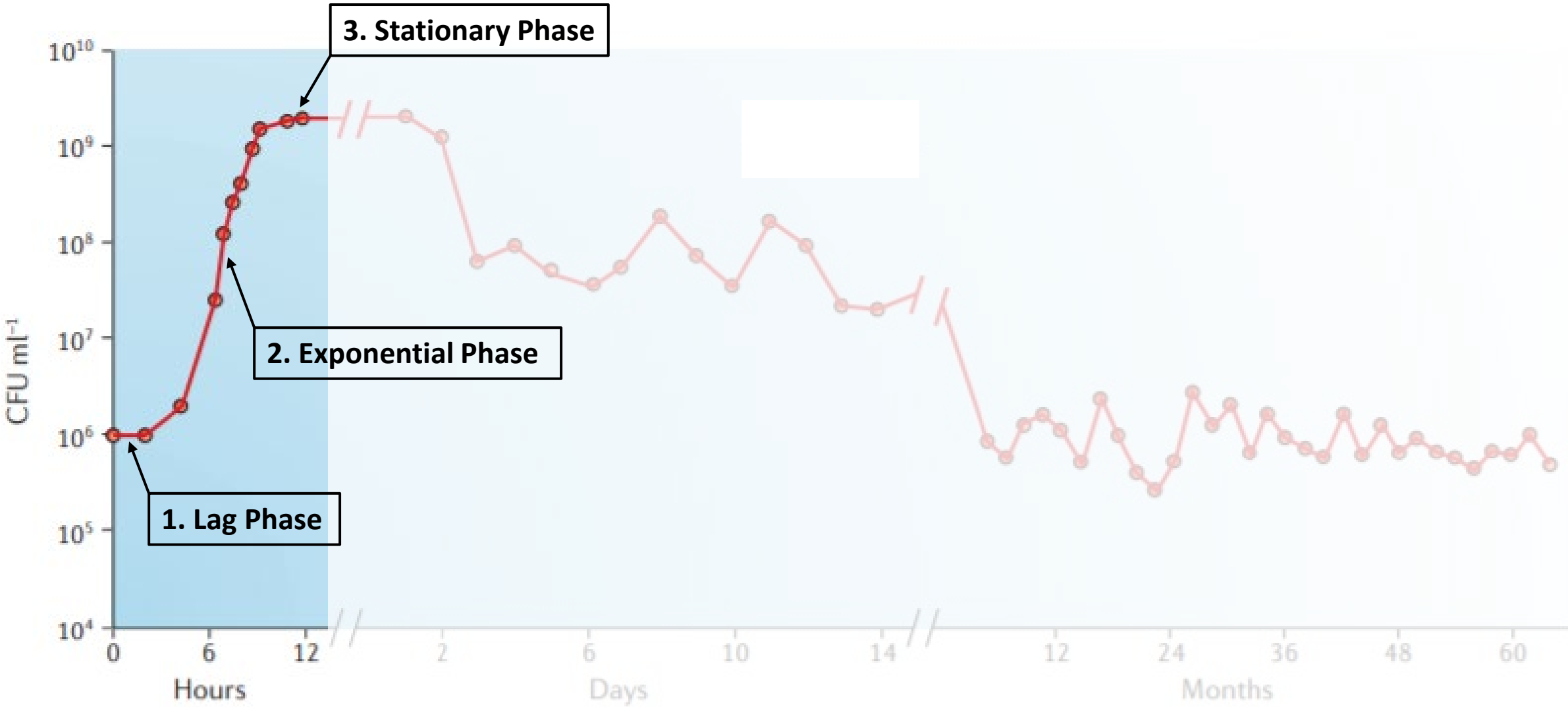
Evolutionary Dynamics in the Long-Term Stationary Phase

Srihari Ganesh

Cluzel Lab

Phases of the Bacterial Life Cycle



S.E. Finkel, *Nature Reviews*, 2006

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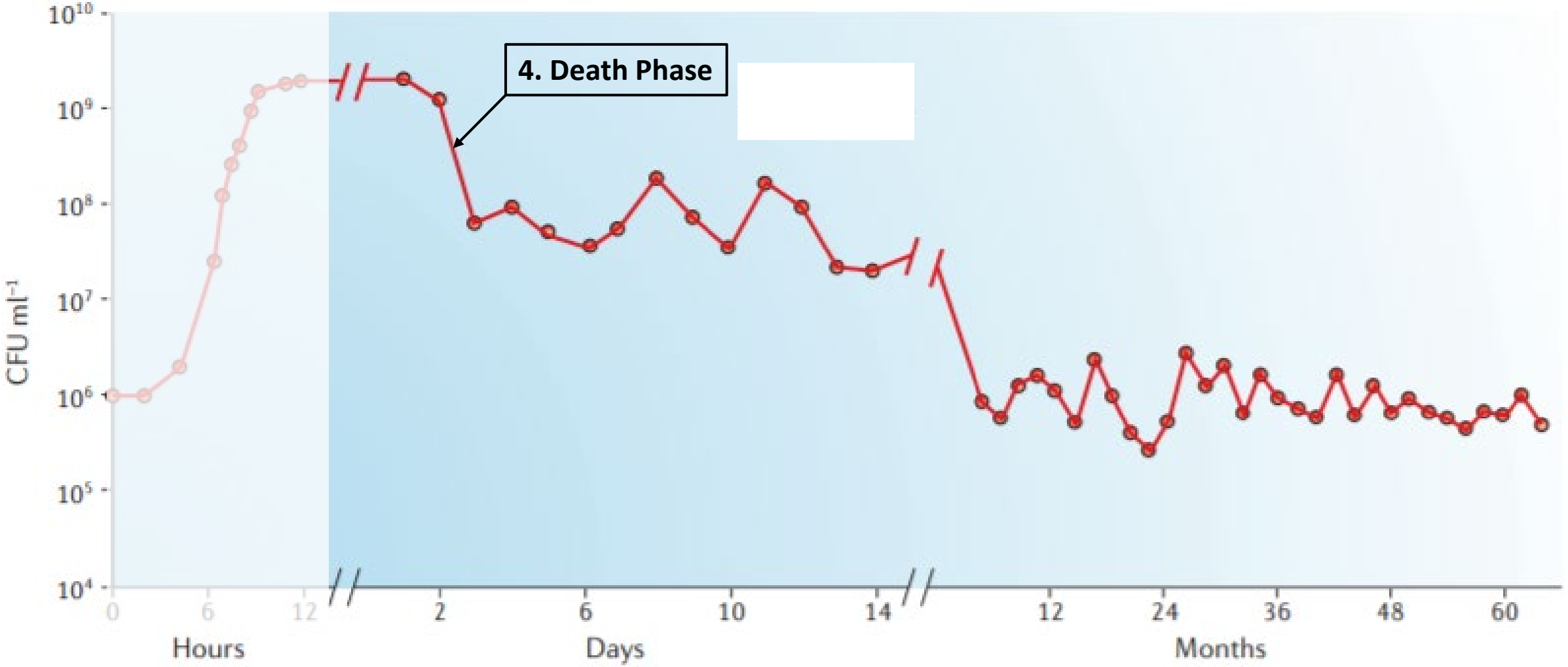

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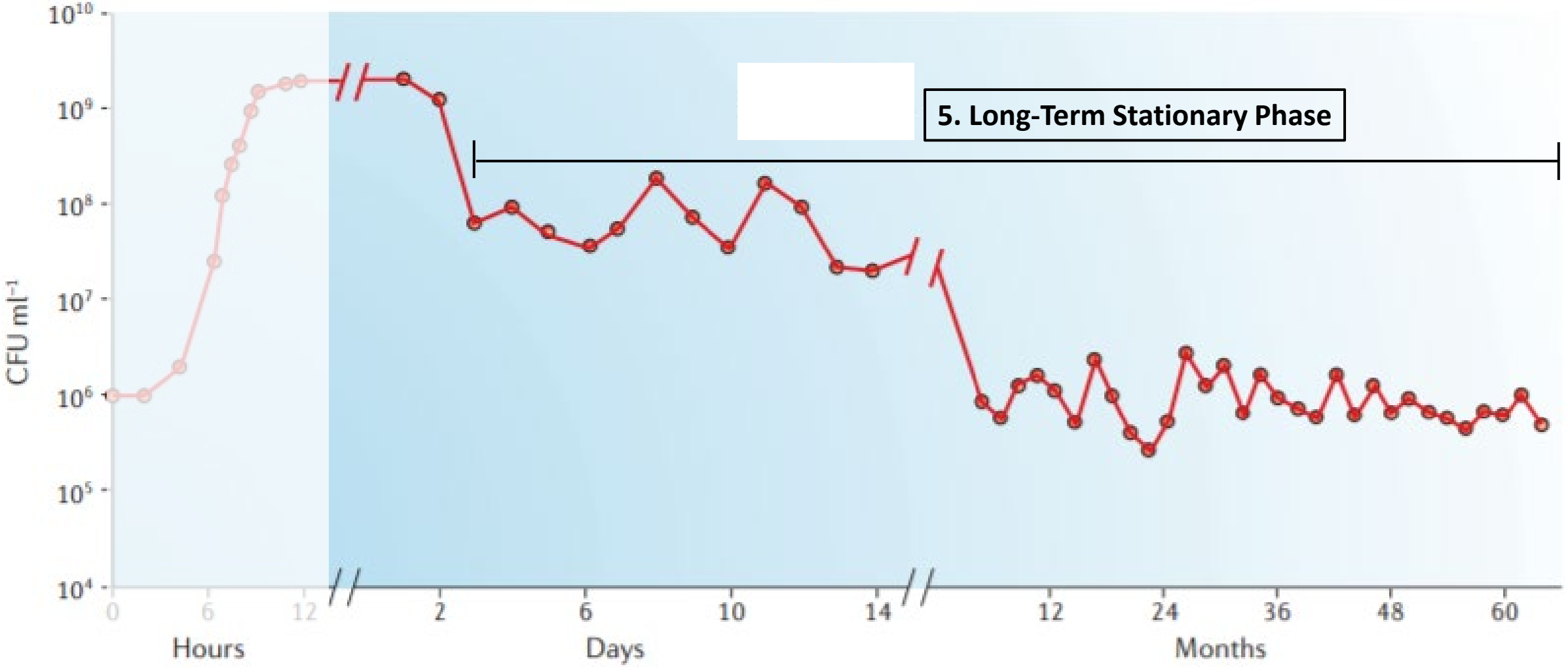

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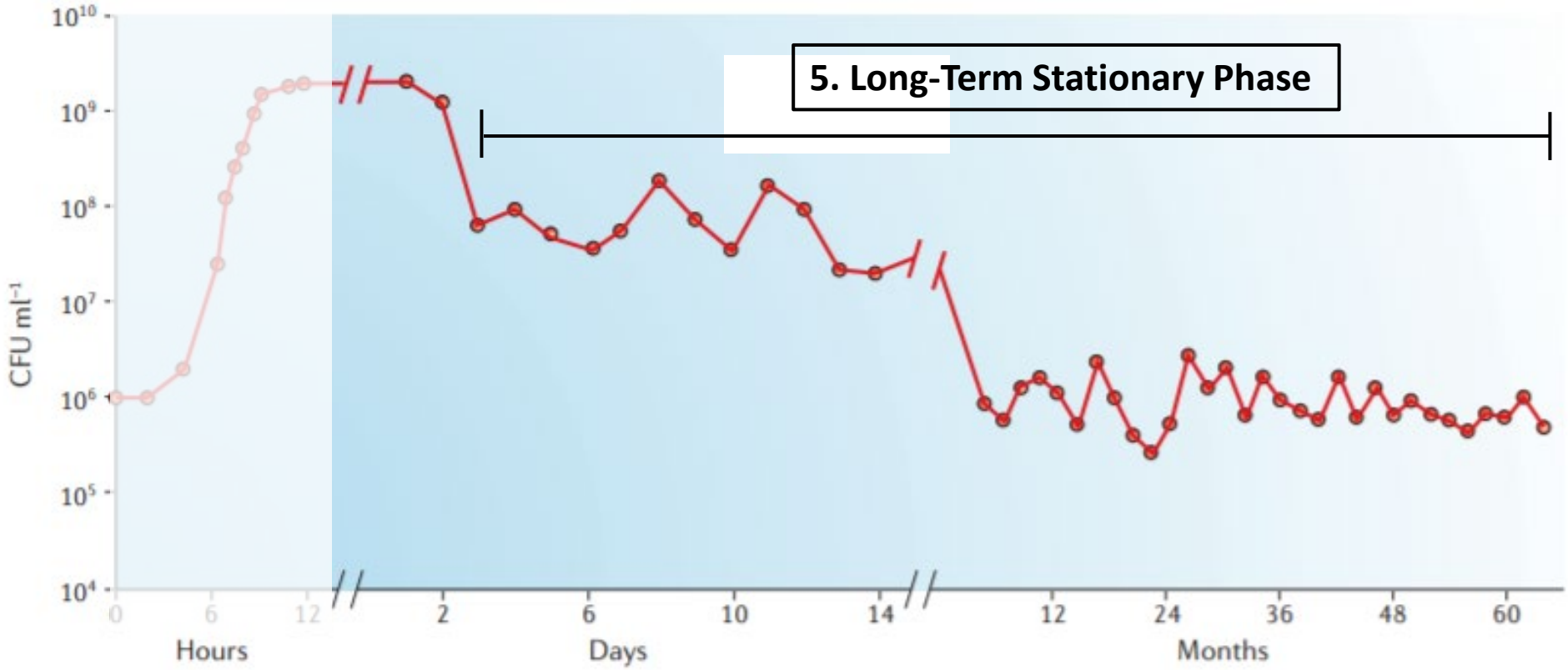
Defining long-term stationary phase (LTSP)

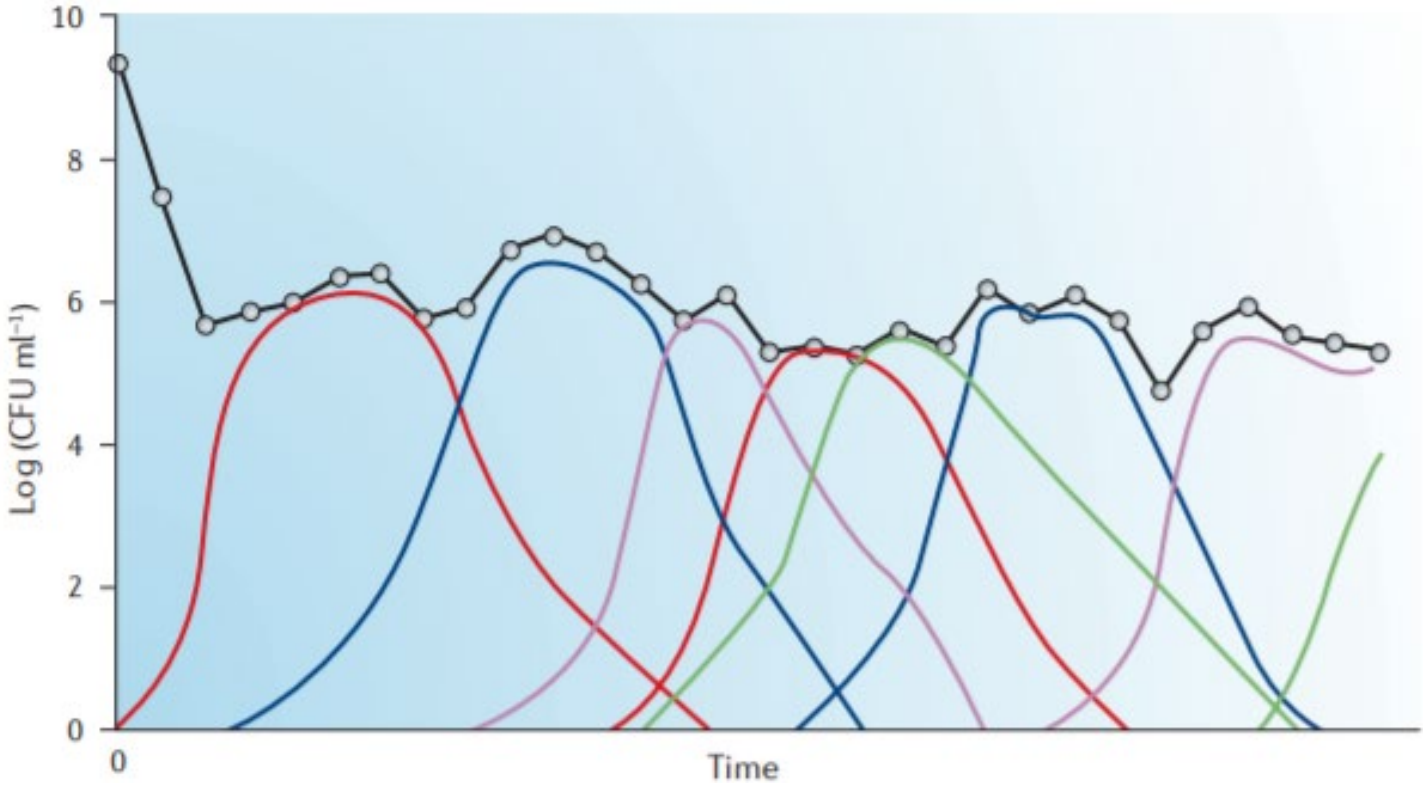
- A state in which bacteria can survive for years without an external food source



S.E. Finkel, *Nature Reviews*, 2006

Evolutionary dynamics in LTSP

- Population in long-term stationary phase (LTSP) is continually evolving
- Interested in modeling the population dynamics of these mutants



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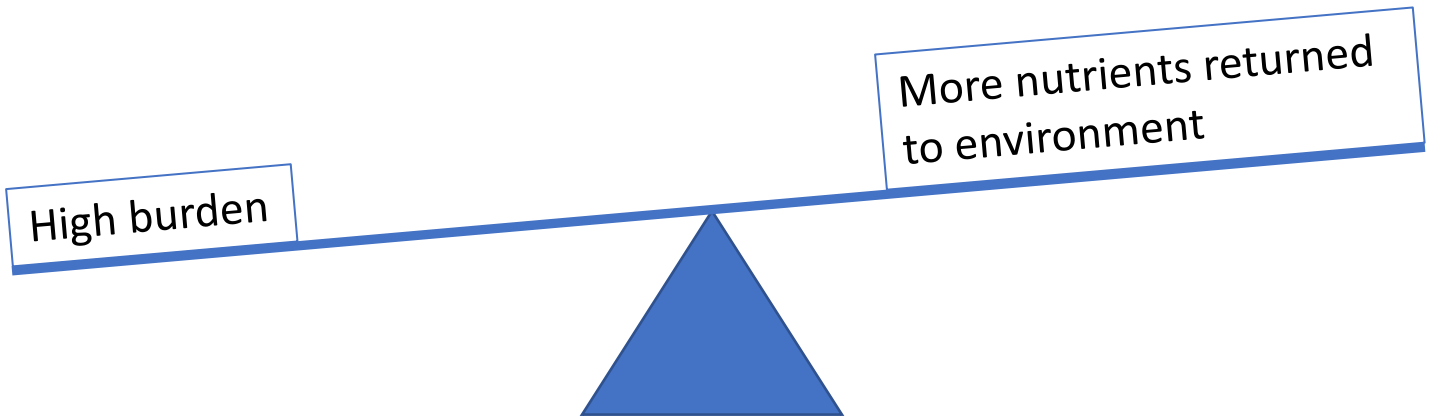
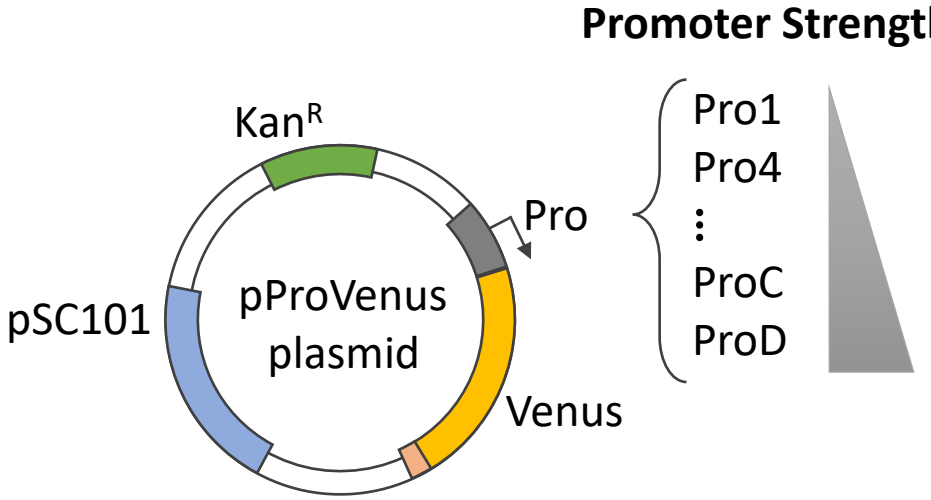
How does the protein burden affect population dynamics?

- Cells often make nonessential proteins
  - Pro: provides more nutrients for other cells to recycle after death
  - Con: is more of a burden through energy usage
- We want to know **how the extra burden impacts dynamics in the long-term stationary phase**
  - Intuition says that a higher burden should still be unfavorable



Experimental Design

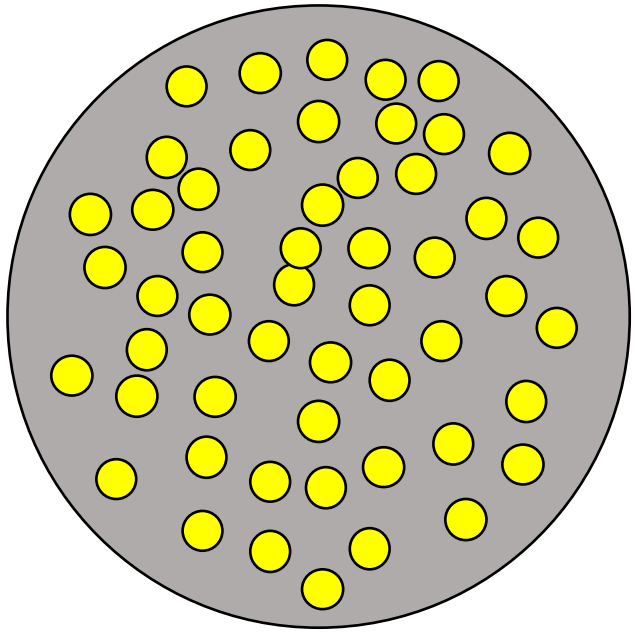
- Varied levels of burden, from low to high, in *E. coli* strains
  - Track burden through fluorescence level
- Expect selection for random mutations that **reduce** burden

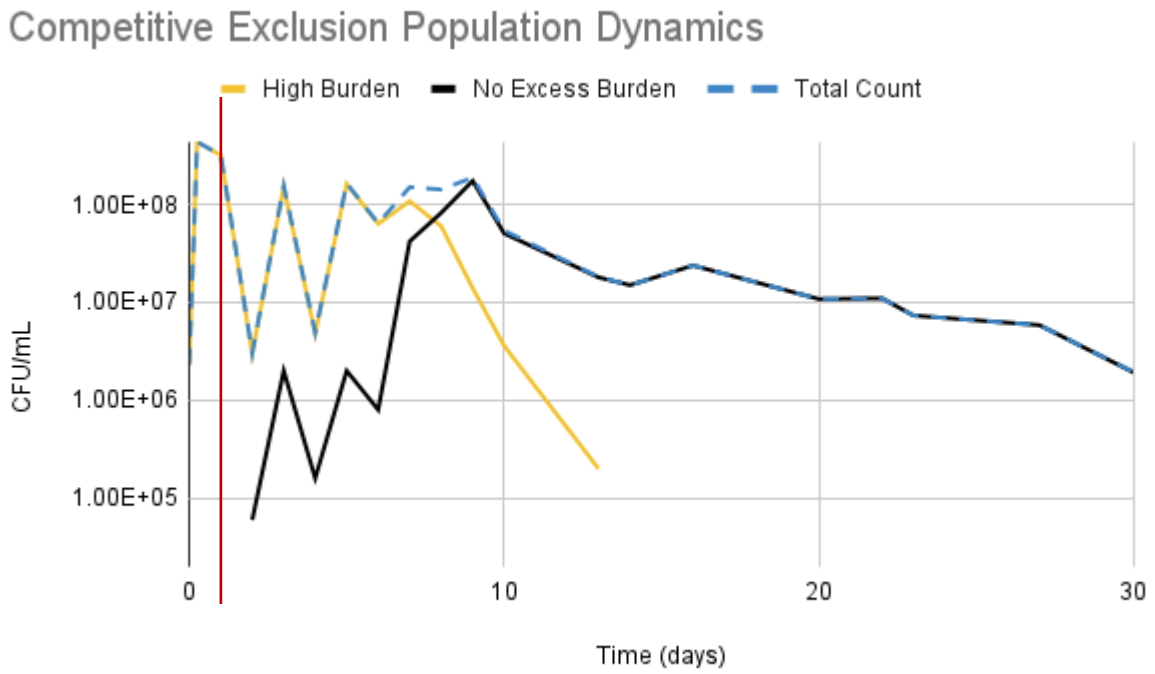


M. García-Alcalá, unpub.

Experimental Competitive Exclusion

- Flask started with only a strain of **high** burden (**high** fluorescence)
- Mutant of parent strain with **lower** protein burden (**no** fluorescence) appeared and took over





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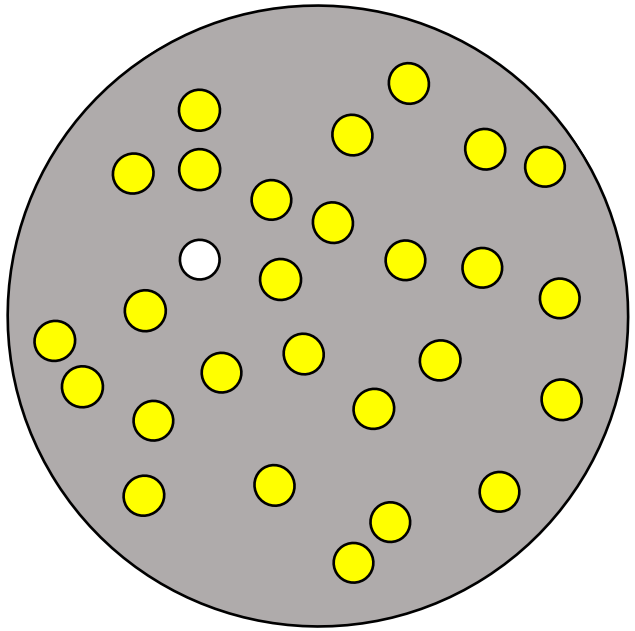

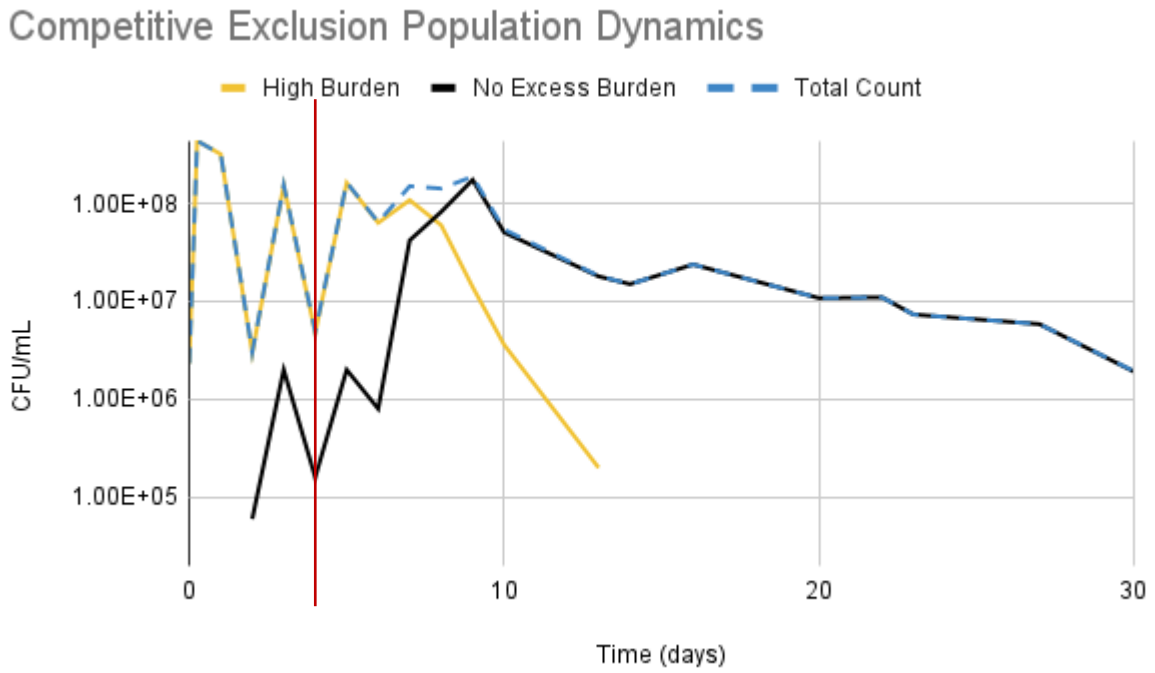

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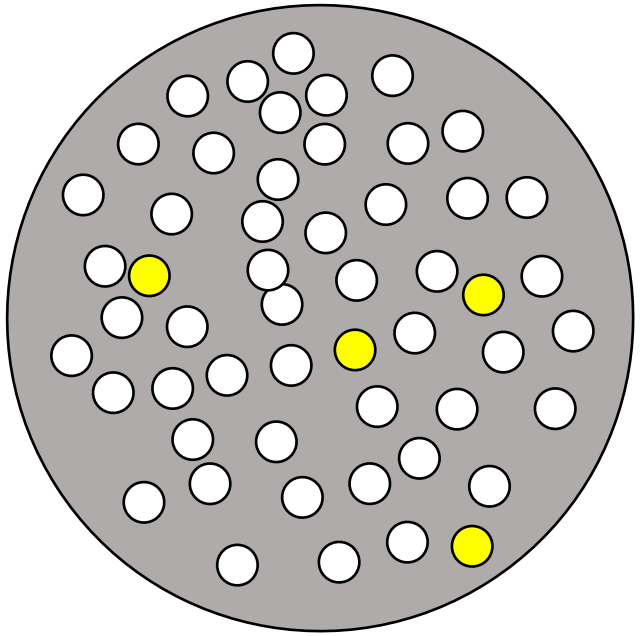

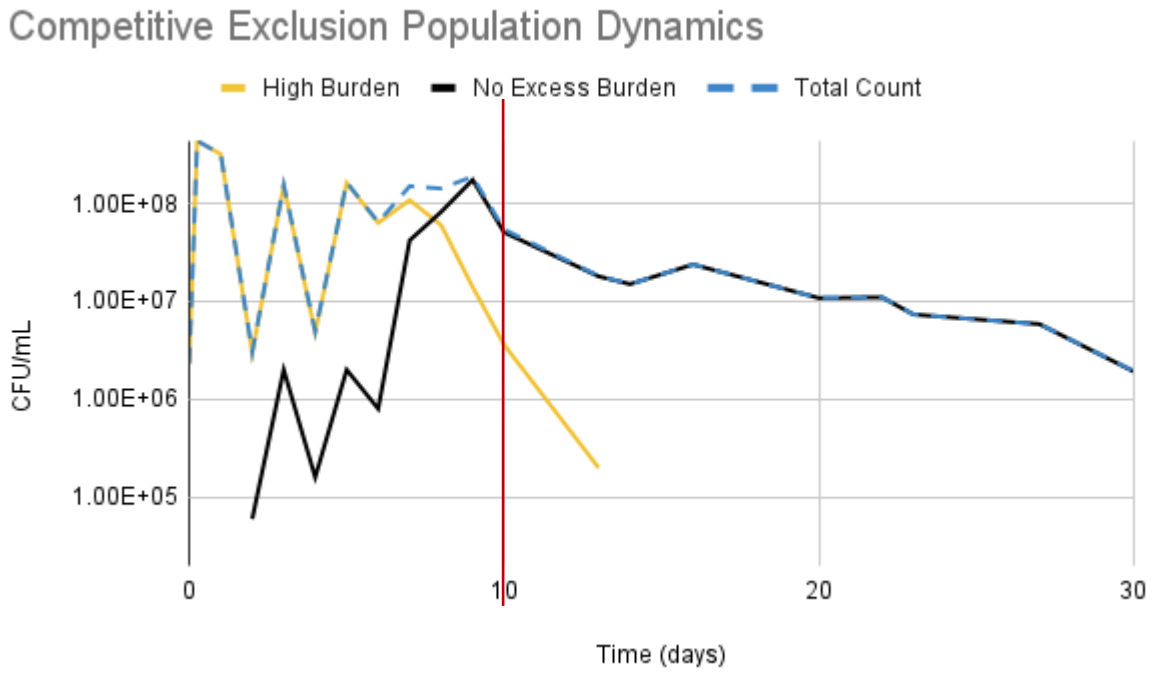

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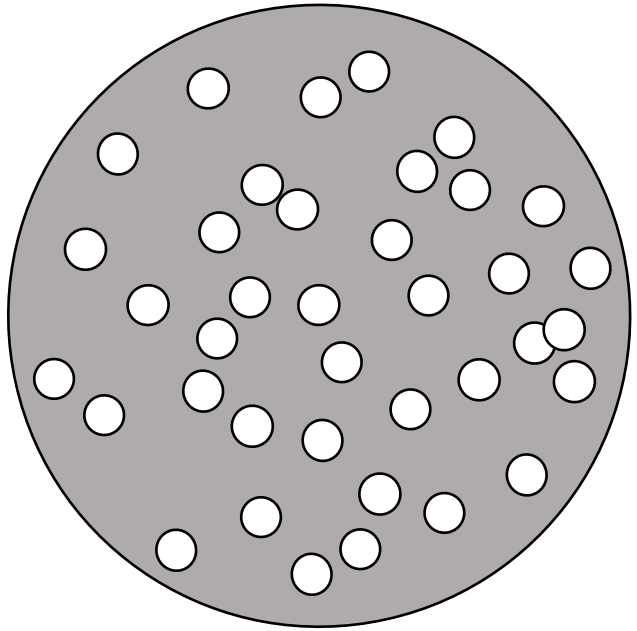
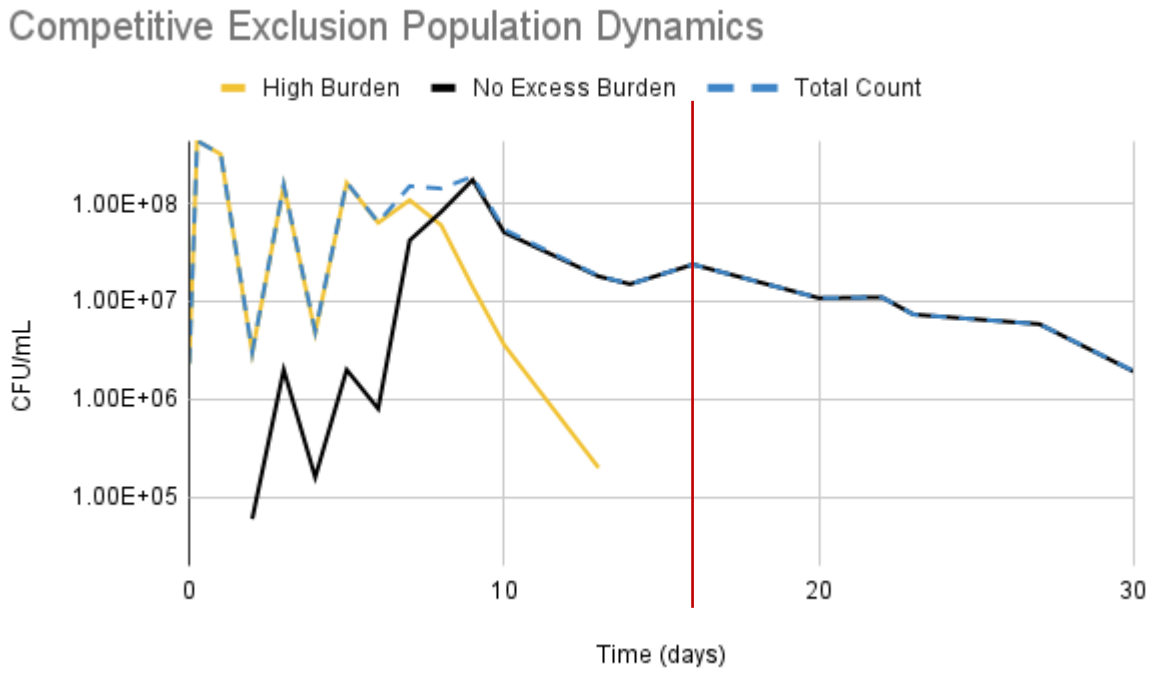
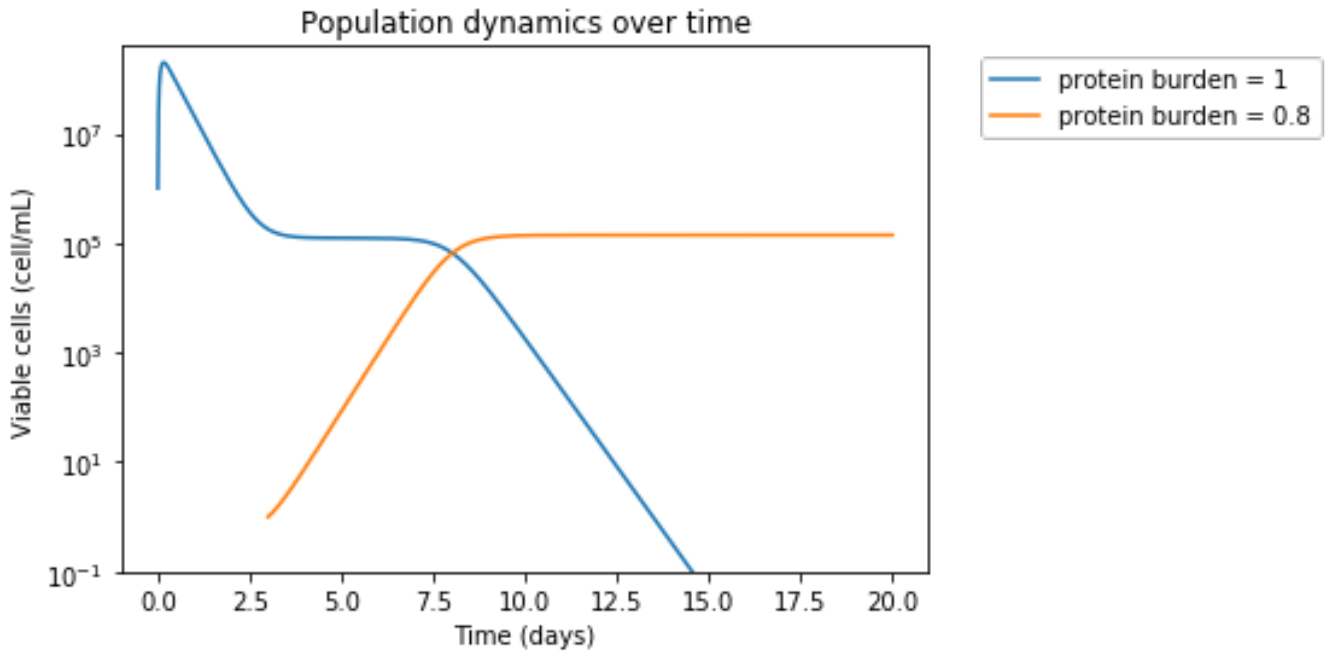




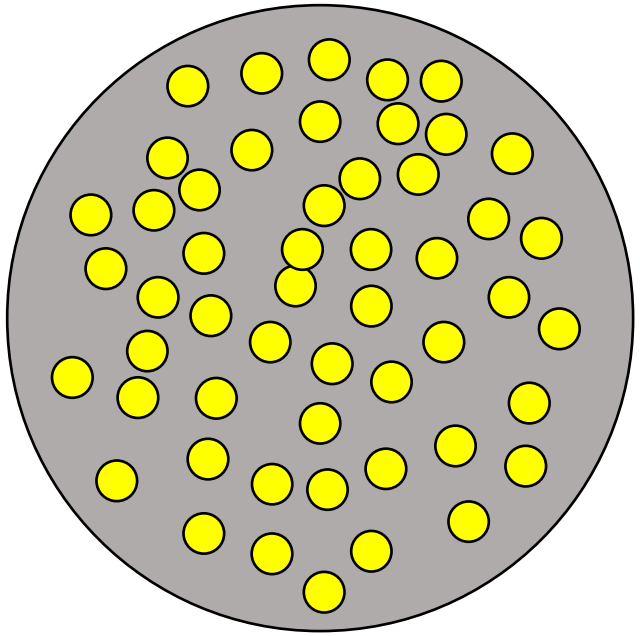
Modeling Competitive Exclusion

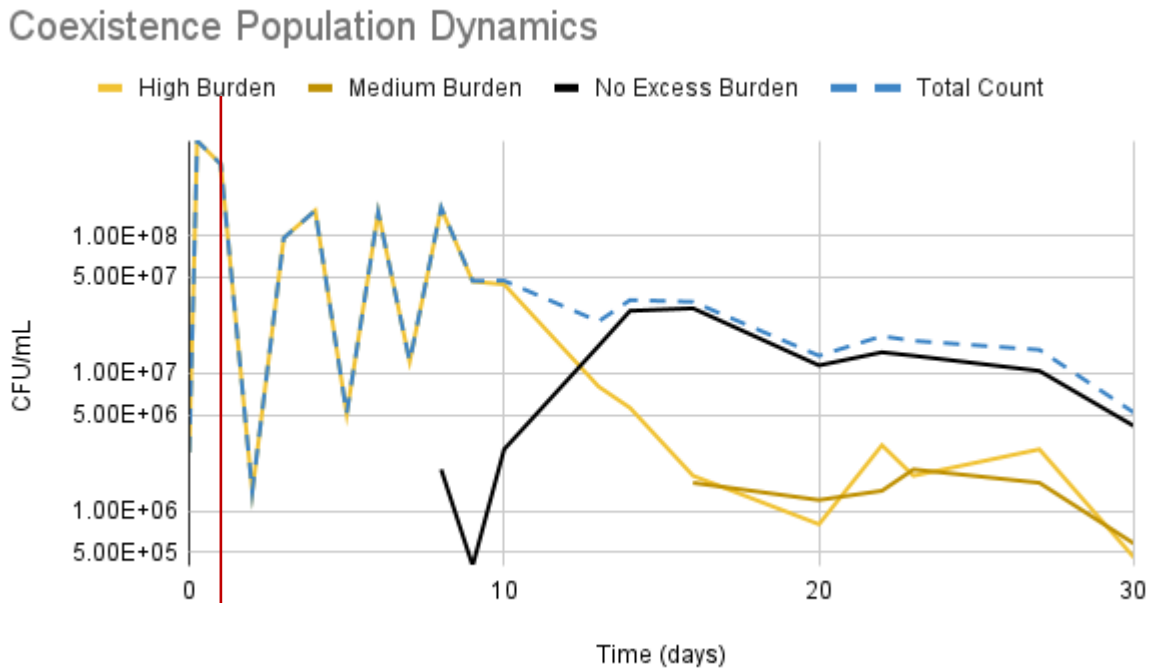
- With a **constant** protein burden, the strain with the lowest burden always takes over in simulations



Experimental Coexistence

- Strains with varying levels of burden can coexist





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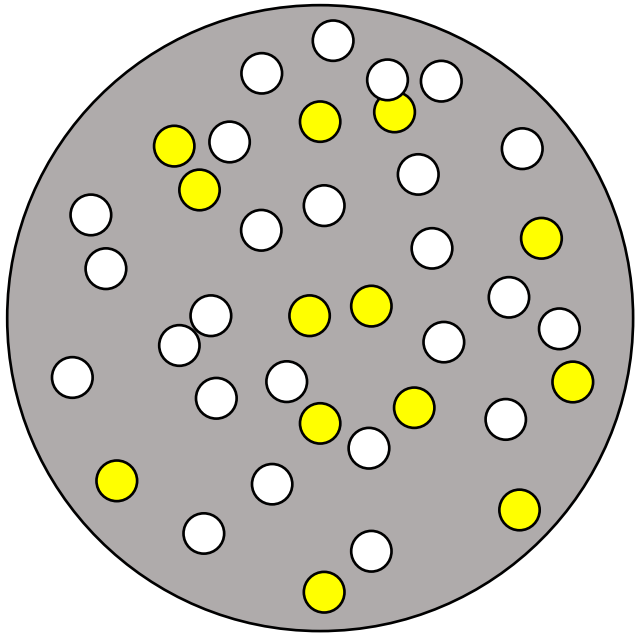

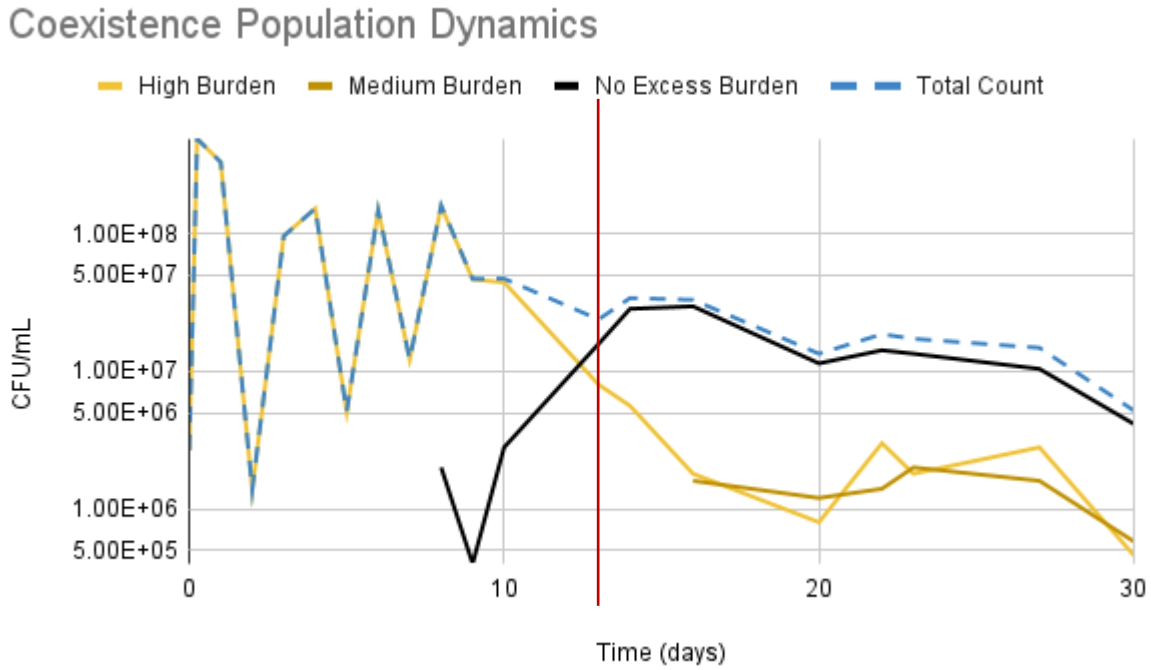

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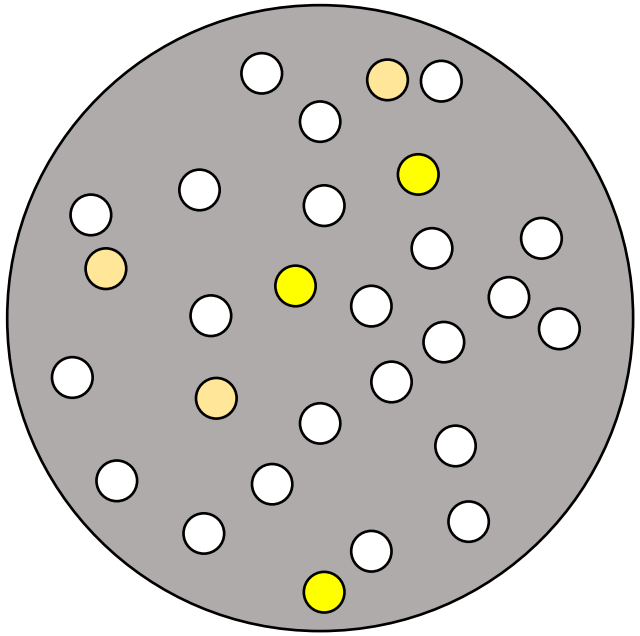
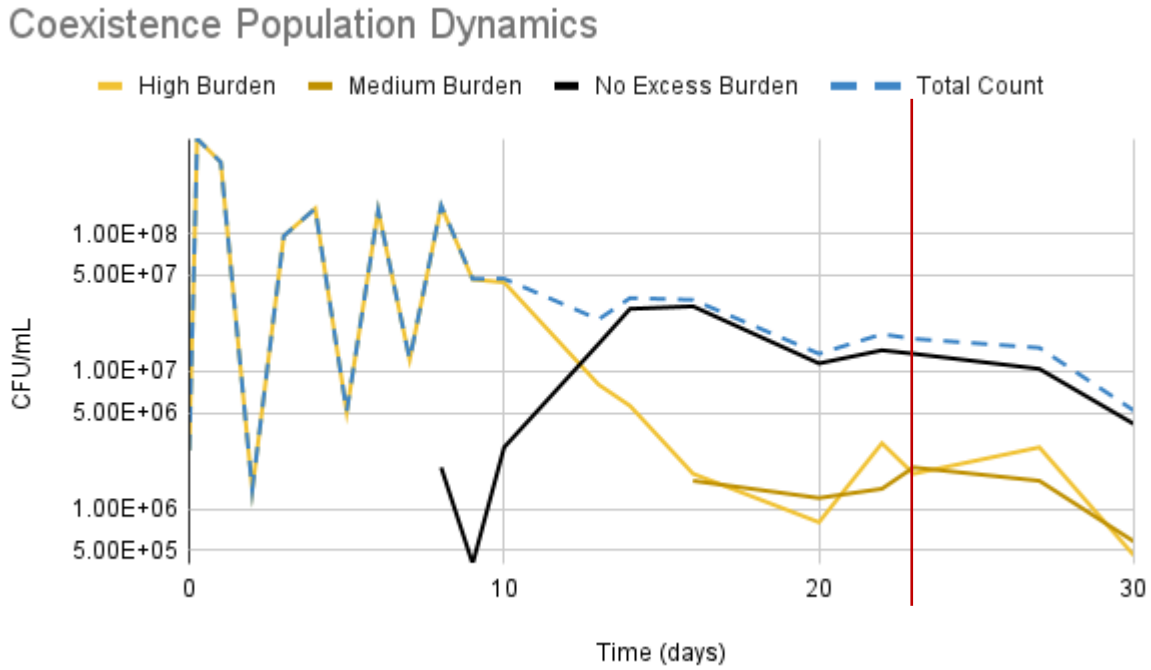
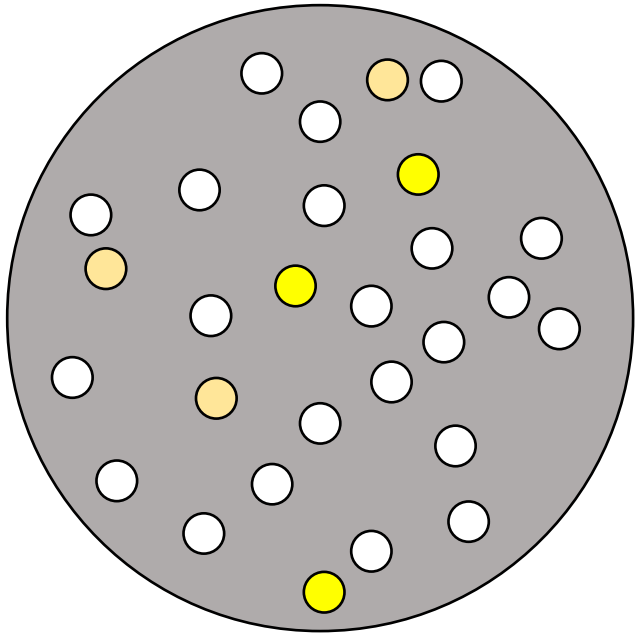
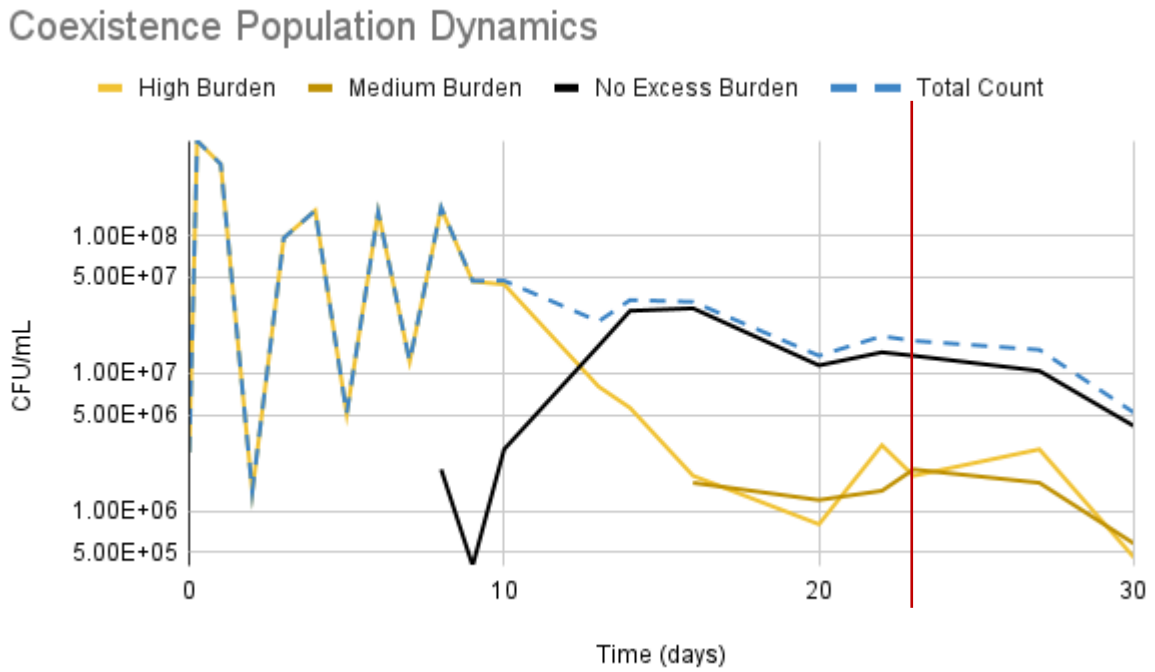




Experimental Coexistence

- Strains with varying levels of burden can coexist
- How do we model coexistence?

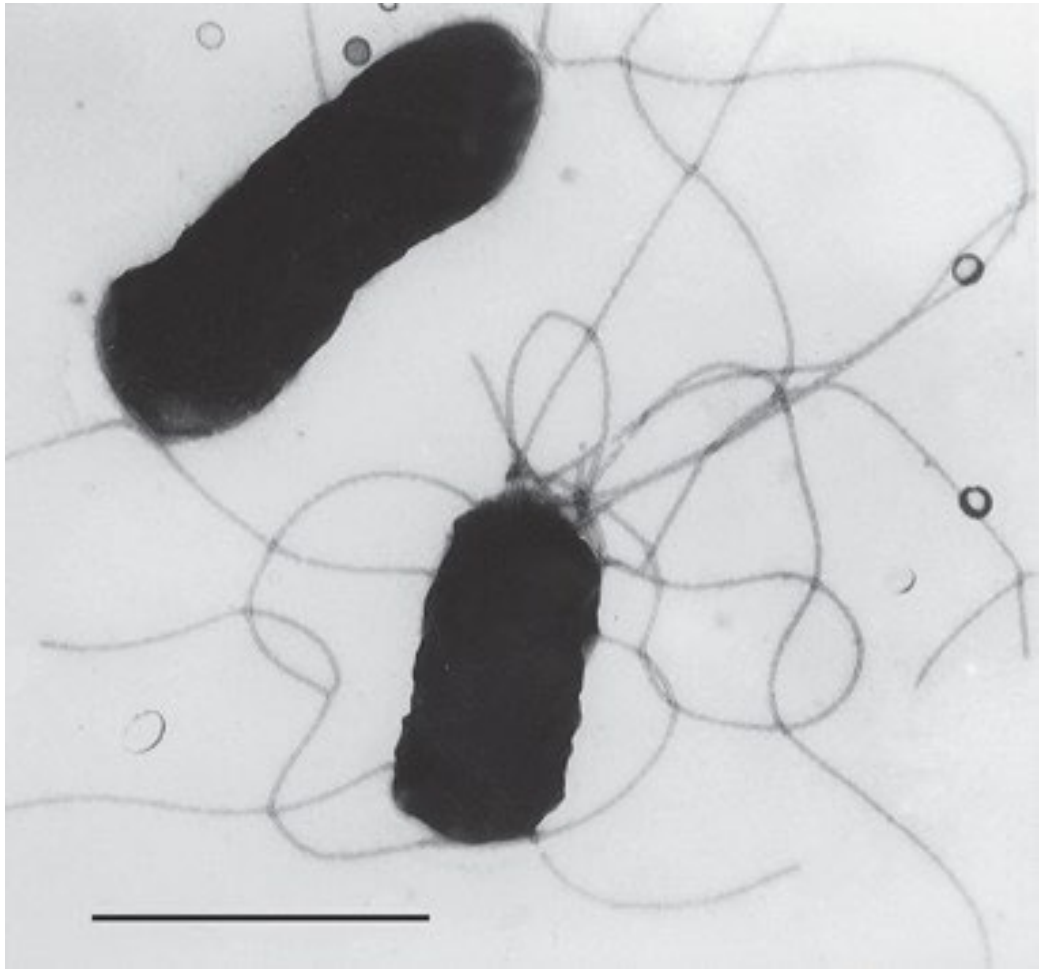


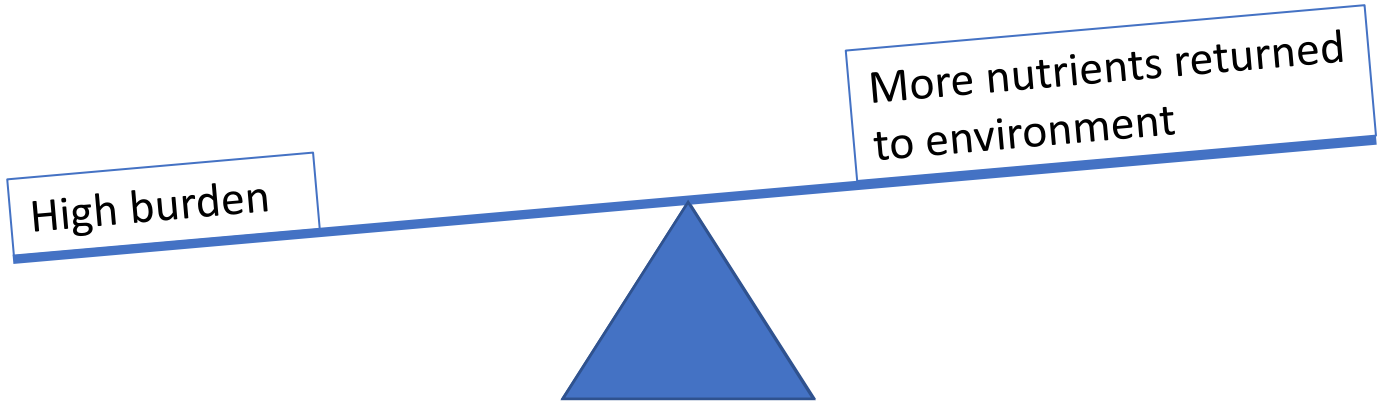


A natural example of protein burden: flagella

- Flagella are massive burdens (20k-30k subunits) –

yet *E. coli* still produce them





M. Eisenbach, Encyclopedia of Life Sciences, 2011

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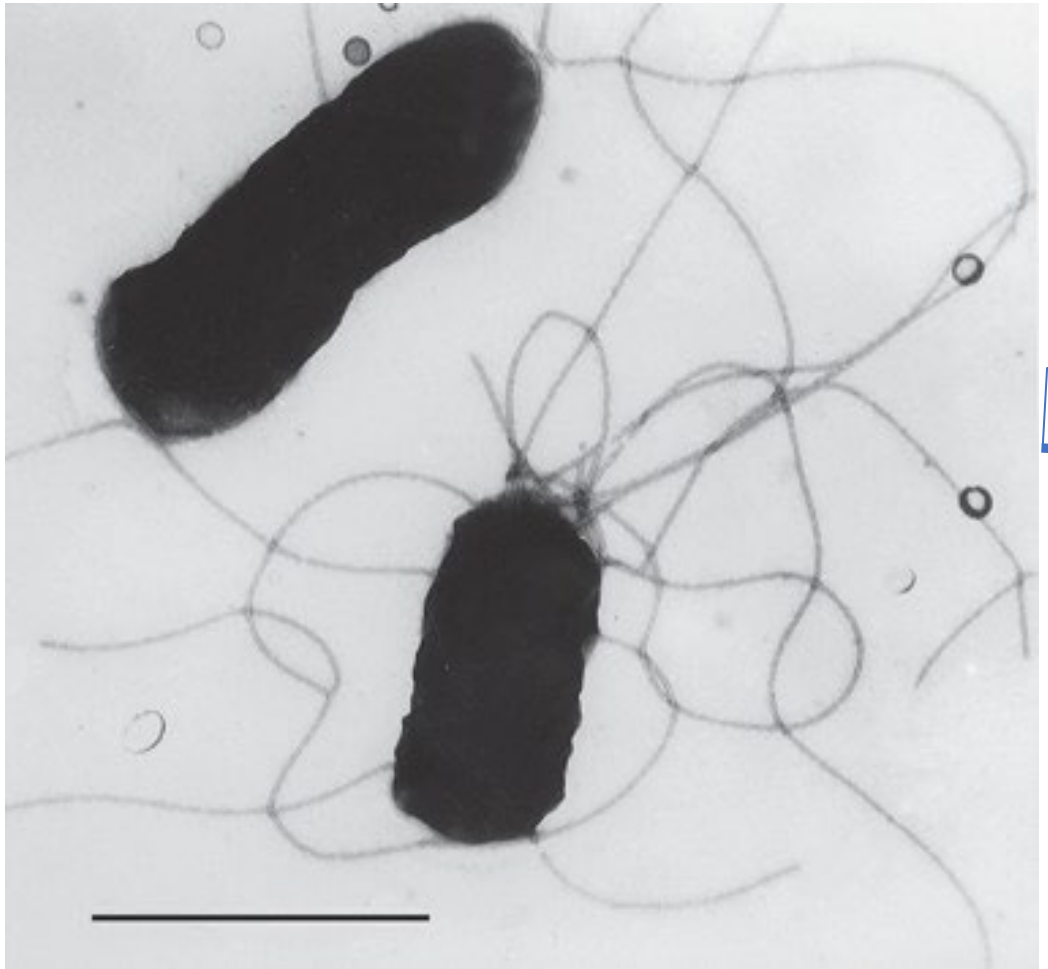

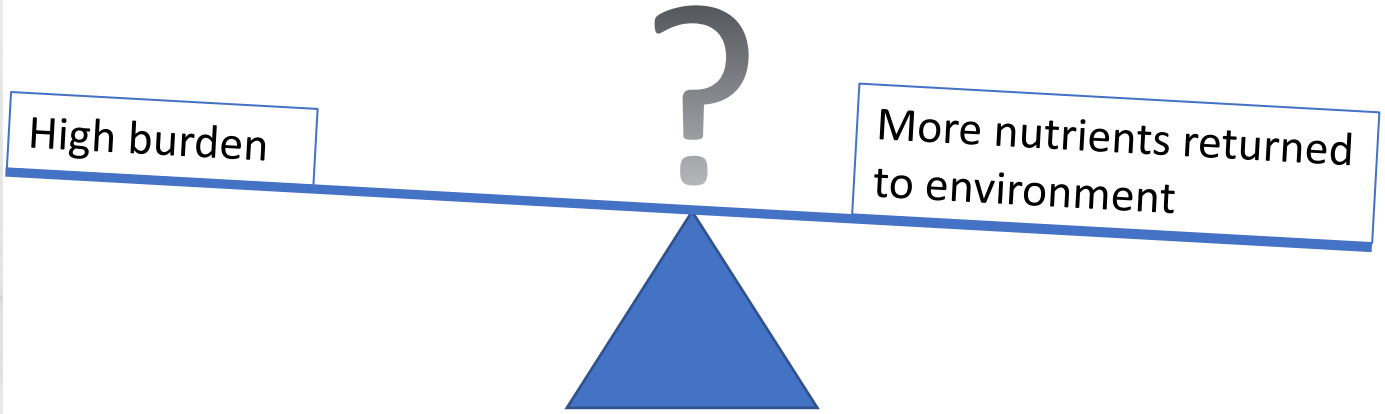

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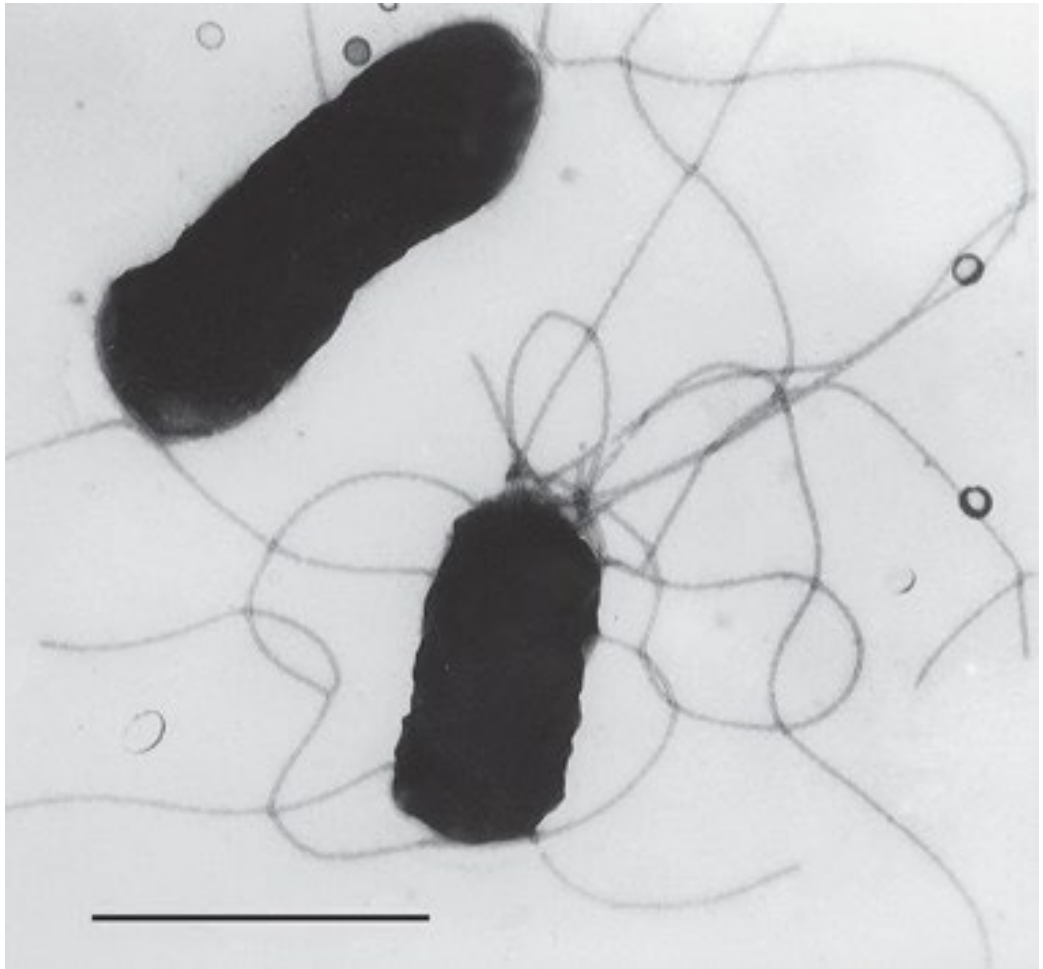
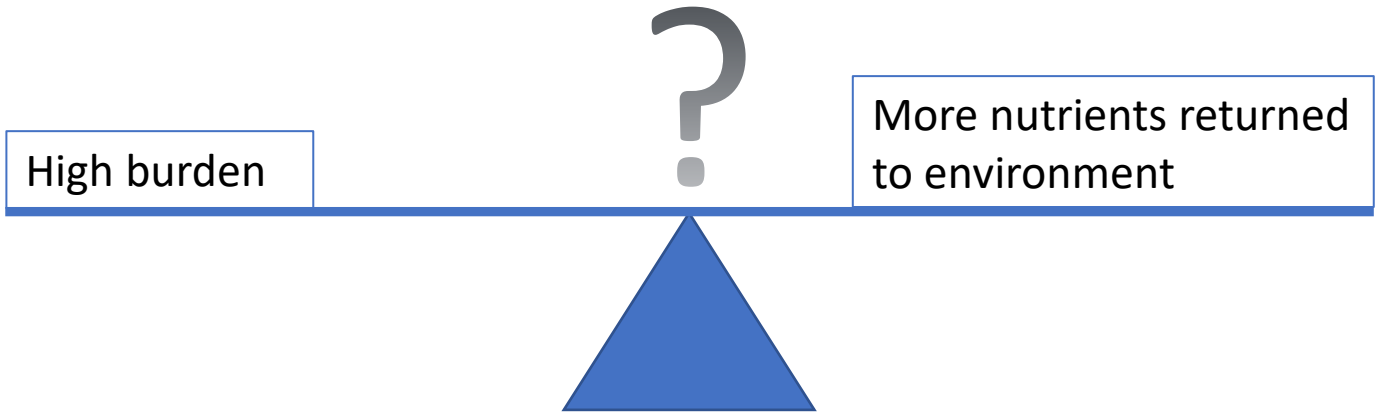
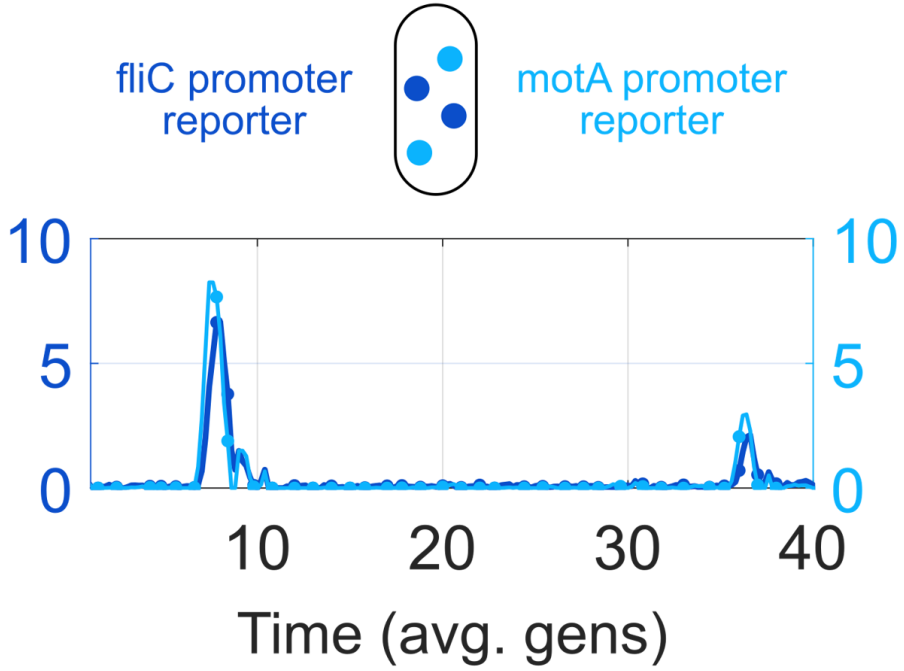




M. Eisenbach, Encyclopedia of Life Sciences, 2011

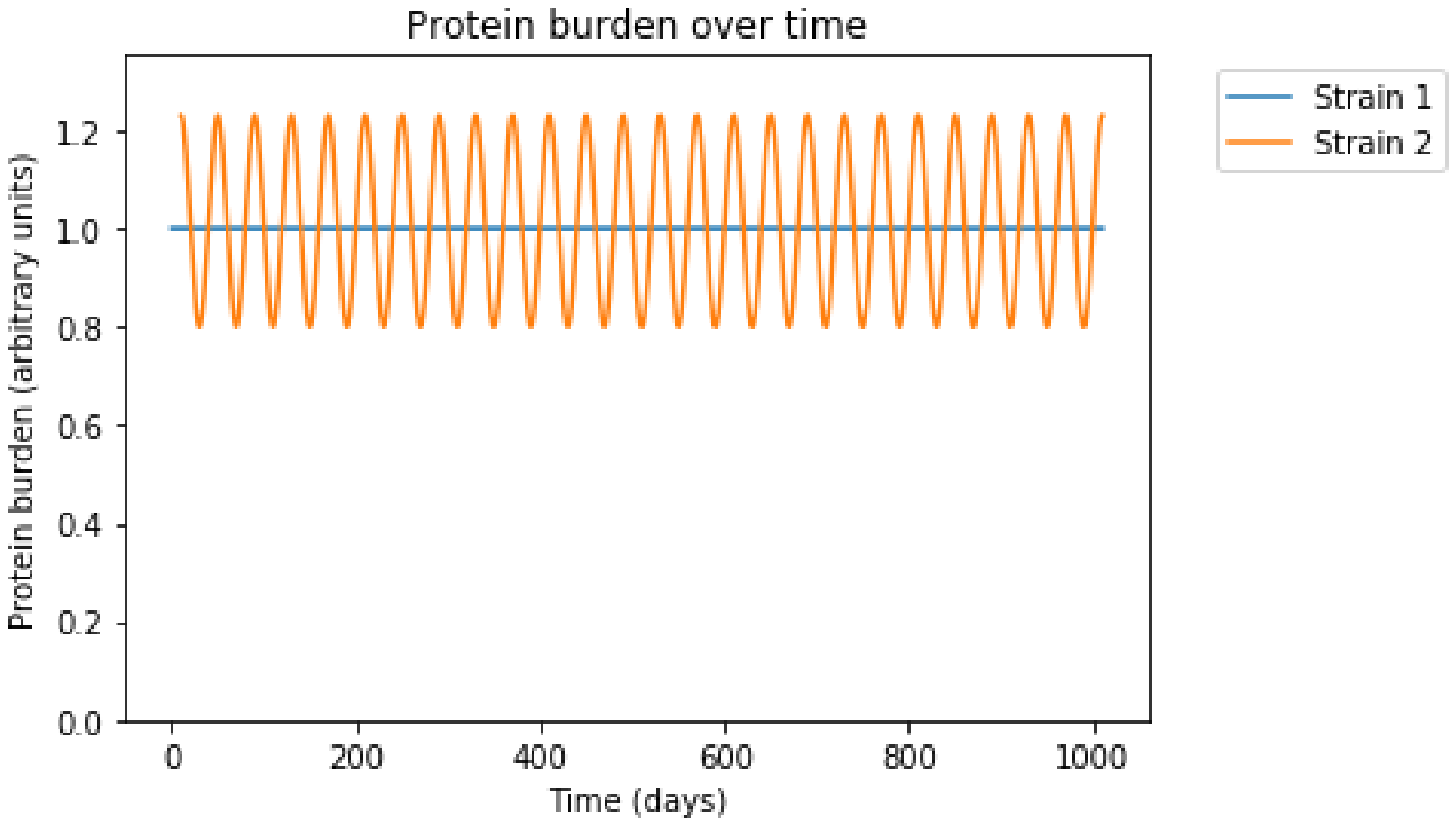
The lowest burden doesn't always take over

- Making flagella is a massive burden, yet **they can still coexist with, or even outcompete, more efficient strains**
  - Wild-type bacteria pulsate flagellum production (through varying promoter strength) as a survival strategy



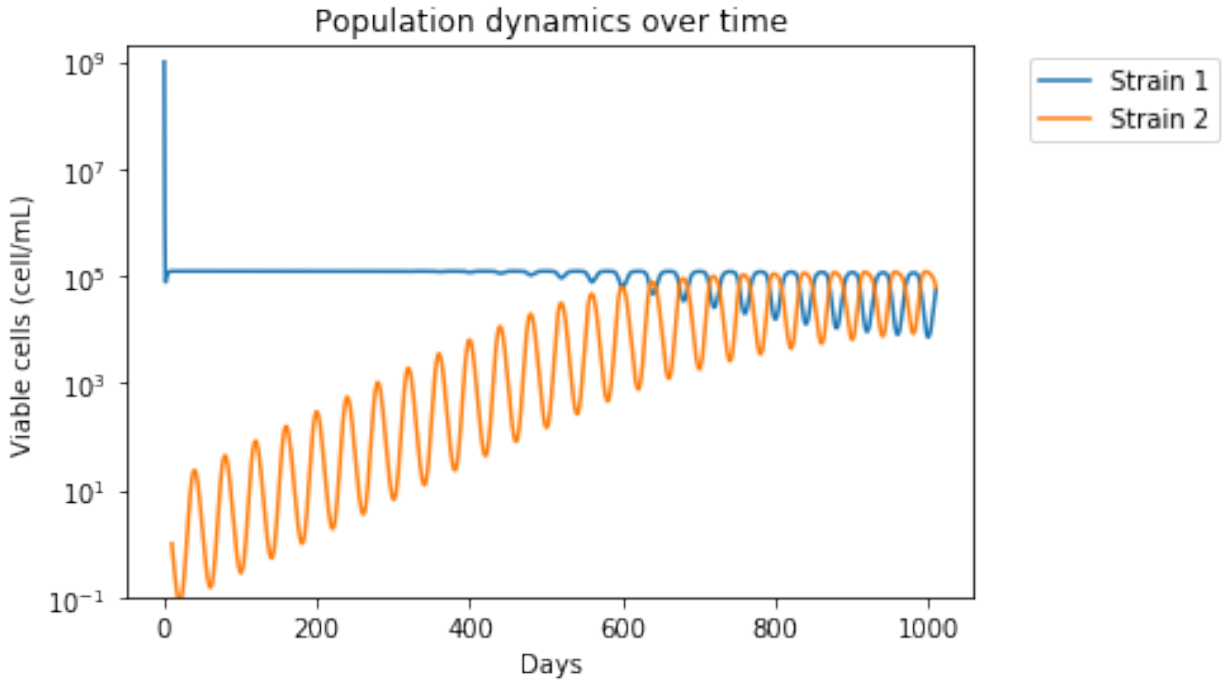
J.M. Kim et al., *Science Advances*, 2020

Simplification: Oscillating the protein burden

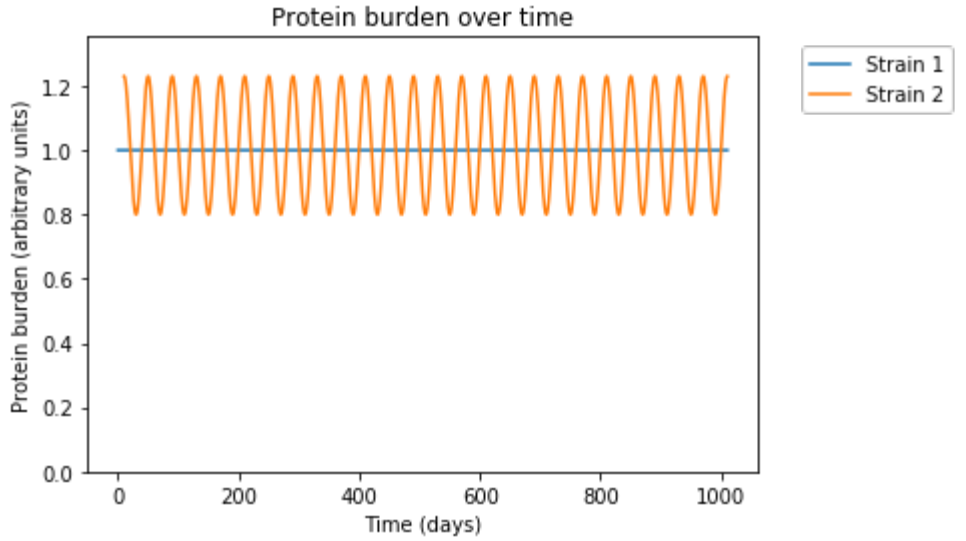


Modeling Coexistence

- An **oscillating** protein burden can be favorable over a constant burden of lower average magnitude



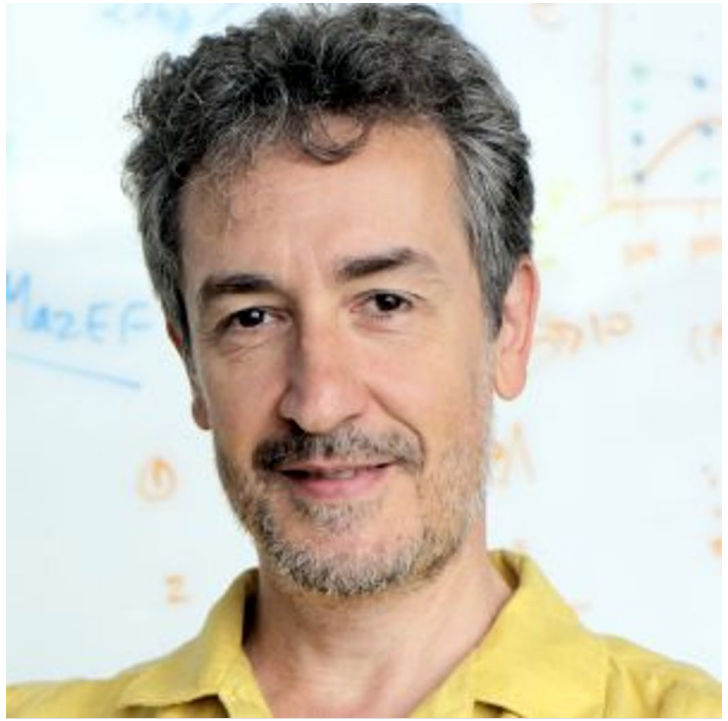
Constant burden of Strain 1 (blue) = 1
Arithmetic mean burden of Strain 2 (orange) ~ 1.02
Geometric mean burden of Strain 2 (orange) ~ 1.003



Future Directions

- Investigate the favorability of oscillating protein burden
  - Match experimentally observed pulsating dynamics
- Fit model to population data in the competitive exclusion case

Acknowledgements



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