



Photo by Daniel Dubois

Graduate student Shannon Faley looks at a microfluidic circuit for trapping T-cells with a microscope. The red spheres on her right are T-cells that have been labeled with fluorescent quantum dots.

A portable detector for HIV-AIDS, measles and other infectious diseases is the object of a new university/industry collaboration

By David F. Salisbury

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A portable device similar to today's home pregnancy tests that can quickly detect the presence of infectious diseases, including HIV-AIDS and measles, as well as biological agents such as ricin and anthrax, is the object of a new university/industry research project.

Vanderbilt University's Institute for Integrative Biosystems Research and Education (VIIBRE) and Pria Diagnostics LLC, a privately held California company that specializes in miniaturized medical diagnostics, agreed to collaborate on the device's development at the end of last year.



Photo by Igor Ges/VIIBRE

A photomicrograph of one of VIIBRE's bioreactors that contains living cells. The reactor is made from a material similar to that used in soft contact lenses. The black shapes are specially coated electrodes that measure the chemical activity of the cells.

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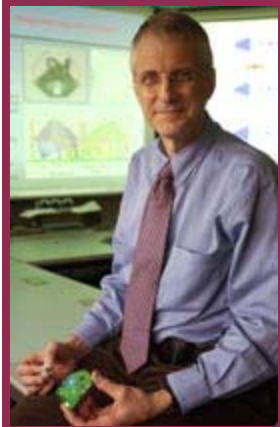


Photo by Daniel Dubois

VIIBRE director
John Wikswo

VIIBRE has spent the last three years developing the ability to measure the metabolism of small groups of cells and studying how they respond to drugs, toxins and pollutants. To do so, the interdisciplinary team has developed two basic technologies: special electrodes that can measure the concentrations of the chemicals that cells consume and excrete in extremely small volumes and the use of fluids flowing through microscopic channels to move and manipulate small numbers of cells reliably. In the process, the group has applied for more than 12 patents.

Meanwhile, Pria has developed a micro-optical fluorescence spectroscopy system and used it as the basis for an inexpensive male fertility detector that can be used in the home to measure sperm motility with an accuracy comparable to laboratory analyses.

"I'm thrilled at how well the VIIBRE and PRIA technologies mesh," says John P. Wikswo, professor of biomedical engineering, physiology and physics at Vanderbilt and director of VIIBRE. "We are already making rapid progress on prototyping portable instruments for clinical diagnosis and biodefense."

"Today the treatment for AIDS is very expensive and there is always a question about when to start and stop anti-retroviral therapy," says Pria's Chief Technology Officer Jason Pyle. "We are developing a device that we hope will allow medical professionals and HIV patients to manage their disease in a way that is similar to how diabetes patients can monitor their condition since the introduction of home blood glucose detectors."



Courtesy of Pria Diagnostics

Jason Pyle, Chief Technology Officer of Pria Diagnostics



Photo by Daniel Dubois

David Schaffer, right, describes Pria's detector with graduate students Shannon Faley and Michael Warnement

The origin of the collaboration is an example of the power of serendipity. It started when David Schaffer, a VIIBRE student who stayed on at the institute as a project engineer after he graduated, was browsing the Web looking for a permanent job.

Although looking for a local position, he inadvertently opened a Web page with listings from California. He came across an interesting opening at Pria, located in Menlo Park, and decided to apply. Although Pria decided that he wasn't the right person for the job, in their correspondence Pyle expressed potential interest in collaborating with VIIBRE. Schaffer passed the information along to Wikswo, who gave Pyle a call. That was in early September. By mid-November a joint research agreement for \$120,000 for the first year was completed and signed.

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The collaboration's goal is to produce its first portable HIV monitor within two years. In addition to such "point of care" devices, Wikswo and Pyle are joining forces to develop "high-throughput" screening systems that can determine the biological activity of large numbers of compounds with extreme rapidity and so could have a major impact on the drug discovery process.

Fifteen years ago a number of start-up companies were created to make the goal of creating a "lab-on-a-chip" a reality. However, putting microscopic arrays of channels, pumps and valves to move around minute amounts of liquid on silicon chips proved to be considerably more difficult than most of the inventors had expected and the products that these companies have created thus far have been too expensive for the point-of-care diagnostics market.



Courtesy of
Pria Diagnostics

Pria's male fertility detector

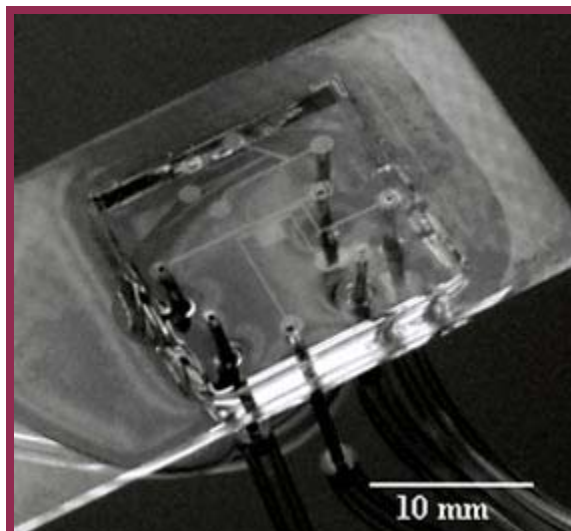
For their home fertility tester, Pria kept costs down by keeping their system as simple as possible. Instead of trying to squeeze everything onto a single chip, Pria designers started with a desktop diagnostic system and shrank it down into a device about the size of a coffee cup.

One of the cost-saving aspects of the design was to keep the fluid-handling components separate from the microelectronics. The resulting device is considerably larger than comparable lab-on-a-chip systems but it is also much less expensive. "That's one of the appealing features about Pria's approach," says Wikswo, "They keep their microfluidics and microelectronics as simple as possible."

"Pria's first product focused on fertility," says Schaffer. "With our capabilities, they can begin applying their technology to a goldmine of different applications."

One of the key VIIBRE capabilities, which was developed by a research team headed by Assistant Professor of Chemistry David Cliffl, is the development of a sensor suite capable of simultaneously measuring the concentrations of the key chemicals that cells consume and excrete—oxygen, glucose and lactic acid—with enough sensitivity to monitor the health of a few thousand cells confined in a small volume.

Under the leadership of Franz Baudenbacher, assistant professor of biomedical engineering and physics, Vanderbilt



Courtesy of David Schaffer/VIIBRE

Close-up of a microfluidic cell sorter shows the tiny channels that carry cells and fluid



Photo by Daniel Dubois

David Cliffl

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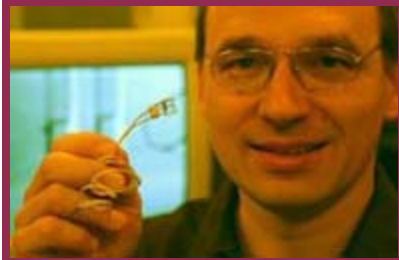
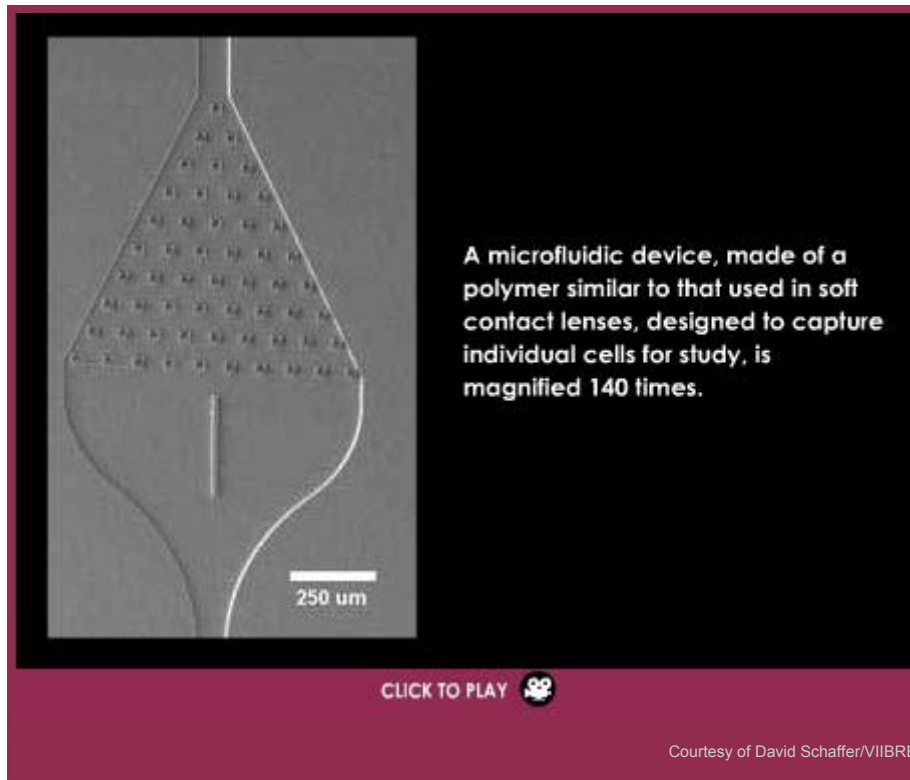


Photo by Neil Brake

Franz Baudenbacher holding microfluidic device

researchers have further miniaturized this sensor technology to record rapid changes in the metabolism and signaling of individual cells. To handle such small numbers of cells, they have adapted a method for molding micro-channels and valves into a material similar to that used in soft contact lenses. This has given them the capability to capture, manipulate, grow and study single living cells in extraordinarily small containers—volumes that are barely larger than the cells themselves.

Most sensors that have been developed to identify toxic agents are single purpose. That is, they can identify the presence of a single toxin, or a limited number of closely related toxins. The ability to monitor the health of small groups of cells, however, makes it possible to detect the presence of unknown poisons as long as they affect cell metabolism. Furthermore, by examining the impact that an unknown agent has on different cell types—such as heart, lung, nerve, skin, etc.—this approach also can rapidly provide critical insights into its mode of action.



“Pria has an outstanding understanding of the clinical and diagnostic device market and the ability to rapidly prototype optical and microfluidics devices,” says Wikswo, “but it is difficult for the company to survey large numbers of possible applications. Yet, here at the university, searching for new applications is one of the things that we do best.”

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