Predicting Plasmid Maintenance and Abundance in Complex Microbial Community

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***Short Abstract* —Predicting whether a plasmid can be maintained in heterogeneous microbial communities is challenging. This is due to the large number of subpopulations and complexity of conjugation networks. Here, we establish a general theoretical framework to describe the dynamics of plasmid distribution across species. With this framework, we derive a general metric to predict plasmid maintenance and abundance in arbitrary microbial community. We validate the predictive power of this metric with simulations of random conjugation networks as well as experimental data found in the literature.**

***Keywords* — plasmid abundance, conjugation, microbial community, segregation, growth burden, plasmid-centric model, species, mathematical modelling.**

I. INTRODUCTION

Plasmids are one of the most important carriers of accessory genes in microbial communities, and reside at the core of horizontal gene transfer [1,2]. A plasmid can replicate itself, transfer from one species to another through conjugation, or be incorporated into the genome of its host [3,4]. Whether a plasmid is maintained or lost within a microbial population, determines whether the functions carried by the plasmid, such as antibiotic resistance, are exhibited [4,5].

Despite its importance, the general understanding of the criterion for plasmid maintenance in heterogeneous microbial communities is lacking. The conventional approach of modelling the plasmid-carrying population, which we call a 'population-centric model' [3], models all possible species-plasmid combinations. Using this approach is challenging because the complexity of the model increases exponentially with increasing numbers of plasmids.

Here, we establish a plasmid-centric model. Compared with the conventional approach, this new framework greatly reduced the complexity of model formulation and mathematical simulation.

II. MATHEMATICAL MODEL

Four dynamic processes are described in this model: (1) species growth, (2) plasmid conjugation, (3) plasmid segregation, (4) system dilution. For a m-species and n-plasmid population, the framework contains two groups of ordinary differentiation equations (ODEs) which describe the population size of each species and the abundance of each plasmid in each species. These equations can be combined into two in the form of matrices, regardless of the numbers of species and plasmid in the community:

$$\frac{dP}{dt} = A \circ U_p \circ P \circ C - D \cdot P,$$

$$\frac{dQ}{dt} = B \circ U_Q \circ Q \circ \bar{C} + (\bar{P} - Q) \circ H \circ \bar{Q} - D \cdot Q - K \circ Q.$$

Here, $\circ$ is the Hadamard multiplication between the matrices. P and Q are the matrices representing species sizes and plasmid abundance, respectively. A and B are the burden or benefit caused by the plasmids. U_p and U_Q are the maximum growth rates. C is the matrix of growth capacity. K is the matrix of plasmid segregation rate constants. H is the matrix of conjugation rate constants.

The population-centric model requires $m2^n$ ODEs and involves $nm^2 2^{2n-2}$ conjugation pairs, while the plasmid-centric model only requires $m(n+1)$ ODEs and nm^2 conjugation pairs.

III. CONCLUSIONS

Despite the complexity of the communities, there exists a universal indicator, ω, for plasmid abundance. ω is defined as:

$$\omega = \frac{\bar{\eta}}{\frac{\bar{\mu}}{\bar{\mu} - \bar{m}D}\left(D + \bar{\kappa} - \frac{D}{1+\bar{\lambda}}\right)}$$

$\bar{\eta}$, $\bar{\mu}$, $\bar{\kappa}$ and $\bar{\lambda}$ are the weighted average of the conjugation rates, maximum growth rates, segregation rates and burdens, respectively. Simulations with randomized parameters show that $\omega > 1$ is the criterion for plasmid maintenance, which provides a simple reference of the fate of each plasmid. The values of ω correspond well with the final abundance of the plasmids, regardless of species number, plasmid number, community connectivity, or species coexistence.

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