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A mathematical model of plasmid spread in microbial communities through horizontal gene transfer mechanisms

Julien Vincent[1], Alberto Tenore[2], Maria Rosaria Mattei[2], Luigi Frunzo[2]

[1]Microbial Ecology Laboratory,
University of Galway, Ireland
julien.vincent@universityofgalway.ie

[2]Department of Mathematics and Applications,
University of Naples, Italy
alberto.tenore@unina.it
mariarosaria.mattei@unina.it
luigi.frunzo@unina.it

Antimicrobial resistance (AMR) poses a critical global challenge with significant implications for public health and environmental sustainability. Antibiotic resistance genes (ARGs) are often carried within plasmids, mobile genetic elements capable of transferring between different microbial cells via horizontal gene transfer (HGT). This occurs primarily through conjugation, which enables direct cell-to-cell transfer, and natural transformation, where bacteria uptake extracellular DNA (eDNA). These processes, along with the presence of metal resistance genes (MRGs) on plasmids, are amplified by metal contamination, which increases selective pressure and facilitates the maintenance and dissemination of antibiotic resistance.

This study presents a multidimensional continuum model for plasmid dissemination in microbial communities via horizontal gene transfer. The model is formulated as a system of nonlocal partial differential equations derived from mass conservation laws and reaction kinetics principles. The microbial domain is modeled as a homogeneous, viscous, incompressible fluid with a velocity given by Darcy's law. The model considers plasmid-carrying cells as distinct volume fractions and their horizontal gene transfer via conjugation and natural transformation. Conjugation is modeled as a density-dependent process, due to the necessity of contact between a donor and a recipient cell to occur. A convolution integral regulates the gene transfer expression to account for its dependence on the presence of potential receptors around a donor, called recipient-sensing. A promotion function is also introduced to account for the burst in conjugation

due to the presence of trace metals. Transformation is modeled as a frequency-dependent process, considering the availability of natural eDNA as the primary factor affecting the process.

The model is solved numerically, and simulations are performed to examine how transformation and conjugation shape the dynamics and ecology of plasmid spread in a two-dimensional system, emphasizing their distinct ecological roles. Additionally, the study investigates how the microbial community regulates, and is in turn influenced by, metal dynamics. Model results confirm relevant experimentally observed evidences in plasmid spread, such as the respective intensity of different horizontal gene transfer mechanisms and the importance of selective pressure.

Keywords: horizontal gene transfer, plasmid dissemination, nonlocal PDEs, metal resistance

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