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Supporting Material

A Structurally Relevant Coarse-Grained Model for Cholesterol

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Supplemental Material for

A Structurally Relevant Coarse-Grained Model for Cholesterol

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Additional simulation details

All simulations were performed within DL_POLY (version 2.14) (1) using the Nosé-Hoover anisotropic thermostat and barostat (2) to maintain the temperature and pressure tensor as needed. The reaction field method with a dielectric constant of 1.0 was used to describe the long-range electrostatic interactions (3) and a 12 Å cutoff used for all interactions. The chosen value of the dielectric constant is consistent with reported experimental values for the dielectric constant of cholesterol derivatives (4). In the atomistic simulations the system was equilibrated for 350 ps followed by 5.0 ns of simulation using a 1.0 fs timestep. To determine the appropriate simulation time the evolution of the crystal structure parameters (energy, density and cell vectors and angles) and the target RDFs was monitored during the simulations. At 298K both longer (20ns) and shorter (1ns) simulations were performed and the average crystal structure, and target radial distribution functions, were found to exhibit minimal differences with the 5.0 ns simulations, indicating the system was equilibrated, and that 1.0 ns of simulation could be used in the CG simulations to minimize the time required to optimize the potential.

In the estimation of the melting point the self-diffusion coefficient was measured during each simulation using the standard Einstein relation

$$D = \lim_{t!} \frac{\left\langle [\mathbf{R}_{cm}(t) \# \mathbf{R}_{cm}(0)]^2 \right\rangle}{6t}, \qquad [1]$$

where $\mathbf{R}_{cm}(\mathrm{t}) - \mathbf{R}_{cm}(0)$ is the time dependent center-of-mass displacement of a given molecule.

Additional details on the coarse-grained model development

The parameters for the bond stretching and bond angle bending potentials were determined from a normalized distribution of the distance between two bonded sites (or the angle between three angled sites) measured from the target atomistic trajectory mapped to the CG level. Before normalization, the angle distributions were weighted by a factor of $\sin(\theta)$ as given in the original RPM method (5), *viz*

$$P(\theta) = f_n p(\theta) / \sin(\theta) \qquad [2]$$

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where f_n is the normalization factor, $p(\theta)$ is the distribution, $P(\theta)$ represents the normalized distribution, and θ is the angle. The parameters of a single-peak Gaussian distribution were then fitted to the histogram and the constants in the force potentials taken from a Boltzmann inversion of the Gaussian. The force constant for a harmonic oscillator and the equilibrium bond length or angle emerge from the simplification of the inversion (5) as shown in equations [3] through [5]:

$$P(\theta) = \frac{A}{w\sqrt{\pi/2}} \exp^{-2\frac{(\theta-\theta_{eq})^2}{w^2}} \qquad [3]$$

$$V(\theta) = -kT \ln\left(\frac{A}{w\sqrt{\pi/2}} \exp^{-2\frac{(\theta-\theta_{eq})^2}{w^2}} \right) \qquad [4]$$

$$V(\theta) = \frac{2kT}{w^2}(\theta - \theta_{eq})^2 + const \qquad [5]$$

where A is the Gaussian area, w the Gaussian width, θ_{eq} the equilibrium angle, k Boltzmann's constant, and T the temperature. As representative examples, the measured distribution of bond lengths and fitted single-peak Gaussian for the bond between the CHM bead and the 1RNG bead is shown in Fig. S1 and the distribution of angles between the 1RNG-ALC-2RNG sites is shown in Fig. S2.

Figure S1. The normalized distribution of the distances between bonded CHM and 1RNG beads (diamonds) in the coarse-grained model and the fitted Gaussian (solid line).

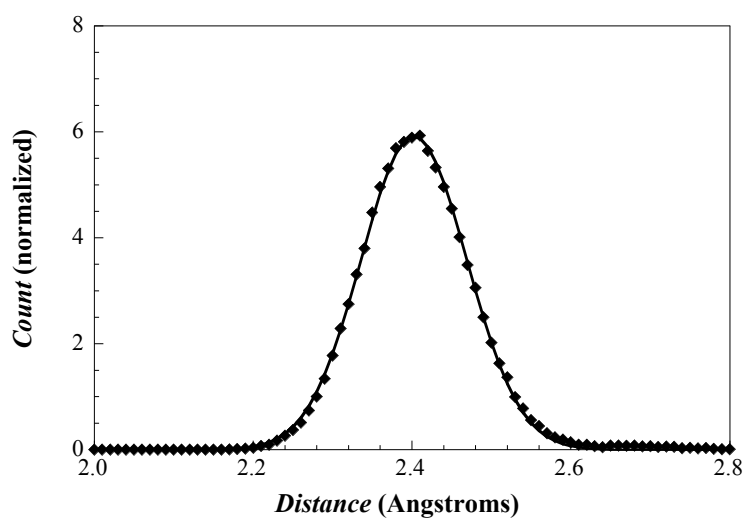
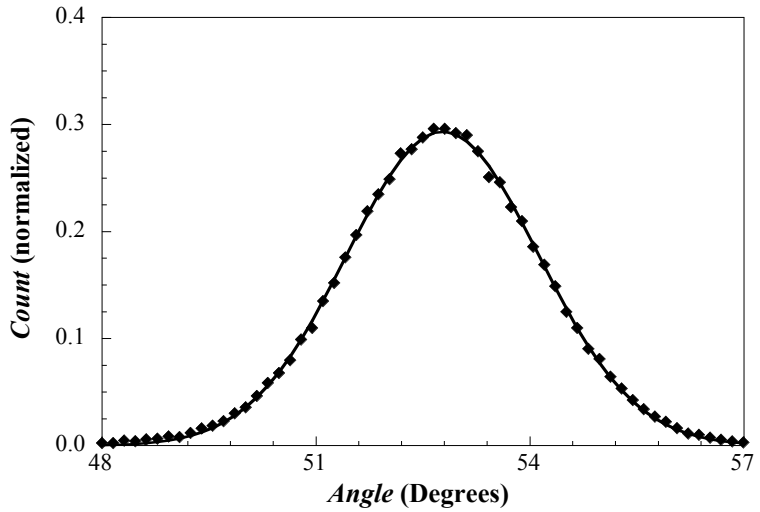


Figure S2. The normalized distribution of the angle between the 1RNG-ALC-2RNG beads (diamonds) in the coarse-grained model and the fitted Gaussian (solid line).



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