

Supporting Information: A simple negative interaction in the positive transcriptional feedback of a single gene is sufficient to produce reliable oscillations

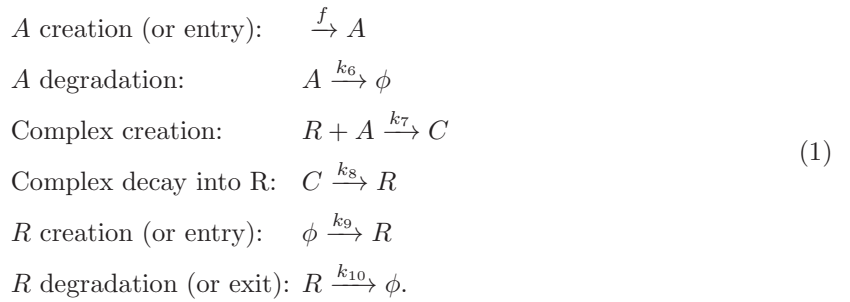
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The negative interaction does not produce an effective high nonlinearity

It has been demonstrated that protein sequestration produces an effective high nonlinearity [1,2]. But this high nonlinearity is not observed if the repressor molecule is recycled (see equation S9 and figure S5 in [1]). The biochemical reactions that describe the negative interaction are as follows:



The dynamics of these reactions are described by the following EDOs:

$$\begin{aligned}
 dA/dt &= f - k_6A - k_7AR \\
 dR/dt &= -k_7AR + k_8C + k_9 - k_{10}R \\
 dC/dt &= k_7AR - k_8C,
 \end{aligned} \tag{2}$$

As in [1], these equations can be solved at steady state to yield:

$$\begin{aligned}
 A &= \frac{fk_{10}}{k_7k_9 + k_6k_{10}} \\
 R &= \frac{k_9}{k_{10}} \\
 C &= \frac{fk_7k_9}{(k_7k_9 + k_6k_{10})k_8},
 \end{aligned} \tag{3}$$

where we observe no nonlinearity in output A as a function of input flux f .

References

1. Buchler NE, Louis M (2008) Molecular titration and ultrasensitivity in regulatory networks. J Mol Biol 384:1106-1119.
2. Buchler NE, Cross FR (2009) Protein sequestration generates a flexible ultrasensitive response in a genetic network. Mol Syst Biol 5:272.