A microchip has been developed that measures the electrical impedance and optical properties of single particles, such as cells, at the same time. Individual cells flow in a high-speed fluid stream through a detection zone, where the device analyzes thousands of cells per minute. This happens in an enclosed microfluidic environment.

Many applications call for fast and accurate analysis of single particles. Blood contains many types of cell that can be discriminated on the basis of their optical properties. This technique, known as flow cytometry, is widely used in hospitals for diagnosing disease, and as a research tool. However, the current technology is expensive and complicated to use.

Conventional flow cytometry is based on ejecting cells from a nozzle at high speed in a tiny droplet of water. Each cell passes through several laser beams so that different optical properties can be measured. There are many limitations to this system. The droplets containing the cells are ejected into the lab air, producing aerosols that may contain infectious pathogens (viruses). The approach also needs large sample volumes. Conventional instrumentation is expensive, requires skilled staff and is generally housed in dedicated laboratories. To address these issues we developed an approach to flow cytometry based on microchip technology. We designed and built a device to measure both the optical and electrical-impedance properties of cells at high speed within a closed system. It is simple and inexpensive enough to be used in routine diagnostics and analysis. The microchip technology can also be integrated into more complex analysis systems.

The properties of the particles (cells) are measured using optical and electrical techniques, as shown in figure 1. The cells pass through a laser and scatter light: the amount of scatter depends on cell size and shape. Cells can also be labeled with antigens, molecules that recognize and bind to specific markers present on the cell surface. The antigens emit light of different colors when excited by the laser, fluorescing to provide an extremely useful but indirect method of identifying different cell types.

The chip also measures the electrical impedance of the cells. This is done by manufacturing chips with microelectrodes precisely positioned in the flow channel. The electrodes are a similar size to a cell (typically 10μm to 20μm wide, with similar gaps) and are energized with an AC signal of a few hundred millivolts. The electrodes are typically 100nm thick and do not protrude into the channel. They are fabricated using photolithography with the channels constructed from polymers. Channel dimensions are typically 40μm wide and high. The entire chip is 25mm long and wide. Cells flow over the electrodes one at a time, so that sensitive circuitry can determine the AC electrical properties of single cells. The electrical impedance signal provides information on the cell’s size, membrane properties, viability and granularity. This type of impedance spectroscopy can discriminate between cells without resorting to labeling.

A major challenge was to develop a way of measuring a broad band of frequencies at once, in the time it takes a cell to pass
through the detection zone. This has been achieved by exciting the cells using a pseudo-random binary signal that contains all of the frequencies of interest. Fast analysis of this signal gives the electrical impedance of the cell across several decades of frequency.

The chip has diverse applications. We are developing a system to measure and characterize marine phytoplankton. We are working with the National Oceanographic Centre, Southampton, to develop microdevices with integrated optics that can be deployed on submarines and used to measure phytoplankton in-situ. Phytoplankton contain fluorescent compounds such as chlorophylls. Species can be distinguished on the basis of their spectral characteristics.

In this work, microchips have been developed to enable fast and accurate analysis of single cells and other micron-sized particles. The system can distinguish cells by measuring both their optical and electrical signals. It may be able to distinguish between many types of cell, including cancer cells. The technology offers a relatively simple and inexpensive approach to multiple analysis of cells. The next steps are to develop even smaller devices that can analyze the properties of smaller particles such as bacteria and viruses at high speed, and to develop a system that can work in arduous or hostile environments, for example a system that can analyze and identify the myriad of small organisms that live in the ocean.

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