Biomechanics of Bacteria

CNF Project Number: 1970-10

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Primary CNF Tools Used: Deep UV Photolithography, AJA Sputter Deposition, ASML, PT 770, Oxford 100, MOS Clean Anneal

Abstract:

In this project we seek to understand the biomechanical properties of individual bacteria as well as bacterial mechanobiology (the response of living bacteria to mechanical stimuli). We have two goals in this project: 1) to understand how physical forces influence bacterial resistance and tolerance to antibiotics; and 2) to understand how to embed and maintain viable bacteria within rigid materials, the so-called "engineered living material."

Summary of Research:

We have designed microfluidic systems that allow us to apply mechanical loads to individual bacteria and observe the cellular response. We manufacture our devices on silica glass wafers using DUV photolithography to achieve nanoscale features (250 nm smallest dimension, Figure 1). We have demonstrated that mechanical stimuli applied to individual bacteria interrupt the assembly of the tripartite efflux pump responsible for removing copper and silver from the bacteria, CusCBA [1].

We recently demonstrated that mechanical stresses within the bacterial cell envelope also interrupt the function of the MacAB-TolC efflux pump which is used by bacteria remove aminoglycoside antibiotics. Additionally, we have developed mechanical modelling methods that allow us to use the results of our experiments as a measure of the elastic modulus of the bacterial cell envelope [2].

In our most recent work, we have demonstrated that mechanical stress within the cell envelope of the pathogen *Vibrio cholerae* stimulates cell wall repair mechanisms through the VxrAB two-component regulatory system [3].

This finding is exciting in that it suggests that mechanical stress and strain regulate maintenance of the bacterial cell envelope, which is the primary load carrying component of bacteria and the primary target of bacteriocidal antibiotics.

We were recently awarded two grants from the National Science Foundation to explore methods of populating rigid materials with living bacteria and the effects of mechanical stimuli on bacterial biomineralization.

References:

[1] Genova, L.A., Roberts, M.F., Wong, Y-C, Harper, C.E., Santiago, A.G., Fu, B., Srivastava, A., Jung, W., Kreminski, L., Mao, X., Sun, X., Yang, F., Hui, C-Y, Chen, P, Hernandez, C.J.. (2019) "Mechanical Stress Compromises Bacterial Toxin Efflux." Proc Natl Acad Sci U S A. 116 (51) 25462-25467, https://www.pnas.org/content/early/2019/11/25/1909562116.

[2] Lee, J., Harper, C.E., Zhang, W., Ramsukh, M., Bouklas, N., Chen, P., Hernandez, C.J. (2022) "Determining the Young's Modulus of the Bacterial Cell Envelope Using Microfluidic-based Extrusion Loading." Submitted.

[3] Harper, C.E., Zhang, W., Shin, J., van Wjingaarden, E., Chou, E., Lee, J., Wang, Z., Dörr, T., Chen, P., Hernandez, C.J. (2023) "Mechanical stimuli activate gene expression for bacterial cell-wall synthesis." In preparation.

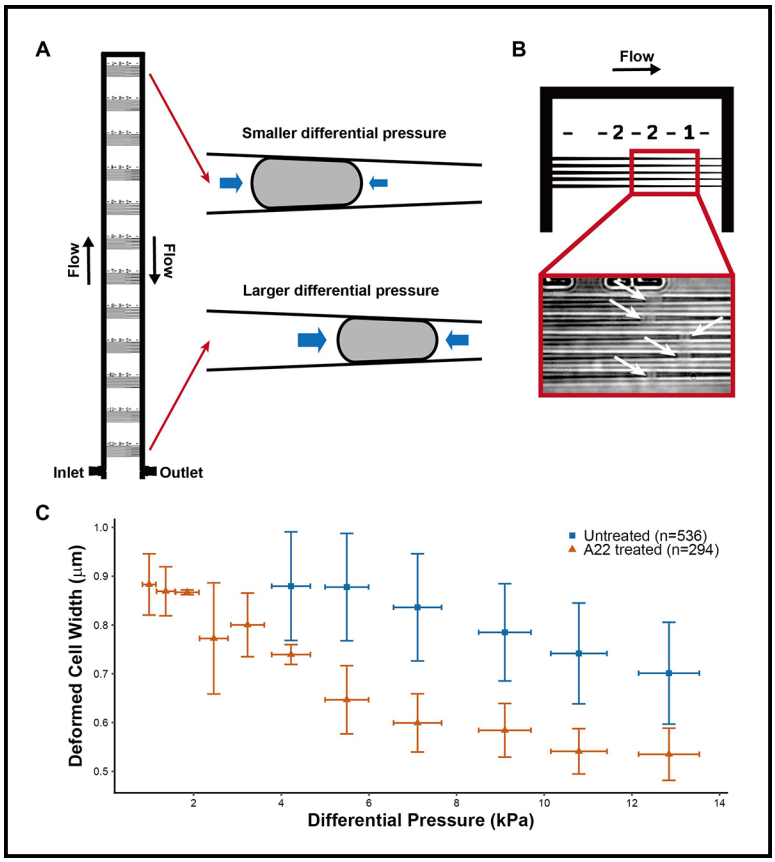

Figure 1: (A) The microfluidic device is shown. Bacteria in liquid media flow through the large bypass channel or become trapped by fluid pressure within the nanoscale tapered channels. The tapered channels are in sets of five, each set providing a different magnitude of differential pressure. (B) E. coli *trapped within the tapered channels are shown. (C) The results of an experiment in which* E. coli *are placed within the device untreated or after treatment with the small molecule A22 that depolymerizes the structural protein MreB, resulting in a less stiff cell as seen from the smaller cell width at each applied differential pressure.*