**20.320 Final Project Implementation Report**

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**Introduction**

In December 2019, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the etiological agent underlying acute respiratory disease, named coronavirus disease 2019 (COVID-19), was discovered in mainland China. Considering the high incidence rate in China and the rapid spread of COVID-19 to other countries, many organizations closely investigated the emerging epidemic. The World Health Organization (WHO) classified the COVID-19 outbreak as a pandemic in March 2020 after the disease’s risk to public health continued to rise globally.

Mainland China, especially the Hubei Province, saw an exponential increase in diagnosed cases as COVID-19 began to reach endemic proportions in early January. Exponential growth of confirmed cases during the initial stages of a novel outbreak is principally unremarkable considering the growth kinetics of the 2014-16 Ebola outbreak in West Africa, the incidence rate of the 2009 influenza A (H1N1) pandemic, and even the daily influenza deaths in Philadelphia during the 1918 influenza pandemic (*1*). However, in mid-January, the growth of confirmed cases in Hubei and many other mainland China provinces dropped to a superlinear rate, measured at the beginning of case reporting – Jan. 21st. This subexponential growth was observed until early February, where the confirmed cases for several mainland China provinces approached an apparent saturation.

Despite regional disparities in healthcare, socioeconomic status, and infrastructure, among other factors (*2*), the number of confirmed cases over time exhibited a similar algebraic growth among many provinces between early stages of exponential growth and later stages of saturating behavior. This similarity among many other inconsistencies suggests that some underlying factors may drive this dynamic.

**Model**

With the intention of leveraging insight into the COVID-19 epidemic process, Maier and Brockman (2020) implemented SIR dynamics into a compartmental model where subpopulations are defined by their state of infection; infected (*I*) represents infectious individuals, susceptible (*S*) represents individuals that may later be infected, and removed (*R*) represents individuals that may no longer become infectious. Under SIR dynamics, epidemics are generally represented by two processes: the spread of infection from I to S, governed by the transmission rate (), and the recovery of an infectious individual after an average infectious period (*T­­­I*), captured by the recovery rate (, where = *T­­­I*)*.*

The average number of susceptible people an infectious person may infect considering free, unhindered spread of disease, or the basic reproduction number (*R*O), can then be described as *R*O = where *R*O is unitless given the units of and are (infection/time) and (time/infection) respectively. Initially, with a small infected population, exponential growth would result given SIR dynamics. Even after the danger to public health becomes apparent and quarantine measures are implemented to reduce *R*O by decreasing the number of contacts, *I(t)* would experience exponential growth given *R*O > 1. As exponential growth did not define the rise of confirmed cases for many provinces in mainland China, another subpopulation was implemented in the model: symptomatic, quarantined infecteds (*X*).

(1)

(2)

(3)

(4)

In Eqs. 1 to 4, preventative measures are implemented through the containment rate (), practically exemplified by social distancing or restrictions of non-essential businesses, and the rate infecteds are quarantined (). This model assumes that the time between sampling and test results is negligible and that *X(t)* is proportional to the confirmed case count, *C(t)*. Assuming that there were enough tests and staff to be well distributed, presuming a negligible testing window is reasonable given the ideal turnover of rapid testing and the time steps represented in *C(t),* one day for Hubei and linearly interpolated half-day increments for the other provinces. If *C(t)* were not proportional to *X(t)* then there would be no modeled subpopulation to fit against observed data. Assuming a strict quarantining policy, *X(t)* is very reasonably proportional to *C(t)*.

**Conclusion**

The algebraic growth of confirmed cases in Hubei was successfully quantified using a scaling law (Fig. 1), though confirmed cases in Hubei began to accumulate at a slower rate – exhibiting some saturating behavior around 9 February. The observed subexponential growth of *C(t)* in the most effected mainland China provinces, not initially expected given SIR dynamics, prompted the addendum of a quarantined subpopulation (X) to the model by Maier and Brockman (2020), represented by Eq. 4.

The ability of SIR-X dynamics to represent the spread of confirmed cases is demonstrated in Fig. 2. The model captured the intermediary superlinear growth phase for all of the most effected mainland China provinces, however, saturating behavior after 9 February was not completely captured for all provinces. For the provinces with saturation behavior captured by the model, the exponential depletion of infecteds drove the accumulation of new cases, assumed proportional to Eq. 4, to zero. The model demonstrates that the kinetics of SARS-CoV-2 spread are dominated by the exponentially depletion of the susceptible population as well as by the accumulation of the quarantined population. These principles illustrate the importance of proactive public health measures enforcing the strict quarantining of infected individuals.

A notable exception to the epidemiological logic of the model is the fit of close to zero in Henan and Hubei (Fig. 2A, 2Cii). This may be in part due to the sensitivity of the solutions to Eqs. 1 – 4 to small perturbations in fitting methods. As such, these provinces demonstrated peculiarly high *public containment leverage* (*P*) values. High *P* values may question whether assuming *X(t)* is proportional to *C(t)* is justified, which, in turn, prompts the reconsideration of fitting methods for future works. However, this seemingly unintuitive result demonstrates the potential for public containment alone to drive the reduction of new confirmed cases. It is important to note that high *P* values are seemingly associated with larger *I(t)* peaks relative to *X(t)* at saturation.

In conclusion, this model has demonstrated the of relevancy of parsimonious SIR-X dynamics in epidemic modeling. Subexponential growth was captured with a scaling law, , and its robust presence throughout heterogeneous subpopulation characteristics illustrates the potency of containment measures in reducing the rate of disease outbreak. Furthermore, the exponential depletion of infectious individuals was principally related to containment and quarantine rates, though both must be implemented synchronously to limit the total number of affected people. These measures allowed a significant proportion of all affected provinces to be shielded by infection provided the consistent and strict implementation of containment measures. As the exponential decay of the infectious population after its peak drove the reduction of new cases, the ability to quantify this behavior may provide insight into the duration of future outbreaks. The SIR-X epidemic model presented by Maier and Brockman (2020) foremost demonstrated the efficacy of policy efforts, quarantine mandates, and behavioral modifications in epidemic containment.

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**Fig. 1. The growth of confirmed cases over time can be represented by the scaling law**

Subexponential growth of laboratory confirmed cases, *C(t)*,was quantified in the Hubei province. *C(t)* followed a scaling law , with fit to a value of 2.46. *C(t)* was processed by removing all *C(i)* equivalent to *C(i-1).* Considering the Hubei province showed an initial phase of exponential growth and later exhibited saturation behavior, represented by dotted line, was fit to *C(t)* data between 24 January and 9 February.

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**Fig. 2. The SIR-X compartmental epidemic model predicted confirmed cases**

Laboratory confirmed cases, *C(t)*, are representable by SIR-X dynamics. The model predictions for *X(t)* and *I(t)* were calculated using Eqs. 1 to 4 with the initial conditions *X(t0)i*=i*C(t0)/N*, *I(t0)*i*=i(I0/X0)X(t0)*, and *S(t0)i=i1 - X(t0) - I(t0),* where *N* represents Hubei’s population and *(I0/X0)* is a constant implemented due to the nature ofconfirmed cases not being fully representative of all possible cases. The solution of Eq. 4, *X(t)*,was fit by the trust-region-reflective method of least squares against *C(t)*, processed as described in Fig. 1,which yielded estimates for the constants *(I0/X0),* , and . and *TI* were allowed ranges of 0.6 - 0.8 (days-1) and 2.6 – 20 (days) respectively to consistently reproduce the observed *C(t)* growth. All fits only considered *C(t)* before 12 February, when, in Hubei, the criteria for determining the confirmed case count changed as clinically diagnosed cases were added to *C(t)* (indicated by the right dotted line). The maximum proportion of infected individuals was also captured by the model, indicated by the left dotted line. All provinces demonstrated similar *I(t)* peak times. The time points for maximum *I(t)* were constant throughout different fitting tolerances, but the size of the peaks was variable. *X(t)* and *I(t)* were very sensitive to the fitting and integration methods applied to Eqs. 1-4.To quantify the efficacy of containment measures, *public containment leverage* ( and *quarantine probability* were compared among provinces. **(A)** The SIR-X model captured the phases of initial exponential growth, the following subexponential growth, and finally the saturating behavior of *C(t)* in Hubei. The fits for , *,* , , and *(I0/X0)*were 0.848, 0.1163, 0.0814, 7.57e-9, and 0.89 respectively. *P =* 1.00 and *Q =* 0.41, indicating that the model predicted public containment measures as the driving force for the protection of the susceptible population. **(C)** The SIR-X model was also applied to the next most effected provinces in mainland china. The fits for **i-viii**, presented as(, *,* , , *(I0/X0)*) were (0.849, 0.146, 0.094, 0.009, 1.39), (0.849, 0.153, 0.088, 4.01e-7, 5.89), (0.849, 0.115, 0.103, 0.034, 3.56), (0.849, 0.093, 0.101, 0.036, 4.97), (0.829, 0.104, 0.075, 0.085, 11.63), (0.849, 0.010, 0.086, 0.052, 5.95), (0.849, 0.079, 0.107, 0.004, 9.87), and (0.849, 0.097, 0.122, 0.002, 3.09) respectively. Q and P were (0.91, 0.41), (1.00, 0.36), (0.75, 0.54), (0.74, 0.60), (0.47, 0.61), (0.62, 0.58), (0.96, 0.58), and (.99, 0.56) for **i-viii** respectively.

**Bibliography**

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