LMU LUDWIG-MAXIMILIANS-UNIVERSITÄT MÜNCHEN

Influence of Neighboring Nucleobases on the Photostability of Uracil

– Quantum Dynamics in Explicit Biological Environments –

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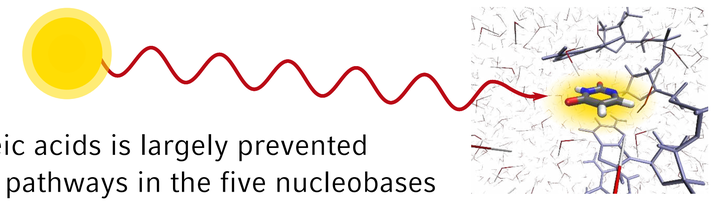
Abstract



Our research interest

- Photochemical damage in nucleic acids is largely prevented by means of ultrafast relaxation pathways in the five nucleobases
- Recent studies elucidate the relaxation process of isolated uracil in the gas phase[1,2]
- Next step: Analyzing the effects of a biological environment on the relaxation path

The challenge

- Appropriate simulation of environmental effects is computationally difficult

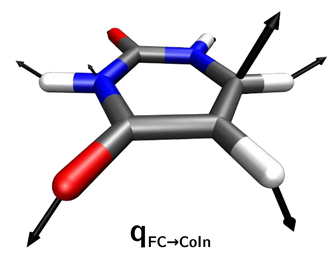
What we present

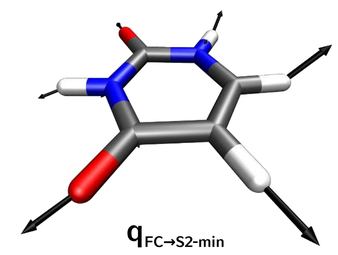
- An approach to simulate wave packet dynamics in explicit solvent environments
- A comparison of the relaxation pathways of uracil in the gas phase and in its native biological environment

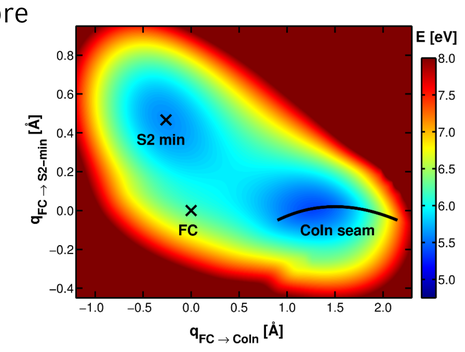
Background: Gas Phase Dynamics

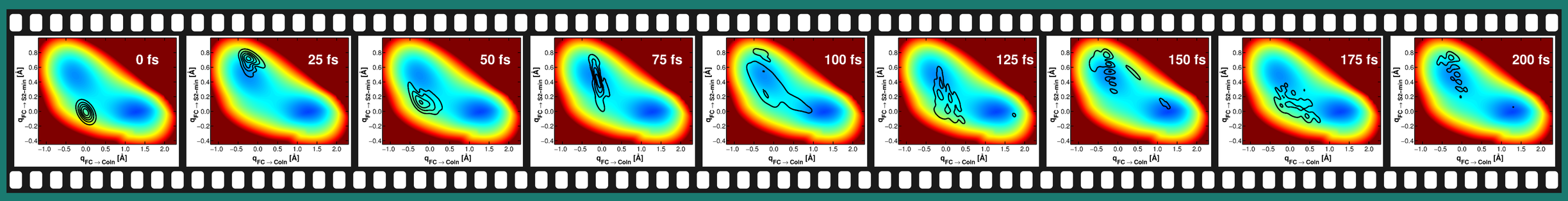
according to Ref. [2]

- Excitation into bright ππ*-state (S2)
- First relaxation step through conical intersection (CoIn) into dark nπ*-state (S1)
- Orthonormal displacement vectors between optimized geometries of Franck-Condon point (FC), S2 min and S1/S2-CoIn (MRCI(12,9)/cc-pVDZ) span coordinate space
- Wave packet evolves into direction of S2 min before decaying through CoIn (see filmstrip below)



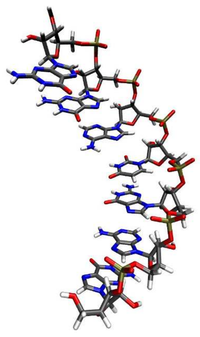






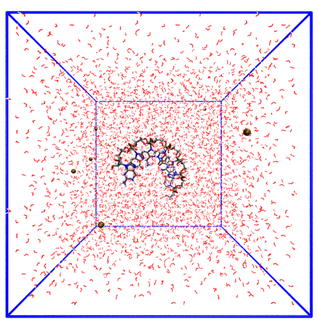
Considering the Environment

based on an approach described in Ref. [3]



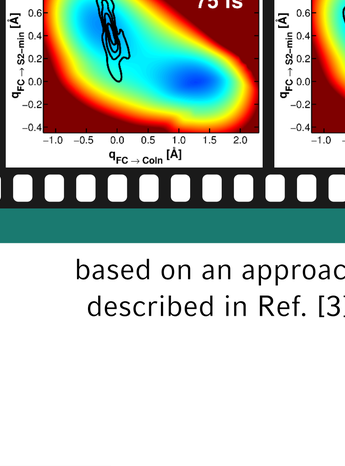
RNA fragment
Sequence: GAGUAGG

add water and Na^+-ions



MD simulation
Water: TIP3P, RNA: Amber14Sb
Simulation time: 100 ps

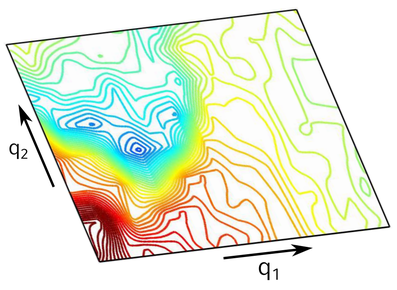
extract 25 random snapshots from 5 MD trajectories



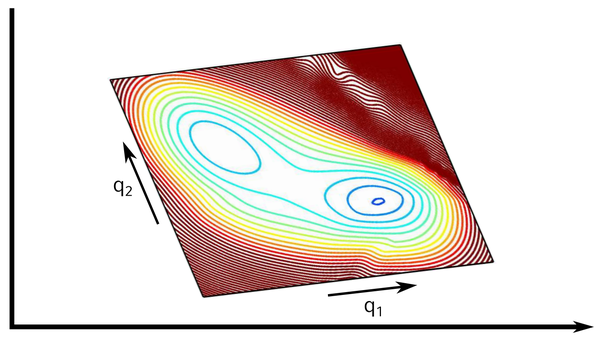
construct QM/MM PES with two neighboring bases in QM region
QM: DFT/M06-2X/6-31G*; MM: Amber14Sb

subtract ground state PES of uracil in the gas phase

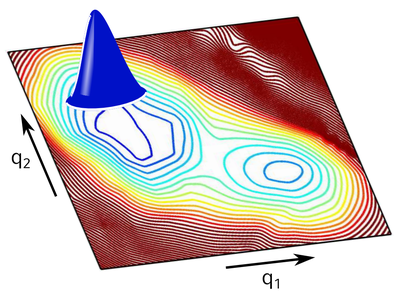
DFT/M06-2X/6-31G*



ground state environment potential



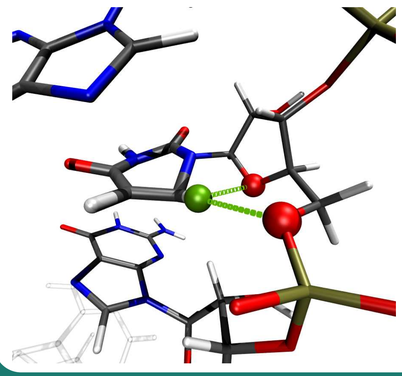
combine environmental PES with high-level S2-PES of uracil in the gasphase
MRCI(12,9)/cc-pVDZ[2]

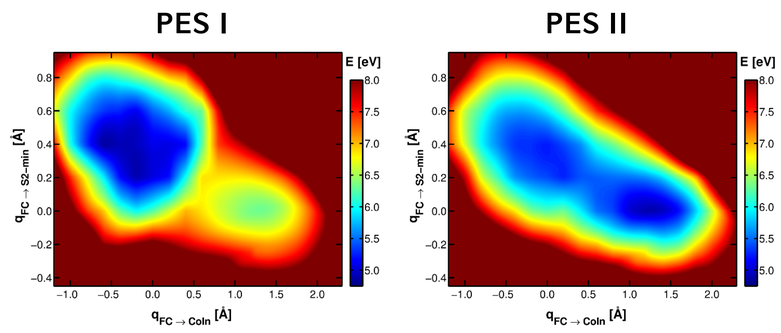


quantum dynamics in an explicit RNA and solvent environment

Environmental Effects on the PES

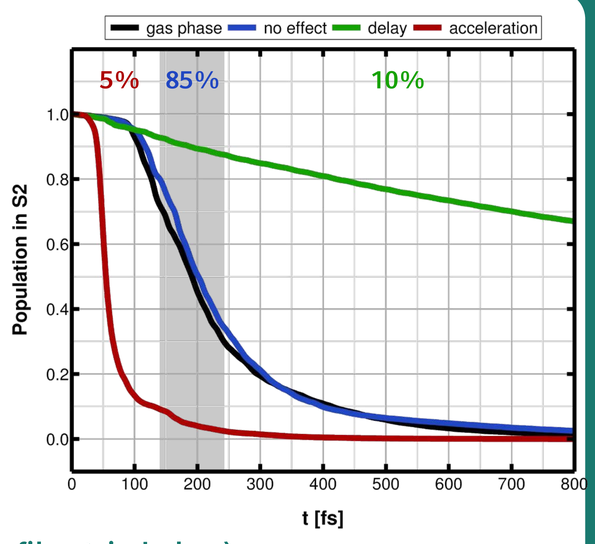
- Majority of cases: no significant environmental influence
- Hydrogen bonds to neighboring bases and to the sugar/phosphate backbone have a strong stabilizing effect
- Stabilization can occur localized (PES I) or delocalized (PES II) across the PES, depending on the specific environmental conformation





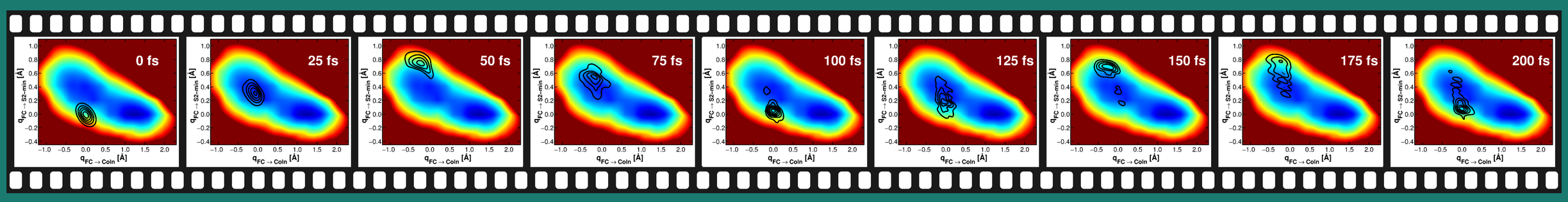
Quantum Dynamics

- Quantum dynamics with non-adiabatic coupling between S2 and S1 states (MRCI(12,9)/cc-pVDZ)
- Sample size: 125 snapshots
- Tolerance of ± 50 fs around the gas phase lifetime (186 fs) defines delay or acceleration
- Most samples resemble the gas phase
- Trapping of the wave packet can be induced by the topology of the PES



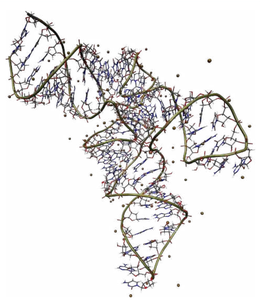
Example: Quantum Dynamics on PES II (see filmstrip below)

- CoIn and barrier are energetically lower than in the gas phase
- But: collision points on PES give less momentum in the direction of the CoIn
- Result: oscillation between FC and S2 min and delayed relaxation



Outlook

- Investigate more RNA fragments with different combinations of neighboring bases
- Increase number of snapshots to improve phase space sampling
- Examine the influence of base-pairing in double-stranded RNA



References

[1] S. Matsika, M. Spanner, M. Kotur, T. C. Weinacht, *J. Phys. Chem. A* **117**, 12796 (2013).

[2] D. Keefer, S. Thallmair, S. Matsika, R. de Vivie-Riedle, *J. Am. Chem. Soc.* **139**, 5061 (2017).

[3] S. Thallmair, J. P. P. Zauleck, R. de Vivie-Riedle, *J. Chem. Theory Comput.* **11**, 1987 (2015).

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