

Generation intervals in space

Understanding the effects of spatial and network structure on links between generation interval and growth rate

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Background

- ► Generation interval (GI) measures time between when a person is infected and when that person infects another person
- ▶ GI distribution, $g(\tau)$, plays an important role in linking exponential growth rate, r, and reproductive number, \mathcal{R} , of an epidemic [1]:

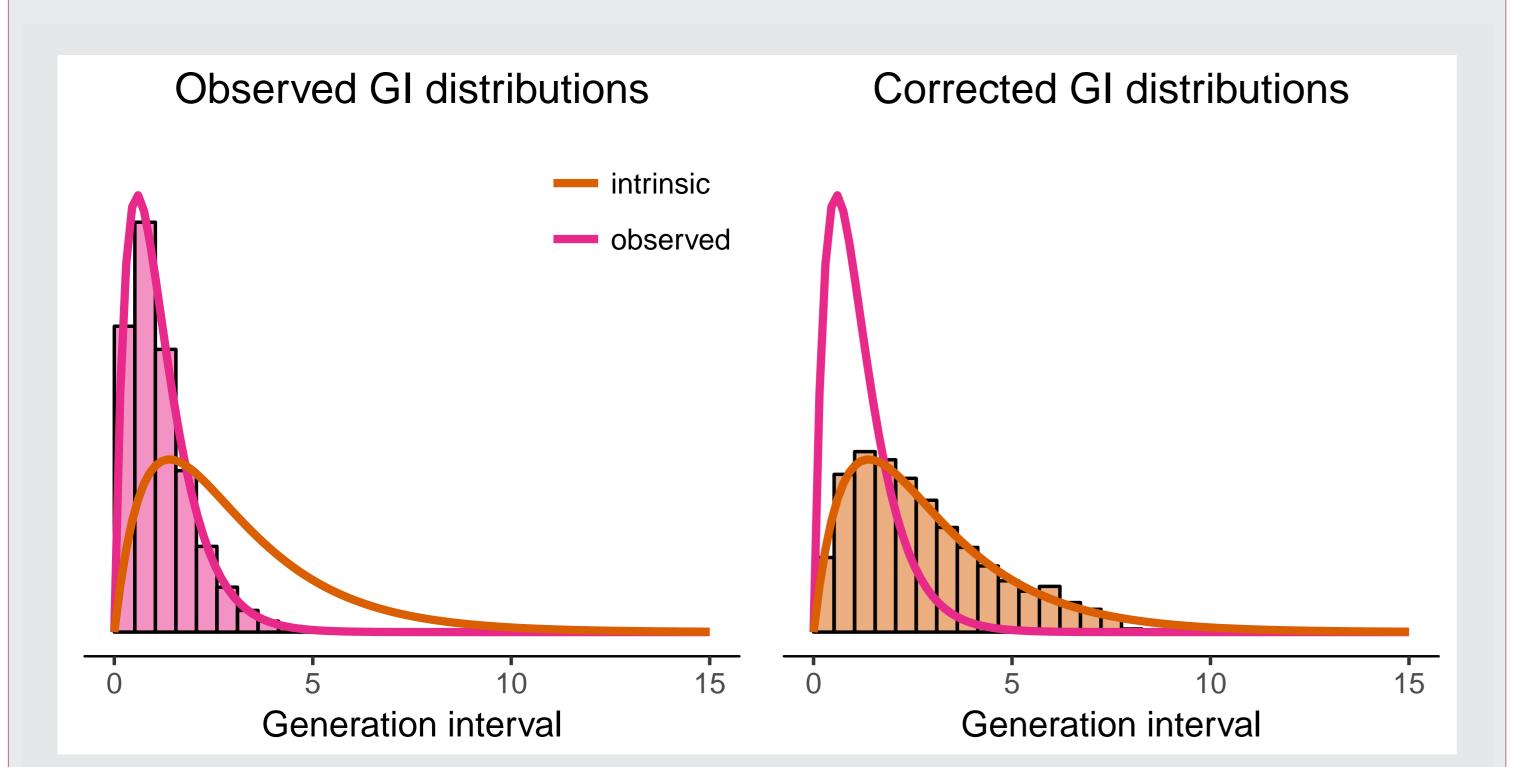
$$1/\mathcal{R} = \int g(au) \exp(-r au) d au$$

- ► Previous work showed that measuring GI through contact tracing data can introduce bias [2]
- ► Trapman *et al.* [3] demonstrated that network structure can affect \mathcal{R} ; ultimately, it changes GI distribution and $r \mathcal{R}$ relationship

Overview Effective GI Locally corrected GI • accounts for spatial (network) • based on degree distribution structure and close contact rate [3] • equivalent to intrinsic GI under homogeneous mixing Exponential correction weight observed periods by $\exp(r\tau)$ Observed GI in early epidemic assumption Intrinsic GI • contact-tracing based • patient based (e.g. titer)

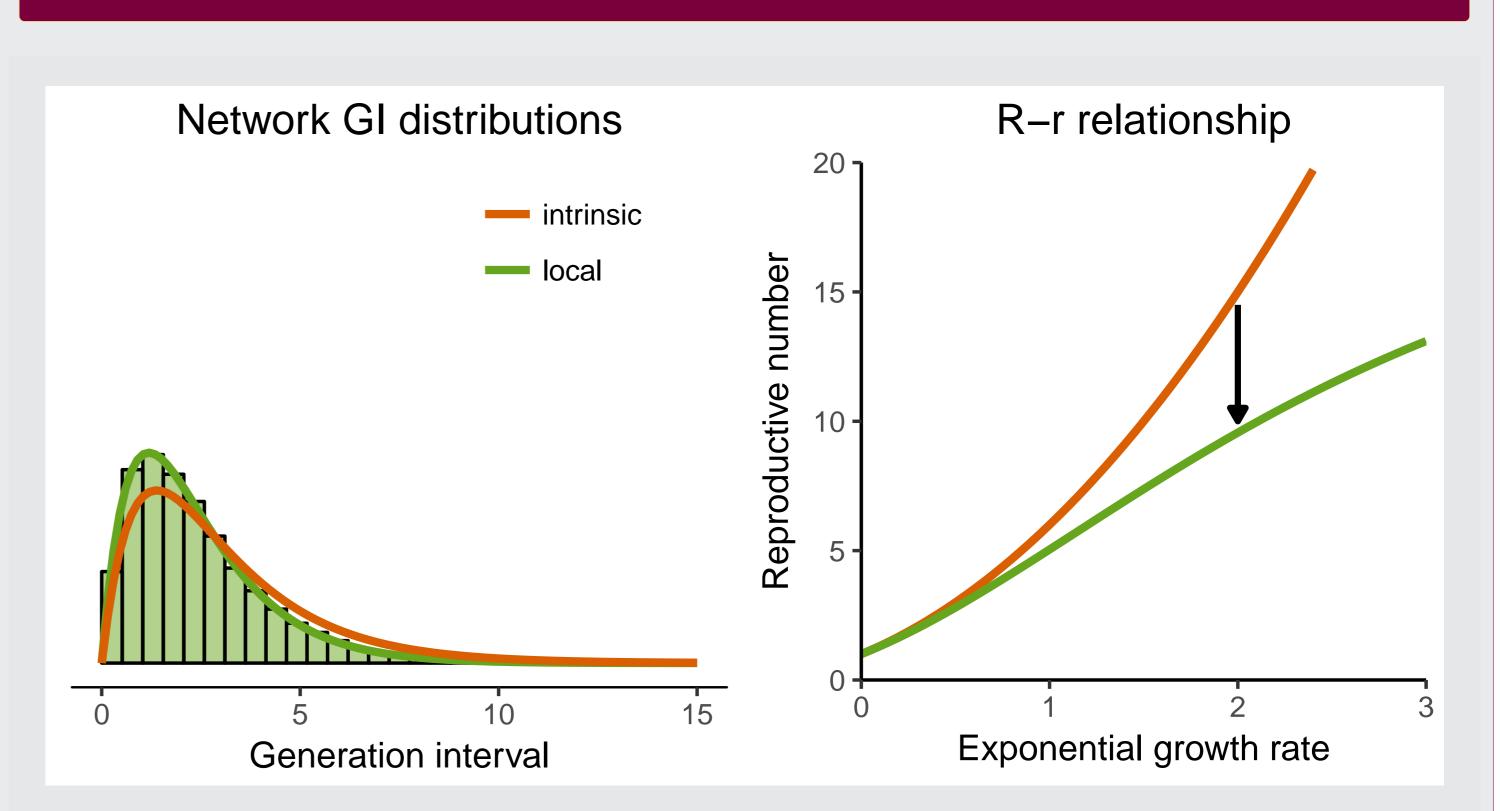
• proportional to $g(\tau) \exp(-r\tau)$

Temporal correction on a homogeneous network



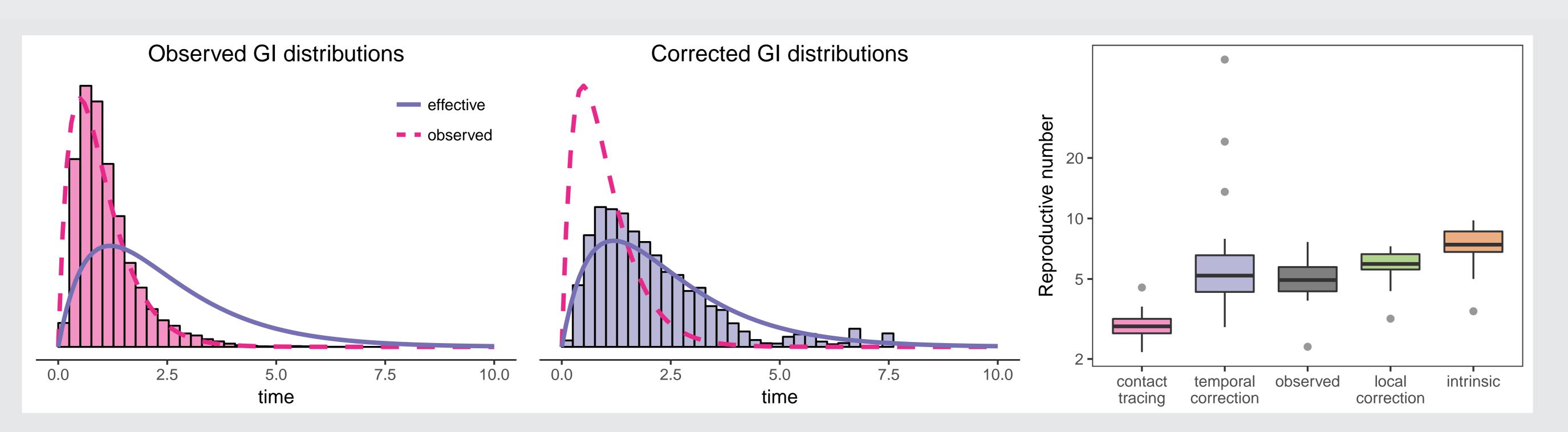
The intrinsic GI distribution can be estimated from observations during an outbreak. During an outbreak, shorter intervals are more likely to be observed (since longer ones may not have completed yet). (Left) Intervals observed during the exponential phase. (Right) The same intervals, but reweighted to remove the sampling bias. These match the known intrinsic GI that was used for the simulations (solid curve). Stochastic SEIR model simulated on a homogeneous network: $\mathcal{R}=6$, mean latent; infectious periods of 1; 2 time units.

Spatial correction on an idealized network



Effects of locality on GI can be calculated in simple cases. Local spatial effects make GIs shorter, because repeated contacts only infect the first time. (Left) Observed GIs from simulations on strictly local networks (close contact rate of 0.2 time⁻¹ per edge). These do not match the known intrinsic GI, but do match the calculated spatial correction. (Right) If a disease is spreading on a network, calculations based on the (longer) intrinsic GI will lead to over-estimates of \mathcal{R} . A simple correction accounts for local effects, but not necessarily other network effects [3].

Simulation on an empirical network



Reproductive number predicted by using the corrected GI distributions matches empirical estimate of the reproductive number. Individual-based observations are expected to overestimate the GI and therefore \mathcal{R} . Contact tracing observations are expected to underestimate the GI and \mathcal{R} . Temporally correcting contact tracing observations yield effective GI and esimate \mathcal{R} similar to observed \mathcal{R} (mean number of individuals infected by first 100 infectees). Stochastic SEIR model simulated on an empirical network [4].

Conclusion and future direction

- ► Gls can be measured in different ways
- ► We can understand how spatial and temporal effects change Gls
- The correct distribution for understanding the link between r and \mathcal{R} differs from both directly measurable distributions (patient-centered and contact-tracing)
- The temporal correction is theoretically sound, but not always statistically robust; more work is needed.

Bibliography

- [1] Jacco Wallinga and Marc Lipsitch. How generation intervals shape the relationship between growth rates and reproductive numbers. Proceedings of the Royal
- Society of London B: Biological Sciences, 274(1609):599–604, 2007.

 [2] David Champredon and Jonathan Dushoff. Intrinsic and realized generation intervals in infectious-disease transmission. 282(1821), 2015.
- [3] Pieter Trapman, Frank Ball, Jean-Stéphane Dhersin, Viet Chi Tran, Jacco Wallinga, and Tom Britton. Inferring r0 in emerging epidemicsthe effect of common population structure is small. *Journal of the Royal Society Interface*, 13(121), 2016.
- [4] Jure Leskovec and Andrej Krevl. 2014 snap datasets: Stanford large network dataset collection. *URL http://snap.stanford.edu/data.*