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Bayesian decision-theoretic analysis of thresholds in Gompertz-mixture models, for robust detection of corona-like viruses in wildlife

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Abstract: Serological assays are used in wildlife populations to detect evidence of previous exposure to viruses of interest. In wild populations, it is not known *a priori* whether previously-infected individuals are present. Peel et al. (2013; *J Virological Methods*, 193(2): 295-303) shows that mixture models may describe clusters of serology values among individuals in a population: those previously infected (seropositive), and those never infected (seronegative). A single cluster arises for populations solely comprising seronegative individuals, with low antibody levels (left bump in Fig. 1). Two clusters will be evident for populations comprising both seropositive and seronegative individuals (two bumps in Fig. 1). Three components are rare. These theoretical expectations focus our inference on 1- or 2-cluster mixture models.

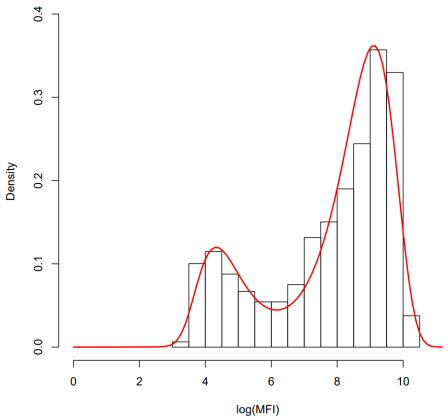

Figure 1. Example fitted Gompertz Mixture (red) and data (histogram)

Our case study considers flying foxes on Christmas Island, near Australia (Pulscher et al., 2022; *Transboundary & Emerging Diseases*, 69(5): e2366-e2377). Interestingly, serology results from some sites were skewed in distribution, so we considered a mixture of Gompertz distributions (Fig. 1, red line), based on the R and C code accompanying Edson et al. (2019; *Epidemiology & Infection,* 147: e240*)*.

For decision-making, ecologists desire a threshold that separates seronegative from seropositive individuals. We tailored Bayesian computation via MCMC to estimate this threshold. A decision-theoretic approach defines the threshold as a parameter in the model, directly simulated at each MCMC iteration. Providing a rich description of uncertainty about the threshold, the posterior distribution can be summarised using a suitable statistic, such as the median posterior threshold together with a credible interval.

In contrast, a widespread practice in wildlife virology adopts a rule-of-thumb, defined as three multiplied by an average of baseline serology values (from assay negative controls). However, when testing procedures are not definitive, the ranges of seronegative and seropositive individuals may overlap (as in Fig. 1). In such cases, the rule-of-thumb may have low specificity, leading to erroneous conclusions that a seropositive individual is seronegative. This false complacency could under-diagnose the extent of viral circulation within a population, with potentially devastating consequences, especially in small populations. We show how a fully Bayesian decision-theoretic approach helps select thresholds, whilst reporting their uncertainty in a meaningful way.

This method is illustrated for different flying fox populations in mainland Australia. The decision-making approach is informed by previous work in plant biosecurity (Low-Choy, 2015, Getting the story straight: Laying the foundations for statistical evaluation of the performance of surveillance, in Jarrad et al. (eds) *Quantitative methods in Biosecurity Surveillance*, CABI). Adopting a Bayesian framework extends these plant biosecurity methods to virology for animal biosecurity, and potentially human biosecurity. Given the known dangers of the *Lyssavirus* in flying foxes transferring to humans, this work also contributes to global efforts to strengthen resilience to pandemics by managing risks of zoonotic transfer of viruses as well as conserving biodiversity for planetary health (Cox & Piccolo, 2020, Environmental health and strengthening resilience to pandemics, *OECD Policy Responses to Coronavirus (COVID-19),* oecd.org/coronavirus).

Keywords: *Bayesian statistical model, Bayesian decision theory, Shifted Gompertz distribution, wildlife disease ecology, model diagnostics, false complacency*