



GEARS: The Repressilator example

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The Repressilator example in GEARS performs parameter estimation on the Repressilator model. The Repressilator model Lillacci and Khammash (2010), is a well-known synthetic gene regulatory network. We consider the model in the form as described by equations 1-9 and figure 1.

$$\begin{aligned}
 \frac{dp_1}{dt} &= \beta(m_1 - p_1) & (1) \\
 \frac{dp_2}{dt} &= \beta(m_2 - p_2) & (2) \\
 \frac{dp_3}{dt} &= \beta(m_3 - p_3) & (3) \\
 \frac{dm_1}{dt} &= \alpha_0 + \frac{\alpha}{(1 + p_3^n)} - m_1 & (4) \\
 \frac{dm_2}{dt} &= \alpha_0 + \frac{\alpha}{(1 + p_1^n)} - m_2 & (5) \\
 \frac{dm_3}{dt} &= \alpha_0 + \frac{\alpha}{(1 + p_2^n)} - m_3 & (6)
 \end{aligned}$$

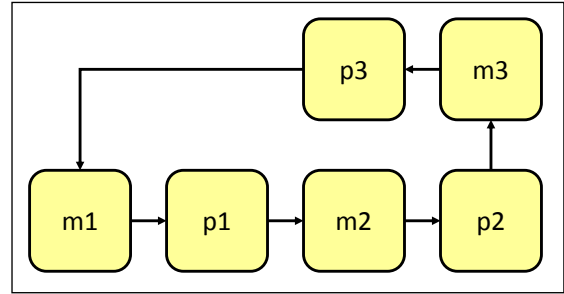


Figure 1: A visualisation of the structure of the Repressilator model.

$$p_{1-3}(t_0) = p_{1-3,0}, m_{1-3}(t_0) = m_{1-3,0} \quad (7)$$

$$\mathbf{y}_F(t_i) = m_3(t_i) \text{ and } \mathbf{y}_V(t_i) = [p_3(t_i), m_3(t_i)] \quad (8)$$

$$\boldsymbol{\theta} = \{\alpha_0, \alpha, \beta, n\} \text{ where } \{\alpha_0, \alpha, \beta\} \in [10^{-3}, 500] \text{ and } n \in [1, 10] \quad (9)$$

Where \mathbf{y}_F is the observation function for the fitting procedure and \mathbf{y}_V is the observation function for the cross-validation procedure. Synthetic data was generated for the Repressilator model for parameter values $\{k_{1-6}, K_i, n\} = [0.05, 298, 8.5, 0.3]$ for the initial conditions $[p_{1-3,0}, m_{1-3,0}] = [10, 0.01, 1, 1, 0.01, 10]$. 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.

A selection of the expected results achieved by running the RP 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 RP example folder.

Parameter	Value	Confidence (95%)	Coeff of variation (%)	Bounds status
α_0	1.0000e-03	± 0.0359519	1834.2819	Lower bound active
α	305.2130	± 22.876	3.8240251	Bounds not active
n	8.8505	± 1.8445	10.63293	Bounds not active
β	0.2978	± 0.0107302	1.8382483	Bounds not active

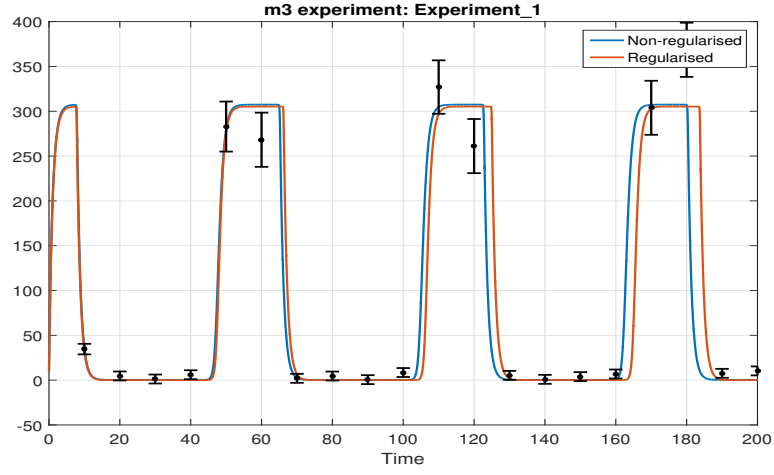
Table 1: A summary of the regularised results from the **GEARS** analysis of the RP model.

Experiment	Regularised estimation	Non-regularised estimation
Experiment 1	3.0621e-03	2.9454e-03

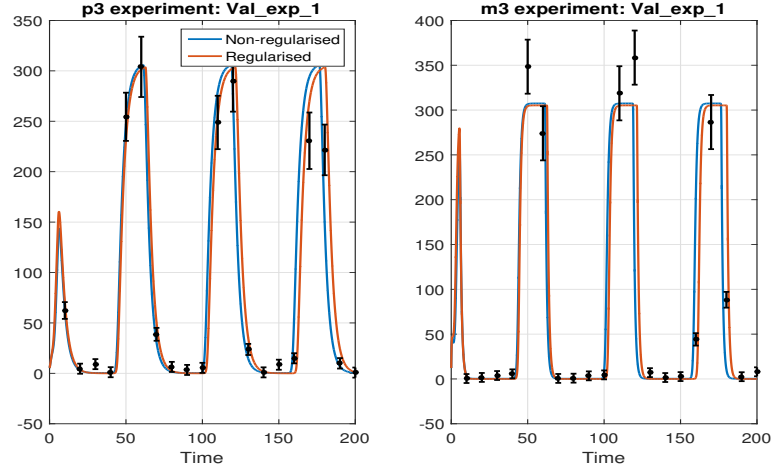
Table 2: The NRMSEs calculated for the fitting of the RP model.

Experiment	Regularised estimation	Non-regularised estimation
All experiments	2.0113e-02	2.0864e-02
Experiment 1	1.1880e-02	1.2588e-02
Experiment 2	2.5845e-02	2.6687e-02

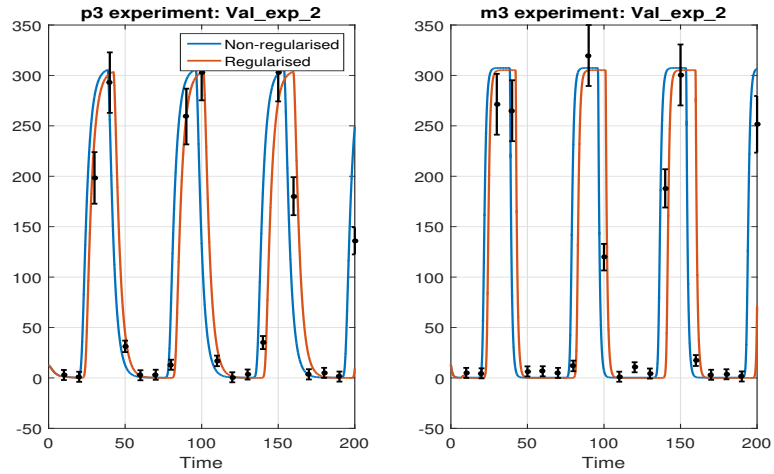
Table 3: The NRMSEs calculated for the cross-validation of the RP model.



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



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



(c) A comparison of the RP 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

Lillacci, G. and Khammash, M. (2010). Parameter estimation and model selection in computational biology. *PLOS Computational Biology*, 6(3):1–17.