scale" approach based on statistical mechanics. The replica exchange method and the string method are examples of this approach. Here, multiple copies of a molecular system and/or its multiple representations with different resolutions are used to enhance sampling or to perform integration along a path connecting distant points in the conformational space. Since the interactions between the systems are much sparser than those within the systems, the communication cost is much smaller and higher parallel scalability can be achieved. To apply the methods of this approach to various problems of slow dynamics of proteins, we have developed a versatile class library that makes it easy to implement novel multi-copy, multi-scale algorithms. The library is written in an object-oriented language, C++, and is parallelized with OpenMP and MPI. We show how to use this library and present the latest results obtained from its applications.

NetworkProfiler to exhibit how gene networks vary from patient to patient according to a modulator. The method uses structural equation model for discovering associations between the differences in molecular mechanisms and the diversity of phenotype traits. This method was applied to microarray gene expression profiles of 762 cancer cell lines and unraveled global changes of networks with 20,000 genes of different EMT (epithelial-mesenchymal transition) expression levels. The computation took 90 days using 1024 cores on the supercomputer at Human Genome Center (6000 cores; 75 TFLOPS at peak). Out of 1732 possible regulators of E-cadherin, a cell adhesion molecule that modulates the EMT, we identified 25 candidate regulators, of which about half have been reported in the literature. Some of them were validated as novel genes for EMT including miRNA. We also try combinatorial methods and results using the supercomputer for modeling dynamics in cancer cells from time-course gene expression profiles that revealed dynamic network changes against anti-cancer drugs and network differences between drug-sensitive and drug-resistant cancer cells.

**1SK-02**

**Molecular dynamics simulations for the protein secretory pathway**

Takaharu Mori1, Yuki Sugita1, 2, 3 (1 RIKEN QBIC, 2 RIKEN AICS, 3 RIKEN ASI)

Advances in massively parallel computing have made possible 1-sec (or longer) simulations of membrane proteins with explicit solvent and membranes, and are beginning to shed considerable light on the biological phenomena in membrane. We have studied molecular mechanisms of the Sec translocase using molecular dynamics (MD) simulations. Sec translocase is a huge membrane protein complex (SecYEG, SecDF, and SecA ATPase) that provides a pathway for secretory proteins to cross membranes, or for membrane proteins to be integrated into membranes. Recently, several crystal structures with different states have been determined for SecYEG, SecDF, and SecA, and it is proposed that each protein undergoes large conformational change during the functional cycle [1,2]. In this study, we performed all-atom MD simulations of the SecY channel to elucidate molecular mechanisms of the conformational transition between the pre-open and closed states. We found that the conformational change is related to the lateral movement of the lipid molecule around the lateral gate region of SecY. We proposed that the intercalation of phospholipids promotes initial entry of the positively-charged signal peptide into the channel [1,3]. We will also present our recent works on the MD simulations of SecDF and other membrane proteins.

2. T. Tsukazaki et al., Nature (published online).
3. T. Mori et al., Biochemistry, 49, 945-950 (2010).

**1SK-03**

**Cytoskeleton Network Analysis**

Hiroyuki Iwamoto (RCAST, The University of Tokyo)

Cytoskeleton network analysis is an essential approach to understanding cell function and to advancing drug development. However, the analysis of such complex systems is computationally demanding. In this talk, we will introduce our method for constructing a Cytoskeleton Network Model (CNM) from experimental data. The CNM is a directed graph that represents the interactions between proteins and is constructed using a hierarchical clustering algorithm. The CNM can then be used to predict the effects of perturbations, such as drug treatment or genetic modification, on cell function.


**1SK-04**

**Uncovering Systems in Cancer by Supercomputer**

Satoru Miyano (Institute of Medical Science, U. Tokyo)

We present computational methods which boost the challenge for hacking cancer systems by the power of supercomputer. It is impossible to build an individual gene network from one patient sample. However, given many patient samples, it turns possible. We developed a computational method named

**1SL-01**

**The present of photosynthesis research**

Miwa Sugiyama (Cell-Free Sci. and Tec. Res. Cent., Ehime Univ.)

The conversion of photon energy to chemical energy by photosynthesis synchronizing with water oxidation is the most important reaction for maintaining all living on the earth, so that the series of photosynthesis reaction occurs quite efficiently. To understand the relationship between the