The role of metabolic spatiotemporal dynamics in modulating biofilm colony expansion

Federico Bocci[1,4], Yoko Suzuki[2], Mingyang Lu[3] and José Onuchic[1]

***Short Abstract* — A recent microfluidic experiment showed that the metabolic co-dependence of two cell populations generates a collective oscillatory dynamic during the expansion of a *Bacillus subtilis* biofilm. We develop a modeling framework for the spatiotemporal dynamics of the associated metabolic circuit for cells in a colony. We elucidate the role of metabolite diffusion and the need of two distinct cell populations to observe oscillations. Uniquely, this description captures the onset and thereafter stable oscillatory dynamics during expansion and predicts the existence of damping oscillations under various environmental conditions.**

***Keywords* — biofilm expansion, phenotypic differentiation, metabolic co-dependence, oscillations, reaction-diffusion system**

I. Introduction

Cell fate determination is typically regulated by biological networks[1][2], yet increasing evidences suggest that cell-cell communication and environmental stresses play crucial roles in the behavior of a cell population[3][4].

The oscillatory expansion of bacterial colonies recently observed in a biofilm system exemplifies how intercellular communication plays a central role [5]. Liu et al supplied a B. subtilis colony with glutamate and observed a transition from steady expansion to oscillatory growth when the biofilm reached a threshold size. Detailed analysis revealed that the spatial regulation of the glutamate biochemical pathway for cell metabolism is critical for the formation of this specific dynamics.

We introduced a scheme to study both temporal and spatial dynamics of the metabolic interactions within the biofilm. This model considers the diffusion of small metabolites by incorporating the spatial dynamics of the bacterial colony. Such features allow us to investigate the spatial organization of cells with different phenotypes, and directly explore the repercussions of the glutamate synthesis pathway on the biofilm development.

II. Results

The proposed model can explain the recurrent oscillatory cycles of the growth rate in terms of the space-dependent interplay between the internal and peripheral phenotypes and reproduce the observed growth dynamics in presence of altered conditions of the growth media. Moreover, we show that he occurrence of oscillations is insensitive to the radius of the biofilm; instead, it is sensitive to the width of the peripheral layer. These findings suggest that the initial onset of the oscillation of the biofilm expansion rate is due to the switch of the bacterial cells from interior to peripheral phenotype, and it is specifically triggered when the peripheral layer increases its width to a certain level. Finally, various types of growth dynamics, including dampened, stable, dissipating dynamics, are revealed by varying the ratio between interior and peripheral cells in the biofilm and modifying the biofilm's external conditions.

III. Conclusion

This modeling scheme provides insights to understand how cells integrate the information from external signaling and cell-cell communication to determine the optimal survival strategy and/or maximize cell fitness in a multi-cellular system.

References

[1] Alon U. Network motifs: Theory and experimental approaches. Nat Rev Genet. 2007;8(6):450–61.

[2] Tyson JJ, Novák B. Functional Motifs in Biochemical Reaction Networks. Annu Rev Phys Chem. 2010;61(1):219–40.

[3] Lee J, Wu J, Deng Y, Wang J, Wang C, Wang J, et al. A cell-cell communication signal integrates quorum sensing and stress response. Nat Chem Biol. 2013;9(5):339–43.

[4] Prindle A, Liu J, Asally M, Ly S, Garcia-Ojalvo J, Süel GM. Ion channels enable electrical communication in bacterial communities. Nature. 2015;527(7576):59–63.

[5] Liu J, Prindle A, Humphries J, Gabalda-Sagarra M, Asally M, Lee DYD, et al. Metabolic co-dependence gives rise to collective oscillations within biofilms. Nature. 2015;523(7562):550–4.

[1] Center for Theoretical Biological Physics, Rice University, Houston, TX, USA. [2] Meisei University, Tokyo, Japan. [3] The Jackson Laboratory, Ben Harbor, ME, USA. [4]Email: fb20@rice.edu.