Prediction and inference for epidemic models using likelihood-based methods

2nd New Zealand Workshop on Uncertainty Quantification and Inverse Problems

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Outline

1. Epidemic Models (brief)

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2. Circumventing Forward Model Simulations

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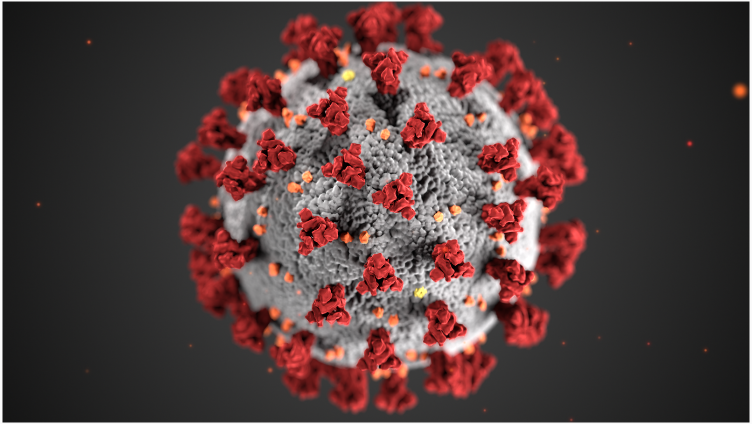
3. Likelihood-based UQ techniques
4. Case Study

Epidemic Modelling

Epidemic modelling is a *severely neglected* field of applied mathematics, due to its *low economic and societal impacts*.



https://www.fda.gov/files/Coronavirus_3D_illustration_by_CDC_1600x900.png

Various ways to model epidemic outbreaks:

- Phenomenological Models
- Deterministic ODEs
- Stochastic SDEs
- Branching Processes
- Agent-based Simulations

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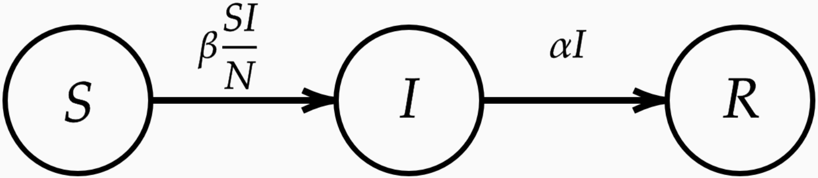
SIR Model



$$\frac{dS}{dt} = -\beta\frac{SI}{N}$$
$$\frac{dI}{dt} = \beta\frac{SI}{N} - \alpha I$$
$$\frac{dR}{dt} = \alpha I$$

Deterministic ODE Models

In general:

$$y = g(x) + \epsilon$$
$$\frac{dx}{dt} = f(x; \theta)$$

Two sources of information:

- the data, y
- the differential equation model, f

How do we use both?

Traditional Methods

Integrate the differential equation for proposal θ

$$\theta \xmapsto{\frac{dx}{dt} = f(x;\theta)} x$$

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$$x(\theta) \xmapsto{y=g(x)+\epsilon} p(y|\theta)$$

Then apply your chosen statistical philosophy to this likelihood

$$p(y|\theta) \xmapsto{\text{magic}} \text{results}$$

Gradient Matching/2-stage NLS

If we had some estimate of x, we could find an estimate of θ pretty easily, without inegration:

$$\frac{d}{dt}x_{\text{est}} = f(x_{\text{est}}; \theta)$$

Gradient Matching/2-stage NLS

If [...]thout

in[...]

We[...]

An example of G

We can do this, for example, using smoothing splines.

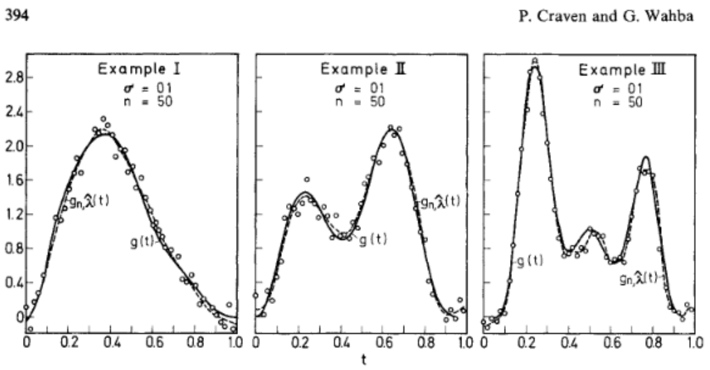

Fig. 2. Examples I, II, and III, $g, g_{n,\hat{\lambda}}$, and the data

from Craven and Wahba (1979), Smoothing Noisy Data with Spline Functions, Numer. Math, 31,377-403

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If we can't find an appropriate G (e.g. when the x is only partially observed), then we cannot use this method.

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We can get around that restriction, if we estimate both x and θ simultaneously.

The differential equation "makes up for" the data we are missing.

Generalised Profiling

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The differential equation "makes up for" the data we are missing.

Can project x onto some smooth basis ($x = \Phi c$), to reduce the dimension of the problem.

Generalised Profiling

Two-level process:

Inner: for a given θ, compute a optimal smooth $\hat{c}$

$$\hat{c}(\theta) = \min_{c|\theta} \left\{ \|y - g(\Phi c)\|^2 + \lambda \left\| \frac{d}{dt}(\Phi c) - f(\Phi c, \theta) \right\|^2 \right\}$$

Outer: Optimise over θ, using the inner to eliminate nuisance parameters (c)

$$\min_{\theta} \left\{ \|y - g(\Phi \hat{c}(\theta))\|^2 \right\}$$

Aside: Profile Likelihood

Given a likelihood:

$$\mathcal{L}(x_1, x_2)$$

Marginal likelihood:

$$\mathcal{L}_{X_1}(x_1) = \int \mathcal{L}(x_1, x_2) dx_2$$

Profile likelihood:

$$\mathcal{L}_{P,X_1}(x_1) = \max_{x_2} \mathcal{L}(x_1, x_2)$$

Aside: Profile Likelihood

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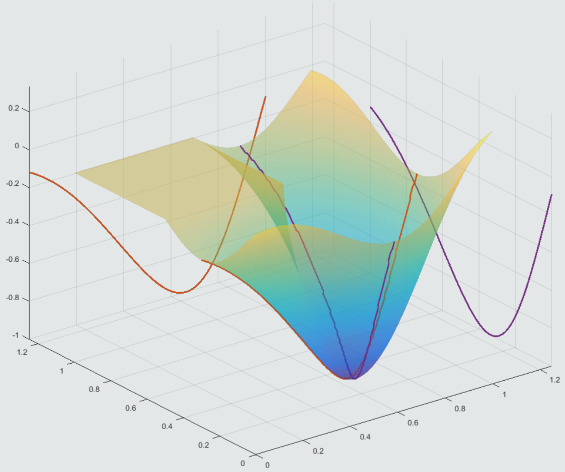
Profiling



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The profile likelihood is more natural under a frequentist lens, since the maximum likelihood estimator is left unchanged:

$$\max_{x_1, x_2} \mathcal{L}(x_1, x_2) = \max_{x_1} \mathcal{L}_{P,X_1}(x_1)$$

GP Likelihood we need a better name

The generalised profiling method feels a lot like taking the profile likelihood of the inner objective.

Using ideas from mixed estimation (Theil & Golberger 1961), we can motivate the inner objective as a likelihood.

$$\mathcal{L}(\theta, c) = \left\| L(y - g(x)) \right\|^2 + \left\| W \left(\frac{d}{dt}(\Phi c) - f(\Phi c; \theta) \right) \right\|^2$$

*Can also add regularisation to this in a justified manner

GP Likelihood

$$\mathcal{L}(\theta, c) = \left\|L(y - g(\Phi c))\right\|^2 + \left\|W\left(\frac{d}{dt}(\Phi c) - f(\Phi c; \theta)\right)\right\|^2$$

Also estimating covariances $(LL^T)^{-1}, (WW^T)^{-1}$.

Can't do this all at once, so choose to use an iterative method (iteratively reweighted least squares).

1. Estimate (x, c) for a fixed (L, W).
2. Estimate (L, W) for a fixed (x, c).
3. Return to Step 1.

UQ (Likelihood-based)

We can optimise the (log-)likelihood to get a point estimate (the MLE).

We really also want confidence sets to go with this.

Profile Likelihood

Claim: The likelihood contains all the information about the uncertainty in the problem.

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All we need to do is to understand the behaviour of the likelihood with respect to quantities of interest.

Profile likelihood is a good way of doing this.

Also gives us information about identifiability.

Bootstrapping

If we have model $y = X(\theta) + \epsilon$, and we estimate MLE as $\hat{\theta}$ and the error as e, we can get an idea of the uncertainty in the estimate by sampling from fits of θ_{BS} for realisations of e.

$$X(\hat{\theta}) + e = X(\theta_{BS})$$

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$$X(\hat{\theta}) + e = X(\theta_{BS})$$

We can also use the randomised maximum likelihood interpretation of this, and sample from the perturbed data instead:

$$y + e = X(\theta_{RML})$$

Case Study

Case Study: 2019 Samoan Measles Outbreak

Measles outbreak in the small South Pacific island nation of Samoa

- September 2019 – January 2020
- Over 5700 cases (pop. 200 000)
- 83 deaths
- Anomalously low vaccination coverage in infants
    - 40% MCV1
    - 28% MCV2

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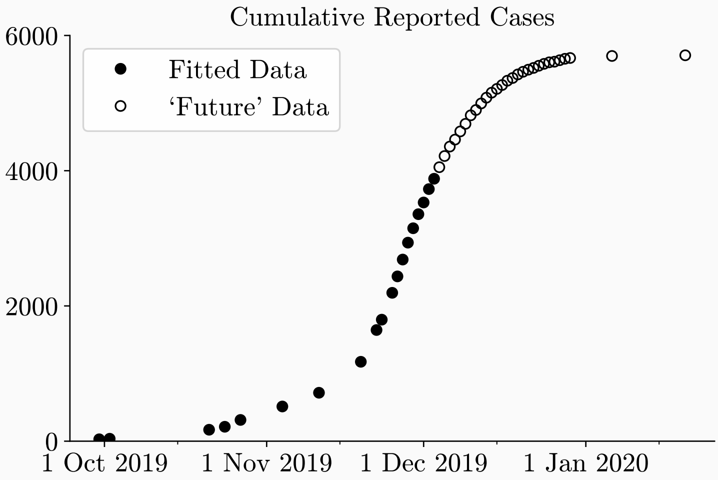

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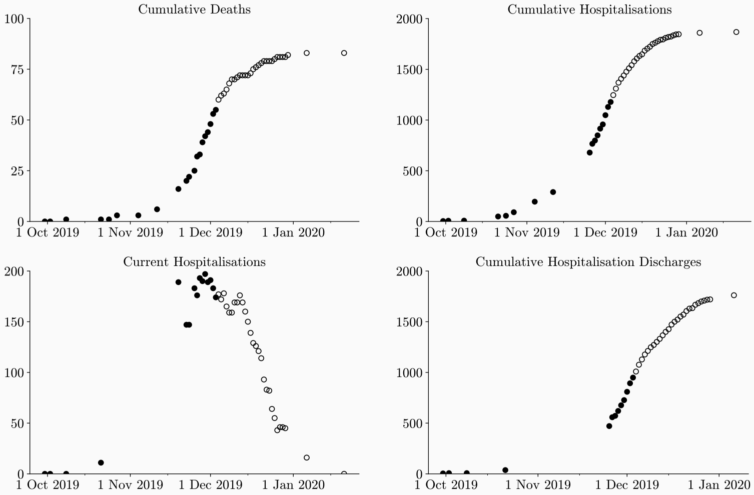
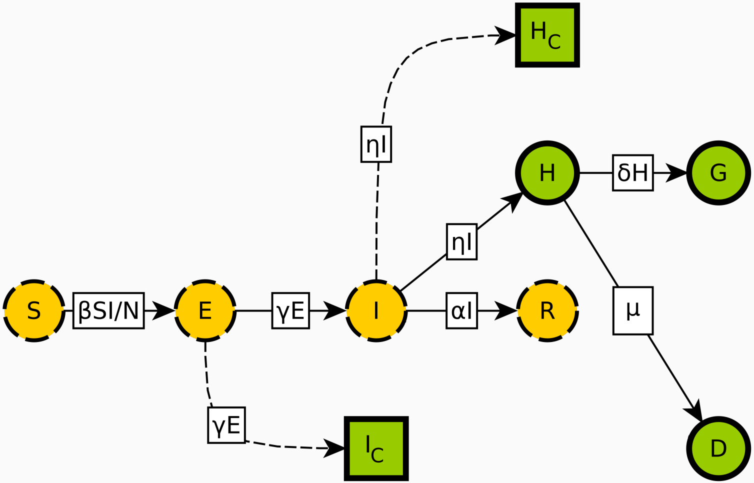
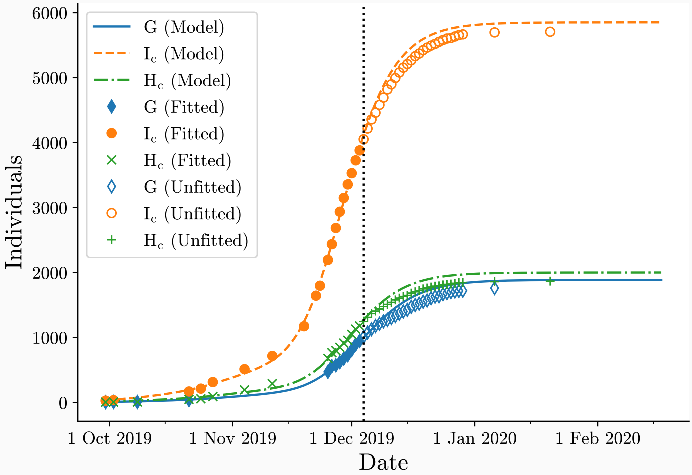


Case Study: Model



Case Study: Results (MLE)



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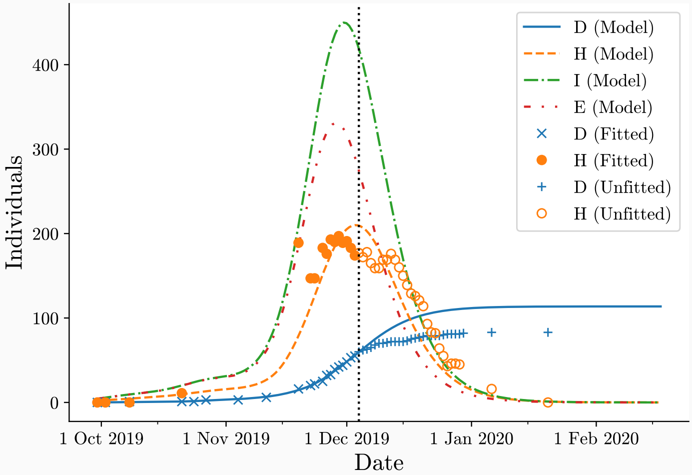
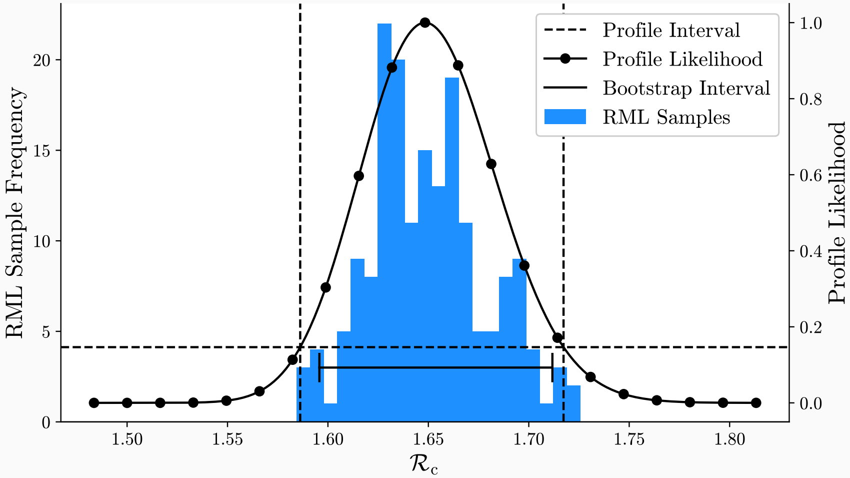


Case Study: Results (UQ)



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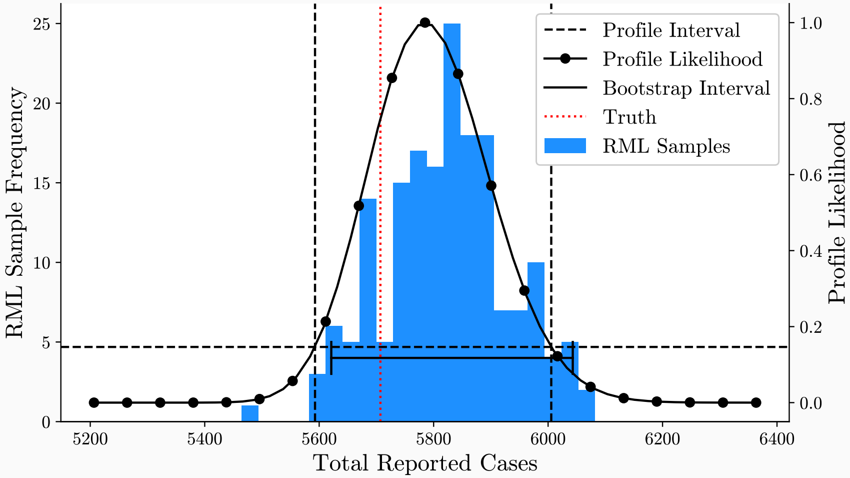

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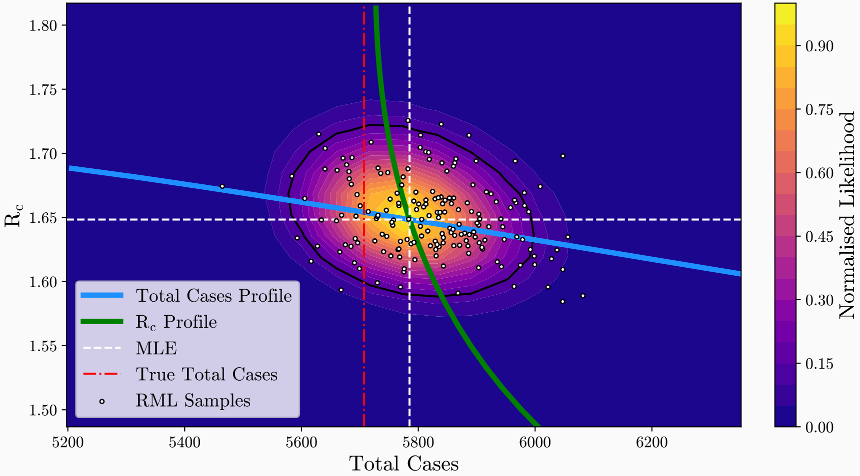

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Closing Remarks

- Can avoid the integration/forward problem solve step by estimating the state and the parameters simultaneously
- There exist frequentist methods (profile likelihood, bootstrapping) to perform UQ on likelihood formulations
- This all seems to work on a case study of real outbreak data
- Though there is some tuning that needs to be done by hand

Thanks for coming!

Questions?

arXiv: 2103.16058

References

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