CONFÉRENCE

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Mapping the relationship between gene expression variation and bacterial growth rate phenotype with CRISPRi

VENDREDI 13 décembre 2024 à 12 h 30

Pavillon Charles-Eugène Marchand, salle Hydro-Québec (1210)

Abstract:

Variation in gene expression and protein abundance lays the foundation for bacteria to respond to the environment, withstand stress, and differentiate to new cell states. However, it remains difficult to predict the effect of changes in gene expression on complex phenotypes like growth. To address this, we recently developed a new approach for mapping expression-growth rate landscapes that integrates sparsely sampled experimental measurements with an interpretable machine-learning model.

In this talk, I will first introduce a mismatch CRISPRi technique for characterizing gene expression/growth rate relationships in high throughput.

Then, I will show how a pairwise model previously used to describe drug interactions can be used to describe and extrapolate from these new data. When trained on pairwise data for a variety of metabolic genes, this model yielded interpretable parameters related to pathway architecture and generalized to predict the combined effect of up to four perturbations.

Based on these results, we propose a strategy using sparsely sampled, low-order measurements to quantify genetic interaction landscapes on the pathway-wide or genomic scale in a single assay. We anticipate this approach will be broadly applicable in optimizing bacterial growth conditions, generating pharmacogenomic models, and understanding the fundamental constraints on bacterial gene expression.

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