Circulatory system on a chip lets scientists mimic heartbeat

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A tiny chip that mimics a circulatory system—right down to the rhythm of a human heart beat—could be an invaluable tool in understanding the causes of cardiovascular disease and developing drug therapies.
The system of tiny valves and channels on the chip mimic blood flow in the body, said biomedical engineering professor Shuichi Takayama, corresponding author of the paper, "Computer Controlled Microcirculatory Support System for Endothelial Cell Culture and Shearing," scheduled to appear in July in the journal Analytical Chemistry.

The design lets scientists study the fluid mechanical effects of blood flow (called shear stress) in certain cells that play a critical role in heart disease. The cells, called endothelial cells, line the inner walls of blood vessels. The changes in ECs caused when blood flows past them at different speeds and rhythms are at least partly responsible for fueling certain diseases—including cardiovascular disease.

Studying endothelial cells in a Petri dish is often ineffective because the test environment is static, like bath water, said Takayama, so the cells are not acting as they would in the body where they are exposed to flow, like in a river. But with the U-M system, scientists can adjust the flow through the channels on the chip so that the ECs think they are inside an artery or vein, or maybe even inside the blood vessels of a couch potato or a regular exerciser, Takayama said.

The system is also capable of mimicking the irregular, surging flow of

blood pumped by the heart. A big question in the study of heart disease and cardiovascular research is how these endothelial cells sense and convert the fluid mechanical stresses associated with blood flowing past the cell into diseases, such as hardening of the arteries or thrombosis. Answering those questions will provide big clues to developing therapies to regulate ECs.

To study this question, scientists have developed systems that model the physiological flow conditions of blood in the body. However, existing model systems cannot perform multiple experiments, are not easily portable, consume large amounts of reagents and can become contaminated easily.

The U-M team's chip differs from others because the intricate system of pumps and channels lets researchers sustain high levels of shear stress on the cells for hours or days, with various patterns of flow similar to how endothelial cells in the body are exposed to changing shear stress levels caused when blood flows past the cell. The microfluidic valving and pumping system lets researchers perform different tests simultaneously in multiple channels on the same chip.

The flow capability is accomplished by blending old and new technology. The central feature is a pin system that was originally meant to be used as part of a device that helps the visually impaired read e-mail, Takayama said. The pins move up and down beneath the reader's fingertips to represent certain Braille letters, thus translating what appears on the computer screen.

In the U-M invention, the pins move up and down to plunge fluid through a system of tiny channels drilled into the chip. The pins function as the heart of the system and the channels as the vasculature. A software program acts as the brain of the system to control pin movement, or the heart beat, and regulates fluid flow patterns, or the pulse, through the

vasculature. The chip with the EC-lined vasculature is assembled in three layers and sits on top of the pin system.

The project is a collaboration between the departments of biomedical engineering and cardiology, restorative sciences, and endodontics. Team members include Jonathan Song, Wei Gu, Nobuyuki Futai, Kristy Warner and Jacques Nor.

The Braille technology also has applications for artificial insemination.

Source: University of Michigan