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Engineering a Global Response to Infectious Diseases

This paper presents a more robust, adaptable, and scalable engineering infrastructure to improve the capability to respond to infectious diseases.

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ABSTRACT | Infectious diseases are a major cause of death and economic impact worldwide. A more robust, adaptable, and scalable infrastructure would improve the capability to respond to epidemics. Because engineers contribute to the design and implementation of infrastructure, there are opportunities for innovative solutions to infectious disease response within existing systems that have utility, and therefore resources, before a public health emergency. Examples of innovative leveraging of infrastructure, technologies to enhance existing disease management strategies, engineering approaches to accelerate the rate of discovery and application of scientific, clinical, and public health information, and ethical issues that need to be addressed for implementation are presented.

KEYWORDS | Bioinformatics; disease; epidemic; genomics; infectious; pathogen

I. INTRODUCTION

Powerful antibiotics and vaccines helped mitigate the threat from infectious diseases for several generations. In 1900, most human deaths were associated with infectious diseases like tuberculosis and influenza. As recently as 2000, the worldwide mortality associated with infectious diseases was 16.4 percent of deaths from all causes. In 2012, this had continued to decline to 11.5 percent. Unfortunately, this means there were still over 6 million deaths associated with infectious diseases [1]. A recent review examined antimicrobial resistance and predicted that by 2050, the impact would include a reduction of the world's potential gross domestic product by 2% to 3.5% and cause an additional 10 million premature deaths a year [2]. Although beyond the scope of this paper, it is worth noting that microorganisms have also been implicated as contributing to or causing many chronic diseases, including some forms of cancer, arthritis, and neurological disease [3].

It is tempting to approach the infectious disease challenge as doing battle with a pathogen enemy where brigades of combatant bacteria or viruses are held back or even defeated by increasingly sophisticated pharmaceutical weapons. There is certainly a place for improved pharmaceuticals; however, a sustainable approach will need to be much more sophisticated. Microbes and their hosts form a complex and dynamic ecosystem, and a long-term strategy for infectious disease control must take into account the fact that diseases can result from changes in the microbe, the host, or the environment. It is time to move beyond the simple war metaphor [4].

To compound the challenge, microbes are notoriously fast in adapting to new environments. This can include bacteria developing antibiotic resistance or acquiring metabolic traits that allow them to thrive in a new environmental niche, and viruses evolving to reduce the effectiveness of antivirals and vaccines. In addition to the evolution of existing pathogens, like the seasonal influenza virus, there are emerging pathogens that are often the result of changing or encroachment upon new ecosystems and the "leap" from a conventional host to a new host species. An example from recent headlines is the Middle East Respiratory Syndrome Coronavirus. MERS-CoV appears to have reached

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humans by direct contact and potentially airborne transmission through animal hosts including camels [5]. The MERS-CoV is related to the coronavirus that caused severe acute respiratory syndrome (SARS). The SARS outbreak began in 2002 and likely spread to humans via bats [6]. Although the viruses are similar, this does not guarantee that utilization of the same medical and public health intervention techniques will be effective. There are many examples of emerging infectious disease outbreaks, including the on-going HIV/AIDS pandemic that has already caused 35 million deaths [7]. Each pathogen involved in an infectious disease outbreak provides an opportunity to identify what scientific data are needed to support effective interventions.

Quoted in the *Global Health Security Agenda* [8], U.S. President Obama said in 2011 "... we must come together to prevent, and detect, and fight every kind of biological danger—whether it's a pandemic like H1N1, or a terrorist threat, or a treatable disease." The *Agenda* complements and supports existing International Health Regulations of the World Health Organization [9], U.S. public health [10], [11], and biodefense objectives [12]–[14]. The framework for data requirements and response priorities used in this paper integrates across these initiatives and regulations. Specifically, in order to manage infectious diseases, capabilities are required for: preparedness, detection, characterization, response, and support for the return to normal, see Fig. 1. This framework is analogous to homeostasis in living organisms. These capabilities are relevant for addressing health interests from the global to the individual organism, e.g., human, animal, plant, or bacterium. The global perspective is studied and implemented by public health, ecological, industrial, and other communities with the principal foci of public benefit, humanitarian needs, scaling, and statistical measures. For an individual human, the perspectives are from medical, economic, relationship, and other personal priorities with the foci of individual health, quality of life, and gaining access to effective care. Integrating frameworks are needed to support optimization of technical, economic, medical, and ethical components of this complex system.

Infectious diseases are a major cause of death and economic impact worldwide. A more robust, adaptable and scalable infrastructure would improve the capability to respond to epidemics. Because engineers contribute to the design and implementation of infrastructure, there are opportunities for innovative solutions to infectious disease response within existing systems that have utility, and therefore resources, before a public health emergency. Examples of innovative leveraging of engineered infrastructure are provided throughout the paper. The next section of this paper discusses opportunities for technology to improve on current approaches to infectious disease management and the following section discusses engineering challenges to accelerate the application of science to infectious disease planning and response at the global scale. I conclude with a brief discussion of the importance and opportunity for engineers to address the ethical issues needed to leverage traditional infrastructure for infectious disease response and help nurture a global culture of responsibility in both healthcare and technical applications.

Fig. 1. ***Infectious disease management for individuals and public health have parallels shown in the inner and outer rings, respectively. Because traditional diagnostics and treatments have long lead development, regulatory approval, and manufacturing lead times, it is challenging to provide timely and effective interventions at a public health scale for an outbreak caused by an emerging or novel pathogen. Approaches to achieving robust, economically viable scaling include improved leveraging of existing infrastructure, establishment of an integrating framework like the Digital Immune System for optimization, and spiral development processes similar to homeostasis.***

II. TECHNOLOGIES TO IMPROVE EXISTING APPROACHES

Leveraging their significant investment in planning and response experience, I adopted from the U.S. pandemic influenza plan [10, p. G-58], infectious disease management goals to provide:

- public health policy-makers with data to guide response, and
- clinicians with scientific data to justify recommended treatments, vaccines, or other interventions.

I have integrated priorities from the influenza plan with a more pathogen-centric approach from the food industry [15] in Table 1 to provide descriptions of priority data to support infectious disease outbreak response.

TABLE 1 Data That Support Managing Human, Animal, and Plant Infectious Diseases Have Been Identified in Planning Scenarios and From Experience in Responding to Natural and Anthropogenic Outbreaks

Data	Purpose
Agent Detection	▪ Identify the source or reservoirs including other hosts ▪ Estimate the amount of agent ▪ Support epidemiology ▪ Support diagnosis ▪ Estimate exposure ▪ Identify the natural evolution of the pathogen, e.g., seasonal, present asymptomatically in different hosts ▪ Estimate global distribution and occurrence
Agent Characterization	▪ Type of agent, e.g., Gram positive bacterium ▪ Strain ▪ Environmental stability on surfaces and airborne
Hazard Characterization	▪ Susceptibility for potential hosts including infection and transmission ▪ Adverse health effects including virulence, pathogenicity ▪ Effect of medical countermeasures on pathogenesis and transmission ▪ Effect of infection controls, e.g., bleach, social distancing

These data can be provided with currently available technologies. However, there are several recurring issues that inhibit global utilization. The issues that can be addressed, even if only partially, by technology are discussed. The key recurring issue is availability. Limited availability is driven by many factors including cost, appropriate sharing of data and materials, and timely manufacture and distribution.

On a more basic level, one of the key factors in sustainable preparedness is infrastructure, and availability is a challenge here as well. Malnutrition due to starvation, unsafe water, and insufficient sanitation all impact infectious disease mortality. In 2004, over half of the deaths of children under five years old were associated with infectious diseases and the significant contributing factor for many of these deaths was under nutrition [16]. Building the infrastructure to eliminate these hazards has historically been the domain of civil and agricultural engineers. Electrical and computer engineers are now providing valuable low-cost information linkages across systems so that weather satellite data can be utilized to help increase local crop yields and prepare water treatment and sanitation plants for adverse weather. The computational algorithms and information networks can be applied worldwide for irrigation and weather prediction for storm and drought management [17].

Remote sensing has been utilized to indirectly detect *Vibrio cholera* [18] and predict a Rift Valley fever (RVF) outbreak [19]. In both of these examples, the disease and environmental biology were shown to correlate with changes that could be measured by air and space borne sensors. For *V. cholerae*, sea-surface temperature and sea height were linked to the inland incursion of water with commensal plankton. Satellite measurements of sea-surface temperature, rainfall, and vegetation changes were used to predict the areas where outbreaks of RVF in humans and animals occurred in Africa. The techniques and data used for RVF may be more broadly applicable to other vector-borne diseases.

In regions with limited infrastructure, it is often difficult or impossible to provide the refrigeration required to maintain the "cold chain" for life-saving vaccines and other medicines. An inspirational consortium of industry, churches, and nonprofits in Zimbabwe, Africa, leveraged the reliable power requirements of cellphone towers to help address the refrigeration storage needs for many vaccines [20]. The initiative has included innovative contributions by wireless providers, refrigerator manufacturers, and others in order to help provide immunizations against polio, measles, and diphtheria.

Another area in which technology is poised to impact infectious disease management is in gaining timely situational awareness of outbreaks. Global and regional travel often make this a difficult task, and data collection and sharing for epidemiologists, care providers, patients, and the public is also limited by other factors such as privacy concerns for individual patients' medical data, governmental goals to protect tourism and other local-to-national interests, the lack of recognized standards for sharing protected data, and an accepted international norm for transfer of public and commercial material during and in response to an infectious disease. Improved network, encryption and access information technologies are also necessary to support managed care organizations and telemedicine applications. A global system addressing these issues and capable of operating on time scales relevant to controlling an epidemic is needed.

A comparison of five outbreak detection algorithms was conducted using a surveillance case study of the seasonal Ross River virus disease [21]. Challenges were identified for making quantitative comparisons of the algorithms as well as in evaluating the performance of each algorithm. A network model has been proposed that has the potential to address algorithm shortcomings for outbreak localization and performance under changing baselines [22]. This is accomplished through modeling the relationships among different data streams rather than only the time series of one data stream compared to its historical baseline. Using measured and simulated data, this approach showed promise for addressing shifts in health data that occur due to special events, worried well, and other population shifts that happen during significant events like pandemics. Another study compared 101 animal and public health surveillance systems, finding challenges due to a limited number of common attributes, unclear surveillance objectives of the design, no common

standard, and insufficient economic data [23]. Privacy issues pose challenges that are difficult to address with technology, but they have been addressed in some applications through voluntary enrollment. For example, the geographic location capability in many cell phones allows applications to push public health and animal disease outbreak information to users based on location. The U.S. Centers for Disease Control and Prevention (CDC) has the FluView application that provides geographic information on influenza-like illness activity [24]. Obviously, the pervasiveness of cell phones improves timely reporting from the field for both the public and the public health profession. Moving forward, addressing privacy issues will be critical so that geographic tracking of a phone's location could be used to help inform an individual of potential contact with infected persons or animals and support automated, anonymous, electronic integration of those data to accelerate the epidemiological detective work of identifying and surveying those same individuals for public health benefit.

Electronic health information systems have made significant progress. However, even as recently as 2014, it was noted: "Despite progress in establishing standards and services to support health information exchange and interoperability, practice patterns have not changed to the point that health care providers share patient health information electronically across organizational, vendor, and geographic boundaries. Electronic health information is not yet sufficiently standardized to allow seamless interoperability" [25]. The U.S. has taken a risk-based approach to health information technology (IT) regulation [26]. Safety in health IT has been recognized as part of a larger system that needs to consider not just specific software, but how it interacts with the IT system and how it will be used by clinicians [27]. Continued development of quality management, human factors, and other standards to support usability and regulatory review are needed.

As the large-scale systems that require computer algorithms to scan and integrate data into summary reports continue to progress, significant benefit is being derived from systems with fairly simple technology. In 1994, ProMED was started as the first e-mail reporting system with curation. It has grown to over 30,000 subscribers in over 150 countries and has roles in outbreak detection including SARS in 2003 [28]. There are many health alert networks (HAN) that utilize websites and electronic communications [29], [30]. A study in New York City showed that most physicians (82%) received Health Department communications, but less than half of those (37%) received the information through the HAN [31]. An important trend is that 47% prefer e-mail distribution of communications and this preference trends with younger respondents.

Looking to the future, achieving the benefits of distributed diagnostics and electronic reporting will depend on both technical and clinical integration. This would improve individual care as well as reduce or eliminate separate data entry and reporting for public health surveillance. In order to realize the benefits of personalized medicine with treatment customized to the individual, the costs, scalability, and compatibility across all data sources must be addressed. Personalized infectious disease medicine might include customization of antimicrobials to an individual patient to improve care and help reduce overuse and misuse of antibiotics. Similarly at the global health scale, timely identification of appropriate virus strains coupled with rapid manufacturing for seasonal influenza vaccination would reduce the disease burden of thousands. In personalized and global applications, the approaches will need to move from diagnostics, characterizations, and interventions aimed at a single specific disease causing pathogen to robust methods that can be adapted for safe and effective use in a timely manner for broad classes of disease. Fully realizing these goals will require improved scientific understanding and new engineering and computational approaches.

III. ENGINEERING TO ACCELERATE R&D AND IMPROVE CARE OF THE FUTURE

There are significant challenges in utilizing traditional engineering approaches in the life sciences. Living organisms are complex by most machine standards. Individual organisms are also typically influenced by peer organisms forming a community, by other living organisms that may be beneficial, neutral or detrimental, and by the environment. There are opportunities for engineers to develop improved measurement, analysis, and model systems to better characterize, predict and manage infectious diseases. Given the complexity of these interacting systems, there are significant challenges to the reductionist approaches familiar to design-based engineering. Fortunately, as the history of vaccination demonstrates, a comprehensive knowledge of the biology is not always required in order to provide healthcare benefits.

With the advent of deoxyribonucleic acid (DNA) sequencing and the efficient detection and laboratory replication of DNA through polymerase chain reaction (PCR) amplification, there are opportunities to organize scientific and medical data using DNA-based indices. The field that has grown up around these technologies, genomics, is an excellent example of how engineering can enable profound advances in biological research. A significant contributor to the organizing principles and demonstrator of this DNA-based approach, Carl Woese, summarized in 2000 the impact as providing "a new and powerful perspective, an image that unifies all life through its shared histories and common origin, at the same time emphasizing life's incredible diversity and the overwhelming importance of the microbial world," [32]. Here, I build on this insight as well as our previous assessment in 2000 of the engineering contributions and opportunities related to DNA sequence

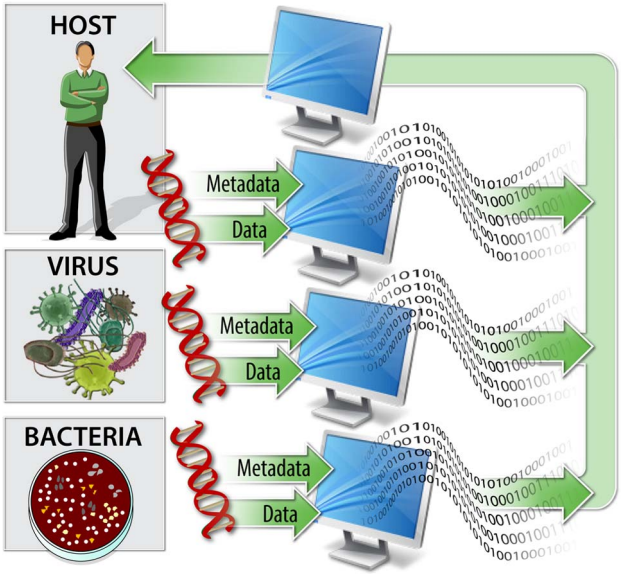

Fig. 2. ***Instrumentation advances have allowed monoculture and complex samples to be converted to nucleic acid sequence data that are easily represented in a digital computer. These data can be used as a framework or index for health and disease related metadata supporting correlative studies across species and providing insight into infectious diseases. Because genetic material is traded among organisms and is often part of complex nonlinear networks within an organism and beyond, increased collection and interpretation of the associations across DNA sequence and metadata are needed. A digital immune system for individuals and populations is envisioned that identifies causation and intervention options to support patient-specific and public health interventions.***

data that describe an organism's genome, transcriptome and proteome [33]. As depicted in Fig. 2, nucleic acid sequence provides a common framework to organize data related to infectious diseases.

Today's DNA sequencing instruments can produce terabases of data in a few days with per-base costs a million-fold lower than a decade ago. Recent studies have demonstrated the power of personalized approaches to major human diseases like cancer. It appears likely that the next few years will bring the personalized human genome and the miniaturized sequencing instrument, each for less than one thousand dollars. Now is the time to innovate and apply the engineering approaches needed to utilize these and other data.

DNA sequencing and the associated bioinformatics tools for analysis provide a powerful methods-based approach to monitoring living systems. DNA and ribonucleic acid (RNA) provide data that help characterize an individual's health status as well as the status of the surrounding environment. Because sequencing converts biological information to digital data, computer networks, data management, integrity, scaling, analysis, privacy, and affordability are keys to expanding access. The "digital immune system" is a powerful concept that generalizes the method to population dynamics and public health [34]. Basing the system on DNA allows correlation techniques to identify patterns in the sequence data—recurring and deviate patterns. These patterns can be indicative of healthy or pathologic host status as well as the absence or presence of pathogens in clinical and environmental samples. The growth of sequence databases with appropriate clinical and environmental metadata will improve the potential quality of the analyses and the impact on individual and public health. Growing databases will also need to address the scaling and privacy issues. One of the most powerful features of the digital immune system approach is the potential to detect a novel pathogen, i.e., one that is not already in the database. The flexibility inherent in this method-based approach is a huge strength and distinguishes it from many of the traditional methods which are not able to detect or characterize a new or emerging pathogen.

Seasonal influenza provides an example of a system of method-based opportunities. The influenza virus changes genetically as it uses an error-prone enzyme to replicate its genome, and mutates further as it migrates from host-to-host, across species—e.g., waterfowl to humans, and across ecosystems of the environment. This mutation process gives rise to a different population of viruses in circulation each year, and poses a challenge to vaccine manufacturers, as one year's vaccine will typically have little value when confronted with the next year's viral strains. Each year's vaccine is constructed specifically to protect against the strains that are projected to be dominant in the upcoming flu season. The current process uses egg-based techniques for manufacturing influenza vaccine and has been successfully utilized for decades as have the techniques for isolating and identifying emerging strains of the virus. Unfortunately, the combined pipeline is relatively slow and does not typically allow for vaccine manufacturing to be based on strains that have been detected at the start of the flu season—vaccine production must be started earlier, and so relies heavily on imperfect predictions as to which strains of influenza will dominate.

RNA sequence data provide a method-based framework for managing influenza response at the global scale. In addition to the detection and identification of the virus, sequence data can be utilized to compare and predict the performance of egg and other manufacturing approaches. As the sequence, clinical, animal, and environmental data are accumulated, there is also the potential to support computational safety and efficacy screening. Shortening the current timeline from detection through vaccination would have significant positive health benefits. There are method-based approaches to vaccine manufacturing with significant potential to improve upon the egg-based approach. Even though the influenza virus has only eight genes and an ominous history of multimillion death pandemics, the scientific understanding is not yet sufficient to avoid the thousands of deaths annually from seasonal influenza nor to mitigate the potential from a pandemic strain.

Fig. 3. *Engineering, process, and other controls allow important infectious disease experiments to be conducted safely. Representative Biosafety Level (BSL) labs are shown. BSL-1 is for agents not known to cause disease in normal, healthy humans. BSL-2 is for moderate-risk agents that may cause disease of varying severity through ingestion or percutaneous or mucous membrane exposure. BSL-3 is for agents with a known potential for aerosol transmission and that may cause serious and potentially lethal infections. BSL-4 is for agents that pose a high individual risk of life-threatening disease resulting from exposure to infectious aerosols, or for agents where the risk of aerosol transmission is unknown. Agents appropriate for this level have no vaccine available, and infection resulting from exposure has no treatment other than supportive care.*

Biocontainment laboratories are needed to safely conduct the research needed to understand pathogens as well as analyze clinical samples. Characterization of existing pathogens increases understanding of current diseases and also helps to prepare for emerging diseases. Laboratories that work with infectious agents are categorized by biosafety level (BSL) ranging from a basic biomedical laboratory (BSL-1) to BSL-4 laboratories (Fig. 3) that can safely handle untreatable disease agents [35]. The engineering systems for automatically controlling airflow and other facility safety components are critical for supporting clinical and research laboratories. Infectious disease research is benefiting from "omic" methods for characterizing proteins (proteomics), metabolites (metabolomics), messenger RNA (transcriptomics), etc. In order to safely produce genomic data more quickly, DNA sequencing instruments have been moved into our biocontainment laboratories. These methods produce large volumes of data, requiring research and clinical labs to have access to traditional engineering disciplines in data management and analysis.

Data management is not the only challenge. So far, our descriptions have implied a single host interacting with a single invading pathogen—the war metaphor. It is not that the metaphor does not work in many cases. For instance, the eradication of smallpox was accomplished through an aggressive worldwide campaign as was the animal and livestock disease rinderpest [36]. It is that the war metaphor is an oversimplification with an often unrealizable aspiration for victory. Consider that most hosts, including bacteria, have associated pathogens and symbiotic microbes.

For example, a tropical grass, fungus, and virus have been found to have a three-way symbiosis that confers heat tolerance [37]. When the virus is removed from the fungus, thermal tolerance is lost by the grass. If the virus is reintroduced to the fungus, thermal tolerance is conferred to the grass. Viruses can also integrate their genes into animal genomes as part of the animal's nuclear DNA affecting inherited traits [38]. Virus infection is one of several naturally occurring changes in the nucleic acid of a genome. Even simple nucleic acid transfers among different biological entities often have difficult to predict results. The complexity compounds as the number of entities increases and community behaviors emerge.

For each of the approximately one trillion human cells in our bodies, there are about ten microbes. The microbes are distributed in different, highly specialized, communities in the gut, mouth, skin, etc. collectively referred to as the microbiota [39], [40]. Given a global population over 7 billion, there are approximately 10^{23} cells/microbes associated with people on the planet. For comparison, it has

Fig. 4. *The global ecosystem is a highly interconnected network of hosts and environments each with its own associated microbiome. Nucleic acids, chemicals, and energy are shared within each environment as well as across the global network. New approaches are needed to visualize and understand the relationships among these environments to improve infectious disease management.*

been estimated that there are 10^{27} cells of *Prochlorococcus* bacteria in the ocean [41]. Equally impressive, there are 10^{30} viruses in the ocean causing roughly 10^{23} viral infections every second [42]. As represented in Fig. 4, whether, grass, animals, or humans, the microbes, the communities, and their host community are sharing chemicals, energy, and nucleic acids.

It is no surprise that clinical, animal, environmental, and other samples often have significant genetic complexity. Information visualization tools like Krona (Fig. 5), support analysis of complex metagenomic data [43]. These types of data can be used to support many applications including investigating food borne disease outbreaks [44]. Genomics helped explain the initiation of the Ebola outbreak in Sierra Leone in 2014 [45]. Genomes from 99 virus samples from 78 patients provided evidence that the index case and associated thirteen initial cases in Sierra Leone had attended the funeral of a traditional healer that had been seeing Ebola patients from nearby Guinea. The sequence data also showed mutations in parts of the genome that might impact diagnostics, vaccines and therapies. Even though the West Africa Ebola virus disease (EVD) epidemic is by far the largest to date, fortunately "the clinical course of infection and the transmissibility of the virus are similar to those in previous EVD outbreaks" [46]. The goal is to be able to make these clinically relevant assessments from the virus genome prospectively—i.e., before the epidemic provides the observations.

Computational algorithms and tools are available to find signatures of existing pathogens as well as recognize patterns that help identify previously unidentified pathogens. Moving forward, computational models for the interactions among the different genes are needed that provide a context for the correlations in data as well as improve predictive capabilities. For instance, going beyond detecting disease outbreaks to being able to assess and predict disease risks is desired. These much more complicated models offer the potential to accelerate disease understanding and the development and safe utilization of medical interventions at both the individual and the global scales. There are multiple initiatives underway that will lay the foundation and strengthen the underlying science. The foundation will enable new engineering approaches that will achieve the greater goals for infectious disease management.

Using an approach that parallels the evolution of electrical circuit design and fabrication, the BioBricks approach is having increasing impact [47]. Perhaps most famous for its student genetic engineering competition

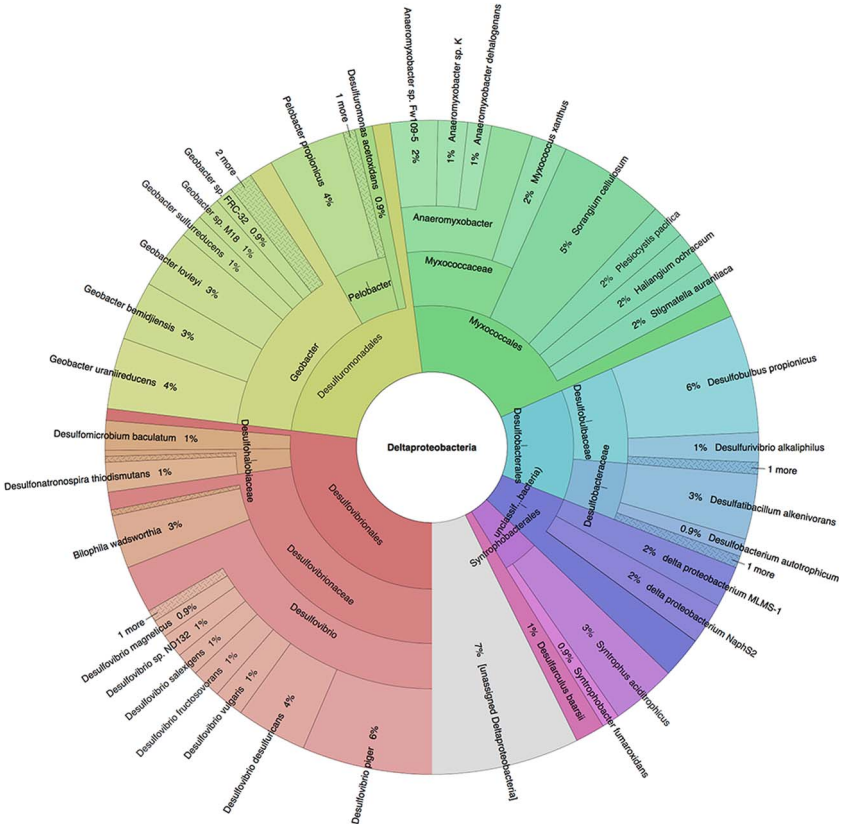

Fig. 5. ***Computational tools are needed to analyze large volumes of complex data that often includes metadata. The output of the Krona tool for visualizing metagenomic data has intuitively displayed estimates of relative abundance.***

iGEM [48], the BioBricks approach of utilizing a library of well-characterized, interconnectable parts is powerful. Just as early circuit designers benefited from standards for circuit fabrication, design, interfaces and modules, aspects of biology are amenable to these approaches. Not only does the approach provide validation of reductionist concepts of each "brick," but the innovative integration of parts also contributes to the characterization and future sharing of more complicated parts. Just as circuit designers can incorporate existing designs or entire functional units like memory or analog to digital conversion, biologists are increasingly able to import others' designs and achieve significantly more functionality. For instance, a rewritable digital memory system has been demonstrated that writes and rewrites nucleic acid bases in a chromosome [49]. Just as DNA sequencing brought a methods-based structure to pathogen detection, approaches like BioBricks bring structure to biological circuits. The electronic circuit analogy continues with the opportunity for software to facilitate design and accelerate testing and evaluation. Just as in our early example for influenza vaccine development, the components of the BioBricks approach are amenable to spiral engineering for both performance and cost.

Building computer architectures and software that can implement *ab initio* test and evaluation calculations for infectious disease trials would require significant advances in algorithms, capabilities, and fundamental biochemical data. While exciting progress is being made in these areas, an alternative approach is to consider the network of interactions among fundamental building blocks and identify correlations with disease and health. This is the domain of systems biology and the building blocks can include DNA, RNA, and peptides.

Progress in systems biology is often paced by access to appropriately curated and calibrated data—not just the underlying nucleic acid content but the associated metadata that describe the host and the relevant associated microbial communities. One of the multiple approaches to address data needed is the Hundred Person Wellness Project of the Institute for Systems Biology. This project is measuring multiple indicators of health over a nine month period and will include lifestyle coaching as part of the study [50]. If successful, the project already has plans to scale to a thousand and then 100 thousand participants. There are similar concepts underway at organizations as diverse as Google X and Human Longevity. Even though these studies do not focus on infectious diseases, they are of significant value in helping to define the baselines for "normal" at different ages, genders, and many other variations that may affect health.

IV. OPPORTUNITIES

Infectious disease is a global issue that remains a significant cause of death and economic impact. Engineers and engineering have many opportunities to help mitigate these diseases ranging from using cell tower power to help deliver vaccines to providing new network analysis software to identify novel viruses in an outbreak.

The joint evolution of engineering and life sciences brings expanded availability and opportunity to understand and design living systems. These are attributes that will be needed to address the medical and infrastructure needs for effective global infectious disease management. However, the zeal to innovate needs to be mediated by a culture of responsibility [51] where the benefits and the risks are considered. The IEEE Code of Conduct [52] is consistent with this ethos and addresses quality of life and privacy topics that have been discussed in this paper. Engineers have an opportunity to provide innovative application of existing infrastructure to infectious disease management and to help nurture a global culture of responsibility in both healthcare and technical applications. ■

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