Advanced Bioengineering

Examples Session on Control Motifs in Biology

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Department of Biosystems Science and Engineering

November 27, 2020

Overview

Today:

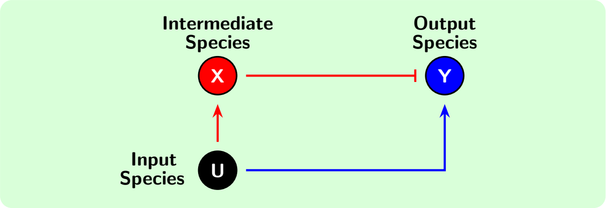
1. Incoherent FeedForward Loops (IFFL)

2. Negative FeedBack Loops (NFBL)

3. Realization of Integral Feedback Control in Biology

Incoherent FeedForward Loop (IFFL)

Topology:



Incoherent FeedForward Loop (IFFL)

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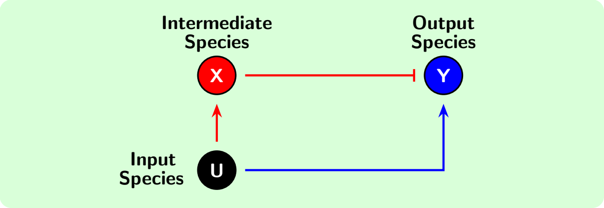

$$\dot{X} = k_x U - \gamma_x X$$

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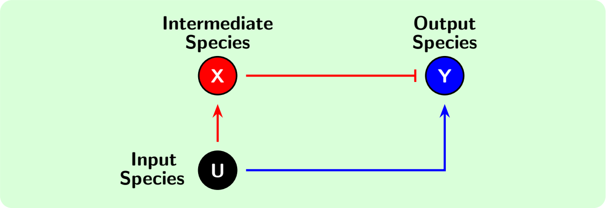

$$\dot{X} = k_x U - \gamma_x X$$

$$\dot{Y} = \frac{k_y U}{1 + X/\kappa} - \gamma_y Y$$

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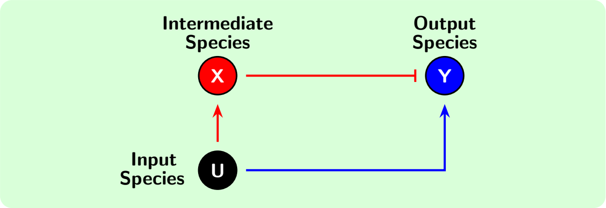

$$\dot{X} = k_x U - \gamma_x X$$

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At steady state: $$\begin{cases} \dot{X} = 0 \\ \dot{Y} = 0 \end{cases}$$

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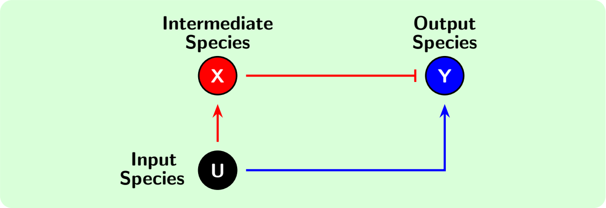

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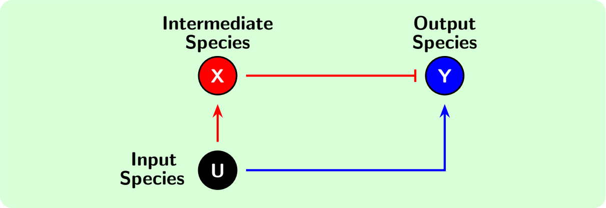

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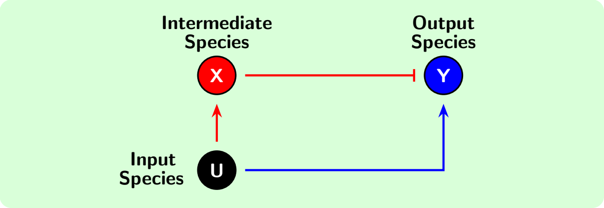

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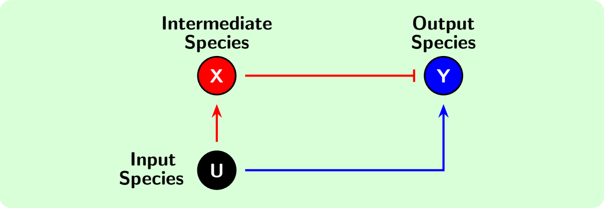

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If $\frac{k_x U}{\gamma_x \kappa} >> 1$

Incoherent FeedForward Loop (IFFL)

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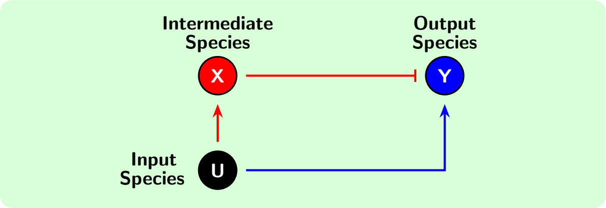

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$$\text{If } \frac{k_x U}{\gamma_x \kappa} >> 1 \quad \Longrightarrow \quad \bar{Y} \approx \frac{\frac{k_y U}{\gamma_y}}{\frac{k_x U}{\gamma_x \kappa}}$$

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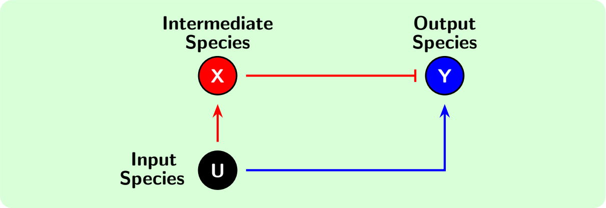

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If $\frac{k_x U}{\gamma_x \kappa} >> 1 \quad \Longrightarrow \quad \bar{Y} \approx \dfrac{\frac{k_y \not{U}}{\gamma_y}}{\frac{k_x \not{U}}{\gamma_x \kappa}}$

Incoherent FeedForward Loop (IFFL)

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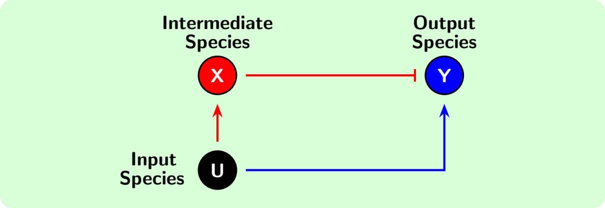

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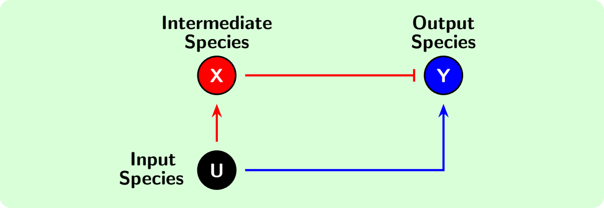

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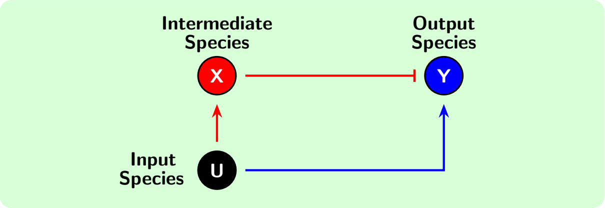

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$$\implies \bar{Y} \approx \frac{k_y \gamma_x}{k_x \gamma_y} \kappa$$

$\implies$ At steady state, the output Y is independent of the input U!

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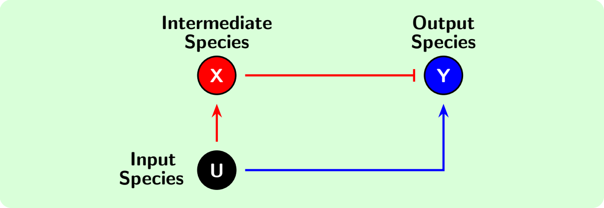

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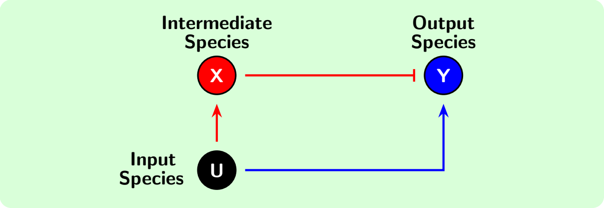
$$\implies \bar{Y} \approx \frac{k_y \gamma_x}{k_x \gamma_y} \kappa$$

$\implies$ At steady state, the output Y is independent of the input U!

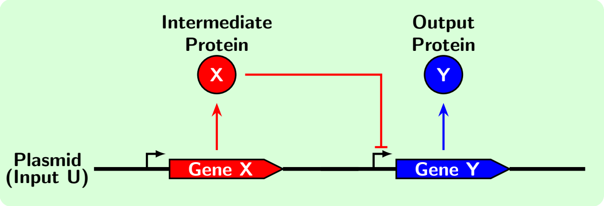
$\implies$ Output is **robust** to the input.

Incoherent FeedForward Loop (IFFL) – Continued

Topology:



Genetic Realization:



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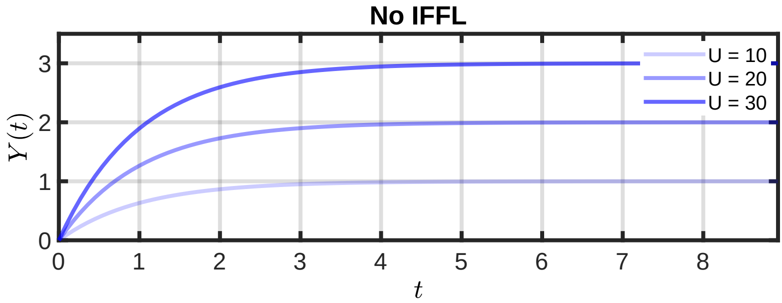
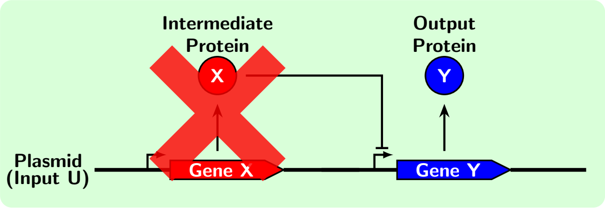


$\gamma_y = 1$

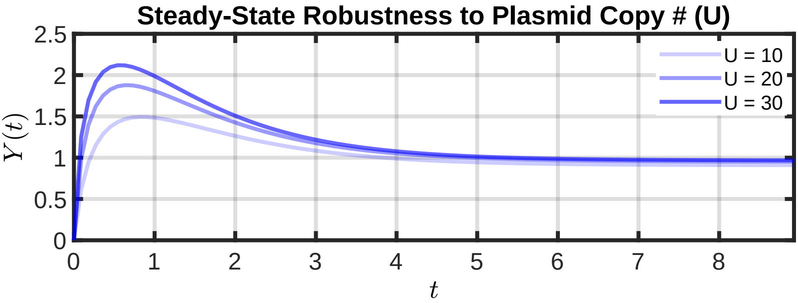
$k_y = 0.1$

Genetic Realization (No IFFL):



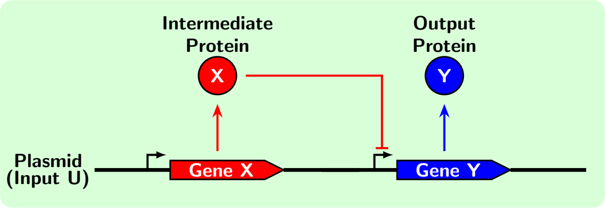
$$\dot{Y} = \frac{k_y U}{1 + X/\kappa} - \gamma_y Y$$

$$\implies \bar{Y} \approx \frac{k_y}{\gamma_y} U$$



$$\gamma_x = 1$$
$$\gamma_y = 1$$
$$k_x = 0.1$$
$$k_y = 1$$
$$\kappa = 0.1$$

Genetic Realization:



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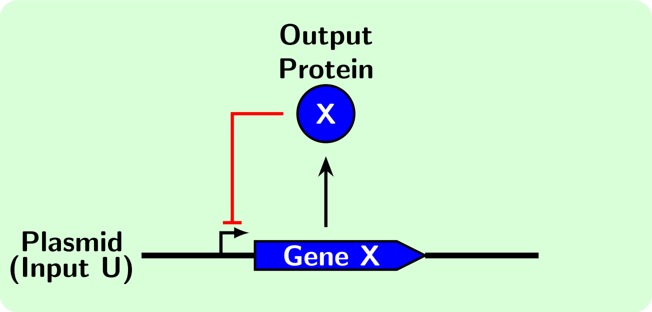
Negative Feedback: Autoregulation



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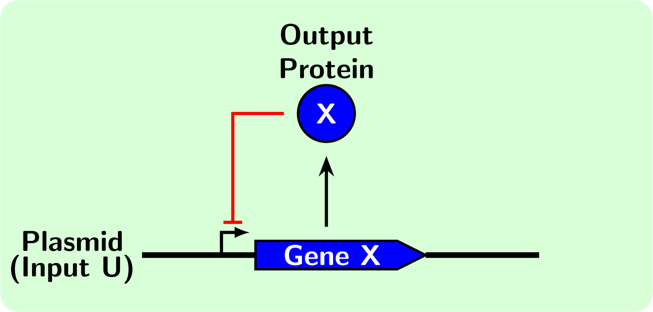
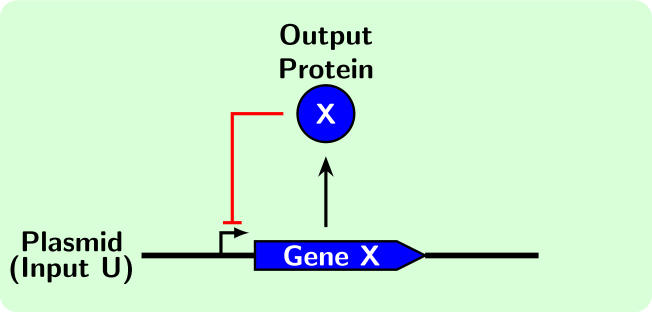


No Feedback:

$\dot{X} = kU - \gamma X$

Negative Feedback: Autoregulation



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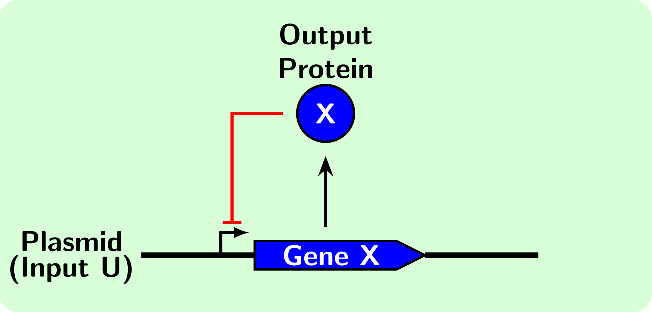


No Feedback:

$\dot{X} = kU - \gamma X$

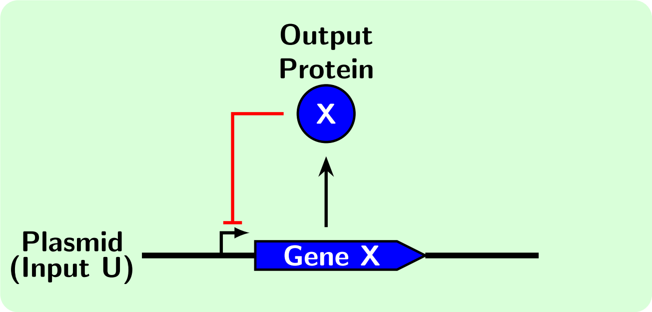
With Feedback:

$\dot{X} = \frac{kU}{1+X/\kappa} - \gamma X$

Let $\bar{X}$ be the equilibrium

$\tilde{X} := X - \bar{X}$ be the perturbation from equilibrium

Negative Feedback: Autoregulation



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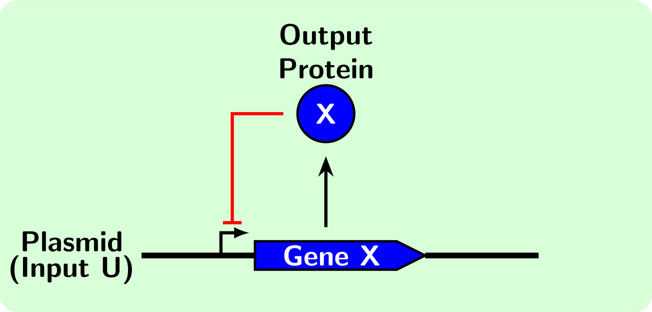
$\Longrightarrow$ linearized dynamics:



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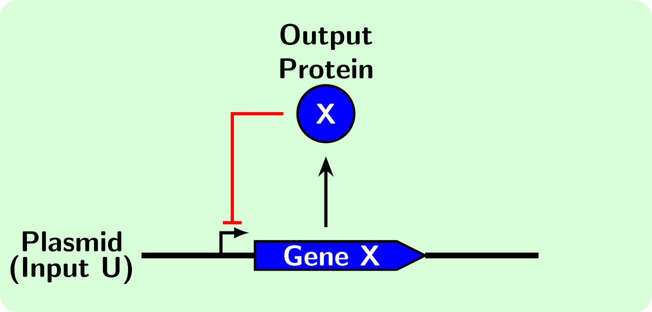
$\implies$ linearized dynamics:

$\dot{\tilde{X}} = -\gamma \tilde{X}$



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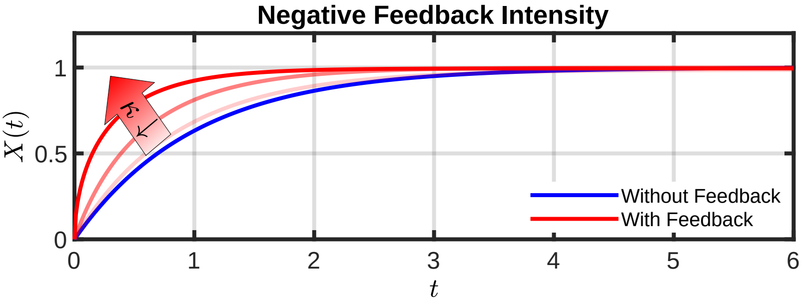
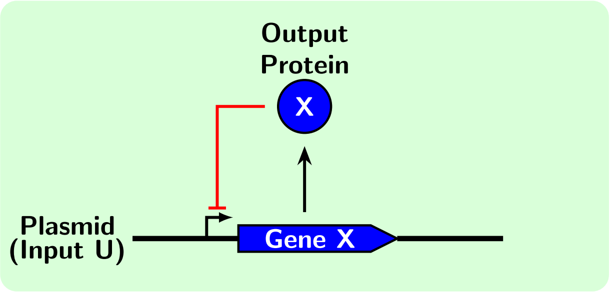
$\implies$ linearized dynamics:

$\dot{\tilde{X}} = -\gamma \tilde{X}$

$\dot{\tilde{X}} = -\left(\gamma + \frac{kU/\kappa}{(1+\bar{X}/\kappa)^2}\right)\tilde{X}$

Negative Feedback: Autoregulation





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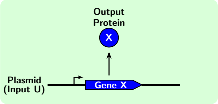
Steady State Robustness WIth Negative Feedback

No Feedback: $\dot{X} = kU - \gamma X \quad \Longrightarrow$ At Steady State: $\quad kU = {\color{blue}\gamma X}$



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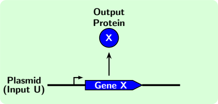

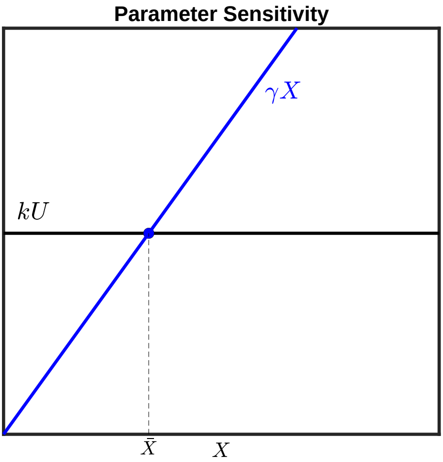

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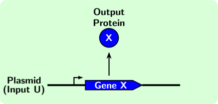

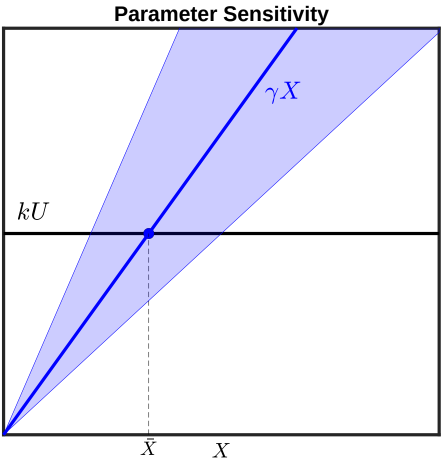

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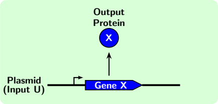
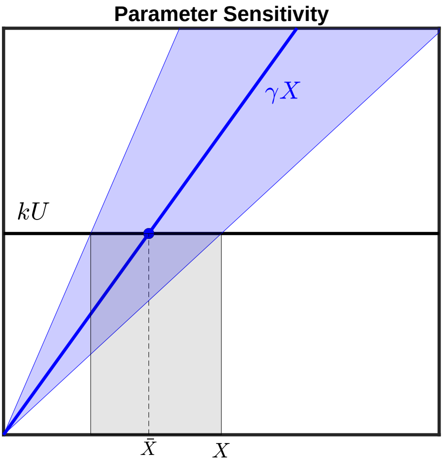
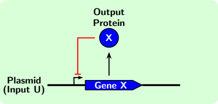




Steady State Robustness WIth Negative Feedback

With Feedback: $\dot{X} = \frac{kU}{1+X/\kappa} - \gamma X \implies$ At Steady State: $\frac{kU}{1+X/\kappa} = \gamma X$



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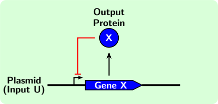

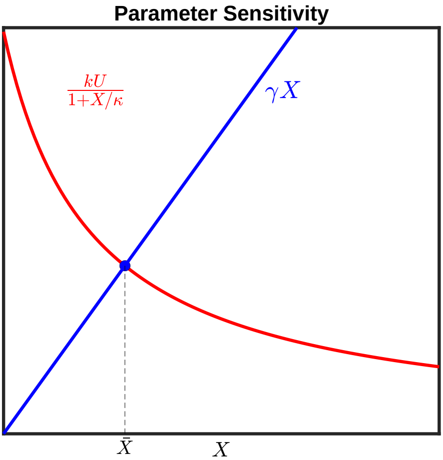

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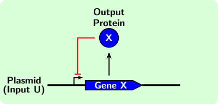

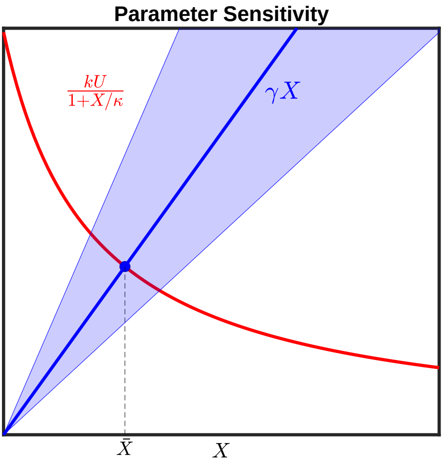

Steady State Robustness WIth Negative Feedback

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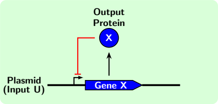
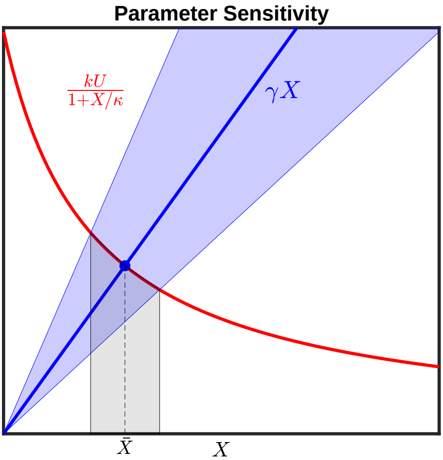
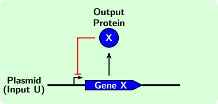




Steady State Robustness WIth Negative Feedback

With Feedback: $\dot{X} = \frac{kU}{1+(X/\kappa)^n} - \gamma X \implies$ At Steady State: $\frac{kU}{1+(X/\kappa)^n} = \gamma X$
$(n = 2)$



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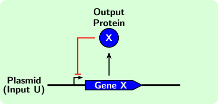

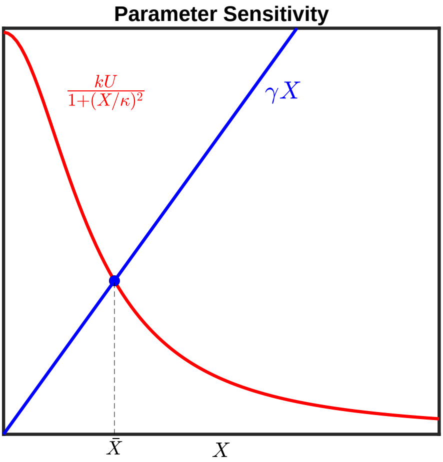

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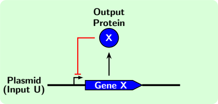

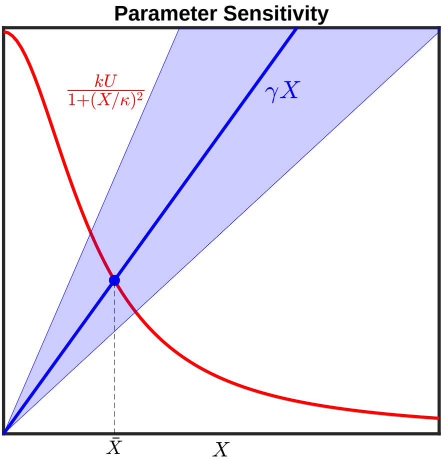

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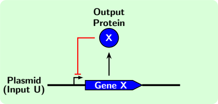

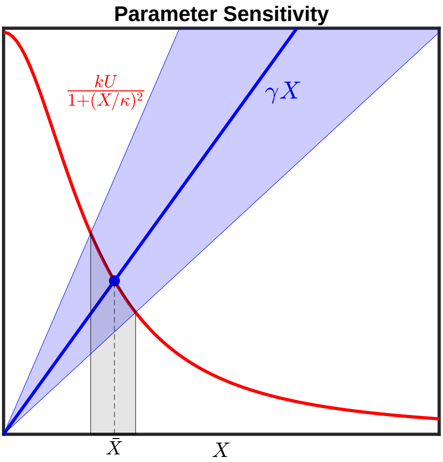

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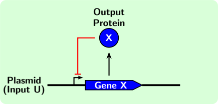
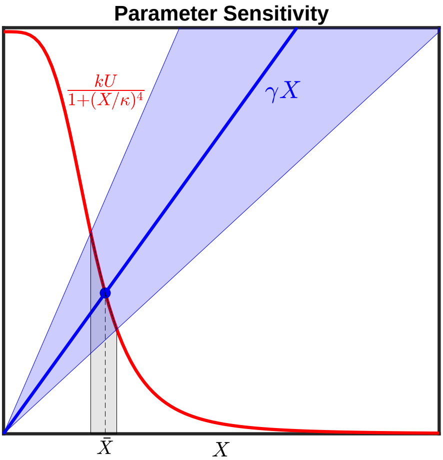
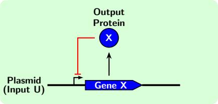
$(n = 4)$

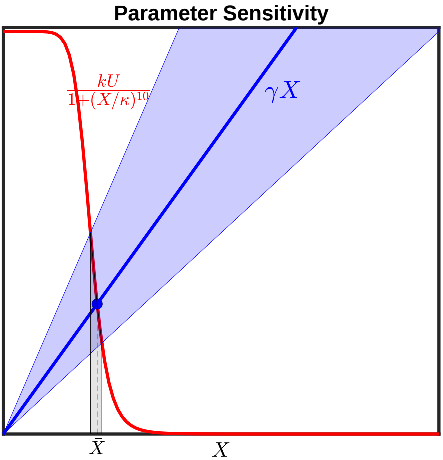




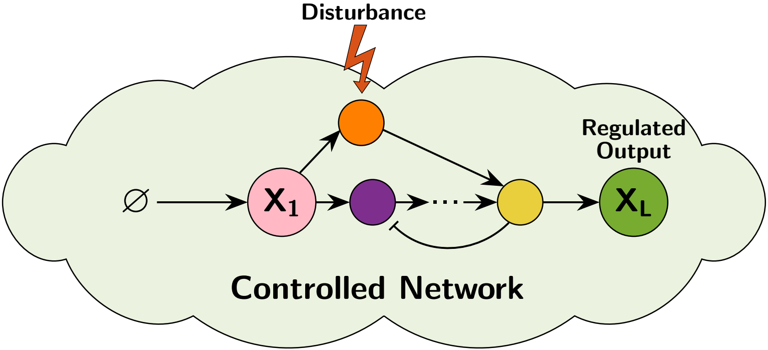
With Feedback: $\dot{X} = \frac{kU}{1+(X/\kappa)^n} - \gamma X \implies$ At Steady State: $\frac{kU}{1+(X/\kappa)^n} = \gamma X$

$(n = 10)$

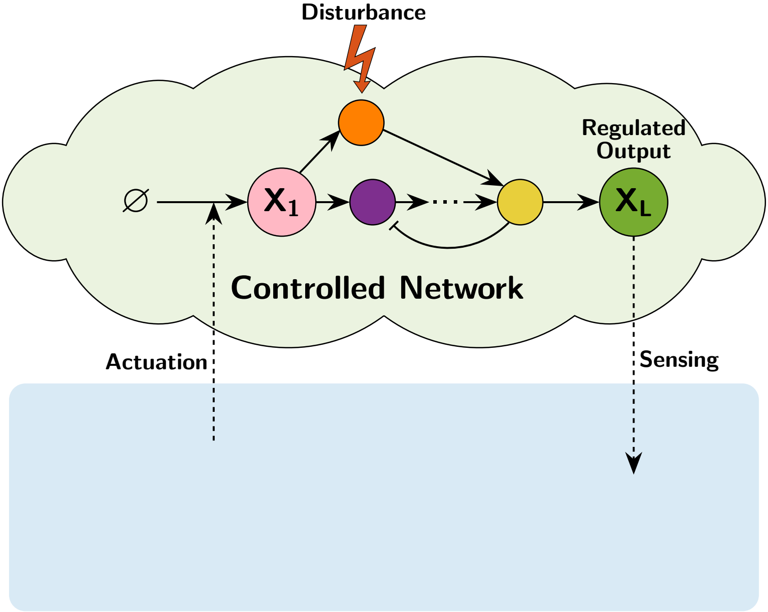




Antithetic Integral Feedback (AIF) Controller



Antithetic Integral Feedback (AIF) Controller



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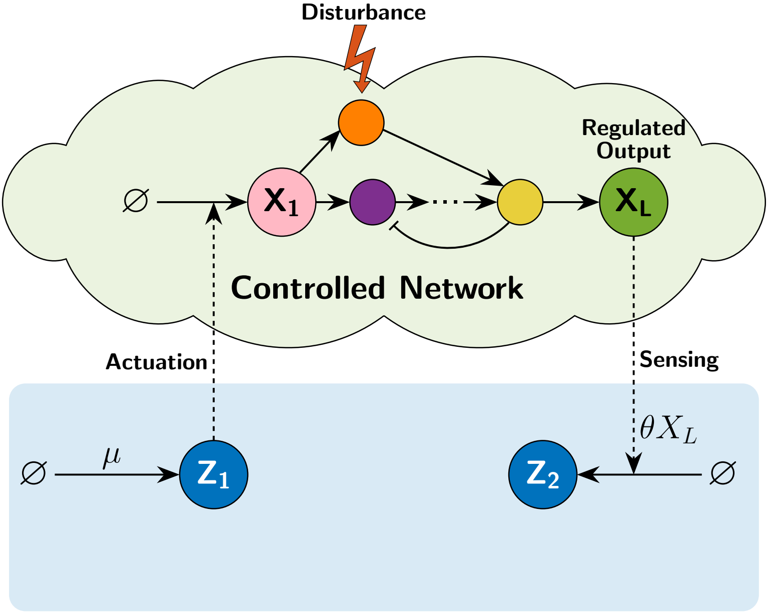
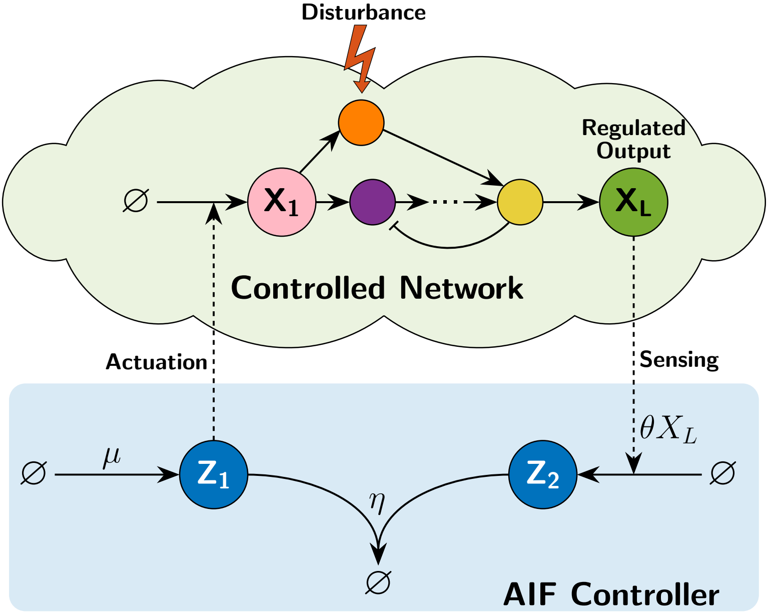
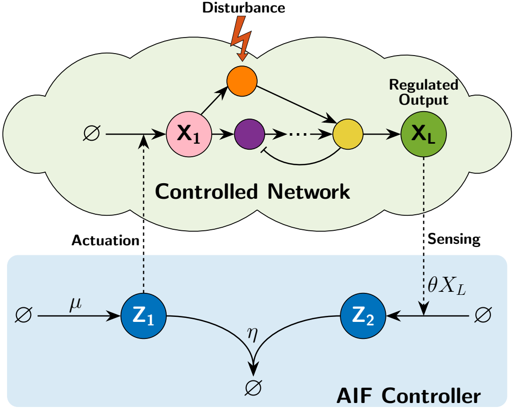


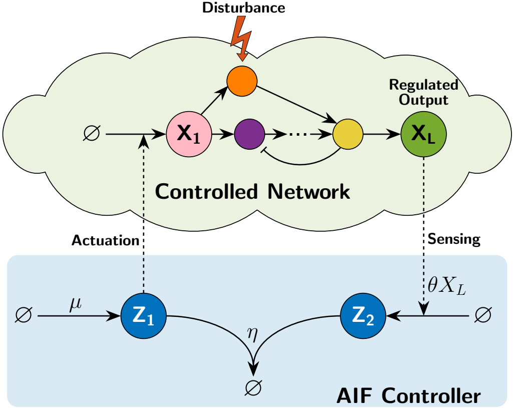
Antithetic Integral Feedback (AIF) Controller



Integral Action

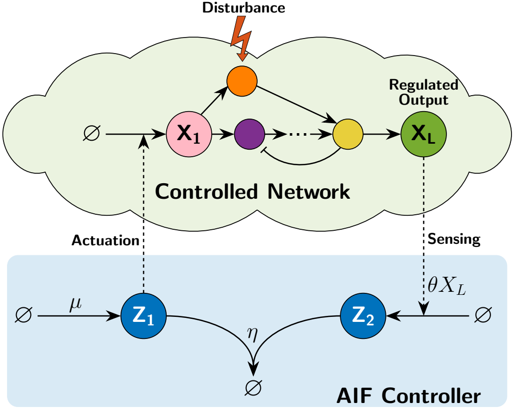


Integral Action



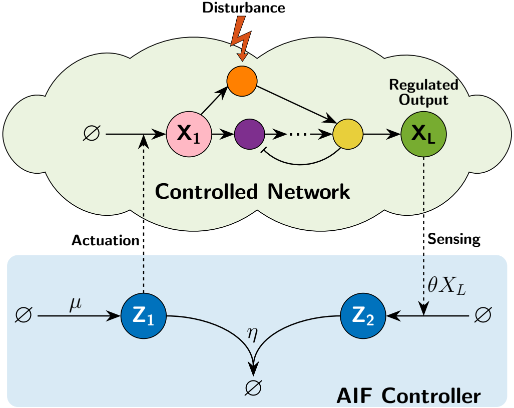
Controller Dynamics: $\begin{cases} \dot{Z}_1 = \\ \dot{Z}_2 = \end{cases}$

Integral Action



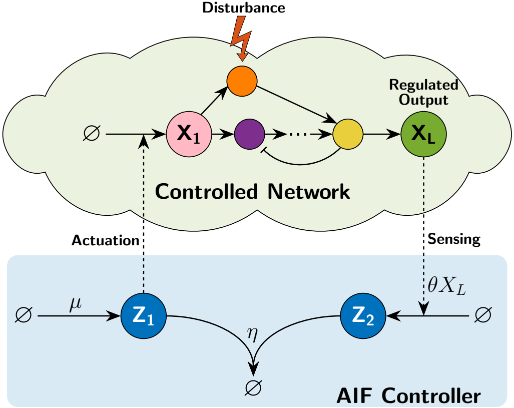
Controller Dynamics: $\begin{cases} \dot{Z}_1 = \mu - \eta Z_1 Z_2 \\ \dot{Z}_2 = \end{cases}$

Integral Action



Controller Dynamics: $\begin{cases} \dot{Z}_1 = \mu - \eta Z_1 Z_2 \\ \dot{Z}_2 = \theta X_L - \eta Z_1 Z_2 \end{cases}$

Integral Action



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Integral Action:

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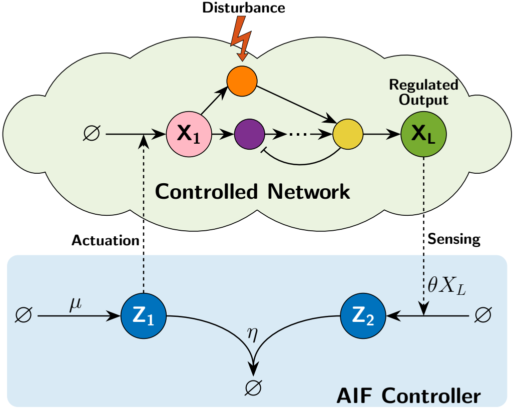

Controller Dynamics:
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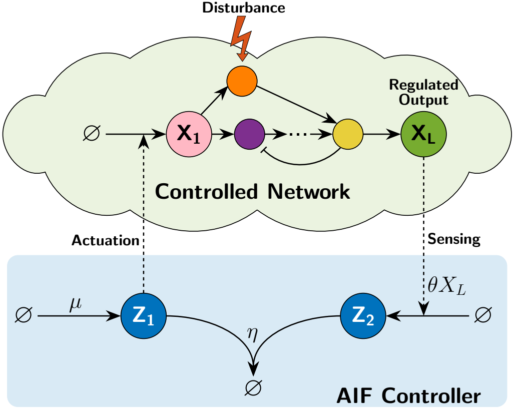
Integral Action:

$$\dot{Z}_1 - \dot{Z}_2 =$$

Integral Action



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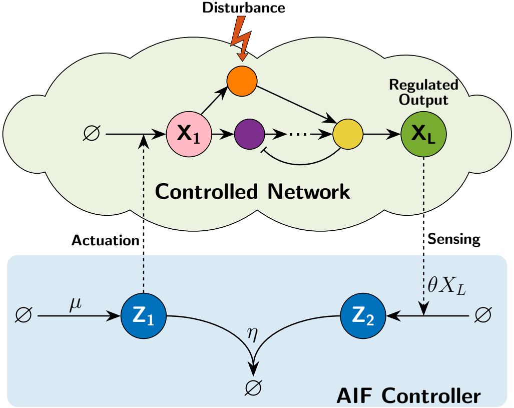
Integral Action:

$$\dot{Z}_1 - \dot{Z}_2 = \mu - \theta X_L$$

Integral Action



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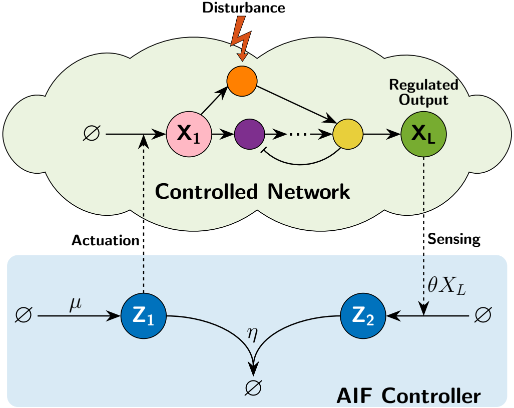
Integral Action:

$$\dot{Z}_1 - \dot{Z}_2 = \mu - \theta X_L \quad \Longrightarrow \quad Z_1(t) - Z_2(t) =$$

Integral Action



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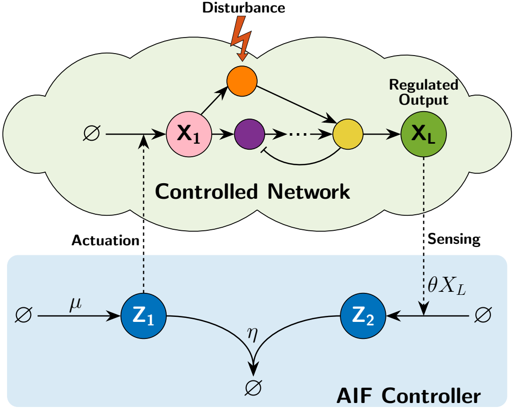
Integral Action:

$$\dot{Z}_1 - \dot{Z}_2 = \mu - \theta X_L \quad \Longrightarrow \quad Z_1(t) - Z_2(t) = \int_0^t \Big(\mu - \theta X_L(\tau)\Big) d\tau$$

Integral Action



Controller Dynamics: $\begin{cases} \dot{Z}_1 = \mu - \eta Z_1 Z_2 \\ \dot{Z}_2 = \theta X_L - \eta Z_1 Z_2 \end{cases} \implies$ Setpoint: $\bar{X}_L = \frac{\mu}{\theta}$

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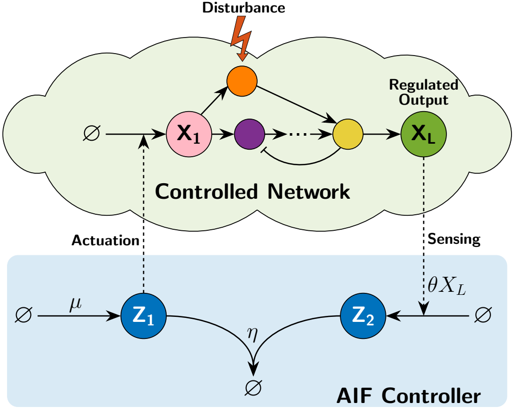
Integral Action



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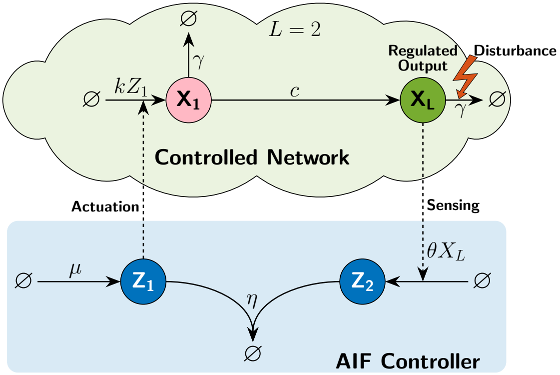
Integral Action:

$$\dot{Z}_1 - \dot{Z}_2 = \mu - \theta X_L \implies Z_1(t) - Z_2(t) = \theta \int_0^t \left(\frac{\mu}{\theta} - X_L(\tau) \right) d\tau$$

AIF Controller: Simulation



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Integral Action:

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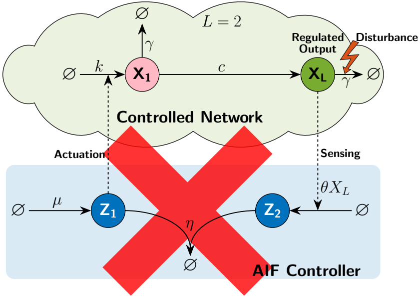
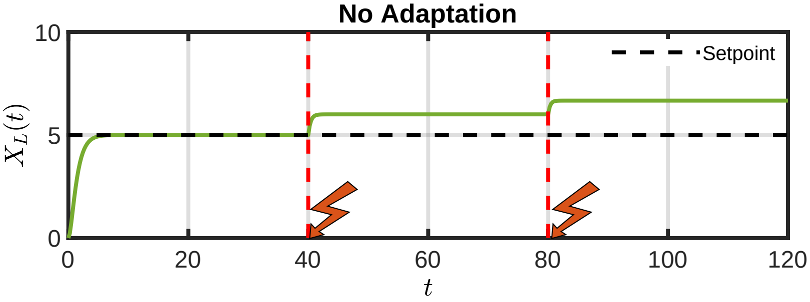
AIF Controller: Simulation





AIF Controller: Simulation