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Structure of Water and Counterions in DNA

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Monte Carlo simulation have been performed to study the hydration of two DNA conformers: the right-handed B-DNA and the left-handed Z-DNA, both in the double helix conformation. The models used to represent the polyelectrolytes consist of three full pitches (60 and 72 nucleotides units for B- and Z-DNA, respectively).

The simulations have been carried out at a temperature of 300 K with 500 water molecules per pitch and as many counterions as necessary to neutralize DNA. In the present studies three different monocharged counterions have been considered: Li^+, Na^+ and K^+. During the Monte Carlo process either the water molecules or the counterions are subject to displacements [1].

The Monte Carlo walks, for these six simulations, have been analyzed in such way to give, for the counterions, information about their position (not yet determined by experiments), and the number of water molecules in their first hydration shell. Some of the counterions have, in the first hydration shell, the same number of water molecules as determined for the same ion in solution [2], but some other lose one or even two water molecules and complete their coordination by binding DNA atoms. There is a preference for the three kind of ions here analyzed, to bind either the PO_4^- groups or the N7 atoms in guanine and adenine [3].

The water structure in the first hydration shell of the DNA is analyzed for specific sites (for example for the nitrogen or the oxygen atoms at the bases) or for groups of sites (for example the bases or the PO_4^-). For both DNA conformers, the polyelectrolyte loses water from the first hydration shell if K^+ is replaced with Na^+ or Na^+ with Li^+.

As known in B-DNA, there are two grooves, the minor and major. The water was found to be highly structured in both grooves. In the minor groove there is either a long filament of water molecules running along the groove or small filaments connecting two phosphate groups belonging to the same strand. In the major groove the water molecules form filaments connecting phosphate groups belonging to two different strands [4]. The first and the last type of filaments are stable for a sufficiently long time as to be detected by X-ray diffraction, as shown recently [5].

These results have been obtained performing, for each of the six simulations, 10^6 displacements (after equilibration). As known, after each displacement the interaction energy of the system, namely, the interaction energy between water–DNA, water–ions, ion–ion, ion–DNA and water–water is computed. In the present study the interaction energies are calculated with potentials obtained by fitting thousands of *ab initio* computations [6]; for the water–water the MCY potential [7], obtained from Configuration Interaction computations, has been used.

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Ion Transport through Membranes: A Computer Experiment

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Gramicidin-A is a linear pentadecapeptide antibiotic, which forms transmembrane channels; these have a number of interesting conductance characteristics [1, 2 and Refs. therein], as for example high specific ion fluxes (a single channel carries about 10^7 sodium ions/sec at 25 °C, 1 *M* NaCl and 100 mV transmembrane d.d.p.) and have a remarkable ion selectivity among the monovalent cations. The permeability ratios with respect to sodium were found to be in the following order $H^+(150) > NH_4^+(8.9) > Cs^+(5.8) > Rb^+(5.5) > K^+(3.9) > Na^+(1.0) > Li^+ (0.33)$. The channel is impermeable to anions and to divalent cations and it exhibits saturation and maxima in conductance as a function of ion concentration, voltage dependence of single channel currents, ion competition and block, and concentration dependence of permeability ratios. These conductance properties make the Gramicidin-A channel in some respects similar to the Na^+ and K^+ transmembrane channels responsible for the excitability of nerve and muscle cells; this enhances the interest in the Gramicidin channel.

The Gramicidin-A channel seems to have two binding sites for monovalent cations, as suggested by NMR experiments using ^{13}C marked Gramicidin molecules [2]. The free energy profile for the transport of Na^+ has also been determined [3].

A number of possible structural models for the Gramicidin channel have been considered [4] involving single helices [5, 6], or double helices [4, 7]. In Urry's model, which seems in agreement with a number of experimental works, two left-handed $\beta^{6,3}_{3,3}$ Gramicidin helices are held together at their N-termini (heads) by hydrogen bonding to form a channel with a length of 26 Å and a pore diameter of 4 Å.

A qualitative mechanism of ion transport and ion selectivity has been proposed [8], arising from the liberation of the carbonyl oxygen into the channel, lining it with negative charges. The general picture of the phenomenon, however, is far from complete. Indeed, other molecular conformations could contribute to the conduction process [4] and even small variations in the conformation of the Gramicidin channel could affect the energetics of channel–ion interactions [1].

In order to help our understanding at the molecular level of some of the above problems concerning the interaction between the Gramicidin-A channel and ions and the role played by water in the ion transport process, we have undertaken computer simulation experiments on this system, assuming Urry's model for the channel. As for similarly large systems previously investigated [9, 10], our initial effort has been directed to the evaluation of pair potentials for the interactions between atoms of the residues and of the backbone, and sodium ion/water molecule. This step, which makes possible Monte Carlo and molecular dynamics simulations, required about one thousand three hundred *ab initio* computations even considering the Na^+ ion only. In addition, more than four hundred *ab initio* computations have been carried out to evaluate pair potentials relative to the interaction between Na^+/water molecule and the phospholipid lysophosphatidylethanolamine, which is used to simulate the membrane moiety of the system. Results of Monte Carlo simulations based on the above models and pair potentials are presented [11].

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Molecular Dynamics Simulations of Aqueous Electrolyte Solutions

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Structural and dynamic properties of various aqueous electrolyte solutions have been calculated from MD simulations where the ST2 and the Central Force model of water were employed [1].

The structural properties of the solutions are discussed on the basis of radial distribution functions, the orientation of the water molecules and their geometrical arrangement in the hydration shells of the ions. An example of the latter case is given in Fig. 1 for a $MgCl_2$ solution [2]. The figure shows that the oxygen atoms of the six water molecules in the first hydration shell of Mg^{++} are positioned at the corners of a regular octahedron, while for Cl^- an octahedral arrangement only is indicated. The four nearest neighbor water molecules around a central one show a tetrahedral structure and the distributions are sharper in the hydrogen atom directions than in the lone pair directions.

Dynamic properties of the solutions such as self-diffusion and rotational diffusion coefficients, reorientation times of the dipole moment vector and residence time of the water molecules in the hydra-