Perfect Adaptation by Zero Control Coefficients

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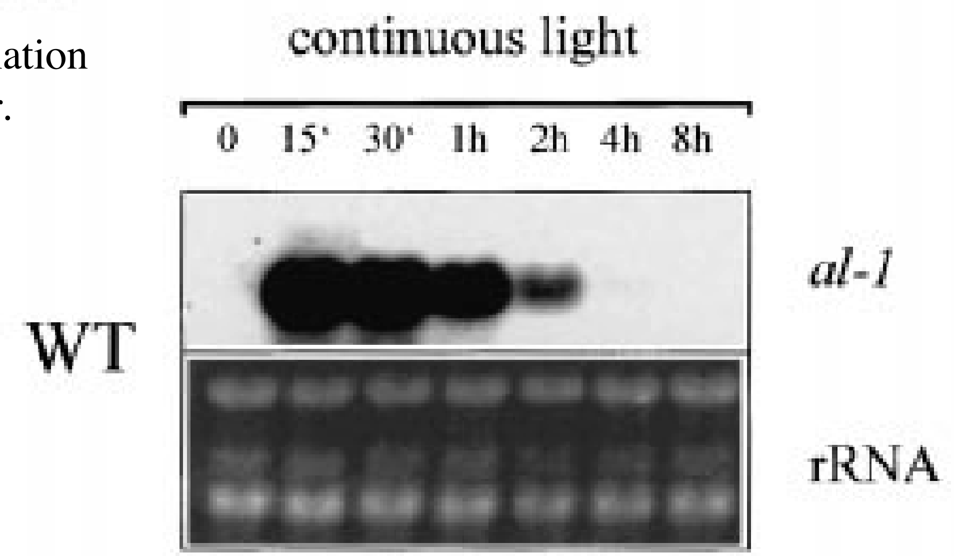
Overview

- what is adaptation, perfect adaptation?
  (few examples)
- Integral feedback control (IFC) for perfect adaptation
- Metabolic control theory (control coefficients)
- kinetic networks with zero control coefficients
  lead to perfect adaptation
- summary; relation to IFC?

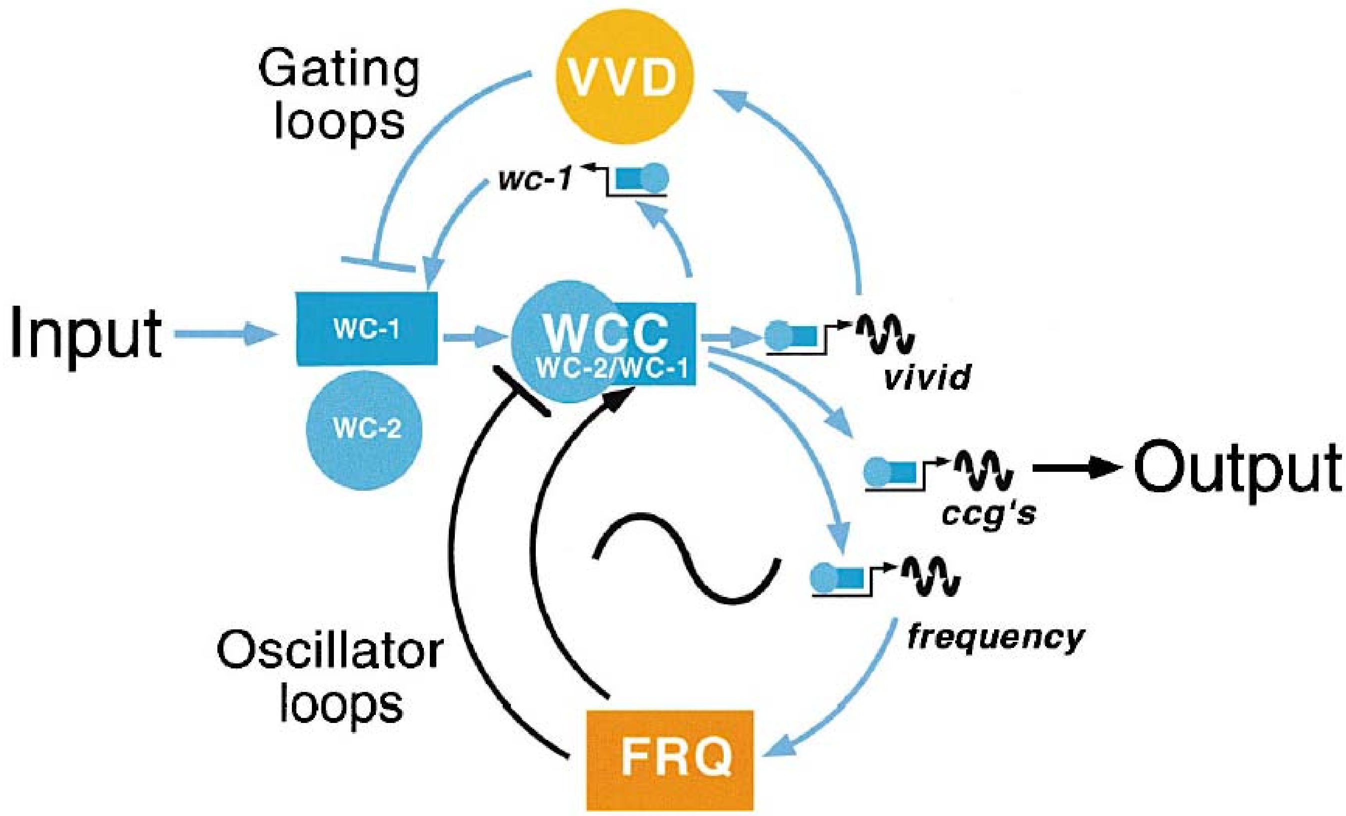
Photoadaptation of the *albino* gene *al-1* in *Neurospora crassa*

The four *albino* genes are induced during conidiation making carotenoids for protection against light. Conidiation is controlled in a circadian manner.



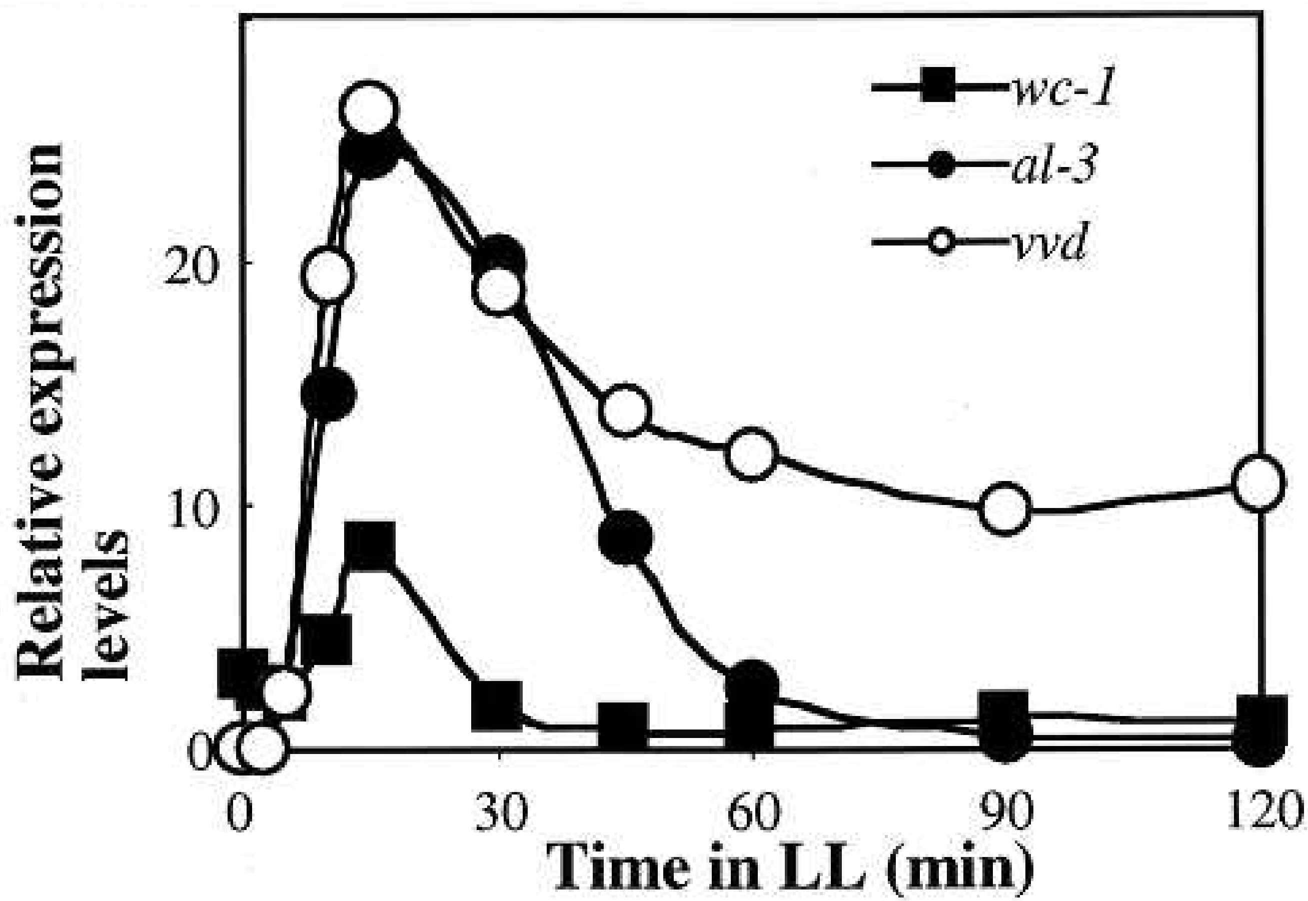
Schwerdtfeger & Linden, Mol. Microbiol. (2001) **39**, 1080-1087

Circadian clock components in *Neurospora crassa*



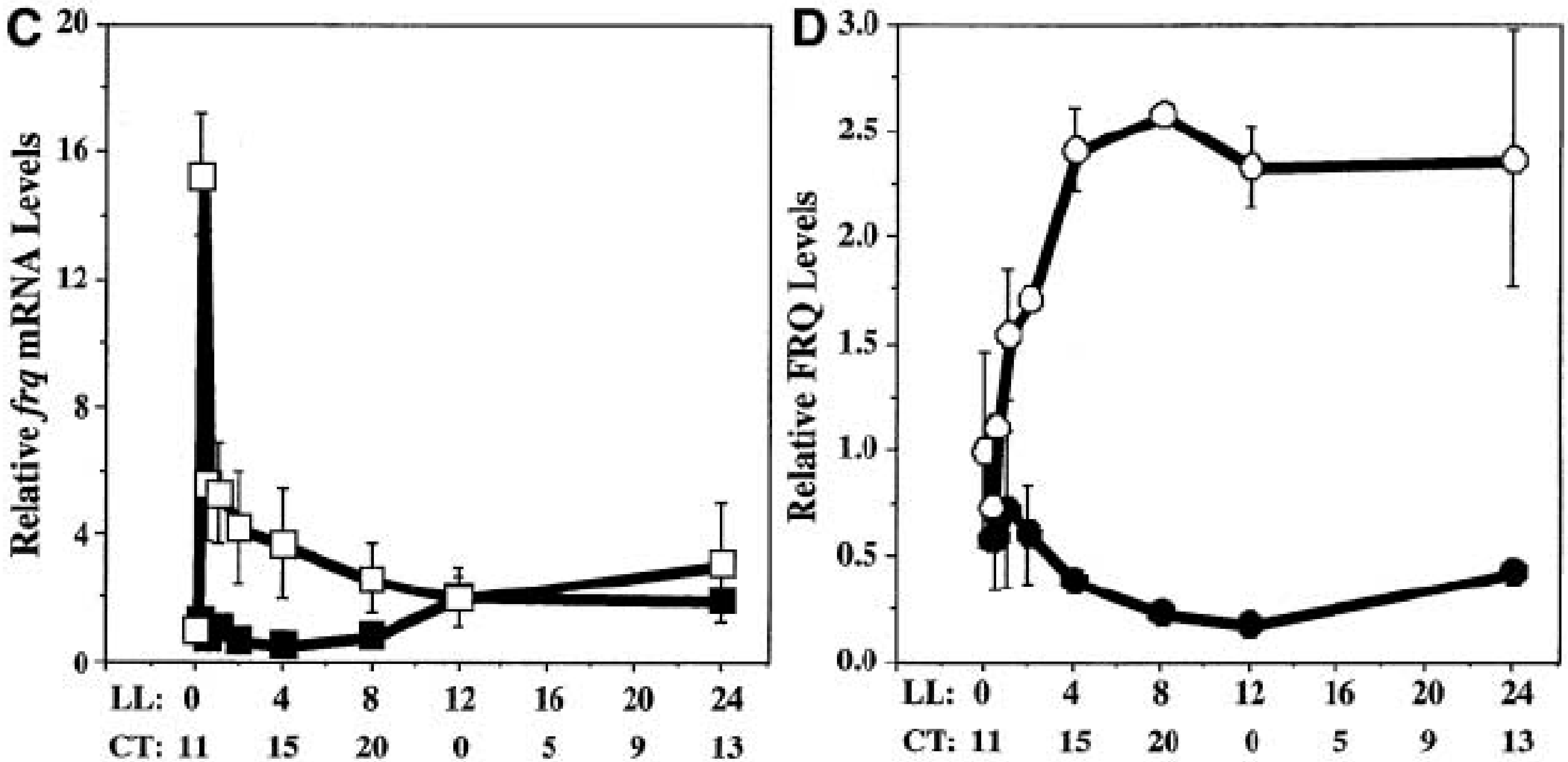
Heintzen *et al.*, Cell 104 (2001) 453-464

Photoadaptation of *al-3, vvd, wc-1* in *Neurospora crassa*



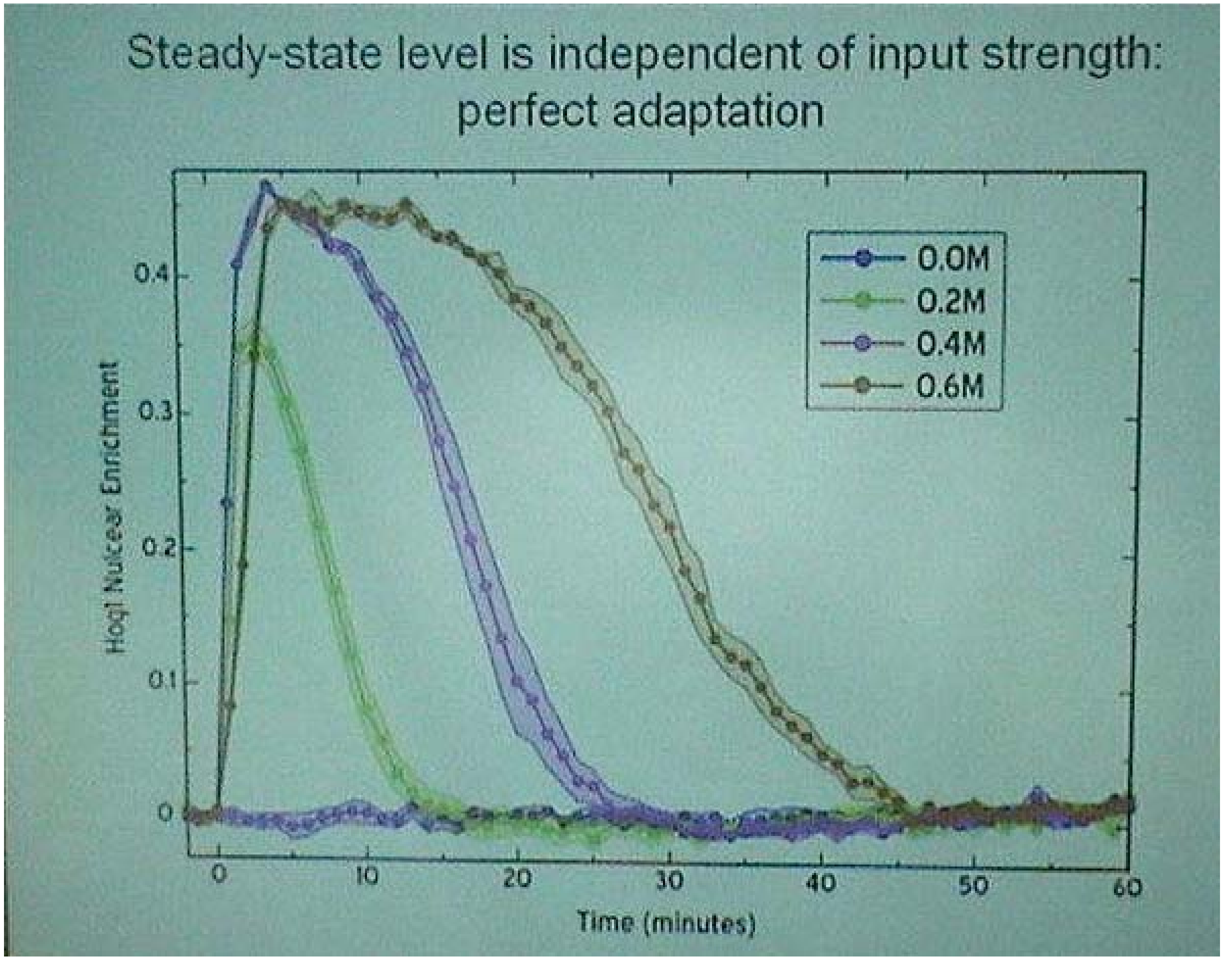
He & Liu, Genes&Development (2005)

Photoadaptation of *frq* and FRQ in *Neurospora crassa*



Collett *et al.*, Genetics **160** (2002) 149-158

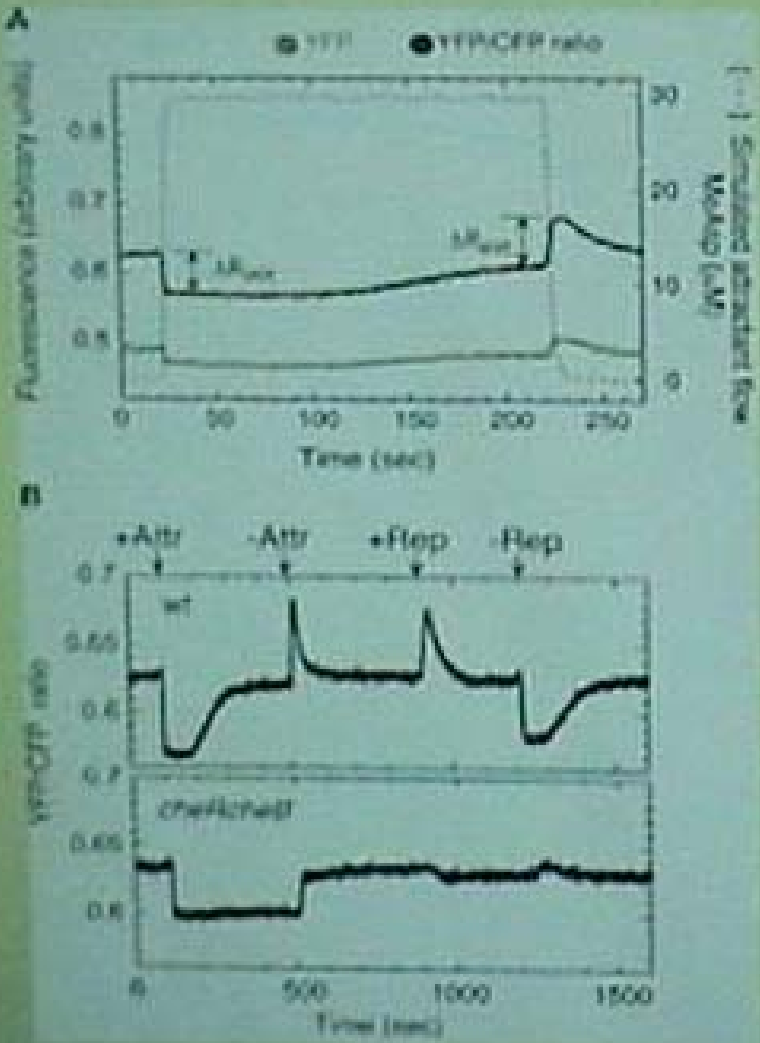
Perfect adaptation:
Nuclear Hog1 steady state levels as a function of NaCl (osmotic) stress in yeast

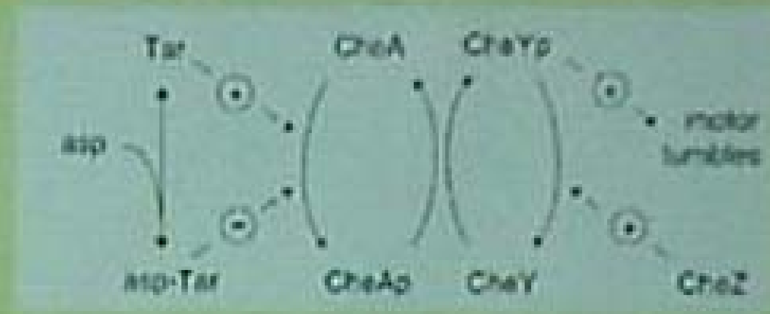


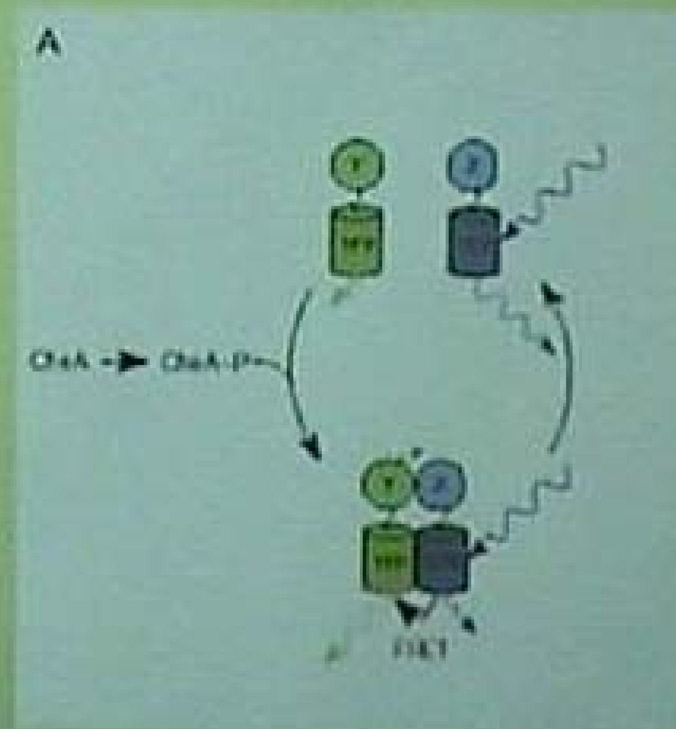
Alexander van Oudenaarden, KITP, July 31, 2007

Perfect adaptation in chemotaxis (E. coli)

Yigal Meir, KITP, July 30, 2007

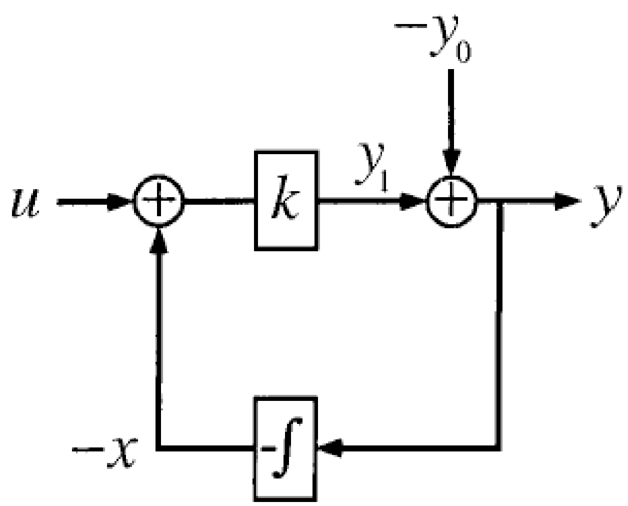






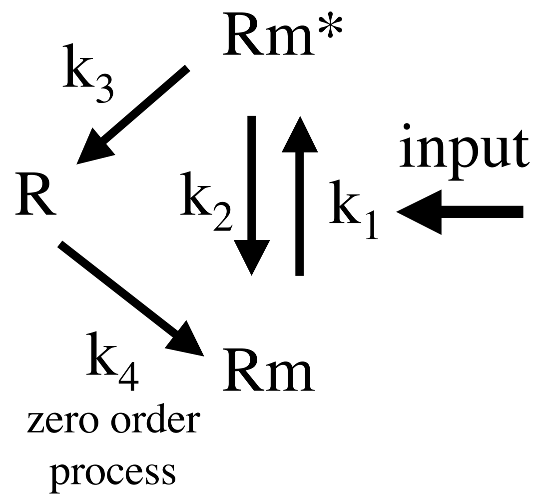
Integral feedback control gives perfect adaptation

(Yi *et al*. PNAS 97 (2000) 4649-4653)



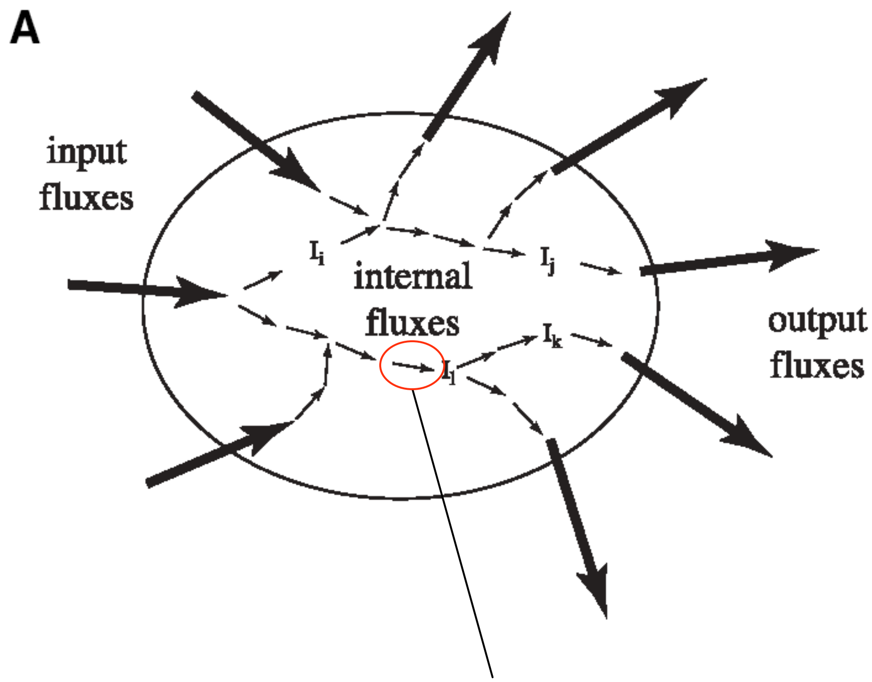
$\dot{x} = y$	$y(t) \to 0$ as $t \to \infty$
$y = y_1 - y_0$	*iff*
$\quad = k(u - x) - y_0$	$k > 0$

Fig. 2. A block diagram of integral feedback control. The variable u is the input for a process with gain k. The difference between the actual output y_1 and the steady-state output y_0 represents the normalized output or error, y. Integral control arises through the feedback loop in which the time integral of y, x, is fed back into the system. As a result, we have $\dot{x} = y$ and $y = 0$ at steady-state for all u. In the Barkai–Leibler model of the bacterial chemotaxis signaling system, the chemoattractant is the input, receptor activity is the output, and $-x$ approximates the methylation level of the receptors.



Barkai & Leibler, Nature 387 (1997) 913-917

Metabolic Control Theory



reaction rate (flux)

$$v$$

Set of N reactions defining a network

$$i \in \{1,2,\ldots,N\}$$

Control coefficient:

$$C_i^v = \frac{\partial \ln v}{\partial \ln k_i} = \left(\frac{\partial v}{\partial k_i}\right)\left(\frac{k_i}{v}\right)$$

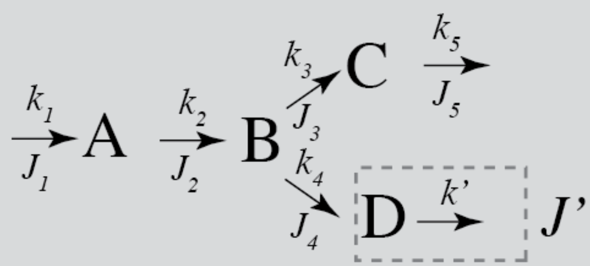
$$\sum_{i=1}^{N} C_i^v = 1$$

Temperature adaptation

Condition: $$\frac{d \ln J_j}{d \ln T} = \frac{1}{RT} \sum_{i=1}^{N} C_i^{J_j} E_a^{k_i} = 0$$

Example:

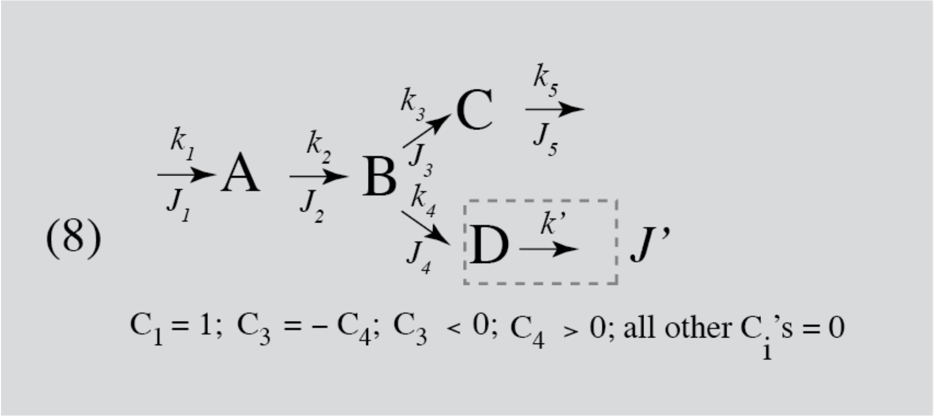
(8)

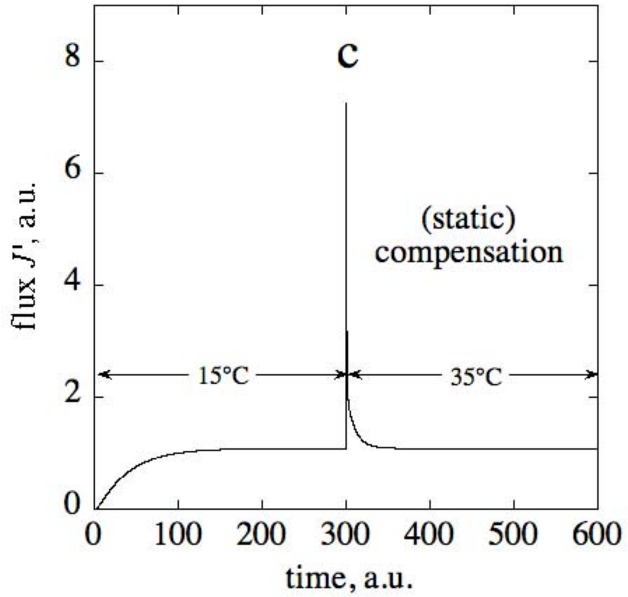


$C_1 = 1$; $C_3 = -C_4$; $C_3 < 0$; $C_4 > 0$; all other C_i's $= 0$

Ruoff *et al*. FEBS J **274** (2007) 940-950.

Perfect Temperature adaptation of flux *J'*

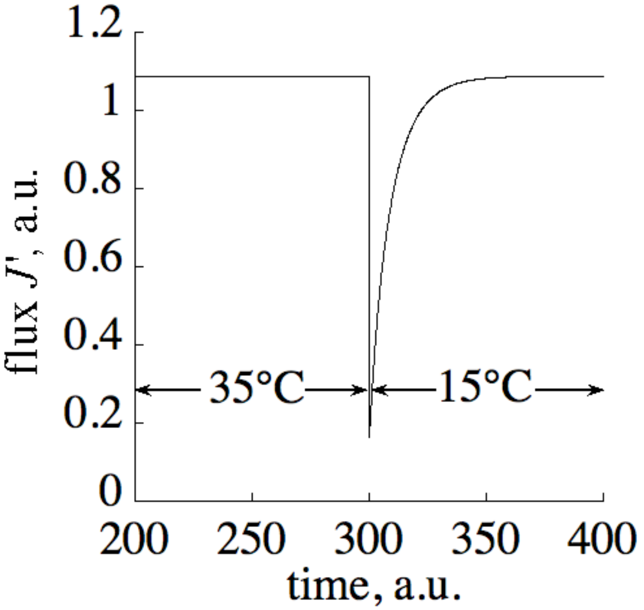




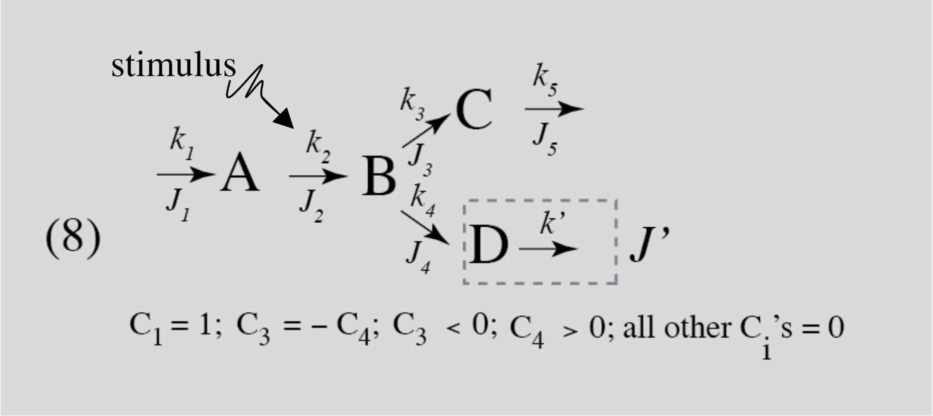
At 25°: k_1=1.7, k_2=0.1, k_3=0.5, k_4=1.5, k_5=1.35, k'=0.7

Initial concentrations of A, B, C, and D are zero.

E_1=26 kJ/mol, E_3=120 kJ/mol and E_4=22 kJ/mol.

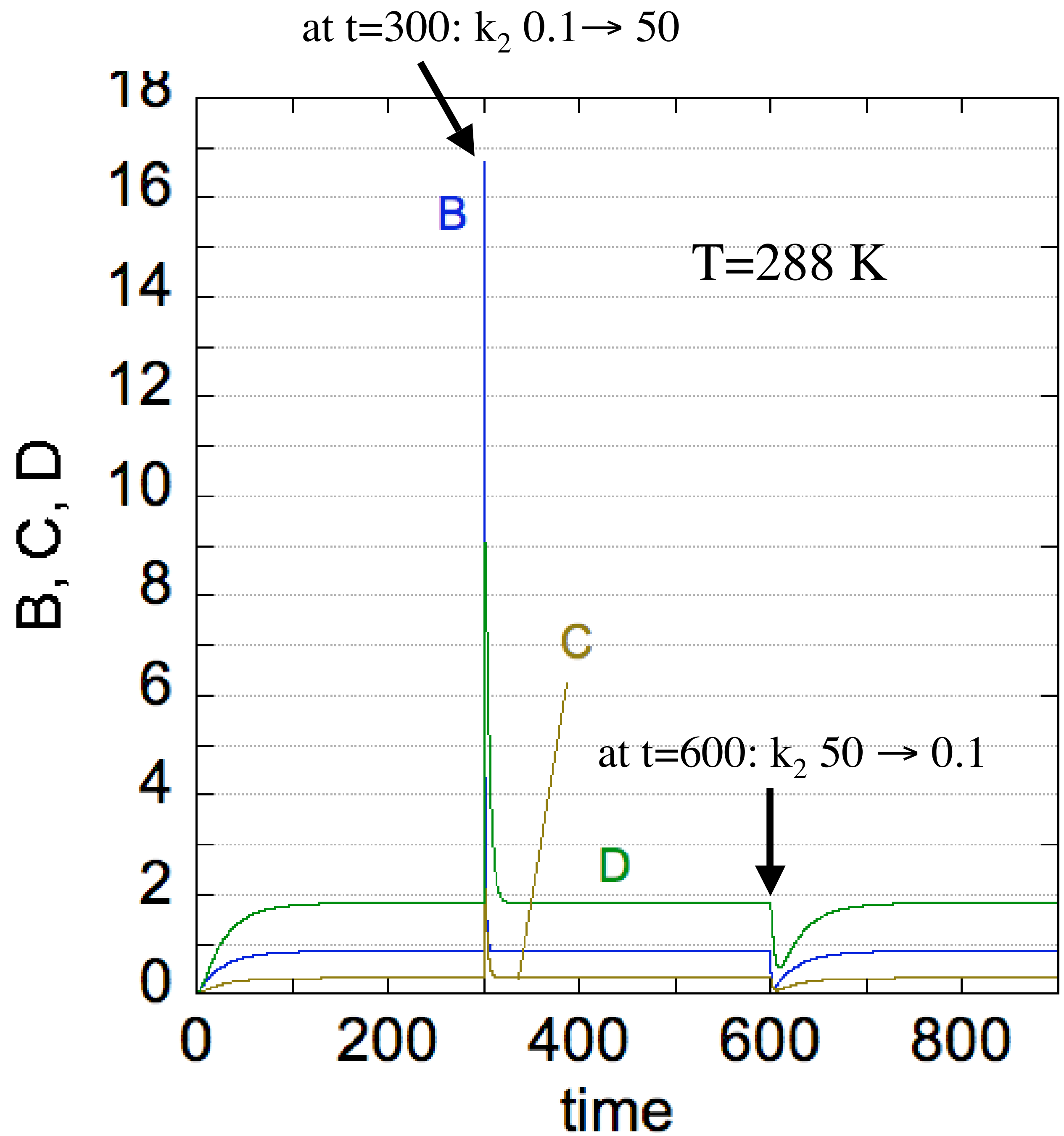


Perfect adaptation of flux *J'* when a receptor is placed there where the control coefficient is zero



Constant temperature.

Change only k_2 as a step-function.



TCMET501_041
0.000,0.1,300.0

K1=1.7D+0
K2=0.1D+0

K3=0.5D+0
K4=1.5D+0

K5=1.35D+0
K6=0.7D+0

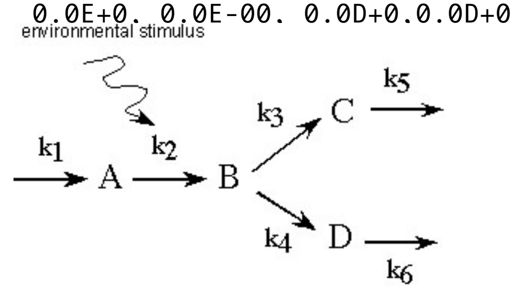
Tref=298.0D+0
Tact1=288.0D+0
Tact2=288.0D+0

2 (rate constant to change)
50.0D+0

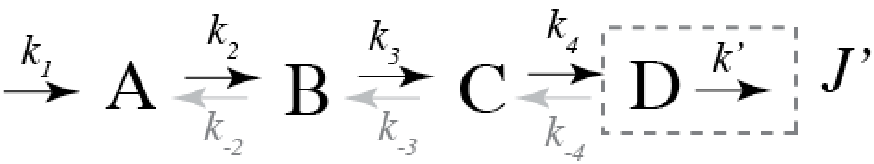
2 (rate constant to change)
0.1D+0

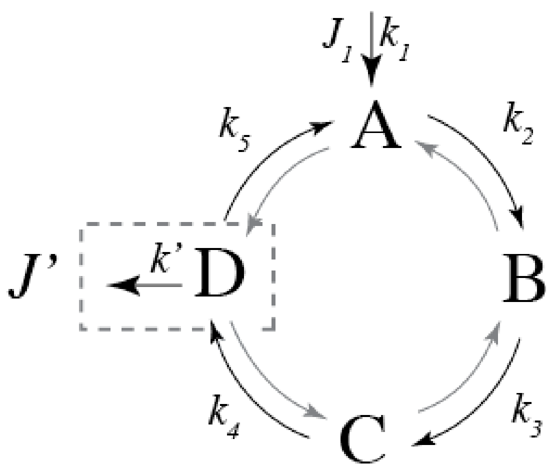
E1=67200.0 J/mol
E2=67200.0 J/mol
E3=67200.0 J/mol
E4=67200.0 J/mol
E5=67200.0 J/mol
E6=67200.0 J/mol

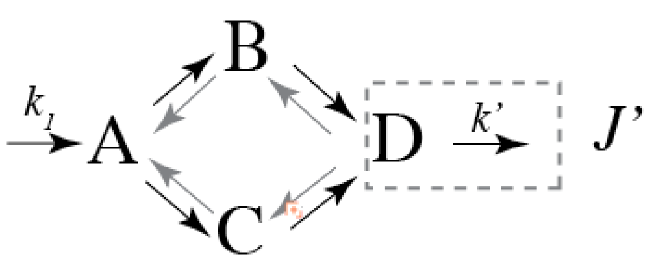
0.0E+0. 0.0E-00. 0.0D+0.0.0D+0



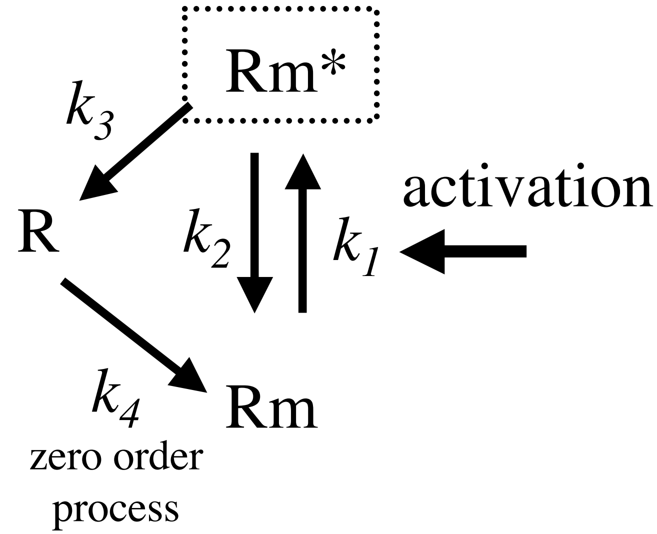
Some reaction sets with zero control coefficients that show perfect adaptation







$C_1 = 1$, all other C_i's are zero

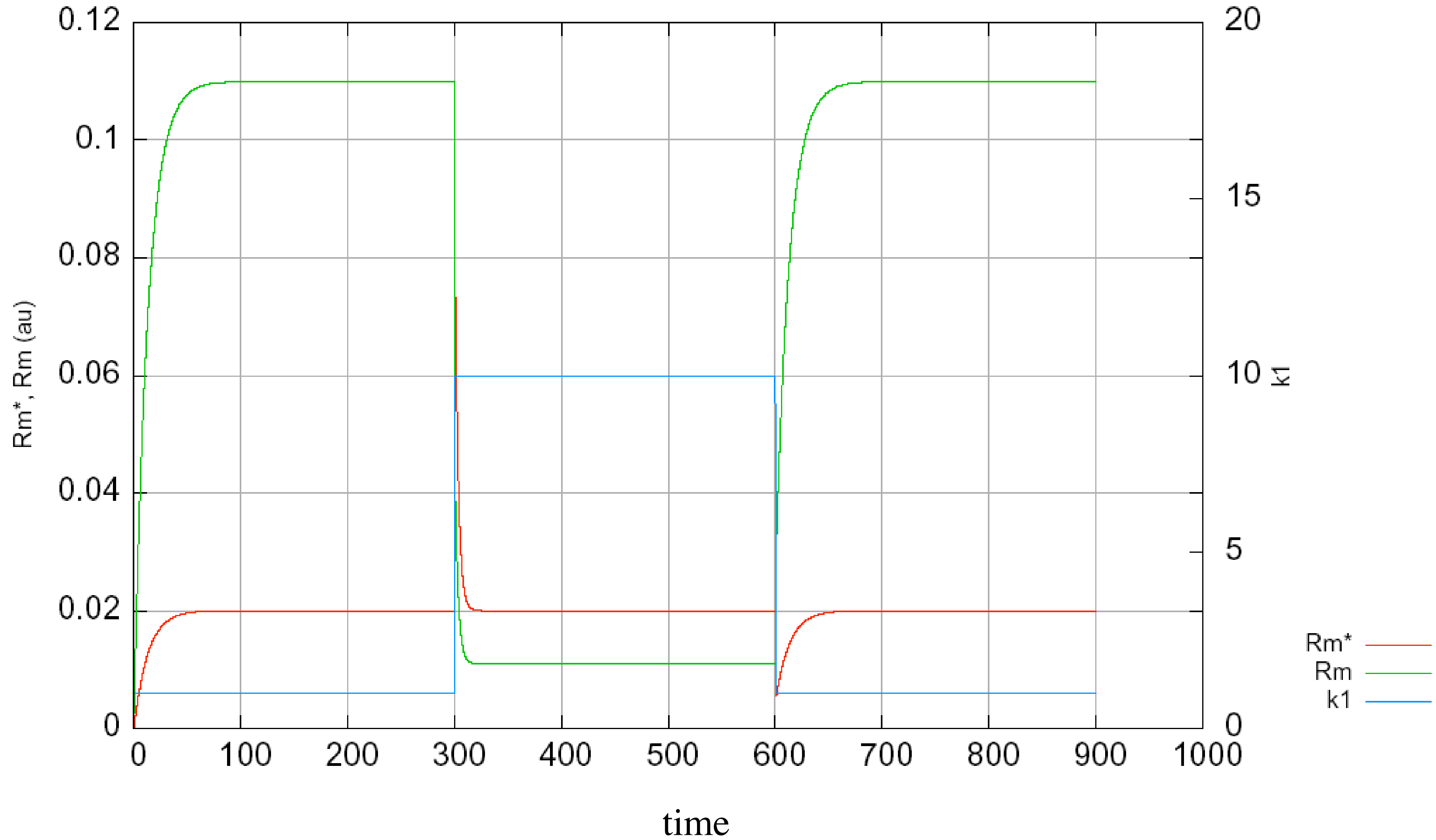


In the Barkai-Leibler model the Rm* steady state is independent of k_1 and k_2:

$[Rm^*]_{ss} = k_4/k_3$.

Therefore, any change in k_1 or k_2 leads to perfect adaptation.

Perfect adaptation in Rm* by changing k_1 stepwise in the Barkai-Leibler model



Summary

- A reaction kinetic system shows perfect adaptation when step-wise changing a rate constant that is associated with a zero control coefficient with respect to a certain flux or steady state concentration.
- No presence of an (explicit) integral feedback control mechanism appears to be required.
- Candidate reactions/rate constants that can show perfect adaptation are easily identified.