nature biotechnology

Why small matters

Starting in the early 1940s, the rise of what we now call molecular biology was characterized by an influx into biology of researchers from the physical and chemical sciences. Physicists such as Max Delbrück, Leo Szilard, Ernst Schrödinger and later Francis Crick all brought to biology an intellectual rigor that made problems that before had seemed insoluble, tractable for the first time. Similarly, as physical chemistry informed Linus Pauling's elucidation of the α-helix and β-sheet, the crystallographic study of minerals inspired scientists, such as Sir Lawrence Bragg, Max Perutz and Desmond Bernal, to tackle the three-dimensional structures of biological macromolecules. Ultimately, biology was transformed from a largely phenomenological discipline to one in which physiological function is predicated on the basis of molecular structure.

In a similar manner, we are now witnessing the emergence of another field in which the physical, chemical and biological sciences are converging. That field is nanotechnology. And the clearest sign that nanotechnology is emerging is that nobody can quite agree on what it is. The US government's National Nanotechnology Initiative defines nanotechnology as 'anything involving structures less than 100 nm in size'. But this arbitrarily excludes a host of other relevant research focusing on fluidics devices and materials that currently is carried out at the micron scale.

The late Richard Feynman is widely credited as founding the field, but it took two scientists working at IBM in the 1980s to finally provide the tools—the scanning tunneling microscope and atomic force microscope—that would allow atomic structures to be observed and manipulated. A few years later, chemists Richard Smalley, Robert Curl and Sir Harry Kroto discovered Buckminster fullerenes—a new form of carbon, later dubbed C60 buckyballs—and Sumio Iijima, Don Bethune and Howard Tennent all independently created carbon nanotubes, materials that have interesting tensile and superconductive properties.

This issue of *Nature Biotechnology* focuses on the interface between biology and nanotechnology—termed (yes, you guessed it) nanobiotechnology. It reflects the increasing importance of nanoscience and nanotools in the creation of novel types of biomaterials for use in tissue engineering and cell patterning, sensors that rely on conformational changes in macromolecules for use in diagnostics, nanopores that allow the passage of single molecules for sequencing DNA, nanomaterials for use in imaging single molecules or cells and devices/materials/particles for use in drug delivery or as therapeutics.

Nobody, however, should expect tangible products and lifesaving medicines from nanobiotechnology anytime soon. As in molecular biology, the delay between basic discoveries and biotechnological application will be long, decades perhaps. It is still too soon to tell which results will turn out to be really useful.

In the meantime, scientists and their sponsors—be they academic, federal, industrial or private investors—must avoid the temptation to hype research, giving the public the mistaken idea that nanotechnology products are further developed and nearer at hand than they really are. Such inaccurate portrayals not only threaten public confidence in the integrity of the science, but also risk a backlash. Already, in the past year, pressure groups, such as Friends of the Earth and the Canada-based ETC group (formerly known as the Rural Advancement Foundation International) have warned of the dangers of nanotechnology, the latter even calling for a global moratorium on the production of all nanomaterials. In April, HRH the Prince of Wales issued dire warnings in a UK newspaper about grey goo destroying the fabric of nature. "Big questions now loom over the world's smallest technologies," he wrote. "The sooner we get to grips with them, the better it will be for all of us."

Partly in response to these safety concerns, the US Environmental Protection Agency has started an assessment of the effects of nanoparticles on biological systems to ascertain whether they do indeed present unique health and environmental risks. At the same time, the US National Institute of Standards and Technology is developing new means of measuring nanotechnology product dimensions, behaviors and properties with a view to establishing standards for quality assurance and control of future nanotechnology products.

In this respect, those who present nanotechnology as the next 'big' thing would do well to learn from the 25-year history of biotechnology. By depicting recombinant DNA as an entirely new and alien approach, the biotechnology industry played right into the hands of the antibiotechnology lobby that successfully caricatured transgenic organisms as unnatural and dangerous. It is therefore very important to make clear from the outset (as was not done, for example, in the field of agbiotech) that each nanotechnology product must be evaluated on the basis of its individual risks and benefits, not as a general product of the technology that produced it.

Nanotechnology derives from the same simple assumption as molecular biology—that from detailed knowledge of structure, one can (often but not always) correctly infer function. Nonetheless, the goal of predicting complex biological phenomena and traits on the basis of 'bottom up' molecular and genomic biology remains frustratingly distant. The requirements of enormous capital investment, automated machinery and high-throughput analytical platforms currently exclude many researchers in smaller laboratories from these high-profile ventures. For them, nanotechnology, offers new and potentially intriguing opportunities that large-scale molecular biology does not. It is of little surprise therefore that this once abstruse area, dominated by physicists and chemists, has now become so attractive to the inheritors of the Delbrück tradition.