X-ray microscopy: freezing complex biological processes

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Microscopes require objects to be static during the capture of a single image, or frame of a movie, or throughout the acquisition of a sequence of images as either the energy is tuned or the specimen is rotated. For biological specimens, radiation damage increases steeply as the spatial resolution is improved; this will likely preclude the study of dynamic processes in single cells or tissues. How then can one study the nanoscale complexity of how biological processes evolve? One possible solution is to use rapid freezing following stimulus, both to stop dynamic processes in time and to mitigate the limitations of radiation damage. Such freezing could be timed with stimuli such as the release of photoactived caged molecules, or electrode activation, or after light scattering or fluorescence has signaled the start of some process. Examples of timed-freezing experiments in biological electron microscopy will be reviewed, cryo capabilities for x-ray microscopy will be discussed, and finally the potential and limitations of short-pulse x-ray microscopy will be considered.