# HDIAC Journal

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HDIAC Journal
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DoDIACs
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# Message from the Director: Better Buying Power 3.0

Stuart Stough
***HDIAC Director***

The Department of Defense continues to seek ways to streamline its processes and discover relevant information and technologies to positively affect the warfighter. In implementing the Better Buying Power 3.0 concept, the DoD had the foresight to drive toward interagency collaboration, which continues to ensure cost and time savings, while eliminating unproductive processes. In part, BBP 3.0, also works to secure the United States' technological superiority.

As the Homeland Defense and Security Information Analysis Center gathers information and establishes academic and industry relationships, the Center helps streamline the acquisition process and present a one-stop-shop of what's relevant and emerging for the DoD and helps the DoD balance its decision-making process. We acquire information on technology with the potential for commercialization and large scale development without huge upfront costs.

In doing this, HDIAC compiles the HDIAC Journal. The Journal is not just a collection of articles on scientific breakthroughs or basic research, but rather it is a catalogue, a way to present those ideas and concepts on the near horizon that have the capacity to impact DoD.

HDIAC uses the Journal to showcase emerging innovations on the "fringe" and get these concepts on the DoD radar. HDIAC seeks the technologies that will be viable acquisitions in the near future. We evaluate technologies that have been minimally funded through research but have not completed the complex product lifecycle.

The HDIAC model functions as a filter by scanning the horizon of research and development in academia and industry and pulling out relevant information from the noise. This data is then converted into a usable format, through the HDIAC Journal, and funneled to the DoD in an easy-to-use tool.

In this issue of the HDIAC Journal, for example, we present information on next generation biofuels, countermeasures for hemorrhagic fevers, real-time assessment of wound severity and smarter camera technology. Each of these technologies could provide cost-savings for the DoD, and using the HDIAC Core Analysis Task would support the BBP 3.0 concept.

The CAT is a way to evaluate the feasibility and technology readiness of these technologies. In a 2015 memo, the Office of the Under Secretary of Defense wrote that "the DoD IACs serve as a proven resource for maximizing the value of each dollar the Department spends, precisely because of the DoD IACs' ability to maximize reuse by building upon previous research, development, and other technical information." [1]

Because the CAT is limited to projects with a ceiling of $500,000 and a 12 month completion time, it is a quick-turnaround vehicle to determine if larger investments should be supported. The CAT is an established process that streamlines STI collection and development and is an ideal model for evaluating proofs of concept, which directly supports BBP 3.0. ■

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## Better Buying Power Focus Areas

1. **Achieve Affordable Programs**
2. Control Costs Throughout the Product Lifecycle
3. **Incentivize Productivity and Innovation in Industry and Government**
4. **Eliminate Unproductive Processes and Bureaucracy**
5. **Promote Effective Competition**
6. **Improve Tradecraft in Acquisition of Services**
7. **Improve the Professionalism of the Total Acquisition Workforce**

# The Next Generation of BIOFUELS for the U.S. Military

**By: Ross Ryskamp, Ph.D.**
**& Daniel Carder, Ph.D.**

The United States Department of Defense is committed to reducing its petroleum energy consumption in an effort to decrease its reliance on foreign oil and the volatile markets that supply it. Title 10 of the USC, § 2911 dictates that the DoD obtain no less than 25 percent of the total energy it consumes within its facilities from renewable sources by the year 2025, and every year thereafter.

Renewable energy sources, such as wind and solar power, provide an excellent opportunity to reduce petroleum consumption at permanent installations; however, other energy sources and/or storage systems are necessary due to the inconsistent energy production of wind and solar power. Furthermore, land and air vehicles, forward deployed military installations, ocean going vessels and other non-stationary military facilities are large consumers of petroleum-based energy that cannot currently be substantially displaced by wind or solar power. Thus, alternatives to petroleum based fuels, such as F-76, JP8 and other compression ignition or jet fuels are essential to reducing the DoD's petroleum consumption.

Biodiesel, as defined by the American Society of Testing and Materials, is a "fuel comprised of mono-alkyl esters of long chain fatty acids derived from vegetable oils or animal fats." [1] Biodiesel, herein, refers to a biofuel suitable for CI engines produced by the primary process of transesterification. The manufacture of biodiesel through transesterification begins with feedstocks containing lipids, such as fats, oils and greases. Recycled and virgin vegetable oils and animal fats are the predominant feedstocks; however, other biological matter composed predominantly of triglycerides may also be suitable for biodiesel production via transesterification. [2]

Through transesterification, triglycerides are chemically reacted with an alcohol, typically methanol or ethanol, to produce esters and glycerol. [3] Esters, namely fatty acid methyl esters, are the resulting biodiesel while glycerol is a byproduct of the reaction. The transesterification process is an equilibrium reaction that can occur fundamentally by mixing the reactants; howev-

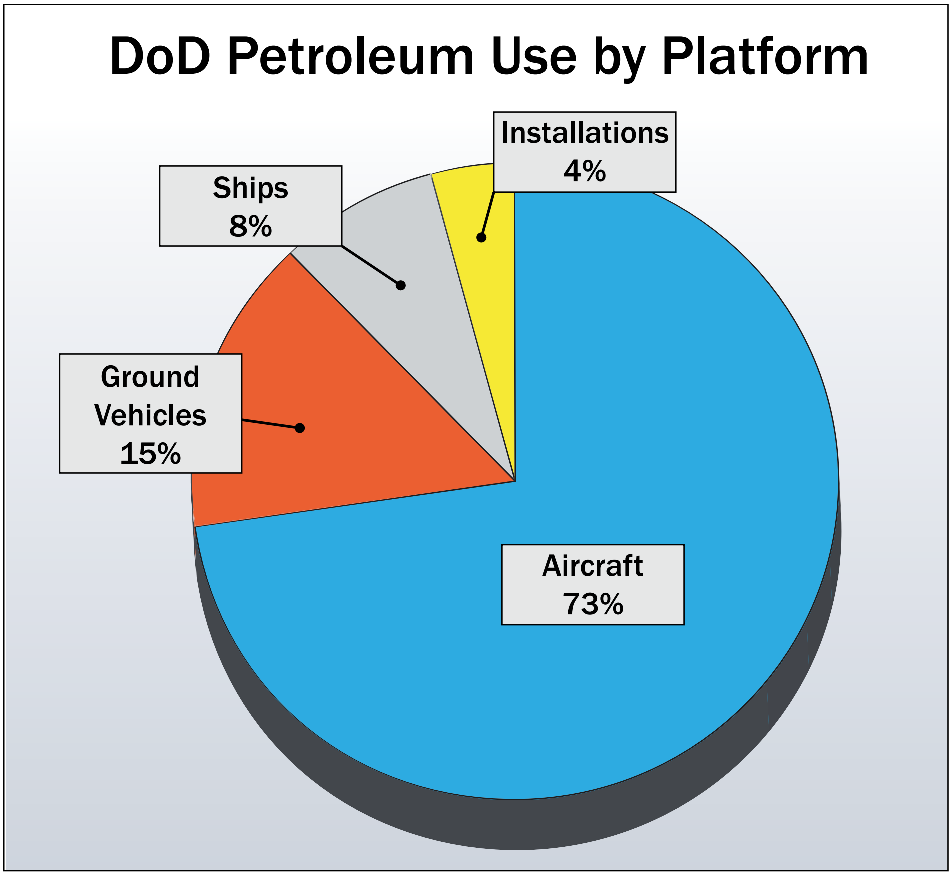


*Figure 1: DoD petroleum use by platform. (Released) [7]*

er, the use of a catalyst, most commonly a strong base such as sodium or potassium hydroxide, is used to accelerate the reaction. [3] The alcohol must be used in excess (approximately 1.6 times the stoichiometric concentration) to ensure a complete reaction, and the reaction can be hindered by other components in the feedstock, such as water and free fatty acids. [4] Thus, prior refinement of the feedstock is necessary for increased yields of FAME suitable for use as a fuel. The FAME can be separated from the glycerol and other byproducts because of the low solubility of glycerol; however, the crude glycerol stream is only approximately 50 percent glycerol and contains excess alcohol, most of the catalyst and soap, which must be removed prior to sale as industrial glycerol. [4]

FAME-based biodiesel, otherwise known as conventional biodiesel, produced by this process is most often used in a form blended with petroleum-derived diesel designated B5, B20 and B100, for example, which describes the ratio of biodiesel to petroleum diesel. It can be used in neat form depending on the application; however, conventional biodiesel has several significant differences from petroleum diesel that complicate its neat use, transport and storage characteristics, as well as its application as a jet fuel.

One such difference is conventional biodiesel contains a modest amount of oxygen, on the order of 10 percent, [5] while petroleum-based diesel contains no oxygen. While this oxygen content can improve soot, carbon monoxide and hydrocarbon exhaust emissions, it detracts from the energy content of the fuel, and possibly even more concerning, it can encourage microbial growth during storage. Furthermore, trace amounts of glycerine remaining in the fuel can form sediment that may plug filters and small passageways. [6] Another concern is the higher cloud point of conventional biodiesel versus petroleum diesel, which makes it more susceptible to gelling and cold flow problems.

These properties of biodiesel make it unsuitable for use as a jet fuel, which is relevant when considering alternative fuels for military applications and the fact that, "when divided by platform type, aircraft are the DoD's largest users of petroleum. According to a 2006 Navy report, in 2003 aircraft accounted for 73% of DoD's petroleum use, ground vehicles accounted for 15%, while ships accounted for 8%. DoD installations accounted for 4%," which is displayed in Figure 1. [7] Due to the incompatibility of biodiesel as a jet fuel, special precautions must be taken during transport and storage to ensure that traces of it do not mix with and potentially contaminate jet fuel, which is a valid concern when diesel and jet fuel share the same transport means or storage tanks.

The next, or second, generation of biofuels for reciprocating CI engines have overcome many of the challenges found with first generation bio fuels (i.e., conventional biodiesel produced by transesterification). One such next generation biofuel is hydroprocessed renewable diesel, often called green diesel or, simply, renewable diesel. This fuel can be produced from all the same feedstocks as conventional biodiesel in addition to others not suitable for the transesterification process. The hydrogenation procedure used to produce HRD easily converts free fatty acids to paraffins, unlike conventional biodiesel production via transesterification for which they can limit the reaction and react with the base catalysts to produce soaps. [6] Furthermore, the hydrogenation process is already in use by petroleum refineries to remove sulfur and other contaminants from petroleum.

Therefore, much of the infrastructure and technology to mass produce this fuel exists and is currently commercially available. The process can also be used to produce hydroprocessed renewable jet fuel suitable for aircraft. The chemical composition of HRD and HRJ is composed wholly of paraffinic hydrocarbons and contains minimal to no olefins, aromatics, naphthenes or oxygen. [8] As such, HRD and HRJ fuels resemble petroleum-based diesel and jet fuels much more than conventional biodiesel, which minimizes storage challenges, compatibility with seals and other fuel system materials, as well as viscosity and cloud point concerns.

While the hydrogenation process is fundamentally the same, there are several variations to the process depending on the feedstock used. As noted, biomass containing substantial components other than triglycerides can be converted to HRD or HRJ with this process, but the level of pretreatment required may increase to ensure the effectiveness of the hydroprocessing catalysts. [6] With regard to vegetable oil, animal fats and other bio-matter comprised predominantly of triglycerides, the process begins with one of two processes, hydrodeoxygenation or decarboxylation to remove oxygen from the triglycerides and form long chain n-paraffins. Both of these processes are performed with the addition of hydrogen and typically some form of a nickel- or cobalt-molybdenum catalyst. [6]

However, the amount of hydrogen required and the byproducts vary depending on the process as well as the feedstock. For example, beginning with rapeseed oil, the hydrodeoxygenation reaction requires 16 moles of hydrogen, produces 1 mole of propane and 6 moles of water, while decarboxylation requires 7 moles of hydrogen, produces 1 mole of propane and 3 moles of carbon dioxide. [6] Note that depending on level of reverse water gas shift reaction and methanation in the decarboxylation process, the required moles of hydrogen can increase to 16. After separation processes, the paraffinic products can be distilled to provide a fuel with similar distillation temperatures as petroleum diesel, high cetane number, but typically poor cold flow or cloud point properties. This fuel and the remaining heavier hydrocarbons can be further refined by hydroisomerization to tailor the cold flow properties of the fuel, effectively converting n-paraffins to iso-paraffins, [9] which is particularly useful for the manufacture of HRJ fuel to be blended with petroleum jet fuel. Figure 2 provides a general comparison of the production processes involved with conventional biodiesel versus HRD fuel.

HRD and HRJ fuel produced by the previously described hydrogenation process exhibit several advantageous properties in comparison to petroleum-based fuel and conventional biodiesel. Notably, these fuels do not contain oxygen and therefore do not share the same concerns with microbial growth and oxidative stability that plagues conventional biodiesel. To the contrary, the absence of oxygen does not provide the soot, hydrocarbon and carbon monoxide oxidation benefits offered by biodiesel; however, the wholly paraffinic chemical composition of HRD offers potential reductions in soot compared to petroleum diesel due to the absence of significant heavy soot forming compounds, such as aromatics and a lower carbon intensity. HRD exhibits a relatively high cetane number, or CN, (70 to 90) when compared to biodiesel (45 to 55) and petroleum-based number 2 diesel (40 to 45). [5]

This high CN can provide improved cold-start ability and performance benefits if engine control is tailored to the fuel properties. Among the three fuels discussed, HRD typically exhibits the highest energy content by mass, slightly higher than petroleum diesel due to the paraffinic composition, and modestly higher than biodiesel mainly due to the lack of oxygen. The cold flow and cloud point characteristics of HRD are much better suited for cold climates when compared to biodiesel and can be tailored to the application via hydroisomerization, which is critical for jet fuel applications and to be an approved DoD fuel.

The use of HRD and HRJ fuel provides the U.S. military with a bio-derived fuel to offset the consumption of petroleum-based diesel and jet fuel. The feedstocks for these renewable fuels can be produced domestically and refined domestically limiting foreign oil dependence petroleum market volatility while helping to achieve renewable energy goals. In fact, trials with HRD and HRJ have already been completed by the U.S. Navy, Army and Air Force.

The Navy's Great Green Fleet is a prime example, a carrier strike group for which the carrier operates on nuclear power while its escort ships utilize a blend of HRD produced from beef tallow and petroleum diesel. [10] Currently, this blend is only 10 percent HRD and 90 percent petroleum diesel; however, the blend is cost competitive with traditional fuels and is considered a "drop in" replacement. [11]

Tests and trials have been performed with neat HRD or HRJ fuels by other groups in the U.S. military. The U.S. Army's Tank Automotive Research, Development and Engineering Center evaluated HRD fuel in a Caterpillar C7 at the TARDEC Fuels and Lubricants Research Facility. [12] The engine was exercised over the 210-hour tactical wheeled vehicle cycle for a total of 840 hours at ambient conditions and 840 hours at desert conditions. Regardless of the environmental conditions, the author concluded that the use of HRD in the Caterpillar C7 "provides adequate performance without any negative impact on engine durability,

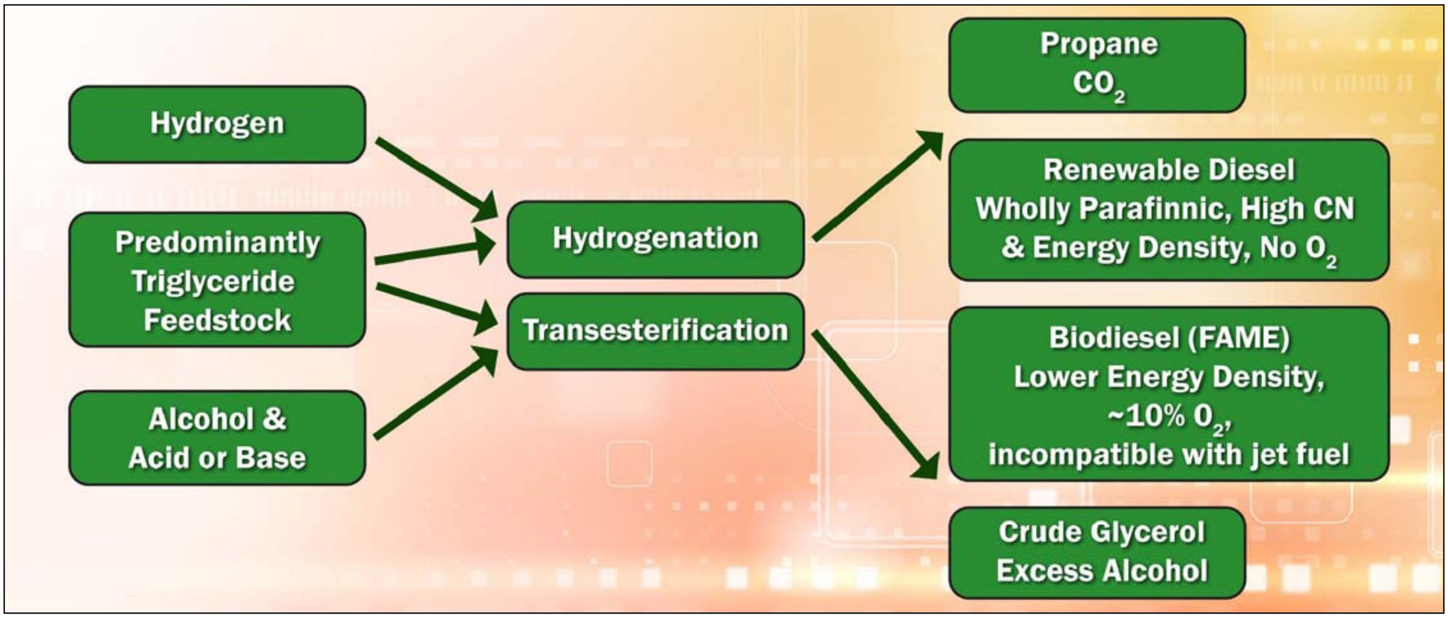


*Figure 2: Overview of production processes for biodiesel and hydroprocessed renewable diesel. (Released)*

emissions, performance, fuel consumption, lubricant degradation, or cleanliness." [12]

The HRD used for this study was considered neat, but it should be noted that it did contain 1.1 percent of petroleum diesel from the supplier for tax crediting purposes. With respect to jet fuel, the Air Force has certified 50 percent HRJ fuel blends with 50 percent petroleum-based jet fuel for use in its entire fleet of aircraft; however, research concerning the use of neat HRJ and other bio-based jet fuels has demonstrated issues preventing their use in neat form. [13] These issues include, "material compatibility (elastomer swelling/shrinkage), tank gauging (density), and additive compatibility (solubility)," which are likely related to the lack of aromatics in the HRJ fuel requiring the blending with petroleum-based fuel. [14]

One potential solution, to provide a 100 percent bio-derived jet fuel, has been developed by Applied Research Associates. Similar to other methods discussed, the process begins with renewable plant oils (i.e., triglycerides) but utilizes a catalytic hydrothermolysis process proceeded by a less intense hydrogenation and distillation (compared to the previously discussed HRJ fuels) that effectively converts triglycerides into "high-density aromatic, cycloparaffin, and isoparaffin hydrocarbons identical to the hydrocarbons in Jet A fuels from petroleum." [15]

With established production methods in place and continuing research on improving the yields, efficiency and quality of biofuels, next generation biofuel research is poised to focus on new feedstocks and advanced processes to exploit them. The production of first generation biofuels often directly competed with food production or indirectly through arable farm land earmarked for food production.

This was especially evident with ethanol produced from corn and biodiesel produced from soy beans. The expansion of biofuel production methods and investment in new production technologies have driven the focus toward feedstocks not involved in the production of food that have high oil outputs and can be grown on non-arable land. Animal waste feedstocks, such as beef tallow, are already in use as feedstocks for biodiesel and HRD production and do not compete directly with food production. However, the scalability to large production quantities presents a challenge.

Several non-edible feedstocks have been identified and are even in use, notably Jatropha, algae and lignocellulosic feedstocks. Regrettably, the excitement about Jatropha, once hailed as a biofuel game changer, has diminished in recent years, as researchers have noted that while Jatropha can be grown on non-arable land, it requires water and nutrients similar to other crops to be a substantial oil producer.

Furthermore, oil is produced from the seeds of Jatropha leaving the rest of the plant as waste. This has led to focus on the conversion of lignocellulosic feedstocks not substantially comprised of triglycerides such as agricultural waste or wood-based paper and pulp byproducts to oils suitable for the hydrogenation process. Prior to the use of lignocellulosic feedstocks in the hydrogenation process the cellulose, hemicellulose and lignin comprising these feedstocks must be broken down into smaller molecules with the use of technologies such as pyrolysis or by thermal or catalytic depolymerization. [6] Unfortunately, this additional process makes the use of these feedstocks less financially and environmentally appealing compared to triglyceride-based feedstocks.

Algae, considered a third, or future, generation biofuel, is an appealing feedstock that has garnered significant interest to produce not only renewable diesel, but also renewable gasoline and other valuable products. Appealing factors include algae's versatility: it can be grown in salt water, fresh water, waste water and brackish water; most species exhibit high growth rates; and many species of algae are inedible, thus it does not compete in terms of land use and food production. Furthermore, $CO_2$ from industrial processes and power plants can be captured and used to grow algae in addition to sunlight.

The versatility and proliferation of algae does have drawbacks, however. There are approximately 55,000 species and 100,000 strains of algae. [16] Of these, only a handful are commercially cultivated worldwide. This raises concerns of cross contamination where species not as well suited for fuel production may infiltrate a farm, potentially ruining the crop.

Nonetheless, this hurdle has led to new innovations, where semi closed algae production units have been developed, such as photo bioreactors, that allow for better utilization of $CO_2$, protect from invasive species and increase production yields with respect to ground space. These type of production units can stack vertically to increase yield density with respect to land use.

The conversion methods to produce biofuels from algae have also garnered significant research attention. One existing approach, hydrothermal liquefaction, is used to produce bio-oil which is a "viscous, corrosive, and unstable mixture of organic compounds." [17] This bio-oil must be further refined through other processes, such as hydrogenation, to produce renewable fuels. One advantage of this method lies in the use of wet algal biomass with little to no preprocessing; however, there are a number of high value components that are destroyed in the process.

An alternative to this process, which retains high value components, yet allows for the extraction of lipids for fuel production, is fractionation. [18] In this process, algal biomass is fractioned into carbohydrate, lipid and protein-rich components where the carbohydrates can be fermented to ethanol, the lipids can be hydroprocessed to HRD and the protein-rich compounds can be converted to biogas via anaerobic digestion for cogeneration of heat and power at the processing facility. [18]

The use of these next generation biofuels in conjunction with new engine and vehicle technologies presents a unique situation to increase fuel efficiency while further reducing petroleum based fuel consumption. A prime example can be found in the advantageous properties of HRD fuel. The high CN of the fuel makes it well suited for advanced combustion strategies that utilize high rates of dilution (exhaust gas recirculation) to limit harmful soot and oxides of nitrogen emissions while retaining high thermal efficiencies.

Furthermore, the lower carbon intensity of this wholly paraffinic fuel has the propensity to produce less soot and CO exhaust emissions during conventional combustion. Dual fuel applications, such as diesel-natural gas engines, which use the compression ignition of diesel to ignite natural gas (or other high octane number fuels), substantially benefit in terms of power density and combustion stability when a high CN fuel is used. [19] This is especially appealing for the algal fractionation approach previously discussed for which biogas and renewable diesel are both produced and could be utilized in a dual fuel engine for power generation and heat production.

Such applications could allow for solar or wind to provide base load power and the use of biofueled internal combustion engines for peak power demands. The parallel path of new technologies such as advanced fuel quantification sensors and in-cylinder pressure and temperature sensors in addition to advanced engine control technologies with these next generation biofuels present further opportunities to reduce fuel consumption. With known fuel properties or feedback on the in-cylinder combustion pressure or temperature, engine control changes such as fuel injection timing, pressure and duration can be made to exploit a particular fuel's properties and combustion characteristics to ensure maximum efficiency and minimal harmful emissions.

The role of the DoD in the evolution of bio-derived fuels is significant. Within the last decade, significant innovations have been made in the realm of bio-derived fuels. The hydroprocessing of renewable feedstocks to HRD or HRJ fuel has overcome many of the restrictions for DoD use found with the use of first generation, conventional biodiesel produced from transesterification. These second generation biofuels can be made from a wider range of feedstocks and have fuel properties much more consistent with petroleum diesel when compared to conventional biodiesel.

Furthermore, it has been proven that HRD fuel can be used in neat form for internal combustion, CI engines and new conversion processes are being refined to use HRJ fuel in neat form for aircraft. The future generation of bio-derived fuels is promising, with research targeting the efficient conversion of lignocellulosic and algae feedstocks to fuels equivalent and potentially improved performance over petroleum fuels. Merging these future bio-derived fuels with advanced engine and combustion technologies provides a promising pathway for significant reductions in petroleum usage by the DoD. ■

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**Daniel Carder, Ph.D., is the director of the Center for Alternative Fuels, Engines and Emissions at West Virginia University. For more than 20 years Carder has specialized in the measurement and control of heavy-duty mobile source exhaust emissions and alternative fuels research. His interests include design and development of exhaust emissions control systems, gaseous and particulate matter measurement and characterization, as well as in-use emissions measurement. His research has spanned most of the transportation sector, including medium- and heavy-duty on-highway, transit bus, locomotive and marine vessels, while his diesel engine research endeavors have covered on-highway, off-highway, mining and portable/stationary applications of both conventional and hybrid designs.**


SEMI
AUTO
SAFE

# LIBS Provides Potential Antidote to Increasingly Dangerous Prospects of Chemical or Biological Warfare

**By: C. David Chaffee**

## Introduction

Keeping technology one step ahead of the bad guys is an important mission of the U.S. government, and an important prospective tool in that fight is laser-induced breakdown spectroscopy, or LIBS. Consider the following scenario:

A mounted LIBS probe on a Stryker vehicle enters a highly contaminated warfare area befouled by unknown, potentially dangerous, toxic chemicals capable of doing great damage to incoming troops if left untreated. The probe scans for chemical warfare agents on nearby asphalt, soil, concrete and vegetation. Within seconds, the probe ablates and analyzes contaminants on these surfaces and localizes the hazard. Armed with this information, ground forces sidestep the hazard and continue their mission without the hindrance of protective overgarments and gas masks.

LIBS partners two tools of modern photonic technology, the pulse laser and the spectrometer. The pulse laser ablates, or vaporizes, a small portion of contaminated material that, when enough energy is applied, becomes plasma. The plasma contains a smorgasbord of scientific information, and the process provides multielement detection (solid, liquid or gas). [1] Included in the plume are the atomic constituents of the target, which are revealed as the resultant, excited microplasma cools. The spectrometer then analyzes and sends the results to the database, which could be a laptop computer, for rapid identification. [2]

LIBS features an "all-optical technique." [3] Frank De Lucia, a research chemist at the Army Research Lab at Aberdeen Proving Ground in Maryland, which has been a leader in LIBS development, said, "It allows you to do standoff—some people have identified materials out to distances of 100 meters. And you don't have to do anything to the sample. You point the laser and get the data back."

## History

The LIBS concept began with the creation of the maser and laser in the late 1950s and early 1960s. [4] In 1962, W.S. Boyle of Bell Telephone Laboratories used a ruby maser pulse to generate plasmas because, "good plasmas were only formed in air, not in inert gases or nitrogen," which Boyle was testing. [5] Encouraged by Boyle's research, Peter Franken of the University of Michigan began similar experiments, but his early attempts to create an acceptable plasma were unsuccessful. [5]

In 1963, John Maxwell provided the first clear description of the instrument: a Q-switched ruby laser head was used with an auxiliary spark source arranged with a pair of carbon atoms. Maxwell used the system to evaluate early geologic samples. [5] Robert Rosan "presented spectra of manganese, iron, beryllium, copper, zinc and calcium in 13 different tissue specimens." [5] Also in 1963, the Ford Motor Co. and researchers in France continued to study processes for developing "laser induced plasma without the auxiliary electrode excitation." [5]

Spectrometers were used in this process at least as early as 1963. Its use was referred to by French researchers J. Debras-Guedon and N. Liodec in work they presented to the French Academy of Science in that year. [5]

The term LIBS was introduced by T. R. Loree and L. J. Radziemski from Los Alamos National Laboratory in 1981. The researchers "were referring to the breakdown of air by laser pulses during the plasma creation phase." [5]

Since then, there has been rising global interest in LIBS. Some 350 papers related to the subject were published in 2005 alone, and the growth in 2007 was called "exponential." [2]

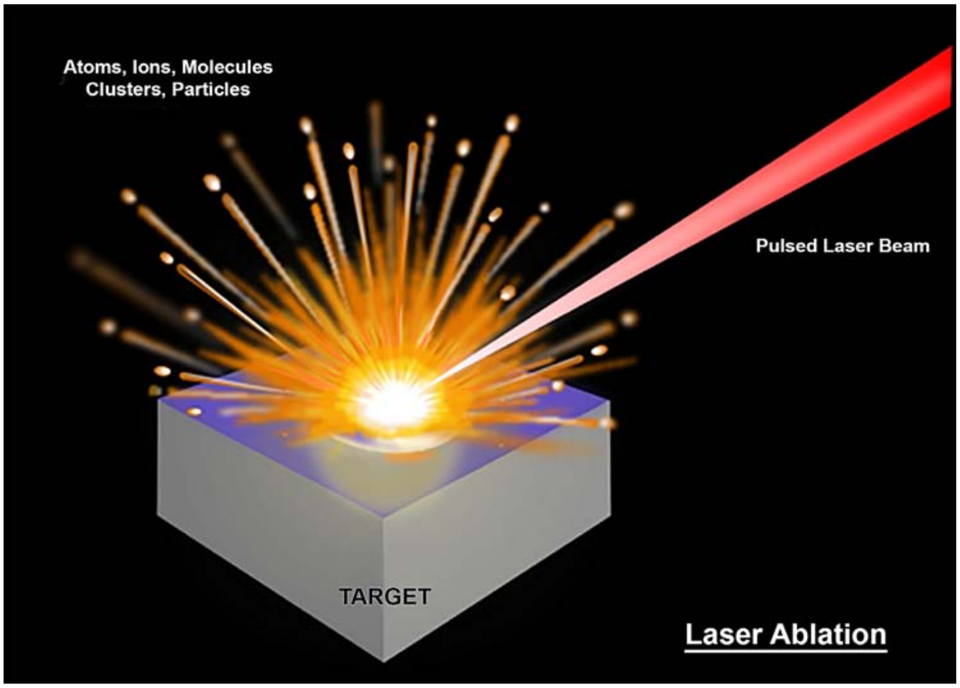


*Figure 1: Laser ablation, which is critical to the LIBS process, is demonstrated here. A wealth of data are included in the resulting plasma cloud. (Released)*

In fact, a community focused on LIBS has emerged over the past 10 years. [6] Indeed, "LIBS has gained enormous popularity and established itself as an analytical spectroscopic tool in several fields of applications." This conclusion is based on the growing number of conferences, papers and citations in publications where LIBS has been the focus. [6]

## How LIBS Works

A pulse laser ablates a sample, and the resulting emission signature is fed to a high-speed spectrometer, which feeds data to a computer to analyze the spectra in near-real time. These are the basic elements.

When the short-pulse laser beam is tightly focused on a target substance, a small volume of the sample material is ablated via both thermal and nonthermal mechanisms and further interacts with a trailing portion of the laser pulse to form a microplasma that contains a wealth of scientific data. This is the "breakdown" of data alluded to in the LIBS name and includes emission information from free electrons, excited ions, atoms and molecules. The induced plasma starts to cool down after the laser pulse ends. During the plasma cooling process, the electrons of the ions, atoms and molecules at the excited electronic states relax into natural ground states and emit light with distinct spectral features.

The most commonly used laser in LIBS is the pulsed Nd:YAG laser because this kind of laser provides a compact, reliable and easy way to produce plasmas in LIBS experiments.

The fundamental mode of this laser is at 1,064 nm, and the pulse width is between 6 and 15 ns.

This laser can provide harmonics at 532, 355 and 266 nm, which are less powerful and have shorter time pulses (between 4 and 8 nm). The fundamental and the first harmonic are the most common wavelengths used in LIBS. The harmonics can be useful to work with different wavelengths in the same environmental conditions because a lot of Nd:YAG lasers can produce all of them. Other kinds of lasers can be used in LIBS, such as carbon dioxide or excimer lasers to work in the far infrared or ultraviolet ranges, respectively. Lasers based on fiber or dye technology can reduce the pulse width if the user is attempting to work with picosecond or femtosecond pulses.

The plasma, induced by the interaction pulsed laser-sample, emits light which consists of discrete lines, bands, and an overlying continuum. These discrete lines, which characterize the material, have three main features: wavelength, intensity and shape. These parameters depend on both the structure of the emitting atoms and their environment. Each kind of atom has some different energy levels which determine the wavelength of the line.

The spectrometer is in charge of diffracting the light collected, with a more or less complex optical system, in order to obtain the spectral signature. Then, the light is detected by using devices

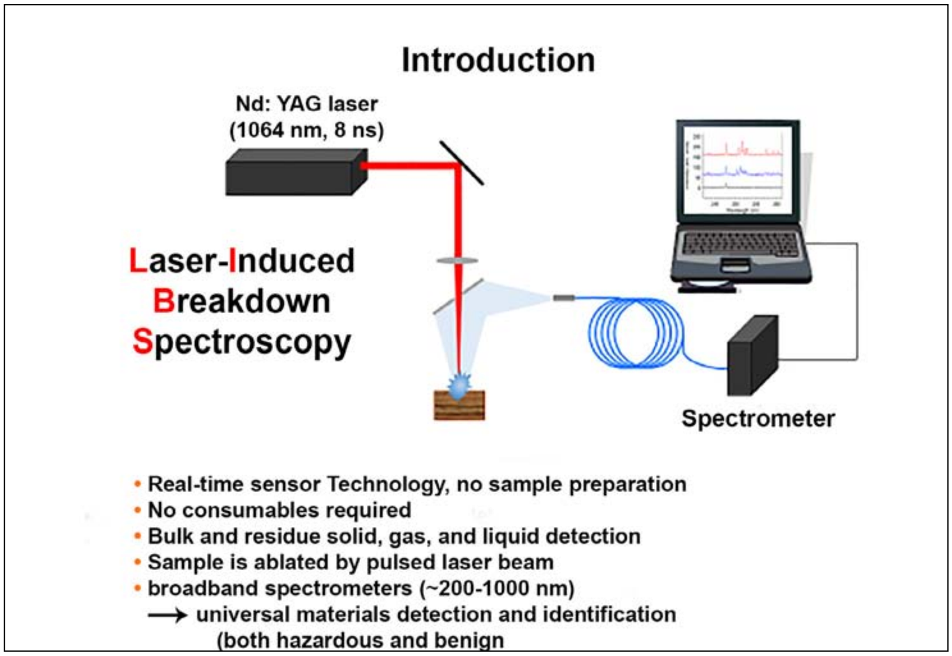


*Figure 2: The component parts of a simple LIBS design. (Diagram courtesy of the U.S. Army Research Lab/Released)*

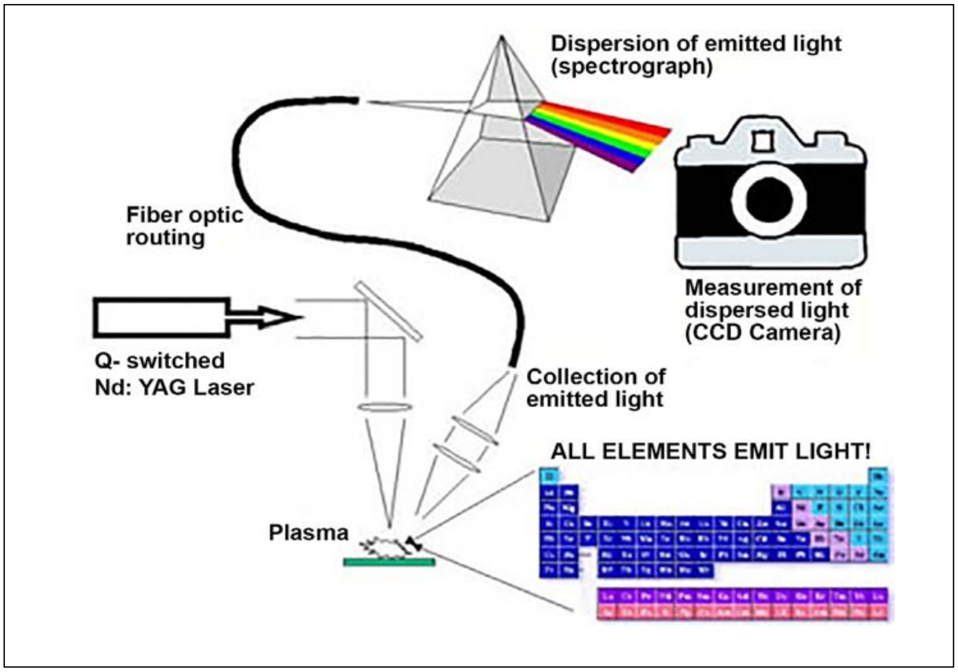


***Figure 3: A brief flow chart of an operating LIBS system. The Nd:YAG pulse laser ignites the sample, which in turn emits light that is then analyzed after traveling through an optical fiber. (Diagram courtesy U.S. Army Research Lab/Released)***

> such as a photomultiplier tube . . . , a photodiode array . . . , or a charge-coupled device . . . [1]

The ability to optimally analyze acquired data has also become a focal area. The use of chemometrics is an important tool in this process, and the ARL has used partial least squares discriminant analysis to good effect here. [3]

## Applications

Sample preparation is not required to use LIBS. [1] Additionally, LIBS has the capability to detect substances up to 100 meters away with reasonable precision. In fact, "LIBS is considered as an attractive and effective technique when a fast and whole chemical analysis at the atomic level is required." [1] Therefore, a wide variety of potential applications exist for LIBS, including soil and mineral analysis in space exploration, explosives detection, nuclear waste management, forensic science, geochemistry, the diagnosis of archeological objects and metal detection in solar cells. [6] Scientists are just now beginning to use LIBS in biomedicine. It potentially holds a bright future for the analysis of biological samples such as human bones, tissues and fluids. For example, LIBS can identify an excess or deficiency of minerals in tissue, teeth, nails or bones. [1] LIBS could also potentially detect cancer and may be able to serve as a surgical instrument that could simultaneously detect and destroy cancerous tumors. [1]

By using standoff configurations or fiber optic probes, LIBS can also operate "in hazardous and harsh environments." [1] This includes the ability to work at a safe distance from nuclear waste or nuclear reactors. Likewise, LIBS can be useful in metallurgy, studying alloy compositions as metals pass through production lines. [1]

Similarly, LIBS is also attractive for certain industrial processes, "because it is a fast analytical tool well suited to controlling some manufacturing processes." [1] For example, LIBS can detect toxic materials "like heavy metals in industrial wastes." [1]

Even the NASA Mars rover, Curiosity, has employed a LIBS spectrometer on the surface of Mars since 2012. It is used for soil and geologic analysis. [5]

In today's uncertain world, mustard gas has shown up in Syria and poisonous chemicals have been used against the Kurds there. Sarin gas was released in a Tokyo subway and anthrax has appeared in U.S. post offices. LIBS seems to be a viable technology that could be implemented by the defense community.

De Lucia said a main Army Research Lab focus has been to identify explosives. "We are looking for carbon, hydrogen, oxygen and nitrogen atomic emission lines for organic explosives. If you are interested in chemical warfare agents, you would also throw in chlorine, sulfur, phosphorous and fluorine, for example," De Lucia said.

De Lucia said an advantage in using LIBS to identify explosives is that the explosives are tactile and sticky and can potentially transfer to other surfaces. Used effectively in such a scenario, LIBS can help to eliminate the threat of such dangerous and deadly chemical agents on the world scene.

## Path to Commercialization

LIBS is an exciting technology that holds much promise, but a variety of obstacles remain before it can reach its full potential.

The general consensus is that a major, necessary goal is for LIBS to achieve recognition as a standard in chemical quantitative analysis. [1,5,6] The achievement of such a goal could place LIBS definitively among the most widely used spectrochemical techniques. Ways of achieving this involve the use of new tools of analysis.

Two new, helpful techniques could speed broader adoption of LIBS, optical catapulting and molecular LIBS. Optical catapulting LIBS, "uses a pulsed laser below the plasma threshold energy on the sample surface to create a solid aerosol which is analyzed with LIBS." [1] Molecular LIBS "analyzes the emission of molecules resulting from sample ablation or from the recombination between target elements and ambient air." [1]

While conventional LIBS reveals the basic elements of samples in the field, carbon, hydrogen, nitrogen and oxygen atoms can form many types of molecules, some harmless and some deadly. Knowing that C, H, N and O exist in the sample does not confirm whether sample contents are explosives such as RDX or HMX, or a harmless byproduct. Efforts to understand the molecular structure in order to more fully understand the sample are ongoing.

Another common problem is the environment or material around the sample. "Say the sample of interest is on wood, the emission intensity will be influenced by the laser material interaction associated with wood," De Lucia said. "The laser-induced plasma

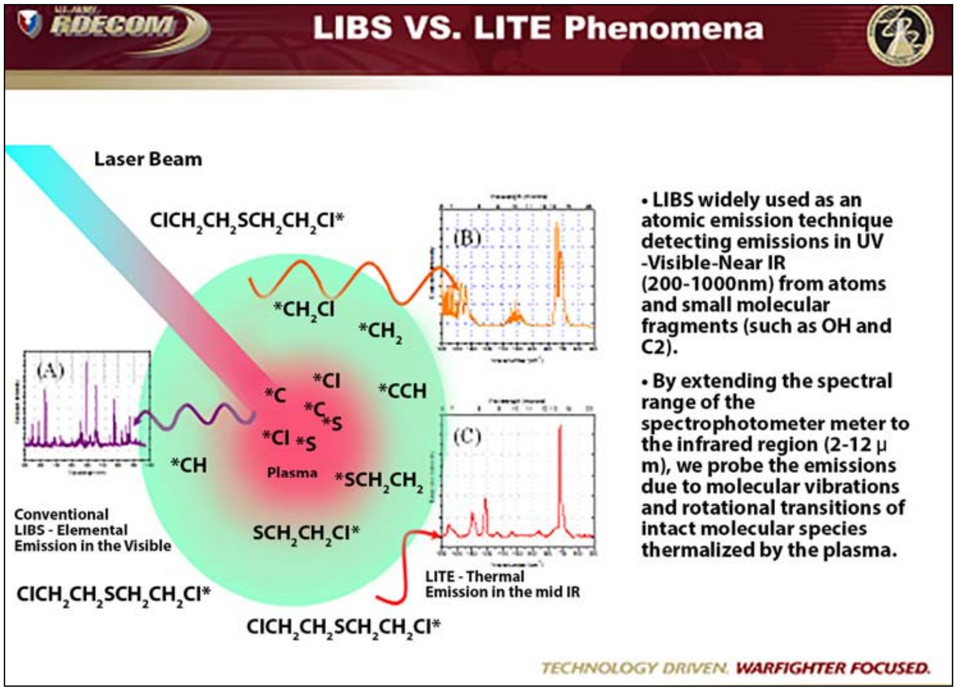


***Figure 4: The graphic illustrates how LITE can be used to expand the focus of LIBS, providing information on the molecular structure of the samples studied. (Diagram courtesy Edgewood Chemical Biological Center/Released)***

samples everything. Whether it is on plastic, a steel drum, dirt, etc., it is included in the data analysis."

In fact, De Lucia said that precisely evaluating only the target is a critical consideration. "If we are evaluating a broadband spectral region, there might be 10,000 elements," he said. "If we know the target specifically, we can reduce that by orders of magnitude by only collecting atomic emission lines associated with our target of interest."

De Lucia also notes that the false positive rate has to be much lower. "Even though it is less than 1 percent, that is not good enough," he says. For example, a biological detector placed in a mall may register 5 or 6 false alarms a day with the response being the emptying of the mall. That is not acceptable.

LIBS is also dependent on distance. The standoff distance changes the optics. For example, a sample taken from hundreds of meters would require a very large and powerful laser and larger collection optics. [3]

Finally, Alan Samuels, Ph.D., a research chemist with the U.S. Army working at the Edgewood Chemical Biological Center, points out that to this point there simply are not enough data to understand the lower levels of contamination for LIBS. "We don't have enough data to prove it will be at or below the fundamental limit of detection," he said. "We would like to get to much lower limits."

He also observes that the ablation process could be a concern in certain instances such as when it occurs on the skirt of a tank where it could impact the electronic control panel.

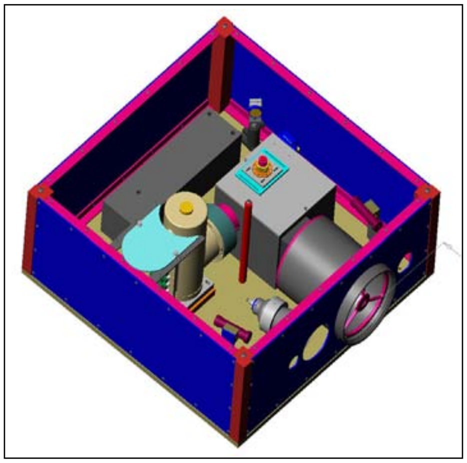

***Figure 5: Set up of the laser and monochrometer used in the long-wavelength LIBS demo. (Diagram courtesy of Brimrose/ Released)***

## LIBS/LITE

Measuring the long-wave infrared spectrum in a LIBS setup, rather than the traditional UV-to-NIR used, can help to reveal the molecular composition of the sample. This is the information sought for defense applications, including chemical and explosive detection and identification, and in commercial applications, such as in the pharmaceutical and chemical industries. [7]

The Brimrose Technology Corporation, Hampton University and the Edgewood Chemical Biological Center were thought to be the first to apply LIBS to detect and resolve molecular vibrational emission. This leap of spectral range greatly improved the detection specificity. During the past few years, the instrument for LWIR LIBS was also significantly improved. For example, the spectrum acquisition time has been reduced from tens of minutes to just a couple of seconds. [7]

For the past eight years, researchers have worked on a new process they believe holds great benefits. They have been working with LWIR LIBS in hopes of attaining both molecular and atomic data configurations. [7]

Scientists are taking advantage of the wealth of data the plasma plume offers. The idea behind laser induced thermal emission is to create a LIBS plasma but to capture data from the IR region, "a new frontier for long-wavelength lasers." [7]

As can be garnered from the name, LITE, the emphasis is on thermal emission. Such an approach allows the operator to largely eliminate the problem of surroundings diluting the plume analysis and focus almost entirely on the sample. [7]

By studying just the thermal emissions, the sample can be distinguished from the surface, "providing us a huge advantage over others capturing protons off of surfaces." [7]

In addition to providing a much cleaner look at the sample, the process holds the potential to at least identify molecular structures as well as atomic ones, thereby opening the door for both chemical and biological analysis and a better, more comprehensive way to identify contaminants. [7]

## Demonstration

The Brimrose Laboratory served as the demonstration site for a LIBS/LITE experiment. In the demonstration, a Quantel laser delivered 72 mJ per pulse at 1.064 microns to ablate black powder. A monochromator was also included. The detector used in the setup was an MCT linear array hybridized with read out IC, making it possible to obtain

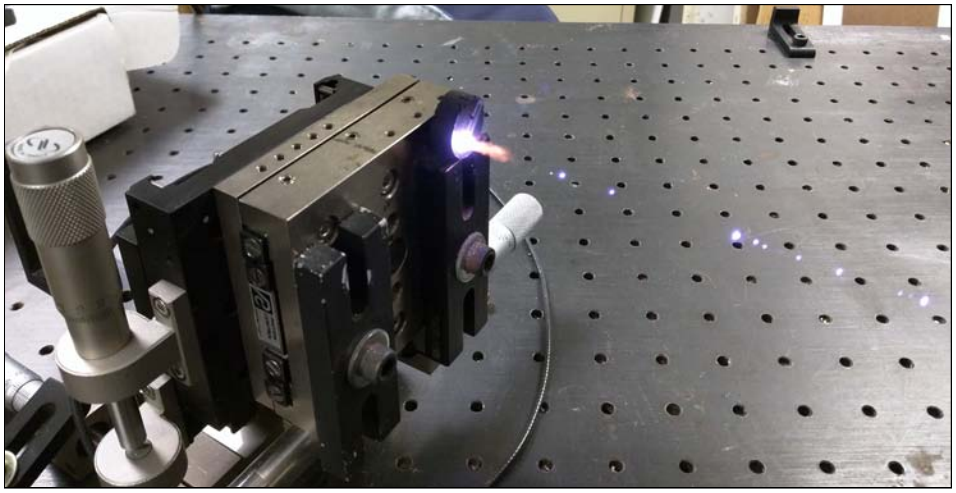

*Figure 6: The black powder used in the demonstration as it is ablated by the Nd:YAG laser beam. (Photo courtesy of Brimrose/Released)*

the entire LWIR spectrum with a single laser pulse. The distance between the laser and the sample was 1 meter. Data were collected simultaneously in both the visible (400-900 nm) and IR (5.6-10 microns) spectral regions. [7]

The pronounced "pop" that occurs the moment when a material is ablated was evident in the demonstration. A lot of energy is focused on a small space that is then converted into a small plasma, which in turn generates elemental emissions in the visible and concomitantly a population of thermally excited intact molecules to yield information about their structure in the infrared. The molecular emissions appear at a slightly longer time (about 100 microseconds) after the peak emission from the plasma, allowing them to be separated from the plasma thermal continuum emission by time grating. [7]

The data collection sequence in the demonstration was as follows:

1. The delay time and integration time for the data collection were set.
2. The laser was activated and created a microplasma on the target sample surface. Simultaneously, the laser sent a trigger signal to the detector.
3. After the detector received the triggering signal from the laser, it waited for the delay time to start collecting data for the duration, according to the integration time that was set.
4. The resulting data (spectra) were then sent to the computer for analysis. [8]

It is believed this experiment, and others like it, will demonstrate proof of principle using LWIR LIBS that may be able to identify both chemical and biological substances. [7]

## Conclusion

LIBS has existed since the invention of the laser, and it holds significant promise as a tool for many applications.

LIBS can precisely identify the atomic elements of a sample, and potentially the sample's chemical formula. This opens the door for numerous applications, including the rapid identification of contaminants in a warzone or hazardous civilian area.

LIBS could be utilized as a significant tool in the war against terrorism and could also serve as a technological tool that could be used in a variety of civilian applications. ■

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# Smarter

# Cameras with Edge Analytics

By: B. Scott Swann
& David Ramsburg

Applying analytic technology at the point of video surveillance capture offers a range of strategic and tactical benefits. Emerging smarter camera solutions built on this premise have the potential to save both time and money for those who implement them. Furthermore, an advanced military surveillance solution architected around this methodology provides a futuristic framework for overcoming challenging issues and maximizing technology to aid situational awareness on the battlefield.

Balancing advancements in technology with efficiency can present daunting challenges that may require agencies to revamp traditional methods for fulfilling a mission. The Department of Defense and several other federal agencies face this dilemma across a range of technology breakthroughs. Although new products present superb opportunities to better protect our troops, advance national intelligence and strengthen our comprehensive security posture, advancing parallel operational policies is a significant hurdle to fully realize the benefits of this modern day innovation.

This article addresses the specific example of how communications network bandwidth is currently a significant bottleneck for camera systems collecting video information. It also describes how edge analytics can greatly reduce the data burden on already overloaded communications networks.

One of the largest obstacles for the full adoption of enhanced sensor technologies has been the limited bandwidth of legacy military communications networks. While these networks have evolved and improved over time, the bandwidth demand has greatly outpaced the supply. The high growth rate of bandwidth demand is driven by two main phenomena:

1. High proliferation of connected devices (such as voice/data handheld radios, sensors, etc.)
2. Increasing data volume produced by each device or sensor suite (For example, a Global Hawk Unmanned Aerial Vehicle currently requires five times the bandwidth of the entire U.S. military during Operation Desert Storm.) [1]

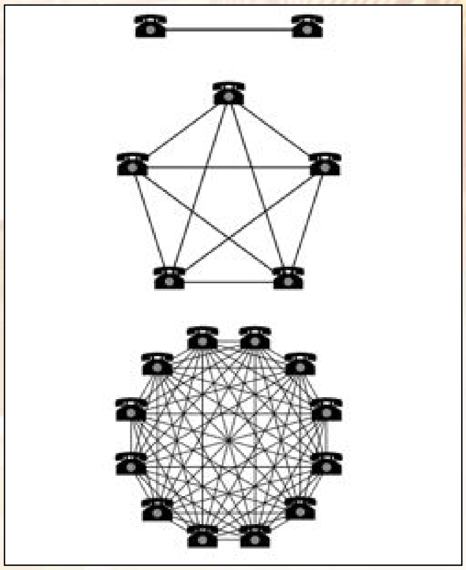

*Figure 1: Illustration of Metcalfe's Law. [2] (Released)*

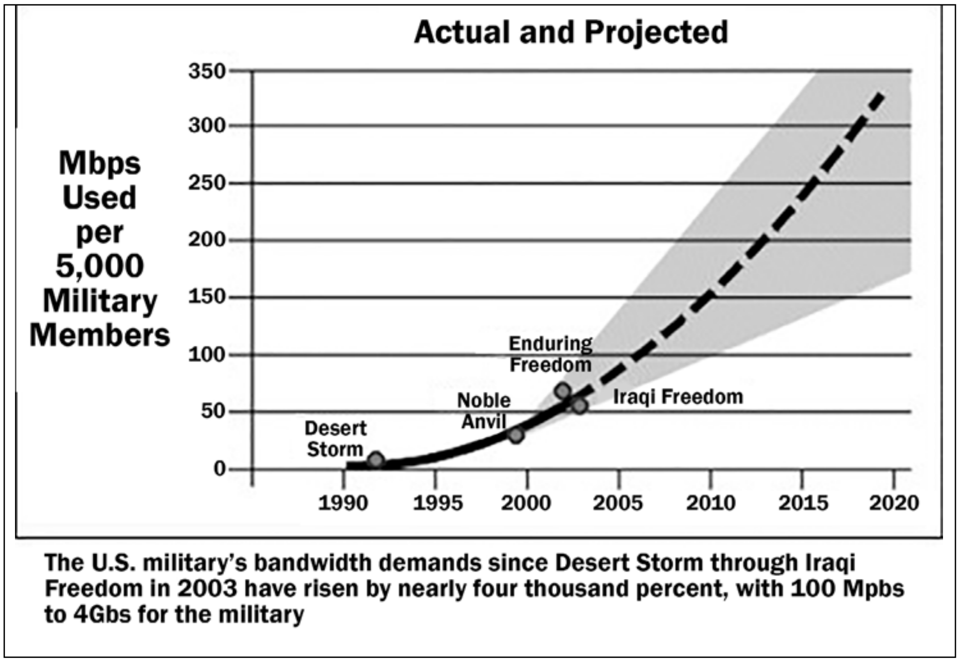


*Figure 2: Growth in SATCOM needed to support 5,000 military members. [10] (Image courtesty of the U.S. Army/Released)*

## Metcalfe's Law

"Metcalfe's law states that the value of a network grows as the square of the number of its users: V ~ N2." [2] The concept of Metcalfe's Law is shown in Figure 1. In this illustration, each user is represented by a telephone. As the number of users in the network increases, the potential connections between users increases by approximately the square of the number of users. As the figure shows, two users can have a single connection, five users can have 10 connections, and 12 users can have 66 connections. The more connections the network has, the higher the potential value of the network. However, the limiting factor for the value of the network quickly becomes the available bandwidth of the network.

A military corollary to Metcalfe's Law is the Iron Law of Bandwidth Usage, which states that, "for military formations, using bandwidth expands to consume whatever amount of bandwidth is provided." [3] This effect makes sense because DoD missions must maximize the value of the network. Therefore, the maximum number of connections must be made, enabling the maximum amount of data flow, and once again causing the network to be the limiting component of the entire system.

Figure 2 shows the increase in bandwidth used by the military from Operation Desert Storm in 1990 through Operation Iraqi Freedom in 2003, with a projection of bandwidth requirement into present day and the future. [1]

## WIN-T Increment 2

In 2013, the U.S. Army began deploying the second tier of a new high-speed, high-capacity tactical communications network, Warfighter Information Network – Tactical Increment 2. [4] The main network enhancement provided by WIN-T Increment 2 is networking on-the-move, which by definition requires multi-node hops across an ad hoc communications network. With the addition of multiple hops between nodes, latency in the network increases creating a reduction in available bandwidth between the nodes.

Figure 3 shows the effect of number of hops on the bandwidth of a wireless network. This figure shows the throughput of a 2 Mbps 802.11 (Wi-Fi) medium access control layer. [5] As can be seen in the figure, the throughput of the network is greatly reduced over the first few hops and eventually stabilizes at a value less than 10 percent of the maximum bandwidth of the system.

In summary, there is, and will likely always be, a shortage of bandwidth within military operations. Trade-offs to best support the mission are in constant competition. Understanding this now, let's inverse our logic to think specifically about sensors.

Today's high-definition camera technology enables the user to focus on objects from far away distances with impressive precision. Analytics such as motion, face and person detection and recognition can analyze this data quickly to attain actionable intelligence. However, egressing the video to a back-end system can be a major challenge.

These high-resolution cameras are bandwidth voracious, and the DoD, especially in theatre, evaluates trade-offs to maximize transmission efficiency. It is common practice for video to be reduced in resolution and frame rate and compressed to support efficiency, but this has negative impacts on video analytics, especially biometric exploitation.

In order to make the data requirements of mainstream video technologies clearer, Figure 4 shows the approximate bandwidth used for common video formats and resolutions. It is easily observed from the chart that as 4K video begins to be used more in the field, the bandwidth requirements of the network will dramatically increase.

Table 1 shows approximate bandwidth requirements for various video formats and examples of interface standards that can accommodate those video streams.

## Current State

Today, video is generally either streamed from the battlefield to a remote location for viewing or stored at the device for subsequent retrieval. Connectivity and bandwidth are drivers for determining if, and at what resolution and frame rates, the streaming of video may occur. The quality of the video impacts how well video analytics can be leveraged.

Video analytics have become a valuable tool for quickly sifting through video content to find specific events of interest. For example, specialized algorithms can save soldier man-hours by quickly analyzing if motion, people, faces, vehicles or other objects appear in a video. When successfully deployed in optimal environmental conditions, video analytics can enable an operator to find actionable intelligence within seconds, or minutes, whereas previous brute force methods could take hours or days.

Algorithms may not be capable of detecting all events. However, video analytics are especially powerful when dealing with large volumes of data too overwhelming for human processing. Video analytics guide analysts to the appropriate data sources to find

| Format | Vertical Lines | Horizontal Lines | Frames/s | Color Bits | Single Frame Size (MB) | Approximate Bandwidth (MB/s) | Interface Standards Which Provide Adequate Bandwidth |
|---|---|---|---|---|---|---|---|
| 480p 24Hz | 640 | 480 | 24 | 32 | 1.17 | 28 | |
| 480p 30Hz | 640 | 480 | 30 | 32 | 1.17 | 35 | 802.11a/g |
| 480p 60Hz | 640 | 480 | 60 | 32 | 1.17 | 70 | |
| 720p 24Hz | 1280 | 720 | 24 | 32 | 3.52 | 84 | 100BaseT |
| 720p 30Hz | 1280 | 720 | 30 | 32 | 3.52 | 105 | |
| 720p 60Hz | 1280 | 720 | 60 | 32 | 3.52 | 211 | |
| 1080p 24Hz | 1920 | 1080 | 24 | 32 | 7.91 | 190 | |
| 1080p 30Hz | 1920 | 1080 | 30 | 32 | 7.91 | 237 | 802.11n |
| 1080p 60Hz | 1920 | 1080 | 60 | 32 | 7.91 | 475 | |
| 4K 24Hz | 4096 | 2160 | 24 | 32 | 33.75 | 810 | GigE |
| 4K 30Hz | 4096 | 2160 | 30 | 32 | 33.75 | 1013 | 802.11ac |
| 4K 60Hz | 4096 | 2160 | 60 | 32 | 33.75 | 2025 | ??? |

*Table 1: Required bandwidth for various video formats and interface standards to support them. (Released)*

the proverbial needle in the haystack.

Nonetheless, the benefits of video analytics are limited to the usability of the data. HD camera optics have matured to enable impressive results with analytics. Unfortunately, if major compromises for bandwidth reduction include poor resolution or lower frame rates, the overall video quality is not likely to support a successful implementation of analytics, especially biometric exploitation of identities.

Emerging video formats and enhanced camera capabilities are enabling much greater information capture. These technologies are driven by the commercial market and demand for higher definition products. By the year 2020, the overall market for 4K video technology is expected to reach $102.1 billion. [6] Likewise, the market for video analytics is estimated to reach $4.23 billion by 2021, with the adoption of cloud-based technologies significantly increasing the demand for video analytics software and services. [7]

The sharpness in pixel density and overall integrity of video provided by 4K cameras is ideal for successful application of analytics. Motion detection, person detection, face detection, color filtering, gender estimation, age estimation, ethnicity estimation, license plate recognition and face recognition are all examples of mature video analytics that run exceptionally well on high quality video. However, 4K cameras also produce extremely large data streams.

The 4K video is more than four times the size of 1080 HD video as shown in Figure 4. Given many military and government infrastructures can hardly handle 1080 HD video streams today, this advancement in camera technology presents substantial bandwidth challenges. These network limitations are not easy to overcome.

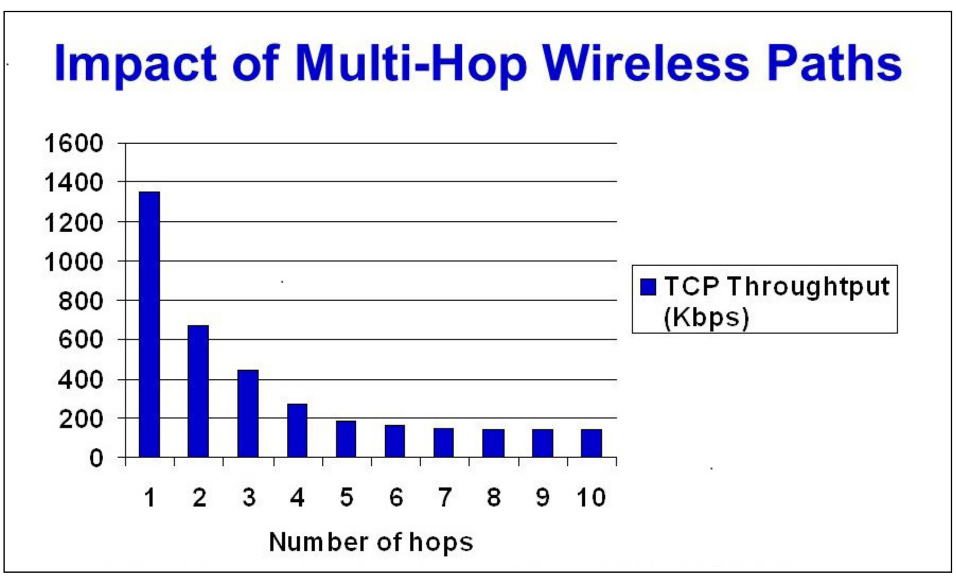


*Figure 3: Impact of multi-hop wireless paths. [11] (Released)*

Applying analytics at the point of capture is the most sensible way to take advantage of HD and 4K cameras. The smart-edge video analytic concept deploys a surveillance infrastructure that utilizes advancements in camera optics capable of producing tailored real-time alert notifications.

## Future State

Is there a silver bullet solution for successfully deploying video analytics in this bandwidth constrained environment? Can the full capabilities of HD camera optics be appropriately exploited with this innovative technology? Yes - by migrating the analytics to what is referred to as 'the edge.'

Processing video locally, at the sensor, provides multiple benefits. First, information extraction is performed on the full-resolution, high-fidelity imagery before the data is compressed, resulting in better actionable information. Second, information can be quickly processed locally because the transmission steps and related latency issues are removed from the process. [8]

Imagine an adaptive surveillance solution that allows an intelligent deployment of analytics to process video at the point of capture. This software-based solution pulls video from a camera and invokes a suite of analytics that run locally on a miniature processor to support a range of transmission options. The edge solution is capable of automatically executing business rules defined by the operator to intelligently maximize bandwidth efficiency based

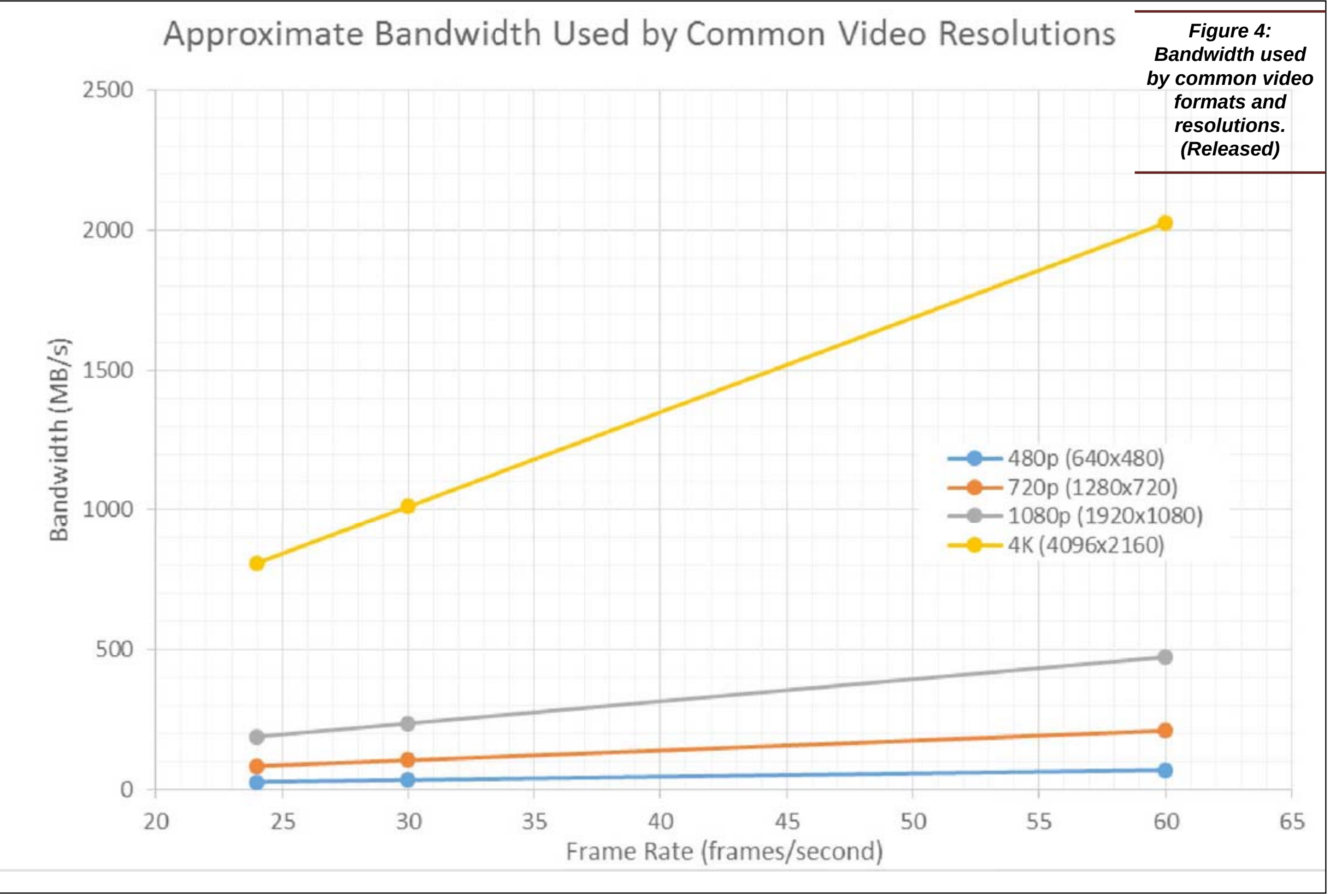


***Figure 4: Bandwidth used by common video formats and resolutions. (Released)***

upon motion, face, person detection and watch-listing. Additionally, modern biometric algorithms can also support multiple watch-lists to be loaded and managed at the edge. This allows the solution to instantaneously compare streaming video with the watch-list photos, subsequently triggering near real-time alerts to a command post or a mobile device.

The overall system infrastructure supports remote management with ground-breaking situational awareness to quickly attain actionable intelligence from video. A variety of enclosure options can be supported with such a solution to include both overt and covert surveillance scenarios. Common smart city cameras can be equipped with small processors to support the overall edge analytic solution as well as more complex implementations that attach a cluster of cameras to a more powerful processing unit. Regardless of the configuration, the edge analytics solution can maintain a forensic recording of video on fully encrypted, detachable drives to support evidentiary testimony.

Consider how this solution might practically support a DoD facility. For example, military base perimeter security encompasses many types of boundaries including access points, fences, buildings, warehouses and many less trafficked areas. It takes substantial manpower to monitor this video feed, and because of the sheer volume of data, it is likely that not all video content is reviewed and analyzed. Running analytics at the point of capture would ensure that each perimeter entry incident is detected and that analysts are alerted. Smart camera systems can also be tied into access control systems. For example, analysts may receive an alert when unauthorized personnel attempt to gain entry into a secure facility. These types of alerts can be driven from a smart camera, edge-based solution that relies on human capital to maximize efficiency. The overall architecture is a force multiplier for military base security fitting within existing standard operating procedures.

Extracting additional content from video, fusing analytic information and better understanding events are all growing areas of research by academia, government and the commercial sector. After the Boston Marathon Bombing, the FBI convened a workshop with both the National Science Foundation and the Defense Advanced Research Projects Agency to better understand "the state of the art in algorithms being developed in academia that can support forensic analysis and identification in large volumes of images and videos." [9] Collectively, these agencies explicitly assessed what is considered the solved, nearly solved and over-the-horizon challenges within image and video analysis. [9] Based on the market opportunity for video, we can expect substantial growth in research to occur within the commercial sector. This increased interest in algorithm development for the purpose of video analysis opens the door for research into video feed security protocols and procedures.

## Summary

Watching today's news broadcasts, it's apparent that video is increasingly associated with tragic events across the globe. Terrorist and foreign fighter groups routinely capture their propaganda and heinous acts of crime on camera. Similarly, other bad actors, such as cartels, leverage video to exploit torturous messages to their rivals, broadcast announcements and facilitate recruitment. This data often gets published on social media and shared across the world. As such, these groups frequently give us a clue to their identity that we can harness for ongoing protection of our troops and citizens – a picture of their face.

Camera technology is rapidly advancing. HD cameras are becoming more affordable, and they capture data with higher integrity. Faces sourced from these high quality recordings are 'usable' for analytics such as face recognition. As such, the video we capture within our surveillance systems must be equally viable.

However, if we depend on backend systems to exploit the video with analytics, it is inevitable we will need to reduce resolution and frame rates due to bandwidth constraints. In this situation, analytics such as face recognition will be much less effective.

It is imperative that more intelligent camera solutions be deployed that can process analytics on the original high-integrity video and leverage the power of this automation to support more actionable intelligence. A smart edge-based camera ecosystem is the future of video surveillance. This ecosystem will allow tactical business rules to be programmed into cameras to determine what information is sent and when.

Why waste bandwidth when there is no motion? If the goal is to only alert the command center when people are present, why not only send video when a person detection algorithm identifies that someone is walking in the surveilled area? If looking for specific terrorists or criminals, how valuable would it be to have access to 30 seconds of video both before and after a specific event, such as the suspect walking by a surveillance point? How valuable would it be to have video content automatically sent to an intelligence operator upon immediate event detection instead of an intelligence operator reviewing hours of video to determine events?

All of these concepts are possible today with smart-camera edge analytics. The systems can be programmed to send video data in appropriate resolutions and framerates for any given network that is deployed. The capabilities of technology will continue to progress, and with the evolution of enabling policies, military surveillance will undoubtedly become more agile and advanced as these intelligent solutions are deployed. ■

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# Secondary

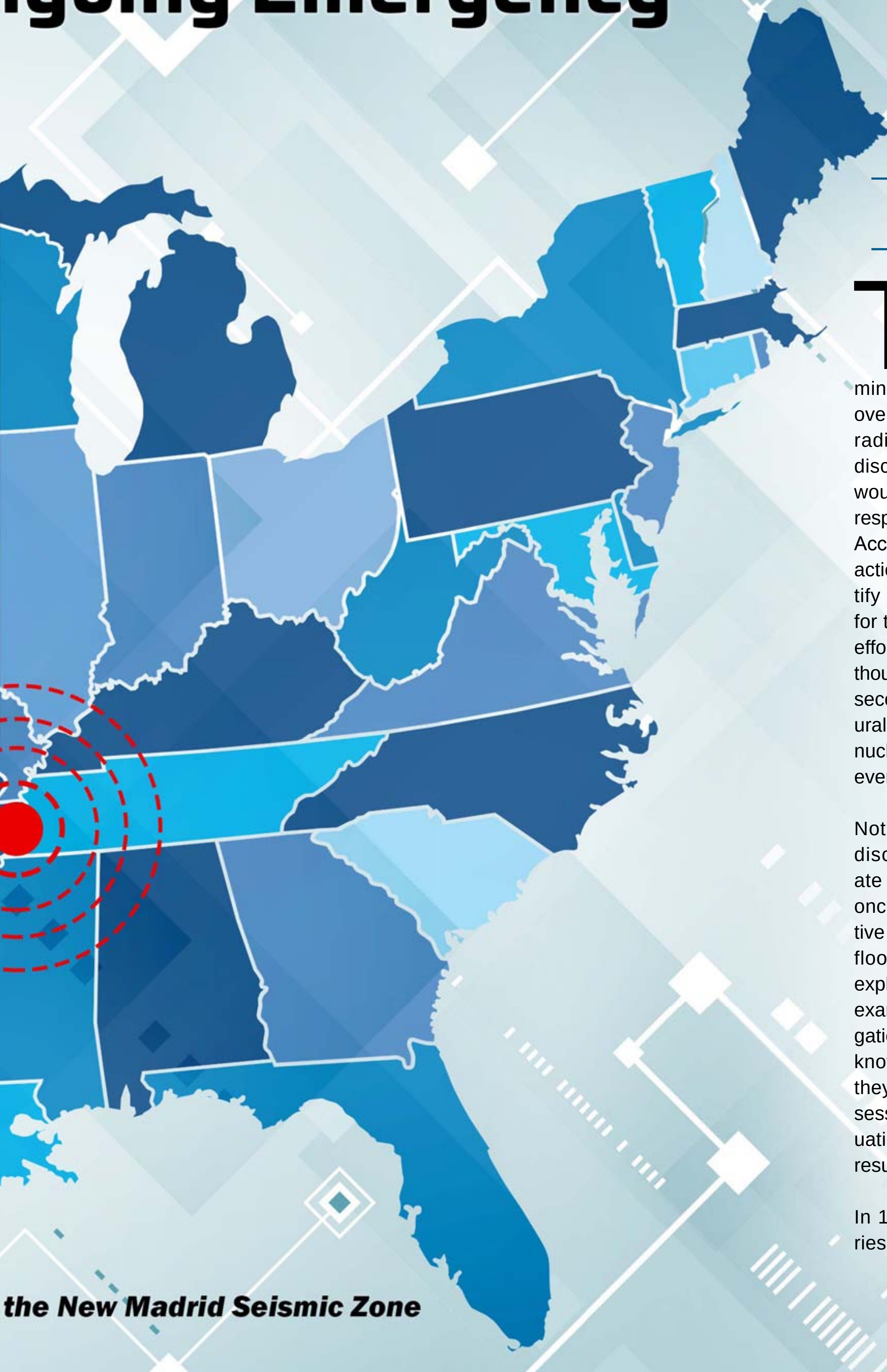
## New Madrid **Seismic Zone:**

## **Response** During an **Or**

*“One of the most commonly used **terrorist bombing techniques** of late is the use of what is called a **“secondary device.”** Most recently a secondary device was planted (but did not go off) in the **Belgium airport bombing**. A recent terrorist attack where the secondary device worked as planned occurred in Thailand … **340 people injured** because they didn’t understand the single most basic concept of terrorist bombings … The first bomb just draws the crowd and the emergency response personnel. **The second one does the majority of the damage.**” [1]*

# Earthquakes

## ngoing Emergency



**the New Madrid Seismic Zone**

**By: Col. Barrett K. Parker
& H. Quinton Lucie, J.D.**

There are emergencies we respond to that have relatively short duration with potentially high consequence. For example, tornadoes are over in minutes. A nuclear weapon burst would be over in seconds, and in a matter of hours its radioactive fallout plume would become a discrete and predictable event. A hurricane would subside in hours or days. By the time response teams arrive, the initial event is over. Accordingly, first responders begin lifesaving actions; planners scale the emergency, identify needed resources and create concepts for the follow-on life-sustaining and recovery efforts. In general, most emergencies can be thought of as discrete, non-continuous events; secondary hazards may linger—perhaps natural gas leaks from a tornado or fallout from a nuclear burst – while the risk from the primary event has ended.

Not all emergencies, however, are single, discrete events. Some emergencies create a continuous hazard to our responders once they arrive on-scene. Consider an active shooter, an Ebola-like disease outbreak, floods or a “secondary device” improvised explosive device scenario in the epigraph are examples of ongoing events that require mitigation. Planners and responders must clearly know and understand which kind of hazard they are addressing. Failing to correctly assess if an emergency is ongoing in certain situations, like the IED attack in Thailand, may result in a greater number of casualties.

In 1811, the New Madrid Seismic Zone series of earthquakes devastated the sparsely

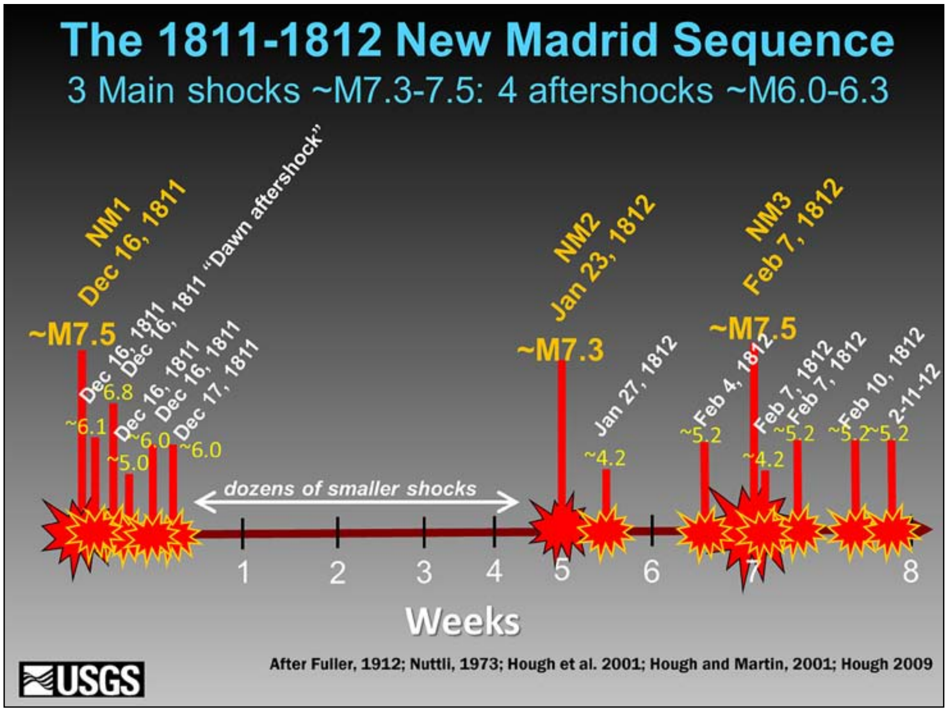



***Figure 1: This historical sequence shows the two month long ongoing emergency that was faced in 1811-12. (Image courtesy of U.S. Geological Surve/Released)***

populated Midwest United States. Three major earthquakes (NM 1-3) and hundreds of significant aftershocks shook the region relentlessly for eight weeks. Today disaster/consequence management planners and exercise designers have generally treated the next NMSZ series of earthquakes as a single, brief, discrete event. While tacitly acknowledging the possibility of aftershocks, plans and exercises understandably focus on immediate life-saving operations, moving to life-sustaining and recovery efforts as soon as the first major earthquake subsides. In reality, it is more likely that recurring, high-end aftershocks will significantly prolong and hamper life-saving efforts, greatly complicate life-sustainment operations and make starting recovery efforts untenable for prolonged periods of time.

## New Madrid Seismic Zone History

Webster defines an aftershock as, “a minor shock following the main shock of an earthquake.” [2] This definition is dangerously misleading if applied to the New Madrid Seismic Zone. The NMSZ earthquake sequence last presented itself in 1811 as a long series of major (magnitude 7.0-7.9) and strong (magnitude 6.1-6.9) earthquakes. As illustrated by the enclosed timeline, the 1811-1812 New Madrid Sequence was a group of four (including the “dawn aftershock” on December 16) major earthquakes and many damaging aftershocks, spread out over an eight-week period. The aftershocks numbered at least four magnitude 6 events and at least five magnitude 5+ events; all of which would have the potential to cause additional damage, especially if there were buildings already damaged by the main shocks. From detailed eyewitness accounts found in journals, diaries and newspaper stories, there were hundreds of smaller earthquakes/events during this time.

This earthquake sequence was not only spread out over time, but also in space, as the earthquake epicenter also shifted in location. The epicenter of the Dec. 16, 1811 event was near Blytheville, Arkansas. Over the next eight weeks, the epicenter of the earthquakes moved steadily northeastward, with the epicenter of the last major earthquake being about 55 miles away, in New Madrid, Missouri. For the major cities in the area, such as St. Louis, Missouri, Paducah, Kentucky, and Nashville, Tennessee, the consequence of the NM3 earthquake was more substantial than the initial event because the epicenter was closer. Thus, large earthquakes, unlike low magnitude events, are not just pinpoint events happening at the epicenter. The ruptures and close-in severe shaking impacts of large earthquakes are spread out over a 20-50-mile linear zone.

Robert Williams, a research geophysicist with the United States Geological Survey Earthquake Hazards Program in Golden, Colorado, clarifies how many aftershocks occurred:

> In total, Dr. Otto Nuttli, who was a prominent and respected seismologist at Saint Louis University, published work in the early 1970s in which he estimated that more than 200 moderate to large aftershocks struck the New Madrid region between Dec. 16, 1811, and March 15, 1812: 10 of these were greater than about magnitude 6.0; about one hundred were between M5.0 and 5.9; and 89 were in the magnitude 4 range. Nuttli also found that about 18 hundred earthquakes of about M3.0 to 4.0 during the same period. Geologists studying the New Madrid seismic zone after Nuttli’s work found that the geologic record contained convincing evidence of large pre-1811 earthquakes. We now know that over the past 3,000-4,000 years, the New Madrid seismic zone has repeatedly produced sequences of major earthquakes that contained earthquakes similar in magnitude to the 1811-1812 events. [3]

The history of the NMSZ demands an “ongoing emergency” concept of response, with the same continuing hazard mindset as a “secondary device” IED attack.

## Looking Forward

Looking forward, the USGS and the Center for Earthquake Research and Information of the University of Memphis now estimate that there is a 7 to 10 percent probability of a repeat of the 1811–1812 earthquakes (magnitude 7.3 to 7.5) sometime over the next 50 years. The probability of a magnitude 6.0 or larger over the same period is much higher, at 25 to 40 percent. [4]

> By studying the geological evidence and the hundreds of detailed personal accounts of people living near the Mississippi River… scientists have built an understanding of the timing and magnitude of the earthquakes occurring during the robust 1811-1812 sequence… Given this history of multiple large shocks… USGS, perhaps in coordination with the Federal Emergency Management Agency and regional State EMA’s, will likely issue a media advisory saying that there is a good chance of additional large main shocks and damaging aftershocks over the

coming months. This announcement may cause thousands of people to leave the region seeking shelter outside the strong shaking zone. [3]

## Exercises Do Not Reflect History Nor Predictions

Over the years, many exercises have focused on the NMSZ hazard. Unfortunately, participants have the impression that an NMSZ event will be much like that of a tornado, where the initial danger will be over within minutes and responders will be free to execute lifesaving and life sustaining operations and transition to recovery operations soon following. Perhaps there will be aftershocks, but they are not included in the response plans or the training scenarios.

The National Level Exercise 2011 followed this exercise design.

In the scenario, the southwest segment of the NMSZ ruptured at a magnitude of 7.7 from near Marked Tree, Arkansas, to near Ridgley, Tennessee. The shaking from this event triggered a magnitude 6.0 event in the WVSZ near Mt. Carmel, Illinois. The earthquakes caused widespread casualties, displaced households and damaged major infrastructure across eight states — Alabama, Arkansas, Illinois, Indiana, Kentucky, Mississippi, Missouri and Tennessee. [5]

While there is little doubt that this represents a near-worst case initial earthquake, in order to support a four-day exercise, the earthquake sequence was scaled and therefore depicted as a single, discrete event. Geologic activity that took eight weeks to culminate in 1811-12 was compressed to an instant, with a stated goal to "respond to and stabilize areas impacted by a catastrophic earthquake within the initial 72 hours." [5]

In response to this scenario, players implemented the following actions over the course of the exercise:

- **Monday, May 16:** Players focused on immediate lifesaving actions and mobilizing responders and resources to locations where critical damage occurred
- **Tuesday, May 17:** Response activities focused on meeting the health and safety needs of those affected by the simulated catastrophic earthquake
- **Wednesday, May 18:** In addition to lifesaving activities, players focused on life-sustaining activities and addressed needs related to infrastructure and housing damage
- **Thursday, May 19:** On the final day of NLE 11, players focused on life-sustaining actions and started shifting to the recovery process [5]

The need to employ all aspects of earthquake immediate response, stabilization and recovery within a four-day exercise overrode the need for a realistic NMSZ Sequence. If the 2011 NLE was overlaid on the historical 1811 timeline, the following actions may have been more indicative of the players' actions over the exercise:

- **Monday, May 16:** Players focused on immediate lifesaving actions and mobilizing responders and resources to locations where critical damage occurred
- **Tuesday, May 17:** Responded to a magnitude 6.1 aftershock. Response activities focused on new immediate lifesaving actions and recovering / refitting response teams affected by aftershock
- **Wednesday, May 18:** Responded to a magnitude 6.7 aftershock. Focused on new immediate lifesaving actions. Most response teams' effectiveness significantly reduced due to aftershocks. Significant new infrastructure and housing damage. Players responded to two new levee failures
- **Thursday, May 19:** Players focused on mobilizing new responders and replacing damaged recovery assets, while continuing lifesaving actions

By compressing the "ongoing emergency" of a NMSZ earthquake, exercises like NLE 2011 have generally overlooked the hazards of conducting rescue operations in a seismically active area. As a result, training scenarios do not force local, state and federal disaster planners to experience having to "restart" and "reinitiate" immediate lifesaving recovery actions. There is no requirement to replace injured response teams, rotate fatigued response teams, replace damaged response equipment or re-assess infrastructure. Simple procedures, such as having engineers assess key bridge trafficability and safety, becomes problematic if 14 earthquakes with a magnitude 4.2 or above occur over eight weeks. Infrastructure reinforcement and repairs become impossible under these conditions.

Local, state and federal disaster planners are also not compelled to conduct lifesaving, life-sustaining and recovery operations all at the same time. By training, responders have prioritized lifesaving operations at the expense of the other aspects of recovery, but will lifesaving still supersede recovery and infrastructure repair if damaged pipelines prevent the flow of essential gasoline or heating oil to the East Coast? Planners must practice and prepare to execute all missions simultaneously.

## Liquefaction: A Special Hazard Consideration

Liquefaction describes a process where a solid is turned into a liquid. In regard to earthquakes, liquefaction occurs when non-clay soils with a uniform particle size become saturated with water and are then subjected to a shock, such as an earthquake. These soils literally become a flowing liquid and lose their strength. The New Madrid area is notorious for liquefaction for two reasons; first, there is a large amount of sand buried just under the surface, and second, the water table is very high due to the close proximity of the Mississippi River. Liquefaction will primarily impact response operations by removing the underlying support from roads, rendering them unusable. Buildings can also fall victim to liquefaction, as their foundations become unsupported and unstable. Liquefaction also causes the infamous "sand blows" or "sand volcanoes" — liquefied sand jets out of the ground, sometimes producing sprays reaching tens of feet in the air and covering significant areas with sand.

Although the USGS has produced maps of both historical and projected liquefaction hazard areas, such as USGS Professional Paper 1336-B The New Madrid Earthquake: An Engineering Geologic Interpretation of Relic Liquefaction Events and Open-File Report 2011-1203 Liquefaction Hazard for the Region of Evansville, Indiana, liquefaction is usually not included in NMSZ exercises. [6]

## Recommendations

When the NMSZ becomes active, regardless if it is with magnitude 6 earthquakes or several earthquakes exceeding magnitude 7, it will be one of America's worst days. The warnings of scientists and experts as well as the lessons of history convey the risk is real and a comprehensive response must be planned. Rudimentary plans exist, and they have been exercised and rehearsed. Plans at all levels, however, must be reviewed to ensure they are coordinated to address an ongoing emergency rather than just a single, discrete event.

Likewise, planning to respond to an incident like the Thailand bombing where a second device is suspected is different from planning for an accidental industrial explosion. Planning for an active NMSZ series, lasting months, must be different from planning for a tornado, lasting minutes. New required capabilities to explore include:

- **Extending lifesaving operations.** Even discrete, instant emergencies like 9/11, lifesaving operations continued for several days. A NMSZ series would cause the "reset" or "re-initiation" of lifesaving operations to occur over a vast area. Recurring aftershocks days and weeks later will generate new civilian and responder casualties. The risk to the population may be exacerbated if secondary earthquakes or significant aftershocks occur during evacuation efforts. Rescue and recovery teams will be highly vulnerable to additional earthquakes as they search compromised infrastructure for survivors. A constant, reliable stream of trained response personnel and equipment will be required to maintain lifesaving operations.

*Figure 2: Liquefaction following the Christchurch Earthquake in New Zealand in 2011. While usually not directly hazardous to humans, liquefaction complicates transportation and can damage buildings and infrastructure. (Image courtesy of the Pacific Northwest Seismic Network/Released)*

- **Conducting simultaneous lifesaving, life-sustaining and recovery operations.** Disaster response priorities have always been clear – lifesaving, then life-sustaining and finally, recovery. Local, state and federal disaster responders will be compelled to conduct all three operations simultaneously during an extended NMSZ series. For example, prescription medicine refills and dialysis support for civilians, normally considered life-sustaining functions, will have to be provided simultaneously with lifesaving functions as the response continues. Recovery efforts, which may include returning critical petroleum product pipelines to service, may overshadow both lifesaving and life-sustaining as the East Coast runs low on the gasoline needed to transport food into major cities and becomes a national concern.
- **Welcoming foreign response teams.** Time and distance considerations and bureaucratic hurdles have generally reduced any consideration of interna-


*Figure 3: New Madrid's Riverfront Park is sited on top of the New Madrid Levee (right), protecting the town from the Mississippi River. This levee, completed in 1927, is typical of infrastructure that would have to be inspected and possibly reinforced after each significant aftershock. (Photos by author/Released)*

tional search and rescue teams to a secondary priority during earthquake exercises. However, in an NMSZ series response lasting months, there will be time to import international response teams. The need for these teams will be high, as U.S. teams are injured, stand down for equipment reset, maintenance or just become exhausted over time. Pre-coordination with some of these international teams, if written into current plans, may greatly reduce their response time and save American lives.

- **Planning on the long-term displacement of citizens.** An evacuation call by USGS and FEMA will create a vast stream of displaced citizens. If months pass before the earthquakes end, and more months pass before electrical and water services are restored, the regional population will have to be moved, housed and cared for. An NMSZ series creates the possibility of a second, preventable tragedy if plans are not in place to ensure proper caretaking of our displaced and vulnerable civilian population.
- **Caution against forward staging.** It is usually desirable to create forward areas to stage teams and supplies in order to reduce the problems associated with long-haul issues. However, with an NMSZ series consisting of several earthquakes and shifting epicenters, forward staging of teams and bulk supplies is a dangerous gamble. An additional concern with forward staging involves liquefaction, which occurs when certain saturated soils lose their strength following an earthquake. New Madrid is notorious for liquefaction, which can remove support from otherwise undamaged roads, rendering them unusable.
- **Planning on second-order disasters generated by follow-on earthquakes.** Levees and similar infrastructure may survive the initial earthquakes only to fail during the second earthquake or major aftershock. Developing training scenarios with these secondary disasters occurring during response operations would provide responders with challenging and realistic training. For example, it was not the initial impact of Hurricane Katrina but the second-order flood resulting from a levee breach that caused the majority of the deaths during the disaster.
- **Conducting simultaneous long-term response and recovery missions.** While many exercises simulate the transition between response and recovery, a brief review did not find exercises where both were conducted simultaneously for extended periods of time. A NMSZ series would create a competition of resources between the two, including the personnel assigned to overseeing both types of operations. Future exercises should explore the division of staffing of the two phases for federal and state governments, and how best to allocate resources. In addition, both of these activities would need to be prepared to conduct sustainable operations with rotational deployment plans and the expansion of reserve personnel cadres, such as the Department of Homeland Security Surge Capacity Force.

## Conclusion

It will be one of the United States' worst days when the NMSZ becomes active. It is certain that this day will come to pass. By looking at history and heading geological forecasts, we must ensure that our response to this enduring disaster is the best that we can devise. There is no reason for us to repeat the mistakes of the responders in Thailand, who missed the secondary device in their desire to save lives. ■

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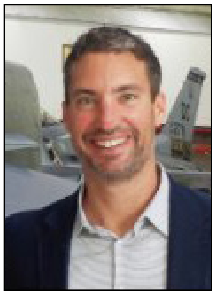

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**By: Gregory Nichols, MPH, CPH**

## Introduction

Technology is advancing at such a rapid pace that it is becoming increasingly difficult to assess the safety and efficacy of each technology before implementation. Furthermore, regulatory oversight and the law, which traditionally lag in regard to technology, are slipping even further behind this wave of technological development. New technologies that are disruptive, untested and not well-established are referred to as emerging. There are many different ways to define an emerging technology, but in general, an emerging technology is one that has the capacity to change the status quo. No matter the definition, all emerging technologies share five key attributes as defined by D. Rotolo:

- Radical novelty
- Relatively fast growth
- Coherence
- Prominent impact
- Uncertainty and ambiguity [1]

It is really the combination of these attributes that not only makes an emerging technology so attractive for positive, societal change, but also generates an environment for potential concern. Apart from environmental, health and safety issues, the concept of emerging technologies has generated apprehension and in some cases fear among military leaders and security experts. NATO has evaluated the impact of emerging technologies on arms control, [2] and a review of U.S. Naval strategy warned that the impact of emerging technologies on mission capabilities is ambiguous. [3] In fact, the latest U.S. National Military Strategy goes as far to state that, "emerging technologies are impacting the calculus of deterrence and conflict management by in-


creasing uncertainty and compressing decision space." [4]

The possibilities of nefarious use and security breaches emanating from emerging technologies have always been cause for alarm. In fact, some of the most notable technological developments in the 20th century (which were emerging in their time) still plague us today: nuclear fission, the internet and rocketry. These technologies have not just opened us up to new worlds of energy production, communication and travel, but also created fear and panic related to the advent of nuclear weapons, social media propaganda and cyber threats.

## The Possibilities for New Threats

Each year the World Economic Forum releases a list of the top 10 emerging technologies to watch for during the upcoming year. Over the past five years, six key groups of technologies are emerging as the most prominent (See Table 1) and are represented in Figure 1.

Aside from being new and not well-established, the aura surrounding many of these technologies is further complicated by the fact that they are considered dual-use technologies, meaning that most legitimate and beneficial uses of the technologies also brings a darker, more sinister application. The challenges associated with dual-use technologies are threefold:

- **Complexity** – Many variables with unknown or unknowable consequences
- **Uncertainty** – Inability to produce usable risk versus benefit assessments
- **Ambiguity** – Often involve conflicts over ethical and professional values [11]

Many of these technologies, if not all, are also being utilized by militaries for use in weapons systems, leading to a resurgence in not only proliferation but state-sponsored scientific research programs that often are used to drive militarization.

The emergence of new technologies, their expected use in military and terror tactics, and a general unawareness of potential consequences has created a new class of security risks that could defy countermeasures used for more classical types of threats, such as nuclear weapons. Nontraditional risks associated with technological innovation can be classified as emerging security challenges and may defy established security agendas. [12] Examples of risks associated with the emerging technologies described earlier can be found in Table 2. These technologies are the most rapidly developing and pervasive, and the potential risks they bring deserve further attention.

## Intellectual Property Theft and Espionage

Theft of intellectual property and espionage are not new crimes; however, the type of information that is being smuggled or potentially stolen is changing all the time. As emerging technologies develop and evolve, the allure they bring in terms of competitive advantage and innovation will become more sought-after, and their value will bring big rewards from some and great loss for others.

In 2014, Jianyu Huang, a former scientist at the Department of Energy pleaded guilty to making a false statement and unlawfully transporting converted government property in interstate and foreign commerce. Huang, a naturalized U.S. citizen from China, was employed at the Center for Integrated Nanotechnologies, which is a user facility jointly operated by Sandia National Laboratories and Los Alamos National Laboratory. From 2009 to 2012, Huang made a series of trips to China in which he brought his government issued laptop containing sensitive information regarding his research with him. He admitted to sharing the information on this laptop with businesses and universities throughout China and was sentenced to one year in prison. [13]

Five men in Taiwan were charged in July 2016 with stealing intellectual property from a nanotechnology company and setting up competing nanotechnology plants in China. The men are former employees of Hsin Fang Nano Technology Co., which developed a novel process for manufacturing nanopowders used in a variety of applications. The men used the information they stole to create Unicat Nan Advanced Materials & Devices Technology Co., and operated it successfully for several years before being apprehended. The estimated financial loss to Hsin Fang is reported to be approximately $82 million U.S. dollars and cost the company 15 years of research. [14]

Apart from nanotechnology, other technologies, such as 3D printing and synthetic biology, pose new risks to IP, particularly in the patenting aspect. Two things are needed to operate a 3D printer: material and a design. The material is either a polymer composite or a metal, and the design is an electronic file (computer-aided design file) that can be developed on special software and even downloaded from the internet. Traditionally, product design has been protected because

| 2012 | 2013 | 2014 | 2015 | 2016 |
|---|---|---|---|---|
| Informatics for Adding Value to Information | OnLine Electric Vehicles | Wearable Electronics | Fuel Cell Vehicles | Nanosensors and the Internet of Things |
| Synthetic Biology and Metabolic Engineering | 3-D Printing and Remote Manufacturing | Screenless Display | Next-generation Robotics | Next Generation Batteries |
| Green Revolution 2.0 – Technologies for Increased Food and Biomass | Self-healing Materials | Human Microbiome Therapeutics | Recyclable Thermoset Plastics | The Blockchain |
| Nanoscale Design of Materials | Energy-efficient Water Purification | RNA-based Therapeutics | Precise Genetic-engineering | 2D Materials |
| Systems Biology and Computational Modelling/Simulation of chemical and Biological Systems | Carbon Dioxide ($CO_2$) Conversion and Use | Quantified Self (Predictive Analytics) | Additive Manufacturing | Autonomous Vehicles |
| Utilization of Carbon Dioxide as a Resource | Enhanced nutrition to Drive Health at the Molecular Level | Brain-computer Interfaces | Emergent Artificial Intelligence | Organs-on-Chips |
| Wireless Power | Remote Sensing | Nanostructured Carbon | Distributed Manufacturing | Perovskite Solar Cells |
| High Energy Density Power Systems | Precise Drug Delivery through Nanoscale Engineering | Mining from Desalination Brine | “Sense and Avoid” Drones | Open AI Ecosystem |
| Personalized Medicine, Nutrition and Disease Prevention | Organic electronics and Photovoltaics | Grid-scale Electricity Storage | Neuromorphic Technology | Optogenetics |
| Enhanced Education Technology | Fourth-generation reactors and Nuclear Waste Recycling | Nanowire Lithium-ion Batteries | Digital Genome | Systems Metabolic Engineering |

*Table 1: The World Economic Forum’s Top 10 Emerging Technologies by year for 2012-2016 with technologies representative of six key groups. (Released) [58,59,60,61,62]*

only the manufacturer has the specifications and the ability to create the item; however, 3D printers are changing that model. The cost of a small 3D printer is only a few hundred dollars, and because CAD files are digital, they can be shared across the internet on file-sharing services, just like movies and music. [15] It is now possible for someone to find the plan online for a product they want to create and simply download and print it on a desktop 3D printer at home.

Somewhat more complex, but maybe even more alarming, is the possibility of patent wars for biological innovations. In 2013, the U.S. Supreme Court ruled in Association for Molecular Pathology et al. v. Myriad Genetics that human genes are not patentable but synthetic DNA is patent eligible because it does not occur in nature. [16] Although this ruling puts limitations on developments in biotechnology related to gene-sequencing, this ruling opens up many new possibilities including a potential war for creating new organisms and being the first to market in order to reap the financial rewards.

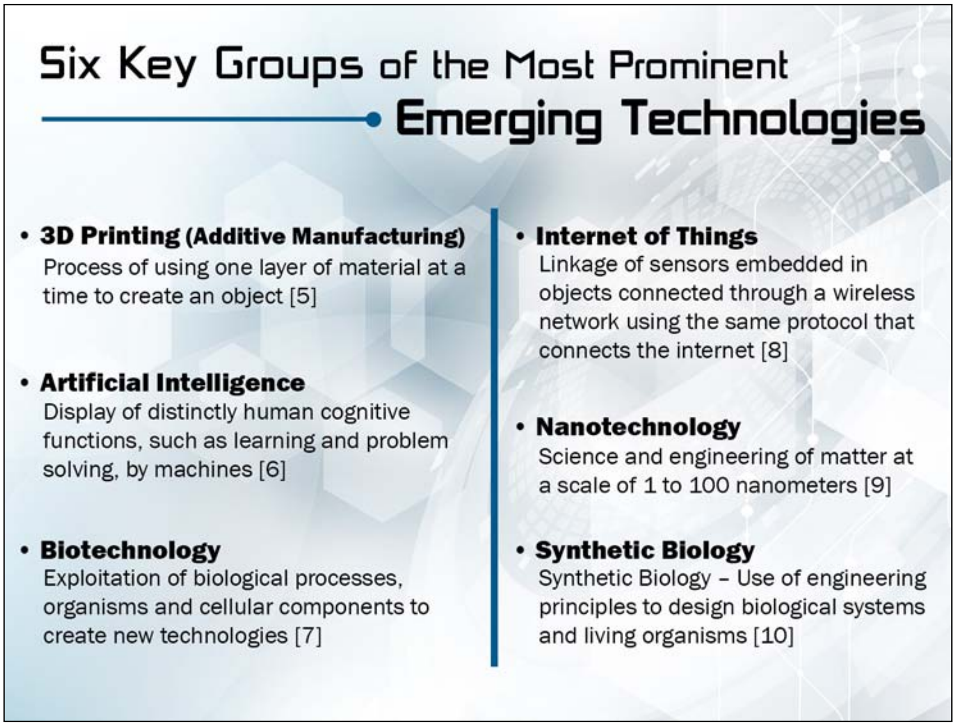


*Figure 1: A representation of the six key groups of the most prominant emerging technologies. (Released)*

## Loss of Control and Sabotage

The connectivity of items to the internet, and the expanded use of electronics and code in general has created a new venue for causing damage and destruction. Sabotage may be one of the oldest threats known to humanity, but technology is opening up the possibility to do this in completely new ways. One example is through 3D printers that are connected to the internet, allowing for remote control. Hackers might be able to target these printers and secretly introduce catastrophic internal defects in the manufacturing process, change the printing orientation or insert fine defects that may manifest at a later time. [17] This may not seem to be a huge concern until the extreme consequences are truly realized. Imagine that thousands of parts used in engines and airplanes are covertly altered and unknowingly placed into service, only to fail at some later time during operation leading to unexplained multiple crashes at once. This is becoming more of a likely scenario as industrial 3D printing becomes more of a widespread reality. [18] These fears apply even to medicine. In August 2015, Aprecia Pharmaceuticals received Food and Drug Administration approval for the first 3D printed drug, Spritam (levetiracetam), which is used to control seizures brought on by epilepsy. [19,20] If the files that drive the printing of the pills were altered in any way, the entire dosing and effectiveness could be manipulated and would potentially compromise the health of anyone taking the drug.

Looking beyond 3D printing, connectivity in general has generated new ways of wreaking havoc on systems. In October 2016, a large portion of the internet was threatened when hackers used the IoT to execute a distributed denial of service attack. [18] A DDoS occurs when a machine receives so many commands that it crashes because it cannot keep up. What is interesting in this case is that hackers utilized something called a "Mirai" botnet that specifically targeted internet-connected devices resulting in more than 500,000 devices being comprised and sending out signals simultaneously and bringing down part of the internet. [21]

More than household devices are connected to the internet. Many aspects of critical infrastructure, such as power plants and dams, are connected to the internet to provide remote and automated access in order to improve the efficiency of operations and reduce the amount of hours a person needs to spend on-site. While this aspect of connectivity does improve operational capacity, for obvious reasons, it creates security threats. For example, sensors are often placed on dams in order to measure water levels and automatically control flood gates if the height of water in the reservoir changes. It is possible to manipulate the sensors and cause the dam's system to think that the levels are too high (a process called spoofing) and open the flood gates lead-

| Risks | Technologies | Examples |
|---|---|---|
| Intellectual property theft/espionage | • 3D printing<br>• Biotechnology<br>• Nanotechnology<br>• Synthetic biology | • Copyright infringement<br>• Security vulnerabilities<br>• Financial loss<br>• Patent wars |
| Loss of control/sabotage | • Artificial intelligence<br>• Internet of things | • Rogue unmanned systems<br>• Spoofing |
| Terrorism/WMD | • 3D printing<br>• Biotechnology<br>• Internet of things<br>• Nanotechnology<br>• Synthetic biology | • Untraceable weapons<br>• Genetically altered diseases Hostile control<br>• Unidentifiable poisons<br>• Untreatable illnesses |

*Table 2: Key emerging technologies, their associated risks, and some examples of concerns. (Released)*

| When | Where | What | Who |
|---|---|---|---|
| 2004 | Berkeley, CA, USA | Protest at Molecular Foundry groundbreaking (Lawrence Berkeley National Laboratory) | Topless Humans Organized for Natural Genetics |
| 2004 | Chicago, IL, USA | Disruption of NanoBusiness Alliance meeting | Topless Humans Organized for Natural Genetics |
| 2004 | Buckinghamshire, UK | Protest at conference of nanotechnology investors | The Heavenly Righteous Opposed to Nano-tech Greed |
| 2005 | Bellevue, WA, USA | Protest outside Eddie Bauer headquarters | Topless Humans Organized for Natural Genetics |
| 2006 | Grenoble, France | Protest outside MINATEC | Students |
| 2009-2010 | 5 cities across France | Protest/vandalism at town halls | Pièces et Main d'Oeuvre |
| 2010 | Zurich, Switzerland | Attempted attack on IBM nanotechnology facility | Switzerland Earth Liberation Front |
| 2011 | 10 cities across Mexico | Series of bomb threats, thwarted attacks, and successful detonations | Individuals Trending Toward Savagery |

***Table 3: Protests and terror incidents involving nanotechnology-related venues. [63] (Released)***

ing to an unplanned and potentially catastrophic release. A group of Iranian hackers gained access to the Bowman Dam in Rye, New York, in 2013. [22] They never gained access to the dam itself, but they did learn information about how the flood gates are controlled.

Artificial intelligence is creating a unique set of risks, in particular one that has frightened humanity for decades, and that is the threat of machines taking over. While the threat may not necessarily be imminent, there is some cause for alarm as both the private sector and the militaries of many nations push to have more autonomous and intelligent machines. In an effort to keep tabs on the activities of semi-autonomous and even autonomous systems, the Department of Defense released DoD Directive 3000.09 prohibiting the creation or use of unmanned systems to, "select and engage individual targets or specific target groups that have not been previously selected by an authorized human operator." [23] This sort of protection becomes imperative when looking at a weapons platform such as the South Korean Super aEgis II, which is the first weapon system capable of recognizing and targeting humans. [24] However, the nature of machine learning in intelligent systems would eventually enable a system to figure out how to get around this failsafe, [25] and at some point, the human would be removed from the equation altogether. Google's Brain deep learning project developed three neural networks named Alice, Bob and Eve that passed each other notes using an encryption method they created themselves. [26] This is the first AI-generated, human-independent encryption.

Understanding what it would mean if a human were unable to gain or regain control of an autonomous, semi-autonomous or intelligent system is the sort of scenario that is becoming more likely. [27,28] "We believe strongly that humans should be the only ones to decide when to use lethal force. But when you're under attack, especially at machine speeds, we want to have a machine that can protect us," Deputy Defense Secretary Robert Work said. [29] In fact, this type of response has already been demonstrated as an AI-controlled drone defeated a pilot in a simulated dogfight. [30] As the DoD continues to develop its Third Offset Strategy [31] and push for more autonomous systems in which humans play a vital role, but not necessarily the lead role, preparing for risks, such as losing control through hacking or intrinsic systems design, will be paramount. Additionally, preparing for attacks from intelligent systems that do not have the same "human in the loop" safeguards will be equally important.

## Terrorism and Weapons of Mass Destruction

In 1346, a Tartar (a subjugated peoples of the Mongol Empire) army laid siege to the city of Caffa on the Crimean peninsula. Sometime after the siege began, the Tartars were stricken with an outbreak of the plague. As the body count mounted, the Tartar commander decided to change the rules of the game and ordered plague-infected corpses to be catapulted into the city. Shortly after, an outbreak of plague erupted inside the walls of Caffa. This event is long believed to have initiated the Black Death that killed one-fourth to one-third of Europe's population in the 14th century. [32]

In 1978, a Bulgarian dissident named Georgie Markov was attacked with an umbrella in London. Unbeknownst to Markov, the umbrella was modified and used to inject a pellet containing ricin into his leg. Ricin is a highly toxic substance found in the castor bean. He died four days after the attack. [33]

In November 2006, a healthy man was admitted into a London hospital with severe gastrointestinal symptoms. He died approximately three weeks later. His death was later determined to be caused by poisoning from Polonium-210, a radioactive substance. [34]

The connection between all three of these events is that they are the first of their kind. No one ever thought these things could or would happen until they did. In many ways, these incidents set the precedent for what it means to be prepared to face emerging security risks. The emerging technologies discussed throughout have the potential to be used as new weapons of terror.

One of the hallmarks of emerging technologies is the uncertainty they naturally harbor, which for obvious reasons, poses unique challenges in preventing attacks as evidenced by a strange report from Russia. Svetlana Zheludeva, a deputy director at the Russian Academy of Sciences, died suddenly after opening a letter containing a white powder. The sender of the letter had sent several similar letters with the white powder to other scientists claiming the powder was a product of his research in nanotechnology; however, no other recipients of the letters died, and test results supposedly showed that the powder was ordinary quartz sand. Russian authorities have stated that there will be no criminal charges and no other information about the case is available. [35]

Even more concerning than bizarre nanotechnology case reports are real instances of biotechnology and synthetic biology used to create more virulent organisms, and, in some cases, completely new ones. A report prepared by the United Nations Interregional Crime and Justice Research Institute called attention to the possibility that beneficial applications of synthetic biology and biotechnology could be suitable for of new or enhanced biological weapons and used by criminals or terrorist. [36] Gene editing techniques, such as clustered regularly-interspaced short palindromic repeats, have the potential to revolutionize medical treatments by altering faulty genes in patients suffering from rare or degenerative disorders; [37] however, CRISPR could also be used to create mutated strains of organisms that could be lethal, and, in fact, CRISPR has already been used to modify human embryos. [38]

Over the past decade and a half, researchers have used genetic engineering techniques to develop hypervirulent strains of viruses in an effort to use that information to create more efficacious vaccine. However, the development of these new viruses and the debate as to whether or not the results of this research should be published openly has created ethical and security challenges. To date, some of the more important biotechnology research includes:

- 100 percent fatal strains of mouse pox created [39,40]
- Genetic characterization of the 1918 influenza pandemic (H1N1) [41]
- Genomic characterization of the Plague that destroyed Europe in the 14th century [42]
- More virulent strain of bird flu (H5N1) engineered [43,44]
- Recreation of 1918 influenza strain (H1N1) using various strains of bird flu (H5N1) [45]

In September 2016 researchers in the United Kingdom created the world's smallest virus, measuring 12 nm in diameter. [46] This was unprecedented considering this was the first artificial virus ever created, but it also opens up a new possibility for biological warfare. No longer do armies or terrorists have to aerosolize existing organisms; they can now create them. These artificial viruses have no known treatments since they have never existed before, which creates new challenges to developing countermeasures and anticipating threats.

Aside from chem-bio attacks, emerging technologies are changing the landscape for how traditional attacks could be carried out. The first 3D printed weapon was successfully fired in 2013, [47] and in August 2016, Transportation Security Administration officers at the Reno, Nevada, airport confiscated a loaded 3D printed handgun in a passenger carry-on bag. [48] More interesting is the fact that the U.S. military has an interest in new 3D printing technology that would allow soldiers in the field to potentially print entire missiles at once. [49] A platform like this could be a game-changer for terrorist organizations in terms of leveling the playing field regarding weapons production and availability.

Finally, new technologies not only bring risk through the potential of creating new types of weapons but the concept of the technology itself poses a threat. Since the early 2000s, a series of attacks and protests aimed at nanotechnology-themed activities and research centers has occurred across the world (Table 3). In many cases, these were harmless protests incited by students or local environmental groups. However, a failed attack on the IBM facility in Zurich and several planned attacks throughout Mexico were orchestrated by known terrorist organizations, and possibly connected to a group known as the Olga Cell, part of an Italian-based internal terrorist organization known as the Federaziane Anarchia Informale. [50]

## Mitigation

Part of the challenge to managing emerging technologies is anticipating what, if anything, could potentially go wrong. The other aspect is to understand what to do in order to manage the fallout of an adverse event. Typically, policy and the rule of law is how most threats are mitigated. In fact, legislators and regulators have looked at existing legal frameworks in order to control emerging threats from technologies. In terms of nanotechnology, biotechnology and synthetic biology, chemical and biological weapons bans and treaties have been deemed appropriate to control the proliferation of new threats. However, biological innovations have always seemed to garner more attention than others, starting with the Ansilomar Conference in 1975 [51] and culminating with the recent announcement of the intent by the National Academy of Sciences and the DoD's Office of the Deputy Assistant Secretary of Defense, Chemical and Biological Defense to assess biodefense given new advances in synthetic biology. [52]

The big problem is that laws are only as good as the people who choose to follow them. The key issue is how to mitigate threats of emerging technologies in the face of any and all environments. Foremost is promoting awareness of not only emerging technologies, but the potential and actual risks they invoke, particularly as everyone, including rogue states and violent non-state actors, are gaining access to the same technology. [52] Recommendations for addressing risks of emerging technologies revolve around awareness, social responsibility and research:

- Increase awareness of the dual role of emerging technologies and their unintended security consequences
- Identify and address emerging security concerns now, even if the threat seems to be remote
- Build emerging security concerns into education curricula and have it addressed within national institutions
- More dialogue around risk governance priorities between industry, academia and government
- Increase funding and priority for research related to risk governance
- Promote a culture of responsibility around innovation
- Include applications of technology in war gaming scenarios used to train military leaders [52,53,54]

Some of these recommendations are already in practice. The FBI launched a program to identify suspicious activity that could be connected to nefarious uses of synthetic biology. The Synthetic Biology Tripwire Initiative is a system in which suppliers of biological products used in synthetic biology or biotechnology alert the FBI when odd requests are made. [55] DARPA announced in September 2016 that it was developing Safe Genes, a program to develop a set of tools used to address potential risks of gene editing. [56] UNICRI is in the process of opening the Center for Artificial Intelligence and Robotics, aimed at raising awareness of the risks and benefits of AI. [57] While these initiatives are a good start, more focus needs to be put on other technologies and include training for first responders.

## Conclusion

In many ways, the title of this article may be misleading. These are not necessarily new risks, but rather relatively common risks that are brought about in ways that have not been used before. However, the fact that most of the world is unprepared to mitigate any one of these scenarios, let alone facing the possibility of several of these scenarios occurring at once, is disconcerting, to say the least. If the 20th century taught us anything, it is that science and technology can be both our greatest friend and our worst enemy. Few people want to think about the impossible or the unknowable, let alone spend money preparing for something that may or may not happen. However, it is always better to plan because each of the events in this article have happened, and these are just the ones we know about. ■

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# Host-Oriented
## as an Innovative Countermeasure


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&

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### The Premise and Need

Our research objective is to develop novel small molecule, broad-spectrum therapeutics against viral infections caused by high priority, bioterror pathogens, including filoviruses and arenaviruses. Currently, there are no Food and Drug Administration approved products to effectively combat severe hemorrhagic fever syndrome induced by several of these deadly viruses, including Ebola, Marburg and Lassa fever. Our innovative approach to develop host-oriented inhibitors that could prevent disease transmission and spread will fill a significant unmet need and will lead the way in identifying first-in-class life-saving therapeutics for these highly devastating, Category A, high priority pathogens.

The expectation is that targeting a cellular protein, instead of a viral target, will greatly diminish or eliminate the frequency of drug resistance-conferring mutations that can occur. If this approach provides potent viral inhibition without toxicity to normal healthy cells, it will facilitate further investigations into the targeting of cellular proteins, so-called host cell factors, for other viral diseases and may lead to a class of better antiviral drugs. Because all viruses, to one extent or another, are dependent on host cell factors for their life cycle, the approach should be applicable to nearly all viral pathogens.

Our anti-viral product that targets Ebola, Marburg and Lassa fever is expected to be used for treatment of infected individuals as well as in prophylactic treatment of soldiers, health care workers or others at high risk. We postulate that emergency administration of such an antiviral therapeutic during an outbreak would both inhibit virus dissemination in infected individuals and reduce the spread of infection, thus slowing disease progression, allowing for more effective viral clearance by the immune system and preventing further viral transmission. As these host-oriented inhibitors are broad-spectrum, they will likely be effective against newly emerging viruses or viral variants. Since these virus-host interactions represent a common mechanism in a range of RNA viruses, we predict that they represent an Achilles' heel in the life cycle of many RNA virus pathogens.

### Value of the Project

This project represents several important value propositions to both the military and to the general public. First and foremost, is the ability to save the lives of people infected with the types of viruses targeted by this drug, namely Ebola, Marburg, Lassa fever

# Therapeutics Against EBOLA & Other Hemorrhagic Fever Viruses

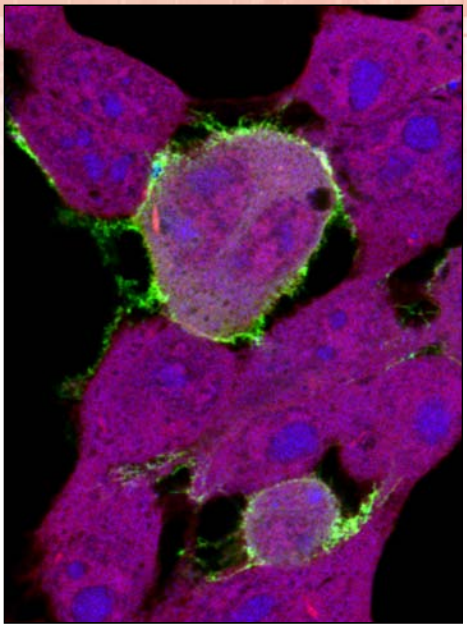
and Junin viruses. Currently, there are no approved products, or any medical measures, which effectively combat virally induced hemorrhagic fever syndrome. HFS is a usually fatal result of viral infection where the infected individual rapidly succumbs to the infection as a result of widespread internal bleeding and organ failure.

Our scientific approach contains several elements that make important contributions to the development of antiviral agents. Chief among these approaches is the targeting of a host cell factor(s) necessary for the virus to be released from an infected cell and disseminated throughout the individual. Nearly all antiviral drugs that have been developed to date target a viral protein essential for virus replication. The continuing problem with this approach is that a great number of viruses are able to quickly mutate to overcome the inhibitory effects of the drug. RNA viruses, which include some of the most pathogenic viruses known, including Ebola and Lassa fever viruses, are especially adept at developing resistance-conferring mutations.

## Virus Egress as a Target for Host-Oriented Therapeutics

Late (L) domains (PPxY and PTAP) are short amino acid motifs that are highly conserved in the matrix proteins of a wide array of RNA viruses (e.g., filoviruses, arenaviruses, rhabdoviruses, paramyxoviruses, henipaviruses and retroviruses). [1] Notably, independent expression of filovirus VP40 or arenavirus Z matrix proteins leads to the production and egress of virus-like particles that accurately mimic budding of live virus, and PPxY L-domains within these matrix proteins play a central role in promoting efficient VLP and virus egress. [2,3,4,5,6]

Moreover, efficient egress of VLPs depends on viral L-domain mediated recruitment of host proteins required for complete virus-cell separation or pinching-off of virus particles



***Confocal image of HEK293T cells expressing GFP-tagged EBOV VP40 (green) and stained with HCS Cell Mask Deep Red and Hoechst dye (blue). GFP-VP40 accumulates at the site of budding at the cell surface and forms VLP projections from the plasma membrane. (Released)***

from the cell surface. [7] For example, recruitment of WW-domain containing cellular E3 ubiquitin ligases (e.g., Nedd4 and ITCH) associated with the host ESCRT1 complex (endosomal sorting complex required for transport) by the viral PPxY L-domain motif is critical for efficient budding of filoviruses, arenaviruses and rhabdoviruses. Based on the critical role of this viral-host interaction during budding, we have used a multifaceted approach to identify, develop and validate two independent series of PPxY budding inhibitors as potent, broad-spectrum antivirals. [8,9,10,11,12,13]

Our strategy represents a new approach toward the treatment of viral infections in that the target of the drug action is a cellular protein rather than a viral target. Concerns regarding the use of host cell-targeted agents due to potential toxicity resulting from inhibition of host protein function are reasonable, but the redundancy present in most cellular functions and a much higher barrier to the development of resistance to antiviral activity may offset these concerns.

## Lead Candidate Budding Inhibitors

Our main objective is to exploit the viral PPxY–host WW domain interaction to obtain broad-spectrum antiviral therapeutics and find suitable chemical equity to move to a full-fledged drug discovery program. Toward this end, we have discovered two series of novel agents that potently interrupt the host Nedd4/viral PPxY interaction, thereby inhibiting viral budding and proliferation. [8,11]

We have made substantive progress in identifying structure activity relationships and improving upon potency for our lead inhibitors 4 and 5. [8,11] Our most potent compounds to date show strong inhibition of Ebola and Marburg VP40 VLP egress as well as inhibition of infectious Ebola and Marburg virus egress at nanomolar concentrations. Moreover, these compounds have in silico properties (MW, cLogD, etc.) and experimental oral drug properties (e.g., metabolic stability) that are predictive of oral drug delivery. [8,11]. We will continue to optimize our lead series to find orally active and safe preclinical drug candidates.

Eventually, we will transition one or more full-qualified PPxY inhibitors into more detailed investigational new drug-directed pharmacokinetic, pharmacodynamic and toxicity studies. Successful completion of these goals will provide a comprehensive package to support advanced development, efficacy testing in nonhuman primates and an IND submission for Phase I safety testing in normal volunteers.

## Summary

There are no approved drugs for the treatment of filovirus or arenavirus infections. Infection with these NIAID Category A pathogens rapidly leads to a hemorrhagic fever syndrome with high rates of fatality. Our lead compounds have shown encouraging antiviral potency in VLP, surrogate virus and live virus assays and mechanistically block a critical interaction between the filoviral VP40 matrix protein and host E3 ubiquitin ligase Nedd4. Our lead compounds possess drug-like properties that are amenable to modification to improve their potency, selectivity, metabolic profile and physio-chemical properties. This work is the result of a multidisciplinary team of established scientists with strong complementary skills in viral biology, virus-host interactions, live cell imaging, medicinal chemistry and drug synthesis and development. ■

***The opinions, conclusions, interpretations, and recommendations are those of the authors and are not necessarily endorsed by the U.S. Department of the Army and the U.S. Department of Defense.***

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**Allen B. Reitz, Ph.D., is chief executive officer of Fox Chase Chemical Diversity Center, Inc. FCCDC conducts early-stage medicinal chemistry and drug discovery activities in direct support of the objectives of the laboratory of Ron Harty at the University of Pennsylvania, and has held a Phase I STTR in the area of virus assembly and budding with Harty as the Principal Investigator. Reitz received his Ph.D. in chemistry from the University of California, San Diego and an Executive Master's from the University of Pennsylvania (Penn Engineering and the Wharton School). Reitz was at Johnson & Johnson in Spring House, Pennsylvania for nearly 26 years before founding FCCDC in 2008.**

# A Novel Approach to Battlefield Wound Assessment & Treatment for Forward Surgical Teams

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**Chitrak Gupta**
&
**Jonathan Boyd, Ph.D.**

As warfare technology has progressed to more sophisticated and deadly tactics, the prevalence and severity of traumatic injury have increased. During Operation Iraqi Freedom and Operation Enduring Freedom, 78 percent of wounds sustained in combat were a consequence of explosions, and extremities were the most commonly affected body region. [1] Due to the severity and frequency of these types of injuries, surgeons working as part of forward surgical teams must think, move and act more quickly to keep pace with patients' needs because mistakes could result in major tissue loss or death.

A study investigating both the frequency and nature of injuries treated by an FST in Afghanistan during the initial phase of Operation Enduring Freedom found that debridement was the most commonly performed procedure. [2] Debridement is the removal of entire sections of damaged tissue, while retaining as much healthy tissue as possible. This process relies on surgical expertise and includes visual and tactile inspection.

Unfortunately for surgeons operating as part of FSTs, extensive wound assessment and treatment options can be restricted, while the clock is ticking on saving tissue and lives. Finding a balance between removing and keeping tissues can mean the difference between risking life-threatening infection and saving a limb. Proper wound debridement is critical for the subsequent wound healing processes, but the current methods for assessment lack precision and require too much time. Injuries to extremities can be expected to persist as the use of explosives in combat continues to rise. Wound assessment will remain a time-consuming and complicated treatment step if new methods are not implemented.

To accommodate the need for more precise treatment, new surgical techniques can be developed to incorporate fluorescent probes that assist surgeon assessments of wounds. By using fluorescently-labeled tags to target tissue that needs to be removed, a surgeon can create a clear and distinct visual boundary between nonviable and healthy tissue. These advances would not only alleviate time pressure but would also improve the quality of care given to patients by establishing a quantifiable method for zone of injury determination.

One prospective option is the use of a biocompatible chemical probe, which may be achieved based on the unique properties of the peptide pHLowInsertionPeptide. The name pHLIP appropriately describes the peptide's mechanism: an increase in the rate of glycolysis within the cells of injured tissues causes a lowered local pH environment, which allows the peptide to insert into cell membranes. pHLIP exists in three conformational states. The first is the free-floating monomeric peptide in solution. If tissue at a physiological pH (~7.4) is exposed to pHLIP, the peptide adopts a conformation that allows it to loosely associate with the cellular membranes that are made up of lipids. When the pH dips below physiological levels, pHLIP assumes a coiled conformation and inserts across the lipid membrane. This characteristic presents a unique opportunity to use pHLIP to monitor any cellular process involving a decrease in the local pH environment, including cancer, tissue damage and more. [3,4,5,6]

Localized acidity targeting is achieved through a relatively simple process. A pH drop causes protonation of aspartic acid and glutamic acid residues of the peptide, increasing the peptide's affinity for lipid bilayers and promoting insertion. [7] Upon insertion, the C-terminus penetrates the cell while the N-terminus remains outside. Researchers can capitalize on this process by attaching fluorescent tags to the N-terminus of the peptide, allowing real-time monitoring of cellular perturbations. In particular, pHLIP can be used to visualize the zone of injury and differentiate between viable and damaged tissue based upon simple pH changes.

While using pHLIP conjugates to identify wound boundaries is novel, pHLIP-fluorophore conjugates have been extensively studied for early detection of cancer and to improve surgical tumor removal. [3,4] The pHLIP-conjugated fluorescent response is directly related to extent of injury, as more serious tumors cause more acidic local environments due to the localized increase in the rates of glycolysis of those tissues. This increased glycolysis will decrease the local pH and ultimately increase the peptide concentration on the tumor surface.

Further, fluorescence can be measured and quantified to improve diagnosis, as targeting changes in glycolysis has been directly correlated with the aggressiveness of tumors. [3] To determine the relationship between fluorescent signal and malignancy, Reshetnyak et al. found higher concentrations of fluorescent pHLIP in tumors with necrotic and apoptotic cores than in tumors with no necrotic tissue. [6] As necrosis is a hallmark of wounds, the same correlation is expected in cases of wound healing. The scope of pHLIP cancer research creates a well-established theoretical base from which researchers can build to expand pHLIP use to wounds.

Fluorescent tools like pHLIP can probe injuries below the tissue surface, and the only criteria for insertion is an acidic environment. Once it targets this region by inserting into diseased or damaged cells, the excess pHLIP conjugate can be distributed and excreted, and only an illuminated zone of injury will remain. After a short clearance time, clinicians can repeatedly use pHLIP conjugates to monitor patient progress and predict the course of treatment.

Wound healing is a complex biological process, beginning with hemostasis and the formation of a platelet plug, then moving to inflammation, when a variety of immune signals are recruited to the wound to prevent infection. During the next phase, cell proliferation, new tissue grows to eventually cover the wound. Finally, the new tissue fully differentiates and matures, which increases the resilience of the closed wound. Complete wound healing can take up to two years, so it is critical that surgeons monitor this delicate process to ensure chronic wounds or infection do not develop.

Wound assessment is an integral part of healing success, and clinicians must evaluate the tissue types, check for presence of inflammation and determine the wound edge. Of these criteria, determining wound edge is the most elusive because there are no well-developed methods to quantify the extent of a wound. Removing the dead or dying tissue is an essential step in initiating wound healing, and successful excision of diseased tissue largely impacts the quality of care. In fact, a study by Cardinal, et al. confirmed a strong correlation between performing surgical debridement and improved wound healing rates, showing that in venous leg ulcers and diabetic foot ulcers, debridement procedures improved wound closure progression. [8]

Unfortunately, improper debridement can result in necrotic tissue remaining at the injured site, providing optimal growth conditions for bacteria and creating a nidus for infection. Complete debridement is important for treating abscesses that, when improperly treated, can develop into infections and cause sepsis. A purely visual estimation of wound edge takes more time and expertise, while increasing the risk of leaving diseased tissue behind. On the other hand, delayed wound healing can also be a consequence of over-debridement, where too much tissue is removed from the injured site. Finding a happy medium between these cases is challenging, and FSTs must make these complicated decisions regularly.

Currently, there are no standardized guidelines for surgical debridement. A certain

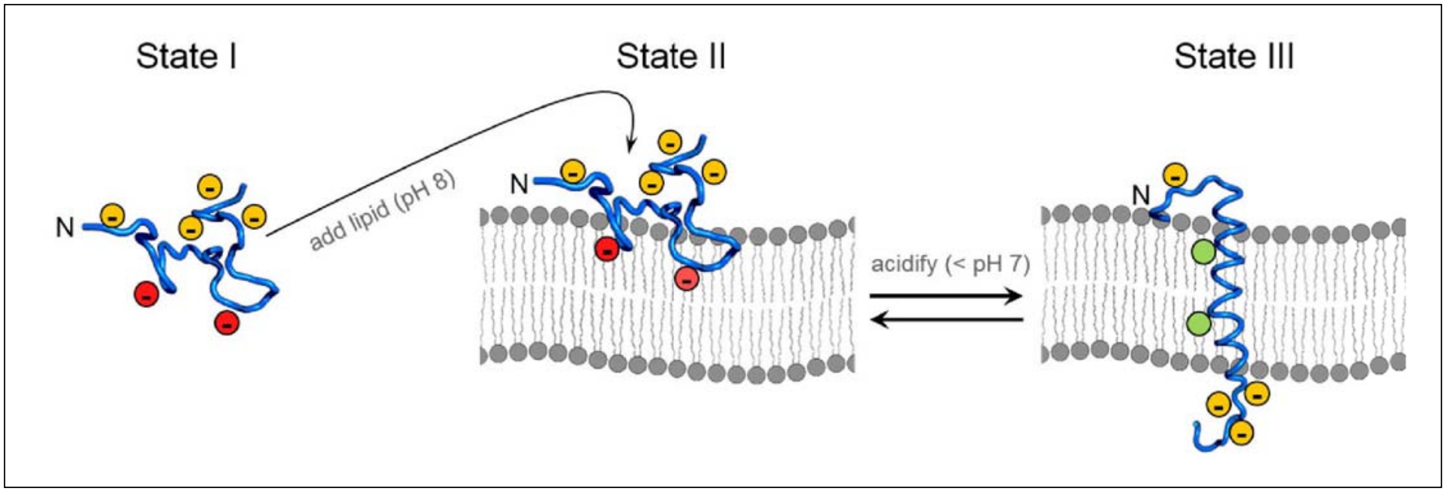


***Figure 1. Biophysical Mechanism of pHLIP insertion. State I is the free-floating, monomeric peptide with deprotonated Asp and Glu residues; red designates the Asp and Glu located in the conserved Leucine coil region. State II illustrates that at physiological pH, the peptide will associate with lipid membranes in solution but remains unstructured. State III is the structured peptide inserted as an α-helix across the lipid bilayer. (Modified with permission from Blake Mertz, Ph.D./Released)***

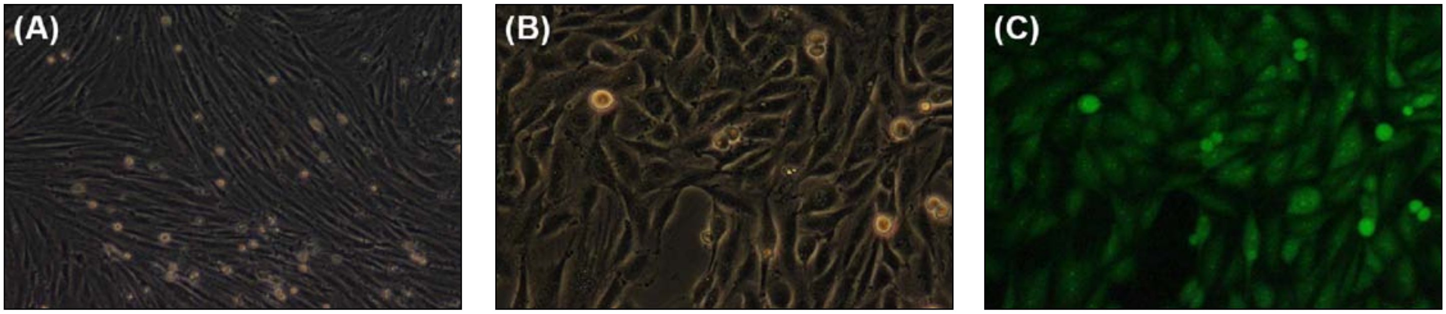


*Figure 2. Induced injury in L6 cells results in strong fluorescent signals. Cells in (a) are normal, differentiated L6 cells before any exposures. L6 myoblasts were differentiated by decreasing serum levels in growth media from the typical 10 percent to 2 percent, as in Lawson . [9] Full differentiation took approximately 72 hours. Cells were exposed to 70 percent methanol to induce cell death. Fluorescently-labeled pHLIP was introduced at a concentration of 0.5µM and pH was monitored. When the pH dropped below pH = 6.5, pHLIP insertion became apparent as shown in (c), where one can see distinct green fluorescence. As expected, this fluorescence created a visualization of injury that could be seen easily under the fluorescent microscope. These pictures show the same frame in (b) normal light and (c) under a fluorescent lens. (Released)*

amount of surgical expertise and time are involved, requiring years of experience and often consultation with other experts. Additionally, attempting to make such an evaluation under pressure can lead to inadequate debridement. This risk necessitates the development of a new tool to assist FSTs in treating injuries sustained on the battlefield. Using pHLIP for more precise debridement would not only drastically improve patient success, but it would also prevent situations where incomplete debridement introduces new complications for patients.

Following a traumatic injury on the battlefield, FSTs have many decisions to make in a short time period. The high frequency of severe wounds requires FSTs to spend a large amount of their limited resources managing these difficult injuries. The development of fluorescent pHLIP diagnostics would provide FSTs a novel tool to help them make quick decisions in the field regarding wound severity and treatment strategies.

To this end, researchers have simulated localized injuries in cell culture and exposed them to pHLIP-fluorophore conjugates that allow for perspicuous visualization. Specifically, L6 rat skeletal muscle myoblasts, which are optimal for emulating the conditions of a wound, grown and fully differentiated into fibroblasts that have the characteristics of smooth muscle tissue, were exposed to pHLIP-1-FITC conjugates under varying acidic or basic environments. The acidic conditions are essentially a simulated injury representative of a wound, while basic environments can serve as a control to ensure that pHLIP will not insert into the membrane at higher pH values.

This early stage research has enabled us to study the interactions of pHLIP as a function of concentration across a pH range to establish a relationship between signal and pH and offered insight regarding pHLIP behavior in different environments. However, in order to appropriately transition this tool for human subjects, there are a number of areas of future study that must be performed. More work should be done to understand the aggregation patterns of pHLIP. Current research suggests there is no danger that pHLIP will aggregate and lose efficacy at concentrations below 50 µM, and the propensity of aggregation can be tuned by altering the sequence of pHLIP. [10] Aggregation studies can help determine what concentration of pHLIP should be used to find a balance between amount of signal and clearance time. The most promising pHLIP candidate is a sequence named pHLIP-1, as it inserts more quickly than other developed variants. [11] It is important to study how the slight sequence variation could affect aggregation, as the primary goal of this research is to develop an injectable product.

Once a well-developed system has been established, it will be possible to build on this knowledge to create a variety of products for different clinical applications. pHLIP technology allows for this type of flexibility by changing the tag on the peptide. While not currently feasible, this technique would have the greatest impact if it could be detected with the naked eye, rather than a fluorophore, and be used practically anywhere. Imagine if FSTs were able to evaluate the severity of wounds in real time on the field, with nothing other than a simple injection upstream of the injured area.

In the meantime, FSTs can employ UV fluorescent or NIR fluorescent dyes, and there are advantages to each. A fluorescent dye like fluorescein provides a cheap, easy-to-use product that could be transported and used almost anywhere. NIR fluorescent dyes, like Indocyanine Green can be used for more sensitive detection, as they reduce the amount of white light interference and background interference from biological sources. Its use would require implementing already existing technologies in hospitals to image the NIR signal. With either product, the goal is an injectable solution of pHLIP that can be rapidly visualized.

pHLIP products are not limited to wound debridement alone and can potentially develop into applications for in situ wound treatment. Drug delivery capabilities of pHLIP have been investigated by several groups, demonstrating the peptide is capable of delivering cell-impermeable cargo across the plasma membrane. pHLIP has delivery potential through another mechanism, as it can also carry cargo by tethering small molecules to the plasma membrane surface. This is the principle behind using the attached fluorescent probes for injury site identification.

Drug delivery feasibility is often guided by Lipinski's rule of five, which suggests drugs should be small and hydrophobic to reach intracellular targets. Many biological inhibitors cannot pass through a membrane unassisted, but pHLIP can translocate these agents with ease. pHLIP has successfully been shown to deliver gold nanoparticles to tumor sites via intravenous injection, allowing for "controlled" toxicity to tumors. [12]

More traditionally, it can inject and release small molecules inside the cell. When small molecules are attached to the C-terminus of the peptide, they are transported inside the cell. The reducing environment of the cytosol results in bond breaking, triggering a release of the cargo. A study of the translocation of phalloidin, a toxic agent that inhibits tumor growth, confirmed the ability of the peptide to effectively deliver cargo. When the toxin was attached to the C-terminus and exposed to cells in an acidic environment, it prohibited tumor proliferation. [13] These findings confirmed pHLIP viability for drug delivery.

Considering the drug delivery capabilities of pHLIP, one can begin to envision the possible applications in wound healing and treatment. pHLIP has already been shown to transport cell-impermeable molecules across plasma membranes to treat tumors [13], so it is not a far reach to apply this technology to wounds. For drug delivery applications, cell-impermeable cargo can be attached to the peptide's C-terminus, as previously stated. The cargo is attached via a disulfide bond that can subsequently be cleaved upon insertion, releasing the cargo into the cytoplasm where it can act therapeutically. [6]

One of the most challenging combat injuries that FSTs face is deep bleeding wounds, such as large chest cavities. These types of wounds cannot be treated with a tourniquet and result in major blood loss. Currently, there is no way to deal with this deep bleeding other than to physically restrict blood flow. Cauterizing and pinching off vessels are the only options but are usually ineffective, as it is extremely difficult to deal with the extent of the cavity. [14] pHLIP peptides could be used to introduce coagulating agents to essentially pinch off arteries and create a sort of molecular tourniquet.

For example, during the inflammatory phase of wound healing, peroxisome proliferator-activated receptor β acts as an anti-apoptotic factor, so survival of cells in the affected area depends on its activation. [15] Peptide delivery of activating factors early on can potentially provide a way to induce wound healing processes at the cellular level earlier than the body would normally be able to accomplish. This application of pHLIP can only be accomplished if researchers understand the steric factors involved, as well as the dynamics of pHLIP that allow it to localize to injured tissues and insert in a few seconds.

Therefore, this type of treatment could act quickly to prevent major blood loss and assist the body's efforts to begin wound healing. Since all pHLIP peptides insert at low pH, it would be possible to deliver a cocktail of different agents to the site, including anti-bacterial and anti-inflammatory agents to reduce the severity of the injury, further assisting the wound healing process. However, there is much work to be done before these types of therapies can be developed.

FSTs face a different set of challenges than a typical operating room, encountering patients whose injuries are so severe that they cannot be transported to a care facility without immediate surgical intervention. One of the challenges faced by FSTs is the pressure to make quick decisions about wound treatment in a short amount of time, but current methods involve time-consuming treatment by highly trained and experienced clinicians. Fluorescent pHLIP products could free up resources by cutting down on time spent for debridement evaluation.

A shift to this technology will allow more confident decisions to be made by FSTs regarding debridement, leading to an increase in tissue preservation. Furthermore, the technique is very intuitive, as it will be administered by simple intravenous injection. FST surgeons would not need excessive training to become familiar with its use, and it will be integrated easily into existing technologies. Therefore, it will not impose high costs for transition.

pHLIP technologies provide promising possibilities for applications in the field by creating new ways to quickly assess injuries, and the key to effective treatment is adaptability to multiple situations. Additional research aimed at deep tissue injuries may lead to an affordable, easy-to-transport tool that is flexible enough to assist in a wide range of medical cases. Different peptide variants can be designed with a variety of fluorophores or cargo molecules to meet the specific needs for many of the disparate circumstances faced by FSTs and general military medicine.

By developing pHLIP conjugated products, physicians will gain access to new treatments for combat wounds, spanning from more precisely identifying the wound edge for debridement to delivery of wound-healing factors that initiate the healing process. This improved accuracy and broadened scope will lead to tissue preservation, decreased rates of infection, enhanced quality of care and better patient outcomes. ■

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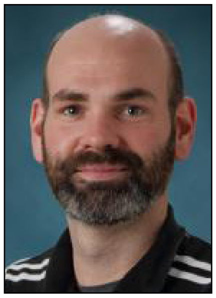

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# Calendar of Events

## May 2017

05/01/17 - 05/04/17 • **Virginia Beach, VA**
**CIP** Joint Service Power Expo

05/01/17 - 05/04/17 • **Fredricksburg, VA**
**HDS** 2017 Armament Systems Forum

05/01/17 - 05/05/17 • **Broomfield, CO**
**HDS** Space Weather Workshop 2017

05/08/17 - 05/11/17 • **Dallas, TX**
**CBRN, CIP, HDS** AUVSI XPONENTIAL 2017

05/10/17 • **Washington D.C.**
**CIP, HDS** 16th U.S.-Sweden Defense Industry Conference

05/15/17 - 05/18/2017 • **Tampa, FL**
**CBRN, HDS** 2017 SOFIC (Special Operations Forces Industry Conference)

05/16/17 - 05/18/2017 • **Scottsdale, AZ**
**AE** Solar Summit 2017

05/22/17 - 05/24/2017 • **Rome, Italy**
**CBRN** 1st Scientific International Conference on CBRNe (SICC)

05/24/17 - 05/25/2017 • **Manchester, UK**
**HDS, WMD** Nuclear Decommissioning Conference Europe

05/25/17 - 05/29/2017 • **St. Louis, MO**
**CIP** International Space Development Conference

05/31/17 - 06/02/2017 •
**Quebec City, Quebec, Canada**
**CBRN, HDS** 9th NATO Military Sensing Symposium

## June 2017

06/06/17 - 06/08/2017 • **Albany, NY**
**HDS** Annual Symposium on Information Assurance

06/18/17 - 06/22/2017 • **Ames, IA**
**CIP, HDS** 28th Rare Earth Research Conference

06/26/17 - 06/29/2017 • **Alexandria, VA**
**CBRN** Biodefense World Summit 2017

06/27/17 - 06/29/2017 • **Sonthofen, Germany**
**CBRN** NCT Europe 2017