Stabilization of protein charges due to their interaction with membrane fluctuations is a subject of growing interest, especially due to possible implications for voltage gating. Two complementary mechanisms governing charge-fluctuation interactions are considered: (1) electrostatic (EM) [1], treating the membrane as an elastic slab (electric bilayer model), and (2) hydrophobic (HM) [2], treating membrane fluctuations as a perturbation to hydrophobic core with a corresponding interfacial tension contribution. In both the linear Poisson-Boltzmann equation is solved via a multi-dimensional continuum model with arbitrarily shaped membrane-water interfaces and a point charge surrounded by a “born sphere” of low dielectric constant. The EM often leads to large membrane thickness fluctuations, far larger than consistent with realistic membrane model descriptions. We show that a switch to EM to HM is unrealistically advantageous in interfacial perturbation amplitudes. To establish the shape of the solvent cavity we apply kinetic Monte Carlo Reaction Path Following (kMCRPF) [2] with the charge’s reaction coordinate as the reaction action. The resulting energy profiles confirm that reverse MD studies [3].

**Introduction**

Coupling of electric fields or charges with the fluctuations of the membrane-solvent interface is important for membrane stability, electroporation, inner transport and voltage gating [4]. We study membrane fluctuations triggered by a single charge bound within the membrane. EM and HM influence are considered. The energy-perturbations from fluctuations reflect the elastic energy of the membrane deformation (2D) and the interfacial tension (3D) [5]. Stabilization arise from wave/dimming of the charges’ electric field, generating the ponderomotive force promoting the fluctuations. Our dimensions using MUMPS (Multifrontal Massively Parallel Solver), a multi-dimensional solver, can be quickly calculate the instability leading to the charge-solvated state and the deformations far beyond the elastic limit. This indicates that at water EM fluctuations must enter to EM state. Fluctuations in the HM model are investigated using an extended family of parameterized shapes that sample a wide range of solute states. Preliminary results indicate that fluctuations typically arise due to electrostatic interaction (EM), which then drive the water mass organization provided by the HM.

**Computational Model**

**Source-Free Poisson–Boltzmann equation, $\Phi_s - \Phi_d = \rho$**

$$A \Phi_s - V_s \Phi_s - \Phi_d = \rho$$

where $d_e = \Phi_s - \Phi_d$, $d_e$ - dielectric constant near the charge, $e_i$ - the coulombic potential constant calculated from $V_s = \Phi_s - \Phi_d$ and $\Phi_d$. Inside the charge sphere $e_i = 1$, and the Poisson-Boltzmann equation is $\Phi_s = 0$. Outside the charge sphere is well-defined, thus:

- **Simulation** due to point charges are eliminated
- **reaction fields** potentials are computed directly

**Boundary Conditions**

- $\phi(\mathbf{r})$ - the point charge
- $\mathbf{n}$ - the normal of the boundary and the point charge

**Parameterized Shapes of Water Pores**

- $\Phi_0$, $\Phi_1$, and $\Phi_2$ - the amplitudes and energy lengths of the lower and upper water dipoles described either by the EM or the HM, and $\alpha$, and $\beta$ the angles of the elliptic water plane described by the HM, for the case of the ellipse with the lower and upper cone, length $\sigma$ are amplitudes of $\Phi$ in the $x$-coordinates

**Electrostatic Energy**

$$\Phi_s = \sum_{i=0}^{n} \frac{q_i}{\sigma_i} \sin \theta_i$$

where $q_i$ - the charge of the $i$-th dipole, $\sigma_i$ - the dipole moment of the point charge

$$E_{EM} = \frac{q_i^2}{2 \sigma_i}$$

**KMC Reaction Path Following (kMCRPF)**

- **Main observation**: An elliptic water–filled pore forms for a charge near mid-membrane.
- **Main observations**: Elliptic pores are greatly reduced due to water plume. The water plume primarily involves the water plume (HM), where the formation is promoted by the elastic fluctuations. The transitions process is strongly affected by the uniformity between the elastic and hydrophobic fluctuations.

**Conclusions**

- **Main observation**: The elastic fluctuations can be strongly promoted by the uniformity of the charge approach mid-membrane. Fluctuations can reduce the barrier to $5-30$ K.T [3], while the corresponding barrier for a planar membrane is $63-85$ K.T. The energy barrier from MD simulations [5] was ~28 K.T.
- **Main observation**: The choice of parameters the water plume (elastic and water interactions) strongly affects the system behavior. The transition barrier broadened with increasing “interfacial tension”. Estimates of the... (change the interfacial tension) and allow for a more accurate comparison between hydrophobic bilayer and future studies.

**References**


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