## S1 Text

# An amplified derepression controller with multisite inhibition and positive feedback 

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# Controller performance towards step-wise changes in $k_{1}$ and linearly increasing $k_{1}$ values 

As shown in the schematic diagram by Fig 7 and Eqs 11 and 12 in the main text, a positive feedback can be implemented by first-order or second-order autocatalysis in C, which increase controller performance in terms of its lifetime.
Here, results with step-wise changes and with linear increase in $k_{1}$ are shown when $C$ is produced by first-order and second-order autocatalysis.

First-order autocatalysis in $C$


Figure S1: Controller performance with first-order autocatalysis in $C$ (Eq. 11 in the main text) and linear increase of $k_{1}\left(\dot{k_{1}}=10.0\right)$. Phase 1: the controller is at steady state at its set-point $A_{\text {set }}=5.0$ with constant $k_{1}=2.0$. Initial concentrations: $A_{0}=5.0, E_{0}=0.9, C_{0}=1.0$. Phase 2 : $k_{1}$ increases linearly, $k_{2}=1 \times 10^{5}, k_{3}=5 \times 10^{2}, k_{4}=1 \times 10^{2}, k_{5}=10.0$, and $k_{6}=1.0 . K_{M}=1 \times 10^{-6}$, $K_{I}=0.1, n=4\left(\mathrm{Eq} 6\right.$ in the main text). Left panel: $k_{1}$ and $C$ as a function of time; right panel: $A$ and $E$ as a function of time.


Figure S2: Controller performance with first-order autocatalysis in $C$ (Eq. 11 in the main text) and step-wise increase of $k_{1}$. Phase 1: the controller is at steady state at its set-point $A_{\text {set }}=5.0$ with constant $k_{1}=2.0$. Initial concentrations: $A_{0}=5.0, E_{0}=0.9, C_{0}=1.0$. Phase 2: $k_{1}=2 \times 10^{4}, k_{2}=1 \times 10^{5}$, $k_{3}=5 \times 10^{2}, k_{4}=1 \times 10^{2}, k_{5}=10.0$, and $k_{6}=1.0 . K_{M}=1 \times 10^{-6}, K_{I}=0.1, n=4$ (Eq 6 in the main text). Left panel: $k_{1}$ and $C$ as a function of time; right panel: $A$ and $E$ as a function of time.

## Second-order autocatalysis in $C$



Figure S3: Controller performance with second-order autocatalysis in $C$ (Eq. 12 in the main text) and linear increase of $k_{1}\left(\dot{k}_{1}=10.0\right)$. Phase 1 : the controller is at steady state at its set-point $A_{\text {set }}=5.0$ with constant $k_{1}=2.0$. Initial concentrations: $A_{0}=5.0, E_{0}=0.9, C_{0}=1.0$. Phase 2: $k_{1}$ increases linearly, $k_{2}=1 \times 10^{5}, k_{3}=5 \times 10^{2}, k_{4}=1 \times 10^{2}, k_{5}=10.0$, and $k_{6}=1.0 . K_{M}=1 \times 10^{-6}$, $K_{I}=0.1, n=4\left(\mathrm{Eq} 6\right.$ in the main text). Left panel: $k_{1}$ and $C$ as a function of time; right panel: $A$ and $E$ as a function of time.


Figure S4: Controller performance with second-order autocatalysis in $C$ (Eq. 12 in the main text) and step-wise increase of $k_{1}$. Phase 1: the controller is at steady state at its set-point $A_{\text {set }}=5.0$ with constant $k_{1}=2.0$. Initial concentrations: $A_{0}=5.0, E_{0}=0.9, C_{0}=1.0$. Phase 2: $k_{1}=2 \times 10^{4}, k_{2}=1 \times 10^{5}$, $k_{3}=5 \times 10^{2}, k_{4}=1 \times 10^{2}, k_{5}=10.0$, and $k_{6}=1.0 . K_{M}=1 \times 10^{-6}, K_{I}=0.1, n=4$ (Eq 6 in the main text). Left panel: $k_{1}$ and $C$ as a function of time; right panel: $A$ and $E$ as a function of time.

