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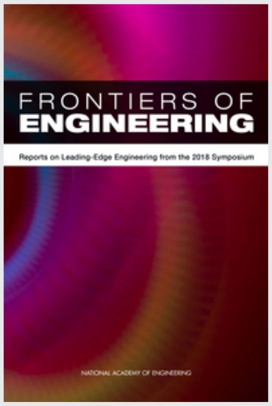

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FRONTIERS OF ENGINEERING

Reports on Leading-Edge Engineering from the 2018 Symposium

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Preface

This volume presents papers on the topics covered at the National Academy of Engineering's 2018 US Frontiers of Engineering Symposium. Every year the symposium brings together 100 highly accomplished young leaders in engineering to share their cutting-edge research and innovations in selected areas. The 2018 symposium was hosted by MIT Lincoln Laboratory in Lexington, Massachusetts, September 5–7. The intent of this book is to convey the excitement of this unique meeting and to highlight innovative developments in engineering research and technical work.

GOALS OF THE FRONTIERS OF ENGINEERING PROGRAM

The practice of engineering is continually changing. Engineers must be able not only to thrive in an environment of rapid technological change and globalization but also to work on interdisciplinary teams. Today's research is being done at the intersections of engineering disciplines, and successful researchers and practitioners must be aware of developments and challenges in areas that may not be familiar to them.

At the annual 2½-day US Frontiers of Engineering Symposium, 100 of this country's best and brightest early-career engineers—from academia, industry, and government and a variety of engineering disciplines—learn from their peers about pioneering work in different areas of engineering. The number of participants is limited to 100 to maximize opportunities for interactions and exchanges among the attendees, who are chosen through a competitive nomination and selection process. The symposium is designed to foster contacts and learning among promising individuals who would not meet in the usual round of professional meetings.

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This networking may lead to collaborative work, facilitate the transfer of new techniques and approaches, and produce insights and applications that bolster US innovative capacity.

The four topics and the speakers for each year's meeting are selected by an organizing committee of engineers in the same early-career cohort as the participants. Speakers describe the challenges they face and communicate the excitement of their work to a technically sophisticated but nonspecialist audience. They provide a brief overview of their field of inquiry; define the frontiers of that field; describe experiments, prototypes, and design studies (completed or in progress) as well as new tools and methods, limitations, and controversies; and assess the long-term significance of their work.

THE 2018 SYMPOSIUM

The topics covered at the 2018 symposium were (1) quantum computers, (2) the role of engineering in the face of conflict and disaster, (3) resilient and reliable infrastructure, and (4) theranostics.

The first session was titled Quantum Computers: Are We There Yet? In recent years there has been a dramatic increase in research and financial investment in developing a quantum computer, which theoretically could solve some problems much faster and more practically than classical computers. A few quantum computational operations have been performed experimentally on a small number of quantum bits, but there are still fundamental scientific challenges to overcome in order to scale up these small quantum systems into large-scale quantum computers. The first speaker in the Quantum Computers session introduced the concept of quantum computing and described possible applications. The next speaker focused on quantum algorithms and the power of quantum systems to process information. This was followed by a talk on logical quantum computing, a method of quantum computation based on logic gates similar to classical digital circuits. The session concluded with a presentation on quantum simulation of phenomena that are too difficult to study otherwise.

The next session, The Role of Engineering in the Face of Conflict and Disaster, addressed the important role of life-saving and community-restoring technologies—from digital, networking, and mapping technologies to those that deliver basic human services in humanitarian crises. An important challenge is ensuring that the technologies in these environments are appropriate for fast-paced and complex situations. The first speaker set the stage by discussing the role of technology from the federal perspective with a focus on mapping technologies utilized during Hurricanes Harvey and Maria. This was followed by a talk that reflected on the role of the engineer within society and in the advancement of peace and social justice. The third presenter provided a perspective on technology implementation in disasters with a focus on digital assistance to facilitate cooperation among responder groups. The final speaker discussed USAID's approach

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to development engineering and disaster relief, describing her experiences with technology implementation in developing regions of the world.

As climate change escalates the possibility of severe weather, infrastructure must be adapted to mitigate against flood impacts and rising temperatures. The session on Resilient and Reliable Infrastructure explored the interconnectivity of water, transportation, energy, and telecommunications infrastructure; how to predict future impacts of disaster events; and solutions that may be incorporated to upgrade these systems to be resilient and reliable. The first speaker introduced the idea of infrastructure resiliency and discussed how to effectively communicate data science evidence to untrained audiences using web applications with graphic interfaces that make the data highly accessible and interactive. The next presenter added the critical cybersecurity element and outlined national programs that expedite communication between researchers and governmental agencies to achieve infrastructure resilience. The final talk described state-of-the-art modeling techniques that further understanding of the impacts of climate change, including gradual stressors such as sea-level rise, on critical infrastructure.

Theranostics—a system in which multifunctional materials combine sensing, imaging, and/or drug delivery that can simultaneously diagnose and detect disease while providing a means to treat the pathology—was the topic of the final session. The presentations described challenges and potential solutions to developing targeted theranostic nanoparticles, synthetic biomarkers for cancer detection and diagnosis, and immune theranostics, which identifies and quantifies immune cells to better monitor those cells during immunotherapy.

In addition to the plenary sessions, the attendees had many opportunities for informal interaction. On the first afternoon of the meeting, a poster session provided an opportunity for attendees to share their research and technical work so that they could get to know more about each other relatively early in the program. On the second afternoon, MIT Lincoln Laboratory arranged tours of its Lincoln Flight and Antenna Test Range Facility, the Lincoln Space Surveillance Complex, and three campus tours that included the Integrated Weather and Air Traffic Control Decision Support Facilities, Wide Area Persistent Surveillance, and Micro Electronics Laboratory.

Every year a distinguished engineer addresses the participants at dinner on the first evening of the symposium. The 2018 speaker, Dr. Grant Stokes, division head of Space Systems and Technology at MIT Lincoln Laboratory, gave a dinner speech titled, *Asteroids—Fact and Fiction*. He talked about the history of asteroid detection, the probability of Earth being hit by an asteroid, and the search for asteroids in a presentation that sprinkled interesting scientific data with humor.

The NAE is deeply grateful to the following for their support of the 2018 US Frontiers of Engineering symposium:

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We also thank the members of the Symposium Organizing Committee (p. iv), chaired by Dr. Jennifer West, for planning and organizing the event.

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Quantum Computers: Are We There Yet?

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Quantum Computers: Are We There Yet?

GRACE METCALFE
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IBM

In recent years there has been a dramatic increase worldwide in scientific research as well as financial investment to develop a *quantum computer*, a device that theoretically could solve specific problems much faster than on any classical computing system, where such efforts are impractical.

Despite a few well-known quantum algorithms, such as Shor's factoring algorithm and Grover's search algorithm, there is a limited set of known specific problems for which a quantum computer is advantageous. A few quantum computational operations have been experimentally performed on a small number of *quantum bits*, units of quantum information analogous to the classical logical bits 0 and 1. There are still several fundamental scientific challenges to overcome in scaling up these small quantum systems to large-scale quantum computers that could not only demonstrate a quantum speed-up for known problems but also help discover new quantum algorithms.

The first speaker, Sara Gamble (Army Research Office), introduced the concept of quantum computing and reviewed some possible applications. As a program manager, she used her broad perspective to provide an overview of the different approaches to achieving such a computational device. Next, Shelby Kimmel (Middlebury College) discussed quantum algorithms and the power of quantum systems to process information. Sarah Sheldon (IBM Thomas J. Watson Research Center) then delved into logical quantum computing, a method of quantum computation based on logic gates similar to classical digital circuits. With her experience in developing the IBM Quantum Experience, Dr. Sheldon also explored cloud-based quantum computing. Finally, Norman Yao (University of California, Berkeley) explained simulation of quantum phenomena that are too difficult to study otherwise.

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Quantum Computing: What It Is, Why We Want It, and How We're Trying to Get It

Sara Gamble
US Army Research Office

Quantum mechanics emerged as a branch of physics in the early 1900s to explain nature on the scale of atoms and led to advances such as transistors, lasers, and magnetic resonance imaging. The idea to merge quantum mechanics and information theory arose in the 1970s but garnered little attention until 1982, when physicist Richard Feynman gave a talk in which he reasoned that computing based on classical logic could not tractably process calculations describing quantum phenomena. Computing based on quantum phenomena configured to simulate other quantum phenomena, however, would not be subject to the same bottlenecks. Although this application eventually became the field of quantum simulation, it didn't spark much research activity at the time.

In 1994, however, interest in quantum computing rose dramatically when mathematician Peter Shor developed a quantum algorithm, which could find the prime factors of large numbers efficiently. Here, "efficiently" means in a time of practical relevance, which is beyond the capability of state-of-the-art classical algorithms. Although this may seem simply like an oddity, it is impossible to overstate the importance of Shor's insight. The security of nearly every online transaction today relies on an RSA cryptosystem that hinges on the intractability of the factoring problem to classical algorithms.

WHAT IS QUANTUM COMPUTING?

Quantum and classical computers both try to solve problems, but the way they manipulate data to get answers is fundamentally different. This section provides an explanation of what makes quantum computers unique by introducing

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two principles of quantum mechanics crucial for their operation, superposition and entanglement.

Superposition is the counterintuitive ability of a quantum object, like an electron, to simultaneously exist in multiple "states." With an electron, one of these states may be the lowest energy level in an atom while another may be the first excited level. If an electron is prepared in a superposition of these two states it has some probability of being in the lower state and some probability of being in the upper. A measurement will destroy this superposition, and only then can it be said that it is in the lower or upper state.

Understanding superposition makes it possible to understand the basic component of information in quantum computing, the qubit. In classical computing, bits are transistors that can be off or on, corresponding to the states 0 and 1. In qubits such as electrons, 0 and 1 simply correspond to states like the lower and upper energy levels discussed above. Qubits are distinguished from classical bits, which must always be in the 0 or 1 state, by their ability to be in superpositions with varying probabilities that can be manipulated by quantum operations during computations.

Entanglement is a phenomenon in which quantum entities are created and/or manipulated such that none of them can be described without referencing the others. Individual identities are lost. This concept is exceedingly difficult to conceptualize when one considers how entanglement can persist over long distances. A measurement on one member of an entangled pair will immediately determine measurements on its partner, making it appear as if information can travel faster than the speed of light. This apparent action at a distance was so disturbing that even Einstein dubbed it "spooky" (Born 1971, p. 158).

The popular press often writes that quantum computers obtain their speed-up by trying every possible answer to a problem in parallel. In reality a quantum computer leverages entanglement between qubits and the probabilities associated with superpositions to carry out a series of operations (a quantum algorithm) such that certain probabilities are enhanced (i.e., those of the right answers) and others depressed, even to zero (i.e., those of the wrong answers). When a measurement is made at the end of a computation, the probability of measuring the correct answer should be maximized. The way quantum computers leverage probabilities and entanglement is what makes them so different from classical computers.

WHY DO WE WANT IT?

The promise of developing a quantum computer sophisticated enough to execute Shor's algorithm for large numbers has been a primary motivator for advancing the field of quantum computation. To develop a broader view of quantum computers, however, it is important to understand that they will likely deliver tremendous speed-ups for only specific types of problems. Researchers are working to both understand which problems are suited for quantum speed-ups and

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develop algorithms to demonstrate them. In general, it is believed that quantum computers will help immensely with problems related to optimization, which play key roles in everything from defense to financial trading.

Multiple additional applications for qubit systems that are not related to computing or simulation also exist and are active areas of research, but they are beyond the scope of this overview. Two of the most prominent areas are (1) quantum sensing and metrology, which leverage the extreme sensitivity of qubits to the environment to realize sensing beyond the classical shot noise limit, and (2) quantum networks and communications, which may lead to revolutionary ways to share information.

HOW ARE WE TRYING TO GET IT?

Building quantum computers is incredibly difficult. Many candidate qubit systems exist on the scale of single atoms, and the physicists, engineers, and materials scientists who are trying to execute quantum operations on these systems constantly deal with two competing requirements. First, qubits need to be protected from the environment because it can destroy the delicate quantum states needed for computation. The longer a qubit survives in its desired state the longer its "coherence time." From this perspective, isolation is prized. Second, however, for algorithm execution qubits need to be entangled, shuffled around physical architectures, and controllable on demand. The better these operations can be carried out the higher their "fidelity." Balancing the required isolation and interaction is difficult, but after decades of research a few systems are emerging as top candidates for large-scale quantum information processing.

Superconducting systems, trapped atomic ions, and semiconductors are some of the leading platforms for building a quantum computer. Each has advantages and disadvantages related to coherence, fidelity, and ultimate scalability to large systems. It is clear, however, that all of these platforms will need some type of error correction protocols to be robust enough to carry out meaningful calculations, and how to design and implement these protocols is itself a large area of research. For an overview of quantum computing, with more detail regarding experimental implementations, see Ladd et al. (2010).

In this article, "quantum computing" has so far been used as a blanket term describing all computations that utilize quantum phenomena. There are actually multiple types of operational frameworks. Logical, gate-based quantum computing is probably the best recognized. In it, qubits are prepared in initial states and then subject to a series of "gate operations," like current or laser pulses depending on qubit type. Through these gates the qubits are put in superpositions, entangled, and subjected to logic operations like the AND, OR, and NOT gates of traditional computation. The qubits are then measured and a result obtained.

Another framework is measurement-based computation, in which highly entangled qubits serve as the starting point. Then, instead of performing manipula-

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tion operations on qubits, single qubit measurements are performed, leaving the targeted single qubit in a definitive state. Based on the result, further measurements are carried out on other qubits and eventually an answer is reached.

A third framework is topological computation, in which qubits and operations are based on quasiparticles and their braiding operations. While nascent implementations of the components of topological quantum computers have yet to be demonstrated, the approach is attractive because these systems are theoretically protected against noise, which destroys the coherence of other qubits.

Finally, there are the analog quantum computers or quantum simulators envisioned by Feynman. Quantum simulators can be thought of as special purpose quantum computers that can be programmed to model quantum systems. With this ability they can target questions such as how high-temperature superconductors work, or how certain chemicals react, or how to design materials with certain properties.

CONCLUSIONS AND OUTLOOK

Quantum computers have the potential to revolutionize computation by making certain types of classically intractable problems solvable. While no quantum computer is yet sophisticated enough to carry out calculations that a classical computer can't, great progress is under way. A few large companies and small start-ups now have functioning non-error-corrected quantum computers composed of several tens of qubits, and some of these are even accessible to the public through the cloud. Additionally, quantum simulators are making strides in fields varying from molecular energetics to many-body physics.

As small systems come online a field focused on near-term applications of quantum computers is starting to burgeon. This progress may make it possible to actualize some of the benefits and insights of quantum computation long before the quest for a large-scale, error-corrected quantum computer is complete.

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Quantum Algorithms: Promise and Perspective

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Middlebury College

Much of the excitement surrounding quantum computers is driven by the possibility of using quantum algorithms to solve problems that are intractable using standard, or "classical," computers. Several prominent examples of quantum speed-ups have been discovered, in particular with applications to cryptography and chemistry. Despite these exciting applications, quantum computers are not a magic bullet for computation; with some problems quantum algorithms give no or only a small advantage. However, because quantum computers are so difficult to simulate and analyze, for many problems and algorithms researchers simply do not know how quantum algorithms will perform. As larger quantum devices and computers come online, it will be possible to test quantum algorithms on them—and discover new problems where quantum computers give an advantage.

EXAMPLES OF QUANTUM ALGORITHMS

Perhaps the most famous quantum algorithm is for factoring (Shor 1994). There is a quantum factoring algorithm whose run time scales roughly like the number of digits in the integer, whereas the best classical algorithm requires nearly exponential time. The assumption that factoring is difficult is critical for the functioning of current cryptosystems, the systems that allow for much of e-commerce. In these cryptosystems, a user encodes information (like a credit card in order to purchase something online), and the only known way that "eavesdroppers" can decode the information is by factoring a very large number. As long as there are no fast methods for factoring, this strategy is good for keeping information private. However, once large quantum computers are developed, they will easily break these codes.

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A second well-known application of quantum computers is modeling chemical and physical interactions. Quantum mechanics is often very difficult to simulate using a regular computer because the amount of space needed to keep track of the quantum system scales exponentially in the number of particles. This fact has made it challenging for scientists and engineers to understand the workings of many important systems and interactions, from high-temperature superconductors to photosynthesis. A quantum computer by its very nature can simulate these many-body quantum systems (Buluta and Nori 2009; Kassal et al. 2011). For example, one of the hopes of quantum computers is that they will improve and speed up the development of drugs and industrial chemistry processes by allowing testing of chemical synthesis and performance in silico.

While quantum algorithms have impressive performance for problems like factoring and quantum simulation, there are many problems where quantum computers provably do not have a large advantage over regular computers. The best-known example is the *parity* problem, which involves determining whether a string of 0s and 1s has an even or odd number of 1s. The best possible quantum algorithm for parity has the same scaling as the best possible classical algorithm (Beals et al. 2001).

Another example of a problem with only a modest quantum speed-up is *search*. While a classical computer can search through the elements of a list to find a certain item in time that scales like the number of items in the list, a quantum algorithm can do this in time that scales like the square root of the number of elements (Boyer et al. 1998; Grover 1996). While this is certainly an improvement, it is not the kind of speed-up that would likely warrant the huge investment required to make quantum computers a reality.

WHY QUANTUM COMPUTERS ARE USEFUL FOR SOME PROBLEMS AND NOT OTHERS

To get perspective on the potential of quantum algorithms, it is important to understand why they have such an advantage for some types of problems and little to no advantage for others. There are three properties of quantum mechanics that are different from standard computation and that are required for quantum speed-ups: superposition, interference, and entanglement. I focus on the first two; while entanglement is necessary for a quantum speed-up (Josza and Linden 2003), it is often implied by the presence of superposition and interference.

Superposition allows quantum systems to be in multiple states at the same time. The most famous example of this is Schrödinger’s cat, which is put in a situation in which it is both alive and dead at the same time. While superposition sounds incredibly powerful, as it seems to imply unlimited parallel computation, there is a catch. A quantum computer can be in a superposition of many states, but when a user tries to get an answer from it, the system collapses to one of

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the states at random. Thus superposition on its own is essentially as powerful as probabilistic computation, where a state of the system is chosen at random.

For superposition to be advantageous to quantum algorithms, it needs to be combined with interference. Whereas in probabilistic computation each state of the computer would be associated with a positive probability, in quantum computing each state of the system can be associated with a complex "probability" or weight. The advantage of having states with complex weighting is that the combination of a positive and a negative weight results in cancellation. In probabilistic computation, where all the weightings are positive, cancellation is not possible.

Therefore, a successful quantum algorithm involves creating a large superposition of carefully weighted states, such that when the states interfere with each other those that don't correspond to solutions cancel out, and those that give the correct solution are reinforced. Certain problems have a structure that allows cancellation to happen quickly, while others require time to amass a proper distribution of weightings. The more structure a problem has, the more likely it is to admit a large speed-up. Parity and search don't have a lot of structure, because flipping a single bit of the input for either problem can change the value of the outcome. Problems like factoring or simulating chemistry are not so sensitive to small changes in the input and instead extract larger-scale structures.

THE FUTURE OF QUANTUM ALGORITHMS

Quantum computers behave in ways that cannot be simulated easily or efficiently with classical computers. While this fact is why quantum computation is exciting, it also hampers the development of quantum algorithms. There are whole classes of quantum algorithms that seem promising, but without being able to simulate their behavior on large problems of interest or analyze them by hand, it is not possible to know how they will perform in practice.

Quantum algorithm designers have developed a toolkit of paradigms. For only some of these approaches and only certain problems has it been possible to analyze their performance. The development of small-scale quantum computers in the coming years will create exciting opportunities to test these algorithms and search for new paradigms.

With the transition from a field that has been purely theoretical to a field that is also "computational" much work needs to be done. Quantum programming languages have just begun to be developed, and for many existing algorithms there is not an easy way to go from the theoretical description to a programming language description. Furthermore, even when an algorithm is described by a quantum programming language, there remain many challenges in converting instructions to quantum machine code, as different physical quantum computers tend to have different sets of basic operations.

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CONCLUSION

Quantum computers are not all-powerful; they do not provide significant speed-ups for all problems. But for problems with appropriate structure, quantum properties like superposition and interference enable significantly better performance than is possible with standard computers. While these applications are exciting, current understanding of quantum algorithms is truly quite limited. As physical quantum computers are developed and quantum algorithms are tested on them, an unprecedented new tool will be available for the development and exploration of quantum algorithms.

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Quantum Computing with Noisy Qubits

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Quantum computing has the potential to revolutionize a wide array of industries, from pharmaceuticals and materials research to finance and logistics, by offering a fundamentally different way of processing information using quantum mechanical systems. The promise of quantum computing lies in its ability to store and process information in quantum bits (qubits), which are notoriously fragile (i.e., they can lose their information easily through interactions with their environment). It is also exceedingly difficult to simultaneously isolate a quantum system from noise and to control it precisely.

INTRODUCTION

The idea of quantum computing first arose in the context of quantum simulation. Richard Feynman (1982) proposed that to properly simulate quantum systems, one must use a quantum computer, but quantum computing was considered impractical because of the inability to control qubits without errors.

Quantum computers are made up of individual qubits that are coupled to noisy environments (stray electromagnetic fields or material defects that can exchange energy with qubits). Unlike classical computers, they cannot rely on redundancy to prevent errors. Additionally, the state of a qubit can be a linear superposition of $|0\rangle$ and $|1\rangle$ and so any error correction must preserve the qubit's additional phase information (Gottesman 2009).

The field of quantum computing was advanced by discoveries of quantum error correction (QEC) codes in the 1990s (Laflamme et al. 1996; Shor 1995; Steane 1996). These codes, along with others since developed, work by encoding a logical qubit (a fault-tolerant qubit that is fully error corrected) into the space of

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many physical qubits (the underlying noisy physical systems). Shor's error correction code, also called the repetition code, works by encoding a logical qubit into nine physical qubits using the following definitions of the logical states:

$$|0_L\rangle = (|000\rangle + |111\rangle) \otimes (|000\rangle + |111\rangle) \otimes (|000\rangle + |111\rangle)$$
$$|1_L\rangle = (|000\rangle - |111\rangle) \otimes (|000\rangle - |111\rangle) \otimes (|000\rangle - |111\rangle)$$

A bit flip can then be detected and corrected based on "majority voting," i.e., the state $|100\rangle + |011\rangle$ with an error on the leftmost qubit is returned to $|000\rangle + |111\rangle$. Similarly, phase flips are detected based on sign changes between the groupings of three qubits.

SURFACE CODE

Quantum error correction codes include stabilizer codes, whose many variants each have different requirements for numbers of qubits and error thresholds.

One typical example of a stabilizer code is the surface code (Bravyi and Kitaev 1998), a topological code defined on a 2D lattice of qubits that is currently popular for those designing hardware around a QEC code architecture. The advantage of the surface code is that it has a relatively high error threshold (the level of errors that can be corrected) and requires only nearest neighbor connectivity.

Recent experiments have demonstrated various building blocks of the surface code architecture (Corcoles et al. 2015; Kelly et al. 2015; Riste et al. 2015; Takita et al. 2016). The number of physical qubits needed to build a logical qubit depends on the type of errors and the error rates present on the physical level. In Shor's QEC code, the logical qubit consists of nine physical qubits (one data qubit and eight ancillae) and corrects for both phase and bit flip errors on the data qubit. Errors can also occur in the ancilla qubits as well as the data qubit; encoding into a larger number of physical qubits is necessary to correct for those second-order errors.

In the surface code framework, the smallest logical qubit that corrects for both phase (Z) and bit flip (X) errors needs 17 physical qubits. A fully fault-tolerant quantum computer based on the surface code assuming realistic error rates is predicted to require millions of physical qubits.

Figure 1(a) shows a schematic for a single logical qubit in a variation called the rotated surface code. The depicted logical qubit is built out of 49 physical qubits on a 5 × 5 square grid (representing 25 data qubits on the vertices and 24 ancilla qubits on the faces) and is tolerant to up to two general errors; a larger number of qubits would be needed to correct for additional errors using the rotated surface code architecture. Errors are detected by encoding the parity of the data qubits on the four vertices of each square onto the ancilla qubits on each face using the quantum circuits from figure 1(b). An error on the data qubit will

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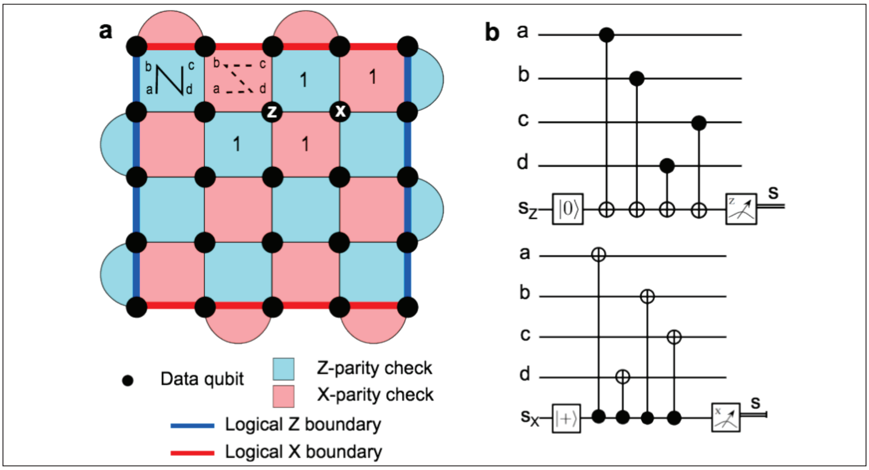

FIGURE 1 (a) Schematic of a rotated surface code, which consists of a square lattice with data qubits (round black circuits) on the vertices and ancilla qubits on the colored square faces. Z- and X-parity of four data qubits, such as the set {a,b,c,d} in the top left corner, are encoded into Z- (blue) and X- (pink) syndrome qubits using the circuits in (b). The ancilla qubit is measured at the end of the circuit. If no error occurred the qubit is measured to be $|0\rangle$. If a bit flip occurs, such as on the data qubit labeled "Z," the parity check on the neighboring Z-check qubits will measure $|1\rangle$ (using the circuit from 1(b) top); likewise for a phase flip on the data qubit labeled "X" and its neighboring X-parity check measurements (1(b) bottom). Reprinted from Gambetta et al. (2017), which was published under a CC BY license (Creative Commons Attribution 4.0 International License).

flip the parity of the neighboring ancilla qubits, allowing the error to be triangulated through ancilla qubit measurements. A logical bit flip gate is performed by individual bit flip gates along the logical X boundaries (indicated in pink). Likewise, phase gates along the Z boundaries (in blue) accomplish a logical phase flip. During computation, the physical qubits are initialized as eigenstates of both X and Z stabilizers, operators like XXXX and ZZZZ that track bit flip parity and phase flip parity, respectively, and are maintained in these states by X and Z parity checks performed by the circuits, as shown in figure 1(b).

HYBRID QUANTUM COMPUTING

Quantum computing devices are now available through cloud services both freely to the public and as commercial offerings, including up to 20-qubit devices on superconducting qubit platforms. While these devices mark significant advances in the field of quantum computing and may be referred to as "quantum computers," they are far from the ultimate goal of fault-tolerant uni-

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versal quantum computers. They are noisy and contain small enough numbers of qubits that they can still be simulated classically (although they are quickly approaching the limits of classical simulation).

Near-term devices pose an interesting problem, however: once devices have enough qubits and can perform long enough depth circuits that they cannot be classically simulated but do not have error correction, can they do anything useful? While development of fault-tolerant quantum algorithms remains a vigorous area of active research, the availability of noisy intermediate-scale quantum devices is stimulating new efforts to find applications that do not require fault tolerance. These applications may include quantum chemistry (Kandala et al. 2017; Yung et al. 2014), optimization, and machine learning.

Recent experiments have demonstrated hybrid quantum-classical algorithms, such as variational quantum eigensolvers (VQE) (Farhi et al. 2014; McClean et al. 2016). These experiments are less sensitive to gate errors because they involve a classical optimization step. The procedure is to prepare a trial state on the quantum processor and then measure some observables (how the state is prepared and which observables are measured depend on the problem being solved); then, based on those observables, the state preparation parameters are updated on a classical computer and run again until a minimum value is achieved. For example, Kandala and colleagues (2017) use VQE to find the ground state energy of small molecules.

In chemistry experiments, a fermionic Hamiltonian is mapped to qubits (Bravyi et al. 2017; Kandala et al. 2017). The trial state is prepared by applying a sequence of alternating single qubit gates and entangling steps, where each single-qubit gate is parameterized by three phases that determine the single qubit rotation caused by the gate. Then the observables that correspond to the qubit Hamiltonian are measured and the energy for that state is calculated. The classical computer updates the phase parameters according to a minimization algorithm (simultaneous perturbation stochastic approximation for this work; Spall 1992), and the cycle repeats until a minimum energy is found. The process is depicted in figure 2.

This approach is called hybrid quantum computing or approximate quantum computing. In addition to having inherently looser requirements on error rates thanks to the optimization process, these experiments can be further improved by techniques like error mitigation (Kandala et al. 2018), which works when the errors all scale with the length of the gates applied during the experiment. One can run the original experiment once and then repeat with all operations slowed down. The repeated experiment will have larger errors, but the two sets of data can be used to extrapolate to the zero-noise limit via Richardson (1911) extrapolation.

LOOKING FORWARD

The outlook for quantum computing involves pursuing both long- and near-term goals. Fault-tolerant universal quantum computing will require improving physical qubits to meet error correction thresholds, building devices with logical

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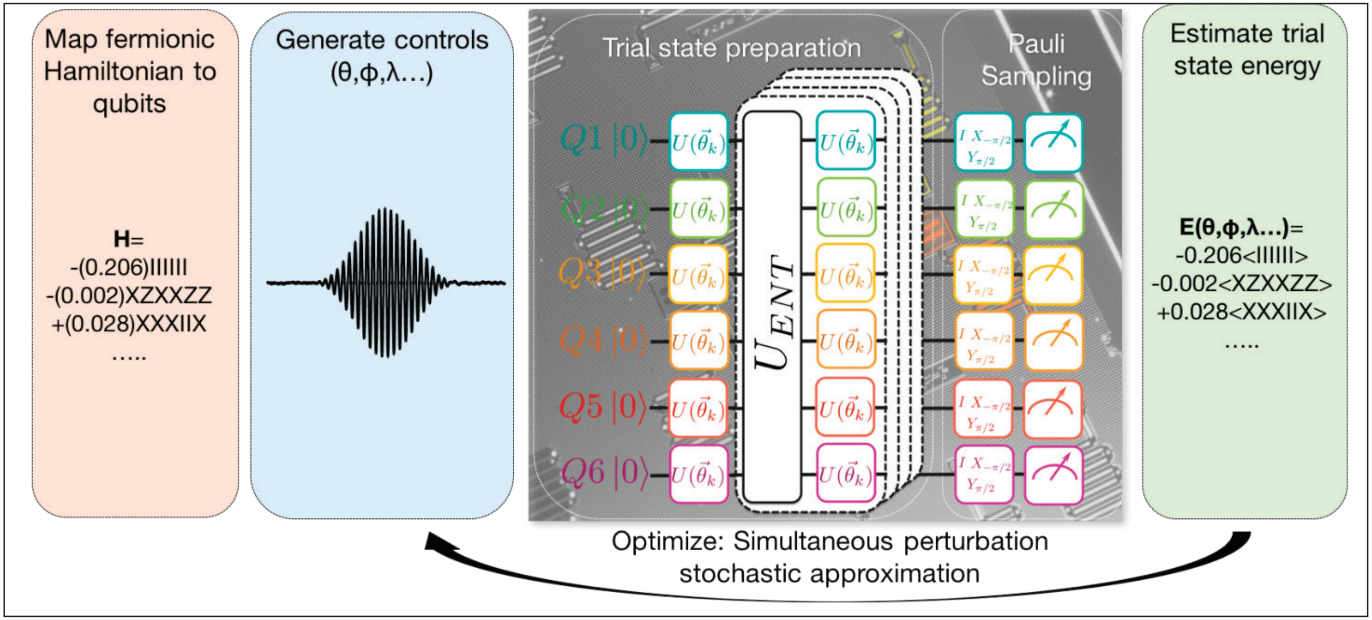

FIGURE 2 Steps for finding ground state energy using variational quantum eigensolvers. First (far left) a fermionic Hamiltonian is mapped to a qubit Hamiltonian, whose operators will be the quantities measured at the end of the loop (far right). Controls, generated by classical electronics, are parameterized so that they can be updated on each iteration of the optimization algorithm. The controls are made up of sequences of single qubit gates, $U\left(\vec{\theta}_k\right)$, interleaved with an entangling set, U_{ENT}. The controls are then applied to the quantum device, the observables from the first step are measured, and the energy corresponding to the qubit Hamiltonian is calculated. This process repeats with new $\vec{\theta}_k$ until the procedure converges on the minimum energy. Figure adapted from Kandala et al. (2017), which was published under a CC BY license (Creative Commons Attribution 4.0 International License).

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qubits, and developing new codes with less stringent requirements on numbers of physical qubits or error rates. In the meantime, there is hope that hybrid quantum-classical approaches, such as the chemistry experiment described above, will demonstrate a quantum advantage long before fault-tolerant devices are available.

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Quantum Simulation: Advances, Platforms, and Applications

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Nearly four decades ago, Richard Feynman gave a visionary lecture, "Simulating Physics with Computers," in which he emphasized the impossible complexity of simulating a quantum mechanical system using a classical computer (Feynman 1960, 1982). Indeed, even describing the full quantum state of ~60 electron spins is well beyond current computational capabilities. To overcome this challenge, Feynman proposed the notion of a "quantum simulator."

The intuition is strikingly simple: Make use of fully controllable quantum building blocks to mimic the interactions that underlie a less accessible quantum system (Buluta and Nori 2009; Lloyd 1996). Experimental progress in this direction has been truly extraordinary, making it possible to isolate single microscopic particles (at the nanoscale), to manipulate and control their internal quantum states, and to detect them with almost perfect fidelity (Cirac and Zoller 2012; Georgescu et al. 2014).

This paper describes three of the major experimental platforms associated with quantum simulation—ultracold atomic systems (Bloch et al. 2012), polar molecules (Moses et al. 2017), and superconducting quantum bits (qubits) (Houck et al. 2012)—and gives examples of the phenomena they can simulate.

MANY-BODY PHASES IN ULTRACOLD ATOMIC SYSTEMS

Ultracold quantum gases provide a number of unique opportunities when it comes to simulating nature. They offer a tremendous amount of control, can be imaged with single-atom resolution, and can mimic the underlying structure of solid state materials (Bloch et al. 2012; Cirac and Zoller 2012). In addition, perhaps the most crucial aspect underlying their broad scientific impact is the

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existence of a flexible array of cooling techniques that can quench the kinetic energy of atomic systems. Indeed, ultracold atomic systems have actually reached subnanokelvin temperatures, revealing phenomena ranging from Bose-Einstein condensation and Cooper-paired superfluidity to Mott insulators and localization.

Despite these successes, the temperature of atomic quantum simulations is still too high to simulate a number of more exotic[1]—and delicate—quantum mechanical phases, including antiferromagnetic spin liquids, fractional Chern insulators, and high-temperature superconductivity. The figure of merit for observing such physics is not the absolute temperature but rather the dimensionless entropy density.

Reaching ultralow entropy densities remains a major challenge for many-body quantum simulations despite the multitude of kinetic cooling techniques. This challenge is particularly acute for gases in deep optical lattice potentials, for which transport, and thus evaporative cooling, is slowed. Moreover, in lattice systems representing models of quantum magnetism, the entropy resides primarily in spin, rather than motional, degrees of freedom. Expelling such entropy through evaporative cooling requires the conversion of spin excitations to kinetic excitations, a process that is typically inefficient.

Two broad approaches have been proposed to overcome this challenge. The first is adiabatic preparation: one initializes a low entropy state and changes the Hamiltonian gradually until the desired many-body state is reached. However, the final entropy density is bounded from below by the initial entropy density, and experimental constraints or phase transitions may preclude a suitable adiabat. The second approach is to "shift entropy elsewhere" (Stamper-Kurn 2009) using the system's own degrees of freedom as a bath. This approach helps to stabilize the Mott-insulating phase of the Bose-Hubbard model, where the low-density wings of the system serve as an entropy sink, allowing for in situ evaporative cooling.

On the applications front, ultracold atomic simulations have raised the possibility of studying topological phases in out-of-equilibrium spin systems. Unlike traditional condensed matter systems, one cannot simply "cool" to a desired topological ground state by decreasing the temperature of a surrounding bath. Rather, preparation must proceed coherently. This necessitates both detailed knowledge of the phase transitions separating topological states from their short-range-entangled neighbors and understanding of the interplay of topology, lattice symmetries, and out-of-equilibrium dynamics.

One particular context where lattice and topology meet is in the notion of fractional Chern insulators–exotic phases, which (as explained in Yao et al. 2013) "arise when strongly interacting particles inhabit a flat topological band structure.

[1] "Exotic" in this context refers to two types of phases of matter: (1) those that have been theoretically predicted to exist but have not yet been observed in nature and (2) those that have been observed but are not yet fully understood.

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Particles injected into these exotic states of matter fractionalize into multiple independently propagating pieces, each of which carries a fraction of the original particle's quantum numbers. While similar effects underpin the fractional quantum Hall effect observed in continuum two dimensional electron gases, fractional Chern insulators, by contrast, are lattice dominated. They have an extremely high density of correlated particles whose collective excitations can transform nontrivially under lattice symmetries." Since the full configuration interaction state generally competes with superfluid and crystalline orders, the resulting phase diagram exhibits both conventional and topological phases.

SPIN LIQUIDS IN POLAR MOLECULES

Polar molecules trapped in optical lattices have recently emerged as a powerful new platform for quantum simulation (Moses et al. 2017). This platform exhibits many advantages, including local spatial addressing, stable long-lived spins, and intrinsic long-range dipolar interactions. Typically, the molecules are subject to a static electric field, and their motion is pinned by a strong laser field (figure 1). This implies that the degree of freedom, which (often) participates in the quantum simulation, is an effective rotational excitation.

These rotational excitations can simulate a large number of interesting many-body quantum phases. In particular, by varying the DC electric field strength as well as the tilt of the electric field vector, one can sharply modify the geometry of the dipoles and introduce additional dispersion into their single-particle band

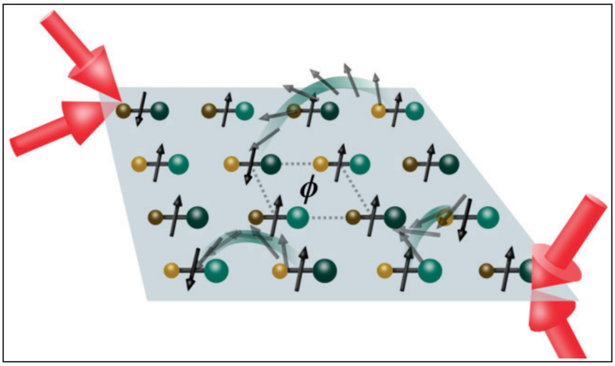

FIGURE 1 Polar molecule quantum simulation. Schematic representation of two-dimensional array of polar molecules dressed by optical beams (red arrows). Each polar molecule is characterized as an effective pseudo-spin-flip, which can hop and interact mediated by the long-range dipolar interaction. ϕ = the angle of the electric field. Colored balls (e.g., green, gold) represent different quantum states of the molecules. Reprinted with permission from Yao et al. (2013).

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structures. At the same time, increasing the electric field strength enhances the long-range interactions. These qualitative differences in the microscopics of polar molecules yield a rich phase diagram exhibiting both conventional and topological phases, including crystalline ordering, superfluids, and chiral spin liquids. The nature of these phases can be characterized using diagnostics such as the ground-state degeneracy and the real-space structure factor.

Of particular interest in the context of polar molecular simulations is the realization of quantum spin liquids. These are characterized by entanglement over macroscopic scales and can exhibit a panoply of exotic properties, ranging from emergent gauge fields and fractionalized excitations to robust chiral edge modes.

Recent work has demonstrated that polar molecule simulations naturally realize the so-called dipolar Heisenberg antiferromagnet. Such simulation requires only a judicious choice of two molecular rotational states (to represent a pseudospin) and a constant electric field. The simplicity of this system stems from the use of rotational states with no angular momentum about the electric field axis and contrasts with previous works where nonzero matrix elements appear for the transverse electric dipole operator, unavoidably generating ferromagnetic spin-spin interactions. Motivated by this physical construction, large-scale numerical studies of the dipolar Heisenberg model (e.g., Yan et al. 2011) find evidence for quantum spin liquid ground states on both triangular and Kagome lattices.

QUANTUM WALKS IN SUPERCONDUCTING QUBITS

Much like their classical stochastic counterparts, discrete-time quantum walks have stimulated activity across a broad range of disciplines. In the context of computation, they provide exponential speed-up for certain oracular problems and represent a universal platform for quantum information processing. Quantum walks also exhibit features characteristic of diverse physical phenomena and thus are an ideal platform for quantum simulation.

It has recently been demonstrated that quantum walks can be directly realized using superconducting transmon qubits coupled to a high-quality-factor electromagnetic cavity (Flurin et al. 2017; figure 2). The quantum walk takes place in the phase space of the cavity mode, and each lattice site corresponds to a particular coherent state of the cavity, while the two logical states of the superconducting qubit form the internal spin of the walker. Coherent spin rotations can be performed using microwave driving, while spin-dependent translations arise naturally from the dispersive coupling between the qubit and the cavity.

A unique application of this particular quantum simulation platform is in the direct measurement of so-called topological invariants. In these protocols, a geometric signature of the topological invariant is imprinted as a Berry phase on the quantum state of the particle; the phase can then be extracted and disentangled from other contributions via a simple interferometric protocol.

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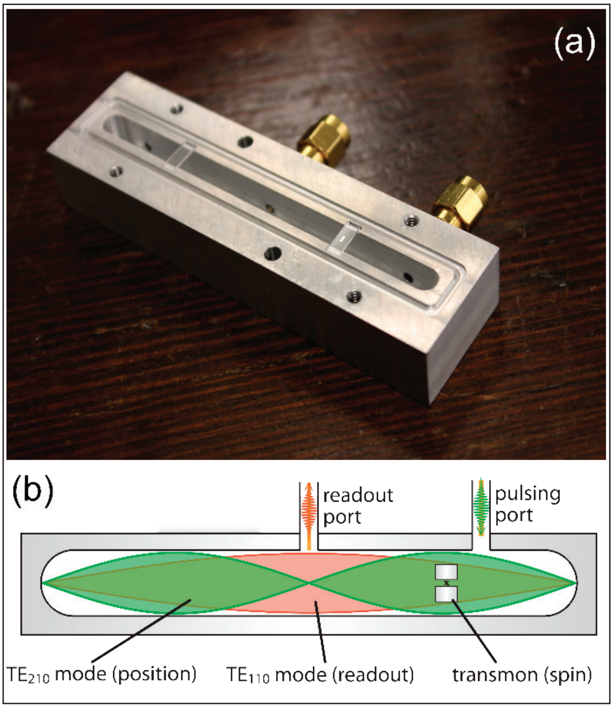

FIGURE 2 (a) Cavity resonator (aluminum box) and coupled superconducting transmon qubit. (b) Schematic of the simulation platform for quantum walks. The fundamental (TE_{110}) mode is used to measure the qubit state. The transmon qubit is dispersively coupled to both cavity modes. Reprinted with permission from Flurin et al. (2017).

CONCLUSION

The quantum simulation community has made remarkable progress in the controlled manipulation of individual quanta (e.g., Lanyon et al. 2011; Simon et al. 2011). These advances have opened the door for the engineering of quantum many-body systems as well as the development of quantum technologies.

Looking forward, the continued dialogue between atomic, molecular, and optical physics, condensed matter physics, and quantum information science promises to be fruitful for both the fundamental and applied sciences, enabling the simulation of macroscopic quantum behavior and providing detailed microscopic intuition.

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The Role of Engineering in the Face of Conflict and Disaster

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The Role of Engineering in the Face of Conflict and Disaster

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Significant humanitarian crises are increasingly prevalent around the world—natural disasters, refugee crises, and drought and famine make headlines on a routine basis. With increased effects from global warming and ongoing conflict around the world, incidents like these will affect the lives of billions of people and continue to present engineering challenges both at home and abroad.

Humanitarian crises present numerous opportunities for the use of life-saving and community-restoring technologies, from digital, mapping, and networking technologies to technologies for the delivery of basic human services. But technology providers must overcome critical challenges to ensure that their solution is beneficial for the affected population. Technologies in these environments must deliver benefits with timely results, be easy to use, adapt to existing structures and communities, often be of low cost and compact form factor, and perhaps most importantly be responsive to the needs of the community. It is essential that engineers understand not only how technology may be used for good but also how it may contribute to conflict. These hurdles can be daunting, particularly for state-of-the-art concepts and startup companies. In addition, for crisis responders, choosing the correct technologies in a fast-paced and complex situation can be a significant challenge.

Speakers in this session addressed the role of the engineer in technology implementation in crisis and postconflict environments and described some technologies being explored for humanitarian assistance and disaster relief. Julia Moline (FEMA) opened the session by explaining the role of technology from the federal perspective, with a focus on recent hurricanes Harvey and Maria.[1] Darshan

[1] Paper not included in this volume.

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Karwat (Arizona State University) examined the role of the engineer in society and particularly in the advancement of peace and social justice. Willow Brugh (Truss) walked through a strategic game design workshop to bridge communication and organizational differences between formal and informal crisis responders. In the final talk, Marissa Jablonski surveyed the USAID approach to development engineering and disaster relief. During the discussions ideas for novel solutions were welcomed for this challenging space, as well as questions about how the role of technology should evolve in today's crises and conflicts.

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Engineering for the People: Putting Peace, Social Justice, and Environmental Protection at the Heart of All Engineering

Darshan Mukesh Arvinda Karwat
Arizona State University

Inequality and injustice are hardwired into current models of technological design and technical work, even in the United States, one of the most technologically advanced and resource-rich nations on Earth. However, the onus for change is not only on those who officially *make* policy—politicians, lawyers, and businesspeople—but also on those who *build* policy and *create* possibilities—engineers. For example, if engineers did not design and build bombs, there would be fewer of them for people to use; engineers can *not* create the possibilities of mass destruction.

On the other hand, engineers *can* create possibilities for deep good by aligning their work with the needs of those who are traditionally marginalized and exploited in and by technical work. In fact, there is a rich history of activism in engineering and science that practicing engineers today can build on to put peace, social justice, and environmental protection at the heart of engineering. I describe different ways in which engineers across the United States are incorporating these ideals, and pose questions for engineers to consider in building a movement of engineering for the people.

BACKGROUND: THE HISTORY AND PRESENT OF ENGINEERING ARE COMPLICATED

I do not have to go back home to Mumbai to find technological inequality and its interplay with poverty and environmental injustice and marginalization. I can simply walk the streets of Phoenix, where many have inadequate access to energy services in the desert summer; or San Francisco, the US tech capital, where poverty levels have shocked UN poverty expert Philip Alston; or Detroit, a poster child for

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the effects of American industrial capitalism, and whose planning and cars helped create not only an American middle class but also urban sprawl and inertia for mitigating climate change; or Hale County in the Black Belt of Alabama, where even today homes are not built to code. In this, the richest country in the world, a country that has driven the international scientific and engineering agenda for many decades, there remains vast technological inequality.

The history of science and engineering is replete not only with incredible and awe-inspiring advances and achievements like refrigeration, lasers, and getting to the moon, but also oppression, marginalization, and racism, mountaintop removal and poisoned waters, and the continued development of the capacity to destroy life and the Earth. While these are certainly matters of social policy, they also concern science, engineering, and technological policy. They concern how we as engineers justify to ourselves the work we do; they are about engineers' stake in the world we help build.

CURRENT EXAMPLES OF CONCERN

It might be easy for engineers or companies to say they are "just doing their job" when they are challenged about what they do, like building surveillance technologies or prisons or weapons or ways to drill for oil in the Arctic. But by saying their work is "just a job," engineers and companies shift the moral burden for bringing politically charged objects into the world from themselves—those who actually do the designing and building—to those who order and pay for those things.

Continued US investment in the development of weapons might be justified by saying that the country needs to maintain military superiority, but such development implicitly devalues the lives of those targeted or affected by the weapons, especially civilians. It is important to remember that while people, politicians, and governments talk about doing something, they do not have the skills to actually do it. Engineers do. This is where engineers and engineering hold power. And because engineering holds power, I believe that engineering has the obligation to systematically do good.

This power is exactly what Google employees exerted when they challenged management about the company's involvement in providing artificial intelligence expertise to a military pilot program called Project Maven, or Algorithmic Warfare Cross-Functional Team (Work 2017), which aimed "to speed up analysis of drone footage by automatically classifying images of objects and people" (Conger 2018). Google employees vehemently protested internally, then wrote a petition to Google CEO Sundar Pichai, stating the following:

> We believe that Google should not be in the business of war. Therefore we ask that Project Maven be cancelled, and that Google draft, publicize, and enforce

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> a clear policy stating that neither Google nor its contractors will ever build warfare technology.[1]

On June 1, 2018, a *New York Times* headline read "Google Will Not Renew Pentagon Contract That Upset Employees" (Wakabayashi and Shane 2018).

Designs are dictated by selected variables and by assumptions of who is considered important. But the world is always more complicated than the variables chosen. For example, the use of mainly white people to train face detection algorithms (Lohr 2018) resulted in Google Photos "recognizing" black faces as gorillas (Breland 2017; Vincent 2018). Engineering is social experimentation: engineers see challenges in the world and develop material interventions, but they often do so without fully knowing the social implications of what they do.

At the same time, the built world of the future needs to look completely different from the world of today, and engineers and engineering are crucial to that. For example, people can talk all they want about mitigating climate change, but if in 10, 15, or 20 years people are using these same roads, these same cars, this same infrastructure—all of which is the outcome of engineering and planning work—the problem of reducing greenhouse gas emissions will not have been meaningfully addressed. How can engineers push social, science, and technology policy to make peaceful, socially just, and ecologically holistic futures possible?

LET'S GRAPPLE WITH VALUES

The idea of "good" is subjective and normative, and questions of dual use are real; building destructive capacity to one person is strengthening national security to another. Thus it is important to be clear in the goals and visions for the future instilled in engineering designs, because engineers legislate the future (Zimmerman 1995) without really knowing it, creating path dependencies for future generations. What we as engineers do now, each day, really matters. We create—or avert—possibilities, opening and closing technological, social, political, economic, and environmental futures. We need more spaces to hash out these challenges and express care for the future. Just like in the Google case, the engineering community has to encourage open debate about the values, motives, and politics in and of engineering.

I can state my motivations simply: I want *all* engineers to instill the values of peace, social justice, and environmental protection in *all* engineering work, from aerospace to naval architecture. I advocate for more engineering and design to benefit the poor and marginalized (including here in the United States), for engineering that reduces the potential for armed conflict, or, for example, to reimagine migration corridors for animals whose ability to migrate is disrupted

[1] https://static01.nyt.com/files/2018/technology/googleletter.pdf.

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by land development. I'm idealistic because it is possible and even practical to create new visions of what engineering should be.

Historical Perspective

This ethos is not new. In the fervor of the anti–Vietnam War movement in the late 1960s, scientists and engineers founded Science for the People (https://scienceforthepeople.org), which raised critical questions about how and why their intellectual labor was used to develop weaponry and perpetuate war. As chronicled by historian Matthew Wisnioski (2012), on March 4, 1969, faculty and students at MIT shut down the Institute for a teach-in that featured panels on military technology, the Vietnam War, and DOD- and ONR-sponsored research being done at Lincoln Laboratory. After the shutdown the MIT Fluid Mechanics Laboratory—which at the time had three full and three assistant professors, a support staff, and approximately 20 graduate students—underwent a complete transformation. It changed the focus of its research from fluids research for military purposes to four other areas: air pollution, water pollution, biomedicine, and desalination (Wisnioski 2012).

All of this comes from the recognition of the deeply political nature of science and engineering. Who decides what to research, what is considered a good design, even the simple act of posing a question—all reflect values and motivations, and circumscribe the tools and methods that can be used to accomplish goals. Engineering is a political endeavor.

Activities That Make a Difference

Here are some examples of engineers, scientists, technical workers, and other leaders who *today* are thinking differently about how engineering and technology can be used to explicitly promote the values of peace, social justice, and environmental protection.

Linking Experts with International Need

On-Call Scientists: Access to technical skills and resources can add significant value to groups that cannot afford to hire technical staff. The American Association for the Advancement of Science program for Scientific Responsibility, Human Rights and Law runs On-Call Scientists (https://oncallscientists.aaas.org/en), which connects scientists, engineers, and health professionals interested in volunteering their skills and knowledge with human rights organizations that need technical expertise. Through On-Call Scientists, a hydrologist enabled a Kenyan human rights group to incorporate social impacts into the requirements of a government-mandated environmental impact assessment for exploratory oil drilling in that country. And when the Syrian government denied that it was using chemical

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weapons on its civilians, Amnesty International and Human Rights Watch were connected with a forensic anthropologist, a pharmaceutical scientist with expertise in toxics, and a biochemist with expertise in the detection of chemical weapons to provide the NGOs with evidence to dispute the denials and build international will to address the war crimes (Harris 2017).

Connectivity for the Overlooked

The Equitable Internet Initiative: A quarter of both urban and rural populations in the United States do not have broadband internet access or can't afford it (Smith 2018), creating a digital and information divide. The Detroit Community Technology Project's Equitable Internet Initiative (http://detroitcommunitytech.org/eii) is increasing access through the distribution of shared gigabit internet connections in three underserved neighborhoods, increasing internet adoption through a training program that prepares residents of those neighborhoods with the skills necessary to bring their communities online, and increasing pathways for youth into the opportunities of Detroit's burgeoning Innovation District through intermediate and advanced digital literacy training.

If You Can See It, You Can Change It

SkyTruth: Throughout the 1990s John Amos worked in the private sector as a geologist who used remote sensing as an exploration tool for the fossil fuel industry. But when he looked at a time series of remotely sensed images of his hometown in Wyoming, he saw the landscape that he grew up in and loved transformed from one of raw beauty to one marred by fossil fuel rigs. That spurred him to lay the groundwork for SkyTruth (https://www.skytruth.org), a nonprofit that uses the view from space to motivate people to protect the environment. In 2010, when the Deepwater Horizon disaster happened, SkyTruth questioned BP's and the US government's estimates of how much oil was being pumped into the ocean and found that the flowrate of the spill was being significantly underreported—by a factor of twenty. That analysis thrust SkyTruth into the spotlight, and since then the company has used satellite technology and remote sensing to monitor threats to the planet's natural resources from urban sprawl, fracking, mountaintop removal mining, and overfishing of the oceans. Their goal is not just to report on disasters but to inspire a global movement where everyone can both easily access the technical resources that SkyTruth uses and be motivated to protect the planet from future catastrophes.

Engineering for Peace

Peace Engineering: Drexel University's Peace Engineering is "the nation's first program dedicated to preventing and reducing violent conflict through education

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and research that integrates innovative technologies, approaches, and policies with the studies and practices of peacebuilders."[2] Important action-oriented engineering projects and research programs can be developed with the goal of creating the conditions for peace and reducing the possibilities of violent conflict. For example, given the current flux in social justice, economic inequity, political fracturing, and ecological degradation, system models can be developed to predict how disparities in health, education, and access to resources affect the dynamics of interacting economic and social systems and can lead to conflict. Such models can also enhance understanding of the impacts of sudden population changes, like those that occur in disasters like hurricanes or armed conflict, on economic and social systems in communities that absorb the displaced population. At their core, programs like peace engineering expand the definition of what engineering can be and what it is for.

Give the People What They Need

Understanding the engineering, science, and technical needs of environmental, energy, and climate justice groups: In the environmental movement, many communities across the country do not have the technical resources they need to be more effective advocates to address environmental and social justice challenges, and are often overlooked by government, academia, and nonprofits. Communities are concerned, for example, about what climate change means for them or, if they are near industrial facilities, about how the facilities are polluting their air, water, and land. What might help these communities? And how can more engineers and scientists be mobilized to address their needs? In my lab group, re-Engineered (www.reengineered.org), we start by asking, What are the scientific, engineering, and technical needs of environmental, energy, and climate justice groups across the United States? What we learn will help shape our engineering research and development work. In addition, we are building an online portal to provide opportunities for the rest of the engineering and science community to be involved and get linked to communities in need.

CONCLUDING THOUGHTS

These examples show that engineering for the people *is* happening. And engineers need to help normalize this kind of work in day-to-day engineering practice, to scale it up, create ways to value it differently, and ensure the proper training of engineers, scientists, and other technical workers to do this work. But such work raises many barriers and questions. First are the connected issues of values, financial security, and debt. It is not only a matter of educating future engineers differently. The vast majority of engineers around the world are not in

[2] http://drexel.edu/engineering/areas-of-study/peace-engineering/.

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school—they are out in the working world, with jobs, families, and maybe a mortgage, and they probably went to college at a time when thinking about issues of social justice and environmental protection and sustainability *in engineering* was not part of their educational experience. How can they be engaged and mobilized?

It seems to me that a lot of engineering jobs take creative, talented people and turn them into cogs in a bureaucratic machine, order takers, with little sense of purpose. In contrast, engineers who engaged with On-Call Scientists, for example, remarked that their experiences completely changed their sense of purpose (Harris 2017). What is needed is to change this work from being pro bono to paid work with a decent paycheck. What are ways to reach engineers in the working world to highlight opportunities for engagement? How can they create these opportunities for themselves?

Student debt can also lead to unfortunate compromises in values. I overheard a conversation among graduating engineers at my alma mater, the University of Michigan, in which one student said, "I really don't want to take this job building missile systems, but I have a ton of student debt, and this would be a good paycheck. So I'm going to try to make the best missiles possible that kill only their intended targets." The problem of student debt thus shifts the moral burden of graduating students from challenging the dominant system of engineering to one in which they are morally conflicted internally. The most socially and environmentally conscious generation of engineers is now graduating. How can more opportunities be created for them to find work that aligns with their values?

We engineers need to be clear about what problems we want to address and solve. That clarity will guide the kind of research and development done. Some might say that there are trickle-down civilian benefits to military research—new materials, new sensing technologies, quieter commercial aircraft, and so on. Sure. But what could be done by engineers and scientists in the United States *directly* for schools and colleges, poverty alleviation, hunger reduction, environmental remediation, the opioid crisis, and climate change resilience with the $200 billion that has been added to the military budget over the past two years (Korb 2018)? I recognize that this question challenges fundamental values and principles that guide US science and technology investment.

The world today has in no small part been created by engineers, and engineers will continue to dictate the design and development of technologies that shape humans' relationship to the Earth. To infuse engineers with ideals of justice, with practical tools to understand the impact of their work on people and the Earth, and with the ability to work closely with those who have different kinds of knowledge, is to change the world.

And so I end this essay with questions I think all engineers should grapple with[3]: Why are we engineers? For whose benefit do we work? What is the full measure of our moral and social responsibility?

[3] From my group re-Engineered's website (www.reengineered.org).

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Combining Formal and Informal Structures in Crisis Response

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Crisis response is often highly fragmented; formal, informal, and ad hoc response entities all spring into action with little coordination or communication. Attempts to improve coordination during crises by synchronizing and planning outside of a crisis setting often fail because of either lack of representation from informal and ad hoc response groups or competing priorities and requirements in formal organizations.

Working with formal and informal response groups, this project sought to improve coordination by creating a game to help responders develop the knowledge, skills, and networking capacities necessary to interact and coordinate with each other in the field. We were able to codify traits of their capacities in a game format from which others can learn. We used a method for facilitation and engagement that optimizes for both the adaptability of the network (informal) and the predictability of the centralized (formal). Understanding the other "side" through this game framework can help response communities learn to coordinate with greater equity, efficiency, and impact.

This project was undertaken with two goals: (1) to foster a bridging process between the two response communities and (2) to develop a tool to improve crisis response by identifying and addressing systemic failures due to gaps between informal and formal crisis response groups. Our research covers the creation of the game and two iterations, but is not an in-depth qualitative study of the interactions that took place during game play. Further improvement of the game through play testing and iteration will allow it to be more playable and useful for its stated goals.

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INTRODUCTION

Tabletop exercises—scripted sessions in which participants talk through how they or the organization they represent would respond to particular events—are a common tool that formal response organizations use to develop concepts and policies. Informal responders, while they may be represented at these sessions, seldom participate at the same level or frequency and so their viewpoints may go unrecognized (Perry 2004).

During our 3-day workshop the sessions provided an opportunity for the development of understanding and cooperation between the formal and informal response communities and of organizational strategies that can improve resiliency, response, and recovery in the face of disasters. Through play testing and iteration during their time together, members of these polarized groups demystified their strengths and limitations by working together to design and create a card game usable during tabletop exercises or otherwise.

The game we developed is now playable by others and open to ongoing improvements. In fact, it has been used in training workshops conducted by offices of emergency services seeking to understand and improve the integration of volunteers and informal response organizations in their disaster response operations, and it led to insights for collaboration opportunities during the responses to Hurricanes Harvey and Irma.

This paper explains the problem, why building a game was the course of action chosen, the methods we used to create the game, and preliminary results.

BACKGROUND: FORMAL AND INFORMAL RESPONSE GROUPS

Response organizations operate along a continuum from the very formal (organizationally stable, with consistent, slow-changing methods) to the very informal (organizationally dynamic, with frequently changing artifacts such as how-to guides and updates about ongoing work). In this paper we focus on the two ends of the spectrum to illustrate the most problematic disconnections in the system.

Formal Agencies

Official (formal) response agencies generally have either professional specialists or operational staff supporting response missions as well as articulated channels for accessing resources needed for response and recovery, but they create encumbered mobility of response and information (Quarantelli 1988). Formal disaster response agencies are (1) government organizations whose overall purpose or specific task is to respond (e.g., FEMA) or (2) nongovernment organizations that exist, plan, and train before the required response (e.g., the Red Cross).

The centralized, hierarchical structures for formal agencies' operations foster vertical communication in the organization but inhibit horizontal communication,

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particularly with external entities: Personnel know how to talk to whom they're allowed to talk to, but that's it. And aid is delivered in big blocks of materials to preestablished points of relief that are accessible for mass deliveries and to majority crowds (Bharosa et al. 2010; Boin and 't Hart 2010; LaPorte and Consolini 1991). For people to receive this aid they must leave their home and be easily mobile, located within reach of a center, and able to use the material (which is made and packaged for large-scale distribution and consumption). They must also be "legible" to the state: documented citizens without any legal issues. Because of these parameters, often the populations most at risk (e.g., marginalized people, the disabled or elderly, undocumented immigrants) are the least likely to be assisted.

Informal Groups

Emergent (informal) response groups—such as Occupy Sandy (http://occupysandy.net/), the "Cajun Navy," and volunteers in Mexico City after the September 2017 earthquake (NPR 2017)—form as a direct result of the crisis itself. They organize quickly through both local and digital networks, and include members of the local population, community leaders, and grassroots and nonprofit networks already established and operating in the area. Remote groups form through similar social and professional ties, but primarily via digital channels.

Informal response entities often have or are able to quickly gather high-resolution information and data. Neighborhood needs are rapidly assessed, support and failure points are known, and local knowledge is quickly disseminated. But they may be unable to respond out of their own capacity, as local material or services are scarce and access to appropriate resources is extremely limited, if available at all. Informal groups may have a comprehensive mapping of pocket populations and their needs, but lack the professional abilities to anticipate and document resource needs, let alone deliver the necessary relief (Sobel and Leeson 2006; Whybark 2007). Large-scale recovery operations—such as removal of debris, provision of acute medical care, and restoration of critical infrastructures—tend to be beyond their scope (Majchrzak et al. 2007).

THE NEED FOR COORDINATION

Given the complementary capabilities, knowledge, resources, information, and access of formal and informal response groups, the potential for increased efficiency, recovery, and accessibility and decreased response time, duplication of efforts, and waste is immense. Yet there are few channels for such coordination, and even less trust between formal agencies and informal groups. Lack of visibility into one another's operations, limited understanding of logistical mechanisms, and cultural differences contribute to the lack of trust (Shklovski et al. 2008).

Faced with this challenge, it is tempting to simply encourage the two actors to behave in ways more similar to each other—the informal more predictably, and

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the formal with more agility (Harrald 2006; Mendonça et al. 2007). But closing the systemic gaps hinges on an understanding between the two sectors, making their operational abilities visible to each other. With understanding comes trust and a willingness to coordinate. When trust is established, dividing tasks and responsibilities becomes part of the response process as information becomes reliable and actors (and their actions) are accountable to a shared mission. Failure to collaborate impacts all crisis responders and the populations affected by their efforts.

The disconnect between formal and informal response systems arises in part from cultural differences (Schneider 1992; Shklovski et al. 2008; Yates and Paquette 2011). "The government" is considered untrustworthy and unreliable to grassroots-level responders, whether because of its bureaucratic structures and histories and perceived agendas or because of a cultural and operational disconnect. And because grassroots groups and their efforts are not formally vetted, hierarchically accountable, or catalogued in a referential manner, formal institutions do not consider them trustworthy or reliable for strategic integration in their efforts.

Visibility and, where possible, transparency open up possibilities for collaboration and cooperative problem solving. Understanding how other groups operate can lead to suggestions for mutual courses of action. Formal and informal response groups working effectively together create a more holistic response ecosystem, with fewer gaps and greater relief capacities (Bharosa et al. 2010; Majchrzak et al. 2007).

To begin the bridging process, this project brought together different types of response groups with the intent of increasing cross-visibility, codifying understanding, and developing trust to improve crisis response.

ORGANIZATIONAL THEORY, COLLABORATION, AND COOPERATION

Formal organizations share certain characteristics—some level of hierarchy, bureaucracy, and norms of internal and external communication—that can be used in organizational theory models to describe and enhance understanding of how they function. Bureaucratic political theory, epistemic community theory, and game theory each provide insights on how cooperation and collaboration[1] can develop in an often discordant emergency response ecosystem (Scott 2003).

Bureaucratic Model of Organization

Allison and Halperin (1972) provide a bureaucratic model of organizations based on three variables: who plays, what determines a player's position, and how

[1] For this game, "cooperation" means simply "staying out of each other's way" and "collaboration" implies actively working to the benefit of the other.

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positions are aggregated into an outcome. The model assumes that cooperation is not the natural state of affairs. The authors describe a noncooperative bargaining process in which "organizations rarely take stands that require elaborate coordination with other players" (Allison and Halperin 1972, p. 49).

The authors argue that a player's stand is largely determined by both the institutional goals and biases that the player represents and the player's personal goals. The model is helpful in our context for understanding why players might take a position that does not support efforts to address a disaster. In addition to the response at hand, individuals representing a formal organization may be concerned about other things, such as availability of resources for future needs, public image, hierarchical pressures not related to the response, or the security of organizational information and systems. Such concerns may draw the players' (disaster responders') positions farther apart as they seek to increase their personal or organizational position, power, and/or resources.

On the other hand, the Allison-Halperin model allows for organizational motivations that move the positions closer together or make cooperation more valuable. These motivations might include the potential to improve the disaster response, an inability to meet certain organizational response tasks, or insufficient resources.

Epistemic Community Theory

Epistemic community theory suggests that cooperation can arise among members of various organizations even when there are significant bureaucratic barriers to it. According to Haas (1992, p. 3), "an epistemic community is a network of professionals with recognized expertise and competence in a particular domain and an authoritative claim to policy-relevant knowledge within that domain or issue-area." Although Haas was writing about international politics, epistemic communities are also found in the disaster response ecosystem. Responders and emergency managers move from organization to organization, attend conferences together, and work together in training exercises and events. Strong epistemic communities help to create trust among individuals across organizations, allowing for cooperation and collaboration even without a bureaucratic mandate for them.

In an alternative model, Axelrod (1984) shows how cooperation can evolve and that an organization's strategy in responding to the actions of other organizations can significantly impact how the cooperation progresses. In Axelrod's model, reciprocation consistently breeds cooperation (pp. 155–158). Variations of this strategy that include some level of "forgiveness" for "defection" can be even more effective.

Game Theory

Recently there has been more focus on deliberate change in organizations seeking innovation and improved collaboration, using models and techniques that

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shift the focus of leaders from "directing" to "enabling" by supporting initiative and risk taking at all levels. The resulting changes (1) have been endorsed by all types of organizations (although they are implemented more readily by organizations that are less rigidly hierarchical), (2) often lead to more intra- and extramural collaboration as individual efforts to collaborate are supported by leadership (Hoskisson et al. 2017), and (3) illustrate the utility of a game-theoretical model of organizational change and collaboration (Arsenyan et al. 2015).

Other changes in organizational norms—such as recognition of the usefulness of play in work (Vesa et al. 2017), the use of design thinking as a mechanism of organizational change (Brown 2009), and globally distributed teams (Jimenez et al. 2017)—can make the use of games a potentially transformational means to improve interaction between the formal and informal aspects of disaster response.

THE PROJECT

In creating and play testing the game, we focused on reducing duplication of effort between formal and informal organizations to support more effective placement of resources; on understanding how trust impacts the ability and motives of various actors; and on building visibility and trust between the different groups.

The objective of the game was to create understanding about why some actors behave the way they do and to thereby create a faster feedback loop around lack of collaboration and ineffective response. The game is meant to instill frustration as systems-level issues become apparent and players who can see each other cannot interact because of arbitrary and stale system mechanics they themselves have perpetuated. Players are encouraged to create new rules to the game, and these may affect how they comport themselves before and during response.

Methods

We undertook this project as action research because it (1) presents a problem that warrants immediate implementation of identified solutions and (2) involves members of both the formal and informal disaster response communities in the identification, design, and development stages (Creswell 1998). We began with several questions about the use of game play:

- Can we create a game that adequately approximates the structure and dynamics of a disaster response ecosystem?
- Does the use of such a game in an organizational setting identify common, recurring, and detrimental barriers to collaboration?
- Does game play induce strategies of cooperative reciprocity among participating individuals and organizations?
- Does use of the game open up opportunities for exploration that other methods don't?

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Gioia and Chittipeddi (1991) provided the methodological foundation for this research. Their study concerned an effort of deliberate change, and the goal of our game-building project was similarly to instigate change in how formal and informal organizations interact in disaster response.

Selection of Game Development Team

To represent formal and informal perspectives, invitees for the game creation group were from local response groups (the Empowered Communities Project, San Francisco Department of Emergency Management, Salvation Army Crisis Response); international NGOs (Save the Children, Oxfam, UNICEF); the private sector (Microsoft, Monkey Brains, Cisco, Airbnb); nonprofits (Meedan, Public Labs, Sarapis, Open Referral, Benetech); and informal groups (Occupy Sandy, anarchist responses to the refugee crisis).

Nine individuals were able to participate: three from informal response entities, two from formal response organizations, one from a nonprofit, two from cross-sector coordination groups, and one from the private sector.

Three-Day Workshop for Game Design

Day 0

- Participants established trust before the start of the planned activities through unstructured time and meals together.

Day 1

- A "Universe of Topics" exercise captured participants' feelings and ideas so that they each felt heard and could see how much/how little their goals overlapped.
- Participants did a visual thinking exercise to describe how their eco-sphere works.
- Participants posited some factors for a game (e.g., players, resources, pain points; figure 1).

Day 2

- Participants played Pandemic (a board game in which players work as a team to treat infections around the world while gathering resources for cures) to immerse in game mechanics and instigate conversation.
- Individuals proposed their own game structures and gave each other feedback.

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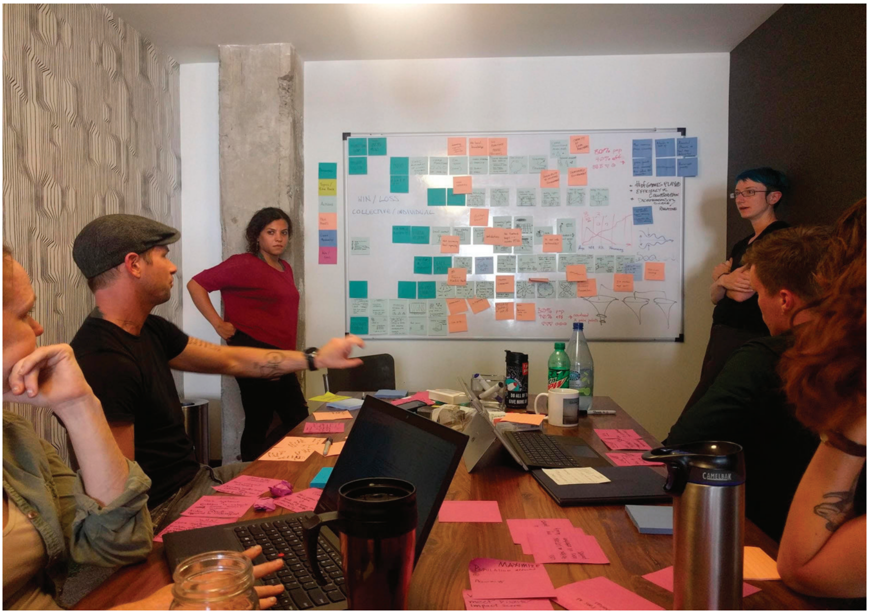

FIGURE 1 Participants in a game design session posit game factors, such as players (teal notes), resources (blue notes), and pain points (coral notes). Photo by Drew Hornbein.

- Participants explored shared factors of their proposed games to coalesce around one game model to develop further together.
- Participants made a prototype, troubleshooting the parts that didn't work. It was okay to be wrong.

Day 3

- Participants visualized the game flow to identify effective aspects (figure 2).
- Play testing revealed what parts were unclear, imperfectly designed (e.g., a player comes out ahead because of ill-conceived math rather than a well-played game), or superfluous.
- The game was revised based on these discoveries and play tested a second time.
- Participants documented how the game works and next steps (while it was fresh in people's minds).

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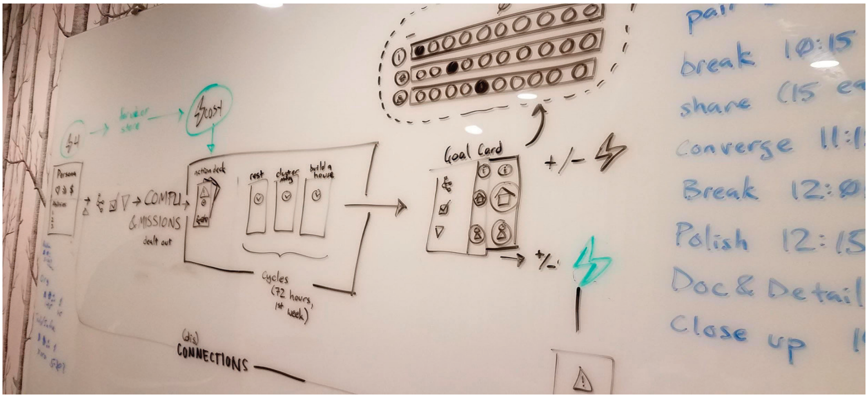

FIGURE 2 Workshop participants illustrated the game flow to identify effective aspects.

Results

The nine participants produced and have since play tested our prototyped card game. It is called ENCAPE (Emergent Needs, Collaborative Assessment, and Plan Enactment) and has four parts:

1. A how-to-play guide
2. A 98-card deck for 4 "personas" (Concerned Citizen, Ad Hoc Response Network, International NGO, and Municipal Government[2]) with 4 connection cards (for one persona to team with another and share resources), 20 special resource/action cards specific to each persona, 30 resource/action cards for any player, 10 missions, 30 updates
3. Templates to generate more cards of each type
4. A process for capturing and enacting feedback from play testers[3]

The game reveals how different player types behave, how duplication of efforts and subsequent waste impact the response ecosystem, and how working together might enhance response efficiency.

IMPLICATIONS

While much research has been done into the workings of formal structures, and some into informal structures, very little has been done into how they overlap

[2] The game still lacks the private sector lens, something we hope to remedy in further play testing.

[3] These resources are available via links at http://blog.bl00cyb.org/2017/08/interfaces-between-formal-and-informal-crisis-response/.

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or what the costs and benefits of doing so might be. ENCAPE revealed two main areas for improvement in disaster response specifically through cooperation or collaboration in formal and informal efforts: duplication of efforts and waste of resources.

Duplication of Efforts

During every crisis there are a few predictable challenges, such as calls for help from stranded or endangered people, individuals separated from their loved ones, basic needs for resources. Although these are well-known and expected elements of a crisis, efforts to address them are often duplicated by formal and informal groups. There is some coordination among groups, but it is limited to one "side" of the spectrum or the other: formal entities share with other formal entities when allowed to, and informal groups share with other informal groups when they are visible to each other.

It is not possible to avoid all duplication of effort. Even formal groups are forced into coordination during a response, regardless of investment of resources in precrisis partnerships. The informal sector is by definition unorganized until an event occurs, with energy expended in doing what it can rather than in becoming familiar with existing resources.

Waste of Resources

Lack of coordination and collaboration can be obvious in the lack of sufficient resources in some places and an excess in others. ENCAPE focuses on three types of resources:

1. Information is necessary for understanding needs and context. Waste in this area shows up as information overload due to lack of data structures (the information becomes overwhelming and inactionable).
2. Materials are necessary for medical services and rebuilding homes, for example. They are wasted when left unallocated or unused (e.g., food rotting on runways) because of unpredictable variation in need-supply flows or complications in distribution.
3. Labor is necessary for the use of both information and materials. Ineffective volunteer and employee management results in a paralyzed workforce constantly seeking direction or permissions, unable to mobilize in a focused and timely manner. This causes a loss of trust in the organization's ability to act intelligently or be worth showing up for.

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Cautions about Findings

This paper describes the impetus and workshop that generated a game to improve understanding of opportunities and barriers in crisis response coordination and collaboration. Deep qualitative research (transcription, coding, and analysis) of the workshop and additional play testing sessions are needed. Much of the understanding of formal/informal issues comes from the authors' direct experience working with emergency response groups.

FUTURE RESEARCH

While some research focuses on informal organizational structures, it is nowhere near as broad or deep in the disaster response sector as research on formal organizations. Benefits from the combination of these two methods will require a deeper understanding of each, as well as of the consequences of doing so.

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USAID Approaches to Engineering Innovation and Disaster Relief

Marissa Jablonski
USAID

The United States Agency for International Development (USAID) is a governmental funding agency that assists with development work all over the world through offices in Washington, DC, and missions located around the globe. The missions have strategic focuses defined in their five-year Country Development Cooperation Strategy (CDCS) under which they are authorized to issue grants or contracts to achieve the agreed upon objectives. The offices in Washington, DC, have either a functional or a regional focus. They primarily support overseas missions through programs and mechanisms or country activities where there is no field mission.

This paper is intended to introduce the reader to eight key departments or offices within USAID that support and utilize innovative engineer-driven solutions to problems. Opportunities mentioned here are broken into three types: (1) funding opportunities that support partnerships between US and overseas institutions; (2) co-creation processes for applicants to work with USAID on multi-party activity design; and (3) offices that use engineering innovation in disaster response. This paper serves as a backdrop and resource for my presentation, which shared revelations discovered during a career of development engineering both within and outside of USAID.

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(1) EXAMPLES OF FUNDING OPPORTUNITIES THAT SUPPORT PARTNERSHIPS BETWEEN US AND OVERSEAS INSTITUTIONS

American Schools and Hospitals Abroad (ASHA)
https://www.usaid.gov/work-usaid/business-funding/grant-programs/american-schools-and-hospitals-abroad

ASHA provides assistance to schools, libraries, and medical centers outside the US that were founded or sponsored by US citizens to serve as study and demonstration centers for American ideas and practices. ASHA awards help cultivate positive relationships between citizens of the United States and other nations through funding for construction or durable commodities. The US nonprofit institutions with which ASHA engages have deep and long-term relationships with their partner institutions overseas that promote mutual understanding and shared fundamental values, ideas, and practices.

Higher Education Solutions Network (HESN)
https://www.usaid.gov/hesn

HESN is a partnership between USAID and seven top universities (the College of William & Mary, Duke, Makerere University, Michigan State, MIT, Texas A&M, and UC Berkeley) designed to channel the ingenuity of university students, researchers, and faculty toward global development. At the launch of the partnership in 2012, each university established a Development Lab and created a Network with a mission to revolutionize development through science and innovation. Now in their fourth year, the HESN Development Labs are researching, incubating, testing, and accelerating solutions in partnership with local universities, organizations, and communities to deliver the greatest impact. The network has created a vibrant framework of cooperation among local actors, development professionals, and academics who know that innovation is key to tackling the complexities of modern-day development challenges.

Middle East Regional Cooperation (MERC)
https://www.usaid.gov/where-we-work/middle-east/merc

MERC was established in 1981 to facilitate research collaboration between Egyptian and Israeli scientists after their two countries signed the Camp David Accords. The program expanded to include Jordan, Morocco, Tunisia, Lebanon, the West Bank, and Gaza Strip in 1993. Arab scientists in the Middle East and North Africa are using science and technology to overcome core development challenges. Working together these scientists have led innovation in agriculture, environment, water resources, and health. Since these are regional challenges, fully realizing potential innovations requires cooperation. Today, at a time of rapid

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change in the Arab world, MERC continues to bring together Arab and Israeli scientists and students to create and share solutions to regional development challenges while promoting a peaceful exchange between neighbors.

Partnerships for Enhanced Engagement in Research (PEER)
https://www.usaid.gov/what-we-do/GlobalDevLab/international-research-science-programs/peer

PEER is an international grants program that funds scientists and engineers in developing countries who partner with US government-funded researchers to address global development challenges. PEER not only catalyzes collaborative research and elevates the use of science and technology to further USAID's development objectives but also establishes long-lasting research relationships that build scientific research capacity, strengthen the research ecosystem in developing countries, and enable collaborators to become better partners in development. The PEER program is designed to leverage federal science agency funding from NASA, NIH, NOAA, NSF, the Smithsonian Institution, USDA, and USGS by directly supporting developing country scientists who work in partnership with current or new colleagues supported by these US government agencies. Technical areas include water resource management, climate change, biodiversity, agriculture, energy, disaster mitigation, nutrition, maternal and child health, and infectious diseases.

(2) CO-CREATION PROCESSES FOR APPLICANTS TO WORK WITH USAID ON MULTIPARTY ACTIVITY DESIGN

Broad Agency Announcements (BAAs)
https://www.usaid.gov/partnership-opportunities/respond-solicitation/baa-process

BAAs are a procurement tool used by USAID to collaborate with the private and public sectors when facing a development challenge that does not have a clear solution and there appears to be an opportunity for innovation. A BAA is not in itself a procurement instrument, but rather a method to communicate interest in solving a development problem. There is no budget allocated and no particular procurement instrument determined in advance. Through a BAA, a problem is defined, solutions are co-developed, competencies are identified, and resources are explored. Often, but not always, BAAs result in a contract, grant, cooperative agreement, memorandum of understanding, fixed amount award, or other type of agreement.

USAID has successfully used BAAs to help solve a variety of development problems, including an Ebola Grand Challenge. BAAs are open for anyone to participate, including the private sector, public sector, nongovernmental, for-profit, nonprofit, and educational institutions, and is often considered a less onerous way to engage with USAID than the traditional procurement process.

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Grand Challenges
https://www.usaid.gov/grandchallenges

USAID Grand Challenges mobilize governments, companies, and foundations around important issues. Through these programs, USAID and public and private partners bring in new voices to solve development problems. They source new solutions, test new ideas, and scale what works. More than 136 million people around the world live in areas experiencing humanitarian crises. Millions of these people are unreachable by traditional humanitarian aid delivery due to armed conflict. As the length, frequency, and scope of the world's conflicts increase, it is becoming more difficult to reach affected people in insecure areas with life-saving and life-improving humanitarian assistance. New solutions are needed that respond to the needs of vulnerable, inaccessible communities, yet less than 1 percent of humanitarian aid is focused on investing in the innovations necessary to reach them.

USAID, the UK Department for International Development, and Grand Challenges Canada partner on Creating Hope in Conflict: A Humanitarian Grand Challenge. Through this Grand Challenge, groundbreaking solutions are sought that engage the private sector and draw from the experiences of affected communities in order to significantly improve, and in many cases, save the lives of vulnerable people affected by conflict. Focus areas include safe water and sanitation, energy (special focus on alternative energy solutions), life-saving access to data and information, and providing quality health care and health products (drugs and equipment).

(3) OFFICES THAT USE ENGINEERING INNOVATION IN DISASTER RESPONSE

Food for Peace (FFP)
https://www.usaid.gov/who-we-are/organization/bureaus/bureau-democracy-conflict-and-humanitarian-assistance/office-food

Alleviating global hunger is critical to US national security: where hunger persists, instability grows. By supporting the world's most vulnerable, Food for Peace is building a more stable world. Through its emergency food assistance activities, USAID saves lives, reduces suffering, and supports the early recovery of people affected by conflict and natural disaster emergencies, including refugees. FFP development activities reduce food insecurity among vulnerable populations for the long term and help build resilience in communities facing chronic poverty and recurrent crises, such as drought. Development food security activities equip people with the knowledge and tools to feed themselves, reducing the need for future assistance.

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The International Food Relief Partnership provides small grants to predominantly faith-based groups to distribute ready-to-use supplementary food and dried soup mix in primarily institutional settings, such as health clinics, schools, and community centers.

Office of Foreign Disaster Assistance (OFDA)
https://www.usaid.gov/who-we-are/organization/bureaus/bureau-democracy-conflict-and-humanitarian-assistance/office-us

OFDA is responsible for leading and coordinating the US government's response to disasters overseas. OFDA responds to an average of 65 disasters in more than 50 countries every year to ensure aid reaches people affected by rapid-onset disasters, such as earthquakes, volcanoes, and floods, and slow-onset crises, including drought and conflict. OFDA fulfills its mandate of saving lives, alleviating human suffering, and reducing the social and economic impact of disasters worldwide in partnership with USAID functional and regional bureaus and other US government agencies.

When disaster strikes, OFDA sends regional and technical experts to the affected country to identify and prioritize humanitarian needs. In the wake of a large-scale disaster, OFDA can deploy a Disaster Assistance Response Team to coordinate and manage an optimal US government response while working closely with local officials, the international community, and relief agencies. OFDA also maintains stocks of emergency relief supplies in warehouses worldwide and has the logistical and operational capabilities to deliver them quickly. OFDA utilizes tested and scaled innovative engineering solutions to solve problems.

CONCLUSION

There are many ways to engage with USAID and obtain assistance in the hopes of expanding the impact of your work through the use of technology and engineering. All information provided here was taken from public USAID websites and referenced accordingly. For further reference, the key website to answer questions about solicitations is https://www.usaid.gov/partnership-opportunities/respond-solicitation.

The key website to help you submit an unsolicited proposal or grant application is https://www.usaid.gov/work-usaid/get-grant-or-contract/unsolicited-proposals.

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Resilient and Reliable Infrastructure

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Resilient and Reliable Infrastructure

Julie Pietrzak
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Hurricanes Harvey (2017), Katrina (2005), and Sandy (2012) are widely considered the three costliest hurricanes in US history. The 2017 Atlantic hurricane season was particularly destructive, with Hurricanes Irma and Maria joining Harvey in contributing to the costliest hurricane season on record. As recovery from these disasters continues—and the possibility of severe weather increases with climate change—research, planning, and design must look to the future to provide resilient and reliable infrastructure.

Resilient infrastructure is not completely shielded from climate change but rather adapted to mitigate against flood impacts and rising temperatures to support rapid recovery after a disaster. Quicker recovery is the key to reliability and the end goal of resilient infrastructure.

In this session speakers considered the interconnectivity of varying types of infrastructure—water, transportation, energy, and telecommunications—and ways to predict disaster impacts as well as potential solutions to upgrade these systems so that they are resilient and reliable. It is imperative that researchers and designers work together with manufacturers and public agencies to develop innovative solutions for implementation in areas susceptible to damage or failure. Incorporating resiliency in the repair and rehabilitation of aging infrastructure is a growing trend across the United States.

The first speaker, Josh Vertalka (Resilient Solutions 21), introduced the idea of infrastructure resiliency and discussed how to effectively communicate data science evidence to untrained audiences, explaining how infrastructure resiliency challenges can be made digestible by using advanced web applications with graphic interfaces to make the data both highly accessible and interactive. Robert Hanson (US Department of Homeland Security) then spoke in more detail about

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challenges associated with critical infrastructure resilience, focusing on the importance of understanding interdependencies to strengthen infrastructure resilience and adding the critical cyber security element.[1] With increasing connectivity of systems, cyber vulnerabilities are a growing threat to resilient and reliable infrastructure. He also described national protection programs and the interface between research and governmental agencies to achieve infrastructure resilience. Finally, Firas Saleh (Jupiter) talked about climate change and the importance of increasing adaptive capacities of infrastructure in a changing climate. He showed how state-of-the-art modeling techniques can enhance understanding of the impacts of natural and anthropogenic hazards and gradual stressors, for example, sea level rise, on critical infrastructure.

[1] Paper not included in this volume.

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Communicating Advanced Infrastructure Resiliency Analytics to Diverse Groups of Stakeholders

Josh Vertalka
Resilient Solutions 21

Data science holds vast potential for providing rich insights into infrastructure resiliency challenges. However, the highly complex, analytical nature of data science is often unfamiliar to people working in disparate professions, and this leads to disinvestment by those who stand to benefit most from these infrastructure resiliency insights.

Little progress has been made toward intuitively communicating the analytical complexity of infrastructure resiliency to untrained audiences. Advanced web applications with graphic interfaces create opportunities to correct this by making data both highly accessible and interactive. Such advances include a model that allows airport security officers to identify combinations of airport security measures that minimize undesired risk events, and a simulation that assists government officials in planning for hurricane risk events by combining probabilistic hurricane paths and flood inundation data.

INTRODUCTION

Emergency managers and disaster planners have faced great challenges from unusually severe hurricanes in the past 25 years. Hurricane Andrew (1992) left large portions of Florida in shambles from its destructive wind. Hurricane Katrina (2005), which steamrolled much of New Orleans and the 9th Ward, might be the best example of resiliency challenges as no one expected the levees to break. In 2017 Hurricane Harvey joined Katrina as one of the costliest hurricanes in US history. It was stationary over the Houston area producing torrential rainfall and wind speeds reaching about 130 mph that devastated the area and left roughly 300,000 people without electricity and thousands of homes and businesses

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destroyed (NCEI 2018). Also in 2017 Hurricanes Maria and Irma, with wind speeds of 150 mph, destroyed Puerto Rico's power grid and over 75 percent of the island's agriculture (NCEI 2017).

Emergency managers (EMs) and disaster planners are tasked with building resiliency for these and other types of destructive events and ensuring safety through a collaborative ground-up approach. EMs need information about the dynamic disaster landscape to effectively execute their jobs (Kapucu et al. 2010, Waugh and Streib 2006). For instance, they may need to address questions such as the following:

- How vulnerable are we to a disaster?
- What disaster impacts will likely be felt by my community?
- How can I better protect the most vulnerable populations?
- What type of recovery efforts will likely be needed after the disaster?
- What can we learn from the disaster to better our response/mitigation efforts in the future?

These questions are complex, and in some cases even chaotic. In addition, the answers are rarely known, especially among EMs with limited resources.

THE CYNEFIN FRAMEWORK

The Cynefin framework describes these types of decision-making problems through operative contexts shown in table 1 (Snowden and Boone 2007).

TABLE 1 Cynefin framework.

Decision level	Description	Math relationship
Simple	Management is straightforward: there is a clear cause and effect relationship and therefore decisions are quite clear.	Direct linear relationship between X and Y
Complicated	Cause and effect relationships are not always apparent to everyone.	The relationship between X and Y is not known but can be worked out. Subject matter experts help dissect complicated problems.
Complex	There is no apparent order or cause and effect relationship; issues are constantly evolving; there is no clear answer at first but with research one eventually emerges.	The relationship between X and Y is unclear and may have feedback loops.
Chaotic	There is no order or researchable order as the system is constantly changing and therefore unmeasurable and unmanageable.	If a relationship between X and Y exists, it is difficult or impossible to identify.

NOTE: Adapted from Snowden and Boone (2007).

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The Cynefin framework can help identify where additional knowledge is needed or where current knowledge needs to be given to the right people. This is true for resiliency too.

Building resilient communities is complex or chaotic when there is a lack of understanding of cause and effect relationships, feedback loops, and interdependencies of the different forces at play. Knowledge and understanding are key in making chaotic, complex, or complicated issues into simpler, more manageable problems. A community may believe, for example, that evacuations are complex because no matter how much planning is involved, there always seem to be traffic jams. If the community understands that traffic jams are caused by improper evacuation routing or a lack of fuel for evacuating motorists, then the problem becomes simpler to correct. Quick, adoptable, intuitive, and useful knowledge provides EMs with the necessary information to plan for resiliency issues that were once more difficult.

Community EMs seek effective and efficient resiliency assessment and decision-making tools to create useful, collaborative, and clearly focused resiliency plans (Ostadtaghizadeh et al. 2015), which are the foundation of disaster recovery (Pfefferbaum et al. 2013). Unfortunately, iterative and stakeholder input is lacking in the creation of scenario-based planning tools (Sharifi 2016), rendering them less effective.

THE NEED FOR BETTER DECISION SUPPORT TOOLS IN AN ERA OF ADVANCED RESEARCH

The 2017 hurricane season highlighted the need for practical, accurate, and user-centric resiliency planning tools. Hurricanes are the most destructive natural hazard experienced by the Eastern and Gulf Coasts of the United States. Most of the fatalities and infrastructure damage are caused by rainfall, storm surge, and high winds.

Emergency managers and disaster planners need decision support tools that overcome the challenges of complicated and easily misinterpreted static map overlays, disparate and discontinuous data sources, and delayed maps, all of which exacerbated hurricane impacts in 2017. Static maps, for example, may provide incomplete spatial information as they require complicated spatial overlays, careful interpretation, and time to digest the information. To make fast and informed decisions, EMs need tools that quickly provide the necessary spatial information and knowledge without requiring convoluted and time-consuming data processing and GIS functions.

Research-driven approaches to creating resilience help build knowledge that EMs use for more effective decision making. The scientific research approaches conducted at RS21 and its partners, including the Department of Homeland Security's Office of Cyber Infrastructure and Analysis and the national laboratories, offer a rich bed of knowledge, including surge and wind modeling. However, the

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scientific research results, in a raw format, can sometimes be obscure for those who need them most. Nonacademic research consumers often have a strong need for cutting-edge research insight but are the least skilled in producing and digesting this information.

This is not to say that these consumers are not intelligent or properly educated. They are. It is also not an issue of scientific research outpacing the needs of practitioners. It is not. It is a matter of connecting the right people with the data insights they need in a consumable way.

USER-CENTRIC APPROACH TO RESILIENCY TOOLS THROUGH CONTEXT BUILDING

User-centric approaches to creating disaster resiliency planning tools involve stakeholder buy-in to create powerful tools that are more widely used. Insight into the complexity of resiliency issues requires an understanding of resiliency problems and approaches, the data needed to solve the problem, who is consuming the information, what information should be presented in a tool, and a host of other considerations. Alignment of these components increases the likelihood that a tool will be useful. At RS21 we have found that the best way to ensure that these components align is through our discovery process.

Collaborative and holistic engagement with stakeholders proves to be effective at both establishing trust and laying a foundation for the development of effective tools. One of the first engagements with our clients is a discovery session to lay out goals, motivations, and challenges. One motivation is to help the client (when necessary) home in on a problem and begin discussing potential solutions through a data science and design lens. This involves examining different analytical approaches and unique datasets needed to solve the problem with the client. This is an iterative approach as the client's problem, the datasets available, and the methods used are intrinsically linked.

Understanding these elements and their interconnectedness helps us identify what type of impacts and insights data science can provide to the client. We catalogue the client's methods, data, and past insights and begin to identify method and data gaps. Our data scientists work with the end users to identify insights that are consumable and important, or human-centric.

For the design perspective, the discovery session begins with a user-centered design approach to help us identify what tool features and elements will help users engage with and understand the data. The approach includes building use cases for the tool, user personas, and mood boards that help maximize connectivity between the users, the tool, and the data. The information gathered in the discovery session allows our development team to efficiently structure the backend databases for the analytical procedures and data and the frontend based on design aspects.

Working in the innovative space of resiliency interfaces, this approach to product development allows for solving not only known challenges but also

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unknowns uncovered during iterative research and brainstorming. It also creates a balance necessary to scope the vast amount of options generated in user-centered design approaches. The end output of pairing user-centered design with design thinking is not just a creative exercise but an effective and user-adoptable system that allows us to provide the best insights in an intuitive, inspiring, and evolving interface.

Furthermore, this process allows teams to create a strategic product roadmap. Instead of reconceiving and creating a tool from scratch when old tools fail, this design thinking approach allows for iterative improvements over time, leading to a much more sustainable, scalable, and cost-effective resiliency product.

This broad framework can be applied not only to the project overall but to any element of a project in progress. Because of this, our workflow is a process of frequent strategic iteration. Just as John Snow did not instantly know how to solve the cholera puzzle, we do not always nail it out of the gate in a product design. While design thinking is a beneficial approach to interactive product design, it is merely creative exploration without a matching iterative development process to realize real-world manifestations of theoretical software. Such a process is crucial to realizing iterative designs in a way that allows for real-time user and stakeholder feedback and testing on a project in flux.

CONCLUSIONS

Disaster management and planning approaches have come a long way in the last few years but still focus on antiquated frameworks and tools. Planning tools have gone from overlaying confusing, disparate, and discontinuous static maps for resiliency scenario–based assessments to GIS-based approaches that require vast datasets and specialized staff.

Custom decision support tools overcome the challenges presented by static maps and GIS applications and enable users to interact with data insights and build different resiliency scenarios through a map interface. Users can toggle switches, zoom in and out of areas, use slide bars to adjust surge levels, and pull levers to change prediction schematics.

For instance, EMs can use our tools to zoom into states, towns, and neighborhoods, then use a slide bar to change the amount of surge flooding in an area. After that, they can examine how multiple levels of expected flooding will impact different infrastructure, including critical lifeline assets, such as hospitals, police stations, evacuation routes, and shelters. This information is immediately available to users, circumventing the need for static maps and GIS tools. Last, our custom tools can be created in 4–8 months using our frameworks and development process.

Overcoming sterile resiliency assessment tools requires human-centric approaches to building tools. Human-centric approaches should not be confused with social science research but instead should focus on the interconnectedness of a problem (resiliency, infrastructure, and other interdependencies) with the people

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who make the decisions. The Double-Diamond technique—a simple visual map of the design process that includes the phases of discover, design, develop, and deliver—offers a cyclical research approach for data-driven research and creative thinking to solve the client's problem. This approach prevents the development of tools without stakeholder and user engagement. Furthermore, human-centered thinking helps connect data and data methods not only to resiliency problems but to the way people engage with solving problems through data. The more connected people are with the data, the more successful the tool becomes.

Our data science, development, and design approach helps resiliency planners and EMs better prepare for hurricanes and other natural disasters by giving them the tools to better leverage knowledge embedded in data. Collaborating with clients in this nonprescriptive approach creates successful custom tools that turn complex problems or pain points in clients' experience into simpler versions, leading to better resiliency.

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Climate Change and Infrastructure Resilience

Firas Saleh
Jupiter

Infrastructure for energy, transportation, and water has evolved over time into inextricably interconnected systems. Traditionally, the engineering design practice of such systems has proceeded on the assumption of "climate stationarity," in which the frequency and magnitude of weather patterns remain unchanged into the future. But climate change is introducing nonstationary stressors, such as rises in sea level and temperature and more frequent and intense storms. Such stressors can affect infrastructure systems at varying spatial and temporal scales and require a holistic understanding.

Recent extreme events have highlighted the importance of understanding infrastructure interdependencies to strengthen resilience and adaptive capacity in a changing climate. Hurricanes Sandy (2012), Harvey (2017), Irma (2017), and Florence (2018) caused disruptions to major US water, transportation, and energy systems that affected the functioning of other critical infrastructure (e.g., for health care and telecommunications). Resilience planning must account for the impacts of both disruptive extreme weather events and long-term climate change–induced stressors, such as sea level rise and drought.

The work presented here focuses on the use of state-of-the-art modeling techniques to better understand the infrastructure impacts of natural (e.g., storms and floods) and anthropogenic (e.g., dam breaks) hazards as well as gradual stressors (e.g., sea level rise). This multidisciplinary research merges the fields of climate change; civil, water resources, and coastal engineering; remote sensing; and high-performance cloud computing to identify critical thresholds in aging infrastructure and failure cascade risks in interconnected systems.

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INTRODUCTION

Climate change is expected to alter the intensity, duration, and/or frequency of climatic extremes over time, a concept termed nonstationarity (Cheng and AghaKouchak 2014).

In general, engineering design metrics and assessment of risk are based on historical statistical analysis in which hydrologic processes fluctuate in an unchanging envelope of variability. Such metrics are essential in guiding engineering design choices.

In inland and coastal urban areas, nonstationary processes are exacerbated by anthropogenic land-cover changes, such as deforestation, urban expansion, and water diversion. In a changing climate, frequent and more intense storms can have more serious implications for vulnerable and aging infrastructure.

Long-term sea level rise is the main driver of accelerated flooding along the US coastline; however, changes in joint distributions from storm surges and precipitation associated with climate change also augment flood potential (Sweet and Park 2014). Hurricane Irene (2011), for example, showed that with a compound event such as storm surge and heavy precipitation, the potential for flooding in low-lying coastal areas is much greater than from either in isolation. Irene's extreme rainfall and resulting flash floods in New York, New Jersey, New Hampshire, and Vermont destroyed or damaged nearly 2,400 roads and 300 bridges (Saleh et al. 2016, 2018a, 2018b). Tropical storm Harvey in 2017 brought more than 51 inches of rain in Texas, breaking the record for the greatest amount of rain recorded from a single tropical storm or hurricane in the continental United States.

The combination of aging infrastructure and increasingly severe climatic stresses sets the stage for future disasters. In that context there is a pressing research need to develop strategies for engineers to (1) better understand climate–infrastructure interactions to recognize the limits and opportunities of the knowledge base on which decisions will be made; (2) account for the effects of climate change in engineering design practice, where appropriate; and (3) clearly justify when such changes are *not* needed for a project of a particular type or scale.

There have been significant advances in considering climate change information in coastal areas, owing to the availability of sea level rise scenarios and analytical methods and tools. But there remains insufficient knowledge of inland and estuarine areas and their preparedness for compound events.

USE CASE: DAMS AND STORM EVENTS

Throughout the United States more than 90,000 dams provide important service and protection to communities and the economy. Their average age is 56 years, which exceeds the average life expectancy of 50 years for certain dams.

Dams are classified based on their hazard potential: high, significant, or low (table 1). As the US population grows and development continues, the number of

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TABLE 1 Dam hazard classification. Based on ASCE's 2017 Infrastructure Report Card (https://www.infrastructurereportcard.org/cat-item/dams/).

Hazard classification	Potential consequences of failure or misoperation
High hazard	Loss of life; significant economic losses, including damages to downstream property or critical infrastructure, environmental damage, or disruption of lifeline facilities
Significant hazard	Significant economic losses, including damages to downstream property, critical infrastructure, environmental damage, or disruption of lifeline facilities
Low hazard	Minor damage to nonresidential and normally unoccupied buildings, or to rural or agricultural land

high-hazard dams is increasing—it was nearly 15,500 in 2016 (see, e.g., figure 1). Many dams were designed based on relatively short hydrologic records; longer accurate instrumental records and future climate modeling are needed to guide their upgrading as well as the construction of new dams.

Overtopping is one of the most common forms of catastrophic dam failure, and may result from an increase in the frequency and intensity of extreme rainfall. In addition, as water levels rise from increased inflows, structural and hydraulic stresses from the weight of the additional water in the reservoir will likely exceed levels either designed for or previously experienced in a given dam.

It is often the case that manmade and natural disturbances do not happen in isolation, and their impacts can vary temporally and spatially. Such compound events are likely to cause tipping points and major disturbances to dams and other critical infrastructure. To address this aspect, a predictive framework was developed in this work to evaluate implications of manmade-induced and natural disturbance scenarios, such as storm surges and intensive rainfall storms that trigger dam overtopping or a dam break.

A test bed located in a complex estuarine system in northern New Jersey (figures 1 and 2) was selected to critically evaluate infrastructure resilience for extreme flood events associated with hurricanes Irene (2011) and Sandy (2012). The two events emphasize the importance of detailed integrated modeling for compound effects of coastal storm surge and riverine flooding.

The test bed captures long- and short-term stressors:

- A coastal environment subject to sea level rise
- A steep gradient in population density
- An infrastructure serving one of the largest metropolitan areas in the United States
- A highly urbanized area with valuable commercial and residential assets
- A history of environmental impacts, ranging from heat waves and hurricanes to localized storms
- A wealth of historic and real-time data and extensive monitoring facilities

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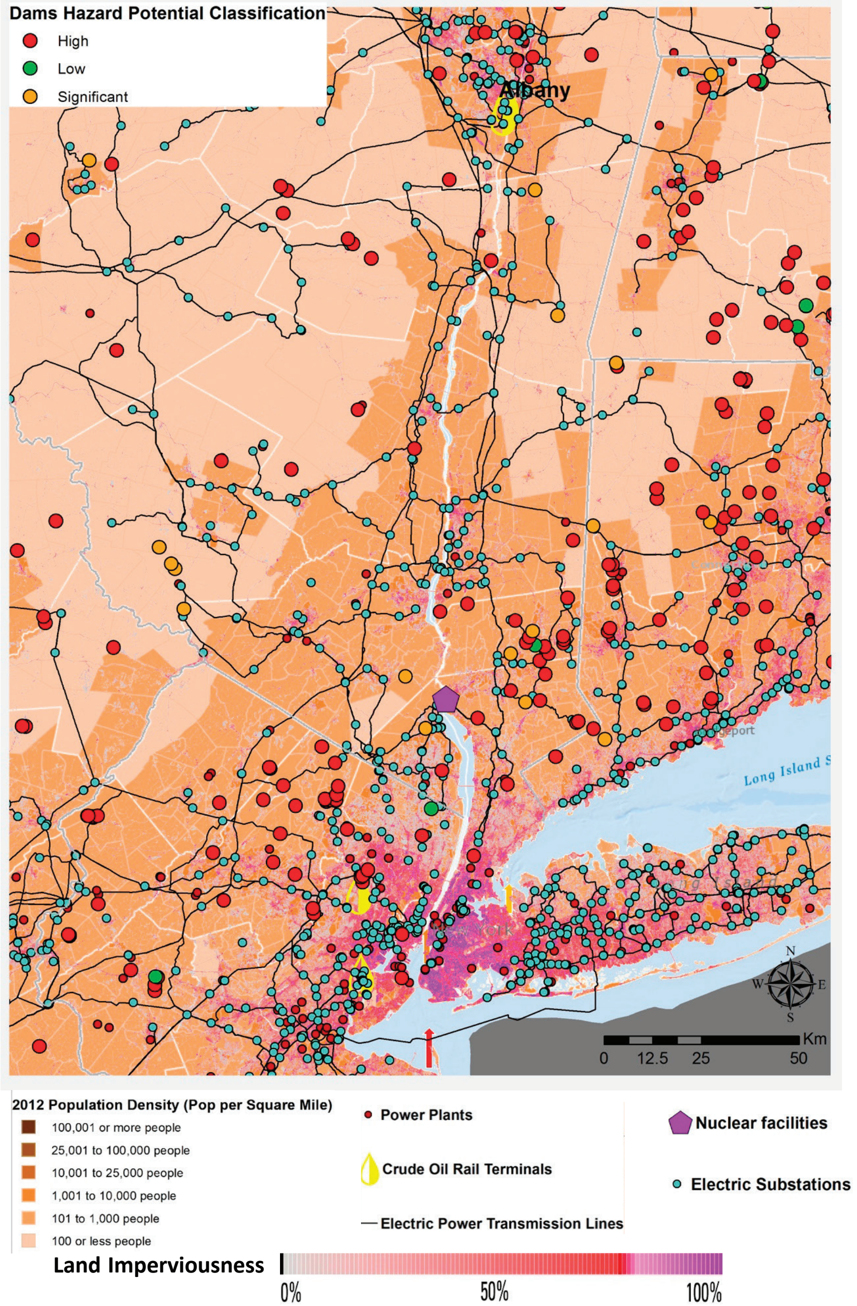

FIGURE 1 Interconnected critical infrastructure in the Lower Hudson Basin, New York.

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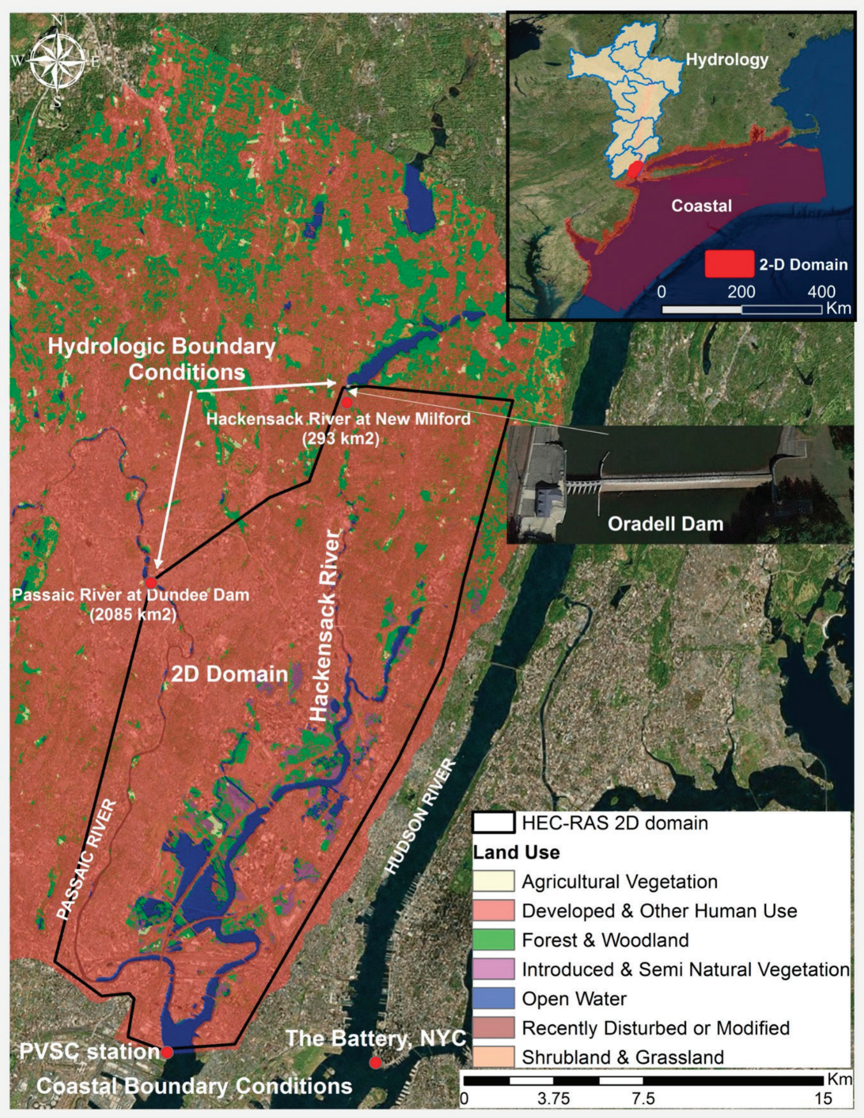

FIGURE 2 Test bed in northern New Jersey showing interconnected system and multi-scale modeling components. HEC-RAS = Hydrologic Engineering Center River Analysis System of the US Army Corps of Engineers; NYC = New York City; PVSC = Passaic Valley Sewerage Commission.

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The area is bounded on the west by the Passaic River at Dundee Dam, on the north by the Hackensack River at New Milford (downstream of Oradell Reservoir, built in 1923), on the east by the Hudson River, and the tidal influence of Newark Bay from the south (Saleh et al. 2017).

To establish baseline inundation extents, the inland hydrodynamic component of the modeling framework was forced with the best available data from the United States Geological Survey and National Oceanic and Atmospheric Administration, represented by measured river discharge and ocean water levels (figure 3). The extents simulated by the model for Hurricane Irene were a combination of storm surge and major flooding. In contrast, flooding associated with Hurricane Sandy was dominated by a coastal storm surge that overtopped all berms and several tide gates in the area of study. The analysis for Hurricane Sandy suggests that the storm surge propagated 36.2 km inland along the Hackensack River up to the Oradell Reservoir dam (figures 2 and 3).

Upon establishing baseline conditions, the framework was then forced with probabilistic and scenario-based projections of sea level rise and change in rainfall to help stakeholders and practitioners understand long-term risks in a changing climate.

DISCUSSION AND CONCLUSION

Modeling frameworks representing hydrosystem components spanning numerous temporal and spatial scales were integrated to provide telescopic capabilities for modeling coastal and inland flooding. The modeling outputs provide important information to quantify integrated processes at decision-relevant scales, identify significant vulnerabilities, and mitigate associated high-impact risks in critical infrastructure. The framework can be used to quantify the impacts on the paired bilateral interfaces of energy–water from natural (e.g., storms and floods) and anthropogenic (e.g., dam break) shocks and explore complex interactions with gradual stressors (e.g., climate change and changes in land use).

Compound events are characterized as (1) two or more extreme events occurring simultaneously or successively (e.g., storm surge, hurricane, Nor'easter, dam failure, and/or precipitation-induced high river discharge), (2) the combination of one or more extreme events and underlying conditions that amplify the impact of the event(s) (e.g., excessive soil moisture, drought, prolonged heat wave), or (3) combinations of events that are not themselves extreme but create an extreme event or impact when combined (e.g., saturated soil, snow melt with temperature anomalies).

Coupling the system-level models of the framework with regional-scale climate change projections can help identify strong and weak linkages between the different components and nonlinear behaviors and responses across spatial and temporal scales. The resulting information can be used to guide decisions about the capacity of infrastructure to withstand projected climate-related hazards.

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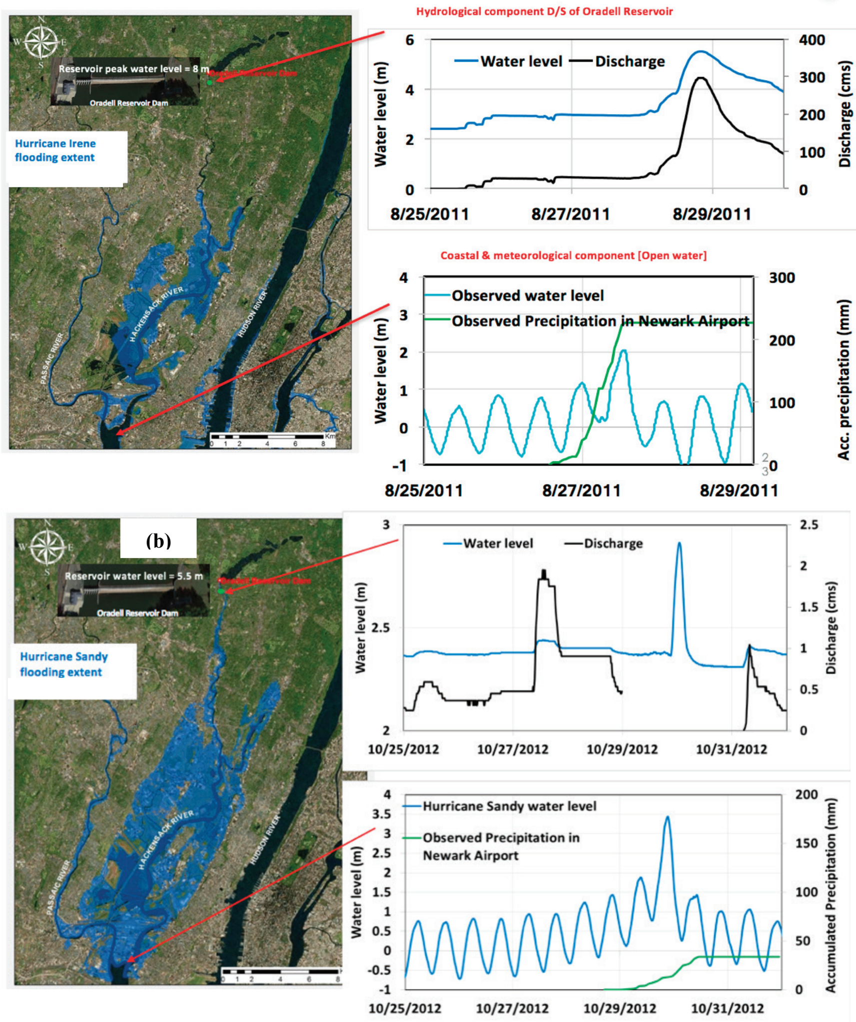

FIGURE 3 Flooding extent for the combined impact of riverine and tidal components during (a) hurricanes Irene and (b) Sandy showing the observed accumulated precipitation and coastal water levels (including surge) at Newark Bay. D/S = downstream

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Theranostics

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Theranostics

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Nanomaterials have been explored as reagents to deliver medicines to disease sites in vivo, to detect the presence of disease, or as contrast agents to allow the imaging of target tissues. A new class of multifunctional materials combines elements of sensing, imaging, and/or drug delivery in a single system: theranostics can simultaneously diagnose/detect disease status and provide a means to treat the pathology, especially in metastatic cancer. This session presented perspectives on these concepts from three leaders in this emerging area and highlighted some promising new approaches in preclinical development.

Andrew Tsourkas (University of Pennsylvania) introduced theranostic nanoparticles and described strategies being developed to improve their tissue penetration and targeting capabilities. He explained that, although many nanoparticles being tested in preclinical studies include a targeting agent to confer specificity for a disease site while minimizing toxicity in healthy tissues, these benefits are not always realized in practice. Next, Ester Kwon (University of California, San Diego) talked about synthetic biomarkers for cancer detection and diagnosis. In her work, diagnostic nanomaterials have been engineered to target the tumor microenvironment and report pathogenic protease activity for the detection of cancer. These nanomaterial sensors can be tools for precision medicine to stratify patients for molecularly targeted therapies. In his talk on immune theranostics, Evan Scott (Northwestern University) presented short- and long-term controlled delivery systems that he and his colleagues have engineered to identify and quantify immune cells after intracellular delivery both in vitro and in vivo. He explained that, because of the complex responses generated by the stimulation of diverse immune cell populations during immunotherapy, it is critical to monitor which cells are targeted during treatment to understand the mechanisms behind elicited responses.

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Developing Targeted Theranostic Nanoparticles: Challenges and Potential Solutions

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It has been nearly 50 years since President Richard Nixon declared "War on Cancer" with the National Cancer Act of 1971. Yet, according to the Centers for Disease Control and Prevention,[1] the cancer death rate has decreased by only about 20 percent since then, paling in comparison to the greater than 65 percent reduction in the death rate for heart disease and stroke (Ma et al. 2015). The development and refinement of targeted theranostic nanoparticles may advance progress on this front.

INTRODUCTION

The vast majority of cancer chemotherapeutics, which primarily consist of small-molecule drugs, have failed to make a major impact on the death rate for most cancer types. This can be at least partially attributed to the substantial risk of systemic toxicity, which limits the dose that can be safely administered. Because of the body's rapid clearance of small-molecule drugs, high doses are needed to achieve a therapeutic effect, but since drugs perfuse both diseased and healthy tissue, there can be undesirable effects in the latter. Small-molecule drugs are also often associated with broad mechanisms of action, which can disrupt unintended cellular pathways.

Initially, it was thought that nanoparticles would provide an immediate solution to all of these problems. Nanoparticles used in therapeutic applications are typically produced at sizes of 10–150 nm to ensure long circulation times after intravenous administration. In general, drugs of less than 10 nm are rapidly cleared by the kidneys, and nanoparticles larger than 150 nm are more efficiently

[1] Expected New Cancer Cases and Deaths in 2020, https://www.cdc.gov/cancer/dcpc/research/articles/cancer_2020.htm.

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cleared by phagocytic Kupffer cells in the liver. Nanoparticles are also designed to be biocompatible (so they do not elicit a significant immune response) and biodegradable (to ensure eventual excretion).

Imaging agents and therapeutic agents are used to facilitate the study and evaluation of nanoparticle pharmacokinetics. Nanoparticles prepared with both a therapeutic and a diagnostic imaging agent are often referred to as "theranostic."

ADVANTAGES AND CHALLENGES OF NANOPARTICLE DRUG DELIVERY

There were many reasons for the initial excitement surrounding nanoparticles as drug delivery vehicles. First, their circulation half-life in serum can be 10- to 100-fold longer than the small-molecule drugs that they carry (O'Brien et al. 2004), giving the drug more time to find its target and often allowing for the use of lower doses. Longer circulation times are also generally associated with reduced toxicity to organs involved in drug excretion (e.g., the kidney and liver), because of slower accumulation in these organs and a lower maximum drug concentration at any given time.

A second advantage of nanoparticles, compared with small-molecule drugs, is that they do not freely perfuse all tissues but are confined to blood vessels and tissues with highly permeable vasculature (i.e., the liver, spleen, and tumor). This results in a lower chance of toxicity to healthy organs. The best known example is the drug doxorubicin: its cardiotoxicity is reduced sevenfold when packaged in a nanoparticle (O'Brien et al. 2004).

Third, nanoparticles can be used to solubilize drugs that are highly hydrophobic and cannot otherwise be administered to patients, thus increasing the number of drug candidates.

Despite the clear advantages of nanoparticles, nanoparticle-based drug formulations have not consistently led to a significant improvement in patient survival compared with free drug. As a result, only six nanoparticles have US Food and Drug Administration approval for the treatment of cancer (Ventola 2017). There seem to be two primary (and related) reasons for the limited efficacy of nanoparticles: low levels of accumulation in tumors and limited penetration into tumor tissues.

A survey of the literature from the past 10 years found that, despite extended circulation time, only 0.7 percent (median) of an administered nanoparticle dose is found in solid tumors (Wilhelm et al. 2016). The accumulation is largely driven by the enhanced permeability and retention associated with the greater vascular permeability of tumors and poor lymphatic drainage.

Once nanoparticles cross the vascular wall, they need to penetrate a dense extracellular matrix in order to reach tumor cells. Unfortunately, nanoparticles typically travel just tens of micrometers over the course of days (Sykes et al. 2014; Wang et al. 2015).

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THERANOSTIC TARGETING

Strategies are being explored to improve both the accumulation and the penetration of nanoparticles in tumors. The most common approach to bolster the accumulation of nanoparticles in tumors involves functionalizing the nanoparticle surface with targeting ligands specific for a tumor biomarker. While targeting alone does not address the challenge of tumor penetration, the penetration has been shown to increase with repeated dosing.

The benefits of targeting probably stem from better retention of the nanoparticles in the tumor rather than a greater quantity of nanoparticles that reach the tumor. Targeting also likely improves the probability of nanoparticle binding and internalization by cancer cells (in relation to surrounding stromal cells), which can enhance drug efficacy. Moreover, the targeting agent may exhibit an additive, or even synergistic, therapeutic effect on target cells when combined with the chemotherapeutic payload in the nanoparticle (Yang et al. 2007).

CHALLENGES AND SOLUTIONS FOR TARGETING STRATEGIES

While targeting is widely considered to be beneficial, studies have shown that receptor targeting does not always make therapeutic nanoparticles more efficacious (Lee et al. 2010; McNeeley et al. 2007). It is now understood that many complicating factors can limit the success of targeted nanoparticles. Not surprisingly, poor tissue penetration remains a significant problem. Heterogeneous antigen expression and/or the loss of cell surface antigen expression during disease progression are also problematic.

Use of the Tumor Microenvironment

One strategy being tested to overcome the high variability and instability of cancer cells involves taking advantage of cues in the tumor microenvironment to promote nanoparticle retention in tumors. For example, numerous nanoparticles have been developed to be retained in tumors in response to the acidic tumor microenvironment, matrix-metalloproteinases, hypoxia, binding of stromal cells, and other factors common to most tumor types (Du et al. 2015). A variation on this approach involves using biological cues to generate smaller nanoparticles in the tumor environment so that they can diffuse more readily through the interstitium (Li et al. 2016; Wong et al. 2011).

While targeting strategies that take advantage of the tumor microenvironment have seemed encouraging in preclinical studies, no single approach can be used in all patients because of patient-to-patient variability. Progress toward personalized medicine is needed to determine which targeting strategies will be effective in individual patients.

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External Stimuli

As an alternative to molecular and environmental signatures for targeting, externally administered stimuli have been used to improve the accumulation and penetration of nanoparticles. Pharmacological stimuli have included enzymes to degrade the extracellular matrix (Parodi et al. 2014), inhibitors to limit matrix generation (Diop-Frimpong et al. 2011), and drugs to alter vascular permeability or blood flow (Chauhan et al. 2012). Physical triggers include radiation (Baumann et al. 2013; Koukourakis et al. 2000) and ultrasound (Mullick Chowdhury et al. 2017; typically in combination with microbubbles). By increasing vascular and tumor permeability both approaches can dramatically improve nanoparticle delivery when timed appropriately.

Magnetic forces can also be used to boost the accumulation and penetration of nanoparticles in tumors. While this has been limited to superficial tissues (Al-Jamal et al. 2016; Schleich et al. 2014) because of the rapid dropoff of the magnetic field gradient with distance from the magnet, proper configuration of multiple magnets can enhance the delivery of magnetic nanoparticles into deep (permeable) tissues.

Physical triggers can also be used to promote the release of drugs from nanoparticles. The hypothesis is that once a drug is released it can more readily perfuse the tumor tissue. A second possibility is that the rapid release of a drug from intratumoral nanoparticles can yield a higher effective dose. Importantly, for this approach, drug release must be limited to the tumor and not be triggered in healthy organs. The most common physical trigger is light irradiation to promote drug release from light- or thermally responsive nanoparticles (Linsley and Wu 2017), but its use is limited to superficial tumors.

Recent work shows that alternating magnetic fields can be used to spatially target the heating of magnetic nanoparticles and trigger drug release from thermally responsive nanoparticles (Tay et al. 2018).

A limitation of all physical triggers is that their effect is confined to the primary tumor. The use of external triggers will therefore need to be complemented with biological targeting strategies to ensure the elimination of metastatic niches.

PROSPECTS

As advances continue in nanoparticle design efforts to overcome the many challenges of treating cancer, there has been a corresponding increase in nanoparticle complexity and cost, and yet there are still very few examples of clinical benefit. Many failures stem from the inability to produce complex nanoparticles at a large scale. Therefore, there seems to be movement toward simplifying nanoparticle designs to achieve high drug encapsulation efficiencies, high drug payloads, and high conjugation efficiencies with few (or no) purification steps required.

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While progress toward effective treatments for cancer is taking longer than expected, researchers are beginning to understand the obstacles that have prevented nanoparticles from significantly reducing the cancer death rate. Innovative solutions are being identified that will one day allow nanoparticles to live up to the lofty expectations of them.

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Synthetic Biomarkers for Cancer Detection and Diagnosis

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Critical to the clinical management of cancer is the ability to detect disease and provide molecular information that can be acted on by therapeutics. Current clinical methods in cancer diagnostics include invasive biopsies of tumor tissue, imaging, and measurement of biomarkers in the blood. These tools can be enhanced by technology that is minimally invasive and could produce functional readouts on tumor activity. Exciting progress toward this goal includes activity-based probes to create "synthetic" biomarkers, methods to image metabolic activity of tumors, and devices for drug micro-dosing. Future goals are to coordinate the readouts from these diagnostic methods with molecular targeted therapeutics for a unified precision medicine approach for cancer treatment.

HETEROGENEITY DRIVES CHALLENGES IN CANCER TREATMENT

Cancer is a leading cause of death worldwide, and in the United States alone cancer care was estimated to cost $147 billion in 2017 (National Cancer Institute). Despite promising recent advances in cancer treatment, the response of patients to therapies is heterogeneous. The evidence for the heterogeneity of human cancer between individuals, tumors, and even within the same tumor is growing as more samples are sequenced and novel methods are developed. Adding to the complexity is the fact that heterogeneity not only is encoded by genetics but can be influenced by the microenvironment of the cancer cell.

At the same time, an increasing number of therapeutics target cancer cells on a molecular basis. This presents the challenge of how to guide clinical decisions

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for patient populations on a quantitative basis to match therapeutics to an individual's cancer in order to maximize efficacy and minimize treatment side effects.

Furthermore, technology that is time-resolved would allow longitudinal monitoring of patients to track their response and capture the development of therapeutic resistance.

All these challenges are embodied in the National Institutes of Health Precision Medicine Initiative, an effort to understand "how a person's genetics, environment, and lifestyle can help determine the best approach to prevent or treat disease."

CANCER BIOMARKERS CAN GUIDE CLINICAL CARE

The timeline of cancer progression is complicated and includes risk assessment, screening, diagnosis of disease onset, response to treatment, and monitoring for relapse after treatment. Biomarkers can provide information about disease status and answer important questions such as, Who has cancer and how advanced is it? What is the best available treatment for an individual and his or her cancer? Is the patient responding to treatment? Is there relapse of disease? The answers to these questions can provide valuable insight to inform clinical actions and improve the clinical management of cancer for reduced side effects and better treatment outcomes.

Biomarkers come in many forms and can include genetic sequencing information, such as the increased risk for breast and ovarian cancer in individuals with BRCA1 mutations (Shattuck-Eidens et al. 1995); analysis of nanometer-scale extracellular vesicles from the urine, such as prostate cancer prediction through sequencing of exosomes (McKiernan et al. 2016); and aberrant overexpression of proteins, such as measuring expression levels of HER2 in biopsies to guide treatment of antibody-based therapies (Slamon et al. 2001).

Given the large diversity of individual patients, the future of cancer diagnostics will likely integrate many inherently noisy biomarker signals using methods developed for "big data."

ACTIVITY-BASED NANOSENSORS AS THERANOSTICS

Although there are promising biomarkers for the diagnosis and monitoring of disease, not all biomarkers are created equal. For example, the serum biomarker prostate-specific antigen (PSA) was widely adopted to screen men over the age of 50 for prostate cancer starting in the 1990s. Although PSA increased diagnostic sensitivity for prostate cancer, many of the cancers were benign. Unfortunately, clinical actions based on the detection of elevated PSA levels increase the risk for complications associated with follow-up procedures, such as biopsies and treatment, leading to what has been recognized as "overtreatment" (Prensner et

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al. 2012). Furthermore, the mechanism for the rise of PSA protein levels in the bloodstream remains unclear, and therefore its link to disease progression is not well understood.

This outcome with PSA reveals a need to reenvision biomarkers as tools that encode information relevant for clinical decisions for treatment, such as how a particular tumor might respond to drug treatment. The pairing of diagnostic information with treatment is embodied in the term “theranostic,” a portmanteau of *thera*py and diag*nostic*.

Enzymes are often the target of cancer therapeutics. A particularly important class of enzymes are proteases, which are known to play critical roles in the progression of cancer (Koblinski et al. 2000). Fluorescence-based small-molecule probes, developed to functionally image protease activity, are important tools to study biology and can also be used in surgical navigation for total tumor resection (Yim et al. 2018). Other groups have engineered imaging probes that, activated by protease activity, fluoresce in the visible and near-infrared wavelengths (Jiang et al. 2004; Weissleder et al. 1999). However, these technologies rely on optical imaging that is limited by imaging depth.

As a complementary technology, we have engineered an exogenously administered nanoscale sensor that is targeted to tumor cells and sheds analytical fragments in response to tumor-specific proteases that can be detected in the urine (Kwon et al. 2017). The advantage of an exogenously administered synthetic system over a naturally occurring blood biomarker is that analyte generation can be engineered for optimal kinetics, specificity, and amplitude using material design. Furthermore, we found that analyte generation was also dependent on ligand–receptor matching between the nanosensor and tumors.

This technology can be developed to include a wider array of protease-sensitive analytes and tumor-specific receptors to precisely stratify patients into treatment groups based on receptor expression that can be matched to therapies such as integrin-targeted therapeutics. Urine-based readouts can be paired with spatial information if nanosensors are built with superparamagnetic nanoparticle cores for magnetic resonance imaging (Kwong et al. 2013).

CONCLUSIONS

A growing number of molecularly targeted therapeutics are available for the treatment of cancer. Diagnostics with activity-based readouts are promising tools to stratify patients for these increasingly precise treatment regimes. The future of clinical management of cancer will include the integration of diagnostic information with molecularly targeted therapeutics.

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Immune Theranostics

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As understanding improves about how the immune system functions, engineers can begin employing principles of rational design to modulate immune responses for therapeutic applications. Key tools in this frontier of immunoengineering have emerged from biomaterials and nanoscale science, such as theranostics: the combined delivery of therapeutic and diagnostic agents. By providing a means of tracking and quantifying cells that are targeted and modulated during vaccination and immunotherapy, theranostics makes it possible to approach the immune system less as a mysterious "black box" and more as an interlinked network of cells and signaling molecules that can be mapped for improved reproducibility and understanding. Immune theranostics holds promise for realizing technologies that harness the full potential of immunotherapy in the treatment of a wide range of inflammatory disorders.

BACKGROUND

The immune system is a dynamic and highly responsive network of bioactive molecules, cells, and tissues. It must continuously maintain the homeostasis of its host body within a strict set of physicochemical boundaries while being ever ready to address an equally complex and evolving repertoire of invading pathogens and heterogeneous cancers. Adding to this complexity is the uniqueness of each patient's immune system—women, men, children, neonates, the elderly, and the diabetic can each have distinct immune responses to the same stimuli. Furthermore, prior exposure to particular inflammatory molecules and conditions, such as certain foods or regional infections, can have significant impacts, even preventing allergic reactions or making some vaccines ineffective in specific parts of the world.

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While the protective abilities of the immune system have long been tapped for the generation of vaccines, its potential to be directed toward the treatment of cancer and inflammatory disorders has been explored only relatively recently in the form of immunotherapy. But what methods are available to controllably and reproducibly modulate this system, which varies from person to person and is based on sex, age, and disease state? To address this need, immunoengineers apply principles of rational design, biomaterials science, nanoscale science, systems analysis, and numerous other engineering disciplines to better assess, control, and customize immune responses for safe and reproducible therapeutic applications.

A NEW FRONTIER FOR ENGINEERING: RATIONAL IMMUNOMODULATION

Immunoengineering is a relatively new field, but its concepts have always been a core component of biomaterials science. Materials development for biological implants and in vivo controlled delivery have historically focused on minimizing inflammation. Biomaterials are therefore usually optimized to inhibit the activation of inflammatory immune cell populations in tissues and biological fluids, to decrease toxicity, increase the therapeutic efficacy of delivered agents, and extend the lifetime of implanted devices.

Now, instead of a focus on preventing inflammation, advances in the development of nanoscale biomaterials (nanobiomaterials, NBMs[1]) permit the design of materials to directly elicit therapeutically beneficial responses from the immune system (Allen et al. 2016; Scott et al. 2017). The immune system interacts with NBMs based on a never-ending battle with viruses. Nanoscale lipid vesicles released by immune cells are essential components of cell–cell communication and signaling, and biomimicry of these nanostructures presents a pathway for probing, modulating, and monitoring immune responses.

With these developments theranostics—the combined delivery of *thera*peutic and diag*nostic* agents—has emerged as a vital tool for identifying and tracking immune cells that are modulated by delivered drugs and immunostimulants (Allen et al. 2018; Karabin et al. 2018). "Immunotheranostic" strategies are significantly enhancing the ability of engineers to reproducibly generate immune responses by monitoring which components are modulated at the organ and cellular level during immunotherapy and vaccination (Du et al. 2017, 2018).

[1] NBMS are broadly defined as any biomaterial with at least one external dimension that is less than 1,000 nm.

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PREVIOUS METHODS OF VACCINE DEVELOPMENT: TREATING THE IMMUNE SYSTEM AS A BLACK BOX

Vaccination is fundamentally the process of training the immune system to recognize and eliminate pathogens either prophylactically or therapeutically and can thus be considered one of the first forms of immunotherapy. Although it may seem obvious that immunology should be a key component of vaccine design, this has not always been the case.

Rational vaccine design requires an understanding of the immune system that has not yet been achieved, but the urgency to aid the sick and prevent the spread of infection has presented no alternative other than the use of trial-and-error methods. As a result, most immunization strategies were developed by treating the immune system as a black box. Antigens (molecular components of pathogens) and adjuvants ("danger signals" that stimulate inflammatory cells) are randomly combined in formulations that serve as the input into the system. The output from the black box is the (hopefully) lasting and protective immune response. With little understanding of the mechanism by which antigens and adjuvants achieve this output, formulations are selected that generate the safest and most effective prevention or removal of infection, with lasting immunological memory to respond quickly to future pathogen exposure.

But complex cell–cell interactions occur, and dozens of signaling molecules known as cytokines are released by inflammatory cells during an immunization. It is critical to know which cells contribute to these responses and whether the same cells can be reproducibly stimulated across different human populations. Importantly, different immune cells express different combinations of cytokines, often in amounts proportional to the extent of their exposure to the adjuvant, and this network of activated inflammatory cells and released cytokines forms an emergent system that can be tailored for specific therapeutic applications.

By employing targeted NBMs to control and monitor which immune cells are modulated during vaccination, theranostics provides a means to explore this black box to better correlate the input vaccine or immunomodulatory formulation with the output immune response.

ENGINEERING NANOBIOMATERIALS FOR TARGETED IMMUNOMODULATION

NBMs are key tools in immunoengineering and have attracted much attention for their ability to deliver therapeutics and imaging agents to specific cells and tissues (Allen et al. 2016; Scott et al. 2017). This versatility has demonstrated improved efficacy and deployment of vaccine formulations by providing triggered or bioresponsive mechanisms for controlled release, transporting combinations of bioactives with diverse solubility, and allowing control over reproducibility, speed, and cost of production (Scott et al. 2017).

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Among the range of available NBMs, self-assembled NBMs composed of synthetic amphiphilic polymers are especially advantageous for vaccination and immunotherapy because of their versatility in chemistry and structure (Allen et al. 2016). These traits allow better mimicry of viruses, which possess physicochemical and structural characteristics that dictate their interactions and processing by critical immune cells known as professional antigen presenting cells (APCs).

Professional APCs—which include dendritic cells, macrophages, and B cells—are the most frequent targets of immunomodulatory NBMs because of their potency for cytokine release and T cell activation. T cells are the effector cells of the immune system that can directly kill virus-infected or cancerous cells (cytotoxic T cells) as well as direct or enhance functions of other immune cells (helper T cells).

Using a military hierarchy as an analogy, T cells can be considered both soldiers and noncombat support troops while APCs are the generals that direct their action. NBMs function as a direct line of communication to the generals by alerting them of imminent danger (adjuvant) and identifying targets (antigen) for elimination. After internalization by APCs, NBMs are degraded in intracellular compartments that contain a variety of enzymes and redox mediators (Owens and Peppas 2006), allowing transported payloads to modulate APC function for the activation of T cells.

THERANOSTICS AS A TOOL TO IMPROVE VACCINE DESIGN AND REPRODUCIBILITY

Continued progress in theranostics will allow early detection of disease, prevent unintended side effects of drugs, decrease the frequency and amount of administered drugs, and allow quantitative assessment of the accuracy of drug delivery in individual patients. Immunotheranostic nanomedicine may thus revolutionize treatments for numerous inflammatory disorders, including cancer and heart disease, by providing powerful new approaches not only for therapeutic delivery and diagnosis but also for personalized medicine and clinically relevant assessment of therapeutic efficacy.

Using viruses, bacteria, and other pathogens as inspiration, biomimetic NBMs can be engineered with physiochemical properties selected to stimulate or suppress specific APC populations while marking them for detection and quantification via multiple diagnostic modalities. As an example, theranostic delivery of a drug regimen to reduce vascular inflammation in patients with cardiovascular disease could allow a clinician to monitor the patient's progress during treatment. Since not all patients will have the same response to anti-inflammatory drugs, the clinician could adjust the treatment as necessary by monitoring the levels of critical inflammatory cells in the patient's arteries. NBMs targeting dendritic cells may serve such a function, as the level of these APCs in vascular lesions directly correlates with the risk of rupture and vascular occlusion (Bobryshev 2010). There is currently no noninvasive method to detect

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such unstable lesions in patients, many of whom could suffer a heart attack or stroke without warning.

ENGINEERING NBMS FOR USE WITH DIAGNOSTIC IMAGING

NBMs can be engineered to be amenable to a variety of diagnostic methods depending on the specific need. Commonly employed imaging modalities include single-photon emission computed tomography (SPECT), positron emission tomography (PET), magnetic resonance imaging (MRI), and fluorescence/luminescence spectroscopy. MRI stands out for safety during repeated use, in contrast to techniques requiring high doses of radiation like SPECT and PET. PET has superior spatial resolution (4–5 mm) to SPECT (10–15 mm) and high sensitivity that can detect picomolar tracer concentrations. Although lower resolution than PET, MRI enhanced with contrast agents (e.g., gadolinium-conjugated NBMs and superparamagnetic iron oxide nanoparticles) can be used to characterize various features of targeted tissues.

While fluorescence is impractical for clinical applications because of poor tissue penetration, it enables unprecedented quantitative analysis of cellular targeting in animal models, where organs and cells can be extracted for analysis by flow cytometry. This immunotheranostic strategy significantly enhances the ability to reproducibly elicit immune responses by monitoring which components are modulated at the cellular level during the development of vaccines and immunotherapies (Dowling et al. 2017).

CONCLUSIONS AND FUTURE DIRECTIONS

Theranostic NBMs hold great promise for diagnostic imaging and controlled delivery of therapeutics during immunotherapy, providing a much-needed method for mapping and understanding the complex network of inflammatory cells that contribute to elicited immune responses.

The immediate future directions of theranostics will likely focus on two critical issues. First, APCs will nonspecifically remove NBMs from circulation regardless of surface-conjugated targeting moieties like antibodies and peptides, making selective APC targeting difficult to achieve. Avoiding uptake by off-target APC populations will require more advanced engineering of the nano/biointerface, such as precisely controlling the surface density and affinity of multiple targeting moieties (Nel et al. 2009), incorporating inhibitory signals like the CD47 ("don't eat me") peptide (Rodriguez et al. 2013), and optimizing NBM structure and size (Yi et al. 2016).

Second, the scalable self-assembly of monodisperse NBMs that mimic the complex nanoarchitectures of viruses remains a challenge. Current methods usually involve impractically complex polymers, low yield of the desired nanostructure, and difficulty with therapeutic loading, particularly dual loading of hydrophobic

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imaging agents and structurally sensitive water-soluble biologics. Recent advances in the commercially scalable technique of flash nanoprecipitation have demonstrated the scalable assembly of complex self-assembled NBMs from poly(ethylene glycol)-*bl*-poly(propylene sulfide) amphiphilic block copolymers (Allen et al. 2017). This method of impinging organic and aqueous phases in confined impingement jet mixers achieves highly reproducible and customizable nanoprecipitation conditions for the fabrication of polymersomes and bicontinuous nanospheres (Allen et al. 2018; Bobbala et al. 2018), which are unique NBMs capable of transporting lipophilic and water-soluble payloads simultaneously.

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Appendixes

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What It Is, Why We Want It, and How We're Trying to Get It
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Robert Hanson, Department of Homeland Security

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