Impacts of epidemic dynamics on the 'effective' generation interval

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Introduction

Accurate models are critical for informing key policy decisions in the midst of an epidemic. Hence, it is crucial to accurately estimate the biological parameters of an infectious disease.

One useful quantity is the distribution of times between infection of infector-infectee pairs, defined as the generation interval. Generation intervals (GIs) are linked to key epidemiological parameters such as the reproduction number R and the growth rate [1].

Our aim is to investigate the impact of transmission-reducing interventions and emergent strain invasion on the generation interval of an infectious disease.

The *intrinsic* generation interval is purely a measure of the infectiousness of an individual and thus can be used in the estimation of the disease's biological parameters. However, as the intrinsic generation interval is not affected by epidemiological changes as the infection progresses, it is not possible to directly measure its value in the real world. Therefore, we introduce two measurable, 'effective' generation intervals:

- **Forwards:** the time τ between an infector's infection at t and an infectee's infection at $t+\tau$
- **Backwards:** the time τ between an infectee's infection at t and the infector's infection at $t-\tau$

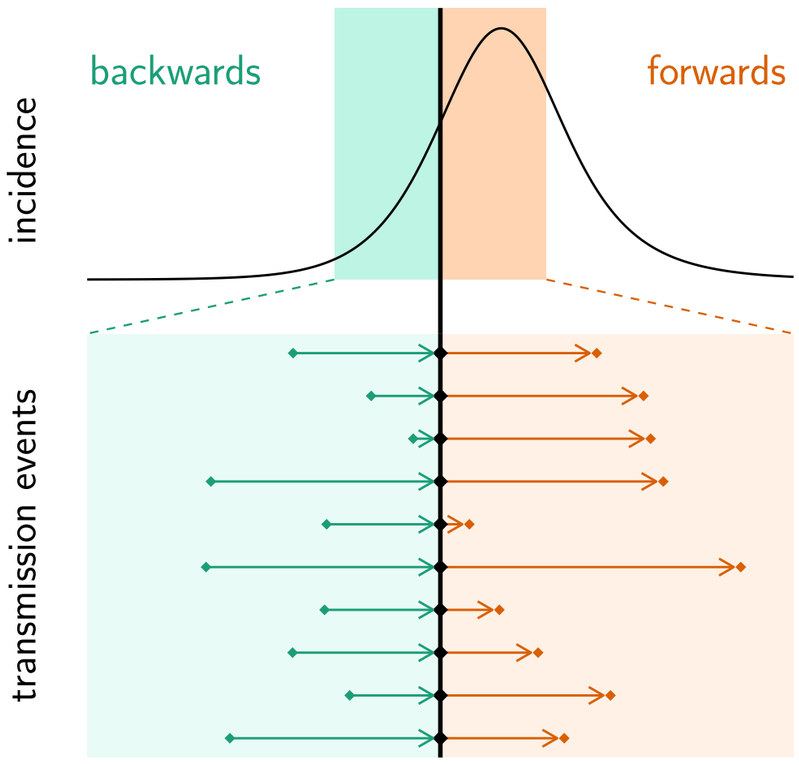

Figure 1. Visual demonstration of the forwards and backwards generation intervals at a given point in time.

Methods

The SEIR model

The classical *SEIR* model separates the population into 4 separate compartments: *susceptible* (S), *exposed* (E), *infectious* (I), and *recovered* (R). The infection can only spread if an individual is in the *infectious* stage. We further define the *incidence* $i(t)$ as the rate of change of susceptibles into the exposed class, that is, $i(t) = \beta(t)S(t)I(t)/N$.

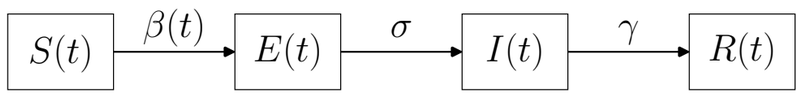

Figure 2. The compartments of an *SEIR* model.

To extend this to a two-strain model, we account for multi-strain dynamics using a cross-protection factor x, and we assume that re-infection with the same strain is not possible (Figure 3).

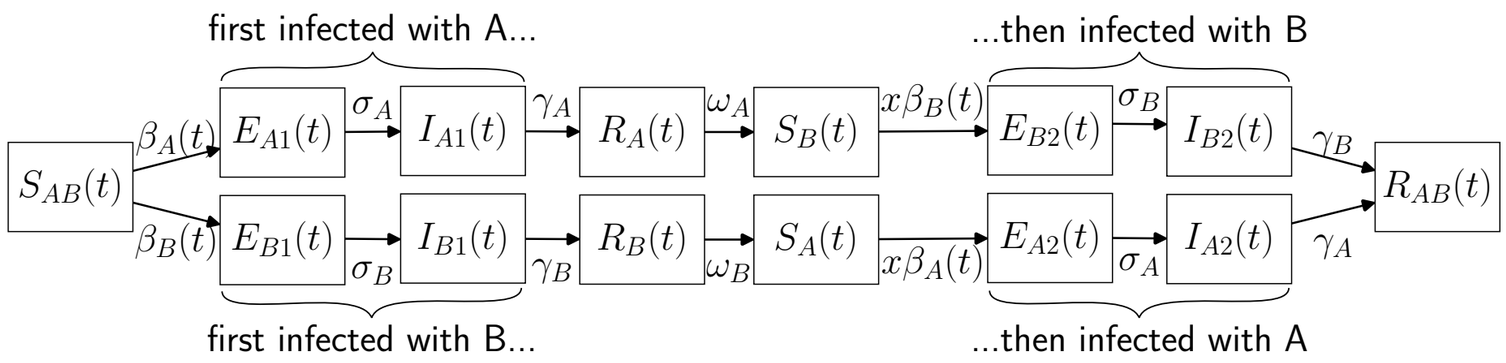

Figure 3. An SEIR model with two competing strains. Partial immunity is denoted by cross-protection factor x.

Generation intervals

For an SEIR model, the intrinsic GI $g_0(\tau)$ is hypo-exponentially distributed with rates (σ, γ).

We introduce time-inhomogenous forwards and backwards generation intervals, which have distributions:

$$g_f(t,\tau) = \frac{g_0(\tau)\overbrace{\beta(t+\tau)}^{\text{rate of transmission at time } \tau \text{ in the future}}\overbrace{S(t+\tau)}^{\text{susceptible people at time } \tau \text{ in the future}}}{\int_0^\infty g_0(\rho)\beta(t+\rho)S(t+\rho)\,d\rho}$$

$$g_b(t,\tau) = \frac{g_0(\tau)\overbrace{i(t-\tau)}^{\text{number of people infected } \tau \text{ time ago}}}{\int_0^\infty g_0(\rho)i(t-\rho)\,d\rho}$$

These formulae are extended to a two-strain model. For strain A, the distribution of generation intervals is given by:

$$g_{f,A}(t,\tau) = \frac{g_0(\tau)\beta_A(t+\tau)\overbrace{(S_{AB}(t+\tau)+xS_A(t+\tau))}^{\text{'effective' susceptibility}}}{\int_0^\infty g_0(\rho)\beta_A(t+\rho)(S_{AB}(t+\rho)+xS_A(t+\rho))d\rho}$$

$$g_{b,A}(t,\tau) = \frac{g_0(\tau)\overbrace{(i_{A1}(t-\tau)+i_{A2}(t-\tau))}^{\text{incidence}}}{\int_0^\infty g_0(\rho)\,(i_{A1}(t-\rho)+i_{A2}(t-\rho))\,d\rho}$$

Results

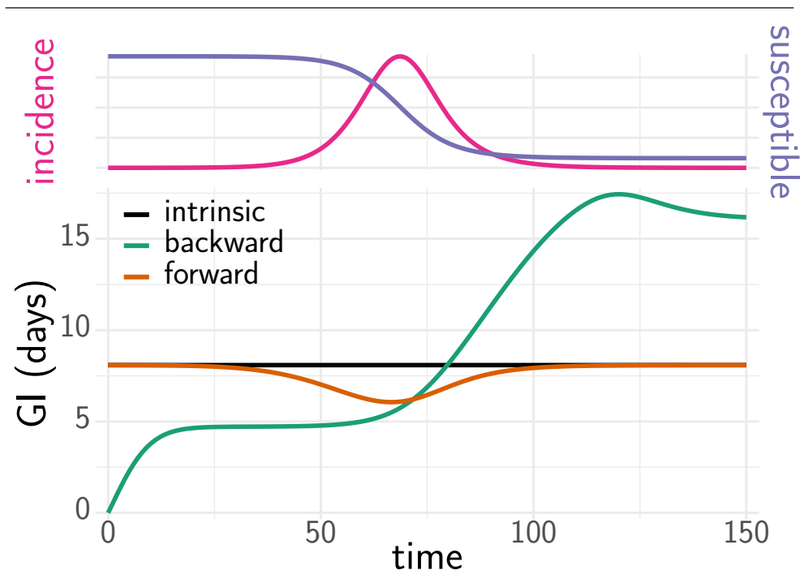

Figure 4. GIs for a single strain model, adapted from Champredon and Dushoff [2].

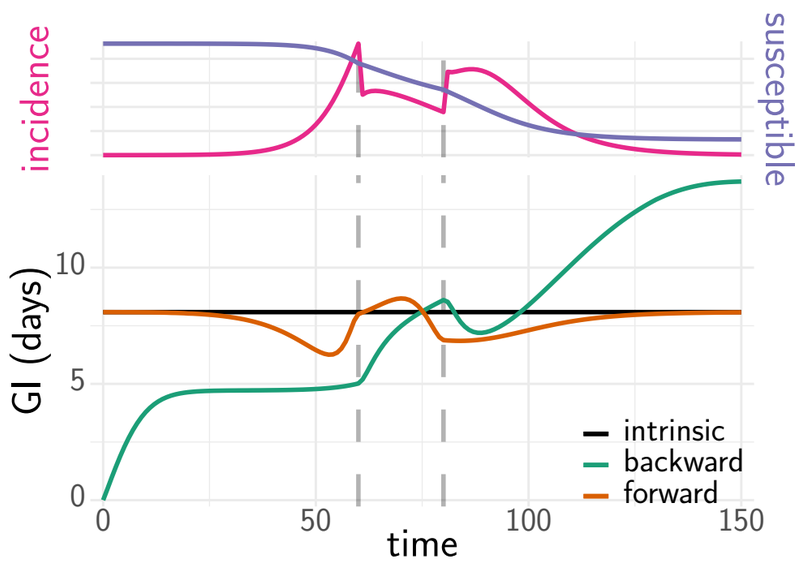

Figure 5. GIs for a single strain model with interventions applied at two time points (dashed vertical lines). At $t = 60$, β is halved, before being restored at $t = 80$.

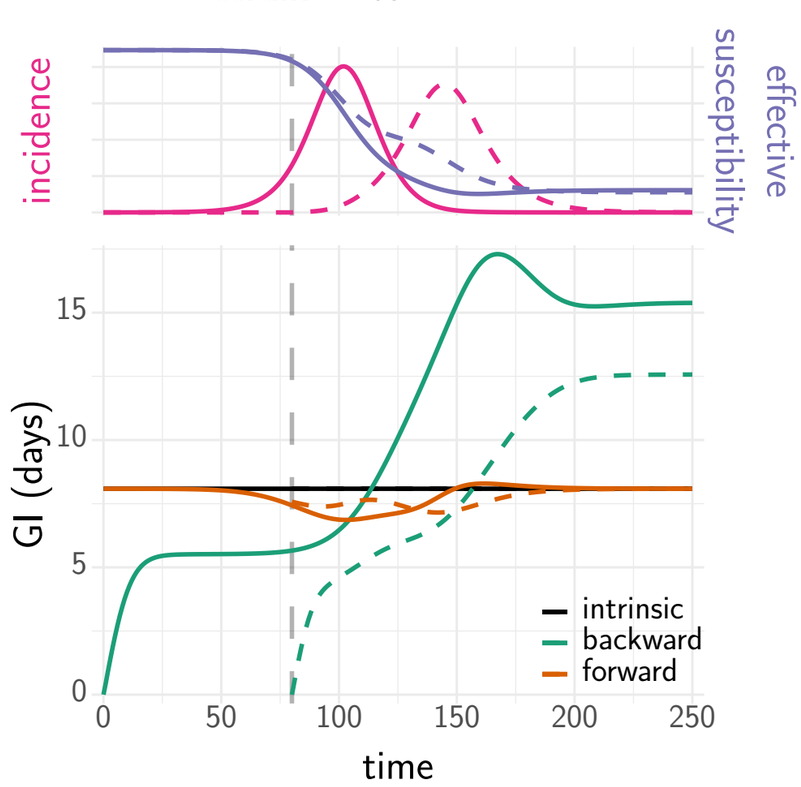

Figure 6. GIs of a two-strain system. At time $t = 80$ (dashed vertical line), strain B emerges in the population. Strain B is 1.8 times more transmissible than strain A.

Discussion and Conclusions

- We have extended previous analyses ([2], [3]) by accounting for changes in β through time, as well as strain emergence.
- We have demonstrated that these changes produce different patterns in the backwards and forwards generation intervals throughout the course of an epidemic.
- The effects of interventions and strain emergence are often not considered in studies that quantify the generation interval from epidemiological data. For instance, Ali et al. [4] attributes changes in the serial interval (often a proxy for the generation interval) entirely to truncation in the generation interval, without acknowledging the inherent effect of intervention.
- Further research to investigate these effects under different scenarios, and to develop estimation methods which account for them, is needed.

References

[1] J Wallinga and M Lipsitch. "How Generation Intervals Shape the Relationship between Growth Rates and Reproductive Numbers". In: *Proceedings of the Royal Society B: Biological Sciences* 274.1609 (22, 2007), pp. 599–604.

[2] David Champredon and Jonathan Dushoff. "Intrinsic and Realized Generation Intervals in Infectious-Disease Transmission". In: *Proceedings of the Royal Society B: Biological Sciences* 282.1821 (22, 2015), pp. 2015–2026.

[3] Hiroshi Nishiura. "Time Variations in the Generation Time of an Infectious Disease:Implications for Sampling to Appropriately Quantify Transmissionpotential". In: *Mathematical Biosciences and Engineering* 7.4 (2010), pp. 851–869.

[4] Sheikh Taslim Ali et al. "Serial Interval of SARS-CoV-2 Was Shortened over Time by Nonpharmaceutical Interventions". In: *Science* 369.6507 (28, 2020), pp. 1106–1109.