



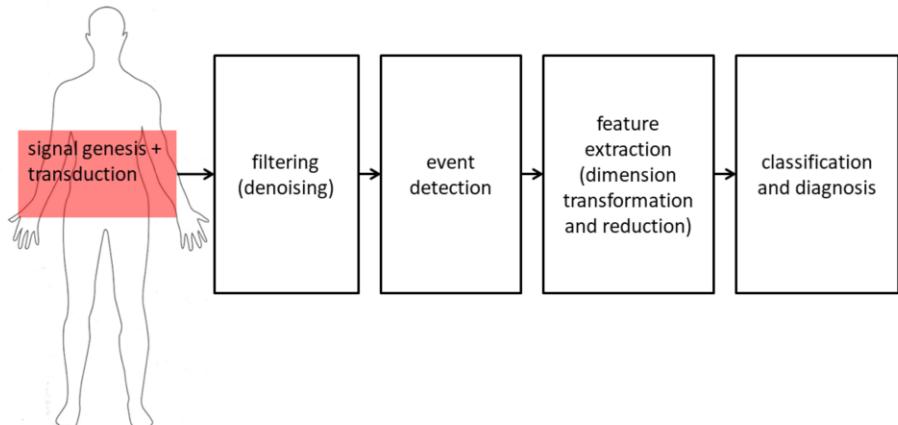
Biomedical Signal Processing

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Signal Genesis - Equations

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Biomedical Signal Processing





Today's goal

Giving a mathematical model for the biomedical signals

Single oscillators

- linear (2nd heart sound)
- non-linear (2nd heart sound, AP, cardiac pacemaker)

Coupled oscillators

- two or more coupled (ECG)
- train of coupled: propagation of AP, blood pressure (BP)

Multiscale events (heart murmur in PPG, EEG)

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What is oscillation? Examples?

All interesting biomedical signals can be said to arise from oscillators.

How can we construct an oscillator using some simple mathematical relations?

Perhaps simplest is $y(k) = -y(k-1)$, representing a pole at $z=-1$

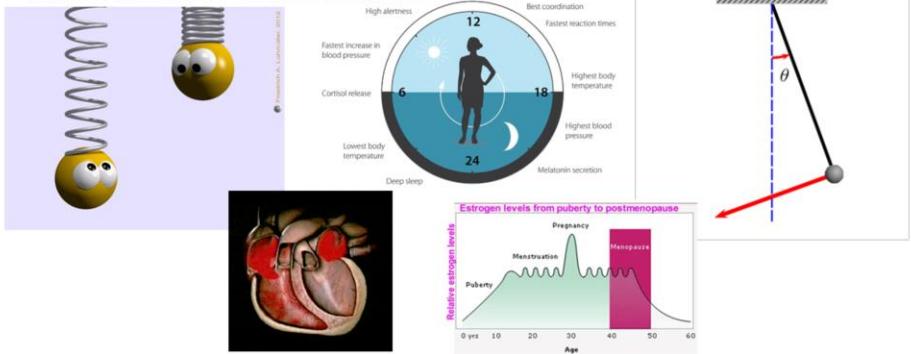
In continuous domain, simplest is $y'' - y = 0$ – **we cannot achieve oscillation with just first and zero order term.**

Why not? 1. Momentum needs to carry object across zero line (no overshoot with $y=-x$)
2. Particle needs to be able to have both +ve and -ve velocities at single position, this cannot be achieved with $y' = f(x)$



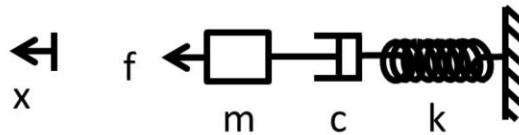
What is oscillation?

Oscillation is the repetitive variation, typically in time, of some measure about a central value (often a point of equilibrium) or between two or more different states.





Mass-spring damper system – a simple oscillator



- **I/O model** ($\ddot{x} + a_1\dot{x} + a_0x = b_1\dot{u} + b_0u$)

$$\begin{aligned}m\ddot{x} + c\dot{x} + kx &= Af \\ \ddot{x} + \frac{c}{m}\dot{x} + \frac{k}{m}x &= \frac{A}{m}f\end{aligned}$$

- **Transfer function (G(s)) and zeros (z) /poles (p)**

$$G(s) = \frac{F(s)}{X(s)} = \frac{\frac{A}{m}}{s^2 + \frac{c}{m}s + \frac{k}{m}}, \quad p_1, p_2 = \frac{-\frac{c}{m} \pm \sqrt{\frac{c^2}{m^2} - \frac{4k}{m}}}{2}, \quad z = \emptyset$$

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As the solution should not explode, poles must be nonpositive \rightarrow stability constrain for the poles to be on the nonpositive halfplane.

Two methods for solving this second-order differential equation:

- **Solving the equation with probe function** : Ae^{st} is the probe function, its derivative is sAe^{st} , second derivative is s^2Ae^{st}

$$\begin{aligned}m\ddot{x} + c\dot{x} + kx &= 0, x = Ae^{st} \\ (ms^2Ae^{st} + csAe^{st} + kAe^{st}) &= 0\end{aligned}$$

the trivial solution is $A = 0$. We devide by Ae^{st} for the relevant solutions

$$ms^2 + cs + k = 0$$

$$\begin{aligned}s_{1,2} &= \frac{-c \pm \sqrt{c^2 - 4mk}}{2m} \\ x(t) &= Ae^{st} = A_1 e^{\frac{-c + \sqrt{c^2 - 4mk}}{2m}t} + A_2 e^{\frac{-c - \sqrt{c^2 - 4mk}}{2m}t}\end{aligned}$$

$A_{1,2}$ can be calculated from the boundary conditions, $x(0), \dot{x}(0)$

- **Solving the equation with the Laplace transform:**

$$\mathcal{L}[\dot{x}(t)](s) = s\mathcal{L}[x(t)](s) - x(0)$$

$$\begin{aligned}
\mathcal{L}[\ddot{x}(t)](s) &= s^2 \mathcal{L}[x(t)](s) - sx(0) - \dot{x}(0) \\
m\ddot{x} + c\dot{x} + kx &= 0, \\
m(s^2 \mathcal{L}[x(t)](s) - sx(0) - \dot{x}(0)) + c(s\mathcal{L}[x(t)](s) - x(0)) + k\mathcal{L}[x(t)](s) &= 0 \\
\mathcal{L}[x(t)](s) \cdot \{ms^2 + cs + k\} - msx(0) - m\dot{x}(0) - cx(0) &= 0 \\
\mathcal{L}[x(t)](s) &= \frac{msx(0) + m\dot{x}(0) - cx(0)}{ms^2 + cs + k} \\
\mathcal{L}[x(t)](s) &= \frac{msx(0) + m\dot{x}(0) - cx(0)}{m(s - s_1)(s - s_2)} \\
&= \frac{A_1}{s - s_1} + \frac{A_2}{s - s_2} \quad / \text{partial fraction decomposition} \\
\mathcal{L}^{-1}[\mathcal{L}[x(t)](s)] &= A_1 e^{s_1 t} + A_2 e^{s_2 t}
\end{aligned}$$

If there is no damping ($c=0$), the solution is a constant oscillation (no real-valued exponential is present):

$$(\text{no damping}) c = 0: s = \pm j \sqrt{\frac{k}{m}}; x = A e^{\left(\pm j \sqrt{\frac{k}{m}}\right)t}$$

Here we can see, that the undamped natural frequency is $\sqrt{\frac{k}{m}}$

If the system is overdamped, there is no oscillation (no imaginary component of the exponential)

$$(\text{overdamping}) c >> 2\sqrt{mk}: s = 0, -\frac{c}{m}; x = A + B e^{\left(-\frac{c}{m}\right)t}$$

Observe that the complex number $\pm j \sqrt{k/m}$ is on the imaginary axis, on the limit of stability \rightarrow the function is neither damped, nor exploding

On the other hand, $-\frac{c}{m}$ has a negative real part, will thus be damped.

The transfer function:

The Laplace transform of the system:

$$X(s) = F(s)$$

$$\mathcal{L}[x(t)](s) \cdot \{ms^2 + cs + k\}$$

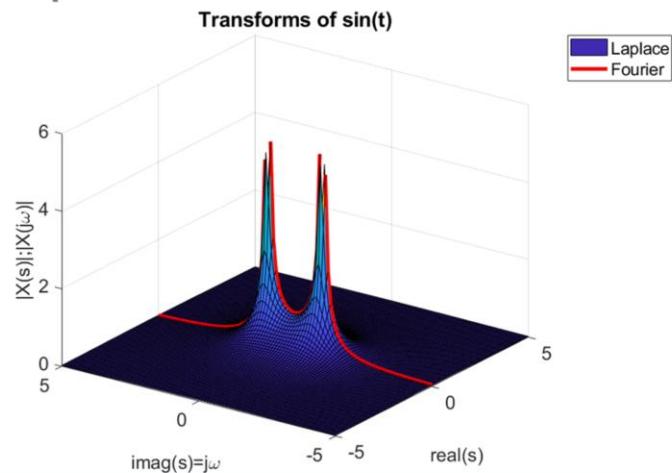
$$= A \mathcal{L}[f(t)](s) \quad / \text{note, that the constant boundary conditions are omitted}$$

$$\frac{\mathcal{L}[x(t)](s)}{\mathcal{L}[f(t)](s)} = \frac{A}{ms^2 + cs + k}$$

We are searching the effect of the system on the input, how the output is different from the input



Fourier vs Laplace



The Laplace transform is a complex-valued function, it takes frequency values on the whole frequency plane. The Fourier transform is real valued, it is drawn along the imaginary axis of the Laplace transform.



Mass-spring damper system

$$m\ddot{x} + c\dot{x} + kx = 0$$

$$\omega_0 = \sqrt{\frac{k}{m}} : \text{undamped natural frequency}$$

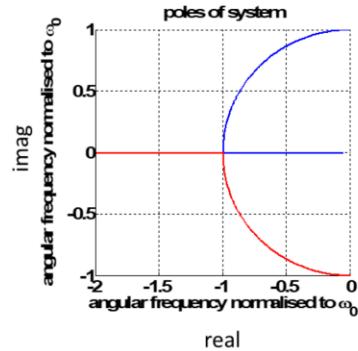
$$\zeta = \frac{c}{2\sqrt{mk}} : \text{damping ratio}$$

$$K = \frac{A}{k}$$

Standard form of stable 2nd order systems without zeros:

$$\ddot{x} + 2\zeta\omega_0\dot{x} + \omega_0^2x = K\omega_0^2f$$

$$G(s) = \frac{K\omega_0^2}{s^2 + 2\zeta\omega_0s + \omega_0^2} \rightarrow G(j\omega) = \frac{K\omega_0^2}{-\omega^2 + 2j\omega\zeta\omega_0 + \omega_0^2}$$



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Omega, zeta and K are the common notations in a standard second order system, and these units will have more engineering relevance.

The poles of the system can be observed on the plot: only the negative half plane is concerned (because of stability). Where conjugate pole-pairs are present, the oscillation will be visible, but when the real part of the pole is less than -1, overdamping will occur.

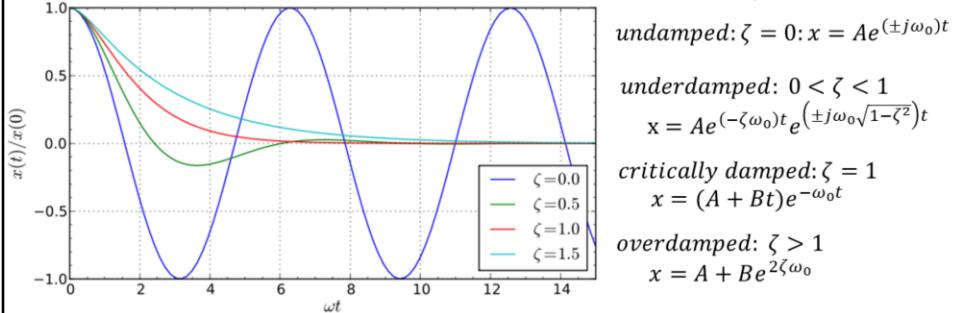
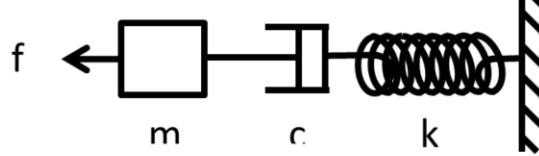
$$p_1, p_2 = -\zeta\omega_0 \pm \sqrt{\omega_0^2(\zeta^2 - 1)}$$

Stability condition:

$$p_1, p_2 < 0 \rightarrow \omega_0, \zeta > 0$$



Mass-spring damper system



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http://en.wikipedia.org/wiki/File:Damping_1.svg

The poles as a function of zeta will have the following values, and the damping can be observed as explained on the previous slides.

$$s = -\zeta\omega_0 \pm \sqrt{\omega_0^2(\zeta^2 - 1)}$$

$$\text{undamped: } \zeta = 0: s = \pm j\omega_0; x = Ae^{(\pm j\omega_0)t}$$

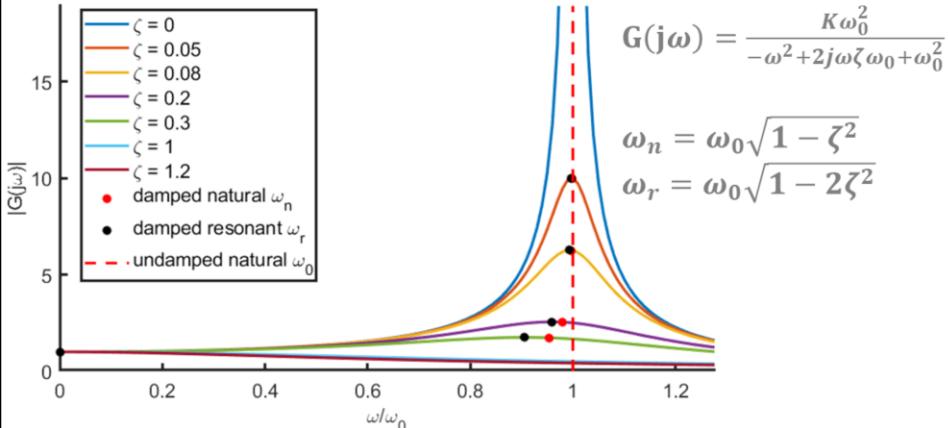
$$\text{underdamped: } 0 < \zeta < 1: s = -\zeta\omega_0 \pm j\omega_0\sqrt{1 - \zeta^2}; x = Ae^{(-\zeta\omega_0)t}e^{(\pm j\omega_0\sqrt{1-\zeta^2})t}$$

$$\text{critically damped: } \zeta = 1: s = -\omega_0; x = (A + Bt)e^{-\omega_0 t}$$

$$\text{overdamped: } \zeta > 1: s = \omega_0 \left(\sqrt{(\zeta^2 - 1)} - \zeta \right), -\omega_0 \left(\sqrt{(\zeta^2 - 1)} + \zeta \right) \approx s_1 + s_2 = 0, -2\zeta\omega_0$$



Natural and resonant frequencies



<https://www.youtube.com/watch?v=5JbpcSH80us>

<https://www.youtube.com/watch?v=urYWaHfel6g>

In the figure above you can see, that under different damping factors (ζ) how the amplitude response of the system for different input forcing frequencies (ω) changes. When there is no damping, - blue line - if the system is forced at its natural frequency (ω_0), the response is infinity – disastrous resonance occurs. If there is some damping, than the maximum response of the system (at its resonant frequency, ω_r) will be finite. If the damped system is left alone, it will resonate at ω_n

The difference between the natural and resonant frequency of a damped system: If you imagine yourself in a swing, if you start swinging from some height, and you stay still, the swing will move with its natural frequency, depending on the length of the chain (and finally stop, depending on the damping factor). But if someone starts pushing you near the natural frequency (not exactly, but close to it), the energy will build up and you will swing higher and higher. This is the resonant frequency, and can be calculated as the maximum of the second derivative of the transfer function.

Frequencies at which the response amplitude is a relative maximum are known as the system's **resonant frequencies**. At resonant frequencies, small periodic driving forces

have the ability to produce large amplitude oscillations, due to the storage of vibrational energy. When damping is small, the resonant frequency is approximately equal to the natural frequency of the system, which is a frequency of unforced vibrations. (wikipedia)

Resonance can be calculated where the amplitude response has its maximum (so the derivative of the function has to be calculated, and where it equals 0, we have the maximum)

$$\frac{X(s)}{F(s)} = \frac{1}{s^2 + 2\zeta\omega_0s + \omega_0^2} = \frac{1}{(s - a_1)(s - a_2)}$$

$$|\frac{X(j\omega)}{F(j\omega)}|^2 = \left| \frac{-1}{\omega^2 - \omega_0^2 - j2\zeta\omega_0\omega} \right|^2 = [(\omega^2 - \omega_0^2)^2 + 4\zeta^2\omega_0^2\omega^2]^{-1}$$

Resonance:

$$\frac{d|\frac{X(j\omega)}{F(j\omega)}|^2}{d\omega^2} = 2 \left[(\omega^2 - \omega_0^2) + 2\zeta^2\omega_0^2 \right] \left| \frac{X(j\omega)}{F(j\omega)} \right|^4 = 0$$

$$\omega_r = \omega_0\sqrt{1 - 2\zeta^2}$$

Natural frequency: previous slide, using the Laplace transform

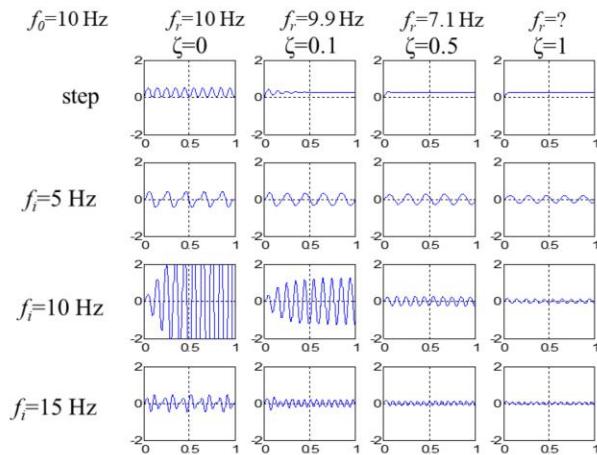
Even your body does have a resonant frequency!

„The main concern is the body's resonant frequency. At the resonant frequency there is maximum displacement between the organ and the skeletal structure, placing biodynamic strain on the body tissue involved.”

<https://ore.exeter.ac.uk/repository/bitstream/handle/10871/19515/C155.pdf?sequence=1>



Example simulations using ode45



We have an oscillation with a natural frequency of 10 Hz. The different columns represent different damping factors in the system, the resonance frequency (f_r) is calculated for each case.

The oscillation is forced by an external impulse (f_i) as listed in the left column.

With the step function as external force no resonance is reached, and with increasing damping the signal flattens out earlier.

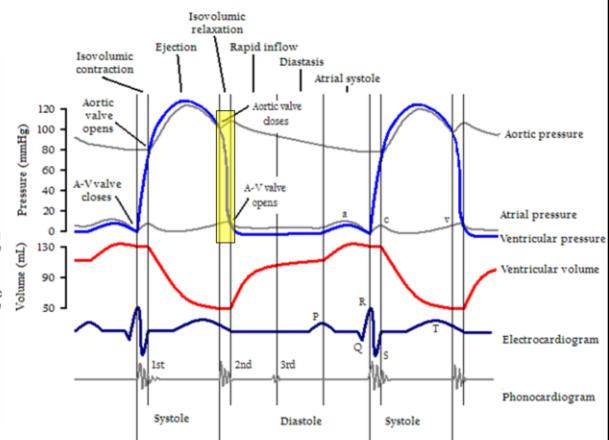
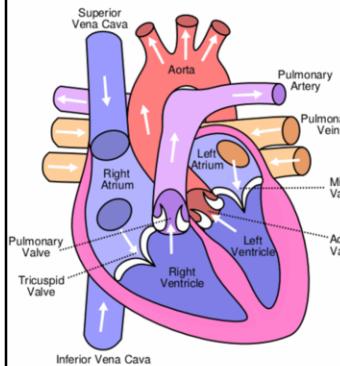
When the external force has a frequency of 5Hz (still far from the resonance frequency), with no damping the two frequency modulate each other. With stronger damping the 10Hz signal disappears from the signal, and only the 5Hz remains.

10 Hz matches the natural frequency, the resonance occurs as expected (disastrous resonance, explosion), with more damping the effect is less prominent (resonant frequency is farther away from the natural, has a lower response)

The 15 Hz signal acts similarly as the 5Hz.



Why is this relevant? Heart sounds



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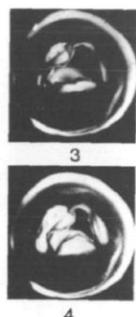
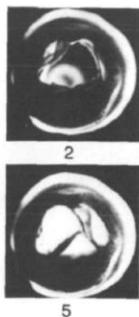
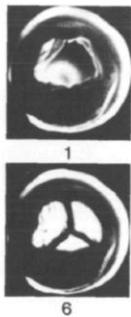
http://commons.wikimedia.org/wiki/File:Heart_labelled_large.png

http://upload.wikimedia.org/wikipedia/commons/9/9a/Wiggers_Diagram.png

The second heart sound can be modeled with a simple Mass-Spring-Damper system.

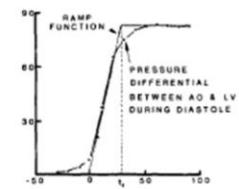
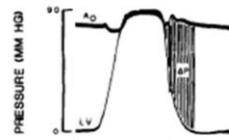
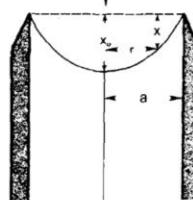


Why relevant? Heart sounds



first mode
vibration

FORCE = ΔP



$$m\ddot{x}_0 + D\dot{x}_0 + Kx_0 = \Delta p\pi a^2$$

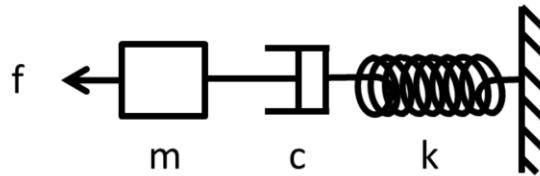
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Sabbah and Stein (1976): Investigation of the theory and mechanism of the origin of the second heart sound

Blick, Sabbah and Stein (1979): One-dimensional model of diastolic semilunar valve vibrations productive of heart sounds



Non-linearization of MSD system



$$m\ddot{x} + c(x)\dot{x} + k(x)x = Af$$

Duffing (non – linear restoring force): $k(x) = 1 + dx^2$

Van der Pol (non – linear damping): $c(x) = \mu(x^2 - 1)$

With non-linear system we can express more biomedical signals.
The damping or the restoring force is not linear ($c\dot{x}$; kx), but a non-linear function of x.



Duffing oscillator

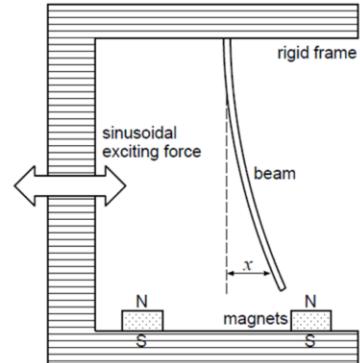
$$\ddot{x} + \alpha\dot{x} + \beta x + \gamma x^3 = \delta \cos(\omega t)$$

amount of damping

Nonlinearity of restoring force

linear stiffness

amplitude of driving force



<http://community.wolfram.com/groups/-/m/t/241732>

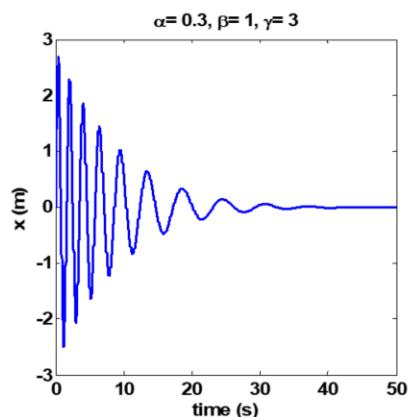
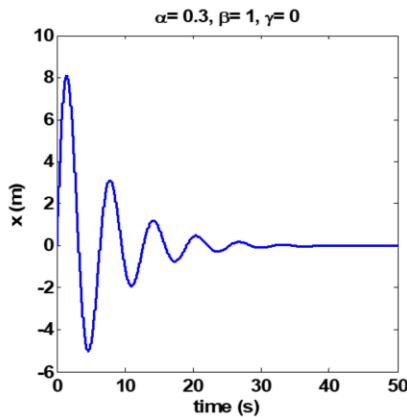
https://www.youtube.com/watch?v=KZF5k4L_Yao

A Duffing oscillator has a non-linear restoring force. In a physical representation a magnet is giving the non-linearity, the resonating frame gives the external driving force, the beam has a stiffness like the spring constant.



Duffing oscillator

$$\ddot{x} + \alpha\dot{x} + \beta x + \gamma x^3 = 0$$



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reason for initial high frequency?
physical example?

https://www.youtube.com/watch?v=KZF5k4L_Yao

The left plot has no non-linearity, simple MSD-system

The right has some non-linearity: the frequency of the oscillation decreases with time

An extension of the pendulum equation.

Pendulum:

[https://en.wikipedia.org/wiki/Pendulum_\(mathematics\)](https://en.wikipedia.org/wiki/Pendulum_(mathematics))

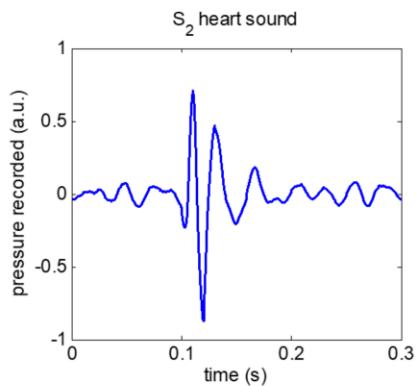
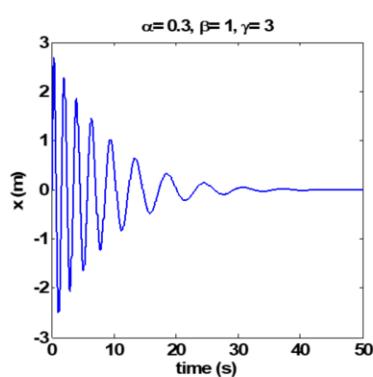
$dd\theta + g/l \sin(\theta) = 0$, linearization of $\sin(\theta)$ to first two terms: $\theta - \theta^3/3!$

Derivation of pendulum equation: force in direction of momentary movement is $mg \sin(\theta)$, so linear acceleration is $g \sin(\theta)$, and angular acceleration is obtained from dividing by length



Duffing oscillator

$$\ddot{x} + \alpha\dot{x} + \beta x + \gamma x^3 = 0$$

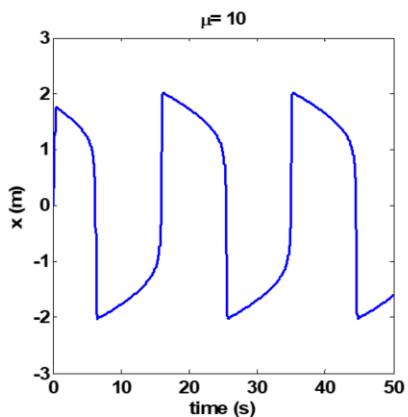


A heart sound can also be modeled by a duffing oscillator. Observe the decreasing frequency of the waveform.



Van der Pol oscillator

$$\ddot{x} - \mu(1-x^2)\dot{x} + x = 0$$



A Van der Pol oscillator can be turned into the FitzHug.Nagumo model.

Apply Liénard's transformation $y \leftarrow x - \frac{x^3}{3} - \frac{dx}{\mu}$
(https://en.wikipedia.org/wiki/Van_der_Pol_oscillator) to get:

$$\begin{aligned}\dot{x} &= -\mu \left(x - \frac{x^3}{3} - y \right) \\ \dot{y} &= \frac{1}{\mu} x\end{aligned}$$

Compare with FitzHugh-Nagumo (simplified Hodgkin-Huxley):

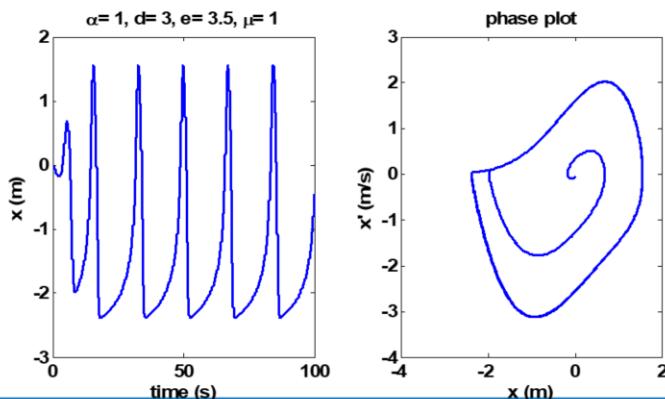
$$\begin{aligned}\dot{x} &= -\mu \left(x - \frac{x^3}{3} - y \right) + \mathbf{I}_{\text{ext}} \\ \dot{y} &= x + a - by\end{aligned}$$



Mix 'em up

$$x + \alpha(x^2 - \mu)\dot{x} + x(x+d)(x+e)/de = 0$$

$$\alpha, d, e, \mu > 0, \mu < d$$



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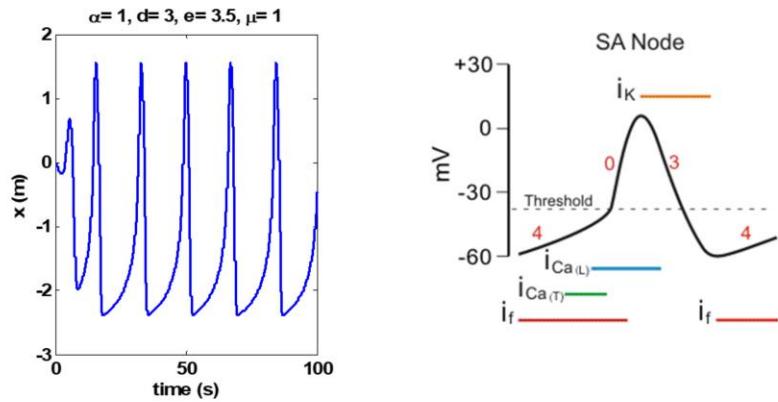
Grudziński and Żebrowski (2004): Modeling cardiac pacemakers with relaxation oscillators

A mixture of the Duffing and Van der Pol oscillator can be used to model the cardiac cycle.

The limit cycle is a stable path on the phase plot, representing a stable oscillation in the time domain, where the system is converging.



Why relevant? Cardiac pacemaker



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Grudziński and Żebrowski (2004): Modeling cardiac pacemakers with relaxation oscillators

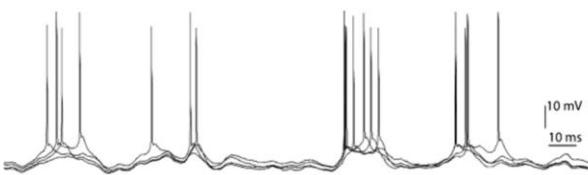
<http://www.cvphysiology.com/Arrhythmias/A004.htm>



Relaxation oscillators

In relaxation oscillators a long relaxation period – during which the system approaches an equilibrium point – is alternating with a short impulsive period in which the equilibrium point shifts.

- Electronic/mechanical relaxation oscillators
- Geysers
- Watermill
- Hodgkin-Huxley model

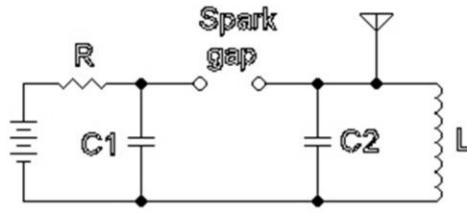


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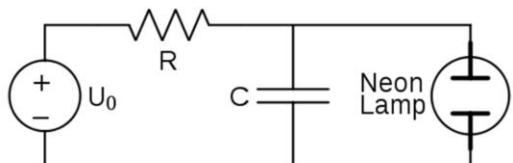
In [electronics](#) a **relaxation oscillator** is a [nonlinear electronic oscillator](#) circuit that produces a [nonsinusoidal](#) repetitive output signal, such as a [triangle wave](#) or [square wave](#).^{[1][2][3][4]} The circuit consists of a [feedback loop](#) containing a switching device such as a [transistor](#), [comparator](#), [relay](#),^[5] [op amp](#), or a [negative resistance](#) device like a [tunnel diode](#), that repetitively charges a [capacitor](#) or [inductor](#) through a resistance until it reaches a threshold level, then discharges it again.^{[4][6]}

In a geyser: ascending gas or vapor becomes trapped beneath the roof of a cavity that is laterally offset from the eruption conduit

The above discussed oscillators (duffing, van der pol), can act as a relaxation oscillator.



Spark-gap transmitter.



Pearson-Anson relaxation oscillator.

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See <https://www.youtube.com/watch?v=Z222teHxi00> for Pearson Anson relaxation oscillator

Spark-gap transmitter. From http://en.wikipedia.org/wiki/Spark-gap_transmitter

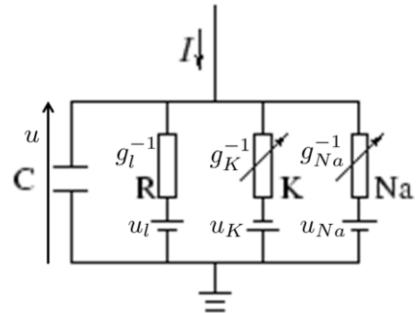
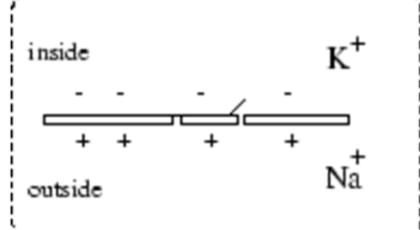
From http://en.wikipedia.org/wiki/Relaxation_oscillator

http://feng-shui-orenda.com/pics/upload/20100706065738_141%20%20water%20mill.JPG

Some more examples for relaxation oscillators. Electrical representation of a sparkgap transmitter and the switch of a neon lamp, and a water mill. The buckets on the wheel of the mill fill up until a threshold is reached, causing a turn of the wheel.



Hodgkin-Huxley



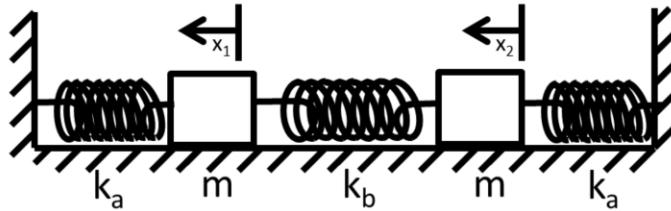
Electrical representation of the cell membrane for the Hodgkin-Huxley model.
Voltage-gated ion channels have electrical conductances that depend on both voltage and time.
A current source („filling the bucket”) excites the membrane, then sudden discharge by voltage gated channels

https://en.wikipedia.org/wiki/Hodgkin%20%93Huxley_model

<http://icwww.epfl.ch/~gerstner/SPNM/node14.html>



Coupled oscillators **after Feynman's LoP**



$$m\ddot{x}_1 + k_a x_1 + k_b(x_1 - x_2) = 0$$

$$m\ddot{x}_2 + k_a x_2 - k_b(x_1 - x_2) = 0$$

Two ways to view system:

1. transfer of energy from one body to another
2. superposition of two constant-amplitude motions

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In nature many times different oscillators are in reaction, they are 'coupled'. It results in a system of differential equations.

In matrix form the Laplace transform of the equation is:

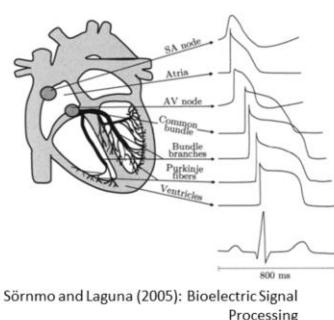
$$\begin{pmatrix} s^2 + \frac{k_a}{m} + \frac{k_b}{m} & -\frac{k_b}{m} \\ -\frac{k_b}{m} & s^2 + \frac{k_a}{m} + \frac{k_b}{m} \end{pmatrix} \begin{pmatrix} x_1 \\ x_2 \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \end{pmatrix}$$
$$\left(s^2 + \frac{k_a}{m} + \frac{k_b}{m} \right)^2 - \left(\frac{k_b}{m} \right)^2 = 0;$$
$$s = j \sqrt{\frac{k_a}{m}}, j \sqrt{\frac{k_a}{m} + \frac{2k_b}{m}}$$

Good demonstration of the modes and the coupling:

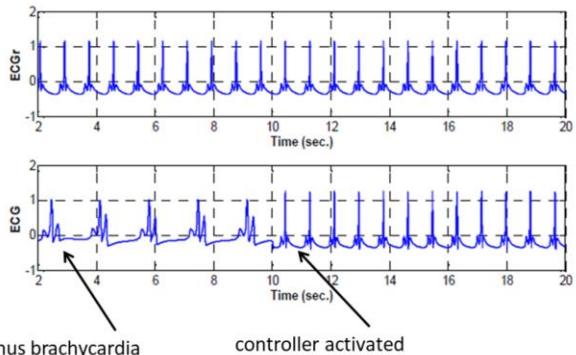
<https://www.youtube.com/watch?v=CjJBvDNxcE>



Why relevant? ECG (coupled action potentials)



Sörnmo and Laguna (2005): Bioelectric Signal Processing



Lopez et al. (?): Simulation and control of heart rhythm dynamics

Biomedical Signal Processing

Lopez et al models oscillator of sinoatrial (SA) node, atrioventricular node (AV), as well as third oscillator to represent propagation through ventricles.

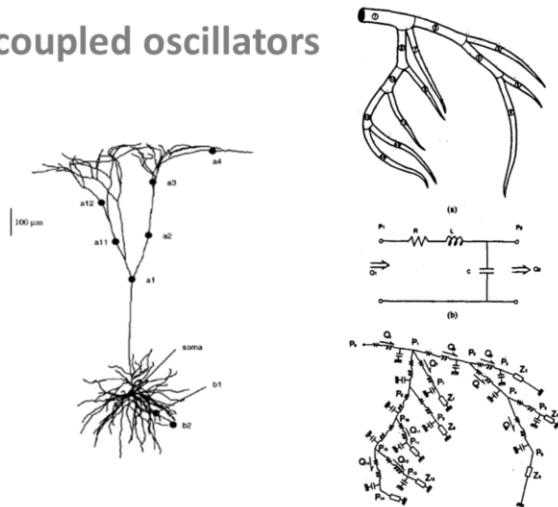
The rythm of the SA node synchronises the rest of the nodes. Ventricular flutter is a result of decoupling between the nodes.

cf Denis Noble from Oxford who did (as far as I know) first modelling of electronic circuitry of heart, as well as later work by Gari Clifford (incl synthetic ECG generator based on phase advance model)



Train of (branched) coupled oscillators

- Cable/1-D wave equation
- Why relevant?
 - propagation of action potentials
 - propagation of blood pressure



Biomedical Signal Processing

When modeling a neuronal network, the branching of the oscillation has to be considered, as well as the coupling between the neurons.

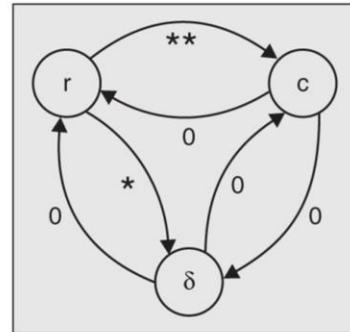
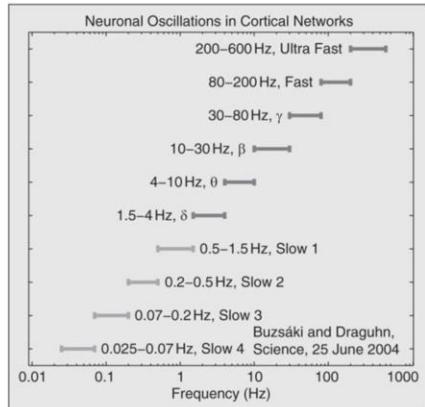
We can model the propagation as coupling between oscillators

Káli: Lecture notes on computational neuroscience

Rangayyan (2002): Biomedical Signal Analysis: A Case Study Approach



Train of (branched) coupled oscillators



Interactions between cardiac (C), respiratory (r), and slow-1 δ EEG (δ) oscillations in rats during deep anesthesia. The strengths of coupling are indicated by the number of stars.

Biomedical Signal Processing

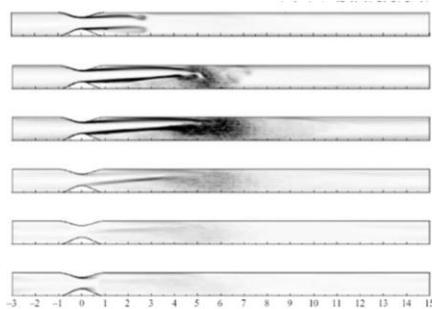
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2931755/>

„We conclude that interactions occur between the oscillatory processes, both within and between the cardiovascular and the neuronal systems. The strengths and directions of these interactions may be used, in principle, for characterization of the state of the organism as demonstrated here for the case of deep anesthesia.”

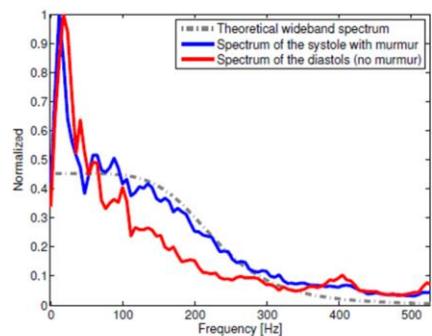


Turbulence as a coupled oscillation

- Example: sound of stenoses



Sequence of normalized averaged vorticity magnitude contours for pulsatile flow through the 75 % eccentric stenosis



The theoretical wideband spectrum is an estimation of the wall pressure fluctuations of a stenosed tube (matches the blue line)

Biomedical Signal Processing

Seeing a 'noise-like' structure in a plot does not mean that it is not useful information.

Turbulances are multiscale events, meaning that it has well separable structures at different scales (fractal patterns). Turbulances are difficult to model, a possibility is to couple large order oscillations to small order oscillations → multiscale event

An example is the stenoses when the vein is pinched at a point, as on the left image. It will lead to turbulence during systolic high pressure.

Nonetheless, the genesis of murmurs is still not completely understood. The mathematical theory behind this question is described by the laws of fluid dynamics, namely by the Navier-Stokes equations

In a pinched, stenosed tube the spectrum (fourier) will have a wideband structure, a quasi white-noise shape. The spectrum can be estimated by:

$$PSD(f) = \rho^2 D u^3 \left(\frac{d}{D}\right)^2 F_{n2} \left(\frac{fD}{u}\right)$$

$$F_{n2} \left(\frac{fD}{u}\right) = \frac{0.00208}{1+20\left(\frac{fD}{u}\right)^{5.3}}$$

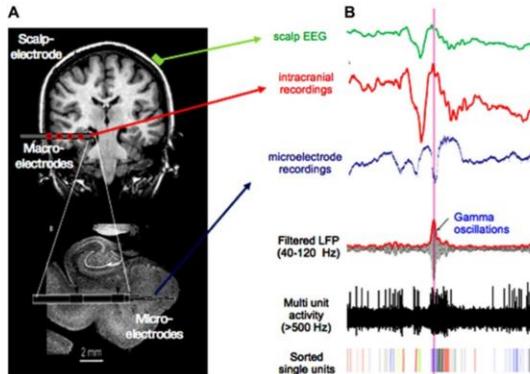
In the right image it can be seen, that the blue systolic heartsound spectrum really

has a wideband spectrum as estimated by the above equation (dashed line), while the diastolic (red) has a normal shape.

Balogh (2012) (top figure taken from Varghese et al., 2007)

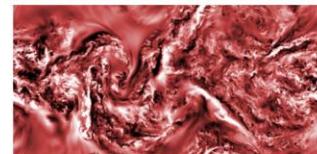


EEG as a multiscale event



„the interaction of different physical processes occurring at largely separated scales”

Both brain activity and turbulence is multiscale



Biomedical Signal Processing

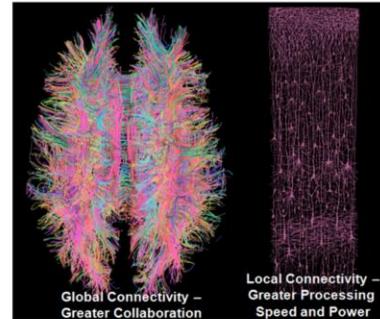
Another example for multiscale processes is the EEG signal. On the scale of the neurons bursts of 300-500Hz can be detected too, but on an EEG signal only lower frequencies, large-field synchronized oscillations can be detected, the single cell will be invisible (alpha-wave).

On the microscale you can see a neuron, on the macroscale you can experience cognition 😊



EEG – signal modifiers among scales

- Individual cells
- Excitation: inhibitory, excitatory + others
- Passive bandpass filtering
- Propagation
- Strong local connections
- Local population
- Small-world oscillations



Biomedical Signal Processing

Some properties of EEG signal genesis.

- The waves are generated by individual neuron → on large scale, however, these are invisible.

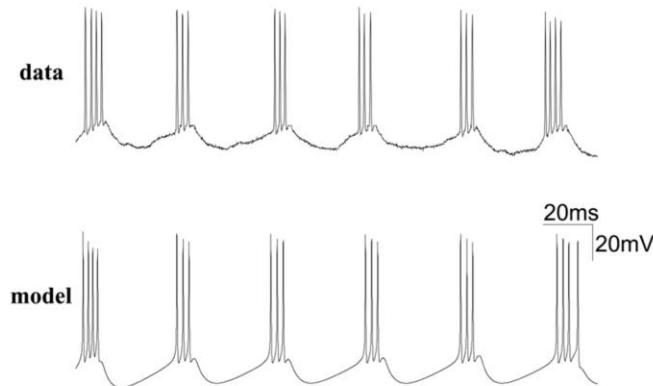
Buzsáki and Draguhn (2004): Neuronal Oscillations in Cortical Networks

Wang (2010): Neurophysiological and Computational Principles of Cortical

http://www.scholarpedia.org/article/Thalamocortical_oscillations



EEG rhythms – Individual cells



Biomedical Signal Processing

Diagram of voltage recording from neuron shows wide class of oscillatory behavior that can be achieved even by one cell in isolation.

Chattering cells (class of pyramidal neurons in neocortex) have intraburst spike rates of 300-500 Hz. To do with currents within cells.

„Bursts may provide a reliable signal for the rhythmicity to be transmitted across probabilistic and unreliable synapses”

(A) A chattering neuron recorded *in vivo* from the cat visual cortex shows rhythmic bursting

in the gamma frequency range. (B) A model chattering neuron endowed with a ping-pong interplay between two electrotonic compartments.

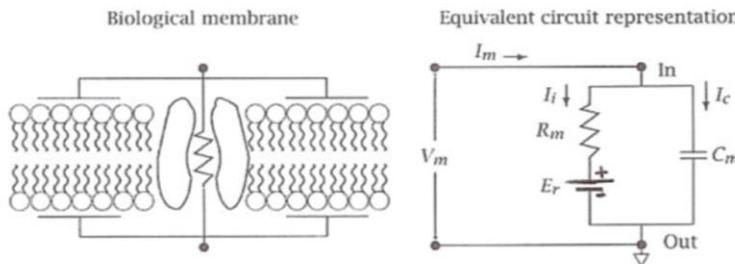
Buzsáki and Draguhn (2004): Neuronal Oscillations in Cortical Networks
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Filtering

On the membrane:

LPF - The charge separation makes the membrane a capacitor



Biomedical Signal Processing

On the membrane:

LPF: The charge separation makes the membrane a capacitor. The leaky channels let ions pass through the membrane, but have some resistance → the passive ion channels are RC circuits, LPFs.

HPF: the flow of cation current can oppose the membrane

hyperpolarization/depolarization in the subthreshold region. (There exist separate ion channels for this purpose, funny currents from prev. lecture) Its kinetics is very slow, filtering out subthreshold slow changes.

BPF: like the 5-10 Hz of thalamic cells

During propagation:

High frequencies will be absorbed in the tissue (like shortwave radiosignals in the air, or good resolution high frequency ultrasound in deeper tissues)

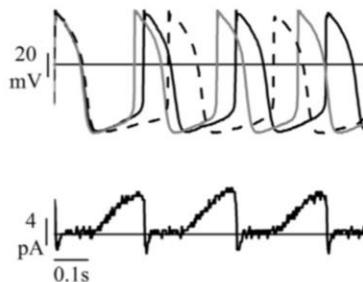
In the synapses a post synaptic potential will only be generated upon a sudden change in the potential, slow electrical waves from the local field potential will not result in the emptying of synaptic vesicles



Filtering

On the membrane:

HPF - slow kinetics of subthreshold cation currents



Biomedical Signal Processing

On the membrane:

LPF: The charge separation makes the membrane a capacitor. The leaky channels let ions pass through the membrane, but have some resistance → the passive ion channels are RC circuits, LPFs.

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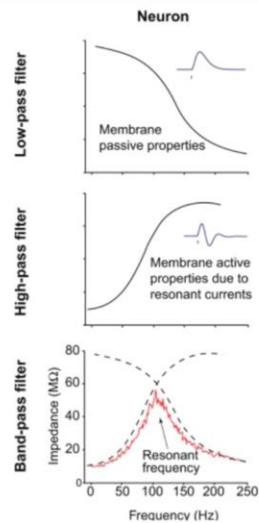
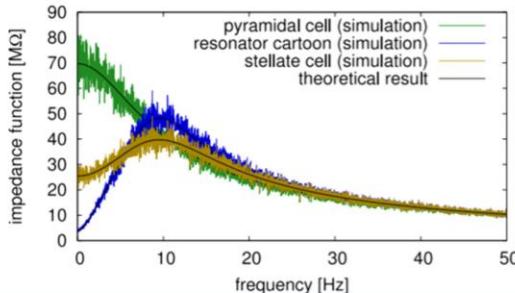
In the synapses a post synaptic potential will only be generated upon a sudden change in the potential, slow electrical waves from the local field potential will not result in the emptying of synaptic vesicles



Filtering

On the membrane:

BPF - If both is present in a cell, they will „resonate”, resulting in bandpass filtering.



Biomedical Signal Processing

On the membrane:

LPF: The charge separation makes the membrane a capacitor. The leaky channels let ions pass through the membrane, but have some resistance → the passive ion channels are RC circuits, LPFs.

HPF: the flow of cation current can oppose the membrane hyperpolarization/depolarization in the subthreshold region. (There exist separate ion channels for this purpose, funny currents from prev. lecture) Its kinetics is very slow, filtering out subthreshold slow changes.

BPF: like the 5-10 Hz of thalamic cells,

https://www.researchgate.net/figure/Principles-of-resonance-and-short-term-plasticity-of-synapses-A-Resonance-in-neurons_fig2_232236950

During propagation:

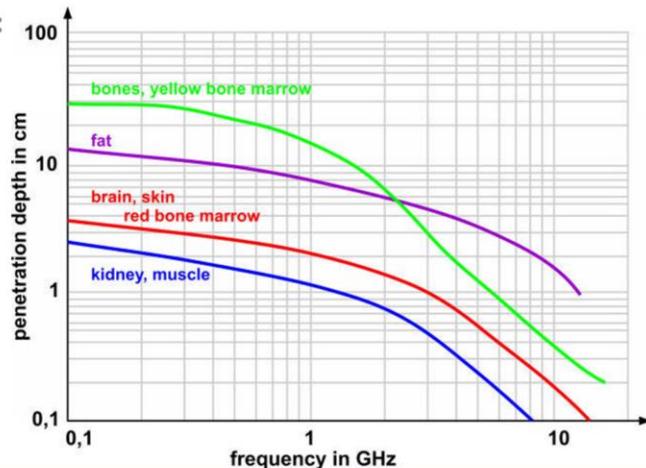
High frequencies will be absorbed in the tissue (like shortwave radiosignals in the air, or good resolution high frequency ultrasound in deeper tissues)

In the synapses a post synaptic potential will only be generated upon a sudden change in the potential, slow electrical waves from the local field potential will not result in the emptying of synaptic vesicles



Filtering

During propagation:
Tissue acts as LPF



On the membrane:

LPF: The charge separation makes the membrane a capacitor. The leaky channels let ions pass through the membrane, but have some resistivity → the passive ion channels are RC circuits, LPFs.

HPF: the flow of cation current can oppose the membrane

hyperpolarization/depolarization in the subthreshold region. (There exist separate ion channels for this purpose, funny currents from prev. lecture) Its kinetics is very slow, filtering out subthreshold slow changes.

BPF: like the 5-10 Hz of thalamic cells

During propagation:

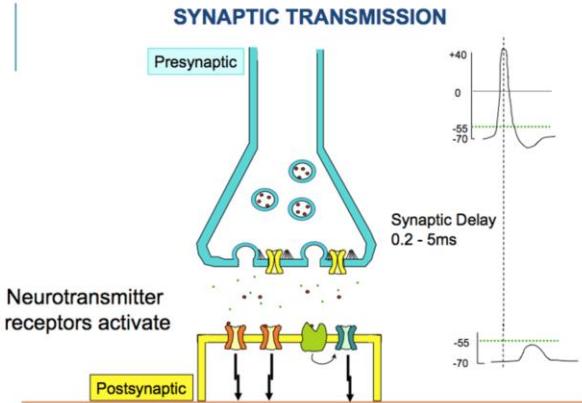
High frequencies will be absorbed in the tissue (like shortwave radiosignals in the air, or good resolution high frequency ultrasound in deeper tissues)

In the synapses a post synaptic potential will only be generated upon a sudden change in the potential, slow electrical waves from the local field potential will not result in the emptying of synaptic vesicles



Filtering

During propagation:
Synapses act as HPF



Biomedical Signal Processing

On the membrane:

LPF: The charge separation makes the membrane a capacitor. The leaky channels let ions pass through the membrane, but have some resistance → the passive ion channels are RC circuits, LPFs.

HPF: the flow of cation current can oppose the membrane

hyperpolarization/depolarization in the subthreshold region. (There exist separate ion channels for this purpose, funny currents from prev. lecture) Its kinetics is very slow, filtering out subthreshold slow changes.

BPF: like the 5-10 Hz of thalamic cells

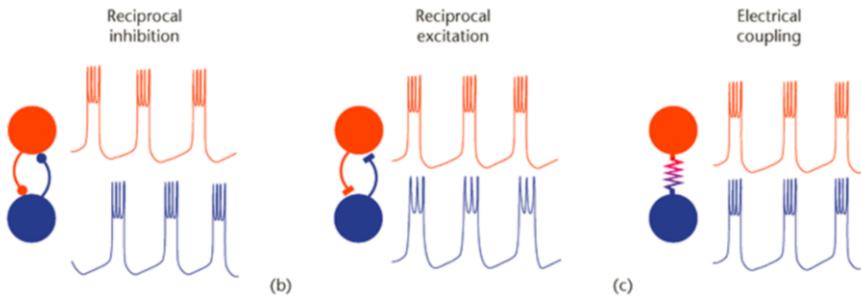
During propagation:

High frequencies will be absorbed in the tissue (like shortwave radiosignals in the air, or good resolution high frequency ultrasound in deeper tissues)

In the synapses a post synaptic potential will only be generated upon a sudden change in the potential, slow electrical waves from the local field potential will not result in the emptying of synaptic vesicles



EEG rhythms – Pair synchrony



Biomedical Signal Processing

Synchronization on a small scale

Some common models of two-cell networks. (a) Two cells that are reciprocally coupled by synaptic inhibition can produce out-of-phase oscillatory activity (half-centre oscillation). (b) Bottom: Two cells coupled with reciprocal excitation can oscillate in phase, but the action potentials are not necessarily time locked. (c) Electrical coupling is due to ion channels (gap junctions) that span the membranes of two cells and allow free flow of ions between the two. Electrically coupled cells typically demonstrate synchronous activity, which may be oscillatory even if the two cells are not rhythmically active in isolation.

<http://www.els.net/WileyCDA/ElsArticle/refId-a0000089.html>

Buzsáki and Draguhn (2004): Neuronal Oscillations in Cortical Networks

Wang (2010): Neurophysiological and Computational Principles of Cortical

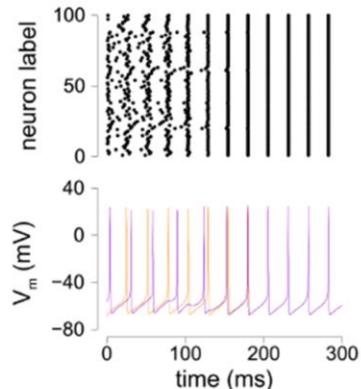
http://www.scholarpedia.org/article/Thalamocortical_oscillations



EEG rhythms – Local synchrony

- Kuramoto model
(http://en.wikipedia.org/wiki/Kuramoto_model)
it is a model for the behavior of a large set of coupled oscillators
- Note what happens when there is phase synchrony.

$$\frac{\partial \theta_i}{\partial t} = \omega_i + \frac{K}{N} \sum_{j=1}^N \sin(\theta_j - \theta_i), \quad i = 1 \dots N$$



Synchronization on a larger scale.

A group of neurons can also generate oscillatory activity. Through synaptic interactions the firing patterns of different neurons may become synchronized and the rhythmic changes in electric potential caused by their action potentials will add up (constructive interference). That is, synchronized firing patterns result in synchronized input into other cortical areas, which gives rise to large-amplitude oscillations of the local field potential. These large-scale oscillations can also be measured outside the scalp using electroencephalography (EEG) and magnetoencephalography (MEG). (Wikipedia, https://en.wikipedia.org/wiki/Neural_oscillation)

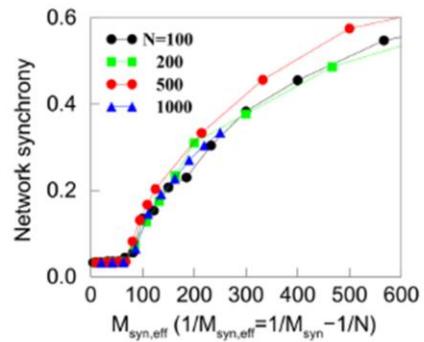
The Kuramoto model explains synchronization of larger populations. See the animation ,phase synchrony'.

Buzsáki and Draguhn (2004): Neuronal Oscillations in Cortical Networks
Wang (2010): Neurophysiological and Computational Principles of Cortical
http://www.scholarpedia.org/article/Thalamocortical_oscillations



Connectedness & Synchronization

- Mean number of connections needs to reach a threshold before synchrony occurs



When mean number of *effective* connections $M_{syn,eff}$ reaches a certain threshold, then synchrony occurs.

Note correction term $1/N$ to account for network size effect.

Network synchrony seems to be defined as average of cross-correlations:

<http://www.jneurosci.org/content/16/20/6402.long>

(Wang and Buzsáki: Gamma Oscillation by Synaptic Inhibition in a Hippocampal Interneuronal Network Model, JNeurosci 1996)

Buzsáki and Draguhn (2004): Neuronal Oscillations in Cortical Networks

Wang (2010): Neurophysiological and Computational Principles of Cortical

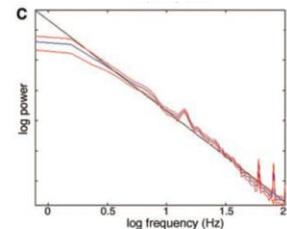
http://www.scholarpedia.org/article/Thalamocortical_oscillations



From micro- to macroscale

What happens with the signal between the micro- and macroscale ?

- the speed of neural communication is limited
- higher frequencies confined locally (filtering)
- Synchronization of activity through coupling (threshold)
- widespread slow oscillations modulate faster local events



The power density of EEG is inversely proportional to frequency in the cortex

Biomedical Signal Processing

Causes of small-world structure (few long range connections)

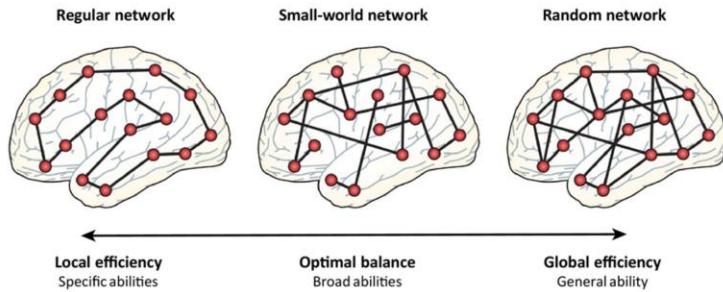
- limited speed of neuronal communication due to axon conduction and synaptic delays
- higher frequency oscillations confined locally, the period of oscillation is constrained by the size of the neuronal pool
- „The power density of EEG or local field potential is inversely proportional to frequency in the mammalian cortex, [...] perturbations at low frequencies can cause a cascade of energy dissipation at higher frequencies [...] widespread slow oscillations modulate faster local events”
- perturbations at low frequencies can cause a cascade of energy dissipation at higher frequencies (the modulation)

figure: Power spectrum of EEG from the right temporal lobe in a sleeping human subject. Subdural recording. Note the near-linear decrease of log power with increasing log frequency from 0.5 to 100 Hz.

Buzsáki and Draguhn (2004): Neuronal Oscillations in Cortical Networks
Wang (2010): Neurophysiological and Computational Principles of Cortical



EEG rhythms – Small-world



The local connections are strong within a small population, leading to a small-world structure. An optimally connected network will lead to local efficiency, meaning that communication among close neurons is cheap, but sending information to farther parts is expensive. However, fueling a random network, where communication among different areas is ideal, needs a lot of energy.



EEG rhythms – Small-world

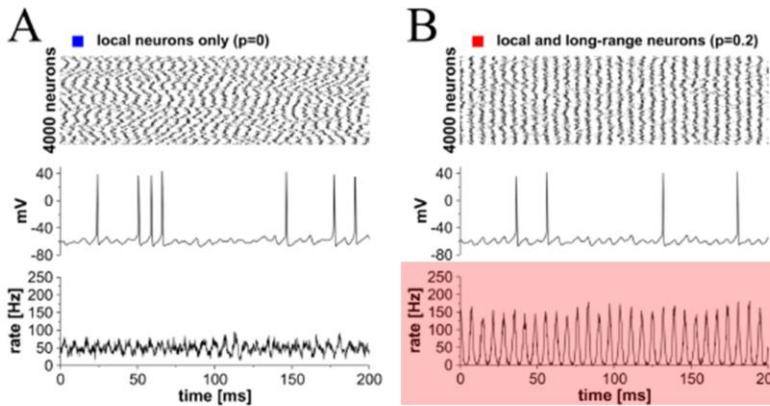


Figure 8. Trade-off between synchronization by long-range connections and minimization of the network wire cost

(A) Oscillations in a network of interneurons coupled by inhibitory synapses, with **local (Gaussian) connectivity** (spatial length is 20 neurons, in a network of 4000 neurons). The network is essentially asynchronous. Upper panel: spike raster of sample neurons; middle panel: the voltage trace of a representative neuron; lower panel: the population firing rate.

(B) Oscillations in a network **with local and long-range connections**. Neurons are connected with Gaussian distributed synapses (as in A) **but $p = 25\%$ of the synapses are reconnected with a power law distribution**. Note strong oscillatory rhythm. (Wang2010)

Buzsáki and Draguhn (2004): Neuronal Oscillations in Cortical Networks
Wang (2010): Neurophysiological and Computational Principles of Cortical Oscillations
http://www.scholarpedia.org/article/Thalamocortical_oscillations



EEG rhythms – Cognition

- „detection and amplification of weak signals”
- shutting out the environment
- temporal coordination
- „consolidation and combination of learned information
- „representation by phase information”

Biomedical Signal Processing

Buzsáki and Draguhn (2004): Neuronal Oscillations in Cortical Networks

Wang (2010): Neurophysiological and Computational Principles of Cortical

http://www.scholarpedia.org/article/Thalamocortical_oscillations

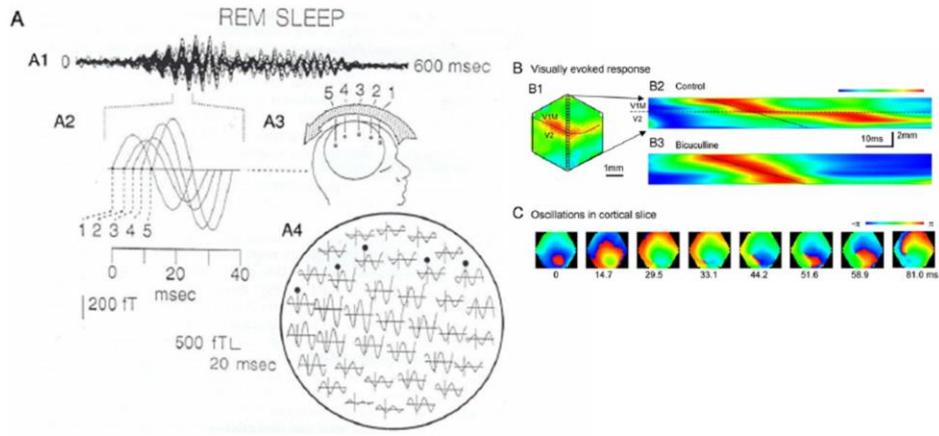
Why is oscillation important on the large scale?

- „detection and amplification of weak signals” (e.g. amplification of thalamocortical oscillations)
- shutting out the environment by the „increased commitment to an oscillatory network” : sleep spindles (7-14 Hz every 1-3 s)
- temporal coordination: <<„binding” of the various features into a coherent cognitive percept>> γ (30-80 Hz)
- „consolidation and combination of learned information” slow (<1 Hz)
- „representation by phase information” θ (4-8 Hz)

Also discussed at previous class ☺



EEG rhythms – Propagation



Biomedical Signal Processing

Sensory processing, decision making, motor action all engage selective neural populations.

Localized neural activity either remains spatially confined in time, or propagates as a wave

among neural pools that are spatially separated but engaged in the same computation or

behavioral state. Wave propagation has been observed on multiple spatial scales.

Figure 9. Propagating waves

(A) Rostrocaudal phase shift of 40 Hz oscillation during rapid eye movement (REM) sleep

as measured using MEG. (A1) shows synchronous activation in 37 channels during a 600 ms

period. The oscillation in the left part of trace A1 has been expanded in trace A2 to show

five different recording sites over the head. The five recording sites of trace (A2) are displayed in diagram (A3) for a single epoch, to illustrate the phase shift for the different 40

Hz waves during REM sleep. The direction of the phase shift is illustrated by an arrow above diagram (A3). The actual traces and their sites of recordings for a single epoch are

shown in diagram (A4) for all 37 channels (ft: femtotesla). (B) Voltage-sensitive dye

imaging of propagating waves in rat visual cortex *in vivo*. A rat visual cortex was imaged

through a cranial window. (B1) A snapshot of visually evoked cortical activity propagating

Buzsáki and Draguhn (2004): Neuronal Oscillations in Cortical Networks
Wang (2010): Neurophysiological and Computational Principles of Cortical
http://www.scholarpedia.org/article/Thalamocortical_oscillations



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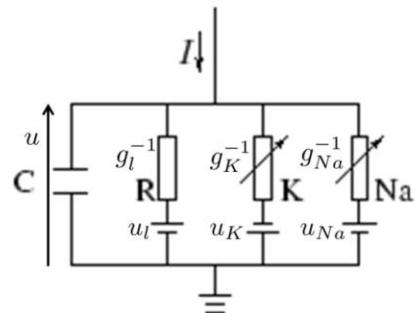
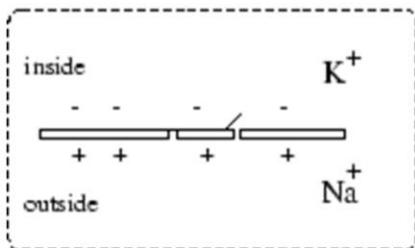
Biomedical Signal Processing



EXTRA MATERIAL



Hodgkin-Huxley



$$I(t) = I_C(t) + \sum_k I_k(t)$$

$$C \frac{du}{dt} = - \sum_k I_k(t) + I(t) = -g_l(u - u_l) - g_K(u - u_K) - g_{Na}(u - u_{Na}) + I(t)$$

Biomedical Signal Processing

Voltage-gated ion channels have electrical conductances that depend on both voltage and time.

A current source („filling the bucket”) excites the membrane, then sudden discharge by voltage gated channels

https://en.wikipedia.org/wiki/Hodgkin%20%93Huxley_model

<http://icwww.epfl.ch/~gerstner/SPNM/node14.html>



Hodgkin-Huxley

$$C \frac{du}{dt} = - \sum_k I_k(t) + I(t) = -g_l(u - u_l) - g_K(u - u_K) - g_{Na}(u - u_{Na}) + I(t)$$

$$g_l = \text{constant}$$

$$g_K = \bar{g}_K n^4$$

$$g_{Na} = \bar{g}_{Na} m^4 h$$

$$\frac{dn}{dt} = \alpha_n(1 - n) - \beta_n n$$

$$\frac{dm}{dt} = \alpha_m(1 - m) - \beta_m m$$

$$\frac{dh}{dt} = \alpha_h(1 - h) - \beta_h h$$

