Center for Research on Biological Structures created at UCSD

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Media Contacts: Devine Hagen, (619) 534-2920, dhagen@ucsd.edu

From the arrangement of atoms that makes up enzymes, proteins, and the body's vast chemical communications networks to the scaffolding of tissues and organs that gives an organism its inner support and outer strength, all life is built on increasingly complex layers of interacting structures.

To better understand the nature of these structures and how they work with each other in living systems, the Center for Research on Biological Structures (CRBS) has been established at the University of California, San Diego (UCSD). Among the center's goals are the creation of new tools to understand complex cell functions such as those involved in muscle contraction, cardiovascular networking, and activities of the nervous system such as thinking, memory and emotion.

"This center holds great promise for deepening our understanding of biological systems by applying sophisticated state-of-the-art technologies to explore new and uncharted areas--a merging of chemistry, physics, and computer science with biology and medicine," said Susan Taylor, professor of chemistry and biochemistry at UCSD, co-director of the Computational Center for Macromolecular Structure, and chair of the new center's executive committee.

"We shall have the breadth to move rapidly from atoms to whole animals, with the discovery of new drugs as one obvious long-range target of this work," she added.

With the aid of recent technological advances, the center will focus on major levels of biological structures, from the atomic and molecular level to the cellular and tissue level and beyond. The center, recently approved by Chancellor Robert Dynes and the UCSD Academic Senate, includes researchers from a cross section of disciplines--from physics, mathematics, chemistry and biology to neuroscience, psychiatry, bioengineering, computer science and pharmacology. The center draws on the expertise of the UCSD campus, the UCSD School of Medicine and the San Diego Supercomputer Center.

"If you look at the history of science, you often see really big gains resulting from the interactions of different research disciplines and exposure to advances in different technological areas," said Mark Ellisman, professor of neurosciences, director of the National Center for Microscopy and Imaging Research at the UCSD School of Medicine, and director of the new center. "These new interactions and technologies enable people to see things in a very different way."

CRBS researchers will deploy advanced computer-assisted instruments allowing them to see biological structures as never before. These newer tools for collecting data include high-power electron microscopes capable of revealing the three-dimensional structures of living cells and their internal components, X-ray and magnetic resonance techniques that capture the atomic structure of simple and complex proteins, and confocal microscopes that allow researchers to visualize molecules tagged with fluorescent markers as they pass chemical messages to each other.

Not only has the computer ushered in a new era of data collection, it also has yielded innovative ways to analyze and store data. Rapid advances in high-performance computing and sophisticated graphics tools are producing colorful three- dimensional computer models of enzymes, hormones, and viruses, and split-second video simulations of previously unseen biological structures and their activities. Applying large-scale computational tools for the analyses of these systems, and for eventual drug design, will be a major activity of this center.

Among the structures coming under study by the UCSD group will be protein kinases, a family of enzymes that form the heart of a molecular relay team in the body. Kinases hand off chemicals called phosphate groups to other enzymes, much as relay runners pass a baton to each racer in a series until one reaches the finish line. At this point, the final enzyme in the path initiates some cellular function--the breakdown of fat stored for energy, cell motility, cell division, or gene transcription, to name a few. It's estimated that the kinase family contains about 2,000 members, with many other players contributing to this signal transduction relay.

Working with computational researchers, the center will establish computer databases such as those containing information on genetics, protein structure, molecular dynamics, and diseases linked to the function or malfunction of kinases and other molecules critical for cell signaling. At the same time, new techniques are being developed to allow scientists to rapidly access and manipulate this centrally stored data from their own laboratories. Combined, the database and the new ways of accessing this data could shed light on chemical inhibitors that may represent new drugs against diseases, including Alzheimer's disease and cancer.

"There's an overwhelming amount of information," said Taylor. "Our goals are to extract the knowledge from all this information. We also want to be able to make these capabilities widely accessible to everybody."

Among the groups interested in this information is a\line mushrooming biotechnology industry around Southern California.

"We want to forge new interactions with biotech and biocomputing-related companies for technology transfer," said Ellisman.

The center--which will operate from a central campus facility at the San Diego Supercomputer Center and "satellite" units at Urey Hall on UCSD's main campus, and the Basic Science Building at the School of Medicine--also will help train a new generation of researchers interested in biological structures and how they interact with each other.

"We see this unit as increasing the relevance of education and training for the rapidly changing needs of industries in California," said Ellisman. "Consistent with the mission of the university is the improvement of the quality of life of the citizenry who pay taxes to support it. Strengthening industry is a big, big piece of that."

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