



Generation intervals in space

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

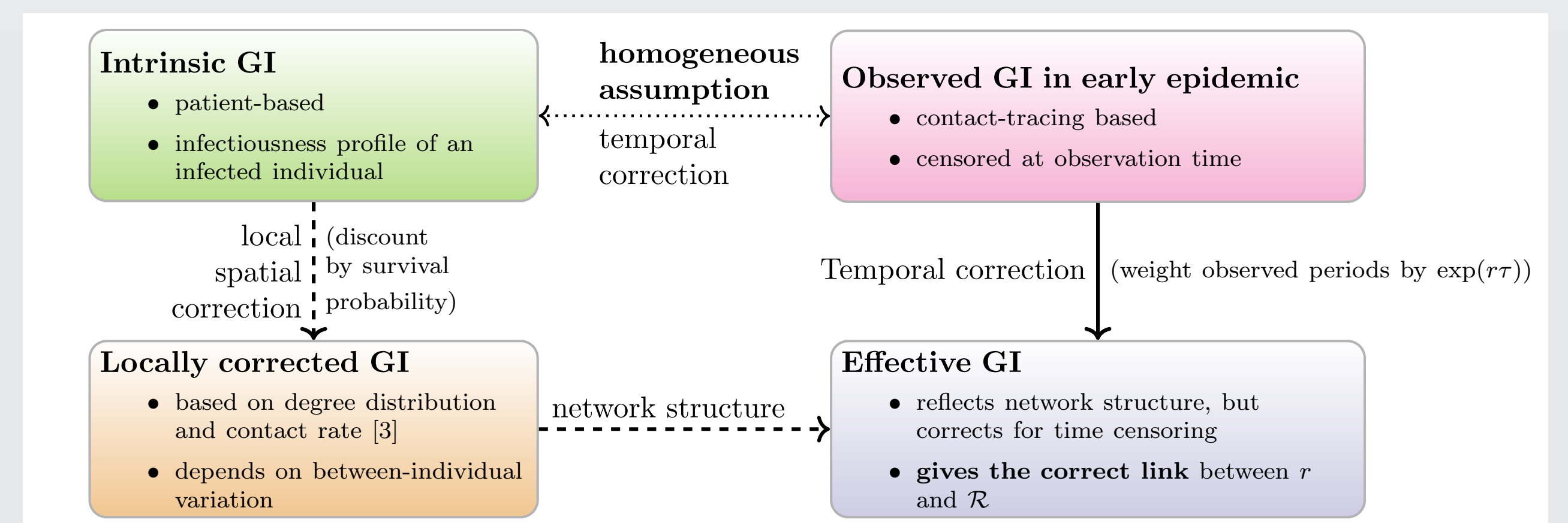
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Background

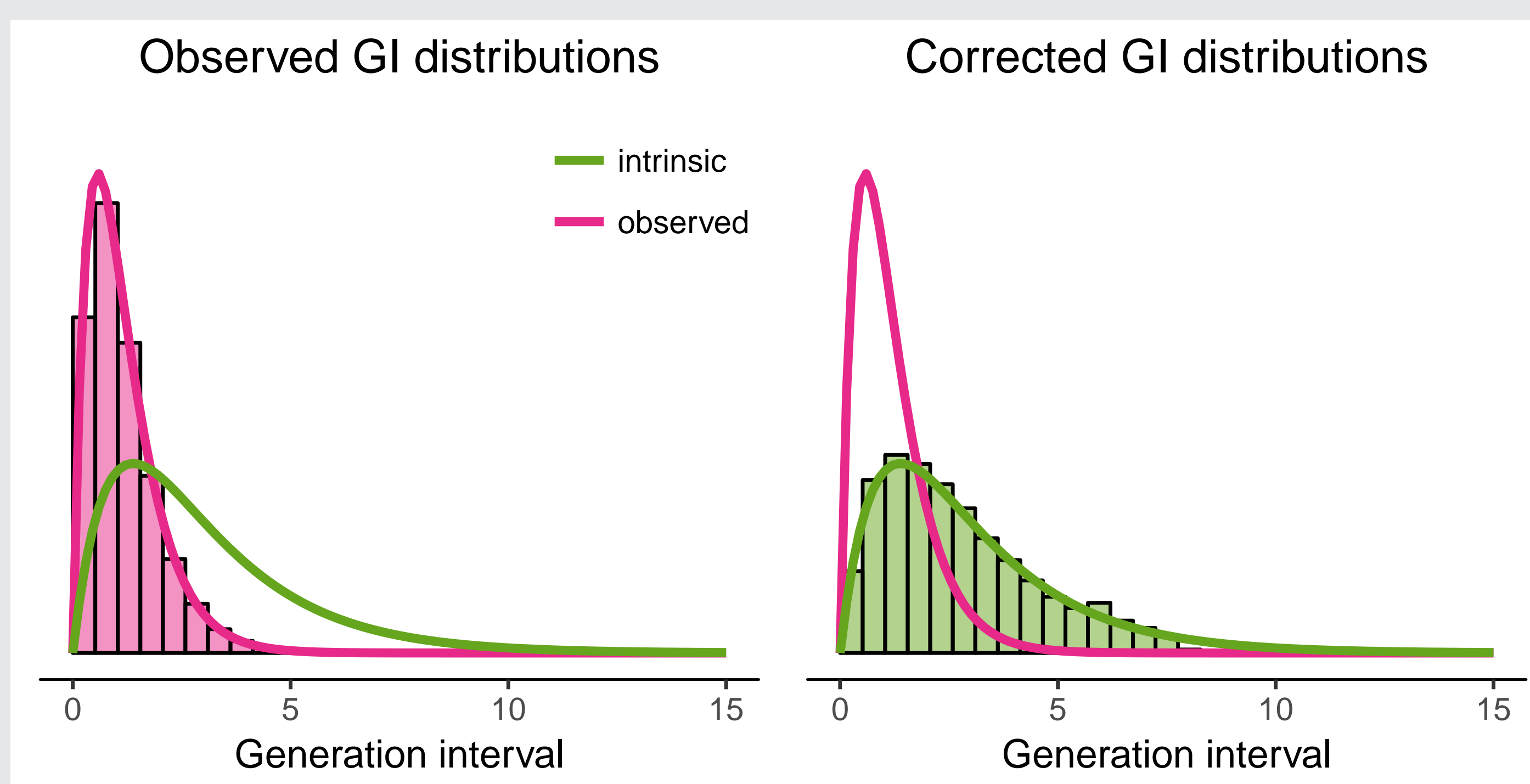
- ▶ Generation interval (GI) measures time between when a person is infected and when that person infects another person
- ▶ GI distribution, $g(\tau)$, links exponential growth rate, r , and reproductive number, \mathcal{R} , of an epidemic [1]: $1/\mathcal{R} = \int g(\tau) \exp(-r\tau) d\tau$
- ▶ If r is known, longer generation times imply higher estimates of \mathcal{R} .
- ▶ Measuring GI through contact tracing data can introduce bias [2]
- ▶ Trapman *et al.* [3] investigated the effects of network structure on the relationship between r and \mathcal{R} .

Overview



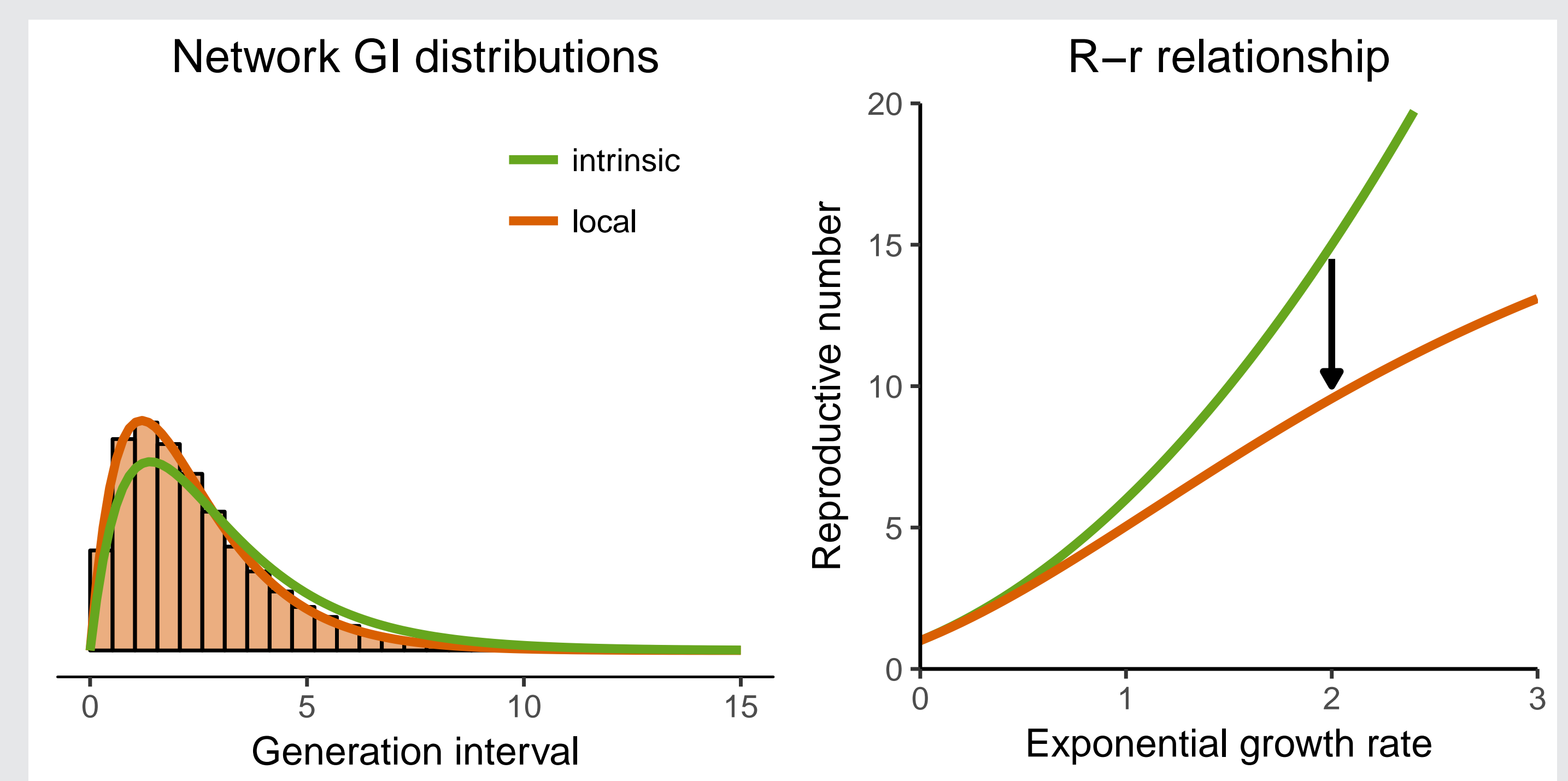
Patient-based GI observations do not account for spatial effects, while contact tracing introduces temporal bias (especially early in outbreaks).

Temporal correction on a homogeneous network



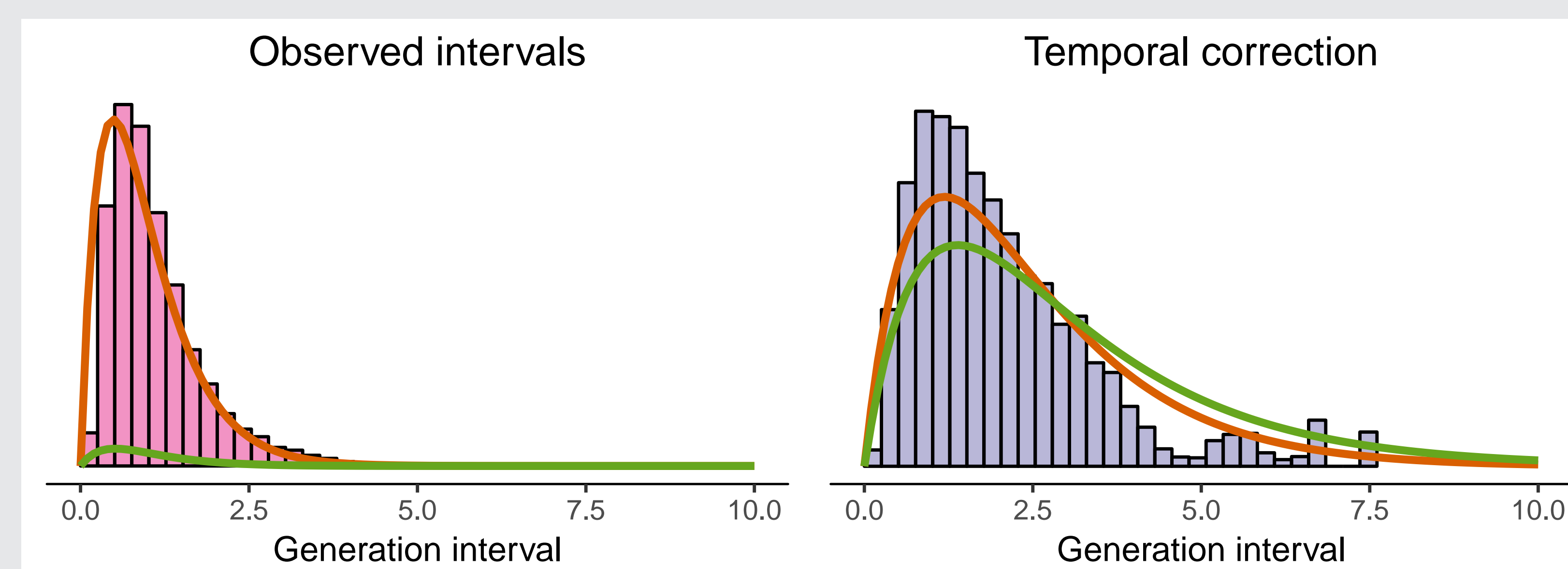
The intrinsic GI distribution can be estimated from observations during an outbreak. During an outbreak, shorter intervals are more likely to be observed (since longer ones may not have completed yet). (Left) Intervals observed during the exponential phase. (Right) The same intervals, but reweighted to remove the sampling bias. Stochastic SEIR simulation on a homogeneous network (histograms) match analytically derived distributions (solid curves). Model parameters: $\mathcal{R} = 6$, mean latent, infectious periods of 1, 2 time units.

Local correction on an idealized network



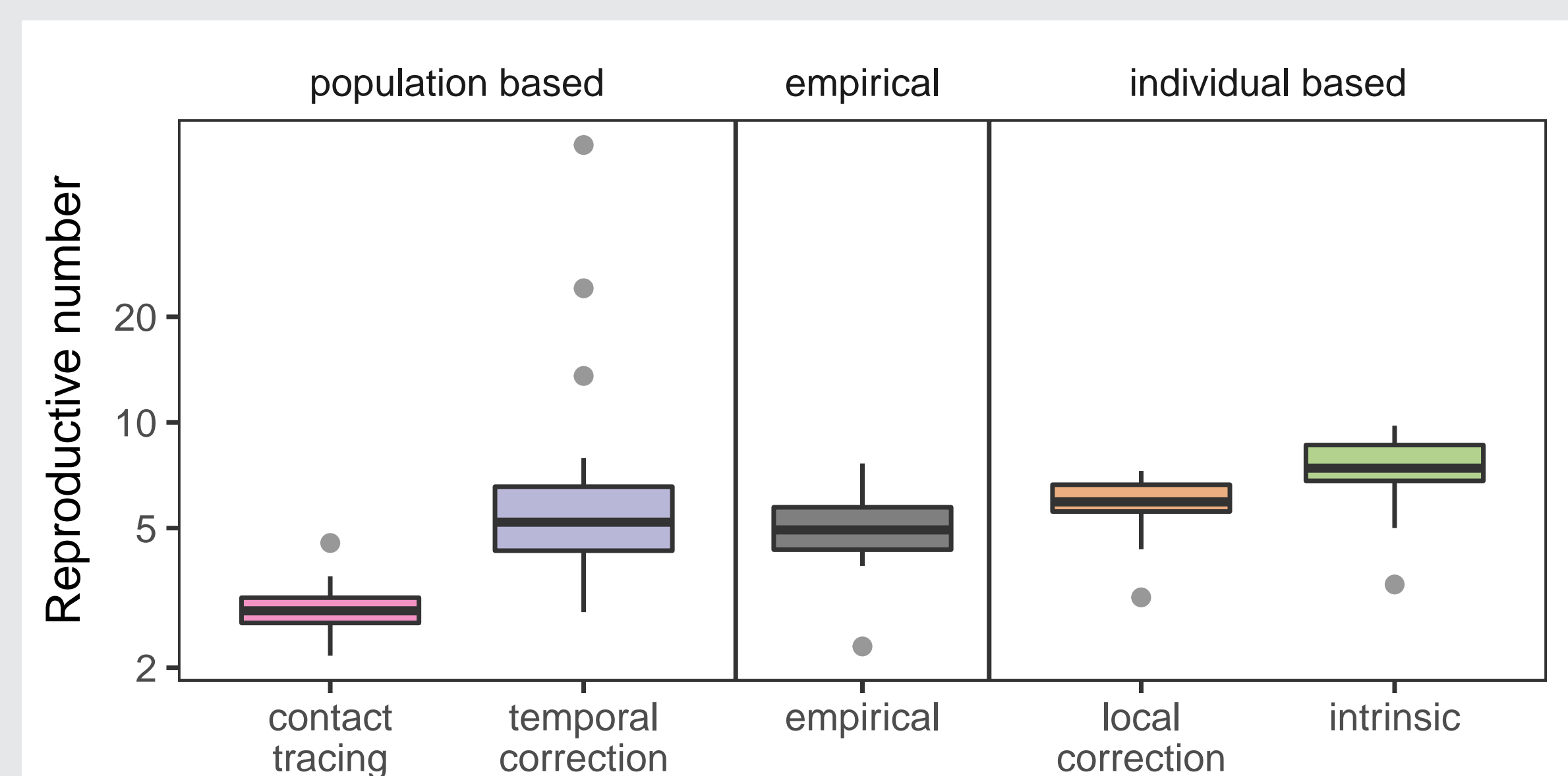
Effects of locality on GI can be calculated in simple cases. Local spatial effects make GIs shorter, because repeated contacts only infect the first time. (Left) Observed GIs from simulations on idealized, strictly local networks. These do not match the known intrinsic GI, but do match the calculated local 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} . The local correction accounts for local effects, but not other network effects [3].

Estimating GIs on an empirical network



Local correction partially accounts for spatial effects on an empirical network [4]. (Left) Early contact-tracing intervals observed in simulation. (Right) Intervals corrected for censoring. The curves show estimates based on the intrinsic GI, with (ORANGE?) and without (GREEN?) the local correction [3]. The local correction requires an estimate of degree distribution, and either an explicit model structure (e.g., SEIR) or information about individual-level variation in infectiousness.

Estimating R on an empirical network



Appropriate corrections improve estimates. Estimates of \mathcal{R} using directly observed GIs either result in under-estimates (contact tracing) or over-estimates (intrinsic). Temporal correction of censored contact-tracing GIs can produce unstable estimates. Local correction of intrinsic GIs [3] is difficult and approximate (previous box).

Conclusion and future direction

- ▶ Different approaches measure different GIs
- ▶ Naive use of intrinsic GI may over-estimate \mathcal{R} , while naive use of contact-tracing GI may underestimate \mathcal{R} . We can understand how spatial and temporal effects change GIs
- ▶ Spatial corrections are difficult, and sensitive to individual variation
- ▶ The temporal correction is theoretically sound, but not always statistically robust

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 Dherain, Viet Chi Tran, Jacco Wallinga, and Tom Britton. Inferring r_0 in emerging epidemics: the 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>.