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Supplemental Information

Hard Limits and Performance Tradeoffs in a Class of Antithetic Integral Feedback Networks

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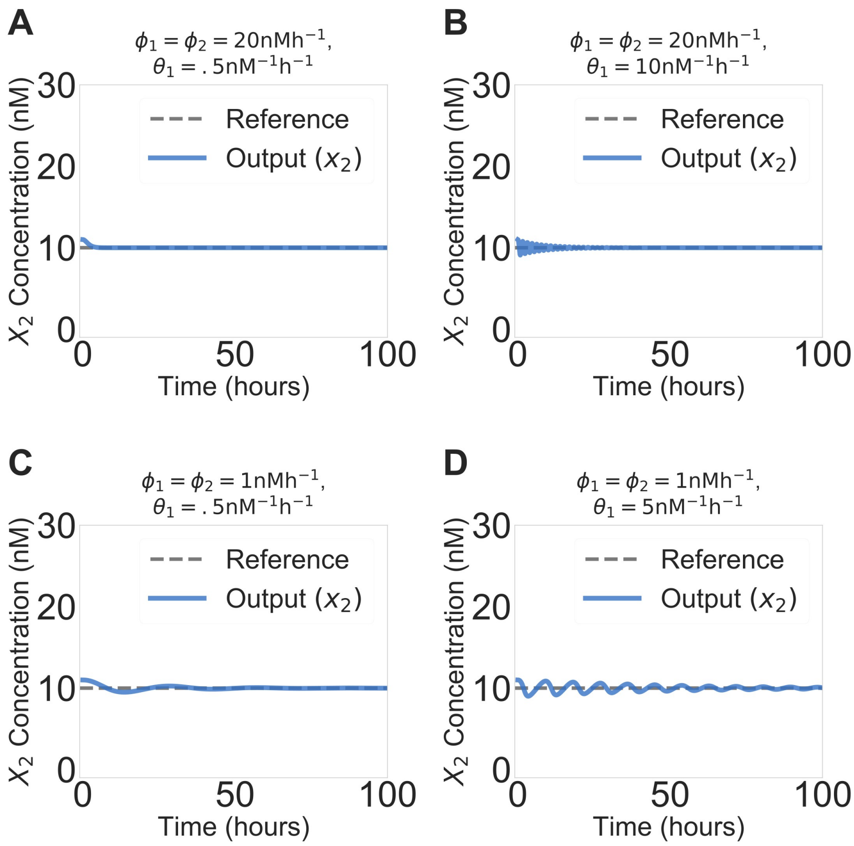

Figure S1: Linear stability of equation (S22). Related to **STAR Methods**. Each panel shows the concentration of the output species X_2. In each panel, we simulate equation (S22) with initial conditions very close to the equilibrium value determined by equation (S23). $x_1(0)$, $z_1(0)$, and $z_2(0)$ are set exactly by equation (S23), and $x_2(0) = \mu/\theta_2 + 1 = 11$. We see that, when the system is initialized near the equilibrium, stability is well-characterized by inequality (S24). In all simulations $k = 1\,\text{nM}^{-1}\,\text{h}^{-1}$, $\theta_2 = 1\,\text{h}^{-1}$, $\eta = 1000\,\text{nM}^{-1}\,\text{h}^{-1}$, and $\mu = 100\,\text{nM}\,\text{h}^{-1}$.

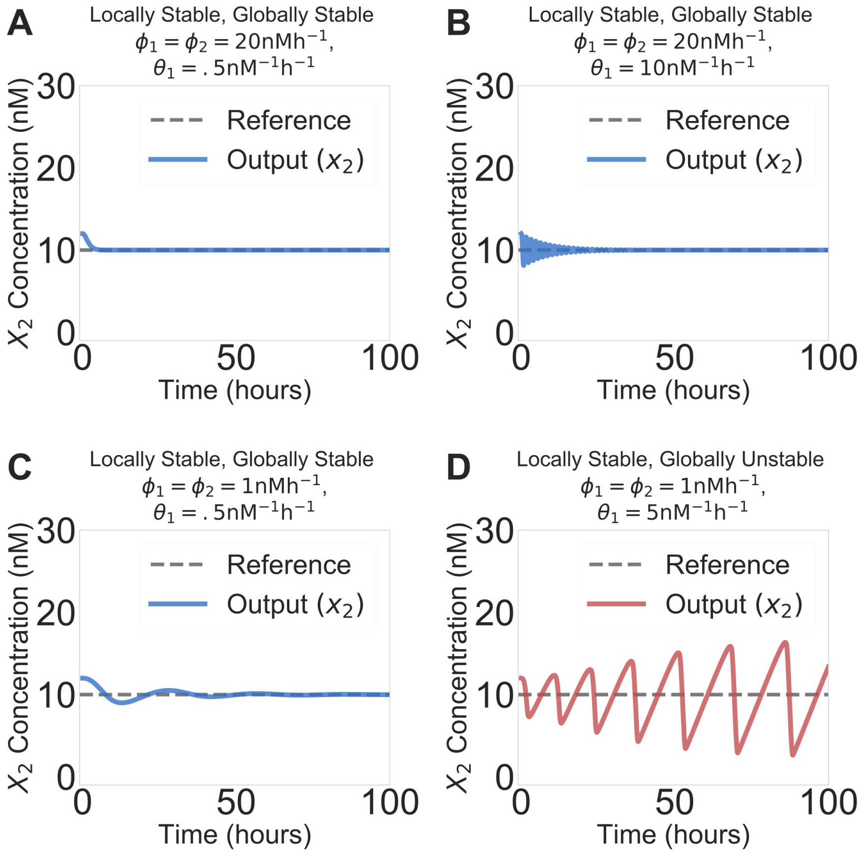

Figure S2: Nonlinear behavior of equation (S22). Related to **STAR Methods**. Here we simulate the circuit described in equation (S22) and show that it can exhibit nonlinear behavior that is not captured by linear stability analysis. Each panel shows the concentration of the output species X_2, with the initial conditions of $x_1(0)$, $z_1(0)$, and $z_2(0)$ set exactly by equation (S23), and $x_2(0) = \mu/\theta_2 + 2 = 12$. In panels **A** and **B**, we see that the circuit's dynamics are well characterized by linear analysis, where even parameters that are both close and far from the stability boundary from inequality(S24) yield stable dynamics. In contrast, panels **C** and **D** both use parameters for which inequality (S24) predicts stability, yet only **C** is actually globally stable. Panel **D** is locally stable, however it appears to converge to an equilibrium characterized by an attracting limit cycle. This is fundamentally nonlinear behavior that cannot be captured by strictly linear analysis. In all simulations $k = 1\,\text{nM}^{-1}\,\text{h}^{-1}$, $\theta_2 = 1\,\text{h}^{-1}$, $\eta = 1000\,\text{nM}^{-1}\,\text{h}^{-1}$, and $\mu = 100\,\text{nM}\,\text{h}^{-1}$.