During the past 10 years, the application of synchrotron radiation to the solution of protein structure has undergone a steady and impressive evolution: from the determination of the three-dimensional structures of individual proteins to the more challenging structures of protein complexes (proteins typically function in cells by binding to and altering the activity of other proteins), to the even more formidable undertaking of solving the structures of large complexes consisting of many proteins. These ever expanding achievements in x-ray crystallography are providing answers to the most important questions in biology, including how the brain functions, how we develop from single cells to the nearly incomprehensible array of cells that comprise a human being, and why we age and eventually die. There is no other place where these remarkable accomplishments are more prominently on display than at the macromolecular crystallography resource at Cornell’s MacCHESS.

MacCHESS can be proud of a number of truly spectacular successes throughout its history and continuing right up to the present. Among these are the recent accomplishments of Tom Steitz and colleagues from Yale University in determining the
FOR A NUMBER OF YEARS, THE OVERARCHING INTERESTS OF MY RESEARCH GROUP AT CORNELL, MOLECULAR MEDICINE/ CHEMISTRY AND CHEMICAL BIOLOGY, HAVE BEEN UNDERSTANDING AND IDENTIFYING THE REGULATORY CUES THAT DICTATE WHETHER CELLS GROW NORMALLY OR BECOME CANCEROUS.
The laboratories of Brian Crane and Steven Ealick, Chemistry and Chemical Biology, are using synchrotron radiation to obtain structural information about proteins that are essential to the basic survival of bacteria, providing what is certain to be extremely valuable information for designing new drugs to combat pathogenic organisms.

For a number of years, the overarching interests of my research group at Cornell, Molecular Medicine/Chemistry and Chemical Biology, have been understanding and identifying the regulatory cues that dictate whether cells grow normally or become cancerous. During efforts to assemble the genes and proteins that regulate how cells grow, however, it became clear that detailed structural information on how these proteins function and bind to their signaling partners was absolutely essential. Aided by the MacCHESS staff and facility, students from our laboratory gained the necessary training to solve the three-dimensional structures of a number of proteins and protein complexes relevant to cancer. This information is now elucidating new strategies for therapeutic intervention.

Cornell has many examples of how exciting new advances in biology and the possibilities for novel therapeutic approaches are emerging from taking advantage of MacCHESS. Quan Hao, director of MacCHESS, and his colleagues are solving the three-dimensional structures of proteins that play essential roles in the immune response and are obtaining information that may relate to AIDS. The laboratories of Brian Crane and Steven Ealick, Chemistry and Chemical Biology, are using synchrotron radiation to obtain structural information about proteins that are essential to the basic survival of bacteria, providing what is certain to be extremely valuable information for designing new drugs to combat pathogenic organisms.

Watching Cellular Machines Work

The future holds even more exciting possibilities. Scientists can now dream of seeing single protein molecules go through their many molecular rearrangements, which occur on a time scale of fractions of seconds and culminate in essential biological activities. Researchers may even anticipate being able to watch the massive protein complexes that function as cellular machines produce the signals that form the very essence of life. With the application of new methods to harness and utilize energy—for example, through the development of the ERL—these experiments, which a few years ago seemed several decades beyond reach, will soon become reality.

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