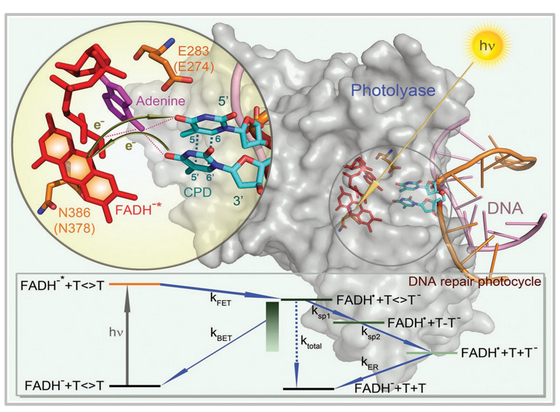
Karlsruher Institut für Technologie

Institute of Physical Chemistry
Theoretical Chemical Biology

Non-Adiabatic Charge Transfer Simulation of Photoactivation in *E.Coli* DNA Photolyase

Gesa Lüdemann, Benjamin Woiczikowski, Thomas Steinbrecher, Tomas Kubar and Marcus Elstner

DNA Photorepair



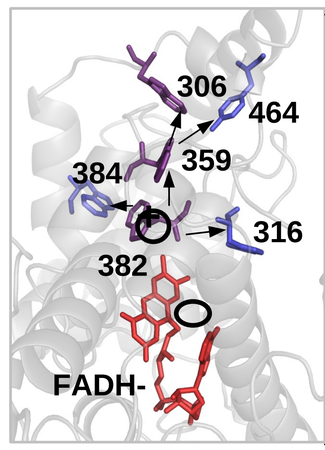
Zhong et al. *PNAS* (2011) **108**, 14831

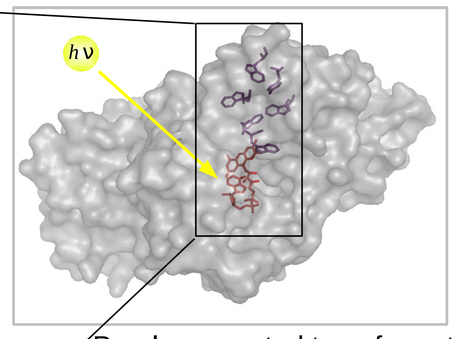
Photolyases bind to UV-damaged DNA and repair CPD lesions via electron transfer from the FAD cofactor to the dimerized pyrimidines.

During **photoactivation** an electron is transferred from the protein surface to the partially oxidized flavin cofactor.

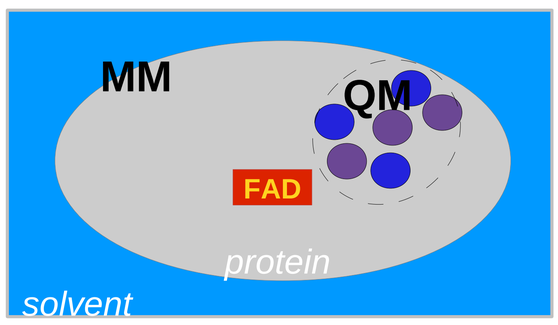
- ➔ dynamic and heterogeneous environment
- ➔ transfer over long distances and long timescales
- ➔ Rate of transfer ≈ environmental reorganization energy

2nd Mechanism: Photoactivation





Purple: accepted transfer path; Blue: residues possibly involved in transfer; Structure by Park et al. Science (1995) 268, 1866



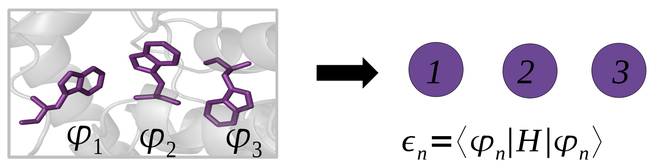
- nuclear and electronic systems are propagated simultaneously via mean field method [2] by coupled equations of motion:

$$M_\alpha \ddot{R}_\alpha = \frac{\partial E^{MM}(q_\alpha, q_A^0)}{\partial R_\alpha} \quad \text{and} \quad \dot{a}_m = i \sum_n a_n H_{nm}$$

=> Charge is free to (de)localize, no *a priori* assumption of CT mechanism

Multi-Scale Simulation Scheme

Coarse Graining of quantum system



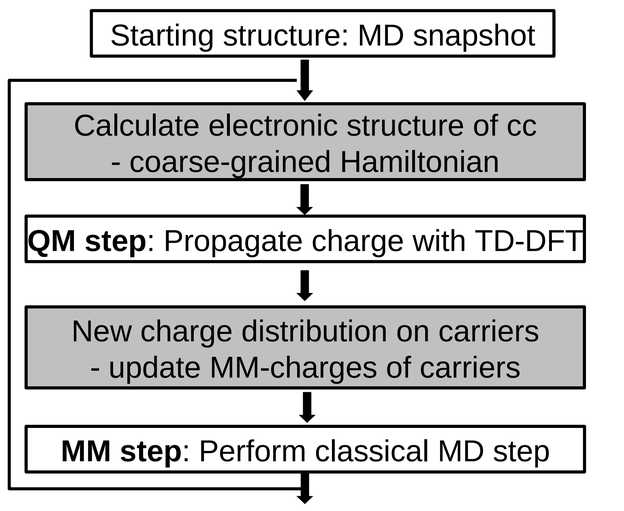
$$\Psi = a_1\varphi_1 + a_2\varphi_2 + a_3\varphi_3 + \ldots = (a_1, a_2, a_3 \ldots)$$

$$\epsilon_n = \langle \varphi_n | H | \varphi_n \rangle$$

$$T_{nm} = \langle \varphi_n | H | \varphi_m \rangle$$

QM/MM Embedding

- Polarisation of QM system by environment: H_{nm} is evaluated with QM/MM-environment represented by point charges
- Influence of changing charge distribution on classical environment: Mapping fraction of fragment charge onto atomic charges



Simulation details

- Simulations based on structure by Park et al.
- carried out with Gromacs and in-house developed quantum chemistry code based on SCC DFTB [3]

Non-adiabatic Ehrenfest Dynamics

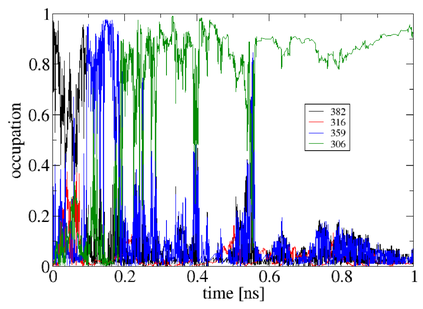
Comparison with rates from Marcus Theory and Experiment

rates in 1/ns

Step	Non-ad	Marcus	Exp
1->2	12	5	100
2->3	15	0.002	30

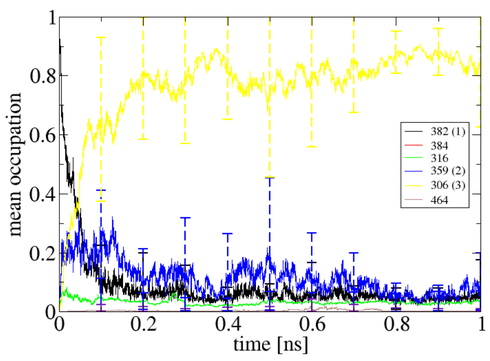
➢ Classical CT theory cannot describe fast 2->3 transfer

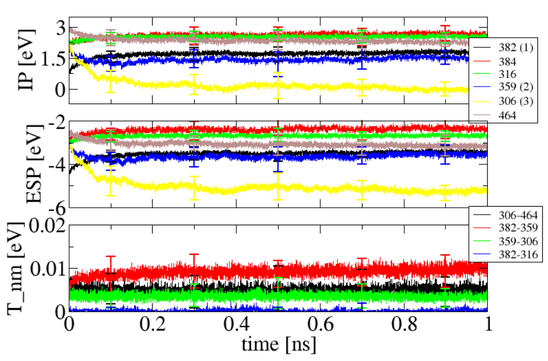
Example of single CT trajectory



- All six amino acids included in QM Zone
- Transfer from 382 to 359 to 306 with slight delocalization

Averages over 30 simulations





- Broad variety of charge transfer characteristics
- On average charge transfer occurs within 50 ps
- Charge resides mainly on Trps 382, 359 and 306
- Small partial occupation of Trp 316
- Drop in ESP leads to drop in IP –stabilization of hole on 306

Electronic Polarisation of environment

- Nonpolarizable forcefields can lead to overestimation of environmental reorganisation energy.
- Scaling of MM charges by suitable constant [4]

$$V_m^{ESP} = \sum_{MM\ atoms} \frac{1}{\varepsilon_{MM}} \frac{q_A^0}{R_{mA}}$$

- We compare values of 1, 1.4 and 2 for ε_{MM}

- Transfer occurs within 25 ps resp 10 ps for the two scaling factors

Summary and Outlook

- Trp 316 might be involved in the transfer process; originally not considered in transfer path
- ESP scaling is important in order to reproduce experimental values
- Charge transfer dynamics can be reproduced very well without prior assumption of the involved amino acids

-> tool to identify ET path from QM/MM simulations which can be applied to multitude of systems e.g. other enzymes of the photolyase/cryptochrome family

References:
1. Woiczikowski et al. *JPCB* (2011) **115**, 9846
2. Kubar and Elstner *JPCB* (2010) **114** 11221
3. Elstner et al. *PhysRevB* (1998) **58**, 7269
4. Blumberger and Lamoureux, *MolPhys* (2008) **10**, 5651

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