Jarzynski's equality

System S, heat bath B at temperature T

compound SB evolves according to Hamiltonian

$$H_\lambda^{SB}(\Gamma, \Theta) = H_\lambda^{S}(\Gamma) + H^{B}(\Theta)$$

λ : parameter than can be controlled externally by performing work W e.g. distance between a molecule and another one moved by an optical tweezer

Partition function

$$Z_\lambda^{SB} = \int d\Gamma \, d\Theta \, e^{-\beta H_\lambda^{SB}(\Gamma, \Theta)}$$

$$= \int d\Gamma \, e^{-\beta H_\lambda^{S}(\Gamma)} \int d\Theta \, e^{-\beta H^{B}(\Theta)}$$

$$= Z_\lambda^{S} Z^{B}$$

is factorized

parameter change during time τ

$$(\Gamma_0, \Theta_0) \xrightarrow{\Lambda} (\Gamma_\tau, \Theta_\tau)$$

canonical ensemble: prob. distr.

$$\frac{1}{Z_0^{SB}} e^{-\beta H_0^{SB}(\Gamma_0, \Theta_0)}$$

Work = increase in energy

$$W = H_\Lambda^{SB}(\Gamma_\tau, \Theta_\tau) - H_0^{SB}(\Gamma_0, \Theta_0)$$

Application : Protein N particles with $\overset{3N\text{-dim}}{\vee}$ position vector $\vec{r}$ and momentum $\vec{p}$

$\xi(\vec{r})$: reaction coordinate

Potential of mean force $\Phi(\xi)$:

$$e^{-\beta \Phi(\xi')} = \int d\vec{r}\, d\vec{p}\;\, \delta(\xi(\vec{r}) - \xi')\, e^{-\beta H(\vec{r},\vec{p})}$$

Helmholtz free energy profile along reaction coordinate

prob. of observing r.c. at ξ is proportional to $e^{-\beta \Phi(\xi)}$

AFM / SMD :

guiding potential

$$h_\lambda(\vec{r}) = \frac{k}{2}\left[\xi(\vec{r}) - \lambda\right]^2$$

$$\tilde{H}_\lambda(\vec{r},\vec{p}) = H(\vec{r},\vec{p}) + h_\lambda(\vec{r})$$

$\lambda(t) = \lambda(0) + vt$ move constraint w. constant vel.

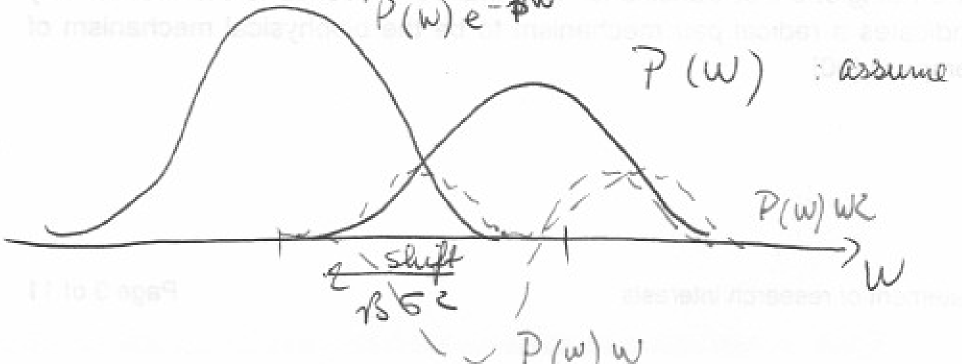
$$\boxed{F_{\lambda(\tau)} - F_{\lambda(0)} = \frac{1}{\beta} \log \langle e^{-\beta W(\tau)} \rangle} \quad \text{Jarz. eq.}$$

$$\left(e^{-\beta F_\lambda} = \int d\vec{r}\, d\vec{p}\; e^{-\beta \tilde{H}_\lambda(\vec{r},\vec{p})} \right)$$

Problem: sampling

$P(W)$: Prob. distr. of work

$$\langle e^{-\beta W} \rangle = P(W)\, e^{-\beta W}$$



reasonable overlap only for $\beta\sigma$ small

i.e. work fluct σ comparable to kT

Average of exponential work

$$\langle e^{-\beta W} \rangle = \int d\Gamma_0 \, d\Theta_0 \, \frac{1}{Z_0^{SB}} e^{-\beta H_0^{SB}(\Gamma_0, \Theta_0)} \times$$

$$\times \, e^{-\beta \left[H_\Lambda^{SB}(\Gamma_\tau, \Theta_\tau) - H_0^{SB}(\Gamma_0, \Theta_0) \right]}$$

$$= \int d\Gamma_0 \, d\Theta_0 \, \frac{1}{Z_0^{SB}} e^{-\beta H_\Lambda^{SB}(\Gamma_\tau, \Theta_\tau)} =$$

$$d\Gamma_0 = \underbrace{\frac{\partial \Gamma_0}{\partial \Gamma_\tau}}_{1} d\Gamma_\tau$$

Liouville Theorem

$$= \int d\Gamma_\tau \, d\Theta_\tau \, \frac{1}{Z_0^{SB}} e^{-\beta H_\Lambda^{SB}(\Gamma_\tau, \Theta_\tau)}$$

$$= \frac{Z_\Lambda^{SB}}{Z_0^{SB}} = \frac{Z_\Lambda^{S} \; Z_B}{Z_0^{S} \; Z_B} = e^{-\beta \Delta F^S}$$

$$\boxed{\langle e^{-\beta W} \rangle = e^{-\beta \Delta F^S}}$$

For a transformation between two equilibrium states of a system in contact with a heat bath at temperature T, the work W done on the system during the transformation can be related to the free energy difference ΔH between the two equilibrium states acc to Jarzynski's equality.

Problems with sampling $e^{-\beta W}$ can be mitigated by stiff spring approximation
→ leads to Gaussian distribution $P(W)$
$P(W)e^{-\beta W}$ can be described fully by knowledge of $P(W) \cdot W$ $P(W) W^2$

Problem: even $P(W)$ is not sampled well
MD biases against negative work

Better: Crooks' transient fluctuation theorem

$$\frac{P_F(W)}{P_R(-W)} = e^{W_d F}$$

$$W_d = \left(\overline{W}_F + \overline{W}_R\right) / 2$$