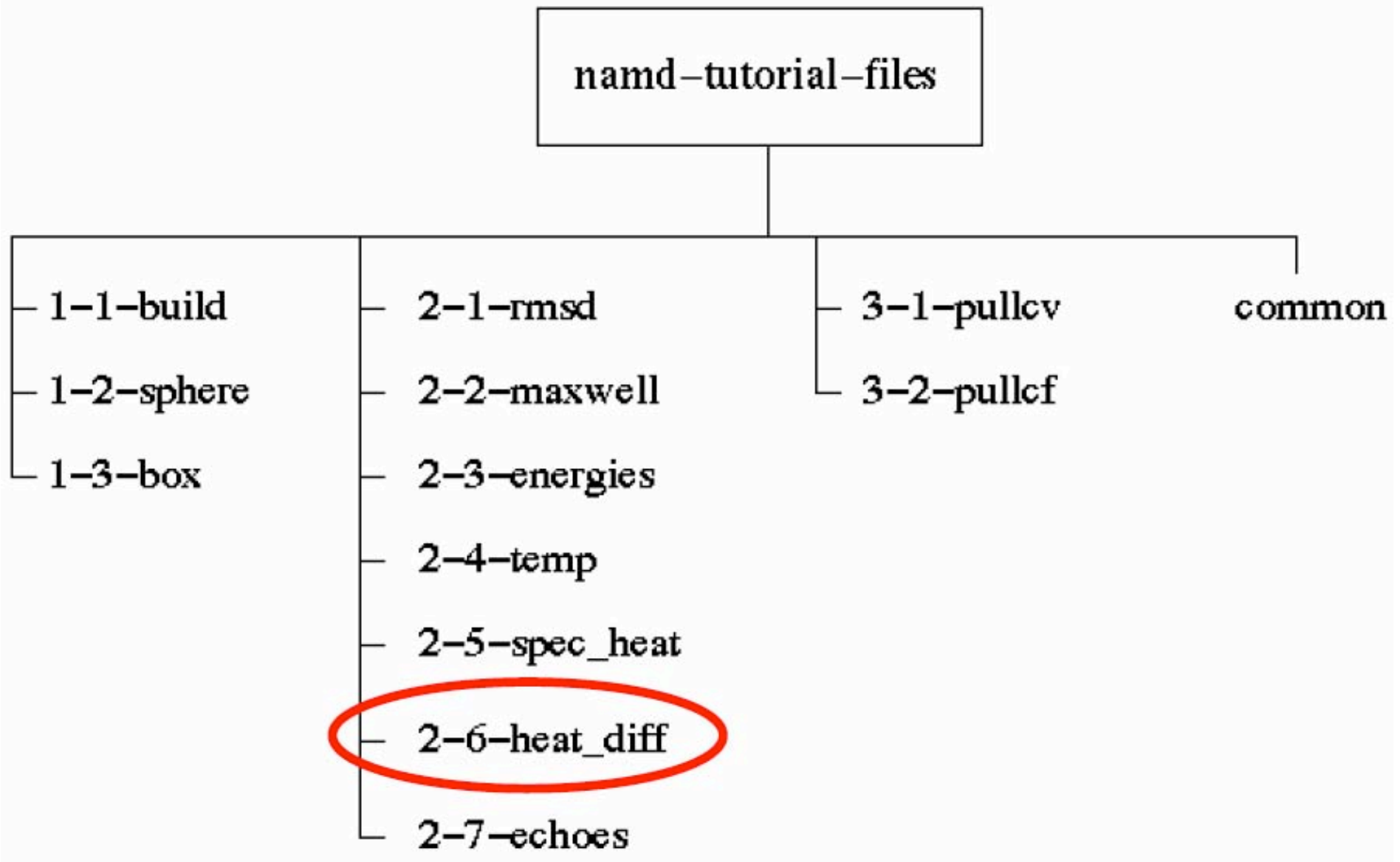


NAMD Tutorial (Part 2)

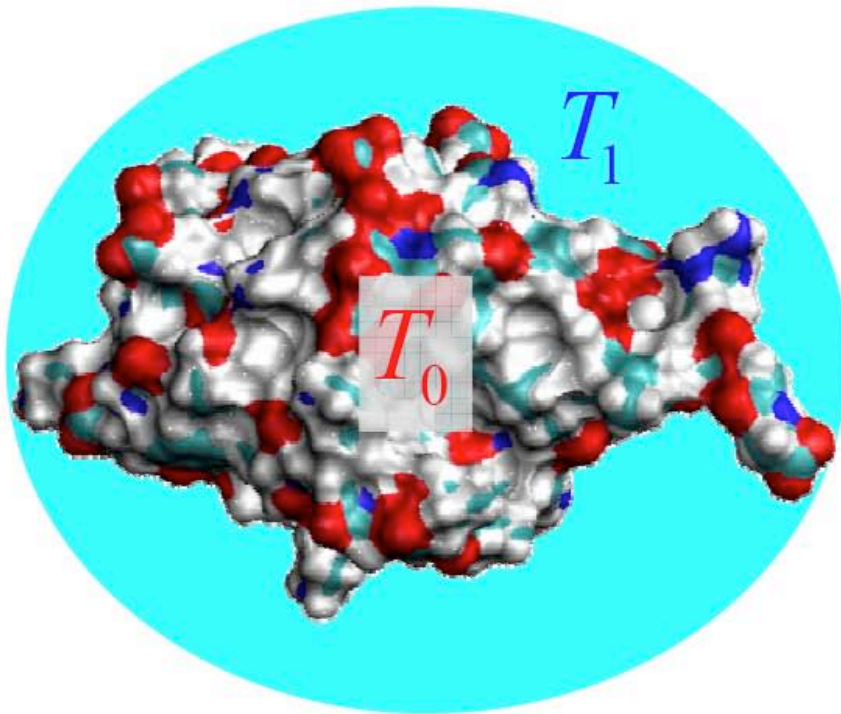
- ▶ **2 Analysis**
 - ▶ 2.1 Equilibrium
 - ▶ 2.1.1 RMSD for individual residues
 - ▶ 2.1.2 Maxwell-Boltzmann Distribution
 - ▶ 2.1.3 Energies
 - ▶ 2.1.4 Temperature distribution
 - ▶ 2.1.5 Specific Heat
 - ▶ **2.2 Non-equilibrium properties of protein**
 - ▶ **2.2.1 Heat Diffusion**
 - ▶ 2.2.2 Temperature echoes

Organization of NAMD Tutorial Files



Simulated Cooling of Ubiquitin

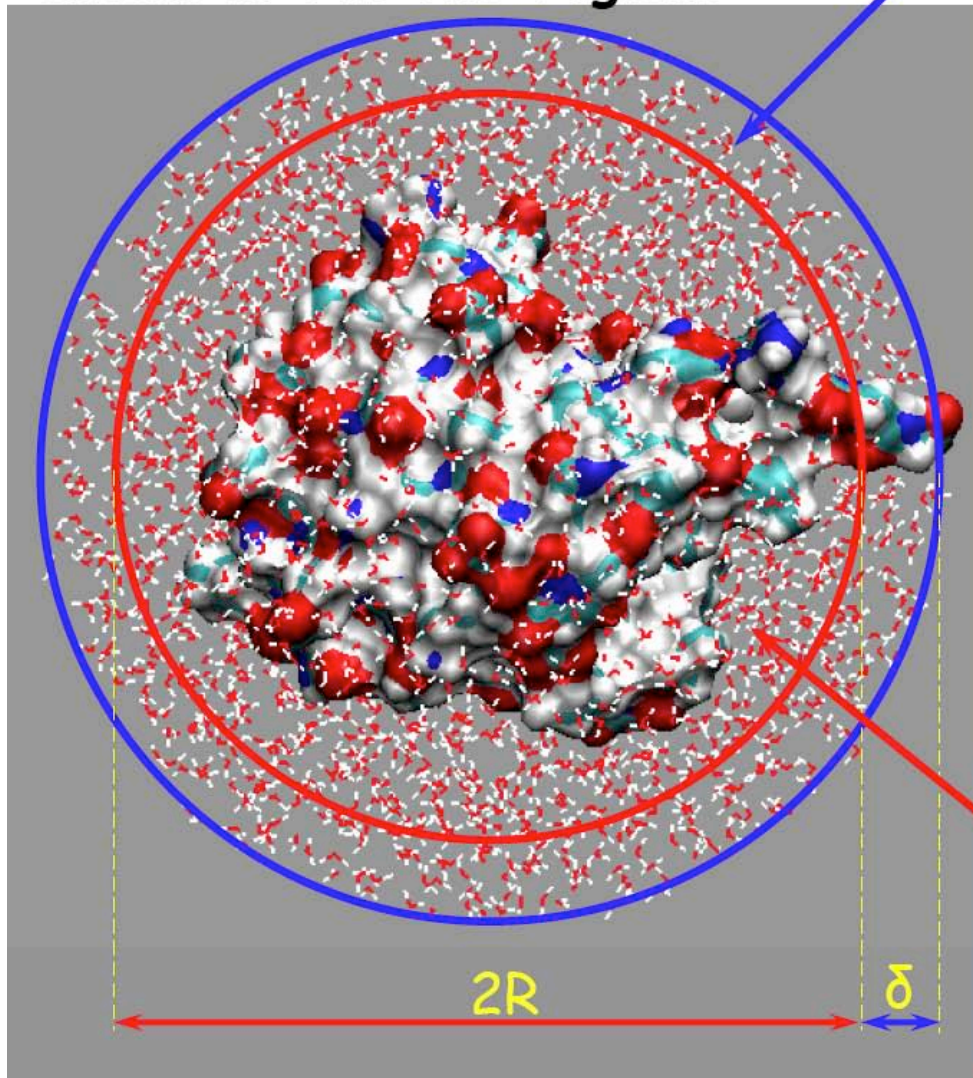
- Proteins function in a narrow (physiological) temperature range. What happens to them when the temperature of their surrounding changes significantly (temperature gradient) ?
- Can the heating/cooling process of a protein be simulated by molecular dynamics ? If yes, then how?



- What can we learn from the simulated cooling/heating of a protein ?

How to simulate cooling ?

Heat transfer through mechanical coupling between atoms in the two regions



coolant layer of atoms

motion of atoms is subject to stochastic Langevin dynamics

$$m \ddot{\mathbf{r}} = \mathbf{F}_{FF} + \mathbf{F}_H + \mathbf{F}_f + \mathbf{F}_L$$

\mathbf{F}_{FF} → force field

\mathbf{F}_H → harmonic restrain

\mathbf{F}_f → friction

\mathbf{F}_L → Langevin force

atoms in the inner region follow Newtonian dynamics

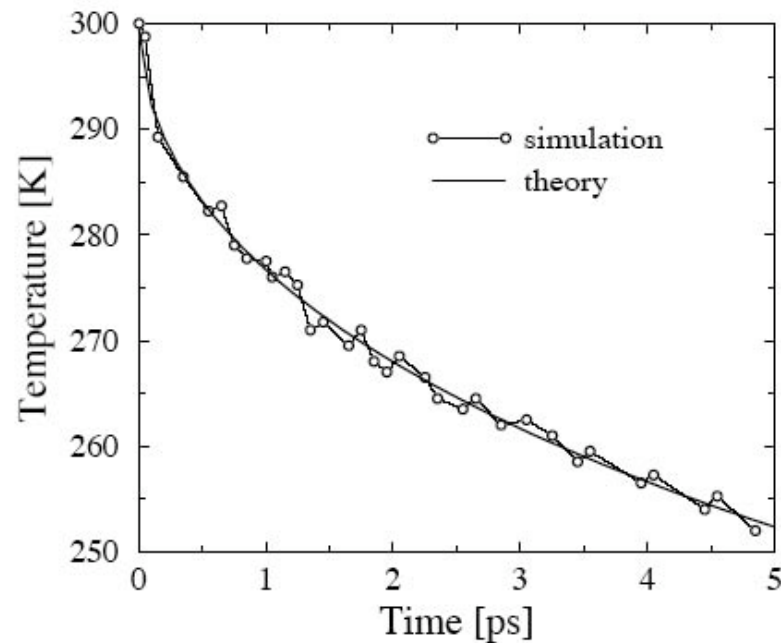
$$m \ddot{\mathbf{r}} = \mathbf{F}_{FF}$$

Solution of the Heat Equation

t	$\langle T_{sim} \rangle$	t	$\langle T_{sim} \rangle$	t	$\langle T_{sim} \rangle$	t	$\langle T_{sim} \rangle$
0.05	298.75	1.05	276.00	1.95	267.00	3.25	261.00
0.15	289.25	1.15	276.50	2.05	268.50	3.45	258.50
0.35	285.50	1.25	275.25	2.25	266.50	3.55	259.50
0.55	282.25	1.35	271.00	2.35	264.50	3.95	256.50
0.65	282.75	1.45	271.75	2.55	263.50	4.05	257.25
0.75	279.00	1.65	269.50	2.65	264.50	4.45	254.00
0.85	277.75	1.75	271.00	2.85	262.00	4.55	255.25
1.00	277.50	1.85	268.00	3.05	262.50	4.85	252.00

Result from simulation

Table 1: Mean temperature $\langle T_{sim} \rangle$ [K] of the protein as a function of time t [ps].



Heat Conduction Equation

$$\frac{\partial T(\mathbf{r}, t)}{\partial t} = D \nabla^2 T(\mathbf{r}, t)$$

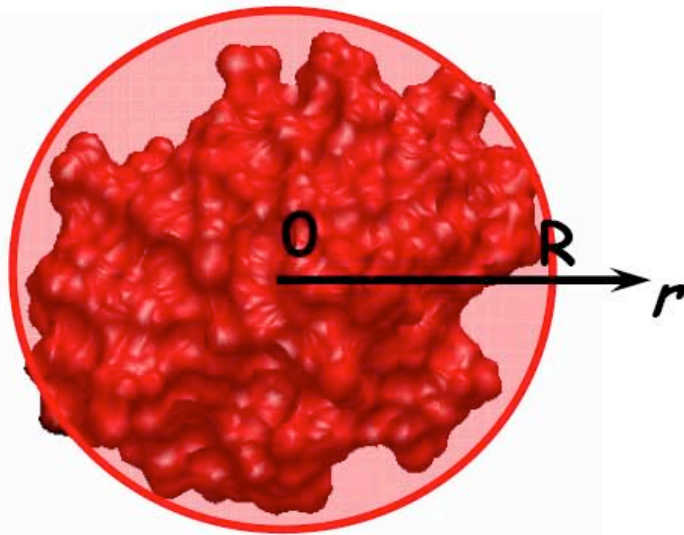
thermal diffusion
coefficient

$$D = K / \rho c$$

mass density

specific heat

thermal conductivity



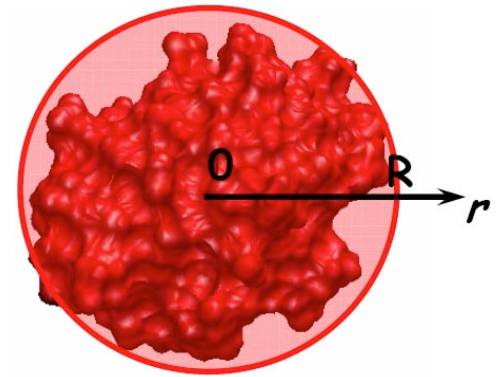
- approximate the protein with a homogeneous sphere of radius $R \sim 20 \text{ \AA}$
- calculate $T(r, t)$ assuming initial and boundary conditions:

$$T(r, 0) = T_0 \text{ for } r < R$$

$$T(R, t) = T_{bath}$$

Solution of the Heat Equation

$$\frac{\partial T(\mathbf{r}, t)}{\partial t} = D \nabla^2 T(\mathbf{r}, t) ,$$
$$D = K / \rho c ,$$



Initial condition

$$T(\mathbf{r}, 0) = \langle T_{sim} \rangle(0) \quad \text{for } r < R ,$$

Boundary condition

$$T(R, t) = T_{bath} .$$

Solution of the Heat Equation

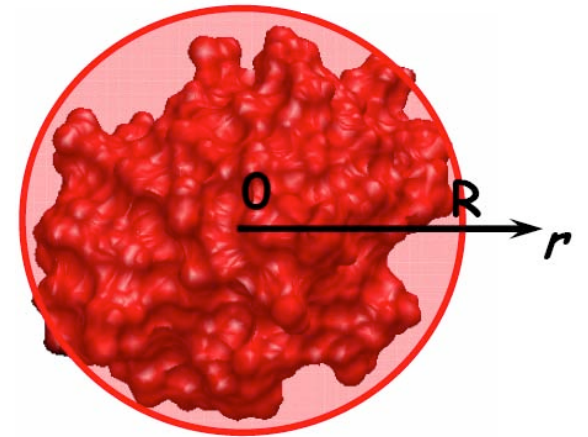
Spherical symmetry

$$\frac{\partial T(r, t)}{\partial t} = D \frac{1}{r} \partial_r^2 r T(r, t) \quad T_{bath}$$

We assume

$$T(r, t) = T_{bath} + \sum_{n=1}^{\infty} a_n e^{\lambda_n t} u_n(r)$$

difference from bath



Here u_n are the eigenfunctions of the spherical diffusion operator

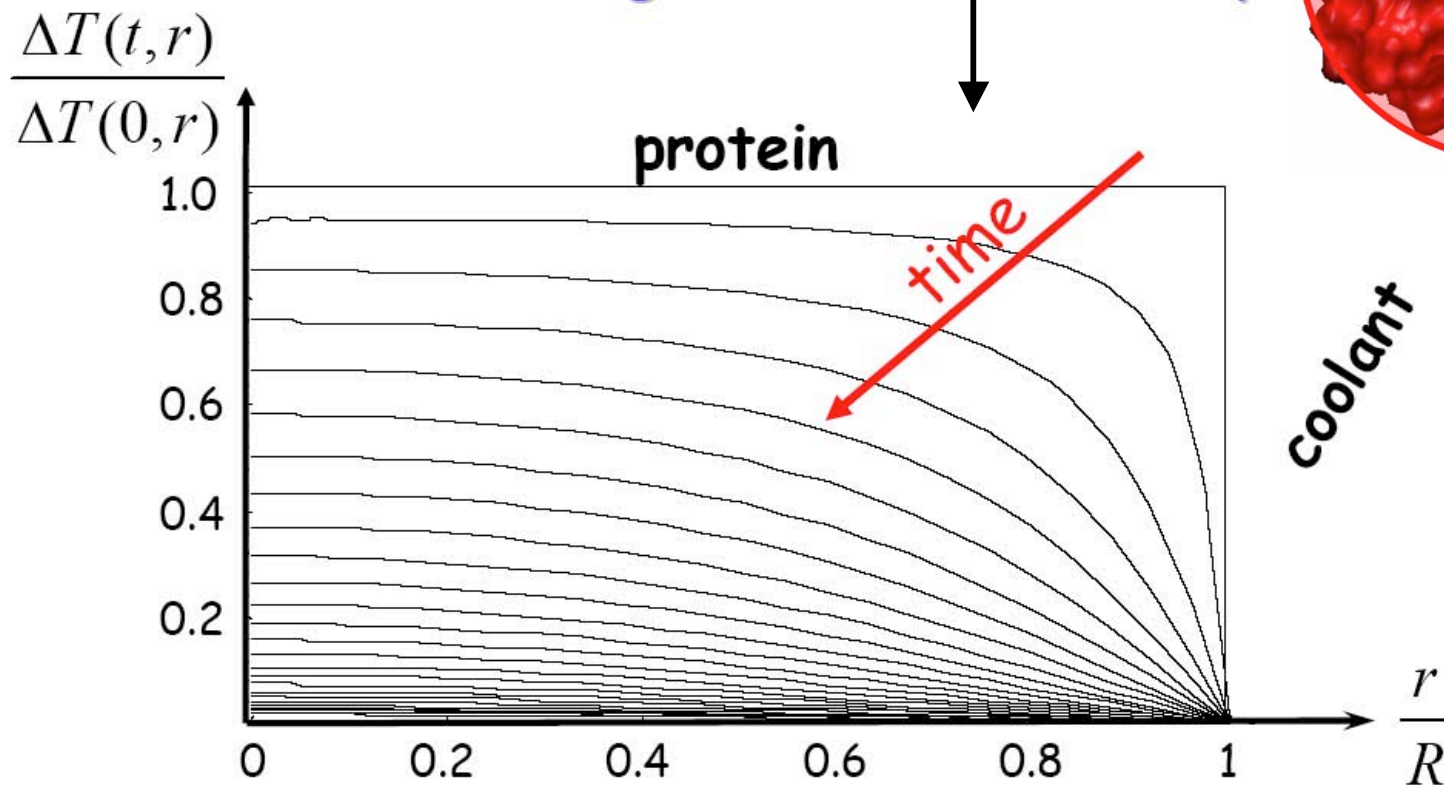
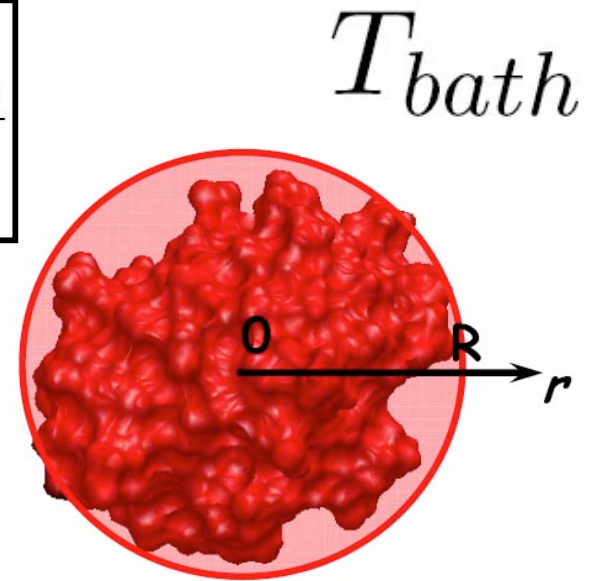
$$L \equiv \frac{D}{r} \frac{d^2}{dr^2} r$$

$$\frac{D}{r} \frac{d^2}{dr^2} r u_n(r) = \lambda_n u_n(r) \quad , \quad u_n(0) = \text{finite} \quad , \quad u_n(R) = 0$$

Solution of the Heat Equation

$$T(r, t) = T_{bath} + \sum_{n=1}^{\infty} a_n \exp \left[- \left(\frac{n\pi}{R} \right)^2 D t \right] \frac{\sin (n\pi r / R)}{r}$$

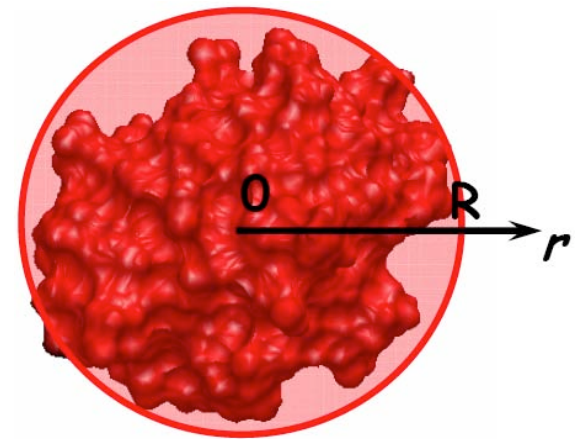
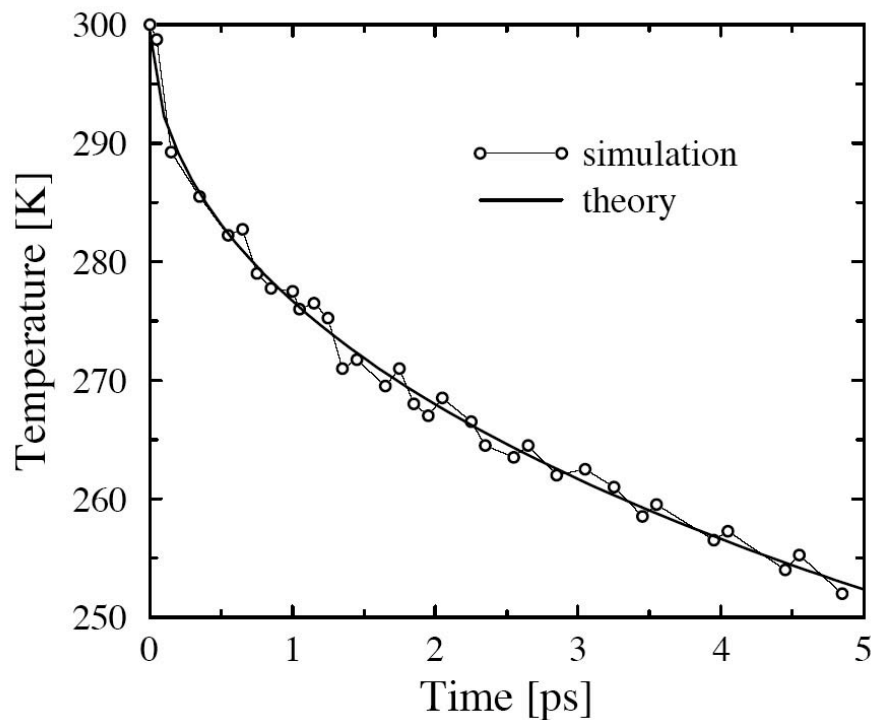
$$a_m = \frac{2R}{m\pi} \Delta T (-1)^{m+1}$$



Solution of the Heat Equation

Temperature averaged over volume

$$\begin{aligned}\langle T \rangle(t) &= \left(\frac{4\pi R^3}{3} \right)^{-1} \int d^3\mathbf{r} T(\mathbf{r}, t) = \frac{3}{R^3} \int_0^R r^2 dr T(r, t) \\ &= T_{bath} + \sum_{n=1}^{\infty} a_n \exp \left[- \left(\frac{n\pi}{R} \right)^2 D t \right] \frac{3}{R^3} \int_0^R r dr \sin \left(\frac{n\pi r}{R} \right) \\ &= T_{bath} + 6 \frac{\Delta T}{\pi^2} \sum_{n=1}^{\infty} \frac{1}{n^2} \exp \left[- \left(\frac{n\pi}{R} \right)^2 D t \right]\end{aligned}$$



$$D \approx 0.38 \times 10^{-3} \text{cm}^2 \text{s}^{-1}$$

$$\text{water } 1.4 \times 10^{-3} \text{cm}^2 \text{s}^{-1}$$

NAMD Tutorial (Part 2)

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