Development of a Multiplexed Microfluidic Detector for Biological Agents

Chung-Yan Koh, Sandia National Laboratories
Betty Mangadu, Sandia National Laboratories
Anup Singh, Sandia National Laboratories

An urgent need exists for developing next-generation detection devices for screening individuals exposed to and intoxicated with biological threat agents or detecting these agents in environmental samples. Biological toxins remain the most acutely poisonous substances known, with the potential to incapacitate hundreds of thousands of people per gram. These devices need to be capable of rapid, sensitive, and specific detection to enable effective countermeasures including therapeutic intervention. Such systems must also be easy-to-use, automated and self-contained, and preferably have a small footprint to allow use in point-of-care and point-of-incident settings.

Our goal is to develop a device capable of fulfilling these requirements for use in field forward diagnostic facilities and other potentially constrained resource environments. We utilize a microfluidic device which uses centrifugal force-driven flow to implement a bead-based sandwich immunoassay and activity assay in a plastic disk. Due to the large surface area provided by the microparticle beads and the confined volumes afforded by the microfluidic architecture, results can be rapidly and sensitively obtained from only a few microliters of sample. The channels in the plastic disk allow for multiplexing of assays from a single sample or from multiple samples. The platform, owing to its bead-based assay format, is readily adaptable to detection of other pathogens and disease markers with no changes to the overall device or platform architecture. The device requires no off-device sample preparation and is compatible with multiple clinical sample types including whole blood, serum, saliva, and urine; device operation is one step for the user. For analysis in stool sample preparation is limited to dilution. This device has a cube form factor, 13 cm on a side and 2 kg in weight, battery powered, compact, and portable. Disposable plastic disks are 10 cm in diameter.

We have demonstrated sensitive and specific detection of a panel of toxins including biothreat agents such as botulinum neurotoxins, staphylococcal enterotoxins, Shiga toxins, aflatoxins, and public health concerns such as cholera, Zika, Dengue, and diphtheria. In a single microfluidic disk, up to 20 assays can be performed. Limit of detection in these assays is better than 1 ng/mL for all assays and as sensitive as 0.02 ng/mL in several cases. We have observed assay insensitivity to sample matrix with linear response across a variety of sample types. We have also adapted the platform for detection of host response markers such as serology assays. The microfluidic method compares favorably with gold standard washed, chemiluminescent microtiter plate ELISA. Correlation between the two methods was very high ($r^2 > 0.998$). Preliminary work in stabilizing assay components as dried reagents has shown promise with minimal loss of sensitivity.

As a field forward diagnostic platform, this technology could lend itself to rapidly detecting and distinguishing biological threat agents in a constrained resource environment.

Sandia National Laboratories is a multi-mission laboratory managed and operated by National Technology & Engineering Solutions of Sandia, LLC., a wholly owned subsidiary of Honeywell International, Inc., for the U.S. Department of Energy's National Nuclear Security Administration under contract DE-NA0003525. SAND2017-5863A

Research reported in this abstract was supported by the National Institute of Allergy and Infectious Diseases of the National Institutes of Health under award number R01AI098853 and by the Science and Technology Directorate of the Department of Homeland Security. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health or the Department of Homeland Security.