Tips and tricks of the trade

Cell Phone Cytometer

Keeping up with the latest mobile phone is getting harder every month, while it seems that every day brings forth a new cell phone "app" you just have to try out. But how about this for an app: a device that converts a cell phone into a fully functional fluorescent imaging cytometer?

Lab Hint

The increasing use of cell phones around the world hardly needs commenting on, with the International Telecommunication Union claiming that some five billion were being used worldwide at the end of 2010, most of which are in the developing world. Handy that – having lots of high tech floating around where there is the greatest medical need.

Not surprising then, that there is a trend towards exploiting this availability with a range of point-of-care cell-phone applications. For example, taking pictures of skin complaints to identify diseases or even for ophthalmology. Most, if not all, of these medical applications are based on static images but what about exploiting the ease, with which cell phones can capture movies? Think of cell phones being used for counting the number of parasites in drinking water or even bringing blood-cell analysis to remote developing areas.

This was the motivation for the cell-phone device built by Aydogan Ozcan's group at University of California, Los Angeles (*Anal. Chem.*, Article ASAP DOI: 10.1021/ac201587a). It is a clip-on attachment that you stick onto a cell phone, converting it into a microfluidic, fluorescent imaging cytometer. The principle is simple: a plastic and glass chamber that acts both as a microfluidic duct and as a light guide fits directly over the lens of a cell phone. The chamber is constructed using the standard Poly(dimethylsiloxane) (PDMS) moulding technique and two light-emitting diodes (LEDs) sit on the sides of the chamber to provide the excitation light.

No beam splitter needed

The glass slide and the PDMS that comprise the chamber also act conveniently as a light guide, so the light passes tangentially through the chamber and the sample, and not into the lens of the cell phone, thus eliminating the need for a beam splitter. A cheap lens is interposed between the chamber and the cell phone lens to give spatial resolution, and you choose one with a focal length to match the spatial resolution demanded by the application. A simple plastic sheet between the chamber and the camera provides the emission filter, and the whole device fits neatly over the cell phone's lens, its size matching the area covered by the phone's CMOS chip.

Simple tracking algorithm

The moving images captured by the camera are analysed to produce the cell count. Particles (e.g. white blood cells stained with a fluorescent label) are identified using a standard edge detector, such as thresholding a contour gradient.

The simplest possible tracking algorithm is used: assuming a uniform rate of flow, objects are matched between frames according to their proximity. To reduce the inevitable errors with such a tracking method, the counts are performed by an array of "virtual counters" covering different parts of the visual field.

The analysis is coded in an open source framework (the authors use the well-known and freely-available OpenCV image analysis library), so it can be adapted for more complex demands. What is more, as the OpenCV library is available for both the iOS and Android platforms, the whole analysis could even be embedded in the cell phone itself, eliminating the need for any further computing hardware altogether.

Does it work? The authors compared the performance of the system with an established haematology analyser (Sysmex KX-21N) and found that the two methods agreed to within 5% error over a range of white blood cell counts. The spatial resolution, too, compared favourably with a benchtop fluorescent microscope, with adjacent fluorescent beads of 2μm centre-to-centre diameter being resolved.

But what about throughput? Using a standard cell phone with the standard camera frame rate of seven frames per second, a cell count is performed in about five minutes. But the limiting factor is the frame rate of the camera and, since cell phones with camera frame rates of up to 120 frames per

The imaging cytometer sits on the cell phone

second are available, the process could be speeded up to about 20 s per sample.

There have been other approaches to creating point-of-care analysers that overcome the present need for expensive, well-equipped laboratories. Many of these exploit cell imaging along with other metrics such as impedance. But the main advantages of the cell-phone analyser are its cost (the authors spent no more than five US dollars for the lens, filter and diodes), its weight (about 18g) and the way it leverages a technology (the cell phone), which is already abundant even in developing countries.

More possibilities

Sure, it isn't as sophisticated as some other point-of-care devices. It can't calculate the ratio of white blood cells to leukocytes, lymphocytes, monocytes and granulocytes like Rao *et al.*'s Chempaq CBC analyser can (Rao *et a*l. 2008, *Clinica Chimica Acta*, 389, 120-125). But then again, the cell phone device's simplicity may actually be a boon: it only requires imagination and some hacking of the analysis code to turn it into a water-borne parasite counter.

STEVEN BUCKINGHAM