nature structural & molecular biology

Get the party started

This year marks the centennial of Einstein's achievements in 1905, a year in which he published five seminal papers on energy, light and time that forever altered physics and impacted all areas of science. To commemorate his achievements as well as bring the excitement of physics to the public, 2005 is being called the World Year of Physics, the International Year in Physics, or simply Einstein's Year. Regardless of the name, it is clear that the world is throwing a big party to celebrate Einstein's exceptional logic and imagination as well as the many contributions of physics to our lives.

> "Logic will get you from A to B. Imagination will take you everywhere." —*Albert Einstein*

Einstein's impact on science was highlighted recently during a series of symposia and lectures cosponsored by the American Association for the Advancement of Science and American Physical Society. One of the most enlightening talks was that from Dr. Elias Zerhouni, director of the National Institutes of Health, who discussed the contribution of physics in general, and of Einstein in particular, to the biological and biomedical sciences. He noted that perhaps the first gift of physics to medicine occurred in the early 14th century when corrective lenses were fashioned for our eyes. Indeed many advances in physics have allowed us to see both large and small molecules in exquisite detail. Dr. Zerhouni, drawing on his own experiences, discussed the recent contributions made in medical imaging, and the ways he imagines biology and physics coming together in the 21st century.

For biologists, the most relevant of Einstein's work to what we do today was done between 1900–1921. Think of Einstein and relativity comes to mind. However it was his dissertation and the least famous paper of 1905, which analyzed the movement of dust particles in solution that changed the way we think about molecules. Einstein proposed that water molecules continuously collided with dust particles and randomly moved them. He suspected that this movement was Brownian motion—first studied in 1827 by botanist Robert Brown—but did not have sufficient data to confirm his theory. In his 1905 paper, Einstein proposed a quantitative relationship, the Stokes-Einstein equation, between the relative sizes of the dust particles and how they diffused through the medium and provided persuasive theoretical evidence for the existence of atom-sized molecules, which was still being debated among physicists at that time. Today we use the Stokes-Einstein equation to analyze our centrifugation and dynamic light scattering data to estimate the effective size of a molecule in solution.

Einstein wasn't the only physicist changing science in the early 1900s. A quick glance at the list of Nobel Prizes in Physics shows Röntgen receiving the first Nobel for his discovery of X-rays. He was followed a few years later by von Laue who showed that particles in an ordered lattice could diffract X-rays. W. Bragg and L. Bragg expanded this concept and developed theoretical and experimental techniques to determine the crystal structures of molecules. These and other advances in the 1930s (development of cyclotrons) and 1990s (high-resolution electronic detectors) improved X-ray techniques and marked the beginning of our love affair with atomic structures of small and large molecules.

While the X-ray crystallographic revolution raged on, other macromolecular imaging techniques, especially those tailored for studies of cellular organization emerged. In the 1930s, Ruska designed the first working transmission electron microscope (TEM) and cells haven't looked the same since. TEM images objects on the order of a few Ångstroms and this characteristic makes it a valuable tool in biological and materials research. While Ruska waited for his Nobel, Zernike invented the phase-contrast microscope that allowed the study of colorless and transparent biological materials. In 1986, Ruska shared the Physics Prize with Binnig and Rohrer, who developed a different way to look at objects, the scanning probe microscope (SPM). In contrast to the classical microscopes, which use an incident beam to image objects, SPM imaging relies on sensing the force between a very sharp probe and the sample surface and hence provides an atomic level three-dimensional image of the surface of objects. One form of SPM, the atomic force microscopy (AFM) is now an important tool for studying macromolecules and their complexes.

Another contribution from physics, the laser, has advanced our understanding of the mechanical properties of biomolecules. Einstein first described the process of stimulated emission that makes lasers possible in 1917, but it wasn't until the 1950s that physicist developed a functional laser. Many decades later laser physics chilled out when Chu, Cohen-Tannoudji and Phillips found a way to cool and trap atoms with laser lights. These studies ushered in the use of optical traps as a powerful tool for manipulating objects, even those as small as a single atom, without mechanical contact to understand their physical properties.

Not to be outdone, spectroscopy was also making strides and winning prizes, and it was the early studies in the 50s and 60s that inspired the chemists to discover the most widely used spectroscopic method, nuclear magnetic resonance (NMR). Likewise, the early physical studies of radioactive materials and isotopes allowed chemists and biologists to develop techniques and enhance existing methods such as NMR to utilize these isotopes in their studies.

It is difficult to predict which of the current trends in physics will impact the biological sciences in the 21st century or who will be the next Einstein. Dr. Zerhouni notes "The role of physics grows in proportion to the emerging complexity of biology." This is because physics describes the fundamental behavior of matter. The current move from studies of individual macromolecules to large interactive systems, for example, in chemical signaling and in neural function, suggests that physics will continue to change and enhance the way we study complex biological systems. ■