# Oscillations

week 6

# 1. Oscillations in nature

# 1. Oscillations in nature

Concepts of **equilibria** play fundamental role in nature

- Chemical substances placed in a box will quickly go to equilibrium, called **chemical equilibrium**
- A hot cup of coffee in a cooler room will go to an equilibrium temperature with the environment: **thermodynamic equilibrium**
- Doctrine of homeostasis: body regulates all physiological variables (temperature, hormone levels, ...), to be in **physiological** equilibrium
- A population rises or falls until it reaches the ecosystem's carrying capacity at which point the system is in **ecological equilibrium**

# 1. Oscillations in nature

If **equilibrium** truly described all scientific phenomena, we could stop the investigation right here and begin to look for **point attractors** in all of our models of natural phenomena.

But are systems in nature really governed by equilibrium dynamics?

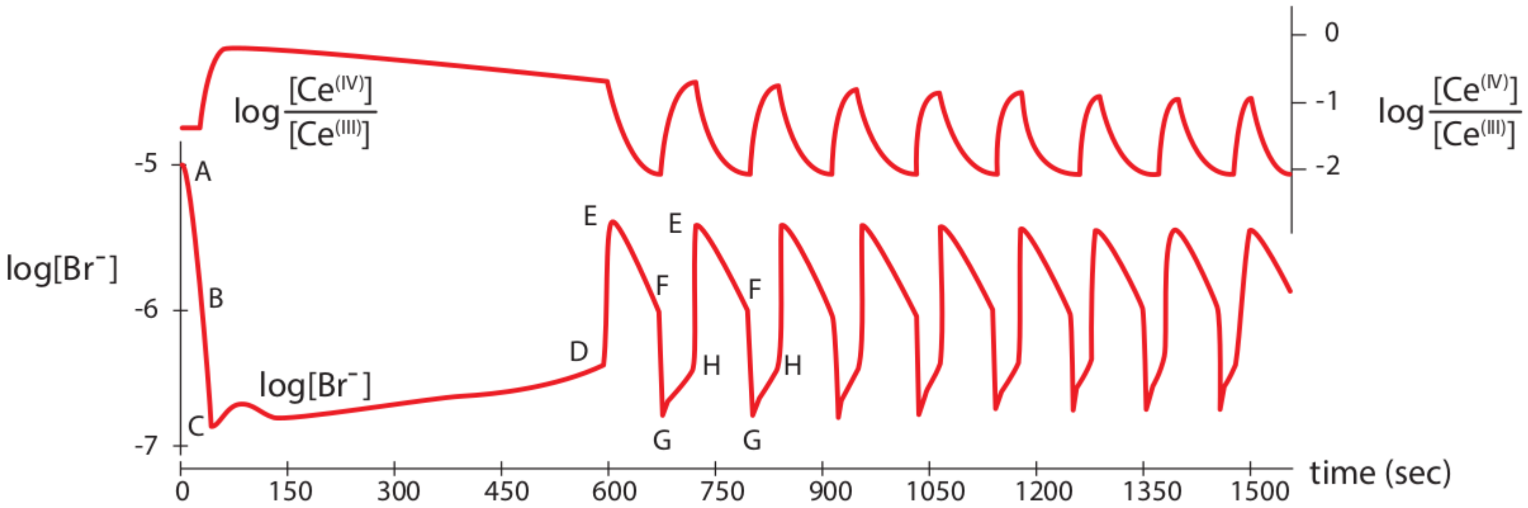
**The doctrine of equilibrium behavior is factually wrong or at least incomplete**

In many types of systems the fundamental behavior is oscillation, not equilibrium

# 1. Oscillations in nature

**Oscillations in Biochemistry**

- In 1958, chemist B.P. Belousov studied the reduction of **bromate by malonic acid**, a well-known laboratory model for the Krebs cycle.
- The colorless liquid turned yellow → colorless → yellow → ... for hours
- Was first reliable oscillatory chemical reaction ever observed



# 1. Oscillations in nature

**Oscillations in Biochemistry**

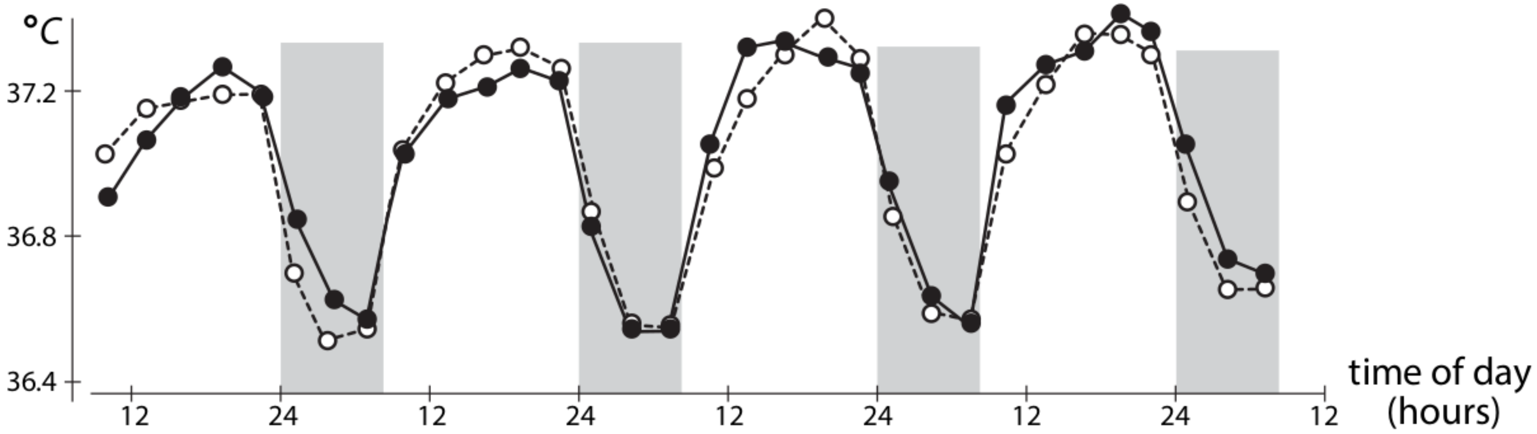
https://www.youtube.com/embed/jRQAndvF4sM?enablejsapi=1

Paper was rejected, because nobody believed this was possible.

Critics → failed to grasp, this was not a perpetual oscillator, only one that oscillates for a long time

# 1. Oscillations in nature

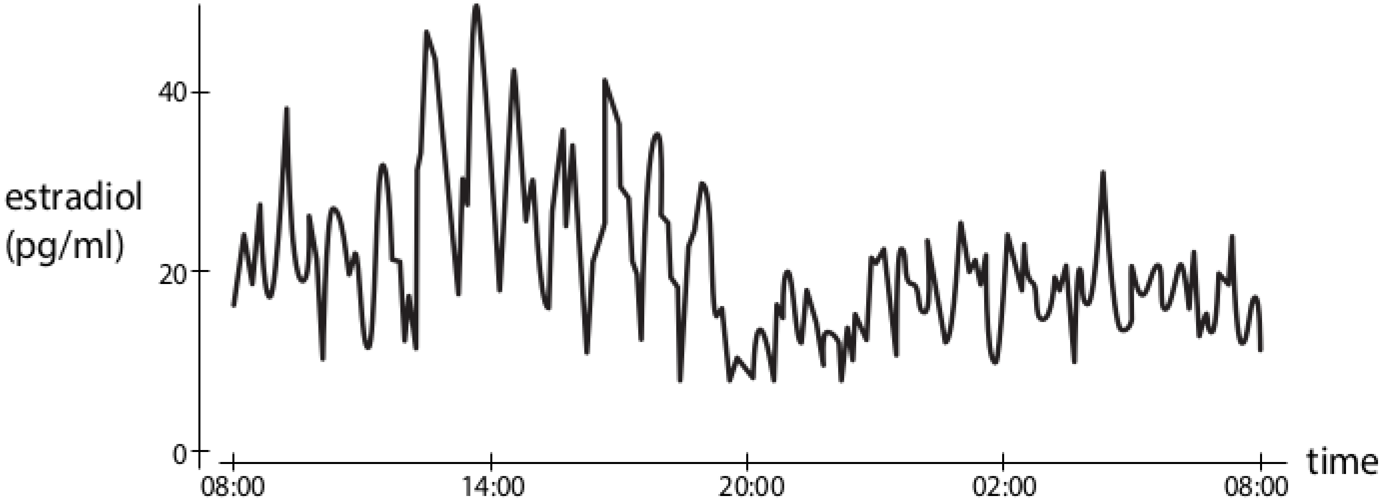
**Oscillations in Physiology - body temperature**




- Can be different up to 1 degree during the day!
- Even persists in complete darkness

# 1. Oscillations in nature

**Oscillations in Physiology - hormones**

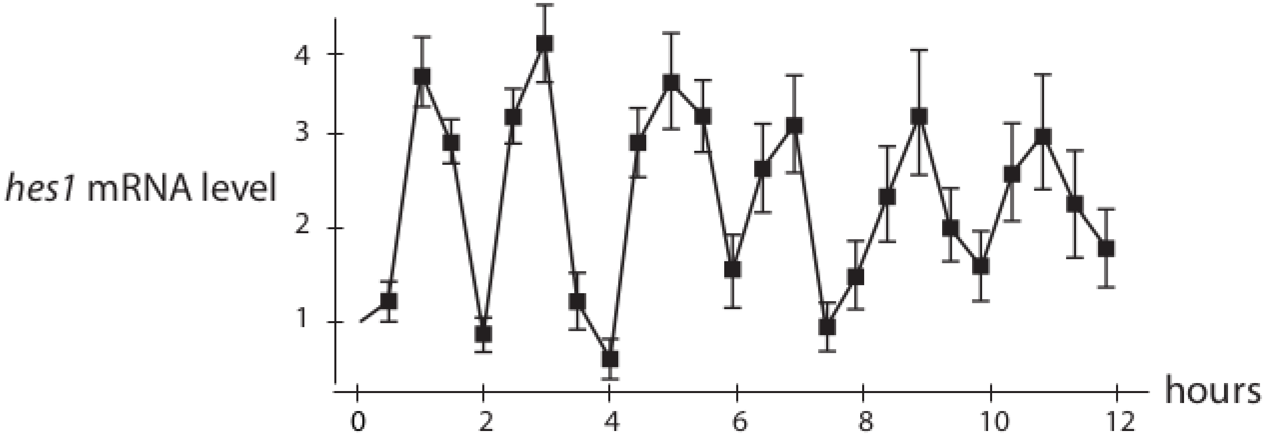



estradiol = major female sex hormone

- Oscillations in the 1-2 h scale, as well as the 12h scale

# 1. Oscillations in nature

**Oscillations in Physiology - gene expression**




**Gene expression**: process by which information from a gene is used in the synthesis of a functional gene product.

- often proteins
- non-protein-coding genes such as transfer RNA (tRNA) or small nuclear RNA (snRNA) genes, the product is a functional RNA

# 1. Oscillations in nature

**Transient versus long term behavior**

1. What is transient behavior?

you start with initial condition → system reacts and evolves
e.g. epidemics: start with single infected and see what happens

2. What is long term behavior?

behaviour for $t \rightarrow$ infinity
e.g. ecological systems

# 1. Oscillations in nature

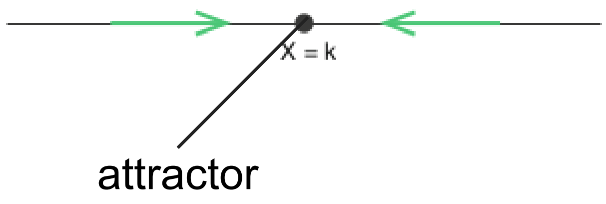
**Attractor**

An **attractor** of a dynamical system on the state space $X$ is a set $A$ contained in $X$ such that for a neighborhood of initial conditions $X_0$, the trajectories going forward from $X_0$ all approach $A$, that is,

$$\text{the distance } d\Big(X(t),\ A\Big) \to 0 \text{ as } t \to \infty$$

example: do you see an attractor?

$$X' = bX - \frac{b}{k}X^2$$



# 1. Oscillations in nature

**Attractor**

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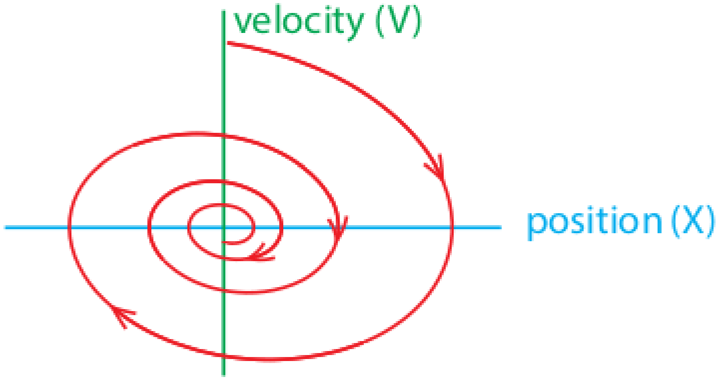
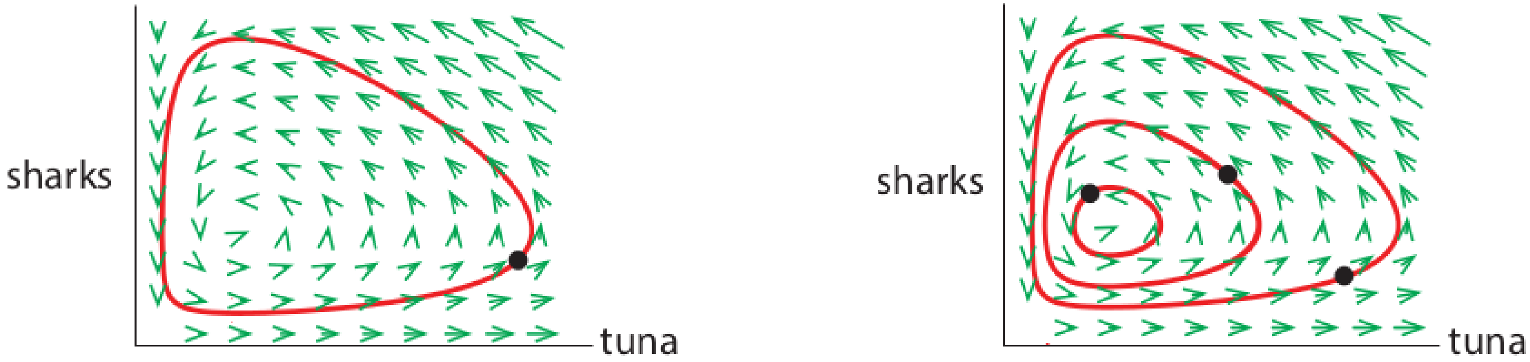
example: do you see an attractor?

spring with friction



# 1. Oscillations in nature

**Stable oscillators - Shark-Tuna model**

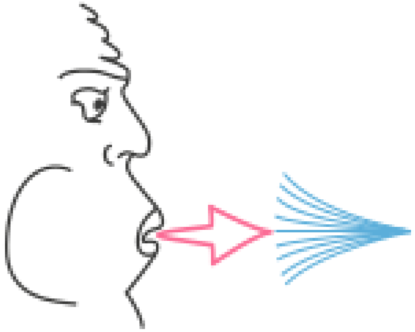


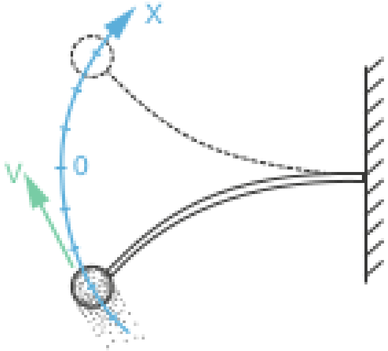

1) If $X$ is a state variable, the function $X(t)$ is an oscillation if and only if it is periodic; that is, if there is a constant $P$ (called the *period* of the oscillation) such that for all times $t$, $X(t+P) = X(t)$. In other words, the function $X(t)$ repeats itself after $P$ time units.
2) In state space, a trajectory represents an oscillation if and only if it is a closed loop, which is often referred to as a closed orbit.

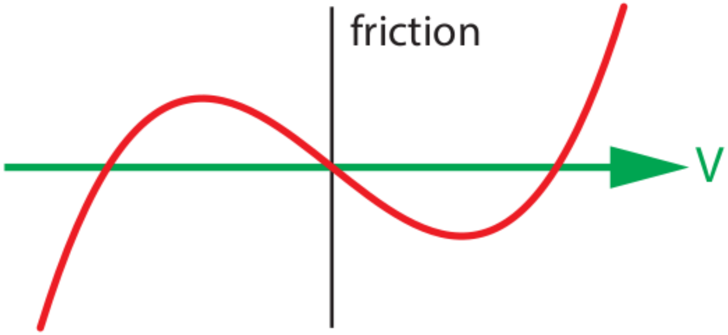
Not robust: slightly change conditions → you are on another orbit = **neutrally stable oscillation**

# 1. Oscillations in nature

**The Rayleigh Oscillator** stable oscillation?






$$X' = V$$
$$V' = -X - (V^3 - V)$$

# 1. Oscillations in nature

**The Rayleigh Oscillator** stable oscillation?

$$X' = V$$
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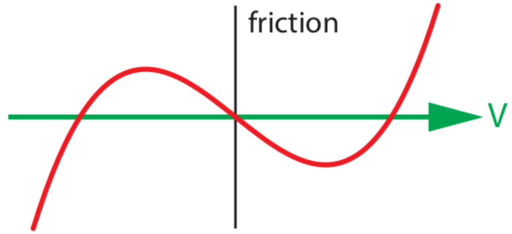
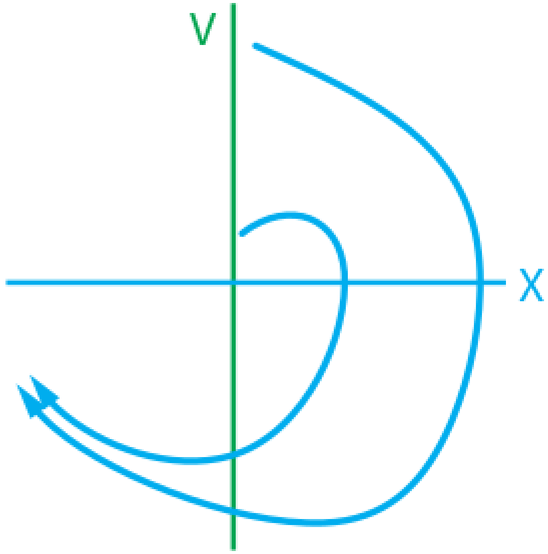
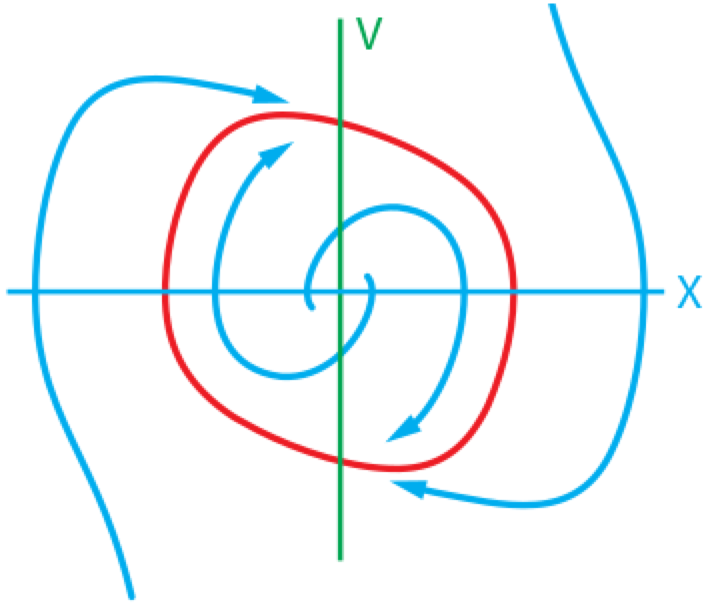
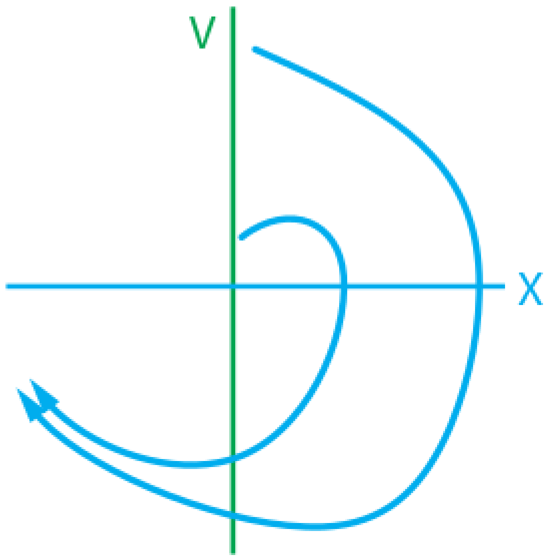


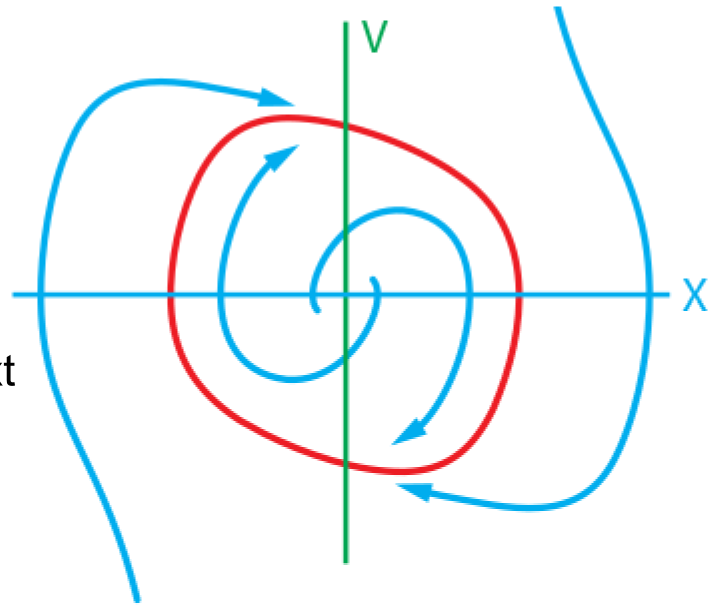



# 1. Oscillations in nature

**The Rayleigh Oscillator** stable oscillation?



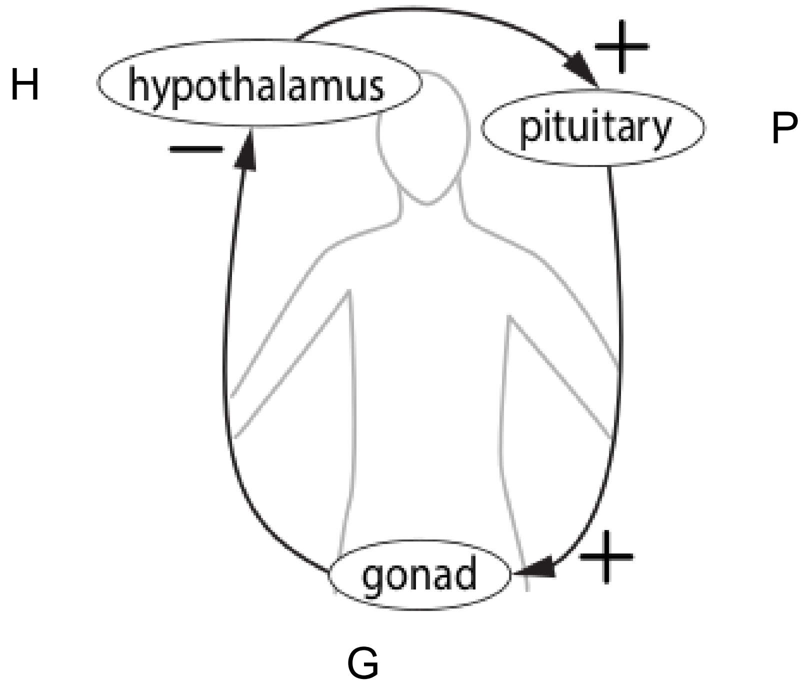

Text

Is an attractor! Any point in the neighbourhood will come closer to the red orbit = limit cycle = stable limit cycle

# Exercise 5.1.1

# 2. Mechanisms of oscillations

# 2. Mechanisms of oscillations - negative feedback



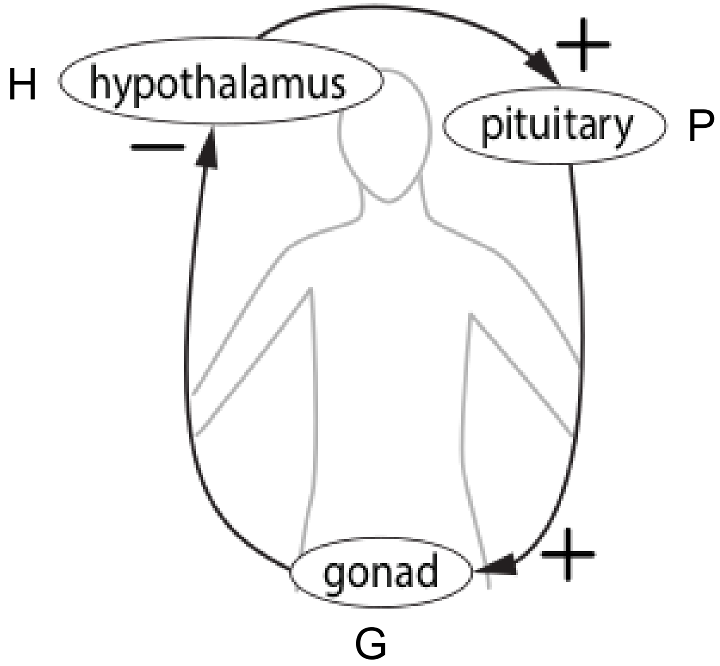

more H → more P → more G → G too high, less H

# 2. Mechanisms of oscillations - negative feedback

$$H' = \text{☁} - k_1 H$$

$$P' = H - k_2 P$$

$$G' = P - k_3 G$$




- We assumed that P' ~ H  (factor 1)
- We assumed that G' ~ P  (factor 1)

☁ decreases as G increases but never goes negative!

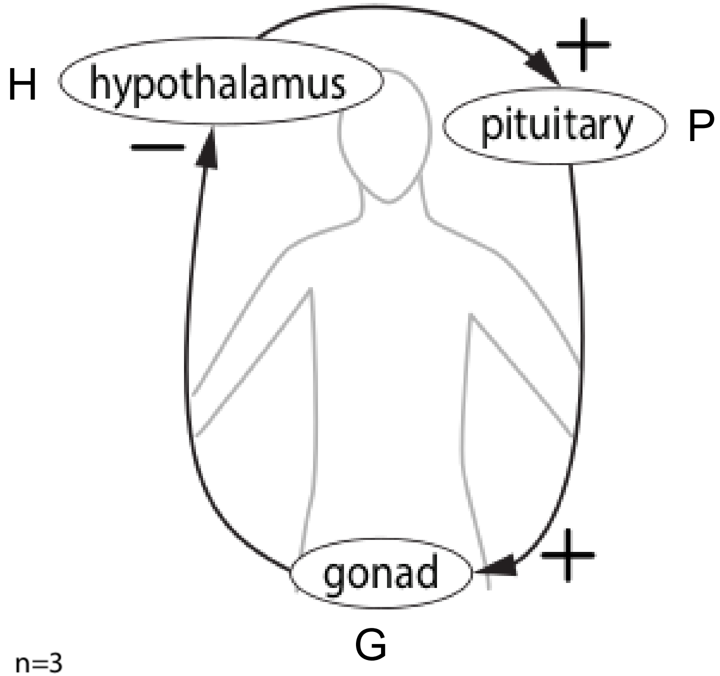
$$\text{☁} = \frac{1}{1 + G^n}$$

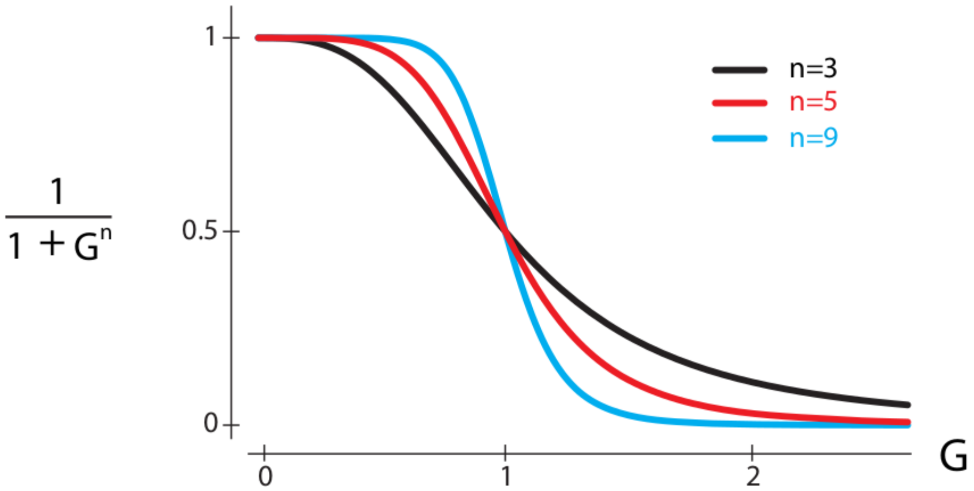
# 2. Mechanisms of oscillations - negative feedback

$$H' = \frac{1}{1+G^n} - k_1 H$$

$$P' = H - k_2 P$$

$$G' = P - k_3 G$$



# 2. Mechanisms of oscillations - negative feedback

$$H' = \frac{1}{1 + G^n} - k_1 H$$

$$P' = H - k_2 P$$

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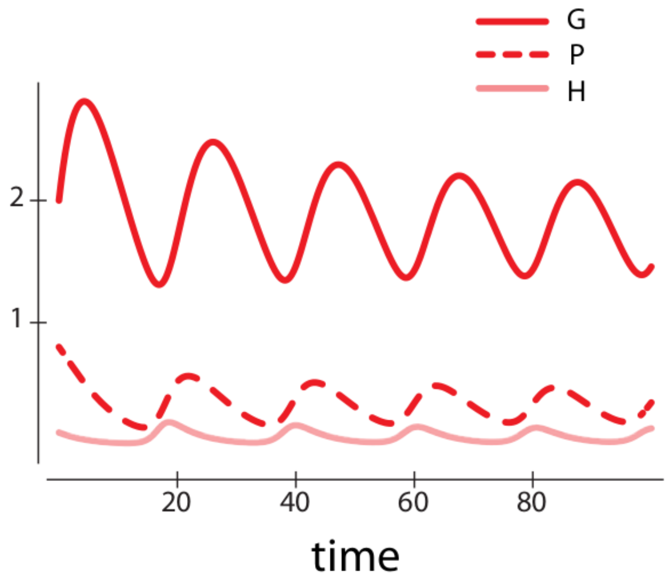
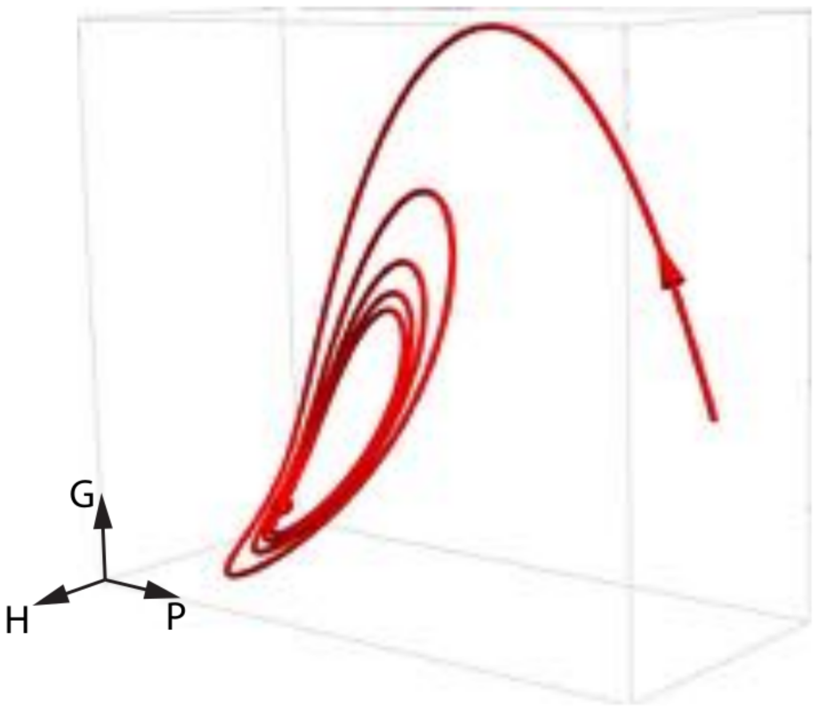


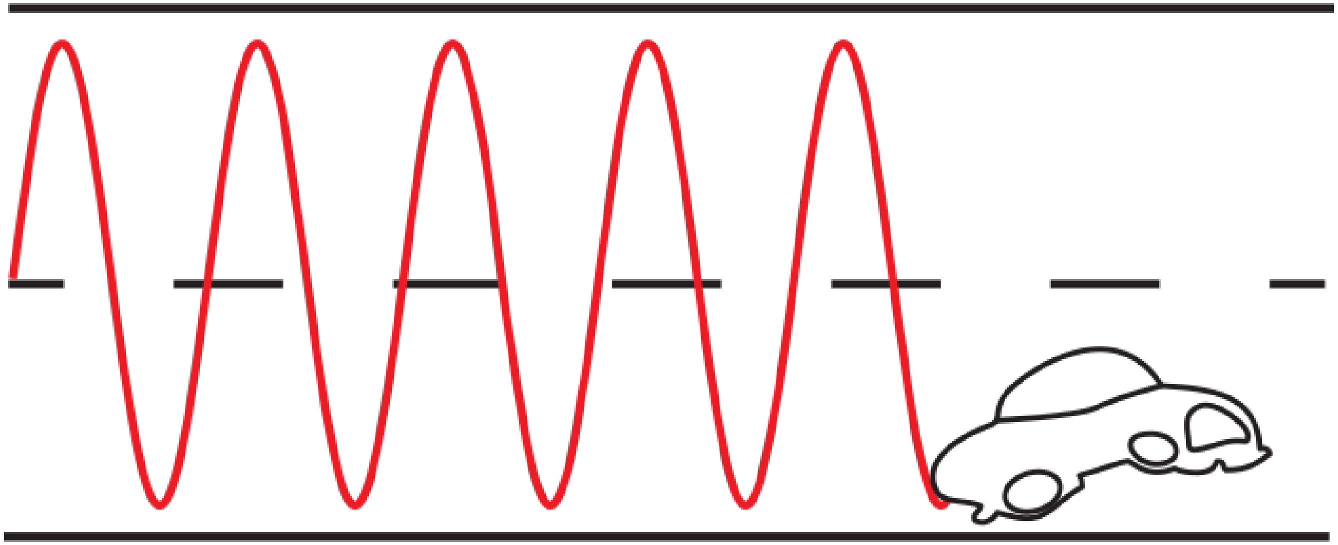




k1 = k2 = k3 = 0.2; n = 9

# Exercise 5.1.2

# 2. Mechanisms of oscillations - negative feedback

Highly sensitive negative feedback loops are one of the major causes of oscillations in biological systems.



# 2. Mechanisms of oscillations - negative feedback

We need the time delay!

$$H' = \frac{1}{1+G^n} - k_1 H$$
$$G' = H - k_3 G$$

This model does not oscillate!

# 2. Mechanisms of oscillations - time delay

**Example: Mackey - Glass model of respiratory control of CO2**

X = amount of CO2

$$
\begin{aligned}
X' &= \text{things that increase } CO_2 - \text{things that decrease } CO_2 \\
&= \text{body metabolism} - \text{ventilation}
\end{aligned}
$$

- when CO2 is high → increase breathing rate
- controlled by chemoreceptors in brain → instructions to the nerves controlling the lung

# 2. Mechanisms of oscillations - time delay

**Example: CO2**

$$X' = \text{things that increase } CO_2 - \text{things that decrease } CO_2$$
$$= \text{body metabolism} - \text{ventilation}$$

L = cte

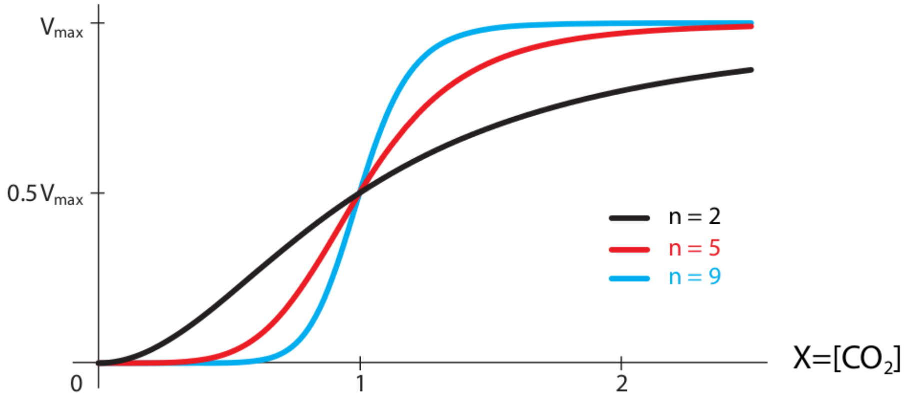
$CO_2/\text{breath} \times \text{breaths/minute}$

X

$$\frac{V_{max} \cdot X^n}{1 + X^n}.$$

ventilation rate

$$\frac{V_{max} \cdot X^n}{1 + X^n}.$$




Hill function

# 2. Mechanisms of oscillations - time delay

**Example: CO2**

$$X' = \text{things that increase } CO_2 - \text{things that decrease } CO_2$$
$$= \text{body metabolism} - \text{ventilation}$$

$$= L - \frac{V_{max} \cdot X^n}{1 + X^n} \cdot X$$

current CO2 level in the lungs

**CO2 concentration of some time ago**
**CO2 monitoring neurons in the brain**

Problem!

# 2. Mechanisms of oscillations - time delay

**Example: CO2**

$$X' = \text{things that increase } CO_2 - \text{things that decrease } CO_2$$
$$= \text{body metabolism} - \text{ventilation}$$

$$= L - \frac{V_{max} \cdot X^n}{1 + X^n} \cdot X$$

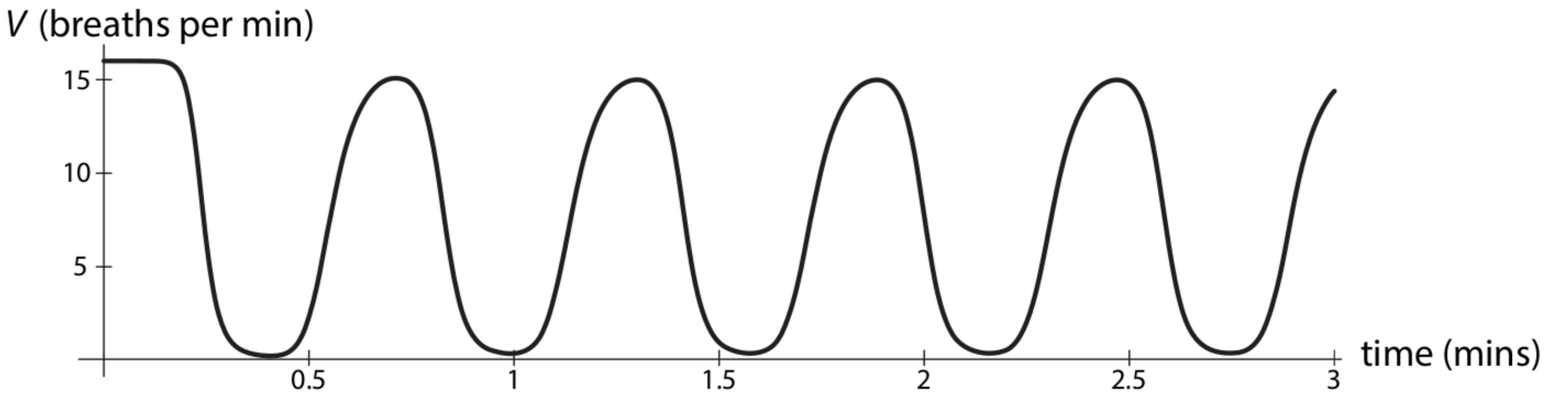
$$X' = L - \frac{V_{max} \cdot {X_\tau}^n}{1 + {X_\tau}^n} \cdot X \qquad X_\tau = X(t - \tau)$$

# Exercise 5.2.1

# 2. Mechanisms of oscillations - time delay

**Example: CO2**

$$X' = L - \frac{V_{max} \cdot {X_\tau}^n}{\boxed{1 + {X_\tau}^n}} \cdot X \qquad X_\tau = X(t-\tau)$$




→ Cheyne - Stokes breathing:

- heart failure patients: longer circulation times (pumping efficiency lower) → τ ↑
- stroke patient: reflex reactions ↑ (hyperflexia) → n ↑

# 2. Mechanisms of oscillations - time delay

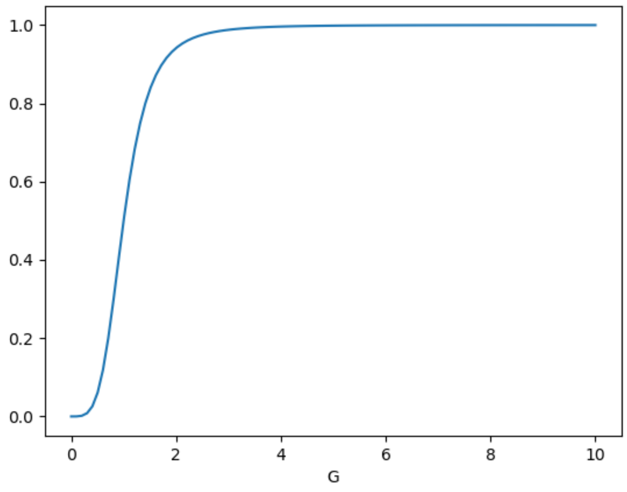
**Example: insulin glucose**

- Insulin is a hormone that is released by the pancreas in response to a rise in blood glucose, for example after a meal
- The insulin then facilitates the entry of glucose into muscle cells, where it is metabolized
- The dynamics of “glucose makes insulin go up, insulin makes glucose go down” is then a classic negative feedback loop

# 2. Mechanisms of oscillations - time delay

**Example: insulin glucose**

$$I' = \underbrace{\frac{k_1 \cdot G^4}{1 + G^4}}_{\text{glucose spurs insulin production by the pancreas}} - \underbrace{k_2 \cdot I}_{\text{degradation of insulin}}$$




a sigmoid!

# 2. Mechanisms of oscillations - time delay

**Example: insulin glucose**

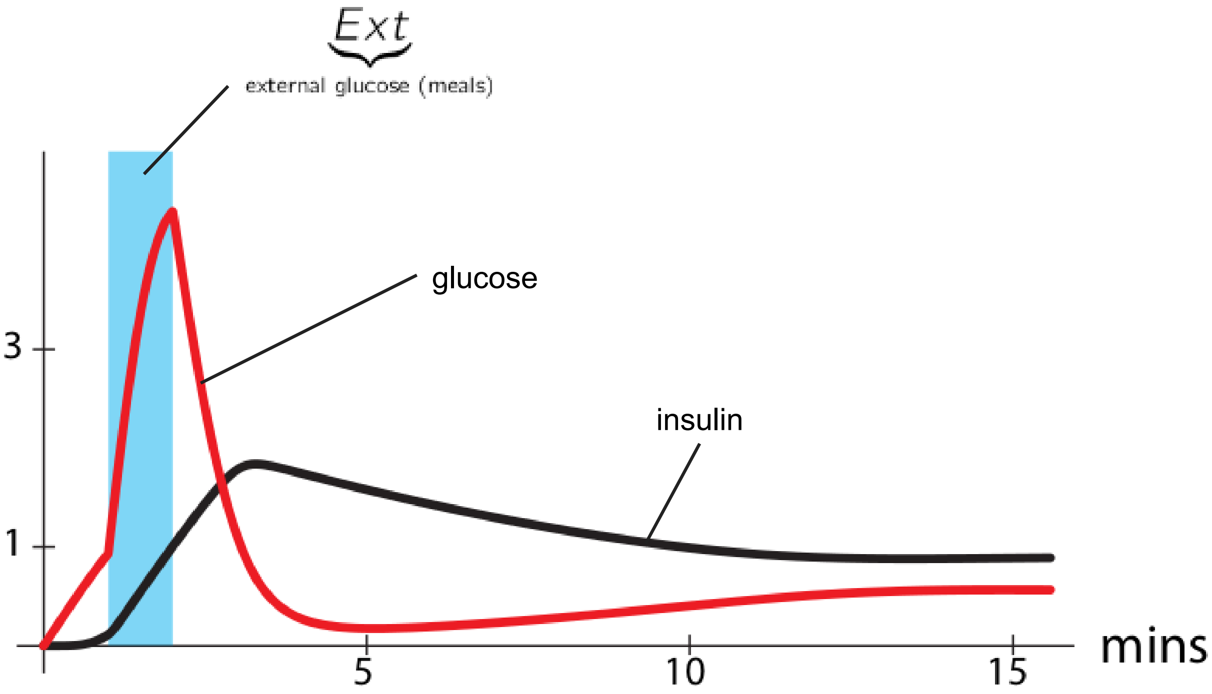
$$I' = \underbrace{\frac{k_1 \cdot G^4}{1 + G^4}}_{\text{glucose spurs insulin production by the pancreas}} - \underbrace{k_2 \cdot I}_{\text{degradation of insulin}}$$

$$G' = \underbrace{\frac{k_3}{1 + I^2}}_{\text{Insulin inhibits glucose production in the liver}} + \underbrace{Ext}_{\text{external glucose (meals)}} - \underbrace{k_4 \cdot G}_{\text{degradation of glucose}} - \underbrace{G \cdot I}_{\text{insulin facilitates glucose utilization by muscle}}$$

- G goes up by external sources (meals)
- G goes up by glucose production by the liver. This production is inhibited by insulin (I)
- G is degraded at a rate k4
- G combines with I in the muscle to metabolize G

# 2. Mechanisms of oscillations - time delay

**Example: insulin glucose**



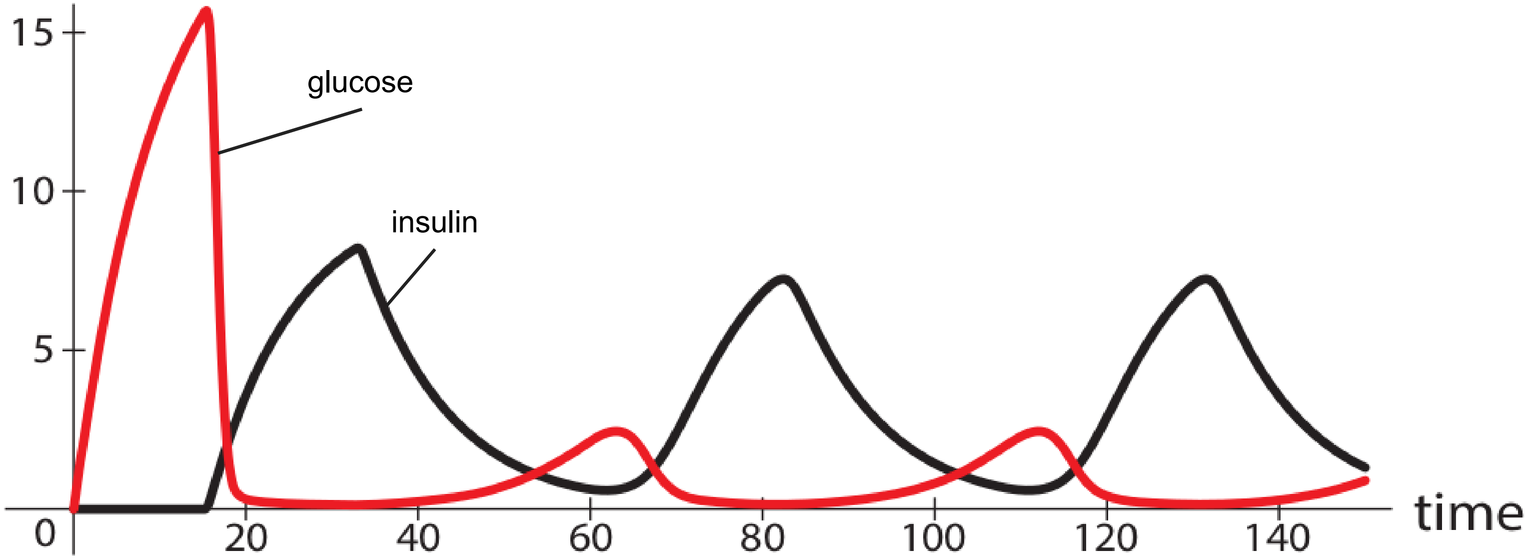

Model does not correspond to reality!

$$k_1 = 1, k_2 = 0.1, k_3 = 1, k_4 = 0.1, Ext = \begin{cases} 5, & \text{if } 1 < t < 2 \\ 0, & \text{otherwise} \end{cases}$$

# 2. Mechanisms of oscillations - time delay

**Example: insulin glucose**

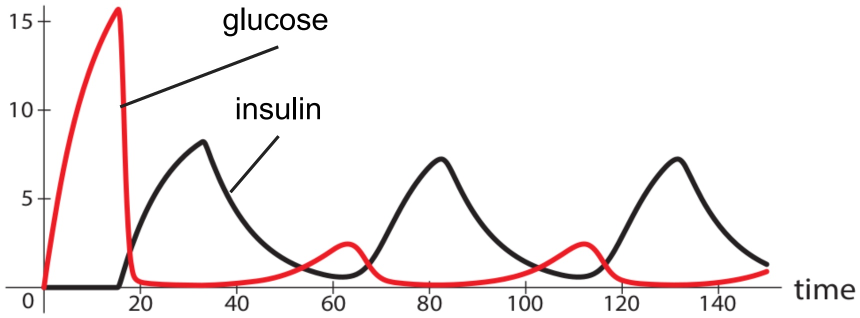
there is a time delay of 15 min, before glucose intake has an effect on insulin



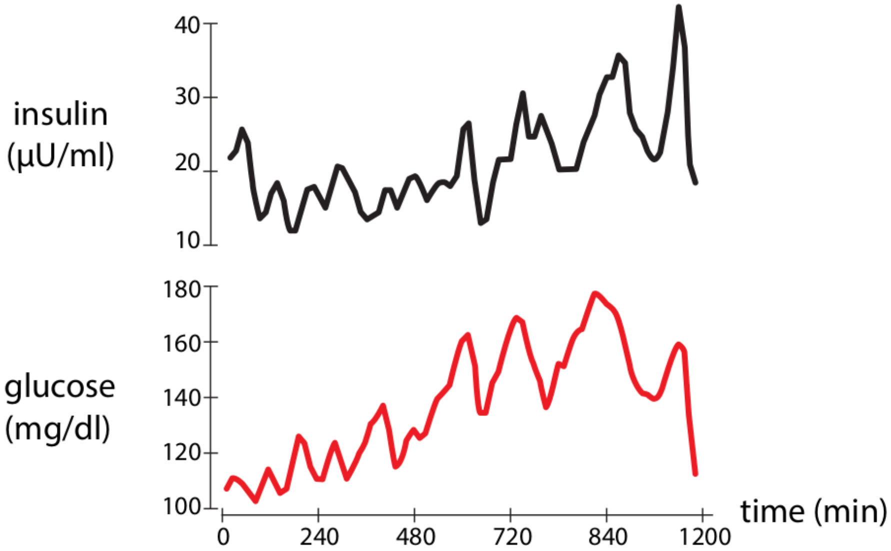

constant intake glucose

# 2. Mechanisms of oscillations - time delay

**Example: insulin glucose**

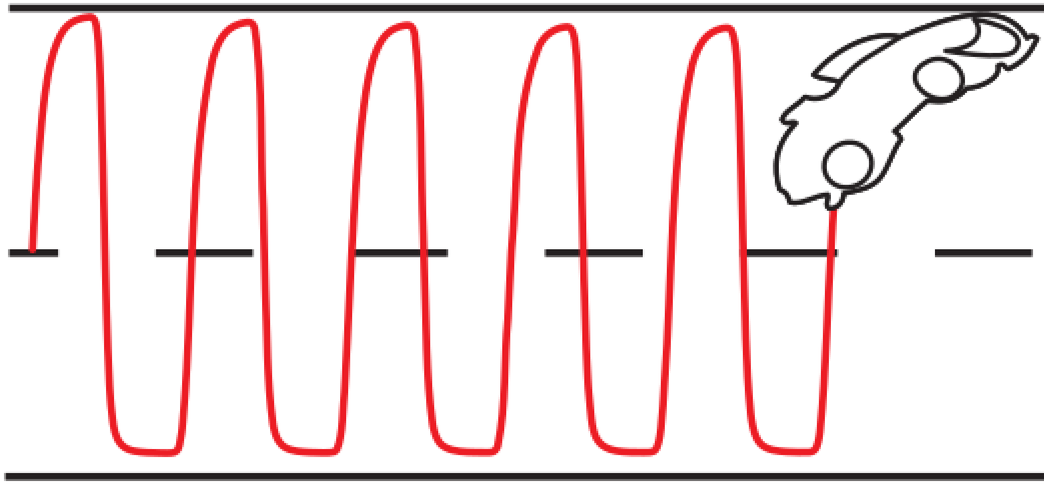



constant intake glucose



# 2. Mechanisms of oscillations - time delay

Under what conditions would this happen in real life?



# 2. Mechanisms of oscillations - time delay

**Example: car towing trailer**

https://www.youtube.com/embed/6mW_gzdh6to?enablejsapi=1

# 2. Mechanisms of oscillations - time delay

**Example: gene expression**

https://www.youtube.com/embed/T4LC0kSf7_s?enablejsapi=1