interaction. Therefore we evaluated various docking simulation algorithms to suggest the best complex structure by integrating outputs of several docking algorithms.

First, we extracted PDB data of protein-protein and protein-nucleotide complexes and split into each protein. Then, some existing docking algorithms were applied to each protein to see whether it reconstructs an original complex. Based on these results, we report the assessment of each algorithm by comparing reconstructed complex with an original complex using RMSD and cluster analysis. In addition, using the algorithms examined here, we discuss the predicted binding site of protein-protein complexes which binding site is still unknown by experimental methods.

2P-297 タンパク質立体構造予測モデルの評価関数の検討

Validation of statistical functions for evaluating protein structural models

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The availability of a structural model of a protein is one of the keys for understanding biological processes at a molecular level. Usefulness of a protein structure model depends on its accuracy. Thus, it is necessary to estimate accuracy of a three-dimensional (3D) model before it is used.

We have previously developed a protein structure prediction pipeline system, FORTE-SUITE, in which all generated 3D models are evaluated by combined scores of two statistical functions[1]. Prediction experiments showed that the system had worked well in temperature-based modeling[1], but that it left some for improvement of model evaluation.

In this study, we analyze the effect of the combination of statistical functions for discriminating between comparative models with correct and incorrect folds. The tested statistical potentials were Verify3D[2] and Prosa2003[3]. We also considered the effect of combined use of amino acid composition of a protein surface. Recently a propensity for ligand binding (PLB) index, which was developed on the basis of the idiosyncratic amino acid composition profile of ligand-binding site, has been reported to have ability to predict ligand-binding sites fast and accurately[4]. We explored the potential of extended use of amino acid composition profile for estimating the accuracy of protein structure models.

[1] Tomii, K., et al. (2005) *Proteins*, Suppl. 7, 114-8211;121.
[2] Luthy, R., et al. (1992) *Nature*, 356, 83-8211;85.
[3] Sippl, M.J. (1993) *Proteins*, 17, 355-8211;362.
[4] Soga, S. et al. (2007) *J. Chem. Inf. Model.*, 47, 400-406.

2P-298 SVMによるドメイン境界予測法の改良

Improvement of SVM prediction of domain linker regions

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The practical importance of the prediction of structural domains in un-annotated amino acid sequences has increased as they represent valuable targets readily characterized by high throughput methods.

Here we report a support vector machine (SVM) prediction of domain linkers, which are loop regions separating two structural domains. The SVM training data set comprised 182 protein sequences from SCOP database, which contained at least one domain linker regions. Using this data set, we constructed a SVM based domain linker predictor, which used a position specific scoring matrix (PSSM) and predicted secondary structure information (PSS) as input data.

A five-fold cross validation test indicates that the sensitivity, the specificity and the area under the ROC (receiver operating characteristics) curve (AUC) value, which represent the prediction performance, were 0.463, 0.578 and 0.833, respectively. Our previous SVMs, which used only amino acid sequence information, indicated sensitivity, specificity and AUC value were 0.369, 0.272, and 0.693, respectively. The performances of our new prediction method were also higher than previously reported methods such as Armadillo (AUC: 0.610, Dumontier et. al., *J. Mol. Biol.* 2005), and neural network-based methods (AUC: 0.642, Miyazaki et. al., *BMC Bioinformatics* 2006; AUC: 0.810, Sim et. al., *Proteins* 2005). These results demonstrate the efficiency of including PSSM and PSS information for predicting domain linkers.

2P-299 リガンドの共通部分構造を認識する脂質シグナル系タンパク質部位の探索

Searching for the binding-sites for common-substructures of ligands among lipid-signaling proteins.

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The proteins in the lipid-signaling pathway, such as nuclear-receptors (NR) and fatty acid-binding proteins (FABP) interact with various lipid-derived molecules to control cellular responses. We are developing a method for predicting the binding-sites and ligand structures of NRs and FABPs by referring to empirical rules derived from the known 3D structures. This method uses the information of the distribution of amino acid residues and their preference for the proto-groups (common sub-structures of ligand molecules) at the binding sites. The non-redundant structures of NR and FABP in PDB had 181 and 132 occupied ligand-binding sites, respectively, and these binding sites were divided into 4542 and 2196 proto-group binding-sites, respectively. These proto-group binding-sites were used to construct the empirical rules (the relationship among amino acid type, site position, and preferred proto-group) to predict the cognate ligands of the proteins. The prediction method was tested on 189 NRs and 228 FABPs. The empirical rules predict a set of proto-groups for a test protein, and a prediction was though to be successful if more than 70% of the proto-groups in the cognate-ligand were detected. As a result, 69% of the NRs and 22% of FABPs were successfully related to their ligands. The low ability of this method for FABPs appeared to come form a greater variety of structures of FABP proto-group binding-sites . The details of the prediction methods, and the detected ligand-binding structures of the proteins will be discussed over the poster.

2P-300 化学反応系のマクロ記述の不安定性について

Instability of macroscopic description of chemically reacting systems

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A well-stirred chemically reacting system generally has two description modes. One is the macroscopic and deterministic description by the reaction rate equation which describes the continuous change of molecular concentrations of chemical species. The other is the microscopic and stochastic description by the chemical master equation which describes the discrete change in the number of molecules. Recent development of systems biology reveals that the former description mode is not adequate when one simulates chemical systems with small number of molecules in a cell. The latter description mode is necessary. [Gillespie, J. Chem. Phys. 113, 297, (2000)] proposed the chemical Langevin equation in order to bridge the two description modes. He estimated the condition that the approximation of the chemical master equation by the reaction rate equation is legitimate. The condition changes as the number of molecules evolves following the chemical master equation. At certain time the condition may not be satisfied. In this sense the macroscopic description of a chemically reacting system is unstable. By examining the condition proposed by Gillespie we propose an index that quantifies the instability of the macroscopic description of chemically reacting systems. We also show some results on the relationship between the proposed index and the stability of equilibrium points.

2P-301 周期閃光刺激に同調する脳波の刺激強度・周波数依存性

Dependence of spatiotemporal characteristic of brain wave entrained to flicker stimuli on stimulus intensity and frequency

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[Objective] Nonlinearity of brain wave is crucial for not only elucidating its underlying mechanism but also applying the brain wave to a brain-computer interface which assists disabilities. We have investigated spatiotemporal characteristics of brain wave entrained to flicker stimuli (steady-state visually evoked potential, SSVEP). The present study focuses to clarify dependence of SSVEP characteristics on stimulus parameters; intensity and frequency. We measured SSVEP for more than 20 subjects under the conditions of the stimulus intensity I_s and stimulus frequency f_s in the range from $I_s < 10$ to $I_s > 300$ (lx) and 5 to 16 (Hz), respectively. SSVEP characteristics are analyzed in terms of its amplitude and phase.

[Results] Grand mean of SSVEP amplitude increases with increasing I_s and fixed f_s, but tends to saturate under the condition $I_s > 200$ (lx). For dependence of the SSVEP amplitude on f_s, the amplitude takes a maximum under the condition that f_s is in the region of the alpha wave (8-13 (Hz)) independently on I_s, indicating significant contribution of the entrained alpha wave to the SSVEP. Although spatial phase relationship of the SSVEP from front to occipital lobe shows a property of standing wave under the condition of $I_s < 60$ (lx) and $f_s < 10$ (Hz), a ratio of phase structure belonging a traveling wave exceeds that belonging the standing wave around I_s=100 (lx). These results suggest that the spatiotemporal properties of the SSVEP reflect parametric dependence of nonlinear oscillators which are responsible for SSVEP.

2P-303 細胞レベルとシステムレベルの動的応答を繋ぐ

Connecting cell-level and system-level dynamical responses

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A theoretical study on dynamical responses of a rhythmicelement (i.e., an oscillator) and its population is reported.When an oscillator is subject to a weak pulse-like stimulus, thedynamical response to the stimulus depends on the timing, ormore precisely, on the phase of the oscillator. Such a responseproperty is characterized by the phase response curve (which isthe function of the phase) describing the phase shift induced bya stimulus given at the phase. For those cells showing rhythmicactivity, such as neurons under certain conditions and circadianclock cells, the phase response curves against some types of stimulican be defined and actually have been measured experimentally.On the other hand, a population- or system- level phase responsecurve can also be defined. For example, phase response curve ofcircadian clocks can be measured from animal behaviour. Here, aninteresting question is on the relationship between thecell-level response and the system-level response. To addressthis problem, we consider a population of coupled oscillators anddeveloped a theory for connecting individual responses and apopulation response. It is shown that the population response isnot a simple linear ensemble of individual responses due to thenontrivial effect caused by interactions between oscillators.The implications for the phase response curves of circadian clockswill be discussed as well.