

Ultrafast Photorelaxation of Uracil Embedded in an RNA Strand

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Abstract. Ultrafast photorelaxation of uracil can be hindered by its natural RNA environment. Multiscale quantum dynamical simulations show that the wave packet can be trapped in the photoexcited electronic state, which could potentially lead to photodamage.

1. Photorelaxation of uracil: gas phase vs RNA

Ultraviolet (UV) radiation can trigger photochemical reactions in nucleic acids and weaken the integrity of the genetic code. The formation of harmful photolesions is however mostly prevented by means of ultrafast relaxation processes occurring in all five nucleobases [1]. Photodamage can happen when these pathways are blocked, and the nucleobases remain trapped in the excited state [1]. Such events are extensively investigated both experimentally and theoretically, mainly for isolated nucleobases. In this context, a recent quantum dynamical study using high-level multireference potential energy surfaces (PESs) of photoexcited uracil demonstrated the possibility of trapping a nuclear wave packet (WP) in the S_2 state with a tailored laser pulse, while an unbiased UV excitation always induces ultrafast relaxation [2]. In our current study, we consider uracil in its native RNA environment, where steric hindrance by the sugar phosphate backbone and/or adjacent nucleobases (fig. 1) can influence the PES. The question we want to address is whether this can delay the relaxation back to the ground state and thus potentially be responsible for photodamage.

2. Multiscale quantum chemistry to characterize the environmental influence

We employ a combined approach (fig. 1) of molecular dynamics (MD) and quantum dynamics (QD) that has recently been developed in our group [3]. Therefore, we sample conformations of several different RNA sequences solvated in water by computing MD trajectories and extracting snapshots at random geometries. Multiscale quantum mechanics/molecular mechanics (QM/MM) calculations then enable us to simulate the effects of an atomistic environment and construct an environmental PES for each snapshot. These are subsequently combined with a high level (MRCI(12,9)/cc-pVDZ) gas phase PES

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of the S_2 state of uracil, containing the geometries of the S_2 -minimum and a conical intersection (CoIn) to S_1 [2]. Finally, we simulate the relaxation through the S_2/S_1 CoIn by performing WP dynamics on the thus obtained PESs.

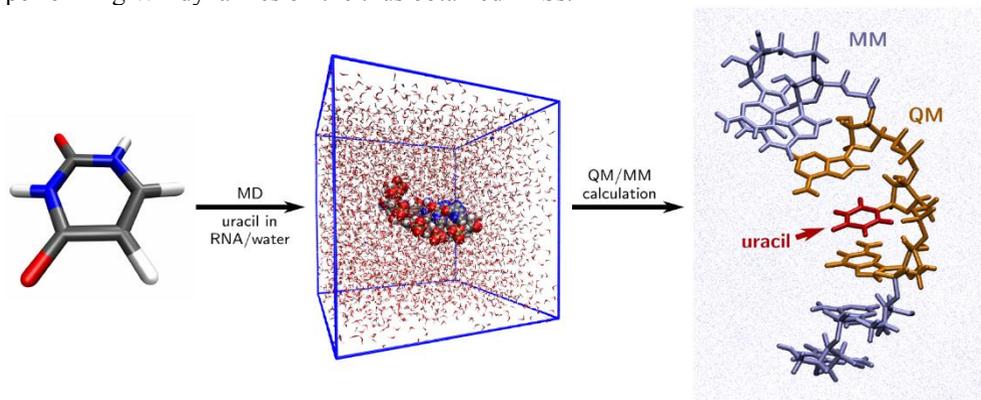


Fig. 1: Uracil in RNA. Left: gas phase geometry of uracil; Middle: MD simulation box containing an RNA sequence solvated in water; Right: QM/MM setup with uracil, RNA backbone and neighboring nucleobases.

3. Wave packet simulations to determine excited state lifetimes

The influence of the RNA environment alters the gas phase PES (fig. 2a) of uracil. We observed effects such as a lowered barrier between S_2 minimum and CoIn (fig. 2b), strongly stabilized minima (fig. 2c) and even additional minima (fig. 2d). Most of the 250 calculated PESs however closely resemble their gas phase counterpart. To determine excited state lifetimes, we performed quantum dynamical simulations with the wave packet starting at the FC point, where it enters the S_2 state after UV excitation. In 82% of the snapshots, the WP follows the gas phase pathway (fig. 2a) and undergoes two oscillations between FC point and S_2 minimum before crossing the barrier and decaying through the CoIn seam. The half-life of this relaxation process is 192 fs, which is in good accordance with gas phase experiments [4]. In 12 snapshots (5%), the relaxation time is decreased, while we observe long excited state lifetimes and even WP trapping for 13% of the snapshots (fig. 2b – d). This means that long excited state lifetimes are rare events, which is in line with the extraordinary photostability of uracil. However, our simulations show that trapping in the electronically excited state can occur in uracil solely through the influence of its natural environment. In the literature, delayed relaxation is usually attributed to the delocalization of excited states, such as excimer or exciton formation [5]. In contrast, our studies show that these critical states can also occur without the need for delocalization events.

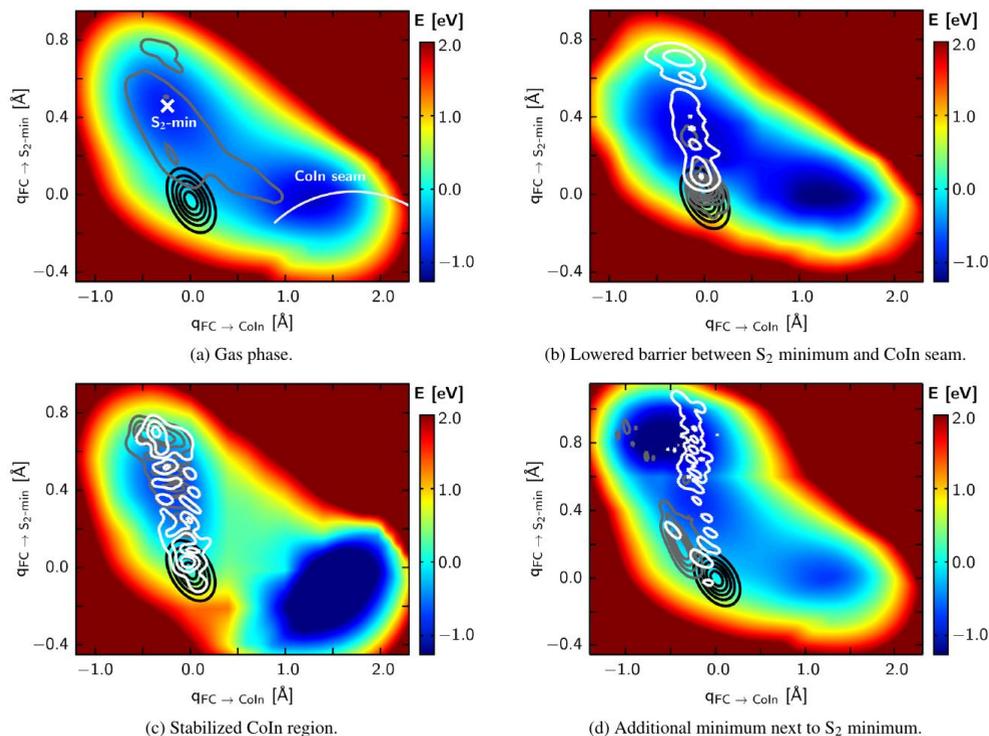


Fig. 2: Nuclear WP starting at the Franck-Condon (FC) point on the S_2 PES of uracil in the gas phase (a) and in an RNA strand (b – d) at 0 fs (black), 100 fs (grey) and 400 fs (white). In the gas phase, the population has completely decayed through the CoIn after 400 fs, while the WP is trapped in the excited state under environmental influence.

4. Different neighbouring base sequences

In the 250 snapshots tested above, we also used 10 different sequences of neighbouring bases to investigate whether there are more or less favourable configurations. This was however not the case, since the distribution of slower (>242fs), faster (<142fs) and similar (192 ± 50 fs) lifetimes as compared to the gas phase was roughly the same for all ten sequences. The possibility of trapping the WP in the S_2 excited state and potentially facilitating photodamage is thus suggested to be base independent.

References

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