J. Quertinmont | 22.04.2026

Principles of Accurate Molecular Dynamics Simulations

Key principles

Integrator Correctness

Energy fluctuations should scale with the squared integration timestep

$$\frac{\sigma(\mathcal{H}(\Delta t_1))}{\sigma(\mathcal{H}(\Delta t_2))} = \frac{\Delta t_1^2}{\Delta t_2^2}$$

Kinetic Energy and Equipartition

- The total kinetic energy must strictly align with an analytical gamma distribution dependent on the number of degrees of freedom and the temperature.
- This is true across any subset of degrees of freedom (e.g. solute vs. solvent or a molecule's translational, rotational, and internal modes).

Thermodynamic Ensembles

The probability ratios of configurational observables (such as volume V and energy E) across different simulated state points must fit ensemble dependencies:

$$\log \frac{P(E|\beta_2)}{P(E|\beta_1)} \sim -(\beta_2 - \beta_1)E \qquad \text{NVT}$$

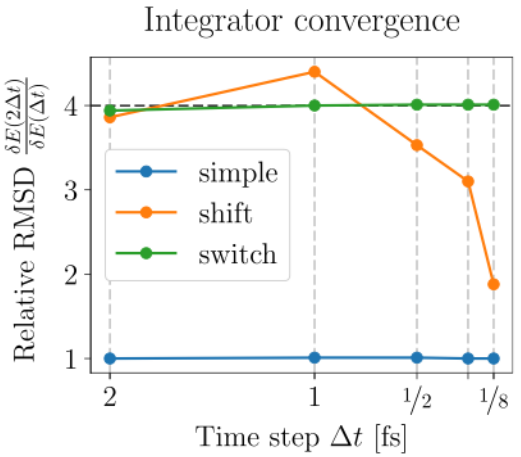
$$\log \frac{P(E,V|\beta_2,P_2)}{P(E,V|\beta_1,P_1)} \sim -(\beta_2 - \beta_1)E - (\beta_2 P_2 - \beta_1 P_1)V \qquad \text{NPT}$$

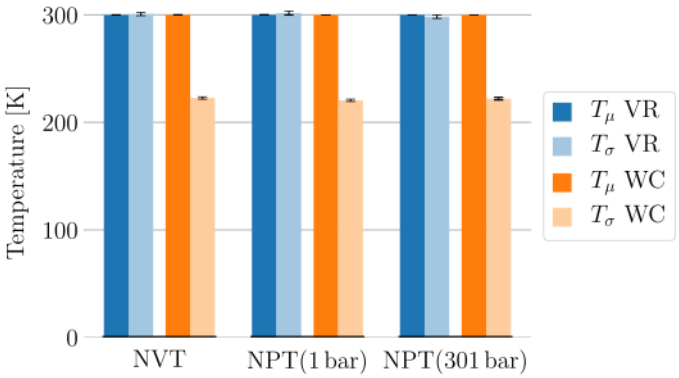
Key tests

Integrator (Δt) convergence:

relative RMSD (expected value = 4) *vs* time step for three cutoff schemes on Lennard-Jones system.

➠ "switch" passes the test.





Kinetic energy test:

T_μ and T_σ are the effective temperature corresponding to the average kinetic energy μ of a distribution of width σ. For a water system of 900 TIP3P molecule, using weak-coupling (WC) or velocity-rescale (VR) algorithm.

➠ "VR" passes the test.

Merz, P. T.; Shirts, M. R. Testing for Physical Validity in Molecular Simulations. PLOS ONE 2018, 13 (9), e0202764. https://doi.org/10.1371/journal.pone.0202764. Images are reproduced under the CC BY 4.0 open access license.