JSTO in the News

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April 2022 | Vol. 12 No. 3

The Sum is Greater Than Its Parts

Keeping the Powder Dry

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CHEMICAL AND BIOLOGICAL TECHNOLOGIES DEPARTMENT MISSION

Lead DoD science and technology to enable the Joint Force, nation, and our allies to anticipate, safeguard, and defend against chemical and biological threats.

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Research and Development Directorate
Chemical and Biological Technologies Department
Joint Science and Technology Office for the
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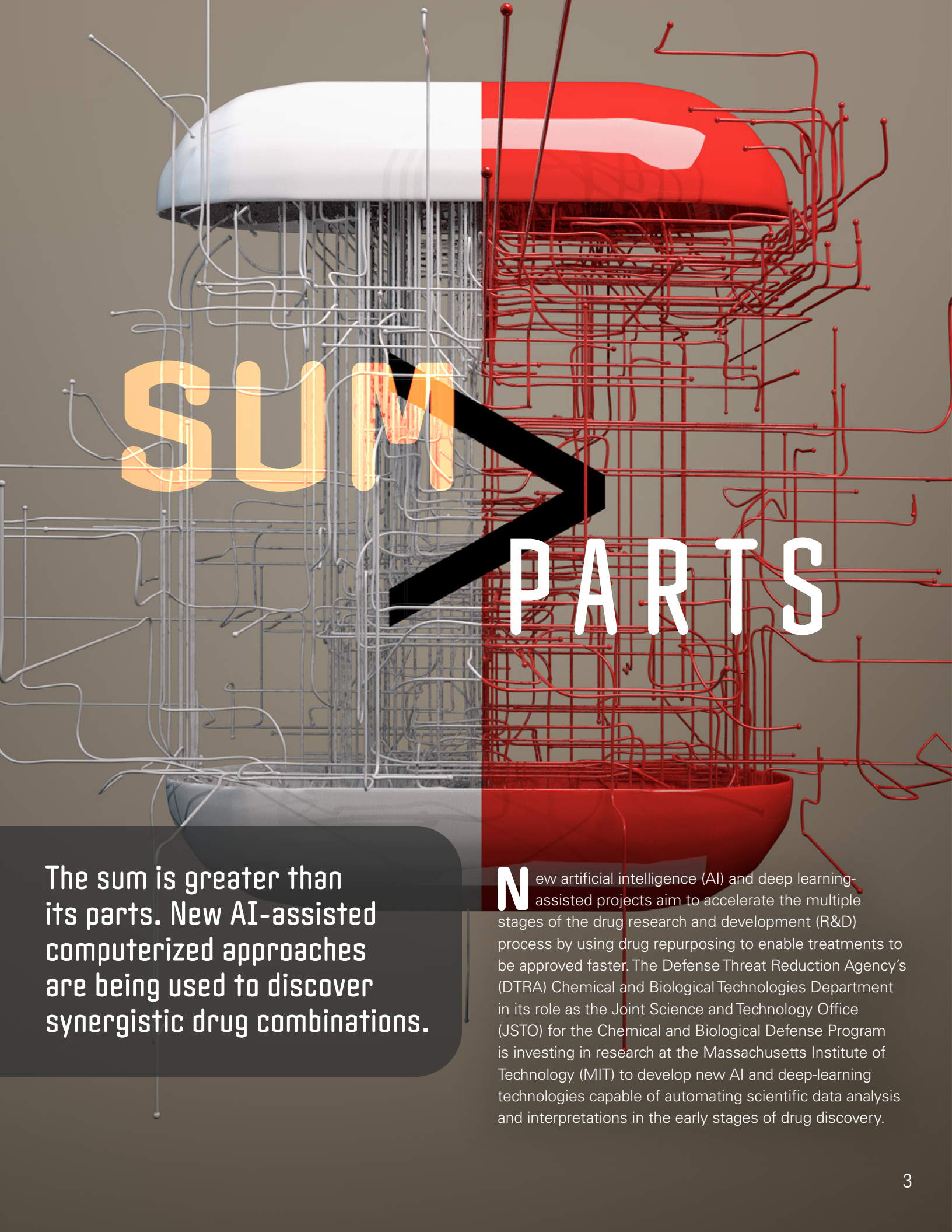
Front cover: The Innovations Automated Robotics Dispensing System, also known as "Roberta," counts medication and fills a prescription bottle. Roberta guarantees safety by using barcode technology to ensure the prescriptions are properly filled. (U.S. Air Force photo by Caleb F. Butler)

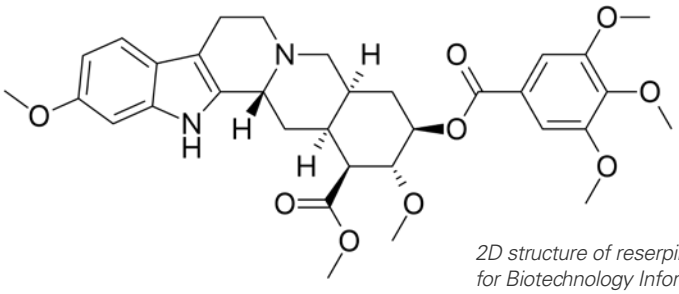
Inside cover: U.S. Air Force Staff Sgt. Sarah Walser demonstrates the use of a reactive skin decontamination lotion sponge at a chemical, biological, radiological, and nuclear defense training facility. (U.S. Air Force photo by John R. Wright)

Back cover: Tech. Sgt. Hannah Harris processes prescriptions at Kadena Air Base, Japan. The pharmacy fills 86,000 prescriptions annually. (U.S. Air Force photo by Yosselin Perla)



The sum is greater than its parts. New AI-assisted computerized approaches are being used to discover synergistic drug combinations.

New artificial intelligence (AI) and deep learning-assisted projects aim to accelerate the multiple stages of the drug research and development (R&D) process by using drug repurposing to enable treatments to be approved faster. The Defense Threat Reduction Agency's (DTRA) Chemical and Biological Technologies Department in its role as the Joint Science and Technology Office (JSTO) for the Chemical and Biological Defense Program is investing in research at the Massachusetts Institute of Technology (MIT) to develop new AI and deep-learning technologies capable of automating scientific data analysis and interpretations in the early stages of drug discovery.



2D structure of reserpine. (National Center for Biotechnology Information image)

Recently, the U.S. Government supported accelerated COVID-19 therapeutic drug trials, and investigators began a rigorous selection process of the vast number of candidate drugs with potential benefits. Scientists have made significant progress in treating presymptomatic and early stage COVID-19 cases using repurposed drugs, such as molnupiravir that DTRA-JSTO had invested in for development as a Venezuelan equine encephalitis virus treatment; however, more advanced tools are needed to prioritize drugs and predict repurposed drug combinations that can be beneficial across all disease stages.

Advanced AI combined with deep learning will automate repurposed drug prioritization with increasing sophistication and reduce the need for hands-on, time-consuming experimentation. The drug-development process normally lasts years, and sometimes decades, beginning with a discovery phase, progressing to R&D, testing in human clinical trials, and then achieving FDA approval if the drug is shown to be safe and effective. The ongoing COVID-19 pandemic illustrates how critical it is to reduce timelines at each stage of drug-development from decades or years to months or weeks.

For medical personnel, an indication—a sign, symptom, or medical condition—leads to their recommendation for a treatment, test or procedure. Researchers explore drug repurposing to discover new disease indications for pharmaceuticals that have already been tested in clinical trials so they can skip most of the safety and toxicity testing already completed. The MIT research team has gone a step further than others in this field by developing a new AI-assisted computerized approach for discovering drugs that work together with increased effectiveness, or synergism, to alleviate COVID-19 symptoms. They described their approach in a recent article, "Deep learning identifies synergistic drug combinations for treating COVID-19." (See link in sidebar on page 5.)

Remdesivir is a broad spectrum anti-viral drug used to treat COVID-19 infection as well as high blood pressure. (Gilead Sciences, Inc. photo)

Synergistic drug combinations are frequently used to treat many diseases, including cancers, asthma, diabetes, hypertension, cardiovascular disease, and some infectious diseases like HIV, viral hepatitis, and tuberculosis. The "one bug, one drug" development approach has a low historical success rate for treating infectious diseases. By contrast, discovering synergistic drugs that act on the infected human, rather than just on the bug, has potential for treating more than one infectious disease.

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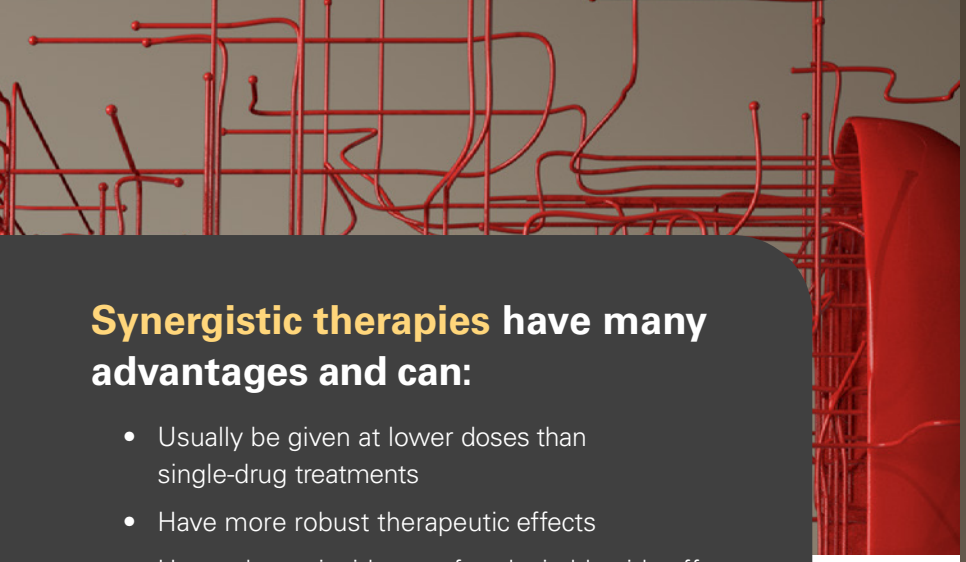


Synergistic therapies have many advantages and can:

- Usually be given at lower doses than single-drug treatments
- Have more robust therapeutic effects
- Have a lower incidence of undesirable side effects
- Reduce the likelihood of developing single-drug resistance in viral and bacterial infections

Current machine-learning approaches have limited capacity for predicting drug combinations for emerging diseases because they require large quantities of data, like those for cancer and diabetes. This amount of data is not readily available for most infectious diseases and to a lesser extent for emerging diseases such as COVID-19. Even less data is available from drug-combination screening studies, making it difficult to discover synergistic treatments.

To address the lack of available data for infectious and emerging diseases, computer scientists at MIT developed new deep-learning methods and created a drug-prediction tool named ComboNet that improves drug-target and drug-drug synergy predictions. ComboNet can perform the following actions with better accuracy than preexisting tools and can predict:

- If a drug binds to a specific biological target
- Each drug's antiviral activity
- How two drugs interact

The MIT computer scientists used ComboNet to identify two new drug combinations that could be used to combat COVID-19: (1) remdesivir plus reserpine, and (2) remdesivir plus IQ-1S. Recently, the FDA expanded approval for using remdesivir to treat patients 28 days of age and older, including those both hospitalized and not hospitalized, for mild-to-moderate COVID-19. Remdesivir has FDA approval for treating high blood pressure. IQ-1S is an experimental drug. In cell viability experiments, both combination medicines demonstrated potent SARS-CoV-2 antiviral activity.

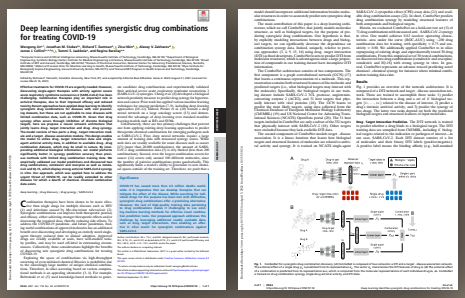
The new machine-learning method and ComboNet drug prediction tool enables scientists to rapidly identify new combination treatments for emerging infectious diseases with greater accuracy than previous tools, which will help minimize the health impacts of infectious diseases and biological warfare threats to the Joint Force. ●

U.S. Government supported accelerated COVID-19 therapeutic drug trials

NIH

Click here to learn more

Proceedings of National Academy of Sciences "Deep learning identifies synergistic drug combinations for treating COVID-19"


Deep learning identifies synergistic drug combinations for treating COVID-19

Click here to learn more

KEEPING THE DRY

Researchers are developing new immediate skin decontamination prototype devices for the Joint Force with the goal of having fewer logistical and operational limitations and a lower cost than the Reactive Skin Decontamination Lotion (RSDL) Kit that is part of regularly issued decontamination equipment. The Defense Threat Reduction Agency's (DTRA) Chemical and Biological Technologies Department in its role as the Joint Science and Technology Office (JSTO) for the Chemical and Biological Defense Program is working with the U.S. Combat Capabilities Development Command Chemical Biological Center (DEVCOM CBC), the University of Hertfordshire in the United Kingdom, and industry partners to develop and test improved, low-cost, skin decontamination prototype devices.

Dry powders could outpace lotions for a readily available, shelf-stable chemical decontaminate for anywhere in the field.

Zirconium hydroxide powder is an inexpensive, commercially available chemical that does not dissolve in water and can absorb and reactively destroy chemical agents.

A soldier in MOPP 4 protective equipment tests for chemical agents to confirm the area is decontaminated after a chemical attack at the National Training Center in Fort Irwin, Calif. (U.S. Army photo by Capt. Katherine Zins)

During a chemical warfare agent (CWA) attack, Joint Force members enter what is called Mission Oriented Protective Posture (MOPP) 4 by donning a complete set of protective garments including a mask, overgarment, boots, and gloves. Getting into this apparel takes time and risks skin exposure to dangerous chemical agents. If warfighters contact chemical agents, they must immediately decontaminate their skin to minimize any hazardous health effects and continue their mission. Currently, the Joint Force can effectively decontaminate nerve and blister agents on skin using RSDL, but it has a limited shelf life, restrictive storage requirements, and high cost.

The new skin decontamination prototype will be designed to overcome current logistical and operational limitations by likely having a longer shelf life, unrestrictive storage requirements, and improved immediate decontamination for the full spectrum of CWAs on skin. Other research seeking improved solutions for wound decontamination in separate but parallel efforts may overlap or complement the skin decontamination prototypes.

DEVCOM CBC and the University of Hertfordshire began testing candidate materials for an improved skin decontamination solution and saw that zirconium hydroxide powder efficiently neutralized chemical agents, which led the research team to choose it to develop for prototype devices. Zirconium hydroxide powder is an inexpensive, commercially available chemical that does not dissolve in water and can absorb and reactively destroy chemical agents. DTRA-JSTO has successfully used zirconium hydroxide powder to develop new chemical filters and equipment decontaminants.

Researchers are investigating zirconium hydroxide by measuring the amount of chemical agent absorbed and destroyed by the powder or released into the environment (called off-gassing) to determine exactly how much powder is needed for effective decontamination and compatibility with current Joint Force equipment. Experiments include using laboratory skin surrogates and specialized chambers called diffusion cells, which measure the amount of chemical agent that penetrates skin, and the efficiency of removal by prototype

Air Force Reserve Staff Sgt. Casey Godwin, aircrew flight equipment specialist, 327th Operations Support Squadron, pats down Staff Sgt. Michael Hopson, loadmaster, 327th Airlift Squadron, with activated charcoal from an M295 Individual Decontamination Kit during a training scenario. (U.S. Air Force photo by Master Sgt. Jeff Walston)

technologies. The researchers will study zirconium hydroxide powder performance in laboratory-simulated extreme hot and cold environments.

Current research is looking at how much loose zirconium hydroxide powder applied to the skin is needed for thorough decontamination. The goal is to use the zirconium hydroxide powder in a form, such as the M295 mitt, for immediate decontamination of exposed skin with similar results as the loose powder. A prototype mitt can be used immediately to absorb chemical agents from skin and reactively destroy CWAs, providing improved immediate decontamination in all environmental conditions, and enabling safe and easy disposal of the mitt.

The next phase of the project is to develop prototype devices using zirconium hydroxide that can be readily used by the Joint Force, potentially including mitts, wipes, and gloves. Industry partners will design prototypes that can:

- Be stored, carried, and used in a variety of operational environments
- Rapidly absorb CWA gross contamination within 2 to 15 minutes
- Neutralize the CWAs

DTRA-JSTO will present this new skin-decontamination concept at the 2022 Chemical Biological Operational Assessment Concept Tent to collect warfighters' feedback on the design of an ideal form and its use in terms of time requirements and application methods.

The decontamination effectiveness and safety data produced from this program will support companies submitting a medical device application to the U.S. Food and Drug Administration for consideration and approval. ●

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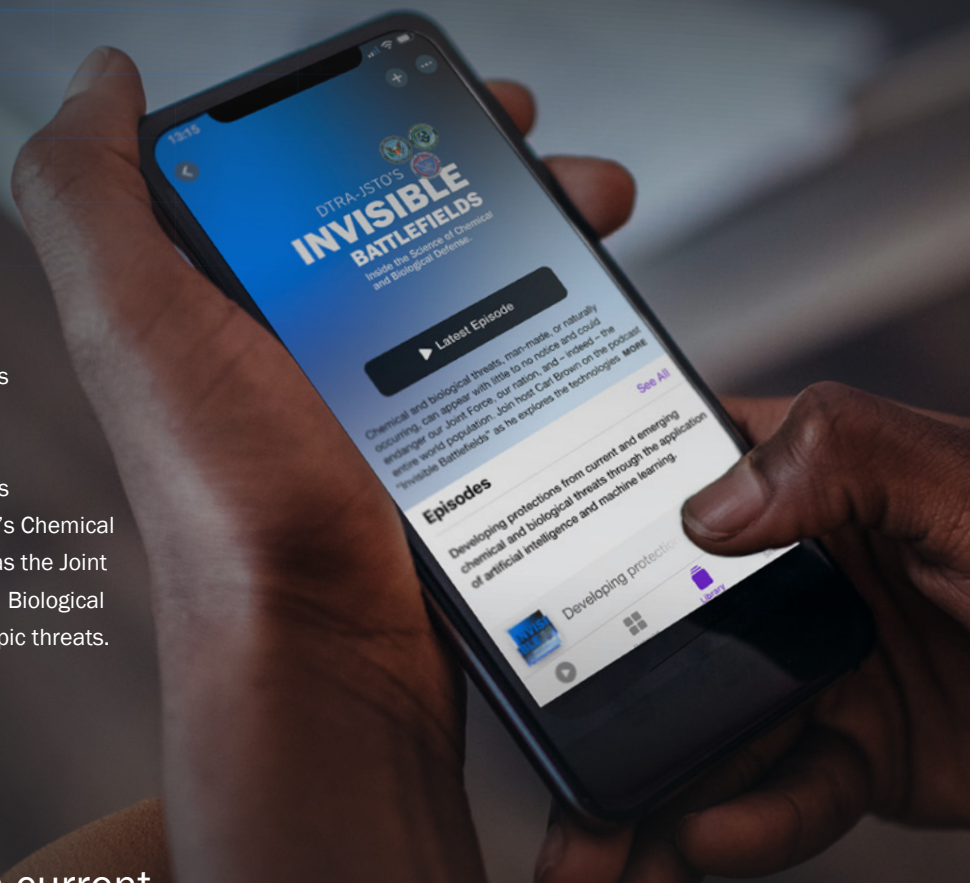
Invisible Battlefields: Inside the Science of Chemical and Biological Defense



Invisible Battlefields is a podcast meant to engage with the Chemical and Biological defense community and is another platform providing a voice highlighting the continuous collaborations that the DTRA-JSTO program explores with industry partners, academia, and other government agencies concerning chemical and biological threats and protecting our Joint Force against them.

Join host Carl Brown as he explores the technologies developed by the Defense Threat Reduction Agency's Chemical and Biological Technologies Department in its role as the Joint Science and Technology Office for the Chemical and Biological Defense Program to protect against these microscopic threats.

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EPISODE 01

Developing protections from current and emerging chemical and biological threats through the application of artificial intelligence and machine learning.

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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 the Chemical and Biological Defense Program. This publication highlights the department's advancements in protecting the Joint Force and citizens from chemical and biological threats through the innovative application of science and technology.

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