tical to those of the wild-type. This opens the possibility of protein engineering for changing channel properties [9]. The report includes the porins from *R. capsulatus* and *R. blastica*, as well as the maltoporin from *Salmonella typhimurium*. Purification for crystallization of these porins and other membrane proteins will be described.

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MS04.03b.02 STRUCTURAL BASIS OF SUGAR TRANSLOCATION THROUGH MALTOPORIN CHANNELS. T. Schirmer, R. Dutzler, Y.-F. Wang*, J.P. Rosenbusch* Departments of Structural Biology and *Microbiology, Biozentrum, University of Basel, CH-4056 Basel, Switzerland.

Maltoporin (LamB), an integral membrane protein from *E. coli*, facilitates the diffusion of maltooligosaccharides across the outer membrane. The structure exhibits a trimer of 18-stranded antiparallel β-barrels. Each barrel contains a channel with an exposed hydrophobic patch formed by six aromatic residues ('greasy slide') that are linearly arranged. Apart from this the channel is lined exclusively by ionizable residues.

Crystal structures of maltoporin in complex with maltooligosaccharides of various lengths reveal that the sugars are bound to the channel constriction and are in apolar contact with the 'greasy slide'. A multitude of H-bonds that are formed between the sugar hydroxyl groups and residues from the channel lining explain affinity and specificity of this interaction. A complex structure with sucrose reveals non-productive binding above the channel constriction. The structural data will be discussed with respect to function and a detailled path for sugar translocation will be proposed.

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MS04.03b.03 THE STRUCTURE OF PROSTAGLANDIN SYNTHASE: A MEMBRANE-BOUND ENZYME. R. Michael Garavito, Department of Biochemistry, Michigan State University, East Lansing, MI 48824-1319.

Prostaglandin H synthase (PGHS) is an integral membrane enzyme which converts arachidonic acid, an essential fatty acid, into the prostaglandin precursors PGG_2 and PGH_2 by means of a free radical mechanism. Nonsteroidal anti-inflammatory drugs (NSAIDs), which inhibit prostanoid biosynthesis by targeting the cyclooxygenase activity of PGHS, are used to treat certain symptoms of inflammatory and cardiovascular diseases as well as cancer; in the latter, aspirin is now a proven anti-cancer prophylaxis. Two isoforms of PGHS have been discovered: PGHS-1 is involved in homeostatic or "house-keeping" prostaglandin biosynthesis while PGHS-2 induced by cytokines during inflammatory events.

We have refined the structure of ovine PGHS-1 to 3.1 Å resolution and have characterized PGHS-1 complexed with four NSAIDs: bromoaspirin, flurbiprofen, iodosuprofen and iodoindomethacin. I will also discuss the nature of enzyme-drug interactions and structure-function relationships, with particular focus on the mechanisms of substrate and NSAID interactions as well as the functional differences in NSAID binding between PGHS-1 and PGHS-2.

An unexpected conclusion from the crystal structure of PGHS-1 is that it is a monotopic membrane protein: a symmetric dimer of PGHS apparently integrates only into one leaflet of the lipid bilayer. Moreover, there is increasing evidence that specific sites on the PGHS molecule interact with other proteins in the lumen of the endoplasmic reticulum (ER), particularly those involved with membrane protein targeting. The nature of integration of PGHS into the membrane bilayer and the mode of targeting the enzyme to the ER membrane and nuclear envelope will be major points of discussion.

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MS04.03b.04 THE STRUCTURE OF AN INTEGRAL MEMBRANE PROTEIN LIGHT-HARVESTING COMPLEX N.W. Isaacs, R.J. Cogdell#, A.A. Freer, A.M. Hawthornthwaite-Lawless*, M.Z. Papiz*, S.M. Prince, and G. McDermott. Depts of Chemistry and #Biochemistry, University of Glasgow, Glasgow, G12 8QQ, UK. and *CCLRC Daresbury Laboratory, Daresbury, Warrington, WA4 4AD, UK.

The crystal structure of the integral membrane light-harvesting complex from *Rhodopseudomonas acidophila* strain 10050 showed that the active assembly consists of two concentric cylinders of single helical protein subunits which enclose the pigment molecules. Eighteen bacteriochlorophyll *a* (Bchl *a*) molecules are sandwiched between these membrane-spanning helices to form a continuous overlapping ring with their bacteriochlorin planes perpendicular to the plane of the membrane surface. A further nine Bchl *a* are positioned between the outer helices with their bacteriochlorin ring planes parallel to the membrane plane. Carotenoid molecules span the assembly making van der Waals contacts to both types of Bchl *a* pigments as well as the protein helices. A close analysis of the structure shows a beautiful interlocking of the protein and pigment molecules to allow for the optimisation of energy transfer between pigments in a single complex and between adjacent complexes, connecting to the reaction centre where charge separation takes place.

This work has been supported by the BBSRC.

MS04.03b.05 8.5 Å PROJECTION MAP OF THE LIGHT HARVESTING COMPLEX I FROM RHODO SPIRILLUM RUBRUM REVEALS A RING COMPOSED OF 16 SUBUNITS. Simone Karrasch, Per A. Bullough, Robin Ghosh, MRC Laboratory of Molecular Biology Hills Road Cambridge CB2 2QH, U.K

Two-dimensional crystals from light-harvesting complex I (LHC I) of the purple non-sulphur bacterium Rhodospirillum rubrum have been reconstituted from detergent-solubilized protein complexes. Frozen-hydrated samples have been analyzed by electron microscopy. The crystals diffract beyond 8 Å and a projection map was calculated to 8.5 Å. The projection map shows 16 subunits in a 116 Å diameter ring with a 68 Å hole in the centre. These dimensions are sufficient to incorporate a reaction centre in vivo. Within each subunit, density for the α- and the β-polypeptide chains is clearly resolved and the density for the bacteriochlorophylls can be assigned. The experimentally determined structure contradicts models of the LHC I presented so far.