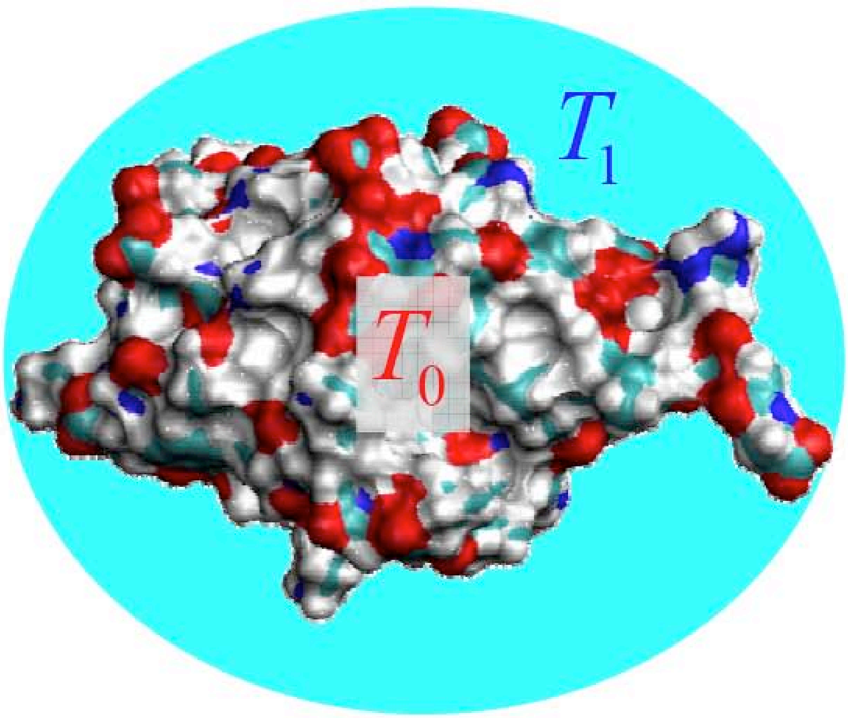
Simulated Cooling of Ubiquitin

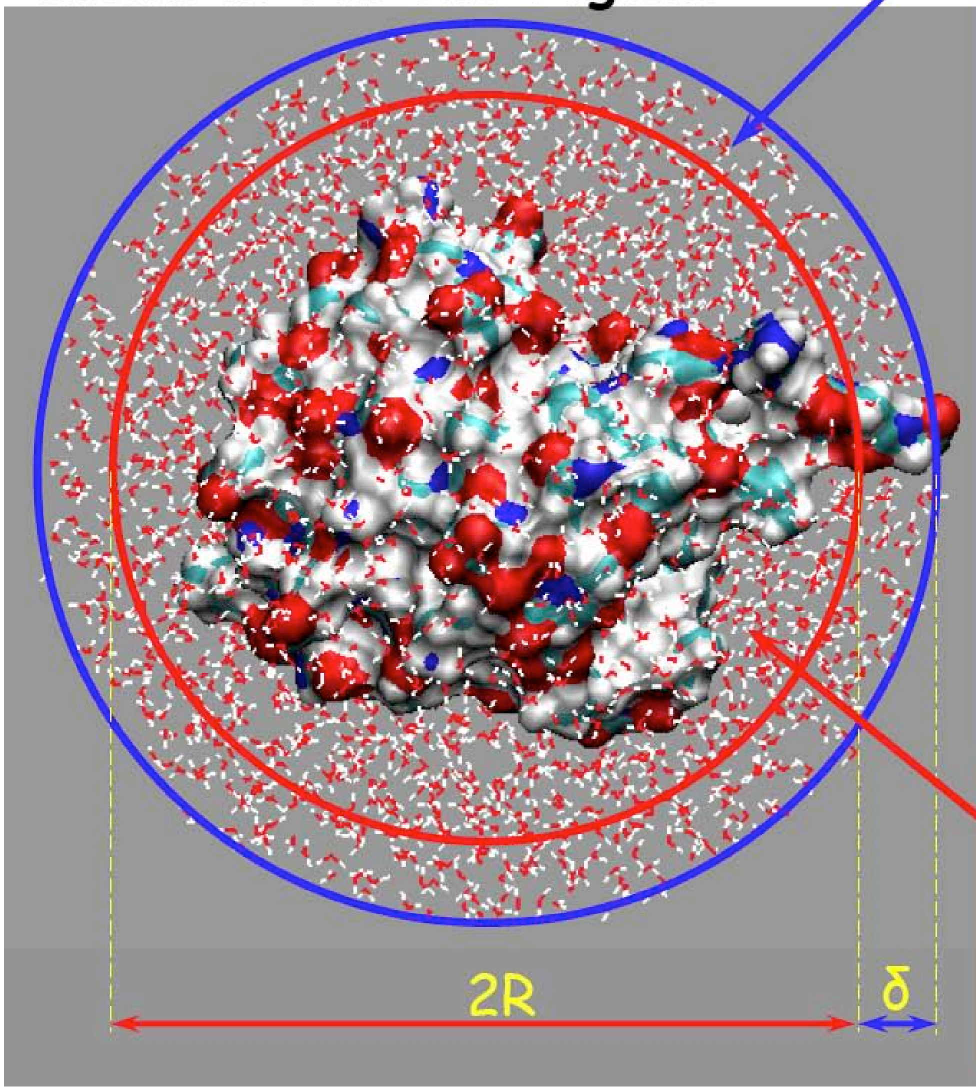
- Proteins function in a narrow (physiological) temperature range. What happens to them when the temperature of their surrounding changes significantly (temperature gradient) ?
- Can the heating/cooling process of a protein be simulated by molecular dynamics ? If yes, then how?



- 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

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

$\boldsymbol{F}_{FF} \rightarrow$ force field

$\boldsymbol{F}_H \rightarrow$ harmonic restrain

$\boldsymbol{F}_f \rightarrow$ friction

$\boldsymbol{F}_L \rightarrow$ Langevin force

atoms in the inner region follow Newtonian dynamics

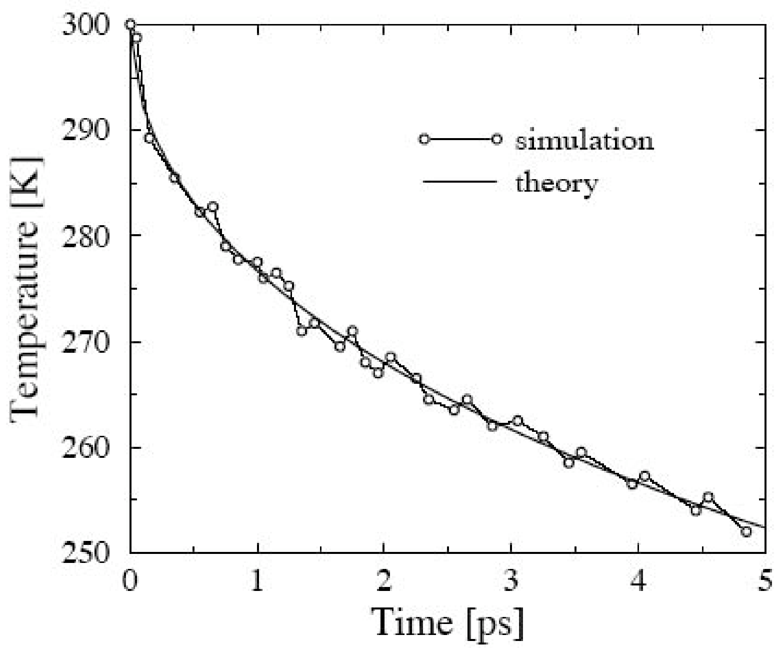
$$m\ddot{\boldsymbol{r}} = \boldsymbol{F}_{FF}$$

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

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

Result from simulation



Heat Conduction Equation

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

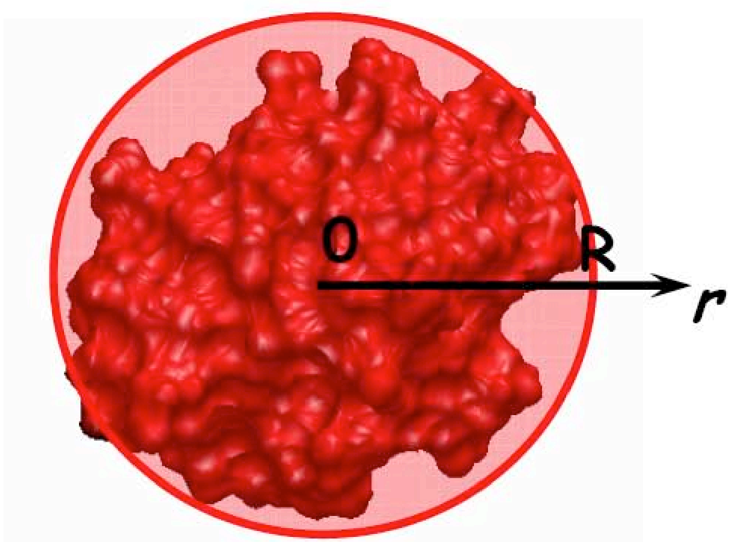
$$D = K/\rho c$$

thermal diffusion coefficient → D

mass density → ρ

specific heat → c

thermal conductivity → K



- approximate the protein with a homogeneous sphere of radius R~20 Å
- calculate *T(r,t)* assuming initial and boundary conditions:

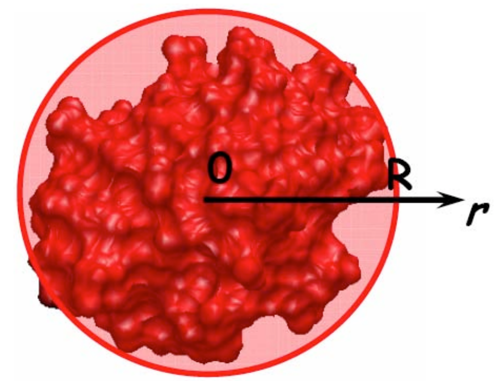
$$T(r,0) = T_0 \;\; for \;\; r < R$$

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

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

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

Boundary condition

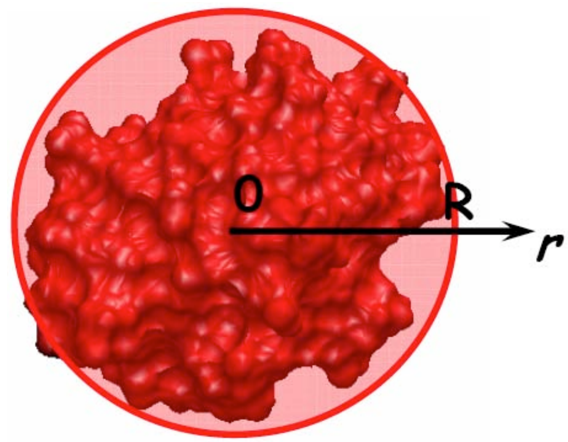
$$T(R,t) = T_{bath}\ .$$

Solution of the Heat Equation

Spherical symmetry

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

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

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

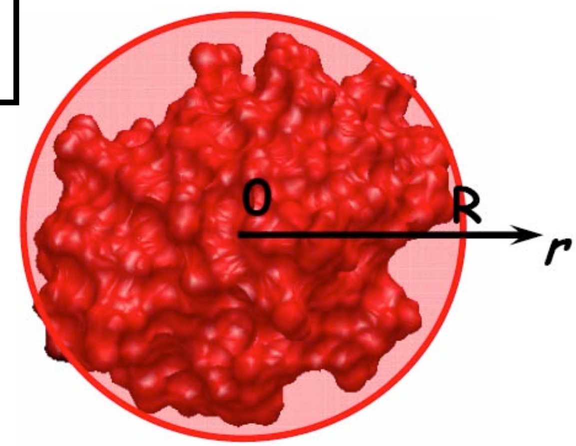
$$\frac{D}{r}\frac{d^2}{dr^2} r u_n(r) = \lambda_n\, u_n(r) \quad , \quad u_n(0) = \text{finite}\ , \quad u_n(R) = 0$$

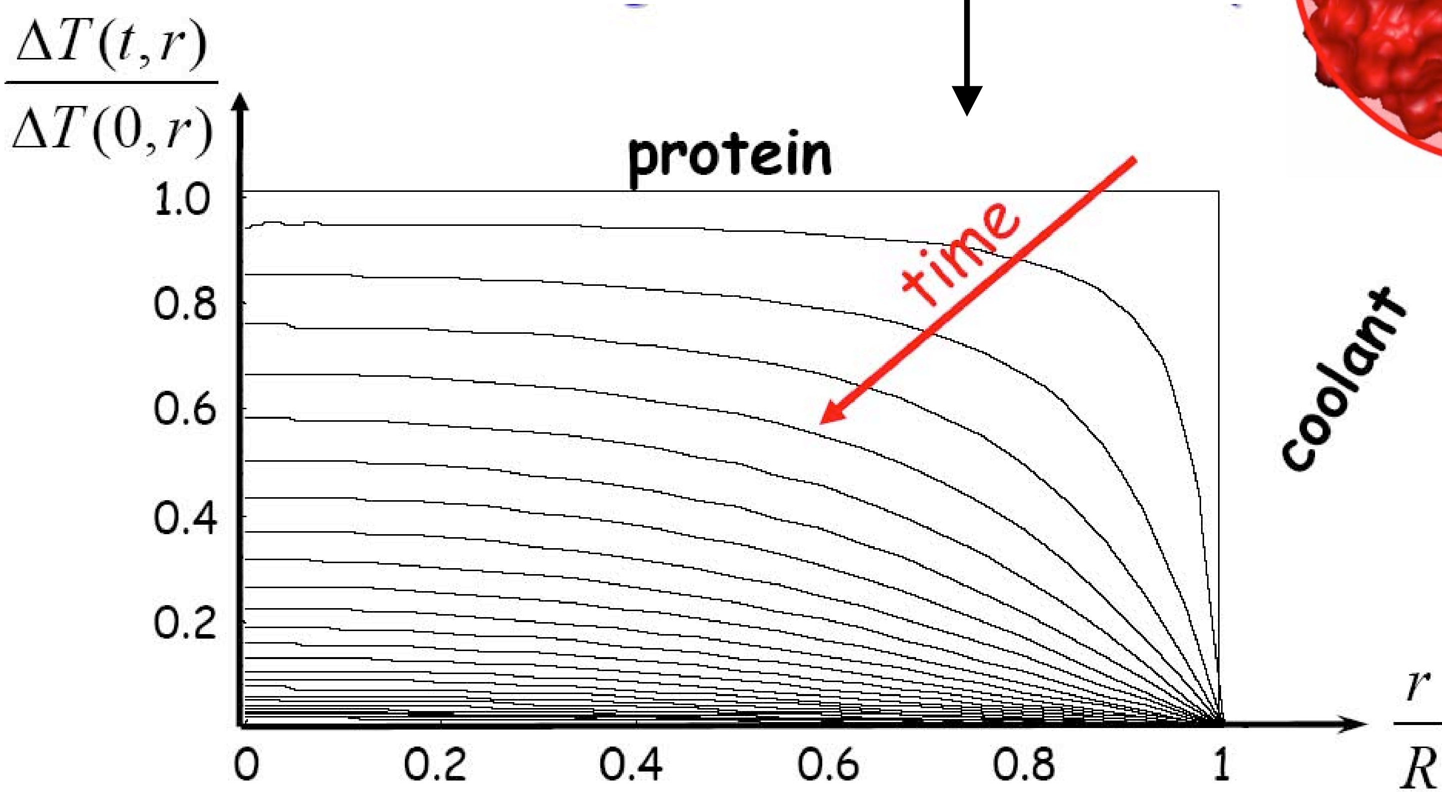
Solution of the Heat Equation

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

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

T_{bath}

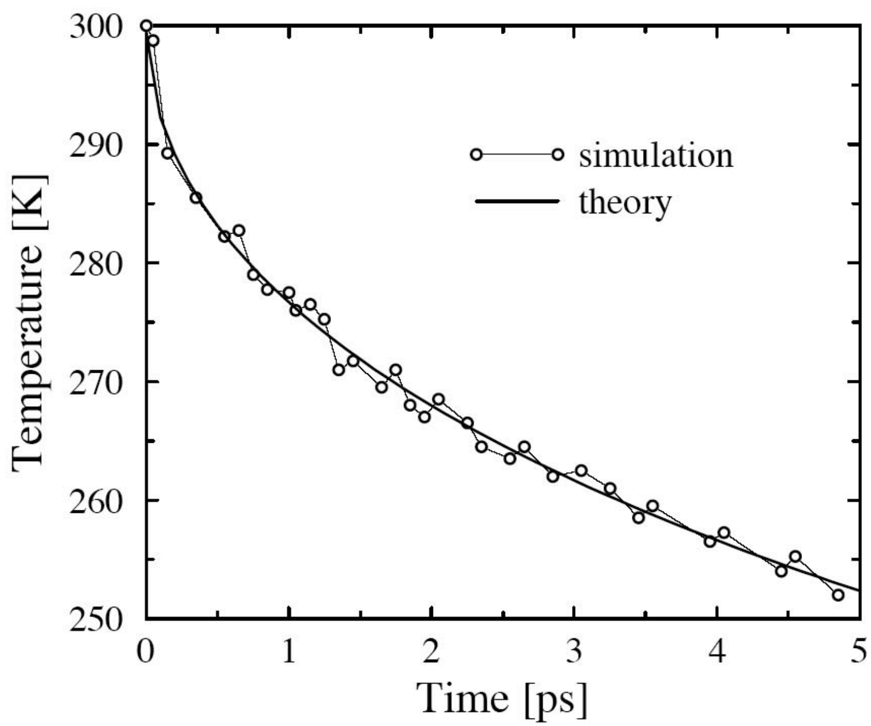


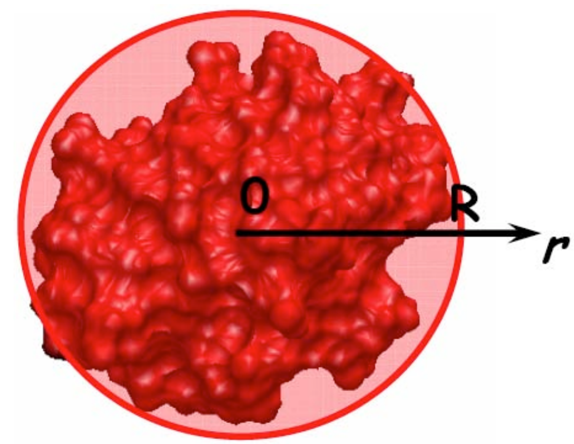


Solution of the Heat Equation

Temperature averaged over volume

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





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

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