

cells from other regions. In the case of suspension cells, harvesting is performed upon the infusion of fresh nutrient medium. Incorporated into the miniature culture system is a temperature-control system and gas-control loop. The inclusion of these two systems will enable the miniature culture system to be autonomous.

*This work was done by Steve R. Gonda of Johnson Space Center and Stanley J. Kleis and Sandra K. Geffert of the University of Houston.*

*In accordance with Public Law 96-517, the contractor has elected to retain title to this invention. Inquiries concerning rights for its commercial use should be addressed to: Emmanuelle Schuler, Ph.D*

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## **Electrochemical Detection of Multiple Bioprocess Analytes**

**Key analytes can be detected using sample volumes of only 100  $\mu$ L.**

*Lyndon B. Johnson Space Center, Houston, Texas*

An apparatus that includes highly miniaturized thin-film electrochemical sensor array has been demonstrated as a prototype of instruments for simultaneous detection of multiple substances of interest (analytes) and measurement of acidity or alkalinity in bioprocess streams. Measurements of pH and of concentrations of nutrients and wastes in cell-culture media, made by use of these instruments, are to be used as feedback for optimizing the growth of cells or the production of desired substances by the cultured cells. The apparatus is designed to utilize samples of minimal volume so as to minimize any perturbation of monitored processes.

The apparatus can function in a potentiometric mode (for measuring pH), an amperometric mode (detecting analytes via oxidation/reduction reactions), or both. The sensor array is planar and includes multiple thin-film microelectrodes covered with hydrous iridium oxide. The oxide layer on each electrode serves as both a protective and electrochemical transducing layer. In its trans-

ducing role, the oxide provides electrical conductivity for amperometric measurement or pH response for potentiometric measurement. The oxide on an electrode can also serve as a matrix for one or more enzymes that render the electrode sensitive to a specific analyte. In addition to transducing electrodes, the array includes electrodes for potential control. The array can be fabricated by techniques familiar to the microelectronics industry.

The sensor array is housed in a thin-film liquid-flow cell that has a total volume of about 100  $\mu$ L. The flow cell is connected to a computer-controlled subsystem that periodically draws samples from the bioprocess stream to be monitored. Before entering the cell, each 100- $\mu$ L sample is subjected to tangential-flow filtration to remove particles. In the present version of the apparatus, the electrodes are operated under control by a potentiostat and are used to simultaneously measure the pH and the concentration of glucose. It is anticipated that development of procedures

for trapping more enzymes into hydrous iridium oxide (and possibly into other electroactive metal oxides) and of means for imparting long-term stability to the transducer layers should make it possible to monitor concentrations of products of many enzyme reactions — for example, such key bioprocess analytes as amino acids, vitamins, lactose, and acetate.

*This work was done by R. David Rauh of EIC Laboratories, Inc., for Johnson Space Center. Further information is contained in a TSP (see page 1).*

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## **Fabrication and Modification of Nanoporous Silicon Particles**

**Biodegradable drug carriers allow sustained drug release for days or even weeks.**

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Silicon-based nanoporous particles as biodegradable drug carriers are advantageous in permeation, controlled release, and targeting. The use of biodegradable nanoporous silicon and silicon dioxide, with proper surface treatments, allows sustained drug release within the target site over a period of days, or even weeks, due to selective surface coating. A variety of surface treatment protocols are

available for silicon-based particles to be stabilized, functionalized, or modified as required. Coated polyethylene glycol (PEG) chains showed the effective depression of both plasma protein adsorption and cell attachment to the modified surfaces, as well as the advantage of long circulating.

Porous silicon particles are micromachined by lithography. Compared to the

synthesis route of the nanomaterials, the advantages include: (1) the capability to make different shapes, not only spherical particles but also square, rectangular, or ellipse cross sections, etc.; (2) the capability for very precise dimension control; (3) the capacity for porosity and pore profile control; and (4) allowance of complex surface modification. The particle patterns as small as 60 nm can