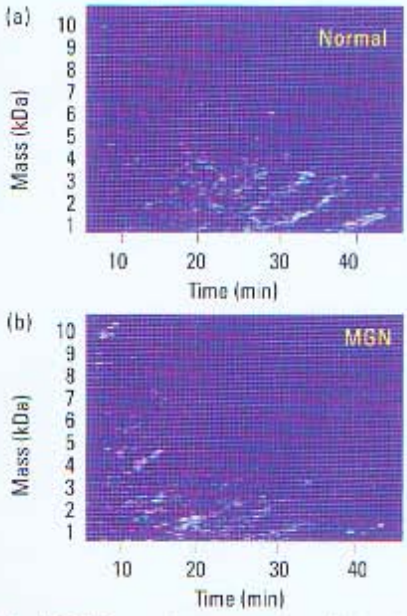
ANALYTICAL CURRENTS

SELDI/MS or CE/MS?

Instead of relying on the presence or absence of one biomarker in a body fluid to indicate disease, researchers are turning to proteomics methods, such as surface-enhanced laser desorption/ionization (SELDI)/MS and CE/MS, to follow multiple biomarkers. To determine which method yields the better discriminatory protein patterns, Harald Mischak and colleagues at Medizinische Hochschule Hannover and Mosaiques Diagnostics and Therapeutics AG (both in Germany) and at the University of Glasgow and the Beatson Institute for Cancer Research (both in the U.K.) compared SELDI/MS and CE electrospray ionization TOF MS head-to-head. They analyzed urine samples from healthy individuals and patients with the kidney disorder membranous glomerulonephritis (MGN).

After extensive analysis of the CE/MS data, the researchers found 200 proteins that were unique to the MGN patients. In comparison, when they tested the same samples using SELDI/MS with a weak cation exchange chip, which primarily binds proteins with high isoelectric point (pI) values, they found only three potential biomarkers for MGN.

SELDI/MS produced spectra of lower resolution and complexity than CE/MS, which the researchers attribute to the selective retention on the SELDI chip. Because only those proteins with high pI were retained, the pool of proteins that were ultimately analyzed was greatly reduced. (*Rapid Commun. Mass Spectrom.* **2004**, *18*, 149–156)

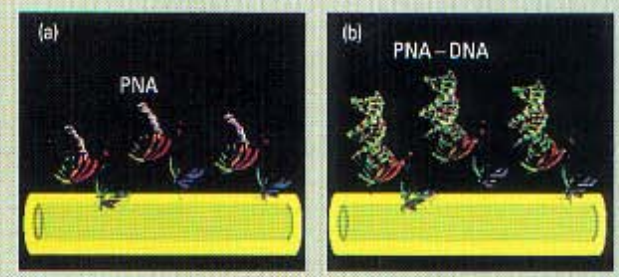


Typical CE/MS protein patterns from (a) healthy individuals or (b) MGN patients. (Adapted with permission. Copyright 2003 John Wiley & Sons, Ltd.)

DNA detection on a wire

By taking advantage of the electrical properties of silicon nanowires (SiNWs) and the intrinsic charge of DNA, researchers have created highly sensitive, label-free DNA detectors. Z. Li and colleagues at Hewlett-Packard report picomolar detection of target DNA with single-stranded DNA probes on SiNW surfaces (*Nano Lett.* **2004**, 10.1021/nl034958e). Pushing the limit even further, Charles M. Lieber and Jong-in Hahm at Harvard University report femtomolar detection of DNA and DNA mismatches using a SiNW sensor modified with peptide nucleic acid (PNA) receptors (*Nano Lett.* **2004**, *4*, 51–54).

PNA receptors are known to bind to DNA with high affinity and stability. Although it should be possible to use other genetic markers of disease, Lieber and Hahm used PNA receptors that can differentiate between wild-type DNA and the ΔF508 mutation in the cystic fibrosis transmembrane receptor gene. Cystic fibrosis is a fatal genetic disease, and detection of the ΔF508 mutation serves as an indicator of the disease.



(a) A silicon nanowire sensor modified with PNA receptors. (b) PNA receptors bind to DNA.

After adding femtomolar levels of wild-type DNA samples, Lieber and Hahm observed a rapid (<10 s) increase in conductance followed by a more gradual increase over hundreds of seconds. The increase is consistent with an increase in negative surface charge associated with the binding of negatively charged oligonucleotides to the surface. They observed no change in conductance when no DNA was added and no substantial long-term change when mutant DNA was introduced.

Likewise, Li and colleagues observed an increase in conductance following the binding of complementary DNA to their receptor probe. For a 12-mer oligonucleotide probe, they were able to easily detect 25 pM of target DNA. They observed no change in conductance in control experiments with noncomplementary DNA with a single-base mismatch.

The new real-time SiNW sensors could be the first step toward real-time, high-throughput, multiplexed DNA analysis for applications such as biowarfare detection and screening for genetic diseases.