Fast ODE Parameter Estimation Using Gaussian Processes

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1. Introduction

Ordinary differential equations (ODEs) are often used to **model biological processes** in Systems Biology.
Characteristically, ODEs have a number of **unknown parameters** that need to be **inferred from the observed data**.

2. Problem

"Traditional" parameter estimation methods involve

1. **simulating from the model** using a trial set of parameters,
2. seeing how the simulated and real data match up
3. **repeating** the steps above with adjustments to the parameters, **until a desirable fit is achieved**.

The main disadvantages are:

- The estimation **process is slow** and **computationally costly**.
- The optimisation method **may fail to converge** to the global optimum in the presence of local optima.

3. Alternative Approach

A **"faster" approach** is provided by the so-called **"two-step" methods** which **avoid solving ODE's** numerically, and involve two steps, i.e.;

1. **use of non-parametric methods** to estimate solution of ODE; and
2. minimisation of a given distance function.

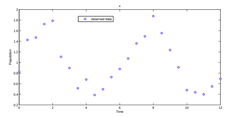
4. Contributions

1. Investigating the efficiency of the two-step approach employing a **Bayesian non linear regression** method : **Gaussian process regression** (GPR).
2. **Speeding up ODE parameter estimation** in "**fully observed**" systems.
3. Estimating parameters of **partially observed systems**.

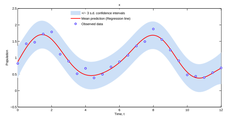
5. Method

Given an ODE $\frac{dx}{dt} = f(x;\theta)$, for $t = 1,\ldots,n$

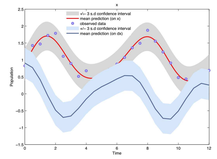
1. Observe data, $x(t)$



2. Fit GPR model to data



3. Fit GPR model to corresponding derivative process



4. Sample from posterior distributions

Obtain $\hat{x}(t)$ and $\frac{d}{dt}\hat{x}(t)$

5. Estimate θ by minimising objective function

$$\underset{\theta}{\text{minimize}} \quad \sum_{i=1}^{n}\left\{\left(\frac{d}{dt}\hat{x}(t_i) - f(\hat{x}(t_i);\theta)\right)^2\right\}$$

6. Applications and Results

We present two examples of the applications of GPR to ODE parameter estimation.

A. GPR is employed to **estimate the parameters of a "fully observed" Lotka-Volterra model**:

$$\frac{dx}{dt} = ax - xy, \qquad \frac{dy}{dt} = bxy - y.$$

Results

GPR obtains **estimates within fractions of a second** and is **more accurate** than the traditional simulation method,

1. with standard deviation ($\sigma = 0.1$)
2. with varying levels of noise (σ)

Method	$\hat{a}$ (1)	$\hat{b}$ (1)	Time (seconds)
Simulation	0.9888	1.0083	0.6318
GPR	1.0038 ± 0.0558	0.9730 ± 0.0557	0.0091

Table 1: *Parameter estimates obtained using the simulation and GPR methods. The "true" parameter values are shown in parentheses. The mean GPR estimates are shown with their corresponding standard deviations.*

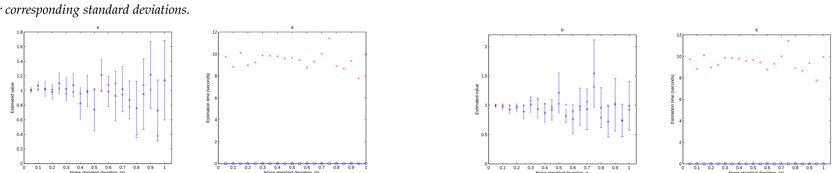


Figure 1: *Comparison of the two methods at different noise (σ) values. The plots on the left show the estimated parameter values for the simulation (red stars) and GPR (blue error bars) methods. The blue stars indicate the mean GPR estimates, while the dotted horizontal lines indicate the true values. The plots on the right show the average estimation times for the simulation (red stars), and GPR (blue circles) methods.*

B. GPR is also employed in **estimating the parameters, α, γ, ρ and ν, of a "partially observed" SIR model using "real" data**:

$$\frac{dS}{dt} = \alpha - \gamma SI - \rho S, \qquad \frac{dI}{dt} = \gamma SI - \nu I - \rho I, \qquad \frac{dR}{dt} = \nu I - \rho R$$

Data

day	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
I(t)	1	1	3	7	6	10	13	13	14	14	17	10	6	6	4	3	1	1	1	1	0
R(t)	0	0	0	0	5	7	8	13	13	16	16	24	30	31	33	34	36	36	36	36	37

Table 2: *Data on the cases of common-cold within a small community in Tristan da Cunha.The data were recorded in October 1967 (Hammond and Tyrrell, 1971)*

Assumptions:

- There were no births during the 21 days, $\alpha = 0$.
- There were no deaths during the 21 days, $\rho = 0$.

Results

Both methods estimated the parameters closely, as shown by the trajectories in **Figure 2**.

Method	$\hat{S}$	$\hat{\gamma}$	$\hat{\nu}$	Time (seconds)
Simulation	37.0059	0.024	0.2413	4.7998
"GPR+simulation" (mean)	41.4129	0.0213	0.27616	0.4282
Original study (1971)	44	0.016	…	…

Table 3: *Parameter estimates obtained using the simulation and "GPR+simulation" methods.*

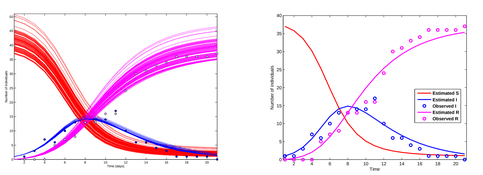


Figure 2: *Trajectories of the model predicted data using the simulation method (left), and the hybrid method (right).The observed data are represented by circles while the estimated data are represented by lines.*

7. Conclusions

- **Without any prior knowledge of the initial conditions** of the system, we may employ GPR to estimate the parameters of a model.
- The GPR approach **works** well for **models that are linear in their parameters**.
- The GPR approach **works well in combination with simulation** in order to **infer unknown initial states**.
- Further applications of this method need to be explored.

References and Further Reading

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