Spatiotemporal Two-Pathogen Dynamics on Metapopulation Networks

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Outline

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1. Introduction
2. Reaction-Diffusion (RD) Systems
3. Multiplex Bi-Virus Reaction-Diffusion (MBRD) Framework

Epidemic Modeling

- Predict severity of infectious diseases and new case counts.
- Inform policy decisions including issued public health emergencies, lockdowns, and mask mandates.
- Examples include COVID-19 pandemic, 2009 H1N1 pandemic, and 2024 Chicago measles outbreak.

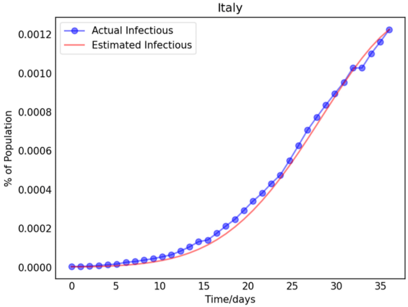


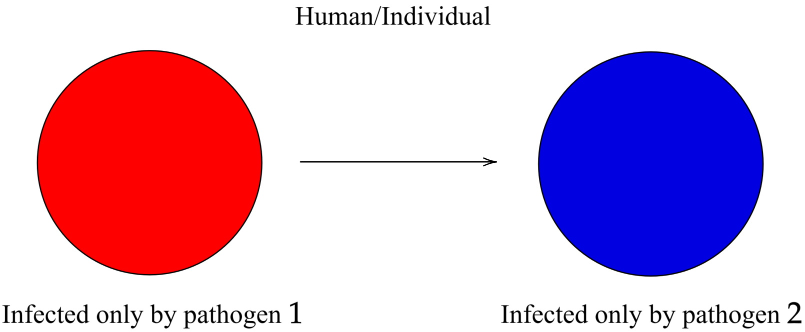
Figure: Modeling of COVID-19 infections in Italy [3].

Epidemics involve interacting pathogens with coupled dynamics. Capturing these multi-pathogen interactions is essential for more realistic models.

Two-Pathogen Interactions: Super-Infection

We consider co-circulation of two viruses or two strains of the same virus.

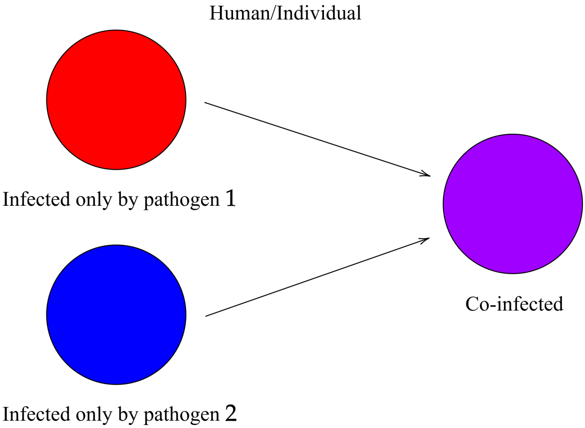
- **Super-Infection:** One pathogen can replace another pathogen in a host (e.g., super-infection of Hepatitis strains).



Two-Pathogen Interactions: Co-Infection

We consider co-circulation of two viruses or two strains of the same virus.

- **Co-Infection:** A host can be infected with both pathogens simultaneously (e.g., COVID-19 and influenza co-infection).



Metapopulation Networks

- Nodes represent local regions (e.g., cities, towns).
- Edges represent human movement between regions.

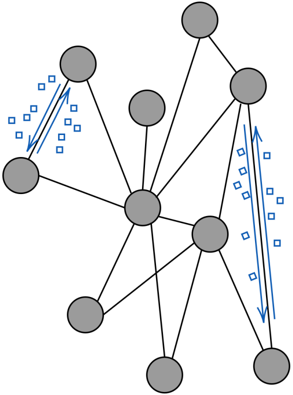


Figure: Metapopulation network example.

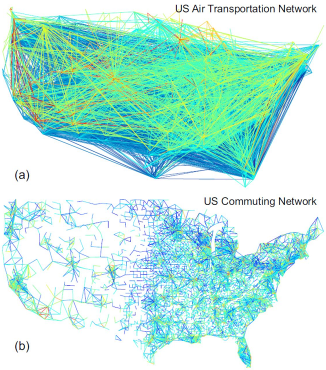
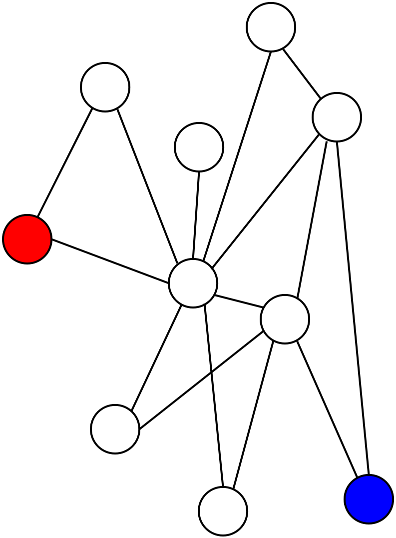


Figure: Metapopulation networks of USA [8].

Spatiotemporal Two-Pathogen Dynamics



- Red: Pathogen 1 infection severity.
- Blue: Pathogen 2 infection severity.

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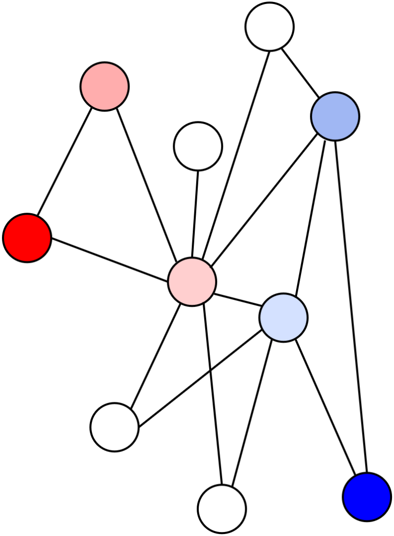

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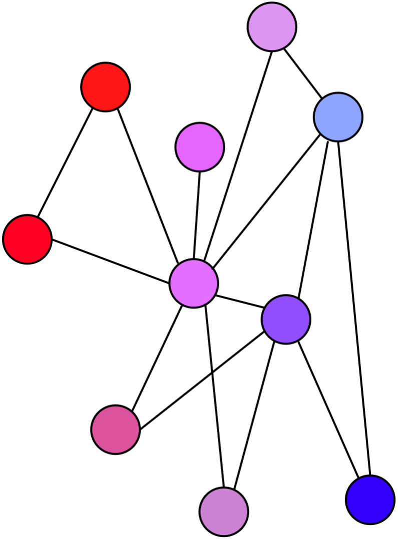

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Turing Patterns

- Appear in animal pigmentations, vegetation patterns, limb formation, synthetic biology, etc.
- Instabilities arise from small perturbations to a uniform state.
- Morphogens react and diffuse to form stable patterns of varying concentrations throughout spatial region.
- Proposed by Alan Turing in his 1952 paper "The Chemical Basis of Morphogenesis" [7].

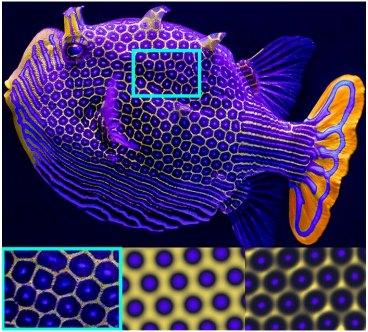

Figure: Turing pattern in boxfish pigmentation [2].

Reaction-Diffusion Systems

- Turing patterns are modeled with reaction-diffusion systems.
- Composed of a reaction and diffusion components.

Definition (Reaction-diffusion system of two morphogens)

The simplest form of a reaction-diffusion system of two morphogens in one-dimensional space is:

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- u and v: concentration of morphogens over space x and time t.
- f and g: reaction functions.
- D_u and D_v: diffusivity coefficients.

Cross-Diffusion

- Gradients of the morphogens are influenced by each other.
- Often induces instability.

Definition (Reaction-diffusion system with cross-diffusion)

Reaction-diffusion equation of two morphogens with cross-diffusion:

$$\frac{\partial u}{\partial t} = f(u, v) + D_u \frac{\partial^2 u}{\partial x^2} + D_{uv} \frac{\partial^2 v}{\partial x^2},$$

$$\frac{\partial v}{\partial t} = g(u, v) + D_v \frac{\partial^2 v}{\partial x^2} + D_{vu} \frac{\partial^2 u}{\partial x^2},$$

- u and v: concentration of morphogens over space x and time t.
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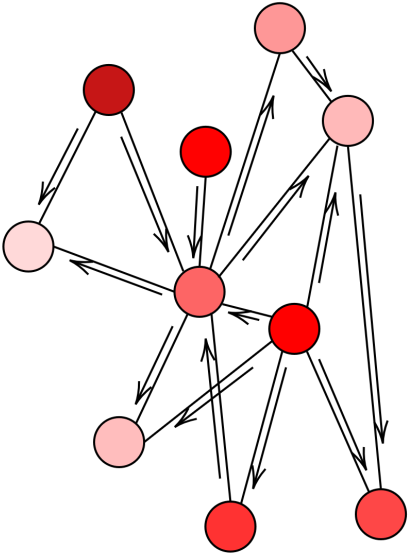
- D_u and D_v: diffusivity coefficients.
- D_{uv} and D_{vu}: cross-diffusivity coefficients.

Diffusion on Networks

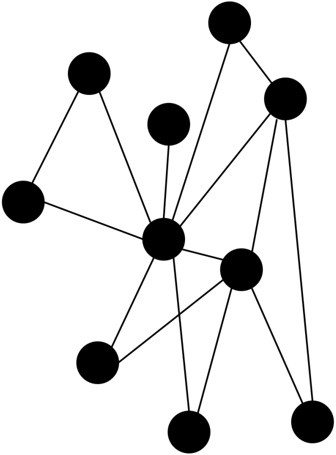


Can we model Turing patterns on networks?

We first consider the diffusion of a single morphogen.

Diffusion on Networks

Consider an unweighted and undirected network $G := (V, E)$ with $|V| = N$, where an edge between nodes i and j is denoted by (i, j).



Diffusion on Networks

- Let u_i be the concentration of morphogen 1 on each node i, and D_u be its diffusivity coefficient.

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The diffusion of a morphogen from node j to node i is of rate $D_u(u_j - u_i)$. If we add these rates, the amount of the substance entering node i is

$$D_u \sum_{j=1}^{n} A_{ij}(u_j - u_i) = D_u \left(\sum_{j=1}^{n} A_{ij} u_j \right) - D_u k_i u_i = D_u \sum_{j=1}^{n} L_{ij} u_j,$$

Definition

We define $L_{ij} := A_{ij} - \delta_{ij} k_i$, where $\delta_{ij} := \begin{cases} 1, & \text{if } i = j, \\ 0, & \text{otherwise} \end{cases}$. Moreover, we define $\boldsymbol{L}(G)$ to be the $N \times N$ matrix with entries L_{ij}. This is also the negative of the graph Laplacian.

Reaction-Diffusion on Networks

Definition (Reaction-diffusion system on networks)

In a network, the simplest form of a two-morphogen reaction-diffusion system is

$$\frac{du_i}{dt} = f(u_i, v_i) + D_u \sum_{j=1}^{n} L_{ij} u_j,$$

$$\frac{dv_i}{dt} = g(u_i, v_i) + D_v \sum_{j=1}^{n} L_{ij} v_j.$$

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- u_i and v_i: morphogen densities for each node $i = 1, 2, \ldots, n$.

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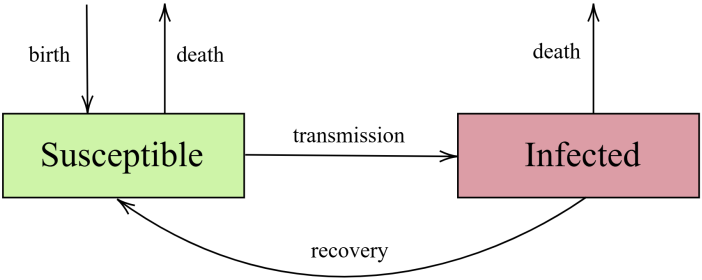
Multiplex Bi-Virus Reaction-Diffusion (MBRD) Framework

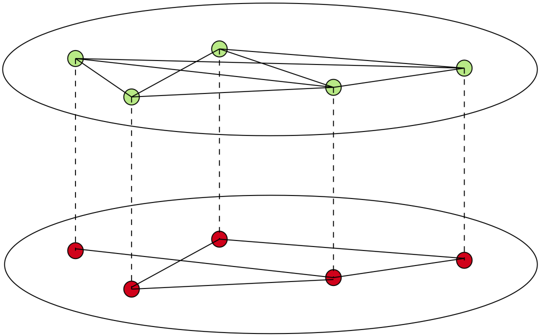
- Framework consisting of two models: superinfection model (**MBRD-SI**) and co-infection model (**MBRD-CI**).
- Based on Susceptible-Infected-Susceptible (SIS) dynamics, where individuals do not gain long-term immunity.



Multiplex Metapopulation Networks

Goal: Model differing population movement patterns between susceptible and infected individuals.

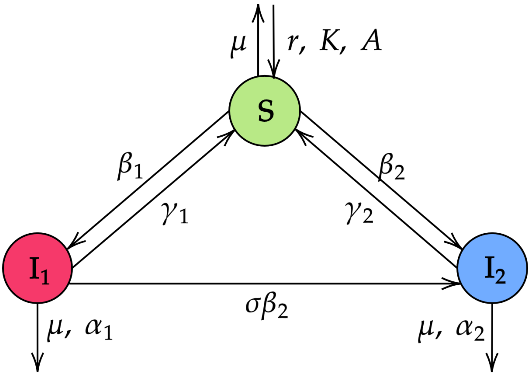
Considering a simple scenario with only one circulating pathogen, we separate a metapopulation network into two layers (with the same nodes), one housing susceptible densities, and the other housing infected densities.



Super-Infection Model (MBRD-SI)

We consider the following three states:

- S, susceptible;
- I_1, pathogen 1-infected;
- I_2, pathogen 2-infected.



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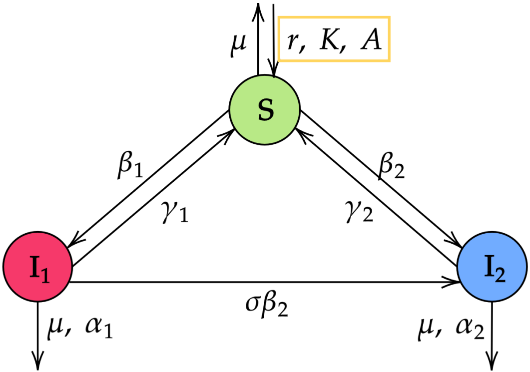

$\boxed{r, K, A}$: birth rate based on carrying capacity.

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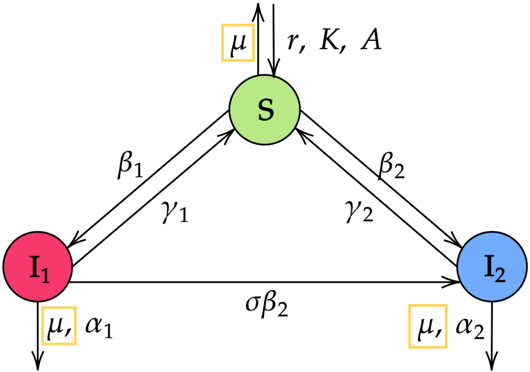

$\boxed{\mu}$: natural death rate.

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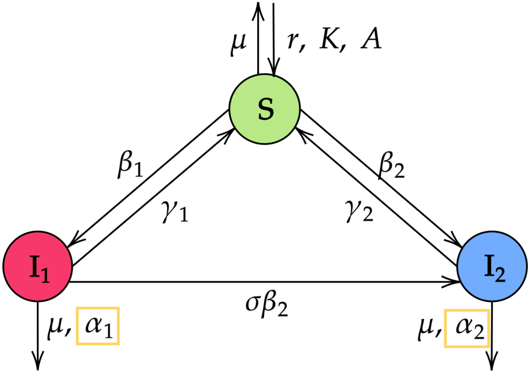

$\boxed{\alpha_1, \alpha_2:}$ infection-induced death.

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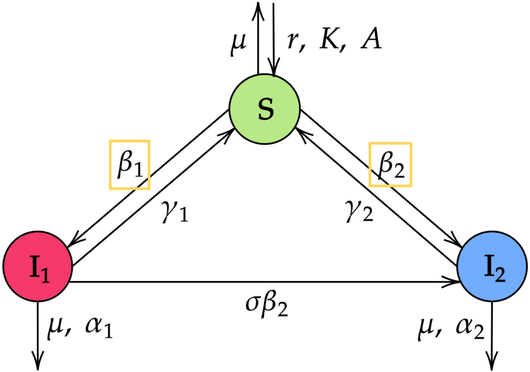

$\boxed{\beta_1, \beta_2:}$ infection transmission.

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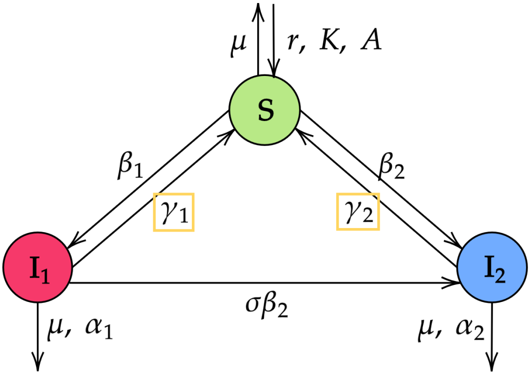

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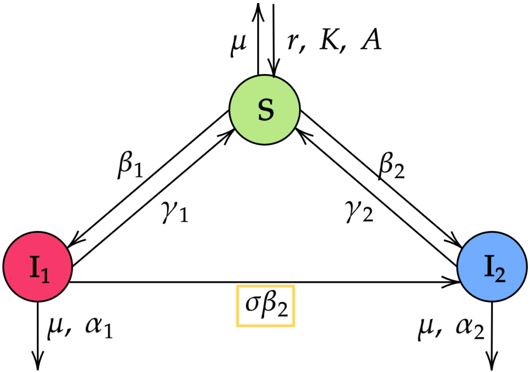
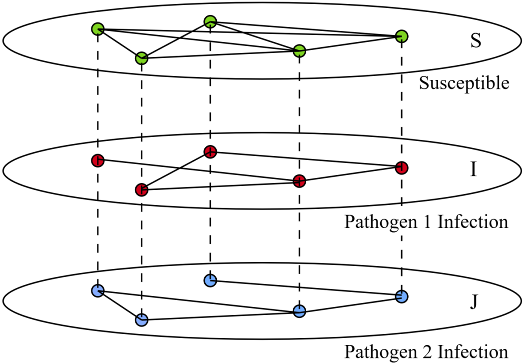


$\boxed{\sigma\beta_2:}$ rate of superinfection.

Super-Infection Model (MBRD-SI)

- We consider a three-layer multiplex network, with the first, second, and third layers denoted G_S, G_I, and G_J and housing the S, I, and J densities, respectively. We treat the densities on each layer as morphogens.
- We incorporate cross-diffusion such that the diffusion in the S layer is also dependent on infected densities in the other two layers.



Super-Infection Model (MBRD-SI)

Recall the definition of $\boldsymbol{L}(G)$ from the last section. We let $\boldsymbol{L}^{(S)} := \boldsymbol{L}(G_S)$ with entries $L_{ij}^{(S)}$, $\boldsymbol{L}^{(I)} := \boldsymbol{L}(G_I)$ with entries $L_{ij}^{(I)}$, and $\boldsymbol{L}^{(J)} := \boldsymbol{L}(G_J)$ with entries $L_{ij}^{(J)}$.

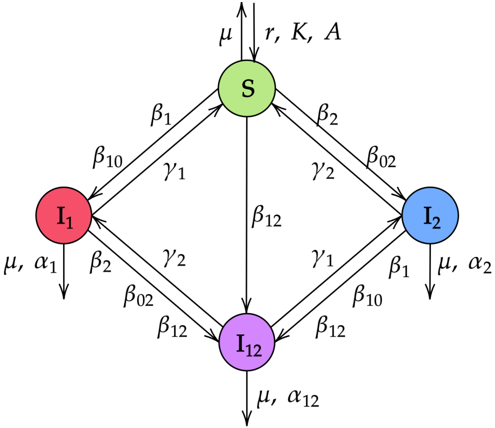
Definition (MBRD-SI)

$$
\begin{aligned}
\frac{dS_i}{dt} &= rS_i\left(1-\frac{S_i}{K}\right)\left(\frac{S_i}{A}-1\right)-\frac{(\beta_1 I_i+\beta_2 J_i)S_i}{S_i+I_i+J_i}+\gamma_1 I_i+\gamma_2 J_i-\mu S_i \\
&\quad +d_{11}\sum_{j=1}^{N} L_{ij}^{(S)} S_j + d_{12}\sum_{j=1}^{N} L_{ij}^{(I)} I_j + d_{13}\sum_{j=1}^{N} L_{ij}^{(J)} J_j, \\
\frac{dI_i}{dt} &= I_i\left(\frac{\beta_1 S_i}{S_i+I_i+J_i}-\mu-\alpha_1-\gamma_1-\frac{\sigma\beta_2 J_i}{S_i+I_i+J_i}\right)+d_{22}\sum_{j=1}^{N} L_{ij}^{(I)} I_j, \\
\frac{dJ_i}{dt} &= J_i\left(\frac{\beta_2 S_i}{S_i+I_i+J_i}-\mu-\alpha_2-\gamma_2+\frac{\sigma\beta_2 I_i}{S_i+I_i+J_i}\right)+d_{33}\sum_{j=1}^{N} L_{ij}^{(J)} J_j.
\end{aligned}
$$

Co-Infection Model (MBRD-CI)

We consider the following four states:

- S, susceptible;
- I_1, pathogen 1 mono-infected;
- I_2, pathogen 2 mono-infected;
- I_{12}, co-infected.



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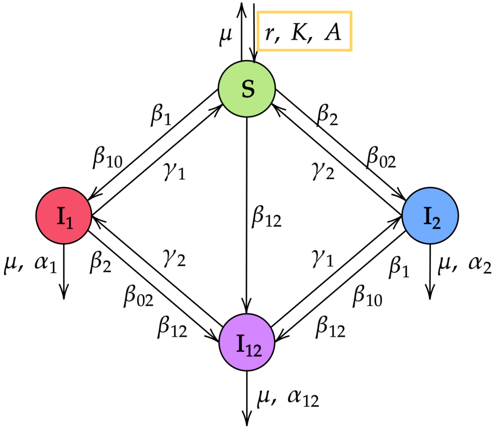

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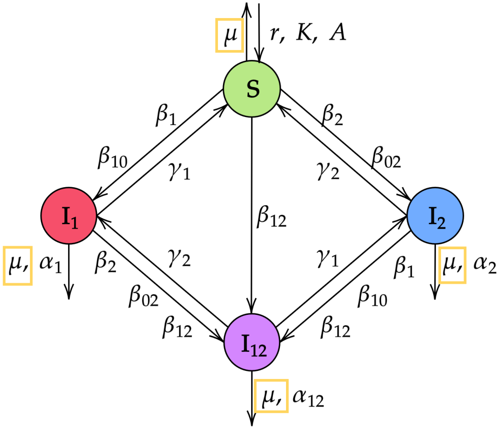

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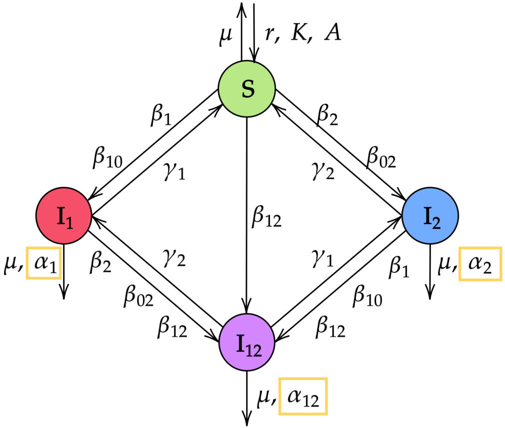

$\boxed{\alpha_1, \alpha_2,\ \alpha_{12}:}$ infection-induced death.

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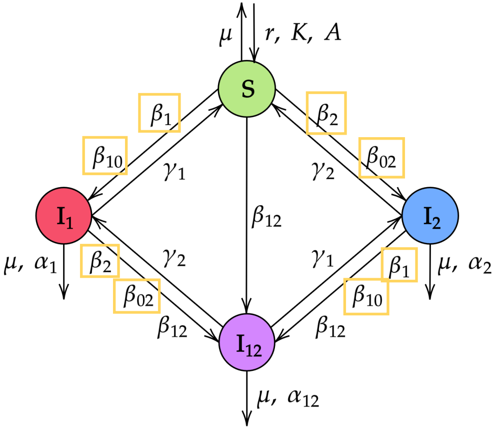

$\boxed{\beta_1, \beta_2, \beta_{10}, \beta_{02}:}$ infection transmission.

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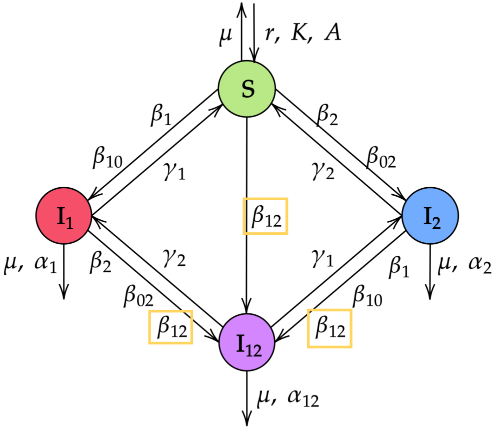

$\boxed{\beta_{12}:}$ co-transmission

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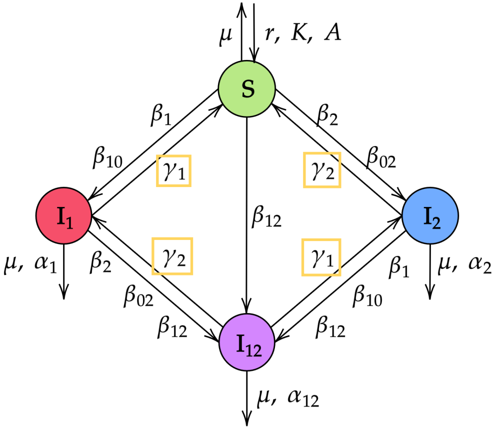

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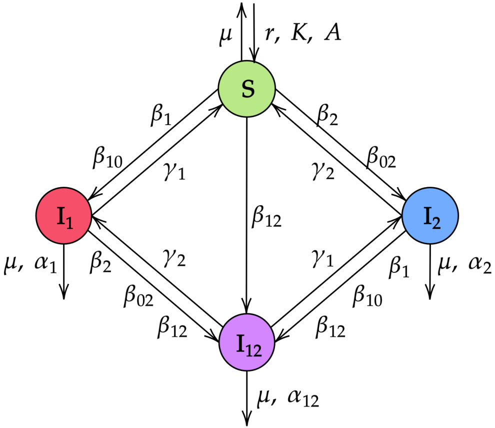

We obtain new reaction functions f, g, h, l.

Co-Infection Model (MBRD-CI)

- We consider a four-layer multiplex network, with the first, second, third layers denoted G_S, G_I, and G_J and housing the S, I, and J densities, respectively. The fourth layer houses the C densities and contains no edges. We treat the densities on each layer as morphogens.
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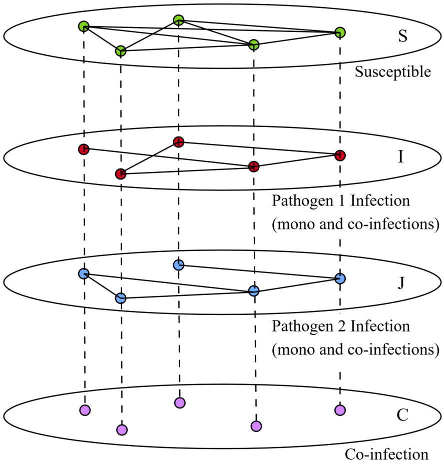

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Definition (MBRD-CI)

$$\frac{dS_i}{dt} = f(S_i, I_i, J_i, C_i) + d_{11}\sum_{j=1}^{N} L_{ij}^{(S)} S_j + d_{12}\sum_{j=1}^{N} L_{ij}^{(I)} I_j + d_{13}\sum_{j=1}^{N} L_{ij}^{(J)} J_j,$$

$$\frac{dI_i}{dt} = g(S_i, I_i, J_i, C_i) + d_{22}\sum_{j=1}^{N} L_{ij}^{(I)} I_j,$$

$$\frac{dJ_i}{dt} = h(S_i, I_i, J_i, C_i) + d_{33}\sum_{j=1}^{N} L_{ij}^{(J)} J_j,$$

$$\frac{dC_i}{dt} = l(S_i, I_i, J_i, C_i),$$

Pattern Formation in Lattice Networks

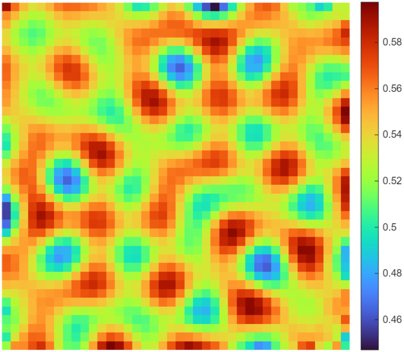

Figure: Pattern in super-infection dynamics, layer I, $t = 1800$.

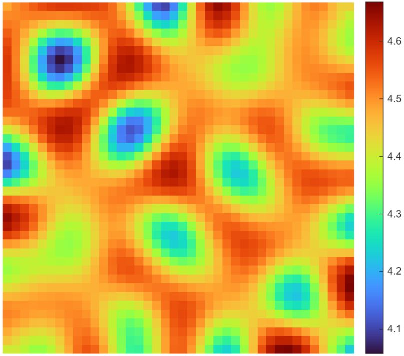

Figure: Pattern in co-infection dynamics, layer I, $t = 550$.

Applications

The Multiplex Bi-Virus Reaction-Diffusion (MBRD) framework can be adapted for other contagion processes such as:

- **Information Propagation:** Spread of conflicting or related rumors in a network of societies.
- **Malware Propagation:** Analyze computer virus and anti-virus dynamics, or pairs of viruses that support one another's survival by infecting the same host computer (e.g. Vobfus and Beebone).
- **Election Forecasting:** Modeling spatial dynamics between voting intentions of states and regions can predict election outcomes and explain spread of political ideologies throughout a country.

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