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15 January 2004

Nanowires track down mutants

Ultra-sensitive, rapid and direct detection of DNA is needed for efficient genetic screening. A device made from a silicon nanowire might have what it takes.

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A nanowire electronic device that can detect specific sequences in DNA in real-time with unprecedented sensitivity might enable instant or high-throughput genetic screening.

The device exploits a change in the conductivity of a silicon nanowire induced by binding of DNA at recognition sites on its surface. Jong-in Hahm and Charles Lieber of Harvard University in Cambridge, Massachusetts, have demonstrated[1] the detector by distinguishing between a wild-type ('normal') DNA sequence and a mutation of the sequence associated with cystic fibrosis, at concentrations down to 10 femtomolar (10^{-15} M).

It's not the first use of nanowires or nanotubes for detection of biological molecules. In earlier reports, for example, carbon nanotubes functionalized with binding sites were used as sensors for proteins[2,3]. The sensitivity of such systems results from the fact that binding of a molecule on a nanowire surface can alter the distribution of charge carriers in the wire sufficiently to be 'felt' across the entire cross-sectional conduction pathway.

This kind of detection strategy contrasts with traditional DNA detection methods, many of which involve some form of labelling to signal a binding event. For example, fluorescently labelled DNA may be bound to complementary single strands localized at specific sites in a detection array. The device developed by Hahm and Lieber[1], in contrast, requires no labelling and works more or less instantly.

The researchers grow silicon nanowires about 20 nm wide using chemical

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vapour deposition onto catalytic gold nanoparticles. To make a device, a nanowire is simply deposited onto a surface and electrical contacts are fabricated at each end by electron-beam lithography.

The molecular-recognition elements on the nanowire surface consist of peptide nucleic acid (PNA) groups bound by biotin linkers to avidin proteins attached to the wire (avidin binds biotin very tightly). PNA is a hybrid of a nucleic acid and a peptide, in which the peptide replaces the sugar-phosphate backbone of DNA. It is capable of binding a complementary-DNA strand with high affinity and stability.

Hahm and Lieber used PNA oligomers with a 10-base sequence complementary to that which spans the so-called ΔF508 mutation region of the gene for the cystic fibrosis transmembrane receptor protein. This mutation of the wild-type gene — three missing bases, corresponding to the absence of the 508th codon of the gene — is responsible for three in four of all incidences of cystic fibrosis. The ability to detect it rapidly in DNA samples could greatly facilitate genetic screening of embryos at risk of developing the disease.

The PNA probes contained the full sequence, and so were able to bind wild-type DNA sequences; the presence of the ΔF508 mutation prevented specific binding. When the functionalized nanowire device was exposed to wild-type DNA, there was an abrupt (around 10 s), roughly twofold increase in conductance through the wire. Hahm and Lieber reason that this is consistent with the binding of negatively charged DNA, and thus an increase in negative surface charge density, at the surface of the p-type (hole-conducting) semiconducting nanowire.

However, exposure of the device to mutant DNA also leads to a similar change in conductance, owing to non-specific binding of the DNA. But this does not prevent the two types of DNA from being distinguishable. Whereas mutant DNA can be easily removed from the nanowire surface by washing with DNA-free solution, reversing the conductance change, wild-type DNA becomes securely bound to the PNA receptors and cannot be removed.

The researchers find that wild-type DNA produces a clear, long-term conductance change, even at concentrations as low as 10 femtomolar. They think that the sensitivity could be improved still further, for example by varying the concentration of dopants in the wires (their p-type silicon nanowires contained small quantities of boron). Moreover, they found very similar behaviour for two different nanowire devices, showing that the response is reproducible.

References

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