Spatial-temporal modeling and analysis of infectious disease.

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Main Theoretical Problems For Epidemic Models

- Persistence: Basic reproduction number or effective reproduction number.
- Final State: Final epidemic size($\mathcal{R}_0 < 1$); Endemic Equilibria (EE, $\mathcal{R}_0 > 1$)
- Control(eradiction, mitigation): The impact of parameters on $\mathcal{R}_0$, Final epidemic size, EE

Without Heterogeneity: SIS ODE model

$$\begin{cases} \frac{\mathrm{d}S}{\mathrm{dt}} = -\beta\frac{SI}{S+I} + \gamma I, \\ \frac{\mathrm{d}I}{\mathrm{dt}} = \beta\frac{SI}{S+I} - \gamma I, \\ N = S(0) + I(0). \end{cases}$$

- Persistence: $\mathcal{R}_0 = \frac{\beta}{\gamma}$
- Final State, EE: $\left(\frac{N}{\mathcal{R}_0}, N\left(1 - \frac{1}{\mathcal{R}_0}\right)\right)$
- To control (eradicate, mitigate) the disease, controling $\mathcal{R}_0$ is enough.
- Spatial homegeneous epidemic model often underestimate the risk of the disease. (1) misestimated $\mathcal{R}_0$; (2) misconception on $\mathcal{R}_0$.

  For spatial heterogeneous epidemic model, smaller $\mathcal{R}_0$ may induce larger epidemic size. $\mathcal{R}_0$ is NOT enough to tell us how large an epidemic will be. (Song, Xiao 2022 JMB; RB Salako, Lou, Song 2023 JMB)

SIS reaction-diffusion model

[Allen-Bolker-L.-Nevai[1]]

$$\begin{cases} S_t = d_S \Delta S - \beta(x)\dfrac{SI}{S+I} + \gamma(x) I, & x \in \Omega,\ t > 0, \\ I_t = d_I \Delta I + \beta(x)\dfrac{SI}{S+I} - \gamma(x) I, & x \in \Omega,\ t > 0, \\ \nabla S \cdot \mathbf{n} = \nabla I \cdot \mathbf{n} = 0 & x \in \partial\Omega,\ t > 0, \\ \int_\Omega [S(x,0) + I(x,0)]\mathrm{d}x = N. \end{cases} \tag{1}$$

- $S(x,t), I(x,t)$: density of susceptible and infected individuals
- d_S, d_I: diffusion rates of susceptible and infected
- $\beta(x), \gamma(x)$: disease transmission and recovery rates
- $N0$: total number of individuals at $t = 0$
- $H^- = \{x \in \Omega : \beta(x) < \gamma(x)\}$ and $H^+ = \{x \in \Omega : \beta(x) > \gamma(x)\}$ are nonempty.

[1] Asymptotic profiles of the steady states for an SIS epidemic reaction-diffusion model, DCDS-A 21 (2008) 1-20

Monotonicity of $\mathcal{R}_0$

- Definition of the basic reproduction number

$$\mathcal{R}_0 = \sup_{\varphi \in H^1(\Omega)} \left\{ \frac{\int_\Omega \beta \varphi^2}{\int_\Omega d_I |\nabla \varphi|^2 + \gamma \varphi^2} \right\}$$

- Threshold dynamics: if $\mathcal{R}_0 < 1$, DFE is GAS; if $\mathcal{R}_0 > 1$, a unique EE is feasible.
- Open problem: GAS of EE.

Theorem (Allen-Bolker-L.-Nevai,2008)

$\mathcal{R}_0$ is a monotone decreasing function of d_I with $\mathcal{R}_0 \to \max\{\beta(x)/\gamma(x) : x \in \bar{\Omega}\}$ as $d_I \to 0$ and $\mathcal{R}_0 \to \int_\Omega \beta / \int_\Omega \gamma$ as $d_I \to \infty$. $\mathcal{R}_0(PDE) > \mathcal{R}_0(ODE)$

Asymptotic behaviours of EE as $d_S \to 0$

Theorem (Allen-Bolker-L.-Nevai,2008)

$(\tilde{S}, \tilde{I}) \to (S^*, 0)$ *in* $C^1(\bar{\Omega})$ *as* $d_S \to 0$ *for some* $S^*(x) \in C^1(\bar{\Omega})$.

A disease may persist but it can be controlled by limiting d_S.

- Transforming the environments to include low-risk sites, such as through treatment or vaccination.
- Restricting the movement of the susceptible individuals, such as isolation or lock down.

Other studies on SIS model

- Multi-strain model: [N. Tunver, M. Martcheva 2011; N. Tunver, M. Martcheva, Y.X. Wu 2016]; [Y.Lou, RB Salako 2022, 2023, JDE, JMB, many]...
- Mass action model: [K. Deng, Y.X. Wu 2016; Y.X. Wu, X.F. Zou 2016]...
- Model with recruitment: [H. Li, R. Peng, F.B. Wang 2016]...
- Advection: [R.H.Cui, Y.Lou, 2016; R. Cui, K. Y. Lam, and Y. Lou, 2017]
- Patch models: [Wang-Mulone 2003; Wang-Zhao 2005; Cui et al. 2006; L. J. S. Allen, B. M. Bolker, Y. Lou, and A. L. Nevai, 2007; D. Gao and S. Ruan, 2011; Arino et al. 2016; S. Chen, J. Shi, Z. Shuai and Y. Wu, 2019; H. Li and R. Peng, 2019]...
- Temporal periodicity: [R. Peng and X.Q. Zhao, 2012]; [S. Liu and Y. Lou, 2021 JFA]...
- Nonlocal: [FY Yang, WT Li, SG Ruan 2019 JDE]; [K Hao, SG Ruan 2021 JMB]; [YX Feng, WT Li, SG Ruan ,FY Yang 2022 JDE]; ...
- Others: [R. Peng, 2009; R. Peng and S. Liu, 2009; R. Peng and F. Yi, 2013; H. Li, R. Peng, and T. Xiang, 2019; H. Li, R. Peng and Z. Wang, 2018; K. Kuto, H. Matsuzawa and R. Peng, 2017]......

SEIRS PDE model

[P. Song, L-, Y. Xiao, JDE 2019]

$$
\begin{cases}
\partial_t S = d_S \Delta S - \dfrac{\beta(x) S I}{S+I+E+R} + \alpha R & x \in \Omega, \ t > 0, \\
\partial_t E = d_E \Delta E + \dfrac{\beta(x) S I}{S+I+E+R} - \sigma E & x \in \Omega, \ t > 0, \\
\partial_t I = d_I \Delta I + \sigma E - \gamma(x) I & x \in \Omega, \ t > 0, \\
\partial_t R = d_R \Delta R + \gamma(x) I - \alpha R & x \in \Omega, \ t > 0, \\
\nabla S \cdot \mathbf{n} = \nabla E \cdot \mathbf{n} = \nabla I \cdot \mathbf{n} = \nabla R \cdot \mathbf{n} = 0 & x \in \partial\Omega, \ t > 0.
\end{cases}
$$

- S, E, I and R: density of susceptible, exposed, infected and recovered individuals;
- σ: proportion of exposed individuals that become infectious;
- α: proportion of recovered individuals that lose immunity.

Main Questions For SEIRS PDE Model

- SIS: $\mathcal{R}_0$ is a monotone decreasing function of d_I.
  SEIRS: Monotonicity of $\mathcal{R}_0$ with respect to d_E, d_I?
- SIS: $\mathcal{R}_0(PDE) > \mathcal{R}_0(ODE)$
  What about SEIRS?
- $(\tilde{S}, \tilde{I}) \to (S^*, 0)$ in $C^1(\bar{\Omega})$ as $d_S \to 0$
  What about SEIRS?

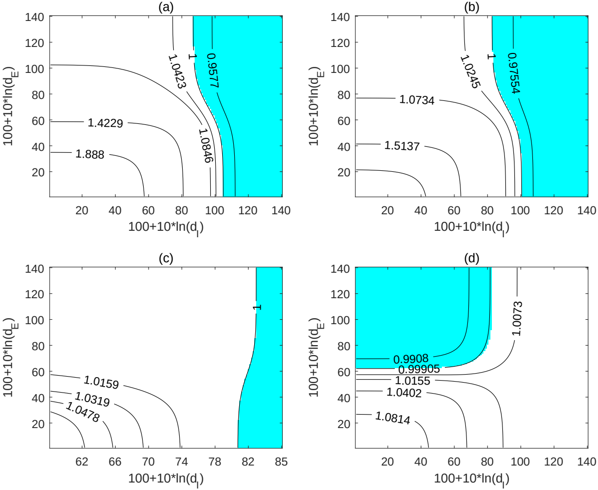

Figure: $\mathcal{R}_0 < 1$ in dyed region. (a) β increasing, γ decreasing; (b) β decreasing, γ increasing; (c) β increasing, γ increasing, $\mathcal{R}_0$ non-monotone in d_E; (d) β decreasing, γ decreasing, $\mathcal{R}_0$ non-monotone in d_I;

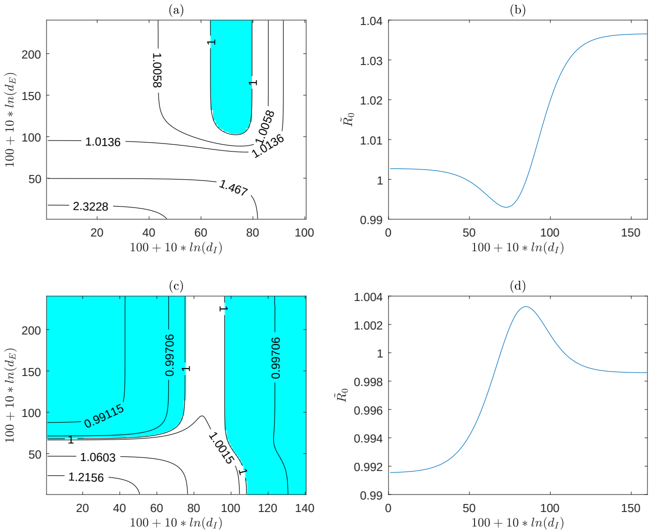

Figure: (a) Medium d_I leads to disease extinction; (c) Large or small d_I leads to disease extinction; (b) $\mathcal{R}_0$ in heterogeneous environment smaller than in homogeneous environment

A numerical counterexample

- A numerical case satisfying $\mathcal{R}_0 > 1, \lambda_1(-d_R\Delta + \alpha(1 - \frac{\gamma}{\beta}))0.$

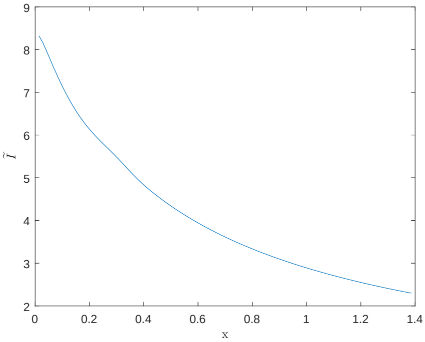

Figure: $\widetilde{I}$ does not converge to zero as $d_S \to 0$; the movement of recovered individuals may increase the number of infected individuals and enhance the endemic.

SEIRS PDE model

[P. Song, L-, Y. Xiao, JDE 2019]

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\begin{cases}
\partial_t S = d_S \Delta S - \dfrac{\beta(x) SI}{S+I+E+R} + \alpha R & x \in \Omega, \ t > 0, \\
\partial_t E = d_E \Delta E + \dfrac{\beta(x) SI}{S+I+E+R} - \sigma E & x \in \Omega, \ t > 0, \\
\partial_t I = d_I \Delta I + \sigma E - \gamma(x) I & x \in \Omega, \ t > 0, \\
\partial_t R = d_R \Delta R + \gamma(x) I - \alpha R & x \in \Omega, \ t > 0, \\
\nabla S \cdot \mathbf{n} = \nabla E \cdot \mathbf{n} = \nabla I \cdot \mathbf{n} = \nabla R \cdot \mathbf{n} = 0 & x \in \partial\Omega, \ t > 0.
\end{cases}
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- S, E, I and R: density of susceptible, exposed, infected and recovered individuals;
- σ: proportion of exposed individuals that become infectious;
- α: proportion of recovered individuals that lose immunity.

Basic reproduction number

Lemma

The eigenvalue problem

$$\begin{cases} -d_E\Delta\varphi_E + \sigma\varphi_E = \mu\beta(x)\varphi_I, & x \in \Omega, \\ -d_I\Delta\varphi_I + \gamma(x)\varphi_I - \sigma\varphi_E = 0, & x \in \Omega, \\ \frac{\partial\varphi_E}{\partial n} = \frac{\partial\varphi_I}{\partial n} = 0, & x \in \partial\Omega \end{cases}$$

admits a unique positive eigenvalue, denoted by μ_0, with a positive eigenfunction. Moreover, the basic reproduction number, denoted by $\mathcal{R}_0$, satisfies

$$\mathcal{R}_0 = \frac{1}{\mu_0}.$$

Remark: $\mathcal{R}_0$ is independent of d_S and d_R.

Another eigenvalue problems

- Principal eigenvalue, denoted as λ_1:

$$\begin{cases} -d_E\Delta\phi_E - \beta(x)\phi_I + \sigma\phi_E = \lambda\phi_E, & x \in \Omega, \\ -d_I\Delta\phi_I + \gamma(x)\phi_I - \sigma\phi_E = \lambda\phi_I, & x \in \Omega, \\ \frac{\partial\phi_E}{\partial n} = \frac{\partial\phi_I}{\partial n} = 0, & x \in \partial\Omega. \end{cases}$$

- The following relationship holds:

$$sign(1 - \mathcal{R}_0) = sign(\lambda_1). \tag{2}$$

- The adjoint problem

$$\begin{cases} -d_E\Delta\phi_E^* + \sigma\phi_E^* - \sigma\phi_I^* = \lambda_1\phi_E^*, & x \in \Omega, \\ -d_I\Delta\phi_I^* - \beta(x)\phi_E^* + \gamma(x)\phi_I^* = \lambda_1\phi_I^*, & x \in \Omega, \\ \frac{\partial\phi_E^*}{\partial n} = \frac{\partial\phi_I^*}{\partial n} = 0, & x \in \partial\Omega. \end{cases}$$

Threshold dynamics

Theorem

(i) *If* $\mathcal{R}_0 \leq 1$, *then* $E(x,t), I(x,t), R(x,t) \to 0$ *uniformly in* $\overline{\Omega}$ *as* $t \to \infty$, *and* $\int_\Omega S(x,t)dx \to N$ *as* $t \to \infty$;

(ii) *If* $\mathcal{R}_0 > 1$, *there exists some constant* $\epsilon_0 0$ *such that*

$$\liminf_{t\to\infty} \|(S(t,\cdot), E(t,\cdot), I(t,\cdot), R(t,\cdot)) - (\frac{N}{|\Omega|}, 0, 0, 0)\|_{L^\infty(\Omega)} \epsilon_0.$$

Moreover, there is at least one endemic equilibrium.

Remark: Lyapunov functional

$$L(E,I) = \int_\Omega (E(x,t)\phi_E^*(x) + I(x,t)\phi_I^*(x))dx.$$

An alternative method: [R. Cui, K. Y. Lam, and Y. Lou, 2017]

Monotonicity of $\mathcal{R}_0$ with respect to d_E, d_I

- $\mathcal{R}_0$ for SIS: $\mathcal{R}_0$ is decreasing in d_I; Self-adjoint elliptic operator and variational characterization.

$$\begin{cases} -d_I\Delta\varphi + \gamma(x)\varphi = \frac{1}{\mathcal{R}_0}\beta(x)\varphi, & x \in \Omega, \\ \nabla\varphi \cdot \mathbf{n} = 0, & x \in \partial\Omega. \end{cases}$$

- $\mathcal{R}_0$ for SEIRS: The movement of exposed individuals makes $\mathcal{R}_0$ more subtle: Lack of variational structure.

$$\begin{cases} -d_E\Delta\varphi + \sigma\varphi = \frac{1}{\mathcal{R}_0}\beta(x)\psi, & x \in \Omega, \\ -d_I\Delta\psi + \gamma(x)\psi - \sigma\varphi = 0, & x \in \Omega, \\ \nabla\varphi \cdot \mathbf{n} = \nabla\psi \cdot \mathbf{n} = 0, & x \in \partial\Omega. \end{cases}$$

Monotonicity of $\mathcal{R}_0$ with respect to d_E, d_I

Theorem

If either β or γ is a constant function, then $\mathcal{R}_0$ is a monotone decreasing function of d_E and d_I. Moreover, the strict monotonicity holds if and only if one of them is non-constant.

- Nonlocal eigenvalue problem:

$$\begin{cases} -d_E\Delta\varphi + \sigma\varphi = \frac{\sigma}{\mathcal{R}_0}\beta(x)\left(-d_I\Delta + \gamma(x)\right)^{-1}\varphi, & x \in \Omega, \\ \nabla\varphi \cdot \mathbf{n} = 0 & x \in \partial\Omega. \end{cases}$$

- $\gamma = constant: (-d_E\Delta + \sigma)(-d_I\Delta + \gamma)\psi = \frac{\sigma}{\mathcal{R}_0}\beta(x)\psi$

Monotonicity and non-monotonicity of $\mathcal{R}_0$

Theorem

Assume Ω is one dimensional, and one of β and γ is monotone decreasing and the other is monotone increasing. Then $\mathcal{R}_0$ is a monotone decreasing function of d_E, d_I, and the strict monotonicity holds if and only if β or γ is non-constant.

Theorem

If assume

$$\frac{\int_\Omega \beta}{\int_\Omega \gamma} > \frac{1}{|\Omega|}\int_\Omega \frac{\beta}{\gamma},$$

then there exist d_E^0 and $d_I^1 < d_I^2$ such that

$$\mathcal{R}_0(d_E^0, d_I^1) < \mathcal{R}_0(d_E^0, d_I^2).$$

Non-monotonicity of $\mathcal{R}_0$ in d_E

Theorem

Let $\nu_0 = \frac{\int_\Omega \gamma(x)dx}{\int_\Omega \beta(x)dx}$ *and* φ_1, ϕ_1 *be the unique solutions of*

$$-\Delta\varphi_1 = \nu_0\beta - \gamma, \quad x \in \Omega \quad \textit{with} \quad \frac{\partial \varphi_1}{\partial n} = 0, \quad x \in \partial\Omega$$

$$-\Delta\phi_1 = \frac{\nu_0}{|\Omega|}\int_\Omega \beta dx - \gamma, \quad x \in \Omega \quad \textit{with} \quad \frac{\partial \phi_1}{\partial n} = 0, \quad x \in \partial\Omega,$$

respectively. If

$$\int_\Omega (\gamma - \nu_0\beta)(\varphi_1 - \phi_1)dx 0, \tag{3}$$

there exist d_I^0 *and* $d_E^1 < d_E^2$ *such that* $\mathcal{R}_0(d_E^1, d_I^0) < \mathcal{R}_0(d_E^2, d_I^0)$.

Asymptotic behaviours of EE as $d_S \to 0$

Consider the linear eigenvalue problem

$$-d_R\Delta\phi + \alpha(1 - \tfrac{\gamma}{\beta})\phi = \lambda\phi \ \text{ in } \ \Omega, \quad \nabla\phi \cdot \mathbf{n}|_{\partial\Omega} = 0, \tag{4}$$

where the smallest eigenvalue is denoted by $\lambda_1(-d_R\Delta + \alpha(1 - \frac{\gamma}{\beta}))$.

Theorem

Assume $\mathcal{R}_0 > 1$ and $\lambda_1(-d_R\Delta + \alpha(1 - \frac{\gamma}{\beta})) < 0$.

(i) *There exist positive constants C_1, C_2 such that for sufficiently small d_S,*

$$C_1 \leq \frac{\widetilde{E}}{d_S}, \frac{\widetilde{I}}{d_S}, \frac{\widetilde{R}}{d_S} \leq C_2;$$

(ii) *As $d_S \to 0$, subject to a sequence, $\widetilde{S} \to \widetilde{S}^*$ for some $S^* \geq, \not\equiv 0$.*

A numerical counterexample

- A numerical case satisfying $\mathcal{R}_0 > 1, \lambda_1(-d_R\Delta + \alpha(1-\frac{\gamma}{\beta})) > 0$.

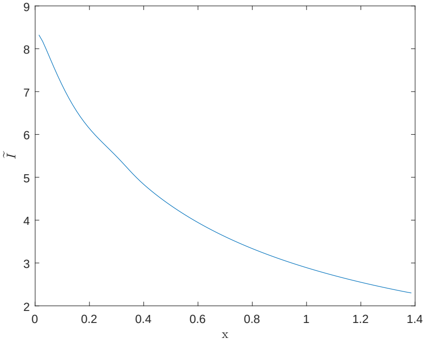


Figure: $\widetilde{I}$ does not converge to zero as $d_S \to 0$; the movement of recovered individuals may increase the number of infected individuals and enhance the endemic.

SEIRS model: discussions

- SIS: $\mathcal{R}_0$ is a monotone decreasing function of d_I.
  SEIRS: Monotonicity of $\mathcal{R}_0$ with respect to d_E, d_I holds in special cases but not in general.
- SIS: $\mathcal{R}_0(PDE) > \mathcal{R}_0(ODE)$
  SEIRS: $>$, $<$, both possible
- $(\tilde{S}, \tilde{I}) \to (S^*, 0)$ in $C^1(\bar{\Omega})$ as $d_S \to 0$
  SEIRS: depending on diffusion rate of recovery individuals.

Some references of basic reproduction number theory

- Next generation operator: [O. Diekmann et.al 1990 JMB; H. Thieme 2009 SIAP]...
- Reviews: [J. Heffernann 2005 Van den Driessche 2017 IDM; Zhao 2017 book Chapter 11; H inaba 2017 book Chapter 9]
- Periodic Abstract Functional Differential Equations : [Zhao 2017 JDDE; Liang, Zhang and Zhao 2019 JDDE]
- Periodic nonlocal dispersal systems with time delay: [Liang,Zhang and Zhao 2019 JDE]
- Periodic reaction-diffusion systems: [Liang,Zhang and Zhao 2017 SIMA]; [Shuang Liu 2021 JFA]
- Age Structure: [Hao Kang 2023 JMB]
- Ecology BRN: [Mark A. Lewis et.al 2019 JMB;H. W. Mckenzie 2012 SIADS]
- ......

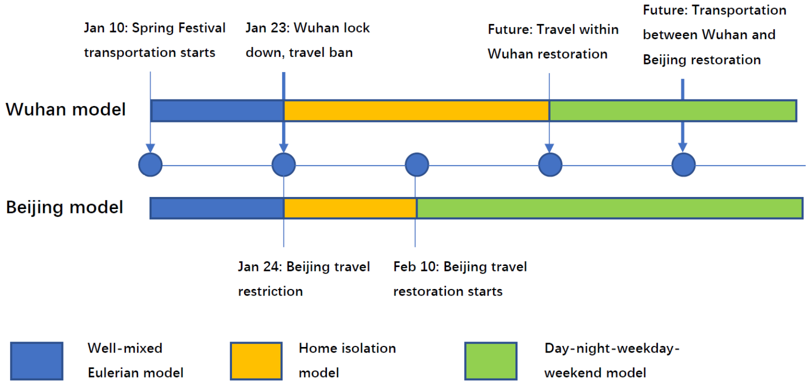
Outline

Background

动机：评估早期武汉封控策略的效果。

观察：不同阶段有不同的风控措施 (居家隔离，市内交通管制，封城)

问题：如何对这种政策多阶段性下扩散模式建模？如何对城市内，城市之间这种不同尺度之间的扩散建模？



Shortages of Theoretical Epidemic Models

- Advantages: theoretically profound and explainable
- Shortages: not practically.
- $t \to \infty$: what about finite t.
- Human doesn't move like animals. (Critical issue: What is the human mobility pattern? How to define the diffusion map? Of course, we need add "If we have human mobility data")

Characteristics of a good practical infectious disease model

[Song-Lou-Zhu-Jiang-Li [2]]

Effectiveness and Adaptability

- Temporal multi Stage: Sporadic, Outbreak, Epidemic, Endemic, Pandemic. Human interventions.
- Spatial multi scale: within and between cities (provinces, states, countries). Spatial heterogeneity.

[2] Song PF, Lou Y, Zhu LP, Li WN, Jiang H. Multi-stage and multi-scale patch model for emerging diseases and the case study of novel coronavirus. Acta Mathematicae Applicatae Sinica, 2020

Previews work on spatial epidemic models

Classification of spatial epidemic models:

- Patch(Reaction-diffusion)Model: [Arino J et.al., 2006, Review]; [L Sattenspiel, 2009, Book]; [Brauer F, et.al., 2019, Book]; ...
  More patch models: [Wang-Mulone 2003; Wang-Zhao 2005; Cui et al. 2006; Allen et al. 2007; Gao-Ruan2011; Arino et al. 2016; Chen et al. 2019; Li-Peng 2019; Gao 2019-20]...
- Individual-based model (Agent based model, ABM): Review Paper [L Willem et.al., 2017, BMC infectious disease]
- Network Model: 靳祯孙桂全刘茂省著《网络传染病动力学建模与分析》; [Mark Newman, Networks, Second Edition, 2018]; [Mark Newman, 2003, SIAM Review]; Series work of Matt J. Keeling.....
  our focus is on patch models.

Previews work on patch epidemic models

- Day-night model: [Pei Sen et.al, 2018 PNAS]
- Gleam (Global Epidemic and Mobility) model: [Vittoria Colizza et.al 2005, PNAS; Duygu Balcan et.al, 2009 PNAS; Duygu Balcan et.al, 2009 BMC Medicine; Michele Tizzoni et al, 2014 Plos Computational Biology; Zhang Qian et al, 2016 PNAS; Matteo Chinazzi et.al 2020, Science]......
  Gleamviz open source software.
- Imperial College in Lond: [Riley Steven, 2007 Science; Max S. Y. Laua et.al 2016 PNAS; Michal Ben-Nun et.al 2019 Plos Computational Biology; David J. Haw et.al 2019 Plos Computational Biology].....
- Lagrangian model: [Chris Cosner, SG Ruan et.al 2009 JTB; Carlos Castillo-Chavez et.al 2016 PNAS; Esteban Vargas, preprint, personal communications]
- Human mobility pattern: [Marta C. Gonzalez et.al, 2008 Nature, Zif's Law; Filippo Simini et.al, 2012 Nature]

Eulerian and Lagrangian (Fluid) Dynamics

Euler 观点：盯着空间某个点 i，观察经过此点的粒子或者流体动力学.

$$\begin{aligned}
\frac{dS_i}{dt} &= A_i - d_iS_i - \beta_i(I_i)\frac{S_iI_i}{S_i+I_i} + \gamma_iI_i + \sum_{j=1}^{p} m_{ij}S_j, \quad 1 \leqslant i \leqslant p \\
\frac{dI_i}{dt} &= \beta_i(I_i)\frac{S_iI_i}{S_i+I_i} - (d_i + v_i + \gamma_i)I_i + \sum_{j=1}^{p} n_{ij}I_j, \quad 1 \leqslant i \leqslant p.
\end{aligned}$$

e.g., Gleam Model ([Colizza et.al, 2006, PNAS];[Zhang et.al, 2016, PNAS]; [Chinazzi et.al, 2020, Science]

Eulerian and Lagrangian (Fluid) Dynamics

Lagrangian 观点：在每个粒子上放置一个标签 (家庭住址 i), 盯着这个粒子，然后研究每个被标记的粒子轨迹.

$$\dot{S}_i = b_i - d_i S_i + \gamma_i I_i - \sum_{j=1}^{n} (S_i \text{ infected in Patch } j)$$

$$\dot{I}_i = \sum_{j=1}^{n} (S_i \text{ infected in Patch } j) - \gamma_i I_i - d_i I_i$$

$$\dot{N}_i = b_i - d_i N_i$$

$$[S_i \text{ infected in Patch} j] = \underbrace{\beta_j}_{\text{the risk of infection in Patch } j} \times \underbrace{p_{ij} S_i}_{\text{Susceptible from Patch } i \text{ who are currently in Patch}} \times \frac{\sum_{k=1}^{n} p_{kj} I_k}{\sum_{k=1}^{n} p_{kj} N_k}$$

Derivation of a general theoretical model

The SEIR meta-population model, to forecast the spatial transmission of emerging disease within and between cities (provinces or countries), includes two kinds of dynamics.

- Epidemic dynamics layer
- Transportation dynamics layer including

  Mobility between cities chracterizing by Eulerian method

  Recurrent Commuting within cities chracterizing by Lagrangian method
- Intervention Layer

Epidemic dynamics

- Four classes: susceptible (S), exposed(E, latent infected without symptoms), infectious (I, infected with symptoms) and recovered (R);
- The susceptible individuals can be infected by exposed and infectious individuals.

Recurrent Commuting within cities

Let $c = 1, 2, ..., K$ denote a finite number of cities and n_c denote the total number of patches for city c.

- The whole population in city c is devided into $n_c \times n_c$ subpopulations $\left\{N^{c,w,h}\right\}_{n_c \times n_c}$. w, h are labels of each individual meaning living patch h (home), working in patch w.
- The probability of subpopulation $N^{c,w,h}$ that locates (due to work-induced fixed recurrent commuting diffusion, *Lagrangian* spatial approach) in patch i at time t within city c is given by $P_i^{c,w,h}(t)$, which implies the number of total people locating at patch i

$$N_i^{c,w,h} = P_i^{c,w,h}(t) N^{c,w,h}$$

Recurrent Commuting within cities

The number of suspected, exposed, infected and recovered individuals locating in patch i at time t are denoted respectively as

$$S_i^c(t) = \sum_{w,h=1}^{n_c} P_i^{c,w,h}(t) S^{c,w,h}(t),$$

$$E_i^c(t) = \sum_{w,h=1}^{n_c} P_i^{c,w,h}(t) E^{c,w,h}(t),$$

$$I_i^c(t) = \sum_{w,h=1}^{n_c} P_i^{c,w,h}(t) S^{c,w,h}(t),$$

$$R_i^c(t) = \sum_{w,h=1}^{n_c} P_i^{c,w,h}(t) S^{c,w,h}(t),$$

$$N_i^c(t) = S_i^c(t) + E_i^c(t) + I_i^c(t) + R_i^c(t).$$

Mobility between cities: leaving

- The number of individuals traveling from city a to b is

$$l_{ab} = D_{ab} m_{ab} N^a,$$

$N^a := \sum_{w,h=1}^{n_a} N^{a,w,h}$ is total population in city a
D_{ab} is the distance dependent movement rate from city a to b
m_{ab} is the transition probability from city a to b.

- The infected individuals living in h, working in w and leaving city c is

$$\sum_{b \neq c} l_{cb} \frac{I^{c,w,h}}{N^c} = \left(\sum_{b \neq c} D_{cb} m_{cb} \right) I^{c,w,h}.$$

Mobility between cities: entering

- The total number of immigrants entering city c

$$\sum_{b \neq c} l_{bc} \frac{I^b}{N^i} := \sum_{b \neq c} D_{bc} m_{bc} I^b.$$

- The probability of the immigrants to city c ending up living in h and working in w,

$$q^{c,w,h} = \frac{S^{c,w,h} + E^{c,w,h} + I^{c,w,h} + R^{c,w,h}}{N^c}.$$

- The number of infected immigrants ending up living in h, working in w and entering city c

$$q^{c,w,h} \sum_{b \neq c} l_{ic} \frac{I^i}{N^i} = q^{c,w,h} \sum_{b \neq c} D_{bc} m_{bc} I^b.$$

A general model: within cities

$$
\begin{cases}
\dfrac{\mathrm{d}S^{c,w,h}}{\mathrm{d}t} = -S^{c,w,h}\displaystyle\sum_{i=1}^{n_c} P_i^{c,w,h}(t)C_i^c(t)\left(\beta_{iI}^c(t)\frac{I_i^c(t)}{N_i^c(t)} + \beta_{iE}^c(t)\frac{E_i^c(t)}{N_i^c(t)}\right) \\
\qquad - \displaystyle\sum_{b\neq c} D_{cb}m_{cb}S^{c,w,h} + q^{c,w,h}\sum_{b\neq c} D_{bc}m_{bc}S^b, \\
\dfrac{\mathrm{d}E^{c,w,h}}{\mathrm{d}t} = S^{c,w,h}\displaystyle\sum_{i=1}^{n_c} P_i^{c,w,h}(t)C_i^c(t)\left(\beta_{iI}^c(t)\frac{I_i^c(t)}{N_i^c(t)} + \beta_{iE}^c(t)\frac{E_i^c(t)}{N_i^c(t)}\right) - \sigma^c E^{c,w,h} \\
\qquad - \displaystyle\sum_{b\neq c} D_{cb}m_{cb}E^{c,w,h} + q^{c,w,h}\sum_{b\neq c} D_{bc}m_{bc}E^b, \\
\dfrac{\mathrm{d}I^{c,w,h}}{\mathrm{d}t} = \sigma^c E^{c,w,h} - \displaystyle\sum_{i=1}^{n_c}\left[\alpha_i^c(t) + \gamma_i^c(t)\right] P_i^{c,w,h}(t)I^{c,w,h} \\
\qquad - \displaystyle\sum_{b\neq c} D_{cb}m_{cb}I^{c,w,h} + q^{c,w,h}\sum_{b\neq c} D_{bc}m_{bc}I^b, \\
\dfrac{\mathrm{d}R^{c,w,h}}{\mathrm{d}t} = \displaystyle\sum_{i=1}^{n_c}\gamma_i^c(t)P_i^{c,w,h}(t)I^{c,w,h} - \sum_{b\neq c} D_{cb}m_{cb}R^{c,w,h} + q^{c,w,h}\sum_{b\neq c} D_{bc}m_{bc}R^b.
\end{cases}
\tag{5}
$$

A general model: between cities

$$
\begin{cases}
\dfrac{\mathrm{d}S^c}{\mathrm{d}t} = -\displaystyle\sum_{i,w,h=1}^{n_c} S^{c,w,h} P_i^{c,w,h}(t) C_i^c(t) \left(\beta_{iI}^c(t) \frac{I_i^c(t)}{N_i^c(t)} + \beta_{iE}^c(t) \frac{E_i^c(t)}{N_i^c(t)} \right) \\
\qquad - \displaystyle\sum_{b \neq c} D_{cb} m_{cb} S^c + \sum_{b \neq c} D_{bc} m_{bc} S^b, \\
\dfrac{\mathrm{d}E^c}{\mathrm{d}t} = \displaystyle\sum_{i,w,h=1}^{n_c} S^{c,w,h} P_i^{c,w,h}(t) C_i^c(t) \left(\beta_{iI}^c(t) \frac{I_i^c(t)}{N_i^c(t)} + \beta_{iE}^c(t) \frac{E_i^c(t)}{N_i^c(t)} \right) - \sigma^c E^c \\
\qquad - \displaystyle\sum_{b \neq c} D_{cb} m_{cb} E^c + \sum_{b \neq c} D_{bc} m_{bc} E^b, \\
\dfrac{\mathrm{d}I^c}{\mathrm{d}t} = \sigma^c E^c - \displaystyle\sum_{i,w,h=1}^{n_c} \left[\alpha_i^c(t) + \gamma_i^c(t) \right] P_i^{c,w,h}(t) I^{c,w,h} \\
\qquad - \displaystyle\sum_{b \neq c} D_{cb} m_{cb} I^c + \sum_{b \neq c} D_{bc} m_{bc} I^b, \\
\dfrac{\mathrm{d}R^c}{\mathrm{d}t} = \displaystyle\sum_{i,w,h=1}^{n_c} \gamma_i^c(t) P_i^{c,w,h}(t) I^{c,w,h} - \sum_{b \neq c} D_{cb} m_{cb} R^c + \sum_{b \neq c} D_{bc} m_{bc} R^b.
\end{cases}
\tag{6}
$$

Application: *Eulerian* model

The population is well mixed and the medical resources are distributed homogeneously within cities

$$P_i^{c,w,h}(t) = \frac{1}{n_c}.$$

$$\begin{cases} \dfrac{\mathrm{d}S^c}{\mathrm{d}t} = -S^c C^c(t)\left(\beta_I^c(t)\dfrac{I^c(t)}{N^c(t)} + \beta_E^c(t)\dfrac{E^c(t)}{N^c(t)}\right) - \sum\limits_{b\neq c} D_{cb} m_{cb} S^c + \sum\limits_{b\neq c} D_{bc} m_{bc} S^b, \\ \dfrac{\mathrm{d}E^c}{\mathrm{d}t} = S^c C^c(t)\left(\beta_I^c(t)\dfrac{I^c(t)}{N^c(t)} + \beta_E^c(t)\dfrac{E^c(t)}{N^c(t)}\right) - \sigma^c E^c - \sum\limits_{b\neq c} D_{cb} m_{cb} E^c + \sum\limits_{b\neq c} D_{bc} m_{bc} E^b, \\ \dfrac{\mathrm{d}I^c}{\mathrm{d}t} = \sigma^c E^c - (\alpha^c(t) + \gamma^c(t))\, I^c - \sum\limits_{b\neq c} D_{cb} m_{cb} I^c + \sum\limits_{b\neq c} D_{bc} m_{bc} I^b, \\ \dfrac{\mathrm{d}R^c}{\mathrm{d}t} = \gamma^c(t) I^c - \sum\limits_{b\neq c} D_{cb} m_{cb} R^c + \sum\limits_{b\neq c} D_{bc} m_{bc} R^b. \end{cases} \tag{7}$$

Application: *Lagrangian* model

$D_{ab} = 0, a, b = 1, 2, 3, ..., K,$ cities lockdown.

$$
\begin{cases}
\dfrac{\mathrm{d}S^{c,w,h}}{\mathrm{d}t} = -S^{c,w,h} \displaystyle\sum_{i=1}^{n_c} P_i^{c,w,h}(t) C_i^c(t) \left(\beta_{iI}^c(t) \dfrac{I_i^c(t)}{N_i^c(t)} + \beta_{iE}^c(t) \dfrac{E_i^c(t)}{N_i^c(t)} \right), \\
\dfrac{\mathrm{d}E^{c,w,h}}{\mathrm{d}t} = S^{c,w,h} \displaystyle\sum_{i=1}^{n_c} P_i^{c,w,h}(t) C_i^c(t) \left(\beta_{iI}^c(t) \dfrac{I_i^c(t)}{N_i^c(t)} + \beta_{iE}^c(t) \dfrac{E_i^c(t)}{N_i^c(t)} \right) - \sigma^c E^{c,w,h}, \\
\dfrac{\mathrm{d}I^{c,w,h}}{\mathrm{d}t} = \sigma^c E^{c,w,h} - \displaystyle\sum_{i=1}^{n_c} \left[\alpha_i^c(t) + \gamma_i^c(t)\right] P_i^{c,w,h}(t) I^{c,w,h}, \\
\dfrac{\mathrm{d}R^{c,w,h}}{\mathrm{d}t} = \displaystyle\sum_{i=1}^{n_c} \gamma_i^c(t) P_i^{c,w,h}(t) I^{c,w,h}.
\end{cases}
\tag{8}
$$

Application: Home quarantine spatial model

$$P_i^{c,w,h}(t) = 1, i = h; P_i^{c,w,h}(t) = 0, i \neq h,$$

$$\begin{cases} \dfrac{\mathrm{d}S^{c,w,h}}{\mathrm{d}t} = -S^{c,w,h} C_h^c(t) \left(\beta_{hI}^c(t) \dfrac{I_h^c(t)}{N_h^c(t)} + \beta_{hE}^c(t) \dfrac{E_h^c(t)}{N_h^c(t)} \right) \\ \qquad - \sum\limits_{b \neq c} D_{cb} m_{cb} S^{c,w,h} + q^{c,w,h} \sum\limits_{b \neq c} D_{bc} m_{bc} S^b, \\ \dfrac{\mathrm{d}E^{c,w,h}}{\mathrm{d}t} = S^{c,w,h} C_h^c(t) \left(\beta_{hI}^c(t) \dfrac{I_h^c(t)}{N_h^c(t)} + \beta_{hE}^c(t) \dfrac{E_h^c(t)}{N_h^c(t)} \right) - \sigma^c E^{c,w,h} \\ \qquad - \sum\limits_{b \neq c} D_{cb} m_{cb} E^{c,w,h} + q^{c,w,h} \sum\limits_{b \neq c} D_{bc} m_{bc} E^b, \\ \dfrac{\mathrm{d}I^{c,w,h}}{\mathrm{d}t} = \sigma^c E^{c,w,h} - \left(\alpha_h^c(t) + \gamma_h^c(t) \right) I^{c,w,h} \\ \qquad - \sum\limits_{b \neq c} D_{cb} m_{cb} I^{c,w,h} + q^{c,w,h} \sum\limits_{b \neq c} D_{bc} m_{bc} I^b, \\ \dfrac{\mathrm{d}R^{c,w,h}}{\mathrm{d}t} = \gamma_h^c(t) I^{c,w,h} - \sum\limits_{b \neq c} D_{cb} m_{cb} R^{c,w,h} + q^{c,w,h} \sum\limits_{b \neq c} D_{bc} m_{bc} R^b. \end{cases}$$

Application:Day-night-weekday-weekend model

- During weekdays: the daytime (9am-5pm for example)

$$P_i^{c,w,h}(t) = 0, i \neq w; P_w^{c,w,h}(t) = 1,$$

and the night time (5pm-9am for example)

$$P_i^{c,w,h}(t) = 0, i \neq h; P_h^{c,w,h}(t) = 1.$$

- During weekends: the daytime (9am-5pm for example), well mixed,

$$P_i^{c,w,h}(t) = \frac{1}{n_c},$$

and the night time (5pm-9am for example)

$$P_i^{c,w,h}(t) = 0, i \neq h; P_h^{c,w,h}(t) = 1.$$

Data cooperation

Time and policies dependent parameters.

- $\beta_{iE}(t), \beta_{iI}(t)$ and data corresponding to temperature, relative humidity and viability of virus;
- $c_i(t)$ and data on mass media or searching index;
- $\gamma_i(t), \alpha_i(t)$ and data on medical resources (sickbeds);
- $P_i^{w,h}(t)$ and data on working commuters;
- D_{cb}, m_{cb} and data on qianxi beween cities (Baidu qianxi open resources).

Case study: Covid-19 outbreak in Wuhan and Beijing

Data: Accumulated and newly confirmed Covid-19 cases in Wuhan and Beijing from Jan 10 to March 1. Population in 16 districts in Beijing and 13 districts in Wuhan. Baidu Searching index data of Wuhan Covid-19.

- Retrospectively investigating the effect of travel ban between Wuhan and Beijing.
- Retrospectively investigating the effect of NPI within Wuhan and Beijing.
- Forecast the effect of traffic restoration within Wuhan on May 1.
- Forecast the effect of transportation restoration between Wuhan and Beijing on June 1.

Timeline and models of Covid-19 in Wuhan and Beijing

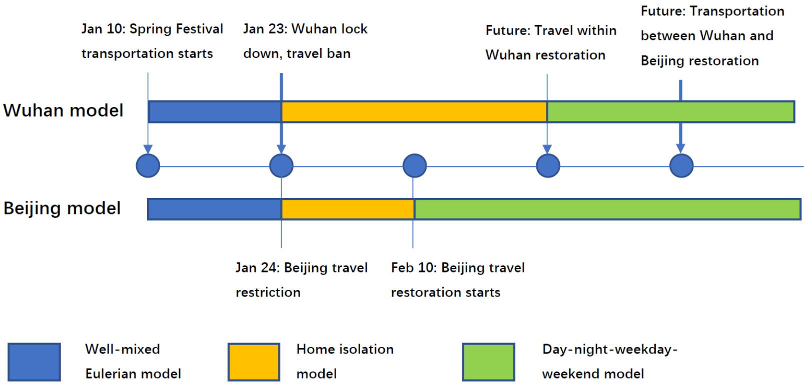


Figure: Timeline models of Covid-19 outbreak in Wuhan and Beijing.

The effect of travel ban between Wuhan and Beijing

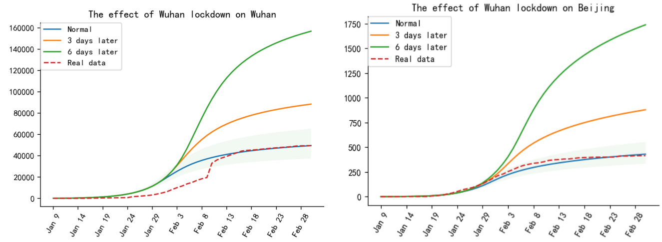


Figure: The effect of travel ban between Wuhan and Beijing.

Ban delay	Accumulated Cases in Wuhan on March 1	Beijing
Normal	49663 (95% CI37603-65525)	431 (95% CI 334-555)
3 days later	88828(1.80)	884(2.14)
6 days later	157703(4.22)	1751(3.16)

The effect of NPI within Wuhan and Beijing

NPI: (non-pharmaceutical interventions) travel restrictions, wearing mask, social distance et.al

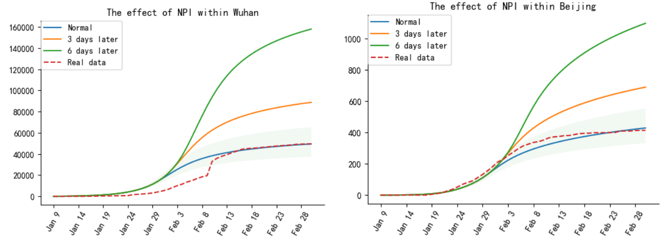


Figure: The effect of NPI within Wuhan and Beijing.

NPI delay	Accumulated Cases in Wuhan on March 1	Beijing
Normal	49663 (95% CI37603-65525)	431 (95% CI 334-555)
3 days later	89107 (1.80)	694 (1.70)
6 days later	158706 (3.66)	1106 (2.67)

Traffic restoration within Wuhan on May 1

Accumulated cases in Wuhan

Table: The effect of traffic restoration within Wuhan on May 1

Restoration or not	April 1	May 1	June 1	July 1
Not	53728	54788	55005	55052
Yes	53728	54788	55135	55388
Difference	0	0	130	336

Transportation restorations between Wuhan and Beijing on June 1

Accumulated cases in Beijing

Table: Transportation restorations between Wuhan and Beijing on June 1

Restoration or not	April 1	May 1	June 1	July 1
Not	482	515	521	523
Yes	482	515	521	526
Difference	0	0	0	3

Outline

Discussions

- Effect of asymptomatic infected individuals' diffusion
- Interaction between environmental heterogeneity (spatial and temporal) and human heterogeneity (susceptibility or exposure).
- How to connect with data and some specific diseases.
- Evolution issues

Thank you!