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Original Investigations

An SCF *ab initio* Investigation of the "Through-Water" Interaction of the Phosphate Anion with the Na^+ Cation

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SCF *ab initio* computations in the supermolecule approach were carried out for the study of the hydration scheme of the dihydrogen phosphate anion, of the sodium cation and for the investigation of the direct and the through-water interaction of these two charged species. It is found that the energy balances of the direct phosphate–Na^+ binding, involving their prior dehydration, or their through-water binding, allowing them to conserve their hydration shells, are of the same order of magnitude, indicating the competitivity of the two processes. This situation results in the existence of multiple possibilities for phosphate–Na^+–water association. Appreciable energies of interaction exist between the different subunits of such systems. The Na^+ cation and to a somewhat lesser extent the phosphate anion have a polarizing effect upon the charge distribution in the system over relatively appreciable distances. On the contrary, the charge transfers between the different components of the system are interpretable essentially in terms of displacements between adjacent units only.

Key words: Through water interaction – Phosphate anion interaction with Na^+ cation

1. Introduction

The elucidation of the interactions capable to exist in the system phosphate anion–water–alkali cations is of fundamental importance for the understanding of the structural and probably also functional properties of nucleic acids, phospholipids, and other phosphate containing biomolecules. In our laboratory it represents also a part of a general program of investigation of the interaction of electrophiles with nucleic acid components in view of the possible significance of such interactions in the electronic mechanisms of chemical carcinogenesis (see e.g. [1]).

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In previous publications we have studied the binary interactions phosphate–water [2, 3], phosphate–cations [4, 5] and recently have also considered the simultaneous interactions of these three entities [6]. In this last study, we examined Na^+ binding to a hexahydrated dimethylphosphate anion (DMP^-) in which the molecules of water were all situated in the first hydration shell of the substrate. It is likely, however, that more complex interactions, involving in particular a larger number of intermediate water molecules, may occur between the phosphate anion and alkali cations and the present work is devoted to an exploration of this possibility and to the determination of its energetic and electronic characteristics.

2. Method

The computations are performed by the SCF *ab initio* procedure in the supermolecule approach as in Ref. [6] with two changes, however. In the first place, for reason of economy and because of the increased dimensions of the system to be explored, the computations have been carried out with dihydrogen phosphate $PO_4H_2^-$ instead of DMP^-. The two hydrogens of $PO_4H_2^-$ were, however, barred from participating in any direct interactions with water, so as to mimic the situation existing in DMP^- and, in general, in phosphodiester linkages. In the second place, the STO 3G basis set [7] used in our previous computations, which has been found to yield too strong binding energies and charge transfers [8], has been replaced by a more appropriate basis of Gaussian functions: 10*s*, 6*p*, 1*d* on phosphorus, 7*s*, 3*p* on the first row atoms, and 3*s* on hydrogen, contracted to minimal. As discussed in Ref. [5], this basis insures an appropriate representation of the pentavalent phosphorus atom and of the anionic character of the compound. The basis set utilized for Na^+ is that of Ref. [8] which associated with the previous one on the other atoms has been shown to yield reasonable values of the binding energies.

Although the main object of our studies was the $PO_4H_2^- \cdots (H_2O)_n \cdots Na^+$ system, the necessity of a more thorough analysis of the results has induced us also to study the properties of the subsystems $PO_4H_2^- \cdots (H_2O)_n$, $(H_2O)_n \cdots Na^+$ and $(H_2O)_n$.

3. Results and Discussion

3.1. Hydration Characteristics of $PO_4H_2^-$

In view of exploring the problem studied in this paper, our attention centered first on the hexahydrate of $PO_4H_2^-$ expected, by analogy with DMP^-, to represent $PO_4H_2^-$ with its complete first hydration shell. In this form the six water molecules are located at the E_{13}, E_{14}, E_{12}, E_{31}, E_{34} and E_{32} sites (Fig. 1), defined in Ref. [3], three of them around each of the P–O_1 and P–O_3 axes. The global interaction energy of this system equals -65.9 kcal/mole which corresponds to -11 kcal/mole per water molecule. (This last number may be compared with -17.3 kcal/mole found for the system $DMP^-/6H_2O$ using the STO 3G basis set [3].) It may be useful to add here that this "symmetrical" hexahydrate is in fact somewhat less stable than the one obtained from it by rotating by 60° one of the two groups of

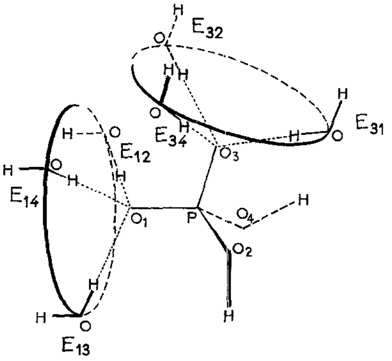
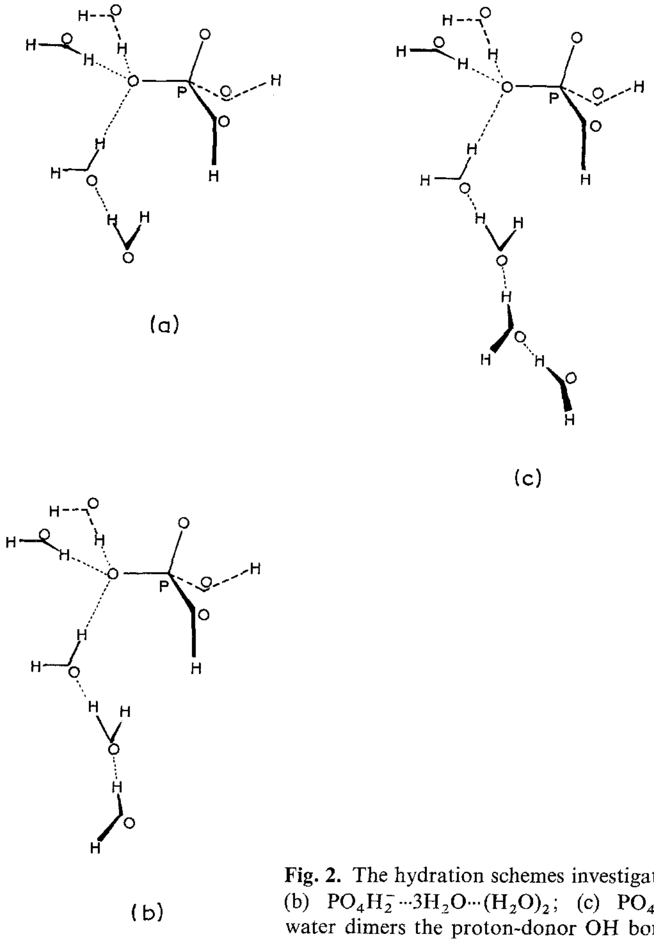


Fig. 1. Hexahydrate of $PO_4H_2^-$. All the water molecules are in the first hydration shell with $O_1 \cdots H = O_3 \cdots H = 1.8$ Å (optimal $O_1 \cdots H$ distance $= 1.7$ Å in the monohydrate)

three waters, in such a way that the two groups become "staggered" with respect to one another. The energy of binding per water molecule in the staggered hexahydrate is -11.5 kcal/mole.



(a)

(c)

(b)

Fig. 2. The hydration schemes investigated (a) $PO_4H_2^- \cdots 3H_2O \cdots H_2O$; (b) $PO_4H_2^- \cdots 3H_2O \cdots (H_2O)_2$; (c) $PO_4H_2^- \cdots 3H_2O \cdots (H_2O)_3$ (in all water dimers the proton-donor OH bond was placed along the bissectrix of the water proton acceptor with an O $\cdots$H distance of 1.9 Å)

With a lesser extent of hydration the energies of binding per molecule of water come out somewhat larger. Thus for the monohydrate $PO_4H_2^- \cdots H_2O$ in the optimal position corresponding to E_{13}, the interaction energy is -17.8 kcal/mole (-28.6 for DMP^- in the STO 3G basis set); for the trihydrate $PO_4H_2^- \cdots 3H_2O$, in positions E_{13}, E_{14}, E_{12}, i.e. with the three water molecules bound to the same anionic oxygen, the interaction energy per water molecule is reduced to -12.9 kcal/mole, thus close to the energy in the hexahydrate.

For the sake of economy the addition of water in the second and further hydration shells was studied only upon this last trihydrate. Up to three water molecules were added "linearly" to the water molecule E_{13} following the scheme of Fig. 2. We shall use the symbol $PO_4H_2^- \cdots 3H_2O \cdots H_2O$ to designate the Scheme 2a (three water molecules in the first hydration shell around $P{-}O_1$ and one in the second), the symbol $PO_4H_2^- \cdots 3H_2O \cdots (H_2O)_2$ to designate the scheme of Fig. 2b (three water molecules in the first hydration shell around $P{-}O_1$, one in the second and one in the third shell) and the symbol $PO_4H_2^- \cdots 3H_2O \cdots (H_2O)_3$ to designate the scheme of Fig. 2c.

Table 1. Binding energies in the systems $PO_4H_2^- \cdots 3H_2O \cdots (H_2O)_n$

System (the sign $\rightsquigarrow$ indicates the subsystems considered)	Interaction energy[a] (kcal/mole)
$PO_4H_2^- \cdots 3H_2O \rightsquigarrow H_2O$	-9.5
$PO_4H_2^- \cdots 3H_2O \cdots H_2O \rightsquigarrow H_2O$	-7.8
$PO_4H_2^- \cdots 3H_2O \cdots H_2O \cdots H_2O \rightsquigarrow H_2O$	-8.2
$PO_4H_2^- \cdots 3H_2O \rightsquigarrow H_2O \cdots H_2O$	-12.4
$PO_4H_2^- \cdots 3H_2O \rightsquigarrow H_2O \cdots H_2O \cdots H_2O$	-13.9
$PO_4H_2^- \cdots 3H_2O \cdots H_2O \rightsquigarrow H_2O \cdots H_2O$	-11.0

[a] The interaction energies in Tables 1 to 4 are computed in each case as the difference between the energy of the total system and the sum of the energies of the two subsystems indicated.

The energy characteristics of the interaction are shown in Table 1 from which it can be seen that they may be looked upon from different viewpoints corresponding to different divisions of the supermolecule into components. Thus when the external water molecule is considered, its interaction energy with the remaining part of the supersystem equals -9.5 kcal/mole in $PO_4H_2^- \cdots 3H_2O \cdots H_2O$, -7.8 kcal/mole in $PO_4H_2 \cdots 3H_2O \cdots (H_2O)_2$ and -8.2 kcal/mole in $PO_4H_2^- \cdots 3H_2O \cdots (H_2O)_3$. Worth noting is the fact that these values are always greater than the interaction energy of two water molecules (in the same relative configuration) which, in the present set, is equal to -5 kcal/mole.

In the supersystems one may, however, consider also the interaction energies of other subunits: in $PO_4H_2^- \cdots 3H_2O \cdots (H_2O)_2$ these could be $PO_4H_2^- \cdots 3H_2O$ and $H_2O \cdots H_2O$. The corresponding energy is -12.4 kcal/mole. In $PO_4H_2^- \cdots 3H_2O \cdots (H_2O)_3$ we may consider the interaction energies of the subunits $PO_4H_2^- \cdots 3H_2O$ with $H_2O \cdots H_2O \cdots H_2O$ or of the subunits $PO_4H_2^- \cdots 3H_2O \cdots H_2O$ with $H_2O \cdots$

H_2O. The two energies equal, respectively, −13.9 and −11 kcal/mole. It must be underlined that in each case these numbers represent the interaction energies between the whole subsystems considered and not just of the two hydrogen-bonded water molecules. In every case again, the values are larger than the interaction energies of the same water subsystem with another water molecule (see Table 2).

Table 2. Binding energies in the linear systems $(H_2O)_n$ ($O \cdots H = 1.9$ Å)

System (the sign ⌇ indicates the subsystems considered)	Interaction energies (kcal/mole)
H_2O ⌇ H_2O	−5.0
$H_2O \cdots H_2O$ ⌇ H_2O	−6.6
$H_2O \cdots H_2O \cdots H_2O$ ⌇ H_2O	−7.0
$H_2O \cdots H_2O$ ⌇ $H_2O \cdots H_2O$	−8.7

Another aspect of the hydration scheme which needs to be considered concerns the distribution and the displacements of electronic charges. Fig. 3a represents the distribution of net electronic charges, in millielectron units, obtained for free $PO_4H_2^-$ and H_2O molecules with the basis set adopted in this paper. Fig. 3b represents the charge distribution in a monohydrate with a water molecule fixed at the E_{13} site. An overall transfer of charge is observed from the phosphate to the water molecule. It amounts to 0.057 e (indicated in a circle) and is thus appreciably smaller than that obtained with the STO 3G basis set [3]. As discussed elsewhere [3, 6, 9] it corresponds to a partial transfer of the anionic character of the phosphate to water and to its subsequent activation for interactions with electrophiles. As shown in Fig. 3c the average transfer of charge, per water molecule, decreases somewhat when the trihydrate upon the $P{-}O_1$ axis is considered. A slight further decrease is observed in the hexahydrate (average value: 0.038 e).

The charge transfer corresponding to the presence of water molecules in the further (second, third or fourth) hydration shell is of particular interest. In $PO_4H_2^- \cdots 3H_2O \cdots H_2O$ (Fig. 3d) it is seen that the water molecule located at the E_{13} site and the water molecule bound to it in the second hydration shell carry an equal excess of charge: −0.024 e each. The sum of the two is only slightly larger than the excess carried by the E_{13} water molecule in $PO_4H_2^- \cdots 3H_2O$ (Fig. 3c) and this may be considered at first sight as if it were simply a very limited further "discharge" of the phosphate by the addition of a water molecule in the second hydration shell. In fact the situation is more complex and may be better understood when looking on the particularly striking aspect of the charge transfer in $PO_4H_2^- \cdots 3H_2O \cdots (H_2O)_3$ shown in Fig. 3f. It corresponds to the distribution of charges in the hydrogen-bonded chain of water molecules starting at E_{13}. Contrary to what might be expected by superficial reasoning, the charge excess on each water molecule does not decrease progressively along the chain as one moves further away from the E_{13} site. The excess of charge is concentrated equally on the phosphate-bound water

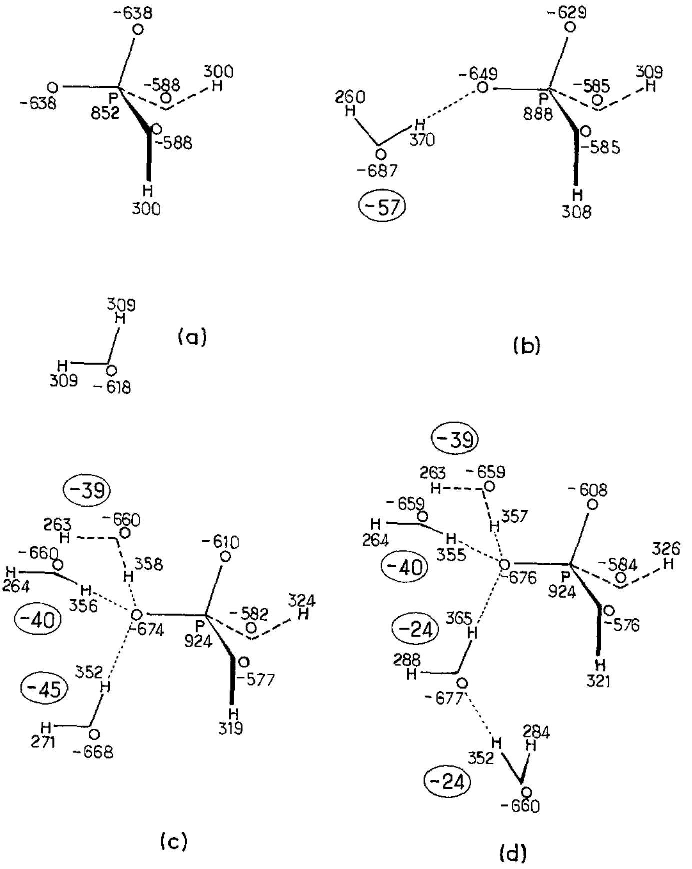


Fig. 3. Distribution of net electronic charges. Numbers in circles indicate the intermolecular charge transfer (in millielectron units).

(a) Isolated $PO_4H_2^-$ and H_2O.

(b) Monohydrate with H_2O in the E_{13} site.

(c) Trihydrate $PO_4H_2^- \cdots (3H_2O)$. All water molecule in the first hydration shell.

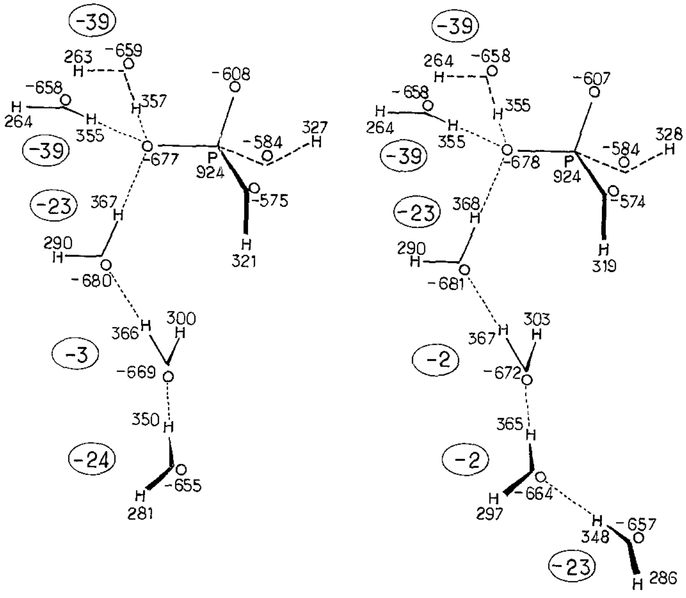
(d) $PO_4H_2^- \cdots 3H_2O \cdots H_2O$. Three water molecules in the first hydration shell and one in the second.

(e) $PO_4H_2^- \cdots 3H_2O \cdots (H_2O)_2$. Three water molecules in the first hydration shell, one in the second and one in the third.

(f) $PO_4H_2^- \cdots 3H_2O \cdots (H_2O)_3$. Three water molecules in the first hydration shell and one in the second, third and fourth hydration shells

molecule E_{13} (-0.023 e) and on the terminal water molecule of the chain (-0.023 e). The two intermediate water molecules are nearly neutral (-0.002 e each).

This situation becomes clarified when one considers the nature of charge displacements occurring in a *water dimer* and in *water oligomers*. Those are illustrated in Fig. 4. It is seen that in the dimer (Fig. 4a) the proton-donor water molecule acquires an excess of 0.019 e and the proton-acceptor water molecule a deficiency of 0.019 e. In the trimer (Fig. 4b), the intermediate water molecule, which acts both as a proton donor and a proton acceptor, has its overall charge displacement



(e) (f)

compensated by this donor-acceptor situation and is practically neutral (+0.001 e), while the terminal water molecules behave, one as a proton donor only and the other as a proton acceptor only and carry thus the corresponding excess or defect of charges, only slightly different from their values in the dimer. The same situation prevails in the water tetramer (Fig. 4c) where the two central water molecules, acting simultaneously as proton donors and acceptors are nearly neutral.

The situation which occurs in $PO_4H_2^- \cdots 3H_2O \cdots (H_2O)_2$ (Fig. 3e) and $PO_4H_2^- \cdots 3H_2O \cdots (H_2O)_3$ (Fig. 3f) correspond basically to the same phenomenon, modified somewhat, however, by the influence of the phosphate anion. As remarked above, in the system of Fig. 3f, the E_{13} and the terminal water molecules carry an excess of negative charge, equal in both cases to 0.023 e, while the two intermediate water molecules are nearly neutral. The situation is now easily understandable: the excess of 0.023 e on the E_{13} water molecule is the result of the partial neutralization of the transfer from the phosphate group to this water molecule ($\simeq 0.040$ e) by the electron-withdrawing effect from it due to its role as a proton-acceptor for the water molecule of the second hydration shell ($\simeq 0.020$ e). The negative charge -0.023 e on the water molecule in the 4'th hydration shell results from its functioning as a proton donor with respect to the water molecule in the 3'rd hydration shell. The two intermediate water molecules, being both proton donors and acceptors, are nearly neutral.

The interpretation of the charge transfer scheme in $PO_4H_2^- \cdots 3H_2O \cdots H_2O$ (Fig. 3d) can be understood within the same type of reasoning. It should not be interpreted uniquely as the transfer of the anionic character of the phosphate towards the water molecules but as a result of this transfer and the one inherent in the formation of water–water association.

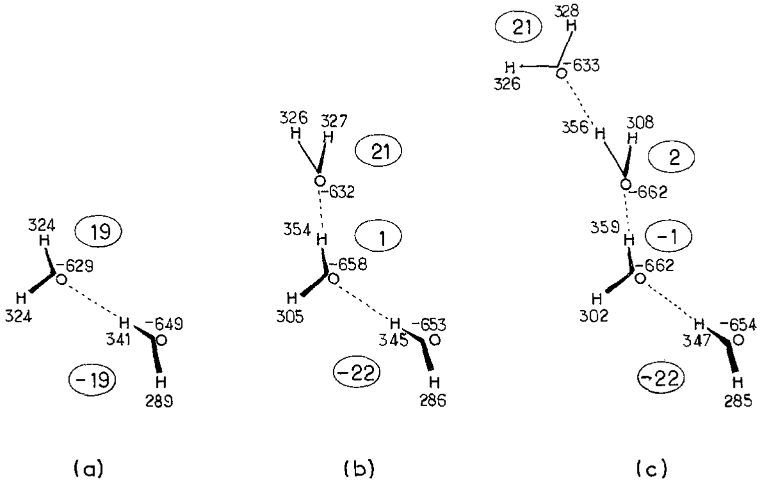


Fig. 4. Distribution of net electronic charges in water dimer and oligomers. Numbers in circles indicate the intermolecular charge transfers. (In millielectron units.)

It must be stressed that the intermediate water molecules of Fig. 3e and 3f although *globally* nearly neutral, have a strongly polarized charge distribution and are thus different from an isolated neutral water molecule. This is evident from the analysis of the modifications of the electronic charges on the individual atoms upon hydrogen bonding.

In this respect, it is instructive to compare the charge displacements in water upon hydrogen bonding to the phosphate to those occurring in the polymers of water alone. In agreement with earlier findings [10–12] the formation of the dimer of water (compare Figs. 3a and 4a) increases the net negative charges on the two bound oxygens (in particular on the one belonging to the proton donor molecule). It increases the net positive charge on the proton engaged in the hydrogen bond and on the two hydrogen atoms of the water acting as proton acceptor. It decreases the net positive charge on the second hydrogen atom of the proton donor molecule. (The increase of the positive charge on the proton engaged in hydrogen bonding is a global description of the depletion of electron density in the region of the hydrogen bond put into evidence as its general feature by more refined descriptions using global density difference maps (see e.g. [13–15]) and confirmed by recent studies combining accurate X-ray and neutron diffraction data (e.g. [16, 17].

The increase in negative charge on the oxygen at the proton-donor molecule of the dimer and the decrease in positive charge at its non-bonded proton allow us to rationalize the fact that "sequential" further addition of one more water molecule on the oxygen atom is favored over a "branching" addition to the proton.

The same type of charge variations, in particular the increase of the net negative charges of the two hydrogen-bonded oxygens, the increase of the net positive charge of the proton engaged in hydrogen bonding and the decrease in the positive charge of the non-bonded proton occur in the hydrogen bonding of water to

$PO_4H_2^-$. The stronger polarizing effect of the anion is seen in the larger values of the charge displacements. Note in particular the large increase in the negative character of the oxygen of the bound water and the large decrease in the positive charge of its non-bonded hydrogen (compare Figs. 3b or 3c and 4a). This makes the water bound in the first shell of the phosphate a better further proton acceptor than an isolated water and also a better one than a water molecule bound to water itself (compare Figs. 4b (or 4c) and 3a). Similarly the strong discharge of the non-bonded proton makes it a much poorer proton acceptor than water alone and also poorer than the corresponding proton in water bound to water. The same thing occurs for the water molecule of the second hydration shell (compare Figs. 3d and 4b). This indicates that sequential binding of a further molecule to an anion–water chain will be more favored with respect to branched binding than it is in a pure water–water array. Such a situation should favor the formation of chains of water molecules departing from the ion, rather than of branched structures. Our results parallel Clementi's finding [18] that "filaments" of water molecules are characteristic of the fine structure of water clusters around ions. In Clementi's study these filaments appear as a consequence of only two-body interactions. It is evident from the present investigation that the effect of polarization due to many-body interactions should enhance this tendency.

It is interesting that the polarizing effect of the phosphate on the electron distribution in the sequential array of water molecules bound to it does not extend significantly beyond the second water molecule: compare for instance the terminal water molecule in Fig. 3e with that of Fig. 4b or the terminal water molecule of Fig. 3f with that of Fig. 4c. In other words, the terminal molecule of a water trimer is very little perturbed by the binding of the other end of the trimer to the phosphate anion (this is not true of the intermediate molecule). Interestingly, considering the reciprocal polarizing effect of water on the phosphate anion it appears that the essential modifications are acquired upon the formation of the first hydration shell and that the further sequential addition of water molecules does not produce a significant effect on the phosphate charge distribution (compare Figs. 3c, d, e and f).

3.2. *Hydration Characteristics of* $Na^+ \cdots (H_2O)_n$

The prior investigation of the hydration characteristics of the $Na \cdots (H_2O)_n$ system may be equally helpful for the better understanding of the results relevant to the "through-water" interaction between $PO_4H_2^-$ and Na^+. In our notation n refers to successive hydration shells so that e.g. $Na^+ \cdots (H_2O)_2$ refers to the system $Na^+ \cdots H_2O \cdots H_2O$ etc. Studies have been carried out up to $n = 4$.

The energy characteristics of these systems are summed up in Table 3 while Fig. 5 presents those concerned with the distribution and displacement of electronic charges. The binding energy of Na^+ with $(H_2O)_n$ which is found equal to −28.9 kcal/mole for one water molecule [8], increases progressively up to −45.0 kcal/mole in the system $Na^+ \cdots (H_2O)_4$. It must be underlined again that e.g. this last number represents the interaction energy of Na^+ with the *global* system of four hydrogen-bonded water molecules. It is instructive for comparison to compute

Table 3. Binding energies in the systems $Na^+ \cdots (H_2O)_n$

System (the sign ϟ indicates the subsystems considered)	Interaction energies (kcal/mole)
H_2O ϟ Na^+	−28.9
$H_2O \cdots H_2O$ ϟ Na^+	−38.6
H_2O ϟ $H_2O \cdots Na^+$	−14.8
$H_2O \cdots H_2O \cdots H_2O$ ϟ Na^+	−42.7
$H_2O \cdots H_2O \cdots H_2O \cdots H_2O$ ϟ Na^+	−45.0

what would be the individual energies of interaction between Na^+ and each "distant" water molecule isolated in the global system, using the appropriate $Na^+ \cdots H_2O$ relative dispositions as they occur in $Na^+ (H_2O)_4$ and suppressing the intermediate water molecules. The results of such a computation are shown in Fig. 6, together with the related charge distributions. The sum of such individual interactions amounts to 41 kcal/mole which is about 4 kcal/mole short of the result of the global interaction illustrating thus the enhancing effect of the polarization of the water molecules in the real system, a feature not taken into account in the $Na^+ \cdots$water interactions of Fig. 6.

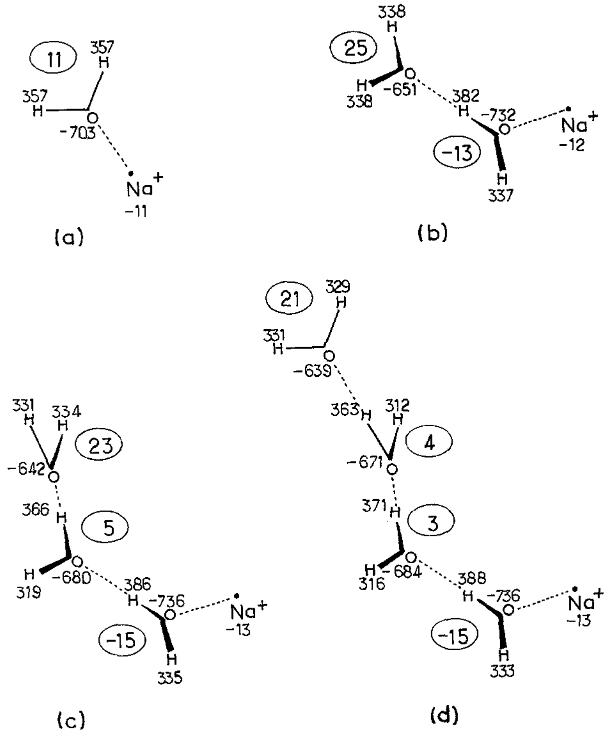


Fig. 5. Distribution of net electronic charges. Numbers in circles indicate charge transfers. (In millielectron units.)
(a) $Na^+ \cdots H_2O$.
(b) $Na^+ \cdots H_2O \cdots H_2O$.
(c) $Na^+ \cdots H_2O \cdots H_2O \cdots H_2O$.
(d) $Na^+ \cdots H_2O \cdots H_2O \cdots H_2O \cdots H_2O$

In this case again, one could subdivide each system into different subunits: e.g. in the system $Na^+ \cdots H_2O \cdots H_2O$ consider the interaction energy of the subsystems $Na^+ \cdots H_2O$ and H_2O. It amounts to −14.8 kcal/mole.

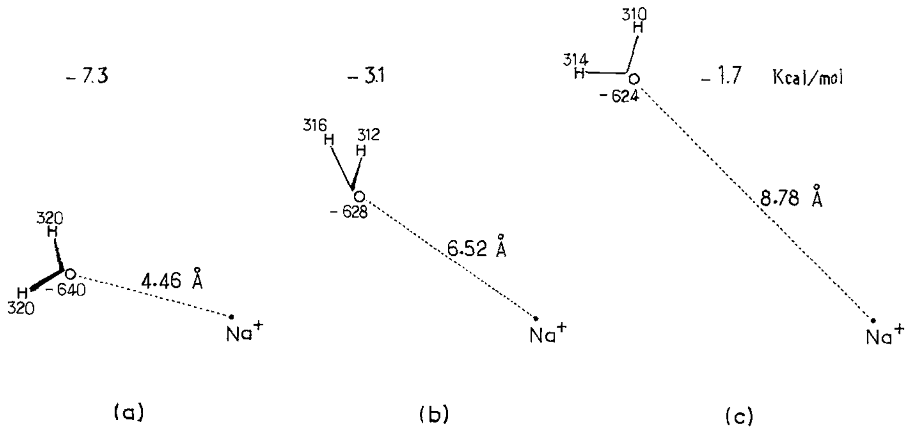


Fig. 6. Interaction energies and charge distributions between Na$^+$ and distant water molecules of Na$^+$ ···$(H_2O)_4$, at the appropriate intermolecular distances, with the intermediate water molecules disregarded. (In millielectron units.)
(a) Na$^+$ and the 2'nd water molecule.
(b) Na$^+$ and the 3'rd water molecule.
(c) Na$^+$ and the 4'th water molecule.

The examination of the charge distribution and transfers (Fig. 5) in relation with those of water–water association (Fig. 4) is equally instructive. It is observed (Fig. 5a) that the interaction of a water molecule with Na$^+$ produces a small charge transfer (0.011 e) from the water to Na$^+$. When this is combined with what we learned above about the charge transfer in a water dimer it enables a clear understanding of the significance of the results obtained with the higher Na$^+$ hydrates. Thus let us consider directly the hydrate Na$^+$ ···$(H_2O)_4$ (Fig. 5d). In this hydrate the H_2O molecule directly attached to Na$^+$ carries an excess of negative charge of 0.015 e, the most distant one an excess of positive charge of 0.021 e and the two intermediate ones are close to neutrality (+0.003 and +0.004 e). The most distant water molecule acts as a proton acceptor and carries therefore the typical charge defect characteristic of such water molecules. The two intermediate water molecules function simultaneously as proton donors and proton acceptors and are therefore close to neutrality. The water molecule attached directly to Na$^+$ has a tendency to loose about 0.011 e towards this cation. It acts, however, also as a proton donor towards the neighbouring water molecule and by this mode of association tends to gain about 0.021–0.023 e. Its resultant net negative charge of −0.015 is a compromise between these two tendencies.

On the other hand it must be noted that while the charge transfer between water and Na$^+$ is relatively small (11 millielectron units), the polarization of the electronic distribution of the water molecule by the bound cation is rather strong (Fig. 5a) as seen in the great increase of the net negative charge on the oxygen atom (85 millielectron units) and the concomitant strong increase of the net positive charges on the hydrogens (48 millielectron units on each). This polarization, in particular of the oxygen bound to Na$^+$, increases further in the systems $(H_2O)_n$ ···Na$^+$, in particular when passing from $n=1$ to $n=2$. It decreases naturally for the more distant water molecules. In all cases one may interpret quite satisfactorily the variations of the charge distribution by considerations based on what we learned about the effect of neighbouring units, H_2O or Na^+.

Finally it may be noticed (Fig. 6) that no charge transfer occurs between Na^+ and water at distances corresponding to the positioning of the second water molecule or beyond in the chain $Na^+ \cdots (H_2O)_n$ whereas the polarization effect remains detectable at large distances [8, 19], even in the fourth position. The polarizing effect of Na^+-binding to the end of a tetramer is still felt slightly at the other end of the chain (compare Figs. 4c and 5d), whereas the corresponding distant effect of phosphate binding is negligible (*vide supra*). This is in keeping with the relative strength of the sodium–water and phosphate–water binding ($\Delta E = -29$ and -18 kcal, respectively, in the present basis set). (To be sure, the comparison should really be made with the system $PO_4H_2^- \cdots H_2O \cdots (H_2O)_3$ or between systems where both $PO_4H_2^-$ and Na^+ carry their complete first hydration shells. Preliminary calculations [20] with fully hydrated ions seem to conserve the result.) A similar difference between the relative influence of F^- and Li^+ on distant water shells has been inferred from CNDO computations [21].

3.3. *The Through-Water Binding of $PO_4H_2^-$ and Na^+*

We can now come back to the main subject of this paper, namely the characteristics of the through-water binding of $PO_4H_2^-$ and Na^+.

Table 4. Binding energies in through-water binding in the system $PO_4H_2^- \cdots (H_2O)_n \cdots Na^+$

System (the sign ∿ indicates the subsystems considered)	Interaction energies (kcal/mole)
$PO_4H_2^-$ ∿ Na^+ (at E_{13})	-120.5
$PO_4H_2^- \cdots H_2O$ ∿ Na^+	$-\ 99.6$
$PO_4H_2^- \cdots 3H_2O$ ∿ Na^+	$-\ 87.9$
$PO_4H_2^- \cdots 3H_2O \cdots H_2O$ ∿ Na^+	$-\ 80.6$
$PO_4H_2^- \cdots 3H_2O \cdots H_2O \cdots H_2O \cdots H_2O$ ∿ Na^+	$-\ 75.6$
$PO_4H_2^- \cdots 3H_2O$ ∿$\overset{6.37\ \text{Å}}{\cdots\ \cdots\ \cdots\ \cdots}$ $\cdots H_2O \cdots Na^+$	$-\ 33.4$
$PO_4H_2^- \cdots\ \cdots\ \cdots\ \cdots$ ∿$\overset{9.78\ \text{Å}}{\cdots\ \cdots\ \cdots\ \cdots\ \cdots\ \cdots\ \cdots}$ $\cdots\cdots Na^+$	$-\ 31.9$
$PO_4H_2^-$ ∿ $H_2O \cdots Na^+$	$-\ 89.6$
$PO_4H_2^- \cdots H_2O$ ∿ $H_2O \cdots Na^+$	$-\ 67.9$
$PO_4H_2^- \cdots 3H_2O$ ∿ $H_2O \cdots Na^+$	$-\ 61.2$
$PO_4H_2^- \cdots 3H_2O \cdots H_2O$ ∿ $H_2O \cdots H_2O \cdots Na^+$	$-\ 47.9$
$PO_4H_2^- \cdots 3H_2O$ ∿ $H_2O \cdots H_2O \cdots H_2O \cdots Na^+$	$-\ 46.8$

The main energy characteristics of this interaction are described in Table 4. With the basis set used presently, the binding energy of the direct $PO_4H_2^- \cdots Na^+$ association (with Na^+ at the E_{13} site, upon which we shall explore the effect of water) amounts to -120.5 kcal/mole. (The strongest interaction which occurs when the Na^+ occupies the B_{13} position amounts to -154.4 kcal/mole.) The through-water association of Na^+ with the systems $PO_4H_2^- \cdots 3H_2O$ (Na^+ attached to the water molecule placed at E_{13}), $PO_4H_2^- \cdots 3H_2O \cdots H_2O$, $PO_4H_2^- \cdots 3H_2O \cdots (H_2O)_2$ and $PO_4H_2^- \cdots 3H_2O-(H_2O)_3$ vary from -87.9 kcal/mole for the first association to -75.6 kcal/mole for the last one. They are thus very appreciable and decrease relatively slowly with the elongation of the water chain.

It may be interesting to determine in, say, the largest of these systems, $PO_4H_2^- \cdots 3H_2O \cdots (H_2O)_3 \cdots Na^+$, the part in the global interaction energy springing from the distant $PO_4H_2^- \cdots Na^+$ interaction. This may be computed approximately by placing the two unpolarized entities at their distance in the hydrated system ($O_1 \cdots Na^+ = 9.78$ Å) but suppressing the intermediate water molecules. This interaction energy amounts to -31.9 kcal/mole. It represents essentially the electrostatic interaction (for the sake of comparison: the interaction of two unit point charges of opposite signs at the same distance equals -33.9 kcal/mole). In a similar computation, in which the trihydrate $PO_4H_2^- \cdots 3H_2O$ and the monohydrate $Na^+ \cdots H_2O$ are placed at their relative distance ($O \cdots H = 6.37$ Å) in $PO_4H_2^- \cdots 3H_2O \cdots (H_2O)_3 \cdots Na^+$, but the two remaining intermediate water molecules are suppressed, the interaction energy comes out to be -33.4 kcal/mole. Similarly when the complete systems are subdivided differently as in the last five lines of Table 4, appreciable interaction energies are maintained. All these results point to the possibility of Na^+ and $PO_4H_2^-$ interacting through large water intermediate chains.

A particularly interesting problem is that of the preference between direct $PO_4H_2^- \cdots Na^+$ interaction (implying their dehydration) and their "through-water" binding. For dealing with this problem, one must evaluate the associated energy balance. Let us consider three simplified model systems: I, II and III.

I) $PO_4H_2^- + H_2O \cdots Na^+$
The problem consists of evaluating the relative values of the energy changes associated with two possibilities:
a) $PO_4H_2^- \cdots Na^+ + H_2O$ (direct interaction involving the dehydration of Na^+)
or:
b) $PO_4H_2^- \cdots H_2O \cdots Na^+$ (through-water binding).
Process a) is associated with an energy gain of -120 kcal/mole (energy gained by the direct $PO_4H_2^- \cdots Na^+$ interaction) diminished by $+29$ kcal/mole (energy lost upon the dehydration of Na^+), a total gain of -91 kcal/mole.

Process b) is associated with an energy gain of -89.6 kcal/mole (Table IV).

II) $PO_4H_2^- \cdots H_2O + Na^+$
The two possibilities to be considered are in this case the formation of:
a) $PO_4H_2^- \cdots Na^+ + H_2O$
b) $PO_4H_2^- \cdots H_2O \cdots Na^+$

The energy of the first possibility is (energy gained by sodium binding to phosphate diminished by energy loss due to the dehydration of phosphate -120 kcal/mole + 18 kcal/mole = -102 kcal/mole; that of the second possibility -99.6 kcal (Table 4).

III) $PO_4H_2^- \cdots H_2O + H_2O \cdots Na^+$
The two possible products to consider are:
a) $PO_4H_2^- \cdots Na^+ + 2H_2O$
b) $PO_4H_2^- \cdots H_2O \cdots H_2O \cdots Na^+$

The energy balance of the first transformation is -120 kcal/mole + 29 kcal/mole + 18 kcal/mole = -73 kcal/mole. That of the second transformation amounts to -67.9 kcal/mole (Table 4).

In the three examples studied the energy balances of the two types of interaction, a) direct phosphate-cation interaction involving the dehydration of these units, or b) their "through-water" interaction allowing the conservation of their hydration shells, are of the same order of magnitude, indicating the competitivity of the two processes. The small advantage for the direct interaction shown in the computations cannot be considered as significant in view of the approximations involved in the simplified models, in particular in the very fragmentary representation of the hydration shells around $PO_4H_2^-$ and Na^+. Till a further refinement we prefer therefore to consider our results as indicating the approximate equivalence of these two types of interaction, as far as the enthalpies of interaction are concerned, of course.

The charge displacements and perturbations which accompany these through-water interactions are indicated in Fig. 7. It is seen that the direct interaction of Na^+ with $PO_4H_2^-$ in their stable association in which Na^+ occupies the E_{13} site (Fig. 7a) is accompanied by a charge transfer of 0.026 e from $PO_4H_2^-$ to the cation (and an appreciable polarization of the charge of the phosphate). In the through water association in $PO_4H_2^- \cdots 3H_2O \cdots Na^+$ (Fig. 7b) the Na^+ and the H_2O molecule to which it is attached carry both an excess of negative charge, quantitatively close to those carried by these two units when bound individually to H_2O or $PO_4H_2^-$ (respectively Figs. 5a and 3c). All the units attached to the phosphate in the $PO_4H_2^- \cdots 3H_2O \cdots H_2O \cdots Na^+$ chain (Fig. 7c) carry an excess of negative charge although the numerical values of this excess are now substantially reduced in the two intermediate water molecules bridging $PO_4H_2^-$ and Na^+. In the large $PO_4H_2^- \cdots 3H_2O \cdots (H_2O)_3 \cdots Na^+$ complex (Fig. 7d) there is still a net negative charge on the E_{13} water molecule and on the water molecule directly bound to Na^+ (and on Na^+) but the two remaining water molecules of the chain are practically neutral.

These situations are easily understandable if one bears in mind the nature of charge transfers occuring between the adjacent components of the chain, considered pairwise. Thus the charge neutrality of the two intermediate water molecules in the last complex springs naturally from the fact that they act both as proton donors and proton acceptors for H-bonding with the water molecules on their two sides. The relatively high net negative charge (-0.022 e) on the E_{13} water molecule is the result of charge acceptance from the phosphate anion ($\simeq -0.040$ e) and its charge donation, as a proton acceptor to the next water molecule ($\simeq +0.020$ e). The smaller net negative charge of the water molecule bound to Na^+ is due to its behavior as a proton donor with respect to the adjacent water molecule ($\simeq -0.020$ e) and to its interaction with Na$^+$ which provides it with a defect of about $+0.010$ e.

The charge transfers are thus interpretable to a large extent in terms of local electron

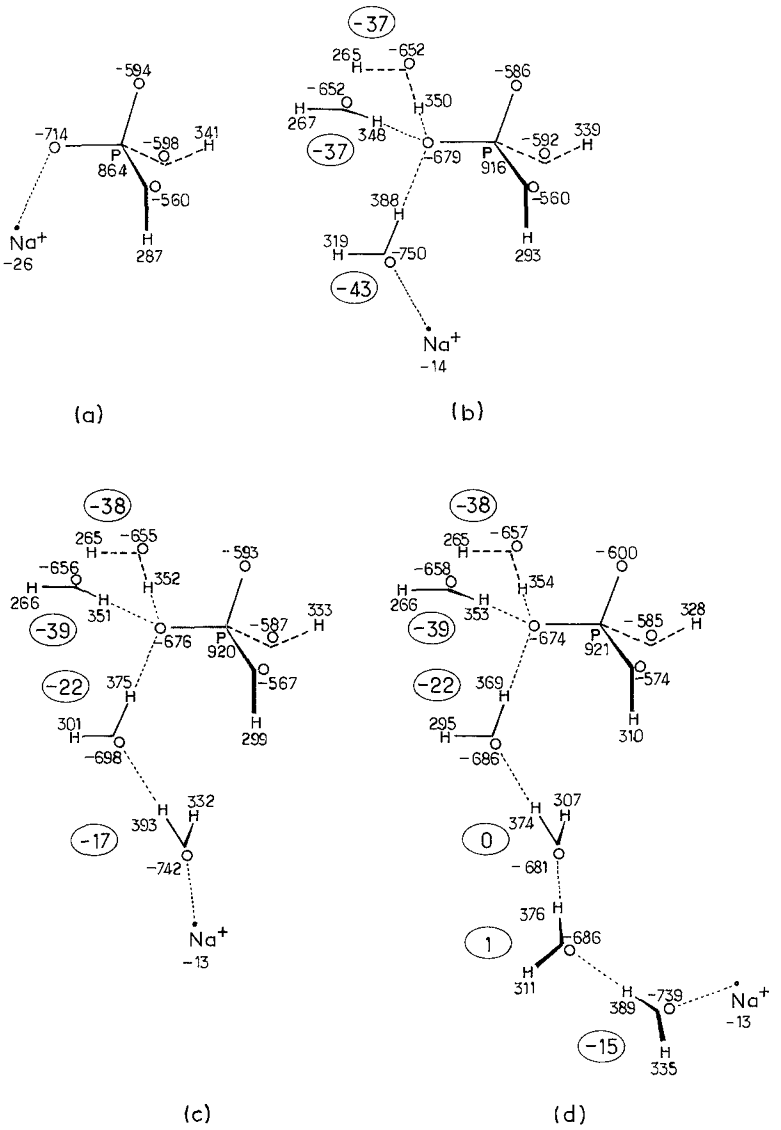


Fig. 7. Distribution of net electronic charges. Numbers in circles indicate charge transfers. (In milli-electron units.)

(a) $PO_4H_2^- \cdots Na^+$ adduct. Cation at E_{13} site.

(b) $PO_4H_2^- \cdots 3H_2O \cdots Na^+$ (the cation attached to the water molecule at the E_{13} site).

(c) $PO_4H_2^- \cdots 3H_2O \cdots H_2O \cdots Na^+$.

(d) $PO_4H_2^- \cdots 3H_2O \cdots H_2O \cdots H_2O \cdots H_2O \cdots Na^+$.

transfers between adjacent units in the chain, only moderately perturbed by the interaction among more distant units. An explicit computation shows that at the distance $O_1 \cdots Na^+$ of 9.78Å which is that between $PO_4H_2^-$ and Na^+ in $PO_4H_2^- \cdots (3H_2O) \cdots (H_2O)_3 \cdots Na^+$ there is no direct charge transfer whatsoever between the two ions. This situation does not prevent a strong interaction to exist between these distant subunits. Computed between the non-perturbed $PO_4H_2^-$ and Na^+ entities in the appropriate relative position, it amounts to −31.9 kcal/mole (Table 4).

Here again the global quasineutrality of the two central water molecules does not prevent them being appreciably polarized (Fig. 7d) with respect to an isolated water molecule (Fig. 3a), or an isolated dimer (Fig. 4a).

The charge displacements within each unit of the chain, as a result of their mutual polarization are again interpretable easily and satisfactorily by the consideration of the effects associated with the bound units.

The comparison of the isolated water tetramer (Fig. 4c) with the same tetramer bound at one end to the anion (Fig. 3f) or to the cation (Fig. 5d) and at both ends simultaneously (Fig. 7d) indicates an enhancement of the polarization when both ions are present: compare for instance the charges at the $O \cdots H$ atoms in the central hydrogen bond which pass from −0.662 e, +0.359 e in the free tetramer to −0.672 e, +0.365 e and −0.671 e, +0.371 e in the anion-bound and cation-bound chains respectively, and to −0.681 e, +0.376 e in the anion–chain–cation adduct. This should correspond to a gradual tightening of the water–water intermediate interaction.

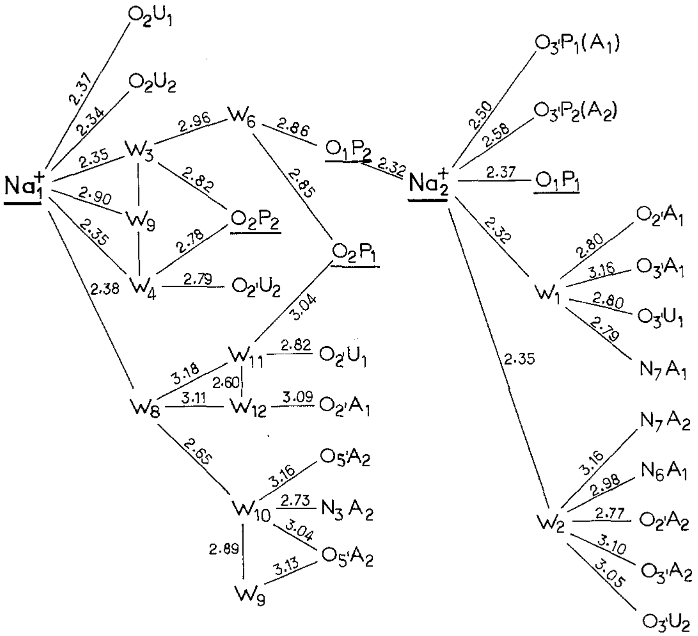


Fig. 8. A part of the interactions between water, Na^+ ions and ApU in the crystal structure of sodium ApU hexahydrate (based on Ref. [22])

4. Conclusion

The principal result of this investigation is to demonstrate that the enthalpy balances of the two types of interaction: direct phosphate–Na^+ binding involving their dehydration or their through-water binding allowing them the conservation of their hydration shells are of the same order of magnitude, indicating the competitivity of the two processes. This situation which results from the existence of appreciable energies of interaction between the different possible subsystems points to the multiplicity of possibilities capable of existing in a phosphate–Na^+–water system. Fig. 8, illustrating a part of such interactions observed in the crystal structure of sodium adenylyl-3′, 5′-uridine hexahydrate (ApU) [22] substantiates their diversified reality.

A significant result is also the demonstration that charge transfers between the different components of the phosphate–Na^+–water system are interpretable essentially in terms of displacements between adjacent units of the system. On the other hand, the polarization effect upon the electronic distributions extends over longer distances. It extends further for Na^+ than for $PO_4H_2^-$ and attains its maximum when the two units are present at opposite ends of the system so as to be able to reinforce each other's effect.

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