enantiomorphous shapes. In the case of infinite series the possible solutions may not be enantiomorphous. An example of two different pyramidal bodies is considered. Another type of ambiguity is associated with numerical instability of solution. The dependence of solution dispersion from the maximum scattering angle is considered. Several numerical examples which demonstrate an optimum data angular range existence are given. The main conclusion that prior to experimental data interpretation one should to perform modelling of the expected structure to estimate the degree of ambiguity and to choose both data weighting functions and angular range is shown by the results of model calculations.

Keywords: *ab-initio* structure determination, nonlinear optimization, numerical methods and simulation techniques

P03.10.30

Acta Cryst. (2008). A**64**, C227

Development of a scoring method for predicting protein complex structures

Yuko Tsuchiya[1], Eiji Kanamori[2], Daron M Standley[3], Haruki Nakamura[3], Kengo Kinoshita[1]

[1]Institute of Medical Science, the University of Tokyo, Human Genome center, 4-6-1 Shirokane-dai, Minato-ku, Tokyo, 108-8639, Japan, [2]Biomedicinal Information Research Center, 2-41-6 Aomi, Koto-ku, Tokyo, 135-0064, Japan, [3]Institute for Protein Research, Osaka University, 3-2 Yamadaoka, Suita, Osaka, 565-0871, Japan, E-mail：yukoo@hgc.jp

The information about protein-protein interactions increases much more rapidly than the increase of the number of the tertiary structures of those protein complexes. Therefore, precise prediction of protein complex structures by protein-protein docking simulations is required. When the protein complex is re-built from its component protomers which derive from experimentally determined complex structure (native structure) by docking, the complex models with rmsd < 10Å from the native structure (near-native model) could be obtained, along with a great number of false positives (decoy). The separation of near-native models from many decoys is therefore needed in the prediction of complex structures by docking. In this study, we developed the method for scoring docking models so that the near-native models were higher in rank than decoys, based on the assumption that the interfaces of near-native models are more complementary in terms of surface properties and shapes compared to those of decoys. We used 125 non-redundant hetero-dimers (native structures) as targets. For each target, maximum 500 complex models were generated by our docking method. We also observed these targets in terms of the shape of the interfaces of their native structures. As a result, we found that these targets could be classified into two groups according to their interface shapes, and moreover, that this classification correlated with another classification which was based on the number of models with high docking score, namely, the difficulty in the separation of near-native models. We therefore only focused on 75 targets classified as difficult targets which need the separation. So far our method could separate the near-native models from the decoys in 70% of these targets.

Keywords: complex structure prediction, protein-protein docking, analysis of protein-protein interfaces

P03.10.31

Acta Cryst. (2008). A**64**, C227

3D homology structure model for a pyrazinamide susceptibility test in *Mycobacterium tuberculosis*

Luis R Castillo

Universidad Peruana Cayetano Heredia, Biochemistry, Molecular Biology and Pharmacology/Unidad de Bioinformatica, Av. Honorio Delgado 430, Urb. Ingeniería, San Martin de Porres, Lima, Lima 31, Peru, E-mail：eloluis87@yahoo.com

Pyrazinamide (PZA) constitutes one of the First-Line Drugs for Tuberculosis treatment and appears to be the most important drug killing the latent *M. tuberculosis*. It is hydrolyzed by *Mycobacterium tuberculosis* pyrazinamidase / nicotinamidase (PZAse) to pyrazinoic acid (POA), the bactericidal agent. X-Ray fluoresecence Spectroscopy analysis shows that PZAse is a metalloenzyme that contains Zn^{+2}, and metal depletion of PZAse using EDTA decreases significantly its activity. Analysis of all PZA resistant strains reported in Peru and Worldwide shows that 90% of resistance are due to single point missense mutations on the PZAse sequence which are not homogeneously distributed along PZAse sequence, but clustered in the region near to the hypothetic PZAse Metal Coordination Site (MCS). Further analysis evaluating distinct amino acid physicochemical parameters and relative distances among the mutated residues in the PZAse 3D Homology Model shows that, those strains which have the highest PZA resistance(>1200 Minimum Inhibitory Concentration (MIC)), have mutations on residues which side chains aim at the MCS ($p<0.02$). These data indicate that PZAse coordinates, at least, a metal ion (Zn^{+2}), which is required for its enzymatic function, and the presented PZA Resistance Prediction Model, which is based on the analysis of the PZAse MCS, could be used in Low-Income countries for rapid and low-cost PZA susceptibility tests.

Keywords: pyrazinamidase (PZA), *Mycobacterium tuberculosis*, homology modelling of proteins

P03.10.32

Acta Cryst. (2008). A**64**, C227-228

Homology modeling of *Arabidopsis thaliana* glycolipid transfer protein

Lenita Viitanen, Tiina A Salminen

Abo Akademi University, Biochemistry, Tykistokatu 6, Turku, Turku, 20520, Finland, E-mail：lenita.viitanen@abo.fi

Glycolipid transfer protein (GLTP) is a 24 kDa cytosolic protein that can transfer glycolipids between membranes *in vitro*, but its function *in vivo* is still unknown. GLTPs have been found in various organisms and recently also in plants. Three different forms of GLTP are expressed in *Arabidopsis thaliana*: AtGLTP_1, AtGLTP_2 and AtGLTP_3. Our collaborators have tested the lipid transfer preferences of the AtGLTPs with a transfer assay. Using the known crystal structures of human GLTP [1, 2] as templates, I have constructed homology models of the AtGLTPs in complex with glycolipid ligands. I have studied and compared the models and templates in order to find structural characteristics that explain the differences in lipid transfer preference of GLTPs. The project is done in collaboration with the research groups of Dr. Johan Edqvist (Linköping University) and Dr. Peter Mattjus (Åbo Akademi University).

[1] Malinina et al. (2004) Nature, 430, 1048-1053
[2] Malinina et al. (2006) PLoS Biol, 11, e362

Keywords: homology modelling of proteins, protein-lipid interactions, structure-function relationships

P03.10.33

Acta Cryst. (2008). A**64**, C228

Relationship between sequence and structure of CDR-H3 in antibodies

Daisuke Kuroda[1,2], Hiroki Shirai[3], Masato Kobori[3], Haruki Nakamura[1]
[1]Institute for Protein Research, Osaka University, 3-2 Yamadaoka, Suita, Osaka, 565-0871, Japan, [2]Graduate School of Frontier Biosciences, Osaka University, [3]Molecular Medicine Laboratories, Astellas Pharma Co., Ltd., E-mail：dkuroda@protein.osaka-u.ac.jp

Antibody modeling is widely used for the analysis of antibody antigen interaction and for the design of potent antibody drug. Antibody combining site is composed of six complementarity determining regions (CDRs). The CDRs except for CDR-H3 is known to have limited numbers of canonical structures, and one can identify one of the canonical structures from the amino acid sequence. CDR-H3 lies in the center of antigen-binding site and shows significant variability in its length, sequence, and structure. Although it is not enough to accurate modeling, the method to classify CDR-H3 structure from the amino acid sequence was also proposed. However, after these methods to classify CDR structures were developed, many more antibody crystal structures were determined. It has enabled us to revise H3-rules, the method to classify CDR-H3 structure. In this work, we show recent progress of H3-rules based on systematic analyses of other five CDRs. As a consequence of the relative spatial positions in the CDRs, some basic residues on VL domain affect the conformation of CDR-H3. We also show the usefulness of whole structural feature of CDR-H3 prediction from the amino acid sequence. We can determine whether the hydrogen bond ladders or beta-turn are formed or not by H3-rules. Our revised H3-rules have the high accuracy of CDR-H3 structure prediction compared to the other methods. Since modeling the antibody structures is crucial for the design and analysis of potent antibody drugs for specific antigens, our empirical rules derived from large amount of structural data are expected to be used in antibody structure analysis and drug discovery. Structural analysis server, H3-rules 2007, can be accessed on the web: http://www.protein.osaka-u.ac.jp/rcsfp/pi/H3-rules/.

Keywords: antibodies structure, molecular modelling, sequence analysis

P03.10.34

Acta Cryst. (2008). A**64**, C228

Comparative analysis of putative NADPH- and NADH-dependent ketopantoate reductase

Sukanta Mondal, Chioko Nagao, Kenji Muzuguchi
National Institute of Biomedical Innovation, 7-6-8, Saito Asagi, Ibaraki, Osaka, 567-0085, Japan, E-mail：suku@nibio.go.jp

The pantothenate (vitamin B_5) biosynthesis pathway has been proposed as a potential target for antimicrobials. Ketopantoate reductase (KPR, E.C. 1.1.1.169) is the second enzyme in the pathway and catalyzes the NADPH-dependent reduction of ketopantoate to pantoate. In an extensively studied *E.coli* KPR ternary complex (PDB code: 2OFP) the cofactor is bound in the active site cleft between the N-terminal Rossmann-fold domain and the C-terminal α-helical domain; a significant hinge bending encloses the active site around ketopantoate to provide a solvent-inaccessible environment in which catalysis occurs. Structural genomics projects have provided two more putative KPR crystal structures from *E.faecalis* (PDB code: 2EW2) and *P.gingivalis* w83 (PDB code: 2QYT). All three proteins adopt similar overall structures with conserved catalytically important residues, suggesting that their reaction mechanisms are similar. The putative NADPH 2'-phosphate binding-site of 2QYT (Arg42) is similar to that of *E.coli* KPR (Arg31) but differs in 2EW2 (Asp30). Comparative analyses of cofactor binding domains of homologous proteins suggest that 2EW2 is NADH-dependent and 2QYT is NADPH-dependent. We have predicted cofactor and substrate binding sites and their binding mode using docking studies. Based on the sequence analysis of KPR family members including Methicillin-resistant *S.aureus* (MRSA) we have hypothesized that both NADPH- and NADH-dependent KPR are widely distributed in different organisms. As a case study, we have modeled the putative KPRs Q2FV20 and Q2FVH3 from *S.aureus* (strain NCTC 8325) and our analysis suggest that they are NADPH- and NADH-dependent, respectively. These models could contribute in understanding their reaction mechanisms and eventually to designing novel inhibitors.

Keywords: computer-aided molecular modelling, docking, cofactors

P03.12.35

Acta Cryst. (2008). A**64**, C228

Dynamics of EcoO109I studied by small-angle X-ray scattering and molecular dynamics simulation

Tomotaka Oroguchi, Hiroshi Hashimoto, Toshiyuki Shimizu, Mamoru Sato, Mitsunori Ikeguchi
Yokohama City University, International Graduate School of Arts and Sciences, 1-7-29 Suehirocho Tsurumi-ku, Yokohama, Kanagawa, 230-0045, Japan, E-mail：oroguchi@tsurumi.yokohama-cu.ac.jp

EcoO109I is a type II restriction endonuclease, which forms homo dimer. Upon DNA-binding, the two subunits rotate counter-clockwise relative to each other and the two catalytic domains undergoes a large structural change to capture the DNA. Using 150 ns of molecular dynamics simulation of the DNA-free form, we investigated intrinsic dynamics of EcoO109I in solution and its relation with the structural change. In the simulation, the overall structure fluctuated largely, which led to large fluctuation in the radius of gyration. The small-angle X-ray scattering profile calculated from the simulation, in which the scattering from explicit water molecules were taken into account, has shown an excellent agreement with the experimental profile. We performed a principal component analysis and found that the main dynamics was the counter-clockwise motion of the two subunits, which is observed in the structural change. We also found that the dynamics of the catalytic domains correlates well with the structural change. These strong correlations between the intrinsic dynamics and the structural change indicate that the structure of EcoO109I is very flexible in the direction of its functional movement intrinsically, and therefore can effectively achieve its structural change upon binding.

Keywords: small-angle X-ray scattering, intrinsic dynamics, structural change