Biochimica et Biophysica Acta, 771 (1984) 151–164
Elsevier

BBA 72034

WATER STRUCTURE IN THE GRAMICIDIN A TRANSMEMBRANE CHANNEL

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(Received July 26th, 1983)

Key words: Gramicidin A; Water structure; Transmembrane channel; Iso-energy mapping

The interaction energy and the structure of water molecules either inside the Gramicidin A transmembrane channel or at its two extremities is examined with the use of iso-energy maps and Monte Carlo simulations. The shape of the channel as experienced by water is analyzed in detail. Variations in the hydration structure due to the presence of a sodium ion placed at several positions along the channel are simulated, analyzed and discussed. Preliminary data on Li^+ and K^+ interacting with Gramicidin A and the system of water molecules are reporeted. The Gramicidin A atomic coordinates have been taken from Urry's recent papers (Urry, D.W. (1971) Proc. Natl. Acad. Sci. U.S.A. 68, 672–676 and Urry, D.W., Trapane, T.L. and Prasad, K. U. (1982) Int. J. Quant. Chem. Quant. Biol. Symp. 9, 31–40).

I. Introduction

The primary function of a biological membrane is the selective control on the flow of chemicals. As is well known, simple inorganic cations, for example, Na^+ and K^+, can be transported across membranes; the difference in ionic concentration at the two sides of the membrane brings about electrical potential differences of basic importance especially in neuron's firing membranes. One of the possible mechanisms for an ion to cross a membrane is migration through a molecular transmembrane channel. The peptide Gramicidin A can act as a molecular channel specifically for monovalent cations. This notable discovery by Hladky and Haydon [1] was soon followed by proposals on the structure of Gramicidin A; in this context, we recall works by Urry [2], Ramachandran and Chandrasekharan [3], Veatch et al. [4], Ovchinnikov and co-workers [5], and Lotz et al. [6]. Recent accounts of two somewhat different proposals for the structural representation of a Gramicidin A channel can be found in publications by Ovchinnikov and Ivanov [7] and Urry et al. [8].

This paper will analyze the structure of water molecules interacting with a Gramicidin A channel modeled according to Urry's atomic coordinates [8]. It is our pleasure to acknowledge Professor D.A. Urry for having provided us with an updated list of the atomic coordinates of Gramicidin A, prior to their publication.

We recall that the primary structure of Gramicidin A is: HCO-LVal[1]-Gly[2]-LAla[3]-DLeu[4]-LAla[5]-DVal[6]-LVal[7]-DVal[8]-L-Trp[9]-DLeu[10]-LTrp[11]-DLeu[12]-LTrp[13]-DLeu[14]-LTrp[15]-$NHCH_2CH_2OH$. In Fig. 1 we report three-dimensional representations of Gramicidin A. In the top-left inset, Gramicidin A is projected onto the *xz* plane (the *Z* axis is the long axis of the channel): from the top-right inset (a projection into the *xy* plane) one can see clearly the cavity constituting the channel (the cross gives the projection of the *Z* axis) and the amino acid residues disposed around the two monomers backbones. The bottom inset of Fig. 1 shows the 15

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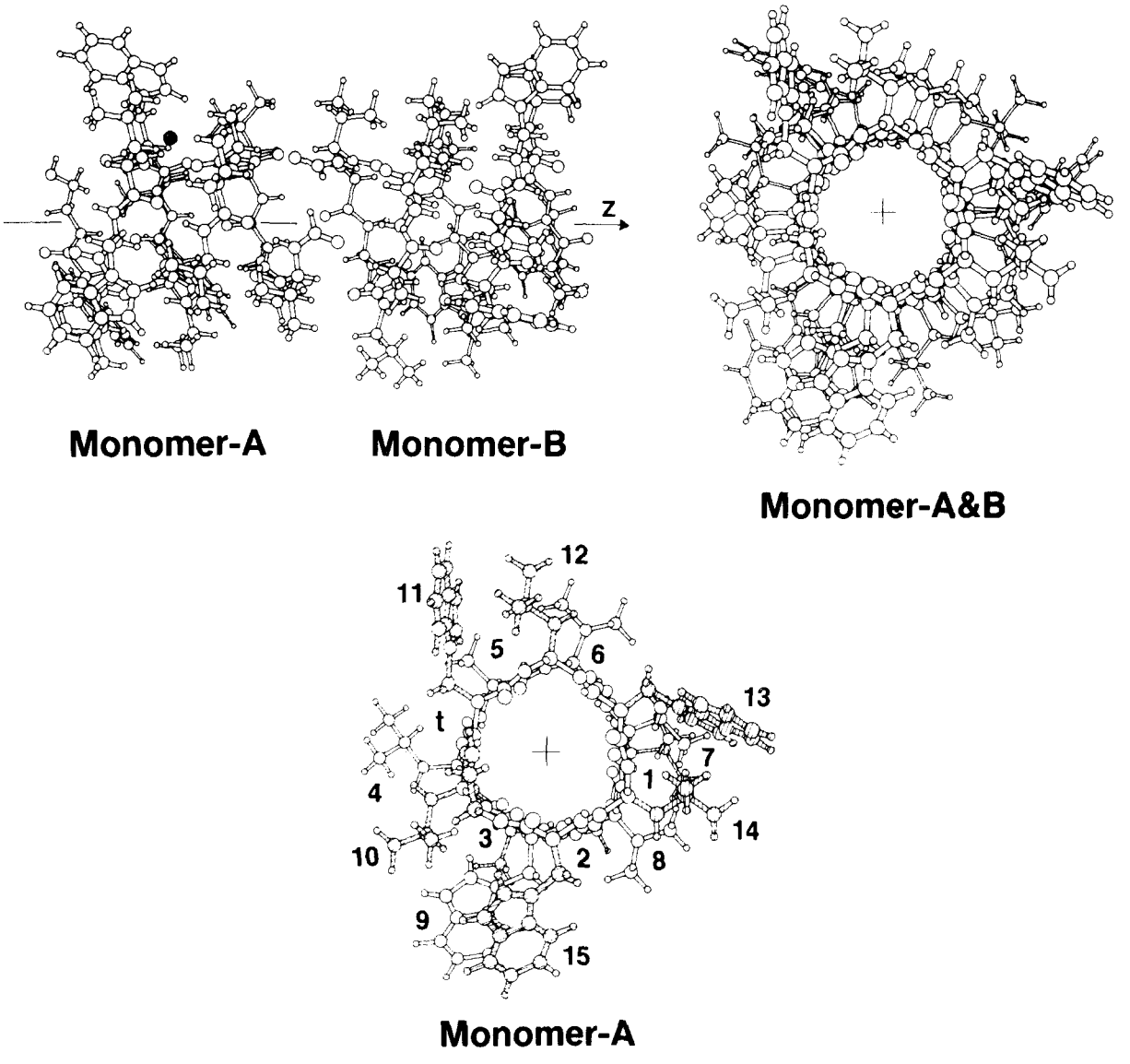


Fig. 1. Top: projections of Gramicidin A onto the *xz* plane (left) and *xy* plane (right); Bottom: projection of the A monomer of Gramicidin A onto the *xy* plane with labels for the 15 residues.

residues of only one monomer; we have used different shading to allow a clear visualization. To facilitate discussions following this paper, we have explicitly labeled the 15 amino acid residues of the A monomer.

In this work we shall discuss, (1) the number of water molecules which can be placed inside the Gramicidin A channel, (2) the interaction energy of the water molecules with the channel and among themselves, and (3) the structure of the water molecules at the two extrema of the channel. In addition, we shall analyze the structural variations for the water molecules which follow the insertion of a monovalent cation at different positions along and nearby the channel. The cations we shall consider are the monovalent cations Li^+, Na^+ and K^+. The above discussions are based on data obtained from Monte Carlo computer experiments [9,10].

Before discussing the system Gramicidin A hy-

drated by many molecules of water at room temperature, we shall analyze Gramicidin A interacting with one water molecule placed at many positions relative to Gramicidin A at zero temperature. In this way we shall discuss 'typical' hydration sites of Gramicidin A [11]; this analysis is performed by using iso-energy contour maps. As known, the iso-energy contour maps yield only a preliminary representation, which is, however, useful even if it cannot be related directly to any laboratory experiment. Realism in the modeling is restored with the Monte Carlo simulation where non-zero temperature, water-water interactions, and statistical weighting factors are no longer neglected.

II. Introductory discussion on the hydration sites in Gramicidin A

A water molecule at a given position and orientation relative to Gramicidin A experiences an interaction energy, E, which to an approximation of the first order can be written as the sum of all the atom-atom pair-wise interactions $V(i,j)$ between an atom i on Gramicidin A and an atom j on H_2O, namely, $E(k) = V(k; i, j)$ (k specifies the geometrical relations between Gramicidin A and H_2O). For one water molecule interacting with amino acids [10] or with a polypeptide chain [11], atom-atom potentials have been derived from ab initio computations. As discussed elsewhere in detail [10], the atoms of the macromolecule are grouped into 'classes'. We recall that a 'class' characterizes the electronic environment of an atom within the molecule. This characterization is obtained by selecting as criteria (1) the atomic number, (2) the hybridization of the atom (number of bonds), (3) the atomic net charge [12], and (4) the energy difference of the atom either when in the molecule or isolated [13]. An atom, i, belonging to the class a and an atom, j, belonging to the class b interact with an energy approximated as:

$$V(i,j;a,b) = B(a,b)/R(i,j)^{12} - A(a,b)/R(i,j)^{6} + C(a,b)q(i)q(j)/R(i,j)$$

where $R(i,j)$ is the internuclear distance for the two atoms, $q(i)$ and $q(j)$ their net charges and $A(a,b)$, $B(a,b)$, and $C(a,b)$ are numerical constants, previously derived [14,15]. The particular constants used for each class of atom of the Gramicidin A are given in a technical report [16], available upon request. We recall that the charges, also reported in the technical report [16], are obtained with Mulliken's algorithm [12] from ab initio Self Consistent Field computations using a minimal basis set which has been reported elsewhere [17], consisting of seven s-type gaussian functions and three 2p-type gaussian functions. Earlier computations [14,15] used three s-type functions for the hydrogen atoms. In the last few years we have used four s-type functions, mainly to decrease the basis set superposition error. These computations have been performed with a computer program discussed previously [18].

The position of the hydration sites in Gramicidin A can be obtained rather easily by probing with one water molecule inside or nearby the channel. Computer programs written to obtain the interaction energy for an optimally oriented water molecule with the oxygen atom placed at the grid points on a predetermined plane, the iso-energy plane, are available [19].

We have obtained the iso-energy contour maps for a plane bisecting the Gramicidin A channel as shown in Fig. 2. The left inset reports a low resolution (the selected grid mesh is 1 a.u.) iso-energy map of the entire channel and of the regions at the two extrema. The contour-to-contour interval is 1 kcal/mol. Notice that the length of the channel is from $Z = 0$ to about $Z = \pm 24$ a.u., namely about 48 a.u.; we have reported the iso-energy contours expanding up to $Z = \pm 47$ a.u. Two hard core areas (the repulsive energies have been cut off at 5 kcal/mol) border the channel. In the central and right-hand inset we report detailed views (grid meshes = 0.5 a.u.); at the center we detail the area enclosed by the dotted line perimeter in the left-hand inset. Only a few of the contours and the minima are labeled to allow easy reading of the interaction energy values. Notice the very prominent minima (E is given in kcal/mol) at the entrance of the channel and the sequence of energy minima along the channel. The three-dimensional 'shape' of the channel can be appreciated by rotating the cross section plane by 90° and presenting the corresponding iso-energy

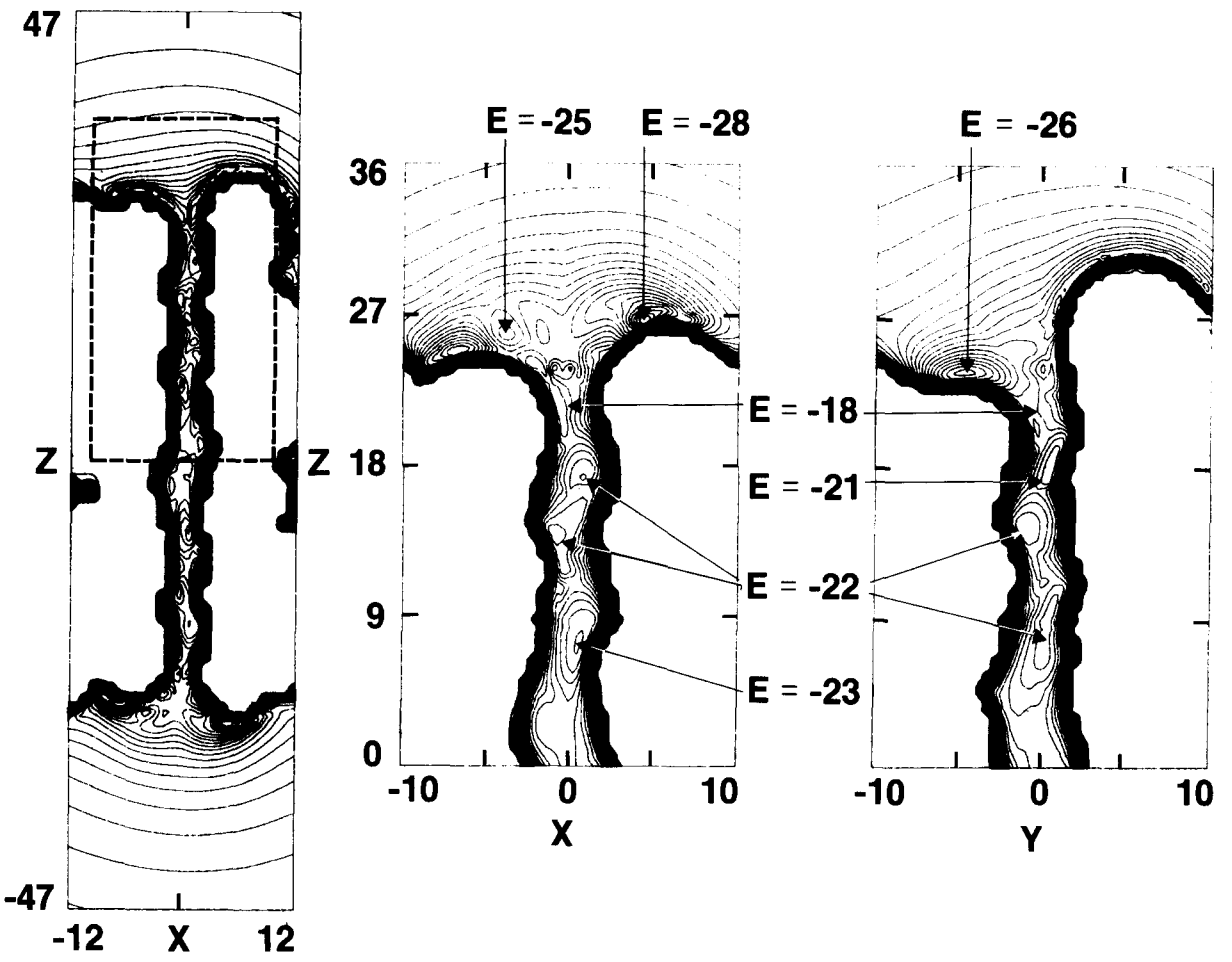
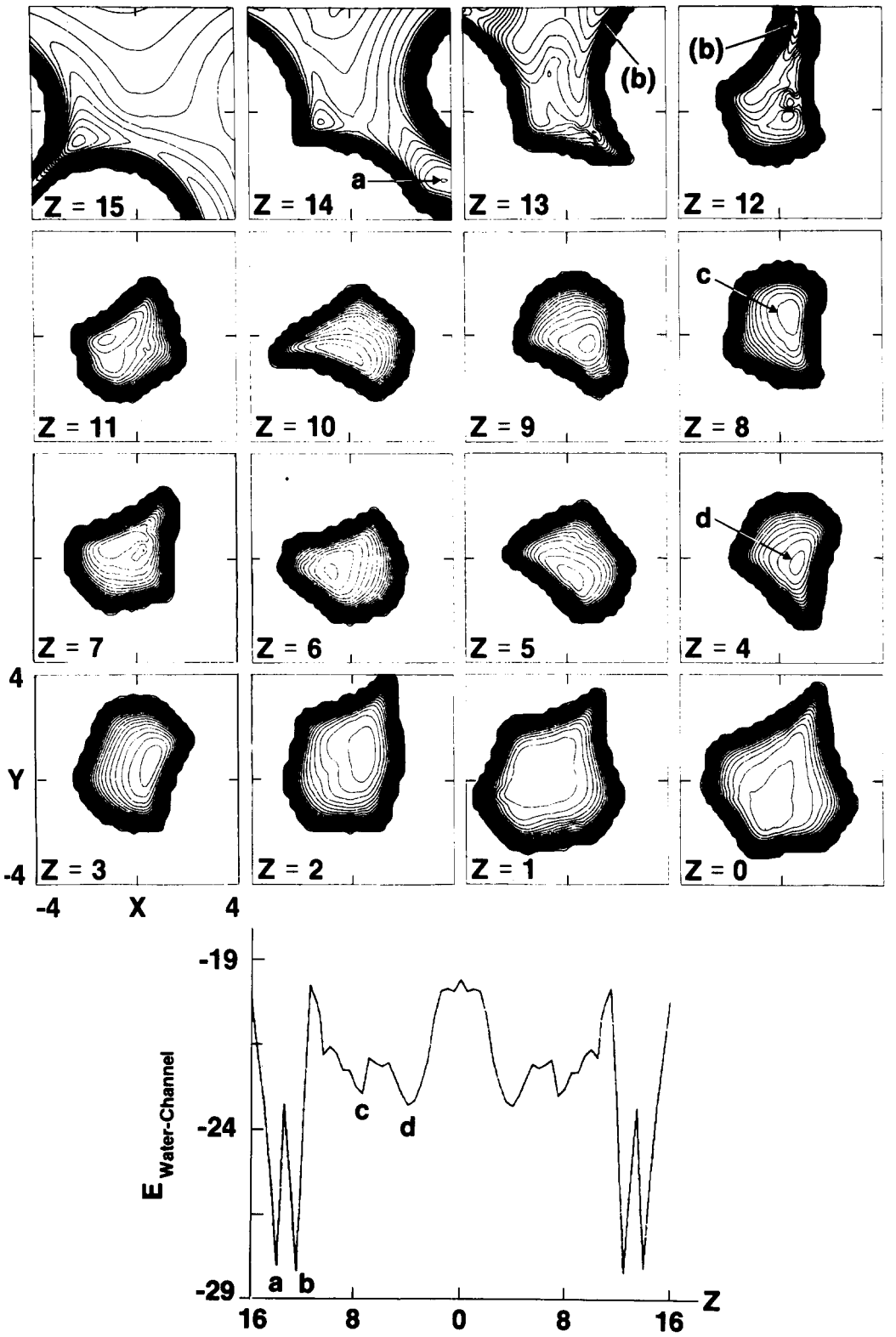


Fig. 2. Left: low resolution iso-energy map for Gramicidin A interacting with water (xz cross section). Center: detail of inset on the left. Right: same as center but for cross-section rotated by 90° around Z axis (yz cross-section). Coordinates (X, Y, Z) and interaction energies (E) are given in a.u. and kcal/mol, respectively.

contour map as in the right-hand inset of Fig. 2.

It is clear and evident that the channel is very attractive to a water molecule. A water molecule, moving along the channel, will find itself in regions of variable attraction separated by energy barriers of about 3 kcal/mol. Notice, for example, the relatively less attractive region at the middle of the channel at $Z = 0$ a.u. These energy variations can be enhanced and time modulated if one takes into account the vibrational modes specific for Gramicidin A. We refer to the paper by Urry et al. [8] for comments on the role of the librating peptide C=O groups at the channel wall. In this context we recall, that among the early computer simulations on Gramicidin A, Fischer et al. [20], did perform molecular dynamics simulations with a model where Gramicidin A is approximated simply by an helical arrangement of polar carboxyl groups with properly parameterized electrostatic charges. The same model has been more recently used by Schröder et al. [21], where qualitatively good agreement was found between molecular dynamic simulations and the diffusion constants for the ions.

Fig. 3. Sixteen cross-sections of the channel from $Z = 0$ Å to $Z = 15$ Å and minimum interaction energy as function of the channel length. Coordinates (X, Y) and interaction energies (E) are given in a.u. and kcal/mol, respectively.


Z = 15
Z = 14
a
Z = 13
(b)
Z = 12
(b)
Z = 11
Z = 10
Z = 9
Z = 8
c
Z = 7
Z = 6
Z = 5
Z = 4
d
Z = 3
Z = 2
Z = 1
Z = 0
4
Y
-4
-4
X
4
-19
-24
-29
E Water-Channel
a b
c
d
16
8
0
8
16
Z

A very detailed view of the channel energetic is now given in Fig. 3, where sixteen iso-energy maps are reported for *xy* cross-sections of the channel for $Z = 0, 1, \ldots, 15$ Å (grid meshes = 0.25 a.u.). At the bottom of the figure we report a graph giving the lowest energy determined in each map. The positions a, b, c, and d in the energy profile (bottom inset), also reported in the *xy* cross-sections (top inset), identify the energy minima; whereas a and b are outside the channel region, the minima at c and d are definitely within the channel. It is noteworthy that four potential-energy minima, each one separated by a barrier, are postulated by Eisenman et al. [22] in order to account for the experimental transport rate [22,23]. At $Z = 0$ Å, the attraction of Gramicidin A to one molecule of water is pronounced even if it is relatively weaker than at any other Z value, an exception being made for positions very near the two ends of the channel (immediately before the most attractive sites (positions a and b)) previously noted in Fig. 2. Notice that the cross-section of the channel is not circular, but assumes rather irregular shapes which gradually evolve and change with Z. Notice also that the most attractive position for water (energy minimum) is, in general, not exactly at the center of the *xy* cross-section (positions c and d in the top inset), but close to it. From these cross-sections we can conclude that the channel ends at $Z = 12$ or $Z = 13$ Å; namely that the channel is 25 ± 1 Å long. Thereafter, there is a 'estuary' region which ends up at about $Z = 15$ or

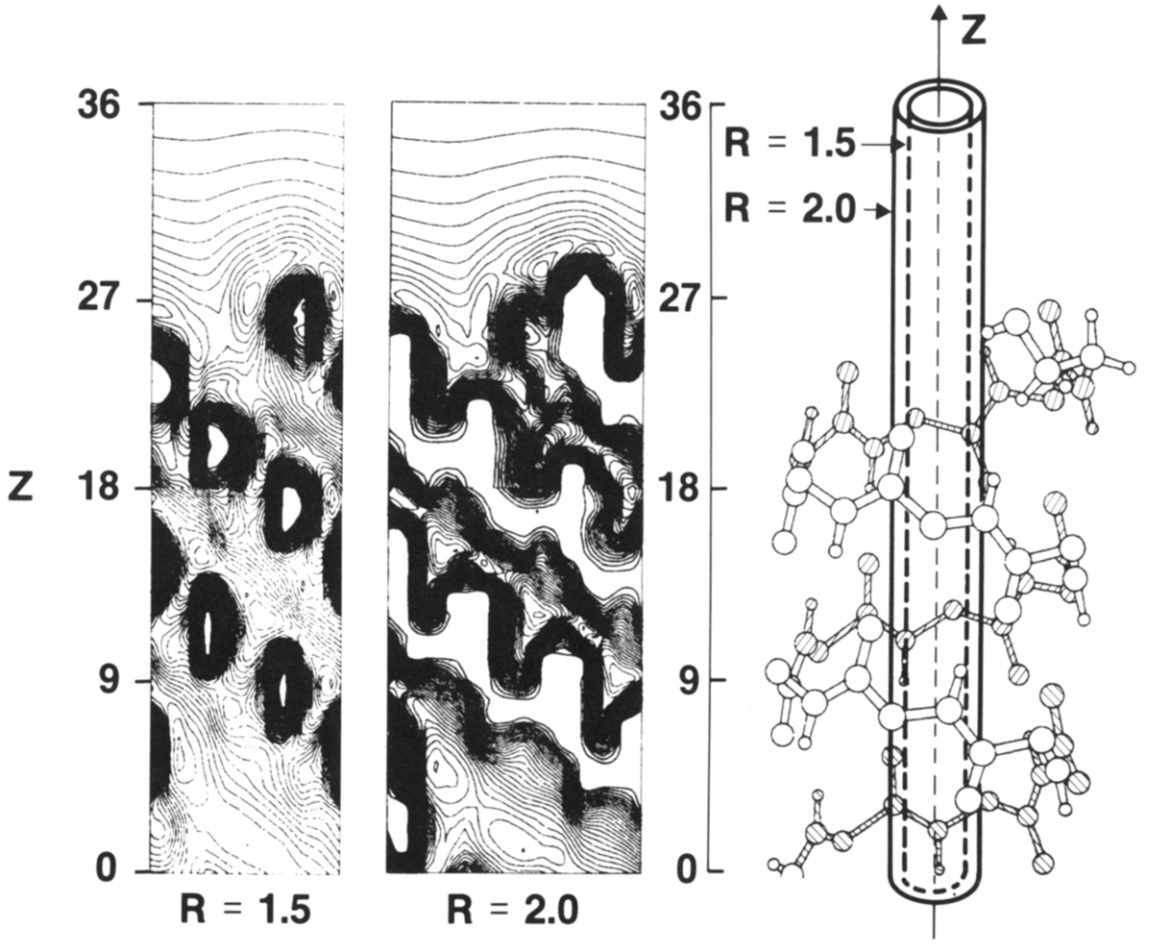


Fig. 4. Cylindrical iso-energy maps flattened out; the cylinder's radii are $R = 1.5$ and $R = 2.0$ a.u., respectively. Z coordinates are given in a.u. The right-side inset is a representation of the helical backbone only.

16 Å. However, the attraction to water extends much further; this informs us that one cannot properly talk of 'bulk water' if not for Z equal or larger than possibly ± 20 or ± 25 Å. In this sense the channel makes itself felt for a length of 40 to 50 Å, a value no much shorter than the standard thickness of many biological membranes.

Before reporting on the Monte Carlo simulations we shall discuss one more detail at the single water level. In Fig. 4 we consider two cylindrical iso-energy maps obtained by selecting cylinders with a radius of 1.5 and 2.0 a.u., respectively (grid meshes = 0.5 a.u.). The cylindrical maps are flattened out in order to allow for a full display. Notice that the hard core appears in the map of $R = 1.5$ a.u. and becomes more prominent for the map of $R = 2.0$ a.u. As one can see by inspection of the insets in Fig. 3, between $R = 3$ a.u. and $R = 4$ a.u. the hard core becomes the only feature. Notice in addition that the backbone of Gramicidin A extends much further than $R = 2.0$ a.u., as evident from the right-hand inset of Fig. 4. Combining the information of Figs. 2, 3 and 4 it seems clear that the channel is much more like a spiral than a cylinder. This is due to the helical nature of Gramicidin A. Any loosening and tightening of the spiral will bring about not only a lengthening and a shortening of the channel but also the possibility of 'occlusion' for the channel which is relatively very narrow, with hard core protrusions extending up to $R = 1.5$ a.u., nearly blocking the channel. In this context it is clear that, with Gramicidin A encircled by phospholipids, the dynamics of the phospholipid layers in the membrane can have profound effects on the 'geometry' of the channel and hence on the ionic transport mechanism. In this paper we have neglected the interaction with the phospholipids, which will, however, be included in a forthcoming work.

III. Monte Carlo simulations

In order to obtain a more realistic representation of the structure and interactions of many water molecules with Gramicidin A, we must introduce (1) a temperature different from zero degree Kelvin and consequently distributions of conformations Boltzman's weighted, and (2) the interactions not only of the water molecules with Gramicidin A but also among themselves. This aim is ideally reached by performing Monte Carlo simulations as described originally in the report of Metropolis et al. [9] and many times thereafter as for example in Refs. 10, 24 and 25. Within a cylindrical volume we place a number of water molecules (about 80) surrounding Gramicidin A. The volume length of the cylinder is 48 Å and the radius of the circular base is 5.5 Å; the cartesian coordinate frame is therefore the same as previously described in Fig. 2. With the above choice for the number of water molecules and the corresponding volume, the liquid water density is about one. The water molecules are constrained to stay within the cylindrical volume. The Gramicidin A is constrained to remain rigid.

The Monte Carlo computer experiments we have performed are exemplified by the insets in Fig. 5, where we report one specific configuration for the water molecules positioned both inside and outside the channel (bottom inset), and the probability distribution, $P(Z)$, for the oxygen atoms (full line) and for the hydrogen atoms (dotted line) as function of the Z axis (top inset). Notice that Gramicidin A is not shown in Fig. 5 in order to simplify the figure; it occupies the volume around the long water filament, namely, the area shown as empty in the bottom inset of the figure, as evident by comparing Fig. 5 with Fig. 2. In our experiments we either exclude or include a cation (Li^+, Na^+ or K^+) which is placed at fixed positions within the cylinder. For each experiment, namely, for each position of the cation, we consider about $2 \cdot 10^5$ different Monte Carlo steps or configurations for the water molecules after equilibrium; the latter was reached after about $4 \cdot 10^5$ Monte Carlo steps. Each configuration is obtained from a previous one by random selection of water molecule and by random displacement (the displacements are for distances not greater than 0.3 Å and for rotations not larger than 18°). The simulated temperature is 300 K.

In the first experiment we consider a system composed of 81 water molecules and Gramicidin A. As shown in the top inset of Fig. 5, the water molecules form a single file within the channel in accordance with the electrokinetic measurements of Rosenberg et al. [26,27] and Levitt et al. [28]. There are nine water molecules between $Z = -12$

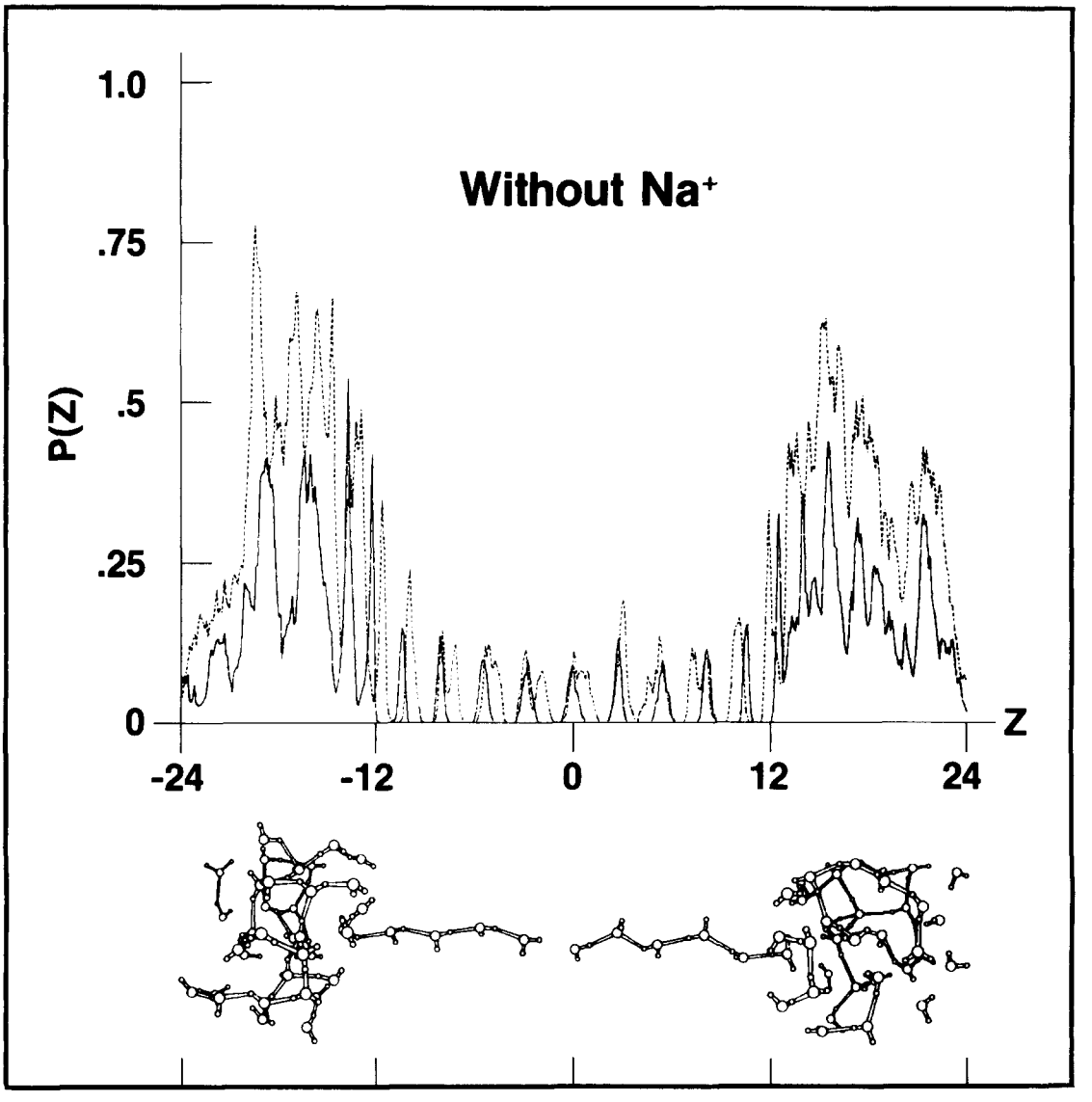


Fig. 5. Top: water's oxygen (full line) and hydrogen (dotted line) probability distributions along the Z axis (in Å) of Gramicidin A. Bottom: a statistically significant configuration of the water molecules.

Å and $Z = 12$ Å. We recall that the channel is about 26 Å in length (from $Z = -13$ to $Z = 13$), the exact definition depending on where one assumes the beginning of the two outlets.

The water molecules are hydrogen bonded together as clearly shown either from the bottom inset or from the statistical distribution (top inset). We recall that we display a hydrogen bond between two water molecules whenever the O-O internuclear separation is not larger than about 3.50 Å and the O-H bond of one water molecule points toward the oxygen atom of the second molecule with an $\hat{OHO}$ angle between 180° (linear bond) and 150° (bent hydrogen bond). An alternative way is to report all the water molecule pairs with an O-O separation smaller than or equal to some threshold value which corresponds either to a hydrogen-bonded pair or to a repulsive pair; note that the latter possibility is very unlikely because of Boltzman's distribution. If the threshold is very tight, then only strong hydrogen bonds are selected; this is the case used in our figures. The

TABLE I

POSITIONS (Å) OF THE CATION AND COMPUTED (MONTE CARLO SIMULATIONS) WATER-WATER, GRAMICIDIN A-WATER AND CATION-WATER AVERAGE INTERACTION ENERGIES

Figures are given in kJ/mol, means ± S.D. of determinations. All data are per water molecule. GA, Gramicidin A.

	$E\ H_2O.H_2O$	$E\ GA/H_2O$	$E\ Ion/H_2O$
Without ion	−25.54 ± 0.07	−50.08 ± 0.07	-
Na^+ at $Z = 24.00$ Å	−24.94 ± 0.10	−48.23 ± 0.04	−7.87 ± 0.23
Na^+ at $Z = 20.00$ Å	−23.29 ± 0.11	−49.42 ± 0.05	−10.02 ± 0.05
Na^+ at $Z = 14.00$ Å	−25.26 ± 0.06	−47.59 ± 0.08	−8.22 ± 0.04
Na^+ at $Z = 12.50$ Å	−25.55 ± 0.08	−47.69 ± 0.05	−7.63 ± 0.06
Na^+ at $Z = 11.20$ Å	−25.82 ± 0.05	−47.76 ± 0.06	−6.73 ± 0.05
Na^+ at $Z = 10.63$ Å	−25.93 ± 0.11	−48.40 ± 0.05	−6.33 ± 0.04
Na^+ at $Z = 10.00$ Å	−26.26 ± 0.07	−47.79 ± 0.05	−5.89 ± 0.03
Na^+ at $Z = 7.50$ Å	−26.30 ± 0.11	−47.79 ± 0.06	−5.10 ± 0.02
Na^+ at $Z = 5.00$ Å	−26.24 ± 0.09	−47.98 ± 0.07	−5.13 ± 0.02
Na^+ at $Z = 2.50$ Å	−25.88 ± 0.06	−48.40 ± 0.08	−4.86 ± 0.02
Na^+ at $Z = 0.00$ Å	−26.69 ± 0.06	−48.35 ± 0.07	−4.94 ± 0.02
Li^+ at $Z = 0.00$ Å	−25.49 ± 0.12	−49.21 ± 0.04	−6.04 ± 0.03
K^+ at $Z = 0.00$ Å	−26.01 ± 0.09	−48.84 ± 0.06	−3.01 ± 0.02

water-water network is also strongly connected at the two channel ends. The corresponding probability distribution intensity increases immediately outside the channel, as expected. Inside the channel, due to its narrowness, one can have an accurate count of the water molecules and of the hydrogen-bonding pattern. Comparing the two insets, we notice that the water molecules of the single configuration have a structure which very closely corresponds to the probability distribution.

In the remaining Monte Carlo experiments we have placed a sodium ion at different fixed positions along the Z axis. The positions are tabulated in Table I where we report the water-water, the Gramicidin A-water and the ion-water average interaction energies in kJ/mol (all data are per water molecule).

Fig. 6 corresponds to the experiment where we have fixed a Na^+ at $X = 0$, $Y = 0$, and $Z = 0$ Å. The top inset again reports the statistical distribution of the oxygen and hydrogen atoms, whereas on the bottom inset we report a specific conformation. Comparing the two insets, it appears that the specific conformation is statistically representative. Notice that this is due to the combined effect of (a) the narrowness of the channel, (b) the two deep energy minima (or the two very stable water sites) at the entrance of the channel, and (c) by keeping the position of the cation fixed. The last fact is probably the least important; indeed, in Fig. 5 one can see that the single conformation representation and the statistical distribution are very close one to another. In both Figs. 5 and 6, notice that there is a strong indication that the water molecules inside the channel use one O-H to make an hydrogen bond, and the second one rotates water to water because it follows the spiraling nature of the channel. The breaks (reported in the single conformation representation as well as in the statistical probability distribution) in the water filament are due to the selection of a threshold for O-O of 3.0 Å; by increasing this value to 3.5 Å the filament has no break if not at the ion.

In Fig. 6 we report the probability distribution of the of the oxygen and hydrogen atoms along Z. Since there is no reason to assume that the distribution is isotropical, in Fig. 7 we report the probability distributions projected onto the xy plane for the six water molecules designated by the six peaks a, b,,...,f in Fig. 6. In order to offer as much chemical insight as possible, the probability distributions of Fig. 7 are given separately for the

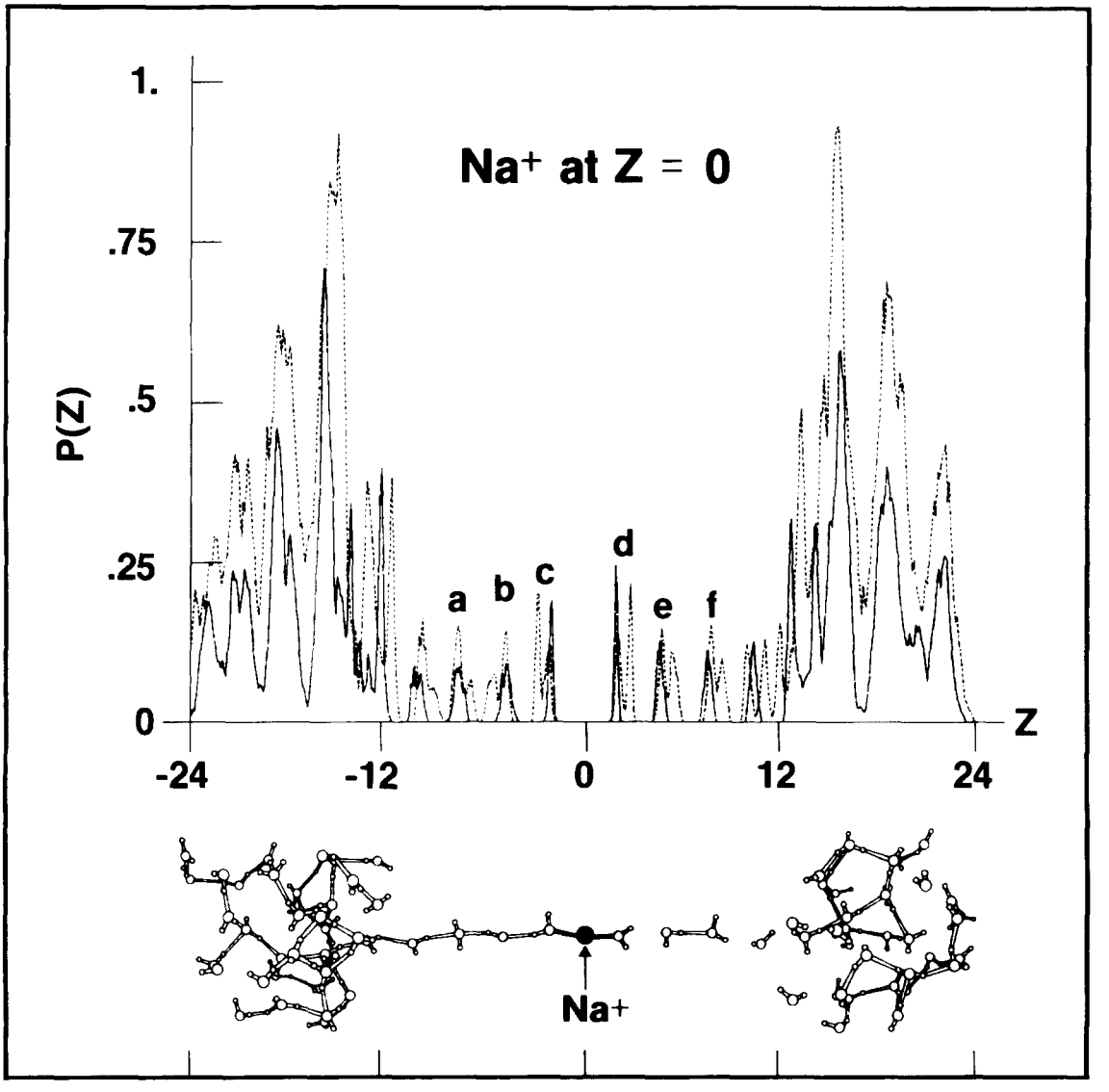


Fig. 6. Top: water's oxygen (full line) and hydrogen (dotted line) probability distributions along the Z axis (in Å) of Gramicidin A with a fixed sodium ion at $X = 0$, $Y = 0$, and $Z = 0$ Å. Bottom: a statistically significant configuration of the water molecules (see Fig. 7 for additional details).

hydrogen atoms (at the right) and for the oxygen atoms (at the left). The insets for the oxygen atom probability display in addition information on the location where the hydrogen probability is large and on the backbone of Gramicidin A with indication of the connected residue (same label a in Fig. 1). From the probabilities along Z and into the xy plane one can visualize the sterical organization of the water molecules to the left and to the right of the ion and the amount of mobility of each water molecule even keeping the cation fixed.

In Fig. 8 we compare four statistically significant single configurations (the probability distributions are presented in the technical report [16]) obtained when the Na^+ is at (a) $Z = 14$ Å, (b) 12.5 Å, (c) 10.63 Å, and (d) 5 Å; namely, we consider the ion immediately outside the channel end, at the very beginning, at the experimental binding site close to the C=O group of L-Trp[11] [8], and around the middle of one monomer. In presence of

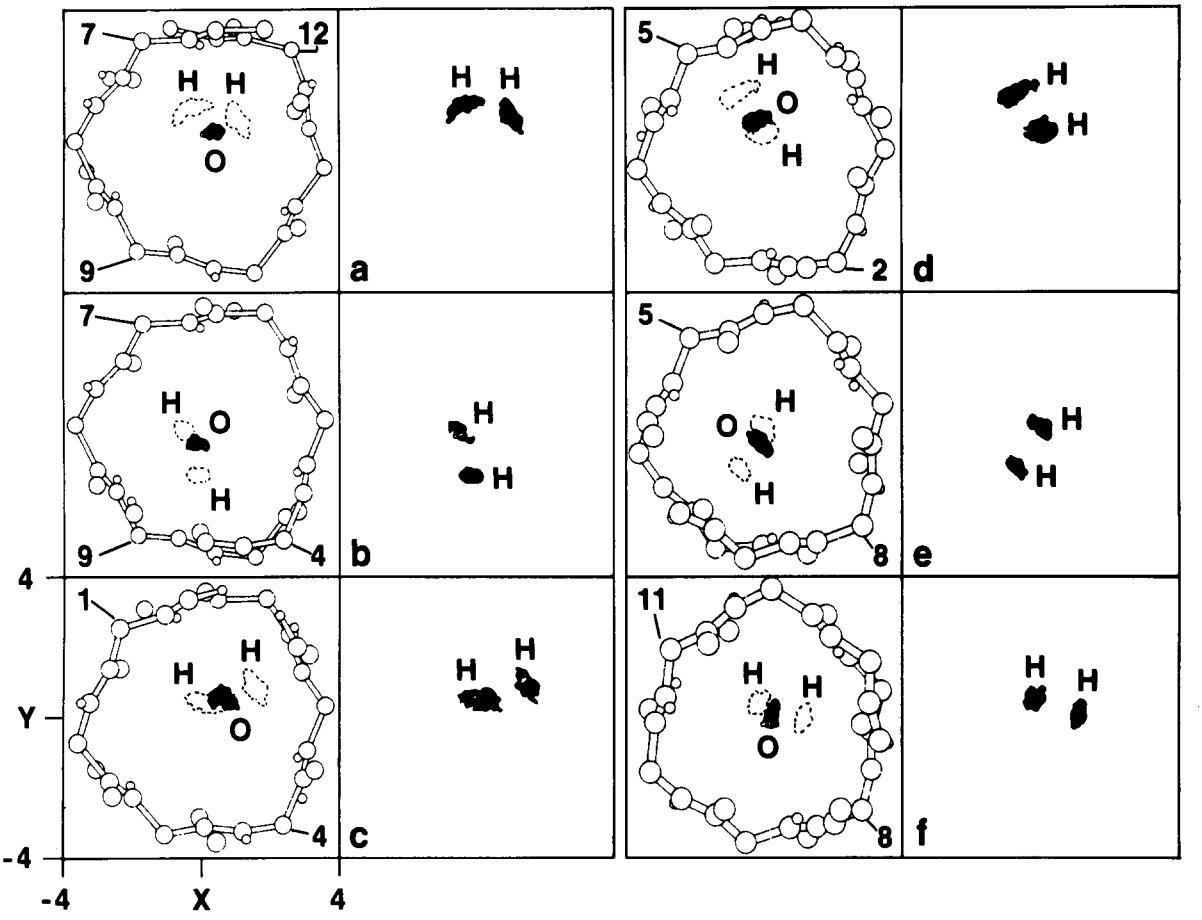


Fig. 7. Oxygen and hydrogen atoms probability distribution maps projected onto the *xy* plane (in a.u.) for six selected regions of the Gramicidin A channel corresponding to the probability peaks of the six water molecules in Fig. 6. The Gramicidin A backbone atoms nearest to water molecules are shown. The number connected to the C atom indicates the connected residue.

one fixed cation, between $Z = -12$ Å and $Z = 12$ Å, we observe eight (Fig. 6) or seven water molecules (Fig. 8) within the channel, an intermediate value between the number of water molecules coupled to the transport of Na^+ deduced experimentally by Rosenberg [26,27] (6–7 water molecules) and the one observed by Levitt [28] (12 molecules).

Notice, also, from the Fig. 8 that when the ion is at the border of the channel it can still coordinate more than two water molecules (for $Z = 14$ Å and $Z = 12.5$ Å the Na^+ coordination number of the first shell is three). When the ion reaches the binding site (10.63 Å), only two water molecules find room to solvate it. This variation in the solvation characteristic is also shown by the interaction energies of Table I, which decreases from about 10 to 5 kJ/mol. The value at $Z = 24$ Å should be ignored, since the cation is located close to the boundary selected for our cylinder; indeed the values at $Z = 24$ Å are reported only to show the boundary effects. The introduction of the cation lowers the attraction Gramicidin A-water, since water is displaced in order to make room for Na^+ (we could talk of 'local' dehydration). The above energetic losses are compensated by the attraction Gramicidin A-Na^+ which is zero when Na^+ is far from the channel and increases when the Na^+ penetrates the channel. In a forthcoming paper we shall analyze this delicate balance in detail.

In our last experiment we compare Na^+ at $X = 0$, $Y = 0$, and $Z = 0$ Å with Li^+ or K^+ at

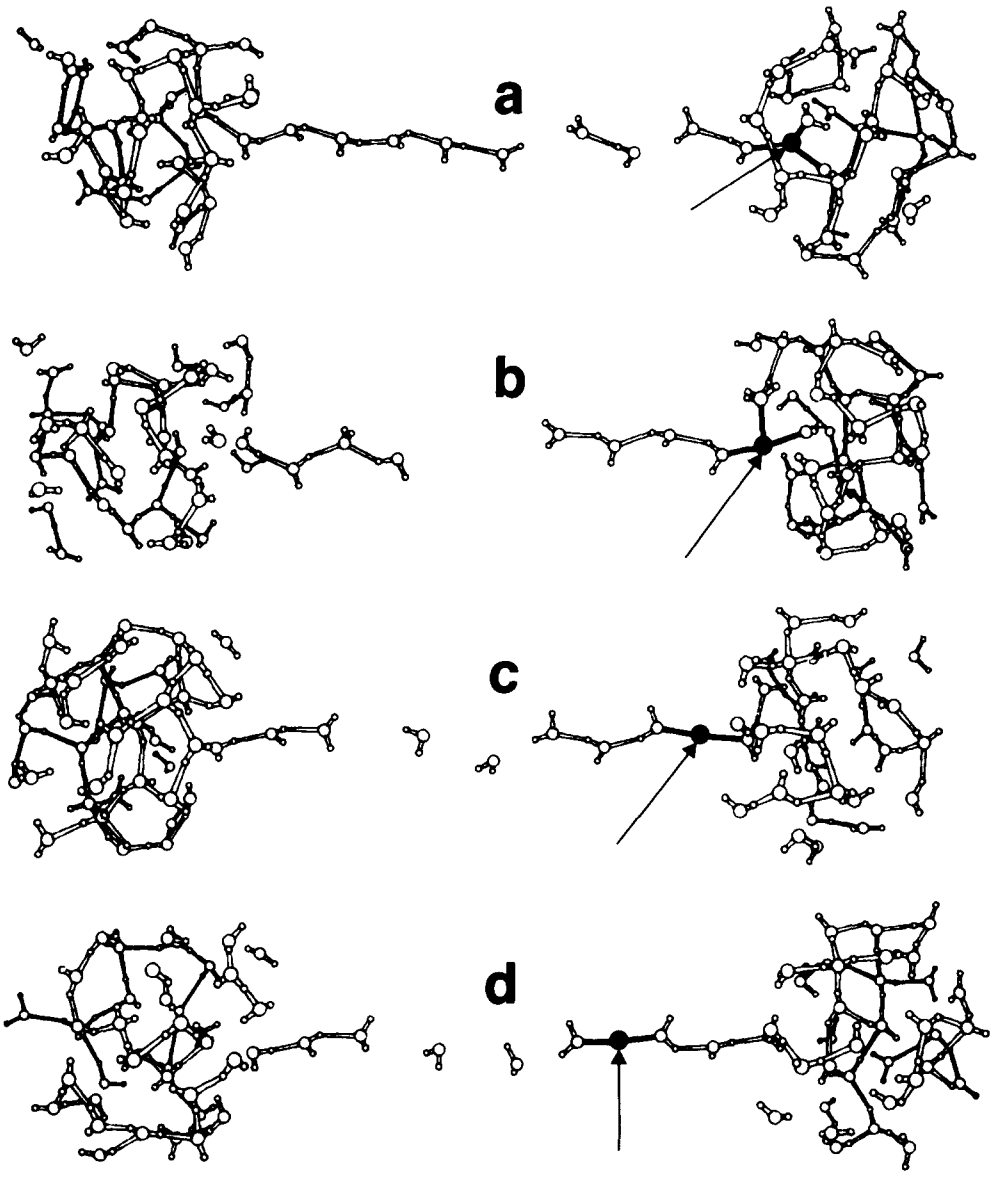


Fig. 8. Statistically significant configurations for water molecules with Na^+ at $Z = 14$(a), 12.5(b), 10.63(c), and 5 Å(d). Arrows point to the sodium ions.

$X = 0$, $Y = 0$, and $Z = 0$ Å (Fig. 9). In all cases, the ion, when in the channel, is coordinated to two water molecules; the directional interaction of the oxygen atoms of the Gramicidin A carbonyl groups with the ion compensates for the loss of the coordinating water molecules of the ion in bulk water. In this sense, the coordination remains nearly constant for the ion both in the solvent water and in the Gramicidin A channel. The cation-water interaction increases in the order $Li^+ > Na^+ > K^+$, but these energy differences are relatively small, of the order of 1 to 2 kJ/mol, not at all as large as the differences in solvation energy in bulk water (see Table I). The water-water interaction for the experiments with Li^+ and K^+ are essentially the same as those found for the Na^+ experiment. Therefore the main source of specificity in the Gramicidin A-ion mechanism is in the differences of the interaction energy between Gramicidin A and different ions (Fornili, S.L., Vercauteren, D.P.

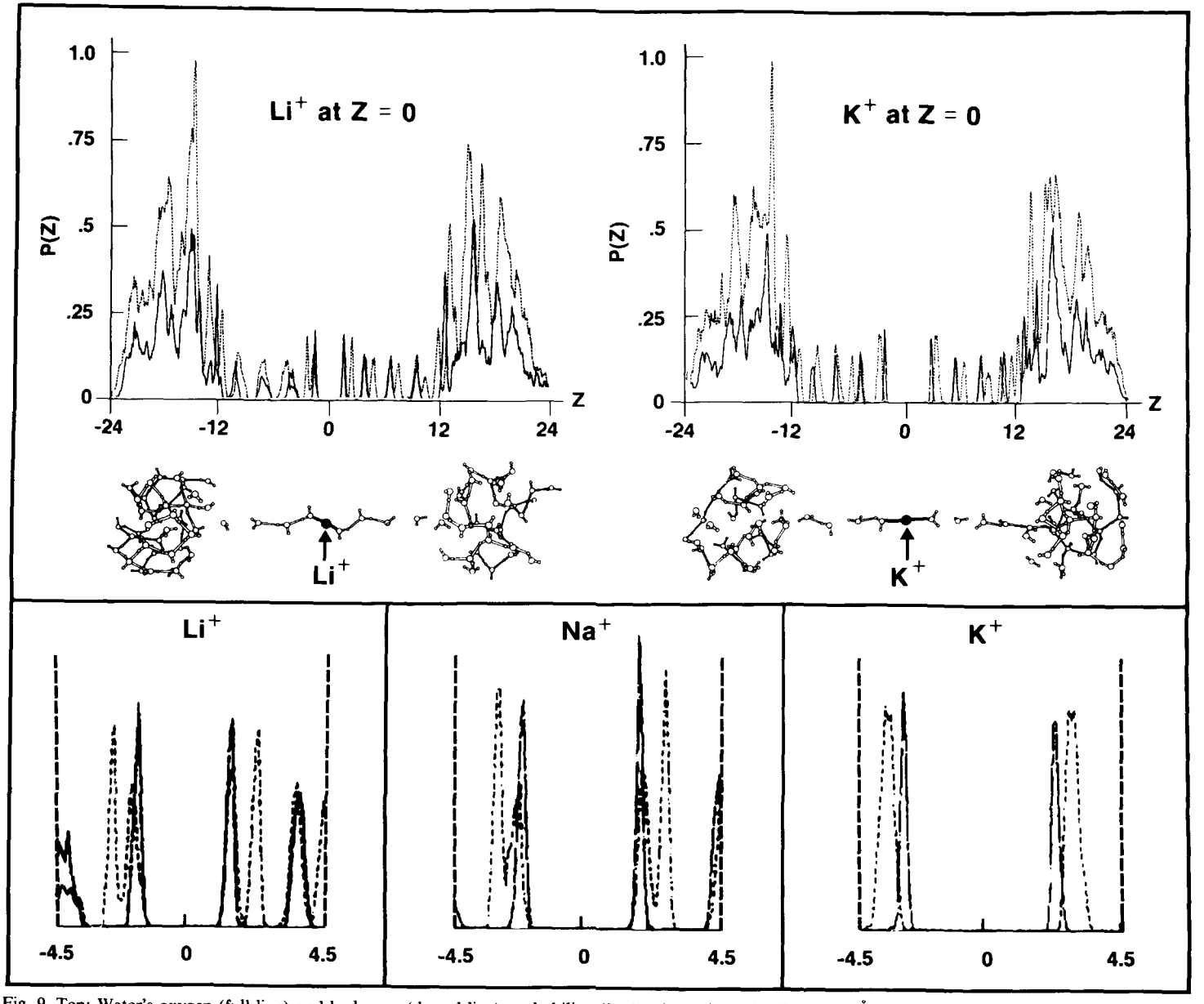


Fig. 9. Top: Water's oxygen (full line) and hydrogen (dotted line) probability distributions along the Z axis (in Å) of Gramicidin A with Li^+ or K^+ at $X = 0$, $Y = 0$, and $Z = 0$ Å. Bottom: detailed distributions for the two water molecules coordinating Li^+, Na^+, and K^+ in Gramicidin A at $X = 0$, $Y = 0$, and $Z = 0$ Å.

and Clementi, E., unpublished data), and also in the elastic properties of the channel (see for example Refs. 8 and 21). These two factors require rather detailed knowledge of the interaction energy potentials between an ion and the full Gramicidin A channel and of the influence of the phospholipids on the Gramicidin A dynamics.

Acknowledgement

One of us (D.P.V.) would like to thank the National Foundation for Cancer Research (NFCR) for its financial support.

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