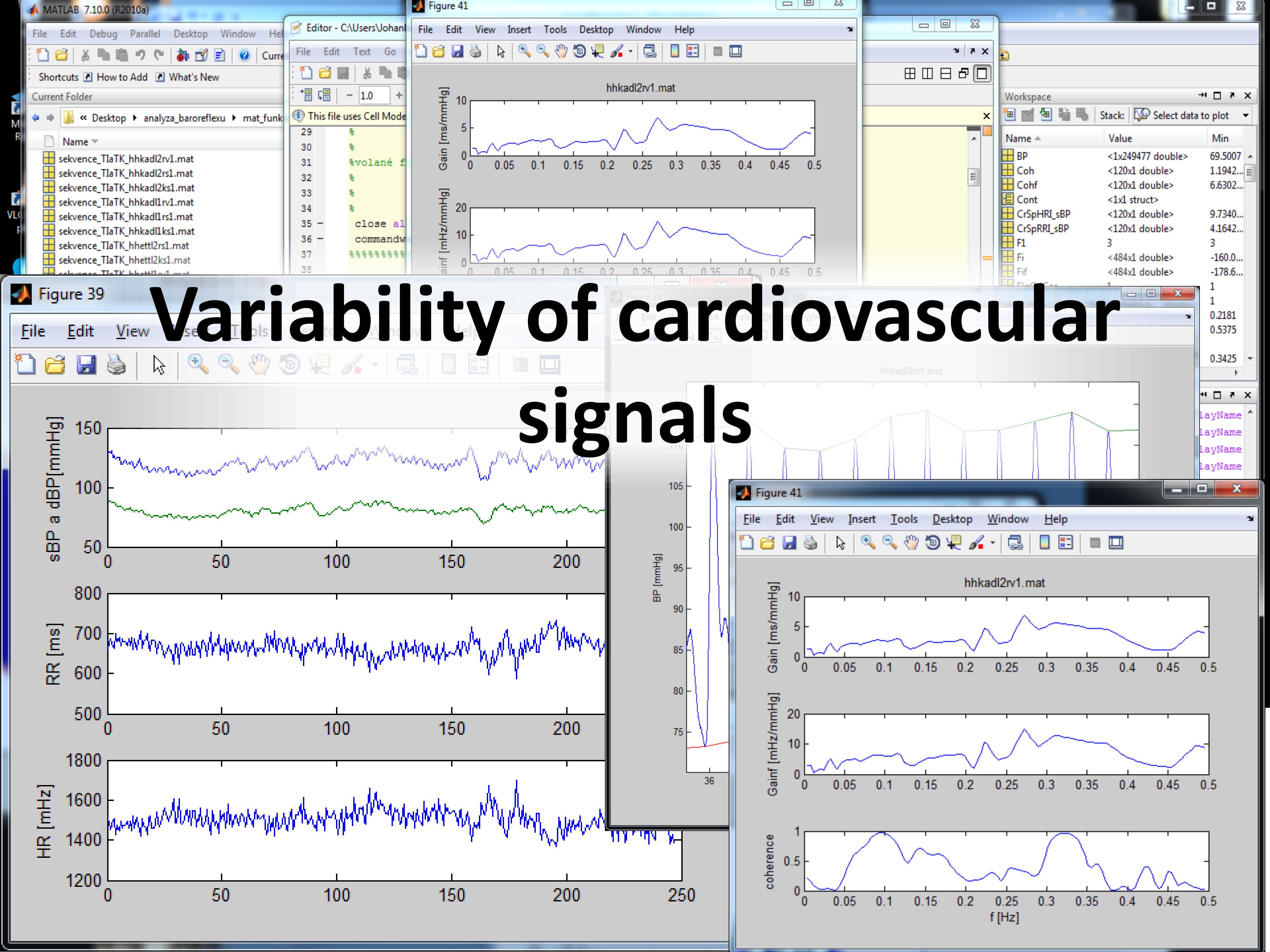
Variability of cardiovascular signals



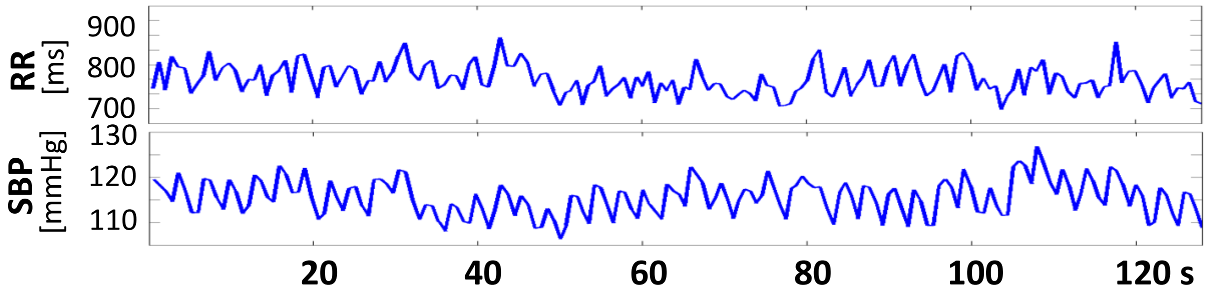
Cardiovascular signal variability

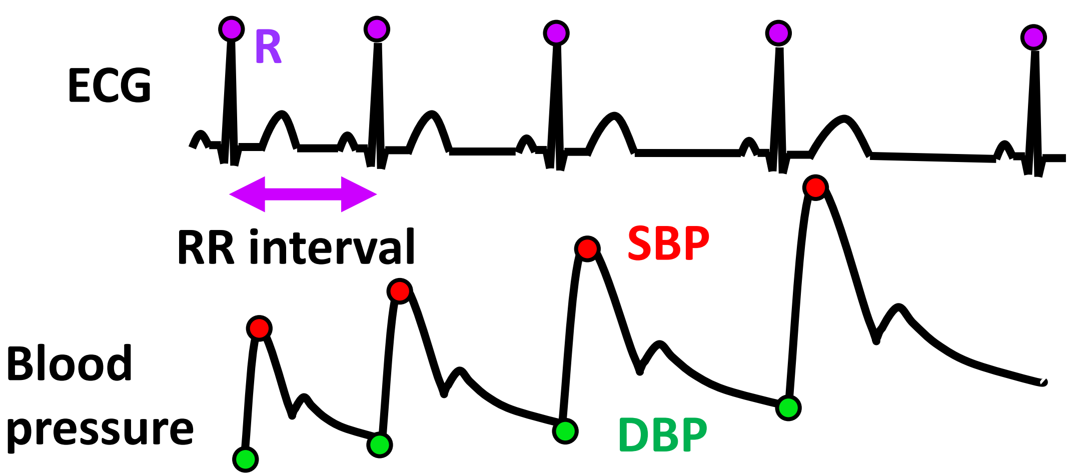
- **Cardiovascular signals (C-V signals)**
  - Easy to measure
    - EGG: RR intervals, heart rate - HR (1/RR)
    - Blood pressure: systolic (SBP), diastolic (DBP), mean (MAP), pulse pressure (PP)
  - Difficult to measure directly (bioimpedance method), can be evaluated indirectly from blood pressure 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

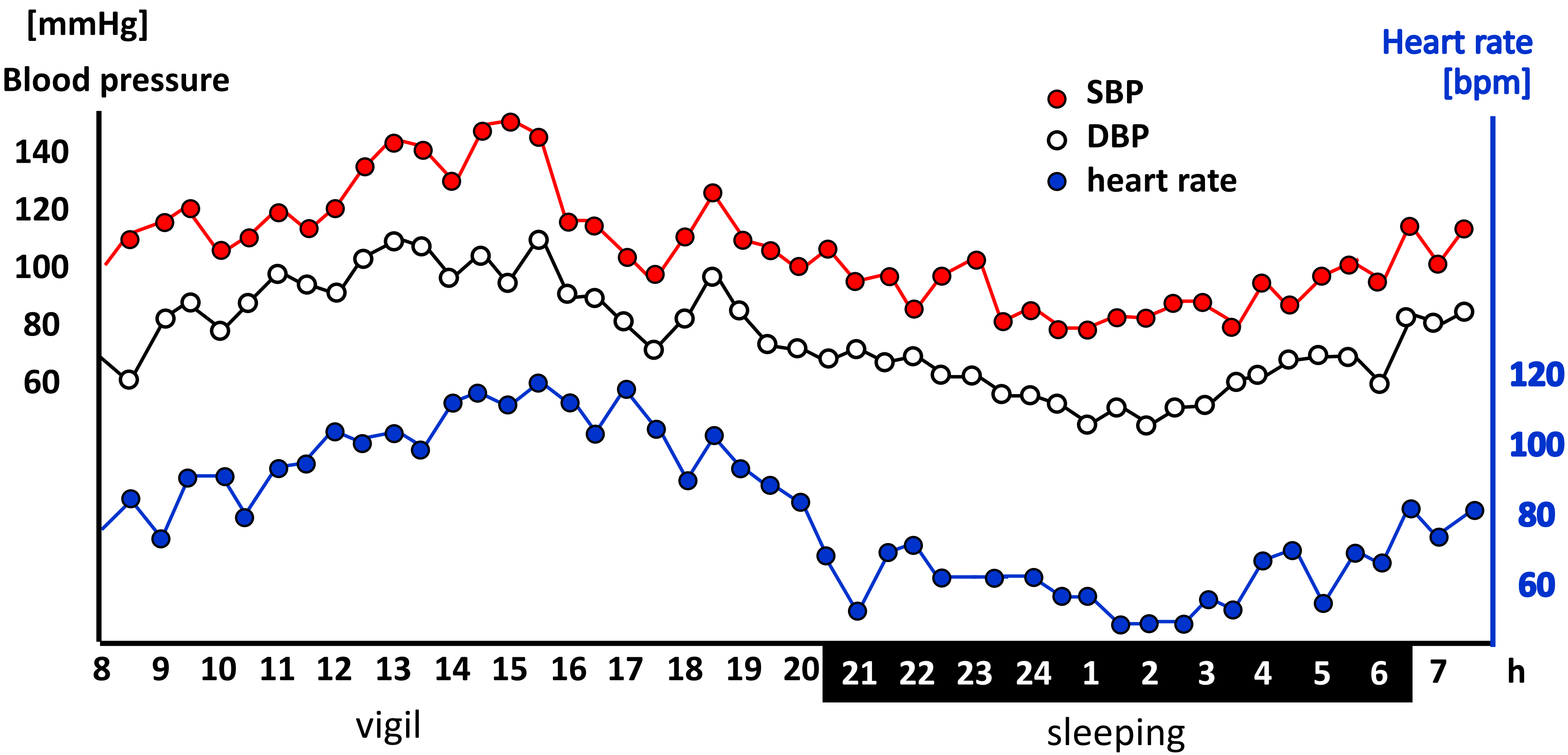




Signal: time series

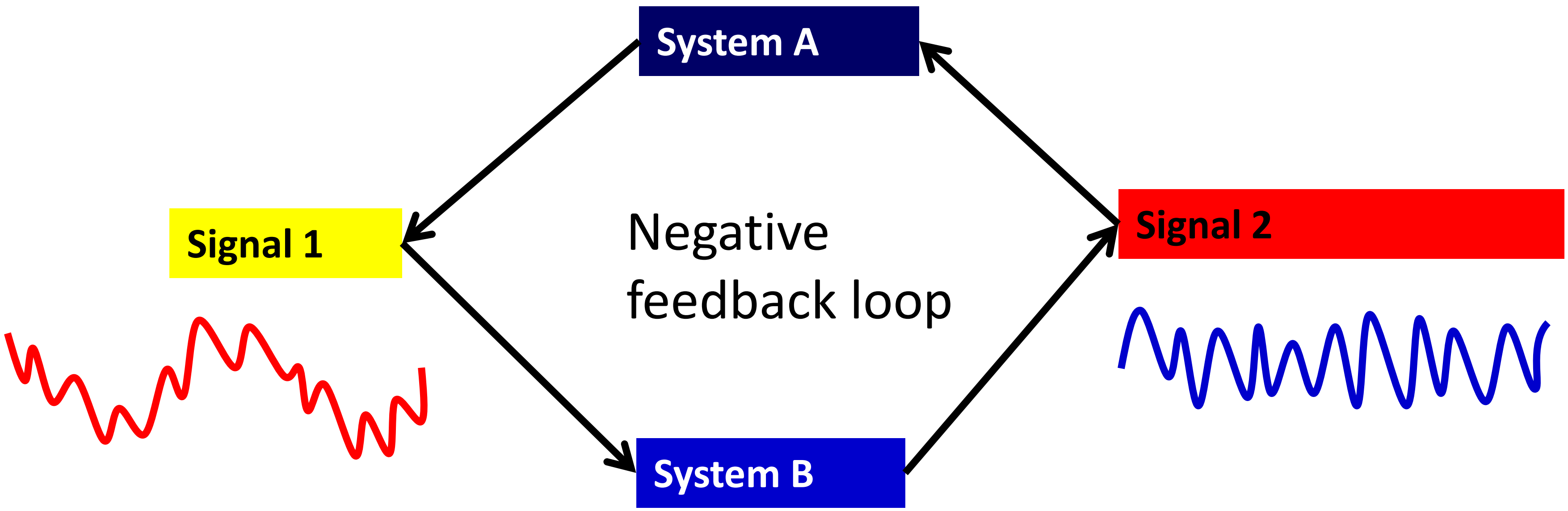
Every 15 minutes

- 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

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

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

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

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

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

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

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

Brief introduction in theory of systems

$-k$

$_{1,n}z^{-p} \quad a_{12,1}z^{-1} + a_{12,2}z^{-2} + \cdots + a_{12,n}z^{-p}\Big)$

$a_{21,n}z^{-p} \quad a_{22,1}z^{-1} + a_{22,2}z^{-2} + \cdots + a_{22,n}z^{-p}\Big)$

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

$S \quad),$

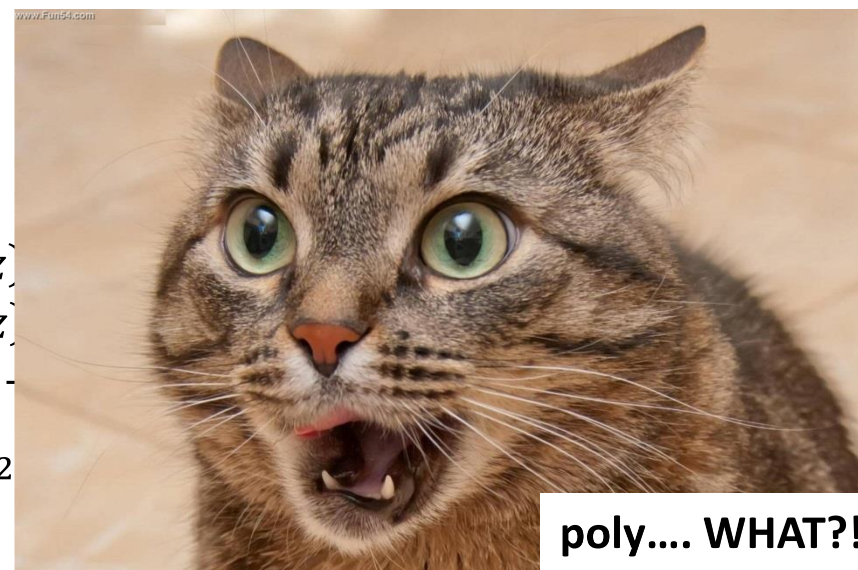
$$\Lambda = \begin{pmatrix} \lambda_1^2 & 0 \\ 0 & \lambda_2^2 \end{pmatrix}$$

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

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

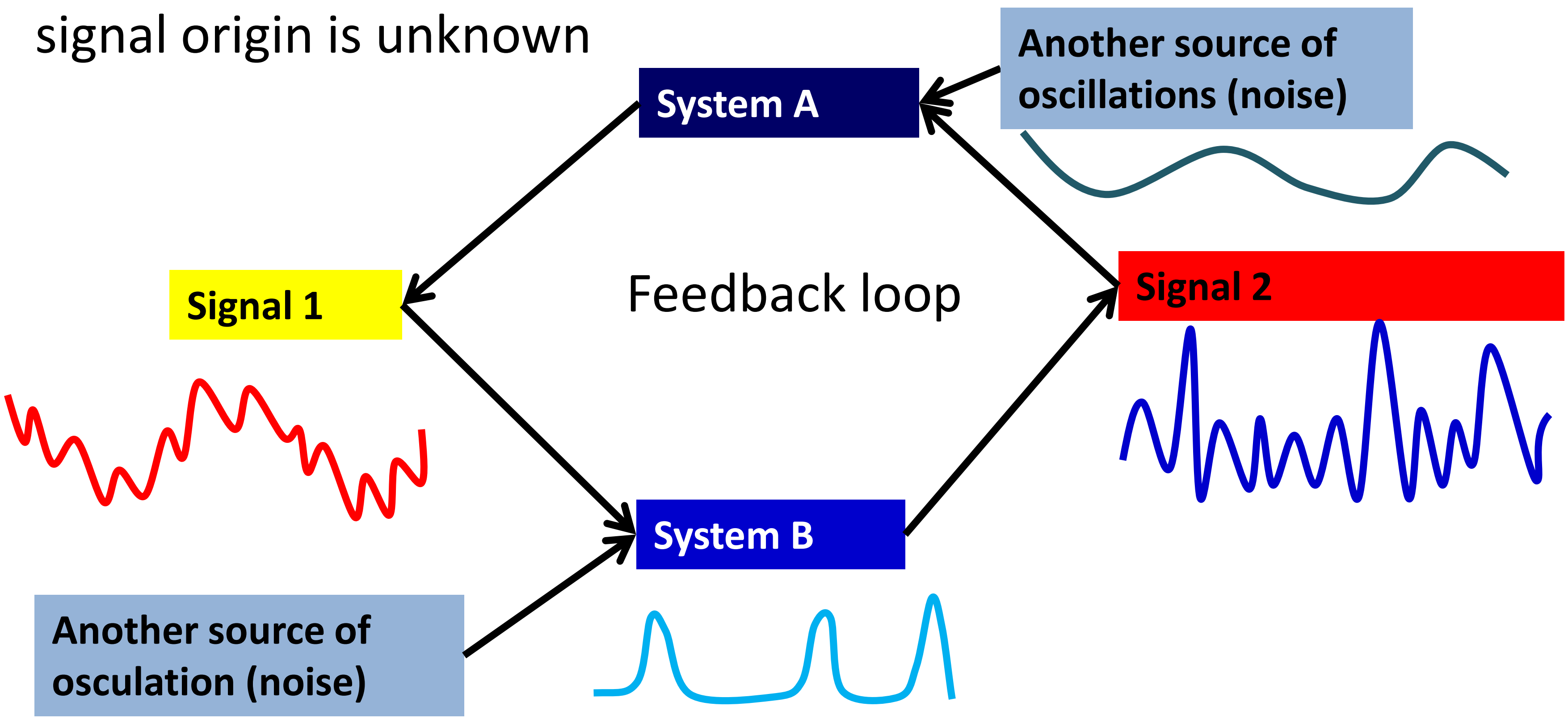
$S_{12}(f) = |\Delta(z)|^2 \cdot [(1 - A_{22}(z))A_{21}(z^{-1})\lambda_1^2 -$

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

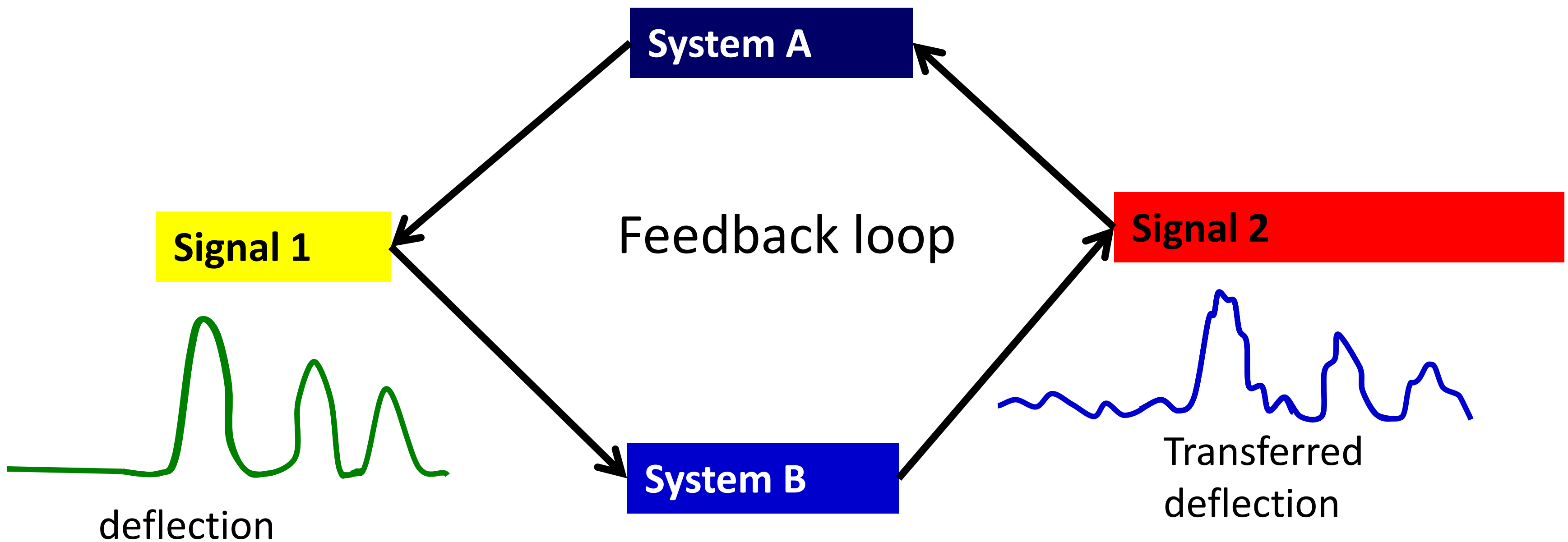


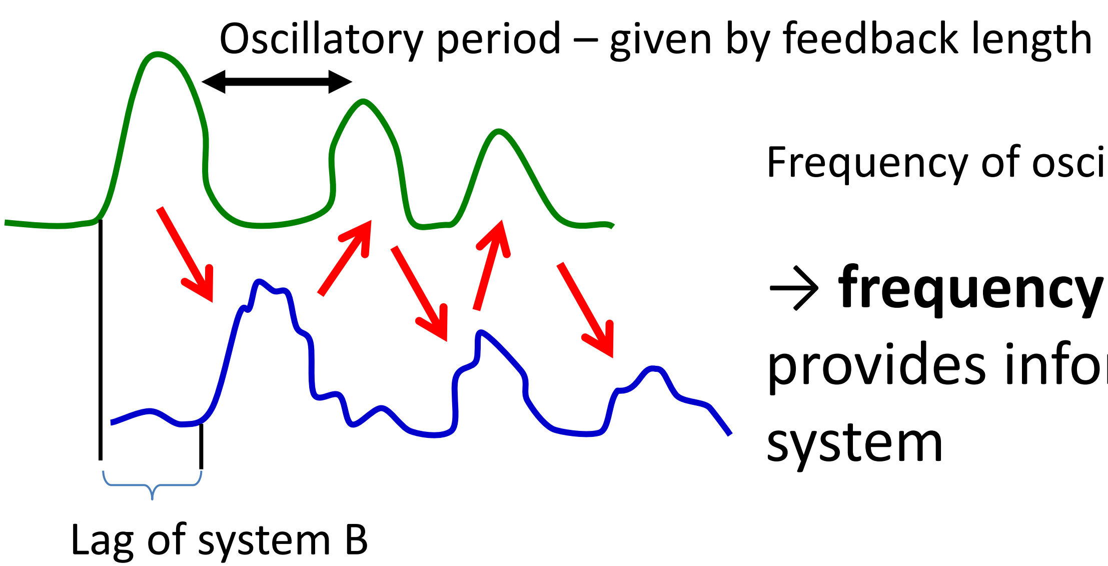
Brief introduction in theory of systems

- 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 system
- noise: another input signal – we do not care about signal and/or signal origin is unknown



Source of oscillations

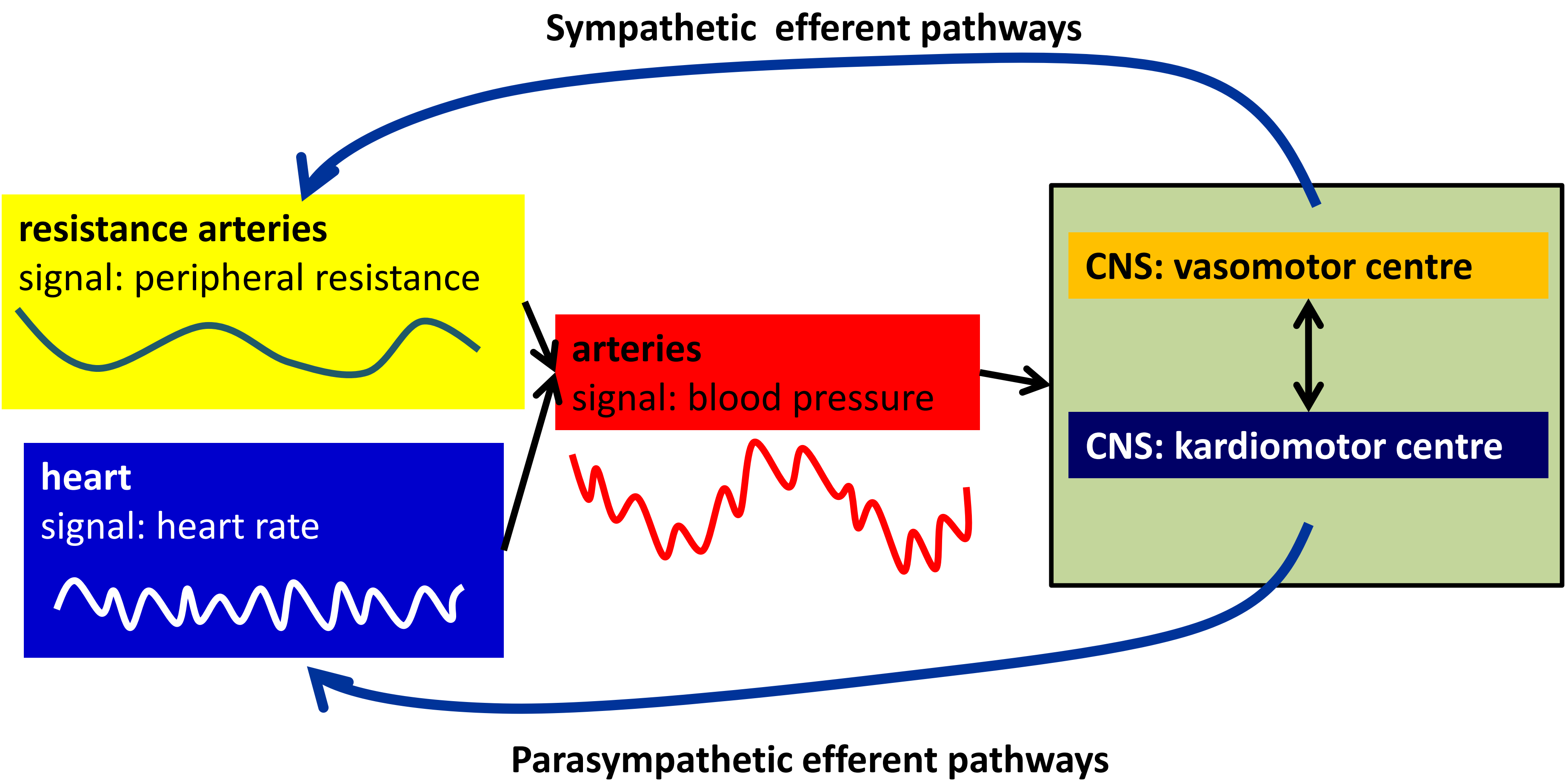




Frequency of oscillation = 1/period

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

Feedback loop - baroreflex



Methods of the variability assessment

methods

Time-domain methods

- Statistic methods
- Geometric methods

Frequency-domain methods

Non-linear methods

(index of ireversibility, entropy based indices, symbolic analysis…)

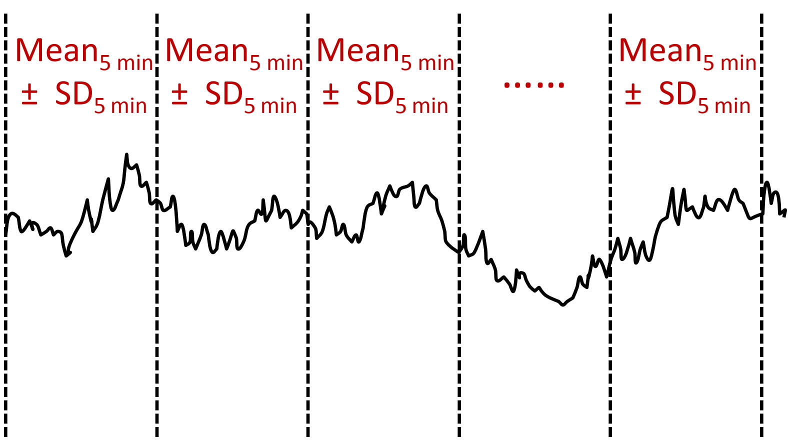
Statistic methods

(Variations on Standard Deviation)

24-hour record of RR intervals

$Mean_{24\text{-}h} \pm SD_{24\text{-}h}$

24-hour record of RR intervals divided into 5-min segments ($Mean_{5\ min} \pm SD_{5\ min}$)



$SD_{24\text{-}h}$ counted from all RR-intervals in 24 hours — **SDRR**

$SD_{24\text{-}h}$ counted from all normal RR-intervals in 24 hours — **SDNN**

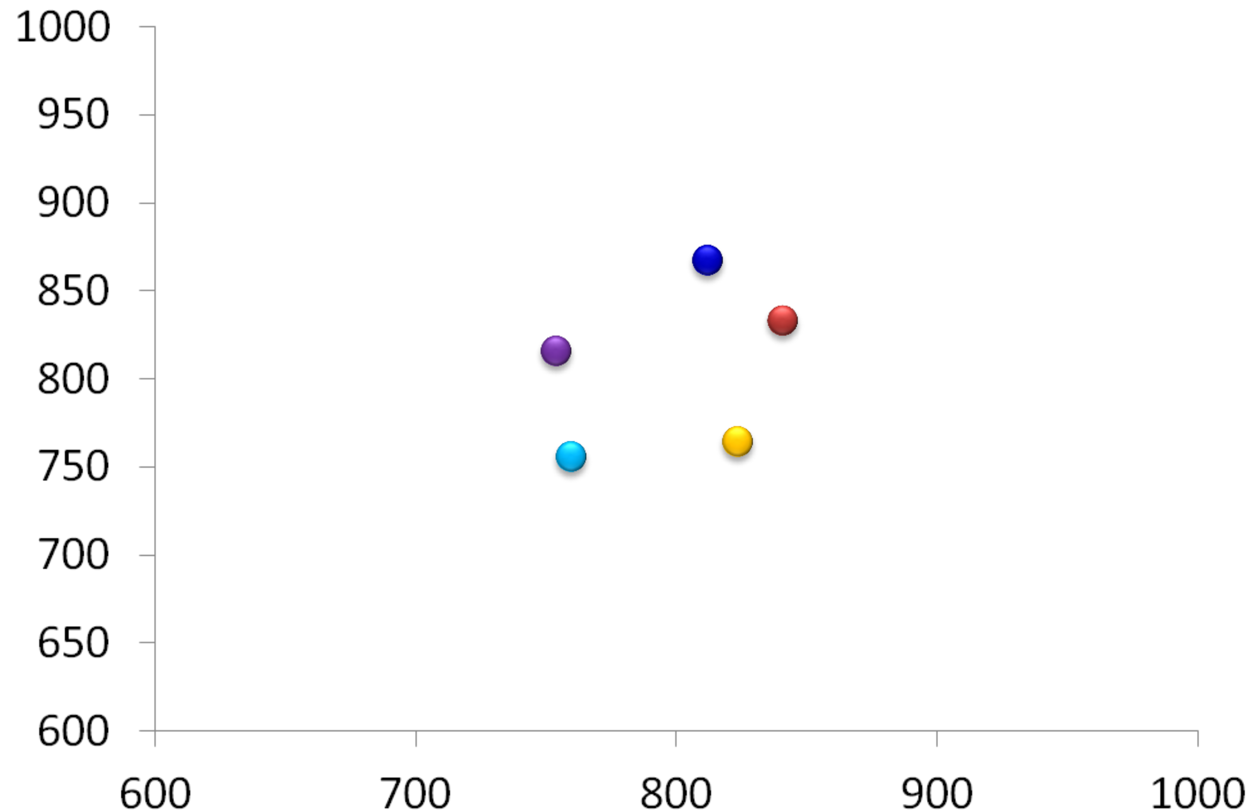
SD counted from all $Mean_{5\ min}$ — **SDANN**

SD counted from all $SD_{5\ min}$ — **SDANNIDX**

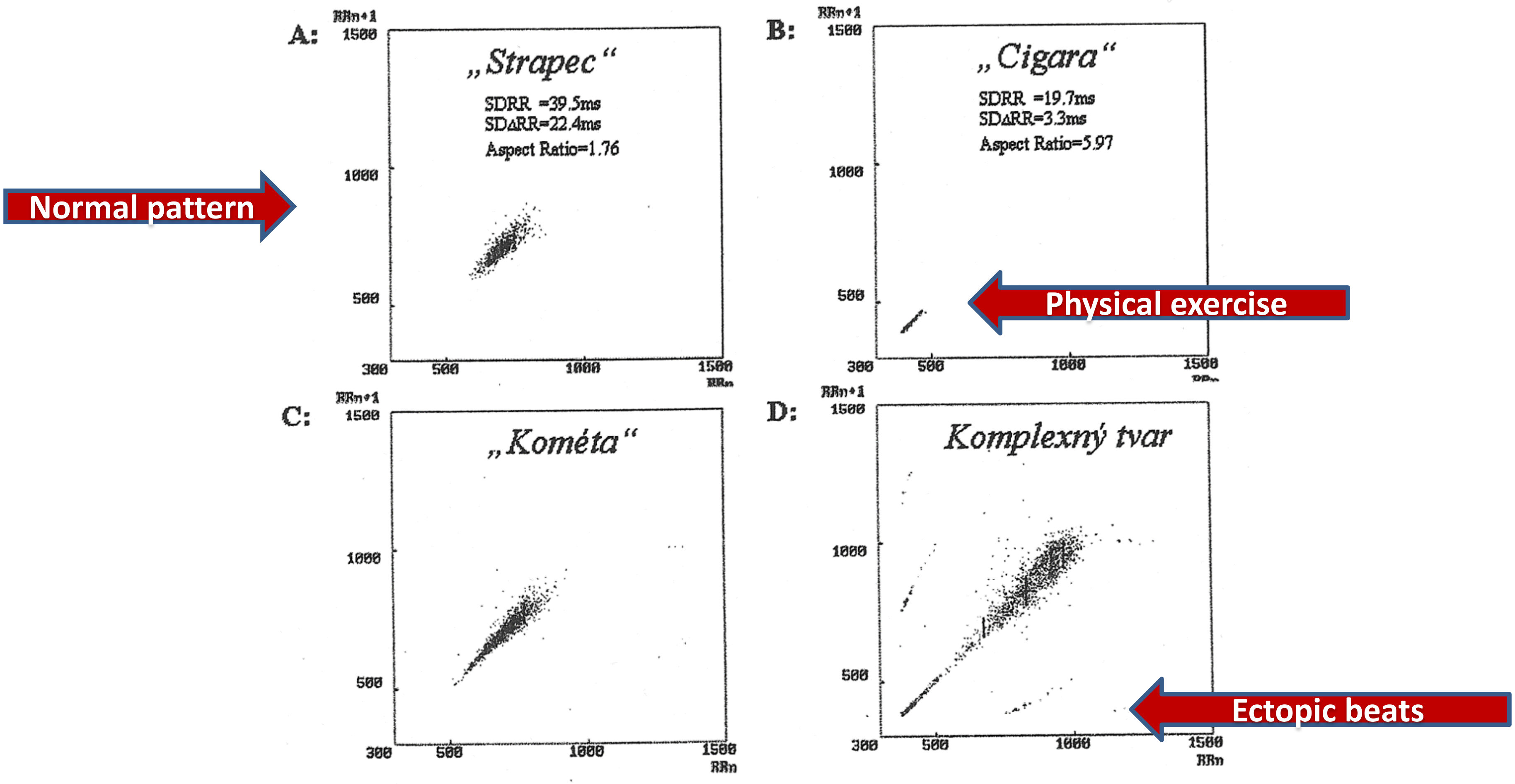
Geometric methods

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

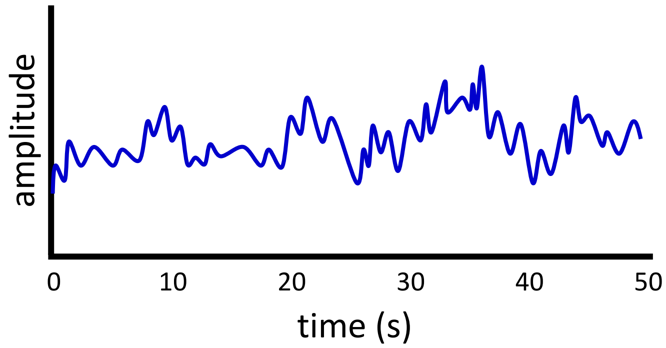


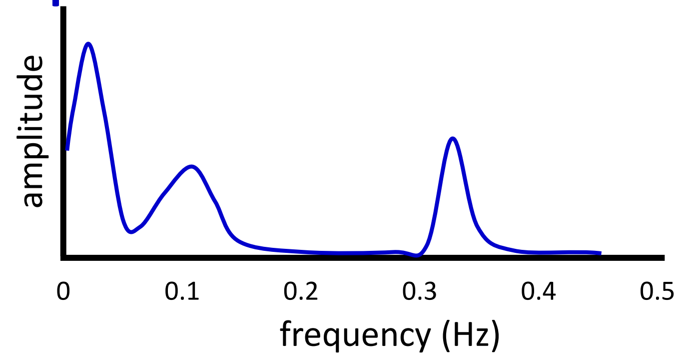
Frequency domain methods – spectral analysis

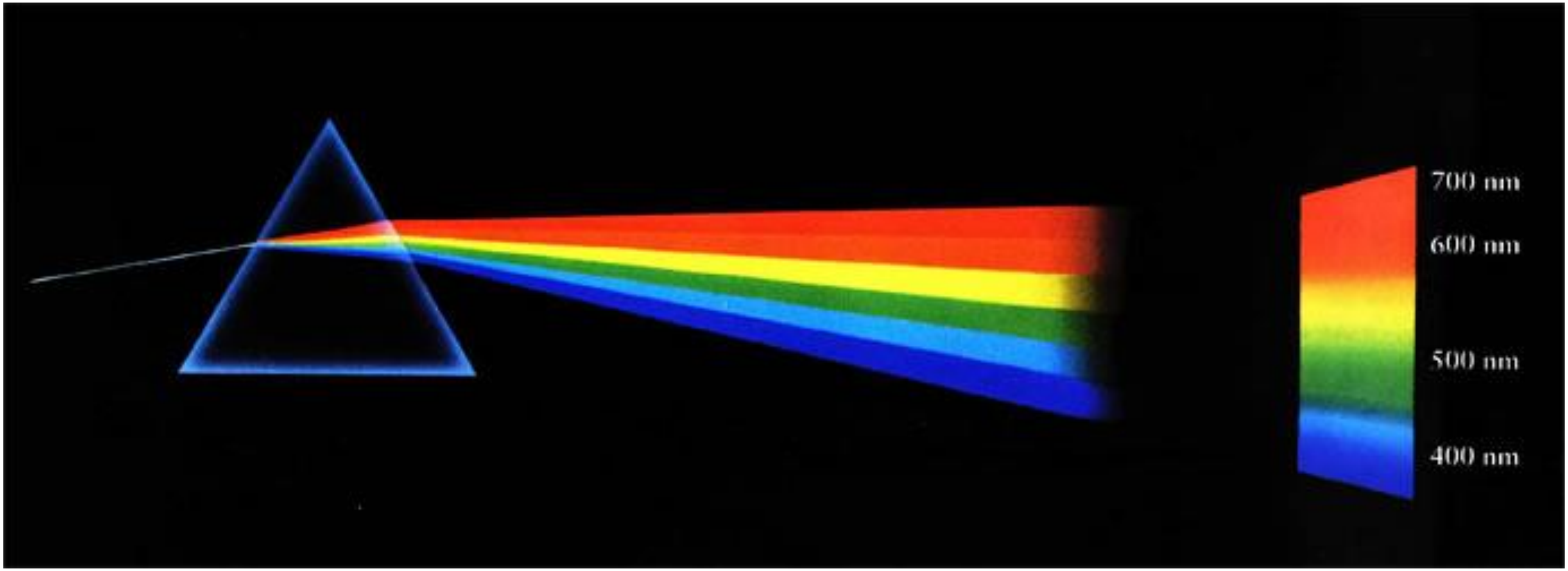
Time series
Signal in time domain

Spectrum
Signal in frequency domain

Signal is decomposed in individual frequencies





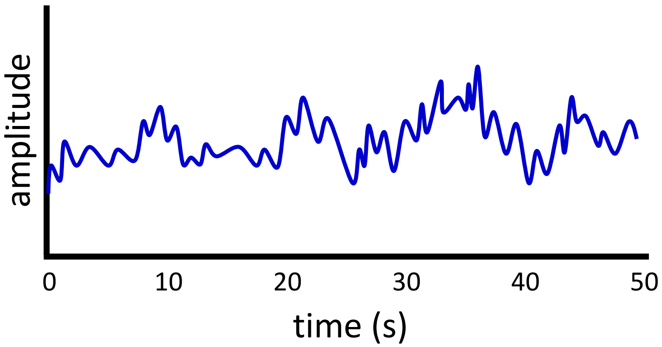


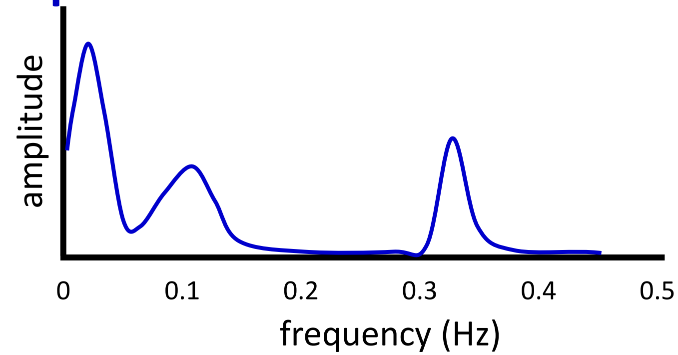
Frequency domain methods – spectral analysis

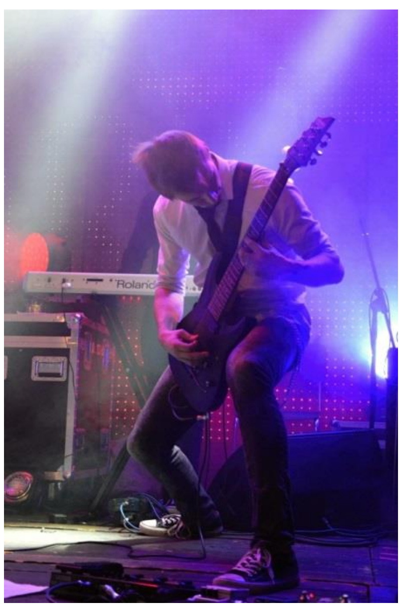
Time series
Signal in time domain

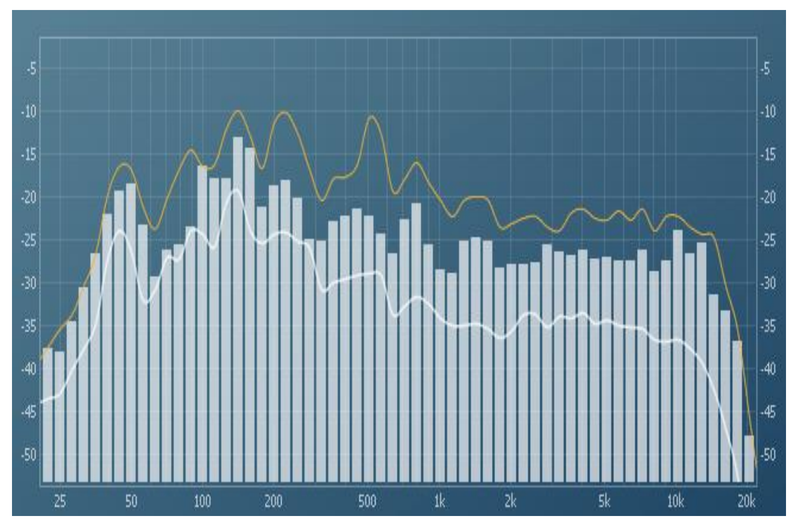
Spectrum
Signal in frequency domain

Signal is decomposed in individual frequencies





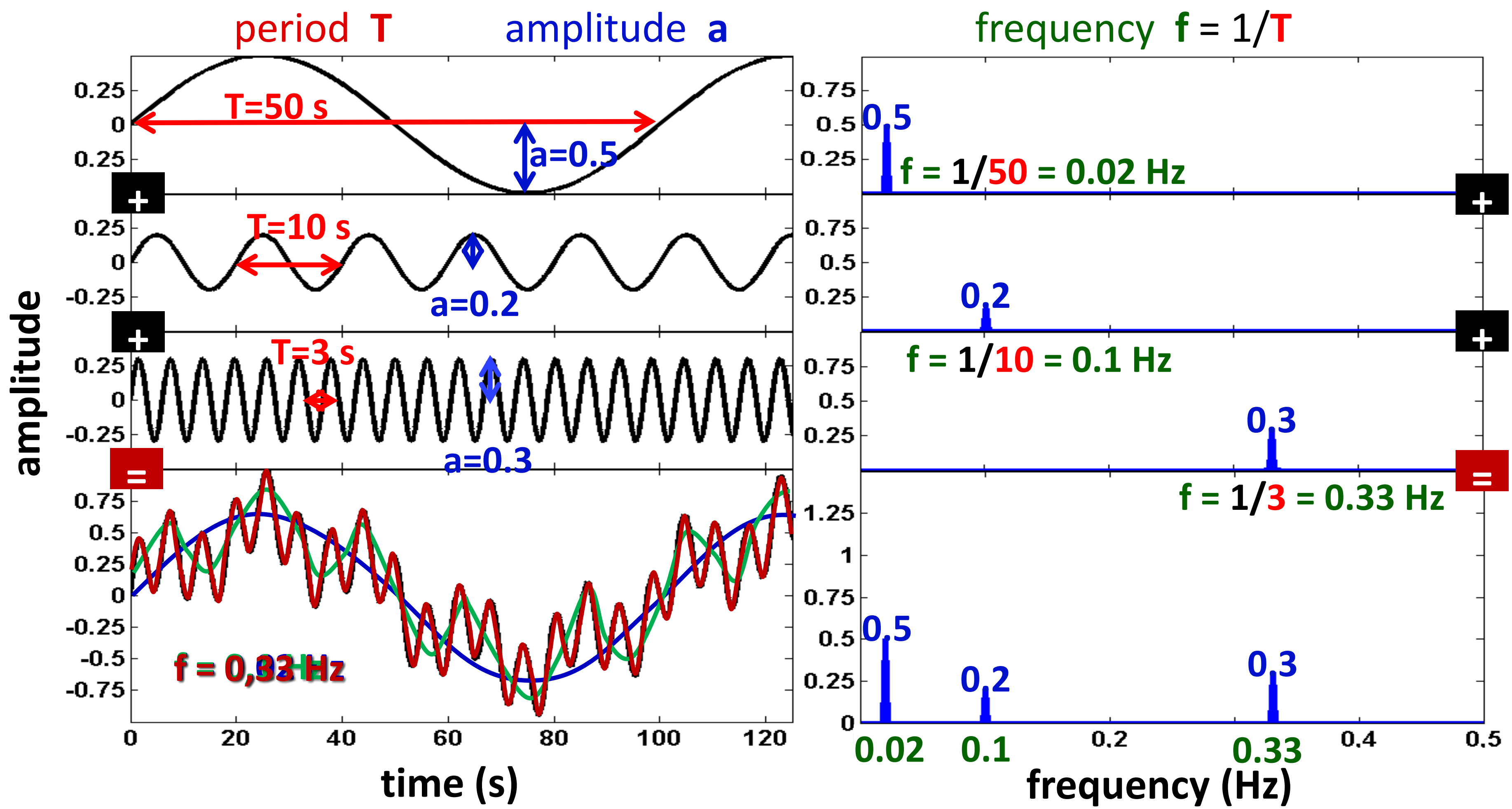




How the spectrum is formed?

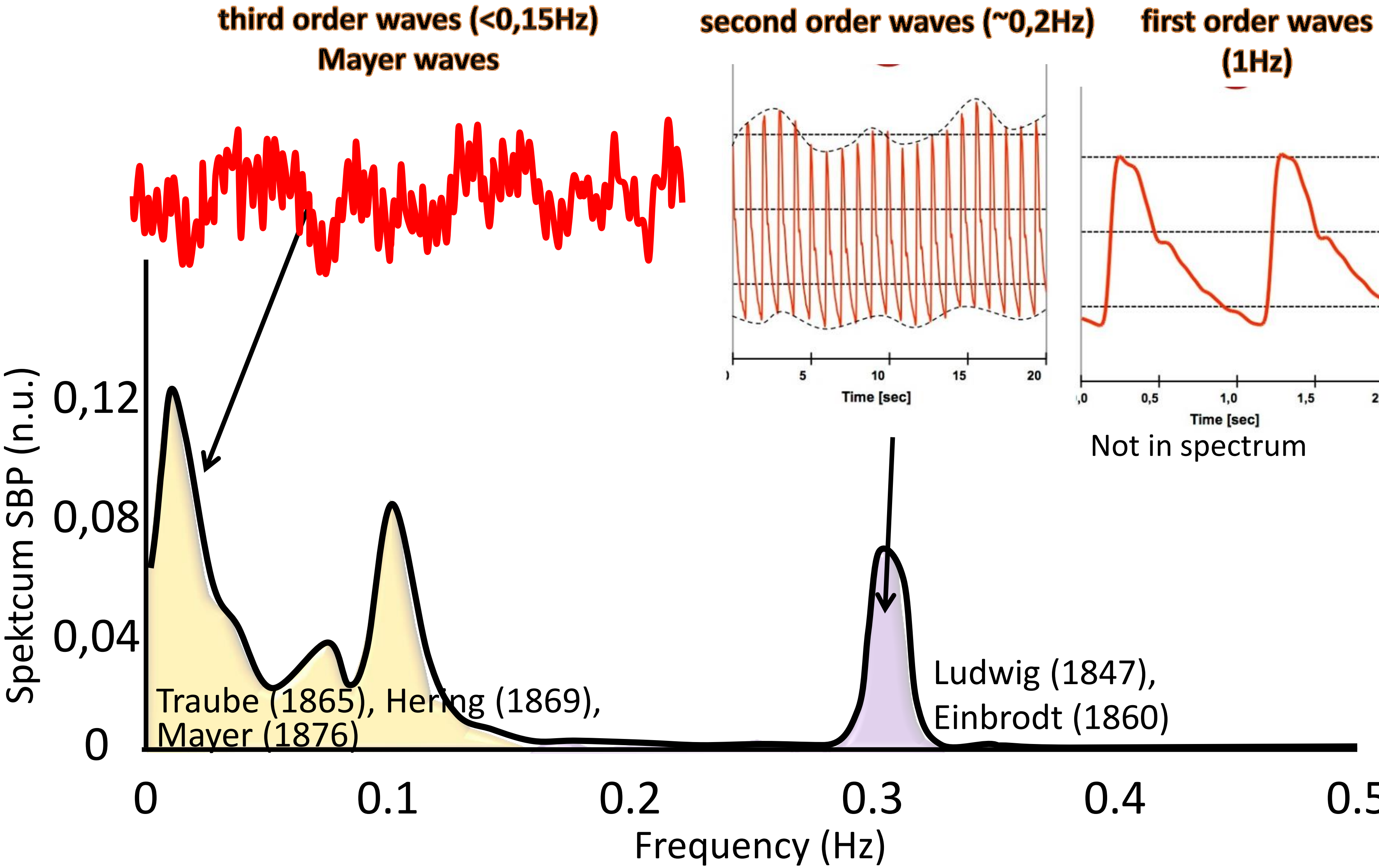
Time domain

Spectrum
Frequency domain



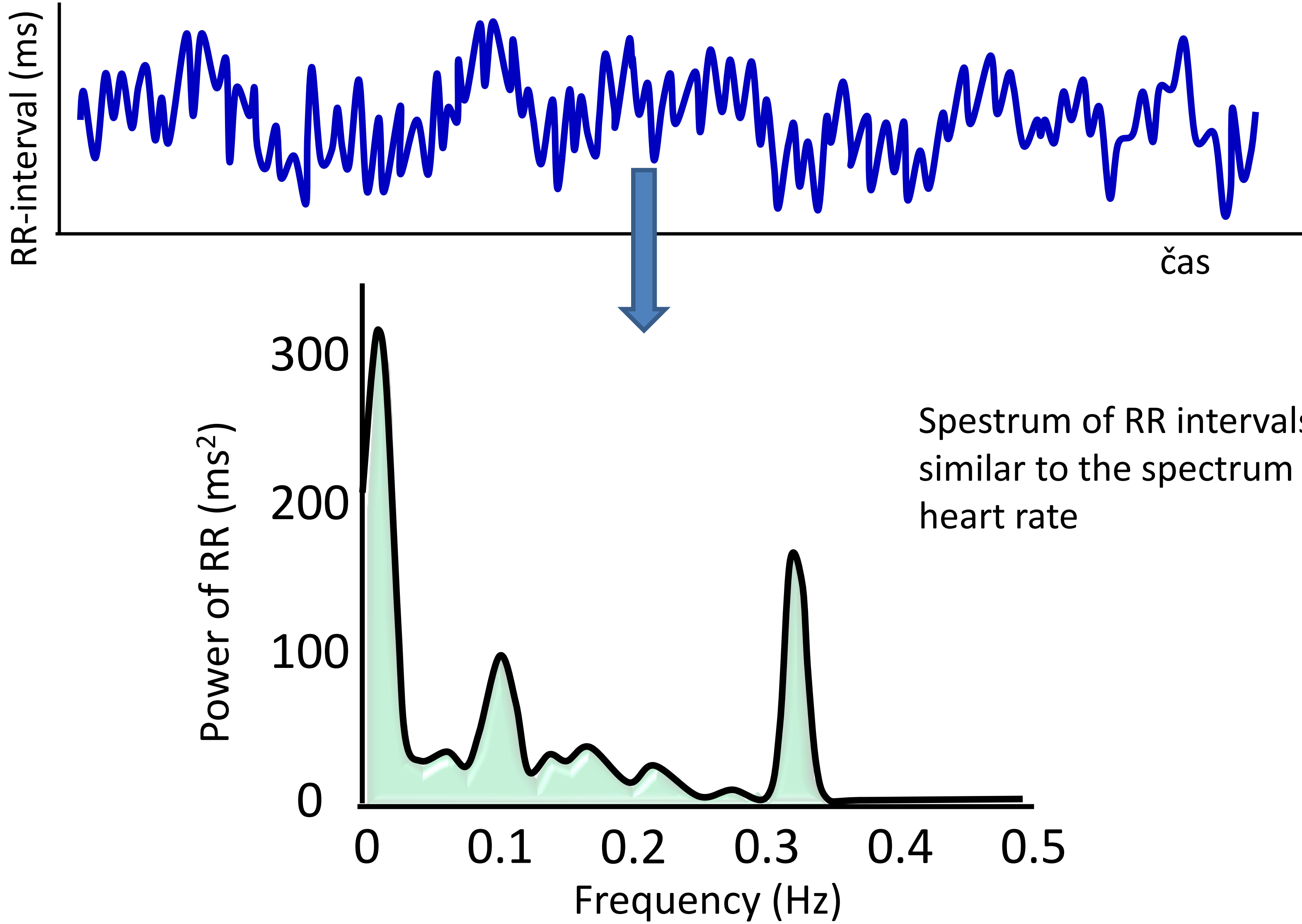
Blood pressure variability – spectrum of SBP

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



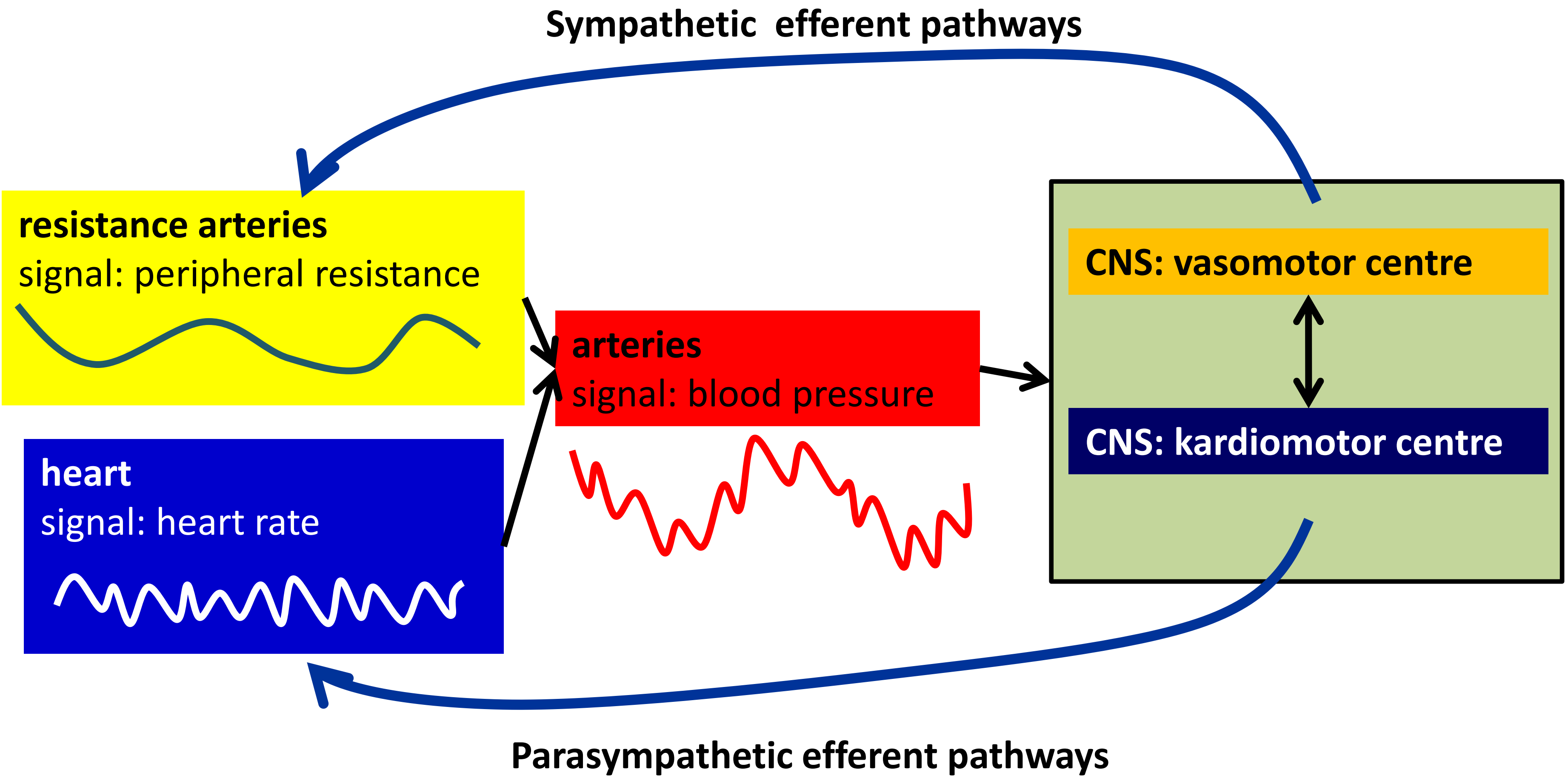
Heart rate variability (HRV)

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

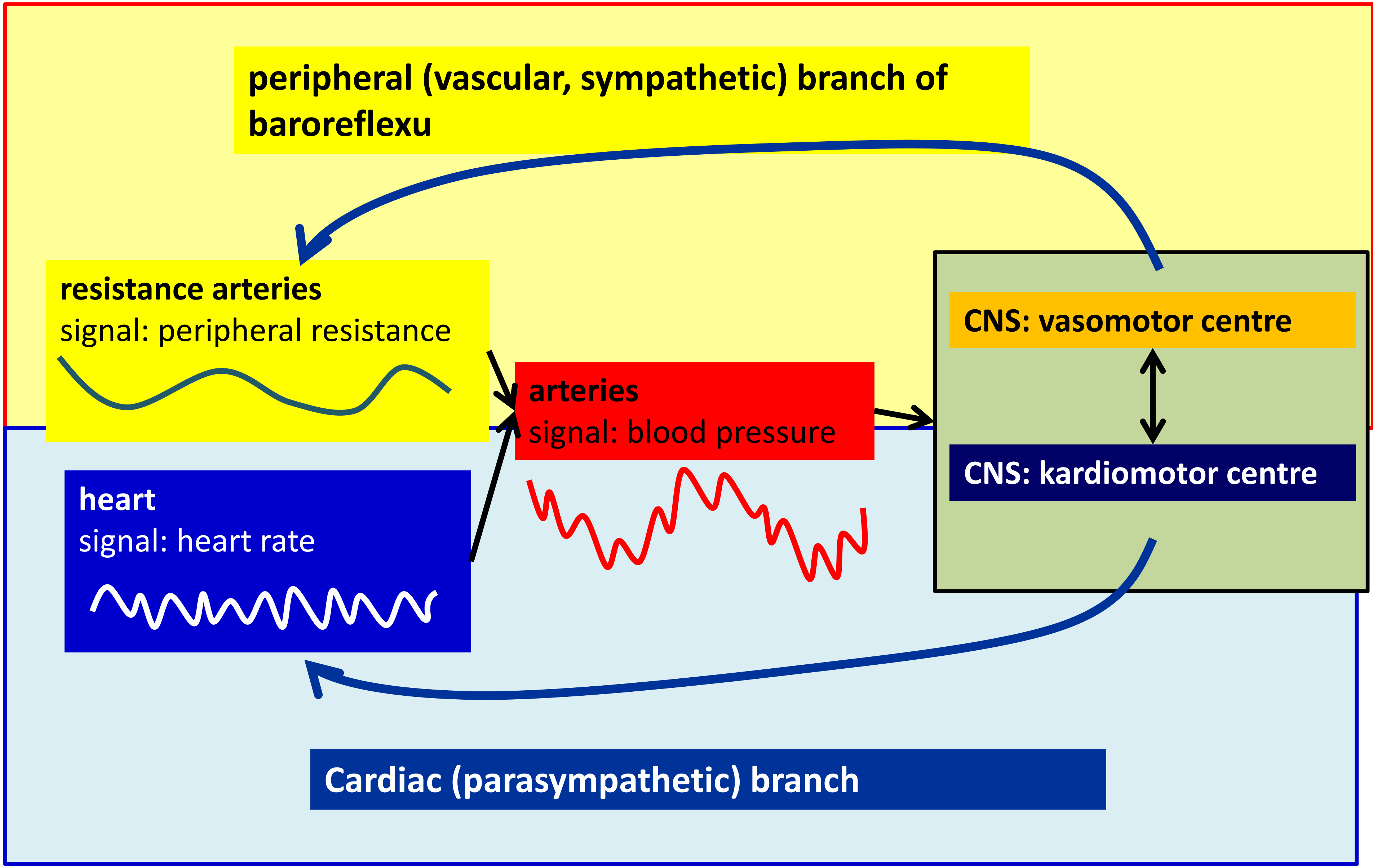


Spestrum of RR intervals is similar to the spectrum of heart rate

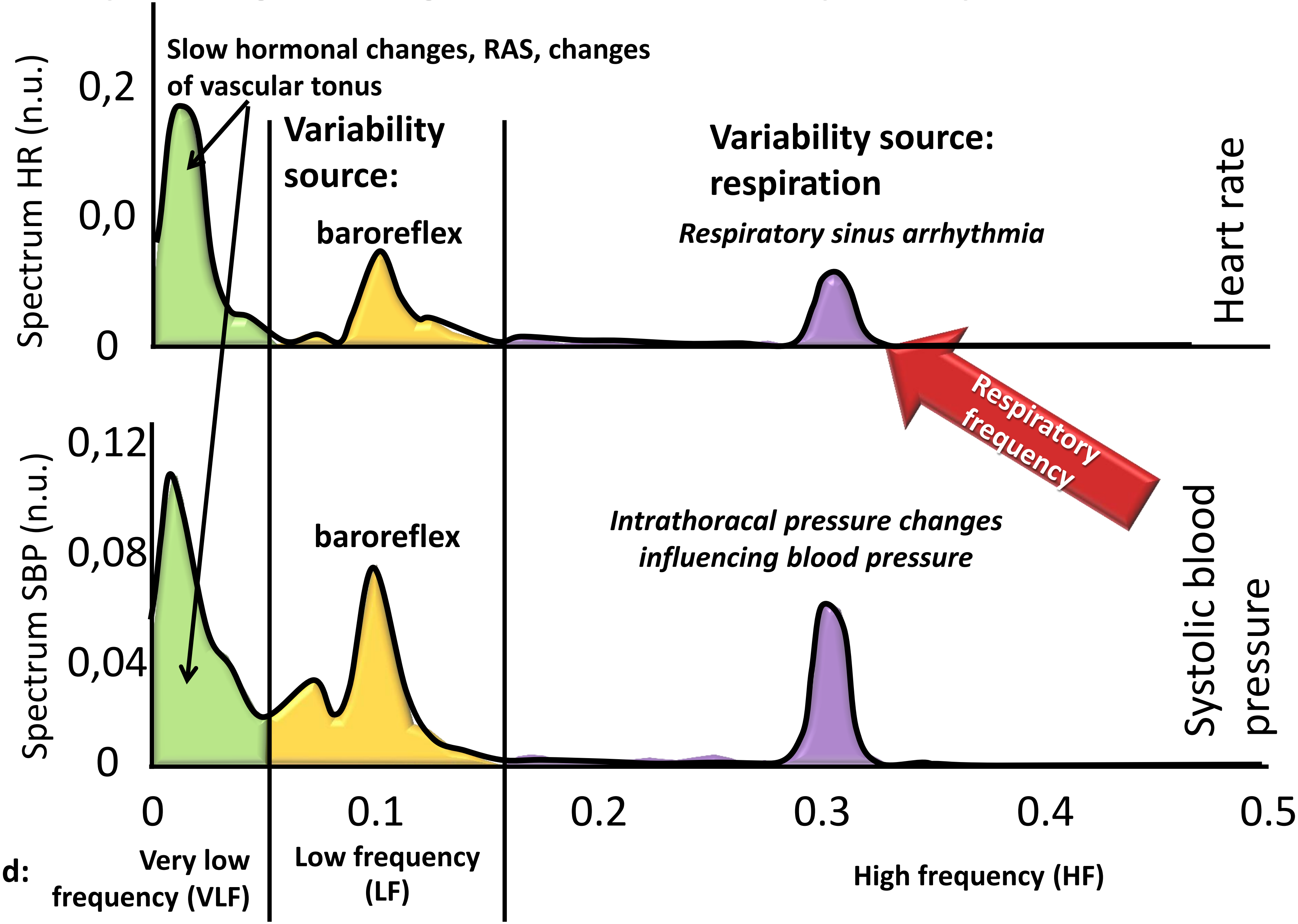
Baroreflex

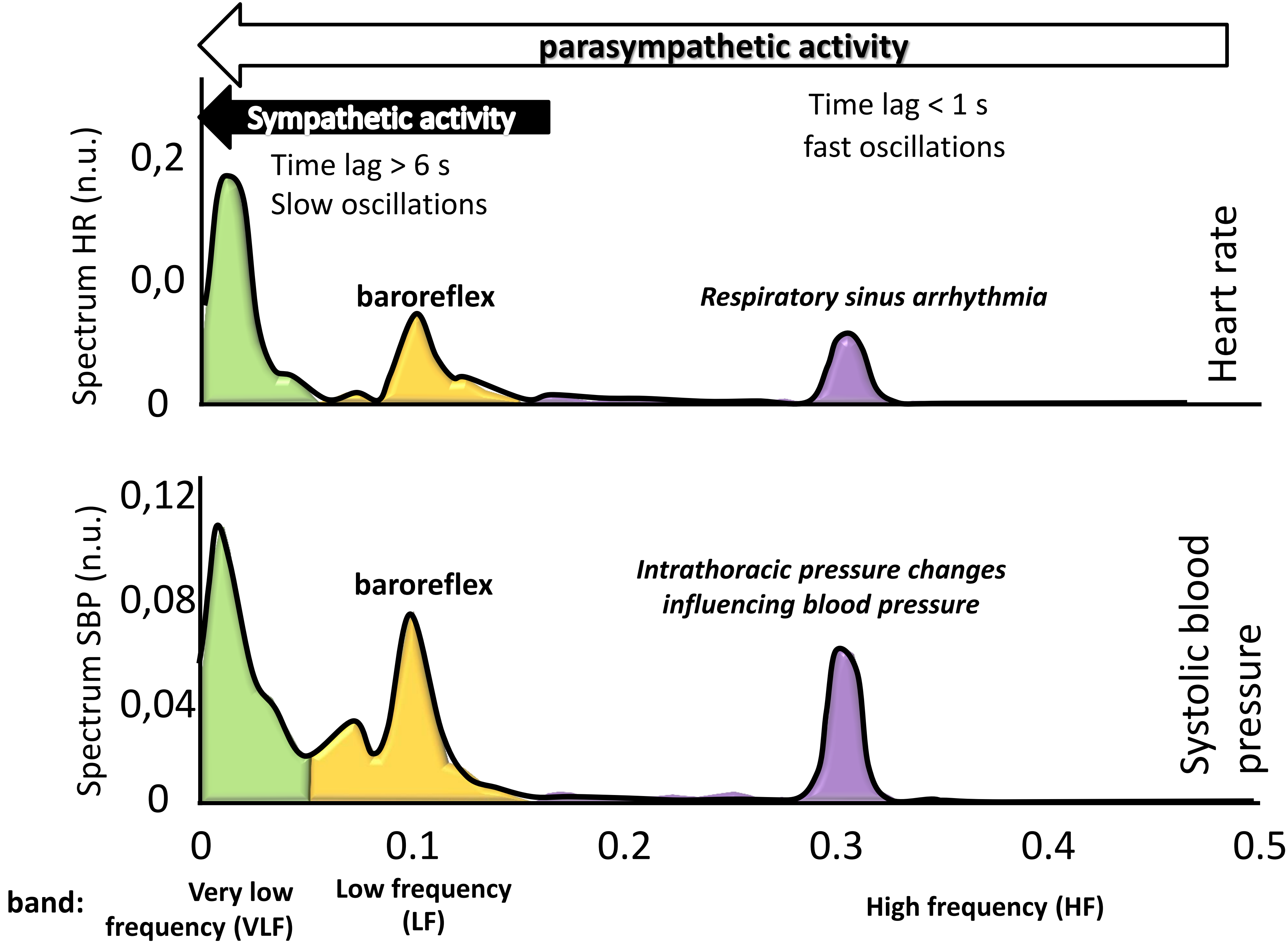

Sympathetic efferent pathways
resistance arteries
signal: peripheral resistance
heart
signal: heart rate
arteries
signal: blood pressure
CNS: vasomotor centre
CNS: kardiomotor centre
Parasympathetic efferent pathways

Baroreflex

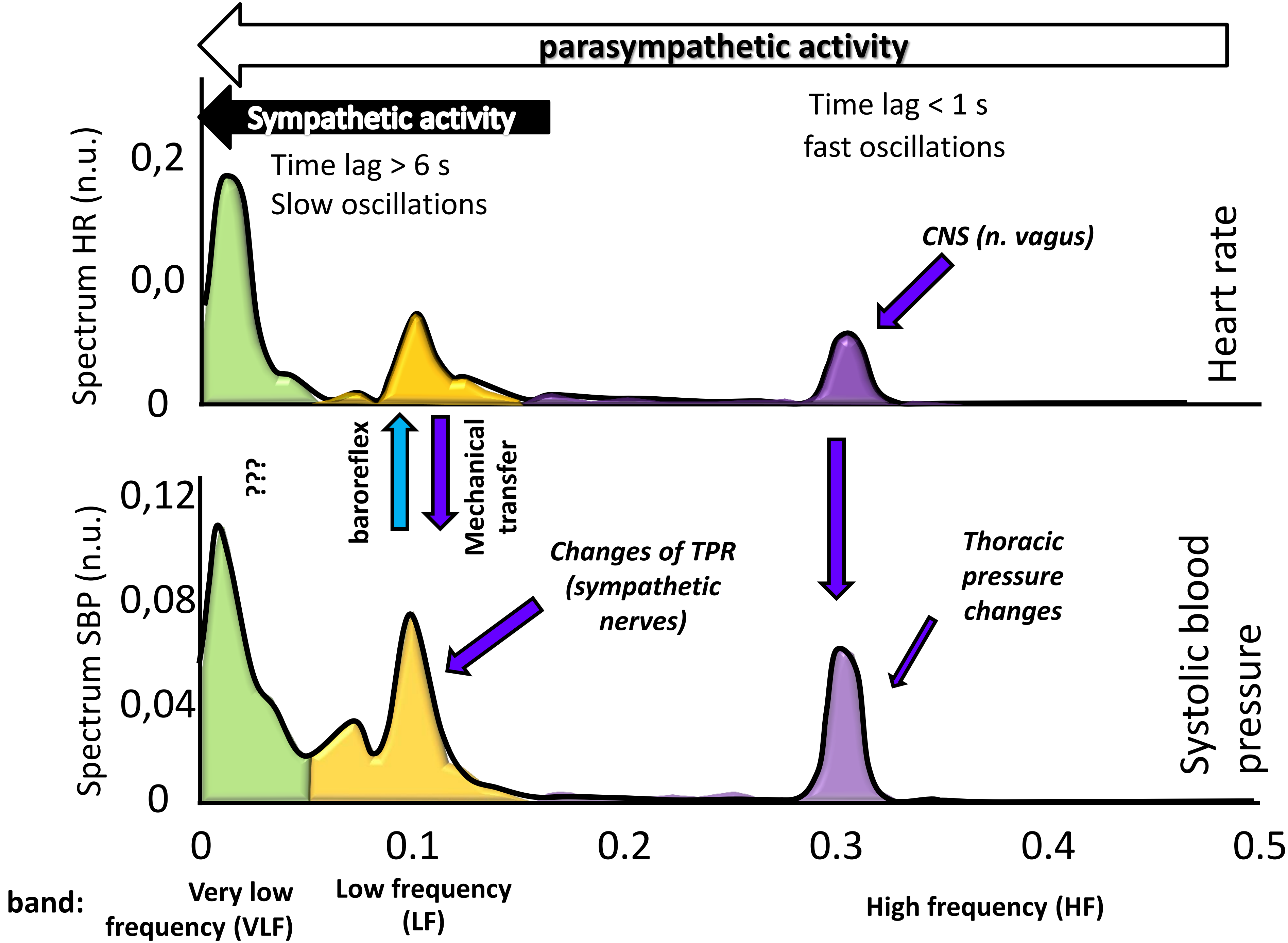

peripheral (vascular, sympathetic) branch of baroreflexu
resistance arteries
signal: peripheral resistance
arteries
signal: blood pressure
CNS: vasomotor centre
CNS: kardiomotor centre
heart
signal: heart rate
Cardiac (parasympathetic) branch

Physiological significance – frequency bands





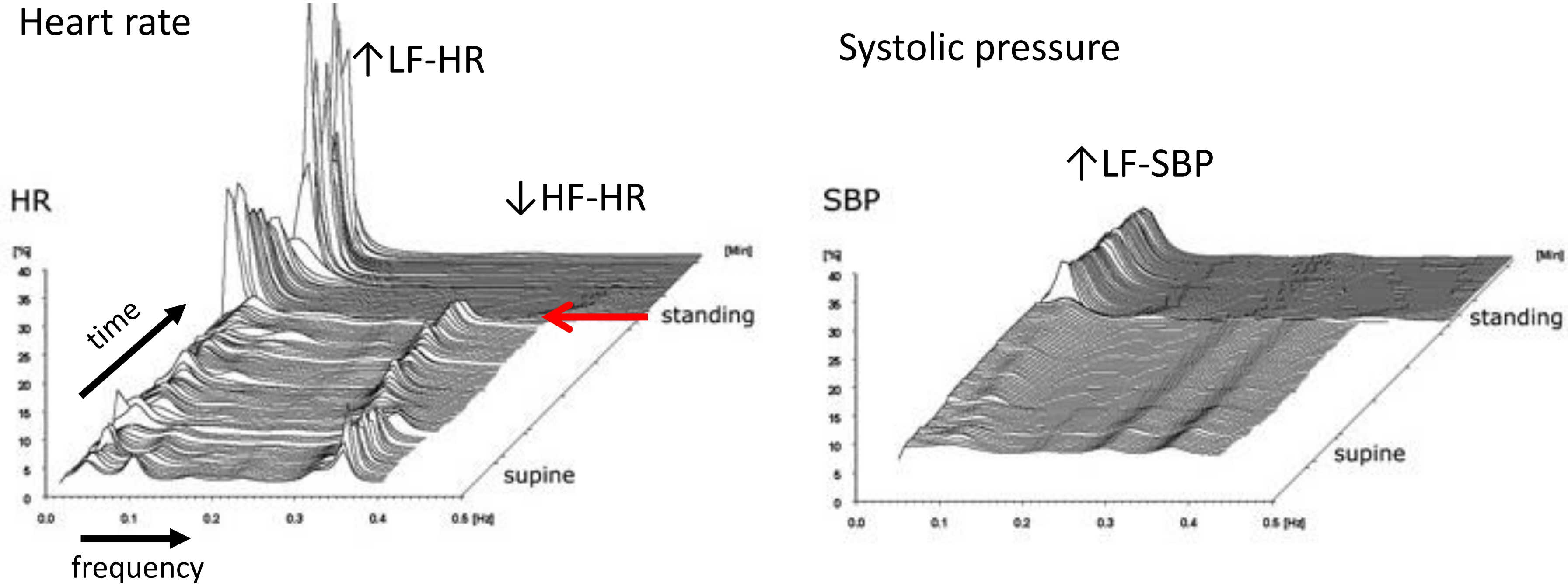
parasympathetic activity
Sympathetic activity
Time lag > 6 s
Slow oscillations
Time lag < 1 s
fast oscillations
Spectrum HR (n.u.)
0,2
0,0
0
baroreflex
Respiratory sinus arrhythmia
Heart rate
Spectrum SBP (n.u.)
0,12
0,08
0,04
0
baroreflex
Intrathoracic pressure changes
influencing blood pressure
Systolic blood
pressure
0
0.1
0.2
0.3
0.4
0.5
band:
Very low
frequency (VLF)
Low frequency
(LF)
High frequency (HF)



parasympathetic activity
Sympathetic activity
Time lag > 6 s
Slow oscillations
Time lag < 1 s
fast oscillations
CNS (n. vagus)
Heart rate
Spectrum HR (n.u.)
0,2
0,0
0
baroreflex
Mechanical transfer
???
Changes of TPR (sympathetic nerves)
Thoracic pressure changes
Systolic blood pressure
Spectrum SBP (n.u.)
0,12
0,08
0,04
0
0
0.1
0.2
0.3
0.4
0.5
band:
Very low frequency (VLF)
Low frequency (LF)
High frequency (HF)

Variability changes: orthostatic challenge

Sympatho-vagal ratio LF-HR/HF-HR

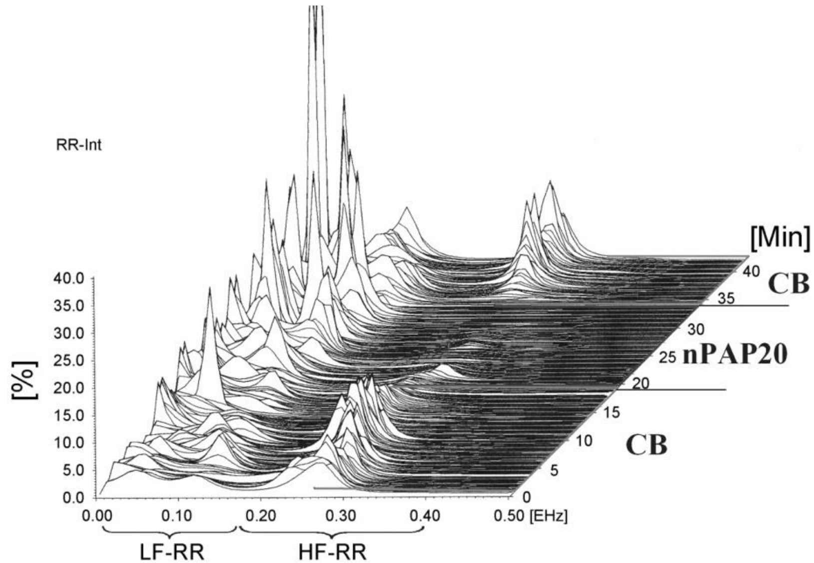


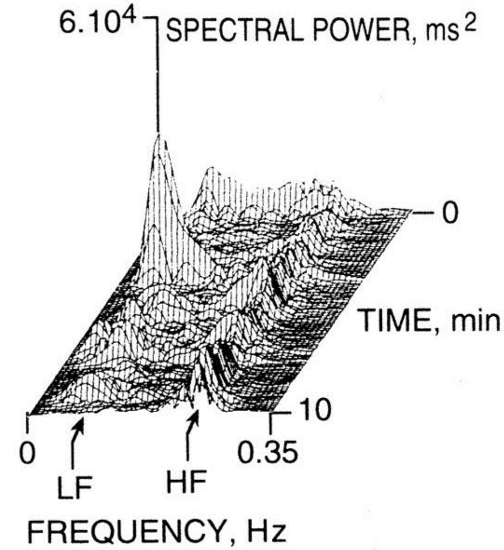
Orthostatic challenge:

- 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**

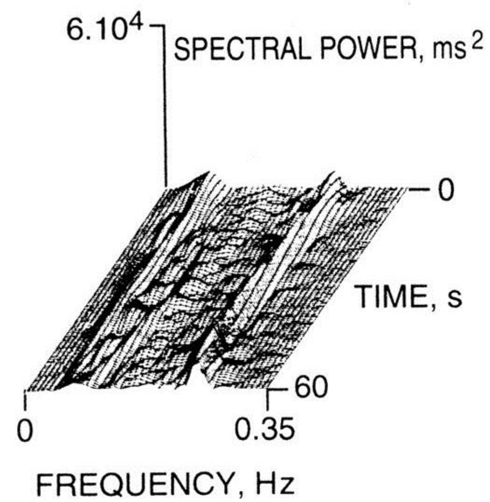
Heart rate variability (HRV) changes



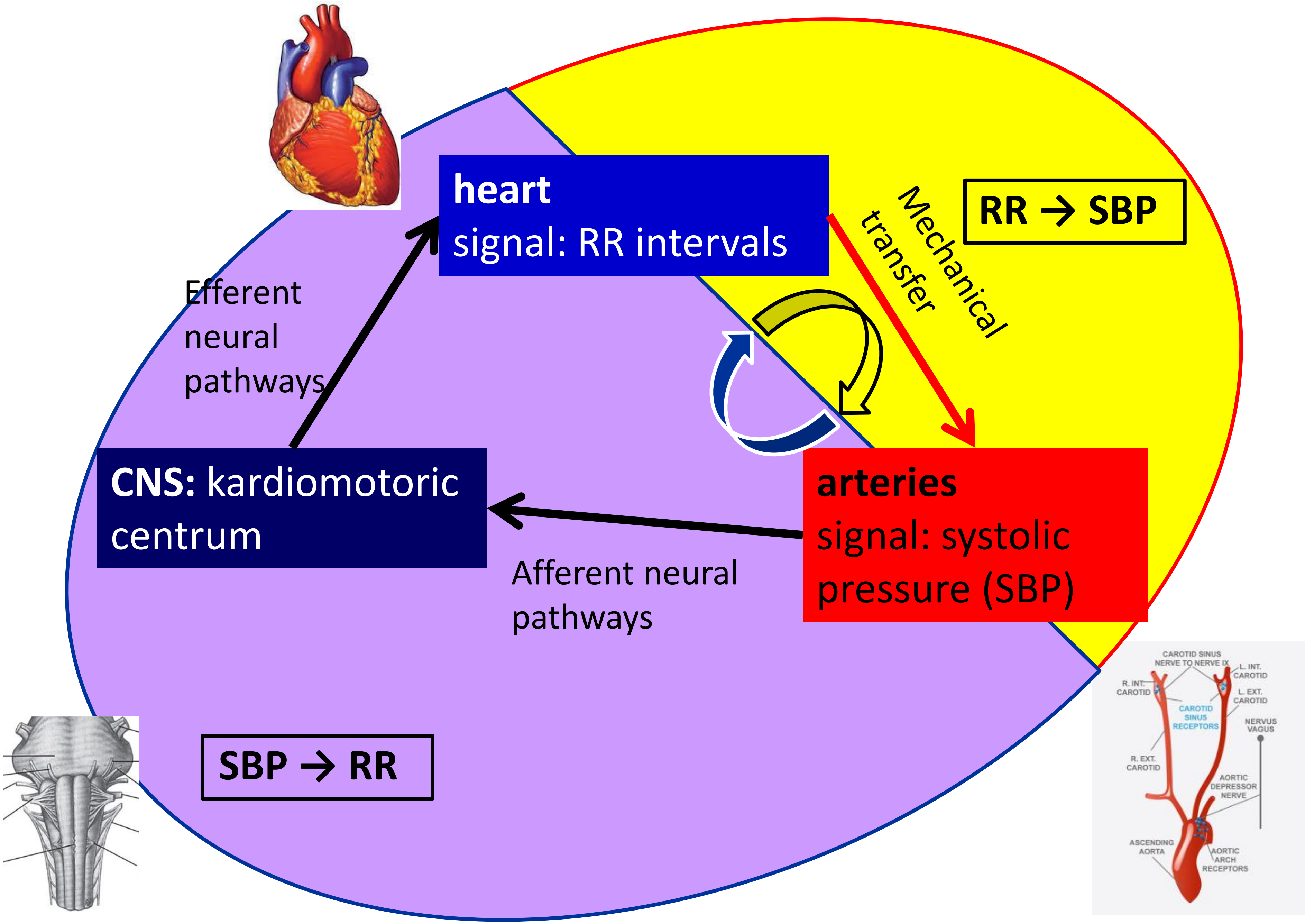


HRV in respiratory frequency decreases in stress situations (↑sympathetic activity)

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

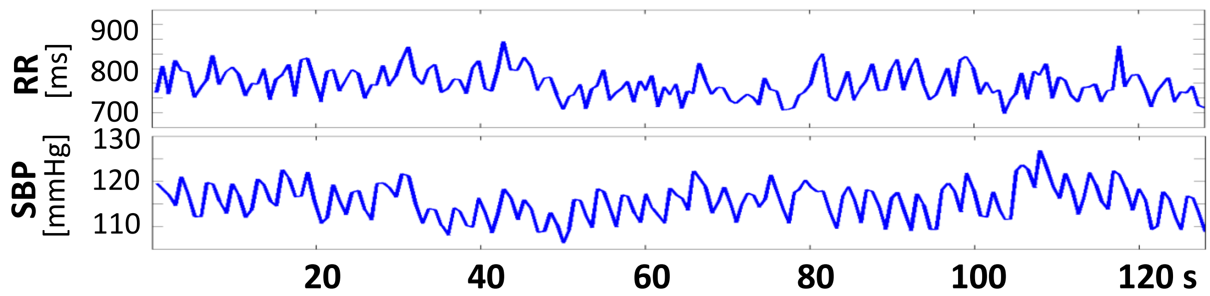


Evaluation of baroreflex function

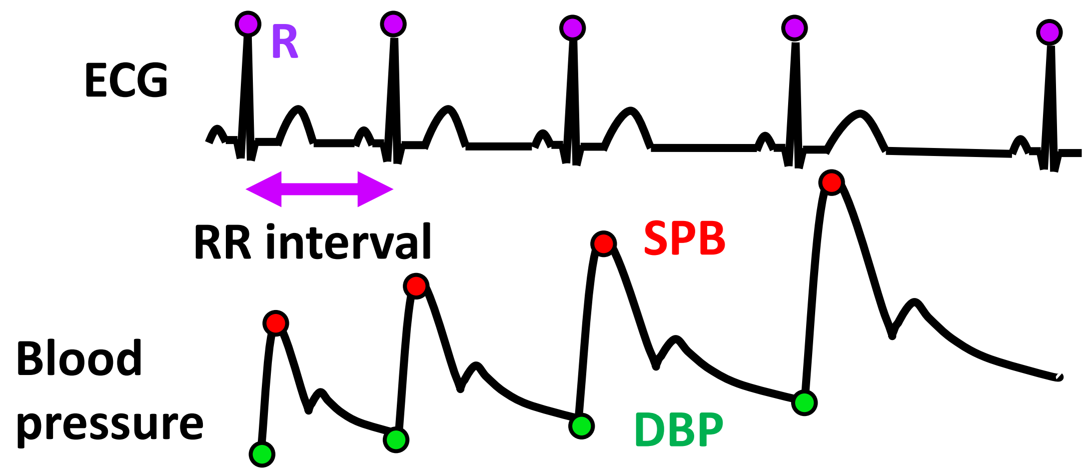


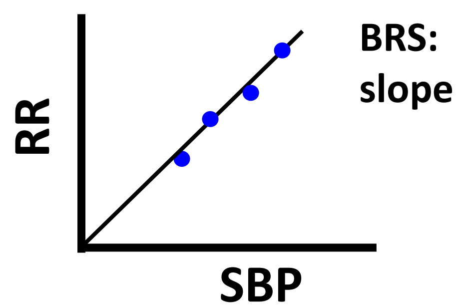
Baroreflex sensitivity (BRS)

Cardiac baroreflex can be evaluted 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:

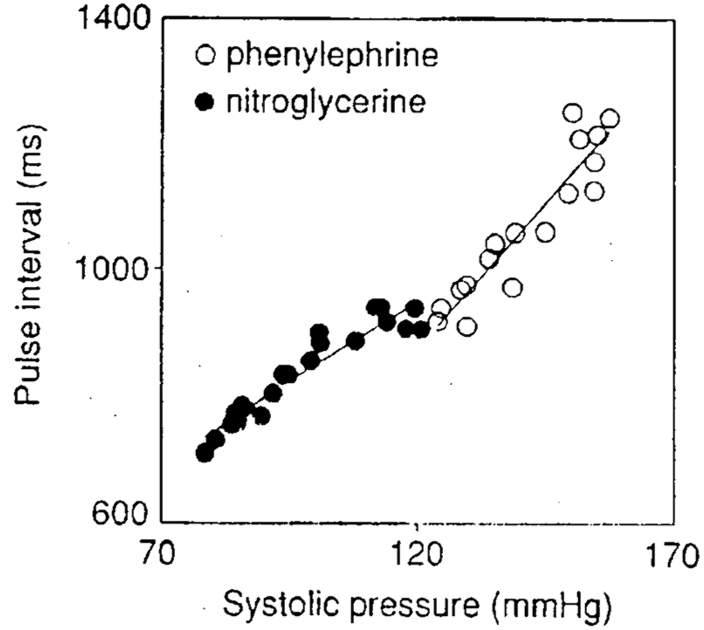
- Phenylephrin application (standard)
- neck suction
- Valsalva manoeuvre

Spontaneous methods:

in time domain: sequence analysis

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

Bolus injections of vasoactive drugs



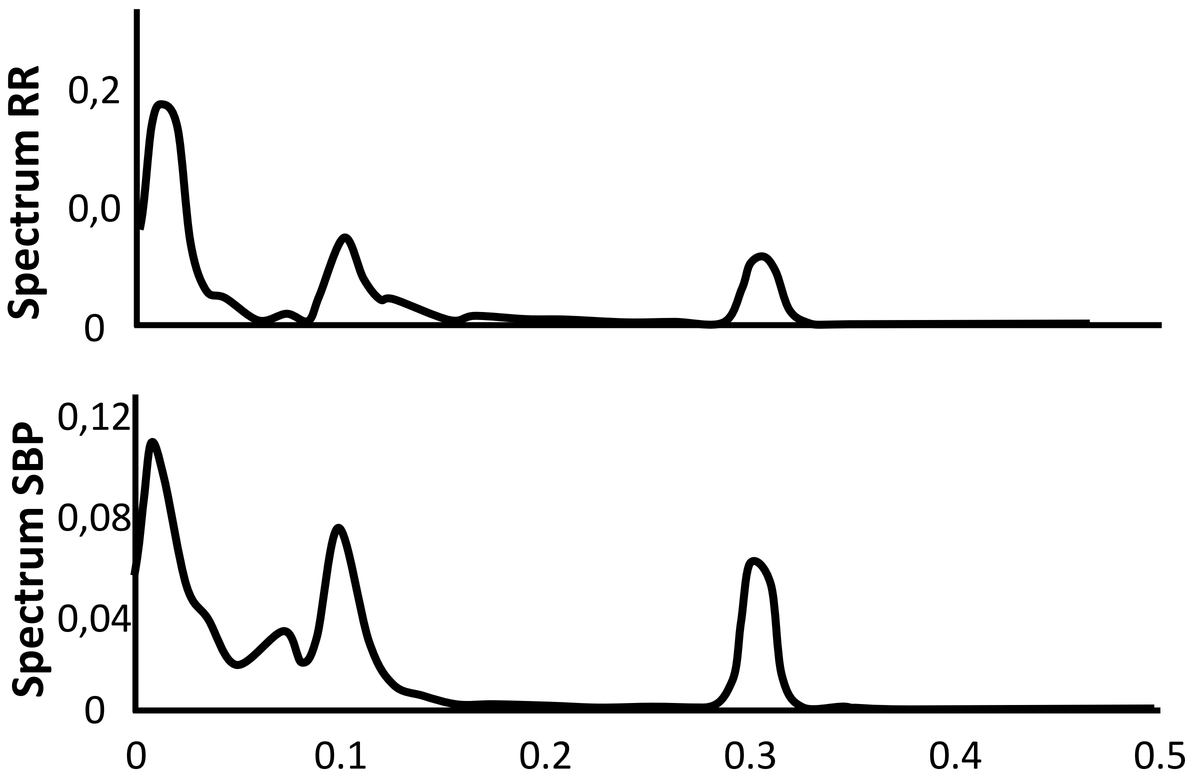
Spectral methods

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

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

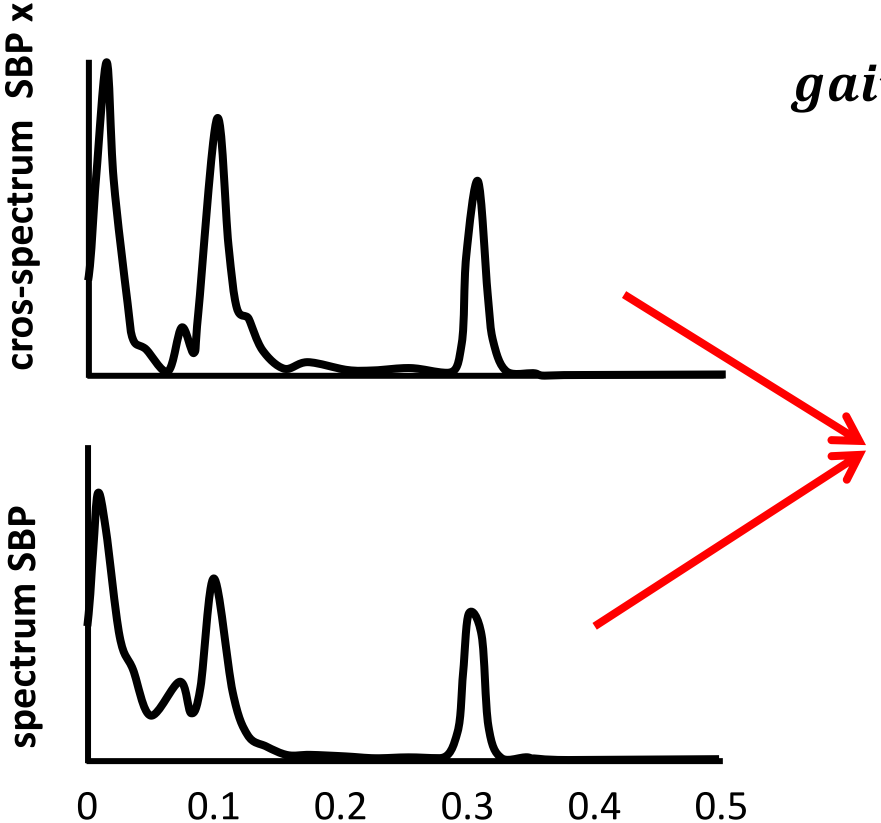
- Complication – not every oscillation in RR is caused by oscillation in SBP



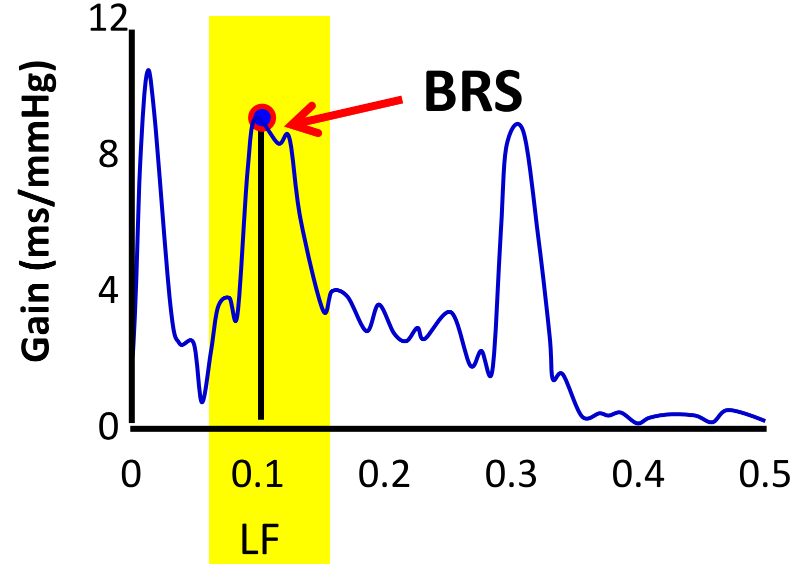
Spectral methods

Cross -spectrum RR and SBP:

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



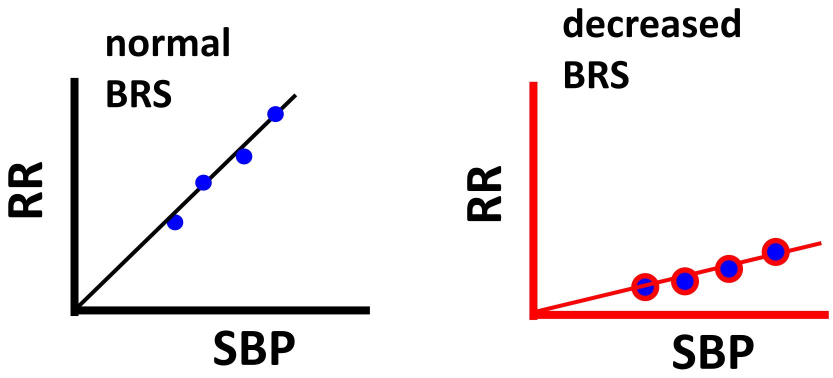
$$gain = \frac{cross - spectrum\ RR\ x\ SBP}{spectrum\ SBP}$$



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

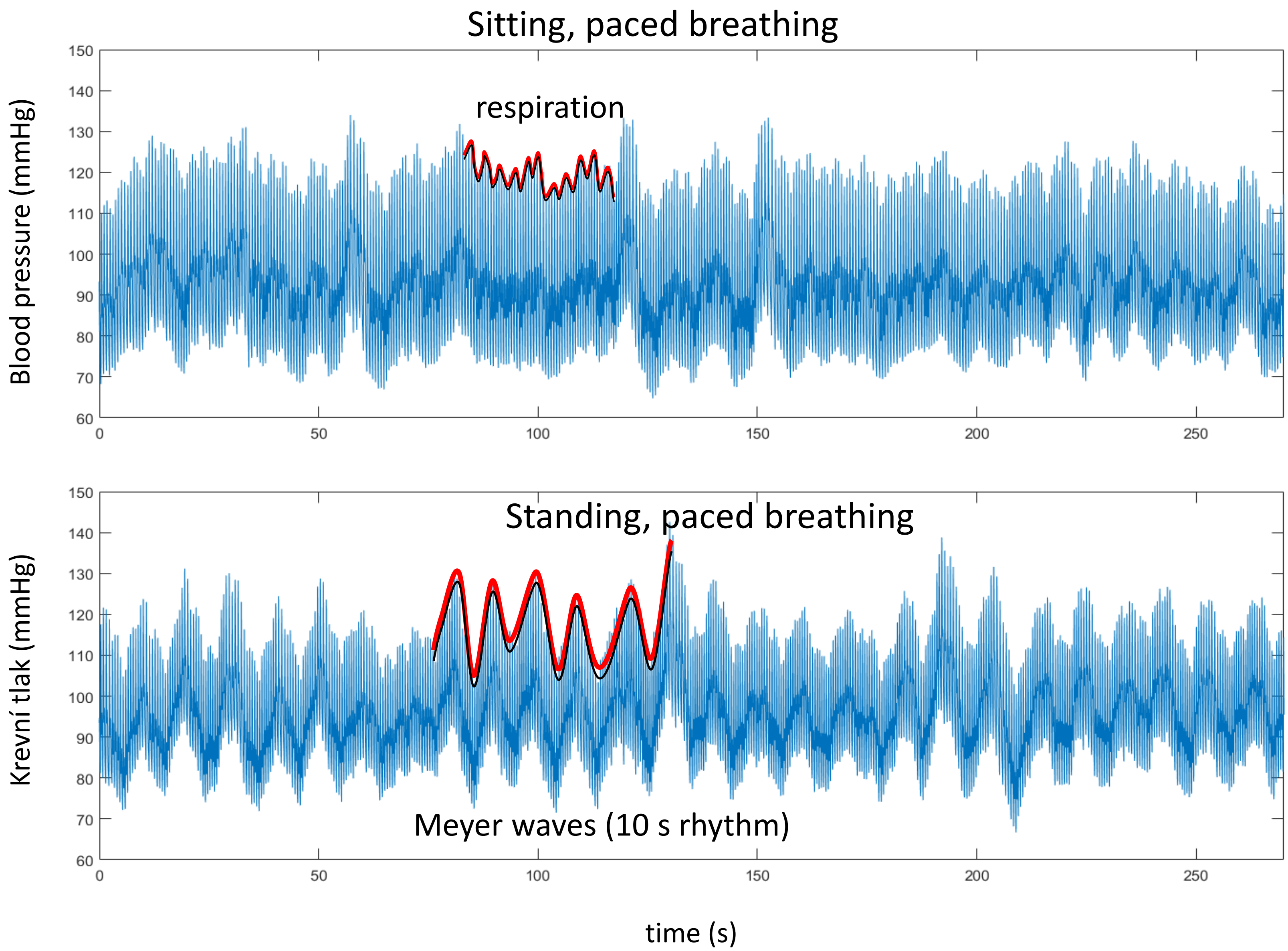
- Physiologically
  - psychic stress – increased sympathetic activity
  - Physical exercise – increased sympathetic activity
  - In old age

- 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

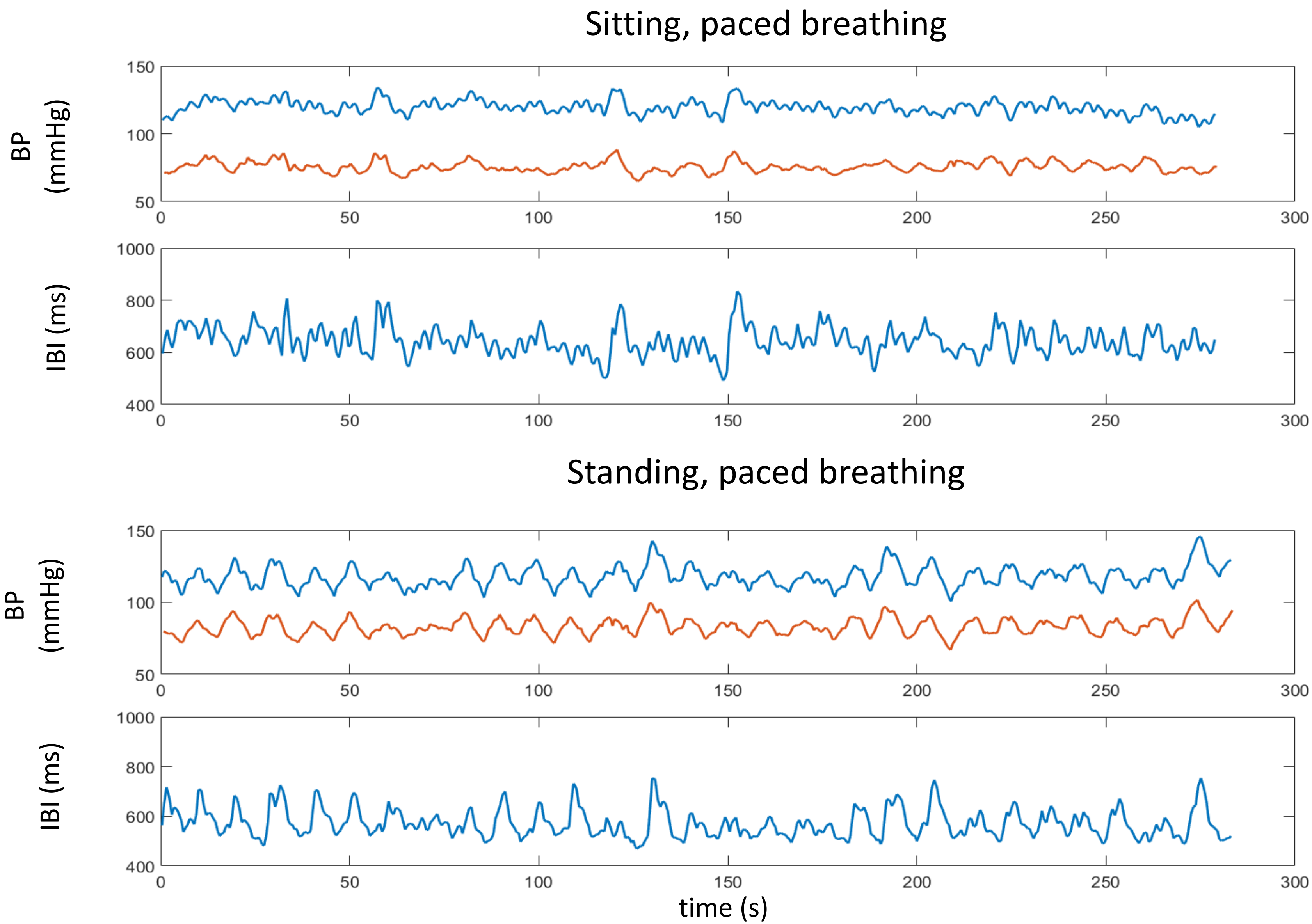
Disadvantages of methods

- Only sinus rhythm without ectopic beats can be analysed
- 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

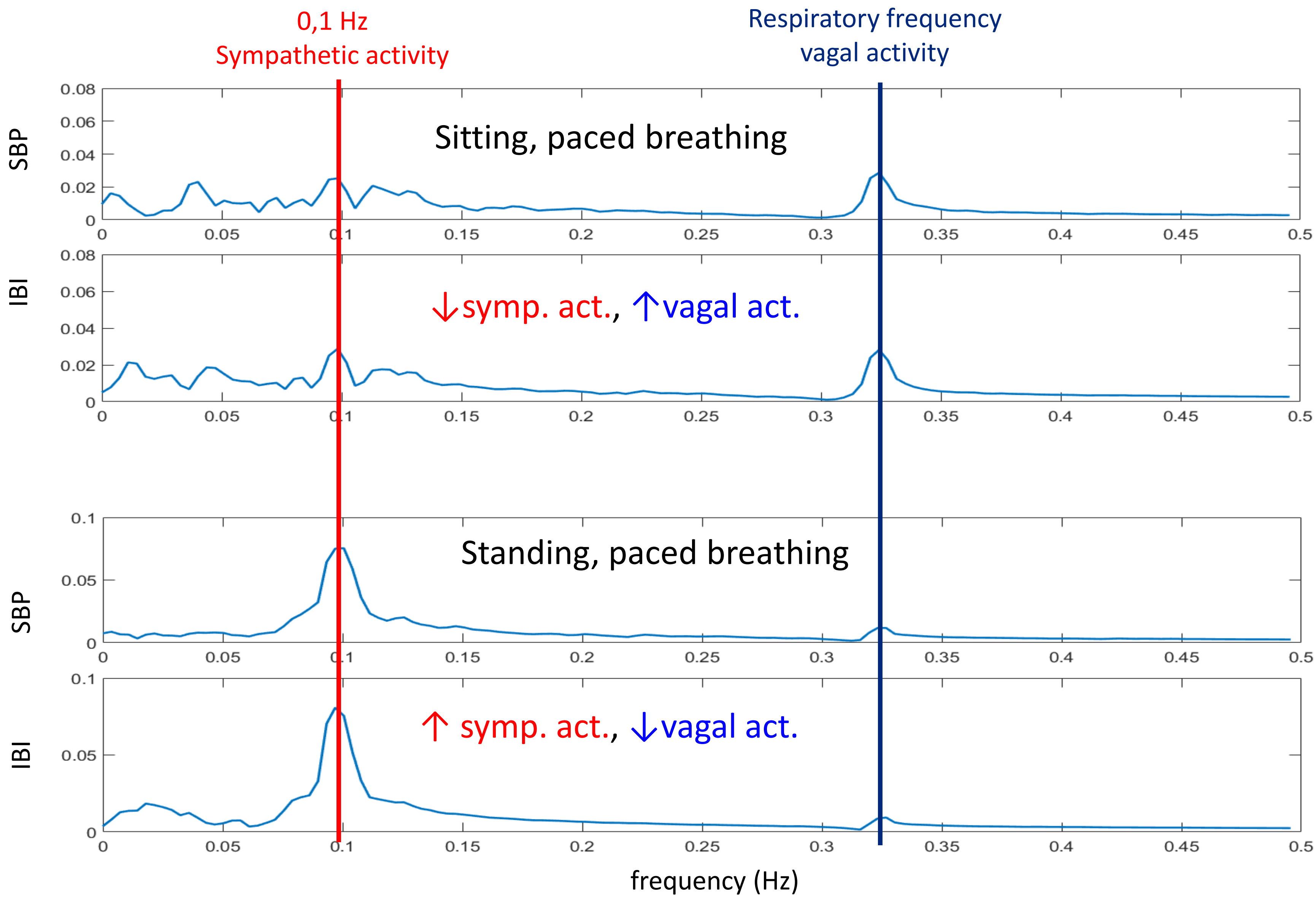
Blood pressure signal (270 s) - example



sequentions of SBP, DBP and inter-beat intervals (IBI) - example

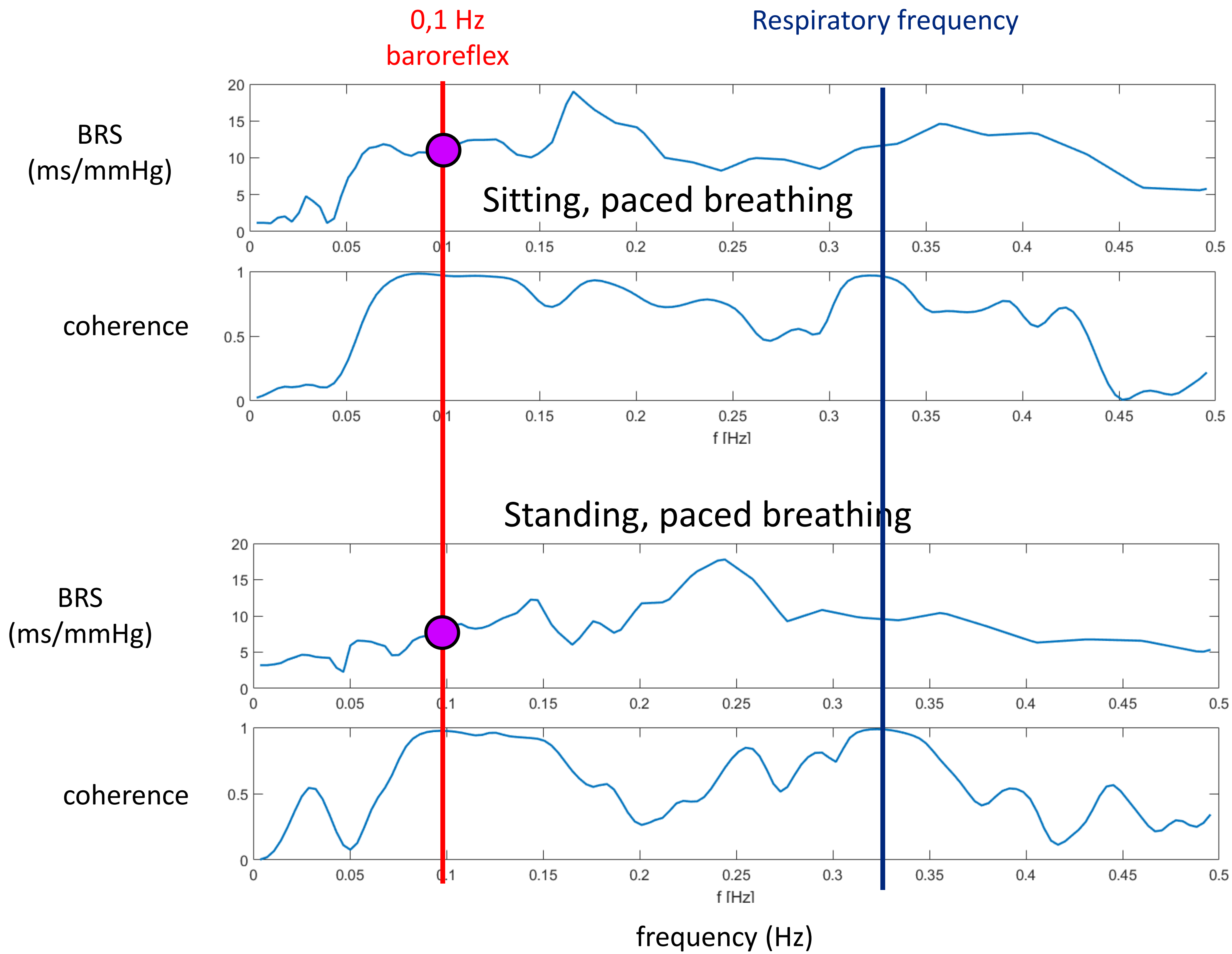


Spectra of SBP and IBI - example



Coherence a BRS - example

coherence: synchronization between signals (correlation on particular frequency)



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)
  - increased – 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 od sudden cardiac death: zero values of BRS and HRV
- Spectra RR and SBP
  - Frequency bands (VLF, LF a HF)
    - HF (0.15-0,5Hz): parasympathetic activity, respiration
    - LF (around 0,1 Hz): sympathetic/parasym. activity, baroreflex
    - VLF (< 0,03): low changes in vascular system (hormones, TPR, RAS,…)

Thank you

Thank you