Synchrotron Radiation Protein Crystallography in the Genomics Era

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Protein crystal structure determination in the context of genome sequencing presents huge challenges and opportunities. The potential for genome level of numbers of protein crystal structure determinations will involve synchrotron radiation (SR) sources and coordination between facilities on a global level, which is practical in the "internet age." There are at least three levels at which this project [e.g., of a human 3-D genome (proteome) project] can be approached. The first level involves predicting from amino acid sequences where a new protein 3-D fold would be likely. The second involves a systematic chromosome by chromosome approach of all 100,000 proteins (although 40% are membrane bound, and probably very difficult to "guarantee" crystals). The third approach is where one genome is not enough (i.e., where protein 3-D structure and amino acid sequence comparisons between different human genomes will be pursued; for example, to investigate in detail the genetic basis of relevant diseases). In addition to inter-SR facility coordination, the efficiency of the protein crystallography technique is a critical objective; yet atomic resolution coordinate quality must not be sacrificed. MAD and ultra-high resolution data collection optimisation (including combined protocols), more efficient detectors (like the pixel detector), more automatic crystal sample changing, microfocus beams to work with smaller and smaller crystals, and rapid but accurate structure validation are all needed to increase the rate of determining structures. But can we grow the protein crystals fast enough?

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