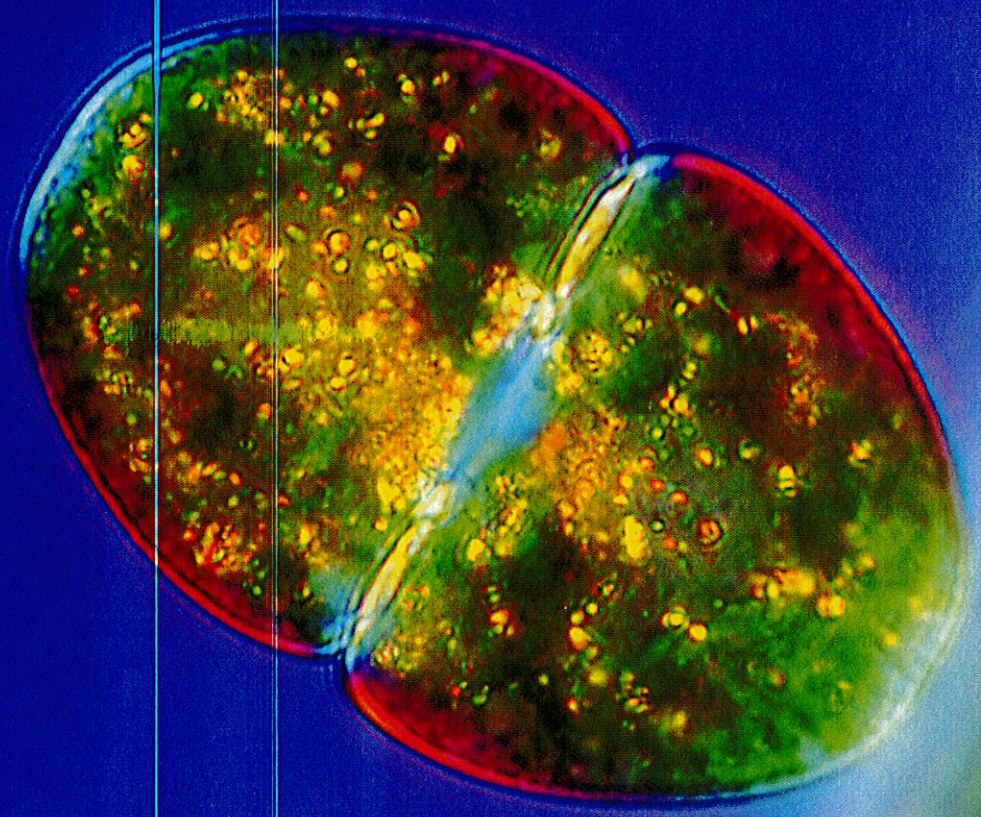
AUSTRALIAN
Life Scientist

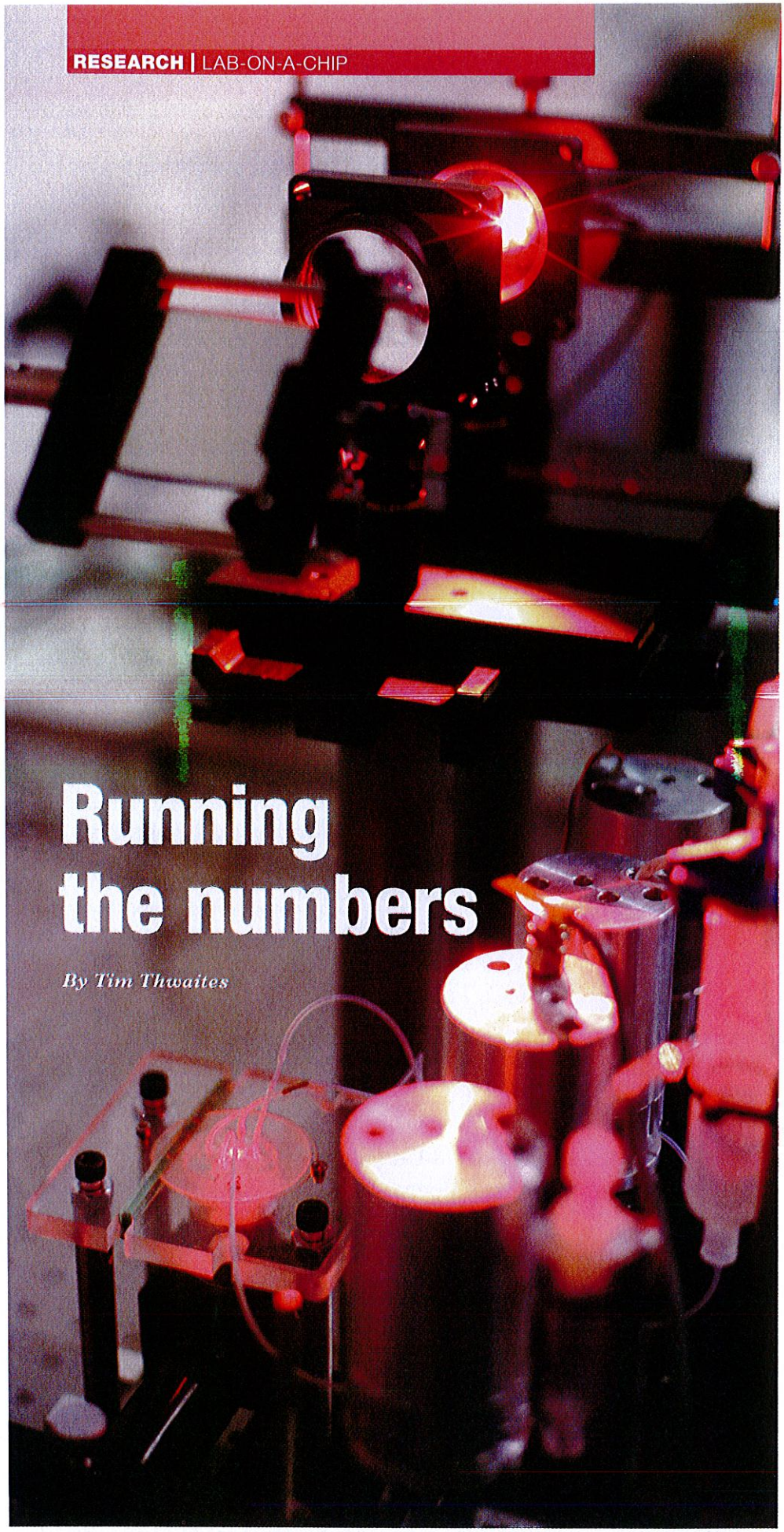
$12.95 (GST included)
Vol 9 Issue 6 • November/December 2012



Vital science

HEALTH AND MEDICAL RESEARCH | IMMUNOLOGY
EPIGENETICS | MICROSCOPY

P&P approved 255003/06813 ISSN 1448-9791



Running the numbers

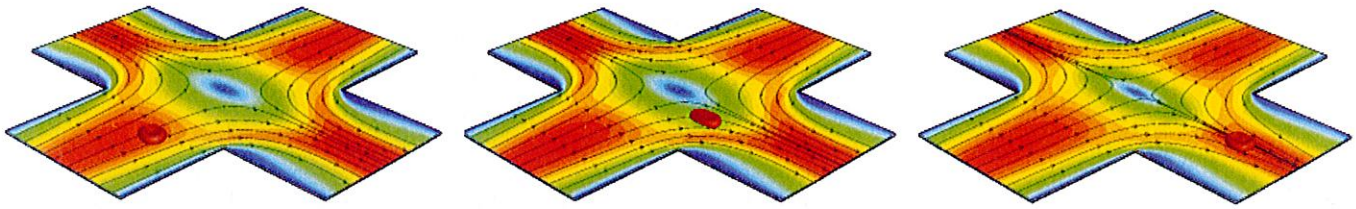
By Tim Thwaites

Clinicians may soon be able to diagnose and track the progress of diseases such as diabetes and malaria under particular treatment regimes through a lab-on-a-chip diagnostic device developed by researchers at Monash University.

IT TURNS OUT THAT UNHEALTHY blood cells are less 'squishy' than their healthy counterparts. This curious phenomenon has now become the basis for an experimental lab-on-a-chip device developed by engineers at Monash University. The intention is to use it as a diagnostic to test living blood cells for diseases such as malaria and diabetes.

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

The challenge lies in determining how changes in the cell affect the flow of blood in such a rarefied environment. "When blood cells become unhealthy, their mechanical properties alter. There's increasing evidence showing the cells lose their elasticity – their membrane stiffness, internal viscosity and deformability all change," says Sheard.



A simulation of a red blood cell being trapped and strained for measurement in the Monash device. (Photo: Yann Hennon, Andrew Fouras & Greg Sheard)

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, and clearly not suited as a conventional diagnostic procedure.

The new lab-on-a-chip device will potentially accelerate this process by more than 100-fold as well as increasing the range of measurements able to be taken. "It's very exciting," says Sheard. "Transformative."

Sheard and his team were able to design their lab-on-a-chip by running highly computationally intensive simulations derived from the complex equations of computational fluid dynamics. To gain an edge, they turned to the supercomputers at the Victorian Life Sciences Computation Initiative (VLSCI) to design their lab-on-a-chip.

"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."

The concept of the device is actually very simple. The 'chip' is about the size of a microscope slide and 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 are portals into which fluid can be injected or withdrawn.

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. Each cell is then measured automatically to determine its state, and they can be ejected down one of the arms for collection and future study or culture.

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, and the technology may eventually lead to a commercial product.

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," he says. ALS

"It's very exciting," says Sheard. "*Transformative.*"

Greg Sheard

Dr Greg Sheard (rear, second from right) observes a laboratory demonstration of the patented microchannel cell-mechanics measurement device. L to R: Imaging specialist and lead inventor Dr Andreas Fouras, biologist Dr James Armitage, and PhD students Michael Curtis (seated) and Yann Henon. (Photo: Dr Greg Sheard)