Bacterial filamentation: a bet for survival in stressful environments

Jesús Vélez Santiago

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Welcome

Abstract

Scientists have extensively studied the mechanisms that orchestrate the growth and division of bacterial cells. Cells adapt their shape and dimensions in response to variations in the intracellular and extracellular environments by integrating information about the presence of nutrients or harmful agents in the decision to grow or divide. Filamentation is a process that occurs when rod-shaped cells stop dividing but continue to grow, thus producing elongated cells (Wang et al. 2014; Wang, Yin, and Chen 2014; Jaimes-Lizcano, Hunn, and Papadopoulos 2014; Sheryl S. Justice et al. 2008). Some cells can naturally grow as filamentous, while others only do so under stressful conditions (Cayron, Dedieu, and Lesterlin 2020; S. S. Justice et al. 2006). Here, we use mathematical modeling and computational simulations to evaluate a toxic agent's intracellular concentration as a function of cell length. We show that filamentation can act as a strategy that promotes the resilience of a bacterial population under stressful environmental conditions.

Acknowledgements

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Introduction

Antimicrobial resistance (AMR) can be considered one of the most critical health problems of the century. That is, microorganisms' ability to grow despite exposure to substances designed to inhibit their growth or kill them. In April 2014, the World Health Organization (WHO) published its first global report on AMR surveillance ("Editorial Board" 2014). Taking out of the darkness a common fear, a possible post-antibiotic future in which common infections or minor injuries can kill. Therefore, understanding the mechanisms of avoiding antibiotic action is essential for producing knowledge and developing strategies that reduce the generation of resistant bacteria.

Bacterial adaptability to hostile environmental conditions can be explained by different elements, not necessarily exclusive. For instance, mutational phenomena that allow bacteria to evade the mechanisms of action of certain antibiotics have been one of the most studied (Dever and Dermody 1991; Andersson 2005). However, the continuous technological development has allowed us to explore hypotheses where phenotypic heterogeneity is considered in detail, allowing us to study emergent behaviors in isogenic populations (Ackermann 2015). Thus, we have gone from studying bacterial communities as a whole to studying them from each of the cells that compose them and their emergent properties.

Single-cell microfluidics is one of the technologies that has made it possible to create and maintain the microenvironments necessary for studying bacteria (Yin and Marshall 2012). Among the most outstanding utilities of microfluidics, we can find the engineering of bacterial systems, microbial ecology, bacterial cell cycle, homeostasis, even cell shape, and geometry. The latter is one of the characteristics that allow the study of bacterial filamentation, a phenomenon that occurs when the cell stops dividing but continues to grow, thus producing elongated cells in the form of filaments.

Mathematical modeling is among the most common strategies to address the AMR problem. Mathematical modeling allows to pose real-life problems in a space filled with mathematical language, solve them, and test their solutions in a real-life living system (Verschaffel, Greer, and Corte 2002). Therefore, this approach can also be used to analyze in detail why a particular biological phenomenon is occurring, how its behavior can be modified, and, finally, to design specific experiments to determine their accuracy and usefulness.

This thesis describes and discusses how and why bacterial filamentation may be a general mechanism for cell survival upon exposure to toxic agents, such as antibiotics, based on experimental analyses and mathematical modeling. We divided this thesis into three chapters that

explain the methodologies used and take us one step closer to understanding filamentation with each chapter.

Chapter @ref(image-processing) describes the fundamental process to identify and quantify the properties of each cell over time, for example, its length, the amount of internal toxin, and the amount of resistance to the toxin.

Chapter @ref(experiment-analysis) used the data processed in the previous chapter to explore bacterial filamentation at the population and single-cell level. Data exploration allowed us to simultaneously observe the behavior of filamentation and its properties in heterogeneous populations. For reference, one population with an antibiotic resistance gene located on the chromosome and another on multicopy plasmids.

Finally, in chapter @ref(model-analysis), we postulated a mathematical model that considers the relationship of cell surface area and volume to the uptake of a toxic agent diffusing into the medium. This model allowed us to specifically evaluate the effect of filamentation in an environment similar to that observed experimentally. Thus, experiments and models work together to learn more about a biological phenomenon to help understand and combat the AMR problem.

1 Summary

In summary, this book has no content whatsoever.

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