

Practical guide to fitting SIR models

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1 Introduction

Over the last few decades, a plethora of computational tools have been developed to study epidemic time series. Central to these methods are mechanistic models. These models allow us to study the qualitative dynamics of a system and infer underlying mechanisms that drove the observed patterns in the data. For example, we now know that the complex dynamics of measles outbreaks were driven by seasonal transmission patterns (Earn et al., 2000).

The SIR model is one of the most basic mechanistic models. It describes how individuals move from susceptible (S) to infected (I) and to recovered (R) states in a homogeneously mixing population:

$$\begin{aligned}\frac{dS}{dt} &= b(t) - \left(\beta(t) \frac{I}{N} + \mu \right) S \\ \frac{dI}{dt} &= \beta(t) S \frac{I}{N} - (\gamma + \mu) I \\ \frac{dR}{dt} &= \gamma I - \mu R\end{aligned}\tag{1}$$

where $b(t)$ is the natural birth rate (or recruitment rate to susceptible population), $\beta(t)$ is the transmission rate, γ is the recovery rate, and μ is the natural death rate. Despite its simplicity, the SIR model is still widely used to study outbreaks, such as measles, plague, HIV, and influenza. The main difficulty in analyzing these systems comes from estimating transmission rate, $\beta(t)$.

One way to estimate $\beta(t)$ is by matching the deterministic solution of the system 1 with the observed number of cases. This method is referred to as trajectory matching. Similarly, it is possible to match *gradients* of the system 1 given if all state variables are observed. Unlike trajectory matching, gradient matching does not require parametric forms of the rates to be specified beforehand and allows for flexible modeling of the system. While these methods are computationally efficient and easy to implement, they do not allow us to take demographic stochasticity into account explicitly.

On the other hand, Monte Carlo methods allows us to model *all* sources of variation (e.g., observation error and process error) explicitly.

This is not at all an exhaustive list of all existing methods. Generalized profiling balances between trajectory matching and gradient matching by fitting a deterministic model (Hooker et al., 2010). Laplace approximation based methods are also available.

Of all these methods, the time series SIR (TSIR) method has been particularly successful in studying dynamics of ??? diseases, especially measles.

There are many ways to estimate underlying parameters of the SIR model 1; yet their differences are unclear because they all rely on different set of assumptions. Which one should one use? Here, we compare TSIR each method against simulated data and study how differences in the assumptions affect our conclusions. Then, we apply each method to measles time series from Boston and discuss implications.

2 Simulated data

3 Fitting methods

3.1 TSIR

$\beta I^\alpha/N$ approximates $1 - \exp(-\beta I/N)$. Hence, we can find $\hat{\beta}$ such that

$$\hat{\beta} \bar{I}^\alpha/N = 1 - \exp(-\beta \bar{I}/N)$$

4 SIR model

The susceptible-infected-recovered (SIR) model is one of the simplest epidemic models which describe how disease spreads in a homogeneously mixing population.

$b(t)$ represents recruitment rate to the susceptible population, μ represents natural mortality rate, and γ represents per-capita recovery rate. $\phi(t)$ represents force of infection, which is defined as the rate at which a susceptible individual acquires infection. We write $\phi(t) = \beta(t)I/N$ to represent *frequency*-dependent action or $\phi(t) = \beta I$ to represent *density*-dependent action, where $N = S + I + R$ is the total population size. For this study, we focus on $\phi(t) = \beta(t)I/N$.

Typically, data suffers from under-reporting and we may want to understand the dynamics of ρI instead, where ρ is the reporting rate. Then, we can write

$$\begin{aligned} \frac{dS}{dt} &= b(t) - \beta S \frac{\hat{I}}{\rho N} \\ \frac{d\hat{I}}{dt} &= \beta S \frac{\hat{I}}{N} - \gamma \hat{I} \end{aligned} \tag{2}$$

4.1 Incidence, prevalence, and mortality

We want to distinguish among different kinds of data: prevalence, incidence, and mortality. Prevalence is defined as the total number of infected individuals present in the population and corresponds to $\hat{I}(t)$. Incidence is defined as the number of newly infected cases. Hence, incidence report at time t corresponds to the integral of the total infection rate from the previous reporting period $t - \Delta t$ and current reporting period t :

$$\int_{t-\Delta t}^t \beta(s) S \frac{\hat{I}}{N} ds. \tag{3}$$

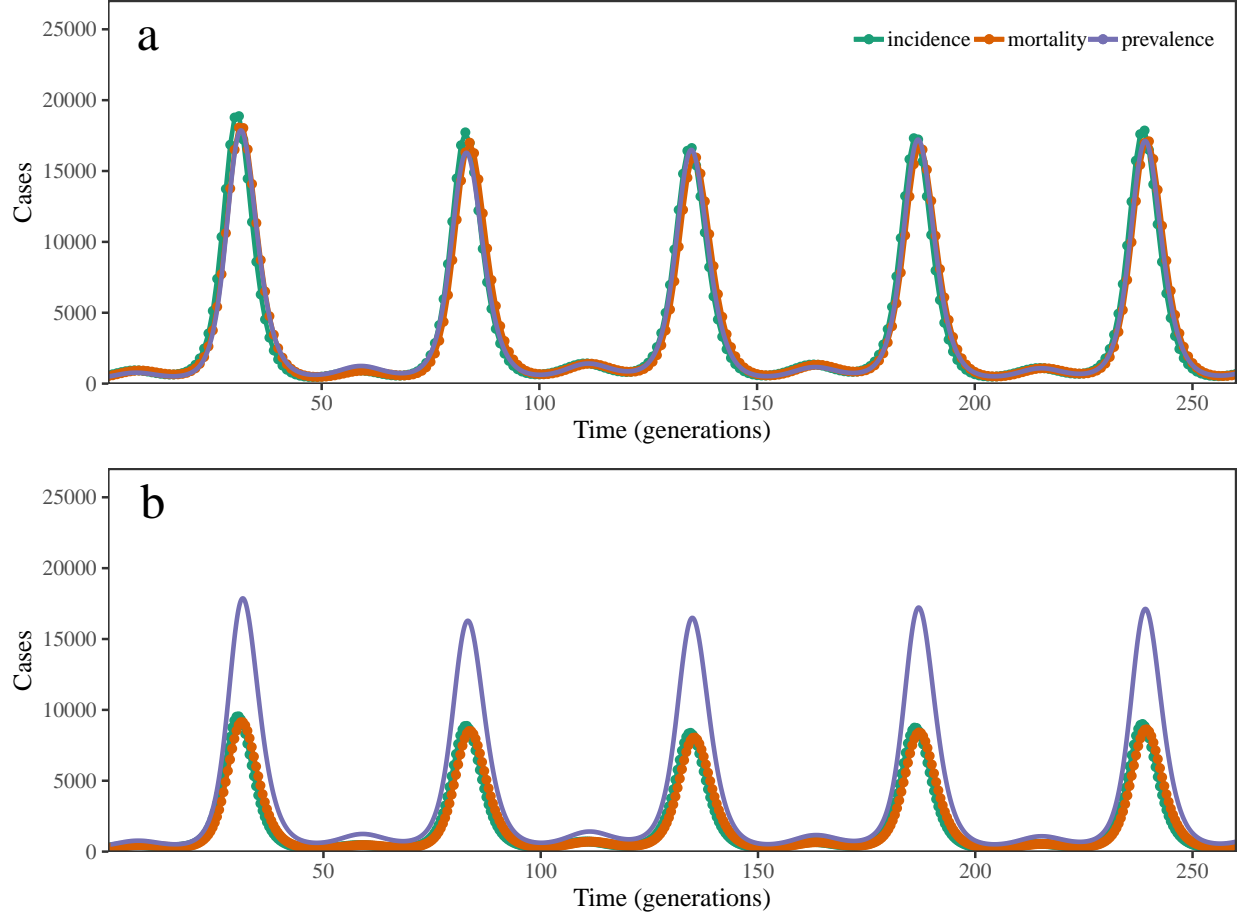


Figure 1: This is not a caption.

Finally, mortality is defined as the number of individuals that died over a time period. Like incidence, mortality can be written as the integral of the total death rate:

$$\int_{t-\Delta t}^t \gamma \hat{I} ds. \quad (4)$$

The main difference among the three types is that prevalence counts provide a direct observation of a state variable whereas incidence and mortality counts do not. As a result,

In this article, we focus on fitting to incidence data only. In particular, we consider two kinds of models: continuous deterministic models and discrete stochastic models. We do not consider fitting continuous stochastic models because they are computationally too expensive.

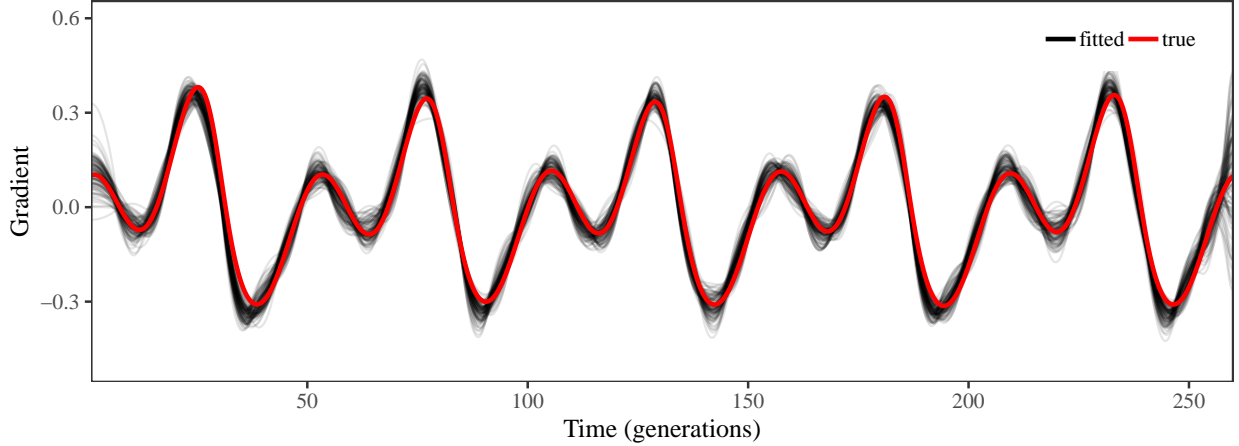


Figure 2: This is not a caption.

5 Fitting continuous models

5.1 Trajectory matching

Trajectory matching is one of the simplest fitting methods. As its name suggests, the goal is to find a set of parameters such that the simulated trajectory, from the ODE model, best matches the observed data. This method assumes that there is only measurement error and no process error. The measurement model can be written as:

$$y_t \sim \text{NegBinomial} \left(\mu_t = \int_{t-\Delta t}^t \beta(s) S \frac{\hat{I}}{N} ds, \phi \right), \quad (5)$$

where ρ is reporting rate and ϕ is dispersion parameter. We prefer this model compared to the binomial or beta-binomial model because fitting binomial or beta-binomial models may not work if there are any irregular patterns in the data.

5.2 Gradient matching

When *all* state variables are observed, we can fit smooth curves to the data and obtain an estimate of the gradients of the ODE by taking the derivatives of the estimated smooth functions. Gradient matching methods seek to estimate the rate equation using nonparametric regression. However, for most epidemics, it is impossible to have data of all state variables. When only incidence is provided, we have no direct

observations of any state variables. If we can reconstruct the dynamics of the susceptible population and assume that incidence is sufficiently similar to prevalence, we can still be able to apply gradient matching methods.

Observe that

$$\frac{d \log \hat{I}}{dt} = \beta(t) \frac{S}{N} - (\gamma + \mu), \quad (6)$$

If we can obtain a reasonable estimate of the gradient $Z_i = d \log \hat{I} / dt(t_i)$, we can write

$$Z_i + (\gamma + \mu) = \exp(\log \beta(t_i) + \log S_i - \log N) + \epsilon_i \quad (7)$$

and estimate β , given that we can reconstruct the susceptible dynamics S_i . Estimate of β can be done using nonparametric regression by treating $\log S_i$ and $\log N$ as offset terms.

First, we want to test whether gradients can be reliably estimated from incidence data alone by simulating a deterministic SIR model with measurement error. We use natural cubic spline with knots placed every 6 biweeks. It works generally well but there is systematic bias. When gradients are at their local maxima (and minima), we tend to overestimate (and underestimate) the gradients. This is because incidence precedes prevalence???

If we simply construct confidence intervals based on equation ?? we underestimate uncertainty significantly by ignoring the uncertainty in the estimated gradients Z_i .

Conditions:

- See Jost and Ellner (???)
- sampled sufficiently
- not too much error
- Brunel Parameter estimation of ODE's via nonparametric estimators

5.3 Generalized profiling

Generalized profiling combines trajectory matching with gradient matching.

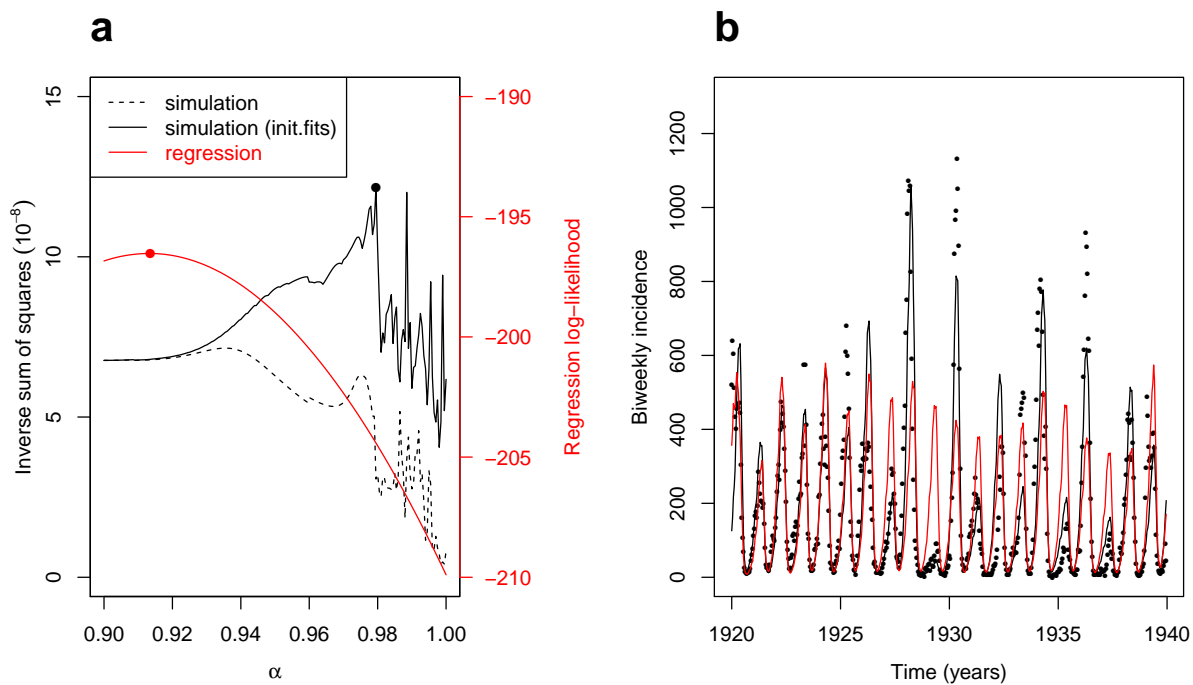


Figure 3: This is not a caption.

5.4 Spectral matching

What is this? Read Reuman et al. 2006

6 Fitting discrete time models

6.1 Time-series SIR

The time-series SIR (TSIR) method was introduced by Bjørnstad et al. (2002) to estimate seasonally varying transmission rates of measles. It relies on reconstructing the susceptible dynamics from birth and case reports and using linear regression, conditional on knowing “true susceptible dynamics”, to estimate transmission rates. Initial conditions are often estimated to improve goodness of fit.

The TSIR method begins by discretizing the infection process, assuming that disease generation-time is

equal to reporting interval:

$$S_{t+1} = B_t + S_t - I_{t+1}I_{t+1} = \beta_t S_t \frac{I_t^\alpha}{N_t} \quad (8)$$

where α is often referred to as a conversion factor from continuous-time model to discrete-time model or a heterogeneity parameter [CITE]. True incidence, I_t , is inferred from the observed incidence, y_t , and estimated reporting rate ρ_t : $I_t = y_t/\rho_t$. Taking log on both sides, estimation of transmission rates β_t becomes a regression problem:

$$\log I_{t+1} = \log \beta_t + \log S_t + \alpha \log I_t - \log N_t + \epsilon_t. \quad (9)$$

The estimation process is deterministic, but the TSIR method is analogous to fitting a stochastic model: equation ?? models step-ahead prediction as a function of previous state and process error, ϵ_t . Coupled with a deterministic susceptible reconstruction and estimation of reporting rate, the TSIR method attributes all errors to one-step process noise and oversmooths the likelihood surface (figure ?). Several studies have associated dynamics of the deterministic model (equation ??) with the inferred parameters from the regression but they are intrinsically different models.

We can make several interesting observations about TSIR model. First of all, the model exhibits a sub-exponential growth.

6.2 Particle filtering

Particle filtering provides a way of approximating the likelihood for stochastic models. In this paper, we focus on mif2 method.

$$\begin{aligned} S_{t+\Delta t} &= B_t + S_t - S_t \left(1 - \exp \left(-\beta_t \frac{I_t}{N_t} \Delta t \right) \right) \\ I_{t+\Delta t} &= S_t \left(1 - \exp \left(-\beta_t \frac{I_t}{N_t} \Delta t \right) \right) + I_t - I_t (1 - \exp(-(\gamma + \mu) \Delta t)) \end{aligned} \quad (10)$$

Tries to account for variation in ... but still ... When are these assumptions appropriate?

6.3 Incidence-based models

Li et al. (2018) compared incidence-based models across several Bayesian platforms. In our case, we can write a similar model as:

$$\begin{aligned}
 S_{t+\Delta t} &= B_t + S_t - I_{t+\Delta t} \\
 \phi_t &= \sum_{i=1}^{\ell} k(i) I_{t-\ell+i} \\
 I_{t+\Delta t} &\sim \text{BetaBin}(1 - e^{-\phi_t}, S_t, \delta_P) \\
 \text{Obs}_t &\sim \text{NegBin}(P_{rep}, \sum I_t, \delta_{obs})
 \end{aligned}
 \tag{11}$$

When reporting period is same as the mean generation time, we want to simulate the model on a finer scale.

Disadvantage: unable to model mechanisms; difficult to deal with prevalence or mortality data. Advantage: flexible generation time distribution.

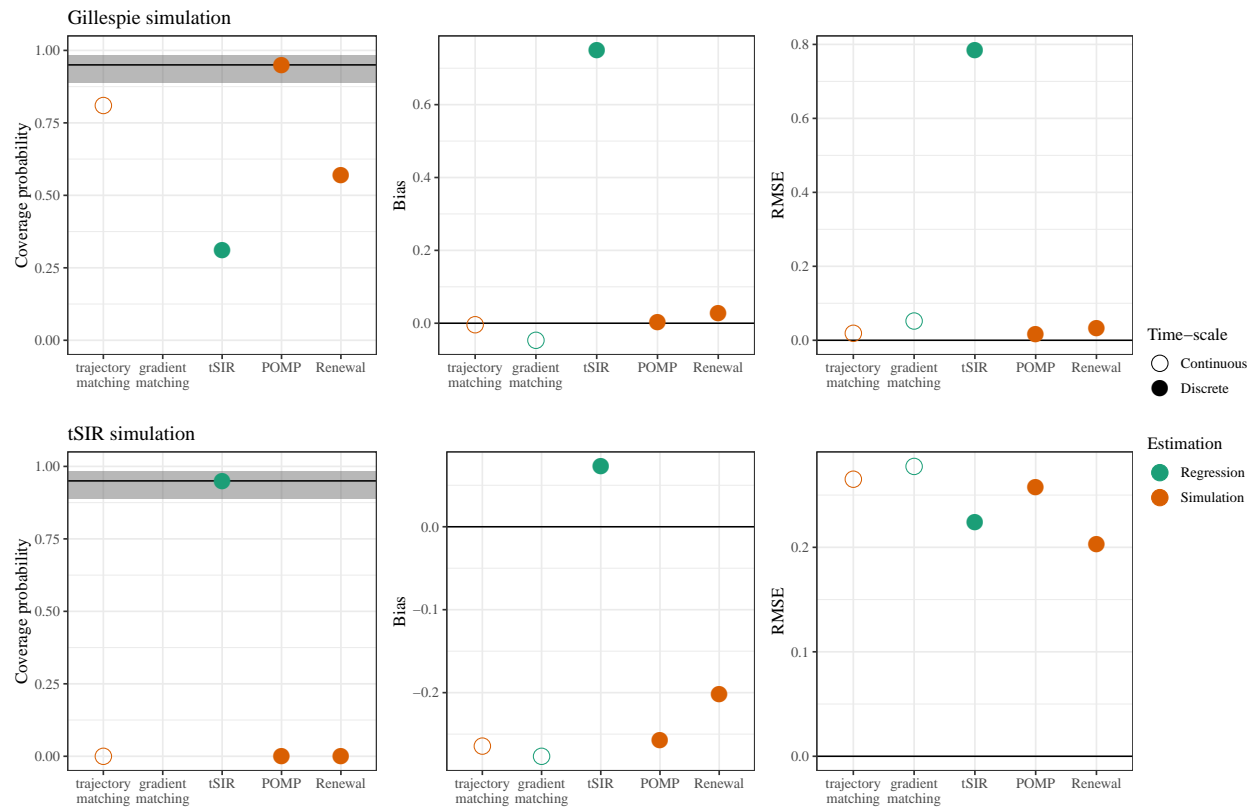
6.4 Probe-based methods

7 Results

7.1 Statistical inference

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8 Appendix

8.1 Derivation of growth rate in discrete-time SIR model

Derivation:

$$\begin{aligned} S_{t+\Delta t} &= S_t - S_t(1 - \exp(-\beta I_t \Delta t / N)) \\ I_{t+\Delta t} &= S_t(1 - \exp(-\beta I_t \Delta t / N)) + I_t - I_t(1 - \exp(-\gamma \Delta t)) \end{aligned} \quad (12)$$

Assuming that S_t is approximately equal to N , we get

$$I_{t+\Delta t} = N(1 - \exp(-\beta I_t \Delta t / N)) + I_t \exp(-\gamma \Delta t) \quad (13)$$

When $I_t \approx 0$, $\exp(-\beta I_t \Delta t / N) \approx 1 - \beta I_t \Delta t / N$ and so

$$\begin{aligned} I_{t+\Delta t} &\approx I_t \beta \Delta t + I_t \exp(-\gamma \Delta t) \\ &= I_t (\beta \Delta t + \exp(-\gamma \Delta t)) \end{aligned} \quad (14)$$

Substituting $\hat{\gamma}$, we get

$$I_{t+\Delta t} = I_t \left(1 + \beta \Delta t - \frac{\Delta t}{\mu} \right), \quad (15)$$

Therefore,

$$I_t = I_0 \left(1 + \beta \Delta t - \frac{\Delta t}{\mu} \right)^{t/\Delta t} \quad (16)$$

and the initial growth rate is given by

$$r = \frac{1}{\Delta t} \log \left(1 + \beta \Delta t - \frac{\Delta t}{\mu} \right). \quad (17)$$

8.2 Probability of infection

In both the TSIR model and the hazard-based model, transition from the susceptible compartment, S , to the infected compartment, I , is represented as a product of number of susceptible individuals and probability of infection between two time steps t and $t + \Delta t$. The TSIR model assumes that the probability of infection is a linear function of prevalence I_t . This formulation is based on the Euler approximation to the solution of the ordinary differential equation. On the other hand, the hazard-based model assumes that the probability of infection is an inverse exponential function of prevalence I_t . Besides their differences in the relationship

between prevalence and probability of infection, there are two more assumptions that we need to consider: (1) force of infection remains constant over two time steps and (2) new susceptible individuals have zero probability of infection between the two time steps.

8.3 Infectious period

Geometric distribution with probability of $1 - \exp(-\gamma\Delta t)$ and unit of Δt . Then, mean infectious period and generation interval is given by

$$\frac{\Delta t}{1 - \exp(-\gamma\Delta t)}. \quad (18)$$

An important but often overlooked component is the variance of the distribution. Squared coefficient of variation for this distribution is equal to $\exp(-\gamma\Delta t)$, which necessarily depends on pre-specified time-step Δt . If we want to match the mean of the distribution to a fixed value μ regardless of our choices of Δt , we obtain

$$\hat{\gamma} = -\frac{1}{\Delta t} \log \left(1 - \frac{\Delta t}{\mu} \right) \quad (19)$$

Then,

$$\text{CV}_{\text{Infectious period}}(\Delta t)^2 = 1 - \frac{\Delta t}{\mu}. \quad (20)$$

We expect changes in variation in infectious period to affect variation in stochastic realizations.

This means that the relationship between r and \mathcal{R} changes. For this generation-interval distribution, we have

$$\mathcal{R} = 1 + \frac{\exp(r) - 1}{(1 - \exp(-\gamma\Delta t))} \quad (21)$$

Substituting

$$r = \frac{1}{\Delta t} \log \left(1 + \beta\Delta t - \frac{\Delta t}{\mu} \right), \quad (22)$$

as well as $\hat{\gamma}$, we get

$$\mathcal{R} = 1 + \frac{\mu}{\Delta t} \left(1 + \beta\Delta t - \frac{\Delta t}{\mu} \right)^{1/\Delta t} \quad (23)$$

Then, we can obtain a relationship between \mathcal{R} of a discrete-time system and that of a corresponding continuous time system, assuming that contact rate β and mean generation-time μ are the same:

$$\mathcal{R}_{\text{discrete}} = 1 + \frac{\mu}{\Delta t} \left(1 + \frac{(\mathcal{R}_{\text{continuous}} - 1)\Delta t}{\mu} \right)^{1/\Delta t} \quad (24)$$

On the other hand, we may want to match choose β and μ to match true r and \mathcal{R} .