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2038-28

Conference: From DNA-Inspired Physics to Physics-Inspired Biology

1 - 5 June 2009

Mediating Role of Alkaline Earth Metal Ions in Electrostatics of DNA: the Long-Range Effects of Solvent Dielectric Saturation

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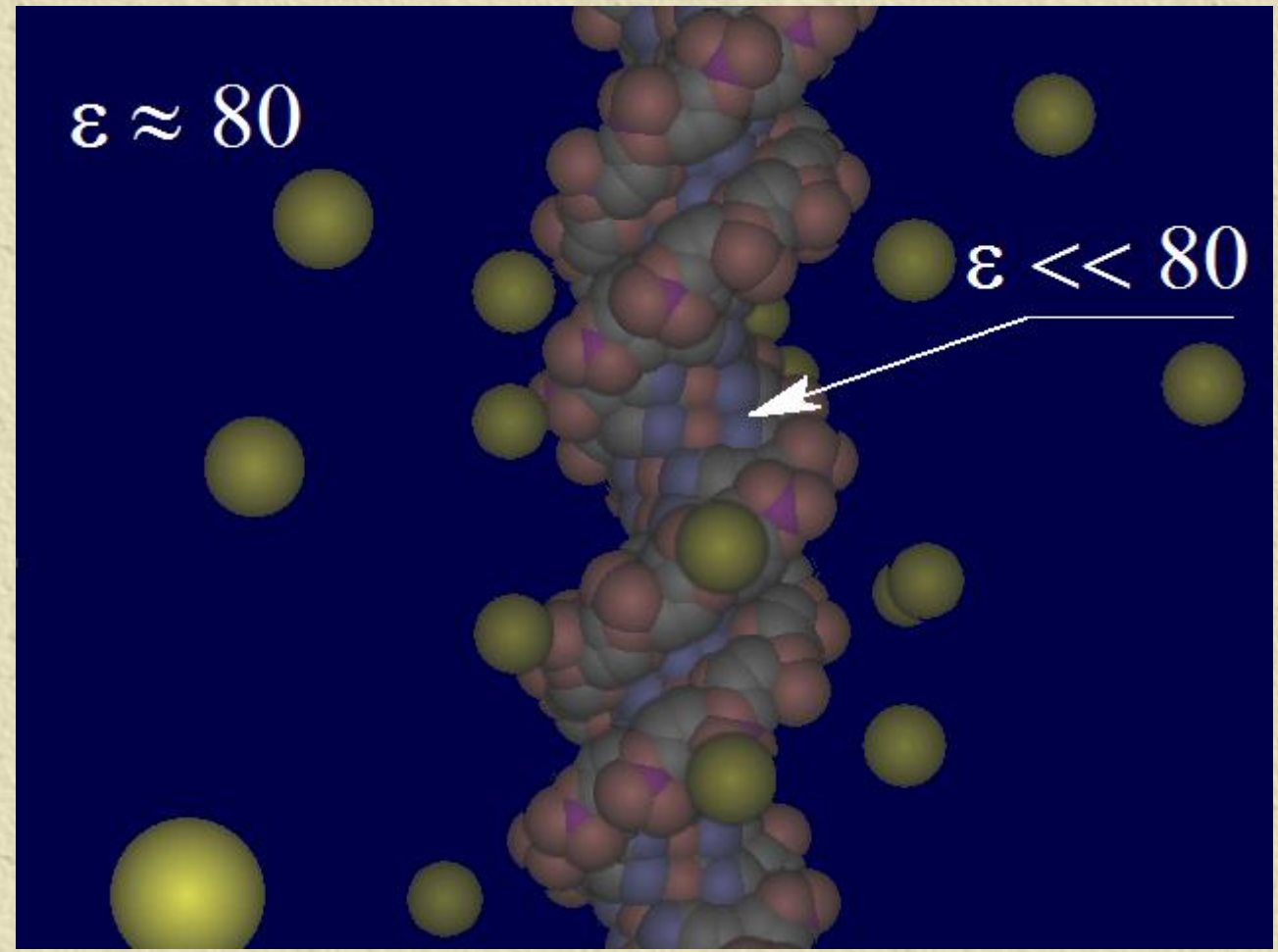
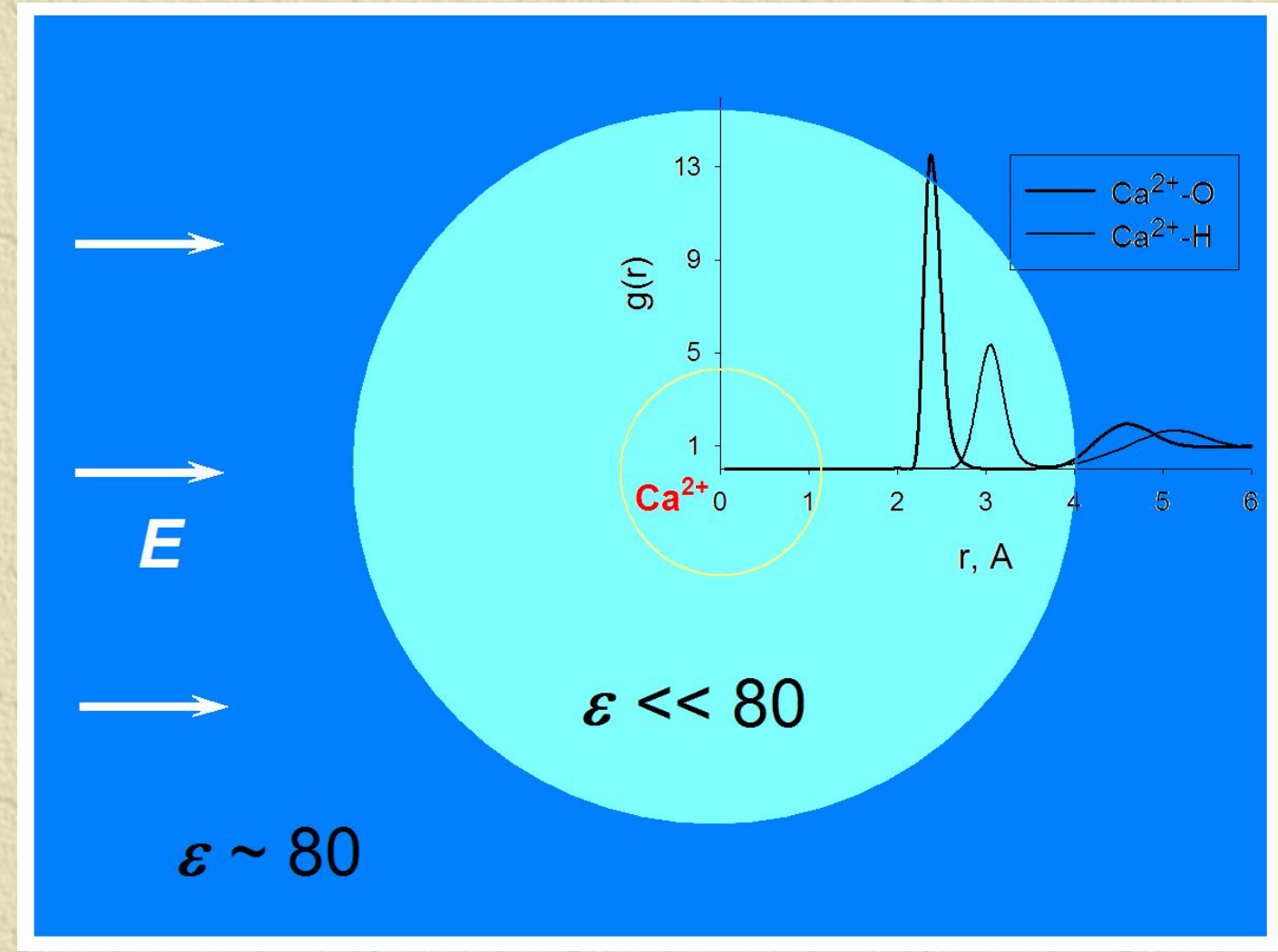
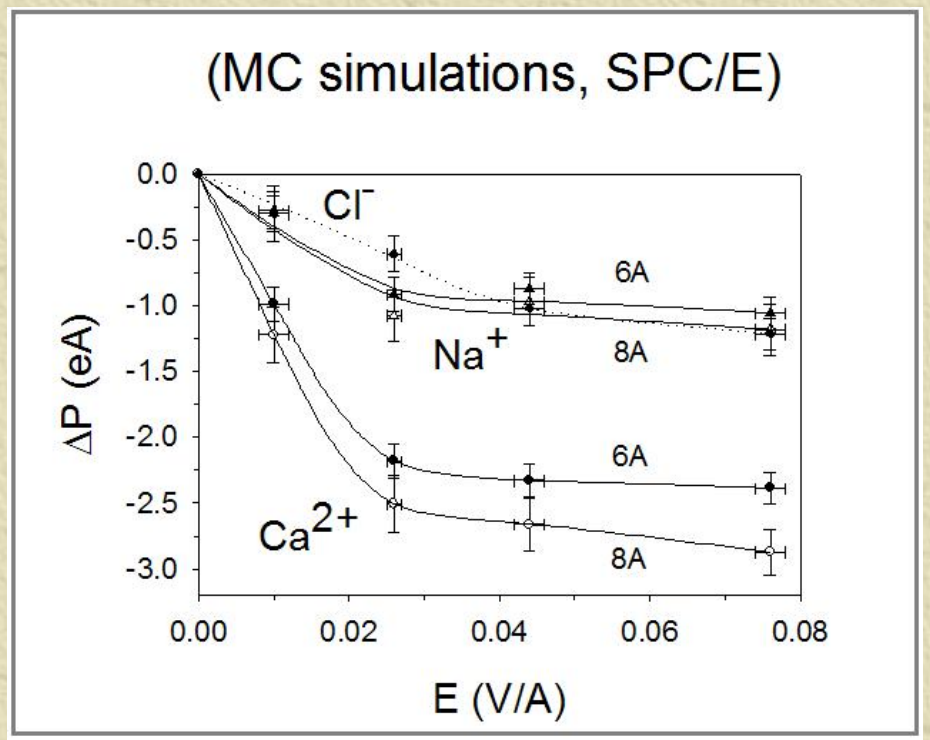
Role of Dielectric Effects near the Polyanion

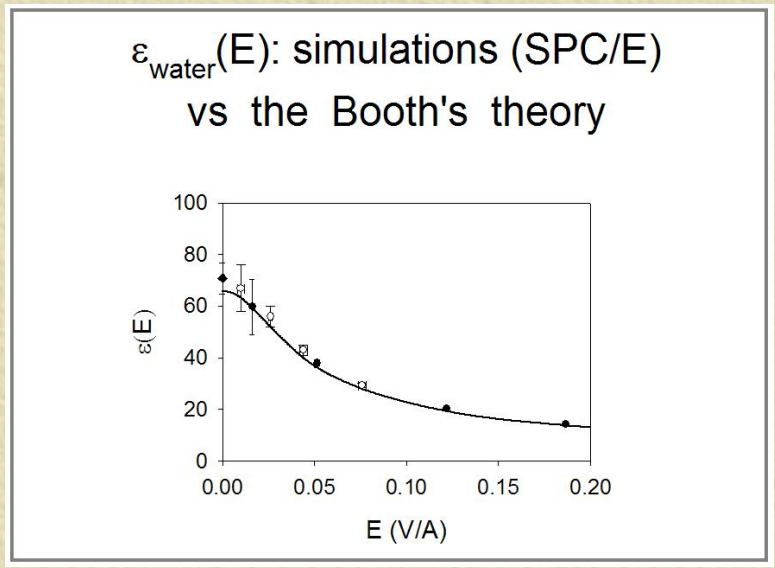


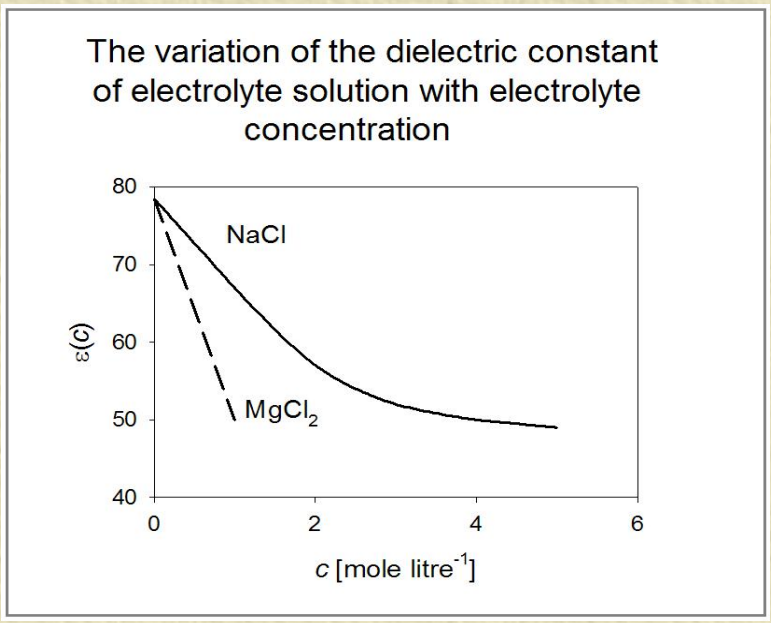
Approximate Dielectric Model of a Hydrated Cation in the External field



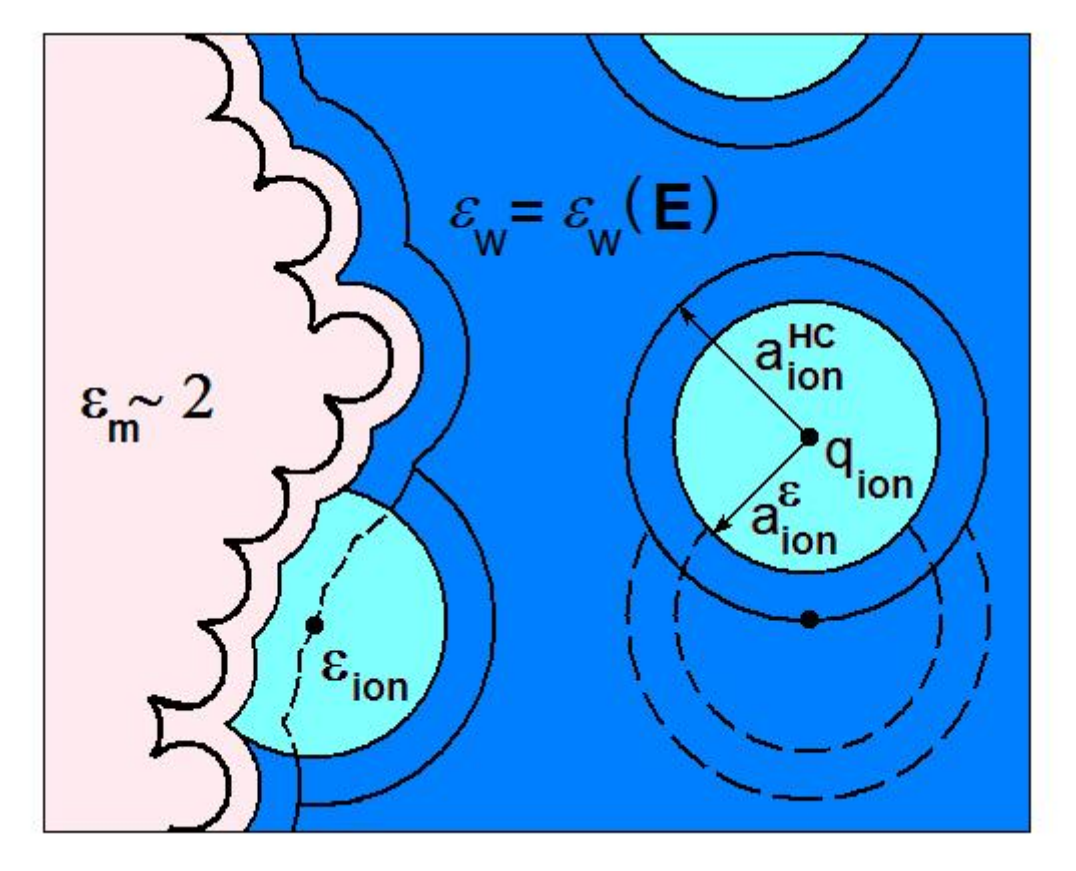
Polarization Deficiency of the Ion Hydration Shell in the External Field





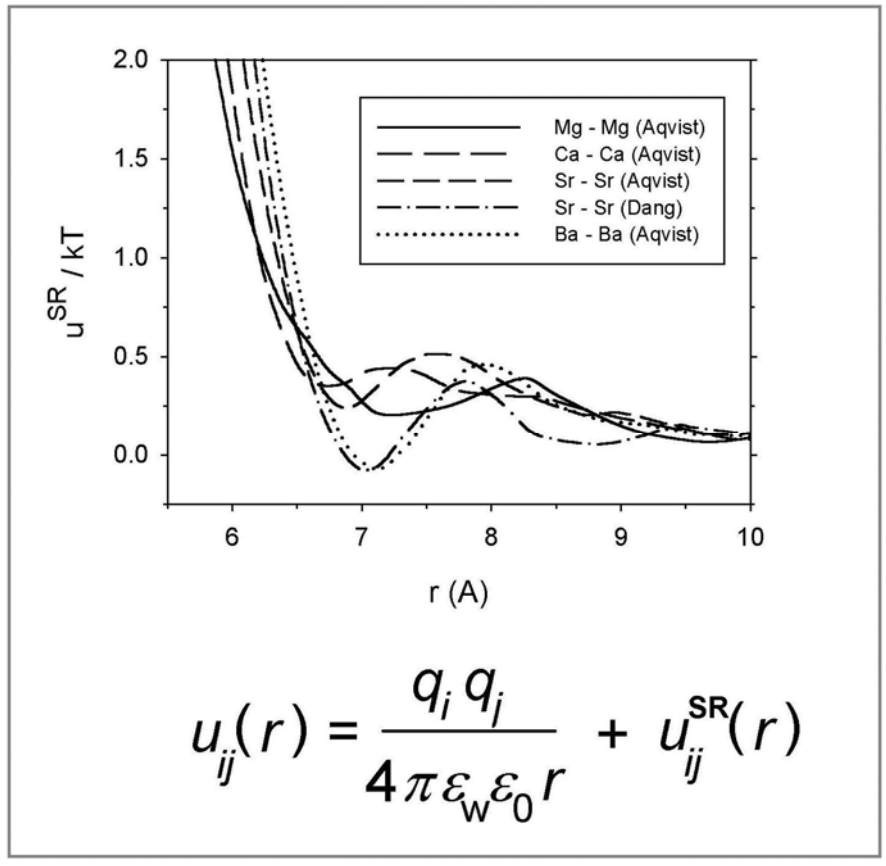


Implicit Solvent Model of Hydrated Ions – the Primitive Polarization Model (PPM)

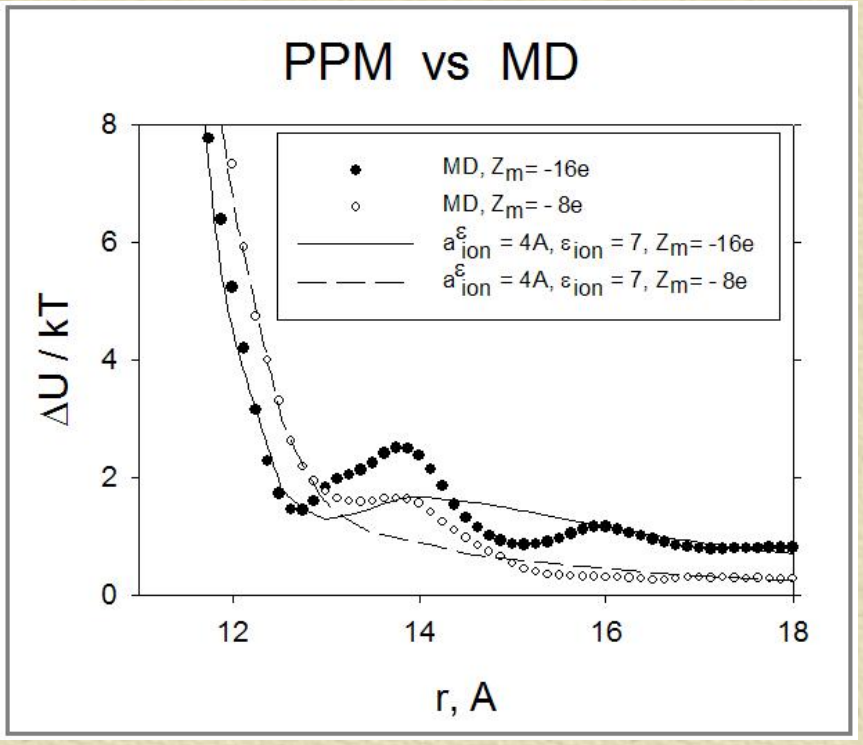


Ion	a_i^{ε}/Å	ε_i	a_i^{HC}/Å
Na^+	3.8	25	4.5
Ca^{2+}	4.0	7	6.0
Mg^{2+}	4.1	7	6.0

Implicit Solvent Model of Hydrated Ions – the Primitive Polarization Model (PPM)



$$u_{ij}(r) = \frac{q_i q_j}{4\pi\varepsilon_w\varepsilon_0 r} + u_{ij}^{SR}(r)$$



Implicit-Solvent Calculations of Ionic Distributions and Free Energy

Calculations	Ion PMF	Ion Model
Poisson-Boltzmann (PB)	mean field	point-like ions
modified PB (MPB), HNC, MC	mean field + interionic correlations + finite ion size	primitive model (PM)
ε–MPB	mean field + interionic correlations + finite ion size + ion hydration shell polarization	PPM

ε-MPB Equations

PB

$$\ln g_i(\mathbf{r}) \approx -\beta q_i \psi(\mathbf{r}) \quad , \qquad (1)$$

where

$$n_i(\mathbf{r}) = g_i(\mathbf{r}) n_i^0$$

and

$$\nabla(\varepsilon(\mathbf{r})\nabla\psi(\mathbf{r})) = \begin{cases} -\sum n_k(\mathbf{r}) q_k / \varepsilon_0, & \text{outside} \\ -\rho_{\mathrm{m}}(\mathbf{r}) / \varepsilon_0, & \text{inside} \end{cases} , \qquad (2)$$

$$\varepsilon(\mathbf{r}) = \begin{cases} \varepsilon_{\mathrm{W}}, & \text{outside} \\ \varepsilon_{\mathrm{m}}, & \text{inside} \end{cases}$$

ε-MPB Equations

ε-MPB

$$\ln g_i(\mathbf{r}) \approx \sum_k \left(\frac{4}{3}\pi (a_{ik}^{\mathrm{HC}})^3 n_k^0 - \int_{|\mathbf{r}'-\mathbf{r}|<a_{ik}^{\mathrm{HC}}} n_k(\mathbf{r}')d\mathbf{r}' \right) - \frac{\beta}{2}\int_{\text{inside}} \rho_m(\mathbf{r}')\phi_i^0(\mathbf{r},\mathbf{r}')d\mathbf{r}' \quad (1)$$

where $\beta \frac{q_i}{2}\left(\eta_i(\mathbf{r}) - \eta_i(\infty)\right) - \beta q_i\left(\tilde{\psi}(\mathbf{r}) + \phi_i^0(\mathbf{r},\mathbf{r})\right)$

$$\nabla(\varepsilon(\mathbf{r})\nabla\tilde{\psi}(\mathbf{r})) = \begin{cases} -\sum n_k(\mathbf{r})q_k / \varepsilon_0, & \text{outside} \\ -\rho_{\mathrm{m}}(\mathbf{r}) / \varepsilon_0, & \text{inside} \end{cases} \quad (2)$$

$$\varepsilon(\mathbf{r}) \approx \frac{(1-\sum p_j(\mathbf{r}))\varepsilon_{\mathrm{W}} + \sum \zeta_j p_j(\mathbf{r})\varepsilon_j}{(1-\sum p_j(\mathbf{r})) + \sum \zeta_j p_j(\mathbf{r})},$$

$$\zeta_j = \frac{3\varepsilon_{\mathrm{W}}}{2\varepsilon_{\mathrm{W}} + \varepsilon_j}, \qquad p_j(\mathbf{r}) = \int_{|\mathbf{r}-\mathbf{r}'|<a_j^{\varepsilon}} n_j(\mathbf{r}')d\mathbf{r}', \qquad \varepsilon_{\mathrm{W}} \approx \varepsilon_{\mathrm{Booth}}(|\nabla\tilde{\psi}(\mathbf{r})|)$$

ε-MPB Equations

fluctuation potential

$$\eta_i(\mathbf{r}_1) = \lim_{\mathbf{r}_2 \to \mathbf{r}_1} [\phi_i^{\delta}(\mathbf{r}_1, \mathbf{r}_2) - \frac{q_i}{4\pi\varepsilon_0 \varepsilon_i r_{12}}] \quad ,$$

$$\begin{cases} \nabla(\varepsilon(\mathbf{r})\nabla\phi_i^{\delta}(\mathbf{r}_1,\mathbf{r})) - \kappa_i^2(\mathbf{r}_1,\mathbf{r})\phi_i^{\delta}(\mathbf{r}_1,\mathbf{r}) = 0, & |\mathbf{r}-\mathbf{r}_1| > \min\limits_k a_{ik}^{\mathrm{HC}} \text{ or inside} \\ \nabla(\varepsilon_i(\mathbf{r}_1,\mathbf{r})\nabla\phi_i^{\delta}(\mathbf{r}_1,\mathbf{r})) = -q_i\delta^3(\mathbf{r}-\mathbf{r}_1)/\varepsilon_0, & |\mathbf{r}-\mathbf{r}_1| < \min\limits_k a_{ik}^{\mathrm{HC}}, \text{ outside} \end{cases} , \qquad (3)$$

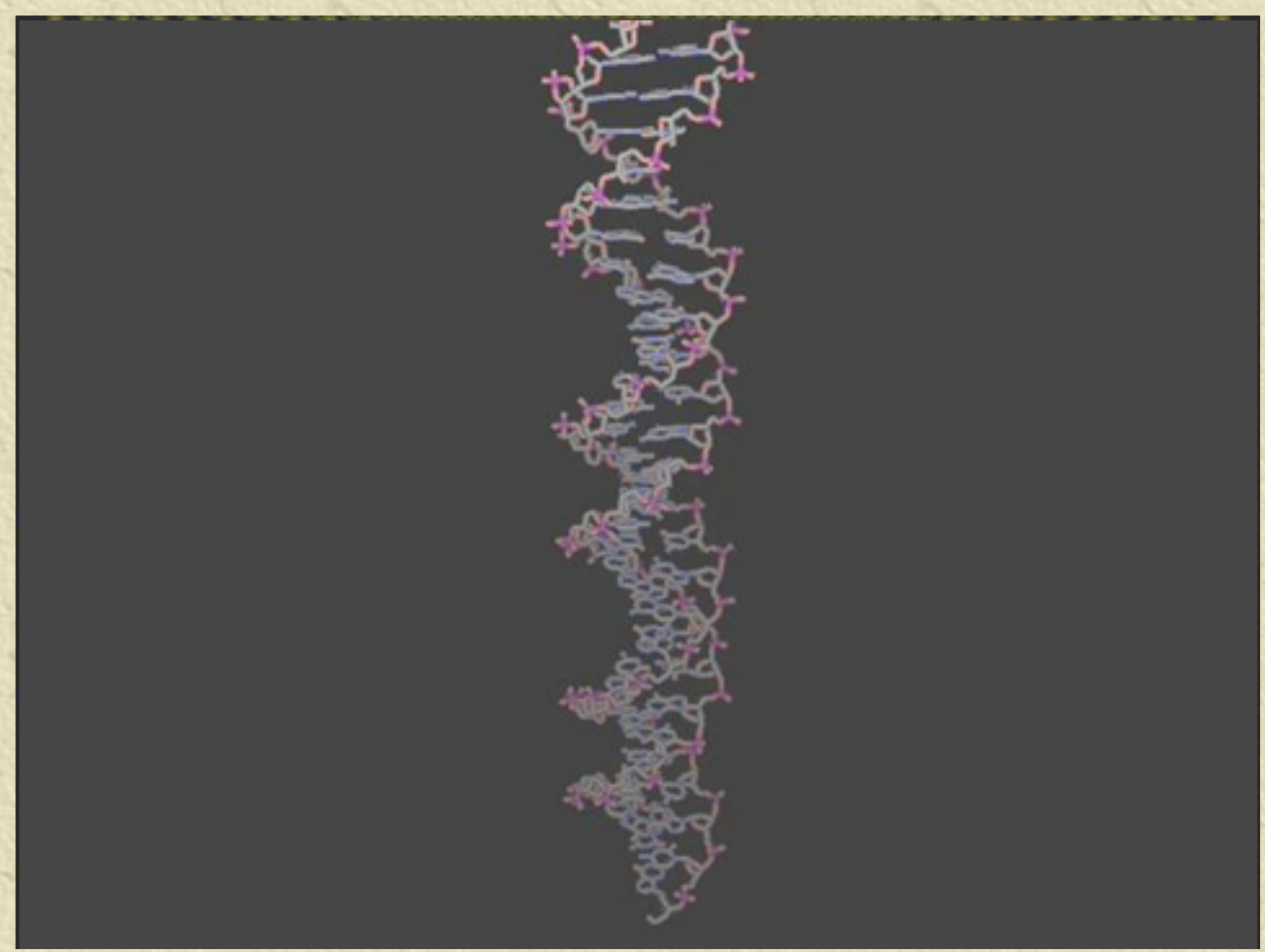
$$\begin{cases} \nabla(\varepsilon(\mathbf{r})\nabla\phi_i^{0}(\mathbf{r}_1,\mathbf{r})) - \kappa_i^2(\mathbf{r}_1,\mathbf{r})\phi_i^{0}(\mathbf{r}_1,\mathbf{r}) = \sum(1-s_{ik}(\mathbf{r}_1,\mathbf{r}))n_k(\mathbf{r})q_k/\varepsilon_0, \\ \qquad\qquad |\mathbf{r}-\mathbf{r}_1| > \min\limits_k a_{ik}^{\mathrm{HC}} \text{ or inside} \\ \nabla(\varepsilon_i(\mathbf{r}_1,\mathbf{r})\nabla\phi_i^{0}(\mathbf{r}_1,\mathbf{r})) = -\nabla(\varepsilon_i(\mathbf{r}_1,\mathbf{r})\nabla\tilde{\psi}(\mathbf{r})), \\ \qquad\qquad |\mathbf{r}-\mathbf{r}_1| < \min\limits_k a_{ik}^{\mathrm{HC}}, \text{ outside} \end{cases} , \qquad (4)$$

where

$$\varepsilon_i(\mathbf{r}_1,\mathbf{r}) \approx \begin{cases} \varepsilon_i, & |\mathbf{r}-\mathbf{r}_1| < a_i^{\varepsilon} \\ \varepsilon(\mathbf{r}), & |\mathbf{r}-\mathbf{r}_1| > a_i^{\varepsilon} \end{cases} , \qquad \kappa_i^2(\mathbf{r}_1,\mathbf{r}) = \beta\sum s_{ik}(\mathbf{r}_1,\mathbf{r})n_k(\mathbf{r})q_k^2/\varepsilon_0 \quad ,$$

$$s_{ik}(\mathbf{r}_1,\mathbf{r}) \approx \begin{cases} 0, & |\mathbf{r}-\mathbf{r}_1| < a_{ik}^{\mathrm{HC}} \\ 1, & |\mathbf{r}-\mathbf{r}_1| > a_{ik}^{\mathrm{HC}} \end{cases}$$

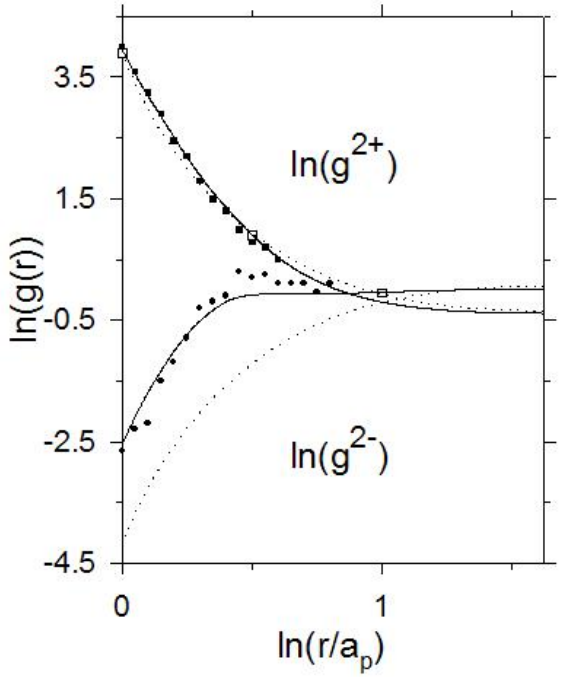
Centers of the Fluctuation Potential Calculations



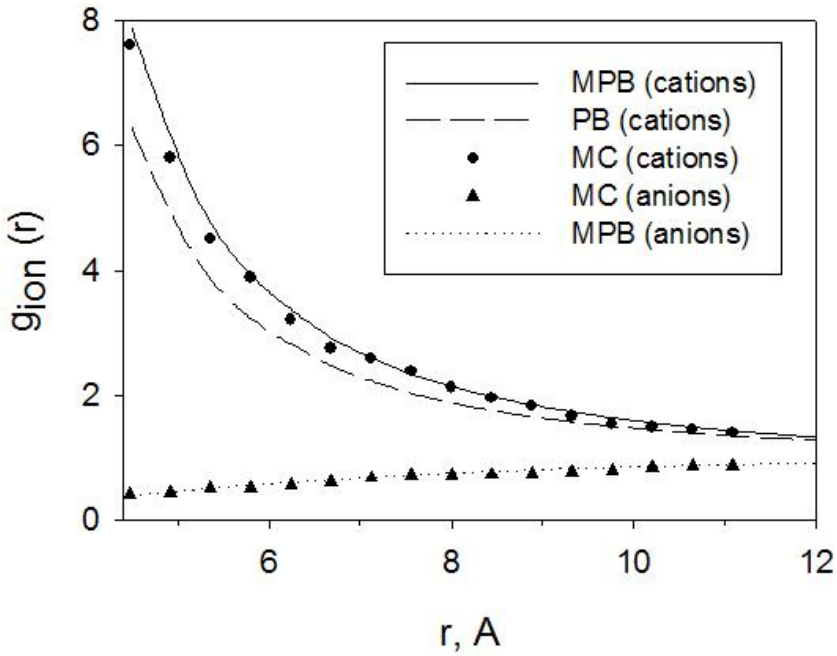
movie

PM Ions: Comparisons between MPB and MC Results

2:2 PM electrolyte around a cylindrical model of DNA, a^{HC}=4A, c=0.05 M, R_{cell}= 65 A,
MC results from J. Phys. Chem. 99, 410 (1995)



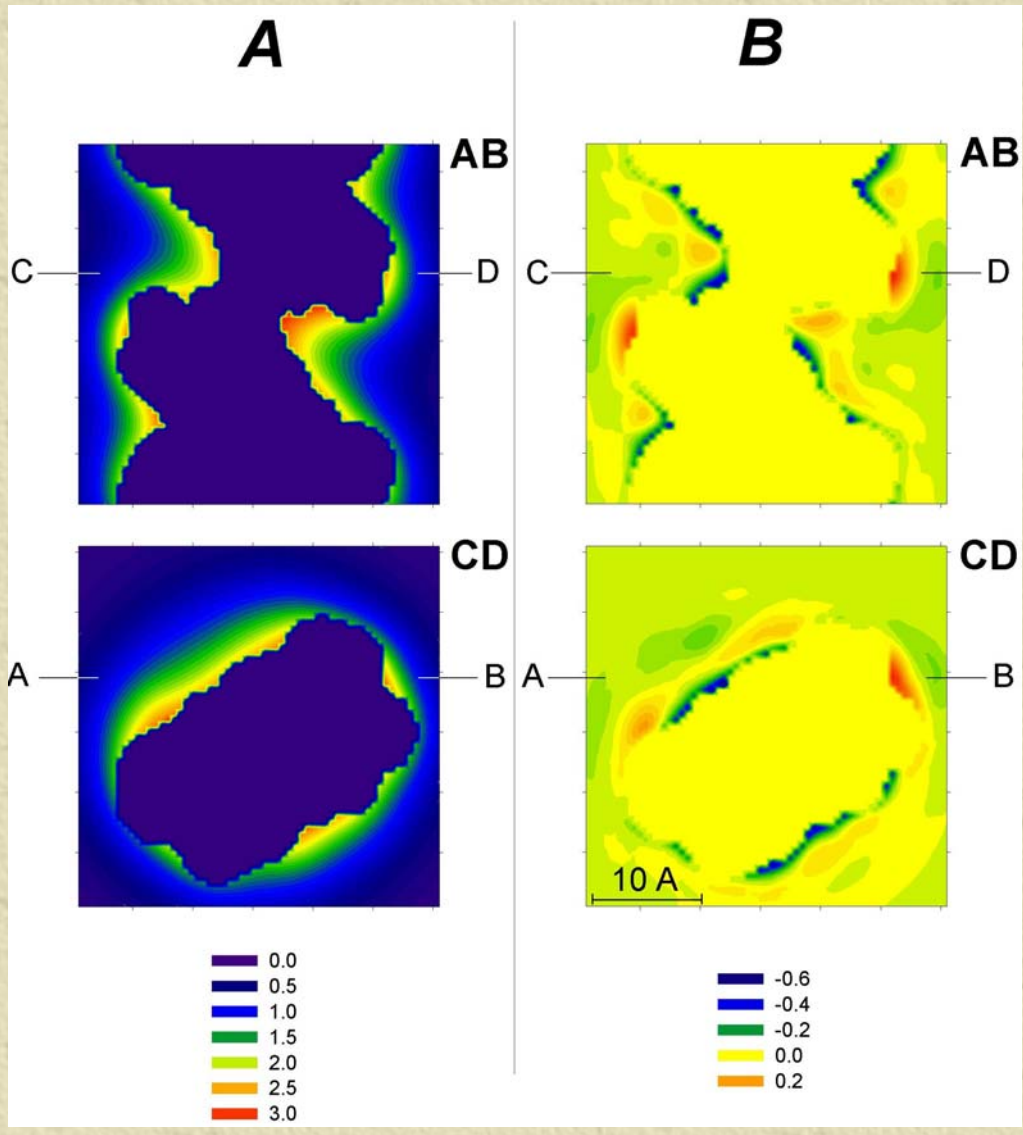
Bulk 2:1 PM electrolyte, c = 0.05 M, a^{HC} = 4.2 A, distributions around anion (-1e), MC simulations from J. Comp. Chem. 19, 893 (1998)



ε–MPB Distribution of Na^+ around B-DNA, c_{NaCl} = 0.5 M

$A - \ln g^{PB}{}_{Na}(\mathbf{r})$

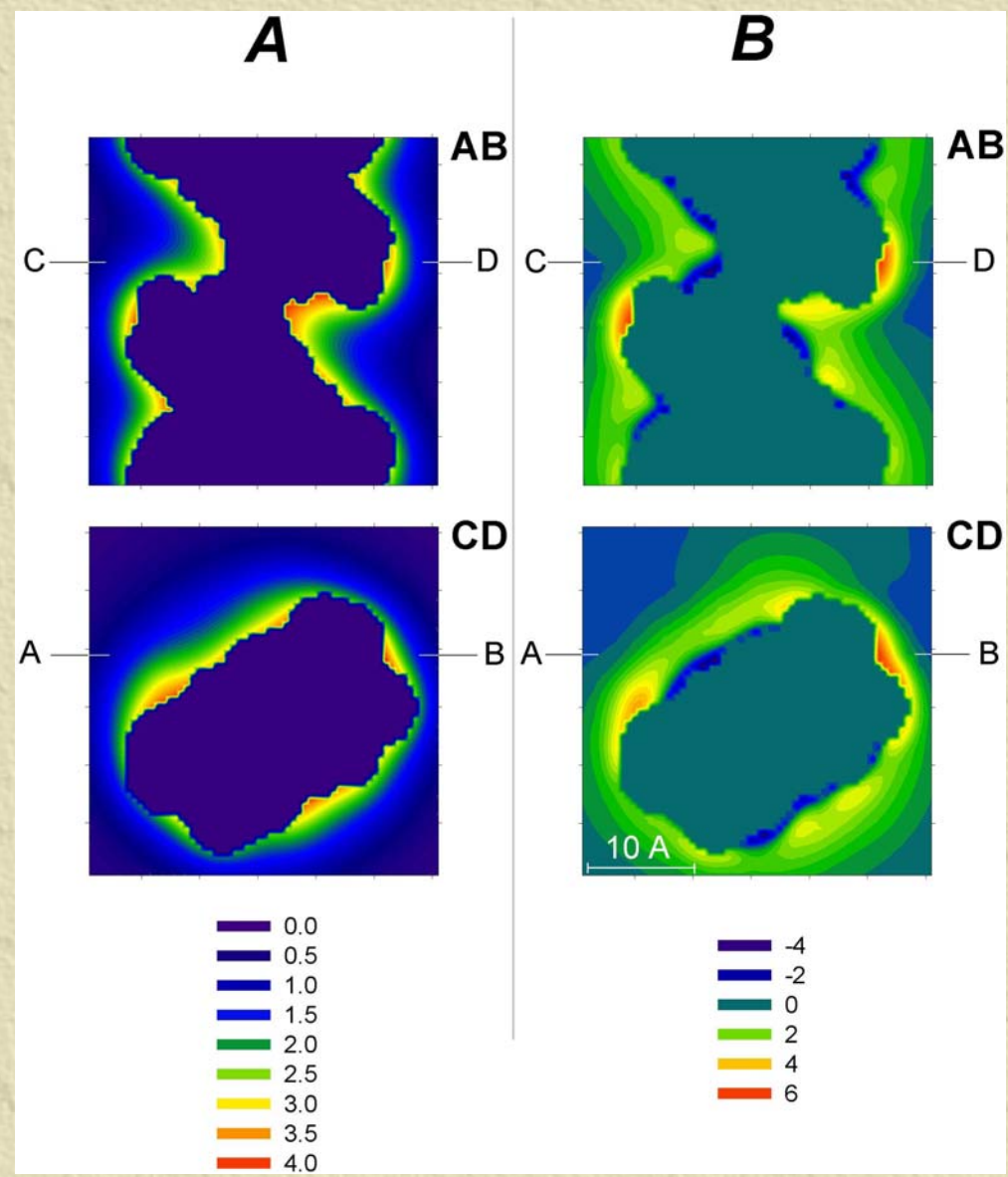
$B - (\ln g^{\varepsilon\text{–}MPB}{}_{Na}(\mathbf{r}) - \ln g^{PB}{}_{Na}(\mathbf{r}))$



ε–MPB Distribution of Ca^{2+} around B-DNA, c_{CaCl2} = 0.167 M

$A - \ln g^{PB}_{Ca}(\mathbf{r})$

$B - \ln g^{\varepsilon-MPB}_{Ca}(\mathbf{r})$

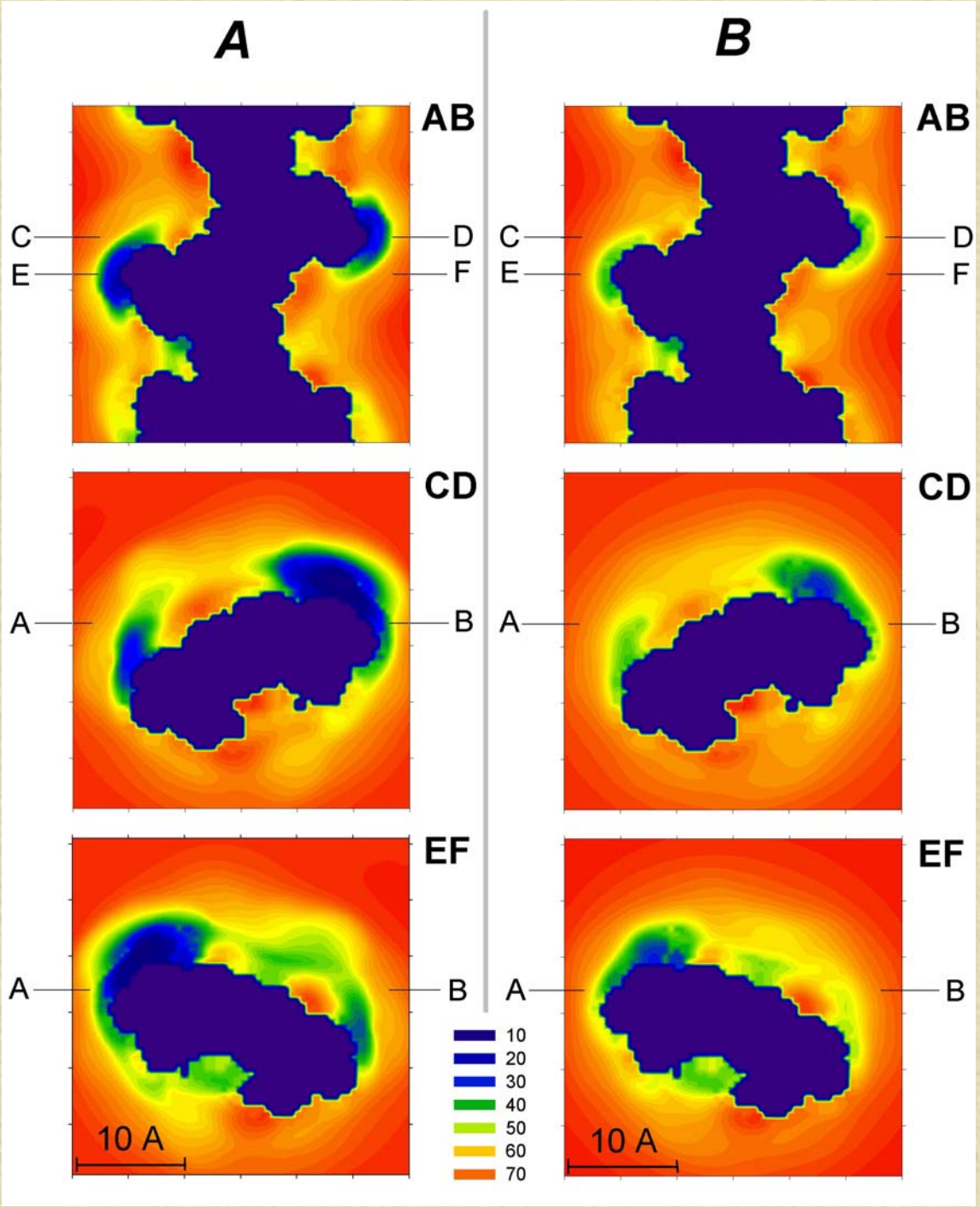


Mean Permittivity $\varepsilon(\mathbf{r})$ around B-DNA

A – 0.167 M $CaCl_2$

B – 0.5 M NaCl

$\varepsilon_{DNA} = 2$

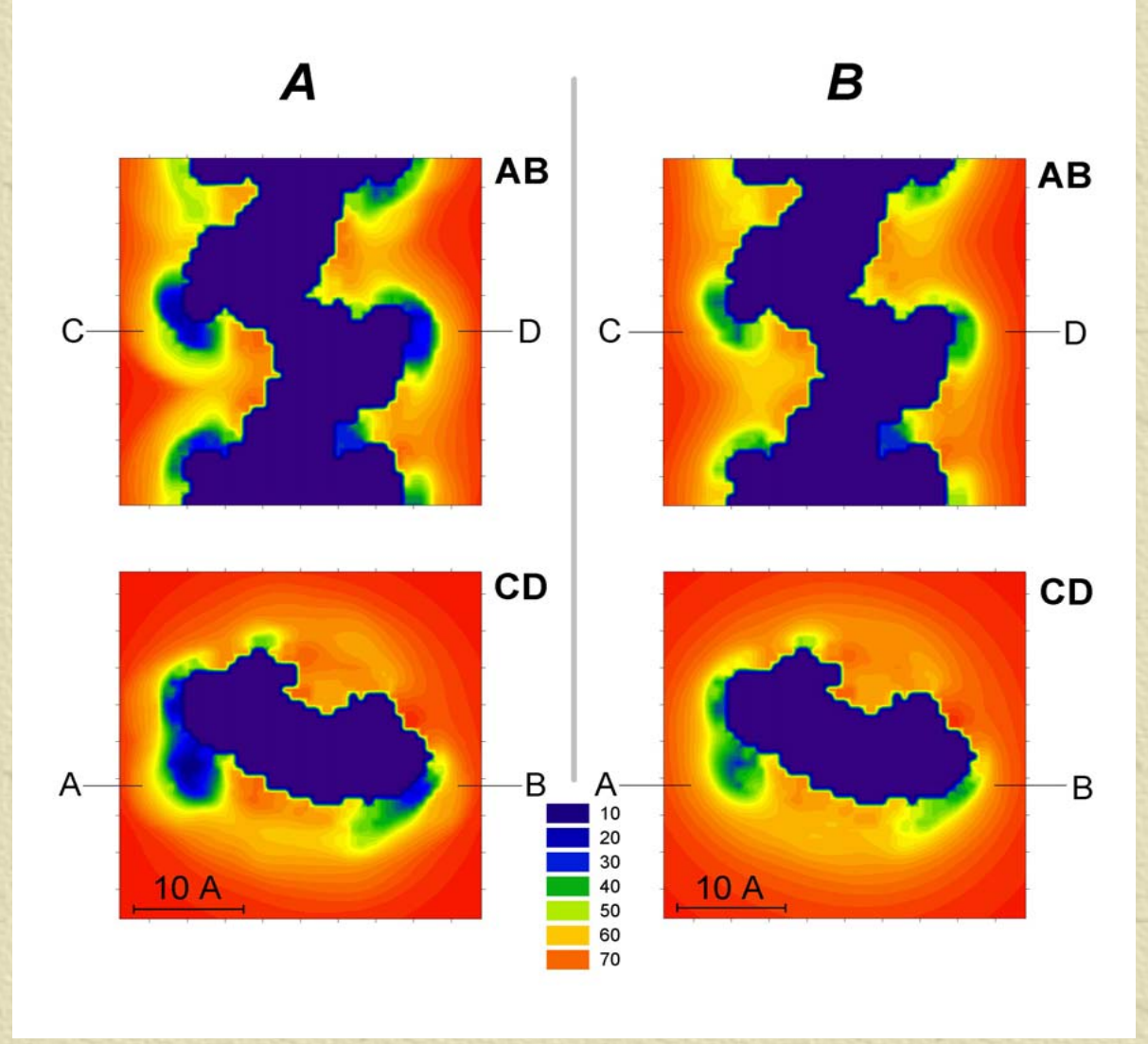


ε–MPB Calculations for B-DNA in 60 mM NaCl + 10 mM $MgCl_2$

$\varepsilon(\mathbf{r})$

A – 60 mM NaCl + 10 mM $MgCl_2$

B – 90 mM NaCl

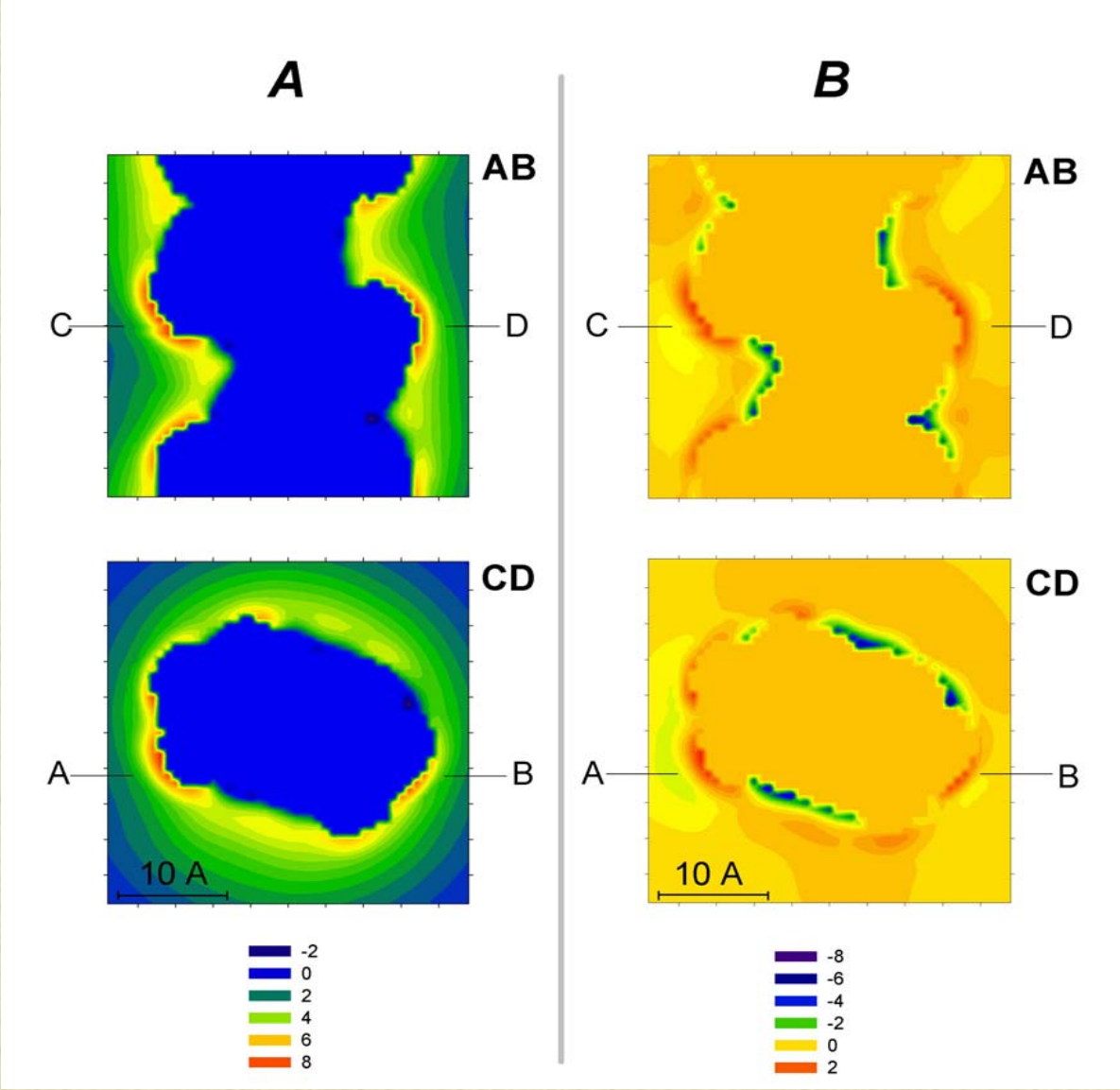


ε–MPB Calculations for B-DNA in 60 mM NaCl + 10 mM $MgCl_2$

$g(\mathbf{r})$

$A \quad - \quad \ln g^{\varepsilon\text{–MPB}}{}_{\text{Mg}}(\mathbf{r})$

$B \quad - \quad (\ln g^{\varepsilon\text{–MPB}}{}_{\text{Mg}}(\mathbf{r}) - \ln g^{\text{PB}}{}_{\text{Mg}}(\mathbf{r}))$

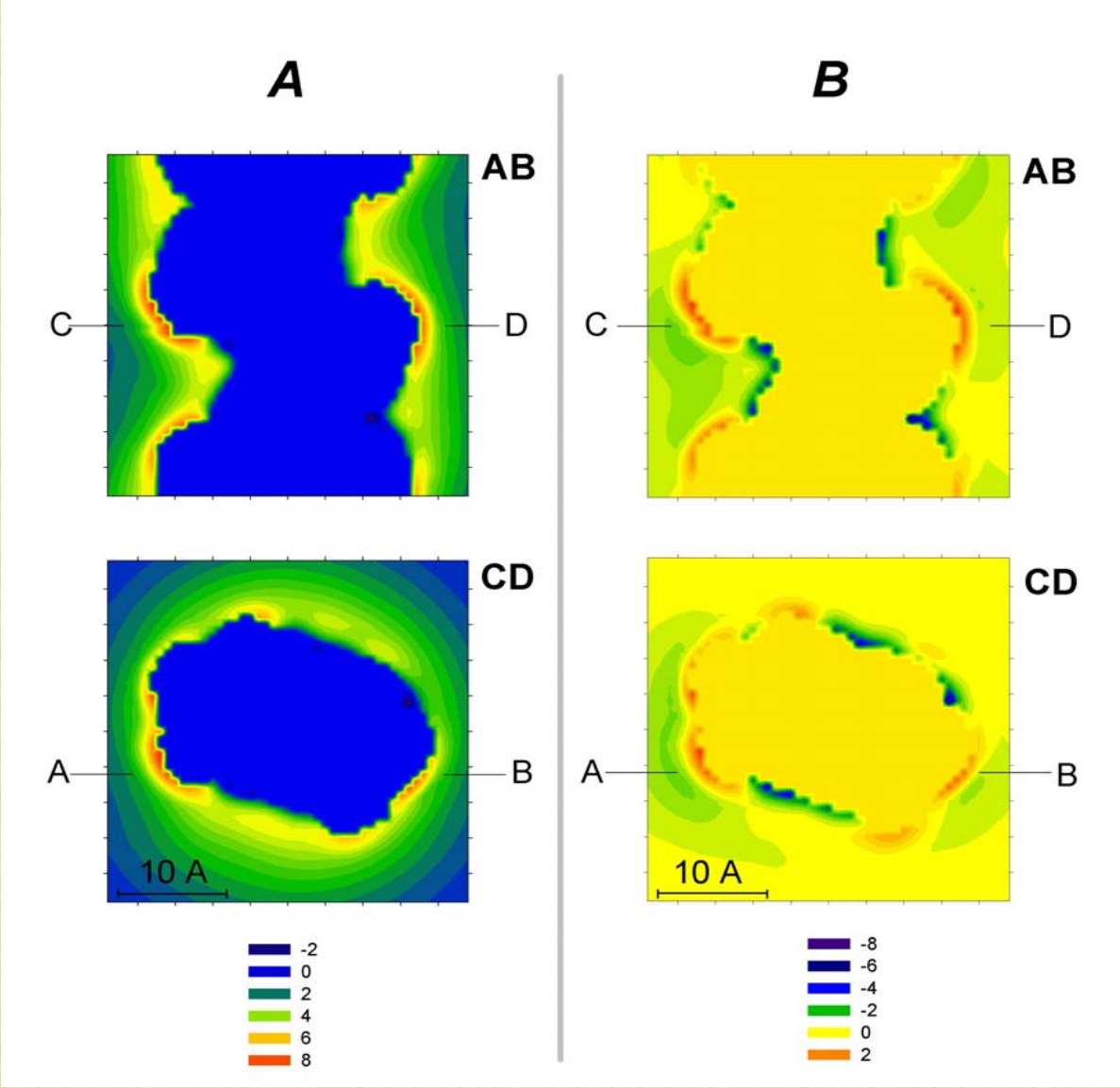


ε–MPB Calculations for B-DNA in 60 mM NaCl + 10 mM $MgCl_2$

$g(\mathbf{r})$

$A \quad - \quad \ln g^{\varepsilon\text{–MPB}}{}_{\text{Mg}}(\mathbf{r})$

$B \quad - \quad (\ln g^{\varepsilon\text{–MPB}}{}_{\text{Mg}}(\mathbf{r}) - \ln g^{\text{MPB}}{}_{\text{Mg}}(\mathbf{r}))$



all-atom MD: residence of Mg^{2+} (60 mM KCl + 10 mM $MgCl_2$)

Figure 7 from J. Mol. Biol. 281, 675 (1998)

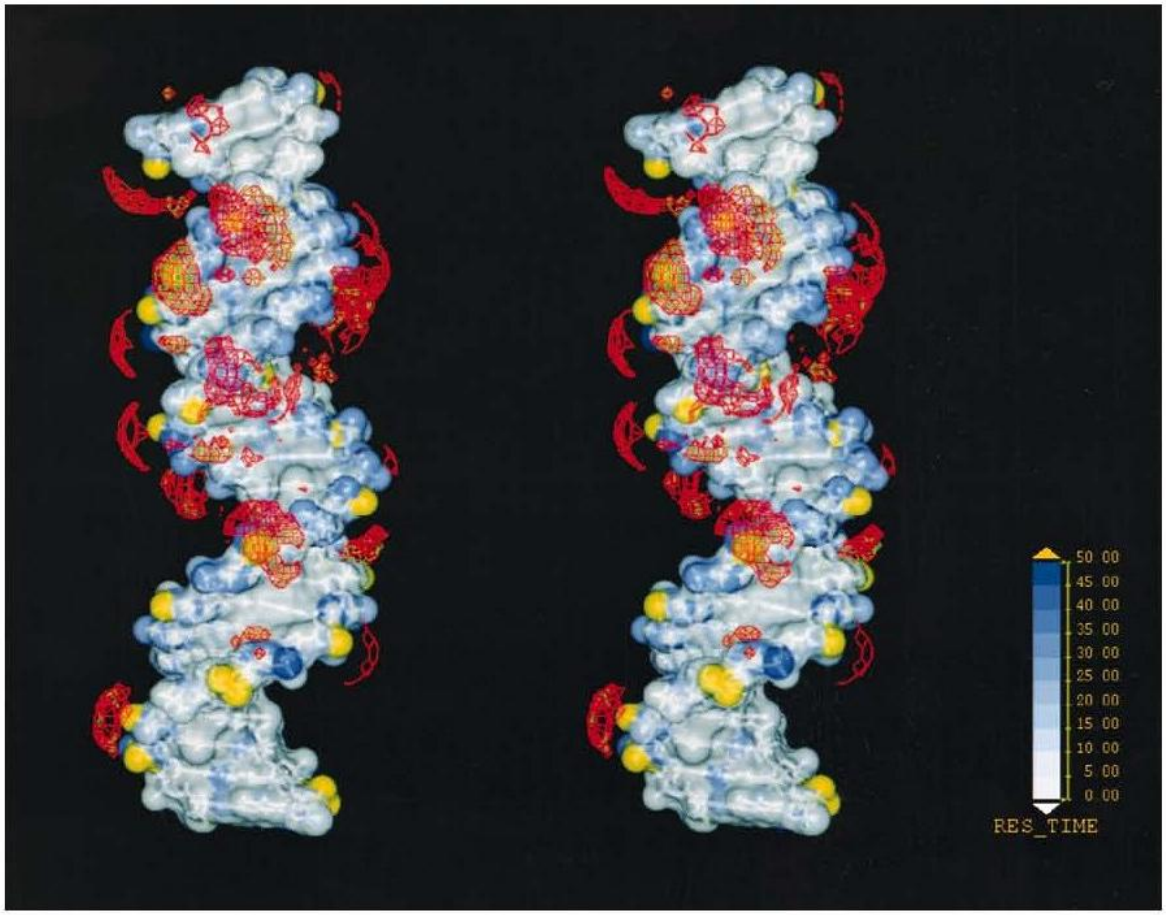
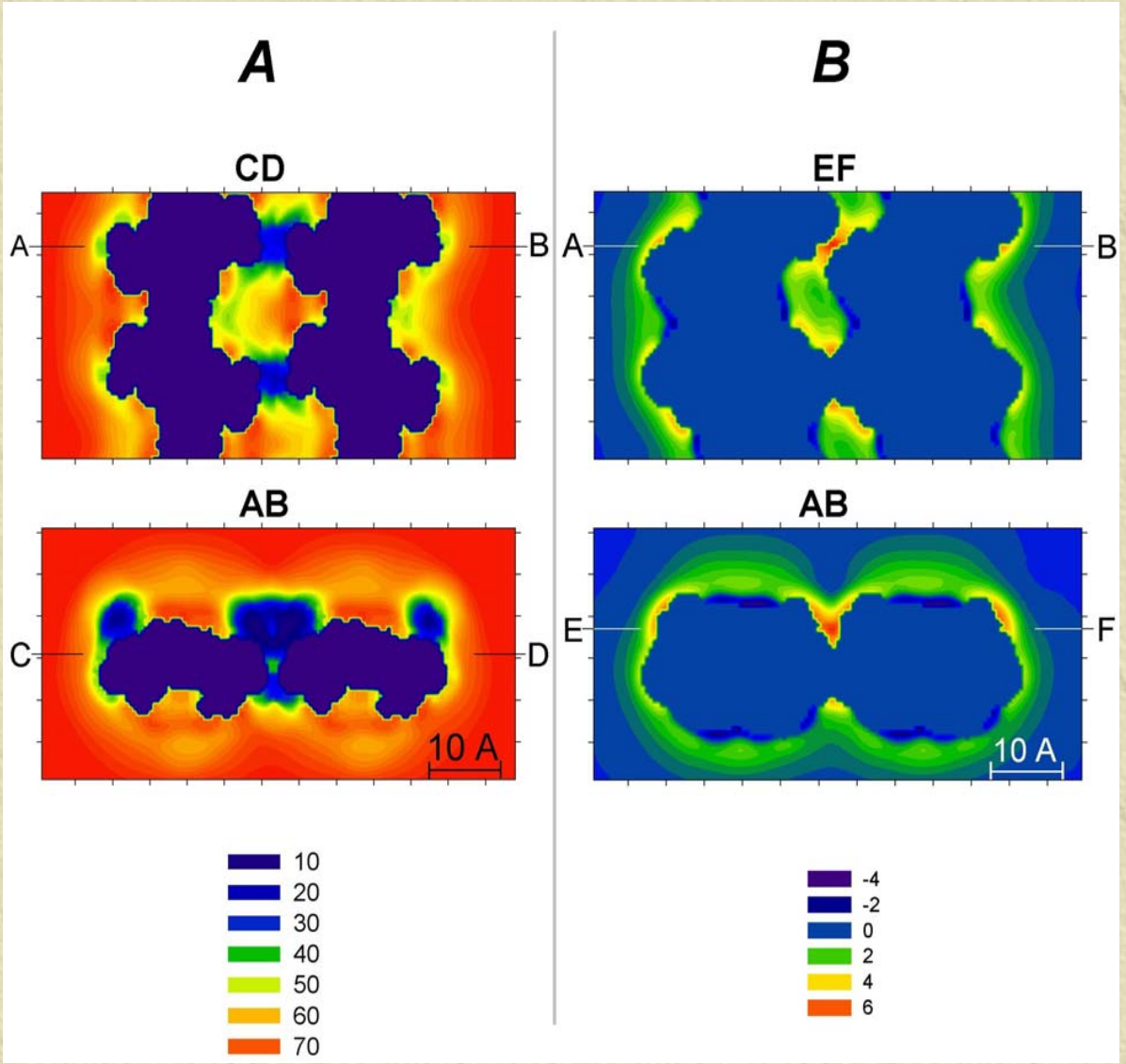


Figure 7. Local reference frame probability distribution and residence times of Mg^{2+} interactions with the phased A-tract DNA sequence (simulation (c)). Two mesh iso-concentration contours are plotted: 10× bulk (green) and 5× bulk (red). The solvent-accessible surface of the stereo image pair is colored to indicated the average residence time of Mg^{2+} with each atom. Interaction times are colored according to the scale on the right (in ps). All DNA-Mg^{2+} interactions are mediated by at least one water molecule.

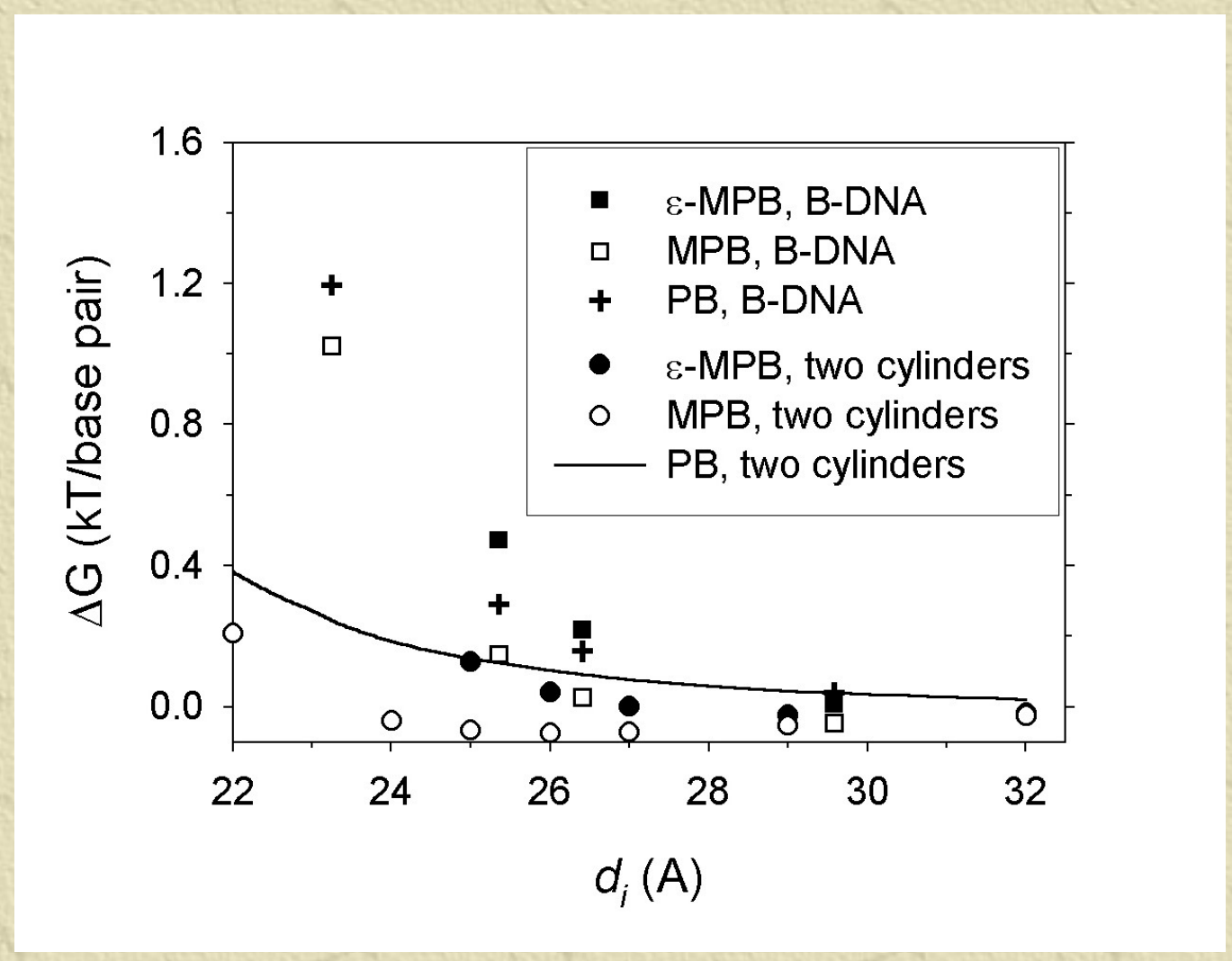
DNA-DNA Interaction, 0.167 M of $CaCl_2$

A – $\varepsilon(\mathbf{r})$

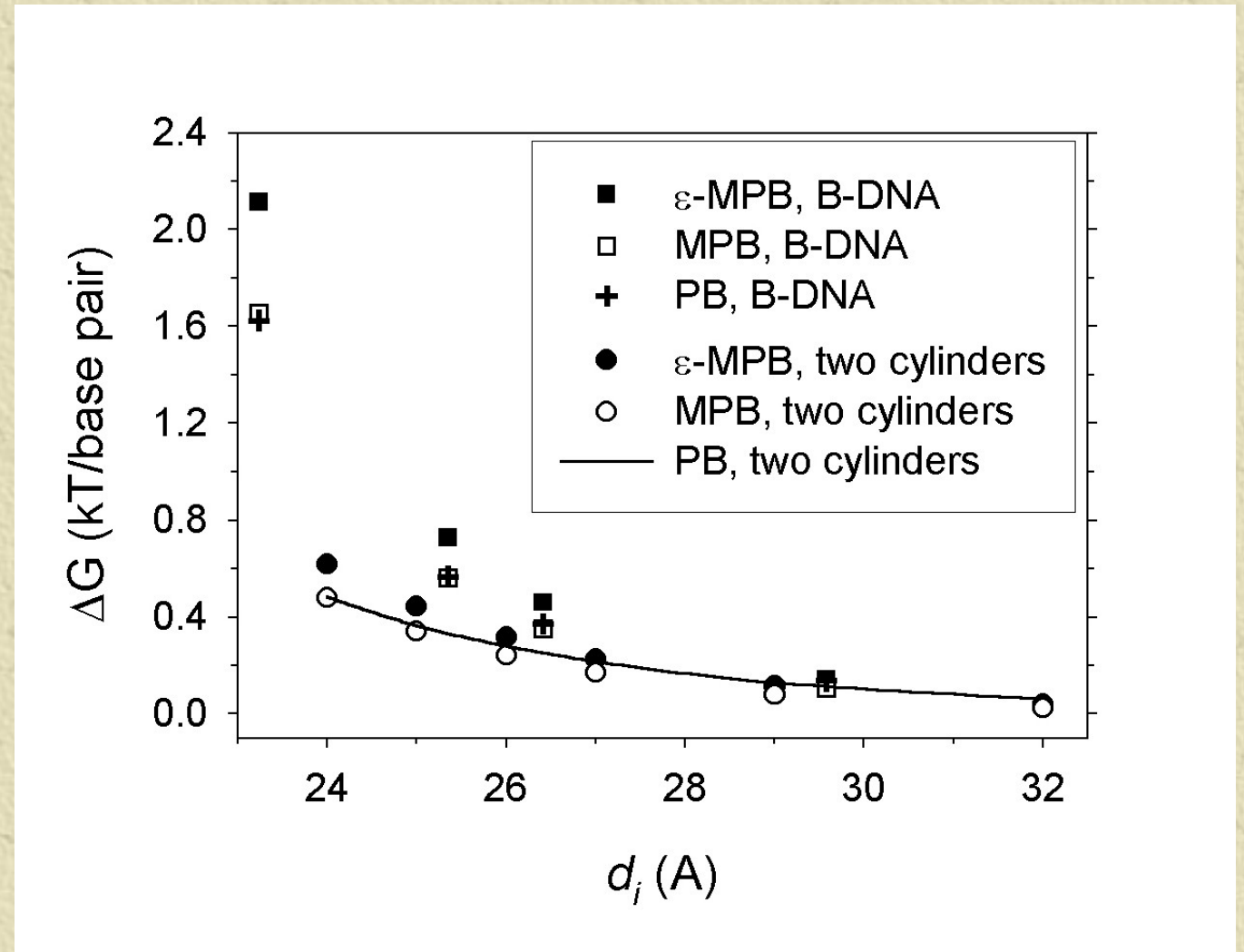
B – $\ln g^{\varepsilon-\mathrm{MPB}}{}_{\mathrm{Ca}}(\mathbf{r})$



DNA-DNA Interaction Energy, 0.167 M $CaCl_2$

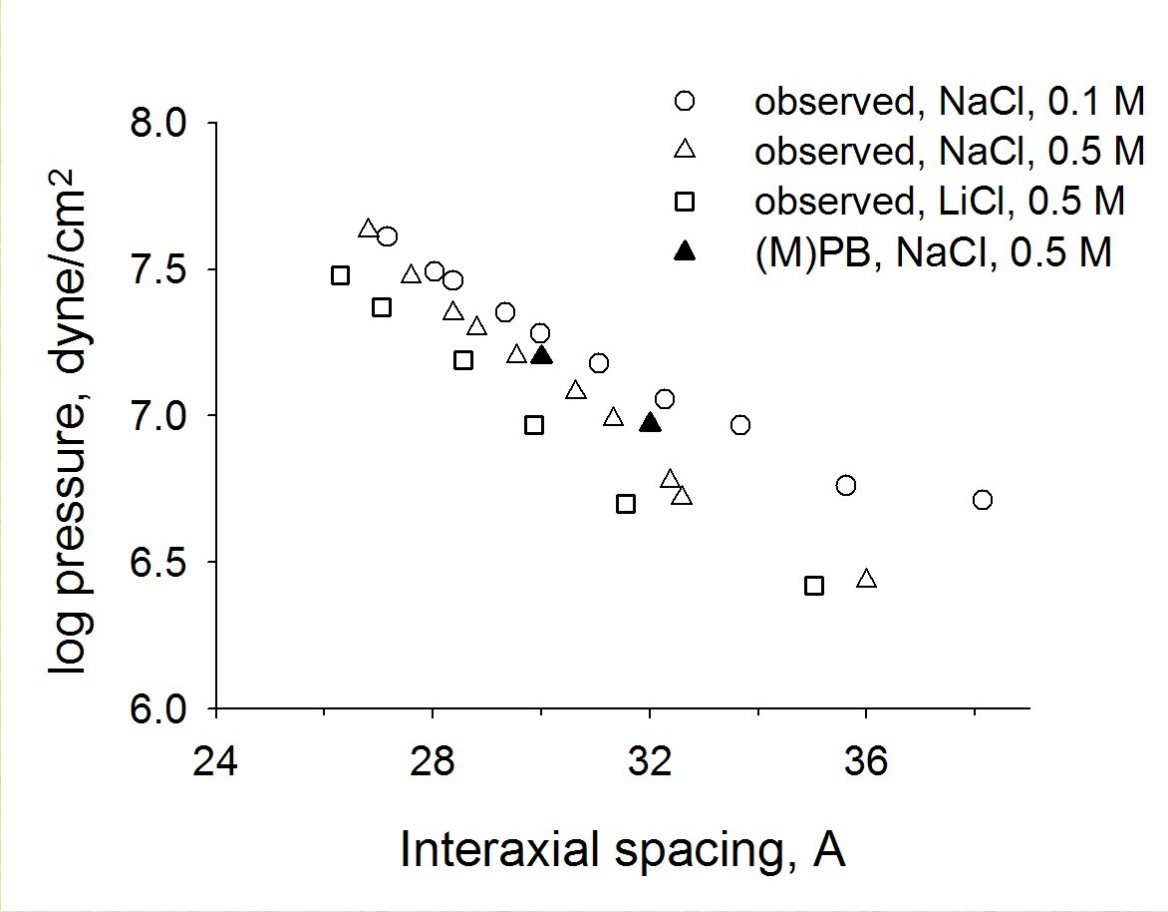


DNA-DNA Interaction Energy, 0.5 M NaCl



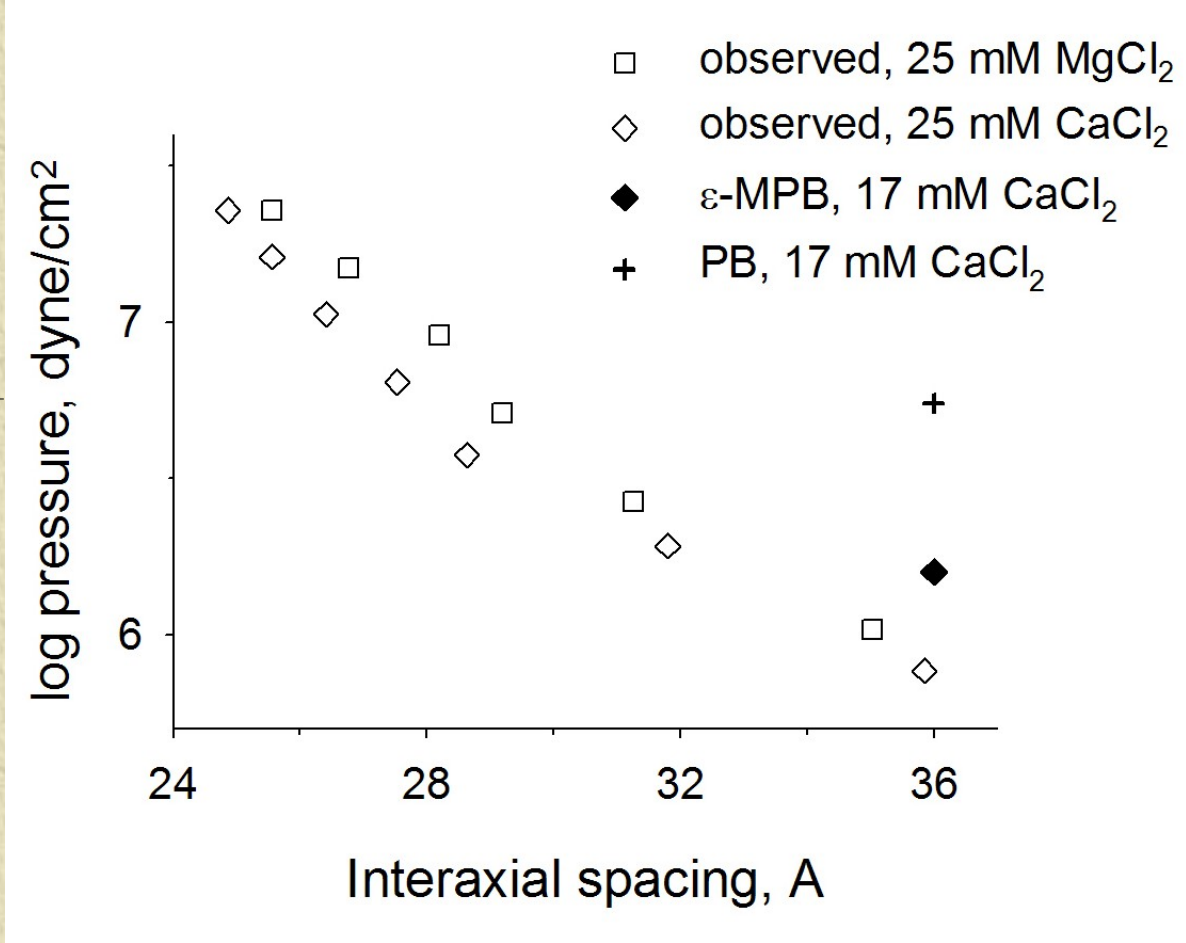
DNA Osmotic Pressure in the Hexagonal Lattice (NaCl)

$$\pi_{\text{osm}} = \frac{\sqrt{3}}{d_i} \frac{d\Delta G_{\text{DNA-DNA}}}{dd_i}$$



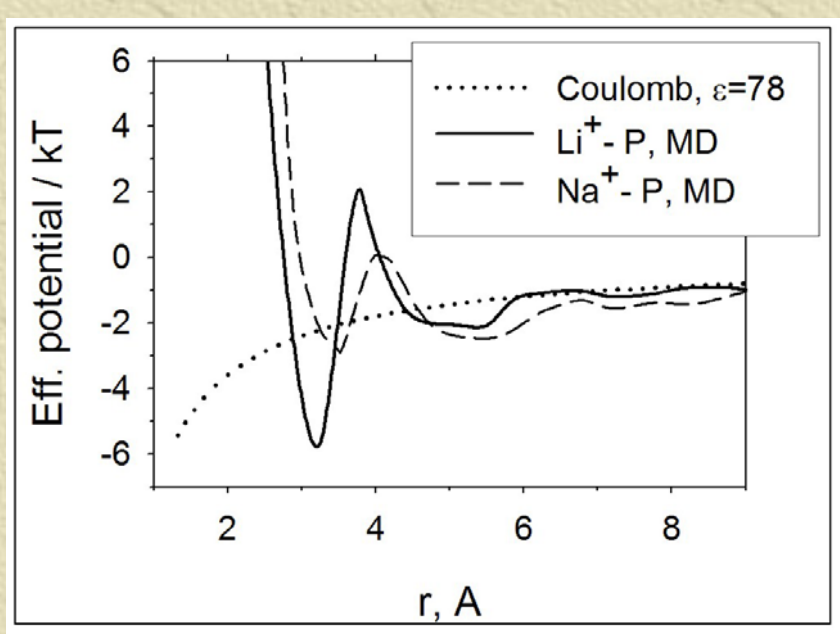
DNA Osmotic Pressure in the Hexagonal Lattice ($CaCl_2$)

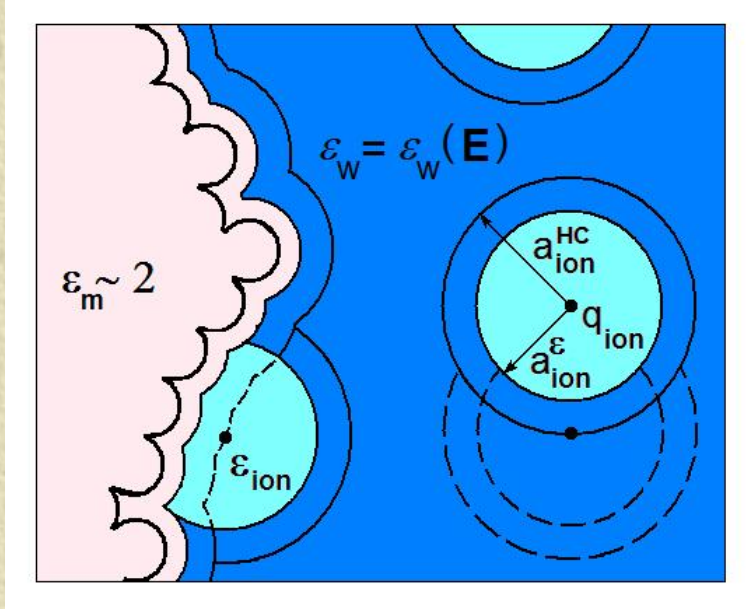
$$\pi_{\text{osm}} = \frac{\sqrt{3}}{d_i} \frac{d\Delta G_{\text{DNA-DNA}}}{dd_i}$$



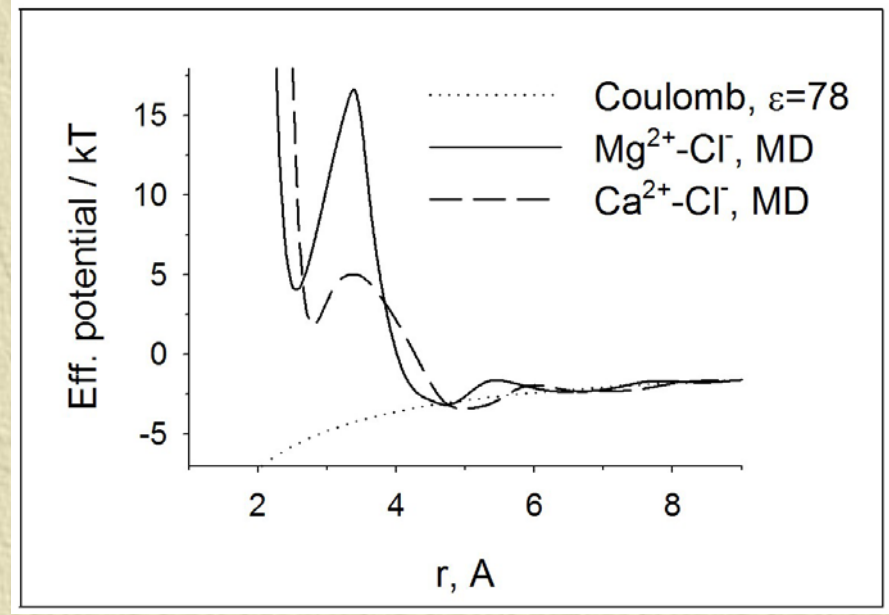
Ion-Specific Partial Reduction of DNA Charges

$$u_{\nu i}(\mathbf{r}) = u_{\nu i}^{\mathrm{SR}}(\mathbf{r}) + u_i^{\mathrm{el}}(\mathbf{r})$$

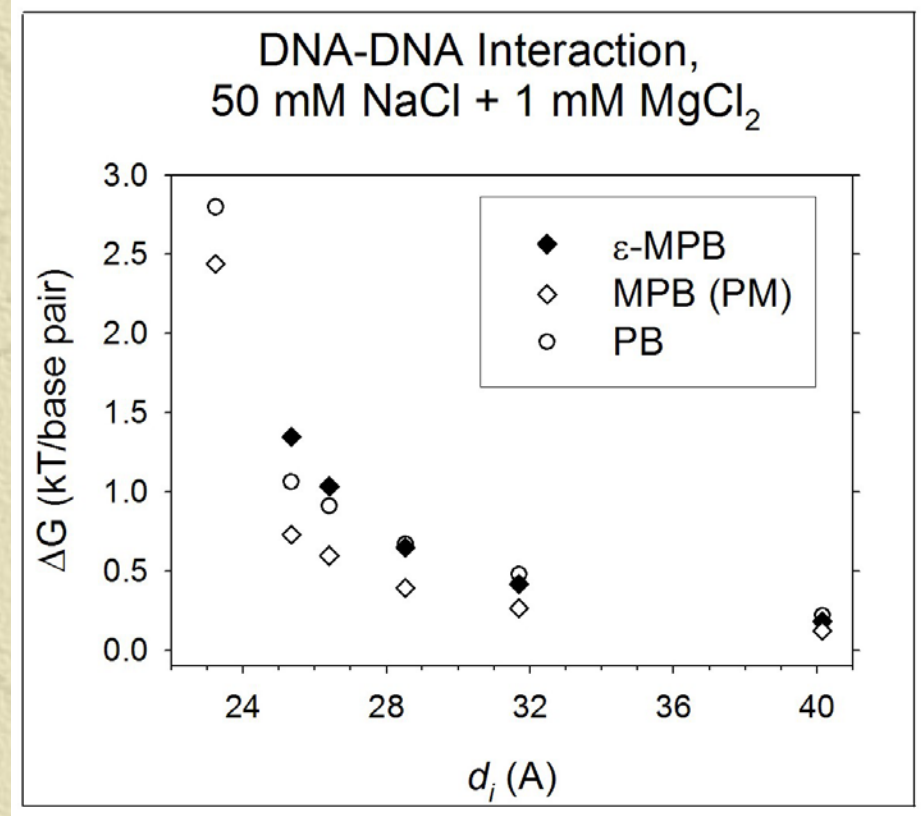


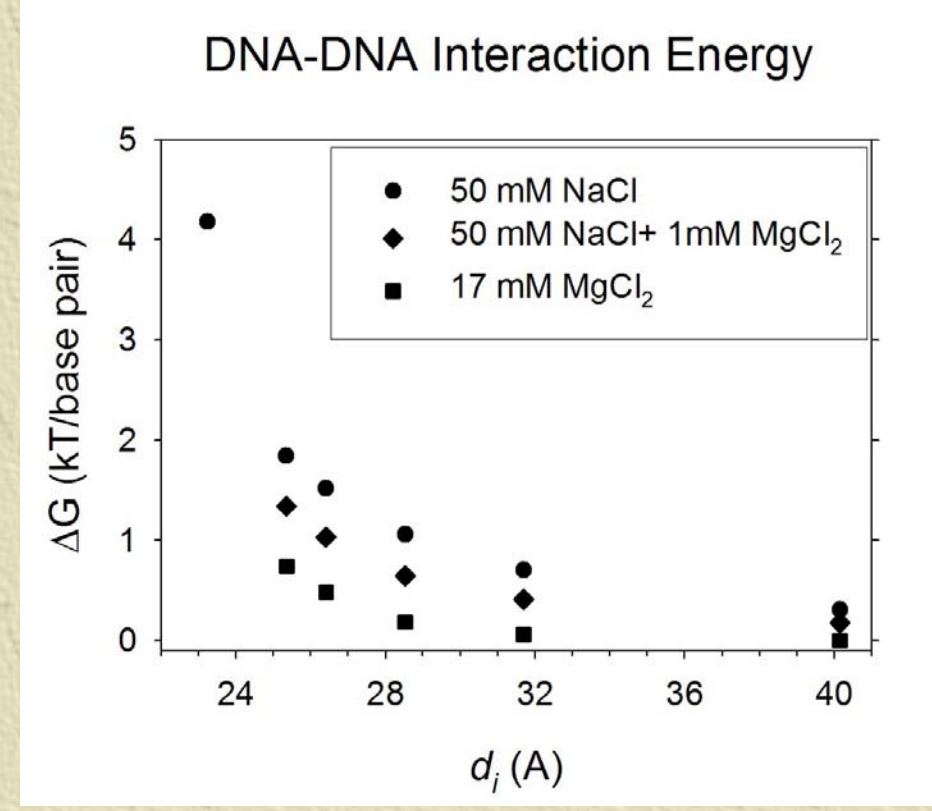


$$\Delta q_\nu = \sum n_i^0 q_i \int_{|\mathbf{r}-\mathbf{r}_\nu|<a_\nu^{\mathrm{HC}}} \exp(-\beta u_{\nu i}(\mathbf{r}))d\mathbf{r}$$



Mediating Role of Alkaline Earth Metal Ions in DNA Electrostatics





Conclusions

- The PPM of hydrated ions can be applied to the MPB equations
- The resulting ε-MPB equations predict high affinity of ions Ca^{2+} and Mg^{2+} to $[PO_2]^-$ groups of DNA
- The ε-MPB calculations predict repulsion of two DNAs in $CaCl_2$ or $MgCl_2$ solution
- The ε-MPB calculations allow evaluation of ΔG^{el} for large macromolecular systems