

Hello, this is Kevin O'Donovan, and I'd like to welcome you to the National Institute of Environmental Health Sciences Superfund Research Program monthly Research Brief podcast.

This month, we're discussing a new dilution tool to facilitate high-throughput assay techniques.

The Research Brief, Number 256, was released on April 6, 2016, and was written by SRP contractor Sara Mishamandani in conjunction with SRP-supported researcher Tingrui Pan.

A new tool provides a quick and easy way to dilute samples for biochemical and biological analyses. The microfluidic dilution generator, developed by researchers led by Dr. Tingrui Pan at the University of California, Davis Superfund Research Program Center, can serve as a simple dilution device in research laboratories, point-of-care clinical settings, and low-resource environments.

Generating a series of dilutions is a routine practice in labs and a gold standard to obtain quantitative readings for a variety of biological and biochemical assays. For example, serial dilutions are used to dilute blood serum to determine the exact amount of proteins and antibodies, develop standard curves to detect and quantify anything from environmental chemicals to DNA, and create dose-response curves based on enzyme activity.

To date, standard dilutions rely heavily on manual dilution or expensive robotic automation. The new tool developed by Pan and his team provides a simple way to produce serial dilutions without the need for expensive tools or highly trained expertise.

The microfluidic dilution device consists of three layers. The bottom layer contains metering reservoirs for the sample, liquid to dilute the sample, also called the diluent, and any reagents that need to be added in equal amounts to the serial dilution. The middle layer contains a through-hole membrane with horizontal channels that connect the reservoirs in the bottom layer. The top layer is a reconfigurable layer for valve switching. The device's flexible design allows the user to create linear, logarithmic, or arbitrary dilution profiles by adjusting the dimensions of the reservoirs.

Only three steps are needed to create dilutions, which can be applied in a wide variety of biological and biochemical assays for high-throughput and quantitative outcomes. In the first step, a pipette is used to load the sample, diluent, and reagent into the inlets, from where they move horizontally through the distribution channels and fill all reservoirs. The device is then reconfigured by manually removing the top reconfigurable layer, separating each horizontal distribution channel and leaving only the vertical passages connecting the sample, diluent, and reagent. Finally, a pipette is used to vertically pull the sample, diluent, and reagent into the reaction chambers, mixing them together.

The device can easily produce discrete concentration profiles ranging from 1 to 100-fold dilution from a fixed small sample volume of 10 microliters. Although several approaches that dilute samples using a diffusive method are emerging, all of them require a pump or vacuum, which is often unavailable in clinics or point-of-care settings and may require higher volumes of samples. This device reduces the time required and is completely compatible with standard biological protocols for a wide variety of

quantitative assays in laboratories, clinical settings, and in-field testing. Requiring limited steps, this device also makes it easy to use for personnel without extensive training and complicated equipment.

If you'd like to learn more about this research, visit the Superfund Research Program website at www.niehs.nih.gov/srp. From there, click on "Who We Fund" and follow the links to the University of California, Davis research summary. If you have any questions or comments about this month's podcast or if you have ideas for future podcasts, contact Maureen Avakian at avakian@niehs.nih.gov.

Join us next month as we discuss more exciting research and technology developments from the Superfund Research Program.