Parameter Estimation and Simulation of Bacteriophage Infection Model

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SEA PHAGES

Tarleton Math Day
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TARLETON STATE UNIVERSITY
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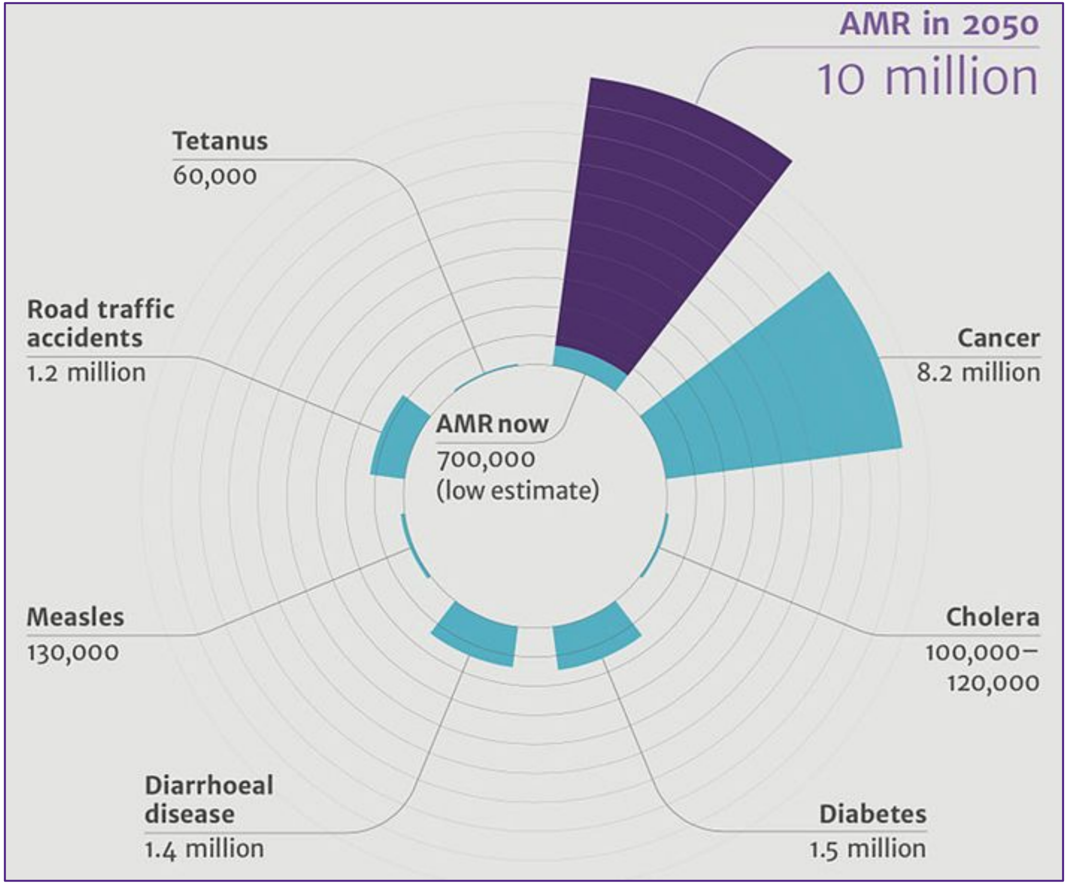
Projected Prognosis



2020

- **700,000 deaths** from **AMR** infections

2030

- **24 million** people forced into **extreme poverty**

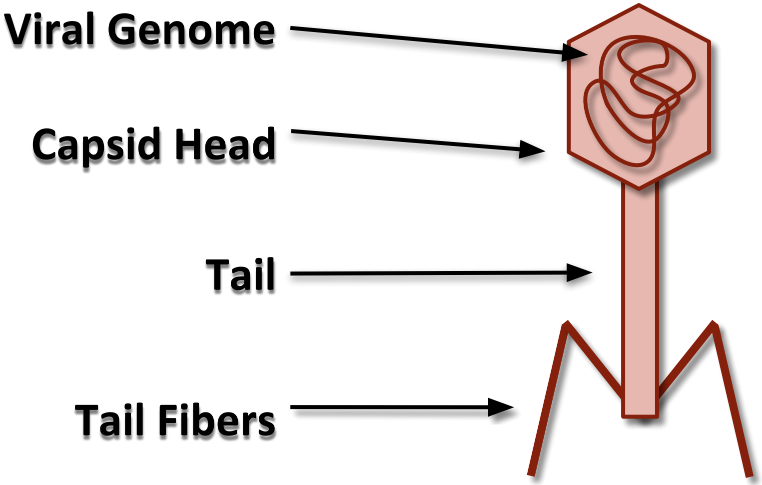
2050

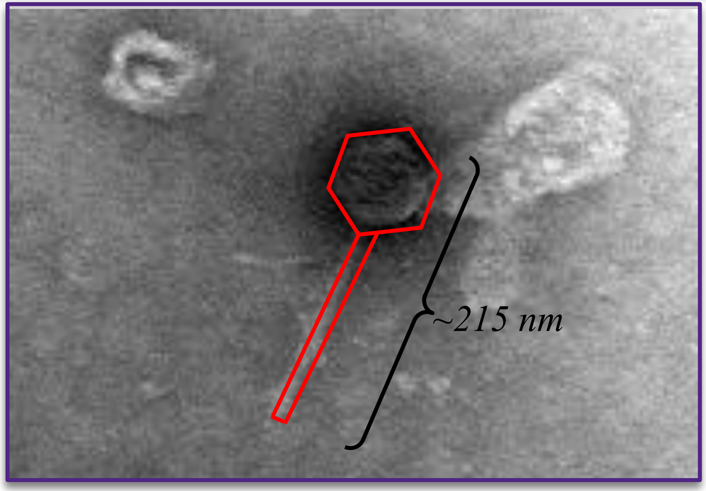
- **10 Million deaths** from **AMR**
- Economic damage akin to 2008-2009 **global financial crisis**

Bacteriophage Background

Bacteriophages

- **Viruses** that infect **bacteria**
- Estimated $\mathbf{10^{31}}$ bacteriophages in the biosphere



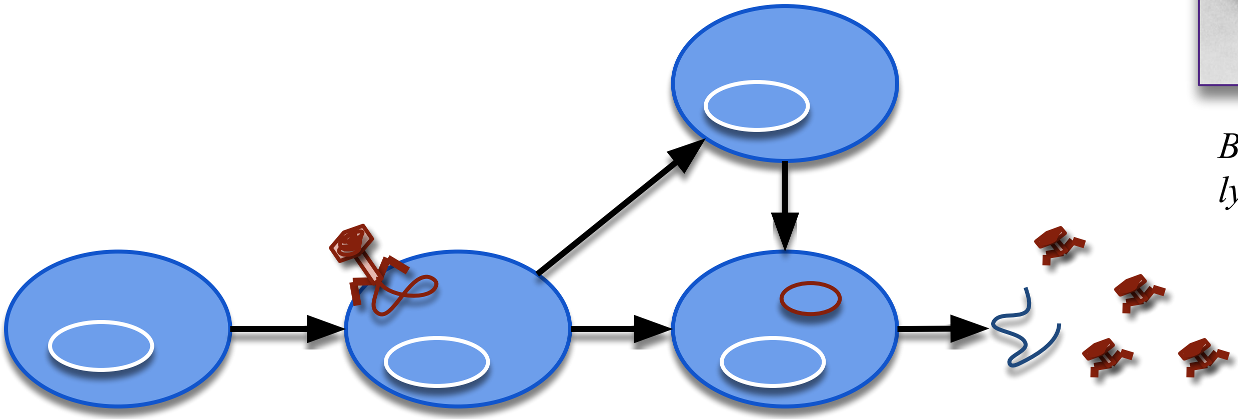


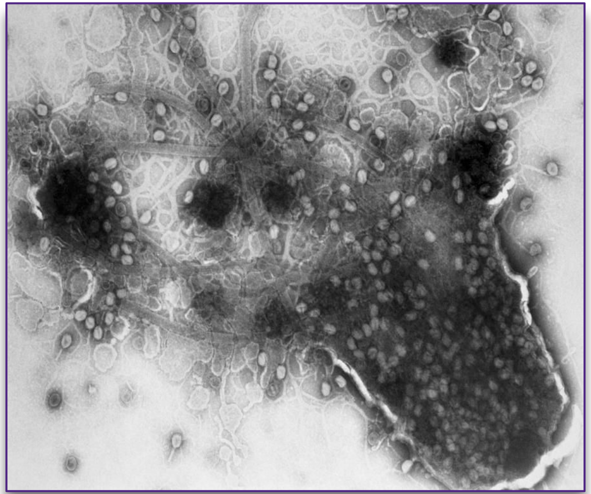
TEM Scan of Microbacterium Phage ***Finny***

Bacteriophage Background

Bacteriophages

- Two infection types: **Lytic** and **Lysogenic**
- **Lysogenic** bacteriophages become **reservoir** hosts
- **Lytic** bacteriophages **produce more** bacteriophages
- Infectious bacteriophage particles called virions





*Bacteriophage **T4** in a lytic infection lysing, and subsequently killing, **E. coli***

Compartmental Diagram

S - Susceptible bacteria

C - Circularized phage genome, choose between lytic and lysogenic infection

I - Lytic bacteria

R - Lysogenic reservoir bacteria

V - Virions created

α - Infection rate

β - Infected to lytic

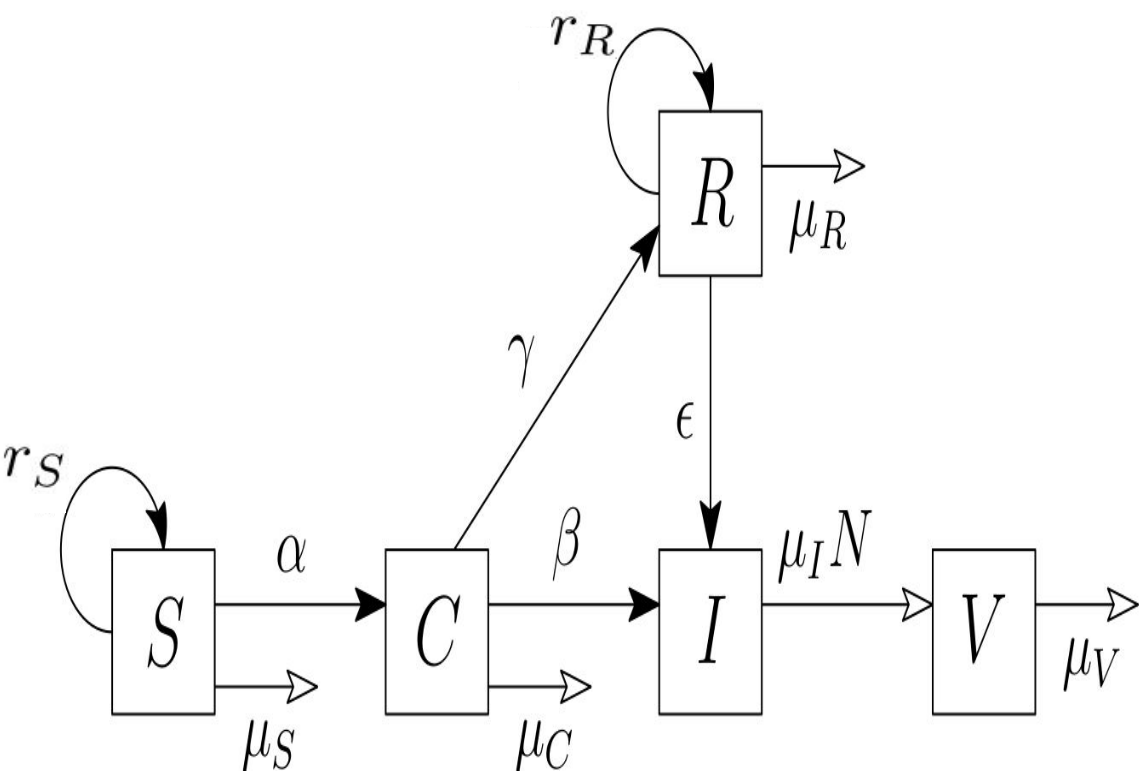
γ - Infected to lysogenic

ε - Lysogenic to lytic

μ - Death rate of a class

rS - Replication rate of the S class

rR - Replication rate of the R class



System of Differential Equations

$$\frac{dS}{dt} = r_S S\left(1 - \frac{S+C+I+R}{\mathbb{K}}\right) - \mu_S S - \alpha SV$$

$$\frac{dC}{dt} = \alpha SV - (\mu_C + \beta + \gamma)C$$

$$\frac{dI}{dt} = \beta C - \mu_I I + \epsilon R$$

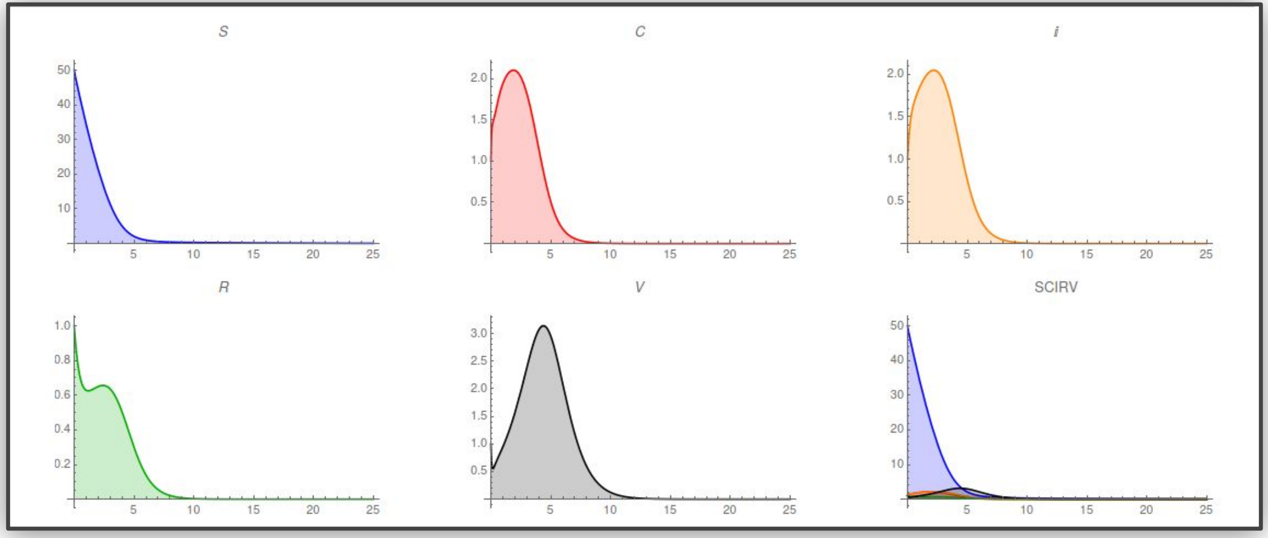
$$\frac{dR}{dt} = r_R R\left(1 - \frac{S+C+I+R}{\mathbb{K}}\right) + \gamma C - (\epsilon + \mu_R)R$$

$$\frac{dV}{dt} = \mu_I N I - \mu_V V - \alpha SV.$$

Search for Stability: Extinction

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

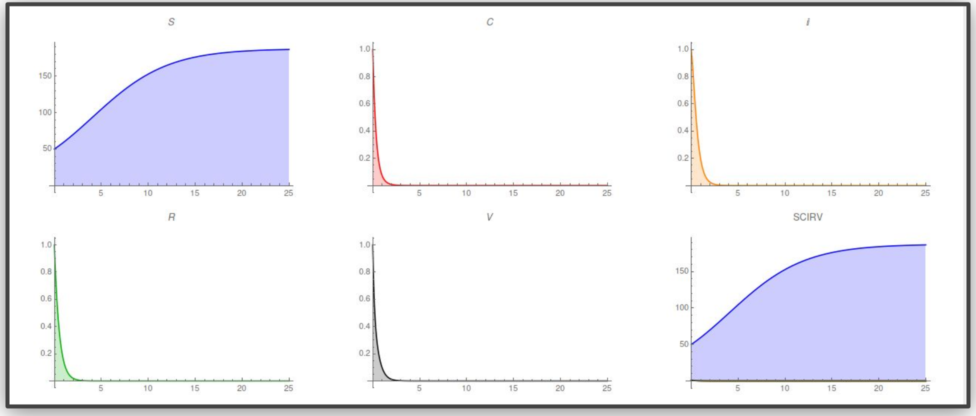
$$r_S < \mu_S \quad \textit{and} \quad r_R < \mu_R + \epsilon.$$



Stability of $(\bar{S},0,0,0,0)$ for Constant Carrying Capacity

Search for Stability: Bacterial Survival

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



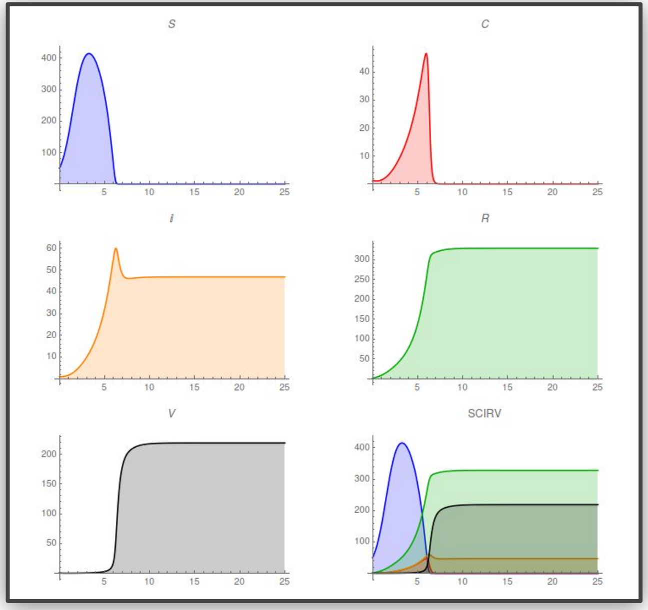
$$\alpha < \min\left\{\frac{\beta+\gamma+\mu_C}{\bar{S}}, \mu_V - N\mu_I\bar{S}\right\}$$

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

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

Search for Stability: IRV Survival

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

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

Future Directions

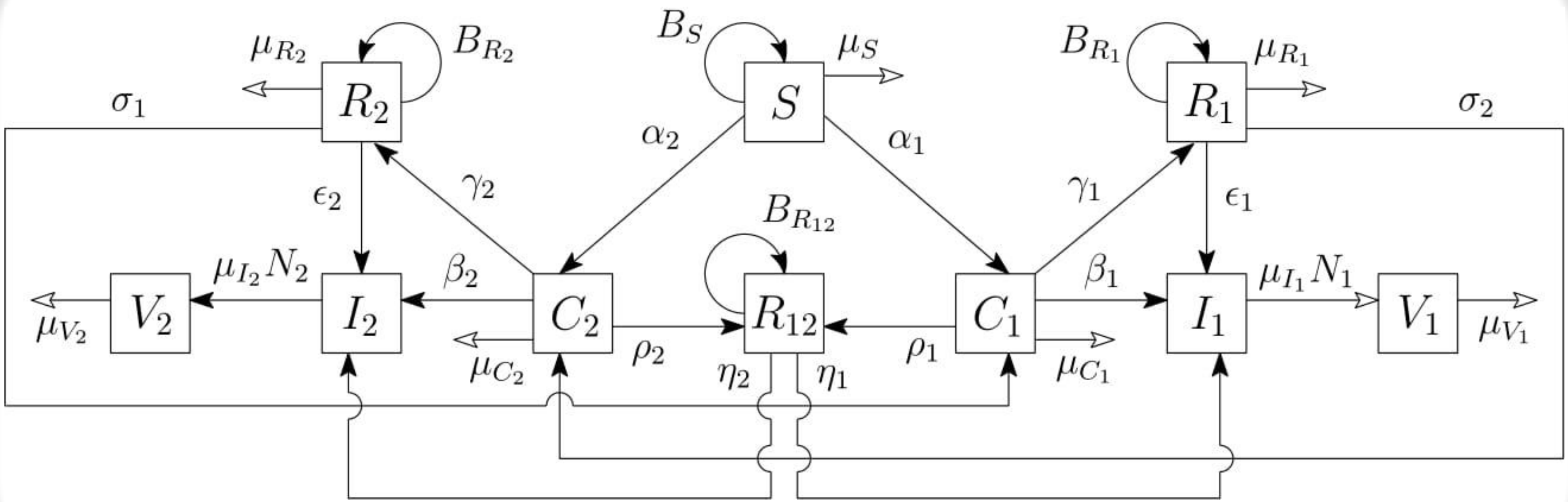
Brauer Theorem

- Ovals of Cassini
- Finding more strict restrictions for S equilibrium

Bacteriophages in Competition

- A complex system of multiple phages interacting
- Models interactions similar to what is seen in medical applications

Future Directions



Acknowledgements

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Thank You!

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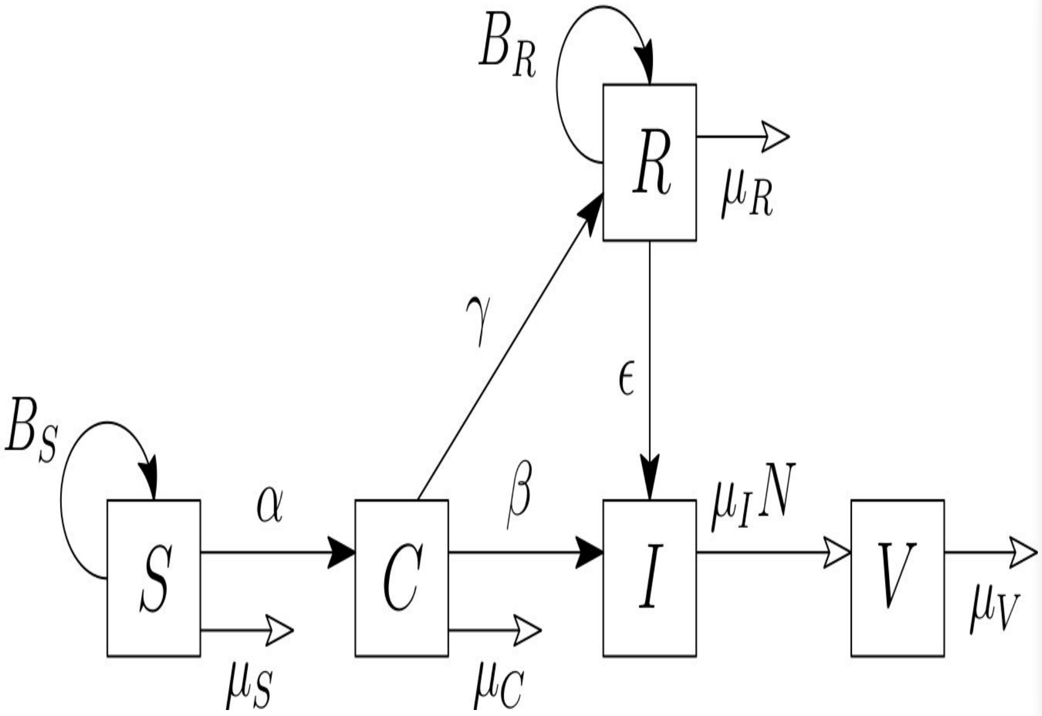
Questions



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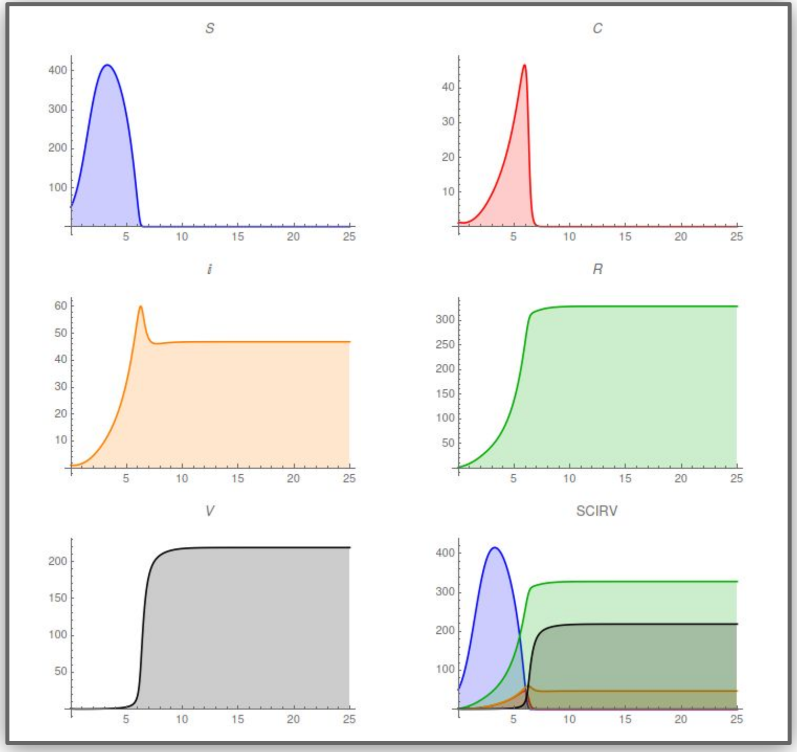

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