NEURO-COMPUTATIONAL MODELING OF
THE GAZE CONTROL SYSTEM

RECREATING FIRING PATTERNS
OF SUPERIOR COLLICULUS POPULATIONS
IN A SPIKING NEURAL NETWORK

Bahadir Kasap
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GENERAL INTRODUCTION

As you read these lines, your eyes make a series of precise rapid movements between the words. These eye movements are called saccades. Fixating the eyes on each word allows us to read because high-resolution vision is limited to about 3-4 letters (1 deg visual angle) only. Saccades are crucial for extracting high-fidelity visual information from the environment.

The Superior Colliculus (SC) orchestrates these eye movements. It is a small nucleus, in monkeys about the size of a pea, sitting on top of the midbrain. When a population of neurons in the SC is activated by the presentation of a sensory stimulus, it makes our eyes (and head) reorient rapidly and precisely to the peripheral target. Recordings have shown that the neural network within the Superior Colliculus generates a signal that fully encodes the kinematic details of the eye-head orienting movement.

This thesis focuses on modeling the signals in the Superior Colliculus that control saccades. Which information is encoded by these signals, which neural mechanisms play a role in the generation of these signals, and what do these signals represent in relation to the response behavior: saccadic gaze shifts? These questions are tackled by a computational modeling approach, which is based on electrophysiological recordings from isolated neurons in the monkey Superior Colliculus.

This introductory section will briefly touch upon the interdisciplinary aspects of computational neuroscience. We will first explain why we move our eyes, followed by a schematic outline of the different brain regions that are known to be involved in the seemingly simple process of reorienting the line of sight from one fixation point to another. We then summarize the role of the midbrain Superior Colliculus in this process. Finally, we describe some relevant properties of neurons, and the mathematical modeling of spiking neural networks.
WHY DO THE EYES NEED TO MOVE?

Voluntary eye movements are crucial for our visual perception because an object can only be identified accurately when its image falls on the fovea (meaning pit in Latin). The fovea is that part of the retina, which, in frontal-eyed animals (such as primates, cats, dogs) provides high-definition vision, as it contains an extremely high density of photoreceptors. However, the human fovea covers only a very small area of the visual field (roughly 2 deg for the human eye), and visual acuity strongly decreases with distance from the fovea (as $1/r^2$). The fovea thus constitutes only 1% of the retinal surface, yet contains about 10% of all photoreceptor cells. Saccadic eye movements have the function to bring objects onto the fovea, as fast and as accurately as possible. As we will see, this requirement, however, calls for a speed-accuracy trade off strategy, as movements cannot be both maximally accurate and fast at the same time.

Eye movements are classified in different (task-related) types; voluntary and involuntary. Each of these eye-movement types are controlled by different, often independent, neural circuits and structures. Briefly, the voluntary eye movements are:

- Conjugate eye movements that coordinate the eyes for binocular fixation on a single object in far visual space (> 1 m away). Both eyes move in the same direction (i.e. the optical axes of both eyes are parallel).
  - *Saccades* are rapid eye movements that quickly change the point of fixation, i.e. jumping from object to object while scanning the environment.
  - *Smooth pursuit eye movements* keep a stable image on the retina of a moving object; such as a flying bird, or a passing car.

- Disconjugate eye movements control the individual gaze directions separately:
  - *Vergence movements* change the angle between the right and left eye, to align the fovea of each eye on nearby targets (<1 m).

Involuntary eye movements are reflexive and aim to keep a stable image of an object on the retina despite self-motion though the environment, or movement of the environment across the retina.

- *Nystagmus* stabilizes the eyes on objects as the head moves or when there are large-scale shifts of the visual field as a result of whole-body movement (as in a riding train, while looking outside).
– *Vestibular nystagmus* combines refixating saccadic fast phases in the direction of the head movement with a compensatory slow-phase ocular shift in the opposite direction, and at the same speed as the head movement.

– *Optokinetic nystagmus* is a similar response of the eyes to large-scale translations of the visual field, e.g. during passive whole-body motion through the world.

While the involuntary eye movements are found in all animal species (frontal-eyed and lateral-eyed), and have three rotational degrees of freedom, the voluntary eye movements occur only in foveate species, and are constrained to two rotational degrees of freedom by Donders’ and Listing’s laws (e.g. Haslwanter, 1995; Opstal, Hepp, et al., 1991). Saccades, smooth pursuit and vergence eye movements are particularly important for foveate animals, which are frontal-eyed predators.

**Saccadic eye movements**

Saccades quickly change the line of sight. Gaze is the direction of the optic axis in space, and is determined by the summed orientations of the eyes in the head, and the head in space (the latter consists of a movement of the head on the trunk, and the trunk in space, but we will ignore trunk movements in this thesis). Programming an accurate gaze shift requires a number of processing steps: first, the target needs to be selected, often from a myriad of distractor stimuli; then the coordinates of the gaze shift should be determined, which often requires a coordinate transformation of the sensory coordinates into the appropriate coordinates for the eye- (and head-) movement, and finally, the decision to trigger the gaze-saccade is made. Together, these processes take about 200 ms to complete in simple visuomotor tasks (one target in otherwise darkness). During the examination of a complex visual scene, the choice regarding target locations has been shown to depend on the required task (they involve top-down modulations) (Fig. 1.1).

Saccadic eye movements are among the fastest motor responses of the body, reaching peak velocities up to about 800 deg/s (even 1300 deg/s in monkey), and the eye-movement duration alone would take typically less than 100 milliseconds. Detailed and reliable eye-movement recordings were acquired by capturing the reflection of an infrared light beam directed on the eye Yarbus, 1967. Such recordings allowed the description of the eyes’ kinematics during saccades by their amplitudes, directions and speed. Saccade amplitude is the
Figure 1.1 Eye-movement traces of the same subject during examination (for 3 minutes) of the painting The Unexpected Visitor (by Ilya Repin, 1884) for two different tasks. In panel 3, the task was to guess the ages of the people in the scene, which requires detailed attention on the faces of each individual person. In panel 7, the observer needs relational cues to estimate the duration of the visitor’s absence (after Yarbus, 1967).

Angular distance between the initial and final orientations of the eye, and the saccade direction is the angle of the line from initial to final position with the horizontal meridian. Amplitude, direction and velocity are typically expressed in eye-centered polar coordinates.

Obviously, the frequency and amplitudes of the saccades are task dependent. For example, Western reading requires many consecutive small saccades in mainly the rightward horizontal direction from one word to another, and a large saccade in the opposite direction to the beginning of the next line. However, while exploring a large-sized painting, or an entire visual scene, there might be many small and large saccades between various locations. Regardless the task, however, there is a tight relationship between the saccade amplitude and its duration, and between the saccade amplitude and its peak velocity. These stereotyped kinematic relationships have been termed the saccadic main-sequence (Bahill et al., 1975): saccade duration increases linearly with saccade amplitude, while the peak eye velocity saturates for large saccade amplitudes (Fig. 1.2).

Even though saccades are voluntary eye movements, conscious control of eye speed is impossible. Once a target location is chosen and the saccade is triggered, the saccadic system orients the eyes fast and accurately towards the goal.

The necessary trade-off between speed and accuracy results in an interesting optimization problem, with which the saccadic system has to deal. Harris and Wolpert, 2006 hypothesized that saccades may optimize speed and accuracy through the main-sequence eye kinematics (Fig. 1.2). Essentially, the velocity
should drop back to zero by the time the eyes approach the target. This ensures accurate fixation. Because of the considerable spatial uncertainty (low resolution) of the peripheral retina, and the long visual delays, the saccadic system runs the risk to overshoot the target, which would require the reprogramming of a correction saccade in the opposite direction. This takes longer than programming an expected correction in the same direction. Computer simulations and mathematical analyses have shown that (i) a deliberate systematic undershoot of the first saccade by about 10%, (ii) in combination with the nonlinear main-sequence behavior (Fig. 1.2) optimizes the system’s performance in overall speed (i.e., the time needed to acquire the target), precision (variability), and accuracy (the mean absolute error).

**Saccadic Feedback Control**

Sensorimotor neuroscience considers goal-directed behavior as a dynamic feedback system (schematically outlined in Fig. 1.3). In this framework, the brain generates a motor command that changes the state of the body. This motor command is forwarded to the muscles. However, an efference copy of the same motor command is also evaluated by an internal (forward) model that predicts the sensory consequences of the planned movement. This internal (learned) model accounts for the properties of body and environment. A state estimator, compares the sensory input (information about the current state) with the predicted outcome (the internal model’s output). This comparison forms the belief about the state of the body and world, and is evaluated to form a new set of motor commands or update the belief about the state.
Figure 1.3 Schematic overview of the conceptual framework of sensorimotor integration. Desired body position is the reference input (goal) to the controller, which generates the motor command signal for the plant, and an efference copy to an internal forward model. The plant represents the system’s biomechanics and generates the movement; the sensory system (e.g., visual and proprioceptive feedback) collects information on the state of body and environment, while the forward model predicts the outcome of the planned movement command. The difference between the sensory feedback and predicted body position forms the internal belief of the system about the state of body and world.

Sensory feedback is compared with the predicted result of the movement by the internal model, and thus forms a state estimate. However, the sensory feedback is typically delayed and noisy (these properties are accounted for by the forward model). For the control of a saccadic eye movement, the delayed sensory feedback during a movement is too slow to be of relevance (dashed line in Fig. 1.3).

The saccadic system has gained particular interest in the study of sensorimotor control because of this lack of (complex) sensory feedback, and the relative simplicity of the biomechanics. Furthermore, the neural circuitry is mainly found in the midbrain and brainstem, which makes it readily accessible for advanced neurophysiological experiments. This has made the system a popular target for neuroscientists and modelers, who aim to understand the neural implementation of motor planning, sensorimotor transformations, speed-accuracy trade-off principles, and the use of internal models in the brain.
NEURAL PATHWAY CONTROLLING SACCADES

As the saccadic behavior and eye kinematics have been well documented, the involvement of the different brain areas and their roles in saccadic control have been studied extensively at the neural level (reviewed in Scudder et al., 2002; Sparks, 2002). We will here briefly summarize the most important principles, deemed relevant for this thesis.

Each eye is controlled by six extraocular muscles that, together with the globe and surrounding fatty tissues, constitute the oculomotor plant. For rapid saccades, the system is controlled by a neural command signal from the midbrain superior colliculus, which is forwarded to fast internal feedback circuits that include the oculomotor brainstem, pons, and cerebellum.

The neural pathway responsible for visually evoked saccades extends from the frontal eye fields in cerebral cortex to the pons in the reticular formation in the brainstem, before the oculomotor muscles are activated (Fig. 1.4). It is well-established that the saccadic circuit has to carry out a spatiotemporal transformation, which converts a spatially encoded retinotopic signal, which is forwarded to striate and extrastriate cortical areas, into the temporal signals of the burst generators that precisely control the extraocular muscles at millisecond precision.

BRAINSTEM CONTROL OF EYE MOVEMENTS

The burst generators in the brainstem encode the kinematics of the horizontal and vertical/torsional saccade components. Their temporal discharges activate the eye muscles to move the eye rapidly in different directions. Saccade direction and velocity are precisely encoded by the different pools of oculomotor neurons. Recordings from the brainstem burst generators have shown precise neural discharges corresponding to the instantaneous velocity of the saccade. These velocity commands are transformed into the pulse-step innervation patterns of the oculomotor neurons. The omnipause neurons form a mutually inhibitory loop with the burst generators; they act as a gate for the saccadic system, mediating the transitions between fixation and saccade (Fig. 1.5; reviewed in Scudder et al., 2002).

The exact location or the neural stage that implements the spatial-to-temporal transformation has been long accredited to the collicular efferent projections to the brainstem. As the temporal encoding of the eye kinematics in the brainstem had long been established, the potential role of the temporal encoding properties of the SC population has long been controversial. Goossens and Van
Figure 1.4 Schematic overview of the major brain regions involved in saccade generation. Interconnected cortical and subcortical regions project onto the intermediate and deep layers of the midbrain superior colliculus. Saccadic command signals generated by the SC are conveyed to several targets: the burst generator in the pons and mesencephalic reticular formation for horizontal/vertical eye saccades, and to the oculomotor nuclei; the reticular formation and cervical spinal cord for the simultaneous control of head movements, and the cerebellum through the NRTP, which in turn modulates the burst generator and reticular formation (LIP: lateral intraparietal cortex, 7a: posterior parietal cortex, SEF: supplementary eye fields, FEF: frontal eye fields, SNpr: substantia nigra pars reticulata, NRTP: nucleus reticularis tegmenti pontis) (after Scudder et al., 2002).

Opstal, 2012; Goossens and Van Opstal, 2006, however, demonstrated that the stereotyped temporal discharge patterns of SC neurons displayed a tight relation to the instantaneous desired eye velocity. Their analysis revealed that the SC signal has both a temporal encoding component as well as a topographical representation of the spatial component. Their analysis further suggested that the burst generators may in fact act as linear systems, as the raw SC signals could be translated into the nonlinear main-sequence saccade kinematics of Fig. 1.2 through a simple linear dynamic ensemble-coding scheme (Opstal and Goossens, 2008).

Superior Colliculus: Spatial Code

The SC is an important node in the saccadic circuit. It sits as a little hill (colliculus) on top (superior) of the midbrain. It is known to act as a multi-sensory-
motor interface, by transforming the sensory input into a fast gaze-orienting motor signal. The SC has long been thought to provide a purely spatial signal to the brainstem, representing the vectorial eye-displacement in a topographi-
cally organized gaze-motor map (Fig. 1.6; Moschovakis et al., 1998; Ottes et al., 1986; Robinson, 1972; Scudder, 1988). The afferent gaze-motor map defines the representation of visual space onto the collicular surface. In this way, the upcoming saccade is encoded by an active population at the appropriate location in the motor map, centered at the stimulus’ point image. This spatial signal encodes the saccade amplitude and direction; the conversion of this signal to the temporal code of the saccade was accredited to the downstream brainstem-cerebellar loops (see above; Fig. 1.5). In this thesis, we challenge this view by taking the spatial-to-temporal transformation already at the level of the motor map.

Figure 1.6 The gaze-motor map is the topographic representation of the visual space on the collicular surface, and is site of an active Gaussian population activity that determines the saccade metrics (direction and amplitude). Here, three saccade vectors in visual space are encoded by three translation-invariant populations on the gaze motor map; the number of spikes from individual neurons in the population depends on their position with respect to the center (Ottes et al., 1986). This static model accounts for the broad, amplitude-dependent, and skewed movement fields of saccade-related cells in the gaze-motor map (Sparks et al., 1976).

Computational models of the SC initially focused on the description of the complex-logarithmic mapping of visual space on the collicular surface, and the distributed encoding of the saccade vector by a large population. The log-polar projection of visual space was quantified from the microstimulation data of Robinson, 1972 and enabled to model the shape of SC movement fields in great
The SC activity could thus be well described by a 2D rotation-symmetric Gaussian function of fixed size, in which the center of the population corresponds to the mapped target location. Ottes et al., 1986 discovered that the population is translation-invariant across the map, with a width (standard deviation) of about 0.5 mm, and a peak activity that could best be quantified by the number of spikes in the burst, rather than by the mean or peak firing rate of the cells.

The first attempt to formulate an ensemble-coding scheme to explain the encoding of the saccade vector on the basis of the afferent mapping with a large active population, was published by Van Gisbergen et al., 1987. In their model, the saccade vector was determined by the total linear sum of cell contributions, which were determined by (i) the activity (number of spikes of each cell), multiplied by (ii) the cell’s efferent connection vector (the inverse of the afferent mapping function). Although this simple model accounts for the properties of movement fields, and can explain how the population encodes the desired eye-displacement vector, it failed to capture results from electrical microstimulation in the SC motor map. For example, double stimulation at two sites was known to produce weighted vector-averaging responses (Robinson, 1972; Schiller and Sandell, 1983), which could not be accounted for by linear summation of cell contributions. An alternative population encoding scheme was proposed by Lee et al., 1988. In their model, the total population coding was based on a center-of-gravity calculation of individual cell contributions, although similar averaging effects could be obtained by the linear summation model, provided that cells in the SC influenced each other through lateral excitatory-inhibitory (McIlwain, 1982; Van Opstal and Van Gisbergen, 1989).

These different static models described how the SC represents the spatial coordinates of the saccade displacement vector, and the subsequent spatio-temporal transformations that underlie the non-linear characteristics of the main-sequence kinematics (Fig. 1.2) are attributed to the local feedback circuits in the downstream brainstem burst generators.

Superior Colliculus: Kinematics Code

The first evidence hinting that the SC signals might also carry information about the saccade kinematics was provided by Berthoz et al., 1986, who reported a relation between the mean firing rate in cat SC cells to the mean eye velocity. Later studies even extended this idea by suggesting that the neural discharges in collicular bursts related to the instantaneous properties of the saccade. However, in those studies, the firing rate was thought to encode the
dynamic motor error signal, which would be constructed by comparing the desired displacement signal (e.g., from cortex) with the dynamic actual eye-displacement through internal feedback (from the brainstem). These models therefore placed the SC inside the dynamic feedback controller of the saccadic system (Opstal and Kappen, 1993; Waitzman et al., 1988).

Single-unit recordings and careful analysis from SC cells during visually-guided saccadic tasks demonstrated how the saccade kinematics were closely reflected in the temporal firing patterns of single SC cells. The temporal characteristics of the SC signals depict stereotyped firing profiles that could potentially form a neural correlate for the main-sequence behavior of saccades (Fig. 1.2). The SC activity exhibited a systematic relationship in the temporal profile of the spike train that depended on both the anatomical position of the cell, and on the saccade in which the cell participated (Goossens and Van Opstal, 2012; Goossens and Van Opstal, 2006). The saccadic command signal could thus encode the full kinematics of the eye movement, and as such the desired trajectory of the eye. In this view, the downstream brainstem circuitry would be responsible for decomposing the spatio-temporal dynamic SC signal into the appropriate driving signals for the extraocular muscles. The brainstem function would thus be simplified to a dynamic linear decomposition stage that transfers the vectorial SC command with the appropriate weights to the different muscles (Fig. 1.7; Opstal and Goossens, 2008).

Goossens and Van Opstal, 2012 demonstrated that the SC motor map embedded a spatial gradient in the cells’ peak firing rates that, in combination with the finding that the total number of spikes in the bursts remains invariant throughout the SC, could underlie the main-sequence properties of saccades (Fig. 1.2). Thus, the non-linear kinematics of saccades would find their origin at the level of the motor map. However, how these characteristics came about had so far not been answered, and will be the main topic of this thesis report.

This thesis treats the SC as a nonlinear dynamical system, and aims to model the observed SC population firing profiles within a large network of spiking neurons. The system accounts for many neurophysiological findings at the single-unit level, and conceptualizes the contributions of different neural mechanisms underlying saccade generation (topographic organization of the motor map, lateral interactions among SC neurons, specific neuronal dynamics across the map) and the saccadic main-sequence.
Spiking neural networks (SNN) have been classified as the 3rd generation of artificial neural network models. Unlike previous models (e.g., Mulloch-Pitts on-off digital neurons as the 1st generation, and activation function neurons as the 2nd generation of continuous signal processing networks), SNNs aim to provide a more realistic neurobiological account of neural processing, by also incorporating the temporal evolution of the neural membrane dynamics, and thus maintaining a realistic temporal code of the system by trains of spikes. SNNs mimic network dynamics at the single neuron level and at millisecond time scale. Therefore, the information is encoded in the form of distributed spike trains (pulse trains) throughout the network.

From an information-theoretical perspective, it may be advantageous to encode and process analog variables by trains of pulses. Temporal-coding is beneficial, especially when the required computations are speed critical. Considering the visual processing speed in pattern classification tasks (around 100 ms;
Thorpe and Imbert, 1989, or saccadic reaction times (200 ms Fischer and Boch, 1983), which complete at millisecond time scales. Rate-coding models will typically fail to capture time-critical spike-based interactions among neurons, leading to only a partial understanding of the underlying neural mechanisms.

Hodgkin and Huxley, 1952 revealed the electrical-chemical properties of the squid giant axon. The squid’s axon allows rapid action potential conduction driving the animal’s escape response. They modeled the neurophysiological principles behind the propagation of action potentials through voltage-gated ion channels. Numerical simulations of the neural dynamics allows the investigation of interactions in neural populations and the construction of functional networks that could imitate realistic neurobiological processes.

In SNN simulations, the neural dynamics are described by a set of differential equations that model the change in membrane potential, $V$, as a function of membrane properties and neural input. At each time step, the membrane potential of a neuron is updated and checked whether it is above its spiking threshold. The change in potential is given by a potential dependent function, such as:

$$\frac{dV}{dt} = f(V, t) + g(I, t)$$

(1.1)

where the change in the membrane potential $dV/dt$ is determined by the internal dynamics and state of the neuron, given by $f(V, t)$, and the external inputs to the neuron are given by $g(I, t)$, which is determined by the activities of other neurons in the network.

In Hodgkin and Huxley, 1952’s description, the neural dynamics are captured by a set of four coupled ordinary differential equations. However, the major neural dynamics can be well approximated by much simpler spiking neuron models, thus greatly speeding up the calculations. Two-dimensional spiking neuron models define the membrane potential change by a set of two coupled differential equations. These models employ quadratic (Izhikevich, 2003) or exponential (Brette and Gerstner, 2005) membrane potential dependence (for $f(V, t)$) and a recovery variable to produce different types of neural dynamics (see Fig. 1.8, for illustrative examples). These simpler models are computationally less expensive to simulate. Yet, they can still capture most neural regimes that are commonly observed, e.g., in motor neurons, but also in SC neurons (Fig. 1.5).

Using the simple spiking neuronal model of Brette and Gerstner, 2005, we built a neural network architecture, which produces spiking patterns that resemble the electrophysiological recordings in the SC motor map during visually-evoked eye movements. In this thesis we follow a computational ap-
proach, in order to better understand the SC network dynamics at the single neuron level.

**SCOPE OF THIS THESIS**

The following six chapters of this thesis focus on the generation of saccadic control signals by the SC network. The work deals with SNN’s to study the emergence of saccadic eye-movement commands in the motor map, and further extends its scope to the full eye-head coordination repertoire of fast gaze shifts.

Chapter 2 focuses on the SC signal itself and the underlying mechanism that generates site-specific firing profiles encoding the saccadic motor command. We introduce a simple one-dimensional spiking neural network (SNN) of the SC motor map. The neuronal dynamics were described by two coupled nonlinear differential equations, describing integrate-and-fire neurons with exponential decay and an adaptation current. The input to the network is provided by a translation-invariant Gaussian population signal at different locations, mimicking the FEF projection onto the SC. This one-dimensional model could reproduce the experimentally observed firing patterns of SC neurons for saccades of different amplitudes. The variation in burst properties across the map was obtained by location-dependent parameters for the neural dynamics and lateral interaction parameters. The lateral interactions among the neurons affected their activity in such a way that all cells in the population fired synchronized bursts.

Chapter 3 proposes a new parallelization method to speed-up spiking neural network simulations by utilizing graphical processing units (GPUs) and an optimal updating strategy. Synaptic updating was considered the parallelization bottleneck of typical spiking neural network computations. In Chapter 3 we compared three different updating mechanisms for a variety of SNNs, and conclude that our new method, which updates the cell’s membrane potential only when the neuron issued a spike, yields by far the fastest simulations for the majority of networks and handles irregular nested paralellism in the spike triggered variable updating. Therefore, the largest computational advantage was obtained for large networks with sparsely firing neurons.

Chapter 4 and Chapter 5 present the extension of the spiking network model of Chapter 2 to the two-dimensional collicular surface, thus producing saccades with all different directions and amplitudes. The network model was designed to also capture the population activity arising from electrical microstimulation experiments. Microstimulation produces normal saccades with normal kinematics for a wide range of electrical stimulation parameters. We here reconcile
our dynamic spike-counting model with these stimulation results by assuming that the stimulation current directly activates only a few neurons near the electrode tip through its electric field. In the model, the lateral synaptic interactions play a crucial role in setting up the large population activity profile with the correct temporal dynamics, just as found for visual-evoked saccades. Chapter 5 further explores the properties of the SNN by studying the effects of electrical double stimulation in the system. The simulations of double-stimulation resulted in saccades that complied with a weighted average of individual stimulation effects. However, this property resulted from the neural dynamics in the SC population, rather than from vector-averaging of cell effects at the downstream brainstem motor circuits.

Chapter 6 extends the idea of SC function from head-restrained saccadic eye movements to combined eye-head gaze shifts. We report results from recordings in head-unrestrained monkey, trained to make fast and slow eye-head gaze shifts. We show that changes in the initial eye position have a strong influence on the gaze kinematics, as well as on the neural activity in the SC. As a result, many cells demonstrated a surprisingly high correlation between the instantaneous gaze velocity and the instantaneous firing rate at the single-trial level. The single-unit data thus further support the hypothesis that the SC population acts as a vectorial gaze pulse-generator, which encodes the desired (straight) trajectory of eye-head gaze shifts. We argue that the output of the motor SC drives, in a feedforward way, the instantaneous kinematics of ongoing gaze shifts.

Chapter 7 introduces a full control model for eye-head gaze shifts that copes with multisensory and multistep localization tasks. Although the ultimate goal will be to capture the behavior of the entire system with spiking neuronal nets (like in Fig. 1.5), we here first identify the functional organization of the system, and the computational algorithms at different stages along the pathway. We discuss the computational challenges faced by the gaze-control system to orient the eye in a complex auditory-visual scene to a target. The model proposes that the system requires access to accurate eye and head orientation signals, that it should account for different internal signal delays, and that it needs to represent target locations and eye- and head motor signals in different reference frames. The main novelty of the model is the proposed role for the SC, by incorporating the recording results of Figure 1.6. The SC signal thus encodes the desired kinematics of the combined eye-head movement vector that will bring the line of sight onto the target. The simulated gaze shifts mimic the observed properties seen in behavioral experiments with monkey and human subjects.


Figure 1.8 Reconstructed membrane potential fluctuations and spiking activity of various neural behaviours. Neural activity is reconstructed by a simple two-dimensional nonlinear model of spiking neurons (Izhikevich, 2003). Electronic version of the figure and reproduction permissions are freely available at www.izhikevich.com.
Abstract

Single-unit recordings suggest that the midbrain superior colliculus (SC) acts as an optimal controller for saccadic gaze shifts. The SC is proposed to be the site within the visuomotor system where the nonlinear spatial-to-temporal transformation is carried out: the population encodes the intended saccade vector by its location in the motor map (spatial), and its trajectory and velocity by the distribution of firing rates (temporal). The neurons’ burst profiles vary systematically with their anatomical positions and intended saccade vectors, to account for the nonlinear main-sequence kinematics of saccades. Yet, the underlying collicular mechanisms that could result in these firing patterns are inaccessible to current neurobiological techniques. Here, we propose a simple spiking neural network model that reproduces the spike trains of saccade-related cells in the intermediate and deep SC layers during saccades. The model assumes that SC neurons have distinct biophysical properties for spike generation that depend on their anatomical position in combination with a center-surround lateral connectivity. Both factors are needed to account for the observed firing patterns. Our model offers a basis for neuronal algorithms for spatiotemporal transformations and bio-inspired optimal controllers.

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2.1 INTRODUCTION

Gathering high-definition visual information requires consecutive gaze shifts, as only the small foveal region in the central retina has a high visual resolution. The rapid step-like gaze shifts between points in the visual field are called saccades. Saccades are straight, extremely fast, goal-directed eye movements, which can reach peak velocities well-over 1000 deg/s in monkey. They demonstrate remarkably stereotyped kinematic relationships, known as the ‘saccade main sequence’ (Bahill et al., 1975): saccade duration increases approximately linearly with saccade amplitude, while peak eye velocity saturates for large saccade amplitudes. Further, the acceleration phase of saccades has a nearly fixed duration for all amplitudes leading to positively skewed velocity profiles (Van Opstal and Van Gisbergen, 1987). These kinematic properties point at a nonlinearity in the system.

These nonlinear kinematics could result from an optimal control mechanism, embedded in the neural pathways for saccade generation (Abrams et al., 1989; Harris and Wolpert, 1998, 2006; Tanaka et al., 2006; Van Beers, 2008). The control overcomes the intrinsic signal-dependent noise within the visuomotor system to achieve an optimal speed-accuracy trade off in line with Fitt’s Law (Fitts, 1954; Goossens and Van Opstal, 2012; Van Opstal and Van Gisbergen, 1989). Consequently, the visuomotor system produces saccades with minimal endpoint variability by moderating the speed of the movement as its amplitude increases.

The neural circuitry responsible for saccadic eye movements extends from the cerebral cortex to the pons in the brainstem. The midbrain superior colliculus (SC), is the final common terminal that specifies the vectorial eye-displacement command for downstream oculomotor circuitry (Moschovakis et al., 1998) and could be in an excellent position to implement the optimal control principles, by mediating the sensorimotor transformations (Goossens and Van Opstal, 2012). Indeed, recent evidence has also implicated a role for SC cells in specifying the nonlinear saccade kinematics (Goossens and Van Opstal, 2006).

The SC contains an eye-centered motor map that relates the anatomical location of the neural population to the intended movement vector (Goossens and Van Opstal, 2006; Ottes et al., 1986). Each saccade command (Fig 2.1-A) is generated by an active Gaussian-shaped population (Fig 2.1-B), the location of which determines the saccade vector, whereas the temporal firing profiles of the neurons (Fig 2.1-C) have been shown to specify the saccade trajectory and kinematics. Small and large saccades are encoded by rostral and caudal populations, respectively. The SC output neurons exhibit bursting behavior in
which the instantaneous firing rates reach up to 900 spikes/s, and saccade-related burst profiles have been characterized by positively skewed gamma functions (Van Opstal and Goossens, 2008). The center of the population corresponds to the image point in the motor map of the saccade vector. Peak firing rate, burst duration and shape of the burst-profile of the central neuron all depend systematically on the cell’s anatomical position in the map. The peak firing rates of neurons recruited for their optimal saccade decrease from rostral (small saccades) (~900 spikes/s) to caudal (large saccades) regions (~400 spikes/s), whereas burst durations increase accordingly (Fig. 2.1-D).

We recently proposed that the neurons in the SC population encode an optimal, straight and fast trajectory of gaze shifts (Van Opstal and Goossens, 2008), and revealed how each SC neuron is involved in different saccades (Goossens and Van Opstal, 2012). In summary, SC neurons exhibit the following firing properties during saccades (schematized in Fig 2.1-D):
(i) each neuron in the motor map elicits a fixed number of spikes for its optimal (preferred) saccade;

(ii) a given neuron’s total spike count varies systematically with the saccade vector into its movement field;

(iii) all neurons in the population have similarly-shaped (scaled and synchronized) temporal burst profiles during a saccade;

(iv) peak firing rate, burst duration, and burst-profile skewness of the central neuron in the population vary systematically across the motor map (Goossens and Van Opstal, 2012).

According to the linear dynamic ensemble-coding model (Fig. 2.1-B, C), the saccade trajectory in two dimensions, $\tilde{S}(t)$, can be decoded from the instantaneous spiking activity of the SC populations in the following way:

$$\tilde{S}(t) = \sum_{n=1}^{N_{\text{pop}}} \sum_{s=1}^{N_{\text{spk}}} \bar{m}_n \cdot \delta(t - \tau_{n,s})$$

(2.1)

with $\delta(t - \tau_{n,s})$, spike of neuron $n$ at time $\tau_s$, weighted by a site-specific, fixed, mini-vector $\bar{m}_n$ (Fig 2.1-C). The latter is given by the efferent motor map (Ottes et al., 1986):

$$\bar{m}_n = \kappa \left[ A \exp \left( \frac{u_n}{B_u} \right) \cos \left( \frac{v_n}{B_v} \right) - 1, A \exp \left( \frac{u_n}{B_u} \right) \sin \left( \frac{v_n}{B_v} \right) \right]$$

(2.2)

and thus fully determined by the location of a neuron in the motor map $[u_n, v_n]$. The SC map parameters $[B_u, B_v, A] = [1.4 \text{ mm}, 1.8 \text{ mm/rad}, 3 \text{ deg}]$; scaling factor $\kappa \lesssim 10^{-6}$ is specified by the assumed constant neural density in the motor map (Goossens and Van Opstal, 2006; Van Opstal and Goossens, 2008).

So far, most computational models of the SC have neglected the spike-level computations taking place in the motor map. One notable exception is the large-scale 7-layer spiking neural network scheme of Morén et al. (2013), which however, does not account for all the physiologically observed bursting properties of SC neurons. For instance, the synchronized firings of saccade related neurons in the recruited population were neglected in that model (property (iii)).

In this study, we construct a biologically realistic, yet simple, spiking neural network model for ocular gaze-shifts by the SC population to a single visual target. Our minimalistic model accounts for the experimentally observed dynamic transformations and the active representation of the saccade vector in
the gaze-motor map (Goossens and Van Opstal, 2012). Spatio-temporal activity patterns of the SC motor map embody the nonlinear saccade kinematics, velocity profiles and eye-displacement vector for optimal saccade trajectories (Van Gisbergen, Van Opstal, et al., 1985). Similarly, our SC model programs the saccadic motor commands by functionally acting as a nonlinear vectorial pulse generator. The resulting activity patterns of our model can be decoded according to the dynamic ensemble-coding scheme of Eqn. 2.1 by the downstream brainstem circuitry, which effectively acts as a linear local feedback loop (Fig 2.1-C). The construction of our model is constrained by the aforementioned firing properties of SC cells during saccades (listed above (i)-(iv)).

We hypothesize that these properties require:

(a) a location-dependent systematic tuning of the neuronal parameters that determine SC spike generation, and the profile of the intracollicular lateral connections, to account for properties (ii), (iii) and (iv);

(b) the input connections to the SC (from cortical sources) set the spike-count properties across the population (properties (i) and (ii)).

Lateral interactions in the SC have been observed by anatomical (Behan and Kime, 1996; Olivier et al., 1998) and electrophysiological (Meredith and Ramoa, 1998; Munoz and Istvan, 1998) studies, and they have been incorporated in several computational models of the SC motor map (Trappenberg et al., 2001; Van Opstal and Van Gisbergen, 1989; Wang et al., 2012). Furthermore, we take the cortical input to the network to be translation invariant, encoding only the selected vector for a saccade target. A fixed input pattern is used to evoke network activity at varying locations in the SC map by topographic feedforward projections according to the afferent mapping. The network generates systematically varying responses at different locations. The temporal differences between burst responses encode the saccade kinematics.

Our model allows the investigation of SC activity as a sensorimotor interface performing spike-level computations that yield the dynamic saccade kinematics. Furthermore, since the model inherently adopts SC functionality, it offers a basis for neural algorithms for bio-inspired optimal control signal generators.
2.2 METHODS

Network architecture

As a starting point, we constructed a one-dimensional spiking neural network with two layers (Fig. 2.2), representing frontal eye field (FEF) neurons (input layer) and gaze-motor map neurons (SC layer), respectively. Each layer consists of 200 neurons uniformly distributed on a 5 mm straight line, which corresponds to the gaze-motor map midline (0° direction). Thus, the network generates motor commands for horizontal saccades over a range of amplitudes from 0 to 104 deg (Eqn. 2.3).

FEF neurons transform the external input current to spiking activity, and relay their signals to the SC neurons through one-to-one, topography-preserving, connections. The SC neurons process the FEF spike trains with their topographically varying biophysical properties. Thus, the instantaneous responses of SC neurons to invariant FEF inputs become dissimilar at different locations within the gaze-motor map, which encode saccade vectors of varying amplitudes.

Log-polar mapping: Visual space to neural coordinates

The afferent mapping translates a target point in visual space to the anatomical position of the center of the corresponding Gaussian-shaped population in both the FEF input layer and the SC motor map. It follows a log-polar projection of retinal coordinates onto Cartesian collicular coordinates (Ottes et al., 1986). In our one-dimensional network model we only considered different saccade amplitudes in the same direction (amplitude $r$, and direction $\phi = 0$ deg). The logarithmic mapping function determines the activation site of a saccade target, $T$, at eccentricity $r$ on the 1D input layer $u_T$ by:

$$u_T = B_u \log \left( \frac{r + A}{A} \right)$$ (2.3)

where $B_u = 1.4$ mm and $A = 3$ deg are the best-fit scaling factors for the monkey SC (Ottes et al., 1986; Robinson, 1972) and determine size and shape of the gaze-motor map.
2.2 Methods

Afferent mapping of saccade amplitude from visual space to the FEF and collicular surface.

<table>
<thead>
<tr>
<th>Saccade Amplitude (deg)</th>
<th>Anatomical position (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>0.5</td>
<td>1.0</td>
</tr>
<tr>
<td>1.0</td>
<td>1.5</td>
</tr>
<tr>
<td>1.5</td>
<td>2.0</td>
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<td>2.0</td>
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<td>7.0</td>
<td>5.0</td>
</tr>
<tr>
<td>8.0</td>
<td>5.5</td>
</tr>
<tr>
<td>9.0</td>
<td>6.0</td>
</tr>
</tbody>
</table>

Spatially translation-invariant input current evokes network activity for different saccade targets.

**Figure 2.2** Schematic overview of the network scheme. Desired SC burst responses by central neurons in each population are generated after Van Opstal and Goossens (2008).

**AdEx neuron model**

We investigated the dynamics of the network model numerically in the Brian spiking neural network simulator (Goodman and Brette, 2008). Simulations ran with 0.01 ms time steps. Brute-force search and genetic algorithms were used for parameter identification and network tuning since there exists no analytical solution for the system.
The neurons in the network are described by the adaptive exponential integrate-and-fire (AdEx) neuron model (Brette and Gerstner, 2005) which accommodates bursting dynamics. The AdEx model is a conductance-based integrate-and-fire model with exponential membrane potential dependence. It reduces the Hodgkin-Huxley biophysical model to only two state variables: the membrane potential, \( V \), and an adaptation current, \( q \). The temporal dynamics of the system are given by the following differential equations for the total membrane current and adaptation current of neuron \( n \), respectively:

\[
C \frac{dV_n}{dt} = -g_L(V_n - E_L) + g_L \eta \exp \left( \frac{V_n - V_T}{\eta} \right) - q_n + I_{\text{inp},n}(t),
\]

\[
\tau_q n \frac{dq_n}{dt} = a(V_n - E_L) - q_n,
\]

where \( C \) is the membrane capacitance, \( g_L \) is the leak conductance, \( E_L \) is the leak reversal potential, \( \eta \) is a slope factor, \( \tau_q \) is the adaptation time constant, \( a \) is the sub-threshold adaptation constant and \( I_{\text{inp},n} \) is the total synaptic input current. All neural parameters are the same for input layer neurons. Thus, input-layer neurons have identical biophysical properties, and only receive an external input current \( I_{\text{inp},n} = I_{\text{ext}} \) to evoke FEF activity. The two parameters that specify SC neurons: adaptation time constant, \( \tau_q, n \) (location dependent), and synaptic input current, \( I_{\text{inp},n} = I_{\text{syn},n} \) (location and activity dependent), however, vary systematically in the network. The remaining SC neural parameters; \( C, g_L, E_L, \eta, V_T \) and \( a \) were tuned for neural bursting behavior. (See Table 2.2 for the list and values of all parameters.)

Furthermore, the AdEx neuron model employs a smooth spike initiation zone instead of a strict spiking threshold. Once the membrane potential reaches the threshold value, \( V_T \), the exponential term dominates and the membrane potential increases without bound. Even though a spike can theoretically occur when \( V \to \infty \), we applied a practical spiking threshold \( V_{\text{peak}} \) for the time-driven simulations. For each spiking event at time, \( \tau \), the membrane potential is reset to its resting potential, \( V_r \), and the adaptation current, \( q \), is increased by \( b \) to implement the spike-triggered adaptation:

\[
V(\tau) \to V_r \quad (2.6)
\]

\[
q(\tau) \to q(\tau) + b. \quad (2.7)
\]

The neuron model has four free parameters (plus the input current) after rescaling the equations (Touboul and Brette, 2008). Two of these parameters characterize the sub-threshold dynamics: the ratio of time constants \( \tau_q / \tau_m \) (with the
membrane time constant $\tau_m = C/g_L$ and the ratio of conductances $a/g_L$. (a can be interpreted as the stationary adaptation conductance). Furthermore, the resting potential $V_r$ and the spike triggered adaptation parameter $b$ characterize the spiking patterns of the neuron (regular/irregular spiking, fast/slow spiking, tonic/phasic bursting etc.).

**Saccade target representation: translation-invariant input current**

We presented the desired saccade-vector to the input layer by evoking a population activity centered around the site $u_T$, according to Eqn. 2.3. Each neuron in the population received input current, whereby the input current amplitudes depend on the distance of the neurons from the center at $u_T$. A spatial-temporal Gaussian-gamma function (Eqn. 2.8) provides the input current to each neuron. Input layer neurons transform the input current to spiking activity and relay to the SC neurons through topography preserving one-to-one connections, which induces an SC population activity. We specified the translation invariant input current profile to the FEF neurons as:

$$I_{ext}(u_n, t) = I_0 \exp \left(-\frac{||u_n - u_T||^2}{2\sigma_{pop}^2}\right) t^\gamma \exp(-\beta t)$$  \hspace{1cm} (2.8)

where $u_n$ is the anatomical position of a neuron on the collicular map, $\sigma_{pop}$ determines the size of the input population recruited for a saccade, $t$ is time, $I_0$ is a constant scaling factor. Time-dependent terms characterize the temporal activity profile by $\gamma$ and $\beta$. The spatial Gaussian function (position, $u_n$) scales the temporal current profile by the distance from the FEF population center.

**The SC synapse model**

The total synaptic input current for an SC neuron is governed by the spiking activity of the input layer neurons and conductance-based synapses:

$$I_{syn,n}(t) = g_{n}^{exc}(t)(E_e - V_n(t)) + g_{n}^{inh}(t)(E_i - V_n(t))$$  \hspace{1cm} (2.9)

where $g^{exc}$ and $g^{inh}$ are excitatory and inhibitory conductances, $E_e$ and $E_i$ are excitatory and inhibitory reversal potentials respectively. These conductances
increase instantly for a presynaptic spike by a factor of synaptic strength between neurons and decay exponentially otherwise, following:

\[
\tau_{\text{exc}} \frac{dg_{n}^{\text{exc}}}{dt} = -g_{n}^{\text{exc}} + \tau_{\text{exc}} w_{n}^{\text{EF}} \sum_{s} \delta(t - \tau_{n,s}) + \tau_{\text{exc}} \sum_{i} w_{i,n}^{\text{exc}} \sum_{s} \delta(t - \tau_{i,s})
\]

\[
\tau_{\text{inh}} \frac{dg_{n}^{\text{inh}}}{dt} = -g_{n}^{\text{inh}} + \tau_{\text{inh}} \sum_{i} w_{i,n}^{\text{inh}} \sum_{s} \delta(t - \tau_{i,s})
\]

with \(\tau_{\text{exc}}\) and \(\tau_{\text{inh}}\), the excitatory and inhibitory time constants; \(w_{n}^{\text{EF}}\), the synaptic strengths between two layers; \(w_{i,n}^{\text{exc}}\) and \(w_{i,n}^{\text{inh}}\) intracollicular excitatory and inhibitory lateral connection strengths, from neuron \(i\) to \(n\), respectively; and \(\tau\), the spike timing of presynaptic FEF (\(\tau_{n,s}\)) and SC (\(\tau_{i,s}\)) neurons.

With conductance-based synaptic connections, spike propagation occurs in a biologically realistic way since the postsynaptic projection of a presynaptic spike is dependent on the membrane voltage of the postsynaptic neuron. In this way, the state of a neuron determines its susceptibility to presynaptic spikes.

**Lateral connections**

We hypothesize that the observed synchronization of bursts of saccade-related neurons in the population arises from lateral interactions between SC neurons. We incorporated a "Mexican Hat"-type lateral connection scheme in the model, where the net synaptic effect is given by the difference between two Gaussians (e.g., Trappenberg et al., 2001, Eqns. 2.11 and 2.12). Accordingly, neurons are connected with strong short-range excitatory and weak long-range inhibitory synapses, which implements a dynamic soft winner-take-all (WTA) mechanism: not only one neuron remains active, but the "winner" affects the activity of the other active neurons. The central neuron governs the population activity, since it is the most active one in the recruited population. As a result, all recruited neurons exhibit similarly shaped bursting profiles as the central neuron.
Two Gaussians describe the excitatory $w_{i,n}^{exc}$ and inhibitory $w_{i,n}^{inh}$ connection strengths between collicular neurons based on their spatial separation:

$$w_{i,n}^{exc} = \bar{w}_{exc} \exp\left(-\frac{||u_i - u_n||^2}{2\sigma_{exc}^2}\right) \text{ for } n \neq i$$  \hspace{1cm} (2.11)

$$w_{i,n}^{inh} = \bar{w}_{inh} \exp\left(-\frac{||u_i - u_n||^2}{2\sigma_{inh}^2}\right) \text{ for } n \neq i$$ \hspace{1cm} (2.12)

with $\bar{w}_{exc} > \bar{w}_{inh}$ and $\sigma_{inh} > \sigma_{exc}$. Self-projections are omitted to prevent neural activity from blowing up:

$$w_{i,i}^{exc} = w_{i,i}^{inh} = 0.$$ \hspace{1cm} (2.13)

**Cross-correlation analysis**

To quantify similarity between burst profiles of neurons at different locations within the population, we computed the cross-correlation between the burst profiles of the central neuron, $P_{cntr}(t)$, with other neurons along the rostral-to-caudal direction from the center, $P_n(t)$. In this analysis, we considered a time window from 10 ms before to 40 ms after the saccade onset ($t = 0$) for each cell. The cross-correlation was calculated after all burst profiles were first normalized with respect to their own peak firing rate, by:

$$r_n = \frac{\sum_t \hat{P}_{cntr}(t) \cdot \hat{P}_n(t)}{\sqrt{\sum_t \hat{P}_{cntr}^2(t)} \cdot \sqrt{\sum_t \hat{P}_n^2(t)}} \text{ with } \hat{P} = \frac{P}{\max(P)}.$$ \hspace{1cm} (2.14)

We restricted our cross-correlation analysis to the population activity within 0.65 mm from the center since the firing rates for cells at larger distances rapidly dropped to zero. Spike density is computed by convolution of a spike train with a Gaussian kernel (width 5 ms).

**Identification of lateral connectivity parameters**

For each saccade amplitude, the recruited population size is the same. The widths of the Mexican-hat connectivity ($\sigma_{inh}$ and $\sigma_{exc}$) are determined based on the size of this active population, because these parameters govern the spatial range of a neuron’s spike influence in the network. The widths are fixed and large enough to yield local excitation and global inhibition. Connection
strengths ($\bar{w}_{\text{exc}}$ and $\bar{w}_{\text{inh}}$), on the other hand, affect spiking behavior and local network dynamics. These values affect how much excitation and inhibition each single neuron will receive from and project to others based on the ongoing activity. Thus, the numerical values of these parameters depend on the parameters of single neurons. Strong excitation would result in a spread of population activity, whereas a strong inhibition would fade out neural activity altogether. Thus, balanced excitation and inhibition is required to establish an active Gaussian population.

To find suitable parameters for the lateral connection strengths, we used a genetic algorithm. In this algorithm, an initial set of 10 $\bar{w}_{\text{exc}}$ and $\bar{w}_{\text{inh}}$ pairs are generated randomly as candidate solutions. This set is considered as the first generation in the genetic algorithm. The network simulations with each pair generated population activity patterns for seven different saccade amplitudes (selected as $r = [2, 5, 9, 14, 20, 27, 35]$ deg). Candidate solutions are subsequently ranked with the fitness function (Eqn. 2.15). Based on their ranks, the two best-fit candidates are chosen as elites and transferred directly to the next generation with 8 new solution candidates, children. Each of these children is generated from a randomly picked pair of parents from the pool of 6 best-fit candidates in the previous generation. The same parent pair is not used to produce more than one child. A child is produced by a random crossover point over a modular representation of parent pair and 5 percent mutation probability. This procedure is repeated until 2 best-fit individuals ranked the same in successive generations.

The genetic algorithm minimized the root-mean squared errors (RMSE) between the spiking network responses and the rate-based model of Van Opstal and Goossens (2008): from the fitness evaluation for each generation, we calculated RMSE between the peak firing rates and the number of elicited spikes from the central cells. Furthermore, the cross-correlations between all active neurons and the central cell are taken into account. This assured that the gaze-motor map characteristics are taken into account for the parameter identification. The fitness function is defined with a weighted RMSE summation;

$$\text{Fitness} = 10^{-1} \times \text{RMSE}(F_{\text{peaks}}) + 10^{1} \times \text{RMSE}(\# \text{of spikes}) + 10^{3} \times \text{RMSE}(\text{cross-correlation})$$

where the weights are empirically chosen to similar ranges since the $F_{\text{peaks}}$ vary from roughly 750 spikes/s to 430 spikes/s, the number of spikes varies between 18 and 22, and the cross-correlation values are below 1.
Peak firing rates of the central neurons from each populations are calculated by convolving the spike trains with a gaussian kernel (with 8 ms kernel width). RMSE values for $F_{\text{peaks}}$ were calculated by applying the firing rate model values:

$$F_{\text{peak}}(r) = \frac{F_0}{\sqrt{1 + \beta r}}$$

(2.16)

where $F_0 = 800$ spikes/s and $\beta = 0.07$ ms/deg (Van Opstal and Goossens, 2008). RMSE of total spike counts from central cells were calculated with respect to $N = 20$ spikes, independent of the saccade vector or neuron position. Synchrony of neural activity was calculated as the RMSE of deviations from 1 for the cross-correlations between the central cell and all other active cells in the population Eq. 2.14.

**Generation of eye movements**

Eye movements are generated by the population activity following the linear ensemble coding model (Eqn. 2.1). The one-dimensional efferent motor map was calculated by Eqn. 2.2 for $v_n = 0$. For any network configuration throughout this paper, scaling factor of the efferent motor map ($\kappa$ in Eqn. 2.2) is calibrated for 21 deg saccade. Resulting eye displacement, $\tilde{S}(t)$ is then interpolated with first order spline for equidistance time points. Finally, the interpolation is smoothed with a Savitzky-Golay filter to compute the derivative, the eye velocity.
<table>
<thead>
<tr>
<th>Input Current</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>$\sigma_{\text{pop}}$</td>
<td>0.5 mm Recruited Population Size</td>
</tr>
<tr>
<td>$\beta$</td>
<td>0.03 Measure for Burst Duration</td>
</tr>
<tr>
<td>$\gamma$</td>
<td>1.8 Skewness and Peak of the Burst</td>
</tr>
<tr>
<td>$I_0$</td>
<td>3 pA Scaling Constant</td>
</tr>
</tbody>
</table>

**FEF Neuron Parameters**

| C         | 50 pF Membrane Capacitance                                                      |
| $g_L$     | 2 nS Leak Conductance                                                           |
| $E_L$     | -70 mV Leak Reversal Potential                                                   |
| $V_T$     | -50 mV Spike Initiation Threshold                                               |
| $V_{\text{peak}}$ | -30 mV Practical Spiking Threshold                                           |
| $\eta$    | 2 mV Spike Slope Factor                                                         |
| $a$       | 0 nS Subthreshold Adaptation                                                     |
| $b$       | 60 pA Spike-triggered Adaptation                                                |
| $V_r$     | -55 mV Resting Potential                                                        |
| $\tau_q$ | 30 ms Adaptation Time Constant                                                  |

**SC Neuron Parameters**

| C         | 280 pF Membrane Capacitance                                                      |
| $g_L$     | 10 nS Leak Conductance                                                           |
| $E_L$     | -70 mV Leak Reversal Potential                                                   |
| $V_T$     | -50 mV Spike Initiation Threshold                                               |
| $V_{\text{peak}}$ | -30 mV Practical Spiking Threshold                                           |
| $\eta$    | 2 mV Spike Slope Factor                                                         |
| $a$       | 4 nS Subthreshold Adaptation                                                     |
| $b$       | 80 pA Spike-triggered Adaptation                                                |
| $V_r$     | -45 mV Resting Potential                                                        |
| $\tau_q$ | 10-80 ms Adaptation Time Constant (varies)                                      |

*Table 2.1* An overview of neural parameters used in the network simulations. Note that for $\tau_q$ the value ranges across the SC motor map coordinates are provided.
### SC Synapse Parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>$E_e$</td>
<td>0 mV</td>
<td>Excitatory Reversal Potential</td>
</tr>
<tr>
<td>$E_i$</td>
<td>-80 mV</td>
<td>Inhibitory Reversal Potential</td>
</tr>
<tr>
<td>$\tau_e$</td>
<td>5 ms</td>
<td>Excitatory Conductance Decay</td>
</tr>
<tr>
<td>$\tau_i$</td>
<td>10 ms</td>
<td>Inhibitory Conductance Decay</td>
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<tr>
<td>$w_{n}^{F-S}$</td>
<td>5-16 nS</td>
<td>Synaptic Strengths (varies)</td>
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### Mexican-hat Parameters

<table>
<thead>
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<th>Parameter</th>
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<tr>
<td>$\bar{\omega}_{exc}$</td>
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<td>Excitatory Scaling Factor</td>
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<tr>
<td>$\bar{\omega}_{inh}$</td>
<td>50 pS</td>
<td>Inhibitory Scaling Factor</td>
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<tr>
<td>$\sigma_{exc}$</td>
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<td>Range of Excitatory Synapses</td>
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<tr>
<td>$\sigma_{inh}$</td>
<td>1.2 mm</td>
<td>Range of Inhibitory Synapses</td>
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</table>

**Table 2.2** An overview of synaptic parameters used in the network simulations. Note that for $w_{n}^{F-S}$ the value ranges across the SC motor map coordinates are provided.
2.3 Results

*Input current evokes spiking activity of FEF layer neurons*

Table 2.2 summarizes the list of parameters of the neurons in the two-layer network. Fig 2.3-A illustrates the input current, $I_{\text{ext}}$ (Methods 2.2, Eqn. 2.8), acting on FEF layer neurons and the resulting spiking response of FEF neurons (Fig 2.3-B) for any saccade target for the chosen parameter values in Table 2.2. For illustration purposes, only a set of uniformly distributed FEF neurons (including the central neuron) is shown. Spike density functions of FEF layer neurons reflect the input current properties; all neurons have scaled spike densities, which decrease as the distance from the central neuron increases. These spike trains impinge onto SC neurons with one-to-one connections (Fig. 2.2).

![Figure 2.3 A Input current, $I_{\text{ext}}$, to FEF layer neurons. B Spike trains and spike densities of FEF layer neurons in response to $I_{\text{ext}}$.](image)

*Figure 2.3* A Input current, $I_{\text{ext}}$, to FEF layer neurons. B Spike trains and spike densities of FEF layer neurons in response to $I_{\text{ext}}$. Spike densities are calculated with a 8 ms gaussian kernel.

*Bursting mechanism of AdEx neuron model*

To illustrate the effect of the relevant neuronal parameters on the response behavior of the AdEx neuron model, Fig. 2.4-A and B show the temporal evolution of the two state variables, membrane potential, $V(t)$, and adaptive current, $q(t)$, for different sets of parameter values. Fig. 2.4-A displays the neural responses for three adaptation time constants and a fixed synaptic input strength (identified by symbols $\Delta$, $\diamond$ and $\triangledown$ in Fig. 2.5), whereas in Fig. 2.4-B the synaptic strengths vary too (indicated by $\triangleleft$, $\triangle$ and $\triangleright$ in Fig. 2.5). The same presynaptic spike train (the peak trace shown in Fig. 2.3-B) impinges on all six illustrated neurons. Thus, the conductance is the same for the three cases in Fig. 2.4-A since the synaptic strengths are fixed (See Methods 2.2). However, the total number of
spikes and burst profiles vary in these three cases since the adaptation current affects the susceptibility of a neuron to incoming synaptic conductance. The differences between responses result from varying the adaptation time constant, $\tau_q$. For fixed synaptic connection values (Fig. 2.4-A), higher adaptation time constant results in fewer spikes, $N_{\text{spk}}$, and a lower peak firing rate (dark blue in Fig. 2.4-C) because $q$ reaches high values faster ($q$ reaches 1 nA in Fig. 2.4-A1 earlier than A2 and A3). This effect results from a fast adaptive current build-up by each consecutive spike in a burst. For lower $\tau_q$ values (Fig. 2.4-A3) the adaptation decay is faster; $q$ decays fast enough to let the next spike occur earlier in the burst. Spike-triggered adaptation in the model is implemented by an instant increase of the intrinsic adaptation current variable, $q$, which is increased by $b$ with each spike (Eqn. 2.6). More importantly, $\tau_q$ affects the inter-spike intervals (ISIs) in these bursts, especially after the peak firing of the bursts; ISIs between consecutive spikes in the burst increase systematically as $\tau_q$ decrease (Fig. 2.4-A3), resulting in the longer tails of the burst profiles (Fig. 2.4-C).

In Fig. 2.4-B, synaptic connection strengths, $w_{F-S}^n$, vary as well. Thus, the total excitatory input current acting on these neurons varies for the identical presynaptic spike trains (Fig. 2.4-B1, B2 and B3). For suitable parameter settings, the number of spikes in the bursts is fixed. A strong adaptation current acting on a neuron with high $\tau_q$ is compensated by an increased conductance through higher synaptic connection strength (B1). On the other hand, a decreased total input current for the fast decaying adaptive current (B3) results in fewer spikes. Varying ISIs result in dissimilar burst profiles (shown in Fig. 2.4-D), both in their peaks and burst durations. Lower peak firing rates are accompanied with longer burst tails, since the number of spikes in the bursts is approximately fixed.

**Parameter tuning for spatial variation of SC burst profiles**

To find suitable parameters for the biophysical properties of SC neurons, we performed a brute-force search procedure. The SC neurons had fixed parameters, except for their adaptation time constants, $\tau_q$, and top-down projections from FEF to SC layer neurons, $w_{F-S}^n$. The fixed parameters for two types of neurons that generate spiking activity of FEF layer neurons and SC bursting behaviour are given in Table 2.2. By varying the adaptation time constant, $\tau_q$, the decay speed of the adaptation current, $q$, could be varied, which accounts for the systematic changes in behavior of SC cells as function of their location in the map. Systematic changes in top-down projections, $w_{F-S}^n$, can compensate for the varying input sensitivity of the neurons resulting from varying adaptive
Figure 2.4 The effect of adaptive characteristics of an AdEx neuron on the evoked neural activity by the input pattern of Fig. 2.3-B. Temporal evolutions of the state variables: membrane potential, $V$, and adaptive current, $q$, for varying adaptation time constants, $\tau_q$ for fixed synaptic input strengths A and for varying synaptic input strengths B. Spike-density functions of the burst profiles for fixed synaptic input strengths C and for varying synaptic input strengths D. Spike densities are calculated with a 8 ms gaussian kernel.

Properties and hence keep the number of emitted spikes constant (as in Fig. 2.4-B). To illustrate the burst properties of the AdEx model neurons, Fig. 2.5 shows the total number of emitted spikes (A) and the peak firing rate (B) of the burst for different $\tau_q$ and $w_{i-S}^{F}$ values, when driven by the same input spike train. It is seen that higher $w_{i-S}^{F}$ and lower $\tau_q$ values result in more spikes and higher
peak firing rates, whereas lower $w^{F-S}_n$ and higher $\tau_q$ values result in fewer spikes and lower peak firing rates. The parameter pairs resulting in 20 spikes in the burst are highlighted (white color in Fig. 2.5).

![Figure 2.5](image)

**Figure 2.5** Brute force parameter search for the adaptation time constant $\tau_q$ and top-down synaptic projections from FEF to SC layers $w^{F-S}_n$. Single AdEx neurons configured with SC parameters are driven by the most active neuron in the FEF population (Eqn. 2.8). **A** Total number of spikes in the burst. **B** Peak firing rate of the burst profile. White points: the neurons emit 20 spikes in their burst, and the contours show the peak firing rates. Black lines depict the parameter values used for SC neurons in the network simulations. They are calculated by a second order polynomial regression of $\tau_q$ and $w^{F-S}_n$ for 20 spikes in burst. Behavior of AdEx neuron at points $\bigtriangleup, \bigtriangledown, \bigtriangledown, \bigtriangledown$ and $\bigcirc$ are illustrated in Fig. 2.4-A and B.

Fig. 2.5-B shows how the peak firing rates (contours) change for the parameter pairs while the total number of spikes in the burst stays fixed (white dots represent 20 spikes in a burst). These analyses lead to a selection of $\tau_q$ and $w^{F-S}_n$ pairs that correspond to observed burst properties in the gaze-motor map. The total number of spikes in the burst remains constant as the peak firing rate drops from the rostral to caudal zone. Thus, we fitted the parameter pairs that yielded 20 spikes in the burst with a second order polynomial (black curve in Fig. 2.5). The fitted values were used in the network simulations to set up the gaze-motor map characteristics of our model.

Fig. 2.6 shows the position-dependent values of $\tau_q$ and $w^{F-S}_n$ used in the network simulations as a function of the anatomical position. The adaptation time constants were chosen to decrease linearly along the SC map from rostral to caudal locations (green line). The corresponding values for the synaptic strengths were then calculated with the second order polynomial fit of Fig. 2.5. In that way, each SC neuron had distinct biophysical properties and their burst profiles varied systematically along the gaze-motor map midline.
Position dependent values of $\tau_q$ and $w_{F-S}^n$ as used in the network simulations to set up spatial variation in the neural activity patterns.

The difference between excitatory and inhibitory intracollicular synaptic projections constructs a Mexican-hat type center-surround interaction within the SC. Wider inhibitory connections width ($\sigma_{inh} = 1.2$ mm > $\sigma_{exc} = 0.4$ mm) with larger excitatory connection weight ($\bar{w}_{exc} = 160$ pS > $\bar{w}_{inh} = 50$ pS) results in local excitation and global inhibition. $\bar{w}_{exc}$ and $\bar{w}_{inh}$ values are optimized by a genetic algorithm to minimize burst profile dissimilarities (Eqn. 2.11 and 2.12). It thus accounts for the synchronization of burst profiles within the population.

Fig. 2.7 depicts the net intracollicular lateral connection strengths from each neuron as obtained from the genetic algorithm. Lateral connections yield short-range excitatory and long-range inhibitory effects of each neuron. Effectively, SC neurons have both excitatory and inhibitory projections among them with different time constants and reversal potentials (summarized in Table 2.2). However, the differences in the synaptic strengths display a center-surround antagonism yielding a Mexican-hat type of lateral connections.
**Central neuron and optimal saccade vector**

A proper selection of $\tau_{q,n} - w_{n}^{F,S}$ parameter pairs along the rostral-to-caudal axis ensures burst profiles that reflect experimentally observed spatial variations in the SC motor map. When these neurons are recruited for their optimal saccades, rostral neurons exhibit higher peak firing rates in their bursts and shorter durations (property iv) when compared to caudal neurons. Figure 2.8-A shows the simulated spike trains and burst profiles for several SC cells along the motor map when they are recruited for their optimal saccade. The temporal profiles of the bursts display a systematic variation of burst duration, skewness and peak firing rate. The peak firing rates decrease from 750 to 550 spikes/s as the saccade amplitude increases from 3 to 63 deg (property iv, Fig. 2.8-B) and the spike counts of the cells stay roughly constant, varying non-systematically between 20 and 23 spikes (property (i)). Note that although these network simulations incorporate lateral interactions, the characteristics of central cell bursts are mostly due to the position dependent distinct properties of SC cells.

![Figure 2.8](image)

**Figure 2.8** A Spike trains and burst profiles for central cells in populations for different saccade amplitudes show increasing burst durations. Burst profiles are aligned to $t = 0$ ms at the first elicited spike, and thus the eye movement onset. Spike densities are calculated with a 8 ms gaussian kernel. B Number of spikes emitted by the central cell is roughly constant between 20 and 23 spikes. The peak-firing rate of the central cell decreases markedly from approximately 750 spikes/s to 550 spikes/s as the saccade amplitude increases from 3° to 63°.

**Synchronized population activity of recruited neurons**

The burst profiles of distinct motor-map neurons do not solely depend on their anatomical positions but also on the saccade vector for which they are recruited.
If the SC were to act as an optimal controller for saccades, the neurons should synchronize their burst profiles so that the net command signal could dynamically reflect a straight trajectory with scaled and optimal vertical and horizontal velocity components. Accordingly, all neurons within the recruited population should exhibit burst profiles that are scaled versions of one another (iii).

Lateral connections with a Mexican-hat shape accounts for this observation (Fig. 2.7). Figure 2.9-A displays bursting profiles of three neural populations in the motor map that encode saccades of amplitudes 5°, 15° and 25°, respectively. The upper panels depict the simulated population activity of a one-to-one network; without lateral connections. The lower panels display the effect of active lateral connections on the bursting profiles. Note that the lateral connections set up a soft winner-take-all mechanism, in which the central neurons dictate their bursting profiles to the other neurons in the population.

Lateral connections correct for the dissimilarities in cell-burst properties arising from the distinct biophysical properties and synaptic strengths. Note that the latencies of peak firing, as well as the variability in burst skewness within the population decrease substantially for the simulations with lateral connections. The net effect of the lateral connections is local excitation and surrounding inhibition from each neuron to the neurons in its periphery. Thus the closer neurons, by exciting each other, are synchronizing their burst profiles. Note that the overall peak firing rates increase in the population when the lateral connections are included. Furthermore, the accumulated inhibition in the network kicks in and affects the burst skewness’ of the neurons after peak firing. This results in more similar burst profiles within the population.

As a quantitative measure of similarity, we computed the cross-correlation of all burst profiles with the central neuron in each population. Fig. 2.9-B displays how lateral connections affect the cross-correlations between the burst profiles of the central neuron and other active neurons in each population. The cross-correlations are naturally high since all firing rates resemble gamma-bursts. However, lateral connections increase the similarity between the burst-profiles, and thus all data points lie further the diagonal.

Spatio-temporal burst dynamics of recruited neurons

Each saccadic motor command is generated by an active Gaussian population. The most active neuron in a recruited population is the central neuron. It elicits the largest number of spikes in the population, and exhibits the highest peak firing rate. The number of spikes elicited by the other neurons decrease with distance from the central cell, both in caudal and rostral directions. Fig. 2.10-A
2.3 Results

A lateral connections synchronize the burst profiles of the neurons in a recruited population. Simulation results without lateral connections (top row in A) display poorer network performance compared to the synchronized activity via lateral connections (bottom row in A). Population activities are normalized by the peak firing rate of the central cell in each population. The peak firing moments are marked to highlight improved temporal aligning via lateral interactions, especially in the population centres.

B Cross-correlation of the burst profiles of the central neuron with the other recruited neurons. Each data point depicts cross-correlations between the neuron pair with and without lateral connections. Neuron’s distance to the population center is color-coded. Dashed lines depict the diagonal unity line. The points below the dashed lines are in favour of lateral connections. Note that this comparison is possible when the lateral connections do not affect the spike counts of neurons in the population (shown in Fig. 2.10).

displays the spike counts of each neuron in the gaze-motor map for three different saccade commands. Fig. 2.10-A captures some important properties that are related to the gaze-motor map: First, a neuron contributes to many different saccade vectors with a different number of spikes described by its movement.
field (Fig. 2.11). Second, the total number of neurons contributing to different saccade vectors is roughly fixed. Since the neurons are uniformly distributed, the widths of the Gaussian populations are the same. Third, the total number of spikes emitted by each population is constant. As such, the number of spikes elicited by the neurons reflects the spatially translation-invariant afferent target encoding scheme as suggested by Ottes et al. (1986).

![Diagram of spike counts and inter-spike intervals](image)

**Figure 2.10** A Spike counts of each recruited neuron for three different saccade vectors. Gaussian curves are plotted in dashed lines only to illustrate similarities between active populations. They are centered around the central cell of each population with a fixed width of $\sigma = 0.4$ mm and a scaling factor of 21 spikes. B Distribution of inter-spike intervals of the spike trains from all neurons in three active populations show that the longer burst durations and lower firing rates are generated with comparable number of spikes for all three populations. Inter-spike interval distribution shifts to longer ISI’s for caudal populations.

However, the temporal characteristics of the bursts do vary with the cell’s locations in the motor map. Fig. 2.10-B shows the ISI histograms for all recruited neurons in the three populations (of panel A). For larger saccade amplitudes, the ISI distribution shifts towards longer intervals. This property reflects the lower firing rates in the spike trains and results from the increased durations of the bursts for the same total number of spikes.

**Saccade-dependent burst profiles of SC neurons**

The spike count for a given neuron varies systematically with the saccade vector into its movement field (ii; Fig. 2.10). Fig. 2.11-A exhibits the spike counts for three neurons in response to varying saccade vectors. The optimal saccade vectors for these three neurons are obtained for the highest number of spikes. Thus, the preferred saccade amplitudes are $\sim 9^\circ$, $21^\circ$ and $33^\circ$, respectively.
counts decrease systematically as the saccade amplitude differs from the preferred saccade amplitude of the neuron. Further, in the spike counts of the three neurons for various saccade vectors, the log-polar characteristics of the gaze-motor map is also apparent. Caudal neurons have a much wider movement field than rostral cells.

Figure 2.11 A Spike counts of the SC neurons in response to different saccade amplitudes determine their movement fields. Preferred saccade amplitudes: $9^\circ$, $21^\circ$, and $33^\circ$, respectively. Spike counts decrease as the contributed saccade diverges from the preferred saccade of the neuron. Note that caudal neurons have broader tuning compared to rostral neurons. That property is a result of the exponential nature of the efferent mapping function. B Burst profiles of one neuron, in response to three different saccade amplitudes: $25^\circ$, $33^\circ$ (its preferred saccade), and $41^\circ$. To emphasize burst profile differences, spike trains are convolved with a gaussian kernel of 3 ms width, normalized by their peaks and aligned to the first spikes for each at $t = 0$ ms.

A neuron’s burst profile, when recruited for different saccade vectors, will also be dissimilar. Fig. 2.11-B depicts the normalized firing rates of the neuron with the preferred saccade amplitude $33^\circ$ when it is recruited for three different saccade amplitudes (highlighted in Fig. 2.11-A by the three symbols): its preferred saccade amplitude ($33^\circ$, diamond), a smaller ($25^\circ$, square) and a larger ($47^\circ$, circle) saccade for which the neuron contributed the same number of spikes. The neuron’s burst profiles are quite different for saccades into its movement field, even when it emits the same number of spikes. The neuron’s spike density decreases faster when it is recruited for the smaller saccade vector, than for a larger one. A direct comparison between these responses and the response profile to the optimal saccade vector is not possible, since it emits more spikes for its optimal saccade vector. Even so, the three saccade burst profiles for the three saccades have different shapes. Hence, the burst shape is not dictated by the location of the cell within the motor map, but by the saccade for
which it is recruited. This property results from the lateral interactions among SC cells.

Eye movements generated by the spiking population

Eye movements are constructed by the linear ensemble coding model with spiking neurons, as a dynamic weighted sum of the SC population spikes (Eqn. 2.1 and 2.2). The trajectories and velocity profiles of three saccades are depicted in Figure 2.12. These are the resulting eye movements of three population activities shown in Figure 2.9. Eye positions show that the population activity results in on target saccades (Fig. 2.12-A). Eye kinematics, on the other hand, differs and synchronized bursts result smoother and more realistic eye movements. Computed eye velocities (Fig. 2.12-B) display that the lateral interactions result in higher peak eye velocities (since the synchronized bursts are integrated dynamically), and that the eye decelerates steadily until the target is reached. Note that the inclusion of lateral interactions results in increased firing rates, synchronized bursts, and much faster saccades.

![Figure 2.12](image)

**Figure 2.12 A** Three eye movements (to saccade targets: 5, 15, 25 degrees) are shown for two cases: with (blue) and without (green) lateral interactions among SC neurons (the associated population activities shown in Fig. 2.9). Eye traces were calculated as a weighted dynamic sum of the elicited population spikes, which are visible as white dots in the eye position traces. Interpolation and smoothing of these data points yield the emerging eye-position traces that allow computation of the associated velocity profiles (See Methods 2.2). **B** Eye-velocity profiles show the strong effect of the lateral connections on saccade performance. Note also that the peak eye velocities increase with saccade amplitude for each population.
Characterisation of lateral interactions

The network is tuned to generate activity patterns that are observed in measured saccade related SC cells. The topographic map and location-dependent firing properties are imposed by site-specific biophysical neural parameters (τ_q and w_{F-S}). Topographical activity properties such as population spike count, number of recruited neurons, spike count of the central neuron and peak firing gradient along the rostral-caudal axis are determined by these biophysical parameters. On the other hand, synchronized population activity is regulated by lateral interactions among neurons, leading to optimized saccade performance. Clearly, also the lateral interaction profiles need to be precisely tuned in order to achieve optimal motor control. These are essentially two free parameters to uniquely define the mexican hat profiles, which we here take as the width and depth of the inhibitory connections. Varying the spatial extent and strength of excitatory and inhibitory connections results in different population activity profiles and eye movement trajectories.

In this one dimensional network model, we quantified the effect of lateral connections on the network performance by the resulting changes in peak eye velocity. The ratio of peak eye velocities for the network with and without the selected lateral connections are shown in Fig. 2.13 for different lateral interaction schemes. Single neurons’ firing frequencies increase as the lateral excitation increases. This results in higher spike counts and higher peak firing rates overall. Yet, since the linear ensemble-coding scaling factor, κ, is calculated by the population spike count, eye kinematics depend on temporal activity of the population. Synchronized bursts result in higher peak eye velocities. Therefore, Fig. 2.13 reads that low w_{inh} values result in faster saccades compared to the baseline eye movement generated by the network activity when the lateral interactions are omitted. The w_{inh} and σ_{inh} pairs that generate the fastest eye movements lie around around w_{inh} = 50 – 70 pS (yellow band). For higher inhibitory strengths, the peak eye velocity may even become slower than the baseline. That is not because of a lack of synchrony of the neurons, but because of stretched firing profiles. As the inhibition builds up too fast, the bursts are no longer gamma-shaped.

To illustrate the behavioral differences, saccades to targets at 11° and 21° are generated from the population activities of four parameter sets (marked □, ◊, ◼ and ◊) in Fig. 2.14. Fig. 2.14-A shows the eye displacements for all four parameter sets to saccade targets. ◊ results in the highest peak eye velocity and more normometric eye displacements for both targets. Associated eye velocity pro-
Figure 2.13 Ratio of peak eye velocity with lateral connections to the peak eye velocity without lateral connections, for different lateral inhibition parameters (inhibitory width, $\sigma_{\text{inh}}$, and inhibitory strength, $w_{\text{inh}}$) and fixed excitatory lateral connections: $w_{\text{exc}} = 160$ pS, and $\sigma_{\text{exc}} = 0.4$ mm. All peak eye velocities are computed for a $21^\circ$ saccade amplitude (see Methods 2.2). Four parameter sets are marked by different symbols (see Figure 2.14). Note that we used the parameter set $\circ$ throughout the paper to demonstrate the network activities. This parameter set was given by the genetic algorithm.

files in Fig. 2.14-B illustrates that high inhibition (◇ and □) results in unusually slow eye movements with a long tail.

Figure 2.14 A Eye movements to two targets (at $11^\circ$ and $21^\circ$) for the four different lateral interaction parameter sets marked in Fig. 2.13. B The associated velocity profiles show markedly different kinematics. Not all lateral interaction profiles lead to optimal saccade behavior (only the two darkest curves correspond to optimal saccades; $\circ$ in Fig. 2.13).
In the present study we studied the properties of a simple, one-dimensional spiking neural network model that accounts for the measured activity patterns of cells in the motor SC and embeds the spatiotemporal transformation that underlie fast saccadic eye-movements. In short, the total ongoing spike count of the recruited population in the motor map encodes the saccade trajectory (spatial code), whereas the instantaneous firing rates of the recruited cells are responsible for optimizing the saccade velocity profile (temporal code).

**Mechanism** Our model describes a biologically plausible scheme, which suggests that the observed burst profiles of SC cells may result from distinct biophysical properties of the neurons, in combination with lateral excitatory-inhibitory interactions within the motor map. In our model, the SC activity is not suppressed by any type of external inhibition, as the SC cells only receive a translation-invariant excitatory input burst from an upstream (cortical) source. After the initiation of spiking activity by the distributed cortical input, the intrinsic neural adaptation of the SC neurons, together with the lateral inhibition, builds up and terminates the neural activity. Adequate tuning of the parameters of the SC cells ensured a fixed number of spikes in the bursts of cells located near the center of the recruited population across the motor map, and to burst durations and peak firing firing rates that systematically varies with the neuron’s location in the map (Goossens and Van Opstal, 2012; Goossens and Van Opstal, 2006).

We varied the adaptation time constant in a linear way as function of the rostral-to-caudal map coordinates from 80 ms to 10 ms, and the top-down projections from the upstream input source varied parabolically from approximately 16 nS to 6 nS (Fig. 2.6). We constrained the parameter pairs to result in different burst profiles that elicited the same number of 20 spikes per saccade (the average number of spikes reported by (Goossens and Van Opstal, 2006)). This fixed spike count results from the neural adaptation mechanism that is incorporated in the AdEx neuron model. The adaptation current, \( q \), acts as an intrinsic inhibitory current on the membrane potential, \( V \), to prevent repetitive high-frequency firing under constant current stimulation. The temporal evolution of the adaptation current affects the response profile of the neuron to tonic input. In this way, neural adaptation can offer a basis for varying the ISI distributions (burst profiles) of SC neurons. We targeted the adaptation time constant, \( \tau_q \), as a critical tuning parameter because it determines how fast the adaptation current will decay. Since \( q \) acts on the membrane potential as an inhibitory current, \( \tau_q \) affects the instantaneous change in the membrane po-
tential, $V$, indirectly, and consequently the burst profile of the neuron. Furthermore, varying the adaptive properties also affects the neurons’ susceptibility to synaptic input. As a result, the spike counts decrease for larger $\tau_q$ values in Fig. 2.4-A because the accumulated total adaptation current, $q$, competes with the total synaptic input to the neuron. As a result, the driving conductances should also vary among the SC neurons to ensure a fixed number of spikes throughout the motor map (i). Fig. 2.4-B depicts the burst profiles of neurons with the same adaptation time constants as in Fig. 2.4-A for different synaptic strengths, $w_{F-S}$. In that way, the neurons can generate gammafunction-like saccade-related bursts with the observed properties (i, iv).

The SC firing patterns all result from intrinsic properties of SC neurons, rather than from external inhibitory suppression, or from negative feedback. Most previous models of the saccadic system assumed that the main sequence kinematics of saccades results from a nonlinear local feedback mechanism in the reticular formation that is known to embed the saccadic burst generators (for example Jürgens et al., 1981; Robinson, 1975; Scudder, 1988; reviewed by Girard and Berthoz, 2005). This assumption includes the recent spiking SC model by Morén et al. (2013) with its external inhibition provided by central mesencephalic neurons. We excluded feedback from the brainstem saccade generator as a putative mechanism to stop the SC bursts, because perturbation experiments have shown that SC activity does not encode dynamic eye-motor error (Goossens and Van Opstal, 2000a,b; Kato et al., 2006; Munoz, Waitzman, et al., 1996; Soetedjo et al., 2002). On the other hand, there is physiological evidence that saccade-related SC neurons have distinct intrinsic membrane properties (Grantyn et al., 1983), and that the bursting profiles might be associated with NMDA receptor activation (Isa and Hall, 2009; Saito and Isa, 2003). Further, the presence of lateral interactions within the SC motor map (Meredith and Ramoa, 1998; Munoz and Istvan, 1998) is well-established. Recent in-vitro multichannel local field potential studies have suggested mexican-hat type lateral interactions in the intermediate and superficial layers of the SC (Phongphanphanee, Mizuno, et al., 2011; Phongphanphanee, Marino, et al., 2014). Those intrinsic circuit properties do not require the motor SC to take part within a feedback loop to generate the observed systematic firing characteristics. Indeed, in our model the saccades are driven in a feedforward way by the SC population. An overview of the underlying intrinsic mechanisms that result in the required SC properties (i-iv) is given in Table 2.3.

**Optimal controller.** The decay of peak firing rates along the rostral-caudal axis in the motor map has recently been argued to embed the nonlinear main-sequence properties of the saccade kinematics (saturating peak eye velocity;
Table 2.3 Overview of the properties of SC activity and the underlying intrinsic SC mechanisms

<table>
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<th>Aspect of SC activity</th>
<th>Model Mechanism</th>
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<td>Translation-invariant input activity temporal profile (Fig. 2.3) through FEF-SC projections, $w_{n}^{F-S}$, and adaptive current, $q$, acting on the membrane potential</td>
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<td>Fixed number of spikes of central cells’ bursts (i, Fig. 2.8-B)</td>
<td>Interplay between adaptation time constant, $\tau_q$, and synaptic input strengths from the FEF-SC projections, $w_{n}^{F-S}$ (Fig. 2.4)</td>
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<td>Gradient of peak firing rates of central cells (iv, Fig. 2.8-B)</td>
<td>Location-dependent variation of adaptation time constant, $\tau_q$, and synaptic input strengths from the FEF-SC projections, $w_{n}^{F-S}$ (Fig. 2.6)</td>
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<td>Synchronization of bursts in population (iii, Fig. 2.9)</td>
<td>Soft WTA lateral interactions in motor map (Fig. 2.7)</td>
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<td>Fixed number of spikes of total population (active gaussian-populations, Fig. 2.10-A)</td>
<td>Translation-invariant input, a fixed density of SC neurons, and the mechanism that creates the movement field of the SC cells (Fig. 2.11-A).</td>
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<td>Saccade-dependent temporal activities of the gaussian populations (Fig. 2.10-B)</td>
<td>Topographic distinct properties (Fig. 2.6) and lateral interactions (Fig. 2.7)</td>
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<td>Spike count of a given SC neuron for different saccade amplitudes (ii, movement fields, Fig. 2.11-A)</td>
<td>Log-polar relationship of the afferent mapping (Eqn. 2.3) and the neuron’s spike count in active gaussian populations (Fig. 2.10)</td>
</tr>
<tr>
<td>Saccade-dependent burst profiles of a given SC neuron (Fig. 2.11-B)</td>
<td>Soft WTA lateral interactions in motor map (Fig. 2.7)</td>
</tr>
<tr>
<td>Saccadic motor commands (Fig. 2.12-A, B)</td>
<td>Dynamic linear summation of spike vectors (Eqns. 2.1-2.2)</td>
</tr>
</tbody>
</table>

Van Opstal and Goossens, 2008). As the function of saccades is to bring the fovea as fast and as accurately as possible to the peripheral target of interest, the main sequence may at first glance seem to counteract this requirement. In early
models of the saccadic system the main sequence properties were typically assigned to (passive) saturation of brainstem burst neurons, which reach peak firing rates up to 1000 spikes/s for large saccades, and hence clearly reach neural saturation levels. Indeed, plotting the instantaneous peak firing rate of a brainstem burst neuron against the instantaneous motor error results in a unique phase curve that resembles the amplitude-peak eye velocity relation of saccades (Van Gisbergen, Robinson, et al., 1981). Because of this, the input-output relation of brainstem burst neurons has been modelled by the same nonlinear, saturating curve. In this way, these models ‘explain’ the saccade main sequence by assuming a nonlinearity in the brainstem pulse generator. However, we recently highlighted several problems with this interpretation (Goossens and Van Opstal, 2012): first, the input signal to the burst neurons is not known, as single-cell recordings can only reveal their output. Therefore, whether the input signal represents dynamic motor error, or a desired eye velocity signal, remains speculative at best. Second, brainstem burst neurons are not the only ones to fire at such extreme firing rates during saccades, as also oculomotor neurons (OMNs) and medial vestibular neurons easily reach these levels. Nonetheless, in the earlier models the OMNs are considered to be linear. Hence, placing the saturating nonlinearity only at the pulse-generating neurons may be somewhat arbitrary. Third, even when a given neuron may have a saturating input-output characteristic, the total neural population may still act as a linear controller. Taken together, the need for a nonlinear transformation at the level of the brainstem burst generator is questionable. To support this argument, we demonstrated that a linear brainstem model, driven by the measured unfiltered spike patterns of recorded SC neurons can indeed fully account for the main-sequence properties of saccades (Eqn. 2.1; Goossens and Van Opstal, 2006).

We therefore argued that the recruited population in the SC motor map acts as a nonlinear vectorial pulse generator, which provides scaled (and coupled) horizontal and vertical eye-velocity signals to the brainstem pulse generators. As a result, the SC population automatically encodes a straight, shortest path, saccade trajectory to the target, which would be expected for a system that needs to be as fast as possible. One may wonder why saccades have to obey a saturating main sequence, especially when neural saturation in the brainstem is not needed to account for the saccade kinematics. Theoretical studies (Harris and Wolpert, 1998, 2006; Tanaka et al., 2006; Van Beers, 2008) have shown that the main sequence might in fact result from an optimal control strategy for a system that has to cope with speed-accuracy trade off in the presence of peripheral uncertainty of the visual field (low spatial resolution of the retina) together with signal-dependent noise in the neural commands. Therefore, the
spatial gradient in the peak firing rates of SC neurons may reveal a deliberate design within the system in order to ensure a saturating, but optimal, kinematic main sequence. In support of this theory, we observed several other properties of the SC firing rates, which are incorporated in our model.

Through our proposed winner-take-all lateral connectivity scheme, the central cell imposes its own temporal profile on all cells in the population. This secondary mechanism thus leads to two important properties of SC burst behavior, which were so far not accounted for by other SC spiking models (Morén et al., 2013): (i) a large degree of burst synchronization of the cells in the recruited population, and (ii) the burst profile of a particular SC cell is not determined by its location in the motor map, but by the saccade for which it is recruited (Goossens and Van Opstal, 2012). Both properties further support the notion that the SC motor map functions as an optimal controller for saccades: burst synchronization leads to a maximally powerful impulsive input to the brainstem burst generator, which thus ensures an optimal acceleration of the eye (see Fig. 2.12). Indeed, the acceleration phase of saccades is virtually independent of the saccade amplitude, with a nearly fixed duration of about 15-20 ms. The latter is presumably mainly determined by the (unavoidable) dynamics of the oculomotor plant (i.e., the short time constant of the eye muscles). Our model accounts for these optimal kinematics through lateral interactions in the SC motor map (Figs. 2.12-2.14).

Current limitations As a proof of principle, we restricted our model to SC activity for visually-evoked saccades in one dimension. The hypothesized input from FEF drives the SC motor map by a translation invariant input pattern (Schlag-Rey et al., 1992; Segraves and Park, 1993) that signals only the location of the saccade target, while providing the same temporal pattern for all saccade amplitudes. Segraves and Park (1993) showed that the FEF activity starts well before the saccade onset and continues for about 90 ms after the saccade is executed. In this model, we have only assumed that the SC is activated by the same input pattern for any saccade amplitude. Clearly, to explain the emergence of different firing patterns of SC cells, despite the same FEF input, the parameters of the SC cells had to vary in a systematic way. Although this simple scheme can explain a wide variety of phenomena with a minimum number of assumptions, several important issues are not yet incorporated in our model:

1. The model needs to be extended to two dimensions to generate saccades in all directions. The current model architecture, however, allows for a relatively straightforward extension and parameter tuning to a two-dimensional network. (In Chapters 4 and 5 we have now incorporated a full two-dimensional motor map.)
2. Electrical microstimulation in the SC with a train of brief high-frequency pulses elicits normometric saccades with normal kinematics, although the stimulation train has no relationship to either saccade duration, or saccade velocity (Robinson, 1972; Stanford et al., 1996; Van Opstal, Van Gisbergen, and Smit, 1990). This may seem problematic for a population model that precisely encodes the saccade metrics and kinematics by its detailed firing patterns. Models that assume that the SC does not play any role in encoding the saccade kinematics regard the temporal firing profiles of SC neurons as immaterial, as only the location of the population matters in driving the saccade. If true, our dynamic ensemble-coding model is in big trouble. Although one may assume that the population activity of SC cells would mimic the rectangular, fixed-frequency envelope of the stimulation train, there is actually no evidence that this is indeed the case. It should be realized that the activity patterns resulting from microstimulation are not known. As the electric field from the microstimulating electrode rapidly decays with distance, it is conceivable that microstimulation only activates a few neurons near the electrode tip, and that the population activity is the result of intrinsic network synaptic transmission. A recent study in FEF has indeed suggested that stimulation at intensities of 10 microamps excites only a few neurons near the electrode (Histed et al., 2009). Katnani and Gandhi (2012) studied the effect of SC microstimulation frequency and intensity on the saccadic behaviour, and showed that different microstimulation procedures result in the same behavior, provided that the total injected charge is equivalent. These results support the idea that once a small set of neurons gets activated, they build up a population activity that yields a normal saccade. Although our model can in principle capture the transmission of neural activity from a centrally activated cell to the rest of the population through the lateral excitatory-inhibitory connectivity scheme, we have not yet incorporated such a mechanism to its full extent (See Chapter 4, where we have worked out this proposal).

3. Our experiments have demonstrated that SC activity during blink-perturbed saccades has a transient decrease in the overall firing rates throughout the entire SC. However, the elicited number of spikes for the (goal-directed) saccade remained unaffected (Goossens and Van Opstal, 2000b), although the saccades lasted much longer, were highly variable, and had much lower peak velocities. Currently, our model has a relatively strong dependence on the input current. In an improved version of the model, the SC population activation should rely less on the details of the input current,
and set up its population activity mainly through lateral connections and intracollicular dynamics (see also the previous point). The external input may therefore act predominantly as a trigger for this process.

4. A more complete model will have to include the separate controls of the eye- and head-motor systems as well, in combination with the vestibular system, to generate gaze shifts with varying contributions of eyes and head, and concomitant changes in the gaze kinematics. Our recent recordings indicate that changes in initial eye-position in the orbit strongly influences the gaze-shift kinematics. Interestingly, this factor also modulates the SC firing rates (in line with their expected role in kinematics control), as well as a subtle concomitant change in the number of spikes (See, however, Chapter 6, for a preliminary account of these neural tuning properties, and Chapter 7 for a computational model of eye-head gaze control).
REFERENCES


DYNAMIC PARALLELISM FOR SYNAPTIC UPDATING IN GPU ACCELERATED SPIKING NEURAL NETWORK SIMULATIONS

Abstract

Graphical processing units (GPUs) can significantly accelerate spiking neural network (SNN) simulations by exploiting parallelism for independent computations. Both the changes in membrane potential at each time-step, and checking for spiking threshold crossings for each neuron, can be calculated independently. However, because synaptic transmission requires communication between many different neurons, efficient parallel processing may be hindered, either by data transfers between GPU and CPU at each time-step or, alternatively, by running many parallel computations for neurons that do not elicit any spikes. This, in turn, would lower the effective throughput of the simulations. Traditionally, a central processing unit (CPU, host) administers the execution of parallel processes on the GPU (device), such as memory initialization on the device, data transfer between host and device, and starting and synchronizing parallel processes. The parallel computing platform CUDA 5.0 introduced dynamic parallelism, which allows the initiation of new parallel applications within an ongoing parallel kernel. Here, we apply dynamic parallelism for synaptic updating in SNN simulations on a GPU. Our algorithm eliminates the need to start many parallel applications at each time-step, and the associated lags of data transfer between CPU and GPU memories. We report a significant speed-up of SNN simulations, when compared to former accelerated parallelization strategies for SNNs on a GPU.

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3.1 INTRODUCTION

Neurocomputing on GPUs

Early GPUs were initially developed and produced for computer graphics, and in particular for video processing and computer gaming. They were built to maximize the device throughput by computing the same function on large quantities of data in parallel. GPUs can speed up computations by running a single instruction on multiple data points simultaneously (SIMD). As such, GPUs have been shown to accelerate computationally demanding complex problems, ranging from game physics to computational biophysics (Owens and Houston, 2008). Theoretical neuroscientists have exploited the use of general purpose computing on GPUs, in neural field model computations and spiking neural network simulations (Baladron Pezoa et al., 2012). Using GPUs as vector processors has recently been adopted for SNN simulators, in order to speed up large-scale simulations, such as NeMo (Fidjeland and Shanahan, 2010), NCS6 (Hoang et al., 2013), and GeNN (Yavuz et al., 2016). However, the advancements in general purpose GPU computing is not yet fully adopted by these simulators.

Time-driven SNN simulations follow a simple routine at every time-step that can be broken down into three major steps: (i) state update, (ii) spike thresholding, and (iii) spike propagation. The state update changes the time-dependent variables of all neurons in the network, according to a set of differential equations, in which each neuron’s membrane potential is computed on the basis of its internal dynamics, synaptic inputs and externally applied currents. Spikes are detected from the updated membrane potentials: if a neuron’s membrane potential exceeds its spiking threshold, it is reset to its resting state, and a spike event is stored in memory. The spike-propagation step calculates the post-synaptic effect of each spike on the connected neurons. Usually, this step is implemented by a weight-matrix multiplication to the synaptic input values of the post-synaptic neurons.

Parallel computing can vastly accelerate the calculations, when these processes are carried out simultaneously. In the optimal scenario, the calculated variables are independent of each other. For SNN simulations, the membrane-potential update and the spike thresholding steps are so-called embarrassingly parallel problems. The state-update and thresholding functions (kernels) can therefore readily run in parallel for individual neurons with different input values or parameters that specify each neuron’s biophysical properties. However, synaptic communication across the network is considered to be the bottleneck
in parallelization (Brette and Goodman, 2012; Zenke and Gerstner, 2014), as it requires a pass through all synapses of the network to update the effect of spikes on the post-synaptic neurons.

Different parallelization strategies have been designed for GPUs (reviewed in Slażyński and Bohte, 2012) with the aim to vectorize these calculations: across neurons (Nageswaran et al., 2009), or across spikes and synapses (Fidjeland and Shanahan, 2010). However, these strategies all have in common that they run many obsolete operations in each time-step, as they typically include also the silent (non-spiking) neurons in the network. Especially, since spikes are relatively infrequent events compared to the size of the network and to the number of time-steps, most computations in existing algorithms introduce substantial additional idle time that merely keeps the computing cores busy. The same problem exists in spiking neural network simulations on other parallel computing architectures (Thibeault et al., 2013).

This problem has partly persisted as a result of technical limitations in GPU programming. General-purpose GPUs have become common for large-scale computational problems. Yet, they pose limitations on the implementation of parallel algorithms as a consequence of the hardware architecture. In particular, memory-handling on the GPU differs from the serial applications that run on the central processing unit (CPU). As GPUs have their own memory, they require that all the data, used for the computations, are available on the device’s memory. Even though the GPU (device) parallelizes the computations, the CPU (host) manages the applications, such as the data transfer between host and device, memory initialization on the device, the initiation of new parallel processes, and the synchronization between parallel processes. This task requires either the device-to-host memory transfer of the spiking neurons’ indices at each time-step, and to initiate the synaptic update kernels for spikes, or to check all synapses in the network to update the spike effects, in case there was a presynaptic spike.

CUDA (Compute Unified Device Architecture) allows the implementation of dynamic parallelism (NVIDIA Corp., 2012), which allows a CUDA kernel to create nested parallel processes on the GPU. When applied to a SNN, this would allow the start of a new parallel operation to update the synaptic values of post-synaptic neurons, only if a neuron emitted a spike. In this way, it would potentially speed-up the simulations, by eliminating idle calculations.

Here, we test an implementation of dynamic parallelism, applied to spike propagation across a SNN. We demonstrate a significant speed-up from dynamic parallelism in a pulse-coupled network of Izhikevich neurons (Izhikevich, 2003). The network consists of randomly connected excitatory and in-
hibitory neurons, which are driven by stochastic input. The same network has recently been used as a benchmark to test the SNN simulator GeNN (Yavuz et al., 2016) on different GPU devices.

Parallel computing on GPUs

A GPU comprises of a GPU chip, and a synchronous graphics RAM (SGRAM, Fig. 3.1A). The GPU chip contains organized sets of streaming multiprocessors, coupled with on-chip registers and read-only texture memories that are private to each processor. The shared memory can be read and written by all processors belong to the same multiprocessor. The SGRAM is used for processor-specific local memory, and for global memory to which each processor has access rights. The access speed and allotted size of these memories will differ. While global memory has the largest space, it has the narrowest bandwidth. Yet, the host can only access the global memory on the SGRAM.

General purpose GPUs typically use C-language programming with application programming interfaces (APIs). Commonly used APIs are NVIDIA CUDA and OpenCL. Here, we will focus on CUDA terminology, for consistency. CUDA provides a set of extension functions to allow the programmer to use computing and memory resources of the GPU. These helper functions allow programmers to allocate memory on the device, transfer memory between device and host, and manage the parallel execution of kernels written in C++.

Parallel computing follows SIMD parallelism (single-instruction multiple data points), where the individual processors run the same instructions on different data points. The instruction code is termed a kernel, as it is the building block of a parallel application. A kernel executes its code simultaneously across a set of parallel threads. A threading structure consists of the arguments and data addresses on the device that will be used by the kernel, and determines a hierarchy of grids of blocks (Fig. 3.1B) that run in parallel. Each thread runs the same kernel, with its unique id, which is used to access and manipulate unique elements in an array or matrix. A thread block is a set of threads that can cooperate through barrier synchronization and access a shared memory (private to that block). A grid is a set of thread blocks that can be executed independently, and only share access to the global memory. Different thread blocks can be executed independently, in arbitrary order. However, within each block, 32 threads (warps) run in parallel, and multiprocessors regulate their execution. When a warp is stuck, the multiprocessor can quickly switch to another available warp to reduce idle time. The GPU scheduler will map the thread blocks onto the multiprocessors, based on the threading structure, and it maintains...
task efficiency by keeping busy as many cores as possible at any given time (Nickolls et al., 2008).

These conceptual differences introduce new challenges that affect programming style. For instance, a race condition arises when concurrent threads need to write to the same memory address. Hypothetically, both may read the same value at the same time, do their own computations on the data, and write one after another to the same location (Fig. 3.1C). In this case, the result from the thread that wrote last will survive, and the computations by earlier threads will be discarded, leading to erroneous results. Such conflicts should be foreseen during code development; writing into a given memory location should thus be sequenced. CUDA API provides atomic operations and memory locks to handle such often-encountered programming problems.

Coalesced memory access refers to combining multiple memory accesses into a single transaction (Fig. 3.1D). When data is organized in the global memory such that the concurrent threads in a warp access contiguous memory locations, then, the whole chunk of memory can be called at once for all threads in a warp. While on earlier GPUs the computing capabilities required aligned and sequential memory calls from a warp (128 bytes for 32 threads), for coalesced memory access, compute capability 3.0 also supports non-sequential accesses if they are aligned (Fig. 3.1D, bottom). Unaligned access patterns do not benefit from memory coalescing for efficient memory calls. Further, coalesced memory access may not always be applied for all algorithms, while un-coalesced access may not be critical for enhanced performance. Yet, especially the algorithms that require repetitive memory accesses will benefit from coalesced memory accesses to improve performance.

In the optimal scenario, (1) the calculated variables would be independent of each other, (2) the data size handled by each processor, and the computational load on the functions (kernels) that process the data, would be balanced, (3) memory access within the device, and memory transfers between device and host would be optimized.

Parallel synaptic updating schemes

We propose a novel parallelization strategy, which utilizes dynamic parallelism for synaptic updating in SNN simulations. To evaluate performance of our algorithm, we compared it to two earlier applied parallel updating algorithms (Fig. 3.2): (1) parallelization across neurons, in which the synaptic currents are calculated for individual neurons in parallel (N-algorithm; Fig. 3.2A; Mutch et al., 2010; Nageswaran et al., 2009), and (2) parallelization
across synapses, which updates the synaptic currents for each synapse in parallel (S-algorithm; Fig. 3.2A; Fidjeland, Roesch, et al., 2009). In contrast, our new algorithm updates all post-synaptic currents for each action potential in parallel (AP-algorithm; Fig. 3.2B). We compared the performance of the three algorithms for different network sizes, by varying the number of neurons (N), and the number of synapses per neuron (S) in the network, and for different spiking regimes, by varying the activity states in the networks.

Each algorithm updates the neural states by N threads. Based on the total current acting on a neuron at a time-step, membrane potential is updated by the differential equation describing the neuron model. If the membrane potential crosses spiking threshold, the spike is recorded to be propagated to the postsynaptic connections. While N- and S- algorithms update synapses at a separate step after state updates are finished for all the neurons, AP- algorithm starts nested processes (Fig. 3.2). This paradigm difference already decreases computation time, because the neural state update computations must be completed for all neurons to continue with spike propagation in N- and S- algorithms. The
A. Parallel update (N-algorithm and S-algorithm)

B. Dynamic parallelism (AP-algorithm)

Figure 3.2 Overview of different algorithms to update state variables and current input at a time-step for $N$ neurons and $S$ synapses per neuron. The main simulation loop determines the duration of the simulation. Boxes summarize what each thread calculates in parallel for different algorithms. For all simulations, states of $N$ neurons are updated in parallel. (A) Parallelization across neurons (N-algorithm), and parallelization across synapses (S-algorithm). (B) Spike-triggered parallelization (AP-algorithm).
threads which complete their calculations earlier wait for the rest of the threads to finish. Therefore, synchronization between neural state update and synaptic update steps hurts throughput. However, the main novelty of the AP-algorithm is the use of dynamic parallelism for spike propagation and decreasing number of running threads per time-step.

Both the N-algorithm and the S-algorithm parallelize the matrix multiplication for synaptic updates. They both calculate an update for each existing synapse in the network (Fig. 3.2A). The N-algorithm starts N threads (across neurons), which each iterate over S synapses to update postsynaptic currents for the neurons that elicit a spike. The S-algorithm recruits N × S threads (across synapses), which each updates the postsynaptic current if there was a presynaptic spike. It is apparent that these two algorithms allot the work in different ways to individual threads. Yet, both algorithms check if there was a presynaptic spike at a connection, and update the postsynaptic current for each synapse with a presynaptic spike. The difference is; the N-algorithm updates the postsynaptic currents with fewer threads, but with more computations per thread, when compared to the S-algorithm. Therefore, the computation duration increases with the number of synapses.

The AP-algorithm combines neuron state update and postsynaptic update steps. It utilizes dynamic parallelism to update all postsynaptic currents from a neuron, whenever it produces an action potential. Each time a neuron’s membrane potential crosses the spiking threshold, a new set of children threads are triggered (Fig. 3.2B). Postsynaptic updates are delivered by S threads, each updating one synaptic end. Therefore, the number of spikes become the main determinant of the number of calculations to be done. AP-algorithm starts S × (# of spikes) threads in total per time-step. Each thread updates a postsynaptic current as in S-algorithm. Compared to the N- and S-algorithms, the AP-algorithm combines spike thresholding with synaptic updating, and thus eliminates the overhead synchronization delays as well. AP-algorithm executes synaptic updates as the spikes occur.

We will demonstrate that each algorithm will have its own optimal performance conditions. As we define algorithm performance by the computation time needed to update the postsynaptic currents, the fastest algorithm is considered the best. The execution time of each time-step is determined by two factors: (i) the time needed for a thread to complete its task, and (ii) the occupancy of GPU multiprocessors. A thread’s runtime depends on the computational load of its kernel; when a kernel must perform many calculations and memory accesses per time-step, it increases processing time. The occupancy of GPU multiprocessors deduces to how well the task is distributed over the
streaming cores to increase throughput. Since the threads are mapped onto the multiprocessors by the GPU scheduler, the more threads there are, the longer it takes for the network to finish.
3.2 METHODS

Network architecture

Performance of the three different algorithms was tested on a SNN that consisted of pulse-coupled Izhikevich neurons, which were driven by stochastic input (Izhikevich, 2003). The change in each neuron’s membrane potential is updated by the following differential equation:

\[
v' = 0.04v^2 + 5v + 140 - u + I
\]  

(3.1)

\[
u' = a(bv - u)
\]  

(3.2)

where \(x'\) designates the time derivative of \(x\), \(v(t)\) is the cell’s membrane potential, \(u(t)\) is the so-called recovery variable, \(I(t)\) is the external (stochastic) input; parameter \(a\) (in s\(^{-1}\)) is the recovery time scale, and \(b\) (dimensionless) is the recovery sensitivity to subthreshold fluctuations of the membrane potential. A neuron emits a spike if its membrane potential crosses its spiking threshold (here set to \(v = 30\)). At the next time step, the membrane potential, \(v\), is reset to its resting value, \(c\), and the recovery variable, \(u\), is increased by a spike-triggered recovery reset, \(d\):

\[
\text{when } v > 30: \quad v = c \quad \text{and} \quad u = u + d
\]  

(3.3)

Because the recovery variable, \(u\), acts on the membrane potential change, \(v'\), as an inhibitory current (Eq. 3.1), its increase is bounded by the internal dynamics of the neuron. When \(u\) reaches high values, the neuron will be hyperpolarized and it will require more synaptic input to elicit another spike. While the neuron is silent, \(u\) will decay exponentially (following Eq. 3.2).

The input current, \(I(t)\), for each neuron in the network consists of two sources: a stochastic input current, and the synaptic currents that it receives from active presynaptic neurons. Formally:

\[
I_j(t_{n+1}) = g_{\text{exc,inh}} \cdot q_j(t_n) + w_s \sum_i S_{ij} \delta_i(t_n)
\]  

(3.4)

where \(q_j\) is a random input to the neuron scaled by an excitatory or inhibitory conductance \(g_{\text{exc,inh}}\), which determines the network’s activity state (either quiet,
balanced or irregular, see below). The total synaptic current is determined by summation over the connectivity matrix elements \( S_{ij} \) from neuron \( i \) to \( j \) for all presynaptic neurons \( i \) that have elicited a spike \( \delta_i(t_n) \) at the previous time step (\( \delta_i = 1 \) if there was a spike at \( t_n \), and \( 0 \) otherwise). \( w_s \) is a fixed synaptic scaling factor that modulates the synaptic input current based on the total number of synapses in the network. Note that \( N - S \) randomly selected entries in the connectivity matrix, \( S_{ij} \), had been set to \( 0 \) for each input neuron \( i \); the remaining \( S \) entries were drawn at random from a uniform distribution for the excitatory and inhibitory neurons.

In the simulations, we varied the number of neurons, \( N \), and the number of synaptic connections, \( S \), per neuron, with \( S \leq N \), to compare the performance of the three algorithms for different network sizes and activity states. While the neuronal parameters \( (a, b, c, d) \) determine the spiking regimes of the individual neurons, the network dynamics are configured by the randomly distributed input conductances, \( g_{\text{exc,inh}} \); the synaptic scaling, \( w_s \), ensures that the activity of each neuron remains stable for different numbers of input synapses.

To set up the network, the initial values of the neuronal variables \( (v, u) \), the neural parameters \( (a, b, c, d) \), and the connectivity strengths, \( S_{ij} \) were selected at random (see Table 3.1, following Izhikevich, 2003). Excitatory cells were tuned for regular spiking and bursting activity with \( (a, b) = (0.02, 0.2) \) and \( (c_i, d_i) = (-65, 8) + (15, -6) \cdot r_i^2 \), where \( r_i \) is a random variable, uniformly distributed on the interval \([0, 1] \). \( r_i = 0 \) corresponds to a regular spiking regime, whereas \( r_i = 1 \) corresponds to a bursting cell. Taking \( r_i^2 \) (instead of, e.g., \( |r_i| \)) introduces a bias towards regular spiking neurons in the network. Inhibitory cells, on the other hand, were tuned by parameters \( (a_i, b_i) = (0.02, 0.25) + (0.08, -0.05) \) and \( (c, d) = (-65, 2) \). Therefore, inhibitory neurons are fast spiking (fast-recovery with \( a = 0.1 \) for \( r = 1 \)) and low-threshold spiking (with \( b = 0.25 \) for \( r_i = 1 \)). In this way, we constructed a heterogeneous network, with different dynamics for each neuron.

In the default network (\( N = 2500 \)), all neurons were connected to \( S = 1000 \) randomly selected postsynaptic neurons, and the \( N \times S \) values in \( S_{ij} \) were initialized randomly from a uniform distribution on \([0, 0.5] \) for excitatory neurons and on \([-1, 0] \) for inhibitory neurons. The ratio of excitatory to inhibitory neurons was kept fixed at 4:1, when we varied the total number of neurons in the network (default SNN: 2000:500). For varying numbers of synapses, we scaled the connectivity matrix with the factor \( w_s = 10^3 / S \), in order to keep the total input strength to the postsynaptic neurons (Eq. 3.4) constant, and having the default \( w_s = 1 \) for \( S = 1000 \) synapses (Izhikevich, 2003).
Table 3.1 Overview of parameters to set up a heterogeneous network with distinct neurons. \( r_i \) and \( q_i \) are random numbers drawn from a uniform distribution on \([0, 1]\).

<table>
<thead>
<tr>
<th></th>
<th>Excitatory neurons</th>
<th>Inhibitory neurons</th>
</tr>
</thead>
<tbody>
<tr>
<td>( a_i )</td>
<td>0.02</td>
<td>0.02+0.08 ( r_i )</td>
</tr>
<tr>
<td>( b_i )</td>
<td>0.2</td>
<td>0.25-0.05 ( r_i )</td>
</tr>
<tr>
<td>( c_i )</td>
<td>-65+15 ( r_i^2 )</td>
<td>-65</td>
</tr>
<tr>
<td>( d_i )</td>
<td>8-6 ( r_i^2 )</td>
<td>2</td>
</tr>
<tr>
<td>( I_i )</td>
<td>2.5 ( q_i ) (quiet)</td>
<td>-1.0 ( q_i ) (quiet)</td>
</tr>
<tr>
<td></td>
<td>5.0 ( q_i ) (balanced)</td>
<td>-2.0 ( q_i ) (balanced)</td>
</tr>
<tr>
<td></td>
<td>7.5 ( q_i ) (irregular)</td>
<td>-3.0 ( q_i ) (irregular)</td>
</tr>
</tbody>
</table>

At each time-step, each neuron’s membrane potential was calculated by Eq. 3.1 based on its input current and internal state. The randomly selected input currents were drawn from a uniform distribution on the interval \([0, 1]\) and scaled by \([g_{exc}, g_{inh}]\) for excitatory and inhibitory neurons, respectively. Different \([g_{exc}, g_{inh}]\) values result in different firing regimes in the network. \([g_{exc}, g_{inh}] = [2.5, 1.0]\) for quiet networks, \([5.0, 2.0]\) for balanced networks, and \([7.5, 3.0]\) for irregularly firing networks (Yavuz et al., 2016).

Parallelization algorithms

The pseudo-codes for the three algorithms are provided below. The state update and thresholding steps were kept identical for all three algorithms. All simulations were performed on a Tesla K40 GPU; the code is made available as open access under https://bitbucket.org/bkasap/dynamicparallelismsnn.
start timer
start a thread for each neuron $i$:
  update state variables:
    $V_i(t_{n+1})$ based on $V_i(t_n)$, $u_i(t_n)$ and $I_i(t_n)$
    if $V_i(t_{n+1}) > V_0$:
      add $i$ to spike list
synchronize: wait until all threads are finished, and ensure that the spike list is complete

(1) N-algorithm
start a thread for each presynaptic neuron $i$:
  for each postsynaptic neuron $j$ (sequentially over $S$ synapses):
    if there is a spike:
      update $I_j(t_{n+1})$ by $S_{ij}$
  synchronize: wait until all threads finish their calculations to proceed to the next time-step
end timer for N-algorithm

(2) S-algorithm
start a thread for each synapse $ij$:
  if there is a spike from the presynaptic neuron $i$:
    update $I_j(t_{n+1})$ by $S_{ij}$
  synchronize: wait until all threads finish their calculations to proceed to the next time-step
end timer for S-algorithm

(3) AP-algorithm
start timer
start a thread for each neuron $i$:
  update state variables:
    $V_i(t_{n+1})$ based on $V_i(t_n)$, $u_i(t_n)$ and $I_i(t_n)$
    if $V_i(t_{n+1}) > V_0$:
      add $i$ to spike list
    start a thread for each postsynaptic neuron $j$:
      update $I_j(t_{n+1})$ by $S_{ij}$
  synchronize: wait until all threads finish their calculations to proceed to the next time-step
end timer for AP-algorithm
Quantifying performance

To quantify algorithm performance, we calculated the total simulation duration, as function of the three different spiking regimes (quiet, balanced, and irregular), spike-propagation algorithm (the N-, S-, or AP-method), and the total number of spikes emitted in the simulation for different network sizes (N: the number of neurons. S: the number of synapses per neuron). The execution times of the time-steps are measured by the time-stamp differences between the start of the state update calculations, until all synaptic currents in the network have been calculated for the next time-step. Even though the neurons were driven by stochastic input, for a given number of neurons and spiking regime, the total number of spikes was fixed. Therefore, a direct comparison is possible between the algorithms by considering their throughput as the number of spikes processed within a millisecond.
Figure 3.3 (A-C) Example raster plots and (D-F) algorithm performance for a network of $N=2500$ neurons, each with $S=1000$ synapses, simulated under three firing regimes during one second: (A) Quiet (194 spikes in the network), (B) balanced (18762 spikes), and (C) irregular firing (41895 spikes). (D-F) The total number of spikes per time-step for the different regimes and algorithms is displayed in the top panels. Results are shown for the first 300 ms of the simulations under (D) quiet, (E) balanced, and (F) irregular firing in the network. Panel D only shows the spike counts for the $S$-algorithm, for clarity. A comparison of the measured execution times of each time-step for the different algorithms is shown by lines in different shades of blue in the bottom panels.

Figure 3.3 depicts the network dynamics of an SNN containing $N=2500$ neurons for the three different activity regimes: quiet (Fig. 3.3A), balanced (Fig. 3.3B) and irregular (Fig. 3.3C) firing. These regimes were obtained by modulating the random input currents, as specified in Table 3.1. Each neuron in the network had 1000 randomly assigned synapses ($S$), with the ratio of excitatory and inhibitory connections set as 4 to 1.

In the quiet regime (A), the network was silent for the majority of time steps. The entire network elicited only 194 spikes during a full second of neural simulation. In that scenario, the execution time for the $N$-algorithm (D) depends only on the existence of a spike at a given time-step. Whenever a neuron spikes, the $N$-algorithm (Eq. 3.3 and Table 3.1) starts $N$ threads, each of which passes
sequentially through the S postsynaptic neurons. Therefore, this algorithm is the slowest of the three when there is a spike, taking about 2.2 ms to complete the cycle. For the balanced and irregular firing regimes (B and C), the execution times of a simulation time-step are not affected for the N-algorithm. In case of many active neurons at a given time-step (as in E and F), the individual threads run sequentially over distinct postsynaptic connections. Thus, the time spent to update the postsynaptic neurons’ current inputs remain the same in the first few milliseconds of high-intensity neuronal firing. When there are no spikes at a time step, as for most time-steps in the quiet regime, or during the silent period after the initial high firing rate in the irregular regime (e.g., between 25-90 ms in Fig. 3.3C and 3.3F), this algorithm takes around 0.8 ms to complete a cycle.

The S-algorithm starts an application with a higher number of parallel processes (given by N x S). Each thread works on an individual synapse and updates the input current of its postsynaptic neuron, whenever the presynaptic neuron is active. Thus, also this algorithm is insensitive to the number of spikes at a given time-step (light-blue lines). Rather, it is bounded by the number of parallel processes that a GPU device can handle simultaneously. In all three firing regimes, the execution time of the S-algorithm stabilizes at around 0.5 ms per time-step.

The AP-algorithm (dark-blue lines) initiates a parallel application with S threads to update the current input to all postsynaptic neurons, whenever a neuron elicits a spike (Fig. 3.2C). Each thread in this case will update a postsynaptic neuron’s input current. The total execution time of this algorithm is most sensitive to the number of active neurons, as compared to the other two algorithms, as each spike will trigger a new parallel process. Yet, taken together, the execution times of each time-step for the three different algorithms show that the dynamic parallelism algorithm is overall the fastest method for spike propagation in the SNN, under all three regimes. The differences become also pronounced in the total execution times.

We noted that the execution times could fluctuate substantially, depending on the number of spikes at a time-step. In the balanced firing regime, between 30 and 50 ms simulation time (in Fig. 3.3B and 3.3E), both the N-algorithm and the AP-algorithm take longer than their mean execution time. Especially, in the beginning of the simulation for irregular firing, where half of the neurons resulted to be active between 0 and 25 ms (in Fig. 3.3C and 3.3F), even the S-algorithm took a longer time. However, this initial high activity in the irregular firing regime seems to be atypical. It is not realistic to have more than half of the neurons active at a time-step in spiking neural network simulations. We
therefore investigated the underlying cause for this high-level transient activity through a phase-plot analysis of the temporal dynamics of a single neuron in the network.

Figure 3.4 Temporal dynamics of a single neuron in the irregular firing regime. (A) The temporal dynamics of the membrane potential (top), $v(t)$, the recovery variable (center), $u(t)$, and the current input (bottom), $I(t)$, shown separately for the stochastic input (light), and the total current input (dark), which includes the synaptic pulses in the network (Eq. 3.4). (B) Phase-plane analysis ($u(t)$ vs. $v(t)$) of this neuron during the first 300 ms shows the relative evolution of the state variables of the neuron. Blue points show the $(u(t), v(t))$ values at each time-step. $u$- and $v$-nullclines are indicated by the dotted curves (for $I = 0$); the vertical dashed line depicts the membrane reset potential (-65 mV); spikes are shown as thin lines, and are labeled in their order of occurrence. During the initial rise of the input current (between 5-25 ms), $u$ increases rapidly during repetitive firing, and the neuron elicits a short high-frequency burst of 5 spikes. The $(u, v)$ trajectory on the phase plane returns back to the system’s stable point (the resting value of both variables, first intersection of the nullclines) after the 5th spike, and the following spikes (6, 7, and 8) occur around this nearly stable $u$ value.

Figure 3.4 shows the dynamics of an excitatory neuron at the first 300 ms of simulation in the irregular firing regime. The transient high firing activity of the network (Fig. 3.3C) results from a high discharge of the neurons in the beginning of the simulation, which resulted to be due to the stochastic input to individual neurons. The temporal dynamics of the three neuronal variables (Fig. 3.4A) show that the initial burst at the start of the simulation results from the high synaptic current input to the network. Nullclines of the neuron model for $u(t)$ and $v(t)$ are shown in Fig. 3.4B. These nullclines (defined by $v' = 0$ and $u' = 0$, Eq. 3.1 and 3.2) intersect at the stable and unstable fixed points of a dynamical system, and describe how the state variables would evolve at a given
The neuron’s stable point (resting state) lies at \((u, v) = (-68, -15)\) where the \(u\)- and \(v\)-nullclines intersect below the reset value of the membrane potential, \(c\). The nullclines depict a snapshot of the neuron’s dynamics at a given time for \(I = 0\). However, the external current input is also a time-dependent variable, \(I(t)\), and is directly added to the membrane potential change, \(v'\) (Eq. 3.1), at each time-step. As a result, the input current shifts the \(v\)-nullcline along the \(u\)-axis. For a positive input current, the \(v\)-nullcline shifts upwards, and the nullclines can lose their intersection points for sufficiently high current values. In this way, the system can become unstable, and the membrane potential starts to increase towards the spiking threshold. With the increase in the recovery variable, \(u(t)\), and the associated membrane-potential reset after each spike, the neuron’s state variables follow a trajectory in the phase plane shown by the blue dots (connected by thin lines for spikes and by dashed lines for decay to the resting potential).

With the initial high rise in the input current, the \(v\)-nullcline shifts upward and drives the neuron into a repetitive firing state. Therefore, the first 5 spikes are accompanied by an increased recovery variable, \(u\), within the first 25 ms of the simulation. The high firing rate is followed by a decay of \(u\) to its resting value, and the following spikes, which occur at irregular intervals, do not increase \(u\) as much as during the initial transient firing. For repeated simulations with different initial parameters in this firing regime the transient high-frequency bursts re-occurred each time, but they were absent if simulations were continued after a deliberate interruption. Thus, the high firing rates at the start of the simulations result from the initial network configuration, rather than from an interesting network effect. In what follows, we therefore discarded this abnormal, transient firing pattern at the start of the simulation, when quantifying the performance of the different algorithms.

Figure 3.5 quantifies the performance of the three algorithms for SNNs with two different numbers of synapses (\(S=1000\) and \(S=2000\) outbound synapses) per neuron, as function of network size (number of neurons, \(N\), from \(2.5 \cdot 10^3\) to \(5 \cdot 10^5\) neurons). For all three algorithms and firing regimes, the simulation runtime increases with the number of neurons, albeit at different rates. The \(N\)-algorithm takes relatively longer for networks with fewer neurons (below \(N = 2.5 \cdot 10^4\)) and starts to be slower with increasing \(N\), in the same way as the \(S\)-algorithm (i.e. according to a power law), for the balanced and irregular firing regimes. For the quiet firing regime, the \(N\)-algorithm is faster than the \(S\)-algorithm for \(N > 10^4\) neurons. Note that the simulation execution times are not affected by the different firing regimes, for either the \(N\)-algorithm, or the \(S\)-algorithm. In the quiet regime, the \(N\)-algorithm outperforms the \(S\)-algorithm,
Figure 3.5 Mean execution time per time-step (bottom) and throughput (top) of the SNN simulations, as function of the number of neurons (on logarithmic scales), and either \( S=1000 \) (blue), or \( S=2000 \) (green) randomly assigned synapses/neuron, for the different parallelization strategies (see legend) under quiet (A), balanced (B) and irregular (C) firing regimes. For networks up to \( 2.5 \cdot 10^5 \) neurons (and larger \( S \)), the PA-algorithm outperforms the N- and S-algorithms for all conditions, as its throughput is higher, and the mean execution time shorter. Note also that, in contrast to the N- and S-algorithms, AP performance is insensitive to \( S \), but it depends more strongly on the firing regime.

since it is faster when there are no spikes at a given time step (Fig. 3.3D). However, both algorithms become slower with increasing number of synapses per neuron. In contrast, the AP-algorithm is insensitive to the variation in \( S \), but is strongly affected by the spike count, as it starts new parallel child processes for each spike. Yet, up to networks with \( N = 2 \cdot 10^5 \), the AP algorithm outperforms the other two computational schemes, when they are densely connected (high \( S \)). When the number of processes exceeds the capacity of the GPU, they have to wait for each other to complete, which will increase the simulation time, also for the AP algorithm.

In Figure 3.6 we compared the performance of the three algorithms (their throughput, and mean execution time) as function of the number of synapses per neuron (between \( S=256 \) and \( 8192 \)), under the three activity regimes, for networks with \( N = 10^4 \) (blue) and \( 10^5 \) (green) neurons, respectively, and for a total neural simulation of 5 seconds. We ensured that the spike counts and neural dynamics of the networks did not vary with the number of synapses, by keeping the total synaptic current fixed in the network. This was achieved by
scaling the range of the uniform weight distributions according to $w_s = 1000/S$, which also ensured that the neural dynamics of the network remained unaffected. Only for networks with a few synapses per neuron some fluctuations in the spike counts may be expected, since the post-synaptic effect of the spikes, and the associated effects of the stochastics, on the postsynaptic currents will be coarser.

The simulations in Fig. 3.6 show that for the AP algorithm the mean execution time per time-step, and total simulation duration were independent of the number of synapses. In contrast, this performance indicator increased steadily with $S$ for the N- and S-methods. Note, that since we kept the spike count fixed for the different configurations, the throughput (top panels) is inversely related to the simulation duration. Taken together, the AP algorithm outperformed the N- and S-algorithms for the smaller networks under all conditions. As the networks grew in size, the AP-algorithm resulted to outperform the other two algorithms for highly connected networks (large $S$).

As our goal was to speed-up the SNN simulations through parallelism, we considered the fastest algorithm for a given simulation condition (determined by the number of neurons, synapses, and spikes) as the winner for that condition. Figures 3.5 and 3.6 indicate that none of the three algorithms wins for all simulation conditions. To provide an overview of the optimal conditions for each algorithm under a wide range of network settings, we varied both the

**Figure 3.6** Mean runtime per time-step and throughput of the simulations, as function of the number of synapses/neuron (logarithmic scale) in a network with $10^4$ (blue) and $10^5$ (green) neurons, for the different parallelization strategies (see legend) under quiet (A), balanced (B) and irregular (C) firing regimes.
number of the neurons, and the number of synapses per neuron in the network, and simulated the networks for the three different firing regimes (Quiet, Balanced and Irregular). For each \((N, S)\) bin we then determined the fastest algorithm, and assigned the associated winner’s color code at that bin. Figure 3.7 shows the results. From these simulations, it is clear that in the quiet regime (Fig. 3.7A), the AP algorithm performs best, regardless the network size and its connectivity. In line with the simulations shown in Figs. 3.5 and 3.6, the AP method is the most efficient algorithm for sparse spiking activity, because it does not trigger the synaptic updating computations when there are no spikes. But when the network activity increases, as in the balanced and irregular network states (Fig. 3.7B and 3.7C), the AP algorithm outperforms the N and S methods especially for the highly-connected networks. In contrast, the N-method is the winner for large networks with relatively sparse connectivity (up to \(S=1024\) synapses/neuron in Fig. 3.7B, and up to \(S=2048\) synapses/neuron in Fig. 3.7C, for networks with \(N=250,000\) neurons), whereas the S-method best suits small and sparsely connected networks. As the S-algorithm requires more threads to be completed at each cycle to update synaptic currents (Fig. 3.2A), the device queues their execution, and start a new batch each time the processors finish their calculations. This introduces additional overhead, because each thread should access memory even when the computation is cheap (in this case, only addition). For the same reason, also the AP-algorithm is hindered by high spike counts per time-step. Instead, the N-method runs fewer threads, as each thread loops over \(S\) synapses. As a result, the N-algorithm performs best for lower \(S\), although its performance is sensitive to the computational load. Thus, if more calculations per synapse were to be required, the AP algorithm would outperform the N algorithm also in these cases. This happens, for example, when synaptic plasticity would be included in the network, as such a mechanism would require additional calculations to account for the synaptic dynamics at each updating time step.
Figure 3.7 Comparative performance of the three algorithms for the three different firing regimes (A: Quiet, B: Balanced, C: Irregular), as function of the number of neurons \(N\) and the number of random synapses per neuron \(S\). In each bin, the winning algorithm has been indicated by color (AP: green, S: red, N: blue). Note that the AP algorithm outperforms the other two algorithms, especially when the spike counts are low (A): it is the fastest algorithm, irrespective of network size in the quiet regime, but also for higher spiking activity, when the number of synapses per neuron is high (B and C).
3.4 Discussion

In this paper, we quantified the performance of three different parallelization algorithms for the simulation of spike propagation within spiking neural networks on a GPU. We showed that the simulation runtimes were highly susceptible to the number of synapses for simulations with the N- and S-algorithms, whereas the spike count was the prominent determinant of simulation runtime for the AP-algorithm. As a result, the AP-algorithm outperforms the other two algorithms when the spike occurrence is sparse in relation to the network size (the total number of neurons and synapses), and to the number of simulation time-steps.

We employed a network architecture of pulse-coupled Izhikevich neurons for the SNN simulations (using the same implementation on CUDA as in Izhikevich, 2003), because this approximate network model allows for easy scalability by varying the number of neurons (N) and synapses (S), while preserving sufficient complexity and variation of different neural states within the network, and easy control of the total spike counts.

However, the simulations had a relatively poor time-resolution (time-steps at 1 ms intervals), while at the same time this simple neuronal model had already been computationally optimized (Izhikevich, 2003) to explain a variety of complex physiological behaviors of neurons under different input and biophysical conditions. The network is thus able to capture different states of synchrony within populations of randomly connected neurons (as coupled nonlinear oscillators).

Note that alternative neural models, which require much higher time precision, will result in many more computations per thread for the neural-state updating steps. This would happen, for instance, when the research question demands more computations per time-step, by including ion-channel-specific computations as in Hodgkin-Huxley model neurons (Hoang et al., 2013; Hodgkin and Huxley, 1952), or when considering current propagation through geometrically complex dendritic trees (Garaas et al., 2009; Gugala et al., 2011). Such architectures and models would require more computations per time-step simply because of the increasing complexity of the models to update neural states or synaptic propagation. Accounting for spike-time-dependent plasticity (Yudanov et al., 2010), or when modeling the high-frequency bursting behavior of neurons in the midbrain Superior Colliculus (Goossens and Van Opstal, 2012; Kasap and Opstal, 2017) would also require additional computations or fine-grained time resolutions, and thus more computations and performance. Also the new class of evolving SNNs require additional computations per time-
step (Schliebs and Kasabov, 2013) and multiple network classes. As long as the spike propagation follows delivery of discrete pulses to a subset of the all neuron population in the network, dynamic parallelism would accelerate GPU based simulations. Because, also under these more demanding dynamic requirements, spikes would be elicited more sparsely during the whole simulation. Because the AP-algorithm eliminates the need to compute synaptic updates for neurons that do not elicit a spike, it will readily speed-up such more demanding simulations. However, this is only valid for spiking neural network implementations. Most of the other neural network modeling frameworks for deep neural networks and machine learning applications are already utilizing GPUs (Torch (Collobert et al., 2011), Tensorflow (Abadi et al., 2015), supported by CUDA cuDNN library in the backend talking to GPU devices (Chetlur et al., 2014)).

We explored the idea of dynamic parallelism for synaptic updating in SNN simulations, by comparing its performance to the two parallelization strategies that are currently available in the literature. However, it should be noted that the actual simulation durations for all three algorithms were longer than reported here because of the considerable time needed for the random number generations, and memory transfers prior to, and following the main simulation loops. The generation of random numbers to initialize the neural parameters and their connectivity within the network introduced considerable latencies, and depended strongly on the number of neurons and synapses in the network. Furthermore, the random number generators that were used for each time-step to provide the time-varying stochastic input current to each neuron, occupied a large portion of the device memory. However, since here we focused on performance differences between the three algorithms, we merely considered the execution time of each time-step from the start of the state updates until all synaptic currents had been calculated for the next time-step.

Our proposed algorithm can readily speed up the computer simulations on GPU where the spike propagation is the limitation factor. Also, the simulation code can be further improved by optimizing the use of device memory during the simulations. However, in this simple network implementation, the comparative performance of the different algorithms would not be affected, since an ongoing thread reads the connectivity matrix element, and writes the synaptic input current only once. Using shared memory and coalesced memory access will potentially accelerate the simulations for repetitive computations on the same data point. This would be the case when GPUs are used to speed-up the neuro-computational simulations with more computations at each synapse updating step, for instance, under synaptic plasticity calculations (Yudanov et
Fiala et al., 2010), or for current propagation within complex dendritic tree geometries (Gugala et al., 2011).

For computationally demanding SNN simulations, different GPU-based simulation frameworks have been introduced: CARLsim (Beyeler et al., 2015), Nemo (Fidjeland, Roesch, et al., 2009), NC6 (Hoang et al., 2013), and GeNN (Nowotny, 2011). The GeNN simulator was developed to implement different SNN architectures with the least amount of code on a GPU (Yavuz et al., 2016). The simulator contains a code-generation process: the user defines a network model, and specifies the neural parameters by a set of predefined functions, upon which the simulator generates and compiles the associated C++/CUDA code for a GPU. Memory usage and access on the device are optimized for various example cases. The GeNN simulator is independent of the operating system and of the GPU device model, and can also be used to generate C++ code for the same network configuration on CPUs. These characteristics make GeNN a versatile simulation tool. However, it limits the user friendliness in easy extensions with new neuron models, in manually specifying the neural dynamics, or in changing the simulator source code. In addition, the GeNN simulator can be optimized by utilizing dynamic parallelism for its synaptic updates.

All GPU devices produced from 2013 onward support dynamic parallelism as described in this study, and thus allow developers to employ this programming paradigm to overcome various programming problems. In terms of spiking neural network simulations, dynamic parallelism substantially accelerates the massive neural computations, by implementing the spike-triggered calculations at each synaptic updating step. In previous parallel SNN implementations, this step was considered to be the bottleneck of the simulations, because the developed algorithms kept running obsolete calculations for spike propagation, even when the presynaptic neuron did not elicit any spike. Especially, the simulations of densely connected neurons operating under sparse spiking regimes (like observed experimentally in the cerebral cortex, or when simulating the neural dynamics at a high temporal resolution) benefit from the considerable speed up via dynamic parallelism. We therefore foresee that spike propagation will no longer be the major determinant of simulation duration of large-scale dynamic neural networks.

The premise of parallel computing is: parallelization accelerates computations. However, parallelization is only possible if the same exact computations are performed again and again on different data points; and these computations are not dependent on each other’s results. Modern GPU’s can run millions of threads in parallel, therefore millions of neural state update and synaptic up-
date can be parallelized. However, the computations can be parallelized only if the calculations are exactly the same, even if with different parameters. Therefore, N- and S- algorithms require to finish all neural state updates to start synaptic propagation. If the neural network architecture requires many small sets of different neuron types, whose behaviours are defined by different equations, GPU utilization would decrease. That would mean, not many calculations are done in parallel and many processors are waiting to be assigned to a calculation. Such scenario would not optimize throughput, thus the architecture of the network is also a consideration for GPU. For full utilization of GPU in calculations, the number of calculations running in parallel should cover the number of threads started at a parallel block.


MICROSTIMULATION IN A SPIKING NEURAL NETWORK MODEL OF THE MIDBRAIN SUPERIOR COLLICULUS

Abstract

The midbrain superior colliculus (SC) generates a rapid saccadic eye movement to a sensory stimulus by recruiting a population of cells in its topographically organized motor map. Supra-threshold electrical microstimulation in the SC reveals that the site of stimulation produces a normometric saccade vector with little effect of the stimulation parameters. Moreover, electrically evoked saccades (E-saccades) have kinematic properties that strongly resemble natural, visual-evoked saccades (V-saccades). These findings support models in which the saccade vector is determined by a center-of-gravity computation of activated neurons, while its trajectory and kinematics arise from downstream feedback circuits in the brainstem. Recent single-unit recordings, however, have indicated that the SC population also specifies instantaneous kinematics. These results support an alternative model, in which the desired saccade trajectory, including its kinematics, follows from instantaneous summation of movement effects of all SC spike trains. But how to reconcile this model with microstimulation results? Although it is thought that microstimulation activates a large population of SC neurons, the mechanism through which it arises is unknown. We developed a spiking neural network model of the SC, in which microstimulation directly activates a relatively small set of neurons around the electrode tip, which subsequently sets up a large population response through lateral synaptic interactions. We show that through this mechanism the population drives an E-saccade with near-normal kinematics that are largely independent of the stimulation parameters. Only at very low stimulus intensities the network recruits a population with low firing rates, resulting in abnormally slow saccades.

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4.1 INTRODUCTION

High-resolution foveal vision covers only 2% of the visual field. Thus, the visual system has to gather detailed information about the environment through rapid goal-directed eye movements, called saccades. Saccades reach peak eye velocities well over ~1000 deg/s in monkey, and last for only 40-100 ms, depending on their size. The stereotyped relationships between saccade amplitude and duration (described by a straight line) and peak eye velocity (a saturating function) are termed the ‘saccade main sequence’ Bahill et al., 1975. The acceleration phase of saccades has a nearly constant duration for all amplitudes, leading to positively skewed velocity profiles Van Opstal and Van Gisbergen, 1987. In addition, the horizontal and vertical velocity profiles of oblique saccades are coupled, such that they are scaled versions of each other (through component stretching), and the resulting saccade trajectories are approximately straight Van Gisbergen, Van Opstal, and Schoenmakers, 1985. These kinematic properties all imply that the saccadic system contains a nonlinearity in its control Smit et al., 1990; Van Gisbergen, Van Opstal, and Schoenmakers, 1985; Van Gisbergen, Robinson, et al., 1981. More recent theories hold that this nonlinearity reflects an optimization strategy for speed-accuracy trade-off, which copes with the spatial uncertainty in the retinal periphery, and internal noise in the sensorimotor pathways Goossens and Van Opstal, 2006; Harris and Wolpert, 2006; Tanaka et al., 2006; Van Beers, 2008.

The neural circuitry responsible for saccade programming and execution extends from the cerebral cortex to the pons in the brainstem. The midbrain superior colliculus (SC) is the final common terminal and a major point of convergence of descending saccade related signals, and it has been hypothesized to specify the vectorial eye-displacement command for downstream oculomotor circuitry Moschovakis et al., 1998; Robinson, 1972; Scudder, 1988. The SC contains an eye-centered topographic map of visuomotor space, in which the saccade amplitude is mapped logarithmically along its rostral-caudal anatomical axis ($u$, in mm) and saccade direction maps roughly linearly along the medial-lateral axis ($v$, in mm; Robinson, 1972). The afferent map (Eqn. 4.1a) and its efferent inverse (Eqn. 4.1b) has been described by Ottes et al., 1986:

\[
\begin{align*}
    u &= B_u \ln \left( \frac{\sqrt{(x + A)^2 + y^2}}{A} \right) \\
    v &= B_v \tan \left( \frac{y}{x + A} \right)
\end{align*}
\]

\[
\begin{align*}
    x &= A \cdot \left( \exp \frac{u}{B_u} \cos \frac{v}{B_v} - 1 \right) \\
    y &= A \cdot \exp \frac{u}{B_u} \sin \frac{v}{B_v}
\end{align*}
\]

(4.1)
with parameters $B_u \approx 1.4$ mm, $B_v \approx 1.8$ mm/rad, and $A \approx 3$ deg. Recently, Hafed and Chen, 2016 provided evidence for an additional anisotropy for upward ($v > 0$) vs. downward ($v < 0$) directions, which would lead to slightly different inverse mapping relations than Eqn. 4.1b (see Discussion). Each saccade is associated with a translation-invariant Gaussian-shaped population within this map, the center of which corresponds to the saccade vector, $(x, y)$, and a width of $\sigma \approx 0.5$ mm Ottes et al., 1986; Van Opstal, Van Gisbergen, and Smit, 1990. It is generally assumed that each recruited neuron, $n$, in the population encodes a vectorial movement contribution to the saccade vector, which is determined by both its anatomical location within the motor map, $(u_n, v_n)$, and its activity, $F_n$.

**Vector averaging vs. linear summation models**

Precisely how individual cells contribute to the saccade is still debated in the literature. Two competing models have been proposed for decoding the SC population: weighted averaging of the cell vector contributions (Lee et al., 1988; Port and Wurtz, 2003; Walton et al., 2005; Eqn. 4.2a) vs. linear summation (Goossens and Van Opstal, 2012; Goossens and Van Opstal, 2006; Van Gisbergen, Van Opstal, and Schoenmakers, 1985; Eqn. 4.2b), respectively, which can be formally described as follows:

$$S_{AVG} = \frac{\sum_{n=1}^{N} F_n M_n}{\sum_{n=1}^{N} F_n} \quad \text{vs.} \quad S_{SUM}(t) = \sum_{n=1}^{N} \sum_{k=1}^{K_n < t} \delta(t - \tau_{n,k}) \cdot m_n \quad (4.2)$$

$N$ is the number of active neurons in the population, $K_n < t$ the number of spikes in the burst of neuron $n$ up to time $t$, $F_n$ its mean (or peak) firing rate, and $M_n = (x_n, y_n)$ is the saccade vector in the motor map encoded at SC site $(u_n, v_n)$ (Eqn. 4.1b).

$m_n = \zeta M_n$ is the small, fixed vectorial contribution of cell $n$ in the direction of $M_n$, for each of its spikes, with $\zeta$ a fixed, small scaling constant that depends on the adopted cell density in the map and the population size, and $\delta(t - \tau_{k,n})$ is the $k$th spike of neuron $n$, fired at time $\tau_{k,n}$.

The vector-averaging scheme of Eqn. 4.2a only specifies the amplitude and direction of the saccade vector, and thus puts the motor map of the SC outside the kinematic control loop of its trajectory. It assumes that the nonlinear saccade kinematics are generated by the operation of horizontal and vertical dynamic feedback circuits in the brainstem Jürgens et al., 1981; Lee et al., 1988;
Robinson, 1975, or cerebellum Lefèvre et al., 1998; Quaia et al., 1999. Note also that vector averaging is a nonlinear operation because of the division by the total population activity.

In contrast, the linear dynamic ensemble-coding model of Eqn. 4.2b encodes the full kinematics of the desired saccade trajectory at the level of the SC motor map through the temporal distribution of spikes by all cells in the population Goossens and Van Opstal, 2012; Goossens and Van Opstal, 2006; Smalianchuk et al., 2018. As a result, the instantaneous firing rates of all neurons in the population, usually estimated by their instantaneous spike-density functions, $f_n(t)$, together encode the desired vectorial saccadic velocity profile:

$$v_{Sacc}(t) = \sum_{n=1}^{N} f_n(t) \cdot m_n$$

with

$$f_n(t) = \sum_{k=1}^{S_n} \frac{1}{\sigma \sqrt{2\pi}} \cdot e^{-\frac{(t-t_{k,n})^2}{2\sigma^2}}$$

where $S_n$ is the number of spikes of cell $n$, with the spikes occurring at times $t_{k,n}$. The Gaussian acts as a linear kernel that smooths the discrete spike into a continuous function (e.g., Richmond et al., 1990).

Although the models of Eqn. 4.2a,b cannot both be right, each is supported by different lines of evidence. For example, electrical microstimulation produces fixed-vector (E-)saccades with normal main-sequence kinematics that are insensitive to a large range of stimulation parameters Katnani, Van Opstal, et al., 2012; Robinson, 1972; Stanford et al., 1996; Van Opstal, Van Gisbergen, and Smit, 1990. If one supposes that electrical stimulation directly activates a large population of SC cells, and that the firing rates follow the (typically rectangular) stimulation profile, a vector-averaging scheme with downstream dynamic feedback circuitry readily explains why E-saccades are normal main-sequence, since the center of gravity of the population specifies the desired saccade vector only, regardless the firing rates.

In addition, reversible inactivation of a small part of the SC motor map produces particular deficits in the metrics of visually-evoked (V-)saccades that may not be readily explained by the linear summation model of Eqn. 4.2b Lee et al., 1988. As the amplitude and direction of a V-saccade to the center of the lesioned site remain unaffected, saccades to locations around that site are directed away from the lesion. For example, V-saccades for sites rostral to the lesion undershoot the target, while V-saccades for sites caudal to the lesion will overshoot the target.

The simple vector-summation model of Eqn. 4.2b yields saccades that would always undershoot targets, as the lesioned population produces fewer output
spikes than under normal control conditions. However, Goossens and Van Opstal, 2012; Goossens and Van Opstal, 2006 observed that their estimate of the total number of spikes from the SC population, was remarkably constant, regardless of saccade amplitude, direction, or speed. Yet, they also observed that many cells in the normal SC fire some post-saccadic spikes. They therefore assumed that saccades are actively terminated by a downstream mechanism, whenever the criterion of a fixed number of spikes, $N_{TOT}$, is reached:

$$\sum_{n=1}^{N} \sum_{k=1}^{K_n} \delta(t - \tau_{n,k}) \leq N_{TOT}$$  \hspace{1cm} (4.4)

They demonstrated, by simulating the summation model of Eqn. 4.2b with actual recordings from ~150 cells, that by including the criterion of Eqn. 4.4 (which constitutes a cut-off nonlinearity in the model), the pattern of saccadic over- and undershoots to a focal SC lesion can be fully explained. In addition, the extended summation model of Eqns. 4.2b and 4.4 also accounts for weighted averaging of double-target stimulation in the motor map Robinson, 1972; Van Opstal, 2016; Van Opstal and Van Gisbergen, 1989. Moreover, although the vector-averaging model (Eqn. 4.2a) correctly predicts the pattern of saccadic dysmetrias, it fails to explain the substantial slowing of the lesioned saccades Lee et al., 1988. As this latter observation is also accounted for by Eqns. 4.2b and 4.4 Goossens and Van Opstal, 2006, it further supports the hypothesis that the SC population encodes both the saccade-vector, and its kine-
matics Smalianchuk et al., 2018.

**Electrical microstimulation in SC**

Interestingly, electrical microstimulation experiments have also shown that at low current strengths, just around the threshold, the evoked saccade vectors become smaller and slower than main sequence Katnani and Gandhi, 2012; Van Opstal, Van Gisbergen, and Smit, 1990. These results do not follow from vector averaging (Eqn. 4.2a, which would always generate the same saccade, but might be predicted by dynamic summation (Eqns. 4.2b and 4.4), if low-amplitude electrical stimulation were to recruit a smaller number of neurons at lower firing rates.

However, if supra-threshold microstimulation would produce a large square-
pulse population profile around the electrode tip (mimicking the profile of the imposed current pulses, as is typically assumed), the summation model would generate severely distorted saccade-velocity profiles, which are not observed in
experiments. Yet, little is known about the actual activity profiles in the motor map evoked by electrical microstimulation, as simultaneous multi-electrode recordings in the SC during microstimulation are not available and would be obscured by the large stimulation artefacts Histed, Ni, et al., 2013.

Under microstimulation, two factors contribute to neuronal activation: (1) direct (feedforward) current stimulation of cell bodies and axons by the stimulation pulses of the electrode, and (2) synaptic activation through lateral (feedback) interactions among neurons in the motor map. How each of these factors contributes to the population activity in the SC is unknown. It is conceivable, however, that current strength falls off rapidly with distance from the electrode tip (at least by $\sim 1/r^2$), and that hence a relatively small number of SC neurons would be directly stimulated by the electric field of the electrode.

Indeed, a two-photon imaging study, carried out in cortical tissue from rodents and cat are V1, showed that microstimulation at physiological current strengths directly activates only a sparse set of neurons directly around the immediate vicinity of the stimulation site Histed, Bonin, et al., 2009. These considerations therefore suggest that the major factor in explaining the effects of microstimulation in the SC motor map may be synaptic transmission through lateral excitatory-inhibitory connections among the cells. Such a functional organization in the SC is supported by anatomical studies Behan and Kime, 1996; Olivier et al., 1998, by electrophysiological evidence Munoz and Istvan, 1998; Phongphanphanee, Mizuno, et al., 2011; Phongphanphanee, Marino, et al., 2014, and by pharmacological studies Meredith and Ramoa, 1998.

**Spiking neural network model**

We recently constructed a biologically plausible, yet simple, spiking neural network model for ocular gaze-shifts by the SC population to visual targets Kasap and Opstal, 2017. This minimalistic (one-dimensional) model with lateral interactions can account for the experimentally observed firing properties of saccade-related cells in the gaze-motor map Goossens and Van Opstal, 2012; Goossens and Van Opstal, 2006, by assuming an invariant spiking input pattern from sources upstream from the motor map (e.g., FEF).

We here extended that simple network model to the full two-dimensional network map that accounts for microstimulation results over a wide range of stimulation parameters. To simplify the analysis of the network properties, and to limit the number of independent parameters that describe the electrical stimulation pulses, we used rectangular current profiles with different heights (current intensities) and durations. In line with the evidence from previous work,
the network was tuned such that microstimulation provides an initial seed that directly activates only a small set of SC neurons, which subsequently sets up a large SC population activity through lateral synaptic interactions. Our results show that stimulating the network indeed sets up a near-normal population activity profile that generates appropriate saccadic command signals across the two-dimensional oculomotor range through the linear dynamic summation mechanism of Eqn. 4.2b.
4.2 METHODS

Log-polar afferent mapping

The afferent mapping function (Eqn. 4.1a) translates a target point in visual space to the anatomical position of the center of the corresponding Gaussian-shaped population in the SC motor map. It follows a log-polar projection of retinal coordinates onto Cartesian collicular coordinates (Eqn. 4.1a; Ottes et al., 1986). To allow for a simple 2D matrix representation of the map in our network model, we simplified the afferent motor map to the complex logarithm:

\[ u(R) = B_u \cdot \ln(R) \quad \text{and} \quad v(\phi) = B_v \cdot \phi \]

with \( R = \sqrt{x^2 + y^2} \) and \( \phi = \tan(y/x) \) \( (4.5) \)

with \( B_u = 1 \) mm and \( B_v = 1 \) mm/rad (isotropic map). Thus, the contribution, \( m \), of a single spike at site \((u,v)\) to the eye movement is computed from the efferent mapping function as:

\[ m_x = \zeta \exp(u) \cos(v) \quad \text{and} \quad m_y = \zeta \exp(u) \sin(v) \quad (4.6) \]

We thus constructed a spiking neural network model as a rectangular grid of 201 x 201 neurons. The network represents the gaze motor-map with \( 0 < u < 5 \) mm (i.e., up to amplitudes of 148 deg), and \(-\pi/2 < v < \pi/2 \) mm. The network generates saccadic motor commands of different directions and amplitudes into the contralateral visual hemispace through a spatial-temporal population activity profile. The location of the population in the motor map determines the direction and amplitude of the saccade target, whereas the temporal activity profile encodes the eye-movement kinematics, through Eqn. 4.2b. As described below, and in our previous study Kasap and Opstal, 2017, the eye-movement main-sequence kinematics result from location-dependent biophysical properties of the neurons within the map, together with their lateral interconnections.

AdEx neuron model

We investigated the dynamics of the network model numerically through simulations developed in C++/CUDA Nickolls et al., 2008. The motor map is represented as a rectangular grid of neurons with a Mexican hat-type pattern of lateral interactions. The neural activities were simulated by custom code utilizing dynamic parallelism to accelerate spike propagation on a GPU Kasap and
Opstal, 2018b. The code was developed and tested on a Tesla K40 with CUDA Toolkit 7.0, Linux Ubuntu 16.04 LTS (repository under https://bitbucket.org/bkasap/sc_microstimulation). Simulations ran with a time resolution of 0.01 ms. Brute-force search and genetic algorithms, described below, were used for parameter identification and network tuning since there exists no analytical solution for the system.

The neurons in the network were described by the adaptive exponential integrate-and-fire (AdEx) neuron model Brette and Gerstner, 2005, which accommodates for a variety of bursting dynamics with a minimum set of free parameters. The AdEx model is a conductance-based integrate-and-fire model with an exponential membrane potential dependence. It reduces Hodgkin-Huxley’s model to only two state variables: the membrane potential, $V$, and an adaptation current, $q$. The temporal dynamics of the system are given by the following differential equations for neuron $n$:

$$\frac{C}{\tau_{q,n}} \frac{dV_n}{dt} = -g_L(V_n - E_L) + g_L \eta \exp\left(\frac{V_n - V_T}{\eta}\right) - q_n + I_{\text{inp},n}(t) \quad (4.7a)$$

$$\frac{\tau_{q,n}}{\tau_{q,n}} \frac{dq_n}{dt} = a(V_n - E_L) - q_n \quad (4.7b)$$

where $C$ is the membrane capacitance, $g_L$ is the leak conductance, $E_L$ is the leak reversal potential, $\eta$ is a slope factor, $V_T$ is the neural spiking threshold, $q_n$ is the adaptation time constant, $a$ is the sub-threshold adaptation constant, and $I_{\text{inp},n}$ is the total synaptic input current. In our previous paper Kasap and Opstal, 2017 the input-layer of Frontal Eye Field (FEF) neurons had identical biophysical properties, and only received a fixed external input current, $I_{\text{inp},n} = I_{\text{ext}}$. In the present simulations, we did not include a FEF input layer, as the electrical stimulation was applied within the SC motor map as an external current.

Two parameters specify the biophysical properties of the SC neurons: the adaptation time constant, $\tau_{q,n}$ (which is assumed to be location dependent), and the synaptic input current, $I_{\text{inp},n} = I_{\text{syn},n} + I_E$ (where $I_{\text{syn},n}$ is a location- and activity-dependent synaptic current, and $I_E$ is the applied microstimulation current). Both variables change systematically with the spatial location of the cells within the network (rostral to causal). The remaining parameters, $C$, $g_L$, $E_L$, $\eta$, $V_T$ and $a$, were tuned such that the cells showed neural bursting behavior (see Table 4.1 for the list and values of all parameters used in the simulations, and Fig. 4.1 for some example responses).

The AdEx neuron model employs a smooth spike initiation zone between $V_T$ and $V_{\text{peak}}$, instead of a strict spiking threshold. Once the membrane potential
crosses $V_T$, the exponential term in Eqn. 4.7a starts to dominate and the membrane potential can in principle increase without bound. We applied a practical spiking ceiling threshold at $V_{peak} = -30$ mV for the time-driven simulations. For each spiking event at time $\tau$, the membrane potential is reset to its resting potential, $V_{\text{rst}}$, and the adaptation current, $q$, is increased by $b$ to implement the spike-triggered adaptation:

$$V(\tau) \rightarrow V_{\text{rst}} \quad \text{and} \quad q(\tau) \rightarrow q(\tau) + b$$  (4.8)

After rescaling the equations, the neuron model has four free parameters (plus the input current) Touboul and Brette, 2008. Two of these parameters characterize the sub-threshold dynamics: the ratio of time constants, $\tau_a/\tau_m$ (with the membrane time constant $\tau_m = C/g_L$) and the ratio of conductances, $a/g_L$ (a can be interpreted as the stationary adaptation conductance). Furthermore, the resting potential $V_{\text{rst}}$ and the spike-triggered adaptation parameter $b$ characterize the emerging spiking patterns of the model neurons (regular/irregular spiking, fast/slow spiking, tonic/phasic bursting, etc.).

**Current spread function**

We applied electrical stimulation by the input current, centered around the site at $[u_E, v_E]$, according to Eqn. 4.5. We incorporated an exponential spatial decay of the electric field from the tip of the electrode:

$$I_E(u,v,t) = I_0 \cdot \exp(-\lambda \sqrt{(u - u_E)^2 + (v - v_E)^2}) \cdot P(t)$$  (4.9)

with $\lambda$ (mm$^{-1}$) a spatial decay constant, $I_0$ the current intensity (in pA), and a rectangular stimulation pulse given by $P(t) = 1$ for $0 < t < D_S$, and 0 elsewhere. Thus, only a small set of neurons around the stimulation site will be directly activated with this input current (see Results). Throughout this paper, we used a fixed input current profile ($I_0 = 150$ pA), $\lambda = 10$ mm$^{-1}$ and $D_S = 100$ ms) except for the final section, where we explore the effect of changing the microstimulation parameters on the resulting saccade. These parameters were determined by the neural tuning of the AdEx neurons in their bursting regime (see Neural tuning and bursting mechanism section in Results).

For simplicity, we incorporated a single rectangular stimulation pulse, $P(t)$, rather than a train of narrowly spaced stimulation pulses. A train of pulses would introduce additional parameters, like pulse height, pulse duration, pulse intervals, pulse polarity, and number of pulses (stimulus duration), each of
which would affect the network response. We have shown before that the spiking neural network model with AdEx neurons and lateral interactions can deal with such spiking input patterns Kasap and Opstal, 2017. However, varying these different stimulations parameters would complicate the analysis, and is deemed a topic for future work (see Discussion). Note also that the AdEx neurons act as leaky integrators for membrane potentials below $V_T$. Therefore, a sequence of pulses and a single rectangular pulse yield qualitatively similar membrane responses.

Remark on the current scale. In SC microstimulation experiments, one typically applies extracellular currents in the micro-Ampere range ($10^{-50}$ µA) to evoke a saccade. In our simulations, we instead take the effective intracellularly applied current, which amounts to only a tiny fraction of the total extracellular current leaving the electrode.

The SC model: synapses and lateral connections

The total input current for an SC neuron, $n$, located at $(u_n,v_n)$, is governed by the spiking activity of surrounding neurons, through conductance-based synapses, and by the externally applied electrical stimulation input (Eqn. 4.9):

$$I_{\text{inp.}n}(t) = g_{\text{exc}}^n(t)(E_e - V_n(t)) + g_{\text{inh}}^n(t)(E_i - V_n(t)) + I_E(u_n,v_n,t) \tag{4.10}$$

where $g_{\text{exc}}^n$ and $g_{\text{inh}}^n$ are excitatory and inhibitory synaptic conductances acting upon neuron $n$, $E_e$ and $E_i$ are excitatory and inhibitory reversal potentials respectively. These conductances increase instantaneously for each presynaptic spike by a factor determined by the synaptic strength between neurons, and they decay exponentially otherwise, according to:

$$\tau_{\text{exc}} \frac{dg_{\text{exc}}^n}{dt} = -g_{\text{exc}}^n + \tau_{\text{exc}} \sum_{i}^{N_{\text{pop}}} w_{\text{exc},i,n}^{i} \sum_{s}^{N_{\text{spks}}} \delta(t - \tau_{i,s}) \tag{4.11a}$$

$$\tau_{\text{inh}} \frac{dg_{\text{inh}}^n}{dt} = -g_{\text{inh}}^n + \tau_{\text{inh}} \sum_{i}^{N_{\text{pop}}} w_{\text{inh},i,n}^{i} \sum_{s}^{N_{\text{spks}}} \delta(t - \tau_{i,s}) \tag{4.11b}$$

with $\tau_{\text{exc}}$ and $\tau_{\text{inh}}$, the excitatory and inhibitory time constants; $w_{\text{exc},i,n}^{i}$ and $w_{\text{inh},i,n}^{i}$ are the intracollicular excitatory and inhibitory lateral connection strengths between neuron $i$ and $n$, respectively (Eqn. 4.12a,b) and $\tau_{i,s}$ is the spike timing of the presynaptic SC neurons that project to neuron $n$. With conductance-based
synaptic connections, spike propagation occurs in a biologically realistic way, since the postsynaptic projection of a presynaptic spike depends on the instantaneous membrane potential of the postsynaptic neuron. In this way, the state of a neuron determines its susceptibility to presynaptic spikes.

We incorporated a Mexican hat-type lateral connection scheme in the model, where the net synaptic effect is given by the difference between two Gaussians Trappenberg et al., 2001. Accordingly, neurons were connected with strong short-range excitatory and weak long-range inhibitory synapses, which implements a dynamic soft winner-take-all (WTA) mechanism: not only one neuron remains active, but the winner affects the temporal activity patterns of the other active neurons. The central neuron governs the population activity, since it is the most active one in the recruited population. As a result, all recruited neurons exhibit similarly-shaped bursting profiles as the central neuron, leading to synchronization of the spike trains within the population Kasap and Opstal, 2017. Two Gaussians describe the excitatory and inhibitory connection strengths between collicular neurons as function of their spatial separation:

\[
\begin{align*}
    w_{i,n}^{\text{exc}} &= s_n \cdot \bar{w}_{\text{exc}} \exp \left( -\frac{||u_i - u_n||^2}{2\sigma_{\text{exc}}^2} \right) \\
    w_{i,n}^{\text{inh}} &= s_n \cdot \bar{w}_{\text{inh}} \exp \left( -\frac{||u_i - u_n||^2}{2\sigma_{\text{inh}}^2} \right)
\end{align*}
\] (4.12a,b)

with \(\bar{w}_{\text{exc}} > \bar{w}_{\text{inh}}\) and \(\sigma_{\text{inh}} > \sigma_{\text{exc}}\), and \(s_n\) is a location-dependent synaptic weight-scaling parameter, which accounts for the location-dependent change in sensitivity of the neurons due to the variation in adaptation time constants.

**Network tuning**

Electrophysiological experiments have indicated that the neural responses are well characterized by four principles: (i) a fixed number of spikes for each neuron associated with its preferred saccade vector \(N_{u,v} \cong 20\) spikes, (ii) a systematic dependence of the neuron’s cumulative spike count on the saccade vector (dynamic movement field), \(N_{u,v}(R, \phi, t)\), (iii) scaled and synchronized burst profiles of the neurons in the population, resulting in a high cross-correlation, \(C_{\text{pop}}(f_n(t), f_m(t)) \approx \delta_{nm}\), between the firing rates of recruited neurons, and (iv) a systematic decrease of the peak firing rate of central neurons in the population, \(F_{\text{peak}}\), along the rostral-caudal axis, together with an increase of burst duration, \(T_{\text{burst}}\), and burst skewness, \(S_{\text{burst}}\).
Goossens and Van Opstal, 2012 argued that these properties follow from a systematic tuning of the gaze-motor map, and that they are responsible for the observed saccade kinematics. Here we applied these principles to determine a similarity measure between our simulated responses, and the experimentally recorded gaze motor-map features. In our network model, these features emerge from the interplay between intrinsic biophysical properties of the SC neurons, and the lateral interactions between them.

**Distinct biophysical properties**

The intrinsic biophysical properties of the neurons were enforced by systematically varying the adaptation time constant, $\tau_{q,n}$, and the synaptic weight-scaling parameter, $s_n$, in the motor map. Changes in the adaptive properties of the neurons result in a varying susceptibility to synaptic input. The synaptic weight-scaling parameter corrects for the total input activity. These distinct biophysical properties capture the systematically changing firing properties of SC cells along the rostral-caudal axis of the motor map, while keeping a fixed number of spikes for the neurons’ preferred saccades $N_{u,v}(R,\phi)$. Following the brute-force algorithm from our recent paper Kasap and Opstal, 2017, the location-dependent $[\tau_{q,n}, s_n]$ value pairs for the neurons were fitted to ensure a fixed number of spikes per neuron under a given microstimulation condition, and the subsequent excitation through lateral interactions (see below, Eqns. 4.15 and 4.16). These parameters were first tuned for isolated neurons. The lateral interactions ensured that the bursting profiles in the population remained scaled versions of each other and had their peaks synchronized (evidenced from a high cross-correlation, $C_{\text{pop}}$, between the burst profiles across the population). The $s_n$ values of Eqn. 4.12a,b were scaled by the number of neurons in the population.

**Lateral connectivity**

The single-unit recordings also suggested that for each saccade the recruited population size, and hence its total number of spikes, is invariant across the motor map. The widths of the Mexican-hat connectivity ($\sigma_{\text{exc}}$ and $\sigma_{\text{inh}}$) govern the spatial range of a neuron’s spike influence in the network, and directly affect the size of the neural population. In our model, these widths were fixed, such that they yielded local excitation and global inhibition. The connection strengths ($\tilde{w}_{\text{exc}}$ and $\tilde{w}_{\text{inh}}$), on the other hand, affect the spiking behavior and local network dynamics, as they control how much excitation and inhibition will be received by each single neuron, and transmitted to others, based on the
ongoing activity. Strong excitation would result in an expansion of the population, whereas a strong inhibition would fade out the neural activity altogether. Thus, balanced intra-collicular excitation and inhibition would be required to establish a large, but confined, Gaussian population.

The parameters for the lateral connection strengths were found by a genetic algorithm, as described in our previous paper (Kasap and Van Opstal, 2017). In the current model we used eight saccade amplitudes for each generation to calculate the fitness of each selection (selected as $R = [2, 3, 5, 8, 13, 21, 33, 55]$ deg, and $\phi = 0$ deg, to cover equidistant locations on the rostral-to-caudal plane: $u = [0.69, 1.08, 1.60, 2.07, 2.56, 3.04, 3.49, 4.00]$ mm, and $v = 0$ mm, respectively).

The genetic algorithm minimized the root-mean squared errors (RMSE) between the spiking network responses and the rate-based model of Van Opstal and Goossens, 2008: from the fitness evaluation for each generation, we calculated the RMSE between the peak firing rates, $F_{\text{peak}}$; the number of elicited spikes from the central cells in the population, $N_{u,v}(R, \phi)$; burst durations, $T_{\text{burst}}$; and burst skewness, $S_{\text{burst}}$. Furthermore, the cross-correlations, $C_{\text{pop}}$, between all active neurons and the central cell were included too to ensure that the experimentally observed gaze-motor map characteristics were taken into account for parameter identification. The fitness function was defined by a weighted RMSE summation:

$$\text{Fitness} = \begin{cases} 10^{-1} \cdot \text{RMSE}(F_{\text{peaks}}) \\ + 10 \cdot \text{RMSE}(N_{u,v}(R, \phi)) \\ + 10^3 \cdot \text{RMSE}(C_{\text{pop}}) \end{cases}$$

(4.13)

where the weights (0.1, 10, 103) were empirically chosen to cover similar ranges, since the $F_{\text{peaks}}$ vary from roughly 430-750 spikes/s, the number of spikes varies between 18 and 22, and the cross-correlation values are < 1.

Peak firing rates of the central neurons from each population were calculated by convolving the spike trains with a Gaussian kernel (Eqn. 4.3; 8 ms kernel width), to determine spike-density functions of instantaneous firing rate. RMSE values for $F_{\text{peak}}$ along the rostral-caudal axis of the motor map were subsequently tuned by approximating the following relation:

$$F_{\text{peak}}(r) = \frac{F_0}{\sqrt{1 + \beta \cdot R}}$$

(4.14)

where $F_0 = 800$ spikes/s and $\beta = 0.07$ ms/deg (taken from Van Opstal and Goossens, 2008. The RMSE of the total spike counts during the burst from
the central cells in the population were tuned to $N_{u,v} = 20$ spikes, and was required to be independent of the neuron’s position in the map. Synchrony of the neural activity within the recruited population was quantified by the RMSE of deviations for the cross-correlations between the central cell and all other active cells in the recruited population.

Generating eye movements

Eye movements were generated by the population activity following the linear ensemble-coding model of Eqns. 4.2b and 4.3. We applied the two-dimensional efferent motor map of Eqn. 4.5. For any network configuration throughout this paper, the unique scaling factor of the efferent motor map ($\zeta$) was calibrated for a horizontal saccade at $(x, y) = (21, 0)$ deg. The resulting eye-displacement vector, $\vec{S}(t)$, was calculated from the spike trains by interpolation with a first-order spline to obtain equidistant time samples. The interpolated data were further smoothed with a Savitzky-Golay filter, to obtain smooth velocity profiles.
Table 4.1 List of all parameters used in the simulations.

<table>
<thead>
<tr>
<th>Microstimulation parameters</th>
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<tbody>
<tr>
<td>$\lambda$</td>
<td>$10 \text{ mm}^{-1}$ Spatial decay constant</td>
</tr>
<tr>
<td>$I_0$</td>
<td>$(40-280) \text{ pA}$ Intracellular current intensity</td>
</tr>
<tr>
<td>$P(t)$</td>
<td>$I_0$ (for $0 &lt; t &lt; D_s$) Rectangular stimulus pulse</td>
</tr>
<tr>
<td>$V_T$</td>
<td>$100 \text{ (25-250) ms}$ Stimulus duration</td>
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<tr>
<th>Neural parameters</th>
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<tbody>
<tr>
<td>$C$</td>
<td>$600 \text{ pF}$ Membrane capacitance</td>
</tr>
<tr>
<td>$g_L$</td>
<td>$20 \text{ nS}$ Leak conductance</td>
</tr>
<tr>
<td>$E_L$</td>
<td>$-53 \text{ mV}$ Leak reversal potential</td>
</tr>
<tr>
<td>$\eta$</td>
<td>$2 \text{ mV}$ Spike slope factor</td>
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<tr>
<td>$V_T$</td>
<td>$-50 \text{ mV}$ Exponential threshold</td>
</tr>
<tr>
<td>$V_{\text{peak}}$</td>
<td>$-30 \text{ mV}$ Spiking threshold</td>
</tr>
<tr>
<td>$V_{\text{rst}}$</td>
<td>$-45 \text{ mV}$ Reset potential</td>
</tr>
<tr>
<td>$a$</td>
<td>$0 \text{ nS}$ Sub-threshold adaptation</td>
</tr>
<tr>
<td>$b$</td>
<td>$120 \text{ pA}$ Spike-triggered adaptation</td>
</tr>
<tr>
<td>$\tau_q$</td>
<td>$10-30 \text{ ms}$ Location-dependent adaptation time constant; varies with $u_n$</td>
</tr>
<tr>
<td>$\zeta$</td>
<td>$5.087 \cdot 10^{-5}$ Efferent map mini-vector scaling factor</td>
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<th>Synaptic parameters</th>
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<tr>
<td>$E_e$</td>
<td>$0 \text{ mV}$ Excitatory reversal potential</td>
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<tr>
<td>$E_i$</td>
<td>$-80 \text{ mV}$ Inhibitory reversal potential</td>
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<tr>
<td>$\tau_{\text{exc}}$</td>
<td>$5 \text{ ms}$ Excitatory conductance decay</td>
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<tr>
<td>$\tau_{\text{inh}}$</td>
<td>$10 \text{ ms}$ Inhibitory conductance decay</td>
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<tr>
<th>Mexican-hat Parameters</th>
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<tbody>
<tr>
<td>$\tilde{w}_{\text{exc}}$</td>
<td>$45 \text{ pS}$ Excitatory scaling factor</td>
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<tr>
<td>$\tilde{w}_{\text{inh}}$</td>
<td>$14 \text{ pS}$ Inhibitory scaling factor</td>
</tr>
<tr>
<td>$\sigma_{\text{exc}}$</td>
<td>$0.4 \text{ mm}$ Range of excitatory synapses</td>
</tr>
<tr>
<td>$\sigma_{\text{inh}}$</td>
<td>$1.2 \text{ mm}$ Range of inhibitory synapses</td>
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<tr>
<td>$s_n$</td>
<td>$&gt; 0.0112 \text{ nS}$ Location-dependent synaptic scaling parameter; varies with $u_n$</td>
</tr>
<tr>
<td>$&lt; 0.0147 \text{ nS}$</td>
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4.3 Results

Neural tuning and bursting mechanism

Figure 4.1 shows the membrane potential traces for three model neurons, differing in their adaptation time constants, $\tau_q$, which were stimulated under different microstimulation paradigms. The electrical stimulus strength increased from a low amplitude ($I_0 = 50$ pA; light blue traces) to a high intensity ($I_0 = 250$ pA, dark-blue traces), for stimulation durations between 25 and 225 ms. Note that for these different microstimulation regimes, the burst onsets and burst shapes (i.e., the instantaneous firing rates) could differ, even when the number of elicited spikes would be the same. These responses illustrate how the biophysical properties of the neurons affected their bursting behavior.

First, the neuron could respond after the stimulation had terminated. Such a feature, as well as the bursting behavior, is only captured by more complex spiking neuron models. Even when the input current amplitude cannot drive a neuron rapidly to its first spike to initialize the burst (light traces), it suffices if the neuron’s membrane potential crosses a certain threshold ($V_T$ in the AdEx neuron). The neuron can then elicit a spike after the stimulation is over (visible for stimulation durations < 75 ms).

Second, the stimulation amplitude determines the response onset: as the amplitude increases, the first spike occurs earlier. Such a behavior is to be expected, since the neuron model acts as an integrator Katnani and Gandhi, 2012; higher input currents thus drive a neuron faster to its spiking threshold.

Third, the different neurons respond differently to long stimulation trains (> 175 ms). While the neuron with a longer adaptation time constant ($\tau_q = 84.6$ ms; Fig. 4.1A) responds with repetitive bursts of 4 to 5 spikes, separated by a silent period, the faster recovering neuron ($\tau_q = 52.4$ ms; Fig. 4.1C) elicits more and more spikes after the initial burst, especially for the higher current amplitudes (dark traces).

Interestingly, the neurons with the intermediate (Fig. 4.1B) and short (Fig. 4.1C) adaptation time constants switch between different bursting behaviors as the current amplitude increases along with longer stimulation durations. Regular short bursts with silent periods in between result from the slow decay of the adaptation current, which acts on the membrane potential as an inhibitory current. Hence, the adaptation time constant determines how fast a neuron will recover after each spike in a burst. Therefore, the strongly adapting neuron with a long will require more input current to elicit another spike (Fig. 4.1A and B for stimulation duration >175 ms), and thus after the fourth spike in the
burst, the adaptation current is already high enough to break the bursting cycle. The fast recovering neuron (Fig. 4.1C, short $\tau_q$) continues its burst with more spikes (dark traces at longer durations (B, C)).

![Figure 4.1 Responses of three SC model neurons to different microstimulation parameters.](image)

The three neurons differed in their adaptation time constants (A: $\tau_q = 84.6\text{ ms}$, B: $\tau_q = 70.95\text{ ms}$, and C: $\tau_q = 52.4\text{ ms}$). Each row shows the membrane potentials, $V(t)$, for the same electrical stimulus, at a particular intensity (see color code for the different lines, top), and delivered at a particular stimulus duration, $D_S$. Note the clear differences in neuronal membrane responses. Stimulus timings and durations are indicated above the traces by black lines, ranging from $D_S = 25\text{ ms}$ (bottom) to $D_S = 225\text{ ms}$ (top). Symbols $\times$, $\circ$, and $+$: selected responses, further analyzed in Fig. 4.2.

A phase plot of the instantaneous adaptation current vs. the membrane potential provides a graphical analysis of the effects of changing the neural parameters, the current input, and the initial state, on the evolution of the dynamical
Figure 4.2 Bursting mechanism of the AdEx neuron model. Phase plots of $V(t)$ vs. $q(t)$ of the neural dynamics of the same three neurons of Figure 4.1. Biophysical parameters of the neurons were selected for their bursting responses to a ramp stimulus, with varying current amplitude and durations (traces are marked in Figure 4.1); the order of spike occurrences is denoted next to the traces in the spike initiation zone: A: a burst with 5 spikes (x); B: two burst cycles with 6 and 5 spikes (o); C: a burst cycle with more than 13 spikes (+).

The q-nullcline follows a linear trajectory, whereas the V-nullcline represents a convex function because of the superposition of two V-dependent parts. For $V < V_T$, the exponential term can be omitted and the linear $V$ dependence will have a slope of $g_L$. For $V > V_T$, the exponential term will dominate with a sharp increase as $V$ increases. When a neuron receives input, the V-nullcline shifts upward by as much as the current density, and the response of the neuron follows a trajectory on the phase plane toward the spiking threshold. The blue trajectories show the evolution of the state variables for three neurons with different $\tau_q$ values, and stimulated at different current strengths. The horizontal arrows show the membrane potential in the spike initiation zone, $V > V_T$. Spikes occur when the membrane potential overcomes the spiking threshold, $V > V_{thr}$. After a spike, the membrane potential is reset, and the adaptation current is increased by $b$ (Eqn. 4.7). The spiking threshold, $V_{thr}$, and the reset potential, $V_{rst}$, are
indicated by the vertical dashed lines. With each spike, the adaptive current increases more and once it reaches values above the V-nullcline, the adaptive current is high enough to suppress the neuron from continued bursting, and hyperpolarizes.

In Fig. 4.2A, the phase trajectory crosses values over $V_{null} = 150$ pA after 5 spikes. Due to the hyperpolarization, the membrane potential starts to drop. The phase plot shows that the microstimulation is finished when the membrane potential decreases to $-58$ mV, and the smooth trajectory is seen disrupted. In Fig. 4.2B, there is a second burst cycle since the microstimulation duration is much longer. After the first burst cycle crosses $V_{null} + 200$ pA with 6 spikes (arrows are placed closer to $V_{thr}$), neuron follows the trajectory to the spike initiation zone for a second burst cycle with 5 spikes. The end of the microstimulation coincides with the second burst cycle and afterwards the membrane potential decreases fast due to the high adaptive current acting on the neuron. In Fig. 4.2C, the neuron gets stuck in its first cycle and continues spiking repetitively. This pattern is due to the fast decay of the adaptive current, which drops by more than b after each spike. Therefore, the neuron would continue spiking repetitively, as long as the current is applied.

The neurons in the network were tuned to respond with a fixed number of spikes in a burst cycle (as in Fig. 4.2A). This initial burst sets up a large population activity through the lateral connections. $V_{null}$ fluctuates for each neuron with the network dynamics, depending on the input from other neurons in the population. Microstimulation parameters were chosen such that the central neuron of the population would respond with a burst cycle of 4-5 spikes (typically, $D_S = 100$ ms, and $I_0 = 150$ pA), independent of the biophysical properties of the neuron. To that end, the adaptation time constant, $\tau_{q,n}$, and the synaptic weight-scaling parameter, $s_n$, for each neuron were determined by applying a fifth order polynomial fit to produce a fixed number of spikes ($N=20$) for self-exciting neurons:

$$s_n = (8.808 \cdot 10^{-9} \cdot \tau_{q,n}^5 - 3.280 \cdot 10^{-6} \cdot \tau_{q,n}^4 + 4.855 \cdot 10^{-4} \cdot \tau_{q,n}^3 - 3.607 \cdot 10^{-2} \cdot \tau_{q,n}^2 + 1.383 \cdot \tau_{q,n} - 8.396) \cdot 10^{-3}$$  \hspace{1cm} (4.15)

The self-excitation mimics the population activity, since the central cell’s burst profile is representative for the entire population activity, due to burst synchronization across the active neurons. The adaptive time constant, $\tau_{q,n}$,
varied from 100-30 ms in a linear way with the anatomical rostral-caudal location of the neurons, according to:

\[ \tau_{q,n} = 100 - 14 \times u_n \quad \text{with} \quad u_n \in [0,5] \ \text{mm} \]  

(4.16)

Microstimulation without lateral interactions

The current density drops rapidly with distance from the microelectrode tip, as given by the current spread function (Eqn. 4.9, with \( \lambda = 10 \ \text{mm}^{-1}, D_S = 100 \ \text{ms}, \) and \( I_0 = 150 \ \text{pA} \)). Figure 4.3A illustrates this decay of current density on the motor map surface. The pulsed input current is presented onto the collicular surface at a site corresponding to the visual image point \((u(R), v(\phi))\) in Eqn. 4.5; Fig 4.3B and C). Microstimulation directly activated only a small set of neurons within a 250 \( \mu \text{m} \) radius. Figure 4.3B and C shows the number of spikes elicited by the activated neurons in the absence of intra-collicular lateral interactions. Each activated neuron elicited only 4-6 spikes within a given input duration range, regardless the electrode’s location. These spikes arose from the initial bursting regime of the neurons until the adaptation current built up with repetitive spikes that canceled the microstimulation input (see Fig. 4.2). The input amplitude affected the response delay of the neurons between stimulation onset and their first spike. Thus, in the model these small neuronal subsets generated only a brief pulse signal that is supposed to set up the entire population activity through lateral connections.

Including lateral interactions

We next tested the collicular network response to the same microstimulation parameters as in Fig. 4.3, while including the lateral interactions. Figure 4.4A-C shows the recruited neural population at the rostral stimulation site. Clearly, the number of recruited neurons had increased substantially as a result of the network dynamics. The diameter of the circular population extended to about 1 mm in the motor map. In addition, the cumulative activity elicited by the central cells had now increased from about 5 to 20 spikes. Figure 4.4B shows the neuronal bursts (top spike patterns) from a number of selected cells in the population, together with the associated spike-density functions. The peak firing rate of the central cells was close to 700 spikes/s and dropped in a regular fashion with distance from the population center. Note also that the cells near the fringes of the population were recruited slightly later than the central cells, but that their peak firing rates were reached nearly simultaneously. Moreover,
Figure 4.3 Spatial properties of input current and neural response. (A) Input stimulus of 150 pA (100 ms), is presented to the network around the vicinity of the tip of the electrode. Current amplitude drops exponentially with distance from the tip location at 0 with $\lambda = 10 \text{mm}^{-1}$ in every direction on the collicular map. (B,C) Spike counts of neurons activated by microstimulation, without including lateral connections in the motor map. The gaze-motor map is stimulated at the corresponding locations prescribed by the logarithmic afferent mapping function (B: $R = 5^\circ, \phi = 0^\circ$; C: $R = 31^\circ, \phi = 30^\circ$).

The bursts all appeared to have the same shape. Figure 4.4C shows the saccade that was elicited by this neural population, together with its velocity profile. The saccade had an amplitude of 5 deg, reaching a peak velocity of about 200 deg/s.

Figure 4.4D-F shows the results for stimulation at the more caudal location in the motor map, yielding an oblique saccade with an amplitude of 31 deg. The size of the resulting population activity is very similar to that of the rostral population, and also the number of spikes elicited by the cells is the same. The peak firing rates of the neurons, however, were markedly lower, reaching a maximum of about 450 spikes/s. As a result, the burst durations increased accordingly, from about 50 ms at the rostral site, to more than 70 ms at the caudal site. Note that the saccade reached a much higher peak velocity (about 900 deg/s) than the smaller saccade in Fig. 4.4C, but its duration was prolonged. Note also that the horizontal and vertical velocity profiles were scaled versions, indicating a straight saccade trajectory.

In Fig. 4.5 we quantified the collicular bursts in response to microstimulation at different sites along the rostral-caudal axis in the motor map. Figure 4.5A shows how the evoked collicular bursts of the central cells in the population systematically reduce their peak firing rates, and increase their duration, as the microelectrode moves from rostral ($R = 2$ deg) to caudal sites ($R = 31$ deg). In Fig. 4.5B we show three major relationships for the bursts of the central cells in the population, for saccade amplitudes between 2 and 65 deg: the peak firing
Figure 4.4 Population dynamics in the gaze-motor map and eye kinematics. (A,D) Spike counts from the gaze-motor map represent the recruited population to microstimulation with lateral interactions. Peak firing rates of the cells decrease with distance from the population center. (B,E) Temporal burst profiles of the recruited neurons (taken at 0.1 mm intervals from the central neuron) portray synchronized population activity, here shown along the rostral-caudal direction in the map. Burst durations increase, but the total number of spikes from the population remains the same. (C,F) Emerging eye displacements and eye velocity profiles, generated by the linear dynamic ensemble-coding model (Eqns. 4.2b and 4.3). Horizontal (green), vertical (yellow), and vectorial (purple) eye-displacement traces.

rate (green) drops from about 750 spikes/s to 300 spikes/s, burst duration (purple) increases from about 40 ms to 125 ms, whereas the number of spikes in the burst (light green) remains constant at \( N = 20 \) spikes. These burst properties, which are due to a precise tuning of the biophysical cell parameters, underlie the kinematic main-sequence properties of saccadic eye movements Goossens and Van Opstal, 2012; Kasap and Opstal, 2017; Van Opstal and Goossens, 2008.

Properties of electrically evoked eye movements

Figure 4.6A shows the amplitudes and directions of 45 elicited saccades across the 2D oculomotor range (stimulation parameters: \( I_0 = 120 \) pA, \( D_s = 100 \) ms). We avoided stimulating near the vertical meridian, as our model included only
Figure 4.5 Central cell firing properties. (A) Spike trains and burst profiles for the central neurons of different populations (electrode tip positioned at $R = 2, 7, 11, 15, 21$ and $31$ deg). (B) Peak firing rates (dark green), number of spikes from the central cells (light green), and the durations of the central cell bursts (purple) for different neural populations between $R = 2$ and $65$ deg. Note that the number of spikes for the central cell is constant at about 20 spikes throughout the motor map, while the peak firing rate at caudal sites drops to barely 50% of the rostral stimulation site. Note also that the durations of the central cell bursts increase monotonically with the movement amplitude.

the left SC motor map (e.g., Van Opstal, Van Gisbergen, and Smit, 1990), and stimulation at very caudal sites ($R > 40$ deg), where edge effects of the finite motor map would lead to truncation of the elicited population at the caudal end. Crosses indicate the coordinates of the corresponding motor map locations where stimulation took place; blue dots give the coordinates of the evoked saccade vectors. There is a close correspondence between the motor map coordinates and the elicited saccade vectors. Only for the most caudal sites the saccade vectors tended to show a slight undershoot. We have not attempted to compensate for these minor effects, e.g. by including heuristic changes to the efferent mapping function. The panels of Fig. 4.6B,C show the evoked saccades for the nine stimulation sites along the horizontal meridian. Note that the saccade duration increased with the saccade amplitude, and that the peak eye velocity showed a less than linear increase with saccade size.

Figure 4.7 presents three examples of saccade position and velocity traces for stimulation at sites encoding three different directions, but with a fixed amplitude of $R = 21$ deg. The elicited track-velocity profiles are direction-independent. Panels 4.7B and C also indicate the behavior of the horizontal and vertical saccade components. As these are precisely synchronized with the saccade vector, the ensuing saccade trajectories are straight (not shown).
Figure 4.6 Saccade endpoints, eye displacement and eye velocity. (A) Saccade endpoints for stimulation at different sites in the motor map. The scaling parameter of the SC motor map was tuned for a 21 deg horizontal saccade (red circle). (B) Eye displacement traces for horizontal saccades (ϕ = 0 deg) [movement amplitudes are highlighted by the thin horizontal lines]. (C) Saccadic eye velocity profiles for the corresponding position traces in B. Note the clear increase in saccade duration, and the associated saturation of peak eye velocity as function of saccade amplitude.

Figure 4.7 Eye-displacement traces and saccadic eye velocity profiles for three directions (ϕ = 0, 30, 60 deg) (A, B, C) with the same amplitude of R = 21 deg. (purple: total vectorial displacement/velocity, green: horizontal, yellow: vertical saccade component).

The main-sequence behavior of the model’s E-saccades is quantified in Fig. 4.8. Figure 4.8A shows the nonlinear amplitude vs. peak eye-velocity relationship, described by the following saturating exponential function:

\[
    v_{\text{peak}} = 1172 \cdot (1 - \exp(-0.04 \cdot R)) \text{ deg/s}
\]  

(4.17)
From Fig. 4.8B, the straight-line amplitude-duration relation was approximated to

$$D_{\text{sacc}} = 28.7 + 1.1 \cdot R \text{ ms}$$

(4.18)

These main-sequence relations were combined into a single, characteristic linear relationship that captures all saccades, normal and slow (Fig. 4.8C) by:

$$v_{\text{peak}} \cdot D_{\text{sacc}} = 1.72 \cdot R \deg$$

(4.19)

All three relations correspond well to the normal main-sequence properties, as have been reported for monkey and human saccades (e.g., Van Opstal and Van Gisbergen, 1987).

Figure 4.8 Nonlinear main-sequence behavior of the model. Shown for stimulation at 16 sites along the horizontal meridian of the motor map. (A) Saturating amplitude-peak eye velocity relation. (B) A straight-line increase of saccade duration with amplitude. (C) Saccade amplitude and the product of peak eye velocity and saccade duration, $V_{\text{pk}} \cdot D$, are linearly related with slope, $k = 1.7$.

Importantly, the main-sequence behavior of E-saccades was largely insensitive to the applied current strength as soon as it exceeded the stimulation threshold. This feature of the model is illustrated in Fig. 4.9, which shows E-saccade peak eye-velocity as function of current strength for a fixed stimulation duration of $D_S = 100 \text{ ms}$ (Fig. 4.9A). The stimulation was applied at three different sites on the horizontal meridian (corresponding to $R = 15$, 21 and 31 deg). Below $I_0 = 80 \text{ pA}$ no movement was elicited, but around the threshold, between 90-120 pA, stimulation evoked slow eye movements, which eventually yielded the final amplitude (Fig. 4.9B). Immediately above the threshold at 130-140 pA, the evoked movement amplitudes and velocities reached their final, site-specific size (Fig. 4.9A,B), which did not change with current strength over the full range between 140-220 pA. The associated peak eye velocity followed a similar
current-dependent behavior for changes in stimulus duration (at a fixed current strength of 150 pA; Fig. 4.9C). Thus, the quantity that determines evoked saccade initiation is the total amount of current (current amplitude times duration; e.g., Katnani and Gandhi, 2012).

Figure 4.9 Effect of stimulation parameters. (A) Peak eye velocity as function of current strength for stimulation at a site corresponding to R =15 (light), 21 (medium) and 31 (dark) deg, for 100 ms stimulation duration. Beyond the threshold at 140 pA, the evoked eye velocity is virtually independent of the stimulation current. (B) Total eye displacement as function of microstimulation strength for stimulation at a site corresponding to R =15 (light), 21 (medium) and 31 (dark) deg for 100 ms stimulation duration. Beyond the threshold at 90 pA, the total eye displacement is independent of the stimulation current. (C) Peak eye velocity as a function of microstimulation duration from the same locations at a fixed stimulation strength of 150 pA.
4.4 Discussion

Summary. The simple linear ensemble-coding model of Eqn. 4.2b Goossens and Van Opstal, 2006; Van Gisbergen, Van Opstal, and Tax, 1987; Van Opstal and Goossens, 2008 seems inconsistent with the results of microstimulation, when it is assumed that (i) the rectangular stimulation input profile directly dictates the firing patterns of the neural population in the motor map, and (ii) that the neurons are independent, without synaptic interactions.

We here argued that these assumptions are neither supported by experimental observation, nor do they incorporate the possibility that a major factor determining the recruitment of SC neurons is caused by synaptic transmission within the motor map, rather than by direct activation through the electrode’s electric field. We implemented circular-symmetric, Mexican-hat like interactions in a spiking neural network model of the SC motor map and assumed that the current profile from the electrode rapidly decreased with distance from the electrode tip (Fig. 4.3A). As a consequence, only neurons in the direct vicinity of the electrode were activated by the external electric field (Fig. 4.3B,C; Histed, Bonin, et al., 2009; Histed, Ni, et al., 2013).

Once neurons were recruited by the stimulation pulse, however, local excitatory synaptic transmission among nearby cells rapidly spread the activation to create a neural activity pattern which, within 10-15 ms, was dictated by the bursting dynamics of the most active central cells in the population (Fig. 4.4). As a result, all cells yielded their peak firing rates at the same time, and the burst shapes of the cells within the population were highly correlated. Similar response features have been reported for natural, sensory-evoked saccadic eye movements Goossens and Van Opstal, 2012, and it was argued this high level of neuronal synchronization ensures an optimally strong input to the brain-stem saccadic burst generator to accelerate the eye with the maximally possible innervation.

Note that the evoked population activity does not grow without limit, but ceases automatically, both in its spatial extent, and in its bursting behavior, while the inhibitory currents acting on the neurons accumulate during the stimulation pulse. These currents are due to the synaptic far-range lateral inhibition, and to each neuron’s own adaptive current. Thus, once the network is perturbed by an excitatory input current, the SC will set up a bursting population activity, without the need of an external comparator, or external feedback by a resettable integrator. Indeed, the adaptive current functionally acts as a putative “spike counter” at the single neuron level. With this spiking neural network model, we thus offer an alternative framework for the oculomotor system, in
which the SC motor map not only provides a spatial signal for the saccade vector, but also the instantaneous eye-movement kinematics, through the temporal organization of its burst profiles.

**Network tuning.** The site-dependent tuning of the biophysical parameters of the AdEx neurons, in particular their adaptive time constants and lateral-interaction weightings specified by Eqns. 4.15-4.16, caused the peak firing rates of the cells to drop systematically along the rostral-to-caudal axis, while keeping the total number of spikes constant (Fig. 4.5). As a result, the saccade kinematics followed the nonlinear main-sequence properties that are observed for normal (visually-evoked) saccadic eye movements (Figs. 6-8). In addition, the long-range weak inhibition ensured that the size of the population remained fixed to about 1.0 mm in diameter, and resulted to be largely independent of the applied current strength and the current-pulse duration (Fig. 4.9).

The lateral excitatory-inhibitory synaptic interactions ensured three important aspects of collicular firing patterns that underlie the saccade trajectories and their kinematics: (i) they set up a large, but limited, population of cells in which the total activity (quantified by the number of spikes elicited by the recruited cells) can be described by a circular-symmetric Gaussian with a width (standard deviation) of approximately 0.5 mm (Fig. 4.4A,D), (ii) the temporal firing patterns of the central cells (their peak firing rate, burst shape, and burst duration) solely depend on the location in the motor map (Eqn. 4.14), but the number of evoked spikes remains invariant across the map, and for a wide range of electrical stimulation parameters (Fig. 4.5), and (iii) already within the first couple of spikes, the recruited neurons all became synchronized throughout the population, in which the most active cells (those in the center) determined the spike-density profiles of all the others (Fig. 4.4B,E).

Here we described the consequences of this model on the ensuing kinematics and metrics of E-saccades as function of the electrical stimulation parameters. We showed that the network could be tuned such that stimulation at an intensity of 150 pA and a total input current duration of $D_S = 100$ ms, sets up a large population of activated neurons, in which the firing rates resembled the activity patterns as measured under natural visual stimulation conditions. As a result, the kinematics of the evoked saccades faithfully followed the nonlinear main-sequence relations of normal, visually evoked saccades (Fig. 4.8). Importantly, above threshold the saccade properties were unaffected by the electrical stimulation parameters (Fig. 4.9).

**Network normalization.** Only close to the stimulation threshold, the evoked activity remained much lower than for supra-threshold stimulation currents, leading to excessively slow eye movements, that started at a longer latency
with respect to stimulation onset. Similar results have been demonstrated in microstimulation experiments (e.g. Katnani and Gandhi, 2012; Van Opstal, Van Gisbergen, and Smit, 1990). The saccade peak eye velocity of the model saccades followed a psychometric curve as function of the amount of applied current (Fig. 4.9). We found that the kinematics of the evoked eye movements at near-threshold microstimulation were much slower than main sequence (Fig. 4.9). Although this property is readily predicted by the linear summation model (Eqn. 4.2b), it does not follow from center-of-gravity computational schemes (like Eqn. 4.2a), in which the activity patterns themselves are immaterial for the evoked saccade kinematics.

Conceptually, the lateral interactions serve to normalize the population activity. Therefore, the total number of spikes emanating from the SC population remains invariant across the motor map, and to a large range of (sensory or electrical) stimulation parameters at any given site. The nonlinear saturation criterion of Eqn. 4.4 is thus automatically implemented through the intrinsic organization of the SC network dynamics, and do not seem to require an additional downstream spike-counting mechanism in order to terminate the saccade response, e.g. during synchronous double stimulation at different collicular sites (see, e.g. Van Opstal and Van Gisbergen, 1989).

Although other network architectures, relying e.g. on presynaptic inhibition across the dendritic tree, have been proposed to accomplish normalization of the population activity and vector averaging Carandini and Heeger, 1994; Groh, 2001; Opstal and Gisbergen, 1989; Van Opstal and Goossens, 2008; Van Opstal and Van Gisbergen, 1989, substantial anatomical evidence in the oculomotor system to support such nonlinear mechanisms is lacking. We here showed, however, that simple linear summation of the effective synaptic inputs at the cell’s membrane, which is a well-recognized physiological mechanism of basic neuronal functioning, can implement the normalization when it is combined with excitatory-inhibitory communication among the neurons within the same, topographically organized structure. Such a simple mechanism could suffice to ensure (nearly) invariant gaze-motor commands across a wide range of competing neuronal inputs.

**Further supporting evidence.** Our model predicts near-normal activity profiles within the SC during microstimulation (Figs. 4.4- 4.6), and hence near-normal recruitment of the downstream brainstem circuits. Although simultaneous recordings in the SC during microstimulation are lacking, Paul and Gnadt, 2006 described recordings from neural populations in the downstream brainstem burst generators (EBNs) and omnipause neurons (OPNs) during SC microstimulation. Their results indicated normal discharge patterns for OPNs and
EBNs, and indistinguishable movement kinematics for stimulation-evoked and volitional saccades Gnad et al., 2001. These results are nicely in line with the predictions or our model (Figs. 4.8 and 4.9), at least for suprathreshold stimulation levels Stanford et al., 1996.

Future work. The two-dimensional extension of our model is a substantial improvement over our earlier one-dimensional spiking neural network model Kasap and Opstal, 2017. It can account for a much wider variety of neurophysiological phenomena. Yet, we have not attempted to mimic every experimental result of microstimulation. A few aspects in our model have not been incorporated yet, or some of its results seem to deviate slightly from experimental observations, which we briefly summarize here.

First, although the network output is invariant across a wide variety of stimulation parameters, and evoked saccade kinematics drop markedly around the threshold (Fig. 4.9), the present model did not produce small-amplitude, slow movements near the stimulation threshold. This behavior has sometimes been observed for near-threshold stimulation intensities Katnani and Gandhi, 2012; Van Opstal, Van Gisbergen, and Smit, 1990. In our model, the saccade amplitude behaved as an all-or-nothing phenomenon (Fig. 4.9B), which is caused by the strong intrinsic mechanisms that keep the number of spikes of the central cells fixed. Although we have not tested different parameter sets at length, we conjecture that a major factor that is lacking in the current model is the presence of intrinsic noise in the parameters and neuronal dynamics that would allow some variability of the evoked responses for small inputs. When near the threshold the elicited number of spikes starts to fluctuate, and becomes less than the cell’s maximum, the evoked saccades will become smaller (and slower) too. Such near-threshold responses would also explain the truncated saccades generated when stimulation train durations are shortened Stanford et al., 1996.

Second, although the main-sequence relations of the model’s E-saccades (Eqns. 4.17 and 4.19) faithfully capture the major kinematic properties of normal eye movements, the shape of the evoked saccade velocity profiles were not as skewed as seen for visually-evoked saccades. As a result, the peak velocity is not reached at a fixed acceleration period, but at a moment that slightly increased with the evoked saccade amplitude (Fig. 4.6C). We have not attempted to remediate this slight discrepancy, which in part depends on the applied spike-density kernels (here: Gaussian, with width $\sigma = 8$ ms, Eqn. 4.3), and in part on the biophysical tuning parameters of the AdEx neurons. However, it should also be noted that a detailed quantification of E-saccade velocity profiles, beyond the regular main-sequence parametrizations Katnani and Gandhi, 2012; Van Opstal, Van Gisbergen, and Smit, 1990, is not available in the published
literature. It is therefore not known to what extent E-saccade velocity profiles and V-saccade velocity profiles are really the same or might slightly differ in particular details.

Third, as explained in Methods, the electrical stimulation inputs were described by simple rectangular pulses, rather than by a train of short-duration stimulation spikes, in which case also the pulse intervals, pulse durations, pulse heights, and the stimulation frequency would all play a role in the evoked E-saccades Katnani and Gandhi, 2012; Stanford et al., 1996. We deemed exploring the potential results corresponding to these different current patterns as falling beyond the scope of this study, which merely concentrated on the proof-of-principle that large changes in the input for the proposed architecture of a spiking neural network led to largely invariant results. Note, however, that in our previous paper Kasap and Opstal, 2017 the presumed input from FEF cells to the SC motor map did indeed provide individual spike trains to affect the SC-cells. We there demonstrated that the optimal network parameters could be found with the same genetic algorithm for such spiky input patterns, as applied here (Eqn. 4.13). The small differences in neuronal tuning parameters for the 1D model with FEF input, compared to the 2D model tuned to electrical pulse input, are mostly due to these fundamentally different input dynamics.

Fourth, Hafed and Chen, 2016 recently reported an asymmetric, anisotropic representation in the afferent mapping for the upper vs. lower visual hemifields, that would explain kinematic differences between upward vs. downward saccades. The underlying mechanism for this anisotropy is not yet clear. For example, it could result from (i) differences in lateral interaction strengths for up vs. down, thus creating different population profiles in the SC; (ii) differences in cell density along the medial-lateral SC coordinate, or (iii) systematic differences in the efferent projection strengths from medial-lateral SC neurons to the up- and down burst generators. In principle, our model could accommodate an anisotropic organization for upward vs. downward saccades by incorporating parametric changes at any of these levels. Here, we focused on a simple scheme, in which the SC was taken fully isotropic (Eqns. 4.5 and 4.6), and the horizontal/vertical burst-generating circuits in the brainstem, including the horizontal/vertical ocular plants, were taken identical Goossens and Van Opstal, 2006. This ensured perfectly straight saccade trajectories in all directions, with homogeneous main-sequence properties, due to a full cross-coupling between the horizontal and vertical movement components (component stretching; see Fig. 4.7).

Any change in this organization (e.g. more realistic eye-position related differences in the oculomotor plants, or different gains and delays in the up- vs.
down vs. horizontal burst generators) will cause saccade trajectories to become curved, and direction and eye-position dependent, and may be made to resemble more closely the idiosyncratic differences observed in measured oblique saccades (e.g. Smit et al., 1990). Although an interesting topic, working out these many different factors, however, falls beyond the scope of this paper.

Fifth, double-stimulation experiments at different sites within the SC motor map have shown that the resulting saccade vector appears a weighted average between the saccades evoked at the individual sites Katnani, Van Opstal, et al., 2012; Robinson, 1972. In the present paper, we have not implemented double stimulation, although an earlier study had indicated that Mexican-hat connectivity profiles in the motor map effectively embed the necessary competition between sites to result in effective weighted averaging Van Opstal and Van Gisbergen, 1989. In a follow-up study, we recently explored the spatial-temporal dynamics of our model to double stimulation at different sites, and at different stimulus strengths Kasap and Opstal, 2018a. Indeed, double stimulation results in weighted-averaged saccade responses, even when the SC activity is decoded by a dynamic linear-ensemble coding scheme, and without the need to implement an explicit cut-off on the total spike count, like in Eqn. 4.4. Thus, our SC scheme with excitatory-inhibitory interactions results to automatically normalize the total activity within the SC motor map (see also above). Hence, double stimulation results do not support the vector averaging scheme per se, as they can be explained by linear summation, in combination with intracollicular interactions, as well. See, however Chapter 5, where we deal with this topic.

Finally, close inspection of the burst profiles in Fig. 4.1 (showing stimulation results for single, isolated neurons) suggests that prolonged stimulation at sufficient current intensities could in principle generate multiple bursts of activity in the SC cells. For example, the top-left trace (I_0 = 250 pA, D_5 = 225 ms) shows a burst of 6 spikes, followed by a second burst of 5 spikes about 150 ms later. In principle, each of these bursts could be part of its own saccade, provided that the total network dynamics (including the lateral interactions) would preserve these properties. Indeed, the literature has shown that prolonged stimulation can lead to a series of eye movements of decreasing amplitude in the same direction (a so-called staircase of saccades; Gnadt et al., 2001; Paul and Gnadt, 2006; Robinson, 1972). Here we haven’t tested our network for its potential to generate staircases, as we limited the stimulation durations to 250 ms. We suspect that the inhibitory currents and neural recovery may have to be balanced better to allow the prolonged input current to overcome the dynamic inhibition.
Yet, although our network was not a priori designed for these staircases, their occurrence would be an interesting emerging property of the model.


DOUBLE STIMULATION IN A SPIKING NEURAL NETWORK MODEL OF THE MIDBRAIN SUPERIOR COLLICULUS

Abstract

The midbrain superior colliculus (SC) is a crucial sensorimotor interface in the generation of rapid saccadic gaze shifts. For every saccade it recruits a large population of cells in its vectorial motor map. Supra-threshold electrical microstimulation in the SC reveals that the stimulated site produces the saccade vector specified by the motor map. Electrically evoked saccades (E-saccades) have kinematic properties that strongly resemble natural, visual-evoked saccades (V-saccades), with little influence of the stimulation parameters. Moreover, synchronous stimulation at two sites yields eye movements that resemble a weighted vector average of the individual stimulation effects. Single-unit recordings have indicated that the SC population acts as a vectorial pulse generator by specifying the instantaneous gaze-kinematics through dynamic summation of the movement effects of all SC spike trains. But how to reconcile the a-specific stimulation pulses with these intricate saccade properties? We recently developed a spiking neural network model of the SC, in which microstimulation activates a relatively small set of neurons around the electrode tip, which subsequently sets up a large population response through lateral synaptic interactions. Single-site microstimulation in this network thus produces the saccade properties and firing-rate profiles as seen in experiments. We here show that this mechanism also accounts for many results of simultaneous double stimulation at different SC sites. The resulting E-saccade trajectories resemble a weighted average of the single-site effects, in which stimulus current strength of the electrode pulses serve as weighting factors. We discuss under which conditions the network produces effects that deviate from experimental results.


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5.1 Introduction

Superior Colliculus. Because high spatial resolution is limited to the central fovea, the primate visual system needs to explore the environment through rapid and precise saccadic eye movements. Normal (human and monkey) saccades display stereotyped ‘main sequence’ characteristics, described by linear amplitude-duration and nonlinear, saturating, amplitude-peak eye velocity relationships (Bahill et al., 1975). In addition, the horizontal and vertical velocity profiles of oblique saccades are tightly coupled, such that they are scaled versions of each other throughout the saccade, and saccade trajectories are approximately straight in all directions (Van Gisbergen, Van Opstal, and Schoenmakers, 1985). These properties imply that the saccadic system contains a nonlinear control stage (Smit et al., 1990; Van Gisbergen, Van Opstal, and Schoenmakers, 1985; Van Gisbergen, Robinson, et al., 1981). Recent hypotheses have suggested that the saccade nonlinearity reflects a speed-accuracy trade-off, which optimally deals with spatial uncertainty in the retinal periphery and internal noise in sensorimotor pathways (Goossens and Van Opstal, 2012; Harris and Wolpert, 1998; Tanaka et al., 2006; Van Beers, 2008).

The neural circuitry underlying saccade planning, selection, and execution extends from the cerebral cortex to the cerebellum, and the pons in the brainstem. The midbrain superior colliculus (SC) is the final common terminal for all cortical and subcortical outputs, and it is known to specify the vectorial eye-displacement command for the brainstem oculomotor circuitry (Moschovakis et al., 1998; Robinson, 1972; Scudder, 1988). The SC contains an eye-centered topographic map of visuomotor space, in which the saccade amplitude is mapped logarithmically along the rostral-caudal axis (u, in mm) and saccade direction roughly linearly along the medial-lateral direction (v, in mm; Robinson, 1972). The afferent map (Eqn. 5.1a) and its efferent inverse (Eqn. 5.1b) are well-described by (Ottes et al., 1986):

\[
\begin{align*}
    u &= B_u \ln \left( \frac{\sqrt{(x+A)^2+y^2}}{A} \right) \\
    v &= B_v \tan^{-1} \left( \frac{y}{x+A} \right)
\end{align*}
\]

\[
\begin{align*}
    x &= A \cdot \left( \exp \frac{u}{B_u} \cos \frac{v}{B_v} - 1 \right) \\
    y &= A \cdot \exp \frac{u}{B_u} \sin \frac{v}{B_v}
\end{align*}
\]

with typical parameter values for the monkey SC given as \( B_u \approx 1.4 \text{ mm}, B_v \approx 1.8 \text{ mm/rad}, \) and \( A \approx 3 \text{ deg}. \) Each saccade is associated with a translation-invariant Gaussian-shaped population within this map, the center of which corresponds (through Eqn. 5.1a) to the saccade vector, \((x_0, y_0)\), and a width \( \sigma_{\text{pop}} \approx 0.5 \text{ mm} \) (Ottes et al., 1986; Van Gisbergen, Van Opstal, and Tax, 1987; Van Opstal, Van
Thus, the activity of neuron \( n \) in the motor map is described by:

\[
F_n(u_n, v_n) = F_{\text{max}} \cdot e^{-\frac{1}{2} \left( \frac{|u_0 - u_n|^2 + |v_0 - v_n|^2}{\sigma_{\text{pop}}} \right)}
\]  

(5.2)

with \( F_{\text{max}} \) the peak activity of the population, quantified by the number of spikes in the saccade-related burst (e.g., Fig. 5.2A). It is generally assumed that each recruited neuron, \( n \), in the population encodes a vectorial movement contribution to the saccade vector, which is determined by both its anatomical location within the motor map, \((u_n, v_n)\), and its activity, \( F_n \) (Goossens and Van Opstal, 2006; Groh, 2001; Lee et al., 1988; McIlwain, 1982; Moschovakis et al., 1998; Ottes et al., 1986; Van Gisbergen, Van Opstal, and Schoenmakers, 1985).

However, the precise mechanism by which the cells contribute to the saccade is still elusive. A major hypothesis in the literature holds that the output of the population is determined by a nonlinear center-of-gravity computation (Lee et al., 1988; Port and Wurtz, 2003; Quaia et al., 1999; Walton et al., 2005). According to this idea, the activity in the SC motor map only specifies the saccade metrics (amplitude and direction of the saccade vector) and is unrelated to the saccade kinematics. Yet, our single-unit recordings have demonstrated a strong (presumably causal) relationship between the instantaneous firing patterns in the SC and associated saccade trajectories (Goossens and Van Opstal, 2006; Goossens and Opstal, 2012).

We therefore proposed and tested an extremely simple linear summation model for the recruited population that explains the encoding of spatial-temporal properties of saccade trajectories through the firing properties of SC burst cells (Goossens and Van Opstal, 2006; Goossens and Opstal, 2012). According to this model, the saccade, \( S(t) \), is generated in the following way:

\[
S(t) = \sum_{n=1}^{N} \sum_{K_n < t} \delta(t - \tau_{n,k}) \cdot m_n
\]  

(5.3)

with \( N \) the number of active cells in the population, \( K_n < t \) the number of spikes in the burst of neuron \( n \) up to time \( t \), and \( m_n = \zeta \cdot (x_{n}, y_{n}) \) the tiny site-specific spike vector emanating from the motor map for each spike from each cell. This spike vector is solely determined by the efferent mapping of SC site \((u_n, v_n)\) (Eqn. 5.1b), where \( \zeta \) is a fixed, small scaling constant determined by the cell density in the map and the population size, and \( \delta(t - \tau_{k,n}) \) is the \( k \)’th spike fired by neuron \( n \) at time \( \tau_{k,n} \).
This entirely linear dynamic model accounts for the full nonlinear kinematics of saccades at the level of the SC motor map (Goossens and Van Opstal, 2006; Goossens and Opstal, 2012). As a result, the instantaneous firing rates of the neurons together encode the saccadic velocity profile (Van Opstal and Goossens, 2008).

Recently, we implemented a simple spiking neural network model for the SC that can generate realistic saccades to visual targets (Kasap and Opstal, 2017). This minimalistic (one-dimensional) model with lateral excitatory-inhibitory interactions among the SC cells accounts for most of the experimentally observed firing properties of saccade-related neurons in the motor map (Goossens and Van Opstal, 2006; Goossens and Opstal, 2012), and yields saccades with normal main-sequence properties. The model takes a fixed Gaussian input from upstream sources (e.g., the cortical frontal eye fields, or FEF), and assumes precisely-tuned biophysical properties of the SC network neurons, and their interconnections.

**Microstimulation.** Electrical stimulation at a particular site in the motor map produces a saccadic gaze shift with metrics that correspond well to the efferent mapping function (Eqn. 5.1b), and with normal main-sequence kinematics (Kattanani and Gandhi, 2012; Robinson, 1972; Stanford et al., 1996; Van Opstal, Van Gisbergen, and Smit, 1990). These studies have also shown that the properties of electrically evoked (E-)saccades are largely invariant to a wide range of stimulation parameters, which might appear problematic for the linear ensemble-coding model of Eqn. 5.3.

Note that two factors contribute to the neural responses to electrical microstimulation: (1) direct (feedforward) current activation of cell bodies and axons by the electric field of the electrode, and (2) synaptic activation through lateral (feedback) interactions among the neurons in the motor map (Kasap and Van Opstal, 2019).

We recently argued that as current strength falls off rapidly with distance from the electrode tip, only a small number of SC neurons will be directly stimulated by the electrode’s electric field (e.g., Histed et al., 2016). Thus, the major factor determining the microstimulation effects would be synaptic transmission. Indeed, several studies have suggested the existence of a functional organization of lateral excitatory-inhibitory interactions within the SC (anatomy: Behan and Kime, 1996; Olivier et al., 1998; electrophysiology: Munoz and Istvan, 1998; Phongphanphanee, Mizuno, et al., 2011; Phongphanphanee, Marino, et al., 2014, and pharmacology: Meredith and Ramoa, 1998).

We thus extended our spiking model to account for single-site microstimulation results over a wide range of stimulation parameters Kasap and Van Op-
The network was tuned such that, above a threshold, the E-saccades were insensitive to changes in the stimulation parameters. This result supports the idea that the excitatory-inhibitory interactions effectively normalize the total SC output. Under microstimulation, the network thus creates a population that is virtually identical to the one elicited by a visual stimulus. It may be expected that such intrinsic normalization could ensure a behavior that resembles (nonlinear) weighted-averaging without the need for a nonlinear, activation-dependent weighting scheme that is implemented downstream from the motor map.

**Double stimulation.** In this paper, we further explore the predictions of our model for synchronous and asynchronous electrical stimulation at two different sites. Robinson, 1972 and Nota and Gnadt (2009) demonstrated that double stimulation in the SC produced eye movements that resemble the weighted average of the individual stimulation effects, with the stimulation current strengths and relative timings acting as weighting factors. Similar weighting effects occur when an electrical stimulus is combined with a behaviorally relevant visual stimulus (Katnani, Van Opstal, et al., 2012). Results such as these have prompted computational modelers to propose a downstream vector-averaging mechanism that acts on the SC output by explicitly calculating the center of gravity of the population (see above; Groh, 2001; Lee et al., 1988; Port and Wurtz, 2003; Quaia et al., 1999; Walton et al., 2005; review in Gandhi and Katnani, 2011). The neural mechanism that would implement such a neural computation, however, remains unspecified.

Figure 5.1 illustrates two extreme outcomes for mechanisms that would both calculate the center of gravity (CoG) of the effects of the total activity: averaging at the level of the motor map (Eqn. 5.5 a), vs. averaging at the level of the brainstem (Eqn. 5.5 b), i.e.:

\[
\hat{S}_{SC\text{ CoG}} = \frac{\sum_{n=1}^{N_{pop}} F_n \cdot \hat{w}_n}{\sum_{n=1}^{N_{pop}} F_n} \quad \text{with} \quad \hat{w}_n = (u_n, v_n) \quad \text{vs.} \quad (5.4)
\]

\[
\hat{S}_{\text{DOWN CoG}} = \frac{\sum_{n=1}^{N_{pop}} F_n \cdot \hat{m}_n}{\sum_{n=1}^{N_{pop}} F_n} \quad \text{with} \quad \hat{m}_n = (x_n, y_n) \quad (5.5)
\]

Note that in the former case (Fig. 5.1A), the resulting saccade is horizontal with a constant amplitude of 20 deg, regardless the direction of the single-site responses. In the case of Eqn. 5.5b, however, response amplitude varies with the angle, \( \phi \), of the single-site stimulation response as \( R_{\text{COG}} = R_{\text{SITE}} \cdot \cos(\phi_{\text{SITE}}) \) (Fig. 5.1B).
Figure 5.1 Geometrical consequences of center-of-gravity averaging at the SC level vs. downstream from the motor map. (A) Hypothetical double-stimulation effects for two sites at eccentricity $R=20$ deg, placed symmetrically around the horizontal meridian at $\phi=0$ deg, with angular separation of 60, 100, and 160 deg, respectively. Weighted averaging within the map (Eqn. 5.5a) would effectively lead to a horizontal movement corresponding to $(R, \phi) = (20, 0)$ deg for all three situations (black dot). (B) If this process occurs downstream from the motor map, the averaged movement (Eqn. 5.5b) would be horizontal, but with an amplitude that systematically depends on the separation angle (colored dots; black dot: result of (A)). (C) Predictions for the two different center-of-gravity mechanisms.

In an earlier modeling study we had shown that lateral excitatory/inhibitory synaptic interactions within the SC motor map, in combination with the linear ensemble-coding scheme of Van Gisbergen, Van Opstal, and Tax, 1987, could account for saccade-averaging effects to (synchronous) double stimulation (Opstal and Gisbergen, 1989; Van Opstal and Van Gisbergen, 1989). However, the model’s output of that study only focused on the saccade-vector endpoints, as it was not equipped to generate saccade trajectories and their kinematics.

Here we employ the dynamic ensemble-coding scheme of Eqn. 5.3 to our spiking collicular network to simulate two-dimensional saccade trajectories under a variety of electrical double-stimulation conditions. We show that linear dynamic ensemble-coding with lateral excitatory-inhibitory interactions in the motor map can account for most of the experimental vector-averaging results to double stimulation (Katnani, Van Opstal, et al., 2012; Port and Wurtz, 2003; Robinson, 1972), without the need for additional computational nonlinearities, such as a downstream population center-of-gravity computation (Port
and Wurtz, 2003; Walton et al., 2005), or a spike-counting cut-off threshold (Goossens and Van Opstal, 2006; Van Opstal, 2016). The results of our model simulations suggest several interesting limiting cases to the averaging behavior, which, to our knowledge, have so far not been investigated in experimental studies. We also discuss to what extent the model’s responses deviate from experimental findings, and suggest some further refinements to the model.
5.2 Methods

The log-polar mapping

Without loss of generality, we simplified the afferent motor map of Eqn. 1a to the isotropic complex logarithmic function, by setting \( B_u = B_v = 1 \), and \( A = 0 \):

\[
\begin{align*}
    u(R) &= \ln(R) \quad \text{and} \quad v(\phi) = \phi \\
    \text{with} \quad R &= \sqrt{x^2 + y^2} \quad \text{and} \quad \phi = \arctan\left(\frac{y}{x}\right)
\end{align*}
\]

(5.6)

Thus, a single spike’s movement contribution to the saccade from a cell at site \((u,v)\) is determined by the simplified efferent mapping relations:

\[
\begin{align*}
    m_x(u,v) &= \zeta \exp(u) \cos(v) \\
    m_y(u,v) &= \zeta \exp(u) \sin(v)
\end{align*}
\]

(5.7)

We modeled the spiking neural network by a rectangular grid of 201 x 201 neurons, representing the gaze motor-map of the right hemifield with \( 0 < u < 5 \) mm (i.e., up to \( R = 148 \) deg), and \( \pi/2 < v < \pi/2 \) mm. Under single-site stimulation, the center location of the recruited population determines the direction and amplitude of the saccade, whereas the temporal activity profile encodes the eye-movement kinematics through Eqn. 3. As described in our previous studies (Kasap and Van Opstal, 2019; Kasap and Opstal, 2017), and briefly summarized below (Eqns. 5.19 and 5.20), the eye-movement main-sequence kinematics result from the location-dependent biophysical properties of the neurons, and their lateral excitatory-inhibitory connectivity profiles.

The AdEx neuron model

We studied the dynamics of the network through simulations developed in C++/CUDA (Nickolls et al., 2008), by custom code that implemented dynamic parallelism on a GPU (Kasap and Opstal, 2018b), developed and tested on a Tesla K40 with CUDA Toolkit 7.0, Linux Ubuntu 16.04 LTS. Simulations ran with a time resolution of 0.01 ms. Brute-force search and genetic algorithms were used for parameter identification and network tuning since there exists no analytical solutions for the system (Kasap and Van Opstal, 2019; Kasap and Opstal, 2017). Sample simulation and analysis code can be found under https://bitbucket.org/bkasap/sc_doublestimulation/.

Neurons were described by the adaptive exponential integrate-and-fire (AdEx) model (Brette and Gerstner, 2005; Touboul and Brette, 2008), which is a conductance-based model with an exponential membrane potential dependence. The nonlin-
ear temporal dynamics of neuron $n$ are described by two coupled differential equations that determine the two state variables: the cell’s membrane potential, $V$, and the adaptation current, $q$:

\[
C \frac{dV_n}{dt} = -g_L(V_n - E_L) + g_L \eta \exp \left( \frac{V_n - V_T}{\eta} \right) - q_n + I_{\text{in},n}(t) \quad (5.8)
\]

\[
\tau_{q,n} \frac{dq_n}{dt} = a(V_n - E_L) - q_n \quad (5.9)
\]

$C$ is the membrane capacitance, $g_L$ is the leak conductance, $E_L$ is the leak reversal potential, $\eta$ is a slope factor, $V_T$ determines the neural spiking threshold, $\tau_{q,n}$ is the adaptation time constant, $a$ is the sub-threshold adaptation constant, and $I_{\text{in},n}$ is the cell’s total synaptic input current.

Once the membrane potential crosses $V_T$, the exponential term in Eqn. 5.10a starts to dominate. To limit the membrane potential, we incorporated a ceiling threshold at $V_{\text{peak}} = -30$ mV for spike generation. For each spiking event at time $\tau$, the membrane potential is reset to its resting potential, $V_{\text{rst}}$, and the adaptation current, $q_n$, is increased by $b$ to implement the spike-triggered neural adaptation:

\[
V_n(\tau) \rightarrow V_{\text{rst}} \quad \text{and} \quad q_n(\tau) \rightarrow q_n(\tau) + b \quad (5.10)
\]

In our model, two biophysical parameters specify the firing properties of the SC neurons: the adaptation time constant, $\tau_{q,n}$ (taken to be location dependent; Kasap and Opstal, 2017), and the synaptic input current, $I_{\text{in},n}$, which is partly determined by the intra-collicular connections (see below). In our model, both depend systematically on the rostral-causal location ($u$) of the cells within the network. The remaining parameters, $C, g_L, E_L, \eta, V_T$ and $a$, were fixed and tuned such that the cells showed neural bursting behavior (see Table 1 for the list and values of all parameters used in the simulations, and Kasap and Van Opstal, 2019, for example responses and phase plots).
Current spread

We applied electrical stimulation by the input current, centered around site $[u_E,v_E]$. We assumed an exponential spatial decay of the electric field from the tip of each stimulation electrode. For stimulation at a single site at time $t_1$:

$$I_E(u,v,t) = I_0 \cdot \exp(-\lambda \sqrt{(u-u_E)^2 + (v-v_E)^2}) \cdot P(t-t_1) \quad (5.11)$$

with $\lambda$ (mm$^{-1}$) a spatial decay constant, $I_0$ the current intensity at site $(u_E,v_E)$ (in pA), and a rectangular stimulation pulse given by $P(t) = 1$ for $0 < t - t_1 < D_S$, and 0 elsewhere. Thus, only a small set of neurons around the stimulation site will be directly activated with this input current (see Kasap and Van Opstal, 2019). In double-stimulation trials, two stimuli were applied at different sites. The total current is then given by:

$$I_E(u,v,t) = \sum_{n=1}^{2} I_{0,n} \exp(-\lambda \sqrt{(u-u_{E,n})^2 + (v-v_{E,n})^2}) \cdot P_n(t-t_n) \quad (5.12)$$

In these simulations, stimulus amplitudes, sites, durations, and their relative timings were systematically varied.

Synapse dynamics and lateral connections

The total input current for neuron $n$ depends on the spiking activity of its surrounding neurons through conductance-based synaptic transmission, and external electric current inputs (Eqn. 5.11 or 5.12):

$$I_{\text{inp},n}(t) = g_{n}^{\text{exc}}(t)(E_e - V_n(t)) + g_{n}^{\text{inh}}(t)(E_i - V_n(t)) + I_E(u_n,v_n,t) \quad (5.13)$$

where $g_n^{\text{exc}}$ and $g_n^{\text{inh}}$ are excitatory and inhibitory synaptic conductances acting upon neuron $n$, $E_e$ and $E_i$ are excitatory and inhibitory reversal potentials, respectively. These conductances increase instantaneously for each presynaptic
spike by a factor that is determined by the synaptic connection strength between neurons, and they subsequently decay over time in an exponential way:

\[
\tau_{\text{exc}} \frac{dg_{\text{exc}}^n}{dt} = -g_{\text{exc}}^n + \tau_{\text{exc}} \sum_i N_{\text{pop}} w_{i,n}^{\text{exc}} \sum_s N_{\text{spks}}^i \delta(t - t_{i,s}) \tag{5.14}
\]

\[
\tau_{\text{inh}} \frac{dg_{\text{inh}}^n}{dt} = -g_{\text{inh}}^n + \tau_{\text{inh}} \sum_i N_{\text{pop}} w_{i,n}^{\text{inh}} \sum_s N_{\text{spks}}^i \delta(t - t_{i,s}) \tag{5.15}
\]

with \( \tau_{\text{exc}} \) and \( \tau_{\text{inh}} \), the excitatory and inhibitory time constants; \( w_{i,n}^{\text{exc}} \) and \( w_{i,n}^{\text{inh}} \) are the intracollicular excitatory and inhibitory connection strengths between neurons \( i \) and \( n \), respectively (Eqn. 5.16a,b) and \( t_{i,s} \) are the spike timings of all presynaptic SC neurons projecting to neuron \( n \).

We incorporated a Mexican hat-type lateral connection scheme (Trappenberg et al., 2001):

\[
w_{i,n} = s_n \cdot (w_{i,n}^{\text{exc}} - w_{i,n}^{\text{inh}}) \quad \text{with:} \tag{5.16}
\]

\[
w_{i,n}^{\text{exc}} = \bar{w}_{\text{exc}} \exp \left(-\frac{||u_i - u_n||^2}{2\sigma_{\text{exc}}^2}\right) \tag{5.17}
\]

\[
w_{i,n}^{\text{inh}} = \bar{w}_{\text{inh}} \exp \left(-\frac{||u_i - u_n||^2}{2\sigma_{\text{inh}}^2}\right) \tag{5.18}
\]

where \( \bar{w}_{\text{exc}} > \bar{w}_{\text{inh}} \) and \( \sigma_{\text{inh}} > \sigma_{\text{exc}} \), and \( s_n \) is a location-dependent synaptic scaling parameter, which accounts for the location-dependent change in neuronal sensitivity that is related to the variation in their adaptation time constants. Figure 5.1B exemplifies the connectivity profile for a single site.

The strong short-range excitatory and weak long-range inhibitory synapses act as a dynamic soft winner-take-all (WTA) mechanism: not just one neuron remains active, but the winner affects the temporal activity patterns of the other active neurons too. The central neuron thus governs the population activity, since it usually is the most active one (but note that under double-stimulation conditions this may change; see Results). As a result, all recruited neurons exhibit similarly-shaped bursting profiles as the most active neuron, leading to spike-train synchronization within the population (Goossens and Van Opstal, 2012; Kasap and Opstal, 2017; Kasap and Opstal, 2018a).
Network tuning

The intrinsic biophysical properties of the neurons were enforced by systematically varying the adaptation time constant, $\tau_{q,n}$, and the synaptic weight-scaling parameter, $s_n$. Changes in the adaptive properties result in a varying susceptibility to synaptic input, while the synaptic scaling corrects for the total input activity. Following the brute-force genetic algorithm from our recent paper (Kasap and Van Opstal, 2019; Kasap and Opstal, 2017), the optimal location-dependent $[\tau_{q,n}, s_n]$ value pairs for the neurons were fitted to ensure a systematic negative rostral-caudal gradient of the peak firing rates ($f_{\text{peak}} \propto 1/\sqrt{R}$ and a fixed number of spikes per neuron for its preferred saccade ($N_{\text{SPK}} = 20$) under a single-site microstimulation condition with $I_0 = 150$ pA and $D_S = 100$ ms.

In short, the algorithm optimized the network fitness, by incorporating the scaled contributions of the cells’ peak firing rates, their total spike counts, and an inter-cellular synchronization index within the recruited population. As a result, the adaptive time constant, $\tau_{q,n}$, decreased linearly from 100 to 30 ms with the anatomical rostral-caudal location of the neuron, $u_n$, according to:

$$\tau_{q,n} = 100 - 14u_n \text{ ms, with } u_n \in [0,5] \text{ mm}$$

(5.19)

The optimal synaptic scaling factor for the lateral excitatory/inhibitory connections (Eqn. 5.16) could be fitted by a monotonically decreasing 5th-order polynomial in $u_n$ (in mm; Kasap and Van Opstal, 2019):

$$s(u_n) = 0.0148 + (-2.52 \cdot u_n + 1.6856 \cdot u_n^2 - 1.49 \cdot u_n^3 + 0.4318 \cdot u_n^4 - 0.04737 \cdot u_n^5) \cdot 10^{-4}$$

(5.20)

Figure 5.2B illustrates the lateral connectivity profile for one of the cells (at $(u,v) = (2.0, 0.0)$ mm) in the motor map, together with the Gaussian population activity around that cell, associated with a small horizontal V-saccade of $[R, \Phi] = [7.4, 0]$ deg (Fig. 5.1A). Note that the lateral interaction profiles are similar in shape and extent across all cells in the motor map, but the absolute values of the excitatory peak and inhibitory trough decrease in a systematic way with the rostral-caudal coordinate, $u$, as $s(0) = 0.0148$ and $s(5) = 0.0113$, from Eqn. 5.20.
Figure 5.2 (A) Population activity profile for a horizontal saccade with an amplitude of 7.4 deg. The cell in the center of the Gaussian population fires 20 spikes and is located at \((u_0, v_0)=(2, 0)\) mm (cross hair); the population width is 0.5 mm (Eqns. 2 and 4). (B) Excitatory-inhibitory lateral connectivity (in pS) for the cell in the center of the population, according to Eqns. 12-14, and Table 1. The strongest lateral inhibition is exerted at about 1.1 mm from the cell (light-blue dashed circle). The red circle indicates the \(w=0\) pS contour, at about 0.6 mm from the cell.
5.3 Results

Single-site stimulation

Figure 5.3A-C shows the recruited neural population at a rostral stimulation site (R = 2 deg, φ = 0 deg) for stimulation with an amplitude of $I_0 = 150$ pA and duration $D_S = 100$ ms. The diameter of the circular population extends to about 1 mm in the motor map, with the cumulative spike count of the central cells reaching ~ 20 spikes. Figure 5.3B provides the neuronal bursts (top spike patterns) from 12 selected cells, together with their calculated spike-density functions. The peak firing rate of the central cells was close to 700 spikes/s and dropped in a regular fashion with distance from the population center. Note also that the cells near the edge of the population were recruited slightly later than the central cells, but that their peak firing rates were reached nearly simultaneously. Moreover, the bursts all appeared to have the same shape. Figure 5.3C presents the saccade of 2 deg (top: as function of time; bottom: as a spatial trajectory) encoded by this population through Eqn. 5.3.

Figure 5.3D-F shows the results for stimulation at a more caudal location in the motor map, yielding an oblique saccade with $R = 21$ deg, $φ = 30$ deg. The size of the evoked population activity is very similar to that of the rostral population, and also the number of spikes elicited by the cells is the same. The peak firing rates of the neurons, however, were markedly lower at the caudal site, reaching a maximum of about 450 spikes/s. As a result, the burst durations increased accordingly, from about 35 ms at the rostral site, to more than 70 ms at the caudal site. Note also that the horizontal and vertical position and velocity temporal profiles are scaled versions of each other, leading to a straight oblique saccade trajectory (Fig. 5.3F, lower panel).

Synchronous stimulation at nearby rostral-caudal sites

Figure 5.4 shows the network response to synchronous double stimulation for two nearby sites, at $R = 10$ and $R = 20$ deg (i.e., $u = 2.3$ and 3.0 mm; Eqn. 5.6a) on the horizontal meridian (i.e., $φ = 0$ ($v = 0$ mm), for both sites). The microstimulation parameters were taken the same at both locations ($I_0 = 150$ pA for $D_S = 100$ ms). After about 30 ms following population activity onset, the highest merged population activity is observed, in which the most active neurons are found between the two stimulation sites (Fig. 5.4A,B). The firing rates of the two neurons closest to the stimulation electrodes are highlighted in Fig. 5.4B. Note that the resulting firing rates at these stimulation sites are markedly lower than at
Figure 5.3 (A,D) Cumulative spike counts in the gaze-motor map in response to microstimulation at two single sites. (B,E) Temporal burst profiles of the recruited neurons at 0.1 mm intervals from the central neuron illustrate synchronized population activity. Peak firing rates of the cells decrease with distance from the population center, which coincides with the location of the stimulation electrode. Burst durations increase for the larger saccade, but the total number of spikes in both populations remains the same. (C,F) Top: Eye-displacement temporal profiles, generated by the linear dynamic ensemble-coding model (Eqn. 3). Horizontal (green), vertical (yellow), and vectorial (purple) eye-displacement traces. Note the longer duration of the larger movement (main-sequence property), and synchronized horizontal/vertical movement components (stretching). Bottom: 2D straight saccade trajectories.

the center of the total population. Note also that these firing rates are highly similar. For single-site stimulation, these firing rates would have been different, due to the tuning properties of the neurons within the motor map (Eqn. 5.19). These interesting equilibrating population dynamics result from the mutual excitatory/inhibitory interactions among the neurons, as given by Eqns. 5.16 and 5.20 (cf. with Fig. 5.2B).
Figure 5.4 Synchronous double stimulation with the same current strengths ($I_0=150\ pA$) at two nearby sites on the horizontal meridian, corresponding to $R=10$ deg (at $u=2.3\ mm$) and $R=20$ deg (at $u=3.0\ mm$), respectively. (A) The neural interactions produce a single population with its peak activity between the two sites. (B) Temporal burst profiles of a set of neurons belonging to the active population. The two neurons closest to the stimulation sites reach similar peak firing rates (highlighted profiles). (C) The resulting saccade (Eqn. 3) has an amplitude of 15 deg, which is at the weighted averaged position.

Synchronous stimulation at widely separated rostral-caudal sites

Fig. 5.5 illustrates the network response to synchronous double stimulation with the same intensity and duration as in Fig. 5.4, at two sites on the horizontal meridian that are separated by nearly 3 mm: $R=2$ deg and $R=35$ deg, respectively (at $u=0.7$ and 3.6 mm). About 30 ms after activity onset, two separated populations can be observed, in which the most active neurons now coincide with the two stimulation sites (Fig. 5.5A). The firing rates of the two neurons closest to the stimulation electrodes are again highlighted in Fig. 5.5B. Note that the peak firing rate at the small-amplitude stimulation site (green line) is markedly lower (by almost 50%) and has a much longer duration than for the single-site stimulation result (cf. Fig. 5.3B). Both populations appear to result in comparable firing dynamics, which again is due to the mutual interactions among the neurons across the motor map (cf. with Fig. 5.2B). However, because the strength of the interaction profiles is site-specific (Eqns. 5.16-5.20), the populations show different onset dynamics, with the caudal site starting later than the rostral site. The resulting horizontal saccade has an amplitude of 31 deg, which differs from the linear summation of the two stimulation effects ($R_{SUM}=37\ deg$).
Figure 5.5 Synchronous double stimulation with the same current strengths at two separated sites on the horizontal meridian, corresponding to $R = 2$ deg (at $u = 0.7$ mm) and $R = 35$ deg (at $u = 3.6$ mm), respectively. Now, the two stimuli generate two separate populations that together produce a saccade of $R = 31$ deg. Note that the peak firing rates and burst durations in both populations are similar, but differ markedly from the single-site stimulation rates (cf. with Fig. 5.3).

**Weighted averaging for rostral-caudal sites.**

We next illustrate the effect of varying the relative current strengths at two stimulation sites on the horizontal meridian (at $R = 20$ deg and $R = 35$ deg, respectively) for synchronous double stimulation. The stimulation amplitude at the rostral electrode was kept constant at $I_{0,1} = 150$ pA, whereas the stimulus intensity at the caudal site was varied systematically between $I_{0,2} = 100$ and 200 pA in 10 pA steps. Figure 5.6 illustrates three stimulus situations: $I_{0,2} = 130$ pA, $I_{0,2} = 150$ pA, and $I_{0,2} = 170$ pA. In all three cases a merged population is seen, in which the center-of-gravity of the activity gradually shifts from the rostral to the more caudal site.

Figure 5.7 shows the result of systematically varying the relative stimulus intensities on the evoked saccade amplitudes (all saccades were horizontal, like in Figs 5.4 and 5.5). The individual stimulation sites produced saccades of $R = 20$ and $R = 35$ deg, respectively (red symbols). Synchronous stimulation at the two sites, with $I_{1,0} = 150$ pA (fixed), resulted in eye-movements with amplitudes that systematically varied as a function of $I_{2,0}$ between 22.4 and 30 deg.

**Double stimulation at medial-lateral sites**

We next illustrate the effects of synchronous stimulation at two sites that encode the same saccade amplitude ($u = \text{constant}$), but different saccade directions (dif-
Figure 5.6 Spike counts of the activated neural populations when the input current at the caudal stimulation site at $R = 35$ deg is varied from $I_{0,2} = 130, 150$ and $170$ pA, with the stimulus strength at the rostral site ($R = 20$ deg) kept fixed at $I_{0,1} = 150$ pA. Note that the center-of-gravity of the merged population shifts in the direction of the stronger stimulation site.

Figure 5.8 shows the SC bursts for a group of selected cells, with the two sites corresponding to the up and down electrode highlighted by the bold green and blue lines, respectively. Note that the stimulation sites are markedly less active than the cells near the horizontal meridian, and also that their firing rates are much reduced (by more than 40%) with respect to the single-site stimulation effect (cf. Fig. 5.3D). The sites near the horizontal meridian, on the other hand, display firing rates (>500 spikes/s) that significantly exceed the peak firing rate (~450 spikes/s) of the single-site stimulation effect at the coordinate for a comparable saccade amplitude.

The resulting saccade is horizontal and has an amplitude of $R = 13$ deg. In other words, the amplitude is much smaller than the saccade corresponding to the site of maximal activity, which would be $R = 20$ deg. It is also somewhat smaller than the projection of the saccade vectors onto the horizontal meridian, which would correspond to an amplitude of $R_{CoG} = 20 \cdot \cos(30) = 17.3$ deg (cf. Fig. 5.1C).

Double stimulation: evoked saccade amplitude depends on medial-lateral separation

To appreciate the complex interactions between the neural populations along the medial-lateral ($v$) axis in the motor map, Fig. 5.9 shows the results for
Figure 5.7 Synchronous double stimulation with varying current strengths at the caudal stimulation site. The input current at \([R, \Phi]=[35,0]\) deg varied between 100-200 pA, while it was fixed to 150 pA at \([R, \Phi]=[20,0]\) deg (same stimulus durations of 100 ms). Varying the stimulation strengths shifted the merged population’s center-of-gravity as in Fig. 5.6. The resulting eye-displacement vectors varied from 22.4 to 30 deg (slope of the linear regression line: 7.8 deg/100pA).

The evoked saccade amplitude (blue symbols) as function of the medial-lateral separation, \(\Delta v\), or, equivalently, as function of the angular separation between the two single-site movements. The figure also indicates the simple predictions from the pure center-of-gravity calculations that would result from the motor map \((R=20\ deg\ for\ all\ sites)\), and from downstream averaging (the red line). It is clear that the evoked saccades follow neither prediction. Although the averaging effects are clearly due to the neural interactions with the SC motor map (as we have not incorporated a downstream center-of-gravity mechanism
Figure 5.8 Synchronous double stimulation at the same current strengths at two separated sites, corresponding to $[R, \Phi]=[20,+30]$ deg, and $[R, \Phi]=[20,-30]$ deg respectively. The two stimuli yield a merged population, and a saccade of $R = 13$ deg, which is directed towards an average location of the two individual stimulation effects.

in our model, see Eqn. 5.3), they clearly differ from the simple scheme of center-of-gravity computation. Instead, the results reflect the intricate neural dynamics as well as the influence of the lateral excitatory-inhibitory interactions (see Fig. 5.2B).

For example, for small spatial separations (up to about 0.7 mm), the two populations strongly overlap (as in Fig. 5.8). As a result, they are partly dominated by the mutual excitatory interactions, leading to a slight increase in the saccade amplitude by about one deg. When the sites are separated by about 1 mm, both populations undergo mostly inhibitory influences, leading to a reduced saccade amplitude. This effect increases up to about $\Delta v = 1.4$ mm, where the evoked saccade (at these current levels) reaches a minimum of 7.0 deg. In this region the inhibitory interactions are the strongest (see Fig. 5.2B). As the electrodes are positioned further apart, the saccade amplitude is still small, but slightly increases up to about 9 deg, because of the slightly lower strength of the lateral inhibition.

**Lateral-medial double stimulation at different current strengths**

Weighted saccade averaging can also occur when the electrodes are positioned along the medial-lateral axis, but the effects resulted to depend strongly on both the electrode separation and on the strengths of the two currents. For example, when one electrode was kept fixed at the supra-threshold stimulation intensity of $I_{0,1}=150$ pA, and the other electrode was varied between $I_{0,2} = 100-200$ pA, the following pattern emerged for all angular separation conditions:
Figure 5.9 Saccade amplitude as function of electrode angular separation $\Delta \Phi$ for medial-lateral sites (separated by $\Delta v$ mm) along the fixed $R=20$ deg radius ($u=3.0$ mm). Note that the stimulation-evoked saccade amplitudes strongly depend on the medial-lateral distance, and that they vary in a very different way than predicted from center-of-gravity computations (cf. Fig. 5.1C; Eqn. 5.5).

(i) For currents below $I_{0,2} = 150$ pA, site 1 always fully dominated, and all saccades were directed towards the first site.

(ii) Above $I_{0,2} = 150$ pA, site 2 dominated and saccades were directed to the second site.

(iii) Only when the currents were equal, $I_{0,1} = I_{0,2} = 150$ pA, averaging was obtained according to the relationship seen in Fig. 5.9. In other words, in these double-stimulation conditions the saccade direction behaved as a bistable variable. This response behavior is illustrated in Fig. 10 for an angular separation of 30 deg ($\Delta v = 0.52$ mm; black symbols).
True averaging of the saccade direction was only obtained when

(i) the fixed stimulation current at site 1 was lowered to slightly above the threshold for evoking a saccade (e.g. to $I_{0,1} = 120$ pA), and

(ii) the two sites were close together.

Figure 5.10 shows the results of such weighted stimulation effects for the same sites (blue symbols). The figure shows that from $I_{0,2} = 130$ pA onwards, a clear weighted averaging pattern was obtained, in which the saccade direction varied systematically with the difference in current strength. Note that for currents below about $I_{0,2} = 130$ pA, also the saccade amplitude started to decrease, as for these cases both currents were getting close to their saccade-evoking thresholds.

*Double stimulation with delay*

In a similar way as observed for the interactions along the medial-lateral coordinate (see sections 5.3 and 5.3), imposing a temporal delay between the two supra-threshold electrode currents (when both at 150 pA) produced different response behaviors, depending on the electrode separations and current strengths. For supra-threshold stimulation at both sites, a curved saccade trajectory would only emerge when the delay is very short (typically, below 6 ms), and the stimulation sites are separated in both the medial-lateral and rostral-caudal dimensions of the motor map. An example of such a stimulation condition is shown in Fig. 5.11. The two sites were at $[R, \Phi] = [5,-45]$ and $[35,+45]$ deg, respectively, and the current strengths were 150 pA at both sites, whereby the stimulation pulse at the second site was delayed by 2 ms. Both electrodes set up a population response, leading to a curved saccade trajectory with an overall amplitude of $R = 19$ deg and a direction of about $\Phi = 40$ deg, which is a weighted average of the individual stimulus effects. When the delay was increased to 4 ms the initial direction of the saccade was horizontal curving towards the final site location in midflight of the response (not shown). At delays above 5 ms, the saccade was invariably directed at the endpoint of the first site, as the second site would be strongly inhibited by the activated first population. As a result, the second site would not be able to set up an appropriate population response to produce a colliding saccadic on its own.

When the stimulation sites and current strengths, as well as the delays were systematically varied, the occurrence of curved saccade trajectories resulted to be quite rare. Instead, we often obtained a bistable response behavior, in which a small change in one of the stimulation parameters (e.g. the current strength at
Figure 5.10 Different double-stimulation response behaviors for the conditions in which the electrode at site 1 (at $(R_1, \Phi_1) = (20, 15)$ deg) was kept fixed and slightly above the saccade threshold at $I_{0,1} = 120$ pA (blue symbols), or well above the threshold at $I_{0,1} = 150$ pA (black symbols), while the current at site 2 (at $(R_2, \Phi_2) = (20, -15)$ deg) was varied from $I_{0,2} = 100$ to 200 pA in 10 pA steps. The former condition (blue) yielded clear weighted averaging between the effects from the two sites, while the latter condition (black) shows bistable response behavior. Red symbols: single-site evoked saccades at $I_0 = 150$ pA.

The first electrode) could fully change the saccadic response from being directed to the first site, towards the second site. An example of this bistable behavior on the stimulation conditions is shown in Fig. 5.12, where the two sites were at $[R_1, \Phi_1] = [20, +30]$ deg and $[R_2, \Phi_2] = [40, -30]$ deg, respectively, and the delay was 10 ms. The stimulation current, $I_{0,2}$, was 150 pA in both cases, whereas $I_{0,1}$ was either 140 pA, or 130 pA. In the former condition, a straight saccade is
Figure 5.11 Supra-threshold (150 pA) double stimulation with a short inter-current delay. (A) Spike counts of the active populations at stimulation sites \([R_1, \Phi_1]=[5, 45] \text{ deg}\) and at \([R_2, \Phi_2]=[35, +45] \text{ deg}\), when the input current at the latter site was delayed by 2 ms. (B) Firing rates of the cells in the active populations are plotted in different colors (blue and green for the first and second population, respectively). (C) Resulting eye-displacement components as function of time (top) and the 2D eye-movement trajectory (bottom). Note that the saccade trajectory is curved, as the initial and final directions of the movement are different.

directed towards site 1, whereas in the latter case, a straight saccade is made in the direction of site 2.

We systematically varied the inter-stimulus delay \(t_2\) from \([2, 5, 10, 20, 50] \text{ ms}\) and \(I_0, 1\) from \([200, 190, \ldots, 80] \text{ pA}\) (\(I_{0, 2}\) fixed at 150 pA), and obtained similar bistable results for many cases. Note, however, that these two sites are separated by about 1.26 mm, which falls in the strongest inhibitory range of the lateral connectivity profile. In the situation of Fig. 5.11 the two sites are further apart, given weaker mutual inhibition and allowing more excitatory interactions (see Fig. 5.2 2B, and Discussion).
Figure 5.12 Double stimulation with a 10 ms delay, for two sites about 1.3 mm apart, showing high sensitivity of the network to small changes in the stimulation parameters. In panels A-C the current at the first electrode was $I_{0,1} = 140$ pA, whereas in panels D-F it was only slightly lowered to $I_{0,1} = 130$ pA. Yet, the resulting saccades differed dramatically, in line with bistable response behavior.
5.4 Discussion

**Summary.** Synchronous double stimulation in a spiking neural network model of the SC with Gaussian excitatory-inhibitory interactions results in saccade responses that display many of the features that have been reported in electrophysiological studies (Katnani, Van Opstal, et al., 2012; Robinson, 1972): when the electrodes were located on an iso-direction line \((v = \text{constant})\) the resulting saccade amplitudes were a weighted average of the individual stimulus effects, with the current strengths acting as weighting parameters (Figs. 5.4–5.7). When the electrodes were positioned along iso-eccentricity lines \((u = \text{constant})\), however, the response patterns appeared to be more complex: weighted averaging was obtained for low stimulation currents at nearby stimulation sites, but when the electrodes were moved further apart and/or the current levels increased, we obtained bistable response behavior (Figs. 5.8–5.10). When a delay was introduced between the first and second stimulus pulse, the averaged saccade trajectories could become curved, provided the delay was short \((<6 \text{ ms}; \text{Fig. 5.11})\). For longer delays, saccades were invariably directed towards the site evoked by the first electrode when its current intensity was above the normal saccade-initiation threshold \((150 \text{ pA})\). In other cases, we obtained bistable response behavior, in which the saccade was directed either to the first site, or to the second site, without averaging (Fig. 5.12).

The weighted averaging effects, which betray a nonlinearity in the system, are entirely due to the neural dynamics (Eqns. 5.9–5.10) and synaptic connectivity patterns (Eqns. 5.16–5.20) within the SC motor map, as the downstream motor circuitry in our model was taken entirely linear (Eqn. 5.3). Yet, the averaging results of our simulations do not correspond at all to the simple prediction of a center of gravity calculation at the level of the motor map either (Eqn. 5.5a; Fig. 5.1B), as for iso-eccentricity stimulation the evoked saccade amplitudes varied strongly with the electrode separation (Fig. 5.9), in a pattern that somewhat resemble the effect of downstream averaging. Whether these predictions truly deviate from observed experimental data on synchronous double stimulation is hard to tell, as precise measurements and quantification of this phenomenon are rare (e.g. Katnani and Gandhi, 2012; Katnani, Van Opstal, et al., 2012). The same may hold for the exact paths followed by curved trajectories evoked by delayed electrical double stimulation Katnani and Gandhi, 2012.

In what follows, we discuss these apparent discrepancies with the experimental data.

**Model structure.** The subtle different behaviors observed for iso-direction vs. iso-eccentricity stimulation are likely caused by the differences in neural orga-
organization for the $u-$ and $v-$coordinates in our model. The tuning parameters of the neuronal dynamics (the adaptive time constant, Eqn. 5.19) and the lateral synaptic projection strengths (the scaling parameter, Eqn. 5.20) both only vary with the rostral-caudal coordinate ($u$), and are assumed constant along iso-eccentricity lines.

These biophysical neural tunings were required to explain the firing behavior of collicular neurons under single-site visual stimulation conditions (Goossens and Van Opstal, 2012; Goossens and Van Opstal, 2006; Kasap and Opstal, 2017), and the nonlinear saccadic main sequence kinematics (see Introduction). From our single-unit recordings we noted that the peak firing rates of SC neurons in the center of the population decreased systematically with the saccade amplitude, meanwhile increasing their burst durations to keep the number of spikes in the saccade-related burst invariant across the motor map for slow, fast, small and large saccades. As single-site microstimulation produces normal saccadic eye movements, we argued that the same population activity would emerge during electrical stimulation and for natural visual stimulation. The neural population dynamics are then explained by synaptic lateral interactions, and are hardly influenced by the externally applied electrical stimulation current. We assumed that the stimulation current directly activates only a small subset of the neurons around the electrode. Indeed, under these assumptions, most single-site microstimulation results could be accounted for as well (Kasap and Van Opstal, 2019).

One discrepancy with experimental observations concerned the near-threshold behavior of the network: around the stimulation threshold, the network’s saccades become much slower than main sequence (as evoked firing rates decrease), but their size (determined by the total number of spikes in the burst) remained unaffected. However, experiments have revealed that near the threshold, saccades become both slower than main sequence and smaller (Katnani, Van Opstal, et al., 2012; Van Opstal, Van Gisbergen, and Smit, 1990). This would suggest that near threshold not only the firing rates are reduced, but also the number of spikes. The current model does not incorporate this possibility.

We here conjecture that the failure to produce different numbers of spikes for near-threshold conditions may also underlie the bistable character of our model to some of the double-stimulation conditions, and its reluctance to readily produce curved saccades. In double stimulation, the two electrodes exert a mutual inhibitory influence, which brings the weaker stimulation site to near- or below-threshold levels under many conditions. Indeed, when the stimulation sites fall in each other’s strongest inhibitory zones, the bistable effects are nearly impossible to overcome (e.g. Figs. 5.10 and 5.12). On the other hand, when the
stimulation electrodes are placed along the u-direction in the map, bi-stability is less common. This is probably due to the decreasing strength of the lateral connectivity patterns along this dimension, as dictated by Eqn. 5.20 (the most caudal sites exert nearly 25% less influence than the most rostral sites).

One possibility to overcome this discrepancy is to introduce variability (noise) in the neural population, e.g. at the level of the synaptic conductances (Eqn. 5.15), and at the adaptive time constants (Eqn. 5.19), that relies on the total input strength to the neuron (multiplicative noise; Goossens and Van Opstal, 2012). This will affect the total number of spikes of the neuron, and therefore could potentially lead to smaller saccades for effectively weak inputs.

**Untested predictions.** The neural interactions, imposed by the two separated electrodes, cause some interesting (and somewhat unexpected) behaviors of the neural firing properties, which so far have not been tested experimentally. Under single-site stimulation, the activity of the central cell, which encodes the ensuing saccade amplitude and direction, fully determines the firing-rate profile of all other cells, as well as the saccade kinematics (neural synchronization; e.g., Fig. 5.3). Under double-stimulation at different nearby sites, however, the most active cells are no longer found at the stimulation electrodes, but at a location in between. The firing rates of these most active cells now determine the full saccade kinematics and the firing profiles of the other cells (e.g., Figs. 5.5, 5.6, and 5.8). Interestingly, the kinematics of the resulting saccades (which are slower) and the firing rates of these most active cells (which are higher) differ from the effects of single stimulation at that most active site. Unfortunately, it is difficult to test this prediction experimentally for the firing rates under electrical double stimulation, because of the strong electrical artefacts produced by the electrodes.

However, the effects of double stimulation on the emerging eye-movement kinematics can be readily assessed. As far as the main-sequence properties are concerned, averaging saccades under double visual stimulation appear to be slower than saccades of the same amplitude to a single visual stimulus, and the associated firing rates in the SC are lower (e.g., Van Opstal, Van Gisbergen, and Smit, 1990). To our knowledge, the detailed velocity profiles under electrical double-stimulation have so far not been quantified in experimental studies.

**Lateral interactions.** The simulations of electrical double stimulation made clear that the shape of the Mexican-hat profile affects the activity profiles of both active neuron populations and of the resulting saccades (e.g. Fig. 10). The presence of lateral interactions within the SC has been well established by both anatomical and physiological evidence (Behan and Kime, 1996; Meredith and Ramoa, 1998; Munoz and Istvan, 1998). Modeling studies have suggested
different synaptic interaction profiles, such as local excitation and global constant inhibition (Van Opstal and Van Gisbergen, 1989), or Mexican-hat type Gaussian profiles (Trappenberg et al., 2001). In the present study, we fixed the ranges of the excitatory and inhibitory interactions (σ_{exc} and σ_{inh}) for all cells and tuned their synaptic strengths in line with the proposal of Trappenberg et al., 2001 (Eqn. 5.20). Although it is conceivable that different profiles with shorter ranges could generate similar population activities (see below), anatomical studies so far do not allow to quantify the connectivity profiles and ranges, except for recent in-vitro studies (Phongphanphanee, Mizuno, et al., 2011; Phongphanpanee, Marino, et al., 2014).

In contrast to the model of Van Opstal and Van Gisbergen, 1989, in the present model the effective range of the electrical current was assumed to be small (Eqn. 5.13; Kasap and Van Opstal, 2018b). This assumption was inspired by recent findings from stimulation experiments with simultaneous calcium imaging in frontal cortical tissue (Histed, Bonin, et al., 2009; Histed, Ni, et al., 2013). In our model, the stimulation profile is subsequently combined with the Mexican-hat interaction function of Eqns. 5.16-5.20. We have shown earlier, using a static population model of the SC, that a weak global constant inhibition in combination with a delta function for the excitatory profile (i.e., only self-excitation) could yield saccade-averaging results if the current-spread function was a Gaussian with a much broader extent as in the present study, and whereby its width depended in a nonlinear way on the applied current strength (Van Opstal and Van Gisbergen, 1989).

Note that for network models such as these, including our own, the overall spatial effect of the stimulation (ignoring time) is in fact given by the convolution of the electrical stimulation profile with the weighting kernel of the excitatory-inhibitory interactions. Each cell’s membrane potential is thus described by:

\[ V_n(u,v) = \int_{(u,v)_{\text{min}}}^{(u,v)_{\text{max}}} w_n(\sigma,\tau) \cdot I_{\text{inp}}(u-\sigma,v-\tau) \cdot d\sigma d\tau \]  

(5.21)

which constitutes one equation for the membrane potential of neuron n, as a multiplicative combination of two functions. It is therefore conceivable that many potential functions could fulfill Eqn. 5.21. However, the nonlinear dynamics of the current model (Eqns. 5.9-5.10) makes a simple analytical approach to find the optimal solution that satisfies all experimental constraints not feasible. Further study is therefore required to analyze the effects of different profiles.
on the total network behavior across a wide range of sensory and electrical stimulation conditions.

As a final note, the electrical stimulation inputs were simply taken as constant rectangular pulses, instead of trains of short-duration stimulation pulses. In the latter case, which is physiologically more realistic, also the pulse intervals (stimulation frequency), pulse durations (stimulus train lengths), pulse heights, pulse interleave times, and pulse polarity may all play a role in the evoked E-saccades under single and double stimulation paradigms (Katnani and Gandhi, 2012; Stanford et al., 1996). Incorporating these different stimulation parameter settings in our spiking neural-network model will require some tedious retuning of the network parameters, but may be worth the effort for its potential to generate novel neural dynamics.
References


MAPS AND SENSORIMOTOR TRANSFORMATIONS FOR EYE-HEAD GAZE SHIFTS: ROLE OF THE MIDBRAIN SUPERIOR COLLICULUS

Abstract

Single-unit recordings in head-restrained monkeys indicated that the population of saccade-related cells in the midbrain Superior Colliculus (SC) encodes the kinematics of desired straight saccade trajectories by the cumulative number of spikes. In addition, the nonlinear main sequence of saccades (their amplitude - peak velocity saturation) emerges from a spatial gradient of peak-firing rates of collicular neurons, rather than from neural saturation at brainstem burst generators. We here extend this idea to eye-head gaze shifts and illustrate how the cumulative spike-count in head-unrestrained monkeys relates to the desired gaze trajectory and its kinematics. We argue that the output of the motor SC is an abstract desired gaze-motor signal, which drives in a feedforward way the instantaneous kinematics of ongoing gaze shifts, including the strong influence of initial eye position on gaze kinematics. We propose that the neural population acts as a vectorial gaze pulse-generator for eye-head saccades, which is subsequently decomposed into signals that drive both motor systems in appropriate craniocentric reference frames within a dynamic gaze-velocity feedback loop.

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6.1 Introduction

Eye-head gaze shifts. A saccadic eye-head gaze shift ($\Delta G$) is the directional change of the fovea in space, which is determined by the sum of the changes of the eye-in-head and the head-on-neck orientations: $\Delta G = \Delta E + \Delta H$. The gaze-control system of human and non-human primates is optimally suited to reorient the fovea as fast and as accurately as possible to a target and to allow vision to identify objects with high resolution during intermittent fixations.

Although any particular gaze shift can in principle be generated by infinitely many combinations of eye and head contributions, under controlled initial conditions the system selects highly reproducible movement strategies. It has therefore been hypothesized (Goossens and Opstal, 2012; Harris and Wolpert, 1998, 2006; Kardamakis and Moschovakis, 2009; Saglam et al., 2011) that gaze shifts result from a control principle that optimizes some performance criterion, such as speed-accuracy trade-off, which minimizes the impact of internal noise and uncertainty, or minimization of motor effort.

Figure 6.1A illustrates a horizontal sound-evoked gaze saccade, in which the initial eye- and head orientations were aligned at straight ahead. It shows the different stages during and around the gaze shift: (i) the fixation phase, during which the vestibular-ocular reflex (VOR) ensures stable fixation, (ii) the gaze shift ($\Delta G = 26$ deg) consists of a large eye saccade ($\Delta E = 22$ deg) to $E_{\text{END}}$, and a small head-movement contribution ($\Delta H = 4$ deg) with the VOR attenuated. (iii) The gaze shift is followed by a remaining head movement (here 14 deg), during which gaze remains stable because of the VOR. (iv) At the end of the head movement ($H_{\text{OFF}}$), the eye orientation may be eccentric in the head (here, $E_{\text{OFF}} = 8$ deg).

Because of the different plant dynamics of eyes and head, and the eye’s limited oculomotor range, not all eye-head combinations are possible or equally efficient in reorienting gaze. Typically, small gaze shifts are associated with small head movements, and large gaze shifts with larger head movements, but the latter also depends on initial eye orientation (e.g., Freedman and Sparks, 2000; Goossens and Van Opstal, 1997; Guitton and Volle, 1987; Kardamakis, Grantyn, et al., 2010. Thus, when a large head movement contributes to the gaze shift, gaze peak-velocity is reduced. This point is illustrated in Fig. 6.1B. Because of the much larger head contribution, the gaze velocity of 60 deg gaze shifts tends to be considerably lower than for gaze shifts with an amplitude of 30 deg.

In this report, we propose a quantitative model that explains this behaviour. The major novelty of our model with respect to earlier proposals (Daye et al., 2014; Freedman, 2001; Goossens and Van Opstal, 1997; Guitton and Volle, 1987;
Figure 6.1 (A) Example of a horizontal gaze shift (25.5 deg amplitude) to an auditory target with the eyes and head initially aligned (signals are shifted by a few degrees for illustrative reasons). The eye- and head displacements that contribute to the gaze shift are measured between gaze on- and offset ($G_{ON}$, $G_{OFF}$; vertical dashed lines). Note that the contribution of the head to the gaze shift ($\Delta H = 3.8$ deg) differs markedly from the overall head displacement (17.6 deg). Note also that the head starts to move slightly earlier than the eyes ($H_{ON}$), inducing a small vestibular counter movement of the eyes to maintain stable gaze fixation. During the fully operating vestibular ocular reflex (VOR) after gaze offset, gaze remains stable (apart from a slow centripetal drift in darkness), while the head continues to move to its final position, $H_{OFF}$. (B) Example gaze- (black) and head- (red) velocity profiles for gaze shifts with an amplitude of about 33 deg (top) vs. 60 deg (bottom). In the latter case, the head contribution is considerably larger, causing the overall gaze velocity to drop (see also Fig. 6.2B). Solid lines: average profiles.

Kardamakis, Grantyn, et al., 2010; Saglam et al., 2011) resides in the assumed role of the midbrain Superior Colliculus (SC) in the control of gaze shifts. Our model is based on results of recent single-unit recordings, taken from the SC of head-restrained and head-free monkeys, which support the idea that the motor SC acts as the nonlinear vectorial gaze-pulse generator of the system.
**Brief background SC.** The SC contains a topographic map of saccadic gaze shifts (Freedman and Sparks, 1997; Ottes et al., 1986; Robinson, 1972). Prior to and during saccades, a population of cells encodes amplitude and direction by the location of its center within the map (Ottes et al., 1986; Sparks and Mays, 1980). SC recordings in head-restrained monkeys demonstrated that the population also encodes saccade kinematics through their firing rates (Goossens and Van Opstal, 2006).

We thus proposed that the SC issues a desired (straight-line) dynamic eye-displacement signal by its total cumulative number of spikes in the saccade-related bursts. Moreover, all cells in the population synchronize their bursts, such that even at the single-unit level each cell encodes the straight desired trajectory of any saccade within its movement field (Goossens and Van Opstal, 2012).

We formulated a simple computational model, in which each spike in the burst from each recruited neuron, \( k \), contributes a tiny movement, \( \vec{m}_k \), to the saccade. This *spike-vector* is determined by the cell’s location in the map, and specifies its connection strength with the brainstem burst generators via the SC-to-brainstem efferent mapping function (Ottes et al., 1986; Van Gisbergen et al., 1987). According to this dynamic ensemble-coding model, the saccade trajectory is encoded by linear cumulative integration of all SC spike vectors:

\[
\Delta \vec{E}(t) = \sum_{k=1}^{N_{\text{pop}}} \sum_{s=1}^{N_{\text{spk,k}}} \delta(t - \tau_{k,s}) \cdot \vec{m}_k \tag{6.1}
\]

where \( \delta(t - \tau_{k,s}) \) is a spike of cell \( k \), fired at time \( t = \tau_{k,s} \).

Simulations with measured spike trains and a linear brainstem burst generator demonstrated that the model fully accounted for the nonlinear main-sequence properties and velocity profiles of fast and slow saccades. As a logical consequence, the main-sequence nonlinearity has to reside in the distribution of spike trains and firing rates in the motor SC (Opstal and Goossens, 2008).

The hypothesis therefore holds that the SC may embed the neural correlate of the optimal controller underlying gaze shifts (Harris and Wolpert, 1998, 2006). Analysis of single-unit responses revealed that its neural mechanism could be described as follows:

(i) A spatial gradient in the peak-firing rates of SC cells from rostral (small saccades, firing rates up to 900 spks/s) to caudal locations (large saccades, about 300-400 spks/s).

(ii) On average, cells fire the same number of spikes for their optimal saccade.
(iii) The population size is the same (diameter of about 1 mm) for all saccades. Hence, the total number of spikes in each recruited population is the same.

(iv) All cells within the population synchronize their bursts.

We here extend these ideas to the head-unrestrained condition. Monkeys generated eye-head saccades with considerable natural variability in their kinematics, induced by varying the initial eye-in-head position. A critical prediction of Eqn. 6.1 is that the same relation should hold for head-unrestrained saccades, regardless gaze-shift kinematics. Thus, the nonlinear gaze kinematics should be reflected in the burst properties of SC cells. To our knowledge, these properties have so far not been documented for head-unrestrained gaze shifts.
6.2 METHODS

Experiments were performed in the laboratory of Dr. EG Freedman at the Department of Neurobiology and Anatomy, School of Medicine and Dentistry of the University of Rochester, NY, while one of the authors (AJVO) was a visiting scientist. Two trained rhesus monkeys (P and S) participated in the experiments. Animals were trained to follow briefly flashed visual targets against a small liquid reward by generating rapid eye-head gaze shifts, while single-unit activity from the left SC was recorded. Details on the surgical procedures, training protocols, and experimental setup are described in full detail in Quessy and Freedman, 2004; Quessy, Quinet, et al., 2010, and Walton and Freedman, 2011. All experimental procedures were approved by the University of Rochester Animal Care and Use Committee, and fully adhered to the National Institutes of Health Guide for the Care and Use of Animals.

We recorded from a total of 52 cells, out of which 30 neurons were isolated long enough for detailed analysis. The movement fields were typically obtained from cells in the caudal SC, where optimal saccade amplitudes ranged from about 30 to 100 deg.

Paradigm. To vary movement kinematics, monkeys elicited gaze-saccades from different initial eye-in-head orientations. At the start of a trial, the animal looked at a straight-ahead LED while aligning one of three head-fixed lasers with the fixation point. The lasers were positioned such that the horizontal head orientation with respect to straight ahead would be either [-18, 0, +18] deg. For example, a target presented at 60 deg rightward, resulted in three different 60 deg eye-head gaze shifts: the head at -18 deg (i.e., the eyes directed 18 deg ipsilateral to the target), 0 deg (eye-head alignment), or +18 deg (the eye-contra condition).

Analysis. To determine the movement field, gaze saccades were elicited in and around the cell’s response field. We counted the number of spikes in the burst from 20 ms before gaze-shift onset to 20 ms before offset (e.g., Fig. 6.3A), and applied the afferent mapping function of Ottes et al., 1986 to each gaze shift to calculate its anatomical coordinates (u,v) in the SC map. In polar coordinates (ΔG, Φ):

\[
\begin{align*}
  u &= B_u \cdot \ln \left( \frac{\sqrt{\Delta G^2 + 2A \cdot \Delta G \cdot \cos \Phi + A^2}}{A} \right) \ mm \\
  v &= B_v \cdot \arctan \left( \frac{\Delta G \cdot \sin \Phi}{\Delta G \cdot \cos \Phi + A} \right) \ mm
\end{align*}
\]  (6.2)
where $B_u = 1.4$ mm, $B_v = 1.8$ mm/rad, and $A = 3.0$ deg determine the shape of the monkey afferent mapping function (Ottes et al., 1986; Robinson, 1972; Fig. 6.4).

We first fitted the static movement field function to all gaze-saccade vectors, and included a potential eye-in-head gain-field modulation (Van Opstal et al., 1995) to the total number of spikes in the burst, $N$, according to:

$$N(G, \Phi, E_0) = N_0 \cdot (1 + \epsilon \cdot E_0) \cdot \exp \left( -\frac{(u - u_0)^2 + (v - v_0)^2}{2\sigma_p^2} \right)$$

(6.3)

This model has five free parameters: $N_0$ is the number of spikes in the burst for the optimal saccade from straight ahead, $(u_0, v_0)$ (in mm) are the SC coordinates of the optimal saccade (Eqn. 6.2), $\epsilon$ (in #spikes/deg) is the eye-position gain, and $\sigma_p$ (in mm) quantifies the tuning width. Optimal parameter values were obtained with the Nelder-Mead Simplex algorithm in Matlab.

Next, the dynamic movement field describes how the cumulative number of spikes in the burst evolves during the straight gaze-displacement along the line connecting start- and end-positions (Goossens and Van Opstal, 2006). According to this model, the cumulative spike count for any gaze shift, regardless kinematics, obeys the following, linear, relation:

$$CS(G, \Phi, E_0, t) = \Delta G(t + \tau) \cdot \frac{N(G, \Phi, E_0)}{\Delta G}$$

(6.4)

where $\Delta G(t + \tau)$ is the desired straight trajectory (increasing monotonically from 0 to $\Delta G$). The neuron’s lead time, $\tau$, was fixed at $\tau = 20$ ms for all neurons. The straight trajectory was obtained by projecting the actual trajectory. $(x(t), y(t))$ onto gaze vector $\Delta G \cdot (\cos \Phi, \sin \Phi)$ (Goossens and Van Opstal, 2006):

$$\Delta G(t) = x(t) \cdot \cos \Phi + y(t) \cdot \sin \Phi$$

(6.5)

The time-independent factor in Eqn. 6.4, $N(G, \Phi, E_0)/\Delta G$, corresponds to the slope of the dynamic phase-relation. It should vary in a systematic way with gaze-shift amplitude and direction (Goossens and Van Opstal, 2006).
6.3 RESULTS

Behavior. Figure 2 shows an analysis of representative gaze shifts from monkey S for the three initial eye positions. These gaze shifts (amplitudes between 20 and 75 deg) were directed into the movement field of neuron s1809. The contribution of the head movement depended systematically on gaze-shift amplitude and initial eye-position (Fig. 2A), and had a strong influence on peak gaze-velocity (Fig. 2B), and gaze-saccade duration (Fig. 2C). Ipsilateral eye orientations (blue) caused consistently larger head movements, and slower gaze shifts. The fastest gaze shifts were obtained for contralateral eye orientations. These findings were robust for all recording sessions and both monkeys.

![Figure 6.2](image-url) Properties of monkey eye-head gaze shifts, measured during single-unit recording of neuron s1809 (see Fig. 6.3). Rightward gaze shifts (N=180) up to 75 deg amplitude were elicited into the cell’s movement field, for three initial eye-in-head orientations (colors). (A) The contribution of the head movement varied systematically with initial eye position. Light open symbols: total head movements (cf. Fig. 6.1). (B,C) The initial conditions had a strong influence on gaze kinematics: larger/smaller head movements yielded slower/faster gaze shifts. Peak gaze velocities thus varied by more than 40%.

Neural responses. The changes in initial eye-position also affected the activity of SC neurons. This is documented in Fig. 6.3 for neuron s1809. Figure 6.3A shows the raw spike trains for the gaze shifts of Fig. 6.2. The neuron fires a prominent saccade-related burst associated with the upcoming saccade. Panel 6.3B presents the phase plots for these spike trains. It shows the cumulative number of spikes, CS(t + 20), as function of the dynamic gaze-shift vector, ΔG(t). Note that each phase trajectory follows an approximately straight line, for which slope and end point differed considerably for each trail. According to Eqn. 6.4, this slope should depend on the total number of spikes in the burst (as determined by Eqn. 6.3), and gaze-saccade amplitude. It is immediately clear
that the cumulative number of spikes in the burst also depends on initial eye position, as blue, black and red phase trajectories fall into different clusters. To test whether the dynamic movement-field model of Eqn. 6.4 captures this variability in the cell’s spiking behavior, we first determined the static movement field of the cell by fitting Eqn. 6.3 to the total spike counts. Figure 6.3D shows the movement field of the cell, together with all 180 gaze-saccade endpoints for this experiment. The optimal parameters for this neuron were: \( N_0 = 40.3 \) spikes, \( \Delta G_0 = 57.2 \) deg, \( \Phi_0 = 9.4 \) deg, \( u_0 = 4.2 \) mm, \( v_0 = 0.28 \) mm, \( \sigma_P = 0.73 \) mm and \( \epsilon = 0.0063 \) spikes/deg.

Figure 6.3 (A) Raw spike trains of cell s1809 for all 180 trials into its movement field, aligned to gaze-shift onset (yellow-dashed line at \( t=0 \)). The motor burst starts 20 ms before gaze onset (red-dashed line). (B) Phase trajectories of the cumulative number of spikes as function of ongoing gaze displacement along the straight gaze vector. (C) Four example trials demonstrating a tight correlation between the cell’s firing-rate profile and instantaneous gaze velocity. For ease of comparison, both variables were normalized to gaze duration and to their maxima. (D) Plot of the movement field (Eqn. 6.3) in gaze-vector coordinates; color specifies number of spikes (dark: low, light: high). (E) The gain-field model captures the data well for all gaze shifts and initial conditions. (F) Test of Eqn. 6.4 on the spike trains during all fast (red), intermediate (black), and slow (blue) gaze shifts into the movement field.
In panel 6.3E we show that the total number of spikes in the burst is predicted well by this model ($r = 0.96$). Fitting the movement field without eye-position modulation yielded $r = 0.90$, which is significantly lower ($p < 0.0001$). We next determined the predictions for the slopes of the spike-train phase trajectories of Fig. 6.3B (Eqn. 6.4). Figure 6.3F shows the predicted cumulative number of spikes for each response vs. the measured cumulative spike count. Note that this plot contains more than 20000 data points. Yet, the correlation between measurements and predictions is very high: $r = 0.96$.

We observed that the neuron’s firing rate had a remarkably good resemblance with instantaneous gaze velocity along the desired trajectory for a large fraction of trials. To illustrate this point, Fig. 6.3C shows four example trials with different gaze-velocity profiles. These normalized traces appeared to correlate very well. We obtained correlations $r > 0.7$ for nearly 50% of the trials in the majority of cells (results to be published elsewhere; see Discussion).

**Model.** Based on the behavioral and neurophysiological results we propose a computational model for the generation of eye-head gaze shifts, in which the SC provides the common drive for the eyes and head as a dynamic desired straight gaze trajectory, $G(t)$, by its total cumulative number of spikes. In other words, the instantaneous firing rate of the total population specifies the desired gaze velocity profile, and as such acts as a vectorial gaze-pulse generator. Details of the model, which is presented in Fig. 6.4, including simulations, were published recently in Kasap and Van Opstal, 2019.

The SC output represents the desired straight-line gaze velocity, $\dot{G}_{\text{DES}}(t)$, which is compared with the true gaze velocity from the oculomotor and head-motor systems to determine a dynamic gaze-error signal:

$$G_{\text{ERR}}(t) = \int_{\text{ON}}^{t} (G_{\text{DES}}(\tau) - \dot{E}(\tau) - \dot{H}(\tau)) \, d\tau \quad (6.6)$$

with eye position to represent the dynamic error of the gaze saccade in a cranio-centric reference frame:

$$H_{\text{ERR}}(t) = G_{\text{ERR}}(t) + E(t) \quad (6.7)$$

This latter signal drives both the oculomotor and head-motor systems. For the eye, the signal can keep eye position within the (soft) oculomotor range (OMR). The dynamic desired eye-in-head position thus becomes:

$$E_{\text{DES}}(t) = \text{OMR}(H_{\text{ERR}}(t)) \quad (6.8)$$
This signal drives the (linear) oculomotor burst generator with dynamic eye motor-error:

\[ E_{\text{ERR}}(t) = E_{\text{DES}}(t) - E(t) \]  

(6.9)

Figure 6.4 Computational scheme for dynamic ensemble-coding of saccadic eye-head gaze shifts by the collicular population. The desired gaze-velocity profile along the straight trajectory, \( \Delta G(t) \), is issued by the SC population, on which the initial eye position, \( E_0 \), exerts a weak, multiplicative modulation. Thus, in line with our recordings, the number of spikes in the burst, and the spike timings, depend on eye position too (e.g., Fig. 6.3 C, E). Eye and head are driven by different signals in head-centered reference frames. The actual contributions of the eye and head movements to the gaze shift, \( \Delta E \), and \( \Delta H \), depend on \( E_0 \) through gain \( g_H \) (inset) and on their relative timings. The VOR gain is modulated between 0 and 1 by ongoing gaze error, \( G_{\text{ERR}}(t) \) (inset). PSG: pulse-step generator and oculomotor plant (not shown). The relative onsets of eye- and head movements depend on stimulus modality, initial eye position, and top-down task-related signals (not shown).

The output of the oculomotor burst generator represents desired eye velocity:

\[ \dot{E}_{\text{DES}}(t) = B_E \cdot E_{\text{ERR}}(t) \]  

(6.10)
with $B_E$ (in $s^{-1}$) a linear gain. Finally, the actual eye velocity during eye-head gaze shifts is obtained after combining this signal with the VOR:
\[
\dot{E}(t) = \dot{E}_{\text{DES}}(t) - g_v(G_{\text{ERR}}(t)) \cdot \dot{H}(t)
\]  
(6.11)

where the VOR gain ($0 < g_v < 1$) is a nonlinear function of gaze error (inset Fig. 6.4). Also the head is driven by the dynamic head-motor error (see inset in Fig. 6.4):
\[
\Delta H_{\text{DES}}(t) = g_H(E_0) \cdot H_{\text{ERR}}(t)
\]  
(6.12)

where the gain $0 < g_H < 1$ is a nonlinear function of initial eye position. The desired head velocity is subsequently generated by a linear head-burst generator:
\[
\dot{H}_{\text{DES}}(t) = B_H \cdot \Delta H_{\text{DES}}(t)
\]  
(6.13)

where $B_H < B_E$. The actual head velocity results after passing the desired motor drive through the head-motor plant:
\[
\dot{H}(t) = \text{PLANT}_{\text{HEAD}}(\dot{H}_{\text{DES}}(t))
\]  
(6.14)

for which we took a simple first-order low-pass filter. Simulations with this model show that it faithfully captures the kinematics and eye-head cross-coupling properties of measured eye-head gaze shifts (Kasap2019).
6.4 Discussion

We extended our SC model of dynamic movement fields (Goossens and Van Opstal, 2006) by including a small, but significant, influence of initial eye-in-head position on the total number of spikes in the burst (gain-field model, Eqn. 6.3). We noted that eye position systematically influenced the SC firing-rate profiles:

<table>
<thead>
<tr>
<th></th>
<th>firing rates</th>
<th>burst durations</th>
<th># of spikes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ipsilateral eye</td>
<td>Lower</td>
<td>Longer</td>
<td>More</td>
</tr>
<tr>
<td>Contralateral eye</td>
<td>Higher</td>
<td>Shorter</td>
<td>Fewer</td>
</tr>
</tbody>
</table>

In many trials (~50%) we found a tight correlation ($r > 0.7$) between the instantaneous firing rate of an SC cell and the straight-line gaze-velocity profile into their movement fields (e.g., Fig. 6.3C). An eye-position signal in the motor SC has been reported before (Van Opstal et al., 1995), but it’s potential role for the control of gaze kinematics in eye-head saccades has not been reported.

Note that the linear spike-counting model (Eqn. 6.1) is a population model. As such, it predicts that the total collicular output faithfully reflects the instantaneous desired gaze displacement (cumulative spike count) and gaze velocity (total cumulative firing rate). The model does not necessarily predict that individual cells should reflect gaze kinematics on a trial-by-trial basis.

To illustrate this point, Fig. 6.5 shows a simulation with rectangular SC bursts (Fig. 6.5B), with the number of spikes determined by the static movement field. The total SC output still produced the required gaze-velocity (Fig. 6.5B) and gaze trajectory, even though none of the cells encode gaze velocity ($r = 0$; Fig. 6.5C). Therefore, the tight correlation illustrated in Fig. 6.3C underscores the role for the motor SC as the nonlinear vectorial pulse generator of the saccadic gaze-controller, as proposed in our model (Fig. 6.4).

In head-restrained monkeys, we found that spike trains correlated well with instantaneous eye-velocity because of the tight synchronization of burst profiles across the population Goossens and Opstal, 2012. We recently reported that this important aspect of neural population activity can be understood from excitatory-inhibitory lateral interactions among the SC cells in a spiking neural network (Kasap and Opstal, 2017, 2018).

We here conjecture that a similar control principle may hold for eye-head gaze saccades, whereby initial eye position influences the characteristics of SC cells in such a way that (i) their burst characteristics vary with initial eye orientation, and (ii) the total number of spikes changes too.
Figure 6.5 Simulation of a hypothetical SC - brainstem saccade model (one-dimensional, for clarity), in which all cells fire rectangular bursts. (A) Population activity in the SC motor map as function of time for a gaze shift of 30 deg. Color code represents mean firing rates. Cells at the fringes of the population start their shorter bursts later than the central cells, so that all cells reach their peak at the same time. (B) Rectangular bursts of all cells; the number of spikes of each cell is determined by the static movement field; burst duration decays exponentially with distance from the central hot spot at \( u = 3.7 \) mm. Continuous curve: instantaneous (normalized) firing rate (c.q. gaze velocity) of the population. (C) The cumulative number of spikes for each individual cell correlates well with instantaneous gaze displacement (blue), but firing rates of individual cells do not correlate at all with instantaneous gaze velocity (red).

In our spiking neural network model (Kasap and Opstal, 2017, 2018), the burst characteristics of spiking leaky-integrate-and-fire neurons depended on two parameters: the time constant of the membrane adaptation current, and the strength of synaptic weights that make up the lateral excitatory-inhibitory interactions. To ensure a fixed number of spikes in the central burst of the population, and a systematic decrease of peak firing-rate with saccade amplitude, both parameters had to depend systematically on the cell’s rostral-caudal location in the motor map. Possibly, initial eye position affects the values of these parameters for the upcoming gaze shift, leading to the observed modifications of the burst characteristics.

As a result of eye-head coupling, the inclusion of the VOR, the oculomotor range, and the eye-position influence on SC cells, each of which introduces its own nonlinearity in the system, the computational complexity of the model is markedly increased when compared to the simple linear eye-movement model of Goossens and Van Opstal, 2006. Moreover, the variable onsets of eye- and head-movements in the gaze shift, and thus their contribution and kinematics, depend on various factors, such as initial eye position, stimulus modality,
and task constraints. Thus, at first sight, one would not immediately expect
that firing rates of SC neurons would correlate so well with the dynamic gaze
trajectory.

As a final note, our model concentrated mainly on the role of the SC in gaze
control, and less on the question whether downstream brainstem-cerebellar-
spinal circuitry operates with a gaze feedback loop (like Fig. 6.4, and in the
models of Goossens and Van Opstal, 1997; Guitton and Volle, 1987; Kasap and
Opstal, 2018; Saglam et al., 2011, or without gaze-feedback by controlling inde-
pendent, but coupled eye-head circuits (like in the models of Daye et al., 2014;
Freedman, 2001; Kardamakis, Grantyn, et al., 2010). We believe that our collicu-
lar data do not rule out either hypothesis, as the SC responses already seem to
reflect all major properties of the ensuing gaze shifts and their kinematics.
REFERENCES


MODELING AUDITORY-VISUAL EVOKED EYE-HEAD GAZE SHIFTS IN DYNAMIC MULTI-STEPS

Abstract

In dynamic visual or auditory gaze double-steps, a brief target flash or sound burst is presented in midflight of an intervening eye-head gaze shift. Behavioral experiments in humans and monkeys have indicated that the subsequent eye- and head movements to the target are goal-directed, regardless of stimulus timing, first gaze-shift characteristics, and initial conditions. This remarkable behavior requires that the gaze-control system

(i) has continuous access to accurate signals about eye-in-head position, and ongoing eye-head movements,

(ii) accounts for different internal signal delays, and

(iii) is able to update the retinal (T_E) and head-centric (T_H) target coordinates into appropriate eye-centered and head-centered motor commands on millisecond time scales.

As predictive, feedforward remapping of targets cannot account for this behavior, we propose that targets are transformed and stored into a stable reference frame as soon as their sensory information becomes available. We present a computational model, in which recruited cells in the midbrain Superior Colliculus drive eyes and head to the stored target location through a common dynamic oculocentric gaze-velocity command, which is continuously updated from the stable goal, and transformed into appropriate oculocentric and craniocentric motor commands. We describe two equivalent, yet conceptually different, implementations that both account for the complex, but accurate, kinematic behaviors and trajectories of eye-head gaze shifts under a variety of challenging multi-sensory conditions, such as in dynamic visual-auditory multi-steps.

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7.1 INTRODUCTION

This paper deals with the spatial updating of target locations for rapid goal-directed eye-head gaze shifts under static and dynamic localization conditions of visual and auditory targets. Gaze is defined as the eye orientation in world coordinates, and is given by the sum of the head-in-world and eye-in-head vectors: $G_W = H_W + E_H$ (see GLOSSARY at the end of this section for a listing of variables and their definitions). We measure spatial coordinates in the world by their azimuth (horizontal plane; $\alpha$) and elevation (vertical, median plane; $\epsilon$) angles, defined in a double-pole coordinate system relative to the center of the upright head and body, when pointing straight ahead (Knudsen and Konishi, 1979).

In a standard goal-directed gaze-orienting task, the subject aligns eyes and head on a central fixation spot, prior to generating a gaze shift to a peripheral target ($T$, either visual, or auditory; Figure 7.1A). In this case, the world-, body-, head-, and eye-reference frames are all aligned (i.e., $G_0 = H_0 = 0$). The coordinates of the goal for the eye- ($\Delta G$) and head ($\Delta H$) motor responses will be identical too, and correspond to the initial sensory coordinates on the retina, or the ears. However, when the eyes are deviated from straight ahead, to $G_0$, like in Figure 7.1B, the error signals for eyes and head will differ, and be (partly) dissociated from the sensory coordinates. For example, in case of a visual target on the retina at $T_E$, the coordinates for the goal-directed head movement will be $\Delta H = T_E + E_0$, with $E_0$ the initial eye-in-head orientation. In contrast, when the target is a sound, presented at head-centered location $T_H$, the signals that should drive the eye movement are given by $\Delta G = T_H - E_0$. Experiments have demonstrated that gaze- and head-movement trajectories are indeed expressed in their appropriate eye-centered and head-centered reference frames, as both remain goal-directed, irrespective of initial conditions, and sensory modality (Goossens and Van Opstal, 1997).

An additional complexity arises when an intervening gaze shift follows target presentation, but precedes the goal-directed eye-head movement to the target. Now, the initial sensory coordinates will be fully dissociated from the required motor commands of eyes and head. This is what happens, for example, in a static double-step trial (Figure 7.1C). Here, two brief stimuli are presented in rapid succession, evoking two consecutive gaze shifts (static refers to the condition that nothing moves during target presentation). In this case, the coordinates of the second gaze shift have to incorporate the intervening eye- and head

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1 For simplicity, we confine our description to two-dimensional (2D) commutative, linear coordinate transformations, thereby neglecting the nonlinear non-commutativity of 3D rotational kinematics.
movements, elicited by the first target (at $T_1$). Because eye- and head-movement trajectories typically differ in a gaze shift, the orientations of eyes and head at the end of the gaze shift will be different too, and the subsequent goal-directed movements will have to be generated in quite different directions. Depending on the sensory modality of the target (visual vs. auditory), the required coordinate transformations for the gaze- and head-movements will differ too. Behavioral experiments in humans (Goossens and Van Opstal, 1997) and monkeys (Van Grootel, Van der Willigen, et al., 2012) have demonstrated that these coordinate transformations are indeed accurately performed.

Arguably, a more challenging localization problem arises when a brief visual or auditory target is presented in midflight of a fast intervening eye-head gaze shift (Figure 7.1D; Vliegen, 2004; Vliegen et al., 2005). In this dynamic double-step paradigm the target is presented at time $t^*$, when the eye, on its way to $T_1$, has reached gaze position $G^*$, while the head may be at $H^*$. To subsequently orient towards the extinguished target location with a goal-directed gaze shift is not trivial, as timing ($t^*$), location, and modality of the target are all unpredictable to the system. As a result, neither the target coordinates ($T^*_E$ and $T^*_H$), nor the appropriate eye-head motor commands ($\Delta H$, $\Delta G$), can be programmed beforehand, which is in principle possible for the other three scenarios (Fig. 7.1A-C). Instead, the sensory signals, coordinate transformations, and updated motor commands have to be determined on the fly, during the rapid gaze shift, within a few tens of milliseconds.

Table 7.1 summarizes the required coordinate transformations for the eye and head, in case of a visual and an auditory target, for the static and dynamic double-step paradigms, respectively, where the symbols refer to Figure 7.1C,D.

Behavioral experiments in humans and monkeys have demonstrated that eye- and head movements remain indeed goal directed, regardless stimulus timing, first gaze-shift characteristics (fast, slow, accurate, or inaccurate), modality (visual vs. auditory), and initial conditions (aligned, unaligned, eye-head onset delay; Van Grootel, Van der Willigen, et al., 2012; Vliegen, 2004; Vliegen et al., 2005). This remarkable behavior requires that the gaze-control system:

(i) has continuous access to accurate signals about eye-in-head orientation, $E_H(t)$, and eye- and head motor errors (see Table 7.1),

(ii) accounts for different internal delays for visual and auditory signals,

(iii) updates visual ($T^*_E$) and acoustic ($T^*_H$) target coordinates into appropriate eye-centered and head-centered motor commands on millisecond time scales.
Figure 7.1 (A-D) Four scenarios for programming a goal-directed eye-head gaze shift to a peripheral target, T, in increasing order of complexity. (A,B) Gaze shifts to a single target with different initial conditions. (C) In the static double-step, the complete intervening gaze shift, \( \Delta G_1, \Delta H_1 \), should account for the target updates. (D) In the dynamic double step, however, only the unpredictable part of the intervening movements after \( t^* \), \( (\Delta G^*_1, \Delta H^*_1) \), should be compensated. See text and Table 7.1, for further explanation.

We have argued that a predictive, feedforward remapping strategy of target coordinates (like proposed, e.g., by Goldberg and Bruce, 1990 and Duhamel et al., 1992, for head-restrained visuomotor tasks) cannot account for this behavior, as the system has no prior access to the unpredictable stimulus properties (timing and modality), nor to the intrinsic, highly variable, partial eye- and head movements that precede and follow target presentation Vliegen, 2004; Vliegen et al., 2005.
### Static double-step

<table>
<thead>
<tr>
<th>Second target modality</th>
<th>Gaze coordinates, $\Delta G$</th>
<th>Head coordinates, $\Delta H$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visual</td>
<td>$\Delta G = T_E - \Delta G_1$</td>
<td>$\Delta H = T_E - \Delta G_1 + E_1$</td>
</tr>
<tr>
<td>Auditory</td>
<td>$\Delta G = T_H - \Delta H_1 - E_1$</td>
<td>$\Delta H = T_H - \Delta H_1$</td>
</tr>
</tbody>
</table>

### Dynamic double-step

<table>
<thead>
<tr>
<th>Second target modality</th>
<th>Gaze coordinates, $\Delta G$</th>
<th>Head coordinates, $\Delta H$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visual</td>
<td>$\Delta G = T_E^* - \Delta G_1^*$</td>
<td>$\Delta H = T_E^* - \Delta G_1^* + E_1$</td>
</tr>
<tr>
<td>Auditory</td>
<td>$\Delta G = T_H^* - \Delta H_1^* - E_1$</td>
<td>$\Delta H = T_H^* - \Delta H_1^*$</td>
</tr>
<tr>
<td>Partial movement after $t^*$</td>
<td>$\Delta G_1^* = \Delta G_1 - \Delta G^*$</td>
<td>$\Delta H_1^* = \Delta H_1 - \Delta H^*$</td>
</tr>
</tbody>
</table>

Table 7.1 Required coordinate transformations for the eye and head in space for static and dynamic double steps, with a visual or auditory second target. $E_1$ is the eye-in-head position after the first gaze shift; $\Delta G^*$, $\Delta H^*$ are the partial gaze- and head movements up to target presentation at $t^*$. Note that $\Delta G_1^*$, $\Delta H_1^*$ correspond to the instantaneous gaze- and head motor errors of the intervening gaze shift at $t^*$ (grey arrows in Fig. 1D).

One possible way to understand goal-directed orienting under these challenging conditions, expands on the original ideas of Robinson, 1975; Robinson, 1973, by assuming that targets are not kept in their original sensory coordinates, but are mapped into a world-centered reference frame, as soon as the sensory information becomes available (at $t = t^*$). In such a scheme, illustrated in Fig. 7.2 (left-hand side), the coordinates of retinal targets are transformed into

$$T_W^{VIS} = T_E(t^*) + E_H(t^*) + H_W(t^*)$$  \hspace{1cm} (7.1)

and the craniocentric acoustic coordinates of a sound source become

$$T_W^{AUD} = T_H(t^*) + H_W(t^*)$$ \hspace{1cm} (7.2)

It is not immediately obvious how Eqns. 7.1 and 7.2 are embedded in the system, given that the visual (about 60-70 ms) and auditory (10-15 ms) sensory delays to the primary cortices and midbrain are quite different. Since the feedback signals should refer to the onset of the stimulus ($t^*$), they should also account for these modality-dependent delays.

Yet, because the world-centered target coordinates of Eqns. 7.1 and 7.2 are invariant to any further intervening eye- and head movements, the system could store target information in a stable spatial memory, and plan a series of spatially
accurate gaze shifts to different targets in the absence of any further sensory input. Another advantage of a single coordinate transformation of targets, is its insensitivity to the accumulation of updating errors, which would occur when target updates would have to be made after every intervening movement (Van Grootel and John Van Opstal, 2009).

In Figure 7.2, we incorporated these world-centered coordinate transformations into a conceptual scheme, in which the population in the gaze-motor map of the midbrain Superior Colliculus (SC) specifies a common dynamic gaze-displacement signal for the brainstem (oculomotor system) and spinal cord (head-motor system). As the eyes and head move, the stable world-centered target coordinates for the next gaze shift are continuously updated into appropriate eye-centered target coordinates, through instantaneous feedback about intervening changes in eye- and head position, e.g. during an ongoing gaze shift:

\[
\Delta G(t) = T_W - E_1(t) - H_1(t)
\]  

(7.3)

At gaze-shift offset (around \(t = t_1\)), this updated signal becomes available to the motor map for the next gaze-shift command in a double-step: \(\Delta G_2 = \Delta G(t_1)\).

**Figure 7.2** Outline of dynamic target-updating, and eye-head gaze control, as described by Vliegen et al., 2005. The scheme incorporates a dynamic update of auditory and visual targets into stable world-centered coordinates, \(T_W\), (Eqns. 7.1 and 7.2) to program the next eye-head gaze-shift (Eqn. 7.3). The SC motor map generates a dynamic gaze command, \(\dot{G}\), that rapidly drives eyes (\(\Delta G_2\)) and head (\(\Delta H_2\)) in their appropriate reference frames to the target (note that all signals represent 2D vectors). Details of the eye- and head motor systems have been omitted, for clarity (see Methods, Figs. 7.3 and 7.4).
We implemented a computational model, based on the scheme of Figure 7.2, in which a population of neurons in the midbrain SC drives the eyes and head to multiple stored target locations. The SC cells encode the desired gaze trajectory, and its kinematics, through their cumulative spike counts, and instantaneous firing rates, respectively (Goossens and Van Opstal, 2012; Goossens and Van Opstal, 2006). Despite a number of simplifications in our model regarding the details of brainstem and cerebellar involvement in the downstream motor circuitry, and the eye- and head motor plants, it accounts for the complex, yet accurate, kinematic behaviors and trajectories of measured eye-head gaze shifts under challenging multi-sensory conditions, such as obtained in static and dynamic visual-auditory multi-steps (Fig. 7.1). An alternative scheme, based on instantaneous gaze- and head- motor-error feedback, is also discussed.
GLOSSARY

- $B(t)$: Oculomotor burst generator output (desired eye velocity)
- $D$: Burst duration of SC output
- $E_{DES}$: Desired eye-in-head position within the OMR
- $G^*,H^*$: Ongoing gaze and head positions at target presentation
- $\dot{G}_{DES}(t)$: Gaze-velocity pulse from SC motor map (rectangular pulse)
- $g_H$: Attenuating gain for the head-motor error vector
- $G_0,H_0,E_0$: Initial gaze, head and eye-in-head positions
- $G_{pk}$: Peak activity of SC output burst
- $G(t),H(t),E(t)$: Gaze-, head-, and eye position at time $t$
- $\dot{G}(t),\dot{H}(t),\dot{E}(t)$: Gaze-, head-, and eye velocity at time $t$
- $g_v(G_{ERR})$: Gaze-error-dependent VOR gain (Fig. 7.4A)
- $\text{OMR}_H,\text{OMR}_V$: Horizontal, vertical oculomotor ranges around straight ahead
- SC: Superior colliculus
- $t^*$: Time of target presentation during ongoing gaze shift
- $T_E,T_H$: Retinal (visual) and head-centric (auditory) target coordinates
- $T_W^V,T_W^A$: Visual and auditory targets-in-world
- $T_W$: Target in world coordinates
- $\alpha,\epsilon$: Azimuth and elevation angles (deviation from straight ahead)
- $\Delta E_{G,0}$: Initial eye-position component in the direction of $\Delta G$
- $\Delta G^*,\Delta H^*$: Ongoing gaze and head motor errors at target presentation
- $\Delta G_{DES},G_{ERR}(t)$: Desired gaze displacement, and current gaze motor error
- $\Delta H_{DES},H_{ERR}(t)$: Desired head displacement, current head motor error
- $\Delta_H(MOD,\Delta E_{G,0})$: Modality, and eye position-dependent head-onset delay
7.2 METHODS AND RESULTS

Simulations were performed in Matlab (The Mathworks, Natwick, USA, version 14a). The Matlab script of the dynamic updating model in world-coordinates is available in the Supplementary material as GazeMultiSteps.m.

**Internal delays.** Suppose a gaze shift is made in some arbitrary direction, with gaze- and head movement trajectories, \( G(t) \) and \( H(t) \) (\( t \) is the current time), and that at time \( t = t^* \), a visual target appears on the retina, with coordinates \( T_{E,RET}(t^*) \). This visual signal reaches the perceptual system (cortex) at time \( t_1 \), after a delay of approximately 60 ms, so that \( T_{E,PERC}(t_1) = T_{E,RET}(t^* + 60) \).

According to Eqn. 7.1, specifying the world-centered location of a visual target at the time of the flash needs eye- and head-position signals that refer to \( t^* \). However, for a rapid gaze shift these positions may differ substantially from those measured at the perceived time \( t = t_1 \). Suppose that the percept of both position signals is delayed by 20 ms, then: \( G_{PERC}(t_1) = G(t_1 - 20) \) and \( H_{PERC}(t_1) = H(t_1 - 20) \). As the signals should be referred to the target flash in the visual field, i.e. at \( t^* = t_1 - 60 \), we get \( G(t^* + 40) \). Thus, the visuomotor system should possess a memory buffer for gaze- and head positions of about 40 ms to correctly map the retinal target into a world-centered reference frame: \( T_{W}^* = T_{E}^* + G^* \). For sounds, the sensory-cortical delay is about 20 ms, so that the memory span for head position to auditory targets would be about 20 ms: \( T_{W}^* = T_{H}^* + H^* \). In what follows, we assumed that these internal delays are appropriately compensated in the system, and we discarded them in our calculations, for simplicity.

**Generating the eye-head gaze shift.** Once \( T_W \) is constructed (and tagged for the next gaze shift), its associated gaze error is calculated from the instantaneous eye- and head positions by Eqn. 7.3. At \( \text{go}^{\text{end}} \) time, \( t_2 \), the population of cells in the SC motor map thus represents the desired gaze-displacement command \( \Delta G_2 \). While this gaze shift is executed, the changing eye- and head positions are used to update the gaze coordinates (Eqn. 7.3) for the next target (if in memory).

The gaze shift is driven by the linear spike-count model of the SC, as proposed by Goossens and Van Opstal, 2012; Goossens and Van Opstal, 2006. Although this model was originally formulated for head-restrained eye saccades, we here extend this concept to eye-head gaze shifts\(^\text{2} \). Now, each spike (\( s \)) from each cell (\( k \)) in the SC contributes a fixed (small) spike vector, \( \vec{m}_{k,s} \), to the desired

---

2 Recordings in head-unstrained monkeys indicate similar spike-count behavior of SC cells for gaze shifts than for head-restrained eye saccades, reported by Goossens and Van Opstal, 2012; Goossens and Van Opstal, 2006: the cumulative number of spikes in the burst encodes a straight gaze shift (Opstal and Kasap, 2019a).
gaze command, the size and direction of which depend solely on the cell’s location in the motor map. The desired gaze shift is then encoded by the linear cumulative sum of all spike vectors from all spike trains in the saccade-related SC bursts:

\[
\Delta G(t) = \eta \sum_{k=1}^{S_k < t} \overline{m}_k \delta(t - \tau_{k,s})
\]

(7.4)

with \(N\) the number of cells in the recruited population, \(\eta\) a fixed scaling constant, and \(\delta(t - \tau_{k,s})\) is a spike at time \(\tau\); thus, \(\tau_{k,s}\) is the timing of spike \(s\) from cell \(k\), and \(S_k < t\) is the cumulative number of spikes from cell \(k\), up to the current time, \(t\).

Note, from Eqn. 7.4, that the firing rates of the neurons directly influence the planned gaze kinematics. Indeed, our recordings have shown that the SC motor map encodes the kinematic main-sequence relations of saccades by a spatial gradient in the peak firing rates of the neurons (high at the rostral zone for small-amplitude saccades, and lower at the caudal SC, for large saccades; Goossens and Van Opstal, 2006), in combination with a fixed number of spikes in the burst (see below, implementation). As a result, the instantaneous firing rates of all SC neurons together encode the (desired) gaze-velocity profile, while the cumulative number of spikes (the time integral of the bursts) encodes the amplitude of the gaze shift (illustrated in the inset of Fig. 7.3A). The nonlinear main-sequence kinematics of gaze shifts are thus entirely encoded by the SC, leaving the brainstem and spinal cord movement generators essentially linear (performing vector decomposition; Goossens and Van Opstal, 2006).

Figures 7.3 and 7.4 show the different steps that specify how a common oculocentric collicular signal generates the goal-directed movements of gaze and head. The head movement is driven by a cranio-centric motor error, which is transformed into a desired head-movement vector in the same direction, \(\Delta H_{\text{DES}}\) (Fig. 7.3B, inset). The amplitude of the head movement is determined by an eye-position dependent gain: \(\Delta H_{\text{DES}} = g_H \cdot H_{\text{ERR},0}\) (see inset, Fig 7.4B). Experiments have demonstrated that if the eye looks contralateral to the target, the head movement contribution will be relatively small, as most of the gaze shift will be carried by the eye. Conversely, if the eye looks into the direction of the target (ipsi), the head-movement contribution is larger (and the gaze shift will be slower; Goossens and Van Opstal, 1997).

**Model implementation.** The simulations ran at a time resolution of 1 ms (i.e., feedback signals arrived with a delay of one sample). The set of equations for the eye- and head-motor signals in the model is described as follows: The pop-
Figure 7.3 Decomposition of the desired gaze-velocity output of the SC population into goal-directed oculocentric and craniocentric motor commands. (A) The difference between desired gaze-velocity (SC output, inset) and feedback from the actual gaze-velocity (sum of the ongoing eye- and head velocities) is integrated (like in Scudder, 1988 model, albeit that the SC command represents a dynamic signal), yielding dynamic gaze-motor error, $G_{ERR}(t)$. To prevent the eyes from running into the oculomotor limits, this signal has to be transformed into a craniocentric error, $H_{ERR}(t)$, by combining it with instantaneous eye position. (B) This craniocentric error subsequently determines the desired eye position within the oculomotor range (OMR) for the gaze shift. Note that $E_{H,DES}$ changes during the gaze shift, because of the gaze- and eye-position feedback. fov: fovea; $E_{H,0}$: initial eye position; $\Delta H_{DES}$: desired head displacement.

ulation of recruited cells in the SC motor map effectively issues a gaze-velocity pulse (by the summed instantaneous firing rates of all neurons), which is given by $G_{DES}(t)$ (see e.g. inset, Fig. 7.3A). In the most straightforward simulations, this profile was approximated by a simple rectangular pulse, with an amplitude that specified the peak gaze velocity, and a duration that increased with gaze amplitude (the integral of the pulse):

$$\Delta G_{DES}(t) = \begin{cases} G_{PK} & \text{for } 0 \leq t \leq D + c \Delta E_{G,0} \\
0 & \text{elsewhere} \end{cases} \text{ with } \begin{cases} D = a + b \cdot \Delta G \\
G_{PK} = \frac{20}{D} \end{cases} (7.5)$$
Figure 7.4 (A) The linear oculomotor burst generator (Goossens and Van Opstal, 2006; Goossens and Opstal, 2012) is driven by instantaneous eye-motor error, $E_{ERR}(t)$, derived from the (dynamic) desired eye position (Fig. 3B). Its output is a desired eye-velocity signal, which is modified by the vestibular ocular reflex (VOR) into the actual eye-in-head velocity, $\dot{E}_H(t)$ ($g_V$ is the VOR gain, which depends on current gaze error, see inset). This latter signal acts as an efference copy for the gaze-velocity comparator (Fig. 3A), and is integrated by the neural integrator in the pulse-step generator (PSG) to provide an efference copy of eye position, $E_H(t)$. (B) The head-movement controller is driven by a desired head displacement, $\Delta H_{DES}$, which is proportional to the initial head motor error (Fig. 3A), head-onset delay, $\Delta t_H$, that depends on initial eye position (inset). The head-velocity feedback for the gaze comparator is derived from the vestibular system, which measures the actual head velocity with respect to the world (SSC: semicircular canals).

where $a (20 \text{ ms})$, $b (1.5 \text{ ms/deg})$ and $c (0.3 \text{ ms/deg})$ are constants, and $\Delta E_{G,0}$ is the initial eye-in-head position component along the gaze-shift vector Fig. 7.5:

$$\Delta E_{G,0} = \frac{\left(\vec{E}_0 \cdot \Delta \vec{G}\right)}{||\Delta \vec{G}||^2} \cdot ||\vec{E}_0||$$  \hspace{1cm} (7.6)

For contralateral eye positions, $\Delta E_{G,0} < 0$ (decrease in SC burst duration, increase of the peak firing rate), and for ipsilateral positions, $\Delta E_{G,0} > 0$. In this way, the cells in the SC motor map specify the nonlinear main-sequence kinematics of saccadic gaze shifts (a straight-line amplitude-duration function, and
a saturating amplitude-peak velocity relation), by adjusting the peak firing rates according to a decreasing spatial gradient along the rostral-caudal (gaze-amplitude) axis of the map (Goossens and Opstal, 2012; Opstal and Goossens, 2008), as well as the dependence on initial eye position. The efferent mapping (synaptic projections to the motor systems) ensures that the integral of the burst encodes the correct gaze-shift amplitude.

Figure 7.5 Example SC burst profiles, as used in the simulations, for different gaze shifts (small, medium, and large), and for different initial eye positions (shown for the center bursts only). Each burst has the same number of spikes (N=20), but its height systematically decreases from the rostral-to-caudal end of the motor map. The efferent projections to the brainstem burst generators weigh the bursts to specify the gaze-shift amplitude and its velocity. Initial eye position influences the burst duration and its peak firing rate: duration increases/decreases for eye positions in the same/opposite direction (ipsi/contra) as the upcoming gaze shift.

The gaze-motor error (Fig. 7.3A) is then determined by the cumulative time integral of the difference between the desired and actual gaze velocity:

$$G_{ERR}(t) = \int_0^t (\dot{G}_{DES}(\tau) - \dot{E}_H(\tau) - \dot{H}_W(\tau)) d\tau$$  \hspace{1cm} (7.7)

Clearly, this gaze error may specify a movement that would exceed the mechanical limits of ocular motion (Fig. 7.3B, inset). To prevent this from hap-
pening, the gaze error is transformed into a craniocentric error, to determine the desired eye-in-head position, $E_{\text{DES}}(t)$, constrained by a soft oculomotor range (OMR; Fig. 7.3B). In our simulations, we described the OMR by a simple rectangle, with the horizontal eye position confined to $|E_{H,x}| < \text{OMR}_{H}$ and $|E_{H,y}| < \text{OMR}_{V}$. When the target remains within the OMR, the desired eye position is simply $E_{\text{DES}} = E_{H} + \Delta G$. When it’s outside the OMR (like in Fig. 7.3B), $E_{\text{DES}}$ is determined by the intersection of the line between fovea and target, and the OMR.

The desired eye position signal drives the eye velocity output of the brain-stem burst generator within a (linear) eye-position feedback loop, just like in Robinson’s influential eye-position feedback model (Van Gisbergen, Robinson, et al., 1981). However, in contrast to Robinson’s original concept:

- the desired eye position (the goal) is a dynamic signal that changes during the gaze shift,
- the input-output characteristic of the burst generator is linear, and
- the actual eye-in-head velocity is modified by the head movement on the output of the oculomotor burst generator (the desired eye velocity signal) through the (gain-modulated) VOR:

$$\dot{E}_{H}(t) = \dot{E}_{\text{DES}}(t) - g_{V}(G_{\text{ERR}}(t)) \cdot \dot{H}(t)$$

(7.8)

where the VOR gain, $g_{V}$, varies in a sigmoid fashion with the instantaneous gaze-motor error: it is close to zero when the gaze error is large, and close to one when the error approaches zero (e.g., Laurutis and Robinson, 1986; Tabak et al., 1996).

Together with the eye movement, the desired head-motor command (issued with an onset delay, $T$, re. gaze onset) is also derived from the collicular desired gaze shift (Fig. 7.3A), and is calculated as follows:

$$\Delta H(t - T) = g_{H}(\Delta G, E_{H}(0)) \cdot \left[ \int_{0}^{t} \hat{G}_{\text{ERR}}(\tau) d\tau + E_{H}(t) \right] + g_{E} \cdot \dot{E}_{\text{DES}}(t)$$

(7.9)

where the head-onset delay, $\Delta t_{H}$, depends on the initial eye-position component along the gaze shift, and on the sensory modality:

$$\Delta t_{H} = p_{\text{MOD}} - d \cdot \Delta E_{G,0} + N(0, 15)$$

(7.10)

where we took $p_{\text{MOD}} = 30$ ms for a visual target, and 10 ms for an auditory target (e.g., Goossens and Van Opstal, 1997), and $d = 0.3$ ms/deg. $N(0, 15)$ is...
a Gaussian random variable with zero mean and std=15 ms. The attenuating head gain, $g_H$, was taken as 0.6 for the horizontal component, and 0.4 for the vertical component. The result of Eqn. 7.10 implicitly determines the actual contribution of the head movement to the gaze shift: it will be large for short delays (auditory targets, ipsilateral eye positions), and small for longer delays (visual targets, contralateral eye positions).

It should be noted that the desired head displacement of Eqn. 7.9 typically differs from the actual contribution of the head movement to the gaze shift. As the latter is determined at gaze-saccade offset, the former may be considerably larger. Especially at long head delays (e.g., for contralateral eye positions), the head movement contribution, $\Delta H_{Goff} = \Delta G - \Delta E_{H,Goff}$, will be relatively small, although the total head movement may still be considerable.

The head velocity (output from a simple first-order head plant) is measured by the VOR, and is subsequently used

(i) to modulate the desired eye velocity from the burst generator ($E_{DES}$; Eqn. 7), and

(ii) to construct the gaze-velocity feedback.

The right-hand term in Eqn. 7.8 accounts for the (small) influence of the oculo-motor burst generator ($g_E$) on the head-motor response (reported by Goossens and Van Opstal, 1997). The integrated outputs of the actual eye- and head velocities are instantaneous eye- and head position, respectively, both of which are used in the world-centric target updates of Figs. 7.2 and 7.5.

Target Updating

**Sampled eye- and head positions.** The switches in the target update mechanism of Fig. 7.2 symbolize the sampling of the eye- and head-position feedback signals at stimulus presentation time. Figure 7.6 illustrates four subsequent target events: two visual targets presented on the retina (at $t_1$ and $t_3$), and auditory targets presented at $t_2$ and $t_4$, where $t_1 < t_2 < t_3 < t_4$.

The system detects and stores each target event, whenever the temporal derivative in sensory space exceeds a threshold. In Fig. 7.6A, we illustrated this for step-like sensory changes, for which the derivatives are mere delta functions
Figure 7.6 (A) Example target appearances in the visual and auditory channels, with the associated triggers at $t_1 - t_4$, representing the sampling switches in Figure 2. (B) Multiplying ongoing eye position with a measure for the rapid sensory change, which approximates a delta function, yields the sampled signal (here: eye position) at target appearance. (C) Calculation of the world-centered target locations, presented during ongoing gaze (black trace) and head (blue trace) movements (generated by a sum of sines, for illustration purposes). Red trace: $E_{11}(t)$. Small squares within the gaze and head trajectories: sampled gaze (red) and head (blue) positions at the four target onsets.

that sample the eye- and head positions precisely at stimulus onset, according to (Fig. 7.6B):

$$
T_{W,1}^V = T_{1}^E + E(t) \cdot \delta(t - t_1) + H(t) \cdot \delta(t - t_1) \\
T_{W,2}^A = T_2^H + H(t) \cdot \delta(t - t_2) \\
T_{W,3}^V = T_3^E + E(t) \cdot \delta(t - t_3) + H(t) \cdot \delta(t - t_3) \\
T_{W,4}^A = T_4^H + H(t) \cdot \delta(t - t_4)
$$

(7.11)

where

$$
\delta(t - t_N) \approx \left| \tilde{S}_N(t) \right| = \left| \left( \frac{\partial S_{x,N}(t)}{\partial t}, \frac{\partial S_{y,N}(t)}{\partial t} \right) \right| 
$$

(7.12)

for visual and auditory targets (Figure 7.6). The derivative reports a sudden sensory change at any (retinal or head-centered) location. Note that this could be a change in target position, in stimulus intensity, in visual contrast, in interaural level difference, etc.
Model responses

The model responses faithfully mimic the natural behavior of measured eye-head gaze shifts. Figure 7.7A illustrates a number of gaze shifts in different directions and amplitudes, all starting from aligned initial conditions from straight ahead. We also added two example trajectories of gaze shifts having unaligned initial conditions. In these two examples, it can be seen that both gaze and head make goal-directed movements, and therefore follow different spatial trajectories. In Fig. 7.7B we plotted the main-sequence peak-velocity behavior of gaze shifts for amplitudes between 5 and 65 deg for three different conditions: initial positions of the eye and head aligned (red), the eye looking in the ipsilateral direction (between +16 to +50%) of the upcoming gaze shift (blue), and in the contralateral direction (between -20 to -100%; green). Note that there is no unique main-sequence relation for eye-head gaze shifts, as the peak velocities depend strongly on the initial eye position: the contralateral condition yields the fastest gaze shifts, while ipsilateral initial conditions produce markedly slower gaze shifts.

The influence of initial eye position on the detailed kinematics of simulated gaze shifts and the associated head- and eye movements is further illustrated in Fig. 7.8, for 50 deg oblique gaze saccades, generated for three initial eye-in-head positions: contralateral (-37%; Fig. 7.8A), aligned (Fig. 7.8B) and ipsilateral (+37%; Fig. 7.8C). Note the different head movements, and the associated changes in the gaze-velocity profiles for the different initial conditions.

An example for static multistep head- and gaze trajectories, made by a monkey towards a series of three visual targets (taken after Bremen et al., 2010) is shown in Fig. 7.9. As the visual targets had a duration 900 ms in this experiment, the three consecutive gaze shifts were all executed under closed-loop static visual-feedback (like in Fig. 7.1B).

Figure 7.10A shows a simulation of eye-, head-, and gaze-trajectories, when the multiple target steps (N =5) were made in an open-loop static localization mode, as in Fig. 7.1C, and to both visual and auditory targets that alternated in the sequence. In this simulation, the brief target flashes (and sound bursts) were presented before the onset of the intervening gaze shift to the previous target (Fig. 7.7B). The model produces spatial trajectories, shown in Figure 7.7, which have a clear resemblance to the head and gaze trajectories of the monkey (Fig. 7.6). Table 7.2 gives the sensory coordinates at the moment of target presentation (for visual: retinal coordinates, for auditory: craniocentric coordinates), as well as the calculated world-centered target coordinates, and evoked gaze shifts.
Figure 7.7 Single-target gaze shifts. (A) Spatial trajectories for 8 gaze shifts to visual and auditory targets in different directions and amplitudes with eye and head aligned at straight ahead (center of the cross). Two example trajectories are shown for incongruent initial conditions: rightward eye fixation for a visual target, and a leftward eye fixation for an auditory target. Note that the gaze- and head trajectories are both goal-directed. (B) The gaze kinematics depend on the initial conditions: with the eyes and head aligned, the gaze shifts follow a nonlinear main-sequence relation (red squares). Faster gaze shifts occur when the eyes fixate in a direction contralateral to the gaze shift (green symbols). Gaze shifts become markedly slower when the eyes fixate in the ipsilateral direction of the gaze shift (blue symbols). See also Fig. 7.8.

Figure 7.11 illustrates the behavior of the model under dynamic localization conditions in a VV sequence (like in Fig. 7.1D), in which target $V_2$ appeared in midflight of the first visual-evoked eye-head gaze shift. The trajectories of the gaze- and head-movements were all goal-directed, despite the considerable differences in initial conditions at the end of the intervening gaze shifts (Fig. 7.11A). Even though both gaze shifts could have amplitudes that would carry the eye beyond the oculomotor range, the complex eye-in-head movement trajectory stayed within the OMR of $[\pm 25, \pm 20]$ deg.

The stimulus timings (magenta lines), as well as the horizontal/vertical time traces of the gaze-, head- and eye-movements, are shown in Fig. 7.11B. In this panel, we also included the simplified SC bursts (rectangular pulses), each scaled for the upcoming gaze-amplitude, according to Eqn. 7.5. The kinematics of gaze, eye and head for the two gaze shifts are presented in panel Fig. 7.11C.

Table 7.3 provides the target and movement coordinates at the moment of presentation during the gaze shifts.
### Table 7.2

<table>
<thead>
<tr>
<th>Target</th>
<th>Sensory coordinates</th>
<th>World coordinates</th>
<th>Gaze shifts</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hor. (°)</td>
<td>Vert. (°)</td>
<td>Hor. (°)</td>
</tr>
<tr>
<td>V1</td>
<td>35.0</td>
<td>10.0</td>
<td>25.0</td>
</tr>
<tr>
<td>A2</td>
<td>0.0</td>
<td>30.0</td>
<td>11.0</td>
</tr>
<tr>
<td>V3</td>
<td>-55.0</td>
<td>0.0</td>
<td>-43.4</td>
</tr>
<tr>
<td>A4</td>
<td>0.0</td>
<td>-20.0</td>
<td>-34.7</td>
</tr>
<tr>
<td>V5</td>
<td>35.0</td>
<td>10.0</td>
<td>-0.2</td>
</tr>
</tbody>
</table>

Table 7.2 Columns 2-3: sensory coordinates (in deg) at the time of stimulus presentation ($t^*$), either on the retina (visual), or relative to the head (auditory). In Fig. 7A the sensory coordinates are shown as red (visual) and blue (auditory) dotted lines between the gaze (visual) and head (auditory) traces, taken at the moment of target presentation ($t^*$; small squares), and the associated target location (as in Fig. 5C). Columns 4-5: The world coordinates correspond to the red (visual) and blue (auditory) squares in Fig. 7A. Columns 6-7: The updated gaze-shift vectors are given in polar coordinates (-90° = down, 0° = right, +90° = up; 180° = left).

### Table 7.3

<table>
<thead>
<tr>
<th>Target</th>
<th>Sensory coordinates</th>
<th>World coordinates</th>
<th>Gaze shifts</th>
</tr>
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<tr>
<td></td>
<td>Hor. (°)</td>
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</tr>
<tr>
<td>V1</td>
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<tr>
<td>A2</td>
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<tr>
<td>A4</td>
<td>45.0</td>
<td>-20.0</td>
<td>9.7</td>
</tr>
</tbody>
</table>

Table 7.3 Simulation results for dynamic multi-steps, shown in Fig. 8, in the same format as Table 7.2. In Fig. 7A, the sensory coordinates are shown as red (visual) and blue (auditory) dotted lines between the gaze (visual) and head (auditory) traces, taken at the moment of target presentation ($t^*$, small squares in the appropriate traces), and the associated target location (as in Fig. 7C). Note that targets 2, 3, and 4 appeared in midflight of gaze shifts 1, 2, and 3.
Figure 7.8 Simulated gaze shifts with fixed polar coordinates, $R=50$ deg, $\hat{N}=37$ deg, but for three different initial eye-in-head fixations. (A) Initial eye position in the contralateral direction ($-37\%$) of the gaze shift, at $E_0=(-15,-11.2)$ deg. (B) The eyes are centered in the head, $E_0=(0,0)$. (C) The eyes look in the ipsilateral direction ($+37\%$) of the gaze shift, at $E_0=(+15,+11.2)$ deg. Left-hand column: eye-, head- and gaze trajectories. Right-hand column: eye-, head- and gaze-vectorial velocities. Note the strong eye-position dependence of the contributions of the eye and head to the gaze shift, as well as to the gaze kinematics and head-onset delay. The fastest gaze shift, with the largest eye movement, and smallest and latest head movement is obtained for the eye in the contralateral initial position (A). The slowest gaze shift with the smallest eye movement and the largest head movement is obtained for the eye in the ipsilateral direction (C).
Figure 7.9 (A) Closed-loop head- and gaze trajectories to a sequence of three visual targets, measured in monkey (after Bremen et al., 2010). Targets were presented as in Fig. 7.1B; gaze shifts could be planned on the basis of visual feedback. (B) Corresponding gaze- and head track velocities. The target presentation times are indicated by the gray horizontal bars, and their onsets by the dotted lines.

Figure 7.10 (A) Simulated open-loop eye-, head- and gaze trajectories to a series of five static multiple-step targets (VAVAV), presented as in Fig. 7.1C. (B) Track velocities of the gaze shifts (black) and of the head (blue). Note the correspondence with the measured trajectories of the monkey. Magenta lines: onsets of the brief visual and auditory targets.
Figure 7.11 Model performance under dynamic double-steps to two subsequent visual targets (VV), where the second target is presented in midflight of the first gaze shift. (A) Visual (red squares) targets are indicated in their order of presentation, in the world-centered coordinate system of the plot. Eye-in-head (green trace) and head-in-space (red trace) started with a gaze shift (black trace) from an aligned initial condition (at 1) to the first target (VIS 1). Note that the gaze- and head traces are goal directed. OMR = oculomotor range in the head. (B) Time traces. Solid lines: horizontal position of eye-in-head (green), gaze- (black) and head-in-space (red); dashed lines vertical position traces. The thin rectangular pulses show the SC bursts for the two gaze shifts, for which the duration and height depend on the gaze-shift amplitude and initial eye position (which is $E_1$ for the second gaze shift; Eqn. 7.5). Magenta lines: stimulus presentation times. VOR: vestibular ocular reflex after gaze offset. Note that the second gaze shift ($AG_2$) starts during the second SC burst. (C) Vectorial velocity profiles of the different movement components during the two gaze shifts. The VOR is indicated. The head movement in the first gaze shift starts simultaneously with the eye at gaze onset; in the second gaze shift it is delayed by ~ 50 ms, resulting in a double-peaked gaze-velocity profile.
We proposed a model for eye-head gaze control that copes with dynamic multisensory and multistep localization problems. As illustrated in Figure 7.1D, and in Table 7.1, these sensory conditions impose several nontrivial updating challenges to the system. Nevertheless, behavioral experiments with humans (Vliegen, 2004; Vliegen et al., 2005) and monkeys (Van Grootel, Van der Willigen, et al., 2012) have indicated that accurate and precise dynamic target updating can operate at millisecond time scales.

To our knowledge, our model is the first to deal with multi-target and multisensory dynamic feedback behavior; the large majority of models so far had been designed to explain the generation of combined eye-head gaze shifts to single (typically visual) targets (as in Figure 7.1A,B; Daye et al., 2014; Freedman, 2001; Galiana and Guitton, 1992; Guitton, 1992; Guitton and Volle, 1987). Moreover, most models were restricted to horizontal gaze shifts, without the additional complexities of cross-coupling the horizontal and vertical movement components, which arise for oblique gaze shifts (with some notable exceptions, e.g., Daye et al., 2014; Goossens and Van Opstal, 1997; Tweed, 1997).

**Major differences with earlier models.** Our model extends earlier proposals in several ways: (i) The midbrain SC acts as a nonlinear vectorial pulse generator, that encodes through its recruited population not only the amplitude and direction of the upcoming gaze shift vector, but also specifies, through the distribution of its spike trains, the desired instantaneous gaze-shift kinematics and trajectories. As head-restrained saccades, with aligned initial conditions, have characteristic main-sequence properties (a saturating amplitude-peak velocity relation), the SC has been proposed to implement this nonlinear behavior through a topographic organization (i.e., a spatial, rostral-caudal gradient) of peak firing rates, burst durations, and burst skewness, within the motor map: cells at the rostral zone, encoding small gaze shifts, are endowed with high peak firing rates and short burst durations, whereas caudal cells fire long-duration bursts at much lower firing rates. Yet, the number of spikes in the SC bursts do not systematically vary across the motor map. This hypothesis was forwarded on the basis of head-restrained collicular recordings, and was supported by quantitative analyses of single-unit responses, and computational modeling (Goossens and Van Opstal, 2006; Goossens and Opstal, 2012; Kasap and Opstal, 2017; Van Gisbergen and Van Opstal, 1989; Van Opstal and Goossens, 2008).

Here we extended this hypothesis to head-unrestrained gaze shifts, by proposing that the SC population specifies an abstract, desired, gaze trajectory (the sum of the eye-in-space and head-in-space trajectories), for which the spe-
specific motoric details (the actual oculomotor and head-motor signals) are extracted downstream from the motor SC within independent brainstem, spinal cord and cerebellar circuitries (Figures 7.3 and 7.4). Recent recordings in head-unrestrained monkeys have revealed that, indeed, the cumulative number of spikes in the SC bursts of single units is better described by the instantaneous straight-line gaze-displacement vector than by the eye-in-head saccade (manuscript in preparation).

Note that our model does not imply that the SC burst (e.g., Fig. 7.5) encodes the detailed changes in the velocity profiles for different contributions of the head, as illustrated in Fig. 7.8. Indeed, our simplified rectangular SC bursts produce clearly differently shaped gaze-velocity profiles (Figs. 7.7-7.11), which result from the (nonlinear) interactions between the eyes and head motor systems, the constraints imposed by the OMR, and the involvement of the VOR. Yet, as the head contribution to the gaze shift is strongly determined by the initial eye-in-head position (contra- vs. ipsi-gaze, e.g. Eqn. 7.10, Figs. 7.4B, 7.7 and 7.8), by the sensory modality (visual vs. auditory), and also by top-down task-related factors (Goossens and Van Opstal, 1997; Laurutis and Robinson, 1986), the SC burst already reflects the resulting influence of the head movement to the gaze shift in its spike trains on the basis of an eye-position signal that enters the SC motor map (introduced in Eqn. 7.5). Evidence for the presence of an eye-position signal in the SC stems from single-unit recordings for saccades under head-restrained conditions (gain field tuning; Stuphorn et al., 2000; Van Opstal, Hepp, et al., 1995. We recently obtained further support for a similar modulation in the head-unrestrained monkey SC, as schematically illustrated in Fig. 7.5 (manuscript in preparation).

(ii) Whereas most models assume nonlinear feedback circuits to control the eyes and head, in our model, the eye- and head feedback control circuits are driven by independent linear burst generators. Although this specific feature is not a critical aspect of our model, it emphasizes that there is no specific need for additional kinematic nonlinearities in the control of the eye- and head motor systems to explain the major main-sequence properties of gaze shifts (saturating peak velocities for large movements, with longer movement durations and increased skewness; e.g., Fig. 7.7B), as these are accounted for by the firing patterns of the SC population. That being said, the limiting oculomotor range is a nonlinearity in our model, as well as the (small) coupling of the oculomotor system on the head-movement trajectory (Eqn. 7.9). Further, the inclusion of more realistic (position-dependent) plant models will require additional nonlinearities in the control circuits. In this paper, we have not attempted to work out the
tedious details to include all these additional factors, but instead to focus on the major functional units that are required to explain the observed behaviors.

(iii) The eyes and head are controlled by signals specified in their respective reference frames: an oculocentric gaze-error signal drives the eyes, and a cranio-centric head-motor error signal drives the head (Fig. 7.3A, Fig. 7.7A). However, to constrain all eye positions to the oculomotor range, the desired gaze error is first transformed into a desired eye-in-head position goal. In this way, the model appears to revive Robinson’s original proposal (Robinson, 1975; Robinson, 1973; Van Gisbergen, Robinson, et al., 1981) that the pontine oculomotor burst generator is driven by a desired eye-position signal, albeit through an entirely different transformation sequence, as the common drive for the eyes and head is now derived from the oculocentric SC motor map.

(iv) In the classical saccadic eye-movement models (Jürgens et al., 1981; Scudder, 1988; Van Gisbergen, Robinson, et al., 1981), the brainstem oculomotor burst generator produces the eye-velocity signal, which appears as a pulse on the oculomotor neurons (the direct pathway), while its integral provides the tonic step-signal to holds the eye in its final position. In our eye-head gaze model this is no longer the case: the oculomotor burst cells instead generate a desired eye-velocity signal. This signal, however, is modified by the VOR during the gaze shift (Eqn. 7.7), to produce the actual eye-in-head velocity for the oculomotor neurons. For that reason, our model predicts that the output of the burst generator, \( B(t) \), should correlate with both the eye- and head-velocity signals:

\[
B(t) = p \cdot \dot{E}_H(t - \tau_E) + q \cdot \dot{H}_W(t - \tau_H)
\]

with \( \tau_E \) and \( \tau_H \) short delays, and \( p \) and \( q \) depend on the gain of the VOR. Such a systematic correlation has indeed been observed across the population of horizontal burst cells in the pons (Cullen, 1996). Yet, as the coefficients \( p \) and \( q \) are not identical, vary from cell to cell, and from movement to movement, the pontine burst does not encode horizontal gaze velocity. The latter depends on the involvement of the VOR: \( B(t) \) equals gaze velocity when \( g_V = 1 \), i.e., when the VOR is fully engaged. However, during rapid gaze shifts the VOR gain is typically low (inset Figure 7.4A; e.g. Laurutis and Robinson, 1986; Tabak et al., 1996).

**Alternative spatial updating strategy.** The world-centered spatial updates of Eqns. 7.1-7.3, and Figure 7.2 (left-hand side) rely on the instantaneous feedback of (absolute) signals about the eye-in-head and the head-on-neck orientations. A potential problem with this scheme, however, already emphasized by the work of Goldberg and colleagues (e.g., Goldberg and Bruce, 1990) is the lack
of neural signatures reflecting a world-centered (or even craniocentric) reference frame. Neural responses in the brainstem, midbrain Superior Colliculus, parietal cortex, and frontal eye fields, all seem to possess signals expressed in oculocentric (displacement) coordinates. This has prompted researchers to propose spatial updating models for saccades, which rely entirely on relative (eye-)displacement signals, rather than on feedback from absolute eye position (Goldberg and Bruce, 1990). It is conceivable, however, that spatial reference frames are encoded by large populations of neurons, rather than by the response properties of single neurons. For example, subtle multiplicative eye-position gain-field modulations of the firing rates of neurons with retinocentric receptive fields could potentially embed the neural representation for a craniocentric target position (e.g., Andersen et al., 1985; Zipser and Andersen, 1988). Similarly, if head orientation would also modulate such neurons, the population code could represent a world-centered target. Although gain-field eye-position modulations have been reported for several stages in the oculo-motor pathways of head-restrained monkeys (e.g. parietal cortex, Andersen et al., 1985; Superior Colliculus, (Stuphorn et al., 2000; Van Opstal, Hepp, et al., 1995), similar gain-field modulations of head position have not yet been studied in head-unrestrained animals, and therefore remain speculative.

Still, keeping targets in absolute world coordinates is not the only way in which the system could ensure dynamic spatial accuracy during fast eye-head gaze shifts. As indicated in Table 7.1, the calculations could also be based (at least in part) on feedback from (relative) dynamic motor errors of the ongoing gaze- and head movements. For head-restrained saccades, such models have been around since the early eighties (Duhamel et al., 1992; Goldberg and Bruce, 1990; Jürgens et al., 1981). If also applicable to head-unrestrained gaze control, there would be no need for a supra-sensory mapping stage of the goal into common world coordinates. Instead, the goal would be kept in its own sensory reference frame: retinocentric for visual targets, and craniocentric for auditory targets. How could this be implemented?

The central defining feature of our model remains the SC motor map, which programs a feedforward desired dynamic gaze-velocity signal for brainstem and spinal-cord circuits. Like in Scudder, 1988 saccade model, this gaze-velocity signal is compared to the current gaze velocity, by integrating the difference. This comparison yields the dynamic gaze motor-error, \( G_{ERR} = \Delta G_1(t^*) \). The presence of such a signal in the system therefore raises an alternative possibility to maintain spatial accuracy, without transforming the target into a suprasensory reference frame. For a visual target, it would thus suffice to subtract
the dynamic gaze error from the retinal target location, which was perceived at time $t^*$ (Figure 7.12):

$$\Delta G_2(t^*) = T_E^* - G_{ERR}(t^*)$$

and

$$\Delta H_2 = \Delta G_2 + E_1$$

(7.14)

Figure 7.12 Dynamic spatial updating schema relying on current gaze- and head-motor errors. Under multisensory conditions, audiovisual integration takes place in a unified, oculocentric reference frame, specifying the desired gaze-displacement vector for the selected target. Note that information about absolute eye position is still required to ensure goal-directed head movements. For reference, the scheme also includes the different delays that should be accounted for in the updating process: different sensory delays for visual and auditory inputs, and a motor delay for the gaze shift. The feedback signals thus have to be stored in short-term memory buffers, from which the correct timing relative to the stimulus event ($t^*$) may be retrieved to ensure accurate updating also in dynamic localization conditions, such as in Figs. 7.1 and 7.11.

Likewise, auditory targets can be kept in their original craniocentric coordinates, as its head-motor error, $H_{ERR}(t)$, is constructed from the instantaneous gaze-motor error, by adding the current eye position at $t^*$ (Figure 7.3A). Also, this signal would be available within the system, as it is required to avoid the
eyes from hitting the limits of the oculomotor range. Hence, for sounds the dynamic updating algorithm reads:

$$\Delta H_2(t^*) = T_H - H_{ERR}(t^*) \text{ and } \Delta G_2 = \Delta H_2 - E_1$$

(7.15)

The multisensory updating process described by Eqns. 7.14 and 7.15 is reminiscent to the proposal of relative coordinate transformations, forwarded earlier by Jürgens et al., 1981, and Goldberg and Bruce, 1990, for head-restrained visual saccades. Here, that concept is extended in several ways, to enable dynamic updating of target locations for auditory and visual-evoked eye-head gaze shifts.

In the earlier proposals, dynamic feedback of eye-motor error was used exclusively to drive the ocular kinematics, encoded by the brainstem oculomotor burst generator (through the so-called local feedback loop). Instead, in our extended model, the instantaneous gaze- and head-motor errors are used to update target locations in the global feedback loop as well (Van Gisbergen and Van Opstal, 1989). Note, however, that accurate knowledge about instantaneous eye-in-head position, $E_H(t)$, and about the eye position at the start of the gaze shift, $E_1$, is still required for either updating strategy. The need for these signals could explain why sound-evoked eye-head gaze shifts to pure tones vary in a systematic way with the initial eye position, despite the fact that changes in eye position have no influence on the sensory (acoustic) input (Van Grootel, Van der Willigen, et al., 2012).

**Multisensory integration.** Although not explicitly modeled in this paper, auditory and visual inputs are combined at the SC motor map (stage AV integration). This notion is in line with the idea that the midbrain SC is a multi-sensory-motor gateway for gaze orienting (Bell et al., 2005; Frens and Van Opstal, 1998; Groh and Sparks, 1996; Jay and Sparks, 1987; Meredith and Stein, 1986; Stein and Meredith, 1993). In the scheme of Fig. 7.12, both sensory modalities express the goal in unified, oculocentric coordinates. The multisensory integration stage is thought to incorporate different factors, which have been shown to include the reliability of each sensory modality (target uncertainty, noise, variability). Psychophysical evidence has shown that in simple two-stimulus AV localization paradigms, the system constructs a multimodal percept that, in the absence of any prior information (i.e., a uniform prior), resembles a weighted average of the visual and auditory target estimates. The unsensory response variances then act as weighting factors (e.g., Alais and Burr, 2004; Hillis, 2002). In the AV stage in our scheme this would translate to:

$$\Delta G_{AV}(t^*) = \frac{\sigma_A^2 \Delta G_A(t^*) + \sigma_V^2 \Delta G_V(t^*)}{\sigma_A^2 + \sigma_V^2}$$

(7.16)
in which $\sigma_X^2$ represents the uncertainty (variance) of sensory modality $X = (A, V)$. Eqn. 7.16 states that when uncertainty about the visual target is much smaller than for audition ($\sigma_V^2 \ll \sigma_A^2$), the weighted average estimate, $\Delta G_{AV}$, will be close to the visual estimate, $\Delta G_V$, and vice versa. Conversely, if both modalities are equally noisy, the bimodal estimate corresponds to the average of the uni-sensory estimates.

Because the construction of the goal is embedded within dynamic sensorimotor feedback loops, our model further proposes that the multisensory integration stage does not only rely on the (multi-)sensory coordinates, but should also incorporate dynamic information about gaze- and head-motor errors. Clearly, given the different coordinate-transformation problems for visual and auditory stimuli with respect to the eyes and head (Table 7.1), this poses interesting challenges for multisensory integration, which, so far, have received little attention in the literature (Corneil and Munoz, 1996; Stein and Meredith, 1993; Van Gisbergen, Robinson, et al., 1981; Van Opstal, 2016).

A further interesting consequence of this concept is that the estimates of the unimodal variances in Eqn. 7.14 may be time-dependent too, i.e., $\sigma_X^2 = \sigma_X^2(t^*)$. For example, the longer the (multi-)sensory processing time (say, for long reaction times), the smaller the sensory uncertainties, and hence the lower the variance in the sensory estimates. However, it is likely that this process strongly depends on the sensory modality, as the sensory processing times (and internal delays) for vision and audition are markedly different.

So far, however, multisensory integration studies have typically dealt with the processing of audiovisual stimuli under static and aligned localization sensorimotor conditions only (as exemplified by Figure 7.1A). New experimental data are needed that reveal the dynamics of multisensory integration in paradigms that require rapid eye-head spatial updating like in Figure 7.1D, and under conditions in which eye, head, and audio-visual stimuli may be either aligned or misaligned in space and time.
REFERENCES


GENERAL DISCUSSION AND SUMMARIES

8.1 GENERAL DISCUSSION

Several computational models have been introduced and tested in this thesis, to investigate the functional implementation of the neural circuitry underlying the gaze-control system. Specifically, we focused on the role of the midbrain superior colliculus (SC) in saccade generation. Below, we discuss the main findings, and provide a possible outlook for this research line.

In Chapters 2, 4 and 5, we introduced a simple spiking neural network (SNN) implementation of the SC motor map that generates the experimentally observed firing patterns of SC populations. In Chapter 2, we specify the crucial firing properties of the gaze-motor map population, and propose a neural implementation within a one-dimensional network for horizontal saccades. We used a homogeneously spiking input layer (representing, e.g. the FEF population) to drive the spiking SC neurons, and show that the experimental firing properties are obtained by assuming a specific, topographical tuning of the membrane parameters, and lateral connection strengths of the spiking neurons. In Chapter 4, we extended the model to 2D to generate oblique saccades in all directions. Furthermore, because the 2D network was set up to explain intracollicular microstimulation experiments, the FEF input layer was discarded, and instead a small subset of SC neurons was driven by the direct current input from the stimulation electrode, which acted as a ‘seed’ for the emerging population activity through the lateral connections. In Chapter 5, we tested the same network implementations during simultaneous microstimulation at two sites, in order to test whether the network could also mimic the results from double-stimulation studies.

In the SNN models of the SC we were able to capture the observed firing patterns through two internal mechanisms: the location-dependent biophysical properties of the adaptive leaky-integrate-and-fire neurons (their mem-
brane time constant and adaptive current), and a Mexican-hat type of lateral excitatory-inhibitory connectivity with the SC. The emerging SC activity is then subsequently decoded into the saccade trajectory through the dynamic linear-ensemble coding scheme proposed by Goossens and Van Opstal. The reconstructed saccade kinematics of the model saccades displayed the same nonlinear main-sequence characteristics (saccade amplitude-duration and amplitude-peak velocity relationships) as observed in real saccades. Note that in our models, the SC motor map controls the full saccade kinematics and metrics, yet is placed outside the dynamic oculomotor feedback loop.

We studied the internal dynamics of the SC as a complex dynamical system. Each neuron’s membrane potential was determined by a set of coupled ordinary differential equations at each time-step, based on its current state and total synaptic input received (through the conduction-mediated external currents from other neurons in the map). At this level of abstraction, mathematical values of the neural variables were assigned to attain gaze-motor map dynamics across the network without breaking the bursting behavior at the neural level. These SNN models recreated firing patterns of SC populations by following the neural principles identified and postulated in the electrophysiological literature. However, the network architecture required some practical choices, for example the neuron type, network size, spike propagation scheme, lateral connectivity profile or input current profile. Computational modeling requires such assumptions, which may not be readily verified experimentally. We have implemented the 2D gaze-motor map of the SNN in a fully deterministic manner, by assuming an all-to-all connected grid (201x201) of neurons. We tested whether indeed the location-dependent biophysical properties and lateral connections could explain the observed gaze-motor map firings. The results show that such a dense network architecture produces smooth gradients in the population firings. Possibly, a smaller network could also capture the gaze-motor map characteristics. Furthermore, the model should be extended with stochastic noise, and external inputs (for example, to incorporate the blink-generation system, and modulation of the firing rates by initial eye position) to study the influence of other inputs.

In Chapter 3, we tackled the increased computational cost of large-scale SNN simulations as resulting from the extension to 2D of the SC model. We exploited general purpose graphical processing unit (GPU) programming for parallel computing, and focused on the synaptic updating (spike propagation) step, which has been identified in the literature as an important bottleneck for parallelization in SNN simulations on GPUs. Dynamic updating capability that is recently introduced in GPUs allows implementing irregular nested paral-
lelism, and thus accelerate the spiking updating step by eliminating redundant calculations. We proposed a simple neural network architecture, which resists scaling of both the number of neurons and the number of synapses with stable firing regimes. This network architecture allowed to benchmark the algorithm and compare it with existing parallelization strategies. Dynamic parallelism accelerates especially densely connected SNN simulations with sparse spiking regimens (considering both time-step and network size).

In Chapter 6, we propose that the SC motor map acts as a vectorial pulse generator for eye-head gaze saccades, and discuss the additional necessary signals and transformations needed for coordinated eye-head movements (incorporating single-unit data from head-unrestrained monkey recordings). The data show that the SC encodes the desired kinematics of eye-head gaze-shifts, and the model proposes that its signal is decomposed downstream for the eye and head motor systems, represented in appropriate oculocentric and craniocentric reference frames, respectively. Systematic changes of the movement kinematics and the neural responses based on the initial eye-in-head orientation show that the gaze control system has instantaneous access to eye and head position signals. The firing patterns in the gaze-motor map observed in head-restrained single-unit recordings do not hold anymore, yet the head-unrestrained burst profiles now tightly correlated with the eye-head gaze trajectories. Our modelling efforts focused on the role of SC in gaze control, and less on the downstream brainstem-cerebellar-spinal circuitry. Our collicular data as such do not address whether the downstream circuitry operates with or without a gaze-feedback loop, yet it is noteworthy that the SC responses already seem to reflect all major properties of the ensuing gaze shifts and their kinematics.

In Chapter 7, we further explored the programming of eye-head gaze shifts in a dynamic multisensory and multi-step setting where new stimuli (either auditory or visual) are repetitively presented to the system during ongoing eye-head saccades. Behavioural evidence had shown that the neural transformations needed for accurate gaze-control take place at millisecond scales, which calls for a chain of nontrivial processes of multisensory integration, target updating, command signal generation and representation of retinal and head-centric control commands in appropriate coordinates. We propose and test a computational black-box model which contains some crucial functional elements for these transformations: the SC generates a common oculocentric gaze-velocity command to the brainstem-spinal circuitry, which is continuously updated from a list of targets stored in the memory. Despite a number of simplifications in our model regarding the details of brainstem and cerebellar involvement in the downstream motor circuitry, and the eye- and head motor plants,
it accounts for the complex, yet accurate, kinematic behaviors and trajectories of measured eye-head gaze shifts under challenging multi-sensory conditions.
In this thesis, several models have been introduced and tested to investigate the functional implementation of the neural circuitry for gaze control. Specifically, we addressed the role of the midbrain superior colliculus (SC) in rapid eye movement (saccade) generation. We modeled the SC as a dynamic spatiotemporal signal generator, in which the population of recruited neurons carries feedforward information about the saccade kinematics and its straight oblique trajectory, rather than the classical notion of a static spatial-encoded population that only specifies the saccade metrics.

In Chapter 2, we constructed a biologically realistic, yet simple, spiking neural network (SNN) model of the midbrain SC. Model-generated spike trains reflected the experimentally observed dynamical patterns and saccade representation in the collicular gaze-motor map (horizontal saccades only). Saccade metrics and kinematics were reconstructed by the linear-summation model of Goossens and Van Opstal from the collicular spike trains, and reflected the well-known nonlinear main-sequence behavior of saccades: a straight-line increase of saccade duration and a saturating peak eye-velocity as function of the saccade amplitude. The input signal to the motor map was taken to be translation-invariant spike trains from sources upstream from the motor map (e.g., frontal eye fields, or posterior parietal cortex). The emerging firing patterns in the SC result from location-dependent biophysical properties of the neural dynamics and lateral interactions among the neurons in the map. Even though the input-signal was location invariant, we varied its projection weights onto the SC layer to compensate for the location-dependent intrinsic inhibitory adaptation current acting on SC neurons. Furthermore, the input layer population outlasted the resulting SC bursts, thus providing the SC neurons always with sufficient driving input. The experimentally observed systematic cell-response properties along the gaze-motor map coordinate was reproduced by introducing lateral interactions. This lateral connectivity synchronized the activity of all neurons in the population with the most active neuron (soft ‘winner-take-all’), by adjusting all firing profiles within the active population.

Our two-dimensional extension of the SC model (described in Chapter 4) enhanced the complexity of the total dynamical system, which strongly increased the number of calculations per simulation step in the SNN simulations. The major factor for this growing complexity resides in the strongly increased number of synapses with the all-to-all Mexican hat-type lateral connections among the grid of neurons within the gaze-motor map (of the order of $200^4 \sim 2 \cdot 10^9$ connections, vs. $(200)^2 \sim 4 \cdot 10^4$ for the 1D map). In Chapter 3, we therefore focused on
methods to optimize the synaptic updating (spike propagation) step, which is identified as the bottleneck of parallelization in SNN simulations on fast graphical processing units (GPUs). Synaptic updating depends on the occurrence of spikes, and since it is not known a priori at which timestep a neuron will emit a spike, in previous parallelization strategies each synaptic connection had to be taken into consideration, even when no presynaptic spike arrived. Thus, in sparsely spiking neural nets, the synaptic updating step may severely hinder parallelization when the size of the network increases. This problem has been classified as "irregular nested parallelism". Our proposed dynamic parallelism algorithm overcomes this issue by allowing to swarm nested parallel routines within an ongoing parallel application. Therefore, unnecessary synaptic updating steps are eliminated for those synapses that do not receive a presynaptic spike. This method is especially beneficial for densely connected large networks with sparse spike occurrences (# spikes / number of neurons x number of simulation steps).

In Chapter 4, we presented the 2D extension of our spiking network model of the SC motor map to generate saccades in all directions. Furthermore, we investigated the potential principles of population recruitment within the SC in order to account for the results of intra-collicular electrical microstimulation studies with the linear dynamic spike-summation model. The driving input to the network was tuned such that it recruited only a small subset of neurons, which subsequently sets up a large synchronized population activity through its lateral (Mexican-hat like) connections. We demonstrated that the bursting SC populations encoded the temporal saccade profiles of natural eye movements, and the linear spike-summation model reproduced the normal main-sequence characteristics of saccadic eye movements. The main-sequence of the saccade kinematics results from the location-dependent biophysical properties of the neurons and their lateral connections, just like adopted in Chapter 2. Furthermore, we showed that in our 2D model, like in real experiments, the population dynamics (and hence, the emerging saccade properties) were largely independent of the microstimulation parameters.

In Chapter 5, we tested the response patterns of the same SC network under various simultaneous double-stimulation scenarios. Simultaneous double stimulation in the SC motor map is known to generate eye movements that resemble a weighted average of the individual stimulation effects, where the current strengths act as weighting parameters. Even though the network responses to simultaneous double stimulation were in line with the published electrophysiological recordings, the introduction of small delays between the electrical stimuli always resulted in bi-stable response patterns, rather than in
systematically strongly curved trajectories towards the goal of the last stimulus. We argue that this effect was probably due to the amount of overlap between the effects of the two stimulus sites, the location-dependent neural parameter tunings with the range of lateral inhibition, and the lack of intrinsic noise in the neural firing. We conclude that the observed nonlinear response characteristics of the network resulted from the neural dynamics within the network, rather than from a downstream center-of-gravity computation from the output of the gaze-motor map.

In Chapter 6, we discussed the role of the SC motor map and a further extension of the idea that it encodes combined eye-head gaze shifts, rather than only the eye saccades. In this chapter we analyzed single-unit responses from the monkey SC during large head-unrestrained eye-head gaze saccades. The data support our model that the signal from the neurons encodes a vectorial pulse that drives the instantaneous desired (straight-line) kinematics of ongoing eye-head gaze-shifts. The SC population burst is decomposed downstream from the motor map into coupled, yet essentially different, signals for the eye- and head motor systems, each represented in their appropriate eye-centered and head-centered reference frames. Furthermore, the inclusion of a limiting oculomotor range and a dynamic gain for the vestibular ocular reflex, in combination with a dependence of the neural firing rates in the SC on the initial eye-in-head position introduce several nonlinearities in the system, which were not included in the models for eye-saccades described in Chapters 2 and 4. Thus, the absolute fixed spike count and the simple, unique gradient in the peak firing rates within the gaze-motor map for single-unit responses may no longer hold for combined eye-head gaze shifts, as it also depends on the initial orientation of the eye in the head. Yet, despite these dynamic nonlinearities, the observed high correlations between the instantaneous firing rates of SC cells and the dynamic gaze trajectories, even at a single-trial level, is quite remarkable, and strongly supports the dynamic role of the SC in gaze orienting.

In Chapter 7, the programming of eye-head gaze shifts was further explored in dynamic multisensory and multi-target simulations, in which several stimuli (either auditory or visual) were presented to the system during ongoing eye-head saccades. Although experimental data from neurons are scarce, behavioral experiments have clearly indicated that the representation of retinal and head-centric control commands update on millisecond time scales in their appropriate reference frames, yielding spatially accurate eye- and head movements. We considered different approaches regarding multisensory integration of visual and auditory signals, and on the decomposition of the gaze-velocity command by independent linear models for eye and head brainstem and spinal
feedback systems. By incorporating different sensory modalities (auditory and visual), a nonlinear range, dynamic modulation of the vestibular ocular reflex, the model generates independent eye- and head-movement components from a common dynamic gaze signal with realistic gaze trajectories and time scales.
8.3 Samenvatting

Dit proefschrift introduceert verschillende modellen om de neurale implementatie van snelle oriënteringsbewegingen van de ogen (zog. "saccades") te onderzoeken. Specifiek hebben we hierbij naar de rol van de superior colliculus (SC) in de middenhersen gekeken. We hebben de SC gemodelleerd als een dynamische, spatio-temporele signaal-generator, waarbij de populatie van gerekruteerde neuronen in de motor kaart van de SC de volledige informatie over de saccade-kinematika en trajectoria bevat, in plaats van het klassieke idee van een statische, spatiale-gecodeerde populatie die alleen de saccade-metriek (amplitude en richting van de oogbeweging) specificeert.

In Hoofdstuk 2 construeerden we een biologisch realistisch, maar eenvoudig, spiking neuraal netwerk (SNN) model van de een-dimensionale SC motorkaart voor horizontale saccades. De model-gegenereerde spike treinen weerspiegelden de experimentele waargenomen dynamische vuurpatronen van SC cellen, en de representatie van de saccade in de SC motorkaart. Saccade-metriek en kinematika werden gereconstrueerd door het lineair-sommatie model van Goossens en Van Opstal op de SC spike-treinen toe te passen, en dit model produceerde het welbekende niet-lineaire gedrag van de saccade kinematika: een lineaire toename van de saccade duur, en een verzadigende pieksznelheid als functie van de saccade amplitude. Het stuursignaal naar de motorkaart werd gemodelleerd als translatie-invariante spike reeksen afkomstig van neurale populaties (zoals Frontal Eye Fields of Posterior Parietal Cortex) voorgaand aan de motorkaart. De activatiepatronen in de SC ontstaan vervolgens door locatie-afhankelijke biofysische eigenschappen van de neurale dynamica van de modelneuronen aan te nemen, tezamen met een specifieke keuze voor de laterale interactiesterkte tussen alle neuronen in de kaart. Hoewel het inputsignaal locatie-invariant was, varieerden we de projectie gewichten vanuit de input naar de SC-laag om de locatie-afhankelijke adaptatiesterkte van SC-neuronen te compenseren. Bovendien was de input populatie altijd langer actief dan de SC cellen, zodat deze laatsten altijd voldoende input kregen. De experimentele waargenomen respons eigenschappen van de SC cellen in de motorkaart kon worden gereproduceerd door de excitati-o inhibitoire laterale interacties. Deze laterale connectiviteit leidde tot gesynchroniseerde activiteit van de neuronen in de populatie, waarbij het meest actieve neuron de temporele structuur van de bursts in de hele populatie bepaalde (‘winner-take-all’ gedrag).

Onze twee-dimensionale uitbreiding van het SC-model (Hoofdstuk 4) verhoogt de complexiteit in het totale dynamische systeem aanzienlijk, waar-door het aantal berekeningen per simulatiestap in de SNN-simulaties eve-
neens sterk toenam. De belangrijkste factor voor deze toegenomen complexiteit ligt in het sterk toegenomen aantal synapsen, vanwege de alles-met-alles Mexicaanse hoed-achtige laterale verbindingen tussen alle neuronen in de motorkaart (orde grootte: ongeveer \((200)^4 \sim 2 \cdot 10^9\) verbindingen in de 2D kaart, tegenover \((200)^2 \sim 4 \cdot 10^4\) verbindingen voor de 1D kaart). In Hoofdstuk 3 hebben we ons daarom gericht op methoden om de synaptische aanpassings stap (d.w.z. de spike propagatie) verder te optimaliseren. Deze stap wordt in de literatuur geidentificeerd als de "bottleneck" van parallellisatie in SNN-simulaties voor snelle grafische processoren (GPU’s). De synaptische aanpassing wordt bepaald door de aanwezigheid van spikes, maar omdat niet a priori bekend is op welk tijdstip een neuron een spike zal uitzenden of ontvangen, moest bij eerdere parallellisatie strategieën elke synaptische verbinding worden meegenomen, ook als er geen presynaptische spikes arriveerden. In dergelijke neurale netwerken kan de synaptische aanpassings-stap de parallellisatie dus ernstig vertragen als de omvang van het netwerk sterk toeneemt. Dit probleem staat bekend als "onregelmatig genest parallellisme". Ons voorgestelde dynamisch parallellisatie algoritme voorkomt dit probleem door meerdere parallele routines bij elkaar onder te brengen binnen een lopende parallele toepassing. Op deze manier worden onnodige synaptische aanpassingen geelimineerd voor die synapsen die een presynaptische spike ontberen. Deze methode is vooral gunstig voor grootschalige sterk onderling verbonden netwerken met schaars voorkomende spikes (# spikes / aantal neuronen x aantal simulatiestappen).

In hoofdstuk 4 presenteerden we de 2D-uitbreiding van ons spiking netwerkmodel van de SC-motorkaart uit Hoofdstuk 2 om saccades in alle richtingen te kunnen genereren. Daarnaast hebben we de principes van populatie rekrutering binnen de SC onderzocht door de resultaten van intra-SC elektrische microstimulatie studies met het lineaire dynamische spike-sommatiemodel te modelleren. De elektrische stimulatie input naar het netwerk werd zodanig afgestemd dat het slechts een kleine subset van neuronen direct rekruteerde, die vervolgens via de laterale verbindingen een grote gesynchroniseerde populatieactiviteit opzette. De simulaties toonden aan dat de hieruit ontstane SC populaties de temporele saccade snelheidsprofielen van natuurlijke oogbewegingen codeerden, en dat het lineaire spike-sommatiemodel nog steeds de normale kinematische karakteristieken van saccadische oogbewegingen kon reproduceren. De saccade-kinematica is het resultaat van de locatie-afhankelijke biofysische eigenschappen van de neuronen en hun laterale verbindingen, net zoals voorgesteld in Hoofdstuk 2. Tenslotte toonden we aan dat in ons 2D-model de populatiedynamica (en de daaruit volgende saccade-eigenschappen) gro-
tendeels onafhankelijk bleven van aanzienlijke variaties in de microstimulatie parameters, net zoals gezien in experimentele data.

In hoofdstuk 5 hebben we de respons patronen van hetzelfde SC-netwerk zoals beschreven in Hoofdstuk 4, getest op verschillende scenario’s met simultane dubbelstimulatie in de motor kaart. Het is bekend dat dubbelstimulatie oogbewegingen genereert die lijken op een gewogen gemiddelde van de individuele stimulatie-effecten, waarbij de individuele stroomsterktes als weging fungeren. Hoewel de responsies van het netwerk op gelijktijdige dubbelstimulatie in overeenstemming waren met de gepubliceerde elektrofysiologische data, resulteerde de introductie van kleine vertragingen tussen de elektrische stimuli vrijwel altijd in bi-stabiele respons patronen, in plaats van in systematisch sterk gekromde banen. Dit effect is mogelijk te wijten aan de mate van overlap tussen de (inhibitoire) effecten van de twee stimuluslocaties (‘winner-take-all’), de locatieafhankelijke neurale parameters, het bereik van de laterale inhibitie, en/of het ontbreken van intrinsieke ruis in het neurale vuurgedrag. We concluderen dat de waargenomen niet-lineaire respons karakteristieken van het netwerk volgen uit de neurale dynamica in het netwerk, in plaats van uit een expliciete zwaartepunt berekening over de totale output van de motorkaart.

de gaze snelheid, zelfs op individueel trial nivo. Dit alles vormt een sterke ondersteuning voor het idee van een dynamische rol van de SC in oog-hoofd gaze saccades.

In Hoofdstuk 7 werd de programmering van oog-hoofd gaze saccades verder onderzocht in een dynamisch black-box model, waarin verschillende stimuli (auditief en visueel) aan het systeem werden gepresenteerd gedurende de uitvoering van snelle oog-hoofd saccades. Experimentele gegevens van neuronen zijn schaars, maar gedragsexperimenten hebben aangetoond dat de representaties van de retinale (visueel, oog) en hoofd-centrische (auditief, hoofd) stuursignalen op milliseconden tijdsschalen worden aangepast in de juiste coördinaten, teneinde ruimte nauwkeurige oog- en hoofdbewegingen te genereren. We beschrijven verschillende varianten voor de multi-sensorische integratie stadia van visuele en auditieve signalen, alsmede voor de representatie van het gezamenlijke gaze-snelheidsignaal voor onafhankelijke lineaire modellen van oog en hoofd. Met verschillende sensorische modaliteiten, een niet-lineair oculomotorisch bereik, en een dynamische vestibulo-oculaire reflex, genereert het model onafhankelijke, maar doelgerichte, oog- en hoofdbewegingen met realistische gaze trajectoria.
Finally, another chapter of my life is closing with this thesis. It has been a great adventure for me since I arrived in the Netherlands. Looking back, I understand better how lucky I was for being surrounded by great people.

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Canim ailem, beni su geldigim noktaya getiren azmi ve sevki bana kazandirdiginiz icin tesekkurler. Yaptigim herseyde yanimdasiniz.
LIST OF PUBLICATIONS


Bahadir Kasap was born in Kayseri, Turkey, and moved to Ankara at early age where he completed secondary education. Afterwards, he moved to Istanbul to study Physics at Koc University. With interest in programming and computing combined with theoretical physics study, he is specialized in Computational Sciences in Engineering during his masters in Technical University of Braunschweig, Germany. His interest in biologically inspired information processing systems resulted in his focus on computational neuroscience during masters thesis at Theoretical Neuroscience & Neuroinformatics department of Free University Berlin. He has studied the effect of unsupervised learning by spike timing dependent plasticity on odor classification task that takes place in honeybee antennal lobe. In December 2012, he started an EU Marie Curie early stage researcher fellowship as part of European Research consortium NETT (Neural Engineering Transformative Technologies) at the department of Biophysics, Donders Institute for Brain, Cognition, and Behaviour, Radboud University, Nijmegen, The Netherlands. His PhD project was accomplished under the supervision of prof. dr. John van Opstal. PhD research focused on neurocomputational modeling of the gaze control system and the role of superior colliculus within. Furthermore, he had additional methodical interest on accelerating spiking neural network simulations by utilizing parallel computing with graphical processing units. During doctoral training, he visited Institute for Complex Systems, Consiglie Nazionale delle Ricerche, Firenze, Italy and Biologically Inspired Computer Vision Lab, Imperial College London, United Kingdom. PhD results presented in this thesis are also previously presented in various international conferences and published in peer-reviewed journals. Since June 2017, he has been working in the industry as a Data Scientist/Data Engineer with currently focusing on streaming data and cloud architecture.
For a successful research Institute, it is vital to train the next generation of young scientists. To achieve this goal, the Donders Institute for Brain, Cognition and Behaviour established the Donders Graduate School for Cognitive Neuroscience (DGCN), which was officially recognised as a national graduate school in 2009. The Graduate School covers training at both Master’s and PhD level and provides an excellent educational context fully aligned with the research programme of the Donders Institute.

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Positions outside academia spread among the following sectors: specialists in a medical environment, mainly in genetics, geriatrics, psychiatry and neurology, specialists in a psychological environment, e.g. as specialist in neuropsychology, psychological diagnostics or therapy, higher education as coordinators or lecturers. A smaller percentage enters business as research consultants, analysts or head of research and development. Fewer graduates stay in a research environment as lab coordinators, technical support or policy advisors. Upcoming possibilities are positions in the IT sector and management position in pharmaceutical industry. In general, the PhDs graduates almost invariably continue with high-quality positions that play an important role in our knowledge economy.

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