Seeing human cells through engineers' eyes

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The human cells as machine hardware, and genetic code as the software required to make them run: that is how a new branch of science, synthetic biology, sees them.

By combining elements of engineering, chemistry, computer science and molecular biology, the new science seeks to assemble the biological tools necessary to redesign the living world.

Singapore is pioneering a new direction in this field. A team from the Research Centre of Excellence in Mechanobiology at the National University of Singapore (NUS), aims to break new ground in studying diseases through the mechanisms of cell and tissue mechanics.

Led by Professor Michael Sheetz, from the Department of Biological Sciences at Columbia University, members who hail from NUS, the Nanyang Technological University, A*Star (Agency for Science, Technology and Research) and international researchers are dissecting the mechanical machinery of cells and describing each machine in an online manual.

Because movement is essential for every aspect of life – from the formation of tissues in the embryo to the constant renewal of the lining of the intestine – mechanobiologists plan to develop a standardised toolkit of specified mechanical parts as well as computer models of cell machines.

Why is this important? Movements gone wild, such as the errant migration of cancer cells during metastasis, represent a broken machine, either in its control or its mechanical drive. Just as a car mechanic refers to manuals in the repair of your car, mechanobiologists hope to develop repair manuals for various tissues in the body based on their knowledge of how the parts should work.

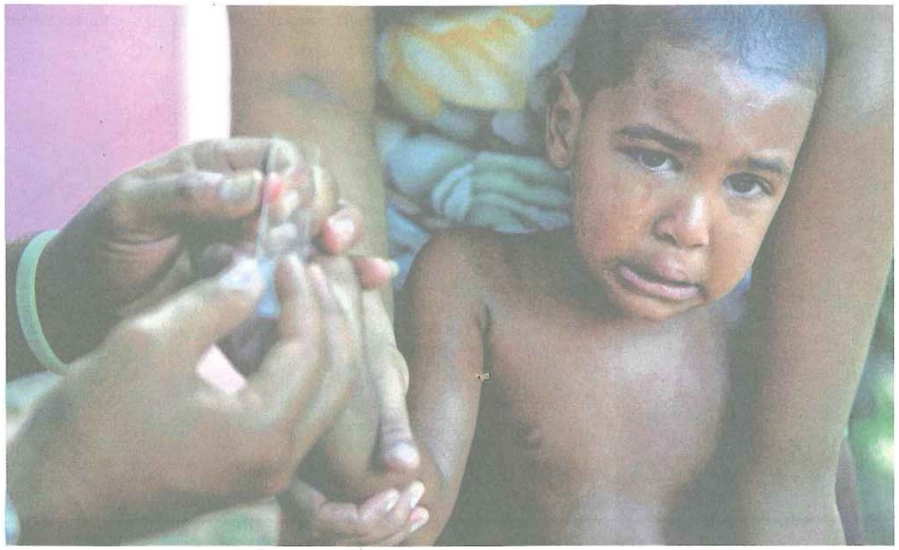

PHOTO: AP

A child in the Dominican Republic cries as a health worker takes a blood sample to test for malaria. Thanks to synthetic biology, a faster and more affordable way has been found to produce a key drug used to fight the disease.

Synthetic biology combines the forward engineering principles of model, design, build and test with the powerful molecular biology methods of manipulating genes. With this engineering focus, a revolutionary breed of biologists, bioengineers and biotechnologists wants to speed up the development of practical solutions to everyday problems.

Early synthetic biologists had a fanciful dream of engineering into a cell the ability to synthesise its own antibiotic when it senses a harmful bacterium nearby.

This notion is perhaps not too far-fetched. Biologists have long recognised that cells respond to a specific input by executing a preset programme of instructions that are stored in the DNA of the cell, in other words by acting as a type of biological computer. Synthetic biologists are now modifying cells to compute by designing computer logic circuits from biochemical reactions. With these new advances, the technologies being developed by synthetic biologists may lead to low-cost drugs, novel materials and new forms of computing.

One example is artemisinin, a drug that holds much promise for combating malaria in the Third World, but is too expensive to extract from plants or to make in a chemical test tube. A team led by Professor Jay Keasling at the University of California at Berkeley has engineered bacteria to make artemisinin by inserting a set of plant genes that control the key steps in artemisinin synthesis into bacteria. He got nature to carry out the difficult chemistry but at a fraction of the time and cost compared to the traditional methods of a chemical laboratory.

However, many technological hurdles prevent more successes from making it out of the research lab.

To circumvent some of these hurdles, synthetic biologists have looked to the Industrial Revolution of the 19th century for one important lesson about engineering nature. "Standards, standards, standards" became the mantra that enabled a machine to be assembled from interchangeable parts made in separate factories. Before the 1800s, parts were custom-made with hand tools. By early 1800, machine tools were invented and a part like the common screw was manufactured to a common specification for the thread. Without standardised parts, the automated assembly line in factories worldwide would not exist today.

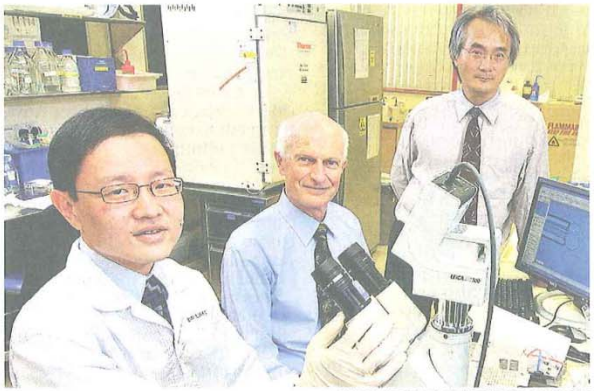

PHOTO: NATIONAL UNIVERSITY OF SINGAPORE

Professors (from left) Lim Chwee Teck, Michael Sheetz and Paul Matsudaira from NUS' mechanobiology team. With members from A*Star, NTU and international researchers, they are studying the mechanical machinery of cells.

With the sequence of the human genome in the last decade and the sequencing of genomes from over 100 different organisms, we have a "parts list" of living systems. Synthetic biologists are now trying to standardise many of the parts like bricks in a Lego set for ease of assembly into a "plug and play" format.

Synthetic biology is becoming so simple that college students with no prior training in biology are designing bugs to do "unnatural" things. At the end of this month, 112 teams of undergraduates from universities worldwide will gather at the Massachusetts Institute of Technology for the annual International Genetically Engineered Machine (iGEM) competition. Taking a cue from electrical engineers who build circuits from a bin of transistors, resistors and capacitors, iGEM competitors design molecular circuits that control the actions of a cell from a bin of standardised biological parts composed of promoters, inhibitors and activators.

At the first competition held in 2004, a University of Texas team produced a biofilm that could capture and display an image. By last year, iGEM had grown from five US teams to 84 teams from 21 countries. The 2008 grand prize winner was a Slovenian team of five undergraduates who beat teams from research powerhouses such as the University of California at Berkeley, Harvard University and the California Institute of Technology with a method for boosting the recognition of bacteria by the immune system of the body.

The writer is head of NUS' Department of Biological Sciences and professor with NUS' Division of Bioengineering. He was helped in this article by the students from the Freshman Seminar on Biological Machines.