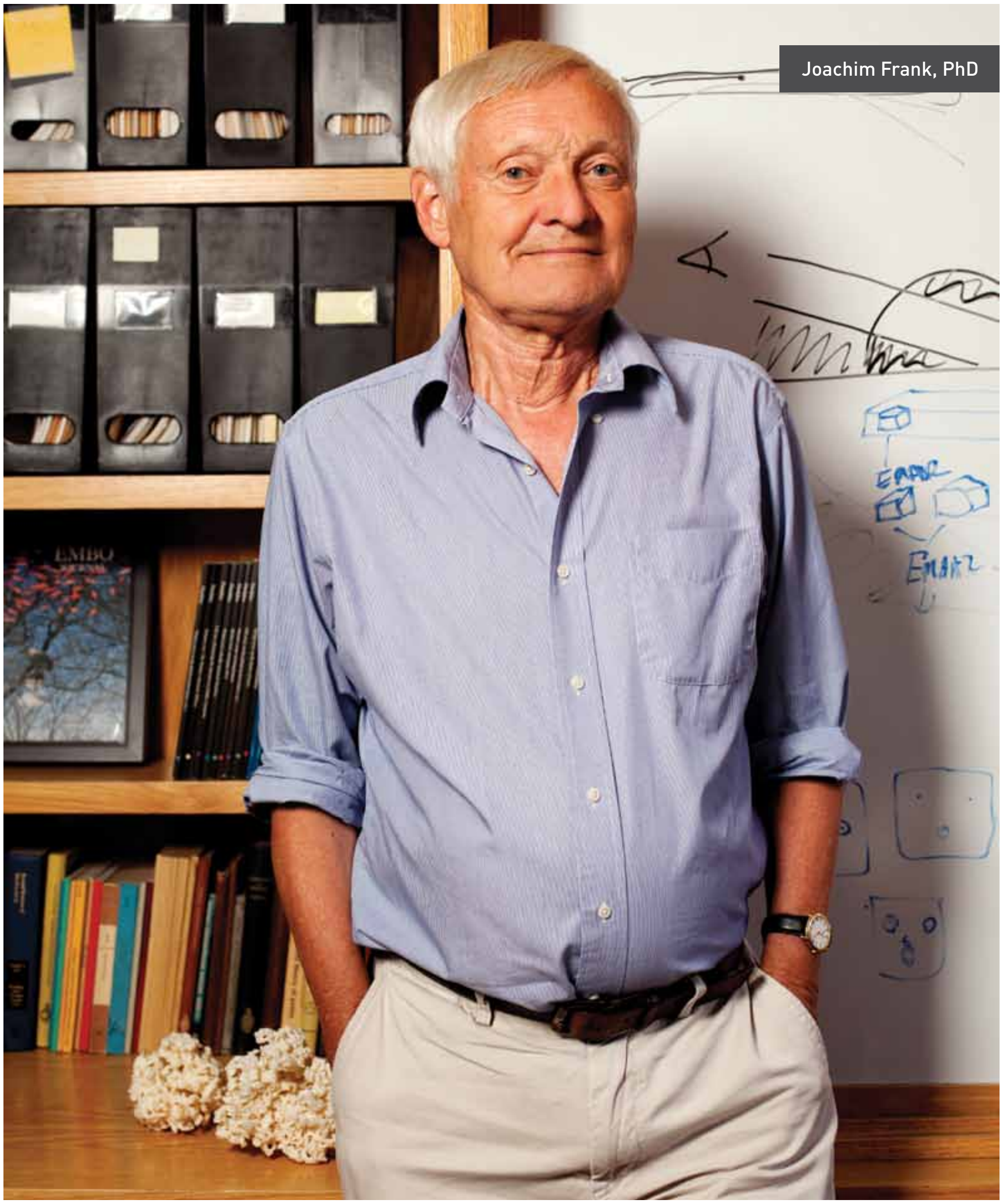
Molecular Microscopy

The uncertainty principle in quantum physics holds that observation has the power to transform the object of our attention. Social scientists know the concept as the Hawthorne effect, after a series of industrial psychology experiments in a Flapper-era Chicago factory of the same name. Biologists see the phenomenon when they deploy an electron microscope to probe samples too small for a light microscope to reveal: Bombard a living sample with electrons, and the fragile molecules within incinerate. Even worse, while biology spans time and space, electron microscopy generates only a two-dimensional image of an inert sample.

Joachim Frank, PhD, took a different approach. Dr. Frank, professor of biochemistry & molecular biophysics and of biological sciences at Morningside and a Howard Hughes Medical Institute investigator, is winner of the 2014 Benjamin Franklin Medal in Life Sciences. The medal—previously awarded to such luminaries as Alexander Graham Bell, Pierre and Marie Curie, Albert Einstein, and Stephen Hawking—celebrates Dr. Frank's development of cryo-electron microscopy, his use of cryo-EM to investigate the structure of large organic molecules at high resolution, and his resultant discoveries regarding the mechanism of protein synthesis in cells.



Joachim Frank, PhD

Dr. Frank's approach, conceived in the 1970s, is simple: Create a 3-D image of a biological molecule, capture images of thousands of identical molecules lying in different orientations, then combine them. Coming up with the concept was the easy part. Much more painstaking was Dr. Frank's development of the computational methods to realize his vision; 35 years later, his techniques are still used by most structural biologists who use electron microscopy.

Using those techniques himself, Dr. Frank has revealed the 3-D shape of ribosomes, complex protein-synthesizing factories in all cells. Combining his mathematical methods with techniques that freeze the ribosome in a thin layer of liquid ice (the cryo in cryo-EM), he obtained the first 3-D image of the molecule that clearly showed its two separate subunits and, later, an even more detailed image that gave scientists new insights into how the ribosome works.

He also has investigated how these molecular machines interact with other molecules during the different steps of protein production. Like multiple still shots for a movie, his studies have revealed how one subunit of the ribosome rotates back and forth in a ratcheting motion to add amino acids during protein production, a process that is the same in all kingdoms of life.

In a study published in Nature, Dr. Frank's team uncovered details of the ribosome from the parasite that causes African sleeping sickness, details that may lead to drugs to kill the parasite. Another Nature paper showed how viral RNA commandeers the ribosome of the virus's host to produce new viruses.

Dr. Frank is a member of the National Academy of Sciences and the American Academy of Arts & Sciences and a fellow of the American Association for the Advancement of Science and the Biophysical Society. He shared the Elizabeth Roberts Cole Award of the Biophysical Society for developing methods of 3-D reconstruction of biological macromolecules.