# Nanobiotechnology:

## MOLECULAR MANUFACTURING FOR THE GENOMIC AGE

When it comes to understanding biology, Professor Carl A. Batt believes that size matters – especially at the Cornell University-based Nanobiotechnology Center that he co-directs. Founded in January 2000 by virtue of its designation as a Science and Technology Center and supported by the National Science Foundation, the center seeks to fuse advances in microchip technology with the study of living systems.

Batt, who is also professor of Food Science at Cornell, recently presented an Academy gathering – entitled "Nanotechnology: How Many Angels Can Dance on the Head of a Pin?" – with a tiny glimpse into his expanding nanobiotech world.

"A human hair is 100 000-nm wide, the average circuit on a Pentium chip is 180 nm, and a DNA molecule is 2 nm, or two billionths of a meter," Batt told the audience.

"We're not yet at the point where we can efficiently and intelligently manipulate single molecules," he continued, "but that's the goal. With advances in nanotechnology, we can build wires that are just a few atoms wide. Eventually, practical circuits will be made up of series of individual atoms strung together like beads and serving as switches and information storage devices."

### SPEED AND RESOLUTION

There is a powerful rationale behind Batt's claim that size is important to the understanding of biology. Nanoscale devices can acquire more information from a small sample with greater speed and at better resolution than their larger counterparts. Further, molecular interactions such as those that induce disease, sustain life, and stimulate healing all occur on the nanometer scale, making them resistant to study via conventional biomedical techniques.

"Only devices built to interface on the nanometer scale can hope to probe the mysteries of biology at this level of detail," Batt said. "Given the present state of the

# Nanoscience & Nanotechnology:

## BUILDING A BIG FUTURE FROM SMALL THINGS

Nanotechnology has gained widespread recognition with the promise of revolutionizing our future through advances in areas ranging from computing, information storage and communications to biotechnology and medicine. How might one field of study produce such dramatic changes?

At the most obvious level nanotechnology is focused on the science and technology of miniaturization, which is widely recognized as the driving force for the advances made in the microelectronics industry over the past 30 years. However, I believe that miniaturization is just one small component of what makes and will make nanoscale science and technology a revolutionary field. Rather, it is the paradigm shift from top-down manufacturing, which has dominated most areas of technology, to a bottom-up approach.

The bottom-up paradigm can be defined simply as one in which functional devices and systems are assembled from well-defined nanoscale building blocks, much like the way nature uses proteins and other macromolecules to construct complex biological systems. The bottom-up approach has the potential to go far beyond the limits of top-down technology by defining key nanometer-scale metrics through synthesis and subsequent assembly – not by lithography.

Of equal importance, bottom-up assembly offers the potential to produce structures with enhanced and/or completely new function. Unlike conventional top-down fabrication, bottom-up assembly makes it possible to combine materials with distinct chemical composition, structure, size and morphology virtually at will. To implement and exploit the potential power of the bottom-up approach requires that three key areas, which are the focus of our ongoing program at Harvard University, be addressed (Figure).

First and foremost, the bottom-up approach requires nanoscale building blocks with precisely controlled and tunable chemical composition, structure, morphology and size, since these charac-

technology, there's no limit to what we can build. The necessary fabrication skills are all there."

Scientists like Batt and his colleagues at Cornell and the center's other academic partners are proceeding into areas previously relegated to science fiction. While their work has a long way to go before there will be virus-sized devices capable of fighting disease and effecting repairs at the cellular level, progress is substantial. Tiny biodegradable sensors, already in development, will analyze pollution levels and measure environmental chemicals at multiple sample points over large distances. Soon, we'll be able to peer directly into the world of nano-phenomena and understand as never before how proteins fold, how hormones interact with their receptors, and how differences between single nucleotides account for distinctions between individuals and species.

The trick – and the greatest challenge

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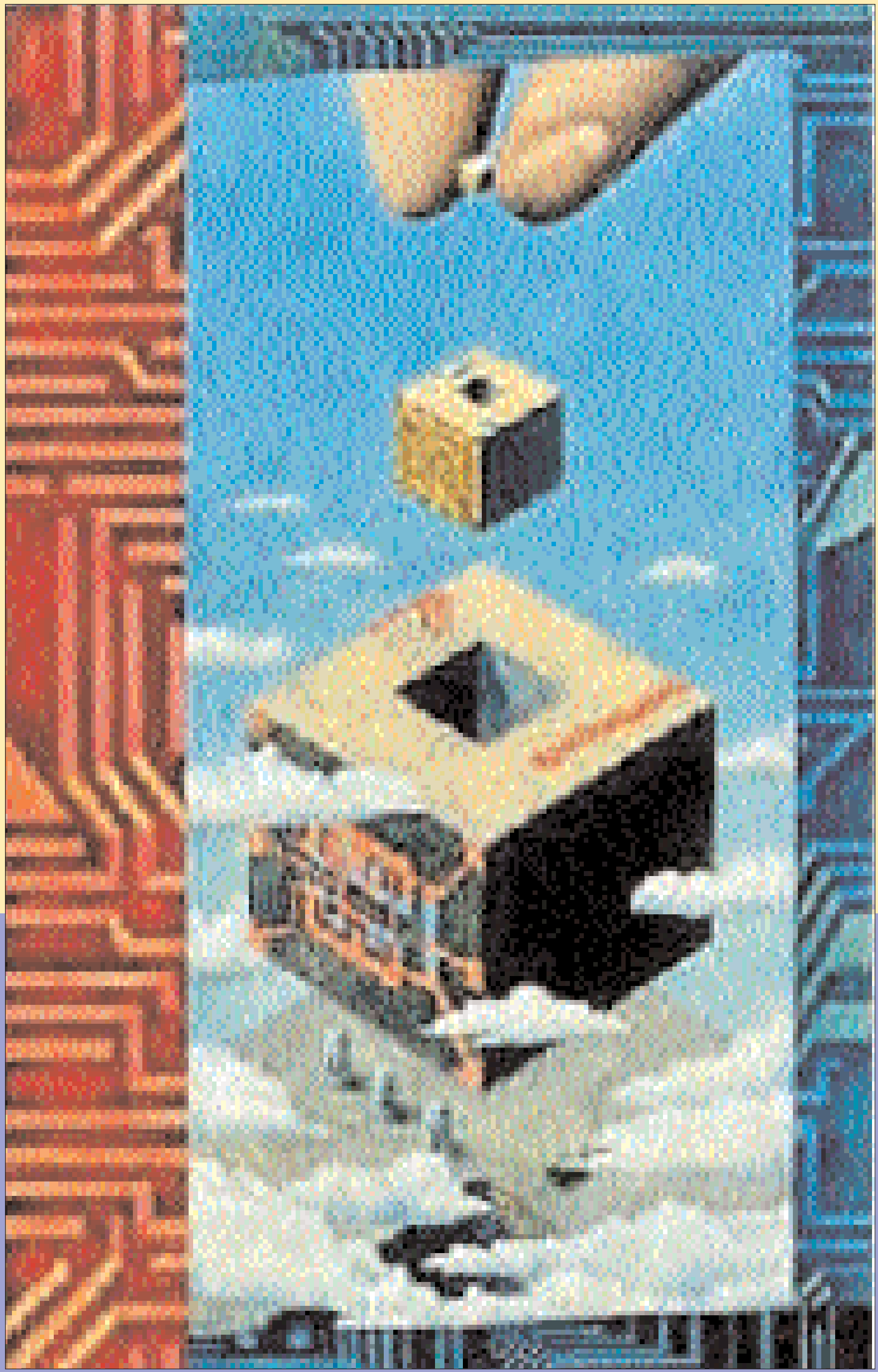

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teristics determine their corresponding physical (e.g. electronic) properties. From the standpoint of miniaturization, much emphasis has been placed on the use of molecules zenges in establishing reliable electrical contact to molecules has limited the development of realistic schemes for scalable interconnection and integration without having key feature sizes being defined by the conventional lithography used to make interconnects.

My own group's work has been focused on the nanoscale wires and, in particular, semiconductor nanowires as building blocks. This focus was initially motivated by recognition that the one-dimensional nanostructures represent the smallest morphology structure for efficient routing of information — either in the form of electrical or optical signals. Subsequently, we have shown that nanowires can also exhibit a variety of critical device function, and thus can be exploited as both the wiring and device elements in functional nanosystems.

Currently, semiconductor nanowires can be rationally synthesized in single crystal form with all key parameters – including chemical composition, diameter and length, and doping/electronic properties – controlled. The control that we have over these nanowire properties has correspondingly enabled a wide range of devices and integration strategies to be pursued. For example, semiconductor nanowires have been assembled into nanoscale field-effect transistors, light-emitting diodes, bipolar junction transistors and complementary inverters – components that potentially can be used to assemble a wide range of powerful nanosystems.

Tightly coupled to development of our nanowire building blocks have been studies of their fundamental properties. Such measurements are critical for defining their limits as existing or completely new types of device elements. We have

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posed by an emerging field that is melding the physical and life sciences in unprecedented ways – is to adapt the "dry," silicon-based technology of the integrated circuit to the "wet" environment of the living cell.

## BRIDGING THE ORGANIC – INORGANIC DIVIDE

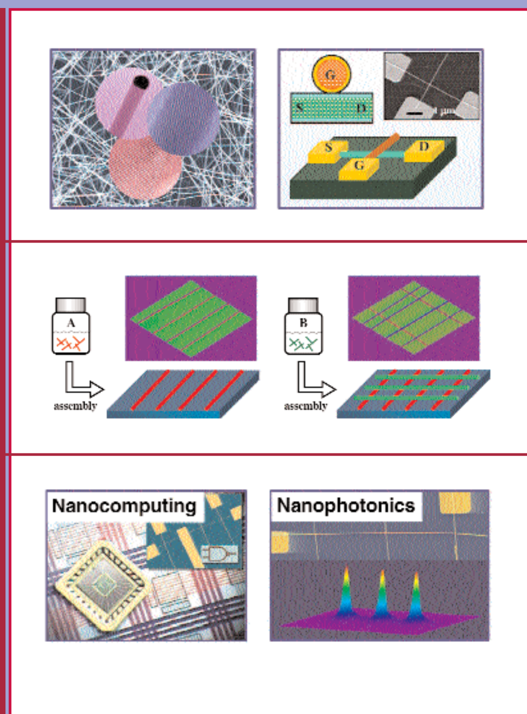
Nanobiotechnology's first order of business is to go beyond inorganic materials and construct devices that are biocompatible. Batt names proteins, nucleic acids and other polymers as the appropriate building blocks of the new devices, which will rely on chemistries that bridge the organic and inorganic worlds.

In silicon-based fabrication, some materials that are common in biological systems – sodium, for example – are contaminants. That's why nanobiotech fabrication must take place in unique facilities designed to accommodate a level of chemical complexity not encountered in the traditional integrated circuit industry.

But for industry outsiders, the traditional technology is already complex enough. Anna Waldron, the Nanobiotechnology Center's Director of Education, routinely conducts classes and workshops for schoolchildren, undergraduates and graduates to initiate them into the world of nanotechnology, encourage them to pursue careers in science, and foster science and technology literacy.

In a hands-on presentation originally designed for elementary-school children, Waldron gives the audience a taste – both literally and figuratively – of photolithography, a patterning technique that is the workhorse of the semiconductor industry. Instead of creating a network of wells and channels out of silicon, however, Waldron works her magic on a graham cracker, a choco-

**Figure Caption. Building the future is as easy as 1-2-3. Key stages of the bottom-up paradigm are illustrated for nanowires: (1) The synthesis of well-defined nanowire building blocks and elucidation of novel properties/ device concepts, such as a crossed nanowire field-effect transistor, which have the potential for massive integration by assembly. (2) Scalable assembly of nanowires into parallel and more complex arrays from fluid solutions, where sequential steps can be used to combine different materials. (3) Implementation of nanowire arrays as functional systems for nanoscale computing and multicolor light sources.**

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developed a new strategy for nanoscale transistors, for example, in which one nanowire serves as the conducting channel and the other crossed nanowire as the gate electrode (1, Figure). Significantly, the three critical device metrics are naturally defined at the nanometer scale in assembled crossed nanowire transistors: (1) a nanoscale channel width determined by the diameter of the active nanowire; (2) a nanoscale channel length defined by the crossed gate nanowire diameter; and (3) a nanoscale gate dielectric thickness determined by the nanowire surface oxide. These distinct nanoscale metrics lead to greatly improved device characteristics such as high gain, high speed and low power dissipation. Moreover, this new approach has enabled highly integrated nanocircuits to be defined by assembly.

Second and central to the bottom-up concept has been the development of hierarchical assembly methods that can organize building blocks into integrated structures. To obtain highly integrated NWs circuits require techniques to align and assemble them into regular arrays with controlled orientation and spatial location.

We have shown that fluidics, in which solutions of nanowires directed in channels over a substrate surface, is a powerful and scalable approach for assembly on multiple length scales. In this method, sequential 'layers' of different nanowires can be deposited in parallel, crossed and more complex architectures to build up functional systems (2, Figure). In addition, the readily accessible crossed nanowire matrix represents an ideal configuration since the critical device dimension is defined by the nanoscale cross point, and the crossed configuration is a naturally a scalable architecture that can enable massive system integration.

Third, combining the advances in nanowire building block synthesis, understanding of fundamental device properties and development of well-defined assembly strategies has allowed us to move well beyond the limit of single devices and begin to tackle the challenging and exciting world of integrated nanosystems. Significantly, high-yield assembly of

late bar and a marshmallow, manufacturing a mouthwatering "nanosmore" chip in a matter of minutes.

Graham crackers are substituted for silicon substrate, while chocolate provides the necessary primer for the surface. Marshmallows act as the photoresist, an organic polymer that, when exposed to light, radiation, or, in this case, a heat gun, can be patterned in the desired manner. Finally, a Teflon "mask" is placed on top of the marshmallow layer and a blast from the heat gun transfers the mask's design to the marshmallow's surface – a result that appeared to leave a lasting impression on the Academy audience as well.

### WHAT'S NEXT?

According to Batt, it won't be too long before the impact of the nanobiotech revolution will be felt in the fields of diagnostics and biomedical research. "Progress in these areas will translate the vast information reservoir of genomics into vital insights that illuminate the relationship between structure and function," he said.

Also down the road, ATP-fueled molecular motors may drive a whole series of ultrasmall, robotic medical devices. A "lab-on-a-chip" will test new drugs, and a "smart pharmacist" will roam the body to detect abnormal chemical signals, calculate drug dosage and dispense medication to molecular targets.

Thus far, however, there are no man-made devices which can correct genetic mutations by cutting and pasting DNA at the 2-nanometer scale. One of the greatest obstacles to their development, Batt said, doesn't lie in building the devices, but in powering them. Once the right energy sources are identified and channeled, we'll have a technology that speaks the language of genomics and proteomics, and decodes that language into narratives we can understand. *–Carl A. Batt*

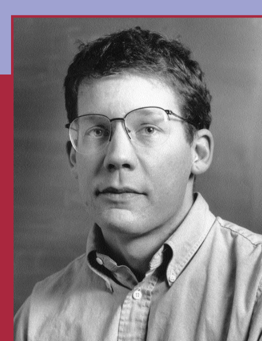
**Microbiologist Carl A. Batt is Professor of Food Science at Cornell University and Co-Director of the Nanobiotechnology Center, an NSF-supported Science and Technology Center. He also runs a laboratory that works in partnership with the Ludwig Institute for Cancer Research.**

crossed nanowire structures containing multiple active cross points has led to the bottom-up organization of OR, AND, and NOR logic gates, where the key integration did not depend on lithography (3, Figure). Moreover, we have shown that these nanologic gates can be interconnected to form circuits and, thereby, carry out primitive computation.

These and related advances have created tremendous excitement in the nanotechnology field. But I believe it is the truly unique characteristics of the bottom-up paradigm, such as enabling completely different function through rational substitution of nanowire building blocks in a common assembly scheme, which ultimately could have the biggest impact in the future. The use of modified nanowire surfaces in a crossed nanowire architecture, for example, has recently led to the creation of nanoscale nonvolatile random access memory, where each cross point functions as an independently addressable memory element with a potential for integration at the 1012/cm2 level.

In a completely different area, we have shown that nanowires can serve as nearly universal electrically based detectors of chemical and biological species with the potential to impact research in biology, medical diagnostics and chem/biowarfare detection. Lastly, and to further highlight this potential, we have shown that nanoscale light-emitting diode arrays with colors spanning the ultraviolet to near-infrared region of the electromagnetic spectrum can be directly assembled from emissive electron doped binary and ternary semiconductor nanowires crossed with nonemissive hole doped silicon nanowires (3, Figure). These nanoscale light-emitting diodes can excite emissive molecules for sensing or might be used as single photon sources in quantum communications.

The bottom line – focusing on the diverse science at the nanoscale will provide the basis for enabling truly unique technologies in the future. *–Charles M. Lieber*



**Dr. Charles M. Lieber moved to Harvard University in 1991 as a Professor of Chemistry and now holds a joint appointment in the Department of Chemistry and Chemical Biology, where he holds the Mark Hyman Chair of Chemistry, and the Division of Engineering and Applied Sciences. He is the principal inventor on more than 15 patents and recently founded a nanotechnology company, NanoSys, Inc.**