Microbes under pressure

L. Holt[a], O. Hallatschek[b], M. Delarue[c]
[a]*Institute for Systems Genetics, NYU Medical Center, NY, USA*
[b]*Physics Department, University California, Berkeley, USA*
[c]*MILE, LAAS-CNRS, Toulouse, France*

Key words: microfluidics, microbiology, mechanical stress

Cells act upon the elastic extracellular matrix and against steric constraints when proliferating in a confined environment resulting, at the population level, in a ***compressive***, ***growth-induced***, ***mechanical stress***. Growth-induced stress is ubiquitous to any cell population proliferating in a confined environment, whether partly or fully, such as microbes found to develop in the form of biofilms embedded in micrometer-sized pores or within biological tissues. Despite their paramount importance, ***compressive mechanical stresses have been largely*** unexplored in contrast to other types of mechanical stress, owing to the technical challenges of confining cells, and in particular microbes.

Microfluidics offers an arsenal of elements that are amenable for the study of microbes under spatial confinement. We developed the ***first microfluidic devices that enable an acute control of the mechanical environment experienced by a microbial cell population***, while keeping the chemical environment constant [1]. Using these microfluidic devices, we elucidated a process by which a partially confined cell population could build-up growth-induced stress: ***We found that when* S. cerevisiae *are grown in confinement, force chains propagate within the population and stabilizes it, resulting in a self-driven jamming***. Growth-induced pressure emerges from jamming, which is strong enough to affect the physiology of the microbes and strain their microenvironment.

We unraveled unique effects of compressive growth-induced stresses on the response of S. cerevisiae, impacting both global biophysical parameters and specific biological pathways. More specifically, we used a new type of nanoparticles [2] to measure that compressive cells have drastically different microrheological parameters leading to a decrease in their growth rate [3]. Moreover, we identified the first mechano-sensitive network, that we termed SCWISh, essential for cell adaptation growing in a spatially-constrained environment: the simple knockout of two genes of the SCWISh network is enough to prevent cell survival under growth-induced compressive stress [4].

Our new microfluidic approach enable for the first time the study of microorganisms under a defined mechanical and chemical environment. It opens avenues for the understanding of compressive stress on various aspects of microbial infections, from its coupling to antibiotics to drive a biological response, to the very invasion of pathogens under a given set of mechano-chemical parameters.

References

[1] M. Delarue et al. "Self-driven jamming in growing microbial populations," *Nat. Phys.*, vol. 12, no. 8, pp. 762–766, 2016.
[2] M. Delarue et al. "mTORC1 controls phase-separation and the biophysical properties of the cytoplasm by tuning crowding," *(in revision in Cell)*
[3] L. Holt and M. Delarue. *(in prep)*
[4] M. Delarue et al. "SCWISh network is essential for survival under mechanical pressure.," *Proc. Natl. Acad. Sci. U. S. A.*, vol. 114, no. 51, pp. 13465–13470, 2017.