THEORETICAL & COMPUTATIONAL
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Simultaneous determination of the free energy profile and effective dynamics along a reaction coordinate

MISSOURI

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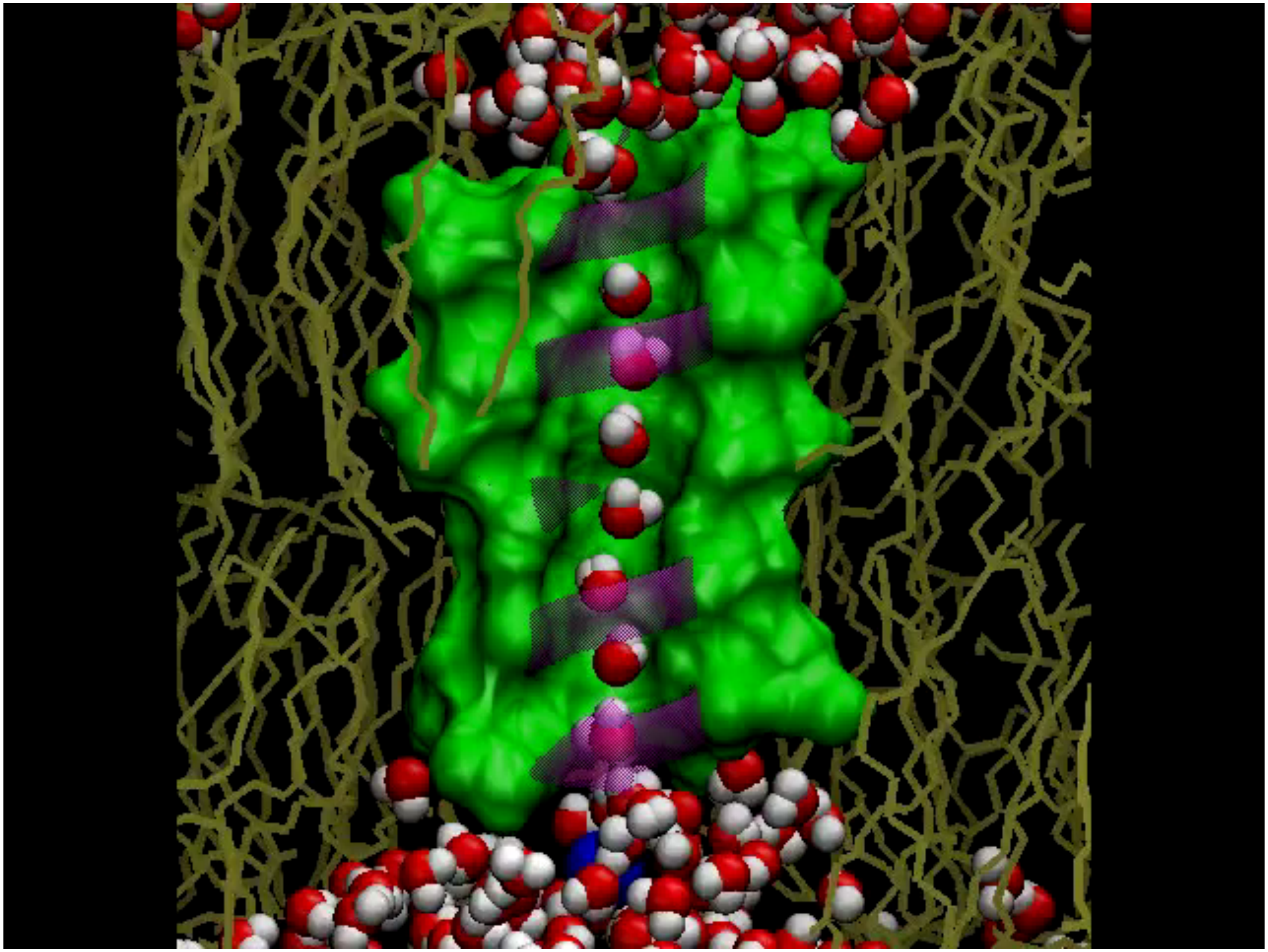
Computer time: HPC resources by RCSS at MU

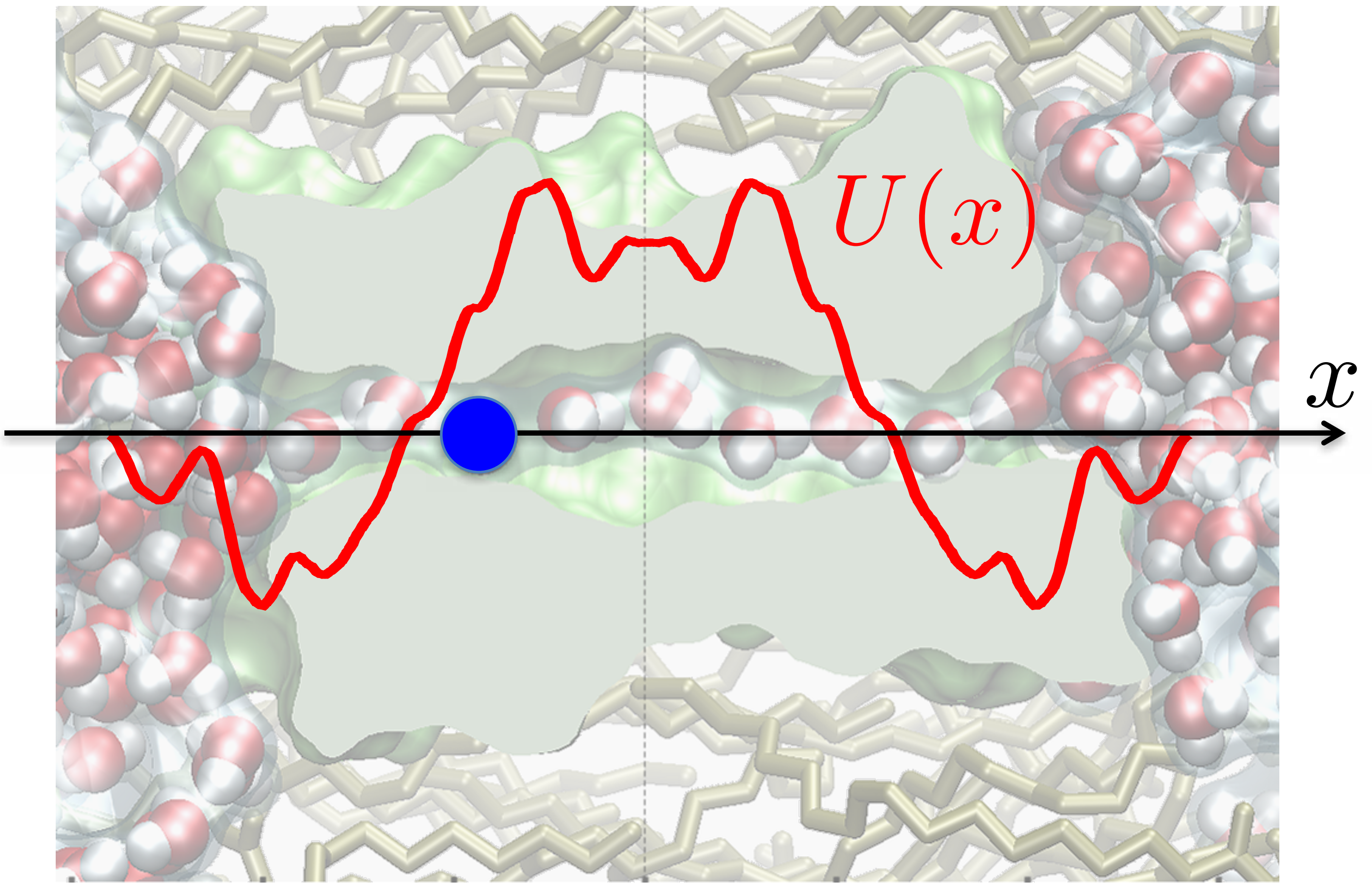
Stochastic dynamics along a reaction coordinate (RC)



Potassium ion transport in gramicidin-A

Effective dynamics along RC

Potassium ion transport in gramicidin-A



Q1: Potential of Mean Force (PMF): $U(x) = ?$

Q2: What is the *effective dynamics* along the RC ?

PMF, $U(x)$, calculation methods

- **Equilibrium methods**
  - Umbrella sampling (with WHAM)
  - Thermodynamic integration
  - ...

- **Non-equilibrium methods**
  - Jarzynski's equality (Fluctuation theorems)
  - Maximum Likelihood Method
  - …
  - *FR Method*

    besides $U(x)$, it can also be used to determine the *effective dynamics* along the RC

Langevin Equation (LE)

Simple (*overdamped*) Brownian motion (dynamics)

$$\gamma_0 \dot{x} = f(x) + F_L(t)$$

$$f(x) = -\frac{dU}{dx}$$

Langevin force = *Gaussian white noise* (no memory)

$$\langle F_L(t) \rangle = 0$$

$$\langle F_L(t) F_L(0) \rangle = 2\gamma_0 k_B T \delta(t)$$

Diffusion coefficient (Einstein relation): $D = k_B T / \gamma_0$

For: $f(x) = 0 \;\Rightarrow\; \langle x^2(t) \rangle = 2Dt$ (linear diffusion)

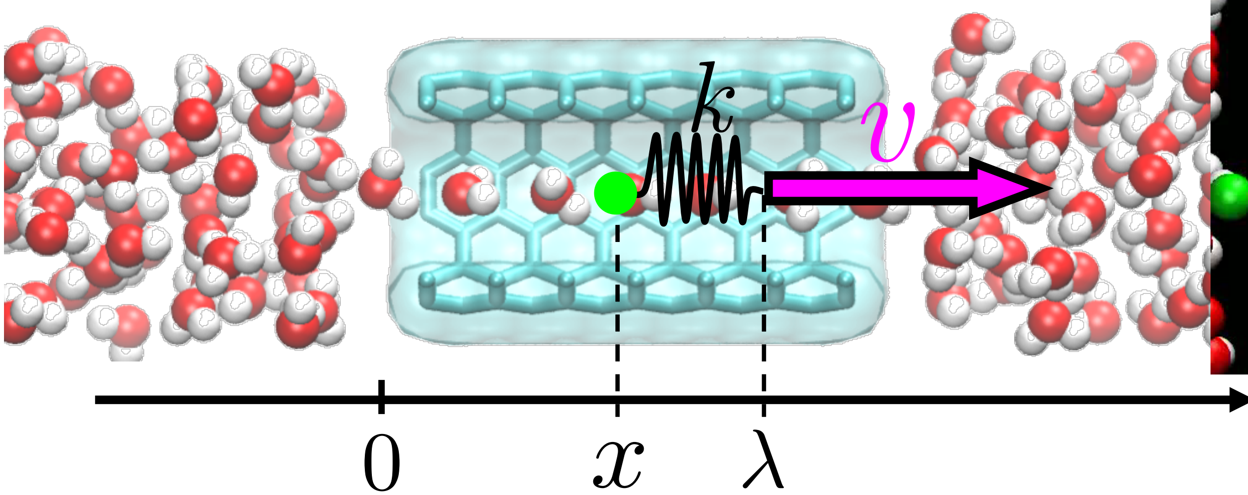
Fast sampling of the RC

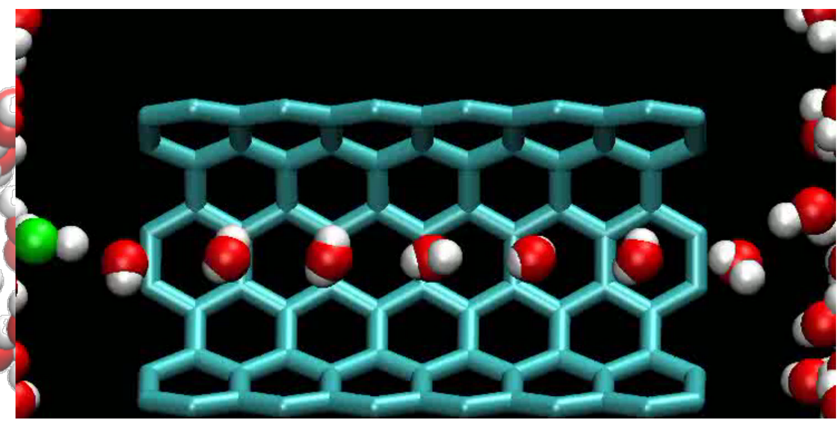
Pulling along RC by using a harmonic guiding potential (HGP)

$$V_\lambda(x) = \frac{k}{2}(x-\lambda)^2, \qquad \lambda = x_0 + vt$$

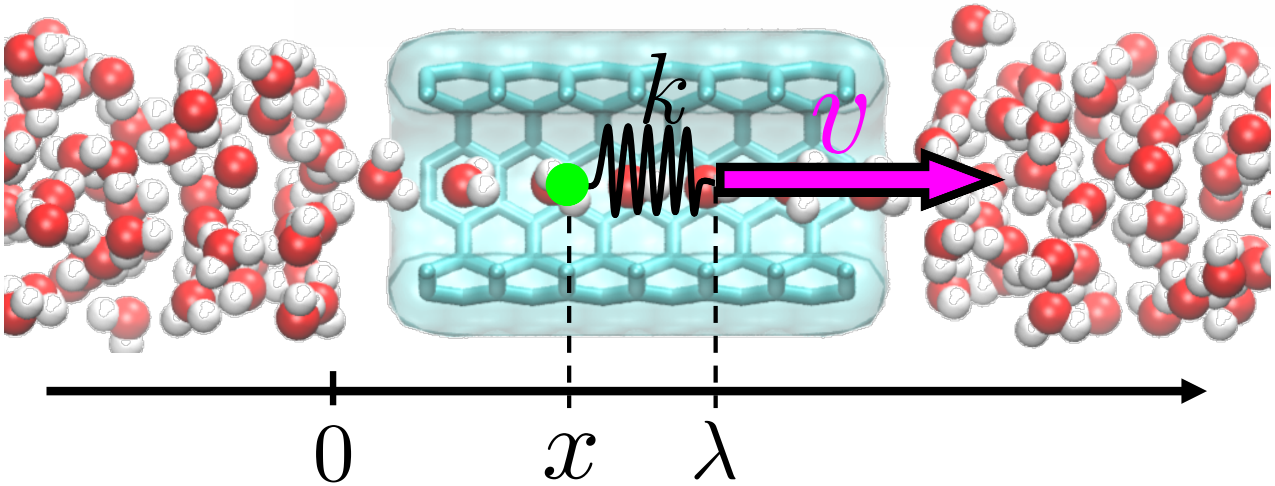
Elastic pulling force: $F_\lambda = -\partial_x V_\lambda(x) = k(\lambda - x)$

Example: constant velocity steered MD (SMD) simulations





Harmonic Guiding Potential (HGP)
Stiff Spring Approximation (SSA)

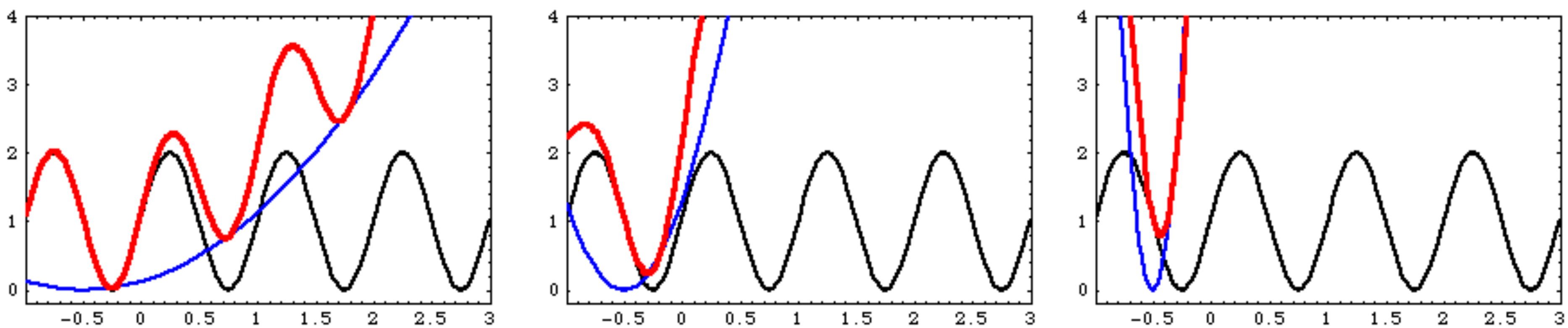


$$V_\lambda(x) = \frac{k}{2}(x-\lambda)^2$$

$$\delta x = x - \lambda$$

$$U_{\text{eff}} = U + V_\lambda$$

SSA: $k \gg 2k_B T/(\delta x)^2$



$k = 1$ $\quad$ $k = 10$ $\quad$ $k = 100$

Overdamped Brownian dynamics

$$\gamma_0 \dot{x} = -\frac{dU}{dx} + F_L(t) + F_\lambda(t)$$

Langevin force = *Gaussian white noise*

$$\langle F_L(t) \rangle = 0 \; ; \quad \langle F_L(t) F_L(0) \rangle = 2\gamma_0 k_B T \delta(t)$$

Nonequilibrium work

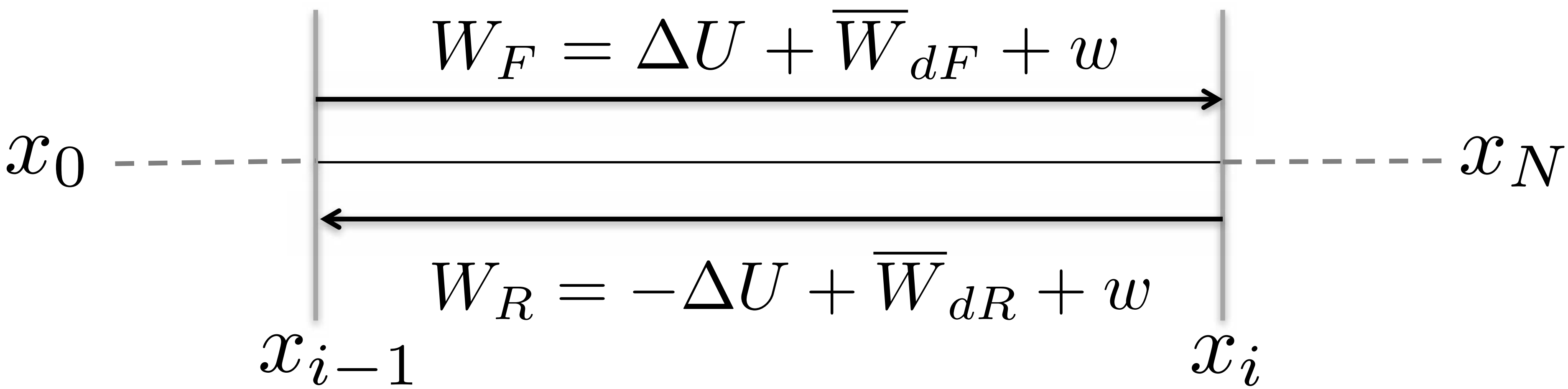
$$W_\lambda = \int_0^\lambda \left(\frac{\partial V_\lambda}{\partial \lambda} \right) d\lambda = \int_0^\tau \left(\frac{\partial V_\lambda}{\partial \lambda} \right) \dot{\lambda}\, dt$$

System is driven out of equilibrium

$$W = \Delta U + W_d \Longrightarrow \overline{W} = \Delta U + \overline{W}_d$$

A1: Determine the PMF $U(x)$

Forward (F) Pulling and Reverse (R) Pulling

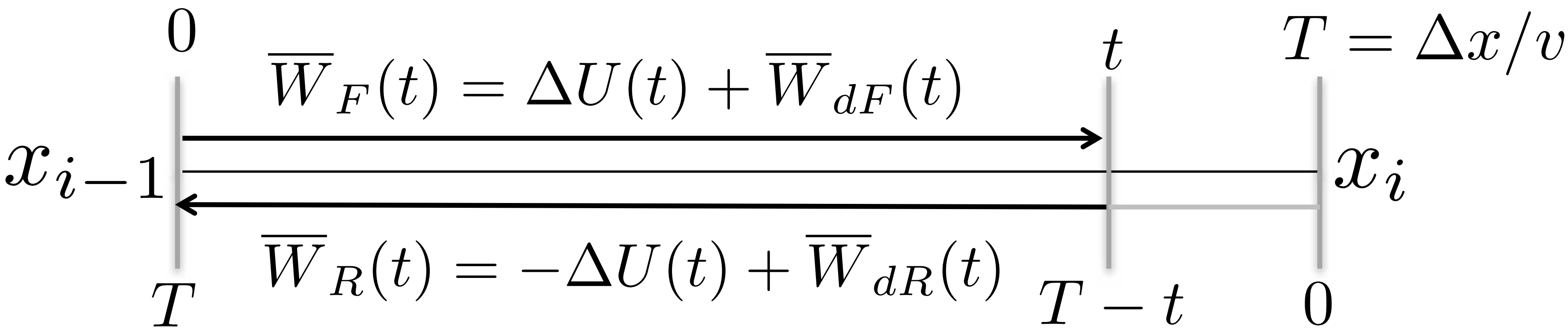


$$\overline{W}_{dF} = \overline{W}_{dR} = \overline{W}_d \ ; \ \overline{w} = 0$$

$$\Delta U = \frac{1}{2}\left(\overline{W}_F - \overline{W}_R\right)$$

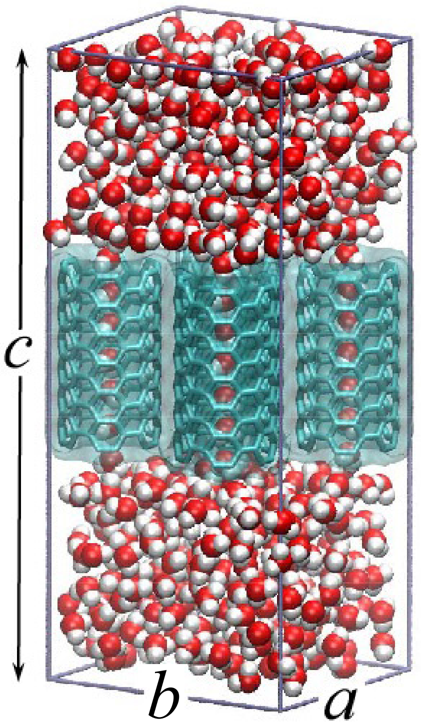
A2: determine the mean dissipative work $\overline{W}_d$

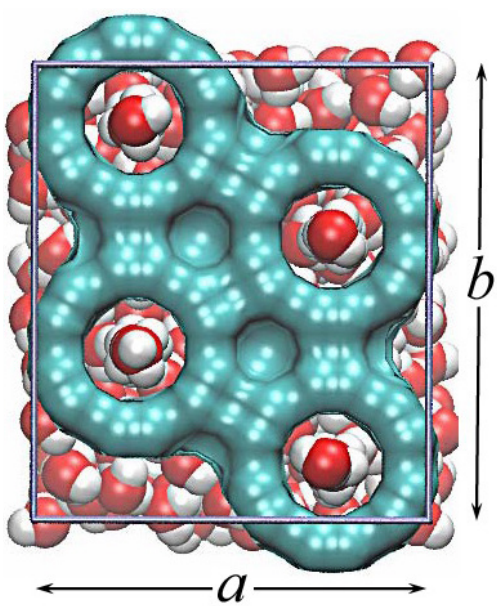
Calculate the mean dissipative work

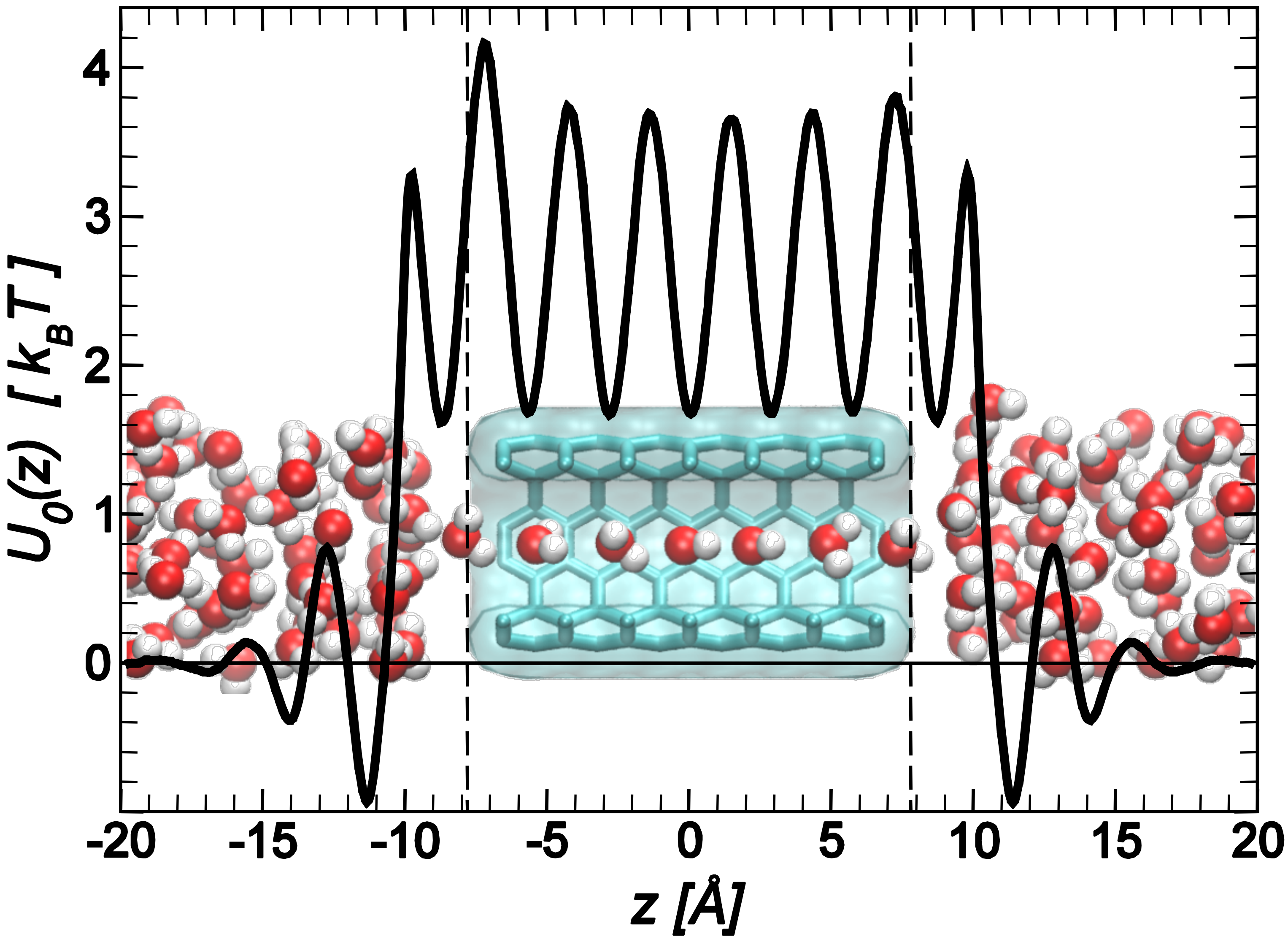


$$\overline{W}_d(t) = \frac{\overline{W}_{dF}(t) + \overline{W}_{dR}(t)}{2} = \frac{\overline{W}_F(t) + \overline{W}_R(t)}{2}$$

Water Transport through SWNT

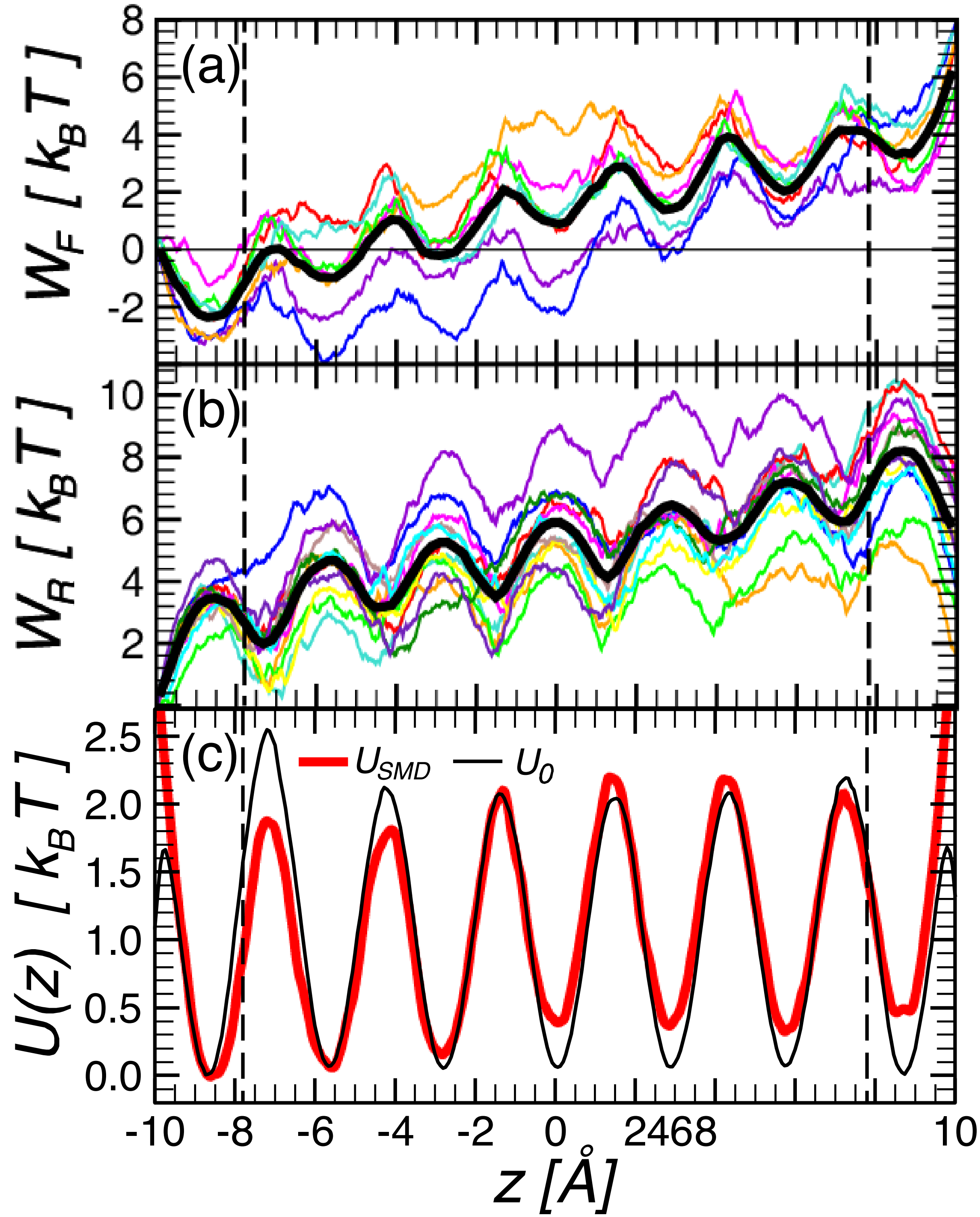




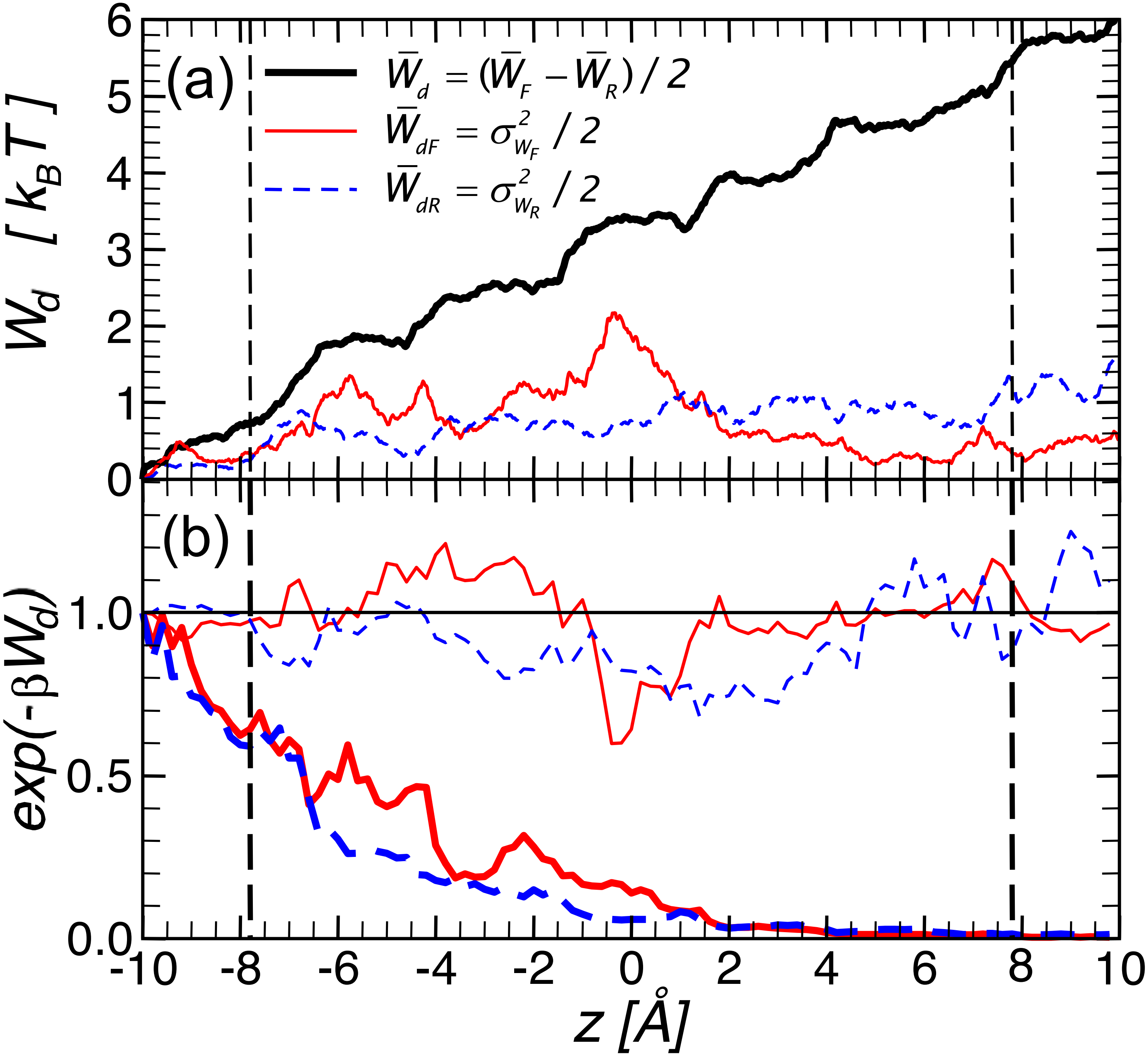


$$U_0(z) = -k_B T \log\left[p_0(z)\right]$$

Water Transport through SWNT



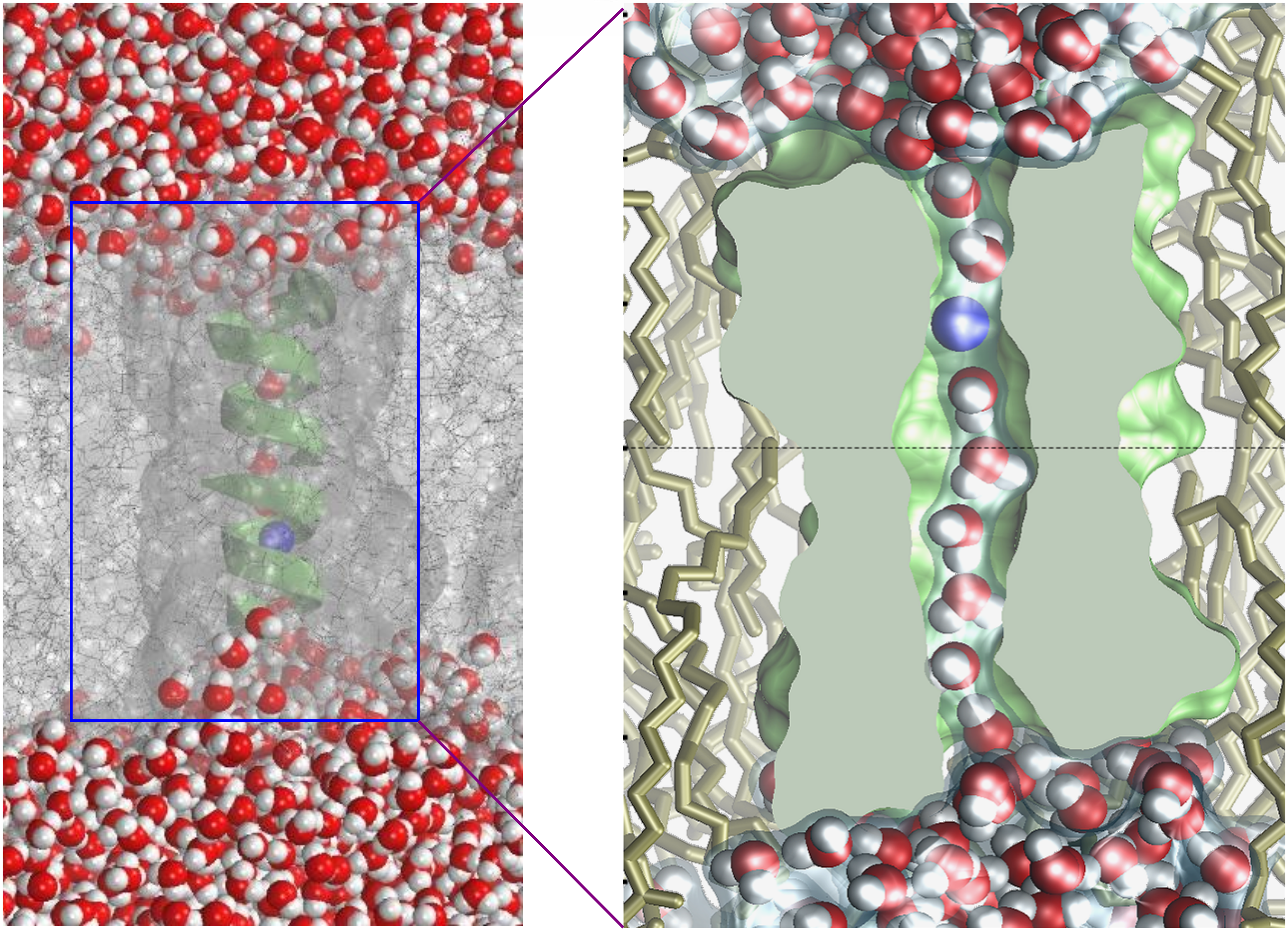
Water Transport through SWNT

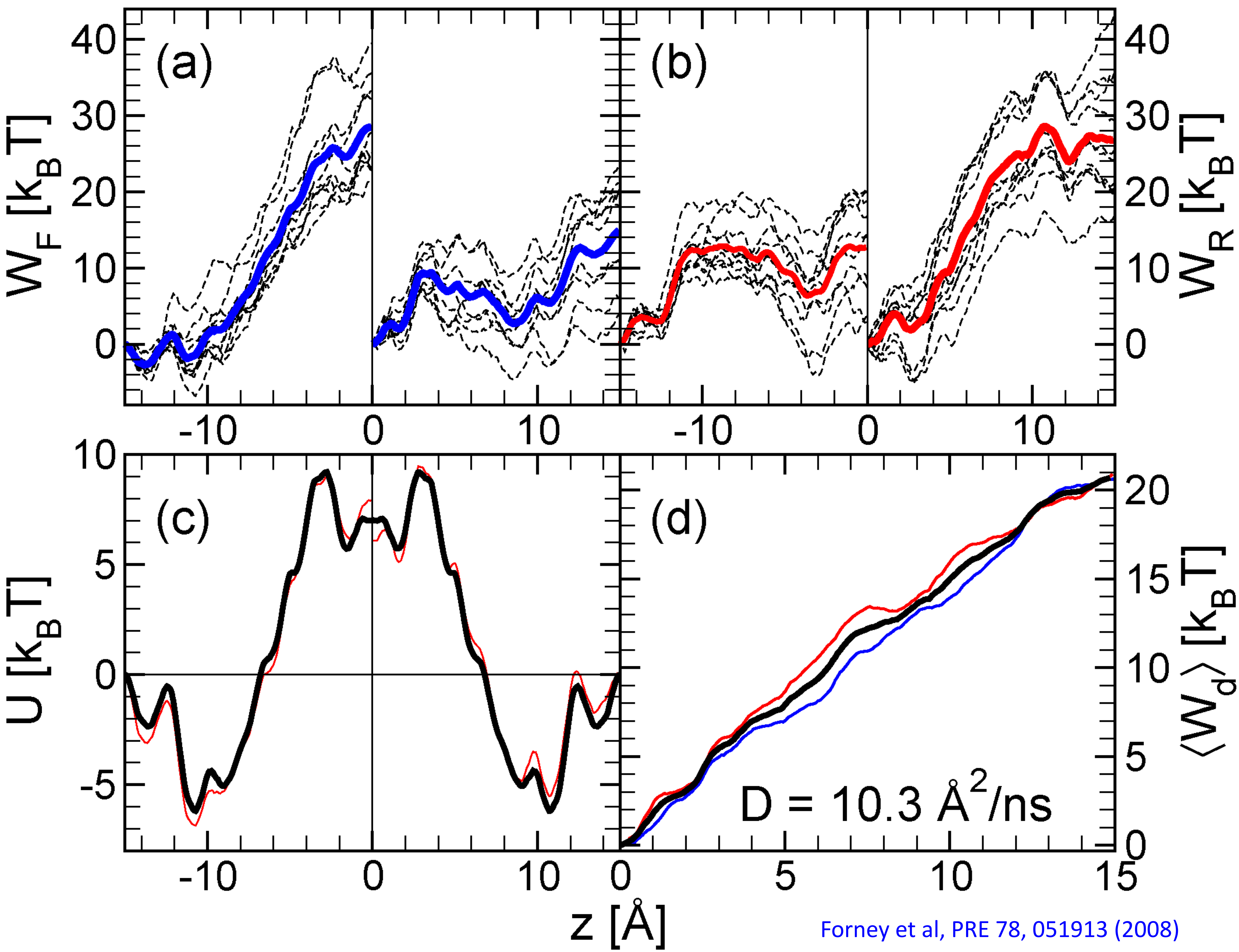


$D \approx 71\ \text{Å}^2/\text{ns}$

$$D_{eff} = a^2/2\tau$$
$$\approx 48\ \text{Å}^2/\text{ns}$$

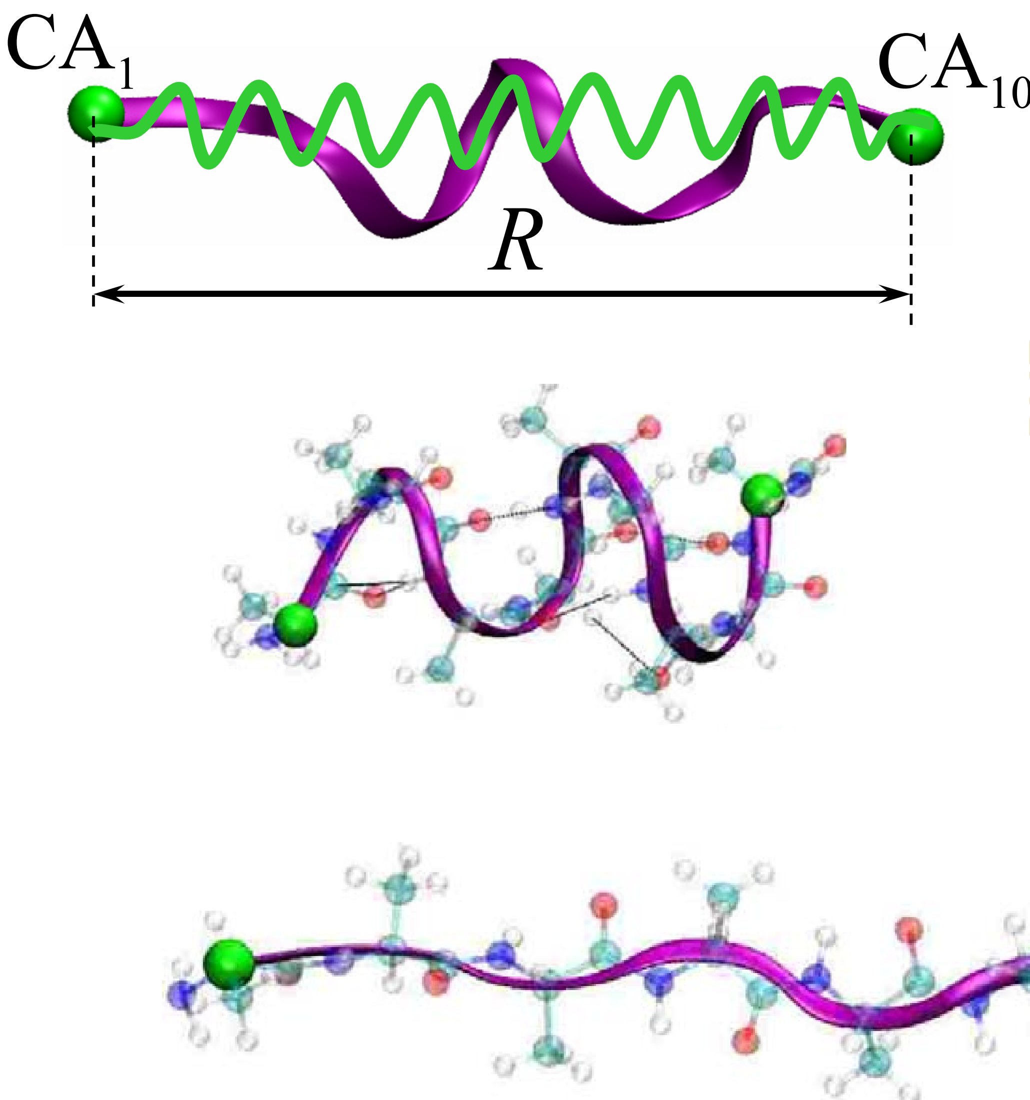
K^+ conduction through gramicidin-A channel

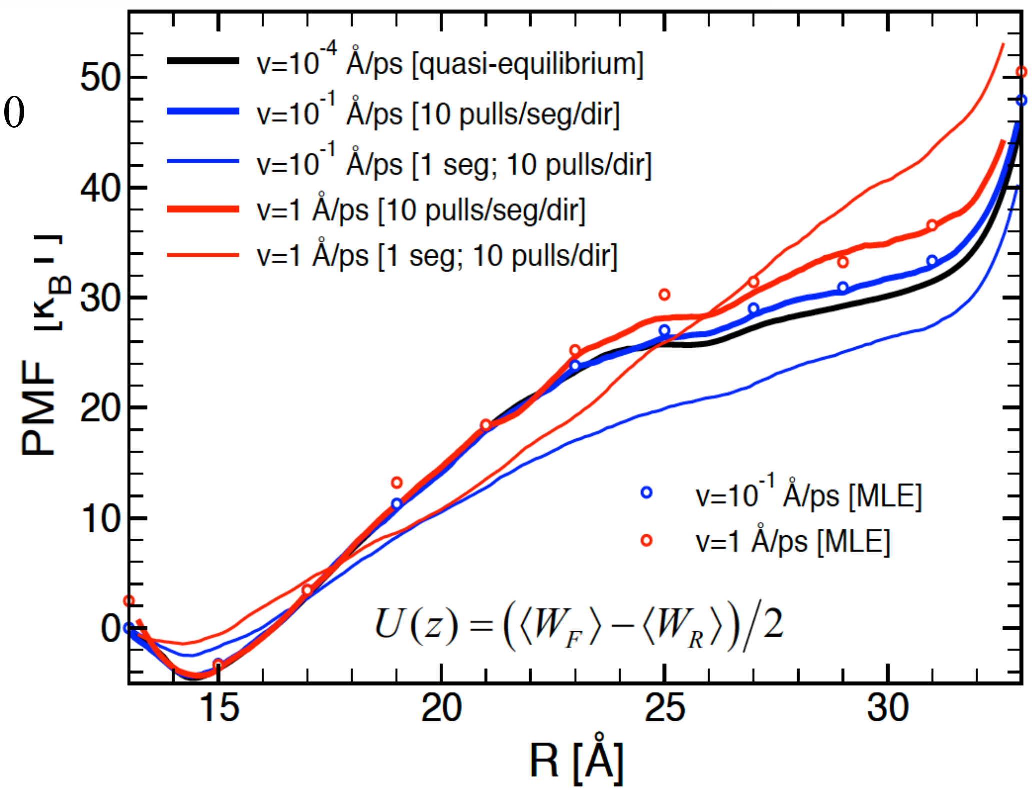




Forney et al, PRE 78, 051913 (2008)

Deca-alanine unfolding/folding





M. Forney, et. al. Phys. Rev. E 78, 051913

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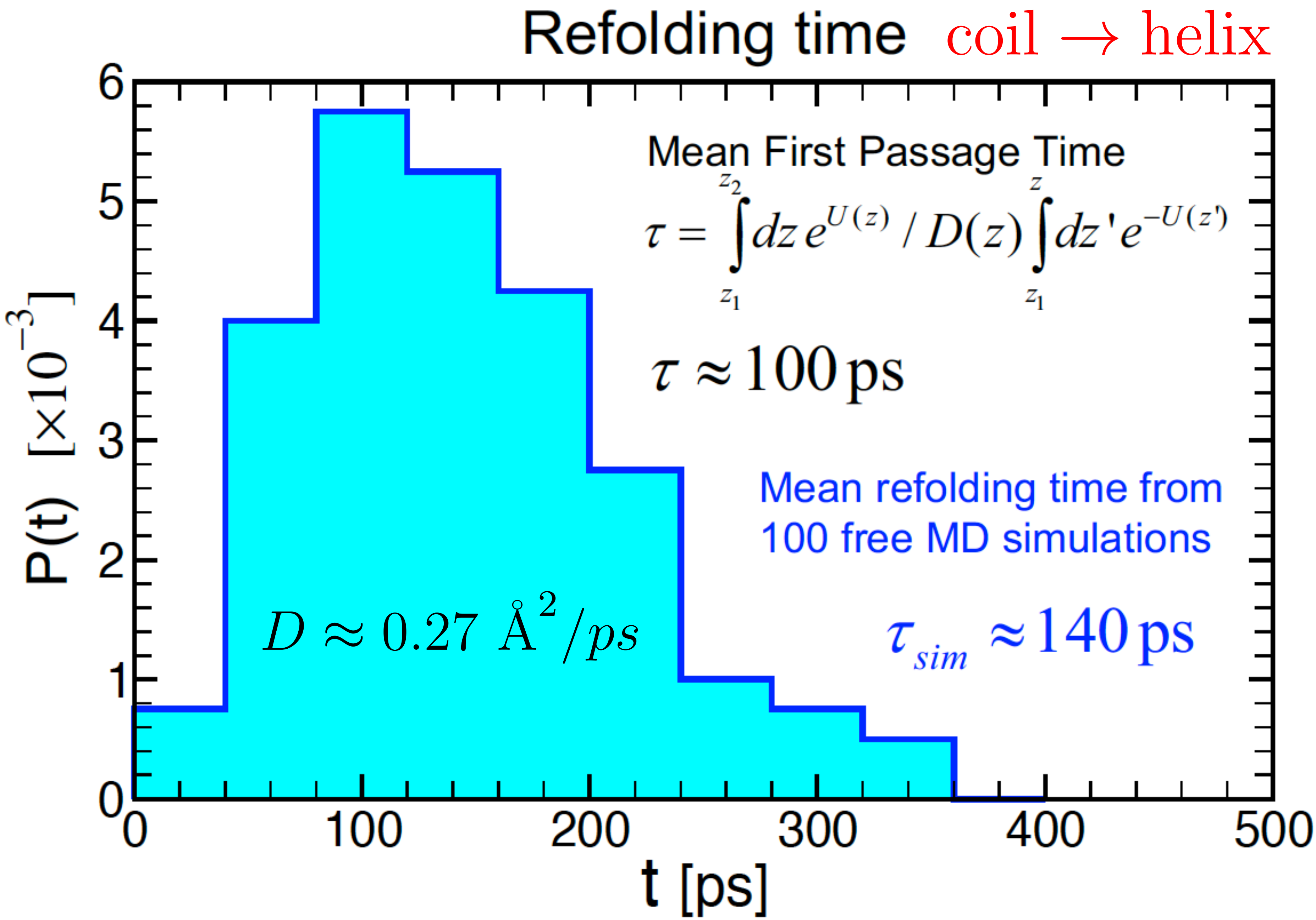

Conclusions

- presented a new method for calculating both the free energy profile (PMF) and the diffusion coefficient from a series of bi-directional pulling processes along a reaction coordinate
- it can identify the effective dynamics along the reaction coordinate
- demonstrated the viability of the method for several cases of interest