Electronic Supplementary Material (ESI) for Integrative Biology.

Supplementary Methods

Simplified model (*toy* model) of the *Pseudomonas putida* TOL network

The model used for simulations is adapted from our previously published model for this network (de Las Heras et al, 2015). Briefly, we assume that XylR, denoted by R_T, is synthesized at a constant background rate k'_{sR} and degraded also at a constant background rate, k_{dR}. XylR synthesis is depends on its own activity, denoted as a_R. Therefore, we write a preliminary differential equation for XylR:

$$\frac{dR_T}{dt} = k'_{sR} + f(a_R) - k_{dR}R \qquad 1$$

We assume that the inducer, *I*, activates XylR by forming a complex, R_c, whose concentration rapidly reaches equilibrium and is described by

$$R_c = R_T \frac{I}{K_D + I} \qquad 2$$

where K_D is the dissociation constant of the XylR-inducer complex. Also, the sum of the complex and the free forms is equal to the total amount of XylR:

$$R_T = R_c + R_f \qquad 3$$

We assume that the DNA binding activity of XylR depends on the concentration of the complex and free forms according to

$$a_R = \lambda R_c + \alpha R_f \qquad 4$$

Where normally $\lambda > \alpha$, and λ is a parameter that indicates how strongly a particular inducer activates XylR, and α indicates the background activity of free XylR. Combining equations 2, 3 and 4 we obtain an expression to describe the level of activity of XylR:

$$a_R = R_T \left(\alpha + (\lambda - \alpha)\frac{I}{K_D + I}\right) \qquad 5$$

With this equation, we can define the function $f(a_R)$ from equation 1. For the model of the wild type network, where XylR inhibits its own transcription in a negative feedback loop, the function f_n from equation 1 is defined as:

$$f_n(a_R) = k''_{sR}\frac{J_R^{nR}}{J_R^{nR} + a_R^{nR}} \qquad 6$$

Where k''_{sR} is the maximum rate of XylR synthesis (when $a_R = 0$), J_R is the a_R level resulting in half-maximal XylR-dependent transcriptional inhibition and n_R is the Hill coefficient which determines how steep is the transcriptional inhibition.

For the network with a positive feedback loop, the $f(a_R)$ function describing transcriptional activation of XylR by itself is:

$$f_p(a_R) = k''_{sR}\sigma \frac{a_R^{nR}}{J_R^{nR} + a_R^{nR}} \quad (7)$$

Where $k''_{sR}\sigma$ is the maximum rate of XylR synthesis; k''_{sR} represents the contribution to the rate made by active XylR and σ takes into account the amount of the σ^{54} factor present in the cell. J_R is the a_R level resulting in half-maximal XylR-dependent transcriptional activation and n_R is the Hill coefficient which determines the steepness of the activation.

For the model in which σ^{54} is controlled by Pu, σ is no longer a parameter, but is itself described by a differential equation:

$$\frac{d\sigma}{dt} = k'_{s\sigma} + k''_{s\sigma}\sigma \frac{a_R^{n\sigma}}{J_\sigma^{n\sigma} + a_R^{n\sigma}} + k_{d\sigma}\sigma \quad (8)$$

Here, $k'_{s\sigma}$ is the background rate of synthesis, $k''_{s\sigma}$ the maximum maximal rate of XylR and σ^{54}-dependent σ^{54} synthesis. J_σ is the a_R level resulting in half-maximal XylR-dependent transcriptional activation of $\sigma^{54}$and n_σ is the Hill coefficient of XylR transcriptional activation.

Finally, we write a differential equation for the concentration of the Lux reporter, whose synthesis is also activated by XylR.

$$\frac{dL}{dt} = k'_{sL} + k''_{sL}\sigma \frac{a_R^{nL}}{J_L^{nL} + a_R^{nL}} + k_{dL} \quad (9)$$

Where k'_{sL} is a small background synthesis rate $k''_{sL}\sigma$ is the maximum rate of XylR and σ^{54}-dependent Lux synthesis. J_L is the a_R level resulting in half-maximal XylR-dependent transcriptional activation of *lux* and n_L is the Hill coefficient which determines the steepness of XylR transcriptional activation.

We used MATLAB to simulate these systems of ODEs. Parameters are shown in Supplementary table 1. Rate constants (k) have a dimension of time^{-1}, while all the other parameters are dimensionless. For rate constants, values were empirically chosen to reflect credible relative relationships and dynamics.

Table 1. Parameter values for the mathematical model of the TOL network

Parameter	Value
k'_{sR}	0
k_{dR}	1
K_D	1
λ	1 (optimal inducer), 0.45 (sub-optimal inducer)
α	0.01
k''_{sR}	1
J_R	0.2
nR	3
k'_{sL}	0.5
k''_{sL}	1

k_{dL}	0.5
J_L	0.2
nL	3
$k'_{s\sigma}$	0.5
$k''_{s\sigma}$	1
$k_{d\sigma}$	0.5
J_σ	0.2
$n\sigma$	3
σ	1 for wild-type σ^{54}, 2 for Psal-σ^{54}
I	0 (before induction), 20 (after induction)