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The background of the poster is a collage of four microscopic images, each in a different color and separated by white diagonal lines. The top image is red and shows large, rounded bacterial cells. The second image is purple and shows elongated, rod-shaped bacteria. The third image is green and shows spherical bacteria. The bottom image is yellow and shows a complex, textured biofilm structure.

The 7th Stevens Conference on Bacteria-Material Interactions

June 11 and 12, 2025



Dept of Chemical Engineering and Materials Science

1 Castle Point Terrace
Hoboken, NJ 07030
stevens.edu

Dear Colleagues:

The Stevens Conference on Bacteria-Material Interactions has run on the odd years since 2011 with a gap in 2021 because of the pandemic, and it is my pleasure to welcome you to the 7th Stevens Conference, which, like its six predecessors, focuses on infection associated with tissue-contacting biomedical devices. This highly resistant form of infection continues to be a significant and almost entirely unresolved clinical problem.

The 7th Stevens Conference addresses the themes of the clinical and patient perspectives of the device-infection problem, how device infection can be prevented from occurring, how it can be detected and how it can be cured if it occurs, how novel technologies can be translated from ideation to clinical use, and how the treatment of device-associated infection is affected by disparities across the healthcare system.

Convergence continues to be a prominent element needed to advance solutions, because solutions require expertise from a very wide range of very different disciplines. Among them are engineering, basic physical science, microbiology and biofilm science, immunology, clinical practice, patient needs, regulatory science, and public policy. An objective of the 7th Stevens Conference is thus to provide a convergence point where expertise from all of these disciplines can find common ground to conceive of and advance solutions more quickly and more effectively going forward.

Thank you for participating in and adding to this important event.

Sincerely yours,

Matthew R. Libera
Professor
mlibera@stevens.edu
Conference Chair

Agenda

Wednesday, 11 June, 2025

Time		Title	Presenter	Affiliation
8:00 - 9:00		Registration and light breakfast		
9:00 - 9:10		Welcome and Conference Overview	Matt Libera	Stevens Institute of Technology
Session 1		Clinical & Patient Perspectives <i>Moderator: Matt Libera, Stevens Institute of Technology</i>		
9:10 - 9:45	1	<i>The pathology of device-associated infection in plastic and reconstructive surgery</i>	Peter Taub, MD	Mt. Sinai Health System
9:45 - 10:20	2	<i>Case studies of infection associated with soft-tissue reconstruction</i>	Anna Kaltsas, MD	Memorial Sloan Kettering Cancer Center
10:20 - 10:50		Break and Poster Viewing		
10:50 - 11:15	3	<i>Patients with Biofilm Infections: Big Decisions, Imperfect Data</i>	Andy Miller, MD	Hospital for Special Surgery
11:15 - 12:00		<i>Interactive discussion: Living with a device-associated infection</i>	Patient A with Drs. Miller and Kaltsas	
12:00 - 1:00		Lunch		

June 11

Agenda

Wednesday, 11 June, 2025

Time		Title	Presenter	Affiliation
Session 2		Interventions <i>Moderator: Greg Caputo, Rowan University</i>		
1:00 - 1:45	4	<i>The journey from concept to patient for a commercially available antibacterial surface for permanent implants</i>	Jordan Katz Gene Kulesha	Orthobond Onkos Surgical
1:45 - 2:00	5	<i>Computational approaches to identify next-gen antimicrobials</i>	Shikha Nangia	Syracuse University
2:00 - 2:05	RF1	<i>Novel Bioactive Glass S53P4 cream and its eluate: A promising strategy against Staphylococcus aureus biofilm and bone infection</i>	Deeksha Rajkumar	Amsterdam UMC
2:05 - 2:10	RF2	<i>Polymyxin B Peptide Hydrogel Coating: A Novel Approach to Prevent Ventilator-Associated Pneumonia</i>	Milan Wouters	University of Antwerp
2:10 - 2:15	RF3	<i>Bioinspired fouling control with mucin-coated active topography</i>	Zehui Han	Syracuse University
2:15 - 2:20	RF4	<i>Quantitative diagnosis of periprosthetic joint infection via time-gated single-photon Raman spectroscopy</i>	Yehong Li	Stevens Institute of Technology
2:20 - 2:25	RF5	<i>Synthesis and Characterization of Antimicrobial Elastomeric Material</i>	Karishni Veerabahu Pillai	Cornell University
2:25 - 2:30	RF6	<i>Structure-Property Relationships and Antimicrobial Activity of Synthetic Peptide-Mimetic Polyurethanes</i>	Zixi Chen	Northeastern University
2:30 - 3:30		Conference Photo & Poster Session 1		
Session 3		Broader Perspectives <i>Moderator: Steve Nicoll, City College of New York</i>		
3:30 - 4:00	6	<i>Using Patient-Level Infection Data to Improve Device Design</i>	Joan Robinson	City College of New York
4:00 - 5:00		<i>Panel Discussion: Why aren't we moving forward faster?</i>	Abraham Joy Jordan Katz Andy Miller Joan Robinson Anita Shukla	Northeastern University Orthobond Hospital for Special Surgery City College of New York Brown University
6:00 - 10:00		Hudson River Dinner Cruise		

June 11

Agenda

Thursday, 12 June, 2025

Time		Title	Presenter	Affiliation
8:15 - 9:00		Registration and Light Breakfast		
Session 4		Biofilm Control - 1 <i>Moderator: Dacheng Ren, Syracuse University</i>		
9:00 - 9:30	7	<i>Modulating Innate Immunity to Combat Staphylococcus aureus Biofilm Infection</i>	Tammy Kielian	University of Nebraska Medical Center
9:30- 10:00	8	<i>Biofilm Dispersion and its Role in Infection Control</i>	David Davies	Binghamton University
10:00 - 10:05	RF7	<i>Decoupling Physicochemical and Chemical Interactions of Staphylococcus aureus and Pseudomonas aeruginosa using Nanoculture Systems</i>	Huda Usman	Carnegie Mellon University
10:05 - 10:10	RF8	<i>Impact of attachment to a surface on macrophage engulfment of nosocomial pathogens: insights into immune evasion mechanisms</i>	Bharti Sharma	Binghamton University
10:10 - 10:15	RF9	<i>Characterizing the molecular details underlying biomaterial-associated infections</i>	Laure van Hofwegen	Amsterdam UMC
10:15 - 11:00		Poster Session 2		
Session 5		Biofilm Control - 2 <i>Moderator: Karin Sauer, Binghamton University</i>		
11:00 - 11:30	9	<i>Coacervate Dense Phase Displaces Surface-Established Pseudomonas aeruginosa Biofilms</i>	Abraham Joy	Northeastern University
11:30 - 11:45	10	<i>Viscoelastic Failure Triggers Bacterial Adaptivity to Environmental Stresses</i>	Brandon Peterson	University Medical Center Groningen
11:45 - 12:00	11	<i>Cyclic strain loading of resin composites triggered the pathogenicity of Streptococcus mutans and Enterococcus faecalis</i>	Santiago Orrego	Temple University
12:00 - 1:00		Lunch		

June 12

Agenda

Thursday, 12 June, 2025

Time		Title	Presenter	Affiliation
Session 6		Translation <i>Moderator: Julie Stenken, University of Arkansas</i>		
1:00 - 1:30	12	<i>Navigating the interconnected path of model design, standard test method validation, and regulatory decision making</i>	Darla Goeres	Montana State CBE
1:30 - 2:00	13	<i>Galleria mellonella larvae: a promising animal model to study biofilm maturation in orthopaedic infections</i>	Martijn Riool	University Medical Centre Regensburg
2:00 - 2:15	14	<i>Developing a next generation of resorbable scaffolds for tissue engineering</i>	Hongjun Wang	Stevens Institute of Technology
2:15 - 2:30	15	<i>Sustained Dual-Antibiotic Polymer Implant for Infection Prevention - in vivo Evaluation</i>	Mohammed Labib	NovaFlux
2:30 - 2:45	16	<i>Designing a high-throughput platform for assessing microbial dynamics in native environments</i>	Tagbo Niepa	Carnegie Mellon University
2:45 - 3:00		Break (SHORT)		
Session 7		Concluding Discussion <i>Moderator: Hongjun Wang, Stevens Institute of Technology</i>		
3:00 - 3:45	17	<i>Engineering Opportunities to Combat Antimicrobial Resistance</i>	Anita Shukla	Brown University
3:45 - 4:00		Conference Closure	Matt Libera	Stevens Institute of Technology

June 12

Moderators

Name	Affiliation
Matt Libera	Stevens Institute of Technology
Greg Caputo	Rowan University
Steve Nicholl	City College of New York
Dacheng Ren	Syracuse University
Karin Sauer	Binghamton University
Julie Stenken	University of Arkansas
Hongjun Wang	Stevens Institute of Technology

Moderators

Papers

Paper Number	Presenter	Affiliation	Title
1	Peter Taub	Mt. Sinai Health System	The pathology of device-associated infection in plastic and reconstructive surgery
2	Anna Kaltsas	Memorial Sloan Kettering Cancer Center	Case studies of infection associated with soft-tissue reconstruction
3	Andy Miller	Hospital for Special Surgery	Patients with Biofilm Infections: Big Decisions, Imperfect Data
4	Jordan Katz Gene Kulesha	Orthobond Onkos Surgical	The journey from concept to patient for a commercially available antibacterial surface for permanent implants
5	Shikha Nangia	Syracuse University	Computational approaches to identify next-gen antimicrobials
6	Joan Robinson	City College of New York	Using Patient-Level Infection Data to Improve Device Design
7	Tammy Kielian	University of Nebraska Medical Center	Modulating Innate Immunity to Combat Staphylococcus aureus Biofilm Infection
8	David Davies	Binghamton University	Biofilm Dispersion and its Role in Infection Control
9	Abraham Joy	Northeastern University	Coacervate Dense Phase Displaces Surface-Established Pseudomonas aeruginosa Biofilms
10	Brandon Peterson	University Medical Center Groningen	Viscoelastic Failure Triggers Bacterial Adaptivity to Environmental Stresses
11	Santiago Orrego	Temple University	Cyclic strain loading of resin composites triggered the pathogenicity of Streptococcus mutans and Enterococcus faecalis
12	Darla Goeres	Montana State CBE	Navigating the interconnected path of model design, standard test method validation, and regulatory decision making
13	Martijn Riool	University Medical Centre Regensburg	Galleria mellonella larvae: a promising animal model to study biofilm maturation in orthopaedic infections
14	Hongjun Wang	Stevens Institute of Technology	Developing a next generation of resorbable scaffolds for tissue engineering
15	Mohammed Labib	NovaFlux	Sustained Dual-Antibiotic Polymer Implant for Infection Prevention - in vivo Evaluation
16	Tagbo Niepa	Carnegie Mellon University	Designing a high-throughput platform for assessing microbial dynamics in native environments
17	Anita Shukla	Brown University	Engineering Opportunities to Combat Antimicrobial Resistance

Papers

Posters

Poster Number	Presenter	Affiliation	Title
P1	Deeksha Rajkumar	Amsterdam Univ Medical Center	Novel Bioactive Glass S53P4 cream and its eluate kill Staphylococcus aureus in biofilm, and prevents experimental bone infection
P2	Milan Wouters	University of Antwerp	Polymyxin B Peptide Hydrogel Coating: A Novel Approach to Prevent Ventilator-Associated Pneumonia
P3	Zehui Han	Syracuse University	Bioinspired fouling control with mucin-coated active topography
P4	Yehong Li	Stevens Institute of Technology	Quantitative diagnosis of periprosthetic joint infection via time-gated single-photon Raman spectroscopy
P5	Karishni Veerabahu Pillai	Cornell University	Synthesis and Characterization of Antimicrobial Elastomeric Material
P6	Zixi Chen	Northeastern University	Structure-Property Relationships and Antimicrobial Activity of Synthetic Peptide-Mimetic Polyurethanes
P7	Huda Usman	Carnegie Mellon University	Decoupling Physicochemical and Chemical Interactions of Staphylococcus aureus and Pseudomonas aeruginosa using Nanoculture Systems
P8	Bharti Sharma	Binghamton University	Impact of attachment to a surface on macrophage engulfment of nosocomial pathogens: insights into immune evasion mechanisms
P9	Laure van Hofwegen	Amsterdam Univ Medical Center	Characterizing the molecular details underlying biomaterial-associated infections
P10	Laure van Hofwegen	Amsterdam Univ Medical Center	The fungicidal activity of novel graphene quantum dots against Candida auris and Candida albicans species
P11	Amelia Ryan	City College of New York	An Optical Aptamer-Based Cytokine Nanosensor Detects Macrophage Activation by Bacterial Toxins
P12	Devin Fauver	University of New Haven	Determining the Metabolic Product of Biofilm-mediated Biodegradation for the Design of New Enzyme-Responsive Smart Polymers
P13	Madison Kajuffa	University of New Haven	Effects of skin thinning on bacterial biofilm formation
P14	Asheka Rahman	University of Arkansas	Initial Organ-On-A-Chip Development for Controlling and Quantifying in situ Bacterial Biofilm/Macrophage Biochemistry
P15	Sage Bentlage	University of Arkansas	Co-culture Optimization for Bacterial Biofilm/Macrophage Analysis
P16	Ernest Obeng	Syracuse University	Antimicrobial Hemostatic Shape Memory Polymer Foams for Infection Prevention in Traumatic Wounds
P17	Nicole Gill	Binghamton University	Biofilm Attachment and Survival on Next Generation Antimicrobial Scaffolds
P18	Sevde Nur Can	Syracuse University	The Smarter the Foam, the Better the Healing: Vanillic Acid-Incorporated Polyurethane Shape Memory Polymer Foams for Hemorrhage and Infection Management
P19	Shakira Martinez Vasque	Carnegie Mellon University	Material properties of interfacial films of Brucella pituitosa

Posters

Poster Number	Presenter	Affiliation	Title
P20	Camila Cue	Carnegie Mellon University	Eradicating Candida auris through Physiological Stress and Drug Permeation using Low-Level Direct Currents
P21	Ann Badia	Carnegie Mellon University	Rapid Bacterial Identification and Antimicrobial Susceptibility Testing to Improve Diagnostics and Treatment in Oral Healthcare
P22	Abraham Polanco	Carnegie Mellon University	Engineering DNA Origami Nanostructures for the Detection and Elimination of Candida auris
P23	Yousr Dhaouadi Khattab	Syracuse University	Optogenetic engineering of Escherichia coli for high-level persistence
P24	Hannah Gedde	Carnegie Mellon University	Effect of Interfacial Stress on Pseudomonas aeruginosa Film Composition and Mechanical Properties
P25	Amy Apgar	Carnegie Mellon University	Microfluidic platforms for studying in vitro infection dynamics of Babesia microti in ovine blood
P26	Anita Kundu	Binghamton University	Characterization of multispecies biofilm dispersion induced by cis-2- decenoic acid and by a step-change increase in nutrient loading
P27	Anand Wadurkar	Syracuse University	Machine Learning Driven Optimization of Peptoid Antimicrobial Coatings for Infection Prevention
P28	Wenhan Zhao	Syracuse University	On-Demand Biofilm Removal by Shape Memory Triggered Changes in Surface Topography
P29	Thalma Orado	Syracuse University	Sensitivity and Specificity of a Bacterial Protease-Responsive Polyurethane Shape Memory Polymer for Chronic Wound Infection Surveillance
P30	Chloe Eosso	Rowan University	Fatty acid ionic liquids as antimicrobials
P31	Matthew Urban	Rowan University	Influence of growth media on efficacy of antimicrobial metals
P32	Matthew Urban	Rowan University	Influence of environmental conditions on dissolution properties of antimicrobial thin-film coatings
P33	Carolina Montoya	Temple University	Effect of dental material type and masticatory forces on periodontitis-derived subgingival microbiomes
P34	Zhuozhuo Yin	Stevens Institute of Technology	Uniform and Controllable Deposition of PAA Microgels onto 3D-Printed PCL Scaffolds
P35	Yunhua Guo	Stevens Institute of Technology	Self-defensive microgel-modified antimicrobial surfaces
P36	Matt Libera	Stevens Institute of Technology	A Spray Deposition System to Model Contamination in the Operating Room by Airborne Bacteria
P37	Joseph Ondari Nyakundi	University of Cincinnati	Laboratory assessment of collection and inactivation of viable, airborne Staphylococcus aureus and MRSA
P38	Justin Cross	Northeastern University	Peptidomimetic Cationic Polyurethanes Coupled with Gram-Positive Antibiotics Effectively Treat Gram-Negative Bacterial Infection
P39	Victor C. Igbokwe	Université de Strasbourg	Development of Anti-Biofilm Agarose Hydrogels for Targeting Bacterial Amyloid Fibrils

The pathology of device-associated infection in plastic and reconstructive surgery

Peter Taub, MD
Mount Sinai Hospital
New York, NY

Peter J. Taub, MD, MS, FACS, FAAP, was born and raised in New York City. He graduated from Brown University (1989) and the Albert Einstein School of Medicine (1993) with national Alpha Omega Alpha (AOA) honors and distinction for research in Plastic and Reconstructive Surgery. He completed an internship and General Surgery residency at The Mount Sinai Medical Center in New York (1999). During that time, Dr. Taub spent a year in the Microvascular Research Laboratory and served as the Teaching Resident for the third-year medical students. He went on to complete a second residency in Plastic and Reconstructive Surgery at UCLA Medical Center in Los Angeles and stayed for an additional year of training in Craniofacial Surgery under the direction of Dr. Henry K. Kawamoto, Jr., MD, DDS.

Dr. Taub is board certified in both General Surgery (2001) and Plastic and Reconstructive Surgery (2003). He is a Fellow of both the American College of Surgeons (FACS) and the American Academy of Pediatrics (FAAP). He is active in many national professional societies and Past-President of the Plastic Surgery Research Council (PSRC), the American Society of Maxillofacial Surgery (ASMS), the American Association of Pediatric Plastic Surgeons, the Northeastern Society of Plastic Surgeons (NESPS), and the New York Regional Society of Plastic Surgeons (NYRSPS). He is also active in the American Society of Plastic Surgery (ASPS), the American Cleft Palate Craniofacial Association (ACPA).

Case studies of infection associated with soft-tissue reconstruction

Anna Kaltsas, MD
Memorial Sloan Kettering Cancer Center
New York, New York

Dr. Kaltsas is an Infectious Disease Specialist at Memorial Sloan Kettering (MSK) Cancer Center. Her clinical interests include the management of infectious complications from cancer and its treatment as well surgical infections and abscesses, bone/joint infections, and hardware and recurrent urinary tract infections, among other conditions.

Dr. Kaltsas earned her medical degree from Albany Medical College with honors, followed by an internal medicine residency at New York-Presbyterian–Weill Cornell. She completed a three-year infectious disease fellowship at Albert Einstein College of Medicine/Montefiore Medical Center, during which time she also pursued a master's degree in clinical research.

Dr. Kaltsas has an interest in medical education and oversees the infectious disease fellowship program at MSK, as well as rotations from interested medical students, interns, residents, and fellows from other institutions and other specialties on the infectious disease service. She also serves as assistant professor of clinical medicine at Weill Cornell Medical College.

Patients with Biofilm Infections: Big Decisions, Imperfect Data

Andy O. Miller, MD^{1*}, and the Patient

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With increasing use of lifesaving and function-restoring biomedical devices together with a growing number of people living at the extremes of age and immune function, we are recognizing the burden of device-related biofilm infections. Advances in biomedical engineering offer new ways to prevent, diagnose, and treat these infections. Understanding what patients and clinicians need from basic researchers is key to asking the right questions in the research arena.

In this talk, my patient and I will discuss her biofilm infection, and talk about what knowledge we wish were available when making big clinical decisions – before surgery, in the operating room, and years afterwards. Hopefully, we can help to offer perspective on biofilm infections outside the lab, and in “the real world” of clinical medicine – where patients and their doctors try to make sense of what we know and try to chart safe courses despite all that we do not know.

The journey from concept to patient for a commercially available antibacterial surface for permanent orthopedic implants

Jordan Katz, Ph.D.,¹ Gene Kulesha,²

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On April 5th 2024, Onkos and Orthobond were granted De Novo authorizations for an antibacterial surface modification of a limb salvage implant system and a spine stabilization system respectively. These represent the first ever permanent implants with FDA approved antibacterial claim language. These approvals were the culmination of a decade of development work at Orthobond, including 7 years of co-development with Onkos. In this presentation we will discuss the path to market from the perspective of both companies, including identifying a patient need, developing a concept, working with FDA to gain regulatory approval, scaling a production facility, and implanting our first 150 antibacterial devices in patients.

Computational approaches to identify next-gen antimicrobials

Shikha Nangia,^{1*} Anand Wadurkar¹ Jash Jaliwala,¹ Khuong Pham,¹
Wafiq Khondkar,¹ Matthew Libera,² and Annelise Barron³

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Implant-associated infections affect nearly one million patients annually, often leading to prolonged treatments, multiple surgeries, and, in severe cases, amputations or death. Addressing this critical healthcare challenge requires innovative strategies for infection prevention and control. In this work, we investigate the design of next-generation antimicrobial coatings based on *peptoids* - biocompatible, sequence-specific, cationic polymers - targeted at preventing biofilm formation and disrupting bacterial colonization on medical implants.

We employ a computational approach integrated with machine learning to design and predict the assembly behavior of 7-mer peptoids constructed from three key repeat units. By systematically generating all possible 7-mer combinations (a library of 2,187 peptoids), we trained a machine learning model to classify their clustering behavior, distinguishing between peptoids that form large aggregates versus smaller clusters of two or three units. This framework enables high-throughput screening for identifying candidate sequences with favorable antimicrobial assembly properties.

Experimental validation of the model's predictions is currently underway. By combining computational modeling, machine learning, and experimental feedback, this approach paves the way for the rational design of peptoid-based antimicrobial materials, offering a promising strategy for developing infection-resistant medical implants.

Using Patient-Level Infection Data to Improve Device Design

Joan H. Robinson, JD, PhD*

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In this talk, I provide an overview of sociological approaches to medical technologies, outline important contributions from the last twenty years, and explain how these approaches can inform bacteria-material device design. Numerous sociological studies have examined clinician and patient interactions with technologies in various settings, analyzing issues such as impacts on user-friendliness, the patients' well-being, and compliance, among others. Social scientists have identified a variety of social and medical challenges faced by clinicians and patients when medical devices go home, as well as the complexities associated with the growing field of "replaceable" body parts that often introduce new opportunities for infection.

How could these social science approaches inform bacteria-material device research, design, and use? Like other life-saving treatments, I argue that patient-level infection data, both quantitative and qualitative, should be foregrounded in the development of new devices seeking to prevent, detect, and cure infections. Doing so could identify the greatest areas of patient needs and what patients would consider success. Finally, I explain some of the barriers to obtaining this type of data from hospitals and patients and ways in which they could be overcome.

Modulating innate immunity to combat *Staphylococcus aureus* biofilm infection

Tammy Kielian

University of Nebraska Medical Center
Department of Pathology, Microbiology, and Immunology
Omaha, Nebraska, USA

Staphylococcus aureus (*S. aureus*) is a leading cause of biofilm infections that can form on native tissues such as bone or implanted medical devices. Biofilms are difficult to treat without surgical intervention since bacteria become recalcitrant to antibiotic therapy. This talk will highlight findings demonstrating that the metabolic profiles of immune cells are programmed by the infection microenvironment, which dictates their anti-inflammatory properties to promote biofilm persistence. Select targeting of metabolic pathways has been found to improve biofilm clearance, demonstrating the feasibility of modulating immunometabolism to augment biofilm eradication.

Biofilm Dispersion and its Role in Infection Control

David G. Davies*, PhD

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Of the many characteristics of biofilm bacteria that have come to light, only a handful can be claimed to be apparently universal and unequivocally unique to biofilm cells. Among these is the biofilm dispersion response. This physiologically-mediated response, resulting in the transition of bacteria from a biofilm to a planktonic habit, appears to be required for long-term biofilm survival. This talk will provide an overview of what we currently understand about the auto-inducible biofilm dispersion response as first characterized in *P. aeruginosa*, focusing on physiological changes that occur during the response, our current understanding of its regulation and how this is being used to control biofilm accumulation in beta testing applications. The talk will address changes in global physiology, expression of proteins associated with cellular release from the biofilm, alterations in virulence, and signal transduction and demonstrate how biofilm dispersion can be used to enhance the antimicrobial activity of conventional chemotherapies and immune function.

Coacervate Dense Phase Displaces Surface-Established *Pseudomonas aeruginosa* Biofilms

Abraham Joy,^{1*} Zixi Chen,² Apoorva Vishwakarma,² Amal Narayanan², Francis Dang², Nityanshu Kumar², and Ali Dhinojwala²

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Biofilms are present in over 80% of microbial infections, costing more than \$4 trillion annually. Bacteria within the dense extracellular polymeric substance (EPS) network of biofilms are dormant and tolerant to clinical antibiotics and can establish additional biofilm communities by dispersal to other surfaces. Mechanical dispersal strategies combined with antibiotics and bacterial signal inhibition are common approaches to disrupt surface-established biofilms. Herein, we demonstrate that nonionic, coacervating synthetic polymers that mimic the physicochemical features of marine underwater adhesives remove ~99% of *Pseudomonas aeruginosa* (*P. aeruginosa*) biofilm biomass from underwater surfaces.

In this work we have used peptide-like polyesters that form phase separated condensates at a defined temperature. The dense phase of the polymers has very low interfacial tension and can adhere to underwater surfaces. We took advantage of this property to evaluate their ability to out-compete biofilm EPS and remove the biofilms from surfaces. We demonstrate that the coacervate efficiently removes polysaccharide rich biofilms such as those from *P. aeruginosa* and *K. pneumoniae*, while not being effective against protein-rich *S. aureus* or *E. coli* biofilms. In addition, we demonstrate that an optimal combination of coacervate viscosity, interfacial tension and possible interactions with EPS components are the basis for the observed biofilm removal. We will discuss these aspects with an eye towards developing a framework for effective antibiofilm materials.

Viscoelastic Failure Triggers Bacterial Adaptivity to Environmental Stresses

Z.Cui,¹ V.Carniello,¹ H.J.Kaper,¹ A.M.Slomp,¹ C.L.Hall,² J.Sjollema¹ and
B.W.Peterson^{1*}

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Antimicrobial resistance is a major threat to the global healthcare system. Bacteria are quickly adapting to new antimicrobials creating a shift in scientific development toward targeted delivery. Genetic mechanisms for bacterial resistance have been extensively studied by looking at what has changed. However, why the change happened remains elusive.

By looking more deeply into bacterial adhesion phenomena and using developed mathematical simulation models, we believe we have found a “why” for bacterial adaptation. Using genetically modified bacteria, we linked adhesion force to cell wall permeability, including the penetration of antibiotics. The stronger the adhesion, the more cell wall deformation and the more antimicrobial penetration. Next, we demonstrated with *in vitro* experiments and detailed mathematical modeling that adhesion and detachment events are supported by extracellular molecules that demonstrate properties similar to viscoelastic failure points. Finally, we discovered that adaptation to changes in the environment (bond strengthening) are triggered only after a certain threshold is reached, which is different for individual bacterial species.

Putting it all together, bacterial adhesion is facilitated by extracellular molecules following well known thermodynamic and diffusion equations. Once attached, these molecules bring the bacteria closer to the surface over time, and allow for flexibility to adapt to the surrounding environment. A change in ionic strength, shear stress, and chemical cross-linking are first felt by these extracellular molecules, in a similar fashion as our normal oral flora protect our teeth from changes in the environment related to eating and drinking. When these extracellular molecules reach a viscoelastic failure point, the cell wall/cell membrane of the bacteria senses this change and strengthens the bond to the surface, which then provides more cell wall deformation and increased antimicrobial penetration.

While this research focuses on individual bacterial adhesion events and is not yet linked to changes within a biofilm, viscoelasticity has been shown to play a role in the relaxation within biofilms for stress, indicating a potential target for the adaptation of bacteria to their environment and developing antimicrobial resistance.

Cyclic strain loading of resin composites triggered the pathogenicity of *Streptococcus mutans* and *Enterococcus faecalis*

Carolina Montoya¹, Ryan Yu-Sheng Chang¹, Aayush Deb¹, Santiago Orrego^{1,2,*}

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Objective: *Streptococcus mutans* and *Enterococcus faecalis* are opportunistic pathogens involved in persistent endodontic and secondary caries infections. Their pathogenicity is expressed by robust biofilm formation, extracellular polysaccharides (EPS) synthesis, and degradative enzyme production. While the interaction between oral bacteria and dental biomaterials depends on the surface characteristics, the influence of cyclic strain loading (i.e., mastication) on bacterial behavior has not been thoroughly examined. This study explores how the mechanical loading of resin composites modulates the pathogenic potential of *S. mutans* and *E. faecalis*.

Methods: Single-species biofilms of *S. mutans* and *E. faecalis* were formed over the surface of resin composite samples held static and subjected to cyclic loading. Beams were submerged in the bacterial liquid culture for 2 h to allow bacterial adhesion. Then, the composite beams were subjected to cyclic mechanical strain ($\epsilon=0$ to 0.2%, 2 Hz) throughout the incubation period (24 h). Cell viability, metabolism, biomass, and carbohydrate content in EPS were evaluated to characterize the biofilm. RT-qPCR was conducted to assess changes in the expression of genes involved in pathogenicity.

Results: Our results showed that applying cyclic loading to the beams caused a significant increase in biofilm biomass, number of viable cells, and EPS production compared to static surfaces for both bacterial strains. Specifically for *S. mutans*, the cyclic strain of surfaces increased L-Lactate production and the upregulation of genes related to biofilm formation, cariogenicity, and glucan production (*gbpB*, *vicR*, and *gtfB*). For *E. faecalis*, cyclic loading resulted in the upregulation of genes involved in the production of adhesins, biofilm formation and maturation, and toxin production (*efaA*, *esp*, and *cylL*). Results suggest that cyclic strain is a mechanobiology signal that fuels the pathogenicity of both bacterial strains.

Conclusions: This work showed that applying cyclic strain to a biomaterial fuels bacteria's pathogenicity, evidenced by the increased biofilm formation (additional biomass, number of viable cells, and acid and EPS production) compared to static surfaces. The virulence of the bacteria was also increased, as evidenced by the increased production of virulence genes.

Navigating the interconnected path of model design, standard test method validation, and regulatory decision making

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Regulatory science focuses on developing the tools necessary for informed decision making. As the name implies, these decisions are happening within the regulatory bodies and are tied to bringing products to the market. Multiple factors are considered in the decision-making process, the most important being does the product protect and/or improve human health outcomes. Depending upon the regulatory body, these decisions are based upon data collected using validated *in vitro* standard test methods, animal models, clinical trials or field studies. The pipeline is often linear, with data from the *in vitro* evaluation providing justification to move forward with a more expensive animal study followed by a clinical trial. While animal studies are common, clinical trials are less so. Regardless, using an *in vitro* model that provides translatable data is a fundamentally important first step in the process. Too often though, *in vitro* models fall short either in model design, statistical attributes, or by not providing data that is predictive of a clinical outcome. This presentation will explore key parameters to consider when designing an *in vitro* model from the perspective of regulatory science decision making.

***Galleria mellonella* larvae: a promising animal model to study biofilm maturation in orthopaedic infections**

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Background: Chronic orthopaedic infections associated with implants remain a major clinical concern due to the formation of resilient bacterial biofilms. While traditional vertebrate models offer valuable insights, they are resource-intensive and limited by ethical constraints. *Galleria mellonella* larvae have emerged as an attractive alternative for modelling infection biology, yet their potential in studying chronic biofilm maturation remains underexplored.

Objective: This study aimed to establish a robust and reproducible *in vitro*–*in vivo* hybrid model using *G. mellonella* larvae to simulate chronic orthopaedic implant infections with mature *Staphylococcus aureus* biofilms.

Methods: Three orthopaedic-related *S. aureus* strains were used to form biofilms on Kirschner wires (K-wires) under both static and dynamic (CDC Biofilm Reactor) conditions for up to 7 days. Biofilms were characterized by culture, SEM, 3D-CLSM, and gene expression profiling. K-wires with biofilms matured for 1 or 7 days were implanted into *G. mellonella* larvae to monitor survival, with rifampicin (80 µg/g) treatment serving as a surrogate for therapeutic efficacy.

Results: Seven-day dynamic biofilm maturation led to significantly thicker biofilms and higher bacterial loads (2–4 log₁₀ CFU increase) compared to static conditions, along with enhanced extracellular matrix production. Once implanted into larvae, these mature biofilms showed markedly reduced susceptibility to rifampicin, supporting their clinical relevance. Kaplan-Meier survival analysis of infected larvae confirmed the increased tolerance of mature biofilms to antibiotic treatment.

Conclusion: This study successfully establishes a cost-effective and ethically sustainable *in vitro*–*in vivo* model leveraging *G. mellonella* larvae for the study of biofilm maturation in orthopaedic infections. The use of preformed mature biofilms under dynamic conditions provides a realistic platform for evaluating novel antibiofilm therapies and deepening our understanding of chronic implant-associated infections.

Developing a next generation of resorbable scaffolds for tissue engineering

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Driven by the shortage of donor tissue and organs, tissue engineering has evolved as a forward-looking field with the convergence of cell/molecular biology, materials science, engineering, and translational medicine. Typically, a resorbable scaffold is used to define both the spatial properties and the essential cell-signalling properties that regulate cell attachment, proliferation, migration, and differentiation to form desirable tissues in vitro and/or in vivo. While extensive attention has been geared toward tissue formation, little or limited effort has been focused on the competing problem of scaffold-associated infection. Similar to tissue-contacting biomedical devices, which can be colonized by bacteria and develop into catastrophic infections, resorbable scaffolds are also susceptible to infection. Recognizing such compelling problems has inspired our further endeavour in scaffold design to include infection control. That is, the next-generation scaffolds not only support the development of desirable tissue but simultaneously also inhibit bacterial colonization.

Built on the established advantages of 3D printed scaffolds for bone formation, we have been integrating antimicrobial attributes by uniquely priming the scaffold surfaces with uniform yet discontinuous layer of microgels, which allows the surface to complex and store antimicrobial peptides for subsequent contact killing of approaching bacteria. On the other hand, such a discontinuous layer of microgels increases the surface roughness of the scaffolds for improved adhesion and proliferation of mesenchymal stem cells. This talk will provide the most recent progress while highlighting the future perspectives.

Sustained Dual-Antibiotic Polymer Implant for Infection Prevention – in vivo Evaluation

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Implant-associated surgical site infections (SSIs) often lead to revision surgeries and sepsis, mainly due to biofilms at the device-tissue interface that cannot be eradicated by systemic antibiotics once established. We developed a novel polymer implant loaded with high concentrations (~20% w/w) of minocycline and rifampin in an ethylene vinyl acetate (EVA) matrix, enabling continuous local release of both antibiotics. This high-loading dual-antibiotic platform achieves sustained drug levels far above the minimum inhibitory concentrations (MICs) of common pathogens for over 60 days at the implant site. In vitro, the EVA-based material released minocycline and rifampin at ~100× MIC for at least 48 days, maintaining potent activity against biofilm-forming bacteria including *S. aureus*, *S. epidermidis*, *Acinetobacter baumannii*, and *E. coli*.

In a murine subcutaneous implant model, the antibiotic-eluting implants completely prevented *S. aureus* adhesion, colonization, and biofilm formation on the implant surface, even when challenged with a high bacterial inoculum (10^7 CFU *S. aureus*). Treated mice exhibited no signs of infection and negligible recoverable bacteria at 14 and 60 days post-implantation, whereas untreated control implants showed heavy *S. aureus* biofilm colonization. By contrast, other anti-infective technologies, such as silver coatings or antimicrobial peptide-functionalized surfaces, typically provide only transient antimicrobial activity and often fall below bactericidal levels (sub-MIC) within days, leaving the implant vulnerable to bacterial ingress.

The unique ability of our dual-antibiotic implant to maintain prolonged above-MIC antibiotic concentrations creates a protected zone around the device, effectively guarding against bacterial adhesion and biofilm development. These findings highlight the translational potential of this strategy for preventing device-related infections in long-term implants (including orthopedic hardware, cardiovascular devices, and percutaneous implants), and represent a promising advancement for infectious disease experts and biomaterials researchers.

Designing a high-throughput platform for assessing microbial dynamics in native environments.

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Tools for cultivating microorganisms in their native conditions are essential for bioprospecting and exploring the untapped potential of currently unculturable species. These tools offer the potential to better understand the vast complexity of microbial ecology, predict emergent functions within microbial communities, and identify new microbial-based biotherapeutics. To address this need, we have developed magnetic nanocultures (MNCs) as a high-throughput microsystem platform to sequester environmental microbes and grow them under near-native conditions. MNCs are created as nanoliter-sized bioreactors encapsulated within semi-permeable membranes, which crosslink into magnetic polymeric microcapsules.^{1,2} The magnetic properties are imparted by iron oxide nanoparticles (NPs) embedded in the polydimethylsiloxane-based shells. These composite membranes provide both mechanical stability for robust housing and magnetic actuation, allowing for the retrieval of cultivated microbes from soil-like environments. The magnetic nanocultures are designed and optimized to possess optical and biological properties suitable for encapsulating, growing, and sorting microbial communities. Here, we demonstrate the platform's versatility by investigating a broad range of direct and indirect microbial dynamics. This innovative tool has significant potential for addressing biological challenges related to drug resistance, chronic infections, antibiotic discovery, and microbiome dynamics in complex microbial communities. Our study sets the stage for further exploration of environmental microbes and the discovery of previously unknown microbial species.

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Engineering Opportunities to Combat Antimicrobial Resistance

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Antimicrobial resistance (AMR) has been dubbed a 'silent pandemic,' with the United Nations and other agencies warning of its devastating consequences if left unaddressed for over a decade. Infections caused by antibiotic resistant bacteria cost the United States more than \$4 billion annually. A 2022 study analyzing 2019 data estimated that AMR was associated with 4.95 million deaths globally, surpassing the combined deaths from HIV/AIDS and malaria.¹ The UN Ad hoc Interagency Coordinating Group on AMR further projected that, by 2050, antimicrobial resistant infections could cause 10 million deaths annually and push 24 million people into extreme poverty by 2030.² Engineers have a critical role to play in the fight against AMR, together with clinicians, scientists, and policy leaders. To this end, the National Science Foundation-funded Engineering Research Visioning Alliance recently convened a visioning event on "Engineering Opportunities to Combat AMR," which brought together 55 researchers, industry leaders, and policymakers. This group developed a roadmap identifying five key areas for engineering research investment to tackle AMR: diagnostic biosensors and wearables, engineered antimicrobial surfaces, smart biomaterials, cell engineering for drug-free therapies, and advanced modeling approaches.³ In this talk, I will present the engineering opportunities highlighted in this report, and provide some examples from my own research on smart biomaterials, which have the potential to combat AMR.

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Novel Bioactive Glass S53P4 cream and its eluate: A promising strategy against *Staphylococcus aureus* biofilm and bone infection

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Orthopedic implant-associated infections (OIAIs), predominantly caused by *Staphylococcus aureus*, pose significant challenges due to biofilm formation and antibiotic resistance, leading to persistent and recurrent infections. Bioactive Glass (BAG) S53P4 is a unique material with antimicrobial and bone regenerative properties. A novel BAG cream formulation can be used as an advanced coating solution to prevent or treat OIAIs. In this study we aimed to characterize a novel BAG S53P4 cream, consisting of antimicrobial BAG powder and binder, for its bactericidal and biofilm killing activity *in vitro* and efficacy in a cadaver mouse bone infection model. Since the bactericidal effects is dependent on eluted compounds, we analysed the bactericidal activity of BAG cream, BAG powder, binder and their eluates against *S. aureus*. To study the influence of the elution time, *S. aureus* was exposed to eluates collected at 2, 4, 8, and/or 24 hours. The bactericidal and biofilm-killing activity were quantitatively analysed. A time kill assay was performed to assess the speed of killing of *S. aureus*. The pH was measured to study its relevance for the bactericidal action of BAG. In a cadaver mouse bone infection model, BAG cream was applied to an *S. aureus* infected femoral bone defect. The BAG cream, BAG powder and their eluates eradicated planktonic *S. aureus* and significant killing of *S. aureus* biofilms was observed with the cream and powder eluates. All eluates, including the eluate collected at the earliest elution time of 2 hours, were highly effective against *S. aureus*, indicating rapid release of bactericidal activity from BAG cream and powder. Time-kill experiments revealed rapid bactericidal activity of BAG cream and powder eluates, with killing starting as early as 30 minutes and increasing with longer exposure times. BAG cream applied to an *S. aureus* cadaver mouse bone infection model inhibited bacterial growth effectively. These findings show the potential of BAG cream as an innovative solution for managing OIAIs. As a next step we intend to investigate the *in vivo* antibacterial efficacy and safety of BAG cream applied in a mouse bone fixation plate infection model.

Polymyxin B Peptide Hydrogel Coating: A Novel Approach to Prevent Ventilator-Associated Pneumonia

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Healthcare-associated infections in intensive care units place a major burden on healthcare systems, with ventilator-associated pneumonia (VAP) being the most frequent nosocomial infection. According to the WHO, 96% of hospital-acquired pneumonia cases are linked to mechanical ventilation. The absence of reliable diagnostic criteria complicates treatment, leading to empirical antibiotic use, ultimately contributing to antimicrobial resistance (AMR). This highlights the need for new anti-infective medical devices.

Varying surface engineering strategies to prevent these infections have been established. One promising approach is the incorporation of antimicrobial peptides (AMPs), which have seen a tremendous increase in preventive medicine in the last couple of years. Immobilization strategies of these AMPs include polymer brushes, chemical coupling, layer-by-layer assemblies, and matrix encapsulation.

This research explores a peptide-releasing hydrogel coating incorporating polymyxin B (PMB), a cationic AMP, on a polyvinyl chloride (PVC) substrate. The hydrogel is formed via ultraviolet photopolymerization, enabling localized, dose-specific drug release. The coating demonstrated anti-adhesion and anti-biofilm effects against multiple *P. aeruginosa* strains, confirmed by viable plate count analysis and scanning electron microscopy. While the absolute duration of drug release remains uncertain, the coating retained antibacterial properties for up to 42 days, as evidenced by micro-BCA analysis. Furthermore, surface characterization via atomic force microscopy, Fourier-transform infrared spectroscopy, and Raman spectroscopy confirmed increased roughness and chemical presence of PMB. Water contact angle measurements indicated enhanced hydrophilicity, and biocompatibility was validated per ISO 10993-5 guidelines.

The successful development of an antibacterial, antibiofilm, and biocompatible coating on PVC endotracheal tubing represents a significant milestone for advancing innovative strategies in infection prevention. Beyond its potential to prevent VAP, this coating may also address other device-related infections. Optimizing the coating protocol and incorporating novel AMPs could pave the way for groundbreaking medical devices.

Bioinspired fouling control with mucin-coated active topography

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In the innate immune system of mammals, beating cilia of epithelial cells and the attached mucin proteins prevent the colonization of microbial pathogens. Abiotic biomaterials of medical implants lack such protection and thus are susceptible to microbial colonization, leading to biofilm formation and persistent infections with high-level antibiotic tolerance. To address this challenge, we further developed our new strategy of biofilm control by magnetically driven oscillation of micron-sized pillars on biomaterials. This study is based on a bioinspired design by covalently coating the pillars with mucin, a glycoprotein found ubiquitously in mammalian innate immune systems. The results show that mucin coating significantly enhances the antifouling effects of active topography in both the inhibition of *Pseudomonas aeruginosa* biofilm formation and removal of its mature biofilms. Analysis using scanning electron microscopy (SEM) reveals that mucin coating inhibits bacterial attachment near the pillar base, the area protected from the direct force of beating pillars. In addition, mucin coating enhanced the twitching motility of *P. aeruginosa* but repressed its swarming motility. Both effects contribute to the antifouling activities. A prototype catheter was engineered to further evaluate the antifouling activities of this design. Overall, the findings from this study demonstrate the feasibility of engineering bioinspired antifouling materials for safer medical devices.

Quantitative diagnosis of periprosthetic joint infection via time-gated single-photon Raman spectroscopy

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This study introduces a novel diagnostic approach for periprosthetic joint infection (PJI) through time-gated and time-correlated single-photon Raman spectroscopy, enabling the precise quantification of alpha defensin levels in synovial fluid (SF). Alpha defensin has been established as a highly specific biomarker for PJI, yet current diagnostic methods, such as the Synovasure® Alpha Defensin Test, are costly and require larger sample volumes.

By developing Raman spectra for human alpha defensin and its mixture with SF, the study establishes a linear correlation between photon count and alpha defensin concentration. Our method successfully differentiates PJI-positive (above clinical cut-off) and non-PJI samples, achieving an accuracy exceeding 90%. Compared to current clinical approaches, this single-photon Raman detection technique offers significant advantages, including higher sensitivity, lower sample volume requirements, and cost-effectiveness.

These findings highlight the potential of Raman spectroscopy as a reliable and accessible alternative for PJI diagnosis, paving the way for improved early detection and better patient outcomes.

Synthesis and Characterization of Antimicrobial Elastomeric Material

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Microbial contamination in the food and healthcare industries remains a persistent challenge despite rigorous cleaning and sanitization protocols. Wearable elastomeric components such as O-rings, seals, and gaskets used in medical devices and food processing equipment often develop microscopic cracks and crevices and form ideal niches for microbial colonization and biofilm formation. Conventional approaches to sanitization of these components often involve the use of antimicrobial aerosols. However, persistent use of these aerosol products accelerates antimicrobial resistance by promoting selective pressure on microorganisms. To address this challenge, we have developed an antimicrobial elastomer in which antimicrobial agents are covalently bound throughout the material as a strategy for sustained microbial inhibition without the risk of leaching.

The antimicrobial elastomeric material was synthesized *via* the addition of a pentaamine compound, tetraethylenepentamine (TEPA) to epoxy-functionalized Ethylene Propylene Diene Monomer (e-EPDM) for subsequent quaternization with an alkyl bromide. The chemistry of the functionalized elastomer was characterized using Fourier-transform infrared spectroscopy (ATR-FTIR) and nuclear magnetic resonance (^1H , ^{13}C). Epoxidation of the norbornene moiety in EPDM was confirmed by the appearance of a band at 871 cm^{-1} in the infrared spectrum and signals at 3.02 and 3.08 ppm in the ^1H NMR. In the subsequent step, a band at $1,234\text{ cm}^{-1}$ (C-N stretching) and the quantitative reduction of epoxy-related signals at 3.02 and 3.08 ppm in ^1H NMR indicated successful introduction of TEPA into e-EPDM. Selected alkyl bromides of varying chain lengths were introduced onto TEPA-functionalized EPDM. The assessment of the antimicrobial performance of the resulting elastomeric material will be evaluated against Gram-positive (*Listeria monocytogenes*) and Gram-negative (*Escherichia coli*) bacteria. From this work, we aim to demonstrate the synthesis of covalently bound antimicrobial agents to prevent microbial growth and biofilm formation in health care and food industries, in support of reducing antimicrobial resistance.

Structure-Property Relationships and Antimicrobial Activity of Synthetic Peptide-Mimetic Polyurethanes

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The increasing concerns about antibiotic-resistant bacterial infections require an urgent need for new antimicrobial strategies. Antimicrobial peptides (AMPs), which contain short cationic and hydrophobic moieties, exhibit bacteria membrane-disruption ability, but the potential of proteolytic degradation and production cost limit further applications. To address this, synthetic peptidomimetic polymers that mimic AMPs offer improved stability, function tunability, and ease of manufacturing. Herein, we explore the antibacterial efficacy and structure-property relationships of a platform of polyurethanes, which are designed to mimic primarily lysine (cationic), valine, phenylalanine, or other hydrophobic or polar residues. These polymers were synthesized by step-growth polymerization and characterized for their antimicrobial activity, cytotoxicity, and bacterial membrane-disruptive abilities against Gram-negative strains, *E. coli* and *P. aeruginosa*, and Gram-positive bacteria, *S. aureus* and *S. epidermidis*. Results indicate that cationic/hydrophobic balance critically affects antimicrobial effectiveness. A polyurethane composed of 100% lysine-mimicking pendant groups exhibited strong antimicrobial activity against *E. coli* (MIC = 16 µg/mL) with minimal hemolysis. When combined with 20% hydrophobic units (e.g., valine or phenylalanine-mimicking units), its membrane disruption efficiency increased.^[1] We also found that poly(ester urethane) with lysine-mimetic and hydrophobic phenylalanine-mimetic pendant groups significantly compromised both outer and inner bacterial membranes in *E. coli* at 32 µg/mL.^[2] Our work established key structure-property relationships, showing how pendant group chemistry and hydrophobicity influence antibacterial activity and cytocompatibility. These findings offer a design principle for developing next-generation chemical-based antimicrobial materials.

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Decoupling Physicochemical and Chemical Interactions of *Staphylococcus aureus* and *Pseudomonas aeruginosa* using Nanoculture Systems

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Microbial interactions within polymicrobial infections are influenced by a complex interplay of chemical signaling, metabolic competition, and environmental constraints [1]. *Pseudomonas aeruginosa* (*Pa*) and *Staphylococcus aureus* (*Sa*) often coexist in such infections, where *Pa* secretes antimicrobial metabolites like pyocyanin and HQNO, challenging *Sa*'s survival through adaptive strategies [2]. This study delves into how spatial confinement and external stressors, such as high osmolarity, toxins produced by *Pa*, modulate these interactions in nanoculture systems. Employing fluorescence microscopy for real-time observation, HPLC for precise metabolite quantification, and dynamic growth analysis, we dissect the influence of *Pa*'s secreted factors on *Sa* viability. Our findings reveal an increase in *Pa*'s metabolite production in co-culture, inversely correlated with *Sa* growth. Interestingly, under high osmolarity (1M NaCl), *Sa* demonstrates enhanced survival, suggesting that osmotic stress may protect *Sa* against *Pa*'s antimicrobial actions. Additionally, alterations in the spatial dynamics observed in *Pa* motility mutants indicate that biogeography within co- cultures plays a critical role in shaping interspecies competition as occurring in multispecies biofilm. These insights not only deepen our understanding of microbial behavior under confinement but also highlight the potential of nanoculture systems as platforms for studying complex microbial ecosystems.

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Impact of attachment to a surface on macrophage engulfment of nosocomial pathogens: insights into immune evasion mechanisms

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Implantable medical devices have revolutionized the field of personalized medicine and have several applications in clinical settings. Bacterial infections on implant devices are often fatal and strongly associated with biofilms. Biofilms are antibiotic-tolerant and the immune ability to target them is still widely unexplored. Therefore, it is important to study the interaction of the host immune cells in response to biofilm infections. The goal of this study was to evaluate the ability of macrophages to engulf *P. aeruginosa* and *S. aureus* at various multiplicities of infection (MOIs), both before and after bacterial attachment. This included planktonic bacteria, bacteria adhered to tissue culture-treated surfaces, and bacteria adhered to untreated surfaces. To achieve this, experiments were performed as follows: (1) THP-1 monocytes (10^5 cells/cm²) were differentiated into macrophages and then challenged with the bacteria, and (2) bacterial cells were allowed to attach to the surface, and then macrophages (10^5 cells/cm²) were introduced. Several bacterial concentrations were used including 10 , 10^2 , 10^3 , and 10^4 cells. Macrophage assays were performed for 2 hours, after which the engulfed bacteria were quantified by cell viability and microscopy. We found that when challenged with planktonic bacteria there was a direct correlation between the inoculum concentration and the numbers of bacteria engulfed by macrophages. *P. aeruginosa* was engulfed at a significantly higher rate than *S. aureus*. However, when bacteria were pre-attached to surfaces for 2 hours, no engulfment was detected, independently of whether the plates were tissue culture-treated or non-tissue culture-treated. No macrophage killing was detected. Overall, our findings provide further evidence of the resilience of bacteria to resist engulfment once associated with a surface/device.

Characterizing the molecular details underlying biomaterial-associated infections

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Biomaterial-associated infection (BAI) is the most common complication related to the implantation of a biomaterial. BAI is mainly caused by *Staphylococcus aureus* and *Staphylococcus epidermidis*, which are commensal bacteria that can cause pathology in the presence of a biomaterial. Such infections can lead to chronic inflammation, revision surgeries, and, in severe cases, loss of function. However, the molecular mechanisms underlying BAI are not well understood.

Therefore, we aim to investigate the molecular details of the host response to BAI by studying gene expression profiles. We used a subcutaneous titanium implant *S. epidermidis* infection mouse model, including study groups of mice with only *S. epidermidis* infection to study the role of infection, and a combination of *S. epidermidis* infection with a titanium implant to study the influence of a biomaterial. We collected the tissue surrounding the surgical site at 1 hour, 6 hours, 2 days, 4 days, 9 days, 14 days, and 21 days after surgery and performed microarray analysis, quantitative culture, and histology.

Infection without a biomaterial was cleared after 9 days, while infection with a biomaterial was not cleared after 21 days. Histology showed a lower and delayed macrophage response in BAI compared to infection only. Comparing differentially expressed genes between the BAI and infection group over time can offer molecular/biological insights into the processes affected by the presence of a biomaterial. Based on these data, we aim to identify genes that characterize the host response associated with increased susceptibility to infection due to implanted titanium biomaterials. This information can be used to design follow-up experiments for more detailed studies of key molecules involved in BAI, and can potentially aid in the design of biomaterials not increasing susceptibility to infection.

The fungicidal activity of novel graphene quantum dots against *Candida auris* and *Candida albicans* species

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Candida auris is an emerging opportunistic pathogen that can cause serious infections, for example catheter-related blood stream infections, which result in high morbidity and mortality rates. The traditional antifungal treatment with polyenes, azoles, allylamines or echinocandins is becoming less effective due to resistance development, complicating the treatment of candidiasis. Risk groups for these infections include patients with prolonged hospital stay or a compromised immune system. To combat the rising antifungal resistance, nanoparticles such as graphene quantum dots (GQD) could serve as an alternative treatment. GQD consist of a single layer of carbon atoms arranged in a honeycomb-like structure with photo-activation properties. When activated by light of a specific wavelength, GQD can generate reactive oxygen species (ROS), which have broad microbicidal activity, including fungicidal activity.

This study aimed to evaluate the fungicidal activity of newly developed carboxyl-functionalized graphene quantum dots (cGQDs) against a panel of *C. auris* strains, spanning clades I to V, and *Candida albicans*. The minimal microbicidal concentration assay was used to assess the microbicidal activity of colloidal cGQDs. Photo-activation with a 435nm blue LED light at a light intensity of 5 mW/cm² for 30 minutes showed 99.9% killing of fungi at a range of 12.5 – 25 µg/ml cGQDs for the *C. auris* strains and at 50 µg/ml cGQDs for the *C. albicans* strain. In addition, we developed a novel thin film with alternating layers of cGQDs and polymer applied on glass slides and we tested its surface fungicidal activity using the Japanese Industrial Standard assay. The cGQDs thin film showed promising fungicidal activity against both *C. auris* and *C. albicans*. These findings show that the cGQDs, both in colloidal state and as thin film, have potential for future application to for instance wound dressings or catheters to prevent or treat *Candida* infection, including infections with the difficult to treat *C. auris*.

An Optical Aptamer-Based Cytokine Nanosensor Detects Macrophage Activation by Bacterial Toxins

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Overactive or dysregulated cytokine expression is hallmark of many acute and chronic inflammatory diseases. This is true for acute or chronic infection, neurodegenerative diseases, autoimmune diseases, cardiovascular disease, cancer, and others. Cytokines such as interleukin-6 (IL-6) are known therapeutic targets and biomarkers for such inflammatory diseases. Platforms for cytokine detection are therefore desirable tools for both research and clinical applications. Single-walled carbon nanotubes (SWCNT) are versatile nanomaterials with near-infrared fluorescence that can serve as transducers for optical sensors. When functionalized with an analyte-specific recognition element, SWCNT emission may become sensitive and selective towards the desired target. SWCNT-aptamer sensors are easily assembled, inexpensive, and biocompatible. In this work, we introduced a nanosensor design based on SWCNT and a DNA aptamer specific to IL-6. We first evaluated several SWCNT-aptamer constructs based on this simple direct complexation method, wherein the aptamer both solubilizes the SWCNT and confers sensitivity to IL-6. We tested the sensor against a range of IL-6 concentrations to determine its limit of detection. Continuous acquisition of fluorescence spectra during nanosensor deployment allowed us to investigate sensor kinetics. To test the sensor's ability to detect endogenous IL-6, we treated Raw 264.7 cells with lipopolysaccharide (LPS). These activated macrophages expressed elevated levels of IL-6, as confirmed by ELISA. We deployed our nanosensor in conditioned media from the activated macrophages and compared its response to the cytokine levels measured with ELISA. We identified a 31-nucleotide DNA aptamer that enabled sensitive and specific detection of IL-6 in a variety of testing conditions. The sensor limit of detection, 105 ng/mL, lies in the relevant range for pathological IL-6 levels. Upon investigation of sensor kinetics, we found rapid response within seconds of antigen addition which continued over the course of three hours. We found that this sensor construct is stable, and the aptamer is not displaced from the nanotube surface during IL-6 detection. Finally, we confirmed the ability of this sensor construct to detect macrophage activation caused by LPS in an in vitro model of disease, finding rapid and sensitive detection of macrophage-expressed IL-6. We are confident further development of this sensor will have novel implications for diagnosis of acute and chronic inflammatory diseases, in addition to contributing to the understanding of the role of cytokines in these diseases.

Determining the Metabolic Product of Biofilm-Mediated Biodegradation for the Design of New Enzyme-Responsive Smart Polymers

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Biofilm-mediated biofouling, or rather the formation of biofilms by bacteria and algae on moist surfaces, is a complex production which can lead to destructive structural and functional alternations. To combat against this, an investigation was launched of the activity of enzyme-responsive materials designed to interact with the enzyme chitinase, the enzyme that breaks down chitin. A process which aims to link the material properties of enzyme-responsive polyolefin to their performance in inhibiting and removing bacterial attachment. To observe and examine this removal, proton nuclear magnetic resonance ($^1\text{H} - \text{NMR}$) spectroscopy was used to identify the biodegradation product which caused the detachment of PAO1 biofilms. After analyzing the resulting spectra, biodegradation products were able to be identified showcasing no PAO1 biofilms, with PAO1 biofilms, transparent (NT) products, and supernatant of PAO1 cultures. These results at varying conversion suggest composition changes during biodegradation. Interestingly, within the results an antimicrobial cationic surfactant cetyltrimethylammonium bromide (CTAB), was identified in the supernatant of PAO1, possibly explaining the antifouling efficacy of the degradation products. In this study, we aimed to identify plausible chemical components of the biodegradation products and analyze the variations in intensity of the components. To specify, it was decided to identify the metabolites within the products by using a 50% methanol extraction technique for ($^1\text{H} - \text{NMR}$) spectroscopy sample preparation. By using this technique, methanol as a polar solvent effectively extracts a diverse set of polar metabolites and many other small molecules present in biological samples. We additionally decided to sample both the methanol and chloroform layers, which resulted from phase separation, in order to analyze potential polar and nonpolar components. From this, preliminary results were obtained which presented a mixture of amino acids, such as tryptophan, threonine, serine, and valine, which showed varying intensities when comparing the control samples to the experimental. Once the planned confirmatory test of liquid chromatography mass spectrometry confirms the identification of the components and their intensities within the biodegradation products, the nature of the biodegradation can be explored optimizing antifouling efficacy. With successful implementation of this project's goals, a framework for development of a unique new antifouling strategy can be created.

Effects of skin thinning on bacterial biofilm formation

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Bacteria, such as *Staphylococcus aureus* and *Pseudomonas aeruginosa* (PAO1), form biofilms. Because biofilms are often resistant to antibiotics, it raises concern for those more susceptible to infection via skin. As people age, their skin elasticity decreases, thus increasing their pore size, ultimately affecting elders and individuals with skin conditions. In this study, we aim to test the correlation between pore size, skin elasticity, and infection. We hypothesize that an increase in pore size caused by the decrease in skin elasticity allows for greater bacterial penetration and subsequent biofilm formation mediated infection. To test this hypothesis, we used porcine skin as a medium for manual skin stretching, and the percent change in recovery of the skin was used to determine the change in elasticity when repeatedly stretched and released. Throughout seven trials, it remained consistent that the percent recovery of length linearly increased. The average percent change in recovery of the skin is $-9.180\% \pm 3.613\%$. The next step would be to use microscopy and image analysis to calculate the change in pore size of both unstretched and stretched skin. Additionally, testing how other factors such as UV exposure and different areas of the body stretch differently would also be of interest to further our research.

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Initial Organ-On-A-Chip Development for Controlling and Quantifying in situ Bacterial Biofilm/Macrophage Biochemistry

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Bacterial biofilms are a major problem in healthcare because they can resist the body's immune system and treatment with antibiotics, making infections harder to cure. Utilizing the concepts of macrophage activation for infections, the polarization state of macrophages may play a crucial role in affecting outcomes of biofilm infections. To better study these interactions requires exquisite control of macrophage and biofilm interactions. Such control can be achieved by considering organ-on-a-chip approaches. An initial polydimethylsiloxane (PDMS)-based organ-on-a-chip device was fabricated using soft lithography. The surface of the chip was functionalized with a polydopamine coating, which was prepared by dissolving dopamine in tris-HCl buffer at pH 8.5, to enhance cellular adhesion and biocompatibility. THP-1 cells, were cultured in 89% (v/v) RPMI-1640 medium, 10% (v/v) FBS, and 1% (v/v) antibiotic-antimycotic solution. Monocyte counts were performed using a hemocytometer with a 1:1 ratio of trypan blue and cell culture medium, and 1.0×10^6 cells/mL were added to each flask. Cytokine secretion, specifically CCL2, was quantified using ELISA. Nitric oxide secretion is quantified using the Griess reaction. Data obtained using the organ-on-a-chip device will be compared to standard microdialysis collections from cell culture.

Co-culture Optimization for Bacterial Biofilm/Macrophage Analysis

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Healthcare-associated infections (HCAs) are a direct result from treatment within a clinical setting and impact two major areas, patient well-being and financial costs. Bacterial biofilms are the leading cause of these infections due to the complex extracellular matrix and phenotypic changes, which significantly alter their behavior. This creates challenges when trying to study interactions between host cells and the biofilm. Co-culture models are a synthetic tool used to achieve a coordinated interactions between two populations, such as biofilms and host immune cells. However, the current state of the art prevents the continuous supply of nutrients and removal of waste products, leading to a short life cycle and therefore the inability to fully understand the mechanisms behind this type of infection. This study aims to optimize the co-culturing process to better assess the immune responses and characteristic changes during a bacterial biofilm infection. The design of the system includes a two-peristaltic pump model that would be able to sustain the flow of nutrients for the macrophages during an infected state and control the outflow of waste to a sampling port. A dual flow model could modulate key components within the co-culture environment, including the pH. This model would be more ideal as it aims to mimic an in-vivo system with the regulation of nutrients, metabolic waste, and pH.

Antimicrobial Hemostatic Shape Memory Polymer Foams for Infection Prevention in Traumatic Wounds

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The primary cause of trauma-related deaths is uncontrolled hemorrhage (1). Within a week following injury, 39% of traumatic-wound patients develop a polymicrobial infection (2). Coupled with the high incidence of antibiotic resistance, which alone is responsible for 100,000 deaths annually (3), there is a critical need for hemostatic agents with infection prevention capabilities for use in traumatic wounds. Under biofilm protection, bacteria become resistant to antibiotics and immune responses, which increases the difficulty of treating infections; thus, biofilm inhibition is necessary in any wound healing system. Previous studies have shown the successful incorporation of antimicrobial phenolic acids (PAs) into hemostatic shape memory polymer (SMP) foams by two mechanisms (chemical and physical) to produce dual phenolic acid (DPA) foams, which demonstrate excellent antimicrobial and antibiofilm properties against native *E. coli*; native and drug-resistant *S. aureus* and *S. epidermidis*; and co-cultures of *E. coli* and *S. aureus* (4). Here, we further characterize these foams' long-term antibacterial and antibiofilm capabilities.

Synthesized foams containing vanillic acid (DVA), ferulic acid (DFA), and p-coumaric acid (DPCA) were exposed to methicillin-resistant *S. aureus* (MRSA) and *E. coli*. Resulting biofilms were examined by scanning electron microscopy (SEM) and confocal laser scanning microscopy (CLSM). SEM images showed reduced biofilm attachment on DPA foams, with DVA and DPCA showing the most promising antibiofilm properties against MRSA. 3D images from CLSM confirmed reduced *E. coli* biofilm biomass on DPA foams. To further quantify long term antimicrobial properties, metabolic activity analysis through intracellular adenosine triphosphate (ATP) levels was performed. ATP luminescence assay showed reduced bacterial metabolic activity in DPA foams after subjecting to biofilm forming conditions for 24 and 72 hrs. DPA foams are currently being tested against other fluorescently labelled bacteria strains in biofilm-forming conditions to further characterize their antibiofilm properties. An *ex vivo* porcine skin model will be used to assess biofilm formation, metabolic activity, and colony forming units (CFUs) of different native and drug-resistant bacteria strains over a 7-day period. Ultimately, this work will provide antimicrobial hemostatic dressings to reduce uncontrolled hemorrhage and subsequent infection in traumatic wounds.

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Biofilm Attachment and Survival on Next Generation Antimicrobial Scaffolds

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Device associated infections (DAIs) are considered one of the largest major complications associated with modern medical technologies. Each year, millions of medical devices are temporarily or permanently implanted in humans to administer treatments or replace failing body components. Unfortunately, these life-saving devices can become contaminated by invading bacteria with the ability to compromise the effectiveness of the device as well as the overall health of the patient. Devices are often contaminated due to the existence of microbes within the operating room (OR) from ventilation systems, sneezing by OR personnel, traffic to and from the room, and shedding from clothing. Device-associated biofouling occurs when bacteria opportunistically adhere to and proliferate on the device surface to form biofilms. Once a biofilm has been established it is 10 - 1,000 times more tolerant to antimicrobial agents compared to the same bacteria in bulk liquid suspension, resulting in a persisting and challenging infection to treat. Therefore, we present a self-defensive surface capable of reducing bacterial attachment. A polycaprolactone (PCL) 3D-printed scaffold with anionic microgels deposited on the surface and loaded with Sub5, a cationic antimicrobial peptide, targets bacteria in a contact dependent manner. Sub5 is preferentially released through bacterial contact due to electrostatic interactions between the negatively charged bacterial membrane and the positively charged antimicrobial peptide. To mimic OR contamination, Sub5 loaded and unloaded PCL scaffolds were added to relevant concentrations of cells in suspension for two hours. Samples were then washed, centrifuged, and plated. We demonstrated a 75% reduction in *Staphylococcus aureus* survival and a 40% reduction in *Pseudomonas aeruginosa* survival on the Sub5 modified surface compared to the control surface lacking Sub5. Furthermore, LIVE/DEAD staining confirmed an increased amount of dead cells for both bacterial strains when cells were incubated with the Sub5-modified scaffold demonstrating the success of a self-defensive surface so far.

The Smarter the Foam, the Better the Healing: Vanillic Acid-Incorporated Polyurethane Shape Memory Polymer Foams for Hemorrhage and Infection Management

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Each year, ~1.5 M fatalities occur due to uncontrolled bleeding in traumatic wounds (1-3) with those receiving life-saving immediate medical aid remaining highly vulnerable to infection. There is thus an urgent clinical need to develop a biocompatible, procoagulant, hemocompatible, low-cost, and antimicrobial hemostatic dressing. Because of their excellent biocompatibility, rapid clotting, non-damaging pressures, and wound-filling properties, shape memory polymer (SMP) foams are a potential answer to this unmet need. We earlier chemically incorporated vanillic acid (VA), a type of phenolic acid, into SMP foams. The resulting VA foams demonstrated antioxidant, cytocompatibility, and hemocompatibility characteristics and antimicrobial features against drug-resistant bacteria, showing promise for use as a comprehensive hemorrhage control dressing (4-7). Here we used both chemical and either 1-day (1DVA) or 3-day (3DVA) physical incorporation methods to develop dual vanillic acid (DVA) foams with elevated VA content.

To evaluate their potential as clinical wound dressings, firstly, VA release from DVA foam samples was measured for up to 3 days, and the cumulative release profile showed that physical incorporation increased VA release, with the highest VA release from 3DVA foams. The hemolysis assay conducted with anticoagulated porcine blood demonstrated that DVA foams induced <5% hemolysis and are therefore non-hemolytic. Antimicrobial studies were performed against *E. coli* and native and drug-resistant strains of both *S. aureus* and *S. epidermidis* for 1-, 6-, and 24-hour time points, and results demonstrated 8-9 log reductions in colony forming units (CFUs) at 24 hours compared to clinical control groups. Lastly, to understand *in vivo* wound healing efficiency of our antimicrobial DVA foams, a SAS Sprague Dawley albino rat infected wound model was used for 4, 8, and 12-day periods. Bacterial burden, wound closure, and histological assessment data showed that 3DVA foams promote wound healing and limited bacterial burden in the wounded area.

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Material properties of interfacial films of *Brucella pituitosa*

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Colloidal interactions in solution are a research domain of practical importance in health, personal care, and oil industries. In the last 20 years, interest in active colloids at fluid interfaces has grown. Among these, microorganisms are notable due to their movement in suspension under external fields or self-propulsion (1,2). The dynamic interaction of microbial cells with energy-rich interfaces causes them to adsorb and become trapped, modifying interfacial properties and lowering the free energy of the system (3). However, very little is known about how interfacial tension and associated stresses affect microbial physiology or trigger adaptive responses at fluid interfaces (4). Here, we are investigating *Brucella pituitosa* (BU72), a newly discovered strain isolated from hydrocarbon-polluted Tunisian sediment. The strain exhibits intriguing interfacial behavior by secreting a surfactant-enriched exopolysaccharide (EPS) films while interacting with oil (5). We seek to explore the viscoelastic properties of BU72's EPS across different interfacial energies. We hypothesize that BU72 adapts to energy-rich confinements through carbon source consumption, with the complexity of its EPS being highly dependent on both the available carbon source and interfacial energy levels. To investigate BU72's response to interfacial tension, BU72 films at the air-water and oil-water interfaces were characterized using rheometry and tensiometry to assess how interfacial energy influences EPS structure and viscoelasticity. Interfacial dilatational rheology provided insights into the dynamic mechanical properties of the secreted biosurfactant. SEM/STEM imaging revealed how the structural integrity of BU72's film is altered by interfacial stress, while NMR spectroscopy revealed compositional changes in EPS under different carbon sources. Altogether, these approaches elucidate how BU72 adapts to interfacial confinement and modulates its EPS production in response to environmental stresses. This research lays the foundation for developing novel bacteria-derived biomaterials with potential applications in crude oil bioremediation.

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Eradicating *Candida auris* through Physiological Stress and Drug Permeation using Low-Level Direct Currents

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Candida auris (*C. auris*) is an emerging multidrug-resistant (MDR) yeast responsible for hospital outbreaks worldwide, with mortality rates reaching 60% in invasive infections. Its misidentification, high persistence, and antifungal resistance create a severe challenge for treatment, highlighting the urgent need for new therapeutic strategies. This study explores electrochemical therapy (ECT) as a novel solution against *C. auris*, investigating the impact of low-level direct currents (DCs) on cell viability, morphology, functions, and antifungal potentiation. A *C. auris* cell solution was exposed to ECT treatments for 1h using three current densities (17.5, 35, and 70 $\mu\text{A}/\text{cm}^2$ DC). Results revealed a 99.998% reduction in *C. auris* viability at 70 $\mu\text{A}/\text{cm}^2$ DC, with the most significant morphological alterations observed through SEM. Additionally, performing flow cytometry using Rhodamine 123 and H2DCFDA allowed access to ECT's effect on membrane potential and intracellular levels of reactive oxygen species (ROS). Flow cytometry scatter plots revealed ECT-induced changes in cell size (forward scatter, FSC) and intracellular composition (side scatter, SSC), and the histograms showed increased fluorescent intensity for both dyes, indicating alterations in cellular functions. Furthermore, the combined effect of ECT and antifungal was examined from time-dependent diffusion studies using BODIPY-labeled caspofungin (CSF-BOD). ECT-treated cells at 17.5 $\mu\text{A}/\text{cm}^2$ DC showed rapid drug adherence after 5 minutes, with significant caspofungin uptake after 15 minutes. In contrast, untreated cells exhibited minimal drug uptake after 60 minutes. These findings demonstrate that ECT is a promising alternative for addressing MDR pathogens like *C. auris*. Future research aims to implement ECT through medical devices.

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Rapid Bacterial Identification and Antimicrobial Susceptibility Testing to Improve Diagnostics and Treatment in Oral Healthcare

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Antibiotic-resistant bacteria pose a significant challenge in detecting and treating infections. Infections related to oral disease can lead to severe periodontal complications, including tissue destruction, tooth loss, and bone damage, ultimately impacting quality of life. Current diagnostic methods for identifying pathogens in oral disease are slow and complex due to the diverse bacterial population in the oral cavity. Furthermore, oral infections have been linked to systemic health issues such as cardiovascular disease, diabetes, respiratory infections, and sepsis, highlighting the need for effective prevention and treatment strategies (1-3). Understanding bacterial proliferation is crucial for predicting the spread of disease and improving treatment outcomes. Traditional methods rely on labeling bacteria with markers, which is time-consuming and impractical for clinical applications requiring rapid analysis. Rapid bacterial detection and identification is essential, as delayed treatment can increase mortality rates by up to 8% per hour (4). A promising alternative is a culturomics platform—the nanoculture, a droplet-based microsystem that encapsulates oral microbes. The nanoculture systematically controls, cultivates, and analyzes microbial community dynamics focusing on swimming behavior, growth patterns, and interspecies interaction (5). In this study, we are developing a python-based machine-learning solution to detect and analyze bacterial motion, enabling species differentiation based on movement patterns. This approach will enable rapid detection and identification of bacterial species, predicting microbial pathogenicity and antimicrobial susceptibility based on bacterial motility and growth patterns (6). This novel strategy will enhance the diagnosis of microbial resistance in periodontal disease, transforming diagnostic care and improving patient outcomes.

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Engineering DNA Origami Nanostructures for the Detection and Elimination of *Candida auris*

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Candida auris is a multidrug-resistant (MDR) fungus that is categorized as an urgent threat by the CDC (1). The mortality rate for patients with an underlying condition infected with *C. auris* is 60%. Current treatments rely on three major classes of antifungals: azoles, polyenes, and echinocandins, but *C. auris* has evolved resistance, with some strains exhibiting pan-resistance. The primary challenges associated with *C. auris* are misdiagnosis and antifungal resistance. The increasing threat posed by *C. auris* necessitates novel detection and control strategies (2). DNA origami is a promising nanotechnology-based approach for developing target-specific antifungal strategies. DNA origami nanostructures are assembled from complementary DNA sequences, where a long single-stranded DNA scaffold hybridizes with short staple strands to form precise 3D structures (3). We are designing three structures of DNA which are nanorods, nanotiles and nanospheres. These nanostructures can be functionalized with aptamers and biotin to enhance specificity (4). Gel electrophoresis and atomic force microscopy (AFM) will be used to characterize the DNA origami, while scanning electron microscopy (SEM) and transmission electron microscopy (TEM) will be employed to study *C. auris*. The interaction between DNA origami and *C. auris* will be characterized via confocal microscopy. This study aims to design and evaluate DNA origami-based nanostructures for targeted *C. auris* binding and investigate their potential as a novel antifungal strategy. Future experiments will focus on binding and efficiency to then assess antifungal activity in controlled conditions.

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Optogenetic engineering of *Escherichia coli* for high-level persistence

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Biofilms are complex communities of microorganisms that can attach to surfaces and exist within a self-produced matrix of extracellular polymeric substances. Biofilms can contain up to 1000 times more persister cells than planktonic (free-floating) bacteria. Persister bacteria are implicated in the resilience of biofilm infections to therapeutics, which are of major concern in the failure of implanted medical devices and prosthesis. Therefore, engineering a genuine persister model for use on a plethora of biomaterials would aid in the development of anti-persister and anti-biofilm strategies. The study of persister cells is challenging, however, due to the stochastic nature of persister formation and low persister count in conventional culturing systems (<1%). To address this challenge, we engineered a new method that can precisely control persistence in *Escherichia coli* by controlling the expression of the toxin gene *hipA* and thus inducing persister formation using blue light. Optogenetic control resulted in 100% persistence in both planktonic cultures and surface-attached biofilms when challenged with ofloxacin & ciprofloxacin, and the persistence level can be controlled by light intensity and exposure time. Transcriptomic analysis of blue light-induced persisters revealed gene expression profiles comparable to those induced by the conventional method of arabinose-driven *hipA* expression. Fluorescent growth rate reporter tagging of biofilms and planktonic cultures also provides for real-time identification of persister cells with reduced fluorescent signals and demonstrates the dynamic range between light and dark states. The use of light provides an unprecedented opportunity for spatial control of persistence, which will enable the screening of new anti-biofilm agents both *in vitro* and *in vivo*.

Effect of Interfacial Stress on *P. aeruginosa* Film Composition & Mechanical Properties

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Pseudomonas aeruginosa is an opportunistic pathogen which primarily infects cystic fibrosis (CF) patients and causes infections in burn and wound patients (1). In CF patients, *P. aeruginosa* secretes a mucoidal film that can exacerbate airway blockages. The overproduction of extracellular polysaccharides like alginate protects *P. aeruginosa* from common treatments such as antibiotics and mucolytic drugs. In this study, we aim to elucidate structural and compositional properties of *P. aeruginosa* biofilm that contribute to its persistence in patients (2). To this end, we studied the commonly characterized *P. aeruginosa* PAO1, the alginate overexpressing PAO1*mucA22*, and a mucoid strain isolated from a cystic fibrosis patient (PASL). Nuclear Magnetic Resonance (NMR) compositional analysis of isotope labeled biofilm structures were performed to determine nutrient sources and biofilm composition (3). Tensiometry and rheology measurements were used to quantify interfacial tension and film elasticity, along with biofilm flow behavior and interfacial mechanics (4). Scanning Electron Microscopy (SEM) and Scanning Transmission Electron Microscopy (STEM) imaging of bacteria and biofilm characteristics provided insights into morphology and cell damage under differing interfacial stresses (5). Overall, these results elucidate how interfacial stresses dictate the mechanical properties of *P. aeruginosa* films under interfacial confinement. Understanding the mechanobiology of *P. aeruginosa*, especially of clinically derived specimens, is essential for designing novel strategies to control infection under interfacial stresses.

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Microfluidic platforms for studying *in vitro* infection dynamics of *Babesia microti* in ovine blood

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Babesia microti is an emerging tick-borne pathogen responsible for human babesiosis, a disease with increasing clinical relevance according to the CDC [1]. *In vitro* cultivation and testing with *B. microti* remains challenging, with most researchers relying on *in vivo* cultures in mouse models [2]. Due to this, it can be difficult to capture infection dynamics of the parasite. To address this issue, we are developing microfluidic-based culturing platforms to support growth of *B. microti* in native and atypical biological materials, including human and ovine blood. The ability to culture *B. microti* with alternative blood sources, such as those derived from meat industry waste, reduces ethical and logistical constraints associated with mouse models. In this study, two microfluidic platforms are utilized: (1) a flow focusing microfluidic device to generate nanocultures with semipermeable PDMS shells, allowing for high-throughput detection and cultivation of *B. microti*; (2) an exclusive liquid repellency empowered under-oil open microfluidic system to maintain a monolayer of red blood cells, facilitating real-time assessment of *B. microti* dynamics [3-4]. These systems allow us to investigate preferred microenvironments, infection mechanisms, replication cycles, and host-specific interactions. Complementary analyses with confocal, SEM, and TEM imaging indicate that *B. microti* can invade and reproduce into ovine red blood cells, which were believed to only infect humans and rodents. Our results demonstrate the abilities of *B. microti* to utilize intra- and extra-cellular hemoglobin for proliferation, advancing the development of alternative culture methods for *B. microti*. Future work will aim to optimize microcapsule shells for better nutrient diffusion, as well as optimizing culture conditions and nutrient supplementation to facilitate the growth of *B. microti in vitro*.

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Characterization of multispecies biofilm dispersion induced by *cis*-2-decenoic acid and by a step-change increase in nutrient loading.

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Biofilms are structured microbial communities encased in an extracellular polymeric substance (EPS) matrix and pose significant healthcare challenges due to their strong adherence to surfaces, resistance to antimicrobial treatments and immune clearance. Dispersion is the final stage in the biofilm life cycle, facilitating bacterial survival by relieving overcrowding and enabling the colonization of new niches, thereby contributing to biofilm persistence and the transmission of biofilm-associated diseases. This highly regulated process is driven by various factors, including nutrient availability and cell signaling molecules (eg: *cis*-2-Decenoic Acid). Nutrient induced biofilm dispersion is a phenomenon where biofilms formed under nutrient-limited conditions, disperse in response to a step increase in nutrients –such as glucose or amino acids– by releasing cells into the overlying bulk environment. Nutrients can trigger metabolic reprogramming, leading to the production of enzymes that degrade key components of the biofilm matrix, further promoting dispersion. The cell-to-cell communication molecule *cis*-2-decenoic acid (*cis*-DA), produced by *Pseudomonas aeruginosa*, is a fatty acid that induces biofilm dispersion in Gram-negative and Gram-positive bacteria. Although, Dispersion has been extensively studied in gram negative single-species biofilms, there is limited research on Gram-positive and multi-species biofilm dispersion. This study investigated exogenous dispersion in multi-species biofilms of *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and *Staphylococcus epidermidis* by a step-change increase in concentration of brain heart infusion (BHI) medium and by induction of dispersion with *cis*-DA (310 nM). Results indicated that dispersed cells as a percentage of total biofilm cells consistently ranged between 50% to 60% for single, dual and three species. Although *Pseudomonas* partially inhibits the biofilm formation of both *Staphylococcus* species in dual- or three- species environments compared to their single-species biofilms counterpart. Research on multispecies biofilm dispersion could lead to greater insight into the mechanisms of how these communities regulate and maintain their structure and survival and potentially reveal key targets for antibiofilm chemotherapeutic interventions.

Machine Learning Driven Optimization of Peptoid Antimicrobial Coatings for Infection Prevention

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Implant-associated infections impact nearly one million patients annually, leading to prolonged treatments, multiple surgeries, and amputations. Addressing this requires innovation in prevention, detection, and cure. We investigate peptoids—biocompatible, sequence-specific, cationic polymers—as antimicrobial coatings for medical implants, focusing on biofilm prevention and disruption.

Using computational modeling and experimental validation, we evaluate peptoid-hydrogel complexes on titanium surfaces. Small-angle X-ray scattering (SAXS) reveals that peptoid self-assembly, governed by sequence composition and hydrophobicity, influences antimicrobial activity. We established a design space of 2,187 peptoids, computationally screening 150 candidates based on charge, aromaticity, and halogenation. Machine learning-driven selection enables microsecond-scale simulations to optimize 10–20 peptoid coatings for experimental validation.

By integrating computational modeling, biophysical characterization, and antimicrobial testing, this study provides a translational pathway for peptoid coatings from development to clinical application. We explore their role in reducing healthcare disparities, improving infection outcomes, and advancing biofilm-resistant medical implants, aligning with the goals of antimicrobial prevention, detection, and clinical translation.

Additionally, we investigate the long-term stability and biocompatibility of these coatings to ensure their safety and efficacy in clinical settings. Future work will focus on scaling up production and conducting in vivo studies to accelerate the translation of peptoid-based coatings into real-world medical applications.

On-Demand Biofilm Removal by Shape Memory Triggered Changes in Surface Topography

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Bacterial pathogens form biofilms on implantable biomedical devices, which are highly tolerant to antibiotics. Previously, we reported a new strategy for biofilm removal using dynamic topography via horizontal changes of the bulk material shape of a memory polymer (SMP) [1]. In this study, we further developed this method by testing the hypothesis that biofilm can be removed by vertical changes in the topography alone without altering the bulk shape of the substrate material. An acrylate-based SMP was prepared with a transition temperature of 40 °C to trigger the shape recovery under aqueous condition within 10 min. Instead of the uniaxial stretching done in our previous study, we created a series of micron-scale patterns on the SMP surface by hot compression to create the temporary shape. This allows dynamic changes in surface topography during shape recovery while maintaining the bulk shape of the material. To investigate if the shape and dimension of the surface patterns affect biofilm removal, we created three recessive square-shaped patterns on polydimethylsiloxane (PDMS) molds, and three line patterns on resin-based molds fabricated with 3D printing. Then the programmed SMPs were prepared via thermal compression to create complementary micro-topographies. Biofilm removal was assessed using 3D fluorescent imaging and biomass quantification. The square-shaped patterns with spacing and length of 5 µm, 10 µm, or 50 µm achieved up to ~70% removal of *Escherichia coli* biofilms with almost complete shape recovery. Similarly, larger deformation with 100 µm and 200 µm tall line patterns removed *Pseudomonas aeruginosa* biofilms by $66 \pm 9 \%$ and $77 \pm 6 \%$, respectively. Overall, the results from this study demonstrated the feasibility to remove established biofilms without changing the shape of the bulk material. These findings are helpful for engineering better antifouling materials.

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Sensitivity & Specificity of a Bacterial Protease-Responsive Polyurethane Shape Memory Polymer for Chronic Wound Infection Surveillance

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Current clinical options for chronic wound biofilm detection and quantification are limited in their accuracy, and efficiency¹. We developed a segmented polyurethane (PUR-PEP) shape memory polymer that changes shape in the presence of bacteria to aid in biofilm monitoring in clinical settings². The purpose of this study was to determine the sensitivity and specificity of the material towards bacterial proteases.

Strained PUR-PEP samples (n=3) were incubated in mammalian enzymes (matrix metalloproteinase-1, trypsin, collagenase I and lysozyme), and in bacterial enzymes (*S. aureus* V8 and beta-lactamase) at 37°C for 10 days. Additionally, strained PUR-PEP samples (n=3) were incubated in serial dilutions of *S. aureus* V8 enzyme (500 units) for 7 days at 37°C. Sample dimensions were measured using digital calipers, and recovery ratios were determined based on change in length over time.

Strained PUR-PEP samples underwent significant shape recovery (~55%) ($p < 0.05$) in both mammalian and bacterial enzymes. The material also recovered all the concentrations of the *S. aureus* V8 enzyme, although recovery was larger in higher concentrations of the enzyme, and there was a significant association between enzyme concentration and shape recovery ($F(13,28) = 12.47, 0.001$).

PUR-PEP recovery in mammalian enzymes indicates that the material chemistry requires tuning to improve its specificity towards bacterial proteases. However, the material recovery in all *S. aureus* V8 enzyme concentrations indicated high sensitivity and the potential to be utilized in detecting low grade or early infections in chronic wounds. These results conveyed the potential to use our PUR-PEP system to provide a visual cue of infection in chronic wounds to improve surveillance efforts.

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Fatty acid ionic liquids as antimicrobials

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Antibiotics have become critical in modern medicine, but with that has also come antibiotic resistance. In order to combat this, novel antimicrobials and novel applications of existing antimicrobials is necessary. This includes combinatorial delivery and application of multiple antimicrobials or the combination of an antimicrobial and efficacy enhancer. Ionic liquids are molten salts, liquid at room temperature in the absence of solvents. Ionic liquids are inherently flexible and diverse, with many many having mix-and-match compatibility between cations and anions to create a wide variety of molecular species. Biocompatibility of ionic liquids has been an area of great interest in the last 15-20 years, with increasing focus on how these molecules interact with proteins and lipid bilayers. Some ionic liquids have the ability to destabilize bacterial membranes which make them inherently antimicrobial, but can also improve the delivery of other antimicrobials. We evaluated several fatty acid ionic liquids by testing various ionic liquids with differing alkyl chain lengths and different biologically compatible cations for individual and combinatorial antimicrobial activity. These compounds were screened against a panel of clinically relevant bacteria including *E. coli*, *S. aureus*, *K. pneumoniae*, and *A. baumannii*

Influence of growth media on efficacy of antimicrobial metals

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Superbugs, the inducers of “hard-to-treat” infections, are an ever increasing concern. Many pathogens have specialized functions to render traditional antibiotic therapies ineffective. This continuous challenge holds a greater impact on the immunodeficient; this is often associated with extended hospitalization, alongside procedures endured during such visits. Those who receive biomedical implants, such as stents or pacemakers, often experience such immunodeficiency; it is during these operations that the body is most susceptible to contamination, and subsequent infection. This study is surveying for the antimicrobial efficacy of various metal ions for the application to thin film coatings on biomedical devices. By coating biomedical implants with such metals, the implant surface itself may serve as an antimicrobial agent to resist colonization and/or elute antimicrobial ions to address infections in the area of the implant. This study evaluates the efficacy of silver nitrate (AgNO_3), copper sulfate (CuSO_4), magnesium sulfate (MgSO_4), and zinc sulfate (ZnSO_4) against clinically relevant bacteria. Notably, many pre-clinical studies have demonstrated varying efficacy of different antimicrobial metal ions, of which may be linked to varied growth conditions between studies. Thus, bacteria were sampled in three different nutrient media: Luria Bertani (LB), Mueller Hinton (MH), and Nutrient broth (NB). Surveyed species include *Escherichia coli*, *Staphylococcus aureus*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, and *Bacillus subtilis*. The principal method employed is the minimal inhibitory concentration assay (MIC), with growth curve techniques additionally employed to monitor live growth of bacteria during their logarithmic growth phase. AgNO_3 exhibited the highest antimicrobial activity, followed by ZnSO_4 , then CuSO_4 , with MgSO_4 posing little to no activity. Antimicrobial efficacy was highest in NB media, followed by MH, with LB media demonstrating the least activity. These results can be attributed to robustness of growth of the bacteria in each media type, but ongoing work is aimed at evaluating the role of total ion content and non-antimicrobial metals with the bacteria and the correlation to efficacy of antimicrobial metals.

Influence of environmental conditions on dissolution properties of antimicrobial thin-film coatings

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The past 20 years have witnessed a significant rise in bacterial resistance to nearly every approved antibiotic on the market, and thus it is imperative that novel antibiotics are developed to combat the rise of antimicrobial resistance. In 2019 alone, antimicrobial resistance was directly responsible for the deaths of at least 1.7 million people worldwide, and contributed to the deaths of nearly 5 million people. Patients that receive biomedical implants are especially susceptible to infections that can complicate the recovery process, as 50-70% out of the 2 million nosocomial infections reported by the Centers for Disease Control (CDC) were due to medical implants. Mortality rates caused by infected biomedical implants are device dependent, and thus can highly vary from less than 5% (dental implants) to over 25% (mechanical heart valves). Additionally, delivering antibiotics to the site of infection for bone and joint implants is challenging due to reduced vascular access. This is further complicated by the prevalence of bacterial biofilm formation on these devices which provides an added challenge to antibiotic treatment. As a result, investigation into biomedical implants with thin-film coatings has emerged as a potential solution to treat infected implant sites. These thin-film coatings typically contain one or more metal species that provide antimicrobial activity. Silver has been shown to be one of the most effective as an antimicrobial agent both on the surface of the implants and when eluted into the environment around the implant. This work aims to characterize the kinetics, environmental conditions, and formation of nanoparticles for maximal silver elution. Cyclic voltammetry analysis of the coatings demonstrate the ability of the different coatings to elute into solution upon application of a current. Silver elution analysis via ICP-MS revealed that silver(II) oxide (Ag_2O) coatings are most effective at releasing high concentrations of silver compared to silver(I) oxide (AgO) and pure silver (Ag) coatings. Furthermore, water (H_2O) provides the optimal environmental conditions for maximal silver elution in comparison to Luria Bertani (LB) broth, Tryptic Soy Broth (TSB) and phosphate-buffered saline (PBS). Subsequent parallel analysis through ICP-MS and DLS show that while sodium chloride (NaCl) significantly inhibits silver elution, it is unlikely this phenomenon can be attributed to nanoparticle formation. This data will be used towards the development of stimuable silver-coated biomedical implants to facilitate the release of silver ions that are capable of preventing biofilm formation and treating deep infections.

Effect of dental material type and masticatory forces on periodontitis-derived subgingival microbiomes

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Introduction: Dysbiotic microbial communities play a key role in oral infections such as periodontal disease. However, the contribution of dental materials in driving dysbiosis or symbiosis is under-investigated. This study evaluated the microbiome-modulating properties of three biomaterials, namely resin dental composites, antimicrobial piezoelectric composites, and hydroxyapatite (HA), using an optimized in vitro subgingival microbiome model derived from patients with periodontal disease.

Methods: Saliva-coated beams of the three biomaterial types were inoculated anaerobically with subgingival dental plaque collected from patients with periodontitis (N=7) and incubated in sterile saliva supplemented with 2% (v/v) heat-inactivated human serum at 37°C for 7 days. To mimic mastication and eating periods, biomaterials were subjected to cyclic loading during incubation (2 Hz, 20 min, 5 times/day). ATP assay and 16S rRNA sequence analysis evaluated the changes in the microbiome's viability and composition, respectively.

Results: The highest microbiome viability was observed in the resin dental composite subjected to cyclic loading ($p<0.05$). Piezoelectric composite and HA showed similar viability. There were no significant changes in alpha diversity between the three materials. However, beta diversity revealed significant differences between the microbiomes formed on the composite materials and HA (PERMANOVA, $p<0.01$) under no loading conditions but not under loading conditions. For example, static HA was associated with increased dysbiosis evidenced by the enrichment of *Porphyromonas gingivalis*, *Porphyromonas endodontalis*, and *Fretibacterium* spp., and depletion of *Granulicatella*, *Streptococcus*, and *Veillonella* spp. compared to composites. Interestingly, cyclic loading reversed the dysbiosis of the microbiomes formed over HA but increased the dysbiosis of microbiomes formed over the resin composites.

Conclusions: The results suggest that piezoelectric charges reduce the microbiome's viability, while composites in general seem to support a less dysbiotic microbiome than HA. Findings of this work open new understandings of the effects of different bioactive biomaterials on the modulation of oral biofilms.

Uniform and Controllable Deposition of PAA Microgels onto 3D-Printed PCL Scaffolds

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In tissue engineering, it is highly desirable for scaffold surfaces to exhibit dual functions: directing cellular activities for tissue formation and achieving localized antimicrobial effects for infection control. Our early evidence demonstrated the capability of complexing positive antimicrobial peptides within negative poly(acrylic acid) (PAA) microgels to selectively kill approaching bacteria via a “contact transfer” mechanism.¹ While static incubation of PAA microgels onto a flat substrate surface allows to form discontinuous monolayer, it remains to demonstrate whether uniform deposition of PAA microgels can be achieved throughout the surface of a 3D scaffold with intricate configurations.

Here, we explore a dynamic coating strategy using slow rotation to ensure equal access of PAA microgels to interior surfaces of 3D-printed polycaprolactone (PCL) scaffolds with a three double-layer grid structure. After oxygen plasma treatment and poly(allylamine hydrochloride) (PAH) priming, PCL prints (6 × 6 × 1.2 mm) were placed in a tube with PAA microgel (2–3 µm) suspension and rotated at 7–9 rpm for coating.

Compared to static deposition, our dynamic strategy reduced microgel aggregation at filament intersections and significantly improved the uniformity of PAA microgels on interior PCL filaments. The narrowly distributed microgels were evenly deposited throughout the 3D PCL prints, forming a discontinuous monolayer with inter-microgel spacing below 2 µm. This spatial precision ensures contact between adhering bacteria and antimicrobial microgels, thereby maximizing local bactericidal efficiency. Notably, such microgel-coated surfaces supported the attachment and proliferation of human mesenchymal stem cells.

The new dynamic coating will offer a controllable yet scalable route to engineer infection-resistant scaffolds for bone tissue regeneration and beyond. This study was financially supported by the National Science Foundation (NSF-GCR award number 2219014)

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Self-defensive microgel-modified antimicrobial surfaces

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The electrostatic complexation between antimicrobials and polyelectrolyte microgels can be exploited to create biomedical device surfaces that are self-defensive against a bacterial challenge. We have previously shown that such surfaces can kill those bacteria which physically contact complexation-loaded microgels, and we attribute the killing to the contact-driven transfer of antimicrobial from a microgel to the bacterium. Much remains unknown about this process, however. Notably, the complexation must be strong enough that the antimicrobial remains sequestered within the microgels under physiological conditions but weak enough that transfer to challenging bacteria can occur. Here we study poly(acrylic acid) (PAA) microgels (~2-5 μm dia) synthesized by membrane emulsification and thermal polymerization. These anionic microgels are electrostatically deposited onto polycaprolactone coupons to form a discontinuous sub-monolayer coating. They can then be loaded by exposing them to low-ionic-strength solutions (e.g., $[\text{Na}^+] = 0.01 \text{ M}$) containing cationic small-molecule antimicrobials. We work with colistin, an FDA-approved antibiotic, and Sub5, an antimicrobial peptide. Loading by electrostatic complexation causes microgel deswelling, which we monitor by *in situ* optical microscopy. Under physiologically relevant conditions (pH=7.4, $[\text{Na}^+]=0.137 \text{ M}$), Sub5 remains stably sequestered whereas colistin is quickly released. Coarse-grained molecular dynamics (CGMD) simulations confirm that Sub5/PAA complexation is stronger than colistin/PAA complexation. CGMD also indicates that Sub5 forms dimers and higher-order structures, a prediction supported experimentally by SAXS measurements. Supramolecular structure enhances the complexation strength via entropic mechanisms. An *in vitro* model of hematogenous contamination model finds >90% reduction in *S. aureus* colonization on Sub5-loaded microgel-modified surfaces relative to unmodified controls. CGMD simulations show that Sub5 has a lower complexation strength with the *S. aureus* membrane than it does with PAA and confirms that there is a thermodynamic driving force for antimicrobial transfer. These antimicrobial surfaces nevertheless remain cytocompatible. Human bone marrow mesenchymal stem cells spread and proliferate more effectively on microgel-modified surfaces than on unmodified PCL control surfaces.

A Spray Deposition System to Model Contamination in the Operating Room by Airborne Bacteria

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Infection associated with a tissue-contacting biomedical device is initiated by the microbial colonization of the device surface. One possible source of contamination is the surgical operating room (OR) where viable bacteria in the OR atmosphere can sediment onto a device surface intra-operatively. Increased infection-control practices have reduced sedimentation rates to $\sim 10^3$ - 10^4 CFU/m²-h, but a strong clinical consensus remains that OR contamination is linked to device infection. There is, however, no clear method to evaluate device-modification technologies meant to mitigate the effects of such contamination. To mimic OR contamination, we have been developing an aerosolizing system able to spray small quantities of bacteria onto a surface. This system uses short bursts of pressurized gas to aerosolize liquids - typically buffer containing a known concentration of bacteria - with volumes ranging from ~ 10 -200 μ L. These bursts can contaminate surfaces with areal densities of bacteria on the order of 10^2 CFU/cm². We have sprayed both gram-positive (e.g., *S. aureus*; *S. epidermidis*) and gram-negative (e.g., *P. aeruginosa*) bacteria. Using titanium alloy coupons, we have quantified the fraction of staphylococci that are well adhered to the coupons, those that can be removed by sonication, and those that are not recovered after spraying. We have used this model to demonstrate a statistically significant reduction of bacterial colonization using surfaces rendered self-defensive against bacteria by triggered peptoid release. Moving towards *in vivo* assessment of these self-defensive surfaces, preliminary experiments indicate that unmodified Ti surfaces contaminated using the spray system can reproducibly provoke infection in a rat femur model at concentrations ranging from $\sim 10^2$ - 10^6 CFU.

Laboratory assessment of collection and inactivation of viable, airborne *Staphylococcus aureus* and MRSA

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Methicillin-resistant *Staphylococcus aureus* (MRSA), classified as a serious threat by the CDC, is resistant to beta-lactam antibiotics. The principal transmission mode of most antimicrobial resistant bacteria (ARB) is considered to be through direct contact with infected patients or their clinical samples, and the contribution of airborne transmission needs more attention. Particles laden with bacteria shed by infected individuals can deposit onto surfaces and remain suspended in the air or re-aerosolize from surfaces based on several factors. In lieu of emerging data on potential airborne transmission of ARB, it is critical to efficiently collect airborne bacteria and assess the effectiveness of inactivation methods to protect public health. In this study, aerosols containing *S. aureus* (ATCC BAA934) and MRSA (ATCC BAA1717) were generated using a Collison nebulizer in a custom-designed enclosed chamber. Airborne bacteria were collected using a novel air sampler (the BioCascade impactor) at varying nebulizer concentrations and 2 collection temperatures. Three inactivation methods (UV-C light, personal air purifier and a disinfectant spray) were also tested at varying time intervals (5, 10, 15, 20 and 30 min). In the absence of inactivation methods, the total CFU/mL ranged between 1,440±480 and 52,300±2,404 corresponding to aerosolization times 5-30 min respectively. In the presence of UV-C and the disinfectant, the fraction of viable bacteria declined with time. UV-C was the most effective for both the strains, and no viable colonies were recorded for 30 min exposures. A 10-fold variation was observed between the organisms in terms of viability in the presence of the personal purifier -- For *S. aureus*, the viability reduced by 100-fold (compared to the nebulizer concentrations of ~10⁵ CFU/mL), while there was only a 10-fold reduction for MRSA. Similarly, *S. aureus* was more susceptible to the disinfectant than MRSA. At 30 min trials, no viable *S. aureus* was collected, while ~850 CFU of MRSA/mL was collected at the same sampling duration. The results demonstrate the efficient collection of airborne, viable *S. aureus* and MRSA using the BioCascade impactor. In addition, the study reveals the effectiveness of UV-C in inactivating airborne MRSA at a 30 min exposure time, while other methods require longer durations. Furthermore, development and validation of novel methods to inactivate airborne MRSA are warranted to protect public health.

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Peptidomimetic Cationic Polyurethanes Coupled with Gram-Positive Antibiotics Effectively Treat Gram-Negative Bacterial Infection

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Urinary tract infections (UTIs), caused by bacterial infection of the bladder, urethra, or kidney, are the most common type of outpatient infection in the United States^[1]. The primary culprit behind these infections is Gram-negative bacteria such as *Escherichia coli*. Their outer membrane obstructs hydrophobic diffusion and permits only small hydrophilic molecules across the membrane, rendering many antibiotics and antimicrobial treatments useless. Recent studies have shown the success of combining existing Gram-positive antibiotics with other bioactive molecules in treating Gram-negative infections. Polyurethanes (PUs), known for their ability to disrupt the outer and inner membranes of bacteria, make them a strong candidate for an antibiotic adjuvant. We synthesized low molecular weight ($M_n < 10$ kDa) peptidomimetic cationic PUs to complement Gram-positive antibiotics. Lysine mimic (mLys) and short chain alkoxy (1-OH or 2-OH) pendant groups were added in different ratios to the PU backbone to observe the effect on the minimum inhibitory concentration (MIC) of various antibiotics against different strains of *E. coli*. Regardless of the pendant group composition, the PUs reduced the MIC of rifampicin and erythromycin by 64-fold and 16-fold when treating *E. coli* 25922, respectively^[2]. The MIC of erythromycin decreased, but not below the susceptibility breakpoint, meaning that the PUs did not enhance its permeability enough for clinical use. Against TEM-1, CTX-M-15, or ARR transfected *E. coli*, all PUs in combination with rifampicin proved effective, lowering the MIC^[2]. Lastly, rifampicin coupled with mLys PU and 80:20 mLys:2-OH PU showed a decreased MIC against multidrug-resistant (MDR) *E. coli* isolated from patients, indicating the synergistic effect between rifampicin and PU can overcome MDR *E. coli* ^[2]. In cytotoxicity testing, 80:20 mLys:2-OH PU showed lower cytotoxicity in comparison to mLys PU, demonstrating this can be a promising future adjuvant for antibiotic treatment of UTIs and other Gram-negative infections.

[1] Medina, Martha et al. "An introduction to the epidemiology and burden of urinary tract infections." *Therapeutic advances in urology* vol. 11 1756287219832172. 2 May. 2019 doi:10.1177/1756287219832172

[2] Tantisuwanno, Chinnapatch, et al. "Synergism between Rifampicin and Cationic Polyurethanes Overcomes Intrinsic Resistance of *Escherichia coli*." *Biomacromolecules*, vol.22, no.7, July 2021, pp. 2910–20. <https://doi.org/10.1021/acs.biomac.1c00306>.

Development of Anti-Biofilm Agarose Hydrogels for Targeting Bacterial Amyloid Fibrils

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Targeting bacterial functional amyloid fibrils is emerging as a promising strategy to combat infections caused by bacterial biofilms. Specifically, this strategy aims to inhibit irreversible bacterial anchorage onto surfaces, disrupting biofilm formation without bactericidal action. This study investigated anti-amyloid molecules (AAMs) capable of disassembling BAP and R5T which are amyloidogenic sequences derived from *Staphylococcus epidermidis* and *Escherichia coli*, respectively. Thioflavin T fluorescence assays and transmission electron microscopy revealed that two polyphenols - PP1 and PP2 were the most effective at disassembling BAP and R5T at sub-bacteriostatic concentrations which were also non-toxic to fibroblasts. Additionally, PP1 and PP2 alter the secondary structures of BAP and R5T from a β -rich to disordered conformation. Incorporating these AMMs into an agarose hydrogel, we found that PP1 and PP2 exhibit distinct release profiles: PP1 was rapidly released while PP2 was retained in the bulk and surface of the hydrogel. This research contributes to developing antibiotic-free anti-biofilm hydrogels, addressing a critical unmet need in combating biofilm infections.



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