retrieval process? Both microbiological studies took careful measures to avoid such contamination. Second, do the cells originate from the liquid water of Lake Vostok, or have they arrived in the ice by some alternative transport mechanism? A variety of microorganisms have been isolated from the overlying glacier ice at Vostok (*6*), and the DNA analysis by Priscu *et al.* shows that the microbiota in the deep ice are related to temperate latitude strains. These observations might suggest that the organisms originated in the glacier ice above. The work by Jouzel *et al.*, however, shows that the ice core sections analyzed by Priscu *et al.* and Karl *et al.* are derived from the lake and that their biological and chemical contents are likely to reflect those of the underlying water. Finally, given that the lake contains viable bacteria and organic carbon, are such cells active in the cold, hyperbaric, nutrient-poor, and possibly anoxic conditions that characterize this environment? Definitive answers to all of these questions will require direct sampling of the Lake Vostok water column, but therein lies a new set of problems.

At the 23rd consultative meeting of the Antarctic Treaty in May 1999, Russia tabled a comprehensive environmental statement on the Vostok operations and highlighted a number of reasons for concern (*7*). The drill hole—which does not yet reach the liquid water level of the lake—has been kept open by the addition of drilling fluid, a mixture of aviation fuel and freons. Some 60 tons of this fluid now resides in the hole, and about 1 ton is located in the drilled lake-ice section. The report notes that the quantity of drilling fluid is too large to be removed, recycled, stored above ground, or transported away from the site. It should not, however, be allowed to penetrate into Lake Vostok, where it would pollute one of the last remaining pristine bodies of water on this planet. Calculations show that materials released into the Lake Vostok water column could circulate to the bottom of the lake within days and throughout the entire lake basin within decades (*8*). Biological and chemical contamination are major issues of concern in penetrating the waters of Lake Vostok and are the focus of ongoing international debate and discussion. They are also an issue for sampling ice and water in places beyond Earth.

Interest in Lake Vostok has been especially intense within the astrobiology community. The discovery of ice-water environments on Jupiter's moons Europa and Callisto has raised many questions about their aqueous geochemistry and potential for life (*9*), and Lake Vostok has been seen as an attractive sampling analog for these more extreme environments (*10*). Despite some similarities, however, there are also radical differences in many properties, including chemical composition (*11*), and biological parallels are unlikely. Irrespective of these differences, future exploration will require special efforts to minimize the human footprint on the pristine ice and water environments of Antarctica and elsewhere throughout our solar system.

References

1. A. P. Kapitsa, J. K. Ridley, G. de Q. Robin, M. J. Siegert, I. A. Zotikov, *Nature* **381**, 684 (1996); J. A. Dowdeswell, and M. J. Siegert *Geol. Soc. Am. Bull.* **111**, 254 (1999).
2. W. F. Vincent, *Microbial Ecosystems of Antarctica* (Cambridge University Press, UK, 1988); E. I. Friedmann, Ed., *Antarctic Microbiology* (Wiley-Liss, NY, 1993).
3. J. Jouzel *et al.*, *Science* **286**, 2138 (1999).
4. J. C. Priscu *et al.*, *Science* **286**, 2141 (1999).
5. D. M. Karl *et al.*, *Science* **286**, 2144 (1999).
6. S. S. Abyzov, in *Antarctic Microbiology*, E. I. Friedmann, Ed. (Wiley-Liss, New York, 1993), pp. 265–295.
7. Russia, Submission to the Antarctic Treaty XXIII Consultative Meeting, IP73 (1999).
8. A. Wüest and E. Carmack, submitted to *Ocean Modelling.*
9. J. Hiscox, *Astron. Geophys.* **40**, 22 (1999).
10. R. Stone, *Science* **286**, 36 (1999); M. J. Siegert, *Am. Sci.* **87**, 510 (1999).
11. K. K. Khurana *et al.*, *Nature* **395**, 777 (1998); R. W. Carlson *et al.*, *Science* **283**, 2062 (1999).

PERSPECTIVES: NANOTECHNOLOGY

Tweezers for the Nanotool Kit

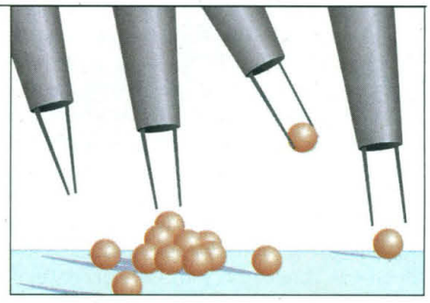
Chad A. Mirkin

Advances in scanning probe techniques have revolutionized the field of nanotechnology. But for the full potential of nanotechnology to be realized, these techniques must be complemented by analogs for macroscopic tools—such as tweezers, pipettes, and pens. On page 2148, Kim and Lieber (*1*) describe such a tool—"nanotube nanotweezers"—which could become an integral part of the nanotechnologist's tool kit for manipulating structures with nanoscopic dimensions.

Many advances—such as the invention of the electron microscope, the development of molecular recognition and self-assembly principles, and the prognostications of visionary scientists like Richard Feynman—contributed to the establishment of nanotechnology as a discipline. But it was undoubtedly the invention of the scanning tunneling microscope (STM) (*2*) and its variants, such as atomic force microscopy (AFM), that catalyzed the explosion of research interest in this field over the past decade. And all signs point to it as one of the biggest growth areas in science and engineering for the next quarter century.

One only has to consider the evolution of the microelectronics industry over the past few decades to understand the payoffs associated with miniaturization. But if we can learn how to routinely prepare and manipulate structures on the nanometer length scale, the resulting future technological advances could make the engineering accomplishments in the trillion dollar microelectronics industry appear trivial. Nanostructures can be exploited in medicine and biology [for example, in medical diagnostics (*3*), ultra-high-density gene chips, and the surface engineering of biocompatible materials], in the further miniaturization of electronic circuitry, in organic devices with molecular components, and in catalysts with highly tailored properties based on catalyst component placement on the nanoscopic scale.

All advances in this field will continue to rely on the development of new analytical tools for making, manipulating, and probing structures on the nanometer length scale. Commercial or custom-built scanning probe microscopes, now to be found in virtually every major research institution in the world, allow one to make electrical measurements across nanoscopic objects (*4*), measure the forces between molecules (*5*, *6*), and probe, push, and manipulate matter on the atomic length scale (*7*). Furthermore, in multiple probe-tip instruments, each tip can be run independently and in parallel fashion (*8*). These advances are paving the way to high-throughput AFM- and STM-based lithographic processing of solid-state materials and are beginning to overcome



How to grab nanoscale objects. This sketch shows how tweezers composed of carbon nanotubes can grab a particle only about 500 nm in diameter (**left**) and move it to a desired location (**right**).

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one of the major limitations associated with single-tip instruments that operate in serial fashion—namely, prohibitive processing times. In addition, these instruments can now operate over substrate areas on the centimeter scale typically associated with lower resolution conventional lithographic methods. Scanning probe lithographies are also being developed for soft (organic) materials, paving the way to devices that use small collections of, or even individual, organic molecules as electronic components. One of the most powerful and promising lithographic methods of this type is dip pen nanolithography (DPN), which uses an AFM as a pen to transport molecule-based inks directly to a substrate (*9*). The direct-write capabilities of DPN and its compatibility with soft materials set it apart from virtually all other scanning probe lithographies, allowing one to pattern multiple chemical components onto a substrate with a current spatial resolution limit of 5 nm.

Collectively, these scanning probe advances allow researchers to fabricate extraordinary structures on a time scale that could enable their transition from research curiosities to commercial processing tools. But absent from this nanotechnology tool kit are analogs to many tools in our macroscopic kits. For example, single, or even multiple-tip scanning probe instruments cannot be used to tweeze or grab nanoscale objects. This is why the advance reported by Kim and Lieber is important. To demonstrate the concept of tweezing on the nanoscopic scale (see the figure) they first patterned a glass pipette probe with two electrodes on opposite sides of the probe and then attached a carbon nanotube to each of the electrodes. Kim and Lieber took advantage of the mechanical toughness and electrical conductivity of the carbon nanotubes to miniaturize a previously demonstrated microscopic phenomenon (*10*), namely that application of an appropriate bias voltage across two tweezer arms can effect a mechanical change in the two arms that results in their pinching together. Removal of the applied voltage relaxes the tweezers but does not open them because of van der Waals interactions between the carbon nanotubes. Application of the appropriate bias voltage reopens the tweezers. The previously demonstrated micrometer-scale tweezers operated at large actuating voltages (45 to 150 V depending on arm composition and size). Besides being substantially smaller and offering the potential for further miniaturization through the use of smaller bundles of single-walled nanotubes, the nanotweezers operate at substantially lower actuating voltages (8.5 V).

Lieber and Kim have demonstrated that their tweezers can be used to grab and manipulate mesoscopic clusters and spheres and even gallium arsenide nanowires. In addition, because the tweezer arms are also individually addressable electrodes, there is the tantalizing prospect of transforming this technology into a two-probe STM device, which could enable electrical measurements over features separated by relatively short distances (*11*). The ability of the nanotweezers to grasp and physically extract a nanoscale component from a complex mixture and then make an electrical measurement across it could make them a valuable analytical tool for studying the intrinsic electrical properties of the components of heterogeneous materials and nanoscale devices. Many other applications for the nanotweezers are within the realm of possibility, including its use in manipulating biological structures on surfaces or even within cells.

Further miniaturization of the device is desirable such that even smaller structures can be picked up and manipulated. Suppression of nonspecific adsorption on the tweezer arms would also substantially improve the concept. Nevertheless, this is a powerful demonstration and an important step toward the development of a useful new tool for the nanotechnologist.

References and Notes

1. P. Kim and C. M. Lieber, *Science* **286**, 2148 (1999).
2. G. Binnig, H. Rohrer, C. Gerber, E. Weibel, *Phys. Rev. Lett.* **49**, 57 (1982).
3. J. J. Storhoff *et al.*, *J. Am. Chem. Soc.* **120**, 1959 (1998).
4. S. Datta *et al.*, *Phys. Rev. Lett.* **79**, 2530 (1997).
5. A. Noy *et al.*, *Chem. Biol.* **4**, 519 (1997).
6. G. U. Lee, L. A. Chrisey, R. J. Colton, *Science* **266**, 771 (1994).
7. M. R. Falvo *et al.*, *Nature* **397**, 236 (1999).
8. S. C. Minne *et al.*, *Appl. Phys. Lett.* **73**, 1742 (1998).
9. S. Hong, J. Zhu, C. A. Mirkin, *Science* **286**, 523 (1999).
10. J. J. Yao and N. C. MacDonald, *Scanning Microsc.* **6**, 937 (1992).
11. A fixed two-probe device has already been demonstrated [S. Tsukamoto, B. Siu, N. Nakagiri, *Rev. Sci. Instrum.* **62**, 1767 (1991)].
12. S. Hong is acknowledged for helpful comments.

PERSPECTIVES: CANCER

Structural Assets of a Tumor Suppressor

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Inactivation of tumor suppressor genes is one way in which cancer cells circumvent normal growth control. Mutations in the stretch of DNA at q23 on chromosome 10 are among the most commonly observed in human cancer and are particularly prevalent in glioblastomas, advanced prostate cancers, and endometrial carcinomas. Early in 1997, two groups reported the discovery of a new tumor suppressor gene at this locus, which they called *PTEN* (Phosphatase and Tensin homolog deleted on chromosome Ten) or *MMAC* (Mutated in Multiple Advanced Cancers) (*1*, *2*). Mutations in *PTEN* are also recognized as the cause of cancer predisposition syndromes, such as Cowden disease (characterized by an increased risk of breast cancer). Since this discovery, rapid progress has been made in characterizing the PTEN protein and its role in regulating the signaling events that control cell proliferation and survival. The latest chapter in this story, published by Pavletich's group in a recent issue of *Cell* (*3*), describes the crystal structure of the PTEN protein and sheds new light on how this phosphatase is regulated.

PTEN contains the signature motif that defines the protein tyrosine phosphatase (PTP) family of enzymes, which remove phosphate groups from other proteins. It was originally described as a dual-specificity phosphatase, that is, it recognizes proteins phosphorylated on tyrosine and on serine/threonine residues. Curiously, PTEN also displays a very unusual specificity for highly acidic substrates (*4*). Insights into the identity of its physiological substrates came with the observation that PTEN has the capacity to dephosphorylate (remove phosphate groups from) inositol phospholipids such as PIP_3 (phosphatidylinositol-3,4,5, P_3). These molecules are crucial secondary messengers in signaling pathways that control proliferation and survival (*5*). A substantial body of data from studies involving disruption of PTEN in mice and in the worm *Caenorhabditis elegans*, together with expression of this phosphatase in tumor cells bearing mutant PTEN alleles, now support the conclusion that PTEN is a lipid phosphatase in vivo (*6*).

The structure of PTEN described by Pavletich's group (*3*) reveals the same overall fold as observed for both phosphotyrosine-specific and dual-specificity phosphatases. However, its active-site cleft is twice as wide as, but of similar depth to, the phosphotyrosine-specific enzymes and both wider and deeper than that of the dual-specificity phosphatases. In addition, the signature motif of PTEN displays a uniquely basic character. Although they do not present the structure of PTEN bound to

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References and Notes

[1] **Nanotube Nanotweezers**
Philip Kim; Charles M. Lieber
Science, New Series, Vol. 286, No. 5447. (Dec. 10, 1999), pp. 2148-2150.
Stable URL:
http://links.jstor.org/sici?sici=0036-8075%2819991210%293%3A286%3A5447%3C2148%3ANN%3E2.0.CO%3B2-V

[6] **Direct Measurement of the Forces Between Complementary Strands of DNA**
Gil U. Lee; Linda A. Chrisey; Richard J. Colton
Science, New Series, Vol. 266, No. 5186. (Nov. 4, 1994), pp. 771-773.
Stable URL:
http://links.jstor.org/sici?sici=0036-8075%2819941104%293%3A266%3A5186%3C771%3ADMOTFB%3E2.0.CO%3B2-L

[9] **Multiple Ink Nanolithography: Toward a Multiple-Pen Nano-Plotter**
Seunghun Hong; Jin Zhu; Chad A. Mirkin
Science, New Series, Vol. 286, No. 5439. (Oct. 15, 1999), pp. 523-525.
Stable URL:
http://links.jstor.org/sici?sici=0036-8075%2819991015%293%3A286%3A5439%3C523%3AMINTAM%3E2.0.CO%3B2-3