MRC Biostatistics Unit

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Bayesian hierarchical regression for SARS-CoV-2 viral load trajectories

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Bayesian inference methods for infectious diseases research workshop

27th March 2023

Question

- How does SARS-CoV-2 viral load vary over individuals and the course of infection?

Dataset

- ATACCC: daily PCR testing of exposed individuals
- Assume that cycle threshold value from PCR is proportional to log viral load
- Max Ct value that can be observed is 40

Analysis here is from a preliminary dataset (unpublished), for a larger dataset with similar analysis see Hakki et al. (2022, Lancet Resp Med)

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Challenges

- Some infections only minimally observed
- Want to generalize to what unseen individuals look like
- False negatives and limit of detection
  - Negative result does not mean absence of virus: could mean too little virus, poor swabbing etc.

Solution

- Hierarchical model: assume that individuals are “similar”
  - Often referred to as “random effects” or “mixed model”
  - Borrows information between individuals
  - After parameters estimated, can simulate unseen individuals
- Bayesian paradigm: natural inclusion of false negative results

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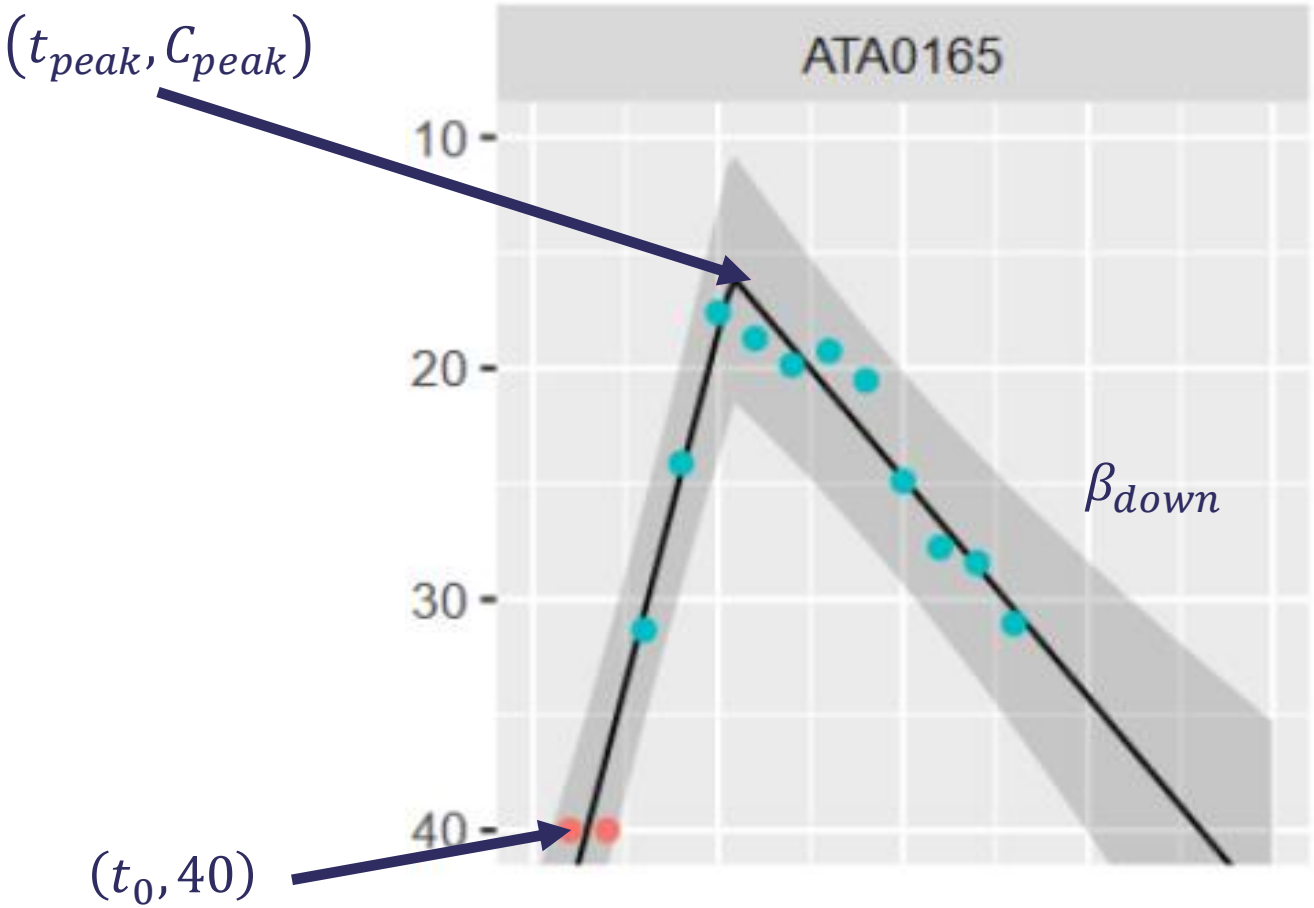
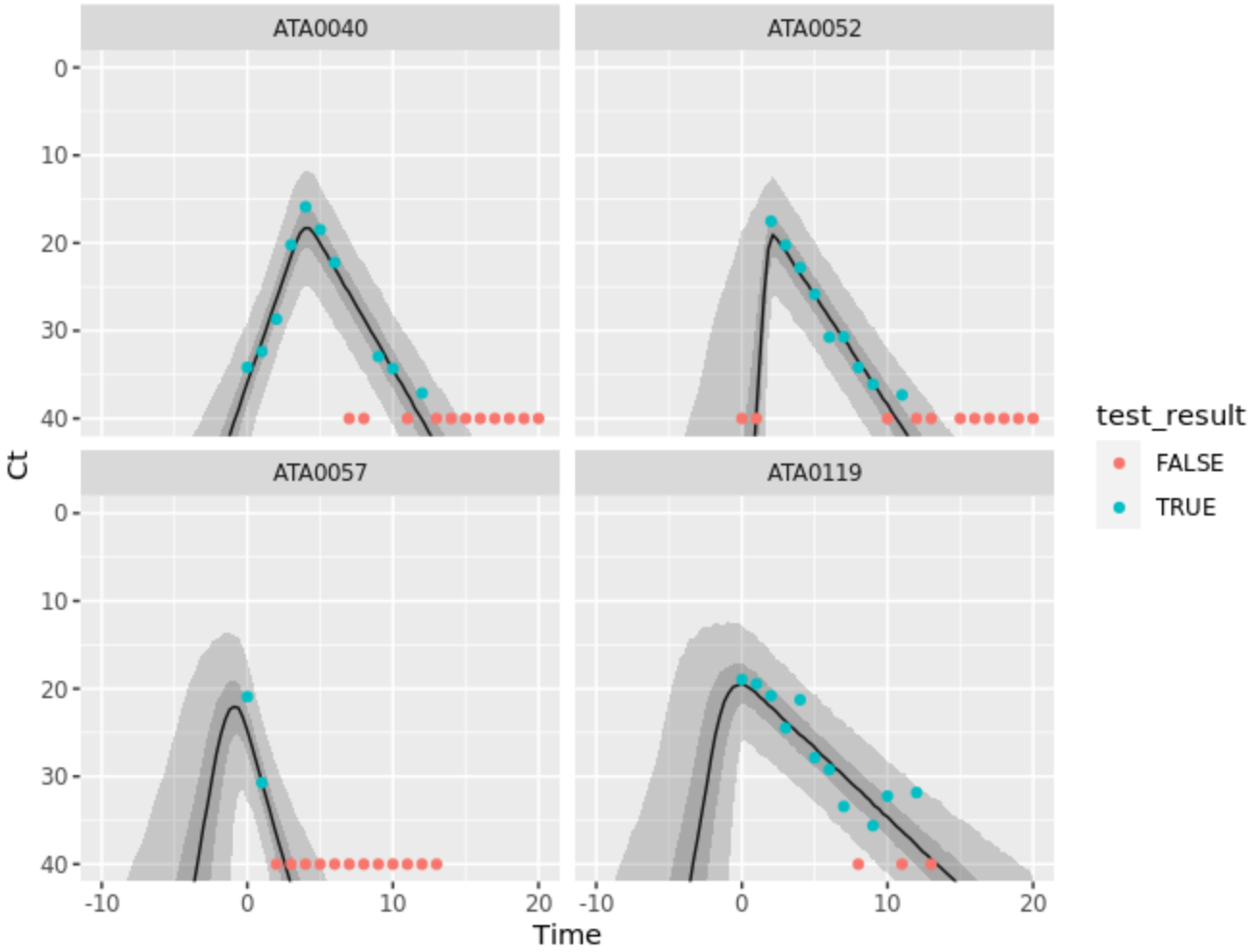
A simple model for viral load



- Piecewise linear model
- Good approximation to more mechanistic ODE-based models

Results



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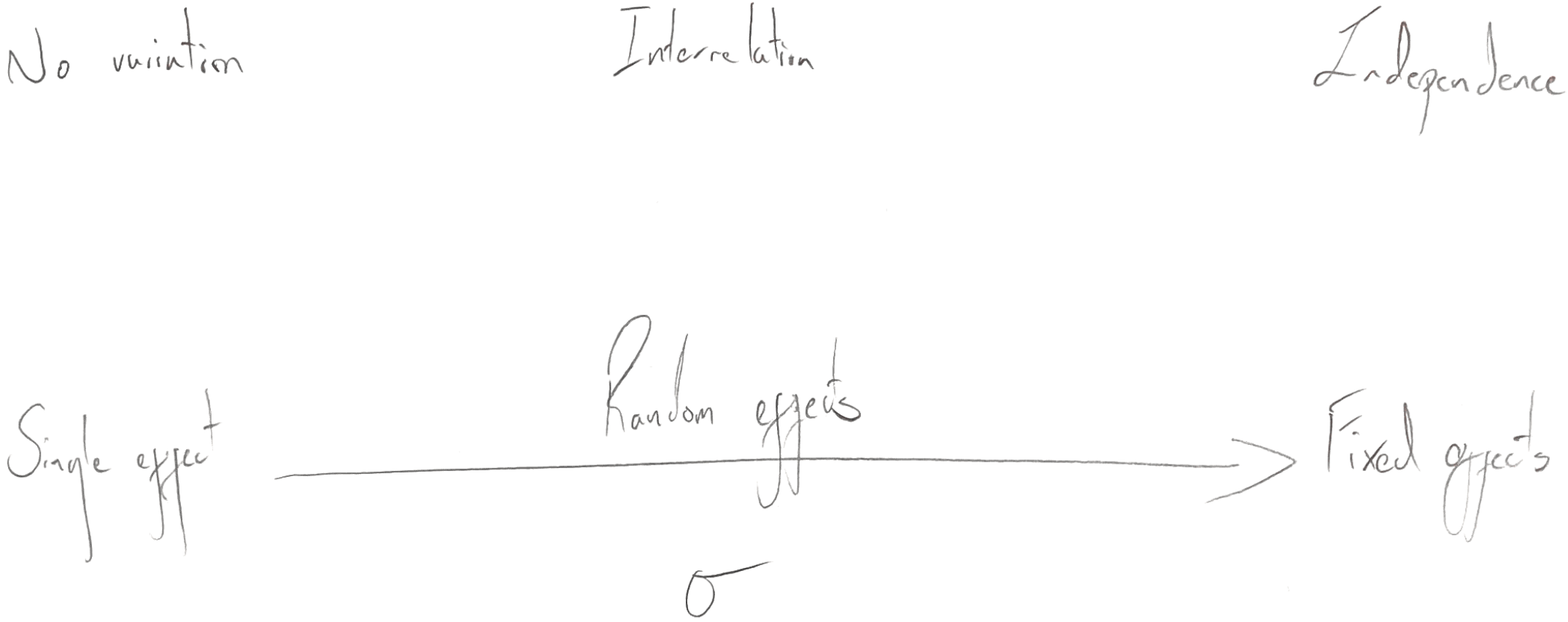
Implementation and today's workshop

- Custom Stan code
  - Allows use of piecewise linear (rather than linear)
  - Custom likelihood for the negatives model
- Modifications for today
  - Use data we have simulated for you
  - Consider just the decline
  - Peak time is time 0
  - Implement in brms: a package for Bayesian linear regression, using Stan on the back-end



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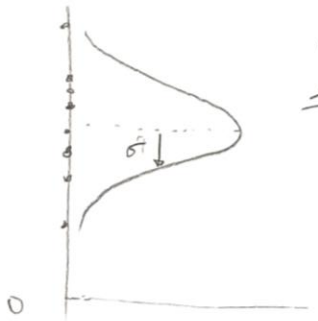
Random Intercept

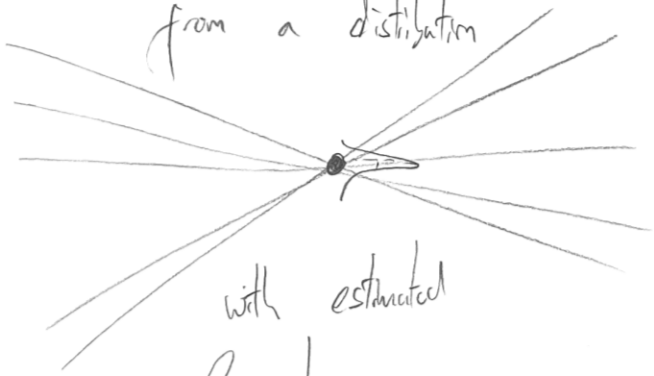


Intercepts are drawn from a distribution with estimated parameters

Generally Gaussian

Random Slopes

Gradients are drawn from a distribution

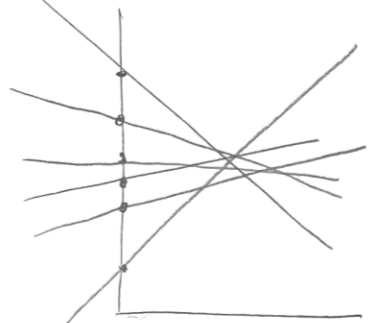


with estimated parameters

Generally Gaussian

Intercepts and slopes may be correlated

Modelled by a joint distribution



Generally multivariate normal