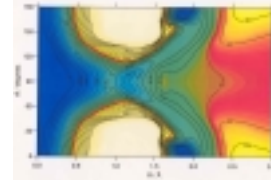




Quantum simulation of biomolecules & clusters

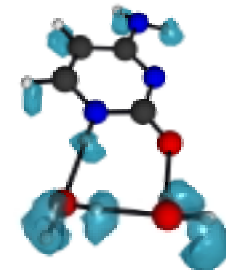
David Clary (Oxford University)

Potentials: **much progress**

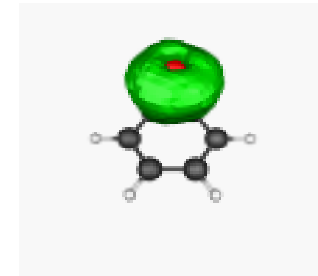


Dynamics / **Classical (eg MD)**
\
Quantum

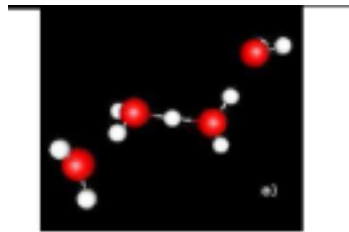
\
structures of
weakly-bound
clusters &
biomolecules



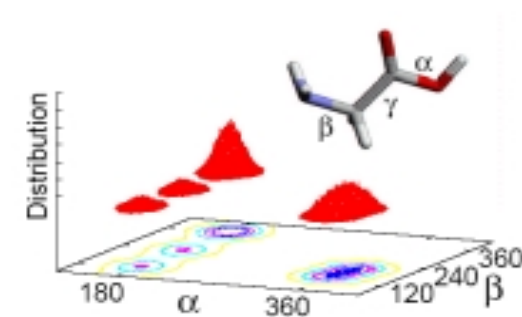
Hydrated clusters: Diffusion Monte Carlo
D Benoit, T van Mourik



Protonated clusters: Diffusion Monte Carlo
Max Mella



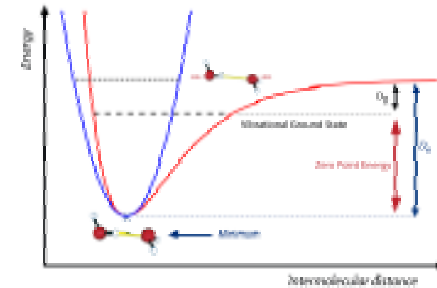
Biomolecule conformations: Torsional path integrals
Tommy Miller



Bound states and structures of weakly bound molecules

1. Harmonic approximation

general but rarely accurate enough



2. Basis functions

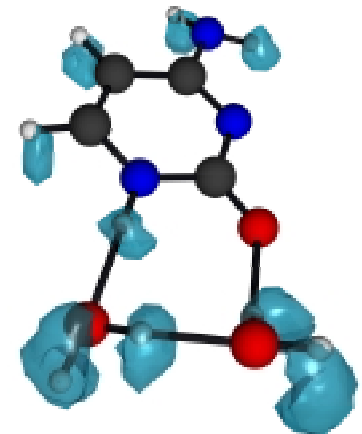
convergence and coordinate problems

Current limit "exact": $(\text{H}_2\text{O})_2$ and $(\text{H}_2)_3$

VSCF applied to larger systems (Gerber)

3. Quantum Diffusion Monte Carlo and Path Integrals

applicable to larger clusters and biomolecules



Diffusion Quantum Monte Carlo (DMC)

$$-i\hbar \frac{\partial \psi}{\partial t} = \frac{\hbar^2}{2m} \frac{\partial^2 \psi}{\partial x^2} - V\psi$$

Substitute $\tau = it / \hbar$

$$\frac{\partial \psi}{\partial \tau} = \frac{\hbar^2}{2m} \frac{\partial^2 \psi}{\partial x^2} - V\psi$$

Diffusion Equation+1st-order rate term:

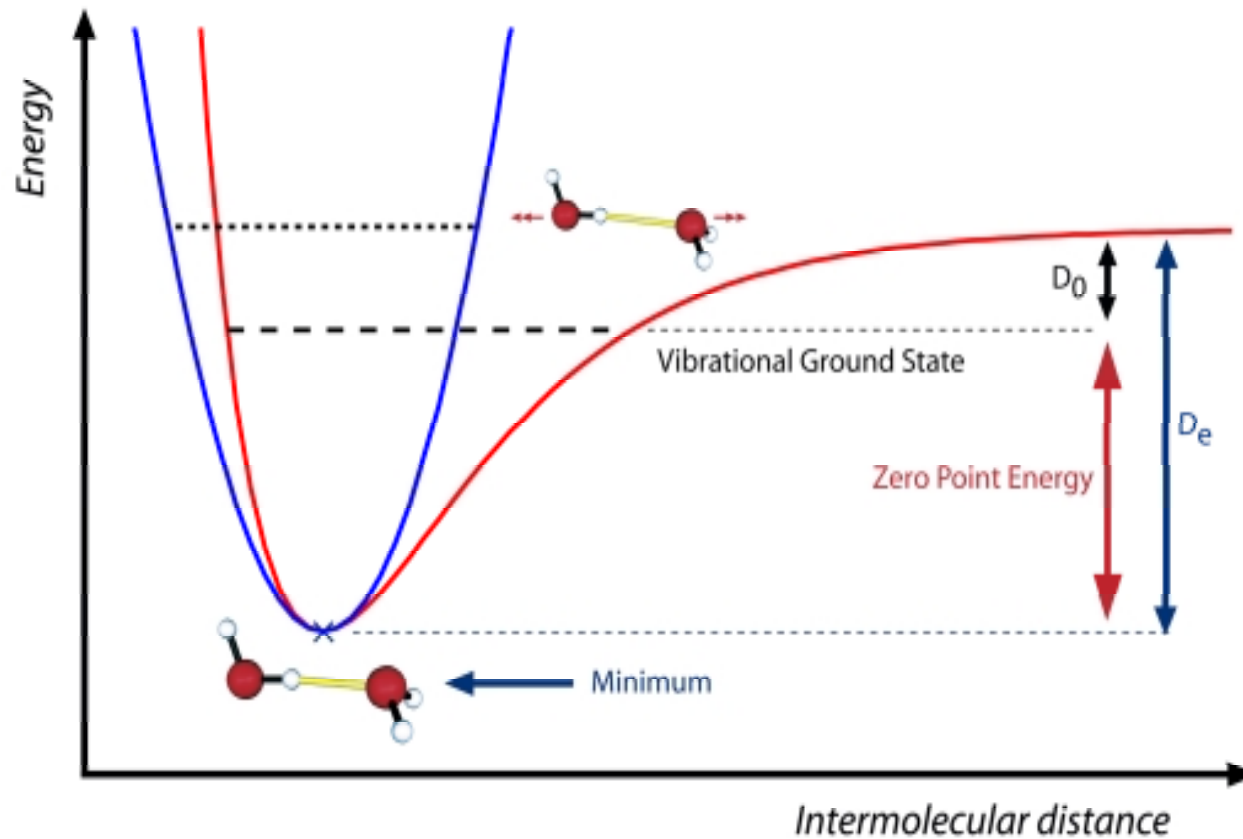
$$\frac{\partial C}{\partial \tau} = D \frac{\partial^2 C}{\partial x^2} - kC$$

Solve with Random Walk algorithm.

$$\psi = \sum_{n=0} c_n \phi_n \exp(-[E_n - E_{ref}] \tau)$$

$E_{ref} = E_0$ gives **ground state** energy

Zero Point Energy correction



OK only!

Diffusion Monte Carlo (DMC)

Electronic structure applications
(eg Anderson, Ceperley, Kalos, Lester etc)

and **vibrational problems**
(Watts, Suhm, Buch, Lewerenz, Whaley etc.)

Buch (1992) factorised out monomer vibrations
Rigid body DMC

D. Benoit and D. C. Clary

"Quaternion formulation of diffusion Monte Carlo for the rotation of rigid molecules in clusters",

J. Chem. Phys, 113, 4105 (2000): **XDMC code**

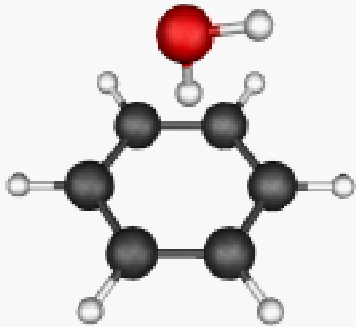
D. C. Clary, J. Chem. Phys., 114, 9725 (2001)

DMC with torsions for proteins:

T-DMC code

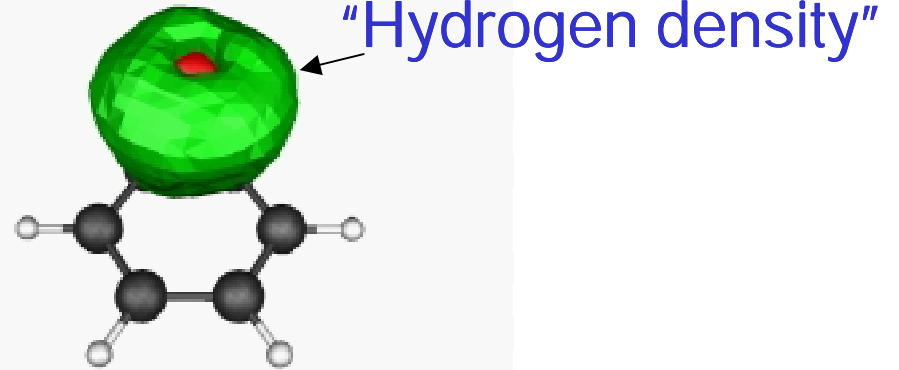
Benzene-water

Classical



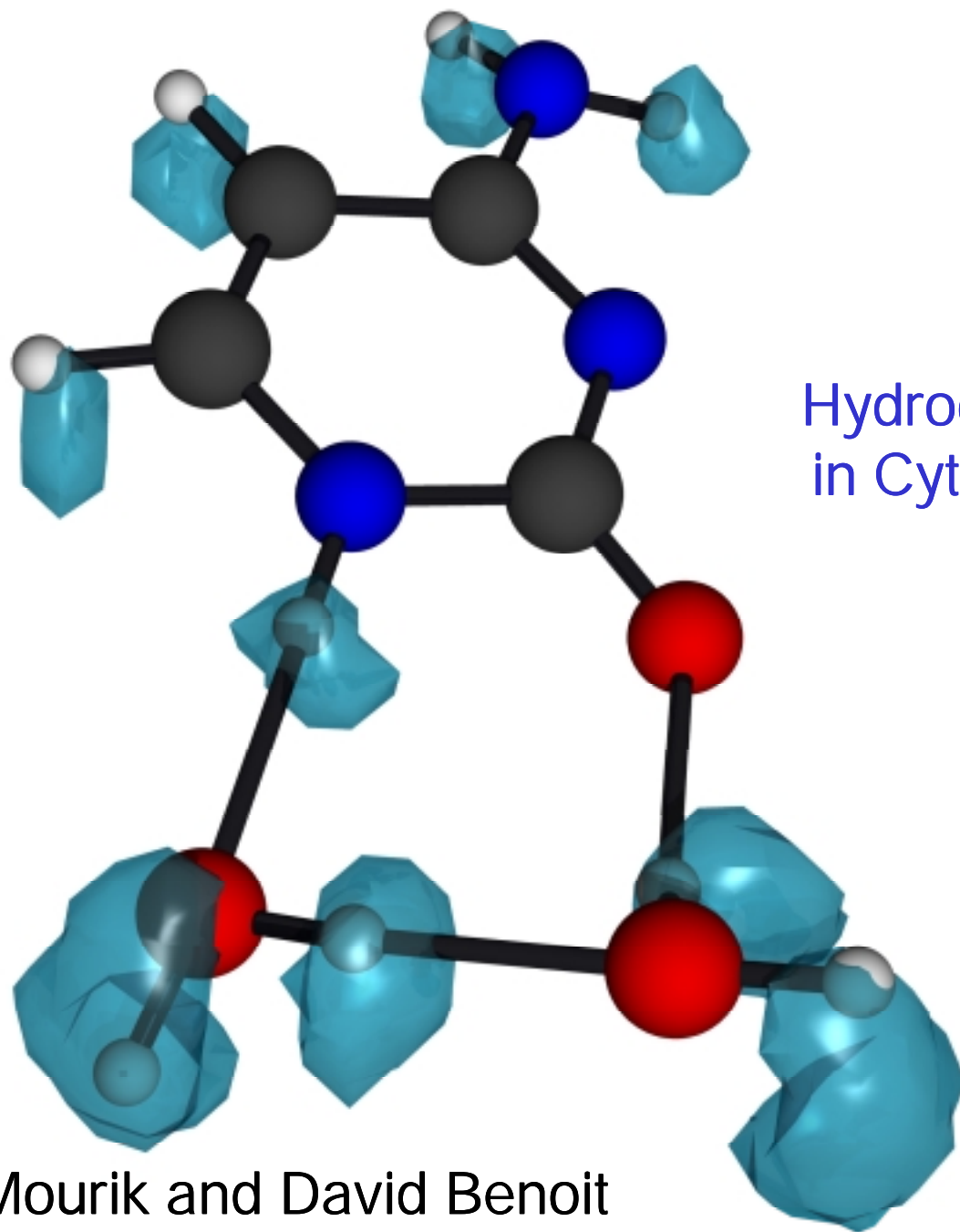
Asymmetric top

Quantum



Symmetric top
(agrees with experiment)

$D_0 =$	2.4 kcal mol ⁻¹ (DMC on Karlstrom potential)
	2.5 kcal mol ⁻¹ Exp (Mons et al)

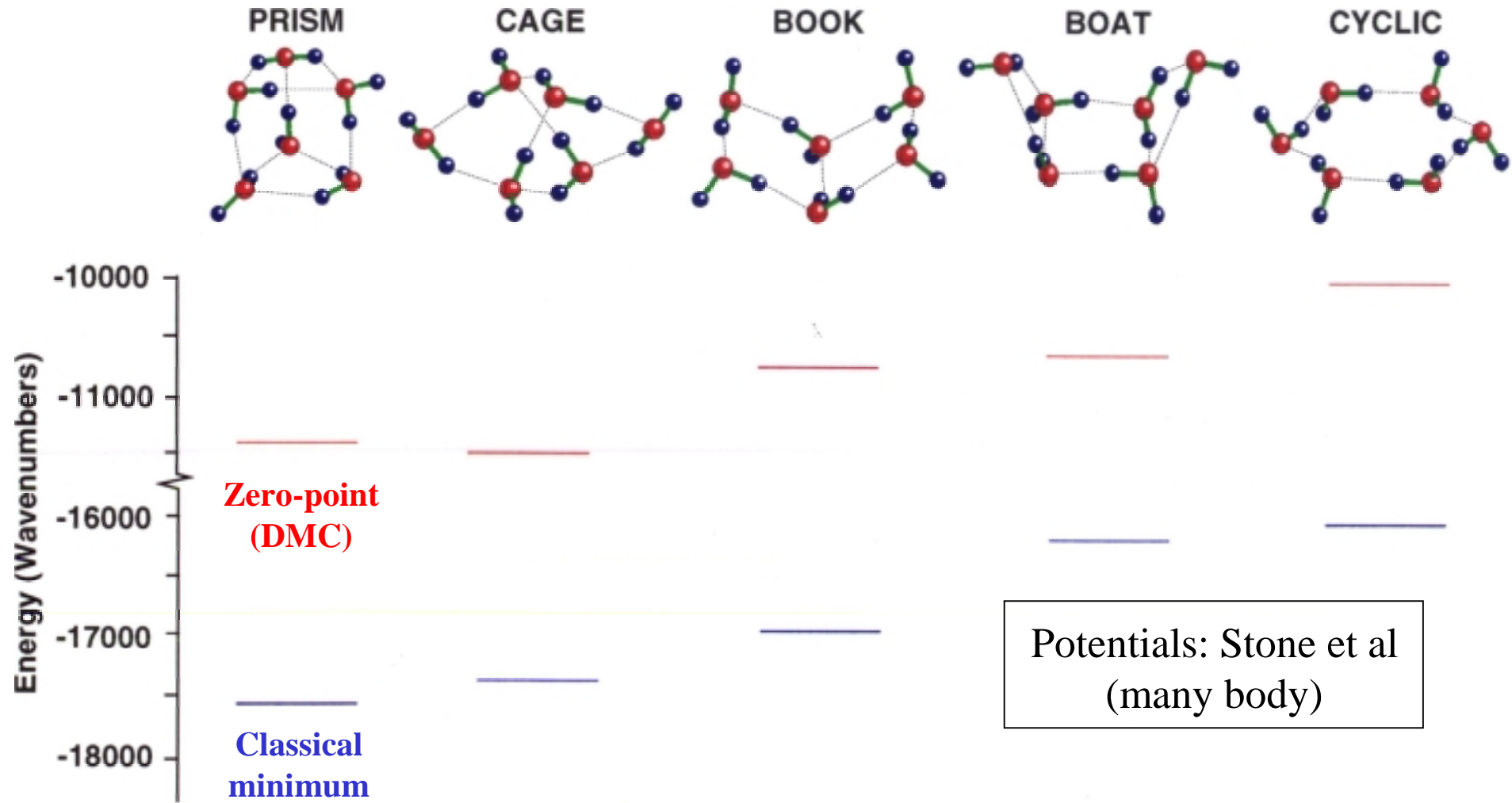


Hydrogen densities
in Cytosine-(H₂O)₂

Tanja van Mourik and David Benoit

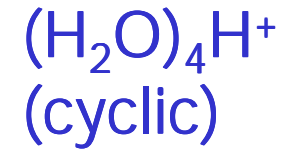
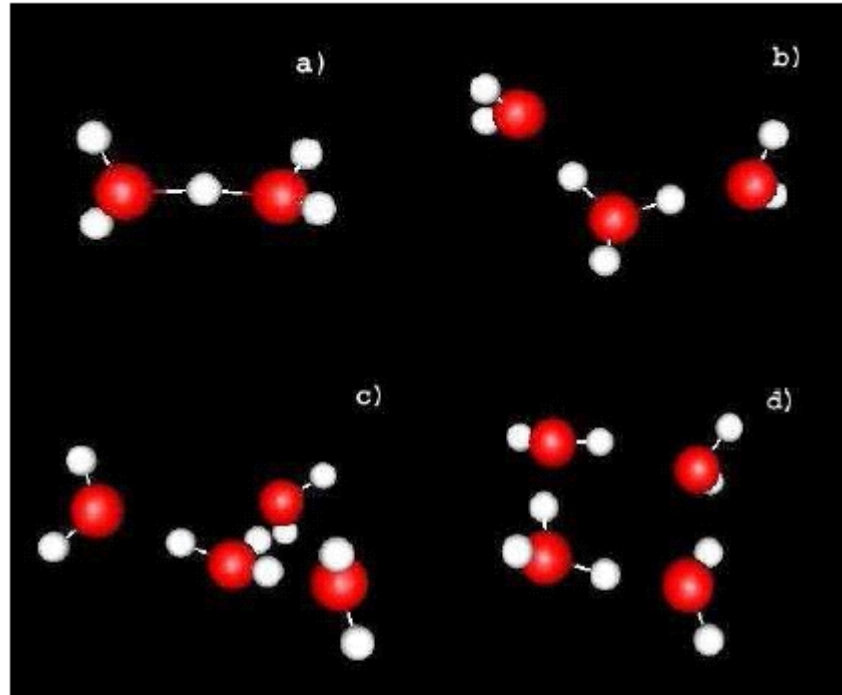
Potentials:
OPLSAA
& MP2

Water hexamer



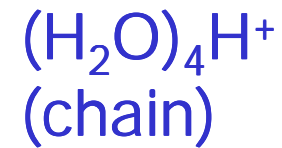
“Cage” found experimentally (Saykally et al)

Max Mella: DMC on $(\text{H}_2\text{O})_n\text{H}^+$

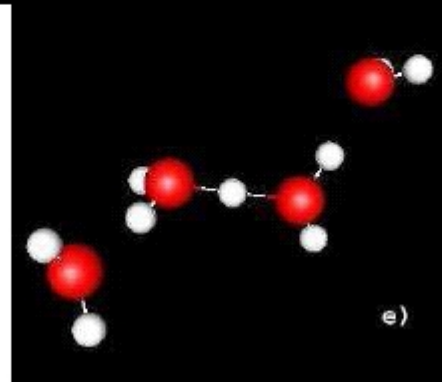


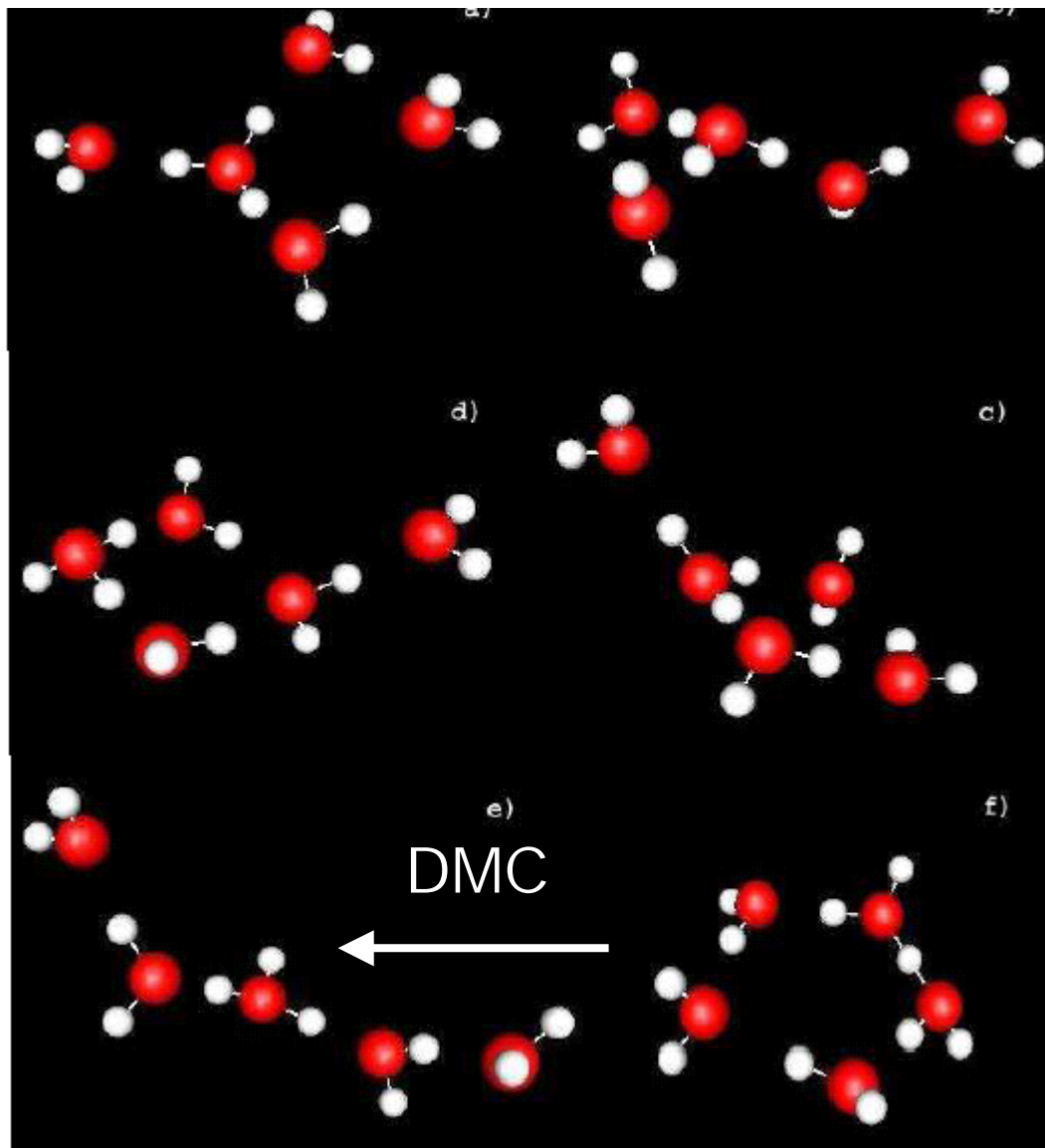
DMC

General
potential of
Singer et al



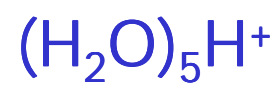
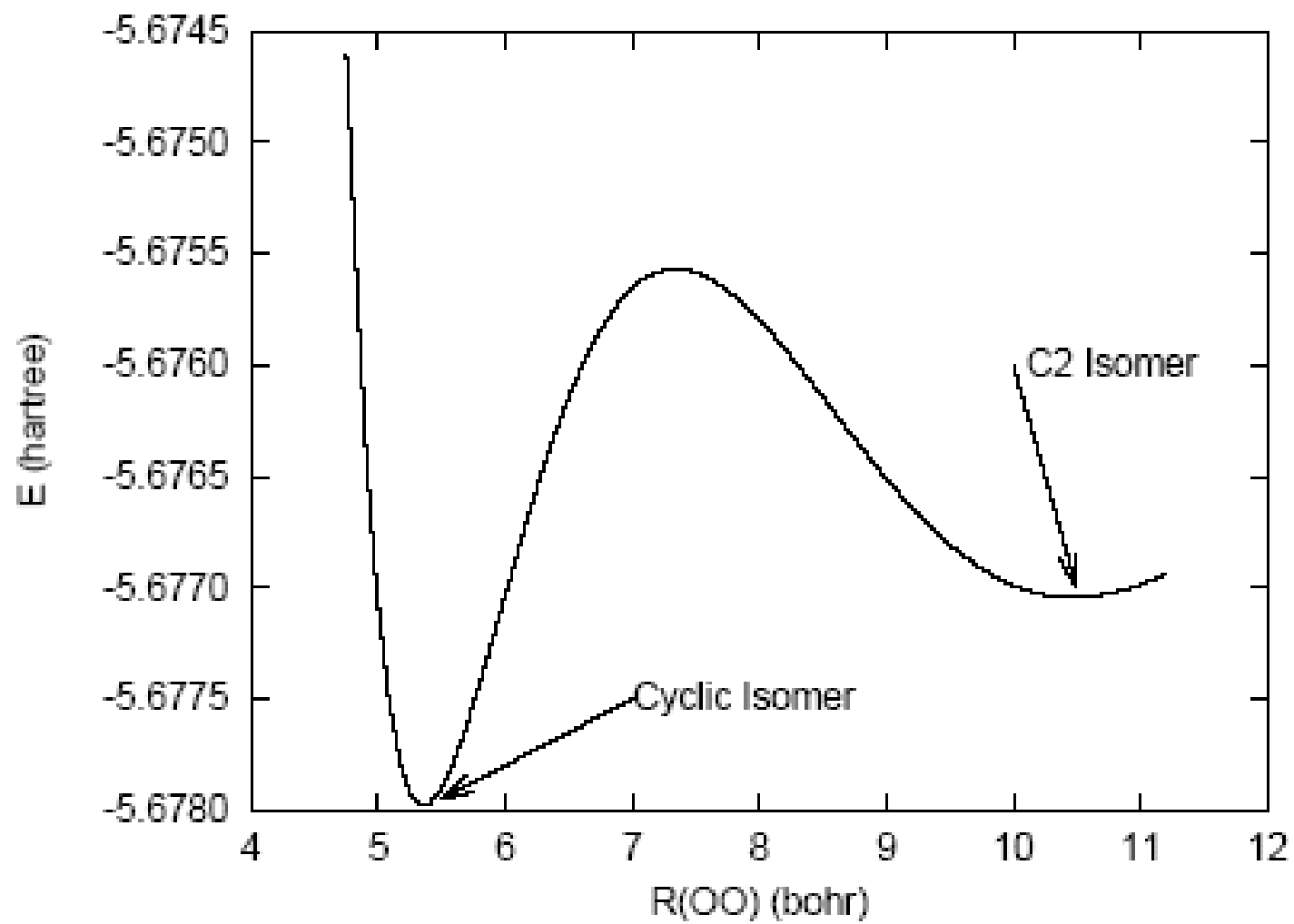
Not rigid body





$(\text{H}_2\text{O})_5\text{H}^+$
(chain)

$(\text{H}_2\text{O})_5\text{H}^+$
(cyclic)



Diffusion Monte Carlo

General way of calculating quantum ground states of weakly-bound systems

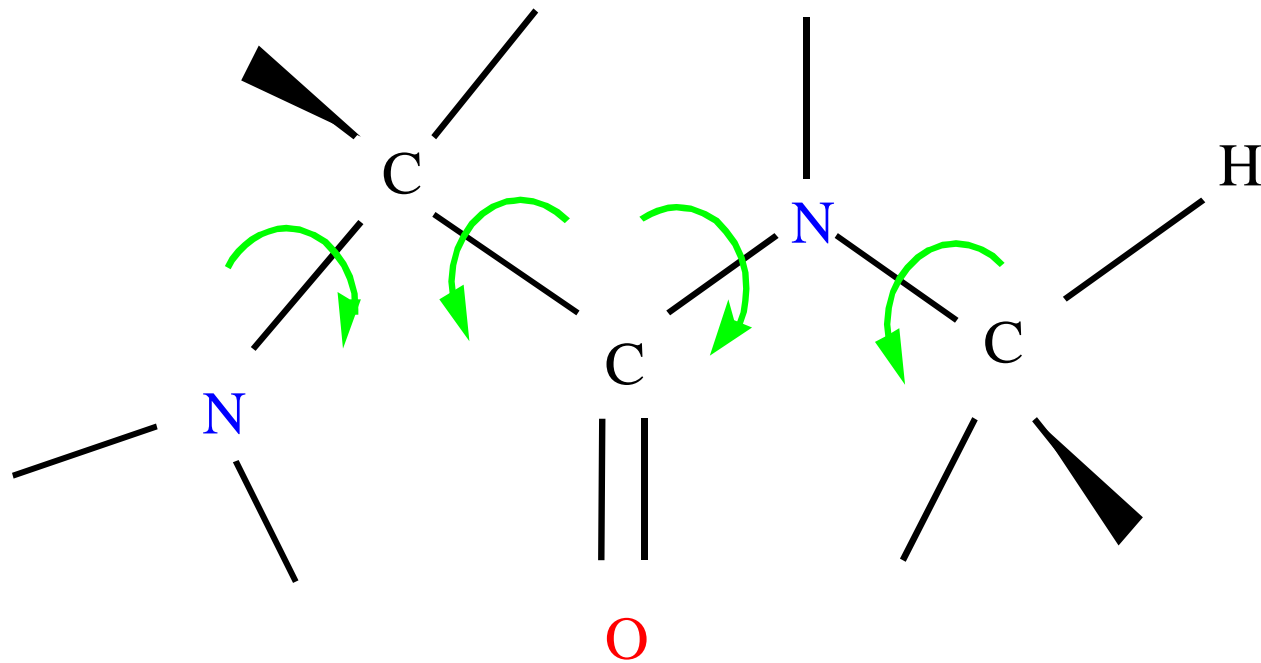
from clusters to hydrated bio-molecules to proteins

Treats effects such as anharmonicity, mode-mode coupling, delocalised nuclear motion, zero-point energy accurately

Provides new concepts such as the H-densities

But is only zero temperature!

Biomolecules



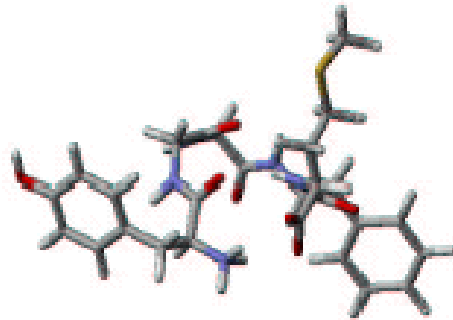
Torsional angles

Quantum nuclear motion for finite temperatures

Torsional **path integral** Monte Carlo:

Tommy Miller

Applied to energy and free energy of peptides

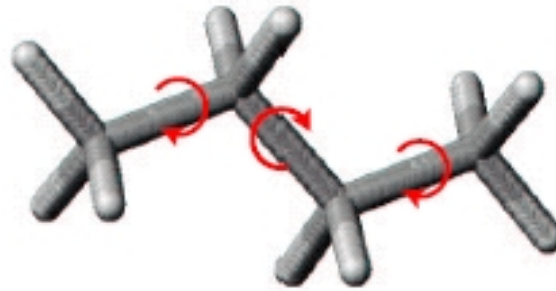


(eg. T M Miller & D C Clary, J Chem Phys, 119 68 (2003))

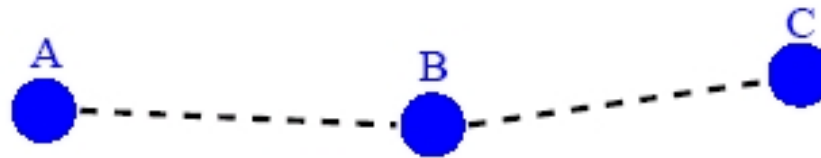
Torsional path integrals

Tommy
Miller

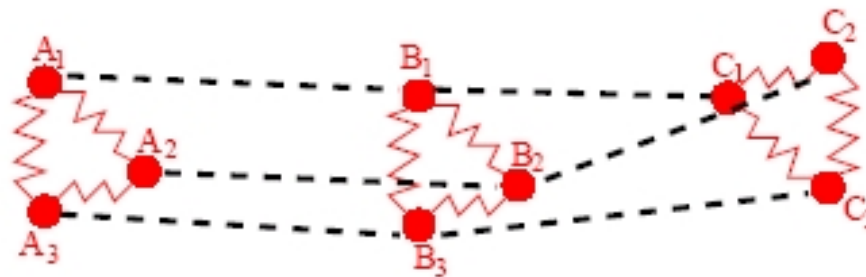
Torsional
Modes



Classical
TPIMC



Quantum
TPIMC



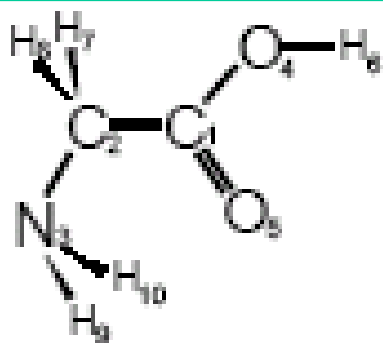
$$Q(T) \approx \left\langle \exp\left(-\frac{\bar{V} + V^{beads}}{kT}\right) \right\rangle$$

Larger the number of beads needed, the more quantum the system

Torsional path integral (TPI)

First tested on simple hydrocarbons and enkephalin

Then applied to predict **free energy & conformation populations**:



Glycine

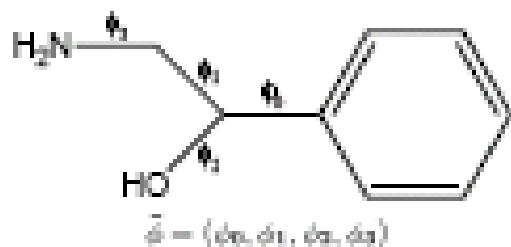
MP2/large basis ab initio potential

IR-matrix spectroscopy:

Ivanov, Sheina, Blagoi, *Spectrochem. Acc. A* 1999, 55, 219.

2-amino-1-phenylethanol (APE).

Using MM3 potential
calibrated against ab initio



UV, and IR-UV ion-dip spectroscopy

Graham, Kroemer, Mons, Robertson, Snoek, Simons,
J. Phys. Chem. A 1999, 103, 9706.

Potentials

Molecular mechanics

Ab initio and DFT (Chris Kriton-Skylaris)

Treating "spectator bonds" (higher frequency bends and stretches)

1. Ignore

2. Optimise geometry on a grid of fixed torsional angles and add vib zpe to potential

3. Calculate full Partition Function (PF) from electronic structure harmonic freqs and multiply by (Tors PI/Tors harmonic) PF

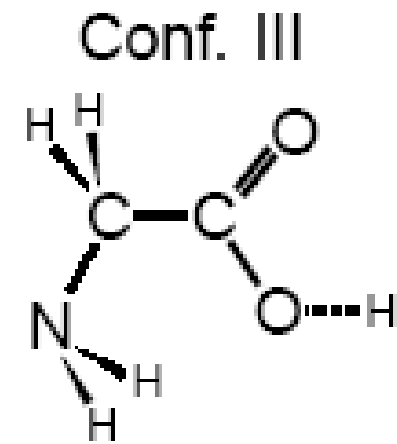
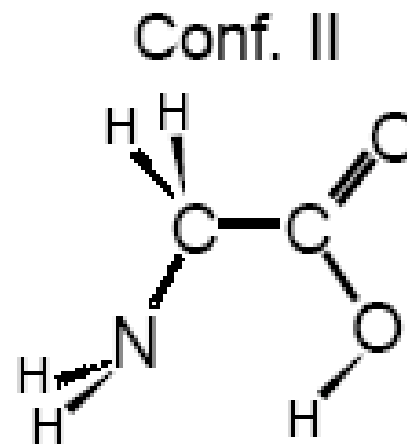
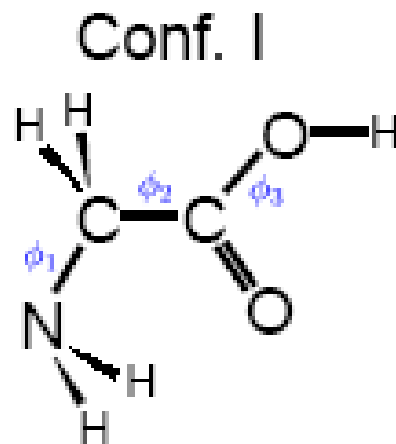
Testing the Method: Conformers of Glycine

How much of each conformer is present?

Challenging for both theory and experiment!

Nine stable structures within **10 kJ/mol** of minimum.

Three conformers observed experimentally:



$$E_{min} = +0.0 \text{ kJ/mol}$$

$$\vec{\phi} = (180^\circ, 180^\circ, 0^\circ)$$

$$+2.2 \text{ kJ/mol}$$

$$(-3^\circ, 12^\circ, 161^\circ)$$

$$+6.7 \text{ kJ/mol}$$

$$(178^\circ, 30^\circ, 2^\circ)$$

Both anharmonic and quantum effects are important.

Ab initio (MP2/6-311++G**) potential

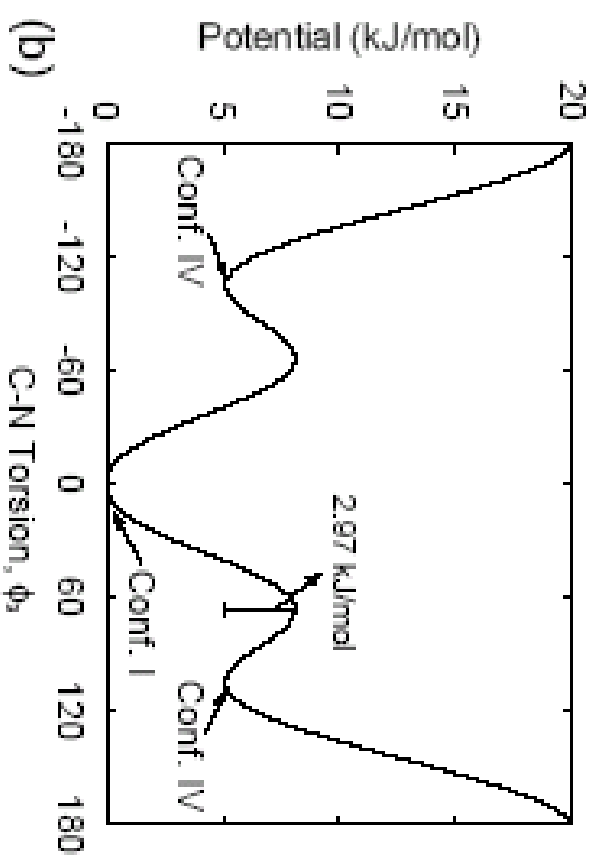
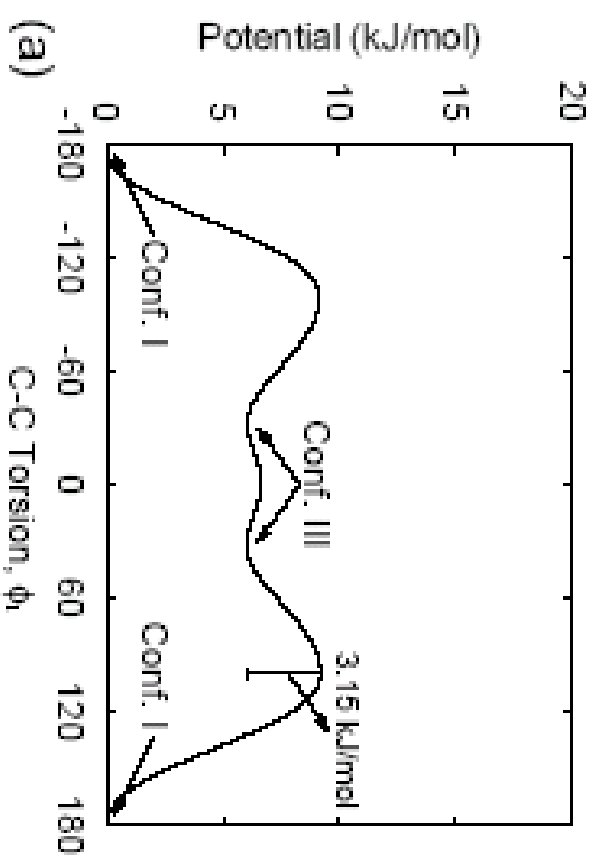
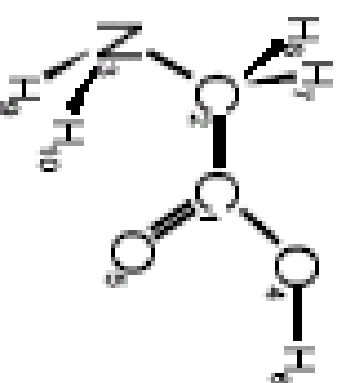
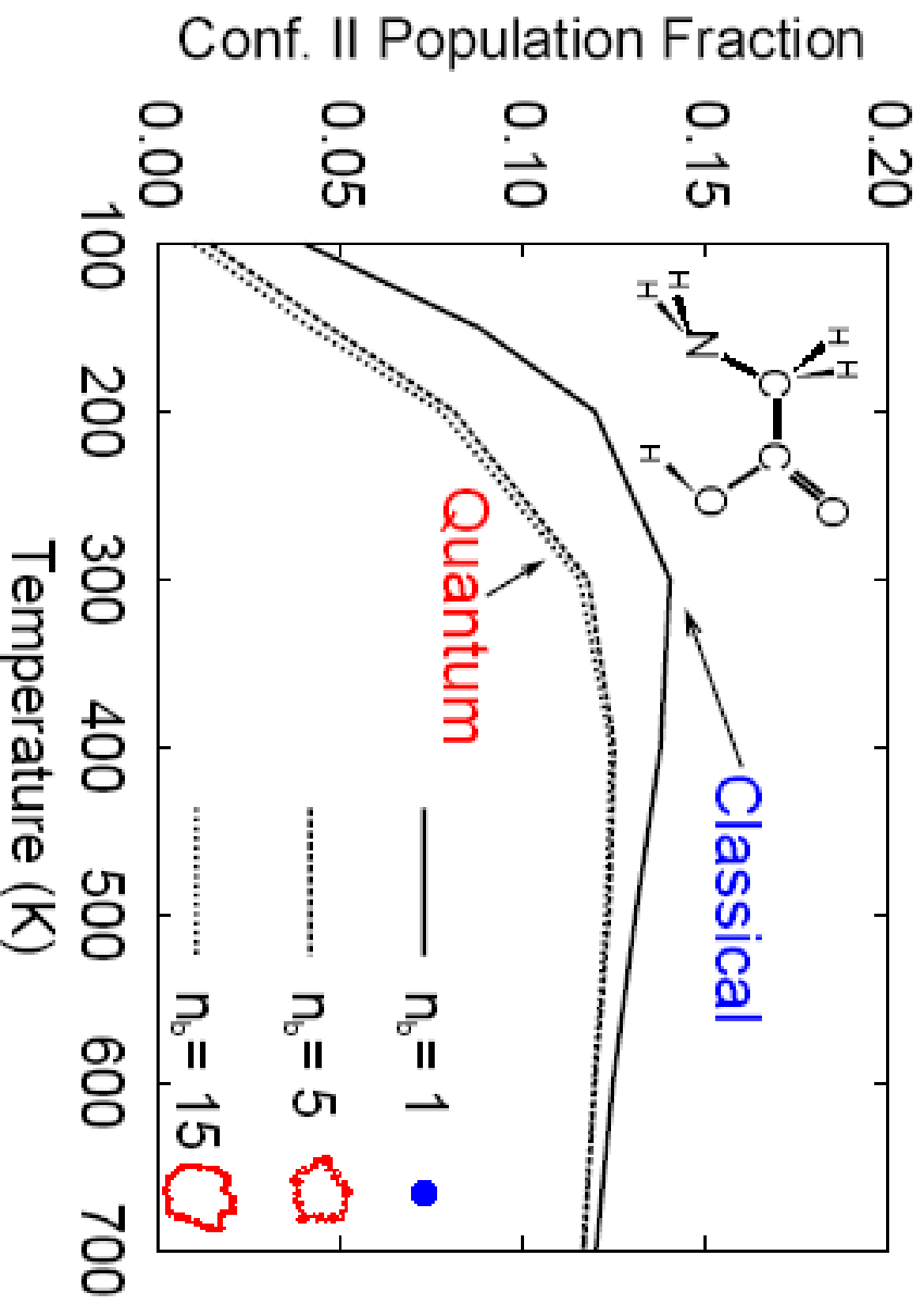


Figure Cross sections of the glycine potential energy surface minimized with respect to (a) the C-C torsional angle ϕ_1 and (b) the C-N torsional angle ϕ_3 .



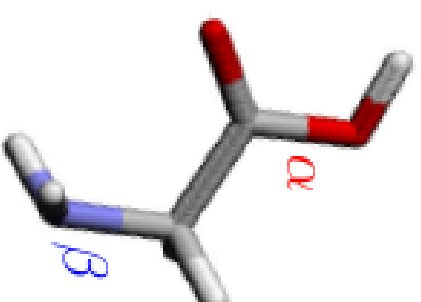
Glycine Conformer II: Quantum Effects



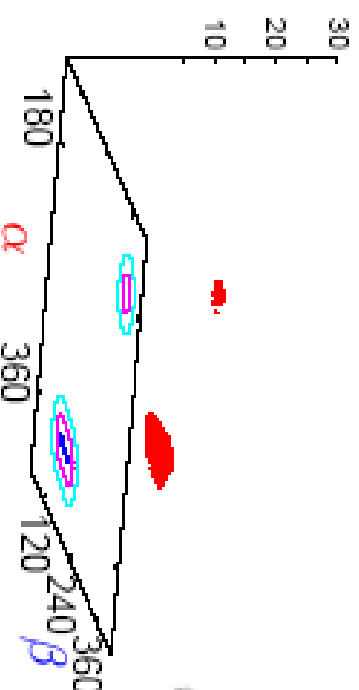
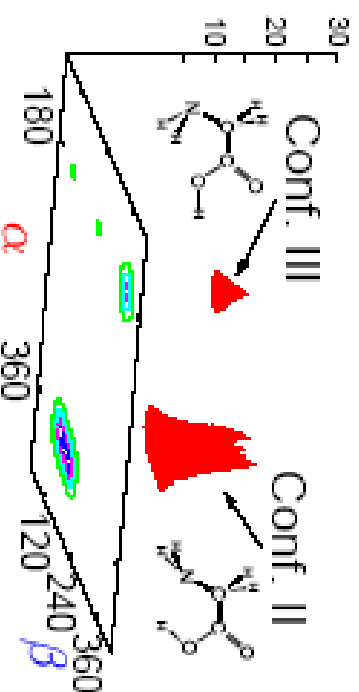
Glycine Torsional Distributions

Classical

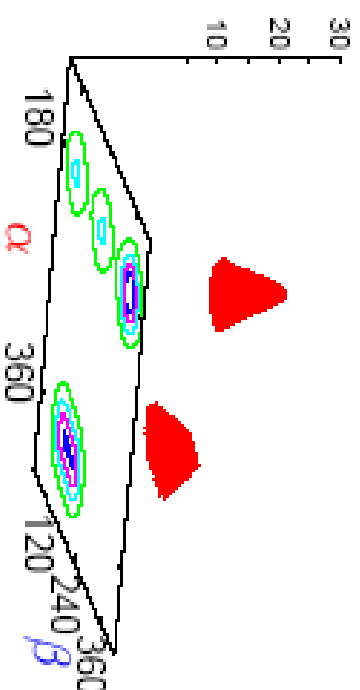
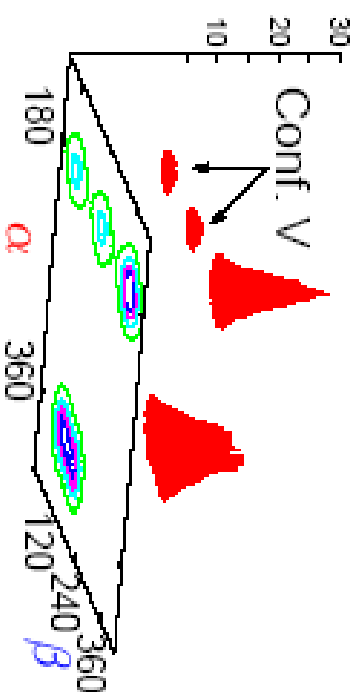
Quantum



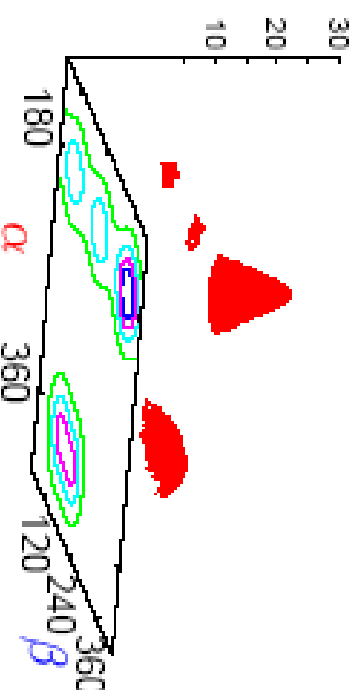
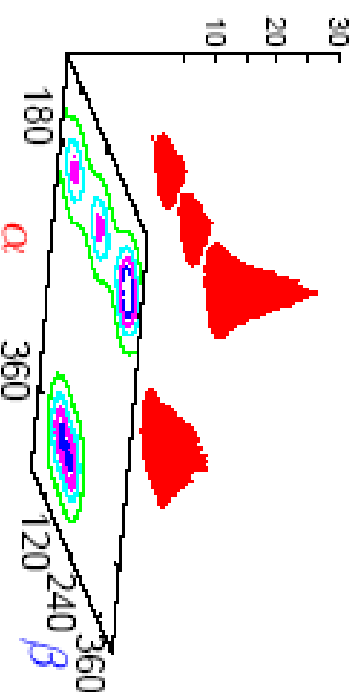
150 K



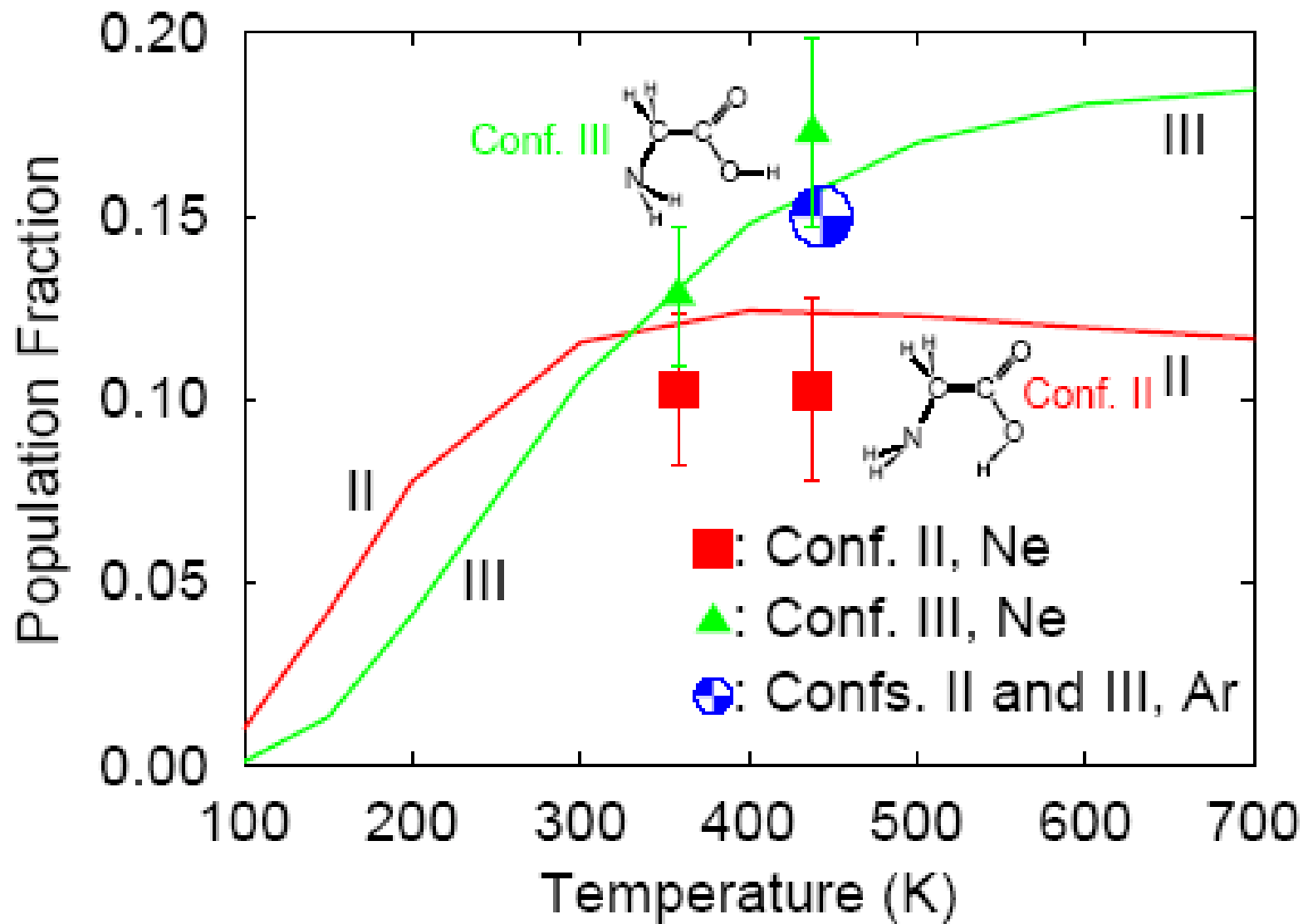
300 K



500 K



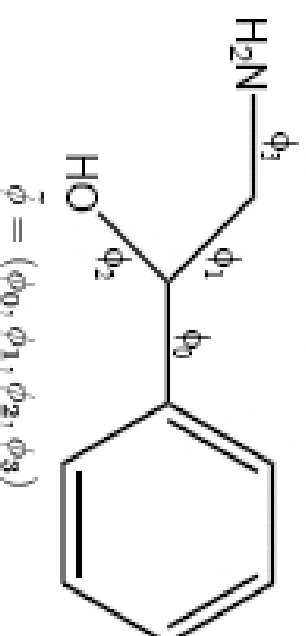
Glycine Conformers: Theory vs. Experiment



(Experiments matrix IR spectroscopy: Stepanian et al 1998; Ivanov et al 1999)

Conformations of APE

2-amino-1-phenylethanol (APE).



Most stable conformers: AG1 and GG1.

Experiment predicts a population ratio of **2.7:1**, but MP2 with ZPE predicts a ratio of **1:1**.



AG1 (0.0 kJ/mol)

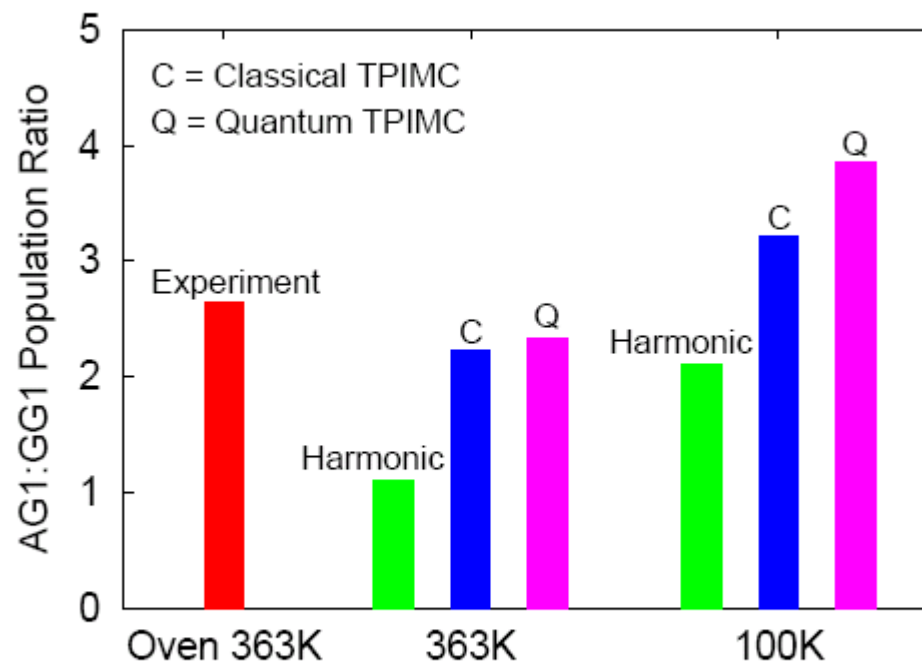
$\vec{\phi} = (100^\circ, 181^\circ, 161^\circ, 292^\circ)$



GG1 (+0.6 kJ/mol)

$\vec{\phi} = (108^\circ, 297^\circ, 89^\circ, 181^\circ)$

APE Population Ratios



MM3 PES used for theoretical results.
HO results are for torsional modes.

Exp: Graham, Kroemer, Mons, Robertson, Snoek, Simons,
J. Phys. Chem. A **1999**, *103*, 9706. UV, and IR-UV ion-dip spectroscopy

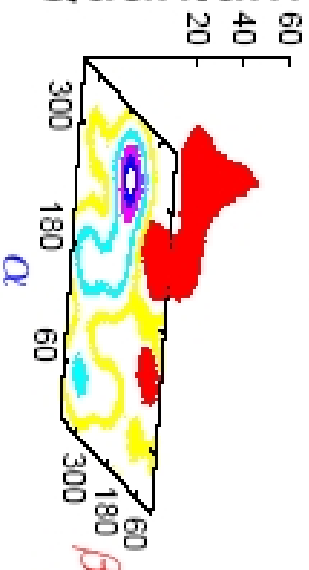
Difference between harmonic and quantum due to Entropy

Torsional Distributions:

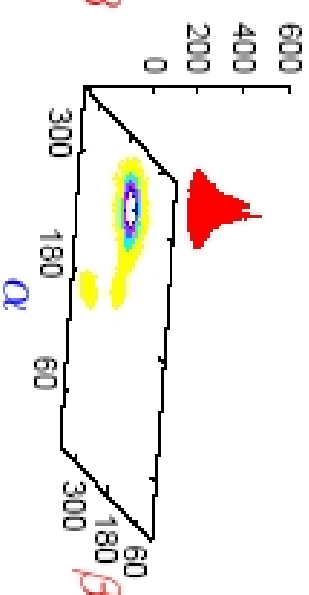


363K

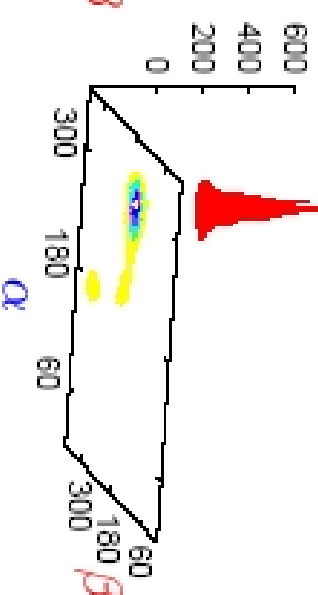
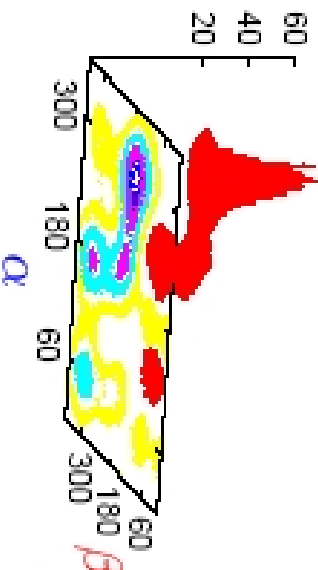
Quantum



100K



Classical



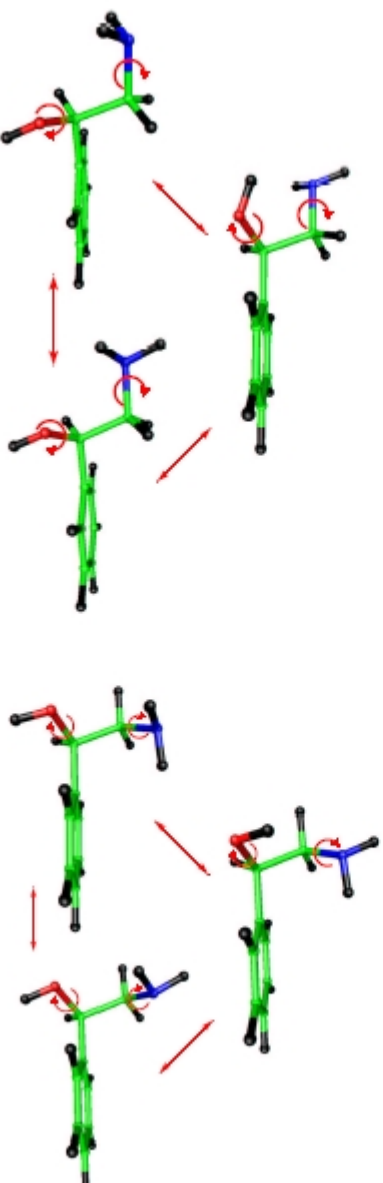
The Four Torsions of APE

The C-C torsion converts between **tail-down** and **tail-up** conformer types.



The -OH and -NH₂ torsions convert between various stable conformers.

Tail-down Conformers



Tail-up Conformers

The C-Phe torsion does not participate in conformer interconversion.



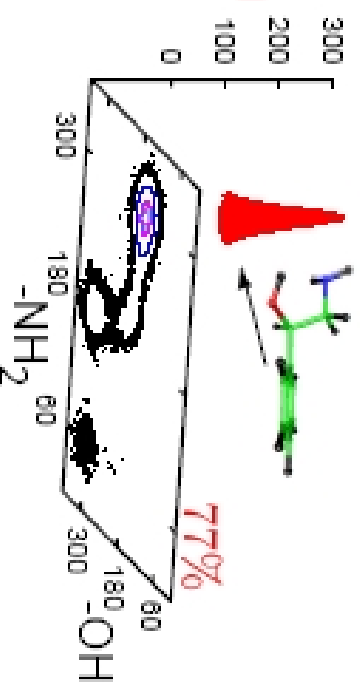
Unhydrated APE at 100 K

Classical

Quantum

Tail-down

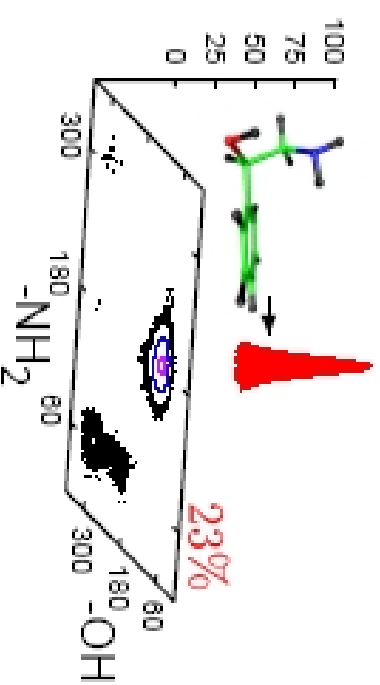
(ρ)



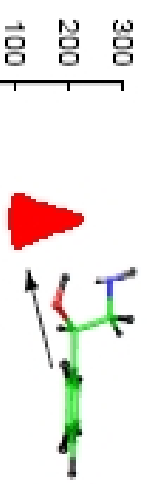
77%

Tail-up

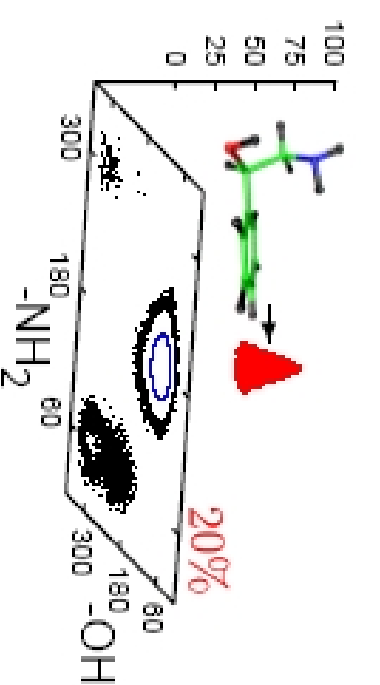
(ρ)



23%



80%

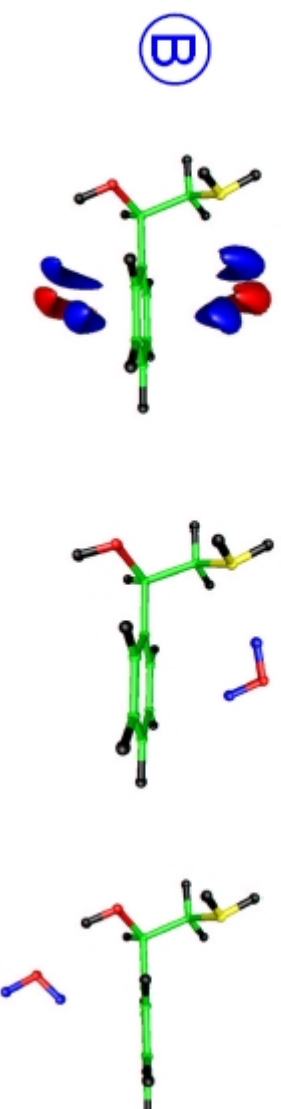
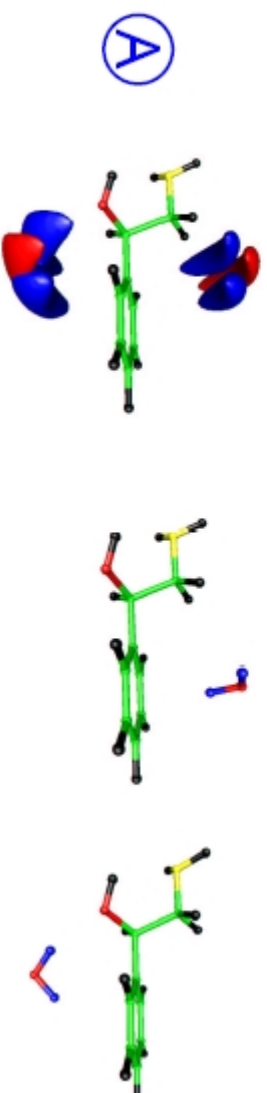
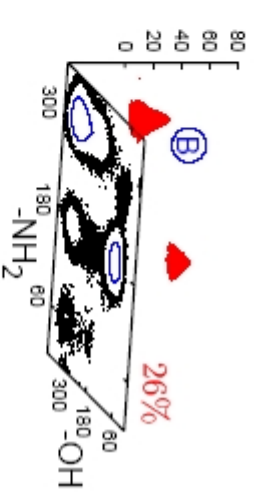
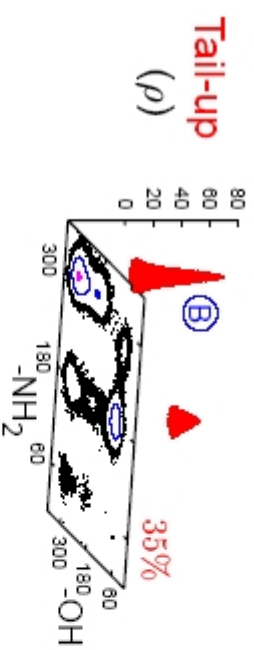
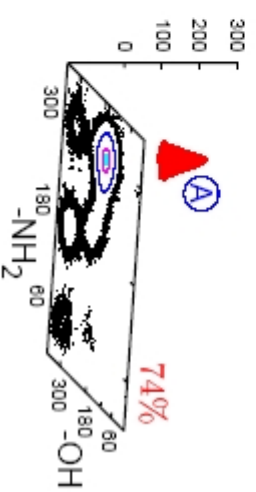
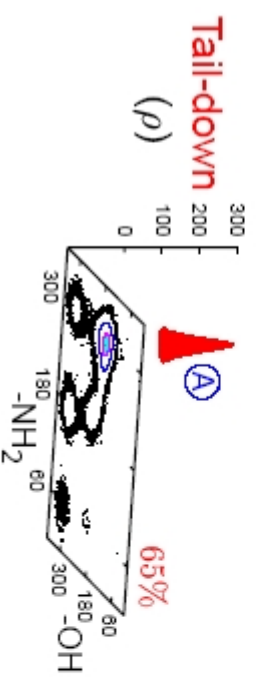


20%

Torsional Distribution of APE + 1 H₂O at 100 K

Classical

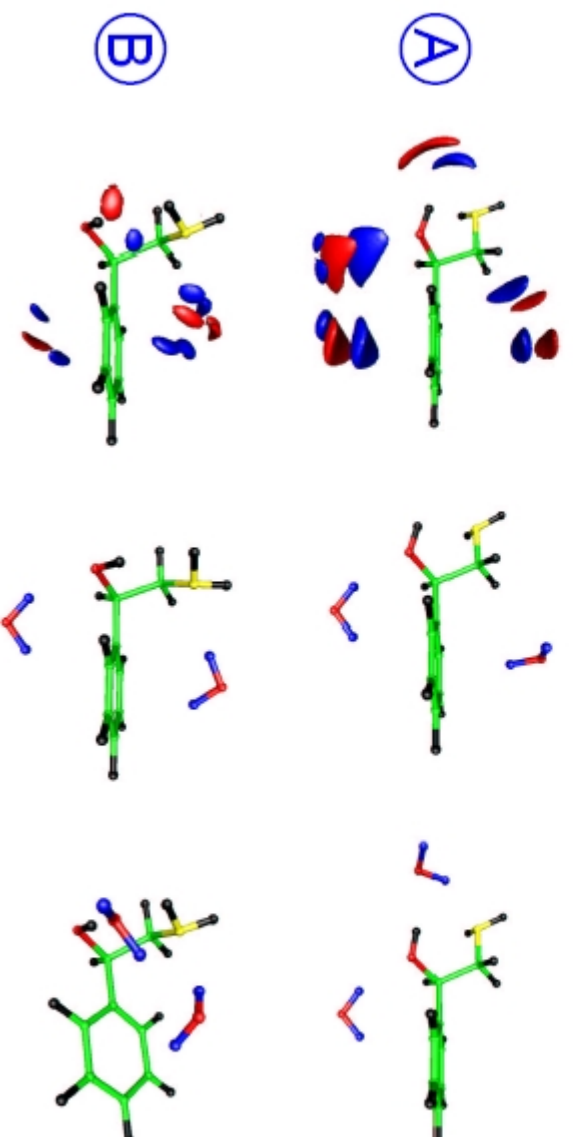
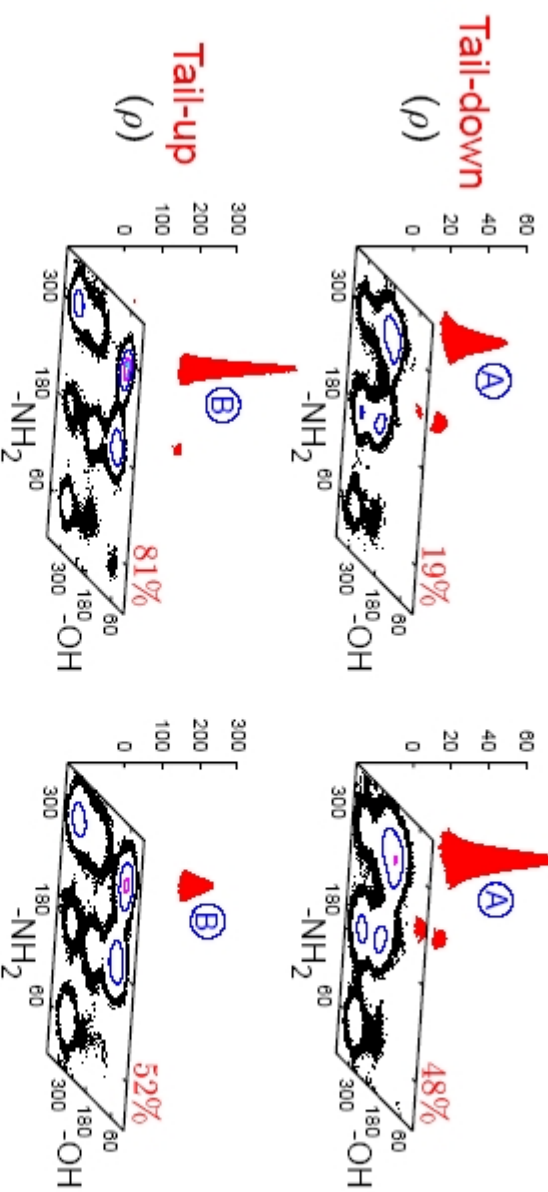
Quantum



Torsional Distribution of APE + 2H₂O at 100 K

Classical

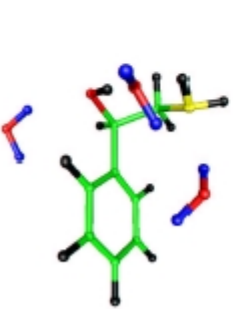
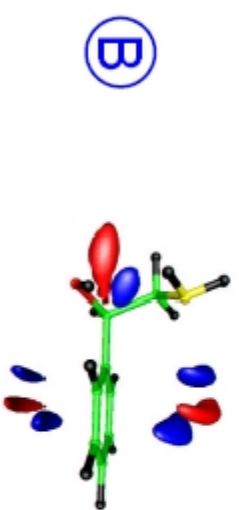
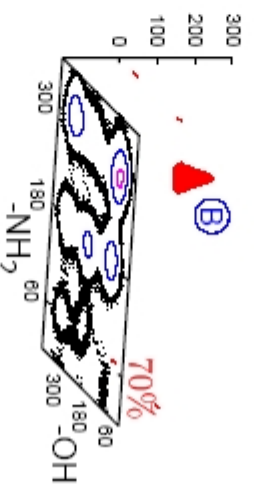
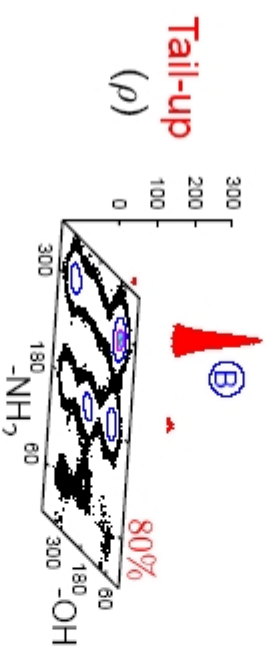
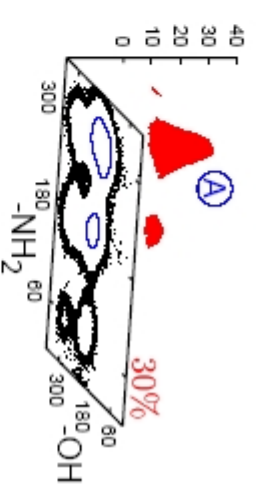
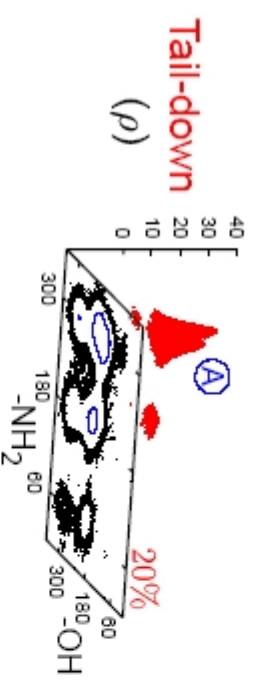
Quantum



Torsional Distribution of APE + 3H₂O at 100 K

Classical

Quantum



Torsional path integral method

Promise for quantum biomolecular simulations
for a range of temperatures

Acknowledgement: Tommy Miller