Modeling Heterogeneity in Microbial Population Dynamics

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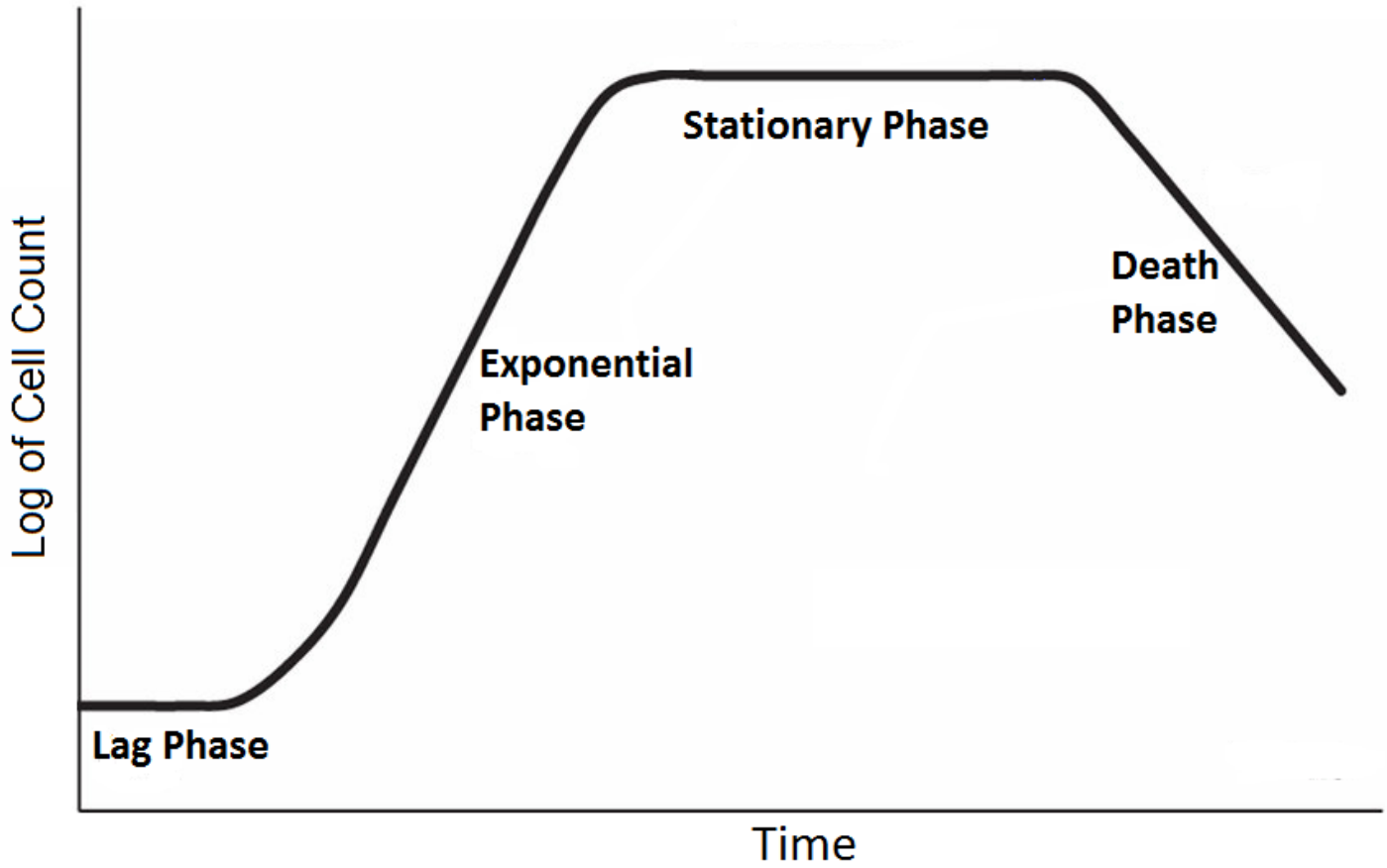
Microbial Growth Models

Diagram of what is considered a typical microbial growth curve



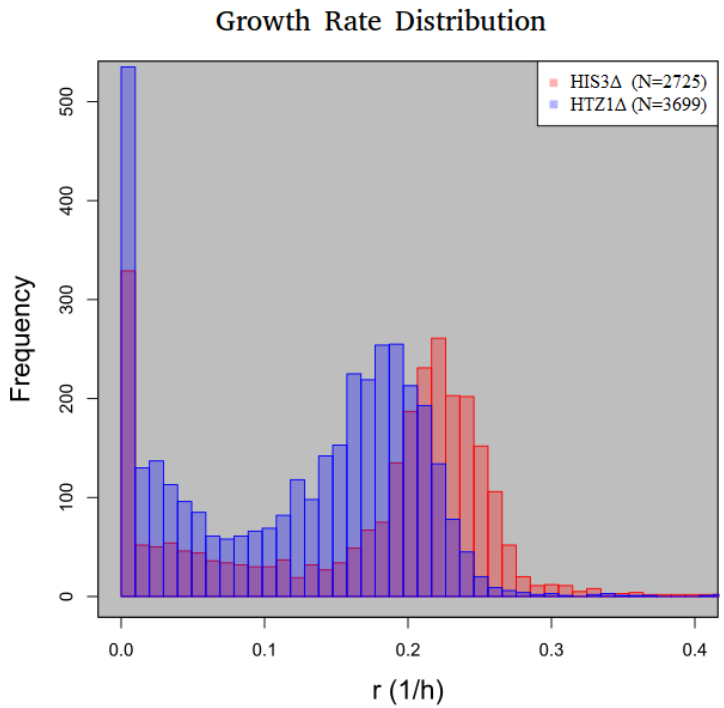
Setting the Scene

Growth Rate

A measure of how quickly cells are progressing through the cell cycle

- Key model parameter when capturing population dynamics
- Important component of evolutionary fitness
- Subject to great selective forces
- Applications in food security, microbial infection modeling, tumorigenesis dynamics, etc.

Research Problem



Growth rate is typically measured at the population scale.

- Assume that observations at that scale apply to **individual cells**.
- Assume that all members of the population behave in the same way...
- Increasing evidence that, even among isogenic populations, there is considerable heterogeneity in growth rates.

Prior Observations

μQFA data by Lawless:

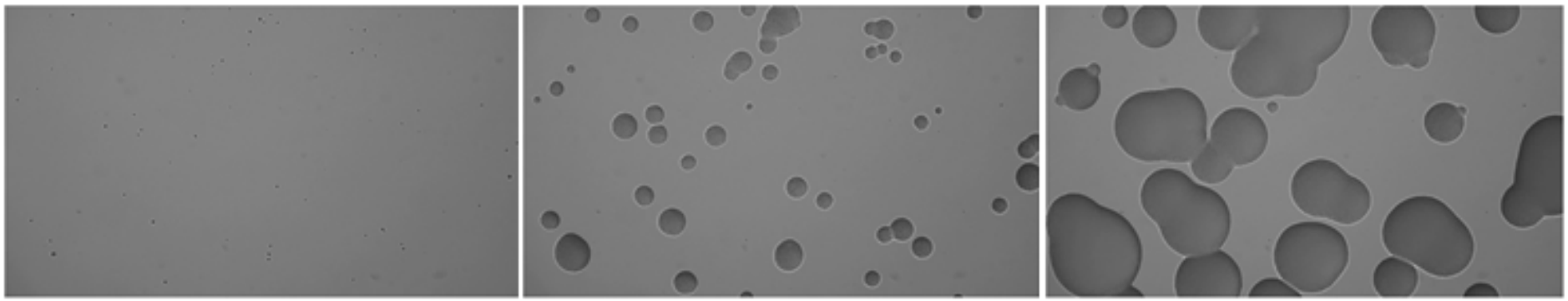
- Little evidence for a lag phase when looking at individual lineages.
- Cells divide almost immediately, with some clones dividing more quickly than others.

- It may thus be plausible that population-level observations of a lag phase are the results of competition between clonal cell lineages.
- We hope to demonstrate that the lag phase can be **apparent at the population level**, despite being **absent at the single cell level**, due to inter-lineage variability in growth rate.

Data, data and more data

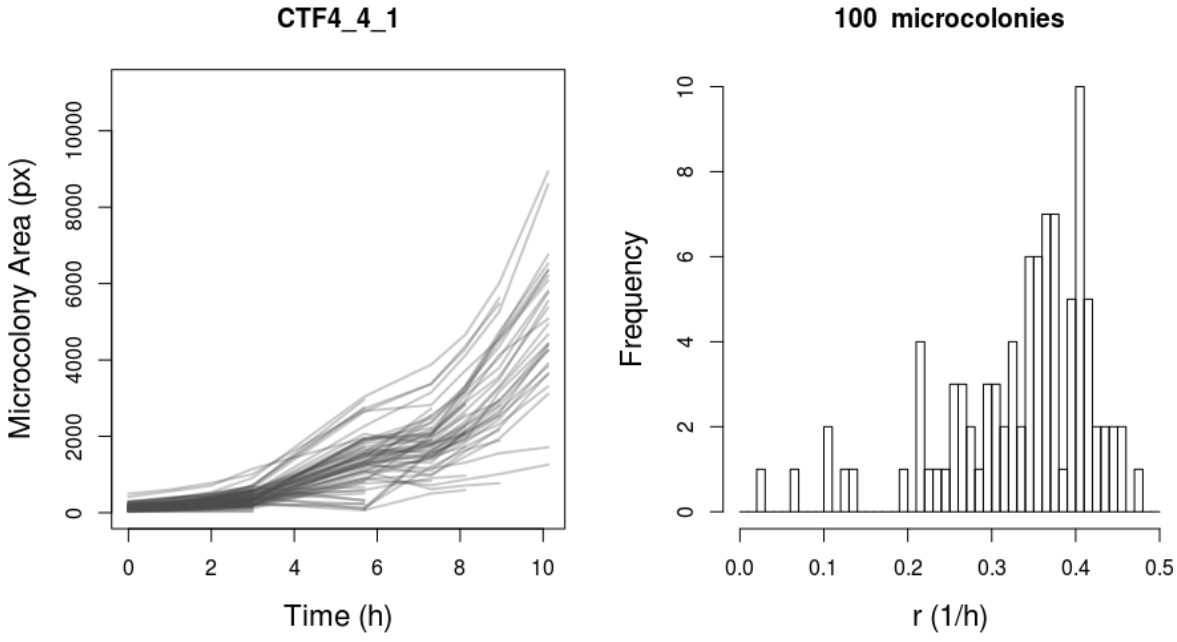
Data sets which will be used to capture growth rate heterogeneity:

1. μQFA data produced by Lawless (unpublished),
2. High-throughput microscopy assay data by Levy et al. 2012,
3. High-throughput microscopy assay data by Ziv et al. 2013.



Proposed Research: Aims

- Find a model which best captures heterogeneity in microbial growth curves through **single lineage observations**.
- Explore the implications which such a model may have on the interpretation of various growth phases.
- Repeat the μQFA experiments with the aim of validating model predictions.



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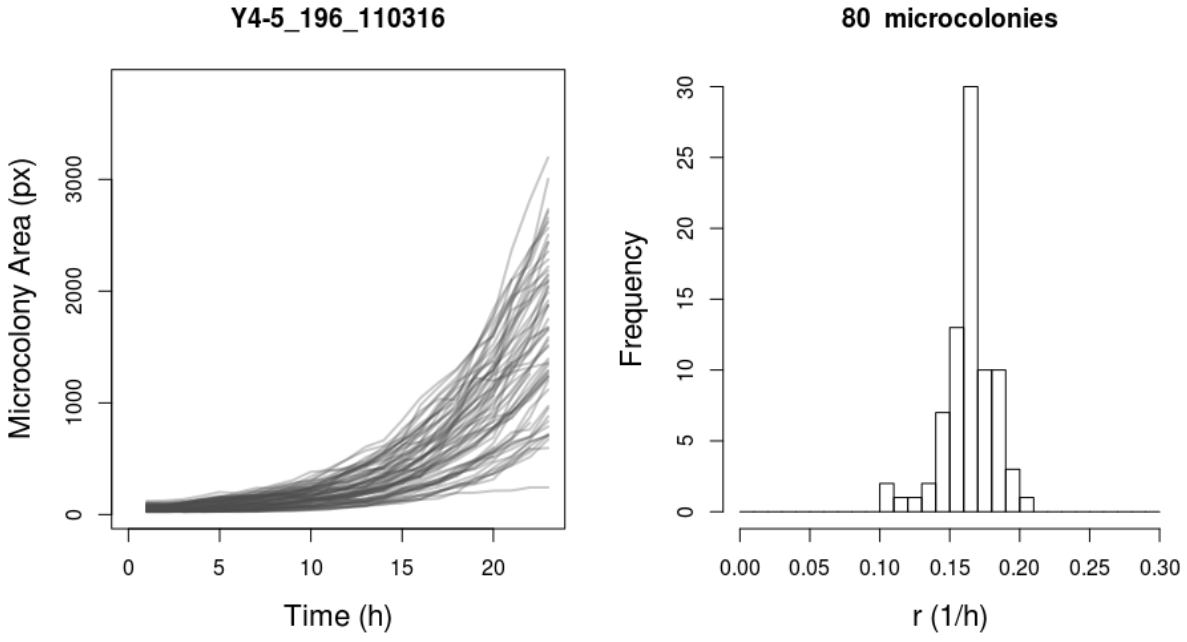

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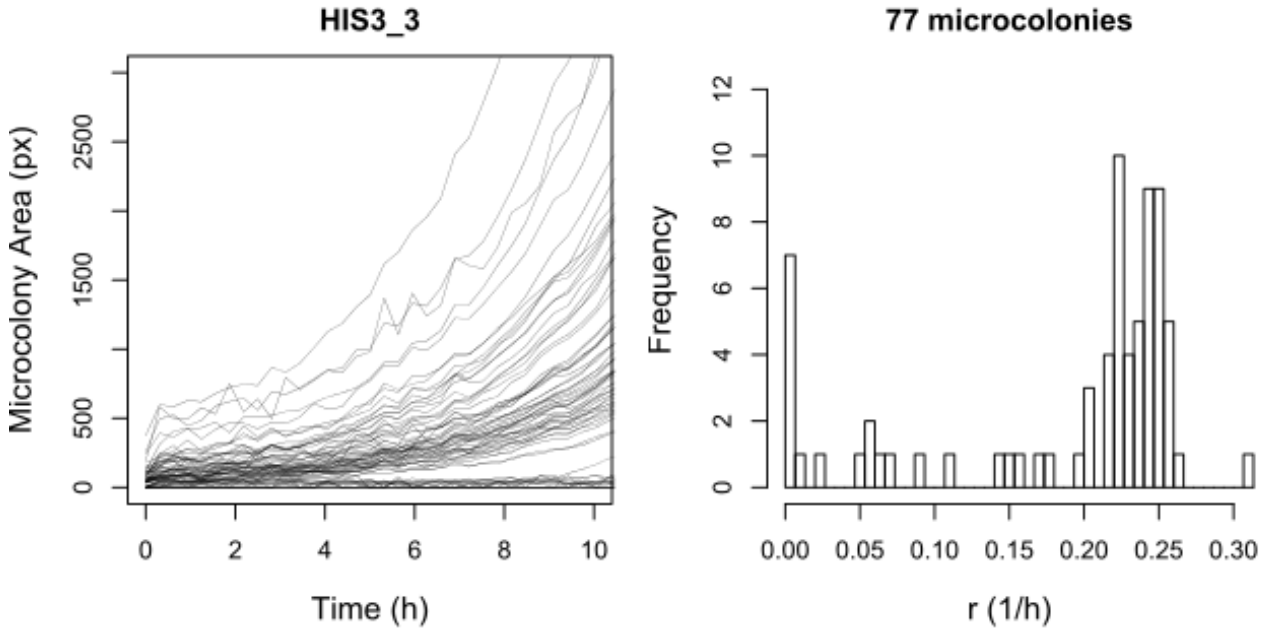

Proposed Research:Objectives

- Data accessibility
- Model development
- Parameter inference workflows
- Model fit
- Mechanistic insights
- Submission

- Logistic deterministic model;
- Standard Gillespie stochastic model;
- Hybrid model combining deterministic and stochastic models.

- birth-only models
- lower bound for time sampling
- switch to a non-dividing stage

Summary

Can we find a stochastic model that **reduces the apparent heterogeneity** of growth rates in data?

Does explicit modeling of cell lineages give rise to an **apparent lag phase** at the population level?

How is **sampling** from different phases affected by heterogeneity?

Research Significance

Microbiology is progressing to become a data-rich science

- Limiting factors in scientific advances often no longer rest in the amount of available data...
- ...but in the quantitative analyses performed on them.
- This project makes efficient use of a vast range of **existing, expensive, experimental** data sets.

Single-lineage stochastic, deterministic and hybrid models

- First time that these models will be considered along-side each other.
- If we are be able to reduce the apparent heterogeneity in population parameters...
- ...the explored mechanistic implications and the developed models will have **vast applications** (e.g. experimental design, risk assessments, tumorigenesis, etc.).

Any Questions?