



RESEARCH TOPIC PRIME4

Mechanostimulation and antibiotic response in biofilm-forming bacteria under fluid flow

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Main facility

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Main field of interest

Biophysics; Microbiology

Abstract

Bacteria often organize into surface-attached communities known as biofilms, which readily form on implanted medical devices and are among the most common sources of hospital-acquired infections1. Clinical isolates, such as those from biliary stents2, display an enhanced capacity for biofilm formation, particularly under dynamic fluid conditions3. This points to an underexplored role of bacterial mechanosensitive channels, which are increasingly linked to infection dynamics and antibiotic resistance. To address this, we propose using recently developed membrane-targeting azobenzene photoswitches4,5 as remote, non-invasive optomechanical tools for the spatiotemporal control and interrogation of bacterial membrane potential, under fluid-induced mechanical stress in microfluidic systems. Complementarily, we aim to assess how such stress influences bacterial susceptibility to antibiotics. This multidisciplinary approach promises new insights into bacterial adaptation in clinically relevant settings and may guide the development of alternative strategies to combat antibiotic-resistant infections.

Main technical approaches

This project will combine advanced microscopy, microfluidic techniques, and quantitative image analysis to investigate bacterial responses to mechanical stress. Fluorescent optical microscopy and live-cell imaging will be employed to monitor bacterial membrane potential dynamics, biofilm development, and spatial organization in real-time. Custom-designed microfluidic devices will mimic physiologically relevant flow conditions, allowing precise control over mechanical stress applied to bacterial populations. These devices will also enable localized photoactivation of azobenzene-based photoswitches for targeted membrane stimulation. High-resolution image datasets acquired during experiments will be





analyzed using automated image processing and quantification pipelines to extract metrics such as biofilm density, morphology, membrane perturbation, and antibiotic susceptibility.

Scientific references

- 1. Caldara M., Belgiovine C., Secchi E., Rusconi R. Environmental, Microbiological, and Immunological Features of Bacterial Biofilms Associated with Implanted Medical Devices (2022) Clinical Microbiology Reviews, 35, e00221-20.
- 2. Blanco-Míguez A., Carloni S., Cardenas C., Dioguardi C.C., Lambroia L., Capretti G., Nappo G., Fugazza A., Capogreco A., Armanini F., Asnicar F., Dubois L., Golzato D., Manghi P., Pinto F., Scuderi C., Casari E., Montorsi M., Anderloni A., Rescigno M., Repici A., Zerbi A., Peano C., Tamburini S., Rusconi R.*, Segata N.* Microbial composition associated with biliary stents in patients undergoing pancreatic resection for cancer (2024) npj Biofilms and Microbiomes, 10, 35.
- 3. Secchi E., Vitale A., Miño G.L., Kantsler V., Eberl L., Rusconi R.*, Stocker R.* The effect of flow on swimming bacteria controls the initial colonization of curved surfaces (2020) Nature Communications, 11, 2851.
- 4. Moschetta M., Vurro V., Sesti V., Bertarelli C., Paternò G.M., Lanzani G. Modulation of Mechanosensitive Potassium Channels by a Membrane-targeted Nongenetic Photoswitch (2023), Journal of Physical Chemistry B, 127, 8869 8878.
- 5. de Souza-Guerreiro T.C., Bondelli G., Grobas I., Donini S., Sesti V., Bertarelli C., Lanzani G., Asally M., Paternò G.M. Membrane Targeted Azobenzene Drives Optical Modulation of Bacterial Membrane Potential (2023) Advanced Science, 10, 2205007.

Type of contract

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