Project 3

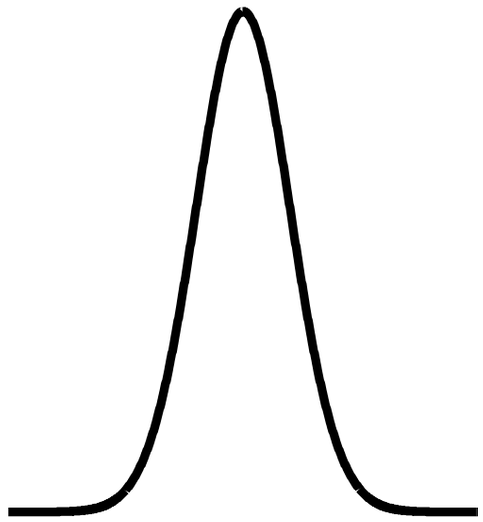
Calculations of Potential of Mean Force with Umbrella Sampling

Assignments

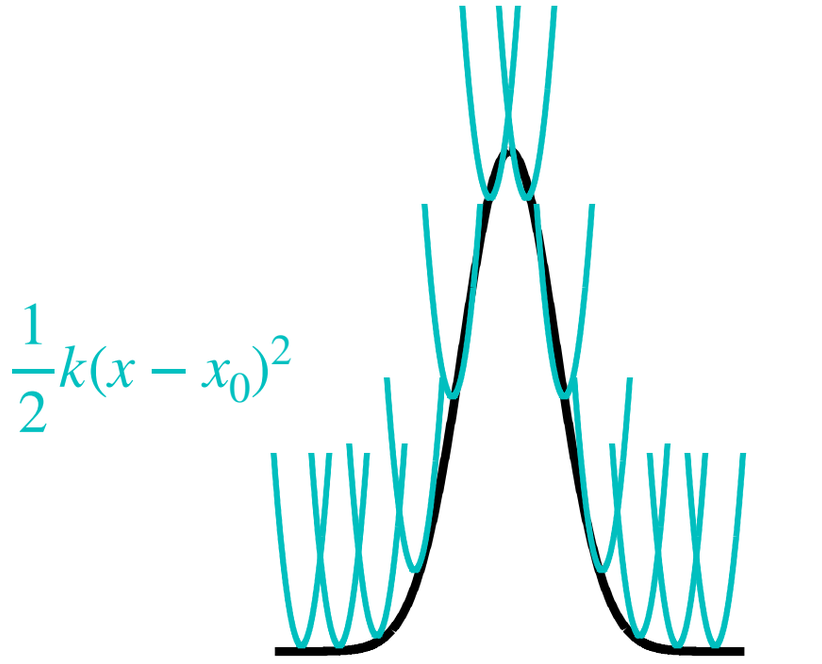
- Write configuration files for umbrella sampling simulations of GROMACS
    - Optional: perform MD simulations based on your settings
    - You can choose either alanine dipeptide or methane dimer
- Write your own WHAM (Weighted Histogram Analysis Method) code to compute potential of mean force (PMF)
- Compute the PMF from your own simulations or my simulation data
    - You can choose either alanine dipeptide or methane dimer

The umbrella sampling method

- When barrier is too high to climb

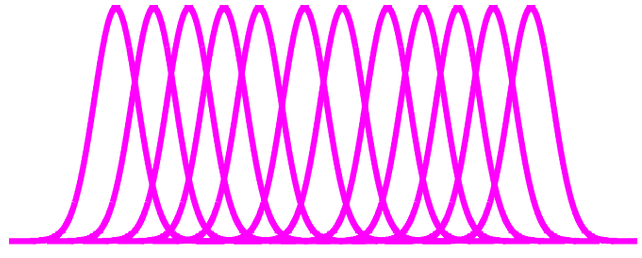


- Umbrella sampling uses harmonic potentials to restrain systems:



$e^{-\frac{1}{2}k(x-x_0)^2}$

$e^{-\frac{1}{2}k(x-x_0+\nabla U/k)^2}$



```
pull                    = yes
pull_coord1_type        = umbrella
pull_ncoords            = 1
pull_ngroups            = 2
pull_group1_name        = MET1
pull_group2_name        = MET2
...

Refer to: https://manual.gromacs.org/documentation/current/user-guide/mdp-options.html#mdp-value-pull-coord1-type-umbrella
```

The weighted histogram method

- The weight of umbrella sampling windows (trajectories):

$$z_i = e^{-f_i} = \sum_{k=1}^{n_{\text{traj}}} \sum_{t=1}^{t_{\text{traj}}} \frac{\exp\left[-\beta_i \sum_{j=0}^{n_{\text{bias}}} \lambda_{j,i} V_j^{(k)}(t)\right]}{\sum_{m=1}^{n_{\text{traj}}} \exp\left[f_m - \beta_m \sum_{j=0}^{n_{\text{bias}}} \lambda_{j,m} V_j^{(k)}(t)\right]}$$

- The weight / PMF of a given bin at x:

$$e^{-\beta_i \text{PMF}(x)} = \sum_{k=1}^{n_{\text{traj}}} \sum_{t=1}^{t_{\text{traj}}} \frac{\exp\left[-\beta_i \sum_{j=0}^{n_{\text{bias}}} \lambda_{j,i} V_j^{(k)}(t)\right]}{\sum_{m=1}^{n_{\text{traj}}} \exp\left[f_m - \beta_m \sum_{j=0}^{n_{\text{bias}}} \lambda_{j,m} V_j^{(k)}(t)\right]} \Theta(\Delta x - |x(t) - x|)$$

- WHAM for umbrella sampling:

$$\lambda_{j,i} = \delta_{j,\#_i} \qquad V_j^{(k)}(t) = \frac{1}{2} k_j (x^{(k)}(t) - b_j)^2$$

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The self-consistent iterations

- A general scheme for self-consistent iterations:

A reasonable initial guess: $f^{(0)}(x)$

A self-consistent equation:

$$f(x) = G(f(x)) \Rightarrow f^{(n+1)}(x) = G(f^{(n)}(x))$$

Convergence control:

$$f^{(n+1)}(x) = wG(f^{(n)}(x)) + (1-w)f^{(n)}(x)$$

Example: solve $x = e^{-x}$

```
Initial guess: x= 1
step= 1 x= 1.000000 exp(-x)= 0.367879
step= 2 x= 0.367879 exp(-x)= 0.692201
step= 3 x= 0.692201 exp(-x)= 0.500474
step= 4 x= 0.500474 exp(-x)= 0.606244
step= 5 x= 0.606244 exp(-x)= 0.545396
step= 6 x= 0.545396 exp(-x)= 0.579612
... ...
step= 25 x= 0.567144 exp(-x)= 0.567143
step= 26 x= 0.567143 exp(-x)= 0.567143
Reference: x= 0.5671432904097838
```

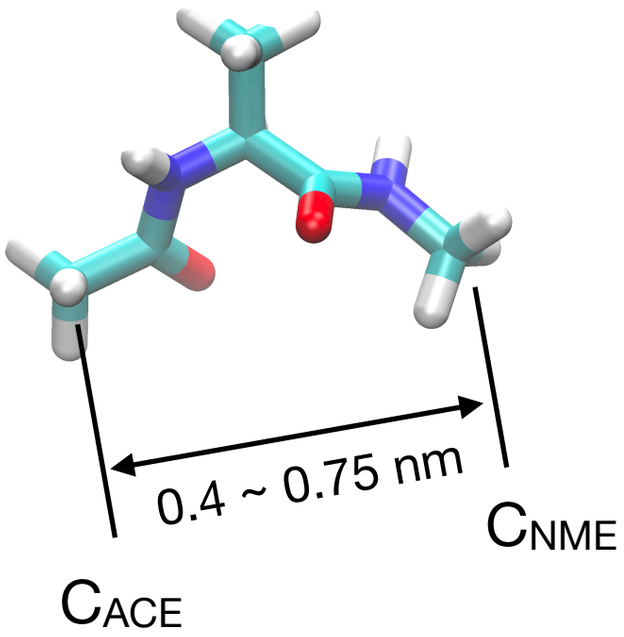
** Advanced convergence control (DIIS, direct inversion in the iterative subspace):

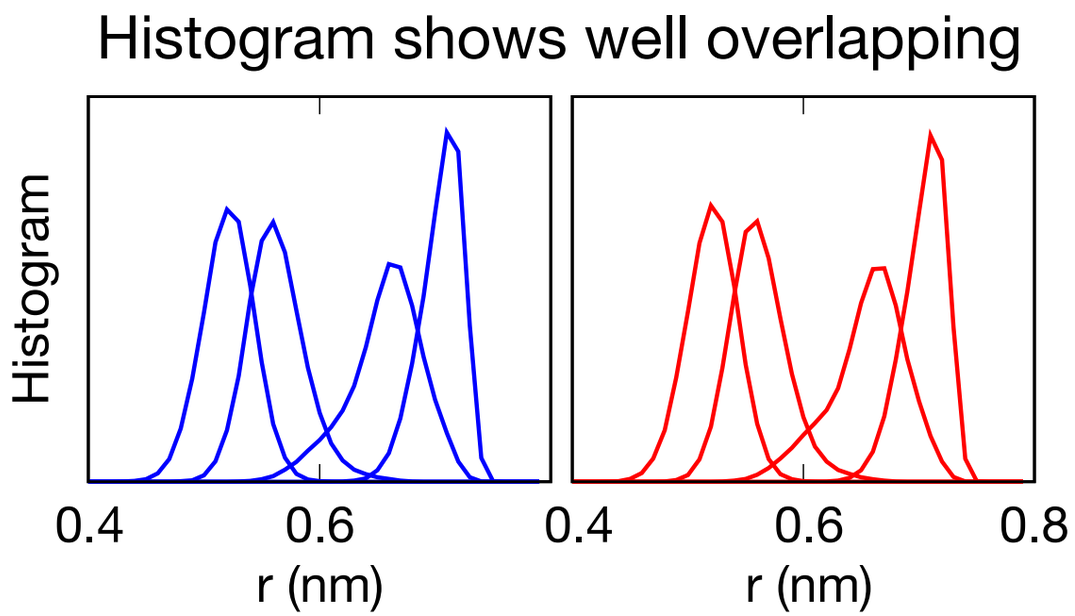
$$f^{(n+1)}(x) = a_0 G(f^{(n)}(x)) + a_1 f^{(n)}(x) + a_2 f^{(n-1)}(x) + \ldots + a_N f^{(n-N)}(x)$$

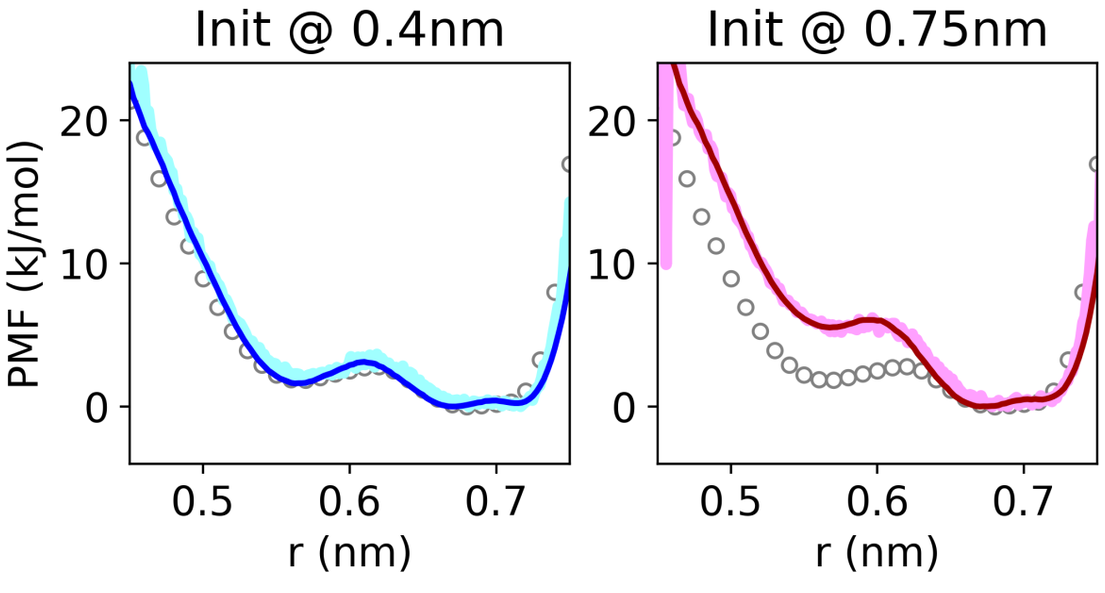
Stop criterium of self-consistent iterations:

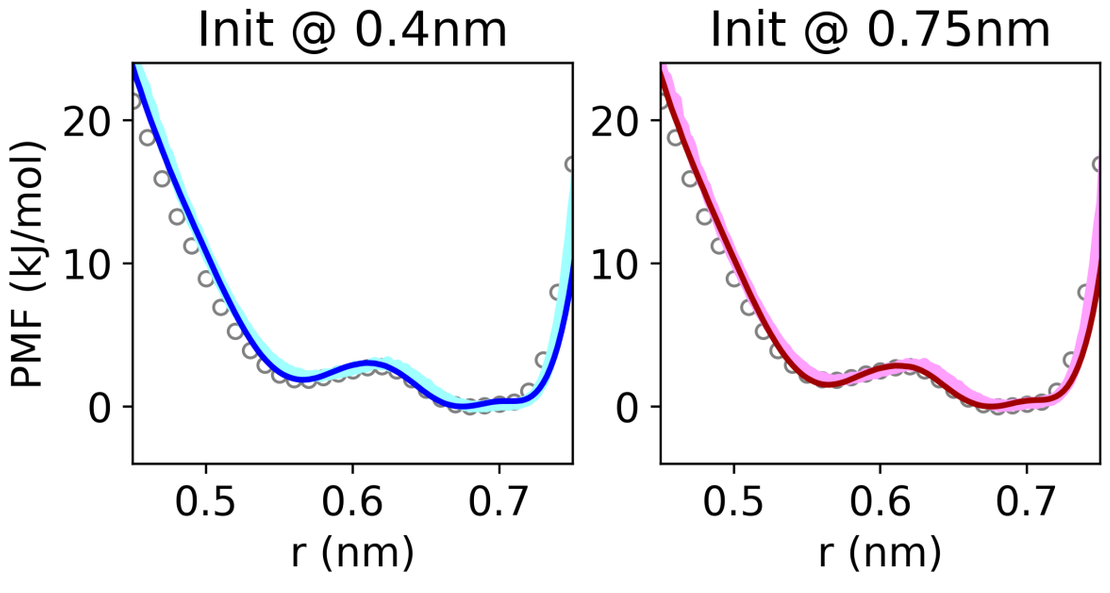
$$\|f^{(n+1)}(x) - f^{(n)}(x)\| < \text{threshold}$$

The folding of alanine dipeptide









** the dimerization of two methanes in water