Microsolvation effects on protonated tryptophan

Matteo Guglielmi

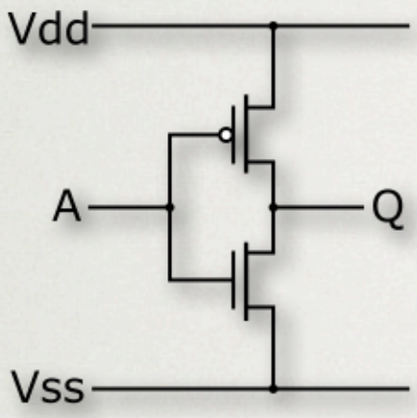
CSRI 2008

Outline

- Who am I?
- Why tryptophan
- Experimental data
- Investigation methods
  (calassical & quantum MD)
- Results
- Conclusions and outlook

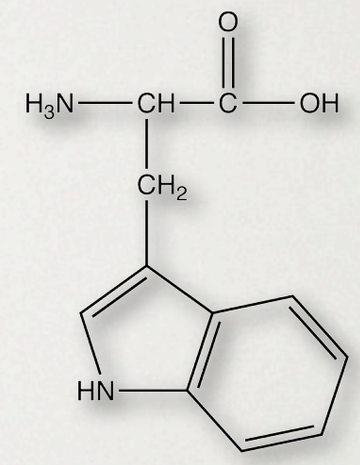
Electronic Engineering

(Bologna - ITALY)



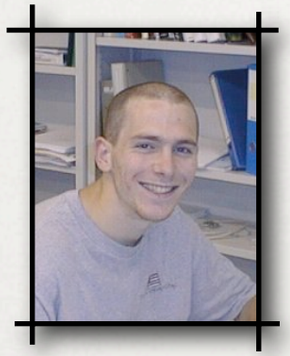
Computational Chemistry

(Lausanne - SWITZERLAND)



Why tryptophan

Thomas R. Rizzo
(Full Professor)



Sebastien R. Mercier
(Ph.D. Student)

Oleg V. Boyarkin
(Senior Scientist)

Anthi Kamariotis
(Ph.D. Student)

A research group in Molecular Physics at EPFL has carried out series of spectroscopic experiments on tryptophan, its fluorescence being widely used to investigate protein structures and dynamics.

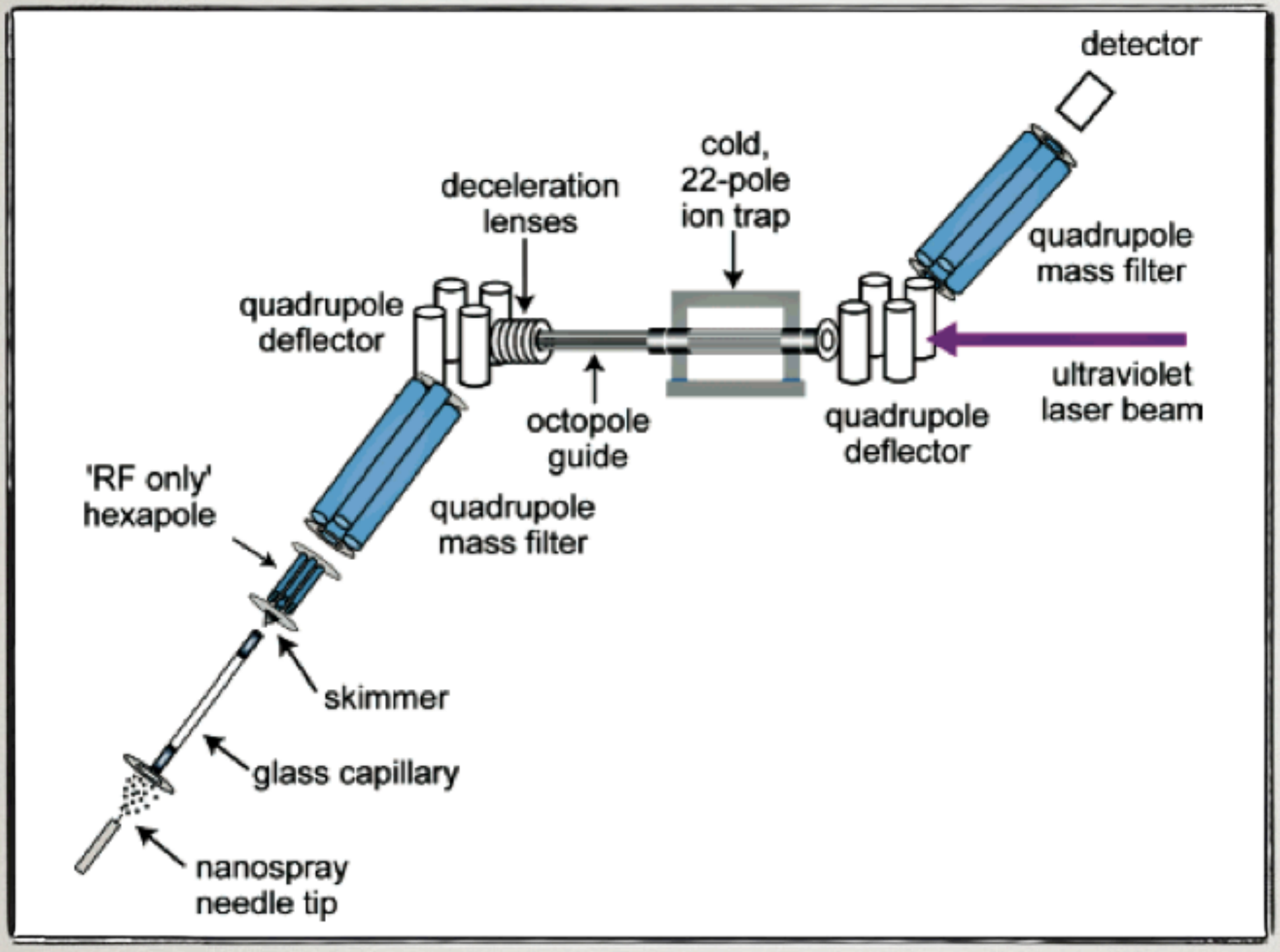
- One of the most important processes that influence the excited state lifetime seems to be charge transfer from the indole ring of tryptophan to a nearby electrophile, a process that is highly sensitive to the local electrostatic environment.

- The local electric field results from the presence of charged groups in the vicinity of the chromophore as well as any water or polar groups that may solvate the charges.

- One way to unravel the effects of local electric field is to investigate ionic forms of tryptophan solvated with a controlled number of water molecule.

EXPERIMENTAL SETUP

"Clusters preparation & photo excitation"



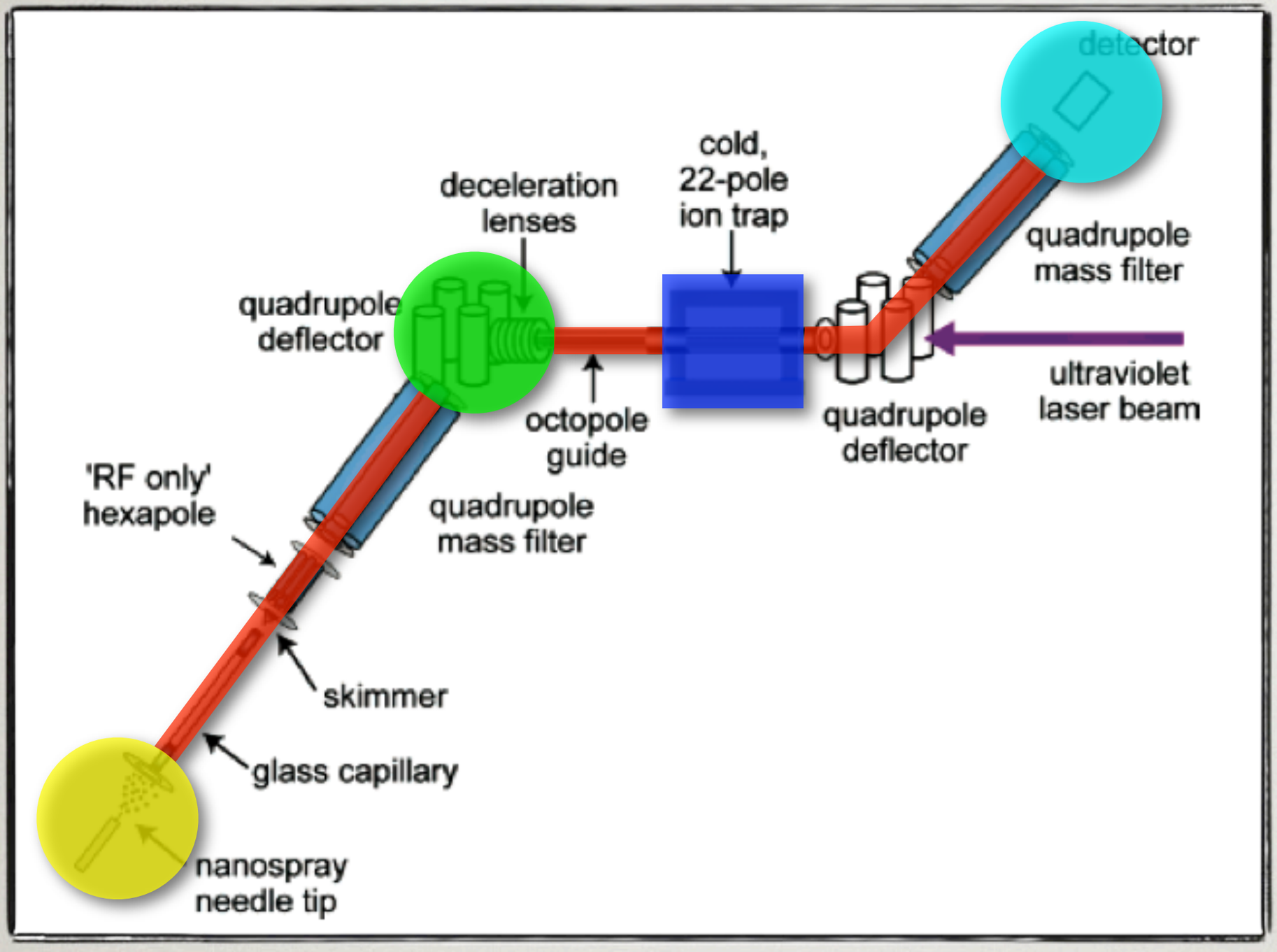
Detector
(cluster frag.s detection)

UV laser pulse
(cluster excitation)

Electrospray
(charged cluster production)

Deflector
(cluster mass selection - “q/m”)

Ion Trap
(clusetr supersonic expansion - T < 10K)



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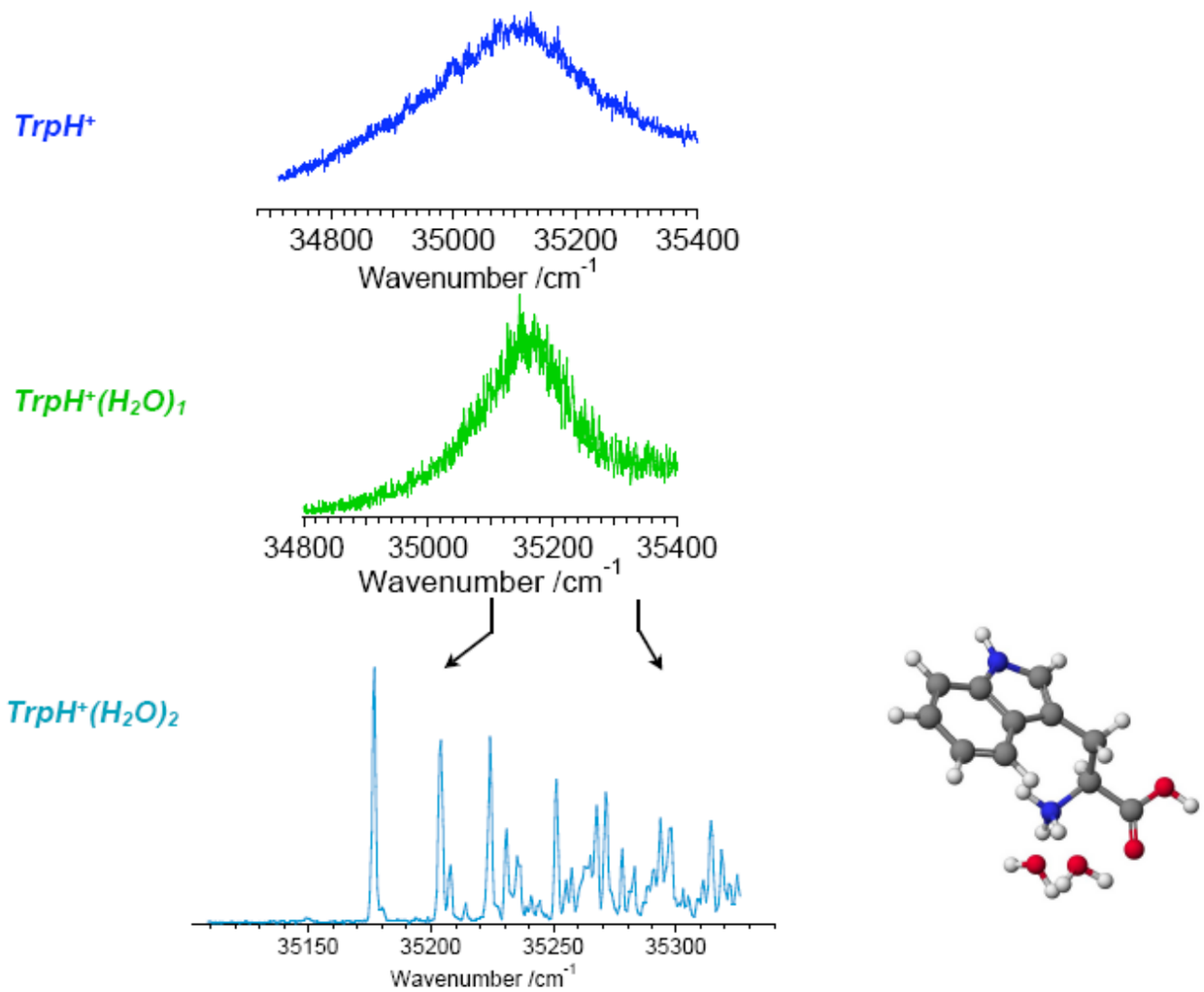
(clusetr supersonic expansion - T < 10K)

What they observed was...

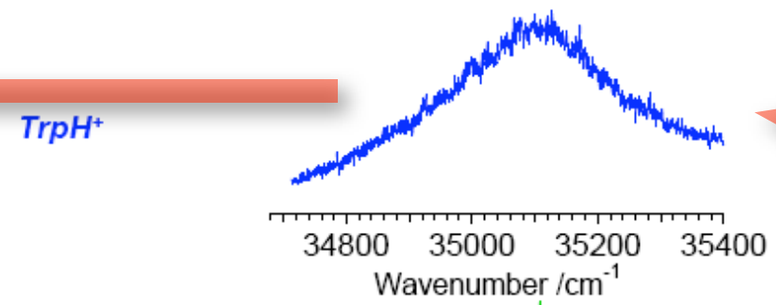
Microsolvation effects on TrpH+ photophysics

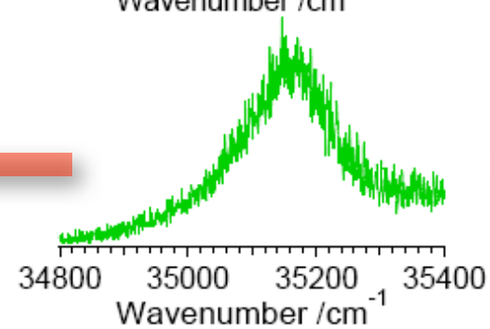


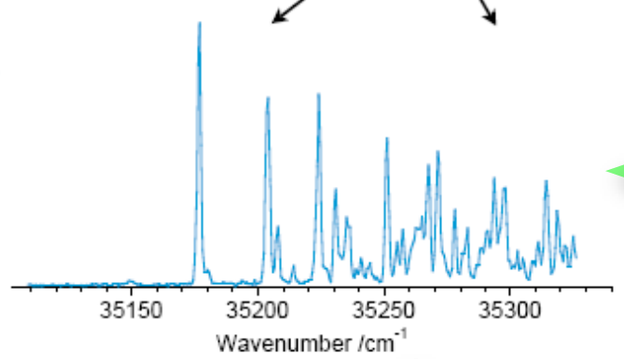
Time-energy uncertainty principle

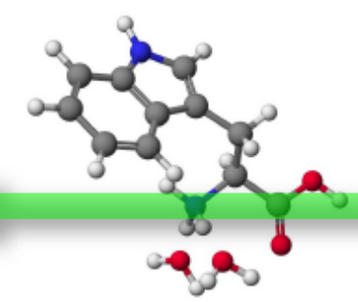
$\Delta E * \Delta t >= h/4\pi$

Microsolvation effects on TrpH+ photophysics









Broad spectra
(high ΔE)

Sharp spectra
(low ΔE)

"**fs**" excited state lifetime
(low Δt)

"**ns**" excited state lifetime
(high Δt)

Time-energy uncertainty principle

$\Delta E * \Delta t >= h/4\pi$

Theoretical methods

(classical dynamics)

Configuration space sampling

Classical MD (300K) / NWChem code

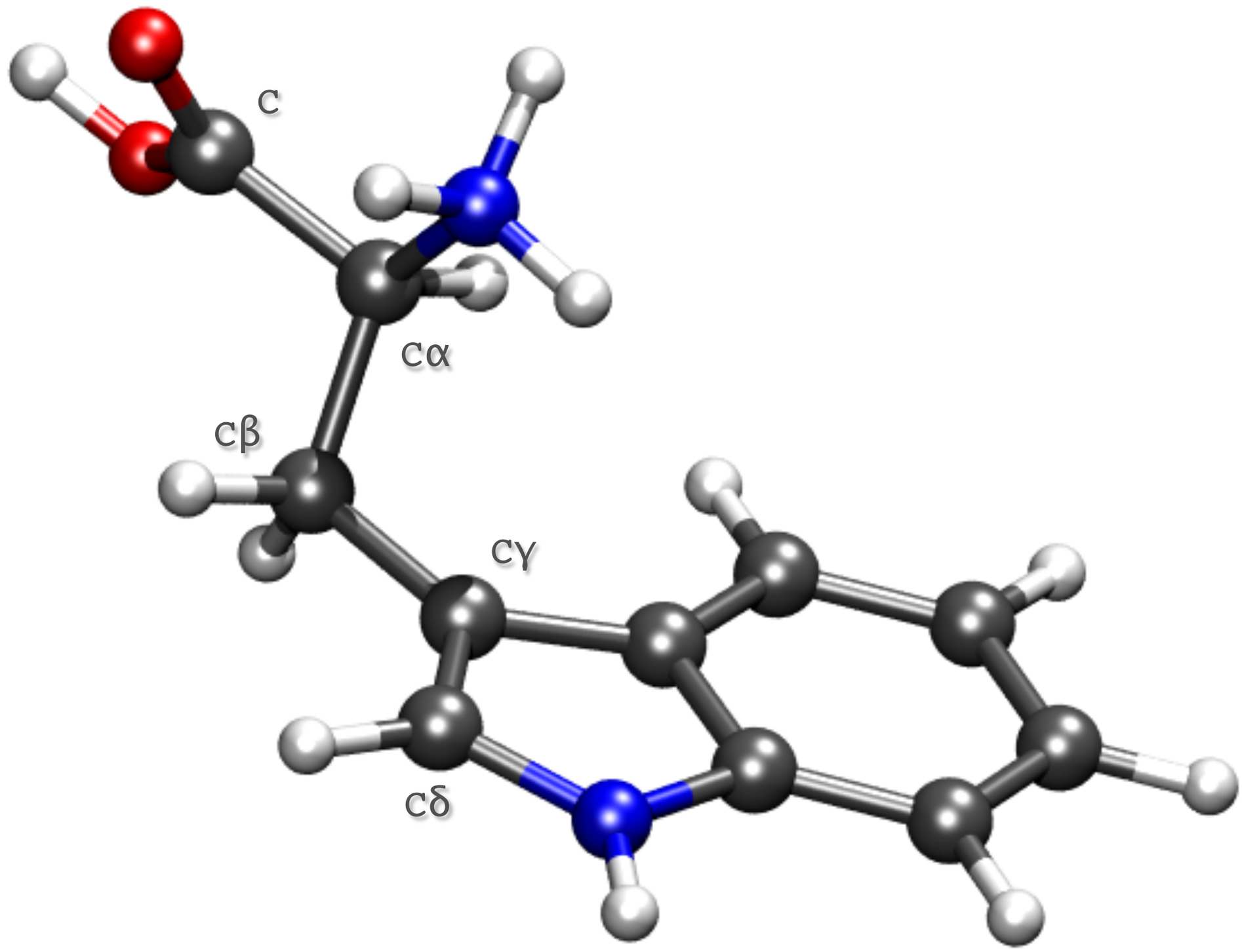
Meta-dynamics (10K) / Gromacs code

Amber force field (parm96)

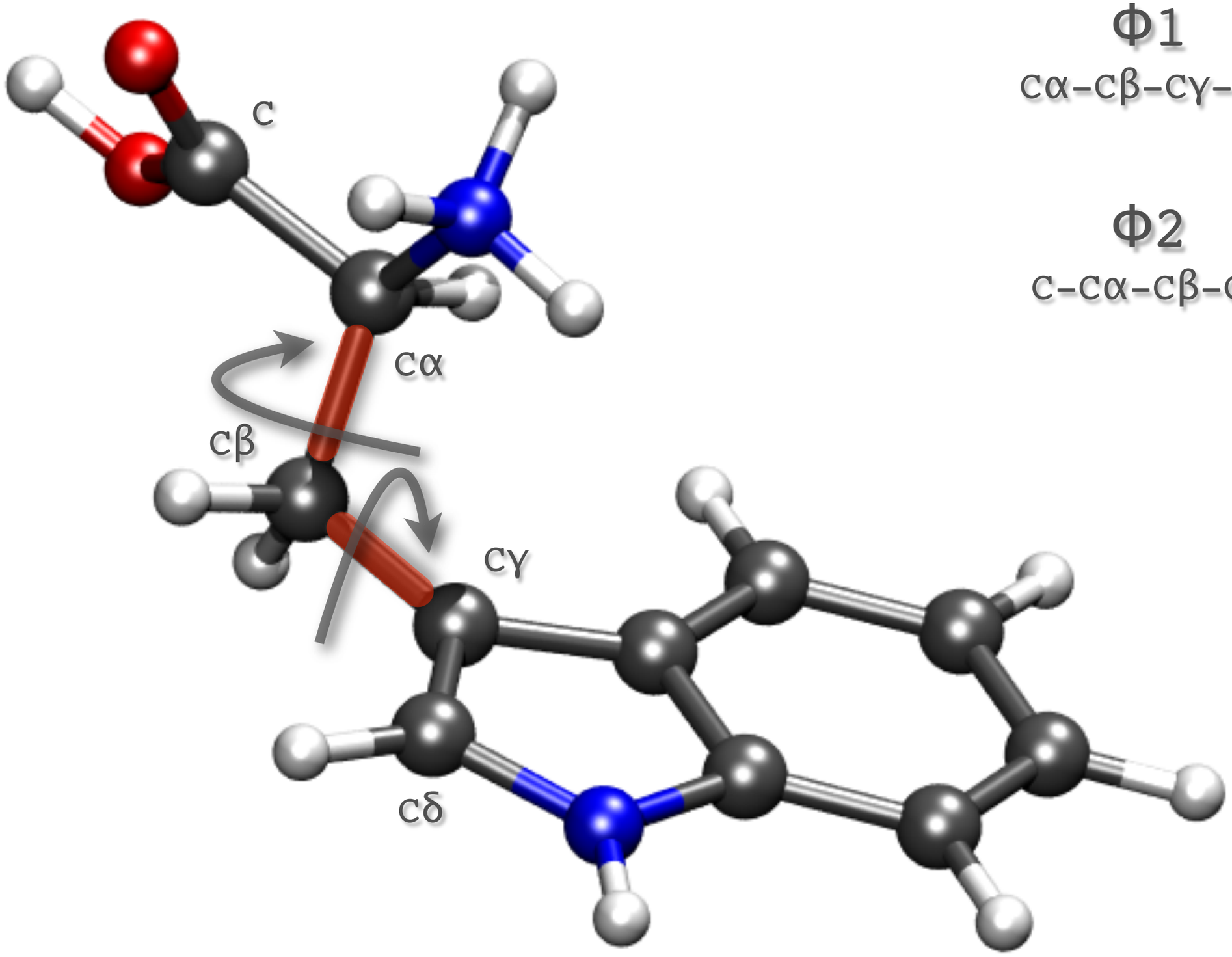
Classical MD

"Searching for the most stable conformers"

Relevant degrees of freedom

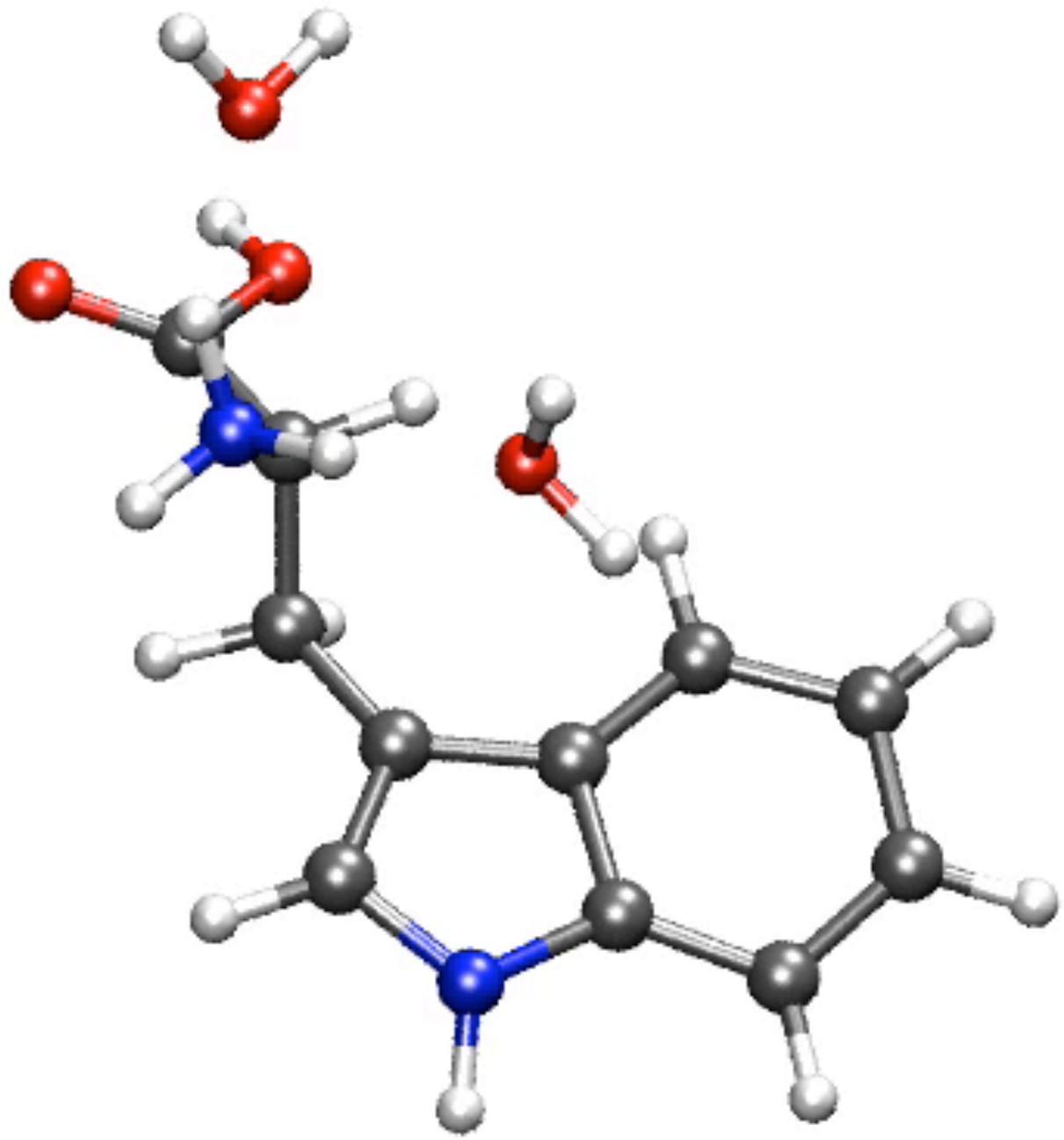


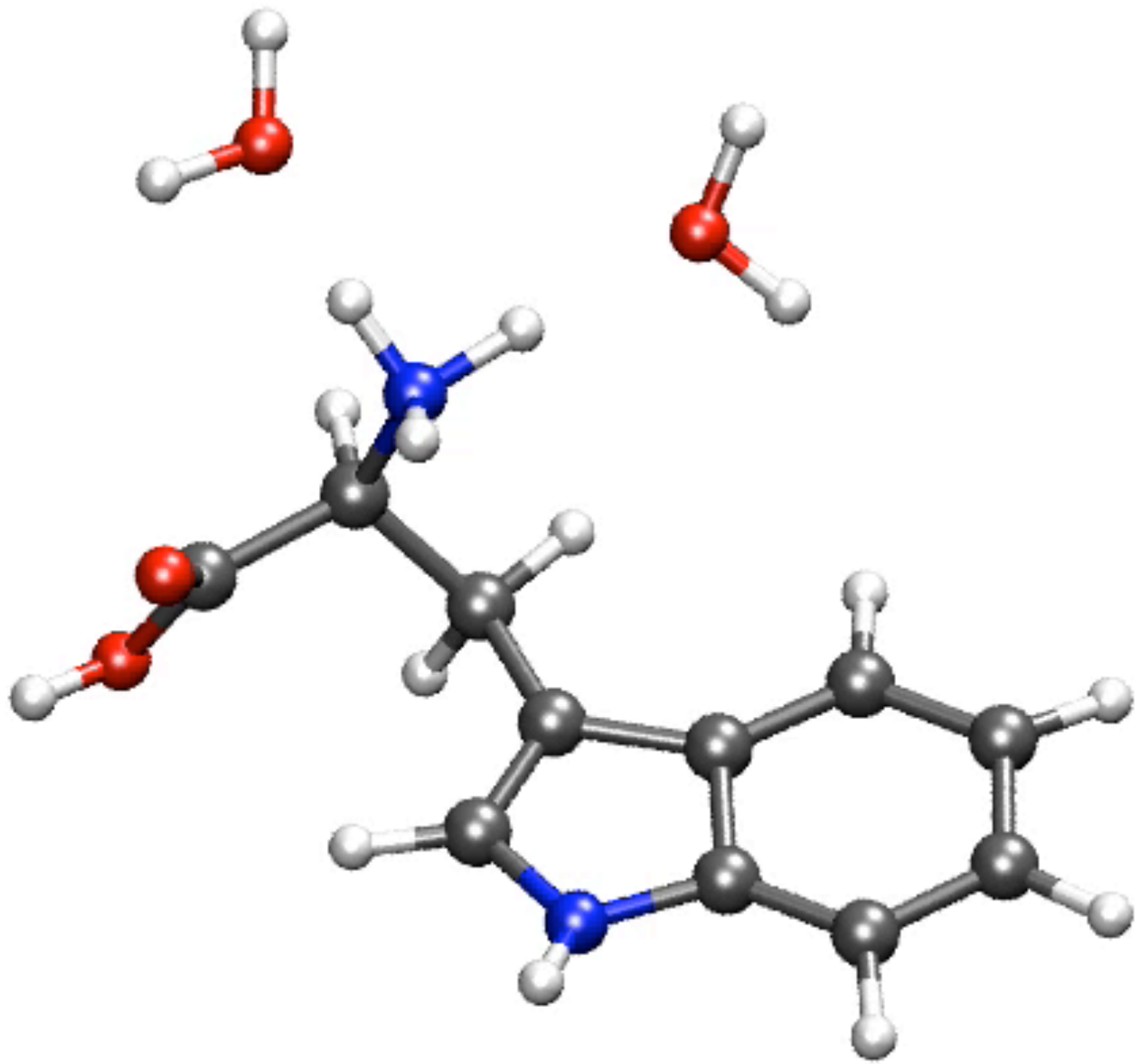
Relevant degrees of freedom



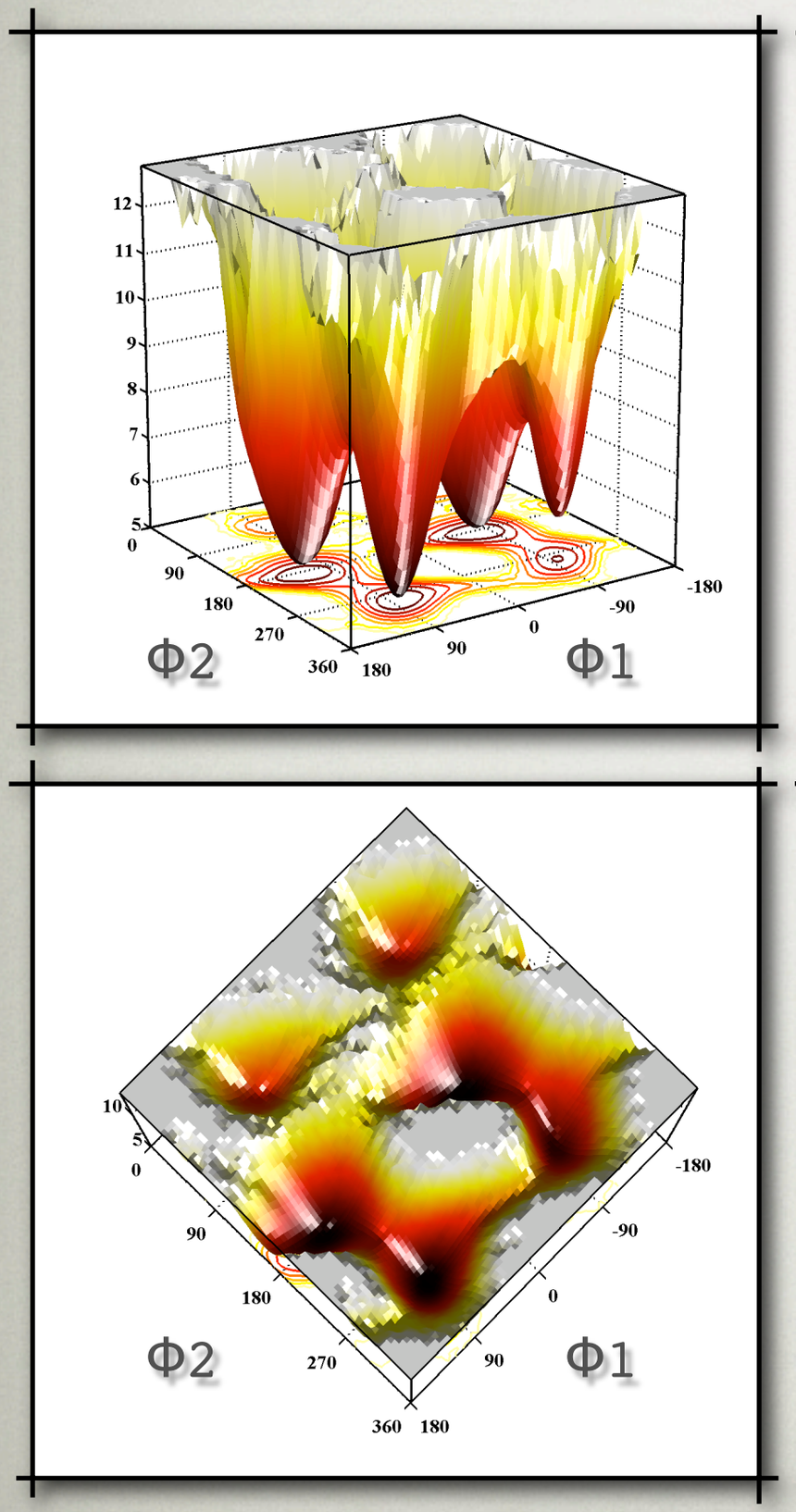
Φ1
Cα–Cβ–Cγ–Cδ

Φ2
C–Cα–Cβ–Cγ

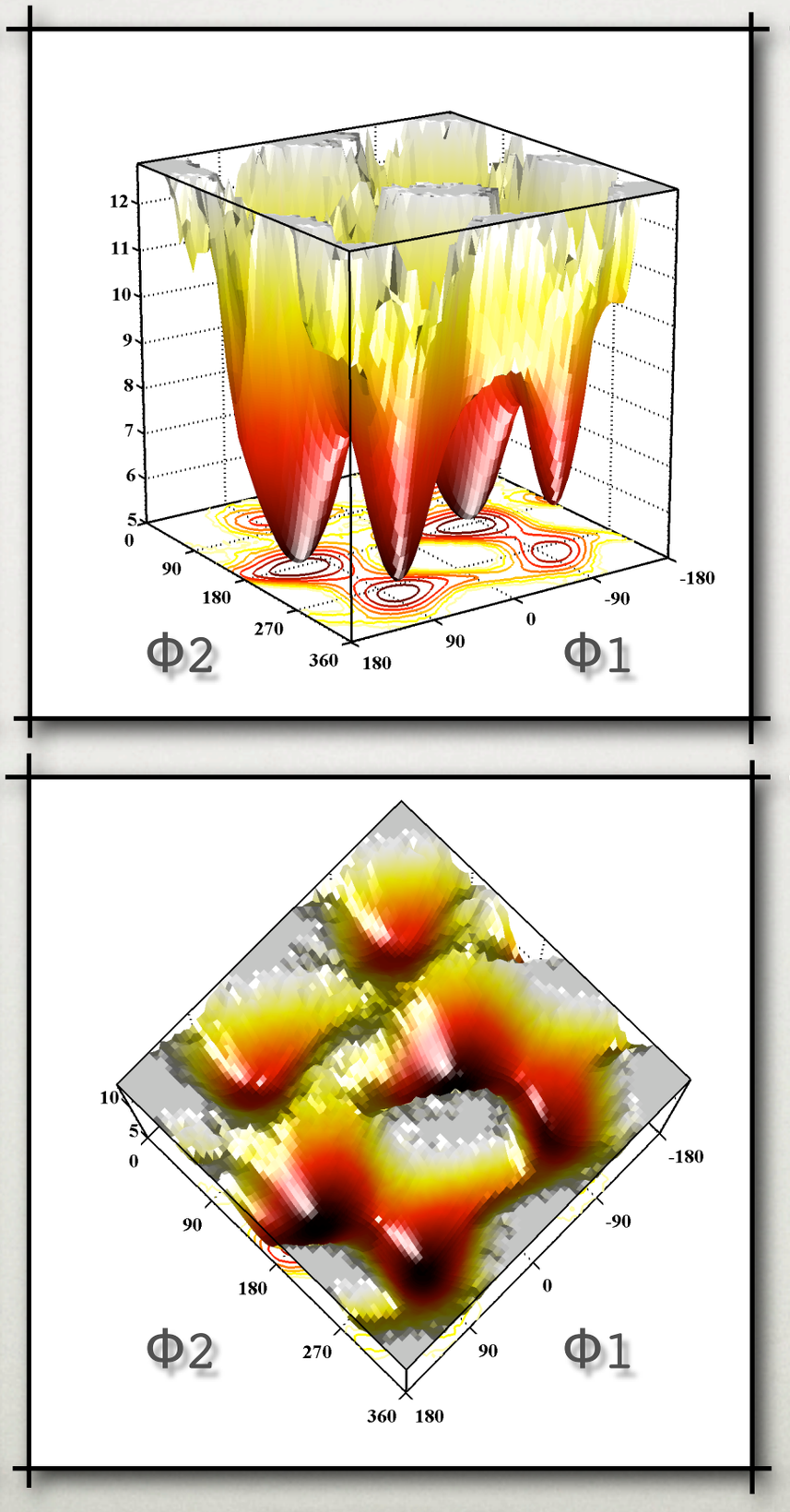




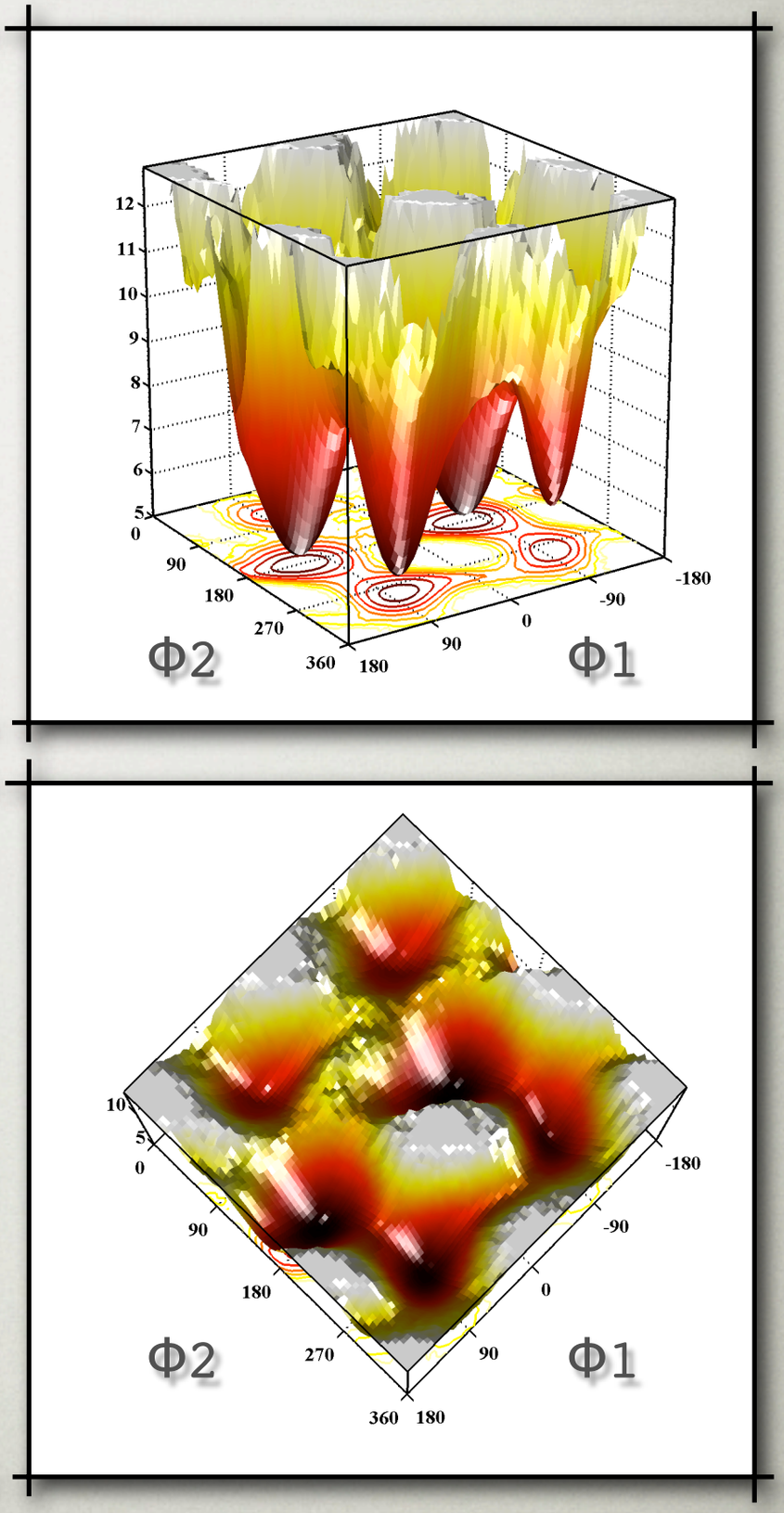
Free-energy profiles (T=300K) along the relevant degrees of freedom Φ1 and Φ2



W^+

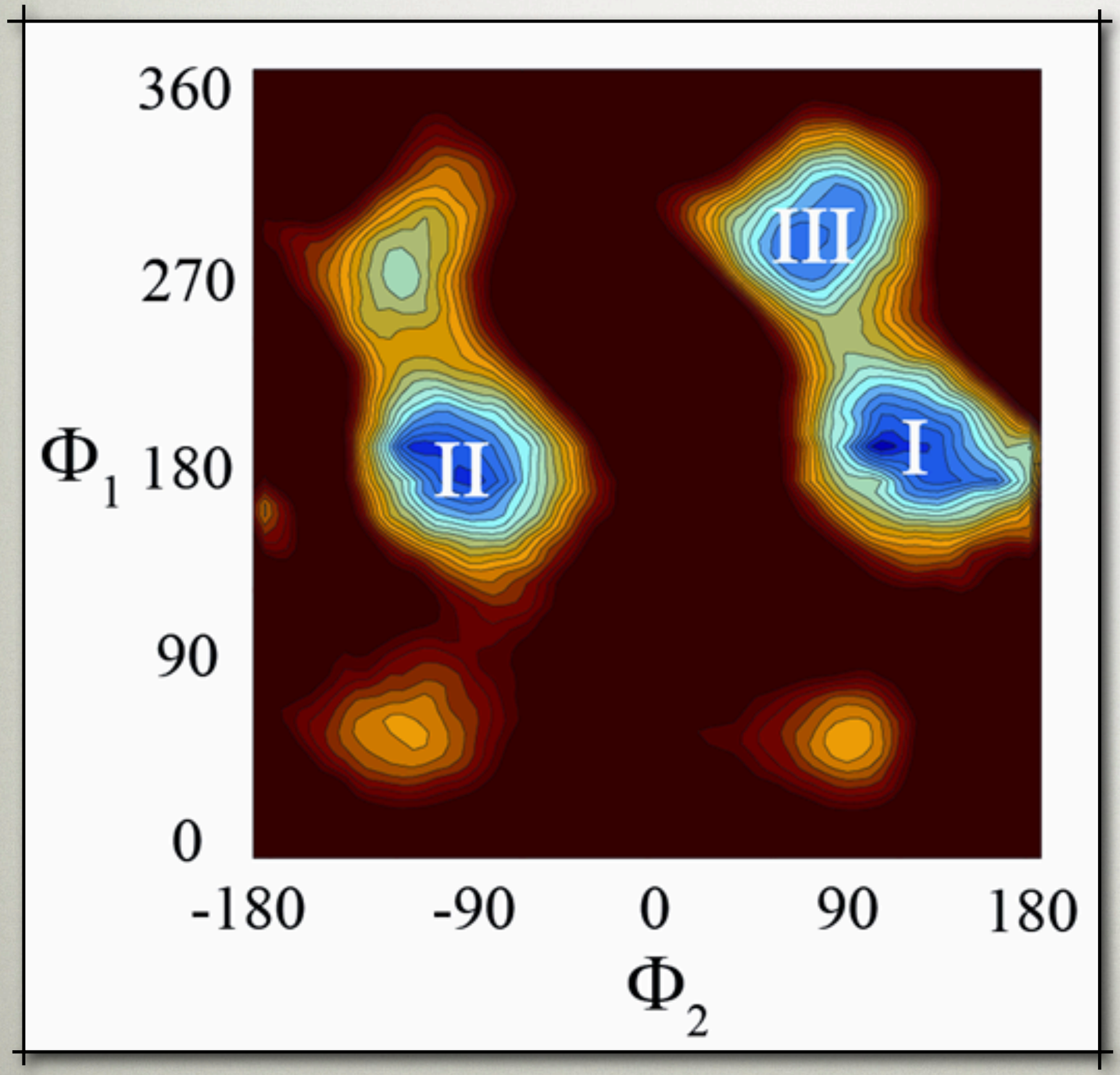


$W^+(1H_2O)$

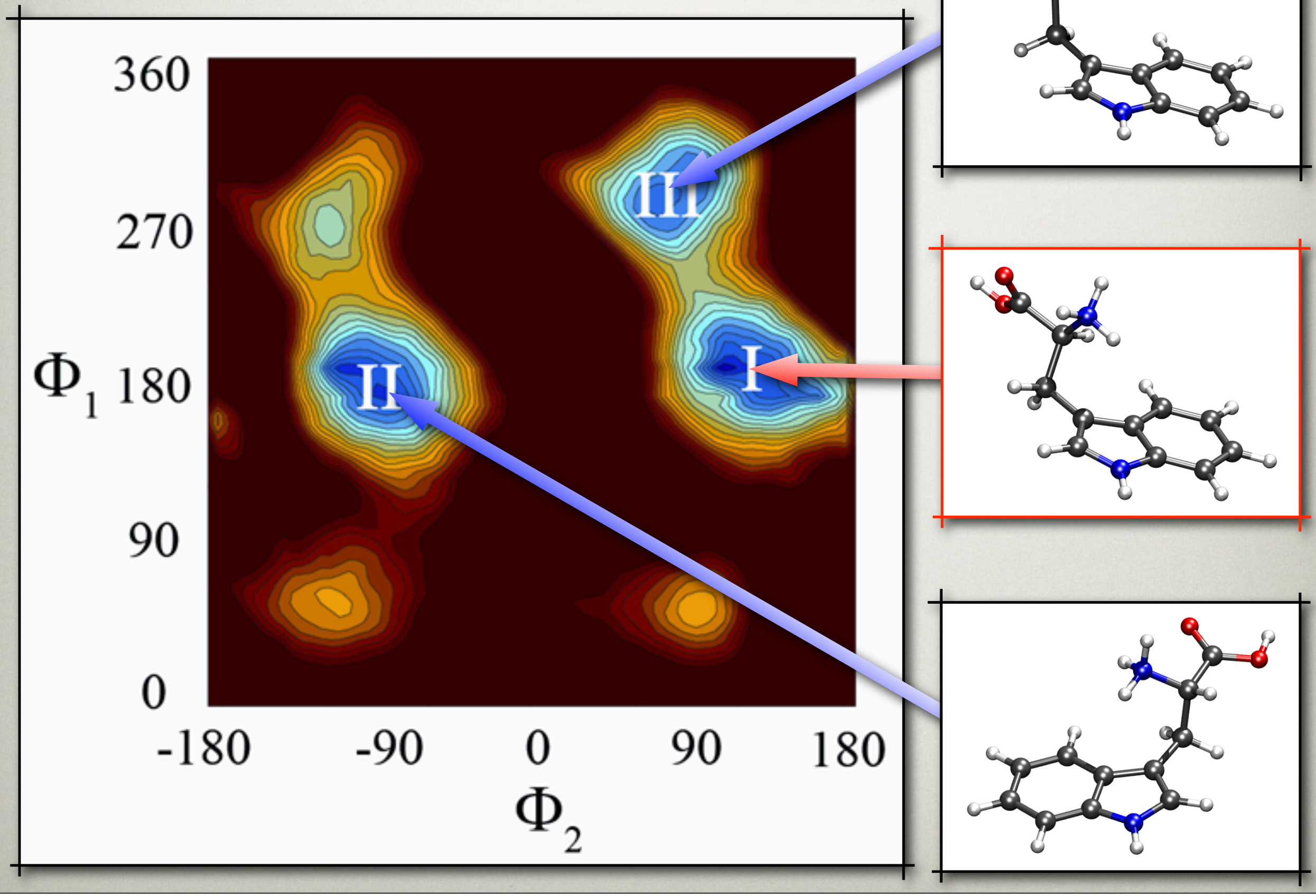


$W^+(2H_2O)$

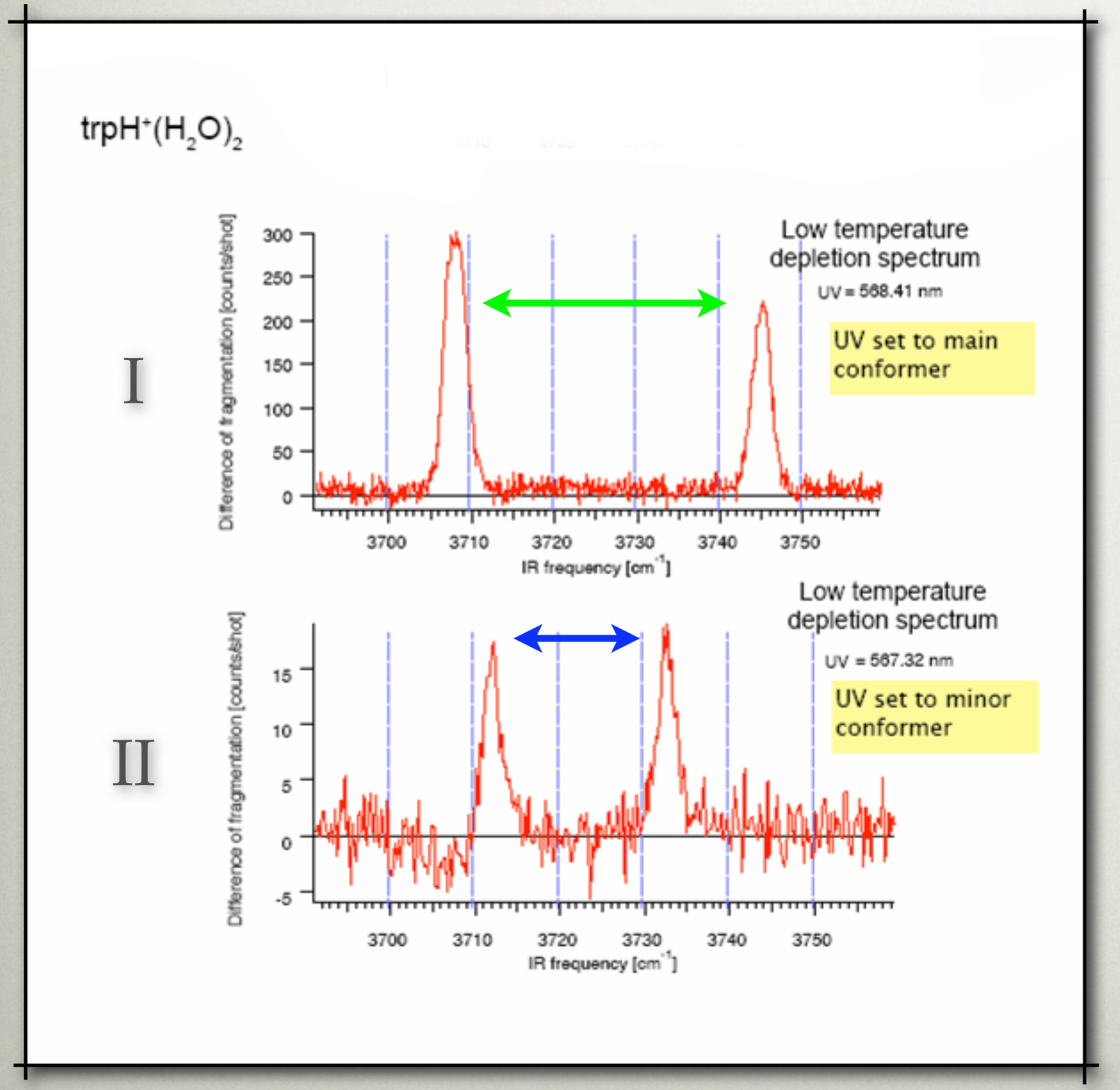
Free-energy profile of W^+ at T=10K

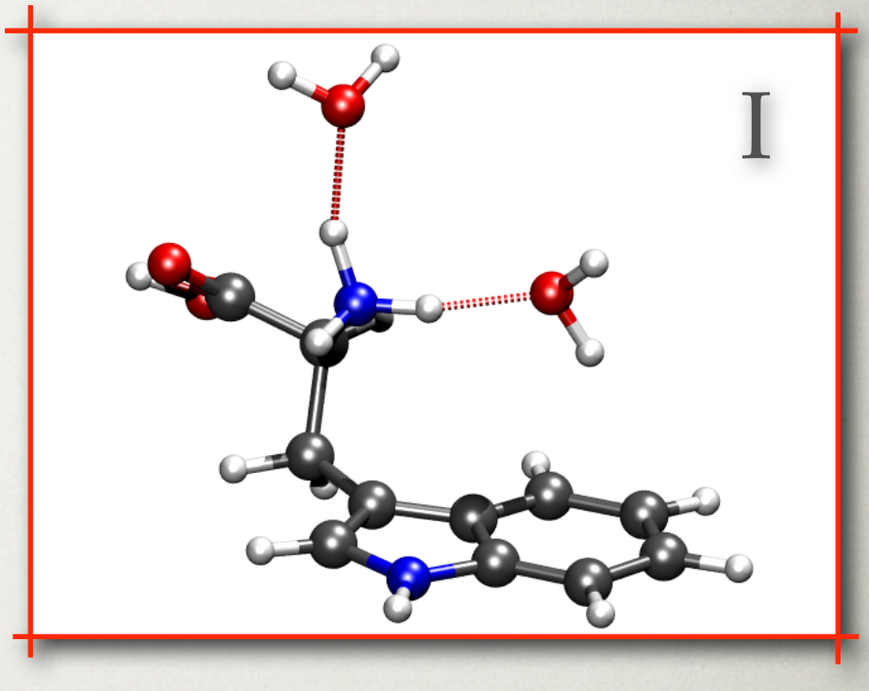


Free-energy profile of W^+ at T=10K



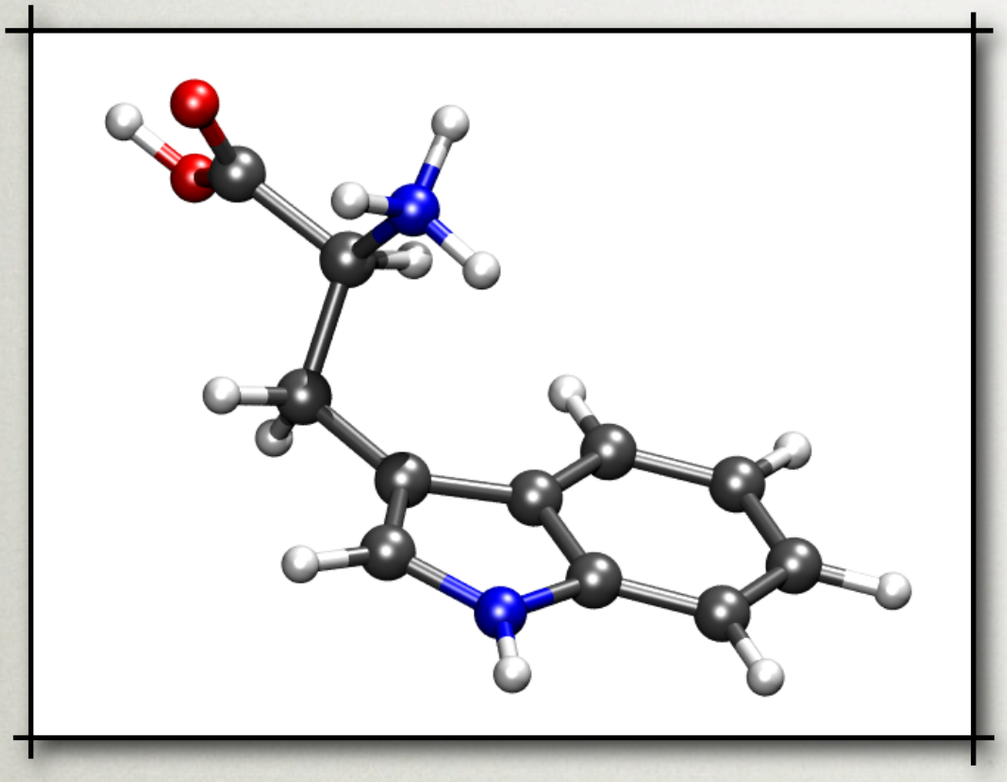
Asymmetric stretches of the two water molecules



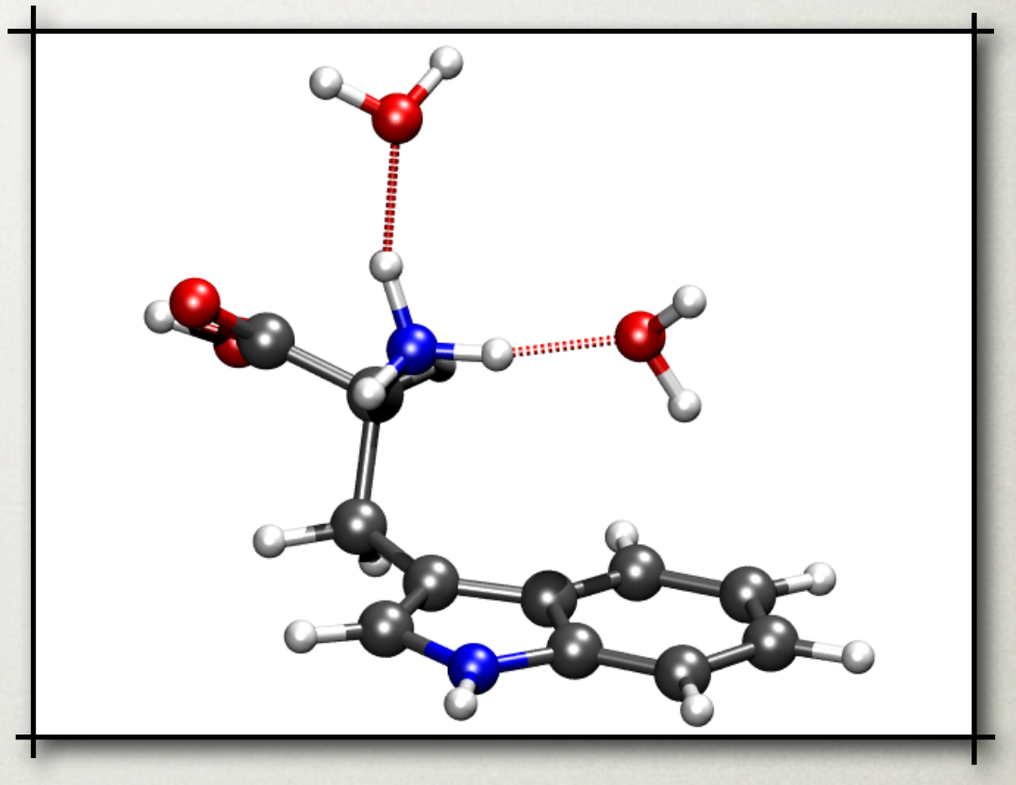


AsyStr		
(expt)	(calc)	
37cm^{-1}	32cm^{-1}	I
20cm^{-1}	25cm^{-1}	II

Initial structures for TDDFT dynamics



W^+



$W^+(2H_2O)$

Theoretical methods

(Quantum dynamics)

DFT/TDDFT

CPMD code: www.cpmd.org, plane wave based, semiclassical ab-initio MD

TDDFT: ALDA, Tamm-Dancoff approx. for energies/forces calculation

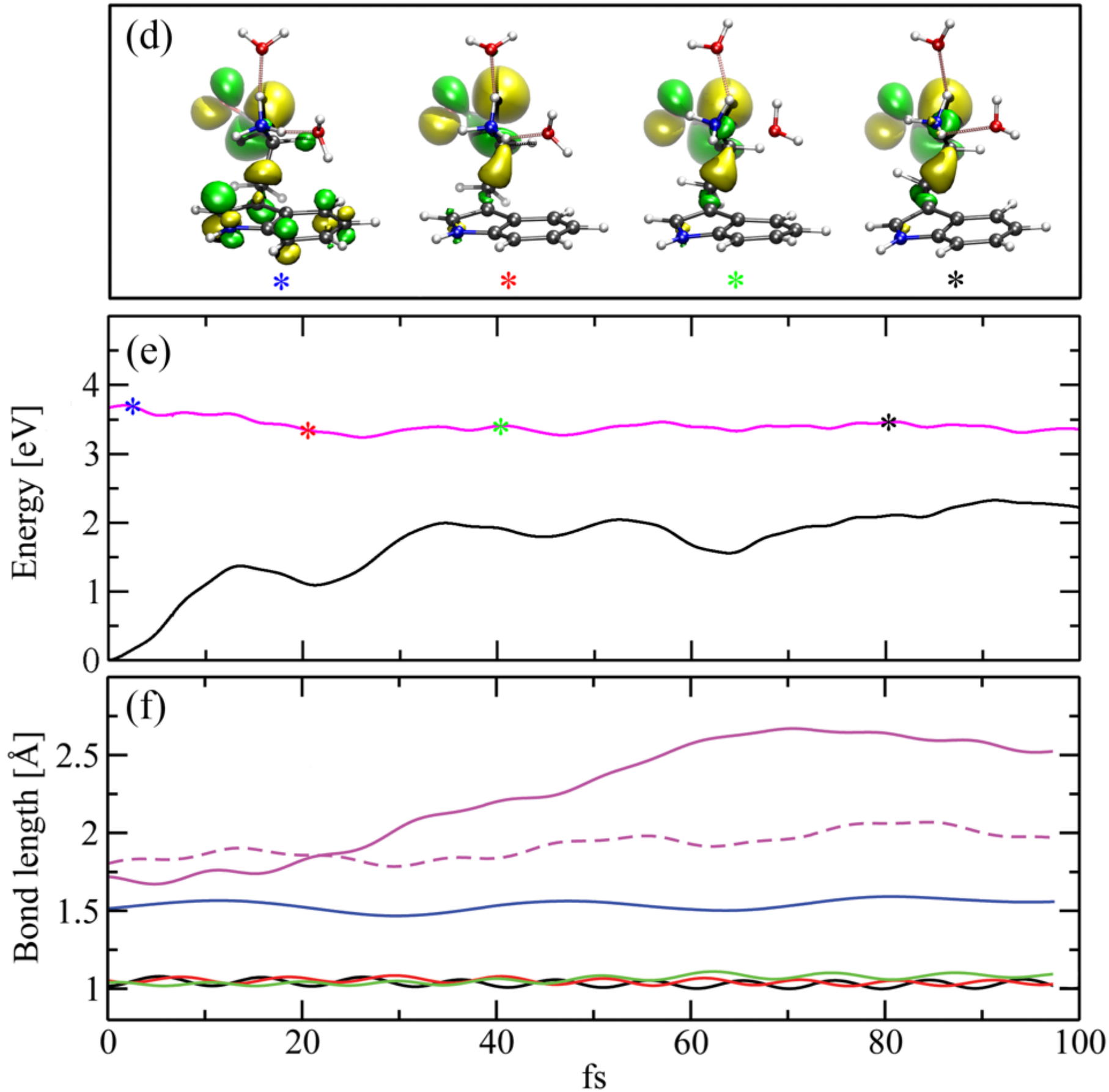
Hutter, J. *J. Chem. Phys.* **2003**, *118*, 3928

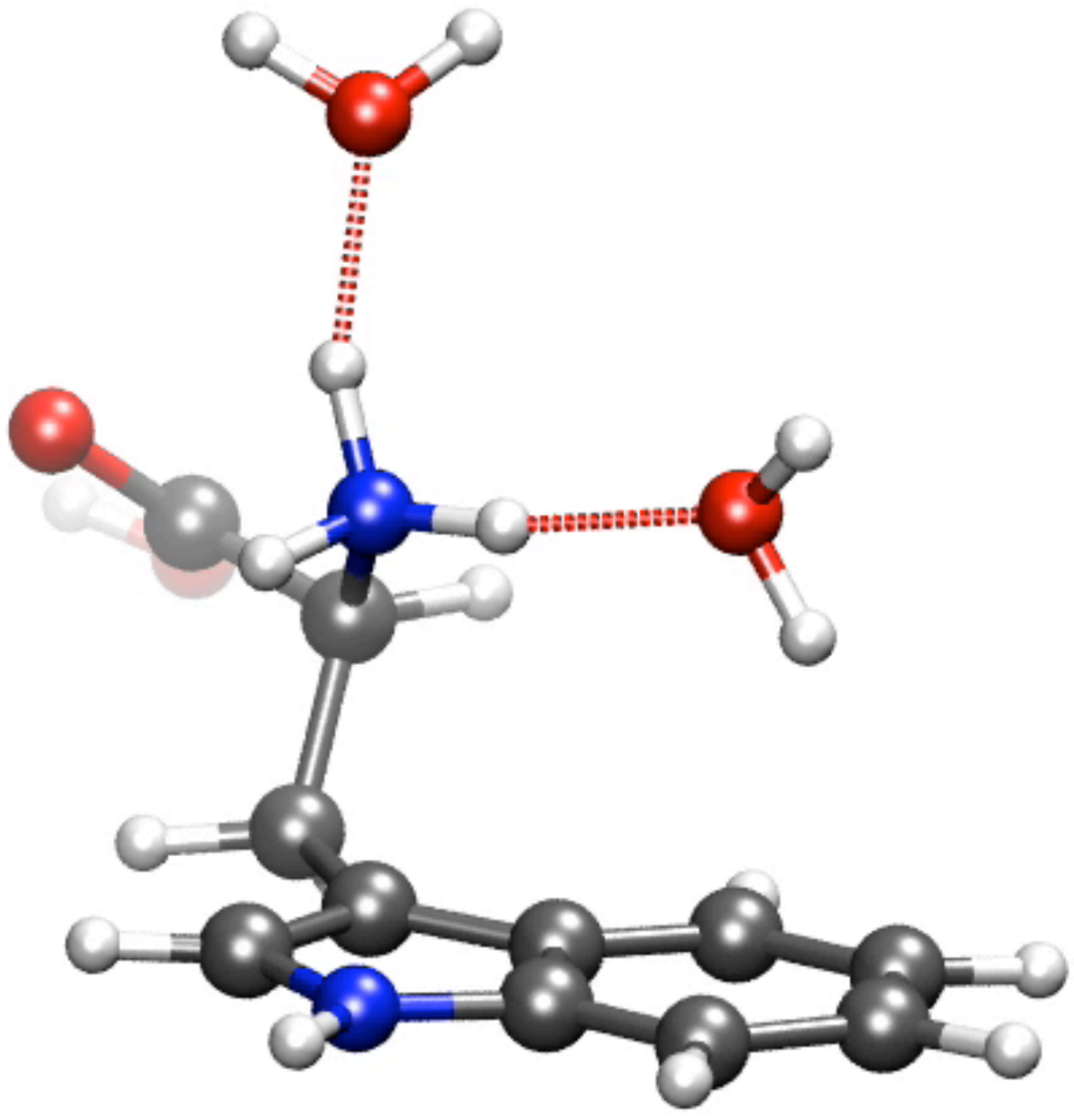
BO/Landau-Zener dynamics: surface crossing probabilities

Wynne, K.; Hochstrasser, R. M. "*In Electron Transfer-from Isolated Molecules to Biomolecules*" Pt 2, **1999**, 107, 263

DFT / TDDFT RESULTS

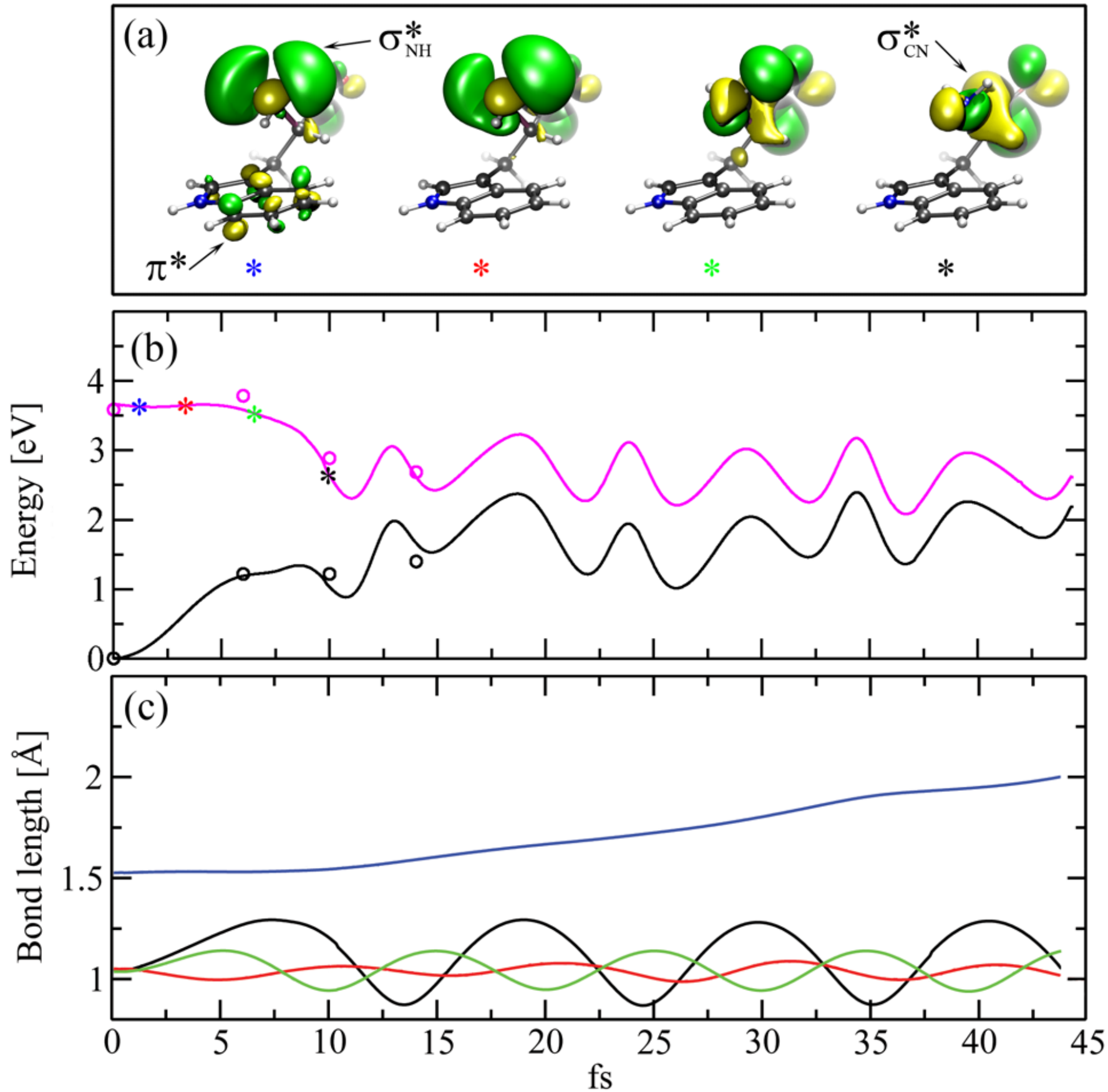
$W^+(2H_2O)$

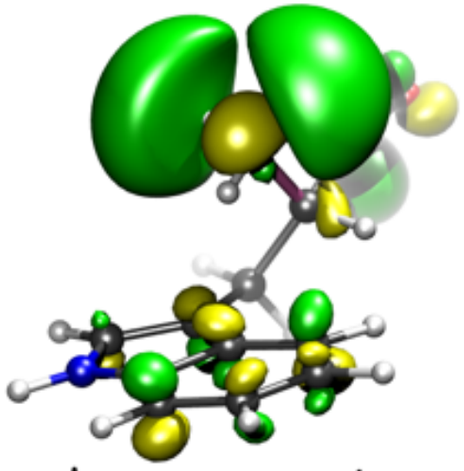
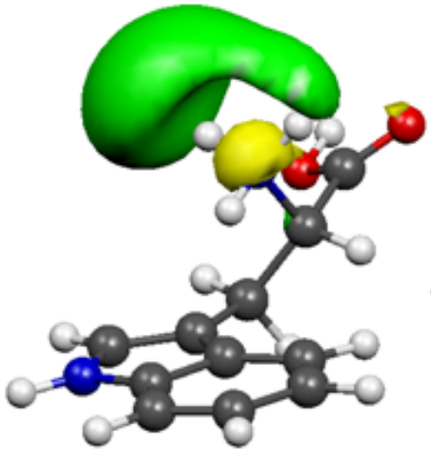
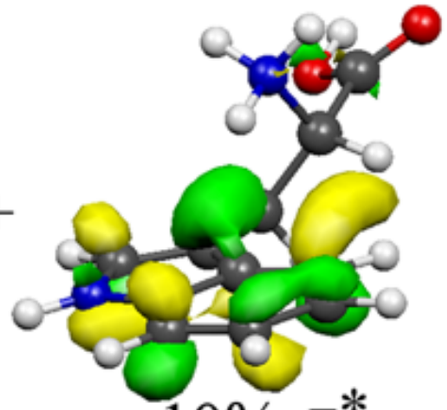
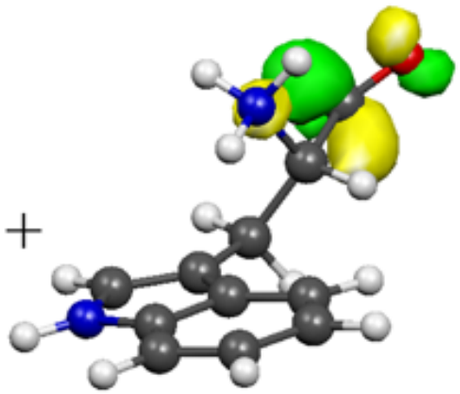
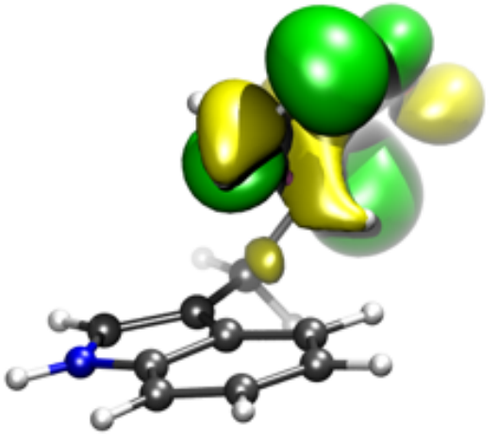
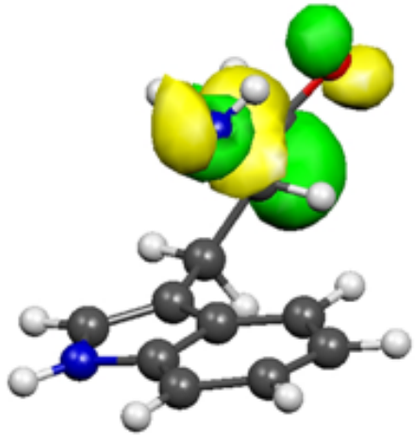
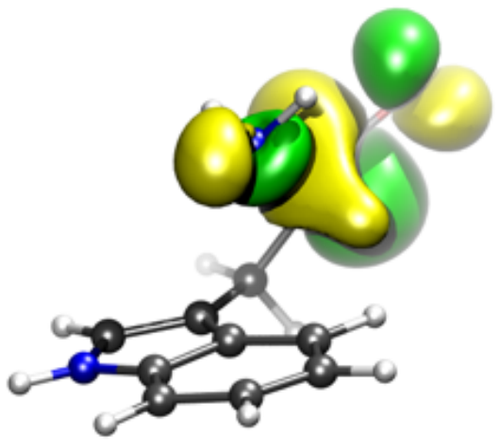
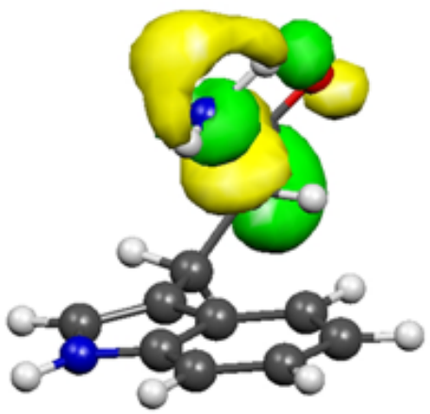

(d)
(e)
(f)
Energy [eV]
Bond length [Å]
fs
0
1
2
3
4
0
20
40
60
80
100
1
1.5
2
2.5

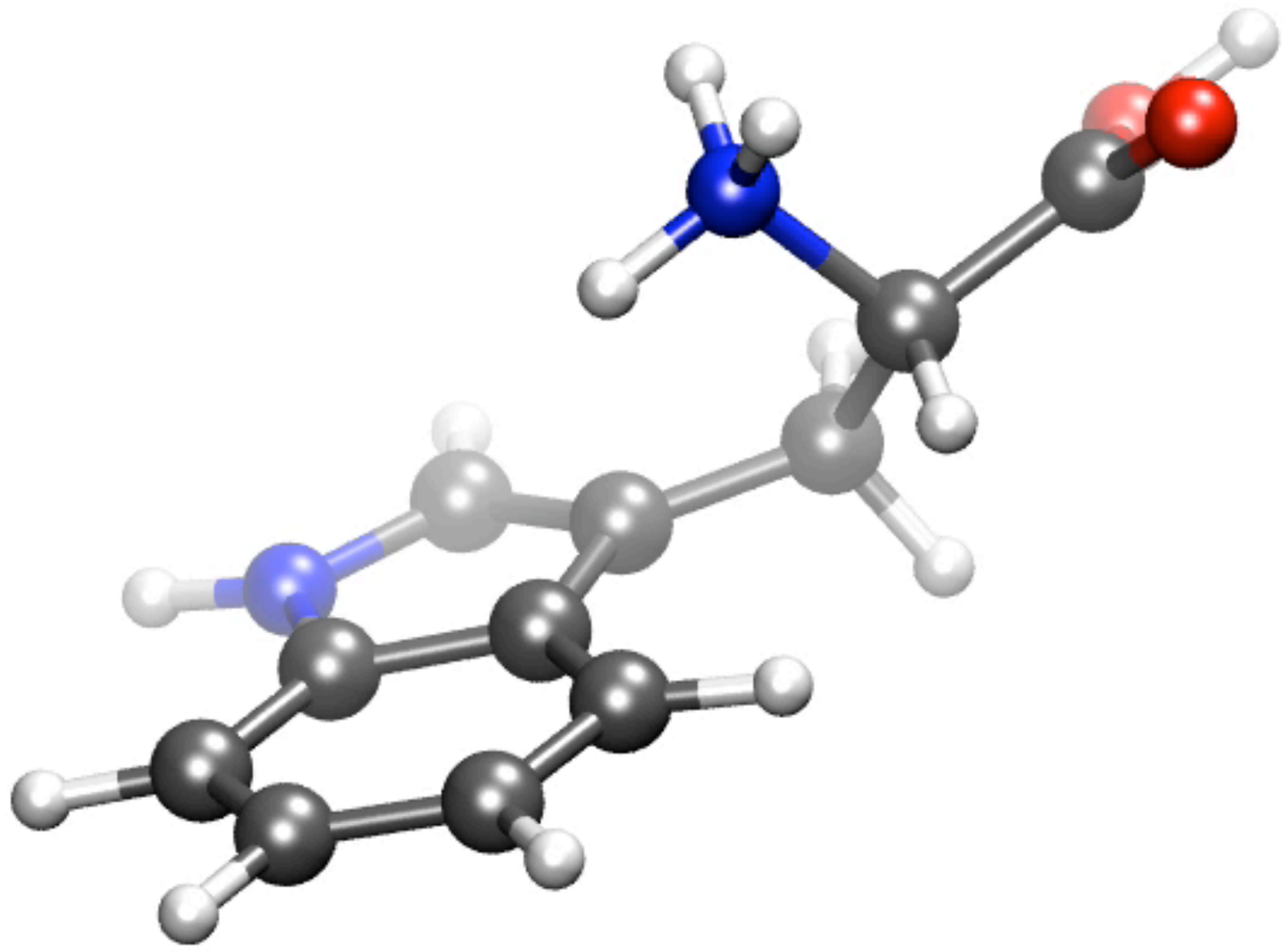


DFT / TDDFT RESULTS

W^+


(a)
σ*NH
σ*CN
π*
(b)
Energy [eV]
(c)
Bond length [Å]
fs

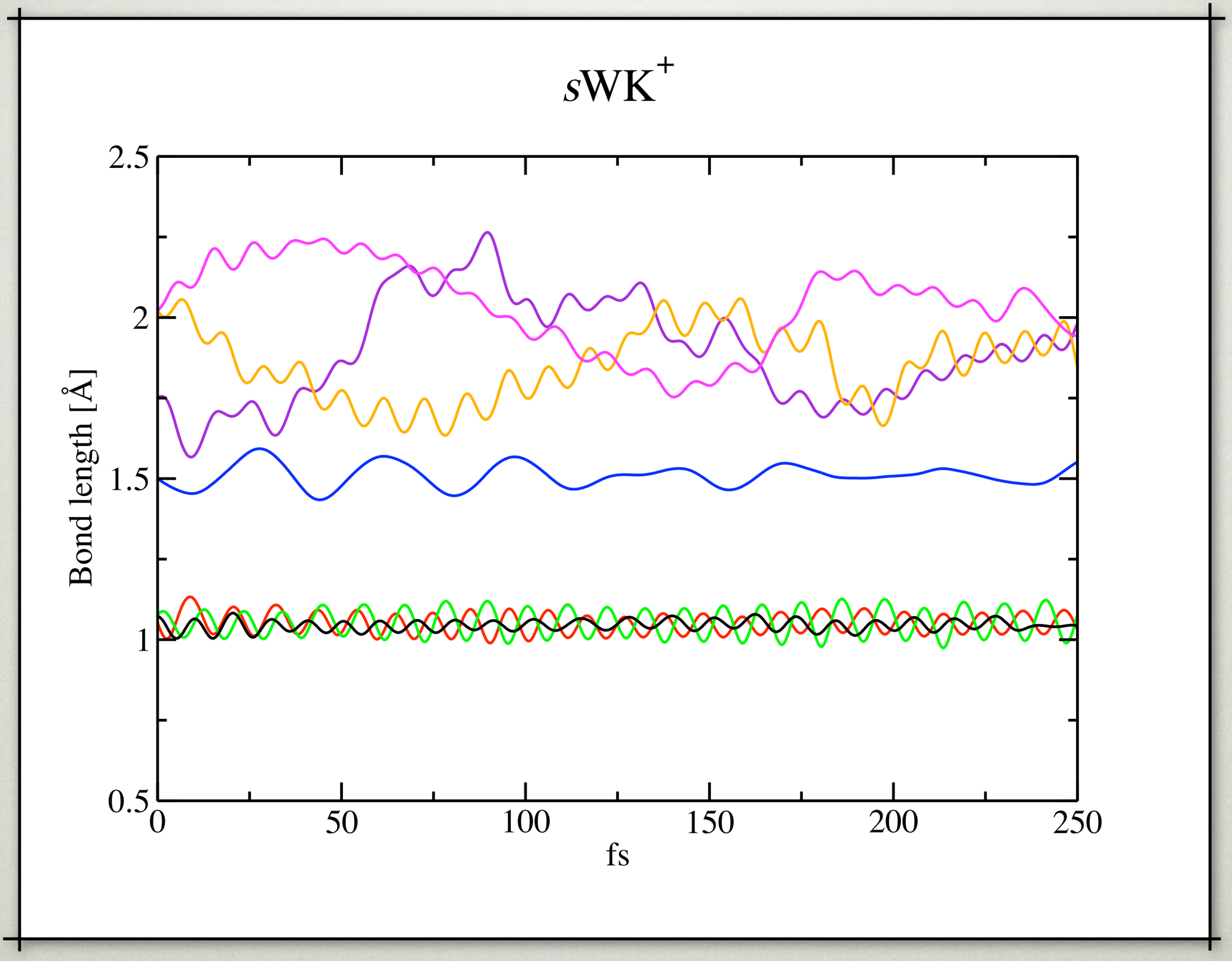
TDDFT	RI-RICC2 (aug-cc-PVDZ)
 63% $\sigma^*_{NH/CN}$, 19% π^*, 8% π^*_{CO}	 +  +  67% $\sigma^*_{NH/CN}$ 10% π^* 6% π^*_{CO}
 99.9%	 81.5%
 99.9%	 79.6%

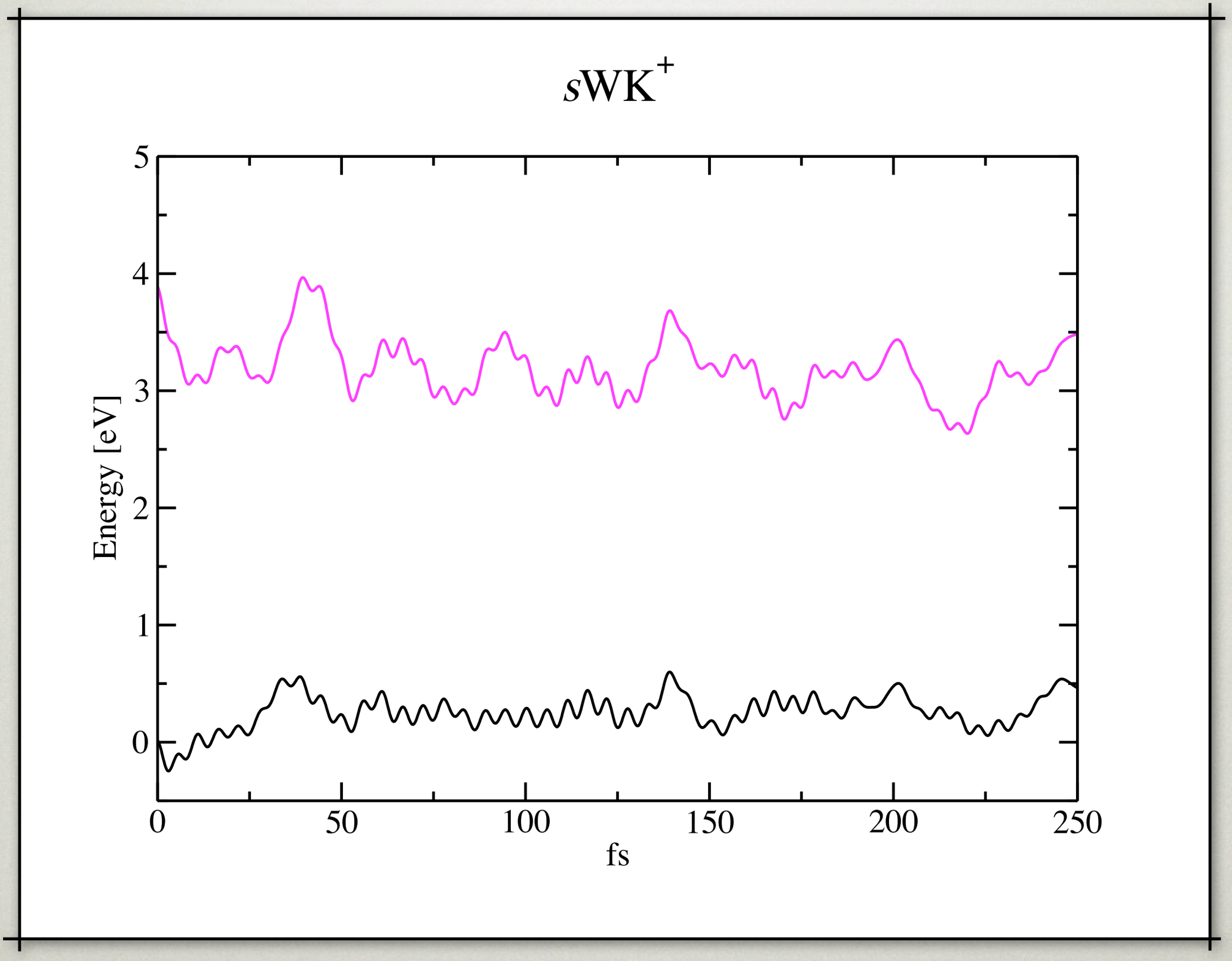


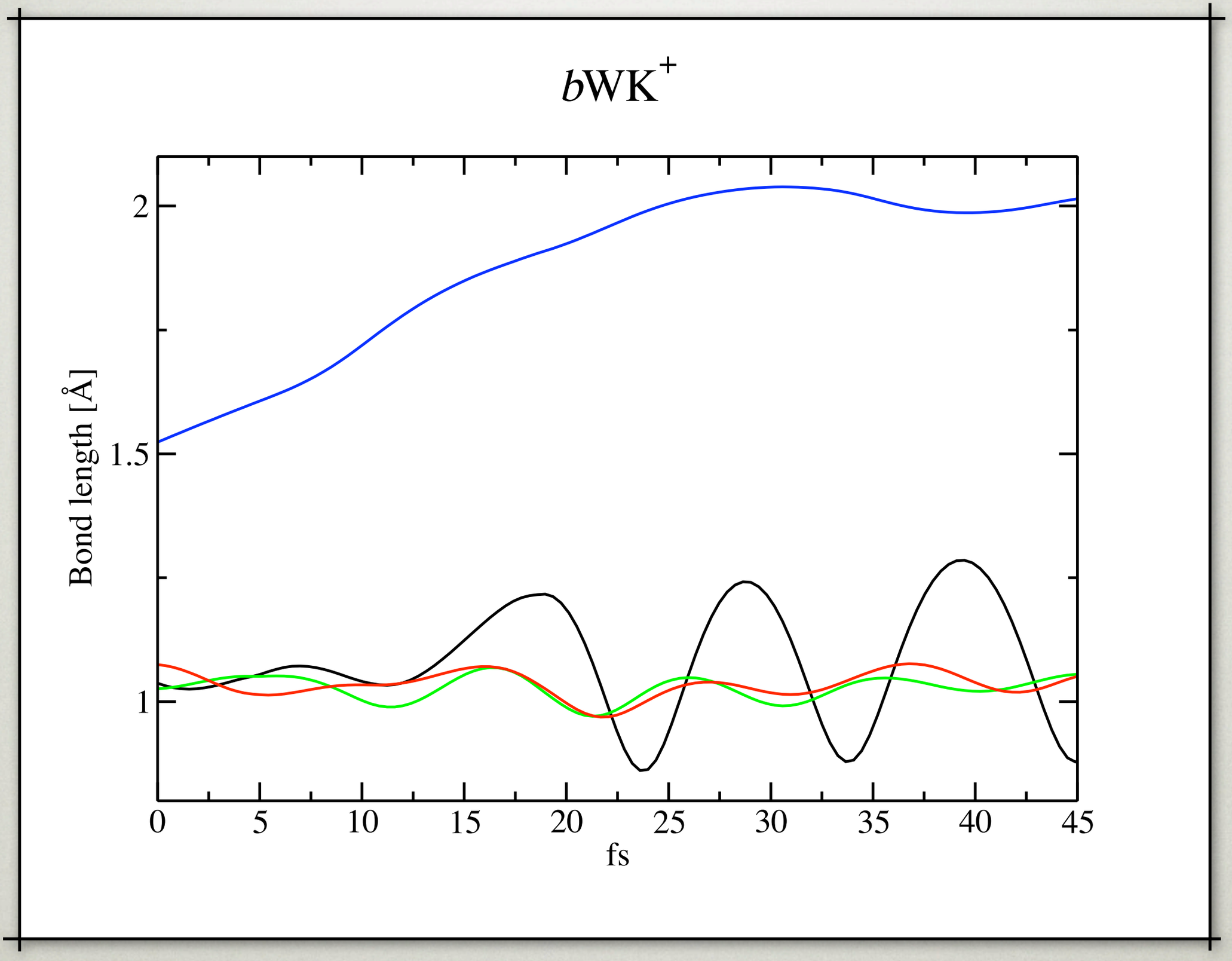
Conclusions & Outlook

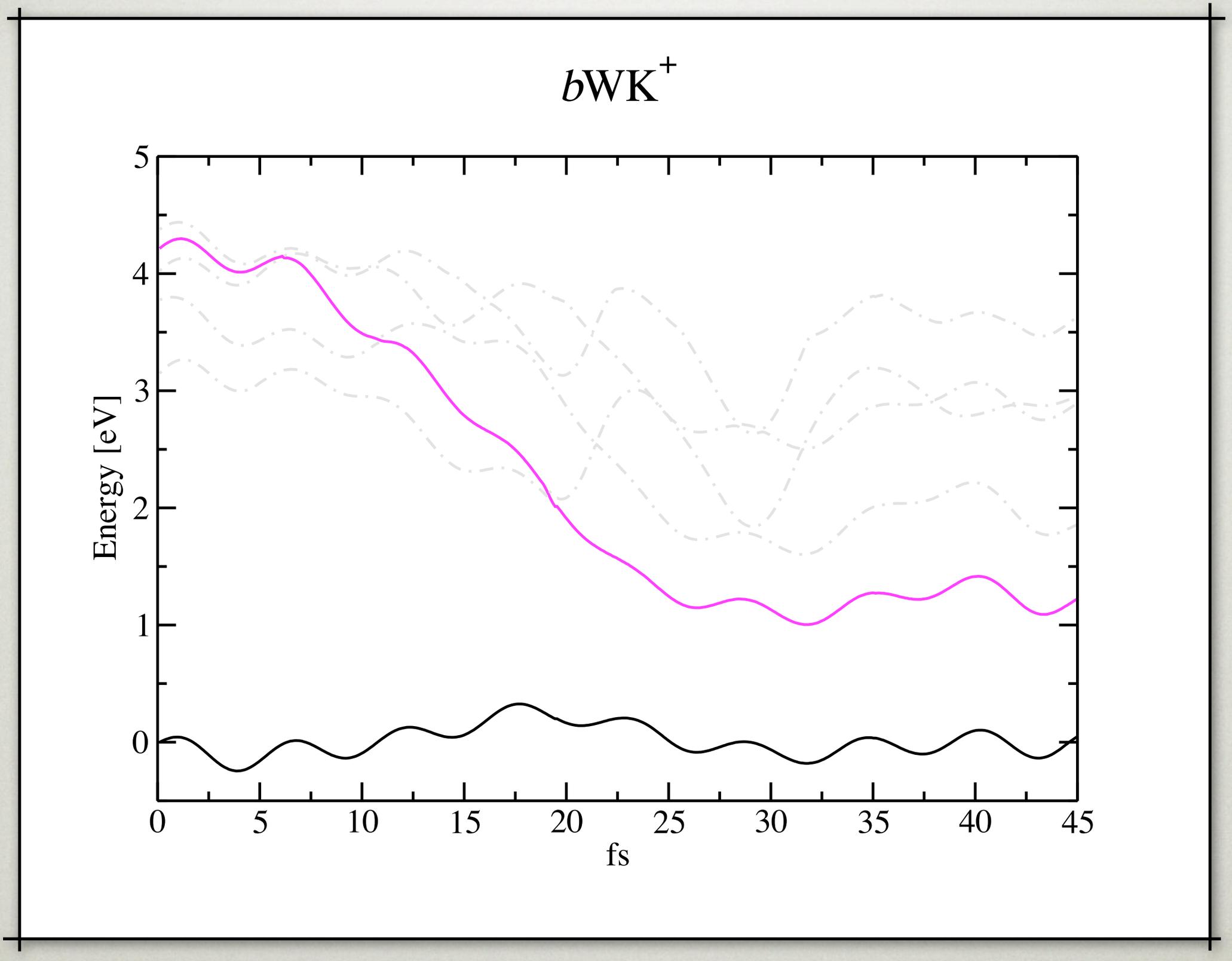
- W^+ does dissociate in the "fs" time scale
- $W^+(2H_2O)$ does not
- Agreement with the experimental fragment observations (NH_3^+ moiety)
- ... but this "test system" was not biologically relevant! Extended QM/MM model:

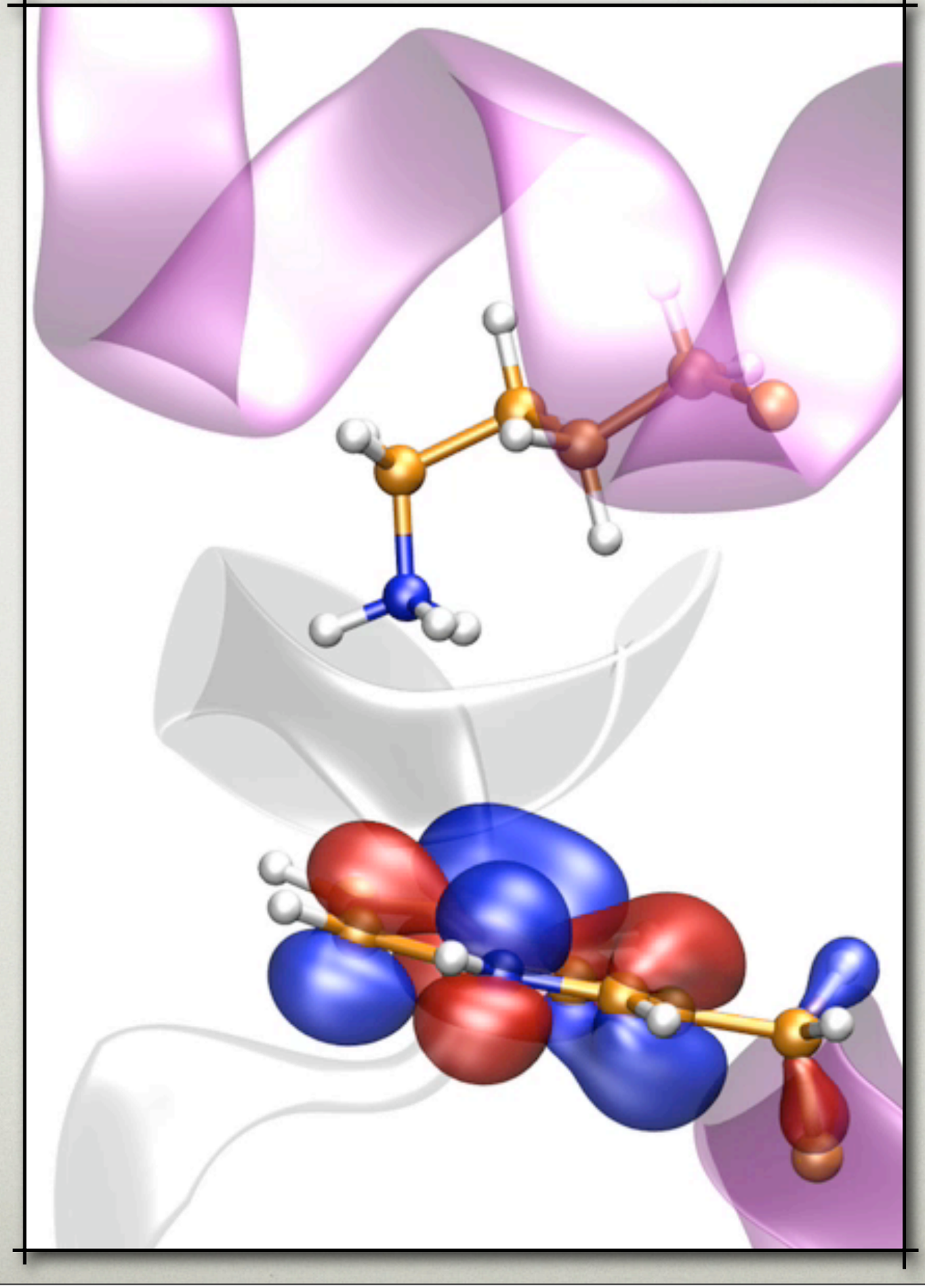
Human Serum Albumin


sWK+
2.5
2
1.5
1
0.5
Bond length [Å]
0
50
100
150
200
250
fs


sWK+
Energy [eV]
5
4
3
2
1
0
0
50
100
150
200
250
fs


bWK+
Bond length [Å]
2
1.5
1
0
5
10
15
20
25
30
35
40
45
fs


bWK+
Energy [eV]
fs
0
1
2
3
4
5
0
5
10
15
20
25
30
35
40
45



Acknowledgements

- All the Coauthors of the $trpH^+$ paper

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J.AM.CHEM.SOC. 2006, **128**, page 16938

- Ute Röhrig (meta-dynamics code), Ursula Röthlisberger (my Professor), Ivano tavernelli (my supervisor)
- Anatole von Lilienfeld and hosts (visit at CSRI)

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ALL OF YOU FOR YOUR KIND ATTENTION