Self-trapped vibrational states in synthetic \(\beta\)-sheet helices†

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Femtosecond vibrational pump–probe spectroscopy on \(\beta\)-helical polysiocyanopeptides reveals vibrational self-trapping in the well-defined hydrogen-bonded side groups that is absent when non-hydrogen bond monomers are mixed in.

In 1973 Davydov hypothesised that the energy-transport mechanism in proteins and enzymes, which remains to this date largely undefined, may actually occur by a vibrational soliton mechanism.\textsuperscript{1,2} It was suggested that in an \(\alpha\)-helix, coupling between the amide I (CO-stretching) mode of the amide units and the NH···OC hydrogen bonds can lead to localisation (self-trapping) of vibrational energy. The vibrational excitation would then be accompanied by a local contraction of the hydrogen-bonded chain. This self-trapping makes it possible to transport the vibrational energy along the hydrogen-bonded chain in the form of a dispersionless wave packet, which would be spread out over only a few consecutive amide units in the hydrogen-bonded chain. As a consequence, the energy generated at one site of the protein could thus be transported to another site without any dispersion of the energy packet.\textsuperscript{1,3}

In order to verify the soliton concept the amide I vibrational self-trapping has been extensively studied over the last decades in particular in crystalline acetanilide, a solid compound with a well-defined array of hydrogen bonds, often used as a model for \(\alpha\)-helices.\textsuperscript{4} Despite this considerable interest, to date only Hamm and co-workers have reported a direct observation of self-trapped vibrational states in an \(\alpha\)-helix.\textsuperscript{2} They observed self-trapping of the NH-stretch (rather than the amide I) mode in poly-\(\gamma\)-benzyl-L-glutamate. Using femtosecond infrared pump–probe spectroscopy Edler \textit{et al.} could directly monitor the self-trapped vibrational states through their anharmonicity.\textsuperscript{2} Upon excitation of the NH-stretching mode, two positive excited-state bands in the pump–probe response were observed, which were attributed to self-trapped NH-stretch excitations. Interestingly, the NH-stretch mode has an energy approximately equal to that of ATP \(\rightarrow\) ADP conversion, relating it to the transport of energy in biological systems.

Here, we investigate whether NH-stretch self-trapping can also occur in \(\beta\)-sheet structures.\textsuperscript{5} To this purpose, we study the self-trapped vibrational states in synthetic \(\beta\)-sheet helices, i.e. polysiocyanopeptides. These helical polymers possess peptide side chains that form well-defined NH···OC hydrogen-bonded networks, which are arranged in the form of four \(\beta\)-sheet type arrays along the polymer backbone. By engineering the structure of this polymer, i.e. by the inclusion of side arms without amide functions, the hydrogen-bonded NH···OC chain in which the self-trapping occurs can be readily modified without significantly changing the secondary structure allowing the self-trapping process to be more easily quantified. Polysiocyanides can be readily prepared by nickel(II) induced polymerisation of isocyanide monomers to give helical macromolecules.\textsuperscript{6} The introduction of a chiral peptide substituent (e.g., L or D-alanine) as side chain both stabilises the helix and induces a preferred helix handedness (Fig. 1).\textsuperscript{7} Dipeptide derived polysiocyanides have a typical MW of \(10^5\) g mol\(^{-1}\) as analyzed by AFM\textsuperscript{7} and possess a highly defined rigid (persistent length of 76 nm)\textsuperscript{8} secondary structure in which the side arms form the above-mentioned \(\beta\)-sheet-like arrays of hydrogen bonds.

The resulting polymers are extremely stable and remain ordered even in competitive hydrogen-bonding solvents such as water. The vibrational excitation of the NH-stretch is strongly reduced in these glassy polymers, whereas in the non-glassy polysiocyanides the NH-stretch vibration is highly enhanced. The internal friction of polysiocyanides with \(\phi\)-helical side chains is reduced by a factor of \(10^4\) in comparison to the polysiocyanides with \(\alpha\)-sheet helices, which is expected to cause a decrease in energy transport through the polymer backbone.

![Fig. 1](image.png)

\textit{Fig. 1} (a) Molecular structure of poly-(\(\tau\)-isocyanolalanyl-d-alanine methyl ester) (LD-PIAA, \(1^\dagger\)) and the random copolymer \(2\) synthesised by random polymerisation of \(\tau\)-isocyanolalanyl-\(\tau\)-alanine methyl ester (DL-IAA, \(4^\dagger\)) and monomer \(3\) (see Scheme 1) used in this study. (b) Schematic drawing of the vibrational self-trapping process. An ultrashort (100 fs) infrared pulse is used to resonantly excite an NH bond in the hydrogen-bonded chain to the \(\nu = 1\) state. This causes contraction of the hydrogen bonds attached to the amide group, which in turn causes a lowering of the stretching frequency of the excited NH bond. The excited NH-group is thus no longer in resonance with its neighbouring NH-groups. This prevents delocalisation of (hence ‘traps’) the vibrational excitation.
The vibrational energy is localised on a single peak, representing absorptions of two-vibron bound states.

(iv) 0.03 equivalents Ni(ClO$_4$)$_2$ pump which is detected in a frequency dispersed manner. The optical response can be observed using a time-delayed probing polarisation dependence implies that the two excited-state result is shown in Fig. 2. The identical delay (see inset) and excitation only a single excited-state absorption peak is observed.

Changing the NH : O fraction in the copolymer allows one to manipulate the degree of connectivity of the hydrogen-bonding network in the side chain initial focus was directed to replace an amide moiety with a carbodiimide chemistry, to methyl (+)-lactate methyl ester. Liberation of the free amine of the ‘dipeptide’ with acid followed by refluxing in ethyl formate in the presence of formamide precursor of (TVBS-II), respectively. To investigate if we could modify or change the self-trapping behaviour without influencing the secondary structure, the transient absorption change of the random copolymers was also measured. It was presumed that the hydrogen-bonding network in the latter polyisocyanopeptide side chains will be partially interrupted, which should lead to isolated NH moieties and consequently a low chance of two neighbouring NH-groups interacting with each other. We chose to incorporate a non-hydrogen bonding isocyanide (with similarities to the bis-alanine derived isocyanide) instead of denaturing the secondary structure (by acid or high temperature), as the latter method would change the overall conformation of the polymer and lead to a complex, inhomogeneously broadened infrared spectrum. To disrupt the one-dimensional hydrogen-bonding network in the side chain initial focus was directed to the incorporation of an N-methylated alanine unit in the isocyanopeptide, but this however proved to be unsuccessful due to cyclisation of the N-methylated monomer into a diketopiperazine (Scheme 1 and ESI†). As a consequence focus was directed to replace an amide moiety with an ester functionality, as illustrated in monomer 3 (Scheme 1 and ESI†). In short, Boc-L-Ala-OH was first coupled, using carbodiimide chemistry, to methyl (R)-(+) lactate methyl ester. Liberation of the free amine of the ‘dipeptide’ with acid followed by refluxing in ethyl formate in the presence of sodium formate generated, after column chromatography, the formamide ([(S)-1-methoxy-1-oxopropan-2-yl]2-formamido-propanoate) derivative. Dehydration of the N-formyl moiety with diphenogse and N-methylmorpholine resulted in the isocyanide derivative 3 which could be subsequently copolymerised. 1H NMR spectroscopy (Fig. S1 and S2, ESI†), however, revealed complete epimerisation of the first ‘amino acid’ residue, as also indicated by the doubling of the signals in the $^{13}$C NMR spectrum. The formamide was optically pure as evidenced by the comparison of the optical rotation of the formamide precursor of 3 ($[\alpha]_D = +17$ (c 1.2, CHCl$_3$)) with the enantiomer of the formamide ($[\alpha]_D = -17$ (c 1.2, CHCl$_3$)).

NH-group (TVBS-I) and on nearest-neighbouring NH-groups (TVBS-II), respectively.

The NH-stretch vibrational self-trapping was followed using femtosecond vibrational pump–probe spectroscopy. Upon excitation of the NH-stretch mode with a short (100 fs) infrared pulse (centre frequency 3260 cm$^{-1}$), the optical response can be observed using a time-delayed probing pulse which is detected in a frequency dispersed manner. The result is shown in Fig. 2. The identical delay (see inset) and polarisation dependence implies that the two excited-state absorption peaks are both due to the NH-stretching mode (Fig. 2). This anomalous response (for normal vibrational excitations only a single excited-state absorption peak is observed) is very similar to the one observed by Hamm and co-workers for self-trapped states in $\alpha$-helices. The two peaks represent absorptions of two-vibron bound states (TVBS) in which the vibrational energy is localised on a single
Fig. 3 Absorption change upon NH-stretch excitation of LD-PiAA and of random copolymer 2 (red line 1 : 15 NH : O). Disruption of the hydrogen-bond network completely eliminates vibrational self-trapping.

excellent model systems for the study of vibrational self-trapping and energy transport in β-sheet-like structures.

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Notes and references


