ANALYTICAL CURRENTS

Micromachined nano-ESI

Electrospray ionization devices for MS encounter problems when they are applied at the extremely low flow rates typical in microfluidic devices. Two approaches are being used to implement nano-electrospray ionization (nESI) on chips: laborious addition of pre-made capillary tips or micromachining tips during chip fabrication. Johan Roeraade and colleagues at the Royal Institute of Technology (Sweden) have produced an on-the-chip structure that more closely resembles a capillary than previous micromachined structures. Previous attempts to form tips on the chip have often resulted in larger-diameter structures than pulled capillaries, and they exhibited more deposit formation than capillaries.

Roeraade and colleagues used silicon-etching techniques such as deep reactive ion etching to create a silicon dioxide tip. The tip resembles a capillary and is 70 μm high, the tip orifice is 10 μm in diameter, and the walls of the tube are 1.5 μm thick.

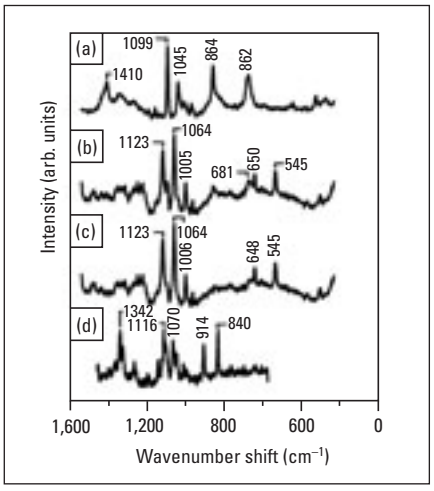
The micromachined tips produced higher peak intensities than added capillary tips but slightly lower S/N. However, the reproducibility of S/N proved to be better than with capillary tips, and the researchers say that micromachining can make even smaller-diameter tips, allowing smaller sample consumption. The researchers see this as a strong complement to MALDI-TOFMS for high-throughput studies of proteomics and drug screening. (*Rapid Commun. Mass Spectrom.* **2003,** *17,* 337–341)

Figure Not Available for Use on the Web

Scanning electron microscope image of micromachined ESI tip. (Adapted with permission. Copyright 2003 John Wiley & Sons, Ltd.)

SERS glucose biosensor

Richard Van Duyne and co-workers at Northwestern University may be a step closer to helping diabetic patients measure glucose levels faster and easier without painful blood sampling. They report the first systematic study of using a biosensor for direct detection of glucose by partitioning glucose onto a silver film substrate, followed by surface-enhanced Raman spectroscopy (SERS) and chemometric data analysis.



(a) 1-DT monolayer on AgFON substrate (λ_{ex} = 532 nm); (b) mixture of 1-DT monolayer and glucose partitioned from a 100 mM solution (λ_{ex} = 532 nm); (c) residual glucose spectrum produced by subtracting (a) from (b); (d) normal Raman spectrum of crystalline glucose for comparison (λ_{ex} = 632.8 nm).

The National Institutes of Health estimate that 17 million people in the United States have diabetes mellitus (types I and II). Most of them measure their glucose levels by withdrawing small samples of blood using a "finger-stick" approach, followed by indirect electrochemical detection of hydrogen peroxide produced by enzymatic oxidation of glucose by glucose oxidase.

SERS detection offers a less-invasive way to measure glucose levels, but glucose has a small normal Raman cross-section and adsorbs weakly—or not at all—to bare silver surfaces. Van Duyne and his team overcame these problems by partitioning glucose into an alkanethiolin monolayer—in this case, 1-decanethiol (1-DT)—that is adsorbed onto a silver film over a nanosphere surface (AgFON), thus preconcentrating the glucose. The glucose now sits within the zone of electromagnetic field enhancement, and a clear SERS spectrum is observed with only 30 s of acquisition time. Using leave-one-out, partial least-squares analysis, the researchers successfully detected glucose over a clinically relevant range of 0–25 mM.

Van Duyne's group is exploring using SERS with near-IR excitation (700–1200 nm), which is a spectral range where skin absorption is minimal. The SERS substrate can be built into a microscale or nanoscale device that can be either implanted underneath the skin or incorporated into a prosthetic lens in the eyes of diabetic patients. (*J. Am. Chem. Soc.* **2003,** *125,* 588–593)