

# Manuscript outline/draft

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## Introduction

The goal is a *brief* (if possible) pedagogically oriented paper, aimed at biomathematicians/students coming for the first time to the idea of fitting curves to epidemic models. Without going too deeply into any one area (likelihood theory, optimization, ...), we aim to provide a primer and pitfall-avoidance guide for fits of simple ODE models (focusing particularly on SIR models) to epidemic data.

## Potential topics

**trajectory-matching vs. gradient-matching** what's the difference? when does it matter? (this paper will focus on trajectory matching) (Ellner et al., 2002; Bolker, 2008)

**early-epidemic vs. whole-epidemic** lots of work on fitting early epidemics, e.g. Chowell et al. (2007), Ma et al. (2014); that's not what we're doing here ... also, we're only going to discuss general principles here, focus on simple SIR (maybe comment on SEIR), but not worry about extensions (waning immunity, Ebola/funeral-transmission ... etc.)

**prevalence vs. incidence** : need to distinguish these cases (typical cases will involve incidence data). Comment on pitfalls of cumulative-incidence approaches (Chowell) without appropriate corrections (maybe discussed elsewhere? King et al. (2015) ?) (Do we need to worry about mortality vs. incidence??)

**least-squares vs. likelihood formulations** equivalence of least-squares and likelihood approaches; advantages of likelihood in providing a framework for inference (confidence intervals). Mention Wald vs likelihood profile CIs.

**optimization issues** multiple maxima (if they exist?); ridges (Polansky et al., 2009). Optimization frameworks (e.g. Nelder-Mead vs quasi-Newton); integrating on  $\log(I)$  scale; sensitivity equations (Raue et al., 2013). Starting points (auto-start methods)

**identifiability/estimability issues** (still in progress!) expected difficulties in optimization, especially with vague starting points. Something about solutions ... fixing parameters (with attendant dangers; Elder et al. (2006). Bayesian priors, bounds ... ?

**advanced methods** *brief* pointers to relevant literature here. Dealing with combined process/measurement error (King et al., 2015); iterated filtering, TSIR, etc.. Bayesian methods (Stan, `debInfer`, ...)

## To do

- what shall we use as a case study? sims; but also some real data set (pref. \*not\* Bombay data set, because of Bacar (2012) ...)

## References

- Bacar, N. (2012, February). The model of Kermack and McKendrick for the plague epidemic in Bombay and the type reproduction number with seasonality. *Journal of Mathematical Biology* 64(3), 403–422.
- Bolker, B. M. (2008). *Ecological Models and Data in R*. Princeton, NJ: Princeton University Press.
- Chowell, G., H. Nishiura, and L. M. Bettencourt (2007, February). Comparative estimation of the reproduction number for pandemic influenza from daily case notification data. *Journal of The Royal Society Interface* 4(12), 155–166.
- Elder, B. D., V. M. Dukic, and G. Dwyer (2006, October). Uncertainty in predictions of disease spread and public health responses to bioterrorism and emerging diseases. *Proceedings of the National Academy of Sciences* 103(42), 15693–15697.
- Ellner, S. P., Y. Seifu, and R. H. Smith (2002). Fitting population dynamic models to time-series data by gradient matching. *Ecology* 83(8), 2256–2270.
- King, A. A., M. D. d. Cells, F. M. G. Magpantay, and P. Rohani (2015, May). Avoidable errors in the modelling of outbreaks of emerging pathogens, with special reference to Ebola. *Proc. R. Soc. B* 282(1806), 20150347.
- Ma, J., J. Dushoff, B. M. Bolker, and D. J. D. Earn (2014). Estimating Initial Epidemic Growth Rates. *Bulletin of Mathematical Biology* 76(1), 245–260.
- Polansky, L., P. de Valpine, J. O. Lloyd-Smith, and W. M. Getz (2009, August). Likelihood ridges and multimodality in population growth rate models. *Ecology* 90(8), 2313–2320.

Raue, A., M. Schilling, J. Bachmann, A. Matteson, M. Schelke, D. Kaschek, S. Hug, C. Kreutz, B. D. Harms, F. J. Theis, U. Klingmüller, and J. Timmer (2013, September). Lessons Learned from Quantitative Dynamical Modeling in Systems Biology. *PLOS ONE* 8(9), e74335.