PS03.05.12 MOLECULAR MODELING ON CALMODULIN FROM ZEA MAIS. Berthold Reich*, Christian Betzel*, Gottfried Wagner**, *Institute of Physiological Chemistry, University of Hamburg, 20246 Hamburg, Germany, **Institute for Botany 1, Justus-Liebig-University, 35390 Giessen, Germany

Modeling on calmodulin from zea mais was performed by using recombinant calmodulin from paramecium tetraurelia (PDB code 1OSA) and the modelling program WHAT IF (1).

Structural refinement was done by debumping and optimizing the H-bond network of the model, using the same program. The final refinement of the maize calmodulin model was done by sequencealignment and superpositioning, using 1OSA as profile, with WHAT IF and FRODO.

(1) "WHAT IF: A molecular modeling and drug design program", J. Mol. Graphics, 1990, Vol.8, March, 52-56

PS03.05.13 A NEW DOCKING PROGRAM (SANDOCK) IDENTIFIES LIGANDS WITH K_d VALUES UP TO 100nM AND BINDING MODES CONFIRMED BY X-RAY STRUCTURE ANALYSIS. By M.D. Walkinshaw# and P. Burkhard*, *Department of Structural Biology, Biozentrum, University of Basel, Switzerland, #Department of Biochemistry, The University of Edinburgh, Scotland.

A new docking program (SANDOCK)[1] was developed to screen large three dimensional databases of small ligand molecules for compounds which are complementary to the active site of a target protein. This program is very efficient as it can screen very large databases with up to a million compounds in a reasonable time and can successfully identify novel binding compounds.

It was possible to identify a series of ligands that bind to three different target proteins FKBP, cyclophilin and thrombin with dissociation constants which are in part as low as 100nM and with binding modes corresponding to that predicted by SANDOCK.

The dissociation constants were determined by applying fluorescence measurements. In addition, the binding of some selected compounds were also confirmed by NMR techniques, which show, that the ligands indeed bind to the predicted region of the protein.

Finally the x-ray structure of thrombin with the small ligand p-Aminobenzamidine shows, that the predicted binding mode of the ligand is correct. The rms difference between the atoms of the docked ligand and the x-ray structure of the ligand is only 0.726 Å, in spite of some conformational changes of the protein upon ligand binding. All hydrogen bonds between the protein and the ligand predicted by SANDOCK are formed, and the predicted distances differ only very little from those found in the x-ray structure.

1) SANDOCK is a further development of DOCK 1.0. [I.D. Kuntz et al. in J. Mol. Biol., 161, 269-288 (1983)]

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Materials Research

MS03.06.01 STRUCTURE PREDICTION. Clive M. Freeman, Alan M. Gorman and Steve M. Levine, MSI 9685 Scranton Road, San Diego CA 92121, USA.

Techniques for predicting and solving crystal structures based on powder diffraction data and simple descriptions of interatomic interaction have advanced dramatically in recent years. Such procedures exploit the standard techniques of computer simulation in combination with hybrid potential energy functions to yield structures which are sterically and experimentally plausible. These methods have been especially useful in the investigation of microcrystalline framework structured materials for which powder diffraction may be the primary experimental route to structural information. In contrast to traditional refinement procedures, which use rapidly convergent but locally biased least squares methods, analogy with physical simulations has prompted the use of simulated annealing as an optimization method in the majority of studies. Metropolis Monte Carlo or Molecular Dynamics based annealing procedures provide significant 'searching' capabilities which yield global minimization properties. Applications to framework structured solids, condensed metal oxides and molecular crystal structures will be described.

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MS03.06.02 CONVENTIONAL DESCRIPTIONS OF NEW PHASES FROM RESULTS OF HIGH PRESSURE INORGANIC STRUCTURE MODELLING. Y. Le Page, D.D. Klug and J.S. Tse, National Research Council of Canada, Ottawa, Canada K1A 0R6. E-mail: yvon.le_page@nrc.ca.

Results of *ab-initio* inorganic structure modelling are often in the form of Cartesian coordinates of atoms in a large, periodical and in general oblique simulation box containing hundreds to thousands of atoms. The contents of that box may correspond to a single crystal, a twin, a mixture of phases or a disordered block of matter. It may also include point, line or plane defects.

The problem of extracting the corresponding crystallographic description, a necessary step in view of full quantum calculations and possible publication, is different from the familiar problem of extracting crystal symmetry and structure from experimental diffracted intensity data. The computer-aided method developed at NRC over the years is based on eye identification on a stereo plot of three pairs of atoms related by conjugate translations in a same single-crystalline region, followed by derivation of fractional coordinates for the atomic content of the corresponding primitive cell. Running this data through the MISSYM program discloses potential symmetry elements of the structure, with their corresponding crystallographic directions.

These potential elements are then critically examined and accepted either as symmetry or pseudo symmetry based on comparison of coordinate deviations between related atoms with the expected magnitude of thermal motion. The conventional cell and space group are then derived from the accepted symmetry elements. All calculations described here can be performed with the NRCVAX system of programs. Examples of simulation boxes and Cartesian models for new members of structural families will be detailed.