DOCTORAL DEFENSE

The Roles of Intergeneration Inheritance and Intrageneration Molecular Dynamics in Shaping Living Cells

Harsh Vashistha



Abstract: We study two important dynamical processes in the bacterium E. coli. The first focuses on understanding how the inheritance of non-genetic components influences cellular properties and restrict heterogeneity in future generations. Heterogeneity in physical and functional characteristics of cells proliferates within an isogenic population due to stochasticity in intracellular biochemical processes and in the distribution of resources during divisions. Conversely, it is limited in part by the inheritance of cellular components between consecutive generations. The aim of this study is to characterize the dynamics of non-genetic inheritance in simple model organism E. coli, and how it contributes to restraining the variability of various cellular properties. We describe the design of a novel microfluidic device that can trap sister cells in the same environment for 10s of generations. We introduce a new method for measuring proliferation of heterogeneity in bacterial cell characteristics, based on measuring how two sister cells become different from each other over time. Our measurements provide the inheritance dynamics of different cellular properties, and the 'inertia' of cells to maintain these properties along time. We find that inheritance dynamics are property specific and can exhibit long-term memory (~10 generations) that works to restrain variation among cells. Our results can reveal mechanisms of non-genetic inheritance in bacteria and help understand how cells control their properties and heterogeneity within isogenic cell populations. In the second study, we turn our attention to the specific question of cell size control in bacteria and focus on the role of the Min proteins dynamics in determining cell size. We demonstrate that the Min proteins, known to exhibit pole-to-pole oscillation responsible for localizing the septal ring to mid-cell in E. coli, play a crucial role in setting the cell size. We show that manipulating the concentrations ratio of the Min proteins in the cell destabilizes their oscillation temporarily and leads to a delay in the formation of the division ring until the cell reaches a size that would stabilize the oscillation again. As a result, cells divide at a new stable size which is longer than observed in earlier cellcycles with the preceding concentrations.

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Zoom ID: <u>982 6888 5790</u>

Non-department members: Contact the **doctoral candidate** or the **Undergraduate Coordinator** (paugrad@pitt.edu) for password.

Research Advisor: Dr. Hanna Salman