JSTO in the News

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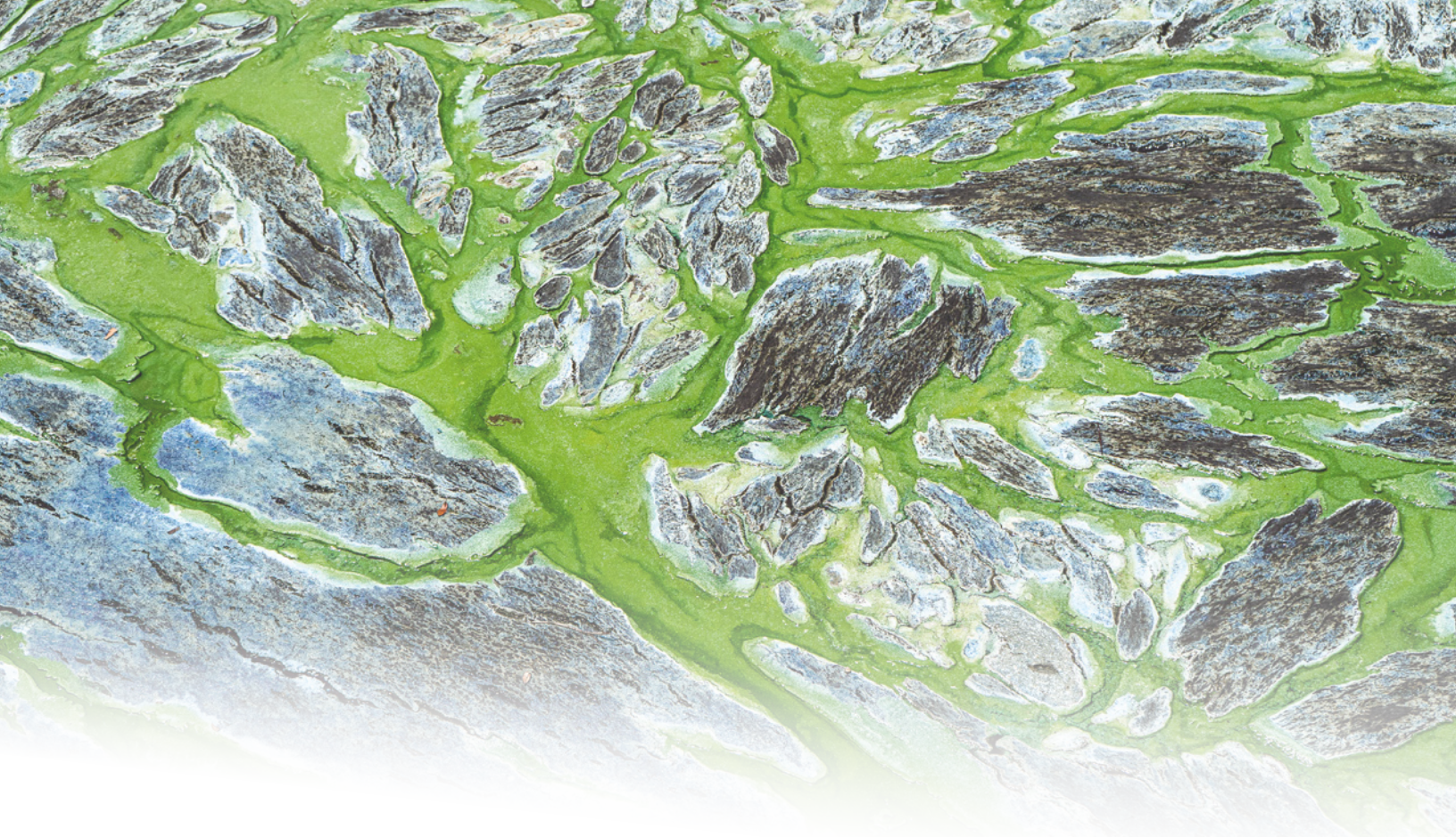
Expertise on TAP

Brain Boost



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Front cover: A U.S Army Officer in Charge of a training chamber that uses tear gas to simulate a deadly gas attack with the 23rd Chemical Biological Radiological Neurological and High-Yield Explosives (CBRNE) Battalion monitors the emission of 2-chlorobenzylidene malononitrile (CS) gas for CBRN training at U.S. Army Garrison Humphreys, Republic of Korea. CS gas capsules are broken and heated to simulate a chemical attack. (U.S. Marine Corps photo by Cpl. Jaye Townsend)

Inside cover: In April 2021, a toxic algal bloom outbreak overwhelmed the Pahokee Marina in Pahokee, Fla. The Florida Department of Environmental protection water test results showed 860 parts per billion of the toxin microcystin. Microcystins are a potent liver toxin and a possible human carcinogen. In addition, the U.S. Environmental Protection Agency found that cyanotoxins can also kill livestock and pets that drink affected water. In 2020, Congress directed the U.S. Army Corps of Engineers to implement a five-year technology demonstration program focused on freshwater Harmful Algal Blooms detection, prevention, and management tools. (Photo by Brigida I. Sanchez)

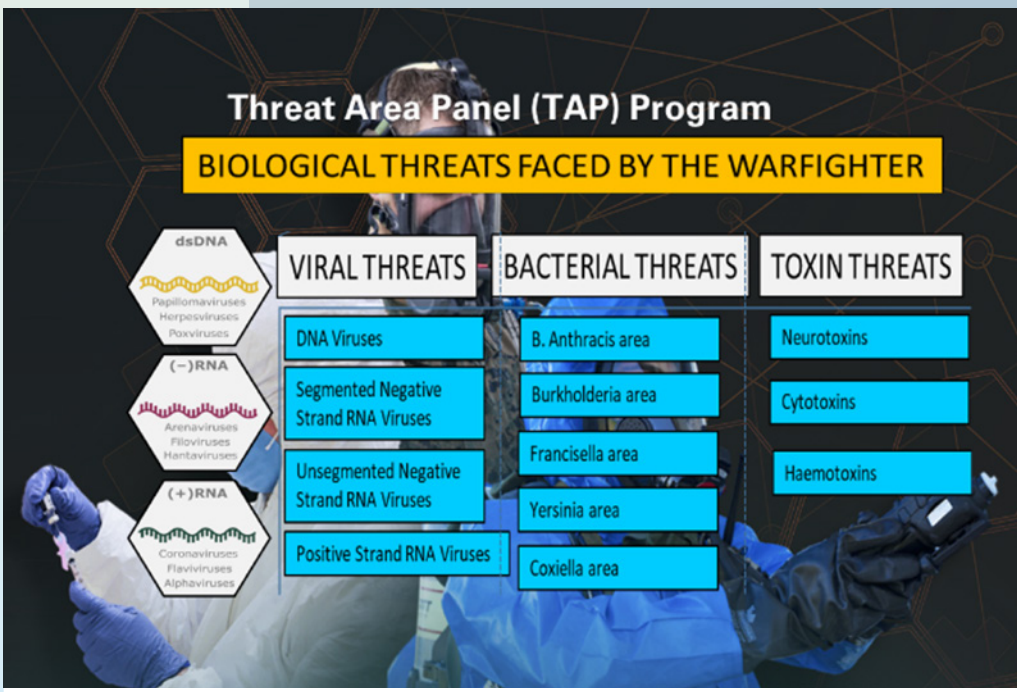
Back cover: An Indiana National Guard soldier with the 438th Chemical Company conducts recon on a chemical spill site during Toxic Lance at Lešť Military Training Area, Slovakia. The State Partnership Program helps position the United States to react effectively to anticipated or unanticipated global scenarios as they emerge. (U.S. Army National Guard photo by Sgt. Hector Tinoco)

Expertise on TAP

The DTRA JSTO Threat Area Panel Program unites experts to characterize and combat emerging biothreats.

The complexity of the biothreat landscape, augmented by advancements in biotechnologies, requires the Department of Defense (DoD) to develop agnostic platforms and programs to rapidly characterize biothreats and accelerate countermeasure development to better protect warfighters, the nation, and our allies.

For this reason, the Defense Threat Reduction Agency's (DTRA) Chemical and Biological Technologies Department in its role as the Joint Science and Technologies Office (JSTO) for Chemical and Biological Defense, an integral component of the Chemical and Biological Defense Program, invested with the U.S. Army Medical Institute for Infectious Diseases (USAMRIID) to establish a streamlined program called the Threat Area Panel (TAP) augmenting their current mission with the rapid assessment of current and emerging biological threats.



DTRA JSTO Threat Area Panel (TAP) Program. Biological threats faced by warfighters have been organized into broad categories and then further broken down into Threat Areas (blue boxes). A matrix of DoD service laboratories in each of these categories, with a SME lead, have been identified to execute Threat Agent Science work up to Biosafety Level 4 (BSL-4) in a streamlined fashion. BSL-4 labs study infectious agents and toxins that can cause life-threatening diseases with no available treatment or vaccine and use strict safety protocols and facility designs to protect staff and the community. Examples of microbes studied in BSL-4 labs include Ebola and Marburg viruses. (DTRA JSTO image)

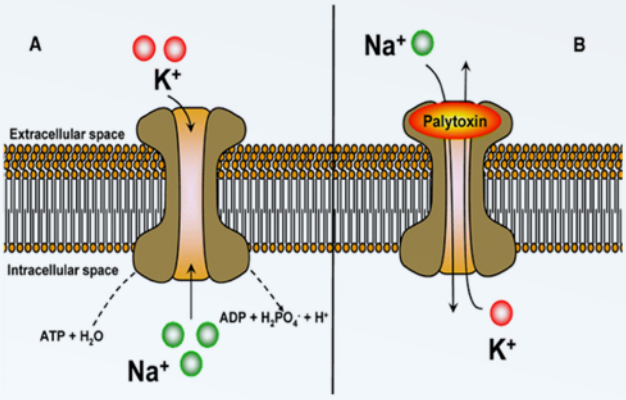
The TAP program brings together subject matter experts in predesignated biothreat areas, or panels, to quickly respond to emerging biothreats, identify knowledge gaps in threat agent science, and assess or maintain unique DoD-owned operational threat characterization capabilities. An incident of companion animal exposure to an unknown toxin shows how the USAMRIID TAP teams, in conjunction with interagency partners, supported the rapid detection and characterization of clinical samples. This opportunity allowed DTRA JSTO to use current characterization capabilities while assessing future needs in personnel, infrastructure, and agnostic methods to be prepared for the full spectrum of biothreats.

USAMRIID TAP received a request from U.S. Food and Drug Administration colleagues to help investigate the death of two companion dogs that reportedly licked rocks containing corals suspected to be contaminated with a marine toxin. The most striking postmortem feature was severe thymic hemorrhage, which is a hallmark of rodenticide toxicity, but this was ruled out by testing. Given the oral exposure to the coral aquarium rocks and other findings during the necroscopic examination, the suspected cause of death was toxicosis by palytoxin (PLTX), which with related compounds are an extremely potent group of marine biotoxins. The toxic activity of PLTX results from the binding to sodium potassium ATPase, converting this critical cellular ionic pump into a nonselective pore with potentially lethal consequences.

Dried zoanthids on rock from Florida companion dog mortality investigation: 300µg to 600µg palytoxin/grams dried zoanthid.

Palythoa *spp. zoanthid collected from a Maryland aquarium store in 2008. 500µg palytoxin/grams wet zoanthid (Deeds et al. 2011)*

...the work highlights the flexibility of DoD capabilities, showing the value the TAP program provides in pre-identifying DoD personnel, using robust DoD capabilities to quickly characterize and counter unknown biological threats, and leveraging inter-agency partners for a coordinated U.S. government response.



(A) Palytoxin (PLTX) and related compounds are an extremely potent group of marine biotoxins. (B) The toxic activity of PLTX results from the binding to sodium potassium ATPase, converting this critical cellular ionic pump into a non-selective pore with potentially lethal consequences. Balanced levels of sodium (Na+) and potassium (K+)—the sodium pump—are essential to muscle contraction and expansion.

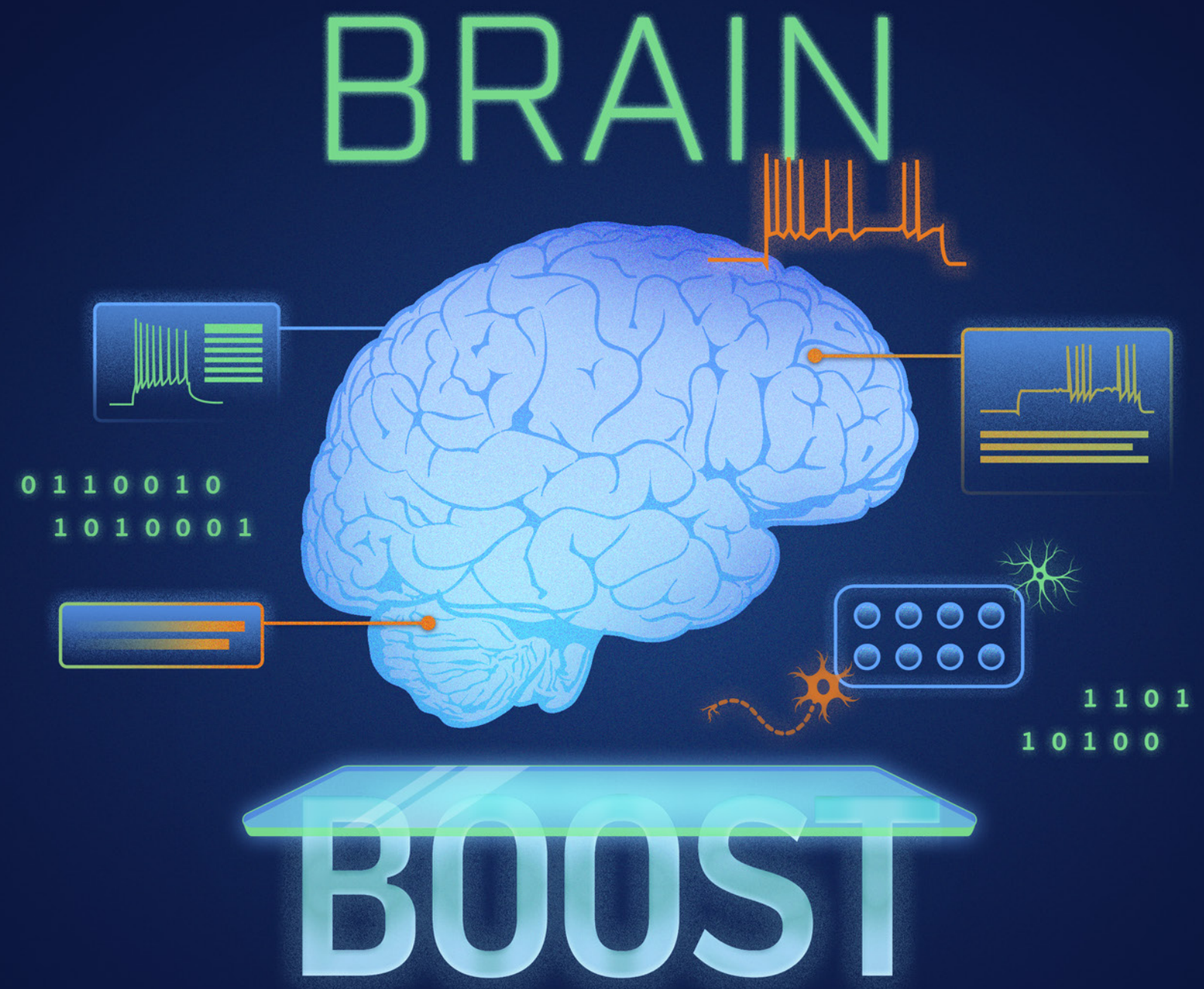
Tissue/Sample	Interpolated PLTX Concentration [µg/mL]
Stomach Content	Not Detected
Liver Blood Sample Dilution	0.18
Kidney Blood Sample 1 Dilution	1.43
Kidney Blood Sample 2 Dilution	0.42
PLTX Control 1:10 Dilution	17.79
Negative Control	Not Detected
Assay Buffer Control	Not Detected

Analysis of stomach content and drained blood samples from tissue using a DTRA JSTO-developed magnetic bead-based sandwich immunoassay detected PLTX at an approximate concentration of 3µg/mL in kidney samples and liver samples. (Results by USAMRIID and DTRA JSTO).

PLTX was confirmed by high performance liquid chromatography and high-resolution mass spectrometry analysis in dried coral samples removed from the rock associated with the exposures. Analysis of the stomach content and blood samples from the livers and kidneys of the deceased dogs revealed levels of PLTX at an approximate concentration of 3µg/mL.

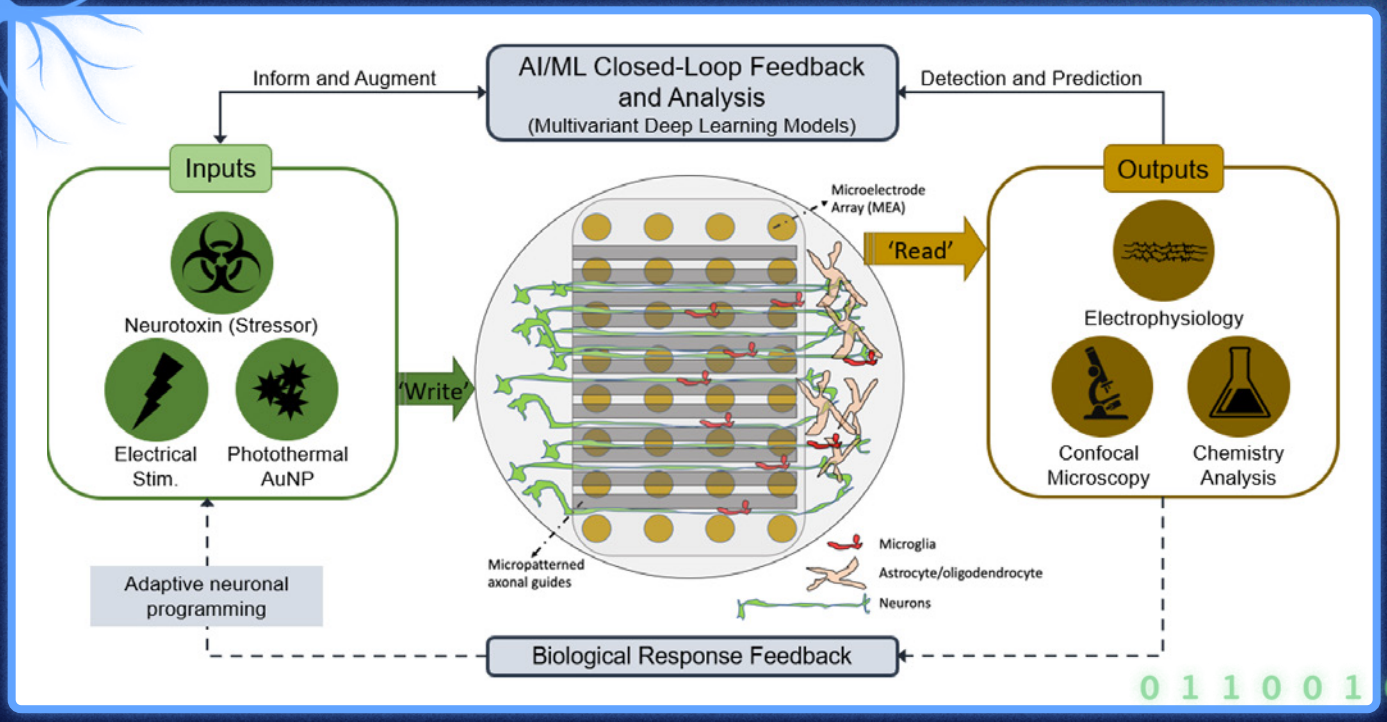
While this case demonstrates a specific veterinary application of diagnostic tools, the work highlights the flexibility of DoD capabilities, showing the value the TAP program provides in identifying DoD personnel, using robust DoD capabilities to quickly characterize and counter unknown biological threats, and leveraging inter-agency partners for a coordinated U.S. government response.

DTRA JSTO's investments in robust threat agent characterization capabilities are vital to national defense and provide key understanding of biological threats critical to detection, diagnostics, and medical countermeasure development. In valuable partnerships with DoD service laboratories, such as USAMRIID, DTRA JSTO provides the Joint Force with the right capabilities to effectively combat an ever-expanding biothreat landscape by limiting technical surprise. ●



Predicting changes to neural activity in asymptomatic cases following exposure to a chemical or biological (CB) threat agent can provide advanced warning to identify and treat at-risk individuals to minimize negative impact to human performance in operational environments. Recent advancements in human organ-on-a-chip technologies that mimic human biomechanics and the physiology of organ systems have enabled researchers to develop minimally invasive means to measure electrophysiological and electrochemical signal data from organoid devices. An organoid is a miniature 3D version of an organ grown in a lab to mimic the structure, function, and complexity of human organs and tissues.

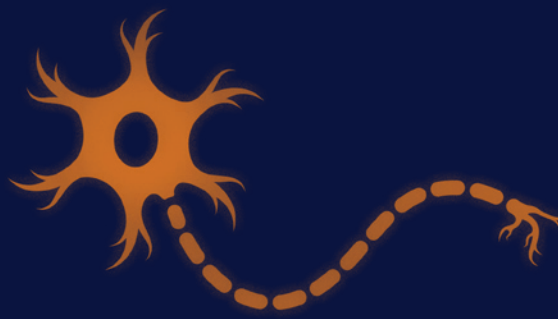
Brain-on-a-chip studies are giving AI/ML algorithms the data they need to harness their predictive capability.



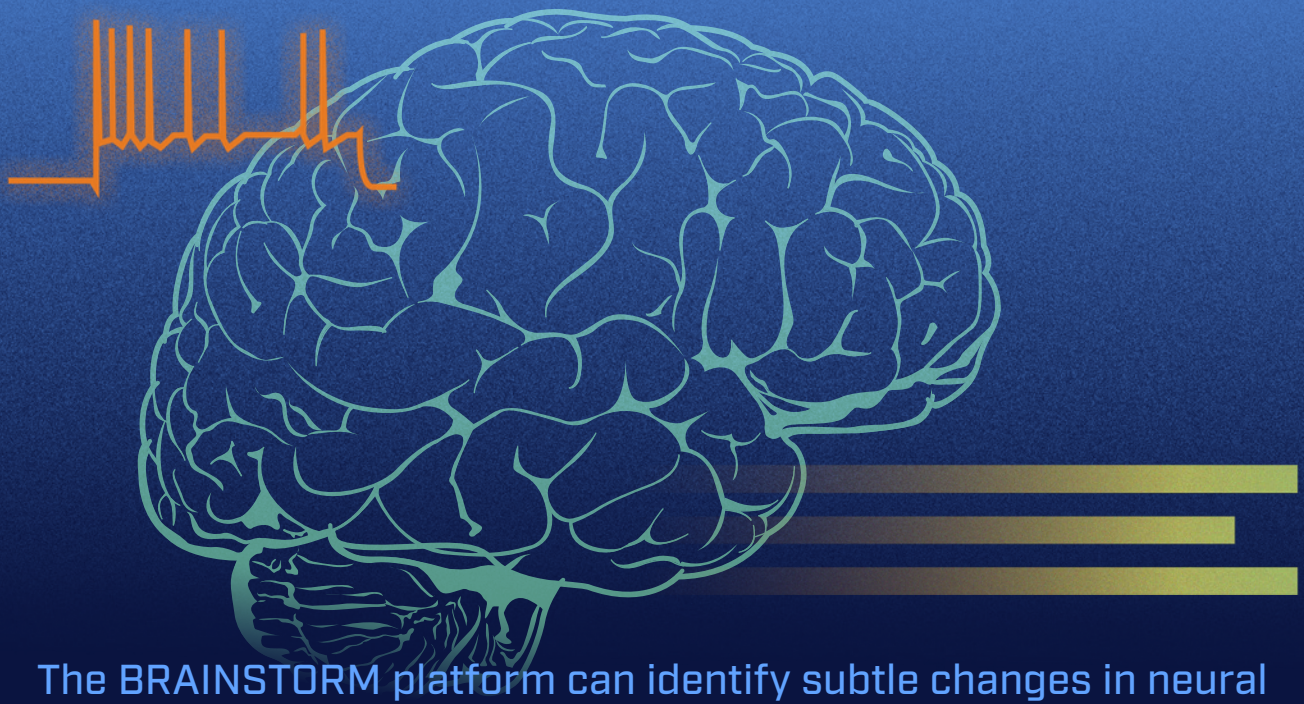
Biomimetic Robotic Architecture for Intelligent Systems and Tissue-Oriented Research and Modeling (BRAINSTORM) uses a brain-on-a-chip platform to evaluate the effects of sublethal doses of a chemical exposure on cognitive neural activity over time by measuring electrical changes in neural activity following exposure to the CB agent. (Image by AFRL)

The deliberate release of a CB agent on the battlefield poses a risk to the operational effectiveness, readiness, and lethality of the Joint Force. Rapid detection of CB threat exposure and the impacts to warfighter health and performance is critical in reducing time to recover, risk to mission effectiveness, and ultimately force lethality. Even nonlethal exposures to CB agents often limit warfighter performance by impacting cognitive neural activity.

Multiple organoids can be combined to form a multiorgan micro-physiological system (MPS) of the human body. Bioelectronic signals from MPS can be analyzed to determine potential adverse health effects of CB exposures to provide dynamic measurements to quantify human performance on the battlefield. When combined with novel computational tools in the domains of artificial intelligence and machine learning (AI/ML), there is an opportunity to classify and reconstruct high-fidelity organoid data to develop ML algorithms able to predict complex cognitive health effect responses within a human system.



This application is one of the drivers for the developing the Integrated Brain-on-Chip for Machine Learning-based Prediction of Warfighter Cognitive Performance (BRAINSTORM) by the Defense Threat Reduction Agency's (DTRA) Chemical and Biological Technologies Department in its role as the Joint Science and Technology Office (JSTO) for Chemical and Biological Defense, an integral component of the Chemical and Biological Defense Program, in collaboration with the Air Force Research Laboratory (AFRL) 711th Human Performance Wing.



The BRAINSTORM platform can identify subtle changes in neural firing patterns that may precede overt symptoms or acute toxicity for identifying potential chemical exposure at sublethal doses.

Existing brain-on-a-chip models provide an advanced platform for detecting and analyzing abnormal neural firing patterns, serving as early indicators of exposure to chemical or biological threats. The BRAINSTORM platform can identify subtle changes in neural firing patterns that may precede overt symptoms or acute toxicity for identifying potential chemical exposure at sublethal doses.

The microfluidics and high-resolution microelectrode array data collected following exposure is also being used by the Naval Research Laboratory (NRL) to develop machine learning models to predict signatures of abnormal neural firing following exposures over time. These computational models derived from brain-on-a-chip data, combined with machine learning techniques, have the potential to predict future exposure scenarios and enable rapid and accurate identification of agents that may have an impact on human performance.

The rapid detection and prediction tools enabled by the integration of the BRAINSTORM platform, developed by AFRL and including ML approaches developed at NRL, offer significant benefits to the Joint Force, our nation, and our allies in terms of efficiency and cost-effectiveness for studying the effects of CB agent exposures on representative human systems.

By harnessing the power of predictive capability, this technology has the potential to provide decision makers with timely and relevant information, minimize impact of chemical exposure to operations, and drive innovative mitigation strategies to maintain warfighter health, performance, and readiness. These advancements by DTRA JSTO will improve the safety, preparedness, and operational effectiveness of military personnel, reducing the risk of cognitive impairment, and enhancing mission success. ●

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Within the Defense Threat Reduction Agency's Research and Development Directorate resides the Chemical and Biological Technologies Department performing the role of Joint Science and Technology Office for Chemical and Biological Defense, an integral component of the Chemical and Biological Defense Program. This publication highlights the department's advancements in protecting the Joint Force, our nation, and allies from chemical and biological threats through the innovative application of science and technology.

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