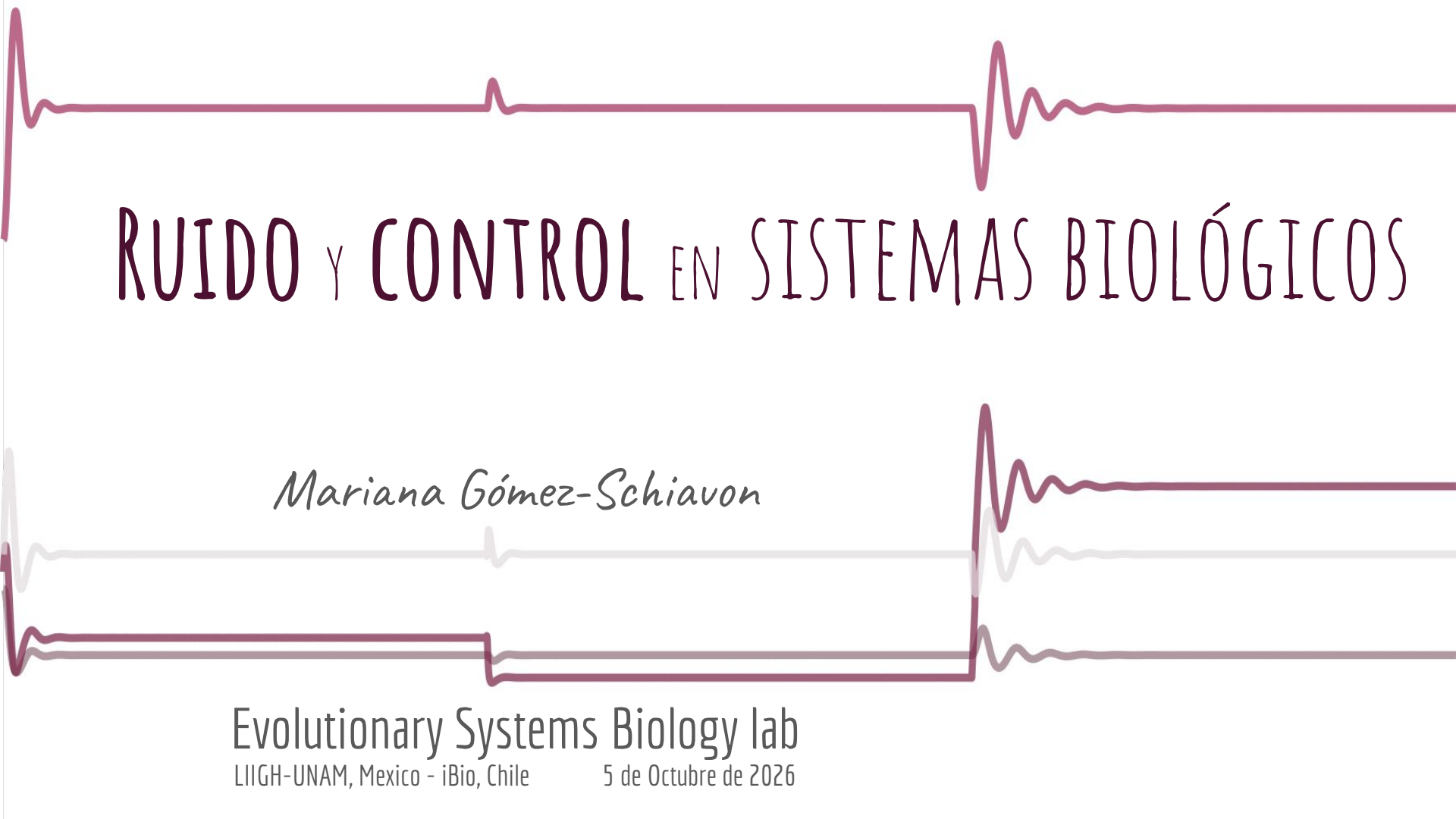




RUIDO Y CONTROL EN SISTEMAS BIOLÓGICOS

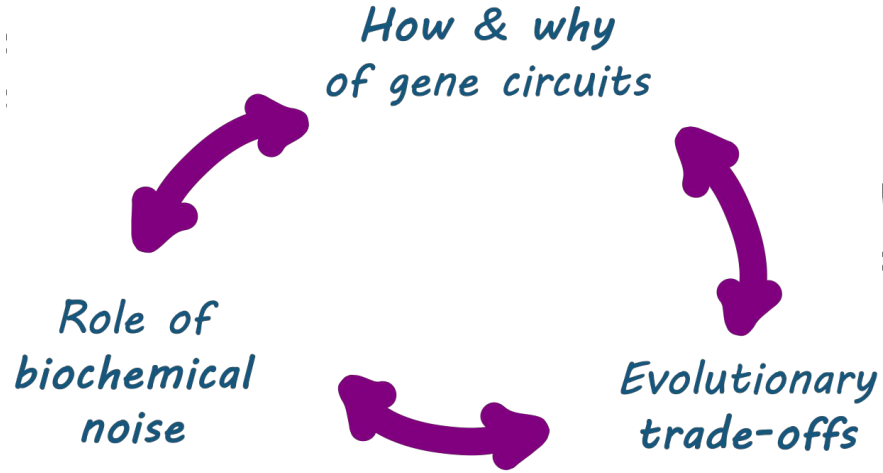
Mariana Gómez-Schiavon

Evolutionary Systems Biology lab

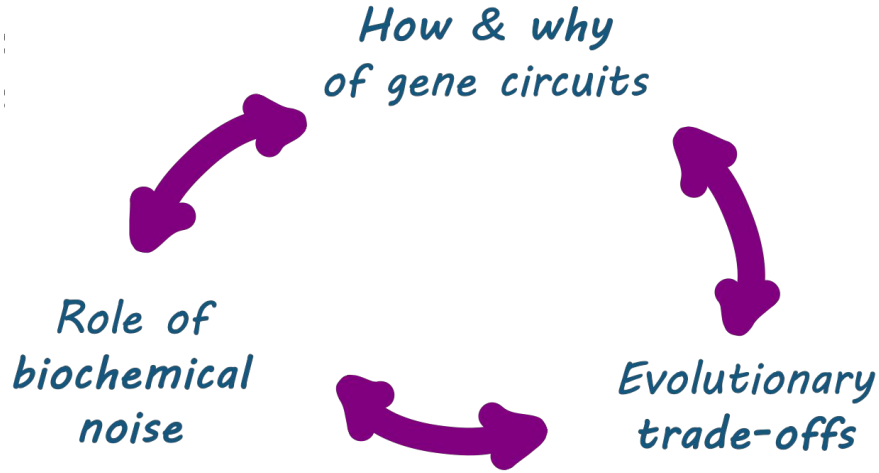
LIIGH-UNAM, Mexico - iBio, Chile

5 de Octubre de 2026

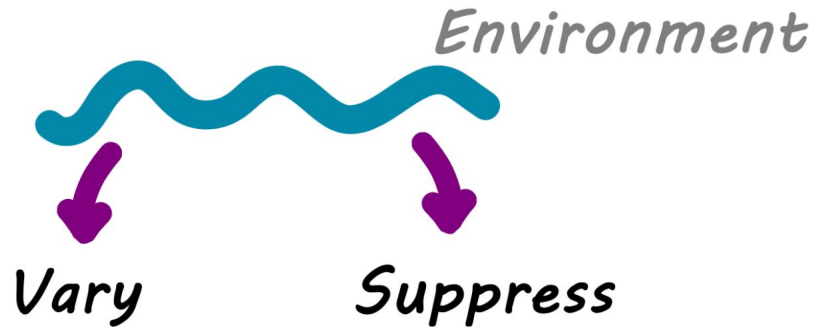
EVOLUTIONARY SYSTEMS BIOLOGY



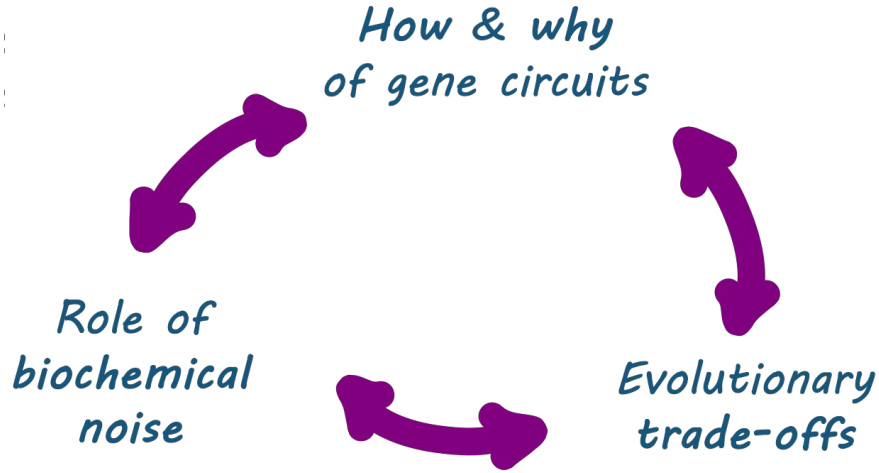
EVOLUTIONARY SYSTEMS BIOLOGY



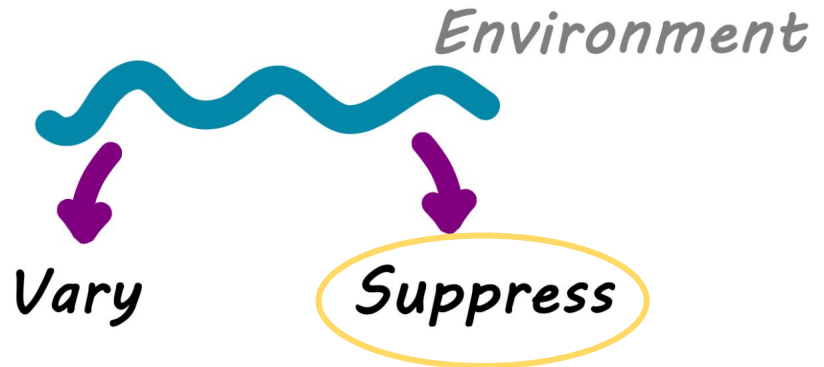
DEALING WITH FLUCTUATING ENVIRONMENTS...



EVOLUTIONARY SYSTEMS BIOLOGY



DEALING WITH FLUCTUATING ENVIRONMENTS...



FEEDBACK CONTROL IN BIOMOLECULAR SYSTEMS

Feedback control is ubiquitous in biological systems:
homeostasis & biochemical adaptation

- Yeast osmoadaptation
- ATP concentration
- Cell growth & tissue size
- Plasma calcium in mammals
- Plasma glucose

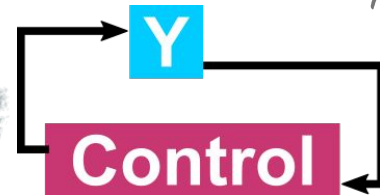
- Bacterial chemotaxis
- Olfactory adaptation

- Synthetic biology!!

Measurement
of the process

Feedback
information

“Corrective”
signal



FEEDBACK CONTROL IN BIOMOLECULAR SYSTEMS

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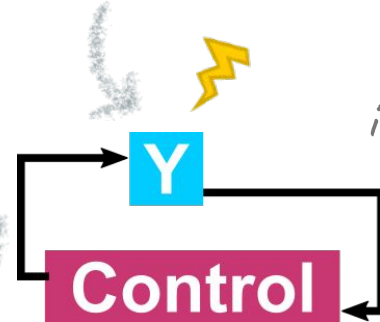
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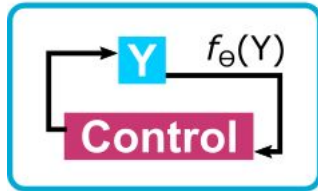
Measurement
of the process

Feedback
information ?



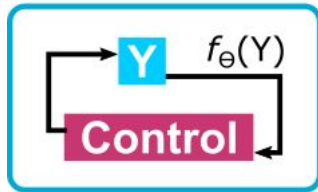
THE CORA CONCEPT

Feedback system

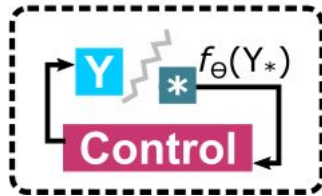


THE CORA CONCEPT

Feedback system



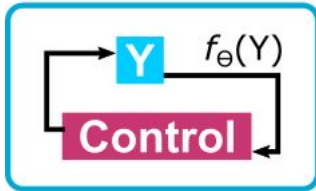
no-feedback system



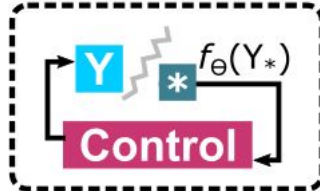
THE CORA CONCEPT

For each condition Θ :

Feedback system



Locally analogous
no-feedback system

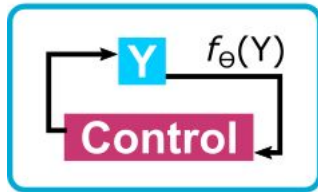


before the perturbation $f_{\Theta}(Y) = f_{\Theta}(Y_*)$.

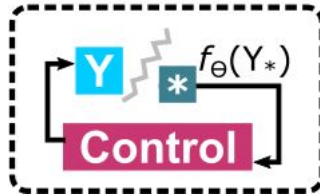
THE CORA CONCEPT

For each condition θ :

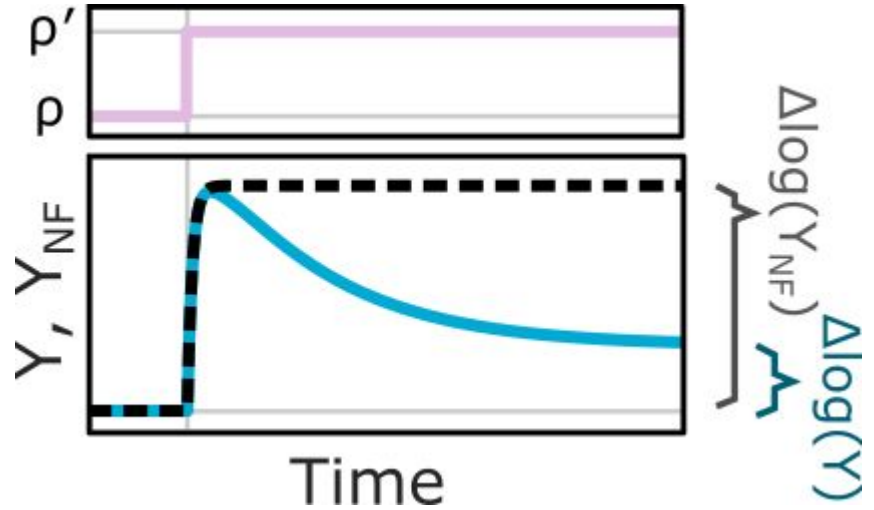
Feedback system



Locally analogous
no-feedback system



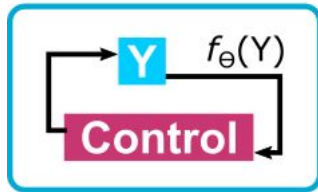
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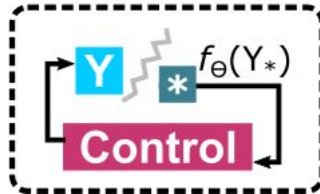
THE CORA CONCEPT

For each condition θ :

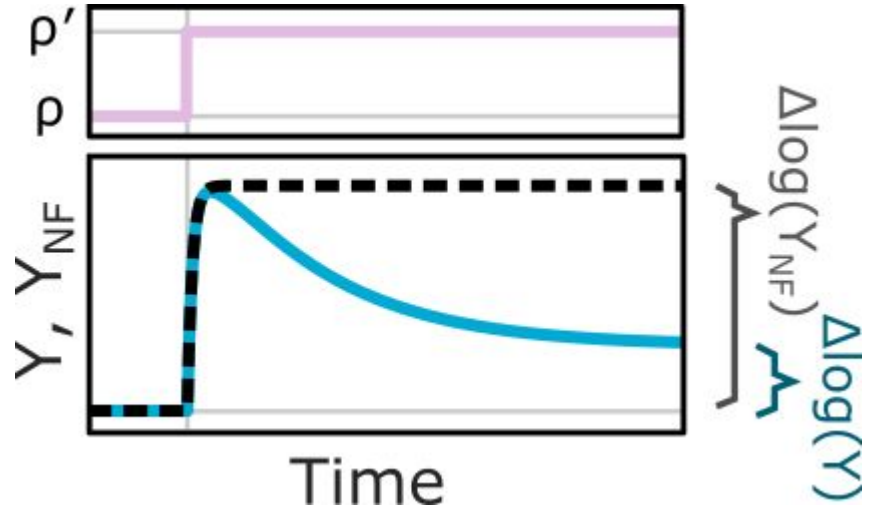
Feedback system



Locally analogous
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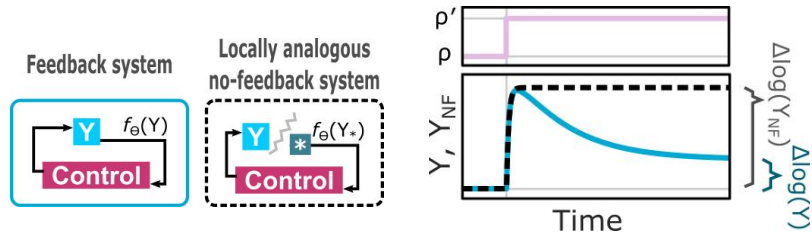


Mathematically Controlled Comparison

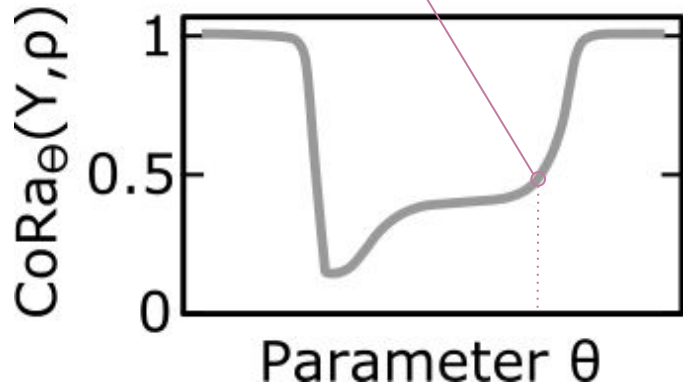
See Alves & Savageau (2000)

Gómez-Schiavon & El-Samad (2022; PNAS)

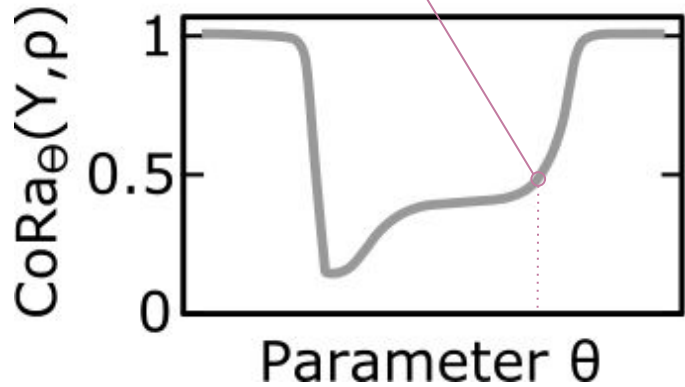
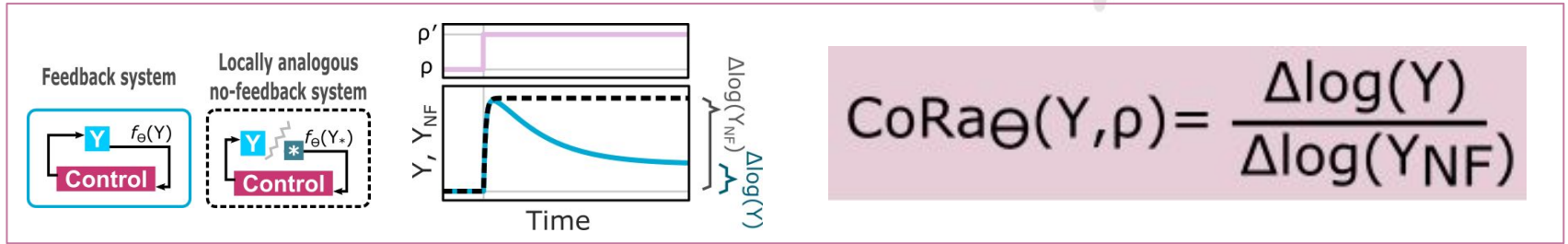
THE CORA CONCEPT



$$\text{CoRa}_{\theta}(Y, p) = \frac{\Delta \log(Y)}{\Delta \log(Y_{NF})}$$



THE CORA CONCEPT



$$\text{CoRa}_{\theta}(Y, \rho) = 1 \Leftrightarrow \text{No control}$$

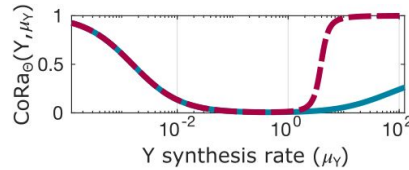


$$\text{CoRa}_{\theta}(Y, \rho) = 0 \Leftrightarrow \text{Perfect control}$$

WHY IS CORA GREAT?

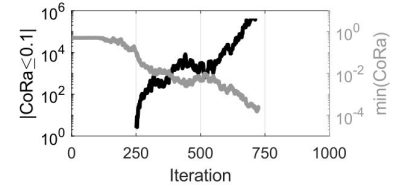
Informative

→ Characterize feedback control systems



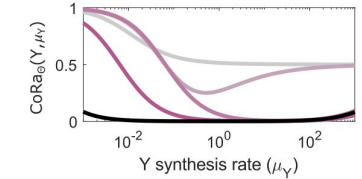
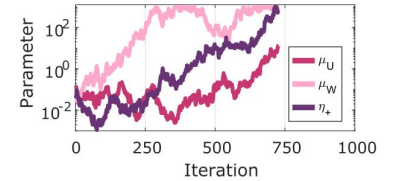
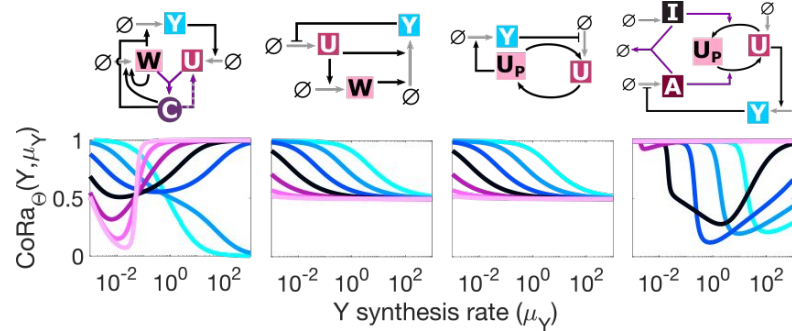
Easy to interpret

→ Design feedback control systems



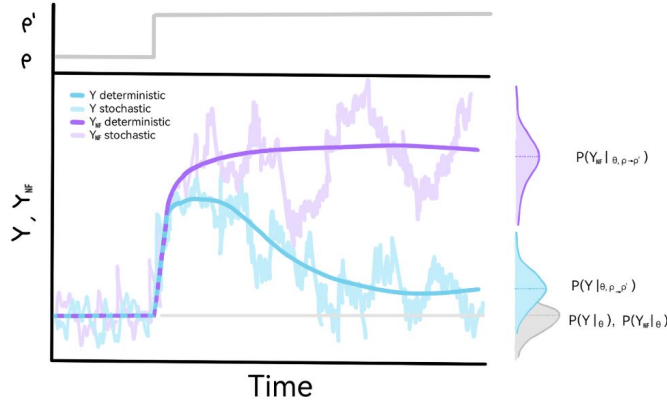
Unifying framework

→ Compare feedback control systems



EXTENDING CORA

1



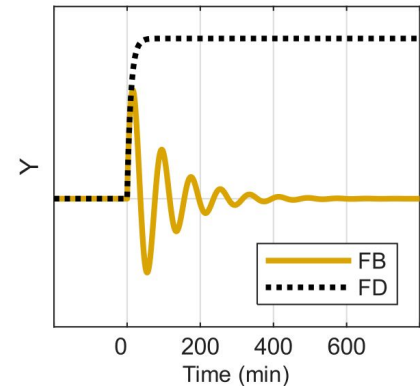
*Between noise from within
& noise from without*

→ *Heterogeneity and control
in biological systems*

2

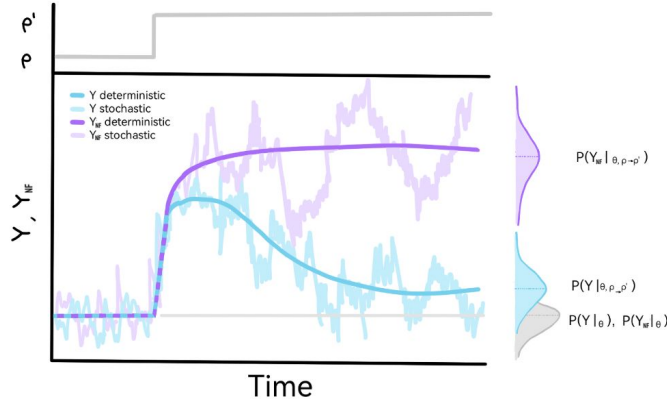
Beyond Steady-State Adaptation

→ *Evaluating the
Dynamic Performance
of Biological Feedback Control*



EXTENDING CORA

1



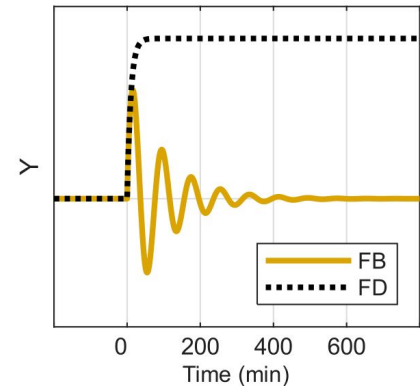
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Beyond Steady-State Adaptation

→ *Evaluating the
Dynamic Performance
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- *Biological systems are inherently stochastic.*
- *Homeostasis as a mechanism to deal with extrinsic noise (i.e., perturbations).*
- *What effect does intrinsic noise have on feedback control?*

- *Biological systems are inherently stochastic.*
- *Homeostasis as a mechanism to deal with extrinsic noise (i.e., perturbations).*
- *What effect does intrinsic noise have on feedback control?*

Adapting the CoRa concept

to evaluate stochastic systems:

- *Locally analogous no-feedback system*
- *Comparing responses*

Stationary distributions

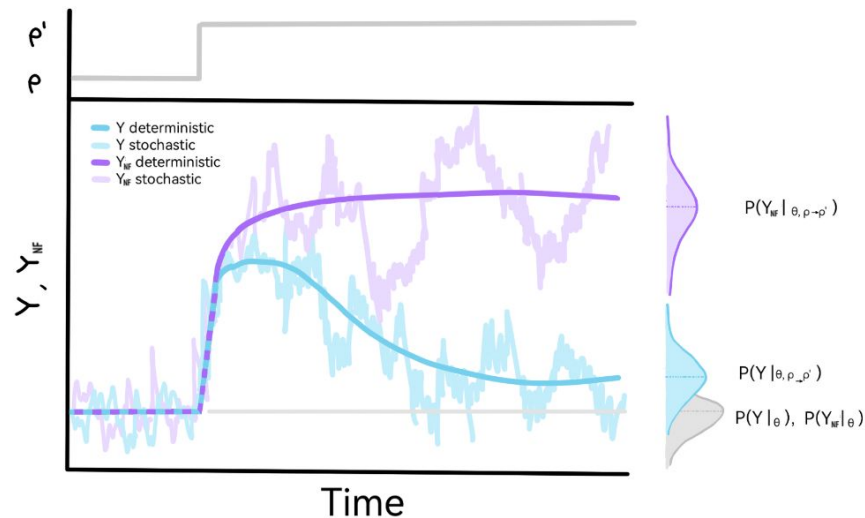


Manuel Hernández
PhD student, BUAP

1

STOCHASTIC RESPONSE OF CONTROL

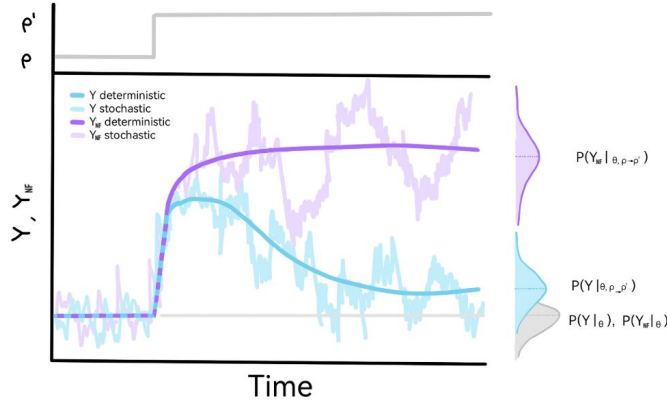
- Feedback also affects *intrinsic noise*!!
→ “Constant environment” CoRa
- How *intrinsic noise* affects homeostatic control (i.e., *extrinsic noise response*)?
→ Stochastic CoRa after a perturbation



Manuel Hernández
PhD student, BUAP

EXTENDING CORA

1



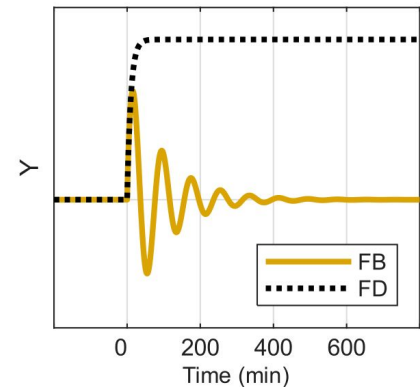
*Between noise from within
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→ *Heterogeneity and control
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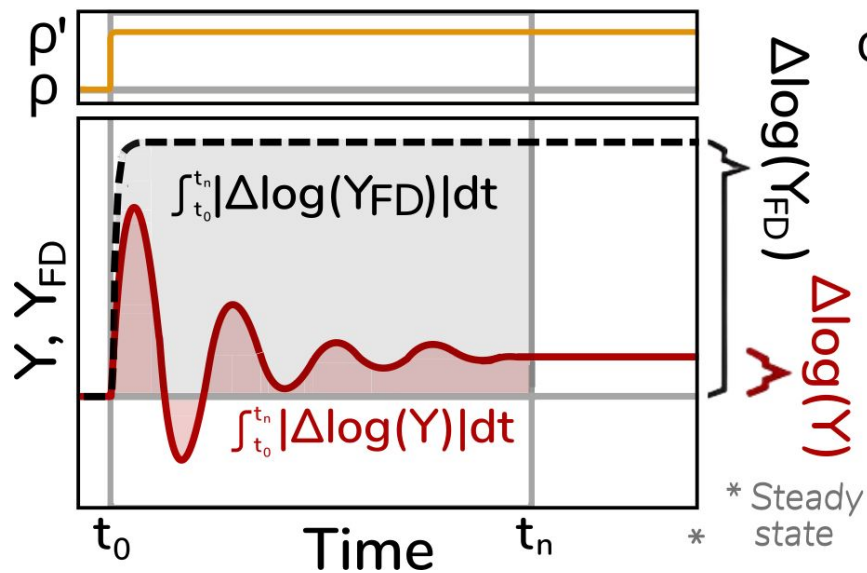
2

Beyond Steady-State Adaptation

→ *Evaluating the
Dynamic Performance
of Biological Feedback Control*



EXPLAINING THE CORADYN APPROACH



$$\text{CoRaDyn } \Theta(Y, p, t_n) = \frac{\boxed{\Delta \log(Y)}}{\boxed{\int_{t_0}^{t_n} |\Delta \log(Y_{FD})| dt}}$$

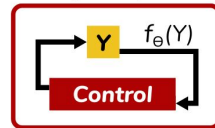
$$= \frac{\int_{t_0}^{t_n} |\Delta \log(Y)| dt}{\int_{t_0}^{t_n} |\Delta \log(Y_{FD})| dt}$$

$$\text{CoRa } \Theta(Y, p) = \frac{\Delta \log(Y)}{\Delta \log(Y_{FD})}$$

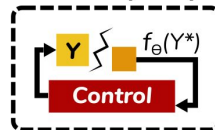


Athena Tamayo
Undergrad student
Thesis research
Graduated June 2024

Original system



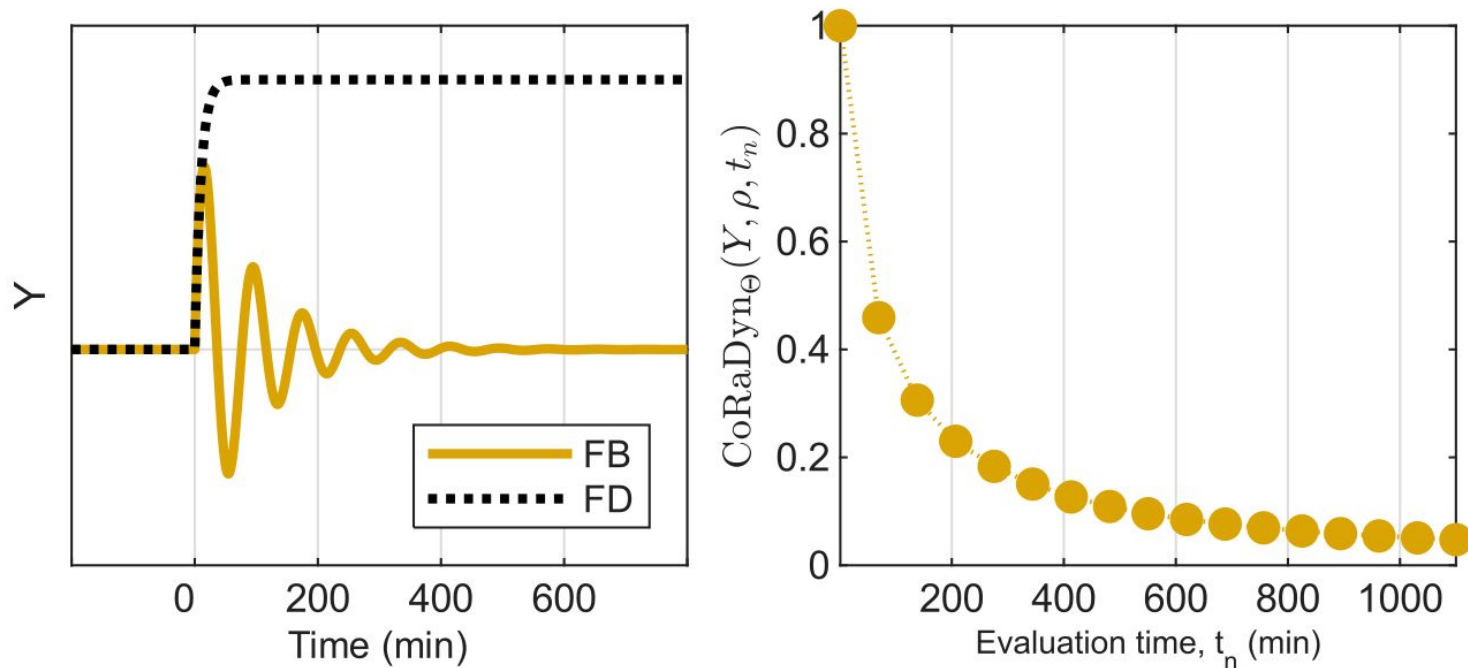
Locally analogous
feedback-disrupted system



- CoRa for a point $\rightarrow$ CoRaDyn for area under the curves.
- Generalizable & comparable to CoRa.

2 TIME-DEPENDENT CHARACTERIZATION OF FEEDBACK PERFORMANCE

CoRaDyn temporal profile

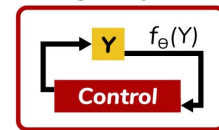


Tamayo-Luisce & Gómez-Schiavon (2026; *bioRxiv*)

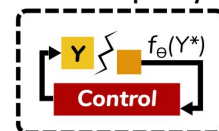


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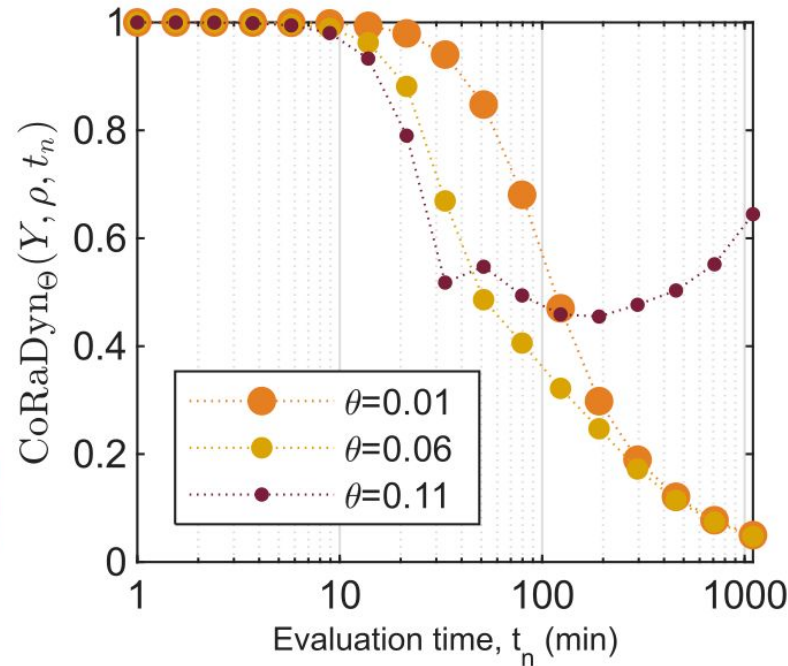
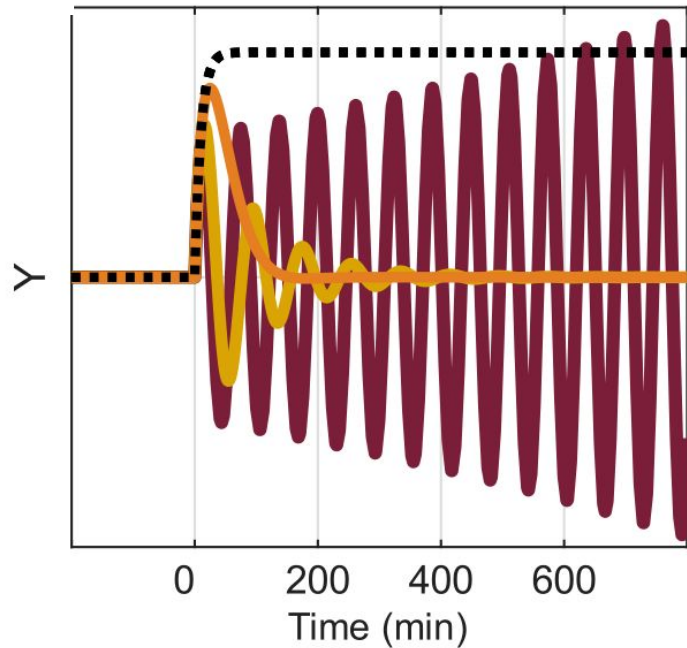


Locally analogous
feedback-disrupted system



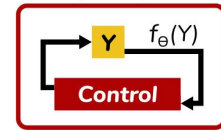
2 TIME-DEPENDENT CHARACTERIZATION OF FEEDBACK PERFORMANCE

CoRaDyn temporal profile across a parameter value, θ , & evaluation time, t_n

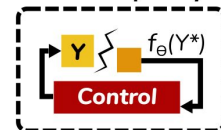


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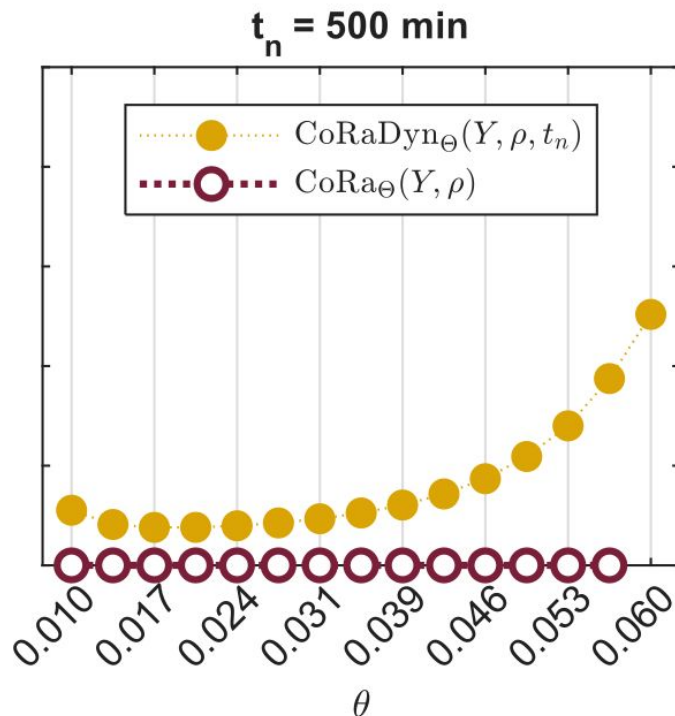
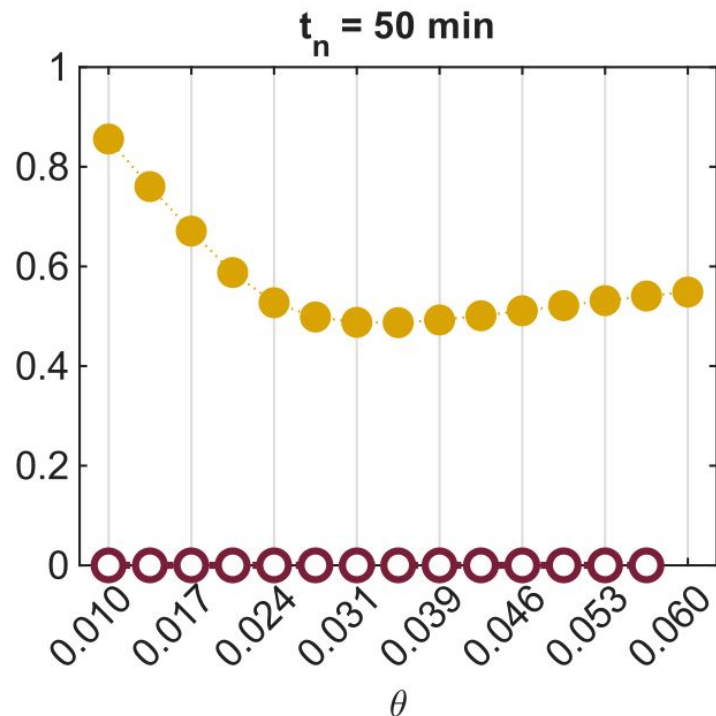


Locally analogous
feedback-disrupted system



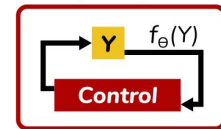
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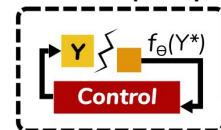


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Original system

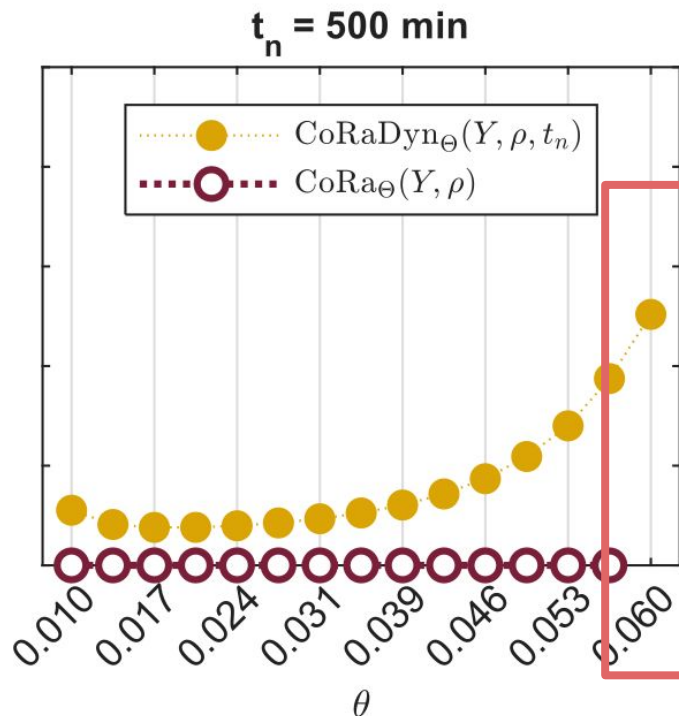
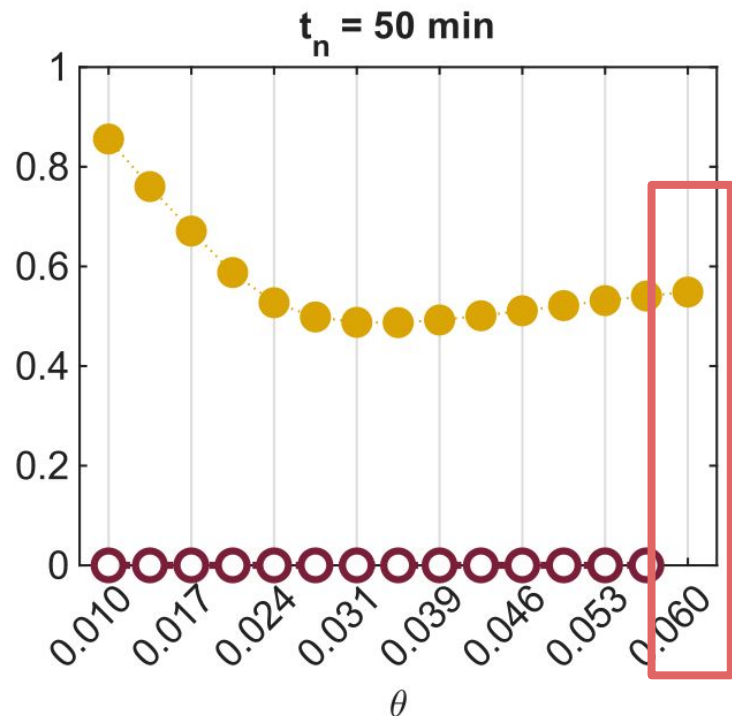


Locally analogous
feedback-disrupted system



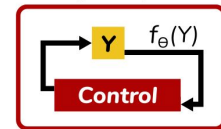
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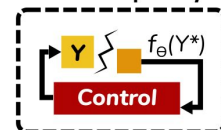


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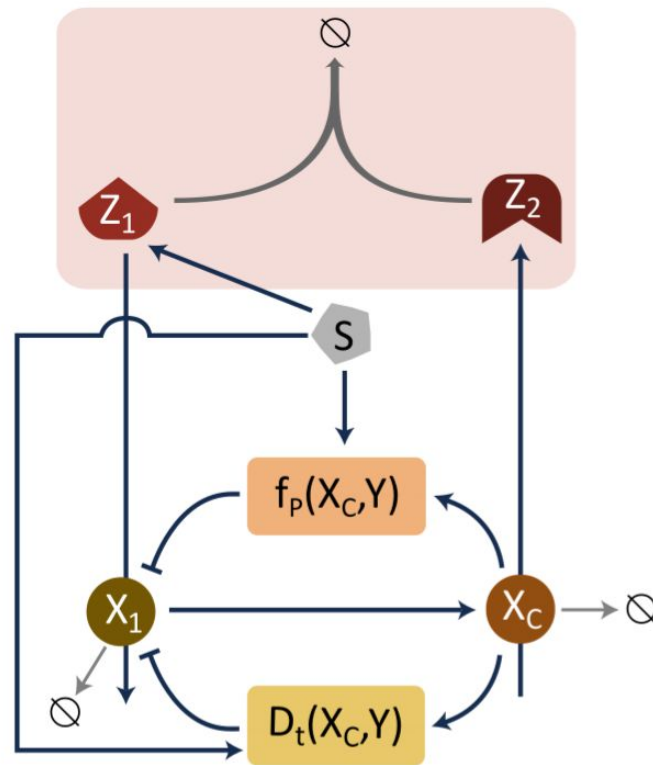
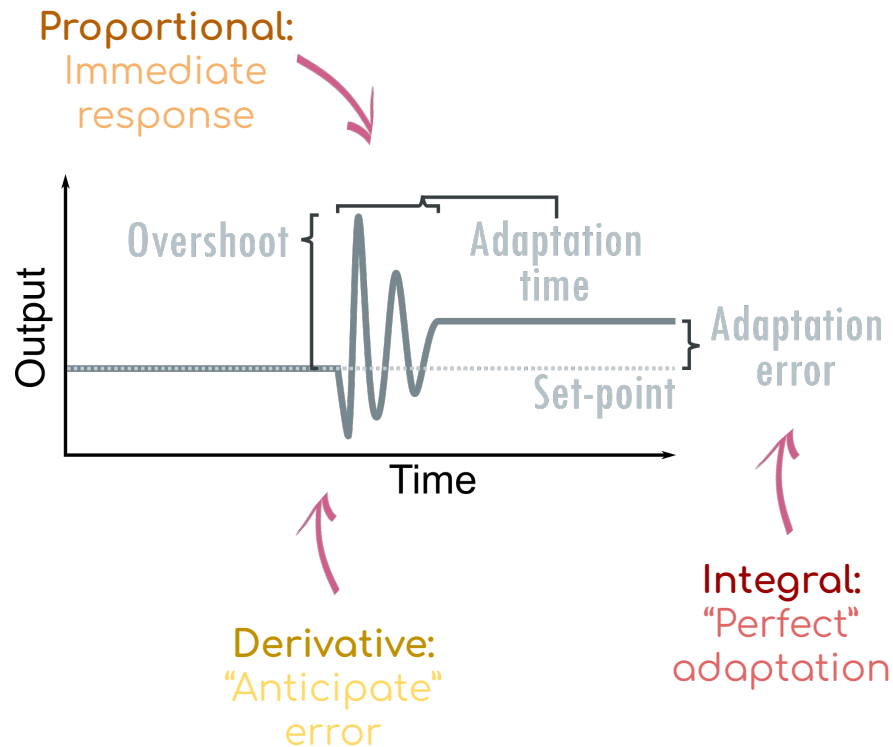


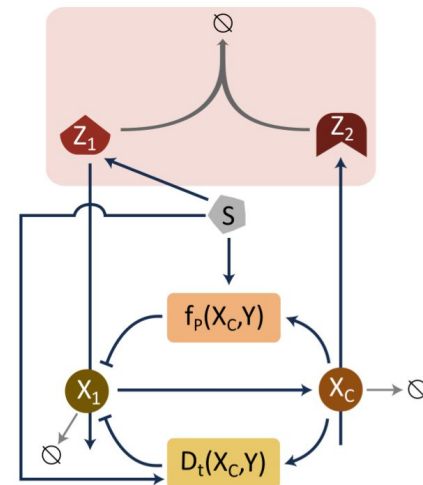
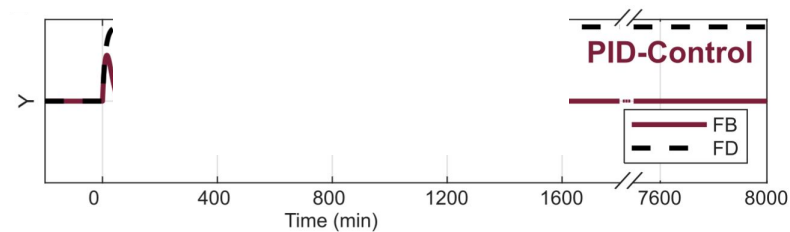
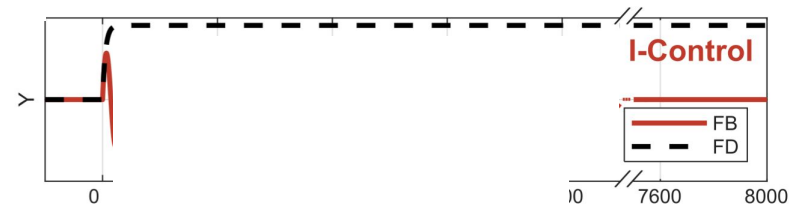
Locally analogous
feedback-disrupted system



2

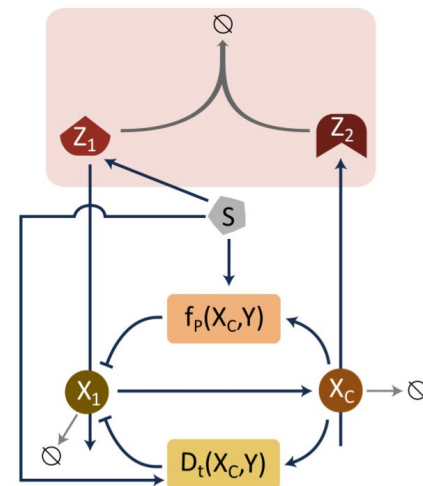
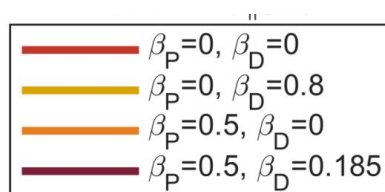
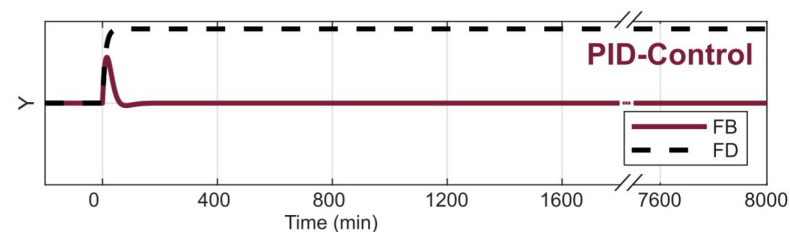
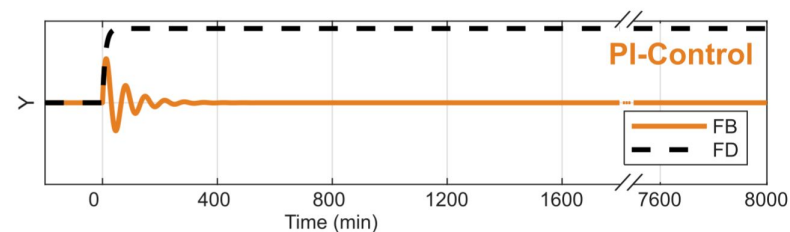
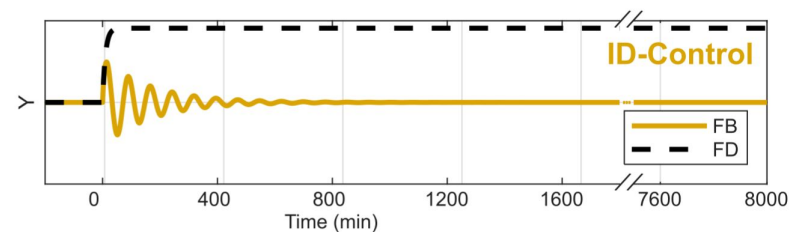
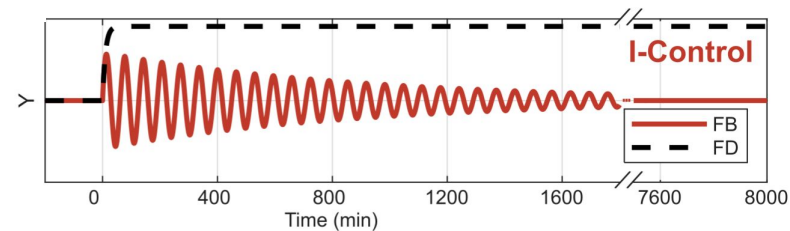
APPLYING CORADYN TO UNDERSTAND PID-CONTROL



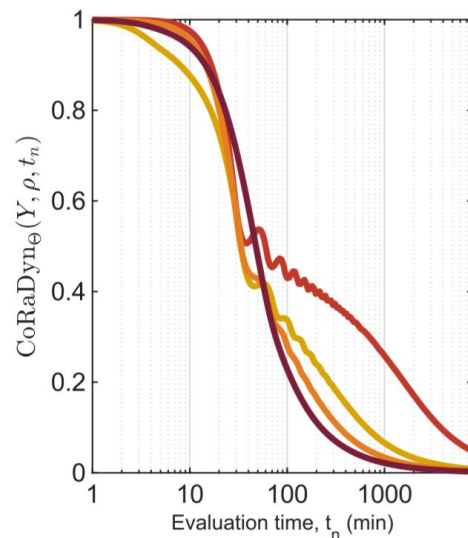
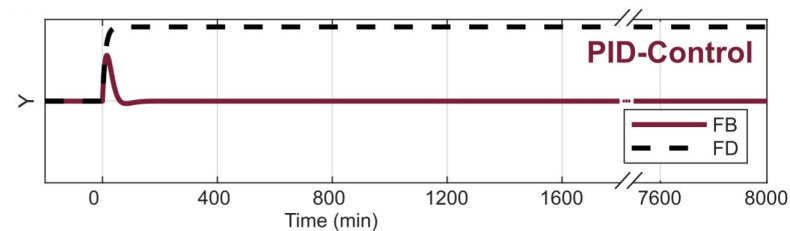
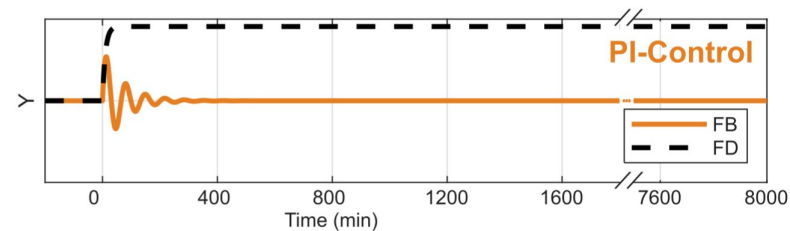
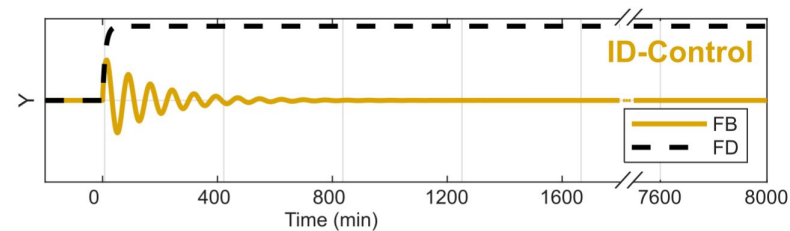
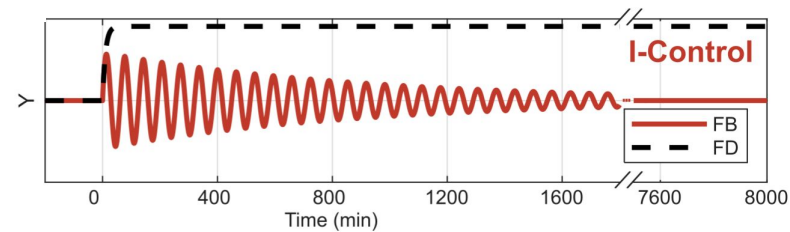


-  $\beta_P=0, \beta_D=0$
 $\beta_P=0, \beta_D=0.8$
 $\beta_P=0.5, \beta_D=0$
 $\beta_P=0.5, \beta_D=0.185$

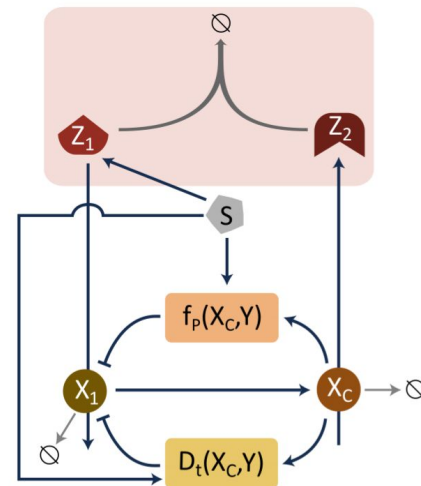
FEEDBACK CONTRIBUTION DEPENDS ON TEMPORAL SCALE OF EVALUATION



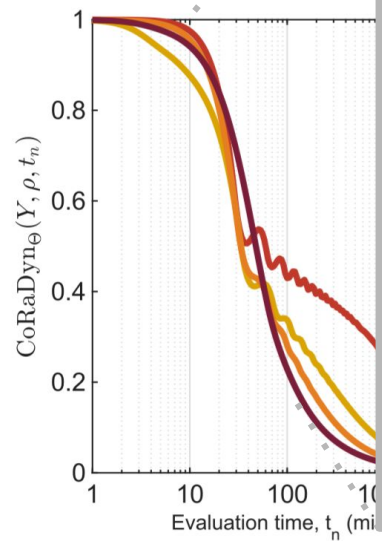
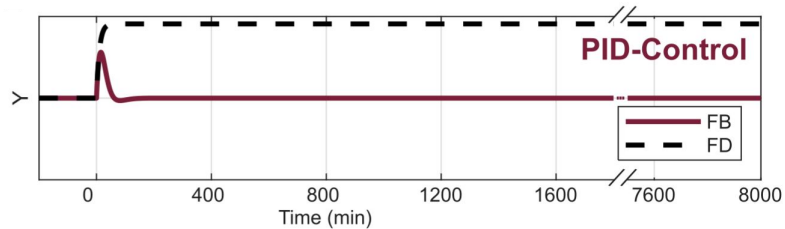
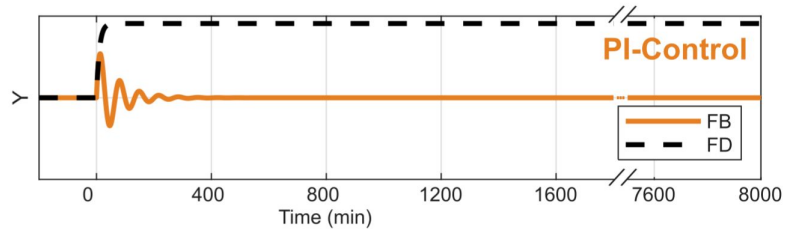
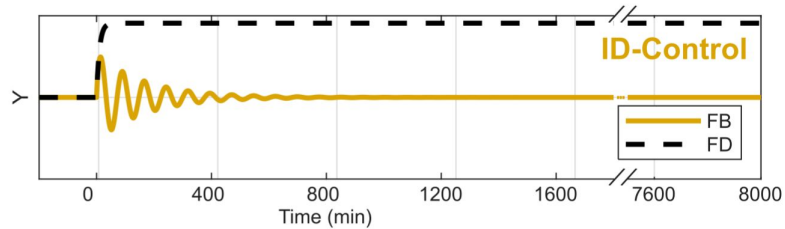
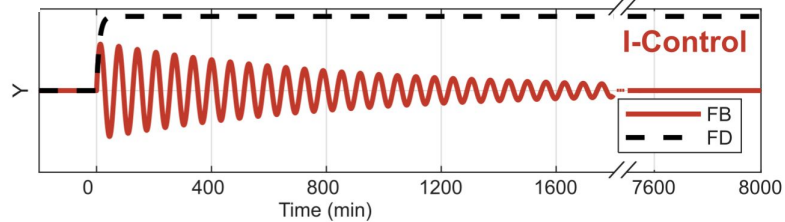
FEEDBACK CONTRIBUTION DEPENDS ON TEMPORAL SCALE OF EVALUATION



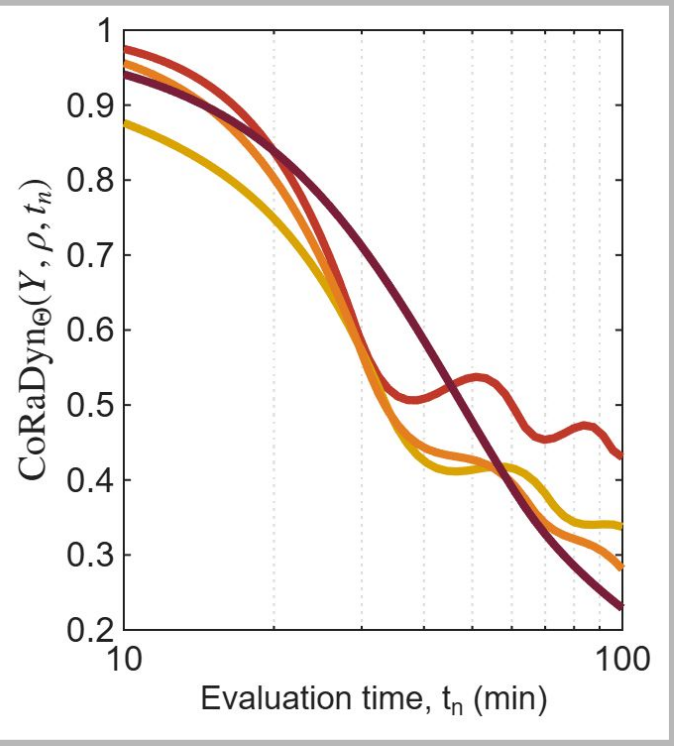
- $\beta_P=0, \beta_D=0$
- $\beta_P=0, \beta_D=0.8$
- $\beta_P=0.5, \beta_D=0$
- $\beta_P=0.5, \beta_D=0.185$



FEEDBACK CONTROL TEMPORAL



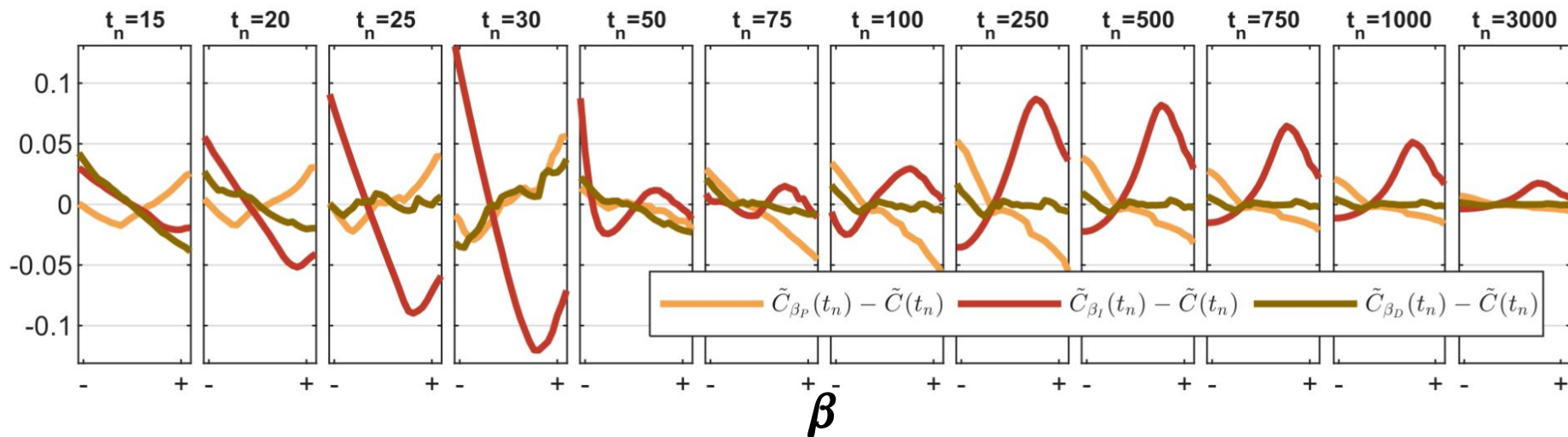
- $\beta_P=0, \beta_D=0$
- $\beta_P=0, \beta_D=0.8$
- $\beta_P=0.5, \beta_D=0$
- $\beta_P=0.5, \beta_D=0.185$



2

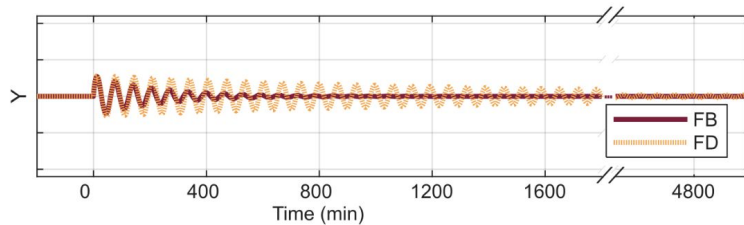
CONTRIBUTION OF P, I, & D CONTROL DEPENDS ON THE EVALUATION TIME

median(CoRaDyn) temporal profile for different control weights, β , & evaluation times, t_n

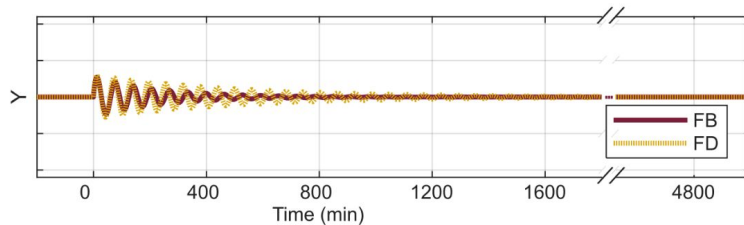


CORADYN ISOLATES DYNAMIC CONTRIBUTION OF OVERLAPPING FEEDBACK LOOPS

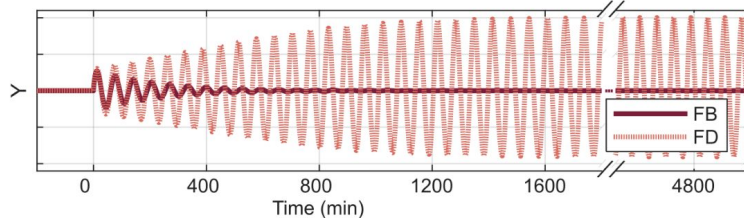
P-Effect



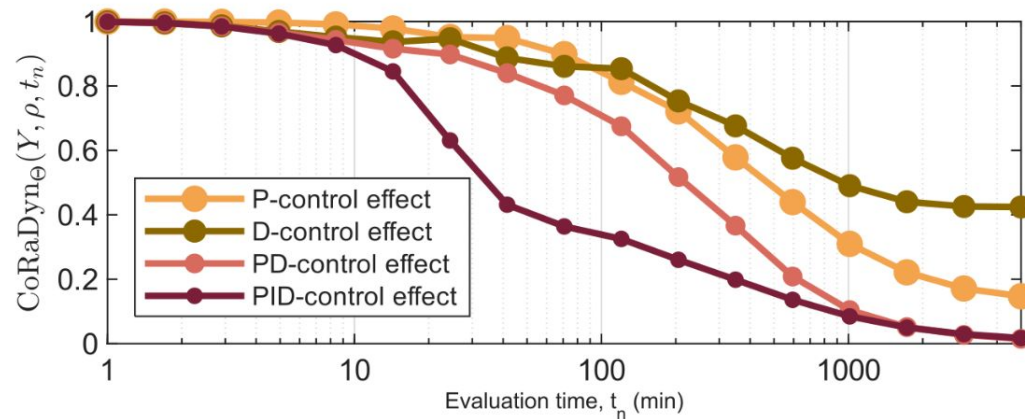
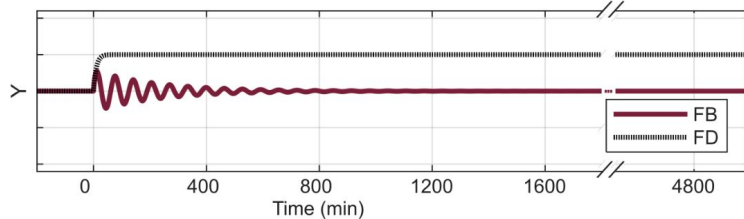
D-Effect



PD-Effect



PID-Effect



CONCLUSIONS

- Feedback control deals with both **intrinsic & extrinsic noise**.
- CoRa approach can be used to evaluate the **feedback performance** in the presence of both.
- **How these two sources of heterogeneity interact?** How much it depends on the feedback control mechanism?
- The CoRa framework can be extended **beyond steady-state adaptation**.
- CoRaDyn quantifies **dynamic feedback performance**.
Transient responses, overshoot & recovery
- CoRaDyn enables meaningful comparisons between feedback strategies.
 - **Distinguishing controllers** with identical steady-state adaptation.
 - Revealing **transient** performance **trade-offs**.
 - **Dissecting** the role of **individual feedback** mechanisms.



THANKS!

- *EvoSysBio Lab*
- *Apoyo del LIIGH*
- *iBio, Chile*

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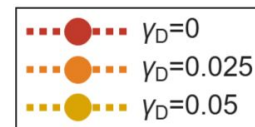
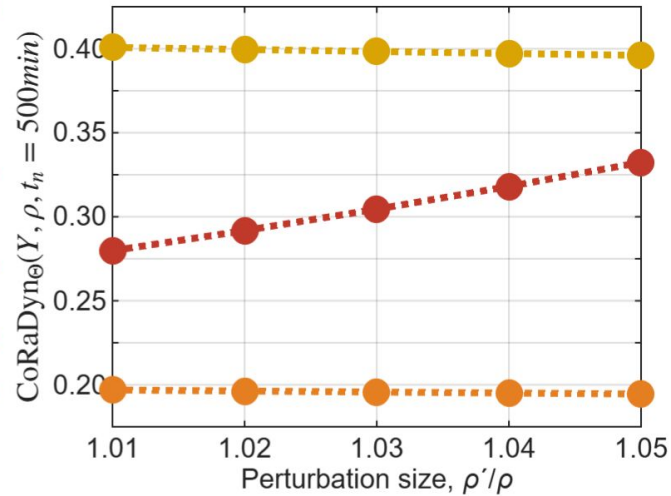
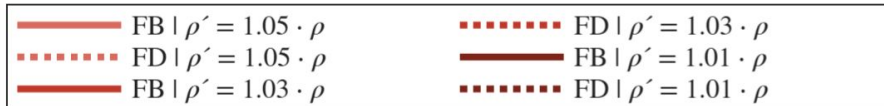
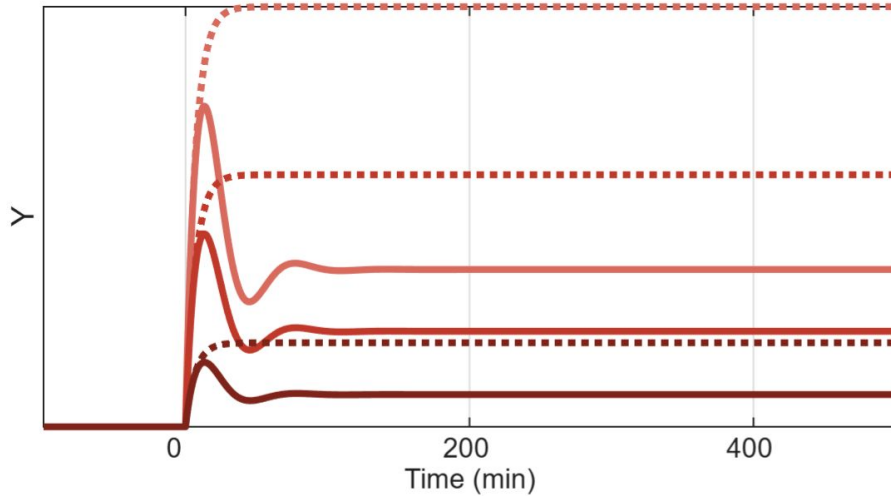
■ LAVIS – UNAM Juriquilla

- Luis Aguilar

- Jair García

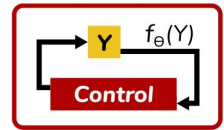
TIME-DEPENDENT CHARACTERIZATION OF FEEDBACK PERFORMANCE

Effect of perturbation size

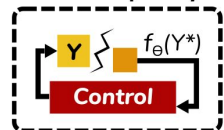


Athena Tamayo
Undergrad student
Thesis research
Graduated June 2024

Original system

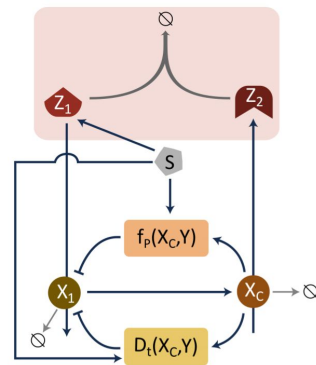
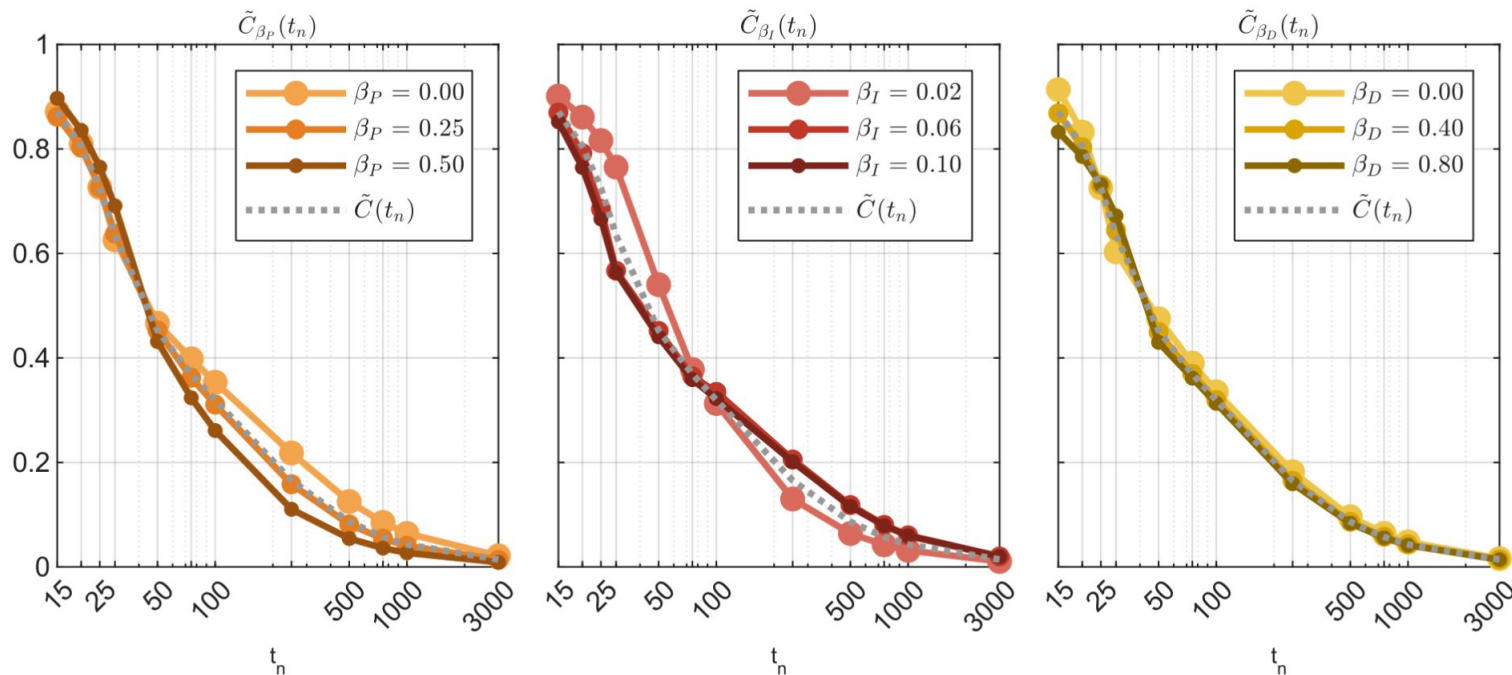


Locally analogous feedback-disrupted system



CONTRIBUTION OF P, I, & D CONTROL DEPENDS ON THE EVALUATION TIME

median(CoRaDyn) temporal profile for different control weights, β



CONTRIBUTION OF P, I, & D CONTROL DEPENDS ON THE EVALUATION TIME

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