

Quantum free energy calculations using path integral molecular dynamics

Kevin Bishop

University of Waterloo

Group Meeting

November 18, 2016

Background

1. Free energy calculations

- ▶ Free energy calculations are an integral part of chemistry
 - ▶ Provide insight into equilibrium structures, reaction rates, etc.
- ▶ Helmholtz free energy directly related to partition function:

$$A = -k_B T \ln(Z) \quad (1)$$

- ▶ In principle, easy to calculate. In practice, Z is very difficult

2. Nuclear quantum effects

- ▶ Important in molecular dynamics simulations¹
- ▶ Use Feynman path integrals

What if we want to do free energy calculations on systems with non-negligible nuclear quantum effects?

¹M. Ceriotti et al., Phys. Rev. Lett. **103**, 030603 (2009), M. Ceriotti et al., Proc. Natl. Acad. Sci. **110**, 15591–15596 (2013).

Outline of project

- Develop procedure to use umbrella sampling alongside path integral molecular dynamics to obtain free energies in real space
 - ▶ Centroid potential of mean force has been studied¹
- The procedure must efficiently determine optimal parameters for umbrella sampling and PIMD simulations
- Test procedure on water dimer system
 - ▶ Use q-SPC/Fw², q-TIP4P/F³ and MB-pol⁴ water models
 - ▶ Should be transferable to other systems and temperatures
 - ▶ Use free energy profiles to obtain B_2 and free energy differences critical to atmospheric chemistry⁵

¹K. Hinsen and B. Roux, *J. Chem. Phys.* **106**, 3567–3577 (1997), T. Yamamoto and W. H. Miller, *J. Chem. Phys.* **120**, 3086–3099 (2004), N. Blinov and P.-N. Roy, *J. Chem. Phys.* **120**, 3759–3764 (2004).

²F. Paesani et al., *J. Chem. Phys.* **125**, 184507 (2006).

³S. Habershon et al., *J. Chem. Phys.* **131**, 024501 (2009).

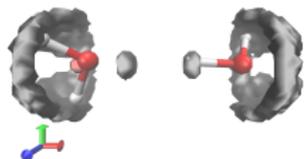
⁴V. Babin et al., *J. Chem. Theory Comput.* **9**, 5395–5403 (2013).

⁵J. S. Daniel et al., *J. Geophys. Res.* **104**, 16785–16791 (1999), J. S. Daniel et al., *Geophys. Res. Lett.* **31** (2004) .

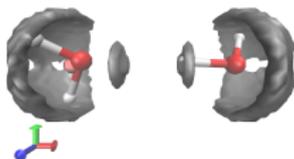
Water dimer with nuclear quantum effects (MC rot.)

Classical molecular dynamics:

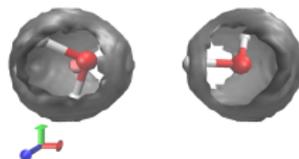
10 K



100 K

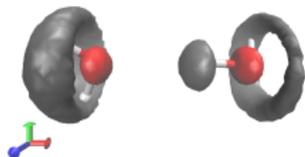


300 K

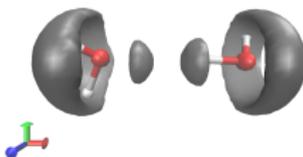


Path integral molecular dynamics:

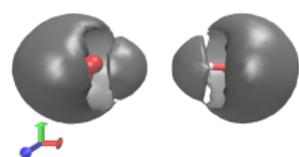
10 K



100 K



300 K



Proposed procedure¹

1. Determine an appropriate k and r_{eq} for umbrella sampling
 - ▶ Sufficient overlap between adjacent windows
 - ▶ **Where do we apply the umbrella sampling potential?**
2. Determine the optimal γ^0 for these simulations from the k
 - ▶ ie. $\gamma^0 = 2\omega_{\text{bias}}$
 - ▶ **Inspired by PILE thermostat**
3. Perform umbrella sampling simulations
 - ▶ Vary P and r_{eq} and temperature
4. Use WHAM to unbiased simulations and obtain free energy profiles
5. Calculate B_2 and ΔA that can be compared to experiment

¹K. P. Bishop and P.-N. Roy, *J. Chem. Phys.* in preparation (2016).

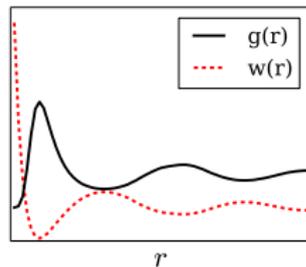
Basics of free energy calculations¹

- Free energy differences are easier to calculate

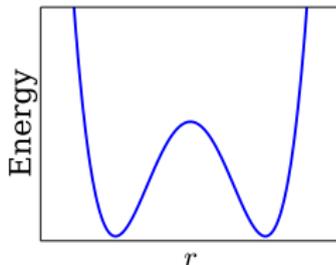
$$\Delta A_{12} = A_1 - A_2 = -k_B T \ln \left(\frac{Z_2}{Z_1} \right) \quad (1)$$

- Free energy over some reaction coordinate, r , is more useful

$$w(r) = -k_B T \ln g(r) \quad (2)$$



- Difficulty:** Need to sample *entire* reaction coordinate
 - Generally high energy barriers



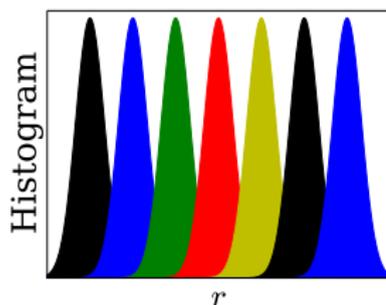
¹C. Chipot and A. Pohorille, eds., (Springer, New York, 2007), T. Lelievre et al., (Imperial College Press, London ; Hackensack, N.J., 2010).

Classical Umbrella sampling¹ and WHAM²

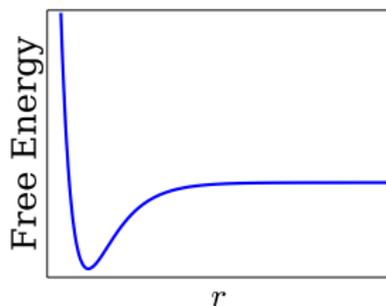
- Umbrella sampling introduces a biasing potential to the system

$$V_{\text{total}}(r) = V(r) + \frac{1}{2}k(r - r_{eq})^2 \quad (1)$$

- Bias is required to sample desired configurations
 - ▶ Water dimer would evaporate at high temperature
- Unbias simulation *windows* using the Weighted Histogram Analysis Method (WHAM)



⇓ WHAM



¹G. M. Torrie and J. P. Valleau, Chem. Phys. Lett. **28**, 578–581 (1974), G. Torrie and J. Valleau, J. Comput. Phys. **23**, 187–199 (1977).

²S. Kumar et al., J. Comput. Chem. **13**, 1011–1021 (1992).

Path integral formalism

Canonical partition function:

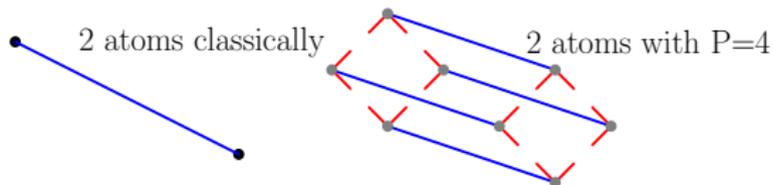
$$Z = \text{Tr}[e^{-\beta\mathcal{H}}] \quad (1)$$

Trotter factorization yields¹:

$$Z = \lim_{P \rightarrow \infty} \left(\frac{mP}{2\pi\beta\hbar^2} \right)^{\frac{P}{2}} \times \int dr_1 \cdots dr_P \exp \left\{ - \left\{ \sum_{i=1}^P \left[\frac{mP}{2\beta\hbar^2} (r_i - r_{i+1})^2 + \frac{\beta}{P} V(r_i) \right] \right\} \right\} \quad (2)$$

interatomic

ring polymer



¹R. P. Feynman and A. R. Hibbs, (McGraw-Hill, New York, 1965), D. Chandler and P. Wolynes, J. Chem. Phys. **74**, 4078–4095 (1981), M. Parrinello and A. Rahman, J. Chem. Phys. **80**, 860–867 (1984), H. F. Trotter, Proc. Amer. Math. Soc. **10**, 545–551 (1959).

Umbrella sampling for path integrals

- Unbiased path integral definition:

$$\begin{aligned} Z &= \text{Tr} \left[e^{-\beta(\hat{K} + \hat{V})} \right] \\ &= \lim_{P \rightarrow \infty} \int dr \left\langle r \left| \left(e^{-\frac{\beta}{P}\hat{K}} e^{-\frac{\beta}{P}\hat{V}} \right)^P \right| r \right\rangle \end{aligned}$$

- Simple solution:

$$\begin{aligned} Z &= \text{Tr} \left[e^{-\beta(\hat{K} + \hat{V} + \hat{V}_{\text{bias}})} \right] \\ &= \lim_{P \rightarrow \infty} \int dr \left\langle r \left| \left(e^{-\frac{\beta}{P}\hat{K}} e^{-\frac{\beta}{P}\hat{V}} e^{-\frac{\beta}{P}\hat{V}_{\text{bias}}} \right)^P \right| r \right\rangle \end{aligned}$$

- Problem: We will need P V_{bias} terms.
 - ▶ No problem simulation wise
 - ▶ Big problem for WHAM, becomes P -dimensional, unstable numerically

Umbrella sampling for path integrals

- Unbiased path integral definition:

$$\begin{aligned} Z &= \text{Tr} \left[e^{-\beta(\hat{K} + \hat{V})} \right] \\ &= \lim_{P \rightarrow \infty} \int dr \left\langle r \left| \left(e^{-\frac{\beta}{P}\hat{K}} e^{-\frac{\beta}{P}\hat{V}} \right)^P \right| r \right\rangle \end{aligned}$$

- Small change to simple solution:

$$\begin{aligned} Z &= \text{Tr} \left[e^{-\beta(\hat{K} + \hat{V})} e^{-\beta\hat{V}_{\text{bias}}} \right] \\ &= \lim_{P \rightarrow \infty} \int dr \left\langle r \left| e^{-\beta\hat{V}_{\text{bias}}} \left(e^{-\frac{\beta}{P}\hat{K}} e^{-\frac{\beta}{P}\hat{V}} \right)^P \right| r \right\rangle \end{aligned}$$

- Only requires 1 \hat{V}_{bias} term
 - ▶ No problem simulation wise
 - ▶ WHAM remains 1-dimensional and numerically stable

Umbrella sampling for path integrals

- We will only apply biasing potential to a single bead
 - ▶ Simple modification to forcefield
 - ▶ Identical to classical WHAM when unbiasing
- We still need to determine the appropriate k and r_{eq} for each window
 - ▶ Property of system and potential energy surface as well as temperature
- We also have to choose a centroid friction parameter

Path integral langevin equation (PILE) thermostat¹

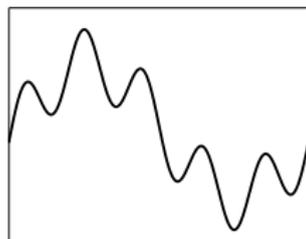
- Uses the Langevin equation² (from classical theory)

$$F_i(t) = -\nabla V(r_i(t)) - \gamma_i p_i(t) + \sqrt{\frac{2\gamma_i m_i}{\beta}} \eta(t) \quad (1)$$

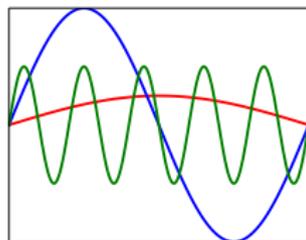
1. Apply Langevin equation to p for $\Delta t/2$
2. Apply interatomic potential for $\Delta t/2$
3. Full Δt evolution under ring polymer potential
4. Apply interatomic potential for $\Delta t/2$
5. Apply Langevin equation to p for $\Delta t/2$

- Requires a single input parameter, γ^0 , the centroid friction

$$\gamma^{(k)} = \begin{cases} 1/\tau_0, & k = 0 \\ 2\omega_k, & k > 0 \end{cases} \quad (2)$$



↓ FFT

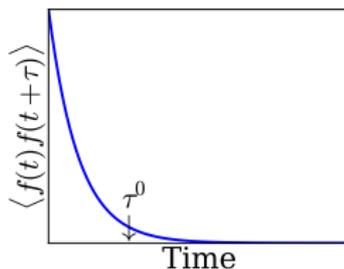


¹M. Ceriotti et al., J. Chem. Phys. **133**, 124104 (2010)

²P. Langevin, C. R. Acad. Sci. **146**, 530 (1908)

Friction optimization

- Centroid friction controls the sampling of the canonical distribution
 - ▶ $\gamma^0 = 0$ provides zero friction and produces microcanonical ensemble for centroid mode
 - ▶ Too large of γ^0 overdamps simulation
- ▶ Standard procedure¹ of calculating γ^0 :
 1. Perform microcanonical simulation
 2. Calculate decorrelation time (τ^0) of autocorrelation function
 3. Optimal $\gamma^0 = 1/\tau^0$
- γ^0 may change with P , ξ_k or temperature
- **Approximation:** Model system with umbrella sampling biasing potential as harmonic oscillator²



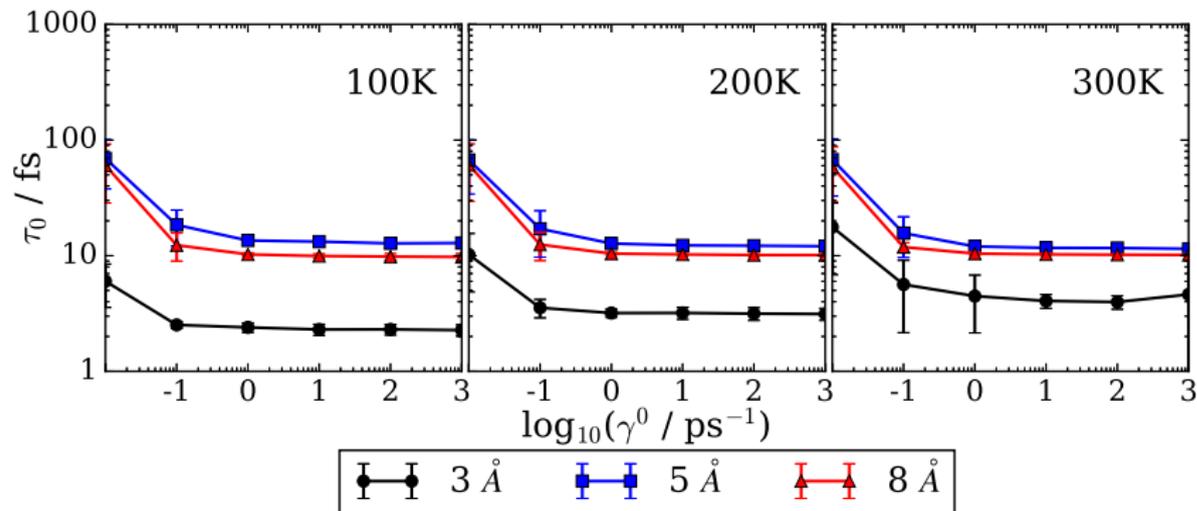
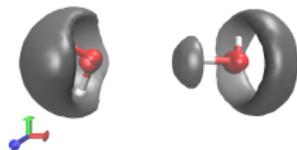
$$\gamma^0 = 2\omega_{\text{bias}} = \sqrt{\frac{k}{\mu}} \quad (1)$$

¹C. Ing et al., J. Chem. Phys. **136**, 224309 (2012)

²K. P. Bishop and P.-N. Roy, J. Chem. Phys. in preparation (2016).

Friction optimization for water dimer

- Results shown for q-SPC/Fw model
- Similar results for other models
- γ^0 is a robust parameter



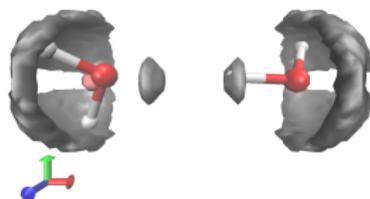
Procedure overview

- Apply biasing potential to a **single** bead only
- Determine the appropriate k and r_{eq} for each umbrella sampling window
- **Choose** centroid friction parameter as $\gamma^0 = 2\omega_{\text{bias}} = \sqrt{\frac{k}{\mu}}$
- Perform all simulations with varying parameters
- Unbias using WHAM

Rigid simulations

Rigid simulations have also been performed using two techniques:

- Applying constraints to classical molecular dynamics
 - ▶ Constraints of the OpenMM¹ package utilize SETTLE², RATTLE³
- Performing Monte Carlo (MC) integration:
 1. Fix centre of mass distance between waters
 2. Randomly sample Euler angles
 3. Calculate potential energy
 4. Sum Boltzmann factors ($e^{-\beta E}$)
 5. Calculate averages
- **Note:** This MC code has been used in a partnership with an external company for classical biomolecules



¹P. Eastman et al., *J. Chem. Theory Comput.* **9**, 461–469 (2013).

²S. Miyamoto and P. A. Kollman, *J. Comput. Chem.* **13**, 952–962 (1992).

³J.-P. Ryckaert et al., *J. Comput. Phys.* **23**, 327–341 (1977).

Monomer simulations

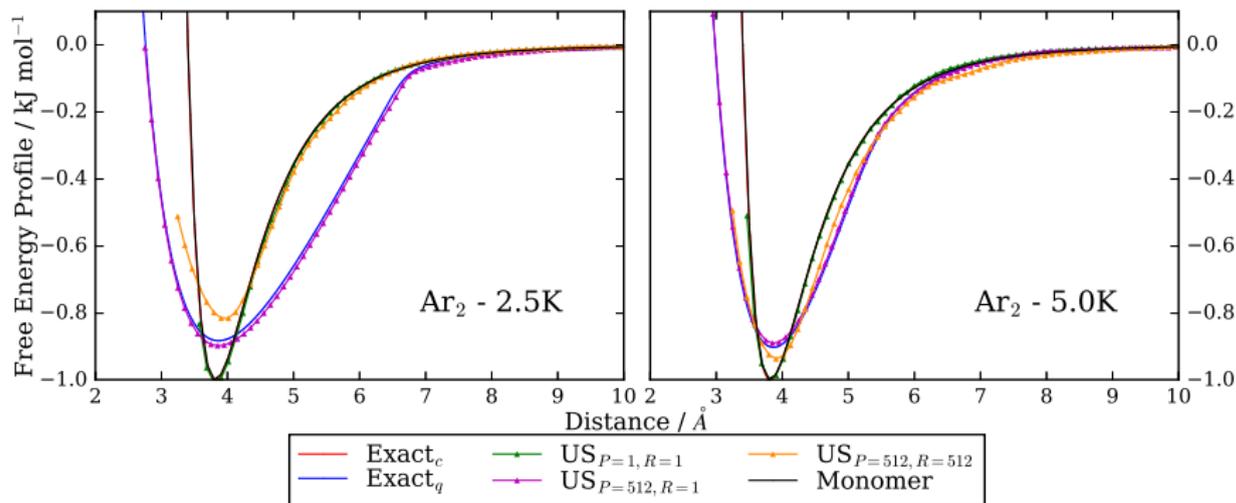
Some work has been done without the need for umbrella sampling. The general procedure is as follows:

1. Perform path integral simulations of water monomer
 - ▶ Provides you with a distribution of the monomer path
2. Place decorrelated configurations of path integral monomers at specific distances and randomly sample Euler angles
3. Build up averages and distributions

Problem: Does not treat reaction coordinate quantum mechanically!

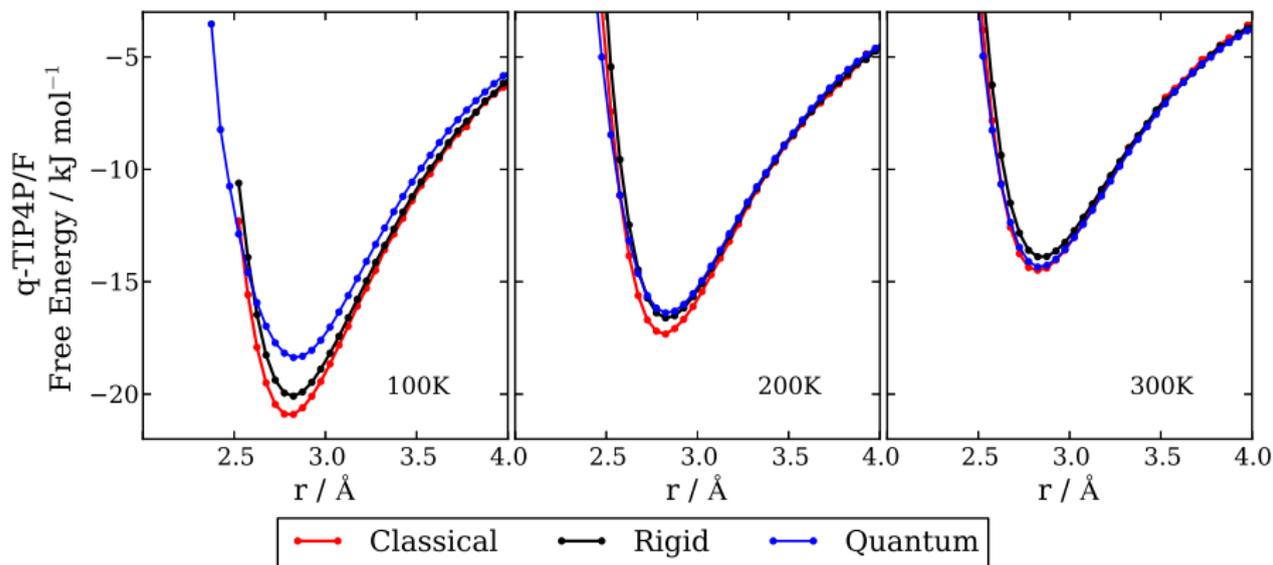
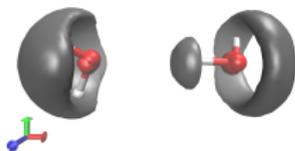
Test Method - Ar₂

- For Ar₂ with a Lennard-Jones potential, we can solve the path integral exactly
- Only our single biasing potential reproduces exact result at low temperature

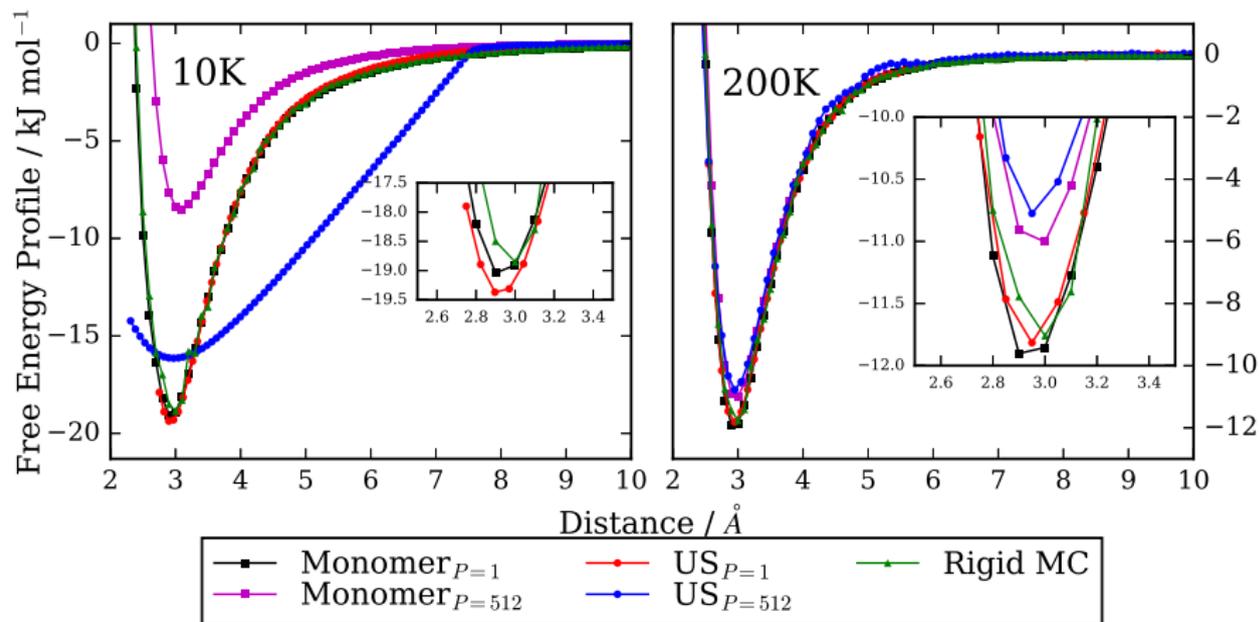


Free energy profiles

- Similar results for q-SPC/Fw model
- Rigid approximation sometimes works if done at correct temperature



Free energy profiles for MB-pol



Second virial coefficients

- Directly related to potential of mean force:¹

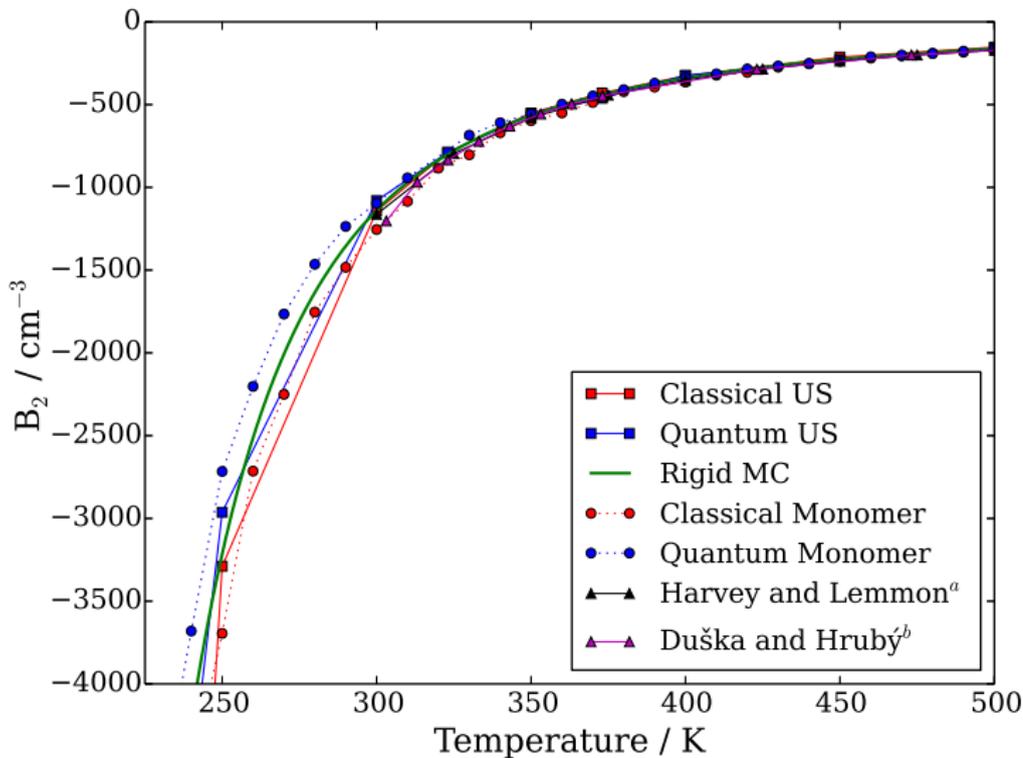
$$B_2(T) = -2\pi \int_0^\infty dr r^2 (e^{-w(r)/k_B T} - 1) \quad (1)$$

- Measured experimentally
 - ▶ Provides measure of quality of the potential used
 - ▶ q-SPC/Fw and q-TIP4P/F are not very good
- More useful results obtained from MB-pol water potential²
 - ▶ Developed using machine learning and the energy calculations of some 40,000+ structures at CCSD(T) level of theory
 - ▶ Successfully implemented within MMTK

¹V. Babin et al., *J. Chem. Theory Comput.* **9**, 5395–5403 (2013).

²V. Babin et al., *J. Chem. Theory Comput.* **9**, 5395–5403 (2013), V. Babin et al., *J. Chem. Theory Comput.* **10**, 1599–1607 (2014).

B₂ results



Using B_2 to connect with ΔA

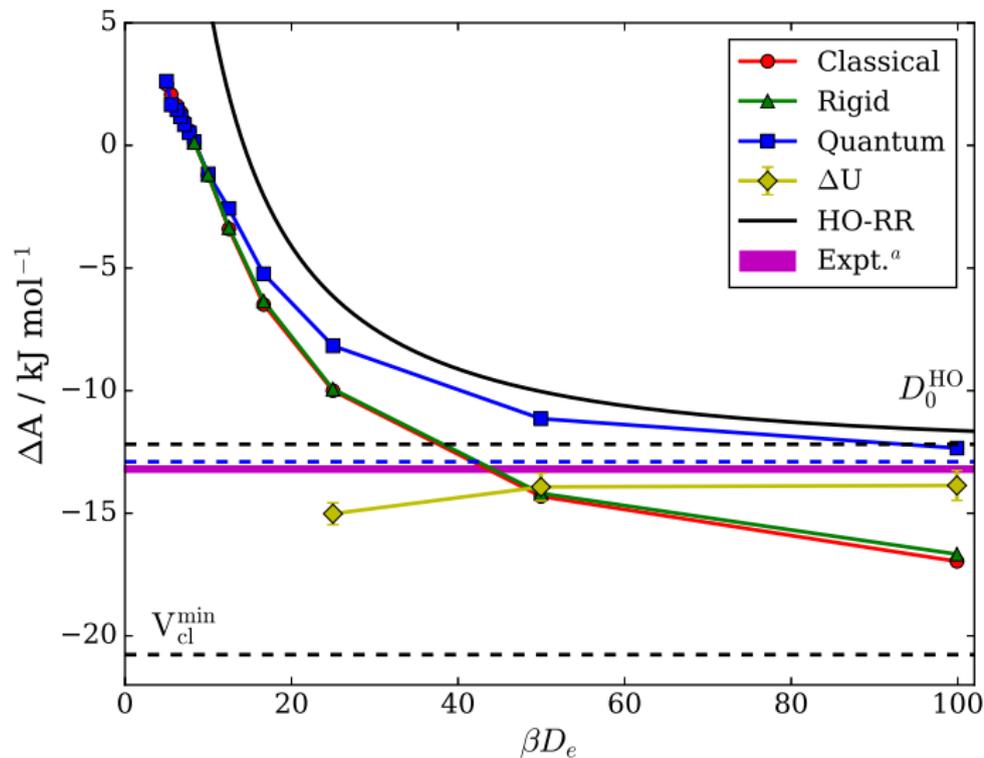
- We can relate B_2 to the ratio of partition functions

$$B_2(T) = V \left(\frac{1}{2} - \frac{Q_d}{Q_m^2} \right) \quad (1)$$

- We can insert this ratio to obtain an expression for ΔA in terms of B_2

$$\Delta A = -k_B T \ln \left(\frac{Q_d}{Q_m^2} \right) \quad (2)$$

$$= -k_B T \ln \left(\frac{1}{2} - \frac{B_2(T)}{V} \right) \quad (3)$$

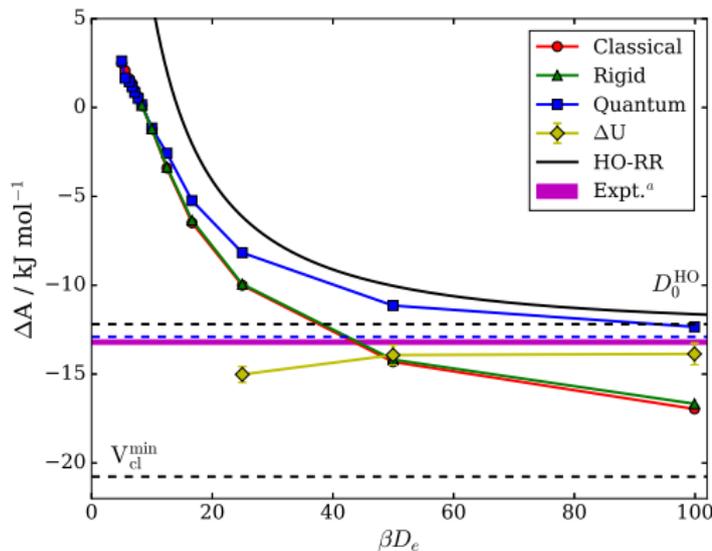
ΔA for MB-pol

PIGS and low temperature behaviour of well depths

- Umbrella sampling difficult at low temperature
 - ▶ Window distributions become very peaked
 - ▶ Distance is a poor reaction coordinate

- Quantum well depths as $T \rightarrow 0$?
 - ▶ $\Delta A = \Delta U$

- Use Langevin equation path integral ground state (Le-PIGS)¹
 - ▶ Preliminary results from Matthew Schmidt
 - ▶ Code in OpenMM

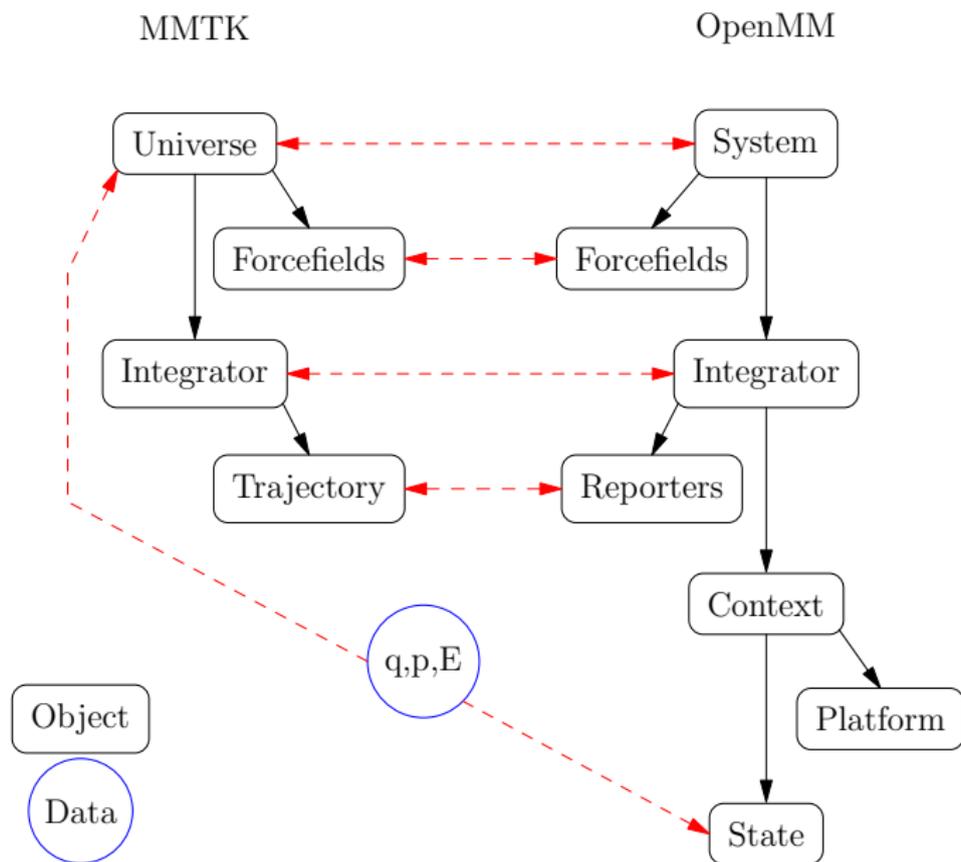


¹S. Constable et al., J. Phys. Chem. A **117**, 7461–7467 (2013), M. Schmidt et al., J. Chem. Phys. **140**, 234101 (2014)

Overview of OpenMM

- Extremely flexible open-source software package for MD
- Supports many architectures including GPU's
- Very efficient algorithms for large *classical* simulations
- Has support for path integral simulations
 - ▶ Algorithms are not as efficient as classical systems
 - ▶ Treats beads sequentially instead of in parallel

MMTK/OpenMM differences



Optimizing OpenMM for large path integral simulations

1. Build system classically
2. Call function that takes classical system and converts to path integral system
 - ▶ Sets up proper interatomic potential terms
3. Use a modified integrator that knows about the changes in the system

Should be transferable to all OpenMM platforms including the GPU platforms

Future Work

- Extend to other systems such as larger water clusters
- Implementing constraints into the PILE thermostat
- Developing a plugin within OpenMM to be more efficient for systems with large numbers of beads
- Working out theory for a quantum potential of mean force

Summary

- Proposed procedure for path integral umbrella sampling
 - ▶ Apply biasing potential to a single bead
 - ▶ Choice of γ^0 is fairly robust
- In the high temperature limit of this work:
 - ▶ B_2 compares favourable to other theoretical work and experiment
- In the low temperature limit of this work:
 - ▶ B_2 is used to calculate ΔA
 - ▶ Compares favourably to theoretical (ground state methods) and experimental D_e

Acknowledgements

Supervisor

- Pierre-Nicholas Roy

Theoretical Chemistry Group

- Matthew Schmidt in particular for Le-PIGS calculations

UNIVERSITY OF
WATERLOO



NSERC
CRSNG