2 Analysis

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- 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**
Temperature Echoes in Proteins

- Coherent motion in proteins: Echoes
- Generation of echoes in *ubiquitin* via velocity reassignments
  1) Temperature quench echoes
  2) Constant velocity reassignment echoes
  3) Velocity reassignment echoes

\[
T(t) = \frac{2}{(3N-6)k_B} \sum_{n=1}^{3N-6} \frac{m_n v_n^2(t)}{2}
\]

kinetic temperature:
Temperature Echoes

- are sharp, resonance-like features in the time evolution of the protein's temperature
- can be produced through 2 consecutive velocity reassignments

Protein in equilibrium

- Synchronization signal
- Probing signal
- Temperature echoes (a kind of "interference" effect!)
Velocity Reassignments

- protein \approx \text{collection of weakly interacting harmonic oscillators having different frequencies}
- at $t_i=0$ the 1$^{st}$ velocity reassignment: $v_i(0) = \lambda_1 u_i$ synchronizes the oscillators (i.e., make them oscillate in phase)
- at $t_2=\tau$ (delay time) the 2$^{nd}$ velocity reassignment: $v_i(\tau) = \lambda_2 u_i$ probes the degree of coherence of the system at that moment
- degree of coherence is characterized by:
  - the time(s) of the echo(es)
  - the depth of the echo(es)

\[ \lambda_1 = \lambda_2 = 0 \Rightarrow \text{temperature quench} \]
\[ \lambda_1 = \lambda_2 = 1 \Rightarrow \text{constant velocity reassignment} \]
\[ \lambda_1 \neq \lambda_2 \neq 1 \Rightarrow \text{velocity reassignment} \]
### Producing Temperature Echoes by Velocity Reassignments in Proteins

<table>
<thead>
<tr>
<th>Time Interval</th>
<th>Condition</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>$t_e$</td>
<td>Equilibration, coupling to heat bath, $T = T_0$</td>
<td>$1^{st}$ velocity assignment</td>
</tr>
<tr>
<td>0</td>
<td>Equilibrium, no heat bath coupling</td>
<td></td>
</tr>
<tr>
<td>$\tau$</td>
<td>Relaxation, no heat bath coupling</td>
<td>$2^{nd}$ velocity assignment, echo</td>
</tr>
<tr>
<td>$\frac{3}{2}\tau$</td>
<td>Relaxation, no heat bath coupling</td>
<td>echo</td>
</tr>
<tr>
<td>$2\tau$</td>
<td>Relaxation, no heat bath coupling</td>
<td></td>
</tr>
</tbody>
</table>

Temperature quench echoes:

\[ v_i(0) = v_i(\tau) = 0 \]

Constant velocity reassignment echoes:

\[ v_i(0) = v_i(\tau) = u_i \]
Generating T-Quench Echo: Step 1

- your system is ubiquitin (1UBQ) in vacuum, pre-equilibrated at $T_0=300K$
- run all simulations in the microcanonical (NVE) ensemble
- psf, pdb and starting binary coordinate and velocity files are available in "common/
- use NAMD2 configuration file "equil.conf" located in "01_equil_NVE/" to complete a 500 fs (# simulation steps) run
- extract the temperature time series $T(t)$ from the NAMD2 log (output) file
- plot $T(t)$
- calculate: $\langle T \rangle$, $\sqrt{\langle T^2 \rangle}$, $C_{TT} = \langle \delta T(t) \delta T(0) \rangle$
Temperature Autocorrelation Function

\[ \Delta T(t) = T(t) - \langle T(t) \rangle \]

\[ C(t) = \langle \Delta T(t) \Delta T(0) \rangle \]

\[ \rightarrow C(t_i) \approx \frac{1}{N-i} \sum_{n=1}^{N-i} \Delta T(t_{n+i}) \Delta T(t_n) \]

\[ C(t) = C(0) \exp \left( -\frac{t}{\tau_0} \right) \]

Temperature relaxation time:

\[ \tau_0 \approx 2.2 \text{ fs} \]

Mean temperature:

\[ \langle T \rangle = 299 K \]

RMS temperature:

\[ \sqrt{\langle \Delta T^2 \rangle} = \sqrt{C(0)} = 6 K \]
Generating T-Quench Echo: Step 2

Perform the 1st temperature quench
- start a new simulation using configuration file “quench.conf” located in “02_quencha/”
- use the restart coordinate file from the previous run
- set all velocities to zero (i.e., set T=0)
- run the simulation for τ number of steps (time step = 1 fs)
- extract (from the log file) and plot T(t)
Generating T-Quench Echo: Step 3

Perform the 2\textsuperscript{nd} temperature quench
- start a new simulation using configuration file “quench.conf” located in “03_quenchb/”
- use the restart coordinate file from the previous run
- set again all velocities to zero (i.e., set T=0)
- run the simulation for 3\tau number of steps (time step = 1 fs)
- extract (from the log file) and plot T(t)

You should discover a temperature echo at 2\tau
Explanation of the T-Quench Echo

**Assumption:** protein \( \approx \) collection of weakly interacting harmonic oscillators with dispersion \( \omega = \omega_\alpha, \quad \alpha = 1, \ldots, 3N - 6 \)

**Step 1:** \( t < 0 \)

\[
x(t) = A_0 \cos(\omega t + \theta_0)
\]

\[
v(t) = -\omega A_0 \sin(\omega t + \theta_0)
\]

**Step 2:** \( 0 < t < \tau \)

\[
x_1(t) = A_1 \cos(\omega t + \theta_1)
\]

\[
v_1(t) = -\omega A_1 \sin(\omega t + \theta_1)
\]

\[
\begin{aligned}
A_1 &= A_0 \cos \theta_0 \\
\theta_1 &= 0
\end{aligned}
\]

**Step 3:** \( t > \tau \)

\[
x_2(t) = A_2 \cos(\omega t + \theta_2)
\]

\[
v_2(t) = -\omega A_2 \sin(\omega t + \theta_2)
\]

\[
\begin{aligned}
A_2 &= A_1 \cos \omega \tau \\
\theta_2 &= -\omega \tau
\end{aligned}
\]
T-Quench Echo: Harmonic Approximation

\[ T(t) \approx \frac{T_0}{4} \left[ 1 - \langle \cos(2\omega(t - \tau)) \rangle - \frac{1}{2} \langle \cos(2\omega(t - 2\tau)) \rangle \right] \]

\[ \approx \begin{cases} 
0 & \text{for } t = \tau \\
T_0/8 & \text{for } t = 2\tau \\
T_0/4 & \text{otherwise} 
\end{cases} \]

\[ \Rightarrow \text{echo depth} = T(2\tau) - T_0/4 = T_0/8 \]
\[ T(t) \text{ and } C_{TT}(t) \]

It can be shown:

\[ \langle \cos(2\omega t) \rangle = \frac{\langle \delta T(t) \delta T(0) \rangle}{\langle \Delta T^2 \rangle} = C_{TT}(t), \quad \delta T(t) = T(t) - \langle T \rangle \]

Accordingly,

\[ T(t) \approx \frac{T_0}{4} \left[ 1 - \langle \cos(2\omega(t - \tau)) \rangle - \frac{1}{2} \langle \cos(2\omega(t - 2\tau)) \rangle \right] \]

\[ = \frac{T_0}{4} \left[ 1 - C_{TT}(t - \tau) - \frac{1}{2}C_{TT}(t - 2\tau) \right] \]
$T(t) \approx \frac{T_0}{2} \left(1 - C_{TT}(t - \tau) - \frac{1}{2} C_{TT}(|t - 2\tau|)\right)$

$C_{TT}(t) = \exp\left(-t/\tau_0\right), \quad \tau_0 \approx 2.2 \text{ fs}$
Dephasing Time of T-Quench Echoes

\[ \Delta T(\tau) = \Delta T(0) \exp\left[-\frac{\tau}{\tau_{\text{dephase}}}\right] \]
Constant Velocity Reassignment Echo?

Can we get temperature echo(es) by reassigning the same set of atomic velocities (corresponding to $T_o$!) at $t=0$ and $t=\tau$?

$$v_i(0^+)=v_i(\tau^+)=u_i, \ i=1,...,3N-6$$

Answer: YES!

$$T(t) \approx T_0 \left[ 1 - \frac{1}{2} C_{TT}(|t-3\tau/2|) \right]$$