Revealing the structural dynamics of biomolecules with x-rays and XFELs

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Macromolecular dynamics are essential to life. They range from local motions that catalyze reactions, through global reorganizations of biopolymers that fold or associate. Over the past 25 years, my group has developed methods to trigger and monitor reactions involving proteins, RNA and DNA, alone and in combination. We use X-ray scattering in both solution and crystallographic modes to reveal macromolecular structural dynamics on time scales ranging from milliseconds through minutes. I will present an overview of experiments that enable dynamic structural measurements on length scales ranging from single Å though nm. The former experiments are uniquely enabled by our home-built mixing injectors, used at x-ray free electron laser sources. I will discuss recent results of these 'structural enzymology' experiments, watching proteins execute the small motions required for catalysis. The latter experiments are enabled by classes of synchrotron compatible microfluidic mixers. We use these mixers to examine structural changes on larger (global) size scales. Problems of interest include the self-assembly (folding) of RNAs into functional structures, or the dynamic interactions of nucleic acids and proteins in important macromolecular complexes like nucleosome core particles or viruses.