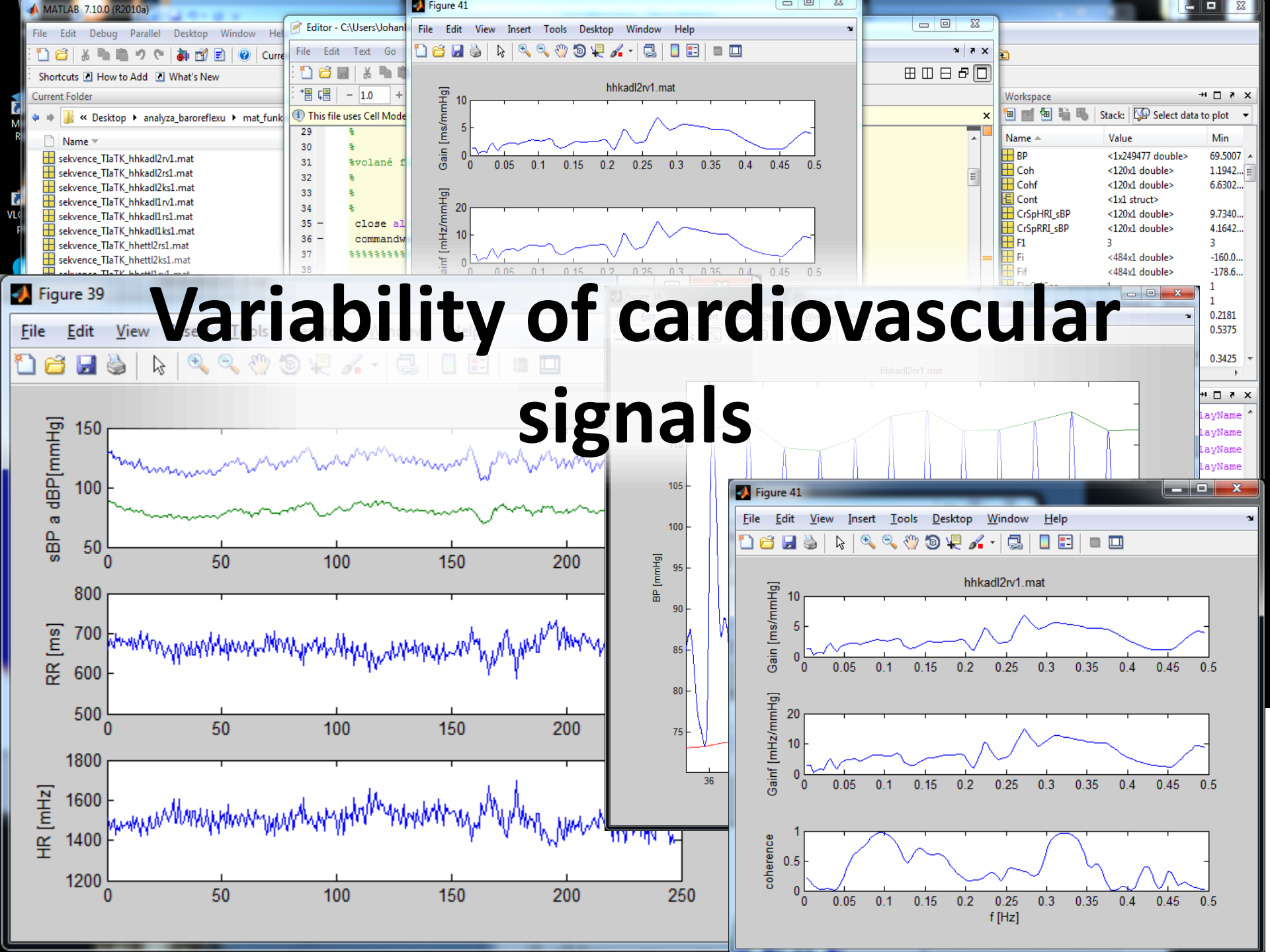


Variability of cardiovascular signals



Cardiovascular signal variability

- **Cardiovascular signals (C-V signals)**

- Easy to measure

- EGG: RR intervals, heart rate - HR ($1/RR$)

- Blood pressure: systolic (SBP), diastolic (DBP), mean (MAP), pulse pressure (PP)

- Difficult to measure directly (bioimpedance method), can be evaluated indirectly from blood pressure wave (Windkessel model)

- Stroke volume (SV), cardiac output (CO), total peripheral resistance (TPR)

- Very difficult to measure directly (invasive measurement)

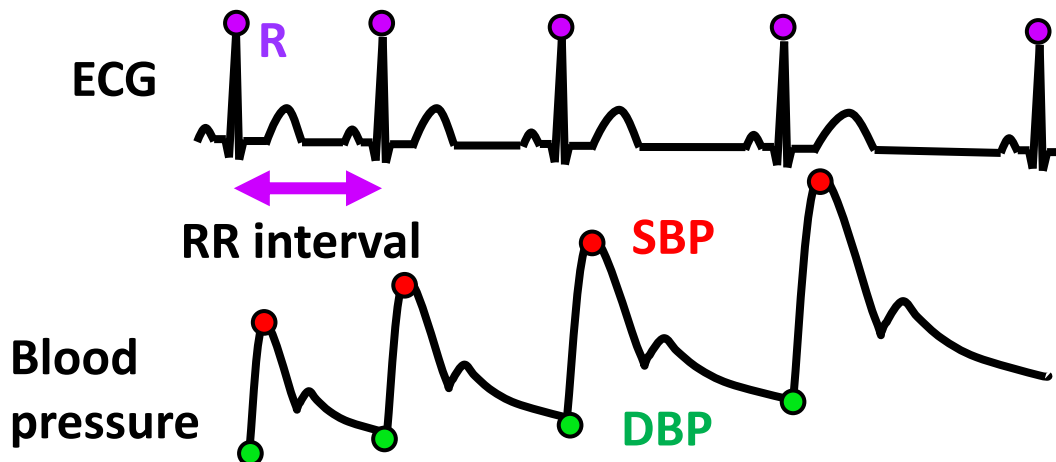
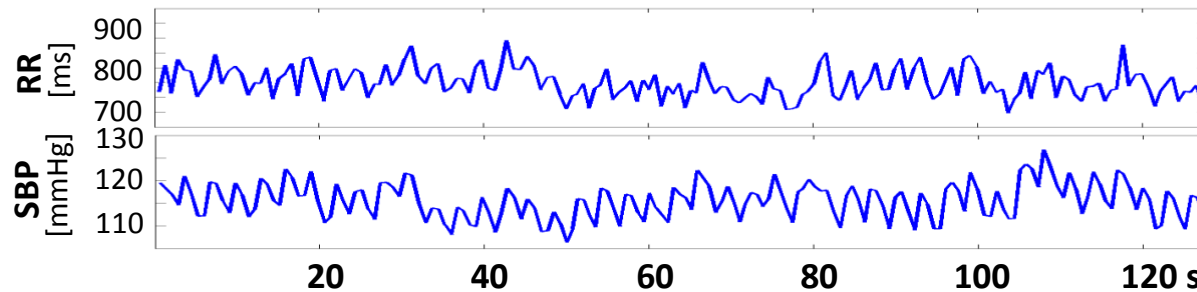
- Blood flow and pressure in various places of vessels



Signal: time series

Beat to beat (for example 5 minutes)

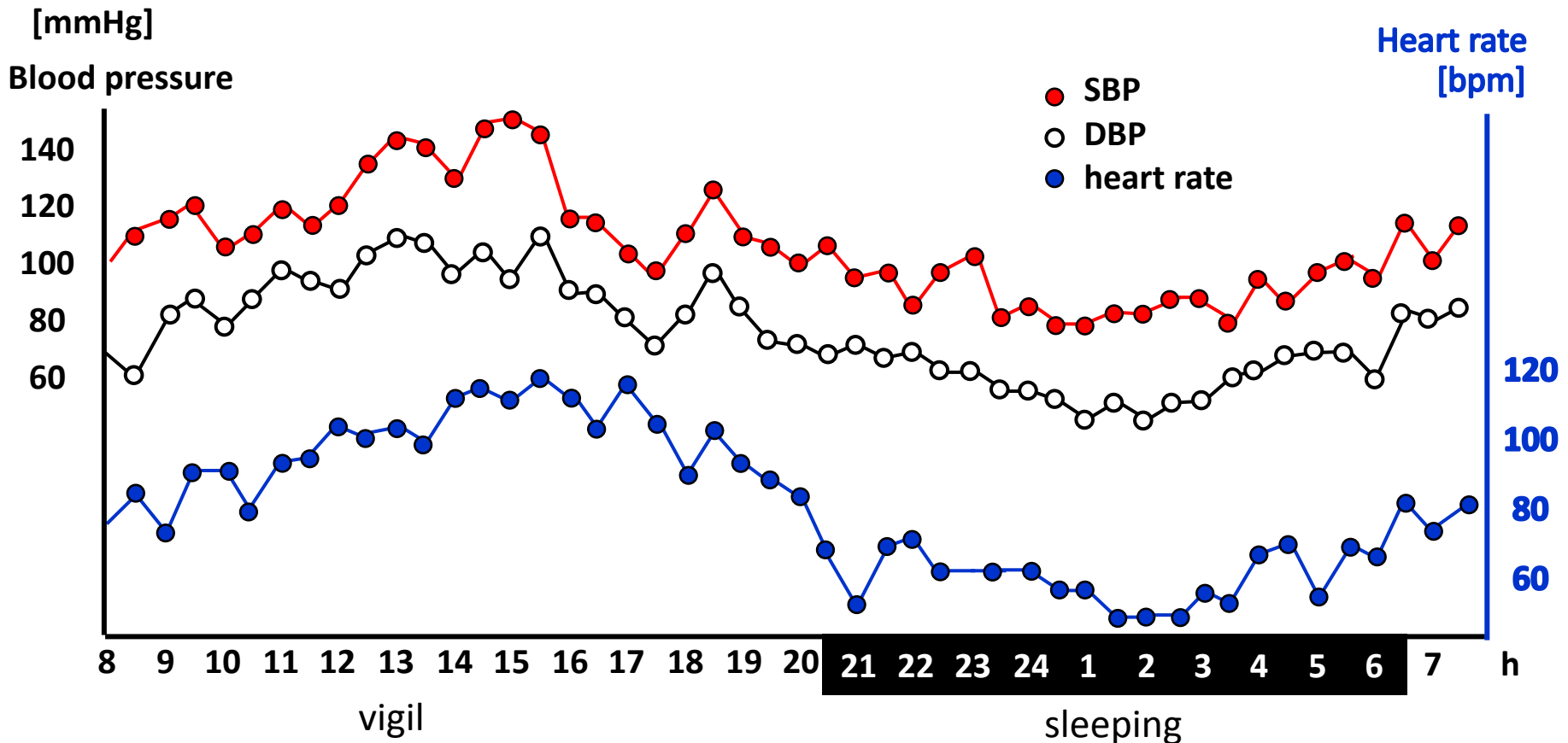
- RR interval: 805, 820, 815, 817, 822, 816,..... ms
- Hear rate: 70, 73, 68, 65, 67, 71,..... bpm
- Systolic blood pressure: 115, 117, 120, 116, 121, 119,..... mmHg



Signal: time series

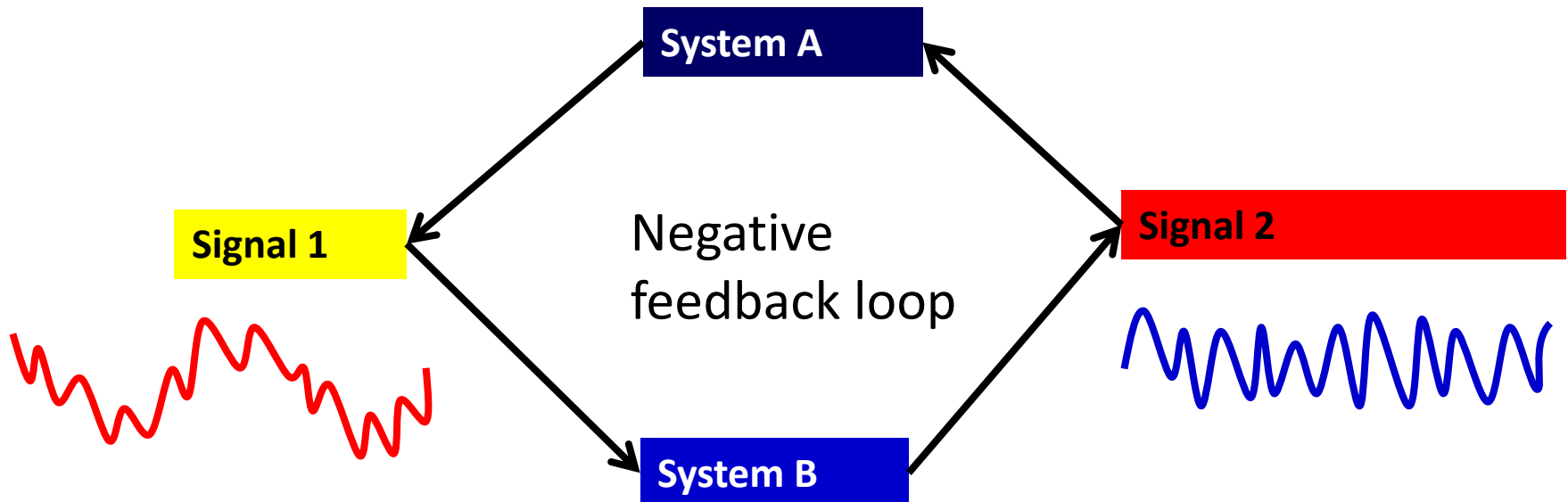
Every 15 minutes

- 24-hour blood pressure measurement, ECG Holter



Variability of cardiovascular signals

- Cardiovascular system is regulated by negative feedback
- Negative feedback forms oscillations in the signals – the longer feedback loop, the slower oscillations
- Analysis of oscillations in the C-V signals contains information about regulatory mechanism



Brief introduction in theory of systems

$$A(z) = \begin{pmatrix} A_{11}(z) & A_{12}(z) \\ A_{21}(z) & A_{22}(z) \end{pmatrix} = \sum_{k=0}^p A_k z^{-k}$$

$$= \begin{pmatrix} a_{11,1}z^{-1} + a_{11,2}z^{-2} + \dots + a_{11,n}z^{-p} & a_{12,1}z^{-1} + a_{12,2}z^{-2} + \dots + a_{12,n}z^{-p} \\ a_{21,0} + a_{21,1}z^{-1} + a_{21,2}z^{-2} + \dots + a_{21,n}z^{-p} & a_{22,1}z^{-1} + a_{22,2}z^{-2} + \dots + a_{22,n}z^{-p} \end{pmatrix}$$

$$H(f) = (I - A(z))^{-1} = \begin{pmatrix} H_{11}(f) & H_{12}(f) \\ H_{21}(f) & H_{22}(f) \end{pmatrix}$$

$$S(f) = H(z) \cdot \Lambda \cdot H'(z^{-1}) = \begin{pmatrix} S_{11} & S_{12} \\ S_{21} & S_{22} \end{pmatrix},$$

$$\Lambda = \begin{pmatrix} \lambda_1^2 & 0 \\ 0 & \lambda_2^2 \end{pmatrix}$$

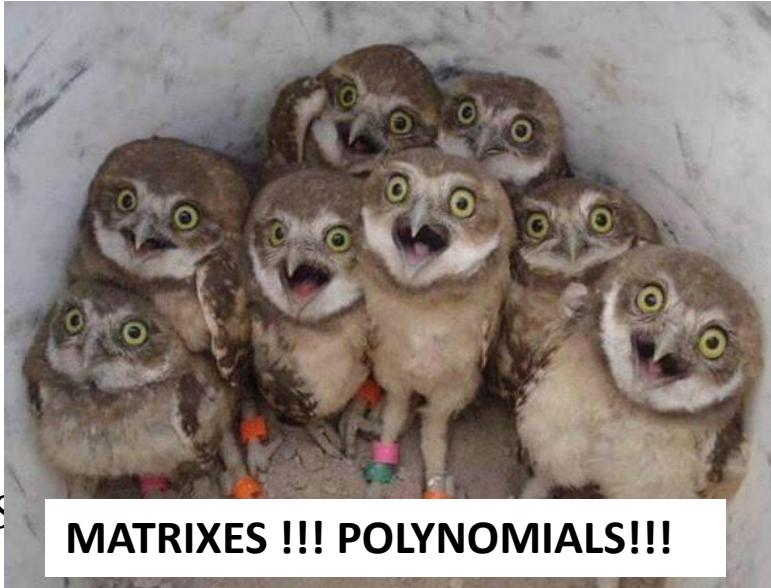
$$S_{11}(f) = |\Delta(z)|^2 \cdot [|1 - A_{22}(z)|^2 \lambda_1^2 + |A_{12}(z)|^2 \lambda_2^2],$$

$$S_{22}(f) = |\Delta(z)|^2 \cdot [|A_{21}(z)|^2 \lambda_1^2 + |1 - A_{11}(z)|^2 \lambda_2^2]$$

$$S_{12}(f) = |\Delta(z)|^2 \cdot [(1 - A_{22}(z))A_{21}(z^{-1})\lambda_1^2 + (1 - A_{11}(z^{-1}))A_{12}(z)\lambda_2^2],$$

$$\text{kde } \Delta(z) = ((1 - A_{11}(z))(1 - A_{22}(z)) - A_{12}(z)A_{21}(z))^{-1}.$$

Brief introduction in theory of systems



MATRIXES !!! POLYNOMIALS!!!

$$\Lambda = \begin{pmatrix} \lambda_1^2 & 0 \\ 0 & \lambda_2^2 \end{pmatrix}$$

$$\begin{pmatrix} a_{11,n}z^{-p} & a_{12,1}z^{-1} + a_{12,2}z^{-2} + \dots + a_{12,n}z^{-p} \\ a_{21,n}z^{-p} & a_{22,1}z^{-1} + a_{22,2}z^{-2} + \dots + a_{22,n}z^{-p} \end{pmatrix}$$

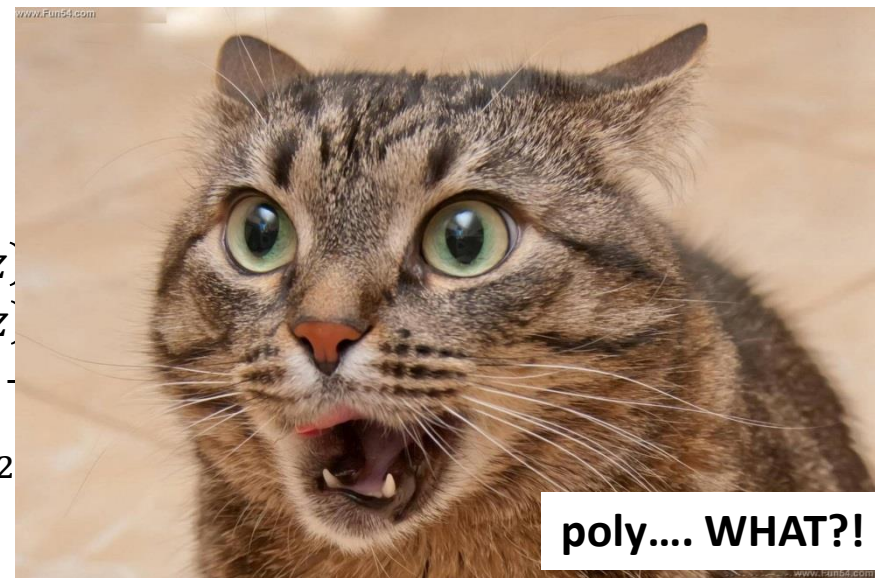
$$^{-1} = \begin{pmatrix} H_{11}(f) & H_{12}(f) \\ H_{21}(f) & H_{22}(f) \end{pmatrix}$$

$$S_{11}(f) = |\Delta(z)|^2 \cdot [|1 - A_{22}(z)|^2 \lambda_1^2 + |A_{12}(z)|^2 \lambda_2^2]$$

$$S_{22}(f) = |\Delta(z)|^2 \cdot [|A_{21}(z)|^2 \lambda_1^2 + |1 - A_{11}(z)|^2 \lambda_2^2]$$

$$S_{12}(f) = |\Delta(z)|^2 \cdot [(1 - A_{22}(z))A_{21}(z^{-1})\lambda_1^2 - (1 - A_{11}(z))A_{12}(z)\lambda_2^2]$$

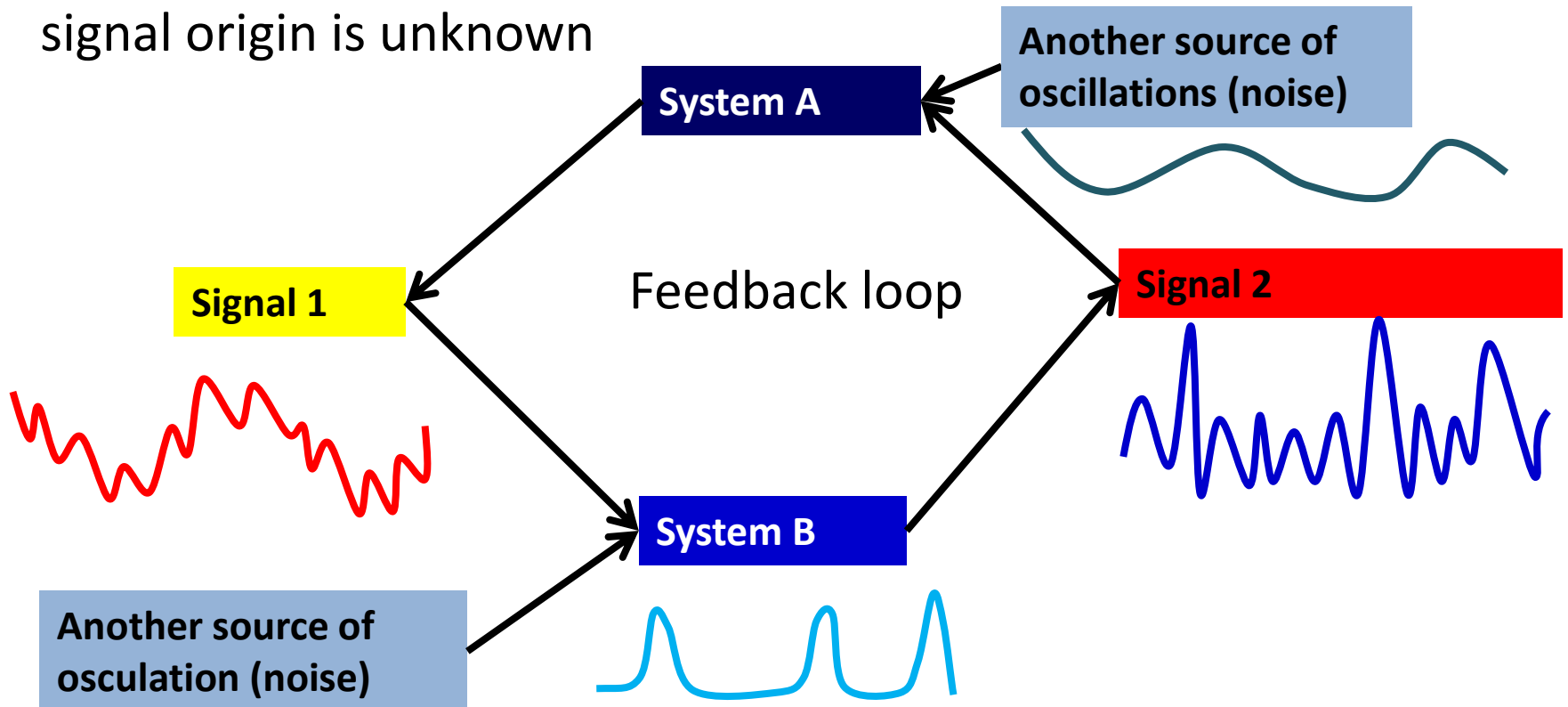
kde $\Delta(z) = ((1 - A_{11}(z))(1 - A_{22}(z)) - A_{12}(z)A_{21}(z))$



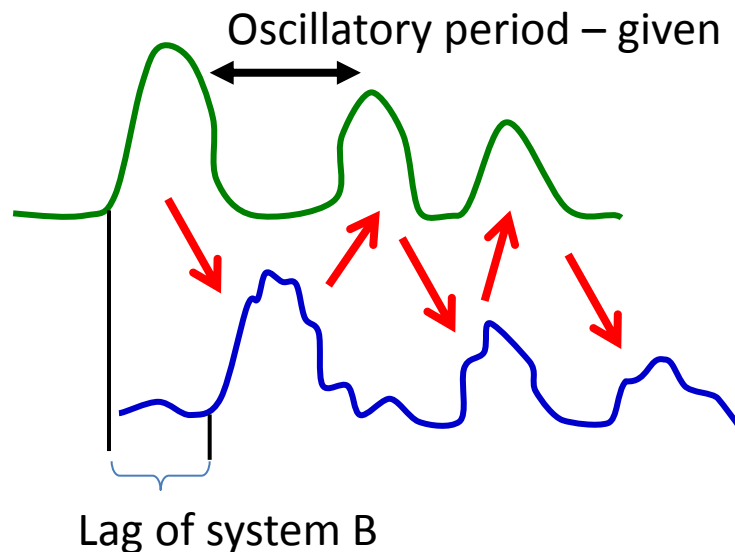
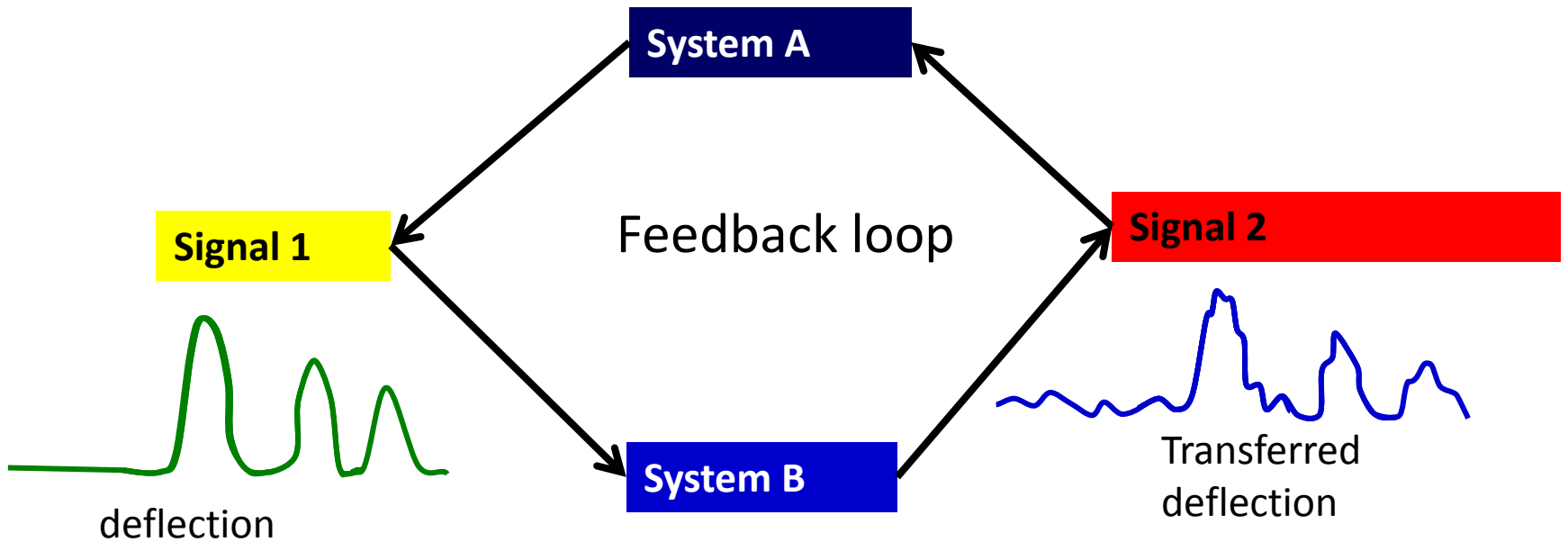
poly.... WHAT?!

Brief introduction in theory of systems

- Biological systems are complex – more than one input, system setting and outputs can change
- System transforms input signal into output signal – analysis of input/output signals helps to understand the sys
- noise: another input signal – we do not care about signal and/or signal origin is unknown



Source of oscillations

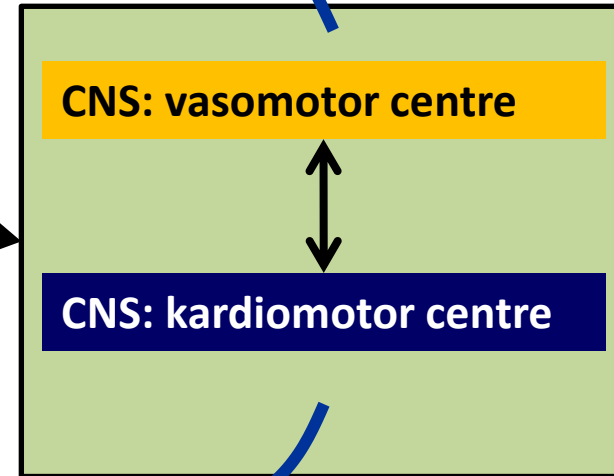
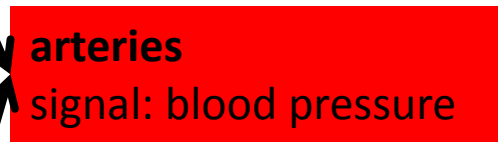
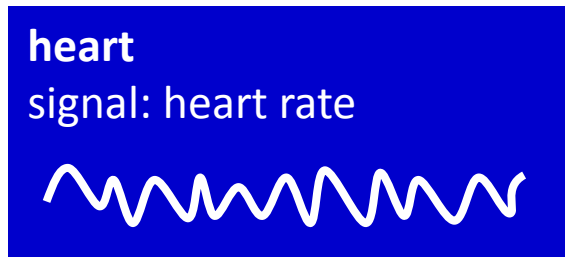


Frequency of oscillation = $1/\text{period}$

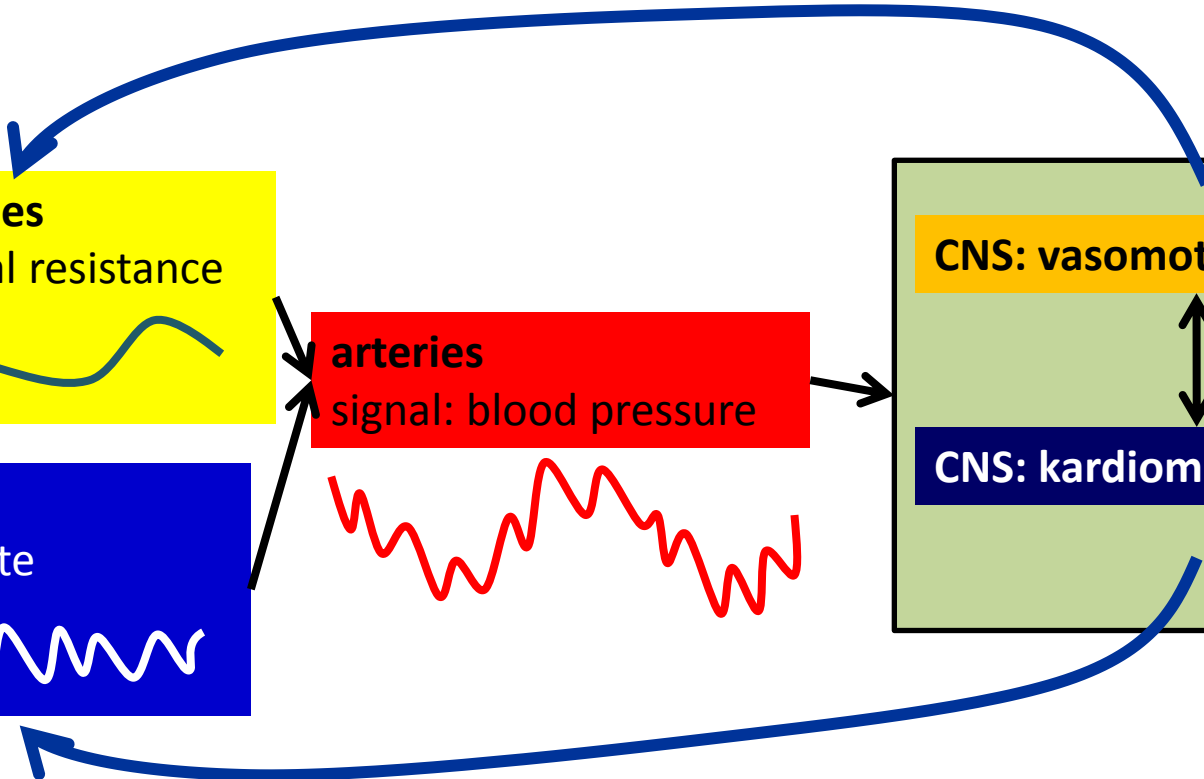
→ **frequency (spectral) analysis**
contain information about system

Feedback loop - baroreflex

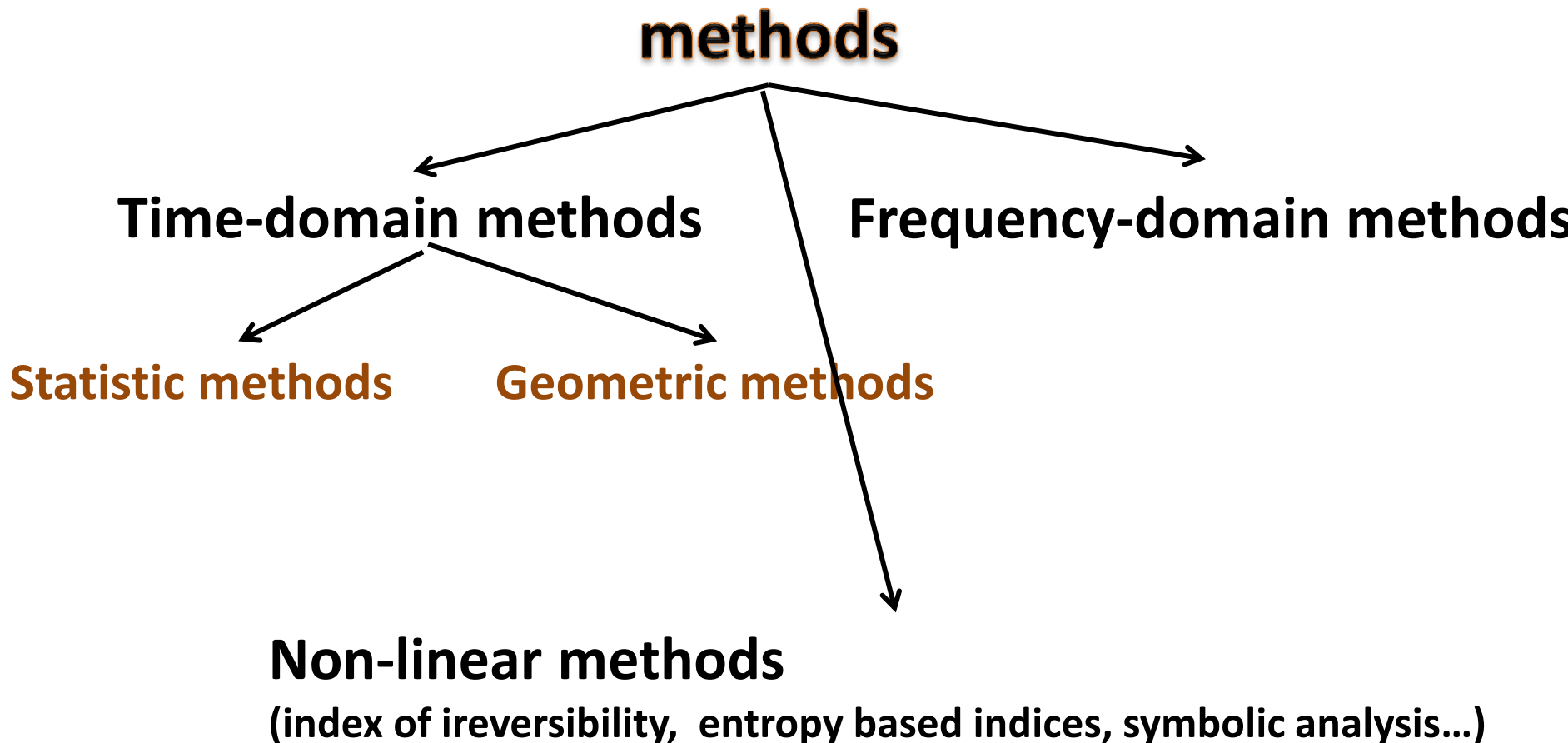
Sympathetic efferent pathways



Parasympathetic efferent pathways



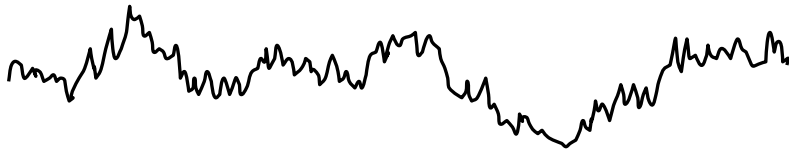
Methods of the variability assessment



Statistic methods

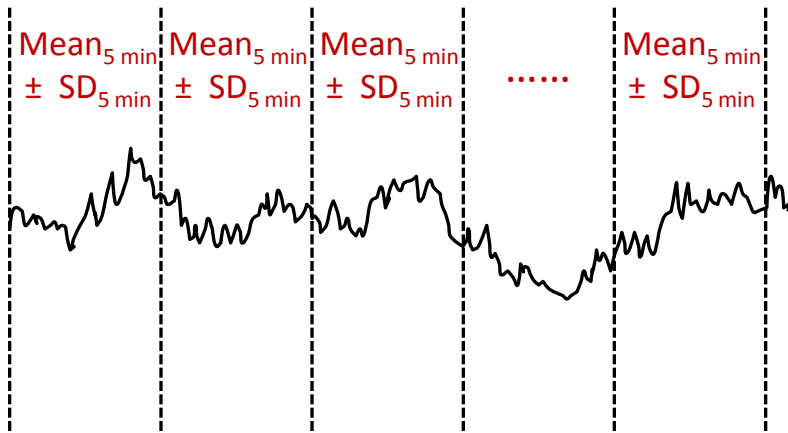
(Variations on Standard Deviation)

24-hour record of RR intervals



$\text{Mean}_{24\text{-h}} \pm \text{SD}_{24\text{-h}}$

24-hour record of RR intervals divided into 5-min segments ($\text{Mean}_{5\text{ min}} \pm \text{SD}_{5\text{ min}}$)



$\text{SD}_{24\text{-h}}$ counted from all RR-intervals in 24 hours

SDRR

$\text{SD}_{24\text{-h}}$ counted from all normal RR-intervals in 24 hours

SDNN

SD counted from all $\text{Mean}_{5\text{ min}}$

SDANN

SD counted from all $\text{SD}_{5\text{ min}}$

SDANNIDX

Geometric methods

RR (ms)

840 **x**

828 **y x**

760 **y x**

756 **y x**

808 **y x**

856 **y**

768

780

808

756

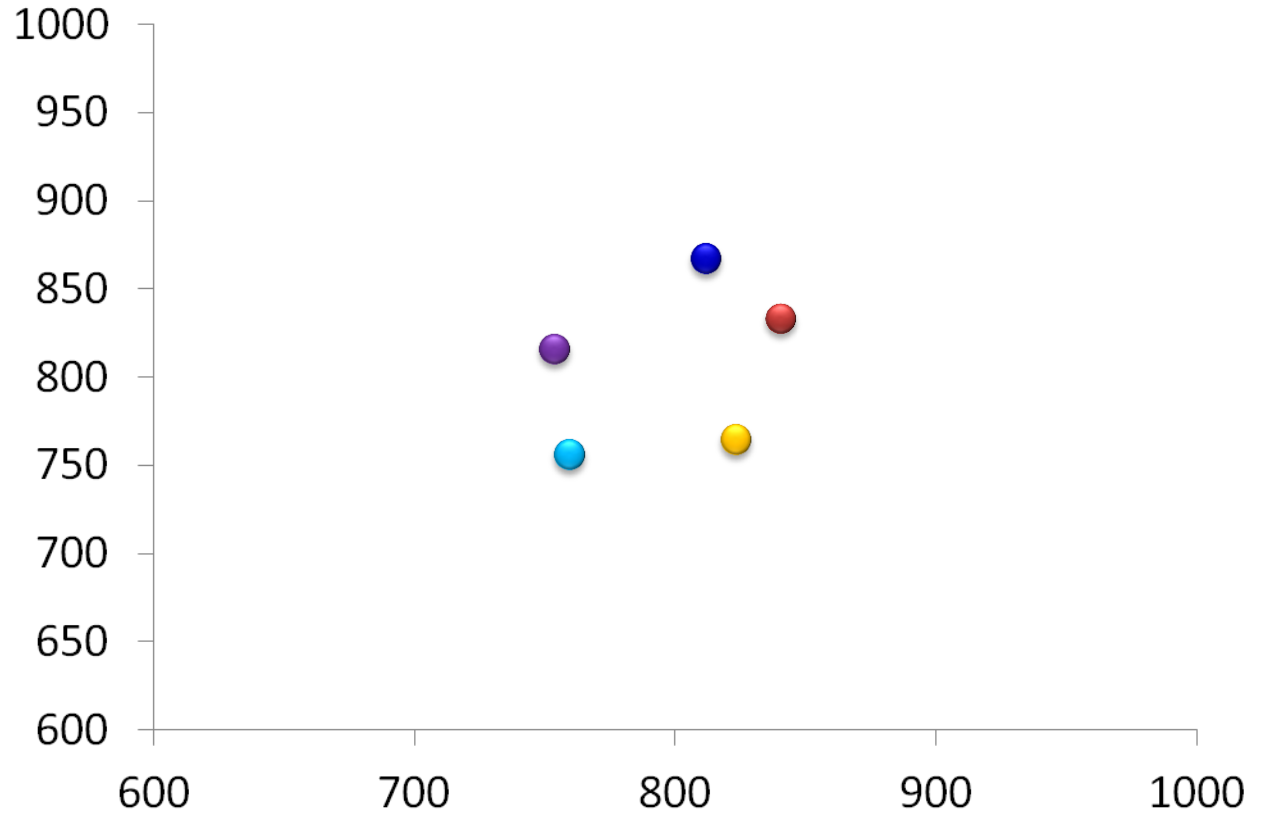
708

728

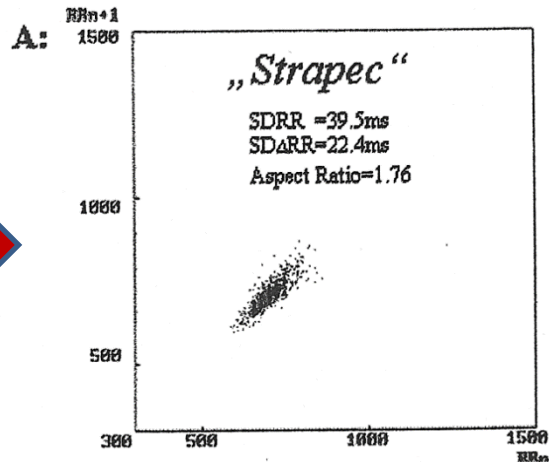
756

732

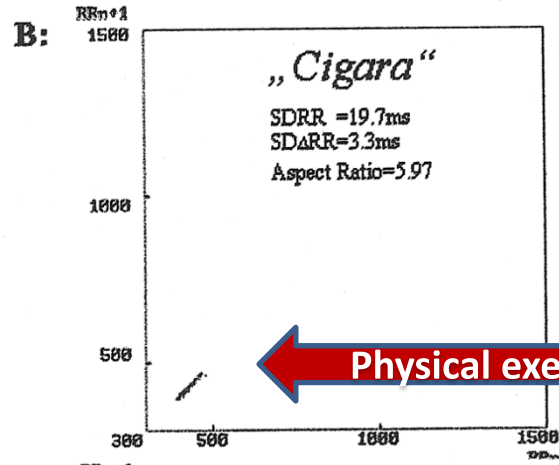
708



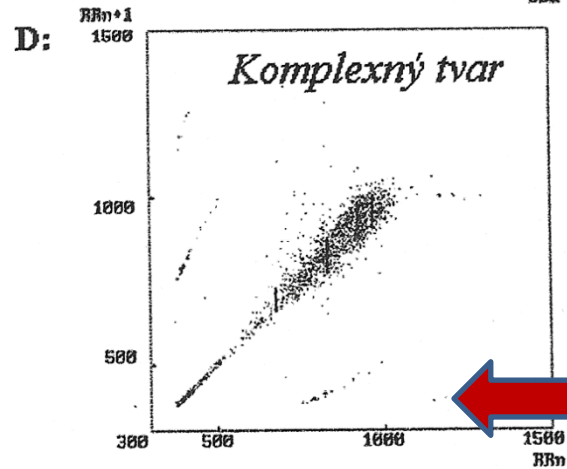
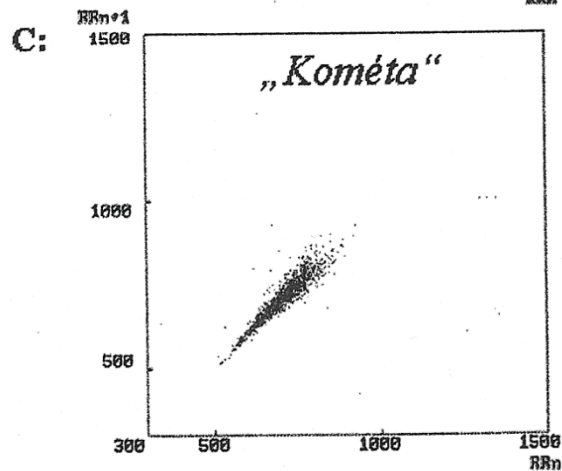
Geometric methods



Normal pattern



Physical exercise



Ectopic beats

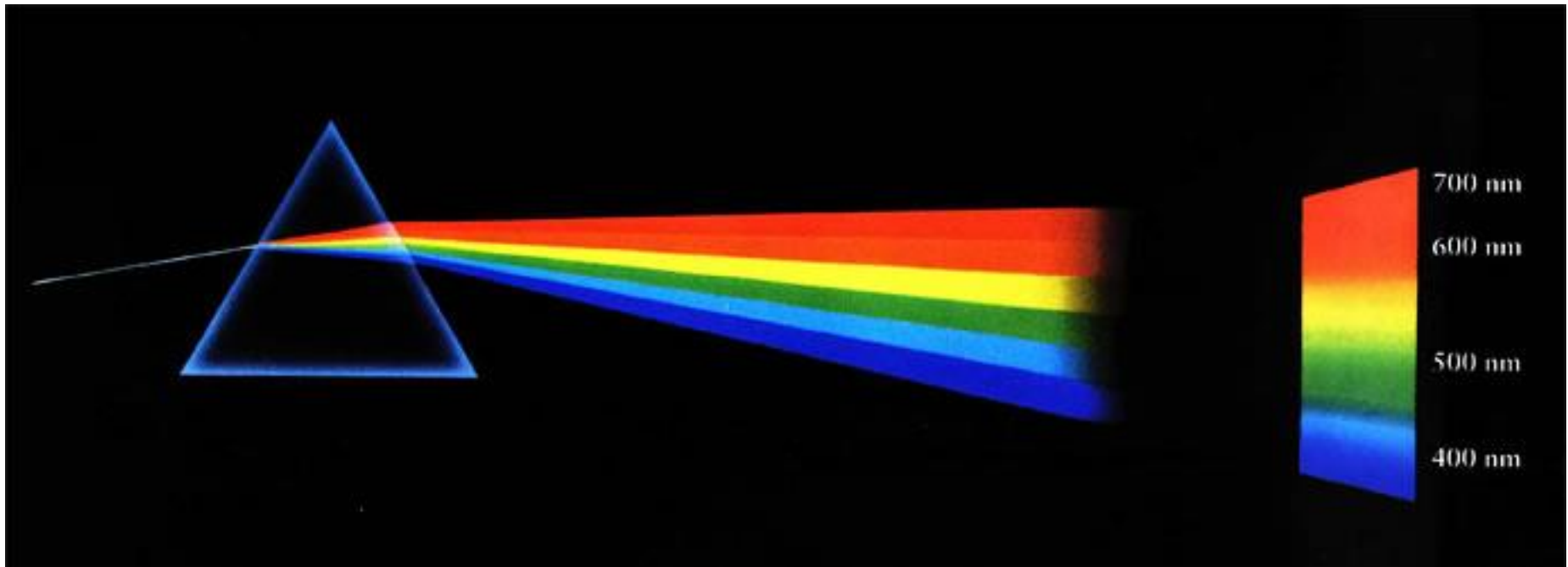
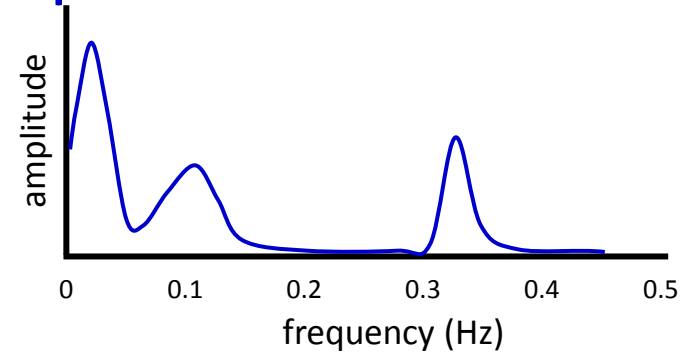
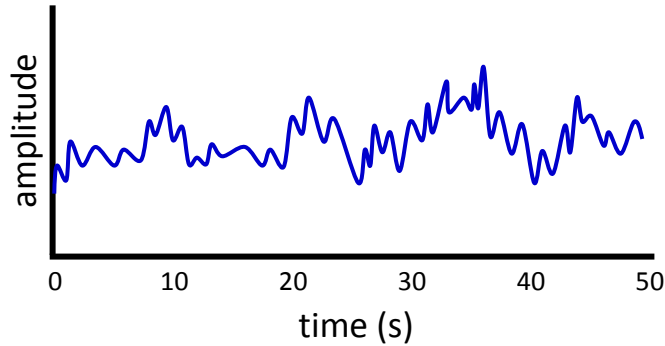
Frequency domain methods – spectral analysis

Time series
Signal in time domain



Spectrum
Signal in frequency domain

Signal is decomposed in individual frequencies



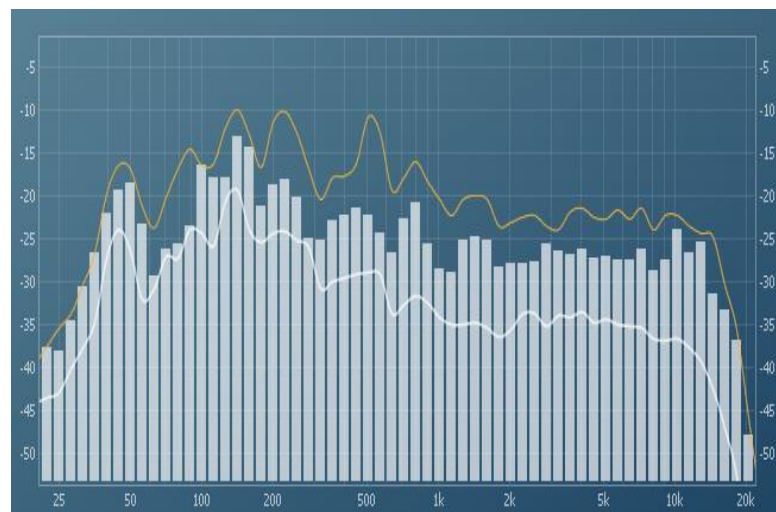
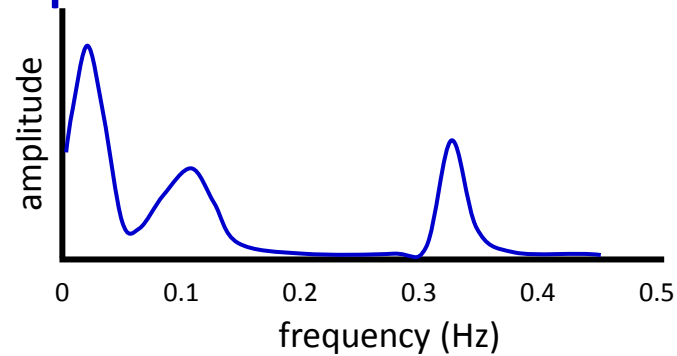
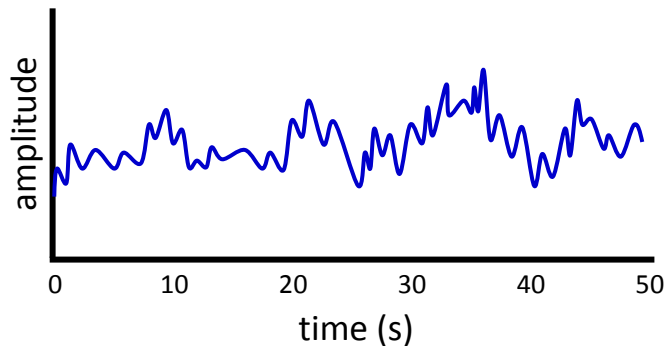
Frequency domain methods – spectral analysis

Time series
Signal in time domain



Spectrum
Signal in frequency domain

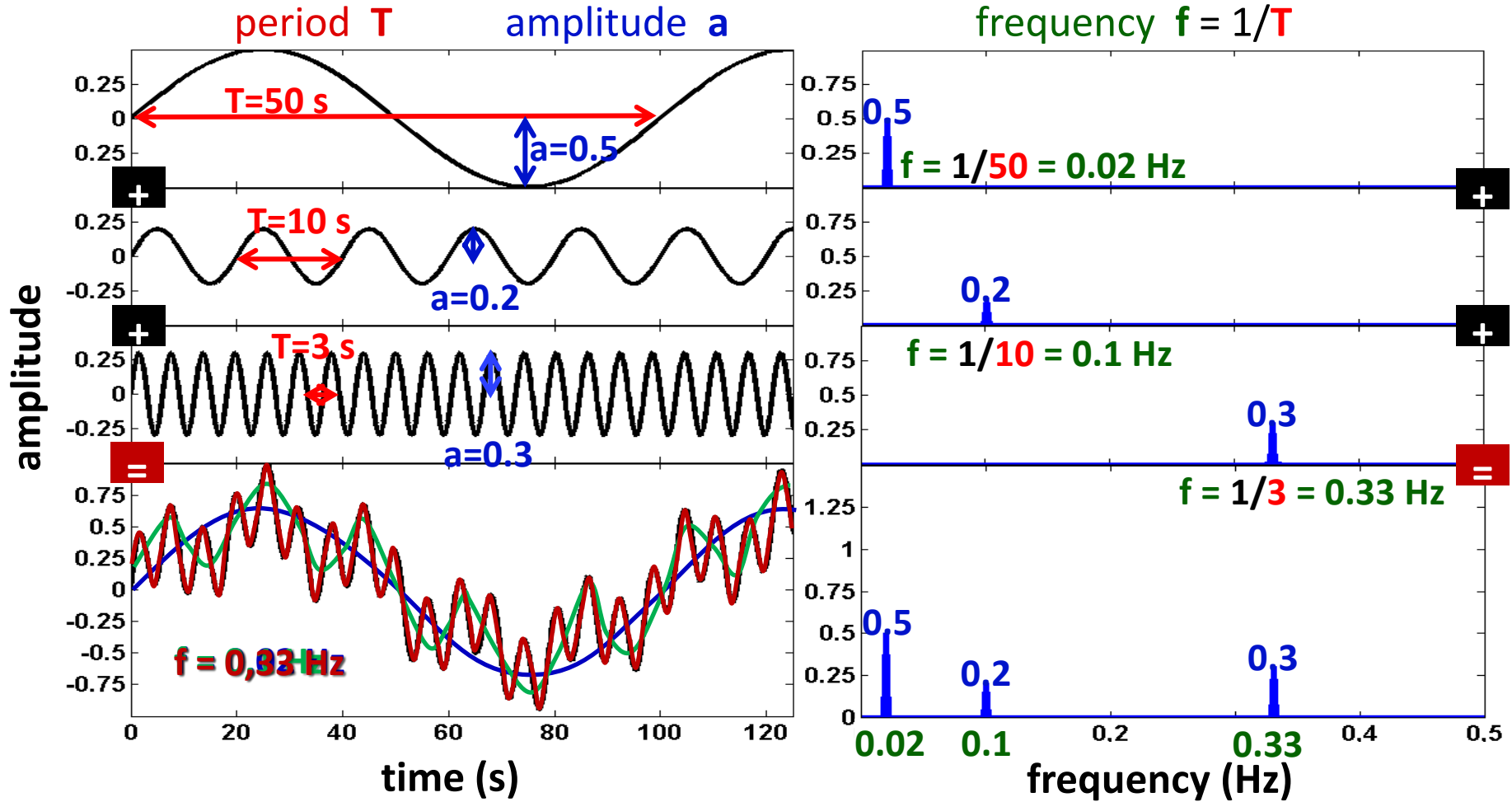
Signal is decomposed in individual frequencies



How the spectrum is formed?

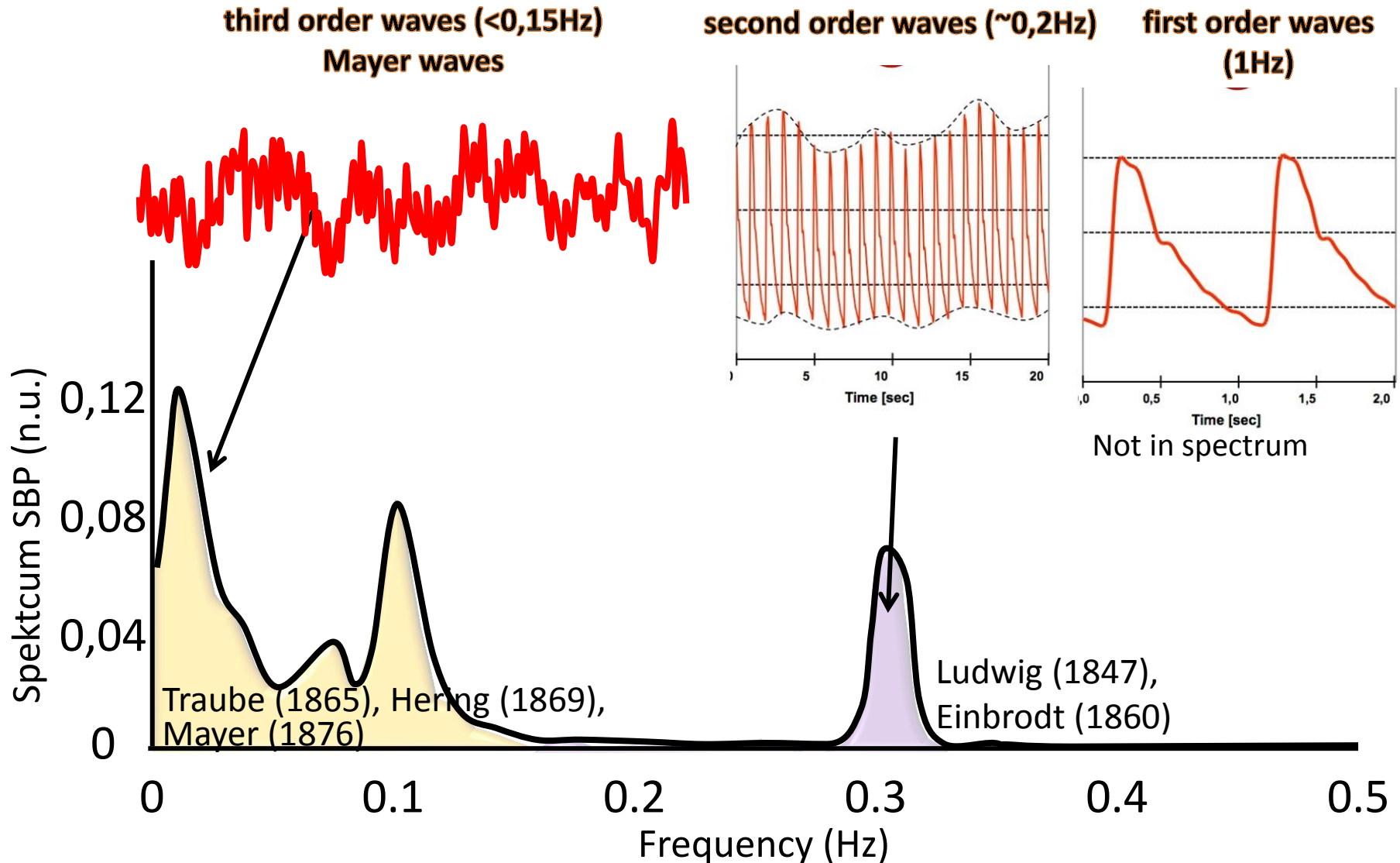
Time domain

Spectrum
Frequency domain



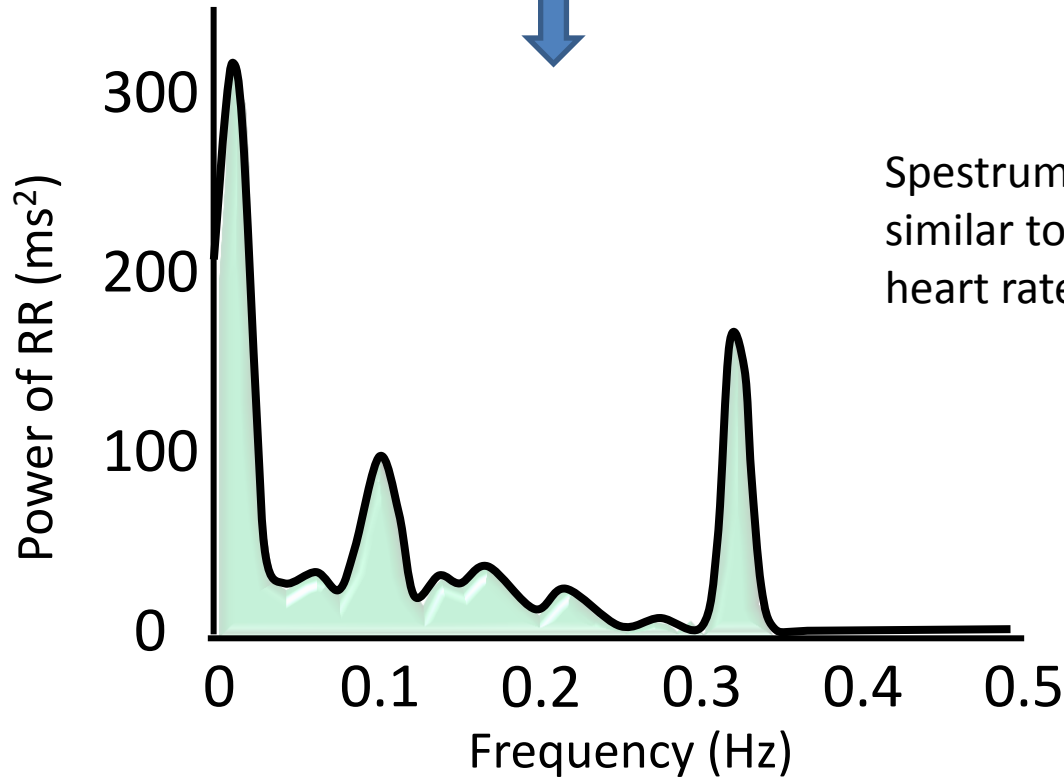
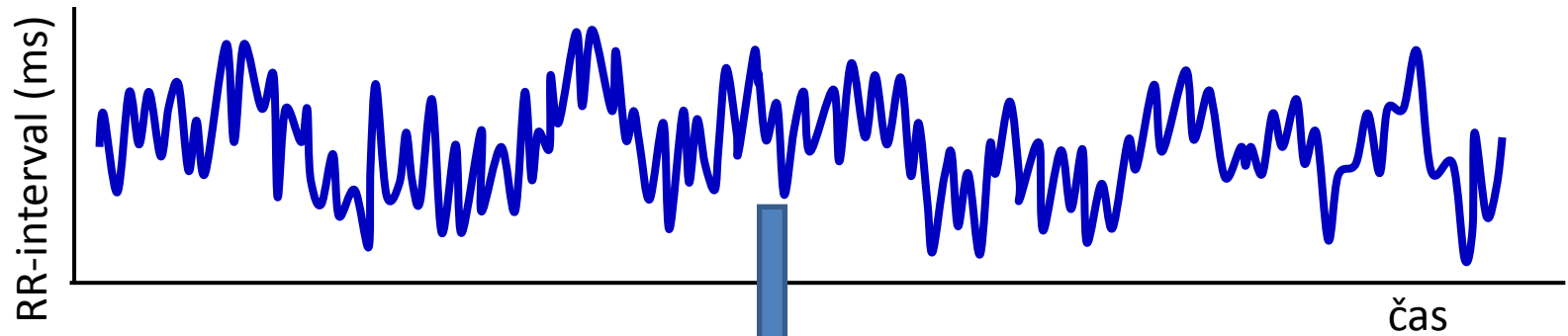
Blood pressure variability – spectrum of SBP

Signal: beat-to-beat series of systolic blood pressure (5 minutes)



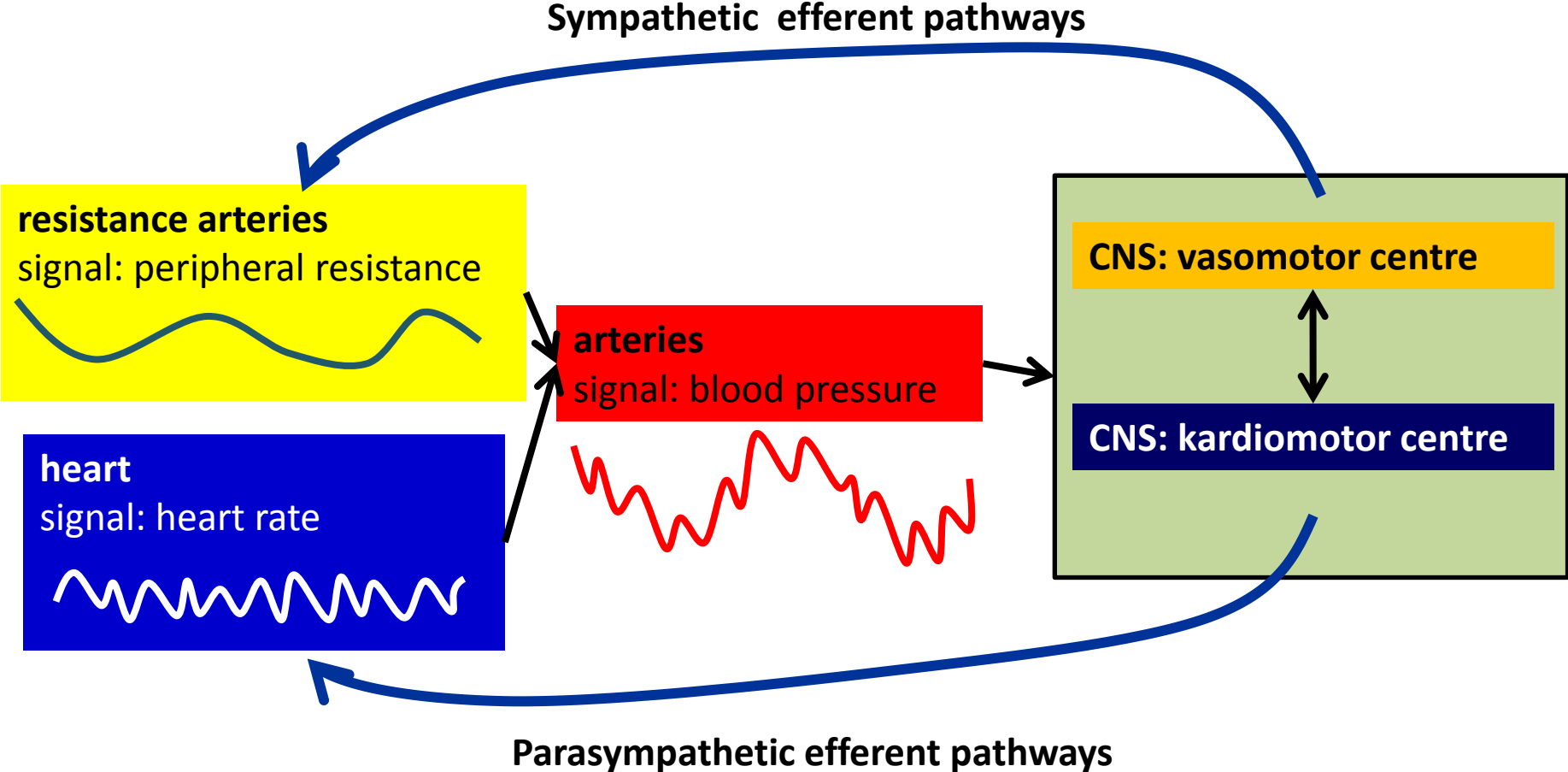
Heart rate variability (HRV)

Signal: beat-to-beat RR-intervals (5 min)



Spectrum of RR intervals is similar to the spectrum of heart rate

Baroreflex



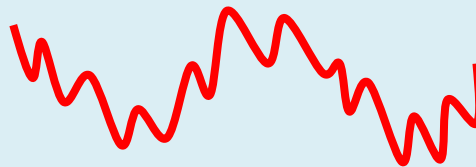
Baroreflex

peripheral (vascular, sympathetic) branch of baroreflexu

resistance arteries
signal: peripheral resistance



arteries
signal: blood pressure



heart
signal: heart rate

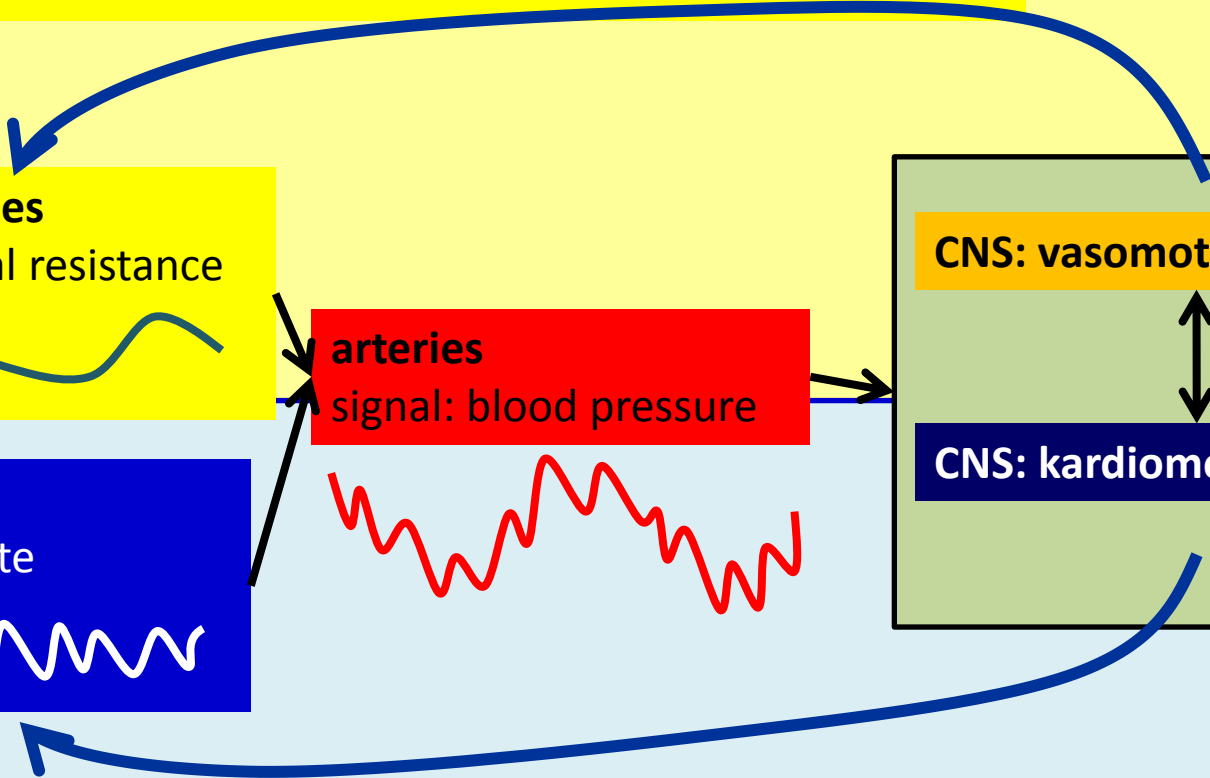


CNS: vasomotor centre

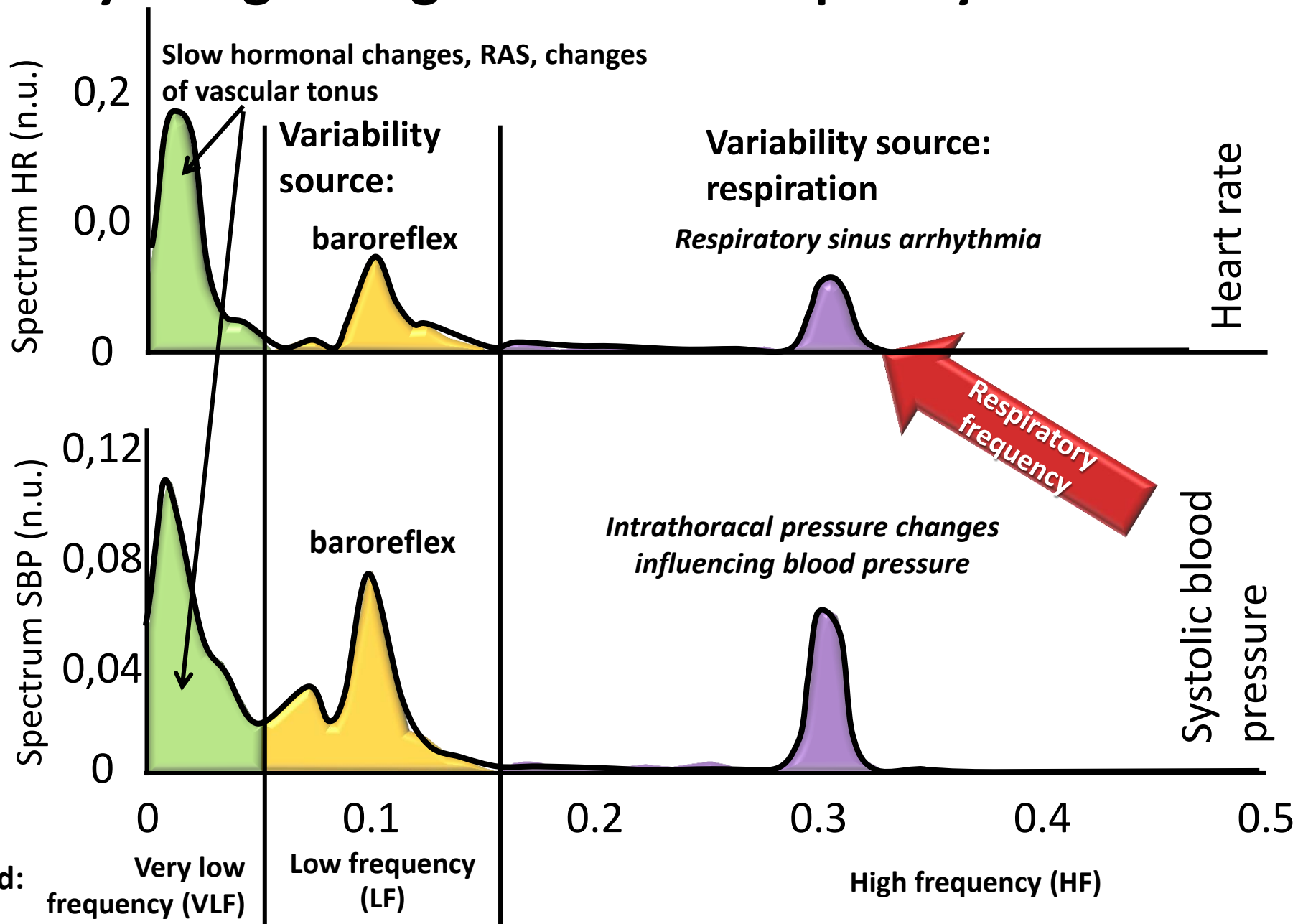


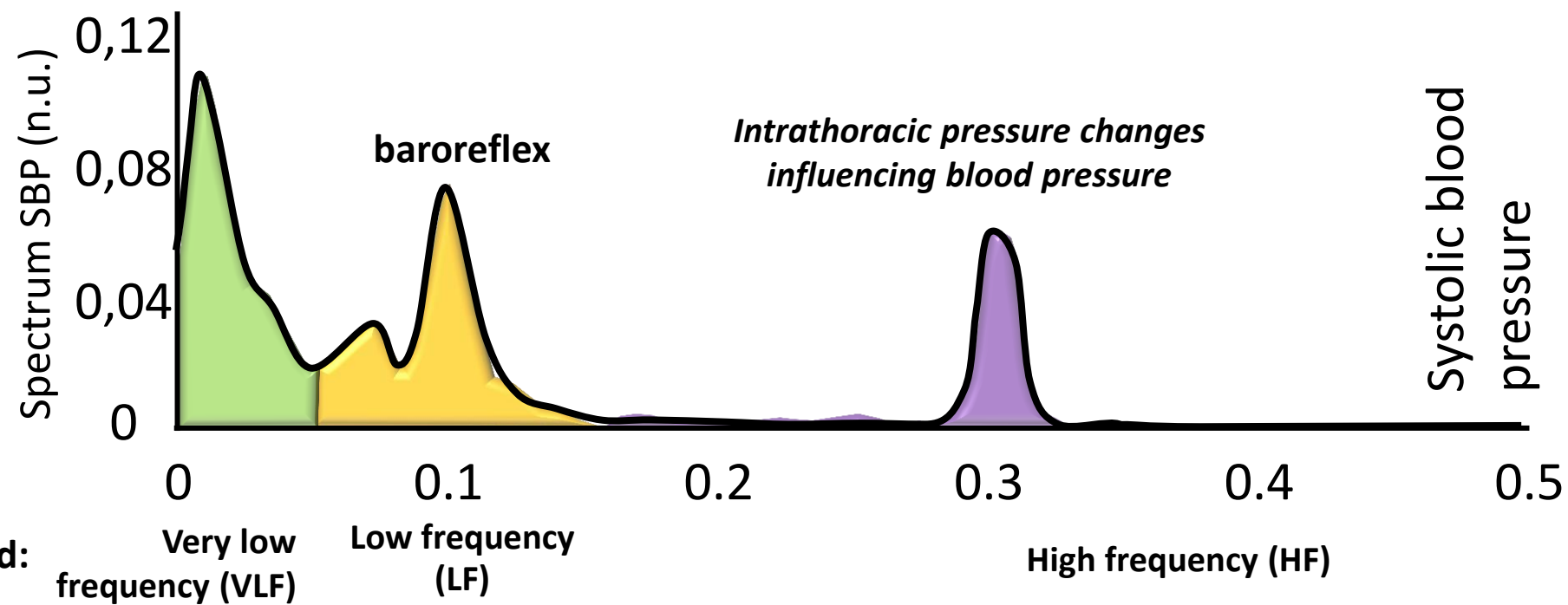
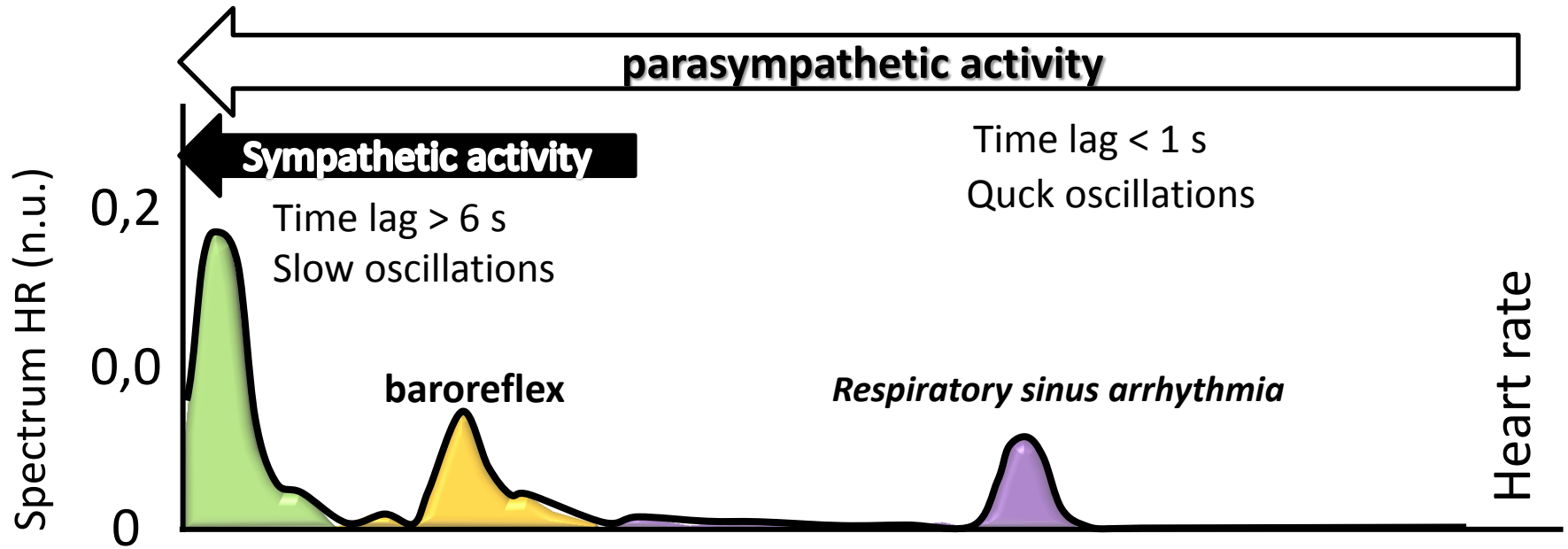
CNS: kardiomotor centre

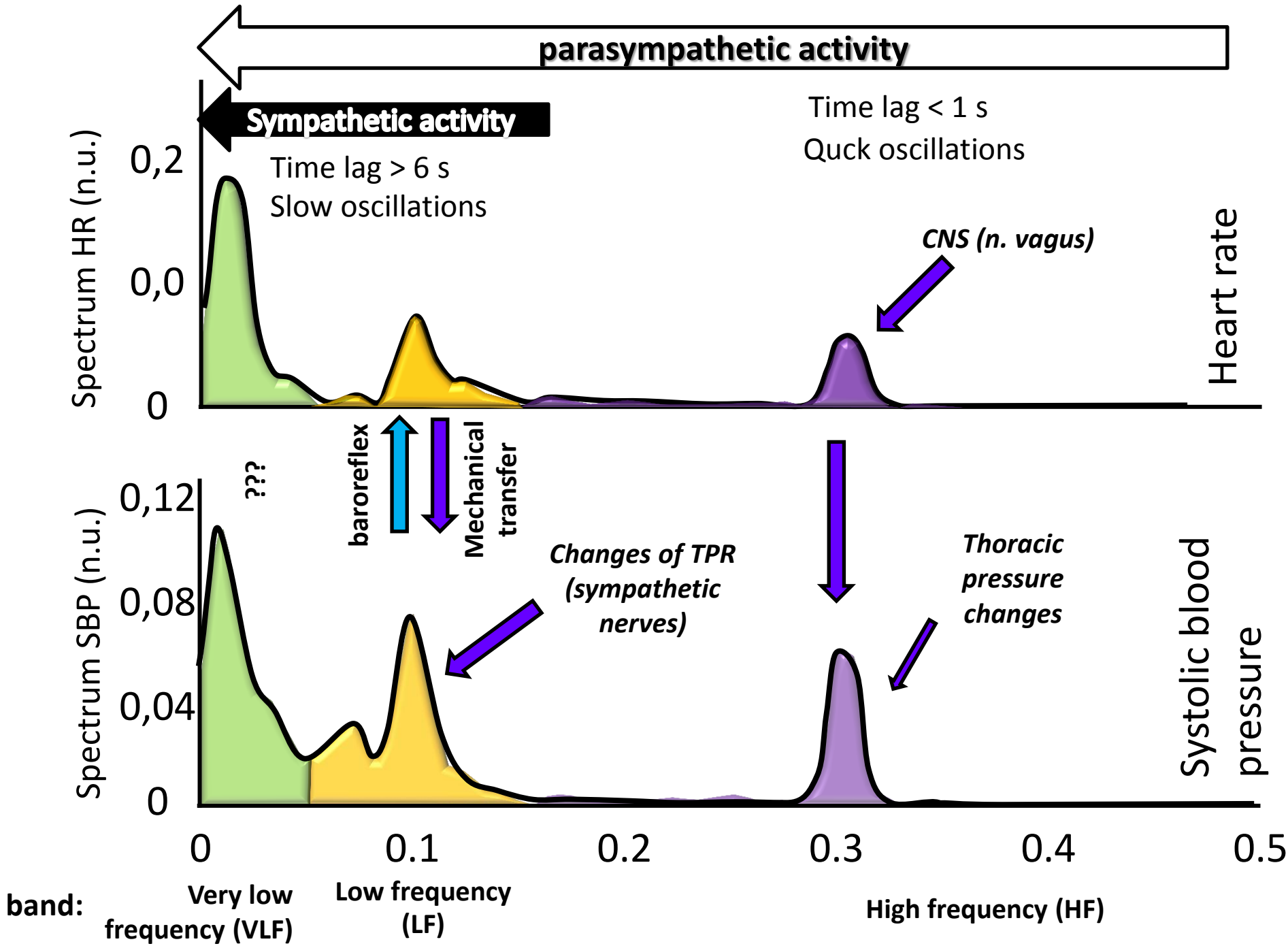
Cardiac (parasympathetic) branch



Physiological significance – frequency bands

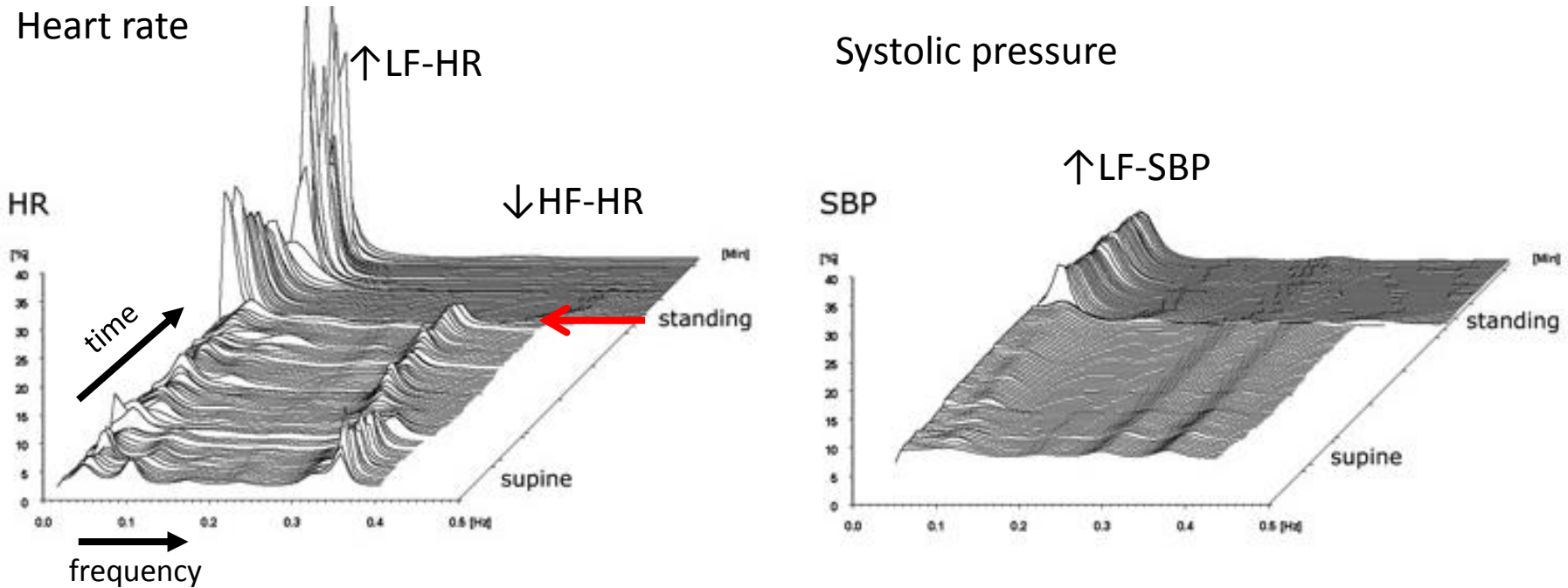






Variability changes: orthostatic challenge

Sympatho-vagal ratio LF-HR/HF-HR

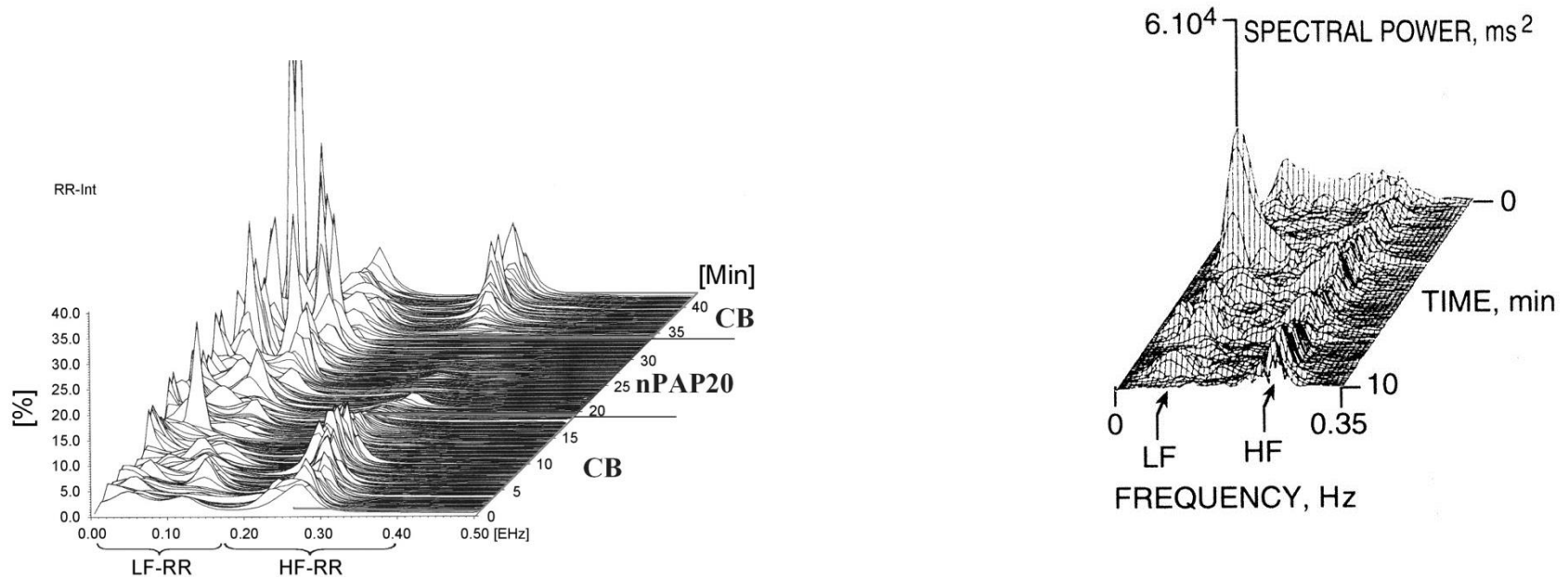


Orthostatic challenge:

- Increase of sympathetic activity → increase of low frequency HR and SBP variability (LF-HR, LF-SBP)
- Decrease of parasympathetic activity → decrease of variability in respiratory frequency (HF-HR)

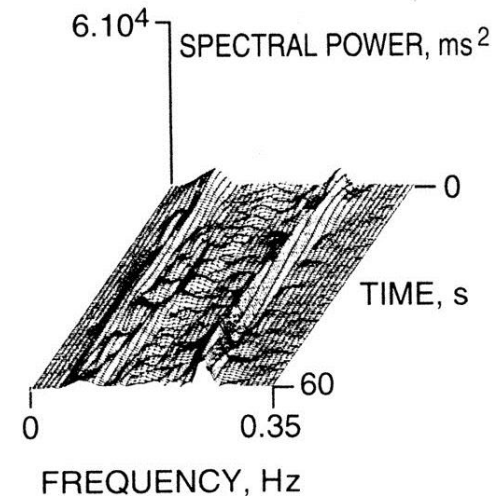
→ analysis of autonomic nervous system function

Heart rate variability (HRV) changes

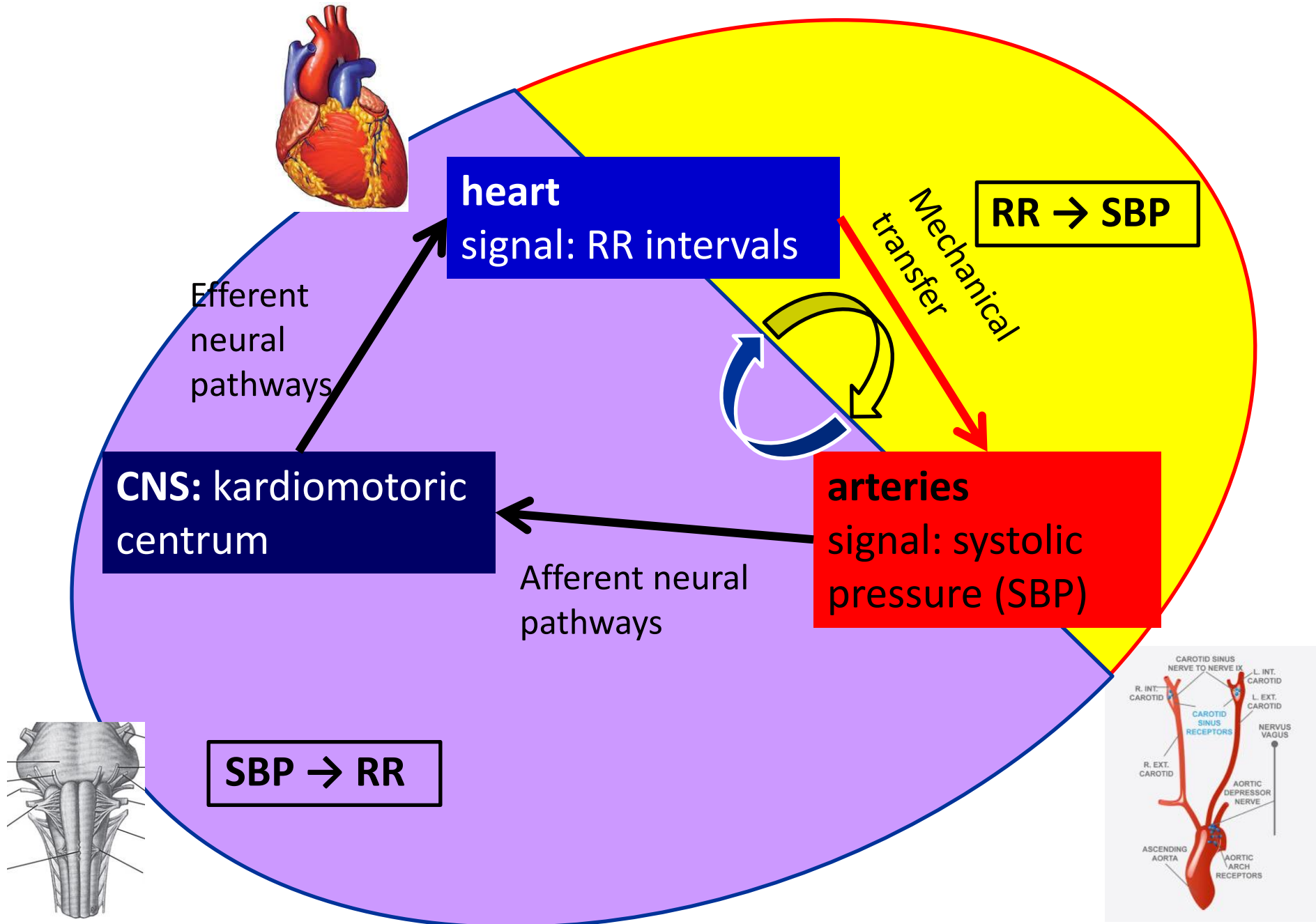


HRV in respiratory frequency decreases in stress situations (\uparrow sympathetic activity)

- Physiologically – sport, mental stress
- Pathologically – diabetes, hear failure
- Transplanted heart
- **Predictor of the cardiovascular risk**



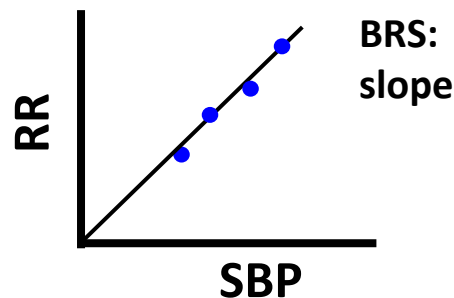
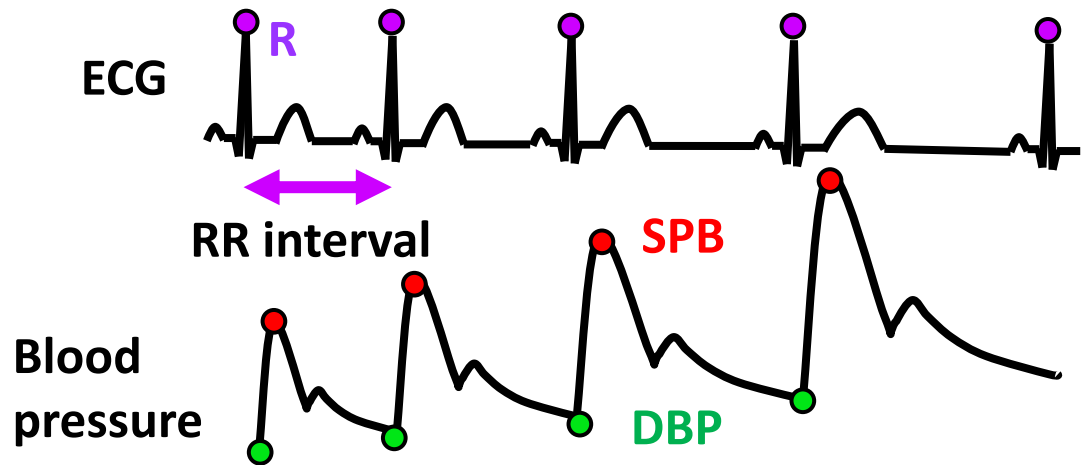
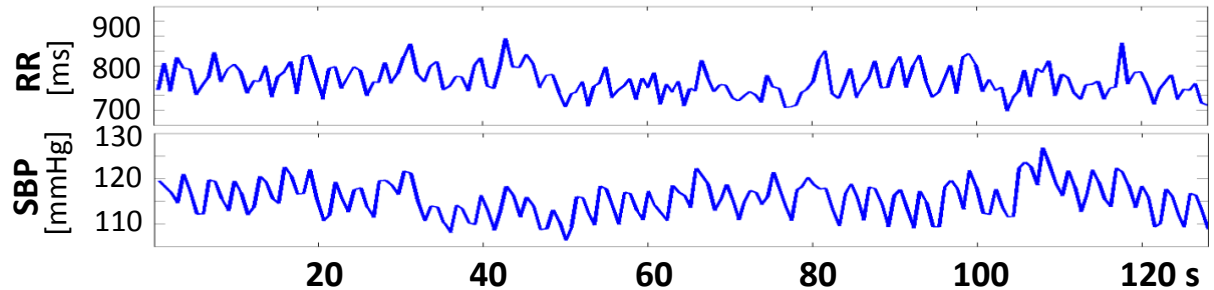
Evaluation of baroreflex function



Baroreflex sensitivity (BRS)

Cardiac baroreflex can be evaluated by analysis of SBP- HR interaction

BRS: change of cardiac cycle caused by change of SBP by 1 mmHg [ms/mmHg]



Baroreflex sensitivity

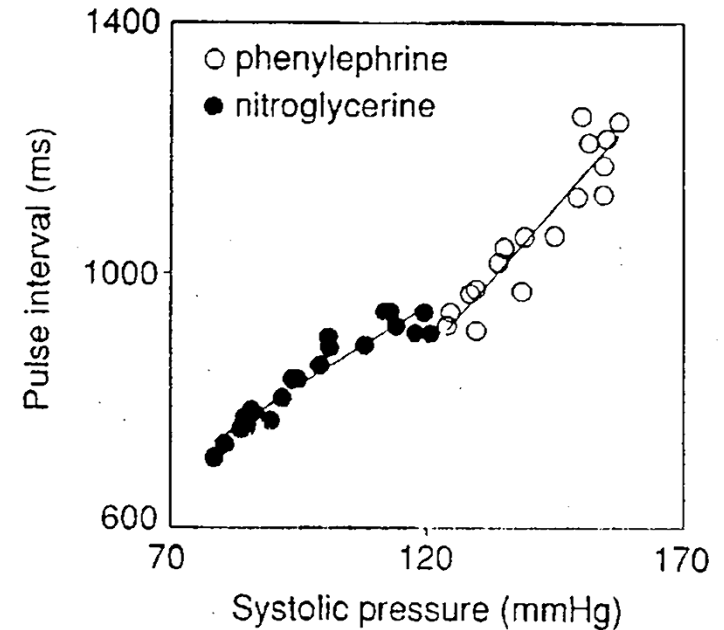
Laboratory methods:

- Phenylephrin application (standard)
- neck suction
- Valsalva manoeuvre

Spontaneous methods:

- in time domain: sequence analysis
- in spectral domain: cross-spectral analysis, α -index

Bolus injections of vasoactive drugs



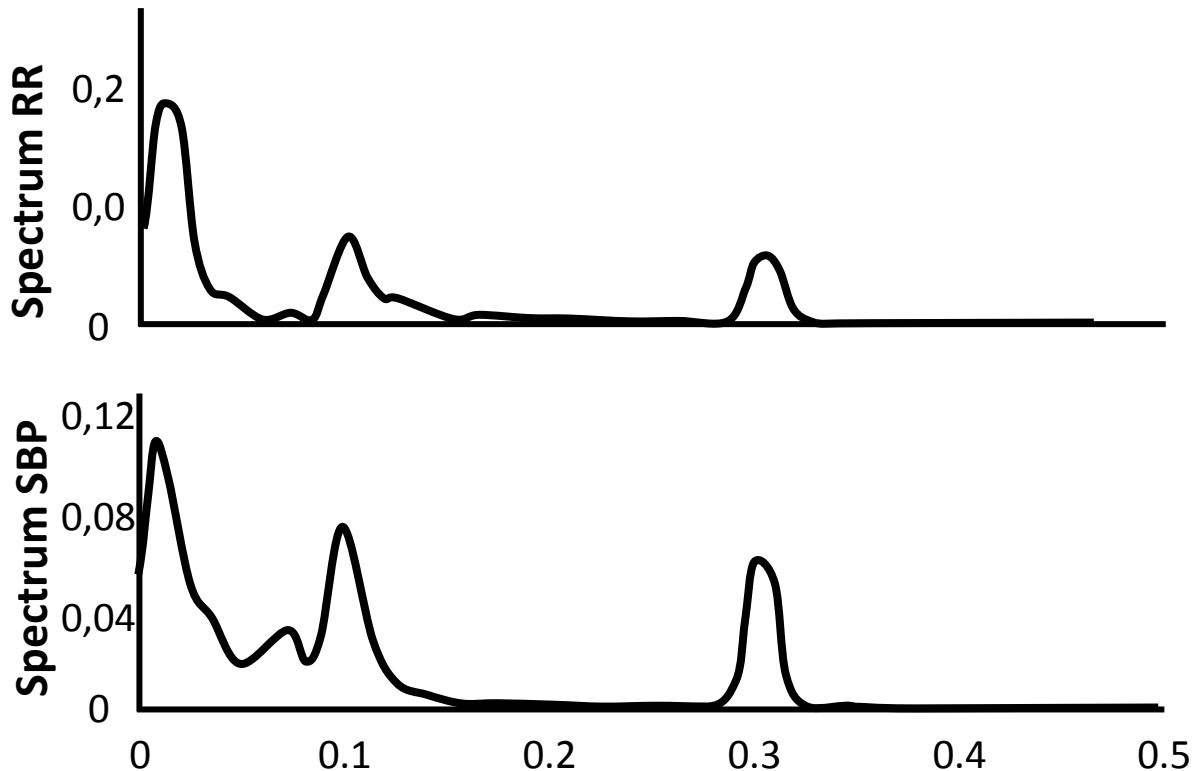
Spectral methods

BRS: change of RR caused by change of SBP by 1 mmHg [ms/mmHg]

- Change of RR – amplitude of RR in the spectrum of RR
- Change of SBP – amplitude of SBP in the spectrum of SPB
- → dividing of spectra → alpha index

$$\alpha \text{ index} = \frac{\text{spectrum RR}}{\text{spectrum SBP}}$$

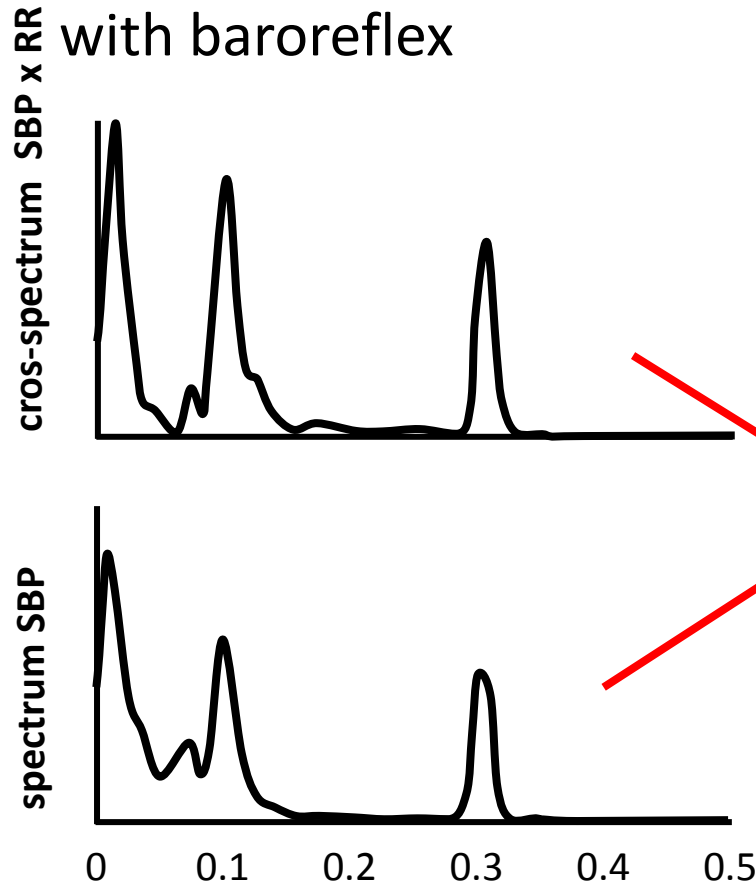
- Complication – not every oscillation in RR is caused by oscillation in SBP



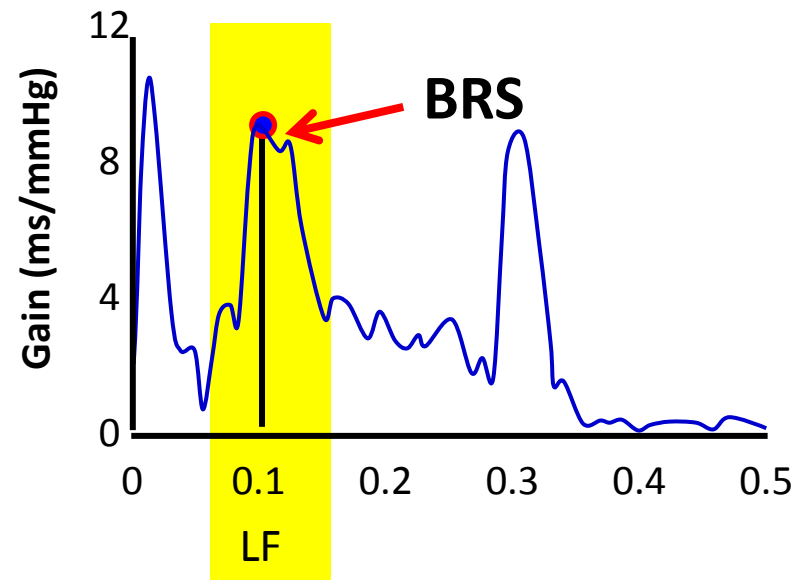
Spectral methods

Cross -spectrum RR and SBP:

- Contains only these frequencies occurring in both signals simultaneously
- Advantage – we can analyse only special frequencies associated with baroreflex

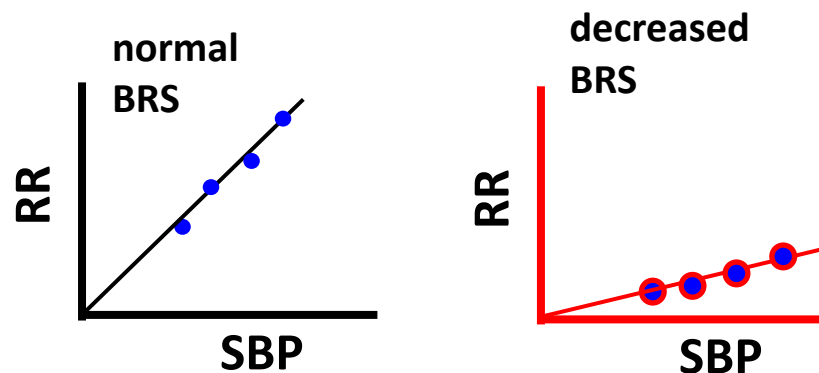


$$\text{gain} = \frac{\text{cross - spectrum RR x SBP}}{\text{spectrum SBP}}$$



Baroreflex sensitivity – physiological significance

- Baroreflex function – regulation of blood pressure changes by changes of HR and TPR
- Cardiac branch of baroreflex is mediated by vagal nerves
 - BRS is increased in higher vagal activity and decreased in sympathetic activity
 - BRS is decreased in stress
 - BRS depends on RR interval length
- **Long-time decreased BRS reflects dysfunction in blood pressure regulation – cardiovascular risk**



Decreased BRS

- Physiologically
 - psychic stress – increased sympathetic activity
 - Physical exercise – increased sympathetic activity
 - In old age
- Pathologically
 - hypertension – decreased baroreceptor sensitivity (atherosclerosis, increased arterial stiffness)
 - diabetes – neuropathy of autonomic nervous system
 - Chronic depression (neurogenic)
 - Heart insufficiency/failure – heart do not response
 - Transplanted heart - denervation
 - Myocardial infarction – heart do not response



Disadvantages of methods

- Sinus rhythm without ectopic beats
- Long recording >5min, stationary signal
- BRS is a parameter of cardiac baroreflex function, information about vascular part of baroreflex is missing
- Causality of RR-SBP is neglected

Take home message 1

- Variability of cardiovascular signals contain information about regulatory mechanisms
- Analysed signals: time series
 - ECG: beat-to-beat RR intervals, heart rate (HR)
 - Continual record of blood pressure: beat-to-beat systolic pressures (SBP)
- Main methods of variability analysis
 - Standard deviations and derived parameters
 - Spectral analysis
- Analysis of RR-SBP interaction: baroreflex sensitivity
(definition: change of RR caused by change of SBP by 1 mmHg)

Take home message 1

- **Heart rate variability (HRV) – assessment of ANS activity**
 - decreased – increased cardiovascular risk
- Blood pressure variability (less analysed)
 - decreased – increased cardiovascular risk
- **Baroreflex sensitivity (BRS)**
 - normal (> 4 mmHg) – baroreflex function is OK
 - decreased (< 3 mmHg) – increased cardiovascular risk
 - Hypertension, diabetes, heart failure, stress
- Predictors of sudden cardiac death: zero values of BRS and HRV
- Spectra RR and SBP
 - Frequency bands (VLF, LF and HF)
 - HF (0.15-0.5 Hz): parasympathetic activity, respiration
 - LF (around 0.1 Hz): sympathetic/parasymp. activity, baroreflex
 - VLF (< 0.03): low changes in vascular system (hormones, TPR, RAS,...)

Thank you

