Supplementary Material

Ion-mediated RNA structural collapse: effect of spatial confinement

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Tightly bound ion model

We recently refined the original TBI model (1–7), which was based on the coarse-grained structural model, into an all-atom structure-based model (8–10). Here, we briefly introduce the new model; see Ref. (1, 8–10) for details.

In the model, the multivalent (z) ions are classified into two types according to the ion-ion correlation strength (1)-(10): the (strongly correlated) tightly bound ions and the (weakly correlated) diffusively bound ions, and correspondingly, the regions where the two types of ions reside are denoted as tightly bound region and diffusive region, respectively. For the diffusive ions, we use mean-field PB approach; for the tightly bound ions, we use an explicit treatment that can account for the strong ion-ion correlations and ion-binding fluctuations. Simultaneously, the monovalent ions are treated as diffusive ionic background with the mean-field approach due to the weak inter-ion Coulombic correlations (6). For a N-nt nucleic acid molecule, the whole tightly bound region is divided into N cells, each around a phosphate. Therefore, there exist a large number of binding modes for different ions binding in different cells, and the total partition function Z is given by the summation over all the possible binding modes M:

$$Z = \sum_M Z_M. \tag{1}$$

Z_M is the partition function for a given binding mode M (1)-(9)

$$Z_M = Z^{(id)} \left(\frac{N_z}{V}\right)^{N_b} \left(\int \prod_{i=1}^{N_b} d\mathbf{R}_i\right) e^{-(\Delta G_b + \Delta G_d + \Delta G_b^{pol})/k_BT} \tag{2}$$

where $Z^{(id)}$ is the partition function for the uniform ion solution (without the polyelectrolyte). N_z is the total number of z-valent counterions and V is the volume of the solution. N_b and $\int \prod_{i=1}^{N_b} d\mathbf{R}_i$ are the number and the volume integral for the tightly bound ions, respectively. ΔG_b is the mean Coulombic interaction energy between all the discrete charge-charge pairs (including the phosphate groups and the tightly bound ions) in the tightly bound region; ΔG_d is the free energy for the electrostatic interactions between the diffusive ions and between the diffusive ions and the discrete charges in the tightly bound region, and the entropic free energy of the diffusive ions. ΔG_b^{pol} is the (Born) self-polarization energy for the discrete charges in the tightly bound region (4, 8). ΔG_b, ΔG_d, and ΔG_b^{pol} have been given in detail in Refs (1)-(4).

Therefore, the electrostatic free energy for a RNA molecule can be computed by

$$G^E = -k_BT \ln \sum_M \left(Z_M/Z^{(id)}\right). \tag{3}$$

The numerical computation and parameter sets are described briefly in the following; see Ref. (4, 8, 9) for details.

Computations and parameter sets

The computation of the TBI model is divided into the following three steps (1)-(10): (*i*) First, we solve the PB equation for an atomic nucleic acid conformation in salt solution, to obtain the $z-$valent ion distributions, from which we determine the tightly bound region for $z-$valent ions. The atomic RNA is defined by the sum of the van der Waals radii of all the atoms in nucleic acid system. (*ii*) Second, we compute the pair-wise potentials of mean force $\Phi_1(i)$ and $\Phi_2(i, j)$ and Born energy $\Phi_0(i)$, with the use of the general Born model (4, 8, 9). The exclusions between ions and nucleic acid atoms are accounted for by a truncated Lennard-Jones potential: $U = u_0(\frac{1}{r^{12}} - \frac{1}{r^6})$ for $r < 1$ and $U = 0$ for $r > 1$, where r is the distance between an ion and an atom in the unit of the sum of the radii for the ion and atom, and u_0 is taken as 0.35 (8–10). The calculated $\Phi_1(i)$ and $\Phi_2(i, j)$ and $\Phi_0(i)$ are tabulated and stored for the later calculations of partition function. (*iii*) Third, we enumerate the possible binding modes. For each mode, we calculate ΔG_b, ΔG_d, and ΔG_b^{pol} (4, 8, 9). Summation over the binding modes gives the total partition function Z (Eq. 1), from which we can calculate the electrostatic free energy for a nucleic acid conformation. For long molecules, we have previously proposed a framework by separately treating high-energy modes and low-energy modes (2).

In the calculations, ions are assumed to be hydrated (1)-(10), and have the radii: Na^+, 3.5 Å; and Mg^{2+}, 4.5 Å (1)-(10), respectively. The dielectric constant ϵ of nucleic acid interior is set to be 20 (4, 8, 9), and the molecule exterior is taken as that of water ($\epsilon = 78$ at 25 °C). When solving PB equation, a thin layer of thickness of a cation radius is added to the molecular surface to account for the excluded volume layer of the cations, and the three-step focusing process is used to obtain the detailed ion distribution near molecules (1)-(10). For each run, the electrostatic potentials are iterated to a convergence of $< 10^{-4} k_B T/q$. The resolution of the first run varies with the grid size to make the iterative process doable (1)-(10), and the resolutions for the second and third runs are 1.36 Å per grid and 0.68 Å per grid, respectively. Our results are stable as tested against different grid sizes.

References

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