

Figure S3. Sampling of partitioned parameter space in a simplified two-component system model. (A) The model was simplified by eliminating as many variables as possible while retaining the capability for negative open-loop gain. (B) Distribution of negative and positive open-loop gain cases for fraction of exogenous phosphorylation flux $J_E/(J_E + J_S)$. Histogram bins containing more than 10⁵ members were cut off for clarity. (C) Distribution of cases with feedback-induced overshoot > 10% over the activated steady state. Intervals for parameter sampling were the same as Table S1 with the following exceptions:

 $k'_{txn} \in [4.33 \times 10^{-5}, 100.]; k'_{txnbasal} \in [4.33 \times 10^{-6}, 1.0]; K_{mb} \in [10^{-4}, 10]. k'_{txnbasal}$ and k'_{txn} are derived from

dividing $k_{txnbasal}$ and k_{txn} by $k_{mRNAdeg}$. Production rates of RR and SHK are $k_{txn} \left(\frac{k'_{txn} [RRP]^2}{K^2_{mtxn} + [RRP]^2} + k'_{txnbasal} \right)$

for $k_{tsn} = k_{tsnRR}$, k_{tsnSHK} , respectively.