AMBERff at scale: Multimillion-atom simulations with AMBER force fields in NAMD

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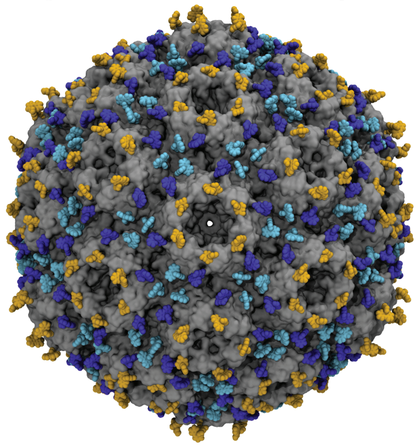
Introduction

The application of all-atom molecular dynamics (MD) simulations to study large-scale biomolecular systems containing millions of atoms can reveal incredible details about viral and cellular processes that are inaccessible to experimental methods. Classical MD simulations rely on “force fields” carefully parameterized for each class of biomolecule to accurately describe molecular motion. Yet, it is not currently possible to use AMBER family of force fields (AMBERff) for multimillion-atom simulations such as the Brome Mosaic Virus (BMV) capsid.

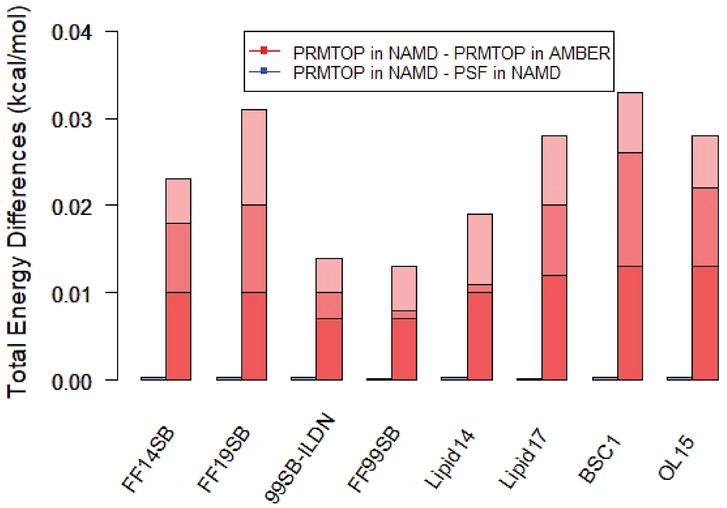
Dye-decorated BMV Capsid



4.2 million atoms

To address this, the authors take advantage of the direct cancellation between the potential energy functions to refactor several popular force fields within AMBERff into the CHARMM file format. These refactored files are compatible with the freely-available NAMD software, which supports MD simulations of biomolecular systems up to two billion atoms on leadership-class supercomputers.

Refactoring Results



Direct comparison of the single point energies for a comprehensive set of test systems show that this process preserves the integrity of the refactored force fields.

Acknowledgement

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Approach

Case sensitivity and the use of symbols, spaces, and numbers are key aspects of AMBERff atom type conventions. We introduce an atom type prefix system that encodes the information lost when ignoring case and symbols, which also conveniently handles numbers.

Prefix	Denotes	Replaces	Example		
U	Uppercase letter	A-Z	CG	→	UUCG
L	Lowercase letter	a-z	cg	→	LLCG
S	Space	“ ”	C	→	USC
N	Number	0-9	C2	→	UNC2
A	Asterisk	*	C*	→	UAC
P	Plus sign	+	Na+	→	ULPNA
M	Minus sign	-	Cl-	→	ULMCL

CHARMMff Equation

$$V_{Total} = \sum^{Bonds} K_r(r-r_0)^2 + \sum^{Angles} K_\theta(\theta-\theta_0)^2 + \sum^{Dihedrals} K_\varphi[1+\cos(n\varphi-\delta)]$$

$$+ \sum^{Sinusoidal\ Impropers} K_\varphi[1+\cos(n\varphi-\delta)] + \sum^{CMAP} f(\Phi,\Psi)$$

$$+ \sum_{i<j}^{van\ der\ Waals} \epsilon_{ij}\left[\left(\frac{R_{min,ij}}{r_{ij}}\right)^{12} - 2\left(\frac{R_{min,ij}}{r_{ij}}\right)^{6}\right] + \sum_{i<j}^{Electrostatics}\left[\frac{1}{4\pi D}\frac{q_i q_j}{r_{ij}}\right]$$

$$+ \sum^{Harmonic\ Improper} K_\phi(\phi-\phi_0)^2 + \sum^{Urey-Bradley} K_{UB}(r_{1,3}-r_{1,3;0})^2$$

AMBERff Equation

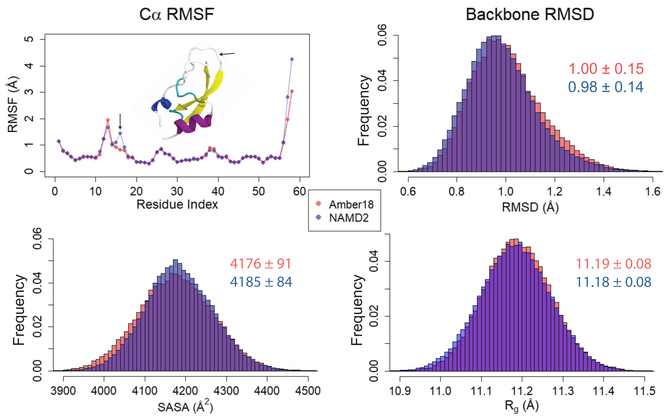
$$V_{Total} = \sum^{Bonds} K_r(r-r_0)^2 + \sum^{Angles} K_\theta(\theta-\theta_0)^2 + \sum^{Dihedrals} \frac{V_n}{2}[1+\cos(n\varphi-\delta)]$$

$$+ \sum^{Sinusoidal\ Impropers} K_\varphi[1+\cos(n\varphi-\delta)] + \sum^{CMAP} f(\Phi,\Psi)$$

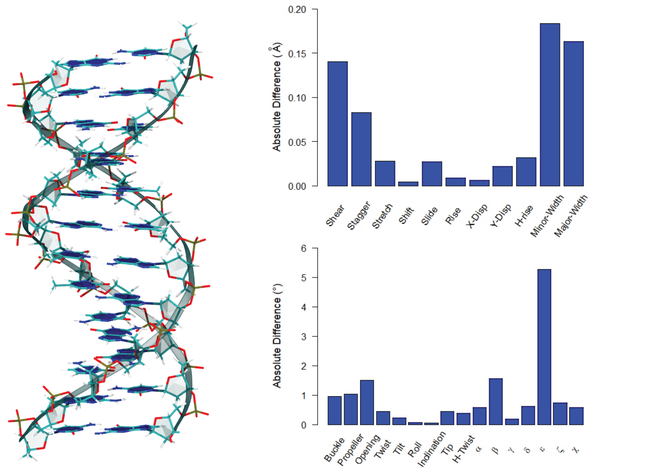
$$+ \sum_{i<j}^{van\ der\ Waals} 4\epsilon_{ij}\left[\left(\frac{\sigma_{ij}}{r_{ij}}\right)^{12} - \left(\frac{\sigma_{ij}}{r_{ij}}\right)^{6}\right] + \sum_{i<j}^{Electrostatics}\left[\frac{1}{4\pi\epsilon_0}\frac{q_i q_j}{r_{ij}}\right]$$

AMBERff is readily substituted for CHARMMff in NAMD2. The contributions of Urey-Bradley and harmonic impropers are eliminated, and CHARMMff equation reduces to the AMBERff equation.

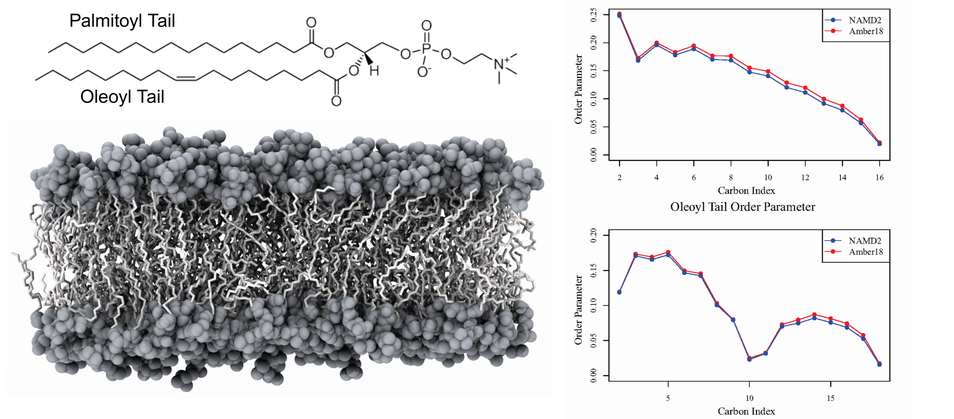
Case Studies



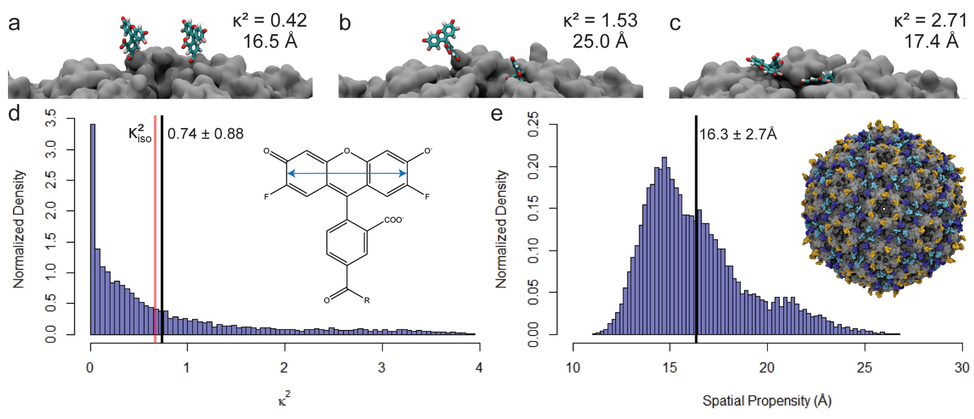
Structural properties of BPTI are preserved between MD engines.



The absolute difference between the means of 27 structural metrics for the Dickerson-Drew Dodecamer are smaller than the fluctuations in these metrics.



The deuterium order parameter for both aliphatic tails of POPC in a 100x100 Å bilayer are in good agreement for simulations performed in AMBER and NAMD.



Using parameters which were refactored as a part of this work, simulations of a dye-decorated BMV capsid in NAMD have revealed dynamics consistent with coordination between dye pairs across asymmetric units.

For more information, scan to visit:
https://sites.udel.edu/jhadden/