GEARS: The Enzymatic Oscillator example

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The Enzymatic Oscillator example in GEARS performs parameter estimation on the Enzymatic Oscillator model. The Enzymatic Oscillator model Decroly and Goldbeter (1982), is a small oscillatory system that exhibits chaotic behaviour. We consider the model in the form as follows:

$$\frac{d\alpha}{dt} = v_{Km1_{r1}} - \frac{\alpha \cdot \sigma_{r2}(\alpha+1)(\beta+1)^2}{10^6 L1_{r2} + (\alpha+1)^2(\beta+1)^2} \tag{1}$$

$$\frac{d\beta}{dt} = \frac{50\alpha \cdot \sigma_{r2}(\alpha+1)(\beta+1)^2}{(10^6 L1_{r2} + (\alpha+1)^2(\beta+1)^2)} - \frac{\sigma_{2_{r3}}(\gamma+1)^2(d_{r3}\frac{\beta}{100}+1)\beta}{(L2_{r3} + (\gamma+1)^2(d_{r3}\frac{\beta}{100}+1)^2)} \tag{2}$$

$$\frac{d\gamma}{dt} = \frac{(\sigma_{2_{r3}}(\gamma+1)^2(d_{r3}\frac{\beta}{100}+1)\beta)}{(50(L2_{r3} + (\gamma+1)^2(d_{r3}\frac{\beta}{100}+1)^2))} - ks_{r4} \cdot \gamma \tag{3}$$

$$\alpha(t_0) = \alpha_0, \beta(t_0) = \beta_0, \\ \gamma(t_0) = \gamma_0 \tag{4}$$

$$\boldsymbol{y}(t_i) = [\alpha(t_i), \beta(t_i)] \tag{5}$$

$$\boldsymbol{\theta} = \{v_{Km1_{r1}} L1_{r2}, \sigma_{r2}, L2_{r3}, d_{r3}, \\ \sigma_{2_{r3}}, ks_{r4}\} \tag{6}$$

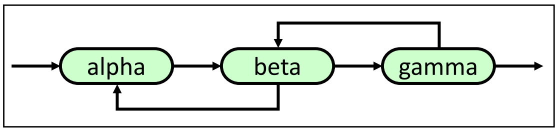


Figure 1: A visualisation of the structure of the Enzymatic Oscillator.

$$\text{Where, } \theta_i \in [10^{-3}, 10^3] \, \forall \, \theta_i \in \boldsymbol{\theta} \tag{7}$$

Where $\boldsymbol{y}$ is the observation function. Synthetic data was generated for the Enzymatic Oscillator model for parameter values $\boldsymbol{\theta} = [0.4, 500, 10, 10, 0.07, 7, 2.5]$ for the initial conditions $[\alpha_0, \beta_0, \gamma_0] = [29.1999, 188.8, 0.3367]$. This data was generated with a standard deviation of 10% of the nominal signal level and a detection threshold of 0.1. This set-up for generating data was used to set up one fitting set of data and two data sets for cross-validation. Initial conditions for the cross-validation sets were varied randomly within a meaningful range. One particular phenomena that effects the EO model is chaotic behaviour. The EO model is capable of producing chaotic behaviour as described in Decroly and Goldbeter (1982). With this in mind we choose parameter values close to but not inside the areas of parameter space in which chaotic behaviour exists.

A selection of the expected results achieved by running the EO example in `GEARS` can be found below. For the full collection of the expected results of the example please consult the expected results folder in the EO example folder.

Parameter	Value	Confidence (95%)	Coeff of variation (%)	Bounds status
$v_{Km1_{r1}}$	0.3787	± 0.631855	85.1185	Bounds not active
$L1_{r2}$	27	± 5.87784	11.10702	Bounds not active
σ_{r2}	2.1896	± 13.7102	319.4597	Bounds not active
$L2_{r3}$	0.0489	± 0.0685321	71.54582	Bounds not active
d_{r3}	0.6115	± 0.373602	31.1694	Bounds not active
$\sigma 2_{r3}$	2.1896	± 19.6767	458.4818	Bounds not active
ks_{r4}	7.2779	± 8.31072	58.26102	Bounds not active

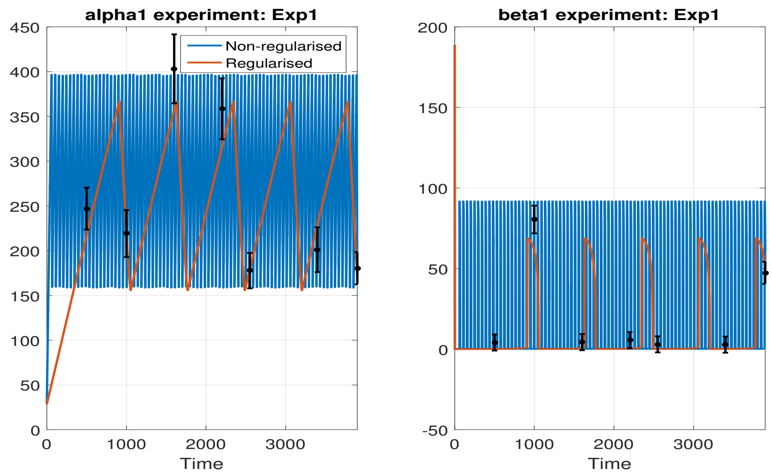
Table 1: A summary of the regularised results from the `GEARS` analysis of the GO model.

Experiment	Regularised estimation	Non-regularised estimation
Fitting experiment	0.010285	0.0065396

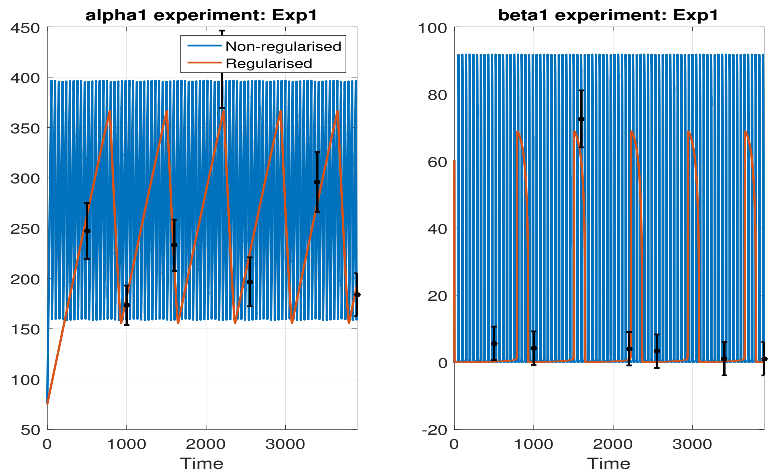
Table 2: The NRMSEs calculated for the fitting of the EO model.

Experiment	Regularised estimation	Non-regularised estimation
All experiments	0.085183	0.10448
Experiment 1	0.008866	0.0077089
Experiment 2	0.12014	0.14755

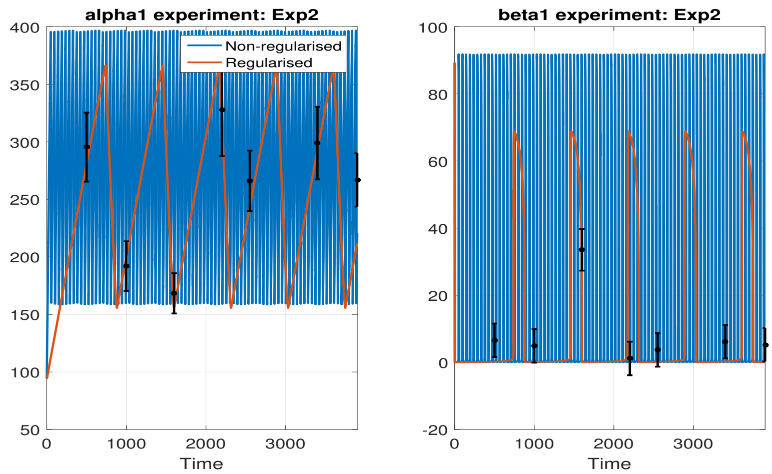
Table 3: The NRMSEs calculated for the cross-validation of the EO model.



(a) A comparison of the EO model fits with and without regularisation.



(b) A comparison of the EO model predictions for the first cross-validation data set with and without regularisation.



(c) A comparison of the EO model predictions for the second cross-validation data set with and without regularisation.

Figure 2: Figures showing the comparison between the regularised and non-regularised fits for both fitting and cross-validation.

References

Decroly, O. and Goldbeter, A. (1982). Birhythmicity, chaos, and other patterns of temporal self-organization in a multiply regulated biochemical system. *Proceedings of the National Academy of Sciences*, 79(22):6917–6921.