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EXPLOITING PROTEIN STRUCTURE IN THE POST GENOME ERA

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The theme of this presentation is to describe computational studies that use information about protein structure to provide enhanced interpretation of biological data. First, a database that describes structural and functional annotation of the proteins in recently sequenced genomes will be reported (1). 40% of the human proteome can be assigned to domains of known structure. Comparative analysis of domain frequencies between different species provides insight into protein evolution. Second, the application of protein structure prediction by fold recognition will be reported (2). Despite the advances of sequence-based methods, fold recognition can identify additional probable remote homologies with its consequential suggestion of protein structure and function. The added value of expert intervention into contemporary algorithms will be assessed. Finally, recent studies to understand the evolution of metabolic networks using structural information to identify remote homologies will be reported (3). Programs available for use by the community are available at www.sbg.bio.ic.ac.uk.

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Keywords: BIOINFORMATICS, PROTEIN MODELLING, PROTEIN EVOLUTION

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THE GOOD, THE BAD AND THE UGLY: EXPERIENCES AT THE SYNCHROTRON

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The availability of synchrotron radiation has very significantly influenced the field of structural crystallography in the last few years. In particular, the macromolecular crystallography benefited enormously from the routine use of very bright radiation sources at the new, third generation synchrotrons. For example, the recent initiative of structural genomics is in large part dependent on the good access to the intense and tunable synchrotron beam lines. The use of the synchrotron radiation is very much appreciated by all involved researchers, but in practice working at the synchrotron has also the darker side. The newest synchrotron beam lines are very bright, which means that the activity at the station is usually very hectic, involving many sleepless nights. In spite of a high degree of automatization, it is not easy to avoid mistakes in such conditions, and several anecdotic stories may illustrate this point. The enormous beam intensity makes it possible to collect meaningful data from very small and weakly diffracting crystals, but it can also quickly destroy the crystalline order in biological samples even if they are frozen, leading to the loss of diffraction. However, the few small bad and ugly synchrotron faces should not obscure the big good and positive face smiling at the synchrotron radiation users

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Keywords: SYNCHROTRON RADIATION, DIFFRACTION, STRUCTURAL BIOLOGY

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PRESSURE-TUNED CRYSTAL CHEMISTRY: H-BONDS VS CENTRAL FORCES AT PHASE TRANSITIONS AND IN POLYMORPHS

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A considerable progress in crystal chemistry has been achieved through systematic studies on thermodynamics, structure-property relations, phase transitions, polymorphism and crystal engineering - and most recently complemented by systematic studies of compressed crystals. Relatively low pressure of few GPa is very efficient in modifying structures, and thus convenient for investigating the role of intermolecular interactions for the formation and transformations of crystals. Crystals are squeezed by pressure and, conversely, the crystal volume can be translated into higher internal pressure (in other words: stronger interactions) exerted on molecules, stronger force constants, or lower amplitudes of thermal vibrations. These interactions are then capable of transforming the conformations of molecules, of modifying their electronic structure, tautomeric forms etc. All these information are essential for understanding the mechanisms governing the crystal chemistry, or even more general problems of physical, chemical and biological sciences. The application of pressures for crystal chemistry will be exemplified by a series of systematic studies on hydrogen-bonded structures. Hydrogen bonds, van der Waals and electrostatic forces react differently to high pressures, and differently contribute to structural transformations and phase transitions. The microscopic structure, aggregation and interactions in crystals determine the thermodynamic character of the phase transitions. The relations obtained for the continuous phase transitions can be extended to the discontinuous ones, to inclusion compounds and to certain polymorphs. They can also explain the structural origins of such thermodynamic features as anomalous thermal expansion or the existence of tricritical point.

Keywords: HIGH PRESSURE, PHASE TRANSITIONS, POLYMORPHISM