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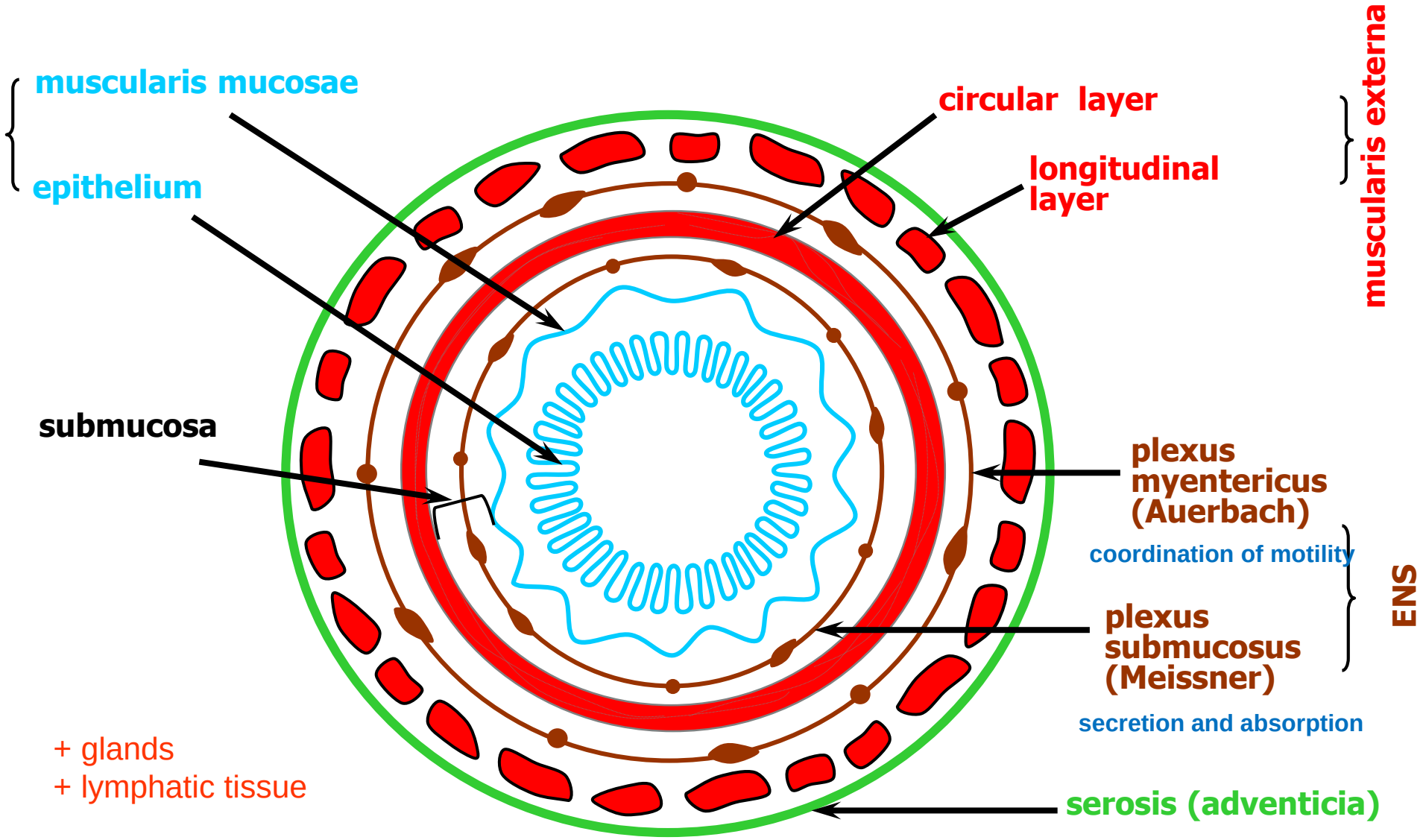
GASTROINTESTINAL TRACT

Introduction

THM

- The GIT is a tube, specialized along its length for the sequential processing of food
- Assimilation of substrates from food requires both digestion and absorption
- Digestion requires enzymes, which are secreted in various parts of GIT
- Food ingestion triggers complex whole-body responses (endocrine, neural, paracrine)
- GIT plays an important role also in homeostasis (absorption vs. excretion, izovolemia, izoionia, etc.) and immunity



Circular muscle layer: inhibitory fibers, contraction – gut is longer and smaller in diameter
Longitudinal muscle layer : no inhibitory fibers, contraction – gut is shorter and bigger in diameter

Modified according to: J. Švíglerová: Fyziologie gastrointestinálního traktu, LF UK Plzeň, 2012

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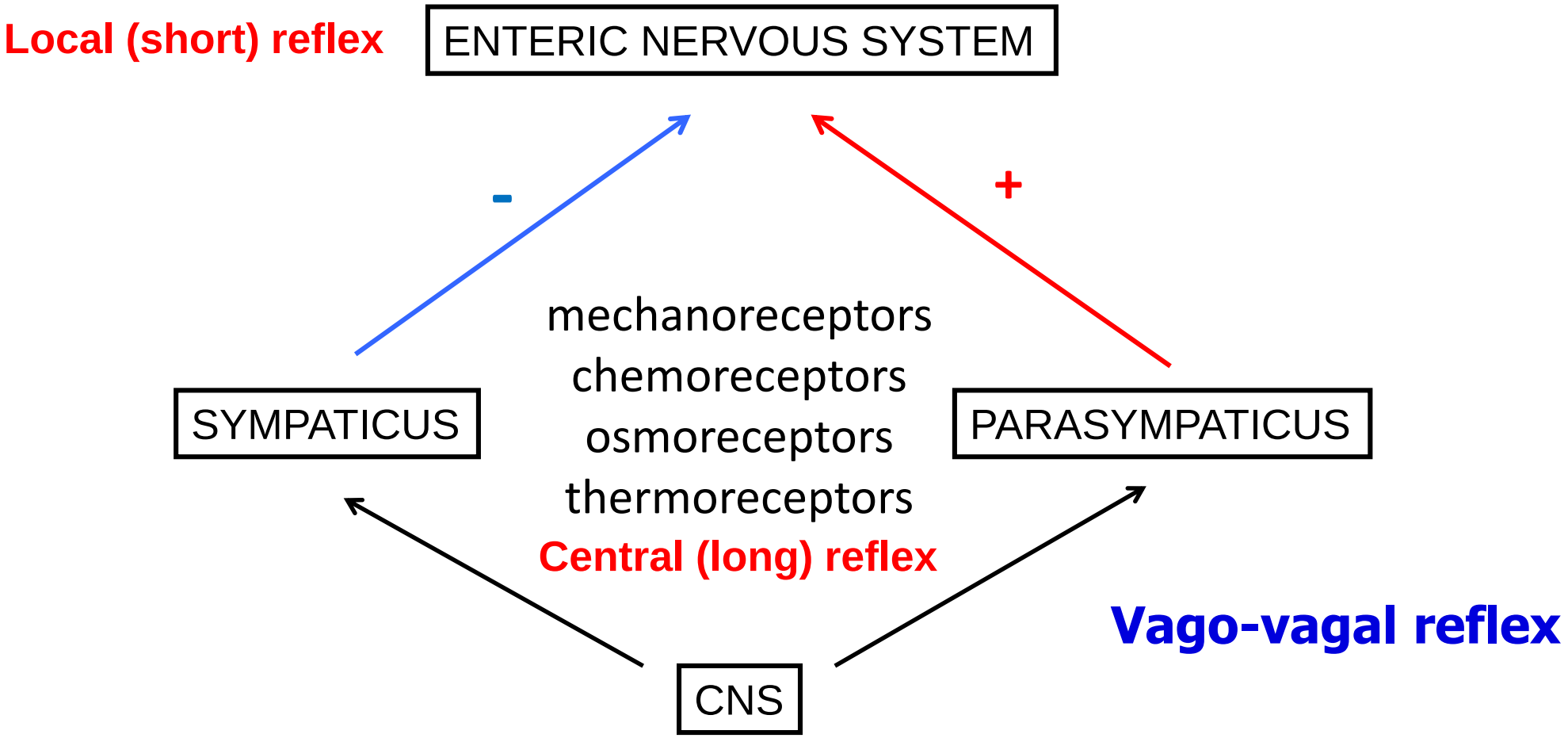
GIT INNERVATION



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GIT MOTILITY

CONTRACTIONS

tonic (stomach, colon)

rhythmic

MOVEMENTS

propulsive (peristalsis, myenteric reflex)

mixing

Receptive relaxation.

These contractions and movements are responsible for churning, peristalsis and reservoir action in GIT.

THM

The regulation of GI function results from an interplay of neural and hormonal influences on effector cells that have intrinsic activities.

The GI tract is innervated by the ANS, which is composed of nerves that are extrinsic and nerves that are intrinsic to the tract.

Extrinsic nerves are distributed to the GI tract through both parasympathetic and sympathetic pathways.

Intrinsic nerves are grouped into several nerve plexuses, of which the myenteric and submucosal plexuses are the most prominent. Nerves in the plexuses receive input from receptors within the GI tract and from extrinsic nerves. This input can be integrated within the intrinsic nerves such that coordinated activities can be effected.

ACh is one of the major excitatory neurotransmitters, and NO and VIP are two of the major inhibitory neurotransmitters at effector cells. Serotonin and somatostatin are two important neurotransmitters of intrinsic interneurons.

THM

Striated muscle comprises the musculature of the pharynx, the oral half of the esophagus, and the external anal sphincter. Smooth muscle makes up the musculature of the rest of the GI tract.

Adjacent smooth muscle cells are electrically coupled to one another and contract synchronously when stimulated. Some smooth muscles contract tonically, whereas others contract phasically.

In phasically active muscle, stimulation induces a rise in intracellular Ca^{2+}, which in turn induces phosphorylation of the 20,000-dalton light chain of myosin. ATP is split, and the muscle contracts as the phosphorylated myosin (myosin P) interacts with actin. Ca^{2+} levels fall, myosin is dephosphorylated, and relaxation occurs. In tonically active muscles, contraction can be maintained at low levels of phosphorylation and ATP utilization.

Periodic membrane depolarizations and repolarizations, called slow waves, are major determinants of the phasic nature of contraction. Slow wave activity results from ionic currents initiated through the interactions of the ICCs with the smooth muscle cells.

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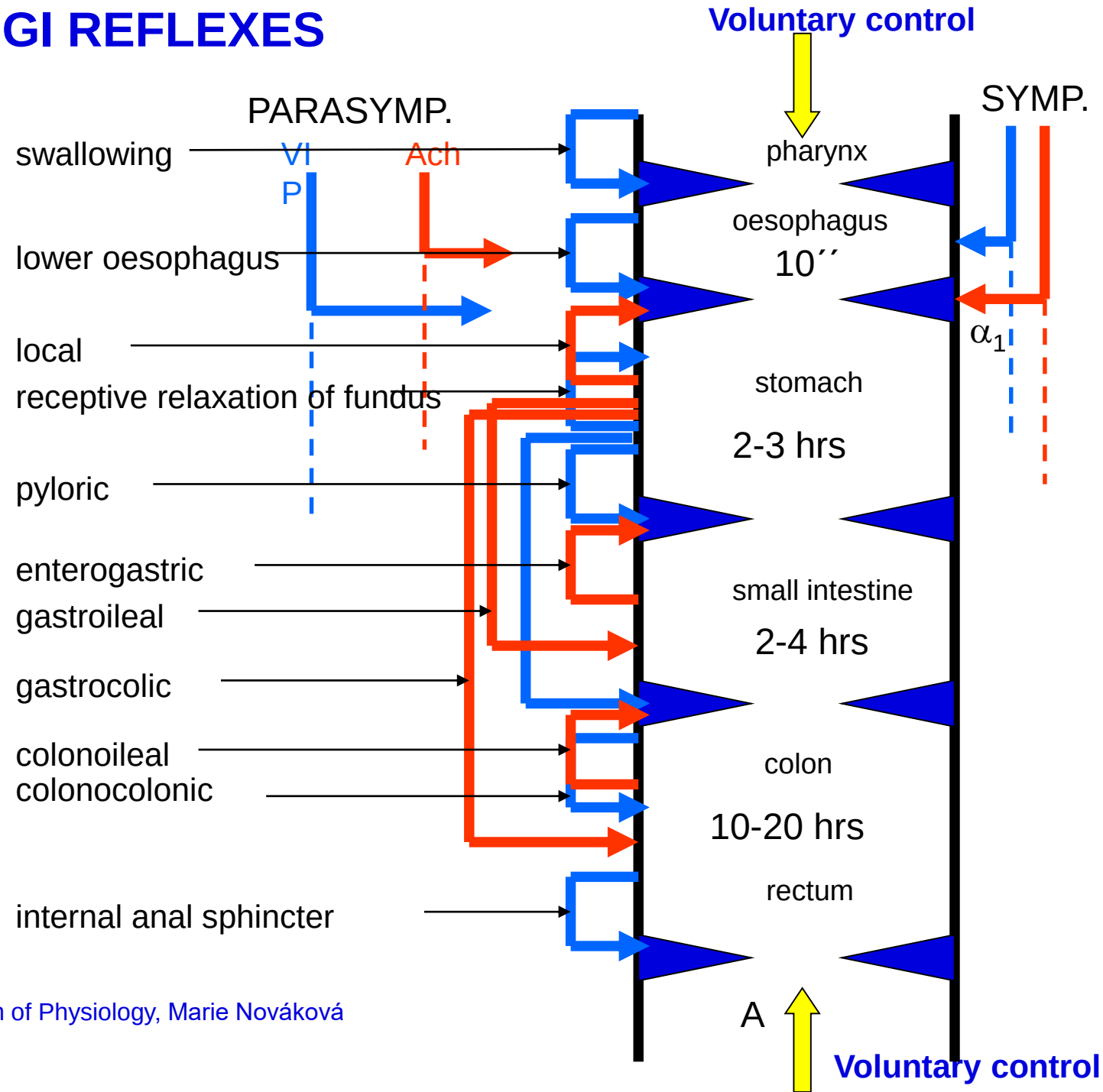
GI REFLEXES



Continuous tonus
S, PS
BALANCE - DYSBALANCE

Signalling:

relax, move on!

slow down!

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SECRETION

- Salivary glands
- Gastric glands
- Small glands of esophagus and intestine
- Exocrine pancreas
- Liver

Common features of secretion:
water, ions, HCO_{3-}, mucin

- Lubrication of food
- Swallowing
- Articulation
- Mechanical protection of GIT
- Chemical protection of GIT
- Enzymes
- Immune function(s)

STIMULATION OF SECRETION
1. Neurocrine
2. Endocrine
3. Paracrine

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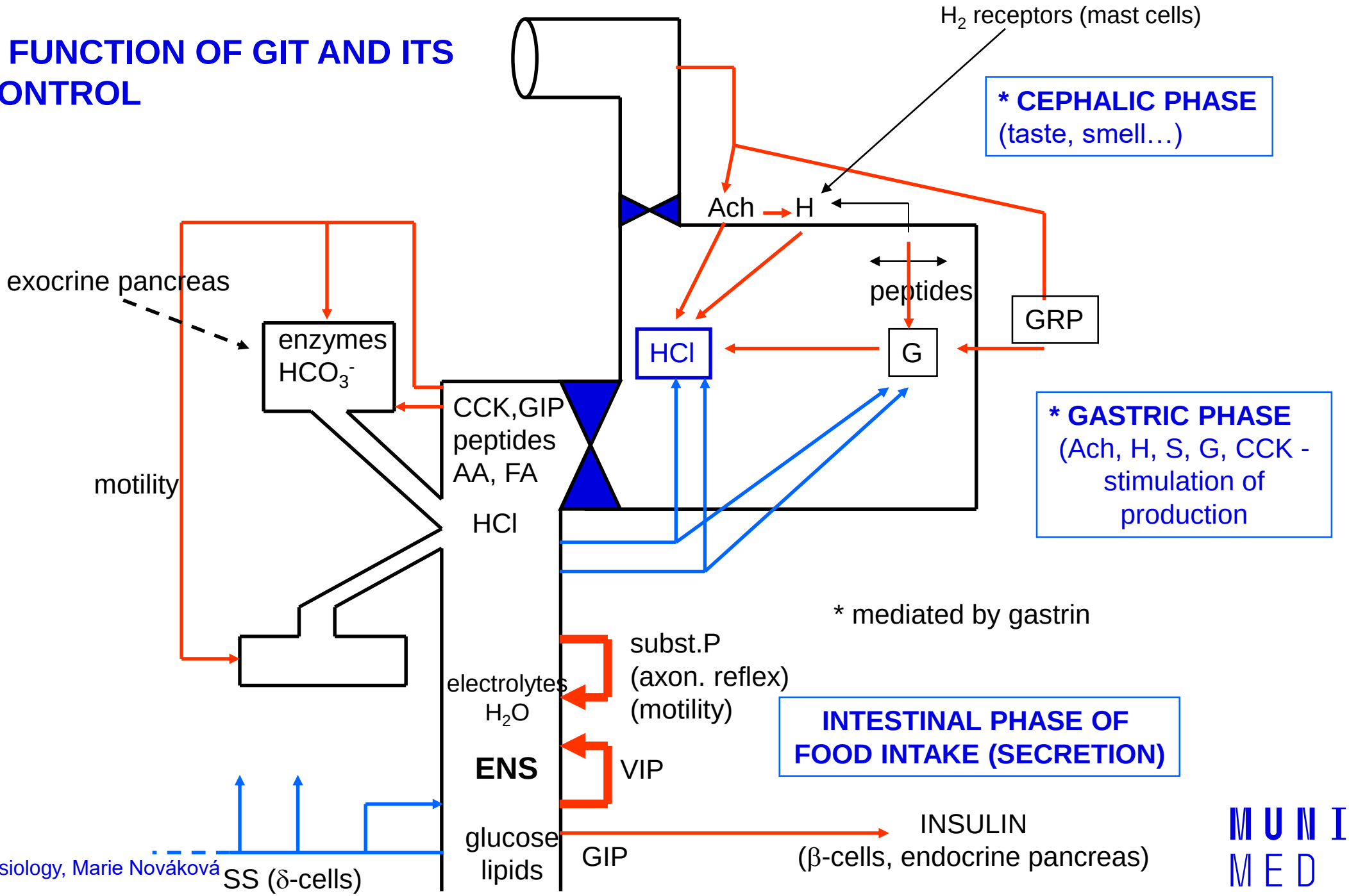
SECRETORY FUNCTION OF GIT AND ITS HUMORAL CONTROL



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The functions of the GI tract are regulated by mediators acting as hormones (endocrine), paracrine, or neurocrine substances.

Two chemically related families of peptides are responsible for much of the regulation of GI function. These are gastrin/CCK peptides and a second group containing secretin, VIP, GIP, and glucagon.

The GI hormones are located in endocrine cells scattered throughout the mucosa and released by chemicals in food, neural activity, or mechanical distention.

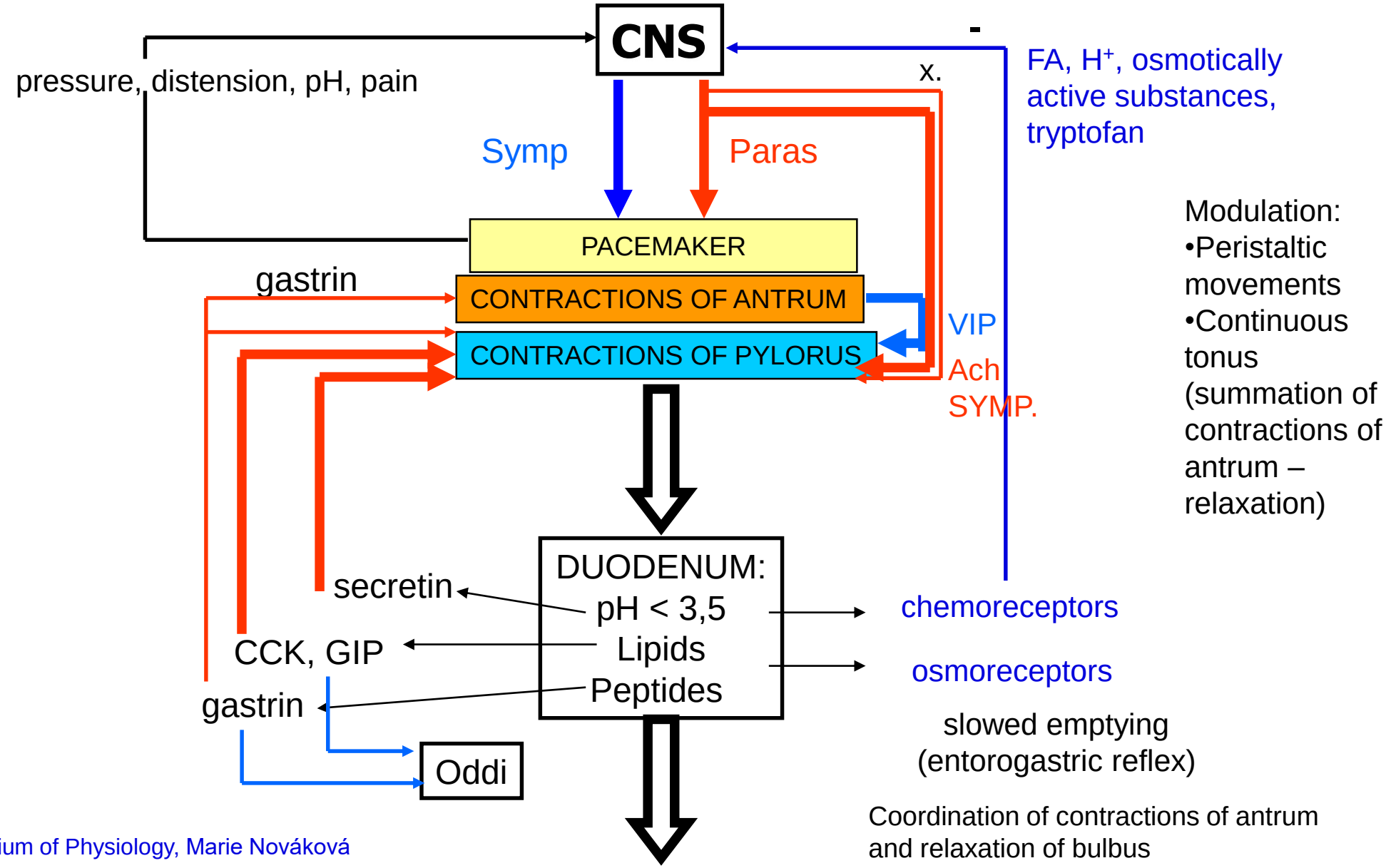
The GI peptides have many pharmacologic actions, but only a few of these are physiologically significant.

Gastrin, CCK, secretin, GIP, and **motilin** are important GI hormones.

Somatostatin and histamine have important functions as paracrine agents.

Neurocrines **VIP, bombesin** (or **GRP**), and the **enkephalins** are released from nerves and mediate many important functions of the digestive tract.

EMPTYING OF STOMACH



Modulation:
- Peristaltic movements
- Continuous tonus (summation of contractions of antrum – relaxation)

Coordination of contractions of antrum and relaxation of bulbus
Duodenogastric reflux

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SECRETION OF GASTRIC JUICE

pH 2, high concentration of K^+ (vomiting) a **Cl^-**

Stimulation of α-receptors – decreased secretion of HCO_3^-
Gastric ulcers
NSA – decreased secretion of HCO_3^- and mucine

Gastric mucose barrier

Mucin (pH 7-8)

Gastric pits (glands)

Surface epithelia

Lamina propria

Mucose cells of neck

Parietal cells (**HCl, intrinsic factor**)
(individual number!!!)

Main cells - zymogenic granula (pepsinogen)

G cells (gastrin)

\+

Ach, G, CCK, secretin

Area:
- Subcardial (mucin)
- Fundus (HCl)
- Pyloric (mucin, G)

Gastric juice: water, salts, HCl, pepsin, intrinsic factor, mucin
Production increases after meal

pepsinogen → pepsin
↑ HCl

Higher secretion – lower pH, lower secretion – more Na^+, (**always more K^+ than in plasma**)

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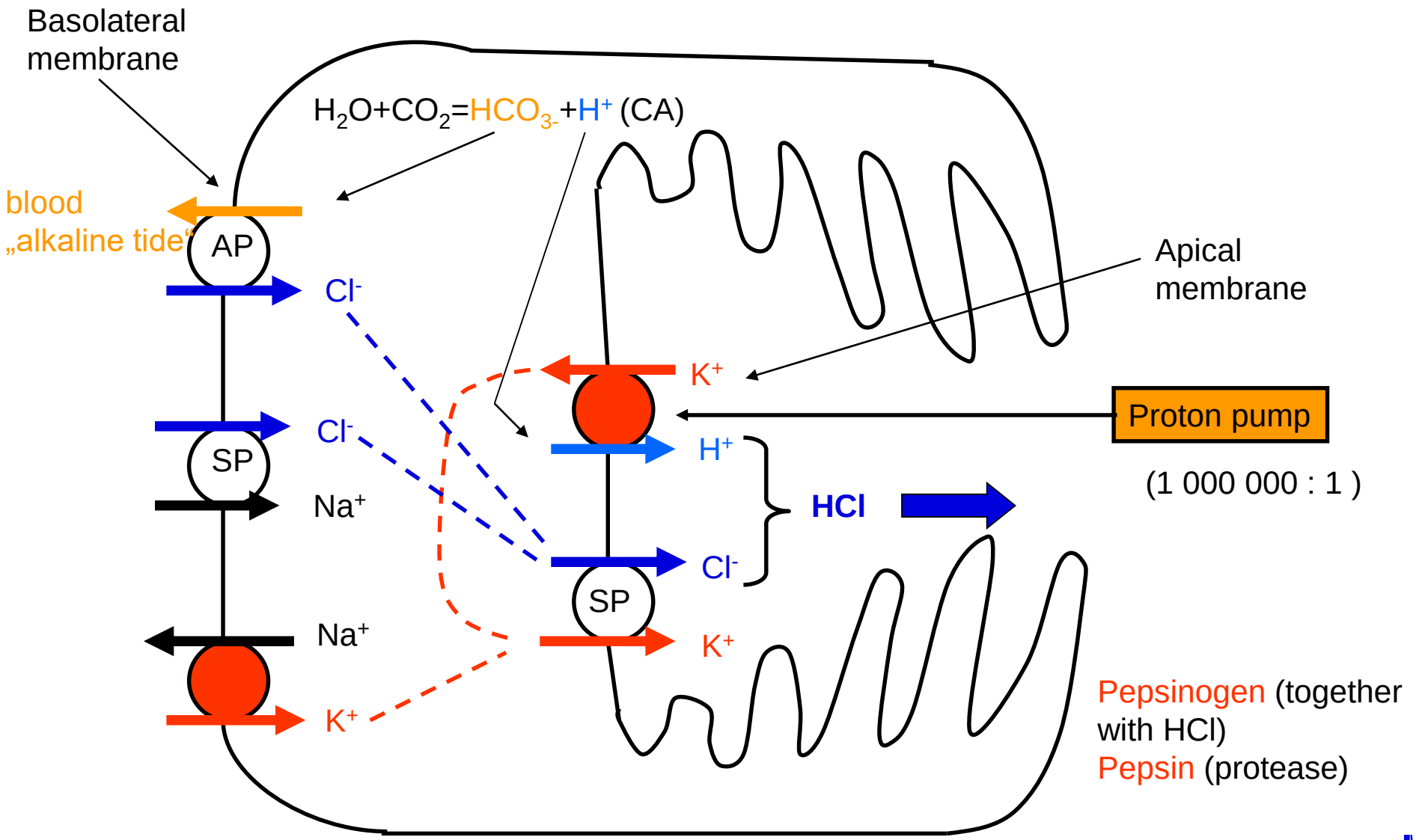
HCl PRODUCTION IN PARIETAL CELL



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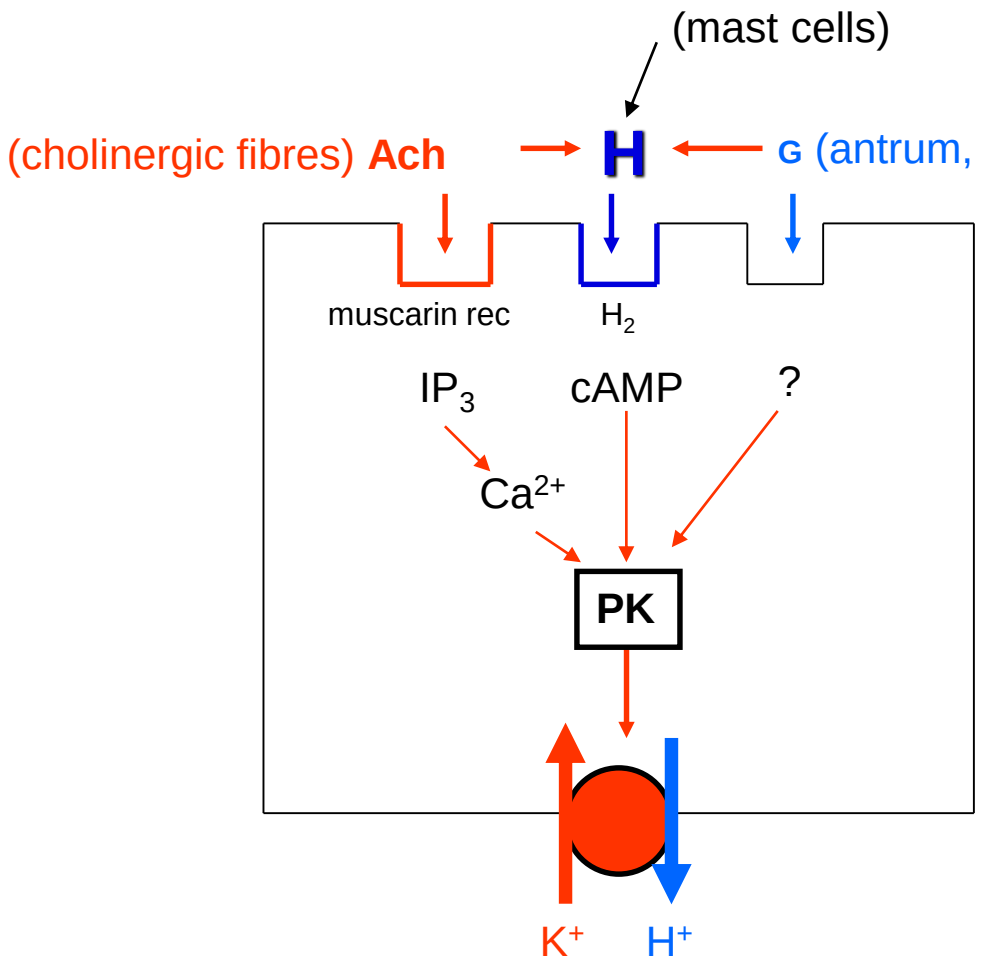
CONTROL OF HCl PRODUCTION IN PARIETAL CELL



Potentiation of stimulation!!!

PGE, somatostatin – **inhibition** of HCl secretion

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Component	Liver Bile	Gallbladder Bile
Na^+ (mmol/L)	150	300
K^+ (mmol/L)	4.5	10
Ca^{2+} (mmol/L)	4	20
Cl^- (mmol/L)	80	5
Bile salts (mmol/L)	30	315
pH	7.4	6.5
Cholesterol (mg/100 mL)	110	600
Bilirubin (mg/100 mL)	100	1000

THM

- Both active and passive mechanisms participate in GIT absorption
- Both paracellular and transcellular movements are involved
- Absorption area is enlarged by folds, villi and microvilli (mostly in small intestine)
- Absorption of water and electrolytes occurs in both small and large intestine,

  absorption of nutrients occurs only in small intestine
- Small intestine absorbs water and electrolytes and secretes HCO_3^-, large intestine

  absorbs water and electrolytes and secretes potassium and HCO_3^-
- Water „follows“ electrolytes, eventually is „drafted“ by osmotically active substances
- Numerous absorption mechanisms depend on sodium gradient

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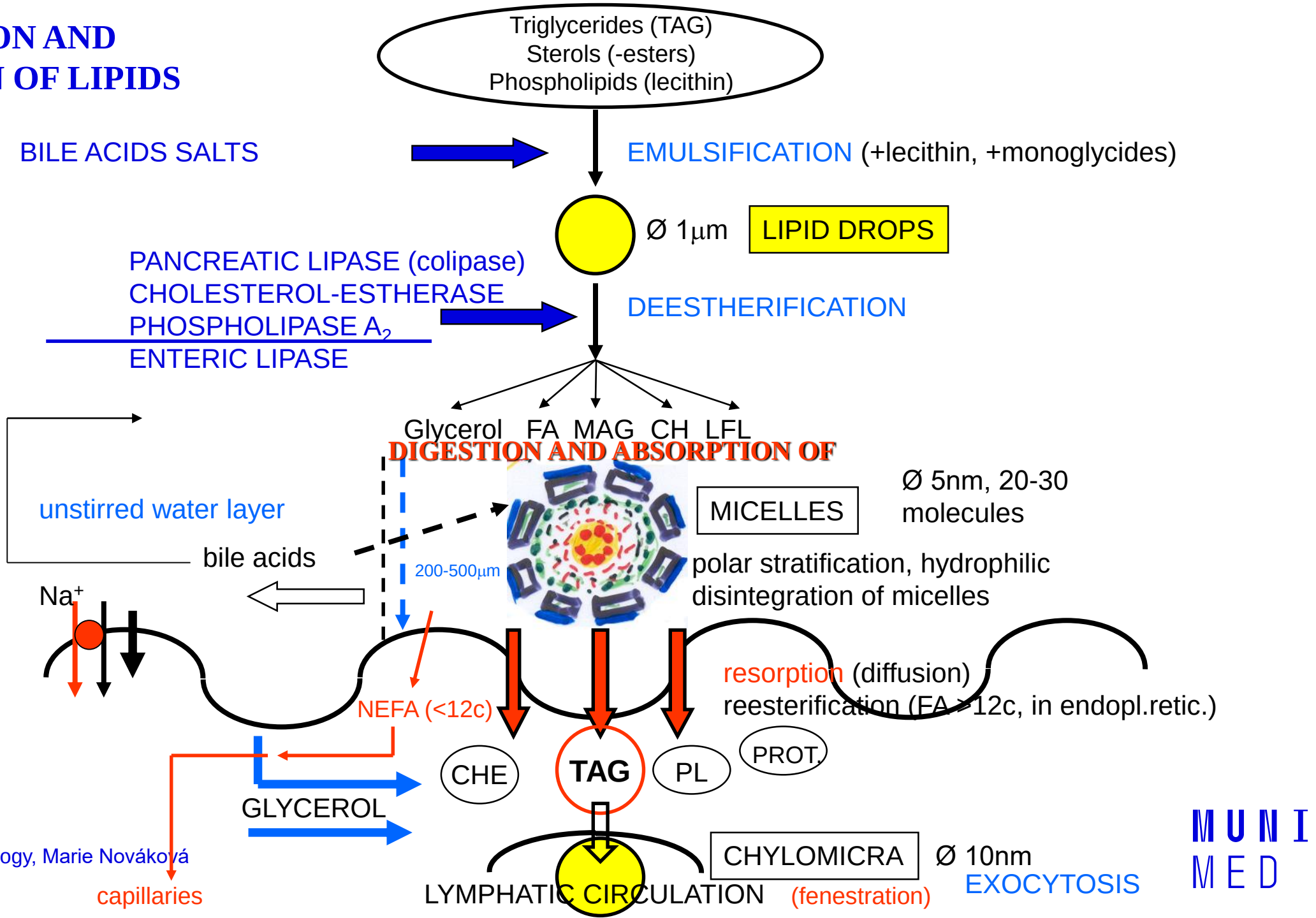
DIGESTION AND ABSORPTION OF LIPIDS



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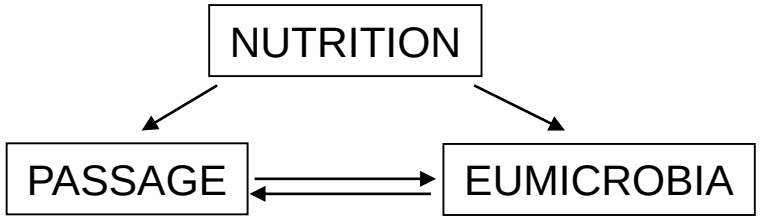
REST OF CHYME

1. Cellulose, collagen
2. Bile acids, epithelia, mucin, leucocytes

- Bacteria **fermenting**: fibre (pectin, cellulose) – lactate, alcohol, acetate, CO_2, methane
- Bacteria **putrescent**: residues of AA – NH_3, SH_2, phenol, indole, solatol (carcinogenic)

Production of vitamin K and vitamins of B group, HOWEVER cannot be absorbed here



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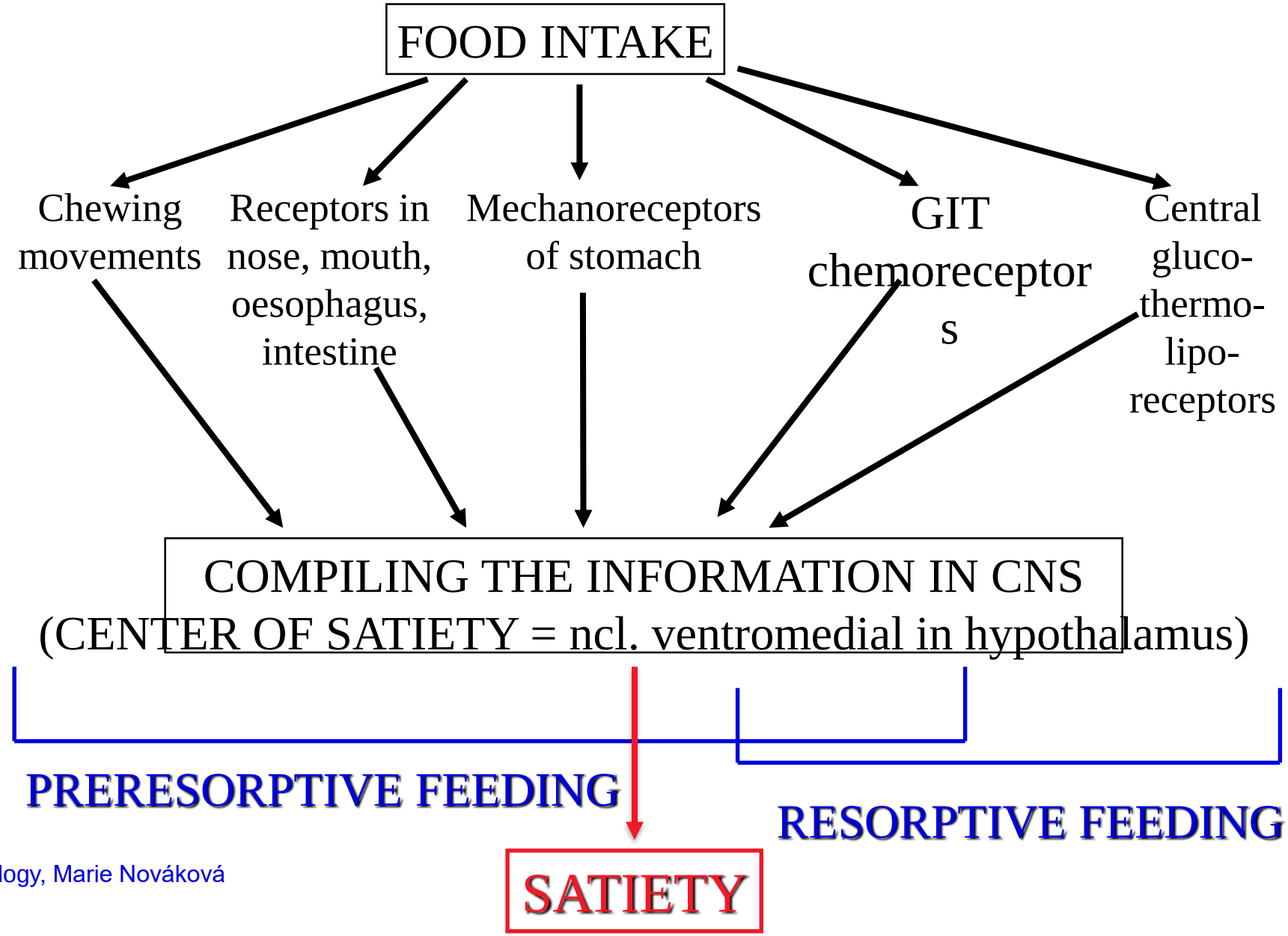
FEELING OF SATIETY



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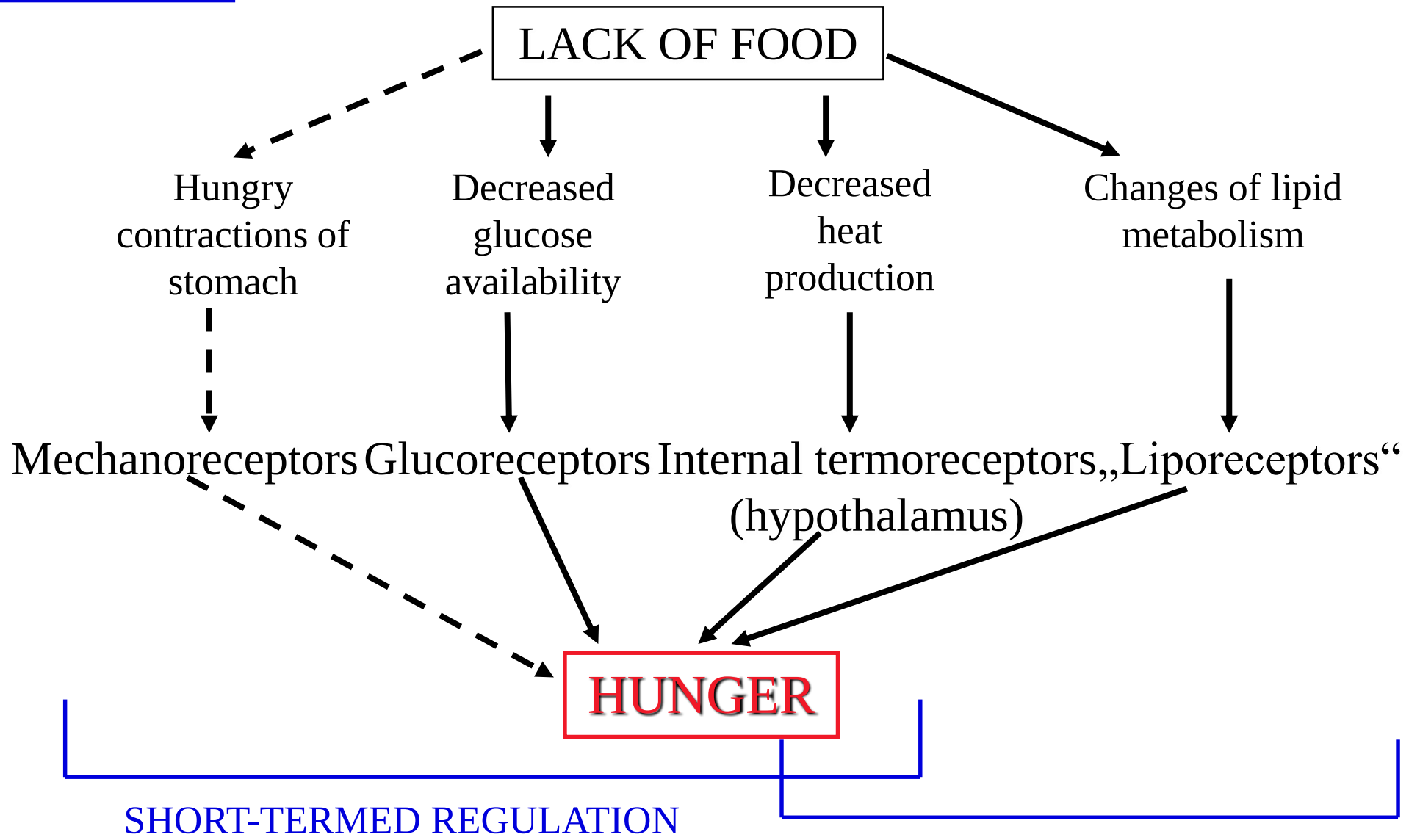
FEELING OF HUNGER



Hormone	Source	Site of Action	Effect
Insulin	Pancreatic beta cells	Hypothalamus	↓Appetite ↑Metabolism
Leptin	Fat cellsEndocrine cells of the stomach	Hypothalamus ↓NPY, AgRP ↑POMC Vagal afferents	↓Appetite ↑Metabolism ↓Ghrelin release
CCK	I cells of the duodenum	Vagal afferents	↓Appetite ↓Gastric emptying
PYY	L cells of the ileum and colon	Hypothalamus ↓NPY, AgRP ↑POMC Stomach	↓Appetite ↑Metabolism ↓Gastric emptying
Ghrelin	Endocrine cells of the stomach, hypothalamus, large and small intestines	Hypothalamus ↑NPY, AgRP Vagal afferents	↑Appetite ↓Metabolism ↓Leptin release

↓, Inhibits; ↑, stimulates *AgRP*, agouti-related peptide; *CCK*, cholecystokinin; *NPY*, neuropeptide Y; *POMC*, proopiomelanocortin; *PYY*, peptide YY.