Organization of NAMD Tutorial Files

- 1-1-build
- 1-2-sphere
- 1-3-box

  - 2-1-rmsd
  - 2-2-maxwell
  - 2-3-energies
  - 2-4-temp
  - 2-5-spec_heat
  - 2-6-heat_diff
  - 2-7-echoes

- 3-1-pullocv
- 3-2-pullocf

common
Objective: Find the average RMSD over time of each residue in the protein using VMD. Display the protein with the residues colored according to this value.
2.1.2 Maxwell-Boltzmann Distribution

**Objective:** Confirm that the kinetic energy distribution of the atoms in a system corresponds to the Maxwell distribution for a given temperature.

\[
p(\varepsilon_k) = \frac{2}{\sqrt{\pi}} \left( \frac{k_B T}{\varepsilon} \right)^{3/2} \sqrt{\varepsilon_k} \exp \left( -\frac{\varepsilon_k}{k_B T} \right)
\]

Normalization condition:

\[
\int_0^{\infty} d\varepsilon \ p(\varepsilon) = 1
\]
Objective: Plot the various energies (kinetic and the different internal energies) as a function of temperature.
2.1.4 Temperature Fluctuations

Temperature time series: 
\[ T(t) = \frac{2}{3k_B} \langle K(t) \rangle = \frac{1}{3Nk_B} \sum_{i=1}^{N} m_i v_i^2(t) \]
\[ = \sum_{i=1}^{N} X_i(t), \quad X_i(t) \equiv \frac{m_i v_i^2(t)}{3Nk_B} = \frac{2\varepsilon_i}{3Nk_B} \]

According to the central limit theorem:
\[ \langle T \rangle = N \langle X \rangle = \frac{2}{3k_B} \left( \frac{m_i v_i^2}{2} \right) = \frac{2}{3k_B} \frac{3}{2} k_B T_0 = T_0 \quad \text{thermodynamic temperature} \]
\[ \sigma_0^2 = \langle X^2 \rangle - \langle X \rangle^2 = \frac{2T_0^2}{3N^2} \Rightarrow \sigma^2 = \sigma_0^2 / N = \frac{2T_0^2}{3N} \]

\[
p(x) = \left( \frac{4\pi T_0^2}{3N} \right)^{-1/2} \exp \left[ -\frac{3(T - T_0)^2}{4T_0^2} \right]
\]
Analysis of MD Data

1. Structural properties
2. Equilibrium properties
3. Non-equilibrium properties

Can be studied via both equilibrium and/or non-equilibrium MD simulations
Time Correlation Functions

\[ C_{AB}(t-t') = \langle A(t) B(t') \rangle = \langle A(t-t') B(0) \rangle \]

since \( \rho_{eq} \) is \( t \) independent!

\[ A \neq B \quad \text{cross-} \]
\[ A = B \quad \text{auto-} \]

\] \] \]

Correlation time: \( \tau_c = \int_0^\infty dt \frac{C_{AA}(t)}{C_{AA}(0)} \)

Estimates how long the “memory” of the system lasts

In many cases (but not always): \( C(t) = C(0) \exp(-t/\tau_c) \)
Free Diffusion (Brownian Motion) of Proteins

- in living organisms proteins exist and function in a viscous environment, subject to stochastic (random) thermal forces
- the motion of a globular protein in a viscous aqueous solution is diffusive
- e.g., ubiquitin can be modeled as a spherical particle of radius $R \approx 1.6\text{nm}$ and mass $M = 6.4\text{kDa} = 1.1 \times 10^{-23}\text{ kg}$

$2R \approx 3.2\text{ nm}$
Diffusion can be Studied by MD Simulations!

*ubiquitin* in water

PDB entry: 1UBQ

**total # of atoms:** 7051 = 1231 (protein) + 5820 (water)

**simulation conditions:** NpT ensemble (T=310K, p=1atm), periodic BC, full electrostatics, time-step 2fs (SHAKE)

**simulation output:** Cartesian coordinates and velocities of all atoms saved at every other time-step (10,000 frames = 40 ps) in separate DCD files
Goal: calculate D and $\tau$

by fitting the theoretically calculated center of mass (COM) velocity autocorrelation function to the one obtained from the simulation

- **theory:**
  \[
  C_{vv}(t) = \langle v(t) v(0) \rangle = \langle v_0^2 \rangle e^{-t/\tau}
  \]
  \[
  \langle v_0^2 \rangle = \frac{k_B T}{M} = \frac{D}{\tau} \quad \text{(equipartition theorem)}
  \]

- **simulation:** consider only the x-component ($v_x \rightarrow v$)
  replace ensemble average by time average

  \[
  C_{vv}(t) \approx C_i = \frac{1}{N - i} \sum_{n=1}^{N-i} v_{n+i} v_n
  \]

  \[
  t = t_i = i\Delta t, \quad v_n = v(t_n), \quad N = \# \text{ of frames in vel.DCD}
  \]
Velocity Autocorrelation Function

\[ \tau \approx 0.1 \text{ ps} \]

\[ D = k_B T / \gamma = \langle v_x^2 \rangle \tau \approx 3.3 \times 10^{-11} \text{ m}^2 \text{ s}^{-1} \]
Probability distribution of $v_{x,y,z}$

\[ p(v) = \left( \frac{2\pi \langle v^2 \rangle}{\tau} \right)^{-1/2} \exp\left( -\frac{v^2}{2\langle v^2 \rangle} \right) \]

\[ = \sqrt{\frac{\tau}{2\pi D}} \exp\left( -\frac{\tau v^2}{2D} \right) \]

with $v \equiv v_{x,y,z}$