Transcription Factors and Their Metabolic Signals

In the model, we use the activity $a_{\text{TF},i}$ of transcription factor *i*. Minimal transcription factor activity is represented by $a_{\text{TF},i} = 0$, while maximal activity is represented by $a_{\text{TF},i} = 1$.

We assume a phenomenological Hill type equation

$$a_{\mathrm{TF},i} = \frac{x_{\mathrm{TF},i}^{n_{\mathrm{TF},i}}}{x_{\mathrm{TF},i}^{n_{\mathrm{TF},i}} + k_{\mathrm{TF},i}^{n_{\mathrm{TF},i}}}$$

that describes $a_{\text{TF},i}$ in dependence on the respective metabolic signal $x_{\text{TF},i}$. For $n_{\text{TF},i} > 0$ transcription factor *i* is activated by its metabolic signal $x_{\text{TF},i}$. For $n_{\text{TF},i} < 0$ it is inhibited. The following table lists the transcription factors together with their metabolic signals x_{TF} used in the model and the according references that motivated the choice of the expression for x_{TF} .

	Metabolic Signal		Parameters	
	x_{TF}	Reference	$k_{TF,i}$	$n_{TF,i}$
FNR	c_{O_2}	[13, 8]	$0.1 \; \mu mol/l$	-2
$\rm ArcA^{a}$	$x_{ArcA}(c_{q8}, c_{q8h2}, c_{mqn8}, c_{mql8})$	[6, 1]	20	-1
CRP	$c_{ m pep}/c_{ m pyr}$	[7, 4]	0.1	1
FruR	$c_{ m fdp}$	[9]	$0.1 \; \mu mol/l$	-1
PdhR	$c_{\rm pyr}$	[12, 11]	$100 \ \mu mol/l$	
AppY	$c_{ m for}$	[5, 2]	$10 \ \mu mol/l$	2
IclR	$c_{ m pyr}/c_{ m glx}$	[10]	10	1

a) The precise nature of the metabolic signal of ArcA is subject to a current debate. Alvarez et al. [1] report that ubiquinone is necessary to deactivate the sensor kinase ArcB and that menaquinole is necessary for activation of the sensor kinase ArcB. In contrast, **Bekker et al.** [3], **Sharma et al.** [14] report that also other quinone species control the activity of ArcB. To be able to capture the different hypotheses we choose the following expression for the metabolic signal of ArcB

$$x_{ArcA} = \frac{k_{dea,q} \cdot c_{q8} + (1 - k_{dea,q}) \cdot c_{mqn8}}{k_{act,q} \cdot c_{q8h2} + (1 - k_{act,q}) \cdot c_{mql8}}, \quad \text{with } 0 \le k_{dea,q}, k_{act,q} \le 1$$

The parameters $k_{dea,q}$ and $k_{act,q}$ determine the relative importance of the ubiquinones over the menaquinones in deactivation and activation of ArcB, respectively. A simulation study with the model (not shown) shows that different choices of the parameters $k_{dea,q}$ and $k_{act,q}$ are able to explain the data that the model uses as a reference. As our model cannot accommodate the influence of the separate redox states of ubiquinol and menaquinol onto ArcA, we have selected to use $k_{dea,q} = 1$ and $k_{act,q} = 0$.

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