The Impact of Synchrotron Radiation on Structural Biology and Biotechnology

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The impact of synchrotron radiation on structural biology and biotechnology must be considered in the context of developments in molecular biology, cell biology, genomics, and macromolecular crystallography in general. During the past 10-15 years, cloning, expression, purification, and crystallization of proteins have made impressive advances. Genomics and the general understanding of biological processes have opened up vast new opportunities to explain biology at continually more complex molecular structural levels. Software to process the data, solve structures, and analyze structural information has grown from poorly organized individual programs to comprehensive software libraries. Crystallography has continued to be the dominant method of determining the three-dimensional structure of increasingly larger and more complex molecular problems. Complexes of multiple proteins and tens of thousands of atoms are being undertaken and solved. Alternatively, proteins can be broken into their functional domains to study their mechanisms or substrate binding at the atomic resolution level. Not only does 3-D structural biology help in understanding biological processes and molecular mechanisms, it allows for the development of methods to rationally modify biological processes to control them. Pharmaceutical research is focusing increasingly on molecular targets involving understood biological processes. Crystallography is an increasingly important tool in the development of new therapeutic agents in a broad range of diseases, but new factors are influencing structure-based drug design including combinatorial chemistry, rapid assaying of structural interactions by NMR, structural genomics, high throughput screening, and informatics.

The impact of synchrotron radiation on structural biology and molecular-targeted drug development relies on the broad band width of x-radiation, high collimation, and brilliance. These properties allow for (1) data collection on very small crystals; (2) data collection on crystals with very large unit cells; (3) structure solution using multiwavelength anomalous scattering; and (4) rapid data collection for time-resolved crystallography, and for rapid determination of large numbers of structures for protein engineering, and study of mutations or protein/inhibitor complexes. Reliance of macromolecular structure scientists on synchrotron radiation has increased dramatically. This is quantified in the 1990 and 1997 surveys used in the BioSync reports on the evaluation of resources and needs[1,2] and on data derived from the Brookhaven Protein Data Bank. During this period, the number of new structures determined involving the use of synchrotron radiation has increased from 18% to 44%, and over 90% of macromolecular crystallographers are using synchrotron radiation. Synchrotron usage has tripled during this period and data collection rates have increased dramatically as a result of improved detector technology and radiation brilliance.

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[1]"Structural Biology and Synchrotron Radiation: Assessment of Resources and Needs," Structural Biology Synchrotron Users Organization (1991).

[2]"Structural Biology and Synchrotron Radiation: Evaluation of Resources and Needs," Structural Biology Synchrotron Users Organization (1997).