ナノビームを用いた構造生物学の将来像

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Prospects of structural biology research using nano beam

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<Synopsis>

Synchrotron radiation has made major contributions to advancements of structural biology research in the last three decades. Energy recover linac (ERL) will not only push the envelope of the structural biology research even further with much higher brightness and capacity, but also enable time resolved diffraction, scattering and spectroscopy experiments with much shorter time resolution in the range of 10 psec to 100 fsec and high repetition rate. Photosysnthesis is a paramount example which would benefit from such experiments. ERL nano beams also require fast two dimensional detectors with very high spatial and time resolution and yet a large number of resolution pixels. A new collaborative project to develop DEPFET pixel detector system will be introduced. Future structural life science research will critically depend on advancement in photon science based on ERL which will need to be combined with other biophysical methods such as electron microscopy and tomography, NMR, and optical live cell imaging in order to reveal the structures and dynamics of machinery of life at atomic resolution.

Synchrotron radiation provides intense, tuneable and very parallel X-ray beams suitable for structural investigations of proteins and their complexes, their atomic structures, dynamics, and higher order architecture of organelles, cells, and tissues. Future light sources are expected to expand these research areas even further leading to a new level of understanding of machinery of life with quantum leaps in some areas. Future directions of the four critical synchrotron techniques, X-ray protein crystallography, scattering, spectroscopy, and imaging will be discussed with needs from biology using our recent research activities in protein transport, membrane remodelling and ubiquitin signalling.

ERL is expected to provide nanobeam, with lower emittance, higher brilliance which will enable protein crystallography to its extreme, i.e., sub-micron nano crystals, extremely large complexes, as well as the highest efficiency in structure determination of proteins and their complexes. Protein complexes are very often fragile, dynamic and transient (i.e., change partners as they go through different stages of function), hence difficult to crystallize. Solution X-ray scattering provides an ideal, complementary technique by providing medium to low resolution structures in solution. In future, exploitation of anomalous signals in solution scattering will bring in important additional information on sub-molecular distances from the labels incorporated in the complexes for understanding of their structure and dynamics. At the higher end of the hierarchical understanding of molecular cell biology, cell/organelle imaging (bio nanoproble) will provide critical understanding of higher order structures combined with higher resolution structures of the components and spectroscopic information. ERL will not only push these even further with much higher brightness and capacity, but also enable time resolved diffraction, scattering and spectroscopy experiments with much shorter time resolution in the range of 10 psec to 100 fsec and high repetition rate. Photosysnthesis is a paramount example which would benefit from such experiments. These biophysical methods are all required to cope with the future needs in investigation of the rapidly growing protein universe: vast interaction networks of biological molecules, metagenomics with several million new protein sequences, non-coding RNAs, and human microbiomes.

To take full advantage of X-ray beams from ERL, it will be equally important to develop fast two dimensional detectors whose capabilities match the excellent properties of the ERL beam, i.e. diffraction limit X-ray beam with very short pulses and high repetition rate. We have recently started a joint project to develop such a system using DEPFET (DEpleted P-Channel FET) sensors in collaboration with Dr. Hans-Günther Moser of Max Planck Institute, München and Drs. H. Ushiroda, S. Tanaka and T. Higuchi of Institute of Particle and Nuclear Sciences, KEK. I will describe the basic concept and design of the detector system which we plan as a novel 2D detector suitable for diffraction and scattering experiments with 20 micron spatial resolution and 20 microsecond time resolution.

Finally, 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.