DOCTORAL DEFENSE

Bacterial Growth Mechanisms and Their Role in Cell Size Homeostasis and Senescence

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Abstract: Growth is a fundamental feature of living organisms, which plays an important role in maintaining cellular characteristics such as cell size and contributes to cellular fitness. It is determined by the rate of biochemical reactions, their efficiency, and their collective organization in a cell, and it is strongly influenced by the environment and the nutrients available to the cell, which can lead to significant fluctuations in the cell's growth rate. To avoid the accumulation of fluctuations over time and prevent processes from diverging, cells utilize control mechanisms to ensure the stability and accuracy of growth. The aim of this study is to better understand the dynamical processes and control mechanisms of self-replication and aging in the simple model organism *E. coli* bacterium, and how they contribute to cell size homeostasis and cellular fitness. We use an experimental setup consisting of a microfluidic device designed to trap single cells while continuously growing, to acquire long-term single cell measurements of cell-size and protein content. We apply new regression analyses methods to the measured growth dynamics, which are not motivated by any preconceived growth control model. Our results reveal dependencies among measured cellular variables that were not considered before, and which point to new growth control mechanisms. By further investigating these dependencies, we find that DNA concentration plays an important role in determining bacterial growth rate, which works to compensate for size differences acquired during cell division and thus allows cells to maintain size homeostasis. We then turn our attention to the effect of metabolism efficiency on growth rate and we study how various metabolic defects affect the ability of cells to grow in different environments. We focus on how these defects affect cellular senescence and contribute to cellular death. Our results uncover aging effects and distinguish different phenotypes of cell death.