Microbial growth dynamics govern conjugation efficiency in the presence of antibiotics

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Short Abstract — **It is generally assumed that antibiotics can promote horizontal gene transfer (HGT). Due to a variety of confounding factors that complicate the interpretation of previous studies, however, how antibiotics modulate HGT remains poorly understood. In particular, it is unclear whether antibiotics directly regulate the efficiency of HGT, serve as a selection force to modulate the population dynamics after HGT has occurred, or both. Here we address this question by quantifying conjugation dynamics in the presence and absence of antibiotic-mediated selection. Surprisingly, we find that antibiotics from all major classes, when dosed at sub-lethal concentrations, do not significantly affect the conjugation efficiency. Instead, our modeling and experimental results demonstrate that conjugation dynamics are dictated by antibiotic-mediated selection. In contrast to conventional wisdom, we further show that antibiotics do not always promote conjugation but instead cause diverse dynamics, depending on how the growth rates of parental strains are influenced by the antibiotics. Our findings may explain the apparently paradoxical observation that HGT appears to be happening to a lesser extent than expected.**

Keywords — **Horizontal gene transfer, antibiotic resistance, synthetic biology**

I. Introduction

HORIZONTAL gene transfer (HGT) has given rise to the rapid, widespread dissemination of antibiotic resistance genes within and among bacterial species [1,2]. It has been speculated that antibiotics can promote HGT based on the observed increase in resistance following antibiotic treatment [3-5]. However, these theories are confounded by the inability to distinguish antibiotic selection dynamics from antibiotic-induced resistance exchange [6,7]. Thus, whether, and to what extent antibiotics specifically modulate conjugation efficiency is still unknown.

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II. Results

To determine whether antibiotics modulate conjugation efficiency, we first decoupled bacterial growth from HGT to quantify the rate of conjugation for increasing concentrations of 10 antibiotics. We show there is no statistically significant effect on the conjugation efficiency up to the highest concentration tested for each antibiotic. We then built a simple mathematical model describing HGT to investigate how antibiotic selection influences population dynamics of conjugants with a fixed rate of conjugation. We identified four main growth scenarios that demonstrate signature dynamics of the relative amount of transconjugants present. In particular, the relative growth rates of the donor and recipient are primarily responsible for the observed increase in transconjugants, and depending on the selection environment, can generate a diverse range of conjugation dynamics. Surprisingly, our results demonstrate that higher concentrations of antibiotics do not always promote conjugation.

We tested these predictions using *E. coli* engineered to undergo HGT in a microfluidic device. We show that experimental results validate modeling predictions, suggesting that antibiotic selection dynamics alone are an accurate predictor of conjugation dynamics.

III. Conclusion

The results from this study demonstrate that antibiotic influence on conjugation efficiency is negligible, but instead selection dynamics are the dominant contributor to observed population dynamics following conjugation. Counter-intuitively, higher concentrations of antibiotics do not necessarily promote conjugation. These findings help elucidate the apparently paradoxical observation that HGT appears to be happening to a lesser extent than expected.

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