INNOVATING CROSS-DOMAIN SOLUTIONS TO DETECT EMERGING BIOLOGICAL THREATS

Multiplexing DNA Sensors and using Pattern Recognition to Detect a Range of Chemical and Biological Threats using a Single Test Platform

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Chemical and biological threats are a major risk to the war fighter and public safety. The ability to detect a wide-range of chemical and biological threats currently require a multitude of testing platforms and analytical methods. This is because these threats comprise vastly different classes of matter: organic chemicals, microorganisms, toxins, inorganic metals, and radionuclides. Each class requires a unique testing platform and trained personnel for analysis. Furthermore, testing involves samples to be collected and sent to a centralized laboratory for analysis. This centralized approach is laborious, time consuming and expensive, ultimately limiting the amount of sampling that can be caried out. Because of these challenges, significant efforts are being devoted to develop inexpensive, onsite detection methods. Such technologies will enable a decentralized approach for monitoring chemical and biological threats, which will allow for increasing the number of testing sites and frequency of testing. Together, this will strengthen our Nation's early detection capabilities and defense.

We are proposing a paradigm shift in chemical and biological threat detection by harnessing the ultra-sensitivity and -multiplexing capabilities of DNA sequencing, and combining this signal readout with the selectivity and programmability of DNA sensors. DNA sensors are emerging as promising tools for rapid on-site detection, which can aid in minimizing exposure. However, sensor activity towards its target analyte is not absolute, so DNA-based sensors have cross-reactivity and high false positives. This is one of the major challenges limiting the wide-scale application of DNA sensors for in-field testing or clinical assays. To address this challenge, we are investigating using a pattern-based readout of a DNAzyme sensor array to improve accuracy of detection of heavy metalsas a proof-of-concept. We measured cross-reactivity between the DNAzyme's respective metal cofactor and common metal interferents and then used t-distributed stochastic neighbor embedding (t-SNE) analysis to quantify the competing metal ion present in solution. Furthermore, we developed a sensing platform for parallel analysis of numerous DNA sensor, which will enable detection of a diverse range of both chemical and biological targets within a single test. With the convergence of multiple technologies, programmability of DNA sensor, parallel sequencing, and artificial intelligence, we believe the field is ready to employ DNA sensors for protecting the warfighter.

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