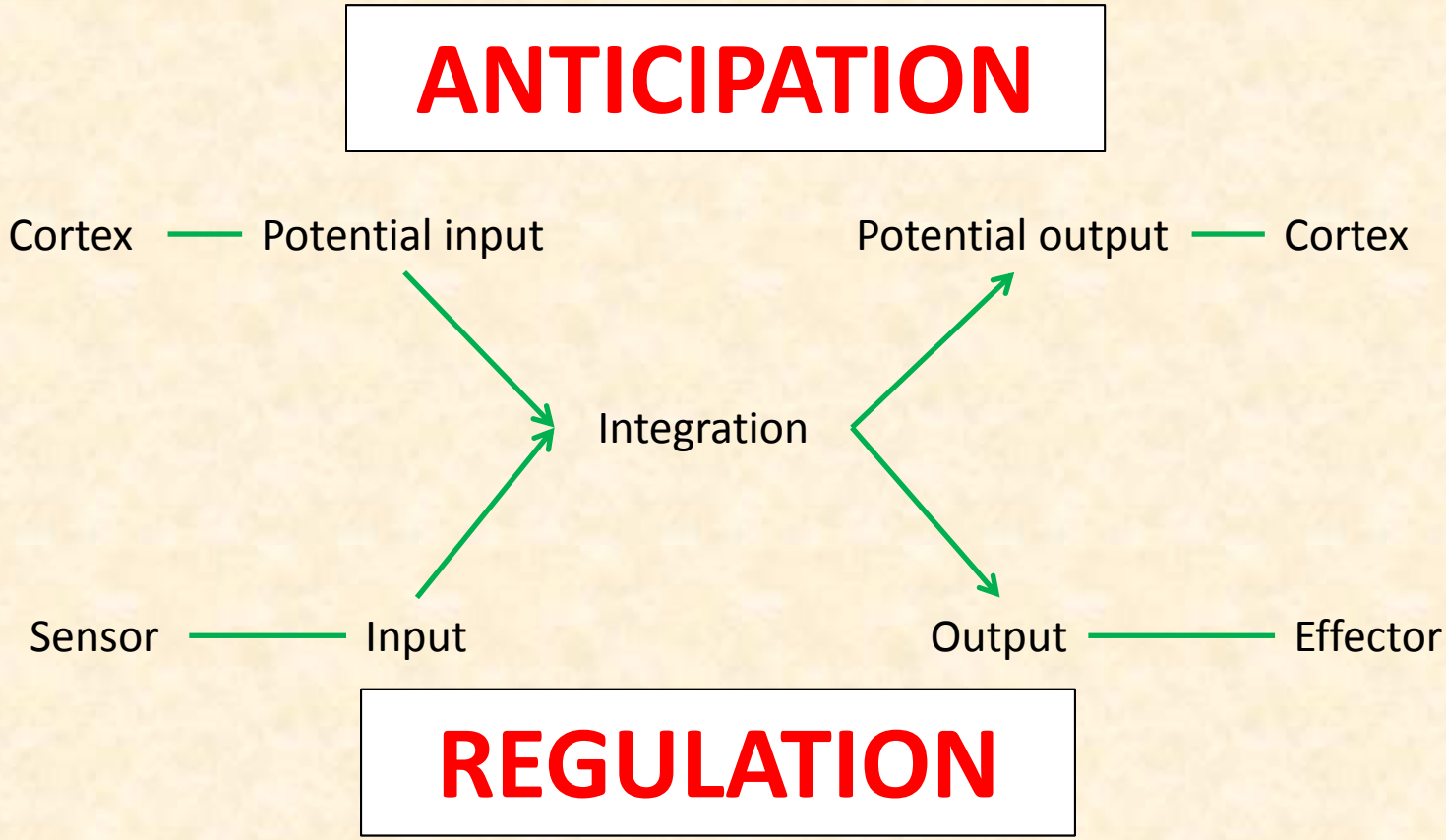
Regulation

in cardiovascular system

The role of nervous system



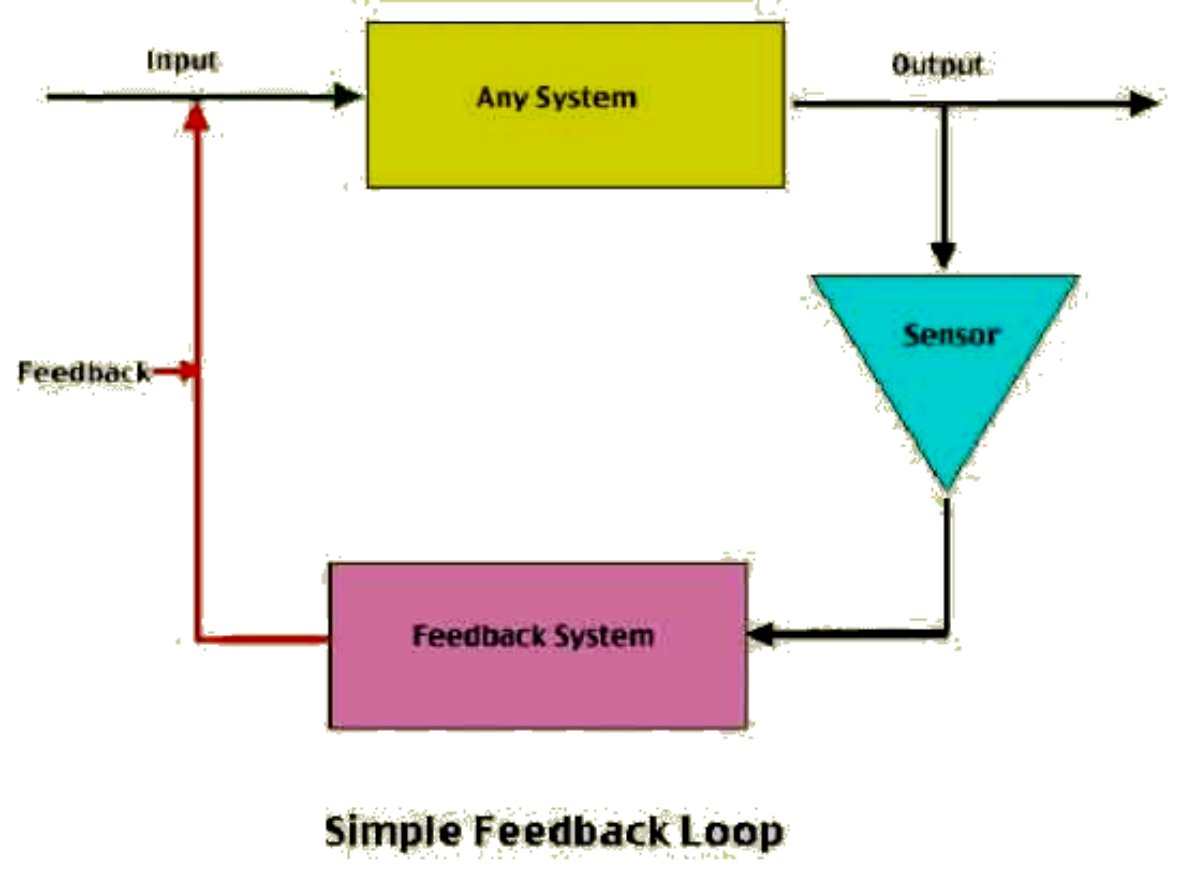
Types of regulation - general view

2 basic types:

- ✓ Nervous regulation
- ✓ Humoral regulation
  - ✓ Feedback control - negative
  - ✓ - positive

autoregulation – local regulation – system regulation

Feedback regulation



http://www.slideshare.net/drpsdeb/presentations

REGULATION IN CARDIOVASCULAR SYSTEM

Main function:

- keep relatively constantaneous arterial blood pressure
- Keep perfusion of tissues

Regulation of vessels tone

- Tone of the vessels = basic tension of the smooth muscle inside of the wall

  (vasoconstriction x vasodilatation)

- Regulation - local autoregulation

  - system regulation

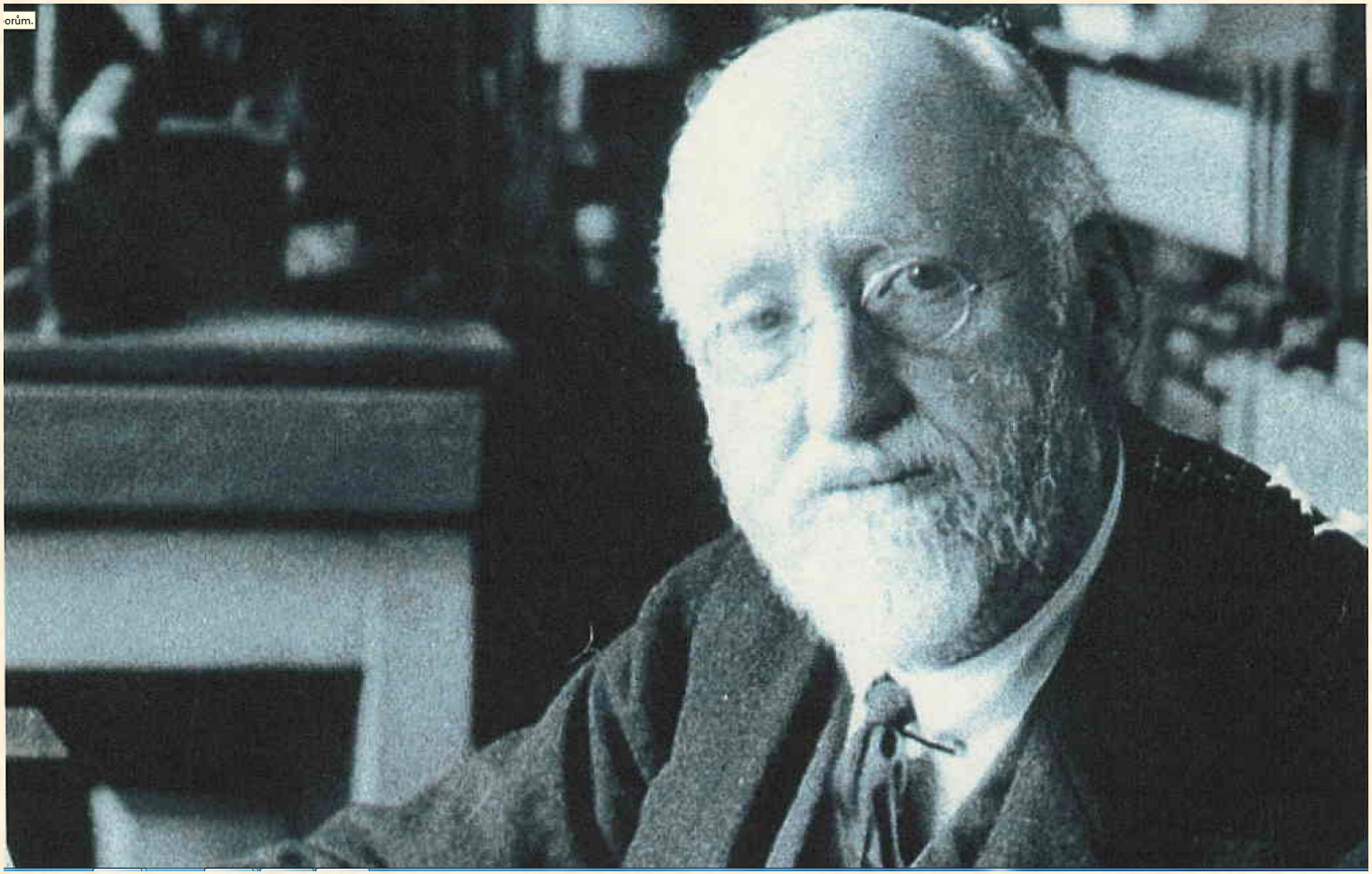
Autoregulation

Autoregulation – the capacity of tissues to regulate their own blood flow

Myogenic theory – Bayliss phenomenon (as the pressure rises, the blood vessels are distended and the vascular smooth muscle fibres that surround the vessels contract; the wall tension is proportional to the distending pressure times the radius of the vessels – law of Laplace:

T=P x r)

orům.



Autoregulation

- **Metabolic theory** – vasodilator substances tend to accumulate in active tissue, and these metabolites also contribute to autoregulation
  - ending products of energetic metabolism – CO_2, lactate acid, K^+
  - effect of hypoxia (circulation: vasodilatation x pulmonary circulation: vasoconstriction)
  - Adenosin – coronary circulation: vasodilatation

Autoregulation

- **by substances which releasing from:**
  - endothelium
  - tissues

Substances secreted by the ENDOTHELIUM

Vasodilatation:

Nitric oxide (NO) from endothelial cells
(originally called: EDRF)

Prostacyclin is produced by endothelial cells

Vazoconstriction:

Endothelins (polypeptids – 21peptides)

three isopeptides: ET 1, ET 2 , ET 3

Substances secreted by the tissues:

Histamine – primarily tissue hormones.

General affect: vasodilatation - decrease periphery resistence, blood pressure

KININS: 2 related vasodilated peptides

Bradykinin + lysylbradykinin (kallidin).

Sweat glands, salivary glands

10x strongers than histamine

Relaxation of smooth muscle, decrease blood pressure

Systemic regulation

By hormones

Catecholamines – epinephrine, norepinephrine
- effect as activation of sympathetic system

RAAS - stress situation

ADH - general vasoconstriction

Natriuretic hormones - vasodilatation

Neural regulatory mechanism

Autonomic nervous system

Sympathetic: vasoconstriction

All blood vessels except capillaries and venules contain smooth muscle and receive motor nerve fibers from sympathetic division of ANS (noradrenergic fibers)

- Regulation of tissue blood flow
- Regulation of blood pressure

Parasympathetic part: vasodilatation

Only sacral parasympathetic cholinergic fibres (Ach) inervated arteriols from external sex organs

Sympathetic nervous system

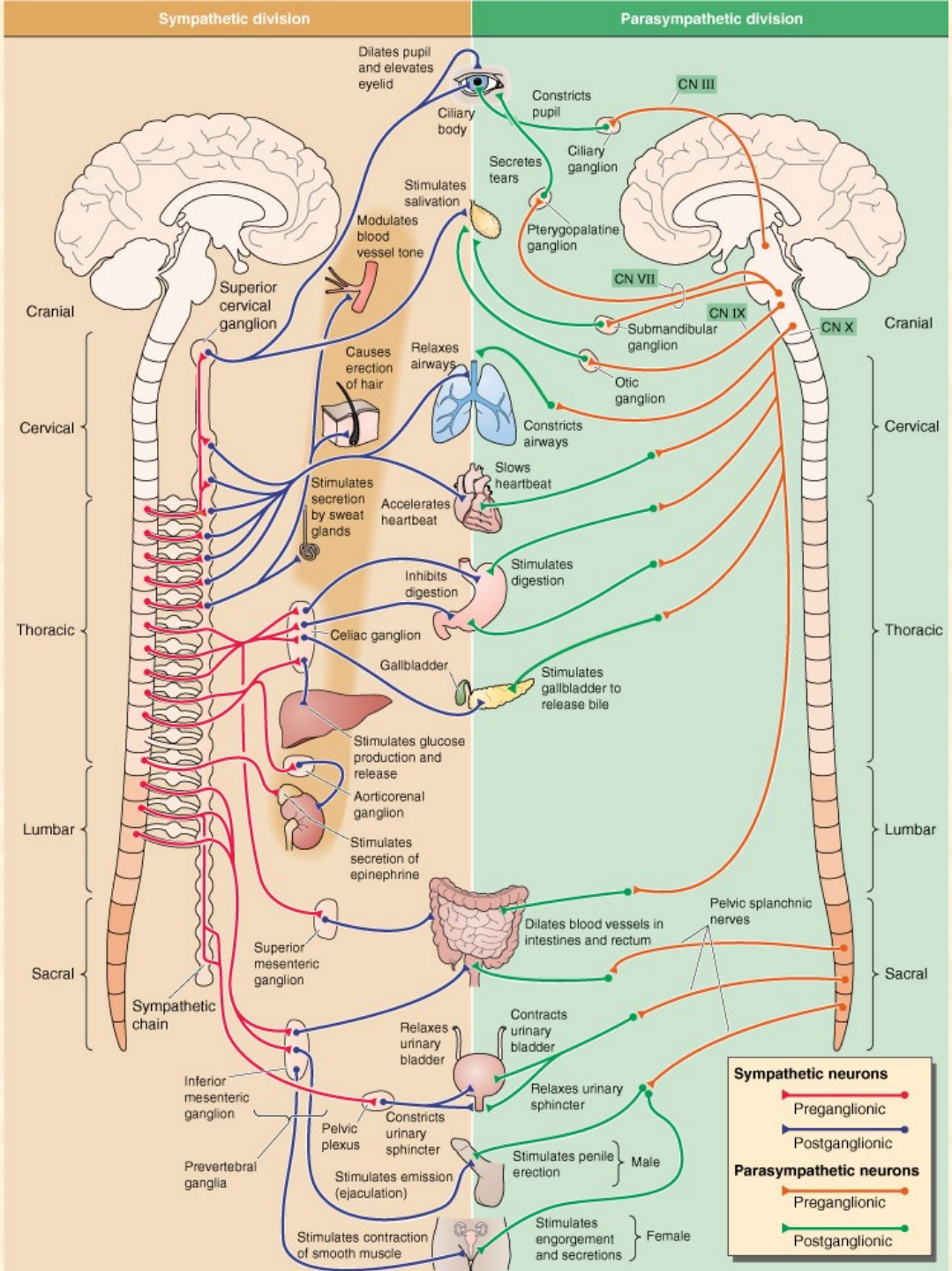
Fight or flight response

Energy/store consumption

Preganglionic neuron
– Spinal cord
-Thoraco - lumbar system

Ganglia
Paravertebral
-Truncus sympathicus
- Majority
Prevertebral
-Plexus aorticus

Mostly diffuse effect



Parasympathetic nervous system

Rest and digest response

Energy conservation/en. store production

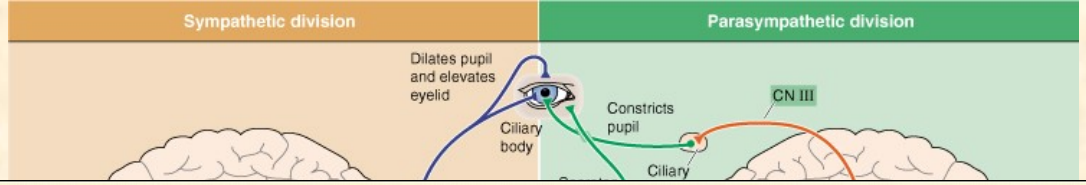
Preganglionic neuron
– Brain stem and spinal cord
– cranio-sacral system

Ganglia
Close to target organs or intramurally

Mostly local effect

Sympatthetic nervous system

Parasympathetic nervous system



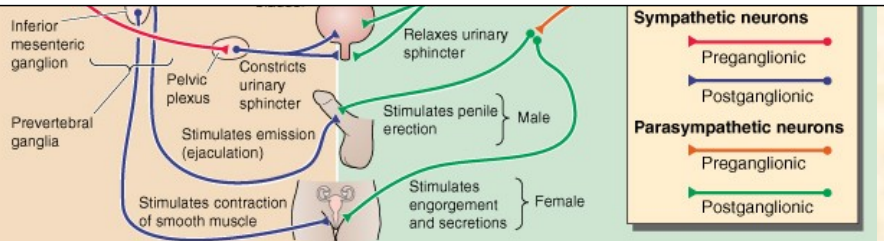
System/function	Parasympathetic	Sympathetic
Cardiovascular	Decreased cardiac output and heart rate	Increased contraction and heart rate; increased cardiac output
Pulmonary	Bronchial constriction	Bronchial dilatation
Musculoskeletal	Muscular relaxation	Muscular contraction
Pupillary	Constriction	Dilatation
Urinary	Increased urinary output; sphincter relaxation	Decreased urinary output; sphincter contraction
Gastrointestinal	Increased motility of stomach and gastrointestinal tract; increased secretions	Decreased motility of stomach and gastrointestinal tract; decreased secretions
Glycogen to glucose conversion	No involvement	Increased
Adrenal gland	No involvement	Release epinephrine and norepinephrine

Fight c… resp… digest… se…

Energy… consu… y… n/energ… duction…

Pregan… neu… ionic… n…
– Spin… nd spinal…
-Thoraco… syst… l system…

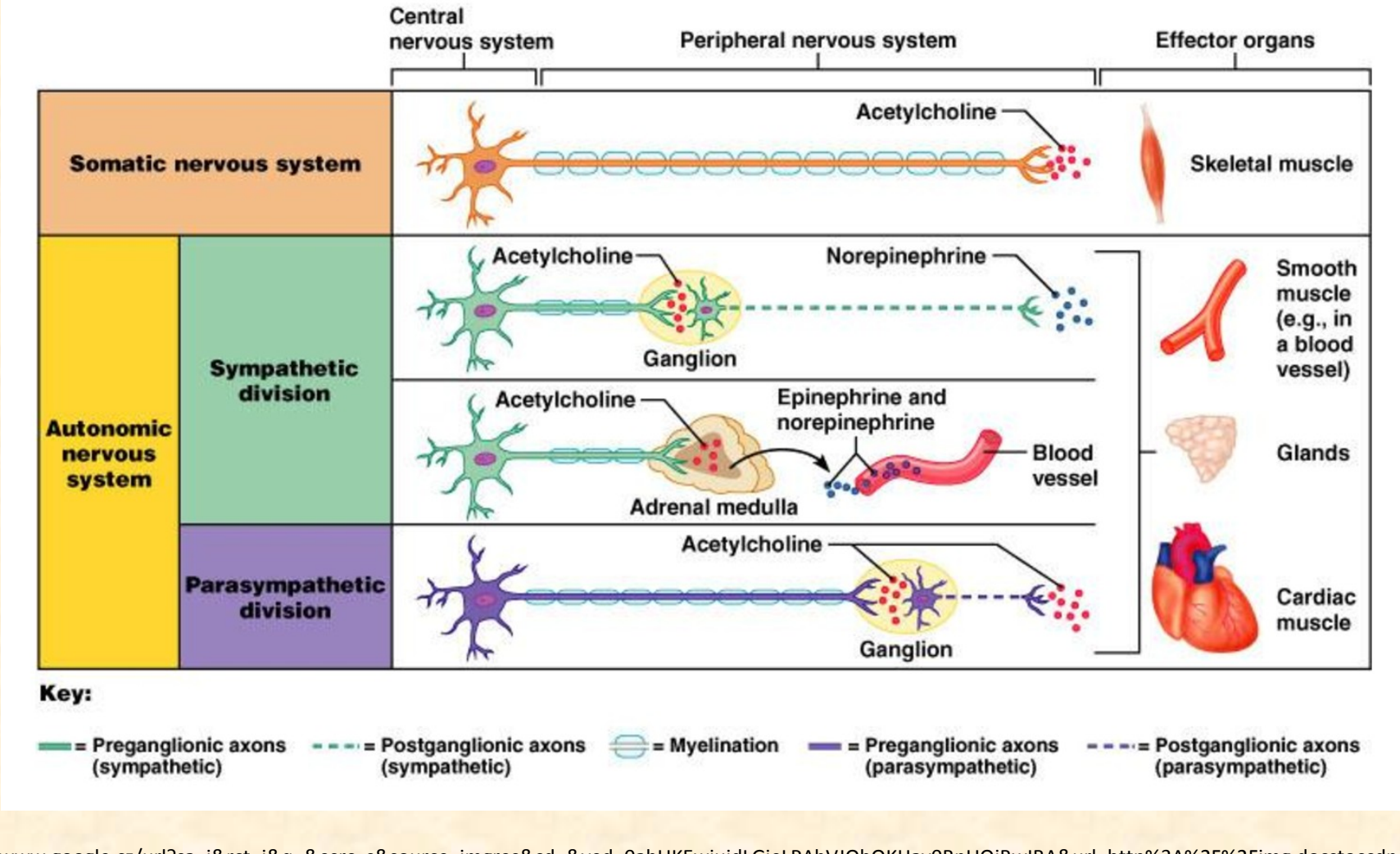
Gan… ia…
Parave… arget…
-Truncus sy… *or*
- Ma… *rally*
Prevel…
-Plexus aorticus



Mostly diffuse effect

Mostly local effect

Mediators of somatic and autonomic nervous system



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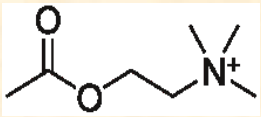
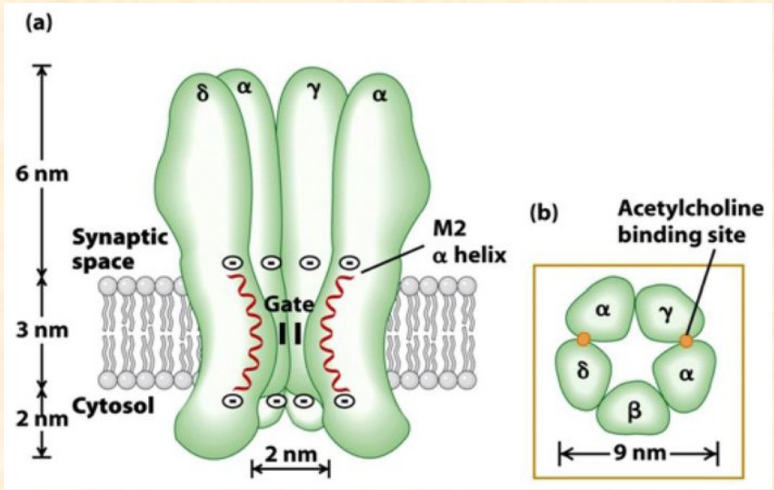


Acetylcholine

Preganglionic fibers

- Sympathetic
- Parasympathetic
- ✓ Nicotinic receptor
  - Ligand-gated ion channels
  - Na+, K+, Ca2+
  - Neuronal (N_N) and muscle (N_M) type
  - Excitatory



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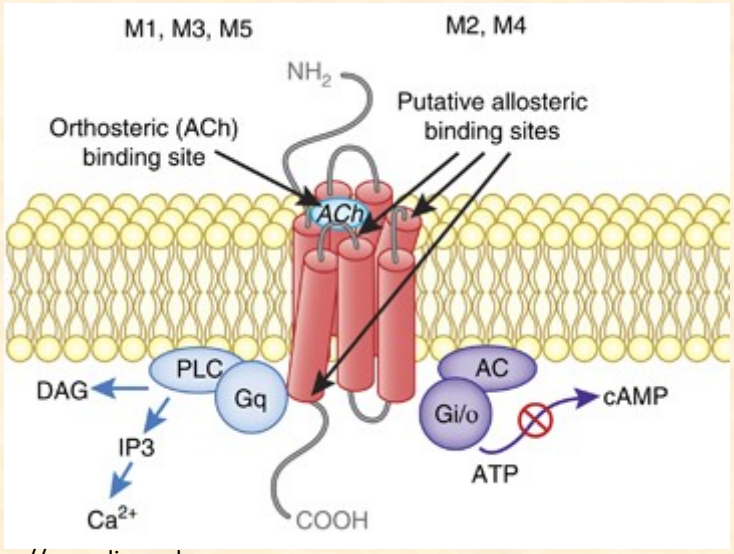
Postganglionic fibers

- Parasympathetic
- ✓ Muscarinic receptor
  - G-coupled
  - Excitatory
    - M1, M3, M5
  - Inhibitory
    - M2, M4



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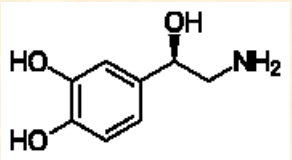
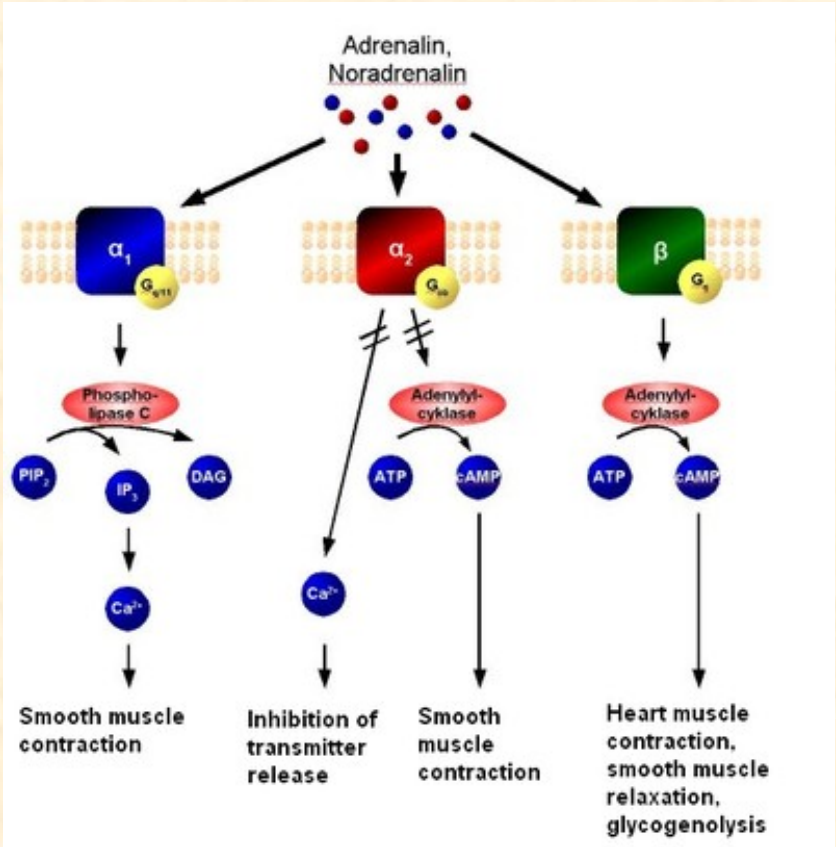


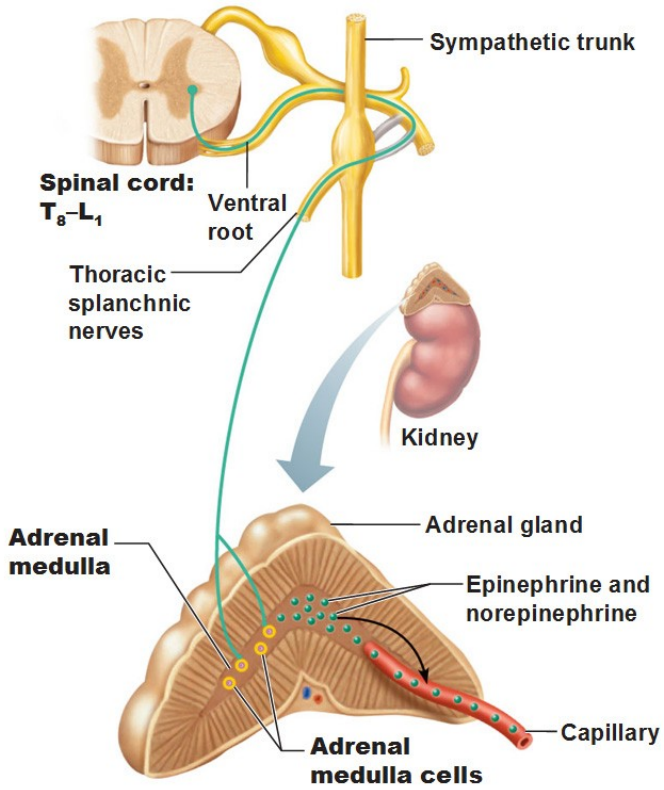
Norepinephrine

- Postganglionic sympathetic fibers
- Adrenergic receptor
  - G-coupled
  - α type– generally excitatory (contraction)
  - β type – generally inhibitory (relaxation) with an exception of !!! heart !!!



https://en.wikipedia.org/wiki/Adrenergic_receptor

- Adrenal medulla
  - Modified sympathetic ganglion
  - „Transmitters“ (stress hormones) secreted into the blood stream
    - Norepinephrine
    - Epinephrine



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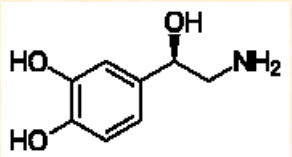

Norepinephrine

- Postganglionic sympathetic fibers
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    with a

- Adrenal medulla
  - Modified sympathetic g
  - Tra

Receptor	G protein and effectors	Agonists	Tissue	Responses
$Alpha_1$	Gq ↑phospholipase C, IP3 and DAG, intracellular Ca^{2+}	**Epi ≥ NE** >> Iso Phenylephrine	Vascular, GU smooth muscle Liver Intestinal smooth muscle Heart	Contraction Glycogenolysis; gluconeogenesis Hyperpolarization and relaxation Increased contractile force; arrhythmias
$Alpha_2$	Gi, Go ↓adenylyl cyclase ↓cAMP	**Epi ≥ NE** >> Iso Clonidine	Pancreatic islets (β cells) Platelets Nerve terminals Vascular smooth muscle	Decreased insulin secretion Aggregation Decreased release of NE Contraction
$Beta_1$	Gs ↑adenylyl cyclase, cAMP, L-type Ca^{2+} channel opening	Iso > **Epi = NE** Dobutamine	Juxtaglomerular cells Heart	Increased renin secretion Increased force and rate of contraction and AV nodal conduction velocity
$Beta_2$	Gs ↑adenylyl cyclase	Iso > **Epi >> NE** Terbutamine	Smooth muscle (vascular, bronchial, GI, GU) Skeletal muscle	Relaxation Glycogenolysis; uptake of K^+
$Beta_3$	Gs ↑adenylyl cyclase	Iso = **NE > Epi**	Adipose tissue	Lipolysis

Epi, epinephrine; NE, norepinephrine; Iso, isoproterenol

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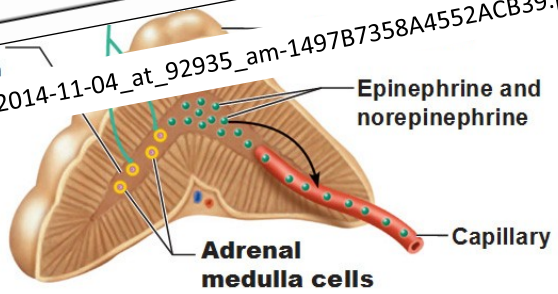

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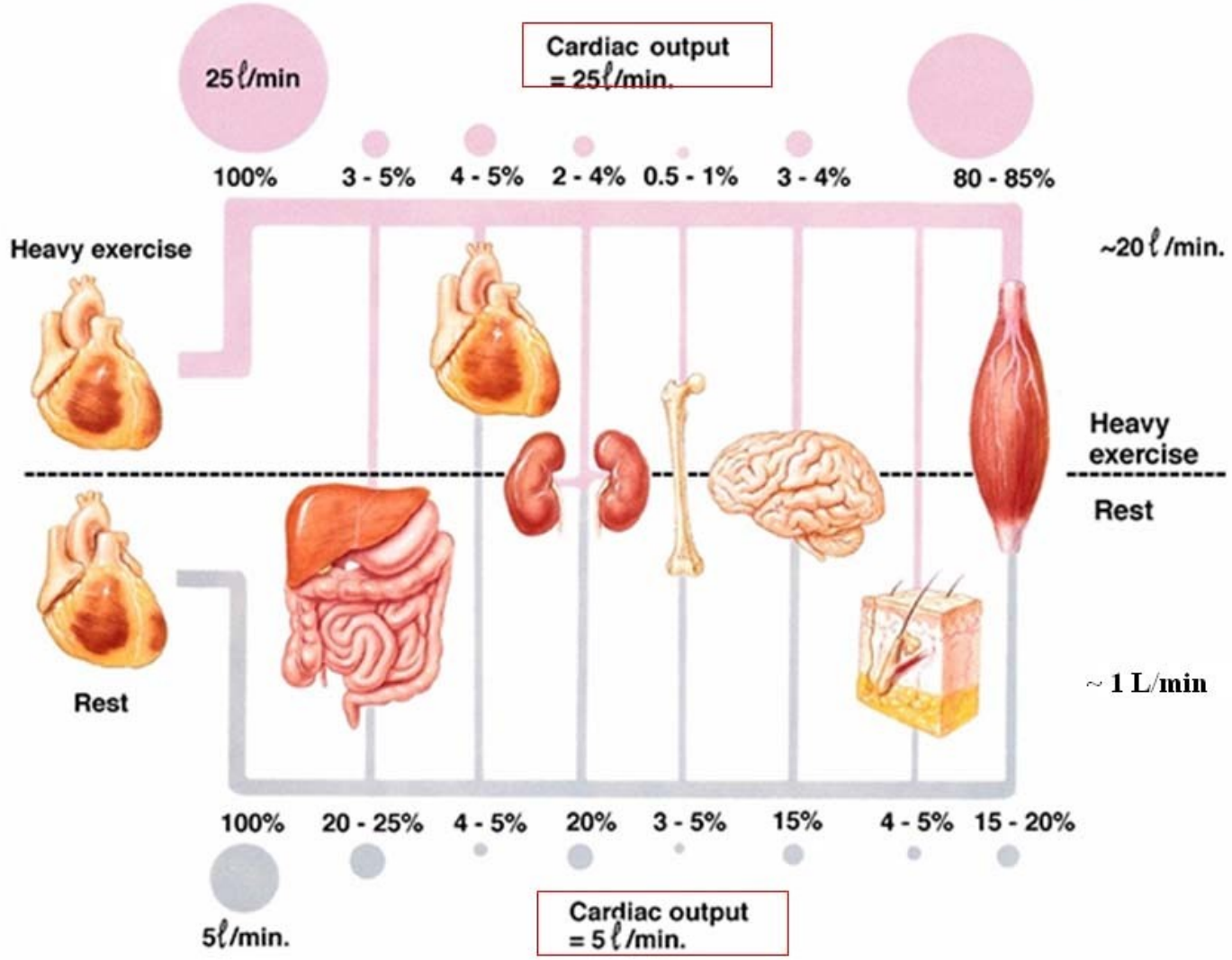
contraction, smooth muscle relaxation, glycogenolysis

Redistribution of Blood Flow During Exercise



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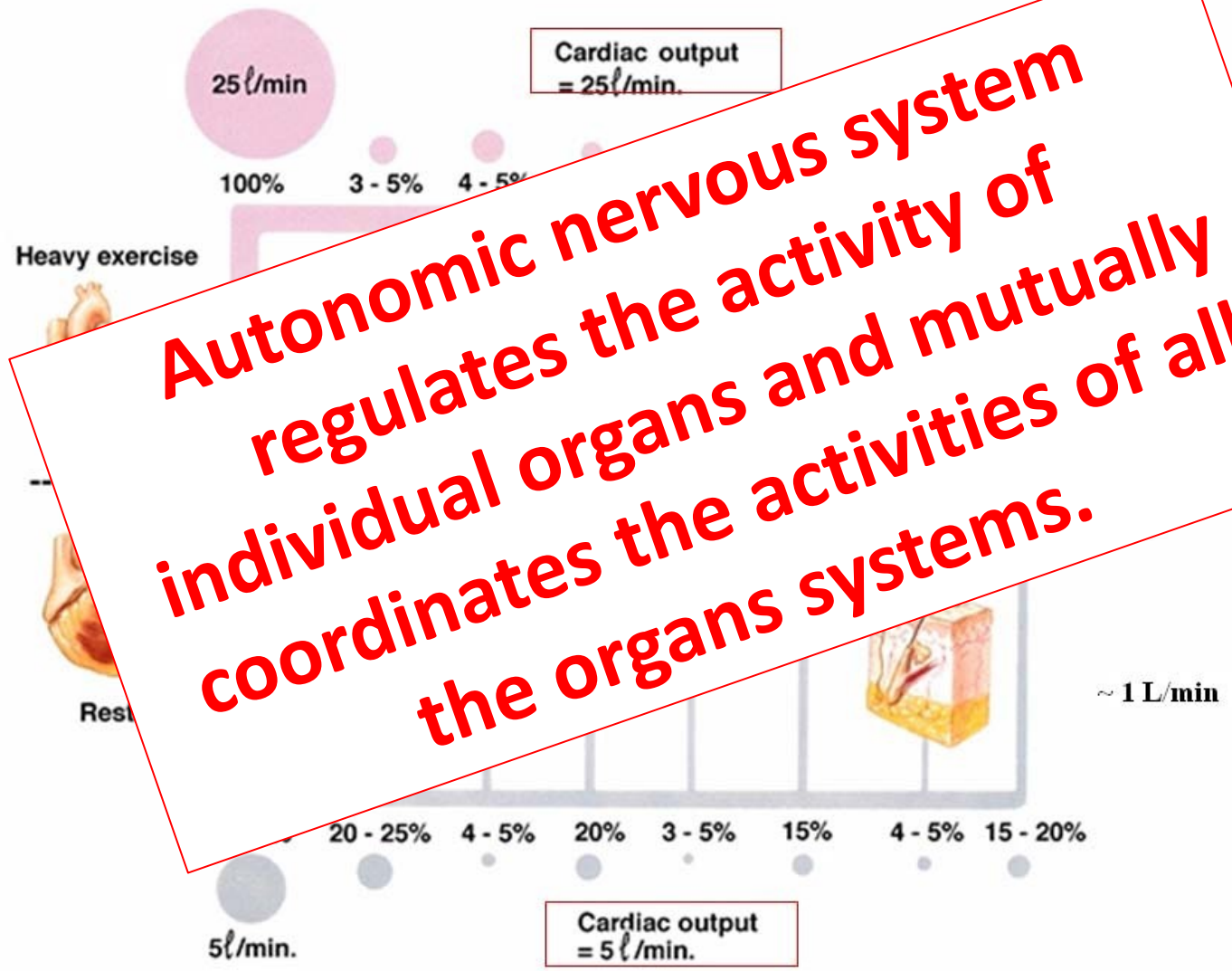
Redistribution of Blood Flow During Exercise



Autonomic nervous system regulates the activity of individual organs and mutually coordinates the activities of all the organs systems.

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INTEGRATION of regulation in cardiovascular system

The regulation of the heart:

– Rami cardiaci n. vagi

Cardiac decelerator center - medula oblongata (ncl.dorsalis, ncl. ambiguus) – parasympathetic fibres of nervus vagus

: vagal tone (tonic vagal discharge)

Negative chronotropic effect (on heart rate)

Negative inotropic effect (on contractility)

Negative dromotropic effect (on conductive tissue)

INTEGRATION of regulation in cardiovascular system

The regulation of the heart:

- nn. cardiaci

Cardiac accelerator center – spinal cord, sympathetic ganglia – sympathetic NS

Positive chronotropic effect (on heart rate)

Positive inotropic effect (on contractility)

Positive dromotropic effect (on conductive tissue)

INTEGRATION of regulation in cardiovascular system

Vasomotor centre (regulation for function of vessels)

Medula oblongata

- ✓ *presoric area* (rostral and lateral part – vasoconstriction – increase blood pressure

- ✓ *depresoric area* (medio-caudalis part – vasodilatation, decrease of blood pressure)

INTEGRATION of regulation in cardiovascular system

- Influence by central nervous system
  - cerebral cortex
  - limbic cortex
  - hypothalamus

Regulation of blood pressure

Short - term regulation

- baroreflex

Middle - term regulation

- humorals regulation

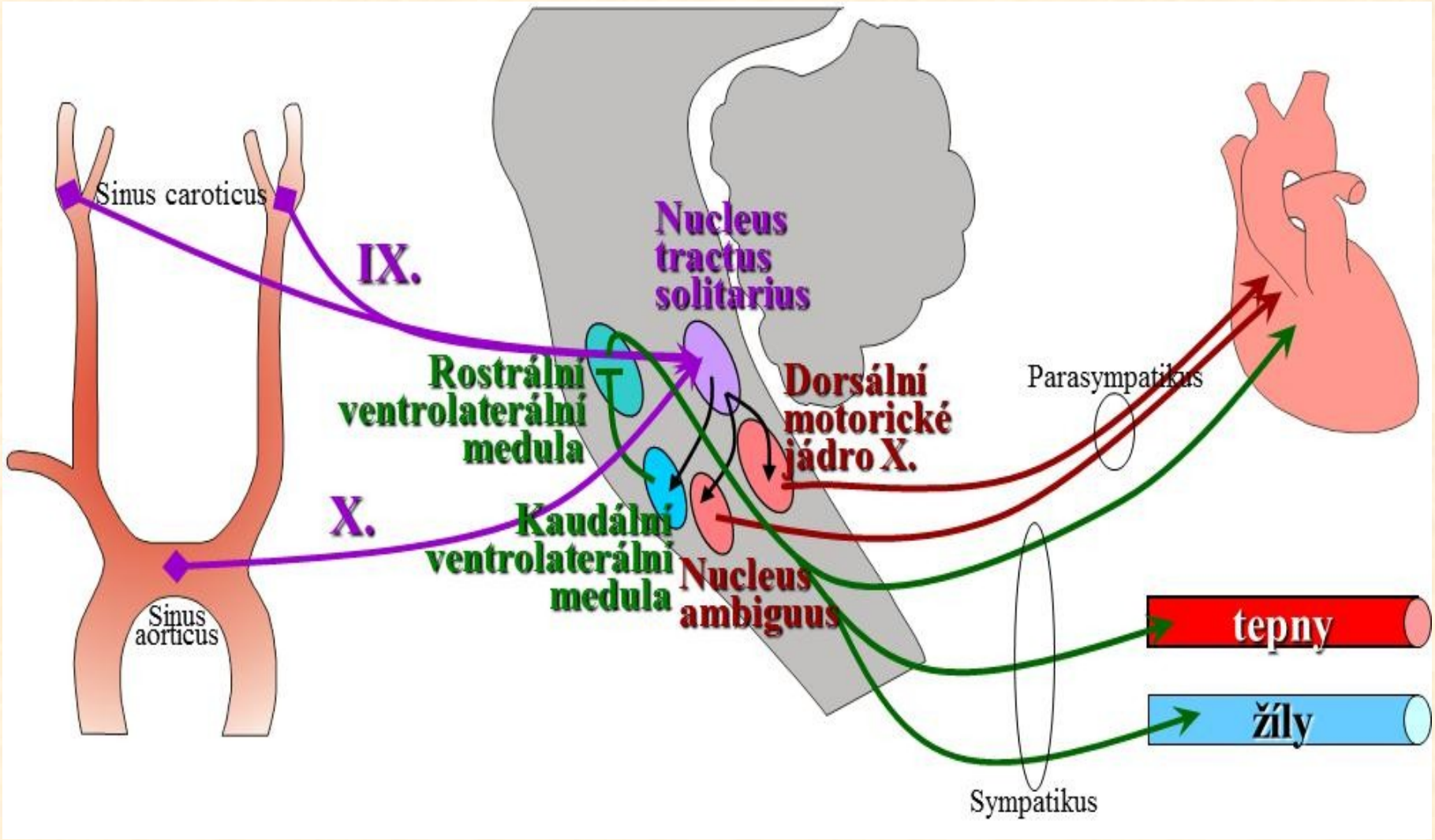
- sympathetic - catecholamines
- RAAS (decrease perfusion pressure in kidney – secretion of renin)
- ADH

Long – term regulation

- kidney regulation

Short term regulation

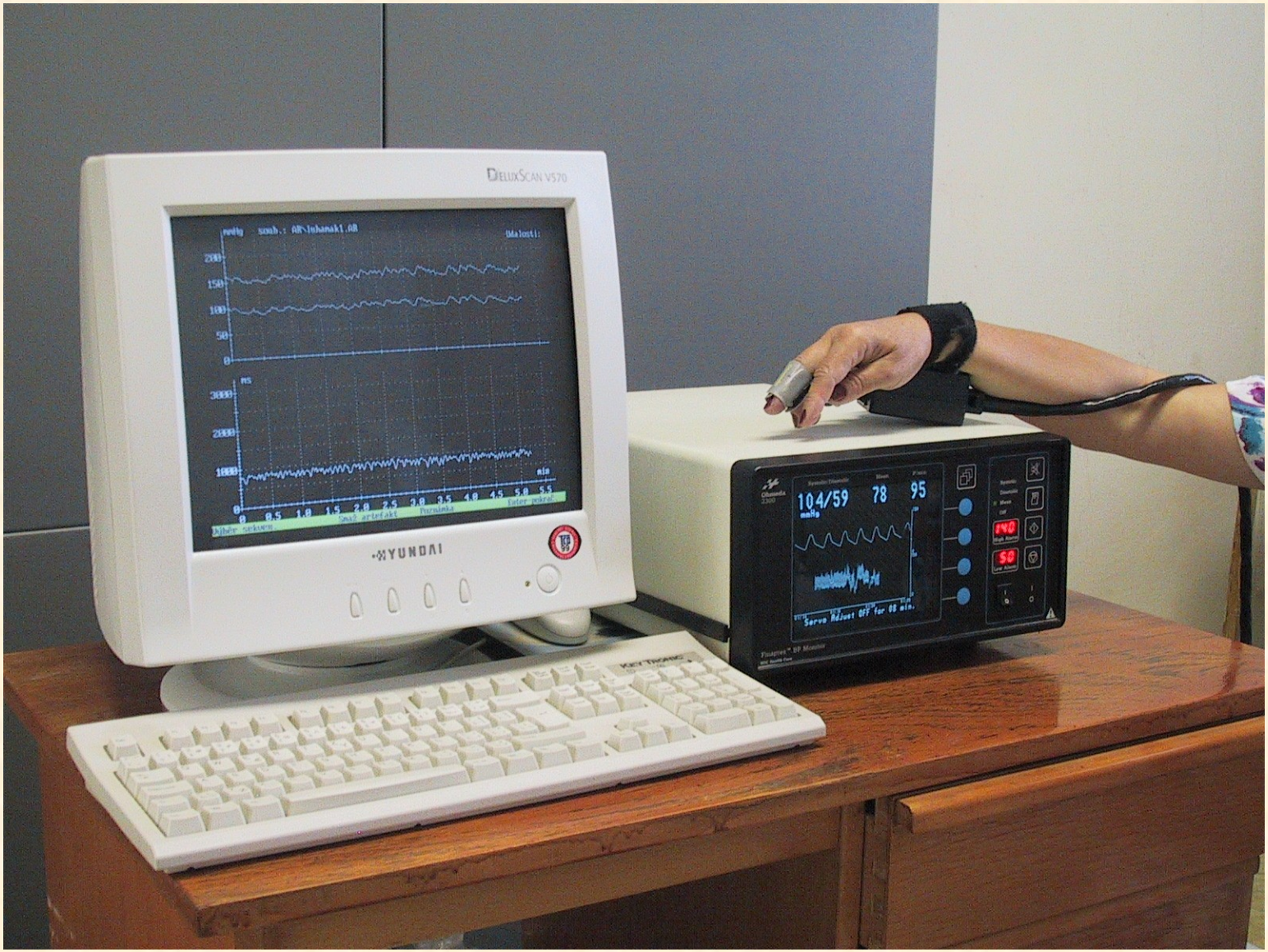
BAROREFLEX



Noninvasive continuously beat-to-beat measurement of finger arterial pressure

- Prof. Jan Peňáz, MD, PhD
- Teacher and researcher on the Department of Physiology, Masaryk university, Brno
- Patent 1969

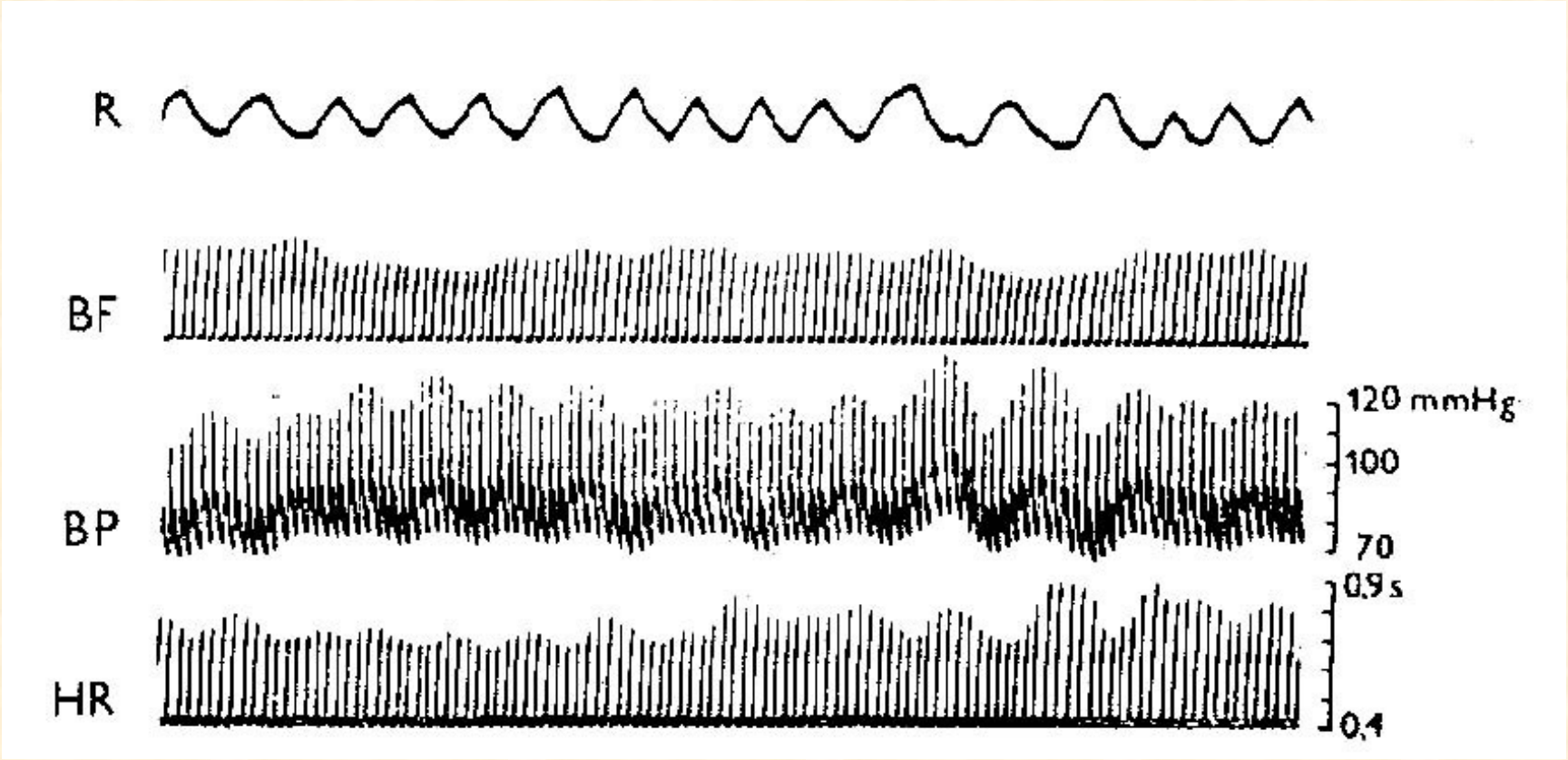
Finapres (Ohmeda, USA)




Finometr (FMS, Nizozemí)
start / stop
FMS Finometer

- We need than **pressure in the cuff corresponded to the pressure of the digital artery**
- **Method: photopletysmography**
- Recorded photoelectric plethysmogram
- The new term: **Transmural pressure** – Pt (the pressure across the wall of the artery)
- BP, Pc (pressure in cuff), Pt
- We estimated: **BP=Pc - - - Pt=0** - - - photoplethysmogram registered the highest amplitude of oscilation --- we measure the **MAP**
- Step by step increase of Pc, in the moment of the highest amplitude – **feed-back loop** started for obtained(keeping) the constant volume of the finger

Records of circulatory parameters



Variability of circulatory parameters

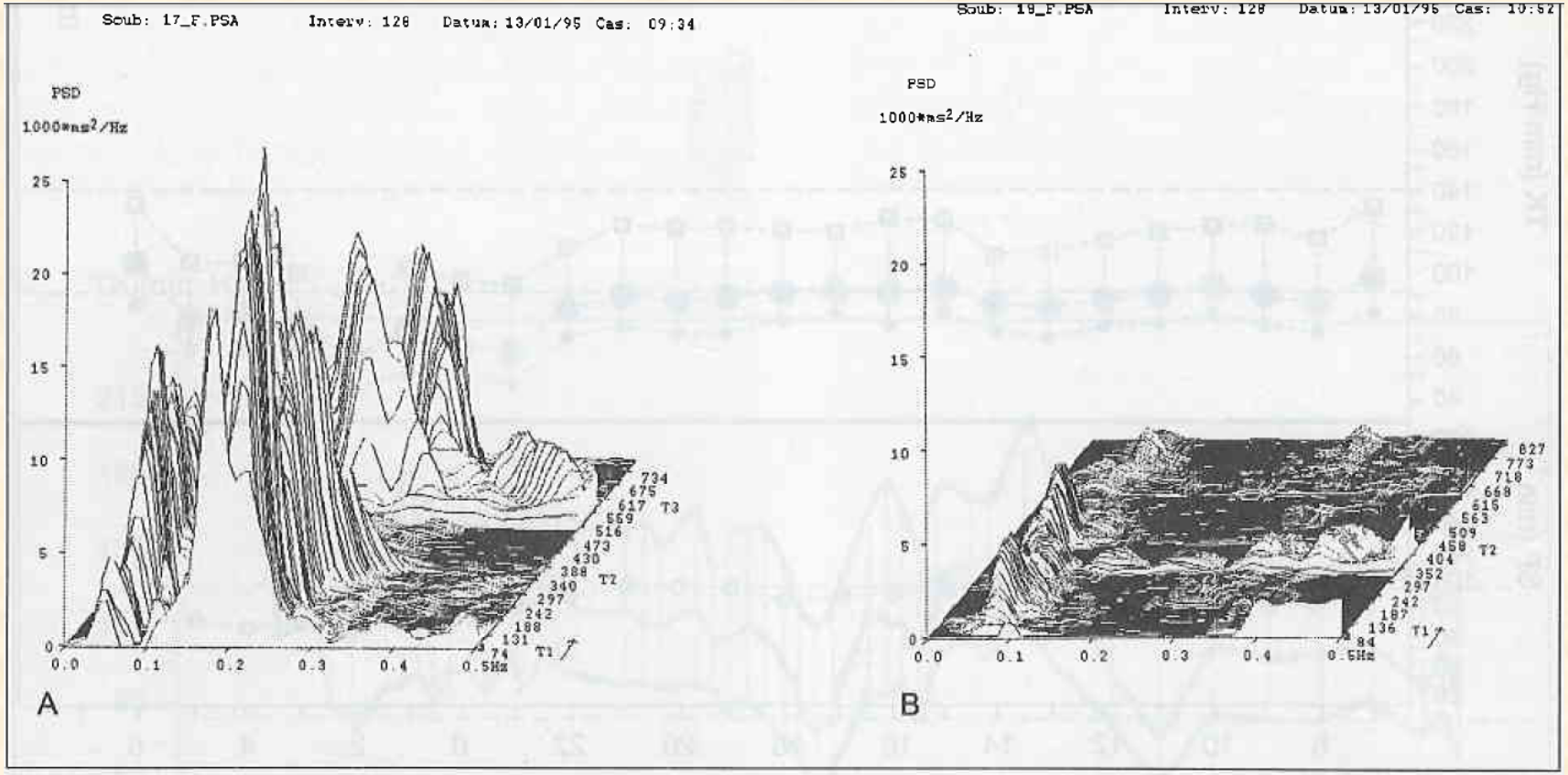
- Heart rate
- Blood pressures – systolic and diastolic

- variability expresses its fluctuation around the average value at certain time intervals (or in various conditions)

Heart Rate Variability (HRV)

- Informs us about the activity of the vagus nerve (tonic activity of n.vagus = vagal tone)
- **Time analysis:**
- from Holter monitoring ECG or 5 - 30min records ECG
- It is basically a statistical evaluation +/-standard deviation
- Disables intervals differing by more than 20% from the average, thus further processed only normal (NN) intervals and evaluated by the standard deviation of all NN sequence for 24h

- **Spectral analysis:**
- Carried out under standard conditions at various maneuvers (supine, standing); evaluated with 300 representative intervals RR / NN /
- Another mathematical processing (Fourier transform) -length RR intervals are converted to cycles in Hz
- The spectrum is divided into several components - low (LF: the sympathetic modulation) and high frequency (HF: vagal modulation)
- People with reduced heart rate variability have a 5 times higher risk of death

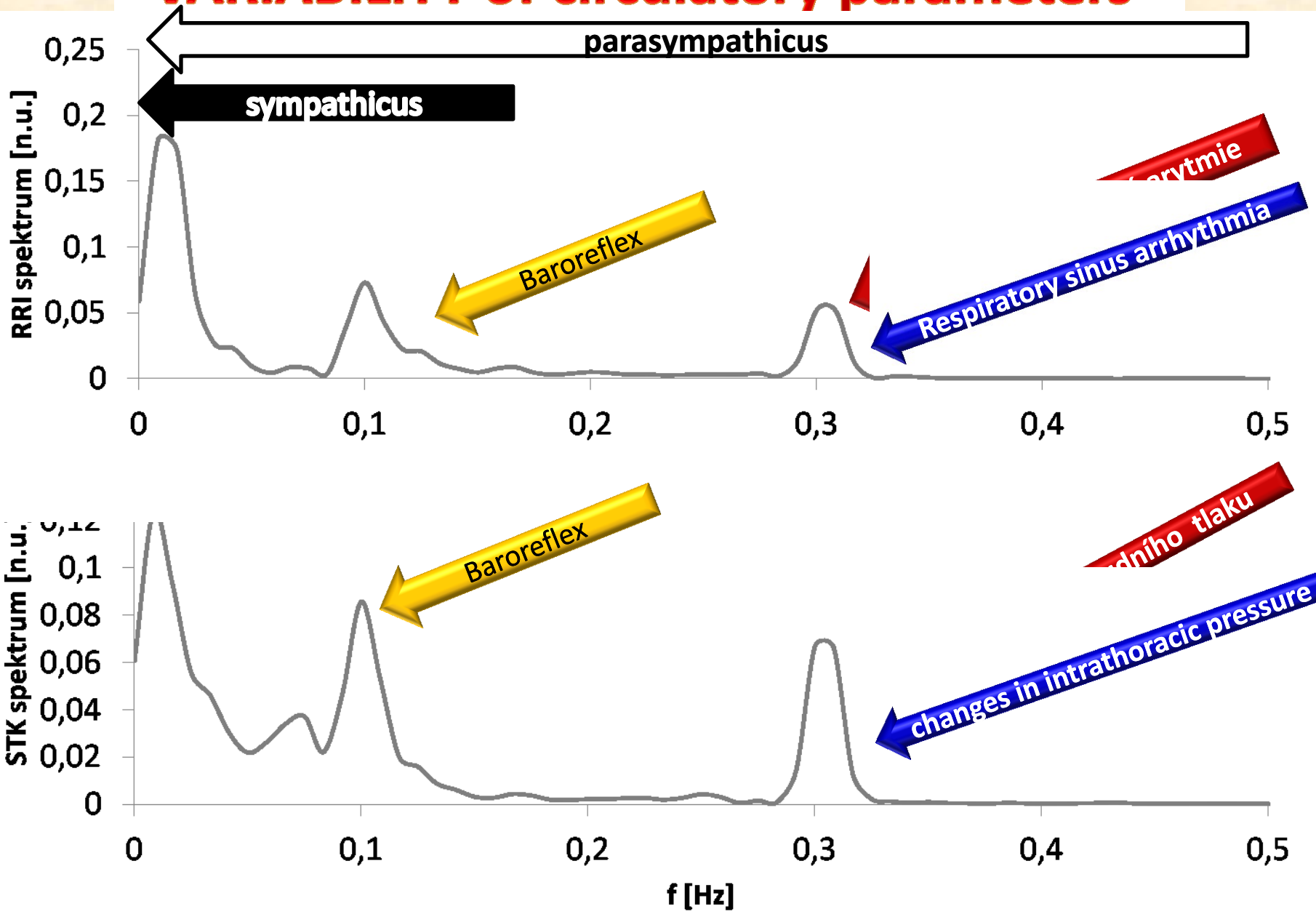


Obr. 9.22 *Spektrální analýza variability srdeční frekvence (VariaPulse TF3)*

Osa x – spektrum cyklů v Hz; osa y – PDS (ms^2 Hz^{-1}); osa z – čas trvání vyšetření v s (T_1 – první řada vleže; T_2 – druhá řada vstoje; T_3 – zadní řada po položení)

A – normální zdravý jedinec: vykazuje dobrou variabilitu vlivem sympatické aktivity v oblasti LF a vysokou variabilitu vlivem vagové tonizace v oblasti HF; B – starší nemocný po srdečních infarktech s komorovými arytmiemi: převažují LF-oscilace posunuté značně k nejnižším hodnotám (0,06 Hz) s nízkým PDS, které svědčí pro převahu sympatiku vzhledem k praktickému vymizení HF-oscilací (0,2 – 0,4 Hz) pro vagovou dysfunkci.

VARIABILITY of circulatory parameters



CIRCULATORY FAILURE

- The main function of circulation is keep a good organ and tissue perfusion

BP = CO x TPR

Circulatory failure is a generalized inadequate blood flow in the body that causes tissue damage due to reduced blood flow - reduced transport of oxygen (and other nutritional factors). The cardiovascular system itself (cardiac muscle, vascular walls, vasomotor system, and other parts of circulation) worsens when coming „circulatory shock“

CIRCULATORY FAILURE

BP = CO x TPR

CO decrease:

- ✓ ***lower volume in circulation*** **– lower venous return**

decrease of filling pressure and by Frank- Starling principle decrease of CO

Clinical: e.g. hemorrhagic shock, hypovolemic shock

Therapy: infusion (e.g. of physiological solution)

CIRCULATORY FAILURE

BP = CO x TPR

CO decrease:

- ✓ ***vasodilatation of venous system*** **- sudden periphery vasodilatation – e.g. sudden loss of vasomotor tone : vasomotor syncope (neurogenic shock-brain damage, deep anesthesia)**
- ✓ **emotional activation of parasympathetic signals to slow the heart and also activation of inverse sympathetic signals to dilate the peripheral vasculature : vasovagal syncope (emotional disturbance-fainting in young people)**

CIRCULATORY FAILURE

BP = CO x TPR

CO decrease:

✓ ***lower pumping*** **function of the heart**

e.g. myocardial infarction, severe dysfunction of the heart valves, cardiac arrhythmias

Resultes: cardiogenic shock

= circulatory shock, which results from the weakened ability of the heart as a pump; (85% of people who develop a cardiogenic shock will not survive)

CIRCULATORY FAILURE

$$BP = CO \times TPR$$

TPR decrease:

- ✓ **toxic vasodilatation (by histamin-allergy) – anaphylactic shock (e.g. bee sting, wasp sting)**
- ✓ **Dysbalance of autonomy nervous system – sympathetic part – decrease of sympathetic tone of vessels**

NYHA classification

Functional Capacity	Objective Assessment
Class I	Patients with cardiac disease but without resulting limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitations, dyspnea, or anginal pain.
Class II	Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea, or anginal pain.
Class III	Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes fatigue, palpitation, dyspnea, or anginal pain.
Class IV	Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of heart failure or the anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort is increased.

Source: Adapted from New York Heart Association, Inc., *Diseases of the Heart and Blood Vessels: Nomenclature and Criteria for Diagnosis,* 6th ed. Boston, Little Brown, 1964, p. 114.