Computational Study of Gram-positive Conjugation: from Single Cell Signaling to Colony Behavior

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Conjugation is a Horizontal Gene Transfer (HGT) phenomenon in which genetic information -coded in plasmids or integrative elements- is mobilized among individuals. Conjugation is well characterized in Gram negative (G-) bacteria. However, in spite of the clinical relevance of Gram positive (G+) species, and the issue of antibiotic resistance dissemination through HGT; little is known about the regulation of conjugation in G+. This work focuses on the study of population-level principles of G+ conjugative regulatory networks, taking the pLS20 plasmid from Bacillus subtilis as a model [1]. For this purpose, the Individual Based Model (IBM) Gro was applied to simulate the dynamics of pLS20 dissemination over a B. subtilis population growing in a solid surface. The analysis was performed from an epidemiology viewpoint, in which the pLS20 plasmid is considered an infectious agent being spread over the bacterial population. Thus, bacterial conjugation can be used as an experimental epidemiology model to extract principles and test strategies regarding agent transmission. The results of this study show the effect of the spatial distribution over plasmid dissemination and the role of noise during the infectious cycle. Interestingly, the analysis reveals the crucial effect of spatial segregation of populations on the dissemination dynamics and the robustness of the system against noise. Finally, this study also highlights the signal inheritance phenomenon, which interferes with the quorum sensing systems dynamics of bacteria colonies growing in solid surfaces.

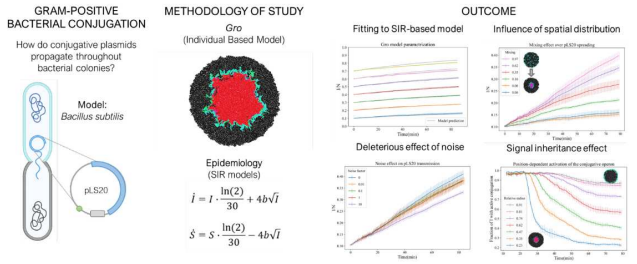

Fig. 1. Bacterial conjugation, snapshot of a colony simulation, simplified epidemic modeling of conjugation plasmid spread, and main outcomes from simulations and their comparison with the epidemic model.

[1] W.J. Meijer, D.R. Boer, S. Ares, C. Alfonso, F. Rojo, J.R. Luque-Ortega, and L.J. Wu, *Multiple layered control of the conjugation process of the Bacillus subtilis plasmid pLS20*. Frontiers in Molecular Biosciences **8**, 648468 (2021).