CONTROL THEORY IN BIOLOGY

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INTRODUCTION

Control Theory is characterized by changing input parameters of a system in order to control a desired output state.

- Goals:

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- Goals:
  - steady
  - no delay
  - no overshoot
  - stable

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OVERVIEW

- Concepts first noted by James Clerk Maxwell: ”On Governors” [Max68]
- Most applications in engineering:
  - Aviation (Autopilot)
  - Ship stabilizers
  - Heating (Central Heating, Furnaces, ...)
  - Solar power plants
  - ...

OVERVIEW

EXAMPLES FROM BIOLOGY

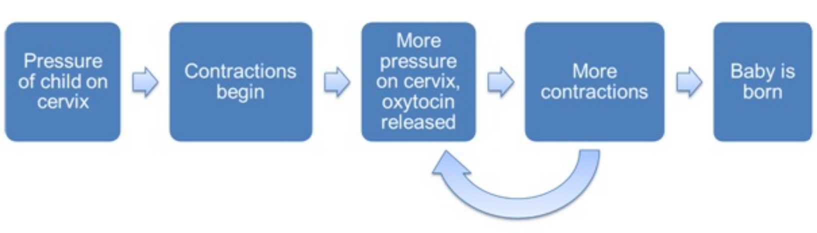
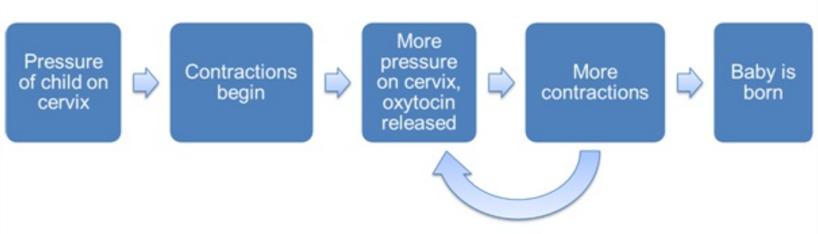


Figure 1: Childbirth [Tea22]

- More pressure



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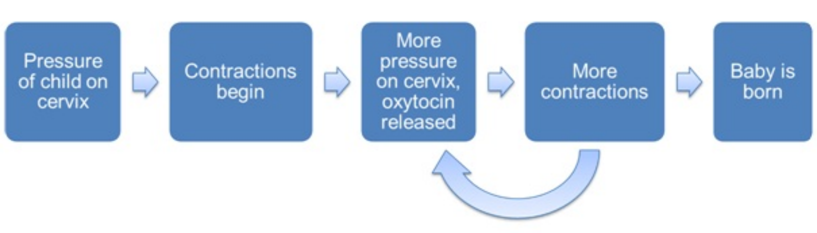

Figure 1: Childbirth [Tea22]

- More pressure
  $\rightarrow$ More contractions
- This is a positive feedback loop.

- More Sweat


Temperature increases
Body begins to sweat; vasodilation
Evaporative cooling occurs; convection cooling occurs
Temperature drops
Goosebumps appear; vasoconstriction
Less convection

- More Sweat
  $\rightarrow$ Less Temperature

- More Sweat
  $\rightarrow$ Less Temperature
- More ...

TEMPERATURE REGULATION

- More Sweat
  $\rightarrow$ Less Temperature
- More ...
  $\rightarrow$ Less ...

- More Sweat

  → Less Temperature
- More ...

  → Less ...
- This is a negative feedback loop.

- Tight calcium regulation in humans

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- Synthetic Biology

MORE EXAMPLES

- Tight calcium regulation in humans
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- Synthetic Biology
- Optogenetics (What we also do)

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- ...

CONCEPTS

We distinguish between two different controllers

- Open Loop Controller
- Closed Loop Controller

  $\rightarrow$ Closed loop control schemes are the biologically more interesting ones.

Figure 3: Open Loop Control System

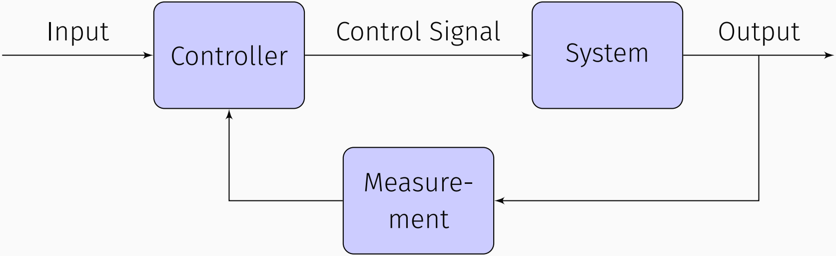

Figure 4: Closed Loop Control System with Measurement and Feedback

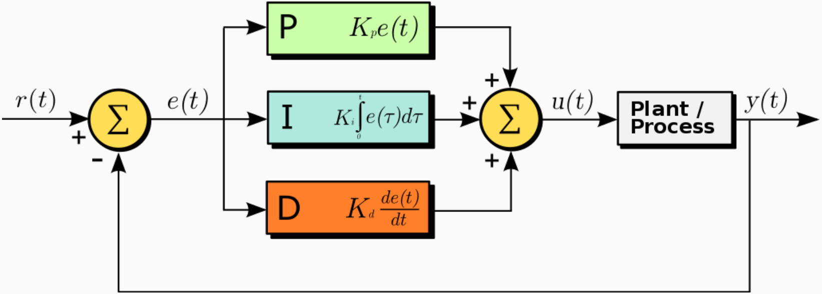

Figure 5: Schematic Overview of a Controller [Urq11]

Relevant values:

u(t) - Response of controller

e(t) - Difference of input signal and setpoint (target)

$$e(t) = r(t) - y(t) \tag{1}$$

$u(t)$ - Response of controller
$e(t)$ - Difference of input signal and setpoint (target)

We want to calculate response $u(t)$ from input $e(t)$.
Use a proportional response

$$u(t) = K_P e(t) \tag{2}$$

$u(t)$ - Response of controller
$e(t)$ - Difference of input signal and setpoint (target)

Differential response

$$u(t) = K_D \frac{\partial e}{\partial t} \tag{3}$$

In discretized version

$$u(t_{i+1}) = K_D \frac{e(t_{i+1}) - e(t_i)}{\Delta t} \tag{4}$$

u(t) - Response of controller
e(t) - Difference of input signal and setpoint (target)

Differential response

$$u(t) = K_I \int_0^t e(\tau) d\tau \tag{5}$$

In discretized version

$$u(t_{n+1}) = K_I \sum_{i=0}^{n} e(t_i) \Delta t \tag{6}$$

We can combine the previously introduced controllers.
PD Controller

$$u(t) = K_P e(t) + K_D \frac{\partial e}{\partial t} \tag{7}$$

PI Controller

$$u(t) = K_P e(t) + K_I \int_0^t e(\tau) d\tau \tag{8}$$

PID Controller

$$u(t) = K_P e(t) + K_I \int_0^t e(\tau) d\tau + K_D \frac{\partial e}{\partial t} \tag{9}$$

...

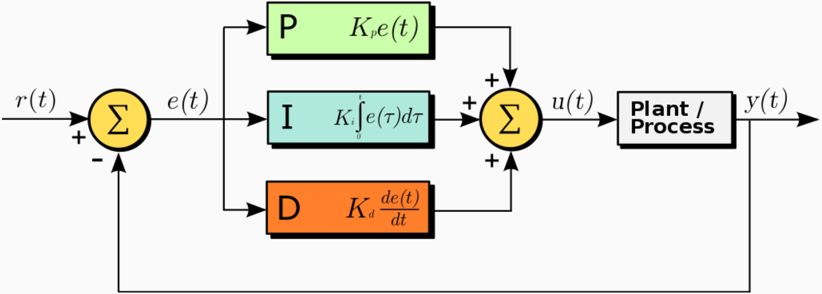

Figure 6: Schematic Overview of a PID Controller [Urq11]

$$e(t) = r(t) - y(t) \tag{10}$$

$$u(t) = K_P e(t) + K_I \int_0^t e(\tau)d\tau + K_D \frac{\partial e}{\partial t} \tag{11}$$

What do the parameters K_P, K_I, K_D do?

$$u(t) = K_P e(t) + K_I \int_0^t e(\tau) d\tau + K_D \frac{\partial e}{\partial t} \tag{12}$$

Alternative representation

$$u(t) = K_P \left(e(t) + \frac{1}{T_I} \int_0^t e(\tau) d\tau + T_D \frac{\partial e}{\partial t} \right) \tag{13}$$

What do K_p, T_I, T_D do now?

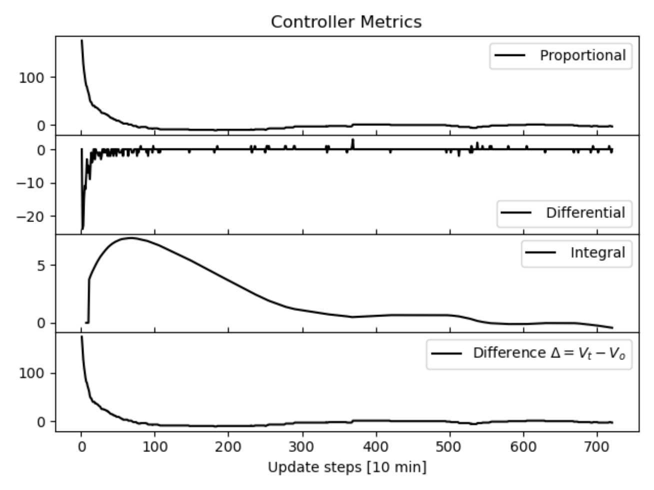

Figure 7: Optimal Control for a given system.

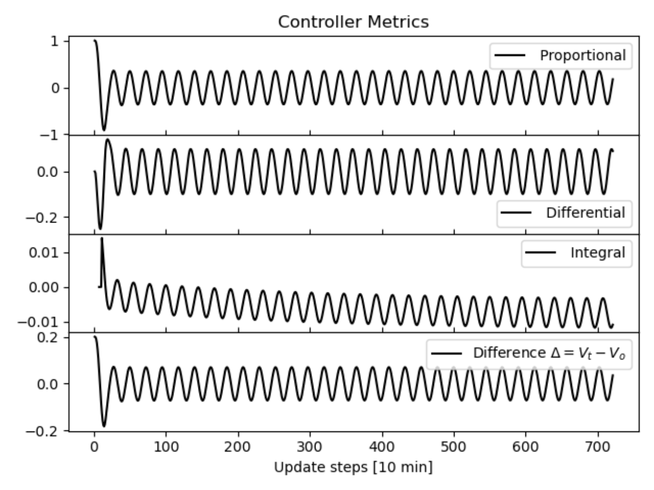

Figure 8: Oscillations can occur upon time-delays are.

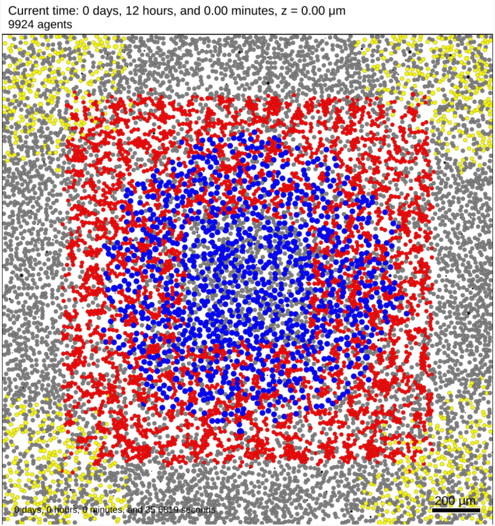

Figure 9: Optogenetic controllers regulate cell densities in different spatial

BIOLOGY AGAIN

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- These findings were simple integral control feedback loop.

RECAP

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”We argue that the key properties of biochemical networks should be robust in order to ensure their proper functioning.” - N. Barkai [BL97]

- These findings were simple integral control feedback loop.
- Robustness results from systems controlling themselves
- Feedback loops and control mechanisms are unavoidable in modern biology

- Noise can play important role in de-/stabilizing systems

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- Almost all biological systems are non-linear (eg. Toggle-Switch)
  $\rightarrow$ some control-schemes do not work as well
- When is control of a system optimal? $\rightarrow$ Can it be optimal?

Questions?

[allowframebreaks]

[BL97] N. Barkai and S. Leibler. Robustness in simple biochemical networks. Nature, 387(6636):913–917, June 1997.

[Max68] James Clerk Maxwell. I. on governors. Proceedings of the Royal Society of London, 16:270–283, December 1868.

[Tea22] The Albert Team. Positive and negative feedback loops in biology, 2022.

[Urq11] Arturo Urquizo. Pid controller overview, 2011.