DNA in Nanopores: Strong Electrostatic Interactions in Cellular Dynamics Processes

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DNA that carries genetic information in living cells is a charged polymer having a unit charge at the phosphate group in every few Angstroms interval along its thread. When the DNA migrates between cellular liquid having the dielectric constant ε_w= 80 through a pore embedded in the cell membrane, the pore both geometrically and electrostatically affects the DNA and ion distributions [1,2]. The membrane is characteristic of the low dielectric constant ε_m=2, thus the electrostatic energy is enhanced roughly by $\varepsilon_w/\varepsilon_m$ (>>1) times as the quantity D=εE should be continuous. In this respect, the electrostatic interactions are expected to be very important in the life processes.

In order to study the behavior of DNA and ions in the nano-sized pore, we have performed molecular dynamics simulations [3]. We take a rectangular box separated into upper and lower compartments by an inserted membrane at the middle. The membrane is pierced by a cylindrical pore extending along the vertical axis, where the pore and compartments are filled with cellular liquid of large dielectric constant ε_w. Salt ions of 1M KCl and (neutral) solvent particles that emulate cellular liquid are put in this volume. Because of the electrostatic interactions and large inhomogeneity of the dielectric constant, the Poisson equation *must* be solved for charge density ρ(r) and dielectric constant ε(r) on top of the short-range Coulomb and Lennard-Jones forces,

$$\nabla \bullet (\varepsilon \nabla \varphi) = -4\pi\rho$$

We adopt the conjugate gradient method to solve the equation in the real space. The DNA is modeled by charged and neutral monomers connected in a row on the backbone, and these correspond to the phosphate groups and sugar rings, respectively; the bases are attached as side chains..

We have shown clearly [3] on the basis of the simple physical model above, that when the DNA is not present in the pore, ions of the isolate form cannot exist in the pore but a few pairs of counterions and coions reside in it because of the electrostatic repulsion from the membrane. When the DNA is present in the pore, it is subject to complete counterions condensation to reduce the electrostatic energy. On the same reason, coions are repelled from the negatively charged DNA and are depleted from the pore. The DNA is elongated in the pore compared to in the bulk phase due to electrostatic repulsion and the geometrical constraint from the membrane and pore.

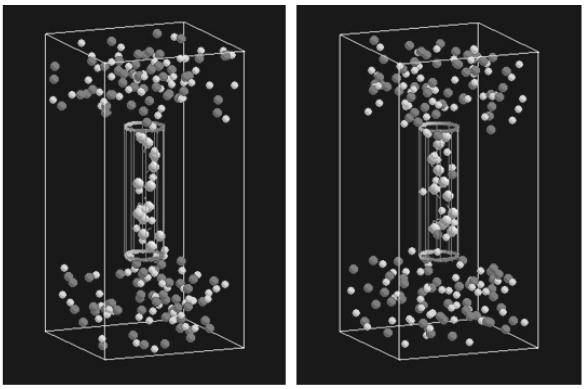

Fig.1 Snapshots of DNA (only charged phosphate monomers are shown), counterions (gray) and coions (dark gray) for the actual ε_m=2 (left), and artificial ε_m=80 (right) dielectric constant cases.

The effects of the electrostatic interactions are best shown in Fig.1, which compares the actual and artificial cases, namely, the membranes having the low ε_m=2 and large ε_m=80 dielectric constants, respectively (the low dielectric constant of the membrane arises from oily nature of the bilayer). The DNA is condensed by counterions and charge neutralized while coions are markedly depleted from the pore in the former, but there are a few coions in the latter case. This clearly proves the important role of the electrostatic effects in the actual life processes.

We are also examining the diffusion of counterions and coions across the pore, and the pore current when a voltage bias is applied between the top and bottom end plates. With the DNA inside the pore, the diffusion rate of counterions, which are the principal carrier of the pore current (coions are depleted) is suppressed by a factor of three compared with that for the DNA-empty pore. This decrease appears to be somewhat less than the α-hemolysin pore current measurement [2]. These results will also be presented at the conference.

References

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