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Modelling horizontal gene transfer of plasmid-mediated resistance in biofilms

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The global spread of antibiotic microbial resistance (AMR) is an increasing health concern, and has been mainly attributed to antibiotics abuse and misuse [1]. Dissemination of AMR is largely associated to plasmids, extrachromosomal genetic elements able to transfer to new host cells through conjugation, which plays a crucial role in the ecological success of plasmids in bacterial communities. Even at subinhibitory concentrations, metals exert a selective pressure on bacterial communities, hence promoting dissemination of AMR. However, in the absence of selective pressure, this ecological success contrasts with the high costs of plasmid maintenance and very low rates of conjugation, generating the so called plasmid paradox [2].

Horizontal gene transfer is even more relevant in biofilms, where close physical contact between bacteria facilitates conjugation. This study presents a mathematical model simulating the social behaviour of bacteria regulating plasmid transfer under selective pressure from metals and more specifically in the case of co-resistance and cross-resistance to antibiotics and metals within a growing biofilm. The model is formulated as a nonlocal system of hybrid PDEs with a convolution integral regulating the transfer genes expression. Gene expression is modelled as a rate depending on environmental conditions: toxic stress from metals and antibiotics, and the presence of potential receptors around a donor, called recipient-sensing. Based on experimental results from literature, a promotion function is also introduced to account for the increase in conjugation in the presence of trace metals.

This mathematical ecology study aims to give an insight into how bacterial social behaviour might answer the plasmid paradox, and how metal contamination participates in the spread of AMR. Numerical simulations showed that the

model is able to qualitatively reproduce the influence of conjugation on plasmid dynamics in a growing biofilm. The relative influence of conjugation and vertical gene transfer was compared, including under selective pressure exerted by trace metals.

Keywords: partial integro-differential equations, nonlocal term, conjugation, plasmid paradox, selective pressure
MSC2020: 92C70, 92D25, 35Q92, 34C60

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