

Understanding the photophysics and photochemistry of biologically relevant chromophores: the road towards cancer therapy and prevention.

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Light-driven processes are important in a myriad of (bio)chemical processes. Following light-irradiation of a given molecular system, an electron may be promoted to a high energy orbital – forming an excited electronic state. The excited molecule represents an exotic state, with a total energy that is usually in excess of many of the transition states associated with ground state reactions. As such, molecular photo-excitation provides a selective means of activating reactions that would be unreactive in the ground state electronic configuration.

Although electronic excitation provides a means of encouraging reactivity, many naturally occurring biomolecules (such as the DNA/RNA nucleobases) remain completely unreactive when photo-excited. Such molecules dissipate the excess energy introduced by photo-excitation and recover their ground state configuration with impressive efficiency. They exhibit photostability and are termed photostable. In the first part of this seminar, I will describe a series of experimental and theoretical methods that have been used to explore the properties of nucleic acids (adenine, thymine, uracil, guanine and cytosine) that give rise to their inherent photostability. The mechanisms of photostability in nucleic acids will then be compared to the excited-state properties of some of the simpler aromatic building blocks (e.g. pyrrole and indole) – in order to reveal the geometric and electronic reasons why the nucleic acids exhibit much greater inherent photostability than their tautomeric and configurational analogues. In the final part of this seminar, I will describe the extent to which the mechanisms of photostability persist upon solvation and in bulk biological environments. In so doing, I will highlight the extent to which the local biological environment introduces rival (potentially detrimental) reactions that reduce photostability and lead to DNA/RNA damage upon prolonged UV-exposure. An understanding of the ways in which natural biomolecules cope with UV-irradiation is vital for the design of more efficient (supra)molecules that offer protection against UV-light (e.g. in commercial sunscreens) and exploit light (e.g. fluorescent probes in biodiagnostics). Future directions will exploit this knowledge in understanding mechanistic details in processes such as interfacial photocatalysis at the molecular level and in developing macromolecular structures for light-induced cancer therapy.