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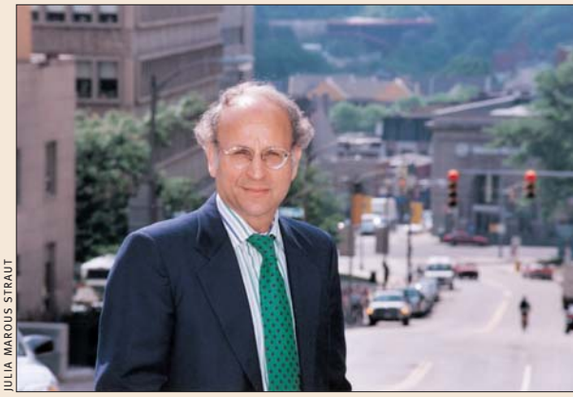
JULIA MAROUS STRAUT

In 1963, the renowned physicist Richard Feynman wrote (*The Feynman Lectures on Physics*) that the most important hypothesis in all of biology was that "...all things are made of atoms, and that everything that living things do can be understood in terms of the jigglings and wigglings of atoms." Not long before Feynman wrote this, Perutz, Kendrew, Crick, Watson, and others in Cambridge—mainly physicists—determined the first macromolecular structures (e.g., a double helix) by analyzing the diffraction of x rays through crystalline solids. Shortly thereafter, Pitt established a Department of Crystallography—then the only one of its kind in the United States. (Pittsburgh also has a rich history in nuclear magnetic resonance, or NMR, another method that allows us to glean structural information on macromolecules important in biology. Paul Lauterbur, a Pitt alumnus, won the 2003 Nobel Prize for work that eventuated in the development of magnetic resonance imaging.) Now, we are establishing a Department of Structural Biology in our medical school; only a handful of American universities have such a department.

At atomic resolution, structural biologists shed light on the 3-D structures and dynamic properties of proteins, nucleic acids, and carbohydrates, illuminating secrets of their biologic activity like function, recognition, and toxicity. X-ray crystallography presents static structures, just as NMR presents dynamic conformations, and cryo-electron microscopy, large structures, e.g., viruses and organelles. As they combine structural findings with other data, these scientists gain insight regarding cellular events and how these events translate into the form and physiology of entire organisms. That can save lives. When x-ray crystallographers at Merck elucidated the structure of the HIV protease, their work immediately led to the design of the first protease inhibitor, yielding an extraordinary increase in the length of survival of patients with AIDS. In the next decade, many new drugs for cancer, infectious and neurologic diseases, and disorders of the immune and cardiovascular systems will follow in the wake of structural biologic studies—for bargain prices. It is estimated that half the cost of drug discovery could be saved if we had structural knowledge of drug targets early on in the process.

The creation of our department is particularly timely, given that what we know of biological 3-D structures is far behind our knowledge of gene and protein sequences. Our new Biomedical Science Tower will house practitioners of the various structural methods in one venue, encouraging their overlapping techniques to yield exciting composites. This new department will also neighbor the Pittsburgh Institute for Neurodegenerative Diseases (see our cover story), fostering what I believe will be landmark studies on the aberrant proteins in Alzheimer's and Parkinson's diseases. I anticipate the department will have 10 full-time primary faculty within a few years, wiggling and jiggling together. Led by Angela Gronenborn, a preeminent structural biologist, they'll address the enormous challenge of relating our one-dimensional knowledge about DNA sequences to the 3-D architectures that they encode and to the complex chemical and physical transformations that underlie all living systems.

Arthur S. Levine, MD
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