The Role of Long-Range Forces in Porin Channel Conduction

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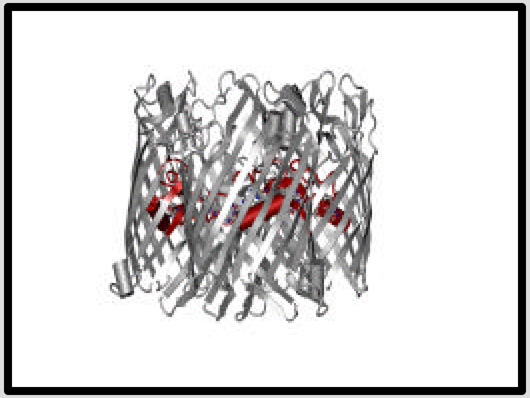
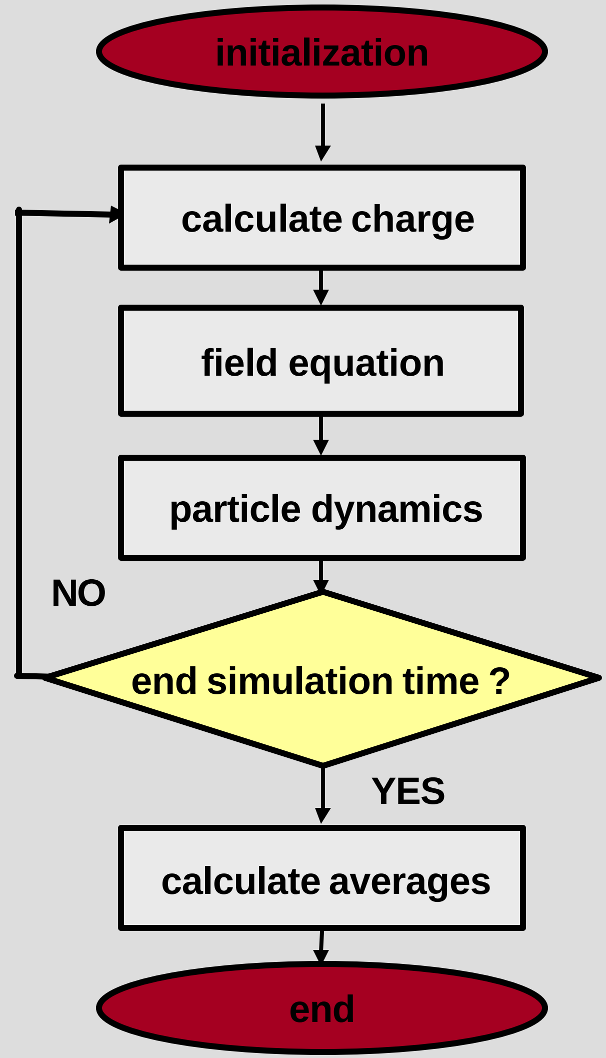
Introduction



Motivation: Examine the influence of a fully self-consistent force field scheme on conduction in ion channels.

- **Particle-Based Simulation Tool**
  - Brownian Dynamics
  - Force-Field Scheme
- **Computational Domain/Results**
  - Electrolyte/Lipid System
  - OmpF Porin Channel
- **Conclusion/Future Work**

Particle-Based Brownian Dynamics Simulation



Langevin Equation

$$m_i \frac{d\vec{v}_i(t)}{dt} = -m_i g \vec{v}_i(t) + \vec{F}_i(\vec{r}_i(t)) + \vec{B}_i(t)$$

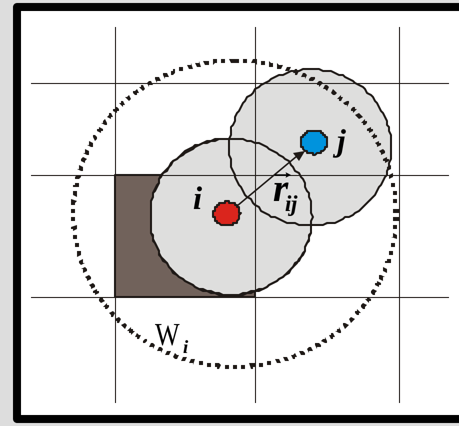
Friction coefficient

$$g = \frac{b}{m} = \frac{k_B T}{mD}$$

Gaussian white noise

3rd order integration scheme: 20 fs timestep

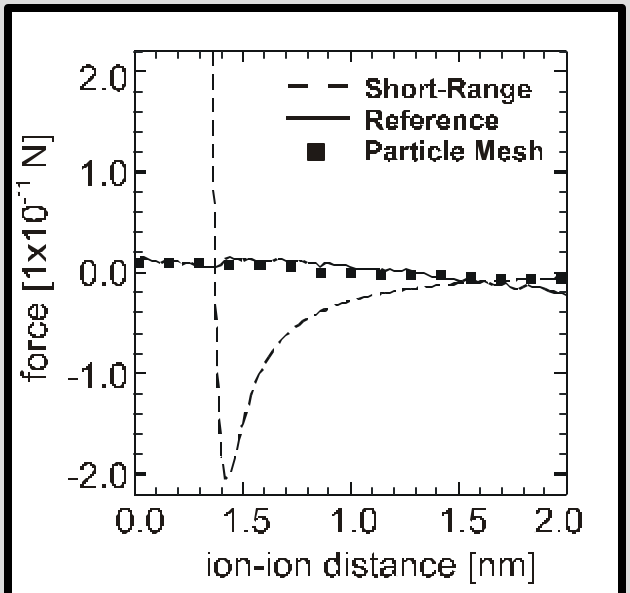
Poisson P³M Force Field Scheme



$$\vec{F}_i = \vec{F}_i^{PM} + \vec{F}_i^{PP}$$

$$\vec{F}_i^{PP} = \vec{F}_i^{C} + \vec{F}_i^{W} - \vec{R}_i$$

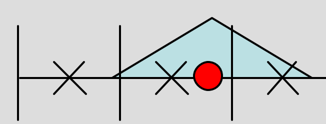
$$\vec{F}_i^{PM}(\vec{r}_p) = -q\nabla f(\vec{r}_p)$$



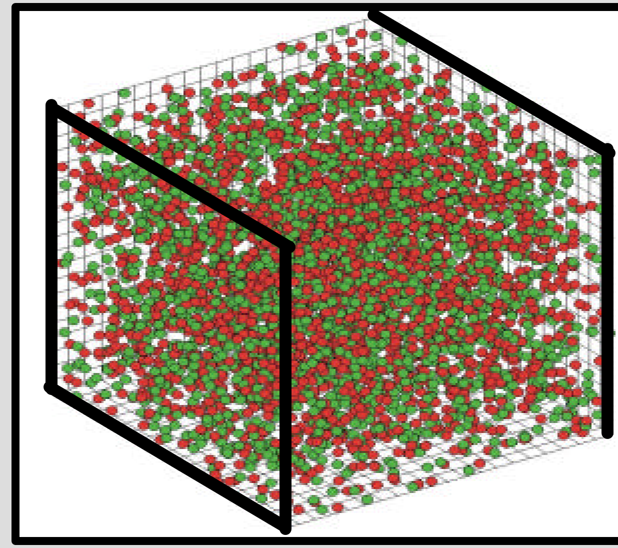
Interaction between cation and anion in a 0.5 M KCl solution.

TSC

$$S(r) = \begin{cases} \frac{48}{\pi a^4}\left(\frac{a}{2} - r\right) & r < a/2 \\ 0 & \text{else} \end{cases}$$



Electrolyte Solution



Boundary Conditions

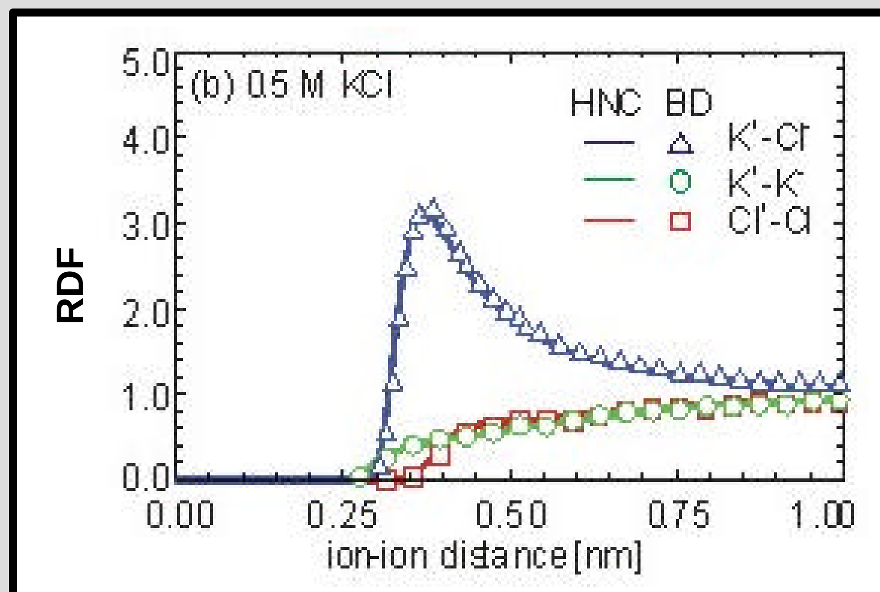
Dirichlet: $f(i,j,k) = V_A$

Neumann: $\frac{\partial f(i,j,k)}{\partial n} = 0$

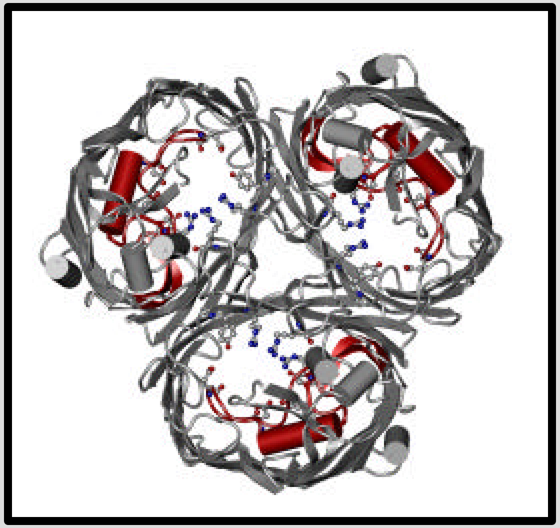
Thermodynamic Properties

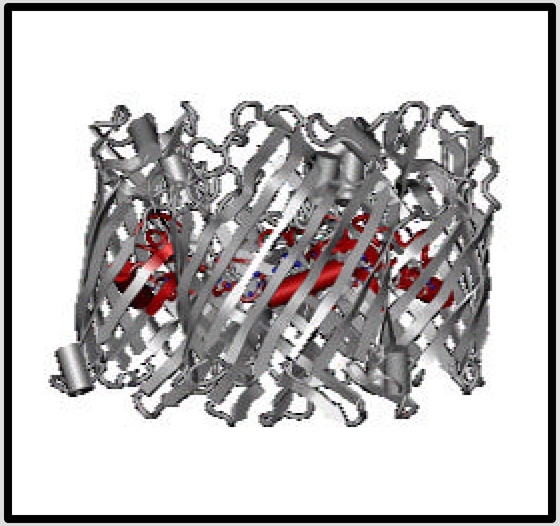
Radial distribution function

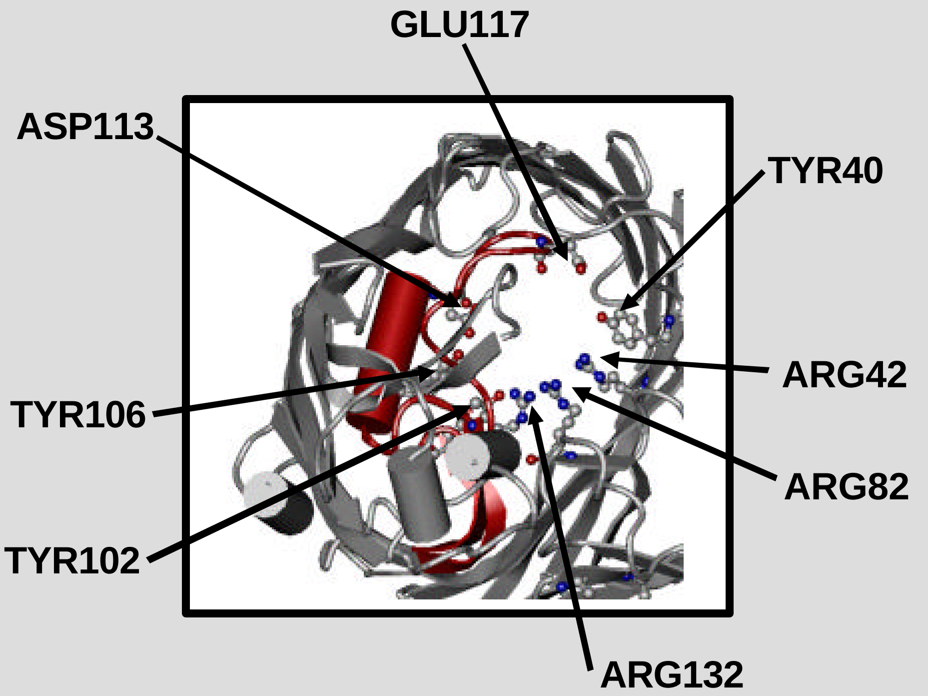
$$g(r) = \frac{1}{\rho N}\left\langle \sum_i \sum_{j \neq i} \delta\left(\vec{r} - \vec{r}_{ij}\right)\right\rangle$$



OmpF Porin Channel





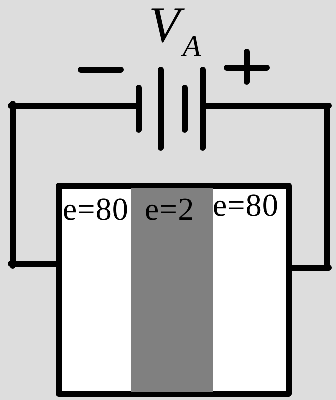


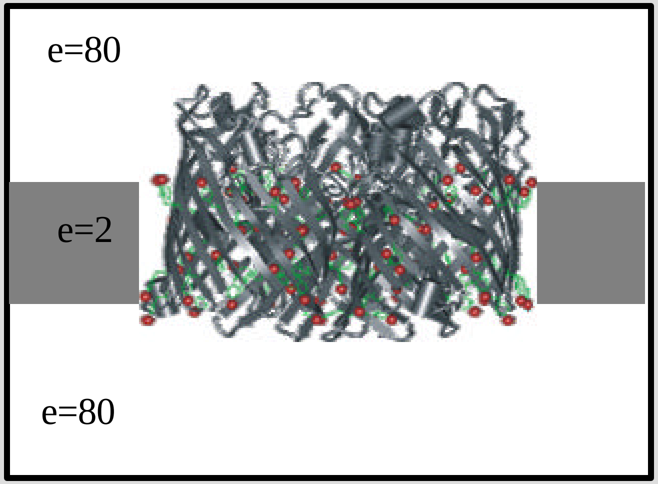
Atomic structure: 2OMF.pdb, *S. W. Cowen et al. Nature 358 (1992)*.

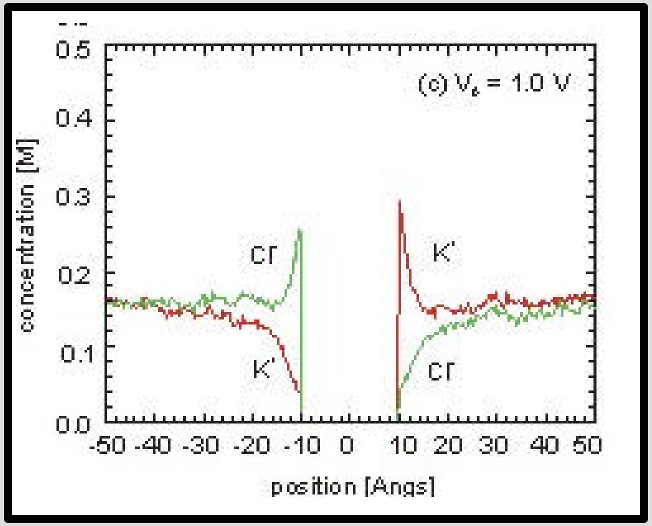
Charge distribution: GROMACS

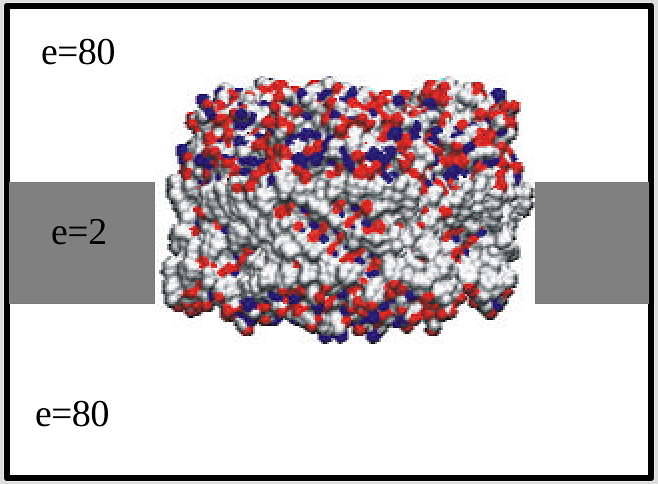
pH=7; total charge: -30*e*

Lipid Membrane/Channel System

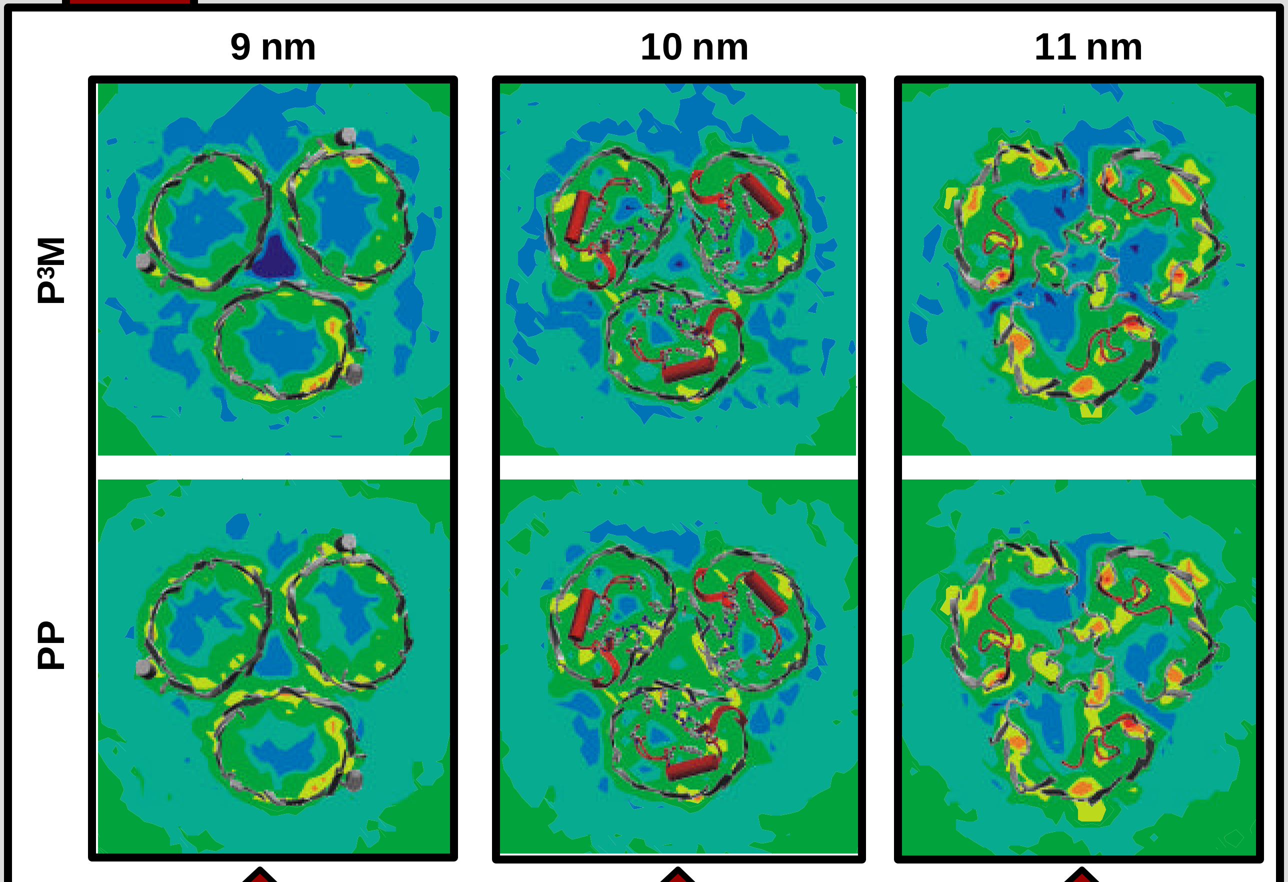


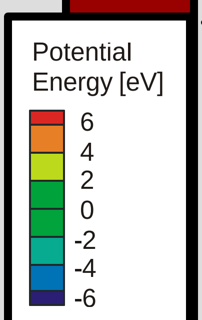


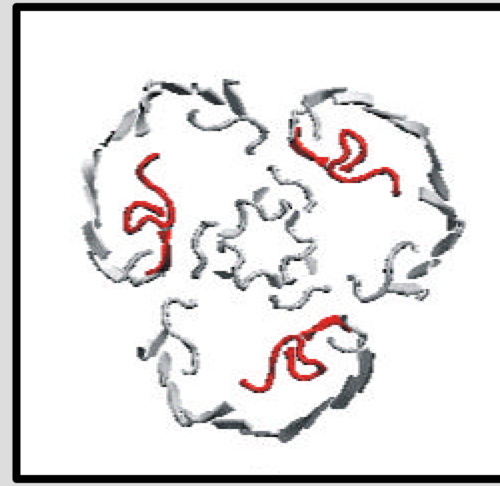


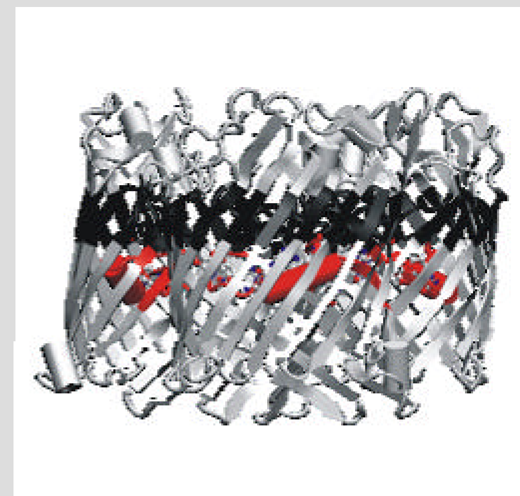


Potential Energy Profile I: P^3M vs PP





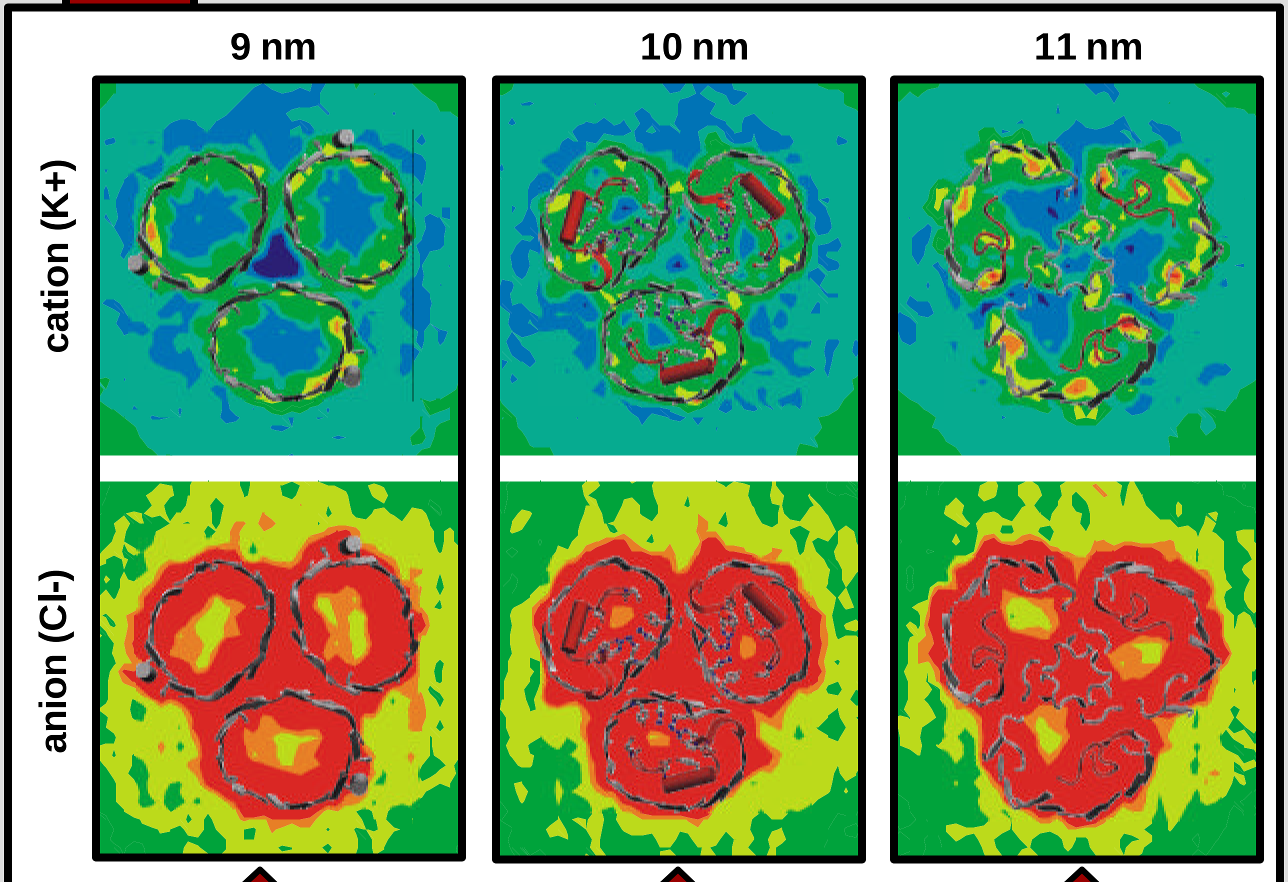


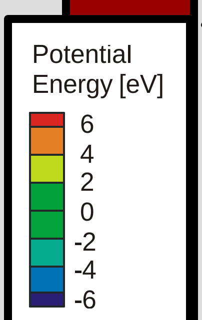


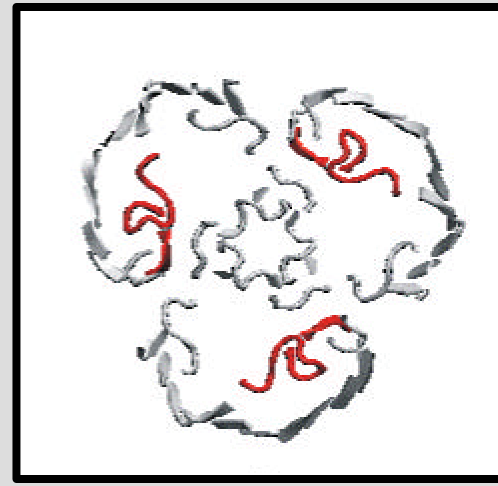
V_A=0.0 V

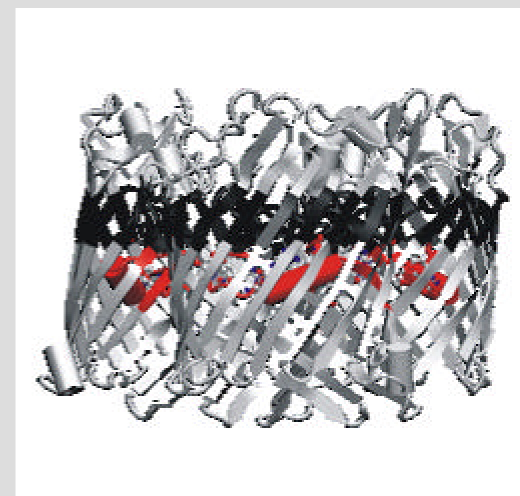
cation (K^+)

Potential Energy Profile II: cation vs anion



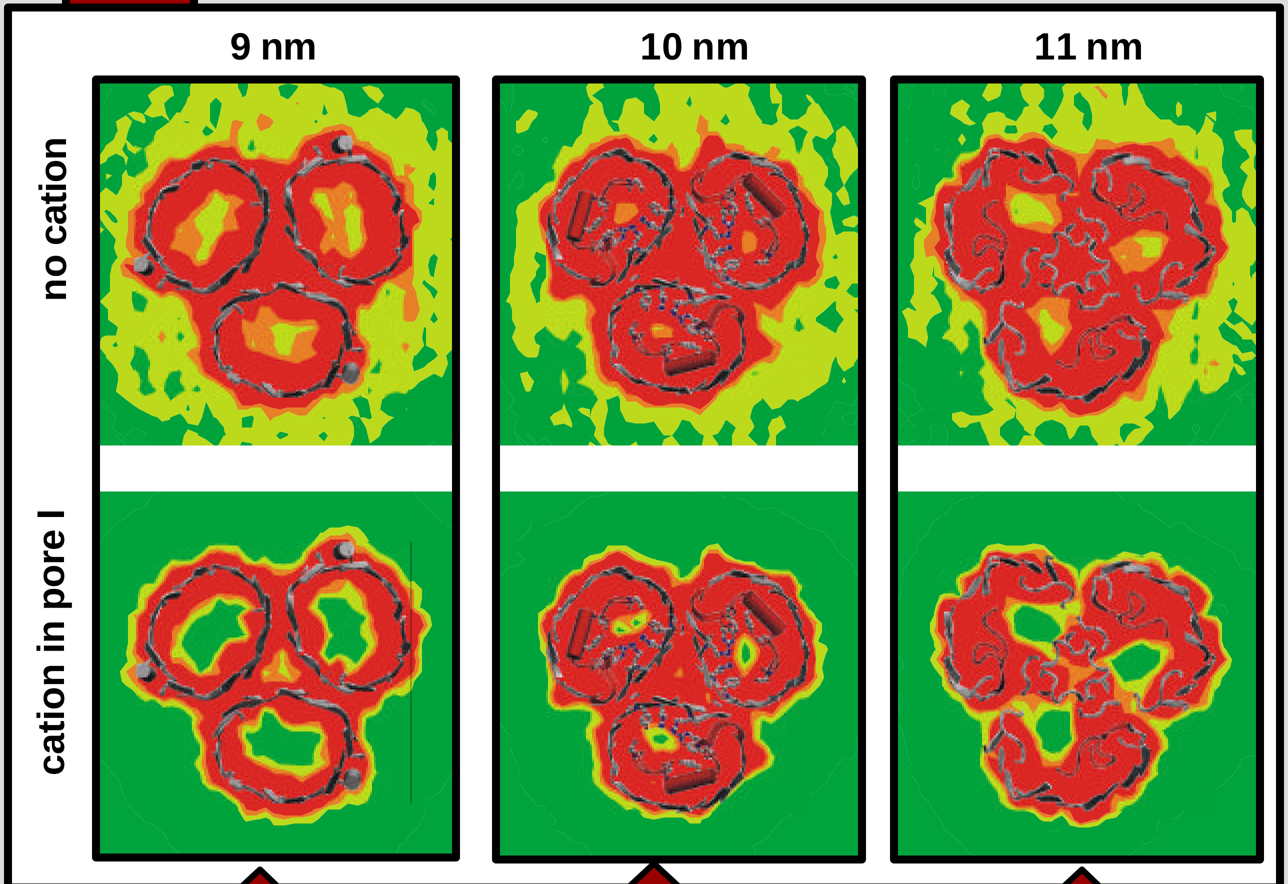


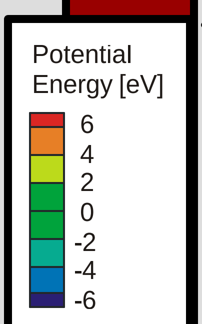


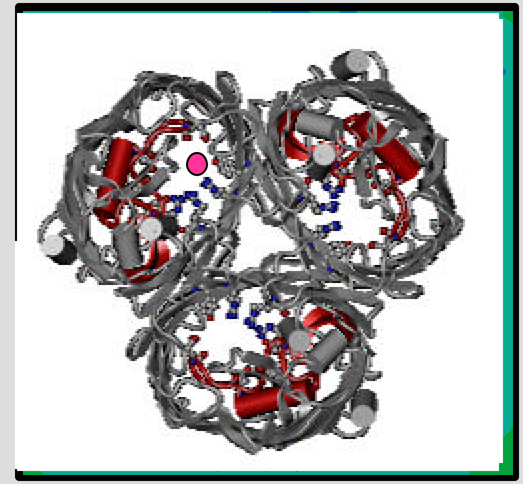


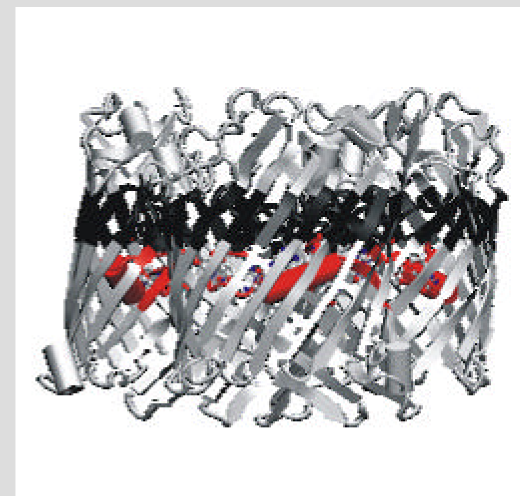
V_A=0.0 V P^3M

Potential Energy Profile III: cation in pore







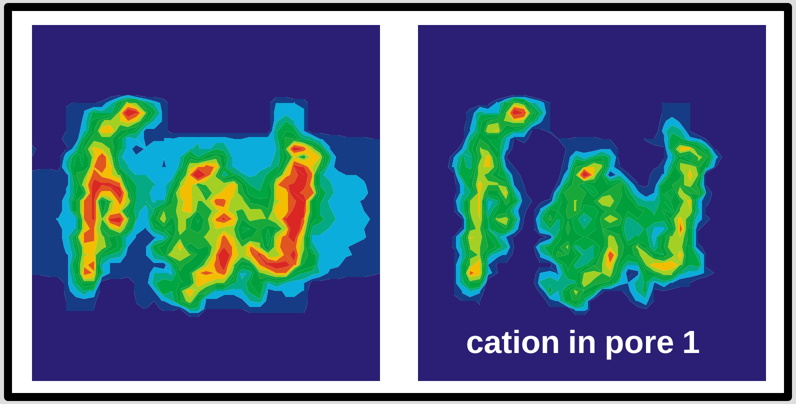


V_A=0.0 V P^3M

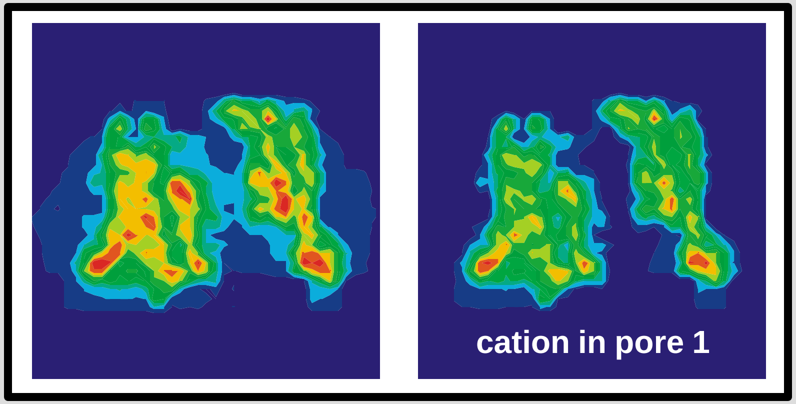
anion (Cl^+)

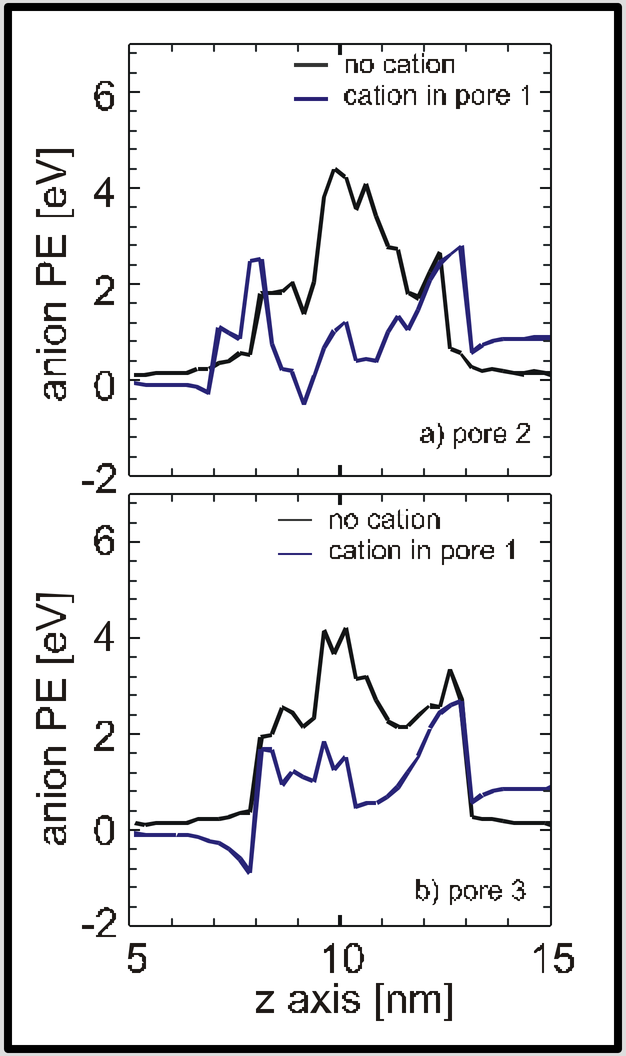
Minimum potential energy pathway

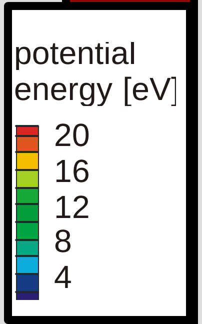
pore 2



pore 3





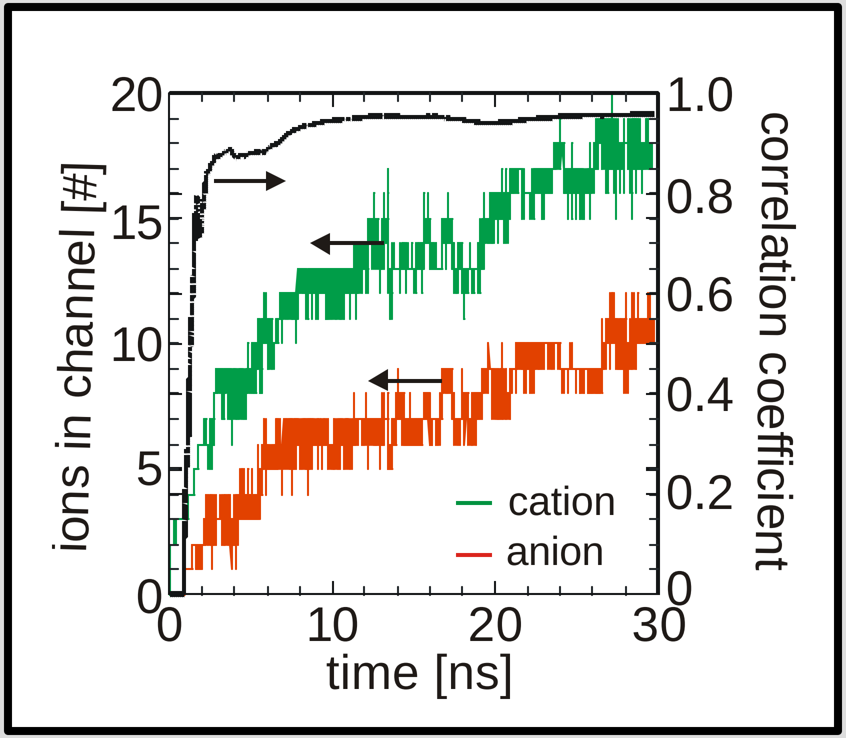


Channel flux correlation

V_A=1.0 V
100 mM KCl

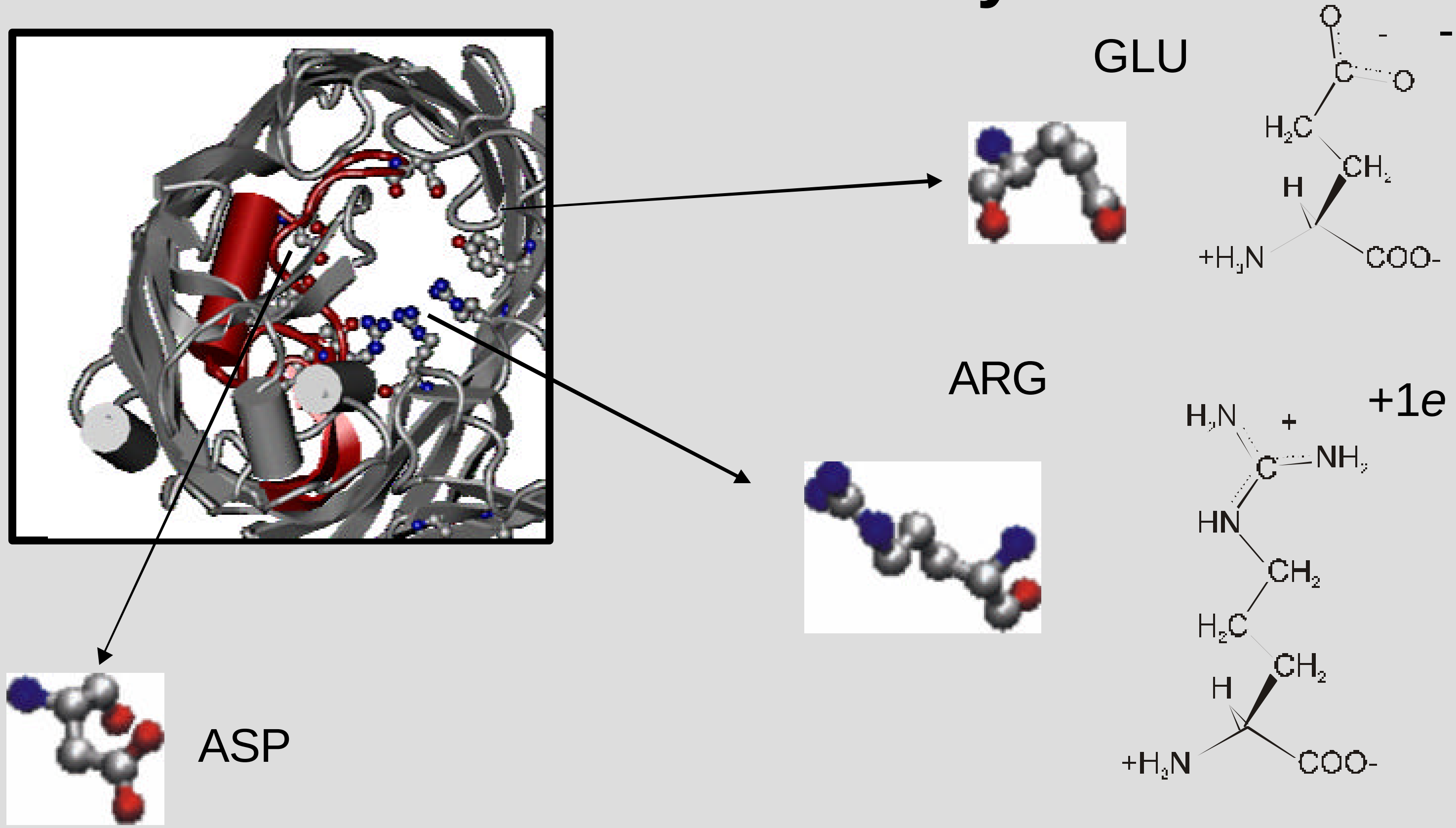
correlation coefficient

$$r_{ac} = \frac{s_{ac}^{2}}{s_a s_c} = \frac{\langle N_a N_c \rangle - \langle N_a \rangle \langle N_c \rangle}{\sqrt{\langle N_a^2 \rangle - \langle N_a \rangle^2}\sqrt{\langle N_c^2 \rangle - \langle N_c \rangle^2}}$$

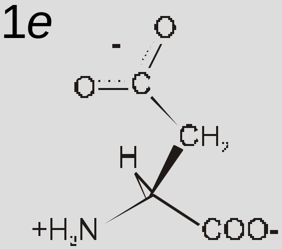


- **Ion-ion pairing within a single pore is observed in BD/MD simulations (W. Im *et al*. J. Mol. Biol. v322 2002).**

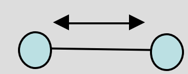
Channel Flexibility



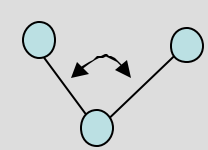
-1*e*



- Bending $V(r_{ij}) = \frac{k_{ij}}{2}\left(r_{ij} - r_{ij,0}\right)^2$



- Rotation $V(q_{ijk}) = \frac{k_{ijk}^{q}}{2}\left(q_{ijk} - q_{ijk,0}\right)^2$



Conclusion

<u>For the specific charge distribution and dielectric constants:</u>

- The long-range interactions are apparent at zero bias.
- The presence of ions in one pore can change the electrostatic profile seen by charges in the other pores.
- The number of positive and negative charges in the 3 pores shows evidence of correlation.

Future Work

- Different charge distribution scheme: *e.g.* CHARM
- Different dielectric constants
- Current-voltage characteristics
- Flexible channel structure