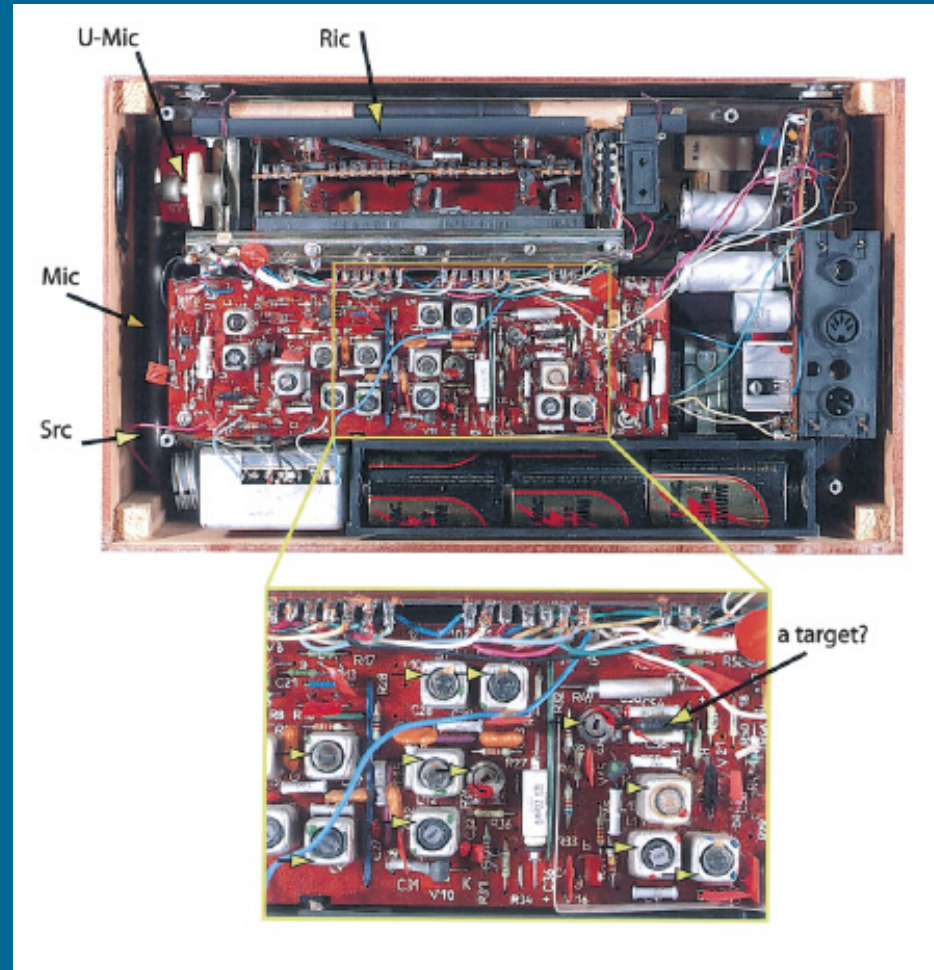


A compositional approach to the stochastic dynamics of gene networks

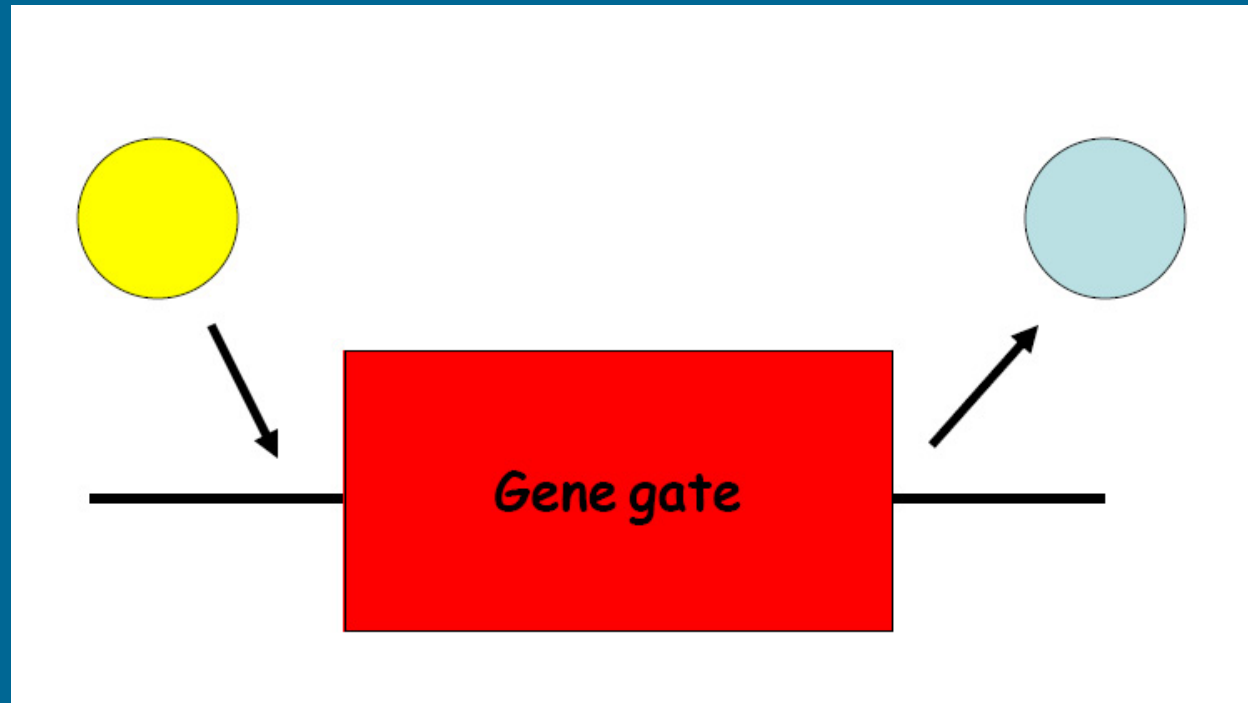
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Gene networks as gene circuits:...engineered modules: a useful paradigm?



Reminder: let's build gene regulatory networks as gene circuits...

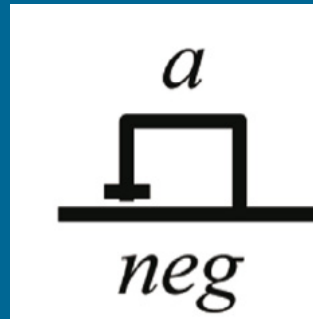


...gate reaction kinetics:

a input, G gate, G' "activated" gate, b output...



... Gate reactions \rightarrow kinetic ODE's...



$$\dot{a} = \varepsilon G - \delta a \quad \dot{G} = \eta N - (\eta + ra)G$$

where $N = G + G' = \text{const.}$

...stationary state: a_0, G_0 .

fast relaxation of activated gate: $\eta \rightarrow \infty$:

$$\dot{a} = \frac{\varepsilon N}{1 + \nu a} - \delta a$$

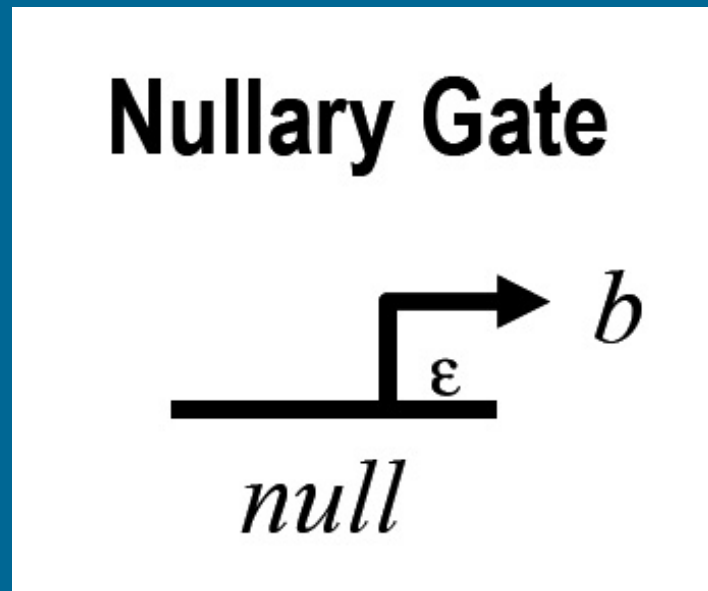
where $\nu = r/\eta = O(1)$.

Hence: equivalent to standard approach.

Here: Hill-coefficient = 1, larger values: more binding partners.

...in stochastic π -calculus

... a gene gate which transcribes constitutively:



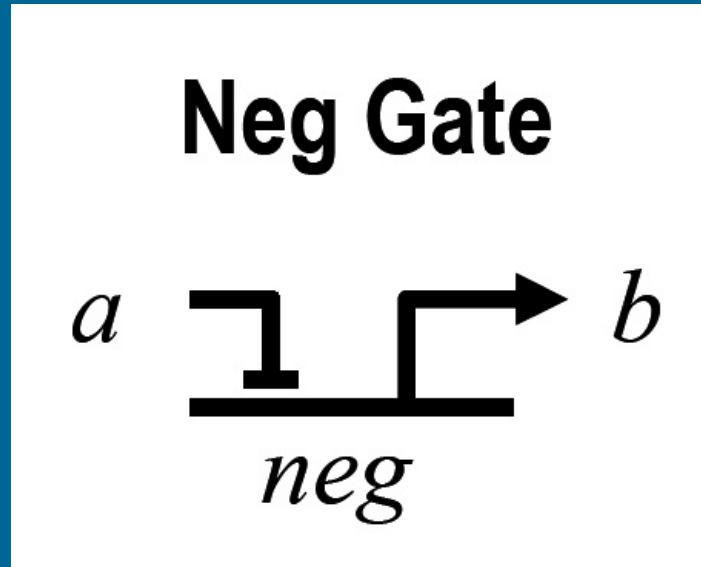
$$null(b) = \tau_\epsilon.(tr(b)|null(b))$$

$$tr(b) = !b.tr(b) + \tau_\delta.0$$

ODE for comparison:

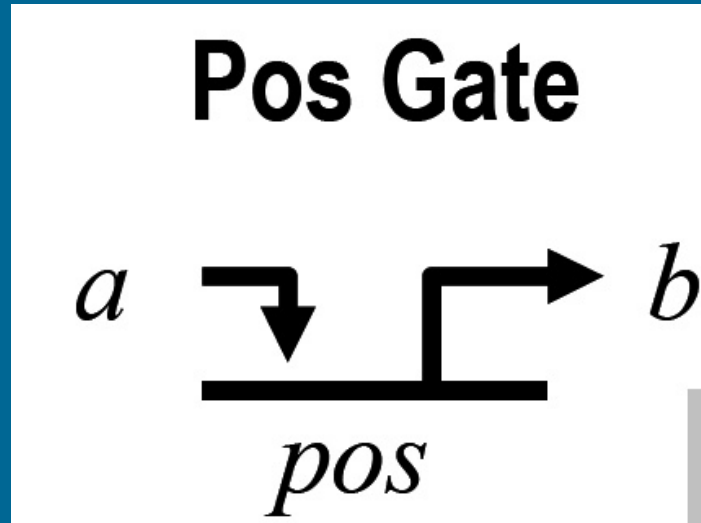
$$\dot{b} = \epsilon N - \delta b$$

...an inhibitory gate:



$$neg(a, b) = ? a \cdot \tau_{\eta} \cdot neg(a, b) + \tau_{\epsilon} \cdot (tr(b) | neg(a, b))$$

...an excitatory gate:



$$pos(a, b) = ? a \cdot \tau_{\eta} \cdot (tr(b) | pos(a, b)) + \tau_{\epsilon} \cdot (tr(b) | pos(a, b))$$

Conclusions:

- there is an exact mapping from reaction kinetics to π and to ODE (Cardelli);
- the ODE's to the compositional model are "equivalent" to the protein/mRNA approach;

Repressilator: ...reminder to EL-ODE modeling ...

$$\frac{dm_i}{dt} = -m_i + \frac{\alpha}{1 + p_j^h} + \alpha_0$$

$$\frac{dp_i}{dt} = -\beta(p_i - m_i)$$

$$i = (lacI, tetR, cI), \quad j = (cI, lacI, tetR)$$

...the repressilator merits more discussion...

- in our model: Hill coefficient $h = 1$ but:
- h only slightly > 1 suffices for EL-dynamics (see Stadler et al., 2006: $h = 4/3$.)
- effects of stochasticity ? Known in principle, but not yet fully analyzed.

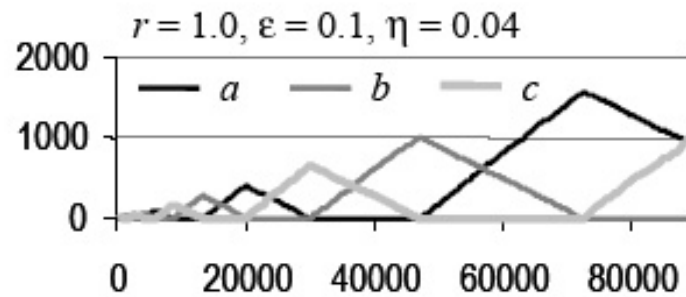
MOCA

Build compositional ODE + π model for cell cycle dynamics.

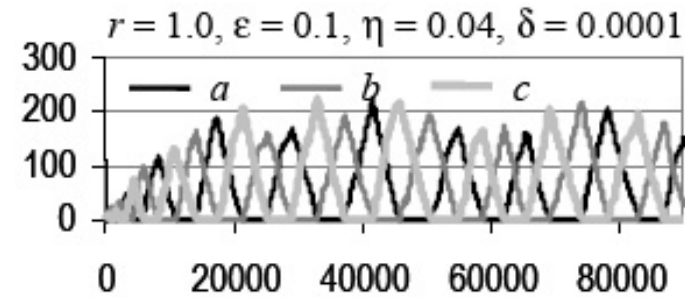
Main feature: "zoom-in".

...example (trivial): protein degradation in the repressilator.

A) $tr(p) = !p.0$



B) $tr(p) = (!p.0) + (\tau_\delta.0)$



C) $tr(p) = (!p.tr(p)) + (\tau_\delta.0)$

