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**

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

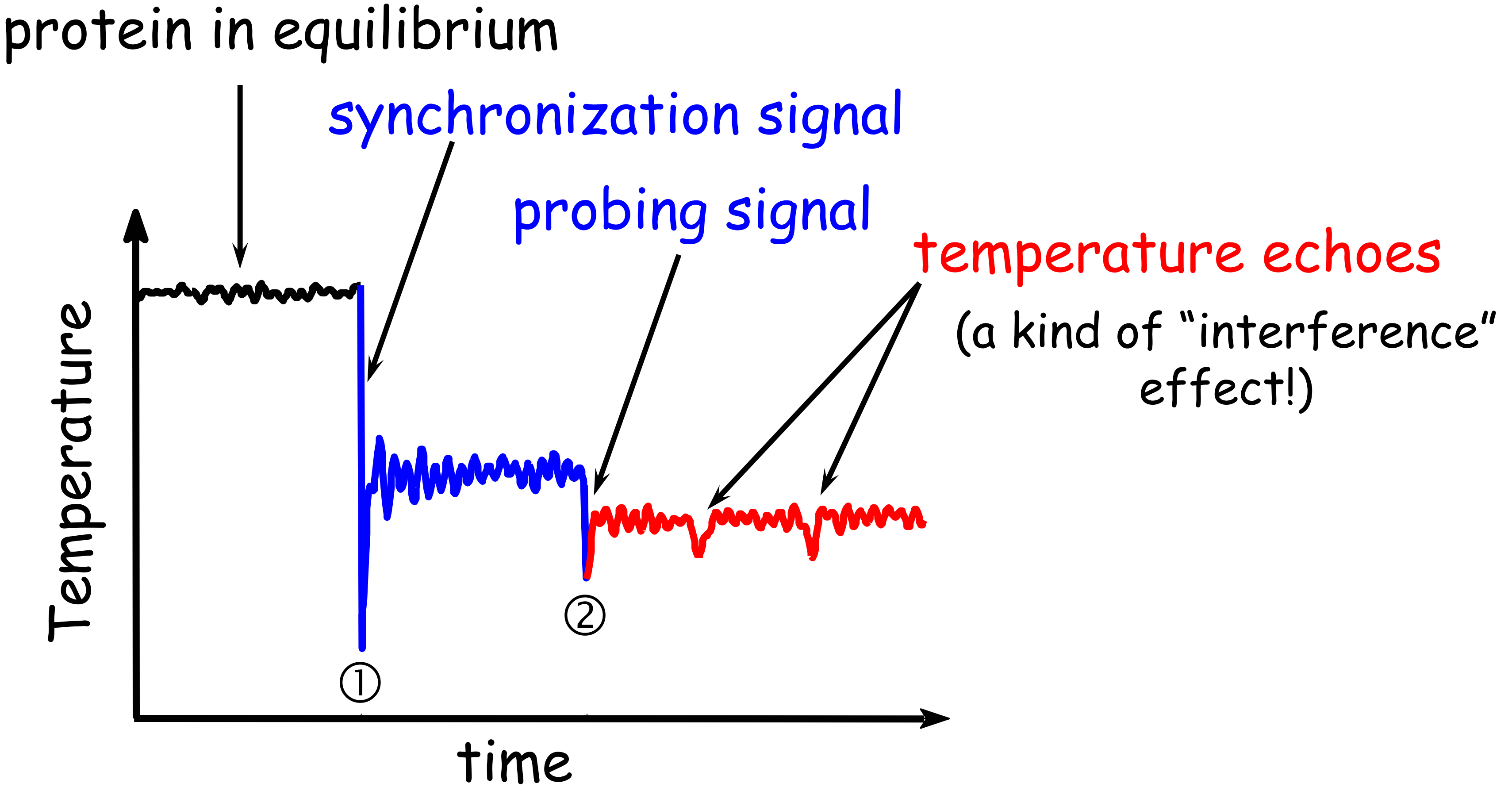
temperature ⇔ velocities

kinetic temperature:

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

Temperature Echoes

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



Velocity Reassignments

- protein ≈ collection of weakly interacting harmonic oscillators having different frequencies
- at $t_1=0$ the 1st 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 2nd 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:

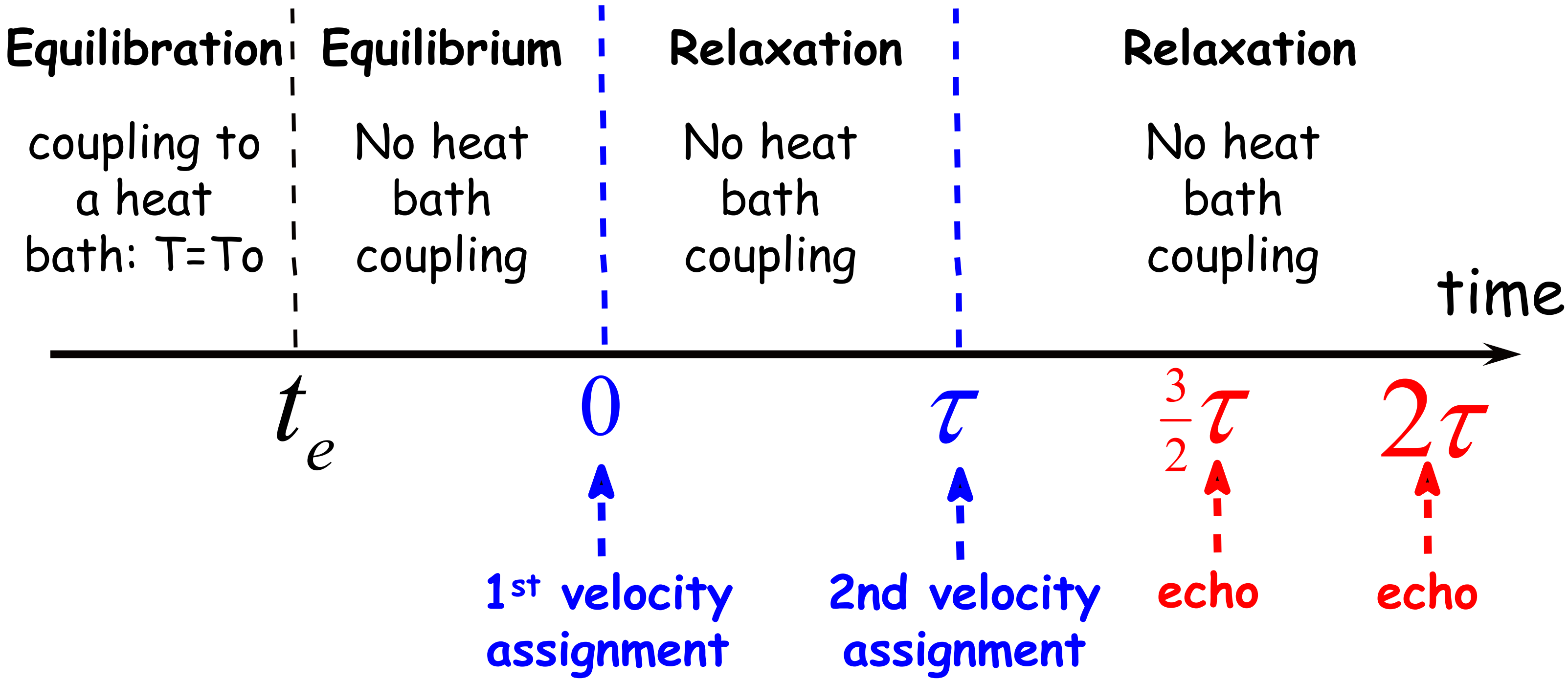
- the time(s) of the echo(es)
- the depth of the echo(es)

$$\lambda_1 = \lambda_2 = 0 \;\Rightarrow\; \text{temperature quench}$$

$$\lambda_1 = \lambda_2 = 1 \;\Rightarrow\; \text{constant velocity reassignment}$$

$$\lambda_1 \neq \lambda_2 \neq 1 \;\Rightarrow\; \text{velocity reassignment}$$

Producing Temperature Echoes by Velocity Reassignments in Proteins

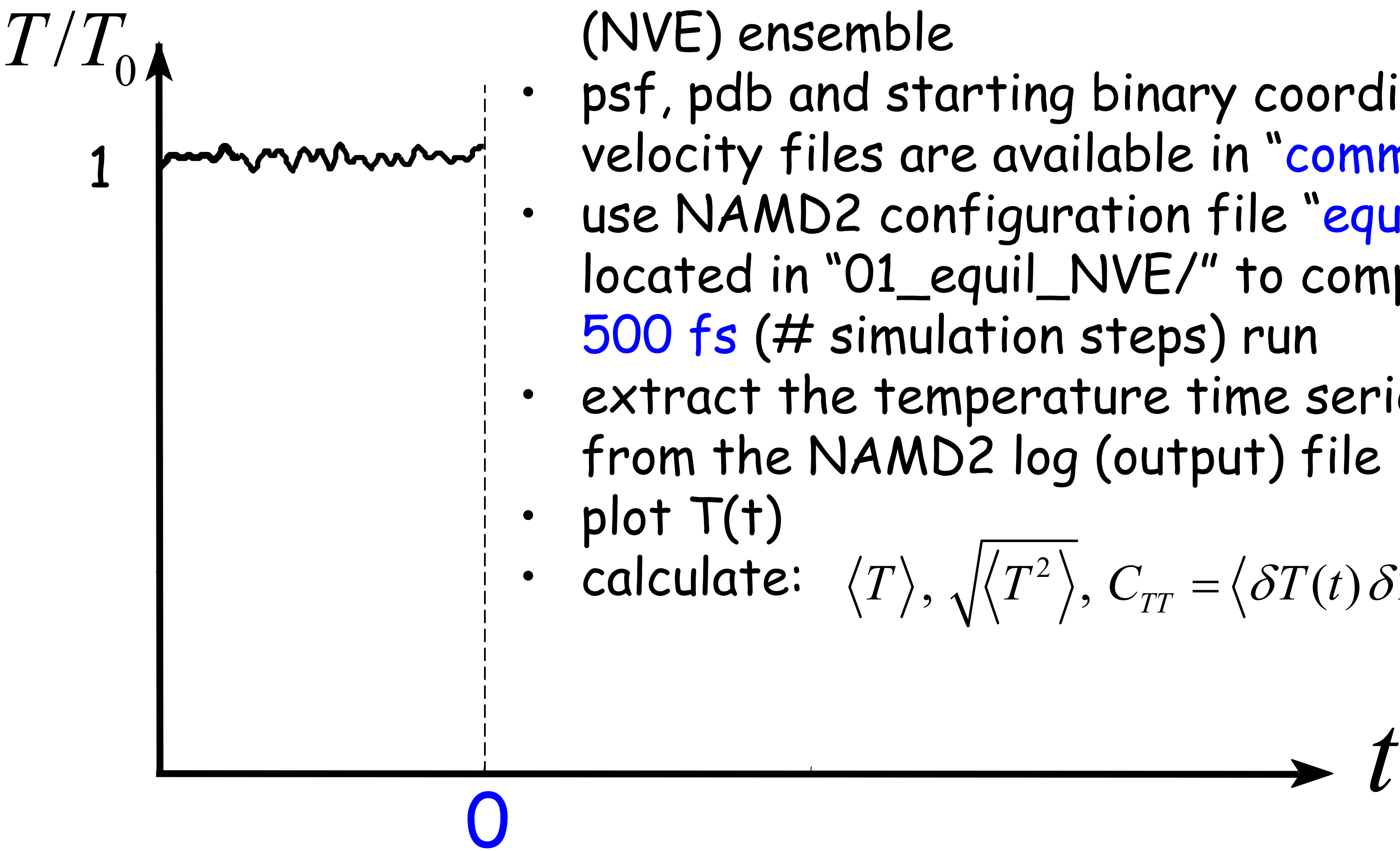


Temperature quench echoes: $v_i(0) = v_i(\tau) = 0$

Const velocity reassignment echoes: $v_i(0) = v_i(\tau) = u_i$

Velocity reassignment echoes: $v_i(0) = u_i \, , v_i(\tau) = \lambda u_i$

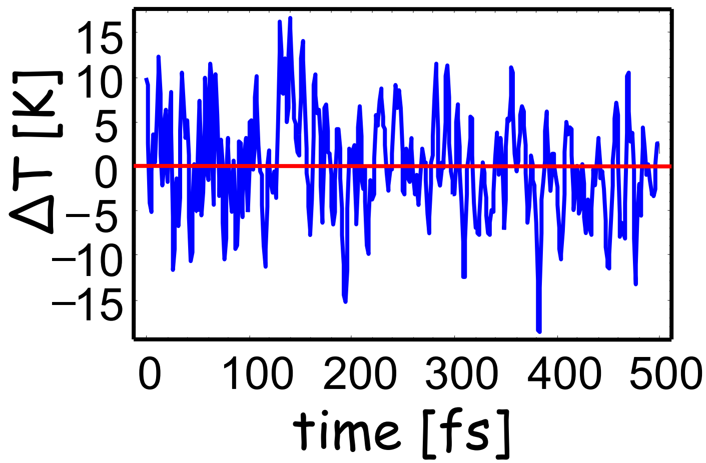
Generating T-Quench Echo: Step1

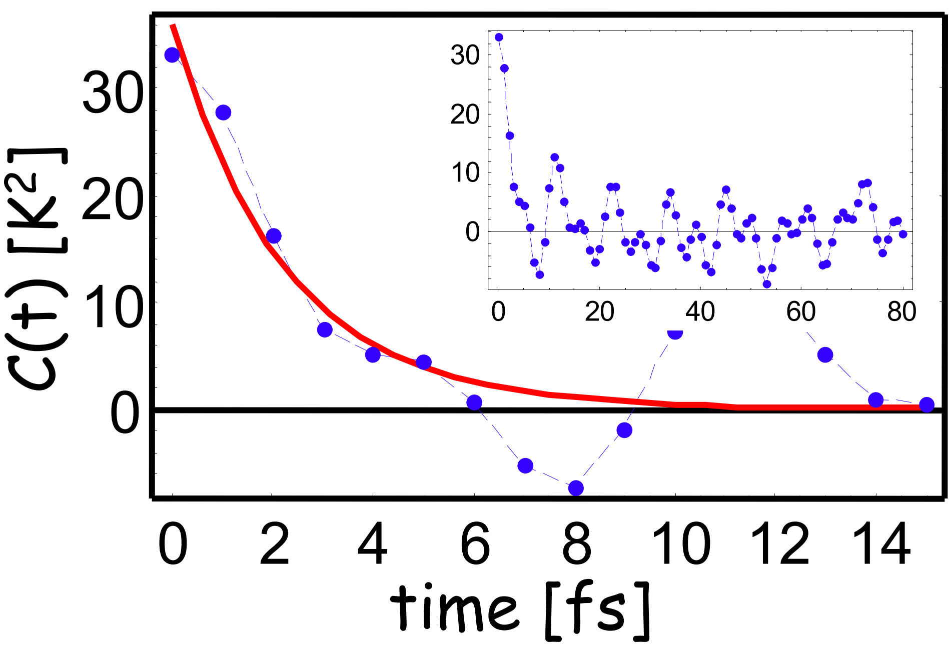


- your system is ubiquitin (1UBQ) in vacuum, pre-equilibrated at T_0=300K
- run all simulations in the *microcanonical* (NVE) ensemble
- psf, pdb and starting binary coordinate and velocity files are available in "common/"
- use NAMD2 configuration file "equil.conf" located in "01_equil_NVE/" to complete 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

$$\Delta T(t) = T(t) - \langle T(t) \rangle$$





$$C(t) = \langle \Delta T(t) \Delta T(0) \rangle$$

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

$$C(t) = C(0) \exp\left(-t/\tau_0\right)$$

Temperature relaxation time:

$$\tau_0 \approx 2.2\ fs$$

Mean temperature:

$$\langle T \rangle = 299\ K$$

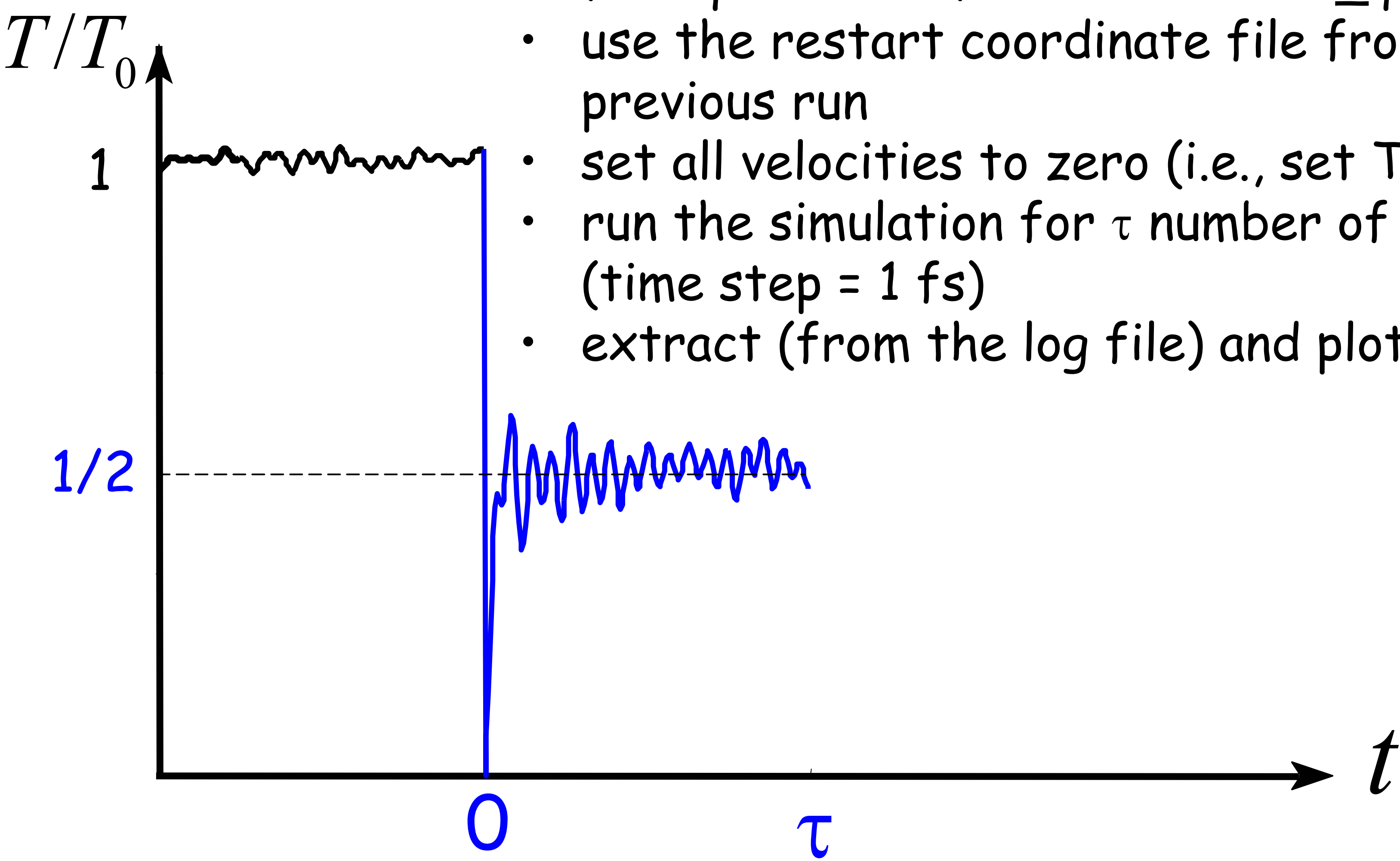
RMS temperature:

$$\sqrt{\langle \Delta T^2 \rangle} = \sqrt{C(0)} = 6\ K$$

Generating T-Quench Echo: Step2

Perform the 1st temperature quench

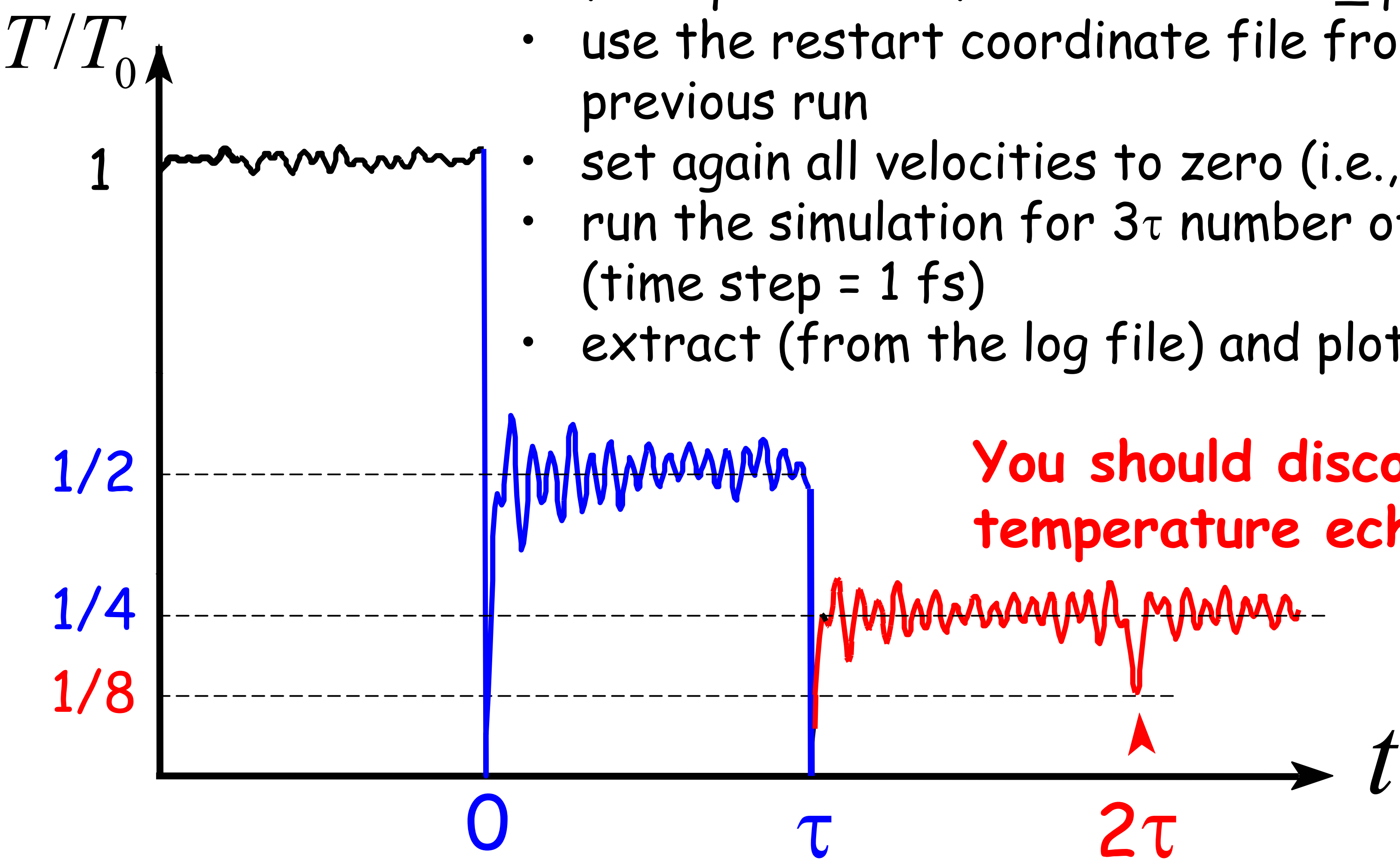
- start a new simulation using configuration file "quench.conf" located in "02_quencha/"
- use the restart coordinate file from the previous run
- set all velocities to zero (i.e., set T=0)
- run the simulation for τ number of steps (time step = 1 fs)
- extract (from the log file) and plot T(t)



Generating T-Quench Echo: Step3

Perform the 2nd 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 3τ number of steps (time step = 1 fs)
- extract (from the log file) and plot T(t)



You should discover a temperature echo at 2τ

Explanation of the T-Quench Echo

Assumption: protein ≈ collection of weakly interacting harmonic oscillators with dispersion $\omega = \omega_\alpha\,,\ \alpha = 1,\ldots,3N-6$

Step1: $t < 0$

$$x(t) = A_0 \cos\left(\omega t + \theta_0\right)$$
$$v(t) = -\omega A_0 \sin\left(\omega t + \theta_0\right)$$

Step2: $0 < t < \tau$

$$\left.\begin{array}{l} x_1(t) = A_1 \cos\left(\omega t + \theta_1\right) \\ v_1(t) = -\omega A_1 \sin\left(\omega t + \theta_1\right) \end{array}\right\} \xrightarrow{v_1(0)=0} \begin{cases} A_1 = A_0 \cos\theta_0 \\ \theta_1 = 0 \end{cases}$$

Step3: $t > \tau$

$$\left.\begin{array}{l} x_2(t) = A_2 \cos\left(\omega t + \theta_2\right) \\ v_2(t) = -\omega A_2 \sin\left(\omega t + \theta_2\right) \end{array}\right\} \xrightarrow{v_2(\tau)=0} \begin{cases} A_2 = A_1 \cos\omega\tau \\ \theta_2 = -\omega\tau \end{cases}$$

T-Quench Echo: Harmonic Approximation

for $t > \tau$: $$T(t) \propto \left\langle v_2^2 \right\rangle = \left\langle \omega^2 A_0^2 \cos^2\theta_0 \cos^2(\omega\tau)\sin^2\left(\omega(t-\tau)\right)\right\rangle$$

The average must be taken over the distribution of initial phases θ_0, amplitudes A_0 and angular velocities ω

equipartition theorem $\Rightarrow \left\langle A_0^2 \cos^2\theta_0 \right\rangle = \frac{1}{2}\left\langle A_0^2\right\rangle = \frac{k_B T_0}{2m\omega^2}$

$$T(t) = T_0 \left\langle \cos^2(\omega\tau)\sin^2\left(\omega(t-\tau)\right)\right\rangle = \ldots$$

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

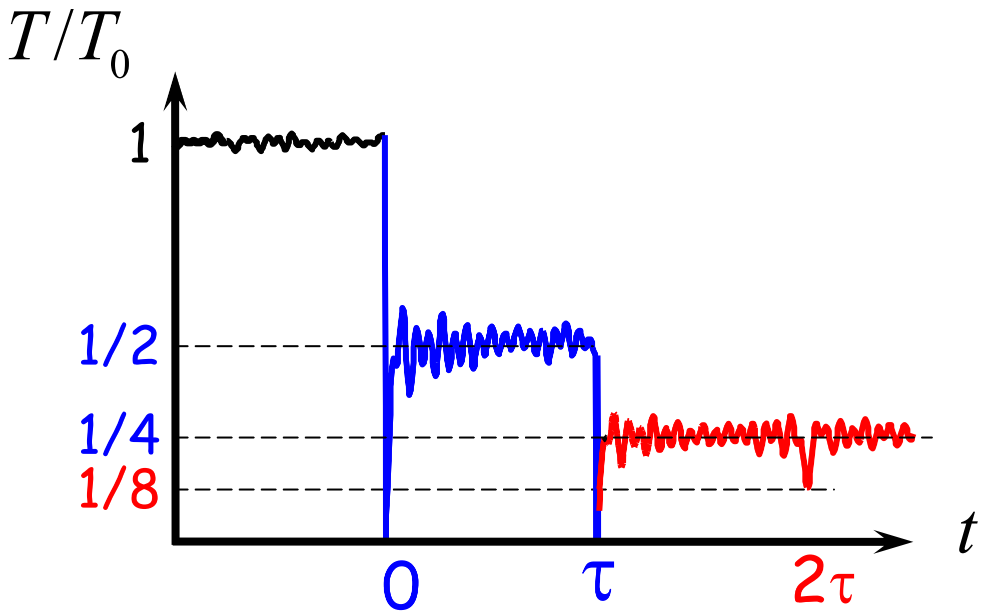
Since : $\left\langle \cos(\omega ?)\right\rangle_\omega \approx 0$ unless $? = 0 \Rightarrow$

T-Quench Echo: Harmonic Approximation

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

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

$\Rightarrow$ echo depth $= T(2\tau) - T_0/4 = T_0/8$



$T(t)$ and $C_{TT}(t)$

It can be shown that:

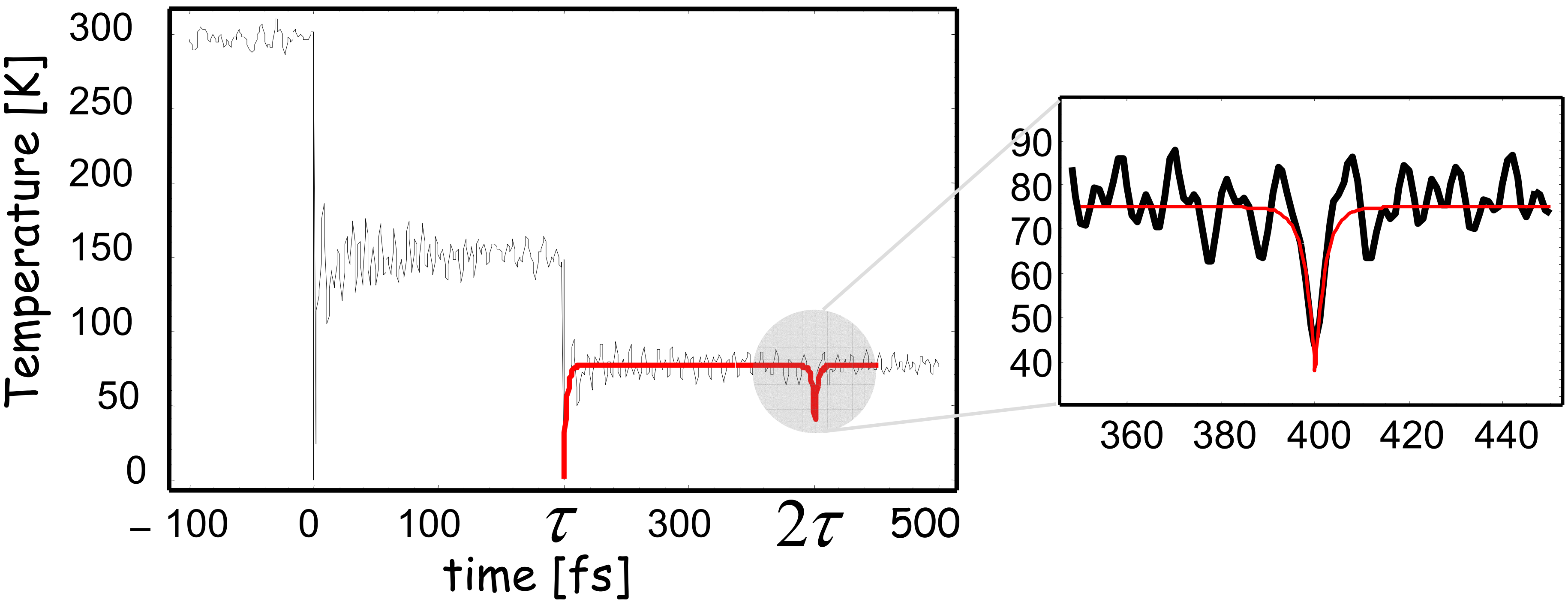
$$\left\langle \cos\left(2\omega t\right)\right\rangle = \frac{\left\langle \delta T(t)\,\delta T(0)\right\rangle}{\left\langle \Delta T^2\right\rangle} = C_{TT}(t), \qquad \delta T(t) = T(t) - \left\langle T\right\rangle$$

$$\Downarrow$$

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

$$\approx \frac{T_0}{4}\left[1 - \frac{1}{2}C_{TT}\left(\left|t-2\tau\right|\right)\right] \quad for \;\; t > \tau$$

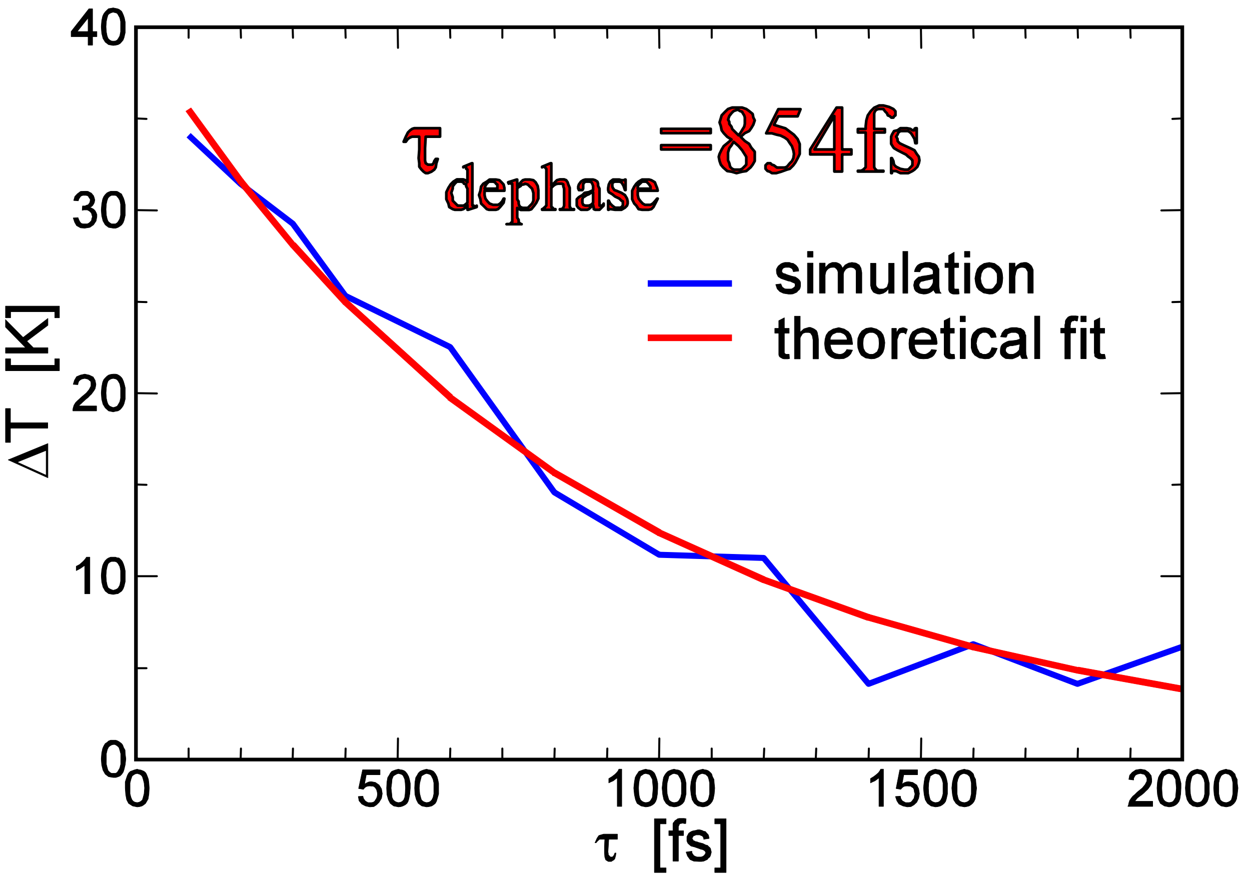
T-Quench Echo: Harmonic Approximation

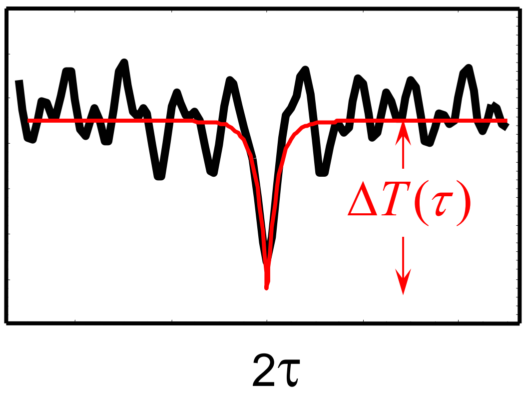


$$T(t) \approx \frac{T_0}{2}\left(1 - C_{TT}(t-\tau) - \frac{1}{2}C_{TT}\left(\left|t-2\tau\right|\right)\right)$$

$$C_{TT}(t) = \exp\left(-t/\tau_0\right), \qquad \tau_0 \approx 2.2\ fs$$

Dephasing Time of T-Quench Echoes





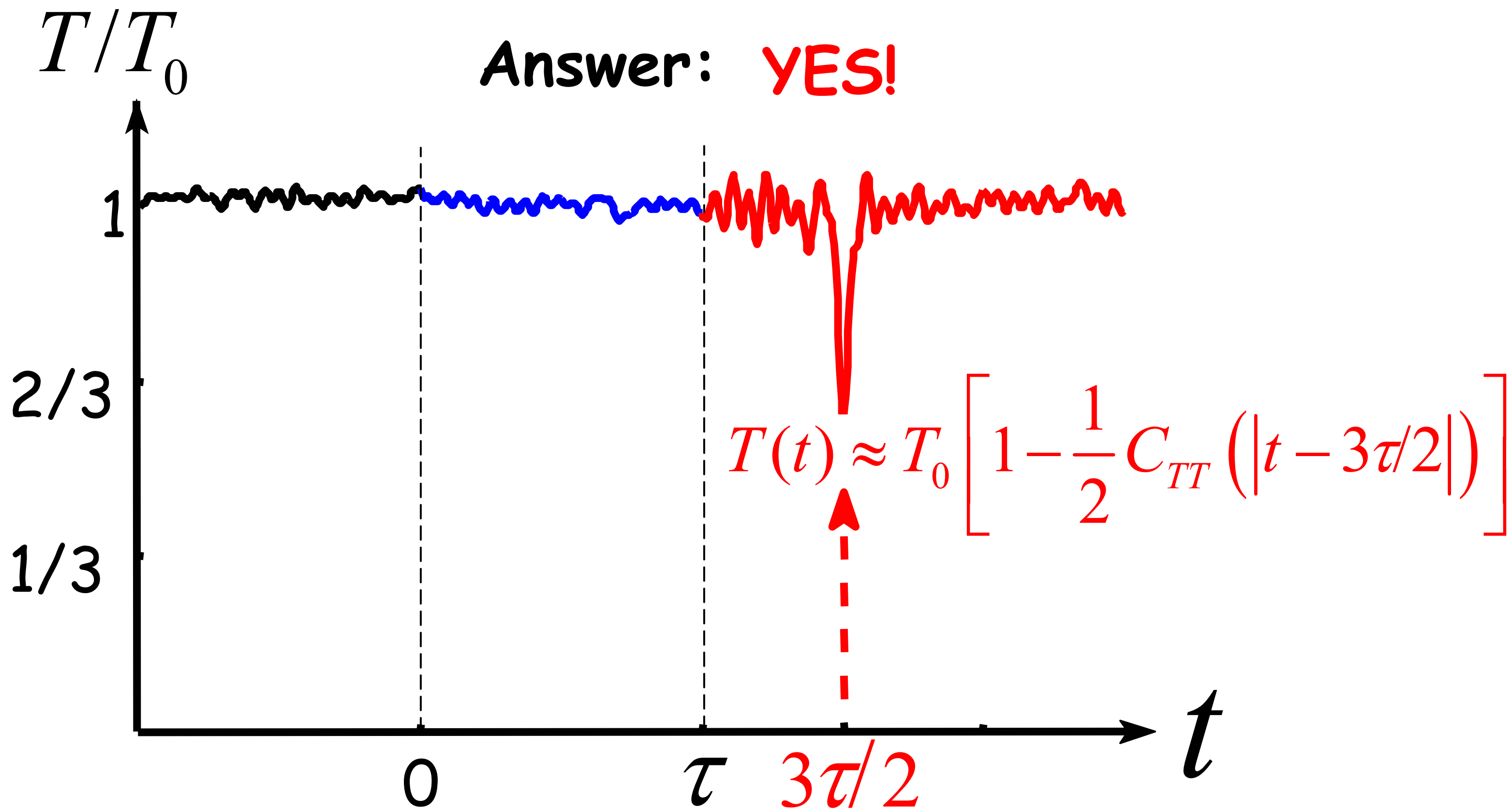
$$\Delta T(\tau) = \Delta T(0)\exp[-\tau / \tau_{dephase}]$$

Constant Velocity Reassignment Echo ?

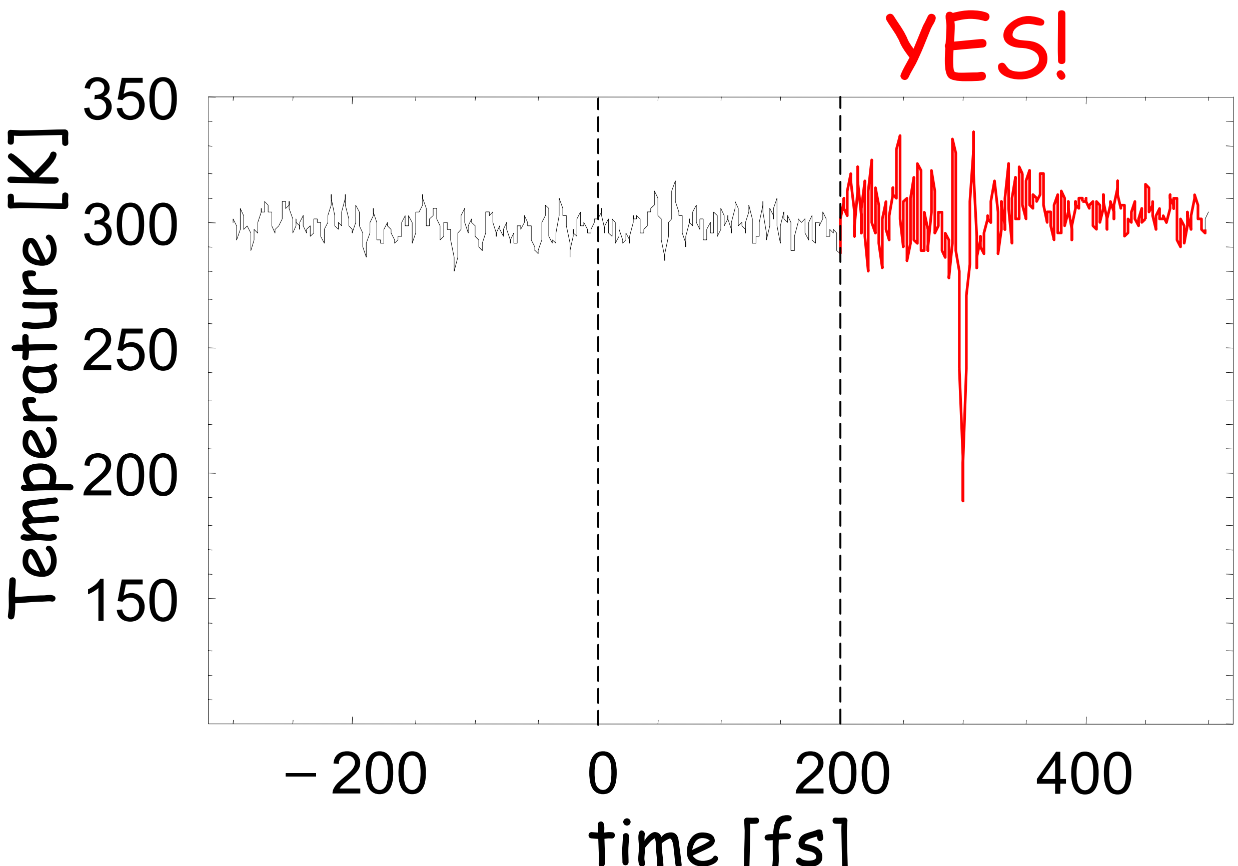
Can we get temperature echo(es) by reassigning the same set of atomic velocities (corresponding to T_0!) at $t = 0$ and $t = \tau$?

$$v_i\left(0^+\right) = v_i\left(\tau^+\right) = u_i\,,\;\; i = 1,\ldots,3N-6$$

Answer: YES!



Is it possible to produce temperature echo with a single velocity reassignment ?



Reset all velocities at time τ to the values at a previous instant of time, i.e., $t = 0$