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Monitoring HIV on a Cheap Chip

A microfluidic chip could measure effectiveness of patient treatments in resource-poor countries.
By Courtney Humphries

Measuring viral load, or the concentration of HIV in the bloodstream, is one of the techniques that physicians use to monitor the effectiveness of HIV treatments. A spike in viral load can be a warning of drug failure or drug resistance, possibly indicating that the patient should be switched to a different drug. But in resource-poor settings, such monitoring is prohibitively expensive and equipment-heavy. A new microfluidic chip designed by the lab of Rustem Ismagilov at Caltech may make it possible to monitor viral load in HIV and other viral infections more cheaply and easily, and the technique could also be useful for other kinds of genetic tests.

Viral load is often measured with PCR, a standard laboratory tool that copies the DNA or RNA in a sample many times. A newer approach, called digital PCR, makes it possible to get much more precise counts. Using microfluidics, the sample is first divided among a multitude of tiny wells, so that each well is likely to hold no more than one molecule. When the molecules are then amplified, the result is a simple yes-or-no signal for each well.

"The bottleneck of those methods comes when you need a measurement with a large dynamic range," Ismagilov says. HIV viral load, for example, can range from 50 to a million molecules per milliliter. A test to measure it must be able to handle large numbers of molecules, yet be sensitive enough count rare molecules. Normally, achieving such sensitivity requires diluting a sample and spreading it out over more and more wells in order to ensure that no more than one molecule is in each well. Ismagilov says that such large numbers of wells can be cumbersome to analyze. At the same time, the sample can't be spread so thin that scarce molecules will be missed.

Ismagilov and his lab members came up with a trick to handle this dilemma: divide the sample into a series of different-sized wells calibrated to detect molecules at different concentrations, which can be calculated together. "Each volume is sensitive to a particular concentration range," he says. "Together these volumes provide more information than any one volume individually."

The technique relies on the SlipChip, a simple microfluidic device developed by Ismagilov. Two overlapping glass or plastic slides can be injected with a fluid sample and then rotated slightly to separate the fluid into the wells. The rotation can also bring certain wells into contact so that chemical reactions can be performed.

In two recent papers in *Analytical Chemistry* and the *Journal of the American Chemical Society*, Ismagilov and his colleagues describe the mathematics of the design and its application in testing viral load in both HIV and hepatitis C. The chips can be designed to perform multiple tests or measure multiple samples, which Ismagilov says adds to their flexibility. Currently, other devices are needed for other stages of PCR preparation and analysis, but the researchers' ultimate goal is for one chip to handle all these steps.