ELECTRONICS

Nanotube computer scaled up

Electronic devices that are based on carbon nanotubes have the potential to be more energy efficient than their silicon counterparts, but have been restricted in functionality. This limitation has now been overcome. SEE ARTICLE P.595

FRANZ KREUPL

For many decades, progress in electronics has been driven by a gradual reduction in the size of silicon transistors (electronic switches). However, this scaling is becoming increasingly difficult and is now yielding diminishing returns. Transistors based on semiconducting carbon nanotubes are clear front runners as replacements for silicon transistors in advanced microelectronic devices. But imperfections inherent in carbon nanotubes, and challenges in handling these tiny objects, have prevented their use in real-world microelectronic applications. On page 595, Hills *et al.*[1] report a major advance in this field: a 16-bit computer that is built entirely from carbon-nanotube transistors.

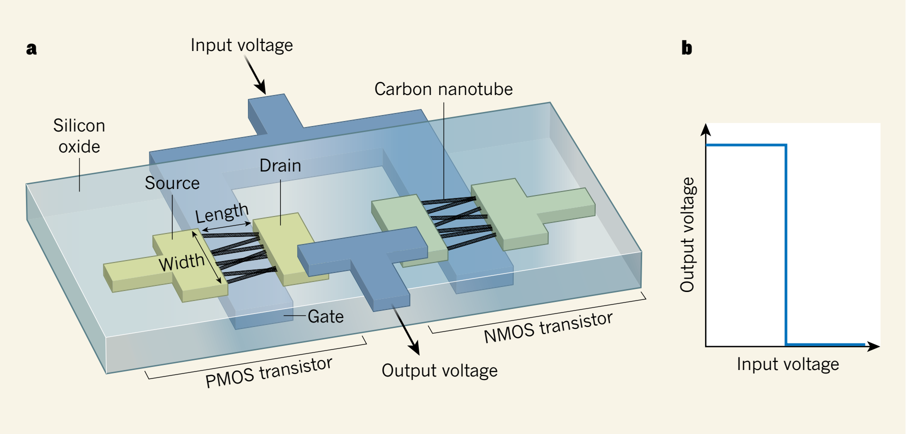

Figure 1 | A carbon-nanotube inverter. a, Hills *et al.*[1] demonstrate a computer that uses basic elements called inverters. Each of these inverters contains two kinds of transistor (electronic switch): a p-type metal–oxide–semiconductor (PMOS) transistor and an n-type metal–oxide–semiconductor (NMOS) transistor. These transistors are interconnected in series and are formed on a silicon oxide substrate. Each transistor consists of three electrodes known as the source, the gate and the drain; the source and the drain are separated by a channel that is formed of semiconducting carbon nanotubes. The micrometre-scale width and length of a channel are indicated. **b,** If a low voltage is applied to the inverter, the output voltage will be high, and vice versa.

To achieve this milestone, the authors needed to develop a viable nanotube-transistor technology that provides two kinds of transistor: p-type metal–oxide–semiconductor (PMOS) and n-type metal–oxide–semiconductor (NMOS). In digital electronics, a computation is divided into a sequence of elementary (logic) operations that are carried out by components called logic circuits. The present design of these circuits in the electronics industry is based on complementary metal–oxide–semiconductor (CMOS) technology, which requires both PMOS and NMOS transistors.

A PMOS (or NMOS) transistor is switched on when a negative (or positive) voltage is applied to an electrode known as the gate. This electrode controls the conductivity of the channel (in this case, formed by carbon nanotubes) between two other electrodes (the source and the drain). When a PMOS transistor and an NMOS transistor are interconnected in series, the result is an element called an inverter (Fig. 1). If a low voltage is applied to such an inverter, the output voltage will be high, and vice versa. This element is the basic ingredient of all the logic circuits used in Hills and colleagues' computer.

The authors made their transistors by forming a network of randomly distributed, high-purity (99.99%) semiconducting nanotubes on a substrate. The formation process resembles pouring a bowl of cooked spaghetti onto a surface and then removing all the strands that are not in direct contact with the surface. The result is a substrate covered with roughly a single-layer of randomly oriented nanotubes.

Hills *et al.* then deposited metal on the nanotubes to connect them to the source and the drain. The work function of this metal (the energy needed to remove an electron from its surface) depended on whether the device was a PMOS or an NMOS transistor. The authors covered the rest of each nanotube with carefully selected and trimmed oxide materials, to isolate the nanotubes from their surroundings and to adjust their properties. In principle, the substrate does not need to be made of silicon; it simply needs to be flat. Moreover, the processing happens at relatively low temperatures (about 200–325 °C), so that stacking of further functional layers would easily be possible.

Contemporary computer design is based on libraries of standard cells — sets of logic operations that can be interconnected for greater functionality. Hills and colleagues devised all the standard cells required to make their computer's architecture using commercially available, conventional design tools. Because the semiconducting nanotubes had a purity of 99.99%, about 0.01% of them were metallic (non-semiconducting) and could have jeopardized the circuits. However, certain combinations of standard cells are more vulnerable to the presence of metallic nanotubes than are others. The authors therefore enforced modified design rules that excluded such vulnerable combinations. Equipped with these tools, they were able to design, fabricate and test their computer by letting it execute 'Hello, World' — a simple program that outputs the message "Hello, World" when run.

Hills and colleagues' nanotube computer is based on CMOS technology, runs 32-bit instructions on 16-bit data and has a transistor-channel length of roughly 1.5 micrometres. It can therefore be compared to the silicon-based Intel 80386 processor, which was introduced in 1985 and had similar specifications. The early 80386 could process its instructions at a frequency of 16 megahertz (see go.nature.com/33clr1a), whereas the nanotube computer has a maximum processing frequency of about 1 MHz. The reason for this difference lies in the capacitances (charge-storage abilities) of the electronic components, and in the amount of current that the smallest transistor can deliver.

Digital logic simply involves charging and discharging the transistor gates and the interconnects. The speed of charging and discharging depends on the amount of current that a transistor can provide, which is related to the width and length of the transistor. A well-designed silicon transistor can deliver roughly one milliampere of current per micrometre of width ($1\,\mathrm{mA}\,\mu\mathrm{m}^{-1}$) (see go.nature.com/2z4wjda). By contrast, the typical nanotube transistors used by Hills *et al.* can provide only about $6\,\mu\mathrm{A}\,\mu\mathrm{m}^{-1}$. This is the main feature that will need improvement in future versions of the computer.

The first step for increasing the electric current is to reduce the transistor-channel length. It has already been demonstrated[2] that the channel lengths of nanotube transistors can be scaled down to 5 nm. The second step is to increase the density of nanotubes in each channel from as little as 10 nanotubes per micrometre to 500 nanotubes per micrometre. For these networks of randomly distributed nanotubes, there might be an upper limit on the achievable density, but a deposition technique has been shown[3] to boost the current in such networks to $1.7\,\mathrm{mA}\,\mu\mathrm{m}^{-1}$. The third step is to decrease the width of the transistors, and thereby the widths of the source and the drain, which would allow these electrodes to be charged and discharged more quickly[4]. These scaled-down transistors are essential for nanotube-based CMOS technology that operates at gigahertz frequencies[5].

Hills and colleagues' achievement is based on averaging the performances of several nanotubes in each transistor channel. In the large-scale nanotube computer of the distant future, the PMOS and NMOS transistors will contain only one nanotube. These nanotubes will need to be semiconducting: no design trick will provide a workaround if one of the two nanotubes in an inverter is metallic.

The authors' work is a great accomplishment that touches on many research topics — from materials science to processing technology, and from circuit design to electrical testing. However, more effort is required before the team will need a sales department. ■

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TUMOUR BIOLOGY

Cells tagged near an early spread of cancer

Cancer cells that travel to a distant site can prompt the normal neighbouring cells at that location to create a tumour-promoting microenvironment. A tool that identifies these normal cells offers a way to study this process. SEE ARTICLE P.603

MARIE-LIESSE ASSELIN-LABAT

Most types of cancer are lethal after tumour cells have left their primary site of growth and moved to colonize a distant organ through a process termed metastasis. Whether a cancer cell will metastasize is determined not only by the cell itself, but also by the microenvironment of that faraway site called the metastatic niche[1]. Only a small number of the cells that reach such a new location will successfully establish a presence there and proliferate[2]. The early processes that aid cancer-cell growth at secondary locations remain poorly understood, partly because of a scarcity of suitable tools with which to analyse these events. On page 603, Ombrato *et al.*[3] describe an innovative *in vivo* method for identifying and isolating the rare normal cells that are in close contact with cancer cells that have just migrated to a secondary site. This approach should help to clarify the early direct interactions between metastatic cells and neighbouring normal cells that help to shape the formation of a metastatic niche.

Ombrato and colleagues engineered mouse breast cancer cells to express a fluorescent protein containing a region of amino-acid residues that make it permeable to lipids (Fig. 1); this feature enabled the protein to be released from the cancer cell in a soluble form that could be taken up by neighbouring cells. The authors studied a model of metastasis in which mouse breast cancer cells that expressed this protein, plus a different fluorescent protein that could be used to specifically monitor cancer cells, were injected into the mouse tail vein and subsequently colonized the lung.

Analysis of lung tissue revealed that healthy cells located within a distance of five cell layers from cancer cells took up the protein, enabling the specific analysis of healthy cells in close contact with an emerging site of tumour growth. Ombrato *et al.* noted a direct correlation between the number of cancer cells in the lung and the number of neighbouring cells that took up the protein. These neighbouring cells included immune cells, which are known[4] to aid the colonization of the lung by breast cancer cells.

Previous studies have used other techniques to identify cells in the vicinity of malignant tumours, by, for example, tagging the cells that specifically receive vesicles released from tumour cells[5]. The advantage of Ombrato and colleagues' technique is that it offers a way to tag probably any type of cell present in the vicinity of a metastatic site.

The lipid-permeable fluorescent protein is

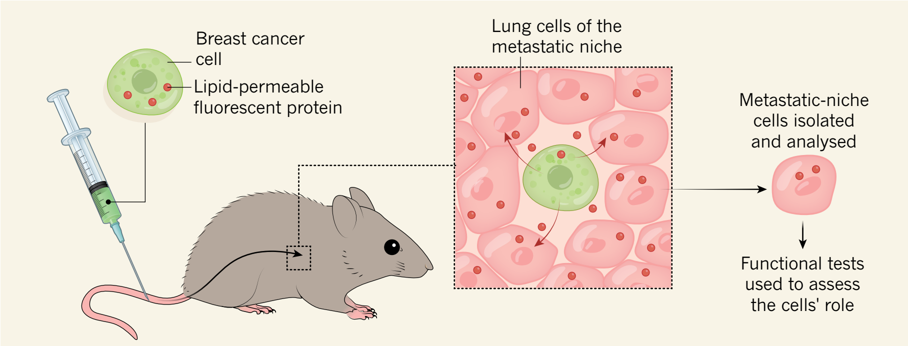

Figure 1 | A tool for identifying healthy cells in the vicinity of cancer cells. Ombrato *et al.*[3] engineered a fluorescent protein to contain amino-acid residues conferring lipid permeability, which enables the protein to enter cells. The authors engineered mouse breast cancer cells to express this protein, and injected the cells into the tail veins of mice. The cancer cells then colonized lung tissue at a site that is termed a metastatic niche. The fluorescent protein released there from tumour cells was taken up by the neighbouring healthy lung cells. The authors carried out direct *in situ* analysis, using approaches such as microscopy, to assess these healthy cells of the metastatic niche. The lung tissue was then removed, and the presence of the lipid-permeable fluorescent protein permitted the isolation and molecular characterization of these cells. This information allowed the authors to carry out functional tests *in vitro* to study how this type of healthy cell affects tumour growth.