02.1-18 A COMPARATIVE MOLECULAR MODEL OF THE Ca^{2+} SENSITIVE REGULATORY PROTEIN CALMODULIN BASED ON TURKEY SKELETAL TROPONIN-C. By Natalie C.J. Strynadka and Michael N.G. James, Medical Research Council of Canada Group in Protein Structure and Function, Department of Biochemistry, University of Alberta, Edmonton, Alberta, Canada T6G 2H7.

Calmodulin (CaM) plays a pivotal role in many Ca^{2+}-dependent intracellular functions. It belongs to the family of proteins that exhibits a common Ca^{2+}-binding structural motif of helix-loop-helix which includes troponin-C (TnC) and parvalbumin. Based on the high sequence identity between CaM and TnC (46%) and with the knowledge of the detailed 3-D structure of TnC, we have constructed an atomic model of CaM. The TnC structure that was used was the one proposed for the 4 Ca^{2+} ion form of TnC (Herzberg et al., J. Biol. Chem. 261, 2638 [1986]). The side chains of TnC were replaced by the homologous residues of CaM using the computer program MUTATE (R. Read). The 2 most significant deletions are the loss of the 11 residue N-terminal helix and a 3 residue Lys-Gly-Lys deletion from the interdomain helix. This latter deletion causes the relative orientation of the N- and C-terminal domains to change by 60° from that of TnC. In order to relieve unacceptably close van der Waals contacts and to correct the geometry at Pro66, 750 steps of conjugate gradient energy minimization, using GROMOS (van Gunsteren), were done on the modelled CaM. In our model, each of the Ca^{2+} binding sites has 5 ligands from the protein and one coordinating water molecule, in agreement with a previous prediction (Herzberg & James, Biochemistry 24, 5298 [1985]). The side chain of Tyr99 is accessible to solvent and stacks against the side chain of Gln135. Tyr138 makes close contacts with Phe89 and Phe141. Regions of conformational flexibility in CaM and TnC are suggested by the differences in certain interhelix angles of these two proteins (Babu et al., Nature 315, 37 [1985]). Hydrophobic patches between helices B and C, and between F and G, suggest the binding sites for the trifluoperazine type drugs.

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02.1-19 THE CRYSTAL STRUCTURE OF MANGANESE SUPEROXIDE DISMUTASE FROM BACILLUS STEAROTHERMOPHILUS. By M.W. Parker and C.C.F. Blake, Laboratory of Molecular Biophysics, University of Oxford, England.

The superoxide dismutases (SOD, EC 1.15.1.1) are a class of metalloproteins containing either copper and zinc or manganese or iron. The enzyme catalyses the disproportionation of superoxide to water and peroxide. The crystal structure of manganese superoxide dismutase from Bacillus stearothermophilus has been solved to a resolution of 2.4Å by the methods of isomorphous and molecular replacement. The crystallographic R-factor after eight cycles of Hendrickson-Konnert refinement is 0.26 and the r.m.s. deviation from ideal bond lengths is 0.025Å. The tertiary fold of the protein exhibits a striking resemblance to iron-containing SODs but bears no resemblance to the copper/zinc-containing SODs. The manganese is tetrahedrally surrounded by three histidines and an aspartate. The active site is lined by an array of aromatic residues. The structure is currently being analysed with the aim of providing a detailed atomic description of the protein's mode of action.

02.1-20 HUMAN CARBONIC ANHYDRASE I - IODIDE COMPLEX: STRUCTURE AND INHIBITION MECHANISM. By Vinay Kumar, Padma Satyamurthy and K.K. Kannan, Neutron Physics Division, Bhabha Atomic Research Centre, Bombay 400 085, India.

Iodide like other anions (CN^-, SH^- etc) is a competitive inhibitor of HCO_3^- reaction and an uncompetitive inhibitor of CO_2 hydration reaction of carbonic anhydrase isozymes. Crystals of Human carbonic anhydrase I isozyme (HCAI) were soaked in a solution of 0.2M NH_4I in 2.5M $(NH_4)_2SO_4$ pH ~ 8.5. Three-dimensional intensity data for HCAI-I^- crystals was collected to a resolution of 2.5Å on an Arndt-Wonacott oscillation camera. Data processing was done on a Scandig-3 microdensitometer controlled by a PDP 11/34 computer (P.K. Pal et al., Int. Sum. School on Cryst. Comp., 1983, Kyoto Japan) followed by 3-dimensional scaling. 48159 reflections were scaled to get 10150 unique reflections. The overall R-factor on F_{obs} was 11.7%. Phases were determined from the refined structure of HCAI (K.K. Kannan et al., Ann. New York Academy of Sciences, 1984, 429, 49-60) with 197 solvent molecules included. (2Fo-Fc) and (Fo-Fc) Fourier maps were computed wherein the Iodide (I^-) position was located and included in the structure. This structure was refined using the restrained least squares (J.H. Konnert, Acta Cryst., 1976, A32, 614-617) method and model building interactive graphics. The initial R-factor was 30.3%. The R-factor after 12 cycles of refinement and one model fitting on a Vector General 3400 graphics system using Frodo (T.A. Jones, J. Appl. Cryst., 1978, 11, 268) programme is 20%. RMS delta and sigma values for covalent bond distances are 0.014 and 0.020, for planar torsion angles 2.5° and 15.0° and for main chain bonded thermal values (B) is 1.3Å² and 1.00Å² respectively. Refined occupancy and B values of I^- ion are 69% and 11.4Å². I^- is inhibiting the enzyme by replacing the catalytically important solvent molecule and is at a distance of 2.57Å from Zn^{2+} ion (Fig. 1). There seem to be two more low occupancy I^- sites with