'Electronic' DNA sequencing: Changes in molecular charge act as signal

March 14 2006

Sometimes it is only individual base pairs that differentiate a diseased gene from a healthy one (point mutations). The systematic exploration of such variations, as well as the diagnosis of genetic diseases, require the simplest, most cost-effective and rapid sequencing methods possible.

Japanese researchers have now developed a new approach for a miniaturized “electronic” process that detects small differences in DNA sequences with high sensitivity. In contrast to prior methods, this technique works without labeling of the bases. It is based on a special semiconducting element called a field effect transistor (FET), which detects changes in the charges on DNA molecules.

The sequencing method developed by Toshiya Sakata and Yuji Miyahara uses a chip with multiple FETs. An FET is a semiconductor component that “feels” electrical fields on its surface. It reacts to changes in the field with a change in the current that flows through its conducting channel. The researchers loaded the surface of such an FET with short, single-stranded pieces of DNA. These probes are the exact counterparts to the sequence at the beginning of the DNA segment being investigated. If a sample containing the target DNA comes into contact with the surface, the target DNA binds to the probes.

The enzyme polymerase could then be used to complete the probe to a complete counterpart of the target DNA, if the four necessary building blocks— the nucleosides adenosine, cytidine, thymidine, and guanosine (A, C, T, and G)—were present in the solution. This is where the special

trick comes in: the chip is dipped alternately into four different solutions, each containing only one of the building blocks. After each dip, the electrical characteristics of the FET are measured.

If and only if a component has been added to the end of the chain, a change is registered. This occurs because each building block brings with it a negative charge, which changes the electrical field on the surface of the FET. In this way, DNA chains of a length up to about ten components can be precisely sequenced. Missing, extra, or changed nucleotides can be rapidly and unambiguously identified.

As electrical signals are measured, this method can easily be standardized. Miniature arrays containing multiple FETs with different probes allow for the parallel analysis of different gene segments.

Source: Angewandte Chemie