I. EXAMPLE: SIMPLE GENE EXPRESSION

mRNA is pumped into the system at a constant rate, k_0. mRNA is converted into protein at a constant rate, k_1, following the law of mass action. mRNA and protein decay proportionally to the amount of each species at rates δ_m and δ_p respectively. The equation governing the dynamics is

$$\frac{d}{dt}\begin{pmatrix} m(t) \\ p(t) \end{pmatrix} = \begin{pmatrix} -\delta_m & 0 \\ k_1 & -\delta_p \end{pmatrix}\begin{pmatrix} m(t) \\ p(t) \end{pmatrix} + \begin{pmatrix} k_0 \\ 0 \end{pmatrix}$$

With exact solution

$$\begin{aligned} m(t) &= m(0)e^{-\delta_m t} + \left(1 - e^{-\delta_m t}\right)\frac{k_0}{\delta_m} \\ p(t) &= \left[p(0) + k_1\left(\frac{k_0}{\delta_m} - m(0)\right)\frac{e^{-\delta_m t} - e^{-\delta_p t}}{\delta_m - \delta_p} \right. \\ &\qquad \left. + \frac{k_1 k_0}{\delta_p \delta_m}\left(e^{\delta_p t} - 1\right)\right] e^{-\delta_p t} \end{aligned}$$

If $\delta_m = \delta_p = 1$, then

$$\begin{aligned} m(t) &= k_0 + (m(0) - k_0)e^{-t} \\ p(t) &= k_1 k_0 + (p(0) + k_1(m(0) - k_0)t - k_1 k_0)\, e^{-t} \end{aligned}$$

If the input, u, is k_0, and the intrinsic parameter set is just k_1. The logarithmic sensitivities are

$$k_1 \frac{d}{dk_1}\begin{pmatrix} m(t;k_1) \\ p(t;k_1) \end{pmatrix} = \begin{pmatrix} 0 \\ k_1 k_0 + (k_1(m(0) - k_0)t - k_1 k_0)\, e^{-t} \end{pmatrix}$$

Then the Fisher information matrix is

$$\boldsymbol{I}(\boldsymbol{\theta}, t) = \int_0^t \left(k_1 \frac{d}{dk_1}\begin{pmatrix} m(t';k_1) \\ p(t';k_1) \end{pmatrix}\right)^T \boldsymbol{\Omega\Sigma^{-1}} \left(k_1 \frac{d}{dk_1}\begin{pmatrix} m(t';k_1) \\ p(t';k_1) \end{pmatrix}\right) dt'$$

Taking $\boldsymbol{\Omega} = \boldsymbol{\Sigma^{-1}} = \boldsymbol{1}$, the fisher information matrix is

$$\begin{aligned} \boldsymbol{I} &= \int_0^t \left(k_1 k_0 + (k_1(m(0) - k_0)t' - k_1 k_0)\, e^{-t'}\right)^2 dt' \\ &= I(0) + \frac{1}{4}e^{-2t}\left[A^2(4e^{2t}t + 8e^t - 2) \right. \\ &\qquad - 2AB(-2t + 4e^t(t+1) - 1) \\ &\qquad \left. - B^2(2t^2 + 2t + 1)\right] \\ &\quad - \frac{3}{2}\left[A^2 - AB - \frac{1}{6}B^2\right] \end{aligned}$$

where

$$\begin{aligned} A &= k_1 k_0 \\ B &= k_1(m(0) - k_0) \end{aligned}$$

The Fisher information matrix is only one entry and is plotted in FIG.1 along with the protein (logarithmic) sensitivity.

The Fisher information is maximized when k_0 is maximized since

$$\begin{aligned} \mathbf{I} &= k_1^2 k_0^2 \int_0^t C_1(t')dt' + 2k_1^2 k_0 m(0) \int_0^t C_2(t')dt' \\ &\quad + k_1^2 m(0)^2 \int_0^t C_3(t')dt' \end{aligned}$$

where,

$$\begin{aligned} C_1(t) &= \left(1 - (1+t)e^{-t}\right)^2 \geq 0 \ \ \forall\, t > 0 \\ C_2(t) &= (1 - (1+t)e^{-t})te^{-t} \geq 0 \ \ \forall\, t > 0 \\ C_3(t) &= (te^{-t})^2 \end{aligned}$$

So increasing k_0 only increases $\mathbf{I}$.

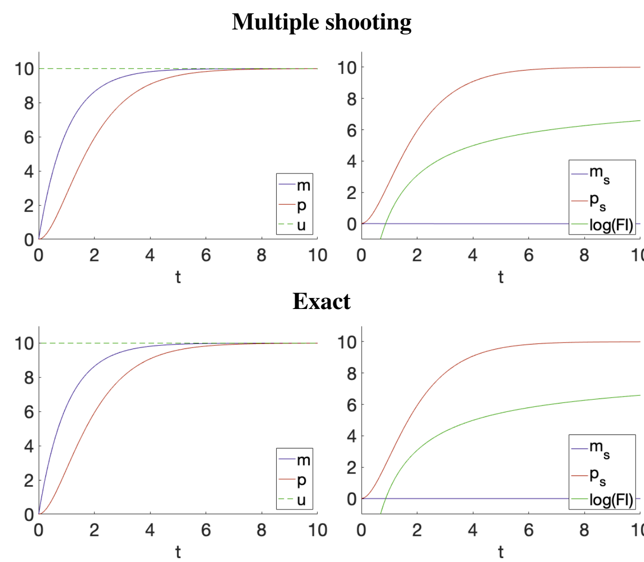

FIG. 1. The state variables, m(t) and p(t), with the optimal input, u(t) (left) and the (logarithmic) sensitivities wrt k_1 with the log of the Fisher information (right). $u(t)$ was computed using multiple shooting, the code used to create the plots is the file SGE.m in the Code folder. Here $u(t) \leq 10$ so that $u(t)$ is the max value in the optimal solution. The curves agree with the exact solutions.