

## **Biological nanomachines and their control**

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Biological nanomachines are nano-meter scale complex machineries such as ribosomes, RNA polymerases, transporters, transport vesicles and signal transduction complexes. They self assemble, move to proper destinations and function as they are programmed, and are recycled after finishing their missions. The cell is extremely congested with such biological nanomachines embedded either in the cytosol (intracellular matrix, i.e., fluid inside the cell), lipid membranes and organelles. Control of these biological nanomachines requires knowledge on their function and atomic scale structure, and their dynamics within the crowded cellular environment.

Among the methods to elucidate their structures and functions, synchrotron radiation protein crystallography has been the most powerful and successful technique revealing the atomic details of large macromolecular complexes, and providing answers for many fundamental biological questions. Synchrotron radiation protein crystallography has come a long way to the present status where high resolution structures can be determined for small to extremely large proteins and complexes with other biological or small molecules. One fundamental constraint of protein crystallography is that one needs to crystallize  $10^6$  to  $10^{12}$  molecules into the crystal lattice which limits free motions of the proteins/complexes. In certain cases where enzymatic reactions can proceed within the crystal lattice with a proper triggering scheme such as light or pH jump, their dynamics can be studied at atomic resolution by time-resolved crystallography. Future SR beams are expected to enable ultimate protein crystallography, i.e., determination of protein structures from submicron crystals. FEL developments hold promise of single molecule structural analyses, which will be extremely powerful in structural studies of well behaving, i.e. with identical structures, protein molecules or their complexes.

There are, however, many other nanomachines which undergo much larger scale conformational changes during their actions or which are intrinsically disordered. This is a very challenging problem for structural biology and every effort is needed in perfecting and combining the existing and new structural analysis techniques, many of which use synchrotron radiation: crystallography, solution scattering, soft and hard X-ray tomographic imaging, and single molecule structure analysis. For full understanding and exploitation of nanomachines, it will be essential that these synchrotron techniques be combined with other structural biology methods such as electron microscopy and tomography, NMR, optical live cell imaging, neutron diffraction/scattering/reflectivity, and other physical and informatics methods to complement the synchrotron molecular cell biology research. Several examples of biological nanomachines will be discussed along with the future needs of X-ray beams and structural analysis methods.