



# Generation intervals in space

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

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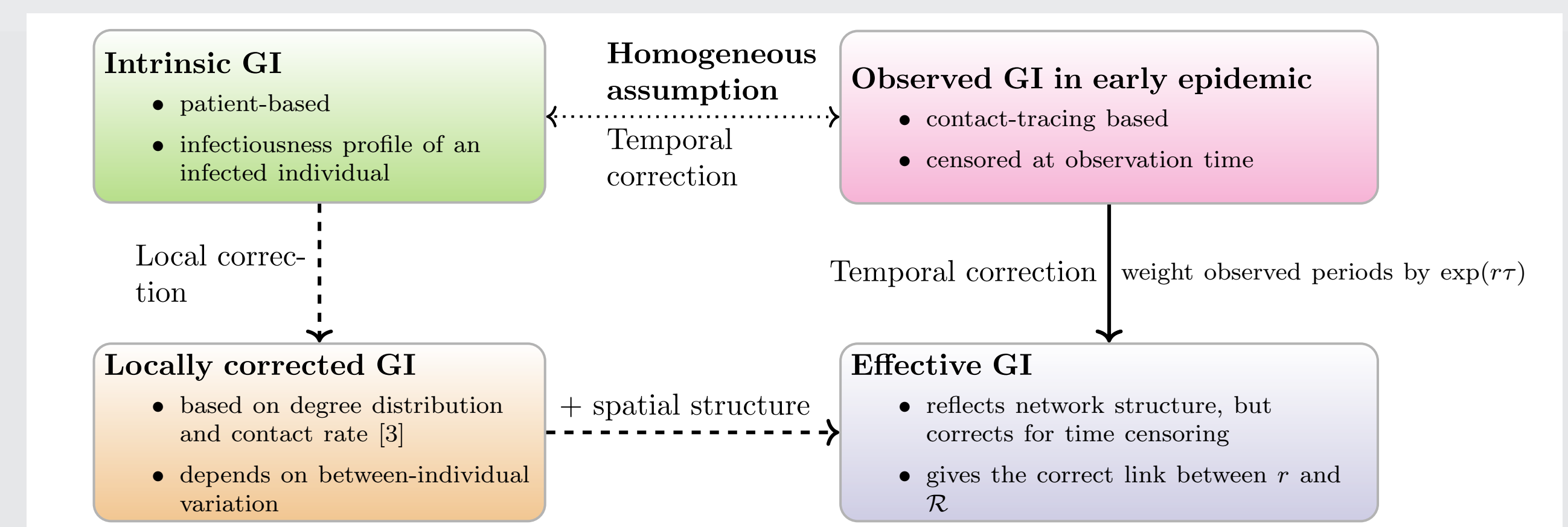
### Background

- ▶ 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]:

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

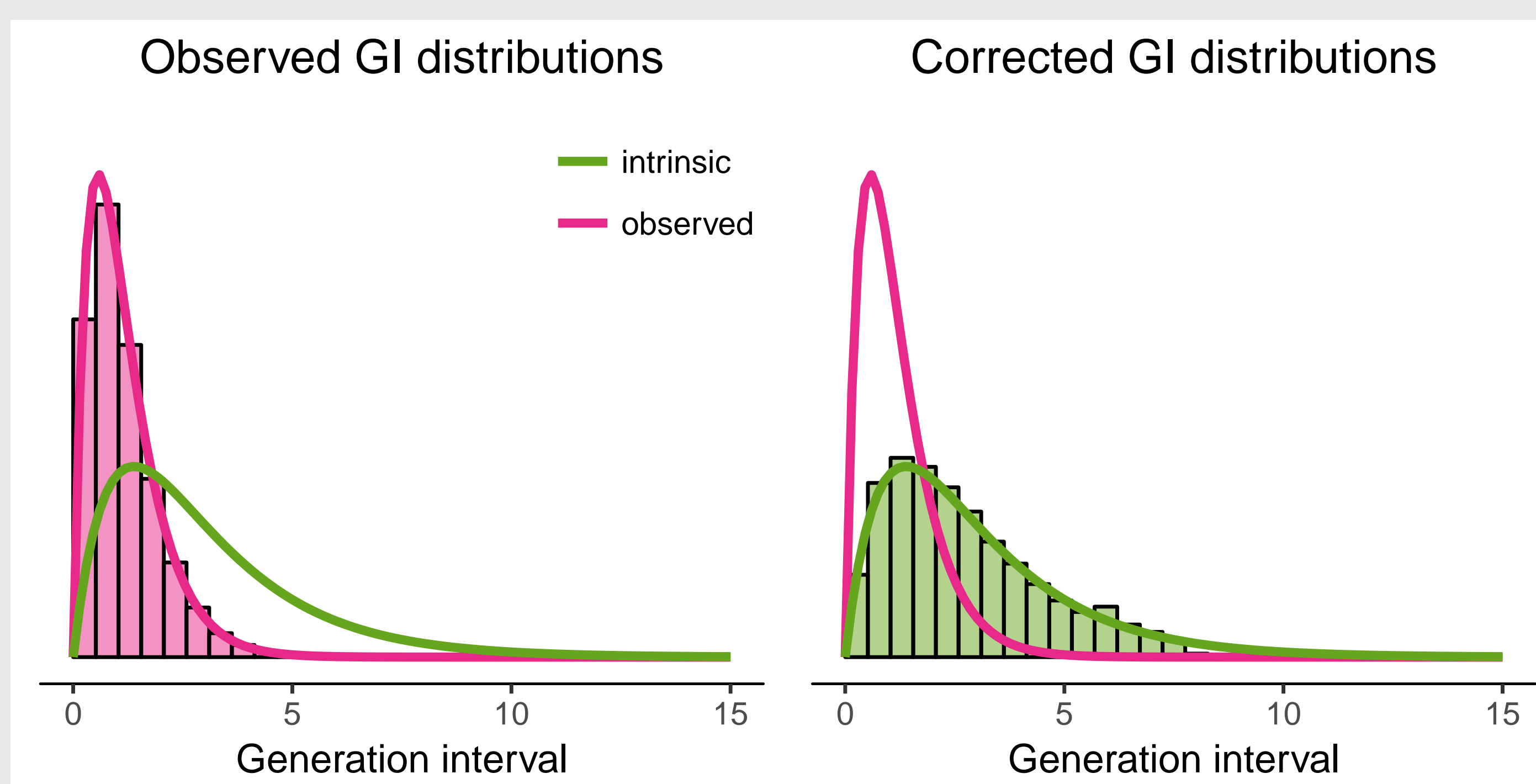
- ▶ Previous work showed that measuring GI through contact tracing data can introduce bias [2]
- ▶ Trapman *et al.* [3] demonstrated that network structure can affect  $\mathcal{R}$ ; ultimately, it changes GI distribution and  $r - \mathcal{R}$  relationship

### Overview



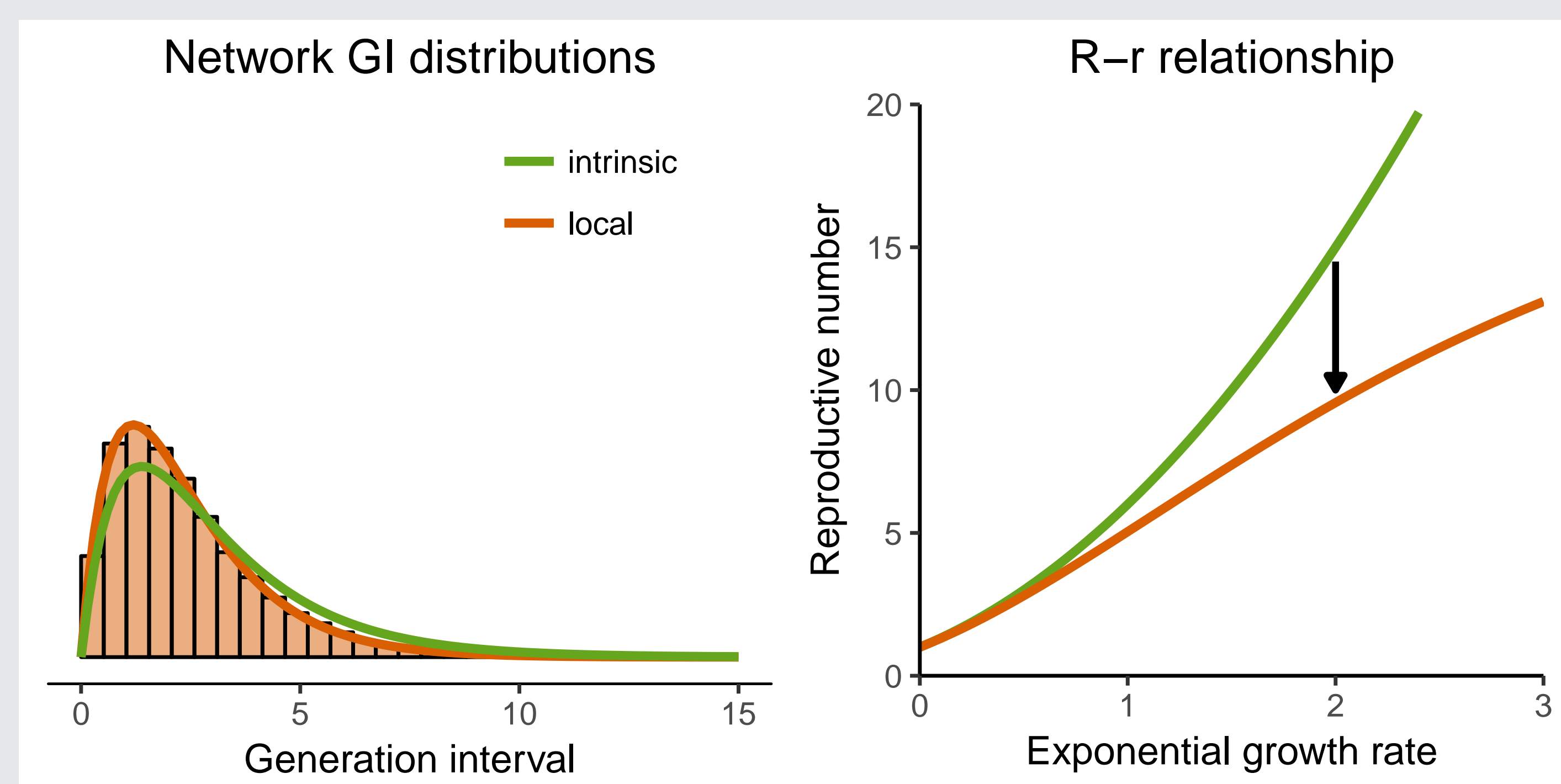
Local correction introduced by [3] accounts for degree distribution but not for any other structures. Observed GIs during an outbreak should implicitly take these structures into account and thus yield effective GIs when corrected for temporal bias.

### Temporal correction on a homogeneous network



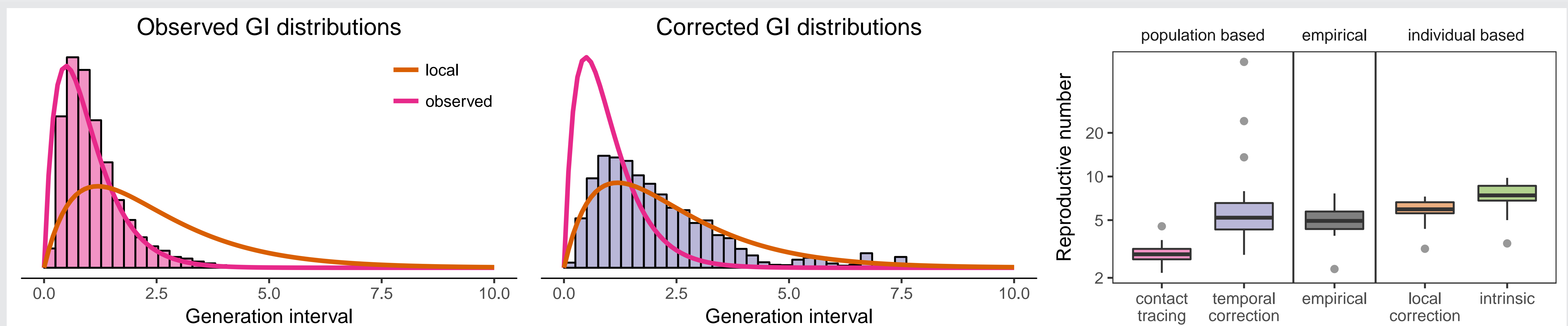
**The intrinsic GI distribution can be estimated from observations during an outbreak.** During an outbreak, shorter intervals are more likely to be observed (since longer ones may not have completed yet). (Left) Intervals observed during the exponential phase. (Right) The same intervals, but reweighted 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.

### 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 (per neighbor contact rate of 0.2  $\text{time}^{-1}$ ). 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 (effective GI) matches empirical estimate of the reproductive number.** (Left) Contact tracing data provides longer GI ( $\approx 1.1$  units; histogram) than predicted GI ( $\approx 1$  unit; solid curve - “observed”) from local correction. (Right) Effective GI ( $\approx 2.1$  units; histogram), obtained by temporally correcting contact-tracing data, is shorter than locally corrected GI ( $\approx 2.4$  units; solid curve - “local”) or intrinsic GI (3 units; not shown). Individual-based observations (intrinsic) are expected to overestimate the GI and therefore  $\mathcal{R}$ . Contact tracing observations (uncorrected) are expected to underestimate the GI and  $\mathcal{R}$ . Temporally correcting contact tracing observations yield effective GI and estimate  $\mathcal{R}$  similar to empirical  $\mathcal{R}$  (mean number of individuals infected by first 100 infectees). Temporally correcting contact tracing data is sensitive to long GIs and can overestimate  $\mathcal{R}$ . Stochastic SEIR model simulated on an empirical network [4].

### Conclusion and future direction

- ▶ GIs can be measured in different ways
- ▶ We can understand how spatial and temporal effects change GIs
- ▶ 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  $r_0$  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>.