Applications of quantum chemistry for mapping electron transfer pathways in photoinduced DNA repair

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Absorption of UV photons by DNA leads to the formation of photodimes between the adjacent pyrimidine bases which is detrimental for DNA biological function. In some organisms these photodimers are inverted by photolyase enzymes operating by means of photoinduced electron transfer. Photoexcited flavin cofactor of photolyases serves as an electron donor to the photodimes. The quantum yield of the repair reaction is determined by competing forward and backward electron transfer reactions. Studies of photolyases [1] are focused on identifying electron transfer pathways that control the repair quantum yield. Determination of the photolyase 3D structure

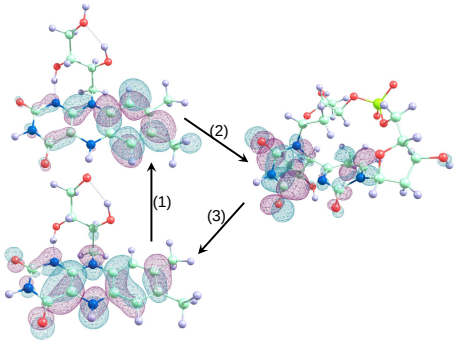

Figure 1: Electron transfer pathways of photoinduced DNA repair. Flavin photoexcitation initiates DNA repair (1), the excited flavin donates an electron to the DNA lesion (2), back electron transfer from the DNA lesion to flavin reduces the repair quantum yield (3). Multireference quantum chemistry calculations provide excitation energies and dipole moments for evaluating electron transfer rates.

initiated computational investigations of the DNA photorepair reactions. One issue to be address by computational studies is evaluation of electron transfer rates to facilitate comparison with experimental findings. We apply multireference quantum-chemistry calculations for characterizing electron transfer between the flavin and DNA lesion (see Figure). In particular, the maximal electron transfer rates are estimated from the excited state calculations with the help of generalized Mulliken-Hush scheme. The obtained maximal rates map the most probable electron transfer pathways and render some previously suggested pathways [1] to be inconsistent with experimental observations. The analysis of maximal rates establishes that energy tuning, e.g. via electrostatic interactions, is crucial for increasing the repair quantum yield. The obtained results pave the way to evaluating controversial proposals and to eventually establishing the mechanism of photoinduced DNA repair by combining computational and experimental results.

Funding The work is supported by the Russian Science Foundation grant no. 22-23-00418.

References

[1] Yamamoto J., Plaza P., Brettel K., 2017, *Photochem. Photobiol.*, 93, 51