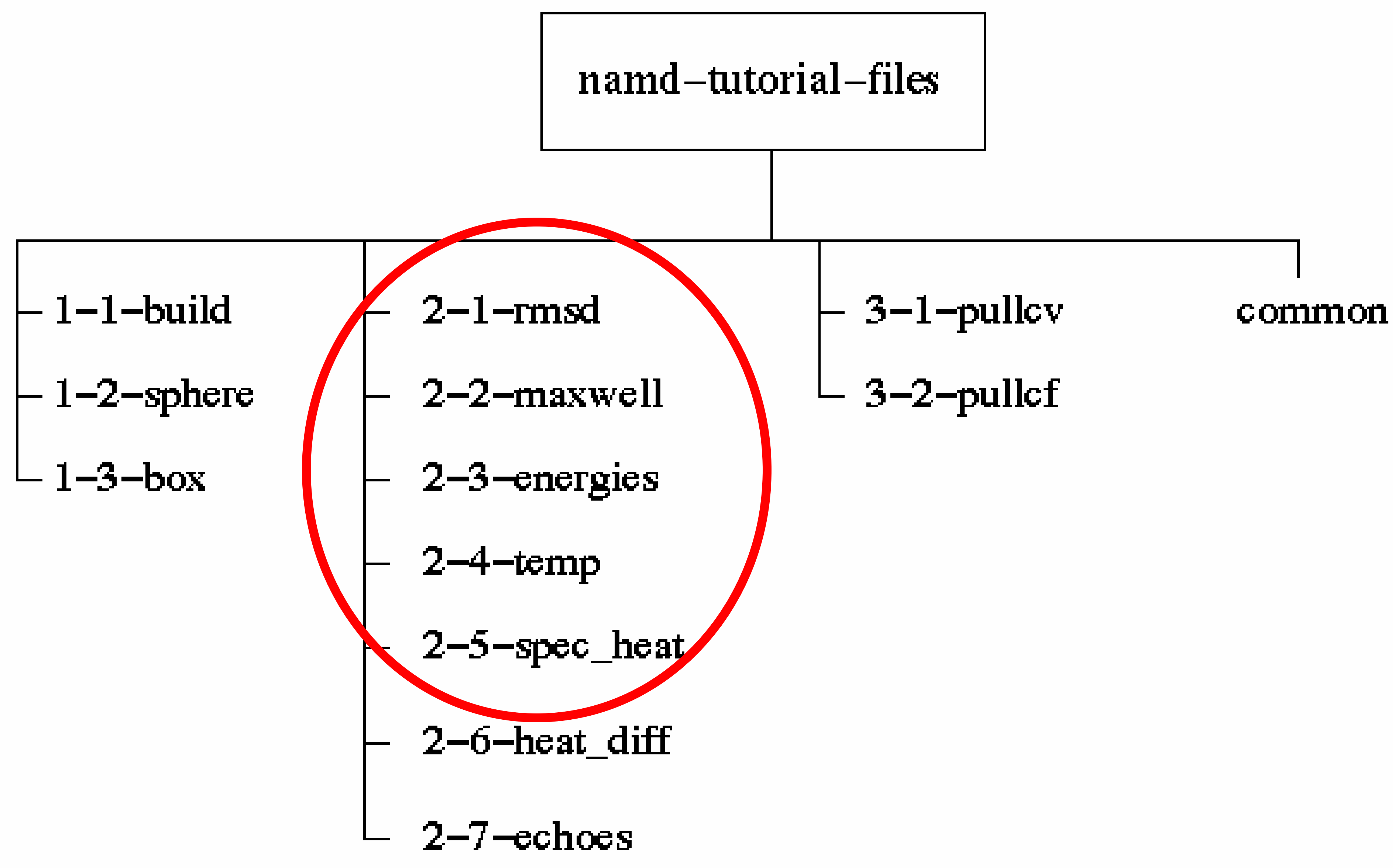
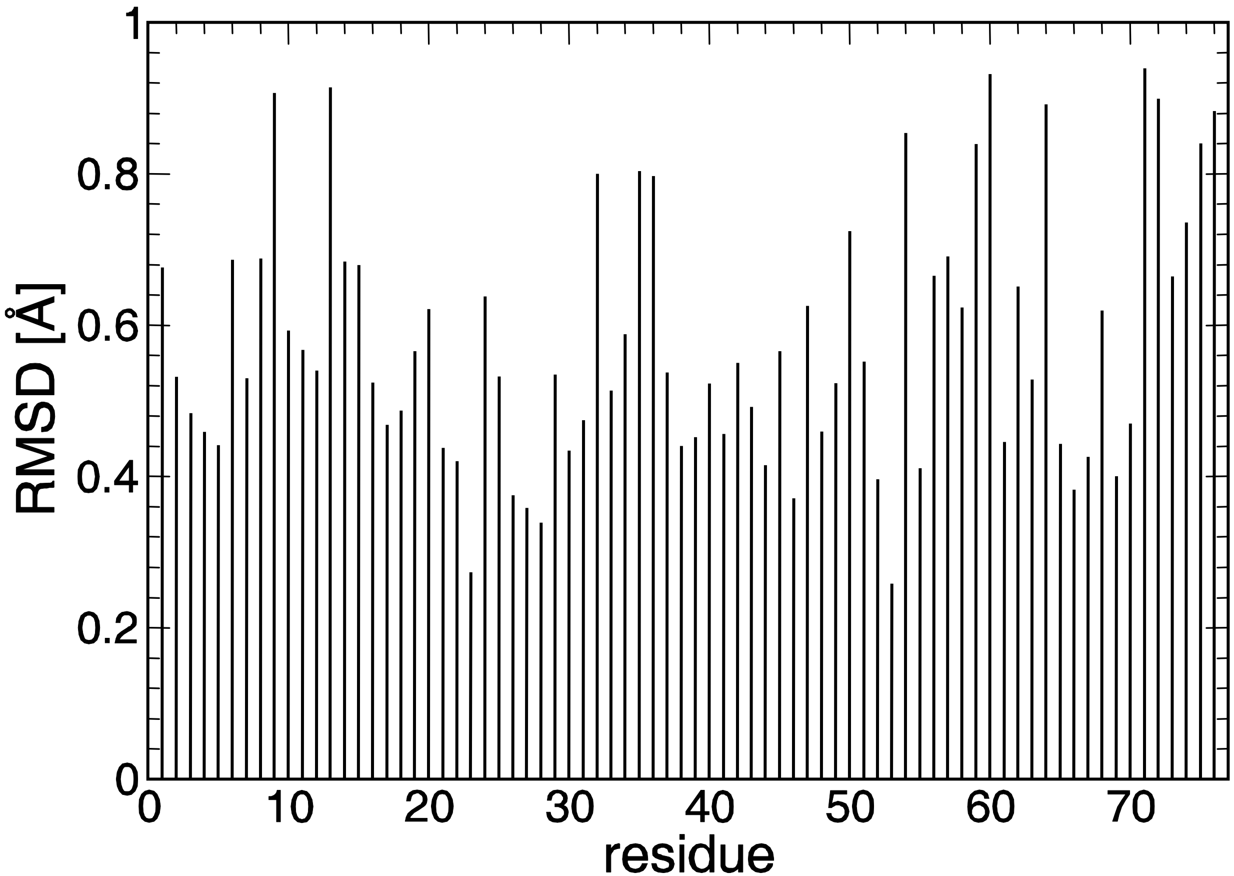
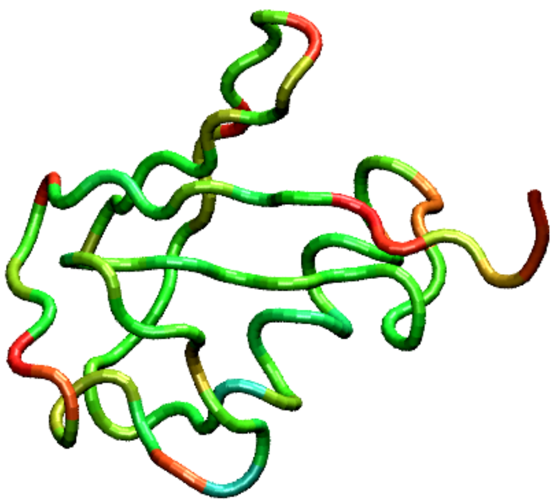
Organization of NAMD Tutorial Files



2.1.1. RMSD for individual residues

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.

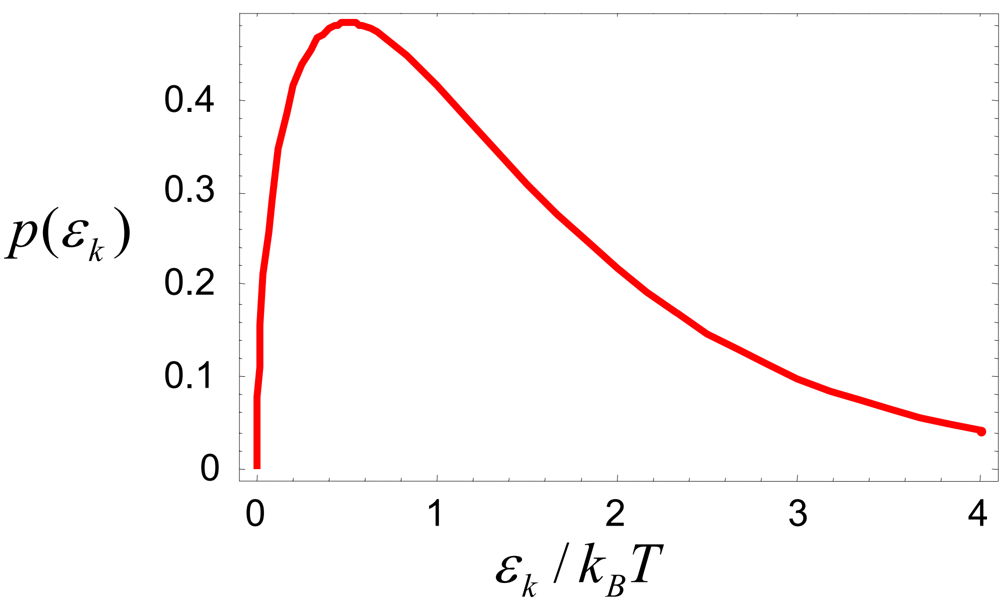




2.1.2 Maxwell-Boltzmann Distribution

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

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



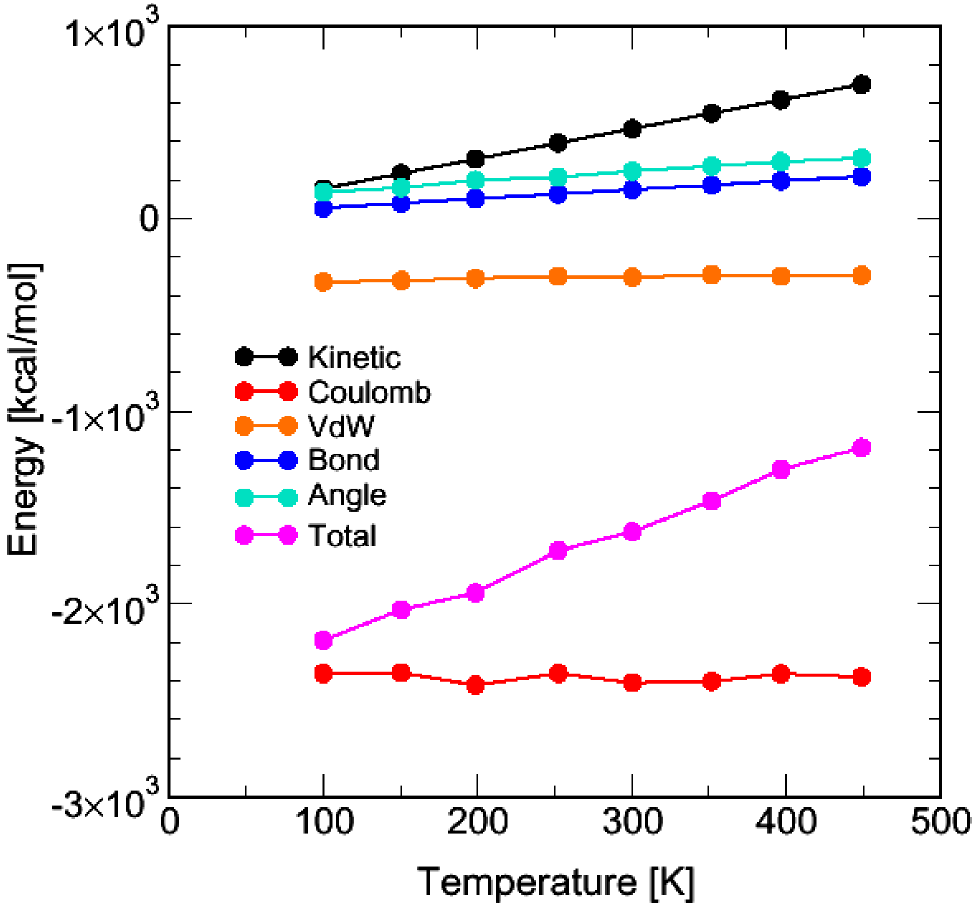
normalization condition:

$$\int_0^\infty d\varepsilon \, p(\varepsilon) = 1$$

2.1.3 Energies

<u>Objective</u>: Plot the various energies (kinetic and the different internal energies) as a function of temperature.

<u>sample</u>:



2.1.4 Temperature Fluctuations

Temperature time series: $T(t) = \frac{2}{3k_B}\langle K(t)\rangle = \frac{1}{3Nk_B}\sum_{i=1}^{N} m_i v_i^2(t)$

$$= \sum_{i=1}^{N} X_i(t)\,, \qquad X_i(t) \equiv \frac{m_i v_i^2(t)}{3Nk_B} = \frac{2\varepsilon_i}{3Nk_B}$$

According to the central limit theorem:

$$\langle T\rangle = N\langle X\rangle = \frac{2}{3k_B}\left\langle \frac{m_i v_i^2}{2}\right\rangle = \frac{2}{3k_B}\frac{3}{2}k_B T_0 = T_0$$

thermodynamic temperature

$$\sigma_0^2 = \langle X^2\rangle - \langle X\rangle^2 = \frac{2T_0^2}{3N^2} \Rightarrow \sigma^2 = \sigma_0^2 / N = \frac{2T_0^2}{3N}$$

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

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

$$C_{AB}(t-t') = \underbrace{\langle A(t)\,B(t')\rangle = \langle A(t-t')\,B(0)\rangle}_{\text{since } \rho_{eq} \text{ is } t \text{ independent !}}$$

$$\left.\begin{array}{ll} A \neq B & \text{cross-} \\ A = B & \text{auto-} \end{array}\right\} \text{correlation function}$$

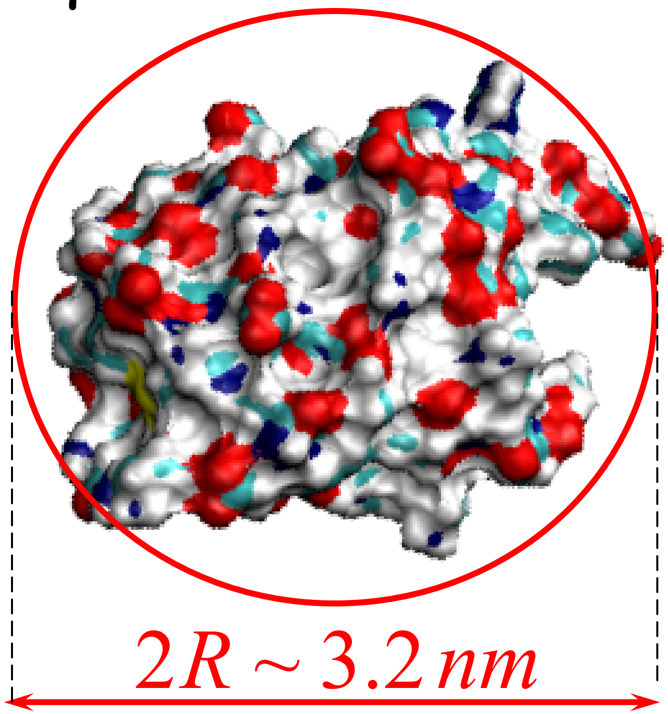
Correlation time: $\tau_c = \int_0^\infty dt\, C_{AA}(t) / C_{AA}(0)$

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

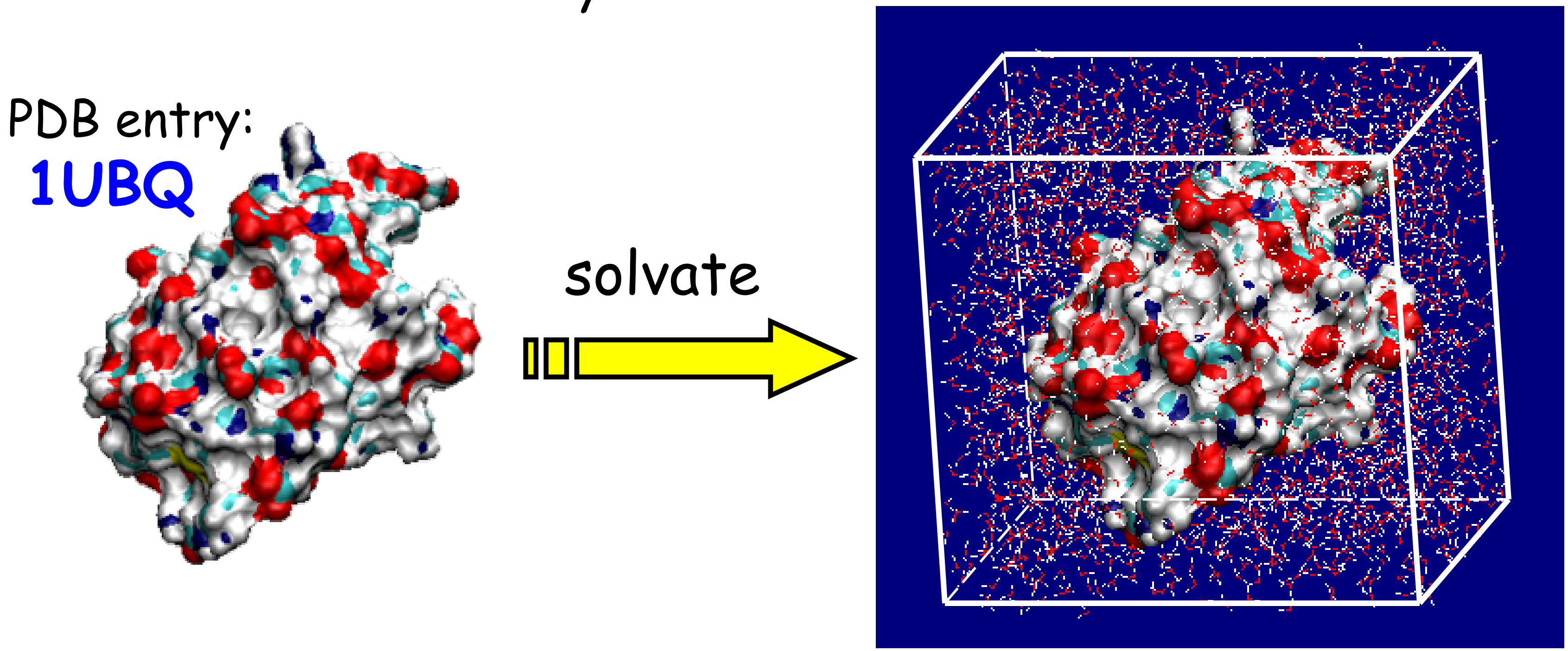
- in living organisms proteins exist and function in a viscous environment, subject to stochastic (random) thermal forces
- the motion of a globular protein in a viscous aqueous solution is diffusive



- e.g., *ubiquitin* can be modeled as a spherical particle of radius R~1.6nm and mass M=6.4kDa=1.1×10^{-23} kg

Diffusion can be Studied by MD Simulations!

ubiquitin in water



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 τ

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

- **theory:** $$C_{vv}(t) = \left\langle v(t)\, v(0) \right\rangle = \left\langle v_0^2 \right\rangle e^{-t/\tau}$$

$$\left\langle v_0^2 \right\rangle = \frac{k_B T}{M} = \frac{D}{\tau}$$ (equipartition theorem)

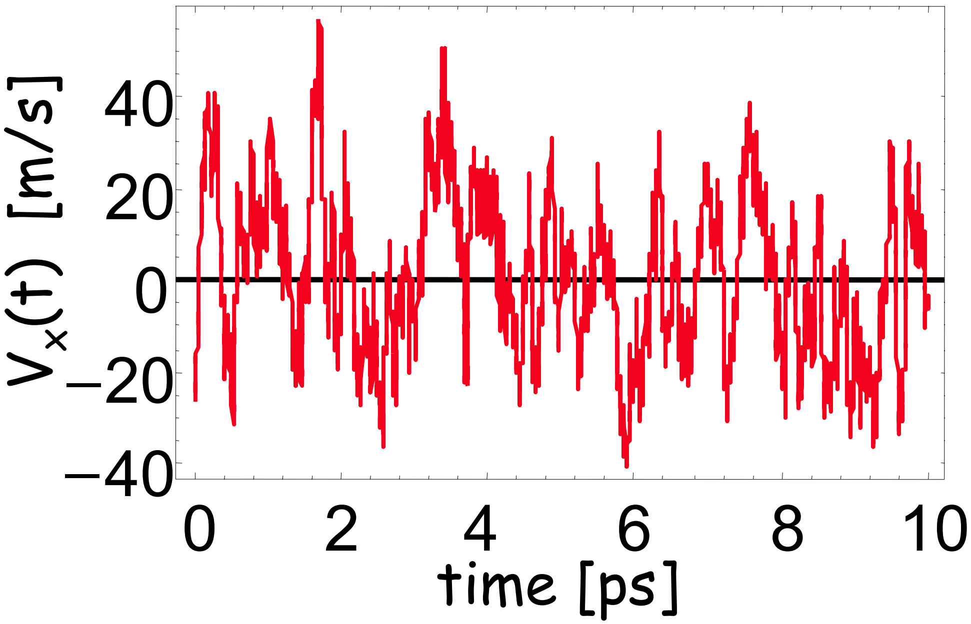
- **simulation:** consider only the x-component $\left(v_x \to v\right)$

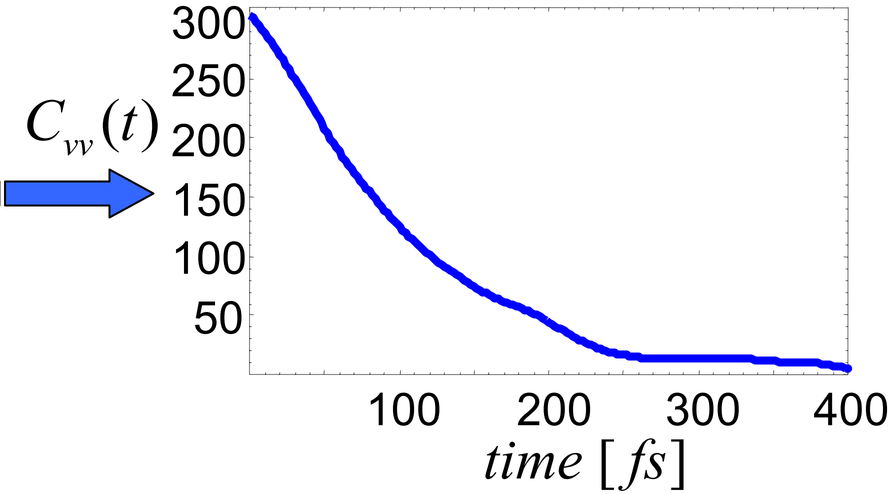
  replace ensemble average by time average

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

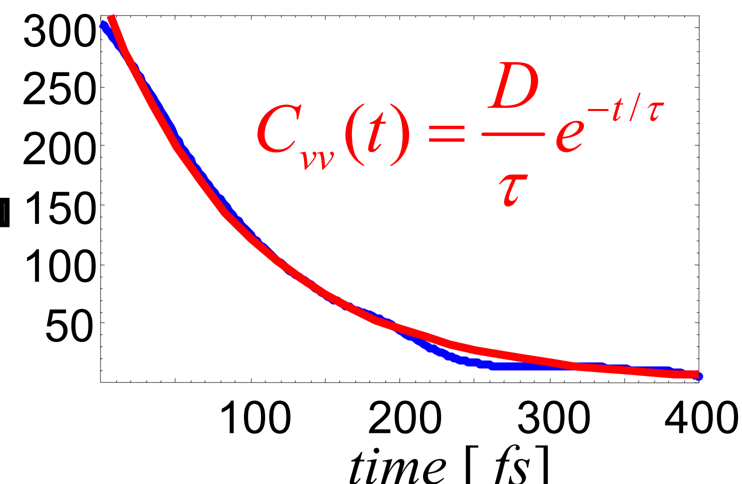
$t \equiv t_i = i\Delta t\,,\ v_n = v\left(t_n\right),\ N = \#$ of frames in vel.DCD

Velocity Autocorrelation Function





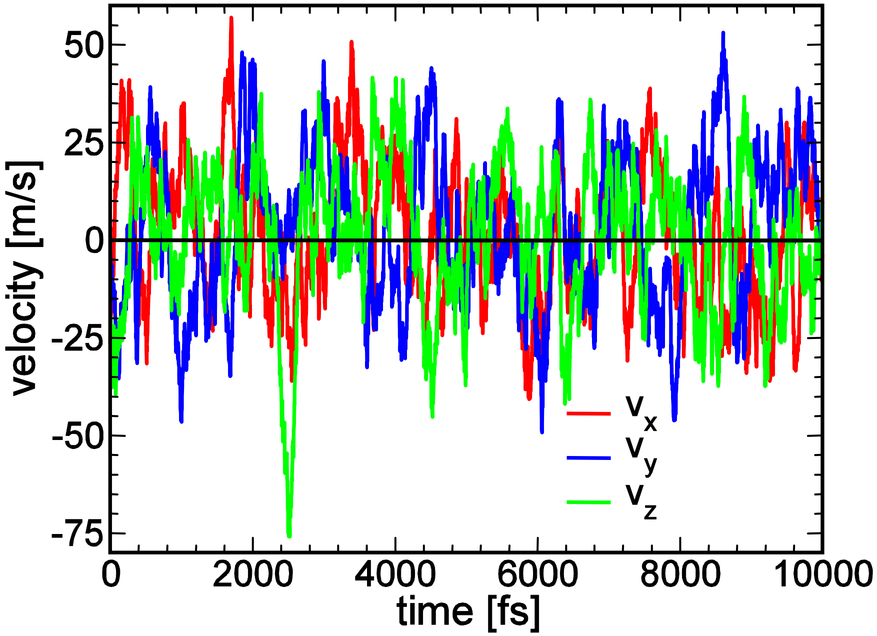
Fit

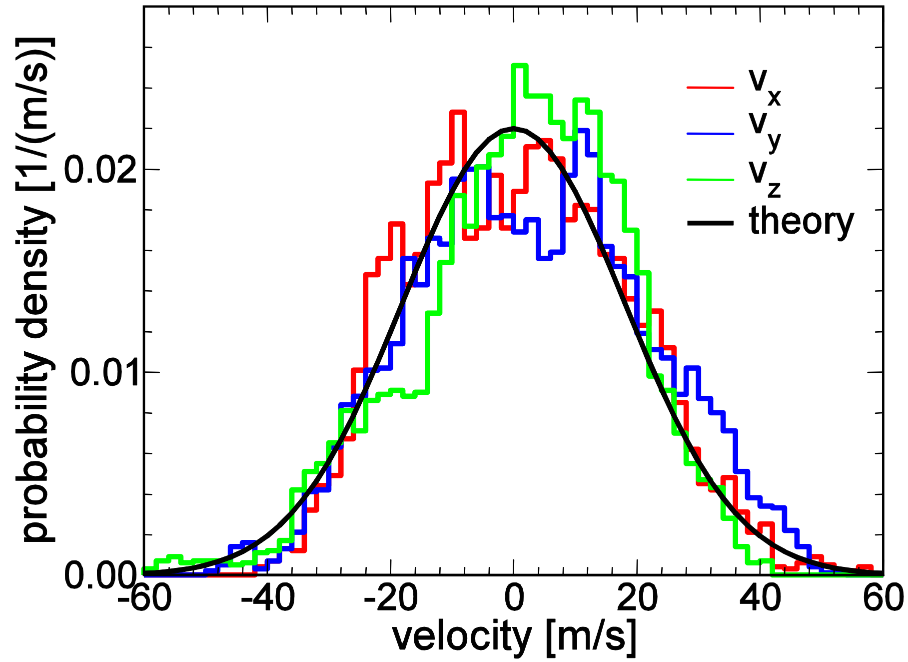


$$\tau \approx 0.1\, ps$$

$$D = k_B T / \gamma =$$
$$= \langle v_x^2 \rangle \tau \ \approx 3.3 \times 10^{-11}\, m^2 s^{-1}$$

Probability distribution of $v_{x,y,z}$





$$p(v) = \left(2\pi\left\langle v^2\right\rangle\right)^{-1/2} \exp\left(-v^2/2\left\langle v^2\right\rangle\right)$$
$$= \sqrt{\tau/2\pi D}\exp\left(-\tau v^2/2D\right)$$

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