A Linear Nonlocal Model for Outbreak of COVID-19 and Parameter Identification

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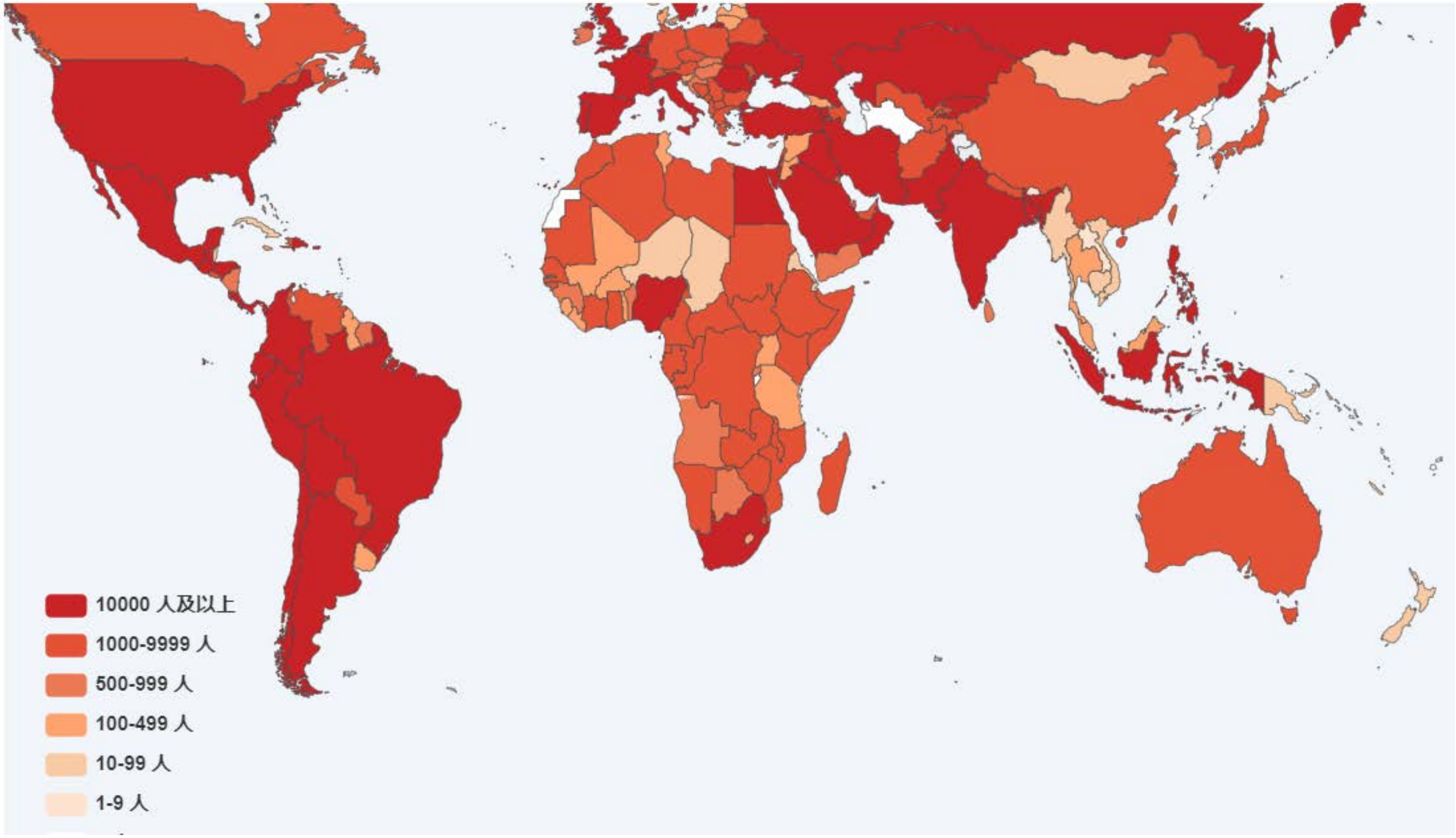
Contents

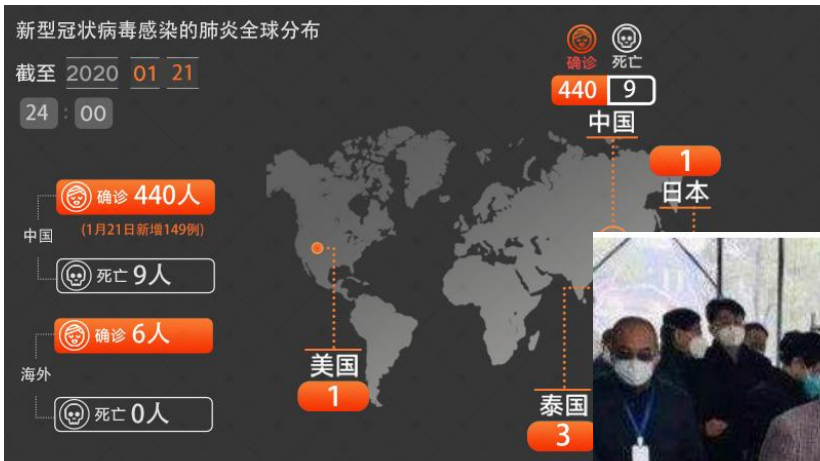
Novel Corona-virus (COVID-19)

- Major event in the world

Confirmed Cases	Death
16059531	641840



Media Coverage



今日：确诊830例，死亡25例，治愈34例

昨日：确诊571例，死亡17例

截至2020.01.23 24:00

Mathematical Models for COVID19

- Why should we establish the "reasonable" mathematical models for COVID?
  - Some information about COVID-19 can not be observed directly
  - We want to predict the trends of the virus epidemic. Especially when the spread of the virus ends

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- **We are trying to describe the problems, not from the medical point of view, but from the general transmission mechanism**

Questions

- Is it possible?
- Are there some existing models?
- What kind models are “reasonable”?
- What is the characteristic of novel corona-virus pneumonia?

Existing Models and Methods

- SI、Logistic models (Nonlinear Quadratic models)
  - It is mainly used in epidemiology. The common situation is to explore the risk factors of a disease and predict the probability of a disease according to the risk factors

$$\frac{dI}{dt} = rI\left(1 - \frac{I}{K}\right), \qquad r = \beta K.$$

- SIR、SIRS、SEIR Models
  - Ordinary Differential Systems

$$\begin{cases} \dfrac{dS}{dt} = -\beta IS, & \dfrac{dE}{dt} = \beta IS - (\alpha + \gamma_1)E, \\ \dfrac{dI}{dt} = \alpha E - \gamma_2 I, & \dfrac{dR}{dt} = \gamma_1 E + \gamma_2 I. \end{cases}$$

Review Analysis for SAR

- Prof. Li Daqian, Prof. Ding Guanghong and their team did the review analysis for SARS, which happened at the end of 2002:
  - Based on SIJR model, which is the simplified model of SEIJR.

论 文　　　　第 49 卷 第 21 期　2004 年 11 月　科学通报

SARS 爆发预测和预警的数学模型研究

刘 畅 丁光宏* 龚剑秋 王 凌 程 珂 张 迪

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The Characteristic of COVID-19

- Latent Period
  - The novel corona-virus can spread in latent period
- The Delay of Data
  - The public data will be announced with some delays due to diagnosis

Some Notations

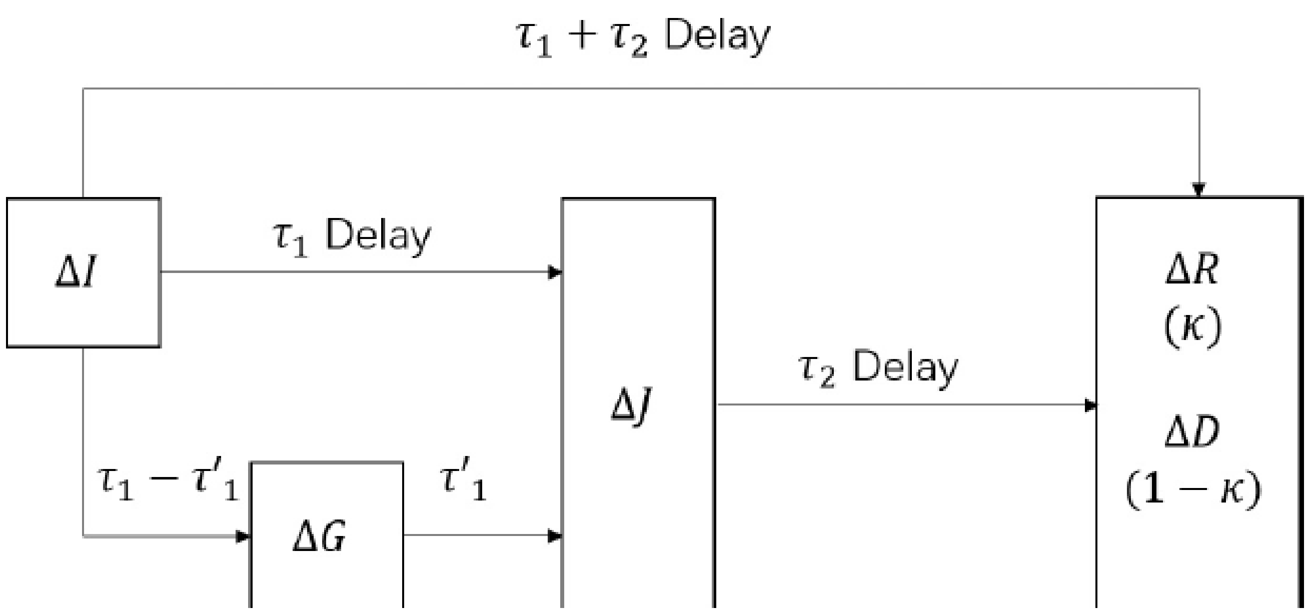
- Notation as follows

Public Data

- $I(t)$: cumulative infected people at time t;
- $J(t)$: cumulative confirmed people at time t;
- $G(t)$: currently isolated people who are infected but still in latent period at time t;
- $R(t)$: cumulative cured people at time t.

Dynamical System with Delays

- The demonstration of the dynamic system



Frame Diagram

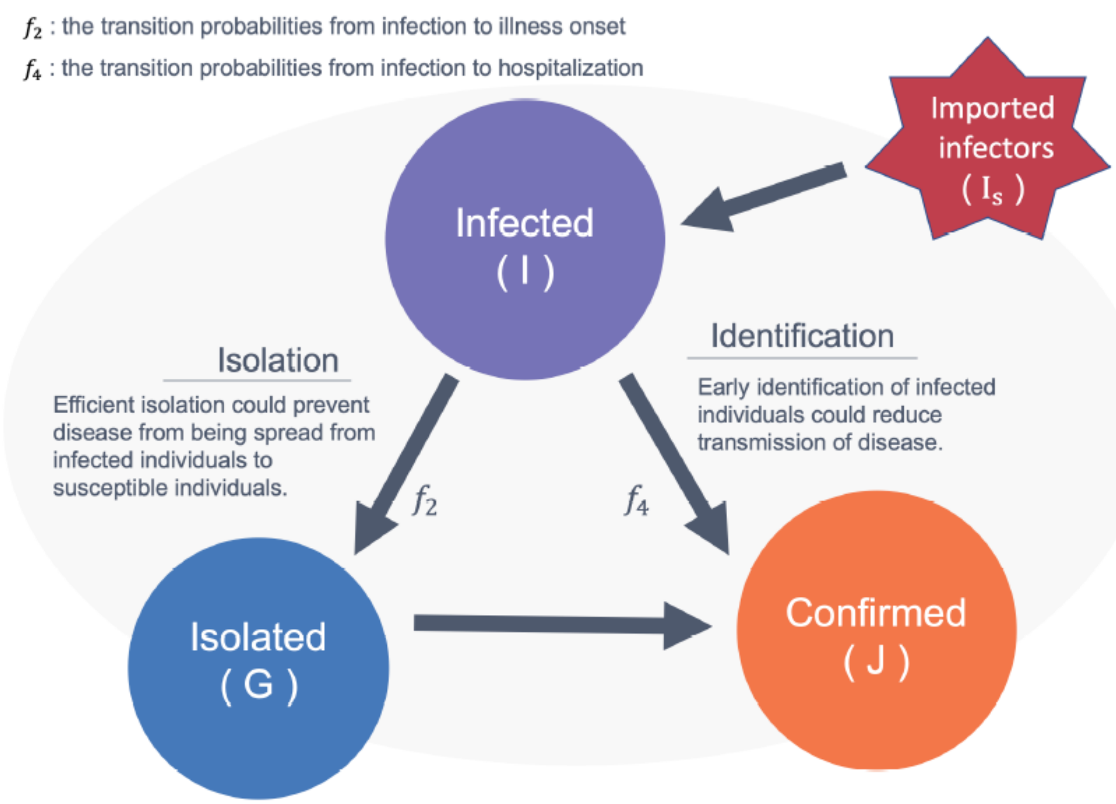


Figure 1: Sketch map of the model.

The Source of Infection

- In the modeling, the most important thing is to consider the source of infection

$$I_0(t) = I(t) - J(t) - G(t)$$

- We focus on the source of infection and establish the dynamical model

The infected cases I(t)

- The changes of the infected cases is proportional to the source of infection

$$I(t+\Delta t) - I(t) = \beta I_0(t)\Delta t$$

$$\Longrightarrow \quad \frac{dI}{dt} = \beta I_0(t)$$

- <u>β defined as spread rate</u>
  - *β, is defined* by the average amount of people becoming infected by this person per unit time

The diagnosed cases J(t)

- The changes of the diagnosed cases is proportional to the source of infected cases in the latent period

$$J(t+\Delta t) - J(t) = \left\{ \gamma \int_0^{\tau_1} h_1(t')\beta(I(t-t') - J(t-t') - G(t-t'))dt' \right\} \Delta t$$

$$\longrightarrow \quad \frac{dJ}{dt} = \gamma \int_0^{\tau_1} h_1(t')\beta(I(t-t') - J(t-t') - G(t-t'))dt'$$

- The coefficient γ is the morbidity
- *The kernel h_1 is a distribution*

The isolated cases G(t)

- The changes of the isolated cases depends on two factors:
  - The source of infection, where ℓ is the rate of isolation;
  - The infected cases, which have been isolated. The term with delay represents the effect

$$G(t+\Delta t)-G(t) = \left\{ l(I(t) - J(t) - G(t)) - l\int_0^{\tau_1'} h_2(t')(I(t-t') - J(t-t') - G(t-t'))dt' \right\} \Delta t$$

$$\Longrightarrow \quad \frac{dG}{dt} = l(I(t) - J(t) - G(t)) - l\int_0^{\tau_1'} h_2(t')(I(t-t') - J(t-t') - G(t-t'))dt'$$

The cured cases R(t)

- Once infected, it needs to go through the incubation period of τ_1 day and the treatment period of τ_2 days to end the treatment

$$R(t+\Delta t) - R(t) = \left\{ \kappa \int_0^{\tau_1+\tau_2} h_3(t')\beta(I(t-t') - J(t-t') - G(t-t'))dt' \right\} \Delta t$$

$$\longrightarrow \quad \frac{dR}{dt} = \kappa \int_0^{\tau_1+\tau_2} h_3(t')\beta(I(t-t') - J(t-t') - G(t-t'))dt'.$$

The kernel functions $h_i(t), \quad i = 1, 2, 3$

- The kernel functions are the probability distributions of delay days with the compact supports and satisfy:

$$\int_0^{\tau_1} h_1(t')dt' = 1$$

$$\int_0^{\tau_1+\tau_2} h_3(t')dt' = 1$$

$$\int_0^{\tau_1'} h_2(t')dt' < 1$$

We can take : δ function or uniform distribution or cut-off Gauss-like distribution..

$$h_i(t) = c_i e^{-d_i t^2}$$

TDD-NCP Model

- Time Delay Dynamic System

- $I(t)$: cumulative infected people at time t;
- $J(t)$: cumulative confirmed people at time t;
- $G(t)$: currently isolated people who are infected but still in latent period at time t;
- $R(t)$: cumulative cured people at time t.

$$\frac{dI}{dt} = \beta(I(t) - J(t) - G(t)),$$

$$\frac{dJ}{dt} = \gamma\beta \int_0^{\tau_1} h_1(t')(I(t-t') - J(t-t') - G(t-t'))dt',$$

$$\frac{dG}{dt} = l(I(t) - J(t) - G(t)) - l\int_0^{\tau_1'} h_2(t')(I(t-t') - J(t-t') - G(t-t'))dt'.$$

$$\frac{dR}{dt} = \kappa \int_0^{\tau_1+\tau_2} h_3(t')\beta(I(t-t') - J(t-t') - G(t-t'))dt'$$

TDD-NCP Model（version 1）

- First version

$$
\begin{aligned}
\frac{dI}{dt} &= \beta(I(t) - J(t) - G(t)),\\
\frac{dJ}{dt} &= \gamma \int_0^t h_1(t-\tau_1, t')\beta(I(t') - J(t') - G(t'))dt',\\
\frac{dG}{dt} &= \ell(I(t) - J(t) - G(t)) - \int_0^t h_2(t-\tau_1', t')G(t')dt',\\
\frac{dR}{dt} &= \kappa \int_0^t h_3(t-\tau_1-\tau_2, t')\beta(I(t') - J(t') - G(t'))dt'.
\end{aligned}
$$

Features of time delay model

- <u>Linear equations</u>
  - With integral terms (nonlocal terms)

- <u>The meaning of parameters are clear</u>

Shortage of the linear model

- If the spread of the virus last for a little bit long time, the prediction results are not so reasonable.

- We are considering two improvements：
  - Locally, use the linear model and try to do the prediction in a short time.
  - Add some nonlinear terms in our models.

Some Remarks on Data

- It should be noted that :
  - In the public data by the government, only the information about the diagnosed cases and the cured cases are provided.
  - $I(t)$ and $G(t)$ usually can not be obtained directly.

Sparsity assumptions

- Due to that the public data can only provide limited information, we have to assume that:
  - The parameters are constants or piecewise constants.

Forward Problems

- Given $\{\beta, l, \gamma, \kappa . \tau_1, \tau_1', \tau_2\}$
- Find the solution of

$$
\begin{aligned}
\frac{dI}{dt} &= \beta(I(t) - J(t) - G(t)), \\
\frac{dJ}{dt} &= \gamma\beta \int_0^{\tau_1} h_1(t')(I(t-t') - J(t-t') - G(t-t'))dt', \\
\frac{dG}{dt} &= l(I(t) - J(t) - G(t)) - l\int_0^{\tau_1'} h_2(t')(I(t-t') - J(t-t') - G(t-t'))dt'. \\
\frac{dR}{dt} &= \kappa \int_0^{\tau_1+\tau_2} h_3(t')\beta(I(t-t') - J(t-t') - G(t-t'))dt'
\end{aligned}
$$

$$
\begin{aligned}
I(t) &= I_0(t), \quad t \le 0 \\
J(t) &= J_0(t), \quad t \le 0 \\
G(t_0) &= G_0(t) \quad t \le 0 \\
R(t) &= R_0(t), \quad t \le 0.
\end{aligned}
$$

Theoretical Analysis

- We have the equation of source infection $I_0(t)$.

$$\frac{dI_0}{dt}(t) = \beta \left(I_0(t) - \int_0^{\tau_1} h_1(t') I_0(t-t') dt' \right) - l \left(I_0(t) - \int_0^{\tau_2} h_2(t') I_0(t-t') dt' \right)$$

$$I_0(t) = \tilde{g}(t), \qquad t \in (-\tau_1 - \tau_2, 0]$$

Dynamical Analysis for the equation of source of infection

- Linear time delay dynamical systems

$$\frac{dI_0}{dt}(t) = (\beta - l)I_0(t) + \int_0^{\tau_1+\tau_2} H(t')I_0(t-t')dt'$$

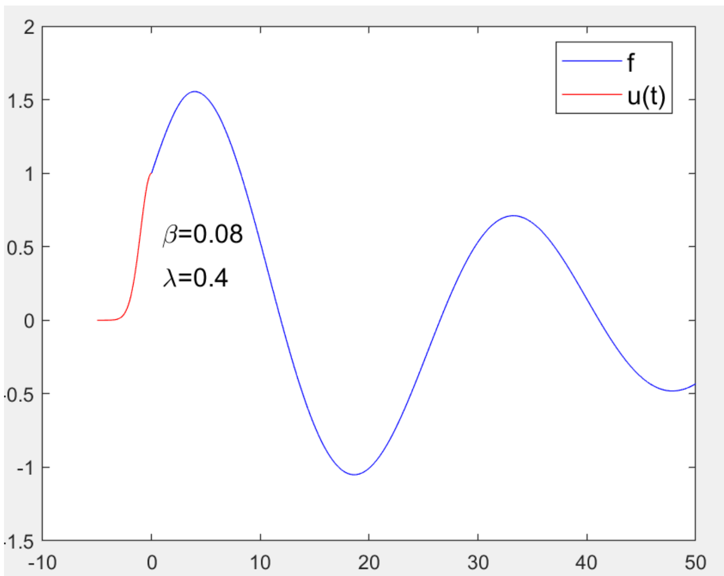
$$H(t) = h_1(t) - h_2(t)$$

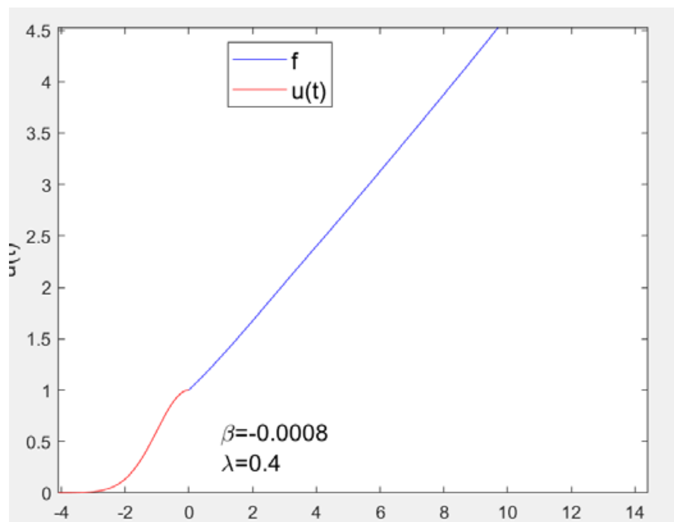
Simplified System

- Simplified system

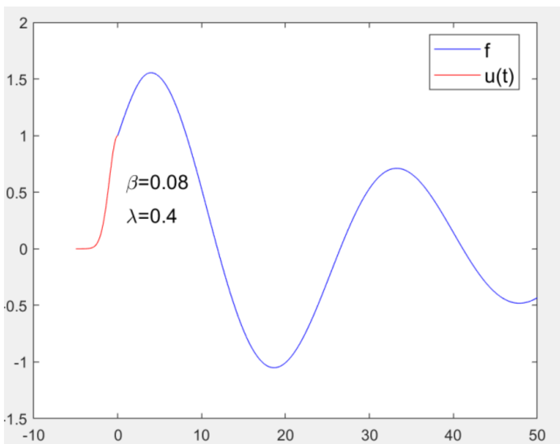
$$\frac{du}{dt} = -\beta u + \lambda \frac{1}{T} \int_{t-T}^{t} (u(t) - u(t'))dt'$$

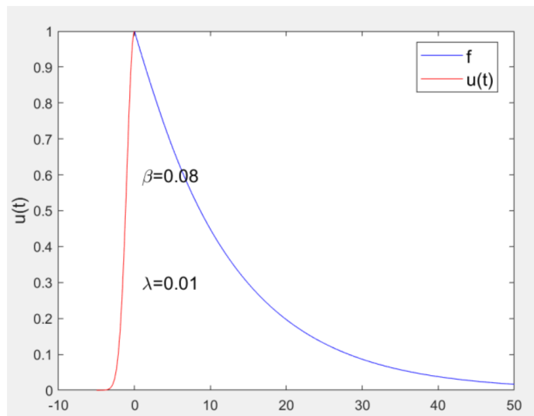
$$u(s) = f(s), \qquad x \in (-T, 0)$$

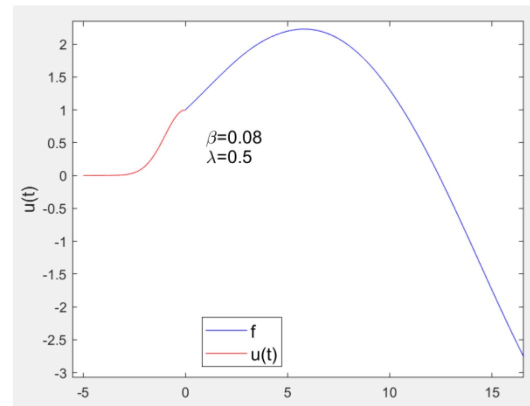




Changes with respect to λ







Conditions for the validity of the model

- The models make sense

$$\frac{dI}{dt} \geq 0,$$
$$\frac{dJ}{dt} \geq 0,$$
$$\frac{dR}{dt} \geq 0.$$

Conditions for validity of model

Conditions for Stopping

The first T, such that $I_0(T) = 0$ and $I_0(t) > 0$ for $t < T$

- The conditions for the validity of equation

- <u>T the stopping time of epidemic situation</u>

$$I_0(t) > 0, \qquad t \in (0, T)$$
$$I_0(T) = 0$$

Inverse Problems and Prediction

- From the public data, determine the parameters in the model
  - Reconstruct the spread rate β， isolated rate l
- By the parameters, which are reconstructed from the public data, we can do the numerical simulation and predict the development of the epidemic situation.
  - Especially, “stopping time T” of the epidemics.

Inversion Scheme

- By the cumulative confirmed cases $J_{obs.}$ and the cumulative cured cases $R_{obs.}$

reconstruct $\theta=(\beta, \ l)$:

$$\min_{\theta} \| J(\theta; t) - J_{Obs.} \|_2$$

$$\min_{\theta,\kappa} \| R(\theta, \kappa; t) - R_{Obs.} \|_2 .$$

Questions

- Whether the mathematical model can well describe the spread of the novel corona-virus?
- Well-posedness of the model?
- Uniqueness of the reconstruction of the parameters ?
- The prediction results are “trustable” ?

Linear integral differential equations

- Existence and Uniqueness（Nonlocal）

$$
\begin{aligned}
\frac{dI}{dt} &= \beta(I(t) - J(t) - G(t)), \\
\frac{dJ}{dt} &= \gamma\beta \int_0^{\tau_1} h_1(t')(I(t-t') - J(t-t') - G(t-t'))dt', \\
\frac{dG}{dt} &= l(I(t) - J(t) - G(t)) - l\int_0^{\tau_1'} h_2(t')(I(t-t') - J(t-t') - G(t-t'))dt', \\
\frac{dR}{dt} &= \kappa \int_0^{\tau_1+\tau_2} h_3(t')\beta(I(t-t') - J(t-t') - G(t-t'))dt'
\end{aligned}
$$

$$I(t) = I_0(t), \quad J(t) = J_0(t), \quad G(t) = G_0(t), \quad R(t) = R_0(t), \qquad t \leq 0.$$

Formulation of the inverse problems

- For TDD-NCP model

$$
\begin{aligned}
\frac{dI}{dt} &= \beta(I(t) - J(t) - G(t)),\\
\frac{dJ}{dt} &= \gamma\beta \int_0^{\tau_1} h_1(t')(I(t-t') - J(t-t') - G(t-t'))dt',\\
\frac{dG}{dt} &= l(I(t) - J(t) - G(t)) - l\int_0^{\tau_1'} h_2(t')(I(t-t') - J(t-t') - G(t-t'))dt',\\
\frac{dR}{dt} &= \kappa \int_0^{\tau_1+\tau_2} h_3(t')\beta(I(t-t') - J(t-t') - G(t-t'))dt'
\end{aligned}
$$

$$
I(t) = I_0(t), \quad J(t) = J_0(t), \quad G(t) = G_0(t), \qquad t \le 0.
$$

- Given other data， we reconstruct **β,l from the measurements of J(t)**

Inverse Problems for the time delay systems

- Inverse coefficient problem (parameters β, l)
  - Uniqueness
  - Stability （with respect to the errors）
  - Algorithms

Based on β,l, Predict the development

- Solve

$$\frac{dI_0}{dt}(t) = (\beta - l)I_0(t) + \int_0^{\tau_1+\tau_2} H(t')I_0(t-t')dt'$$

$$H(t) = h_1(t) - h_2(t)$$

$$I_0(t) = g(t), \qquad t \in (-\tau_1 - \tau_2, 0]$$

- Get the first stopping time T， which satisfies：

$$I_0(t) > 0, \qquad t < T, \quad and \quad I_0(T) = 0$$

If such T does not exists， it means the epidemic will not stop until all people are infected.

Inverse Problems for time delay dynamical system

- Inverse Source Problems (Find the Virus super Disseminator from Data)
  - Uniqueness
  - Algorithms

Case Study I

- By the public data from Jan. 23rd to Feb. 1st, we reconstruct spread rate β and isolate rate l:

中国科学 : 数学　2020 年　第 50 卷　第 3 期 : 1～8
SCIENTIA SINICA Mathematica
《中国科学》杂志社
SCIENCE CHINA PRESS
CrossMark
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论 文

基于一类时滞动力学系统对新型冠状病毒肺炎疫情的建模和预测

严阅[1]，陈瑜[1]，刘可伋[1,2]，罗心悦[1]，许伯熹[1]，江渝[1]，程晋[3*]

Reduce parameters（Sparse assumption）

- Based on public statistics

表 1　参数值

γ	κ	τ_1	τ_1'	τ_2
0.99	0.97	7	4	12

Spread rate and Isolate rate

- Different areas

表 2　参数的估计值

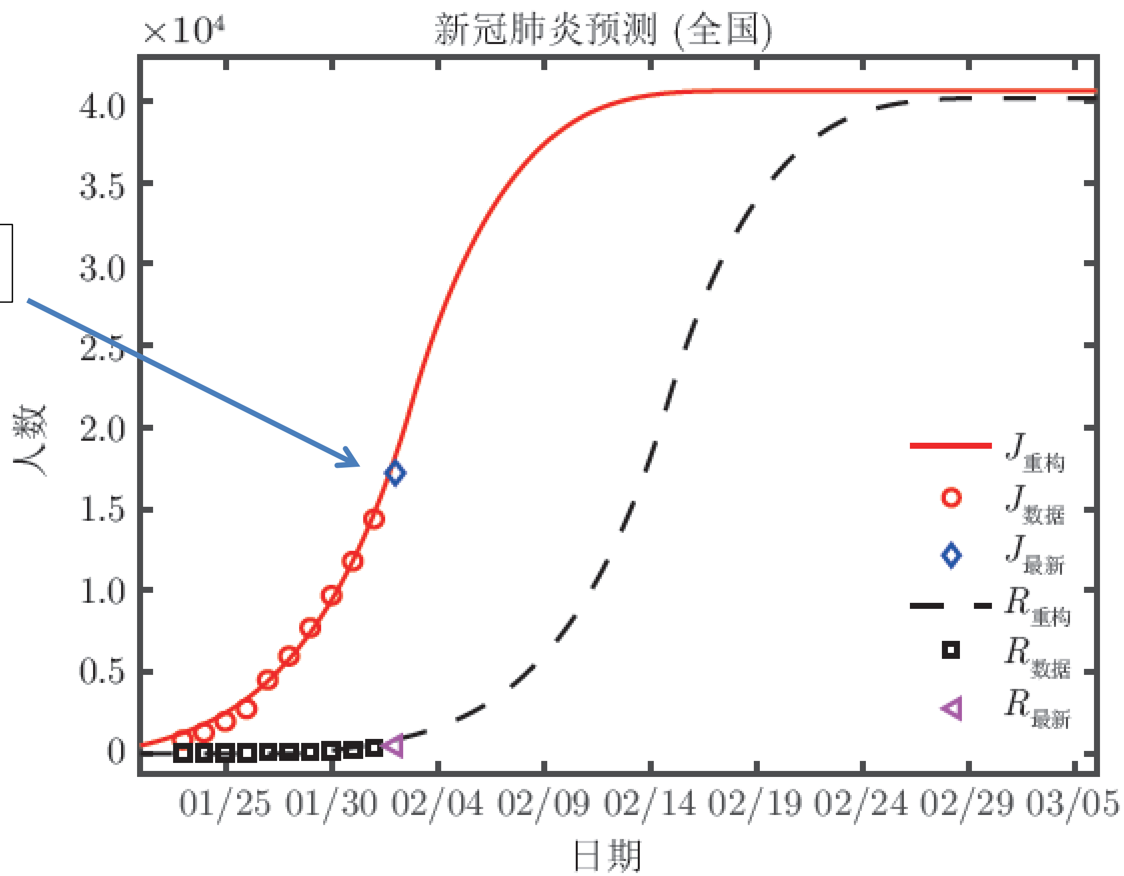
地区	传染率 β	隔离率 ℓ
Whole country	0.2320	0.4202
Wuhan	0.1957	0.5500
Shanghai	0.2113	0.5500
Jiangsu	0.2581	0.5500

Prediction（Whole country）

- Whole country

March 13th **81004**

Feb. 1st 14380

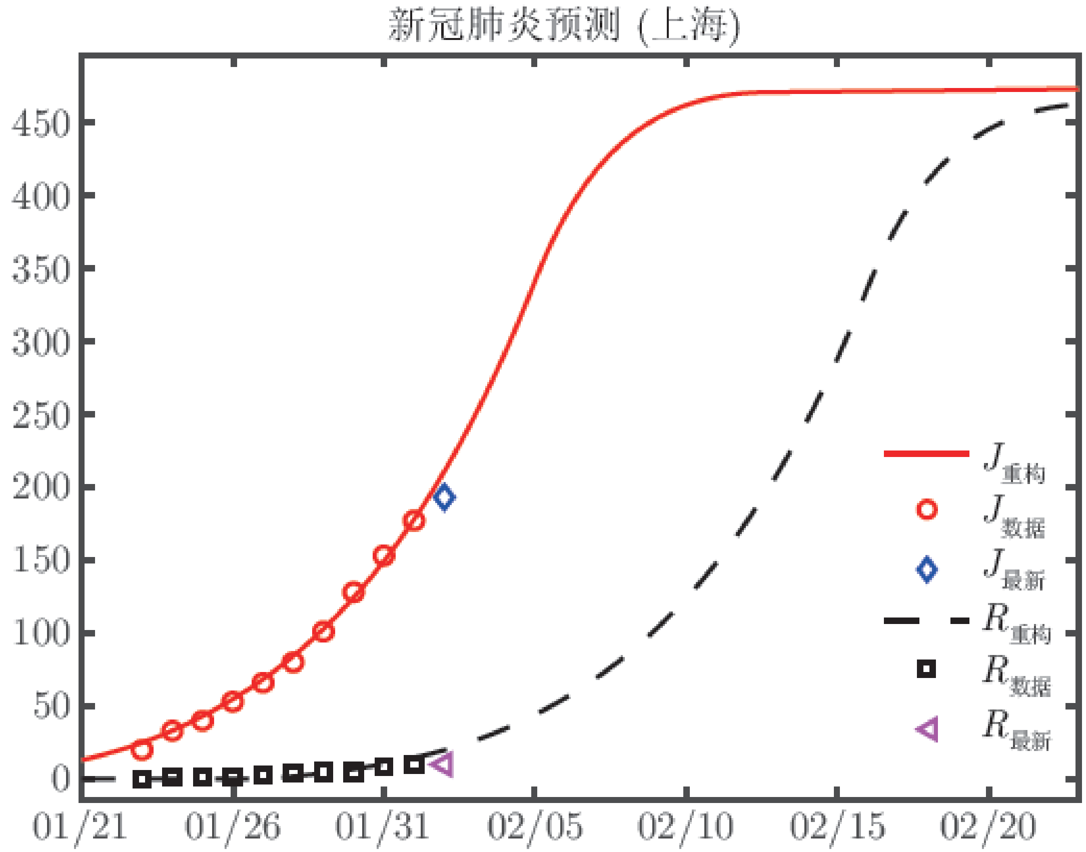


Prediction（Shanghai）

Strengthening of control measures！

March 13th 346

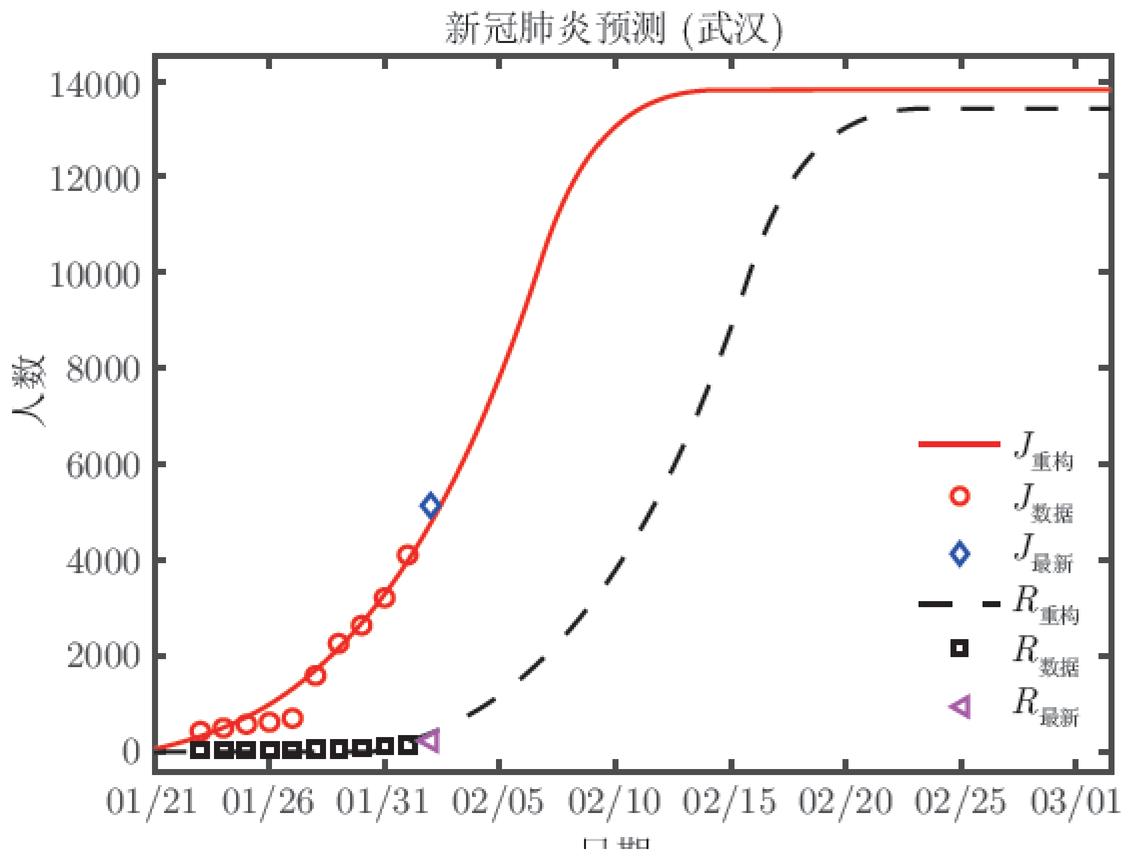
- Shanghai



Prediction（Wuhan）

- Wuhan

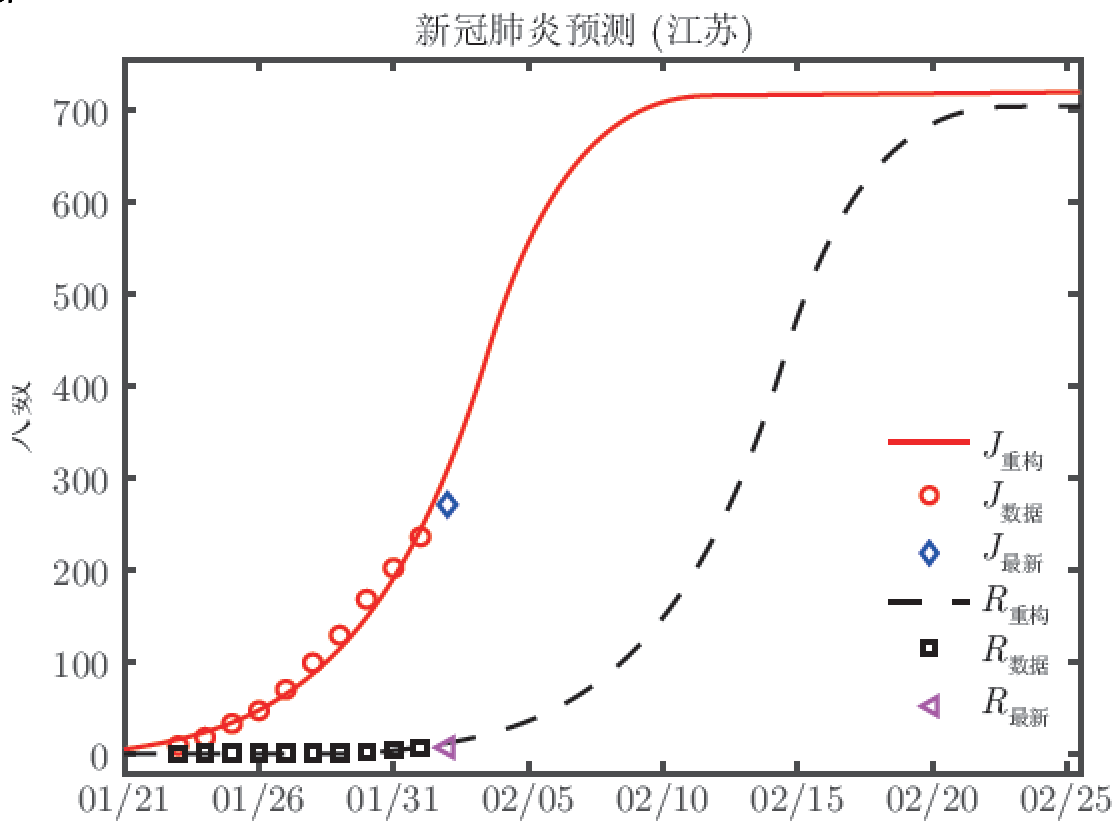
March 13[th] **49991**



Prediction（Jiangsu）

- Jiangsu

March 13th 631



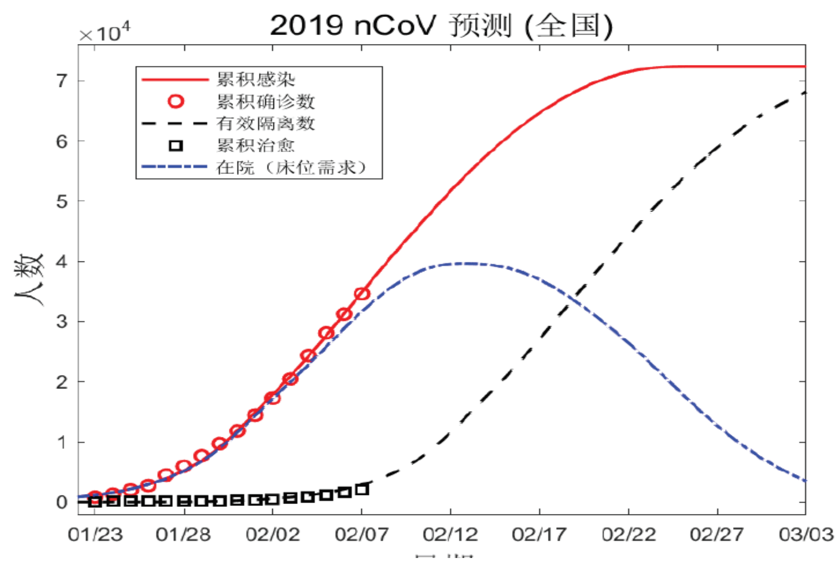
There is a certain gap between the prediction result and the actual facts

- The model is not good?
- The method is not correct?
- Data is not correct?

Research Report

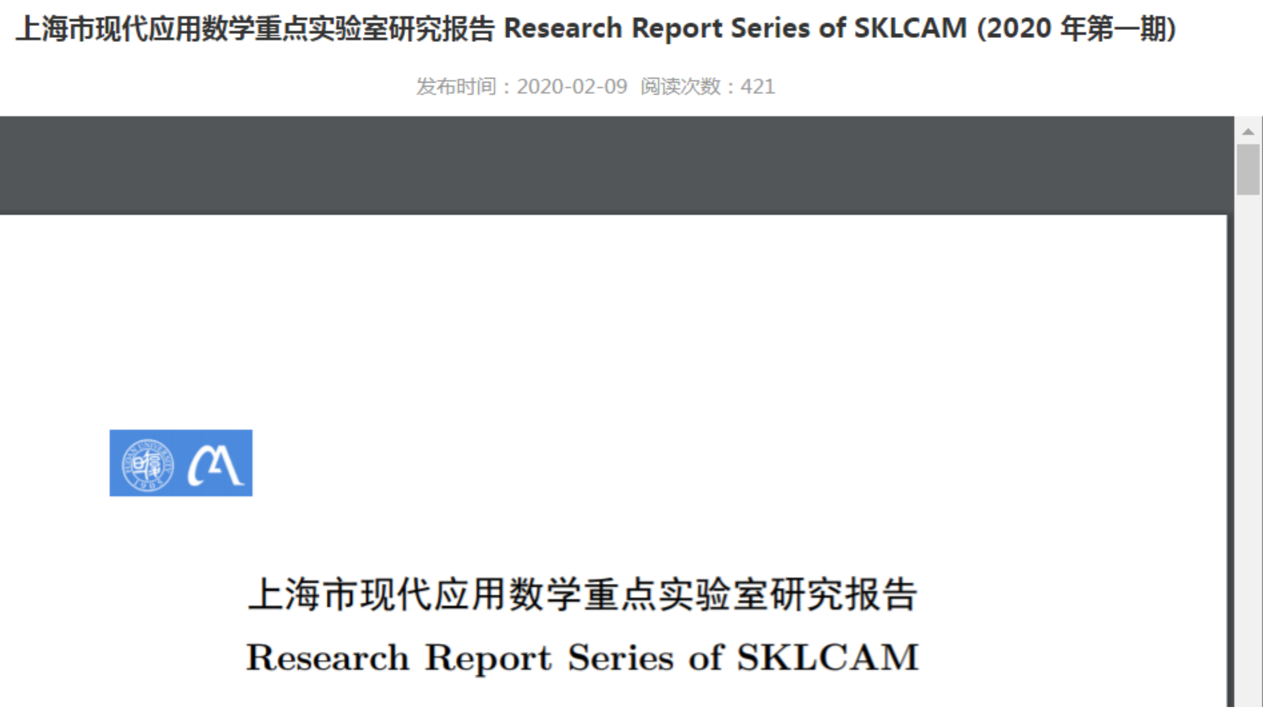
- Prediction for China

基于时滞动力学系统新冠肺炎传播模型的
若干预测分析



Lab. Report

- Feb. 9th, 2020


上海市现代应用数学重点实验室研究报告 Research Report Series of SKLCAM (2020 年第一期)

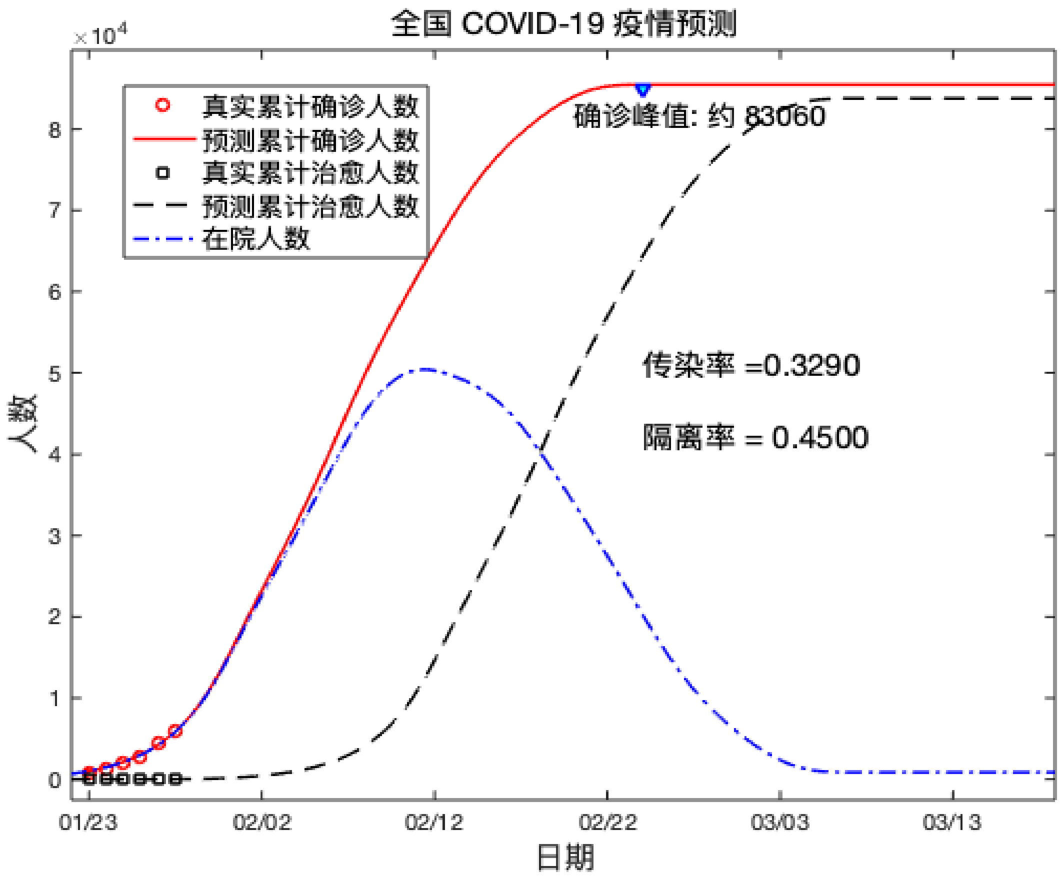
发布时间：2020-02-09 阅读次数：421

上海市现代应用数学重点实验室研究报告

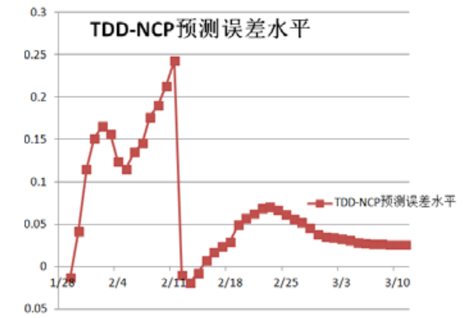
Research Report Series of SKLCAM

Choose suitable Data

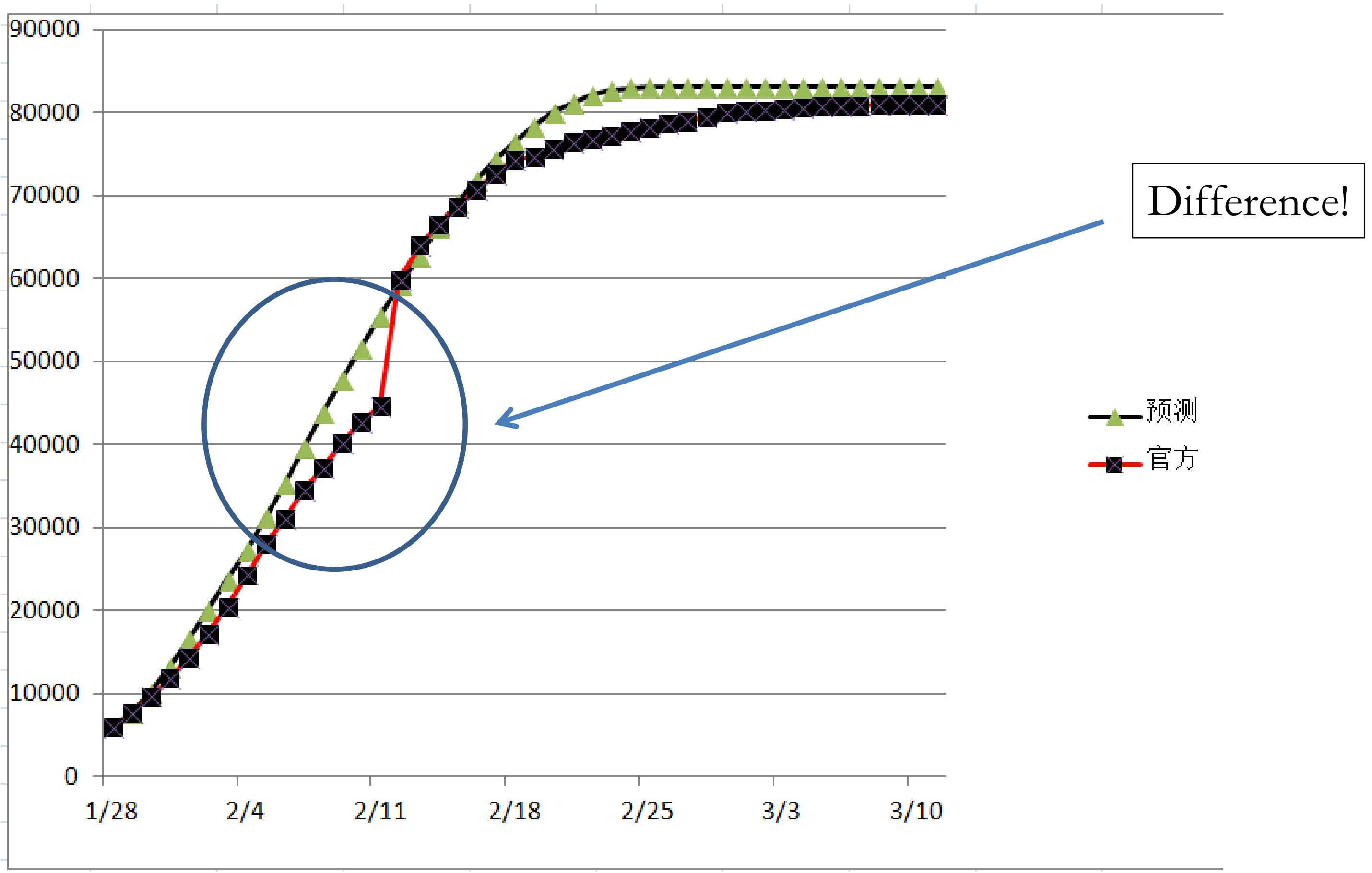
- Data from Jan. 23rd to Jan. 28th, 2020



Prediction



- Public Data and our simulation Results



Problems in simulation

- Credibility of data ?
  - Data at the early stage. Data in US...

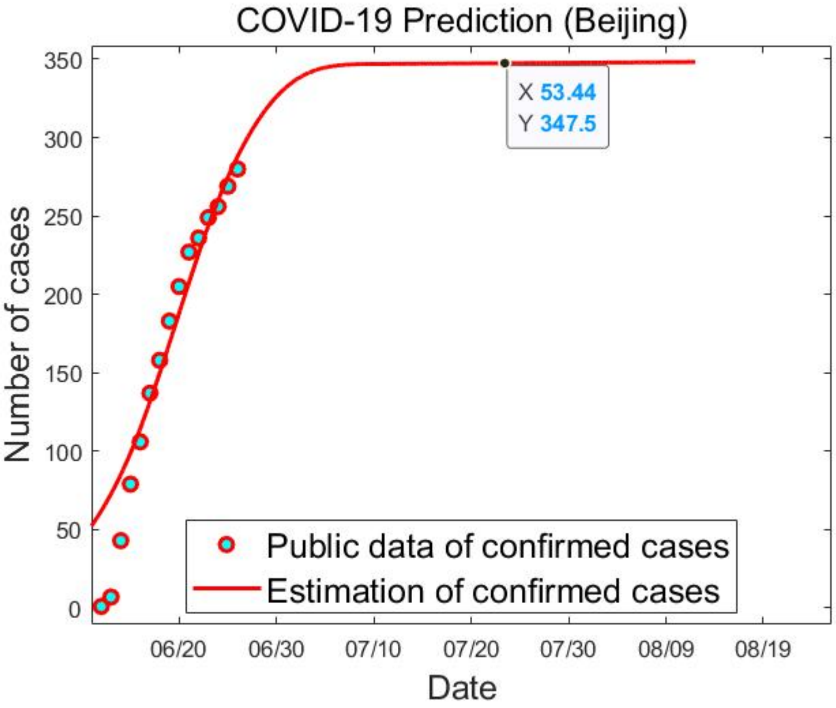
- The reconstruction results heavily depend on the data we choose!
  - Some data is distorted.

- Prediction： Whole Country > Hubei> Other cities
  - Model in the sense of statistical average

Case Study II

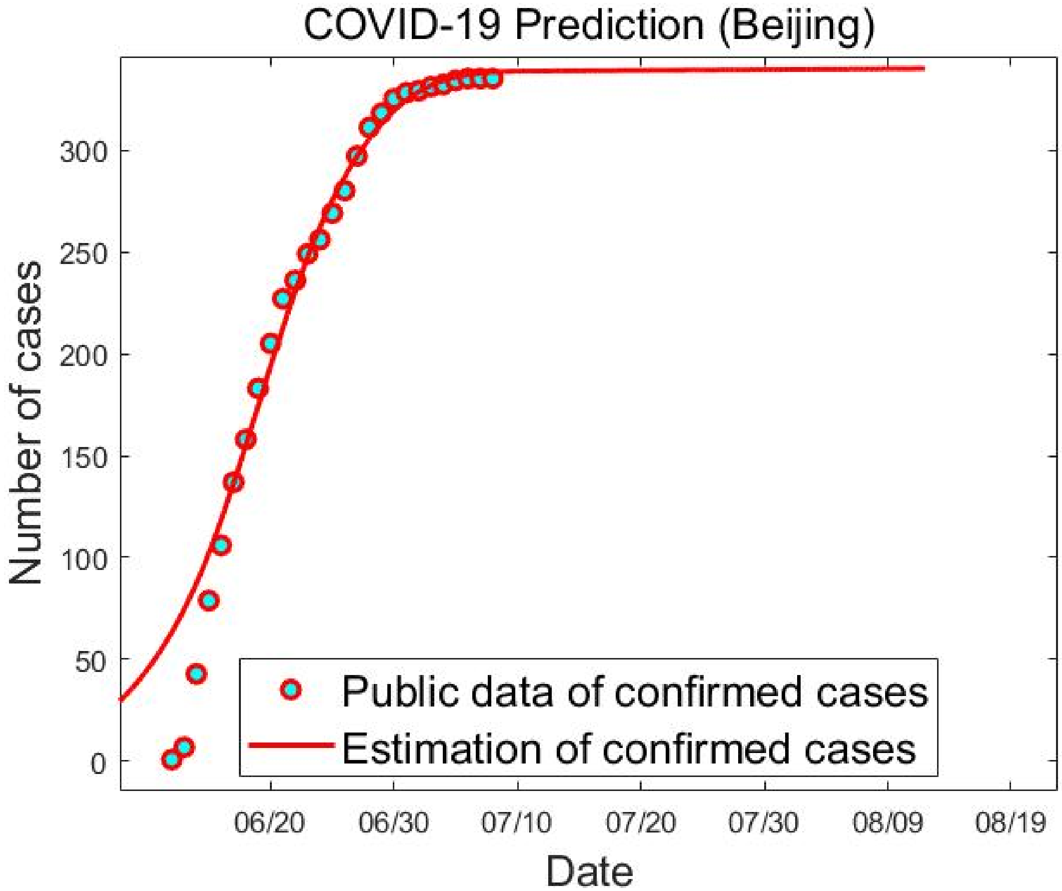
- Beijing,
  - June 11—14,
  - Confirmed Cases 79
  - β=0.20
  - l=0.354

  - Prediction 350



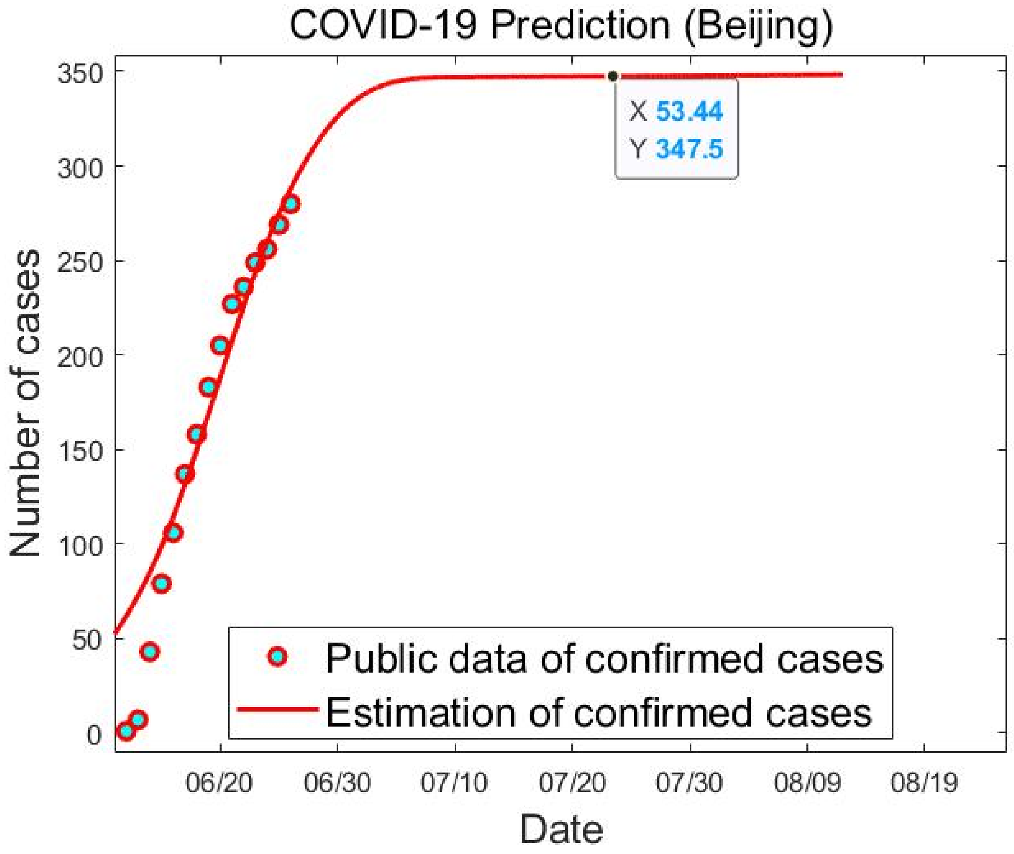
Review

- By all public data



Prediction

- By partial data



Fudan-CCDC Model (Wenbin CHEN)

- Continuous case

$$\frac{\mathrm{d}I}{\mathrm{d}t} = \beta I_0(t),$$
$$\frac{\mathrm{d}J}{\mathrm{d}t} = \beta \int_{-\infty}^{t} f_4(t-s) I_0(s)\mathrm{d}s,$$
$$\frac{\mathrm{d}G}{\mathrm{d}t} = \ell I_0(t) - \ell \int_{-\infty}^{t} f_4(t-s) I_0(s)\mathrm{d}s.$$

- Discrete case

$$I(t+1) = I(t) + \beta I_0(t),$$
$$J(t+1) = J(t) + \beta \sum_{s\le t} f_4(t-s) I_0(s),$$
$$G(t+1) = G(t) + \ell I_0(t) - \ell \sum_{s<t} f_4(t-s) I_0(s).$$

Choose the kernels

- Choose the kernels based on Data from CCDC

$$f_2(t) = \frac{0.5977}{t} e^{-1.105(\ln(t)-1.417)^2}$$

$$f_3(t) = 0.005559 t^{1.641} e^{-0.002105 t^{2.641}}$$

$$f_4(t) = f_2 * f_3(t) = 0.06244 e^{-(\frac{t-10.87}{5.378})^2} + 0.03322 e^{-(\frac{t-15.97}{23.8})^2}.$$

Ongoing works

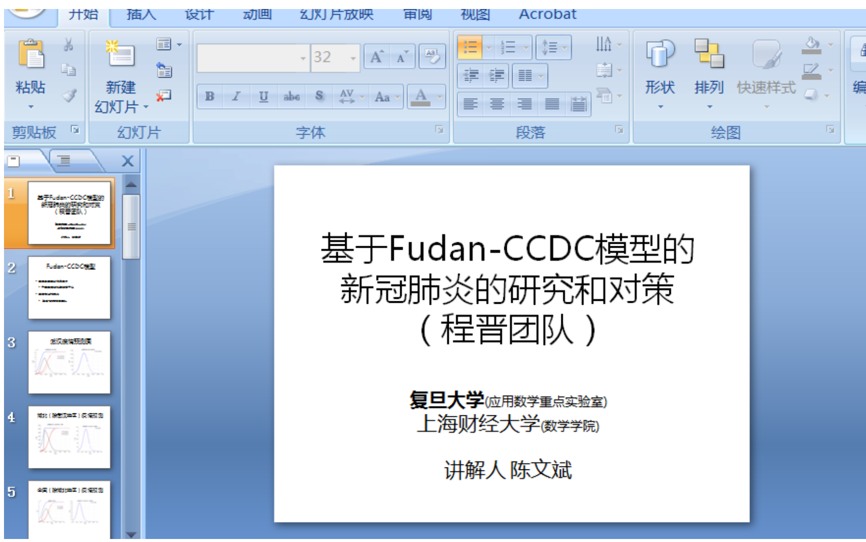
- Improving the time delay models
- Tracking epidemic data across countries
- Study the uniqueness and stability of the inverse problems

Research Results from our team

- **Internal Reports：**
  - Cheng Jin, Chen Wenbin， Report to Shanghai Government on Feb. 16th, 2020.
  - Report of the novel coronavirus disease (COVID-19) epidemic situation, with Wuhan Health Center Information Center, Wei Ning health Artificial Intelligence Laboratory, School of Mathematical Sciences, Fudan University

Presentation on Feb. 16th, 2020

- Presentation in Shanghai



一些政策建议

- 阶梯状逐步放开流动性，流动性的影响可能会延迟出现
- 密切跟踪数据，对隔离出站人员持续定期跟踪（14天）。
- 严防高危地区和人员的追踪，发现病例，马上在一定范围内隔离排查，实行打地鼠挖洞策略
- 建议调整医保慢性病人的取药政策，减少就诊次数
- 建议对幼儿园区、高校等重点区域依然保持严密防守
- 建议错峰出行
- 建议对海外回国人员进行密切关注，防止海外二次输入

One of our suggestions is to **<u>pay attention to overseas personnel to prevent secondary input from overseas</u>**

Some references

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  - 严阅, 陈瑜, 刘可伋等, 基于一类时滞动力学系统对新型冠状病毒肺炎疫情的建模和预测[J/OL], 中国科学: 数学, 50 (3), 1-8, 2020. https://doi.org/10.1360/SSM-2020-0026.
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  - YueYan, et al. COVID-19 in Singapore: another story of success, International Journal of Mathematics for Industry, 已接收, 2020.
  - Nian Shao, Jin Cheng, Wenbin Chen. The reproductive number R0 of COVID-19 based on estimate of a statistical time delay dynamical system, medRxiv 2020.02.17.20023747; doi: https://doi.org/10.1101/2020.02.17.20023747.
  - Nian Shao, et al. CoVID-19 in Japan: What could happen in the future?, https://doi.org/10.1101/2020.02.21.20026070

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  - <ins>Nian Shao, Min Zhong, Yue Yan, HanShuang Pan, Jin Cheng, Wenbin Chen</ins>. Dynamic models for CoVID-19 and Data Analysis, Mathematical Methods in the Applied Sciences, 2020, Accepted.
  - <ins>邵年，钟敏，程晋，陈文斌</ins>. 基于Fudan-CCDC模型对新冠肺炎的建模和确诊人数的预测, 数学建模及其应用,2020,接收。
  - <ins>罗心悦，邵年，程晋，陈文斌</ins>. 基于时滞动力学模型对钻石公主号邮轮疫情的分析, 数学建模及其应用,2020,接收。
  - <ins>刘可伋,江渝,严阅, 陈文斌</ins>. 局部新冠肺炎时滞模型及基本再生数的计算, 控制理论与应用,2020, minor reversion.
  - <ins>邵年，陈瑜，程晋，陈文斌</ins>. 关于新型冠状病毒肺炎一类基于CCDC统计数据的随机时滞动力学模型, 控制理论与应用,2020.

Meaning of Models

- In strict sense, all models are "wrong"
- The models are meaningful
  - Give the rough estimates and prediction
  - See "the light at the end of the tunnel"

Thanks!

Welcome the comments!

All world unite to fight the epidemic