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Source Models in Inverse Electrocardiography

Adriaan van Oosterom

Department of Medical Physics, University of Nijmegen, The Netherlands

Correspondence: A van Oosterom, Dept. Medical Physics, University of Nijmegen, Geert Grooteplein 21, 6525EZ Nijmegen, The Netherlands. E-mail: avo@mbfys.kun.nl, phone +31.24.3614248, fax +31.24.3541435

Abstract. This paper presents an overview of the most prominent models of the cardiac electric generator that have been described in the literature to describe the electrocardiographic signals that are observed on the body surface. The properties of the two most popular surface source models are compared: the equivalent double layer and the epicardial potential model.

Keywords: Source models; Dipoles; Multipoles; Epicardial Potentials; Equivalent Double Layer

1. Introduction

Since the early days of electrocardiography, the development of diagnostic ECG criteria has been accompanied by the development of biophysical models aimed at linking the electrophysiology of cardiac function to the waveforms of the ECG signals observed on the body surface. This applies in particular to the situation where the actual *waveforms* of the observed ECGs play a role in the diagnosis, rather than rhythm analysis.

The need for the use of models stems from the fundamental impossibility of deriving a unique specification of internal bioelectric sources on the basis of observations of the potentials on the body surface: a multitude of different sources may give rise to identical data outside the actual source region.

This fact has been known since 1853 [von Helmholz, 1853], and ever since various ideas have been put forward to come to terms with it. In the terminology of statistics, the electrocardiogram can be classed as being a moderately sensitive, but highly non-specific indicator of cardiac disease.

The use of a biophysical model of the genesis of the electrocardiogram circumvents this problem to some extent. In such models a description of the bioelectric generator is postulated *a priori*: a *source model*. In addition a model is used for describing the passive effects on the observed data of the body tissues that surround the active electric sources: a *volume conductor model*. The computation of the potentials generated by this pair is referred to as the Forward Problem. Through recent advances in the domain of computer science and linear algebra the solution of the Forward Problem is straightforward. What needs to be sorted out is the selection of an appropriate source model and the solution of its parameters, the problem referred to as the Inverse Problem.

In this issue four contributions are included that demonstrate recent promising developments in this field. This contribution presents an overview of the major existing source models. It compares two most popular surface source models: the equivalent double layer and the epicardial potential model.

2. Source Models

The electric current sources generating the observed potentials are not amenable to direct observation; they are *derived* from observed potential fields and measured or assumed conductivity values. The source models discussed in this contribution are the so-called *equivalent* generators, used to describe the potentials at electrodes placed on the thorax. When discussing the nature of such equivalent generators it suffices to characterize the potential distribution that these sources generate in an infinite homogeneous medium. The effect of the inhomogeneities in the electric volume conductor of the tissues surrounding the sources, the torso bound being the most prominent one, on the potentials is handled by a subsequent operator acting on the infinite medium potentials, solving the associated Forward Problem.

At the basis of the cardiac electric sources are the biochemical processes at the membranes of the cardiac myocytes. A study of the physics involved indicates that the currents generated in the extracellular domain are proportional to the spatial distribution of the spatial gradients of the transmembrane potentials [Wilson et al., 1933; Geselowitz, 1989].

2.1. The Dipole

The dipole is probably the best-known model of the cardiac electrical generator. The potentials close to this source tend to infinity. Because of this, the dipole clearly cannot be interpreted directly in terms of the underlying electrophysiology. It is merely an equivalent source description, to be used only for describing the potentials at relatively large distances from the actual cardiac sources. It expresses the lumped contributions of all cells that are active at a given time instant in the region outside the domain of the sources. Since there is no net current generated at any time instant in a bounded medium, the current dipole describes the dominant result at a distance. At any moment in time the dipole is specified by six parameters: three for its position in 3D space and three for its (vector) strength.

The only direct electrophysiology interpretations of the dipole in terms of the underlying electrophysiology are possible in the situations where the electric activity is restricted to a small part of the myocardium. Examples are the time interval directly following activation (e.g. WPW-syndrome, ectopic beats) and during the final phase of the depolarization process.

The dipole is the basis of vectorcardiography (VCG). It can be used as an equivalent generator during the entire QRST interval. In this application a single dipole performs surprisingly well: it accounts for about 80 % (representation power) of the potentials as observed on the body surface. This holds true irrespective of whether a detailed volume conductor model is involved, or the localization of the dipole is allowed to vary with time over the cardiac cycle. When viewed as the solution of an Inverse Problem, the dipole produces a highly robust estimate of cardiac electric activity, albeit a highly non-specific one.

The link with the underlying electrophysiology can be improved by considering *multiple* dipoles. Multiple dipole source models have been used in several simulation studies, the first computer assisted one being the one by Selvester *et al*. [Selvester et al., 1967]. The number of parameters involved when considering *N* dipoles is 6*N*. The nature of the inverse problem is such that, without using prior information, the solution readily becomes highly unstable, as apparent from the ever increasing bounds of the confidence intervals of the estimated parameters.

2.2. Multipole Expansions

The dipole forms the first term in the multipole expansion, a general method from the potential theory as known in physics. The next term in this expansion is the quadrupole. This expansion has also been tested in the application to cardiac source modeling [Arthur, 1968]. The application involves three free parameters for position of the entire configuration, three for its dipole elements and five quadrupole elements. By including the quadrupole, the representation power goes up to 95 % or more. However, here the same reservations apply as mentioned for the dipole. Moreover the quadrupole terms are of a different nature (dimension) than the dipole terms, which makes it difficult to relate these to cardiac electrophysiology. The interest in this type of source description soon waned. However, recently some revival can be witnessed in the form of an application of the multipole expansion to the imaging of epicardial potentials [Arthur and Beeter, 2000].

2.3. The Uniform Double Layer

The uniform double layer model (UDL) is another classic model for describing the electric generator during the depolarization phase of the ventricles. In this model, surfaces carrying elementary current dipoles are implied which represent depolarization wave fronts as they propagate through the myocardium. It was introduced in 1933 by Wilson [Wilson et. al, 1933] and has served very well ever since for explaining ECG waveforms qualitatively [Holland and Arnsdorf, 1977]. It has a direct link with electrophysiology. Conceptual notions derived from the uniform double layer can be found in most basic textbooks on practical electrocardiography.

2.4. Potential Distribution on the Heart Surface

For some decades, a source model is being developed in which the equivalent cardiac electric generator is expressed in terms of the electric potentials on a surface encompassing the myocardium [Martin, 1970]. In most related studies the surface involved is the epicardium. Such voltage sources are based on the theoretical unique one-to-one relationship between the voltage at the surface bounding a volume conductor and those at some interior surface, on condition that the surface is *closed* and that no primary sources are present in between. All active sources are assumed to lie within the inner surface. Inverse methods based on this relationship aim at obtaining a ‘closer look’ at the sources without assuming any a priori knowledge about the character of these sources [Martin, 1970; Colli-Franzone et al. 1985]. In this method the interpretation of the computed potentials in terms of the underlying electrophysiology is derived from the subsequent processing of the inversely computed potentials [Oster et al., 1997]. This may involve, e.g., the differentiation of the inversely computed pericardial electrograms in order to estimate the timing of local depolarization. Based on the fact that the solutions can be mapped onto a surface, the method has been referred to as cardiac source imaging [Greensite, 1992].

2.5. The Equivalent Double Layer

The equivalent surface source (EDL) model expresses the entire electrical activity *within* the myocardium by means of a double layer source situated *on the closed surface* S_h bounding the myocardium. During the depolarization phase this source model is equivalent to the UDL source model. The strength of an EDL source element at any position on S_h is zero until the moment that it is depolarized, after which it takes on the (constant) strength of the UDL. The equivalence is based on the solid angle theory [Cuppen and van Oosterom, 1984; van Oosterom, 2002]. In its application to the depolarization phase, the corresponding invers problem has been termed “Activation time mapping” [Wach et al., 2001].

More generally, for any position on S_h, the time course of the local EDL source strength is proportional to the transmembrane potential, $f_m(t)$, of the cells near S_h. This property can be founded on the bi-domain theory, treating the myocardium as two interpenetrating domains: the intracellular domain and the extracellular domain. In this bi-domain the local gradients of the transmembrane potential, Ñ$f_m(t)$, act as the electric sources throughout the myocardium. The expression as an equivalent surface source, in which the gradient of the transmembrane potential throughout ventricular mass is replaced by the transmembrane potential at the surface bounding ventricular mass, stems from the application of Gauss’s divergence theorem [Geselowitz, 1989; 1992]. Its validity assumes homogeneity of the anisotropy ratio of intracellular and extracellular conductivities. Although this assumption may not always hold true, the application to represent the cardiac sources throughout the entire cardiac cycle during, *i.e.*, including repolarization, has proved to be interesting [van Oosterom, 2001].

Just like the source description based on epicardial potentials, the solutions based on the EDL can be mapped on the surface carrying the sources. These solutions can either be the isochrones of local depolarization time or the instantaneous values of the local transmembrane potential. As such this method can also be classed under the heading of cardiac source imaging.

3. Matrix Formulation of the Forward Problem

The Forward Problem can be expressed in compact form by means of a matrix formulation. This involves the discretization of the electric source *strengths* of N generator elements at T subsequent time instances, leading to a matrix $\boldsymbol{S}$, representing the entire source, having as its elements $s_{n,t}$, $n=1 \ldots N;\ t=1 \ldots T$.

In the same manner, the volume conduction effects can be represented by a transfer matrix $\boldsymbol{A}$, having elements $a_{l,n}$. Each element represents the potential in lead l generated by a unit source element n of unit strength. By using these matrix formulations of source and transfer, the entire forward computation can be expressed simply by a matrix multiplication:

$$\mathbf{F} = \boldsymbol{A}\,\boldsymbol{S}, \qquad (1)$$

with $\mathbf{F}$ a matrix (dimension $L*T$) representing the potentials at L lead positions at T discrete time instants. Applied to a single dipole of fixed location, the value of N is =3 and the rows of $\boldsymbol{A}$ are the lead vectors of the dipole.

This matrix of formulation arises naturally when dealing with the surface sources discussed above. For the source model based on epicardial potentials, the rows of ***S*** represent the time course of the epicardial potentials at all nodes representing the epicardal surface. For the EDL model, the rows of ***S*** represent the time course of the local transmembrane potential at all nodes representing the heart surface S_h (epicardium as well as endocardium).

The transfer matrices ***A*** involved in both source models are different, reflecting the specific nature of the implied sources. Most prominently, the transfer matrix for the pericardial potentials has an eigenvalue 1 with a unit right eigenvector, whereas the transfer matrix for the EDL source model has an eigenvalue 0 a for the unit right eigenvector.

The matrix formulation, Equation 1, can also be used to compute the potentials on both epicardium and endocardium as generated by the EDL source model. This computation should be classed as solving a Forward Problem. For the endocardial potentials to make sense, the volume conductor model involved, expressed by an appropriate transfer A, should include a compartment accounting for the higher electric conductivity of blood. Note that the endocardial and epicardial potentials on S_h and the local transmembrane potentials $f_m(t)$ are of a different nature. The former follows the time course of the monophasic action potential, the latter that of an electrogram. By contrast, the computation of $f_m(t)$ from observed epicardial electrograms entails solving an inverse problem. Ideally, endocardial electrograms should also be used in this computation.

This matrix formulation of the forward problem links the associated inverse problem to the domain of inverse methods discussed in a wider context in the general literature.

4. Source Imaging

Recent efforts towards bypassing the fundamental problem involved in the inverse problem of electrocardiography have led towards the source descriptions specified on surfaces. The matrix formulation of forward problem can be viewed as a mapping of the information (images) on the heart surface the onto the images on the body surface. The spreading out of the electric currents inside the body causes the images of the heart's electric activity to lose contrast and sharpness the further away from the heart the observations are made. The inverse problem can be viewed as a de-blurring problem, a problem that has direct parallels in the domain of picture processing. The produced images are much more amenable to direct interpretations in terms of electrophysiological events than either the vector or multipole expansions. This fact also facilitates the use of physiological prior information to improve the quality of the inverse solution.

In this issue four contributions are included that demonstrate recent promising developments in this field.

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