All-Atom Molecular Dynamics Simulations of Entire Virus Capsid Reveal the Role of Ion Distribution in Capsid's Stability

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We executed our MD simulations using GROMACS. For simulations with GROMOS53a6 force field the SPC water model was used, and for simulations with Amber03 force field the TIP3P water model was employed. Our calculations did not include DNA.

MD simulations for all cases were performed with periodic boundary conditions in a cubic simulation box. The initial configurations with the neutralizing number of ions were prepared as follows. At first, the crystallographic configuration was solvated in water using genbox GROMACS utility. The box was a cube with the edge of 26.6 nm. Then a sphere with radius 3 nm (for the capsid with tails) or 4.5 nm (for the one without tails) positioned in the center of mass of the capsid was extracted from the system using our own software. The radii were selected to cover only water molecules without capsid atoms. Molecules were maintained non-broken, i.e. all atoms, connected with the ones covered by the sphere, were included in the latter. Then the needed number of randomly chosen water molecules in the extracted sphere (407 for the capsid with tails and 606 for the one without tails) was replaced with Cl^- ions using genion GROMACS utility. The obtained solution was placed back into the main system by merging their pdb files in a text editor. After that a spherical layer with radius 11 nm and thickness 0.5 nm was extracted from the system using our own software. As before, it contained only water. Randomly chosen water molecules in the layer were replaced with 227 (for the capsid with tails) or 246 (for the one without tails) Na^+ ions using genion utility. The produced solution was placed back into the main system in a text editor. Finally, Na^+ and Cl^- ions in concentration, corresponding to the physiological solution (0.9% by mass, i.e. 1720 ions of each sign) were added by replacing water molecules using genion utility. The ions were spread uniformly in the whole system, both inside and outside the capsid.

The preparation of initial configurations with the low number of ions was performed by the same algorithm with differences only in number and kind of added ions. In the inner sphere 200 (for

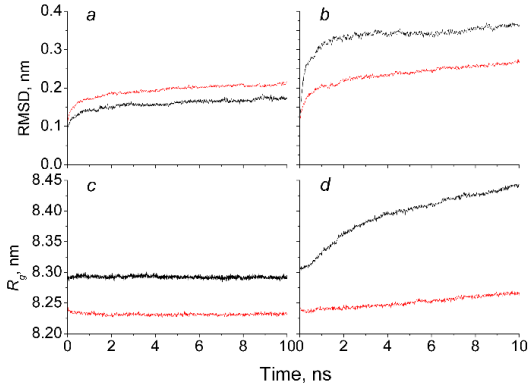

Figure S1. Time change of the root-mean-square deviation, RMSD, (top plots) and radius of gyration, R_g, (bottom plots) of backbone atoms from their initial structure as a reference structure in AMBER force field. The calculations of RMSD and R_g did not include the tail sequence for all structures and consisted of the same number of amino acids. Red is for the capsid with the tails, black is for the capsid without the tails. a,c – the capsids with the neutralizing number of ions, b,d – the capsid with the low number of ions

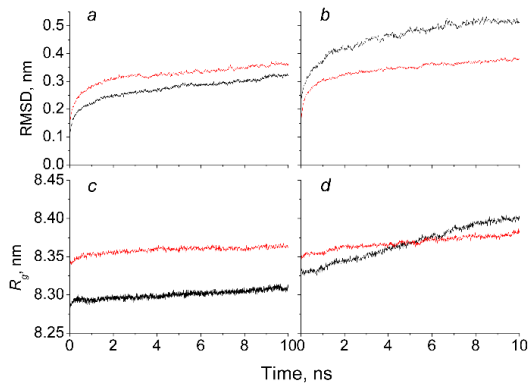

Figure S2. Time change of the root-mean-square deviation, RMSD, (top plots) and radius of gyration, R_g, (bottom plots) of backbone atoms from their initial structure as a reference structure in GROMOS force field. The calculations of RMSD and R_g did not include the tail sequence for all structures and consisted of the same number of amino acids. Red is for the capsid with the tails, black is for the capsid without the tails. a,c – the capsids with the neutralizing number of ions, b,d – the capsid with the low number of ions

the capsid with tails) or 300 (for the capsid without tails) water molecules were replaced with Cl^- ions. In the outer layer 20 water molecules were replaced with Na^+ ions (for the capsid with tails) or 60 water molecules were replaced with Cl^- ions (for the capsid without tails).

Before start of the MD calculation we carried the energy minimization, after that the MD calculation was performed with position restraints of the capsid at T = 200 K and then at T = 300 K. After 1 ns of the equilibration process the MD simulation was carried out without position restraints at T = 300 K during 10 ns.

For production of our simulations we used velocity rescaling thermostat and "Verlet" value of the cutoff-scheme parameter. Cut-off distances for the short-range neighbor list, PME electrostatics and Lennard-Jones interactions were equal to 1.0 nm. All simulation parameters were the same for all systems.

Results of the simulations were analyzed by means of time evolution of root-mean-square deviation (RMSD) and radius of gyration (R_g) values. RMSD and R_g were calculated by GROMACS utilities by the formulas:

$$\mathrm{RMSD} = \sqrt{\frac{1}{M}\sum_{i=1}^{N} m_i \|r_{i0} - r_i(t)\|^2}$$

$$R_g = \sqrt{\frac{\sum_i \|r_i(t) - r_c\|^2 m_i}{\sum_i m_i}},$$

Where M is the mass of the capsid, $r_i(t)$ is the position of atom i at time t, r_{i0} is the position of atom i in the crystal structure, m_i is the mass of atom i, and r_c is the center of mass of the capsid.

RMSD and R_g were calculated taking into account only the backbone atoms with the initial structure as a reference structure. The calculations did not include the tail sequence for all structures and used the same number of the amino acids.

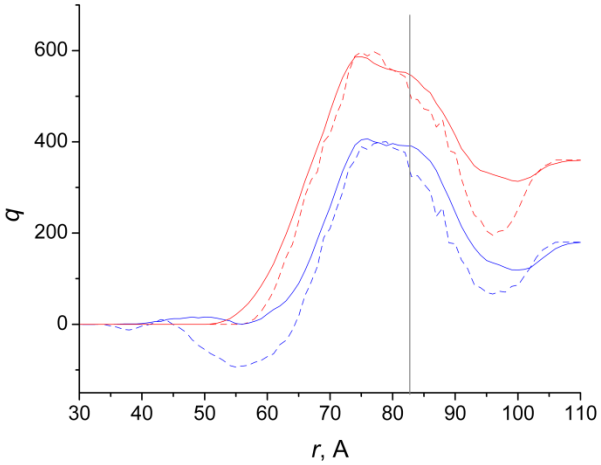

Figure S3. The dependences of integral charge of capsid atoms on the distance from the capsid center of mass. Blue curves correspond to the capsid with tails, red curves correspond to the capsid without tails. Solid curves correspond to the final configurations, dashed curves correspond to the initial ones. The vertical line corresponds to the middle of the capsid wall.