オレゴン大学 Matthews 教授講演会

日時: 2009年3月12日(木)10:45-12:15
会場: 早稲田大学先端生命医科学センター【TWIns】3階 セミナールーム3
〒162-8484 東京都新宿区若松町2-2
(都営大江戸線若松河田町駅/牛込柳町駅から徒歩5分、都営新宿線曙橋から徒歩10分)

Matthews 教授より，以下の話題を提供していただきますが，専門外の研究者・学生の初学者のために，蛋白質構造解析の面白さや，未来の展望についても，分かりやすく語って頂く予定です。
世話人: 早稲田大学 教育・総合科学学術院 教授 加藤尚志 TEL 03-5369-7309

A Talk About Nothing: Cavities in T4 Lysozyme

By Lijun Liu, Walter A. Baase and Brian W. Matthews

Institute of Molecular Biology and Department of Physics
University of Oregon, Eugene, OR, USA

Professor Brian W. Matthews
B.S., University of Adelaide;
Ph.D., University of Adelaide;
D.Sc., University of Adelaide
Protein Crystallography, Protein Engineering, Structural Biology

By replacing larger, non-polar amino acids with smaller ones in the core of T4 lysozyme it is possible to engineer cavities of different sizes. The largest of these, generated by the L99A substitution, has a volume about 150 Å^3. The talk will focus on the properties and uses of this cavity. External ligands can easily move into and out of the cavity. Because solvent is not displaced it serves as a simple model to evaluate the effectiveness of docking procedures used to predict ligands that will bind to a specific site on a protein. The cavity generated by the L99A substitution is largely non-polar, but by making supplemental mutations the polarity can be changed and the consequences for ligand binding evaluated.

The size and shape of the cavity can change to accommodate different ligands. For example, in binding ligands such as C_6H_5X or C_6F_5X where X = H, F, Cl, Br or I the cavity volume increases from 181 Å^3 to 245 Å^3. There is a remarkably close contact of 3.0 Å between the iodine atom on C_6F_5I and the sulfur or selenium atom of Met or SeMet102. This interaction is 1.0 Å less than the sum of the van der Waals radii and is an example of a so-called halogen bond. Notwithstanding this close approach, the increase in binding energy for the halogen bond relative to a van der Waals contact is estimated to be only about 0.5-0.7 kcal/mol.

The effect of high pressure on the cavity-containing mutant lysozyme has been evaluated. Under pressure the cavity does not collapse. Rather, the protein structure is maintained and several water molecules move into the cavity.

There has been ongoing controversy as to whether apolar cavities in proteins are truly empty, or whether they contain disordered solvent which is too mobile to be seen by standard crystallographic analysis. To address this question we have obtained a high-resolution electron density map for the cavity-containing mutant which is based on experimental phases and avoids artifacts that may be introduced during conventional crystallographic refinement. A similar investigation has been carried out for the apolar cavity in the protein interleukin-1β. The results of these experiments will be described.

Recent publications

1. Tronrud DE, Matthews BW. Sorting the chaff from the wheat at the PDB. ***Protein Sci.*** 2009 Jan;18(1):2-5.
2. Liu L, Baase WA, Matthews BW. Halogenated benzenes bound within a non-polar cavity in T4 lysozyme provide examples of I...S and I...Se halogen-bonding. ***J Mol Biol.*** 2009 Jan 16;385(2):595-605.
3. Tronrud DE, Matthews BW. Sorting the chaff from the wheat at the PDB. ***Protein Sci.*** 2009 Jan;18(1):2-5.
4. Liu L, Quillin ML, Matthews BW. Use of experimental crystallographic phases to examine the hydration of polar and nonpolar cavities in T4 lysozyme. ***Proc Natl Acad Sci U S A.*** 2008 Sep 23;105(38):14406-11.
5. Matthews BW. Five retracted structure reports: inverted or incorrect? ***Protein Sci.*** 2007 Jun;16(6):1013-6.
6. Quillin ML, Wingfield PT, Matthews BW. Determination of solvent content in cavities in IL-1beta using experimentally phased electron density. ***Proc Natl Acad Sci U S A.*** 2006 Dec 26;103(52):19749-53.