Lu switches summary

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In their study, [**?**] explored the effect of white Gaussian and shot noise on the multi-state switches. They found that the classical toggle switch, with the repressing transcription factors has two steady states and the toggle switch with added double positive auto-regulation has three steady states. By extending the analysis on these models by using StabilityChecker we can determine the design principles that make a tristable versus a bistable switch. This is another example of a use for StabilityChecker. The system used in their study is defined by two dynamical systems:

$$\dot{x} = f_x(x,y) = g_x\, H^S_{xy}(y)\, H^S_{xx}(x) - k_x x \tag{1}$$

$$\dot{y} = f_y(x,y) = g_y\, H^S_{yx}(x)\, H^S_{yy}(y) - k_y y \tag{2}$$

$$H^S_{xx} = H^-_x(x) + \lambda_x H^+_x(x) \tag{3}$$

$$H^-_x(x) = 1 \big/ \left[1 + (x/a_x)^{n_x}\right] \tag{4}$$

$$H^+_x(x) = 1 - H^-_x(x) \tag{5}$$

0.1 Classical model

For the classical model, in which no self-activation is present, the system reduces to the following equations:

$$\dot{x} = f_x(x,y) = g_x H^S_{xy}(y) - k_x x, \tag{6}$$

$$\dot{y} = f_y(x,y) = g_y H^S_{yx}(x) - k_y y \tag{7}$$

For the parameter values used in the Lu study, as shown in Table 1, the system exhibits three steady states (Figure 1), of which two are stable and one is unstable.

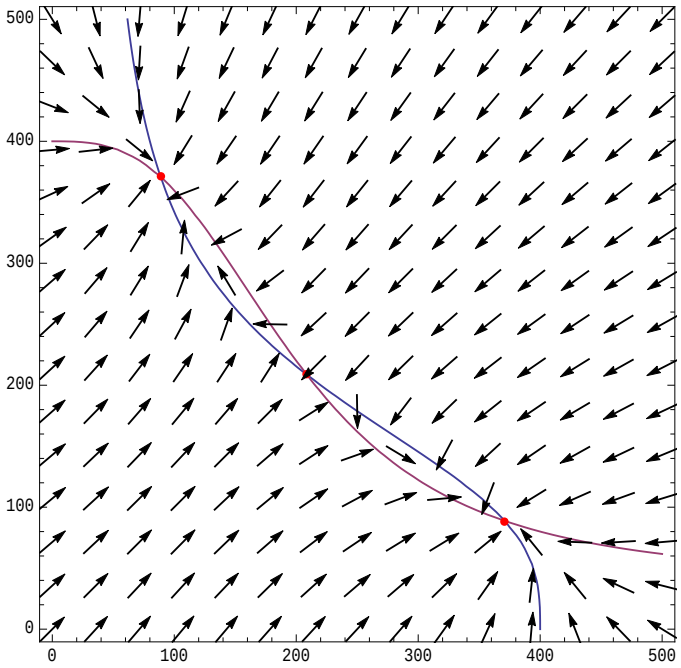

Figure 1: Phase portrait of the Lu classical model with no self activation. There are two stable steady states and one unstable steady state.

Table 1: Lu classical model parameter values

gx	gy	kx	ky	nxy	nyx	xxy	xyx	Ixy	Iyx
40	40	0.1	0.1	3	3	200	200	0.1	0.1

Using StabilityChecker with priors centred around the parameter values used in the original paper (Table 2), we can find the robustness of this bistable behaviour, as well as identify the most important parameters for bistability.

Table 2: Lu classical model priors

gx	gy	kx	ky	nxy	nyx	xxy	xyx	Ixy	Iyx
35-45	35-45	0-0.2	0-0.2	2-4	2-4	150-250	150-250	0-0.2	0-0.2

The posterior distribution of this model is shown in Figure 2. As can be seen from the posterior, the most restrained parameters are kx and ky, the parameters responsible for the degradation of the species involved. This indicates that the rate of degradation of the species is critical for the desired dynamic to occur.

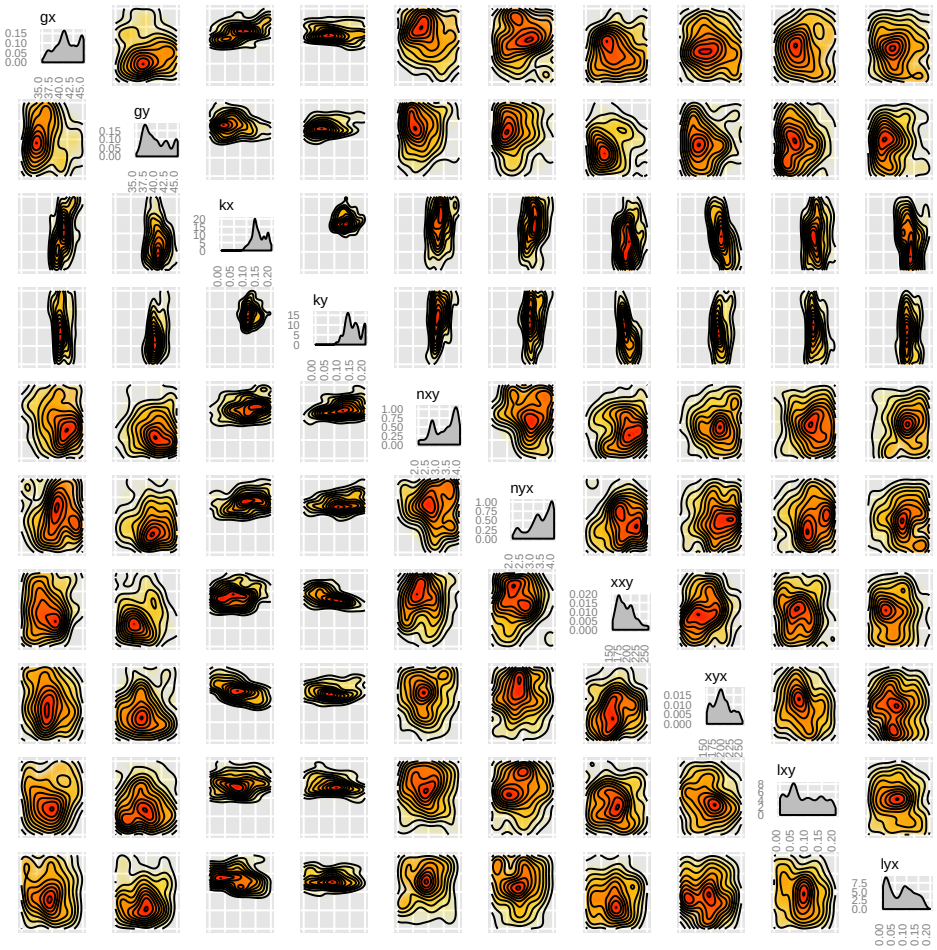

Figure 2: The posterior distribution of the Lu classical model with no self activation. kx and ky are the most constrained parameters.

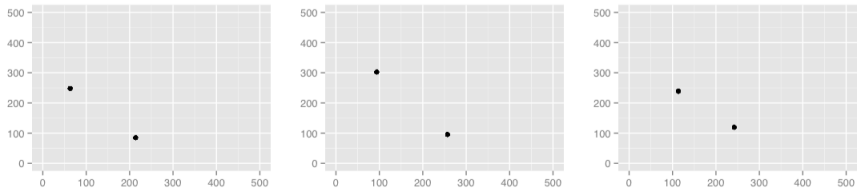

Figure 3: A sample of the phase plots produced from the final population of the Lu classical model.

1 Single positive autoregulation

Table 3: Lu model with single self-activation priors

parameter	range
gx	1-2
gy	20-25
kx	50-55
ky	48-52
nxy	30-35
nyx	0.1-0.2
xxy	2-3
xyx	0.4-0.6
lxy	0.02-0.04
lyx	0.02-0.04
nXX	25-30
nYY	0.01-0.02
xXX	0.4-0.5
xYY	1-3
lXX	65-72
lYY	0.02-0.04

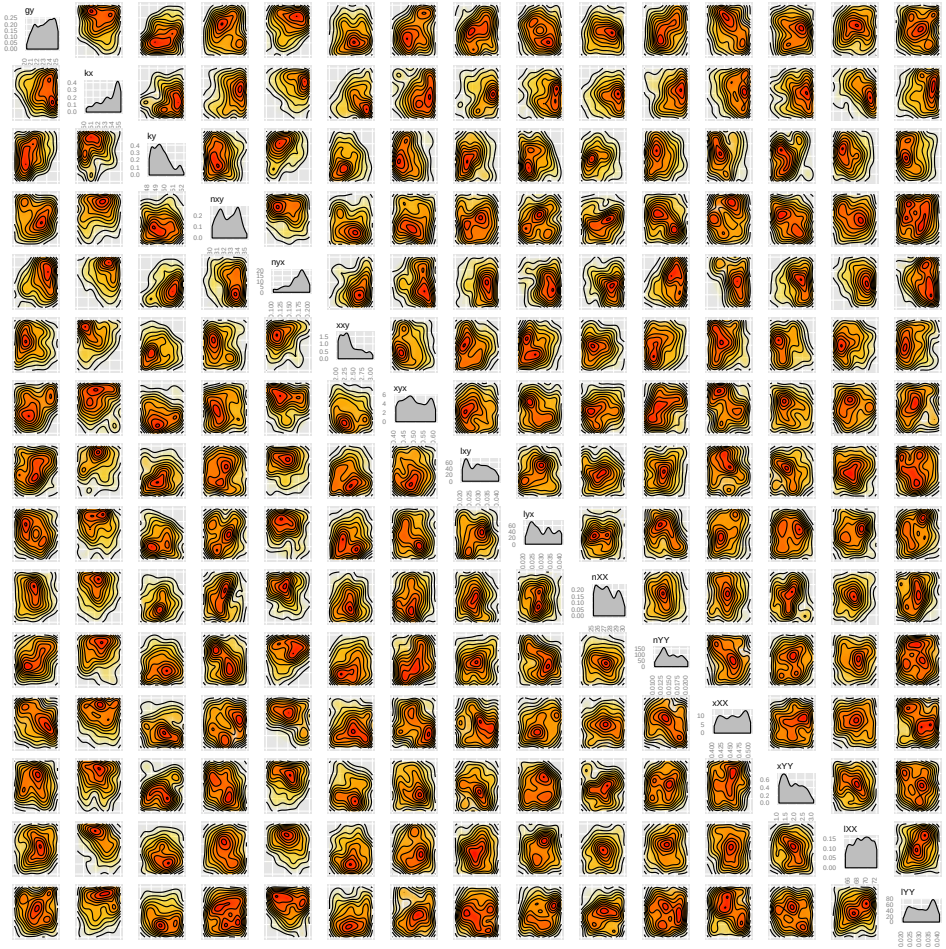

Figure 4: The posterior distribution of the Lu classical model with no self activation. kx and ky are the most constrained parameters.

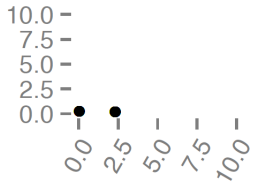

Figure 5: Phase plot of asymmetric Lu toggle switch

2 Double positive autoregulation

If self-activation is included, then the system is that presented in equations 1 and 2 . When values that are presented in Table 4 are assigned to the parameters for the self-activating model, the system exhibits five steady states as seen in Figure 6.

Table 4: Lu model with self-activation parameter values

gx	gy	kx	ky	nxy	nyx	xxy	xyx	Ixy	Iyx
4	4	0.1	0.1	1	1	200	200	0.1	0.1

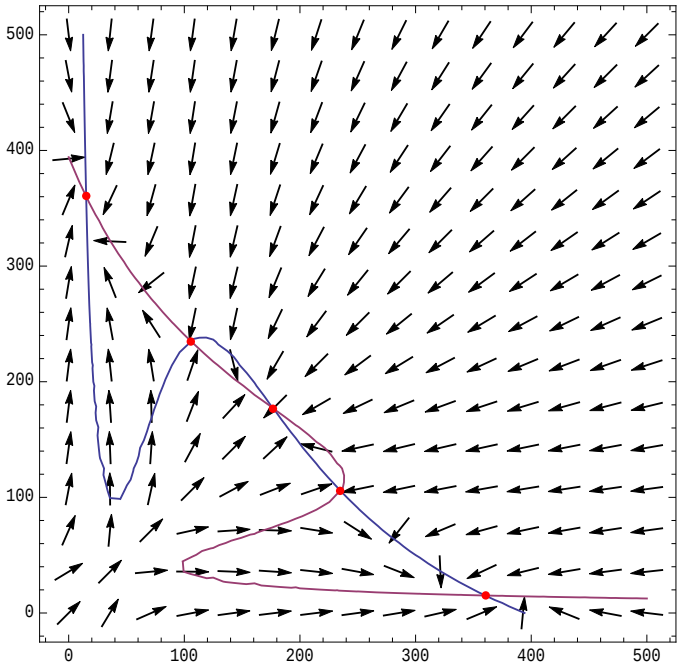

Figure 6: Phase portrait of the Lu model including double self-activation. The model had three stable steady states and two unstable steady states.

Using StabilityChecker and priors centred around the original values, shown in Table 5, we can explore the robustness of this behaviour, in a similar way as done for the classical model.

Table 5: Lu model with double self-activation priors

gx	gy	kx	ky	nxy	nyx	xxy	xyx	Ixy	Iyx
3-5	3-5	0-0.2	0-0.2	0-2	0-2	150-250	150-250	0-0.2	0-0.2

The posterior is shown in Figure 7. The most constrained parameters are kx and ky, similar as in the classic toggle switch case.

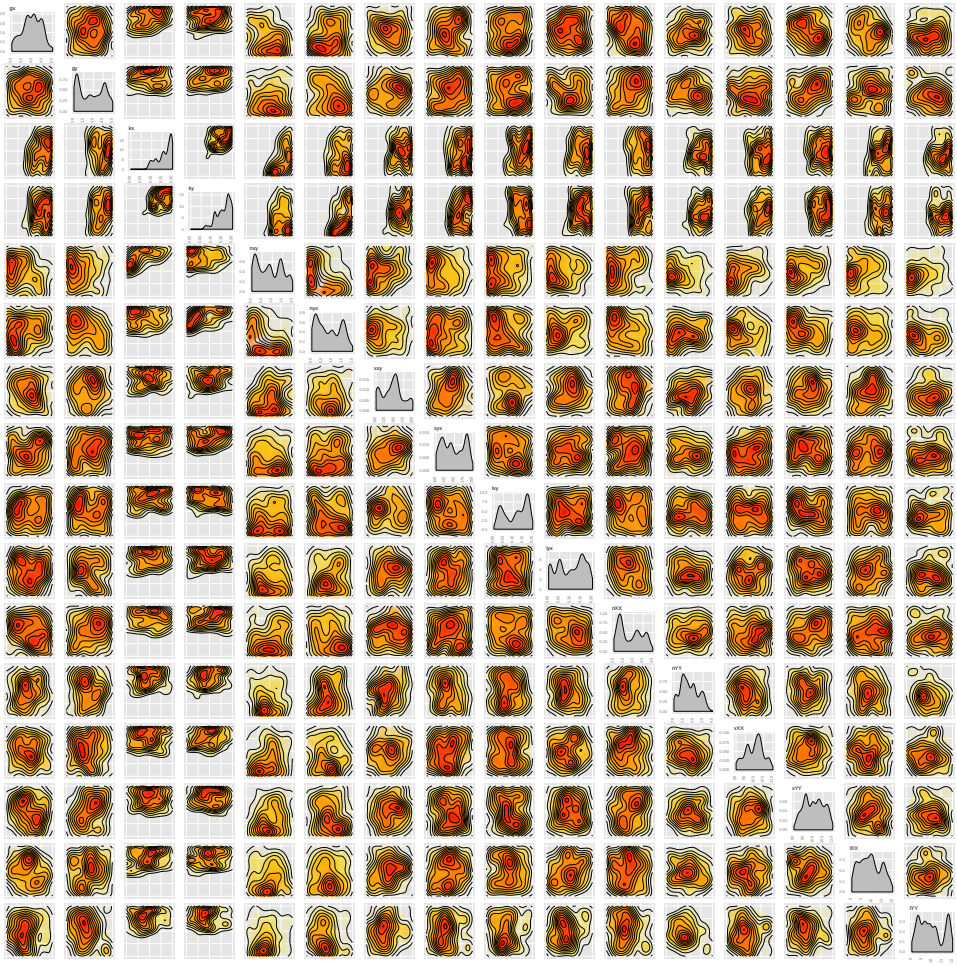

Figure 7: The posterior distribution of the Lu model with double self activation. kx and ky are the most constrained parameters.

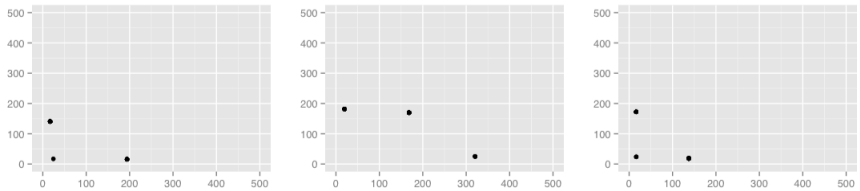

Figure 8: A sample of the phase plots produced from the final population of the Lu tristable model.