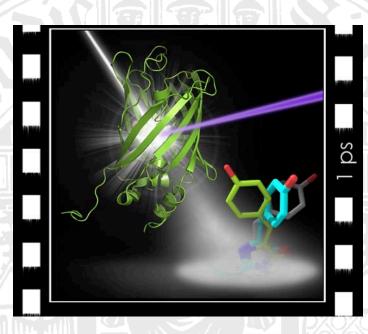




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WATCHING PROTEINS AT WORK WITH X-RAY FREE ELECTRON LASERS

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Proteins are the molecular engines of life. Their broad range of biological tasks and functions is reflected in the large diversity of specific dynamical characteristics they display on a broad time scale. On the femtosecond time scale, atomic bonds vibrate and proteins respond to light stimuli. Amino acid side chains jiggle and wiggle on the pico- to nanoseconds time scale. Within micro-to milliseconds, protein domains change shape and move with respect to each other. Entire proteins are synthesized and fold in seconds to minutes.

A large number of experimental techniques exist that each opens a specific window onto macromolecular dynamics on a particular time scale. Among those, time-resolved crystallography allows watching proteins *at work* at atomic resolution. Recently, the advent of an entirely new generation of X-ray sources, so-called X-ray free electron lasers (or "XFEL"), pushed the resolution in time-resolved crystallography down to sub-picoseconds. These devices generate X-ray pulses of very short duration, of the order of a femtosecond (one millionth of a billionth of a second), with a very high intensity, at the core of an installation several kilometers in length. Exciting possibilities are now opened to structurally follow ultra-fast macromolecular processes such as vision, bioluminescence and other phenomena, which have not been observable to date. As an example, we will show how time-resolved X-ray crystallography at XFELs allowed visualizing photoswitching in fluorescent proteins, which are extensively used as markers in biological imaging (see figure).