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Parameter Estimation and Simulation of Bacteriophage Infection Model

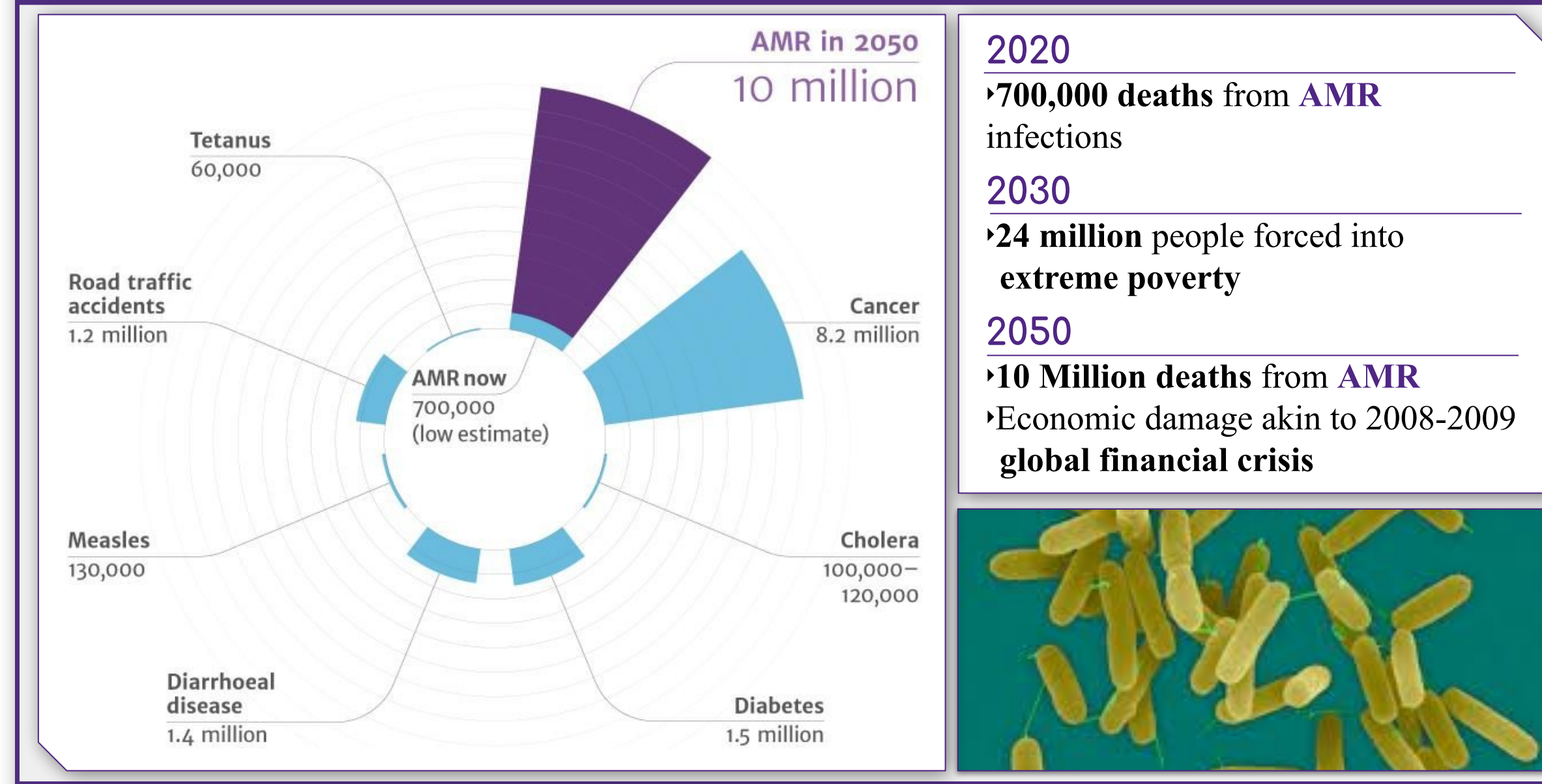
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Abstract

Bacteriophages are a class of viruses that infect and destroy bacteria.

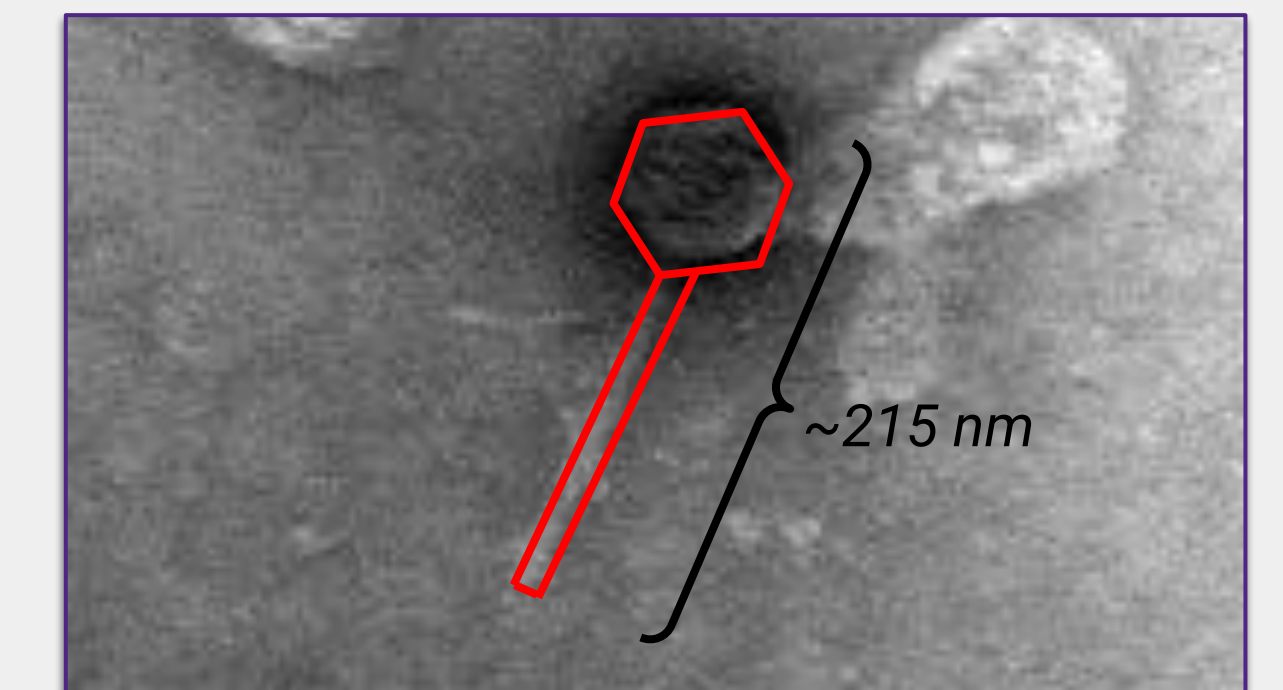
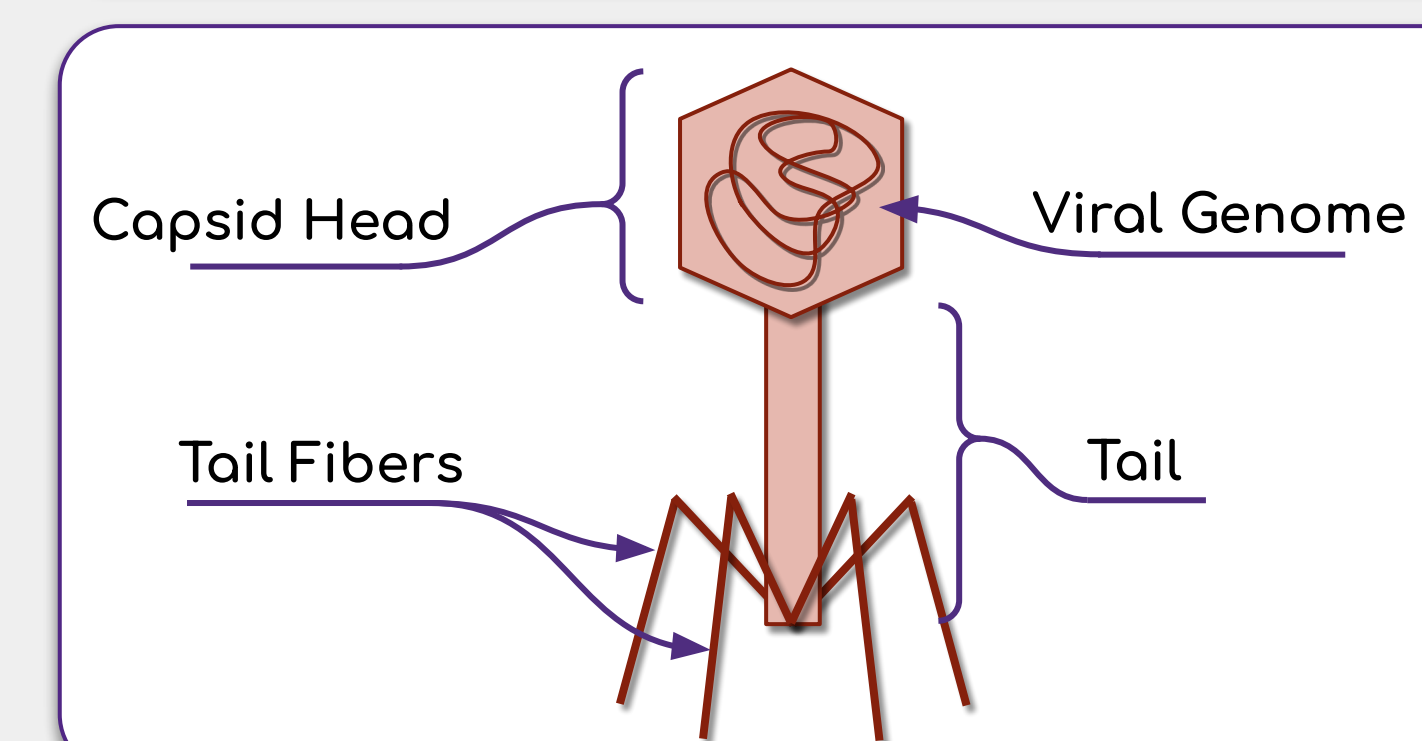
They are an emerging focus in research due to their potential use in treating antimicrobial resistant (AMR) bacterial infections. We are working on an interdepartmental project to create a mathematical model for the complexity of bacteriophage infection of host cells. A system of $4n+1$ differential equations was derived to model these interactions. This system of equations was then used to simulate results for the infection outcomes of the different populations. These results were then evaluated in search of equilibria for populations in a given parameter space. It is our hope that these simulated equilibria can be used to identify infection outcomes for bacteriophages used in clinical settings to speed up testing before usage and effectively improve patient outcomes.

The Threat of AMR Diseases



Bacteriophages

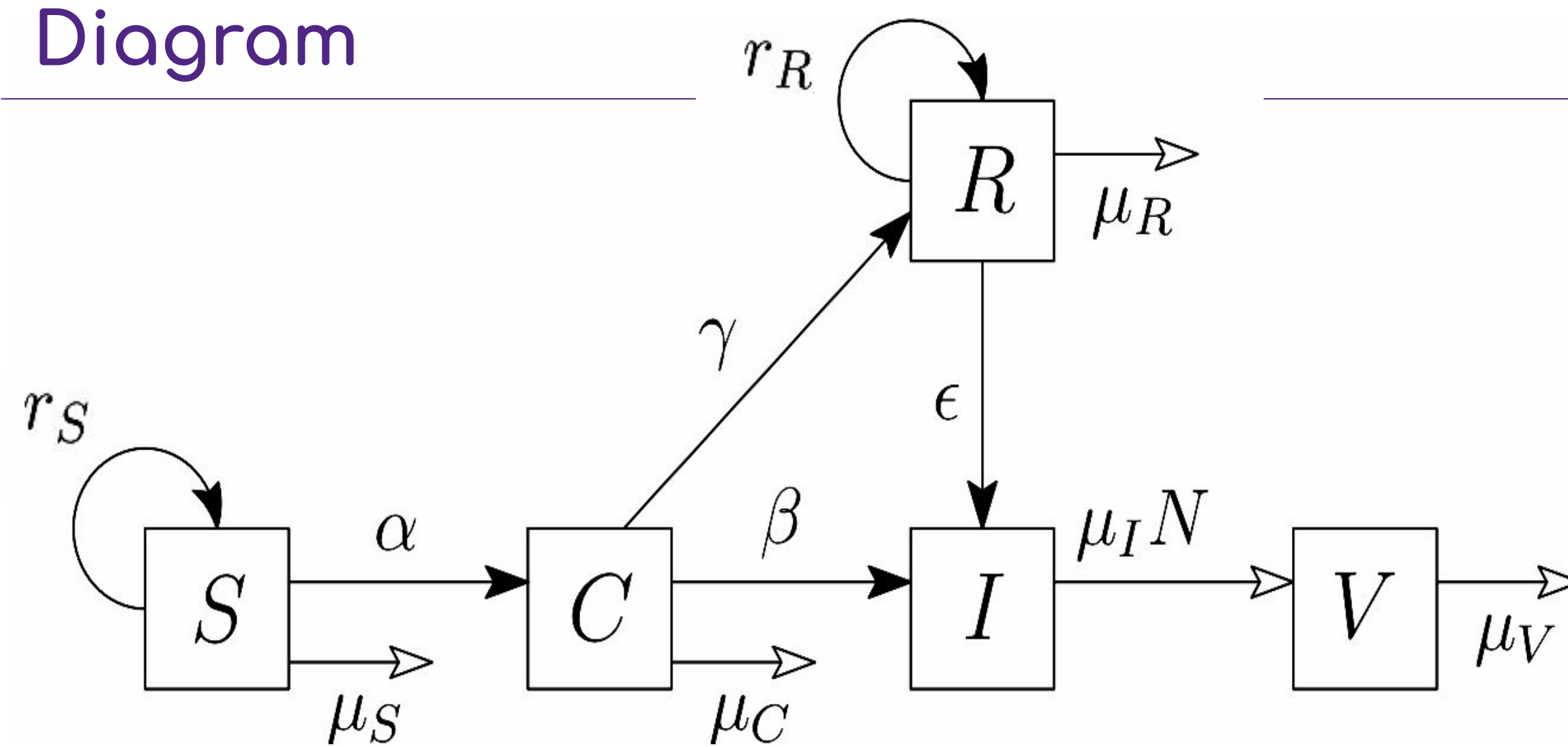
- Viruses that infect bacteria
- Estimated 10^{31} bacteriophages in the biosphere



TEM Scan of Microbacterium Phage Finny

The Infection Cycle: Single Phage

Diagram



Classes

- | | |
|--|---|
| S - Susceptible bacteria | I - Lytic bacteria |
| C - Circularized phage genome
(Can become either lytic or lysogenic) | R - Lysogenic reservoir bacteria |
| | V - Virions released |

Parameters

- | | |
|----------------------------------|---|
| α - Infection rate | μ - Death rate of a class |
| β - Infected to lytic | r_S - Replication rate of the S class |
| γ - Infected to lysogenic | r_R - Replication rate of the R class |
| ϵ - Lysogenic to lytic | |

Equilibria Theorems and Numeric Simulations

Theorem 1 (Extinction Stability for Constant Carrying Capacity, One Phage Only). The extinction equilibrium is locally asymptotically stable provided

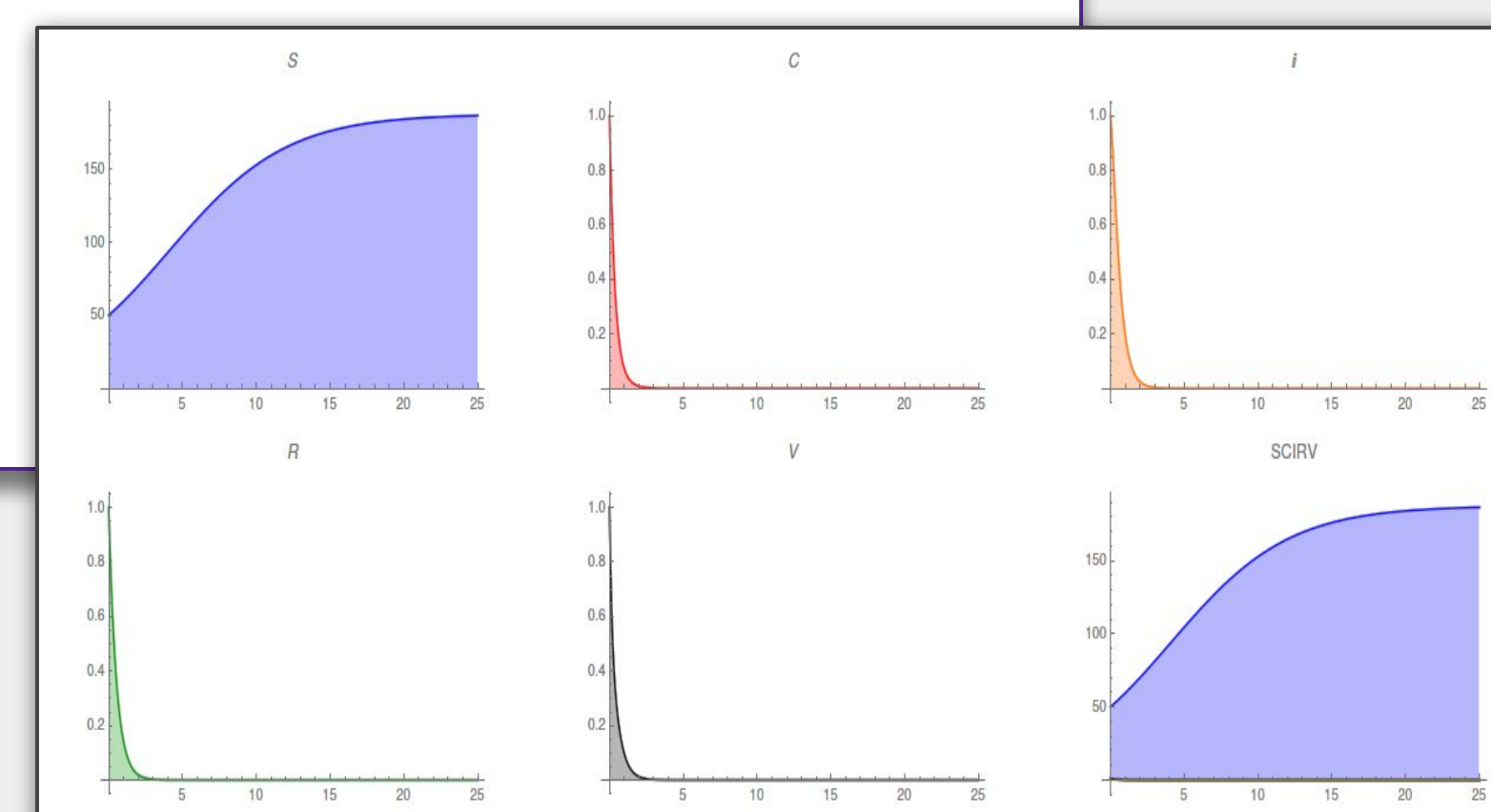
$$r_S < \mu_S \quad \text{and} \quad r_R < \mu_R + \epsilon.$$

Theorem 2 (Stability of $(\bar{S}, 0, 0, 0, 0)$ for Constant Carrying Capacity, One Phage Only). Suppose $r_S > \mu_S$ so that $\bar{S} = \frac{\mathbb{K}(r_S - \mu_S)}{r_S} > 0$. Further assume that $\mu_V > N\mu_I$. Then, a sufficient criteria for local asymptotic stability is

$$\alpha < \min \left\{ \frac{\beta + \gamma + \mu_C}{\bar{S}}, \mu_V - N\mu_I \bar{S} \right\}$$

$$\mu_I > \beta + \epsilon$$

$$\gamma < \epsilon + \mu_R - \frac{\mu_S r_R}{r_S}.$$



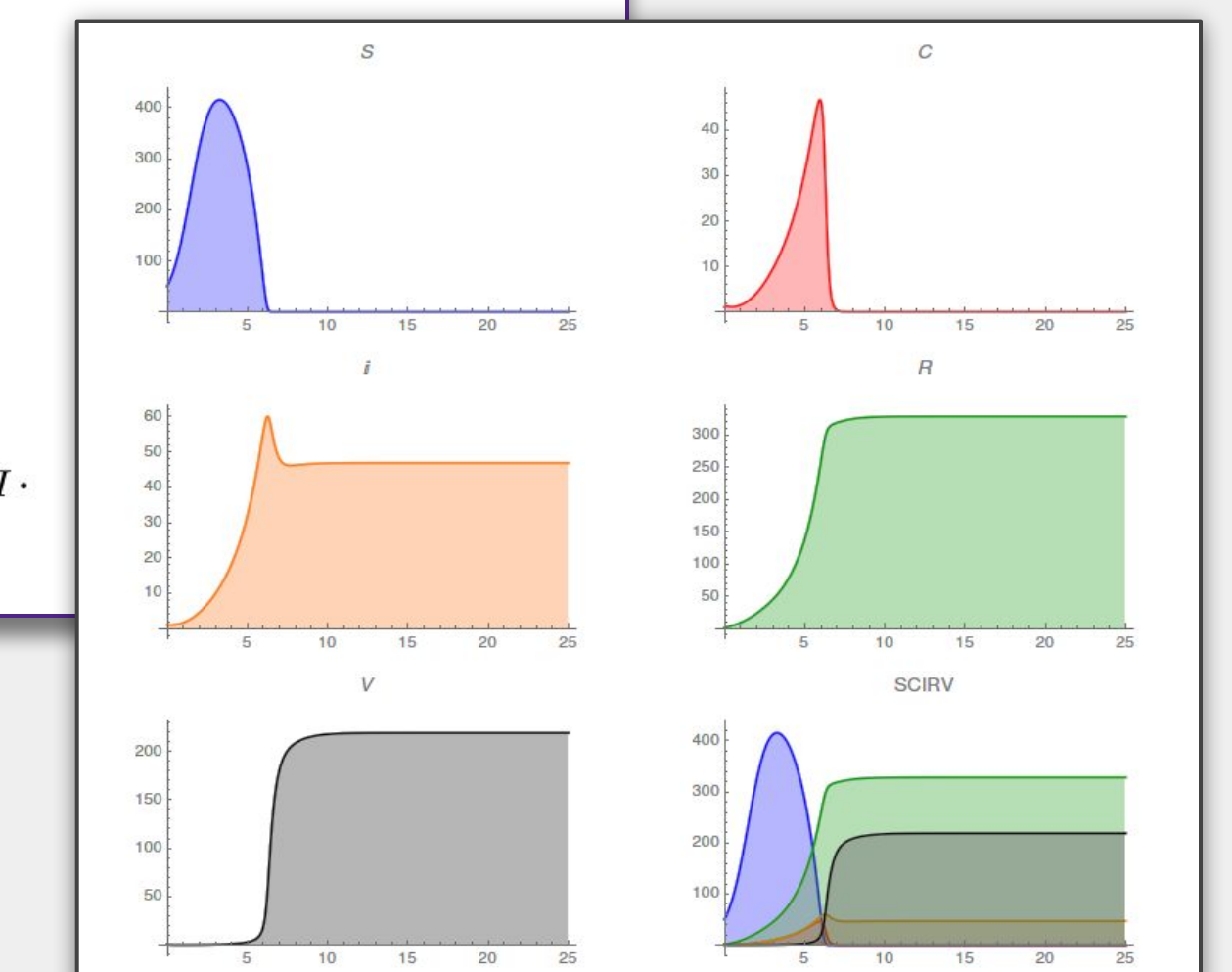
Theorem 3 (Stability Criterion for IRV Equilibrium for Constant Carrying Capacity, One Phage Only). Assume $r_R > \mu_R + \epsilon$. The equilibrium

$$(\bar{S}, \bar{C}, \bar{I}, \bar{R}, \bar{V}) = \left(0, 0, \frac{\epsilon \bar{R}}{\mu_I}, \bar{R}, \frac{N \epsilon \bar{R}}{\mu_V} \right),$$

$$\bar{R} = \frac{\mathbb{K} \mu_I (r_R - \epsilon - \mu_R)}{r_R (\epsilon + \mu_I)}$$

is locally asymptotically stable provided

$$r_S < \frac{r_R (\alpha \bar{V} + \mu_S)}{\epsilon + \mu_R} \quad \text{and} \quad r_R > \mu_R - \mu_I.$$



Future Directions

Brauer Theorem

- Ovals of Cassini
- Tightening bounds for S equilibrium

Bacteriophages in Competition

- Find equilibria for multi-phage interaction models
- Model interactions similar to what is seen in medical applications

