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On the electronic band structure of periodic β-pleated sheet polypeptides in the presence of water and ions*

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The structure of the possible water surroundings of several periodic polypeptides in the β-pleated sheet conformation has been determined by Monte-Carlo calculations. The resulting water positions have been used to calculate the band structure of the polymers in the effective field of these water molecules. In addition, similar calculations have been performed with sodium ions in the solution. It has been found that the changes of the band widths and of the band gaps are less than 1.8 eV in the presence of water and less than 1.1 eV in the presence of water and ions. The band positions themselves are, however, shifted by up to 3.7 eV in the presence of water and by up to 6 eV in the presence of water and ions.

Key words: Polypeptides — Hydration — Band structure

1. Introduction

Most biomolecules like DNA, proteins, etc. occur in vivo in aqueous solution. Electronic structure calculations on such biomolecules should therefore be accompanied by investigations of the effects of the solvation shell on the electronic structure. Indeed, as we shall show in this paper for the polymers considered, the effects of the solvation shell on the energy bands of several polypeptides in the β-pleated sheet conformation (from now on abbreviated as β-conformation)

* Dedicated to Professor J. Koutecký on the occasion of his 65th birthday

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differ not only in magnitude, but also in direction of band shifts and changes of the band widths. This means that explicit calculations of the kind described below are in principle necessary for each individual system if the influence of hydration on the band structure is to be predicted.

The approach followed here is the simulation of the solvent strucure of biomolecules by Monte-Carlo methods as reported by Clementi et al. [1, 2]. We mention, however, that there are also other possible approaches, as for example the supermolecule calculations reported by Pullman et al. [3]. In the Monte-Carlo approach it is possible to obtain information on the electronic structure of the solvated biomolecule by performing Hartree-Fock calculations on the molecule in the field of the surrounding charges. Even for polymers this is possible and has been done for the band structure of a cytosine stack in aqueous solution [4]. Recently, the influence of the solvation shell on β-alanine (a peptide chain of alanine in its β-conformation) has been reported [5]. The purpose of the present study is, on the one hand, a comparison of the interaction of various β-polypeptides with water and, on the other hand, to investigate the influence of solved ions on the electronic structure of biopolymers. Ion-containing solutions and their structure around biopolymers have also been studied by Clementi and Corongiu [6–7] and it has been found that Na^+ ions around B-DNA in solution form well-defined structural patterns. We consider in the present study both pure water solvation and the effect of Na^+ ions in the solution, aiming to determine the position of Na^+ ions in the hydration shell around the β-polypeptides and to calculate the changes in the electronic band structure induced by their presence.

2. Methods

The calculation of the effects of the solvation shell on the electronic structure of a polymer essentially involves two steps: first, the positions of the water molecules (and as the case may be, the ions) surrounding the polymer have to be determined by the Metropolis Monte-Carlo method [8], and second, the band structure of the polymer in the effective field of the surrounding molecules has to be calculated by the *ab initio* crystal-orbital method [9, 10].

The Monte-Carlo simulation was performed with the Metropolis sampling scheme [8] for a temperature of 300 K and a water density of 1.0 g/cm^3. Periodic boundary conditions have been assumed with two amino acid residues in the sample cube. The height of the cube is, therefore, identical to double the translation distance of the polypeptide; length and width are automatically determined by the program so as to include at least two solvation shells and part of the bulk water.

In the case of the calculation with water and sodium ions, two Na^+ point charges were placed in the cube. The water-water interaction potential is the approximate analytical solution fitted to configuration interaction calculations by Clementi et al. [11]. The amino acid-water, amino acid-Na^+, Na^+-Na^+ and water-Na^+ interaction potentials are also approximate analytical solutions fitted to calculations by Clementi et al. [12–14].

The total interaction energy of the system has been calculated for 10 240 cycles (i.e. $10\,240 \times n$ different configurations, where n is the number of water molecules and ions; one cycle implies a move for each molecule separately and successively). The first 5120 cycles were discarded from the statistical analysis; the results are based on averages over the last 5120 cycles. Sub-averages were taken over macrosteps consisting of 128 cycles. As a rule of thumb we chose the step length so that about half of the random configurations were accepted. The minimal energy configuration was reached when the total interaction energy did not change more than 0.8 kcal for at least 1000 cycles.

The Hartree-Fock calculations have been performed by the crystal-orbital method [9, 10]. The β-pleated sheet structure [15] has been assumed and the geometry of the amino acids representing the elementary cell has been built up using standard bond lengths and bond angles [16]. The same geometries have also been used in a previous study of the band structures of periodic polypeptides without surrounding water [17]. All band-structure calculations have been performed in a strict second neighbour interaction approximation (except in one case; see Sect. 3.2), using Clementi's 7s3p and 4s minimal basis sets [18]. Each water molecule has been represented by 23 point charges contributing to the one-electron matrix in the crystal-orbital calculation. The polarization effect by the mutually interacting fields [19] has been found in test calculations to be negligible for larger clusters of water molecules.

Most of the Monte-Carlo and smaller band-structure calculations were performed on an FPS-164 array processor in the single-job execution mode. The larger band-structure calculations have been performed on an IBM 3090 computer with vector-oriented compiled programs (a typical CPU time is 1.6 h for a serine stack in the presence of water).

3. Results and discussion

3.1. Polypeptides with water interaction

In Table 1 we list the band edges, band widths and band gaps for glycine (gly), alanine (ala), serine (ser), cysteine (cys), histidine (his), valine (val), asparagine (asn), and aspartic acid (asp). For all systems the data obtained without water interaction (F for free polymer calculation) and with water interaction (W) are given for the valence band (N) and the conduction band (N+1).

One can distinguish the systems according to the way their bands are shifted by the water point charges: for glycine, cysteine, aspartic acid, serine and aspartic acid both valence and conduction bands are shifted down; for alanine, valine and histidine both valence and conduction bands are shifted upwards; for asparagine the conduction band is shifted down and the valence band is shifted up. The reason for this different behaviour is to be found in the different local orientations of the water molecules which are nearest to the amino acid.

For instance, in the case of serine the nearest water molecule is attractive, as is shown schematically in Fig. 1: water molecule 1 is the nearest to the polypeptide

Table 1. Band structure results for polypeptides in the presence of water (all energies in eV)

System[a]	Type of band[b]	Lower limit	Upper limit	Band width	Band gap
gly	N+1	3.601	4.174	0.573	15.784
F	N	−12.574	−12.183	0.391	
gly	N+1	3.090	3.691	0.601	15.846
W	N	−13.082	−12.756	0.326	
ala	N+1	3.760	4.355	0.595	15.826
F	N	−12.261	−12.066	0.195	
ala	N+1	3.801	5.024	1.223	15.047
W	N	−11.482	−11.246	0.236	
ser	N+1	4.313	4.944	0.631	15.411
F	N	−11.209	−11.098	0.111	
ser	N+1	0.701	1.283	0.582	14.742
W	N	−14.274	−14.041	0.233	
cys	N+1	4.154	4.734	0.580	14.779
F	N	−10.715	−10.625	0.090	
cys	N+1	3.434	4.083	0.649	14.974
W	N	−11.660	−11.540	0.120	
his	N+1	3.233	3.642	0.409	13.501
F	N	−10.291	−10.268	0.023	
his	N+1	4.632	5.157	0.525	12.910
W	N	−8.277	−8.274	0.003	
val	N+1	2.833	3.270	0.437	14.746
F	N	−12.091	−11.912	0.179	
val	N+1	4.133	4.585	0.451	14.691
W	N	−10.764	−10.558	0.207	
asn	N+1	3.988	4.587	0.599	15.572
F	N	−11.704	−11.584	0.120	
asn	N+1	3.047	3.068	0.021	13.985
W	N	−10.976	−10.938	0.037	
asp	N+1	3.169	3.178	0.019	15.057
F	N	−12.109	−11.898	0.211	
asp	N+1	0.646	0.676	0.029	15.256
W	N	−14.790	−14.609	0.181	

[a] For the abbreviations of the polypeptide names see text; F = free-polymer calculations; W = calculation in the presence of water

[b] N = valence band; N+1 = conduction band

and is pointing with the positive hydrogen atoms towards the negative oxygen atom of polyglycine; water molecules 2 and 3 (dashed lines) are already at a longer distance from the polymer (water molecule 2 is actually above the drawing plane, molecule 3 below); the water molecules around the side chain are at greater distance from the polymer than the first three and their influence on the side chain largely cancels. Therefore, the attractive interaction leads to a shifting down of both valence and conduction band.

Not always is the situation as evident and easy to depict as in the case of serine. In the case of histidine, for instance, there are many water molecules at similar short distances. However, it seems that their total influence is repulsive and both valence and conduction bands are shifted up. In the case of asparagine, the point

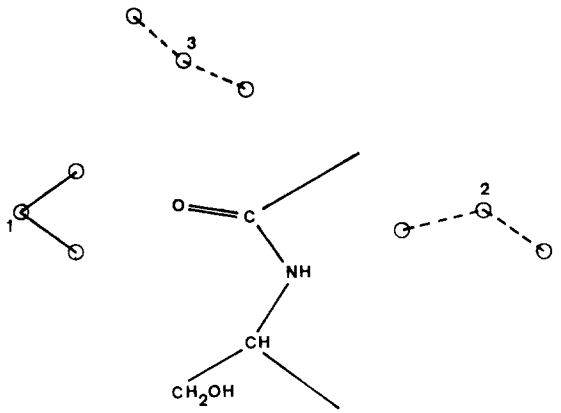

Fig. 1. Schematic projection of the nearest water molecules around a serine residue

charges are repulsive near the backbone, attractive near the side chain; therefore, due to the different localization of the eigenvectors of valence and conduction band on backbone and side chain, the conduction band is shifted down and the valence band is shifted up.

Figure 2 shows a comparison of the situations in glycine and valine. In both cases there are two water molecules near the polymer. For glycine (dashed lines) they are both pointed with the positive charges towards O′ and N; for valine (full lines) one (molecule 1) is pointed with the negative charge towards O′ and is therefore repulsive; the other (molecule 2) has both positive and negative charges near to C′ and N in such a way that it is only slightly attractive. Therefore, the bands are shifted downwards in glycine, while they are shifted upwards in valine.

The change in the band gap depends not so much on the general distance of the water molecules from the whole polymer, but more on the individual distances to the relevant groups (on which the eigenvectors of the bands in question are

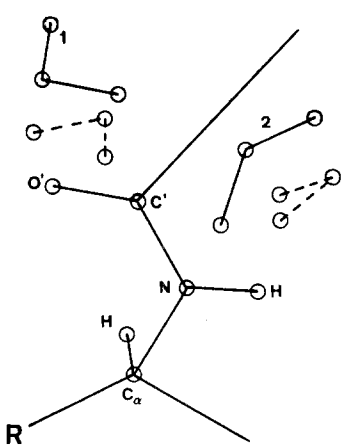

Fig. 2. Schematic projection of the nearest water molecules around a glycine and valine residue, respectively *Full lines* are for valine, *dashed lines* for glycine)

localized). Since the distribution of the water molecules around the individual atoms or groups depends on the chemical character (e.g. hydrophobic or hydrophilic) of that group, the value of the band gap should be a more significant property of a system in aqueous environment than the shifts of the bands. In the case of valine, for example, the upper valence band edge belongs to $k = \pi/a$ (where a is the translation distance) and the corresponding eigenvector is localized more on O than on N. The lower conduction band edge belongs to $k = 0$ and the corresponding eigenvector is localized more on C than on O. The strongly repulsive water, molecule 1 in Fig. 2, thus shifts the upper valence band edge upwards more than it shifts the lower conduction band edge, which is more under influence of the weakly attractive water molecule 2, upwards. The band gap is therefore decreased.

A similar mechanism is operative for the band widths. For the above example of valine the lower valence band edge ($k = 0$) has an eigenvector which is less localized at O′ than that for the upper edge. Therefore, the lower valence band edge is shifted less upwards than the upper one and the valence band width is increased.

One can also classify the systems according to the way their gap is affected by the surrounding water: it is decreased for polyalanine, polyserine, polyhistidine, polyvaline and polyasparagine; it is increased for polyglycine (only very little), polycysteine, polyasparagine$^+$ (only very little) and poly(aspartic acid). The changes in the band gap and band widths are never larger than 1.8 eV, the largest change occurring for poly(aspartic acid) [8]. The shifts of the band positions are somewhat larger: 3.66 eV in the case of poly(serine), where the shift is largest.

3.2. Polypeptides in the presence of water and ions

In Table 2 the different interaction energies (in kcal/mol) between water-water, amino acid-water, Na^+-Na^+, Na^+-water and amino acid-Na^+ are listed. For convenience of comparison with other Monte-Carlo calculations the interaction energies are divided by two, in contrast to the binding energy and the energy partitioning for different regions of the amino-acid residues. E_{WW} is the average water - water interaction energy, i.e. the average of the interaction energies between one water molecule and the other water molecules. E_{WA} is the average amino acid - water interaction energy, i.e. the average of the interaction energies between the two amino-acid units and the water molecules in the cube. E_{II} is the average of the interaction energies between one sodium ion and the other sodium ions. E_{IA} is the average interaction between the two amino-acid units and the sodium ions in the cube. E_{WI} is the average of E'_{WI} and E'_{IW}, where E'_{WI} is the average of the interaction energies between one water molecule and the sodium ions in the cube, E'_{IW} is the average of the interaction energies between one sodium ion and the water molecules in the cube.

The results in Table 2 show that the water-water interaction energy is much less in the case of the polypeptides with sodium ions than for the same system without

Table 2. Interaction energies (in kcal/mol) for Monte-Carlo results for polyalanine and polyvaline

System	Ala without Na^+	Ala $Na^+(2)$	Val without Na^+	Val $Na^+(2)$
E_{W-W}	−8.90	−6.9	−8.8	−7.0
E_{W-A}	−6.4	−1.6	−20.8	−2.0
E_{I-I}		0.1		0.01
E_{I-A}		−29.5		−24.8
E_{W-I}		−66.1		−62.8

Table 3. Band structure results for polypeptides in the presence of water and ions (all energies in eV)

System[a]	Type of band[b]	Lower limit	Upper limit	Band width	Band gap
ala	N+1	3.760	4.355	0.595	15.826
F	N	−12.261	−12.066	0.195	
ala	N+1	3.801	5.024	1.223	15.047
W	N	−11.482	−11.246	0.236	
ala 2	N+1	3.099	3.254	0.155	15.655
W, Na(2), I(2)	N	−12.613	−12.556	0.057	
val	N+1	2.833	3.270	0.437	14.746
F	N	−12.091	−11.912	0.179	
val	N+1	4.133	4.585	0.451	14.691
W	N	−10.764	−10.558	0.207	
val	N+1	0.974	1.375	0.401	14.442
W, Na(1), I(1)	N	−13.582	−13.468	0.114	
asp	N+1	3.169	3.178	0.019.	15.057
F	N	−12.109	−11.898	0.211	
asp	N+1	0.646	0.676	0.029	15.256
W	N	−14.790	−14.609	0.181	
asp^-	N+1	6.404	7.228	0.824	15.103
W, Na(1)	N	−8.796	−8.700	0.096	

[a] For the abbreviations of the names of the polypeptides, see the text; F = free-polymer calculations; W = calculations in the presence of water; W, Na(J), I(J) = calculations in the presence of water, J sodium ions and J negative point charges per elementary cell

[b] N = valence band; N+1 = conduction band

them. The amino acid-water interaction energies also become less in the presence of the sodium ions. The observed trends indicate that the water-water and water-amino acid interactions are considerably weakened by the presence of the sodium ions. The reason is that due to the strong Na^+-water and Na^+-amino acid interactions the positions and (even more important) the orientations of the water molecules, i.e. the structure of the aqueous solution, were changed in such a way that they are polarized away from each other and from the amino acid and towards the sodium ions.

In Table 3 we show the band edges, band widths and band gaps for polyalanine, polyvaline and poly(aspartic acid) in the presence of water and solvated ions.

To keep electric neutrality we have placed negative point charges at suitable

positions in the system in the case of the band-structure calculations on polyalanine and polyvaline with Na^+ ions (see Fig. 3); in the case of poly(aspartic acid) we have chosen the ionic form, i.e. the form where the COOH group is replaced by COO^-, for the calculation with Na^+ ions. (The ionic form occurs in some concentration in solution [20].) The positions of the negative point charges for polyalanine and polyvaline were chosen so that they were compatible with the water structure; namely they were positioned at a distance of 3–3.5 Å from the corresponding Na^+ ion in a direction away from the polymer with small deviations such that a place was found where the surrounding water molecules pointed with the positive ends towards the negative point charge.

This procedure is a compromise which allows us to perform a band-structure calculation for polymers in the presence of sodium ions by keeping the whole system neutral. The negative point charges have only model character in this case and describe the charge balance of the environment. It is true that between the positions of these negative point charges (in contrast to the Na^+ ions) and the polypeptide chain there may be water molecules which would warrant the introduction of a dielectric constant. If this were done only for the negative point charges, but not for the Na^+ ions, an infinite chain would again behave as a

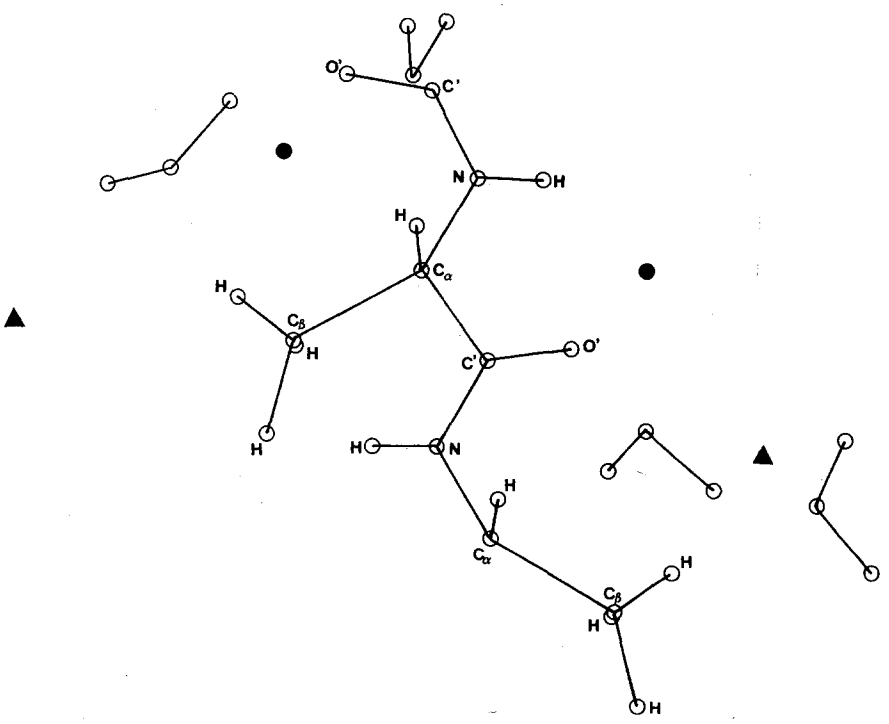

Fig. 3. Schematic projection of the nearest water molecules, sodium ions and negative point charges around alanine residues (*Full circles* represent the sodium ions, the *triangles* represent the negative point charges)

chain with an infinite number of unbalanced charges which, of course, cannot exist. Since in reality a polypeptide chain is always finite and one does not have an Na^+ ion at every site, the best way to model the real situation is - in our opinion - not to introduce a dielectric constant either for the effect of the Na^+ ions, or for the negative countercharges.

The calculations were done in the following way: two Na^+ ions were placed in a cube extending over two alanine units for the Monte-Carlo calculation; the system was heated up to a higher temperature in 128 cycles and then cooled down again during 512 cycles to 300 K. A large unit cell comprising both alanine units was used, employing the first neighbour interaction approximation. (This is not equivalent, but is similar in accuracy to taking a small unit cell of one alanine unit and employing the second neighbour interaction approximation.) The calculations for the other two systems, polyvaline and poly(aspartic acid), were done with one Na^+ ion per small unit cell (containing one amino acid).

The following trends can be observed in the results of the band structure calculations (Table 3), for polyalanine the band gap is decreased by the water interaction and again somewhat increased in the presence of ions to a value still below that of the interaction-free polymer. As shown in Fig. 3, the two sodium ions try to avoid each other and to be close to the CO groups. There they will decrease the influence of the water interaction as discussed above, which in turn leads to a reduction of the effect on the band gap. The situation is, however, different for polyvaline, which has a larger hydrophobic side group and which shows an enhancement of the water effects on the band gap by the ions, namely a further decrease of the gap. For poly(aspartic acid) the gap is increased in the presence of water and again somewhat decreased in the presence of ions to a value still above that of the interaction-free polymer. The band widths are decreased for both polyalanine and polyvaline. For poly(aspartic acid) the conduction band width is increased and the valence band width is decreased.

The effects on band widths and band gap, however, always remain smaller than 1.1 eV, the polyalanine widths showing the strongest changes. The band positions, on the other hand, change by up to 6 eV - in the case of poly(aspartic acid). This means that the ions in the solution influence the electronic levels of the polymers, but that the levels are shifted more or less parallel to lower energies.

It is also interesting to note that the changes of the band positions are quite large in comparison to what one would expect from simple electrostatic considerations. This is due to the rearrangement of the electron populations under the influence of the charges, on the one hand, and the closeness of the Na^+ ions to the polymer (making the use of a dielectric constant problematical), on the other.

4. Conclusions

We have performed calculations on the electronic structure of several β-polypeptides in the presence of water and ions. There are some shifts of the bands in the presence of ions, but the shifts are more or less parallel; this expresses itself

in the fact that the band widths and the band gap are changed to a much lesser degree than the band positions. In the presence of water alone the maximal changes are still smaller than the changes in the presence of water and ions. The behaviour of the shifts in general seems not to be predictable without explicit calculations in each case. However, the smallness of the changes in the band gap values suggests that water and ions should not have too much influence on the conduction properties of polypeptides. This justifies the use of free-polymer calculations in the investigation of the conductivity of periodic [17, 20] and non-periodic-polypeptides [21]. The importance of this conclusion for experimental measurements of the a.c. conductivity of non-periodic polypeptides should also be emphasized, namely, that in a recent investigation on a four-component (gly, ser, cys, asn) disordered polypeptide chain it has been shown that this system can become a good variable-range hopping conductor if free charge carriers are present (in vitro through doping with electron donors, in vivo in a nucleoprotein very probably through charge transfer from DNA to the polypeptide) in its conduction band region [21].

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