

## INNOVATING CROSS-DOMAIN SOLUTIONS TO DETECT EMERGING BIOLOGICAL THREATS

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Agility against future biothreats requires technologies that can rapidly adapt to the ever-changing threat landscape. Such technologies that are also amenable to use in the operational field are especially challenging. Here we describe Dial-a-Threat, which provides nucleic acid detection in a low SWaP-C format as simple to operate as lateral flow immunoassays. Crucially, these assays can be “reprogrammed” by snapping in a different targeting module, enabling stockpiled assays to be readily repurposed to new threats. Underpinning this technology is a synthetic biology-enabled cell-free expression reaction that can perform different functions by simply swapping DNA. In response to an emerging threat, new sensors can be developed quickly in a centralized lab driven by high-throughput experimentation and computer-aided experimental design. The DNA sequence encoding for the new sensor can then be transmitted electronically to forward labs, which can create new targeting modules via benchtop oligo synthesis. In principle, the entire process of new threat to fielded assay could occur in under a week. Using the same system, it is also possible to detect proteins and small molecules of interest in CB defense and beyond. We present efforts to optimize the reactions for speed, enabling detection of biothreats in under 30 minutes. To deploy the reaction to the operational field in a low SWaP-C package, we developed a paperfluidic device in 3D-printed housing with simplified user operation, refined over multiple operational events. The output is an eye-readable color change, which can optionally be paired with a reader for automated analysis and integration with tactical networks. In all, Dial-a-Threat offers a highly adaptable solution to in-field detection needs.

This research is funded by DTRA JSTO project CB10923, Dr. Stephen Francesconi.