Modeling and analysis for bio-circuits design

8th Mar. 2019

Ayush Pandey

Overview

Current practices

- Nonlinear Analysis
- Stability Analysis
- Input to state stability

Overview

- Current practices
- **Nonlinear Analysis**
- Stability Analysis
- Input to state stability

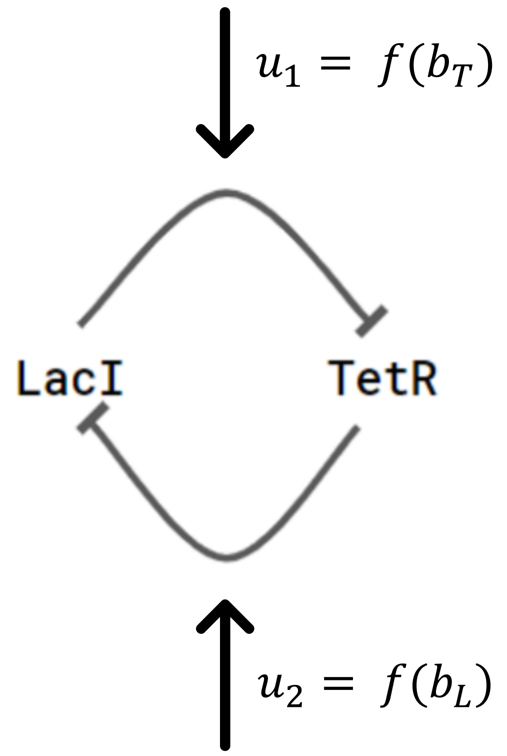
Toggle Switch – Full Model

$$\dot{m}_T = \frac{Kb_T^n}{b_T^n + p_L^n} - d_T m_T$$

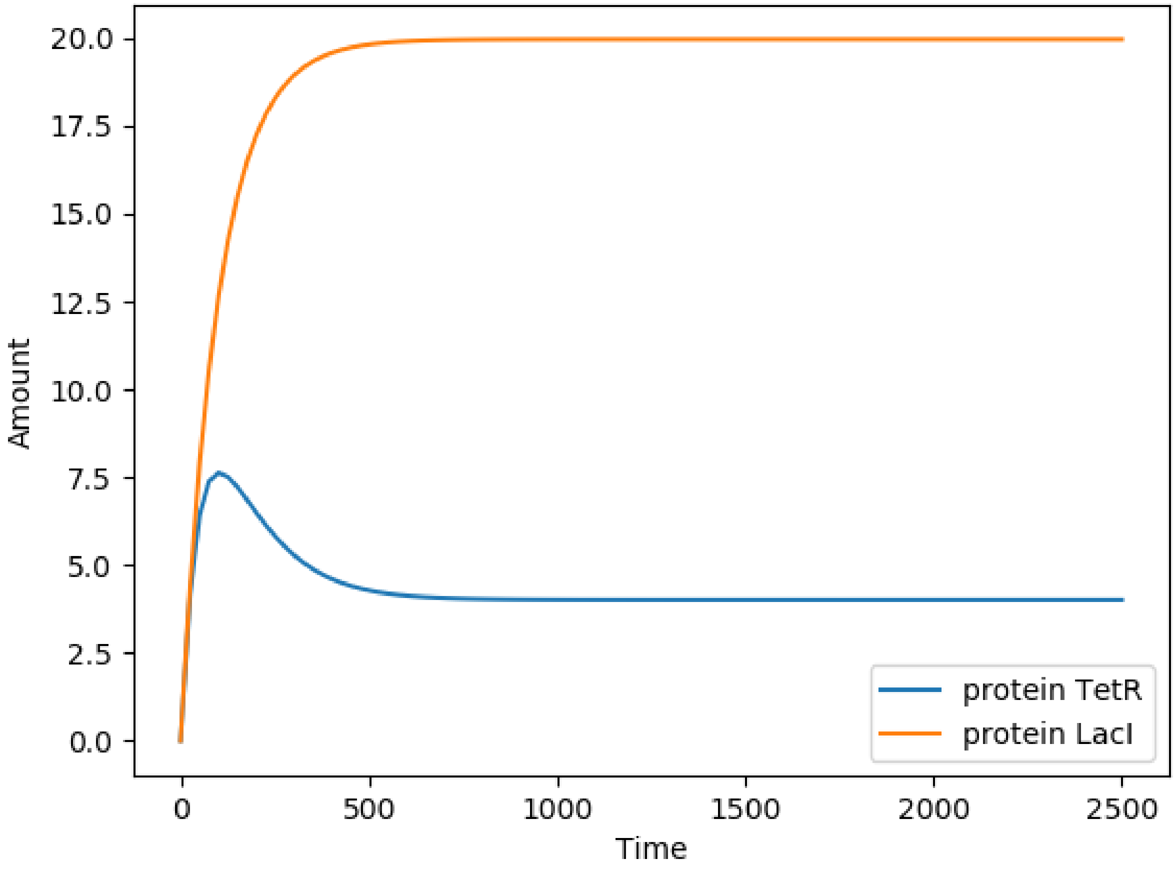
$$\dot{m}_L = \frac{Kb_L^n}{b_L^n + p_T^n} - d_L m_L$$

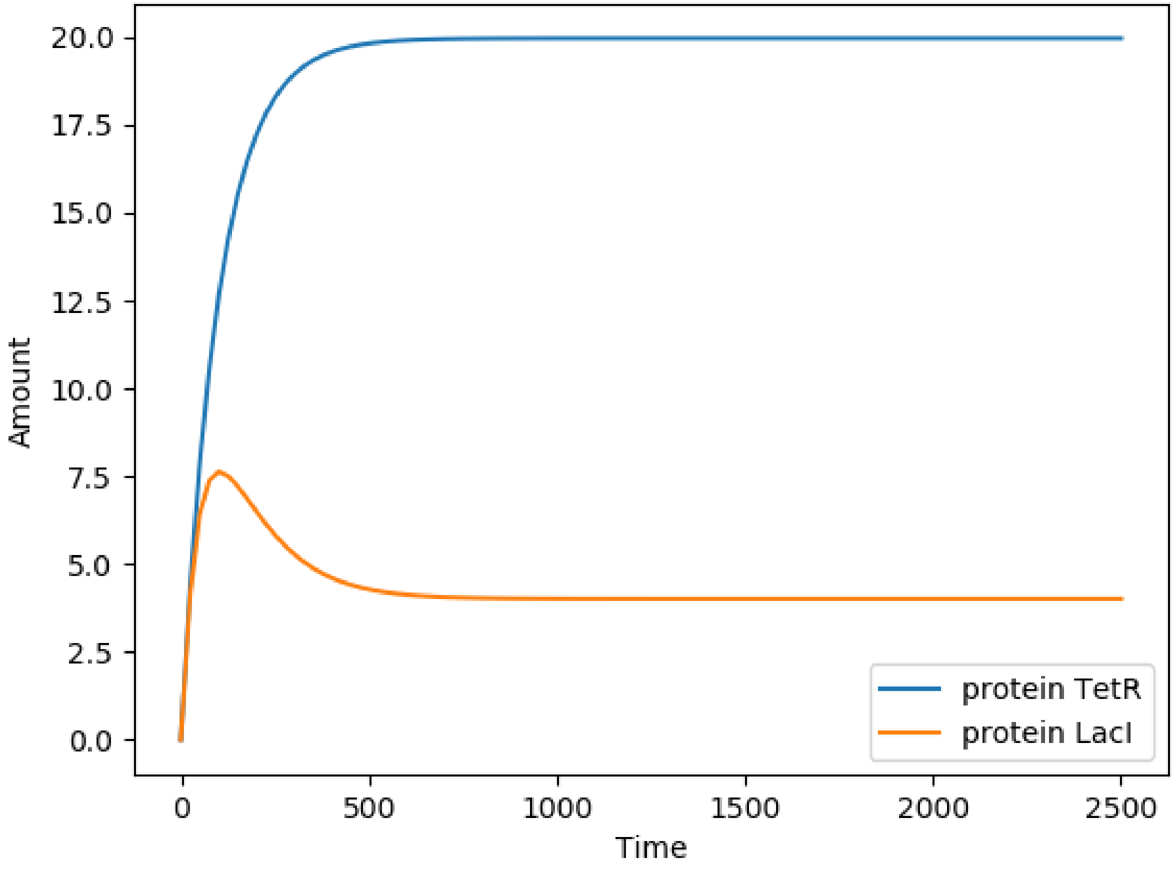
$$\dot{p}_T = \beta_T m_T - \delta_T p_T$$

$$\dot{p}_L = \beta_L m_L - \delta_L p_L$$



Numerical Solutions – Toggle protein expression



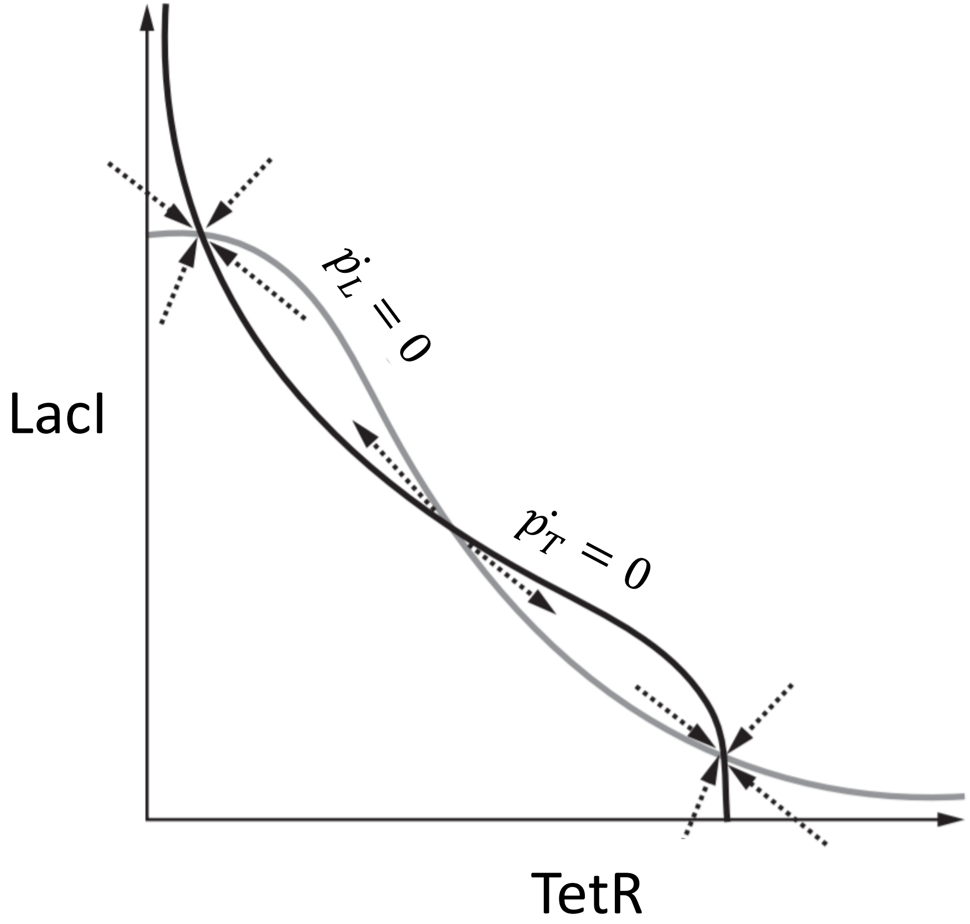


Overview

Current practices	
Nonlinear Analysis	
Stability Analysis	
Input to state stability	

Nullclines and domain of attraction

- Three equilibrium points
- Two stable and one unstable
- Each equilibrium corresponds to a different protein expression
- Induction parameters (input) can be used to drive system.



Results - Stability

- Using the converse Lyapunov theory,
- From the lecture notes,

$$\boxed{\begin{gathered}\dot{x} = f(x) \;\; \textit{is locally exponentially stable} \\ \Updownarrow \\ \dot{x} = Df(0)x \;\; \textit{is exponentially stable}\end{gathered}}$$

gives a constructive approach to find Lyapunov functions for nonlinear systems.

$$V(x) = x^T P x$$

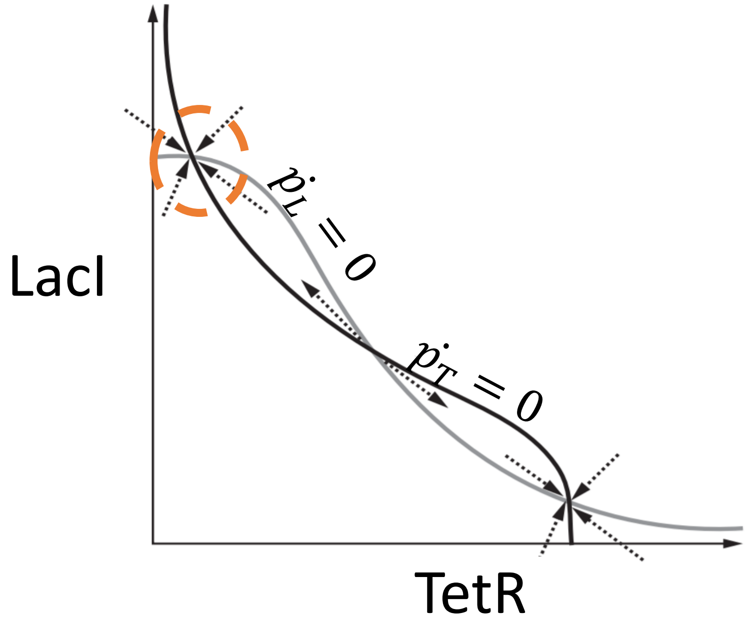
$$P = \begin{bmatrix} 2.672 & -0.436 & 2.362 & -11.549 \\ -0.436 & 1.886 & -9.662 & 1.960 \\ 2.362 & -9.662 & 52.362 & -10.605 \\ -11.549 & 1.960 & -10.605 & 51.960 \end{bmatrix}$$

$$\lambda_P = \begin{bmatrix} 65.392 \\ 43.289 \\ 0.099 \\ 0.100 \end{bmatrix}$$

Estimate of domain of attraction

$$\left\| \int_0^1 Df(\tau x) d\tau - Df(0) \right\| < \frac{\lambda_{min}(Q)}{2\lambda_{max}(P)}, \; x \in \mathcal{B}_r(0)$$

$$\mathcal{B}_{0.086}(0) \subset D_{oa}$$



Overview

- Current practices
- Nonlinear Analysis
- Stability Analysis
- **Input to state stability**

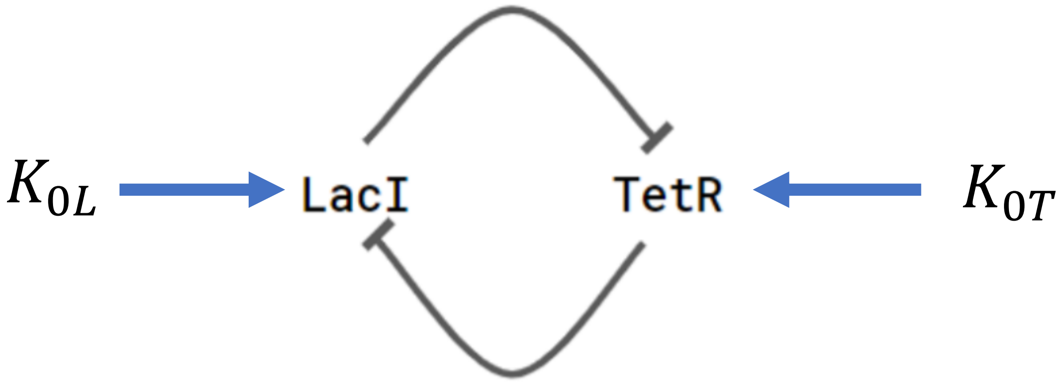
Motivation

- Modeling leaky expression

$$\dot{x} = f(x) + d$$

$$d = \begin{bmatrix} K_{0T} \\ K_{0L} \end{bmatrix}$$

$$\dot{m}_T = \frac{Kb_T^2}{b_T^2 + p_L^2} - d_T m_T + K_{0T}$$
$$\dot{m}_L = \frac{Kb_L^2}{b_L^2 + p_T^2} - d_L m_L + K_{0L}$$
$$\dot{p}_T = \beta_T m_T - \delta_T p_T$$
$$\dot{p}_L = \beta_L m_L - \delta_L p_L$$



Input to state stability

$$\|d\| \leq \frac{1}{4}\frac{\lambda_{\min}}{\lambda_{\max}(P)}\|x\| \iff \|x\| \geq \frac{4\lambda_{\max}(P)}{\lambda_{\min}(Q)}\|d\|$$

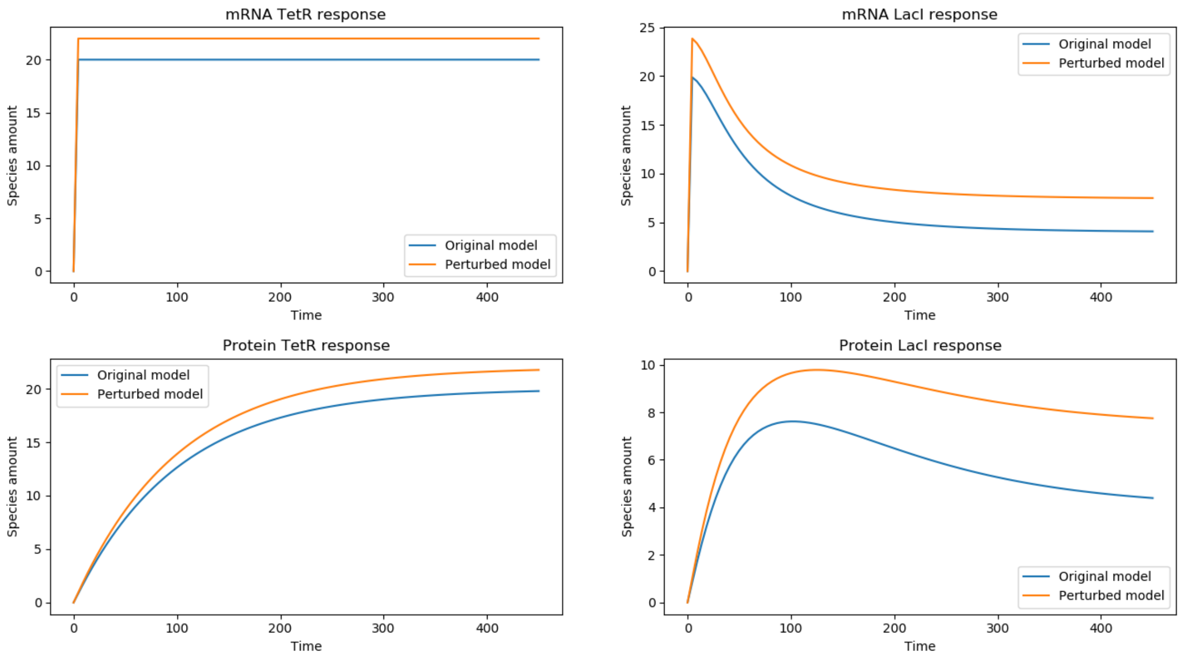
$$\|x(t)\| \leq \alpha_1^{-1}\left(\beta\left(\alpha_2\left(\|x(0)\|\right), t - t_0\right)\right)$$

$$\rho(r) = \frac{4\lambda_{\max}(P)}{\lambda_{\min}(Q)}$$

$$\alpha_1(r) = \lambda_{\min}(P)r^2$$

$$\alpha_2(r) = \lambda_{\max}(P)r^2$$

$$\alpha_3(r) = \frac{1}{2}\lambda_{\min}(Q)r^2$$

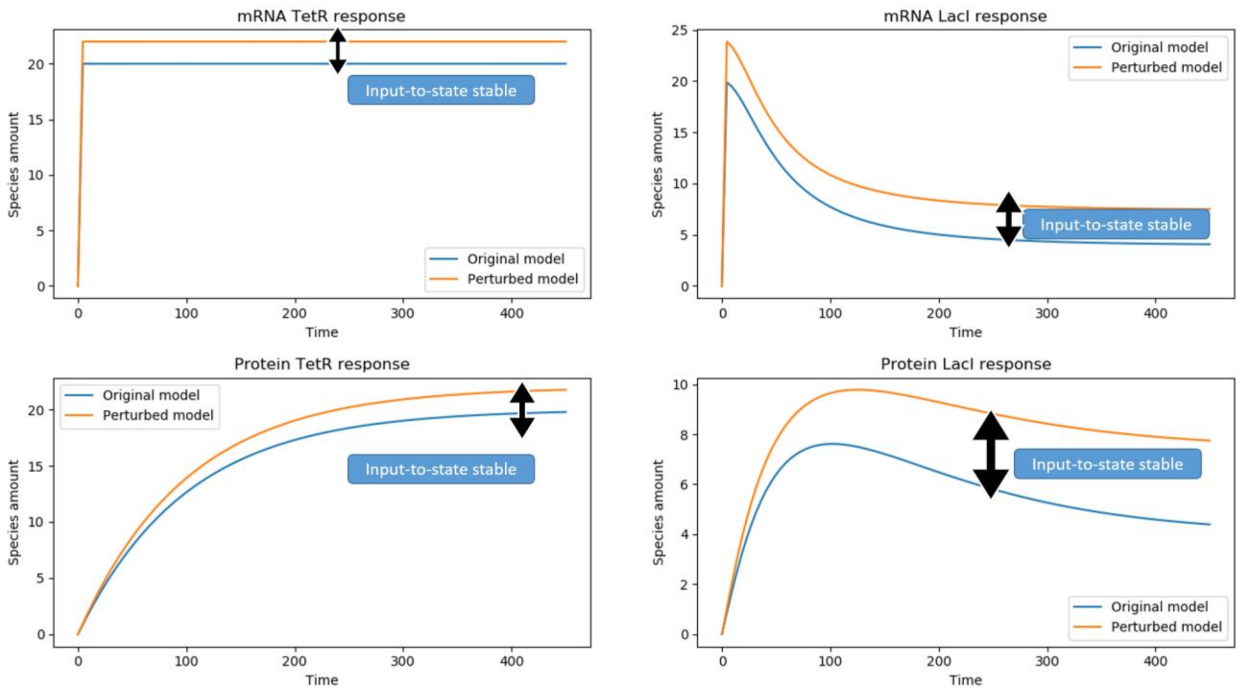


$$\boxed{\|x(t)\| \leq \max\left(\|x(0)\| e^{-\frac{\lambda_{\min}(Q)}{4\lambda_{\max}(P)}t} M^{\frac{1}{2}}, \frac{4\lambda_{\max}(P)}{\lambda_{\min}(P)}\|d\|\right)}$$

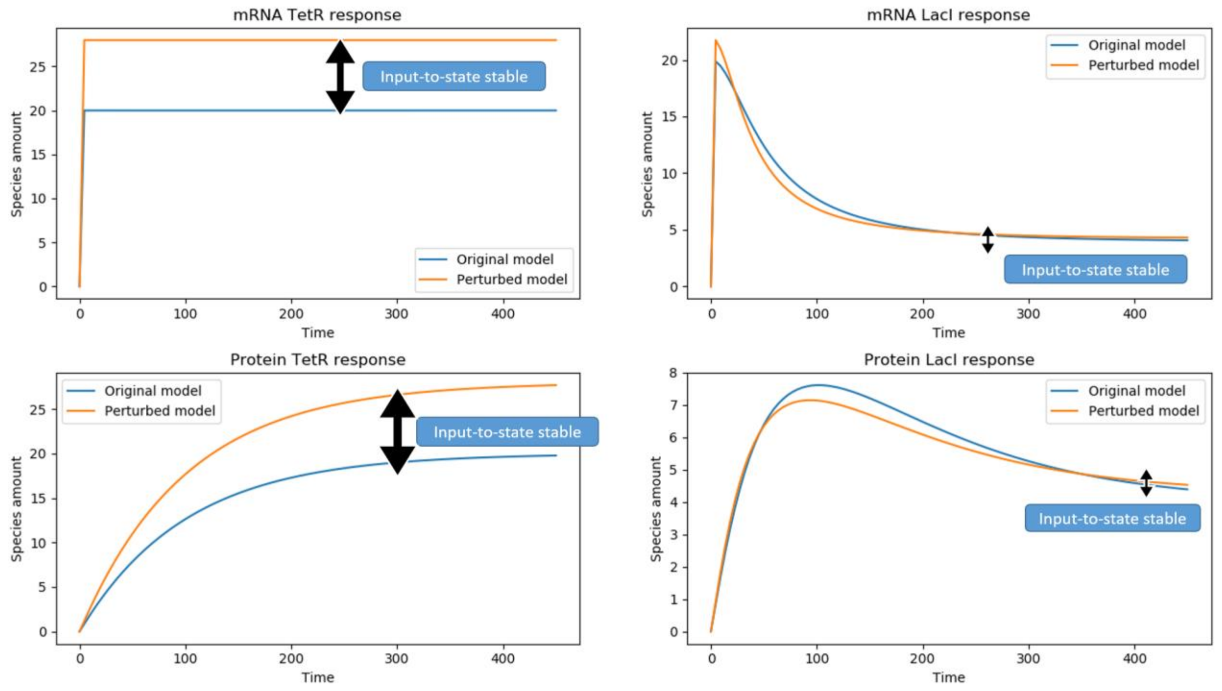
$$M \triangleq x_0^T P x_0$$

Results – Different disturbance bounds

$$||d|| = 30$$



$$||d|| = 50$$



Future directions

- Applications of input to state stability analysis in developing predictive models for bio-circuits.
- Modeling resource sharing – saturation like nonlinearities.
- Design of bio-circuits using nonlinear analysis.

- Questions?