



NSF Engineering Research
Visioning Alliance

Engineering Opportunities to Combat Antimicrobial Resistance

Executive Summary



Antimicrobial test. Source: Canva



Executive Summary

Microbial infections that were once easy to treat are now less responsive to treatment and sometimes impossible to cure. Some microbes, including bacteria and fungi, harbor the ability to circumvent current treatments through a phenomenon known as antimicrobial resistance (AMR), which may result in poor clinical outcomes. The World Health Organization has defined AMR as a critical global health threat, with deaths associated with AMR-related infections surpassing those caused by cancer. Unfortunately, there is a dearth of effective treatment and prevention options. The slow pace of development of novel antibiotics in the pharmaceutical sector, in addition to a lack of antibiotic stewardship, preventative measures, and engineering innovation, create a space for future AMR development. Thus, there is an urgent need to identify and implement novel solutions that treat AMR-related infections and prevent the future development and spread of AMR.

AMR is a multidisciplinary problem that requires interdisciplinary solutions. To develop effective treatments and preventative measures, fundamental concepts within biology, chemistry, physics, and engineering must be combined in a translatable manner. Engineering can function as the key to bridging the gap between fundamental principles and successful implementation into tangible and scalable treatments and tools that both patients and clinicians can use.

At the Feb. 6-7, 2024 visioning event convened by the Engineering Research Visioning Alliance (ERVA), it was the goal of 55 researchers, industry leaders, and policymakers representing a broad range of expertise to create a roadmap of innovative, less-explored lines of multidisciplinary engineering research that can transform efforts to mitigate AMR. During the two-day event, participants actively discussed grand challenges and identified engineering research priorities spanning improved diagnostics, alternative therapeutics and therapeutic delivery systems, drug-free treatment approaches, prevention, and advanced modeling as key components needed to address drug-resistant infections and prevent AMR spread across communities. Specifically, five key areas for engineering research investment were identified. These research areas are listed below, along with key research priorities identified during vigorous discussion.

Grand Challenges

01

Diagnostic Biosensors and Wearables

- Develop new biosensors with improved sensitivity and broad-spectrum detection capabilities.
- Design biosensors to sample biomarkers from a variety of patient specimens, ideally those that are non-invasively collected and/or at low volumes.
- Design biosensors with enhanced chemical stability for improved shelf-life.
- Integrate diagnostic technology into wearable devices for rapid detection of infections in clinical and non-clinical settings

02

Engineered Antimicrobial Surfaces

- Develop antimicrobial surfaces that prevent bacterial and fungal attachment and/or effectively eradicate bacteria and fungi upon contact that are compatible with existing medical devices and high-touch surfaces.
- Explore different surface functionalization strategies (e.g., nanostructures, coatings, chemistries) to ensure the stability of antimicrobial surfaces following exposure to sanitation protocols.
- Incorporate diagnostic/sensing materials into antimicrobial surfaces to improve preventative measures and reduce the spread of AMR.

03

Smart Biomaterials

- Develop smart delivery systems using materials that locally release encapsulated antimicrobials following exposure to bacterial infections.
- Develop and design immunomodulatory materials as novel drug-free therapeutics that can stimulate the host immune response to combat infection.

04

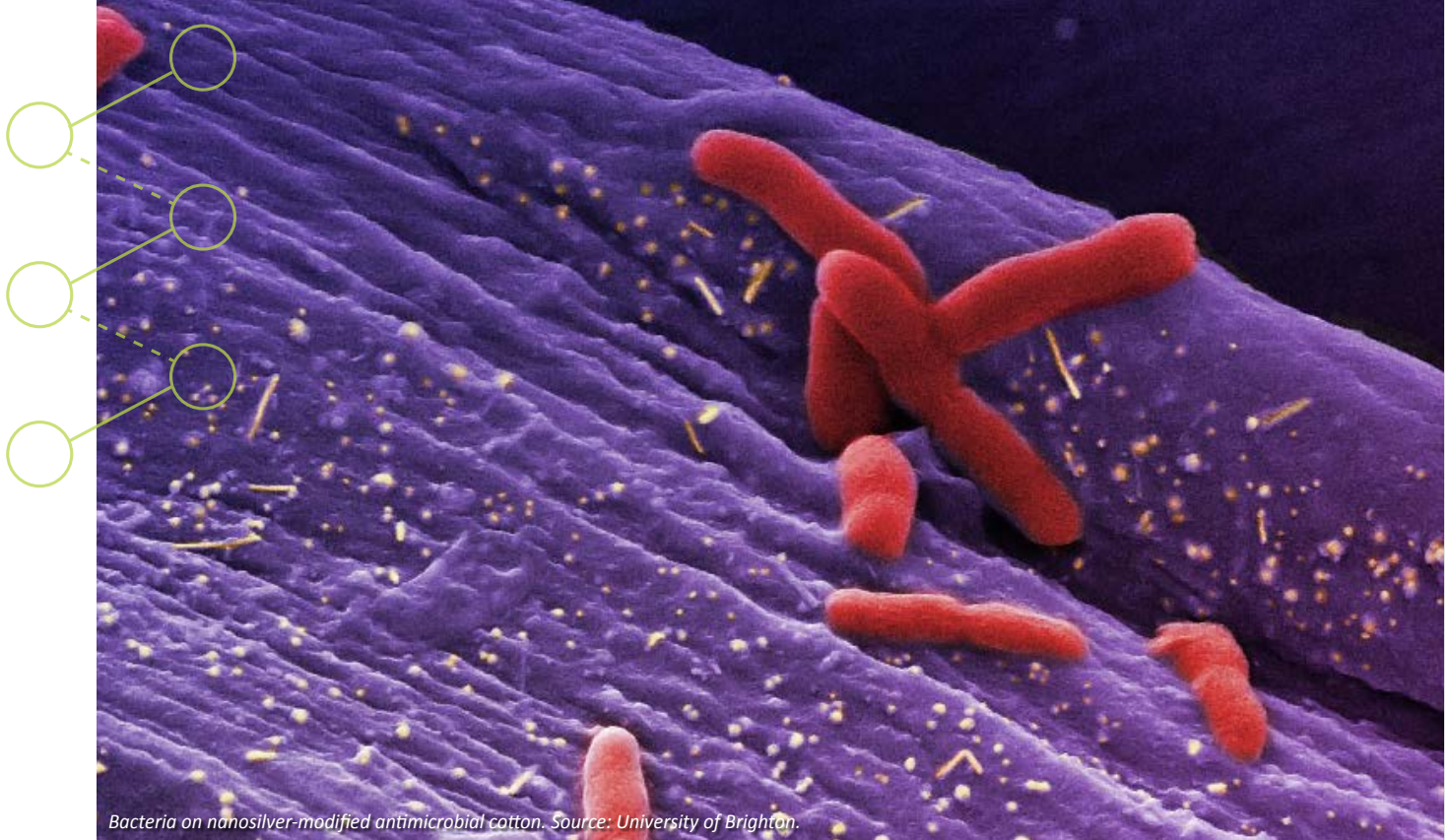
Cell Engineering for Drug-Free Approaches

- Engineer different immune cells to appropriately respond to and treat AMR-related infections.
- Engineer commensal microbial cells to prevent the development of infections originating from within the microbiome and prevent the spread of AMR-related genes within endogenous bacterial communities.
- Investigate ideal administration of engineered immune and microbial cells to ensure viability and therapeutic efficacy.

05

Advanced Modeling Approaches

- Develop *ex vivo* “body-on-a-chip” models that accurately recapitulate complex infection sites or organs to study the response and efficacy of novel therapeutics.
- Design and investigate the efficacy of novel therapeutics that are effective against drug-resistant bacteria utilizing computational and artificial intelligence (AI)-based tools.



Bacteria on nanosilver-modified antimicrobial cotton. Source: University of Brighton.

Taking Action

AMR challenges the clinical treatment of infections daily, and the development of resistance has only been accelerated by inappropriate use of and exposure to antibiotics. Significant improvements are imperative to reduce infections and deaths associated with AMR. Engineering-directed research and technologies are needed to bridge the gap between patient needs and clinical translation. The priorities discussed in this report describe the innovative research needed to prevent or halt the progression of AMR and its consequences in the lives of patients. Engineering research enabling new preventive and therapeutic approaches and modeling can significantly contribute to addressing this global challenge.

Preventative Measures

Preventing the future development of AMR and the spread of AMR-related infections is essential. Several engineering approaches can be adopted to enable preventative measures in the clinic and in our daily lives at home. Diagnostic biosensors could provide accurate information to health care providers while allowing the required treatments to be administered promptly. These biosensors should be designed to diagnose any bacterial pathogen while maintaining sensitivity, stability, and the ability to be integrated into wearable technologies. Novel antimicrobial surfaces can be developed to control the spread of infections for multiple applications. Work on nanostructured surfaces has already shown that it is possible to engineer the shape and size of nanostructures to eradicate specific pathogens. Significant work remains to understand the causal relationship between specific bacteria and the shape and size of repeating structures on surfaces. Beyond identifying effective tailored nanostructures, it is imperative to develop manufacturing technologies that can be scaled to produce large surfaces. While the semiconductor industry has mastered the art and science of creating nanostructures on silicon substrates, it cannot be translated to manufacture large surfaces with such structures. Traditional lithography techniques used today will be far too expensive to create large surfaces with the desired patterns. Other mechanical approaches like nanoimprinting that are insufficiently accurate for the semiconductor industry will work well for low-cost applications. However, challenges related to surface stability will require significant research to overcome as well as investigation into manufacturing requirements.

Novel Therapeutic Approaches

Engineering research is required to develop novel antimicrobial therapeutics and therapeutic delivery systems for controlled release of drugs. Necessary research ranges from drug-free cellular engineering approaches to smart antimicrobial delivery systems. Research into synthetic biology approaches utilizing immune and host-microbial cells is required to successfully integrate these cells within the body without adverse reactions. Smart drug delivery systems must be designed to ensure on-demand, tailored drug delivery under the desired (and often complex) conditions. These delivery systems should prevent inappropriate release of therapeutics to minimize development of AMR. Researchers and engineers must ensure the stability and viability of cell-based therapeutics and encapsulated agents within smart delivery systems. These novel approaches must also be designed as effective therapeutics against pathogenic bacteria without compromising the health of the commensal microbes, the microorganisms that reside on or within the human body normally without harming human health. Importantly, commensal microbiota frequently confers beneficial functionality to the human host.

Modeling Advancements

Research involving both *ex vivo* and computational modeling can generate powerful tools that provide accurate information rapidly without the need for long and expensive experiments. Specifically, *ex vivo* approaches can assist in developing complex models of bacterial and fungal infections containing commensal microbes and components of healthy tissues. Computational modeling abrogates the need for physical materials, allowing for complex system design without the challenges accompanying *in vitro* and *ex vivo* models. These models can be utilized as predictive measures following certain therapeutic approaches or to develop novel antimicrobial therapeutics that are effective against resistant microbes. Integration of AI-based approaches could also significantly improve the development of computational models and improve the design of future therapeutics with enhanced accuracy and speed.

The ideation and directed breakout sessions developed by the Thematic Task Force promoted open discussion, leading to identification of key research areas where engineering can pave the way for progress. The grand challenges discussed throughout this report can be utilized to develop novel antimicrobial therapeutics as well as preventative measures to limit future development and spread of AMR.

This report underscores the urgent need for new approaches to combat AMR and AMR-related infections while identifying specific directions for engineering researchers and funding bodies to pursue that have the potential to significantly address this global health threat.



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Our mission is to identify and develop bold and transformative new engineering research directions and to catalyze the engineering community's pursuit of innovative, high-impact research that benefits society.



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