Korea Institute for Advanced Study

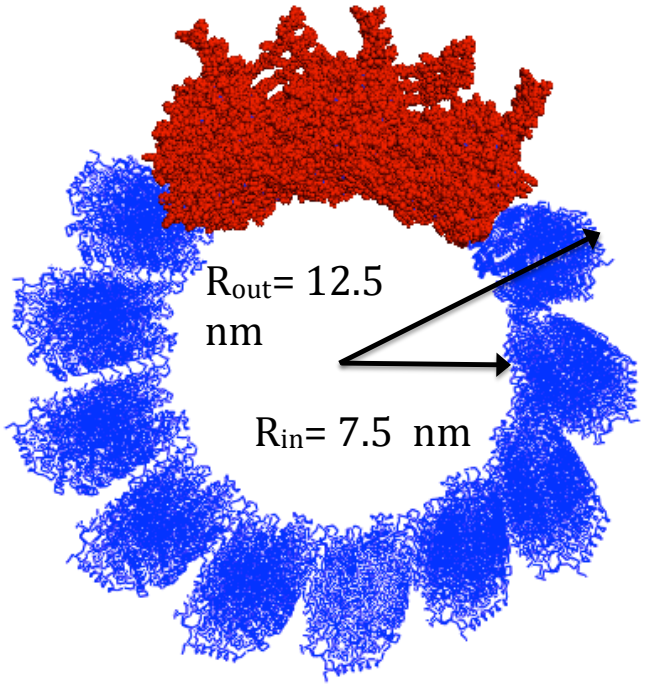
Dynamical Properties of the Solution Environment near the Microtubule Surface and their Implication to the Interaction with Motor Protein

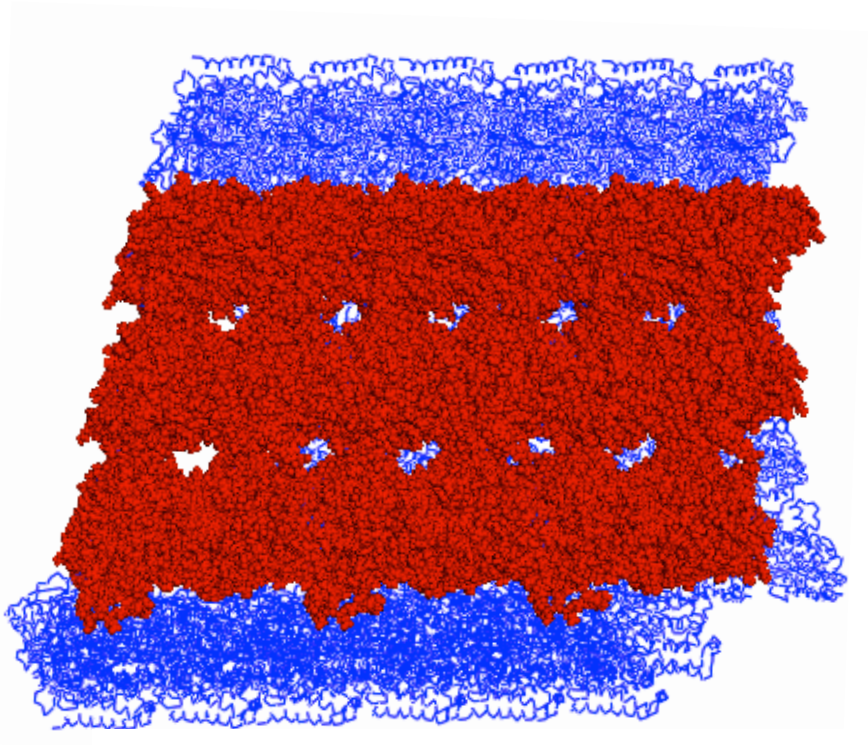
Arash Azari

Importance and Functionality:

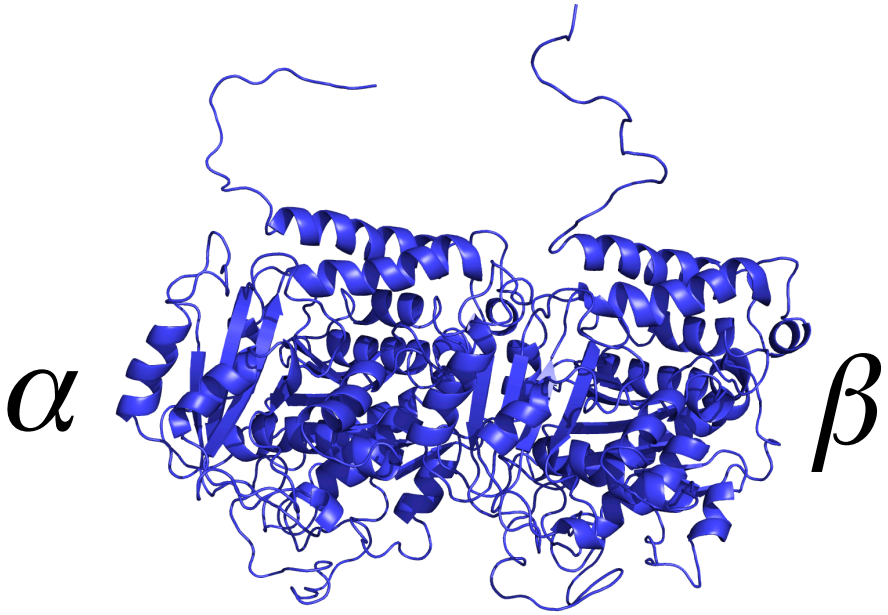
- Segregation of genetic material
- Intracellular transport
- Maintenance of cell shape
- Positioning of cell organelles
- Extracellular transport by means of cilia
- movement of cells by means of flagella and cilia

Structure of MT:





- Polarity, vesicle transport
- 11-18 protofilaments ~13
- ~ 50 e negative charges
- 150 mM NaCl
- 10 mM Ca^{2+} and Mg^{2+}



- Radial Distribution Function (RDF):

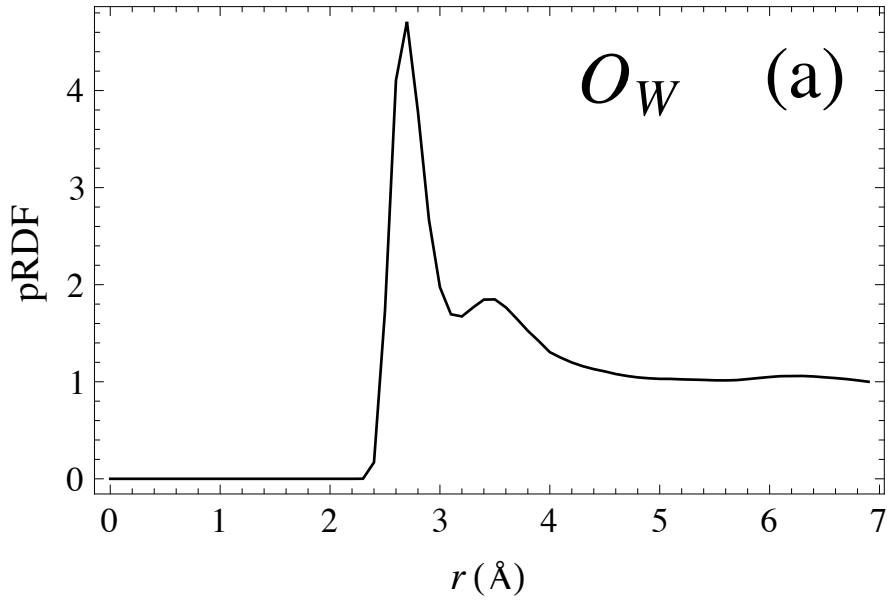
$$g_i(r) = \sum_{t=0}^{T} \sum_{j=1}^{N_W} \frac{\delta\left(\left|\mathbf{r}_i(t) - \mathbf{r}_j(t)\right| - r\right)}{4\pi r^2 N_W \Delta r}$$

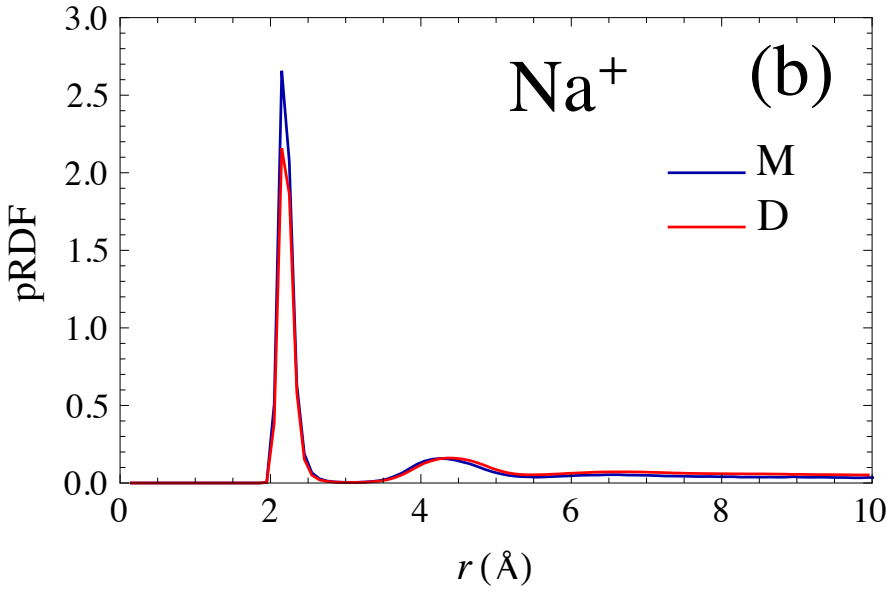
- The normal component, proximal RDF

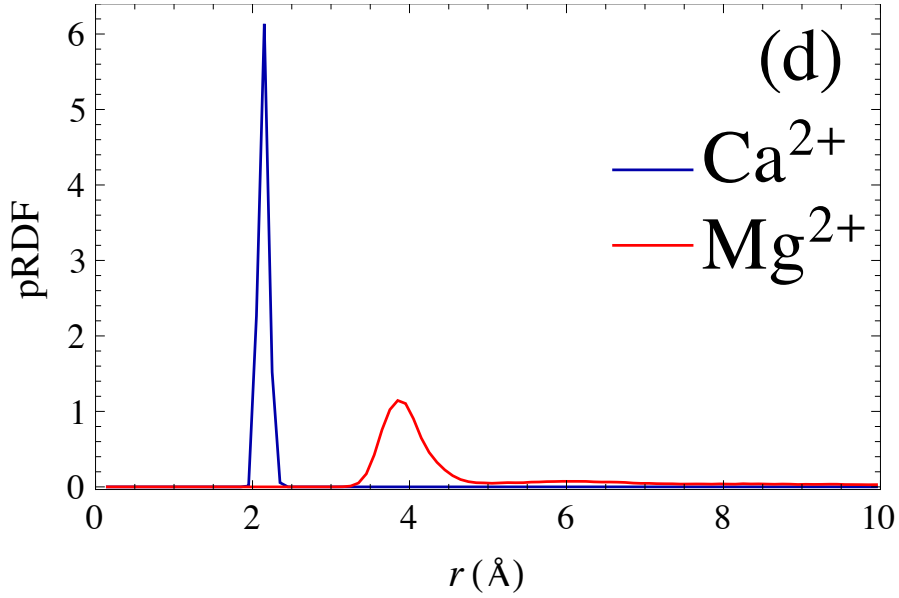
$$g_\perp(r) \propto Inf\left[\left|\mathbf{r}_i(t) - \mathbf{r}_j(t)\right|\right]$$

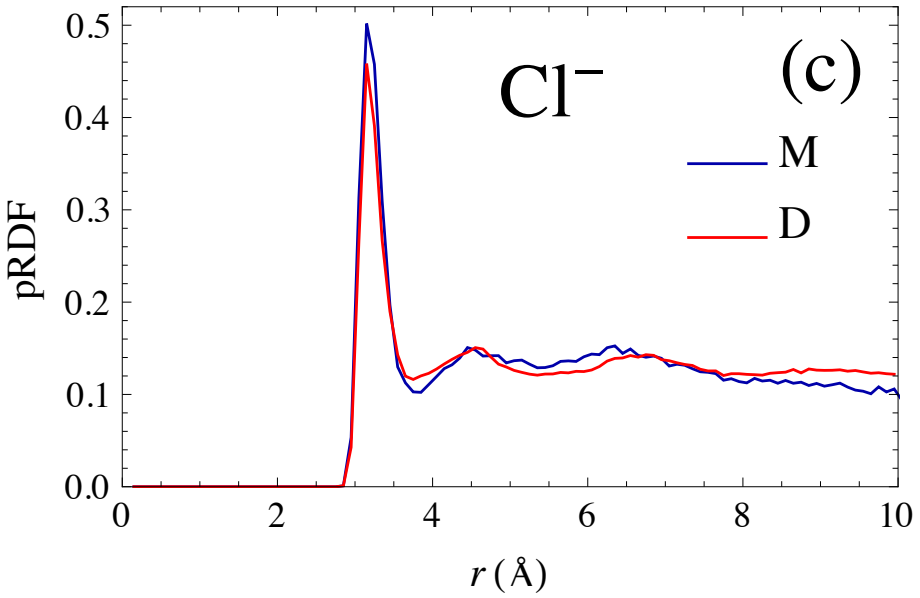
Biophys. J. **66** (3), 601-614, (1994), and Biophys J. **75** (1), 150–158, (1998).

Proximal Radial distribution Function (pRDF):

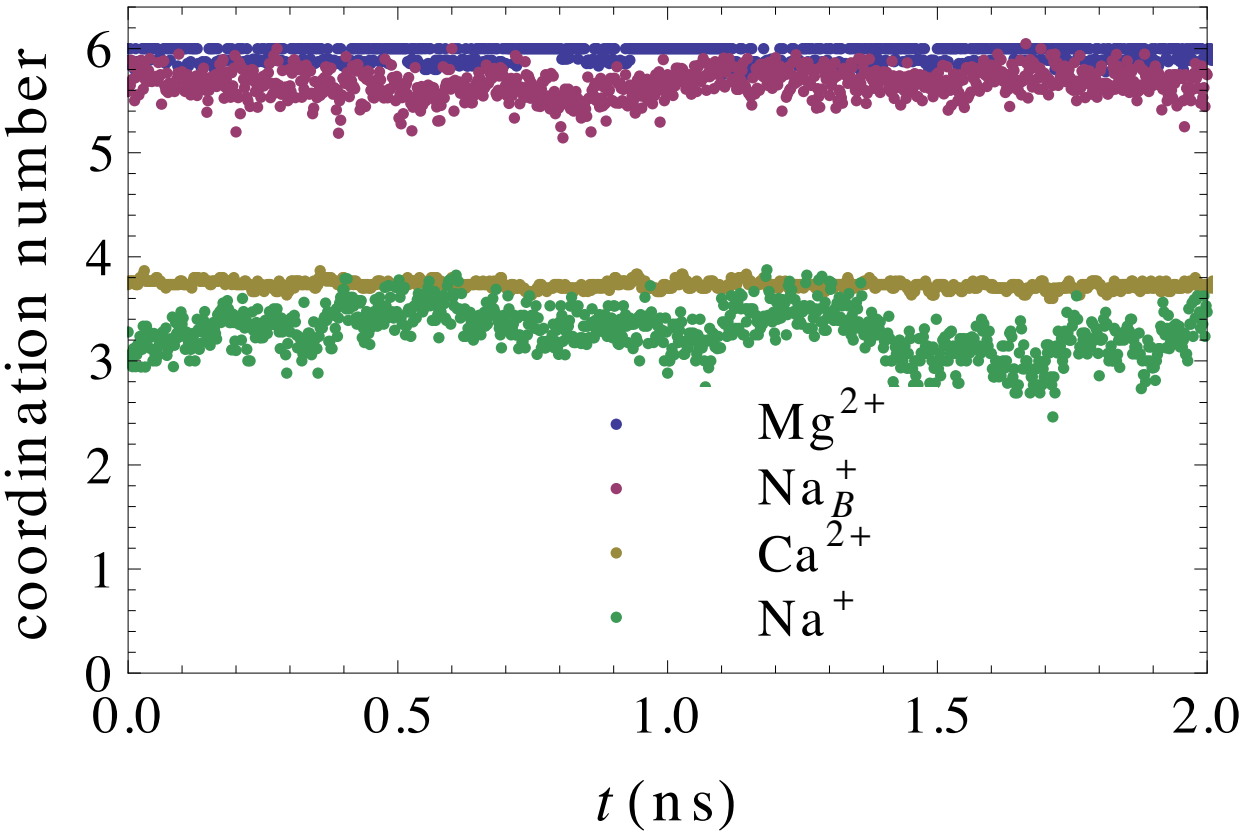








- **Ions Coordination Numbers:**

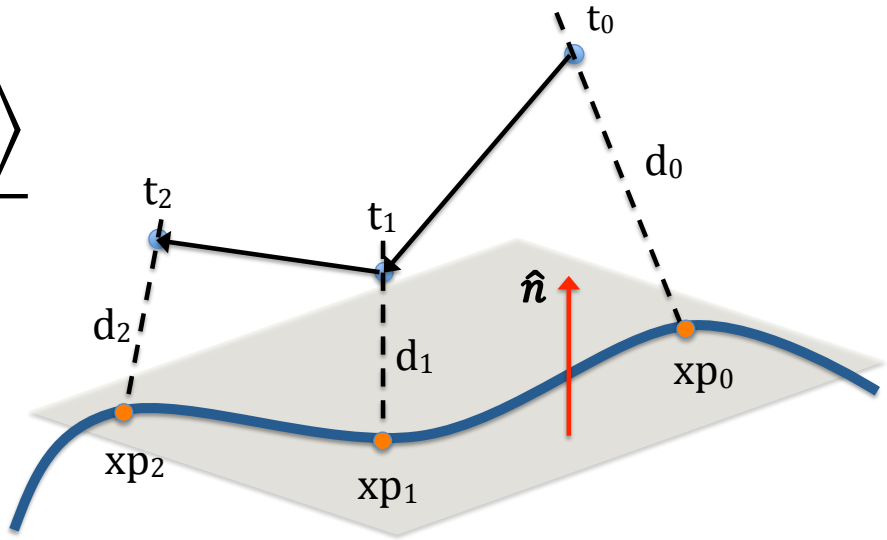


Average coordination numbers: Mg^{2+} 5.9, Na_B^{+} 5.7, Ca^{2+} 3.7 and Na^{+} 3.3.

Translational Diffusion:

$$D = \frac{1}{2d} \lim_{\Delta t \to \infty} \frac{\left\langle \left| \mathbf{r}_i(t) - \mathbf{r}_i(0) \right|^2 \right\rangle}{\Delta t}$$

$$D = \frac{1}{d} \int_0^\infty dt \left\langle \mathbf{v}_i(t) \cdot \mathbf{v}_i(0) \right\rangle$$

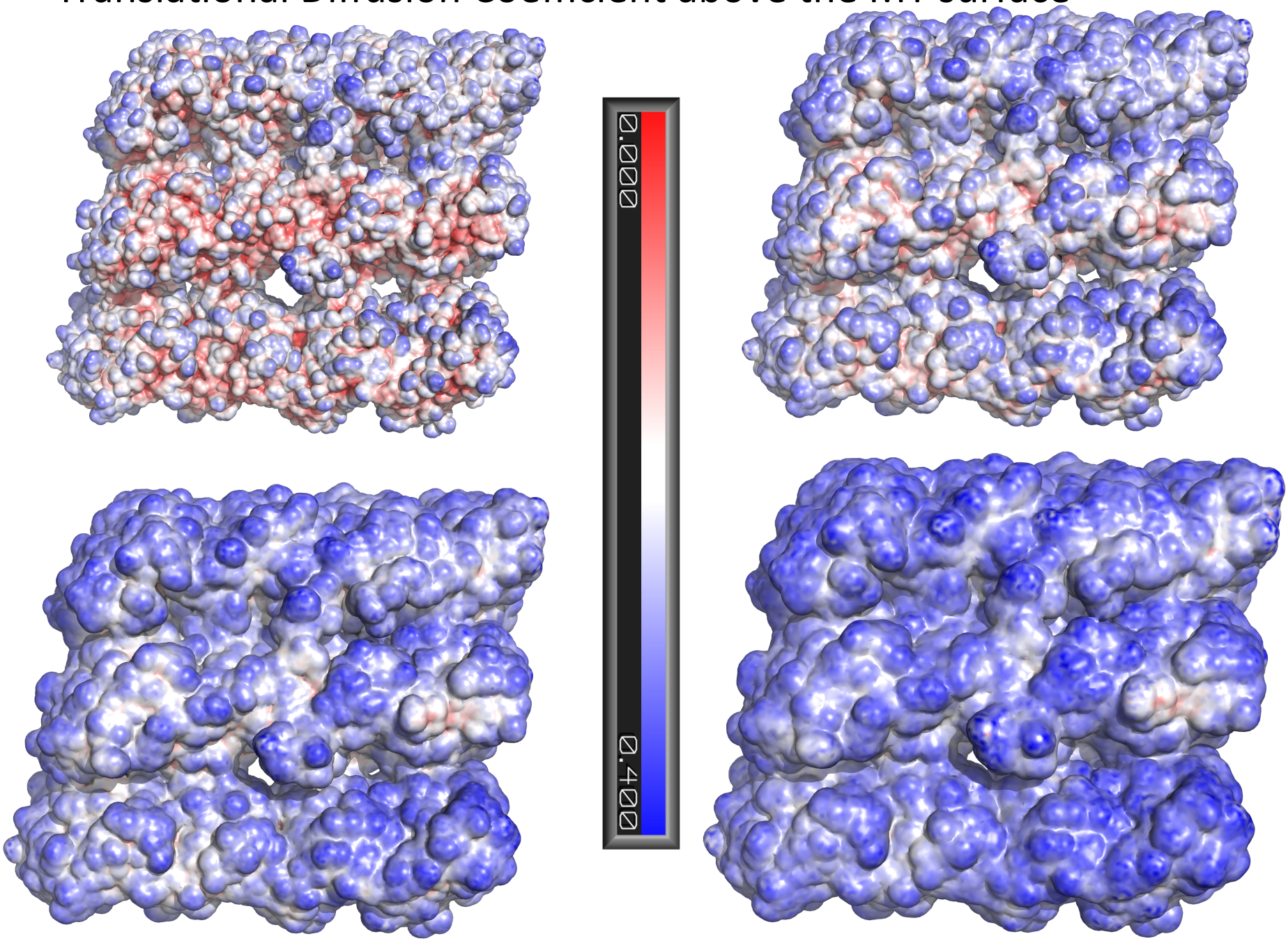


$$D_{uvw} = \frac{1}{2d(t_2 - t_1)} \left(\left\langle \left| \mathbf{r}_i(t_2) - \mathbf{r}_i(0) \right|^2 - \left| \mathbf{r}_i(t_1) - \mathbf{r}_i(0) \right|^2 \right\rangle \right)$$

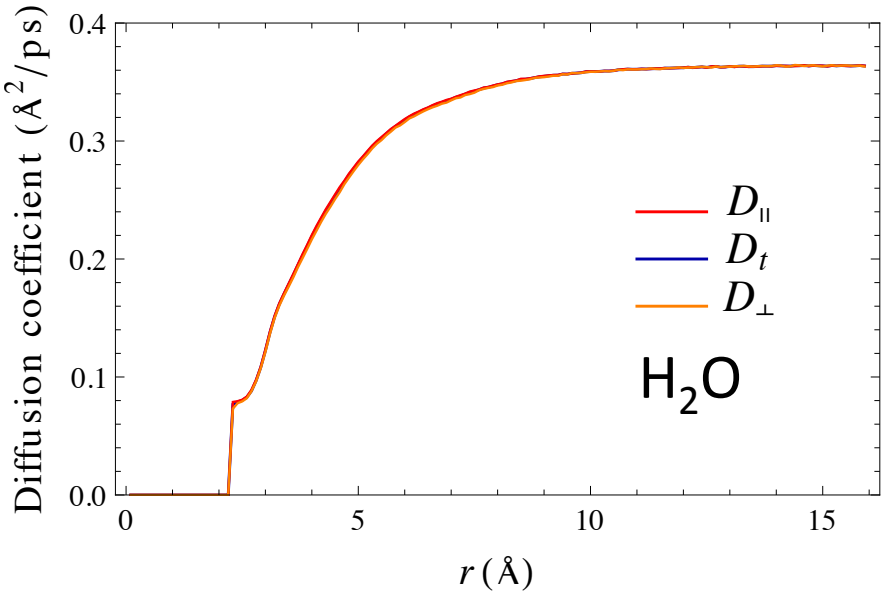
$$\left\langle \Delta r^2 \right\rangle = \left\langle \Delta r_{\parallel}^2 \right\rangle + \left\langle \Delta r_{\perp}^2 \right\rangle$$

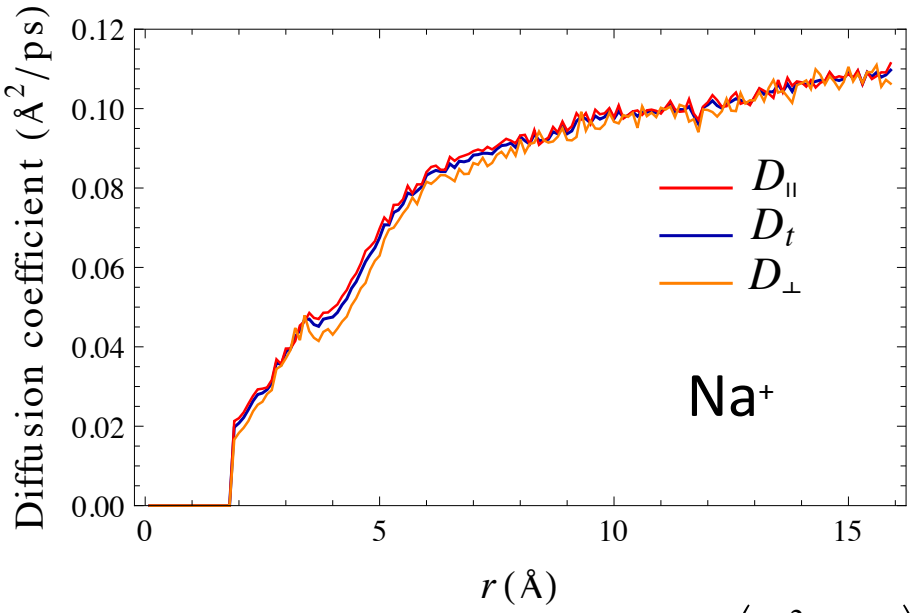
Biophys. J. **66** (3), 601-614, (1994)

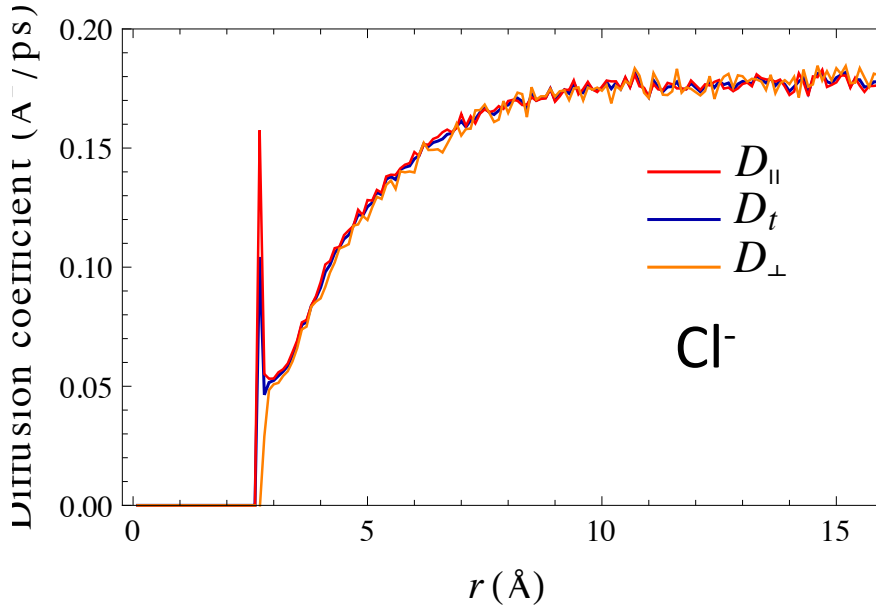
Translational Diffusion Coefficient above the MT surface



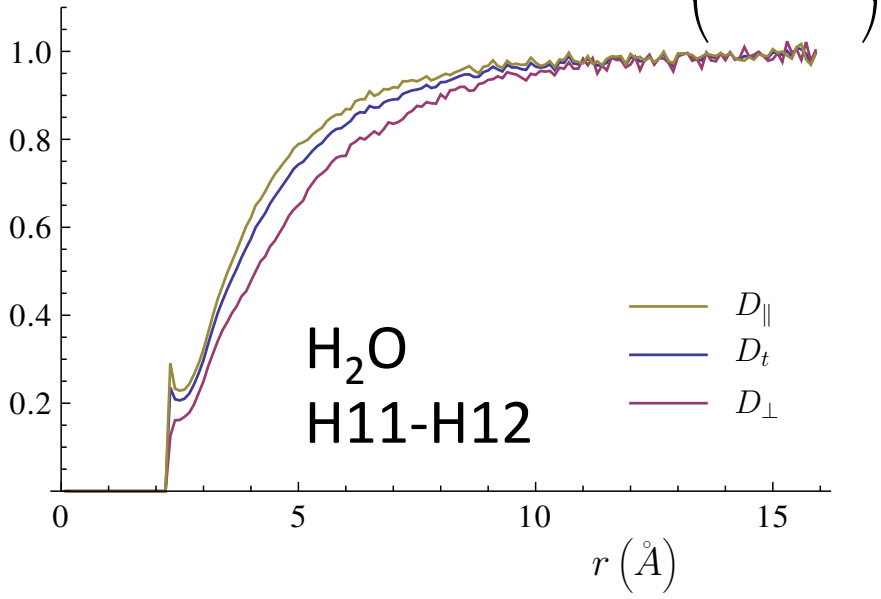
Translational Diffusion Coefficient and its normal and tangential components:



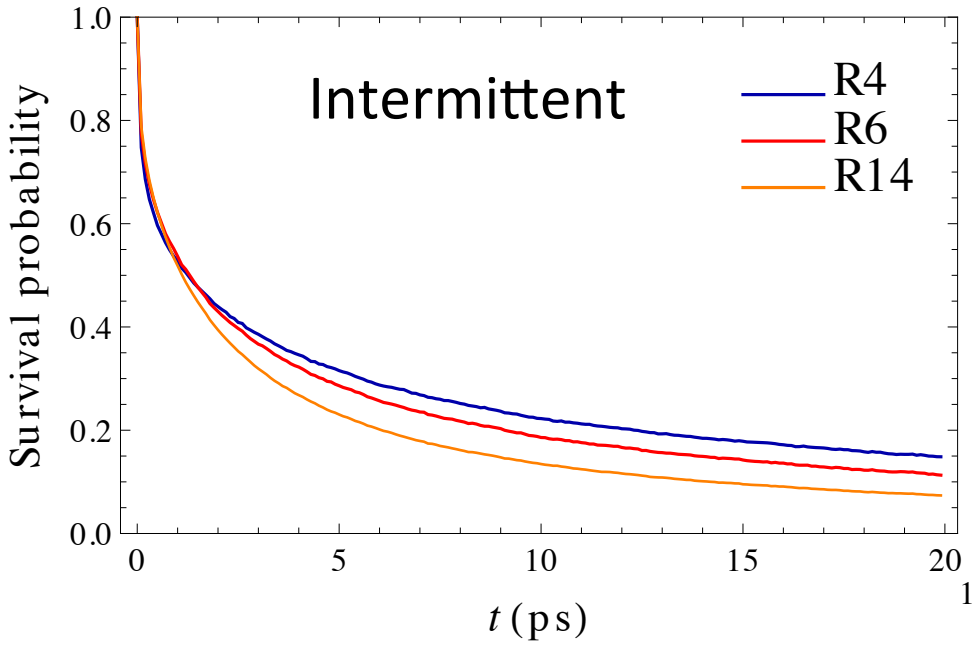




$\frac{D}{D_B}$ Bulk Diffiusion: $D_B = 0.36\left(\mathring{A}^2\, ps^{-1}\right)$



Hydrogen Bonds Survival Probability:



$$P(t) = \frac{\sum_{i,j} p_{ij}\left(t;t^{*}\right)}{\sum_{i,j} p_{ij}\left(t=0\right)}$$

$$\overline{\tau}_{I4} = 7.15(ps)$$

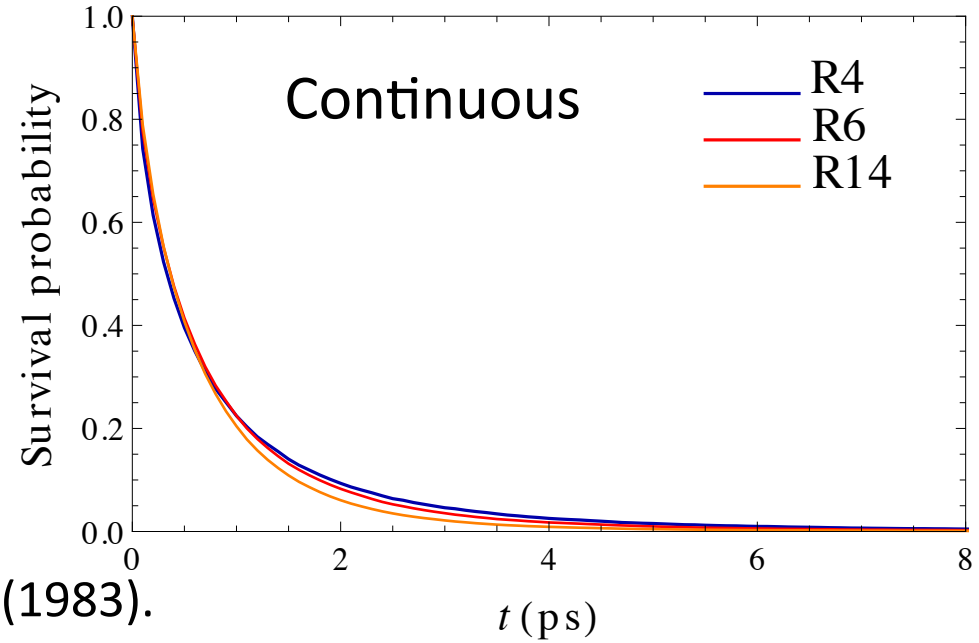
$$\overline{\tau}_{I6} = 5.85(ps)$$

$$\overline{\tau}_{I14} = 4.32(ps)$$

$$\overline{\tau}_{C4} = 0.72(ps)$$

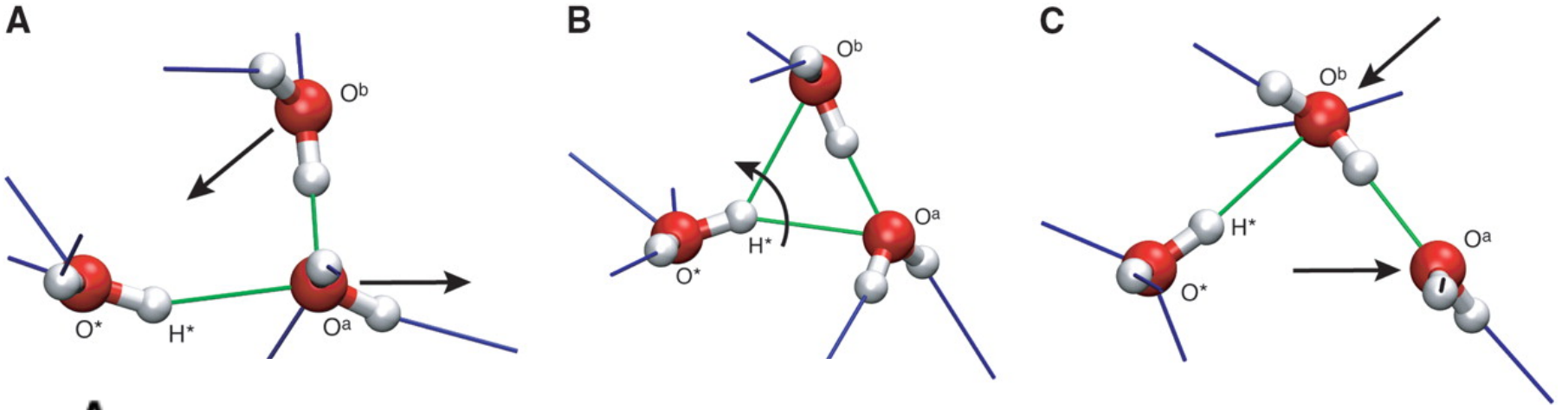
$$\overline{\tau}_{C6} = 0.7(ps)$$

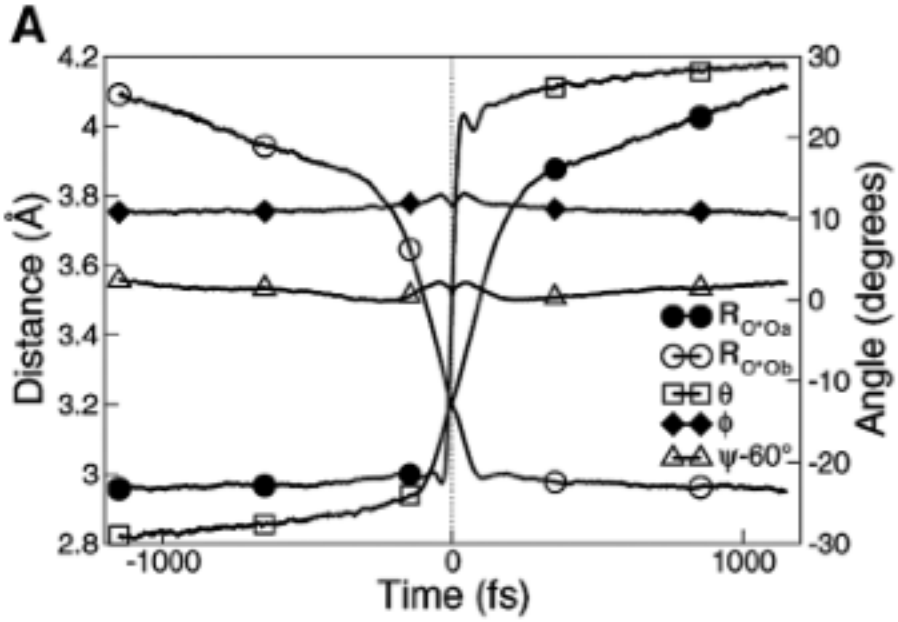
$$\overline{\tau}_{C14} = 0.63(ps)$$

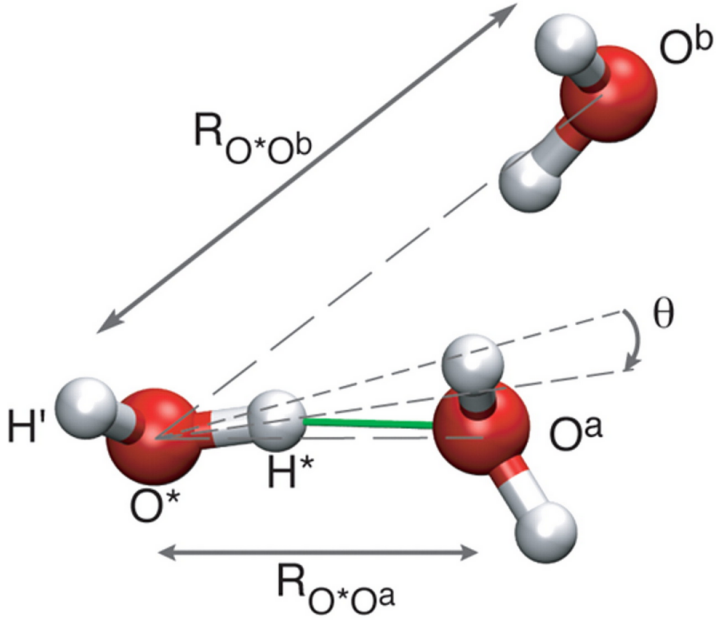


Molecular Physics, **50** (5), 1151-1162, (1983).

H-bond Breaking and Reorientation; Jump:







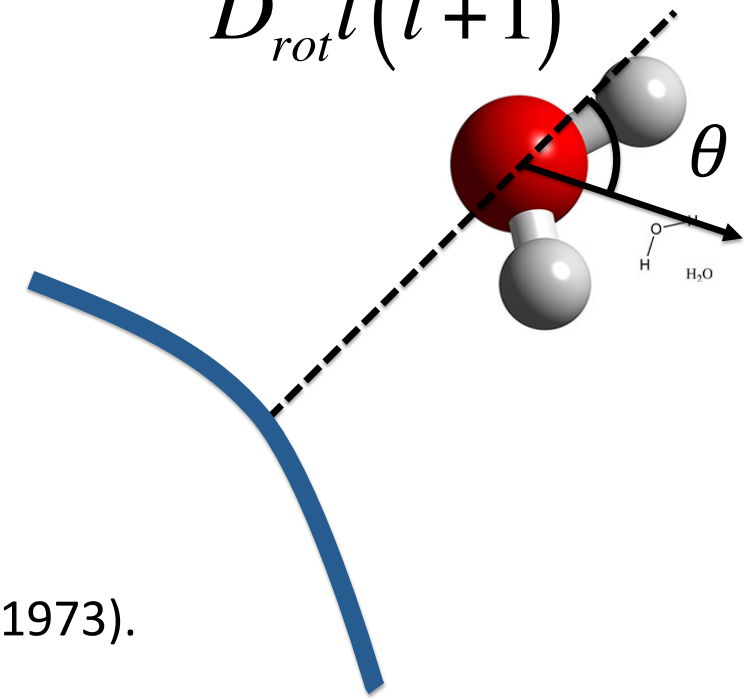
Science, **311** (5762), 832-835, (2006).

Rotational Diffusion:

$$\nabla^2_{\vec{r}} f(\theta,\phi,t) = \frac{1}{D_{rot}} \frac{\partial f(\theta,\phi,t)}{\partial t}$$

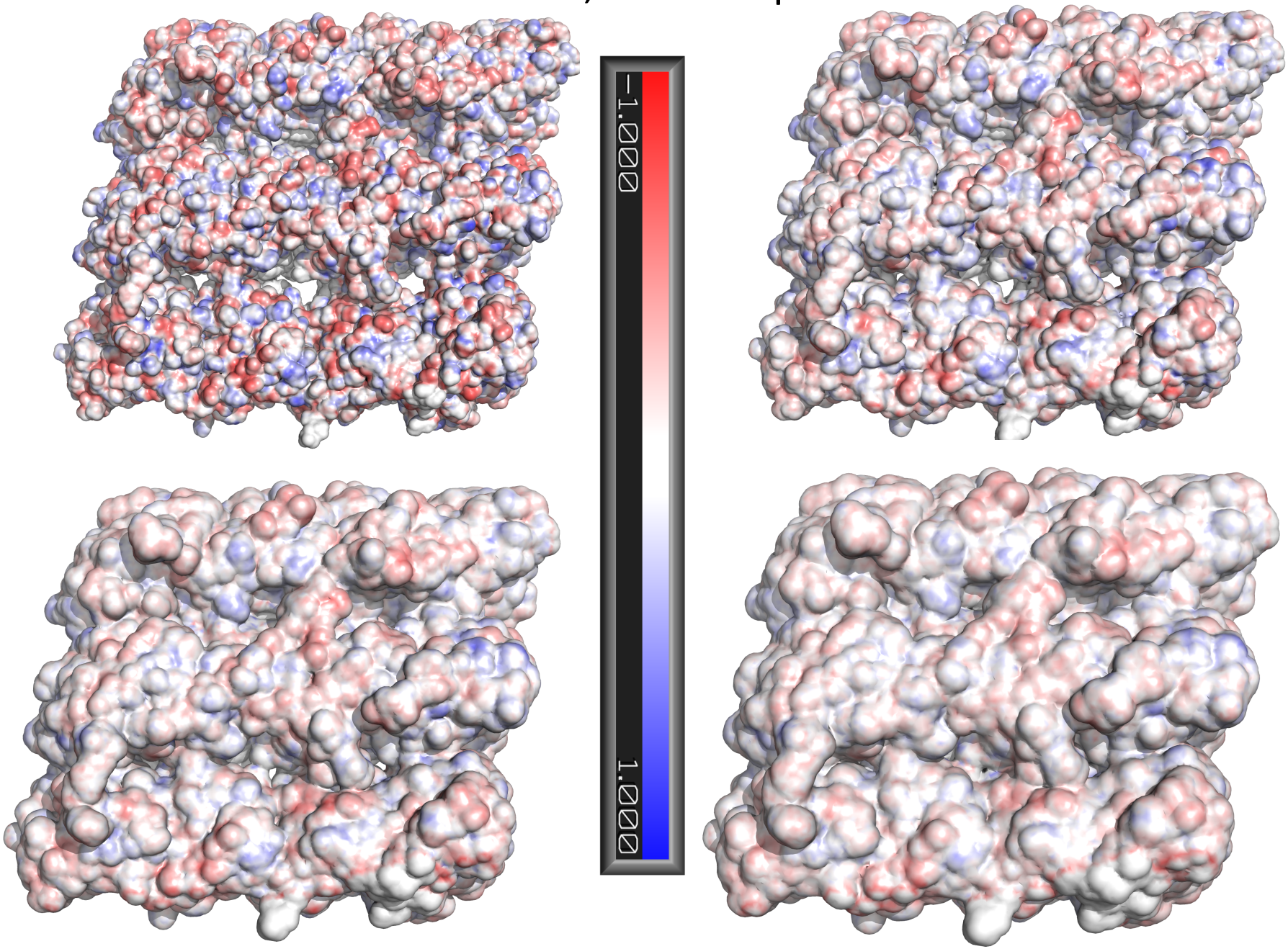
$$f = \sum_l P_l(\theta)\, a_l(t), \qquad \tau^l_{reor} = \frac{1}{D_{rot} l(l+1)}$$

$$\Gamma_l(t) = \left\langle P_l\left(\hat{\boldsymbol{\mu}}(t)\cdot\hat{\boldsymbol{\mu}}(0)\right)\right\rangle$$

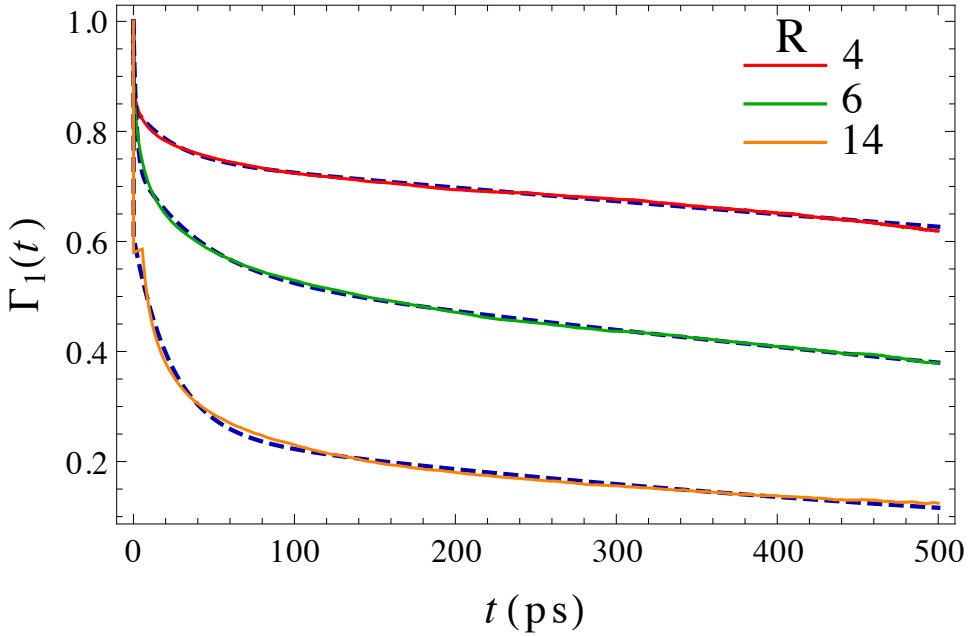


Theory of electric polarization, Elsevier, (1973).

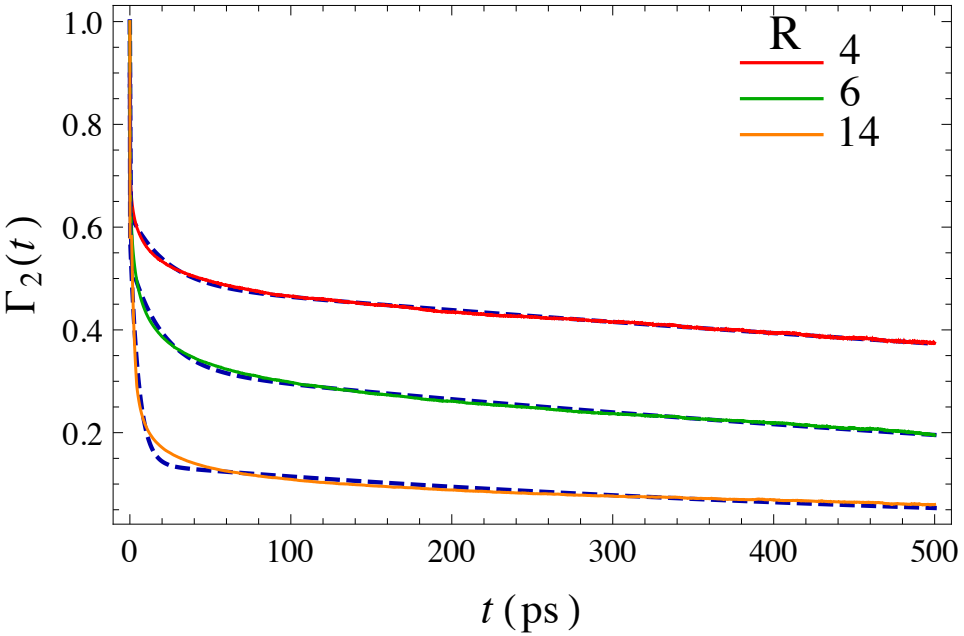
Rotational Diffusion Coefficient, Water Dipole Orientation:



Dipole-Dipole Autocorrelation:



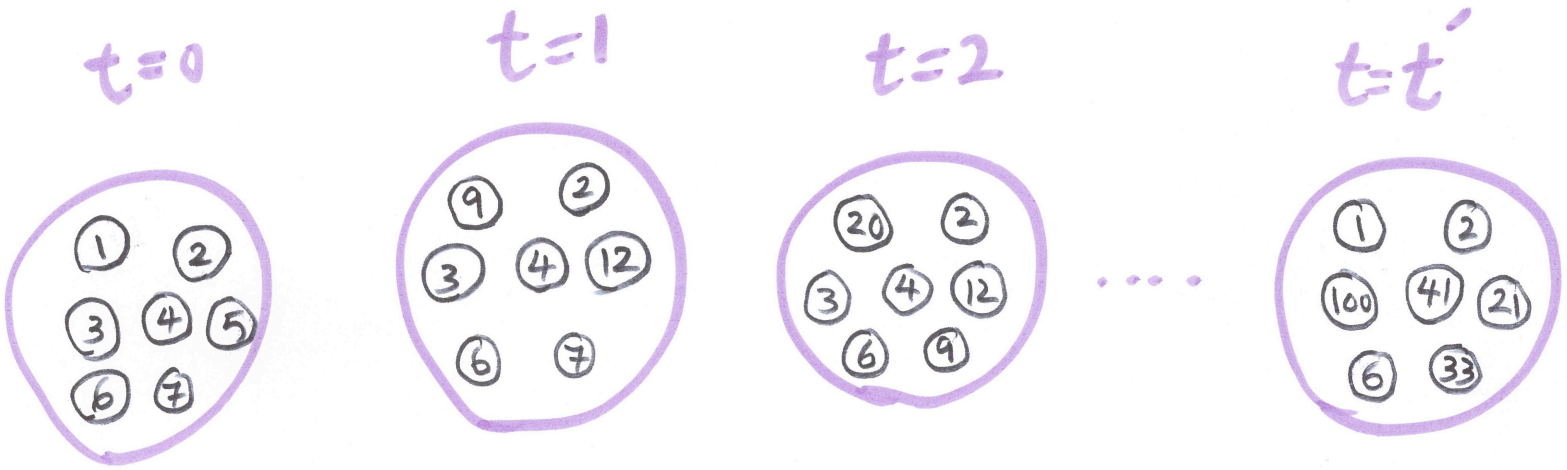
	R 4	R6	R14
A	0.74	0.54	0.25
B	0.15	0.26	0.39
C	0.1	0.2	0.35
$\tau_1(ps)$	2791	1378	634
$\tau_2(ps)$	0.3	1.8	~0.0
$\tau_3(ps)$	24.5	40.7	23.3
$\bar{\tau}(ps)$	2095	761	170



	R 4	R6	R14
A	0.48	0.32	0.13
B	0.37	0.46	0.4
C	0.13	0.21	0.45
$\tau_1(ps)$	1855	985	522
$\tau_2(ps)$	0.17	0.35	~0.0
$\tau_3(ps)$	22	19.8	5.3
$\bar{\tau}(ps)$	910	324	75

Survival Time Correlation:

$$C_R(t) = \sum_{j=1}^{N} \frac{1}{T-t} \sum_{t'=0}^{T-t} P_{R,j}\left(t, t+t'; t^*\right)$$

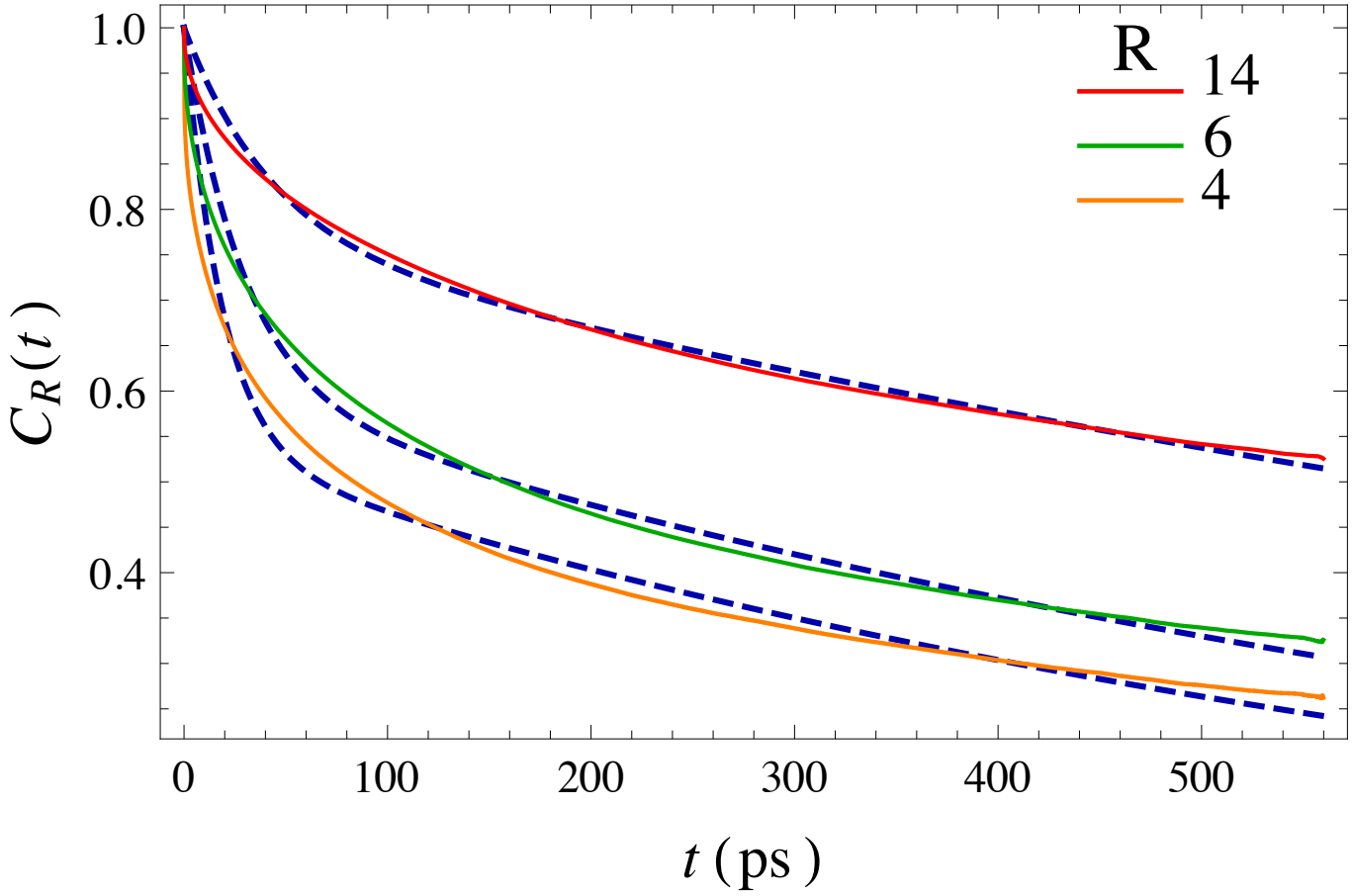


① : if $t' \leqslant t^* \Rightarrow P_{R,1}(t, t+t', t^*) = 1$

$$\begin{cases} t^* = 0 : & \text{Continuous} \\ t^* = \infty : & \text{Intermittent} \end{cases}$$

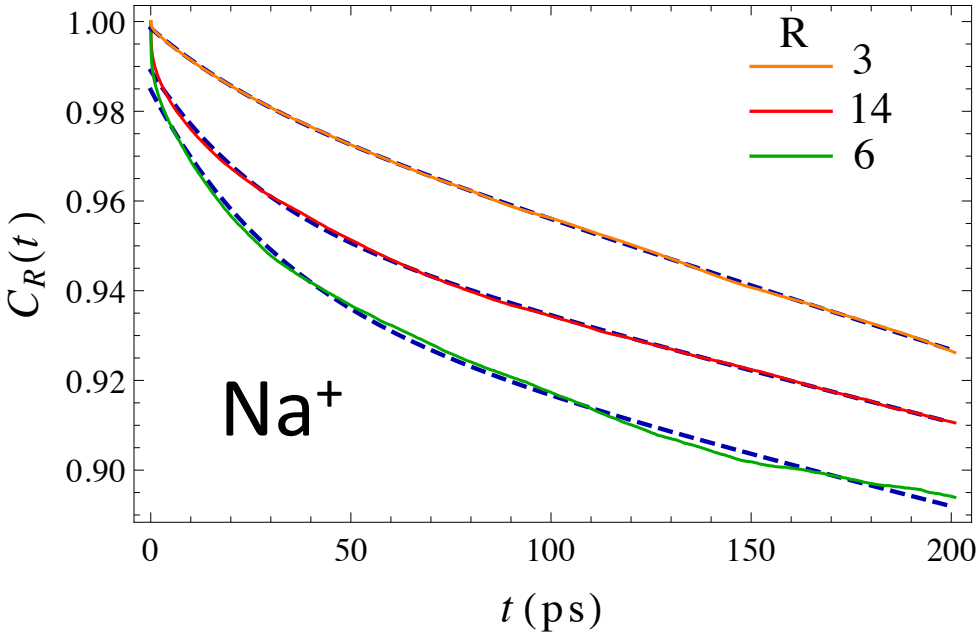
J. Phys. Chem., **87** (25), 5071–5083, (1983).

Water Survival probability:

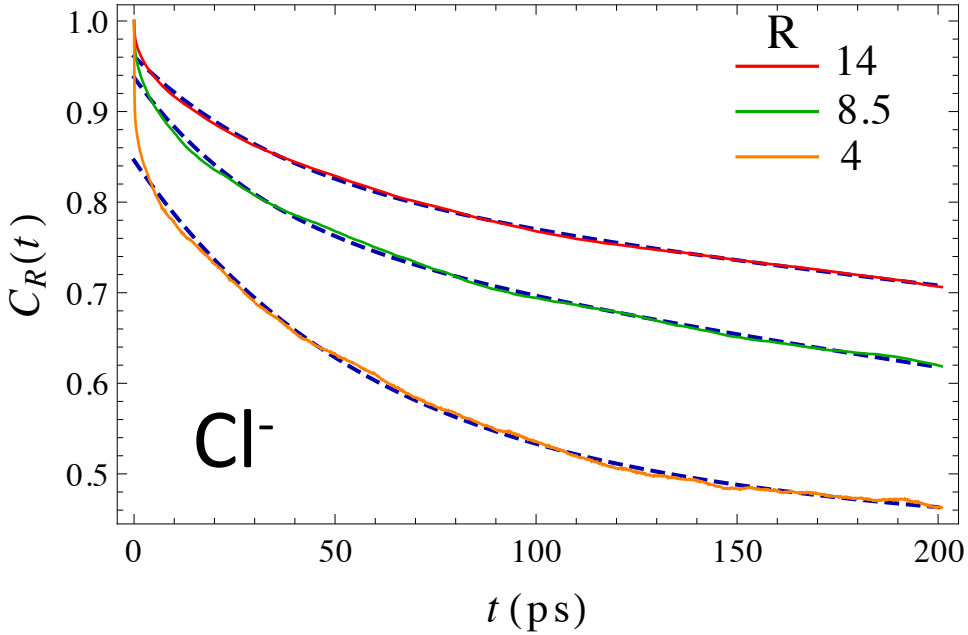


	A	B	$\tau_1(ps)$	$\tau_2(ps)$	$\bar{\tau}(ps)$
R 4	0.53	0.46	705	18.7	386
R 6	0.6	0.4	827	29	511
R 14	0.77	0.22	1382	42	1076

Ions Survival probability:



	R 3	R 6	R 14
A	0.98	0.93	0.95
B	0.01	0.04	0.03
$\tau_1(ps)$	3262	3952	4003
$\tau_2(ps)$	27	31	28
$\bar{\tau}(ps)$	3215	3709	3833



	R 4	R 8.5	R 14
A	0.5	0.78	0.81
B	0.34	0.16	0.14
$\tau_1(ps)$	2108	901	1380
$\tau_2(ps)$	55.5	31	37
$\bar{\tau}(ps)$	1071	700	1134

Electric Conductivity:

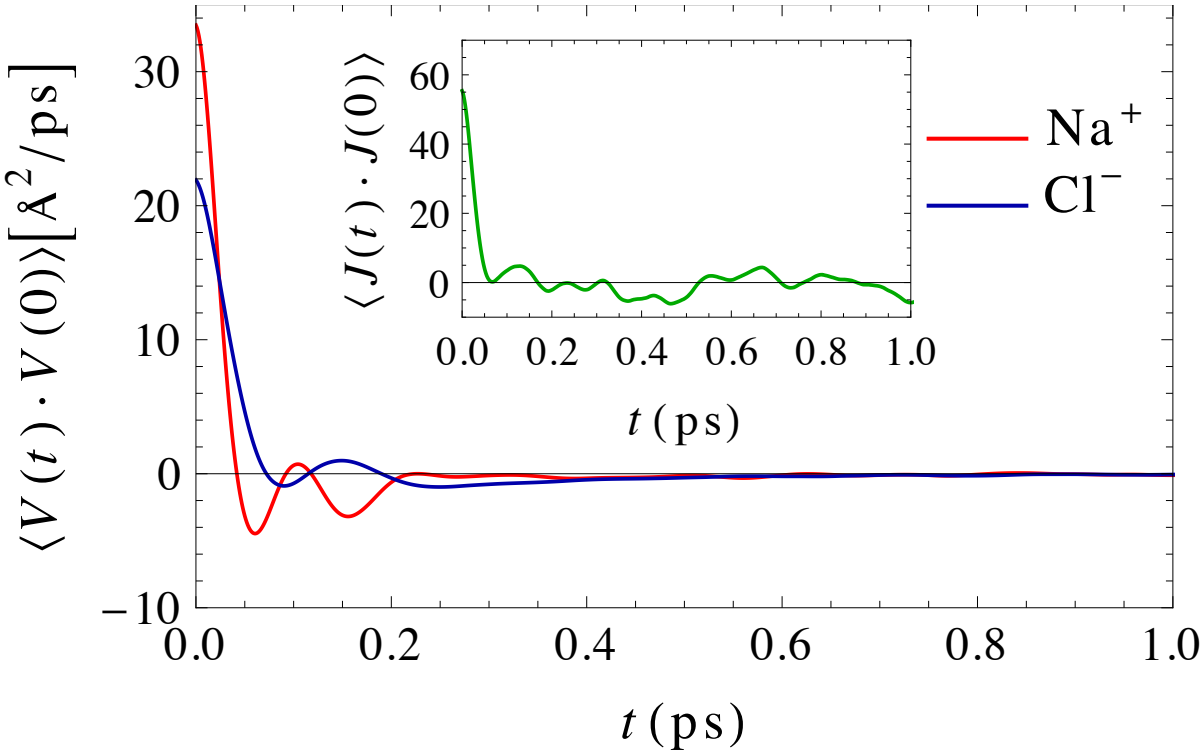
$$\sigma = \frac{1}{3k_B TV}\int_0^\infty \left\langle \mathbf{J}(t)\cdot\mathbf{J}(0)\right\rangle dt$$

$$\mathbf{J}(t) = e\left(\sum_{i_{cat}=1}^{N_{cat}} z_{cat}\mathbf{v}_{i_{cat}}(t) + \sum_{i_{an}=1}^{N_{an}} z_{an}\mathbf{v}_{i_{an}}(t)\right)$$

Nernst-Einstein

$$\sigma = \frac{e^2}{k_B TV}\left(N_{cat}D_{cat} + N_{an}D_{an}\right)$$

Electric Conductivity of MT:



	Conduct. (S/m)	D_{Na}($\text{Å}^2 ps^{-1}$)	D_{Cl}($\text{Å}^2 ps^{-1}$)
Within 3	0.06	0.033	
All	0.76	0.072	0.16
All not within 3	0.68	0.10	0.16
All not within 5	0.42	0.11	0.17

Biophys. J., **90** (10), 3739-48 (2006)

Counterion Condensation; Poisson-Boltzmann:

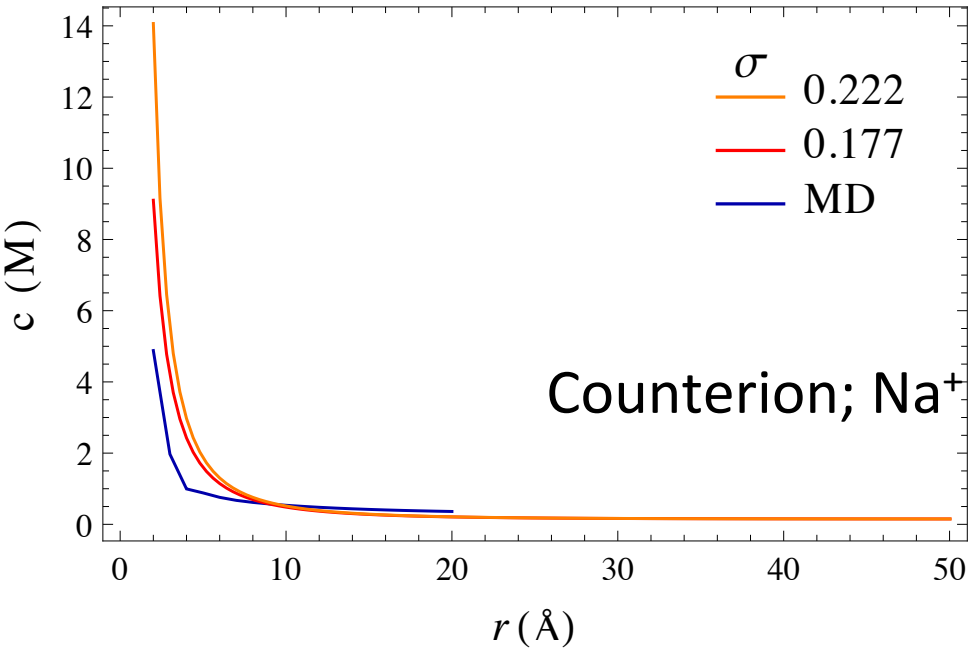
$$\nabla^2\psi(\mathbf{r}) = -4\pi\frac{\rho}{\varepsilon}; \qquad \rho = z_-n_- + z_+n_+, \qquad n_\pm = n_\pm^0 e^{-\frac{z_\pm\psi}{k_BT}}$$

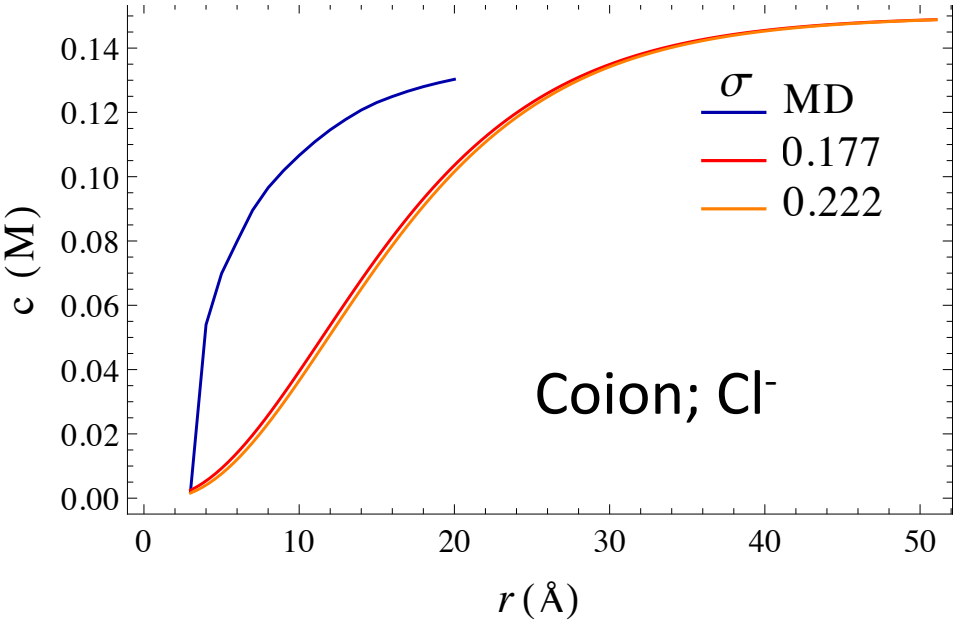
$$\nabla^2\psi(\mathbf{r}) = \frac{8\pi e n^0}{\varepsilon_W} Sinh\left(\frac{e\psi(\mathbf{r})}{k_BT}\right) \qquad \lambda_D = \sqrt{\frac{8\pi e^2 n^0}{\varepsilon_W k_BT}}$$

$$\left.\frac{d\psi}{dz}\right|_{z=boundary} = -\frac{4\pi}{\varepsilon_W}\sigma; \qquad \psi|_\infty = 0$$

Intermolecular and Surface Forces, Academic Press, (2011).

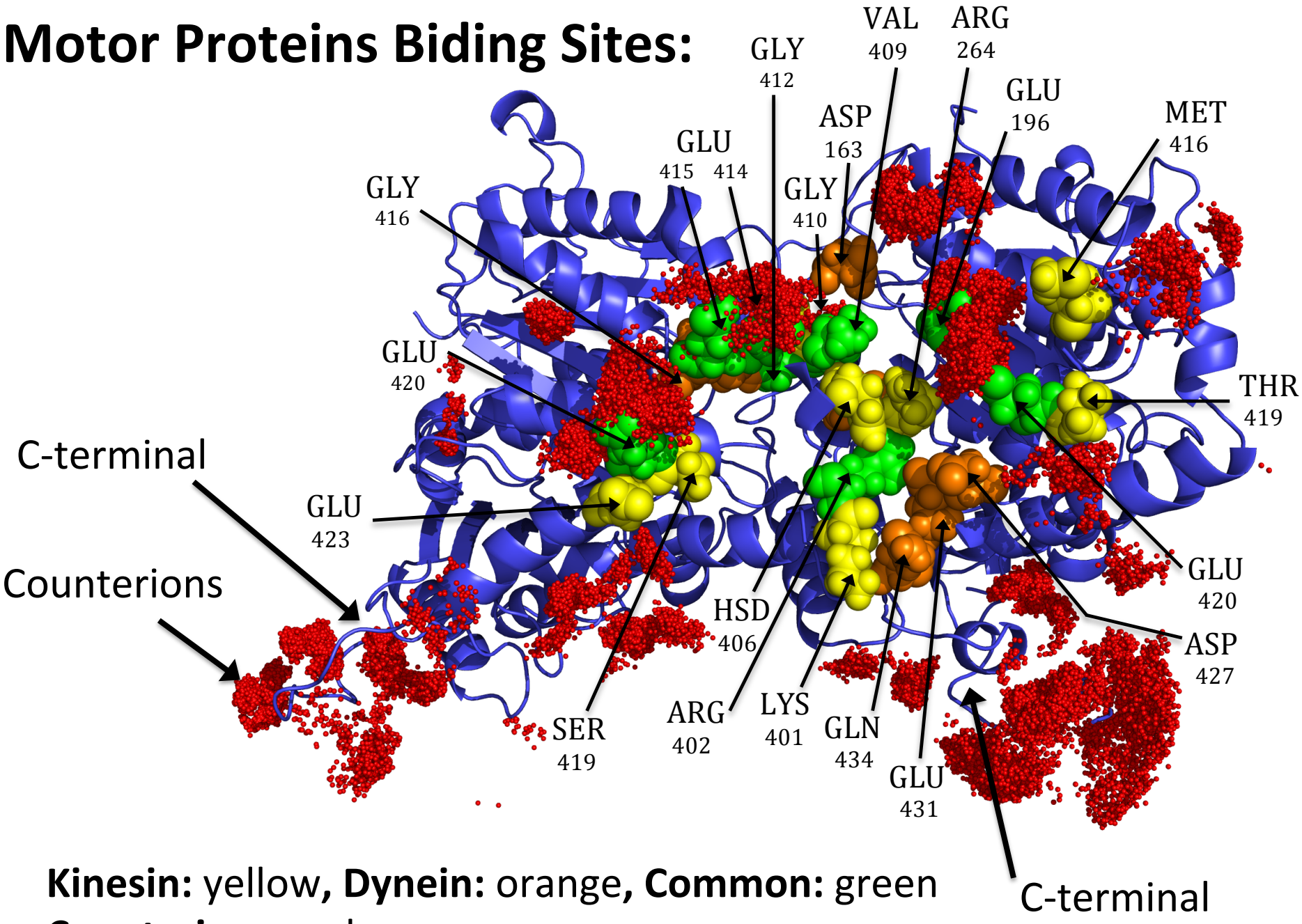
Concentration of Counterion and Coion:





Biological Implication:

Motor Proteins Biding Sites:



Kinesin: yellow**, Dynein:** orange**, Common:** green
Counterions: red

Kinesin and Tubulin contact residue map:

α	LYS 401	ARG 402	HIS 406	VAL 409	GLY 410	GLU 411	GLY 412	GLU 414	GLU 415	SER 419	GLU 420	GLU 423
H	GLU 287	ARG 350	THR 276	LYS 273	LYS 266	LYS 266	LEU 265	LYS 261	ARG 350	ARG 346	ARG 346	LYS 48

β	GLU 196	ARG 264	MET 416	THR 419	GLU 420
H	ARG 307	ASP 308	HIS 171	PRO 172	ARG 307

Residues within 4 Å distance on Kinesin head and α-β tubulin dimer.

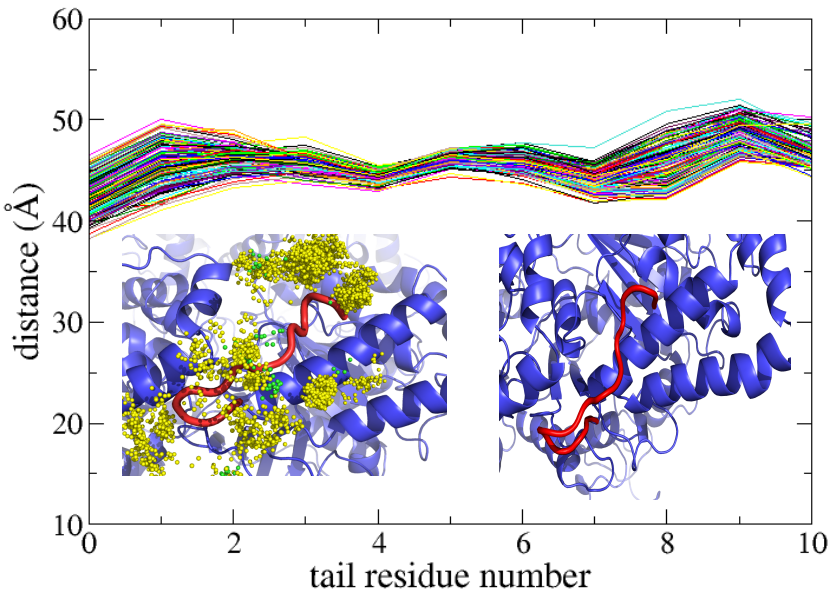
Dynein and Tubulin contact residue map:

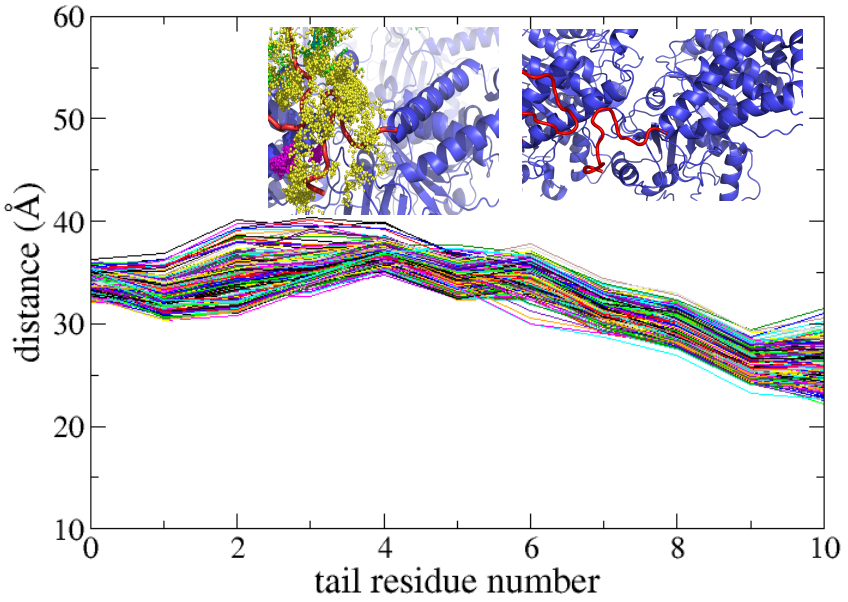
α	ARG 402	VAL 409	GLY 410	GLY 412	MET 413	GLU 414	GLU 415	GLY 416	GLU 420
H	GLU 45	PRO 53	ASN 51	PRO 53	PRO 53	ARG 123	ALA 124	ARG 123	ARG 123

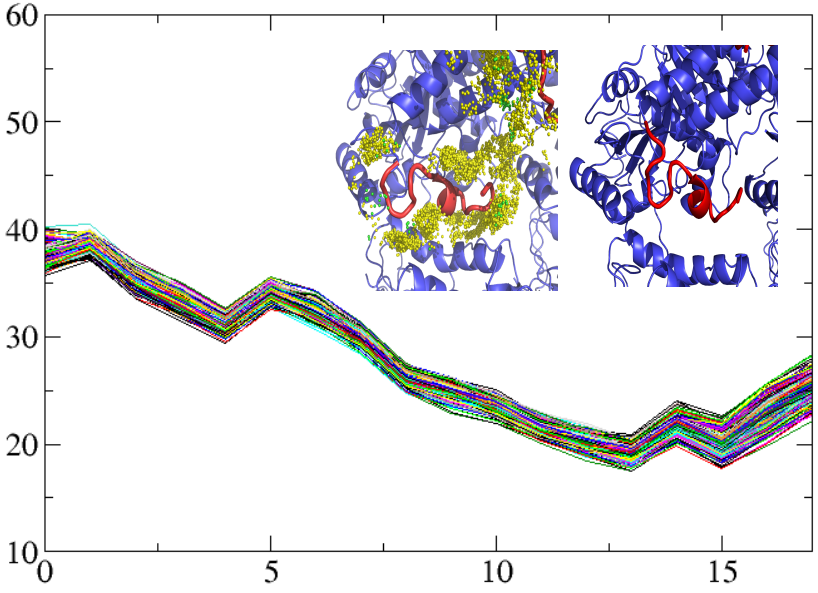
β	ASP 163	GLU 196	PRO 263	GLU 420	ASP 427	GLU 431	GLN 434
H	LYS 75	ARG 47	SER 48	GLU 84	LYS 40	GLN 41	GLN 41

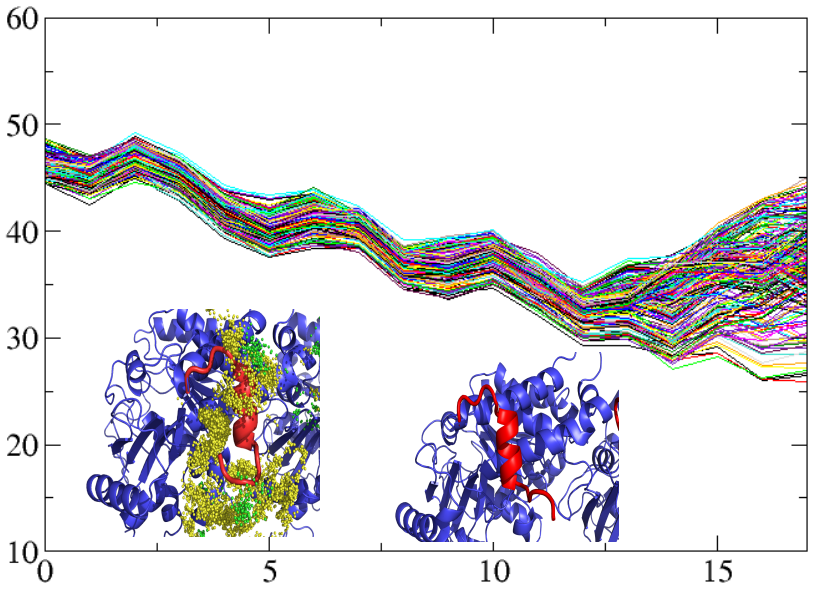
Residues within 4 Å distance on Dynein head and α-β tubulin dimer.

Conformation, counterions and distance (from MT) of the C-terminal tail

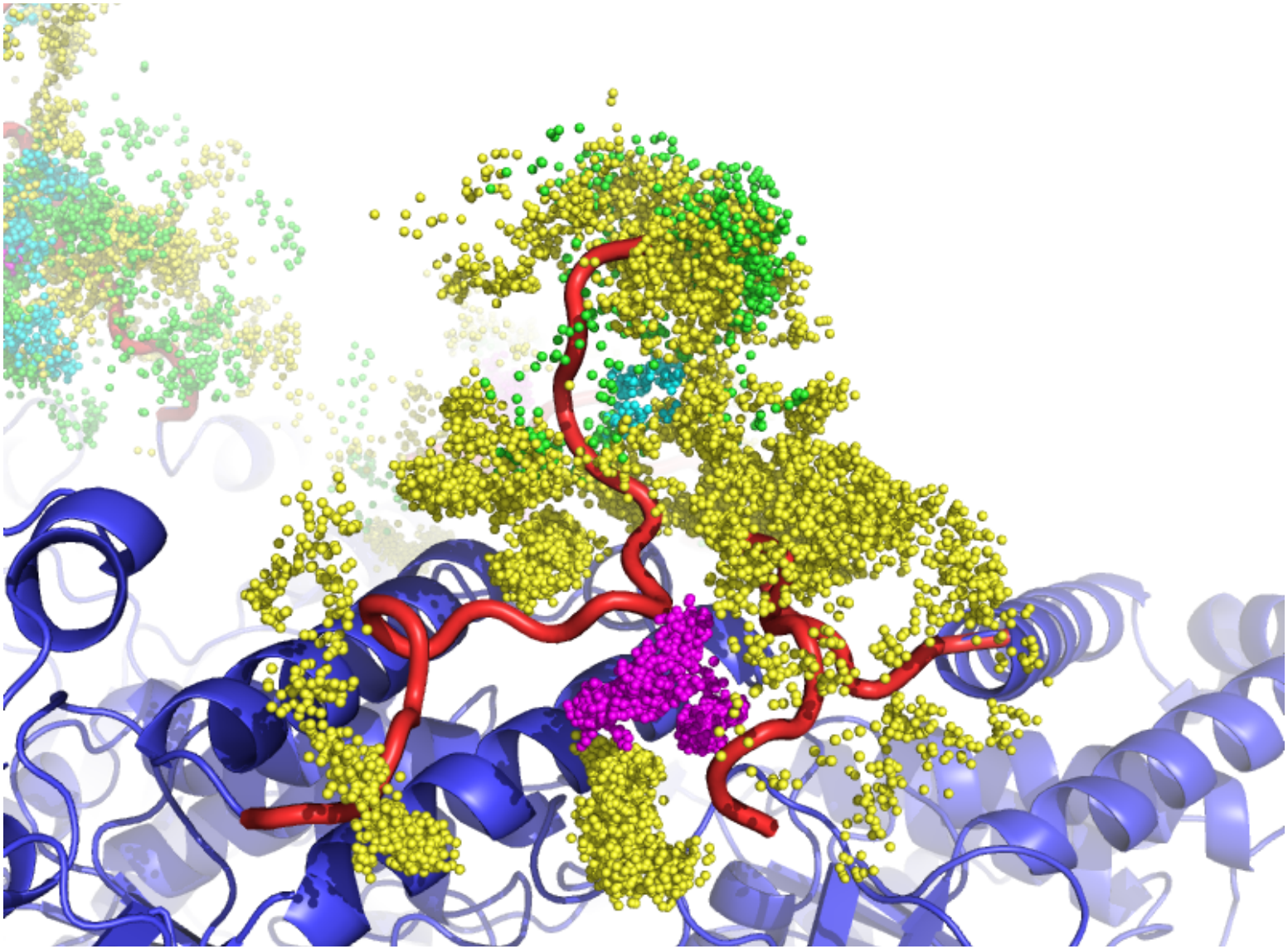




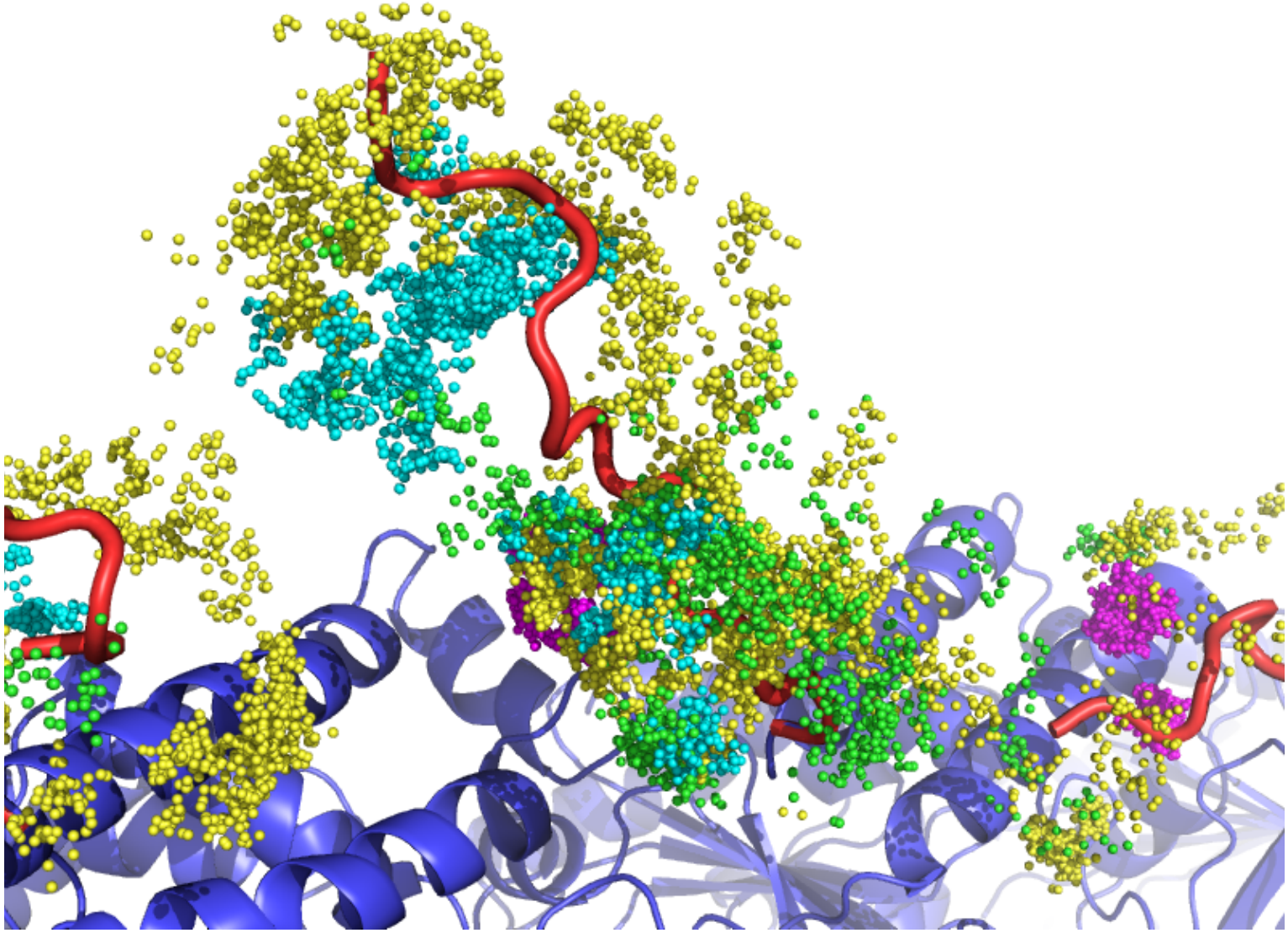




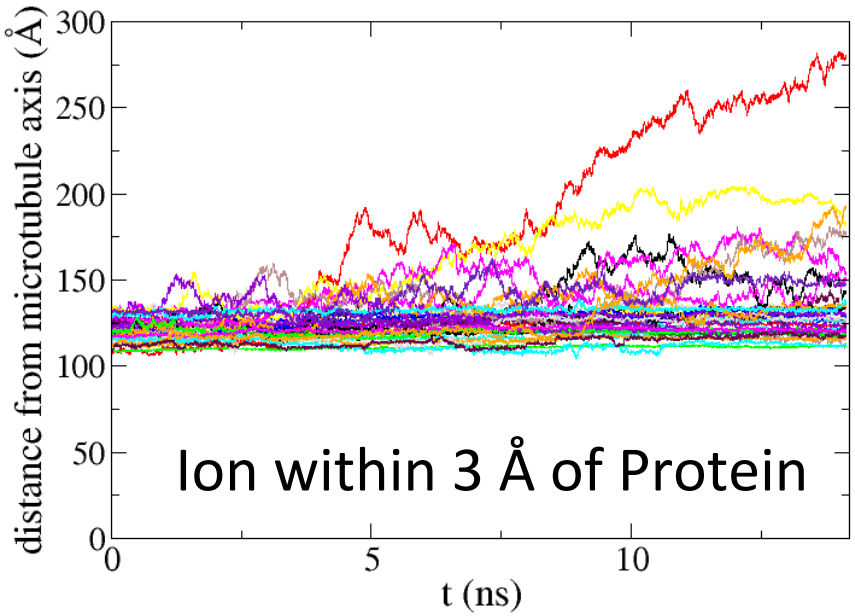
Possible scenarios for C-terminals interaction:

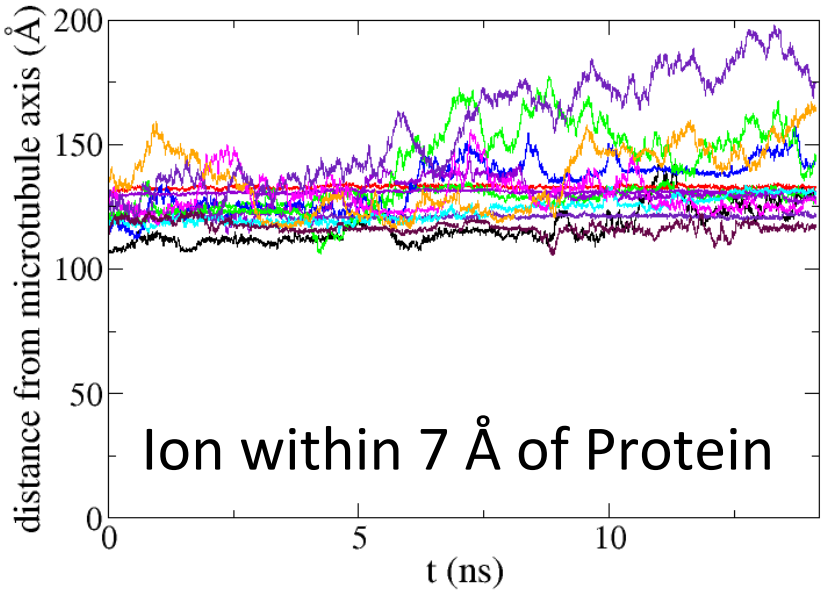


Sodium: yellow, Calcium: magenta, Magnesium: Cyan, and Chloride: Green



Release and Adsorb of Sodium Ion :





Thank you