The activities of biological systems are maintained primarily by chemical reactions, and often modeled as reaction-diffusion systems represented by partial differential equations for the "concentrations" of chemicals. However, this classical scheme requires some preconditions. First, each reaction event is instantaneously completed and not affected by previous reactions. Secondly, the molecules diffuse freely and their excluded volume can be neglected. These conditions are however not always satisfied; many of enzymes are molecular machines whose reaction cycles and motions are coupled, and cells are highly crowded with macromolecules. Moreover, recent experiments have shown that there are a number of "minority" chemicals, existing only one or a few molecules per cell. For such rare species, the notion of continuous "concentrations" is no longer valid, and the classical scheme depending on it breaks down. Using simple autocatalytic models, we previously showed that the molecular discreteness in such rare chemicals, either discreteness in numbers (i.e. integers) or spatial discreteness (i.e. finite space between molecules), may affect the reaction-diffusion behavior. Toward a theoretical framework to predict phenomena in the complex molecular networks in the cell, we have expanded the models for a number of chemical species. In some cases, the behavior strongly depends on the system size, which suggests importance of being moderately small. Relevance to cell behavior and possible experimental designs will be also discussed.

Human genome organization and dynamics
Kazuhiro Maeshima (Structural Biology Center, National Institute of Genetics)

Human genome DNA of around 2 m in length is organized into a cell nucleus having a volume of only 1 picoliter. Each genome has only two sets of genes. In order to activate a certain gene, a protein factor, which is normally considered to be in a small number, has to search the whole genome and target the specific gene. In this process, genome organization must play an important role. In fact, how is the human genome DNA is organized into a nucleus? The DNA is wrapped around histones, forming a nucleosome structure. The nucleosome had been assumed to be folded into a 30-nm chromatin fiber and other helical folding structures. However, our recent cryo-electron microscopy (cryo-EM) and synchrotron X-ray scattering analyses have shown almost no visible 30-nm chromatin fibers or other regular structures in interphase nuclei and mitotic chromosomes. This suggests that chromosomes consist of irregularly folded nucleosome fibers. Thus, nucleosome fibers may be constantly moving and rearranging at the local level. Recently we observed these local nucleosome dynamics, which could be crucial for scanning genome information.

Genetically encoded luminescent probes
Takeharu Naga1,2 (ISIR, Osaka Univ., 1PRESTO, JST)

Optogenetic tools including ChR2, LOV domain, and CALI (chromophore-assisted light inactivation) allows us to operate biomolecule function upon light irradiation, by which we are now able to investigate protein of interest in terms of functional difference according to the existing area inside cells and expression stage with real time resolution. To understand what’s going on after the light-switching of optogenetic tools, many researcher may want to visualize some other molecular dynamics and function by fluorescence imaging. However, excitation light for the imaging should mis-activate or mis-inactivate the optogenetic tools so that we cannot apply the fluorescence imaging in combination with the optogenetic technology. To overcome this problem, we have been developing genetically-encoded luminescent probes which are based on hybrid between a mutated chemiluminescent protein and a fluorescent protein variant. In the symposium, I will introduce our recent achievement such as development of color variant of bright luminescent protein, and the use of them in conjunction with the optogenetic technologies for understanding operation principles of bio-nanosystems.