

How Do Biomolecules Harness the Energy in a Photon to Generate a Signal?

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All chemical and biochemical reactions involve dynamic, not merely static structures, in which atoms move from their positions in reactants via intermediate structures towards those in products. Atomic motion in biomolecules spans an extremely wide time range, from femtoseconds to seconds or even to the generation time of the organism. How shall this atomic motion be probed and the reaction mechanisms identified? Are these chemical kinetic mechanisms based on a relatively small number of discrete intermediate states and well-defined pathways for interconversion among these states? Or, is there essentially a continuous distribution of intermediate states?

We explore these questions by studying light-sensitive biomolecules and in particular, signaling photoreceptors. Such molecules absorb a photon in the visible region of the spectrum, undergo structural changes over a wide time range that constitute a thermodynamic signal, then ultimately respond to this signal by a change in the “behavior” of the organism e.g. a change in the swimming behavior of bacteria or the light-dependent developmental processes of plants (1). That is, signaling photoreceptors harness the energy in a photon to generate information, in contrast with processes such as photosynthesis in which the energy in the photon ultimately generates chemical energy and drives metabolic processes. Harnessing light energy is non-trivial; the energy in a visible photon is 50 – 70 Kcal/mole which far exceeds the free energy of stabilization of a typical protein, ~ 10 Kcal/mole. Thus if inappropriately harnessed, the photoreceptor may be unfolded or denatured and thus rendered biologically inactive.

We apply a combination of ultrafast time-resolved X-ray crystallography (2,3) and UV/visible spectroscopies (see e.g. 4) to explore the static and dynamic structures of signaling photoreceptors, in crystals and in solution. Some photoreceptors absorb blue light e.g. flavin-based LOV receptors; others absorb red/far red light e.g. bilin-based bacteriophytochromes. The primary photochemistry differs from system to system: isomerization about a double bond, rupture of a covalent bond, formation of a covalent bond, or electron transfer (1).

Do these light-dependent processes in any way resemble the more widely studied ligand-binding-dependent signaling processes? Obviously, not all biological systems are light-sensitive and techniques devised for natural photoreceptors are not directly

applicable to them. To explore generality, we are implementing biologically-inspired approaches to conferring light sensitivity on light-inert biological systems. That is, we design and engineer artificial biological photoreceptors, in which a desired biological activity e.g. catalysis by a kinase, or binding to a specific DNA sequence is placed under the control of light. This topic is just becoming known as “optogenetics” (5-8).

References

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