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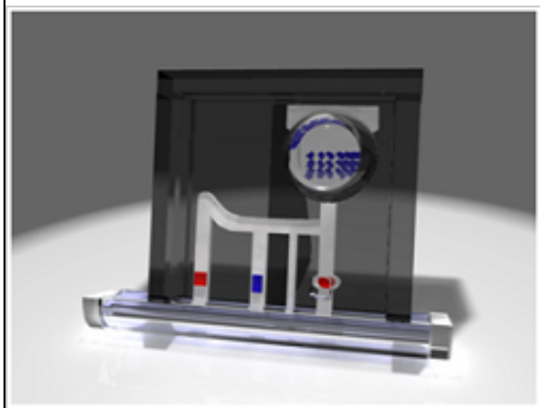

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At the end of a long day spent on a plane and in meetings, Paul Yager was ready for a good night's sleep. Instead, he was lying in a hotel-room bed with his eyes wide open and his mind racing.

He kept thinking about what his next step would be to improve diagnostic field testing. He didn't want to think about it; he wanted to sleep. Watching one of those boring TV infomercials, which he hates, surely would do the trick. Yager flipped on the TV and tried to zone out to the sounds of a pitchman extolling the virtues of a desktop paper cutter for craft projects.

In moments Yager was even more awake. Cutting paper into different shapes could solve a major roadblock in getting laboratory-quality diagnostic testing into situations without labs or trained personnel.

"I had been working for a year or more to figure out what I and my lab could do for an encore after 15 years of developing conventional microfluidic devices and systems," Yager said. "No matter what we did, there was always an instrument needed to push the fluids around or to convert chemical changes into numbers a physician could use for a diagnosis.

"The new idea that evolved that night was the whole instrument to be a disposable piece of paper in a cheap plastic housing, but the chemical processes that would be performed on that piece of paper would be anything we can do today in the lab or in microfluidics. That's the kind of idea that keeps you up the rest of the night."

Now the concept is becoming reality thanks to a two-year, $1 million coveted NIH Challenge Grant in Health and Science Research award Yager received this fall. Only 200 grants were awarded from the 20,000 applications.

By using the same materials as in a simple strip test cut into different shapes, Yager's concept will improve the usability, reliability, and sensitivity of strip testing.

Yager wants to create a method of strip testing that would work like a lab test—a device that could process a sample using multiple steps, but would be inexpensive and could be administered by a lay person. In other words, he wants lab complexity on a strip of paper.

The challenge is to precisely sequence and time the steps of the chemical analysis using only the power of capillary action, the natural absorbing ability demonstrated by a paper towel wiping up spilt milk. By revising the straight strip-test design into one that resembles a comb with teeth of various lengths and widths, Yager and his team will be able to do just that.

Each paper tooth performs a step in the analysis process. The fluid with the shortest path (based on the shape of its channel) reaches the detection zone first, and then stops flowing when its source dries up. Meanwhile, fluids continue to be drawn up the paper teeth at different rates depending on their length and distance from the detection zone. The length and shape of the paper also will determine when a reagent shuts on or off.

"Conventional strip tests are made to be very simple – a user adds a sample and reads the result in a few minutes – but this simplicity limits them to tests that can be done in a single chemical step. By cutting the paper into new shapes, the paper can be programmed to automatically carry out more sophisticated tests without requiring the user to do anything extra," says Barry Lutz, co-investigator on the grant.

The only instrument needed to read the networked test strip would be a cell-phone camera.

"You can calculate the results with a downloadable App, or send the image to the doctor's office for the diagnosis. Either way we piggyback onto existing cell-phone technology, which is nearly universal these days," Yager says.

Once Yager's group works out the correct shapes for various test protocols anyone with a pair of scissors would be able to cut out a complex strip test following a pattern, like a child would cut out paper dolls.

"One thing I find very attractive about this technology is that it is "franchisable", Yager says. "This won't require a big factory in the developed world, but will be a truly global technology."

Other groups around the world, including the Whitesides Research Group at Harvard, have turned attention to new opportunities to use paper in diagnostics. What sets the Yager team's work apart is engineering paper designs to carry out multi-step procedures like those done in laboratories. The group is consulting with PATH experts on strip testing to build a technique that adds to scientists' current understanding of how to control flow in porous materials, which may open up other possibilities.

The Yager lab's success with microfluidics and the DxBox, which also performs tests on nitrocellulose paper, combined with the abilities of complex paper networks, makes it possible to amplify chemicals for more sophisticated analysis without expensive equipment like pumps, controllers and detectors.

This testing platform could help reduce health care costs in the United States by making sophisticated diagnostic testing possible in physicians' offices, nursing homes, schools, hospitals, and even homes. Yager's team sees application to a range of infectious diseases, acute and chronic diseases like myocardial infarction, and cancer. In the developing world the platform could be used to diagnose AIDS, tuberculosis and malaria. Rapid diagnosis of infectious diseases could lead to proper treatment earlier.

NIH Challenge Grants address specific scientific and health research challenges in biomedical and behavioral research that would benefit from two-year start-up funding. Challenge topics focus on specific knowledge gaps, scientific opportunities, new technologies, data generation or research methods and that promise to have high impact on biomedical or behavioral science or public health, according the NIH Web site.