# A Coupled 3-D PNP/ECP Model for Ion Transport in Biological Ion Channels

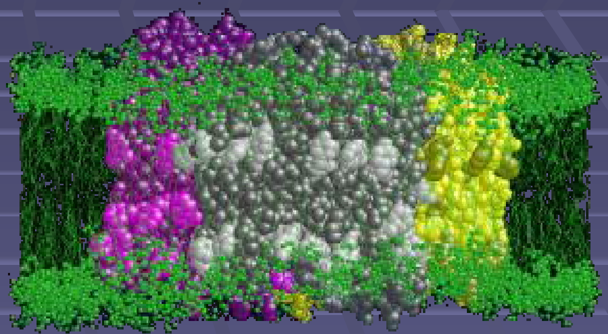
Zhicheng Yang, Trudy. A. van der Straaten and Umberto. Ravaioli

Beckman Institute for Advanced Science and Technology

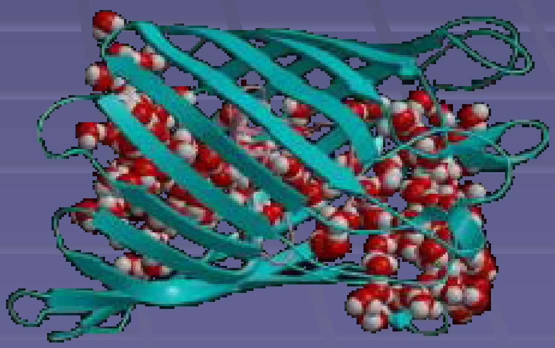
University of Illinois at Urbana-Champaign

# What are ion channels?

- Natural nanotubes in biological cells
- Made of proteins
- With highly localized charge inside the channel
- Controls the flow of ions and water in and out the cells
- Selectivity and Gating



*Porin trimer*



*A porin monomer filled with water*

# Why PNP?

- Molecular Dynamics (MD)
  - Most popular and accurate
  - Limits simulation times to ~100ns
  - Steady-state conduction occurs over much longer timescales
- Poisson-Nernst-Planck (PNP)
  - Known as Drift-Diffusion theory
  - Continuum model
  - Widely used in device simulation
  - Much less computational cost

# Conventional PNP model

- Poisson equation

$$\varepsilon_0 \nabla(\varepsilon(r)\nabla\phi(r)) = -\sum_i z_i e n_i(r) - \rho_{fixed}(r)$$

- Nernst-Planck equation:

$$J_i(r) = -\frac{z_i e}{K_B T} D_i(r)\rho_i(r)\nabla\mu_i^{id}(r)$$

$$\mu_i^{id}(r) = z_i s_i \phi(r) + kT\ln[\rho_i(r)]$$

- Above coupled equations are solve self-consistently

# Problem with PNP

- Continuum model treat ions as a continuum fluid of point particles
- Ignores the size of ions and water molecules
- Ignores non-singular distribution of charge on the ion

  Result:
  - Overestimate Coulomb screening and ion packing
  - Cannot describe ion selectivity

**Free Energy Model for Inhomogeneous Fluid Mixtures:**
**Yukawa-Charged Hard Sphere, General Interactions, and Plasmas**

Yaakov. Rosenfeld, *J. Chem. Phys*, **98**, 8126 (1993).

&

D. Gillespie, W. Nonner, and R. S. Eisenberg, *J. Phys*. **14** 12129 (2002).

# Excess Chemical Potential (ECP)

- ECP is introduced to add these additional effects to the PNP model
- Modified Nernst-Planck equation:

$$J_i(r) = -\frac{z_i e}{K_B T} D_i(r)\rho_i(r)\nabla(\mu_i^{id}(r) + \mu_i^{ex}(r))$$

Where

$$\mu_i^{id}(r) = z_i e\phi(r) + k_B T \ln[\rho_i(r)]$$

$$\mu_i^{ex}(r) = \mu_i^{HS}(r) + \mu_i^{ES}(r)$$

# Excess Chemical Potential (ECP)

- Two components of ECP
  - Hard Sphere (HS)
    - Finite-sized ions
    - Present of water molecules
  - Electrostatic component (ES)
    - Non-singular charge distribution on the ion
- ECP is a function of ion and water densities and can be calculated by DFT

# Coupled PNP/ECP equations

Modified Nernst-Planck equation with the ECP correction:

$$J_i(r) = -\frac{z_i e}{K_B T} D_i(r)\rho_i(r)\nabla(\mu_i^{id}(r) + \mu_i^{ex}(r))$$

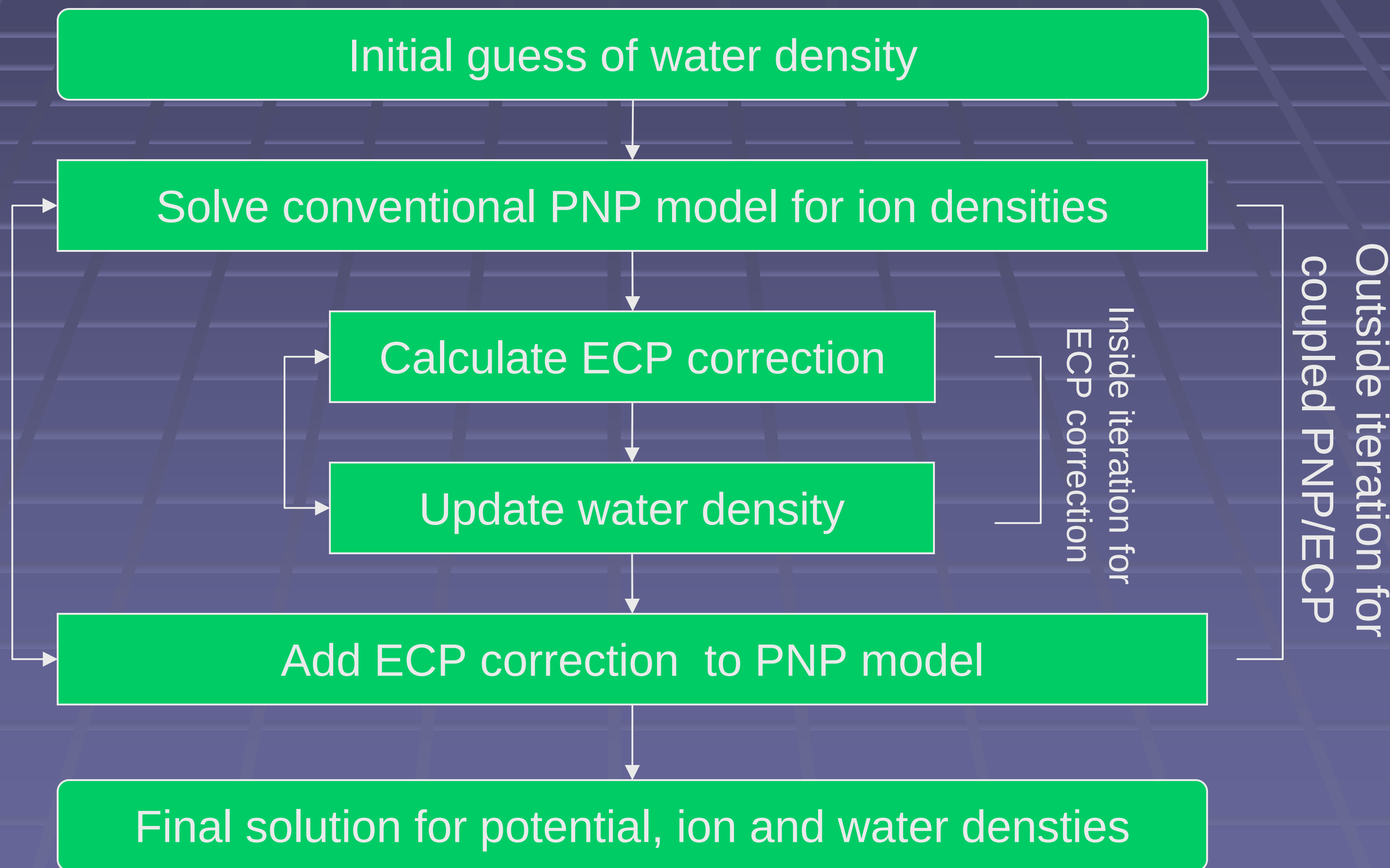
Here $\mu_i^{ex}(r) = \mu_i^{HS}(r) + \mu_i^{ES}(r)$ is a function of $\rho_i(r)$ $\rho_{H_2O}(r)$

Next slide shows how to calculate $u_i^{ex}$ in detail

Poisson equation:

$$\varepsilon_0 \nabla(\varepsilon(r)\nabla\phi(r)) = -\sum_i z_i e n_i(r) - \rho_{fixed}(r)$$

# Flow chart for PNP/ECP model



# Inside Iteration for ECP correction

$\rho_i(x),\ \rho_{H_2O}(x)_0$

$$\mu_i^{HS}(x)=kT\sum_{\alpha}\int\frac{\partial\Phi_{HS}}{\partial n_{\alpha}}(x')\omega_i^{(\alpha)}(x-x')dx''$$

$$\mu_i^{ES}(x)=\mu_i^{ES}(\rho_k^{ref}(x))+\mu_i^{ES}(\rho_k^{nonref}(x))$$

$\rho_k^{ref}(x)_0 \quad s(x)_0$

$$\rho_k^{ref}(x)_m=\int\bar{\rho}_k(x')_m\,\omega(x',x)dx'$$

$$s(x)_m=1/(2\Gamma(x)_m)$$

$$\rho_k^{ref}(x)_{m+1}=\frac{\rho_k^{ref}(x)_m+\alpha\rho_k^{ref}(x)}{1+\alpha}$$

Converge?

$\mu_i^{ES}(\rho_k^{ref}(x))$

$$\mu_i^{ES}(\rho_k^{nonref}(x))=\frac{z_i e^2}{2\varepsilon\varepsilon_0}\sum_j z_j R_{ij} AVC\left\{\left(r^2\frac{\lambda_i+\lambda_j}{\lambda_i\lambda_j}-\frac{r^3}{2\lambda_i\lambda_j}-\frac{r(\lambda_i-\lambda_j)^2}{2\lambda_i\lambda_j}\right)\Delta\rho_j(\bar{r}+x)\right\}$$

$$u_{H_2O}^{ex}(x)=u_{H_2O}^{HS}(x)+u_{H_2O}^{ES}(x)$$

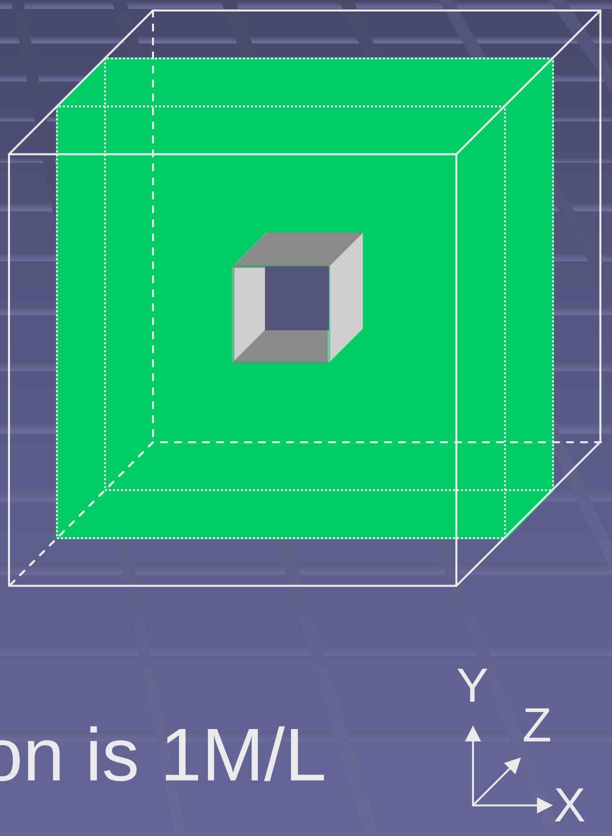
$$kT\ln(\rho_{H_2O}(x))=kT\ln(\rho_{B,H_2O})-u_{H_2O}^{ex}$$

$\rho_{H_2O}$ Converge?

$\rho_{H_2O}(x),\ u_i^{ex}(x),\ u_{H_2O}^{ex}(x)$

# 3D test structure

- Dimension of 96x96x96 Å
- Membrane in the X-Y plane with length 28 Å in Z direction
- Rectangular channel of 8x8x28 Å on the protein wall along Z direction
- Ion concentration at bath region is 1M/L

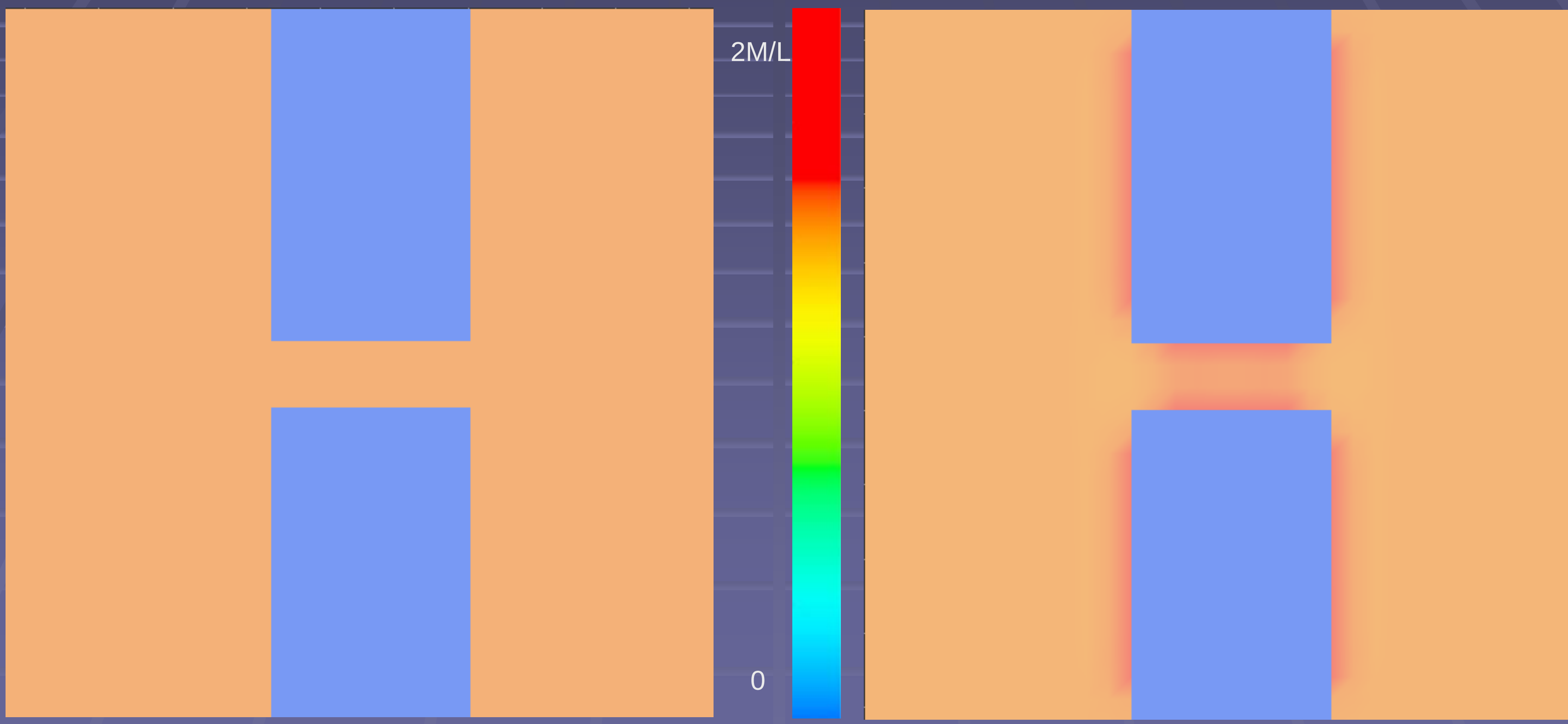


# Cation density without fixed charge

Result from test structure without permanent charge

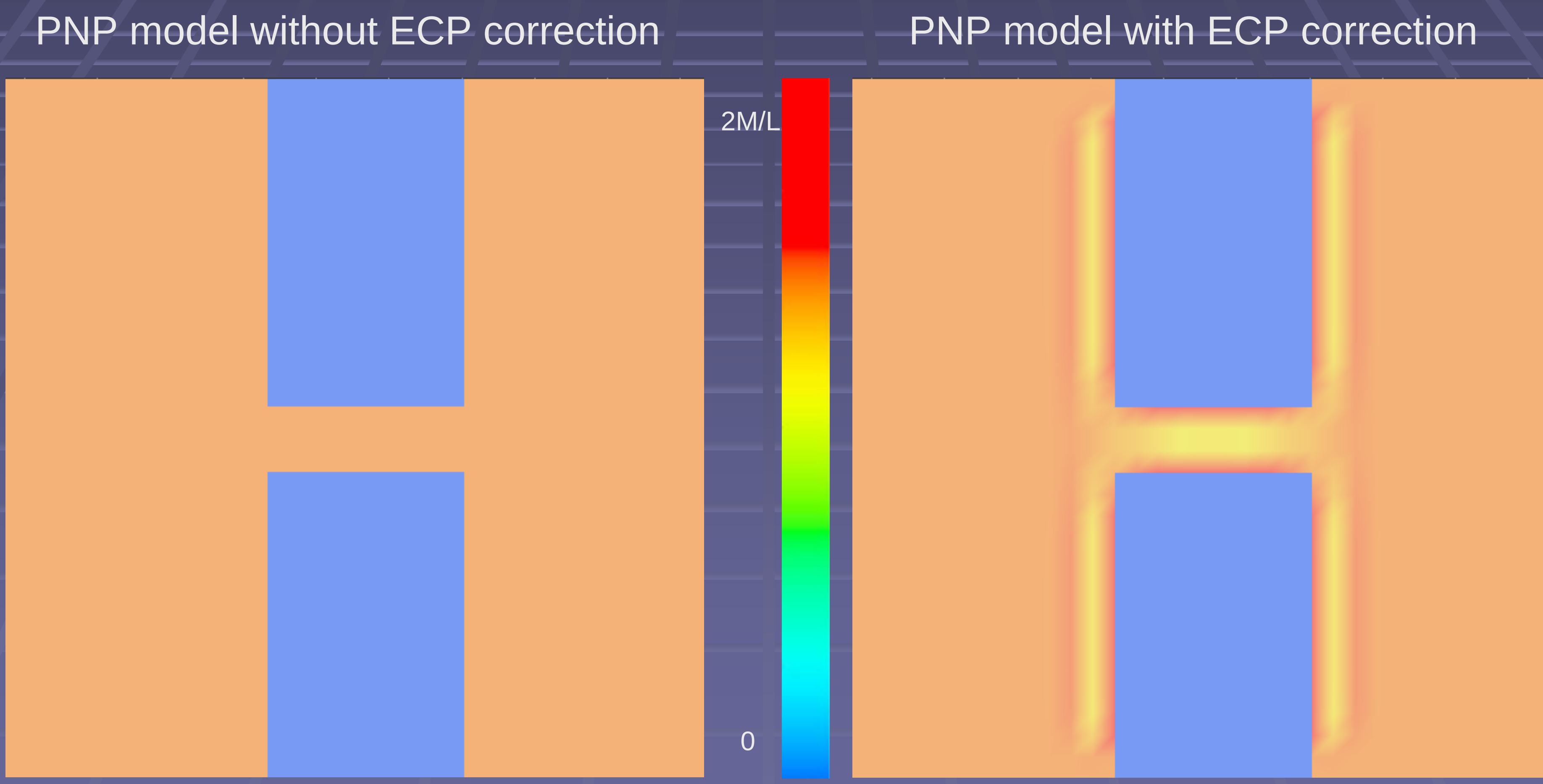
PNP model without ECP correction

PNP model with ECP correction

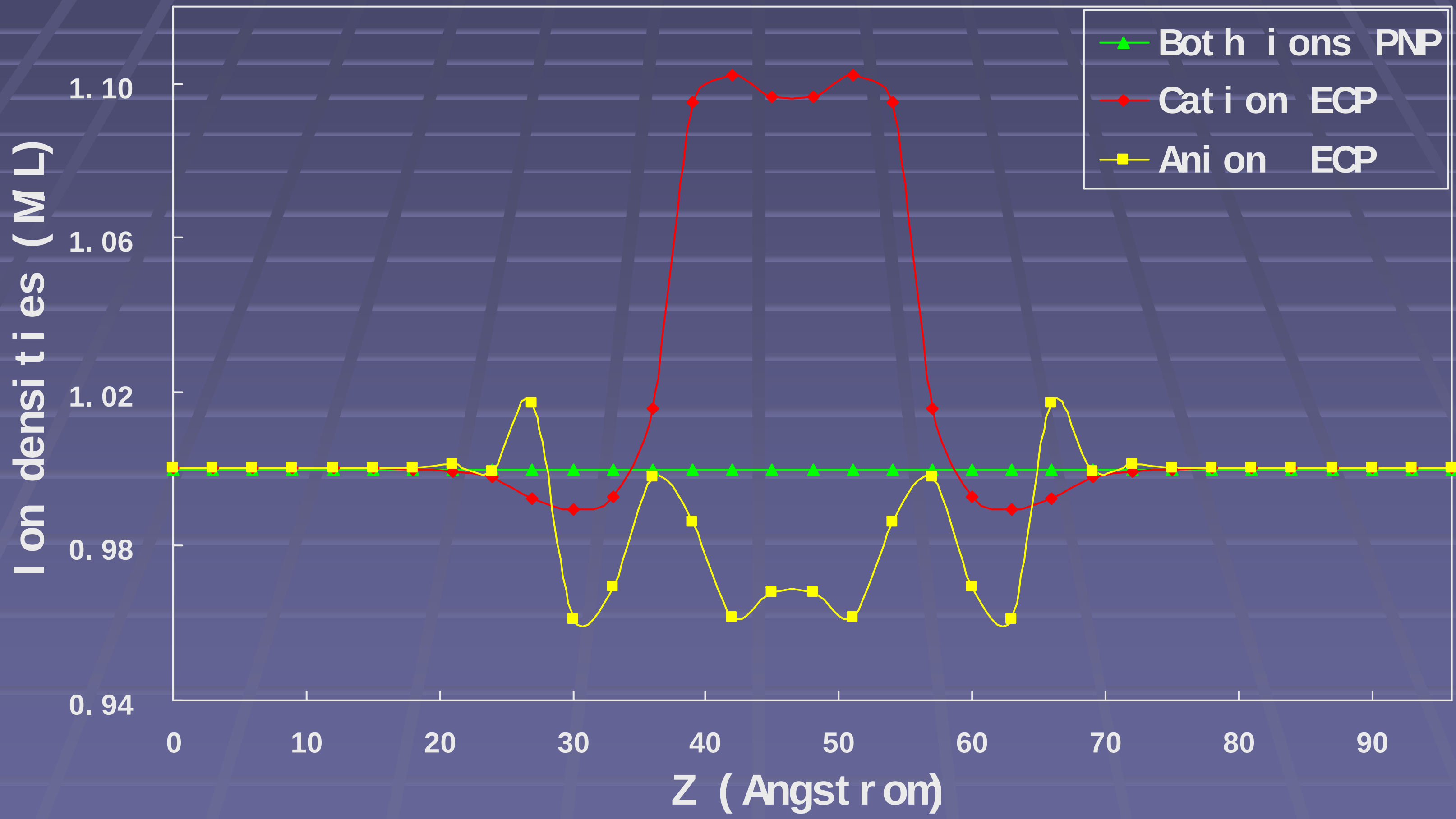


# Anion density without fixed charge

Result from test structure without permanent charge



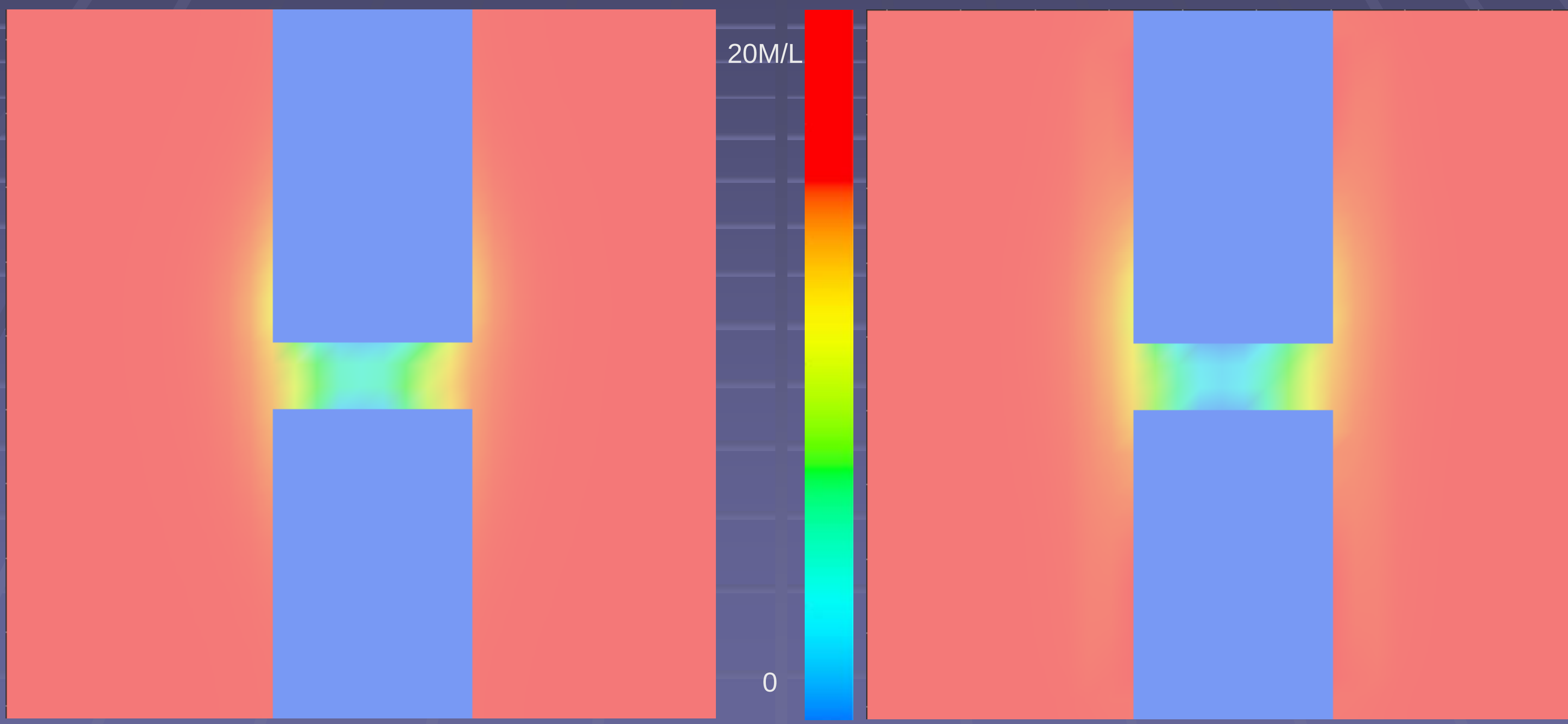
# Ion densities without fixed charge



# Cation density Comparison

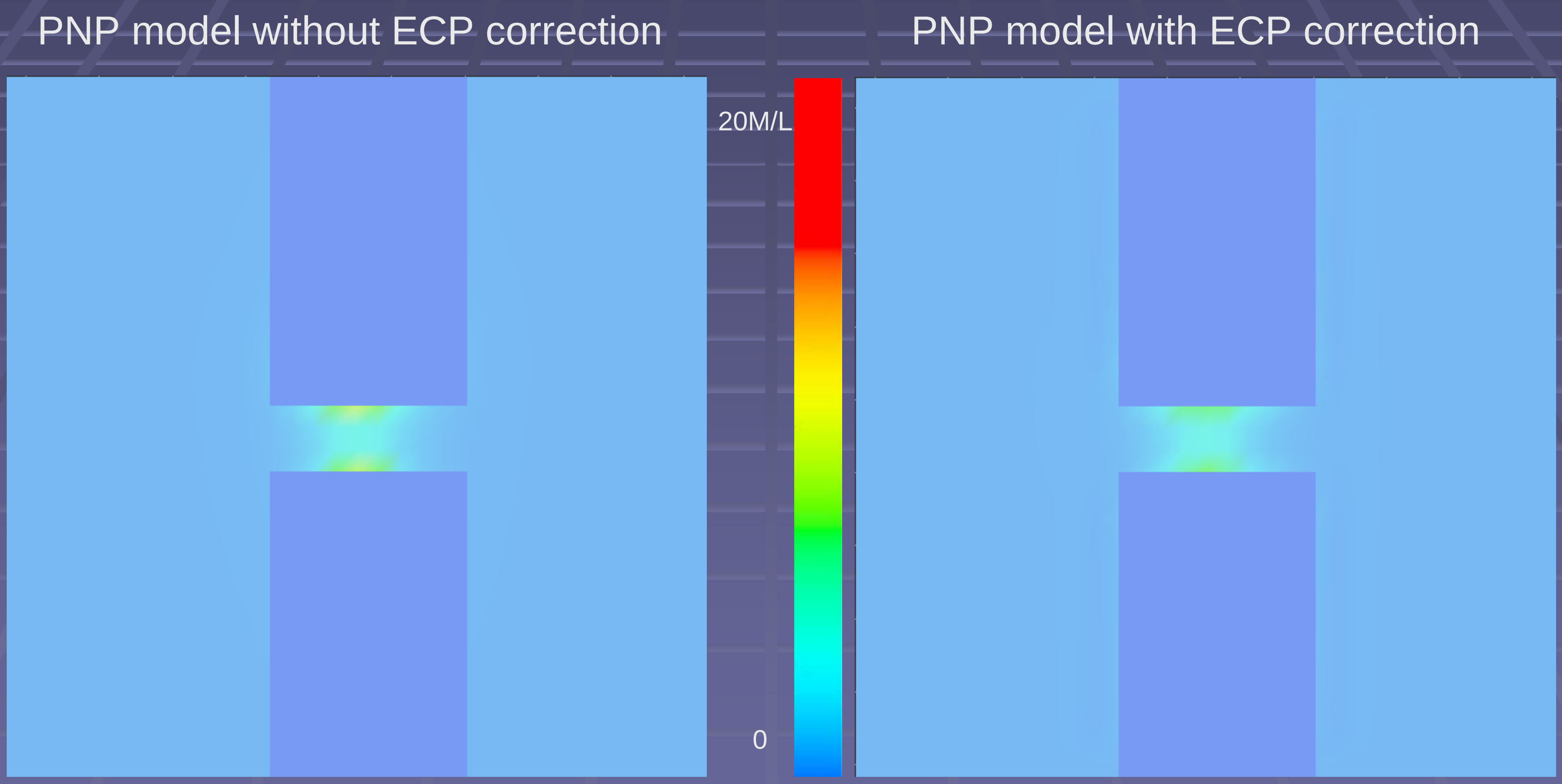
Result from test structure with positive permanent charge

PNP model without ECP correction | PNP model with ECP correction

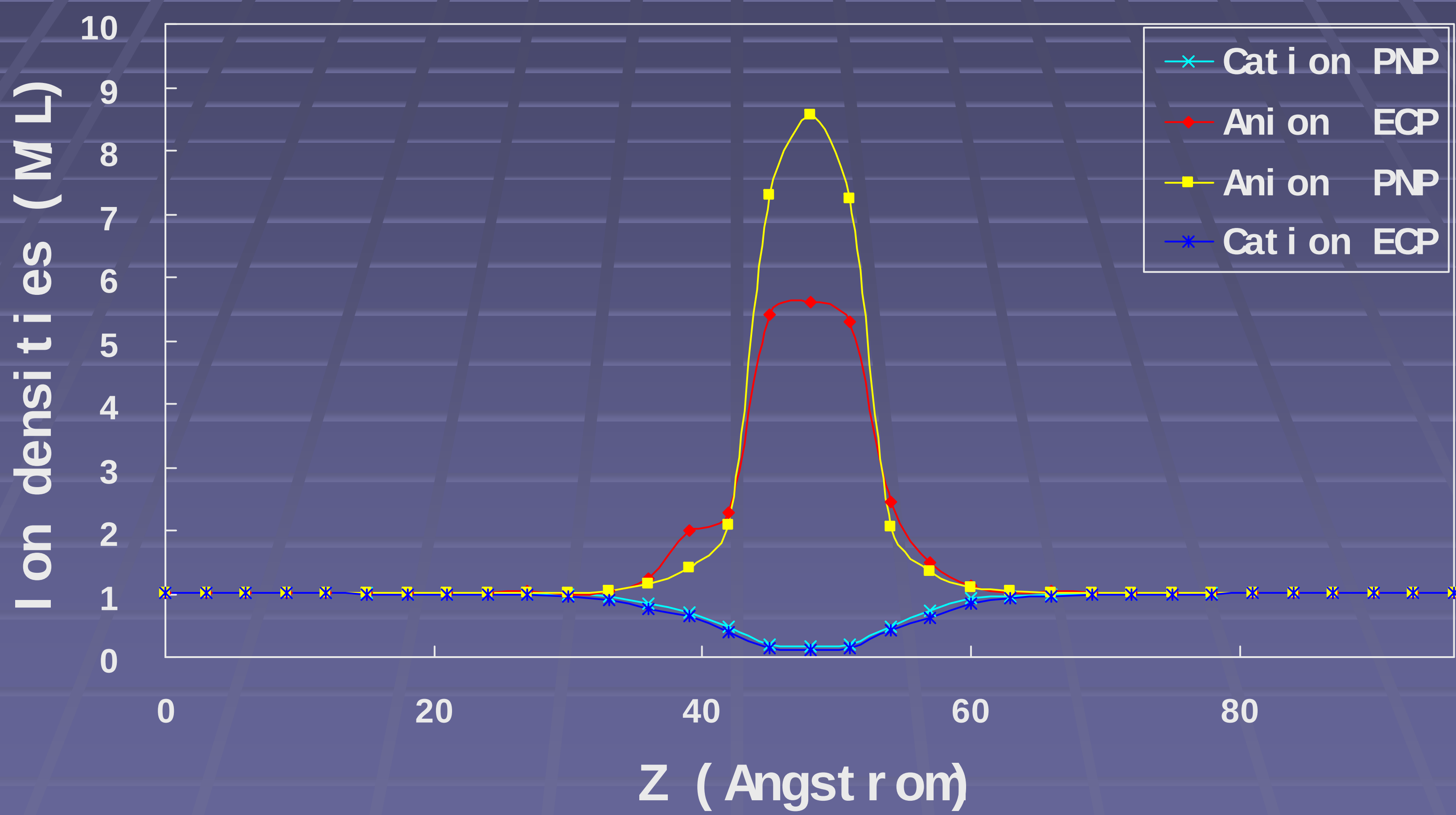


# Anion density Comparison

Result from test structure with positive permanent charge



# Ion densities with fixed charge



# Future Work

- Comparisons with particle simulations
- Implementation of a realistic biological ion channel
- More efficient computational procedure