Homeostasis

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Outline of the lecture

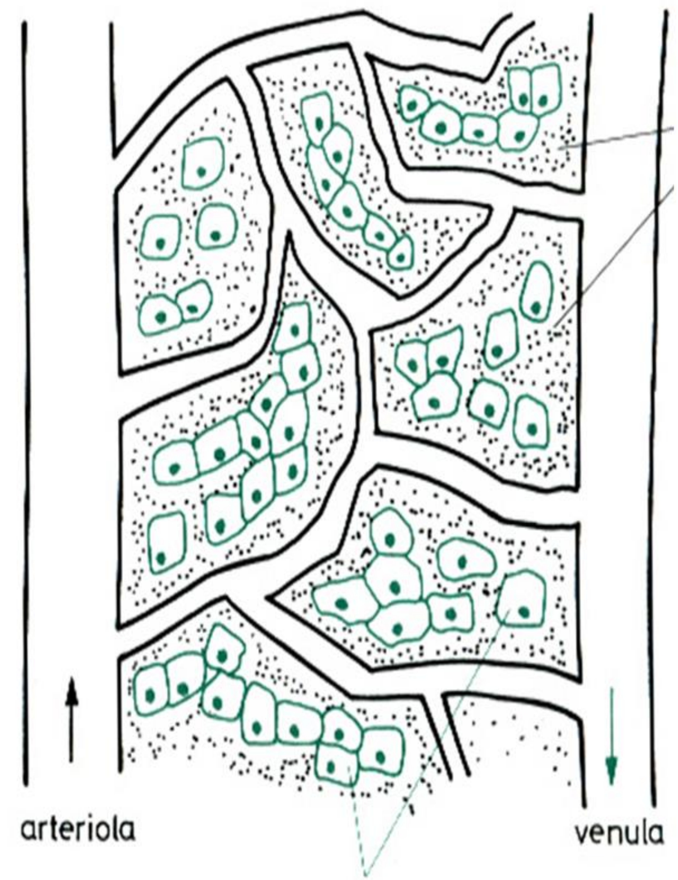
1. Internal environment of living organisms, homeostasis
2. Homeostatic regulations – endocrine system, hormones
3. Examples of homeostatic regulations not requiring the nervous system
   – Potassium level of blood plasma
   – Calcium level of blood plasma
4. Homeostatic regulations – nervous system
   – Elements of the nervous system
   – Hypothalamus
5. Examples of regulations involving the brain
   – Water balance
   – Body temperature regulation

Homeostasis

• Defined as maintenance of a relatively stable internal environment (Walter Bradford Cannon, 1932, The Wisdom of the Body).

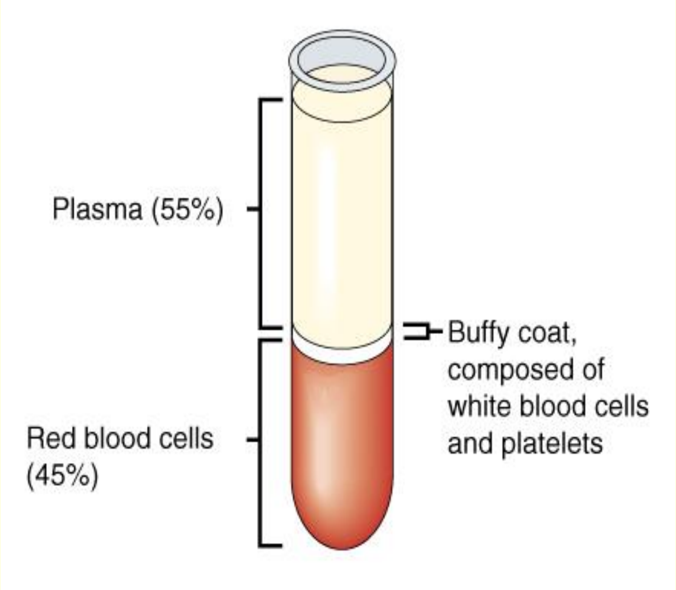
- Homeostasis is essential for survival and function of all cells
- Composition, temperature, and other characteristics are stable, which, however, does not mean that they are absolutely unchanging

Interstitial fluid is in interaction with the blood. Thus, the organisms provide homeostasis to its cells primarily through the regulation of the composition of the blood.



Sejtek az intersticiális térben

Blood composition



Which parameters should be relatively stable?

Plasma composition

- Contains 90% water
- 7% plasma proteins
  - created in liver
  - confined to bloodstream
  - albumin
    - maintain blood osmotic pressure
  - immunoglobulins
    - antibodies bind to foreign substances called antigens and form antigen-antibody complexes
  - fibrinogen
    - for clotting
- 3% other substances
  - Nutrients, electrolytes, gases, hormones, waste products

Some components of homeostasis

Isoionia: homeostasis of ion concentrations and organic small molecules

Ion concentrations in blood plasma:

Na+.......143 mmol/l	Cl-.........................103 mmol/l
K+.............4 mmol/l	HCO3-.. ....24 mmol/l
Ca++......2,5 mmol/l	H2PO4- és HPO4--…1 mmol/l
Mg++.........1 mmol/l	

Some organic small compounds:
Glucose….4.5-5.5 mmol/l
Urea........2.5-6.3 mmol/l

Isosmosis: Osmotic pressure of blood plasma: 290 milliosmol/l

Isohydria: H-ion concentration: $[H^+]$=35-40 nmol/l (pH: 7.38-7.42)

Buffer systems: carbonates, phosphates, hemoglobin, plasma proteins

Physical parameters: **isovolemia** (homeostasis of blood volume), **isothermia**

Causes of deviation from homeostasis

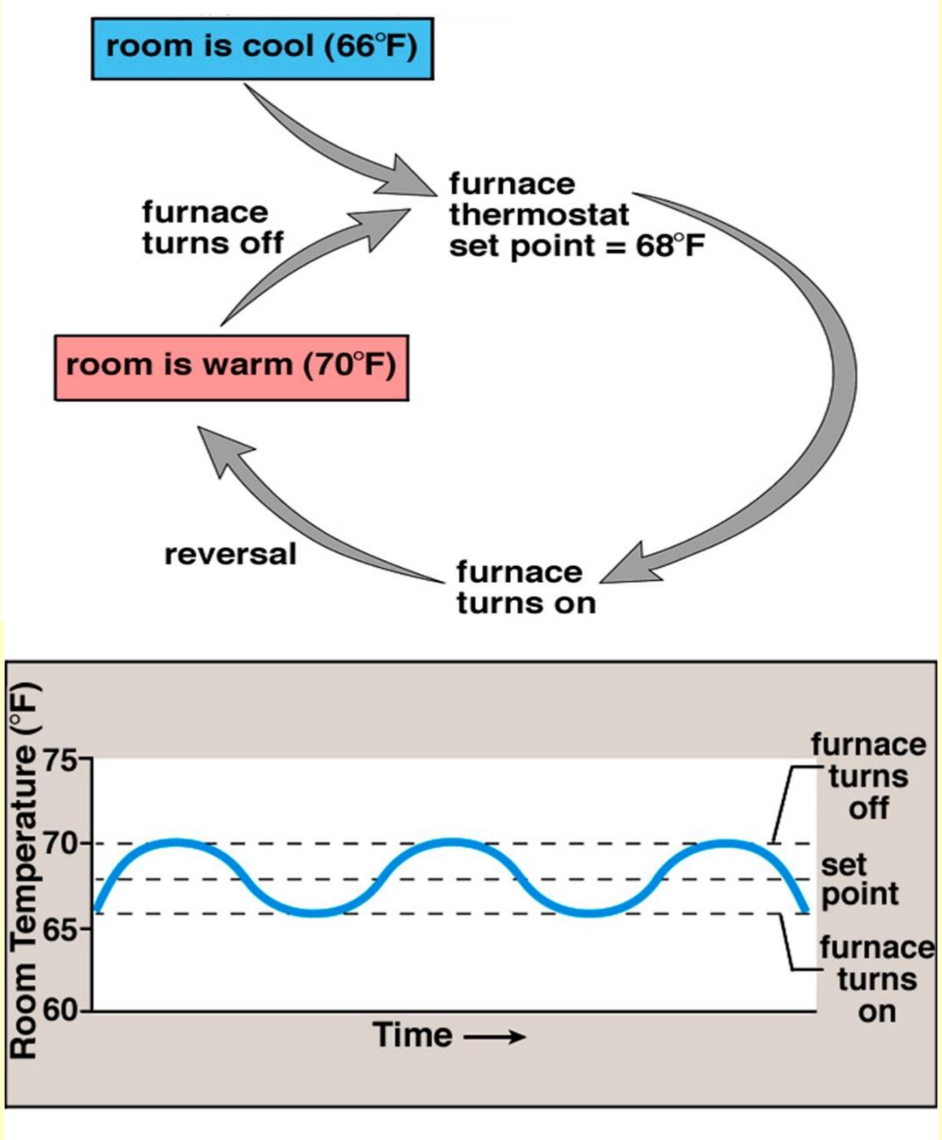
- Homeostasis is continually being disrupted by
  - External threatening stimuli
    - Heat, cold
    - Lack of oxygen
    - Pathogens, toxins
  - Internal stimuli
    - Non-equilibrial processes
    - Food intake, drinking
    - Physical and psychological distresses

Homeostatic control systems

In order to maintain homeostasis, control system must be able to:

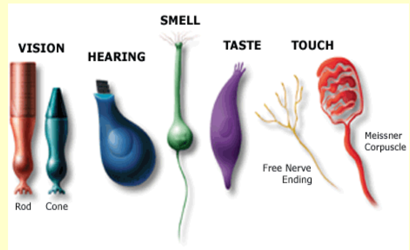
- **Detect** deviations from normal in the internal environment that need to be held within limits
- **Integrate** this information with other relevant information
- **Respond**: make appropriate adjustments in order to restore factors to their desired values (**set point**)

Temperature regulation by thermostat

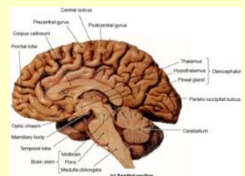


Feedback loop

- Receptor - structures that monitor a controlled condition and detect changes

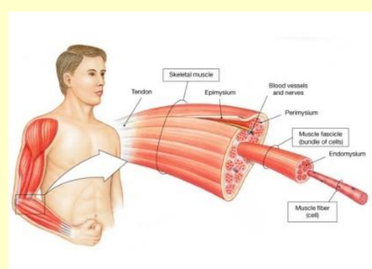


- Control center - determines next action

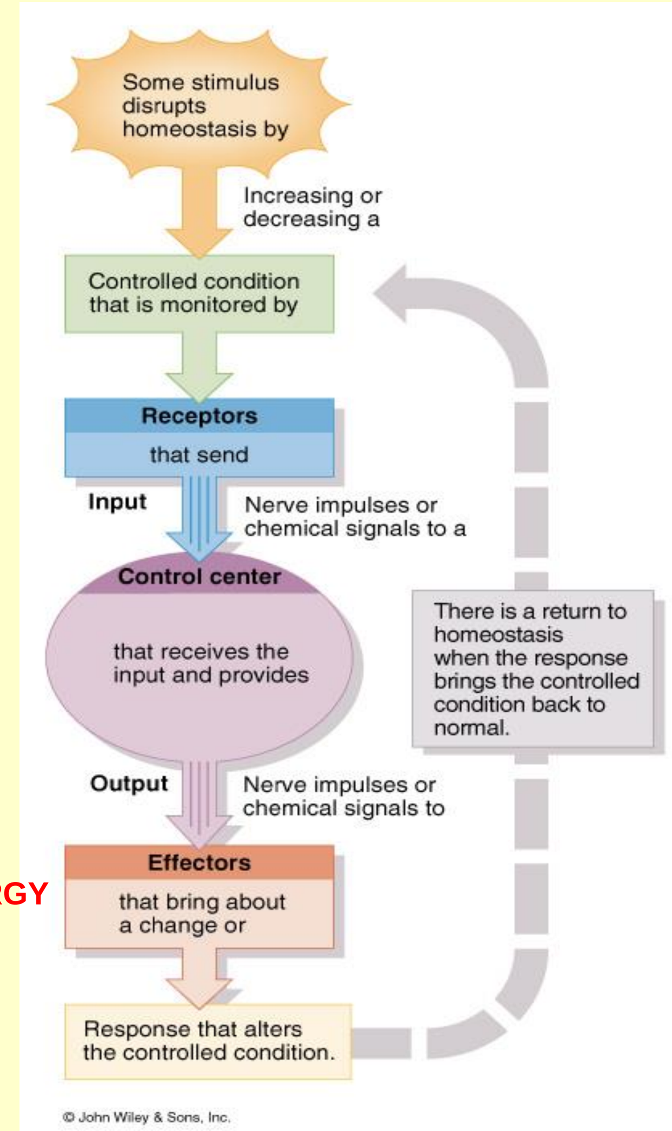


Neuronal, endocrine, or immune system

- Effector
  - receives directions from the control center
  - produces a response that restores the parameter



ENERGY



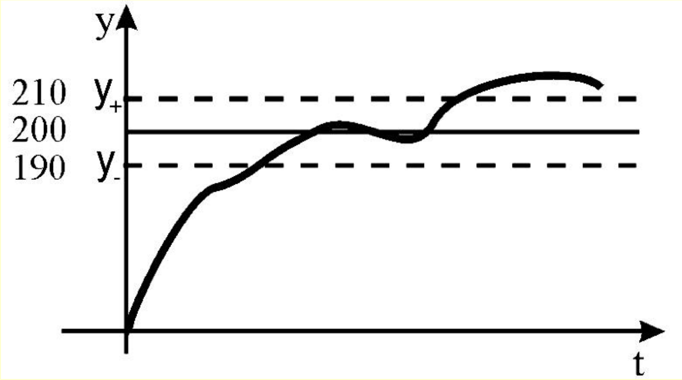
Some characteristics of the regulation

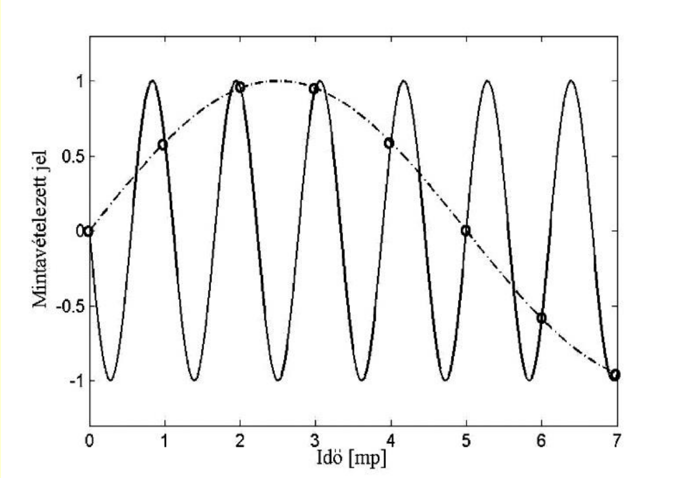
• What are the limits, between which the regulation can keep the parameter (in case of “slow” changes)?

• How quickly can the regulation respond?
- It is important that both the sampling rate of the sensor and the speed of the control process be greater than the expected changes in the process output

• Can the regulation actively control both directions of the process (only takes off the accelerator or also brakes)?

• Is the system multi-stable? (Is the parameter regulated by multiple regulatory systems?)

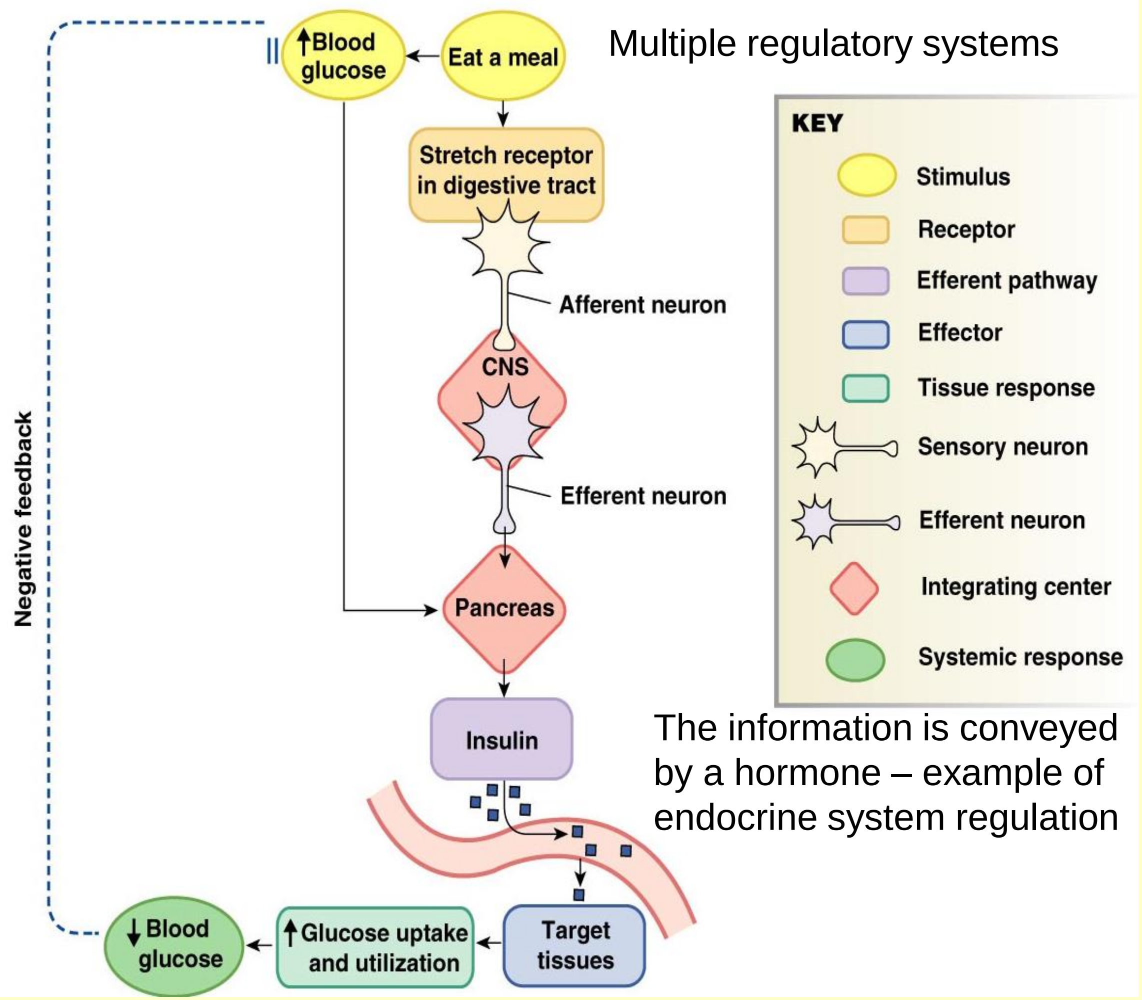




Example of negative feedback loop to control blood glucose concentration

- Blood glucose concentrations rise after a sugary meal (the stimulus)
- The hormone insulin is released and it speeds up the transport of glucose out of the blood and into selected tissues (the response)
- Blood glucose concentration decreases (thus decreasing the original stimulus)
- Characteristics: limit, speed, directions, multiple systems

Multiple regulatory systems

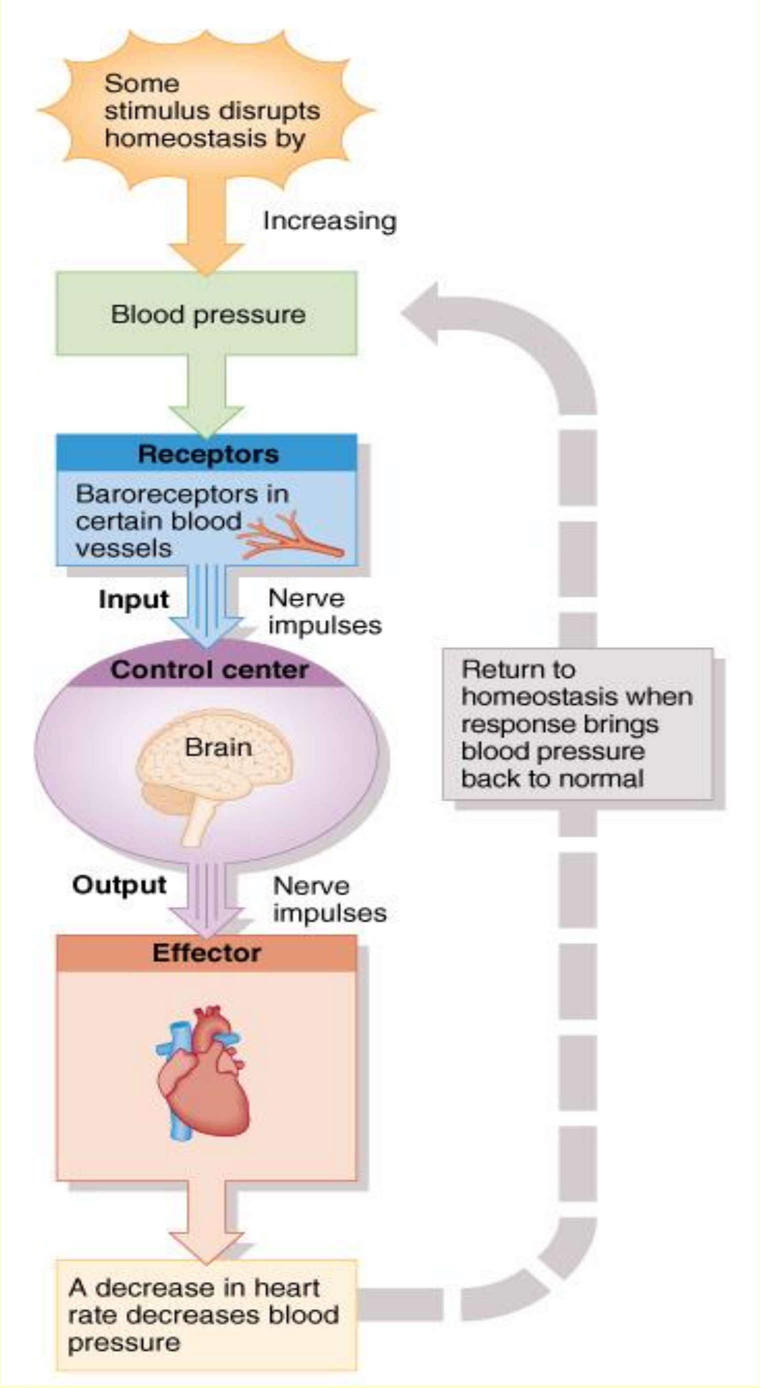


The information is conveyed by a hormone – example of endocrine system regulation

Homeostasis of blood pressure

– an example of neuronal regulation

- Baroreceptors in walls of blood vessels detect an increase in blood pressure
- Brain receives input and signals blood vessels and heart
- Blood vessels dilate, heart rate decreases
- Blood pressure decreases
- Characteristics: limit, speed, directions, multiple systems
- Negative feed-back regulation



Positive feedback during childbirth

- Stretch receptors in walls of uterus send signals to the brain
- Brain induces release of hormone (oxytocin) into bloodstream
- Uterine smooth muscle contracts more forcefully
- More stretch, more hormone, more contraction etc.
- Cycle ends with birth of the baby & decrease in stretch

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Endocrine glands

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4. Thyroid (and parathyroid) gland
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7. Langergans' islands of pancreas
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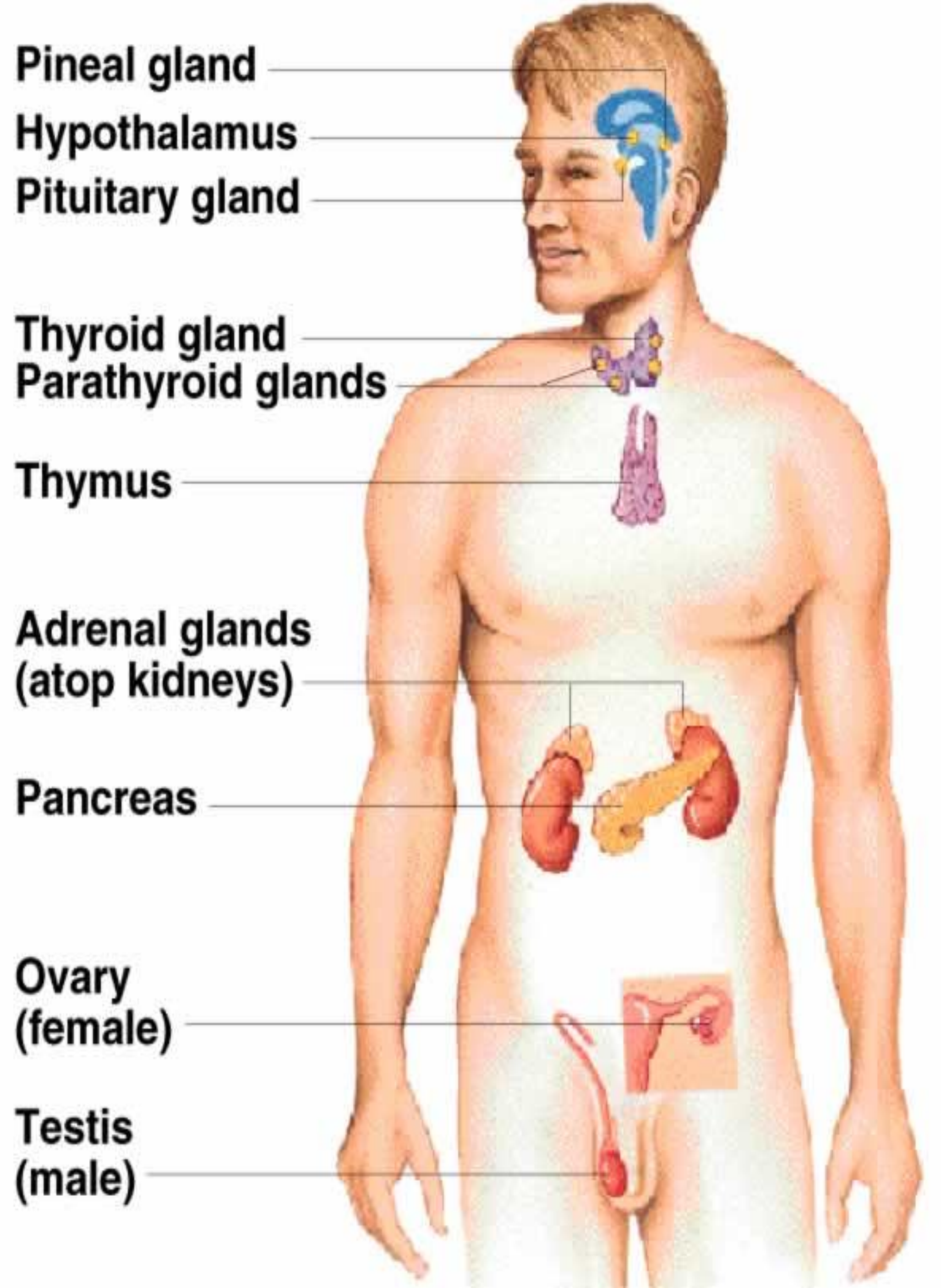
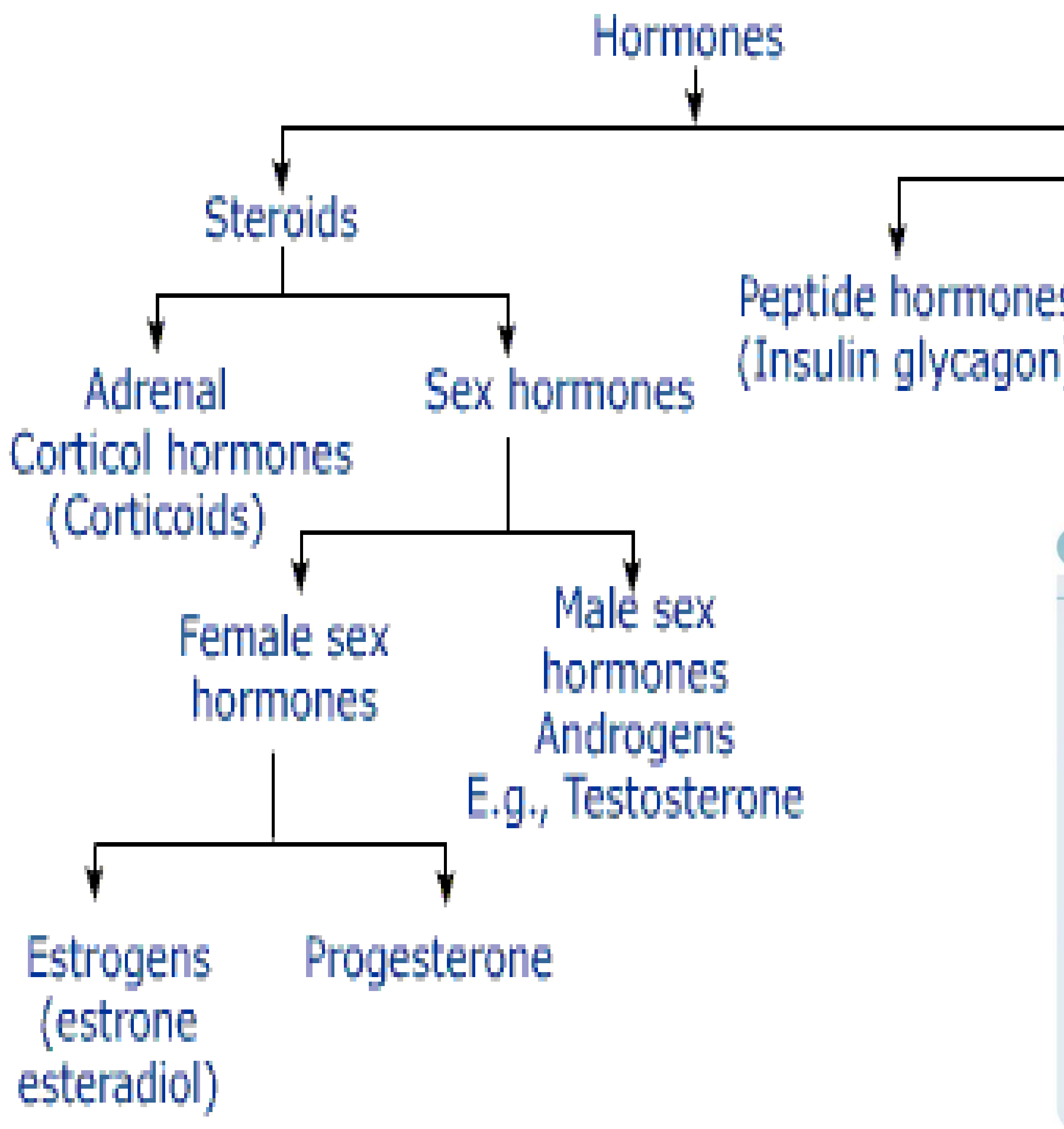


Chemical nature of hormones



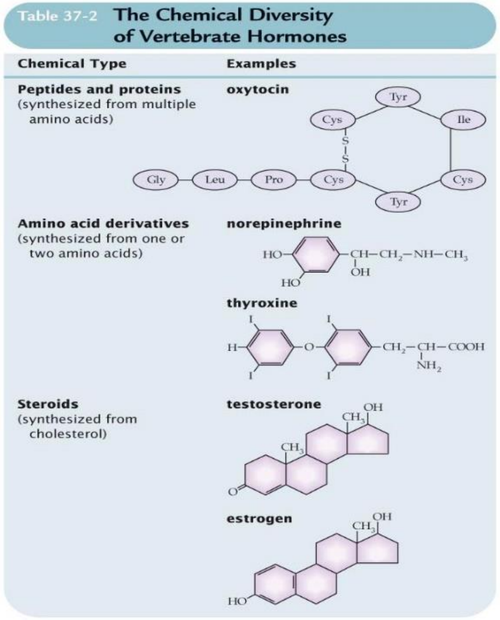


Table 37-2 The Chemical Diversity of Vertebrate Hormones

Chemical Type	Examples
Peptides and proteins (synthesized from multiple amino acids)	oxytocin
Amino acid derivatives (synthesized from one or two amino acids)	norepinephrine; thyroxine
Steroids (synthesized from cholesterol)	testosterone; estrogen

Functional consequences of chemical properties of hormones

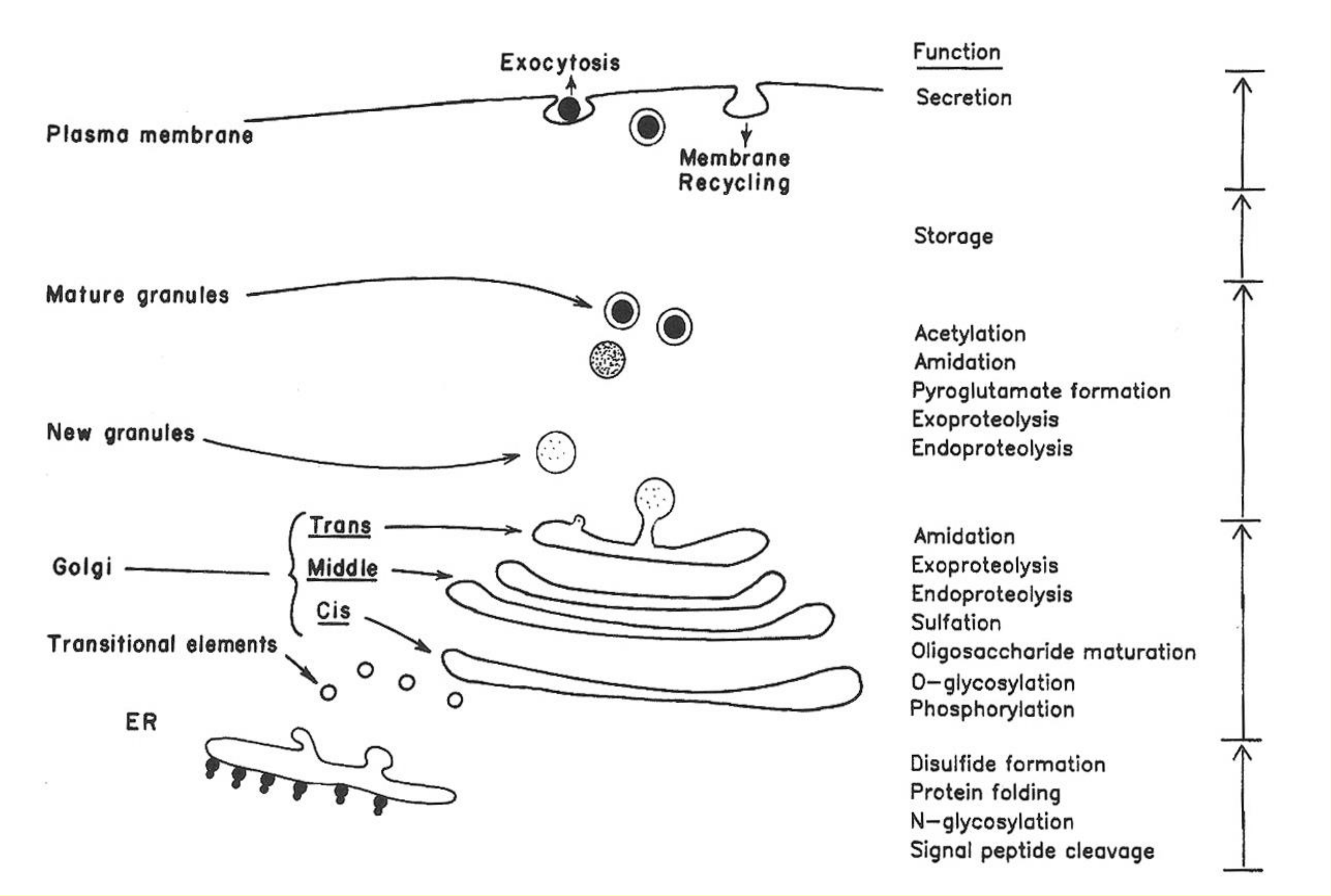
Steroid (and other lipophilic) hormones

- can penetrate the membrane
- are not accumulated in cells as they are released immediately
- their concentration in blood is determined by the speed of synthesis
- are transported in blood by binding proteins
- directly reach the brain for neuronal-endocrine interactions

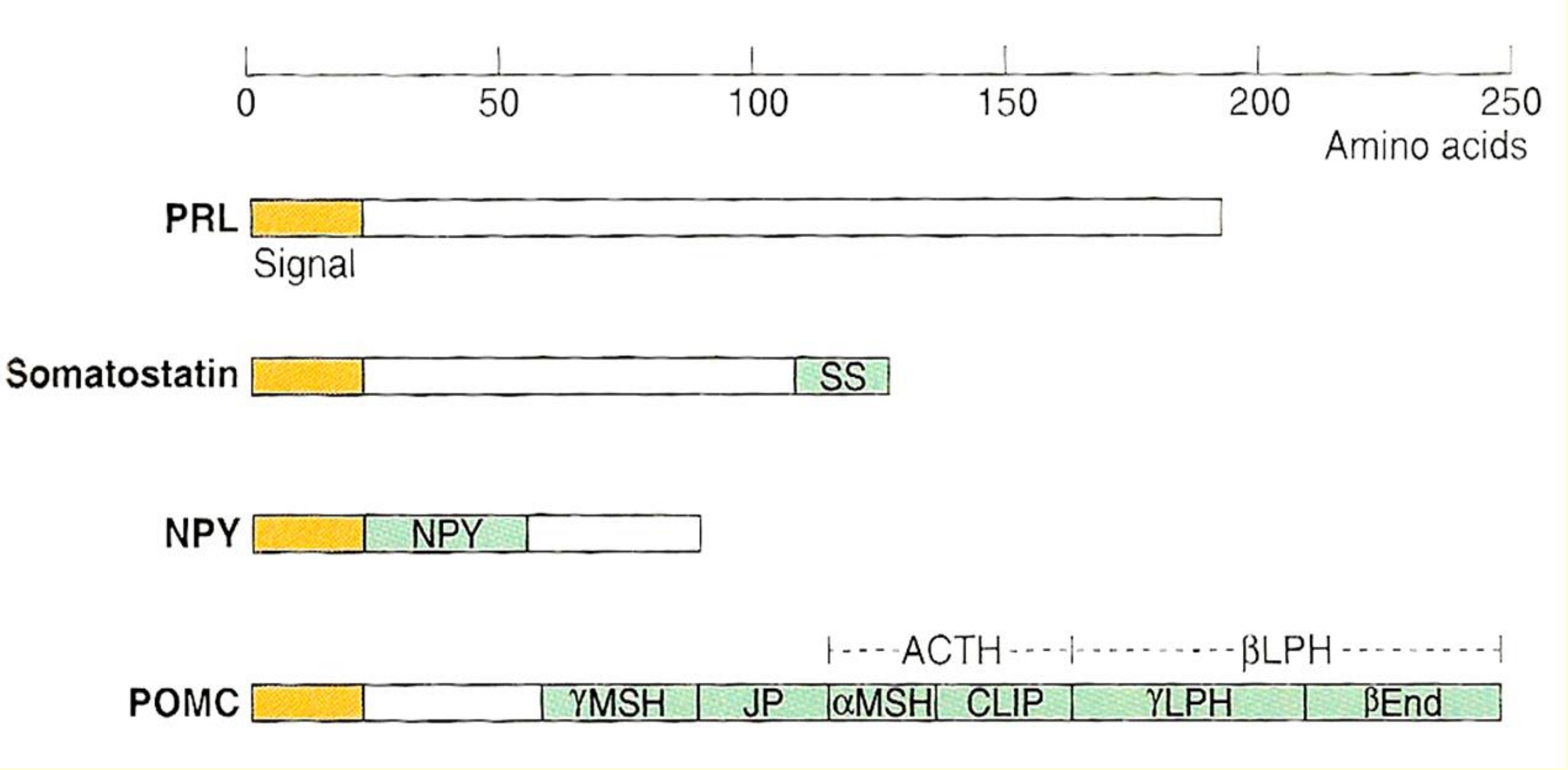
Peptide and protein hormones (always water soluble)

- cannot penetrate membranes
- accumulate within the cells in vesicles and are secreted by exocytosis
- their concentration in blood is determined by their release
- are transported in blood as free molecules
- transporters are needed for their passage to the brain

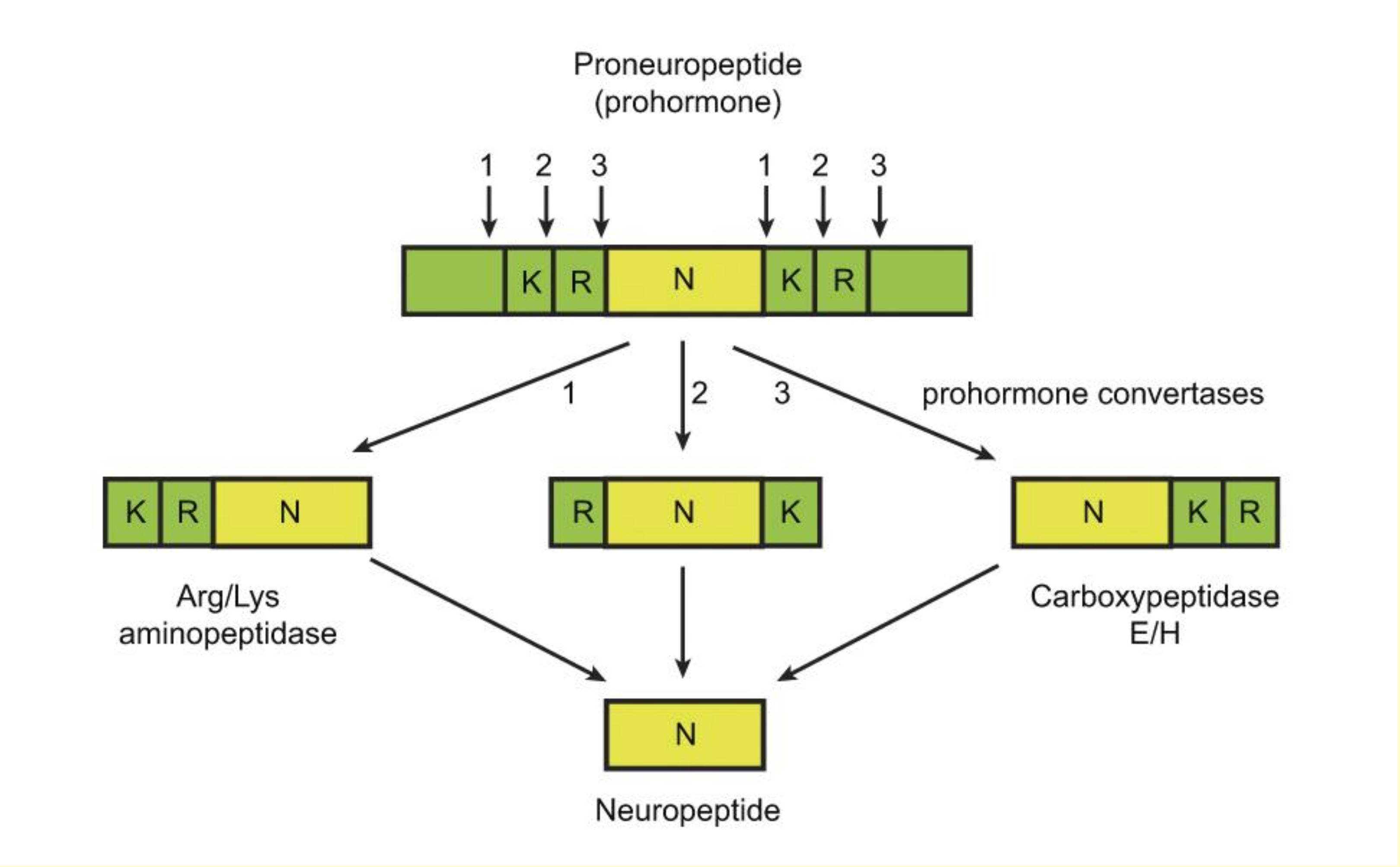
Synthesis, posttranslational modification and secretion of peptide hormones



Examples of the position of peptide hormones in the newly synthesized protein chains



Cleavage of prohormones by endopeptidases (prohormon convertases) in the Golgi apparatus



Action of hormones

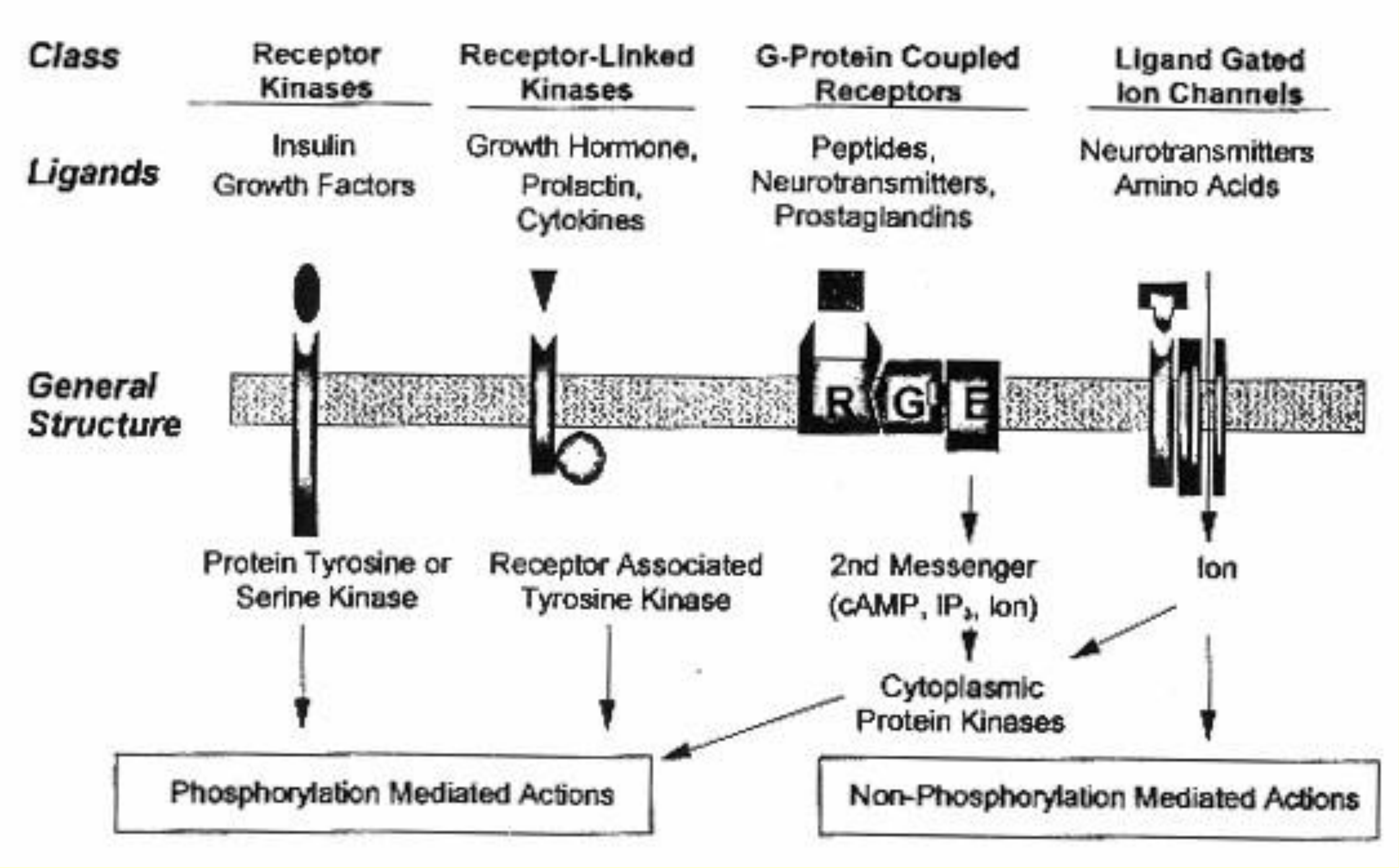
Steroid hormones:

- Steroid hormones enter through the cell membrane and bind to receptors inside of the target cell
- These hormones may directly stimulate transcription of genes to make certain proteins
- Because steroids work by triggering gene activity, the response is slower than peptide hormones

Protein/peptide hormones:

- Protein/peptide hormones do not enter the cells directly. These hormones bind to receptor proteins in the cell membrane.
- When the hormone binds with the receptor protein, a secondary messenger molecule initiates the cell response
- Protein/peptide hormones often produce fast responses

Types of membrane-bound receptors

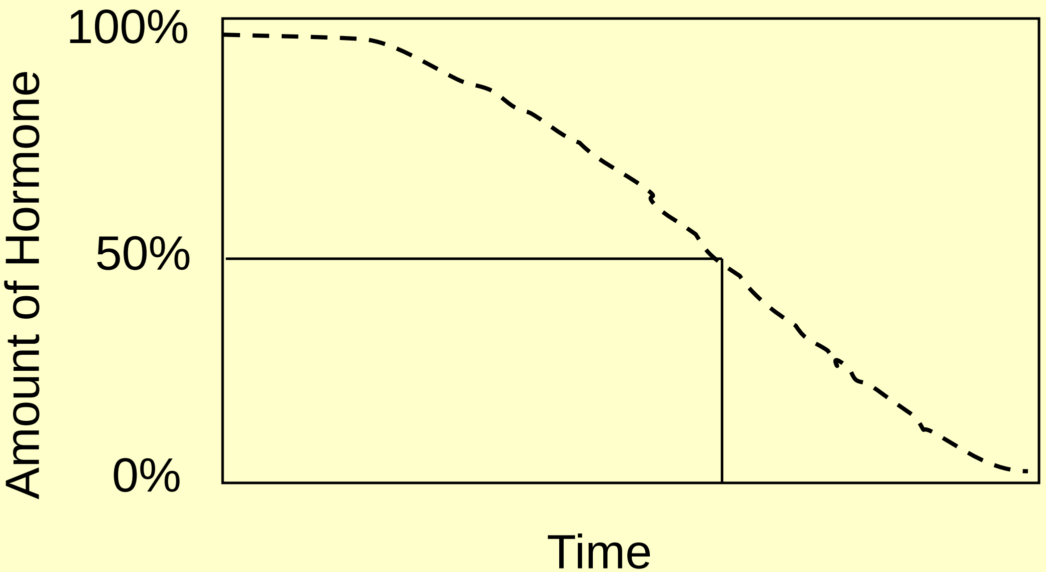


Inactivation of hormones

- Hormones are eventually broken down (metabolized) and/or excreted from the body
- Steroid hormones are inactivated mainly in liver. Inactive metabolites are excreted mainly with urine.
- Peptide/protein hormones are typically inactivated by proteolysis, which takes place in the circulation. The proteases are often produced in the liver.
- The rate of inactivation and removal from the circulation is fairly constant for a given hormone. Thus, typically their synthesis/release and not inactivation is regulated.

Inactivation of hormones – half-life

The length of time it takes to remove half of the amount of a hormone from the circulation is the half-life of that hormone.
The half-life ranges :
- from several min to 20 min – for the majority of peptide and protein hormones
- till 1 h – for steroid hormones
- till 1 week – for thyroid hormones



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Some components of homeostasis

Isoionia: homeostasis of ion concentrations and organic small molecules

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Buffer systems: carbonates, phosphates, hemoglobin, plasma proteins

Physical parameters: **isovolemia, isotermia**

Potassium homeostasis

- Blood plasma concentration: 3.6-5.0 mmol/l
- Excretion: 90% kidney, 10% gut

- Causes of low potassium ion level:
  - reduced oral intake
  - intestinal loss: diarrhea, vomiting
  - renal loss: kidney disease

  Consequence:

  $K_i/K_e \Uparrow$ ➔ muscles cannot properly contract

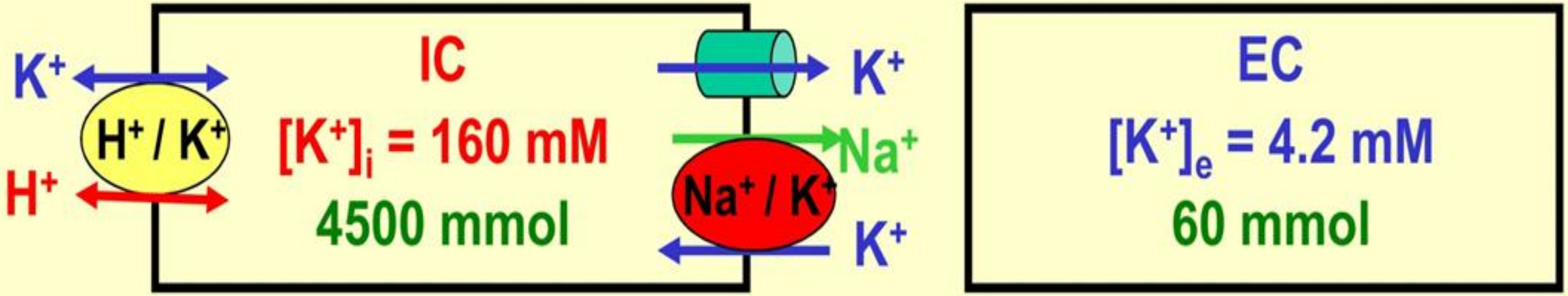
- Causes of high potassium ion level :
  - increased potassium intake (combined with kidney disease)
  - reduced excretion in kidney (e.g. due to digitalis poisining)
  - potassium loss from cells (trauma, hemolysis, cytostatics)

  Consequence: :

  Elevated excitability of muscles: spasms of sceletal muscles, and cardiac problems

Passive regulation of blood plasma potassium ion level from „internal store”

Compartmentalization of potassium ion:



The total amount of potassium ion 75-times higher in the intracellular than in the extracellular space.

Passive control: A small change of the intracellular potassium level, which has no effect on intracellular processes, can significantly compensate potassium ion level in the extracellular space.
Na-K pump, potassium channels and potassion transporters are present in the plasmamembrane of all cells. Extracellular K-ion level acts on the activity of these proteins, which effectively buffers extracellular K-ion levels.

Compartments interacting with the blood: potential surfaces of regulations

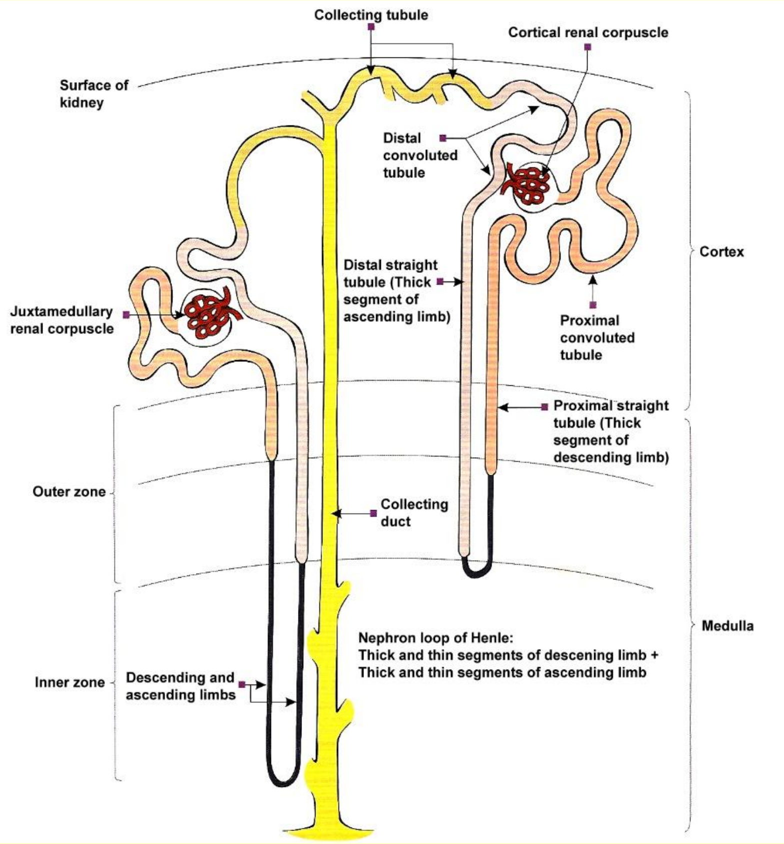
- Gastrointestinal tract
  - Behaviors determining feeding and drinking
  - Regulation of absorption
  - Secretion with faces

- Kidney

- Lung (mostly for gases)

- Sweat

- Internal stores
  - Binding proteins in the blood
  - Intracellular space of the cells
  - Organs specialized for storage



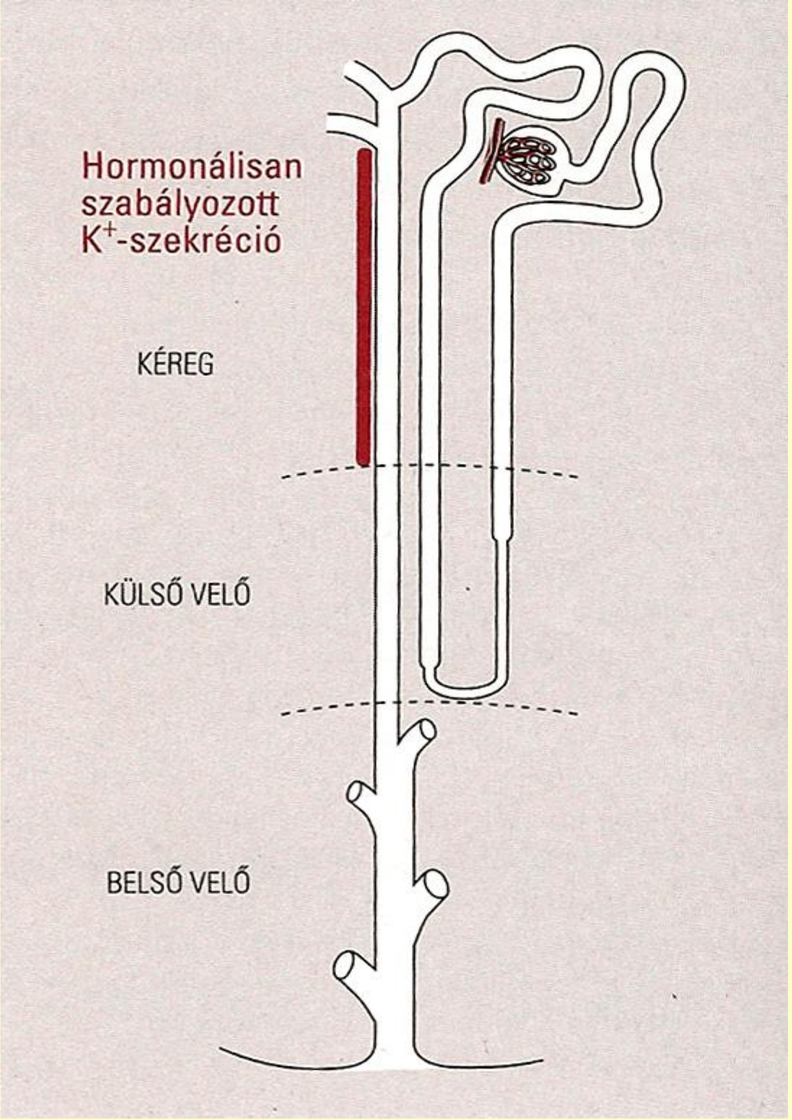
Hormonally regulated active control of blood potassium ion level

- 92% of potassium ion of the primary urine is reabsorbed before the collecting duct

- There is a low speed, non-controlled potassium ion reabsorption in the medulla, which reabsorbes all potassium ion leading to zero excretion without regulation

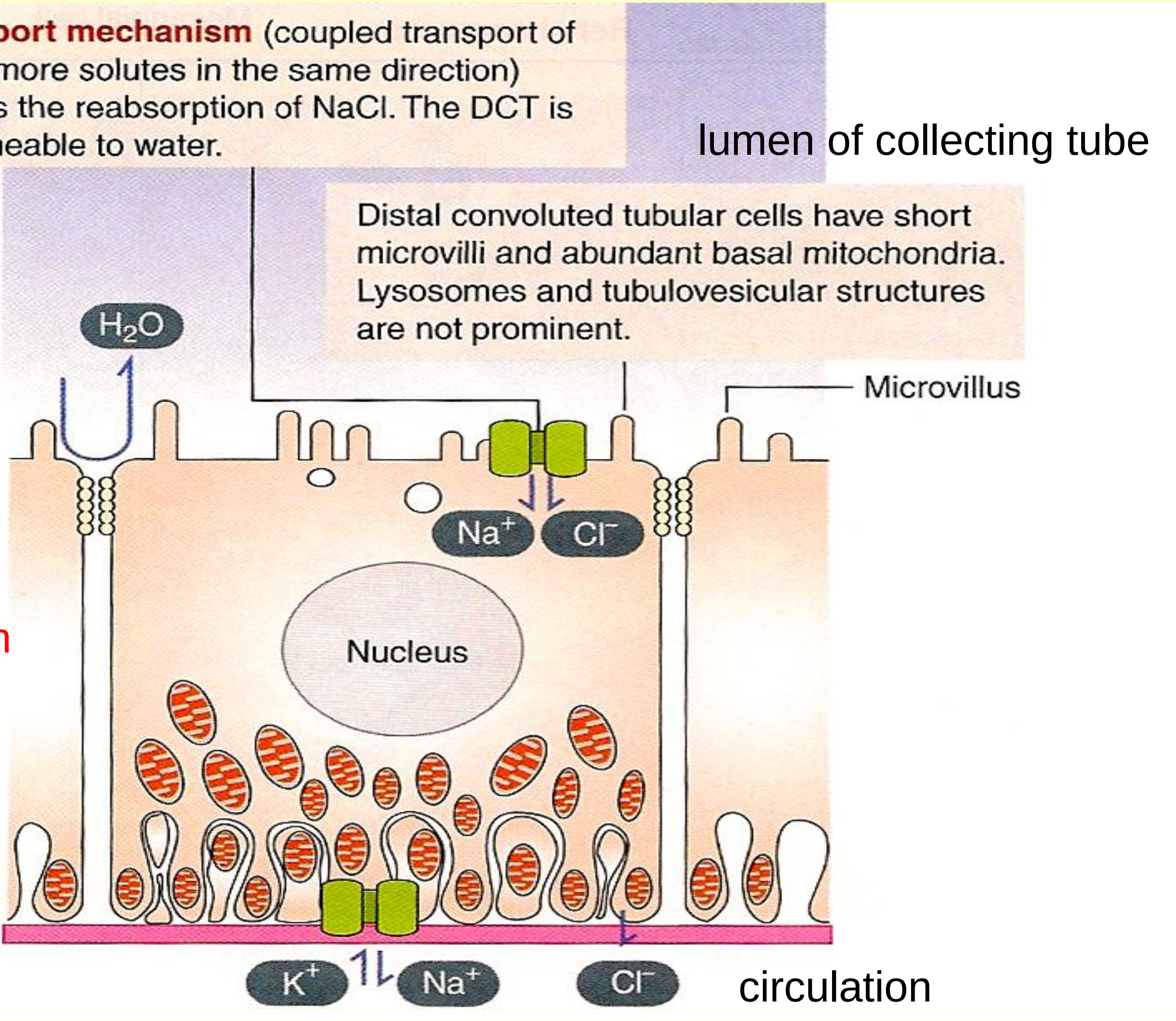
- ***Active regulation*:** **aldosterone**, a mineralocorticoid steroid hormone released from the adrenal gland leads to increased **secretion of potassium** in the initial segment of the collecting duct thereby reducing blood plasma potassium ion level. This is the only active regulation of potassium level of the blood.

- Regulation has only one direction, and is not very strong but still sufficient as passive regulation helps out and potassium intake with food is relatively constant in the long term. Potassium does not even have a specific taste (the salty taste is primarily determined by sodium ion).



Mechanism of action of aldosterone

Aldosterone increases the activity of the Na-K pump thereby increasing intracellular potassium ion level, which leads to its secretion to the lumen of the collecting tube.



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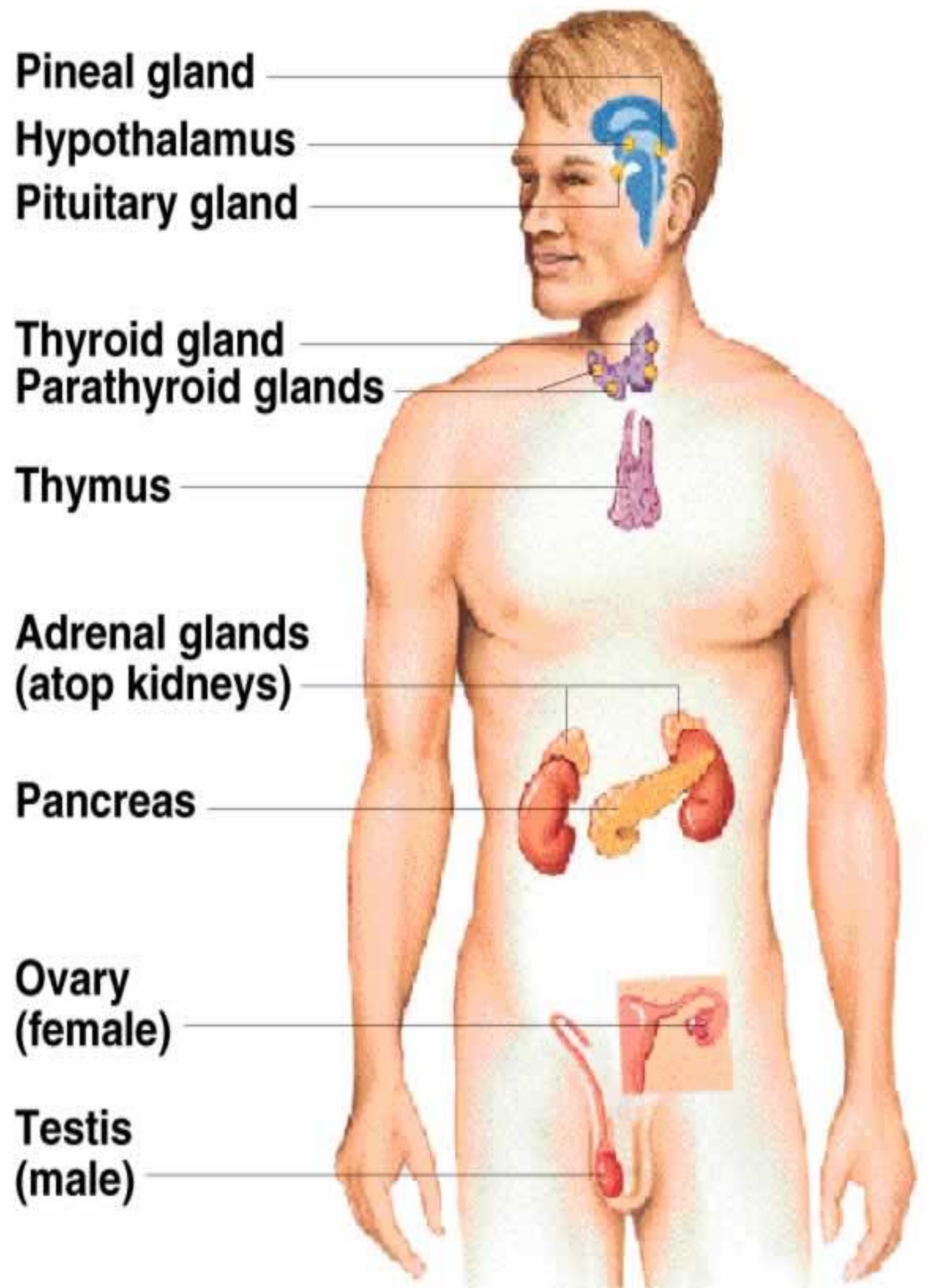
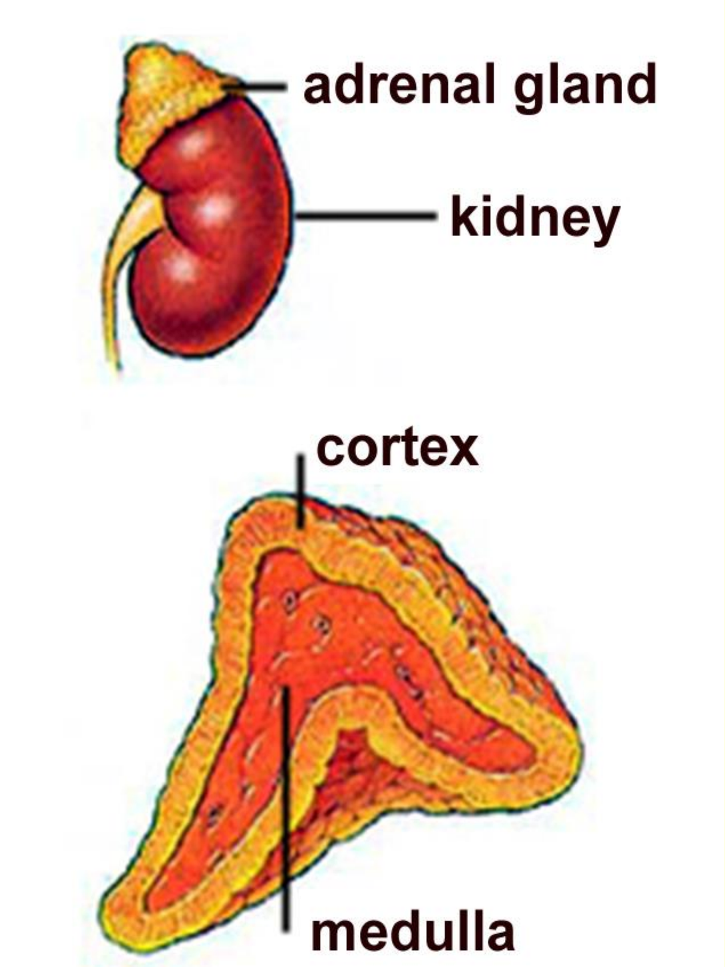


Adrenal gland



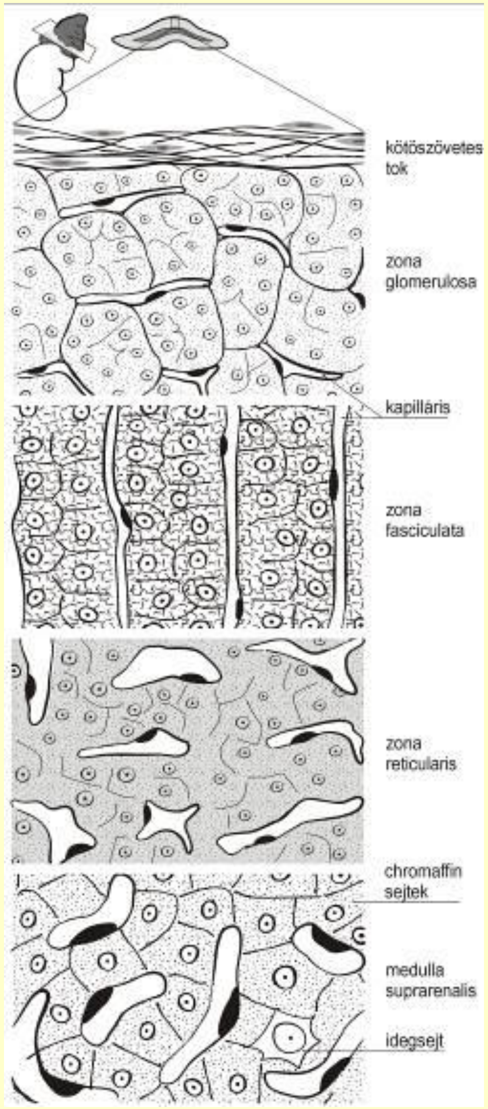
Mineralocorticoids

(aldosterone)

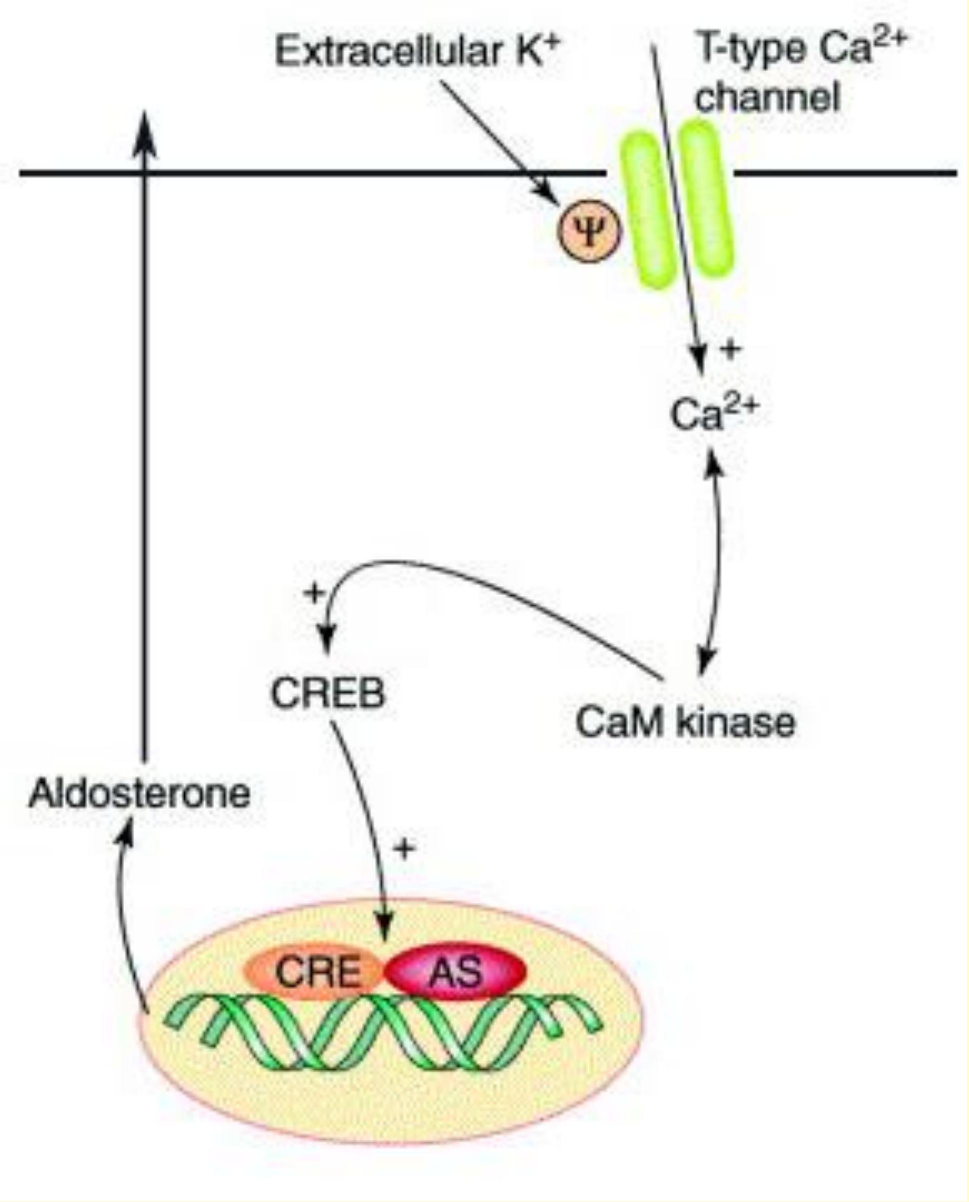
Glucocorticoids

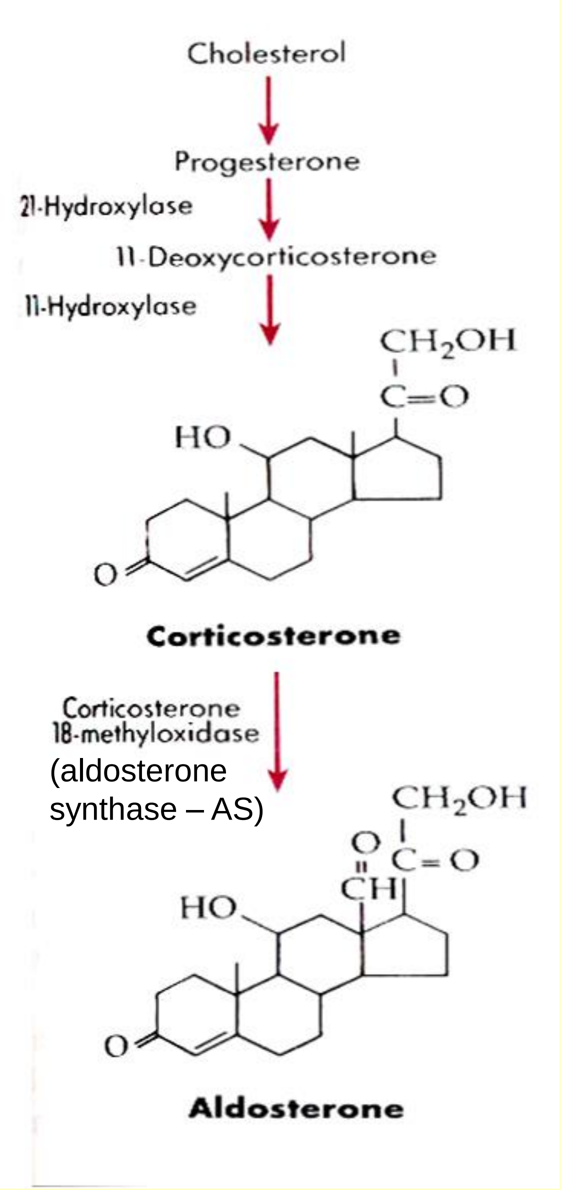
Sexual steroids

Catecholamines



Regulation of aldosterone secretion





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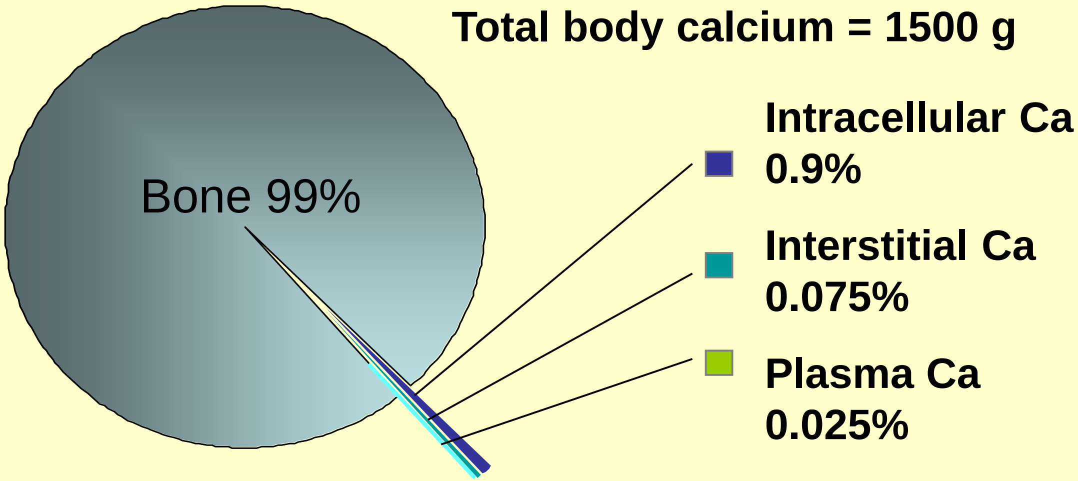
Calcium content of human

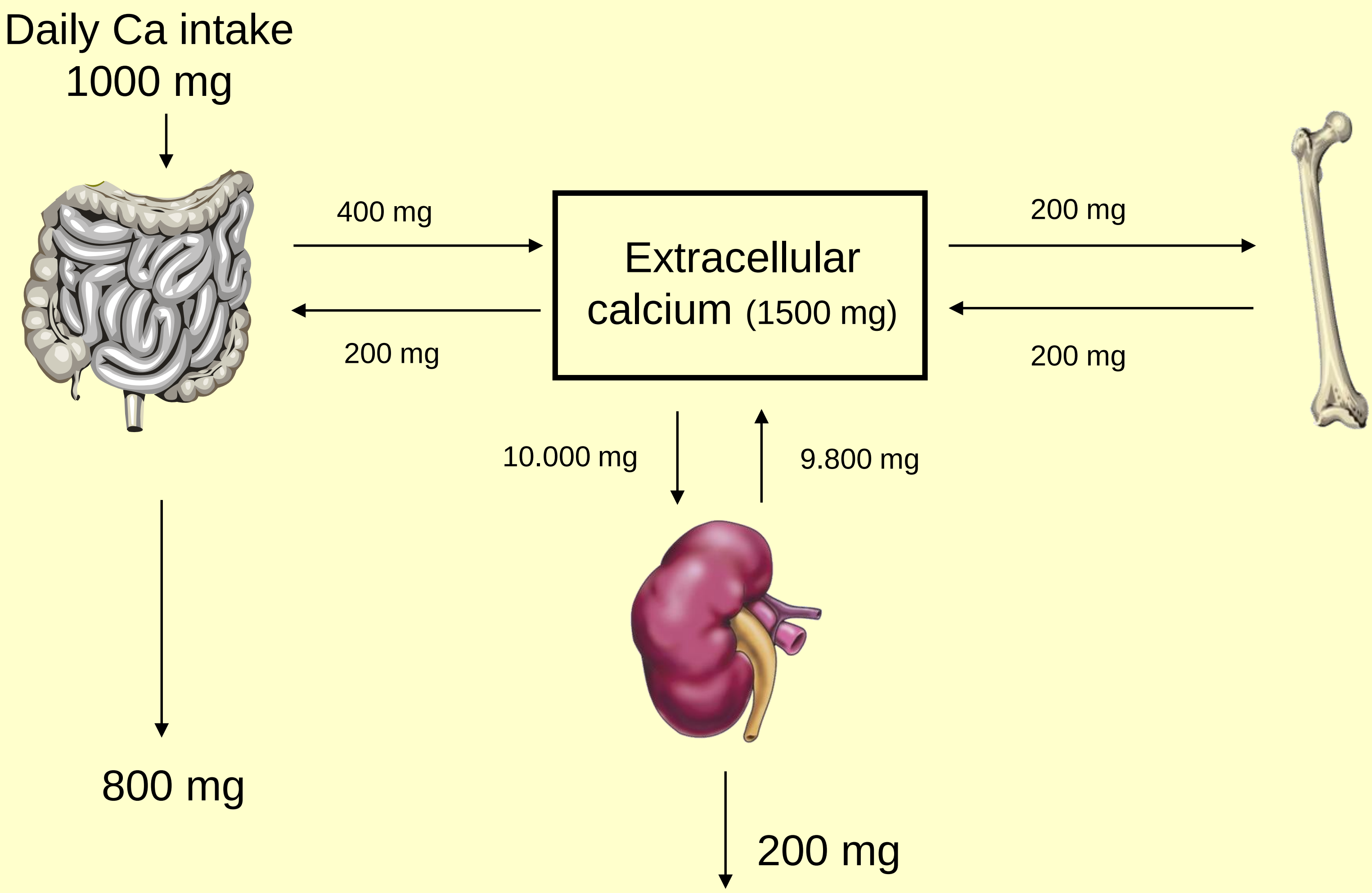


Plasma Ca:

Bound to proteins– 45%
In complexes– 10%
Ionized free Ca – 45%

Biologically active fraction

Calcium homeostasis



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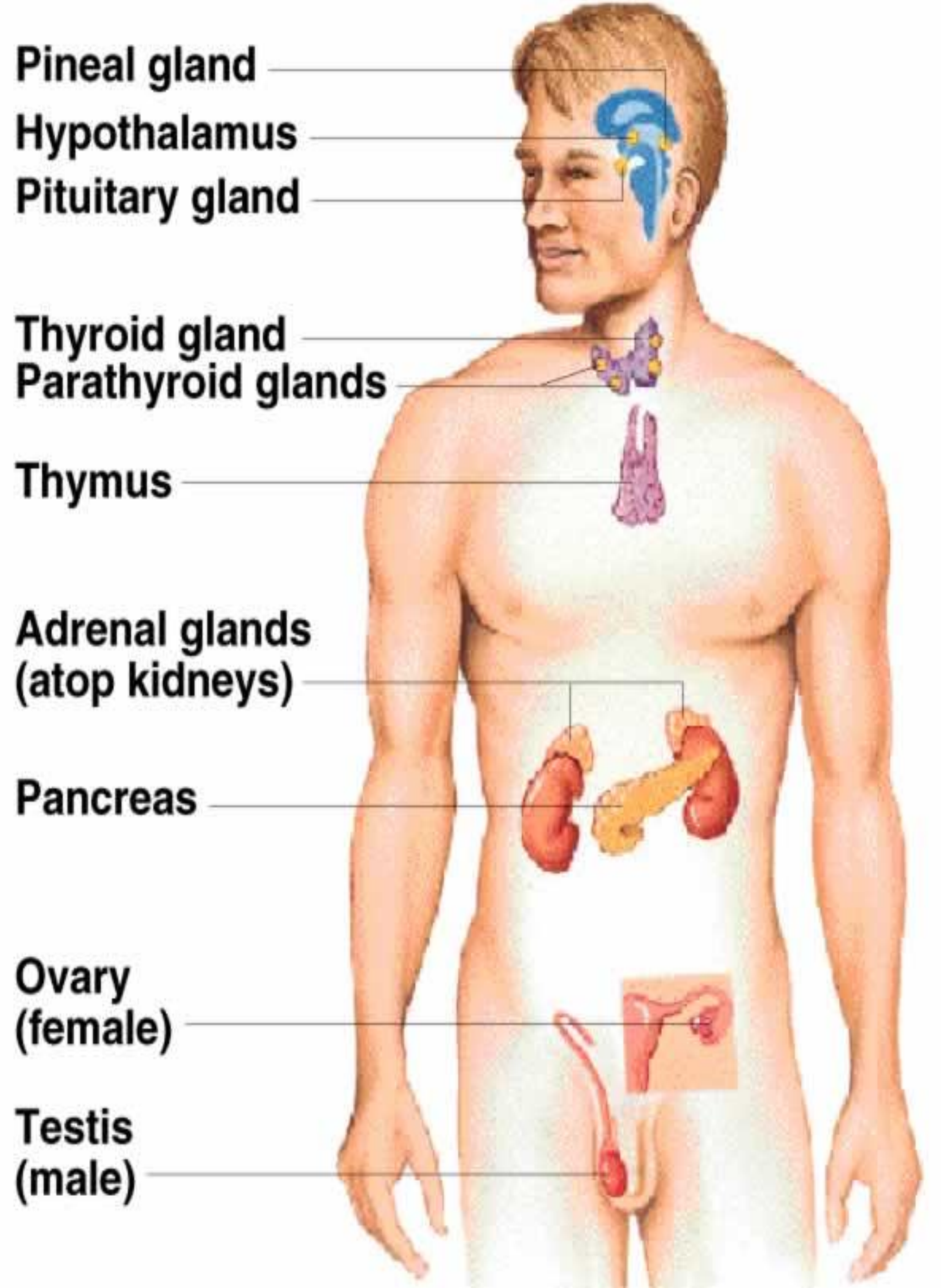


Regulatory hormones of calcium homeostasis

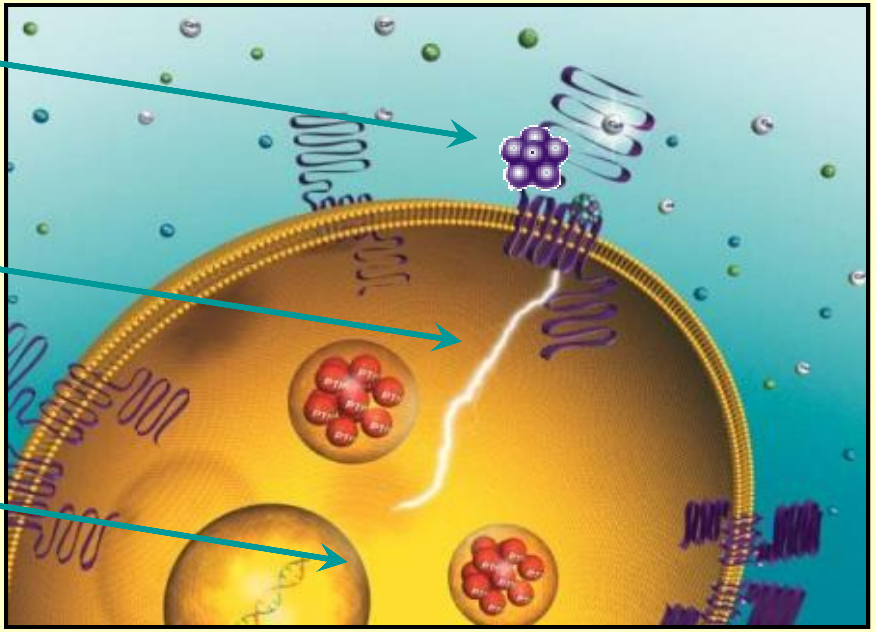
The major regulatory hormone is parathyroid hormone (PTH), which increases calcium ion level in the plasma. PTH is produced in the parathyroid gland when blood calcium ion levels decrease.

Another hormone, calcitonin has the opposite effect, it decreases plasma calcium ion level. Calcitonin is produced in C cells of the thyroid gland.

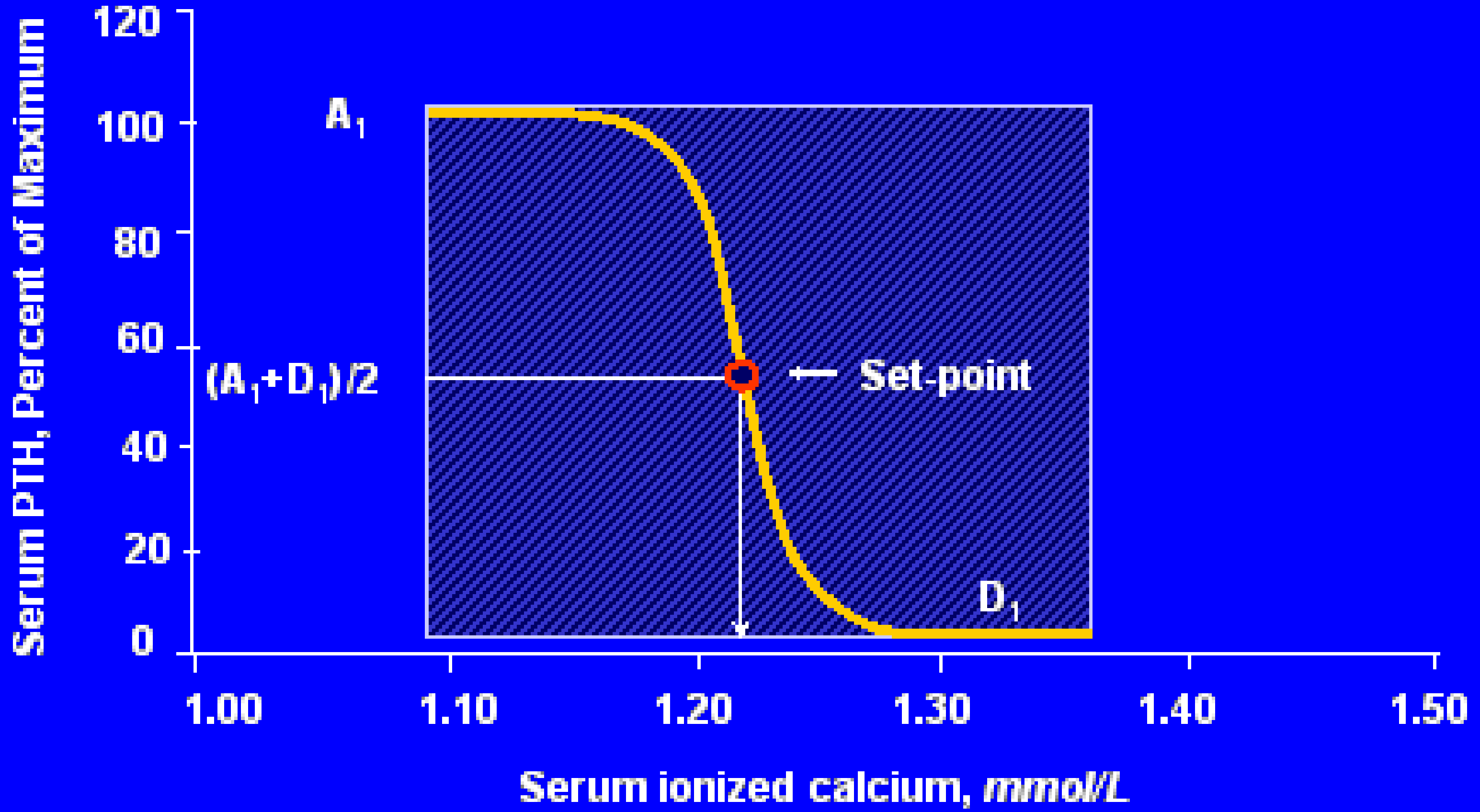
Calcium receptor senses calcium ion level in the plasma

Intracellular signaling of calcium receptor

If calcium ion level increases:
- PTH secretion is inhibited
- Calcitonon secretion is stimulated



Ca regulates PTH – through CaR



Adapted from Goodman WG et al. *Kidney Int.* 1996;50:1834-1844.

Target tissues of hormones regulating plasma calcium ion level

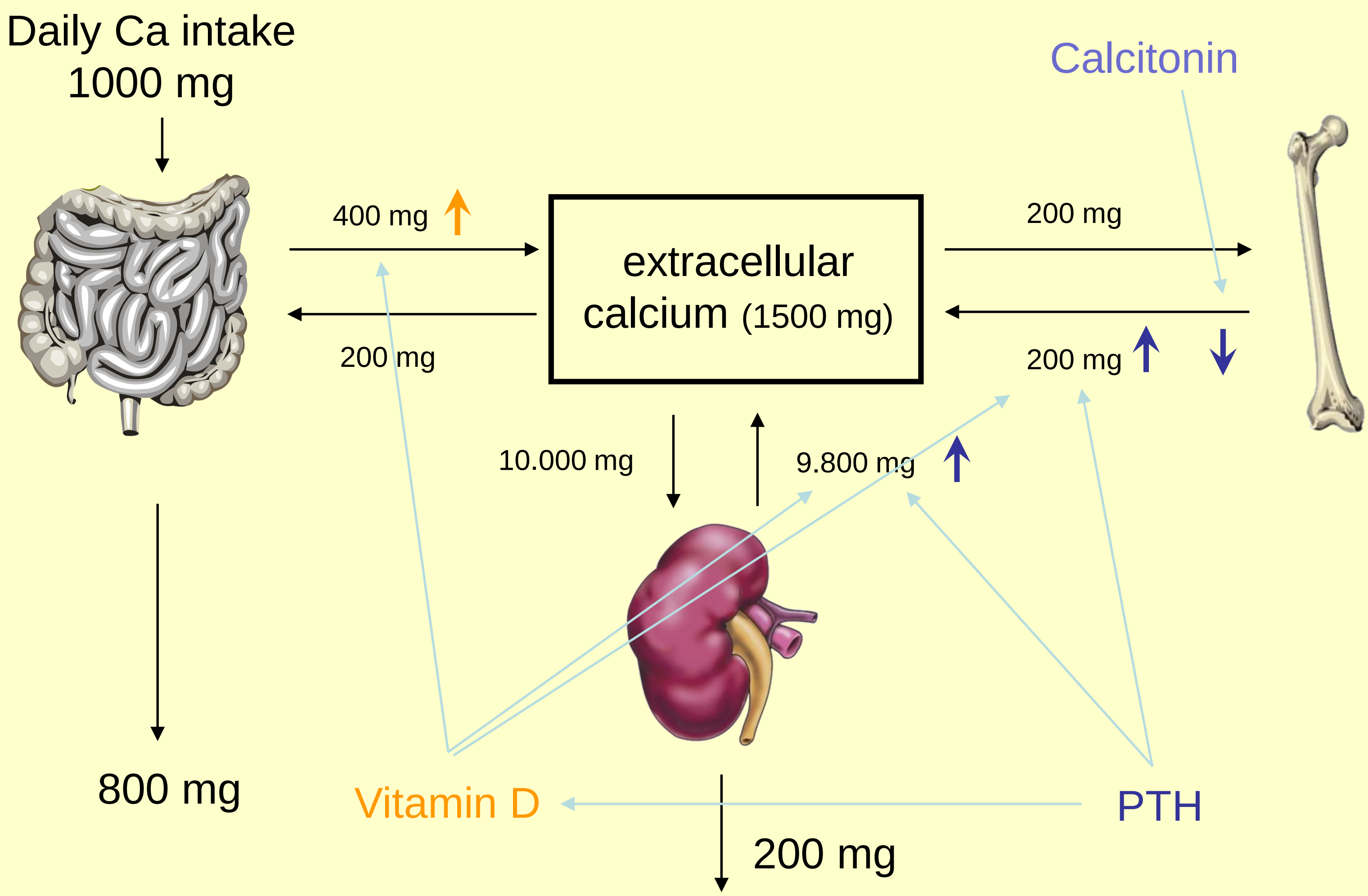
Parathyroid hormone:

- kidney
  - Stimulates calcium ion reabsorption
  - Stimulates the synthesis of vitamin D
- bone
  - Stimulates osteolysis
- gastrointestinal system
  - No direct effect
  - Vitamin D increases the absorption of calcium ion in the small intestine

Calcitonin:

- bone
  - Inactivates osteoclasts thereby inhibits osteolysis

Regulation of calcium homeostasis



Comparison of the regulation of plasma calcium to that of potassium ion

- Parathyroid hormone increases calcium ion level while aldosterone descreases potassium ion level, so the major direction of regulation is the opposite
- Calcium ion level can be actively regulated in both directions as not only parathyroid hormone but also calcitonin plays a role, which has opposite effect on plasma calcium level
- Parathyroid hormone acts to increase calcium ion levels in 3 different tissues while aldosterone regulates potassium ion level only in the kidney
- Parathyroid hormone has indirect effects, too. It includes another hormone, vitamin D in the control of plasma Ca ion level.
- Both regulations are coupled (potassium to sodium, calcium to phosphate), both opposing directions
- Neither regulation involves the nervous system

Comparison of the 2 major regulatory systems of the body

- Endocrine system
  - Secreting glands of endocrine regulate activities based on **internal** information, which require **duration** rather than speed

    E.g. controls concentration of nutrients and, by adjusting kidney function, controls internal environment’s volume and electrolyte composition
- Nervous system
  - Detects changes in **external environment**, too
  - Controls bodily activities that require **rapid** responses
  - Coordinates endocrine system with **behavioral** responses

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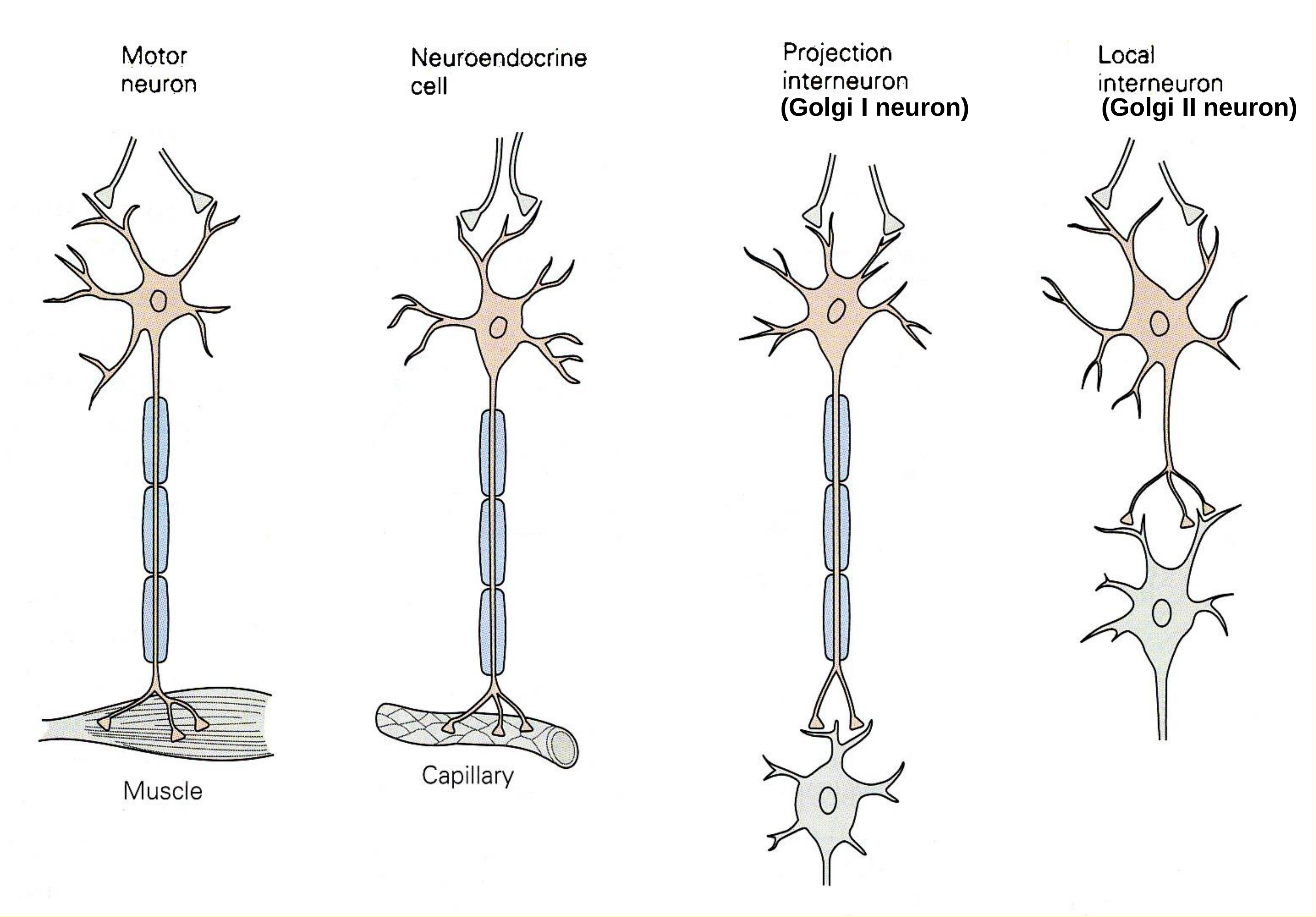
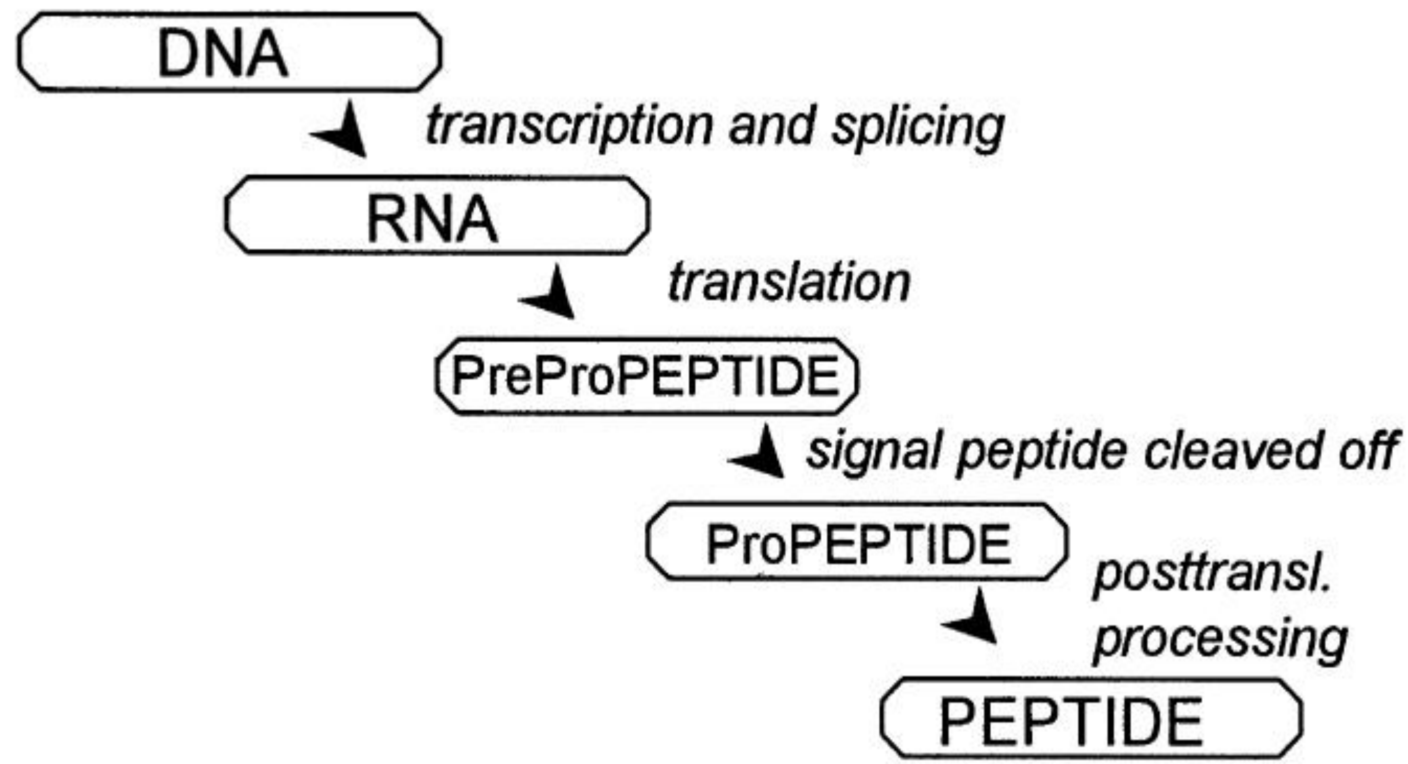
Types of CNS neurones based on their targets



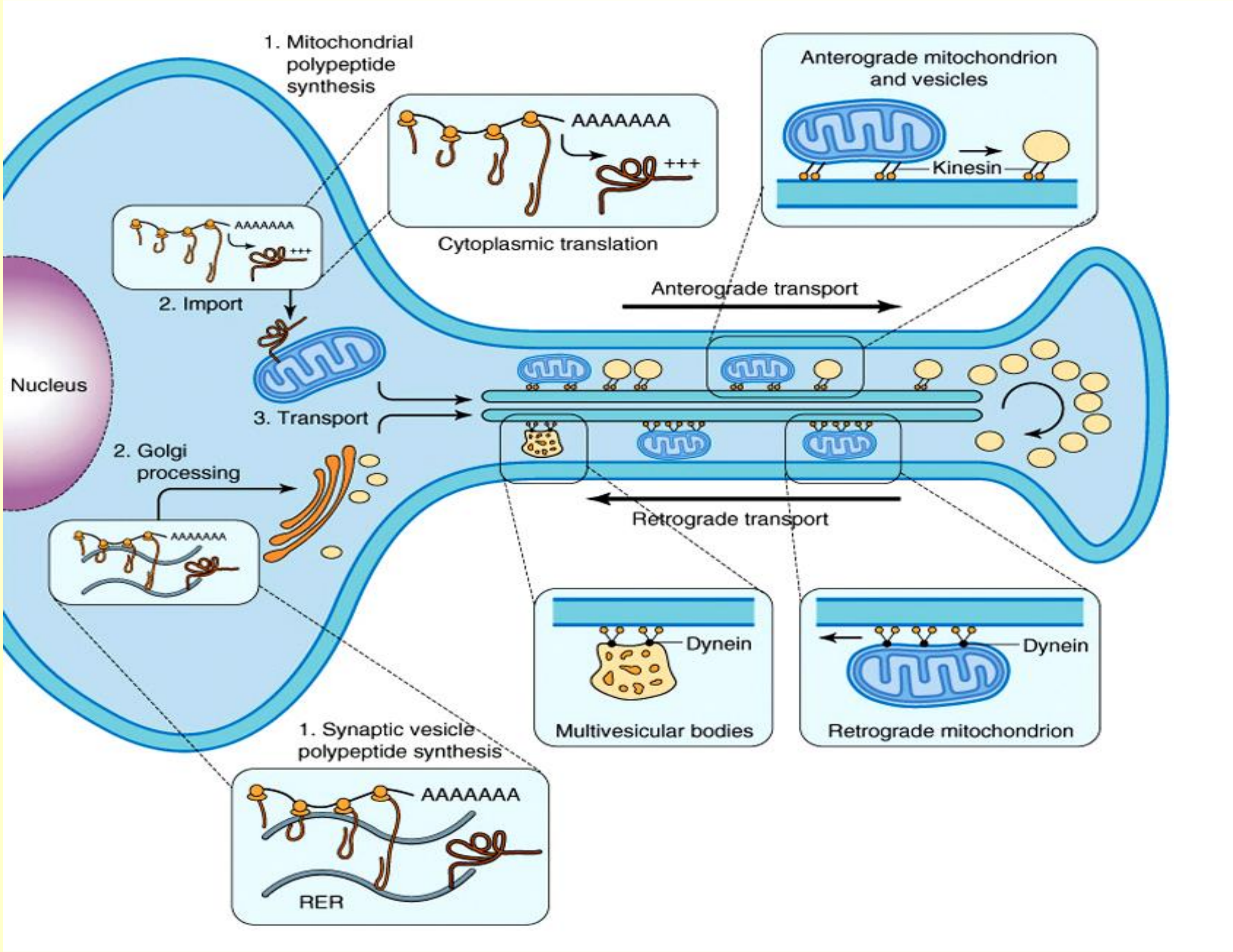
Definition and characteristics of neuropeptides (see similarities to peptide hormones)

- Consist of 3-50 amino acids
- Functions: 1. neurohormonal control of the endocrine system, 2. neuromodulatory function within the nervous system
- They are synthesized as prepropeptide and process through posttranslational modifications
- They are transported in axons towards the presynaptic terminal by vesicular transport
- They are released by regulated vesicular secretion
- Neuropeptides possess high-affinity G-protein coupled, 7TM cell surface receptors

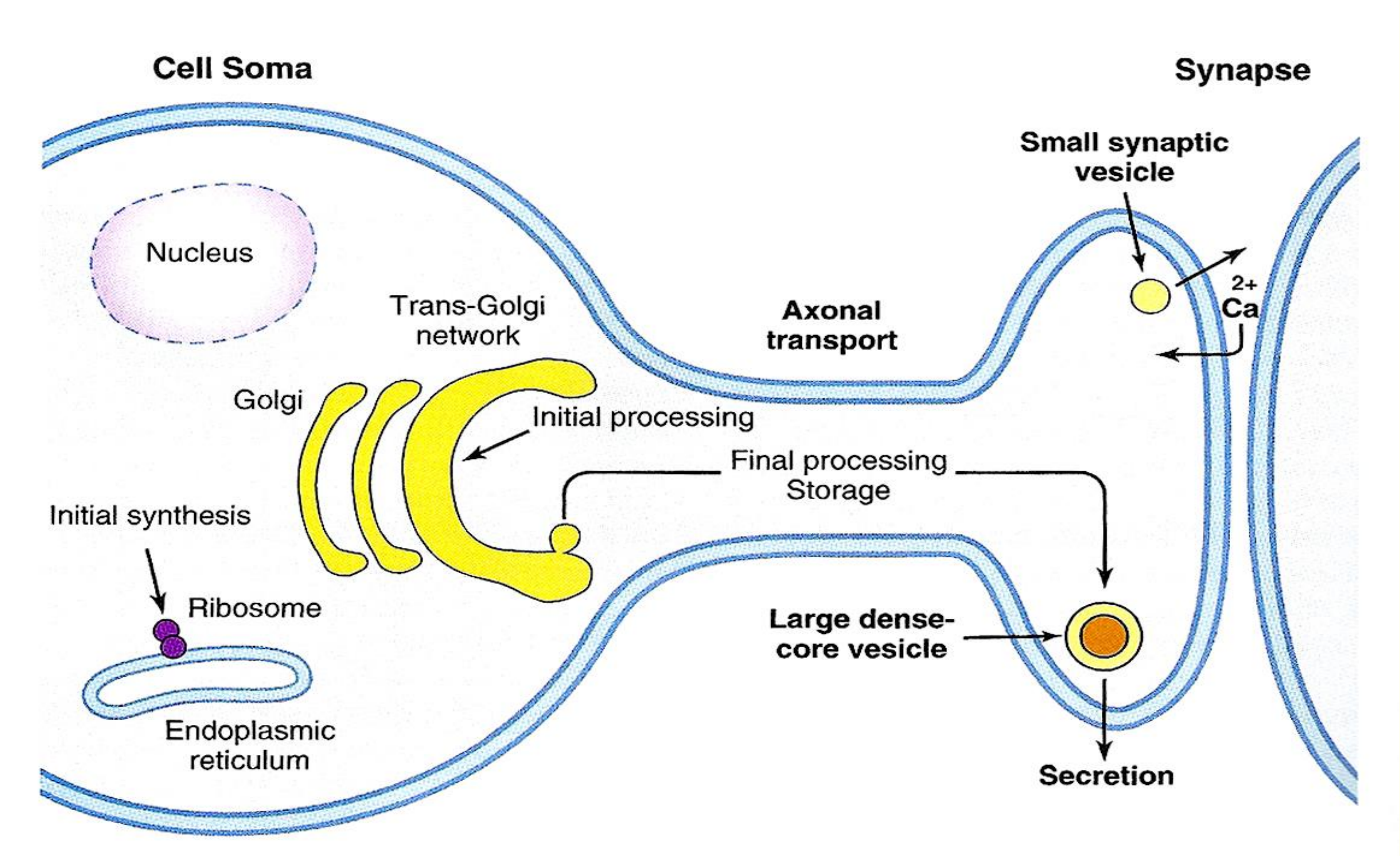
Synthesis of neuropeptides



Axonal transport of neuropeptides

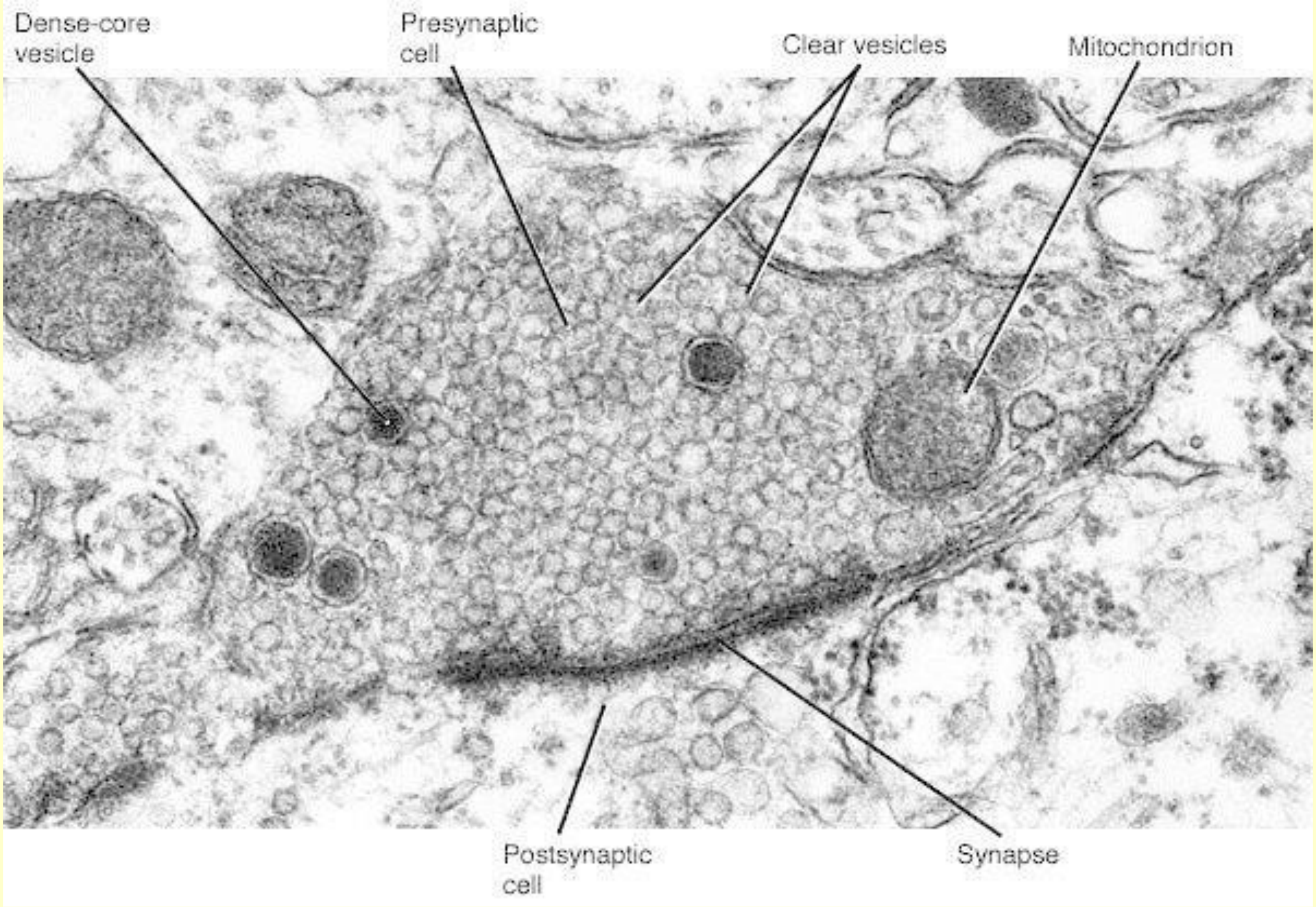


Storage of neuropeptides in presynaptic terminals

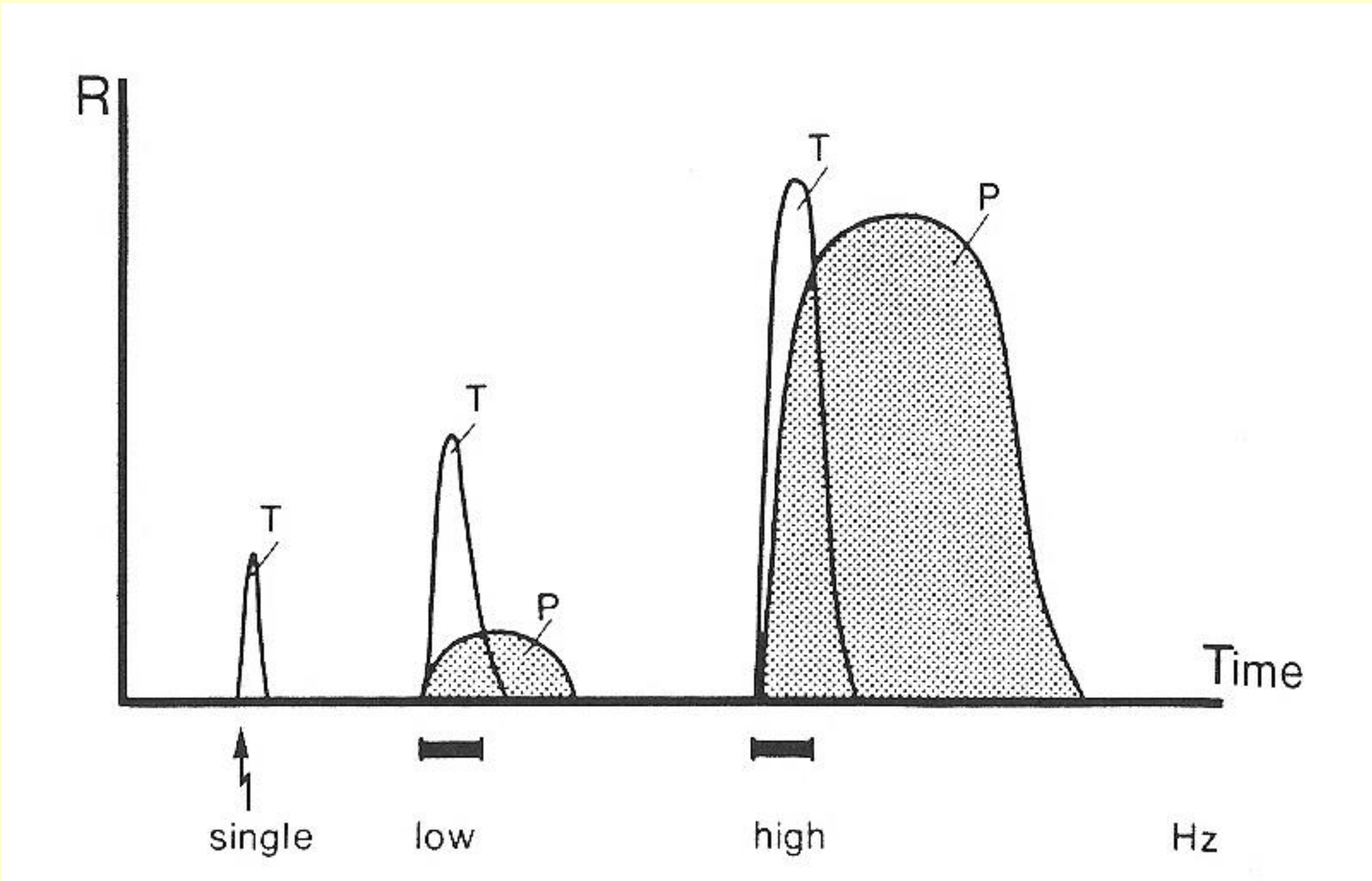


Peptides are stored in „large dense core vesicles" (LDCVs) and not in „small clear vesicles" (SCVs)

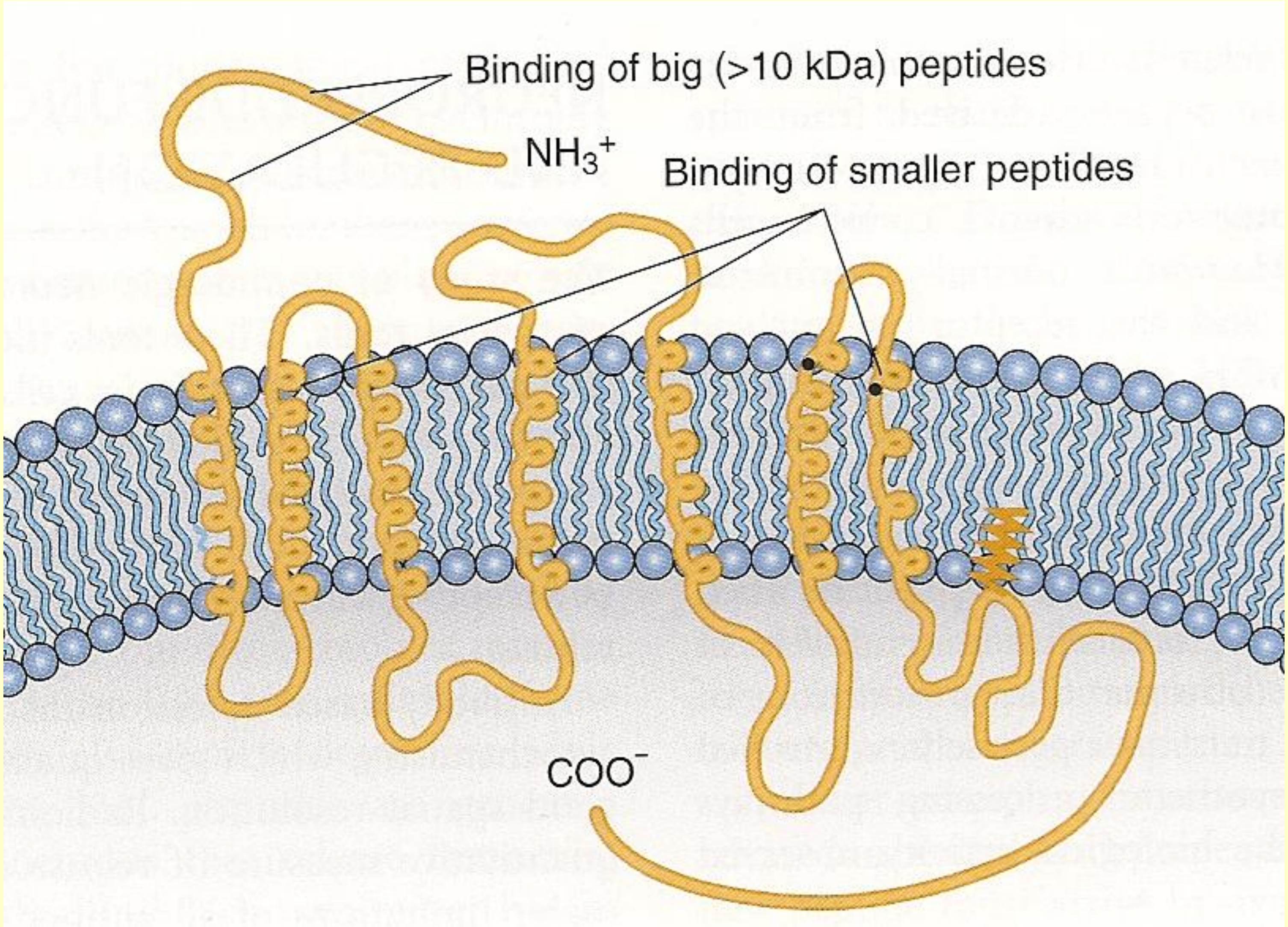
Large dense core vesicles in presynaptic terminals



Release of neuropeptides following neuronal activity



G-protein coupled peptide receptors



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2. Homeostatic regulations – endocrine system, hormones
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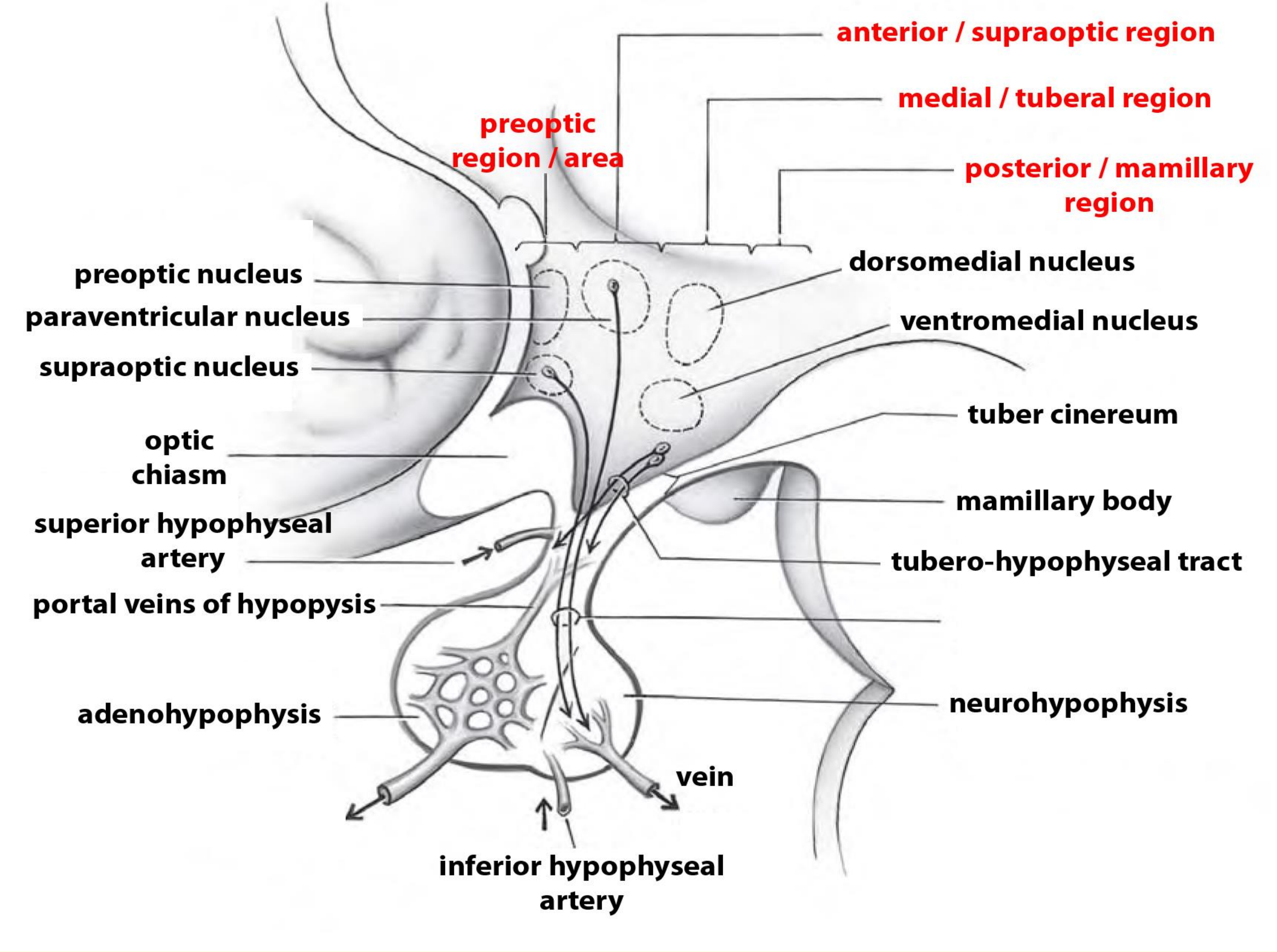
   – Body temperature regulation

Homeostatic center of the brain: the hypothalamus

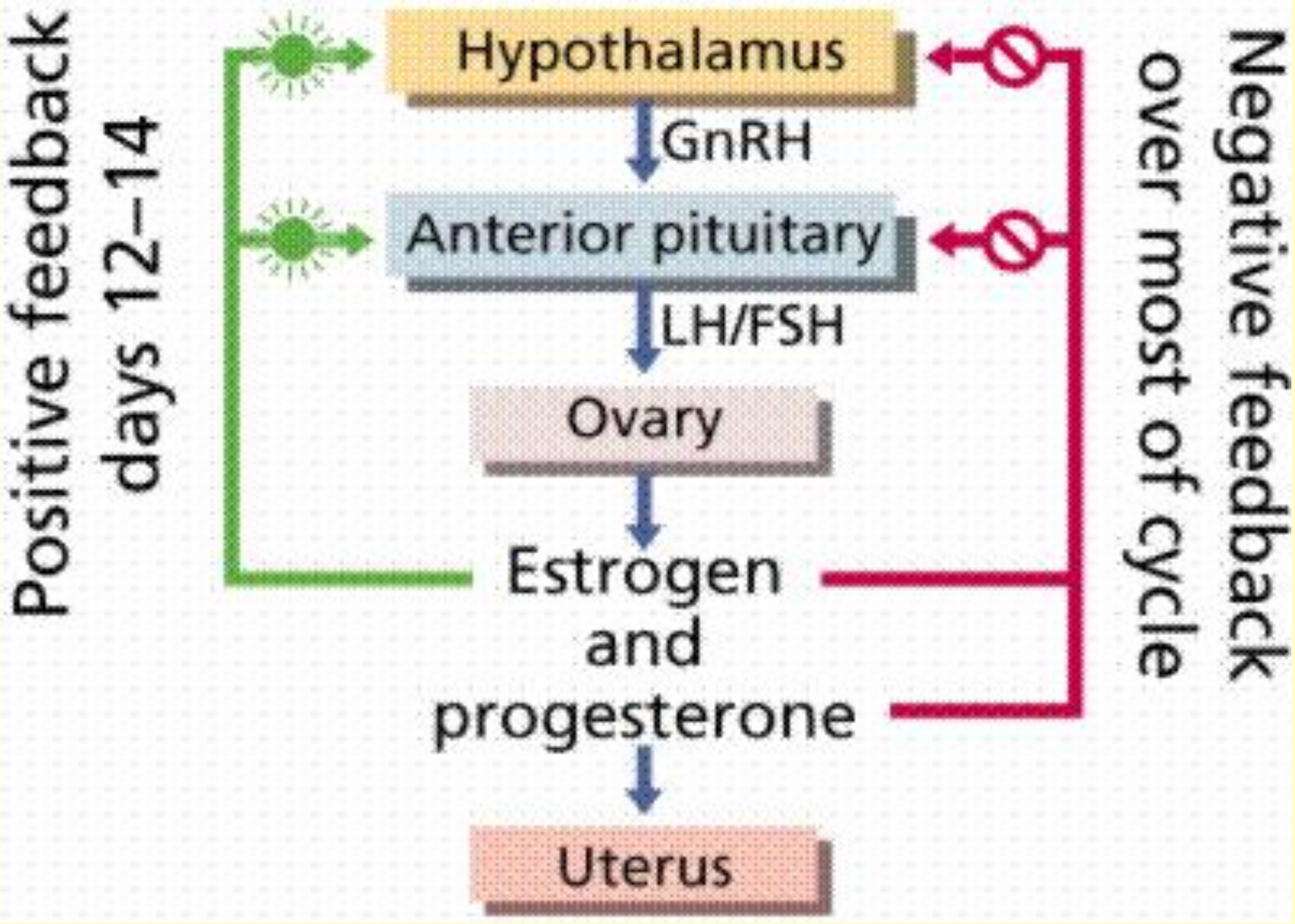
Regulatory functions of hypothalamic nuclei:

- Vegetative regulations (e.g. heart frequency)
- Neuroendocrine regulations (e.g. stress response)
- Salt and water balance
- Food intake and body weight
- Temperature
- Circadian rhythms
- Sleep
- Reproduction

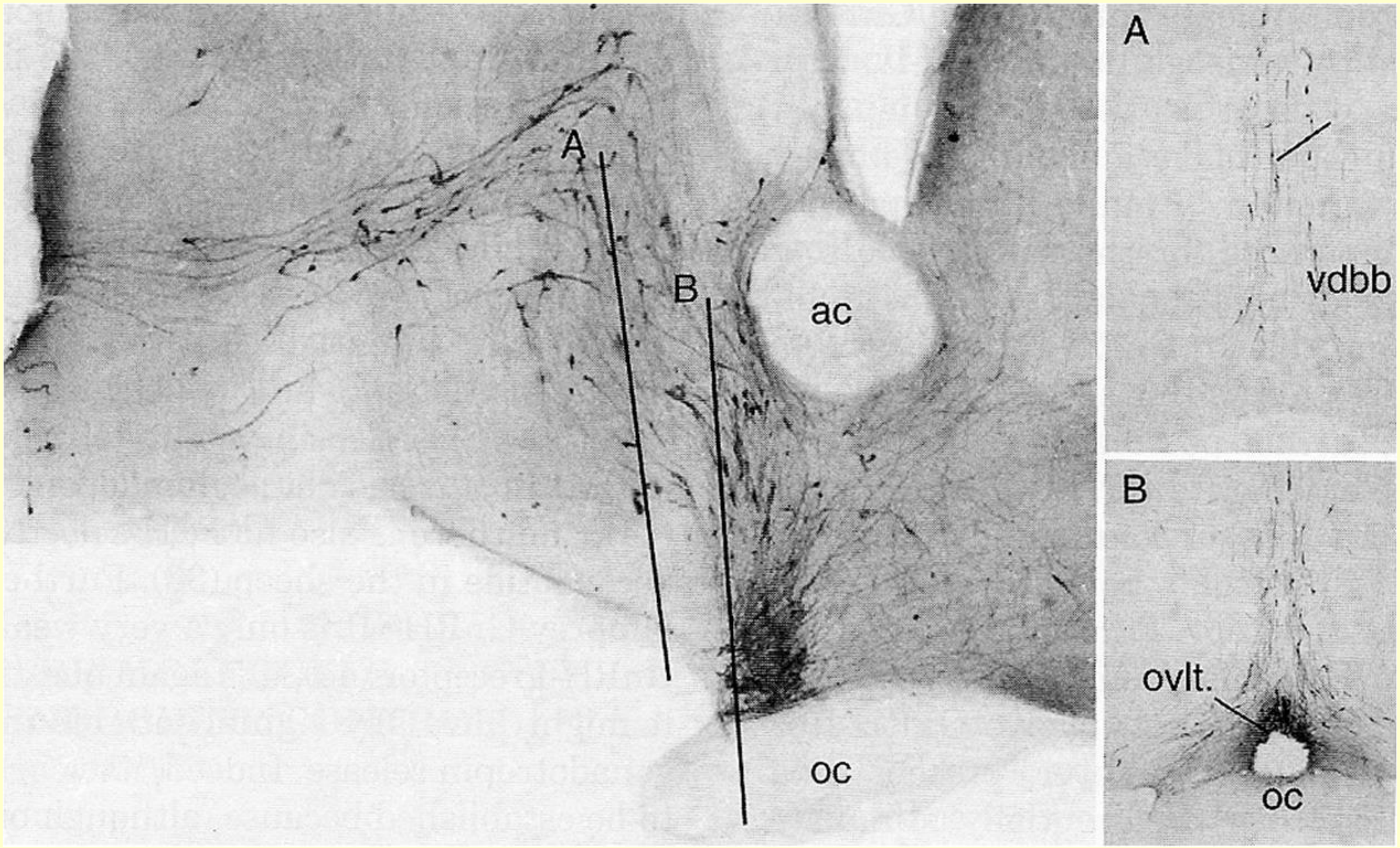
Antero-posterior regions of the hypothalamus



Example of a neuroendocrine regulation: GnRH neurons in the preoptic area of the hypothalamus control estrogen levels

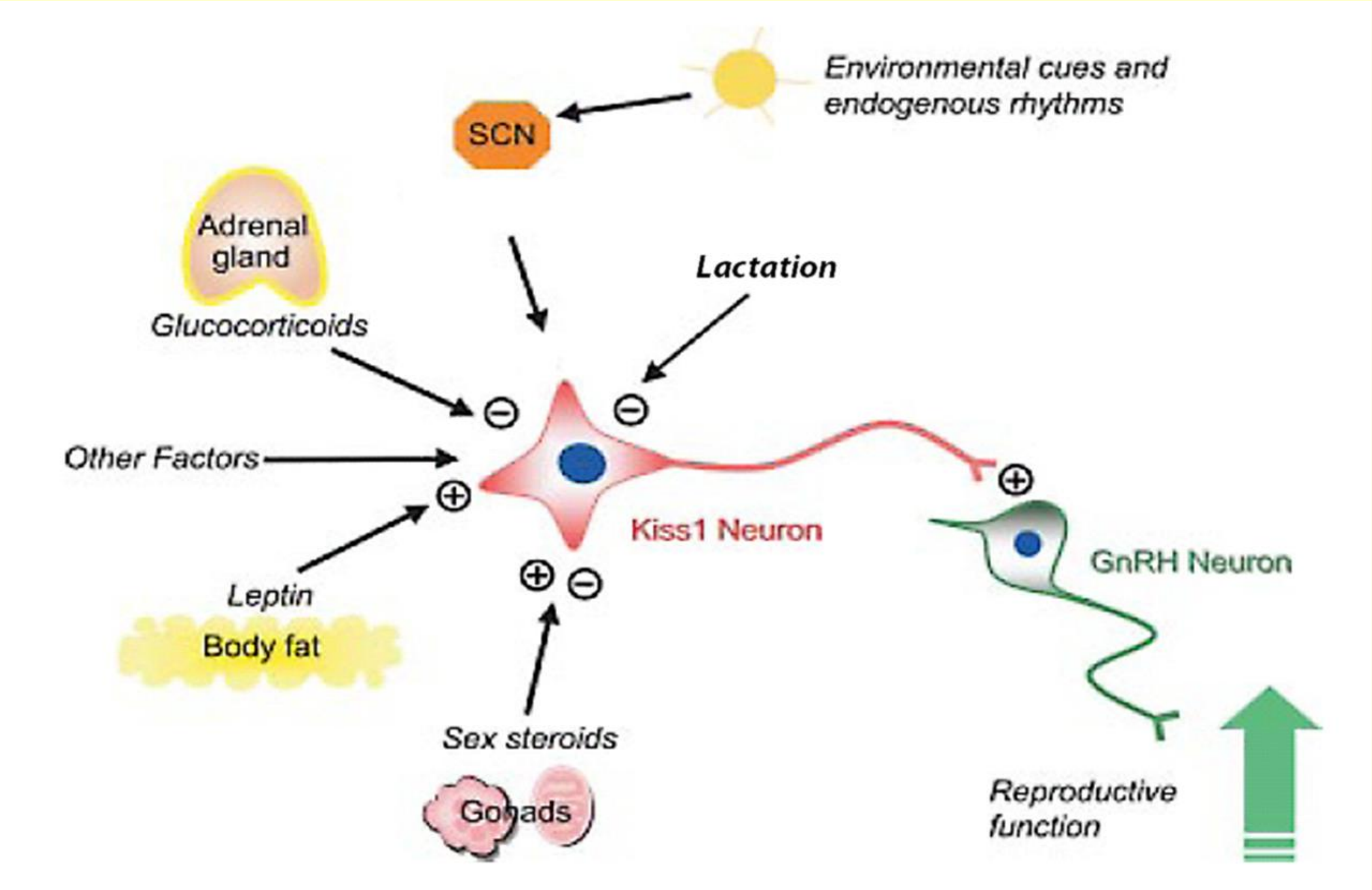


The distribution of GnRH-producing neurons in the preoptic area of the hypothalamus

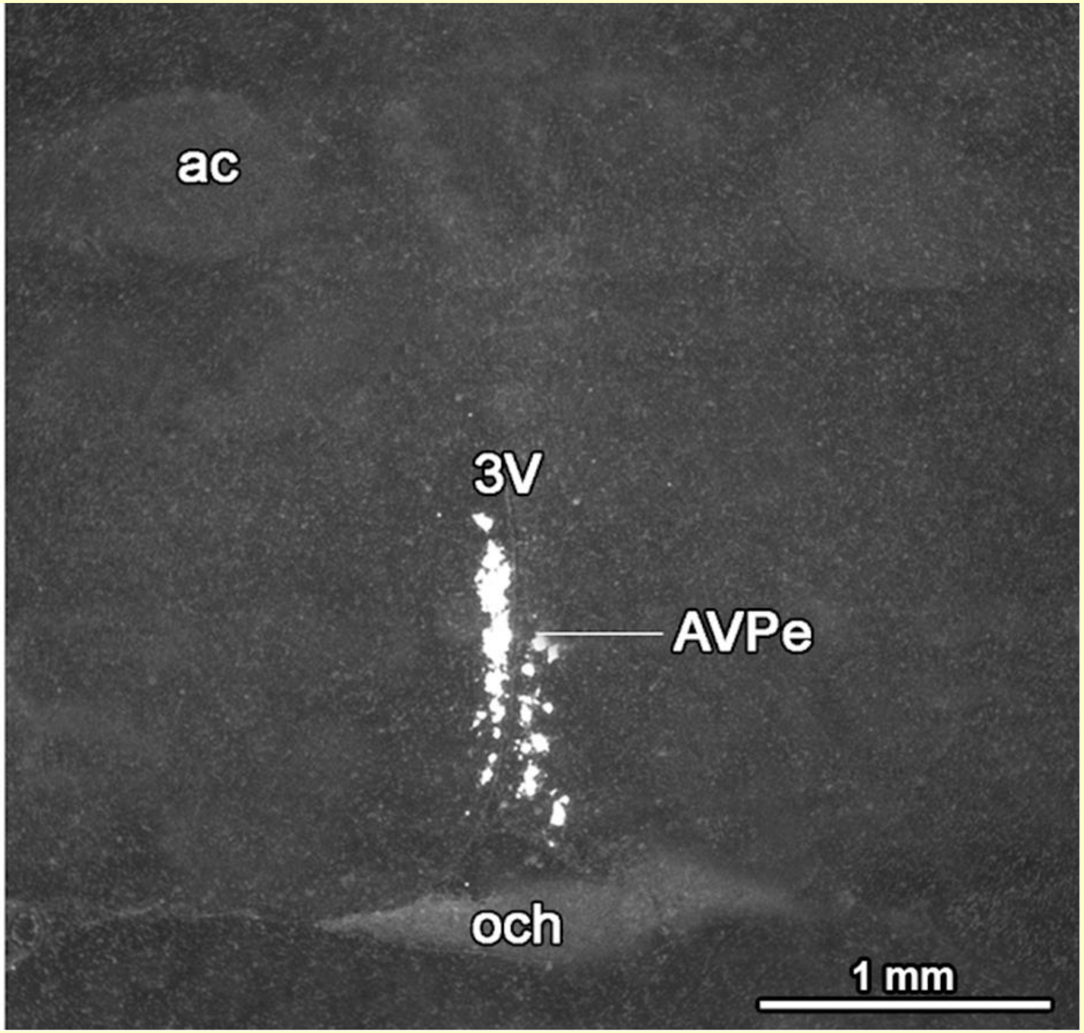


Why is it good to include the brain in the regulation of steroid hormones?

KISS I neurons mediate the homestatic status of the body to GnRH neurons

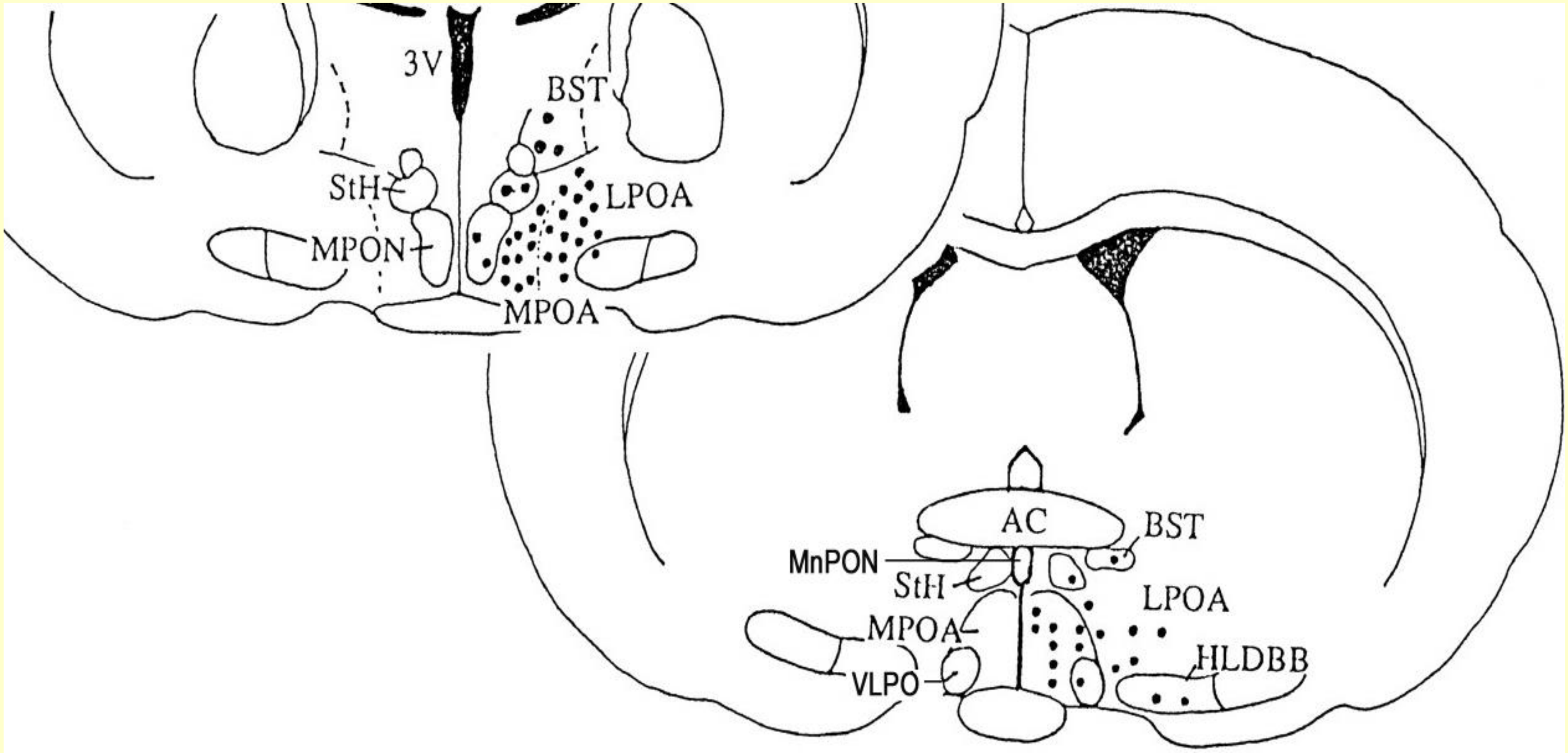


The distribution of kisspeptin-producing Kiss1 neurons in the preoptic area



Other homeostatic functions of the preoptic region of the hypothalamus

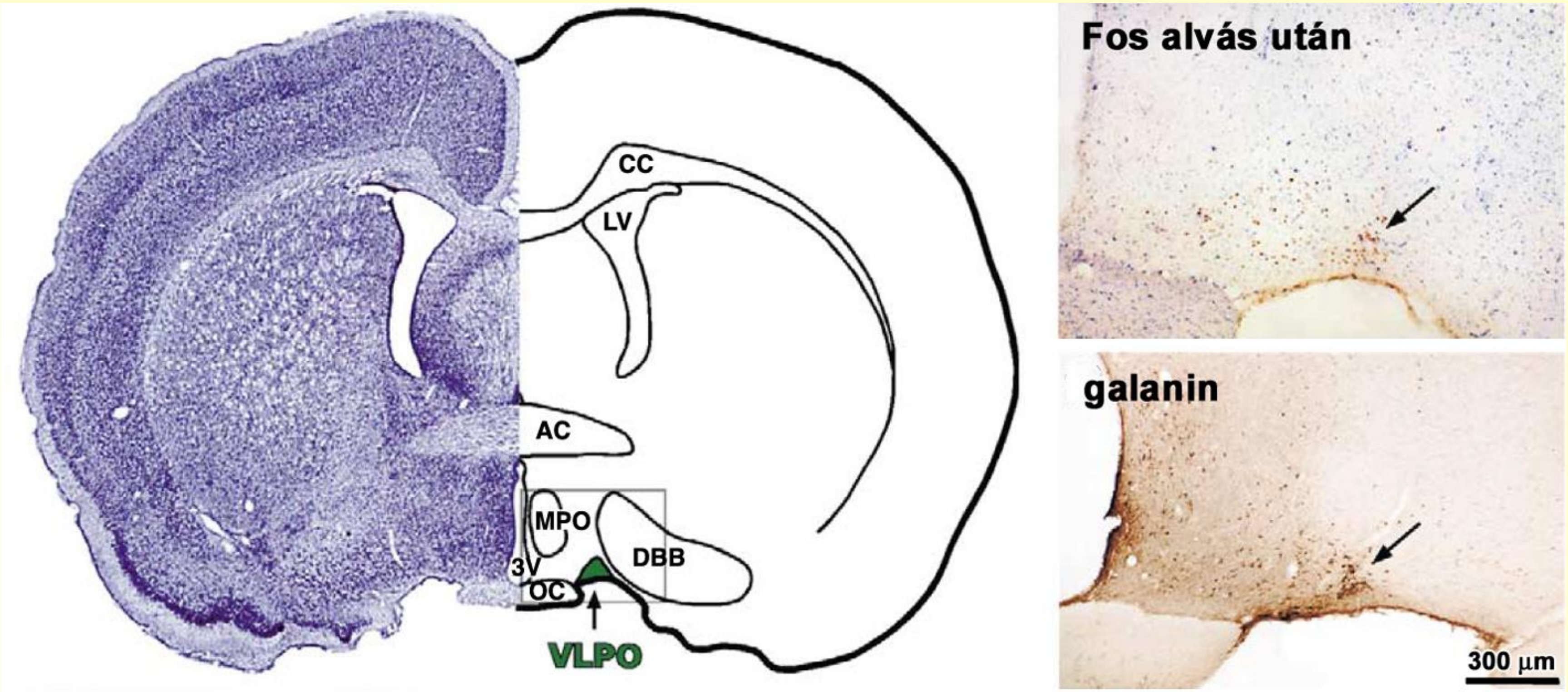
•: Position of neurons participating in the control of body temperature



The thermoregulatory neurons do not form a distinct nucleus

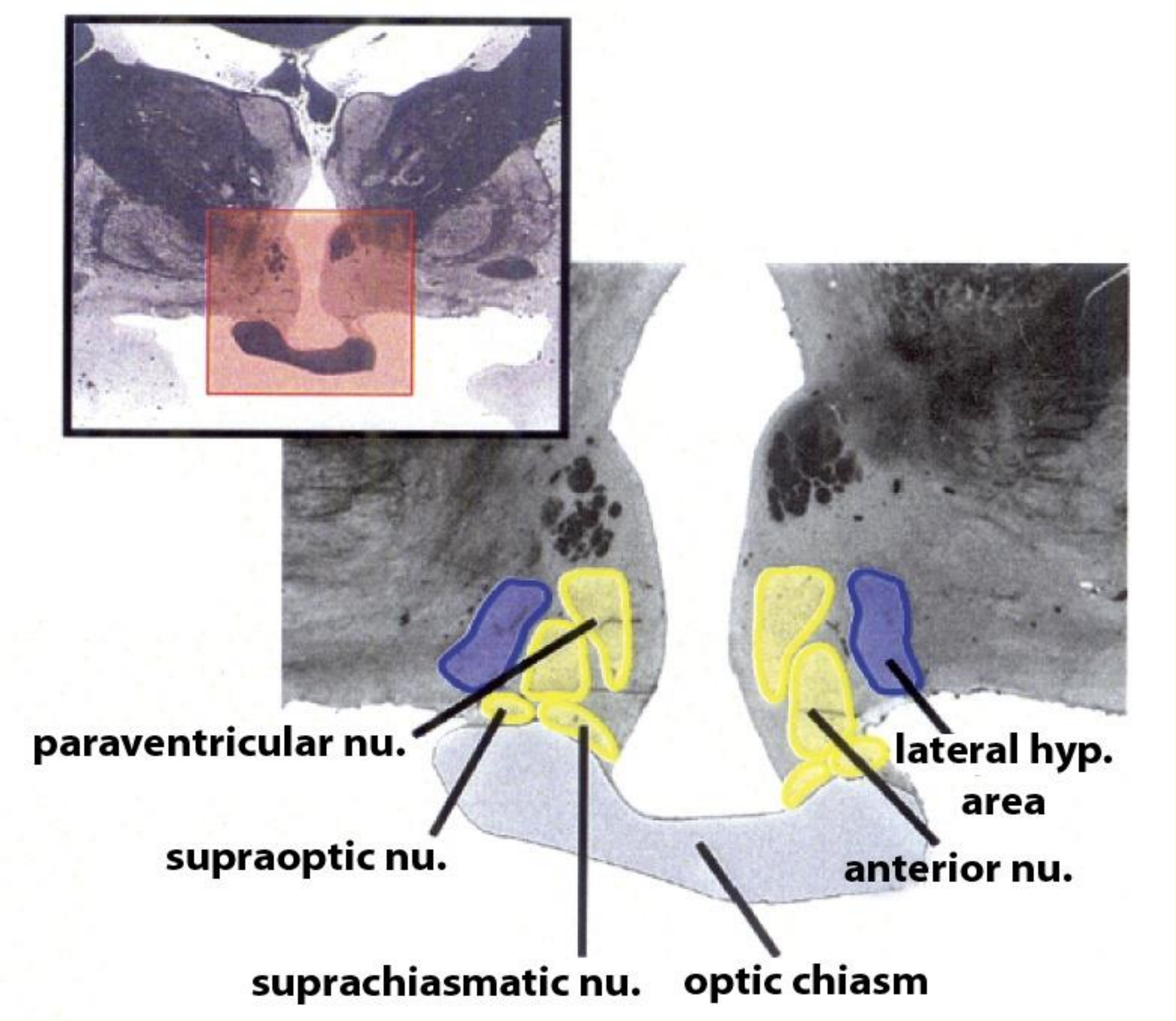
Hypothalamic centers of sleep regulation:

1. ´sleep on´ cells in the VLPO

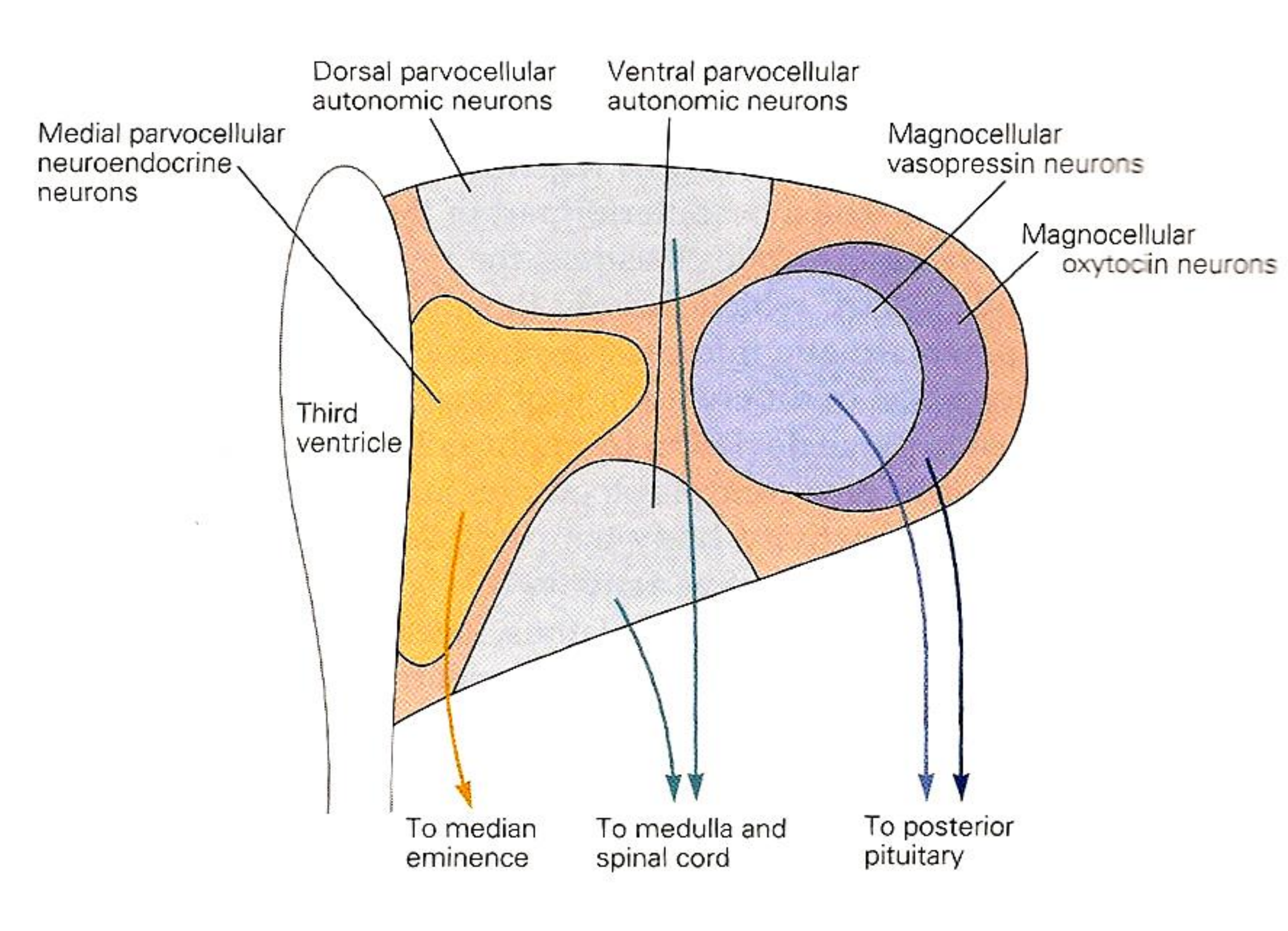


VLPO: ventrolateral preoptic nucleus

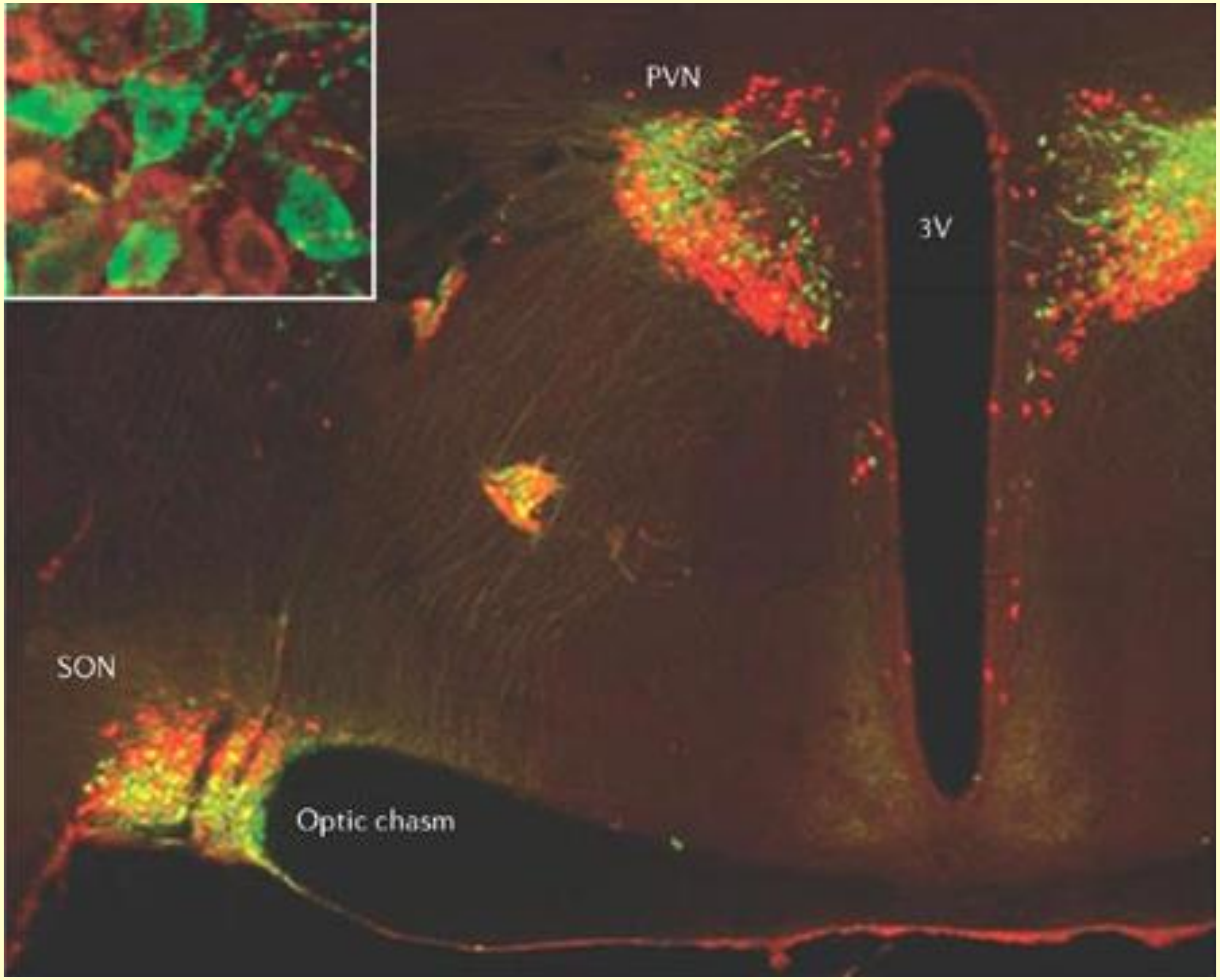
Anterior hypothalamic region

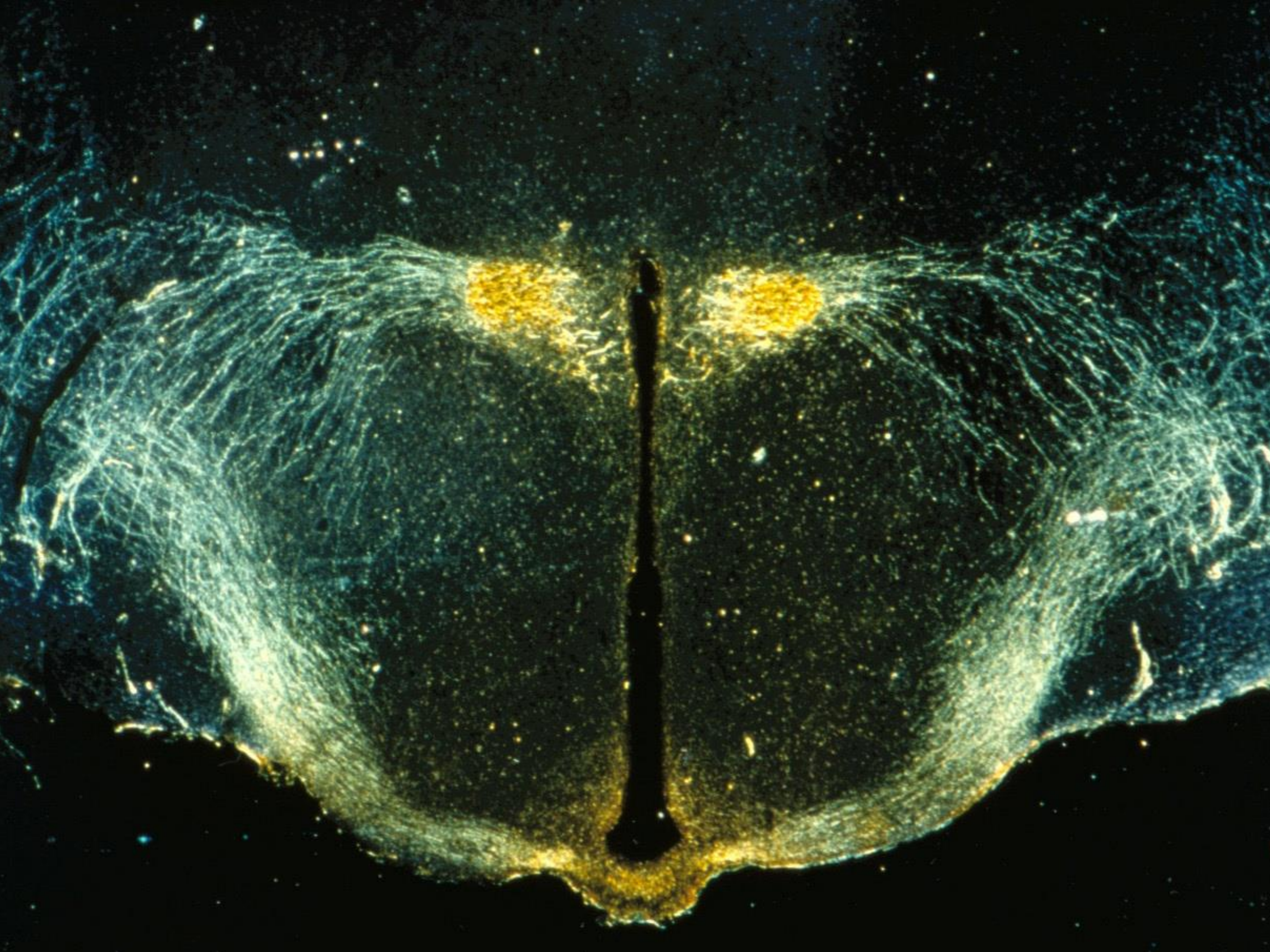


The paraventricular hypothalamic nucleus

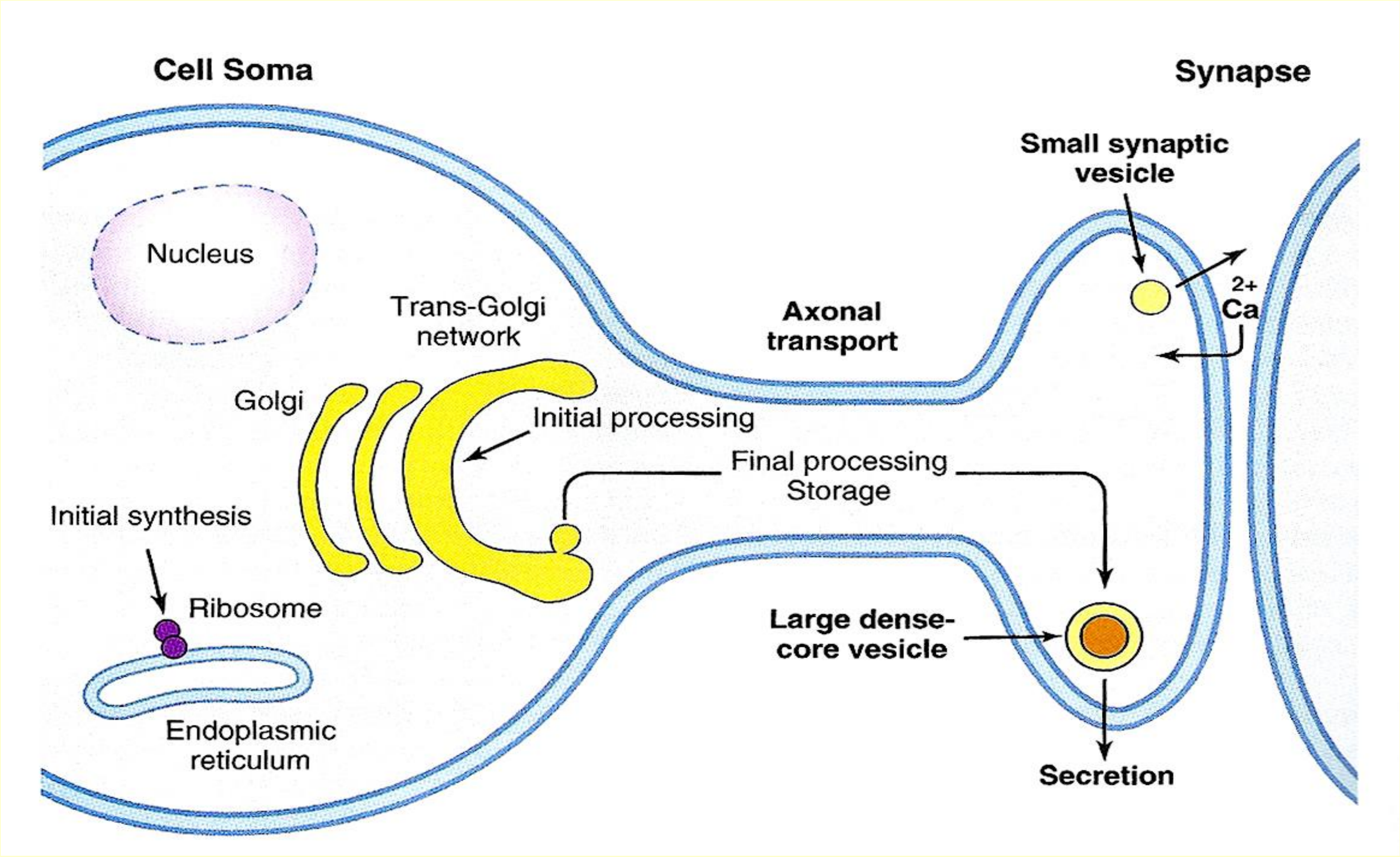


The distribution of oxytocin and vasopressin (ADH) neurons in the hypothalamus



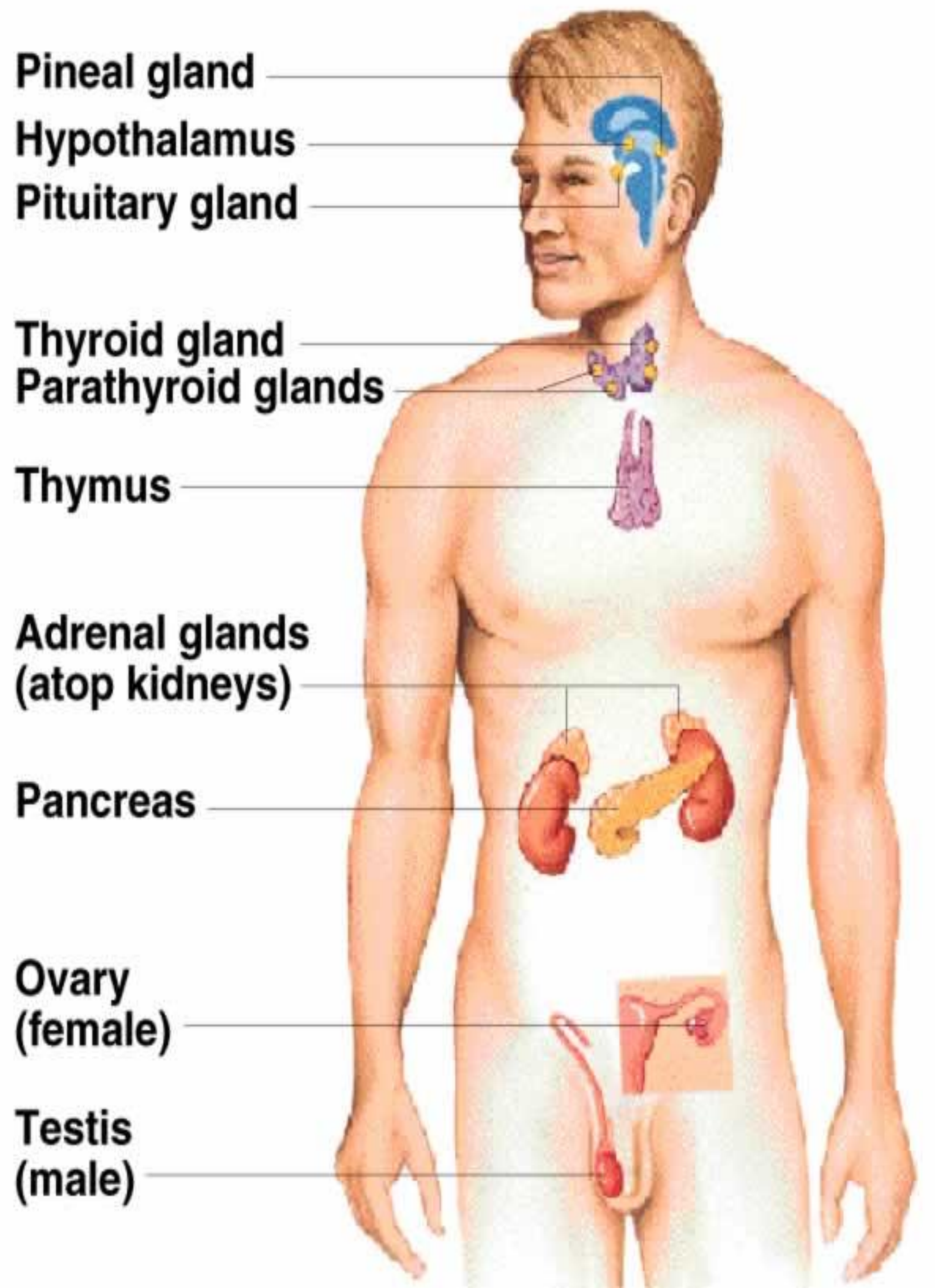


Axonal transport and storage of neuropeptide hormones (e.g. oxytocin) to brain vessels

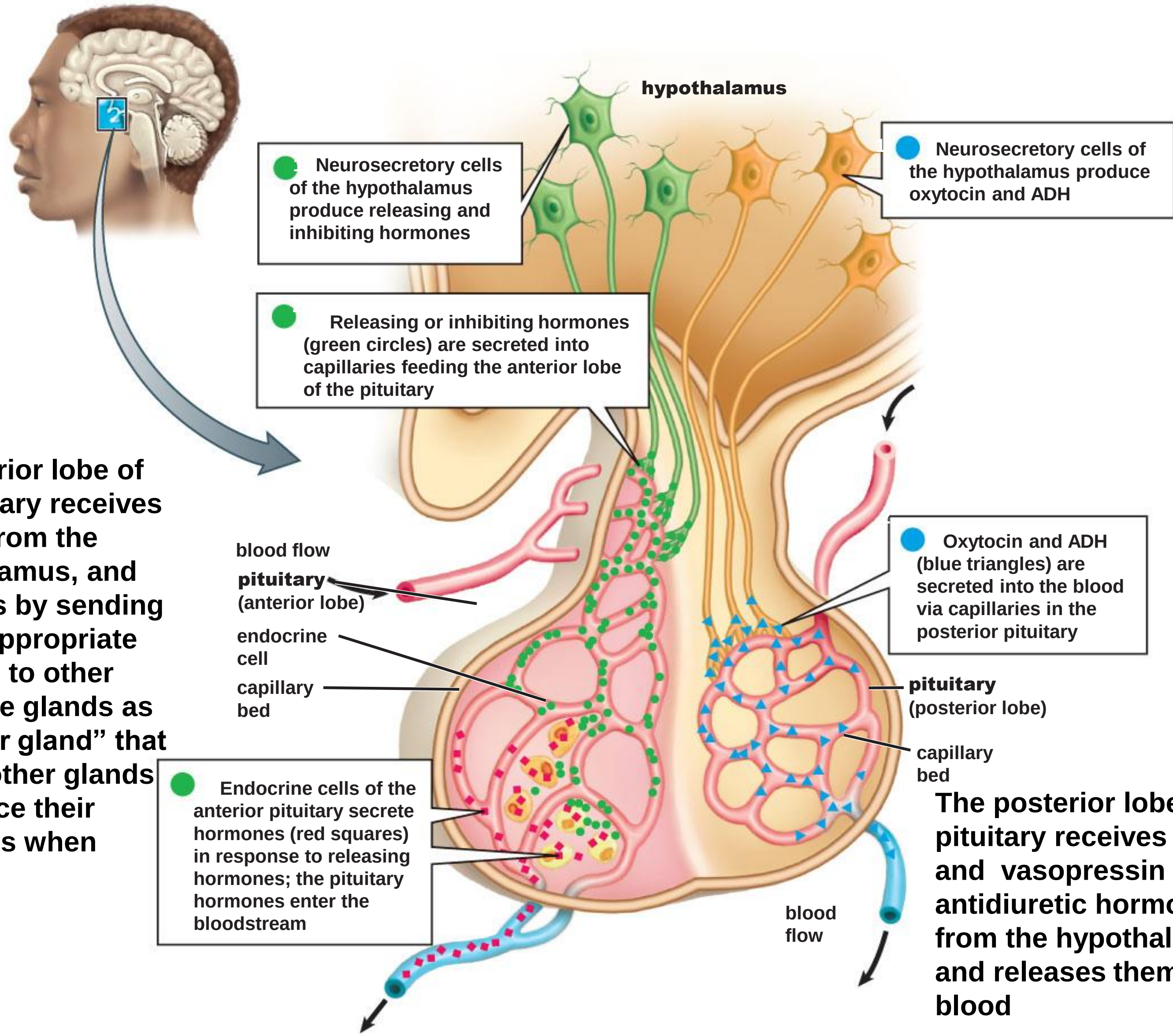


Endocrine glands

1. Hypothalamus
2. Pituitary
3. Epiphysis (pineal gland)
4. Thyroid (and parathyroid) gland
5. Thymus
6. Adrenal gland
7. Langergans' islands of pancreas
8. Sex glands (ovary or testis)



Secretory activity of the pituitary



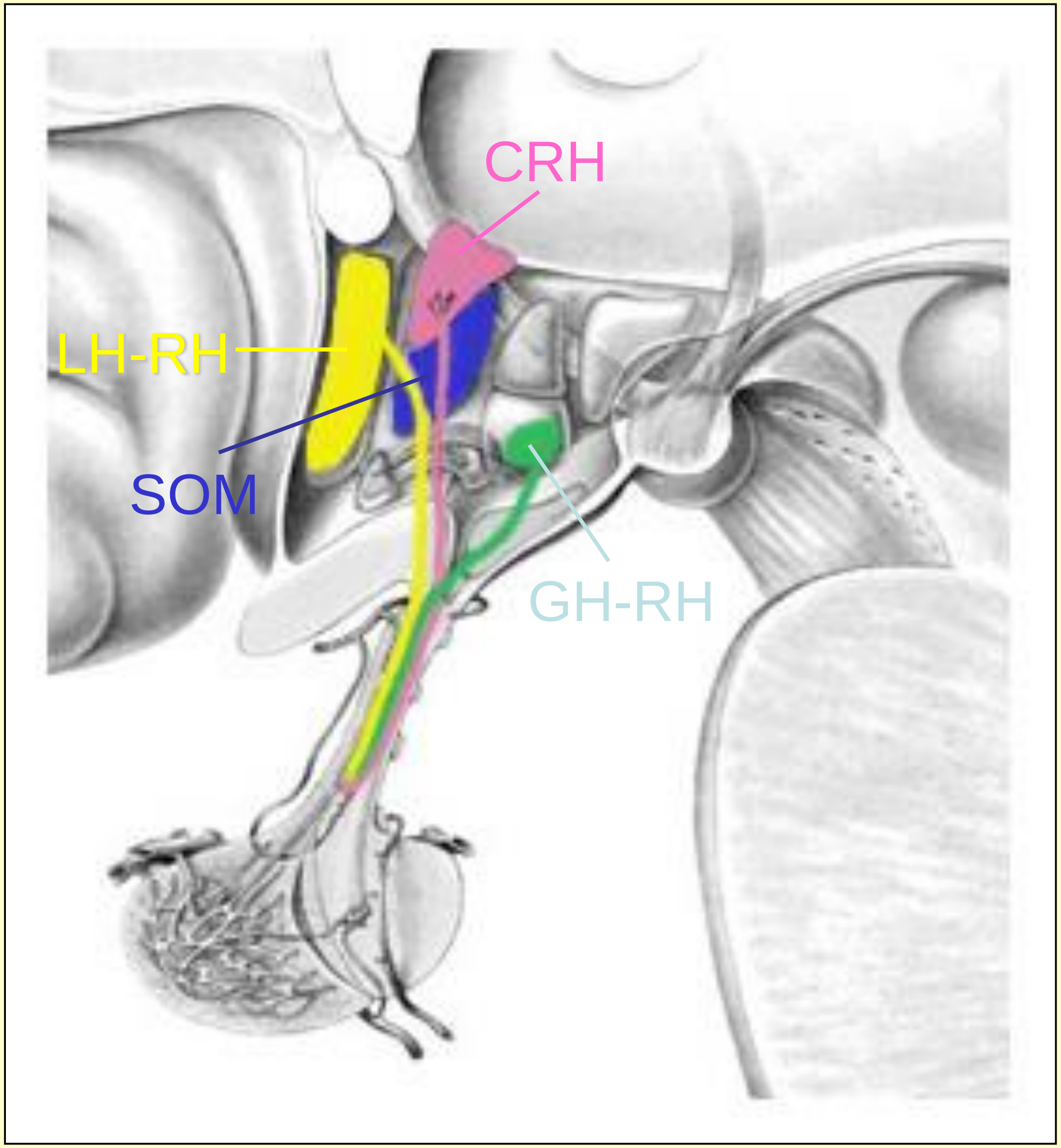
The anterior lobe of the pituitary receives signals from the hypothalamus, and responds by sending out the appropriate hormone to other endocrine glands as a “master gland” that signals other glands to produce their hormones when needed.

The posterior lobe of the pituitary receives oxytocin and vasopressin (or antidiuretic hormone- ADH) from the hypothalamus, and releases them to the blood

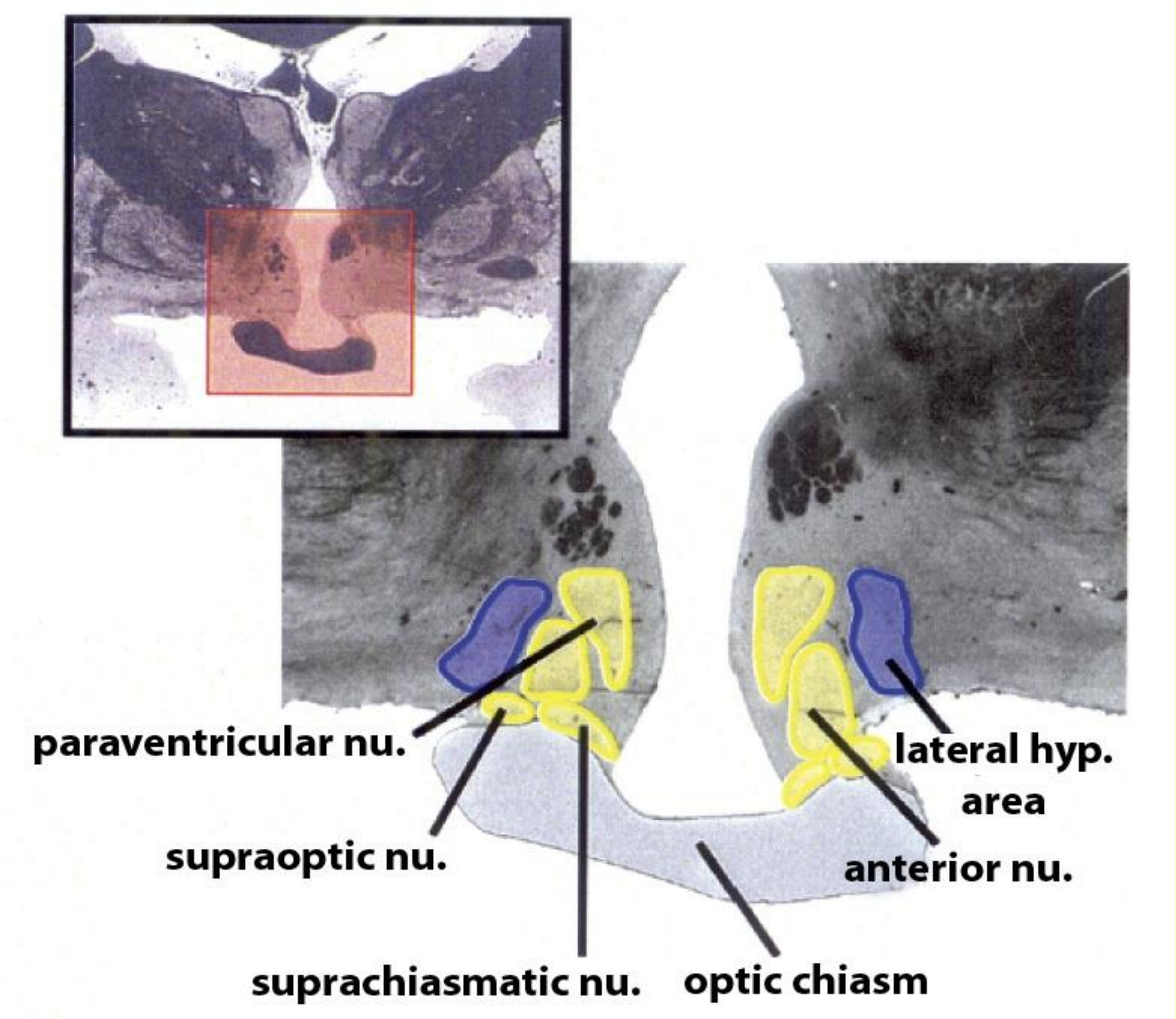
Pituitary hormones

Pituitary Hormone	Functions
Follicle-stimulating hormone	Stimulates maturation of egg in the ovary and release of sex hormones.
Lutenizing hormone	Stimulates maturation of egg and of the corpus luteum surrounding the egg and release of sex hormones.
Thyroid-stimulating hormone	Stimulates the thyroid gland to release thyroxine.
Adrenocorticotropic hormone	Causes the adrenal gland to release cortisol.
Melanocyte-stimulating hormone	Stimulates synthesis of skin pigments.
Prolactin	Stimulates the development of manna and milk production
Growth hormone	Stimulates growth during infancy and puberty.
Antidiuretic hormone	Signals the kidney to conserve more water.
Oxytocin	Affects childbirth, lactation, and some behaviors.

Neuroendocrine regulatory hypothalamic nuclei

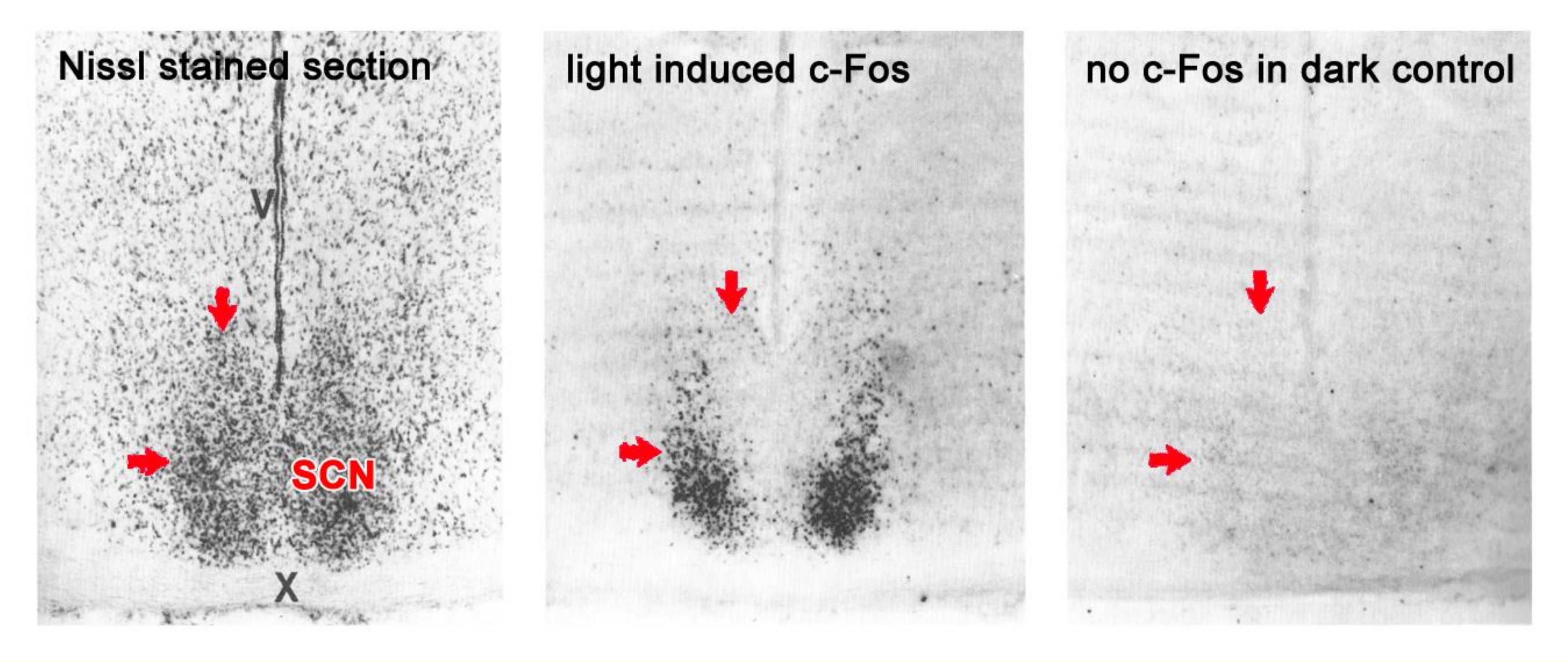


Anterior hypothalamic region

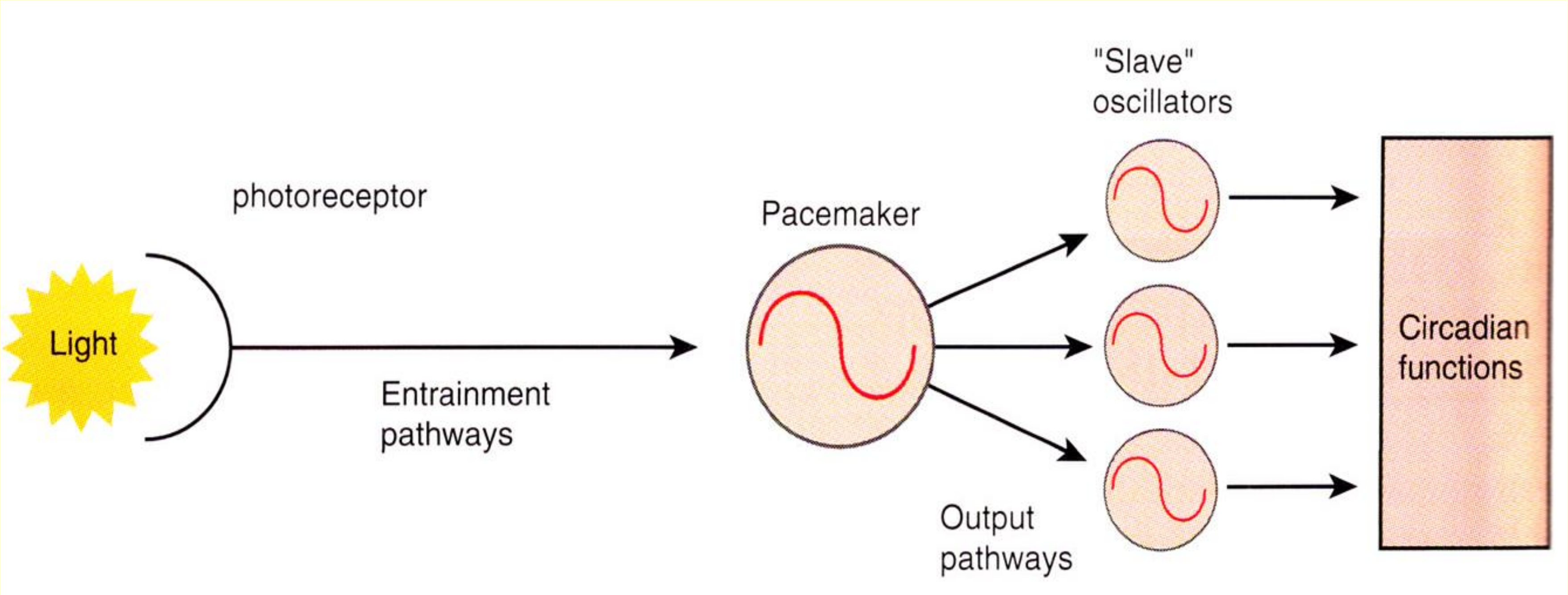


Circadial regulation of neural functions

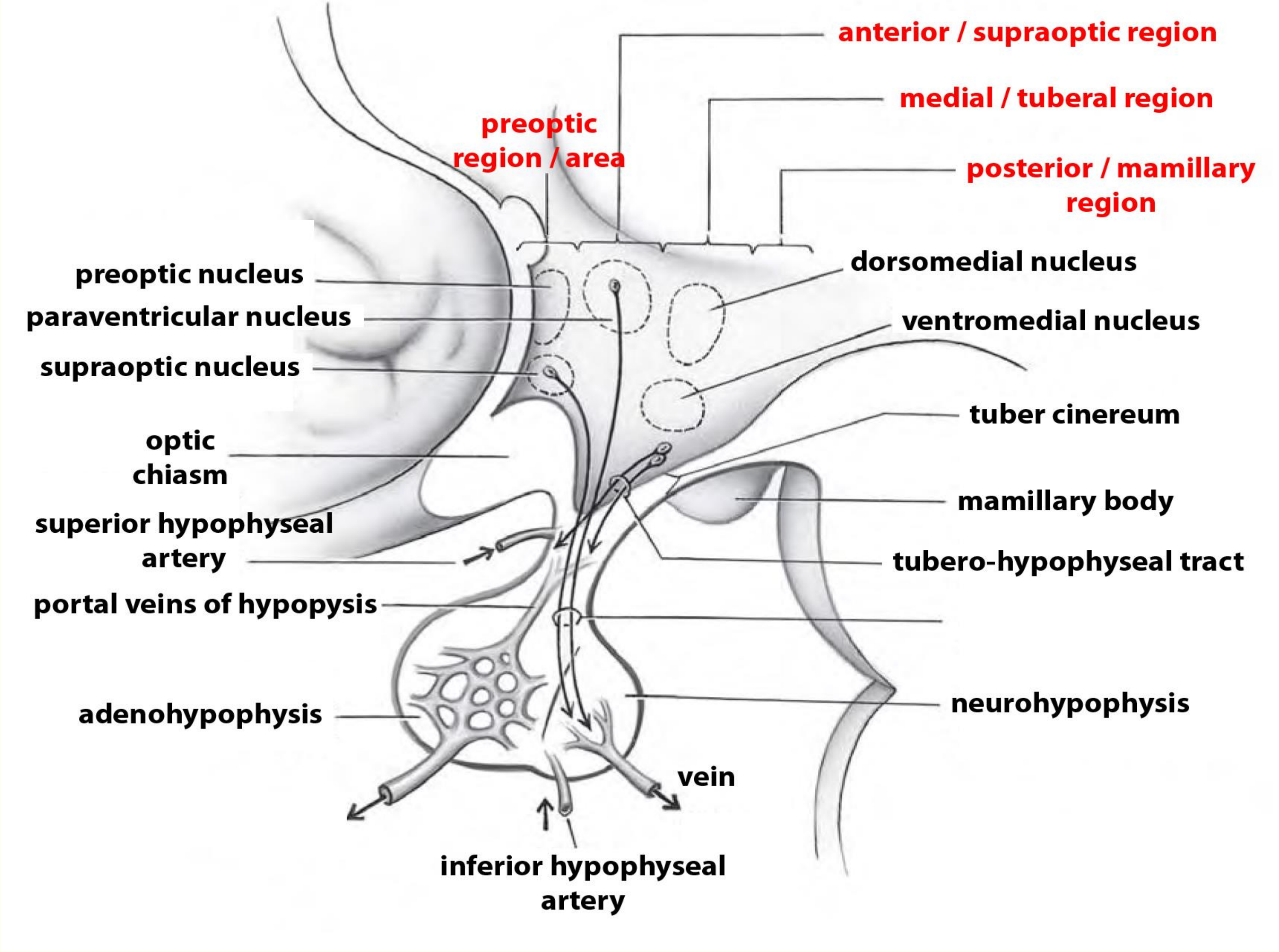
PACEMAKER: **SUPRACHIASMATIC NUCLEUS (SCN)**



Principle of creating circadian (daily) rhythms

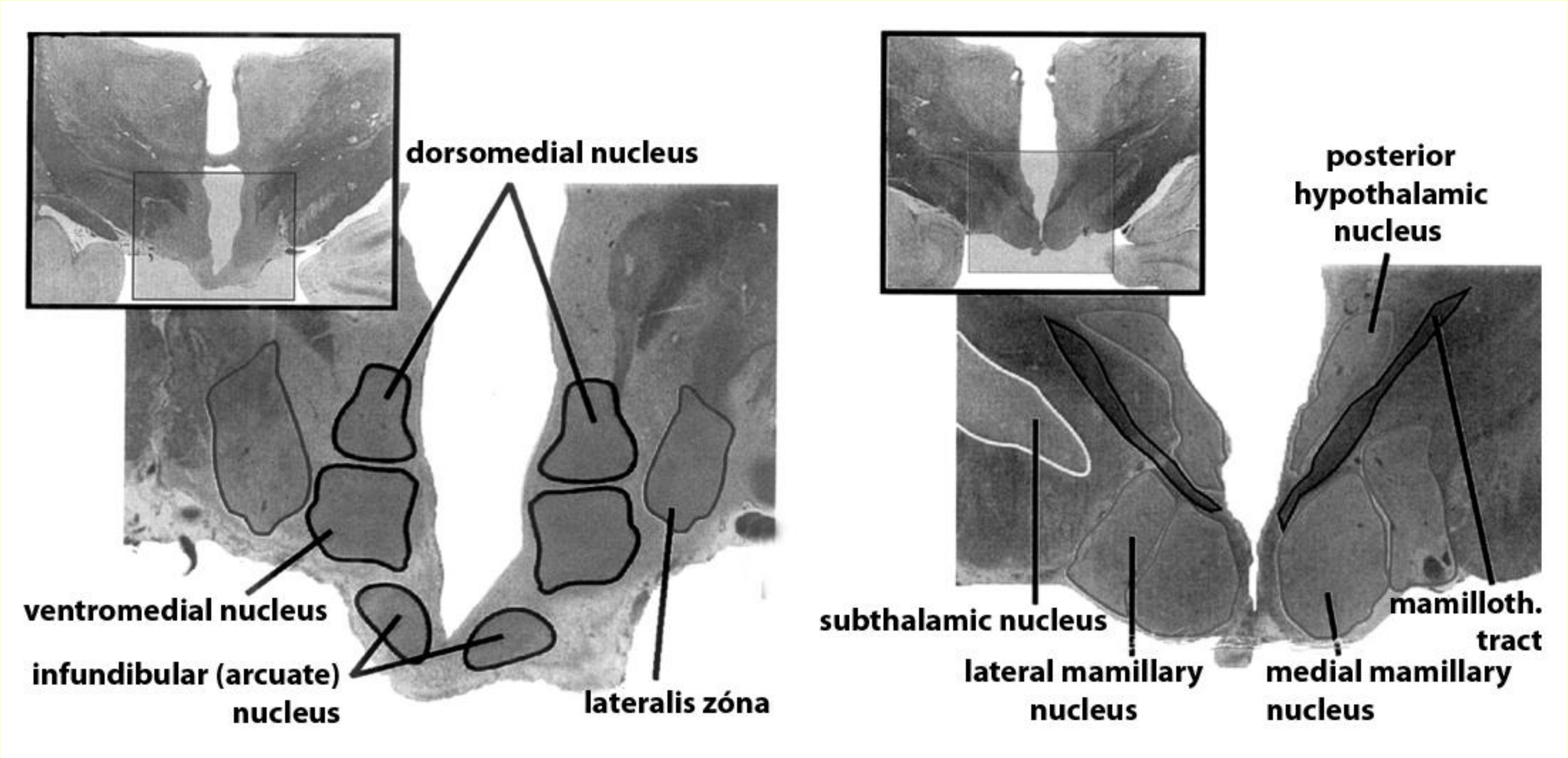


Antero-posterior regions of the hypothalamus

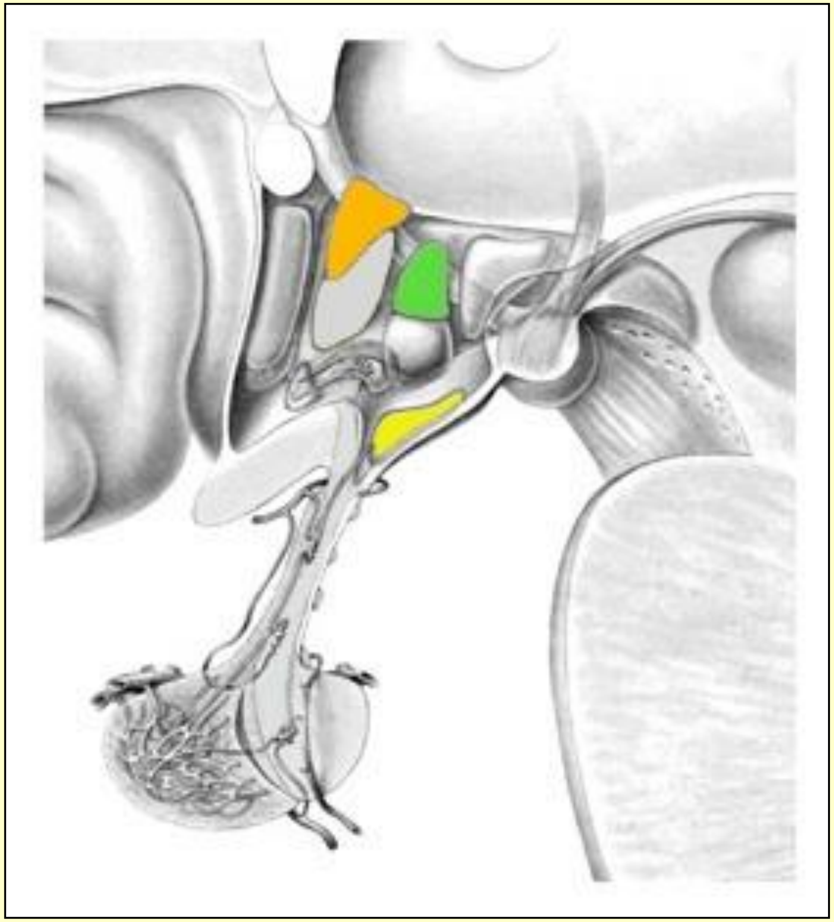


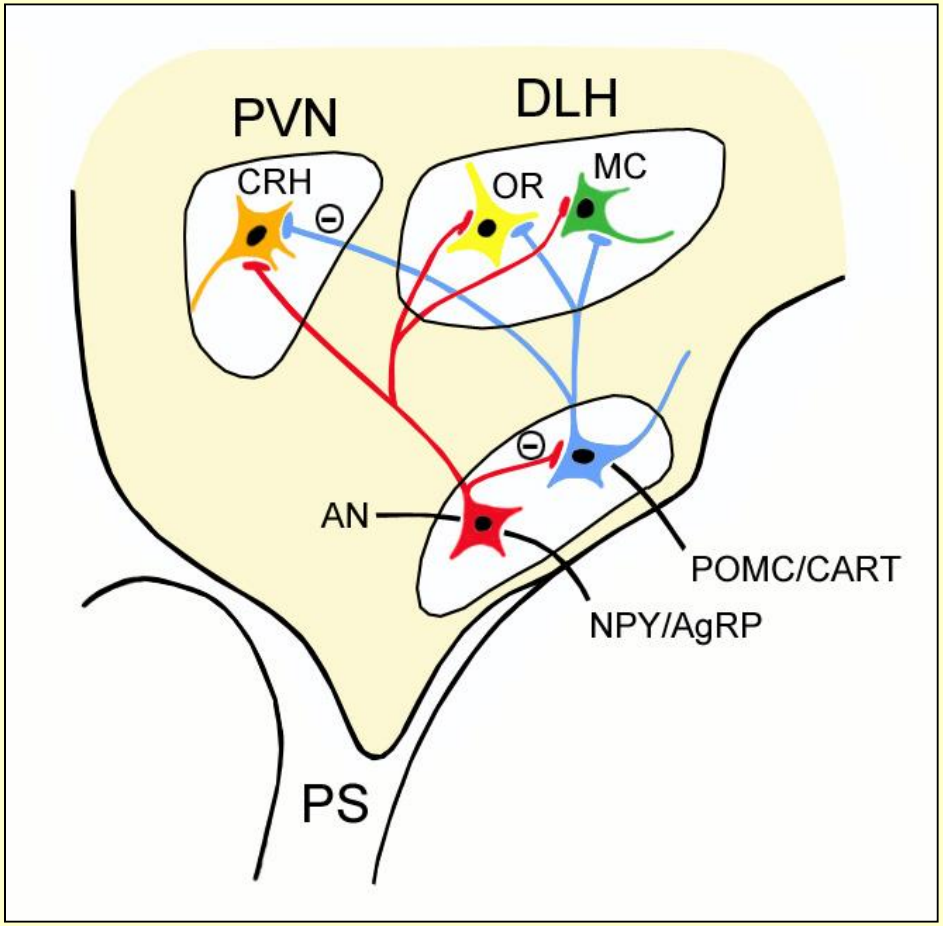
Tuberal and posterior hypothalamic regions

Tuberal hypothalamic region | **Posterior hypothalamic region**

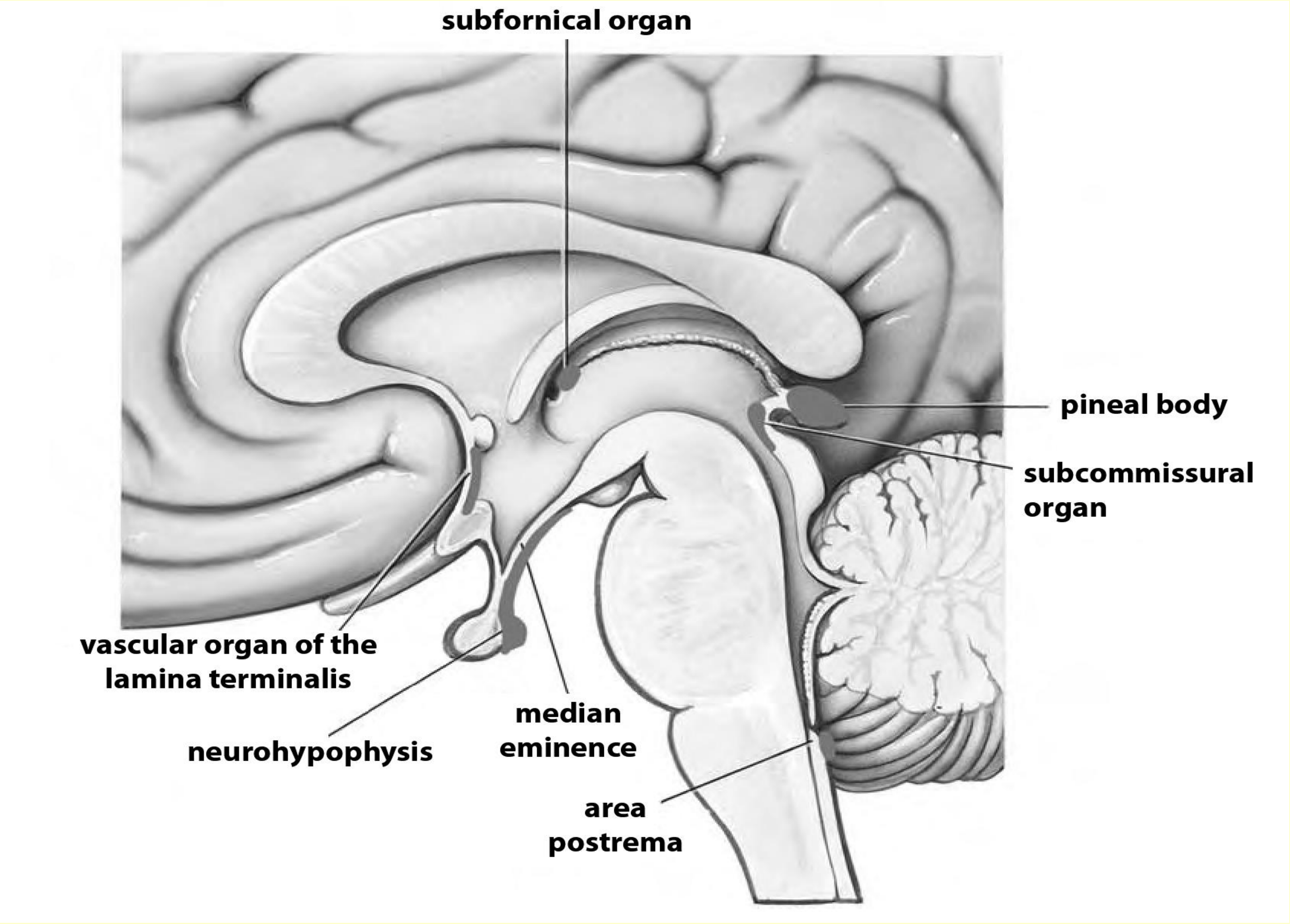


Hypothalamic centers that control food intake and body weight

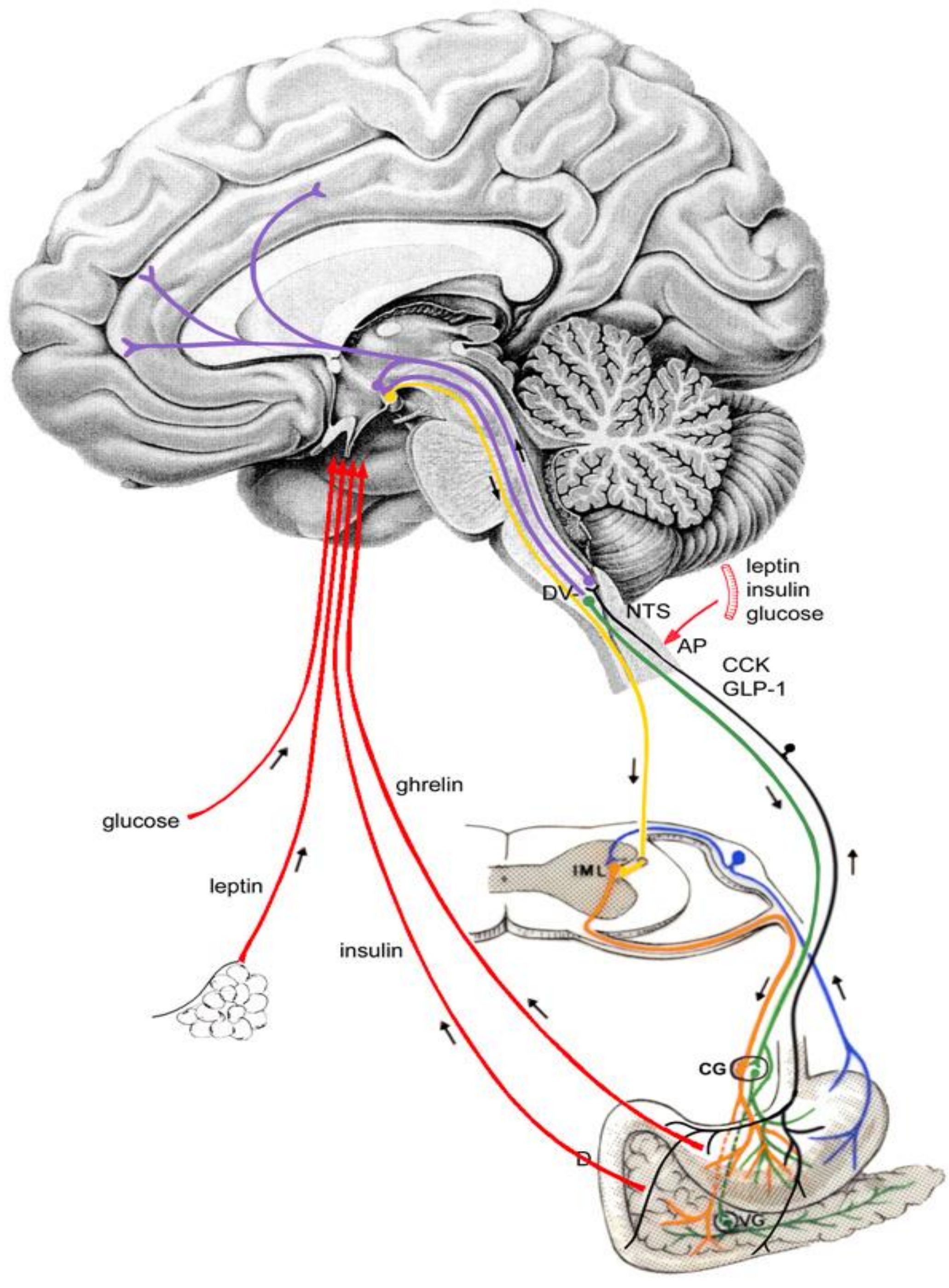




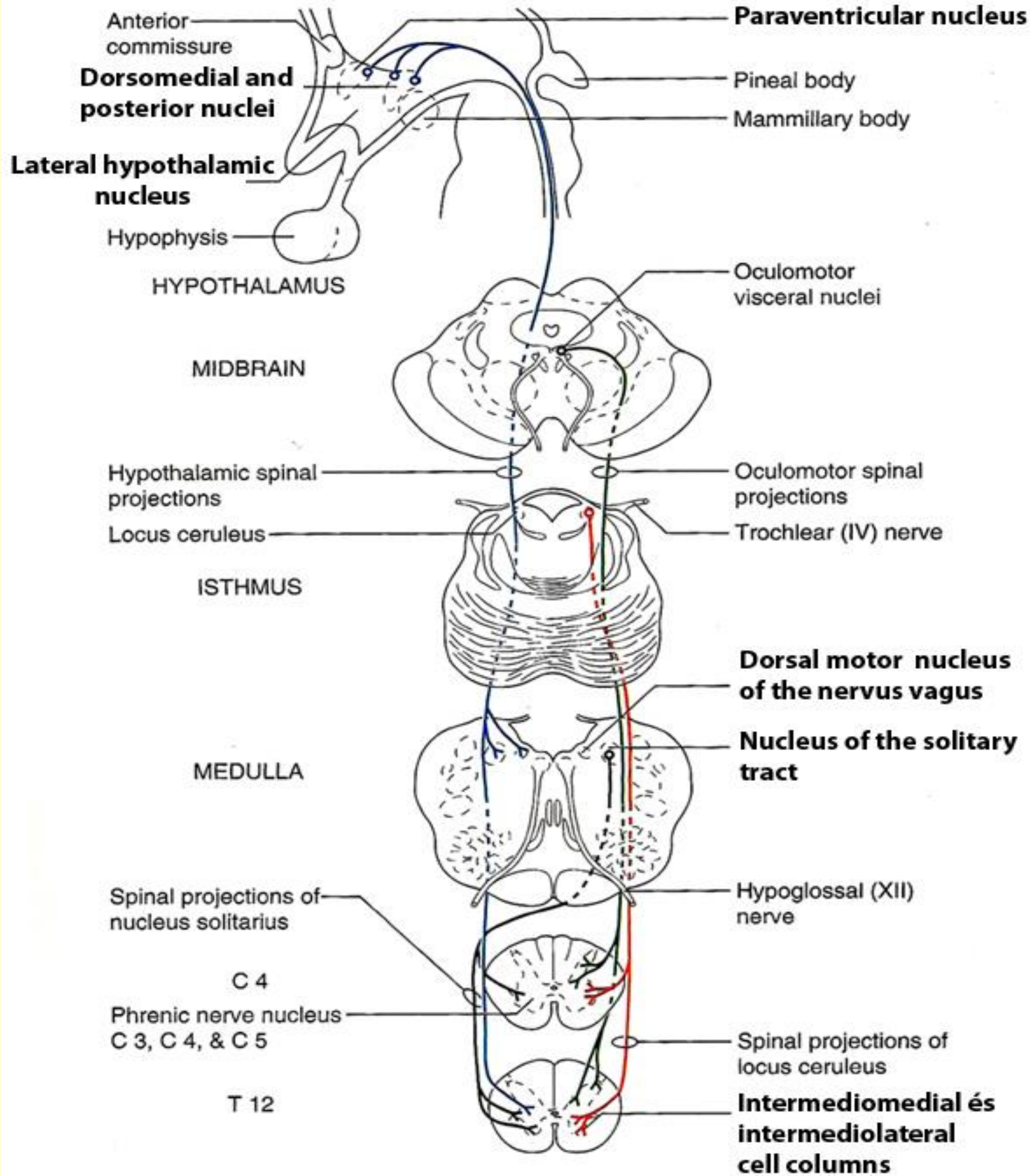
Circumventricular organs – humoral inputs



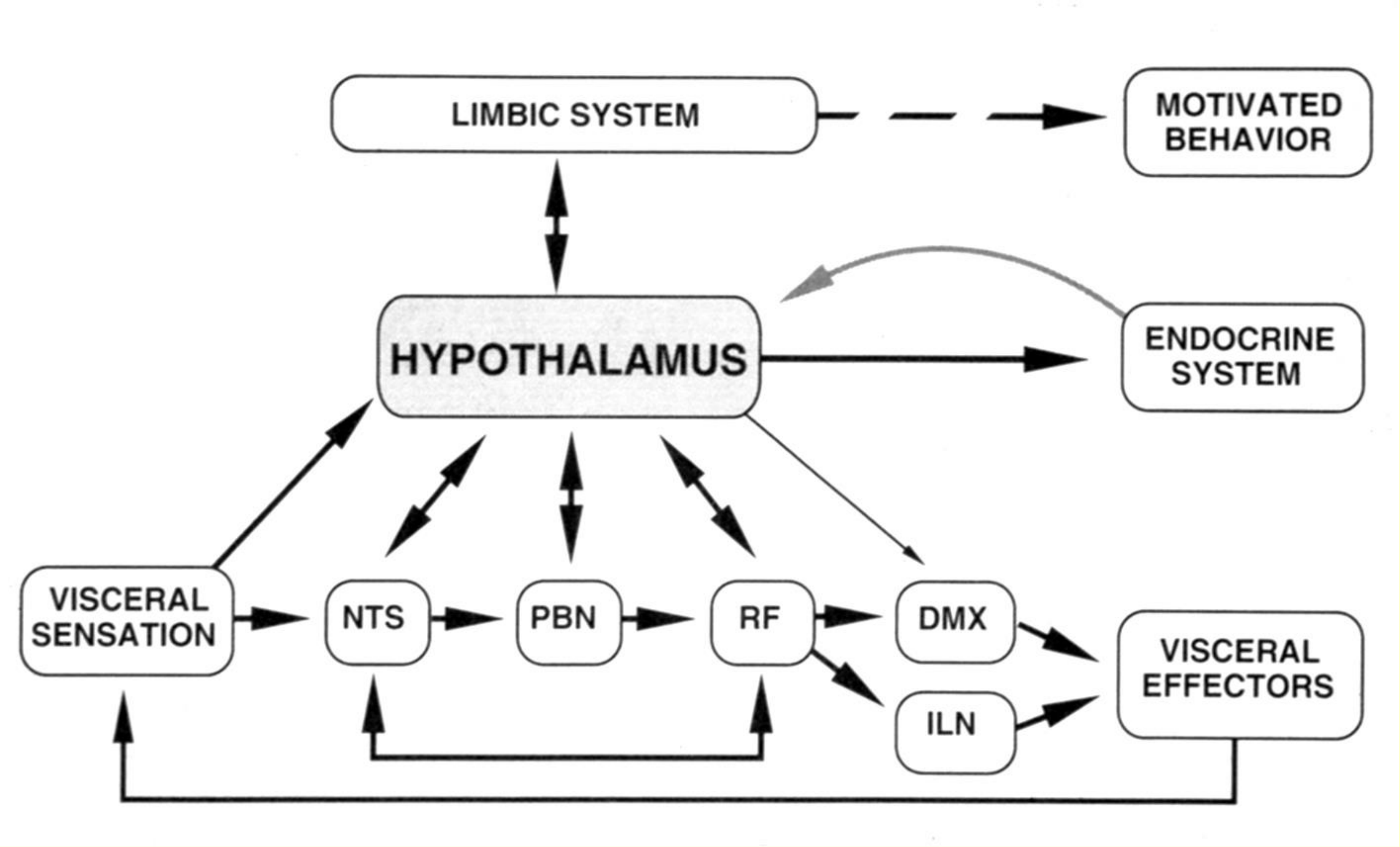
Major pathways regulating food intake



Hypothalamo-spinal tract and other descending pathways regulating vegetative functions



Neural elements of homeostatic regulations



NTS: nucleus of the solitary tract, PBN: parabrachial nucleus, RF: reticular formation, DMX: dorsal motor vagus nucleus, ILN: intermediolateral column (nucleus) of the spinal cord

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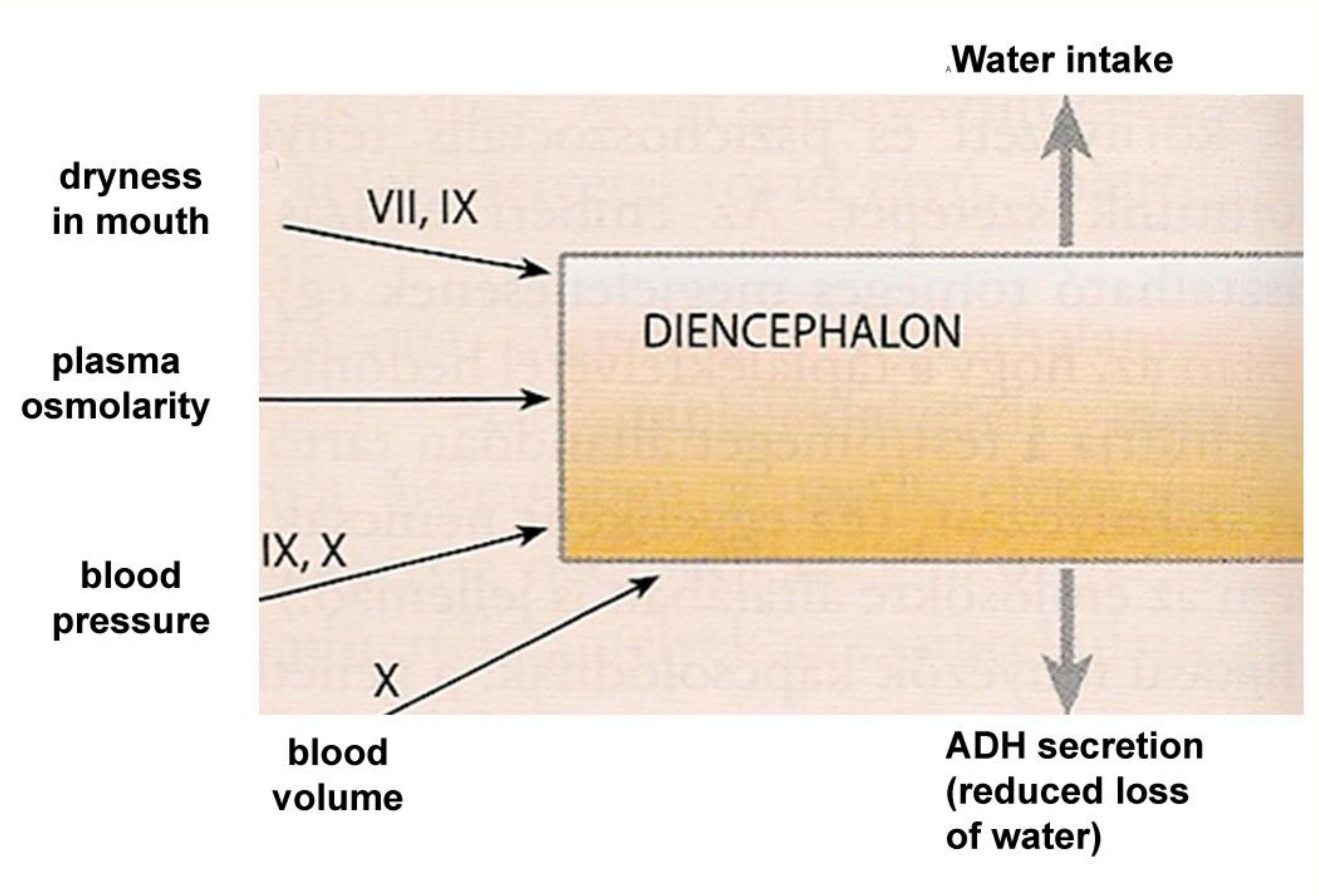
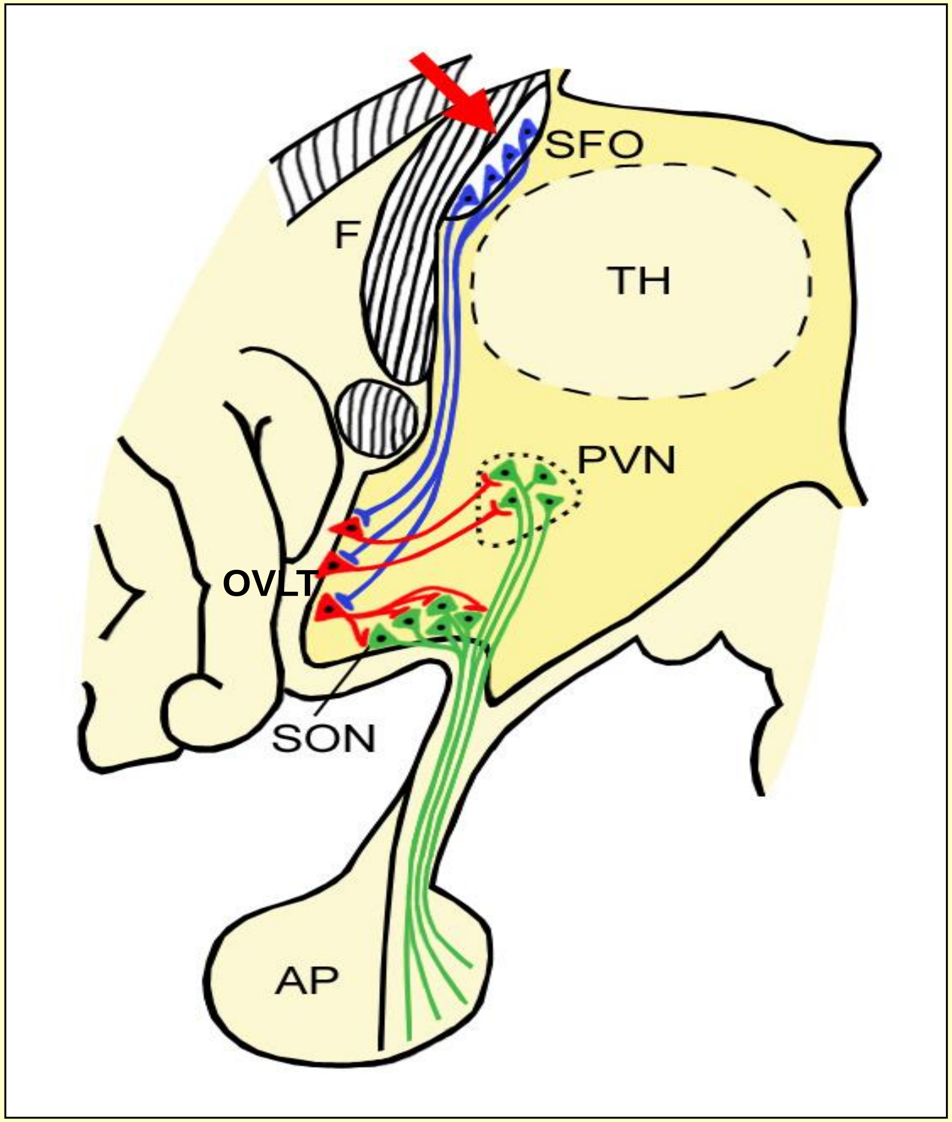
Water balance of the body

Uptake (ml)	Loss (ml)
As fluid: 1000-1500 As food: 700 From metabolism (mainly oxidation of carbohydrates) : 300	Urine (kidney): 1000-1500 Skin-lung: perspiration insensibilis: 900 Faces: 100
Total: 2000-2500	Total: 2000-2500

Regulation of water balance



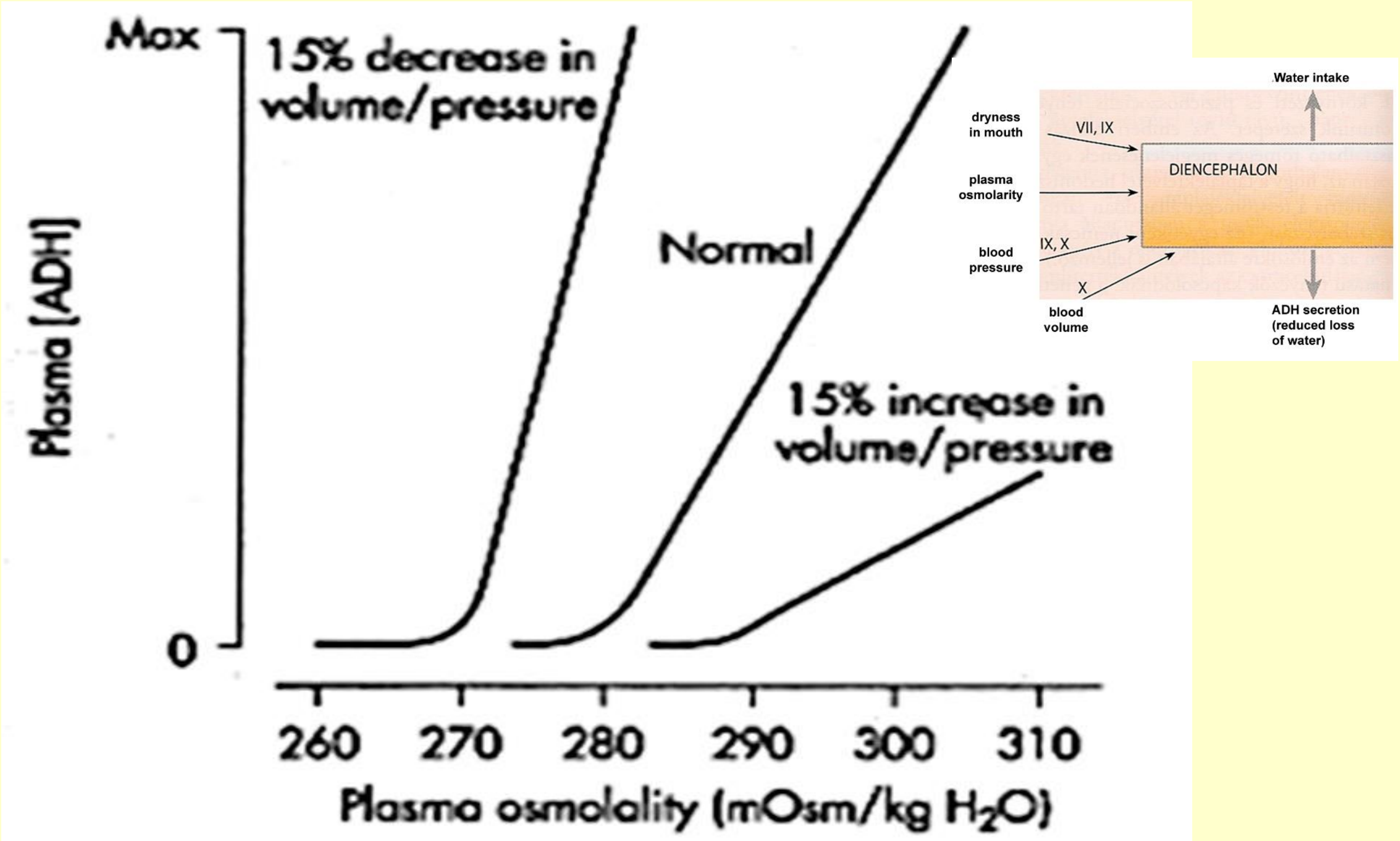
Hypothalamic centers regulating water balance



Osmolarity changes are detected in the subfornical organ (SFO) and the vascular organ of the lamina terminalis (VOLT).

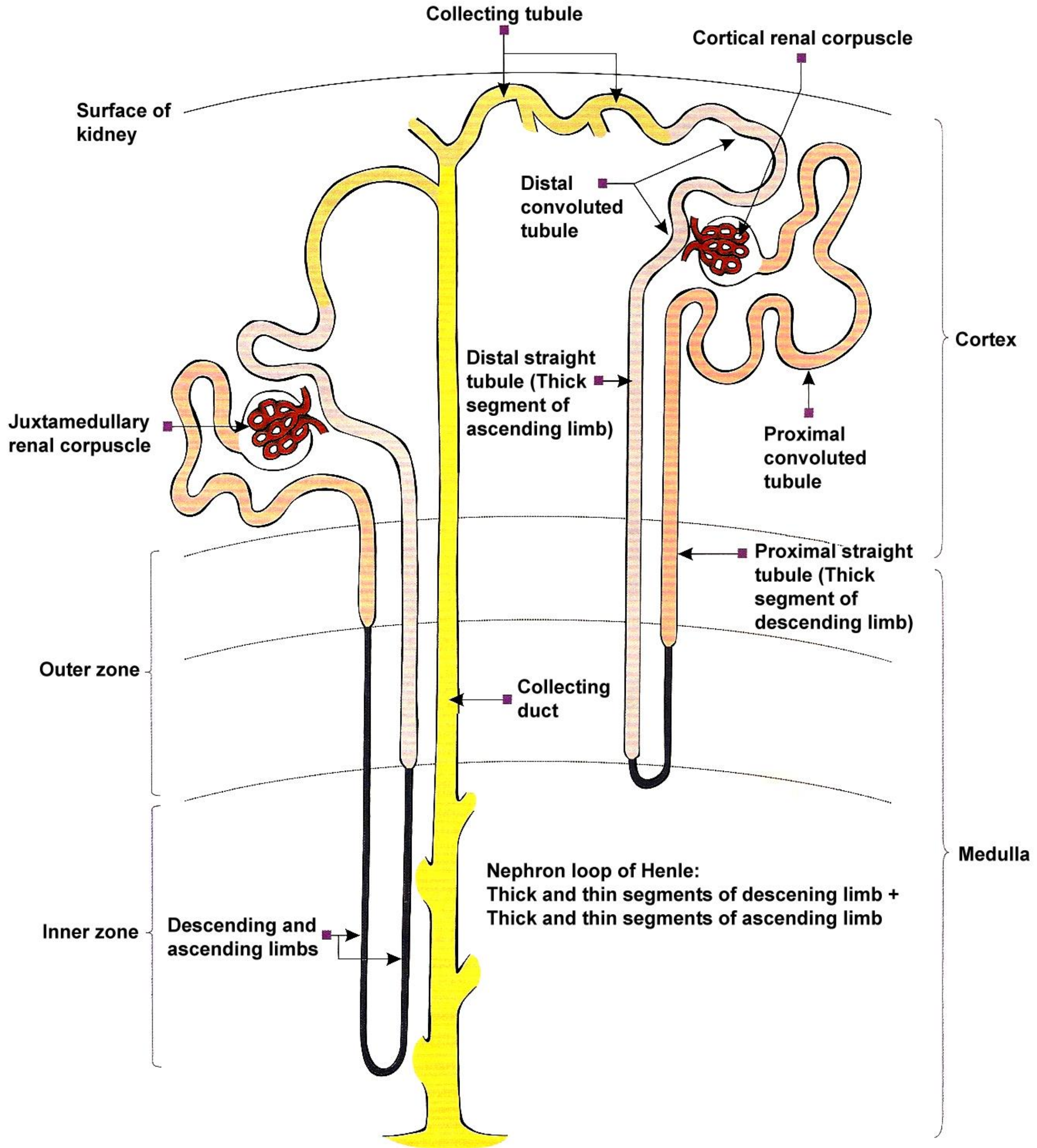
If osmolarity increases, vasopressin (ADH), synthesized in the paraventricular (PVN) and suparoptic (SON) nuclei, is released from the pituitary.

Function of plasma ADH concentration on osmolarity and volume of blood

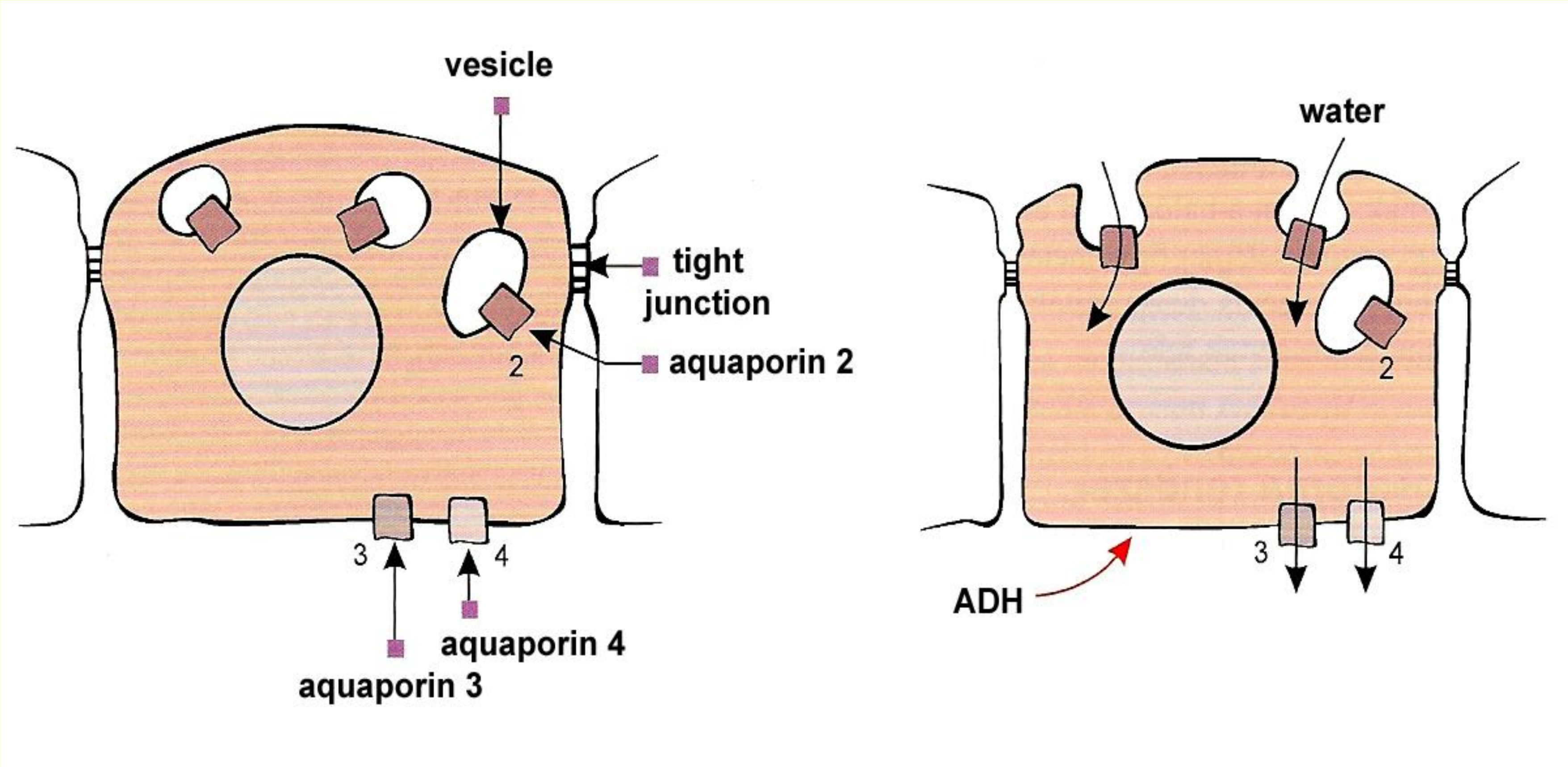


Remark: thirst increases only above 290 mOsm at normal blood volume

Nephron, the functional unit of kidney

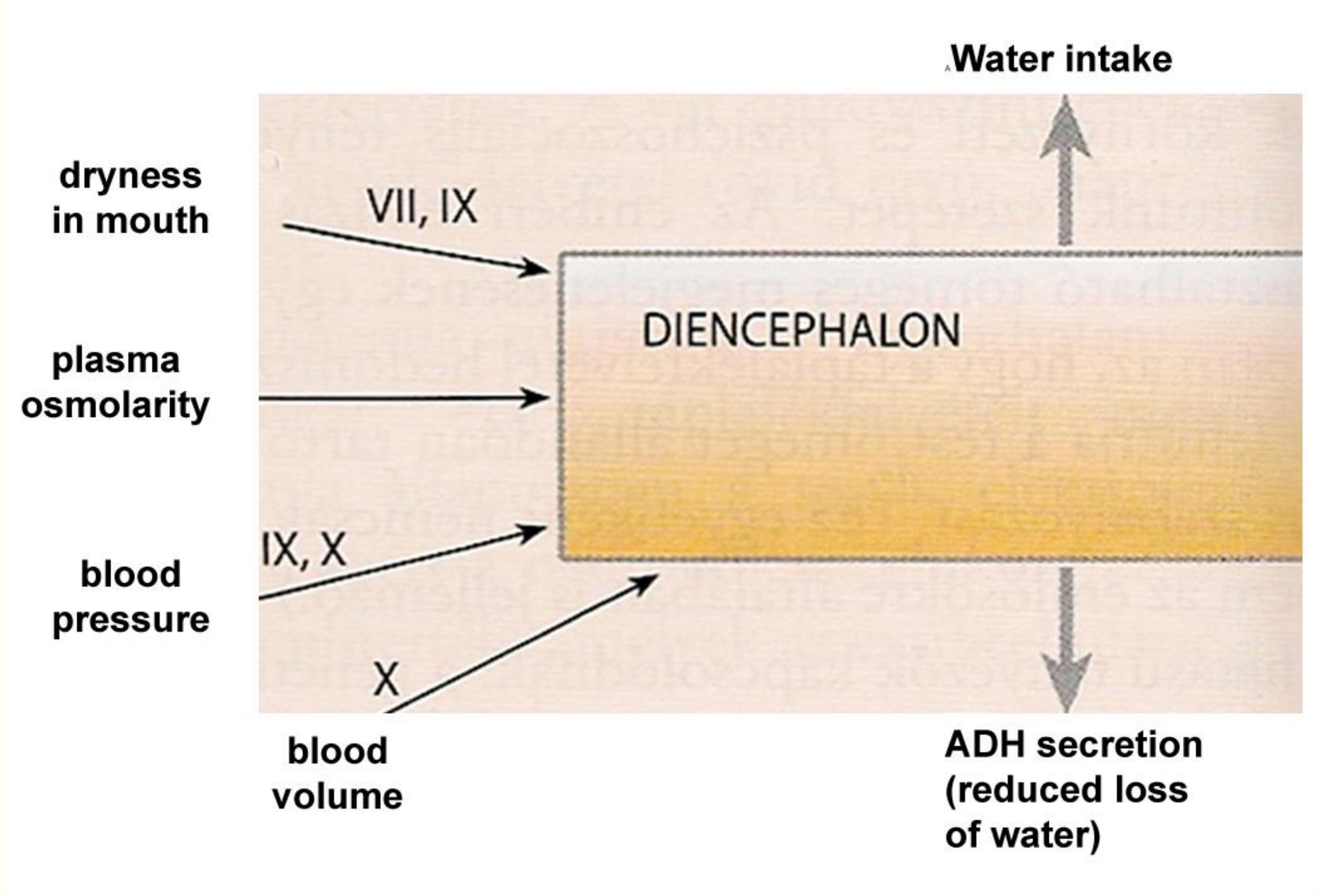


The effect of ADH (antidiuretic hormone, vasopressin) on the cells of the collecting duct

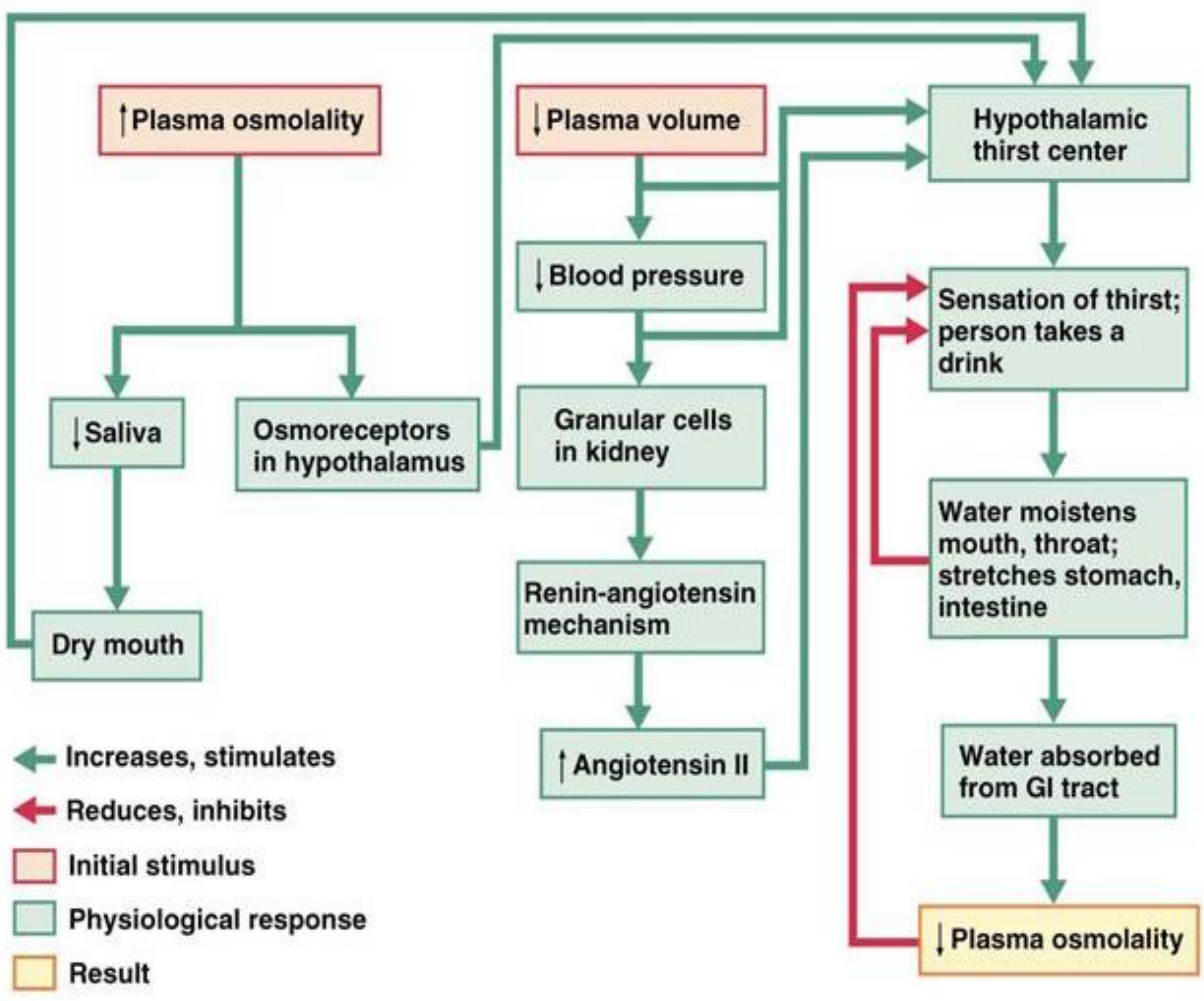


V2 type receptors of ADH is present in the cells of the collecting duct of the renal tube. Their activation leads to the increase of cAMP, which in turn activates protein kinase A, whose final effect is that water channels (aquaporines) get to the apical membrane of the cells, which therefore becomes water-permeable.

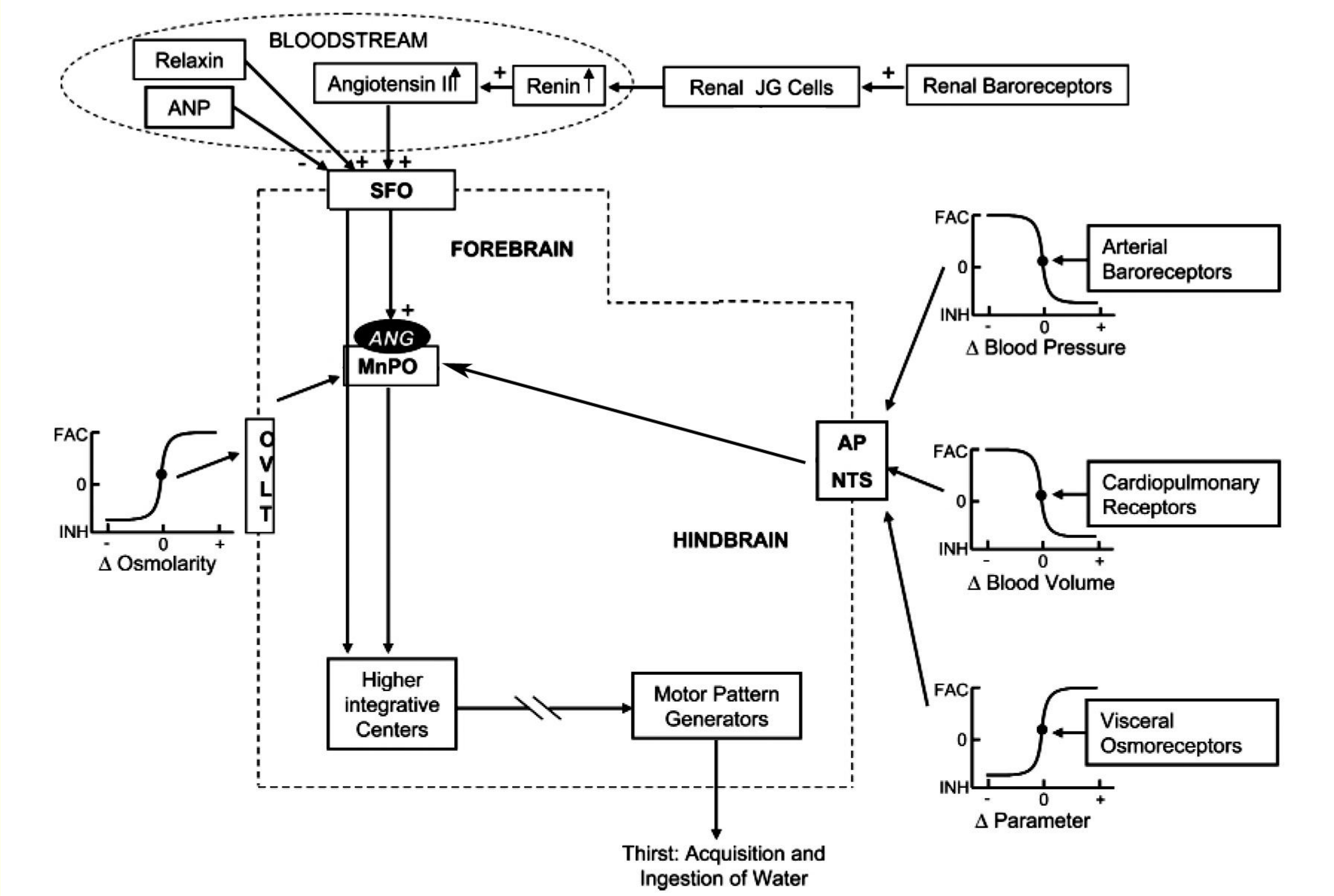
Regulation of water balance



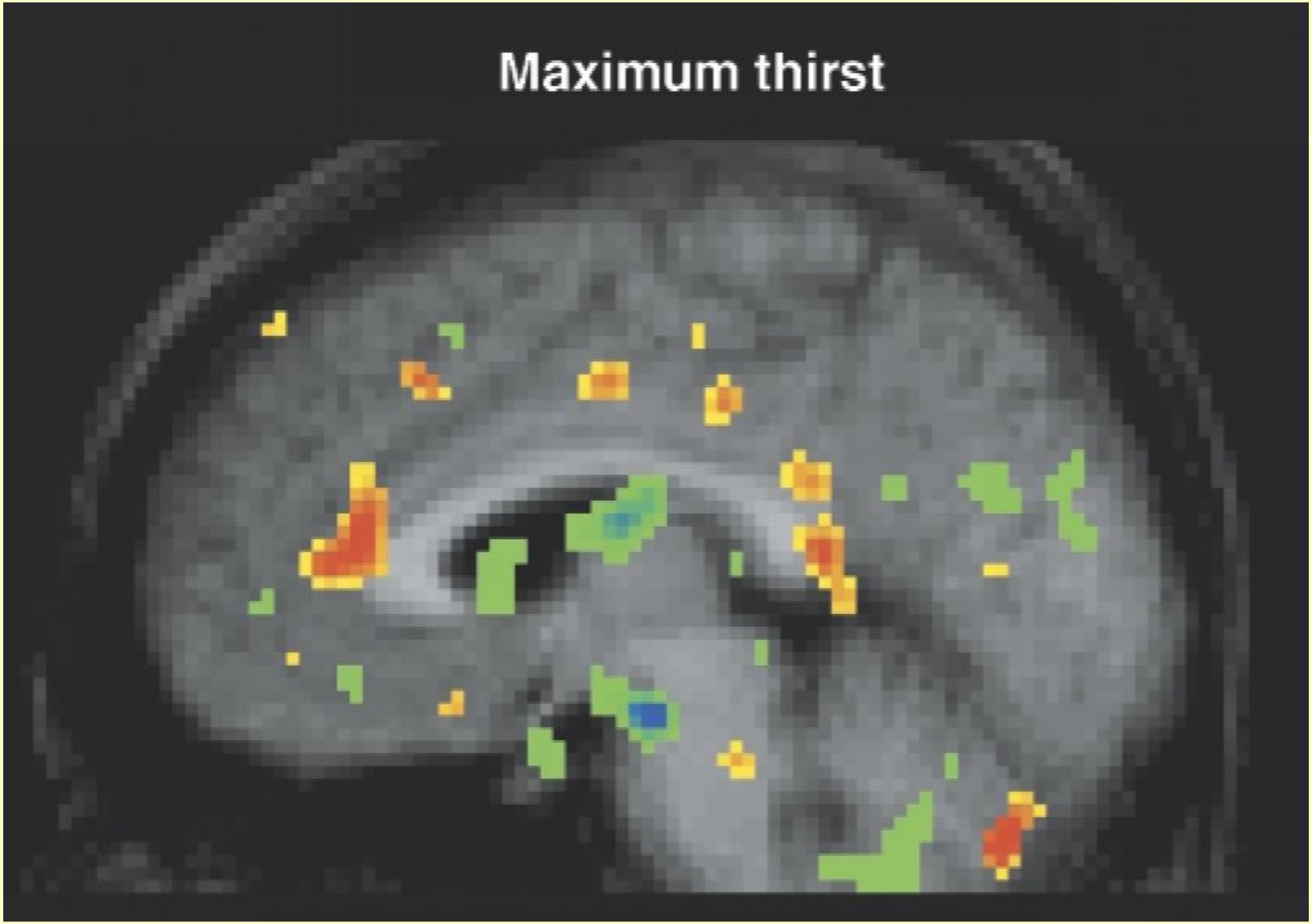
Regulation of water uptake – a behavioural response



Regulatory pathways of thirst



Brain areas activated by thirst



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Heat produced by basal metabolism

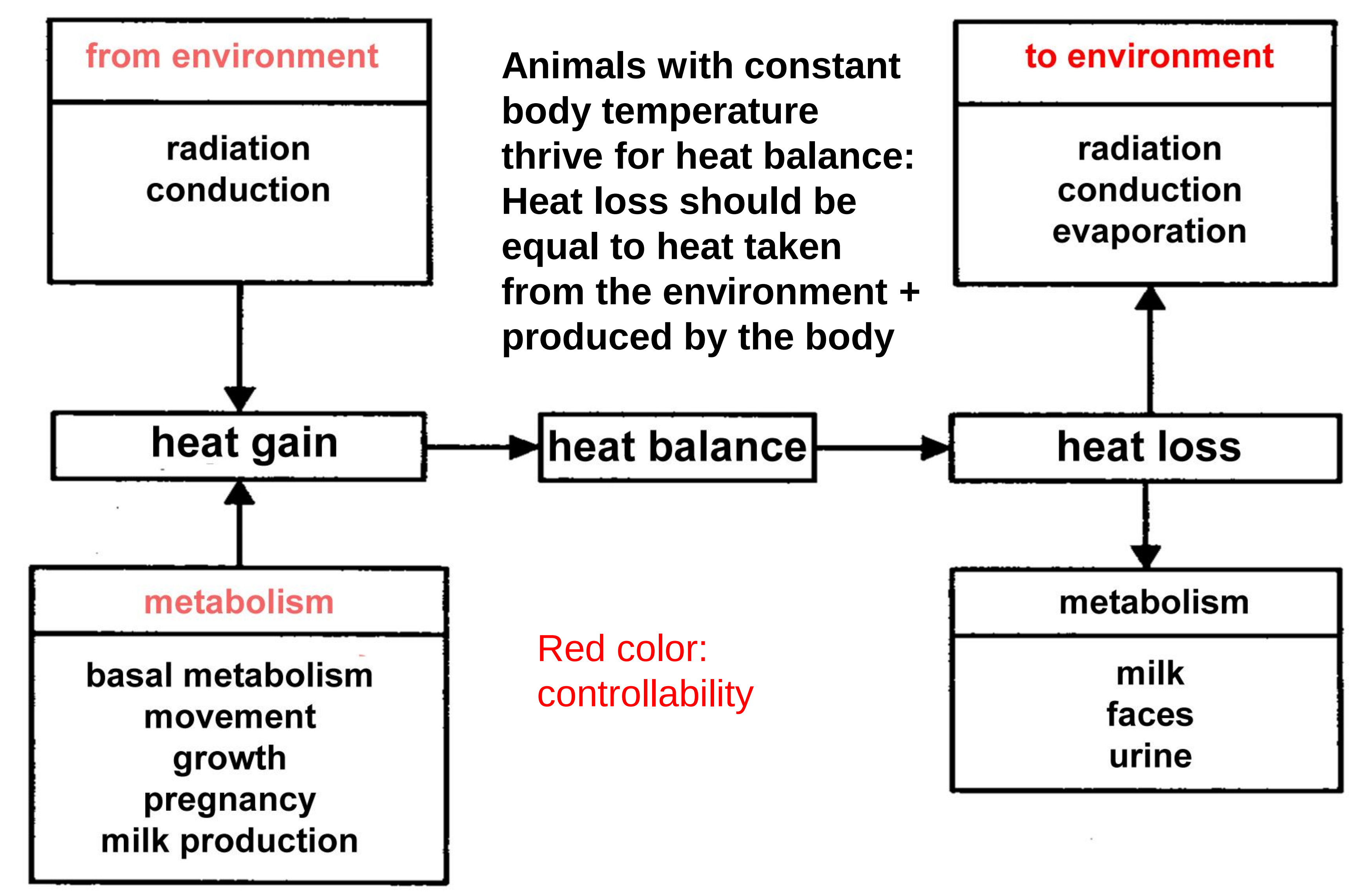
Energy produced by basal metabolism leaves the body in the form of heat. It depends on the size of the animals:

- Heat produced by bigger animals is larger
- Heat produced per body weight decreases with the size of the animal

Rubner's surface area law: heat produced by the basal metabolism of animals is proportional with their surface area rather than their body weight.

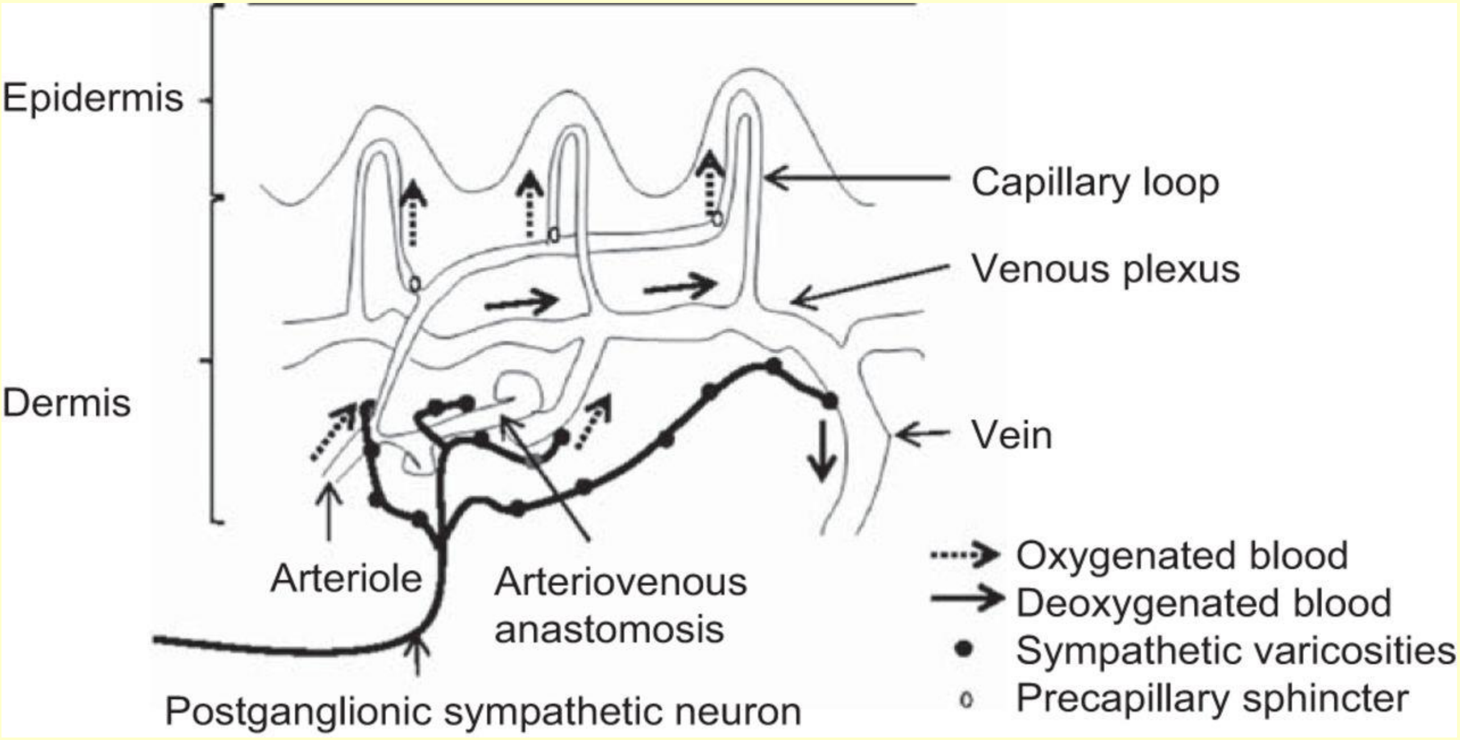
More precisely: Heat produced by basal metabolism is proportional to $W^{0,75}$, where W is the body weight. Thus, heat production is 290 KJ/$W^{0,75}$, and does not depend on individual or the species.

Factors determining heat balance of animals



Body temperature control 1.

1. In response to small alterations from set point body temperature, animals first change the circulation of the skin:
    - If ambient temperature decreases, skin arterioles contract thereby decreasing heat dissipation
    - If ambient temperature increases, skin arterioles dilatate thereby increasing heat dissipation



Body temperature control 2.

In response to larger alterations from set point body temperature:

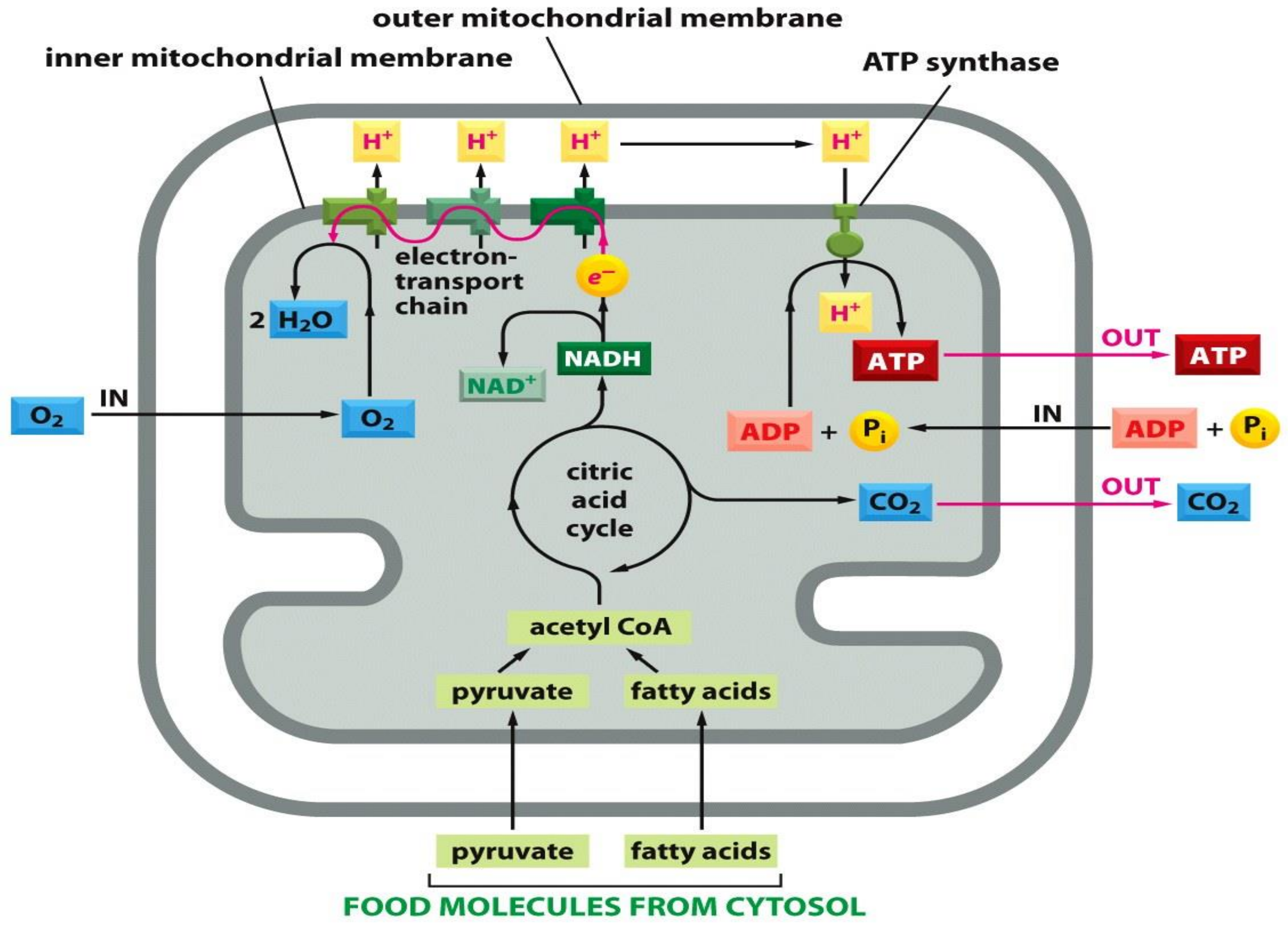
A. In cold environment

- Heat production by the brown adipose tissue is activated
- Muscle contraction can further increase heat production (shivering)
- Activation of thyroid hormone production increases metabolism by enhancing cellular oxidation
- Appropriate behavioral changes

B. In warm environment

- Enhanced ventillation of the lung
- Sweating starts, water evaporates from the skin
- Appropriate behavioral changes

Mechanism of heat production in brown adipose tissue



If the inner membrane of mitochondrium leaks H-ions then heat is produced instead of ATP

Body temperature control 3.

If previous measures were inefficient and body temperature alteration is life-threatening:

A. **In cold environment**

- Due to the activation of stress axis, cellular metabolism is further increased

B. **In hot environment**

- Heart frequency and blood circulation increases

Body temperature control 4.

Slower adaptations to changes of long-time alterations of ambient temperature:

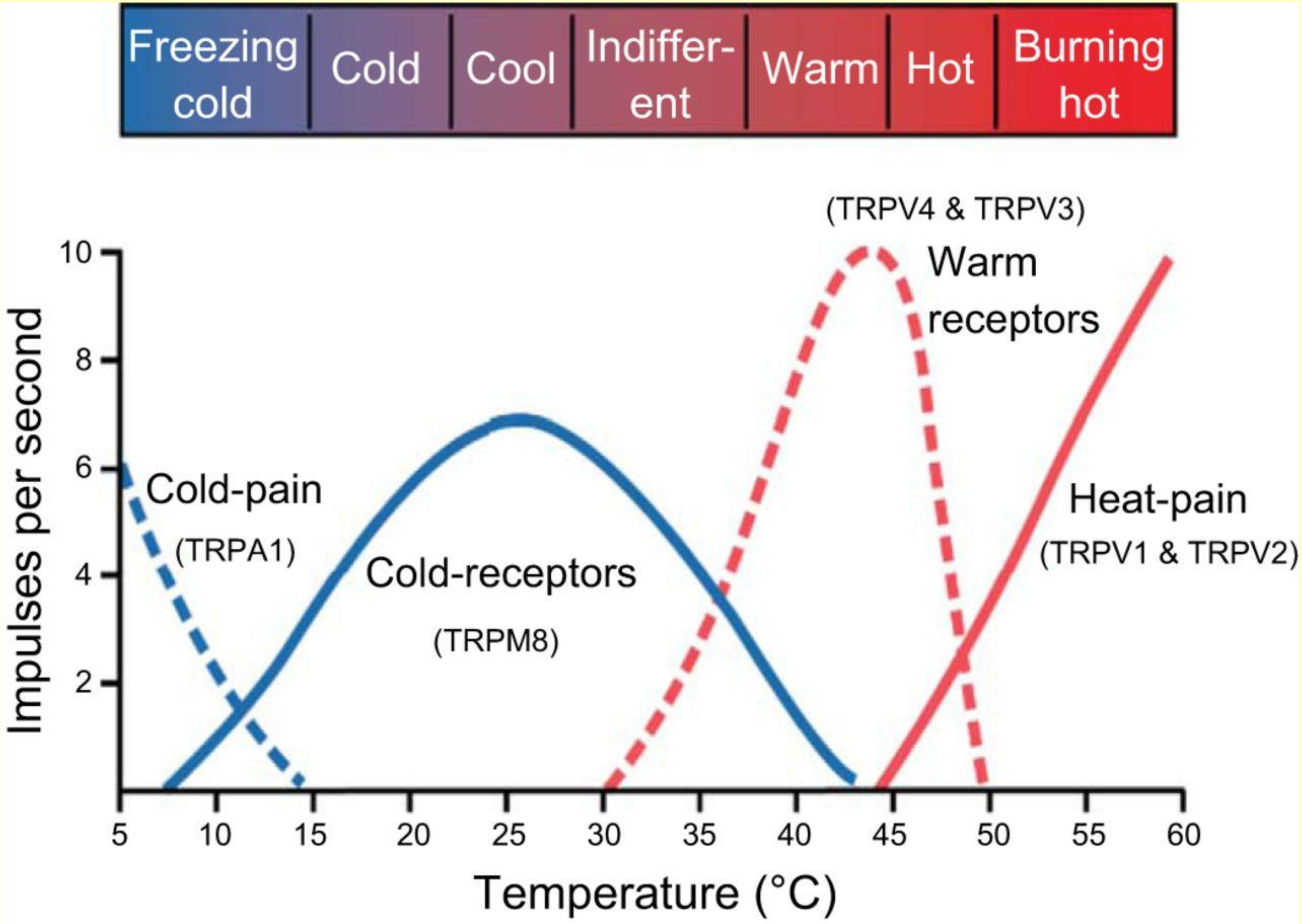
1. Alterations of thermal insulation:

   - adiposity depos build up

   - changes of outer integument take place (e.g. seasonal changes of hair, feather)

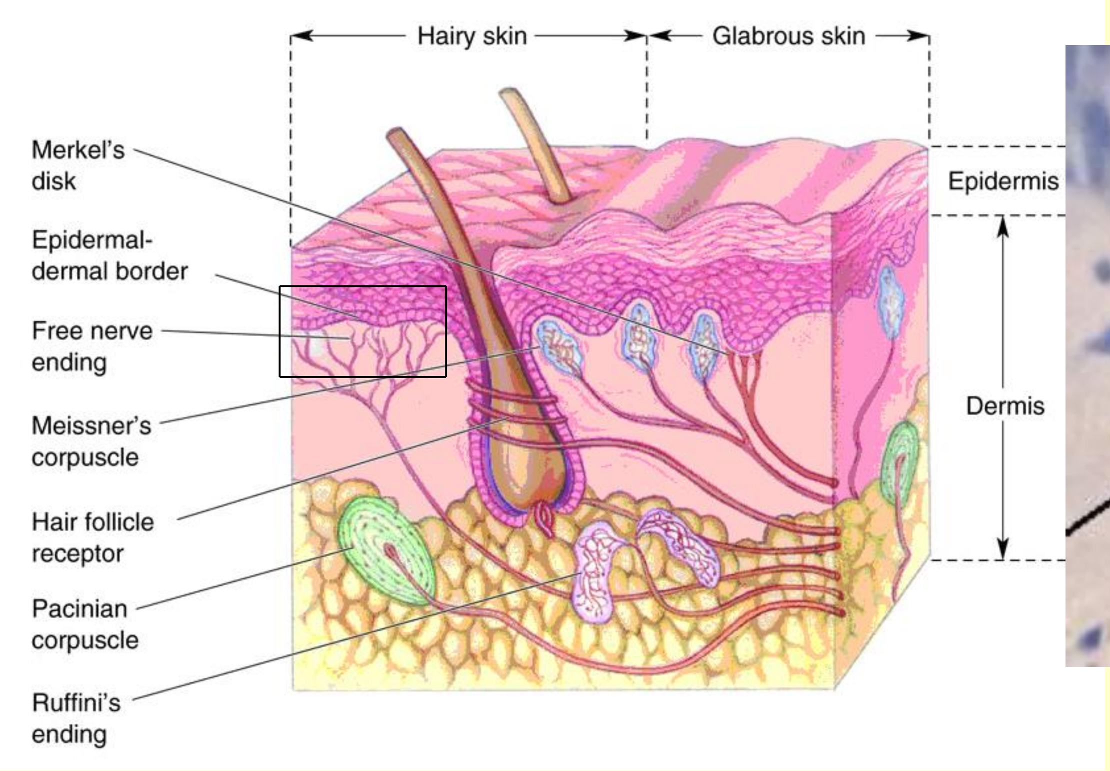
2. Appropriate behavioral changes

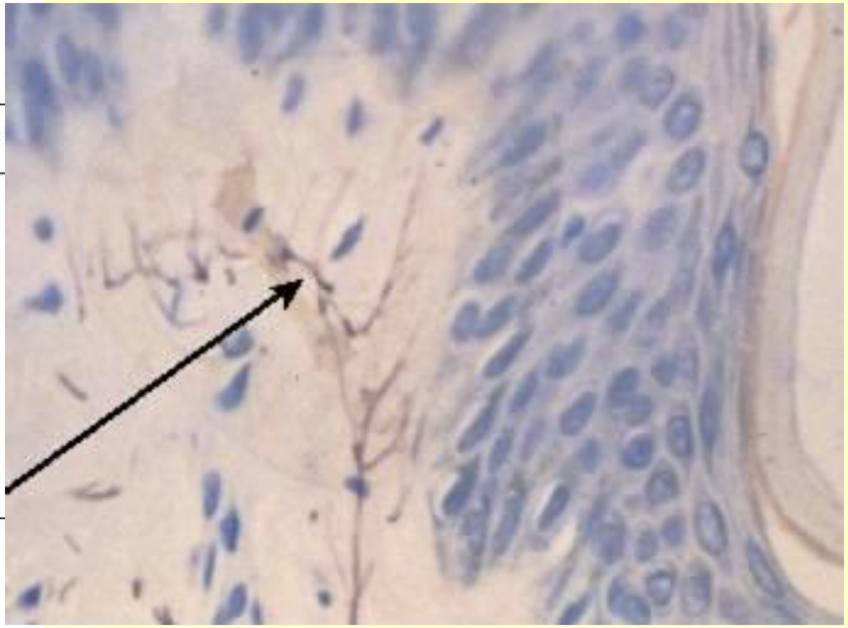
Temperature receptors: transient receptor potential (TRP) channels



Etain A. Tansey, and Christopher D. Johnson Advan in Physiol Edu 2015;39:139-148.

Temperature receptors (TRP channels) are located on free (or bare) nerve terminals in the skin





Thin myelinated (Aδ) or unmyelinated axons (C)

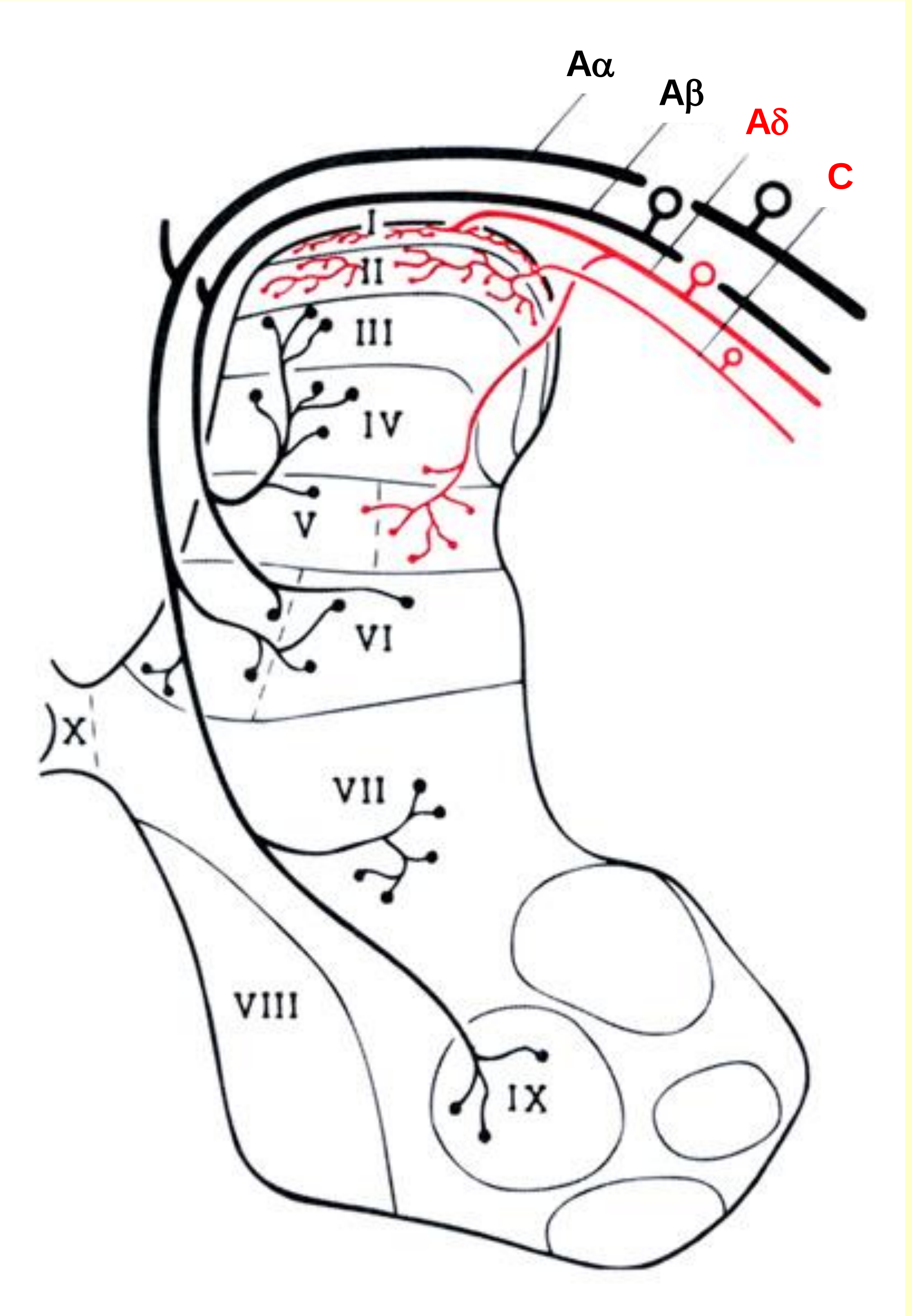
Termination of heat-sensitive primary afferents in the spinal cord

Aδ termosensitive (cold) fibers

termination: lamina I
lamina IIa
lamina V

C termosensitive (warm) fibers

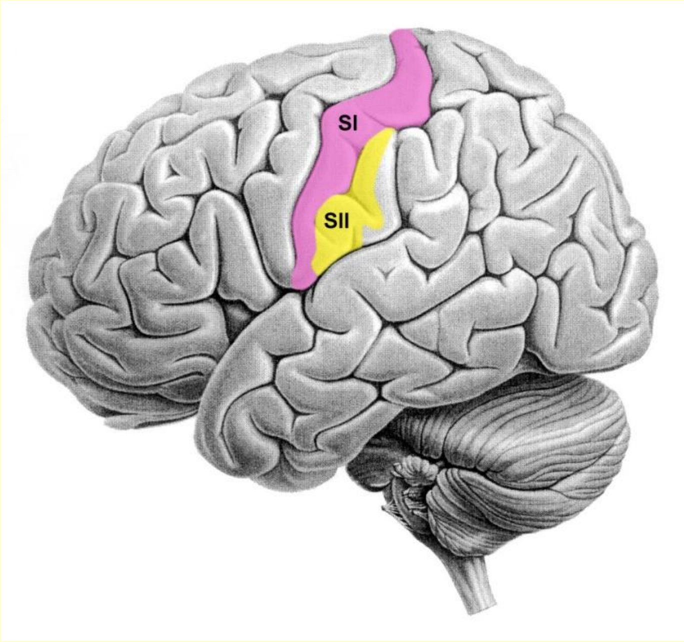
termination : lamina IIb



Neuronal pathways carrying temperature information

Pathways of heat sensation and heat localization (only ascending)

- spinothalamic tract
- trigeminothalamic tract

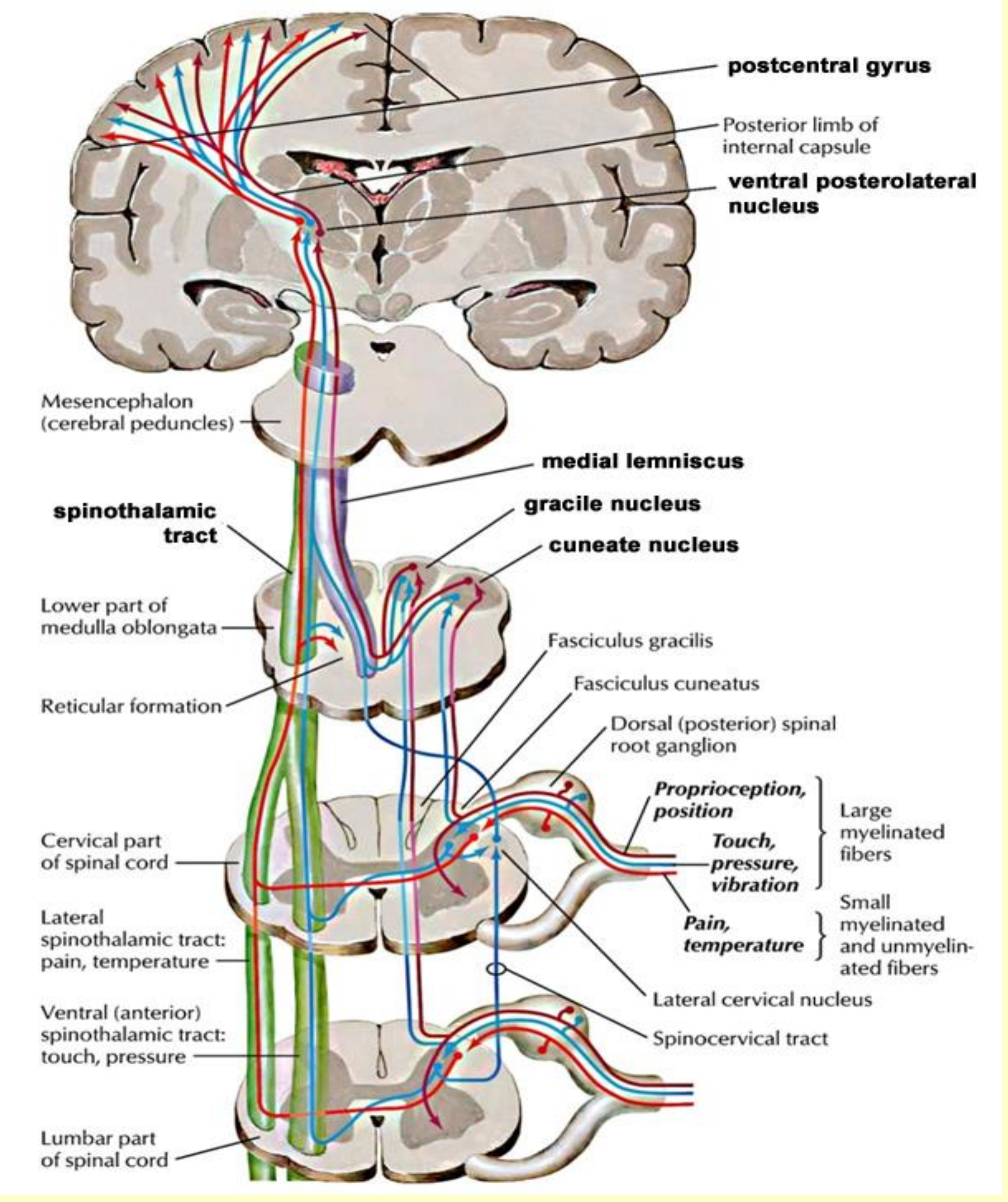


Thermoregulatory pathways

- ascending and descending

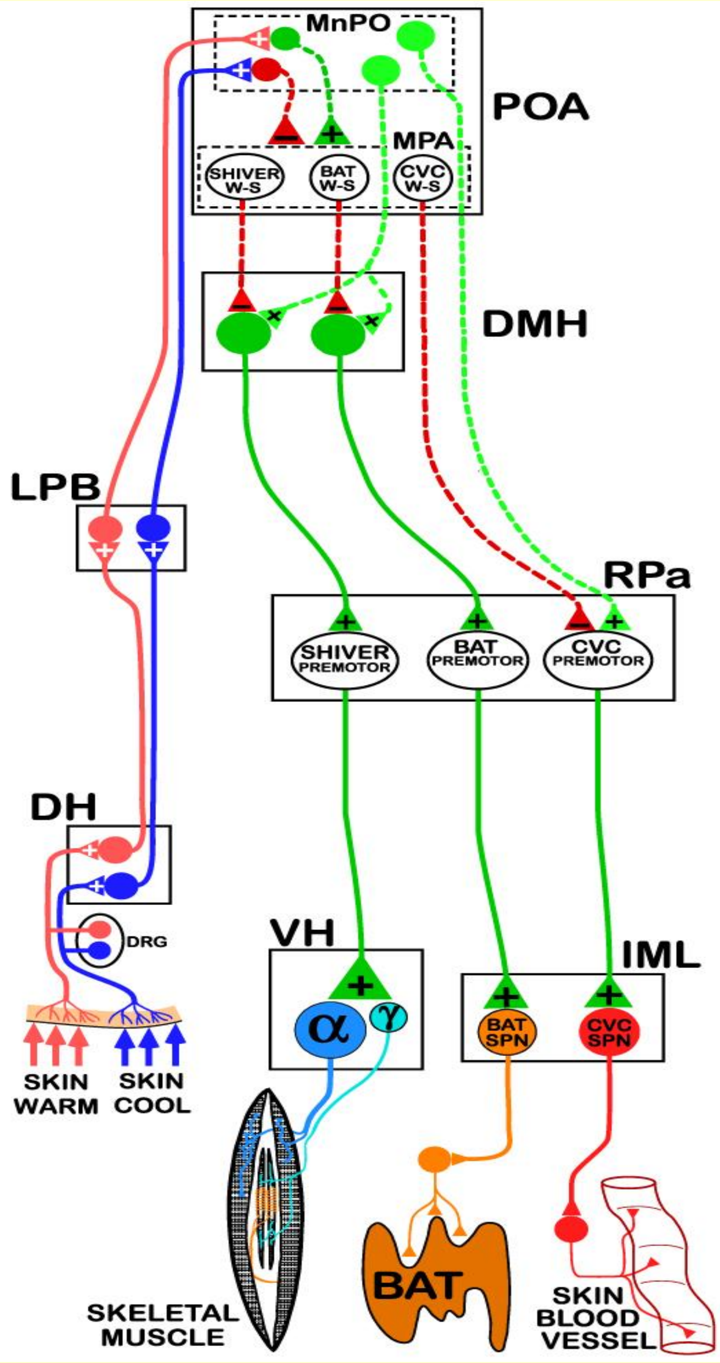
Pathways of thermal stress (only descending)

The ventral posterolateral nucleus of the thalamus (VPL) relays sensory inputs from the body to the cerebral cortex

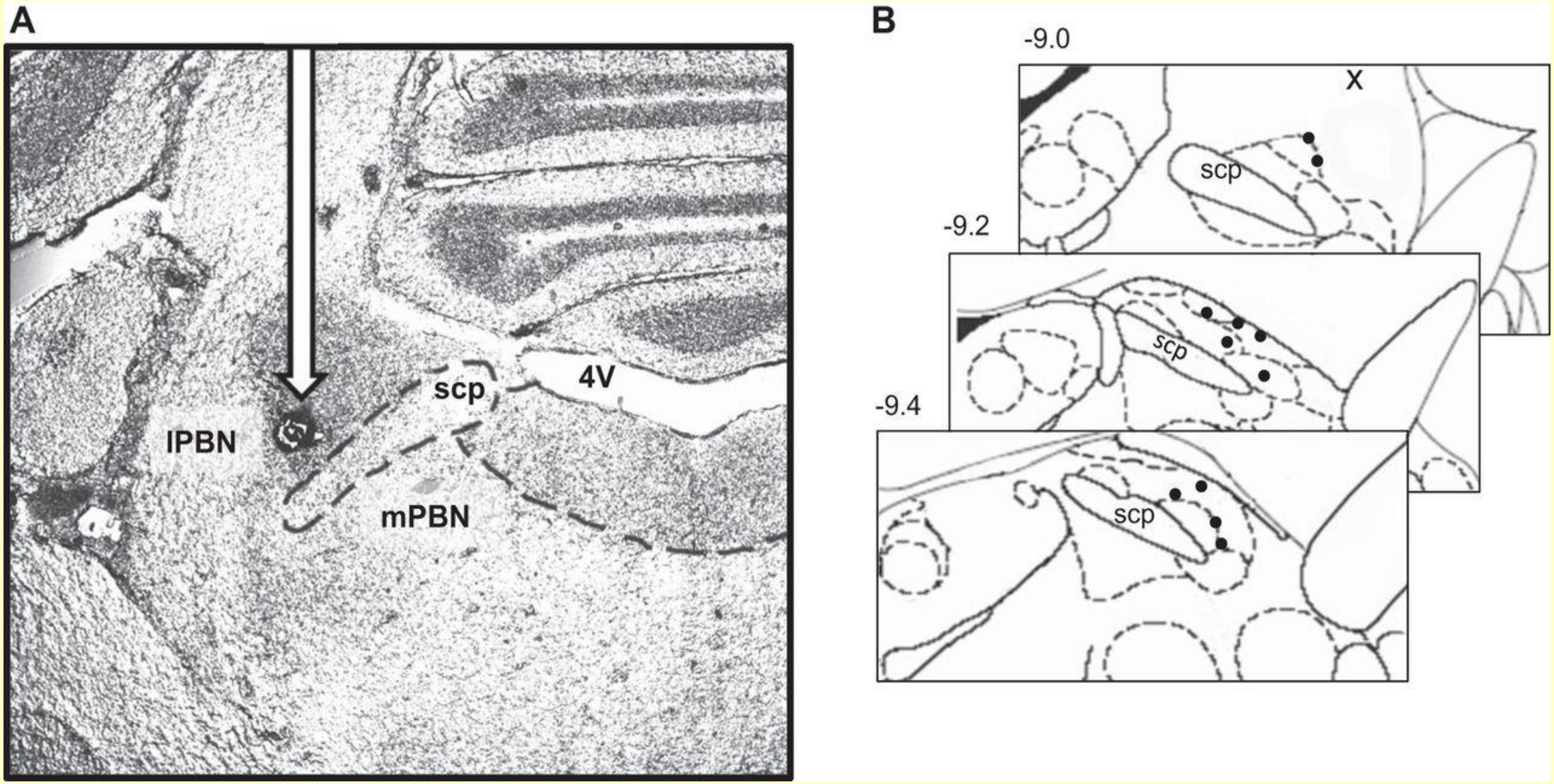


Thermoregulatory pathways

DH: dorsal horn of spinal cord
LPB: lateral parabrachial nucleus
POA: preoptikus terület
MnPO: median preoptic nucleus
MPA: medial preoptic area
CVC: cutaneous vasoconstrictor
W-S: warm-sensitive
DMH: dorsomedial hypothalamic nucleus
rRPA: rostral raphe pallidus
VH: ventral horn of spinal cord
IML: intermediolateral cell column
BAT: brown adipose tissue



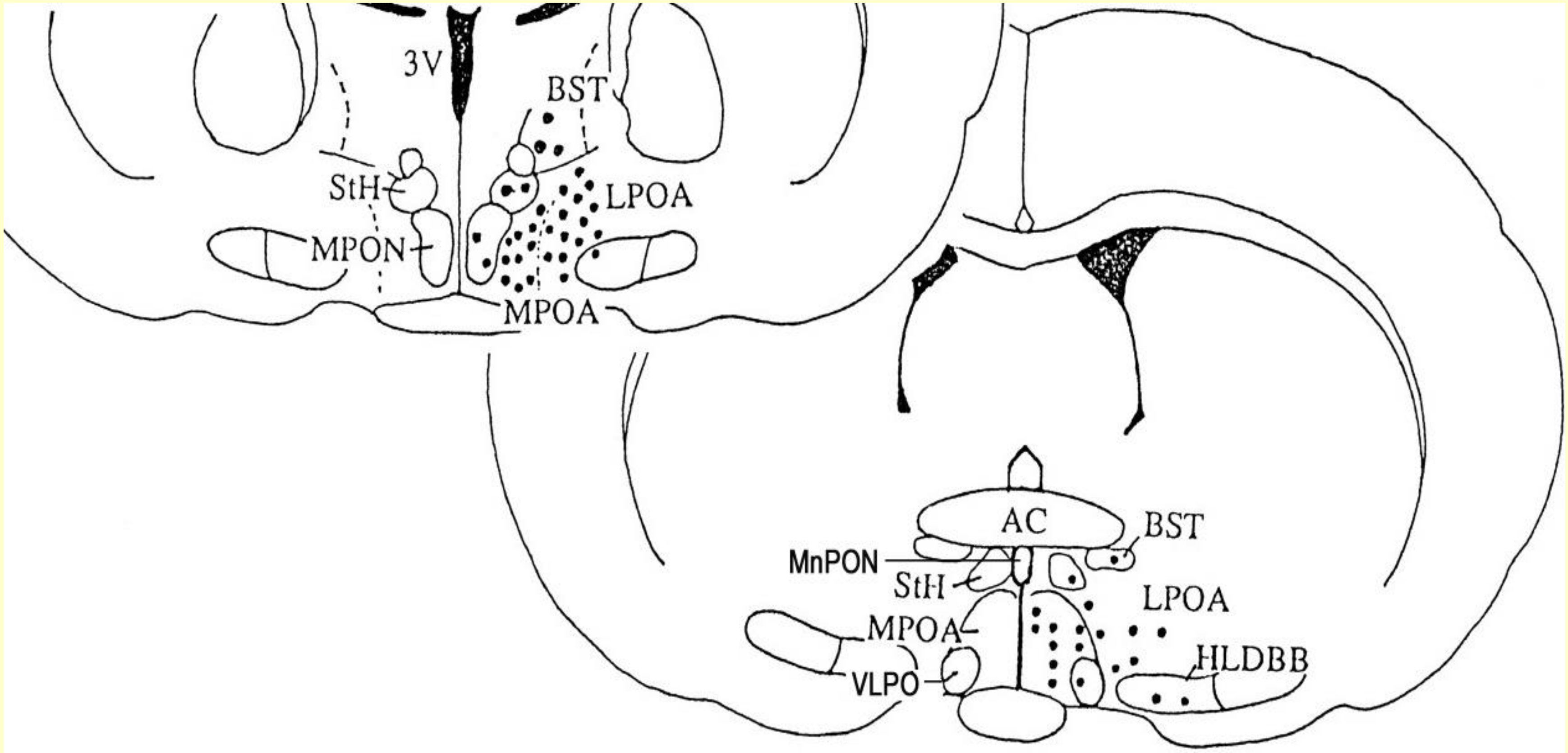
Lateral parabrachial nucleus (LPBN)



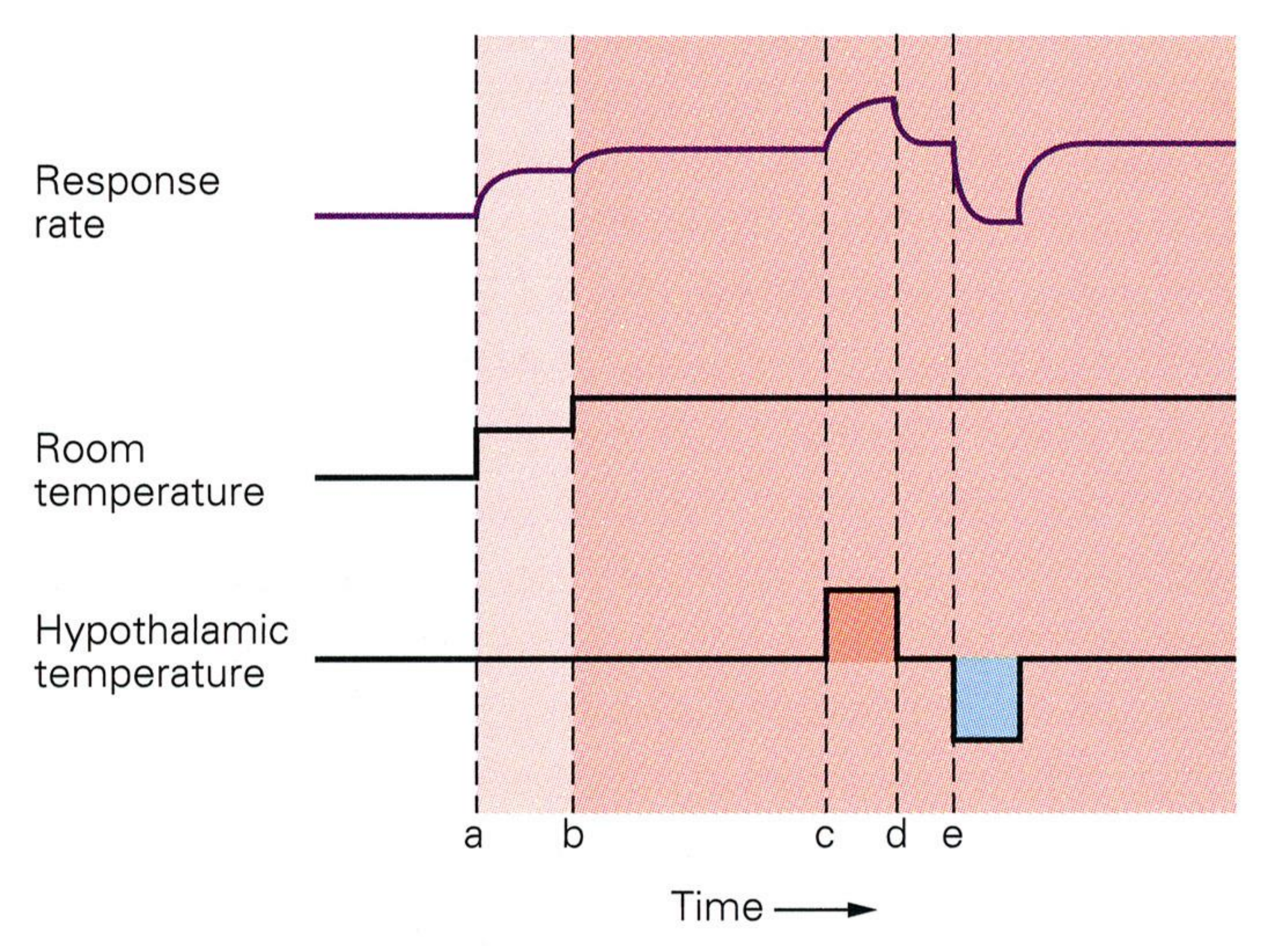
scp: superior cerebellar peduncle = brachium superior

Heat-sensitive neurons in the preoptic region of the hypothalamus

•: Cells reacting to central and peripheral change of temperature



Summation of peripheral and central input on heat-sensitive neurons of the medial preoptic area



a, b: activation of peripheral warm-sensitive receptors
c-d: activation of central warm-sensitive receptors
e: activation of central cold-sensitive receptors

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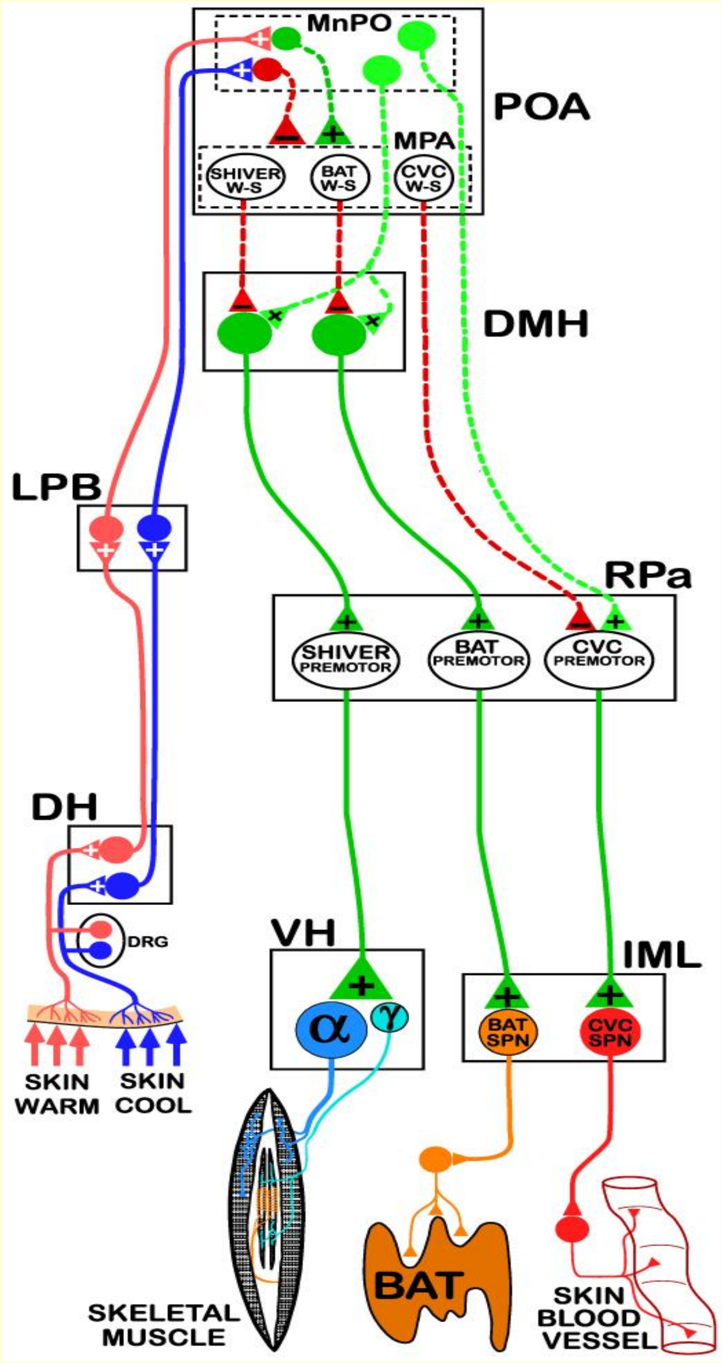
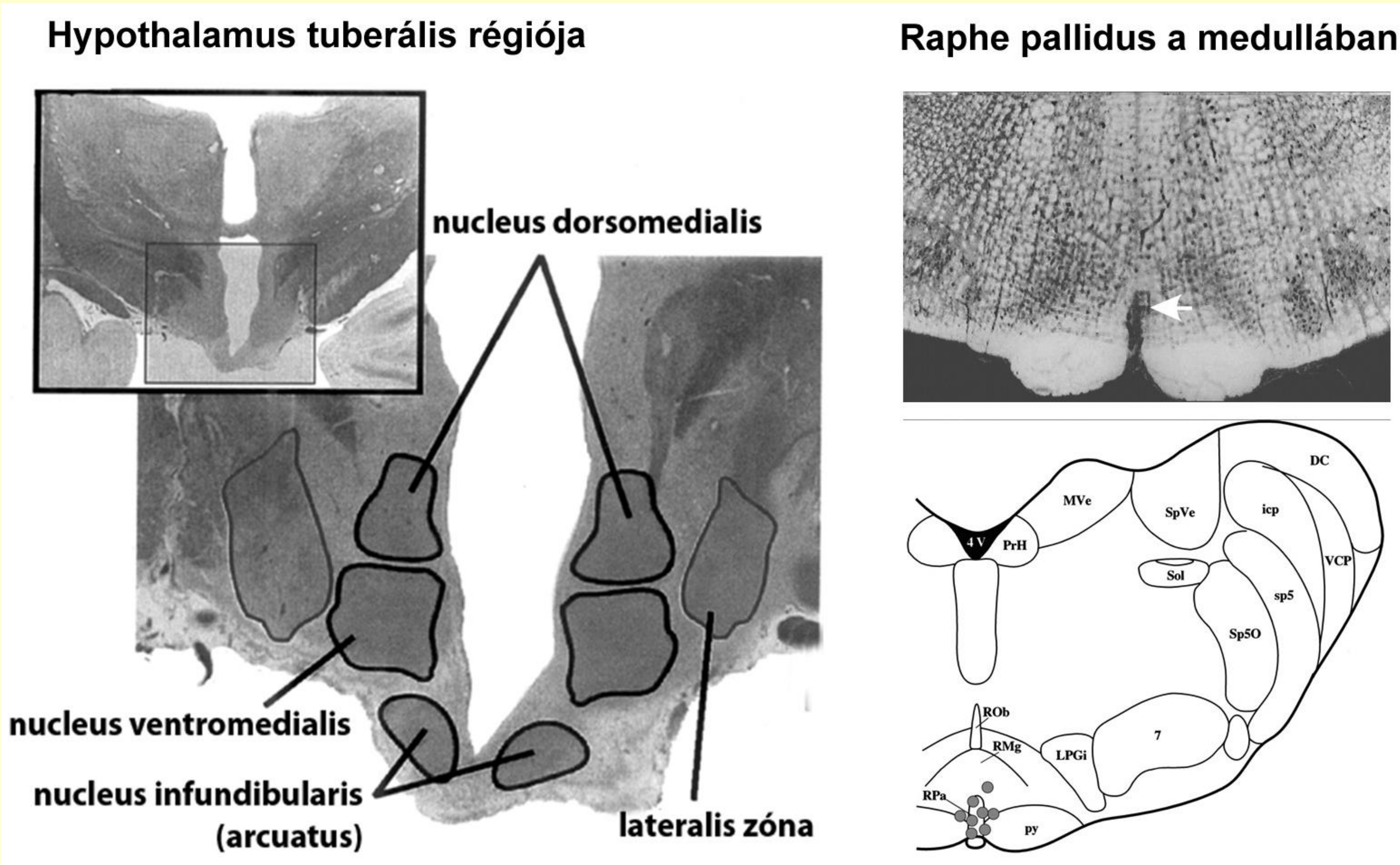
POA: preoptikus terület
MnPO: median preoptic nucleus
MPA: medial preoptic area
CVC: cutaneous vasoconstrictor
W-S: warm-sensitive
DMH: dorsomedial hypothalamic nucleus
rRPA: rostral raphe pallidus
VH: ventral horn of spinal cord
IML: intermediolateral cell column
BAT: brown adipose tissue



Location of the dorsomedial nucleus in the hypothalamus and the raphe pallidus in the medulla



Body temperature control 2.

In response to larger alterations from set point body temperature:

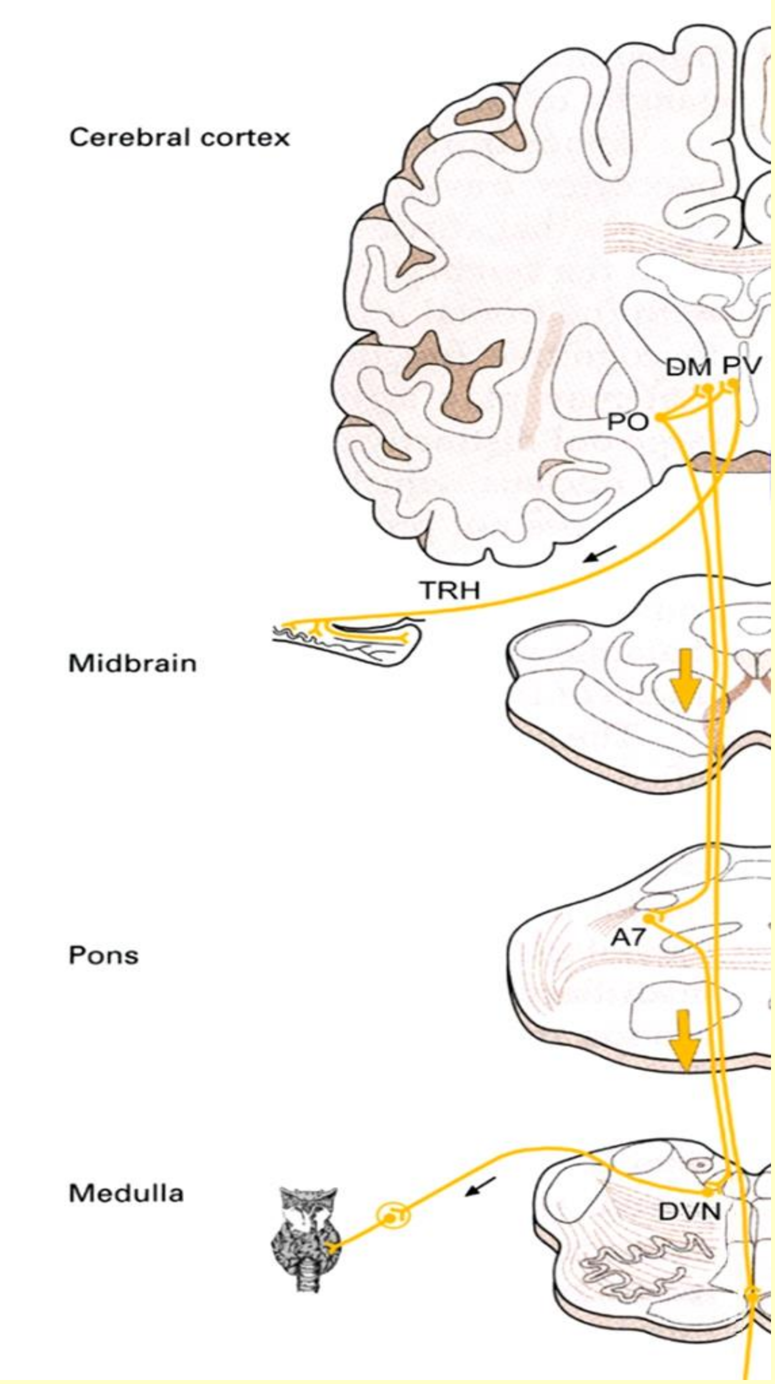
A. In cold environment

- Heat production by the brown adipose tissue is activated
- Muscle contraction can further increase heat production (shivering)
- Activation of thyroid hormone production increases metabolism by enhancing cellular oxidation
- Appropriate behavioral changes

B. In warm environment – neuronal pathways are not known

- Enhanced ventillation of the lung
- Sweating starts, water evaporates from the skin
- Appropriate behavioral changes

Neuroendocrine and descending thermoregulatoy pathways controlling the secretion of thyroid hormones



Body temperature control 3.

If previous measures were inefficient and body temperature alteration is life-threatening:

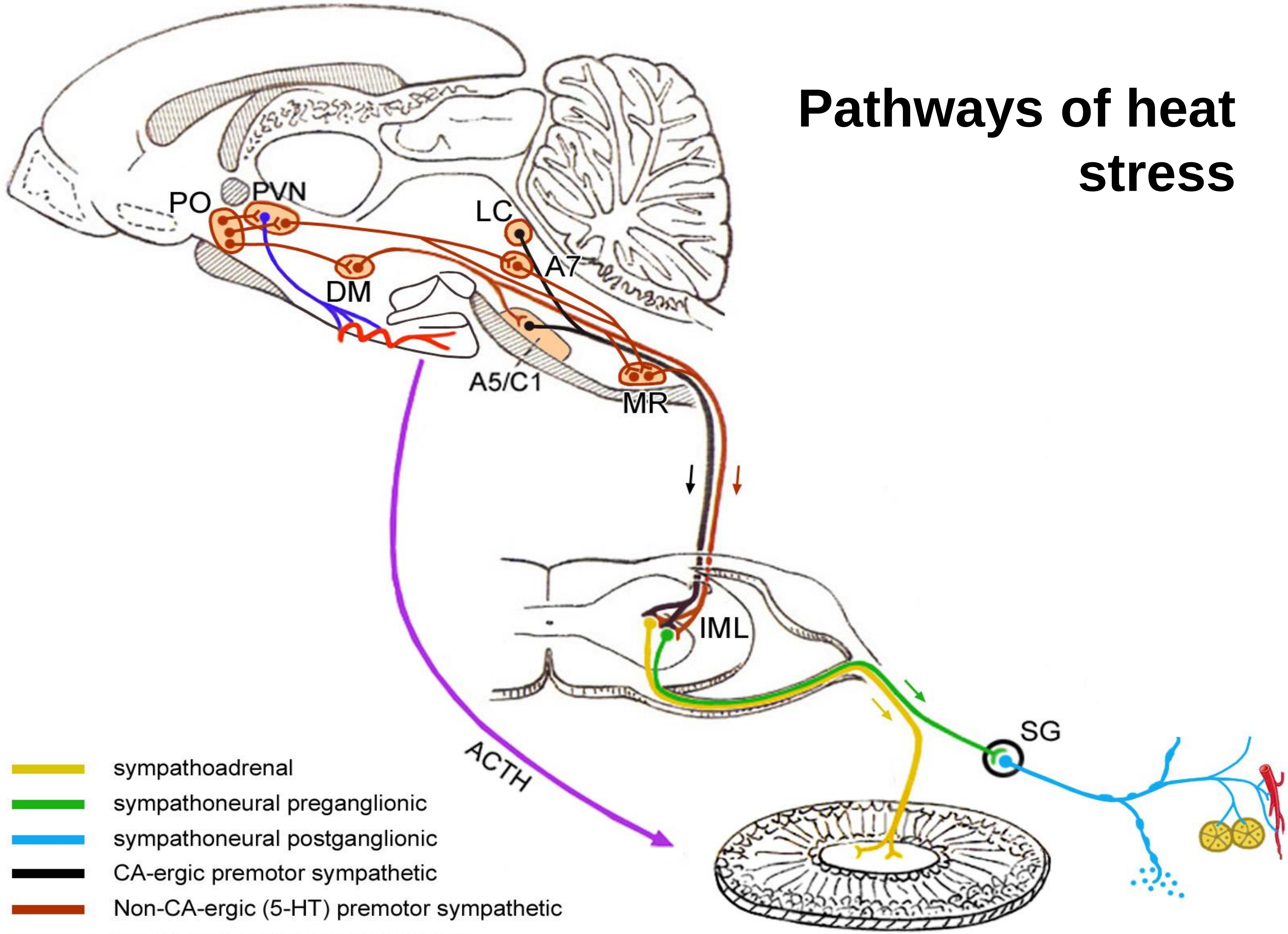
A. **In cold environment**

- Due to the activation of stress axis, cellular metabolism is further increased

B. **In hot environment**

- Heart frequency and blood circulation increases

Pathways of heat stress



sympathoadrenal
sympathoneural preganglionic
sympathoneural postganglionic
CA-ergic premotor sympathetic
Non-CA-ergic (5-HT) premotor sympathetic
hypothalamo-pituitary-adrenal axis

Thank you for your attention!