Cytometer on a Chip

Analyses could be performed rapidly in compact instruments using disposable chips.

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A cytometer now under development exploits spatial sorting of sampled cells on a microarray chip followed by use of grating-coupled surface-plasmon-resonance imaging (GCSPRI) to detect the sorted cells. This cytometer on a chip is a prototype of contemplated future miniature cytometers that would be suitable for rapidly identifying pathogens and other cells of interest in both field and laboratory applications and that would be attractive as alternatives to conventional flow cytometers.

The basic principle of operation of a conventional flow cytometer requires fluorescent labeling of sampled cells, stringent optical alignment of a laser beam with a narrow orifice, and flow of the cells through the orifice, which is subject to clogging. In contrast, the principle of operation of the present cytometer on a chip does not require fluorescent labeling of cells, stringent optical alignment, or flow through a narrow orifice. The basic principle of operation of the cytometer on a chip also reduces the complexity, mass, and power of the associated laser and detection systems, relative to those needed in conventional flow cytometry.

Instead of making cells flow in single file through a narrow flow orifice for sequential interrogation as in conventional flow cytometry, a liquid containing suspended sampled cells is made to flow over the front surface of a microarray chip on which there are many capture spots. Each capture spot is coated with a thin (≈50-nm) layer of gold that is, in turn, coated with antibodies that bind to cell-surface molecules characteristic of the cell species of interest. The multiplicity of capture spots makes it possible to perform rapid, massively parallel analysis of a large cell population.

The binding of cells to each capture spot gives rise to a minute change in the index of refraction at the surface of the chip. This change in the index of refraction is what is sensed in GCSPRI, as described briefly below. The identities of the various species in a sample of cells is spatially encoded in the chip by the pattern of capture spots. The number of cells of a particular species is determined from the magnitude of the GCSPRI signal from that spot.

GCSPRI as used here can be summarized as follows: The cytometer chip is fabricated with a diffraction grating on its front surface. The chip is illuminated with a light emitting diode (LED) from the front. By proper choice of grating parameters and of the wavelength and the angle of incidence of a laser beam, laser light can be made to be coupled into an electromagnetic mode that resonates with surface plasmons and thus couples light into surface plasmons. Coupling of light into a surface plasmon at a given location reduces the amount of incident light reflected from that location. A change in the index of refraction at the surface of a capture spot gives rise to a change in the resonance condition. Depending on the specific design, the change in the index of refraction could manifest itself as a brightening or darkening, a change in the wavelength needed to excite the plasmon at a given angle of incidence, or a change in the angle of incidence needed to excite the plasmon at a given wavelength.

Whereas a multiwavelength laser system with multichannel detection would be needed to detect multiple species in conventional flow cytometry, it suffices to use an LED and a single detector channel in the GCSPRI approach: this contributes significantly to reductions in cost, complexity, size, mass, and power. GCSPRI cytometer chips could be made of plastic and could be mass-produced cheaply by use of molding and other methods adopted from the manufacture of digital video disks. These methods are amenable to a high degree of miniaturization: such additional features as fluidic channels, reaction chambers, and fluid-coupling ports could readily be incorporated into the chips, without incurring substantial additional costs.

This work was done by Salvador M. Fernandez of Ciencia, Inc., for Johnson Space Center. Further information is contained in a TSP (see page 1).

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:

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Principles, Techniques, and Applications of Tissue Microfluidics

This technique can be used in the diagnosis of diseases such as cancer.

NASA's Jet Propulsion Laboratory, Pasadena, CA

The principle of tissue microfluidics and its resultant techniques has been applied to cell analysis. Building microfluidics to suit a particular tissue sample would allow the rapid, reliable, inexpensive, highly parallelized, selective extraction of chosen regions of tissue for purposes of further biochemical analysis. Furthermore, the applicability of the techniques ranges beyond the described pathology application. For example, they would also allow the posing and success-