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Citation on the research work of Sreepadmanabh M

The existence of bacteria has been known to mankind for ~ 400 years. Over this period, almost the entirety of our understanding about bacterial populations—growth, fitness, antibiotic resistence etc.—came from studying bacteria on the surface of flat agar plates or in well-mixed liquid broths. However, strikingly, in their natural niches bacteria inhabit complex 3D environments such as soil, tissues, and mucus. While the role of chemical microenvironments and genetic perturbations in bacterial fitness and survival has been at the forefront of research, the role of physical properties of their surroundings remains largely unknown. Sreepadmanbh's pioneering work has unveiled this area of research and paved the path for understanding the fitness of bacterial species in competeing cultures within mucus-like 3D environments. His work has has primarily discovered, for the first time, that physical confinement in mucus like materials can play a selective role in bacterial growth.

Using a novel 3D growth matrix that captures the physical properties of gut mucus, his research show that the architecture of bacterial colonies growing within this matrix is directly controlled by single-cell shape and the degree of physical confinement set by the porosity and stiffness of the matrix. Under increased physical confinement, low aspect ratio (spherical) cells form compact, rounded colonies, whereas high aspect ratio (rod-shaped) cells form elongated colonies with a higher surface area to volume ratio, allowing better nutrient access, which translates into a direct growth advantage for high aspect ratio cells over low aspect ratio cells. Remarkably, this principle holds irrespective of specific organismal biology or nutrient composition, as well as across two different morphologies of the same species, and even within mixed populations of different cell types. Finally, his work establishes a generalized phase space between growth performance under increased physical confinement and cellular shape – that demarcates two distinct, well-separated populations of poorly performing low aspect ratio bacteria and efficiently performing high aspect ratio bacteria.

Together, his findings show that growth success under 3D confinement is strongly dictated by single cell geometry and the mechanical state of their environment. Critically, this work demonstrates the potential to use such physical constraints to alter bacterial community composition under biomimetic mechanical regimes. This has important implications from a biomedical and therapeutic angle – for instance, while we generally believe that sub-MIC drug concentrations are ineffective at eliminating bacteria, Sreepadmanabh's work here shows how morphologhical alterations under sub-MIC treatments lead to drastically different growth patterns. This idea has immense potential towards improving our understanding of pathogenesis within complex tissue-like systems, as well as identifying and selectively eliminating regimes amenable for microbial growth. Insights from such work are valuable towards developing more effective drug screening platforms which offer more biomimetic testing beds for candidate therapeutic agents.

The outcomes from Sreepadmanabh's work will force a radical rethinking of how we model and predict bacterial community dynamics in complex ecological settings. Rather than relying only on intricate biochemical signalling or stochastic mutational events, this research demonstrates that the physical microenvironment itself actively modulates population compositions over short time scales by tipping the balance in favour of pre-existing morphological traits. This has a direct impact on practical applications in healthcare, agriculture, and bioremediation, where diverse microbiomes abound within complex heterogeneous 3D porous environments such as tissues, mucus, soil, and sediments.

Yours sincerely,
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