Determining travel fluxes for reopening in epidemic areas

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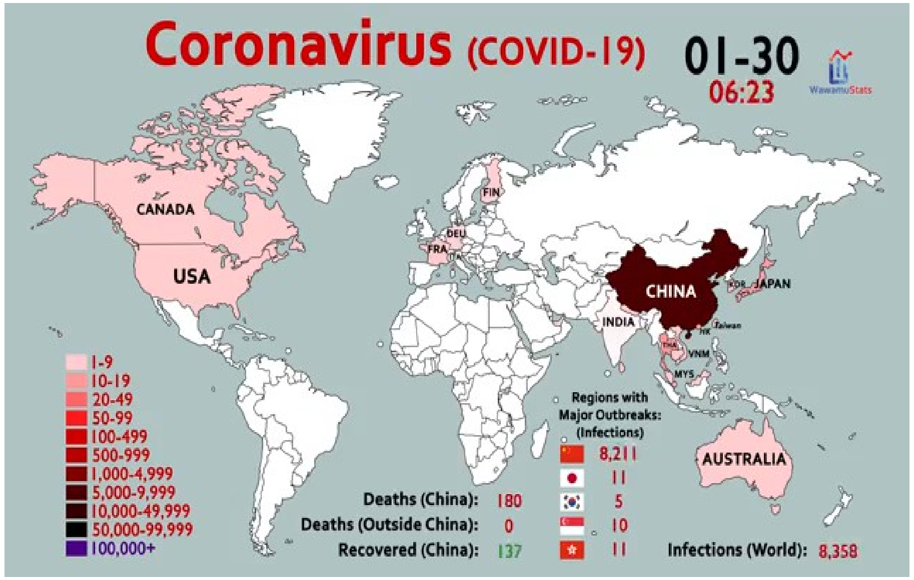
Infectious Disease Outbreaks, Webinar 2020-2021

Outline

- Background and motivations
- How to design a reopening strategy? When, where and how?
  - Effect of mass movements on possible outbreaks
  - The optimal reopening strategies
- Conclusions

Complex spatial spread of COV-SAR-2

Woolley-Meza, et al., Eur. Phys. J. (2011).



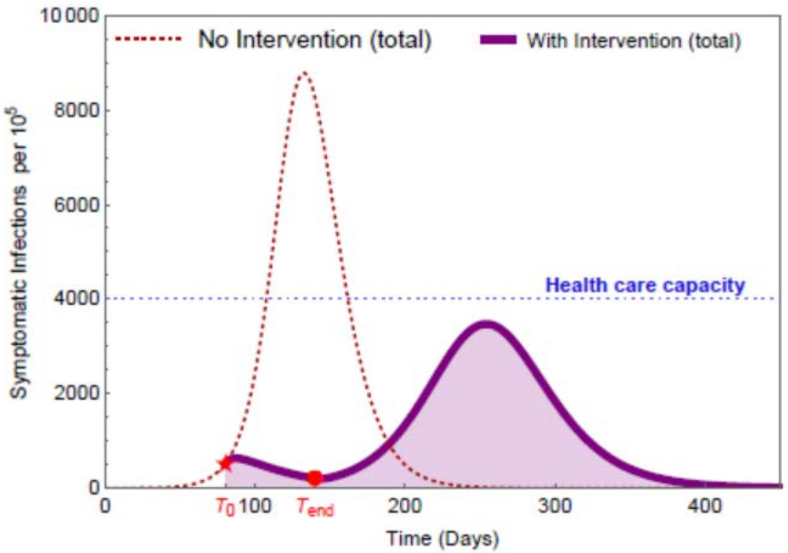
https://www.youtube.com/watch?v=Z7IqpqLV9M0

- The characterization and prediction of spatial spread of infectious pathogen heavily depend on **population mobility**.
- **Transportation network** has reshaped the **geometric feature** of geographical space.
- The geographical distance plays a weaker and weaker role in **regional connection**.

Lockdown strategies Vs relaxing restrictions

□ Strong social distancing (including lockdown, quarantine, isolation) restrictions have been used extensively as part of policies aimed at controlling the COVID-19 pandemic;

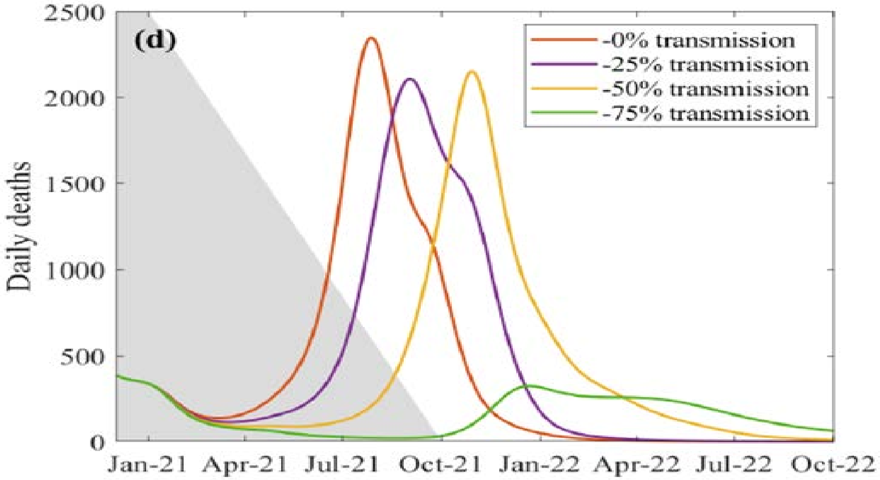
□ To identify less restrictive policies that help restart the economy without cause second wave ?



Various "What if ? "questions

➢ Would lifting the lockdown cause a second wave of infections?

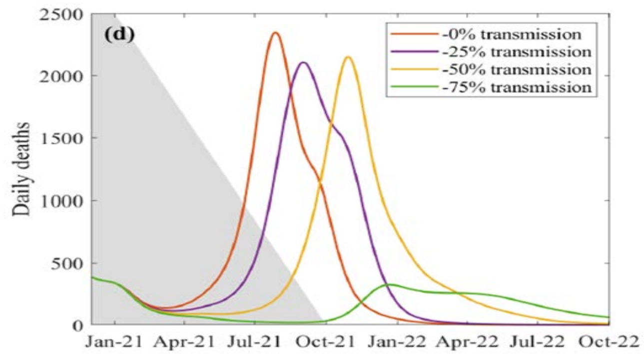
➢ What the number of deaths would have been had the government acted earlier?

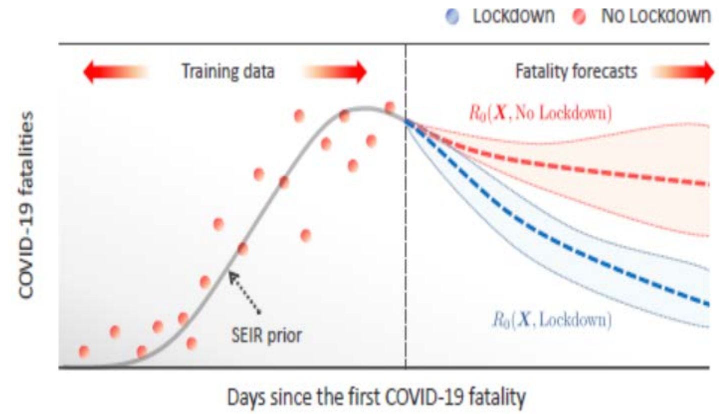


Modelling lockdown exit strategies for COVID-19

Vary the contact rate at a given timing

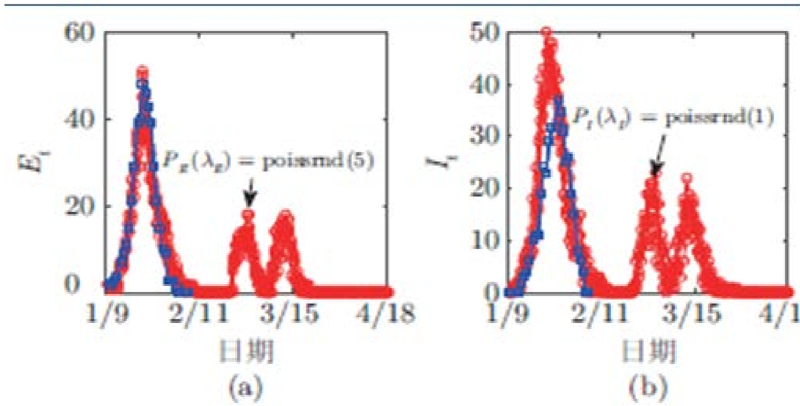
- Keeling et al., 2020
- D'Orazio, 2020;
- Brethouwer, 2020 ;
- Aleta et al., 2020;
- Petersen et al., 2020





Allow individuals to move at a given time period

- Wang et al., China Math, 2020;
- Arion et al 2020
- Shea et al. 2020
- ……



Modelling lockdown exit strategies for COVID-19

◆ Modify the incidence rate

$$\lambda = \mathrm{I} \cdot C(t, N) \cdot \frac{S}{N} \cdot \beta_0(t)$$

→ **Transmission probability (**wear face mask, …)

→ **Contact rates (**contact tracing, quarantine, isolation**)**

◆ Modify the movements

$$E_1' = \beta c(1-q)S_1(I_1 + \theta A_1 + \nu E_1) - \sigma E_1 - \sum_{2}^{n} m_i^E((t)$$

$$\frac{\partial p(t,x)}{\partial t} = \gamma \Delta p(t,x) + R(t,x)p(t,x).$$

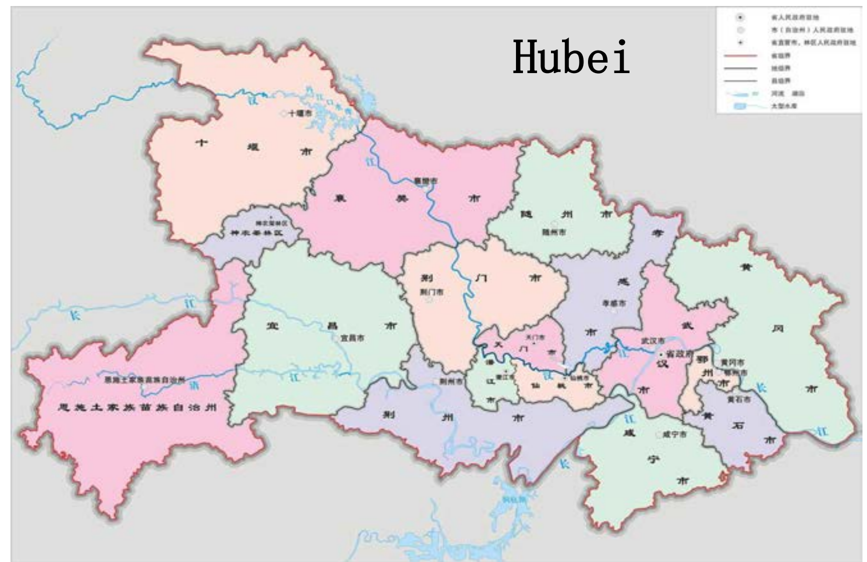
$$R(t,x) = \Lambda(t,x) - \Gamma(t,x)$$

$$\Lambda(t,x) = \beta C(t,x)\frac{s(t,x)}{n(t,x)},$$

Motivations: Optimal reopening strategies: to determine when, where can lift the lockdown, and how to do

Part 1： Effect of mass movements on possible outbreaks

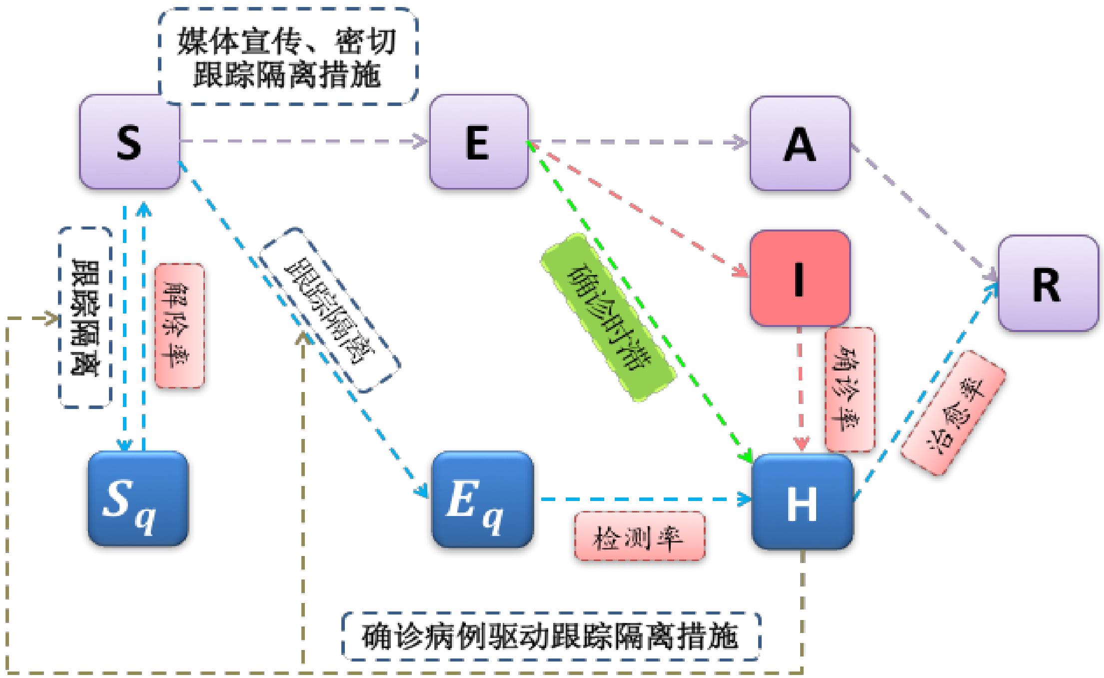
Question: During the late stage of COVID-19 infection in China in 2020, when did individuals return to work (the date of resumption of work) ?



➤ **Methods: a meta-population model, movement network with Hubei province**

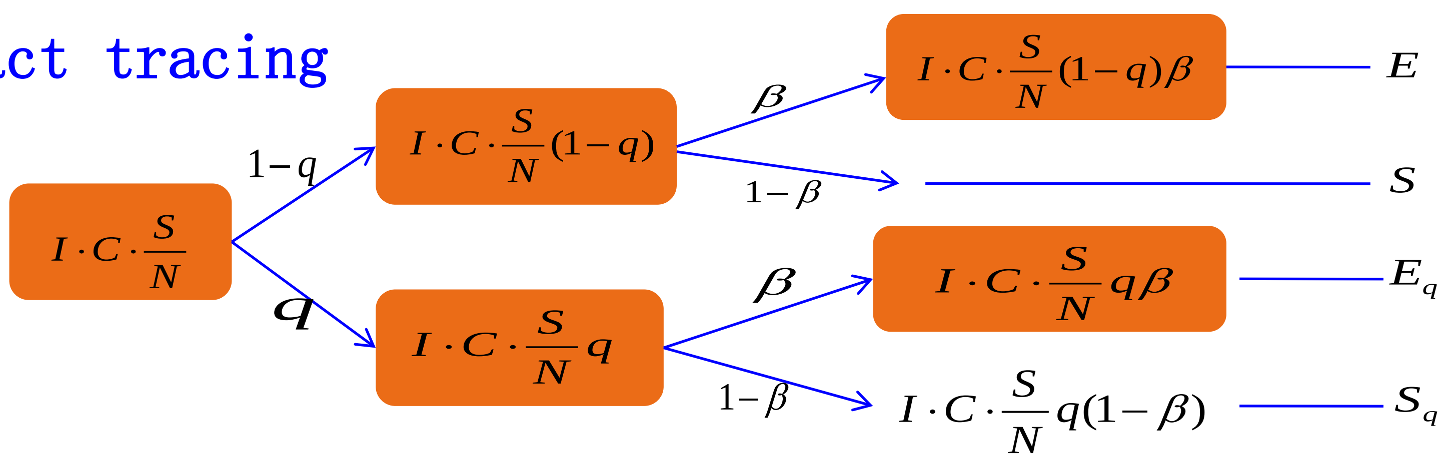
The SEIR-type model with contact tracing

J Clin Med 2020; 9:462.



$$S' = -(\beta c + cq(1-\beta))SI - \vartheta SA + \lambda S_q,$$
$$E' = \beta c(1-q)SI + \vartheta SA - \sigma E,$$
$$I' = \sigma\varrho E - (\delta_I + \alpha + \gamma_I)I,$$
$$A' = \sigma(1-\varrho)E - \gamma_A A,$$
$$S_q{}' = (1-\beta)cqSI - \lambda S_q,$$
$$E_q{}' = \beta cqSI - \delta_q E_q,$$
$$H' = \delta_I I + \delta_q E_q - (\alpha + \gamma_H)H,$$
$$R' = \gamma_I I + \gamma_A A + \gamma_H H,$$

contact tracing



A meta-population model

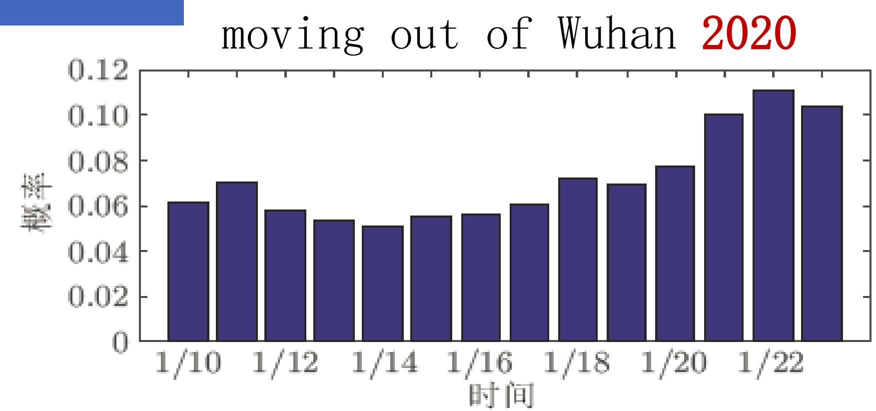
$$
\begin{cases}
S_1' = -(\beta c + cq(1-\beta))S_1(I_1 + \theta A_1 + \nu E_1) + \lambda S_{q1} - \sum_{2}^{n} m_i^S((t) \\
E_1' = \beta c(1-q)S_1(I_1 + \theta A_1 + \nu E_1) - \sigma E_1 - \sum_{2}^{n} m_i^E((t) \\
I_1' = \sigma\rho E_1 - (\delta_I + \alpha + \gamma_I)I_1 - \sum_{2}^{n} m_i^I((t) \\
A_1' = \sigma(1-\rho)E_1 - \gamma_A A_1 - \sum_{2}^{n} m_i^A((t) \\
S_{q1}' = (1-\beta)cqS_1(I_1 + \theta A_1 + \nu E_1) - \lambda S_{q1} \\
E_{q1}' = \beta cqS_1(I_1 + \theta A_1 + \nu E_1) - \delta_q E_{q1} \\
H_1' = \delta_I I_1 + \delta_q E_{q1} - (\alpha + \gamma_H)H_1 \\
R_1' = \gamma_I I_1 + \gamma_A A_1 + \gamma_H H_1
\end{cases}
$$

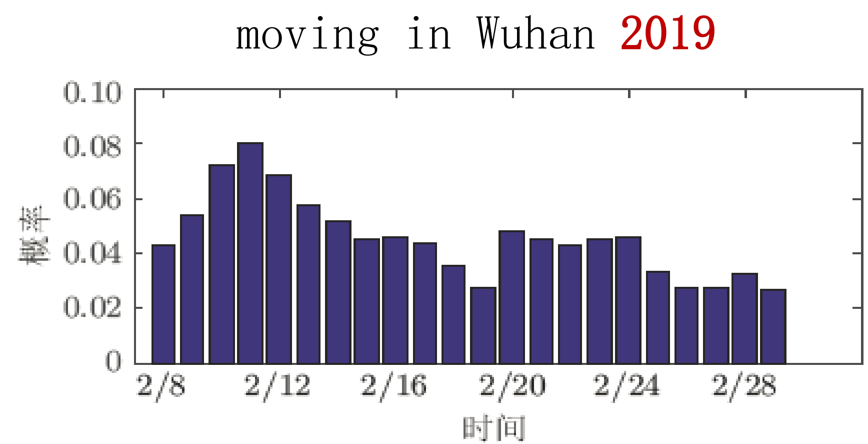
movements

Estimate the movements

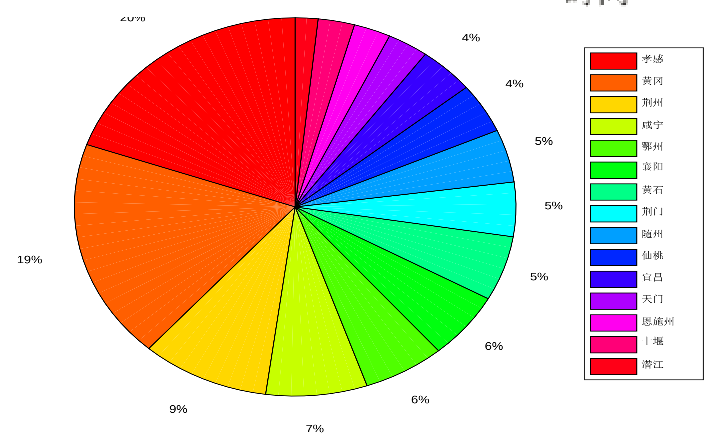
$$m_i^j(t)$$

- **+** Jan 10 – Jan 23
- **○** Jan 23– date of resumption
- **−** resumption





Average distribution of destinations of Wuhan's emigrant population from Jan 10 to Jan 23, 2020



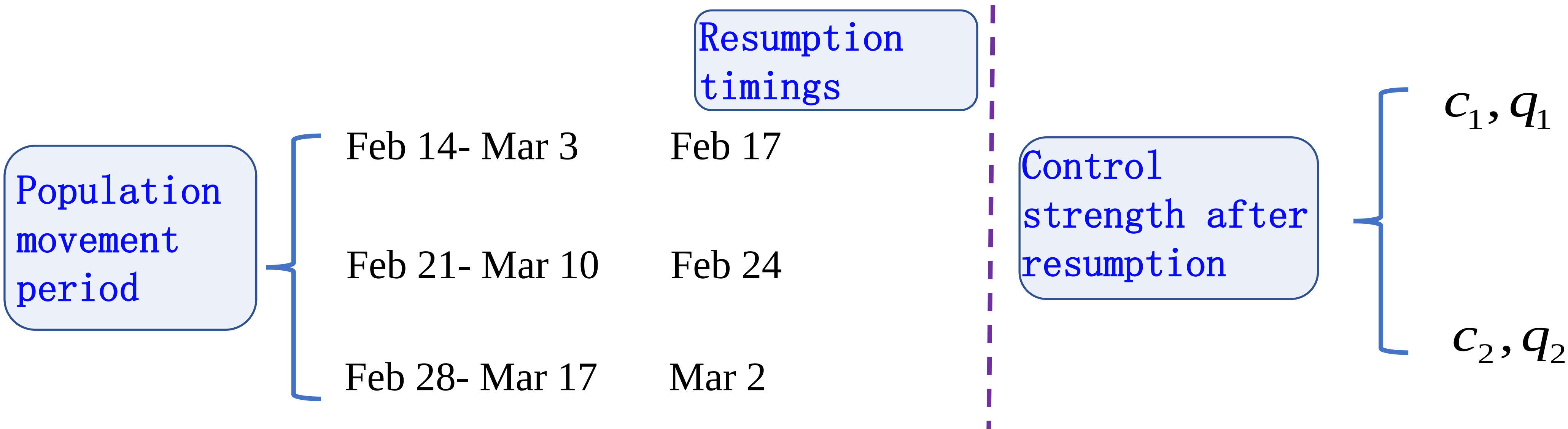
Modelling enhanced interventions

Piece-wise contact rate, quarantine rate

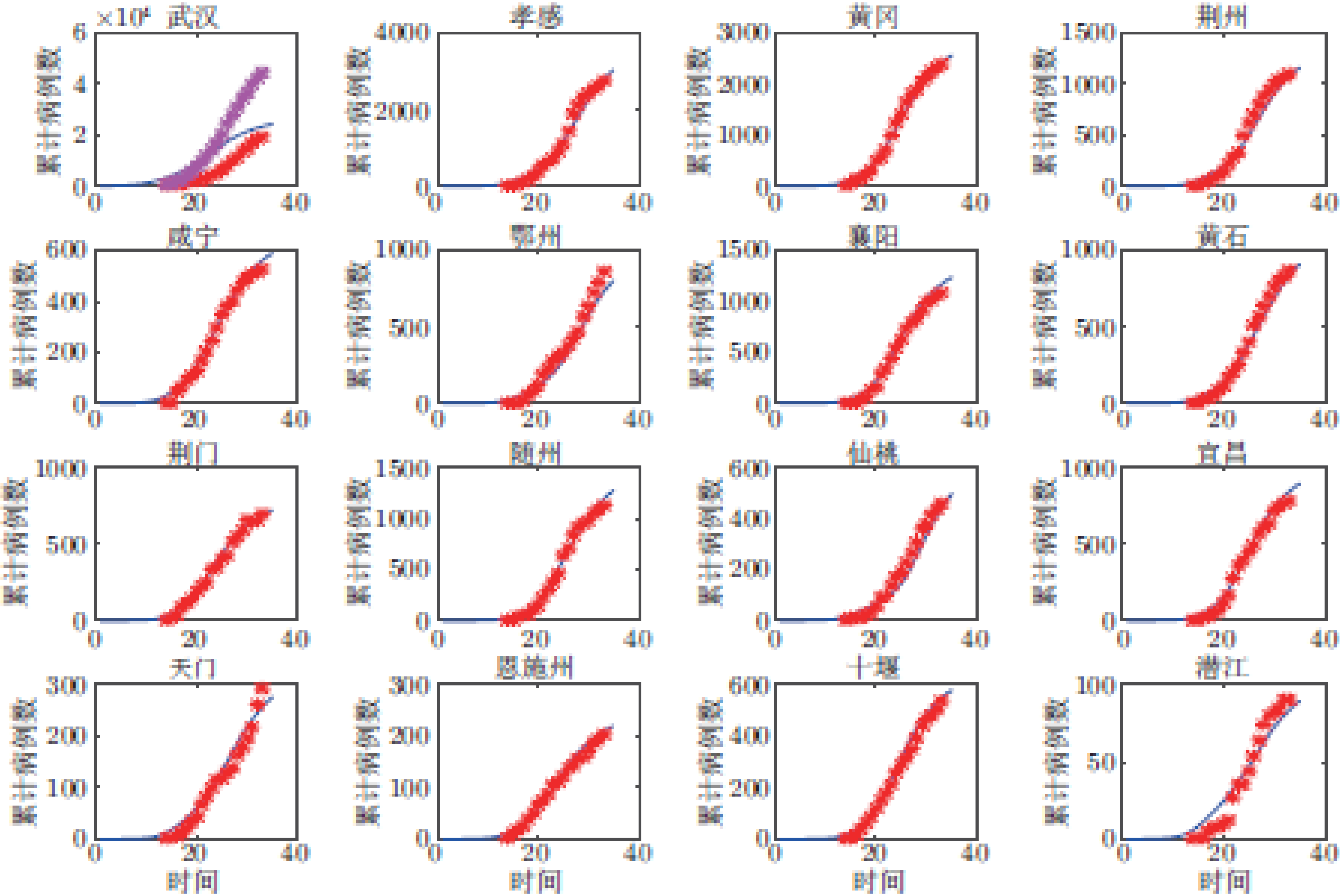
$$c(t)=\begin{cases} c_1, & \text{Jan } 26 \le t \le \text{Jan } 30 \\ c_2, & \text{Jan } 31 \le t \le \text{Feb } 4 \\ c_3, & \text{Feb } 4 \le t \le \text{Feb } 9 \end{cases}$$

$$q(t)=\begin{cases} q_1, & \text{Jan } 26 \le t \le \text{Jan } 30 \\ q_2, & \text{Jan } 31 \le t \le \text{Feb } 4 \\ q_3, & \text{Feb } 4 \le t \le \text{Feb } 9 \end{cases}$$

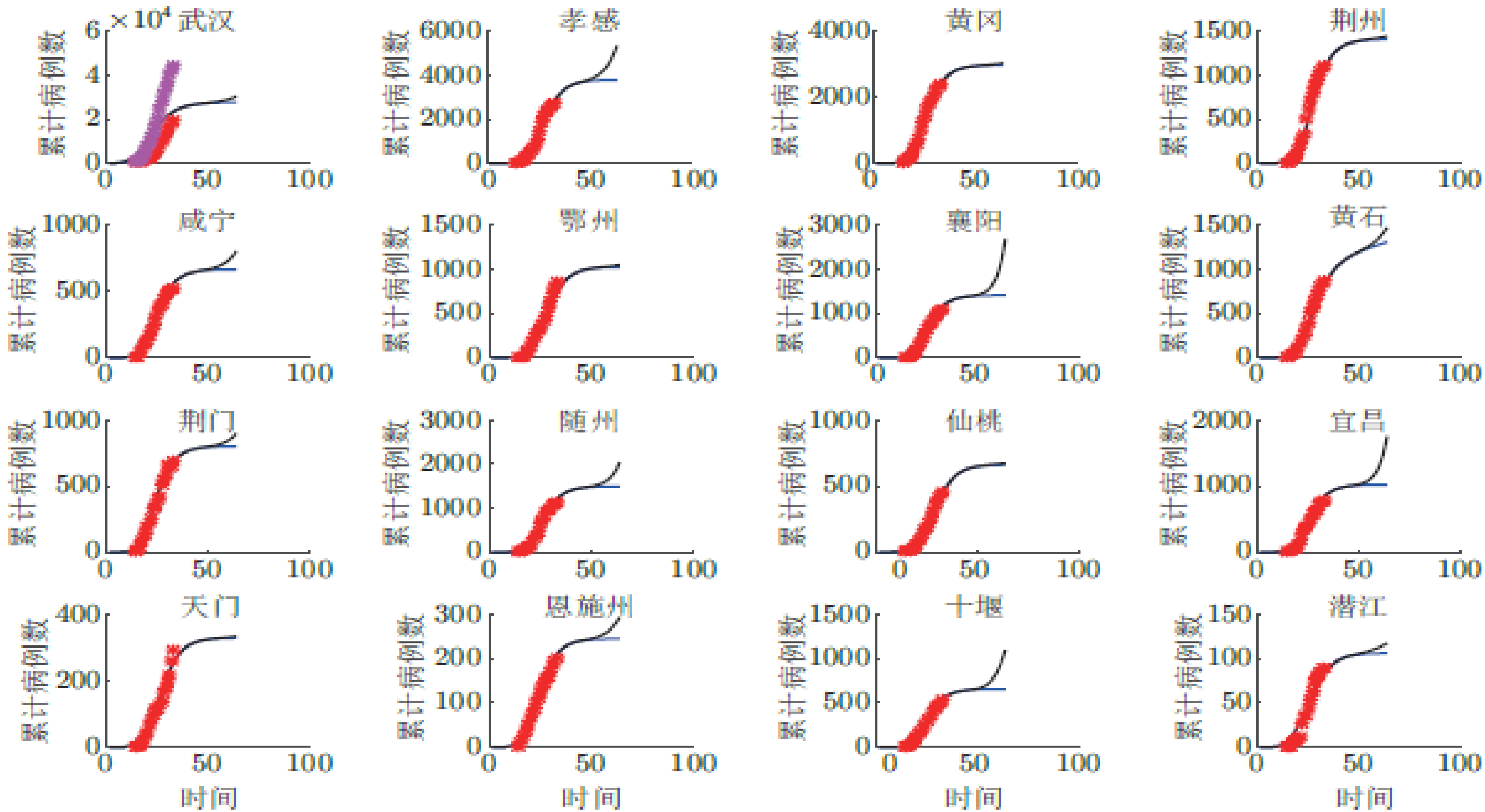
Modelling resumption of work



Data fitting for 16 cities

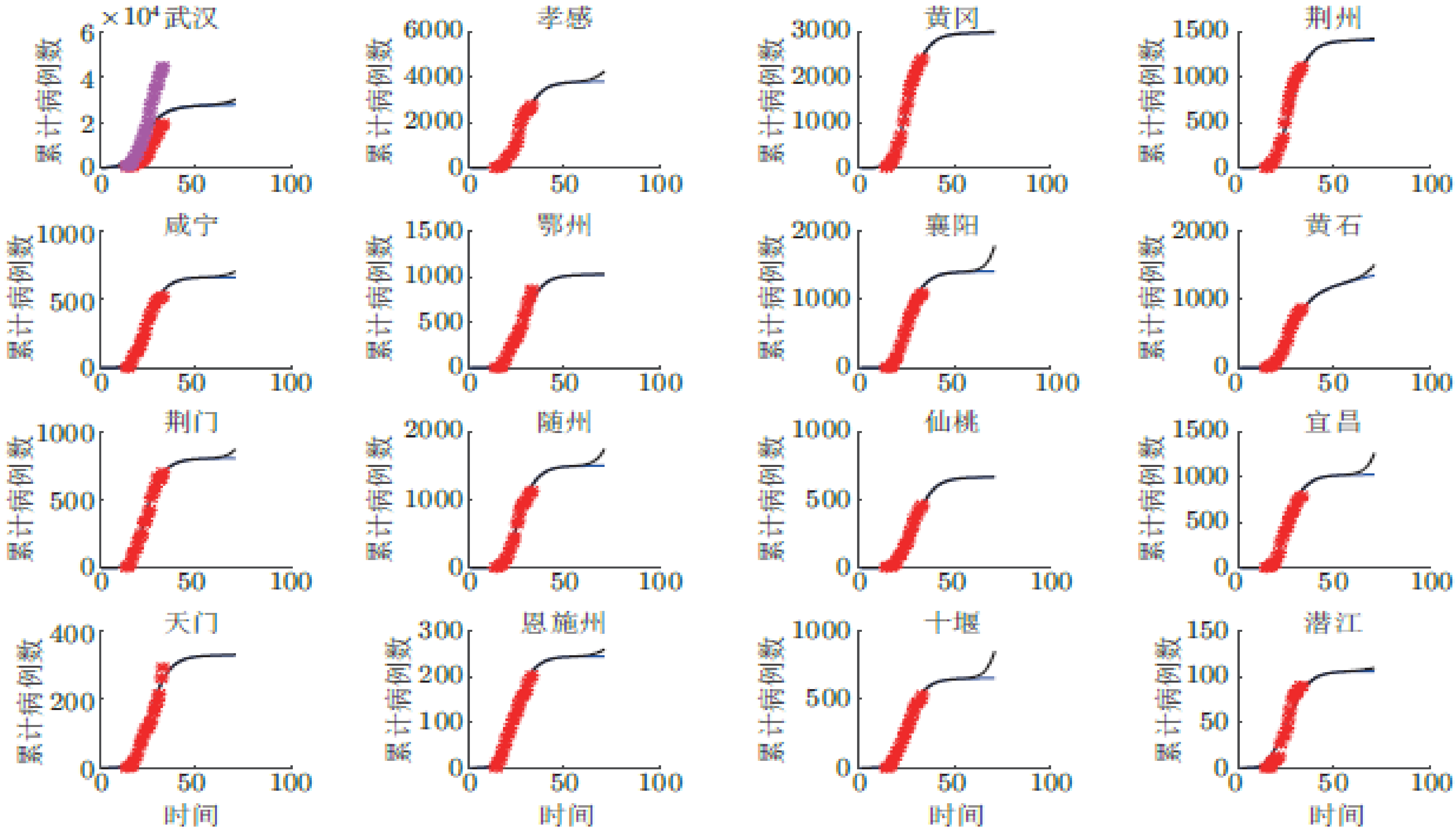


Effect of resumption timings on infection (Feb 24th 2020)



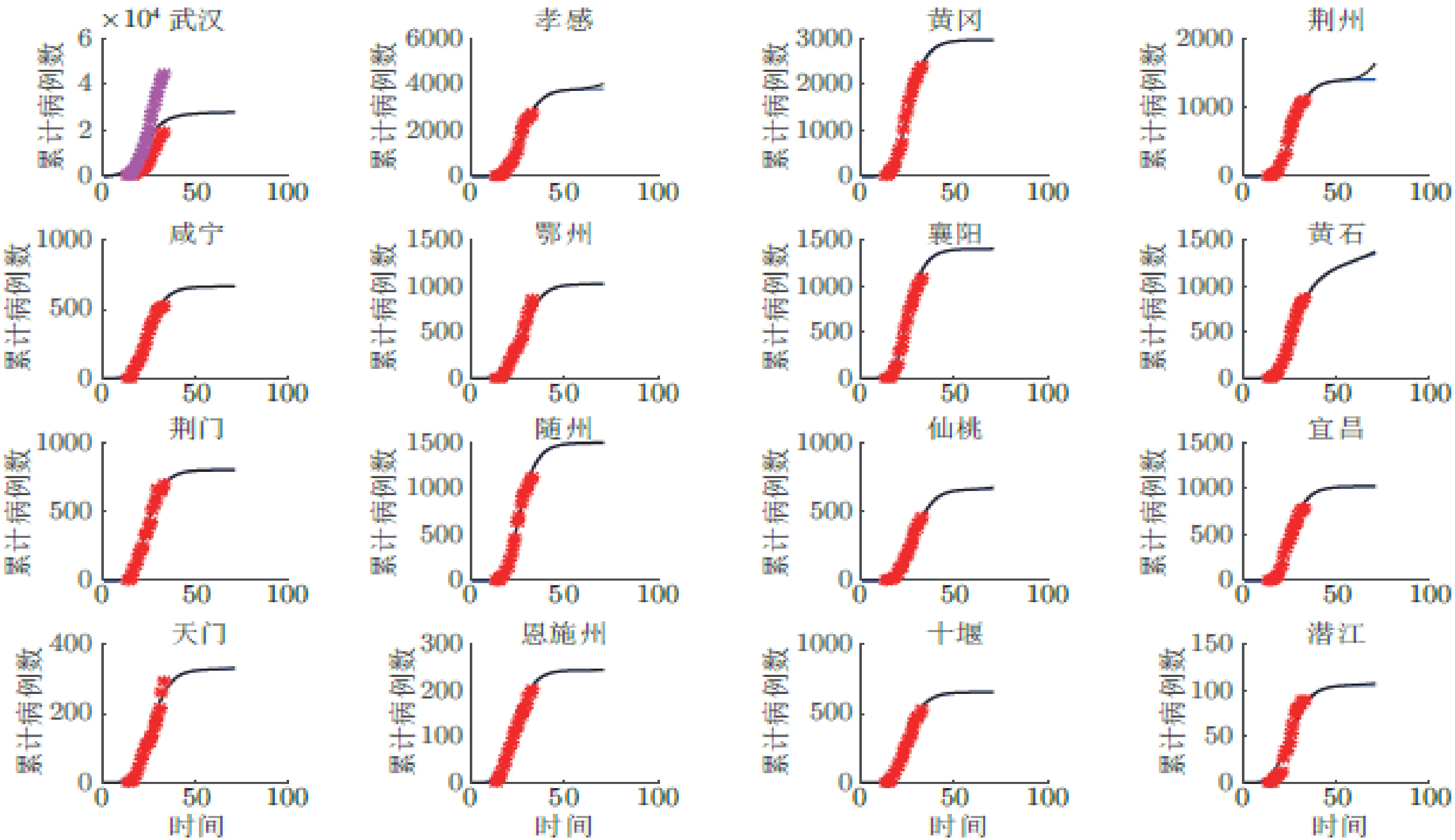
- ➢ Resumption of work will significantly increase the number of cases in most cities, except for Huanggang, Ezhou and Tianmen

Effect of resumption timings on infection (Mar 2nd 2020)



➢ Resumption of work will significantly increase the number of cases in most cities, except for Huanggang, Ezhou, Tianmen, Xiantao, Qianjiang.

Effect of resumption timings on infection (Mar 2nd + 2020)



In reality, on March 10th Hubei began to reopen,
since March 15th movements within the province have been allowed

Part II: Optimal reopening strategies

◆ **The obtained reopening strategies：**

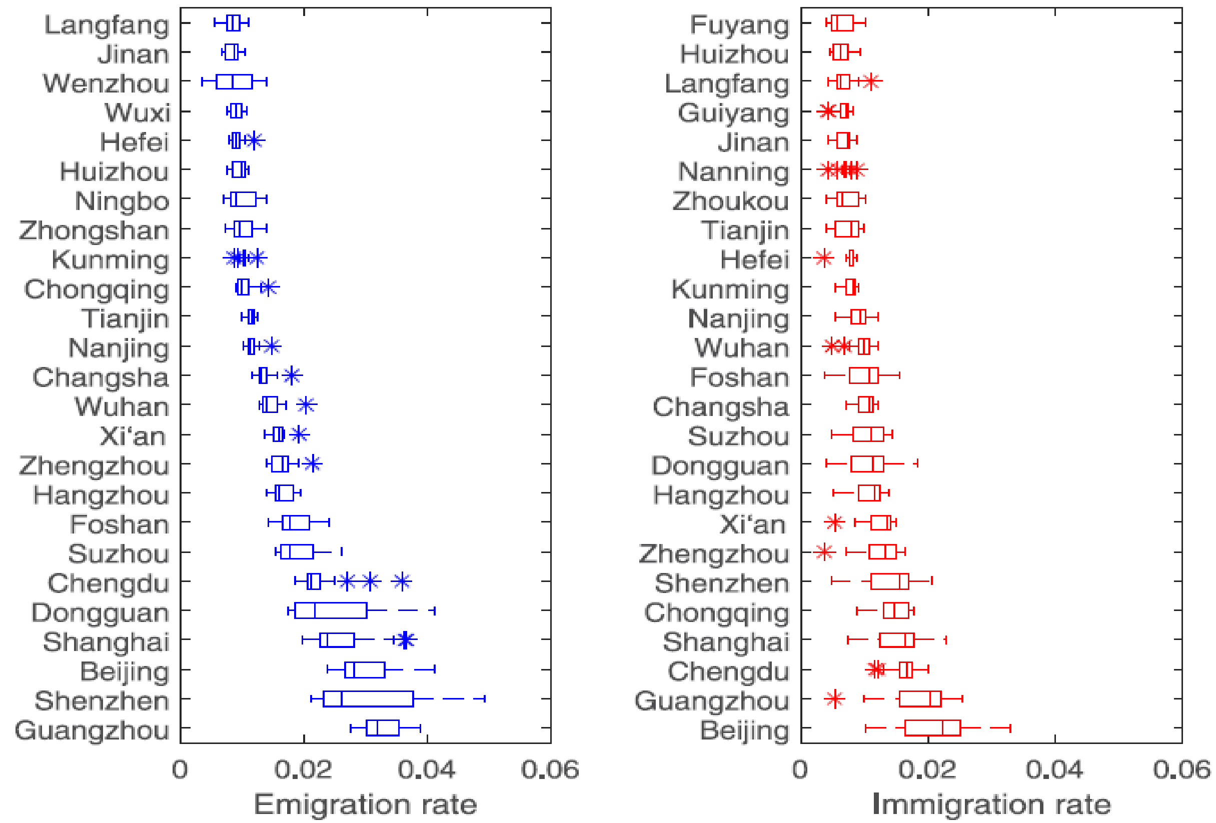
Given flux levels and reopening time, we simulate the proposed model to see whether there is possible outbreak or not

◆ **The optimal reopening strategy:**

To determine the optimal reopening timing, travel flux such that the possible outbreak can be avoided ?

Ref: Daipeng Chen, Yuyi Xue Yanni Xiao*, Determining travel fluxes in epidemic areas. PLoS Comput Biol 2021, 17(10): e1009473. https://doi.org/10.1371/journal.pcbi.1009473.

Related data to population mobility in China



- **Migration index** gives mobility strength of population in each city. Higher migration rate means more inflow (outflow) from a given city.
- There is no direction of individual movements. Other data are required to form a **mobility network**.

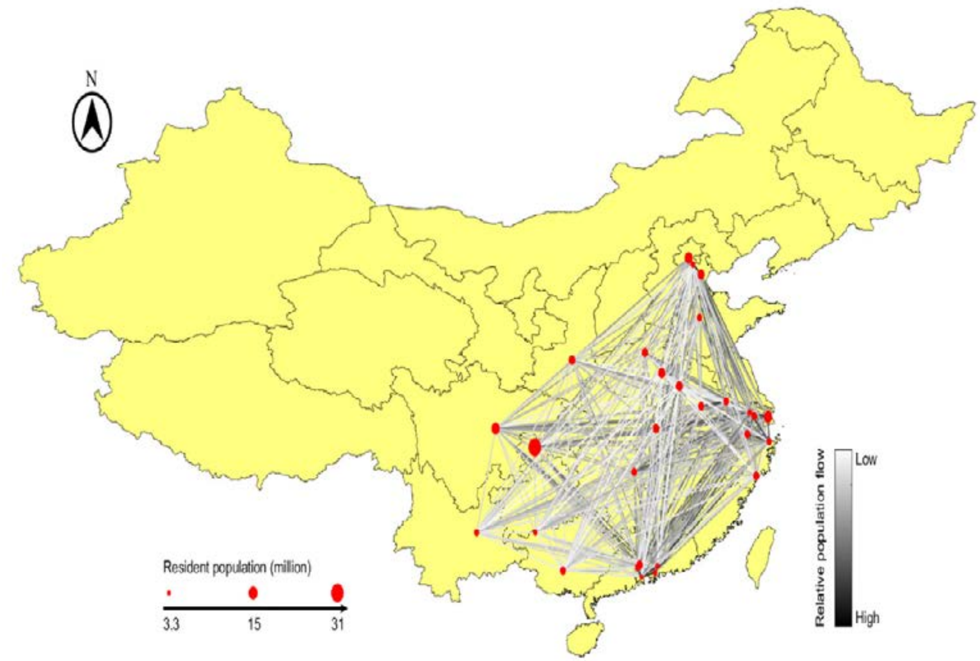
Estimation of mobility network

Mobility Network via Gravity model

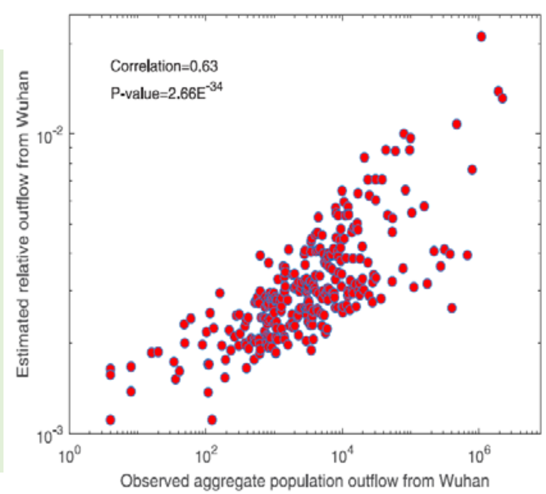
(Erlander and Stewart, 1990.)

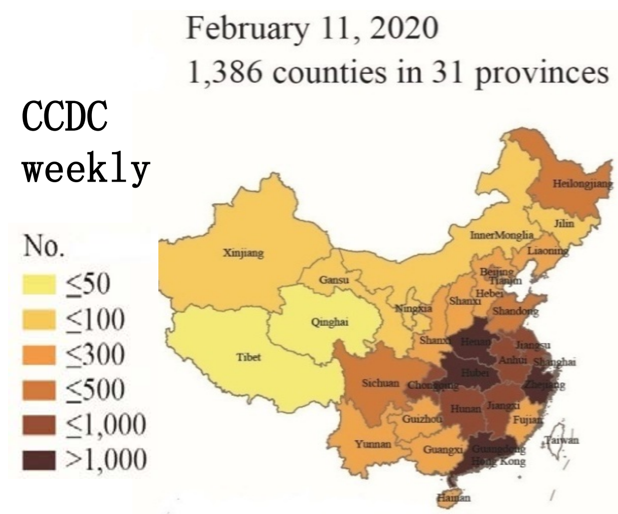
$$W_{ij} = G \frac{{M_i}^{\sigma_1} {M_j}^{\sigma_2}}{e^{r_{ij}/r}} \quad (1)$$

where M_i and M_j are the "mass" (e.g. population size, GDP) of city i and city j. r_{ij} is the georgical distance between cities i and j. Parameter values come from reference.



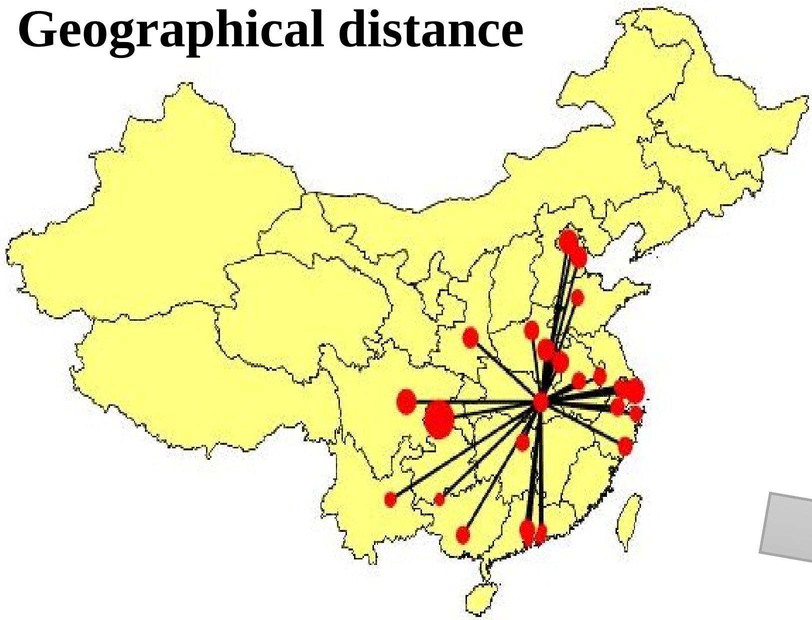
- Estimated relative population flow is consistent with observations.
- There were high population flows among the cities with the larger population sizes and the eastern cities with more developed economies in mainland China.





Transform the mobility network to a new graph

Geographical distance



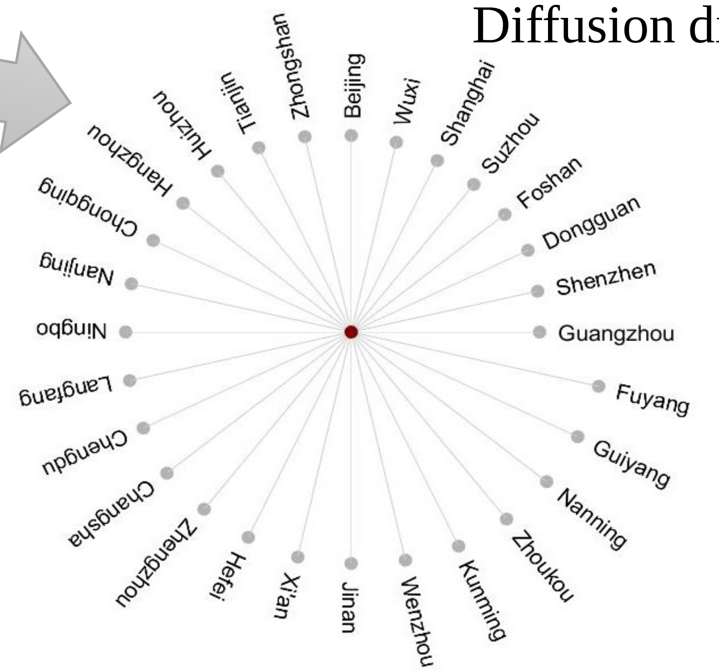
2. Diffusion distance

$$D_l(i,j) = \left(\sum_k \left(P_{ik}^{(l)} - P_{jk}^{(l)}\right)^2\right)^{1/2} \quad (2)$$

where $P_{ik}^{(l)}$ is the element of matrix P^l.

Diffusion map

Diffusion distance



1. Derive a Markov chain

Connectivity: $A_{ij} = \frac{W_{ij}+W_{ji}}{2\sum_{i,j}(W_{ij}+W_{ji})}$ and $A_{ii} = 1$.

Transition probability matrix: $P_{ij} = \frac{A_{ij}}{\sum_j A_{ij}}$.

Remark: We can map the *geographical space* to a *diffusion space* using a general kernel $A(x,y)$.

Modeling the spatial spread of pathogen

Meta-population model
(geographic space)

$$\dot{I}_i = -\sum_{j=1}^{n} L_{ij} I_j + \frac{\beta C_i S_i I_i}{N_i} - \Gamma_i I_i$$

$$i = 1,2,\ldots,n.$$

Reaction-diffusion model
(diffusion space)

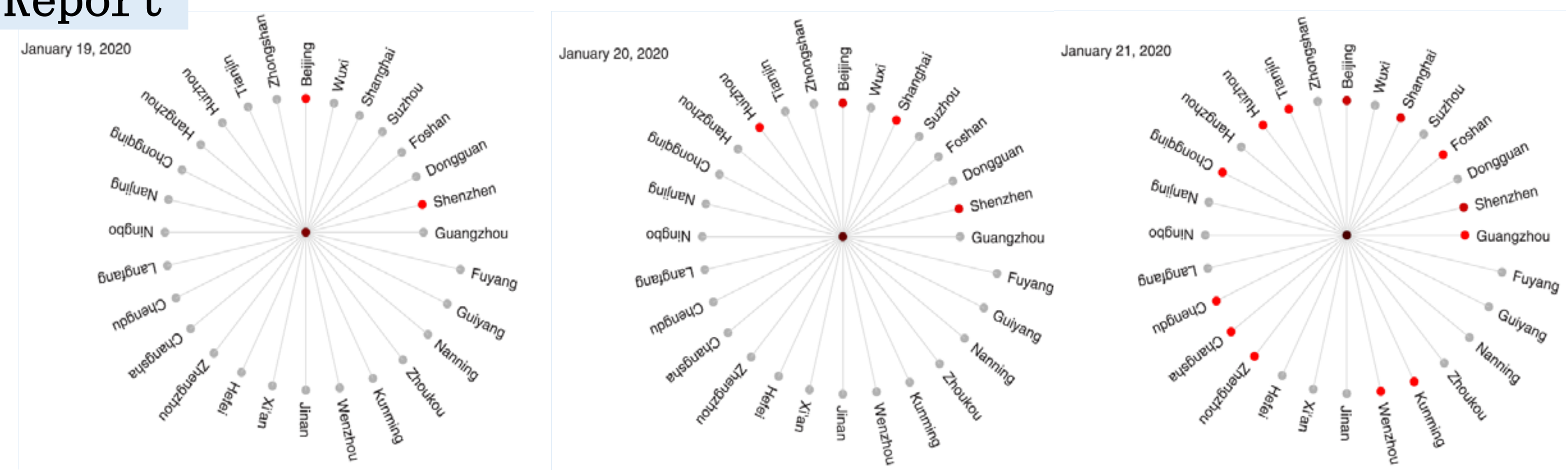
$$\frac{\partial p(t,x)}{\partial t} = \gamma \Delta p(t,x) + R(t,x)p(t,x)$$

$$R(t,x) = \beta C(t,x)\frac{s(t,x)}{n(t,x)} - \Gamma(t,x)$$

Onset

Source: CCDC weekly

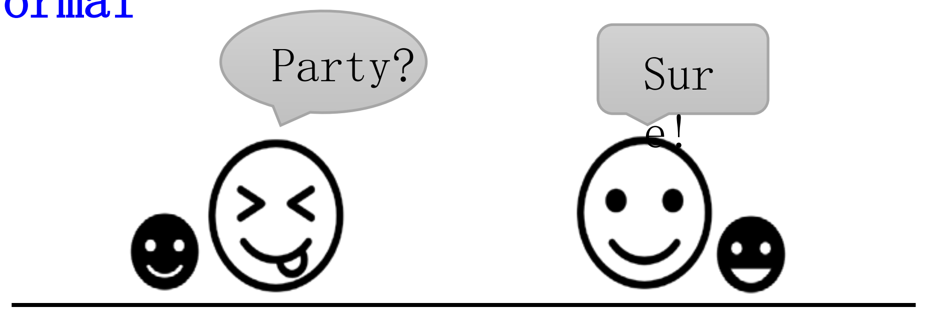
Report



The shorter the diffusion distance to Wuhan, the earlier the confirmed cases appear

Modeling the lockdown strategy

Normal



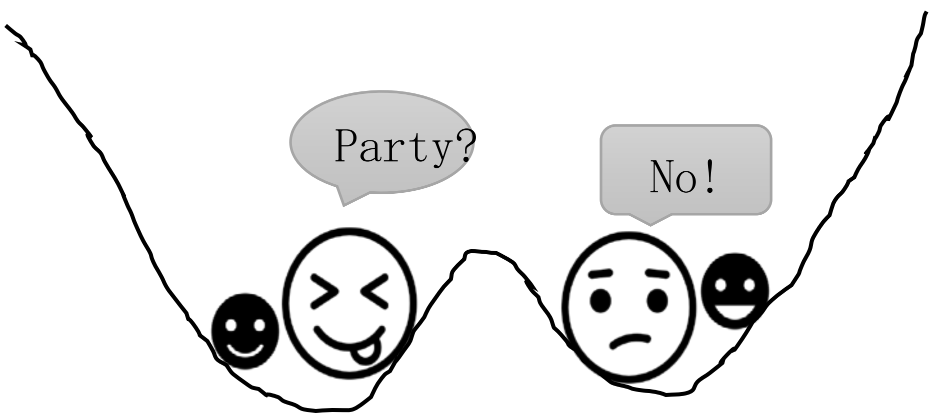
Poteintial U with $\nabla U = 0.$

Reaction diffusion system

$$\frac{\partial p(t,x)}{\partial t} = \gamma \Delta p(t,x) + R(t,x)p(t,x)$$

$$\frac{\partial p}{\partial t} = \gamma \Delta p + \nabla.(p \nabla U) + Rp$$

Lockdown to counteract diffusion



Potential $U = -\gamma \ln(p).$

ODE system

$$\frac{\partial p(t,x)}{\partial t} = R(t,x)p(t,x)$$

Since

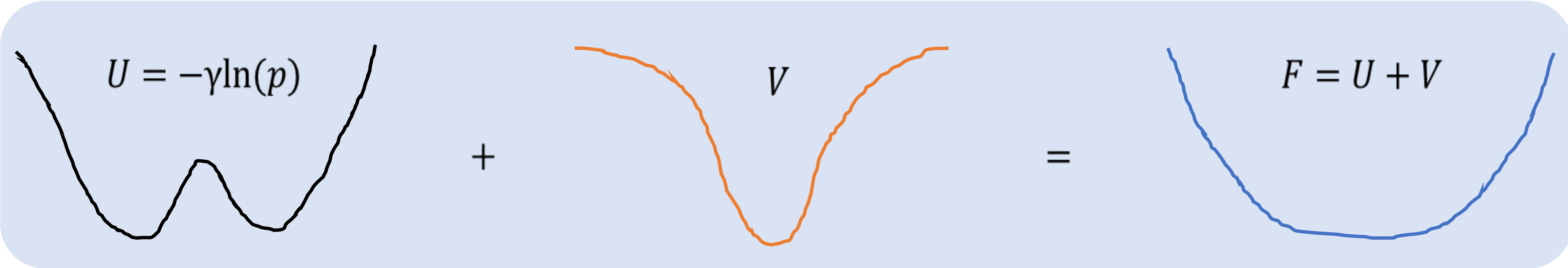
$$\gamma \Delta p(t,x) + \nabla.(p(t,x) \nabla U) = 0\,.$$

The mobility of infectious individuals is restricted

Modeling the lockdown exit strategy

Basic idea

Aim: Find a new potential V to reshape the function U such that the individuals can move following the gradient of the proposed potential function $F = U + V$.



Reaction diffusion-drift system

$$\frac{\partial p}{\partial t} = \gamma \Delta p + \nabla.(p \nabla F) + Rp = \nabla.(p \nabla V) + Rp \quad (3)$$

Note that, $V = 0$ ($\nabla V = 0$) means completed lockdown, and $V = \gamma \ln(p)$ means completed exiting lockdown.

Lockdown exit strategy (task 1 – when and where)

A good lockdown exit strategy should not cause a second outbreak of epidemics

$$\frac{\partial p(t,x)}{\partial t} = \nabla.\left(p(t,x)\nabla V(t_0,x)\right) + R(t,x)p(t,x) \leq 0, \qquad (4).$$

Where $t_0 \leq t < t_1$, t_0 is the initial time of travel flux $-\nabla V(t_0,x)$, and t_1 is the end time of it.

Integrating the inequality (4) on $\Omega = \{\Omega_1, \Omega_2, \ldots, \Omega_m\}$, $R(t,x)$ is homogeneous on Ω_i, we have

$$\sum_{i=1}^{m} R(t,\Omega_i,\epsilon)I(t,\Omega_i) \leq 0 \qquad (5).$$

Since the first term is the sum of inflow and out flow in Ω. Where, $R(t,\Omega_i,\epsilon) = (1-\epsilon)R(t) + \epsilon R(0)$.

Inequality (5) is a **necessary condition** for lifting the strict lockdown. The travel flux $-\nabla V(t_0,x)$ would exist if this condition was satisfied (our paper)!

Estimation of net growth rate

With some assumptions, from

$$\frac{\partial p(t,x)}{\partial t} = \gamma \Delta p(t,x) + R(t,x)p(t,x)$$

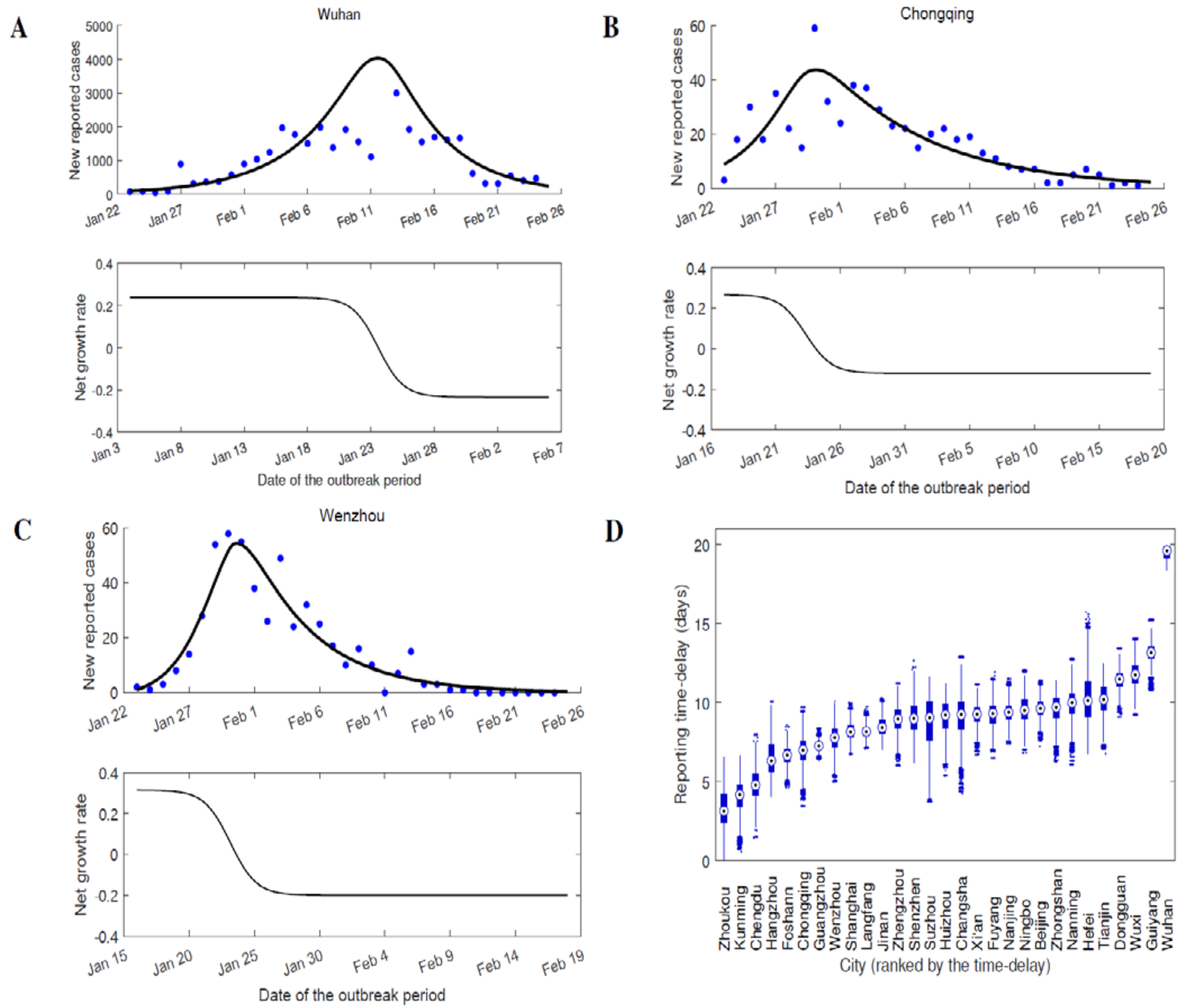
We have, **for initial outbreak city Ω_0,**

$$\frac{dI(t,\Omega_0)}{\partial t} = \gamma_0 I(t,\Omega_0) + R(t,\Omega_0)I(t,\Omega_0)$$

where $\gamma_0 = -\gamma|\partial\Omega_0|/|\partial\Omega_0|$ is the total outflow rate from the initial outbreak city.

For other cities,

$$\frac{dI(t,\Omega_i)}{\partial t} = \gamma_i I(t,\Omega_0) + R(t,\Omega_i)I(t,\Omega_i).$$



Lockdown exit strategy （when & where?）

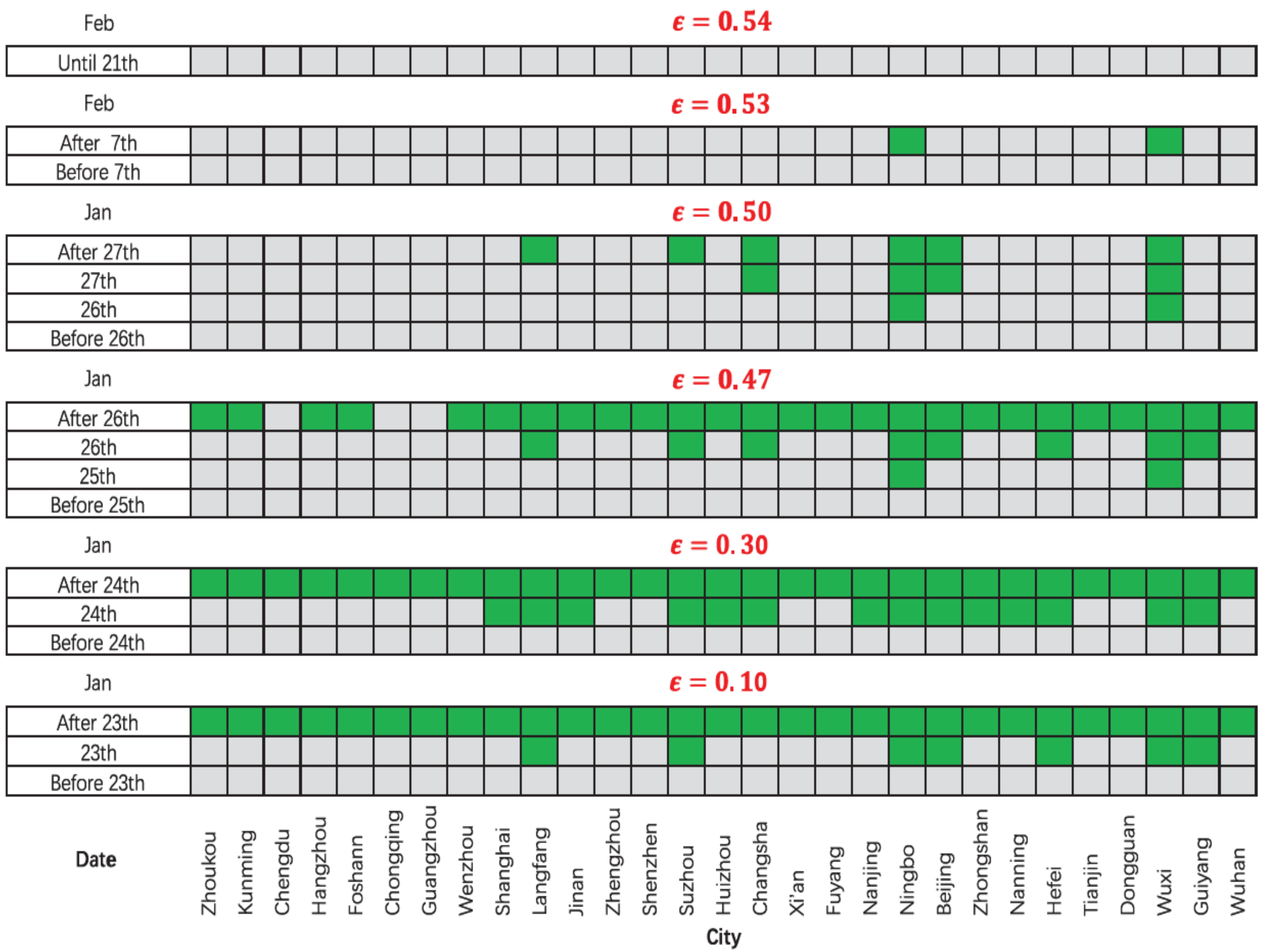
Zero-one programing

$$\max H_1 = \sum_{i=1}^{m} \xi_i , \qquad (5)$$

s.t. $\sum_{i=1}^{m} R(t,\Omega_i,\epsilon) I(t,\Omega_i)\xi_i \leq 0,$

$\xi_i \in \{0,1\}.$

Where $\xi_i = 1$ means subregion Ω_i is selected. We maximize the objective function to get more subregions where the strict travel restrictions can be lifted.



Lockdown exit strategy (task 2 – how?)

No second outbreak

$$\frac{\partial p(t,x)}{\partial t} = \nabla.(p(t,x)\nabla V(t_0,x)) + R(t,x)p(t,x) \leq 0, \qquad (4).$$

Graph Laplacian converges to Kolmogorov operator (Coifman and Lafon, 2005,2006)

$$L_{\delta,m} = 4\delta\left(Q_{\delta,m} - E_m\right) \xrightarrow{m \to \infty} \mathcal{L} = \nabla(\ln(p)).\nabla + \Delta$$

With

$$K_\delta\left(\Omega_i,\Omega_j\right) = \frac{1}{(\pi/\delta)^{k/2}} e^{\delta D_l^2(\Omega_i,\Omega_j)},$$

$$K_{\delta,m}\left(\Omega_i,\Omega_j\right) = \frac{K_\delta\left(\Omega_i,\Omega_j\right)}{\sqrt{\left(\sum_{i=1}^m K_\delta\left(\Omega_i,\Omega_j\right)\right)\left(\sum_{j=1}^m K_\delta\left(\Omega_i,\Omega_j\right)\right)}},$$

$$Q_{\delta,m}\left(\Omega_i,\Omega_j\right) = \frac{K_{\delta,m}\left(\Omega_i,\Omega_j\right)}{\sum_{j=1}^m K_{\delta,m}\left(\Omega_i,\Omega_j\right)}.$$

Note that the model (3) is

$$\frac{\partial p}{\partial t} = p\mathcal{L}V + Rp.$$

Therefore, inequality (4) implies that

$$\left(L_{\delta,m}V^{(m)} + R^{(m)}\right)p^{(m)} \leq 0^{(m)}$$

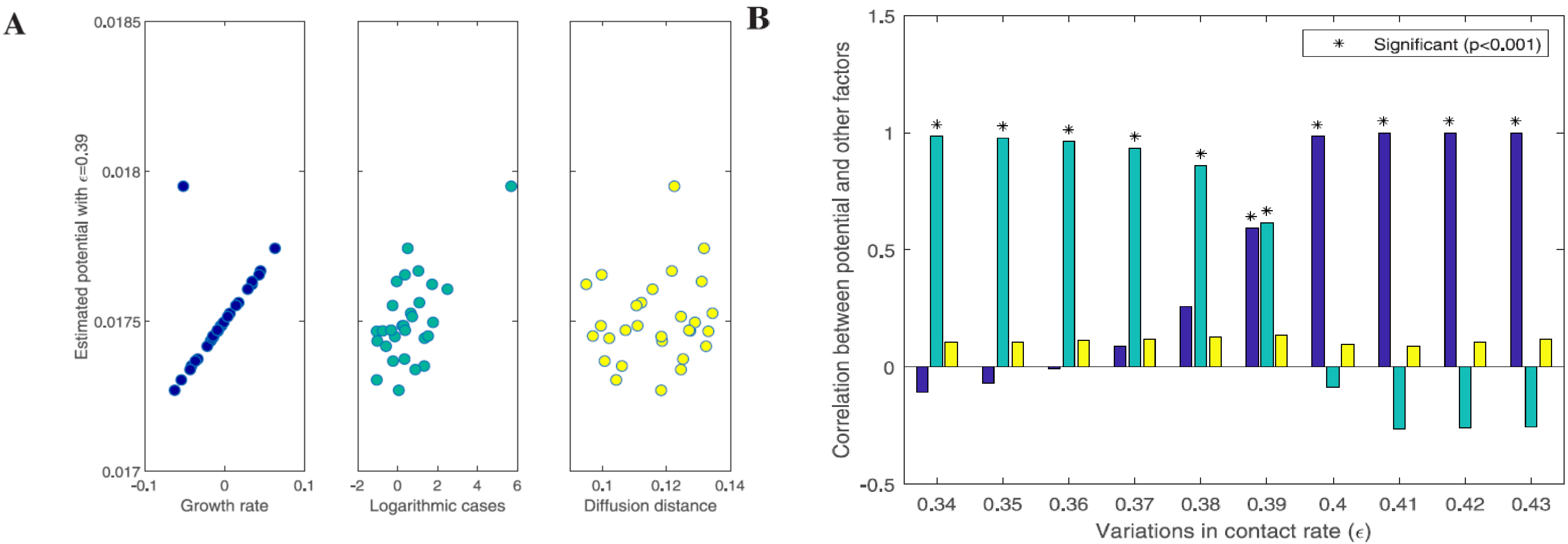
Optimization

$$\min \quad H_2 = \left\|V^{(m)} - \gamma \ln\left(I^{(m)}\right)\right\|^2,$$

$$\text{s.t.} \quad L_{\delta,m}V^{(m)} + R^{(m)} \leq 0^{(m)}.$$

Approximation theory of diffusion maps

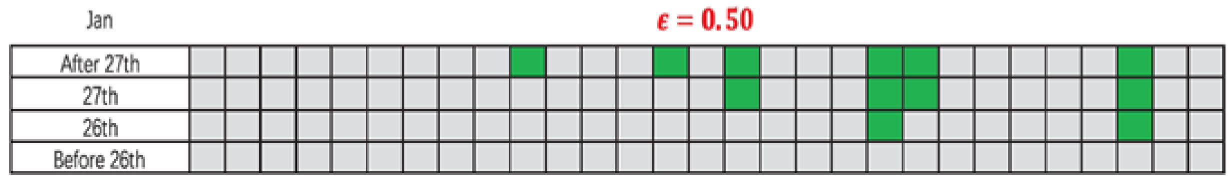
Lockdown exit strategy (how ?)



➢ The cities with larger growth rates and more COVID-19 cases tend to have higher potential, but the estimated potential does not show a clear correlation with diffusion distance;

➢ The estimated potential is significantly correlated with the number of COVID-19 cases when the contact rate is relatively low and is significantly correlated with the growth rate when the contact rate is high .

Lockdown exit strategy (how)



Net flow matrix

$$J_{ij} = \max\left\{\frac{V(t_0,\Omega_j) - V(t_0,\Omega_i)}{D_l(\Omega_i,\Omega_j)}, 0\right\}.$$

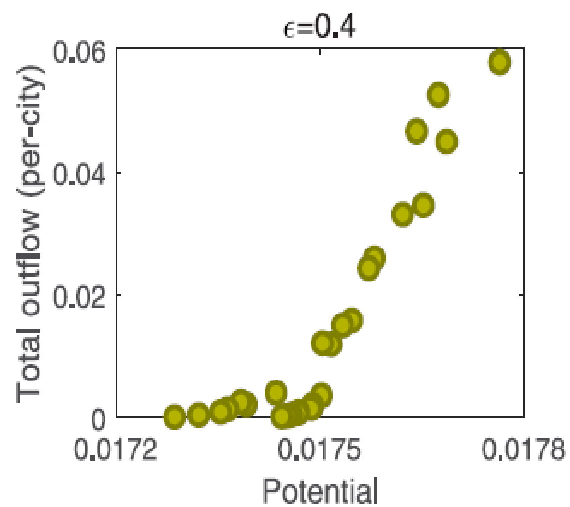
The net population outflow from subregion Ω_j to another Ω_i.

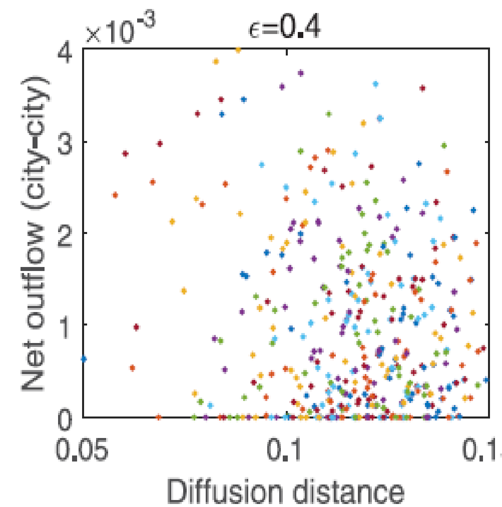
C

Net flow matrix (ϵ=0.5)

	Langfang	Suzhou	Beijing	Changsha	Wuxi	Ningbo
Langfang	0	0	0	0	0	0
Suzhou	0.0008637	0	0	0	0	0
Beijing	0.001385	0.0003912	0	0	0	0
Changsha	0.001023	0.0003554	3.618e-05	0	0	0
Wuxi	0.001256	0.0007197	0.0001107	5.476e-05	0	0
Ningbo	0.001559	0.0009713	0.0005838	0.000469	0.0004979	0

- A city with a higher potential also has more outflows;
- The potential does not show a significant correlation with the diffusion distance, it seems that the outflow population from one city is more likely to reach the closer city





Lockdown exit strategy (how)

Relative flow matrix

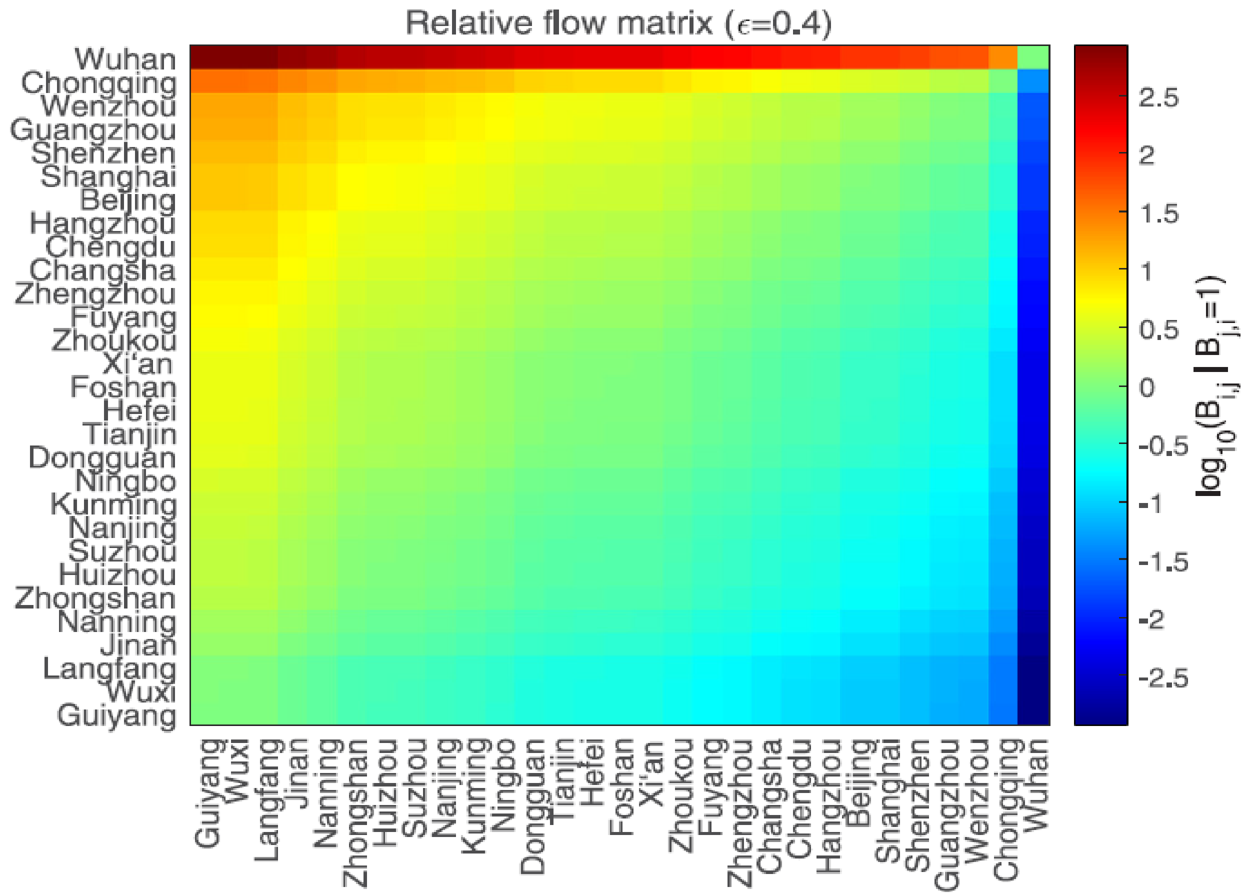
$$B_{ij} = (B_{ji} - J_{ji})\frac{I(t_0,\Omega_i)}{I(t_0,\Omega_j)} + (1+\zeta)J_{ij}.$$

Where ζ is a perturbation to the estimated flow matrix.

let the travel flow $B_{j,i} = 1$,

Note: 每个格子(i, j)中的数字都表示在i到j的移动速率为1的条件下，j到i的移动速率应该是多少

D



- The cells far away from the diagonal are associated with larger absolute values;
- The travel flow from a city with a severe epidemic to a city with a mild epidemic should be smaller than the travel flow in the opposite direction

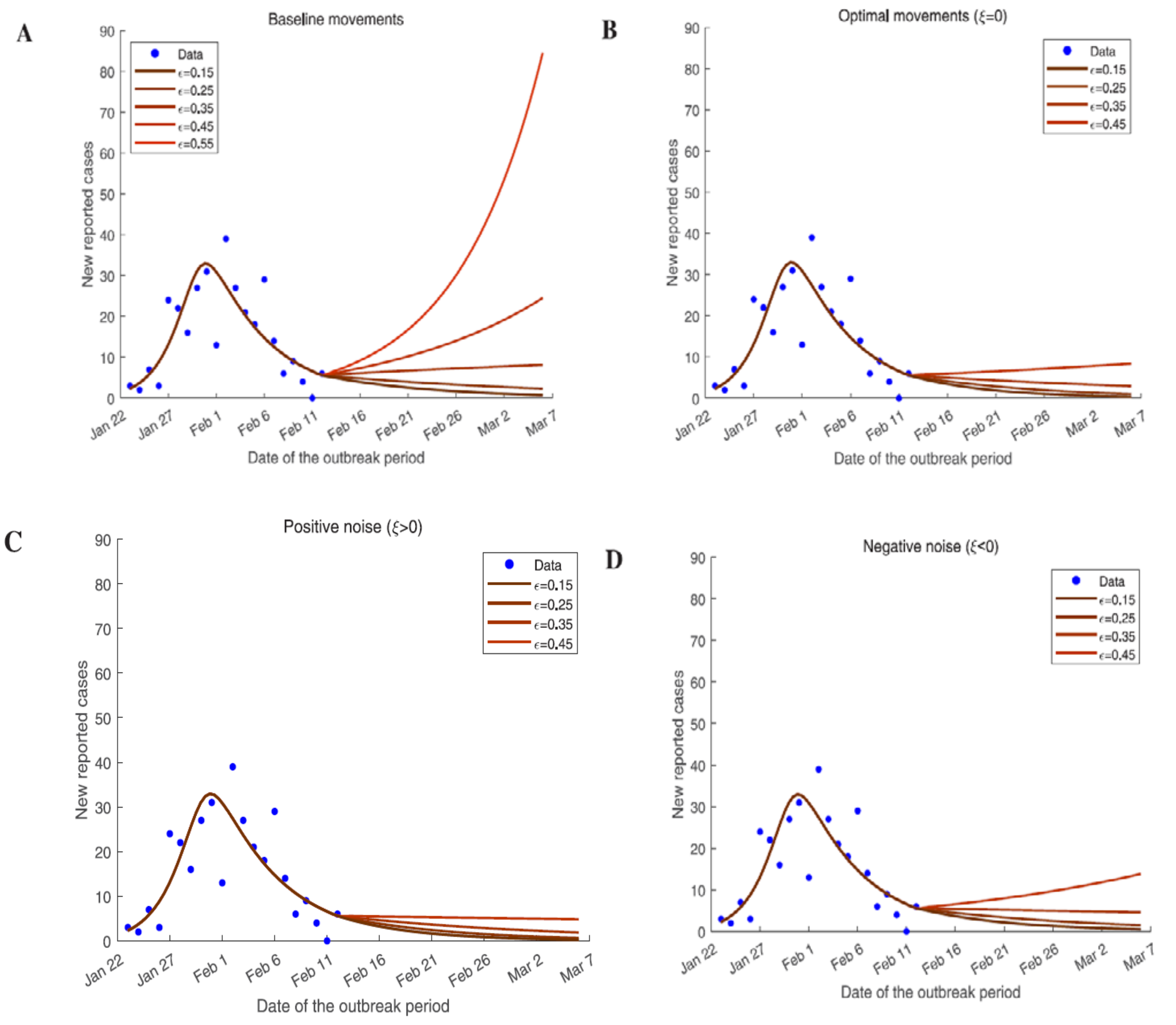
Testable simulation

Meta-population model

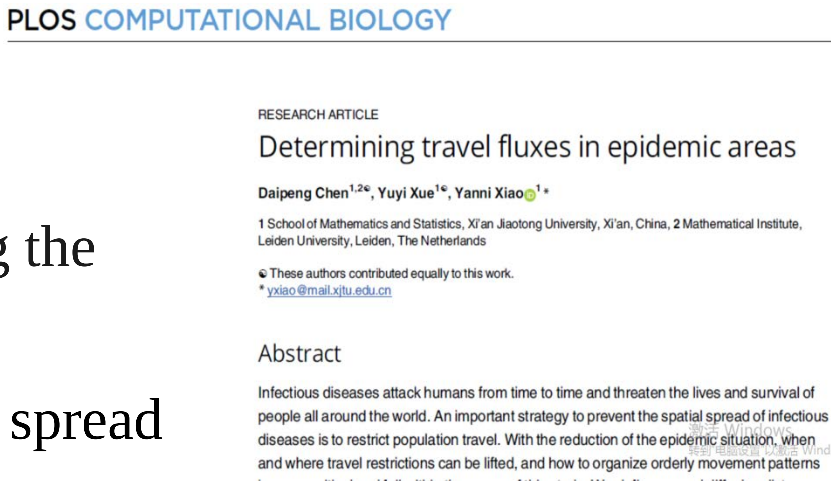
$$\frac{dI(t,\Omega_i)}{\partial t} = \sum_{j=1}^{m} (B_{ij} I(t,\Omega_i) - B_{ji} I(t,\Omega_j)) + R(t,\Omega_i) I(t,\Omega_i).$$

Where B is the estimated relative population flow matrix.

- The population should move from the cities with higher potential to low-potential cities



Conclusions


PLOS COMPUTATIONAL BIOLOGY

RESEARCH ARTICLE

Determining travel fluxes in epidemic areas

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Abstract

Infectious diseases attack humans from time to time and threaten the lives and survival of people all around the world. An important strategy to prevent the spatial spread of infectious diseases is to restrict population travel. With the reduction of the epidemic situation, when and where travel restrictions can be lifted, and how to organize orderly movement patterns

- Population mobility network was reconstructed using the gravity model.
- Define a diffusion distance which reshape the spatial spread of infectious pathogen to a weave-like pattern.
- In the perspective of diffusion distance, the spread of pathogen was modeled by a reaction diffusion system.
- Lockdown was represented by a potential function. A lockdown exit strategy was proposed which answered where, when and how the travel flux can be organized.
- Testable simulation verified the proposed lockdown exit strategy.