THE DISPATCH

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DTRA Helps Fight Ebola Outbreak

An ariel view of one of the Transportable Laboratories provided by DTRA to help fight the Ebola outbreak in Guinea, Sierra Leone and Liberia. DTRA has provided 10,000 sets of personal protective equipment (PPE) for health care workers to help stem the disease's spread, as well as providing additional assistance (labs, diagnostic equipment, etc.) to these countries. (Photo courtesy of DTRA)

In This Issue

J10 - DTRA's Newest Directorate

DTRIAC recently interviewed BG Otey about the stand-up of J10 and his assignment as Director of J10.

▶ 1) How does J10 help "Make the World Safer"?

The establishment of the Nuclear Enterprise Support Directorate (J10) fulfills a commitment Director Myers made in November 2014 "…to elevate and increase our focus on our nuclear mission so that we meet the expectations of the recently completed DoD Nuclear Enterprise Review." The men and women of the Defense Threat Reduction Agency, USSTRATCOM Center for Combating WMD, and Standing Joint Force Headquarters for Elimination (i.e., the "ONE Team") came together to plan, coordinate, and work necessary actions to achieve J10's initial operational capability (IOC) in February 2015 and full operational capability (FOC) in May 2015.

Every day J10 helps secure and strengthen our nation's nuclear deterrent with capabilities stemming from a diverse program portfolio. These capabilities include, but are not limited to: nuclear safety and security policy support; executing a wide array of stockpile logistics activities; technical inspection training and oversight; education and training; nuclear and radiological detection; exercises; and detailed facility and mission assessments. Our nuclear support mission is not exclusive within the

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Obtaining a STARS account

In order to obtain access to the Defense Threat Reduction Agency's (DTRA) Scientific and Technical Information Archival and Retrieval System (STARS), contact STARS Customer Support at the Defense Threat Reduction Information Analysis Center (DTRIAC) at 505-853-0854 or via e-mail at DTRA-DTRIAC@mail.mil and you will be provided with a STARS User Account Request form. Prior to completing the form and submitting it, you must ensure you meet a number of requirements. You must:

- Be a U.S. citizen
- Hold a FINAL DoD Secret, Top Secret Clearance or DOE L/Q Clearance (Interim clearances are not eligible)
- Be able to provide clearance information to the DTRA in the form of a visit request (not required of DTRA CIV or MIL personnel)
- Obtain DTRA sponsorship (not required of DTRA CIV or MIL personnel)

J10 - DTRA's Newest Directorate

• *Continued from page 1*

ONE Team, and, as such, we have sought ways to deepen ties with other nuclear-focused organizations (e.g., Nuclear Technologies).

▶ 2) What are your short-term and long-term plans/goals for J10?
Our focus and primary goal is to do our part to support and improve the safety, security and effectiveness of U.S. nuclear resources as DoD seeks to implement a multitude of recommendations from two extensive 2014 Nuclear Enterprise Reviews. Our longer term goal is to continually assess our capabilities, and, as needed, recommend any organizational changes and/or resource realignments to ensure that we execute our programs in the most effective and efficient manner possible.

▶ 3) What do you want people to know about J10's mission?
I think our mission statement best describes what we "do" in a succinct manner. Specifically, we "provide nuclear enterprise support to the DoD and Interagency stakeholders to ensure the safety, security, and effectiveness of the U.S. nuclear deterrent force, and support to countering weapons of mass destruction threats to the United States, allies and partners to make the world safer." To do this we execute the following programs:

- Nuclear Surety;
- Stockpile Logistics;
- Defense Nuclear Weapons School;
- Nimble Elder (e.g. Technical Support Groups);
- Defense Nuclear Surety Inspection Oversight;
- Nuclear Weapon Accident and Incident Exercises;
- Balanced Survivability Assessments;
- DoD Red Team Assessments;
- Joint Staff Integrated Vulnerability Assessments (note: transitioning to Joint Mission Assurance Assessments in FY16); and
- Foreign CBRNE Exercises

▶ 4) Do you have anything else you would like to add?
I am very fortunate to get to work with the outstanding men and women of the J10 and it continues to be a gratifying experience– we have a team of highly qualified and dedicated professionals working on the tough challenges facing the nuclear enterprise in the coming years. I look forward to continuing our important work in concert with nuclear enterprise stakeholders across DoD and the Interagency to build relationships and accomplish the mission.

FROM THE DTRIAC PROGRAM MANAGER

In this issue of the DTRIAC Dispatch we explore the exciting work done by the Chem-Bio Research personnel at DTRA. We discuss Stealth Nanogels, Novel Protein Therapeutics, Rapidly Shapeshifting Polymers and Plastics, Synthetic Catalytic Material, Synthetic Biology and Quorum Sensing.

With the stand-up of the J10 – Nuclear Enterprise Support Directorate, DTRIAC interviewed its Director, Brig Gen Gregory Otey. General Otey provides insight into the unique role this directorate fulfills within the Nuclear Enterprise.

If you have written an article you would like to have published in the Dispatch or have any questions or comments related to DTRIAC, please e-mail us at DTRA-DTRIAC@mail.mil.

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Harnessing Synthetic Biology to Combat Bacterial Pathogens

Developed in the 1940s, antibiotics are powerful medicines used in the treatment and prevention of bacterial infection to save lives. Yet every year approximately two million people in the United States are treated for a bacterial infection that is resistant to antibiotics. These antibiotic-resistant infections result in an average of more than 20,000 deaths annually.

In addition to posing a threat to the civilian population, antibiotic-resistant bacteria, such as plague or smallpox, are highly contagious and could be used as a biological weapon to thwart our military forces. Thus, the arms race against antibiotic-resistant bacteria necessitates a new generation of antimicrobial therapies that must destroy microbes while considering the secondary effects associated with their use.

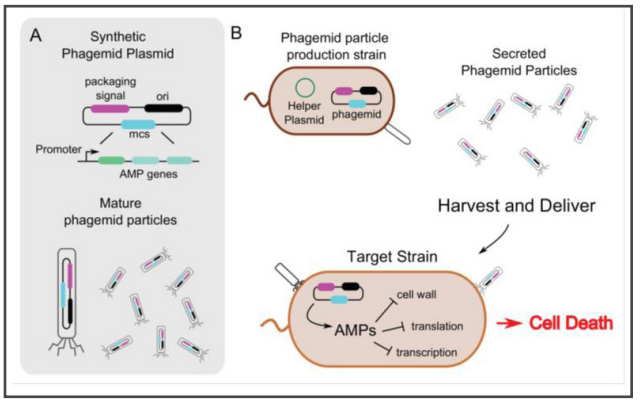
Research funded by the Defense Threat Reduction Agency's Chemical and Biological Technologies, managed by DTRA's Dr. Ilya Elashvili and conducted by Dr. James Collins from the Massachusetts Institute of Technology, developed a delivery system for the next generation of antimicrobial therapies.

Their work, recently published in *Nano Letters* entitled *"Engineered Phagemids for Nonlytic, Targeted Antibacterial Therapies,"* holds promise as a synthetic biology platform that can be rapidly adapted to deliver targeted antimicrobial therapies to counter multi-drug resistant bacteria.

Traditional antimicrobial therapies employ broad-spectrum antibiotics that indiscriminately kill bacteria, often breaking down the cell membrane through a process called lysis. Such techniques create harmful secondary effects including the release of toxic intracellular intermediates and destroying the natural microbial flora. Antimicrobial peptides (AMPs) are an attractive alternative to broad-spectrum antibiotics because they kill bacteria without inducing lysis.

To maximize this non-lytic effect, AMPs must be expressed in situ, thereby overwhelming the microbe's intercellular machinery and rapidly shutting down the cell. Researchers have often used bacteriophages for delivery of synthetic biology constructs in situ, and though effective, they are too unreliable to be widely used as a delivery system for alternative therapies.

Dr. Collins and his team improve on AMP and bacteriophage therapy through the use of phagemids plasmids that contain the f1 origin that can be used as a cloning vector, enabling their packaging and delivery by mature M13 bacteriophage particles. A quirk in M13 biology enables expression of virus particles that lack the ability to reproduce, while retaining the ability to infect cells with their DNA. Once delivered, a phagemid plasmid can replicate inside the targeted bacteria, ensuring high expression levels of AMPs.



Engineered phagemids as a modality for delivery of AMP expression vectors to microbes for induced cell death. (A) Phagemids are plasmids that can be encapsulated and transmitted by bacteriophage particles. As a plasmid, the phagemid can be engineered to accommodate the expression of multiple AMPs, a stable replication in the host strain, and the packaging signal for a specific bacteriophage. (B) A phagemid particle production strain secretes replication incompetent mature phagemid particles that contain phagemid DNA. When applied to a target strain, these mature phagemid particles transfect a target strain population with the phagemid for the specific induction of cell death. Figure developed by Dr. James Collins under DTRA-funded research. (Image courtesy of DTRA funded research)

Additionally, the lack of viral particle reproduction with phagemids prevents resistance to infection in the target cell. This is a critical improvement over traditional bacteriophage therapies where transfected vectors were often unstable and easily rejected by the host. By harvesting and applying M13 phagemid particles containing antimicrobial expressing phagemid plasmids, a target cell population can be converted into an antimicrobial factor system that induces rapid, nonlytic cell death.

Collins and his team compared the ability of a phagemid expression system to the traditional bacteriophage therapy to induce cell death. They transfected E. coli bacteria with phagemid or conventional bacteriophage vectors containing single AMP expression systems known to kill, but not lyse the bacteria.

The survival of cells infected by phagemid particles was reduced by at least an order of magnitude when compared to the survival of cells infected by the conventional bacteriophage vector. Critically, cells infected with the phagemid remained dead throughout the course of the experiment whereas cells infected by the bacteriophage vector began to recover after four hours.

By combining the expression of multiple AMPs on a single phagemid, the researchers enhanced the induction of cell death by another order of magnitude. As an additional benefit, they demonstrated that cells infected by phagemid particles can also be re-infected for additional treatment, unlike conventional bacteriophage therapy where transfected cells gain resistance.

After testing their system in vitro, the authors tested their system in vivo through mice. Mice were infected with E. coli and either treated with AMP expressing phagemid particles or left untreated as a control. The results show that 80 percent of mice treated with AMP expressing phagemid particles survived infection, compared to a 27 percent survival rate in untreated mice. The authors suggest that application of their phagemid platform, in addition to inducing expression of AMPs, may also induce a pro-inflammatory response that further enhances the fight against infection.

Dr. Collins and his team envision phagemids as a platform for delivering the next generation of antimicrobial therapies that can be easily modified to include expression of alternative AMPs, origins of replication and signals to counter new challenges in antimicrobial therapy and target infections. Their work will help realize the full potential of antimicrobial peptides and bacteriophage therapy, protecting the warfighter against antibiotic-resistant microbes.

Novel Protein Therapeutics Reduce the Threat of Deadly Chemical Agents

New research could be used to design cutting-edge protein therapeutics, including those with the ability to catalytically degrade chemical and biological agents. This would enable the warfighter to quickly detect and neutralize harmful agents and save countless lives.

In a project managed by Dr. Ilya Elashvili from the Defense Threat Reduction Agency's Chemical and Biological Technologies, researchers Dr. David Baker from the University of Washington and Dr. Peter G. Schultz from the Scripps Research Institute, used computational protein design methods to engineer a protein that can stay in a prolonged unnatural state.

One strategy proteins use to achieve catalysis is the stabilization of fleeting, high-energy substrate conformations called transition states, which have lifetimes that are less than one billionth of a second. Because the orientations of many protein side chains must be precisely tuned to accomplish this feat, the design of proteins with novel catalytic abilities represents a daunting challenge.

However, in a recent development, a protein with the ability to kinetically stabilize the conformational transition state of the non-canonical amino acid biphenylalanine was reported. In the article, "*Trapping a Transition State in a Computationally Designed Protein Bottle,*" recently published in *Science*, describes the iterative computational and experimental approach that was utilized to achieve this goal.

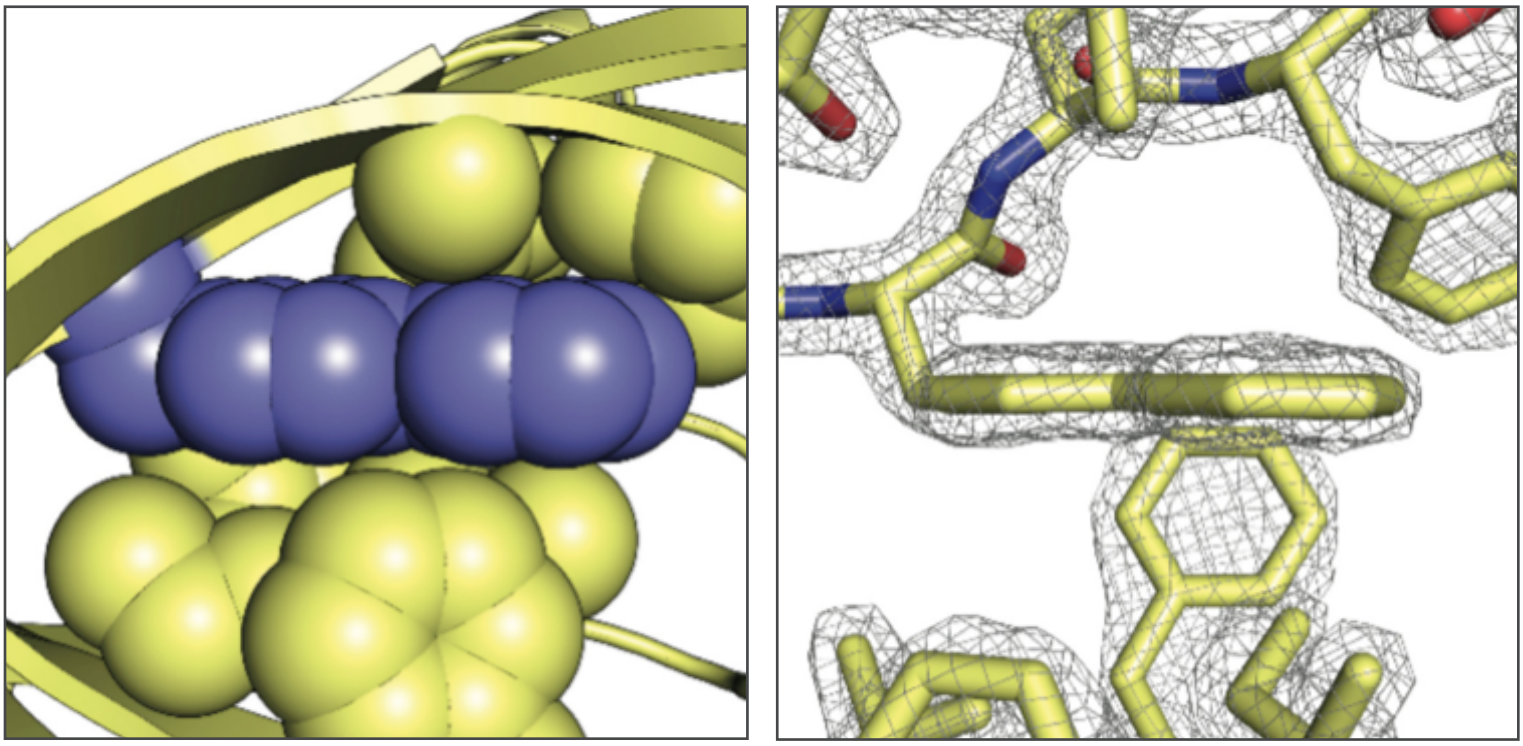
The design strategy was inspired by an earlier, DTRA-supported finding from Dr. Baker reported in the Journal of the American Chemical Society, in which researchers constructed proteins with metal-binding sites containing non-canonical amino acid with atomic level accuracy using computational modeling methods.

Researchers computationally searched approximately 2,300 protein scaffolds of known structure from thermophilic organisms to identify where the biphenylalanine amino acid could be placed within the protein core.

The cores of the candidate proteins were then computationally redesigned to have high complementarity to a model of the non-canonical amino acid in a high-energy, planar conformation. If the team could model this difficult objective, it would pave the way to design and construct proteins that fold into predefined 3-D structures with superb precision.

X-ray crystallographic analysis of one of the designed proteins indicated that the researchers had partially stabilized the desired conformation. This structure was used for further modeling. After two additional rounds of computational and structural analysis, a variant of the original designed protein was identified in which the side chain of the biphenyl amino acid was constrained to exist in a planar conformation. This result is remarkable because the research team reported a crystal structure of a species that normally has a lifetime of less than a billionth of a second.

While the energy of the disfavored biphenyl conformation stabilized in this study is lower than that found in most enzymes, the authors highlight that the protein design from this study can be applied to future enzyme design efforts. The ability to routinely design enzymes with desired functionality could have far-reaching impact for the Department of Defense, enabling stronger detection neutralization of chemical and biological threats the warfighter may face.



A trapped transition state of bond rotation about the central bond of biphenyl is illustrated. On the left, computationally designed packing interactions (yellow spheres) between the core of a protein and the non-canonical amino acid biphenylalanine (blue spheres) are shown. The right panel shows electron density surrounding the planarized biphenyl side chain and surrounding residues. (Image courtesy of Dr. David Baker, University of Washington)

The Next Superpower: New Rapidly Shapeshifting Polymers and Plastics

If you could have any superpower would it be X-ray vision like Superman or lightning speed like The Flash? What about shapeshifting powers like Mystique? You may not be able to pick a power such as one of these, but recently discovered polymers can. Research funded by the Defense Threat Reduction Agency, and conducted by Dr. Scott T. Phillips at Pennsylvania State University, is exploring how shapeshifting polymers and plastics can be utilized to protect the warfighter from the release of toxic chemical agents.

Future detection, identification and medical countermeasure technology capabilities may soon have significant increases in performance and applications due to these shapeshifting polymers and plastics.

Applications for this technology range from plastics that easily alter their size, shape, structure, surface properties, or function to those that detect exposure to target analytes or form the basis of smart capsules for medical applications.

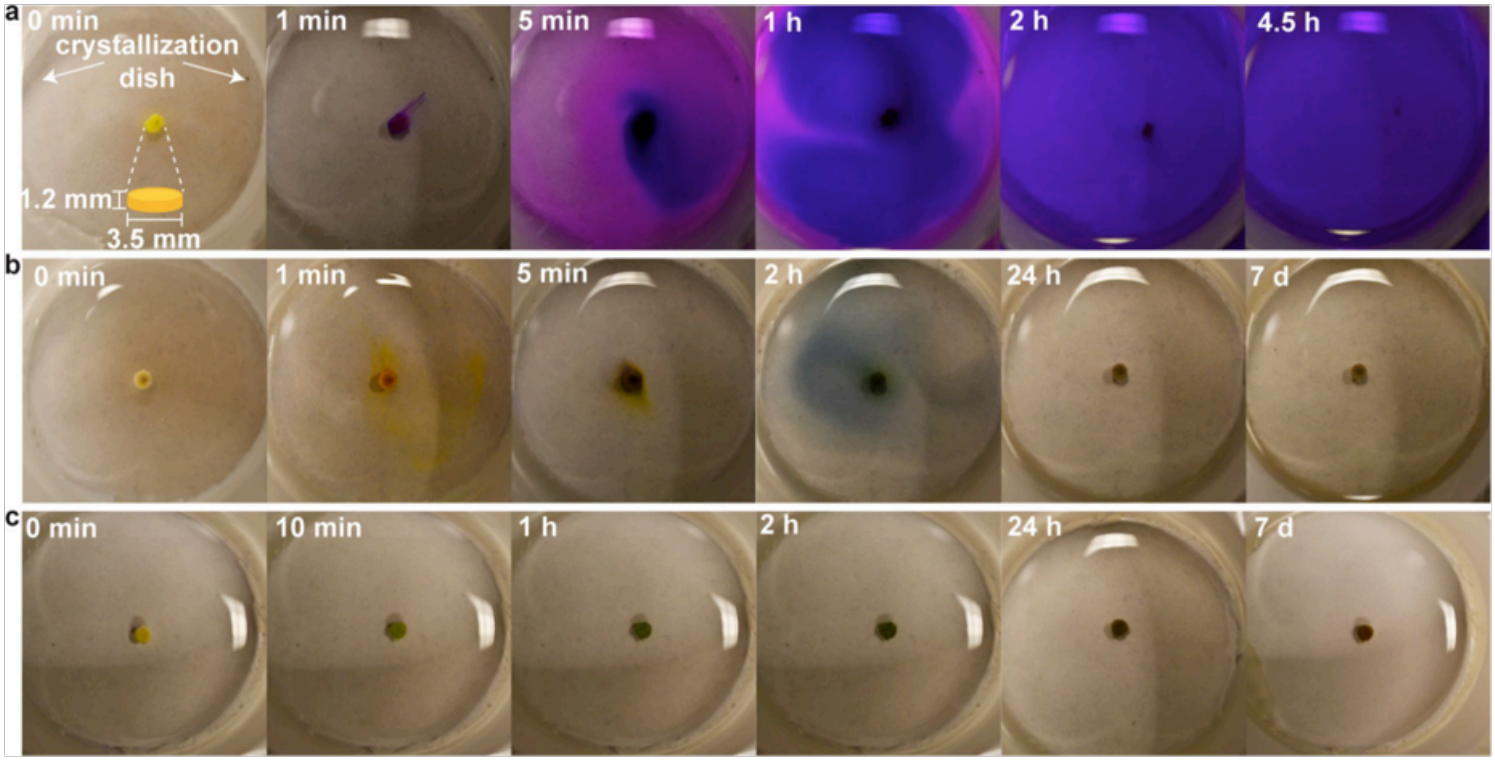
Managed by Dr. Brian Pate, DTRA Chemical and Biological Technologies, Dr. Phillips and his team continue to research the development of self-immolative continuous depolymerization (unzipping) reaction (CDr)-based detection unit polymers. CDr polymers, so named for their behavioral or reactive characteristics, are capable of undergoing continuous and complete depolymerization once the target molecule comes in contact with the polymer trigger or initiation site.

Next, the depolymerization proceeds throughout the entire macroscopic polymeric object until it reaches completion. This reaction is similar to the effect that occurs when an automatic weapon is fired. A finger, or the chemical agent, is placed on the trigger, the target molecule. The pressure applied by an operator's finger on the trigger initiates the chain reaction that empties the magazine due to the spring mechanism that holds the bullets in place. However, instead of bullets, the polymer unzips when it touches the zipper, reacts and is neutralized.

By capitalizing on this strategy to incorporate or tailor the appropriate detection unit (trigger point) design on the polymer, and incorporating the appropriate repeating polymeric unit (referred to as "bullets"), researchers are able to ensure the responding signal induced depolymerizaiton reaction is continuous, complete and provides an amplified response. This ameliorates the previous issues caused by too few detection units that resulted in the rate limiting step in responses for this type of macro plastics.

In addition to this research significantly expanding our knowledge of relationships between reactivity and directed transport in response to specific analyte signals, CDr polymers may be further engineered for specific protective responses such as countermeasures that neutralize chemical and biological agents or trigger another synthetic or biological component to neutralize the threat. Once fully engineered, the polymers could be used for a variety of applications, including protective coatings in warfighter's uniforms to neutralize harmful agents, or for a smart medical application that can release an antidote to harmful ingested agents.

Details of this recent success are published in a *Journal of the American Chemical Society* article *"Surface-Accessible Detection Units in Self-Immolative Polymers Enable Translation of Selective Molecular Detection Events into Amplified Responses in Macroscopic, Solid-State Plastics."*



Photographs showing selective depolymerization at the solid–liquid interface using solvent-cast disks of polymer. (Image courtesy of Dr. Scott Phillips, University of Pennsylvania)

Synthetic Catalytic Material Enables Rapid Destruction of the Nerve Agent Soman

Large-scale chemical weapons have been used for more than 100 years, but the August 2013 attack during the ongoing Syrian conflict highlighted the deadliness of these chemical agents. While it is not clear exactly how many died in the attack, a U.S. government assessment estimated more than 1,400 people perished due to the chemical warfare agent (CWA) sarin. It was the deadliest use of chemical weapons since the Iran-Iraq war. As is evident, to create mass causalities and chaos, an enemy simply needs to release a CWA in a public place or military installation.

To preemptively combat sarin and other CWAs, the Defense Threat Reduction Agency's Chemical and Biological Technologies partnered with Northwestern University and Edgewood Chemical Biological Center to determine fundamental design rules which enable development of robust, highly-adsorptive materials that display enzyme-like catalytic activity for CWA capture and destruction.

These efforts have yielded a new, high-stability material that catalyze the destruction of the nerve agent soman, also known as GD, a more toxic analogue of sarin. Like other organophosphorus nerve agents, soman binds and inhibits natural functions of acetylcholinesterase and other targets in the neuronal and muscular systems, generating several immediate and long-term effects. Effects vary from a mild discomfort to death depending on the type of agent, the exposure amount and route of exposure.

The ECBC team, managed by DTRA's Ms. Tracee Whitfield, has the specialized facilities and the technical expertise to work safely with nerve agents and simulants.

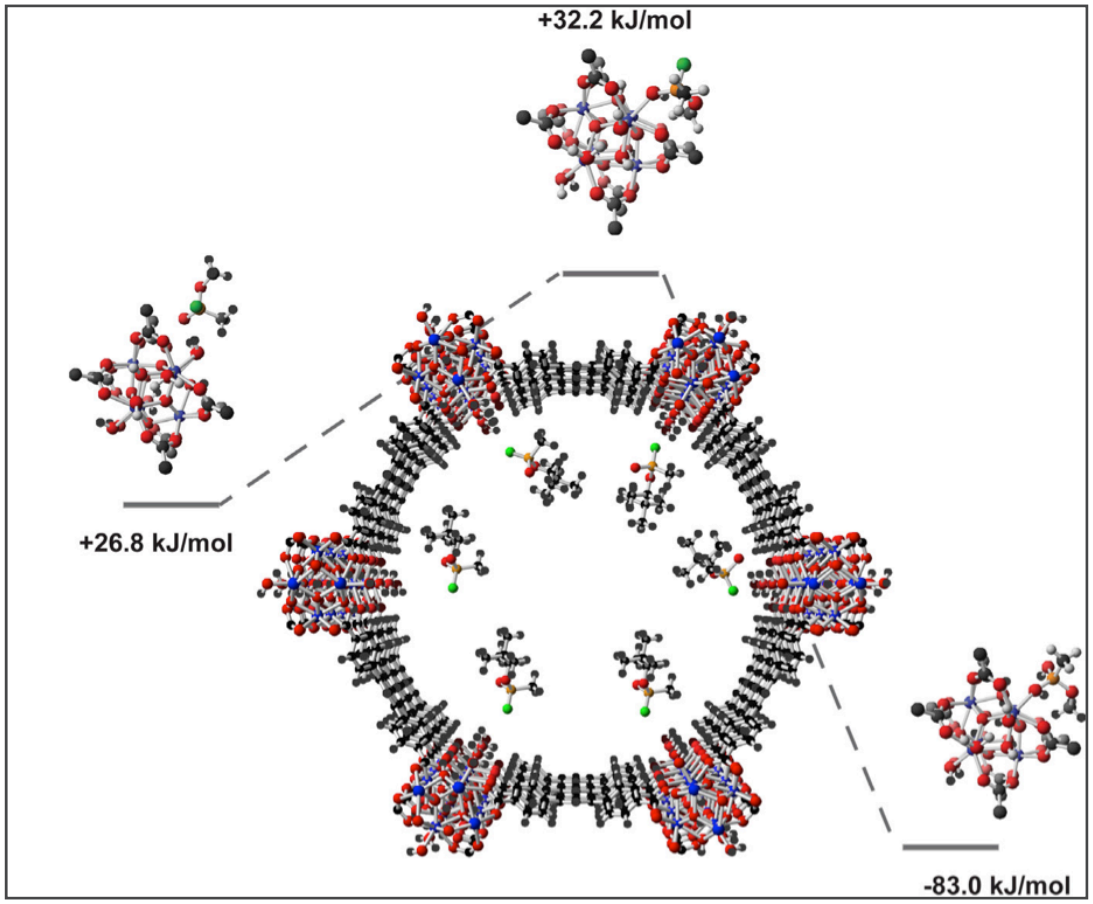
In a recently published article in *Nature Materials*, *"Destruction of Chemical Warfare Agents Using Metal-Organic Frameworks"* researchers at Northwestern University and ECBC describe the efficacy of a highly porous material, NU-1000, and its dehydrated analogue, toward both soman and a safer-to-handle simulant, methyl paraoxon. This man-made material is capable of hydrolyzing the CWA. NU-1000 is undeterred by hydrolysis product formation and continues to rapidly degrade both agent and simulant, unlike the naturally occurring cholinesterases.

The computational team showed density functional theory calculations that the hydrolytic degradation of GD proceeds via interaction with highly Lewis acidic hexa-zirconium/ oxo, hydroxo, aqua clusters. Once bound, the agent is rendered susceptible to selective attack by hydroxide ion at the agent's sole phosphorous-fluorine bond. The innocuous fluorine-free product then rapidly exits from the zirconium-based active site.

As suggested by the computed energies in the figure on page 1, soman reacts with metal-organic frameworks via Lewis acid activation pathways. Displacing water from the metal sites in the metal-organic frameworks would further activate it by increasing the number of Lewis acid sites, which is a slow step in the agent and simulant degradation reactions. Therefore, the researchers hypothesized that by dehydrating the metal-organic frameworks, the overall rate of agent or simulant destruction could be accelerated. They tested their hypothesis by thermally treating NU-1000 to dehydrate it and observed ten-fold accelerated reaction kinetics for the simulant hydrolysis. The paraoxon degradation half-life decreased from 15 minutes to 90 seconds.

In a related study published in Chemical Science, "Exploiting parameter space in MOFs: a 20-fold enhancement of phosphate-ester hydrolysis with UiO-66-NH2," the Northwestern team showed that simulant degradation, catalyzed by related metal-

• *See SOMAN on page 7*



Depiction of a portion of the structure of NU-1000 illustrating its molecular scale porosity. Sketched within the pore are molecules of GD. Shown in the close ups are the agent GD and catalytic node (left and top), and the degradation product and catalytic node (right), together with their computed free energies relative to the isolated agent and catalyst. Notice that the catalytic reaction is initiated by displacement of a water molecule from the catalyst active site and binding of nerve agent via an oxygen atom (shown in red; compare left and top close-ups). Hydrolytic degradation entails severing a fluoride ion (green) from the agent and replacing it with a hydroxyl derived from water (right close-up). The rapid release of the degradation product from the active site is not illustrated. (Image from Dr. Joseph Hupp, Northwestern University, courtesy of DTRA funded research)

Tracker Jacker of Bacteria: Quorum Sensing used to Defeat Deadly Agents

In the popular *Hunger Games* series, tracker jackers are genetically altered wasps that track and pursue anyone who disturbs their nests; their stings inflict great pain and sometimes death. Similar to the tracker jacker, research conducted by Dr. William E. Bentley from the University of Maryland is exploring how to rewire bacteria to sense, track, pursue and defeat infectious agents that afflict the warfighter.

The research, funded by the Defense Threat Reduction Agency's Chemical and Biological Technologies and managed by Dr. Ilya Elashvili, focuses on bacterial quorum sensing (QS), or the molecular communication system that enables individual bacteria to organize, eliciting group behavior.

While the mechanisms and components of the cell's QS circuitry are largely known, the challenge arises when some cells in a given population avoid collective behavior. Bentley's group wants to engineer 'smart' cells to execute these challenging tasks but needs to understand how bacteria normally determine the size of their desired quorums.

Previous reports highlighted the mechanisms and consequences of bacterial QS, but few have the exact fraction of bacteria that exhibit the collective behavior. Not all cells in the population take on the collective phenotype; concepts such as bacterial 'bet hedging' and 'social cheating' have been suggested to describe the emergent populations.

This is partly due to our inability to independently assemble a defined quorum. The quorum of most natural and artificial systems is a consequence of its ecological niche. To deploy engineered 'smart' bacteria in the gastrointestinal tract, scientists must first understand how cells perform by themselves, and then extend this ability to the environment they will eventually inhabit.

In their *International Society of Microbial Ecology Journal* article, *"Directed assembly of a bacterial quorum,"* Bentley and his team describe the assembly of quantized quorums. The team built a system in which they can engineer a fraction of the bacterial population to exhibit a desired behavior. This development creates a system in which quorum sensing hypotheses can be tested.

For example, what is the benefit when 65 percent of the population elicits a coordinated response? Is a benefit maximized at another quantum unit, such as 55 percent? If cells seek out new territory, what fraction needs to go? Do those that depart need to act collectively? Such questions are not easily answered using preexisting methodologies.

"This advance provides a better system to study quorum sensing, enabling scientists to design commensal strains of bacteria that target pathogens harmful to the warfighter."

The new system was made possible by independently engineering the autoinducer signaling system of E. coli and the sensitivity of detector cells, so that upon encountering a particular signal molecule concentration, a discretized subpopulation of cells emerges with the desired behavior. In their new system, the emergent cells all express a marker, a red fluorescent protein, known as DsRed, as an indicator of QS-mediated activity. In future designs DsRed will be replaced by a drug or other behavior-modifying protein. The six-hour process is robust, as detector cells are engineered to produce both large and small quorums.

Bentley and his team also demonstrated how the fraction of QS-responsive cells could serve as a population-based sensor for the QS autoinducer. When exposed to a concentration of autoinducer, a predetermined fraction of cells expressed the DsRed protein, indicating a QS-mediated collective response. The team showed that only a small subset of the overall bacteria population was needed to entice additional bacteria to leave their location. Additionally, this subset of cells did not need to take on the QS-mediated behavior. Instead, only when they arrived to the new location in the company of similar bacteria, did they become QS active.

Specifically, wild-type bacterial cells were immobilized in polysaccharide beads, where they synthesized, secreted and 'called' a small group of engineered 'smart' cells to travel to the first cells' location. After they arrived, the 'smart' bacteria banded together and established QS-mediated behavior; producing the QS-regulated fluorophore.

This advance provides a better system to study quorum sensing, enabling scientists to design commensal strains of bacteria that target pathogens harmful to the warfighter. Like the tracker jacker, antimicrobial 'smart cells' will pursue pathogens until they disarm the invader.

Soman

• *Continued from page 6*

organic framework materials, UiO-66 and UiO- 67, can be substantially accelerated by appending to the frameworks' linkers a simple organic base.

The authors speculate that the appended base serves as a local buffer, facilitating needed proton-transfer reactions such as the formation of reactive hydroxide ions from water molecules. Notably, naturally occurring phosphotriesterases (enzymes that hydrolytically degrade Organophosphorus nerve agent) also position bases close to metal-containing active sites, presumably for related reasons.

Finally, even though the synthetic catalyst NU-1000 yields the same weapons degradation product as the enzyme, it does so by a means that is less dependent on the exact structure and composition of the chemical weapon. The next step, therefore, is to determine the extent to which the synthetic catalyst exhibits broad-spectrum capability toward the nerve agent destruction and to further improve its catalytic effectiveness. Doing so would have far-reaching effects for the safety of the warfighter while mitigating the effects of harmful CWA.

Stealth Nanogels Attack, Defeat Their Target

The U.S. Department of Defense is no stranger to the concept of stealth or low-observable technology. After all, the department began developing its first stealth aircraft, the F-117 Nighthawk, in 1978. The aircraft, dubbed the "Diamond in the Sky," was used in covert operations, notably in 1991 when it slipped unseen past Iraqi radar and successfully attacked 37 targets in the opening hours of Operation Desert Storm.

Although the stealth fighter officially retired in 2008, principal investigator Dr. Liangfang Zhang and his research team from the University of California at San Diego are applying principals of low observable technology to the development of novel biomimetic therapeutic strategies. This research could be utilized to protect the American warfighter from chemical and biological threats through biodetoxification and vaccine development. Moreover, the same research could be applied to novel drug delivery methods for cancer patients.

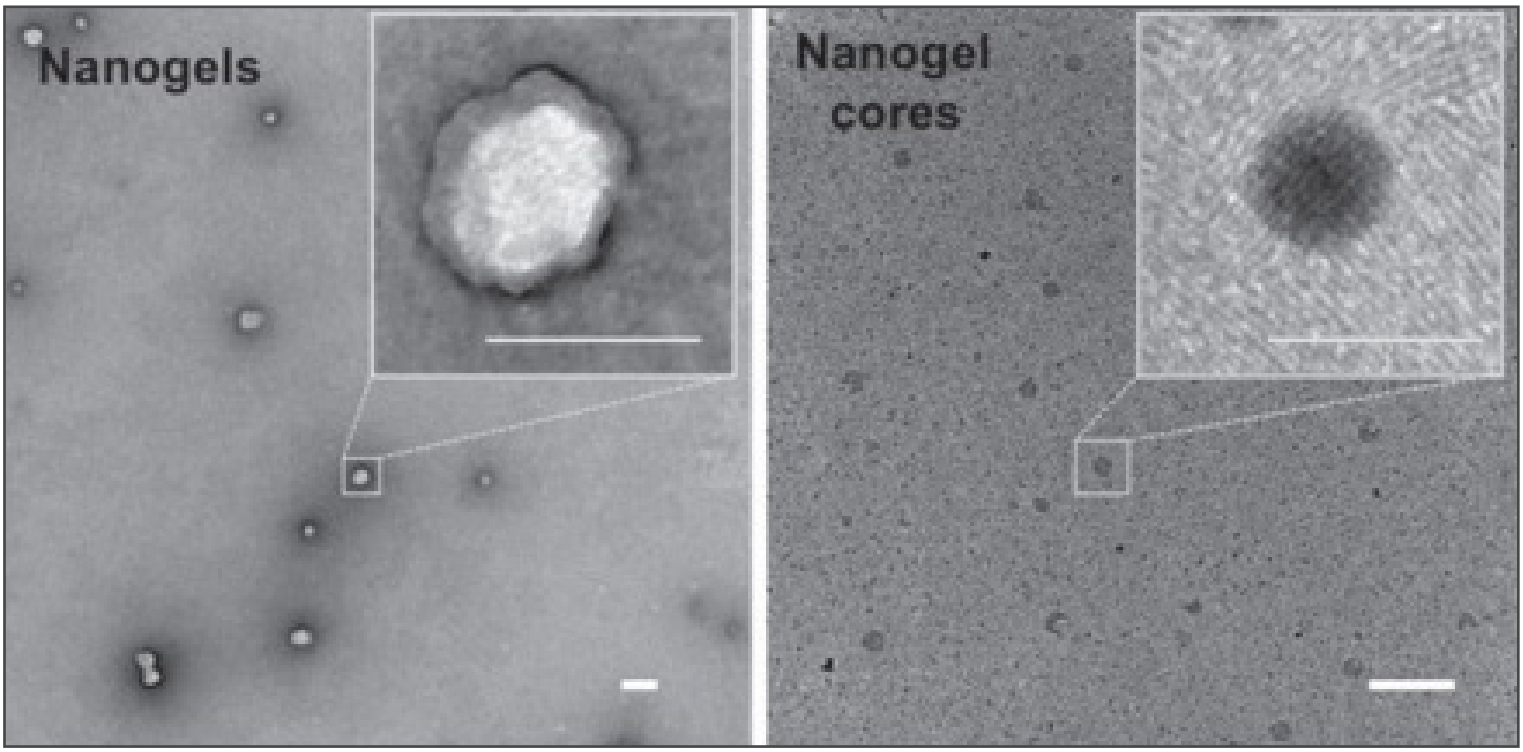
"This fundamental research opens the door to a new class of biomimetic nanoparticles and encourages the development of new medical countermeasure technologies to protect warfighters exposed to chemical and biological threats."

In his recent report published in *Small*, *"Synthesis of Nanogels via Cell Membrane-Templated Polymerization,"* Zhang describes how his team overcame critical nanogel development issues to enable new delivery platforms.

The project, managed by Dr. Brian Pate of the Defense Threat Reduction Agency's Chemical and Biological Technologies, solved critical nanogel development challenges by synthesizing a unique macromolecular inhibitor that is impermeable to cell membranes. This inhibitor also selectively and effectively constrains the polymerization reaction outside of the vesicles, while keeping the inside reaction alive.

These cell membrane-cloaked nanoparticles, also called stealth or low observable nanoparticles, consist of a synthetic polymer core, usually engineered from gold or silica. The natural cell membrane shell acts as a 'cloaking device,' and is made up of red or white blood cells, cancer cells or bacteria. The stealth-like nanogel particles have unique strength in their ability to mimic natural properties of the source cells while preserving a high degree of synthesis flexibility of the cores.

This fundamental research opens the door to a new class of biomimetic nanoparticles and encourages the development of new medical countermeasure technologies to protect warfighters exposed to chemical and biological threats.



Transition electron microscopic images of a red blood cell membrane–coated nanogels and the nanogel cores after the treatment with Triton X-100 and proteinase K (scale bar = 100 nm). Image courtesy of Dr. Liangfang Zhang and the University of California at San Diego, developed under DTRA-funded research. (Image courtesy of DTRA funded research)