Impact of Human Movement on Disease Persistence

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Outline

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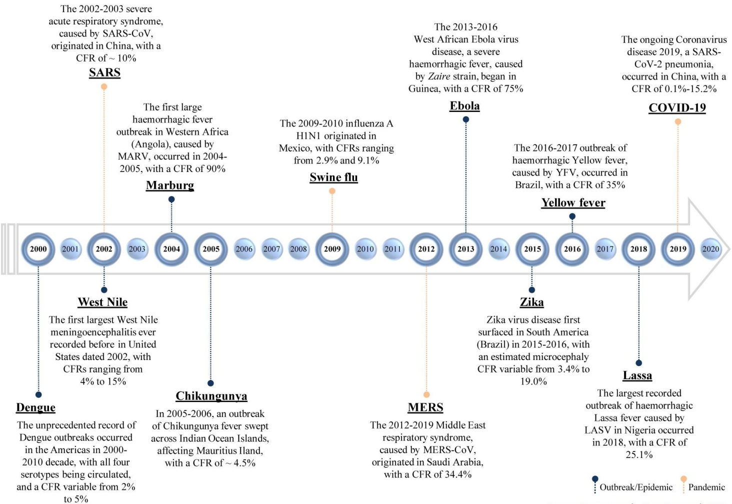
Infectious Disease Outbreaks

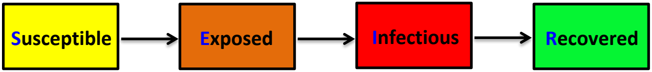
The frequency and scale of disease outbreaks have increased rapidly.



Source: Trovato et al., *Font Immunol*, 2020.

Epidemic Models

- Simplified means of describing the transmission of infectious disease through individuals.
- Useful in understanding disease spread, predicting the future number of cases and designing control policies.
- With respect to disease status, a population is divided into disjoint classes.

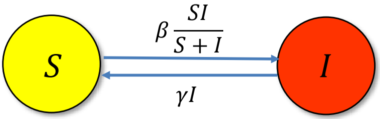


Epidemiological Terms

- Basic reproduction number ($\mathcal{R}_0$): the number of secondary cases produced by a single infection in a completely susceptible population.
- Threshold dynamics: if $\mathcal{R}_0 < 1$, a disease cannot spread; if $\mathcal{R}_0 > 1$, then the disease can spread.
- Disease-free equilibrium: a steady state where there is no disease.
- Endemic disease: a disease that is always present in a certain population or region.
- Endemic equilibrium: a steady state where there is disease.

SIS Model

- The population is divided into susceptible and infectious classes.



Here β is the transmission rate and γ is the recovery rate.

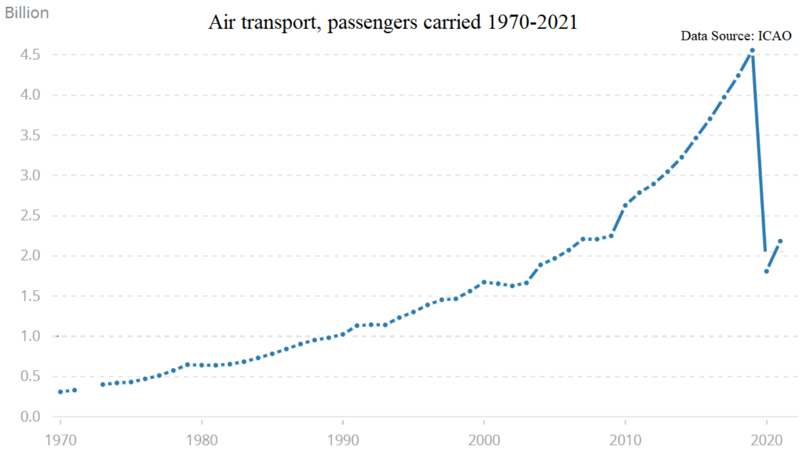
- Model equations ($N = S + I$):

$$\frac{dS}{dt} = -\beta \frac{S}{N} I + \gamma I, \qquad \mathcal{R}_0 = \frac{\beta}{\gamma}.$$
$$\frac{dI}{dt} = \beta \frac{S}{N} I - \gamma I,$$

- If $\mathcal{R}_0 \leq 1$, then $E_0 = (N, 0)$ is globally asymptotically stable (GAS); if $\mathcal{R}_0 > 1$, then $E^* = \left(\frac{1}{\mathcal{R}_0}, (1 - \frac{1}{\mathcal{R}_0})N\right)$ is GAS.

Changes in Travel

More people travel more frequently and farther than ever before.



Human Movement and Infectious Diseases

- Global travel and tourism facilitate the spread of infectious diseases and constitute a major challenge for infection control.
- Mathematical models play a crucial role in characterizing, forecasting, and controlling the spatio-temporal spread of infectious diseases.
- Modeling movement: continuous diffusion in continuous space corresponds to reaction-diffusion models (Fisher 1937) or nonlocal dispersal models (Andreu-Vaillo et al. 2010), while discrete diffusion in discrete space corresponds to patch models (Levin 1969).
- Epidemic patch models are widely used in the study of disease spread in discrete space (Wang 2007, Arino 2009).

Epidemic Patch Models

Specific diseases:

- Baroyan et al. (AAP 1971): influenza
- Dye and Hasibeder (TRSTMH 1986): malaria
- Ruan, Wang and Levin (MBE 2006): SARS
- Gao et al. (BMB 2013): Rift Valley fever
- Tien et al. (JMB 2015): cholera
- Bichara et al. (LBM 2016): dengue fever
- Zhang, Cosner and Zhu (BMB 2018): West Nile fever

Differen factors:

- Sattenspiel and Dietz (MB 1995): acquired immunity
- Wang and Zhao (SIAP 2005): age-structure
- Salmani and van den Driessche (DCDS-B 2006): latent period
- Zhang and Zhao (JMAA 2007): seasonality
- Knipl, Röst and Wu (SIADS 2013): transport-related infection
- Wang et al. (BMB 2015): entry–exit screening

Epidemic Patch Models–Cont'd

- J. T. Wu, K. Leung, G. M. Leung, Nowcasting and forecasting the potential domestic and international spread of the 2019-nCoV outbreak originating in Wuhan, China: a modelling study, *Lancet*, 395: 689–697, 2020.
- M. Chinazzi, et al., The effect of travel restrictions on the spread of the 2019 novel coronavirus (COVID-19) outbreak, *Science*, 368:395–400, 2020.
- R. Li, et al., Substantial undocumented infection facilitates the rapid dissemination of novel coronavirus (SARS-CoV2), *Science*, 368: 489–493, 2020.
- M. Gatto, et al., Spread and dynamics of the COVID-19 epidemic in Italy: Effects of emergency containment measures, *Proc. Natl. Acad. Sci. USA*, 117: 10484–10491, 2020.

Outline

Allen, Bolker, Lou and Nevai, SIAP, 2007

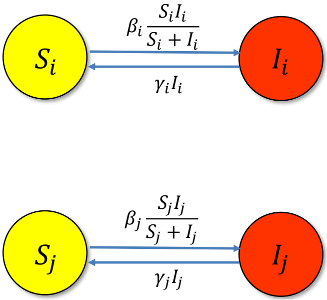
Following the SIS model by adding migration among $n \geq 2$ patches:

- The model of each patch in isolation remains unchanged.
- Different patches are connected by human movement.

No movement

Patch i

Patch j



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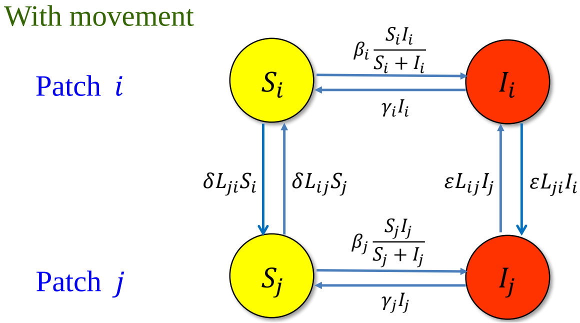


Allen, Bolker, Lou and Nevai, SIAP, 2007–Cont'd

An SIS patch model ($\Omega = \{1, \ldots, n\}$):

$$\frac{dS_i}{dt} = -\beta_i \frac{S_i I_i}{S_i + I_i} + \gamma_i I_i + \delta \left(\sum_{j=1, j \neq i}^{n} L_{ij} S_j - \left(\sum_{j=1, j \neq i}^{n} L_{ji} \right) S_i \right), \ i \in \Omega,$$
$$\frac{dI_i}{dt} = \beta_i \frac{S_i I_i}{S_i + I_i} - \gamma_i I_i + \varepsilon \left(\sum_{j=1, j \neq i}^{n} L_{ij} I_j - \left(\sum_{j=1, j \neq i}^{n} L_{ji} \right) I_i \right), \ i \in \Omega.$$

Denote the total emigration rate of patch i by $-L_{ii} = \sum_{j=1, j \neq i}^{n} L_{ji}$.

$$\frac{dS_i}{dt} = -\beta_i \frac{S_i I_i}{S_i + I_i} + \gamma_i I_i + \delta \left(\sum_{j=1, j \neq i}^{n} L_{ij} S_j + L_{ii} S_i \right), \ i \in \Omega,$$
$$\frac{dI_i}{dt} = \beta_i \frac{S_i I_i}{S_i + I_i} - \gamma_i I_i + \varepsilon \left(\sum_{j=1, j \neq i}^{n} L_{ij} I_j + L_{ii} I_i \right), \ i \in \Omega.$$

Allen, Bolker, Lou and Nevai, SIAP, 2007–Cont'd

An SIS patch model ($\Omega = \{1, \dots, n\}$):

$$\begin{aligned} \frac{dS_i}{dt} &= -\beta_i \frac{S_i I_i}{S_i + I_i} + \gamma_i I_i + \delta \sum_{j \in \Omega} L_{ij} S_j, \ i \in \Omega, \\ \frac{dI_i}{dt} &= \beta_i \frac{S_i I_i}{S_i + I_i} - \gamma_i I_i + \varepsilon \sum_{j \in \Omega} L_{ij} I_j, \ i \in \Omega. \end{aligned} \tag{1}$$

(A1) $S_i(0) \geq 0$ and $I_i(0) \geq 0$ for $i \in \Omega$, and $\sum_{i \in \Omega} I_i(0) > 0$;

(A2) $L = (L_{ij})$ is essentially nonnegative, irreducible, and symmetric;

(A3) $H^- = \{i \in \Omega : \mathcal{R}_0^{(i)} := \beta_i / \gamma_i < 1\}$ and
$H^+ = \{i \in \Omega : \mathcal{R}_0^{(i)} > 1\}$ are nonempty and $H^- \cup H^+ = \Omega$.

The basic reproduction number is $\mathcal{R}_0 = \rho(FV^{-1})$ where

$$F = \mathrm{diag}(\beta_1, \dots, \beta_n) \ \text{ and } \ V = \mathrm{diag}(\gamma_1, \dots, \gamma_n) - \varepsilon L.$$

Allen, Bolker, Lou and Nevai, SIAP, 2007–Cont'd

- Open problem:

  $\mathcal{R}_0 = \rho(FV^{-1})$ is a monotone decreasing function of ε.

- For SIS reaction-diffusion model (Allen et al., DCDS-A, 2008):

$$\begin{aligned} \frac{\partial S}{\partial t} &= \delta \Delta S - \beta(x)\frac{SI}{S+I} + \gamma(x)I, && x \in \Omega,\ t>0,\\ \frac{\partial I}{\partial t} &= \varepsilon \Delta I + \beta(x)\frac{SI}{S+I} - \gamma(x)I, && x \in \Omega,\ t>0,\\ \frac{\partial S}{\partial n} &= \frac{\partial I}{\partial n} = 0, && x \in \partial\Omega,\ t>0, \end{aligned}$$

  the basic reproduction number is

$$\mathcal{R}_0(\varepsilon) = \sup\left\{ \frac{\int_\Omega \beta\varphi^2}{\int_\Omega \varepsilon|\nabla\varphi|^2 + \gamma\varphi^2} : \varphi \in H^1(\Omega),\ \varphi \neq 0 \right\}.$$

Symmetric Movement

Theorem (Gao, SIAP, 2019)

Let $F = \mathrm{diag}(\beta_1, \ldots, \beta_n)$ *and* $D = \mathrm{diag}(\gamma_1, \ldots, \gamma_n)$ *be two positive diagonal matrices and* $L = (L_{ij})_{n\times n}$ *be an essentially nonnegative, irreducible and symmetric matrix with zero column sums. Then* $\mathcal{R}_0 = \rho(FV^{-1})$ *with* $V = D - \varepsilon L$ *is constant if* $\mathcal{R}_0^{(i)} = \beta_i/\gamma_i$ *is constant and strictly decreasing in* $\varepsilon \in [0, \infty)$ *with* $\mathcal{R}_0'(\varepsilon) < 0$ *for* $\varepsilon \in (0, \infty)$ *otherwise.*

Outline of the Proof: By the Perron–Frobenius theorem, there exists a vector $\boldsymbol{v} \gg \mathbf{0}$ such that $V^{-1}F\boldsymbol{v} = \rho(V^{-1}F)\boldsymbol{v} = \mathcal{R}_0\boldsymbol{v}$, or equivalently,

$$\left(\frac{1}{\mathcal{R}_0}F - V\right)\boldsymbol{v} = \left(\frac{1}{\mathcal{R}_0}F - D + \varepsilon L\right)\boldsymbol{v} = \mathbf{0}.$$

We thus have

$$\mathcal{R}_0'(\varepsilon) = \frac{\boldsymbol{v}^T L \boldsymbol{v}}{\boldsymbol{v}^T F \boldsymbol{v}}(\mathcal{R}_0)^2.$$

Karlin's Theorem

Lemma (Reduction Principle in Genetics: Karlin, 1982; Altenberg, PNAS, 2012; Altenberg, SIMAA, 2013)

Let P be an irreducible stochastic matrix (i.e., nonnegative and each column summing to one), and let D be a positive diagonal matrix that is not a scalar multiple of identity matrix $\mathbb{I}_n$ of order $n \geq 2$. Put

$$M(\alpha) = (1-\alpha)\mathbb{I}_n + \alpha P.$$

Then for $\alpha > 0$, the spectral bound of matrix $M(\alpha)D$, denoted by $s(M(\alpha)D)$, has the following properties:

(a) $\frac{d}{d\alpha}s(M(\alpha)D) < 0$. *Thus $s(M(\alpha)D)$ decreases strictly as α increases.*

(b) *$s(M(\alpha)D)$ is strictly convex in α. Thus* $\frac{d^2}{d\alpha^2}s(M(\alpha)D) \geq 0$.

Asymmetric Movement

Assume that: (B1) L is essentially nonnegative and irreducible;
(B2) $\mathcal{R}_0^{(i)}$ is non-constant in $i \in \Omega$.

Theorem (Gao and Dong, PAMS, 2020)

For model (1), *the basic reproduction number* $\mathcal{R}_0$ *is strictly decreasing and strictly convex in* $\varepsilon \in [0, \infty)$. *Moreover,* $\mathcal{R}_0'(\varepsilon) < 0$ *and* $\mathcal{R}_0''(\varepsilon) > 0$ *for* $\varepsilon \in (0, \infty)$.

Fast dispersal inhibits disease outbreaks.

Corollary (Gao and Dong, PAMS, 2020)

For model (1) *with* $\varepsilon \in (0, \infty)$, *the reproduction number* $\mathcal{R}_0$ *satisfies*

$$\min_{i\in\Omega} \mathcal{R}_0^{(i)} < \mathcal{R}_0(\infty) < \mathcal{R}_0(\varepsilon) = \rho(FV^{-1}) < \mathcal{R}_0(0) = \max_{i\in\Omega} \mathcal{R}_0^{(i)},$$

where $\mathcal{R}_0(\infty) = \sum_{i\in\Omega} \beta_i L_{ii}^* / \sum_{i\in\Omega} \gamma_i L_{ii}^*$ *and* $L^* = (L_{ij}^*)^T$ *is the adjoint matrix of* L.

Related work: Chen et al. (JMB 2020, SIAP 2022).

Outline

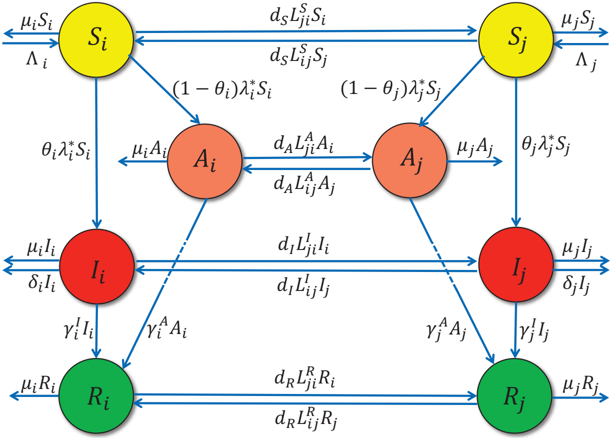
1. Background
2. SIS Patch Model
3. SIAR Patch Model
4. Research Questions

Asymptomatic Infection

- An asymptomatic case is an individual who tests positive but experiences no symptoms throughout the course of infection.
- Asymptomatic infection is very common for many infectious diseases including COVID-19, Ebola, influenza, cholera, chlamydia, Zika fever, dengue fever, yellow fever, and malaria.
- Asymptomatic infectives are hard to detect but may transmit the infection to others, acting as silent spreaders.
- Symptomless people have more contacts with others through normal daily activities, so a significant proportion of new infections could be attributed to asymptomatic transmission.

Flow Diagram

The population in patch $i \in \Omega = \{1, \ldots, n\}$ is divided into classes consisting of susceptible, symptomatic, asymptomatic and recovered individuals, denoted by S_i, I_i, A_i and R_i, respectively.



Model Equations

The transmission dynamics in patch $i \in \Omega = \{1, \dots, n\}$ follow:

$$
\begin{aligned}
\frac{dS_i}{dt} &= d_S \sum_{j \in \Omega} L_{ij}^S S_j + \Lambda_i - \beta_i \frac{I_i + \tau_i A_i}{N_i} S_i - \mu_i S_i, \\
\frac{dI_i}{dt} &= d_I \sum_{j \in \Omega} L_{ij}^I I_j + \theta_i \beta_i \frac{I_i + \tau_i A_i}{N_i} S_i - (\mu_i + \gamma_i^I + \delta_i) I_i, \\
\frac{dA_i}{dt} &= d_A \sum_{j \in \Omega} L_{ij}^A A_j + (1 - \theta_i) \beta_i \frac{I_i + \tau_i A_i}{N_i} S_i - (\mu_i + \gamma_i^A) A_i, \\
\frac{dR_i}{dt} &= d_R \sum_{j \in \Omega} L_{ij}^R R_j + \gamma_i^I I_i + \gamma_i^A A_i - \mu_i R_i,
\end{aligned}
\tag{2}
$$

where $d_\natural$ and $L^\natural = (L_{ij}^\natural)$ with $\natural \in \{S, I, A, R\}$ are dispersal rate and connectivity matrix, respectively, and $N_i = S_i + I_i + A_i + R_i$.

Basic Reproduction Number

Using the next generation matrix method, the basic reproduction number is defined as

$$\mathcal{R}_0 = \rho(FV^{-1}),$$

where

$$F = \begin{pmatrix} F_{11} & F_{12} \\ F_{21} & F_{22} \end{pmatrix} \text{ and } V = \begin{pmatrix} V_{11} & 0 \\ 0 & V_{22} \end{pmatrix}$$

with

$$F_{11} = \mathrm{diag}\{\theta_1\beta_1, \ldots, \theta_n\beta_n\},\ F_{12} = \mathrm{diag}\{\theta_1\tau_1\beta_1, \ldots, \theta_n\tau_n\beta_n\},$$
$$F_{21} = \mathrm{diag}\{(1-\theta_1)\beta_1, \ldots, (1-\theta_n)\beta_n\},$$
$$F_{22} = \mathrm{diag}\{(1-\theta_1)\tau_1\beta_1, \ldots, (1-\theta_n)\tau_n\beta_n\},$$
$$V_{11} = D_I - d_I L^I,\ D_I = \mathrm{diag}\{\mu_1 + \gamma_1^I + \delta_1, \ldots, \mu_n + \gamma_n^I + \delta_n\},$$
$$V_{22} = D_A - d_A L^A,\ D_A = \mathrm{diag}\{\mu_1 + \gamma_1^A, \ldots, \mu_n + \gamma_n^A\}.$$

Since $F_{12} = F_{11}F_{21}^{-1}F_{22}$, it follows that

$$\mathcal{R}_0 = \rho(F_{11}V_{11}^{-1} + F_{22}V_{22}^{-1}) = \rho(V_{11}^{-1}F_{11} + V_{22}^{-1}F_{22}).$$

Threshold Dynamics

By using a Lyapunov function and persistence theory, the basic reproduction number $\mathcal{R}_0$ is shown to be a sharp threshold between disease extinction and persistence.

Theorem (Gao et al., SIAP, 2022)

For model (2), if $\mathcal{R}_0 \leq 1$, then the disease-free equilibrium E_0 is globally asymptotically stable; if $\mathcal{R}_0 > 1$, then the disease is uniformly persistent and there exists at least one endemic equilibrium.

Question: how is $\mathcal{R}_0$ affected by population dispersal, characterized by dispersal rates d_I and d_A, and connectivity matrices L^I and L^A.

Upper and Lower Bounds on $\mathcal{R}_0$

The basic reproduction number of patch i in isolation is $\mathcal{R}_0^{(i)} = \mathcal{R}_{0I}^{(i)} + \mathcal{R}_{0A}^{(i)}$, where $\mathcal{R}_{0I}^{(i)} = \frac{\theta_i\beta_i}{\mu_i+\gamma_i^I+\delta_i}$ and $\mathcal{R}_{0A}^{(i)} = \frac{(1-\theta_i)\tau_i\beta_i}{\mu_i+\gamma_i^A}$.

Theorem (Gao et al., SIAP, 2022)

For model (2), *the basic reproduction number* $\mathcal{R}_0$ *satisfies*

$$\min_{i\in\Omega} \mathcal{R}_{0I}^{(i)} + \min_{i\in\Omega} \mathcal{R}_{0A}^{(i)} \le \mathcal{R}_0 \le \max_{i\in\Omega} \mathcal{R}_{0I}^{(i)} + \max_{i\in\Omega} \mathcal{R}_{0A}^{(i)}.$$

Furthermore, the inequality

$$\min_{i\in\Omega} \mathcal{R}_0^{(i)} \le \mathcal{R}_0 \le \max_{i\in\Omega} \mathcal{R}_0^{(i)}$$

holds if $\theta_i = \theta, \tau_i = \tau$ *and* $\gamma_i^I + \delta_i = \gamma_i^A$ *for all* $i \in \Omega$.

Remark: any value between the lower and upper bounds of $\mathcal{R}_0$ is reachable under appropriate dispersal strategy (d_I, d_A, L^I and L^A).

$\mathcal{R}_0$ vs Dispersal Rates: Two-patch Case

How does $\mathcal{R}_0$ vary with dispersal rates, d_I and d_A?

Proposition (Gao et al., SIAP, 2022)

For model (2) with $n = 2$, if all parameters are positive, then the derivative of $\mathcal{R}_0$ with respect to d_I or d_A has sign-preserving property, i.e.,

$$\operatorname{sgn}\left(\frac{d\mathcal{R}_0}{dd_I}\right) = \operatorname{sgn}\left(\left.\frac{d\mathcal{R}_0}{dd_I}\right|_{d_I=0+}\right) \quad \textit{and} \quad \operatorname{sgn}\left(\frac{d\mathcal{R}_0}{dd_A}\right) = \operatorname{sgn}\left(\left.\frac{d\mathcal{R}_0}{dd_A}\right|_{d_A=0+}\right)$$

for $d_I > 0$ and $d_A > 0$.

So, $\mathcal{R}_0$ is either strictly decreasing or strictly increasing or constant with respect to d_I and d_A. Different from SIS or SIR patch model.

$\mathcal{R}_0$ vs Dispersal Rates: General Case I

Theorem (Gao et al., SIAP, 2022)

Suppose $\theta_i = \theta$ and $\tau_i = \tau$ for all $i \in \Omega$, and L^I and L^A are symmetric. Then the basic reproduction number $\mathcal{R}_0(d_I)$ of model (2) is constant in terms of d_I if $D_I\mathbf{1}$ is a right eigenvector of $F_{11}D_I^{-1} + F_{22}V_{22}^{-1}$ associated to eigenvalue $\mathcal{R}_0(0) = \rho(F_{11}D_I^{-1} + F_{22}V_{22}^{-1})$, i.e.,

$$(F_{11}D_I^{-1} + F_{22}V_{22}^{-1})D_I\mathbf{1} = \mathcal{R}_0(0)D_I\mathbf{1},$$

and strictly decreasing otherwise. If, in addition, $\gamma_i^I + \delta_i = \gamma_i^A$ for all $i \in \Omega$, then $\mathcal{R}_0$ is constant in terms of d_I if $\mathcal{R}_0^{(1)} = \cdots = \mathcal{R}_0^{(n)}$, and strictly decreasing otherwise.

Similar conclusions hold for $\mathcal{R}_0$ with respect to d_A.

$\mathcal{R}_0$ vs Dispersal Rates: General Case II

Proposition (Gao et al., SIAP, 2022)

Assume that: (i) $\theta_i = \theta$ *and* $\tau_i = \tau$ *for* $i \in \Omega$; (ii) *the connectivity matrices* L^I *and* L^A *are equal (i.e.,* $L^I = L^A := L$*);* (iii) *there is a positive diagonal matrix* C *such that* CLC^{-1} *is symmetric. Let* $\boldsymbol{\alpha}$ *be a positive right eigenvector of* L *corresponding to eigenvalue zero. Then the basic reproduction number* $\mathcal{R}_0(d_I)$ *of model* (2) *is constant in terms of* d_I *if* $D_I\boldsymbol{\alpha}$ *is a right eigenvector of* $F_{11}D_I^{-1} + F_{22}V_{22}^{-1}$ *associated to eigenvalue* $\mathcal{R}_0(0) = \rho(F_{11}D_I^{-1} + F_{22}V_{22}^{-1})$*, i.e.,*

$$(F_{11}D_I^{-1} + F_{22}V_{22}^{-1})D_I\boldsymbol{\alpha} = \mathcal{R}_0(0)D_I\boldsymbol{\alpha},$$

and strictly decreasing otherwise. If, in addition, $\gamma_i^I + \delta_i = \gamma_i^A$ *for all* $i \in \Omega$*, then* $\mathcal{R}_0$ *is constant in terms of* d_I *if* $\mathcal{R}_0^{(1)} = \cdots = \mathcal{R}_0^{(n)}$*, and strictly decreasing otherwise.*

$\mathcal{R}_0$ vs Dispersal Rates: General Case III

When symptomatic or asymptomatic individuals do not move between patches, the monotonic result on $\mathcal{R}_0$ holds with no additional restrictions on model parameters.

Theorem (Gao et al., SIAP, 2022)

For model (2), *if* $d_I = 0$ *(or* $d_A = 0$*), then the basic reproduction number*

$$\mathcal{R}_0 = \rho(F_{11}D_I^{-1} + F_{22}V_{22}^{-1})$$

is strictly decreasing with respect to d_A *(or* d_I*) whenever* $\mathcal{R}_0^{(i)}$ *is nonconstant in* $i \in \Omega$*, and constant otherwise.*

In general setting, $\mathcal{R}_0$ can be decreasing, increasing or nonmonotone in d_I or d_A.

$\mathcal{R}_0$ vs Dispersal and Dispersal Rates: Independence

When is $\mathcal{R}_0$ independent of dispersal or dispersal rates, i.e., $\mathcal{R}_0(d_I, d_A, L^I, L^A)$ =const, or $\mathcal{R}_0(d_I, d_A)$ =const?

Proposition (Gao et al., SIAP, 2022)

For model (2), the following statements on $\mathcal{R}_0$ hold:

(a) *$\mathcal{R}_0$ is independent of dispersal if and only if both $\mathcal{R}_{0I}^{(i)}$ and $\mathcal{R}_{0A}^{(i)}$ are constant in $i \in \Omega$.*

(b) *$\mathcal{R}_0$ is independent of dispersal rates d_I and d_A if and only if $\mathcal{R}_0^{(i)}$ is constant in $i \in \Omega$ and $s((D_A F_{22}^{-1} F_{11} D_I^{-1} - d_A L^A F_{22}^{-1})^{-1} - D_I F_{11}^{-1} F_{22} D_A^{-1} + d_I L^I F_{11}^{-1}) = 0$ for any $d_I \geq 0$ and $d_A \geq 0$.*

(c) *$\mathcal{R}_0$ is independent of dispersal rates d_I and d_A if $\mathcal{R}_0^{(i)}$ is constant in $i \in \Omega$ and $D_I \boldsymbol{\alpha}^I = k D_A \boldsymbol{\alpha}^A$ for some $k > 0$, where $\boldsymbol{\alpha}^\natural$ is a right positive eigenvector with eigenvalue zero of matrix $L^\natural$ for $\natural \in \{I, A\}$, but not conversely.*

(d) *$\mathcal{R}_0$ is independent of dispersal rates d_I and d_A if $\mathcal{R}_0$ is independent of dispersal, but not conversely.*

Outline

Question 1: SIS Patch Model

How does disease persistence vary with partial changes in connection?

Let $F = \text{diag}(\beta_1, \ldots, \beta_n)$ and $V = \text{diag}(\gamma_1, \ldots, \gamma_n) - \varepsilon L$.
Namely, $\mathcal{R}_0 = \rho(FV^{-1})$ versus s where $L_{ij} = sK_{ij}$ holds for

(i) a fixed pair of i and j with $i \neq j$ (Gao and Ruan, MB, 2011), e.g.,

$$\begin{pmatrix} -sK_{21} - L_{31} & L_{12} & L_{13} \\ sK_{21} & -L_{12} - L_{32} & L_{23} \\ L_{31} & L_{32} & -L_{13} - L_{23} \end{pmatrix}.$$

(ii) a given i and all $j \neq i$, or a given j and all $i \neq j$, e.g.,

$$\begin{pmatrix} -sK_{21} - sL_{31} & L_{12} & L_{13} \\ sK_{21} & -L_{12} - L_{32} & L_{23} \\ sL_{31} & L_{32} & -L_{13} - L_{23} \end{pmatrix}.$$

(iii) all $i, j \in \Omega_1 \subset \Omega$ and $i \neq j$, e.g.,

$$\begin{pmatrix} -sK_{21} - L_{31} & sL_{12} & L_{13} \\ sK_{21} & -sL_{12} - L_{32} & L_{23} \\ L_{31} & L_{32} & -L_{13} - L_{23} \end{pmatrix}.$$

Question 2: SEIRS Patch Model

The transmission dynamics in patch $i \in \Omega = \{1, \ldots, n\}$ follow:

$$\begin{aligned}
\frac{dS_i}{dt} &= d_S \sum_{j\in\Omega} L_{ij}^S S_j - \beta_i \frac{S_i I_i}{N_i} + \alpha_i R_i, \quad i \in \Omega, \\
\frac{dE_i}{dt} &= d_E \sum_{j\in\Omega} L_{ij}^E E_j + \beta_i \frac{S_i I_i}{N_i} - \sigma_i E_i, \quad i \in \Omega, \\
\frac{dI_i}{dt} &= d_I \sum_{j\in\Omega} L_{ij}^I I_j + \sigma_i E_i - \gamma_i I_i, \quad i \in \Omega, \\
\frac{dR_i}{dt} &= d_R \sum_{j\in\Omega} L_{ij}^R R_j + \gamma_i I_i - \alpha_i R_i \quad i \in \Omega,
\end{aligned} \tag{3}$$

where $d_\natural$ and $L^\natural = (L_{ij}^\natural)$ with $\natural \in \{S, E, I, R\}$ are dispersal rate and connectivity matrix, respectively, and $N_i = S_i + E_i + I_i + R_i$.

Question 2: SEIRS Patch Model–Cont'd

The basic reproduction number is defined as

$$\mathcal{R}_0 = \rho(FV^{-1}) = \rho(-F_{12}V_{22}^{-1}V_{21}V_{11}^{-1}),$$

where

$$F = \begin{pmatrix} 0 & F_{12} \\ 0 & 0 \end{pmatrix} \text{ and } V = \begin{pmatrix} V_{11} & 0 \\ V_{21} & V_{22} \end{pmatrix},$$

with

$$F_{12} = \mathrm{diag}\{\beta_1, \ldots, \beta_n\}, \quad V_{11} = \mathrm{diag}\{\sigma_1, \ldots, \sigma_n\} - d_E L^E,$$
$$V_{21} = -\mathrm{diag}\{\sigma_1, \ldots, \sigma_n\}, \; V_{22} = \mathrm{diag}\{\gamma_1, \ldots, \gamma_n\} - d_I L^I.$$

Threshold dynamics: the disease-free equilibrium is GAS if $\mathcal{R}_0 \leq 1$, while the disease is uniformly persistent and there exists at least one endemic equilibrium if $\mathcal{R}_0 > 1$.

Question 2: SEIRS Patch Model–Cont'd

(i) The basic reproduction number of model (3) satisfies

$$\min_{1\le i\le n} \mathcal{R}_0^{(i)} \le \mathcal{R}_0 \le \max_{1\le i\le n} \mathcal{R}_0^{(i)},$$

where $\mathcal{R}_0^{(i)} = \beta_i/\gamma_i$ is the reproduction number of patch i in isolation.

(ii) Give some sufficient conditions under which $\mathcal{R}_0$ is strictly decreasing in d_E and / or d_I.

(iii) Completely determine the monotonicity of $\mathcal{R}_0$ in d_E and d_I for the two-patch case.

(iv) Find the necessary and sufficient conditions under which $\mathcal{R}_0$ is independent of dispersal rates or dispersal.

(iv) Analytically and numerically explore the effects of population movement on disease prevalence (including the asymptotic profiles of the endemic equilibrium).

Question 3: Connectivity Matrix

Given $\boldsymbol{x} = (x_1, \ldots, x_n)^{\mathrm{T}} \gg \mathbf{0}$, find all connectivity matrices M (essentially nonnegative, irreducible with zero column sums) satisfying $M\boldsymbol{x} = \mathbf{0}$, e.g.,

$$-\sum_{i=1}^{n} x_i I_n + \begin{pmatrix} x_1 & x_1 & \cdots & x_1 \\ x_2 & x_2 & \cdots & x_2 \\ \vdots & \vdots & \ddots & \vdots \\ x_n & x_n & \cdots & x_n \end{pmatrix}$$

and

$$\begin{pmatrix} -x_1^{-1} & x_2^{-1} & 0 & \cdots & 0 \\ 0 & -x_2^{-1} & x_3^{-1} & \cdots & 0 \\ \vdots & \vdots & \vdots & \ddots & \vdots \\ x_1^{-1} & 0 & 0 & \cdots & -x_n^{-1} \end{pmatrix}.$$

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