A SQUISHY CELL IS A HEALTHY CELL

Clinicians may soon be able to diagnose and track the progress of diseases such as diabetes and malaria under particular treatment regimes through a patented Lab-on-a-chip diagnostic device. Behind its development is a team of Monash University engineers, their understanding of the complexities of computational fluid dynamics and the supercomputers at the Victorian Life Sciences Computation Initiative.

Tim Thwaites, Science Writer

Moving from simulation to the laboratory:
A prototype of the team's patented microchannel cell-mechanics measurement device.
Image credit: Mr Michael Curtis and Dr Greg Sheard

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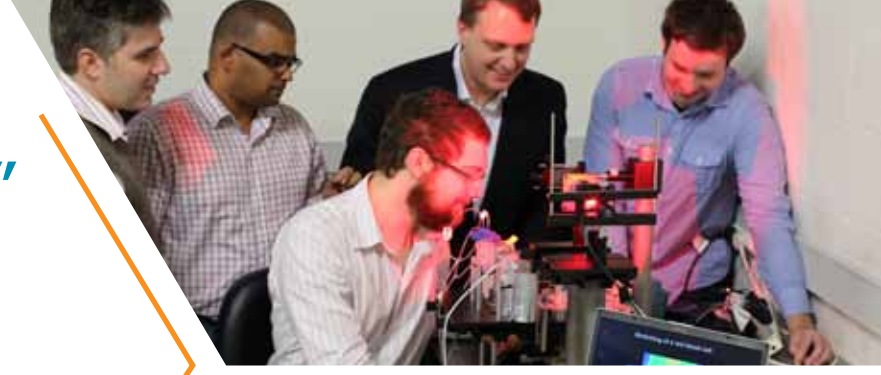


Dr Greg Sheard (rear, 2nd from right) observes a laboratory demonstration of the patented microchannel cell-mechanics measurement device. From left to right, other team members include imaging specialist and lead inventor Dr Andreas Fouras, biologist Dr James Armitage, and PhD students Michael Curtis (seated) and Yann Henon.

Image credit: Dr Greg Sheard

Unhealthy blood cells are less flexible, 'less squishy' than their healthy counterparts. Such differences in stiffness have become the basis for a lab-on-a-chip device developed by engineers at Monash University to test living blood cells for diseases such as malaria and diabetes. It can also be employed to sort the cells, without harming them, for future culturing and experimentation.

The patented device and its accompanying control system have attracted considerable interest from big pharmaceutical and healthcare companies, according to co-inventor Dr Greg Sheard, Senior Lecturer in the Department of Mechanical and Aerospace Engineering. "There is a competitive race on worldwide to develop technologies to measure biological properties in a microfluidic environment."

The operation of the new device depends on an understanding of fluid flows and on simulations derived from the complex equations of computational fluid dynamics. That's why its inventors needed access to the supercomputers at the Victorian Life Sciences Computation Initiative (VLSCI) to design it.

As an engineer with a predilection for playing with such high performance computers, Sheard says he moved into the life sciences area because it threw up interesting problems which also tended to attract funding. "Engineering fluid dynamics, for instance, can be very dry—abstracted from immediate and obvious applications. But in this project, we have developed an instrument that can be used for the diagnosis, treatment and management of disease. You can see much more readily that it has direct benefit to humankind."

"When blood cells become unhealthy, their mechanical properties alter," Sheard says. "There's increasing evidence showing the cells lose their elasticity—their membrane stiffness, internal viscosity and deformability all change." And this makes it much more difficult for them to move through the narrow blood vessels known as capillaries. Even worse, it can damage the blood vessels themselves, leading to blockages and the death of tissue downstream.

In fact, it was medical researchers at Monash in 2002, who first demonstrated these changes in stiffness—in red blood cells infected by the malaria parasite. Each individual measurement for the paper they wrote was made manually using a pipette. It was a difficult and time-consuming task. The new device will accelerate this process by more than 100 times, as well as increasing the range of measurements able to be taken. "It's very exciting," says Sheard. "Transformative."

The concept of the device is actually very simple. About the size of a microscope slide, the 'chip' is etched with micro-channels about a tenth of a millimetre wide in the shape of a cross. At the end of each of the arms of the cross are portals through which fluid can be injected into or withdrawn from the micro-channels.

By careful management and control of the fluid flows down each arm, individual blood cells, less than a hundredth of a millimetre in diameter, can be injected, drawn into and trapped in the centre of the cross. At this point the cell is subjected to a fluid pulse coming down one of the arms. Its deformation and how it restores its shape is recorded using high-speed photography.

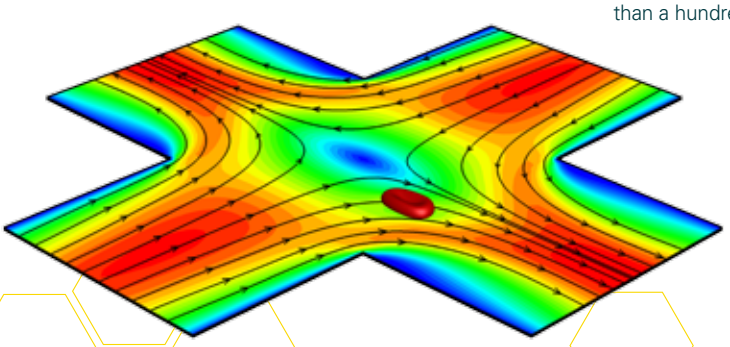
These images can then be analysed to provide measurements of the mechanical properties associated with stiffness. On the basis of the results, blood cells can be diagnosed as healthy or in varying disease states. And, as the pulsing process does no harm to the living cell, each one depending on its state, which has been measured automatically, can then be ejected down one of the arms for collection and future study or culture.

Thus the system, now at prototype stage, can be used to diagnose and track the progress of diseases such as diabetes and malaria under particular treatment regimes. But all this depends on the fine regulation of fluid flows exerted by the control system.

"CFD (computational fluid dynamics)-based modelling and simulation using the computer resources of the VLSCI and our own in-house codes for the cells and fluids played a crucial role in the development of the device," says Sheard. "It allowed us to set up the precise flow rates in the cross slot and to calculate exact pressures and shear forces on cells. It is intrinsic to the intellectual property."

For further information about this research contact Greg Sheard at greg.sheard@monash.edu.

To contact VLSCI, go to www.vlsci.org.au.



A simulated passage of a red blood cell through the device is created using a high-resolution three-dimensional coupled cell-fluid solver, depicting the blood flow on the vertical mid-plane of the microchannel.

Image credit: Mr Yann Henon, Dr Greg Sheard and Dr Andreas Fouras.

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VLSCI is an initiative of the Victorian Government in partnership with The University of Melbourne and the IBM Research Collaboratory for Life Sciences, Melbourne. It exists for all Victorian researchers and as at July 2012, is the largest supercomputer facility devoted to life sciences research in the world.