s3.m2.o3 **From modeling and refinement to refinement with modeling.** D. Turk, *Dept. Biochem. & Mol. Biol., Jožef Stefan Institute, Jamova 39, 1000 Ljubljana, Slovenia*.
Keywords: modeling, automated structure determination, software.

Macromolecular models have to be created before they can be refined. The first models were physically build into electron density maps in so called Richards box and it successors. Refinement was introduced only gradually and with quite some hesitation of the crystallographic community before it was accepted as a valid and inevitable tool of a macromolecular crystal structure determination. As model building progressed from the physical models to the virtual models on a screen of a computer, also lower quality electron density maps could be interpreted and structures completed with the help of refinement tools became a common practice. Meanwhile structure refinement progressed from real space difference density maps to reciprocal space least-square targets and lately to gradients driven by maximum likelihood methods.

The division of tools and procedures on refinement and modeling (electron density interpretation) remained, however, more or less unmodified. Only recently it has become evident that automated structure determination is within reach and integration of tools dealing with model building and structure refinement became the new challenge of the macromolecular structure determination. MAIN approach will be presented only briefly, and will be followed by the other two more detailed talks in the session.

s3.m2.o4 **From maps to molecules in minutes.** T.J. Oldfield, Molecular Simulations Inc., *Dept. of Chemistry, University of York, Heslington, York, YO10 5DD, UK*
Keywords : automated, crystallography, interpretation.

Recent developments in recombinant DNA techniques, crystallisation protocols, X-ray data collection techniques and devices, and computing have led to a substantial increase in the speed and number of protein structure determinations in modern crystallographic laboratories. However, there still remains a number of key stages in the crystallographic process which limit the rate of structure determination. One of these is fitting electron density maps, either in the initial stages of tracing a chain to a new map, or in the manual rebuilding during refinement. This is a particularly onerous task, requiring many days and often weeks of working at a graphics terminal with maps and model.

The presentation will show how methods developed within the program QUANTA can be used to automate the interpretation of electron density maps of proteins. In particular I will show how automation can be used for map tracing, sequence assignment, model building, ligand fitting, water placement/refinement, validation, structure classification and functional assignment.

The level of automation provided by the presented methods is defined by the quality of the data, but this is significant even where the resolution is moderate (3Å) and initial phase error is high (80 degrees). The current version of the application has also been shown to work with 6Å data where phases are of good quality, while at higher resolutions (< 2Å) the structure can be traced completely in seconds.

The validation, structure classification and functional assignment techniques are possible due to recent advances with data mining calculations. These results are in preliminary stages, but large databases of structural fragments and active sites have been generated and can be used to screen protein structures for features of interest.

The electron density applications are already available within QUANTA 98 and represent novel and effective tools for speeding up all aspects of map interpretation. The various modules (X-AUTOFIT, X-LIGAND, X-SOLVATE, X-BUILD and X-POWERFIT) have been developed in close collaboration with the large number of crystallographers working on projects in the Protein Group at York.