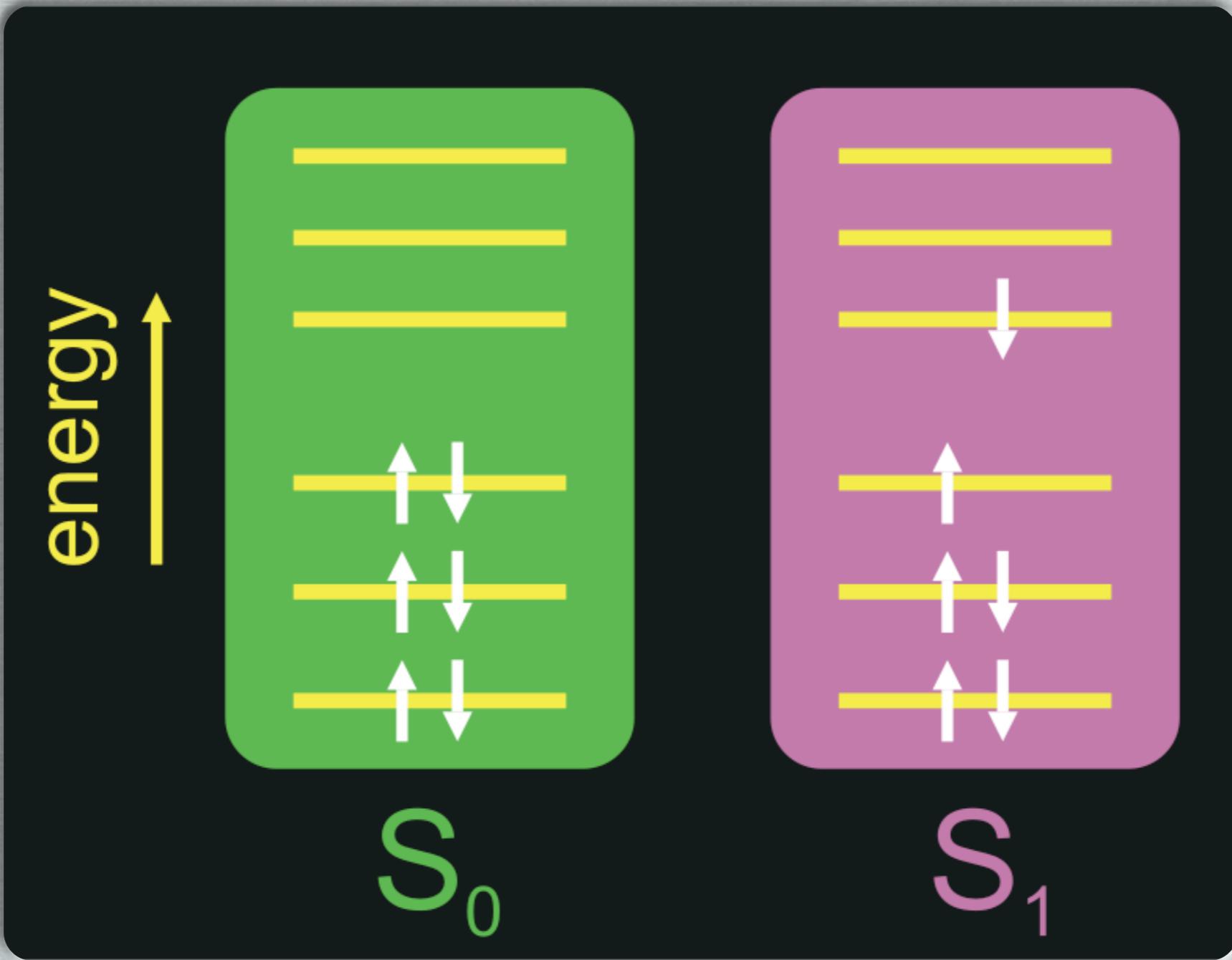


Light-induced processes in biological systems: from first-principles to biotechnology

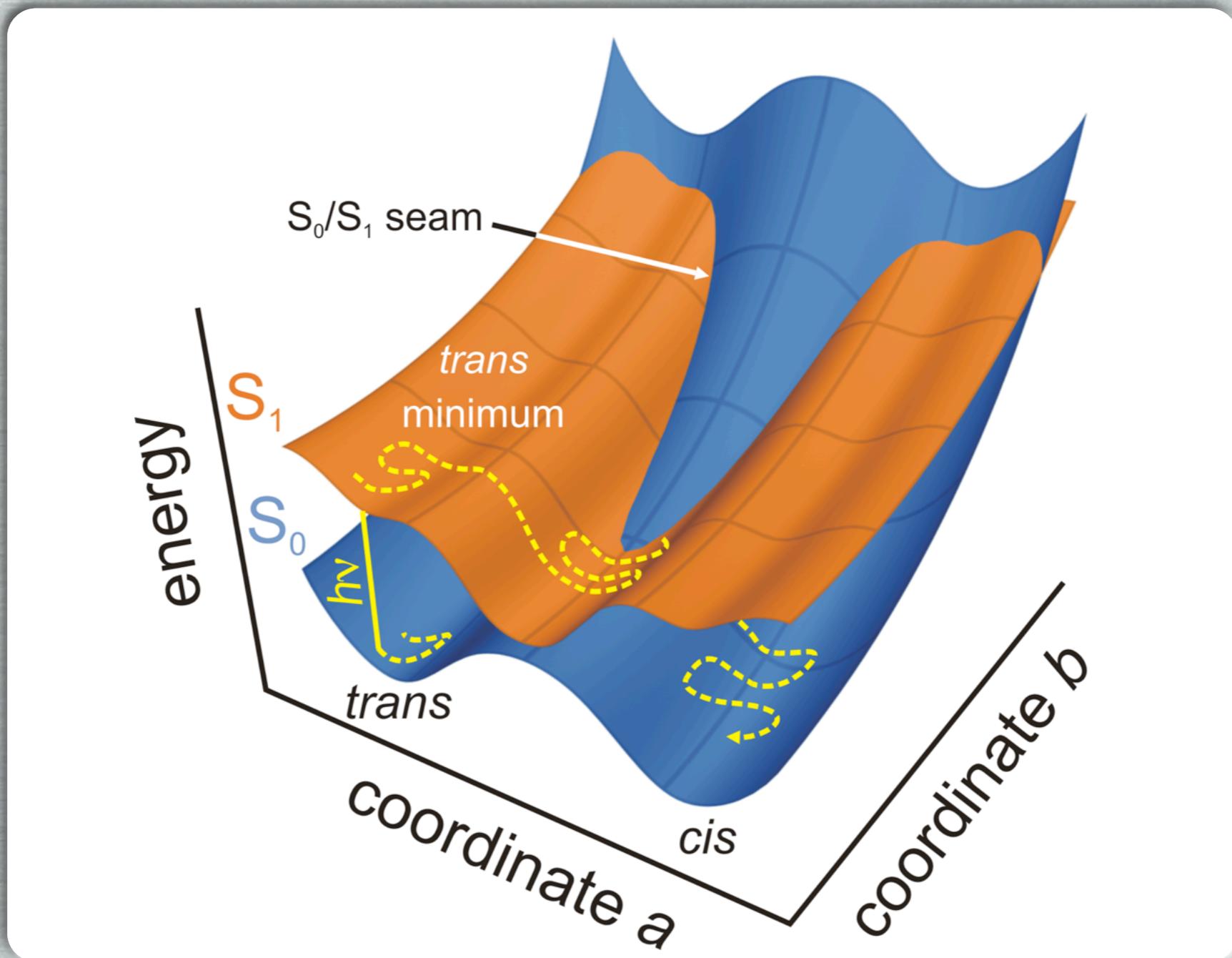
```
real calculate_QMMM(t_commrec *cr, rvec x[],rvec f[],
                     t_forcerec *fr, t_mdatoms *md){
    real
        QMener=0.0;
    t_QMMrec
        *qr;
    t_QMrec
        *qm;
    t_MMrec
        *mm=NULL;
    rvec
        *forces=NULL,*fshift=NULL;
    int
        i,j,k;
    qr = fr->qr;
    mm = qr->mm;
    qm = qr->qm[0];
    snew(forces,(qm->nrQMatoms+mm->nrMMatoms));
    snew(fshift,(qm->nrQMatoms+mm->nrMMatoms));
    QMener = call_QMroutine(cr,fr,qm,mm,forces,fshift);
    for(i=0;i<qm->nrQMatoms;i++){
        for(j=0;j<DIM;j++){
            f[qm->indexQM[i]][j]           == forces[i][j];
            fr->fshift[qm->shiftQM[i]][j] += fshift[i][j];
        }
    }
    for(i=0;i<mm->nrMMatoms;i++){
        for(j=0;j<DIM;j++){
            f[mm->indexMM[i]][j]           == forces[qm->nrQMatoms+i][j];
            fr->fshift[mm->shiftMM[i]][j] += fshift[qm->nrQMatoms+i][j];
        }
    }
    free(forces);
    free(fshift);
}
```

Gerrit Groenhof

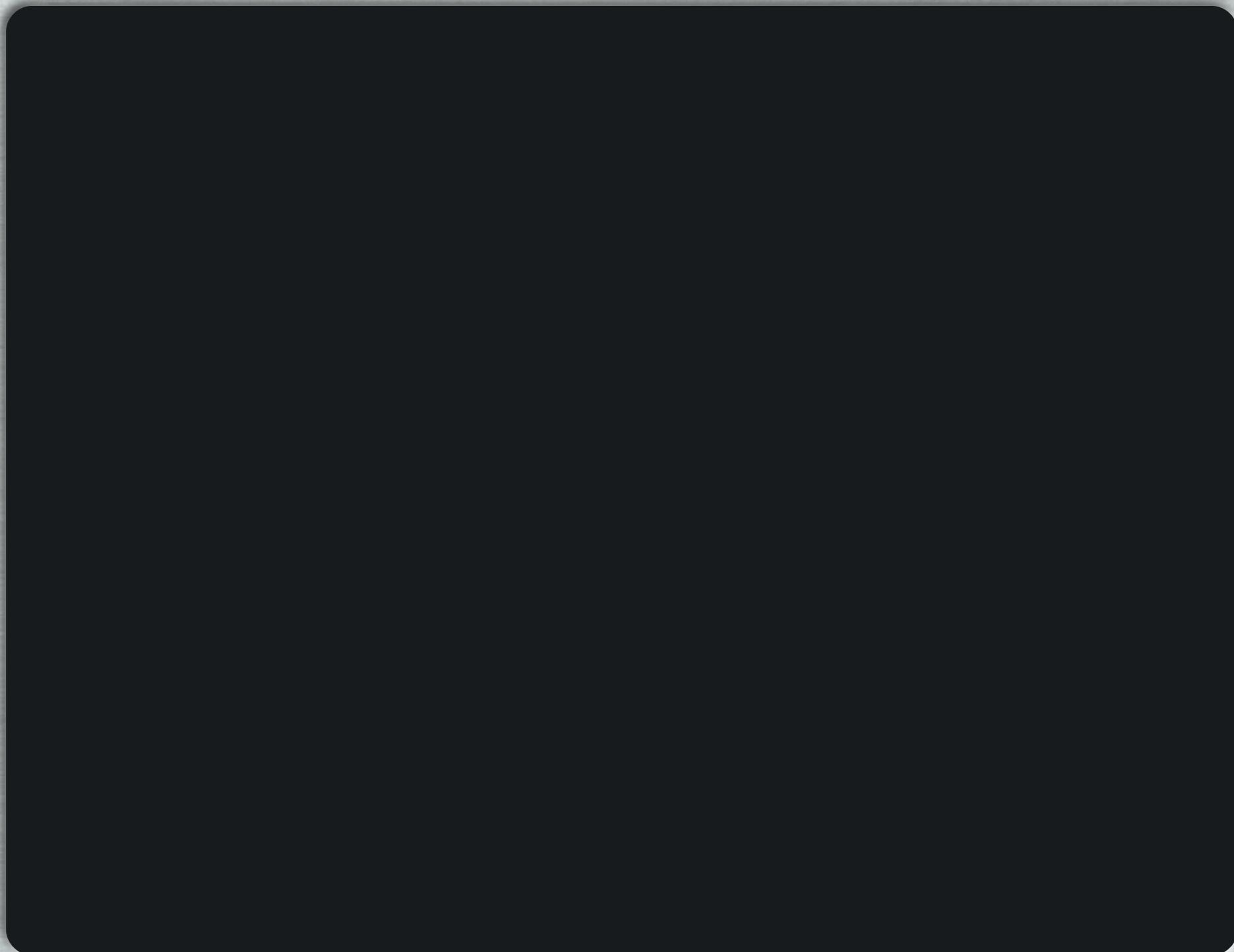
Chemistry in the Excited State



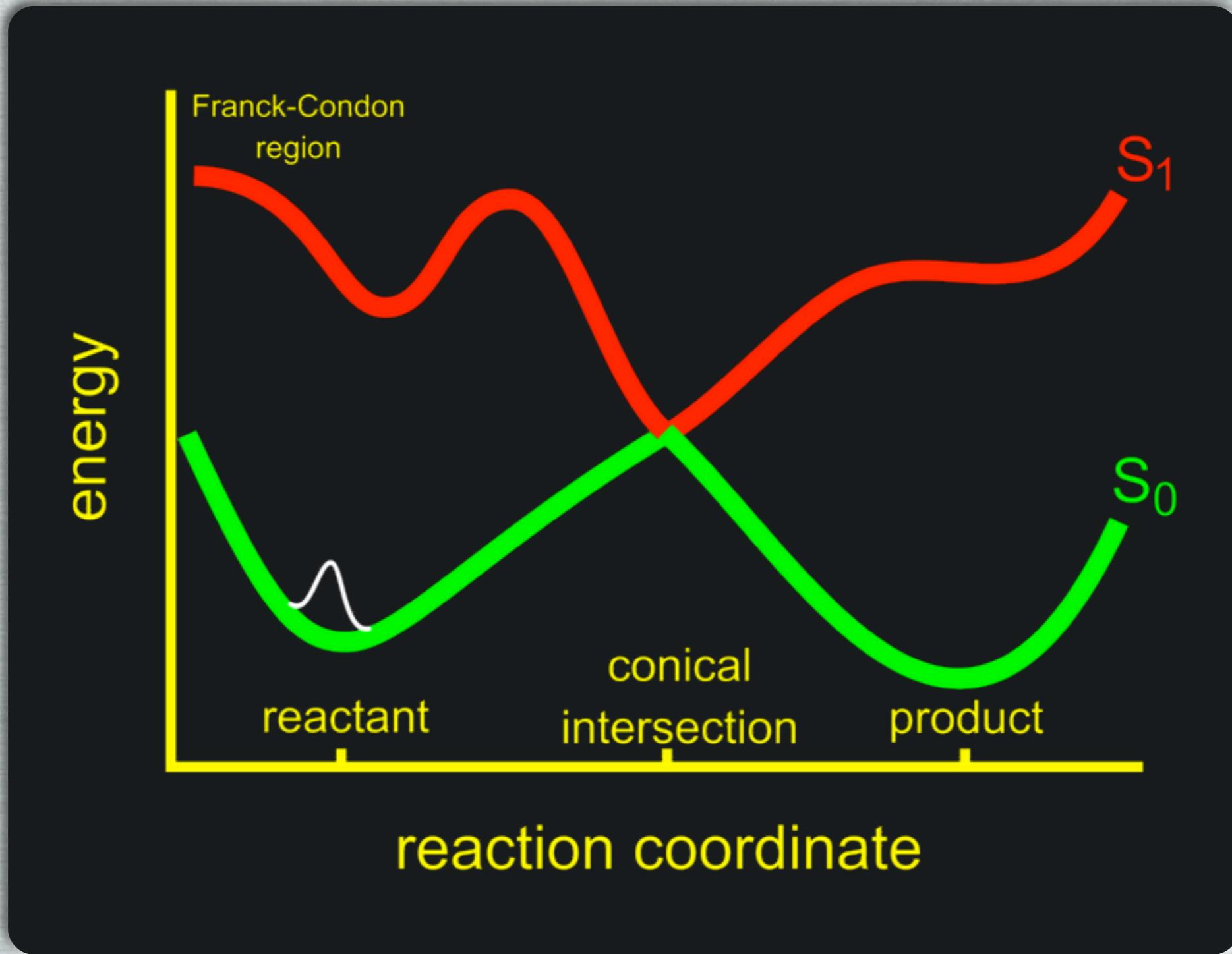
Chemistry in the Excited State



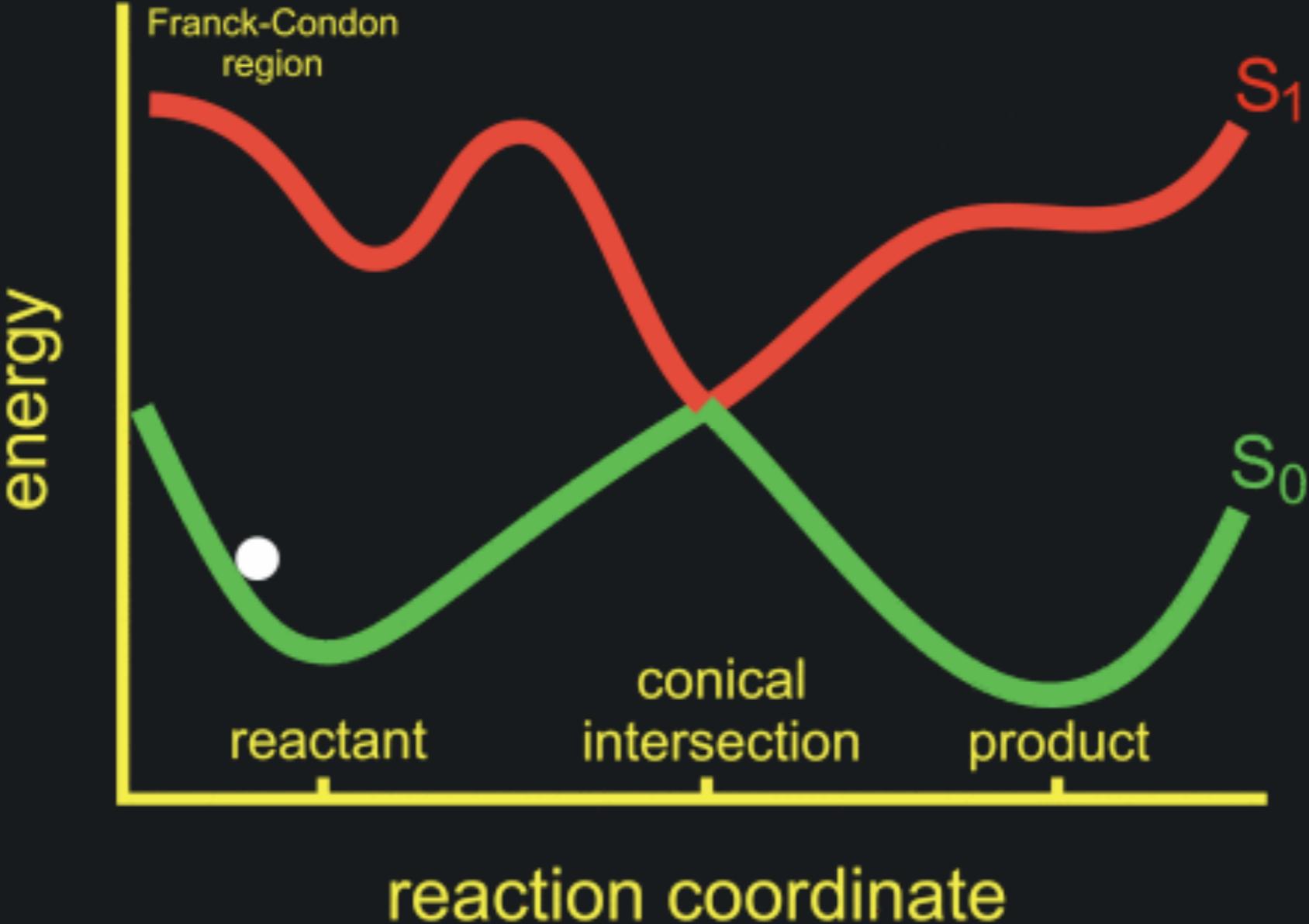
wavepacket dynamics simulation



wavepacket dynamics simulation



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

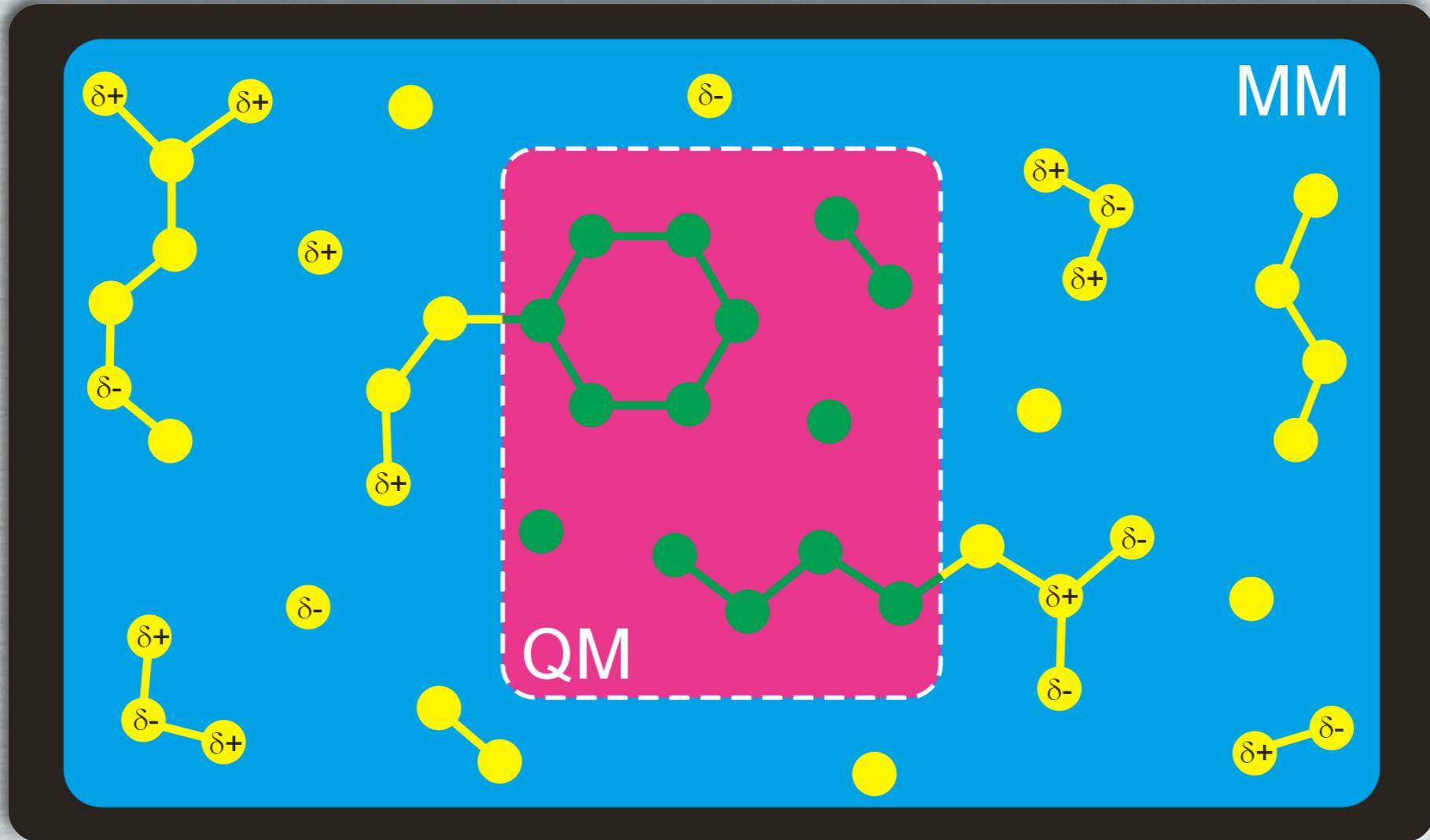
► molecular mechanics forcefield

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

► 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

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

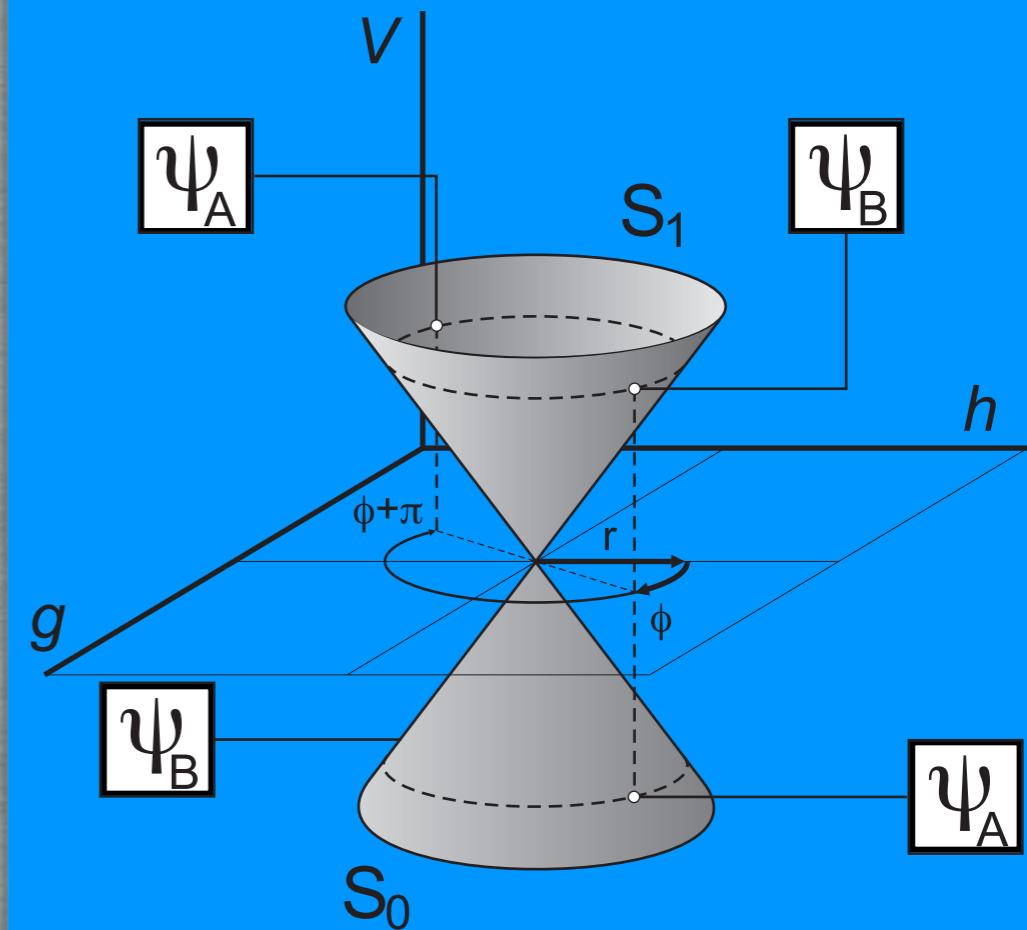
Massey parameter

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

wavefunction overlap

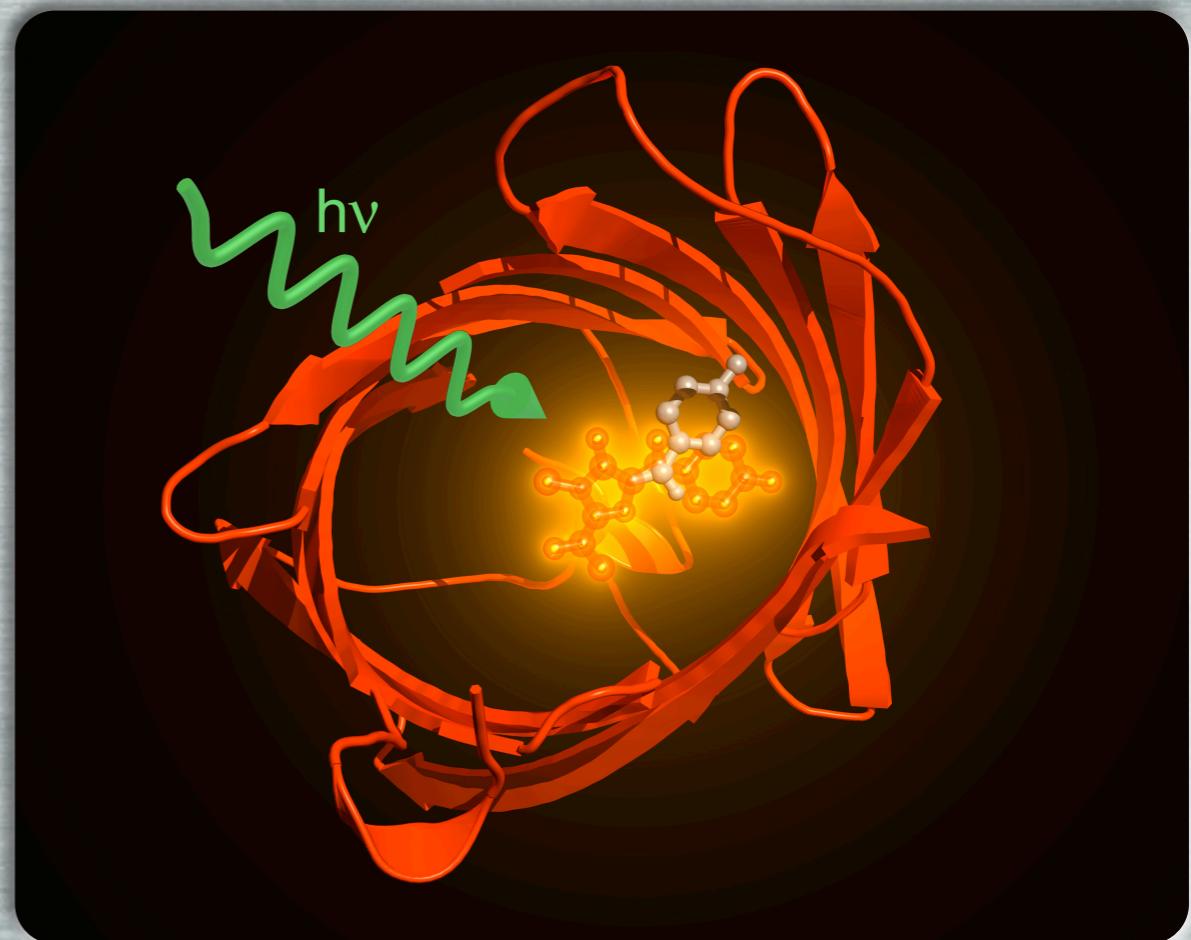
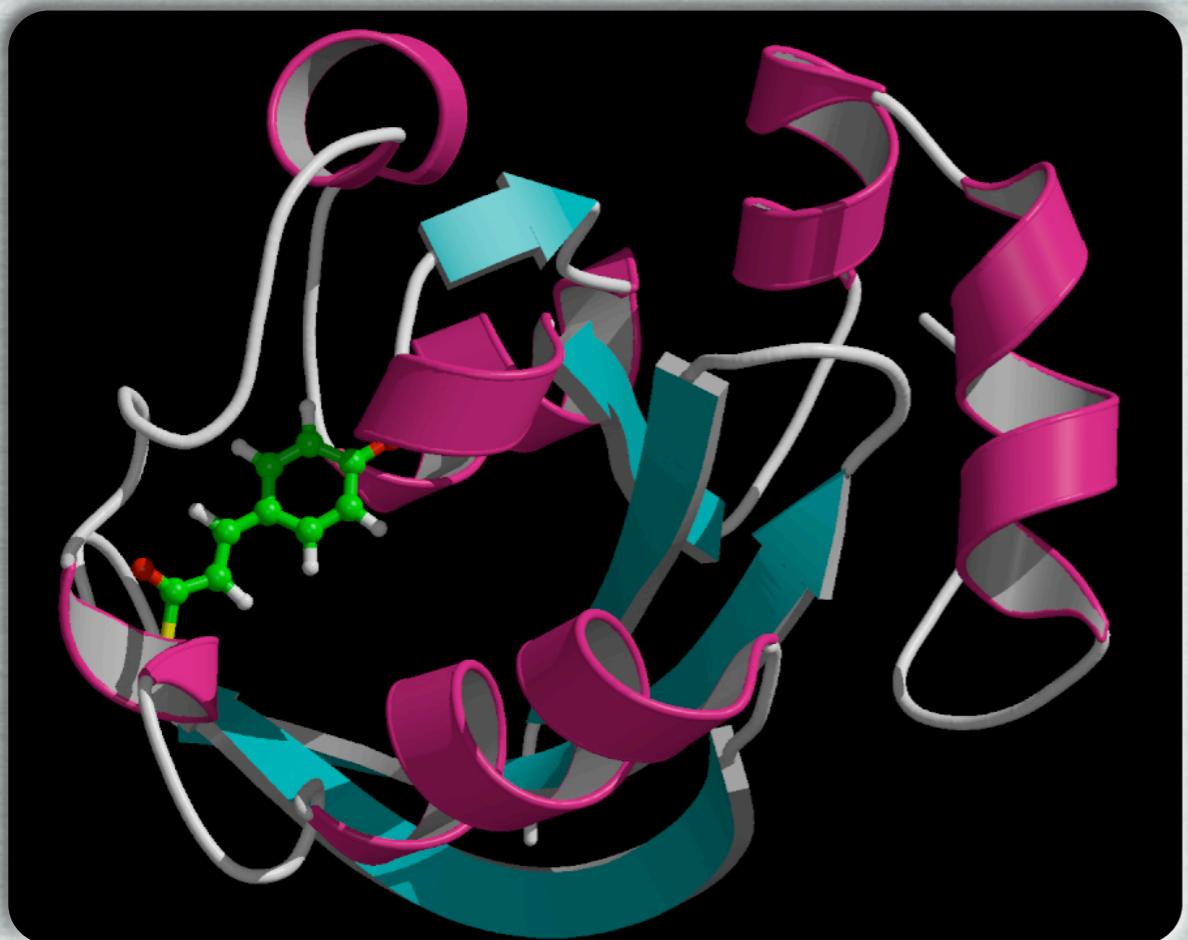
$$\left\langle \Psi_1 \left| \frac{\partial}{\partial t} \Psi_2 \right. \right\rangle \approx \langle \Psi_1(t) | \Psi_2(t + \Delta t) \rangle$$

conical intersection



selected QM/MM applications

- ▶ activation of a photoreceptor protein
- ▶ photo-switching in asFP595



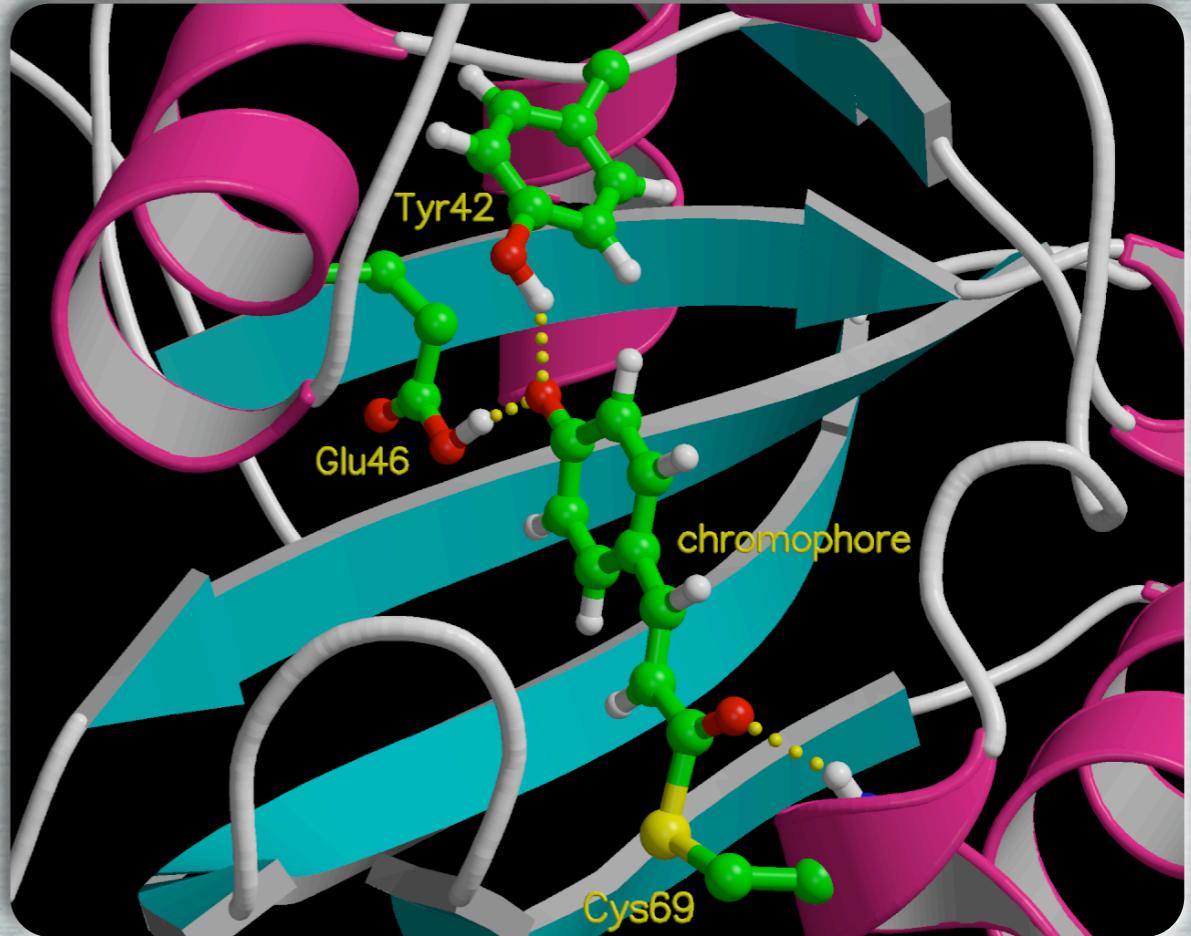
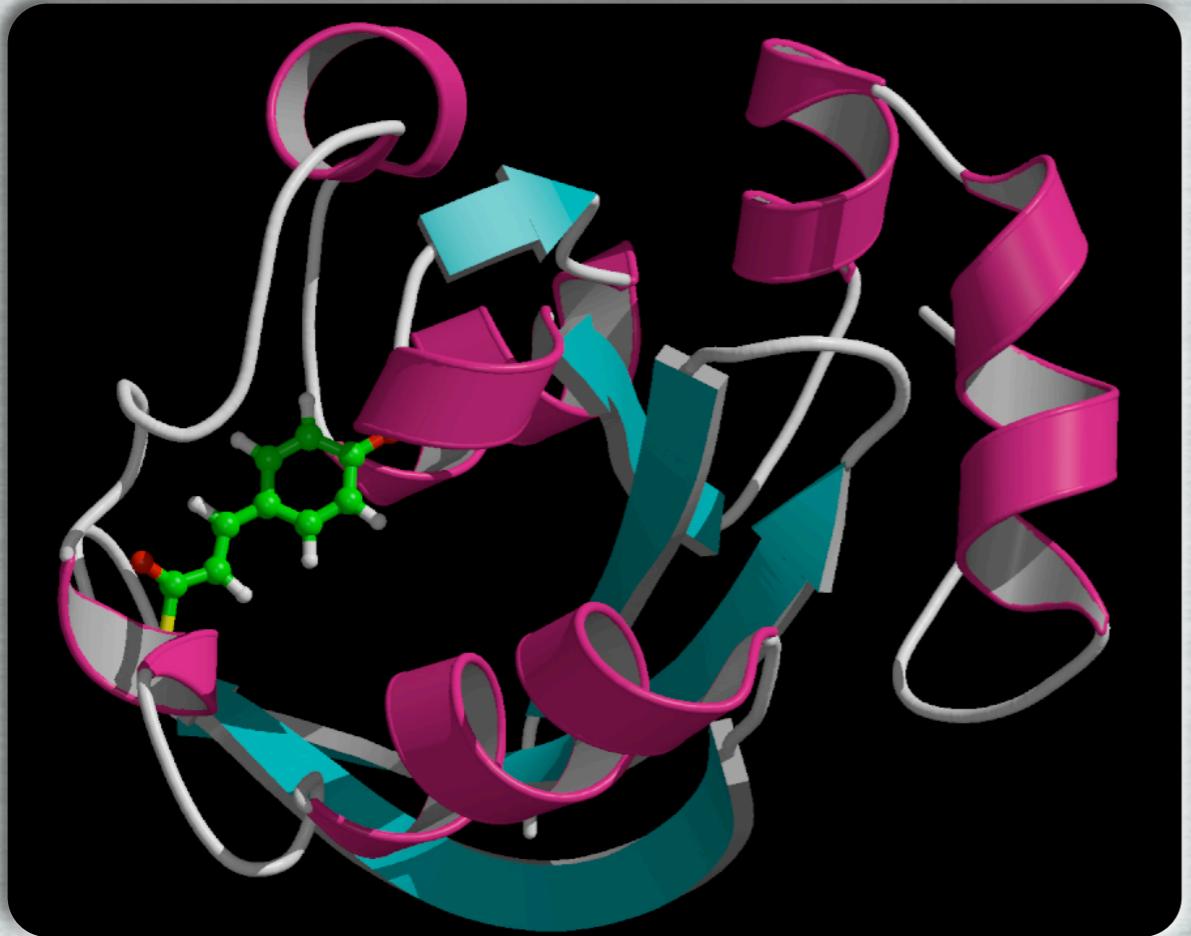
avoiding exposure to UV light



Halorhodospira halophila bacteria

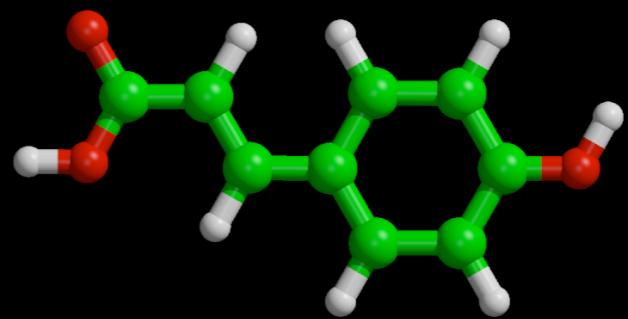
- ▶ negative phototaxis to blue light
- ▶ photoactive yellow protein

Photoactive Yellow Protein



chromophore

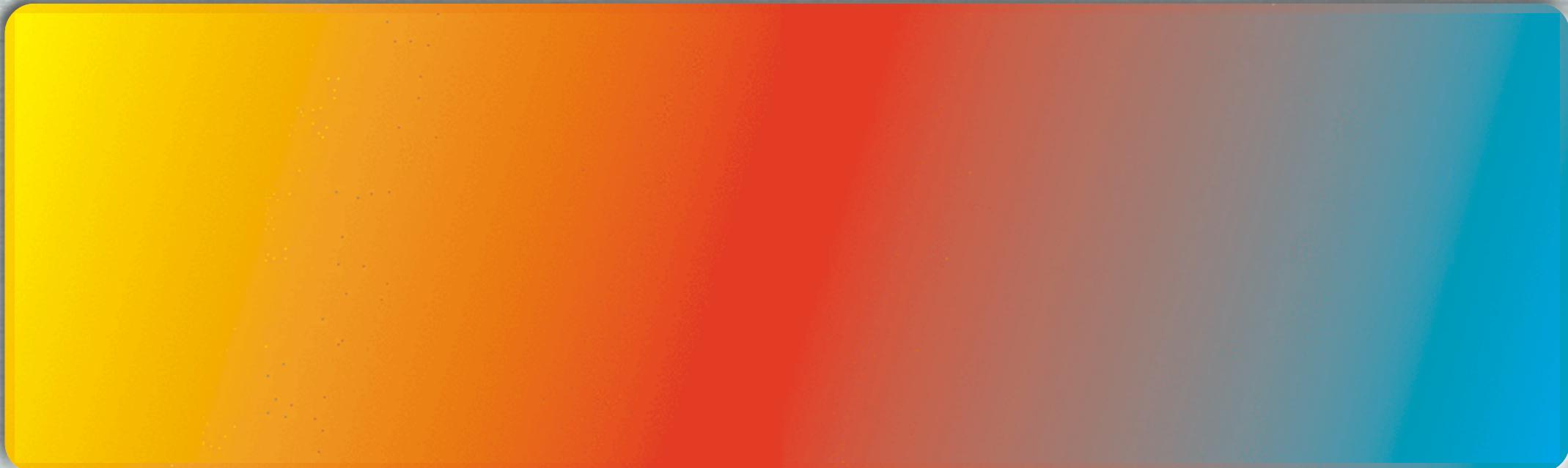
- ▶ β -coumaric acid
- ▶ isomerization



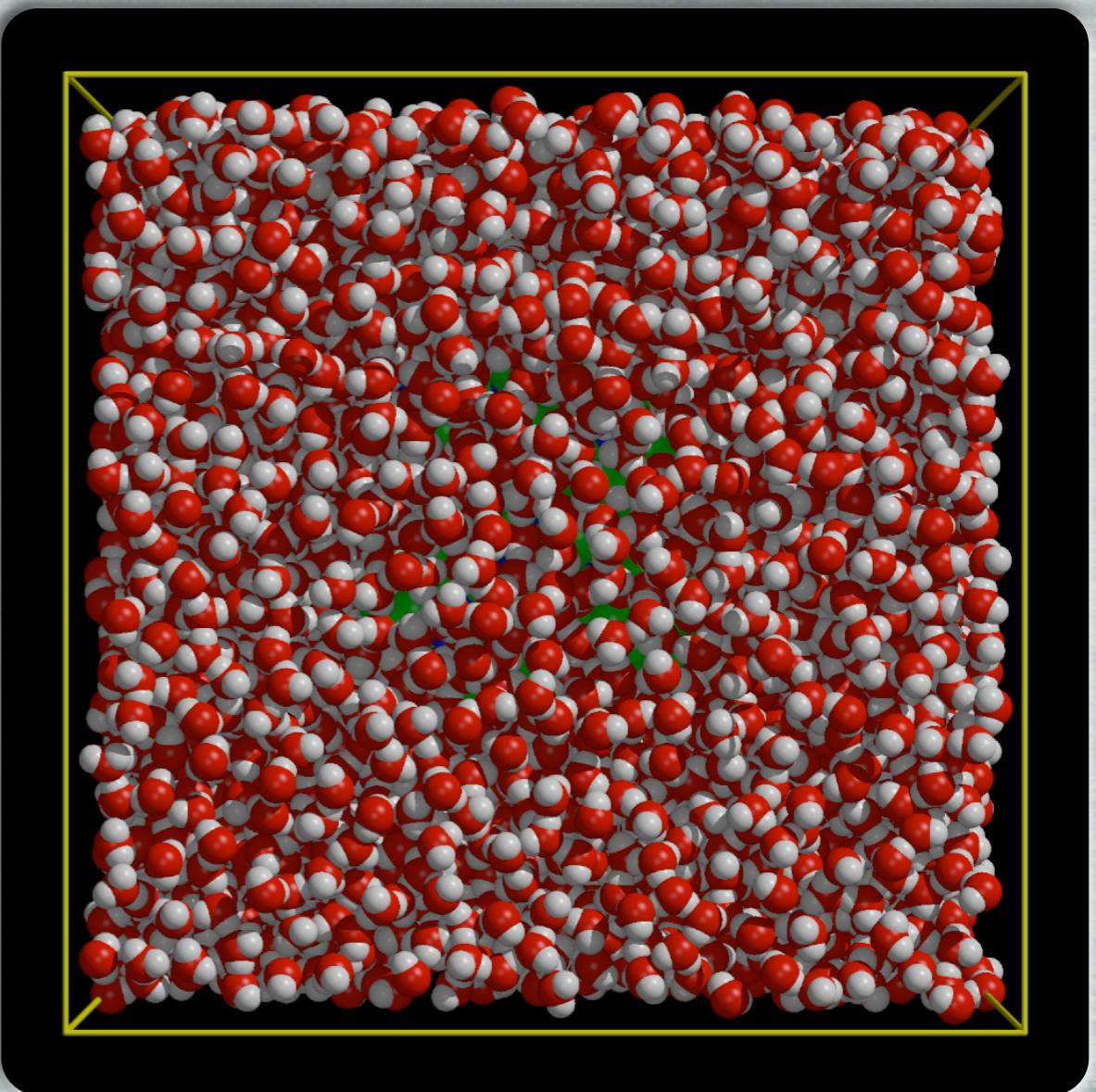
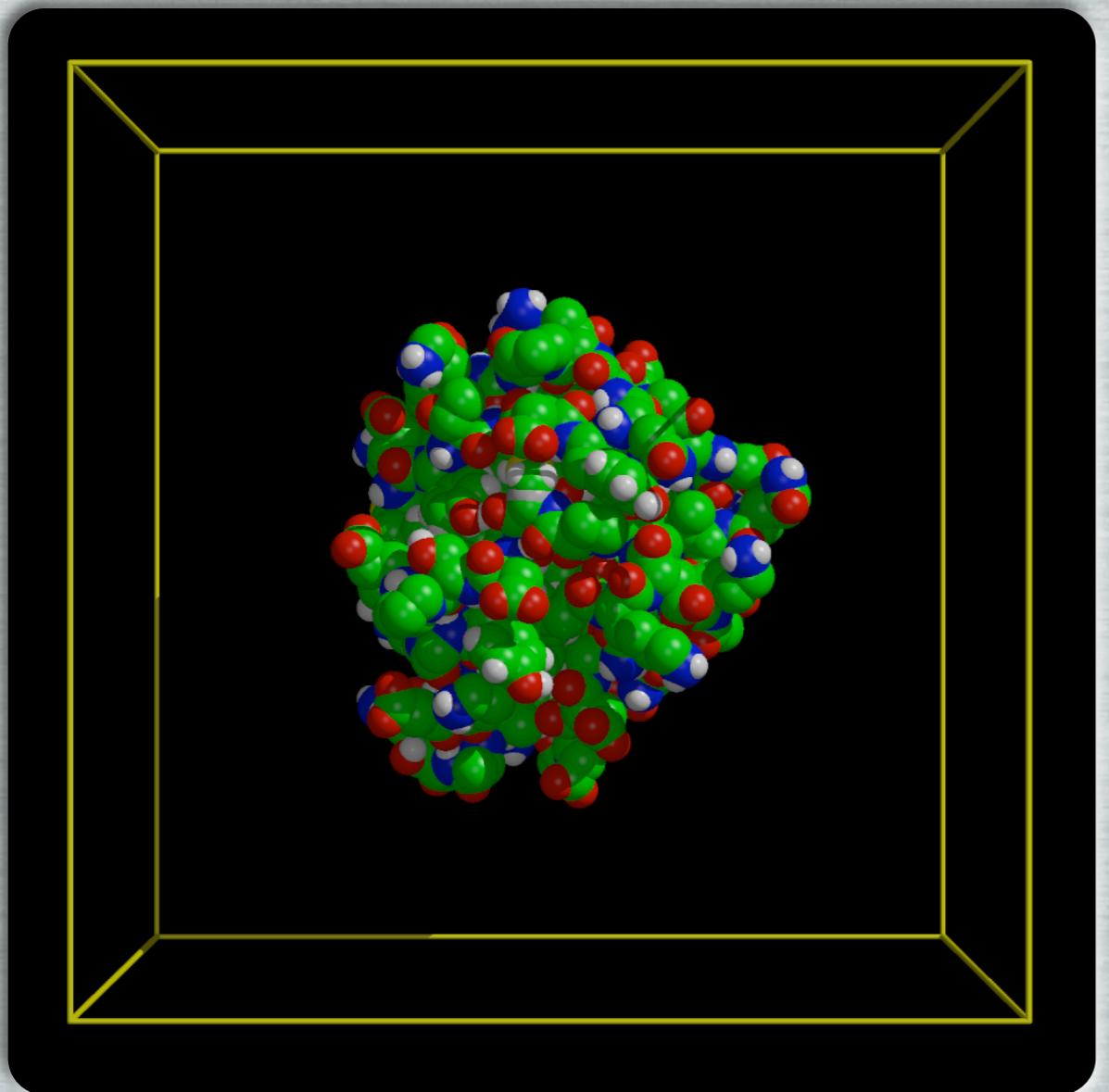
Photoactive Yellow Protein

photocycle

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

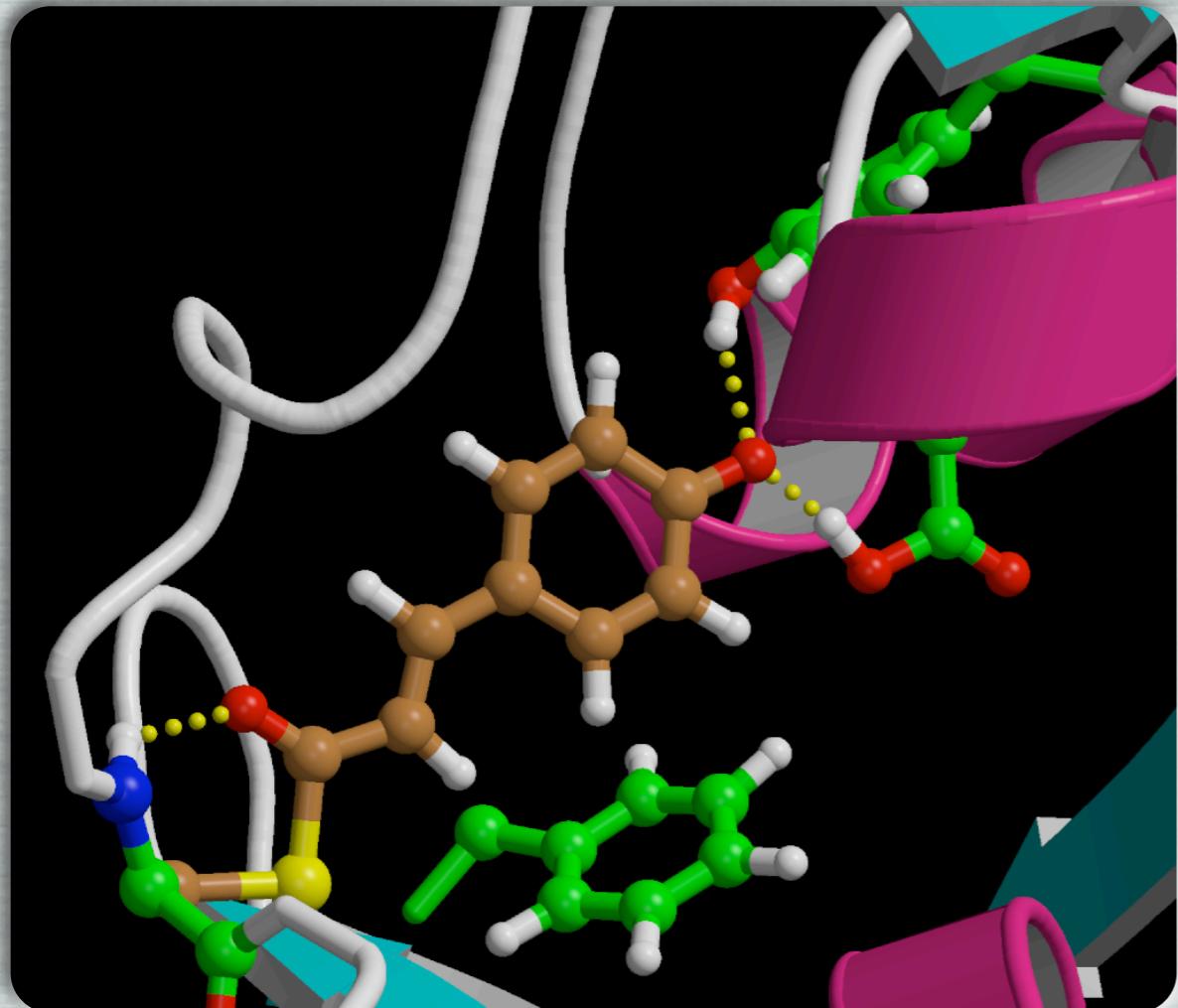


atomistic simulation of excited PYP



atomistic simulation of excited PYP

QM/MM protocol



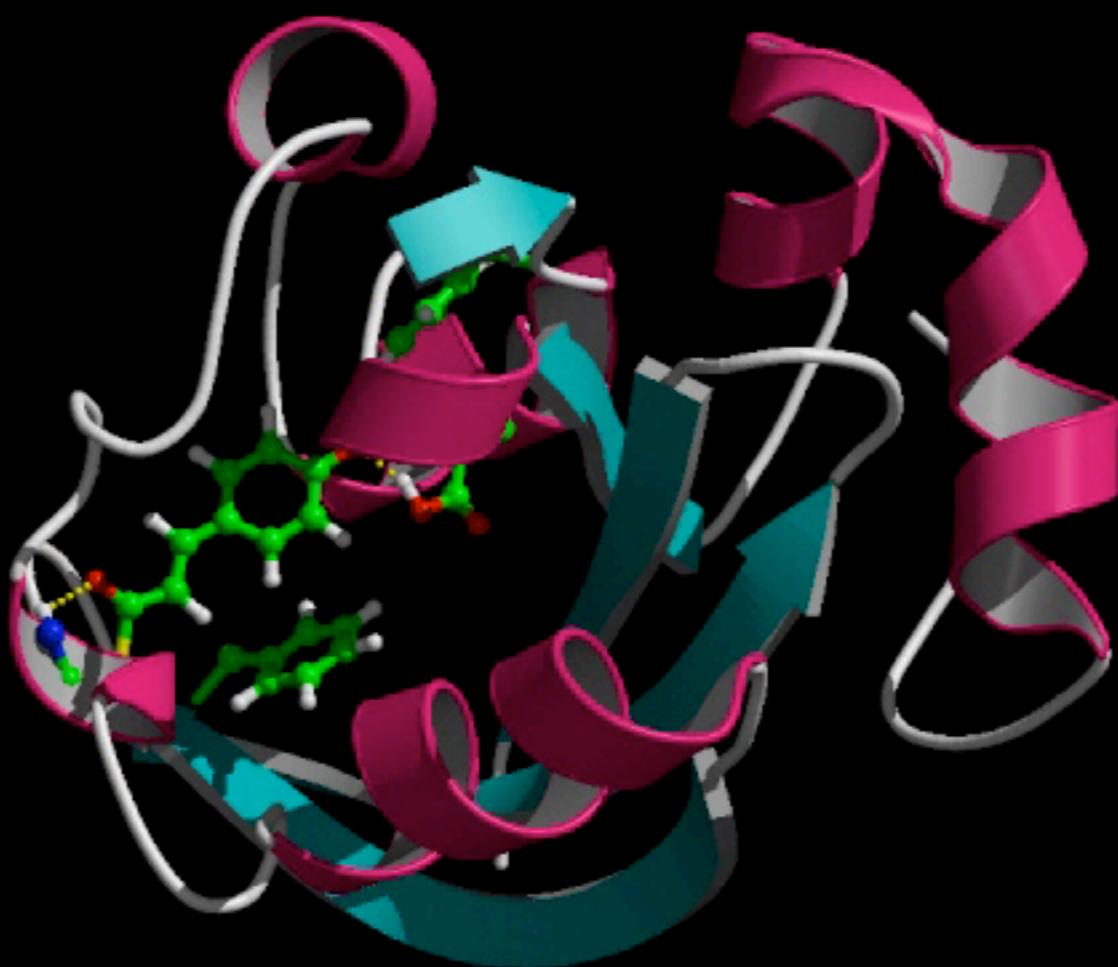
QM subsystem

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

MM subsystem

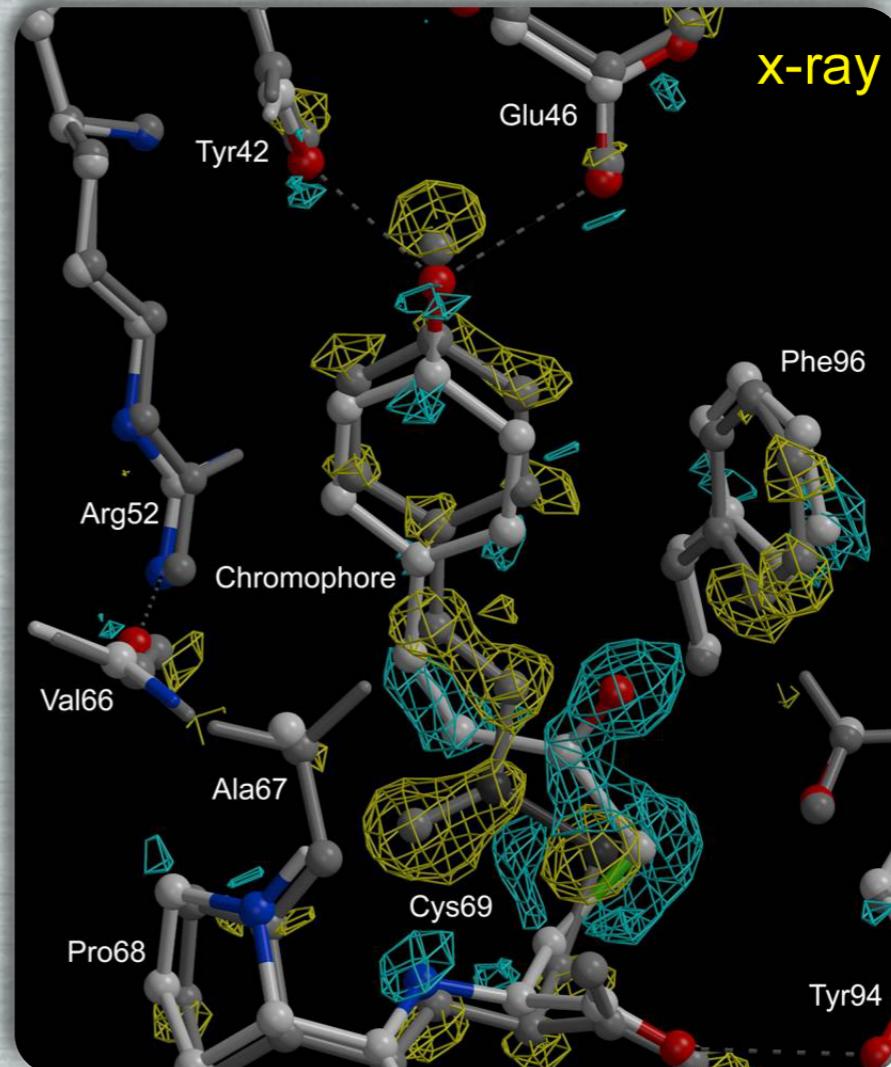
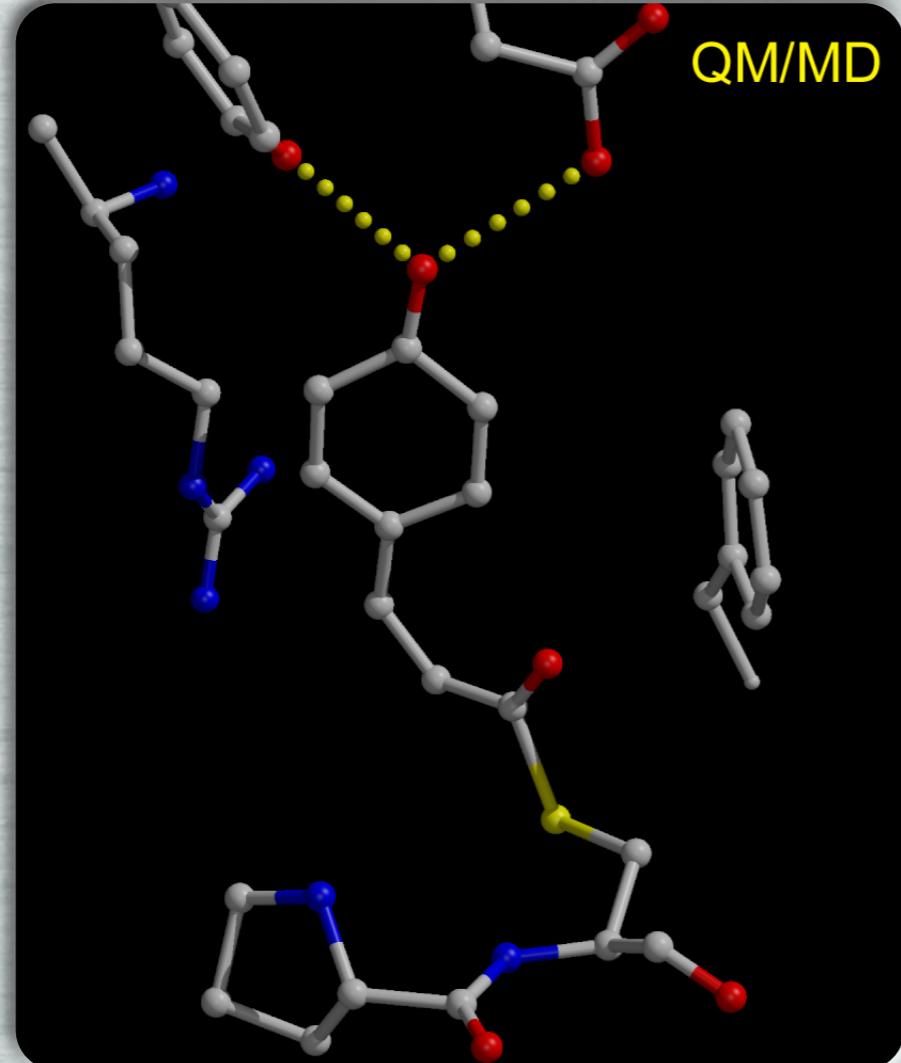
- ▶ apo-protein & water
- ▶ GROMOS96/SPC

atomistic simulation of excited PYP



JACS 124 (2004): 4228

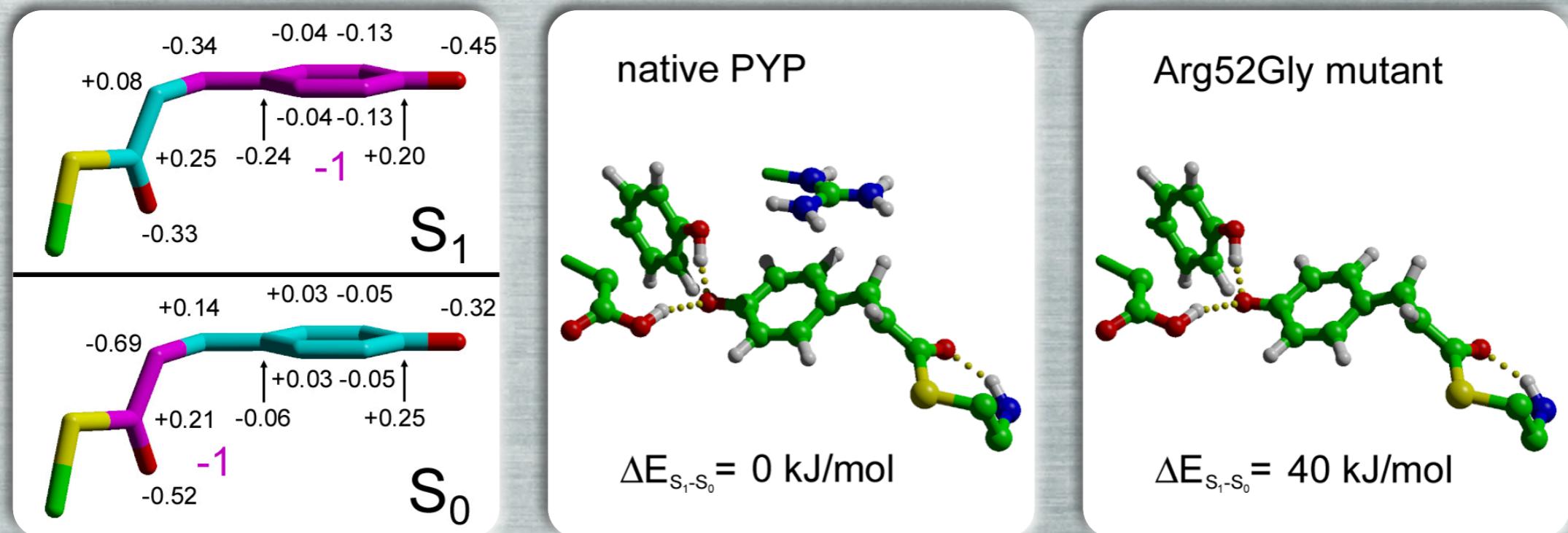
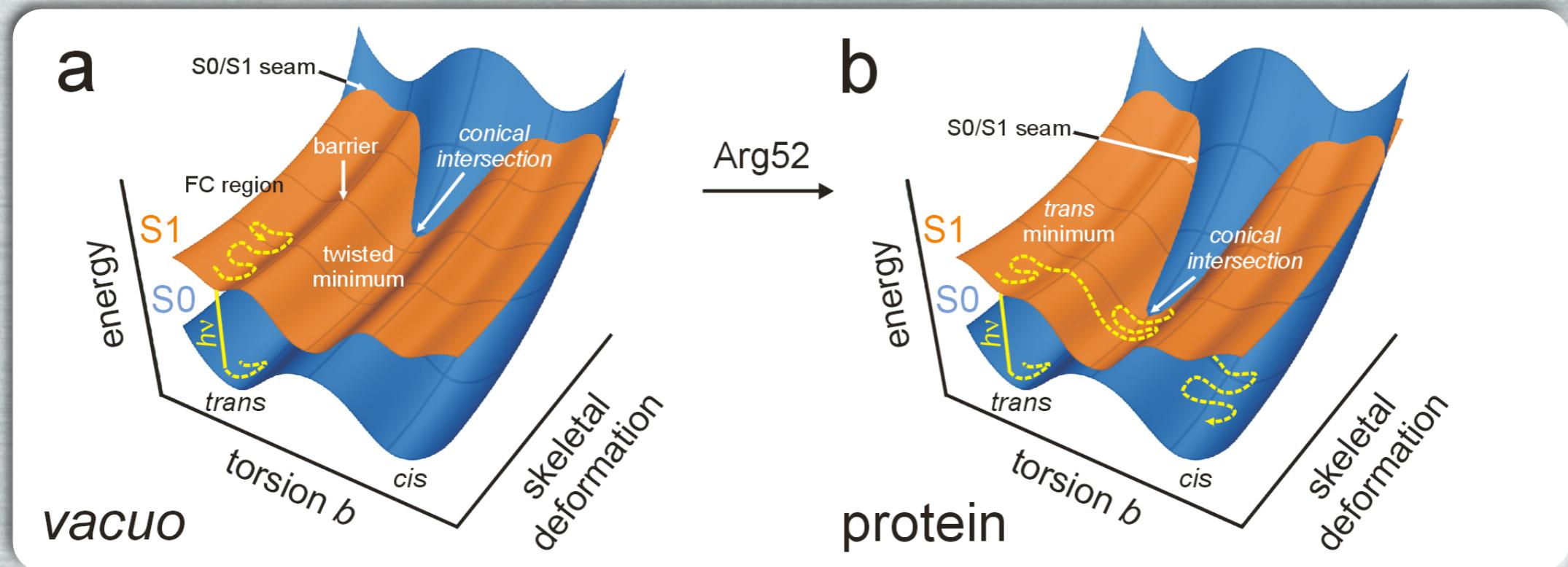
atomistic simulation of excited PYP



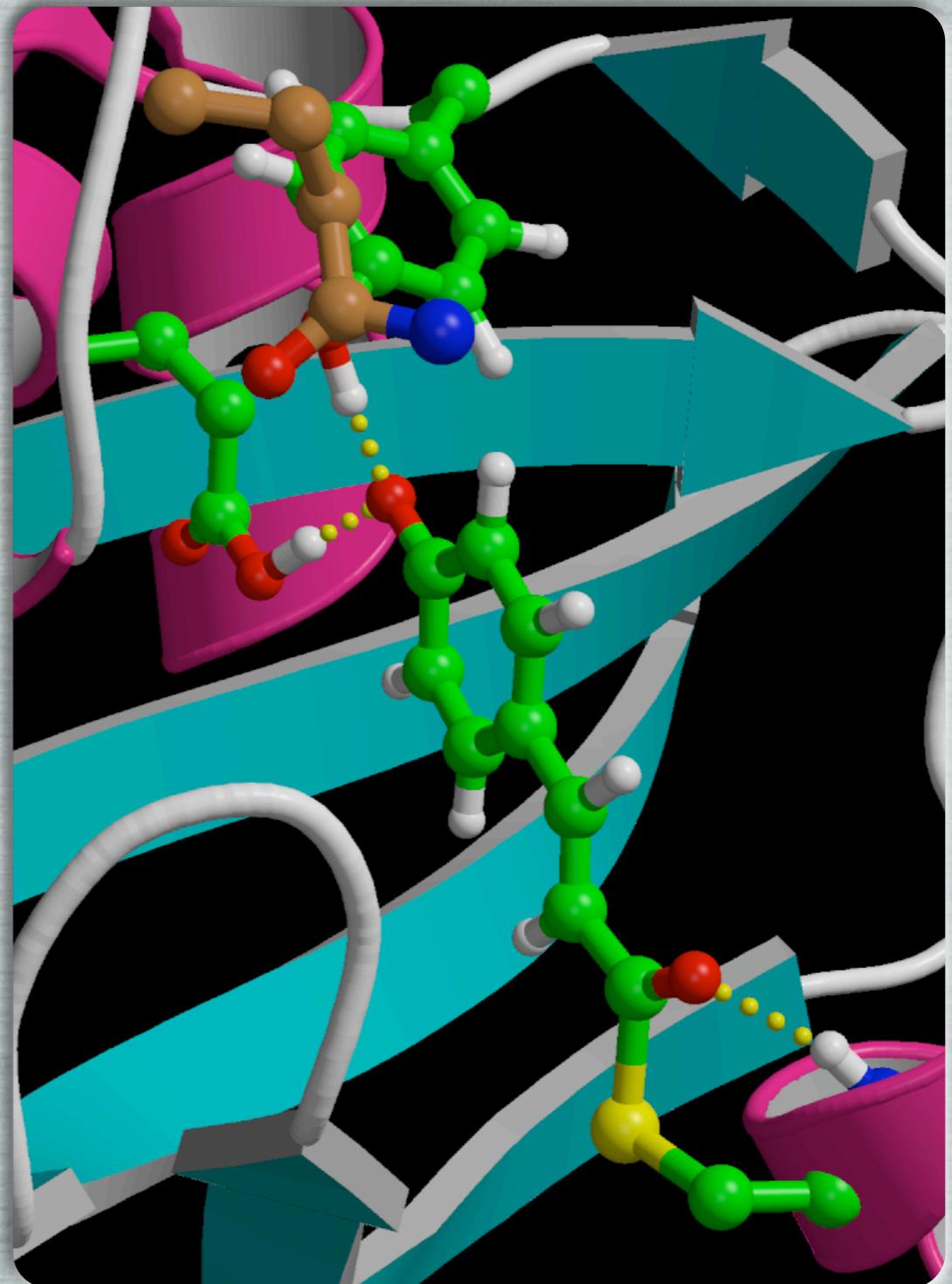
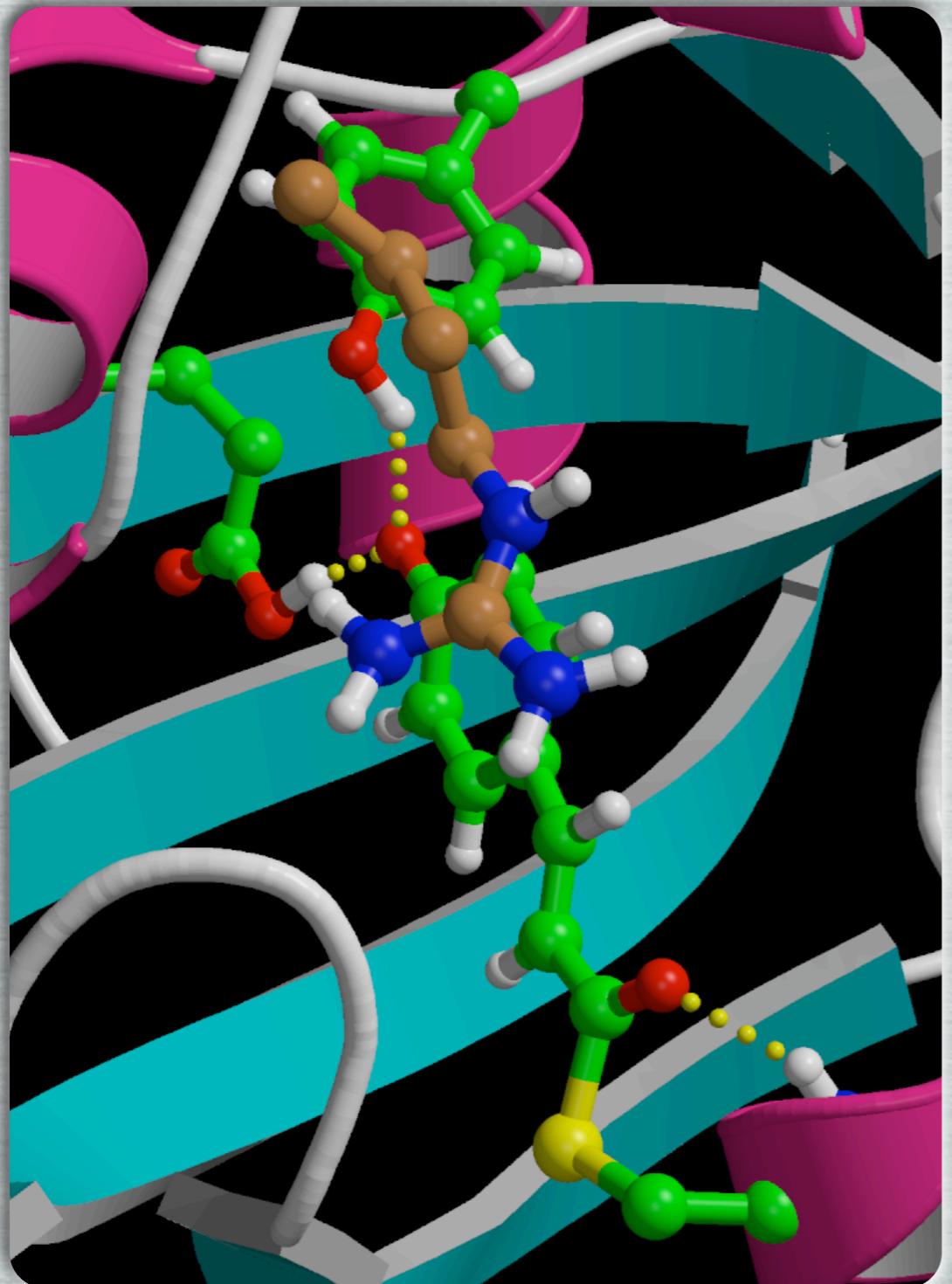
comparison to experimental structure

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

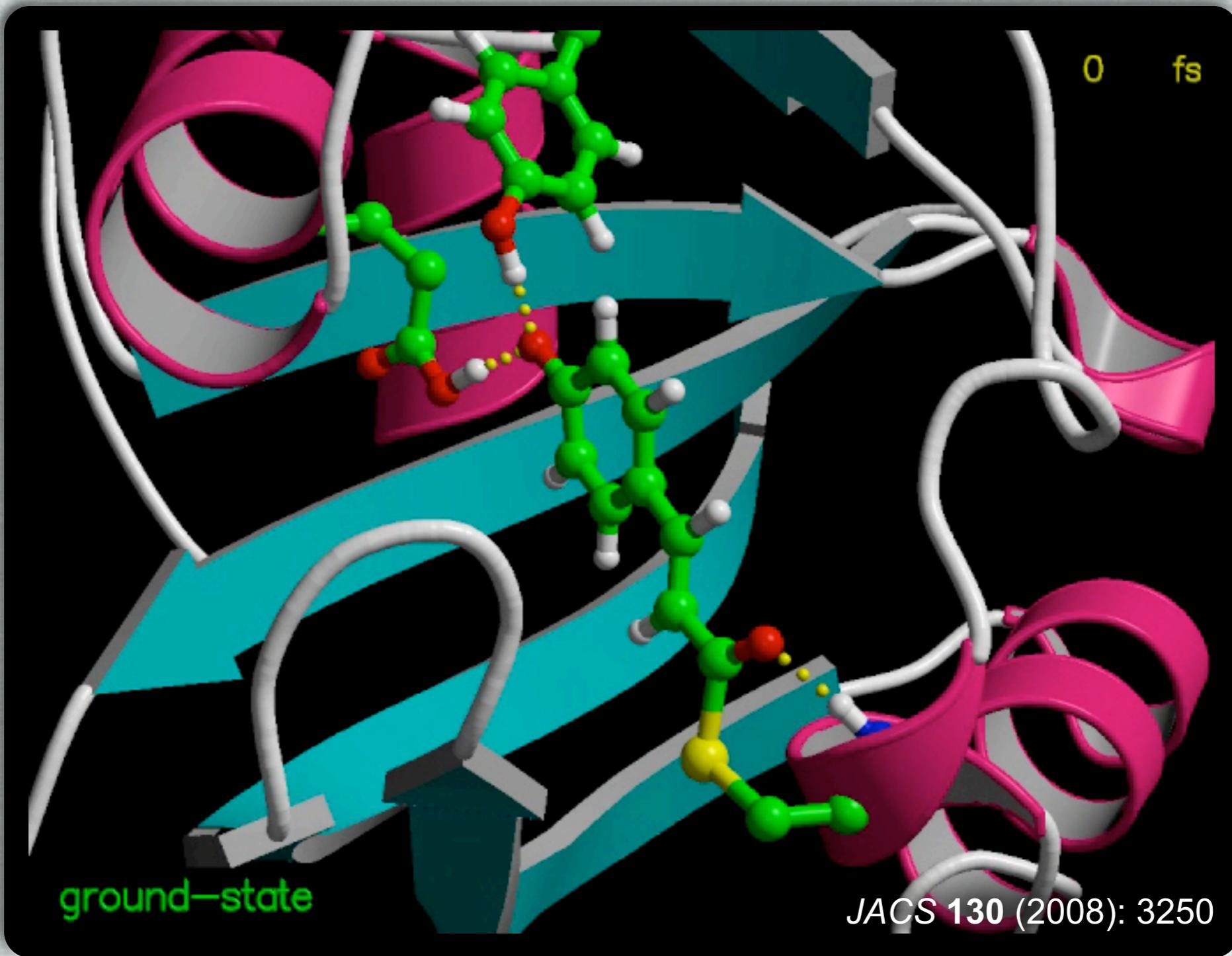
atomistic simulation of excited PYP



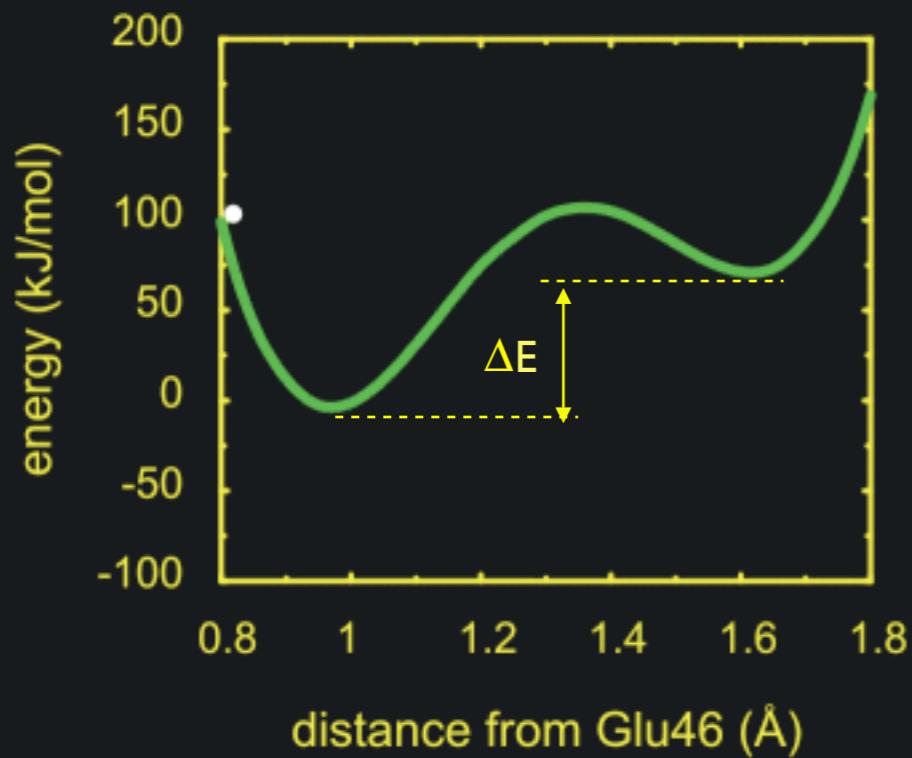
arginine/glutamine mutant



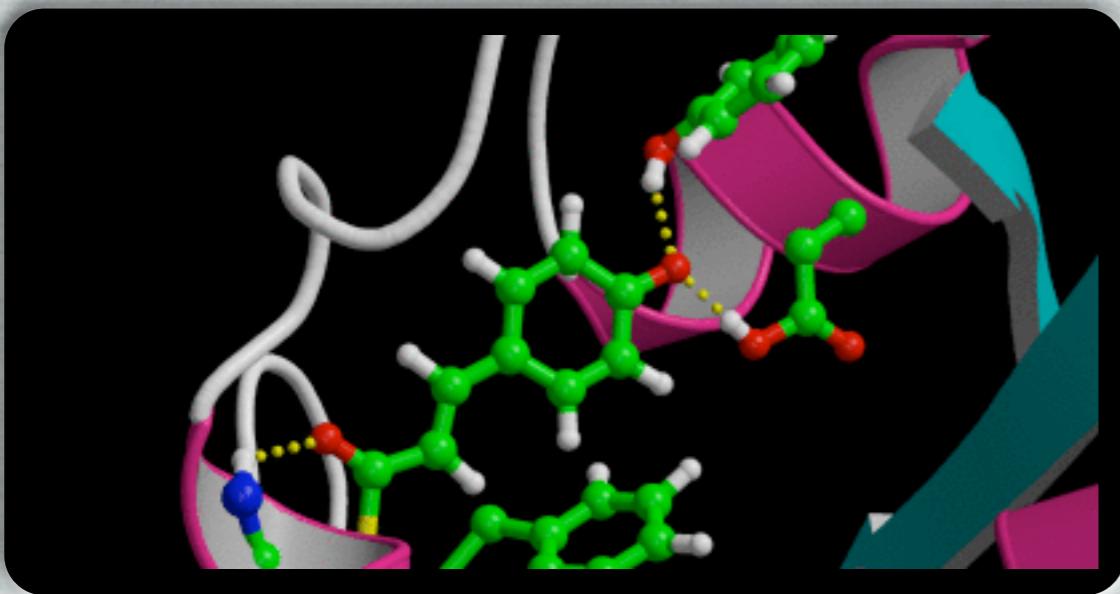
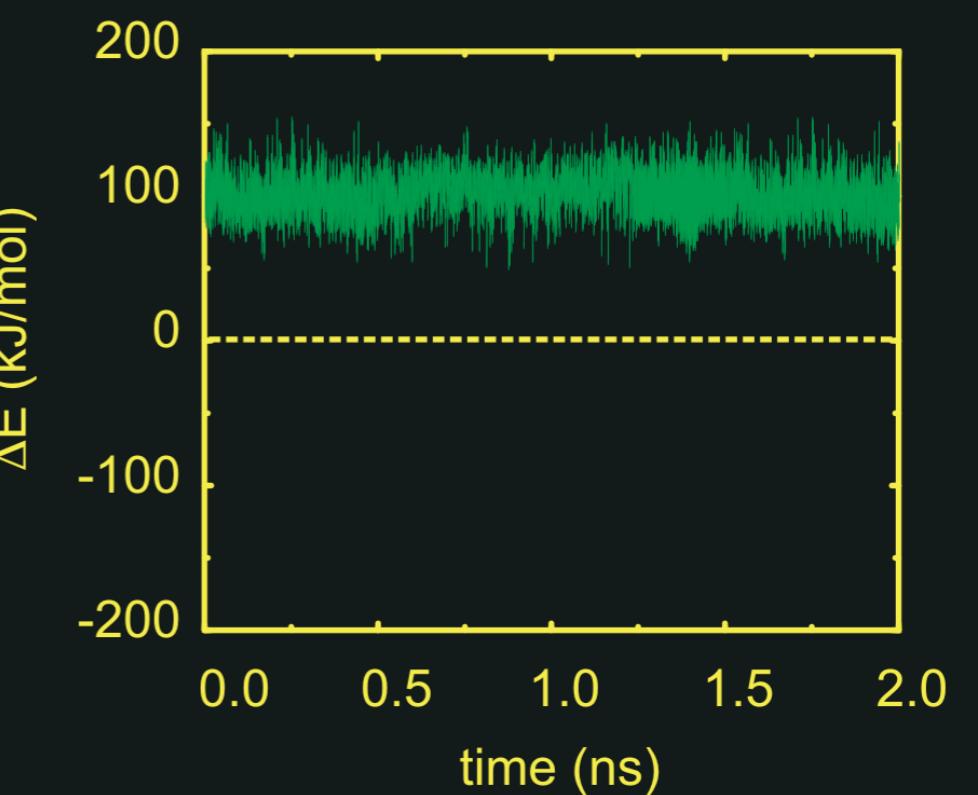
atomistic simulation of excited R52Q



atomistic simulation of excited PYP

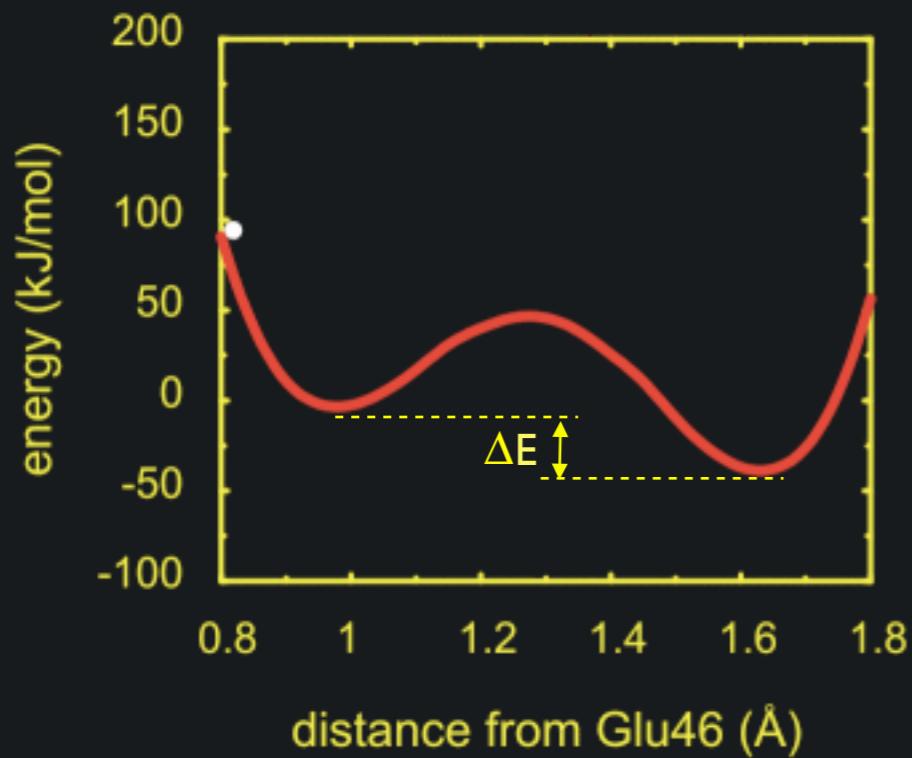


QM/MM (Gromos/PM3)

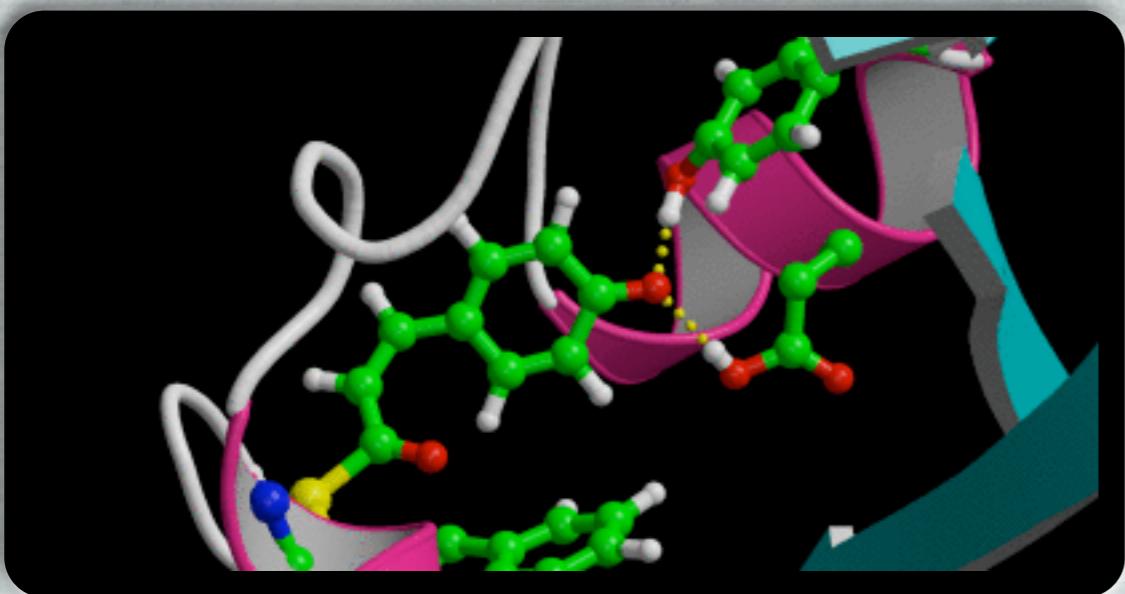
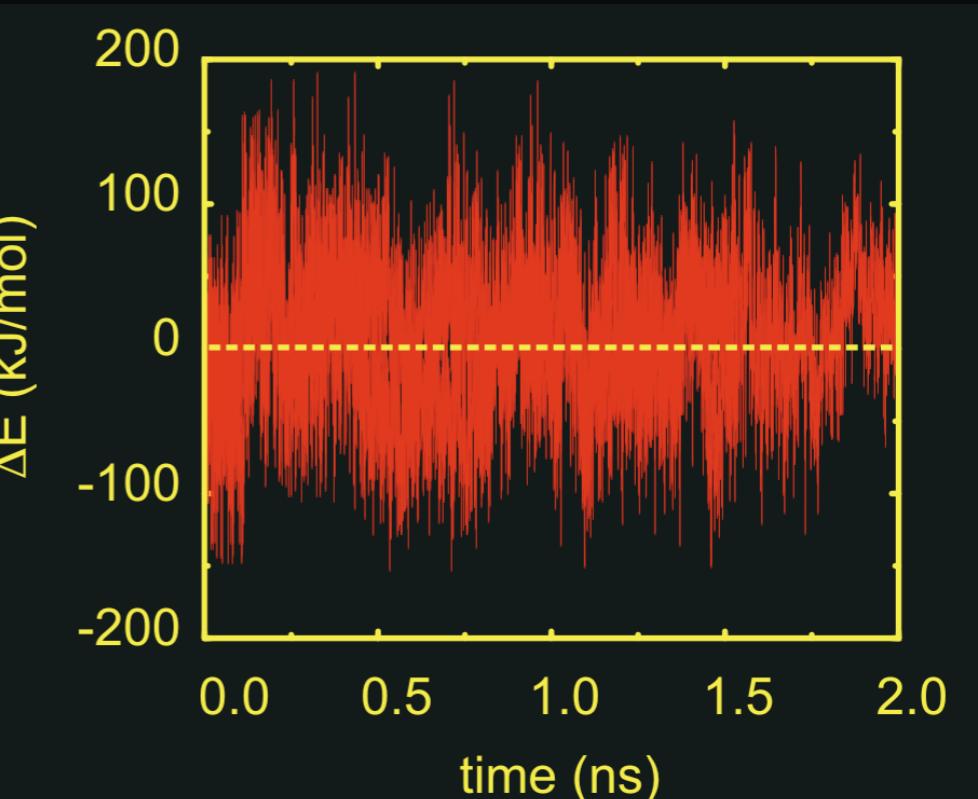


before isomerization
► proton cannot transfer

atomistic simulation of excited PYP



QM/MM (Gromos/PM3)



after isomerization
► proton can transfer

activation mechanism of PYP

photon absorption

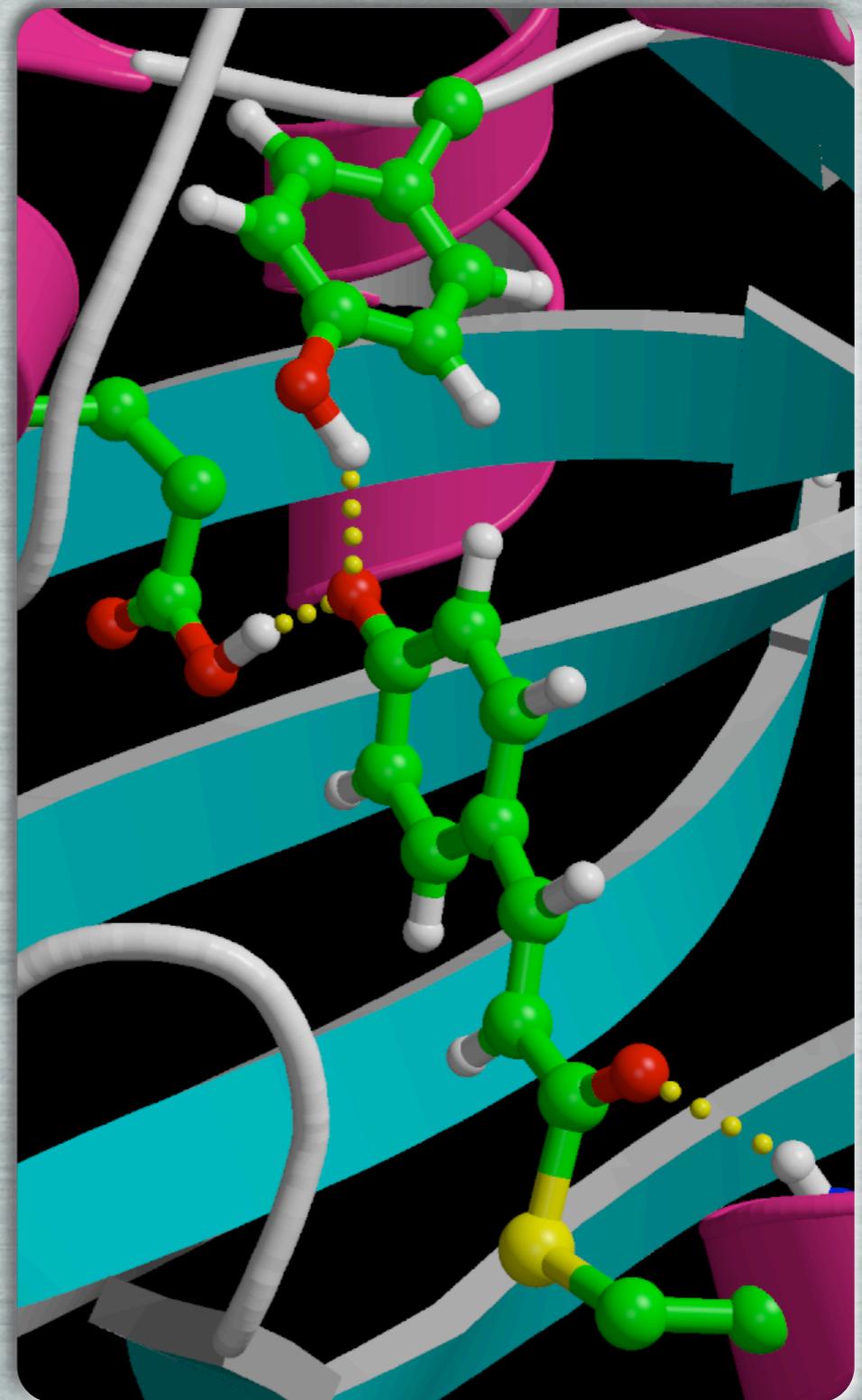
photo-isomerization

carbonyl flip

proton transfer

partial unfolding

signalling state



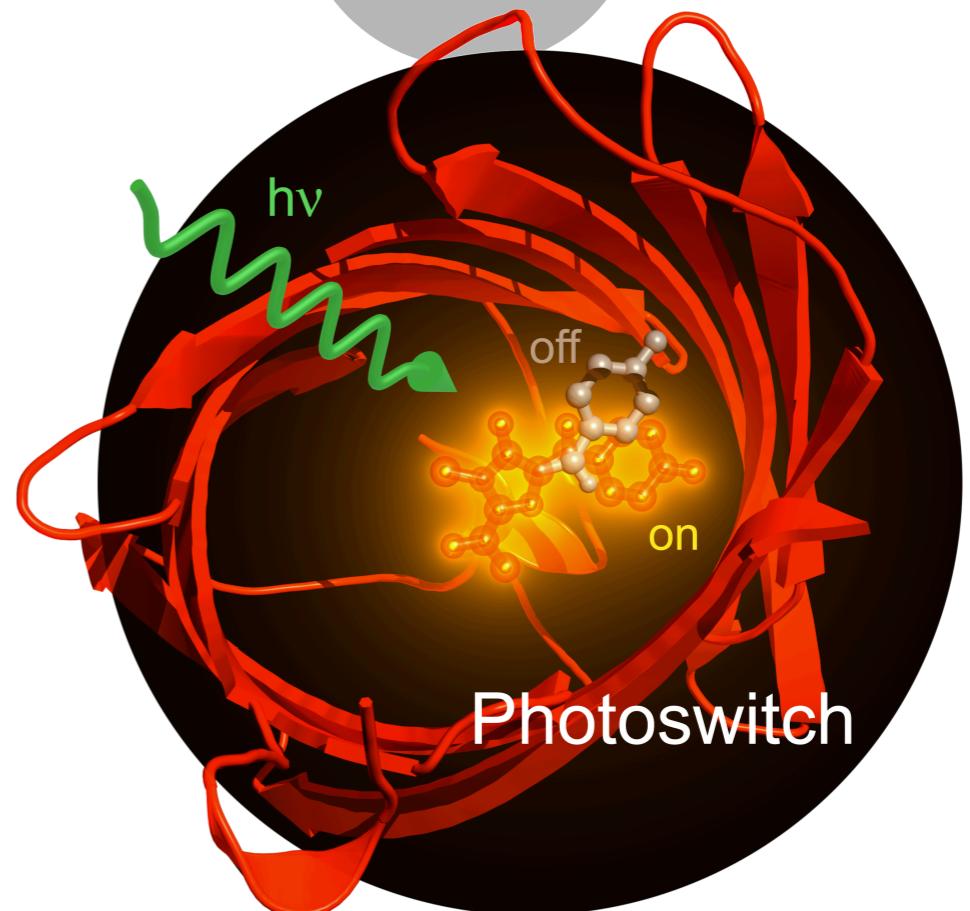
asFP595

chromophore
photoswitchable
▶ on - fluorescent (*cis*)
▶ off - dark (*trans*)
STED microscopy

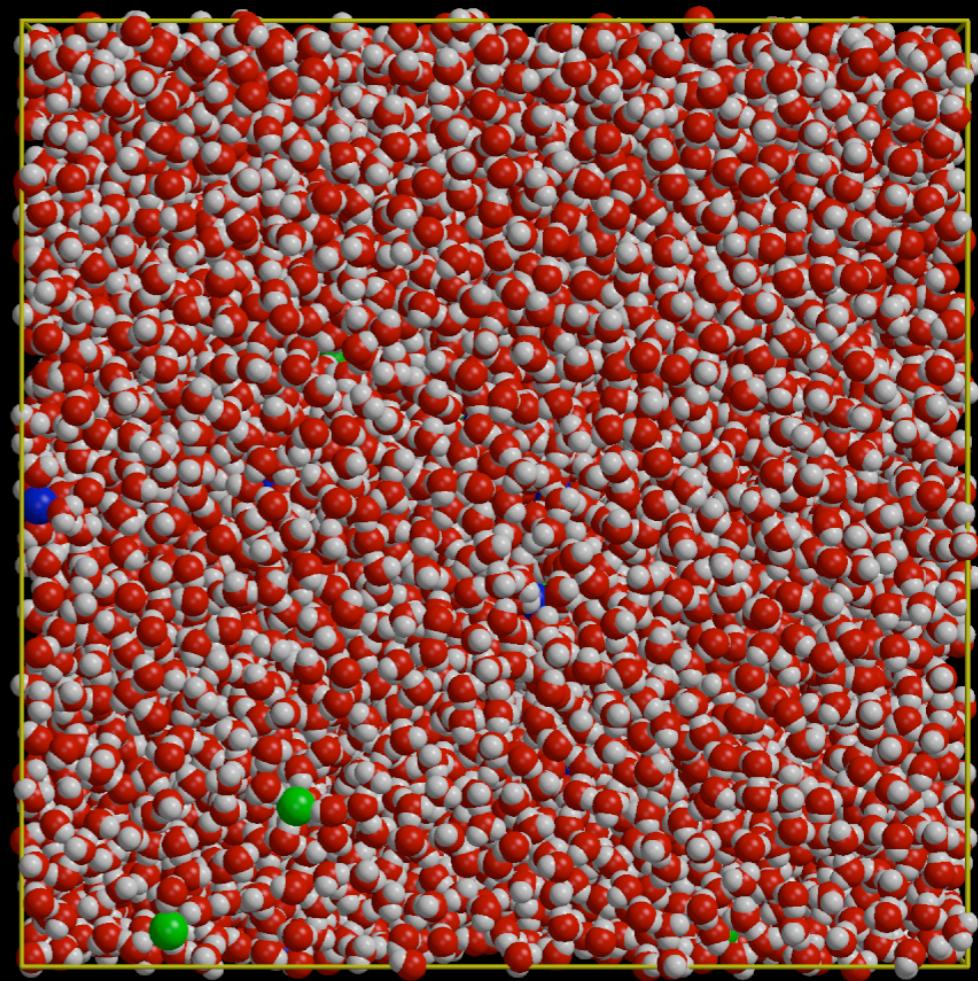
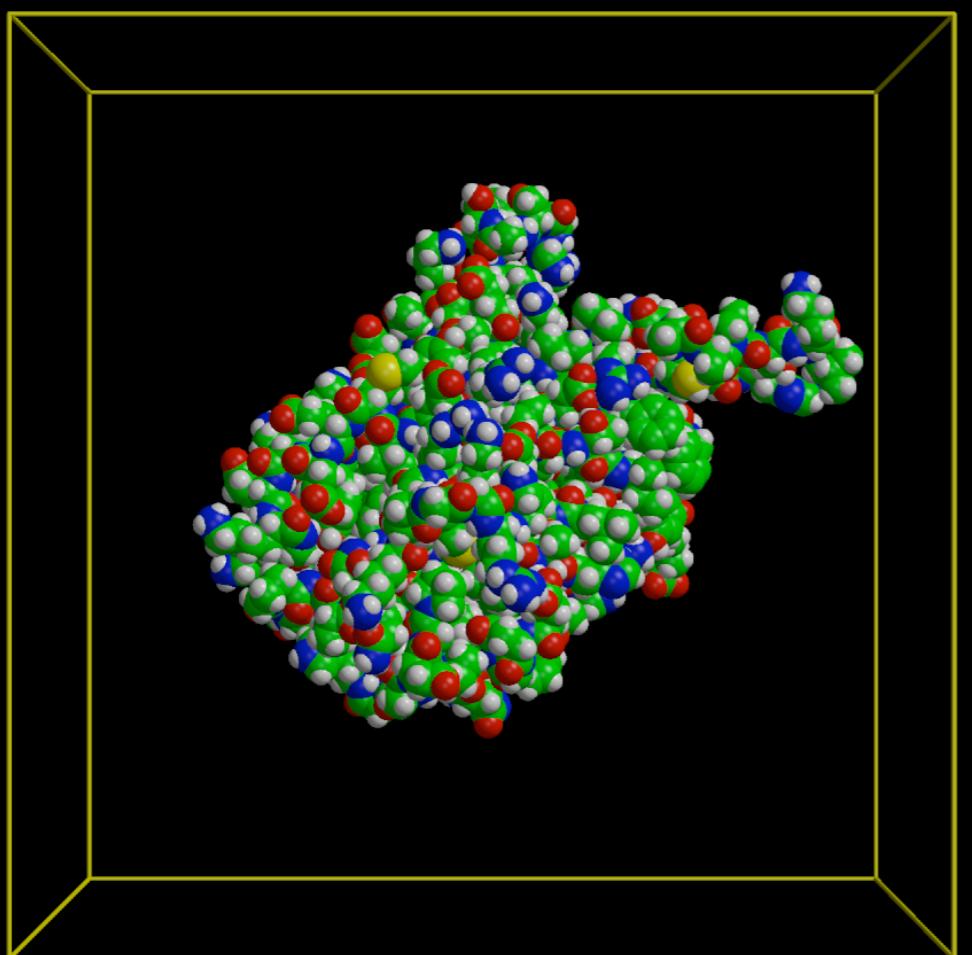
mechanism

- ▶ photo-isomerization
- ▶ protonation changes

Angewandte
Chemie

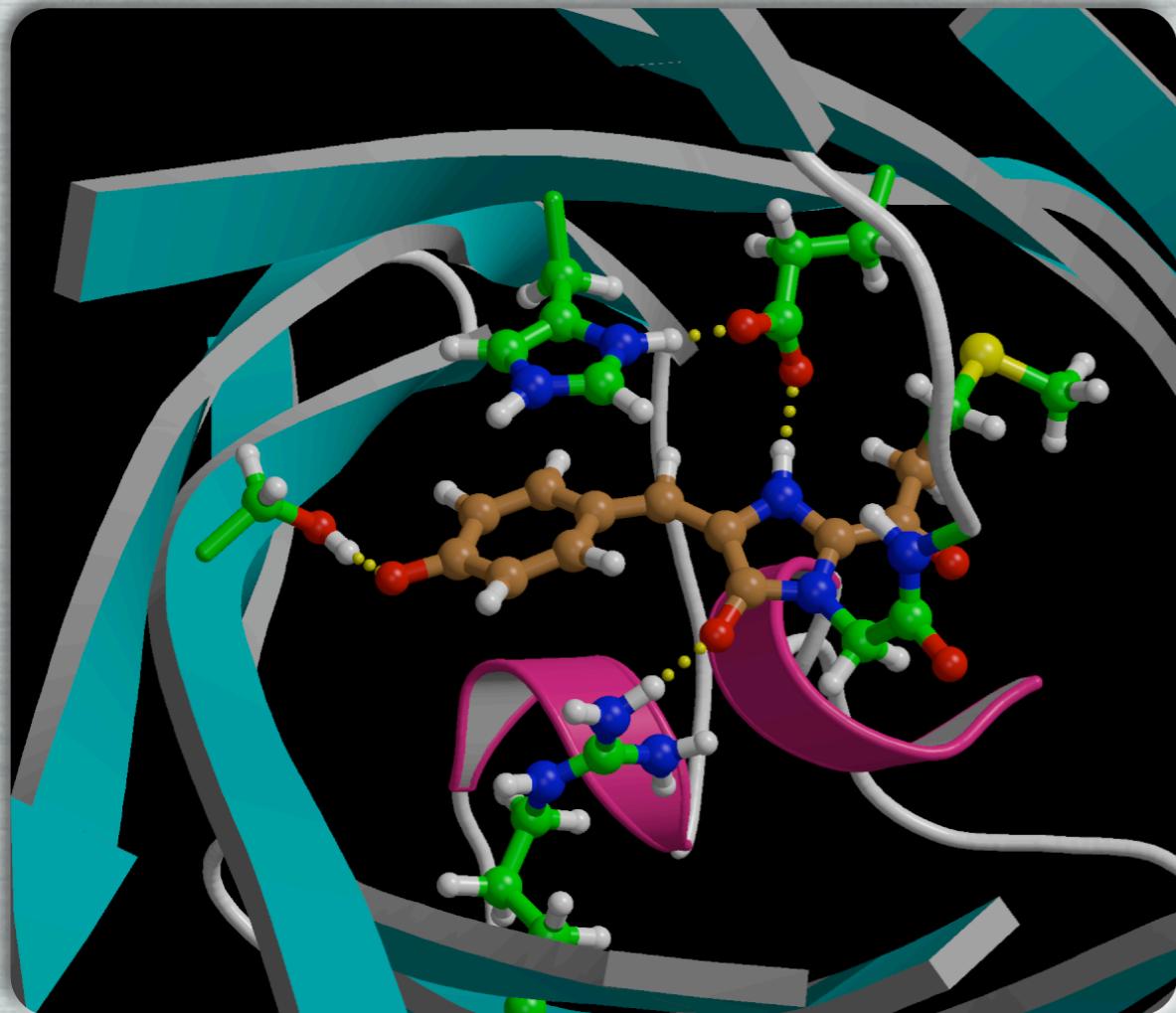


atomistic simulations of asFP595



atomistic simulations of asFP595

QM/MM protocol



QM subsystem

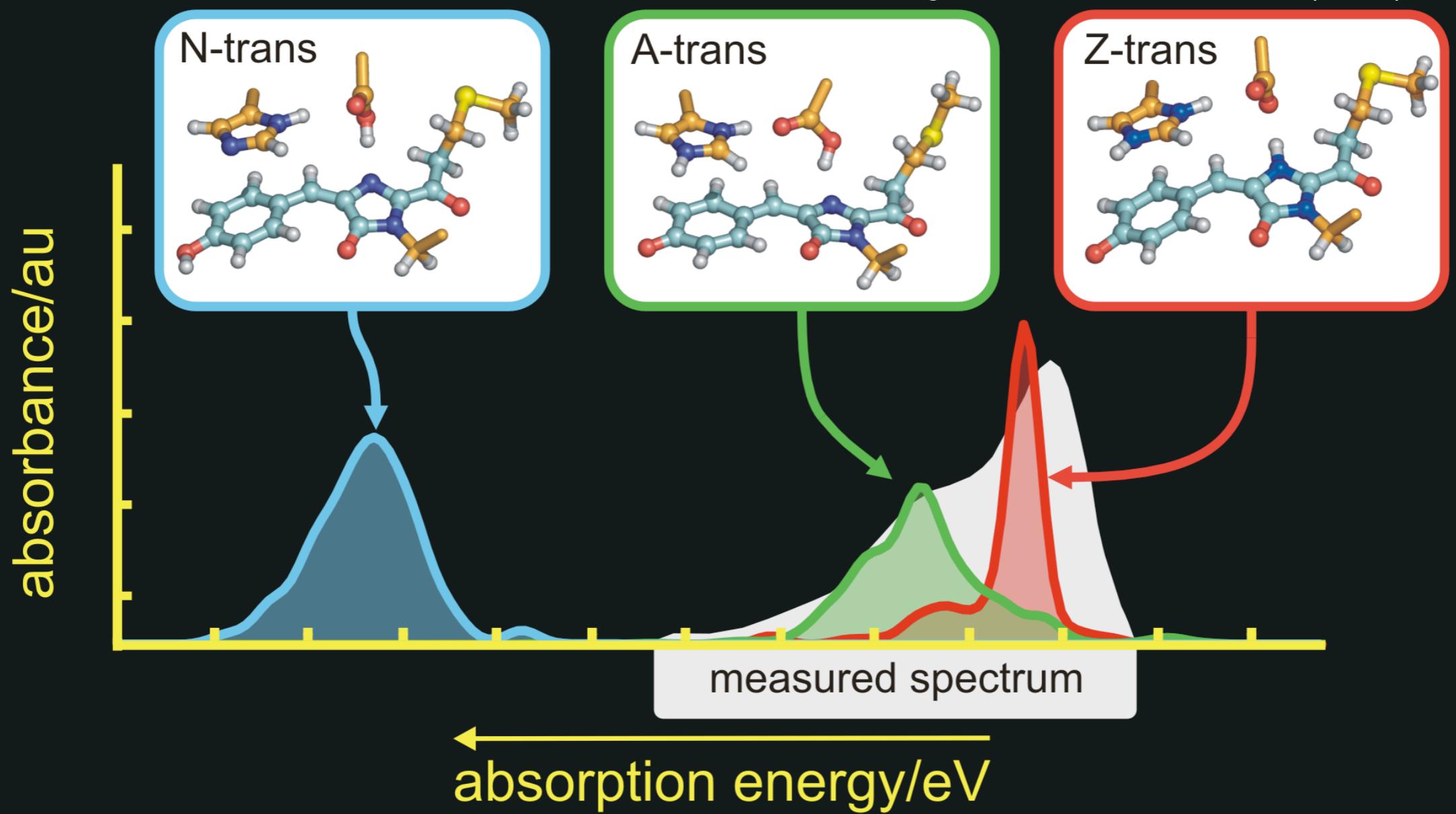
- ▶ chromophore
- ▶ active site residues
- ▶ TD-DFT & INDO/S

MM subsystem

- ▶ protein, water, ions
- ▶ OPLS-AA/TIP4P

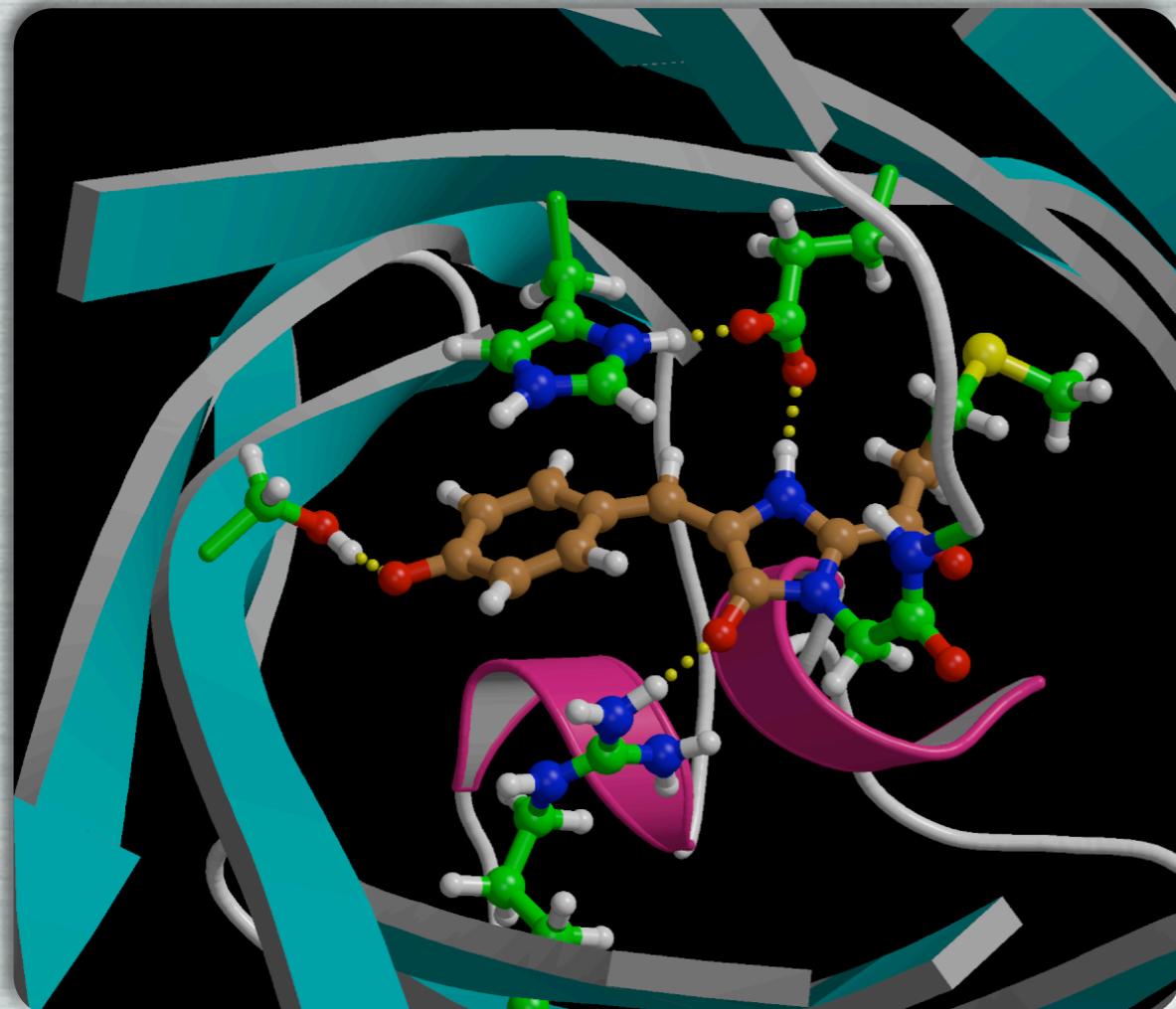
absorption spectra of asFP595

Angew. Chem. Int. Ed. 119 (2007): 536



atomistic simulations of asFP595

QM/MM protocol



QM subsystem

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

MM subsystem

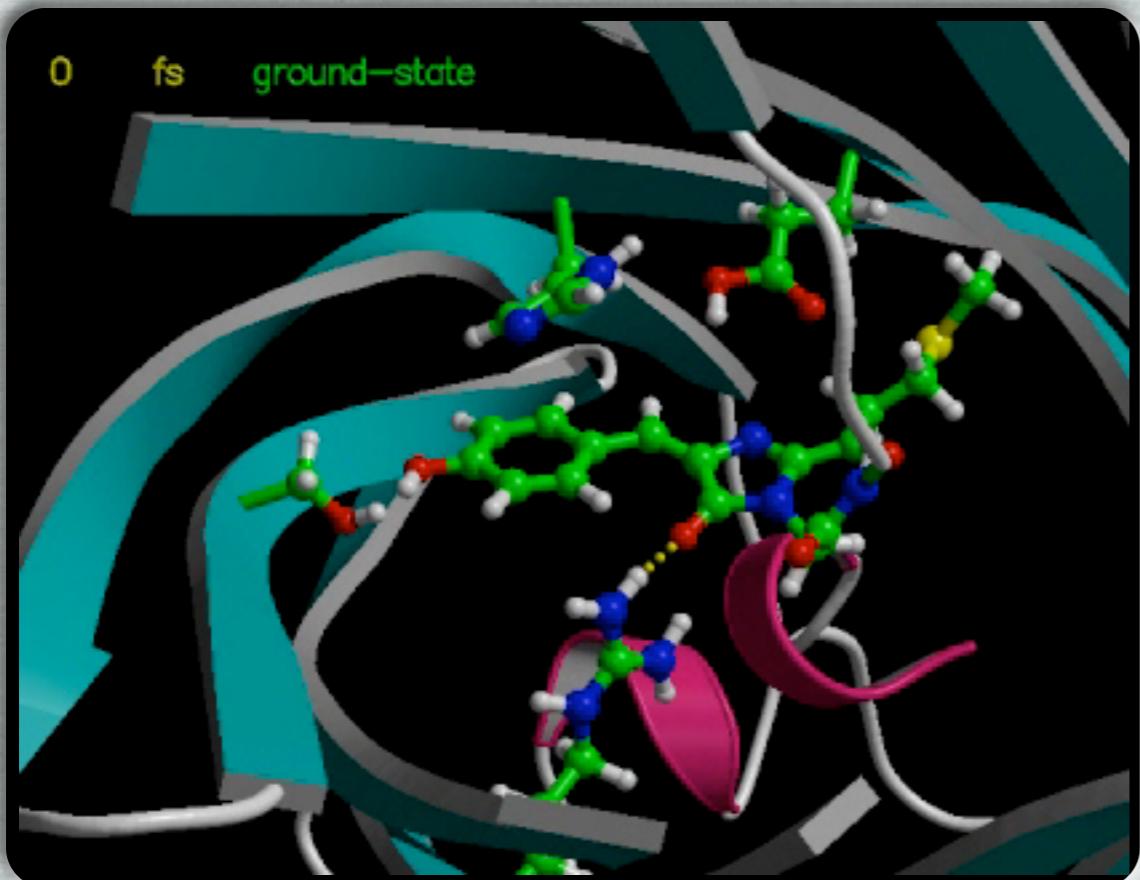
- ▶ protein, water, ions
- ▶ OPLS-AA/TIP4P

neutral: photoisomerization

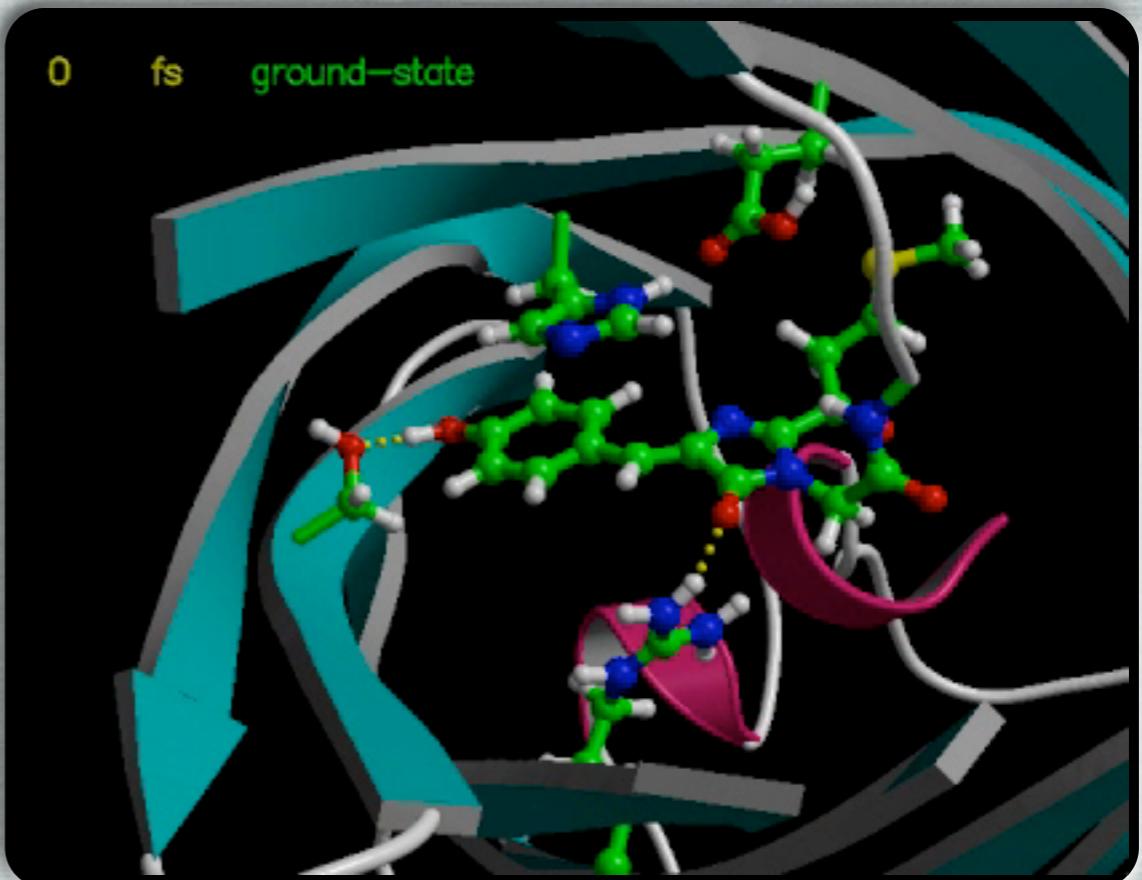
neutral *trans*

neutral *cis*

neutral: photoisomerization

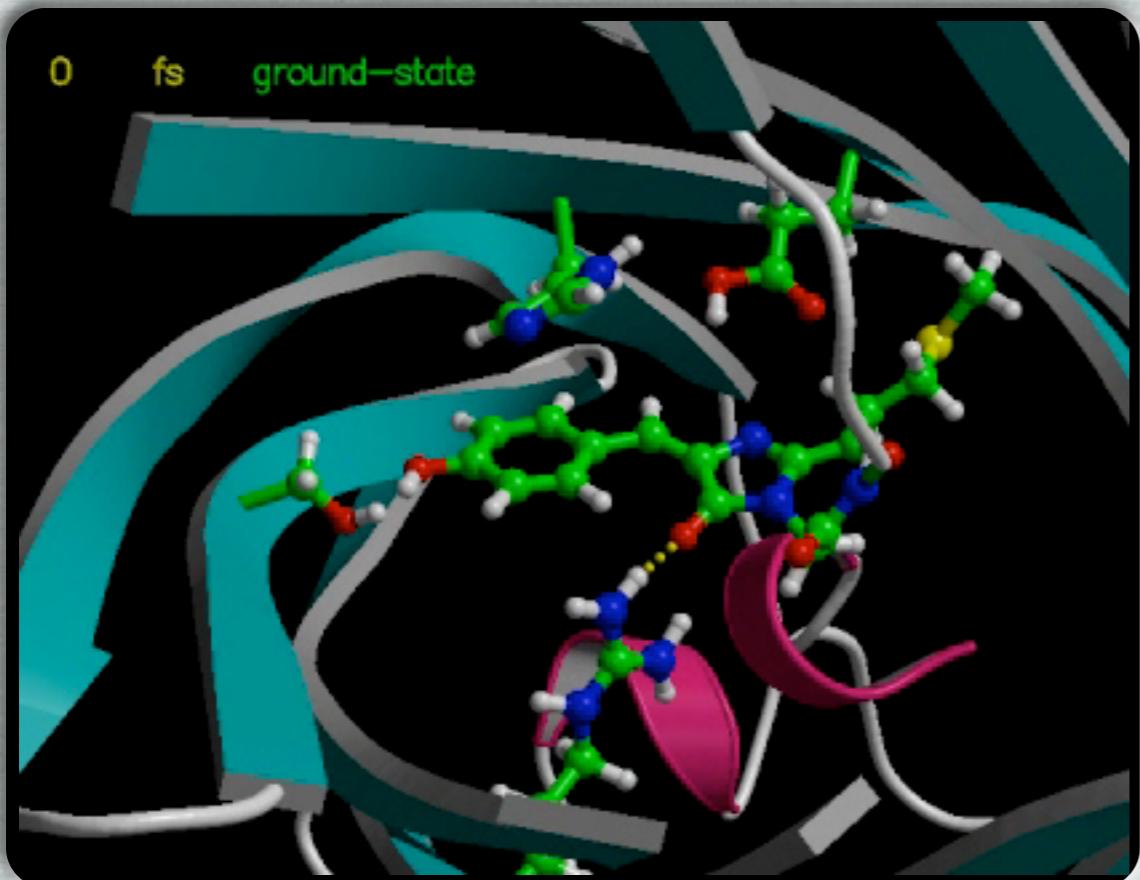


neutral *trans*

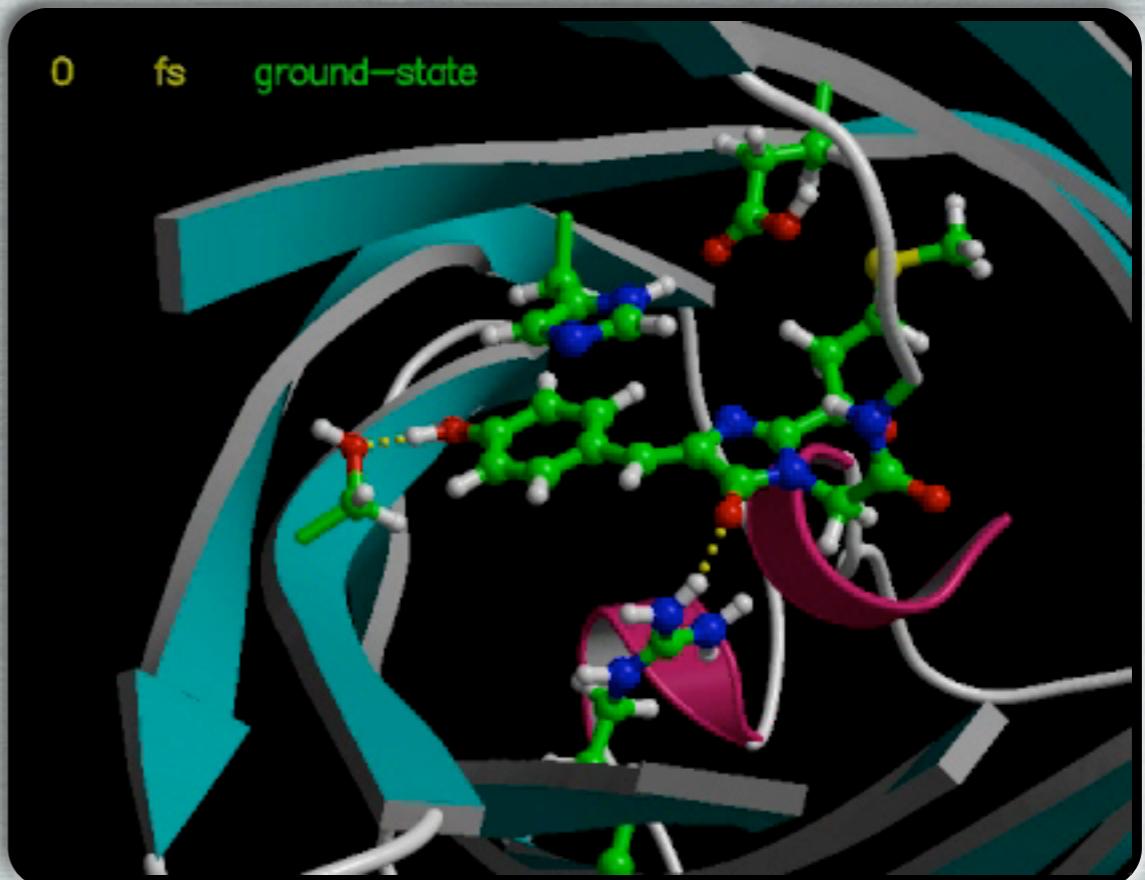


neutral *cis*

neutral: photoisomerization



neutral *trans*



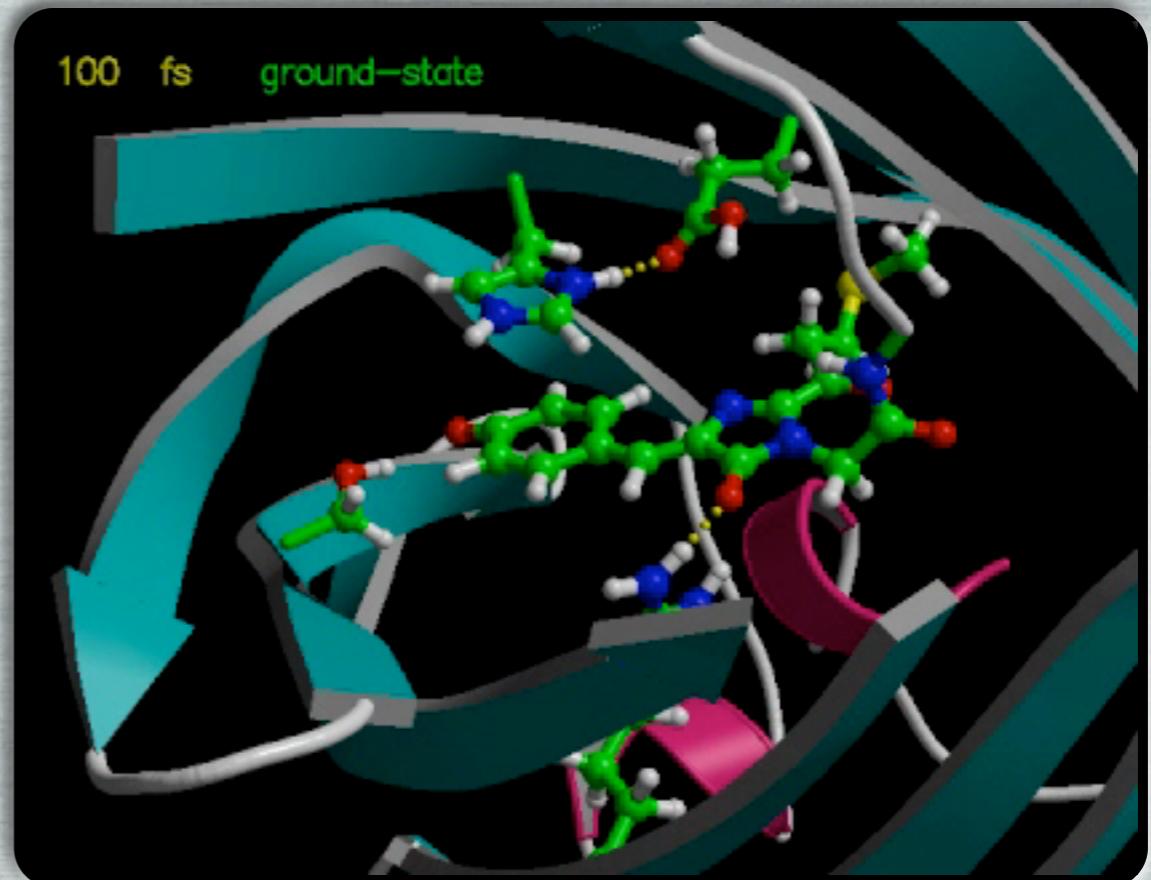
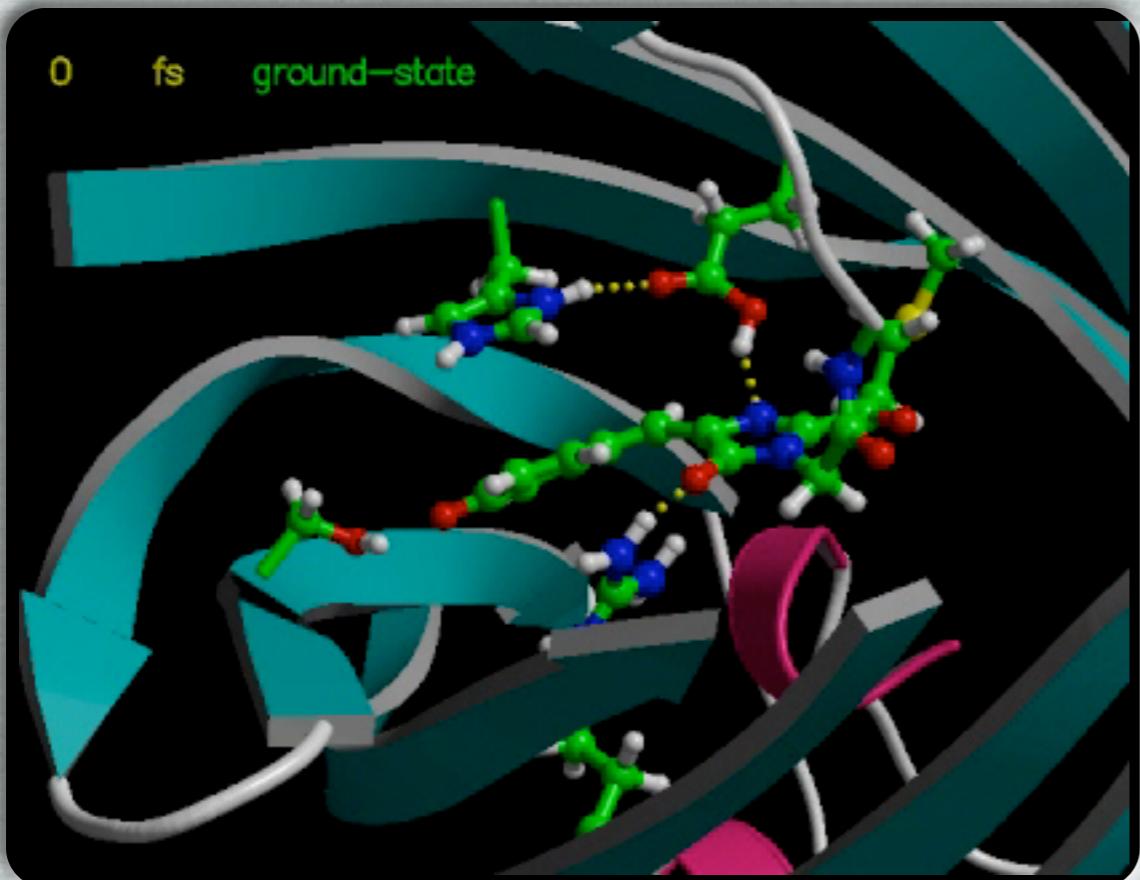
neutral *cis*

anions: radiationless decay (dark)

anionic *trans*

anionic *cis*

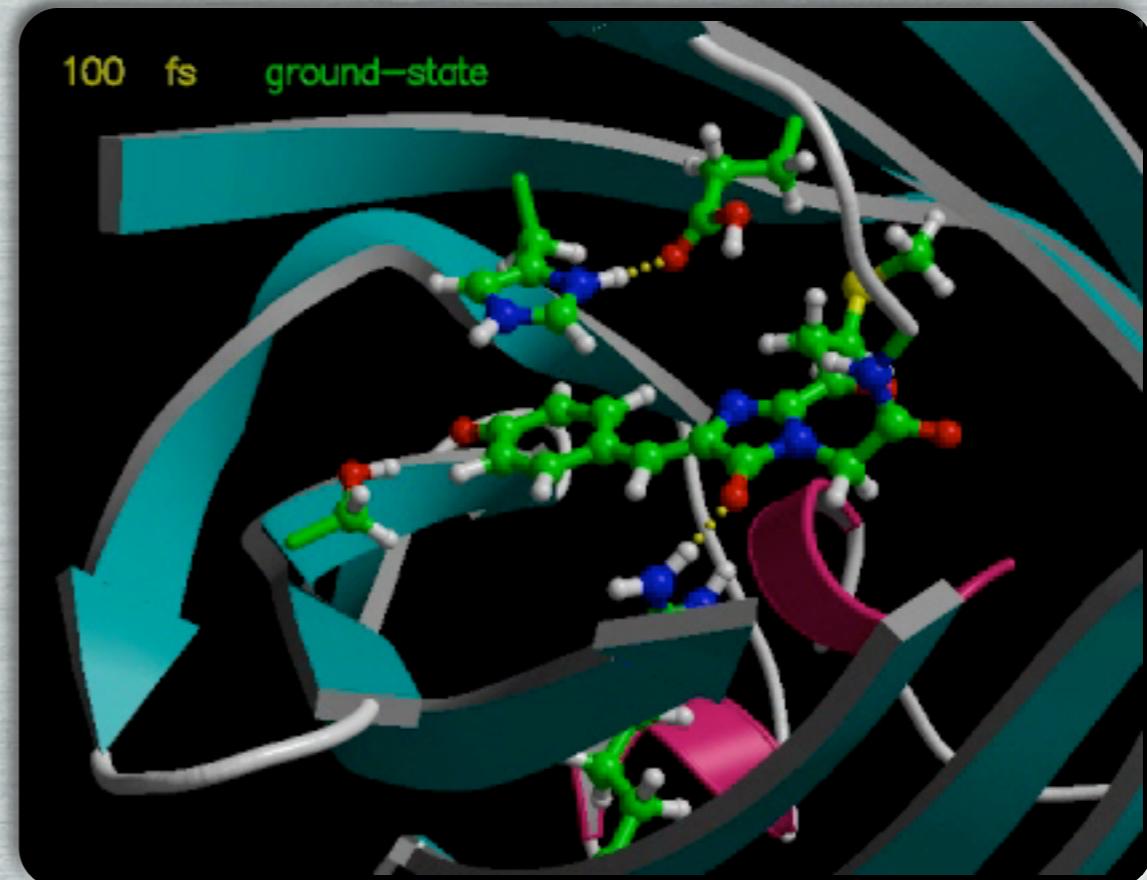
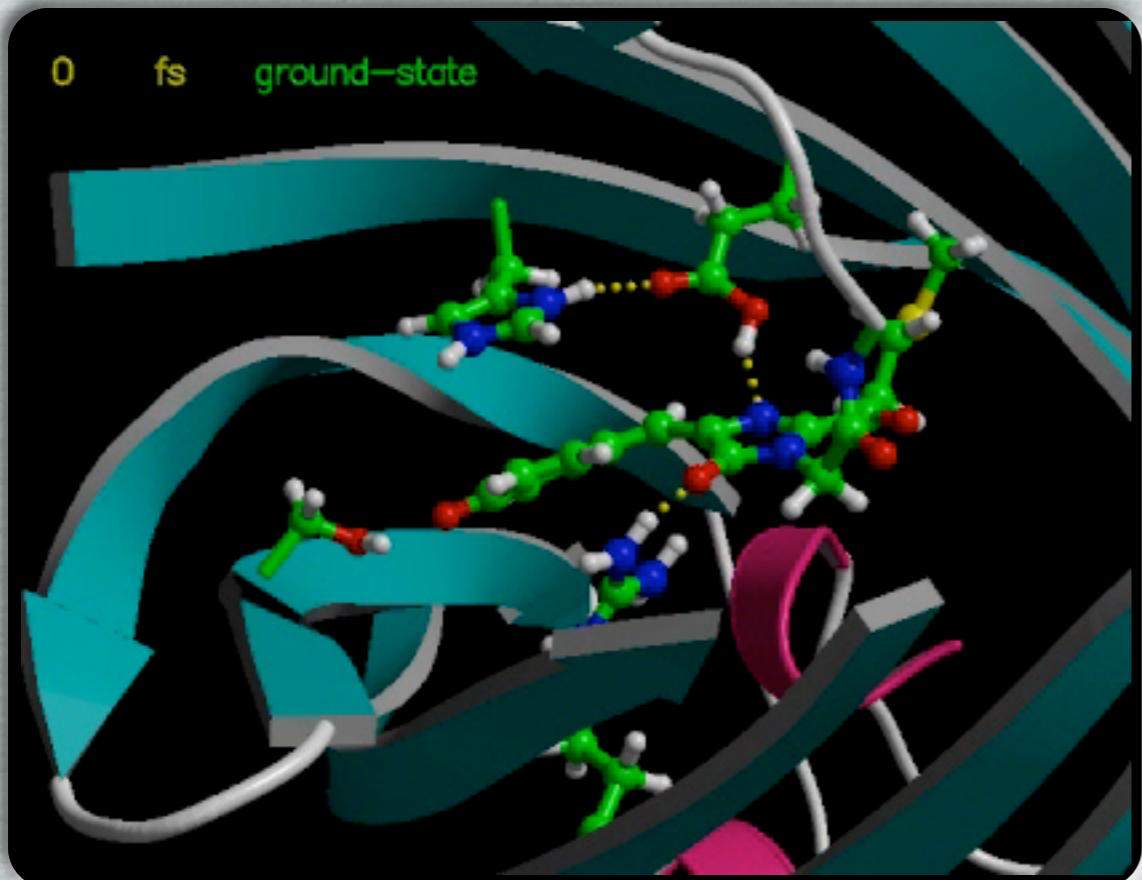
anions: radiationless decay (dark)



anionic *trans*

anionic *cis*

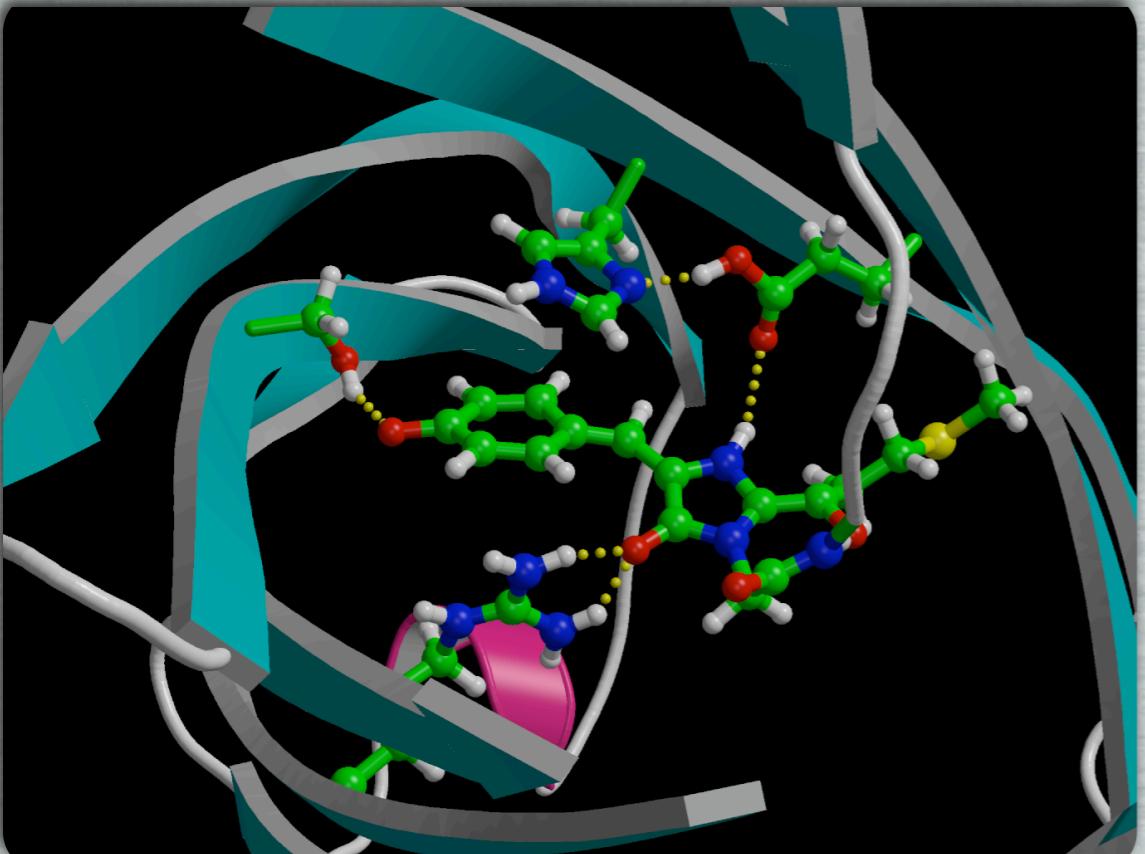
anions: radiationless decay (dark)



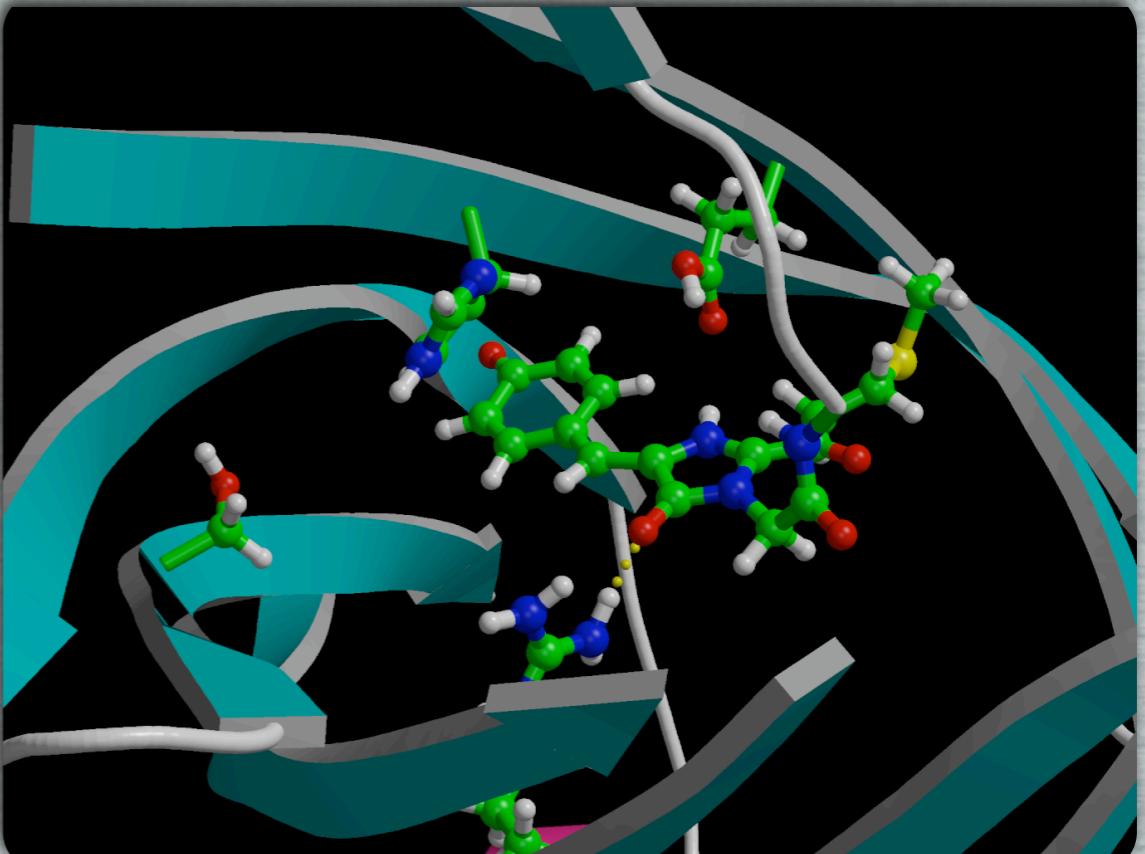
anionic *trans*

anionic *cis*

zwitterions: fluorescence

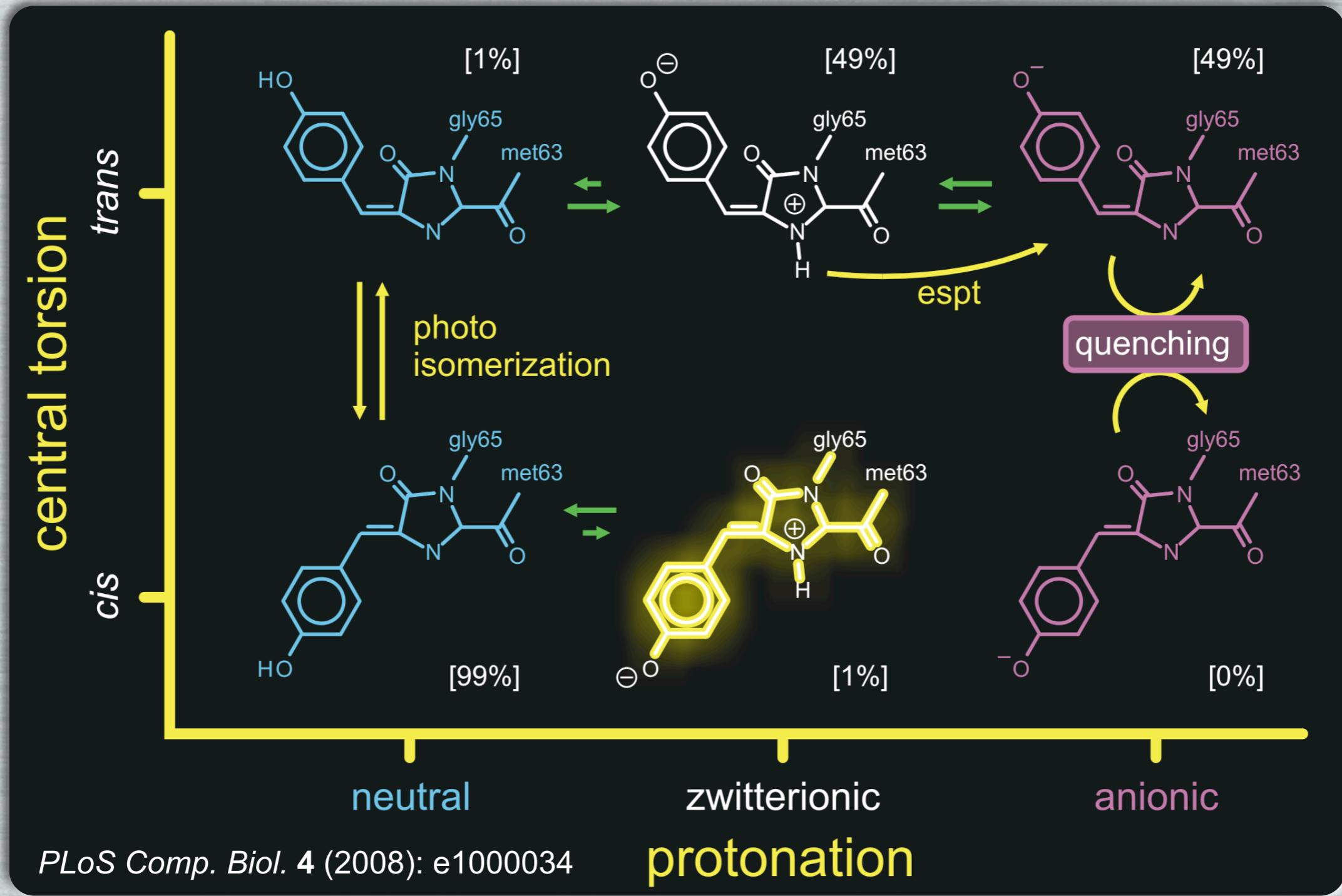


zwitterionic *trans*



zwitterionic *cis*

photoswitching mechanism in asFP



summary & outlook

mixed quantum/classical molecular dynamics

- ▶ photobiology
- ▶ electron transfer
- ▶ ionizing radiation

towards biotechnology

- ▶ protein/chromophore modification
 - ▶ data storage, imaging, ...
-



acknowledgements

Lars Schäfer

Martial Boggio-Pasqua

Michael Robb

Gromacs team

David van der Spoel

Erik Lindahl

Berk Hess

An aerial photograph of a large, modern research facility nestled in a green, hilly landscape. The complex consists of several interconnected buildings with white facades and grey roofs, surrounded by trees and greenery. A road runs along the perimeter of the facility, and a yellow field is visible to the right.

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

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