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The hydration structure of the Na^+ and K^+ ions and the selectivity of their ionic channels

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Abstract

Some ions, mainly Na^+ and K^+, play a fundamental role in the excitability of the nerves and muscles because they are transported through the ionic channels of their cells. The selectivity of these channels is related to the hydration structures of the ions that were determined for Na^+ and K^+ by means of Monte Carlo simulations of systems constituted by water molecules and the ions at infinite dilution. The Na^+ hydration shell, which is formed by three water molecules, is quite stable while the K^+ ion can only perturb the water structure in its immediate neighborhood so that it is unable to attract the water molecules. As a result the diameter of the hydrated Na^+ is about 0.5 nm while the K^+ diameter is equal to its ionic diameter. Taking into account the steric hindrance and the energy profiles, K^+ can pass through 0.3 nm diameter channels while the dimensions of the Na^+ channel must be at least 0.5×0.3 nm^2 so that the ion maintains part of its solvation shell. Grand canonical Monte Carlo simulations were also conducted on water confined in cylindrical channels. In a 0.3-nm diameter rigid channel, the mean water concentration is close to 90% of the bulk one and the mean configurational energy is equal to 50% of the bulk energy. In a 0.5-nm diameter rigid channel, these fractions are 60 and 67% respectively . The results suggest that water molecules can be substituted by a K^+ ion in its channel without large energetic cost and that the exchange between the molecules of the medium and the hydration molecules can occur at a low energetic cost in the Na^+ channel. These results are in good agreement with experimental data on the selective transport of these ions.

Keywords: Ionic channel; Ionic transport; Monte Carlo simulation; Hydration shell; Electrolitic solution

1. Introduction

Ions play an important role in the excitability of nerves and muscles [1]. The excitation, or the electric signal, is generated by the transport of ions through the ionic channels which are the elements of primary excitation in the membranes of the nerve, muscular and other tissues cells. The electrically excitable cells maintain high K^+ and low Na^+ intracellular concentrations when compared to the extracellular concentrations. The concentration gradient results in an electrical potential. The concentration gradients are maintained by the action of the Na^+, K^+-ATPase pump. The resting potential, which is negative inside these cells, is controlled mainly by the ratio between the internal and external K^+ concentrations since the membrane surface is specifically permeable to this ion. The main difference between the cells that are electrically excitable and the others is that the ionic channels of the former ones are sensible to the potential difference between the internal and external surfaces of their membranes. The response of the channels to the membrane potential changes occurs in a few milliseconds by means of a regenerative increase of the permeability to specific ions. Ionic channels in the axon membrane surface are permeable to ions such as Na^+ and K^+. The action potential is generated by the ionic transport of Na^+ and K^+ ions in their respective channels. The Na^+ influx that occurs first due to the Na^+ channels opening is followed by the K^+ outflux due to the K^+ channels opening [1]. The ionic channels are mainly constituted by proteins forming macromolecular pores with diameters of about 0.3 to 0.8 nm. Different kinds of channels can open and close synchronously resulting in electric signals and responses of the nervous system. The opened highly selective ionic channels allow the entry of some kind of ions along the electrochemical gradient with a flux

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of about 10^6 ions/s [1]. The Na^+ channels are very similar while the structure and function of the various K^+ channels are so different that they can be classified as distinct channels [1,2]. The selectivity of the ionic channels is due to the dimension of the selectivity filter (the narrower part of the channels), to the existence or absence of polar groups on the walls, and to the interaction of the ions with the solvent, or water molecules. The internal dimension [1,3] of the Na^+ channels is about 0.3 by 0.5 nm. They are also permeable to some other cations [1,3] such as Li^+ and $HONH_3^+$. The 0.3 nm diameter [1,4,5] K^+ channel is also permeable to the Rb^+ and Tl^+ cations [1,4]. The channels are blocked by external low pH that protonates the acid groups in the interior of the channels [1,4]. The hydration energy and number of solvation molecules constituting the hydration shell of the ions also contribute to the selectivity of the channels since the ions must lose their hydration water molecules to enter the channels. This results in an increase of the interactions with the polar groups of the selectivity filter and in an electrostatic stabilization of the ionic permeation [1].

Many models were developed [6–13] to describe the ionic channels, either for theoretical, or for experimental purposes, such as the gramicidin model [6]. Simulation techniques were applied recently to the study of these systems. They are used as a complement to explain the nature of experimental data, to test theories, to check molecular models, to foresee experimental data or to generate information that experiments cannot procure. These techniques allow one to obtain structural, thermodynamical and dynamical data by means of the Monte Carlo [14–17] and/or the molecular dynamics [14,15] methods. The properties of any system depend on the trajectories of its molecules which can be obtained by means of the integration of motion equations such as the Newton ones. The objective of a simulation is to integrate these equations in some way in order to extract from the different generated configurations the basic information that will be used to determine structural, thermodynamical or dynamical properties. Two methods are available for this purpose. The first one is the numerical integration along time using some definite time step: this is molecular dynamics. The second method considers sets of configurations that are randomly generated as: the coordinates of a molecule are changed randomly. The new configuration is accepted if the energy change between the final and initial state is negative, or is accepted conditionally, using the Boltzmann factor, if the energy change is positive. The coordinates of all the molecules are changed sucessively in the same way or by random choices. Many such cycles are realized along an entire simulation. Both the molecular dynamics and the Monte Carlo method are equivalent for modeling structural and thermodynamical properties while only molecular dynamics is able to obtain dynamical properties. The first step in a simulation is to choose a model that describes fairly well the system to be studied. The choice of a model means to determine how the components of the system interact, i.e., to determine the intermolecular interaction potential. A well-known example is the Lennard-Jones potential.

In the particular case of the aqueous systems, many models are available, all of them containing parameters to be determined empirically from experimental data, and/or from ab initio quantum-mechanical calculations [18–29,31]. Two different potentials will be used in the present work. The first one is the TIP4P model [29] which describes the water molecule as formed by four interaction points: two positive charges on the hydrogen atoms, a negative one located at 0.015 nm from the centre of the oxygen atom in the direction of the dipole moment, and the centre of the oxygen atom which is the origin of the 6-12 potential. The second potential is the SP3 potential [31], which describes the water molecules as formed by rigid spheres with two embedded dipoles together with multipolar contributions. The geometries of the water molecules in both models are equal, i.e., the length of the O–H bond is 0.09572 nm and the H–O–H angle is fixed at 104.52°.

The objective of the present communication is to associate the hydration structures of the Na^+ ion [32] and of the K^+ ion with the ionic specificity of some ionic channels. The solvent structure in the neighborhood of the ions is important information to describe and to understand the dynamical and thermodynamical properties of the electrolyte solutions in physico-chemical and biological systems [1,32–38]. In spite of the increase in experimental and theoretical information on solvation in recent years [32–38], many doubts remain with respect to the shielding mechanisms or to the effect of the solvation shells on the electrolyte solution properties. Many solvent molecules are submitted to the influence of the electrostatic field of an ion in their neighborhood but only some of them are subjected to such intense interactions that they lose part of their degrees of freedom, i.e., the solvent molecules are no longer able to travel with some freedom in all spatial directions. The structure of the shells of solvent molecules close to the ion depends on the intensity of the ionic electrostatic field and on the thermal motion [32,33]. Consequently the closest region, called the solvation shell, is the most important since the electric dipoles have some chances to be parallel with the field presenting an attractive energy. This is the reason why the number of water molecules which remain together when the ion is submitted to external electric fields can frequently be considered as the hydration number. The hydration number is obtained experimentally by thermochemical [35] and transport data [35], or by X-ray and neutron diffraction analysis [39]. The hydration number obtained from these sources are sometimes difficult to compare [35,39] because the final result depends on the specific property used for their derivation. The simulation methods are in these cases useful to help the understanding of solvation properties. Recently it was shown [32,33] that precise structural information on the hydration structure of ions can be obtained, at infinite dilution, from some specific multivariable distribution functions which provide, for example, information about the relative orientation of molecules. It was also shown that the energy profile of solvent molecules in the neighborhood of ions is a stability criterion for the hydration structure [40,42], and important to explain the transport of ions in microchannels.

2. Models and method

The hydration structure of the K^+ ion can be determined by the same methodology that was applied [32] to the Na^+ ion: a system constituted by one ion and 124 water molecules was simulated by the Monte Carlo method in the NpT ensemble [14–17] at 298 K and under an external pressure equal to 101 325 Pa. During the simulation the ion remains fixed at the center of the simulation cube while periodic boundary conditions and minimum image convention are applied to the solvent molecules [14], so that the simulated electrolyte solution is infinitely dilute [32,38,40,41,43]. The water molecules are modeled by the TIP4P potential [29] and the interactions between the water molecules and the K^+ ion by an electrostatic interaction plus a Lennard-Jones potential [30]. No special treatment, such as the Ewald sum, was given to the long-range forces since we are interested in the hydration structure close to the ion [32,38,40,41,43]. The Monte Carlo simulations are performed according to the following procedure: the maximum displacement of the center of each oxygen atom is 0.0014358 nm while a random rotation is obtained by three random rotations (maximum 15°) around each Cartesian axis. Volume variations, maximum 1.3% of the whole volume, are attempted at each 50 complete NpT Monte Carlo cycles. The resulting mean densities are equal to 1.048 ± 0.025 kg dm^{-3} for K^+ and 1.070 ± 0.022 kg dm^{-3} for Na^+ and the mean molar energies are equal to -11.35 ± 0.15 kcal and -11.64 ± 0.14 kcal respectively. These data were obtained over 99 200 000 configurations (800 000 Monte Carlo cycles) for the K^+ ion and 18 600 000 (150 000 cycles) for the Na^+.

The structural and energetic properties of the hydration structures are analyzed [32,40] through:

(1) The radial distribution functions for the pair ion–oxygen atom, $g(R)$, and ion–hydrogen atom, $g(R_H)$ where R is the distance between the ion and the oxygen atom, $R \equiv |\vec{R}_O|$, and R_H is the distance between the ion and an hydrogen atom;

(2) The angular-radial distribution functions are defined by R and the angles formed by $\vec{R}_O$ and the dipole vector, $\vec{\mu}$, or by $\vec{R}_O$ and the vector defined by the two hydrogen atoms of the same molecule, $\vec{HH}$. The corresponding functions are $g(R,\theta)$ and $g(R,R\hat{-}HH)$, respectively;

(3) The angular-angular frequency distributions $F(\alpha, \mu\hat{-}\mu)$ and $F(\alpha, HH\hat{-}HH)$, where $\alpha \equiv R_{O,i}\,\hat{}\,R_{O,j}$, $\mu\hat{-}\mu \equiv \vec{\mu}_i\hat{-}\vec{\mu}_j$ and $HH\hat{-}HH \equiv \vec{HH}_i\hat{-}\vec{HH}_j$ if i and j are the indices of two water molecules that are found inside the solvation shell;

(4) The angular-angular-angular frequency distributions $T(\alpha,\alpha',\alpha'')$ where the angles α' and α'' are defined by three molecules inside the solvation shell and

(5) The mean molar energy, obtained directly during the Monte Carlo simulation, as a function of the distance R, $E_{MC}(R)$, that must tend towards the mean molar energy in the bulk, E_{bulk}, i.e., $E_{bulk} = E_{MC}(R \to \infty)$.

The complete definitions of the distribution functions and the details of their calculations are given elsewhere [32,40]. The radial distribution function, $g(R)$, is the ratio of the concentration observed by a molecule at the distance R by the mean bulk concentration. Consequently a value 2, for example, for $g(R = 0.2)$ nm indicates that the mean concentration at $R = 0.2$ nm is twice the bulk concentration. The $g(R,\theta)$ and $g(R,R\hat{-}HH)$ distribution functions decompose the former information in its components relatively to the orientations of the dipole or of the HH vectors. These functions give consequently informations on the large or small probability for finding a molecule at R with the corresponding orientations. The functions $g(R)$, $g(R,\theta)$ and $g(R,R\hat{-}HH)$ inform only the structure of the pair ion–water molecule. This information is incomplete for understanding how many water molecules are located near an ion. They are completed by the angular-angular frequency distributions $F(\alpha,\mu\hat{-}\mu)$ and $F(\alpha,HH\hat{-}HH)$ which give the angles and distances in the triangle formed by two water molecules and the ion as such as on the relative orientations of the two water molecules. This information is as yet incomplete to reconstruct the tridimensional structure of the solvation shell since from planar structures we are unable to identify the connection between two or more of them. The necessary information is consequently generated by the last structural functions, the angular-angular-angular frequency distributions $T(\alpha,\alpha',\alpha'')$, which complete the information on the positions of triplets of water molecules near the ion. With the aid of these functions we are now able to reconstruct the tridimensional structure of the region perturbed by the ion.

3. The hydration structure of the Na^+ and K^+ ions

The pair radial distribution functions $g(R)$, plotted in Fig. 1, present a first peak higher and narrower for Na^+ (maximum at 10.5) than for K^+ (maximum at 4.0) indicating that the water molecules are located at a more defined distance in the Na^+ case. The radius of the solvation shell, that defines the number of hydration molecules, can be defined at the maximum of the first $g(R_O)$ peak [32,40,41] which is found at $R \approx 0.23$ (Na^+) and ≈ 0.30 nm (K^+). The corresponding numbers of neighboring molecules are

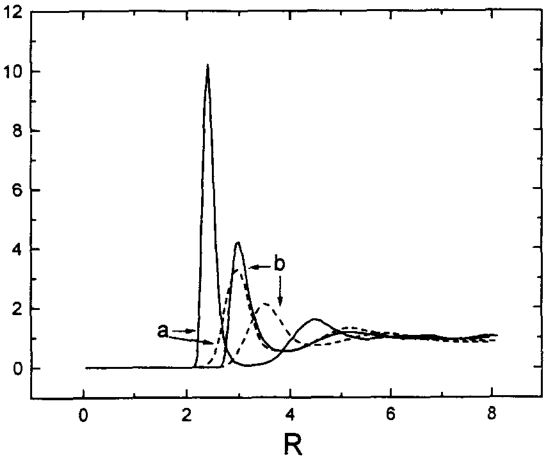

Fig. 1. The radial distribution functions $g(R_O)$ (unbroken line) and $g(R_H)$ (dashed line) vs. R_O (in OH distance units = 0.09572 nm). (a) Na^+ and (b) K^+.

3.09 and 3.5 while these numbers would be 5.1 and 8.5 choosing the position of the first minimum as the hydration shell radius located at $R \approx 0.33$ (Na^+) and ≈ 0.39 nm (K^+). The agreement with experimental data is good for the Na^+ ion [35], while the definition of a hydration number is uncertain in the K^+ case for which the value 3 ± 2 is generally accepted [35–37] from neutrons and X-ray diffraction patterns. The values of the first minimum of $g(R_O)$, 0.1 for Na^+ and 0.5 for K^+, indicate that the interchange of solvent molecules between the hydration shell and the bulk fluid is easier in the K^+ case than for Na^+. A direct consequence of such a behavior can be seen in the $g(R_H)$, Fig. 1, because the first peak is smoother in the K^+ case than in the case of Na^+ ion. Another consequence can be seen in the distances between the first $g(R_O)$ and $g(R_H)$ peaks (0.062 for Na^+ and 0.048 nm for K^+), which correspond to angles between $\vec{R}_O$ and the vector $\vec{OH}$ approx. equal to 40 and 30°, respectively. Consequently, Na^+ is closer to the plane of the hydration molecules [32] than K^+, and Na^+ orients the water molecules better than K^+ since the angle $\vec{R}_O,\vec{OH}$ would be 52° with the ion along the direction of the dipole vector.

The $g(R,R\hat{}HH)$ angular-radial distribution functions are plotted in Fig. 2A for the Na^+ ion and in Fig. 2B for the K^+. The less defined structure of the K^+ solution appears through the first $g(R,R\hat{}HH)$ peak, at the same distance from the first $g(R_O)$ peak, that is lower and broader than in the Na^+ case. The maximum is found at $R\hat{}HH = 90°$ for both ions. At the same distance from the position of the maximum, the peak decreases together with $R\hat{}HH$ and its intensity becomes close to zero near 40° for Na^+ and 20° for the K^+. With increasing $|\vec{R}|$, the structure disappears for K^+ since $g(R,R\hat{}HH)$ approaches one after a decrease only to 0.5. In the Na^+ case, the second peak is separated from the first one by a region where the intensity is close to zero.

The $g(R,\theta)$ distributions, shown in Fig. 3A,B, present the same features as $g(R,R\hat{}HH)$ in Fig. 2, together with the fact that Na^+ orientates more precisely the water dipoles than K^+. In the first case, the range of θ is from 0 to 80°, with the maximum at 30°, while for K^+, the range is wider from 0 to 100°, with a maximum at 60°.

The angular-angular frequency distributions $F(\alpha,\mu\hat{}\mu)$ are plotted in Fig. 4A,B for the Na^+ and the K^+ ion, respectively. These functions are zero for $\alpha < 70°$ (Na^+) and for $\alpha < 45°$ in the K^+ case due probably to steric hindrance. In both cases two main peaks can be observed for $\alpha = 180°$, $\mu\hat{}\mu = 180°$ and for $\alpha = 90°$, $\mu\hat{}\mu = 90°$ with steepest descents along the α than along the $\mu\hat{}\mu$ direction. The intermediate region between the two peaks shows their overlap.

The functions $F(\alpha,HH\hat{}HH)$, Fig. 5A,B exhibits two maxima, the first one located at $\alpha = 180°$, $HH\hat{}HH = 0°$ for both ions and the second at $\alpha = 105°$, $HH\hat{}HH = 85°$ in the Na^+ case and $\alpha = 180°$, $HH\hat{}HH = 75°$ for the K^+. The features of the surfaces are similar to the features of $F(\alpha,\mu\hat{}\mu)$ but the extrema are always better defined for the Na^+ ion.

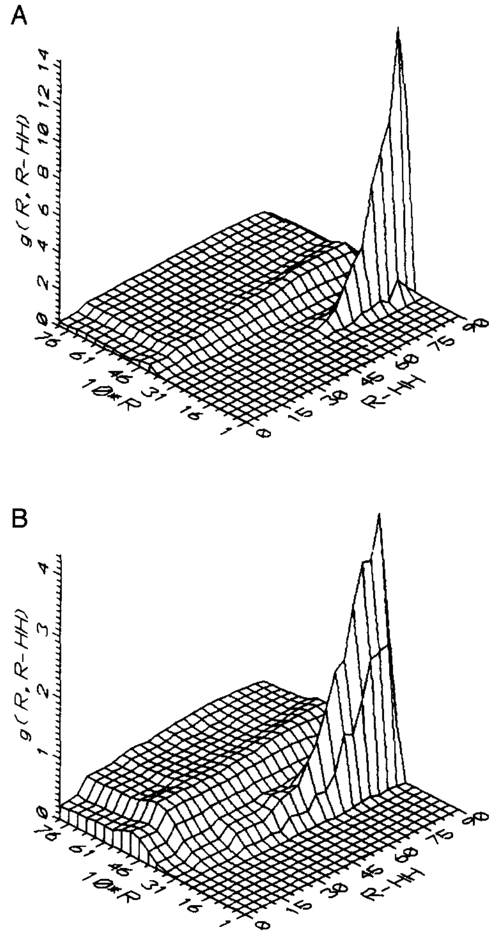

Fig. 2. The angular-radial distribution functions: $g(R,R\hat{}HH)$ for (A) Na^+ and (B) K^+ as functions of R_O (0.09572 nm units). The angles are in degrees.

Two examples of $T(\alpha,\alpha',\alpha'')$ are shown in Fig. 6A,B. A sharp maximum for the Na^+ ion is located at $\alpha = 180°$ and $\alpha' = \alpha'' = 90°$, while no definite maximum can be well identified in the K^+ case.

The $E_{MC}(R)$ energy profiles plotted in Fig. 7 show fundamental differences in the energies of the solvation shell of Na^+ and K^+. The first one is formed under favorable energetic conditions, about 1.5 kcal mol^{-1} below the bulk energy and 1.9 kcal mol^{-1} below an energy barrier at 0.316–0.335 nm from the Na^+ ion. The K^+ case is completely different since the energy of the water molecules, which approach the ion down to 0.3 nm, remains equal to the bulk molar energy: no minimum or energetically favorable region can be identified for the K^+ ion in Fig. 7.

4. The hydration structure and the selectivity of the ionic channels

The selectivity of the ionic channels is an energy problem that, besides dynamical aspects, must focus attention on how the hydrated ions can lose hydration molecules to enter in the channels; on how the hydrated ions can exchange hydration molecules by molecules present in the channels and on how the molecules present in the channels can be removed from their states. The solvation shell of the Na^+ ion is fairly stable as it can be deduced from Fig. 1 to 6A, from Fig. 7 and from Refs. [32,40,42], while it is not possible to identify a defined solvation structure in the case of K^+. The K^+ ion can only perturb its immediate neighborhood since its interaction with the solvent molecules never results in energy decrease (see Fig. 7). In this way, K^+ presents in aqueous solutions a radius close to its ionic radius, 0.133 nm. On the other hand, the Na^+ ion is hydrated by three water molecules as shown in Figs. 11–13 in Ref. [32]. Its diameter must consequently be the sum of the non-hydrated ionic radius, 0.095 nm, plus the distance between the center of the ion up to the surface of the water molecules of the solvation shell. According to Fig. 1, this sum is in the $(0.095 + 0.4) \approx 0.5$ nm range.

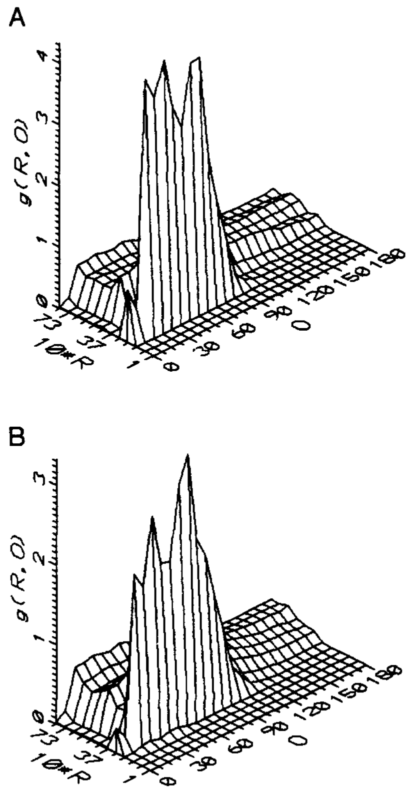

Fig. 3. The angular-radial distribution functions: $g(R,\theta)$ for (A) Na^+ and (B) K^+ as functions of R_O (0.09572 nm units). The angles are in degrees.

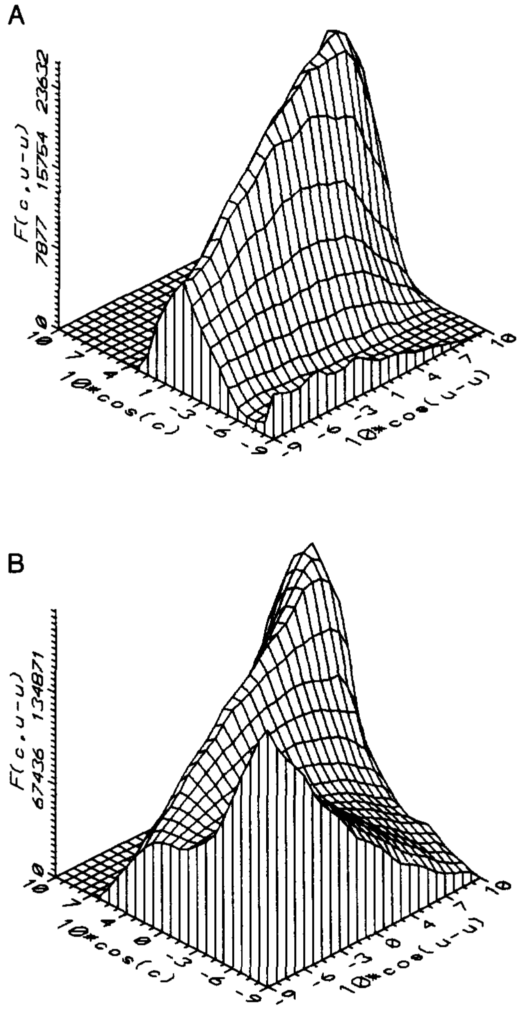

Fig. 4. The frequency distributions: $F(\alpha,\mu\hat{}\mu)$ for (A) Na^+ and (B) K^+.

Experimental data suggest that the selectivity filter of the Na^+ channel is partially constituted by negatively charged ionic groups [1,4] which can form hydrogen bonds with some organic cations for which the Na^+ channel is permeable [44]. In the case of the K^+ channel, recent

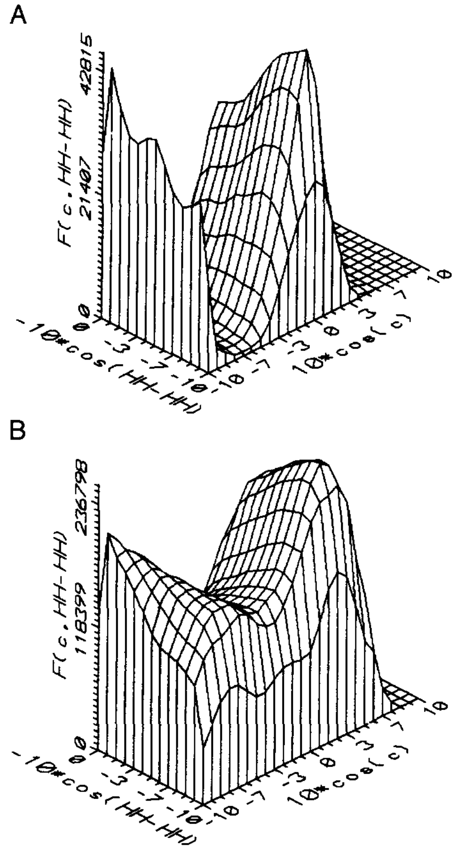

Fig. 5. The frequency distributions: $F(\alpha, HH\text{-}HH)$ for (A) Na^+ and (B) K^+.

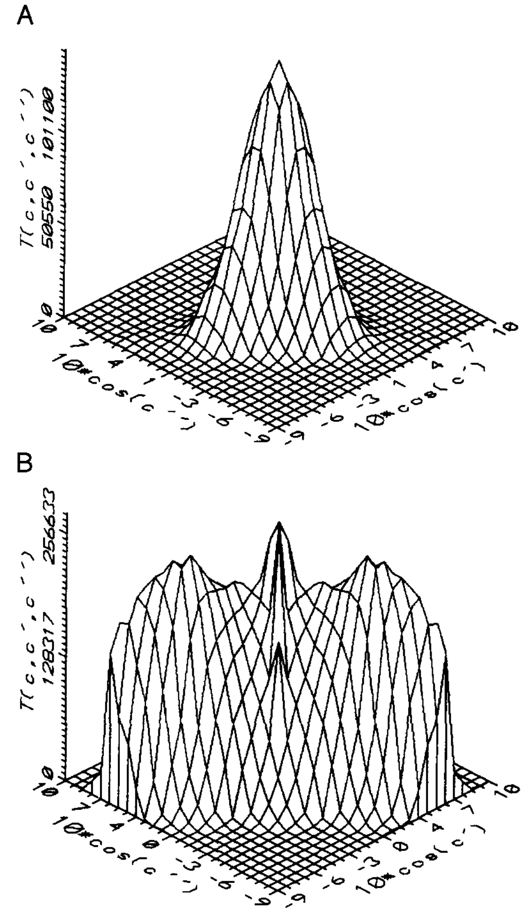

Fig. 6. $T(\alpha, \alpha', \alpha'')$ with $\alpha = 180°$ for (A) Na^+ and (B) K^+.

studies [48] have shown that the selectivity filter can be constituted by aromatic rings that interact preferentially with K^+ in aqueous solution. Joining these conclusions with the hydration structures of the K^+ and Na^+ ions the present results agree with previous ones on the transport of Na^+ and K^+ in their respective ionic channels [1]. One of the factors responsible for the entry of the Na^+ ion in its channel would be the hydrogen bonds [44] that are formed between the hydration water molecules of the ion and the polar groups located on the internal surface of the channel [44]. The resulting attraction allows the ion to penetrate in the channel. Such a mechanism is feasible since the Na^+ hydration shell is fairly stable permitting the exchange of water molecules at low energetic cost. The energetic cost for the removal of the hydration molecule, or the energetic cost for breaking hydrogen bonds between the water molecules and the surface of the channel, is decreased by the energy gain for the hydration of the ion. On the other hand, the selectivity of the K^+ channel is due to the lack of the hydration shell of this ion together with no hydrogen bonding formation between the water molecules present in the channel and the wall. This situation can occur due to the lack of strongly polar groups on the walls. In agreement with these present results, it was shown that aromatic molecules in contact with K^+ aqueous solutions interact

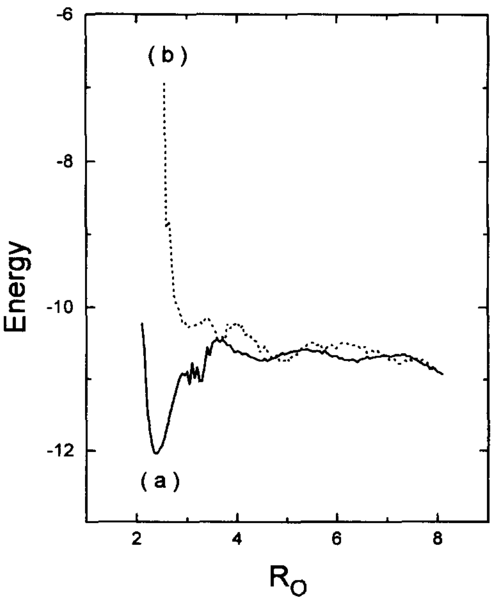

Fig. 7. The energy $E_{MC}(R)$ (kcal mol^{-1}) as a function of R (in 0.09572 nm units) for (a) Na^+ and (b) K^+.

preferentially with K^+ [45]. The interaction between aromatic molecules and hydrated ions cannot occur. This observation suggests that the K^+ channels are more selective than the Na^+ channels [1]. Nevertheless a complete explanation for the selectivity of the ionic channels will be achieved with more information such as the complete knowledge of the nature and structure of the constituents of the channels.

From an energy point of view, the non-hydrated K^+ ion is unable to orient preferentially the water molecules inside the channels because the interaction energy is never attractive [40]. Consequently the transport mechanism of the K^+ ion in the ionic channel can be seen as the ion breaking through against the water molecules in the selectivity filter. Consequently the water molecules cannot be bound by hydrogen bonds to the groups of the wall of the channel. Coincidentally the radius of the water molecules, about 0.14 nm [34–36,46], is very close to the ionic radius of the K^+ ion, 0.133 nm, so that K^+ can substitute a water molecule, avoiding too large perturbations of the medium structure. On the other hand, the Na^+ transport can only go along with extensive perturbations of the medium since the ion either keeps its hydration water, or interchanges them with the water molecules encountered on its way. In this last case, the interchange occurs because the hydration shell becomes unstable when one more water molecule is added [40].

Information about the structure and energy of pure water in the channels can be obtained by grand canonical Monte Carlo simulations [14,46,47], specifically the concentration and molar energy of the confined liquid. We used, keeping in mind this purpose, the SP3 water model [31] confined in rigid cylindrical channels with radii equal to 0.15 and 0.25 nm. The SP3 model describes the water molecules as hard spheres where two dipoles, corresponding to the two OH polar bonds, and a tetrahedral octupole are embedded. This model is easily associated to a hard wall channel. The results are presented in Table 1.

The first basic results are the hydrogen and oxygen atomic densities of the confined water. As usual, the water molecules are preferentially adsorbed on the wall, leaving, in the 0.5-nm channel, some free space in the center of the channel. The same adsorption procedure is also observed experimentally. The number of water molecules near the wall is about 120 times those near the axis. The small diameter in the 0.3-nm channel forces the water molecules, even adsorbed, to remain very close to the axis. This structure is very well described by a pearl necklace, i.e., each water molecule owes only two neighbor molecules located in opposite positions. In both cases, the number of first neighbors is two, less than in the bulk. The pearl necklace structure in the 0.3-nm channel results in an uncommonly high mean concentration for a very thin channel [47] together with a low mean molar energy. Consequently the energetic cost of the transport of the ions in the channels is also aided by the fact that the solvent concentration is lower than in the bulk (see Table 1). At the same time, the configurational energy is less negative since the chemical potential of the water molecules is the same in the channels and in the bulk resulting in water entropy greater in the channels. The important consequence is that the structural reorganization occurs in the channels with energy and entropy costs smaller than they would be in the bulk phase. These procedures favor the transport of the K^+ ion in channels whose diameters can be as small as 0.3 nm since the water molecules are not bound to the wall of these channels and the weak stability allows the intercalation of the ion. For the same reason, the Na^+ ion cannot penetrate in these channels because the energetic cost of the dehydration is too high (greater than the thermal energy) while it can penetrate in its own channel because it meets water molecules strongly bound by hydrogen bonds to the walls. These water molecules are, nevertheless, in a less stable state and in a concentration less than the water of the bulk: the strong electrostatic ionic field together with the destabilization of the hydration shell due to the entry of one more water molecule is favorable to the interchange of the water molecules between the hydration shell and the molecules present in the channel. All the process occurs maintaining the energy of the water molecules that participate lower than the bulk energy. The interchange of water molecules between the medium and the Na^+ solvation shell is still easier when occurring with molecules that the ion does not meet directly on its trajectory avoiding in such a way important destabilization of the structure such as a 180° rotation of the water molecule. Interchanges occurring perpendicularly to the ionic trajectory must be consequently more frequent and more capable of being carried out. These interchanges occur on the directions perpendicular to the axis of the channel. The resulting dimensions of the Na^+ channel perpendicularly to its axis must therefore be about 0.5 nm on a length of the order of two oxygen covalent diameters, i.e., 0.3 nm, so that two water molecules can be located one parallel to the other and to the channel axis. In the same channel, the K^+ ion is unable to displace the water molecules bounded to the polar groups of the channel walls since its lack of hydration molecules and its weak electrostatic field do not make possible the displacement of the bounded water molecules at low energetic cost.

Table 1
Grand canonical Monte Carlo results for SP3 water in cylindrical channels

Channel radius (nm)	Mean molar concentration (mol/l)	Mean molar energy (kJ/mol)
0.15	52 ± 33	-16 ± 11
0.25	32.9 ± 0.9	-20 ± 2
∞	55 ± 3	-30.9 ± 0.6

5. Conclusion

The hydration of the ions is an important factor in the selectivity of the ionic channels. The ionic transport always occurs in a medium that is structured by the highly polar water molecules so that the energetic factors play the important role of allowing or not the passage of the ion in the selectivity filter. Simple models for the channels are able to make easier the understanding of their selectivity. The importance of the interchange of the water molecules between the solvation shell and molecules inside the channel is underlined by analyzing the kind of ions that can be transported in the specific channels. Ions that can pass through the Na$^+$ channels are highly hydrated ions such as Li$^+$ and HONH$_3^+$, the first of them presents a highly structured and stable solvation shell [40]. On the other hand, the Rb$^+$ and Tl$^+$ cations, that can pass through the K$^+$ channels, do not present stable solvation shells due to their size. Finally, a last doubt remains about the validity of studying an essentially dynamic process (the ionic transport) with the aid of a technique that furnishes only configurational information (MC). The ionic transport occurs in millisecond time intervals very much larger than the relaxation times for the interactions water molecules–ions that are typically of the picosecond order. These discrepancies suggest strongly that the ionic transport can be described as successive equilibrium states justifying the use of MC information in the present communication.

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