

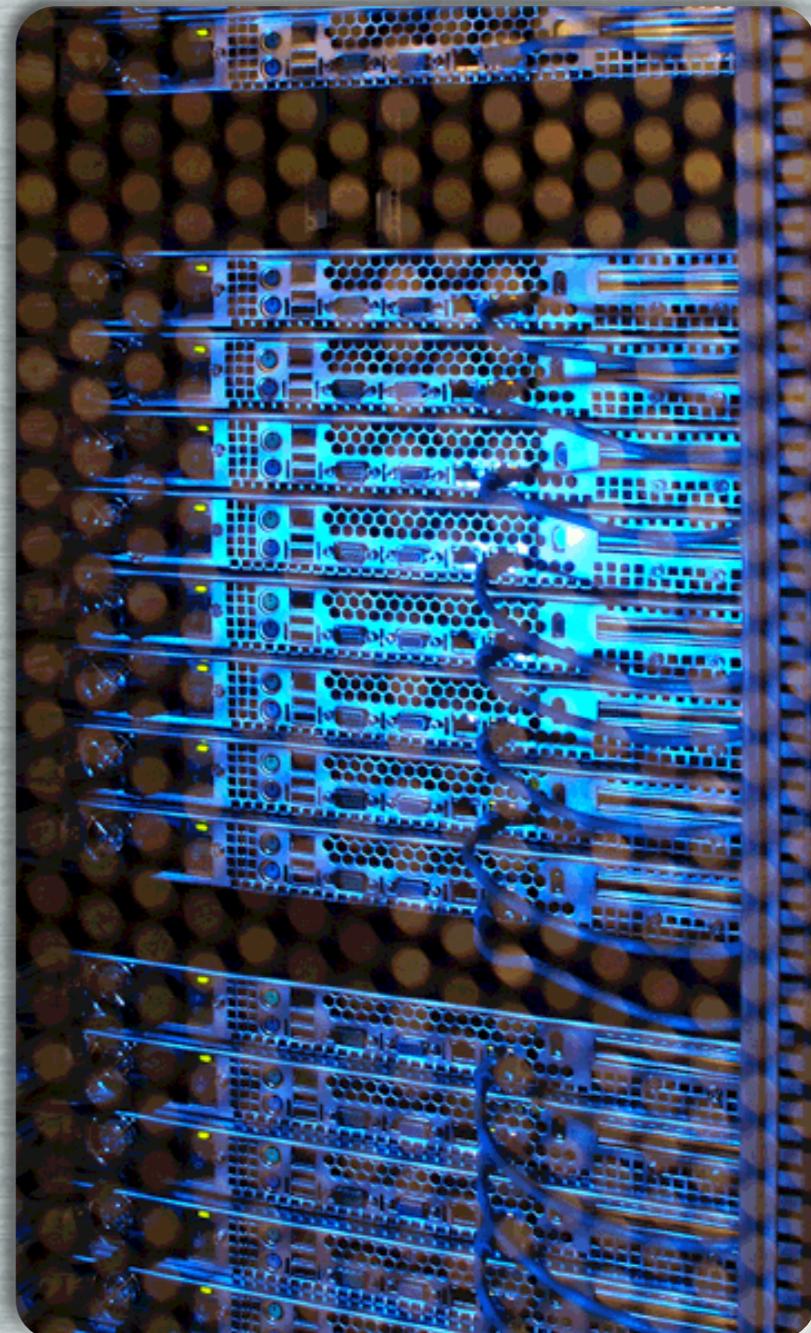
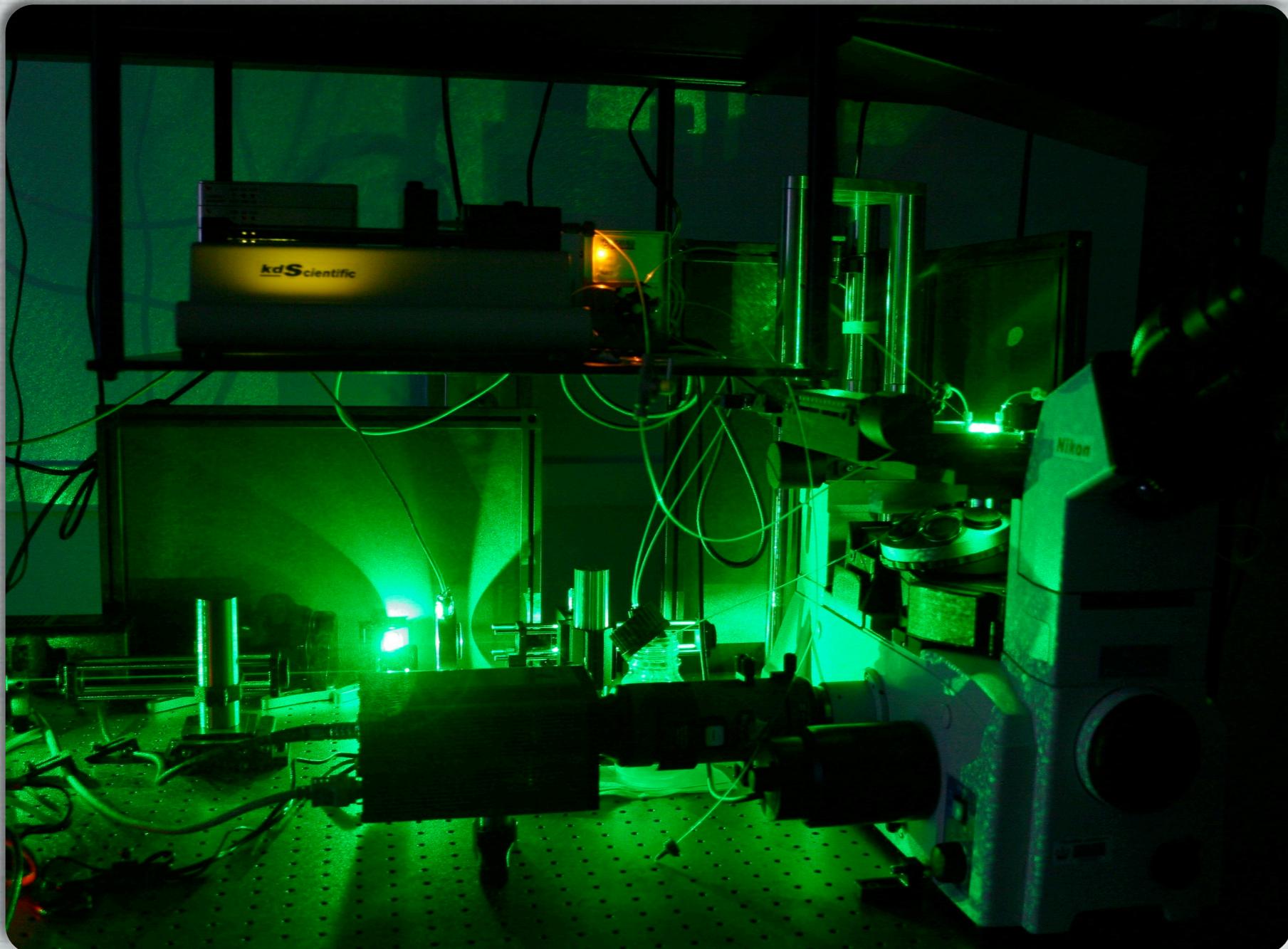
Computer simulations of photobiological processes



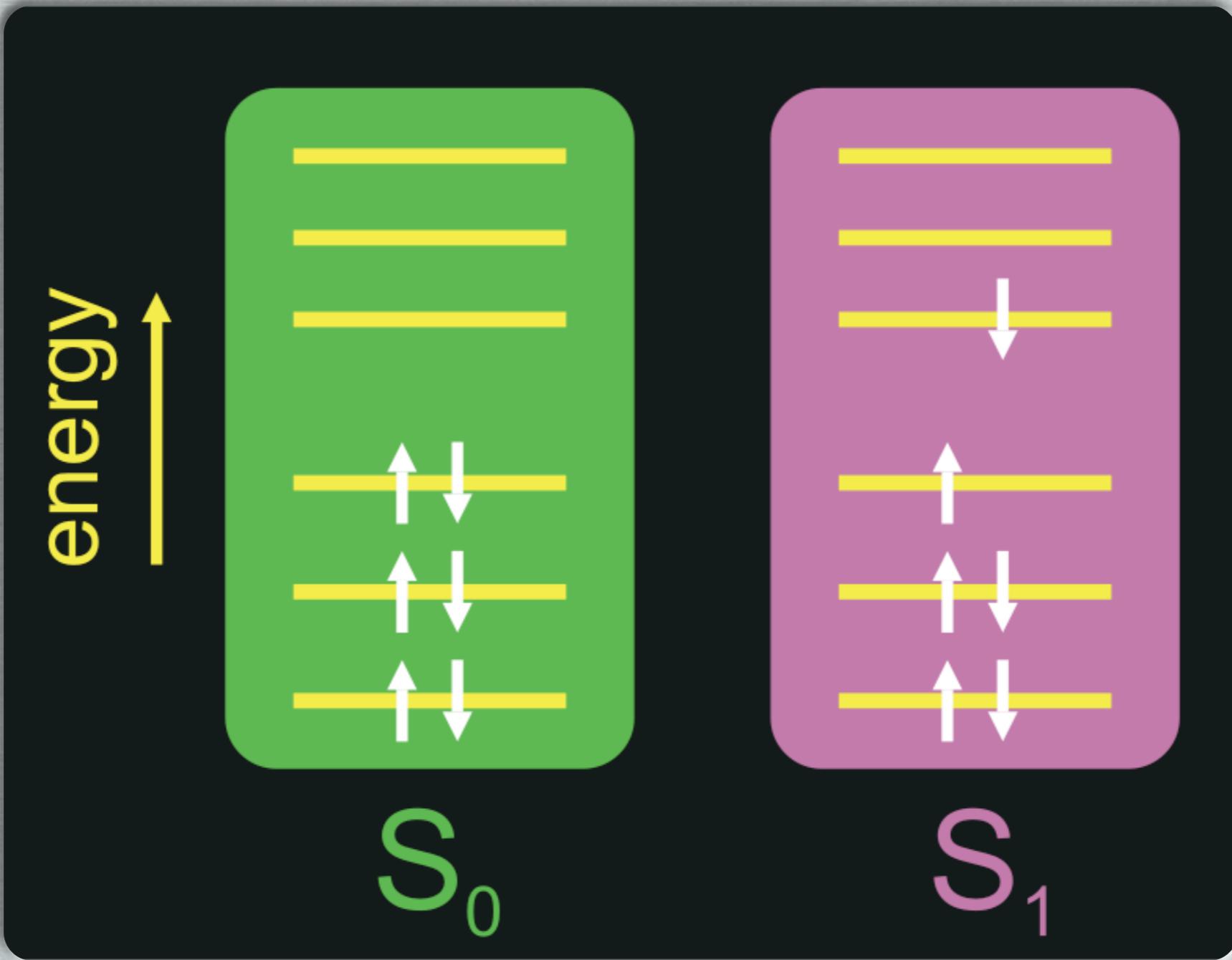
Computational
Biomolecular
Chemistry

the effect of the protein environment

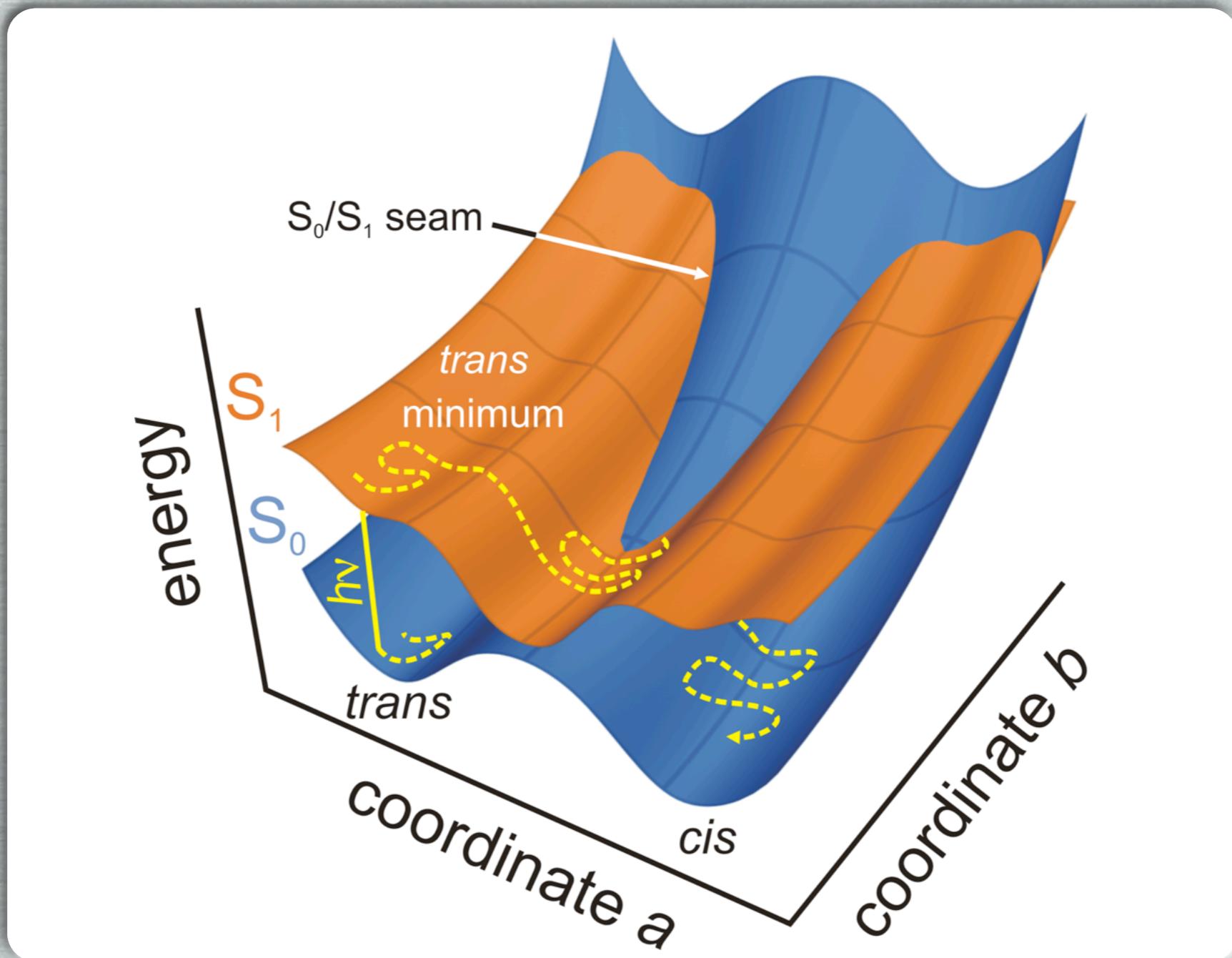
Gerrit Groenhof



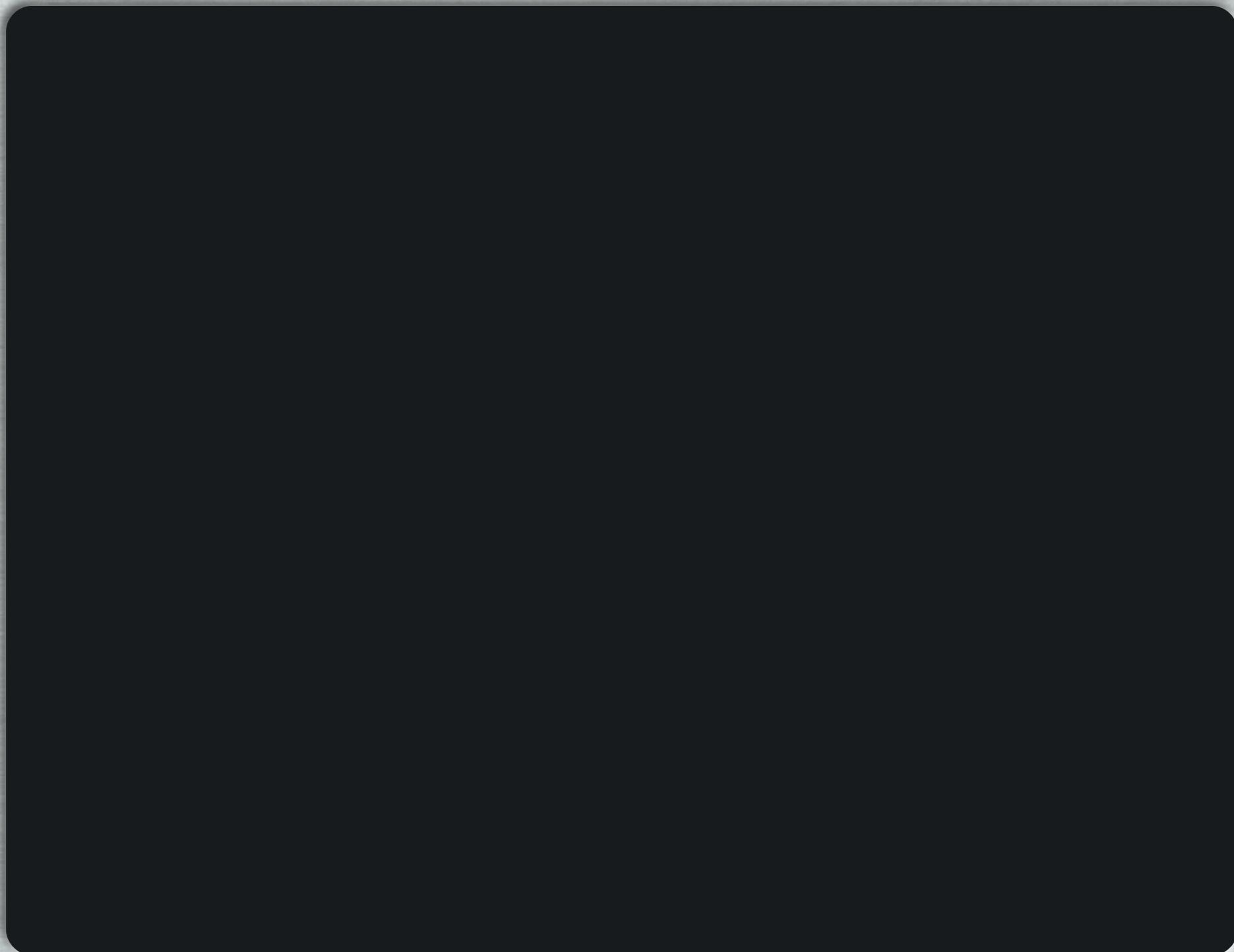
Chemistry in the Excited State



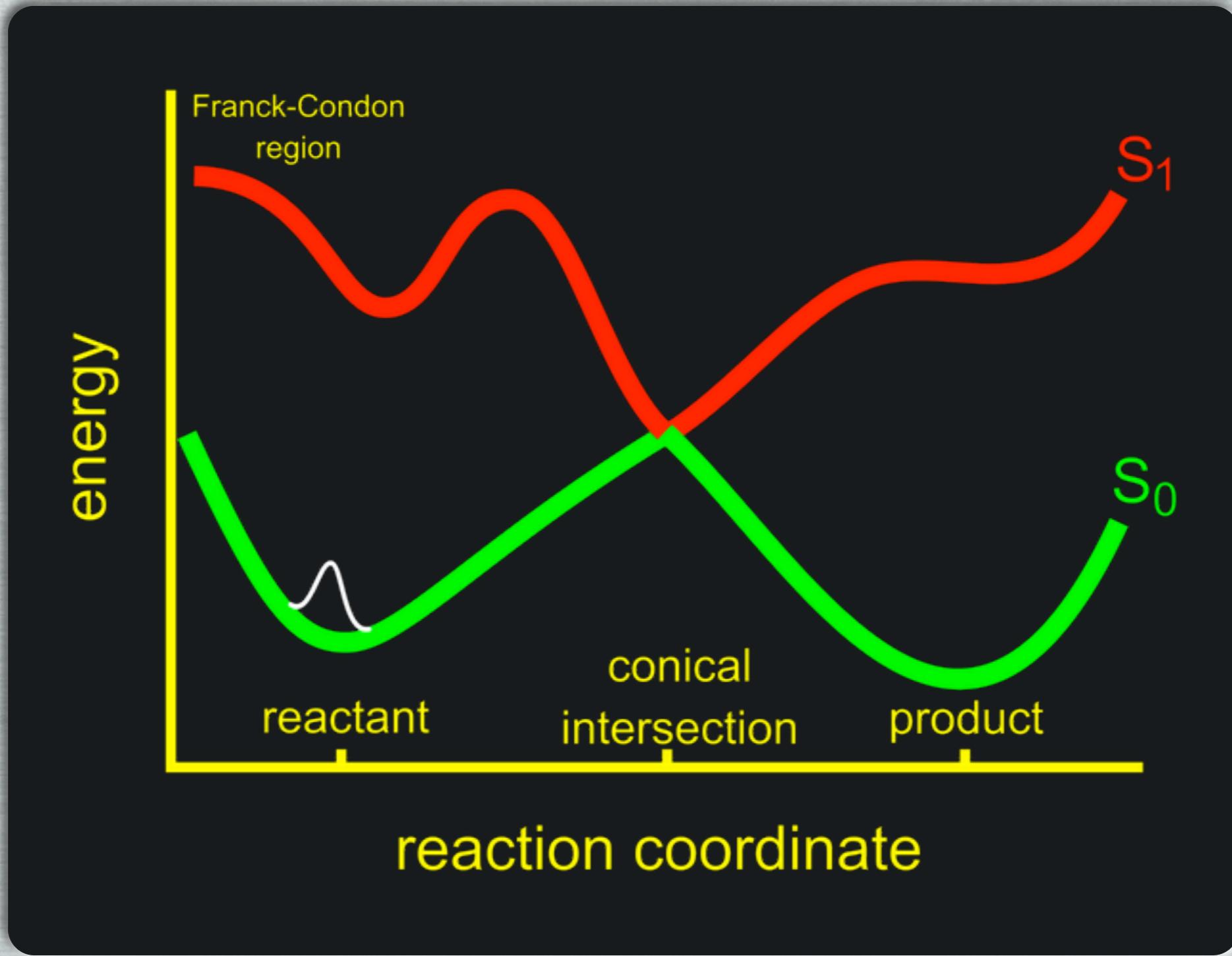
Chemistry in the Excited State



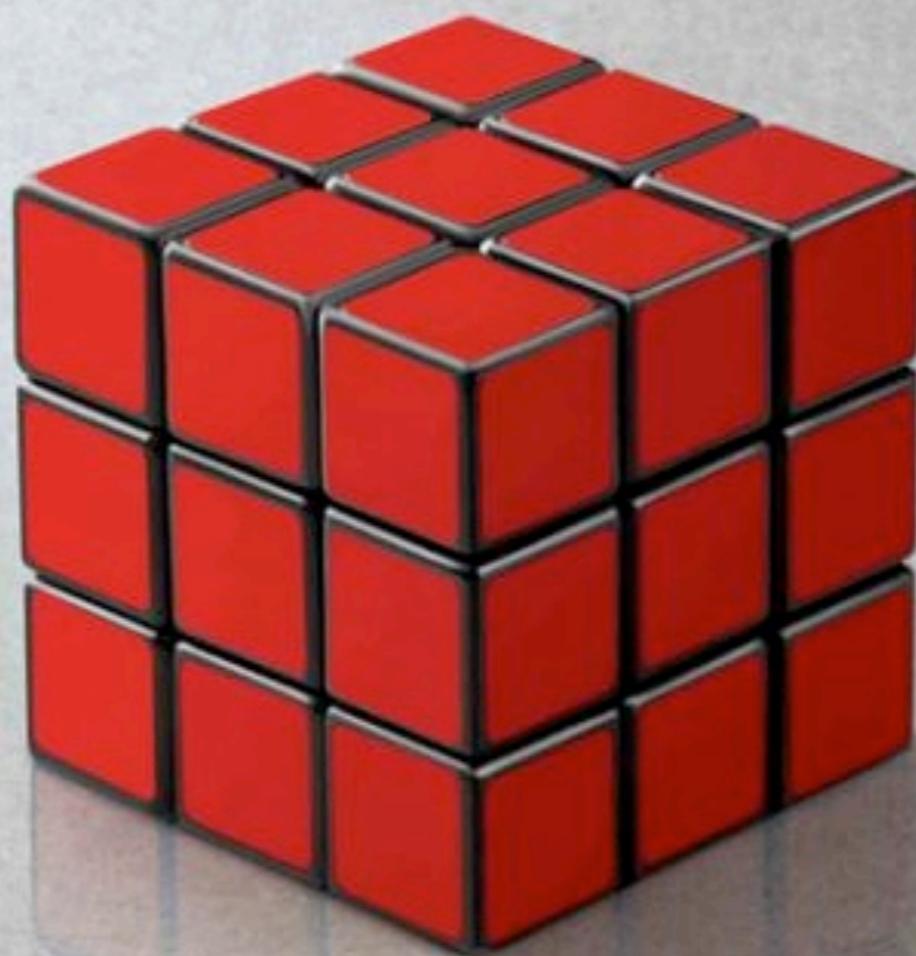
wavepacket dynamics simulation



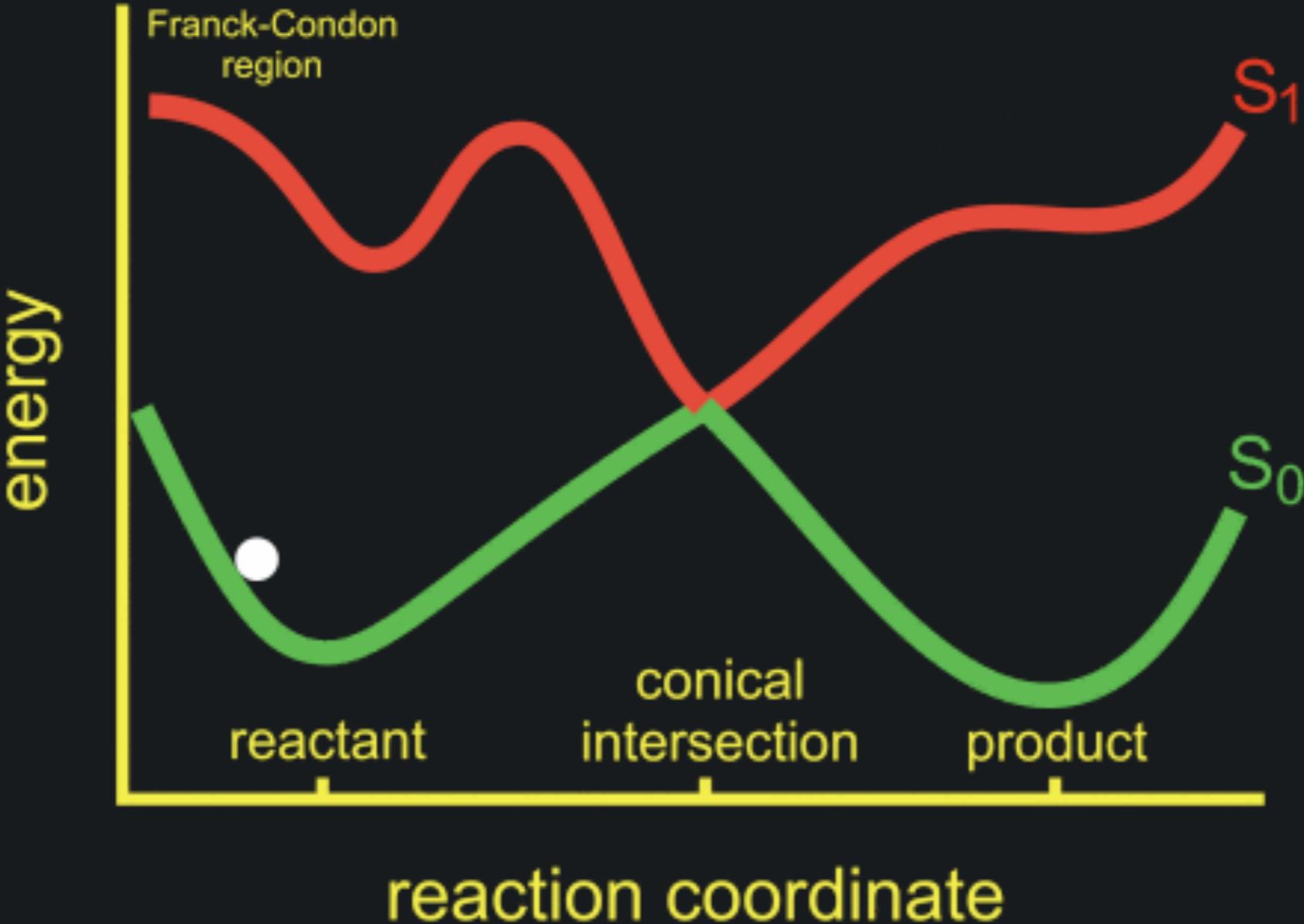
wavepacket dynamics simulation



trying to keep it simple ...



classical dynamics simulation



Molecular Dynamics

nuclei are classical particles

$$F_n = m_n \ddot{x}_n = -\nabla_{x_n} V(x_1, x_2, \dots, x_N)$$

$$x_n(t) = x_n(t_0) + \dot{x}_n(t_0)(t - t_0) + \frac{1}{2} \ddot{x}_n^2 (t - t_0)^2$$

potential energy and forces

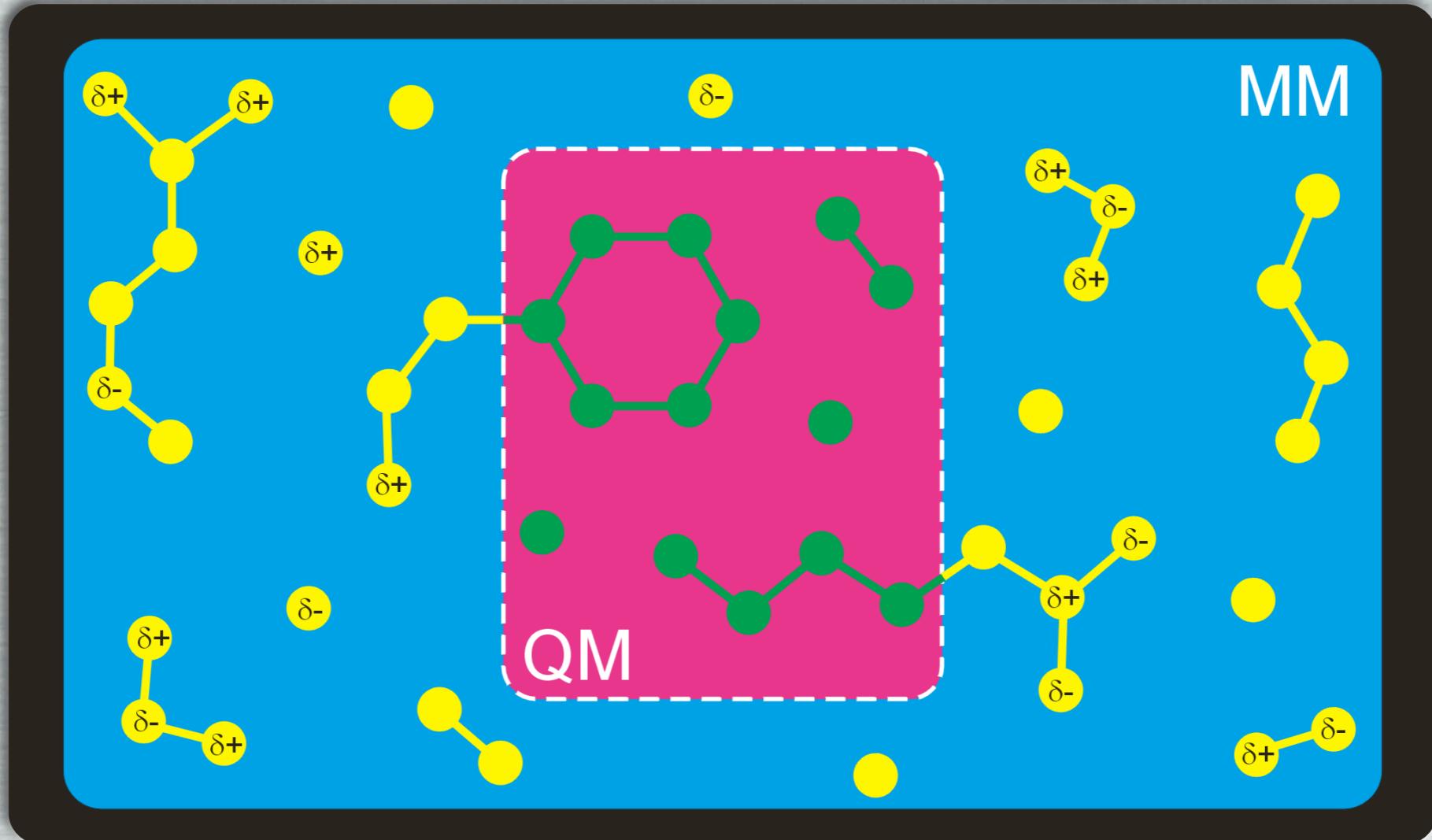
► molecular mechanics forcefield

$$V(x_1, x_2, \dots, x_N) = \sum_k v_k(x; p_k)$$

► molecular quantum mechanics

$$V(x_1, x_2, \dots, x_N) = \langle \Psi_e | \hat{H}(x_1, x_2, \dots, x_N) | \Psi_e \rangle$$

mixed quantum classical simulations



QM subsystem embedded in MM system

radiationless decay: surface hopping

Landau-Zener formula

$$P_{2 \rightarrow 1} = \exp \left[-\frac{\pi}{4} \xi \right]$$

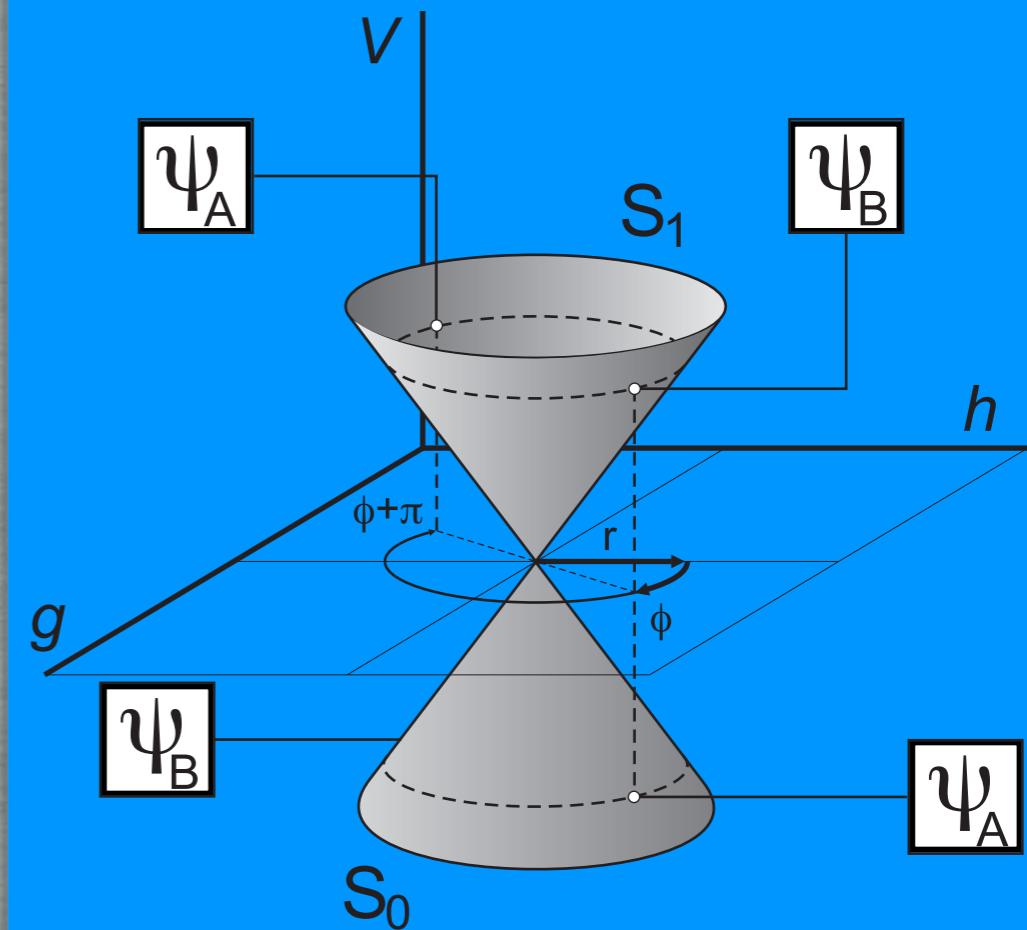
Massey parameter

$$\xi = \frac{\Delta E}{\hbar \left\langle \Psi_1 \left| \frac{\partial \Psi_2}{\partial t} \right. \right\rangle}$$

wavefunction overlap

$$\left\langle \Psi_1 \left| \frac{\partial}{\partial t} \Psi_2 \right. \right\rangle \approx \langle \Psi_1(t) | \Psi_2(t + \Delta t) \rangle$$

conical intersection



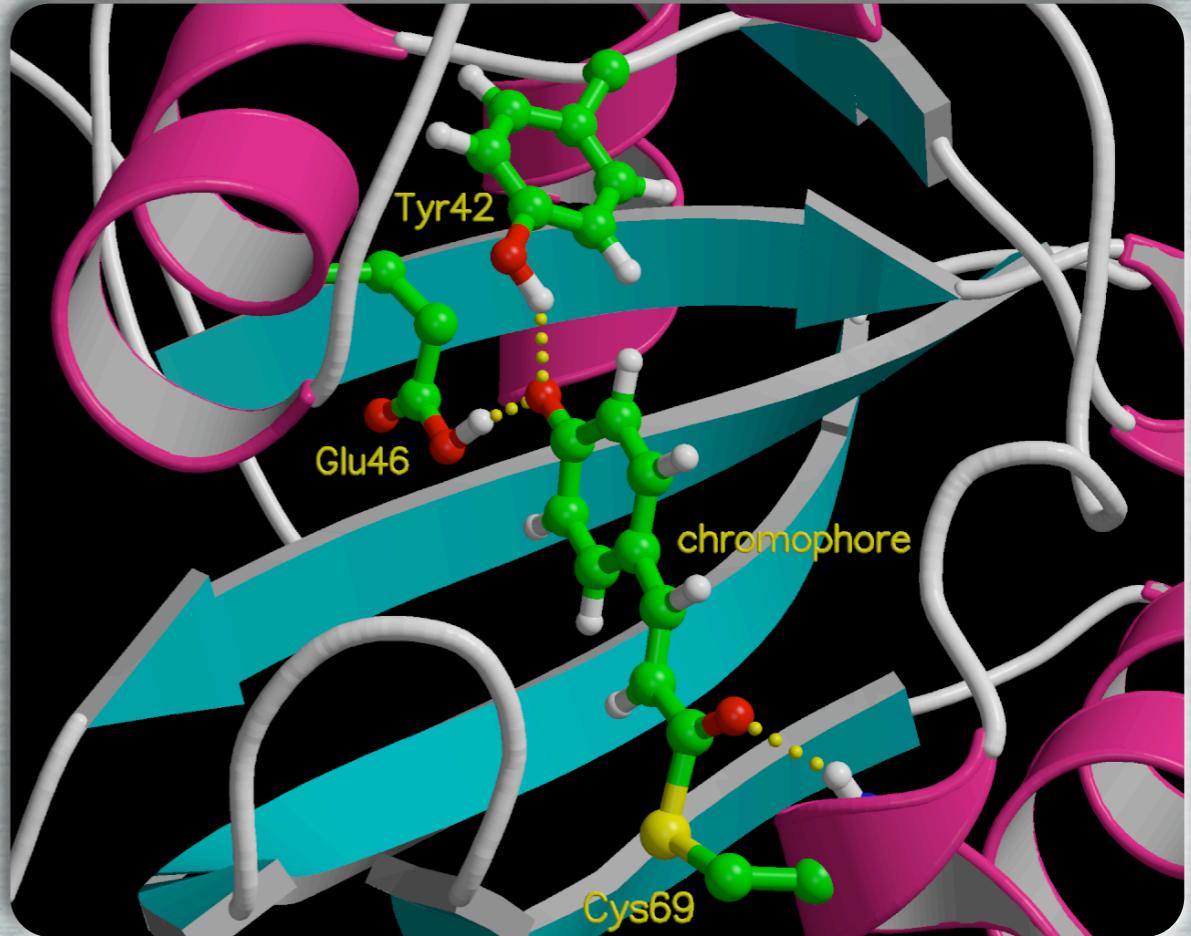
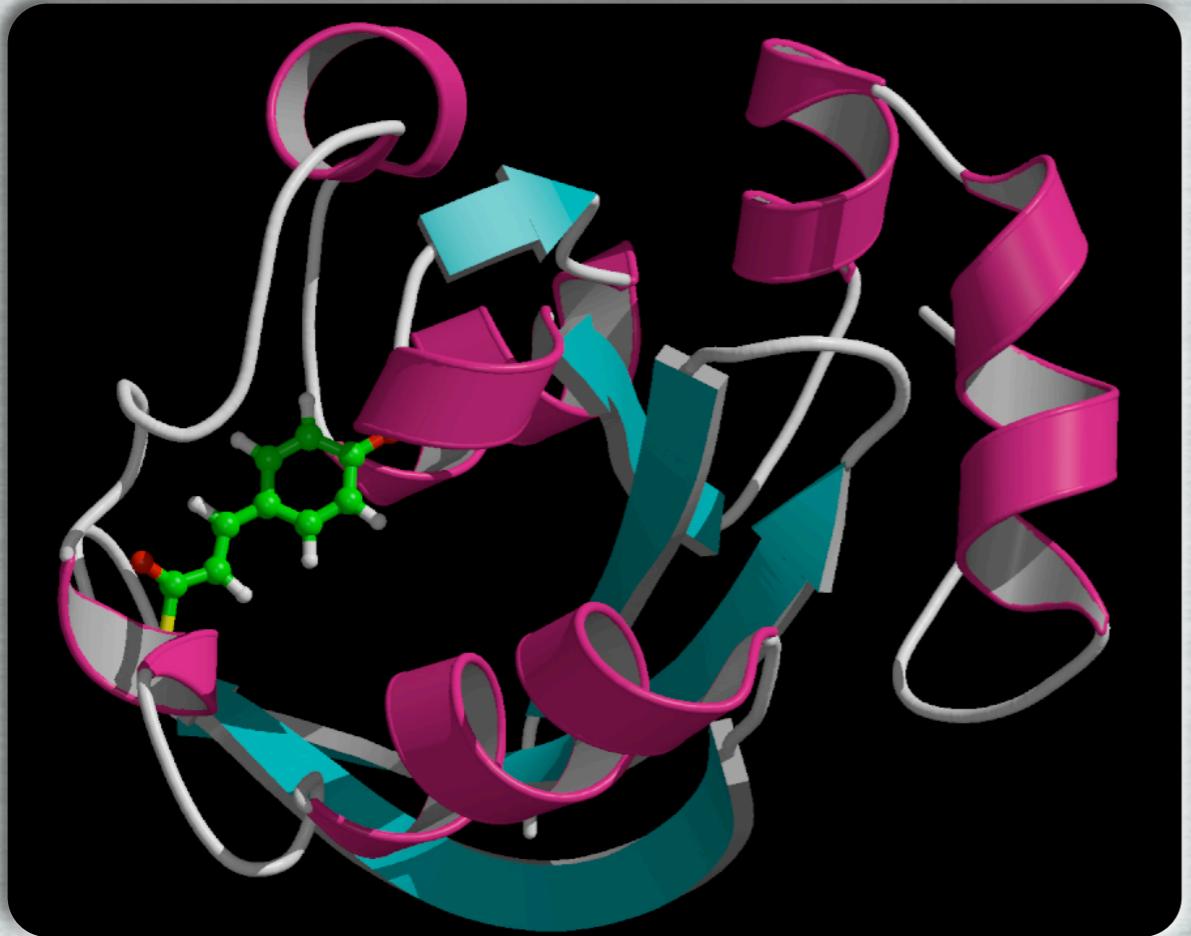
avoiding exposure to UV light



Halorhodospira halophila bacteria

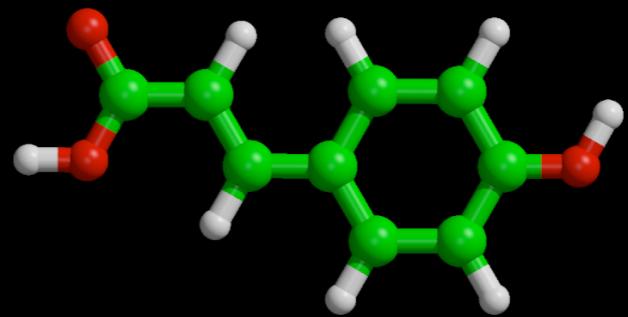
- ▶ negative phototaxis to blue light
- ▶ photoactive yellow protein

Photoactive Yellow Protein



chromophore

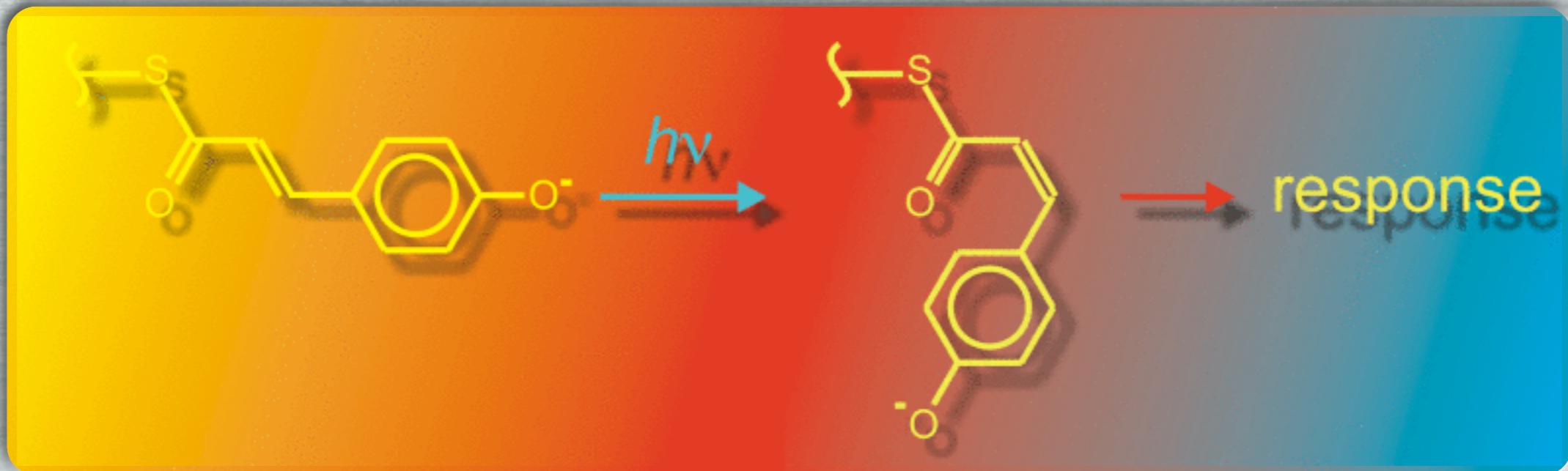
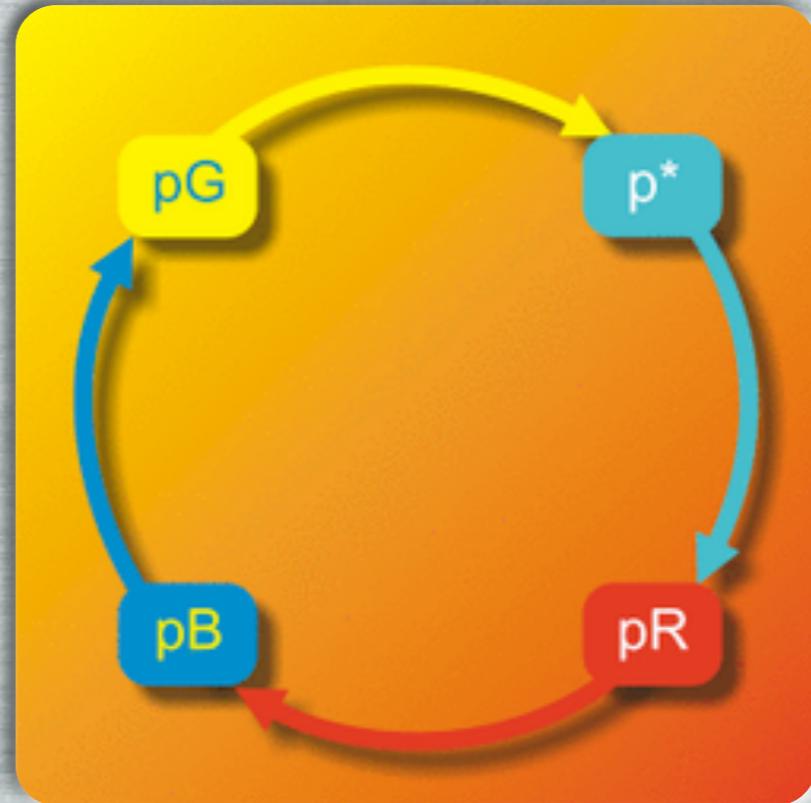
- ▶ β -coumaric acid
- ▶ isomerization



Photoactive Yellow Protein

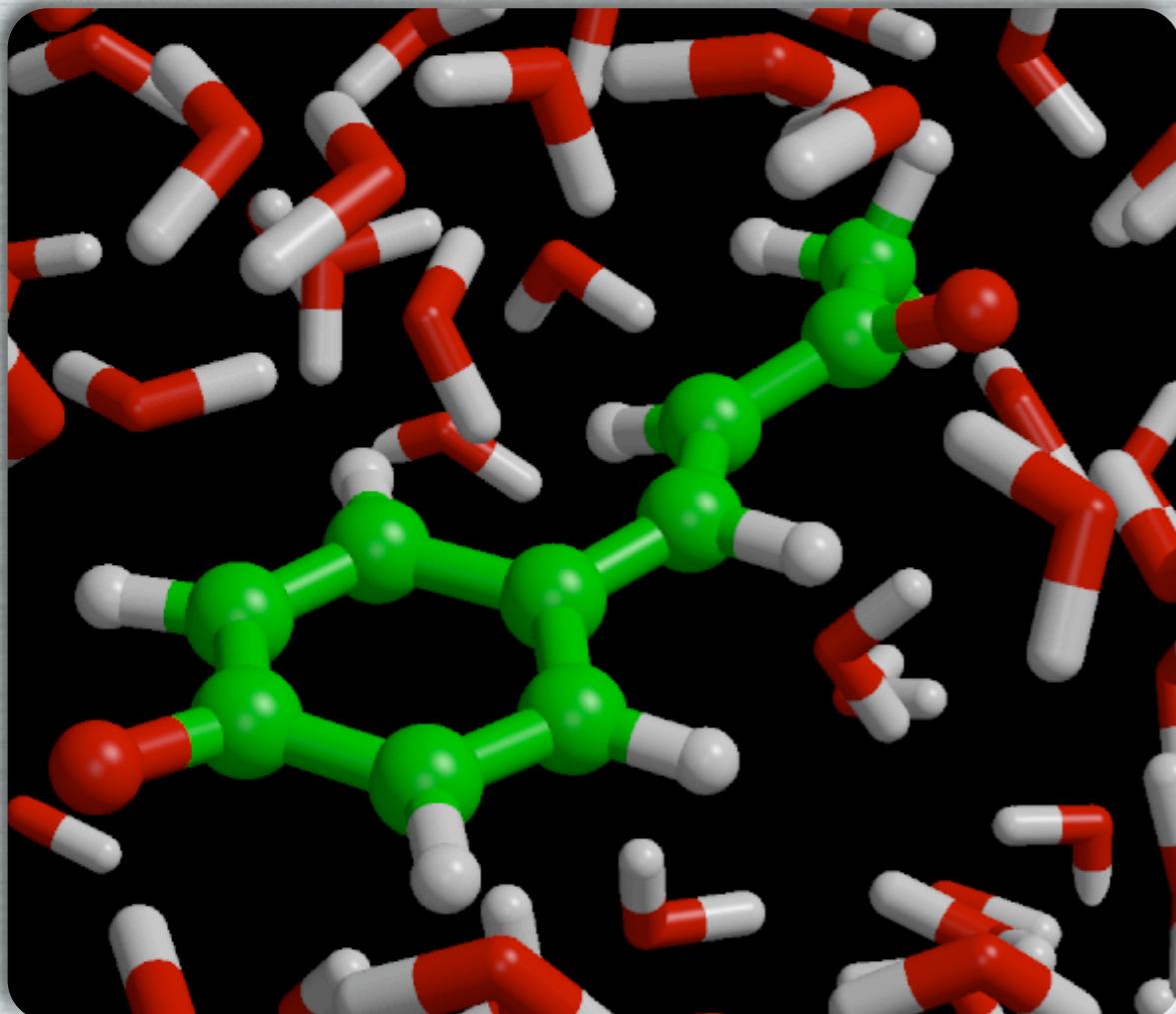
photocycle

- ▶ photon absorption
- ▶ isomerization (ns)
- ▶ partial unfolding (μ s)
- ▶ relaxation (ms)



PYP chromophore in solution

QM/MM protocol



QM subsystem

- ▶ chromophore (pck)
- ▶ CASSCF(6,6)/3-21G
- ▶ surface hopping

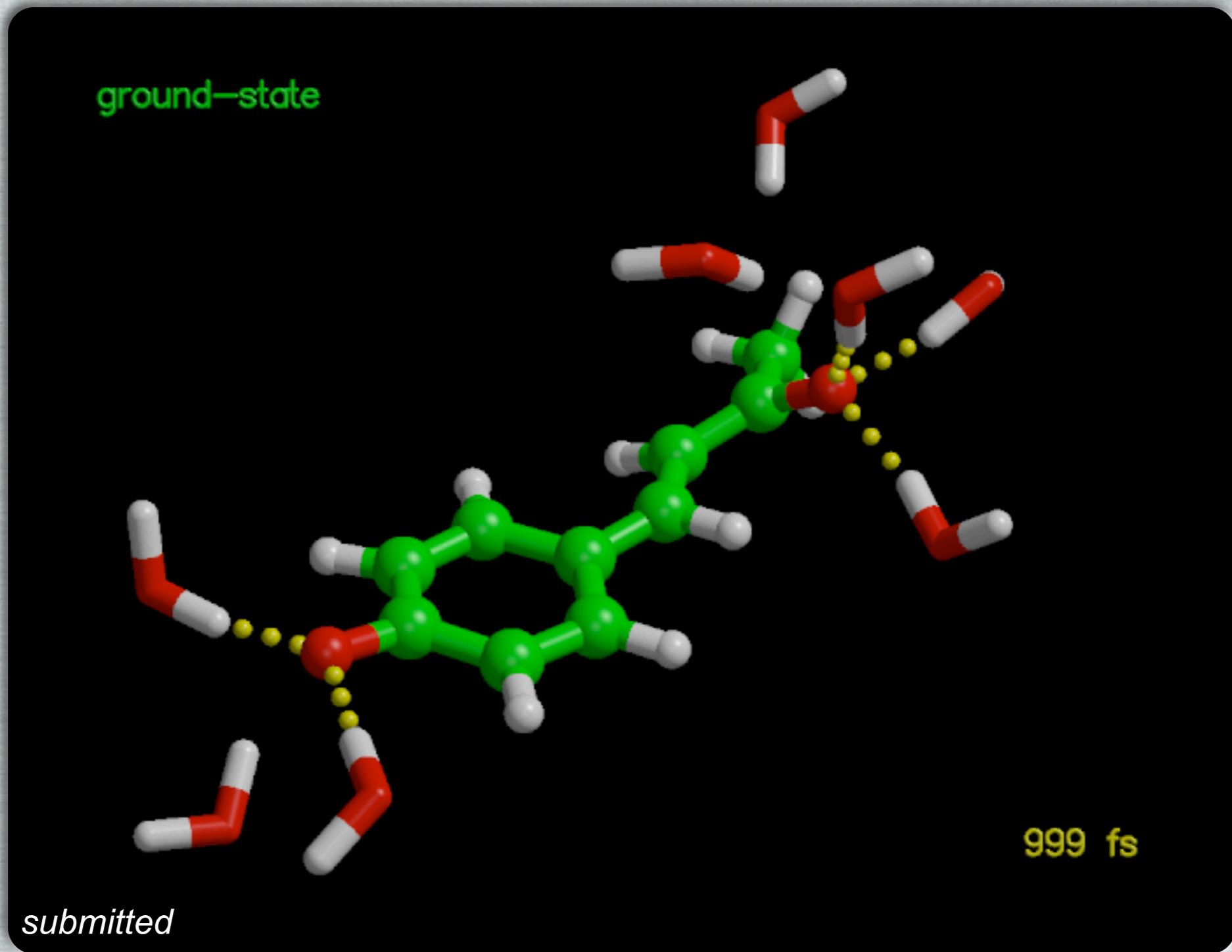
MM subsystem

- ▶ water & ions
- ▶ GROMOS96/SPCE

single bond photoisomerization (88%)

submitted

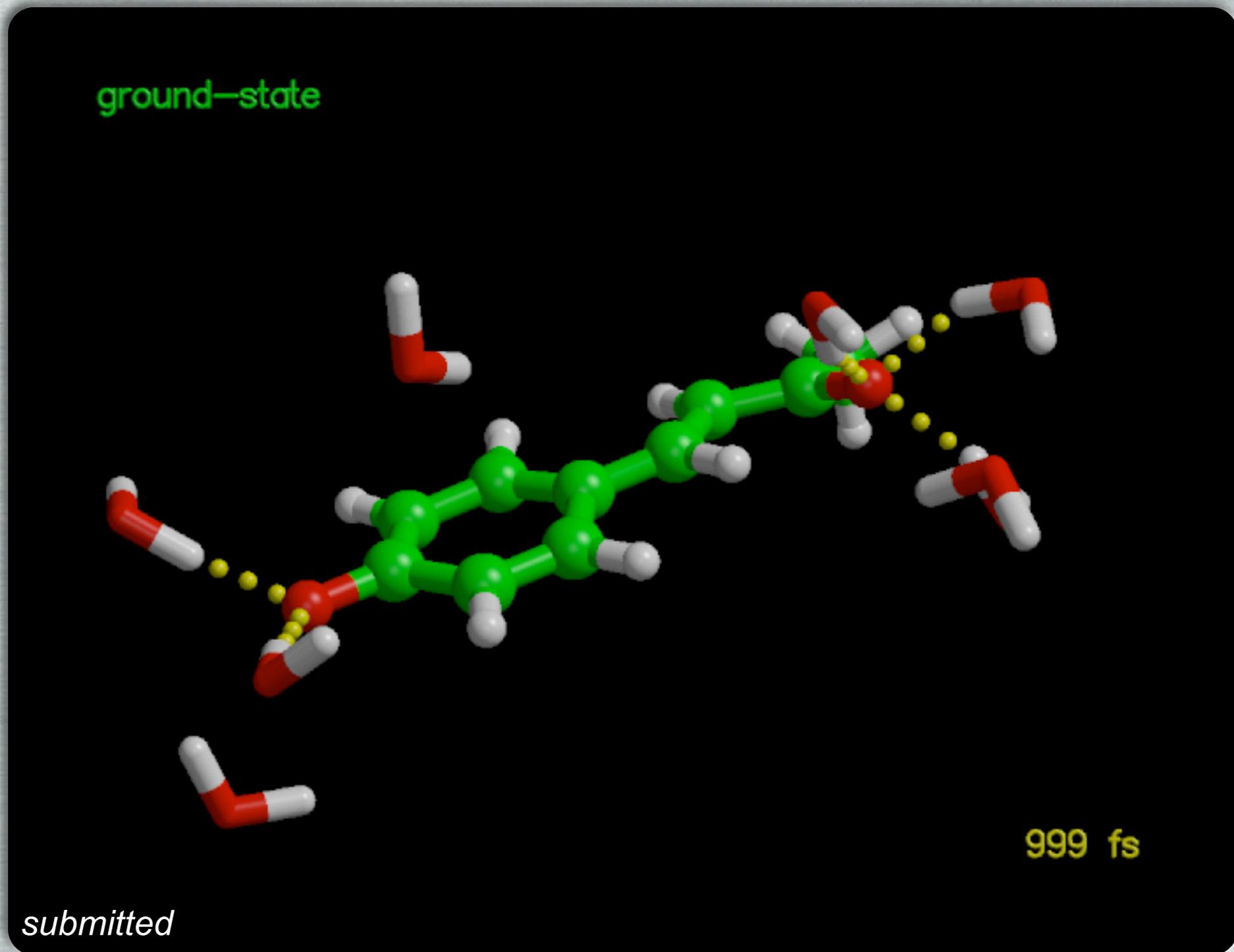
single bond photoisomerization (88%)



double bond photoisomerization (12%)

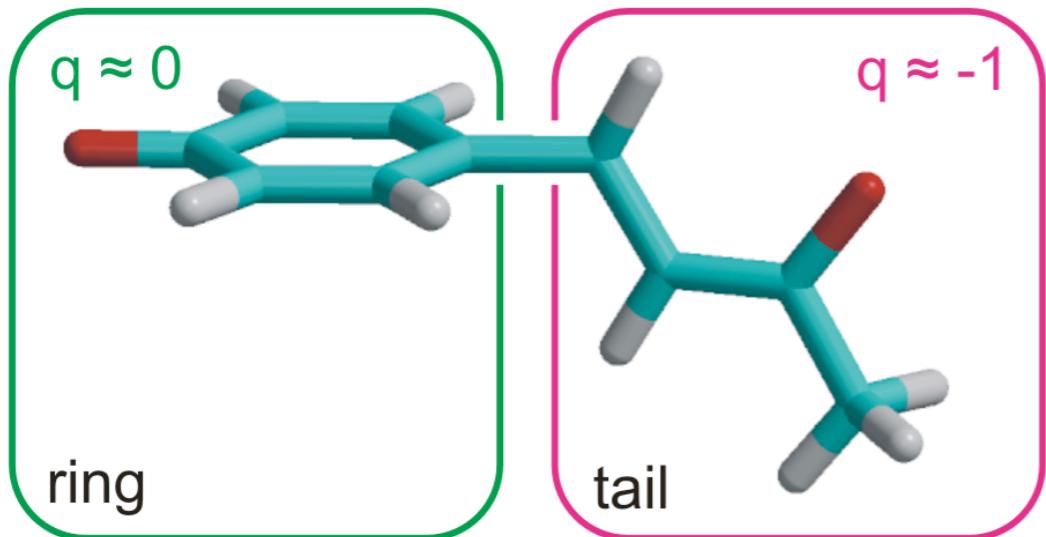
submitted

double bond photoisomerization (12%)



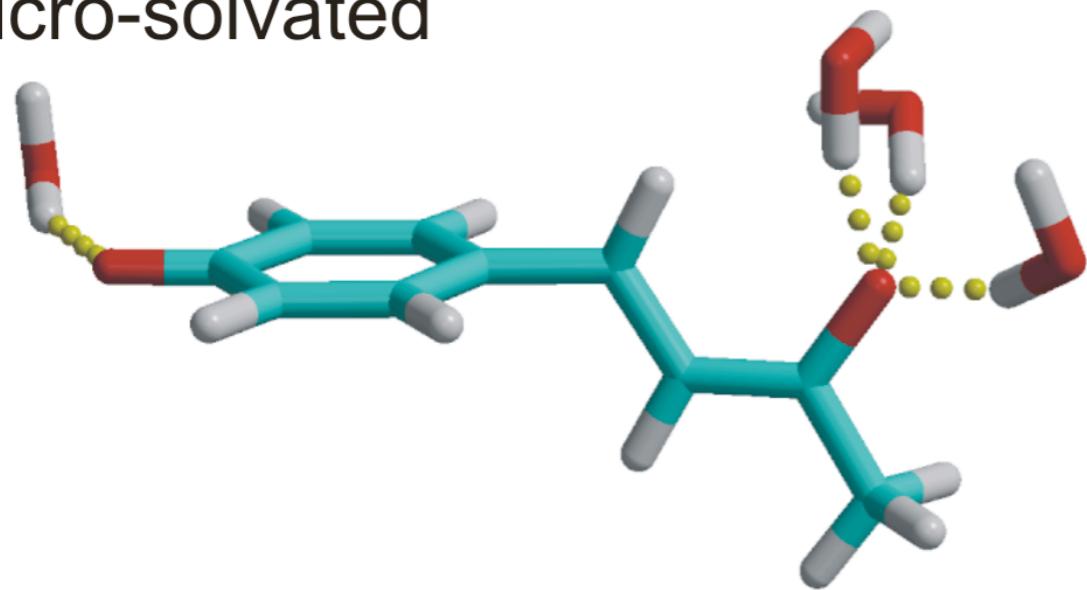
hydrogen bonds are essential

vacuum

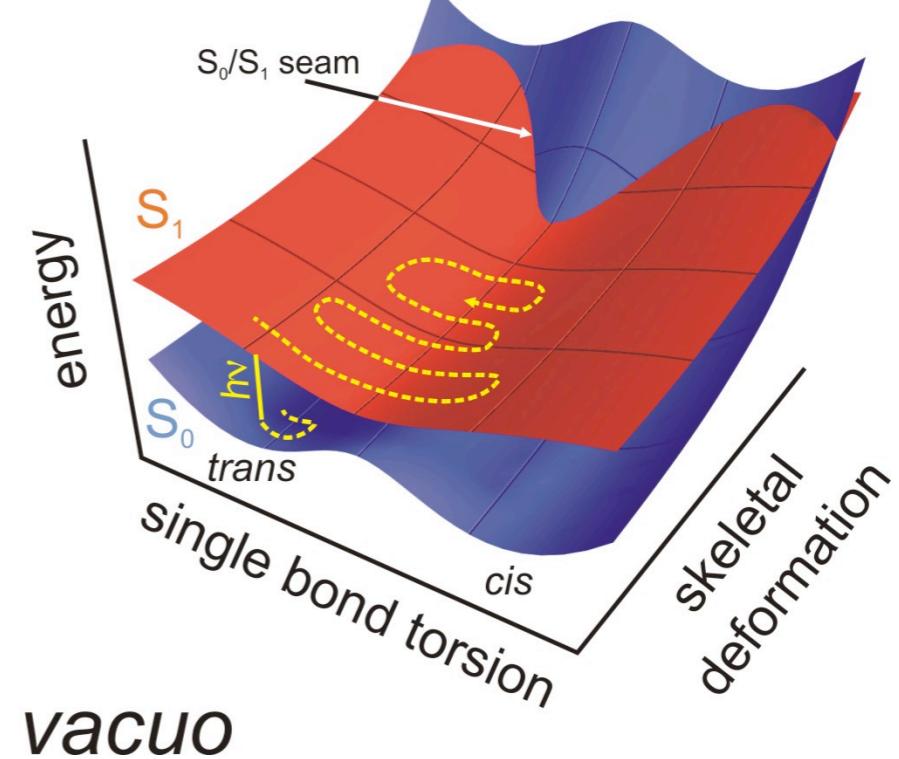


$$\Delta E_{S_0-S_1} = 167 \text{ kJ/mol}$$

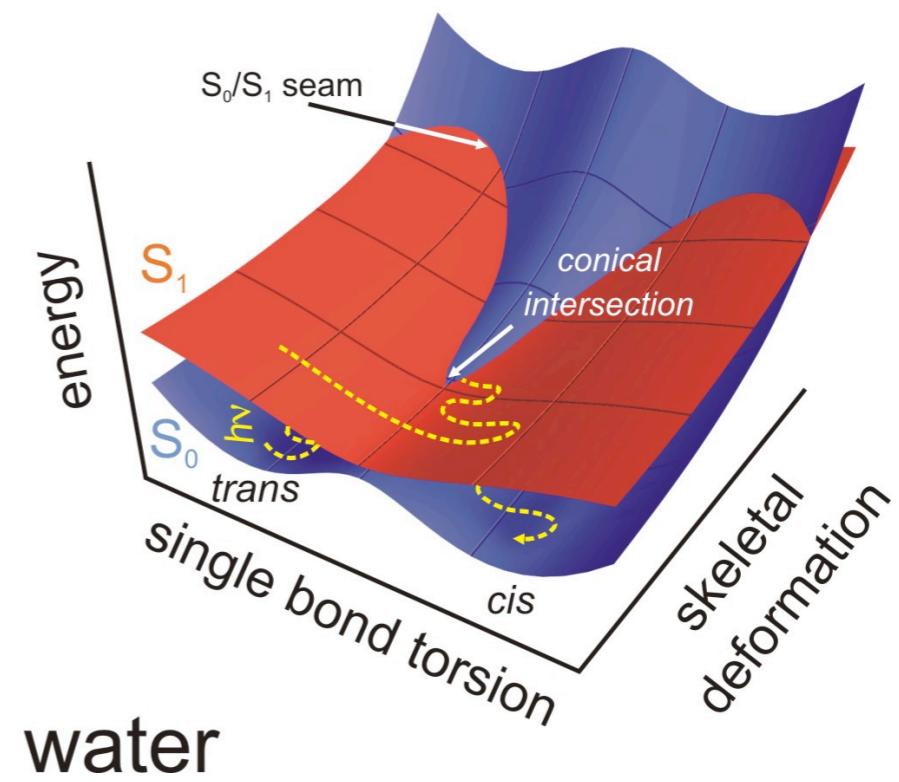
micro-solvated



$$\Delta E_{S_0-S_1} = 0 \text{ kJ/mol}$$



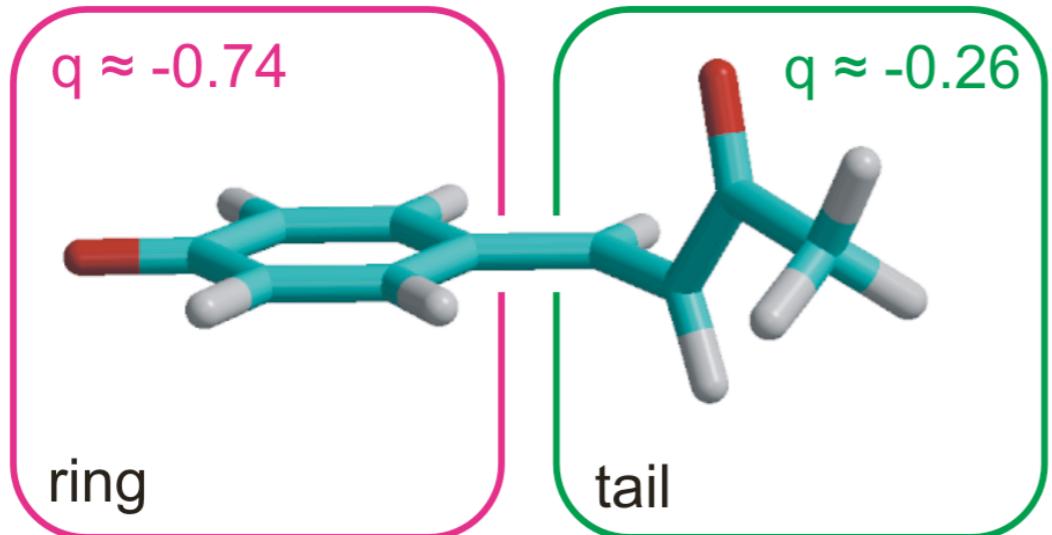
vacuo



water

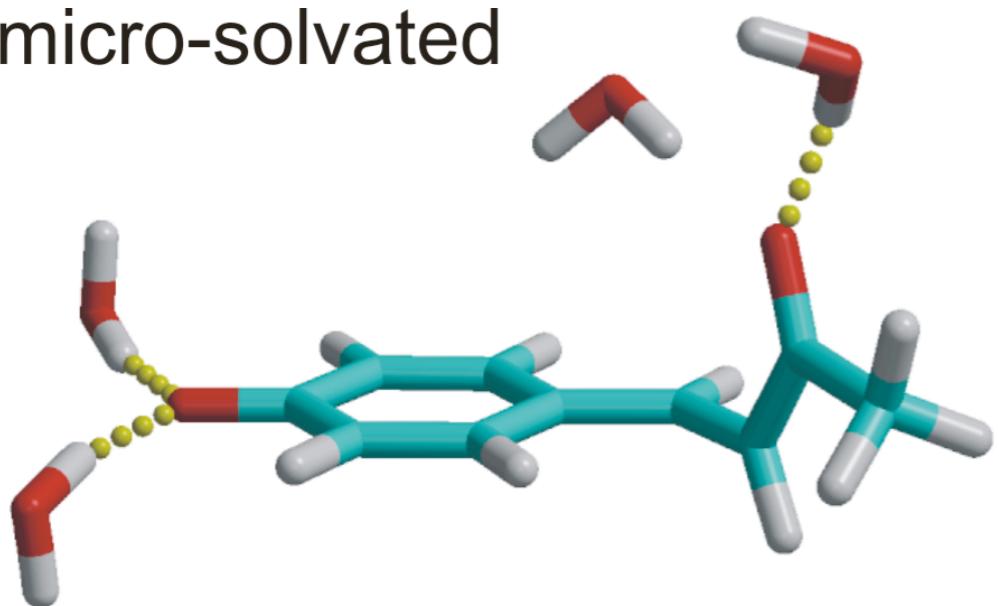
hydrogen bonds are essential

vacuum

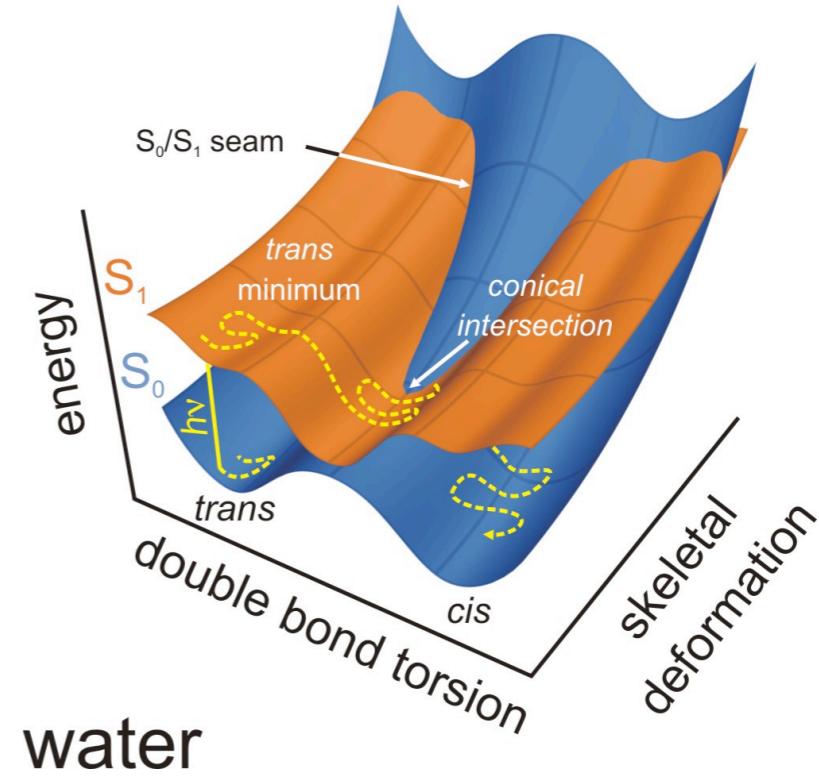
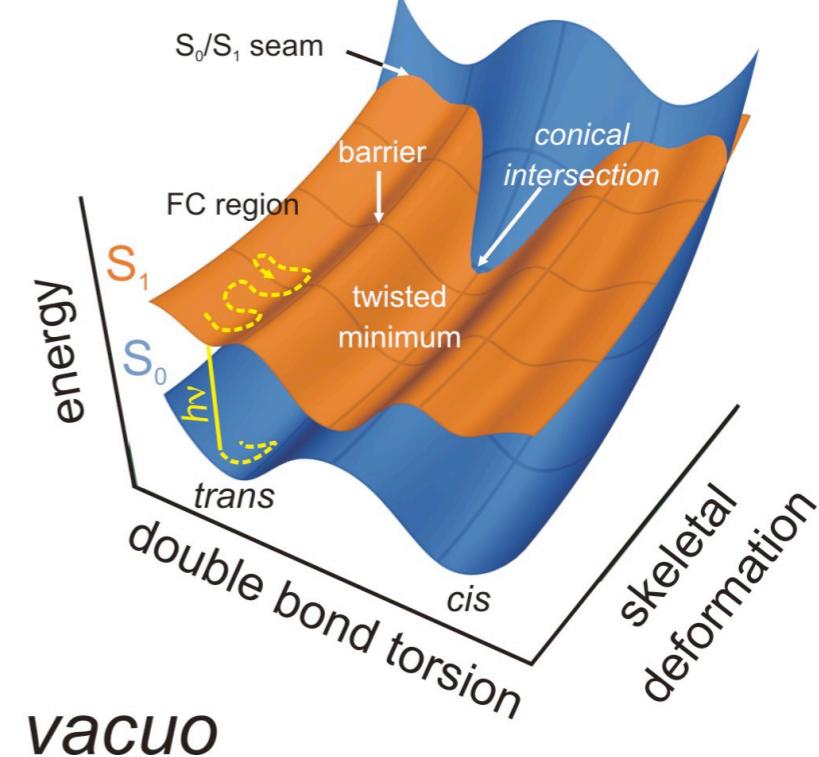


$$\Delta E_{S_0-S_1} = 91.2 \text{ kJ/mol}$$

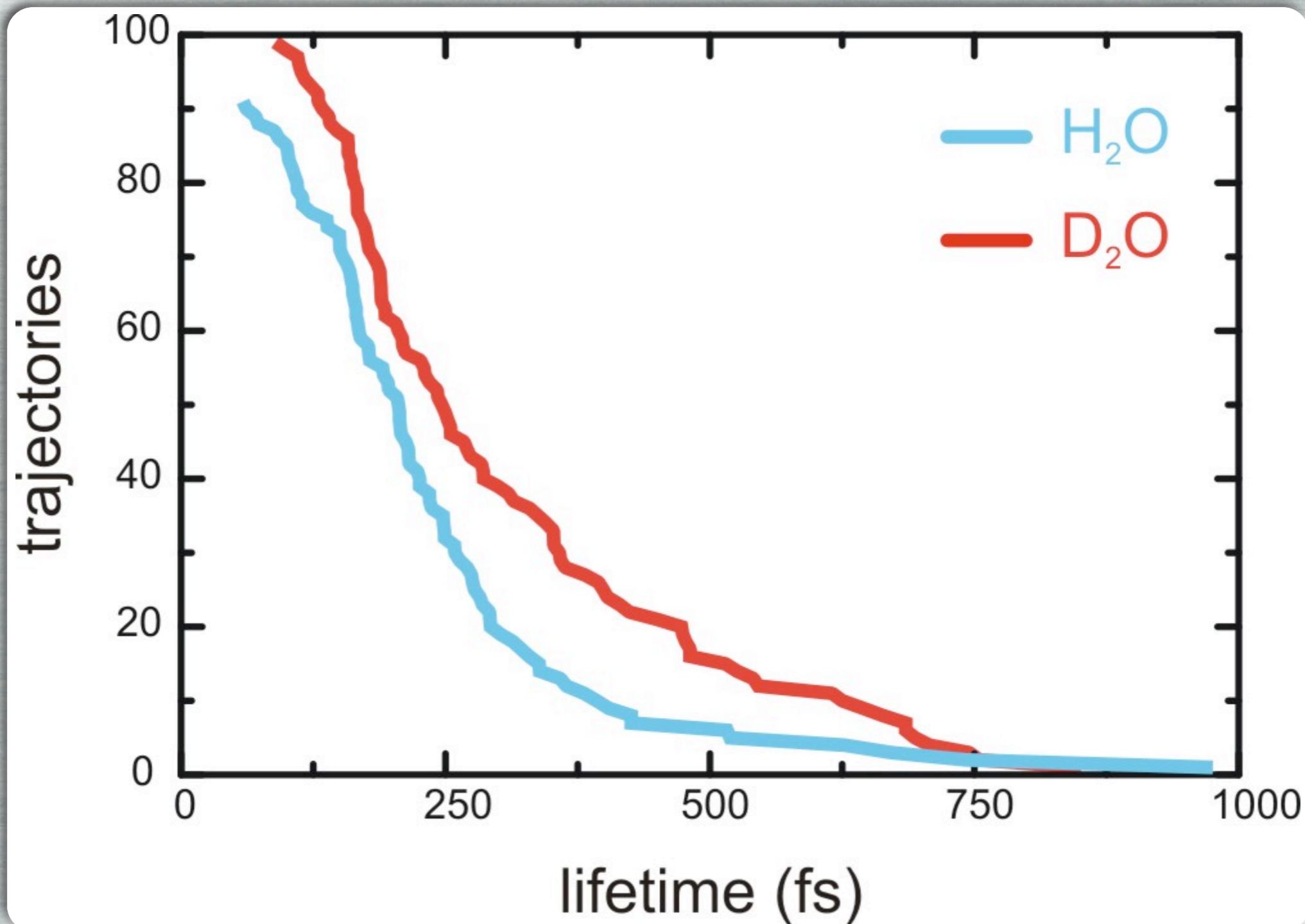
micro-solvated



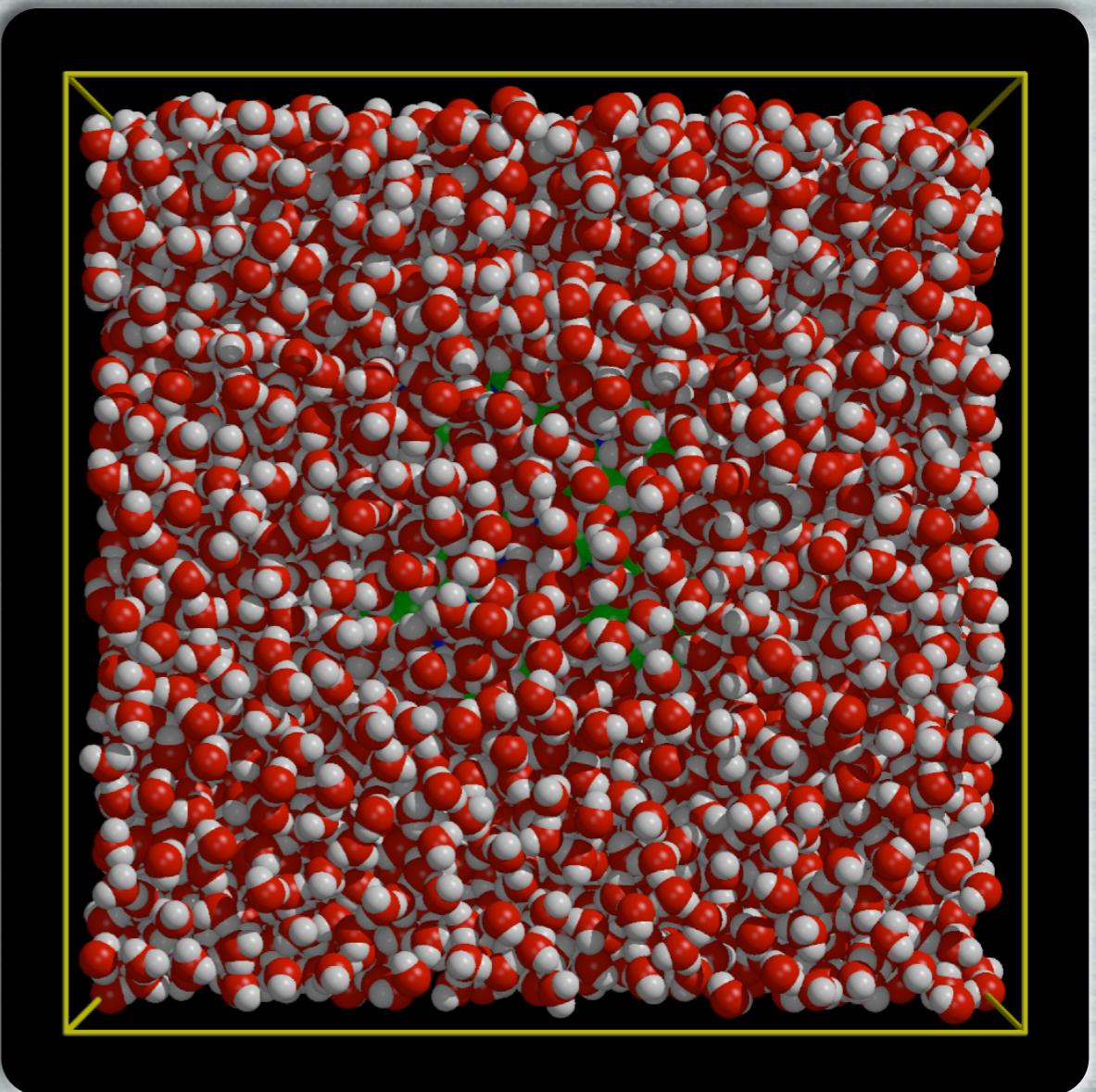
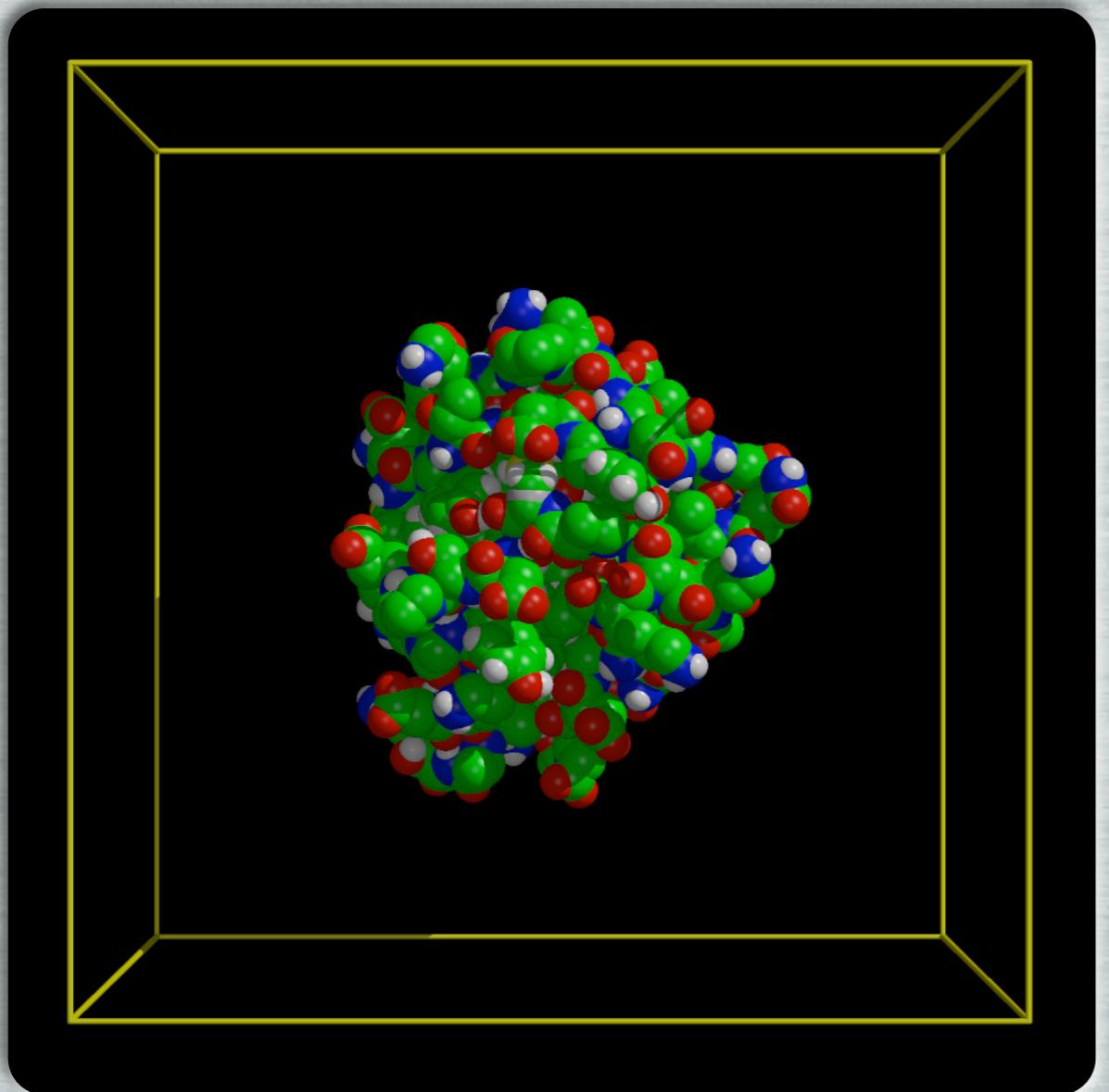
$$\Delta E_{S_0-S_1} = 0 \text{ kJ/mol}$$



isotope effect on re-organization

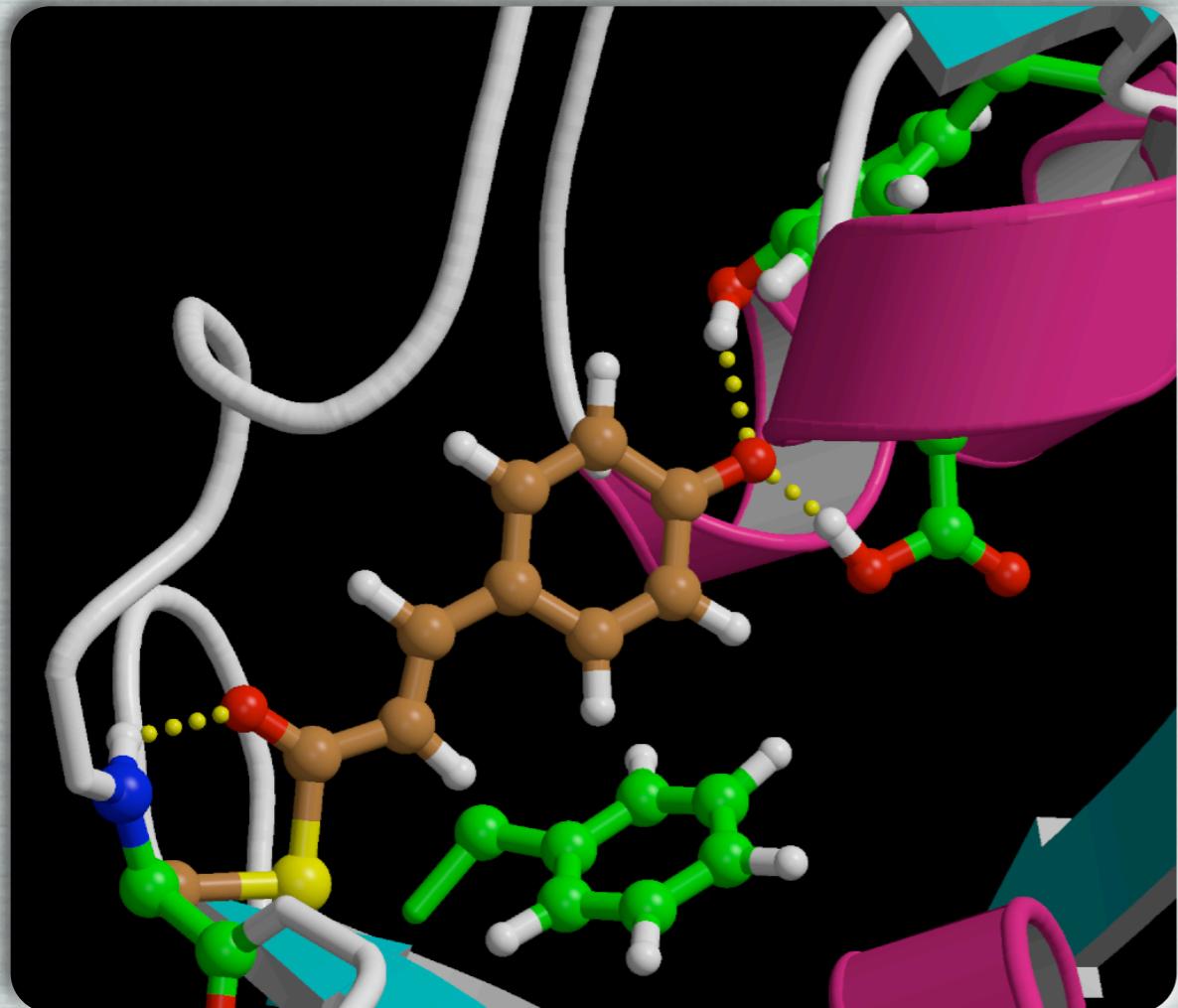


atomistic simulation of excited PYP



atomistic simulation of excited PYP

QM/MM protocol



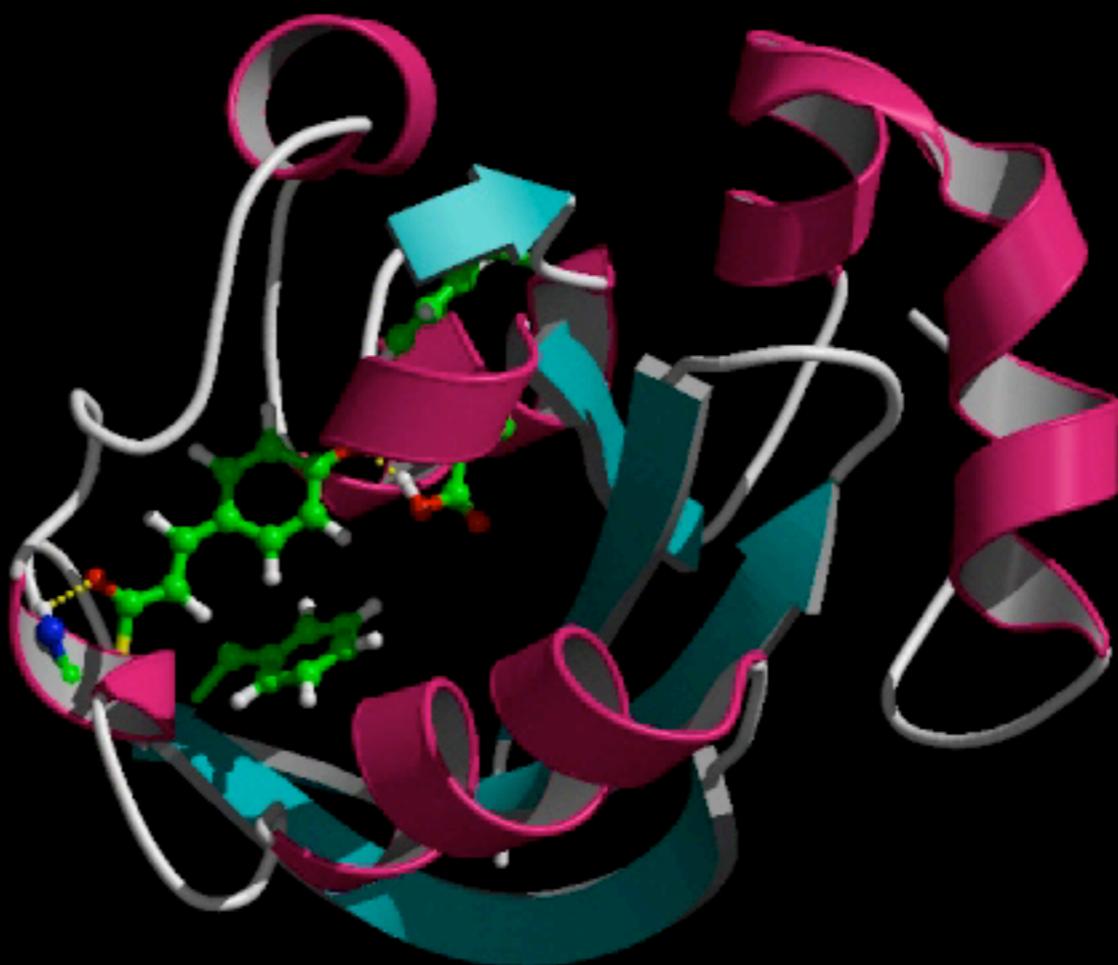
QM subsystem

- ▶ chromophore
- ▶ CASSCF(6,6)/3-21G
- ▶ surface hopping

MM subsystem

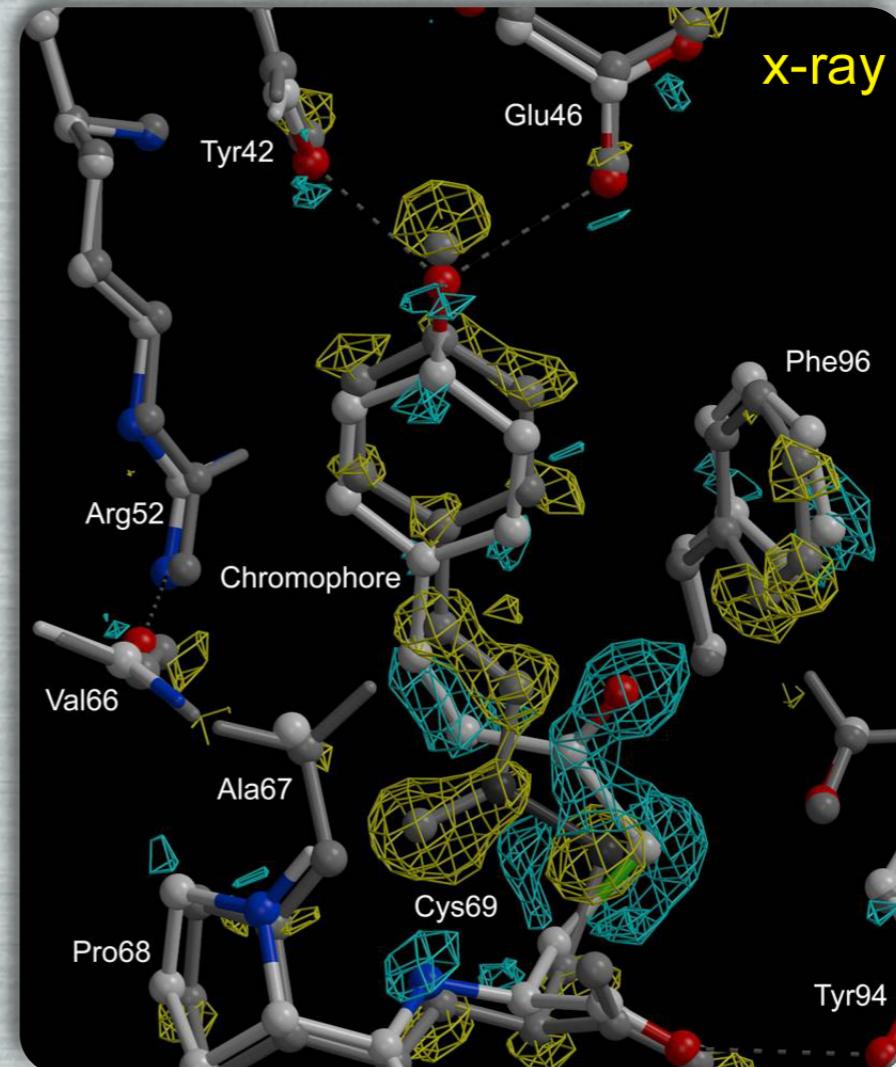
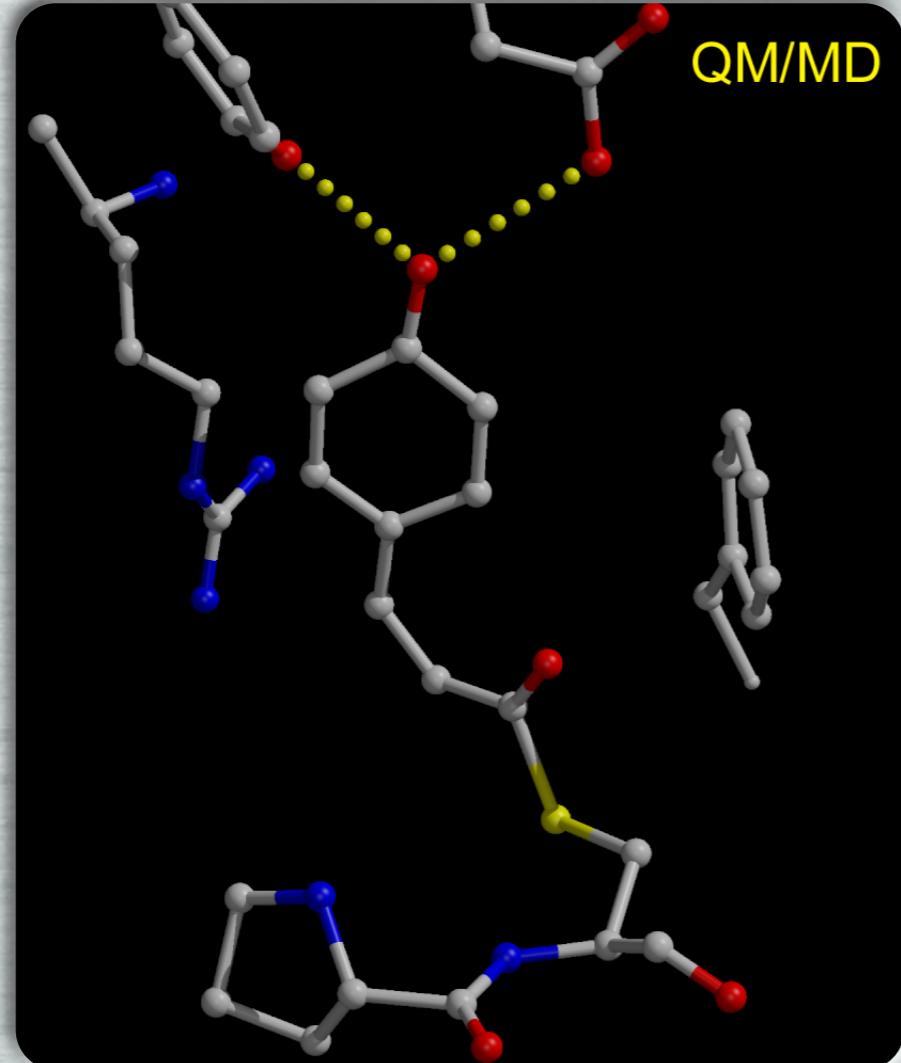
- ▶ apo-protein & water
- ▶ GROMOS96/SPC

atomistic simulation of excited PYP



JACS 124 (2004): 4228

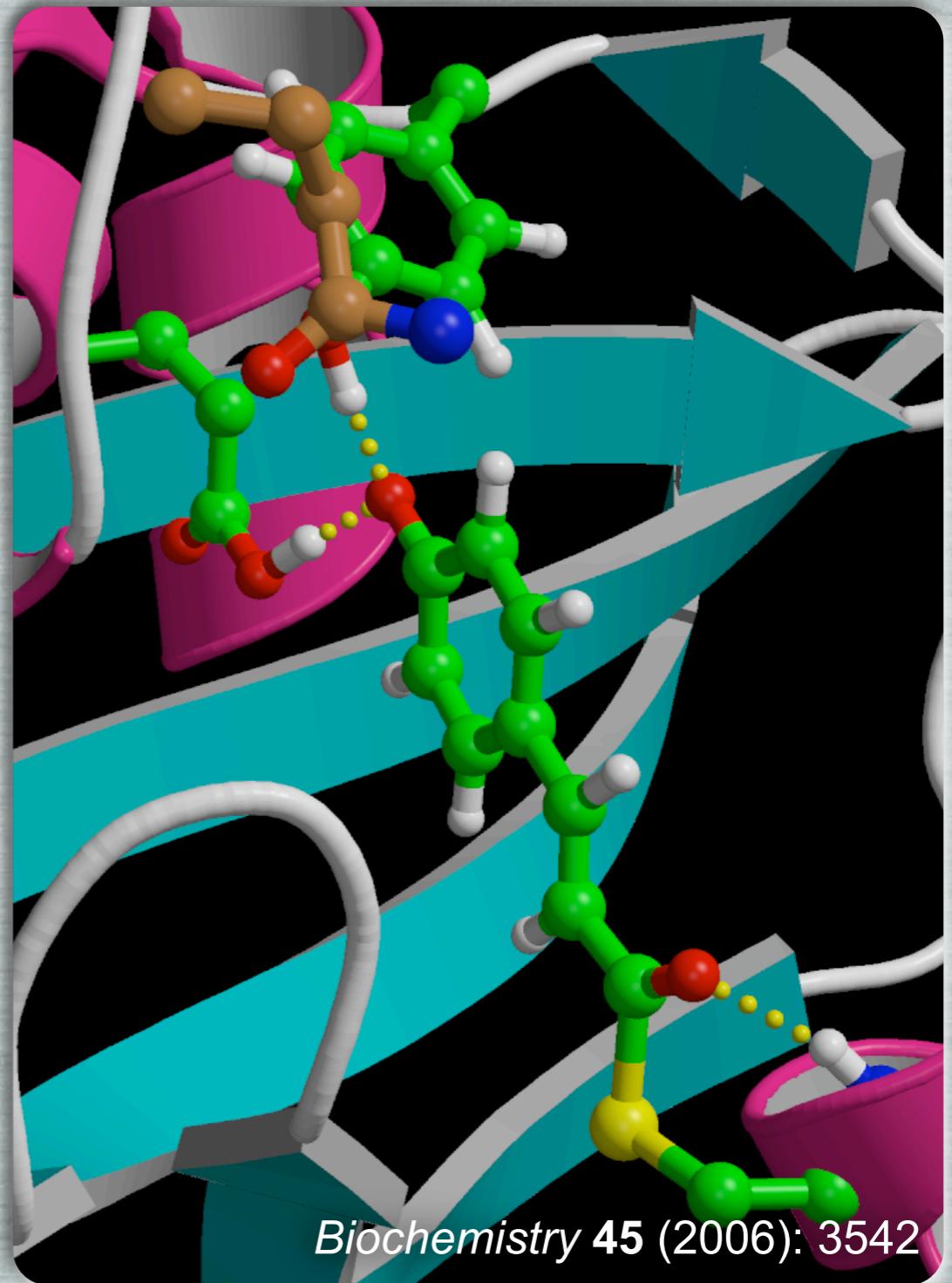
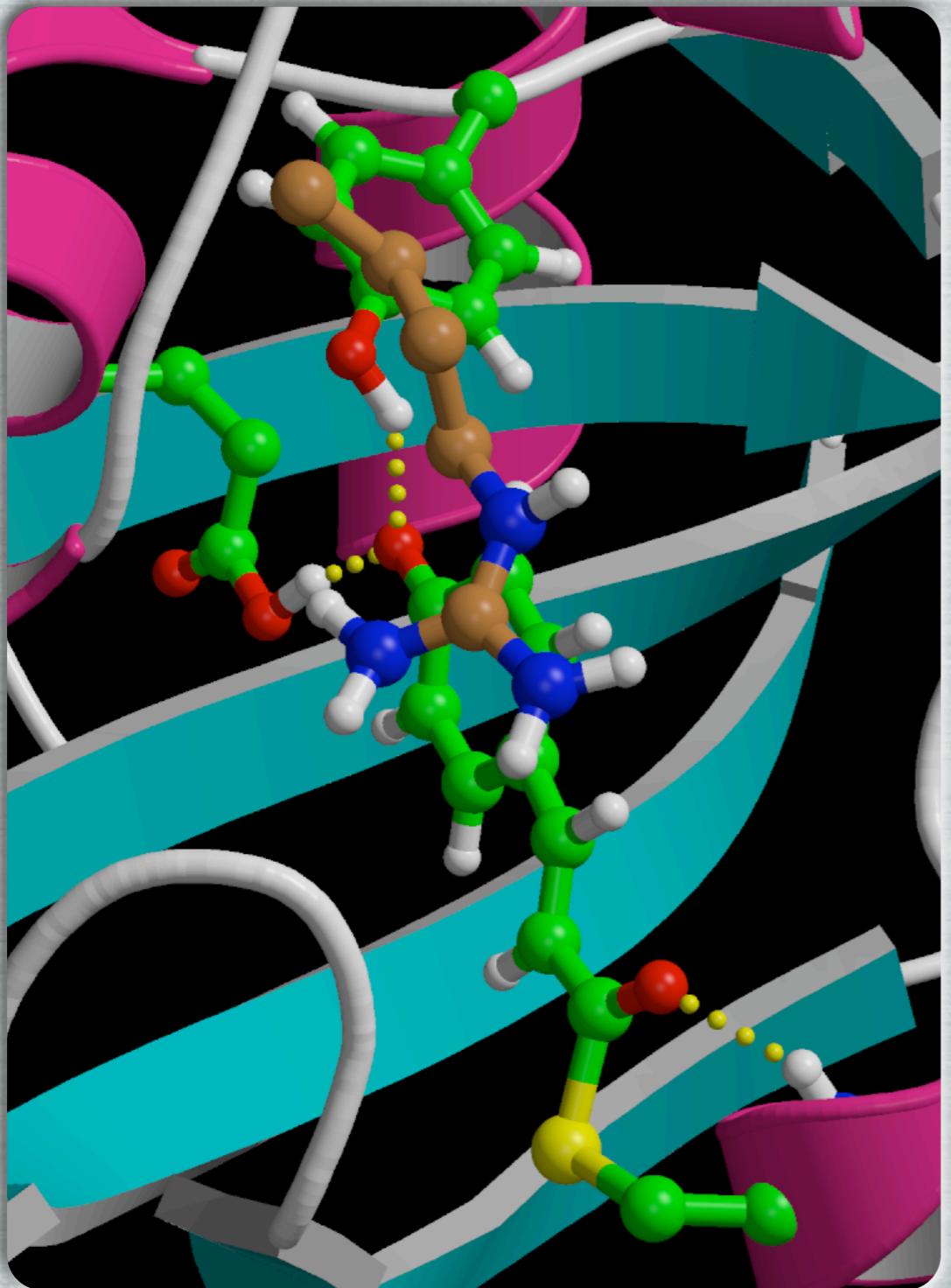
atomistic simulation of excited PYP



comparison to experimental structure

► Kort et al. *J. Biol. Chem.* **279**: 26417-26424 (2004)

arginine/glutamine mutant

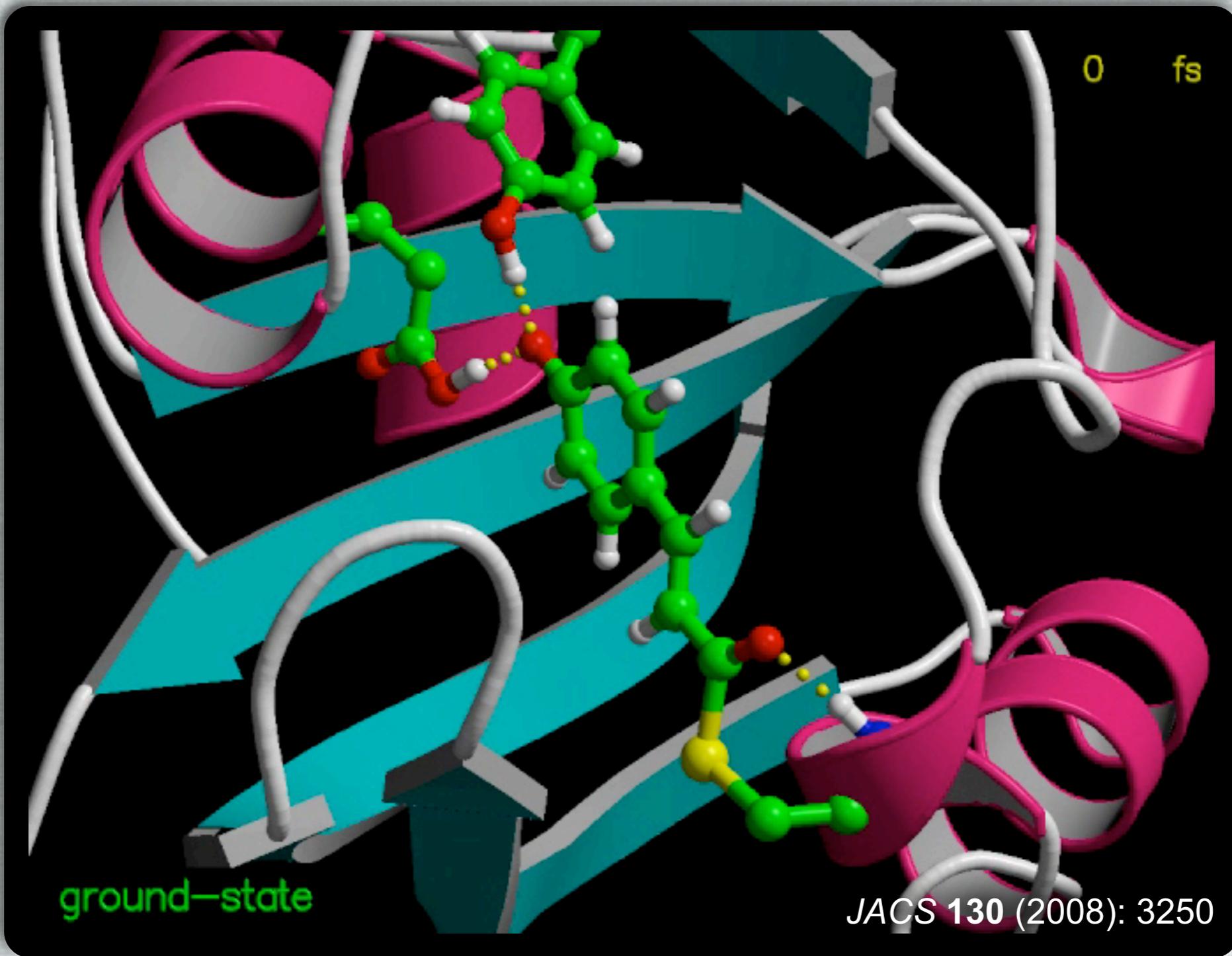


Biochemistry 45 (2006): 3542

atomistic simulation of excited R52Q

JACS 130 (2008): 3250

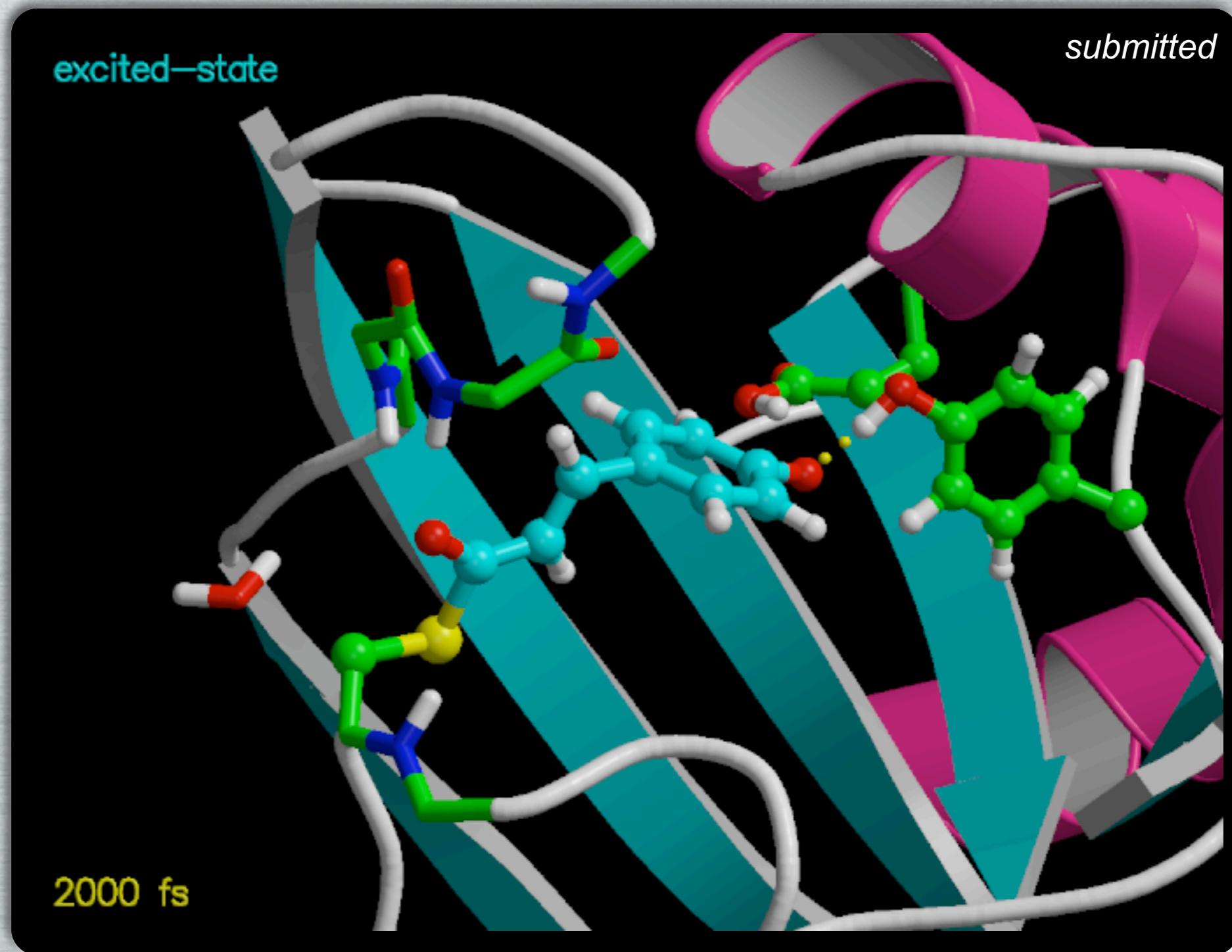
atomistic simulation of excited R52Q



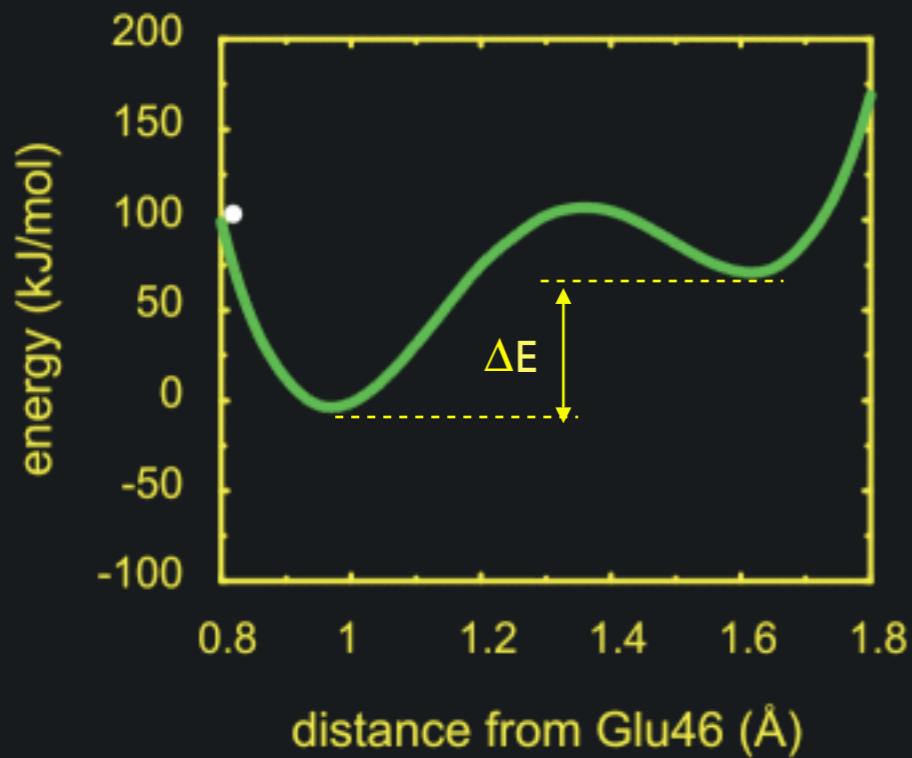
stabilizing H-bonds in R52Q mutant

submitted

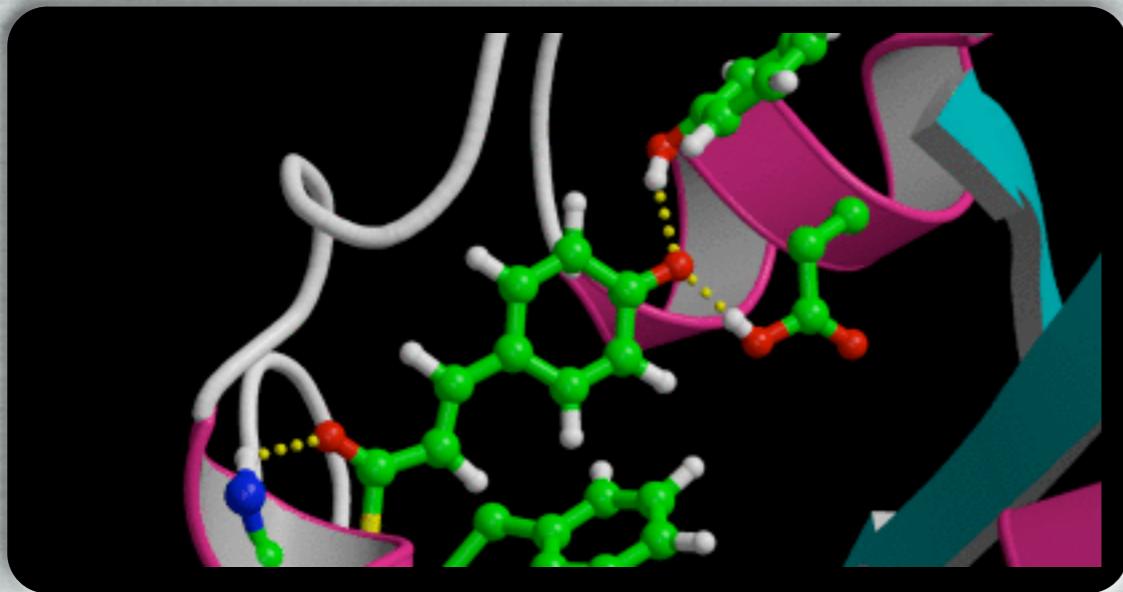
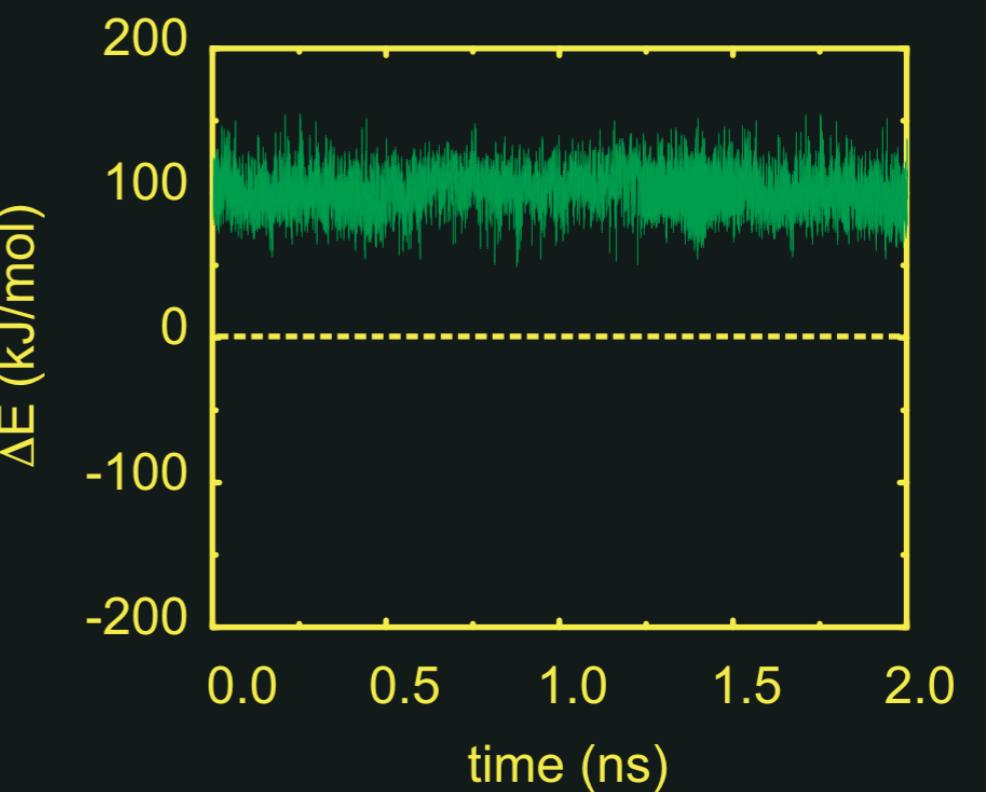
stabilizing H-bonds in R52Q mutant



atomistic simulation of excited PYP

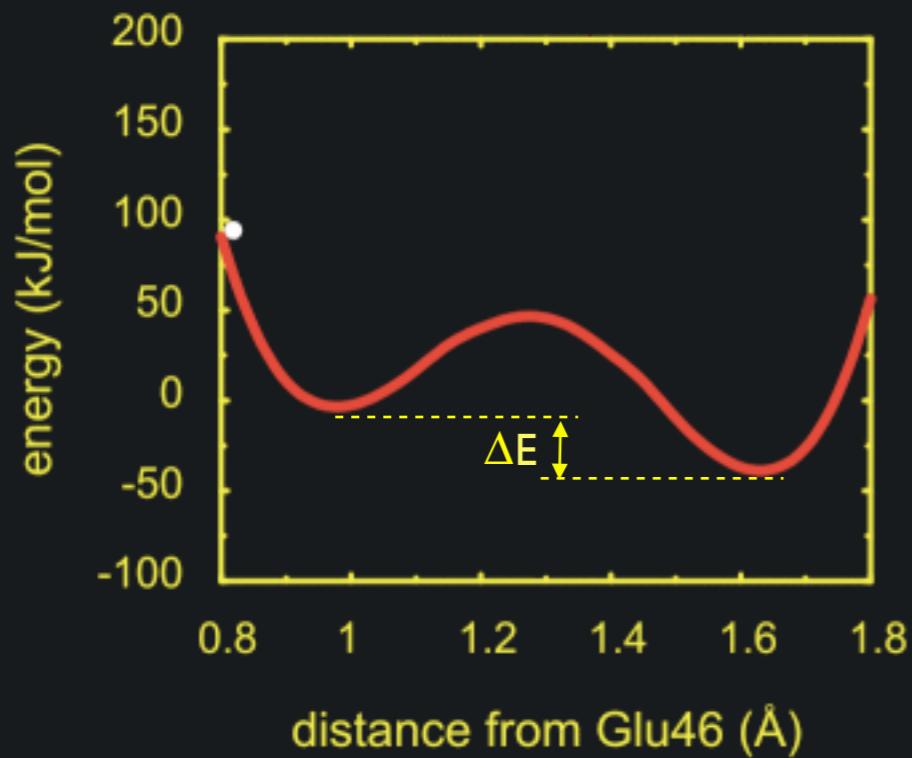


QM/MM (Gromos/PM3)

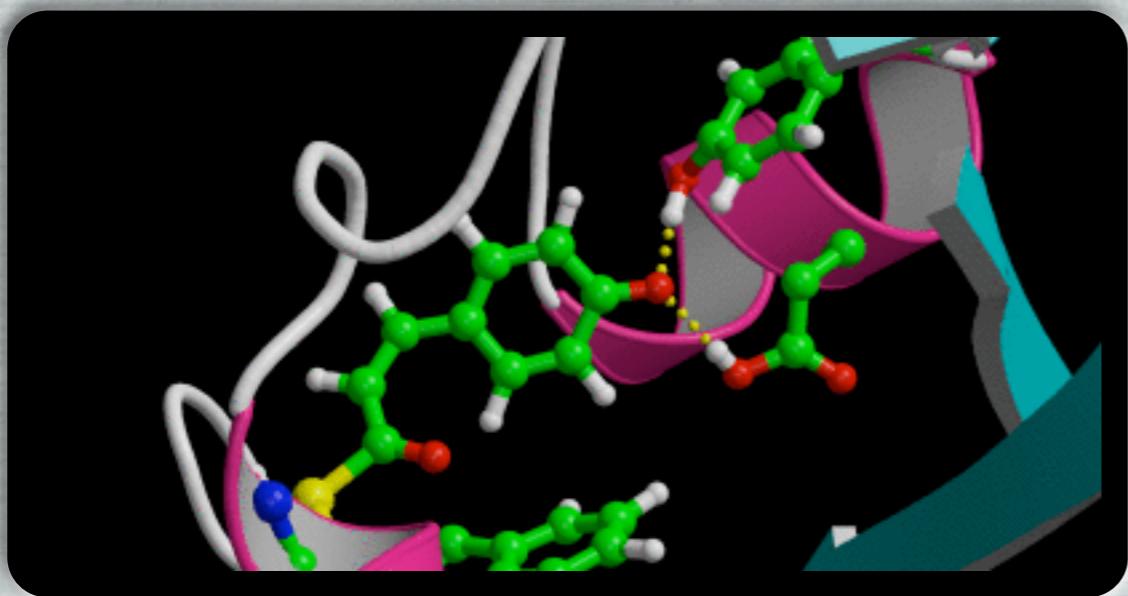
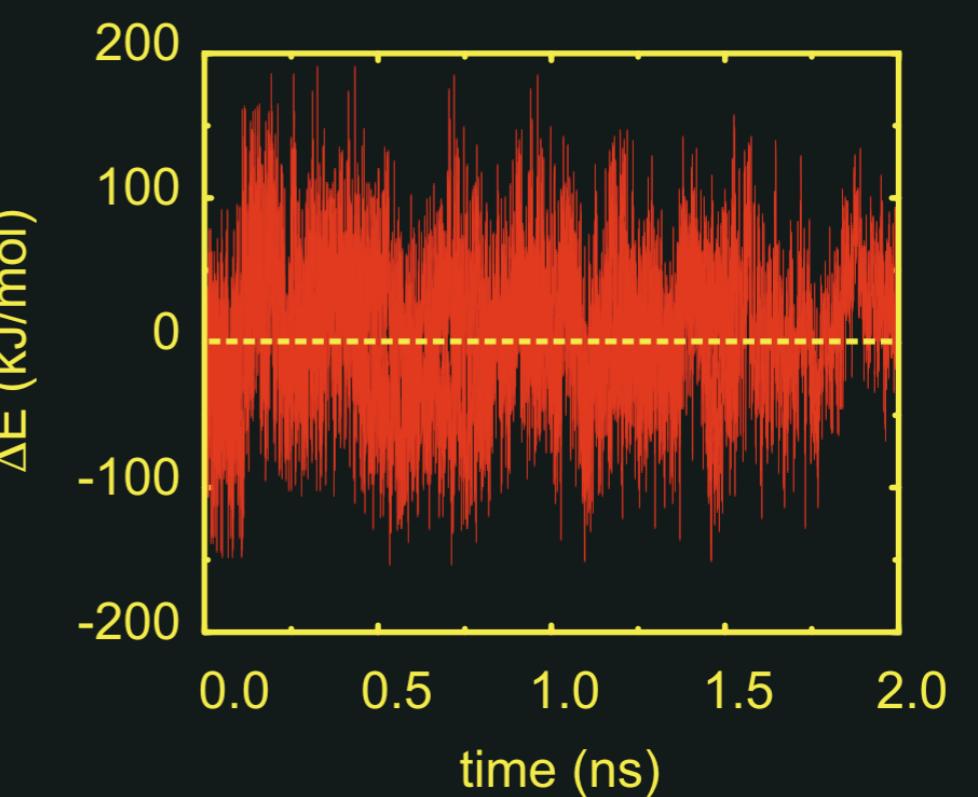


before isomerization
► proton cannot transfer

atomistic simulation of excited PYP

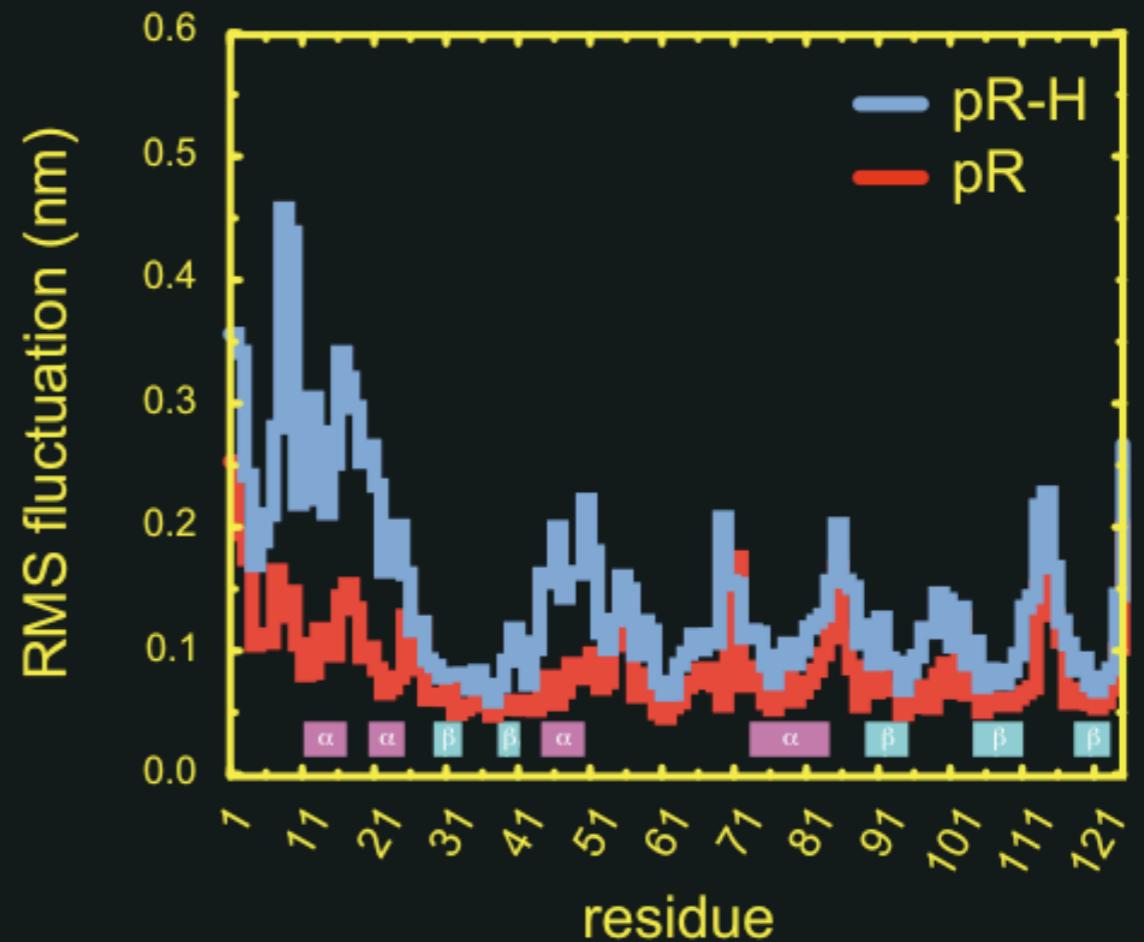
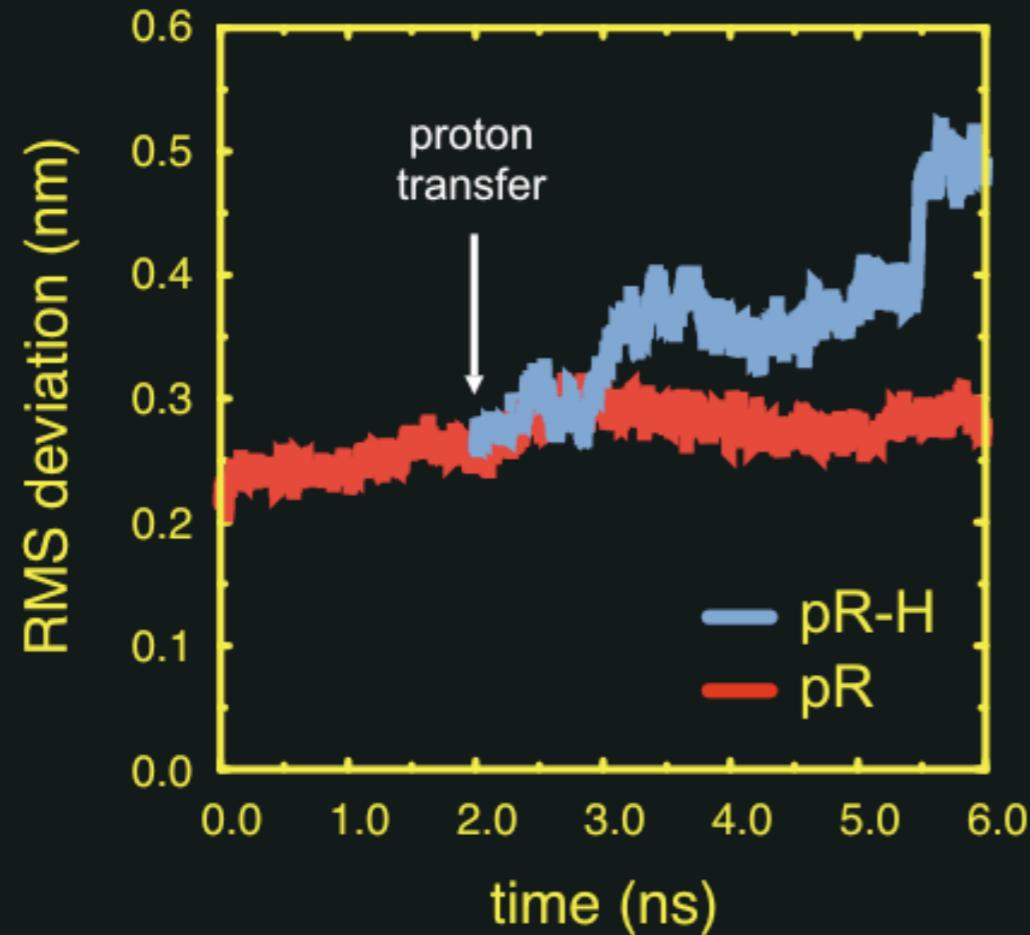


QM/MM (Gromos/PM3)



after isomerization
► proton can transfer

atomistic simulation of excited PYP



proton transfer induces unfolding

activation mechanism of PYP

photon absorption

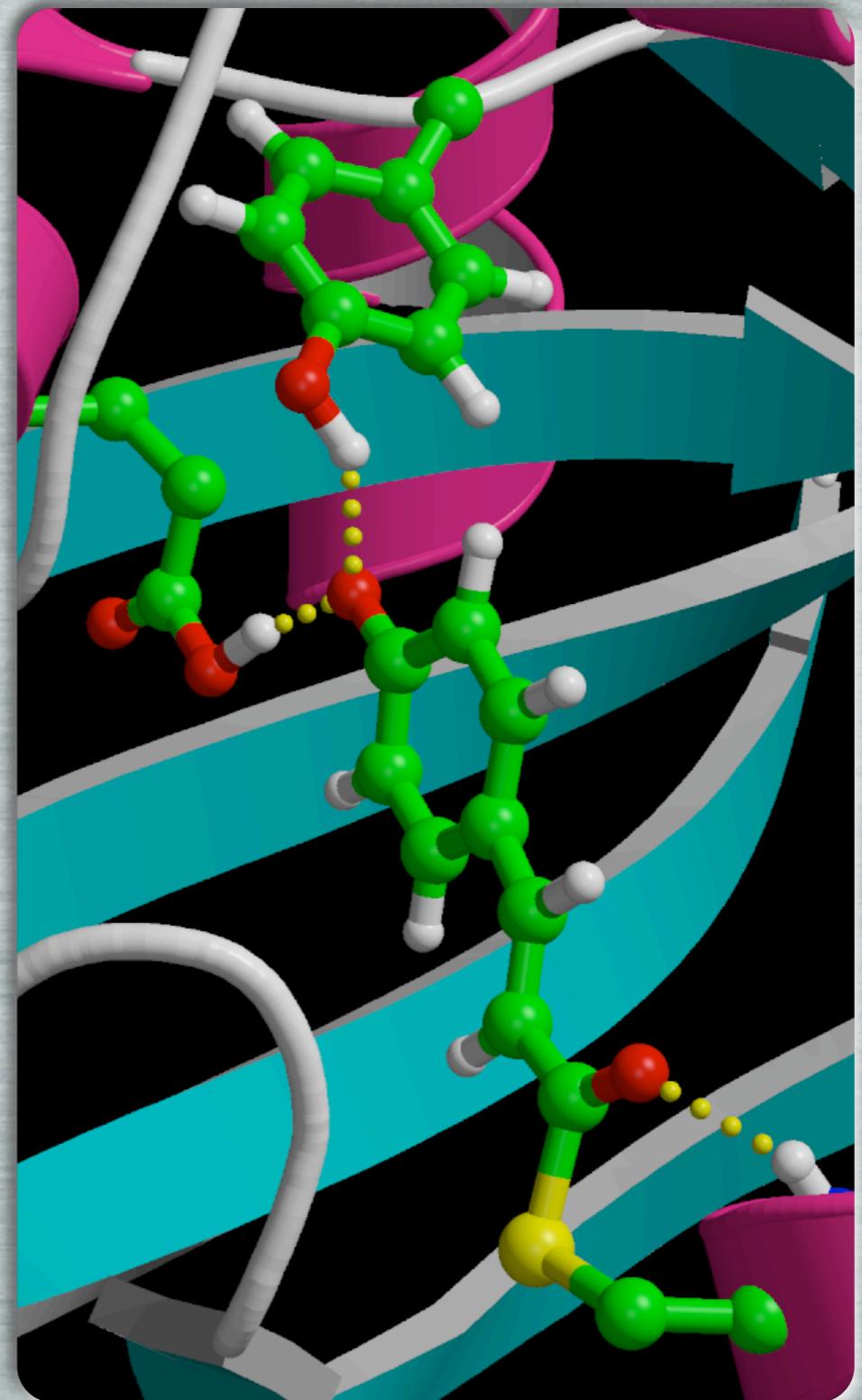
photo-isomerization

carbonyl flip

proton transfer

partial unfolding

signalling state





acknowledgements

Martial Boggio-Pasqua

Lars Schäfer

Michael Robb

Gromacs team

David van der Spoel

Erik Lindahl

Berk Hess



open positions at the
Max-Planck-Institute for biophysical chemistry
Göttingen, Germany

ggroenh@gwdg.de