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The Effect of Screening the Electrostatic Potentials of Reactive Sites Within B-DNA by Metal Cations

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The effect of screening the backbone phosphates by Mg^{2+} ions, in various ways, on the negative electrostatic potential minima associated with the nucleic acid bases in B-DNA is investigated. The results are compared to screening by Na^+ ions and to the corresponding potential minima in unscreened B-DNA.

Key words: Screening of DNA – Magnesium ions – Electrostatic potential.

In a recent publication from this laboratory [1] we have presented calculations of the electrostatic potential minima at sites of the nucleic acid bases, susceptible to electrophilic attack, within a model of B-DNA consisting of one full helical turn of this biopolymer. Subsequently, we have also described the effect on these potential minima of screening the phosphates in the B-DNA backbone by two different cations, NA^+ and $CH_3NH_3^+$ [2].

In the present note we extend these studies on countercation screening to include a divalent cation, Mg^{2+}, bound to the phosphates of the double helix in various ways.

Our studies of Na^+ screening involved a complete neutralisation of the net charge of our B-DNA model, which is to say that one naked sodium ion was directly bound to each phosphate group of the backbone. To obtain a similar neutralisation with the divalent Mg^{2+} ions it is only necessary to bind one such ion to every second phosphate group and this may be done in two ways: configuration (I), in which the screened phosphates in the two backbones are "staggered" (Fig. 1*a*); configuration (II), in which the screened phosphates in the two backbones are "in step" (Fig. 1*b*). It will be noted that in this latter case an exact

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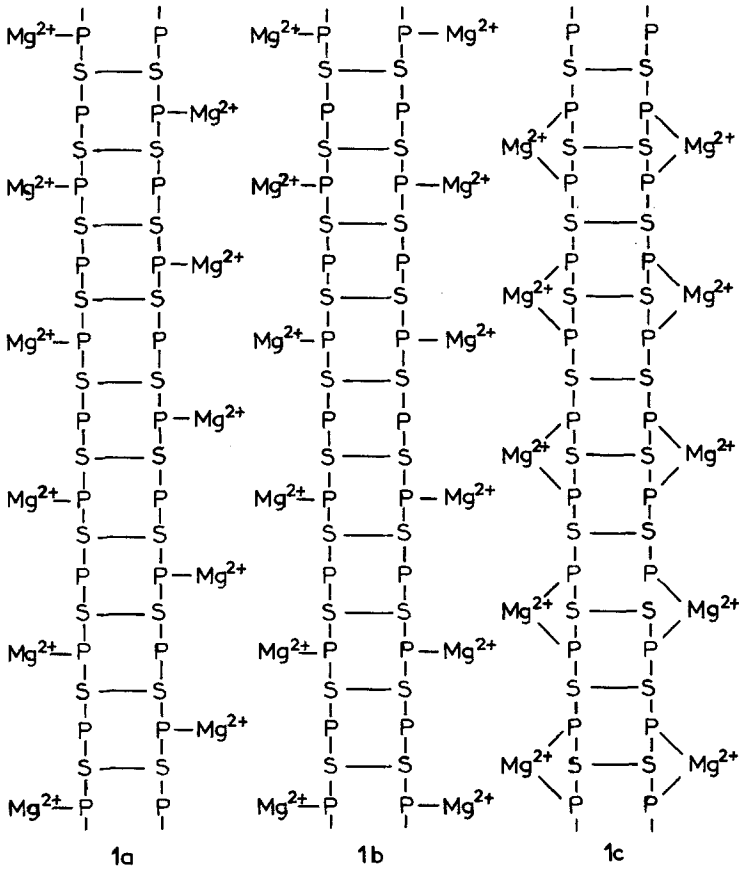

Fig. 1. Schematic diagrams representing the configurations of Mg^{2+} ions screening B-DNA

neutralisation of charge is not possible for the nucleic acid section of 22 phosphate that we have studied and the screened nucleic acid section has a net charge of +2. The position of Mg^{2+} in these cases was between the two anionic oxygens of the phosphate group, in the OPO^- plane with two identical bonds Mg^{2+}–O of 1.95 Å [3]. We have, in addition, studied the screening by Mg^{2+} in a position, with respect to a phosphate group, that could be adopted by this ion surrounded by its first hydration shell of six, octahedrally positioned water molecules. When bound through-water to a single phosphate group this position is again in the OPO^- plane with two symmetric Mg^{2+}–O distances of 3.78 Å [4]. In this case, the configuration of Mg^{2+}'s bound to the B-DNA segment was taken to be as in Fig. 1*a*. A second possibility was also considered where the hydrated Mg^{2+} ion is bound to two consecutive phosphate groups with through-water bonds to one anionic oxygen of each phosphate, yielding two symmetric Mg^{2+}–O distances of 3.78 Å, as for the single phosphate binding described above. The configuration of this scheme of screening, termed (III), is shown in Fig. 1*c*. Note that for this scheme the screened 22 phosphate segment of B-DNA again carries a net charge, −2.

Table 1. The potential minima at nucleic acid bases (kcal/mole)

Site	Nucleotides	B-DNA unscreened	B-DNA screened by Na^+	B-DNA screened by Mg^{2+} configuration (I)	B-DNA screened by Mg^{2+} configuration (II)	B-DNA screened by Mg^{2+} "hydrated" configuration (I)	B-DNA screened by Mg^{2+} "hydrated" configuration (III)
N7(G)	−147 (1)	−683 (1)	−157 (1)	−154 (1)	−120 (1)	−201 (3)	−204 (1)
N3(G)	−108 (7)	−677 (2)	−154 (2)	−147 (2)	−113 (3)	−205 (1)	−203 (2)
N3(A)	−114 (5)	−676 (3)	−153 (3)	−145 (3)	−114 (2)	−204 (2)	−201 (3)
O2(T)	−110 (6)	−663 (4)	−148 (4)	−138 (4)	−101 (4)	−194 (4)	−196 (4)
O6(G)	−115 (4)	−654 (5)	−134 (5)	−128 (5)	−96 (5)	−172 (6)	−178 (6)
N7(A)	−127 (2)	−650 (6)	−123 (7)	−122 (6)	−88 (7)	−168 (7)	−171 (7)
O2(C)	−123 (3)	−645 (7)	−129 (6)	−120 (7)	−95 (6)	−177 (5)	−180 (5)
C8(G)5′	−73 (9)	−630 (8)	−110 (9)	−107 (8)	−73 (8)	−161 (8)	−160 (8)
C8(G)3′	−68 (13)	−623 (9)	−109 (10)	−99 (11)	−64 (11)	−149 (11)	−141 (11)
N2(G)3′	−29 (22)	−623 (10)	−116 (8)	−101 (10)	−70 (10)	−155 (10)	−158 (9)
N2(G)5′	−32 (21)	−623 (11)	−108 (11)	−104 (9)	−73 (9)	−158 (9)	−157 (10)
O4(T)	−97 (8)	−612 (12)	−90 (12)	−88 (12)	−55 (12)	−125 (13)	−134 (13)
C8(A)5′	−69 (12)	−610 (13)	−88 (13)	−86 (13)	−55 (13)	−142 (12)	−141 (12)
N4(C)3′	−51 (19)	−602 (14)	−81 (15)	−78 (14)	−47 (14)	−119 (17)	−130 (14)
N6(A)5′	−52 (18)	−600 (15)	−80 (16)	−75 (16)	−43 (16)	−121 (15)	−127 (15)
N6(A)3′	−51 (20)	−598 (16)	−81 (14)	−76 (15)	−44 (15)	−121 (14)	−124 (16)
C8(A)3′	−60 (16)	−597 (17)	−79 (17)	−71 (17)	−35 (18)	−120 (16)	−114 (19)
N4(C)5′	−53 (17)	−593 (18)	−57 (18)	−70 (18)	−40 (17)	−116 (19)	−120 (17)
C5–C6(T)3′	−69 (11)	−592 (19)	−71 (19)	−66 (19)	−27 (19)	−118 (18)	−117 (18)
C5–C6(C)5′	−71 (10)	−584 (20)	−65 (20)	−60 (20)	−22 (20)	−112 (20)	−112 (20)
C5–C6(T)5′	−61 (15)	−584 (21)	−53 (21)	−48 (21)	−11 (21)	−93 (21)	−98 (21)
C5–C6(C)3′	−64 (14)	−569 (22)	−40 (22)	−37 (22)	+1 (22)	−82 (22)	−88 (22)

We remark that in both screenings by the "hydrated" Mg^{2+} ions the potentials of the water molecules of hydration, very weak in comparison to the potentials of the ions, are not included in the present calculations.

The results for these various Mg^{2+} screenings are presented in Table 1 with, for comparison, the corresponding potential minima for the free nucleotides [1], unscreened B-DNA [1] and B-DNA screened by Na^+ [2]. The minima for guanine and cytosine were calculated for the central base pair in a repetitive sequence GC and those for adenine and thymine for the central base pair in a repetitive sequence AT. All values are given in kcal/mole. After each column of Table 1 the numbers in parentheses denote the order of decreasingly negative potentials. From table 1 several conclusions can be drawn:

(1) A large overall increase in potential and a considerable reordering of the base sites occur between the potential minima corresponding to the free nucleotides and those of the 22 phosphate segment of B-DNA. These changes have already been discussed in our previous publications ([1] and references contained therein).

(2) For the proposed Na^+ and Mg^{2+} screenings, the potential minima are rather similar. much smaller than those for free B-DNA but, nevertheless, more negative, in many cases, than those for the free nucleotides. The principal exception to this observation being the less negative minima for the helix screened by Mg^{2+} in configuration (II), when the segment studied carries a net positive charge, +2, as previously described.

(3) Comparing the *ordering* of the potential minima resulting from unscreened B-DNA or Na^+ screened B-DNA with those for the various Mg^{2+} screenings there is surprisingly little change. For all screenings, N7(G), N3(G) and N3(A) are associated with the deepest minima and moreover when their order is changed from that in B-DNA, for naked Mg^{2+}'s in configuration (II) or hydrated Mg^{2+}'s in configuration (I), there are only a few kcal/mole separating the interchanged sites. For the weaker sites of Table 1 there are again only very few reorderings most of which involve interchanges of no more than one or two places in the ordering scheme.

We thus conclude that, at least for screening of B-DNA involving direct or through-water binding of cations to the phosphate groups, the principal effect is an overall linear shift of the potential minima at the bases with little internal reordering. Further, that even for "saturated" countercation screening the base potentials generally remain more attractive to electrophiles than for free nucleotides.

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