Graduate Studies in Biomedical Engineering and Medical Physics
University of Patras **2020**

Physiology and Pathophysiology for Engineers and Physicists

Teachers:
Elias Kouvelas, Prof. Emeritus, Medical School, University of Patras
*** George Kostopoulos**, Prof. Emeritus, Medical School, Univ. of Patras
Adamantia Mitsacos, Prof. Emeritus, Medical. School, Univ. of Patras

* = Introduction to Physiology and its principles + Neurophysiology

Course Description

Purpose:

Designed to bring to engineering students a **general awareness** of the function of whole organisms, their component cells, organs, and organ systems as well as the basic mechanisms leading to disease

Contents:

An overview of human physiology & Pathophysiology

Cellular physiology (pointers to subjects introduced in previous modules, which are important prerequisites for understanding Physiology)

Circulatory and respiratory physiology

Physiology of the gastrointestinal system

Hormonal control – physiological modelling

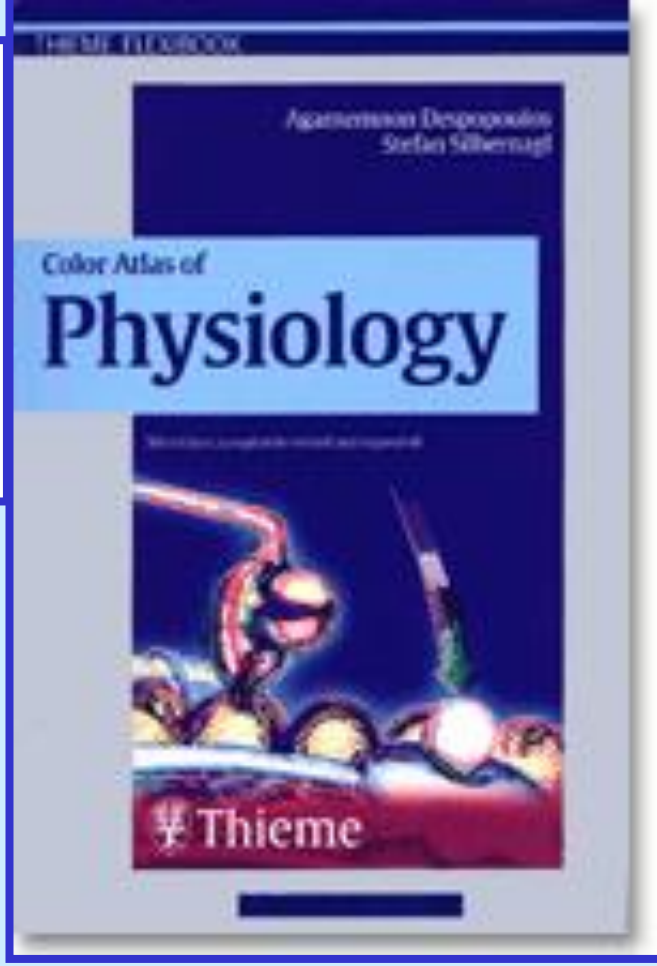
Neural integration and control of body and behavior

Duration: 1 module – 20 X 2 hours

Time: starting 26 October 2020 see calendar

Συγγράμματα Φυσιολογίας:

Despopoulos and S. Silbernagl 2003, "Color Atlas of Physiology", Thieme 5th edition. [και Ελληνική μετάφραση της 2ης εκδ], Ιατρικές Εκδόσεις Λίτσα.



Αλλα συγγράμματα στα Ελληνικά:

Vander MD, Sherman PhD, Luciano PhD, Τσακόπουλος M. Φυσιολογία του Ανθρώπου. Ελλ. Μετάφρ. Εκδ. Πασχαλίδη 2001

2. Koeppen BM and Stanton BS, "Berne & Levy Αρχές Φυσιολογίας". Ελληνική μετάφραση. Εκδόσεις Παρισιάνου, 2003.

3. ***W. Boron & E. Boulpaep:*** *Medical Physiology. A cellular and molecular approach. Σε* Ελληνική μετάφραση, *Εκδ. Πασχαλίδη).*

Προεκτάσεις παθοφυσιολογίας:

S. Silbernagl/F. Lang: **Color Atlas of Pathophysiology** 2000. 406 pp, 180 illustrations, ISBN 0865778663 / 3131165510 Georg Thieme Verlag

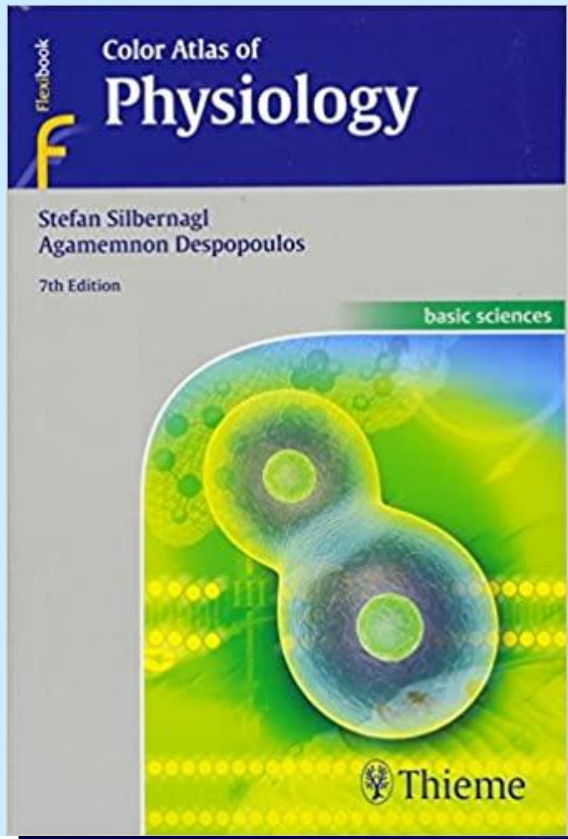
Resources:

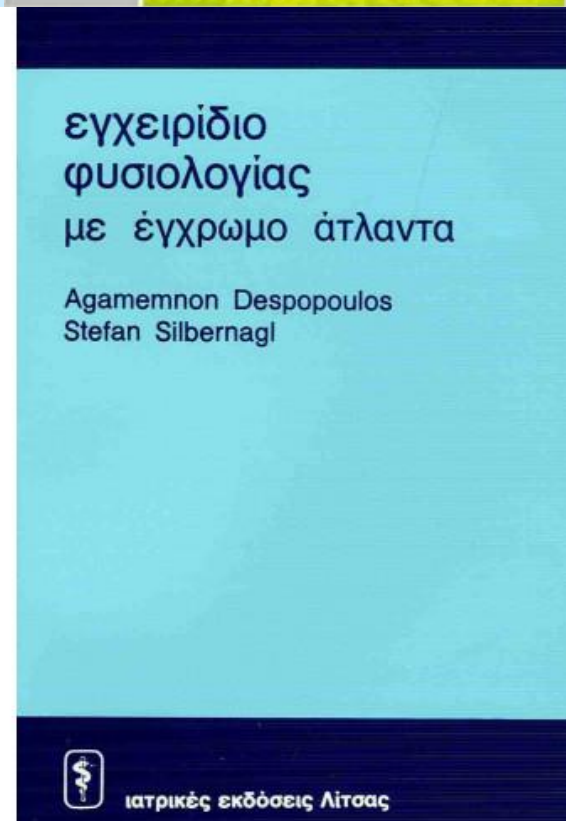
Textbook: (any one, but **mandatory to own**) :

Despopoulos and S. Silbernagl 2003, **"Color Atlas of Physiology",** Thieme 5th edition. Translated in all major languages [και Ελληνική μετάφραση, ΙατρικέPhysiologyς Εκδόσεις Λίτσα]

- **Exams** will be based on material presented and selected from any textbook of Physiology
- **Lectures** are not exhaustive.
- Some **handouts** will be given to you to help with PATHOPHYSIOLOGY – only some elementary stuff.
- **Attendance and active participation in lectures (which demands a good command of English) are mandatory** for allowance to take part in the exams

send me questions at: gkkostop@upatras.gr





Suggested extra supplements:

1. S. Silbernagl/F. Lang: **Color Atlas of Pathophysiology** 2000. 406 pp, 180 illustrations, ISBN 0865778663 / 3131165510 Georg Thieme Verlag

2. DU Silverthorn **"Human Physiology**; An integrated approach" chapter. 1, 6 and 8-13, Pearson Education Int.2001, 185 pages.

3. **"Brain Facts"** 2009, a 74-page primer, published by the Society for Neuroscience (USA) available at
   http://www.sfn.org/index.aspx?pagename=brainFacts

4. **Neuroscience: The Science of the Brian** by BNA free download

5. (advanced – in library) **"Essentials of neural science and behavior"** Appleton &Lange, 1995 / edited by Eric R. Kandel, James H. Schwartz and Thomas M. Jessel / μεταφρασμένο στα Ελληνικά "Νευροεπιστήμη και Συμπεριφορά", από τους Α. Καραμανλίδη, Γ.Χ. Παπαδόπουλο και Χ. Καζλαρή, Πανεπιστημιακές Εκδόσεις Κρήτης 1997)

In translation:

1. **Vander MD, Sherman PhD, Luciano PhD, Τσακόπουλος Μ.** Φυσιολογία του Ανθρώπου. Ελλ. Μετάφρ. Εκδ. Πασχαλίδη 2001
2. **Berne RM and Levy** MN Αρχές Φυσιολογίας. Ελληνική μετάφραση. Παν Εκδόσεις Κρήτης κεφ. 1-3, σελ. 3-52
3. ***W. Boron & E. Boulpaep:*** *Medical Physiology. A cellular and molecular approach. Σε* Ελληνική μετάφραση, *Εκδ. Πασχαλίδη).*

Very brief: **Laurie Kelly McCorry** : ***Essentials of human Physiology for Pharmacy***, *Second Edition* (also electronic) **p.:** 362, 2004, Routledge, USA

Course procedures - Τα διαδικαστικά

Η **εξεταστέα ύλη** είναι από το περιεχόμενο του βιβλίου των Despopoulos and Silbernagl και ότι σημειώσεις σας δοθούν σε εκτύπωση ή σε e-class (ιδιαίτερα για τη Παθοφυσιολογία), οδηγούμενοι και από τις παραδόσεις που θα αναρτώνται στο e-class

Οι **παραδόσεις** δεν εξαντλούν τη διδακτέα/εξεταστέα ύλη, αλλά σας βοηθούν να την κατανοήσετε και να αναγνωρίσετε ποια είναι τα σημαντικότερα σημεία της.

Η **παρακολούθηση** και ενεργός συμμετοχή στο μάθημα αποτελούν προϋπόθεση συμμετοχής στις εξετάσεις

Επικοινωνία:

Γραμματεία Φυσιολογίας: 2610-969155
Γ. Κωστόπουλος gkkostop@upatras.gr

part 1 - general physiology

- Definition of Physiology
- Definition of Pathophysiology
- Elements of an organism
- Homeostasis – define disease
- Control systems and body communication
- Energy balance
- Methods in physiology
- What is life?

What is a Physiologist?

- Physiologists are interested in <u>function *and* integration</u>

  ie how things work *together* at various levels of organisation ⇒ whole organism

- When studying parts of organisms (even single molecules) a physiologist will seek to establish the <u>relevance</u> of any information derived to the function of the whole body

Physiology =

•The study of the functions of a living organism and its component parts. .Includes chemical and physical processes.

•Formalized by 16th century as the study of the vital functions of the human body. .Now includes study of plants and animals.

•Cannot be fully separated from anatomy, the study of structure. .(Form follows function..) Also prerequisites: biology & biochemistry

Physiology – An Integrative Science

• Few unanswered questions remain about how the human body works at the **systems level** – most involve nervous control.

•Bulk of research is at cellular and **molecular level.**

•Must look at links between cells, tissues, and organs to fully understand functions.. – integration

Function Versus Process

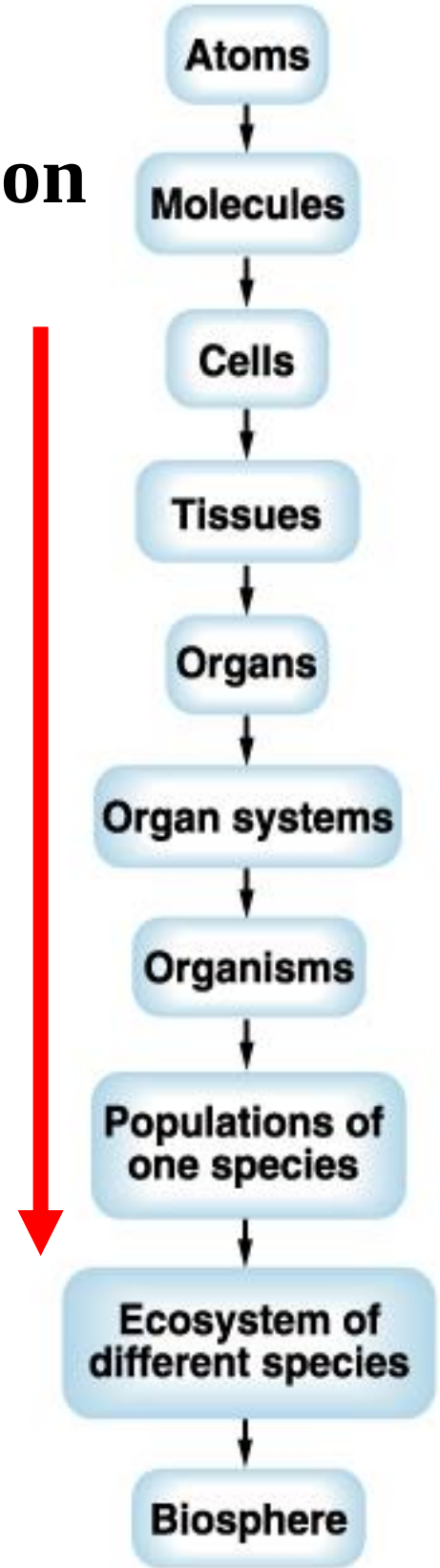
•**Teleological** approach (function) – Why does something exist or occur?

•**Mechanistic** approach (processes) – How does something occur?

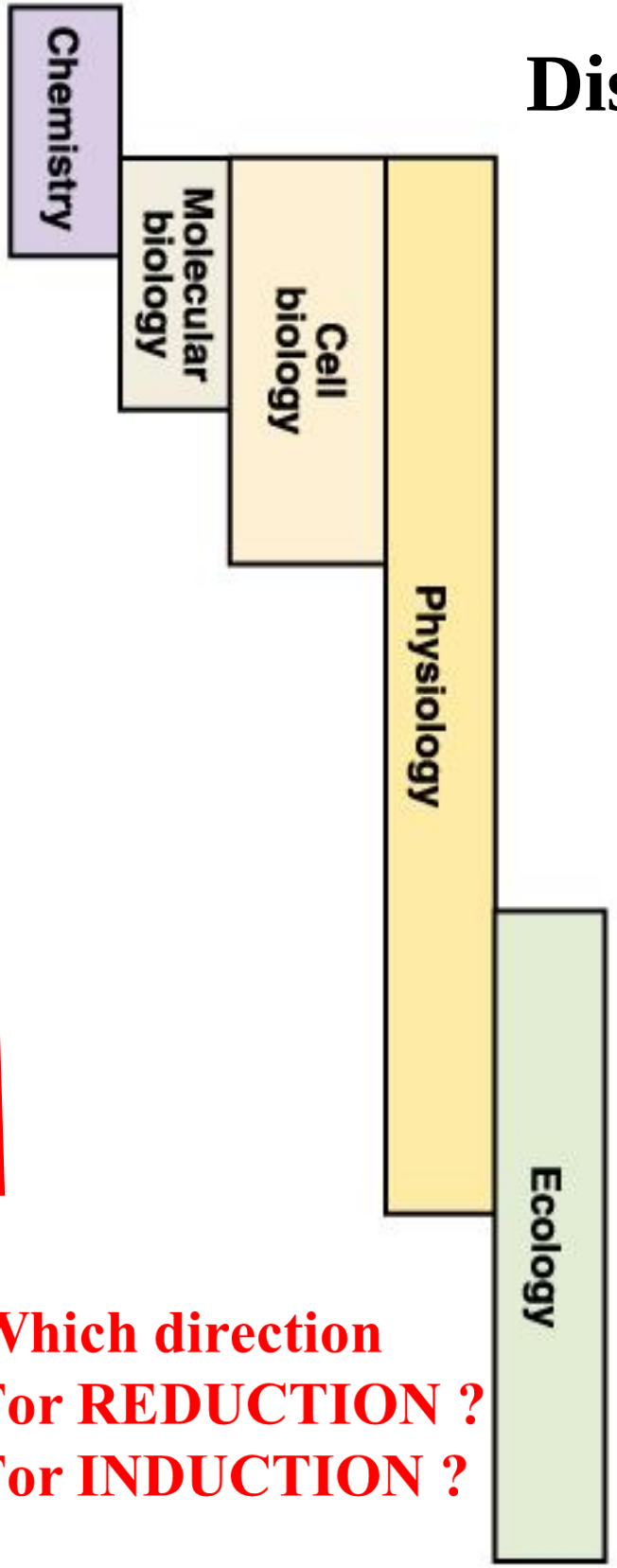
•Use the pumping of blood by the heart or why there are differences in skin color between Caucasians and Africans.to show the difference between a teleological approach to physiology and a mechanistic approach.

The **mechanist view** of life, the view taken by physiologists, holds that all phenomena, no matter how complex, can ultimately be described in terms of physical and chemical laws.
In contrast, **vitalism** is the view that some "vital force" beyond physics and chemistry is required to explain life.
The **mechanist view** has predominated in the twentieth century because virtually all information gathered from observation and experiment has agreed with it.

Levels of Organization



Discipline



Which direction
For REDUCTION ?
For INDUCTION ?

4 levels of organization

1. Cells

- Cells are the **basic structural units** of all plants and animals.
- **All** organisms are composed of one or more cells.
- Cells are the **smallest functioning units** of life.
- All cells **come** from preexisting cells.
- Cells maintain homeostasis.

2. Tissues – Collections of cells that carry out related functions.

3. Organs

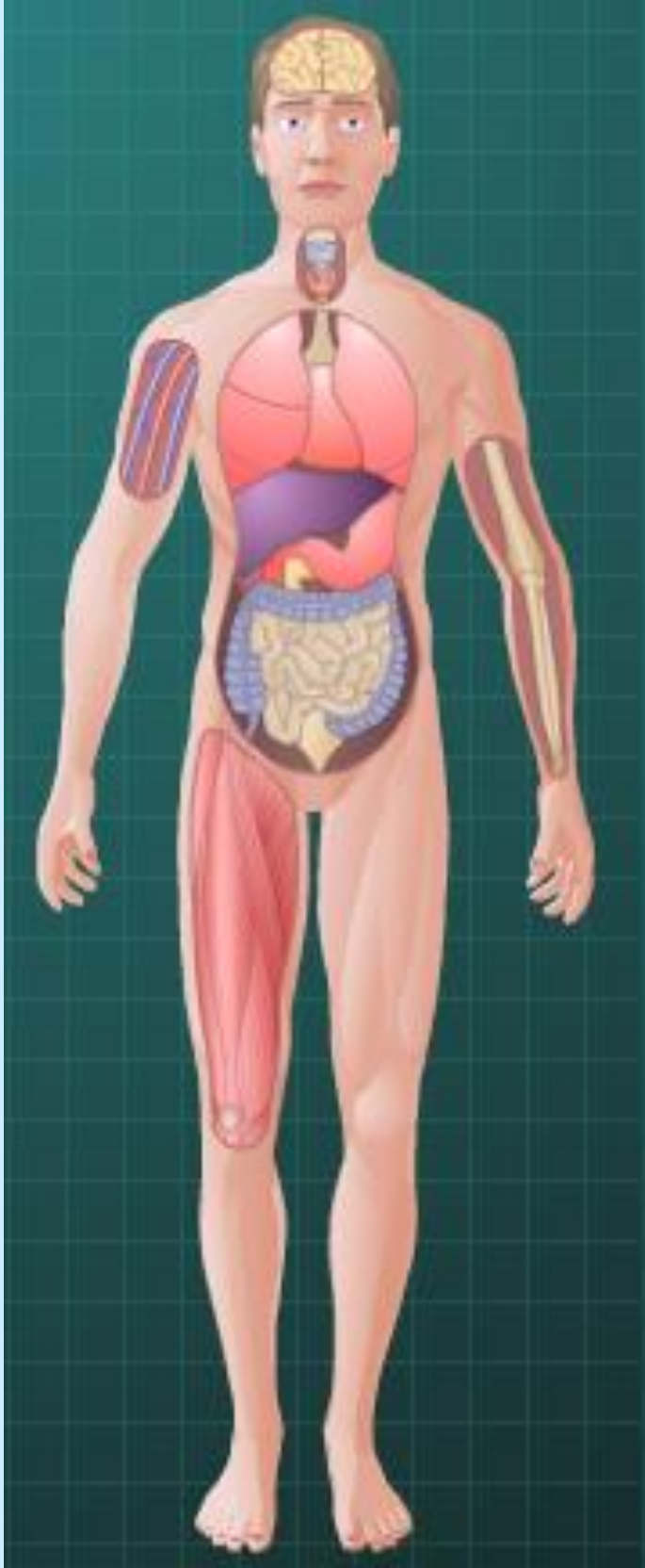
If you disassembled organs into tissues and sorted the tissues into piles based on their basic functions, there would only be 4 categories:

- Epithelium
- Connective Tissue
- Muscle Tissue
- Neural (Nervous) Tissue

•4. Systems

Service Functions

- Cardiovascular system
- Respiratory system
- Digestive system
- Renal system
- Reproductive system
- Musculo-skeletal system
- Nervous system
- Endocrine system
- Immune system



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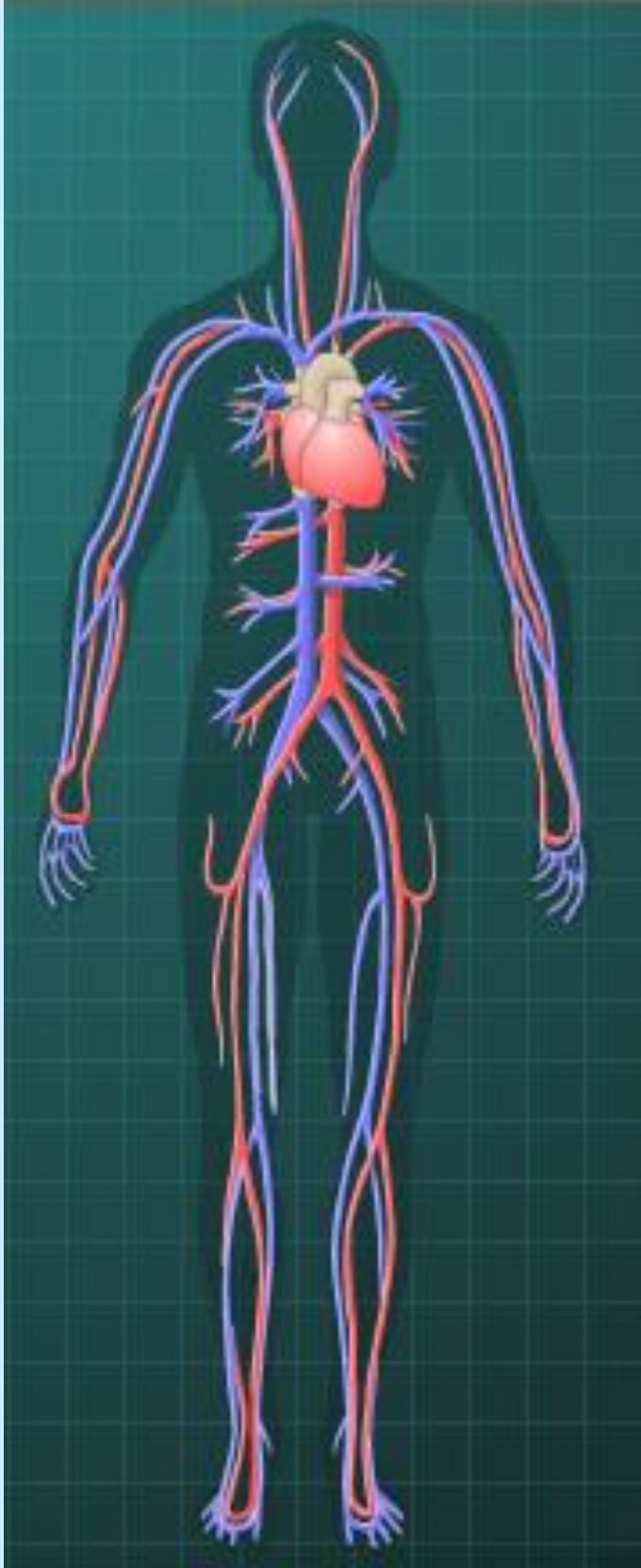

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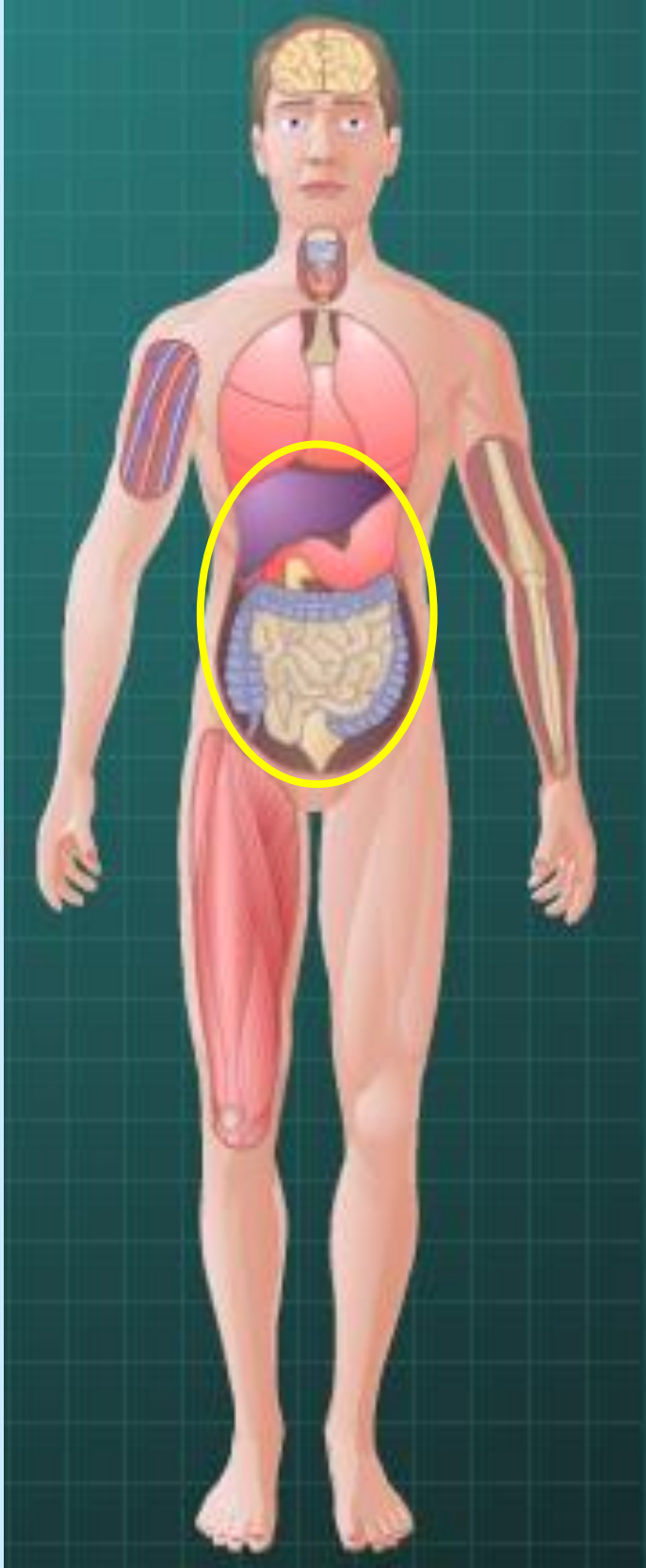

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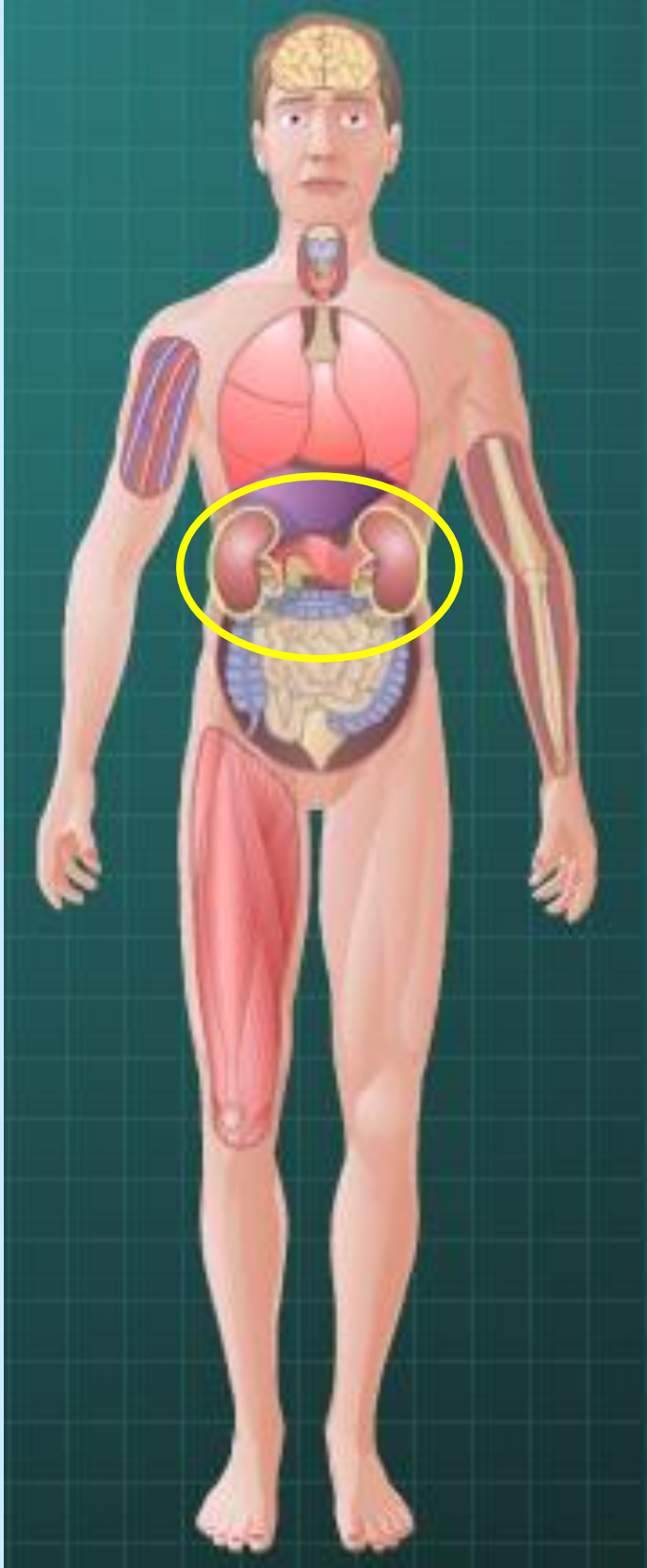

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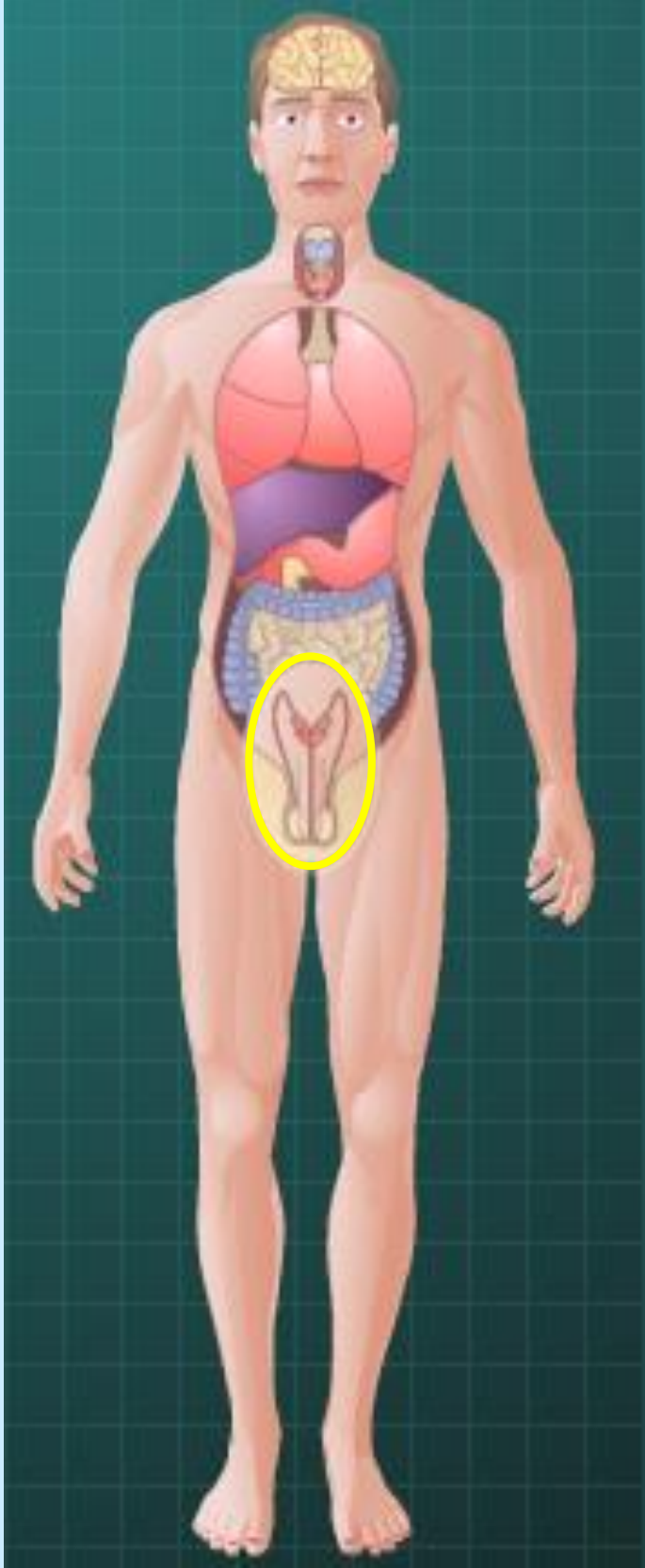

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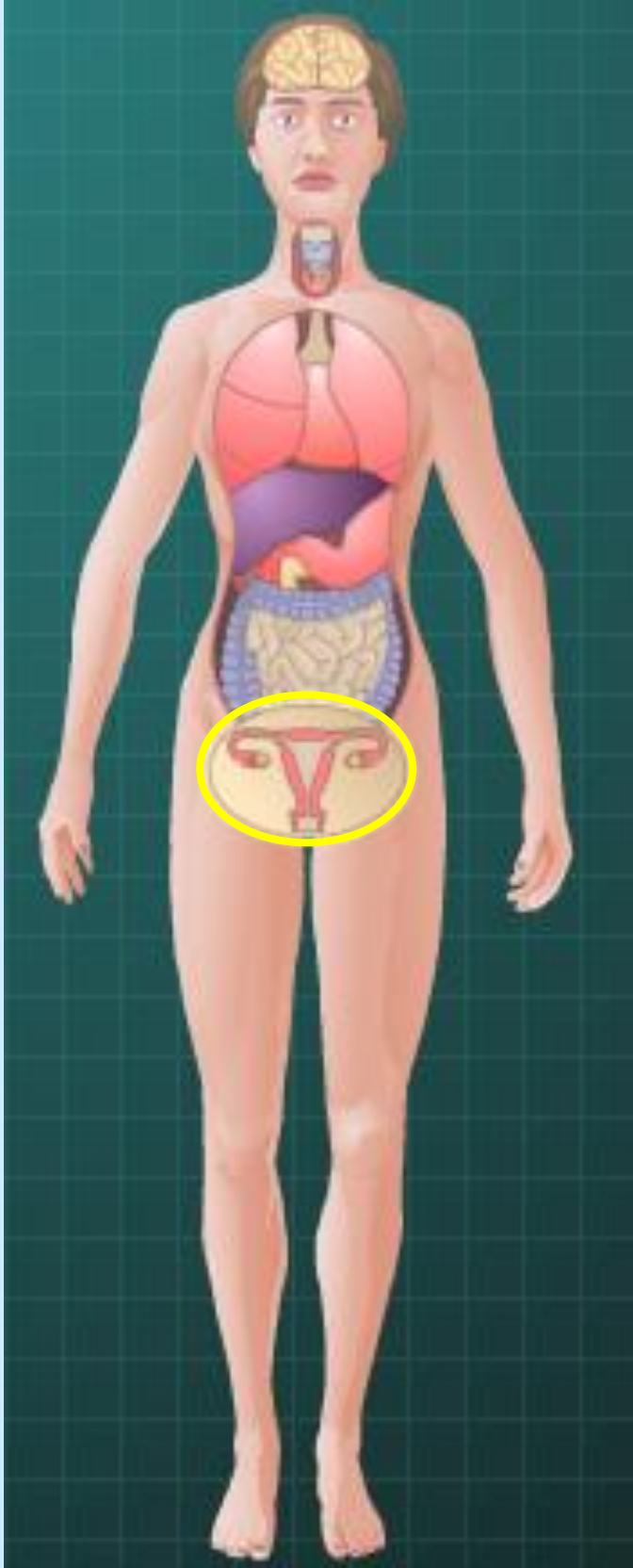

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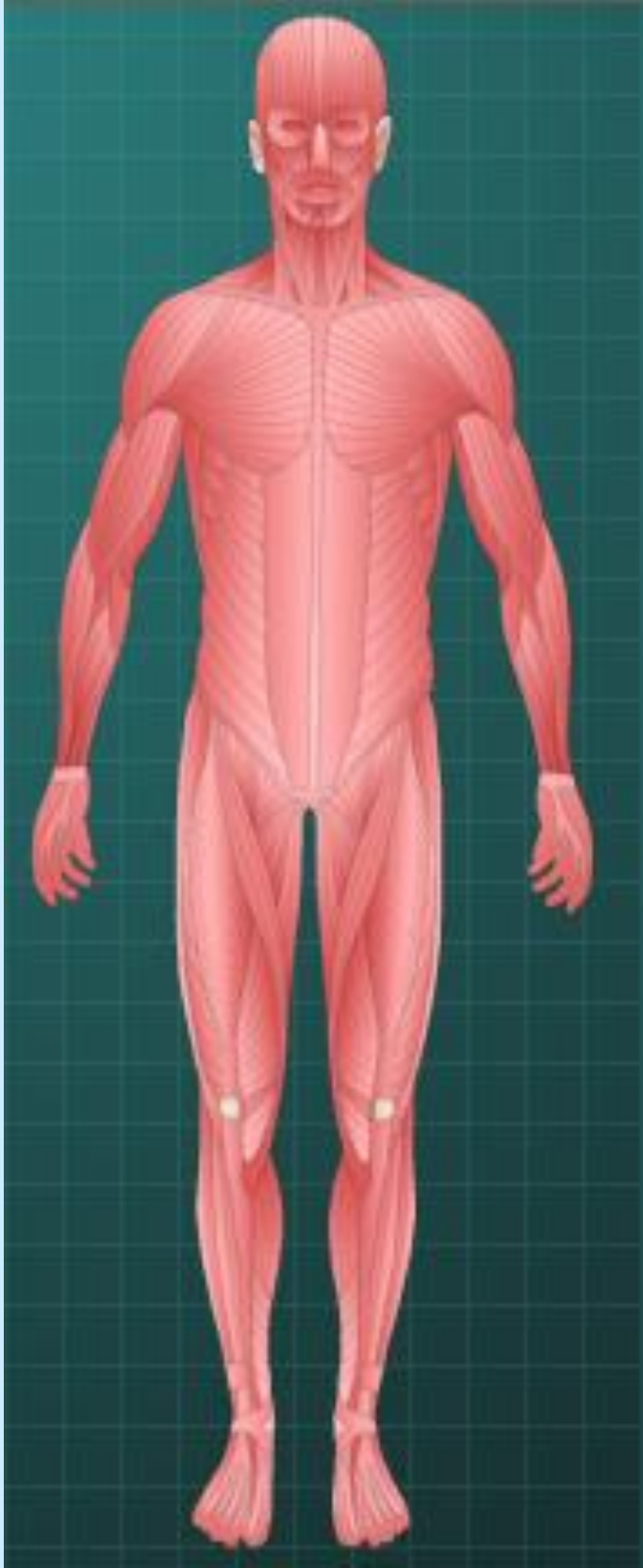

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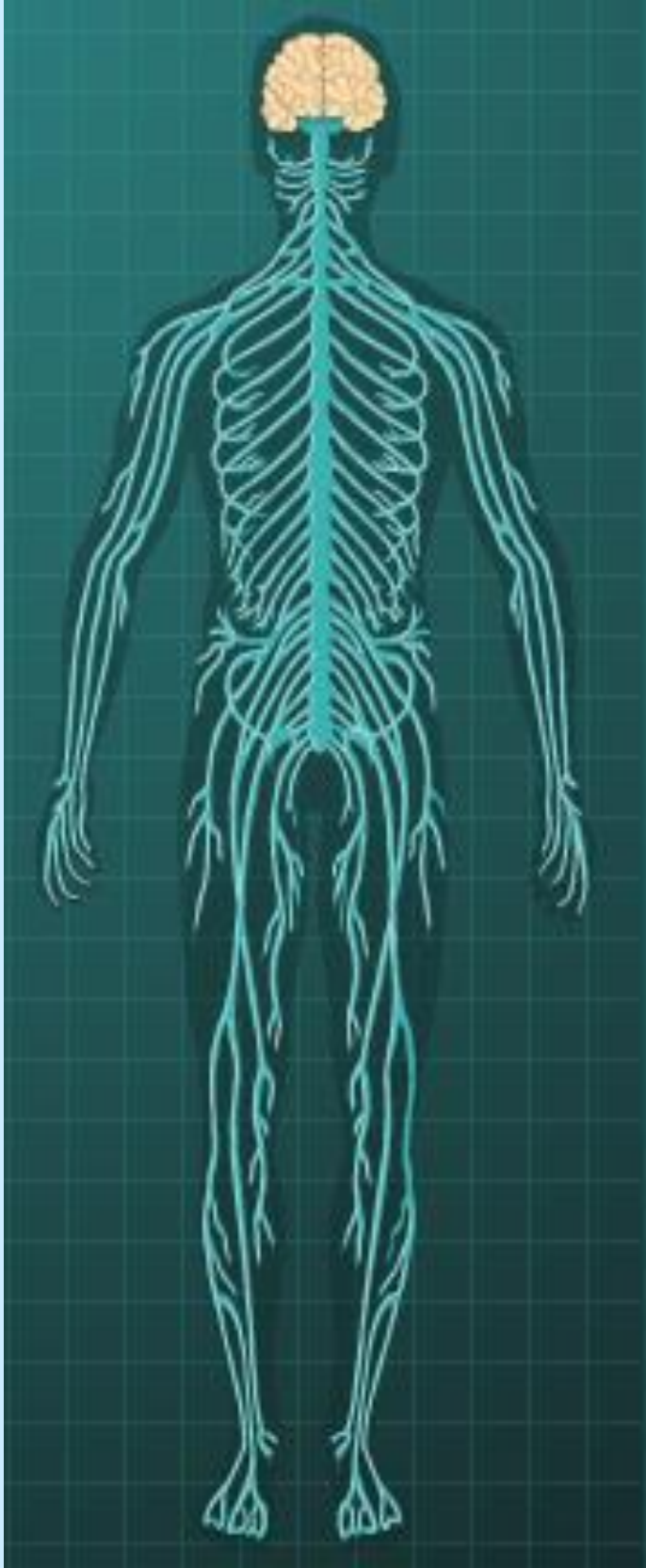

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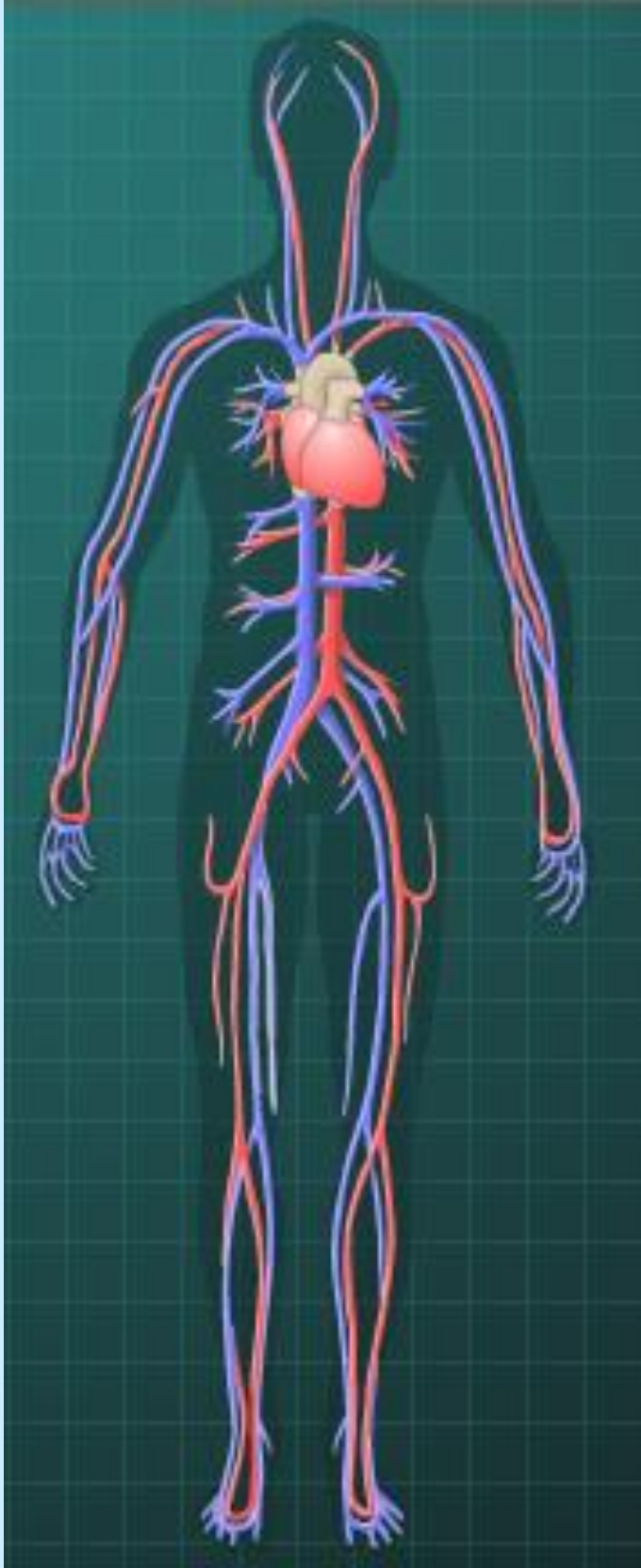

Service Functions

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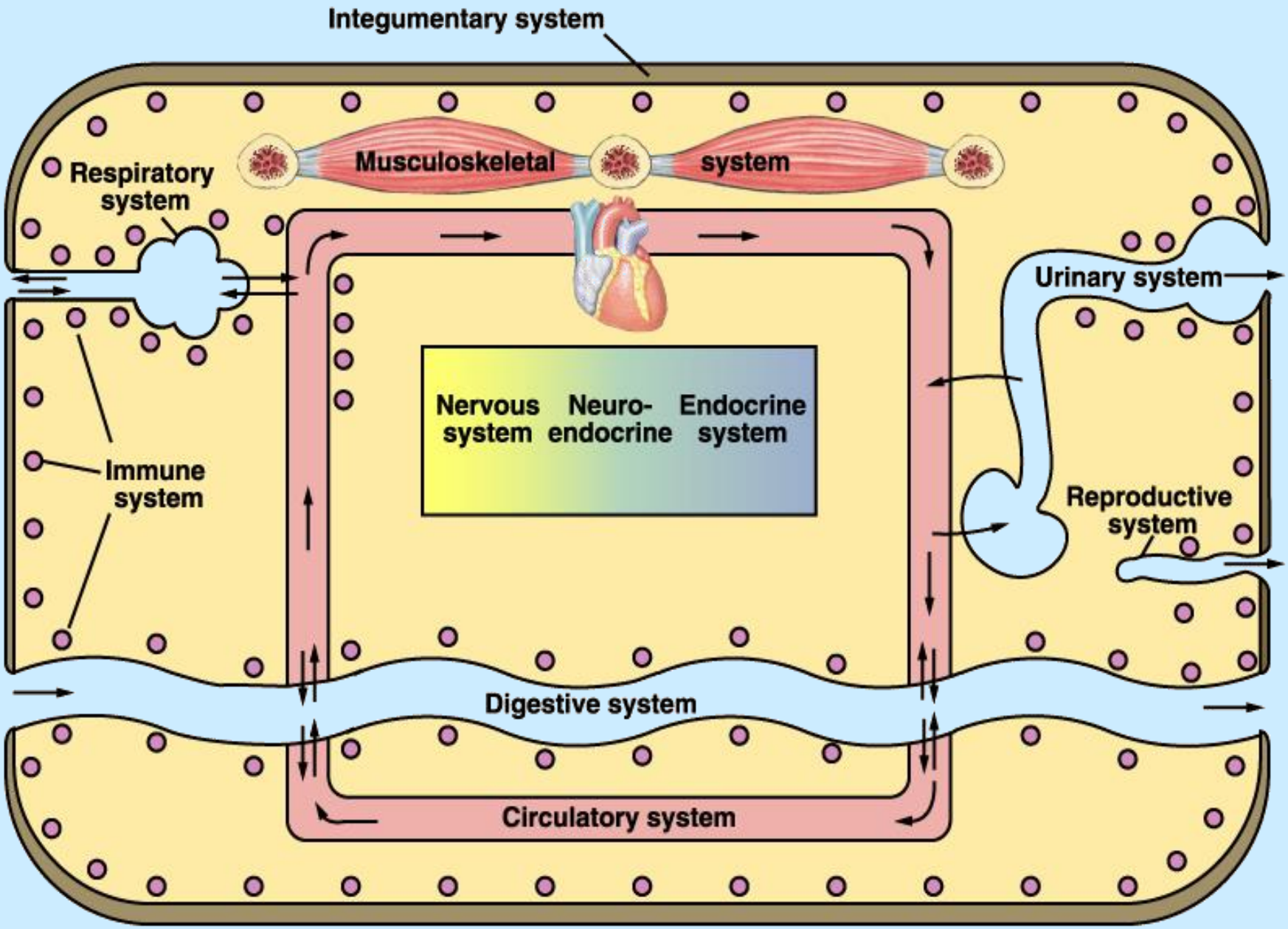
- Endocrine system
- **Immune system**

Any system missing?

Functions of Organ Systems

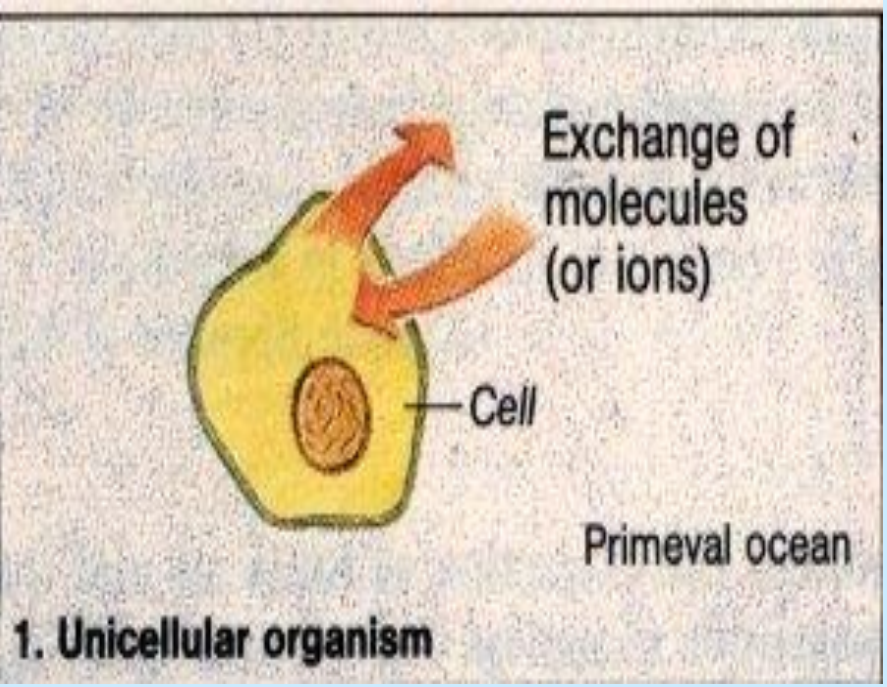
Integumentary - protection and temperature control.
Skeletal - support, protection, mineral storage, blood formation.
Muscular - locomotion, support, heat production.
Nervous - responding to stimuli and coordinating the activities of other organ systems, cognition, planning, consciousness, socializing
Endocrine - directing long-term changes in the activities of other organ systems.
Cardiovascular - internal transportation.
Lymphatic - defense against infection & disease.
Respiratory - delivery air to where gas exchange occurs.
Digestive - processing of food and absorption of nutrients, minerals, vitamins, and water.
Urinary - elimination of excess water, salts, and waste products.
Reproductive - production of sex cells & hormones.

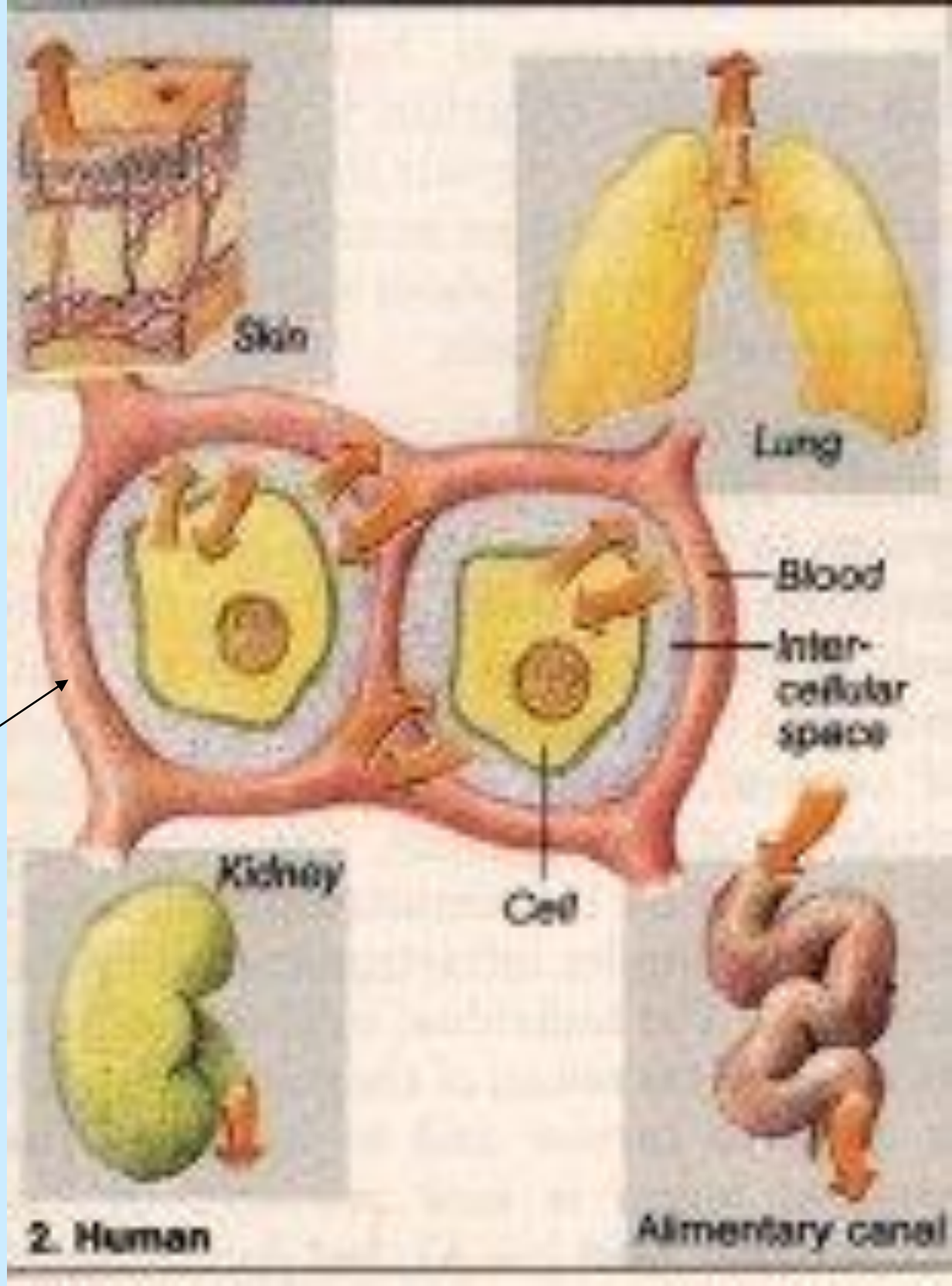
If an alient animal fell on earth… what would it look like?



..a hint of integration?

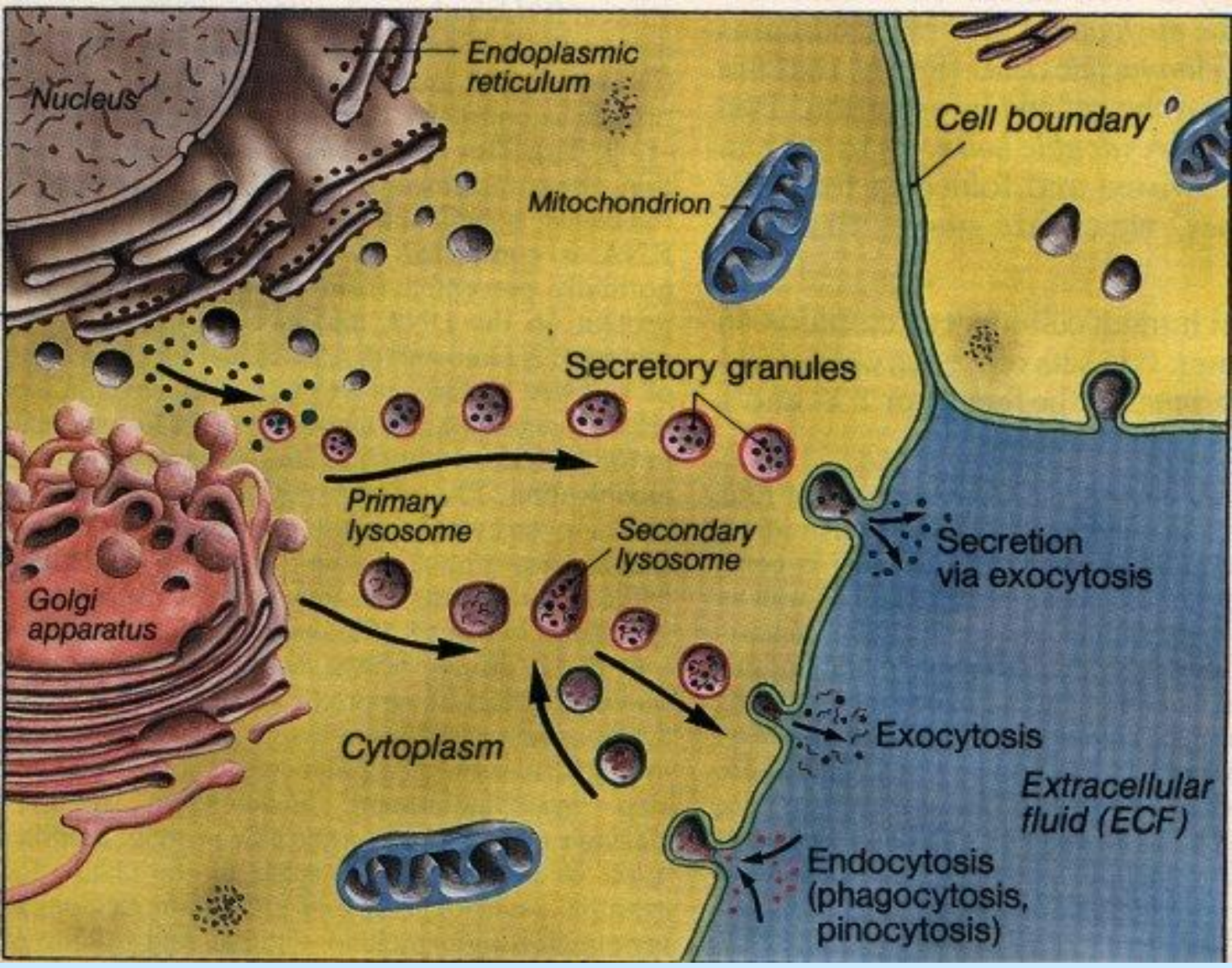
Organisms are made up of systems, which are made up of organs

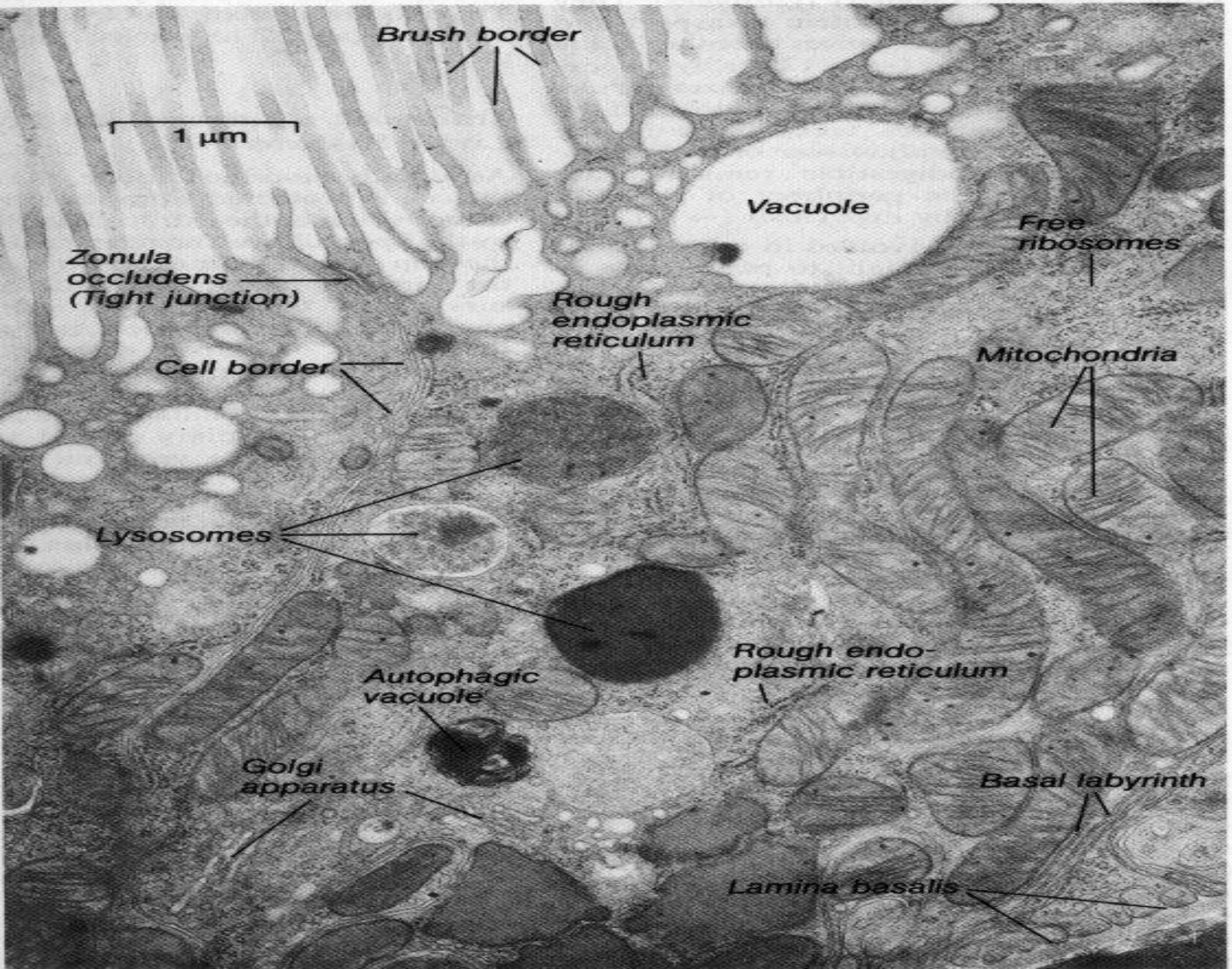


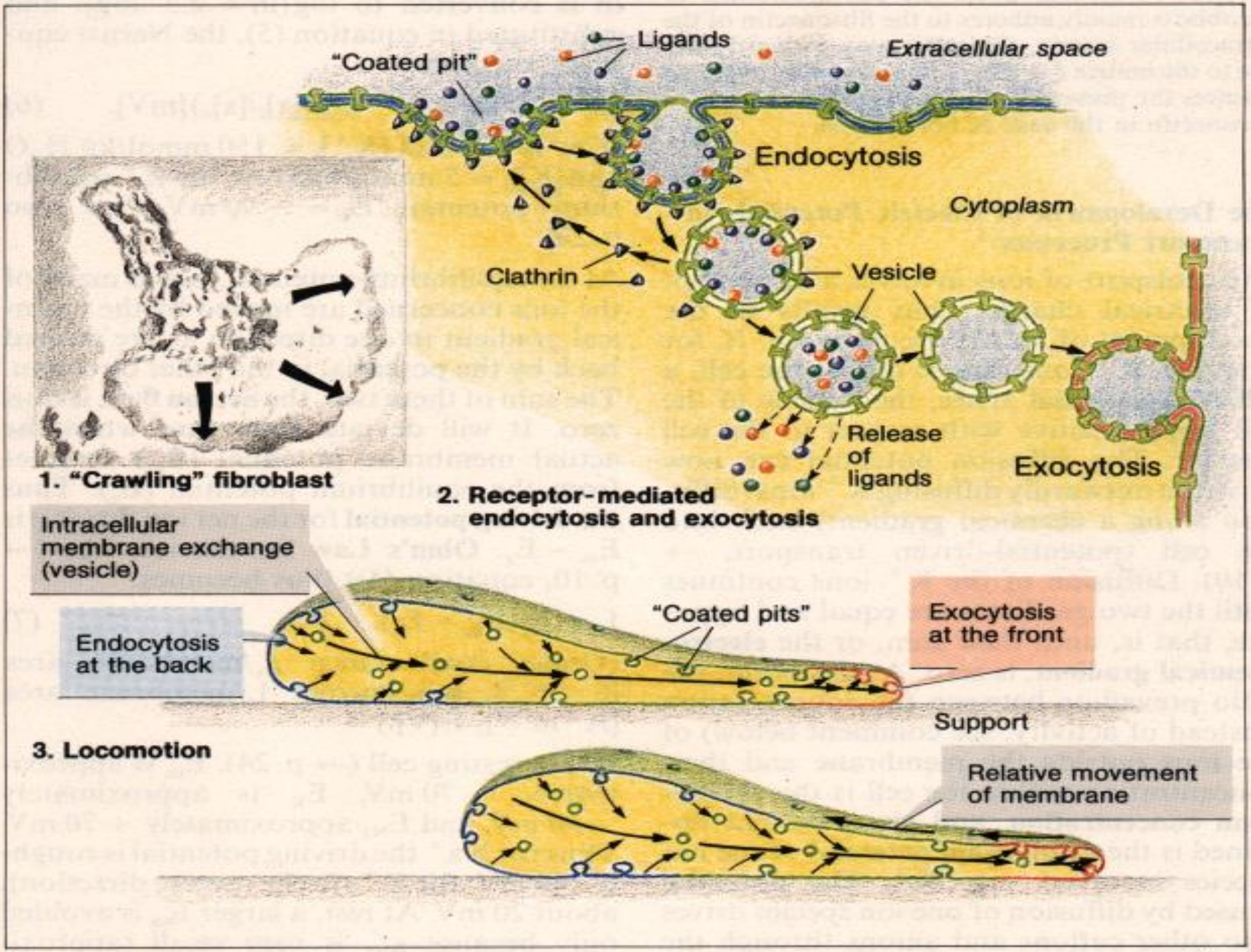


Cardiovascular

External to Internal environment


Endoplasmic reticulum
Nucleus
Cell boundary
Mitochondrion
Secretory granules
Primary lysosome
Secondary lysosome
Secretion via exocytosis
Golgi apparatus
Exocytosis
Cytoplasm
Extracellular fluid (ECF)
Endocytosis (phagocytosis, pinocytosis)


Brush border
1 µm
Vacuole
Free ribosomes
Zonula occludens (Tight junction)
Rough endoplasmic reticulum
Cell border
Mitochondria
Lysosomes
Rough endo-plasmic reticulum
Autophagic vacuole
Golgi apparatus
Basal labyrinth
Lamina basalis



E. Endocytosis and exocytosis as a means of cell locomotion (Explanation see tex

Physiology is quantified by BIOMETRICS

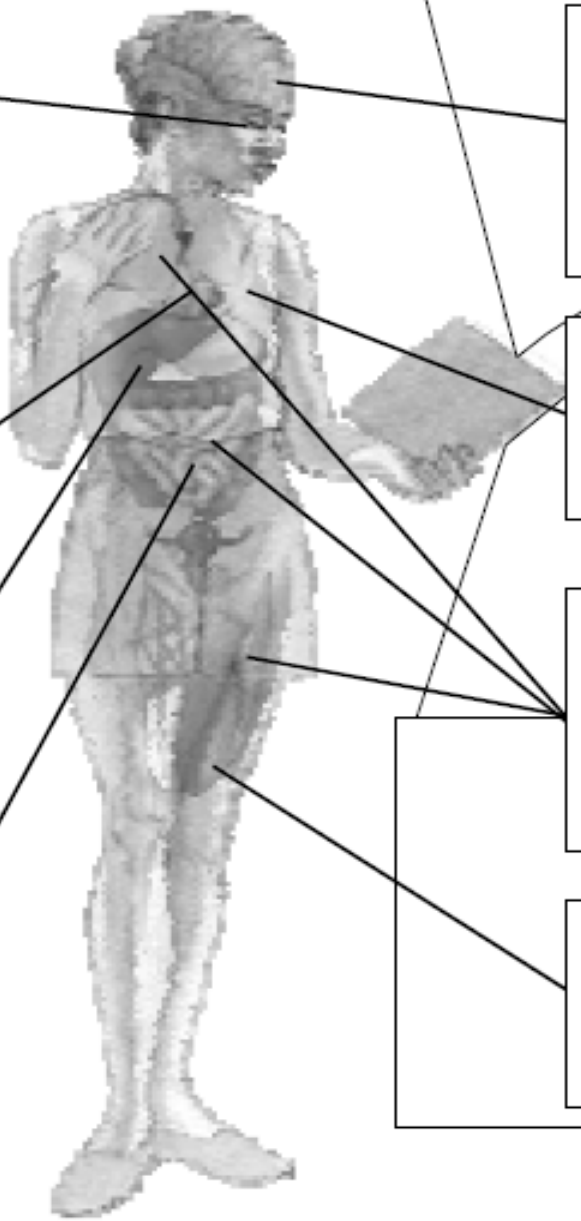
During the minute that it will take you to read this page:

Your eyes will convert the information on this page into electrical signals that will transmit to your brain.

Your heart will beat 70 times, pumping 5 liters of blood to your lungs and another 5 liters to the rest of your body.

Your kidneys will produce 1 ml of urine.

Your digestive system will be processing your last meal for transfer into your bloodstream.



Your brain will send chemical messengers through your nerves to control your body.

You will breathe in and out about 12 times.

Your cells will consume 250 ml of oxygen and produce 200 ml of carbon dioxide.

You will use about 2 calories of energy.

S. Stavrianeas, Ph.D.

Πηγή: http://www.willamette.edu/~stas/physiology/handouts/

Evolution of Physiological Systems

As life crawled from the sea on land, adaptations evolved to cope with changes in the external environment.

- Water conservation – skin, lungs, kidneys.
- Fertilization and fetal development.
- Skeletons to support body weight.
- …
- …
- Locomotion increased the need for better brains. Why?
- Raising kids rather than laying eggs led to the development of what?

… so much about Physiology in general…

…More specifically …

… Physiology tries to answer 3 principal questions:

- mechanisms maintaining **homeostasis**
- // of intercellular **communication**
- **Energy** management in a body.

Θέματα-κλειδιά στη Φυσιολογία

1. **Ομοιόσταση:** Διατήρηση των παραμέτρων του εσωτερικού περιβάλλοντος εντός στενών ορίων. Τα συστήματα στο σώμα μας συνεργάζονται ώστε να προστατεύουν την ομοιόσταση από εσωτερικές και εξωτερικές προκλήσεις
2. **Επικοινωνία:** (από το ενδοκυττάριο και διαμεμβρανικό επίπεδο μέχρι εκείνο του οργανισμού) Είναι ζωτικής σημασίας στην σύνθεση και ολοκληρωση των λειτουργιών και στην ομοιόσταση. Κύτταρα επικοινωνούν με άλλα κύτταρα, ιστούς και όργανα
3. (Διαμερισματοποίηση του σώματος και του κυττάρου και) **Ροή ενέργειας και διατήρηση της μάζας**

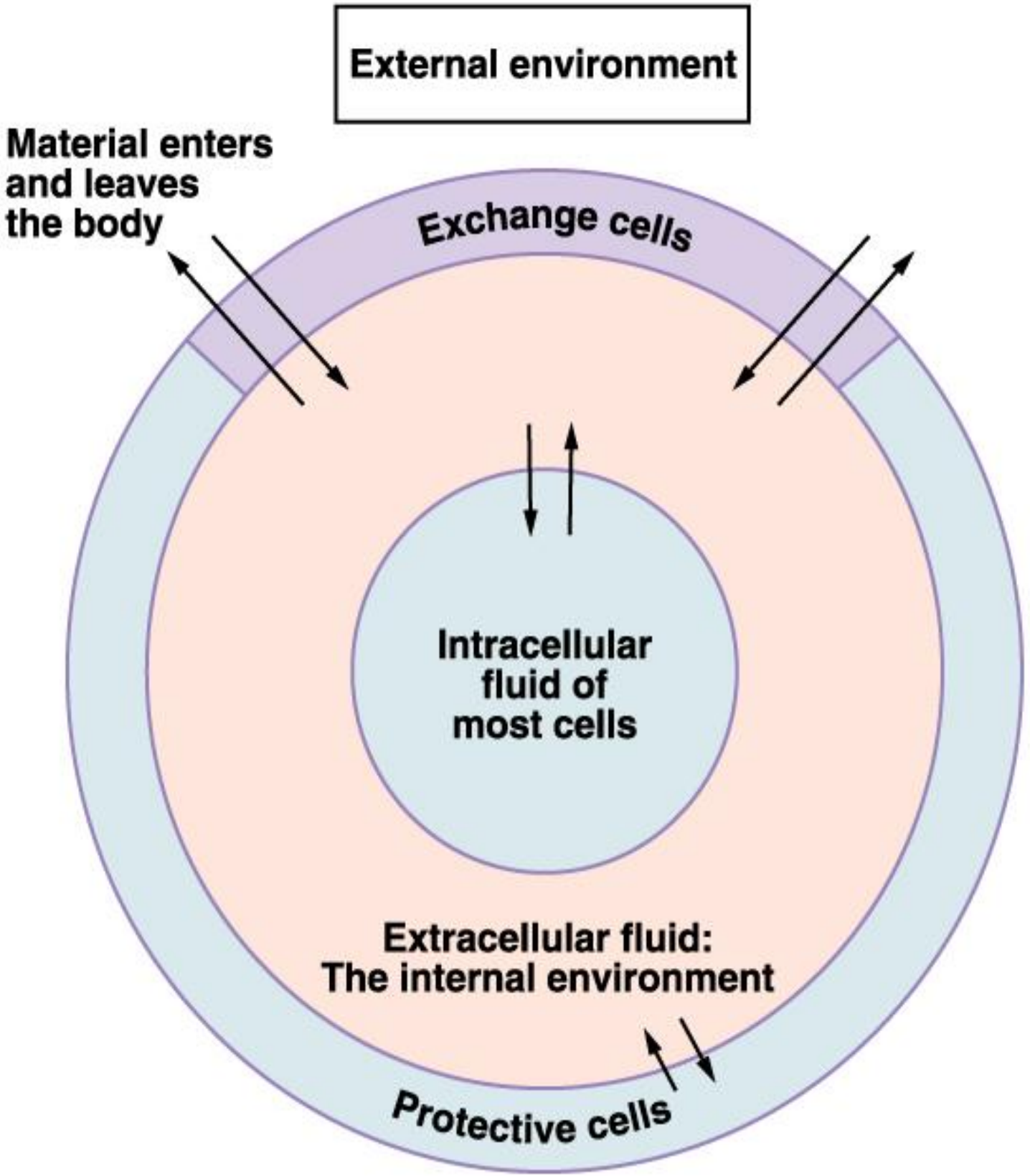
Internal Versus External Environment

Most cells in the human body are not in contact with the external environment.

Extracellular fluid (ECF) – body fluid that surrounds the cells and makes up one-third of the body's total volume.

Intracellular fluid – inside cells. Contains bulk of body's water.

ECF serves as interface between external environment and cells. Maintained within a narrow range of values.


External environment
Material enters and leaves the body
Exchange cells
Intracellular fluid of most cells
Extracellular fluid: The internal environment
Protective cells

Homeostasis is …

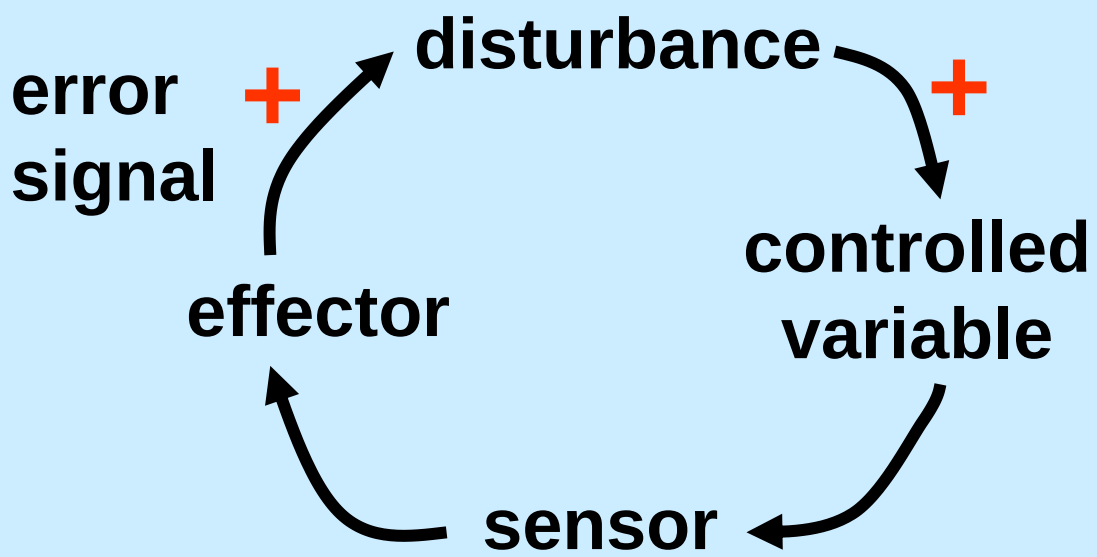
- **… the process of maintaining the composition of the internal body compartments within fairly strict limits (ion concentrations, pH, osmolarity, temperature etc)**
- **… requires regulatory mechanisms to defend against changes in external environment and changes due to activity**
- **Cellular homeostasis - … of the intracellular fluid composition**
- **Organismal homeostasis - … of the extracellular fluid composition**

- Cardiac muscle cell contraction = electrical signals ⇒ changes in intracellular and extracellular [Na^+], [K^+] and [Ca^{2+}]
- If extracellular [K^+] too high ⇒ depolarisation ⇒ contraction ⇒ fibrillation (bag of worms, ταχυαρυθμία) => risk of death

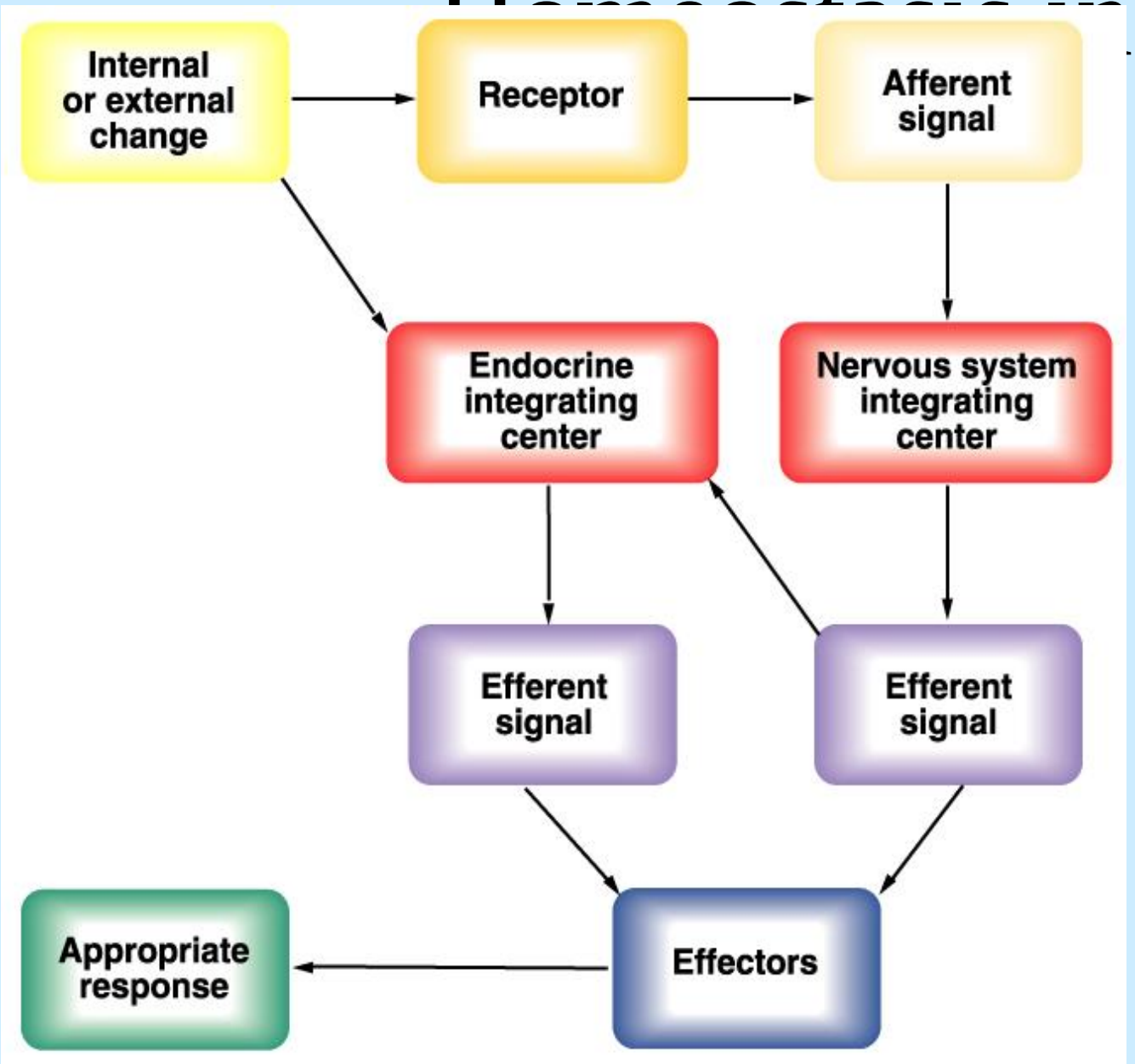
CONCLUSION: Extracellular [K^+] must be kept within narrow range

Positive feedback

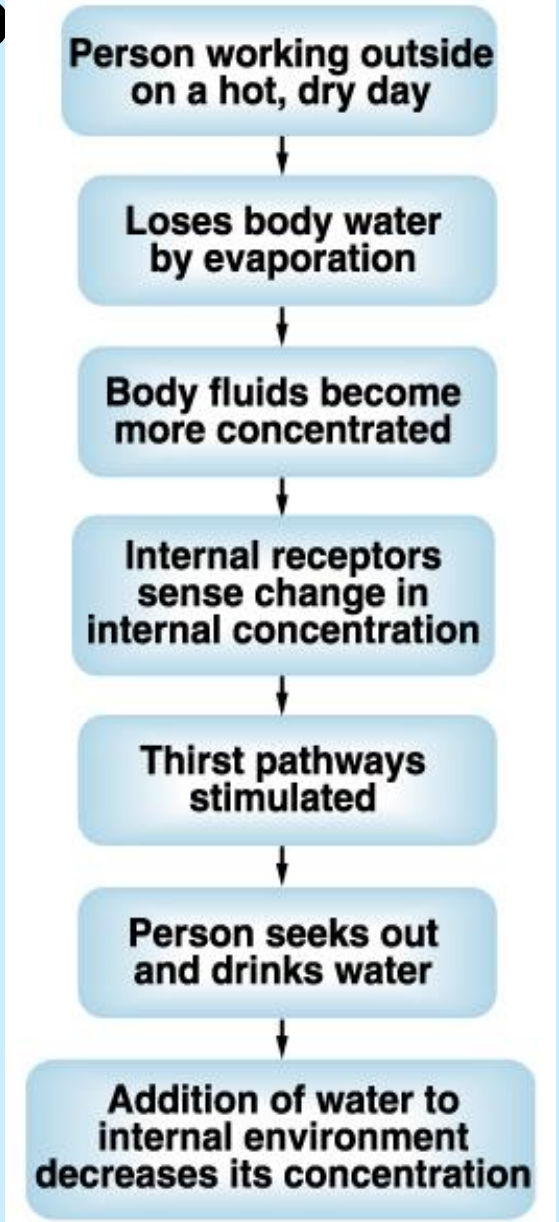
- **Negative feedback - error signal ⇒ *reduce* deviation from reference point**
- **Positive feedback - error signal ⇒ *increase* deviation from reference point (vicious circle)**



Homeostasis in Summary



Theory



Practice

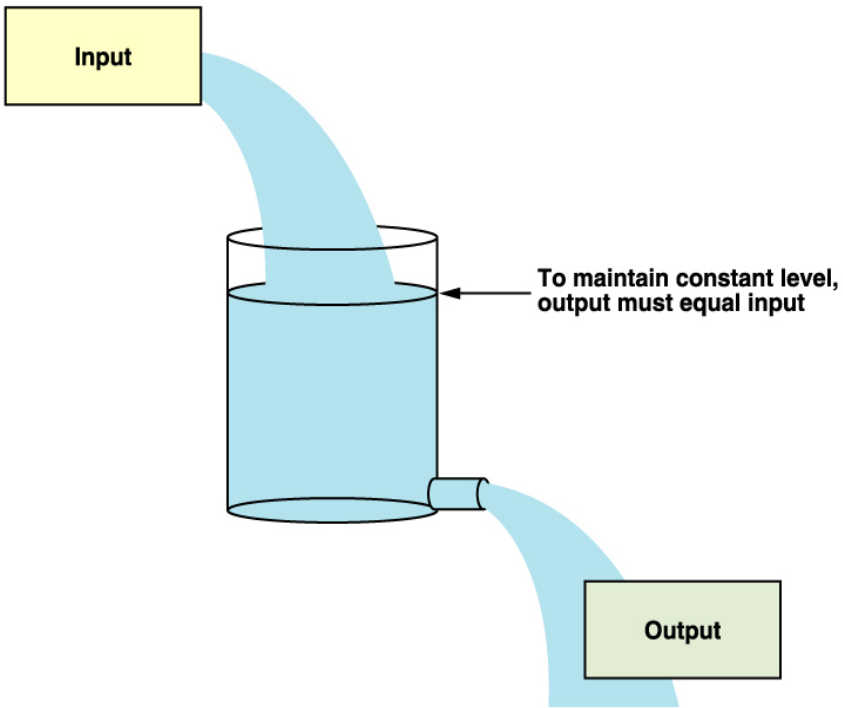
Homeostasis

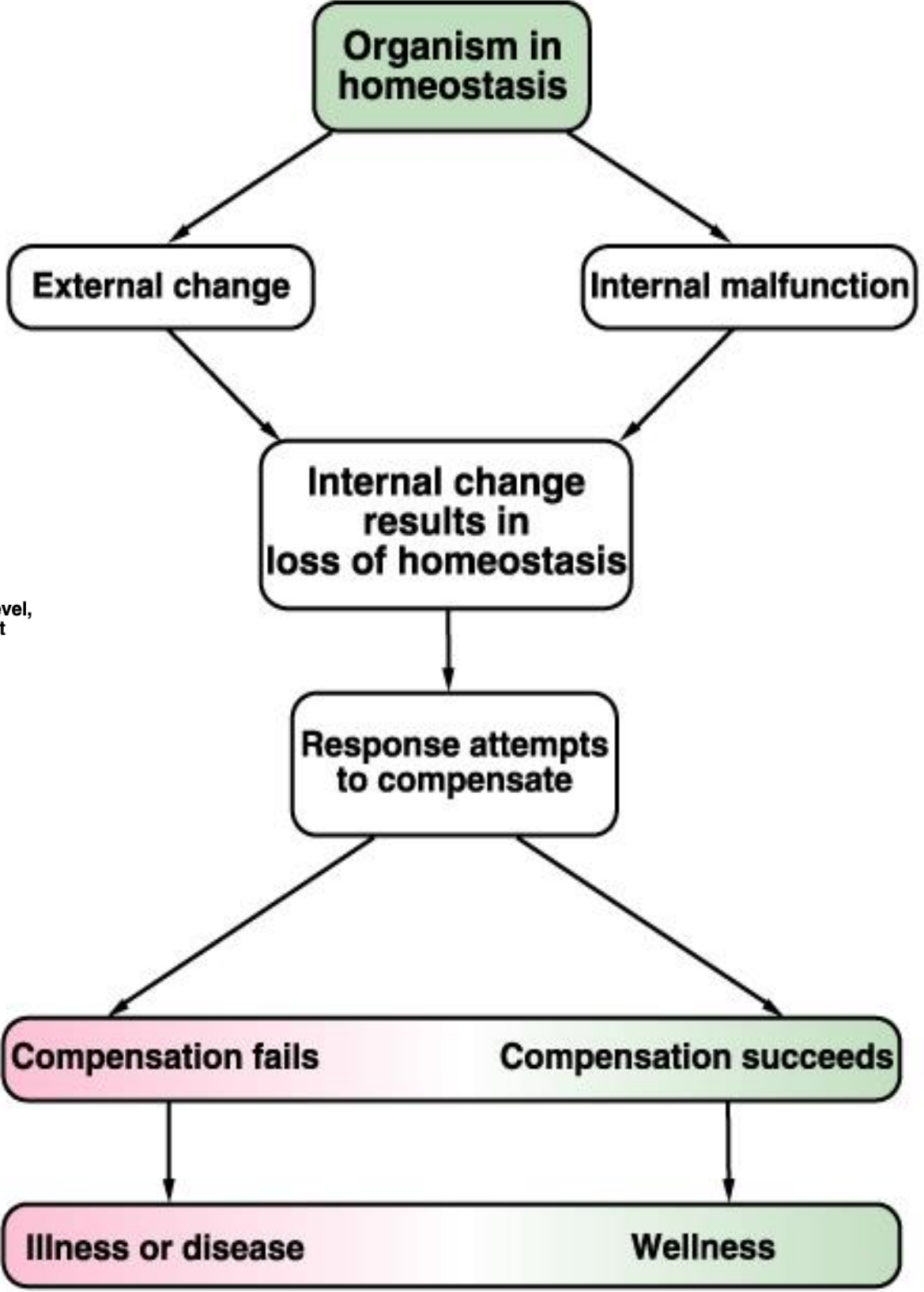
The maintenance of a relatively constant internal environment.

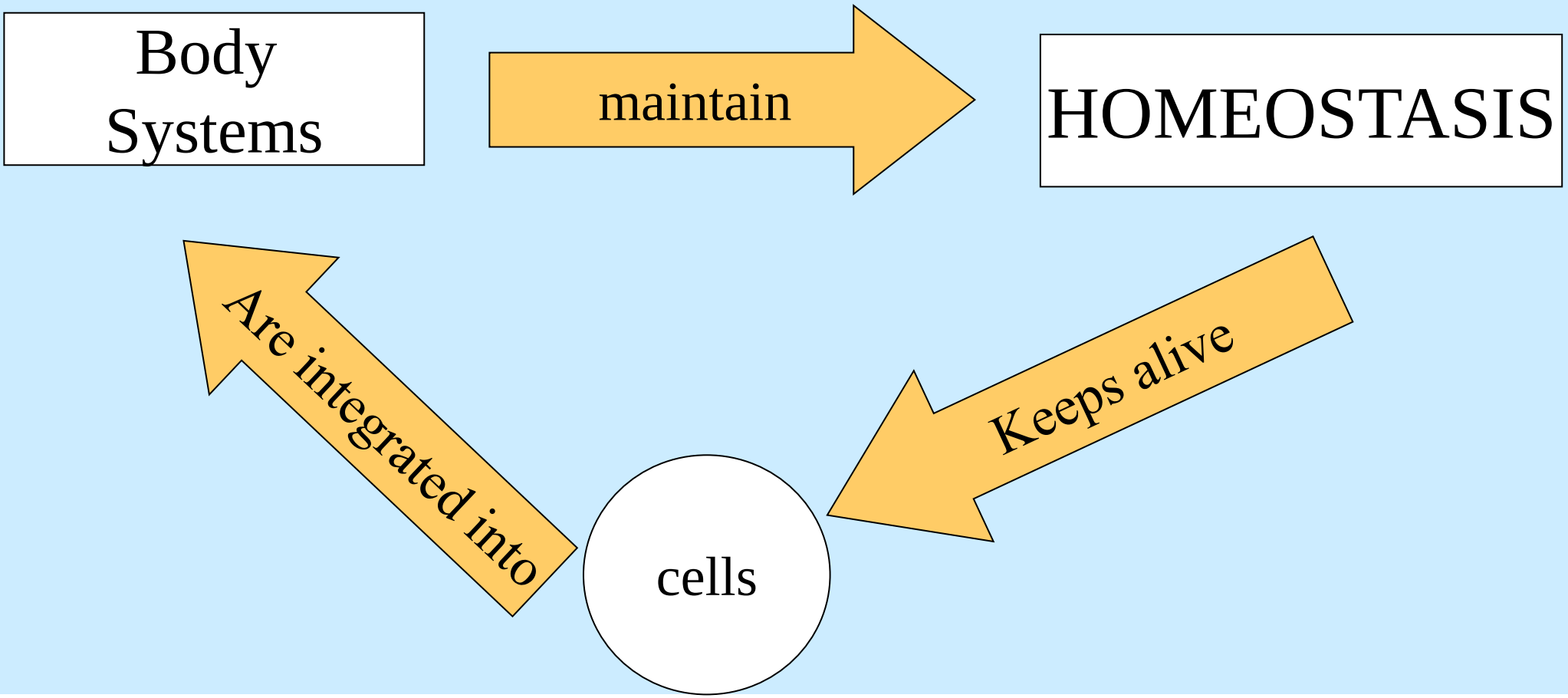
όμοιος (same) + στάσις (a standing).

absence of homeostasis = disease!

Word created in 1929 by Walter B. Cannon.


Input
To maintain constant level,
output must equal input
Output

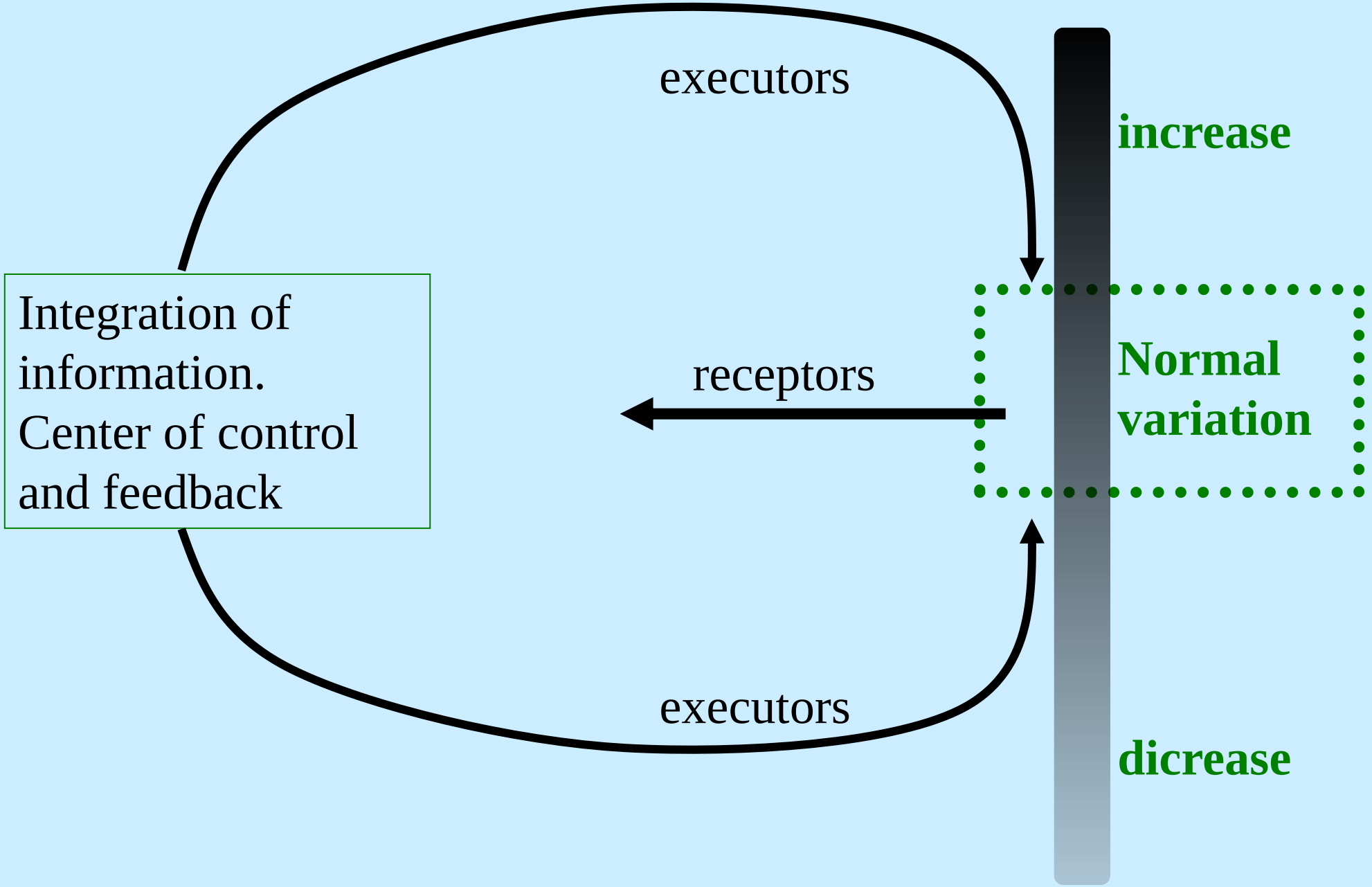

Organism in homeostasis
External change
Internal malfunction
Internal change results in loss of homeostasis
Response attempts to compensate
Compensation fails
Compensation succeeds
Illness or disease
Wellness



Cellular homeostasis ←→ body homesostasis

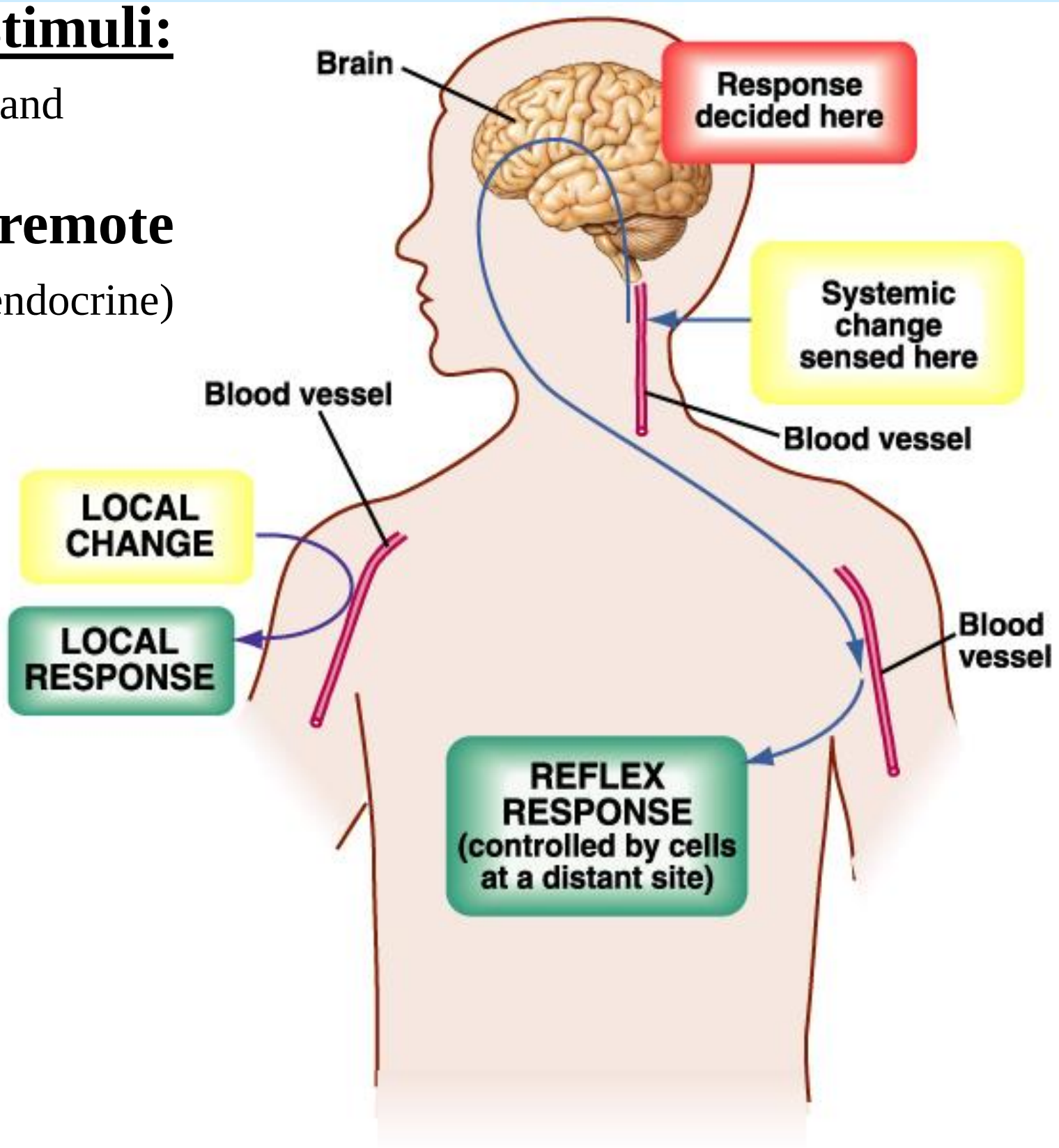
Homeostasis = maintenance of vital parameters of extracellular fluid within set limits

Components of an homeostatic system: receptors, control center, executors



Responses to stimuli:

- **local** (paracrine and autoctocrine
- **reflexive via remote centers** (neural, endocrine)



Receptors

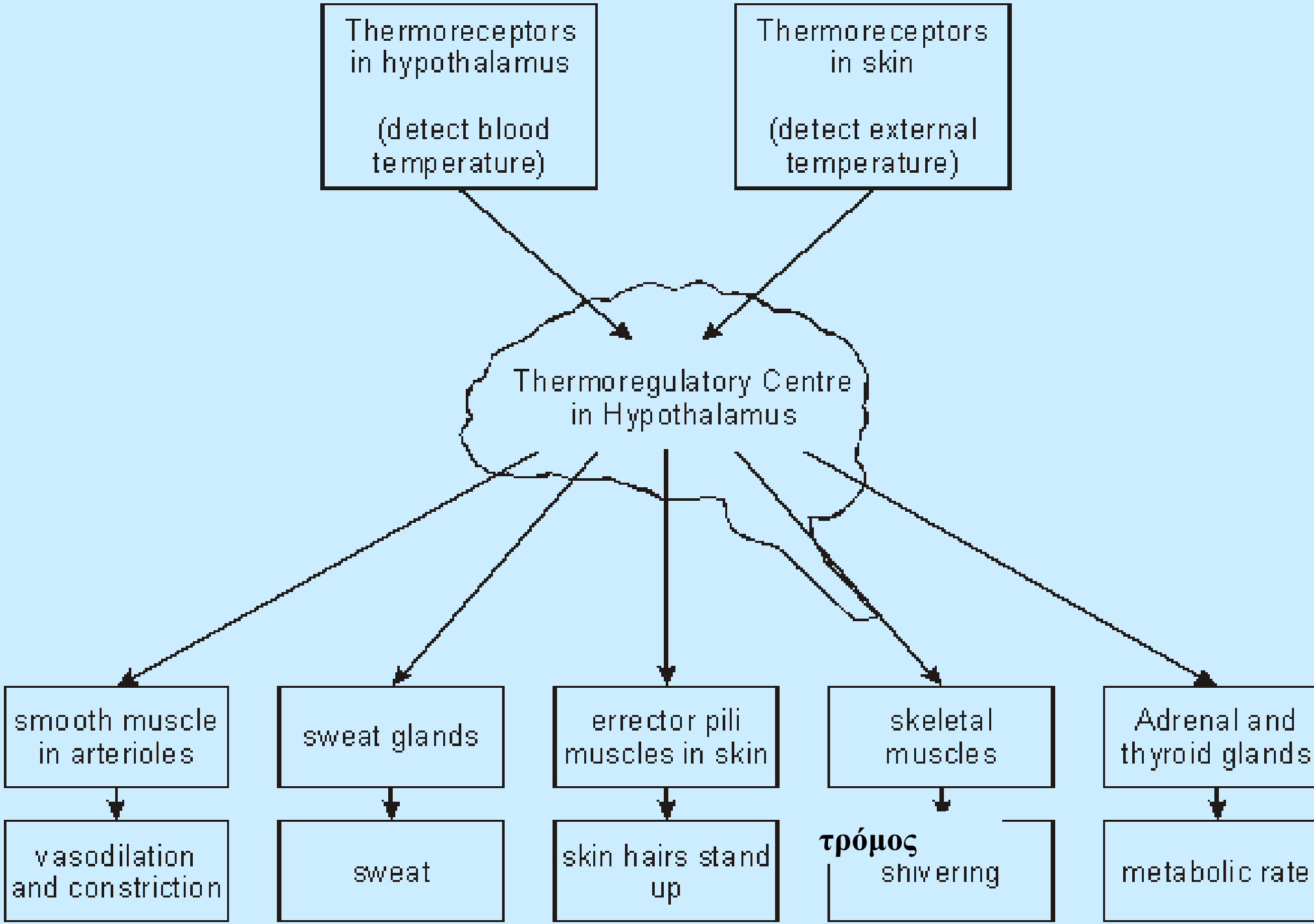
Cell membrane or cytoplasmic receptor proteins

Specialized cells or structures for the transduction of various stimuli into electrical signals

- Chemoreceptor (pH, gases, chemicals)
- Osmoreceptor (osmolarity)
- Thermoreceptor (temperature)
- Baroreceptor (pressure)
- Proprioceptor (body position)
- Other mechanoreceptors (pain, vibration, touch)

Penguins gather close to each other to face the cold.... We ?

MULTIPLE HOMEOSTATIC MECHANISMS CONTROL BODY TEMPERATURE



How is homeostasis achieved?

- **Desired concentration range for each chemical constituent of body ⇒ regulatory mechanisms**

eg

Blood [glucose] ≈ 4-5 mmol.l^{-1}

if [glucose] >> 5 mmol.l^{-1} ⇒ ↑ insulin secretion

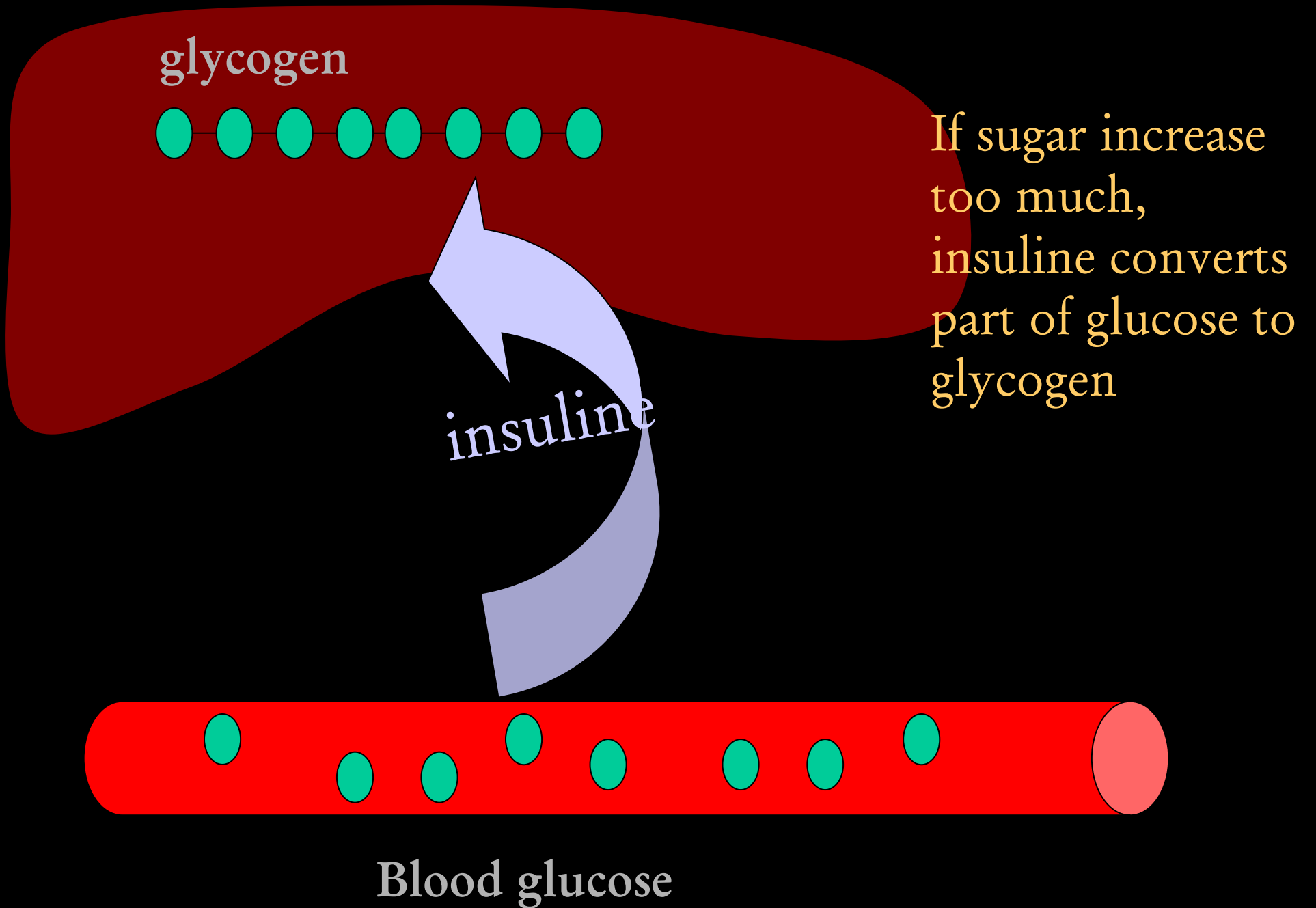
⇒ ↓ [glucose]

if [glucose] << 4 mmol.l^{-1} ⇒ ↓ insulin secretion

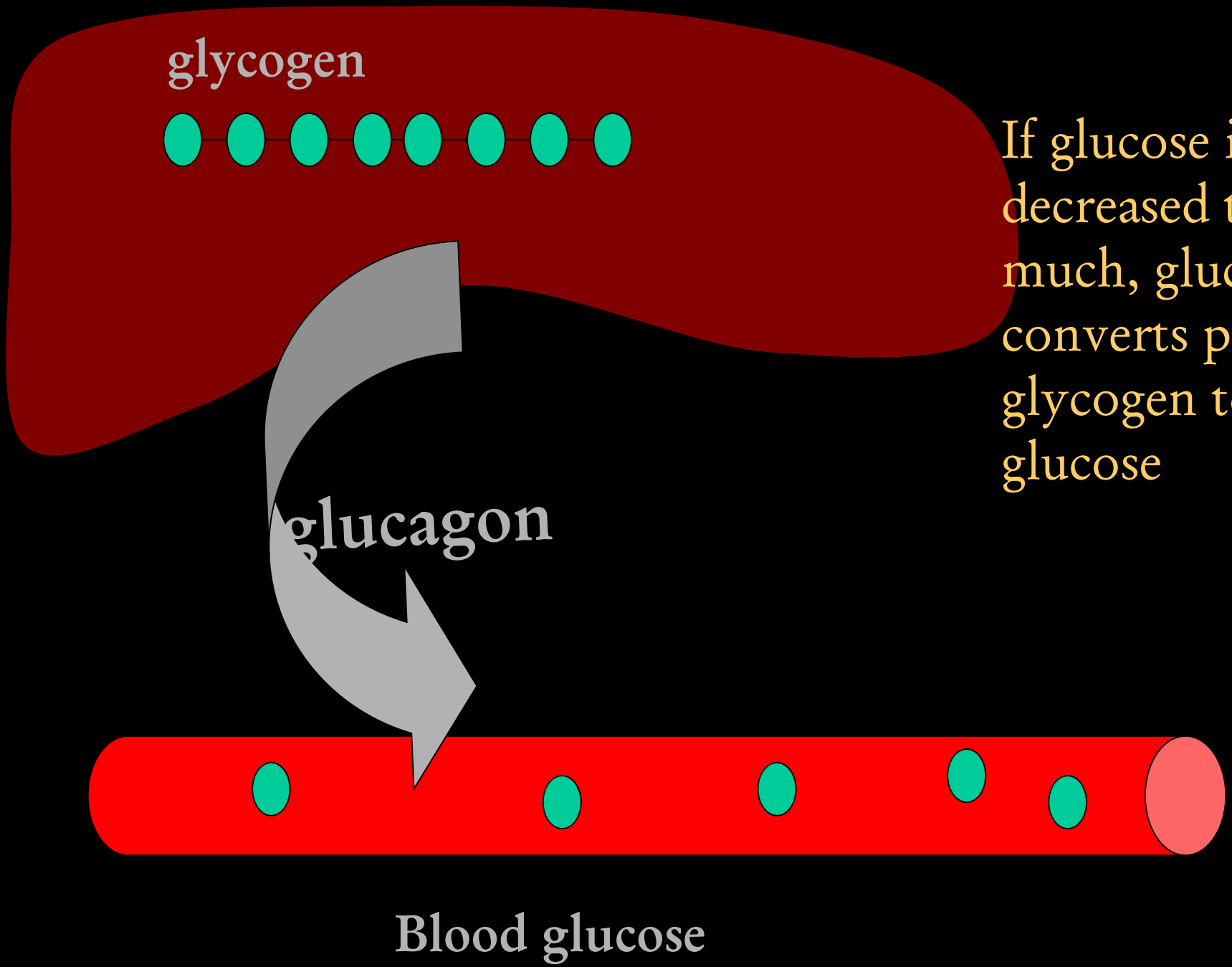
⇒ ↑ [glucose]

***ie* [insulin]$_{blood}$ changes to maintain [glucose]$_{blood}$**

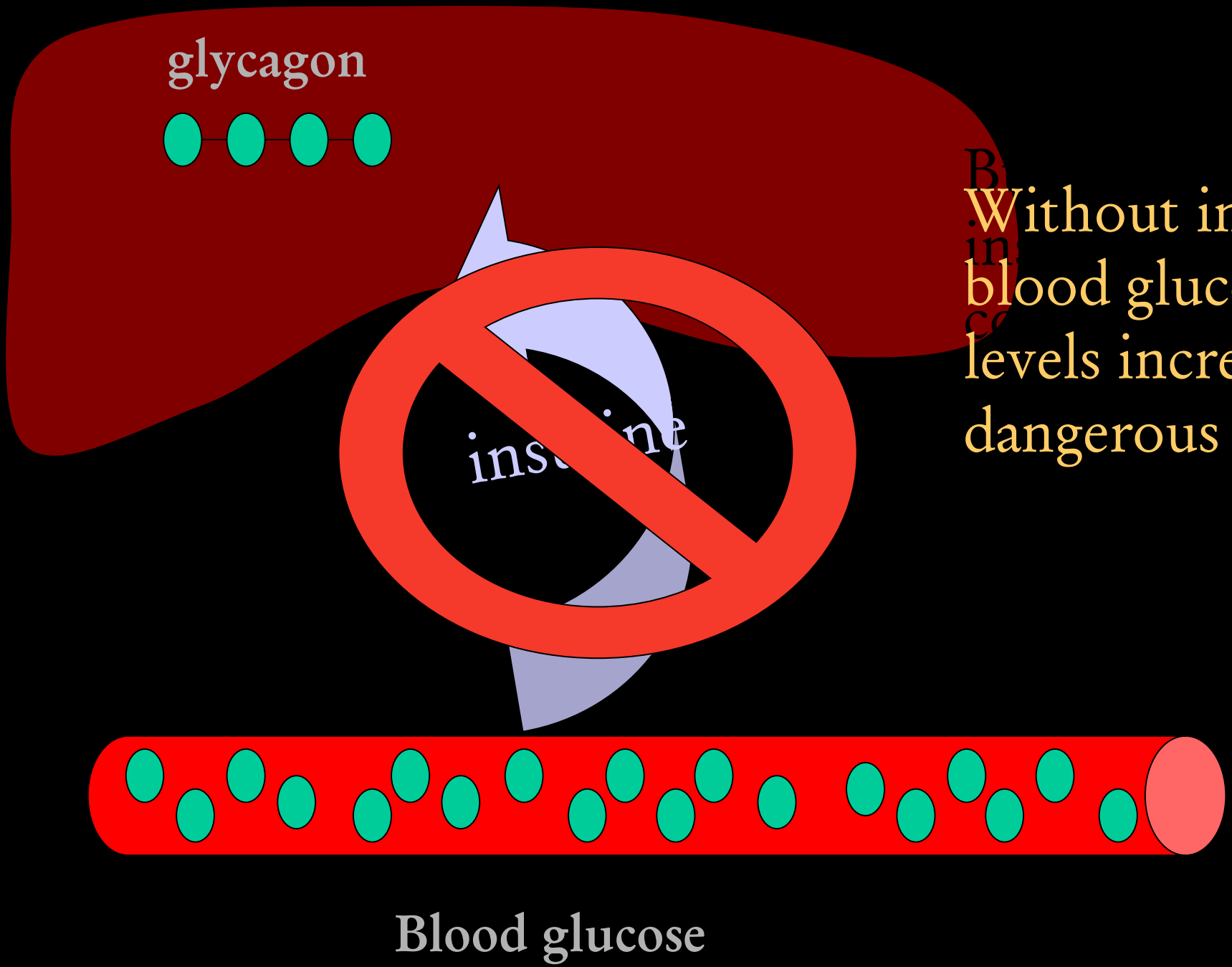
- **Regulation termed - NEGATIVE FEEDBACK**
- **Control system designed to maintain level of given variable (concentration, temperature, pressure) within defined range following disturbance**



If sugar increase too much, insuline converts part of glucose to glycogen

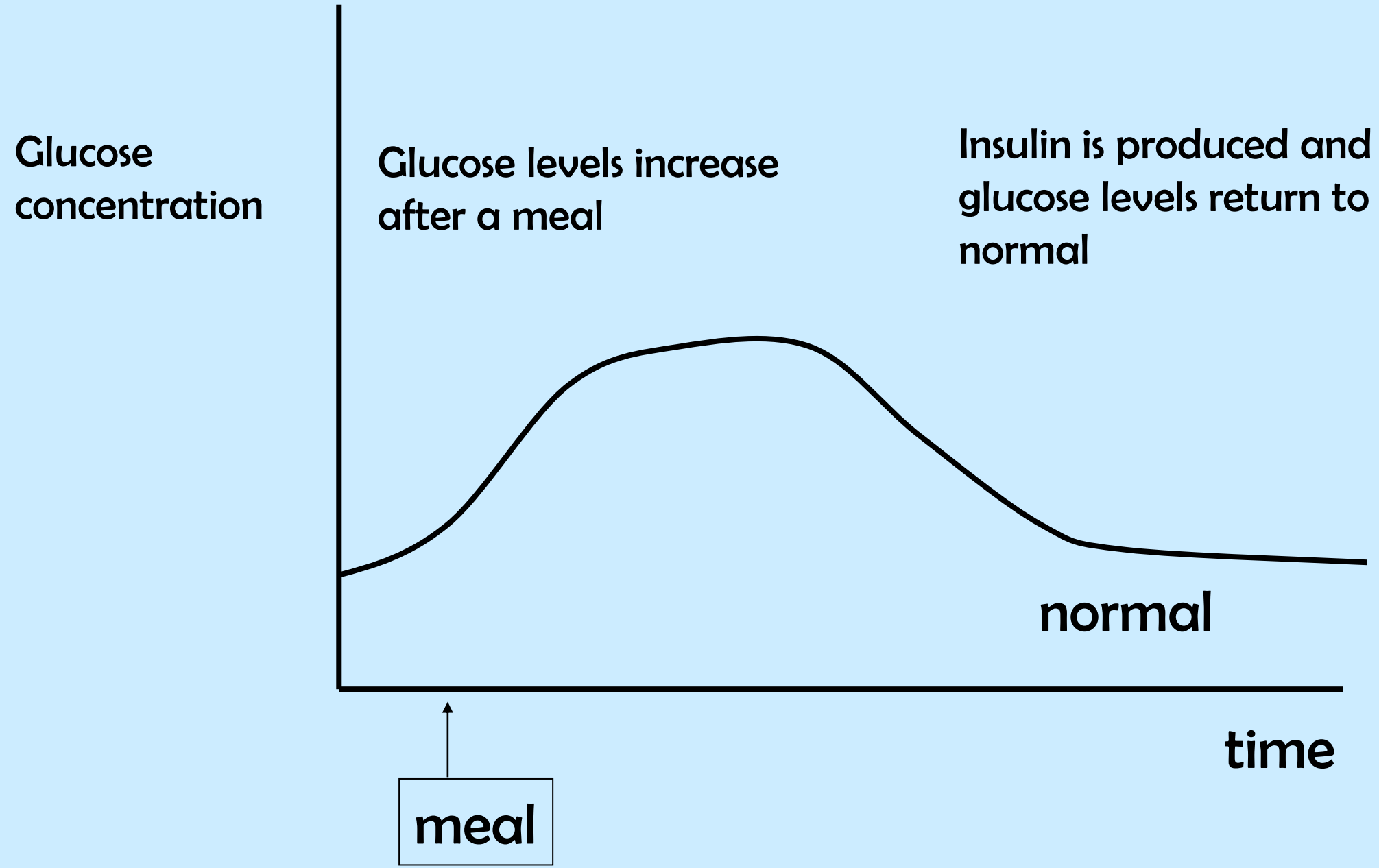


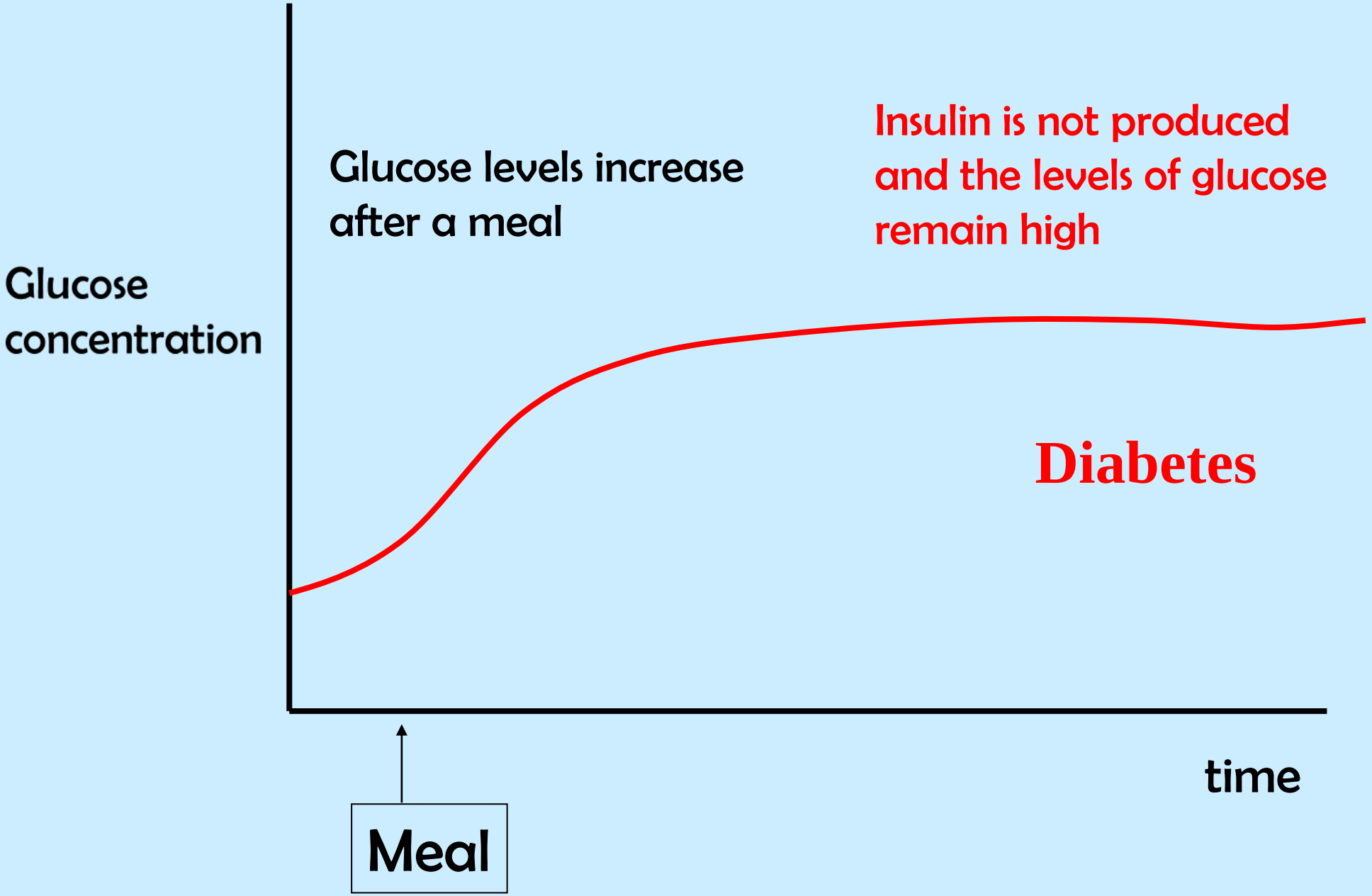
If glucose is decreased too much, glucagon converts part of glycogen to glucose


glycagon
Without insuline blood glucose levels increase in dangerous levels
Blood glucose

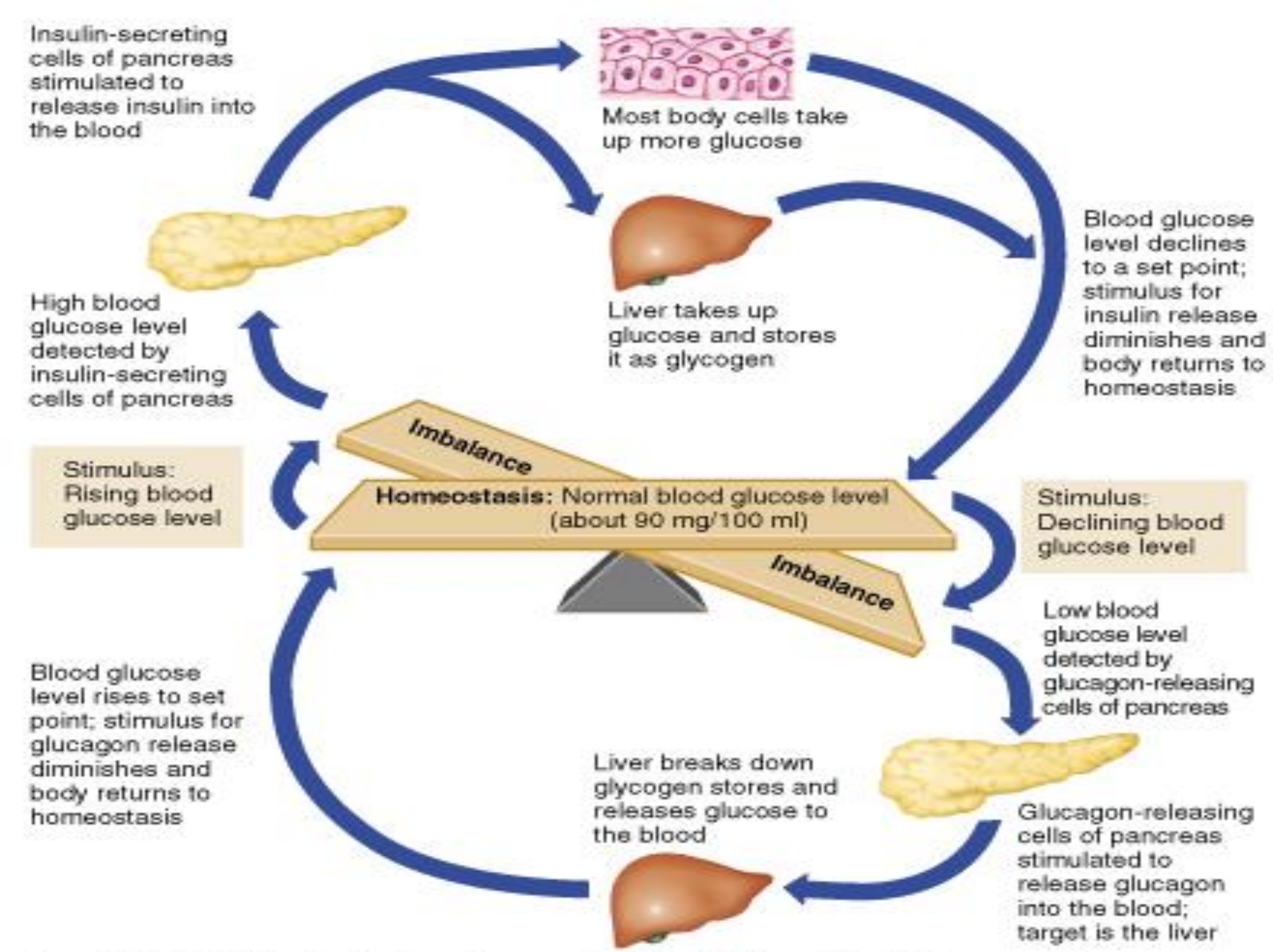
Diabetes

- Some people do not produce enough insulin
- When they eat their blood glucose levels cannot be decreased
- This condition is called diabetes.
- Diabetic patients may need to have insulin injected in their blood. They have to control their diet.


Glucose concentration
Glucose levels increase after a meal
Insulin is produced and glucose levels return to normal
normal
time
meal

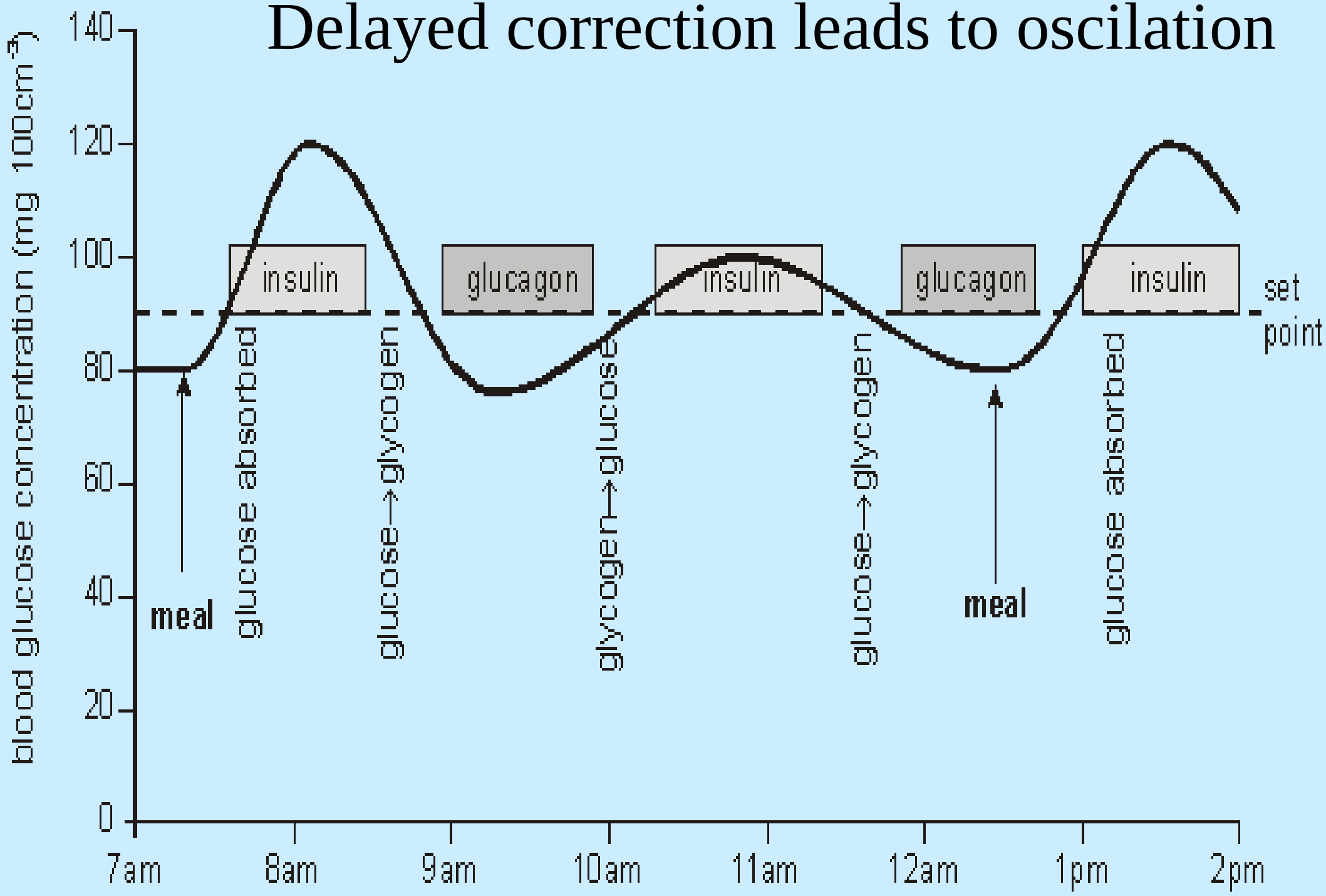

Glucose levels increase after a meal
Insulin is not produced and the levels of glucose remain high
Glucose concentration
Diabetes
time
Meal

Negative feedback: controlling glucose blood levels



HOMEOSTASIS OF GLUCOSE

Delayed correction leads to oscilation



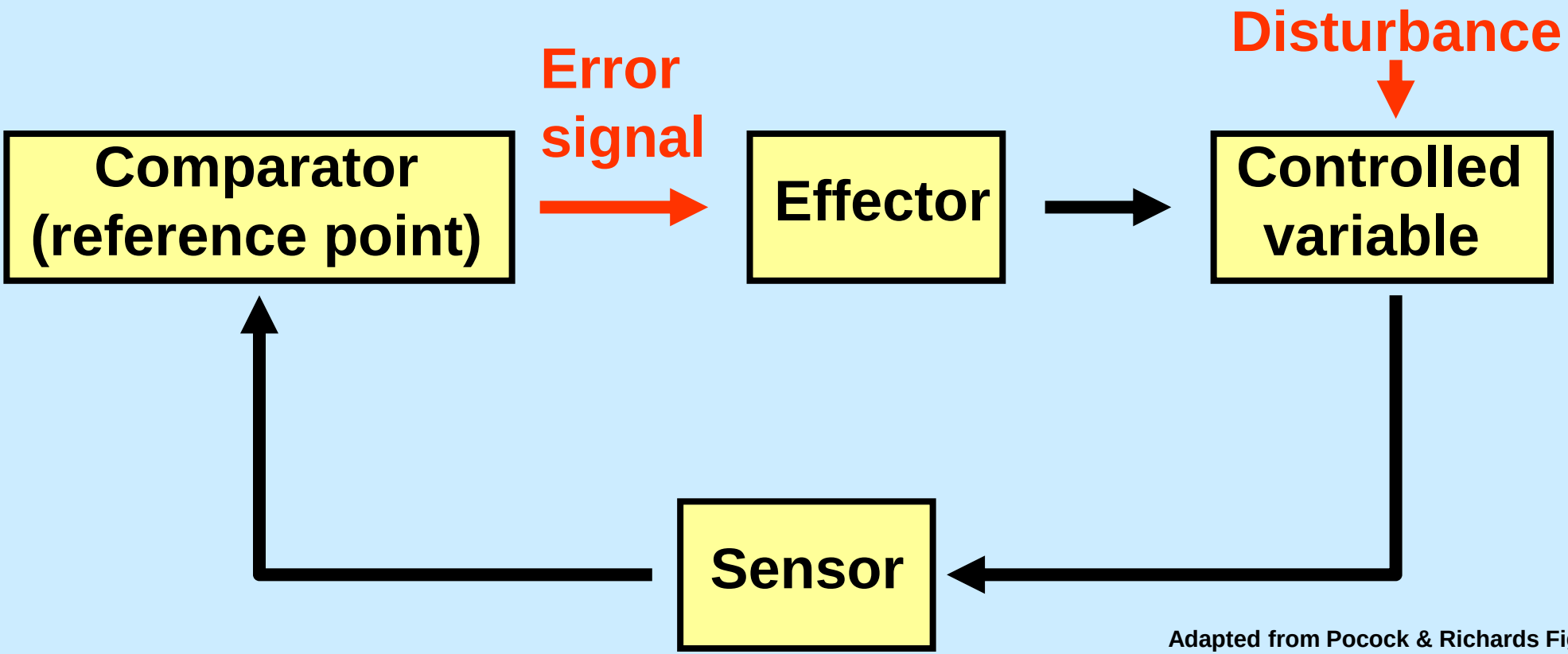
Negative feedback loop

Negative feedback loop requires:

Sensor — specific to variable needing to be controlled

Comparator — reference point for sensor to compare against

Effector — if sensor ≠ comparator ⇒ **Error Signal** ⇒ restore variable to desired level



Adapted from Pocock & Richards Fig 1.1a

Limitations of negative feedback

- **Negative feedback control initiated *after* variable has been disturbed**
- **Amount of correction to be applied assessed by magnitude of error signal ⇒ incomplete correction**
- **Overcorrection ⇒ oscillations in controlled variable**

- **Disadvantages overcome by multiple regulatory mechanisms**

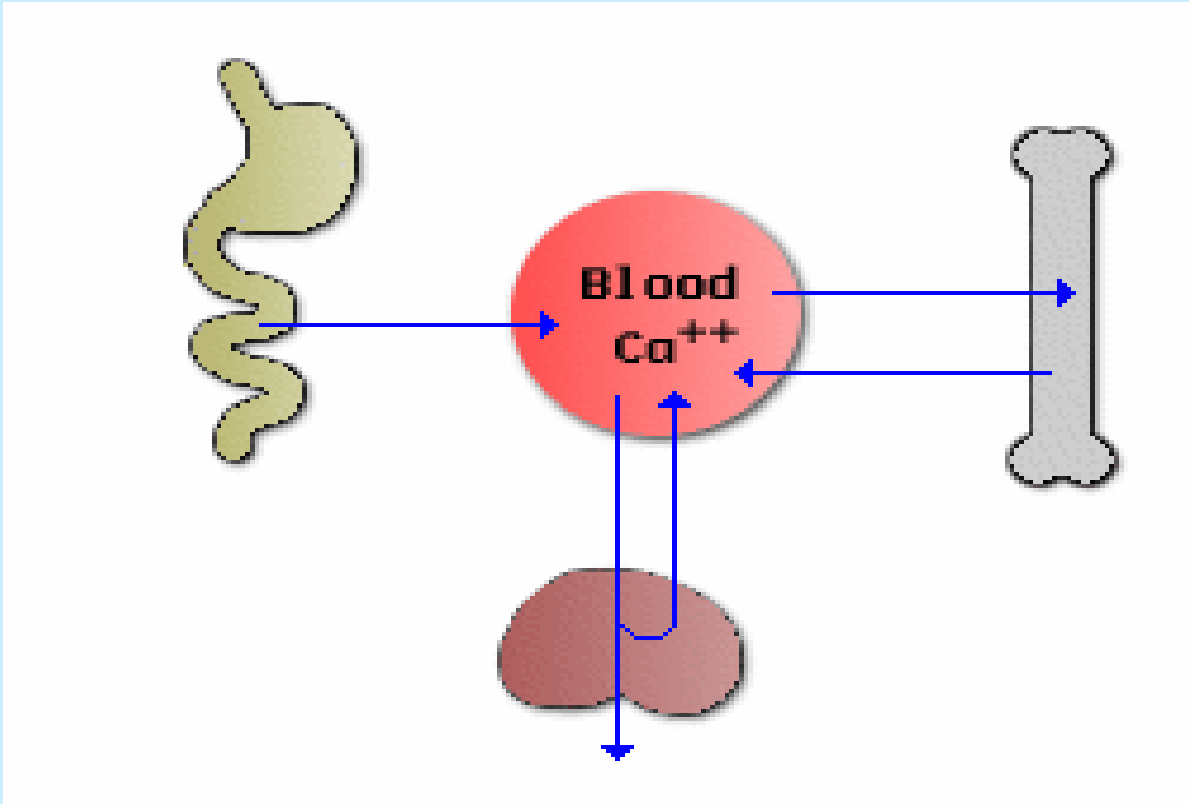
eg

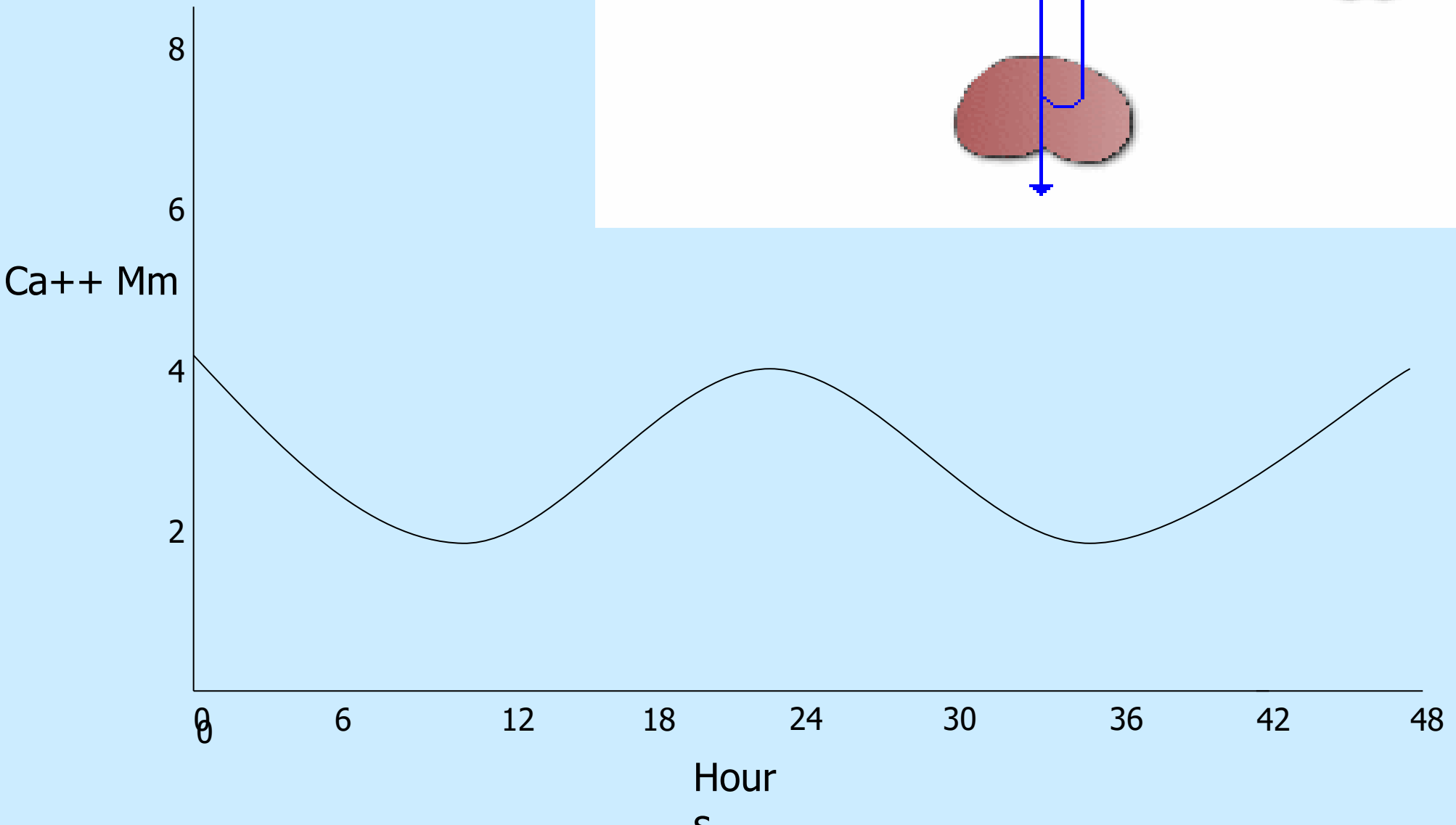
regulation of blood [glucose]

insulin ⇒ ↓ $[glucose]_{blood}$

glucagon ⇒ ↑ $[glucose]_{blood}$

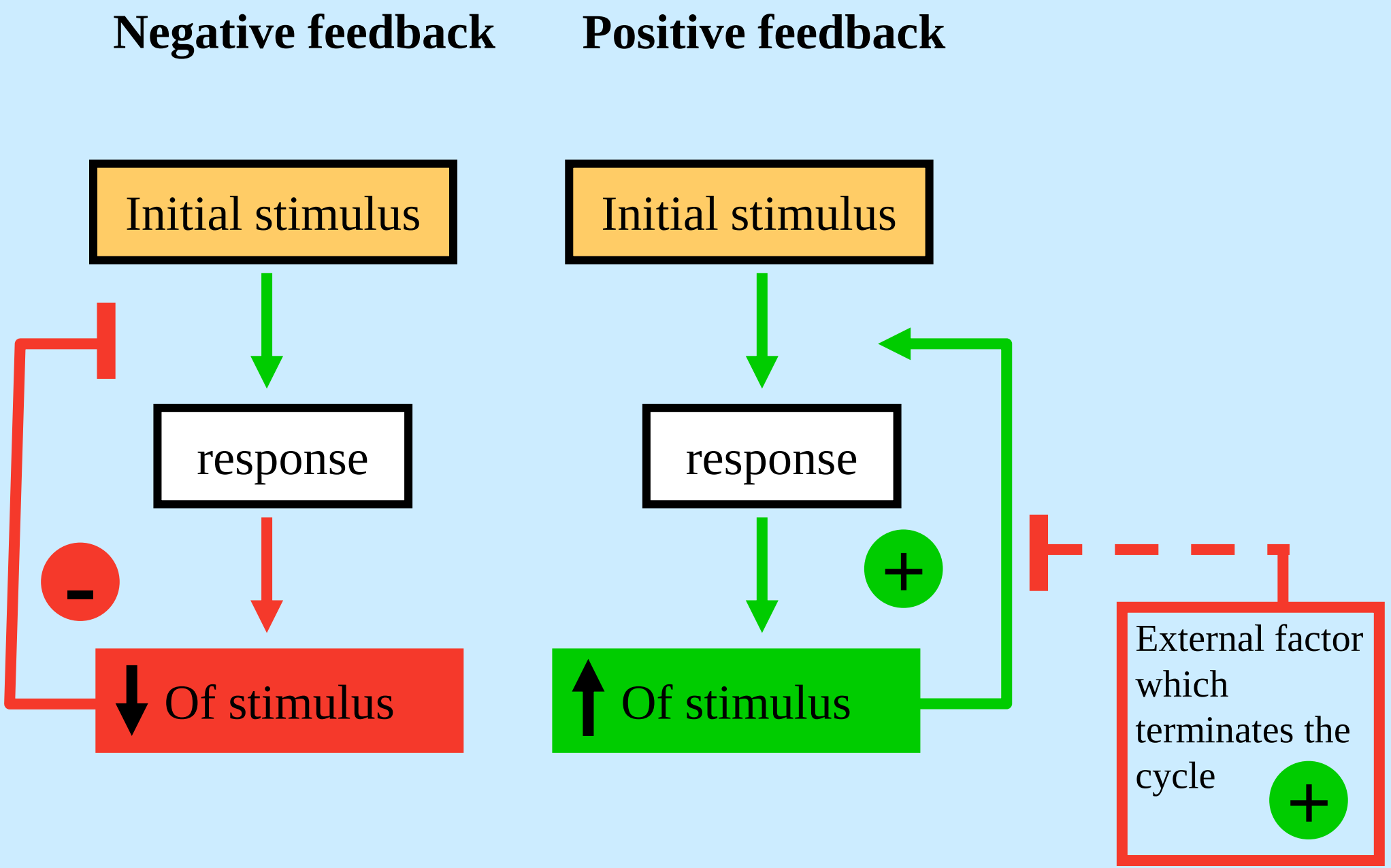
Organs included in Ca++ homeostasis and daily cycle of its levels



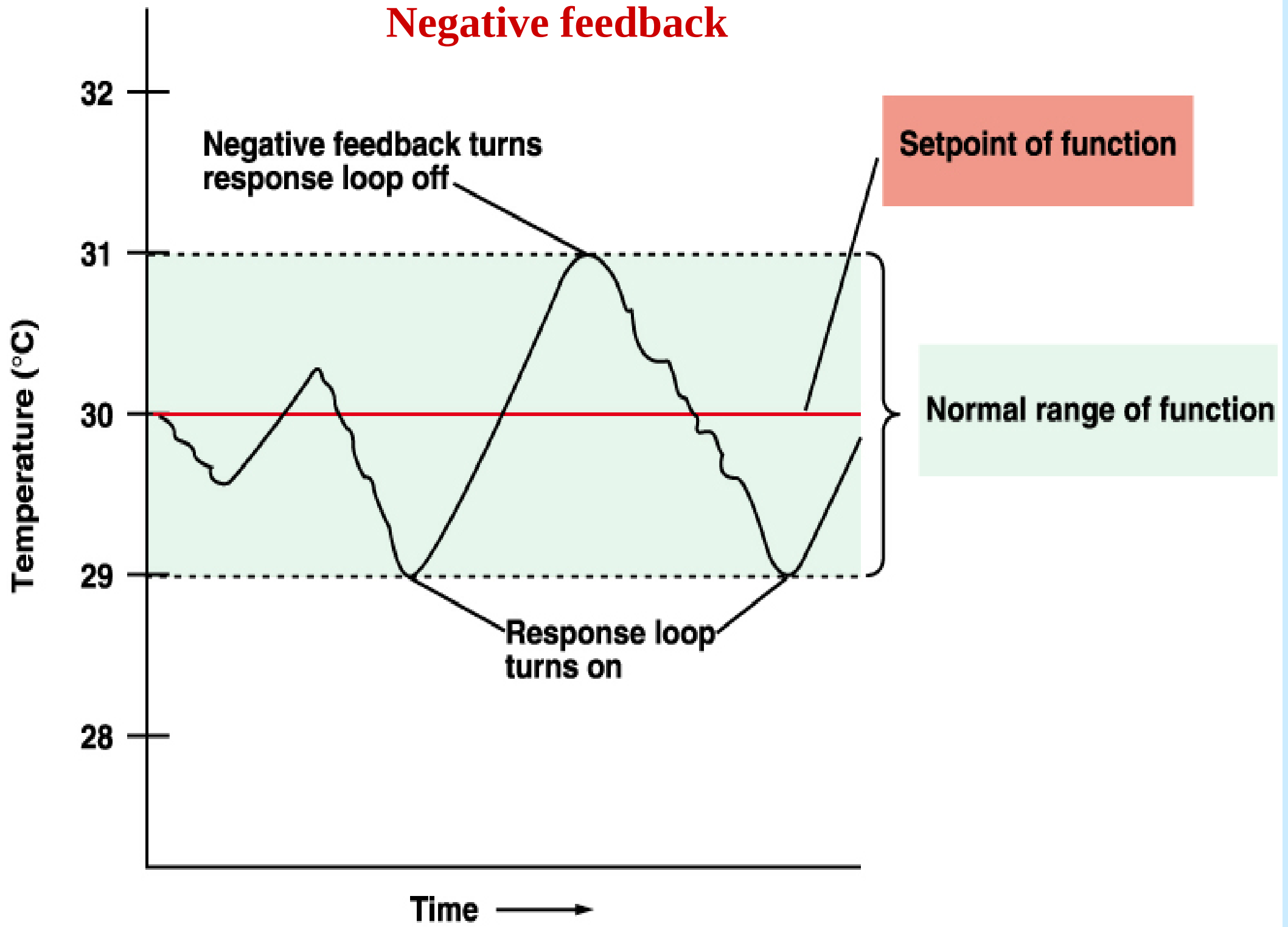


Homeostasis

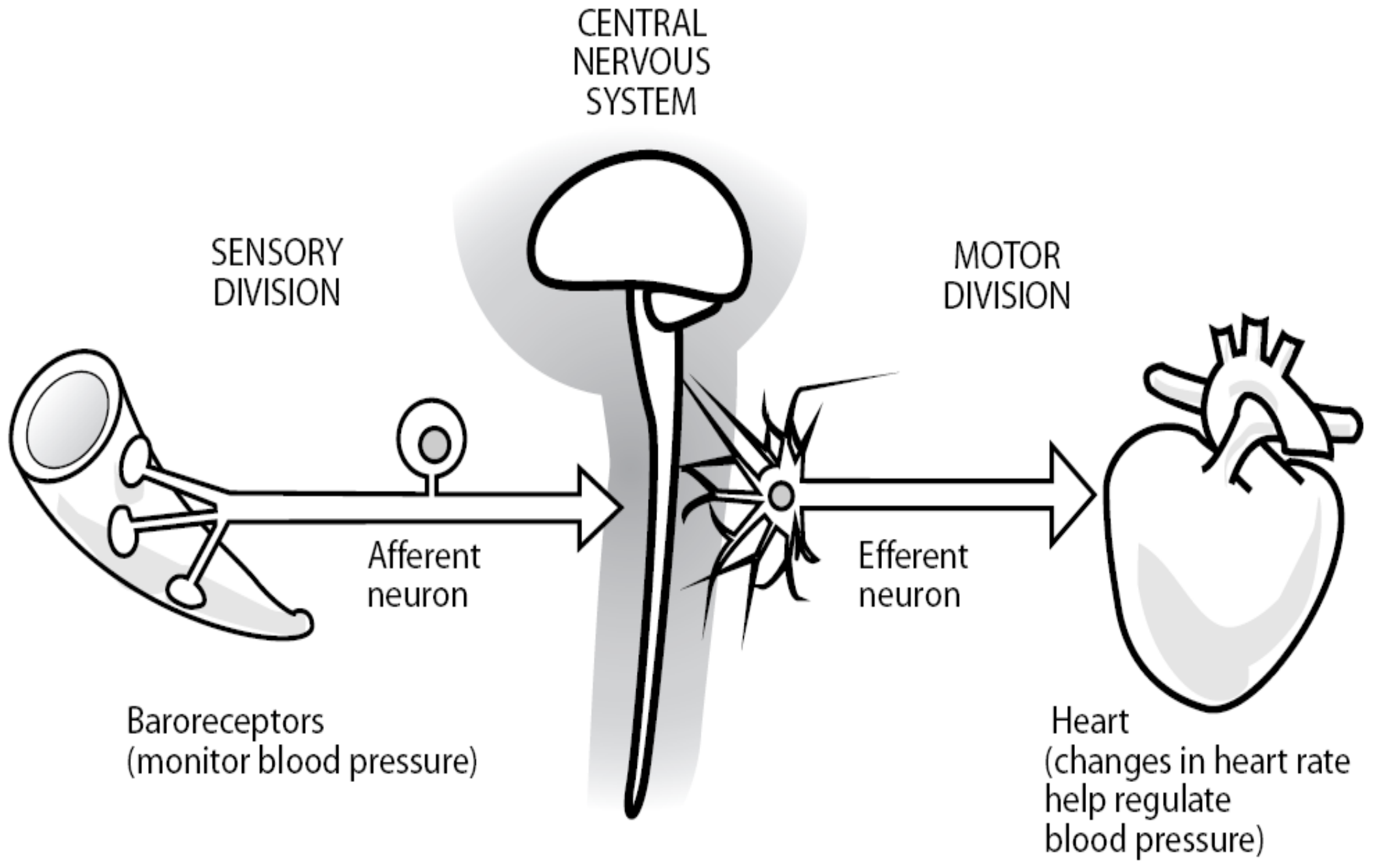
1. is a dynamic balance
2. ... Inspite of a multitude of stimuli
3. ... Maintained by (usualy) negative (and rarely positive) feedback


Negative feedback
Positive feedback
Initial stimulus
response
-
Of stimulus
Initial stimulus
response
+
Of stimulus
External factor which terminates the cycle
+

Negative feedback

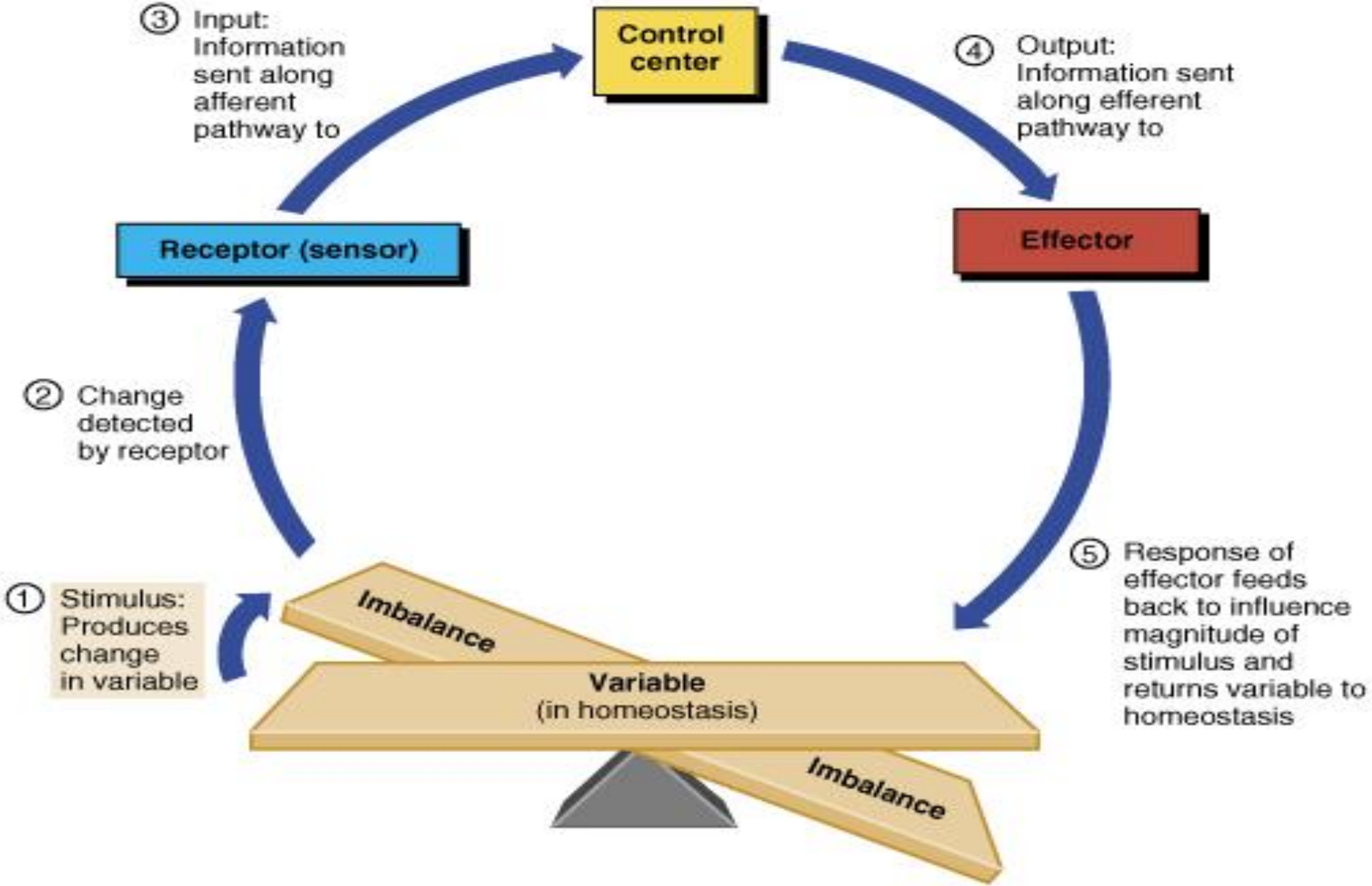


Negative feedback: Changes in blood pressure are being monitored by baroreceptors in the large arteries and through a control by the NS appropriate changes try to reverse these changes and maintain homeostasis



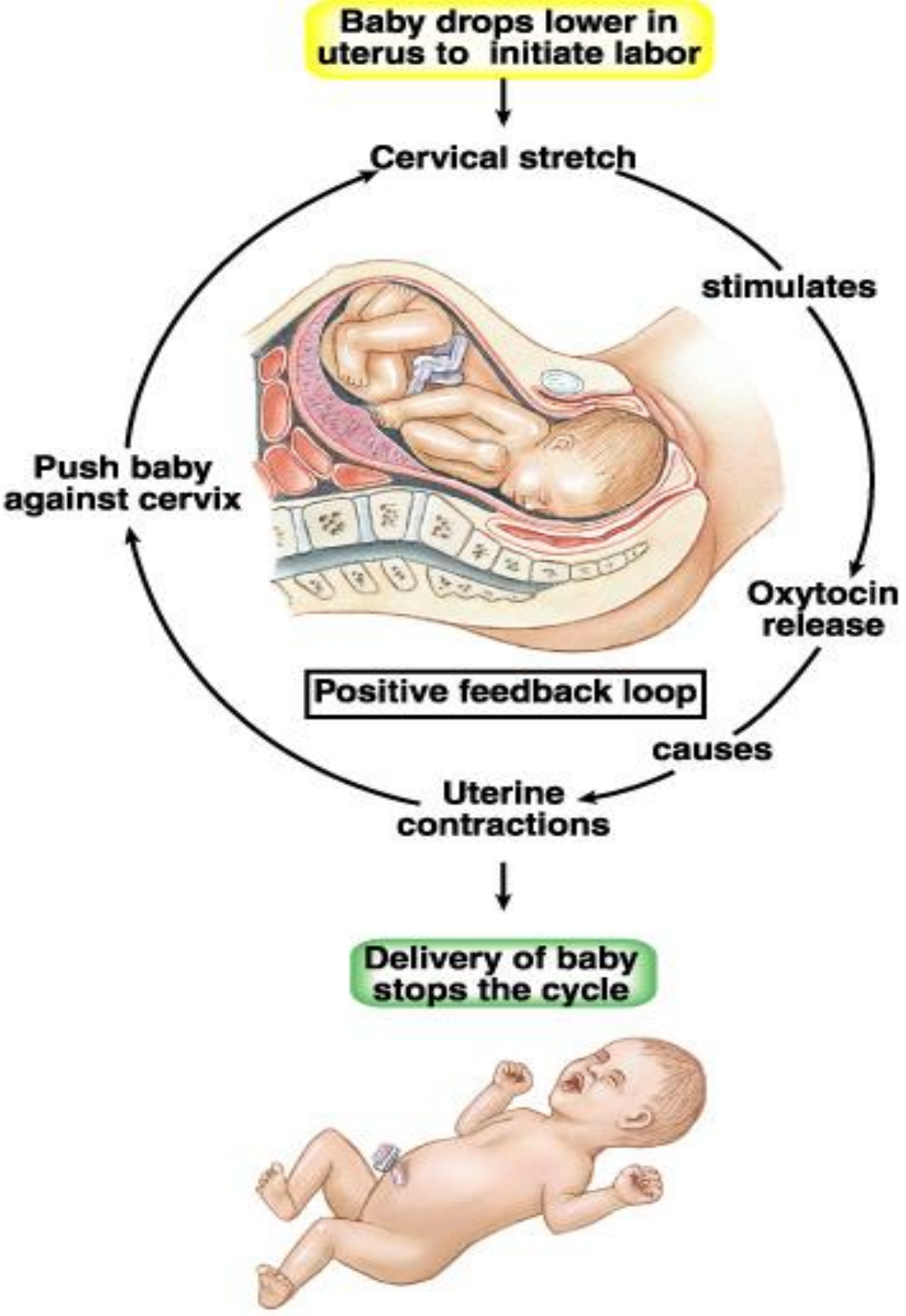
Negative feedback =

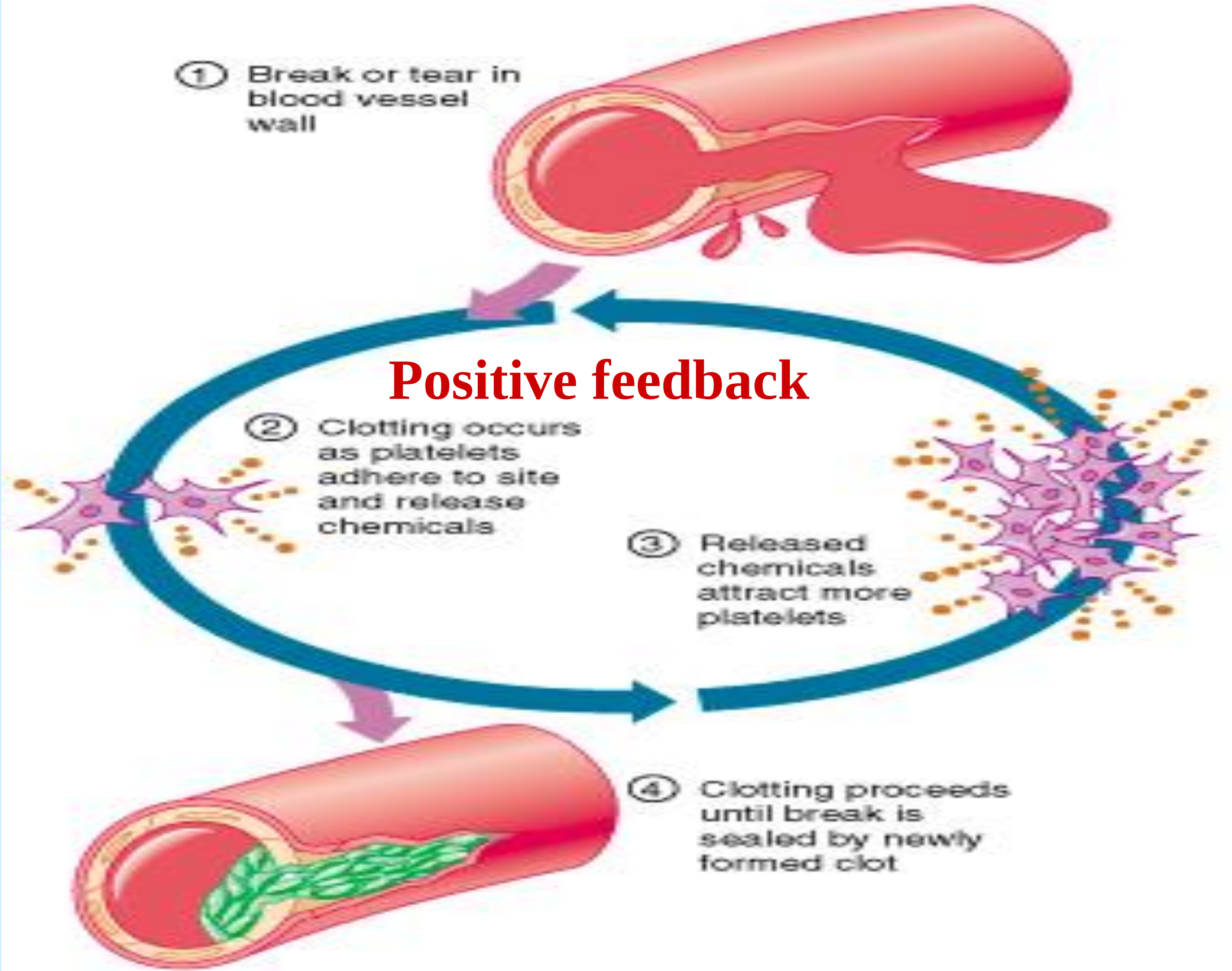
control mechanism in which a change in a monitored parameter evokes a response which counteracts that change



Positive feedback

Rarely used in homeostasis because they are catastrophic, unless they have a limit.




① Break or tear in blood vessel wall
Positive feedback
② Clotting occurs as platelets adhere to site and release chemicals
③ Released chemicals attract more platelets
④ Clotting proceeds until break is sealed by newly formed clot

Disease

The failure to maintain homeostatic conditions.

Can be due to: pathogens or parasites, inherited disorders, loss of normal regulatory control mechanisms, degenerative changes, trauma, toxins, environmental hazards, nutritional factors.

Pathology - the study of disease.

Pathophysiology - the study of the functional changes caused by disease..

Themes in Physiology

- Homeostasis
- Integration of body systems.
- Cell-to-cell communication and coordination.
- Movement of substances and information across cell membranes.
- Compartmentation of the body and cell.
- Energy flow.
- Mass balance and mass flow.

Control Pathways

Three components: stimulus or change in conditions, evaluation of the change and initiating a response, and the response.

Local control – paracrine or autocrine response.

Reflex control pathway – respond to changes that are more widespread or systemic in nature.

.Nervous system

.Endocrine system

.Cytokines

Reflex Pathways

Response loop – input signal, integration of the signal, and output signal. **Integrating center** compares incoming **(afferen**t) signal from sensor **(receptor**) to **setpoint** and alters outgoing **(efferen**t) signal to **effector** accordingly. Receptors have **threshold** which must be exceeded to set reflex in motion.

Feedback loop – modifies response loop. Homeostatic if **negativ**e. **Positive feedback loops** are not homeostatic.

Feed forward Control

Allows body to predict that a change is about to occur.

Response loop starts in anticipation of change, e.g. seeing, smelling, or thinking about food.

Circadian rhythms – evolutionary response to 24-hr day and to seasons.

Control Systems

Specificity – direct contact between nervous system and target cells. Endocrine more general so multiple tissues can respond simultaneously.

Nature of Signal – electrical and chemical for nervous system. Chemical for endocrine.

Speed – Fast for nervous reflexes (120 m/s). Slow for endocrine, min to hr.

Duration of Action – Shorter for nervous control than for endocrine. Neurotransmitters removed rapidly. Depend on multiple repeating signals.

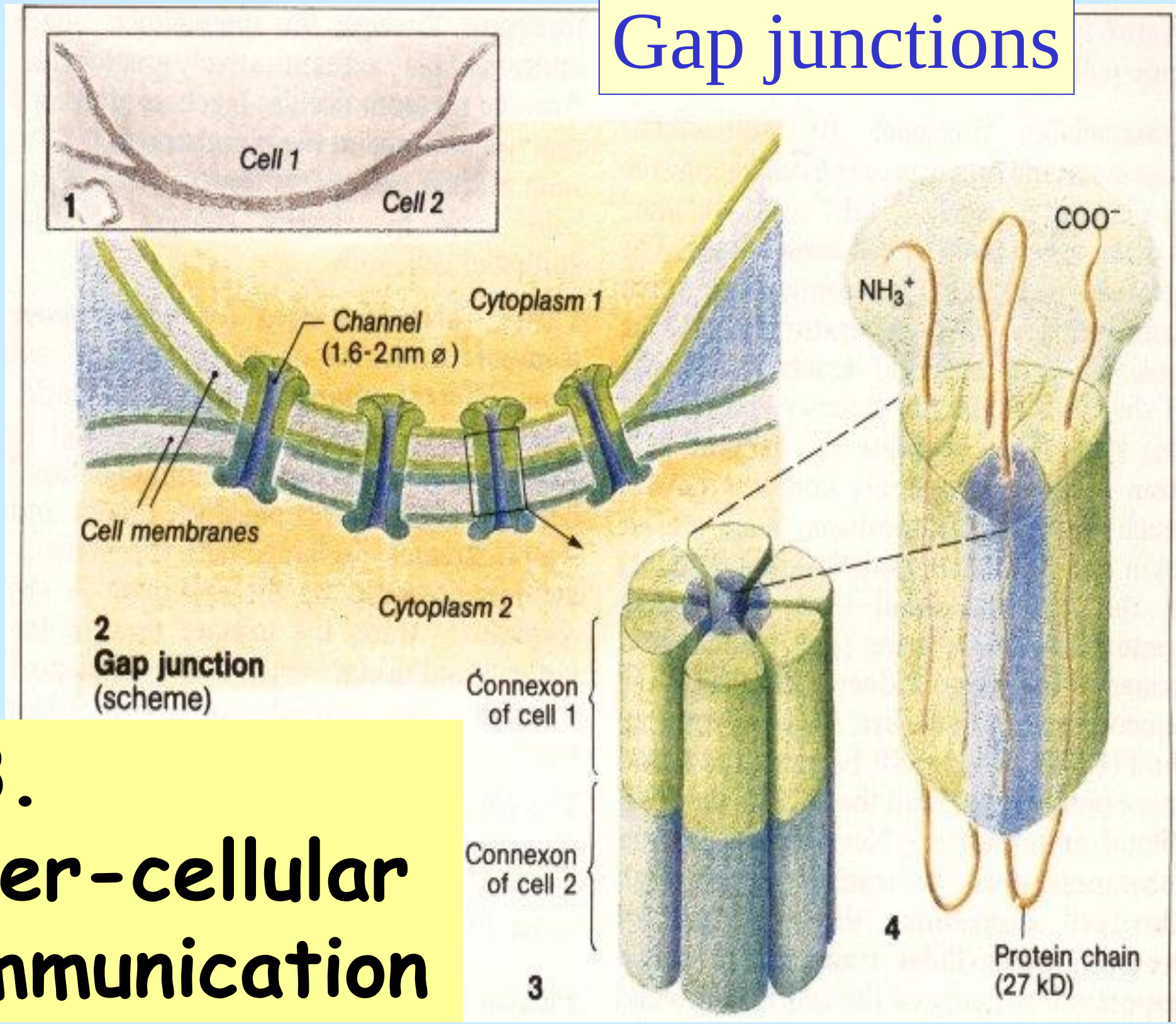
Coding for Stimulus Intensity – depends of frequency of signal for nervous control. Depends on amount of hormone for endocrine control.

Control Pathway Patterns

(1) **Nervous** – neurotransmitter to target.
(2) Nervous – neurohormone to target.
(3) Combined – neurotransmitter to endocrine cell then hormone to target.
(4) Combined – neurohormone to endocrine cell then hormone to target.
(5) Combined – neurohormone to endocrine cell then hormone to endocrine cell then hormone to target.
(6) **Endocrine** – hormone to target.

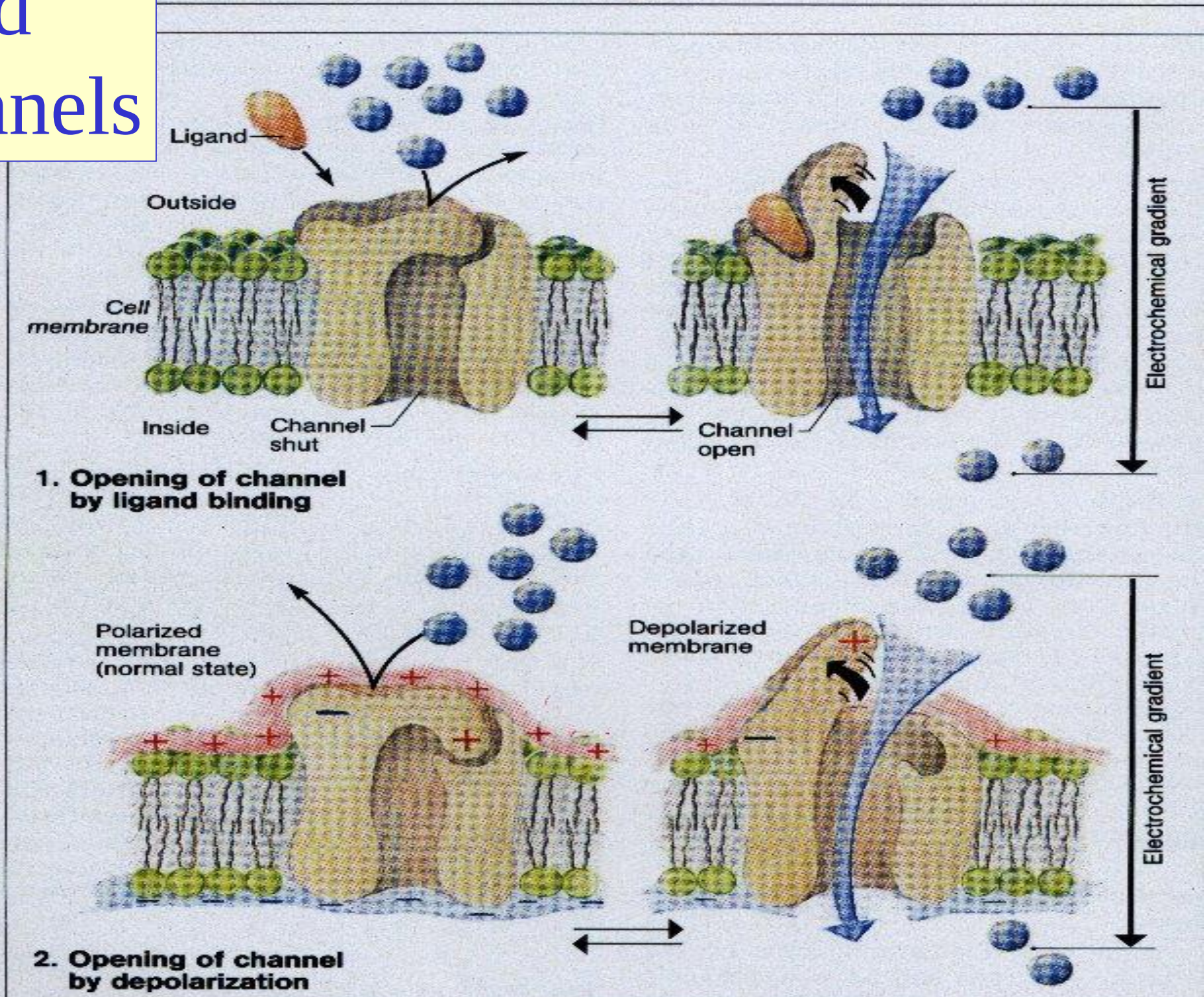
1.1. Defining Physiology
1.2. Homeostasis
1.3. Inter-cellular Communication
1.4. Methods
1.5. Energy

Gap junctions

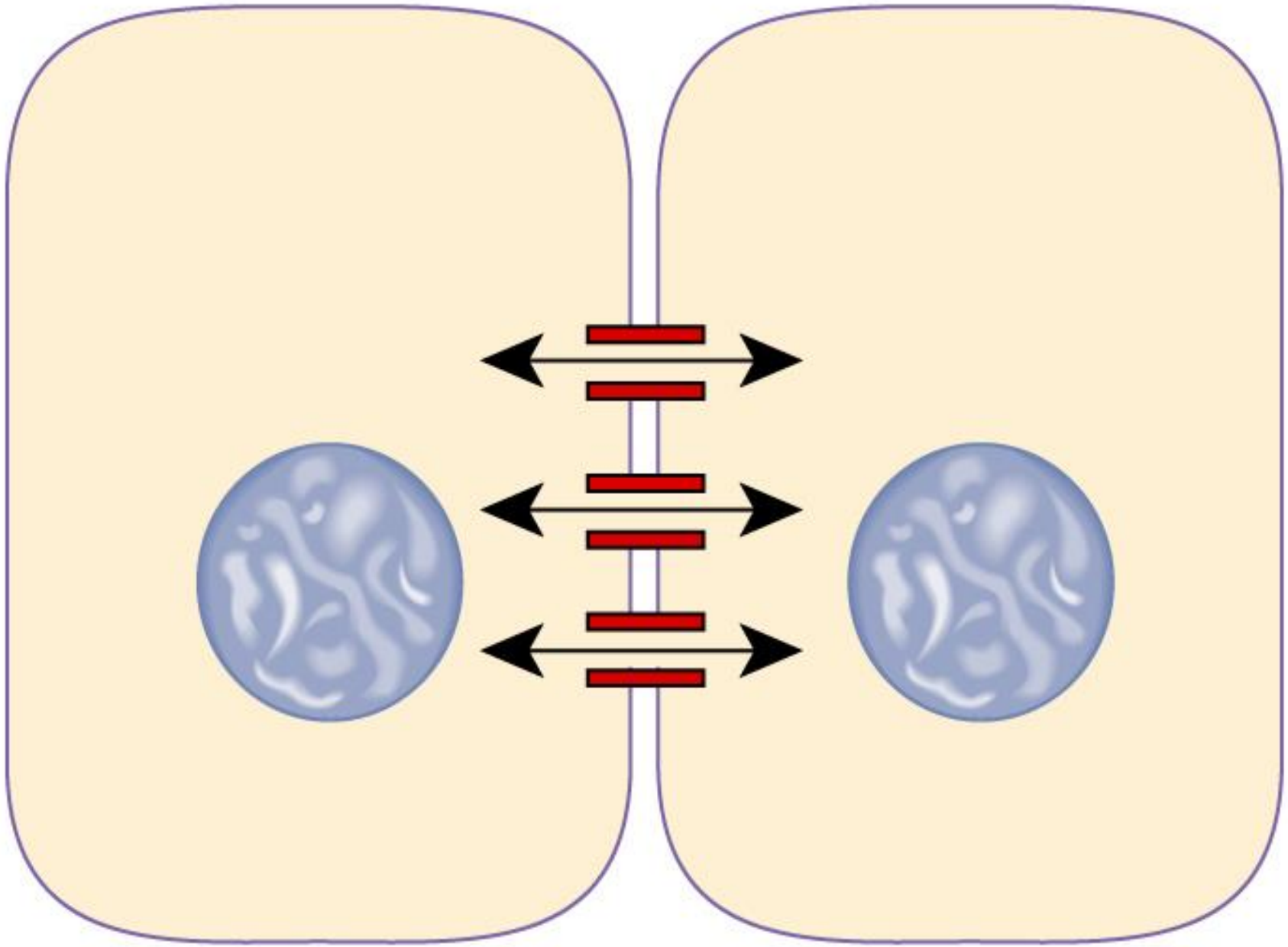


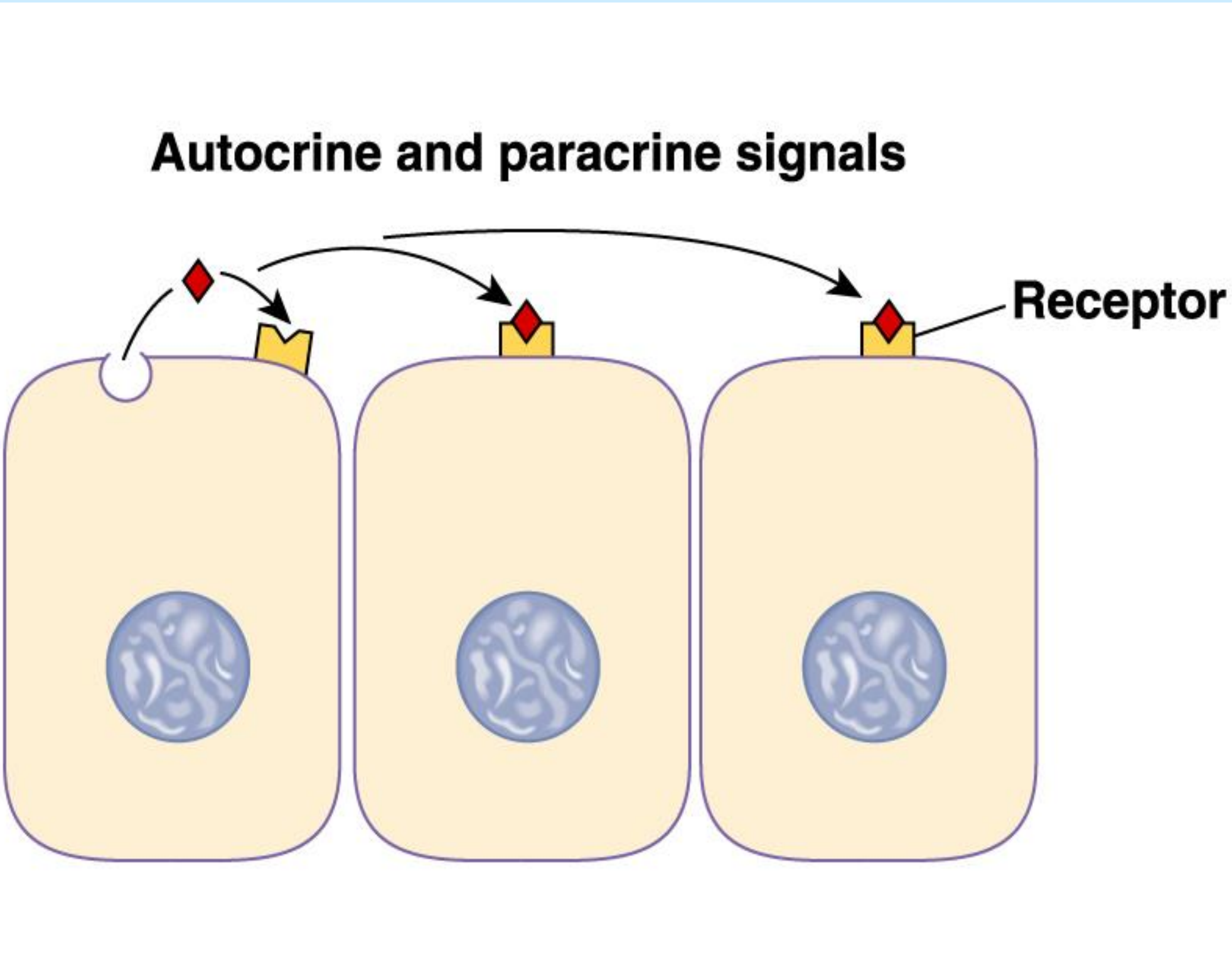
1.3. Inter-cellular Communication

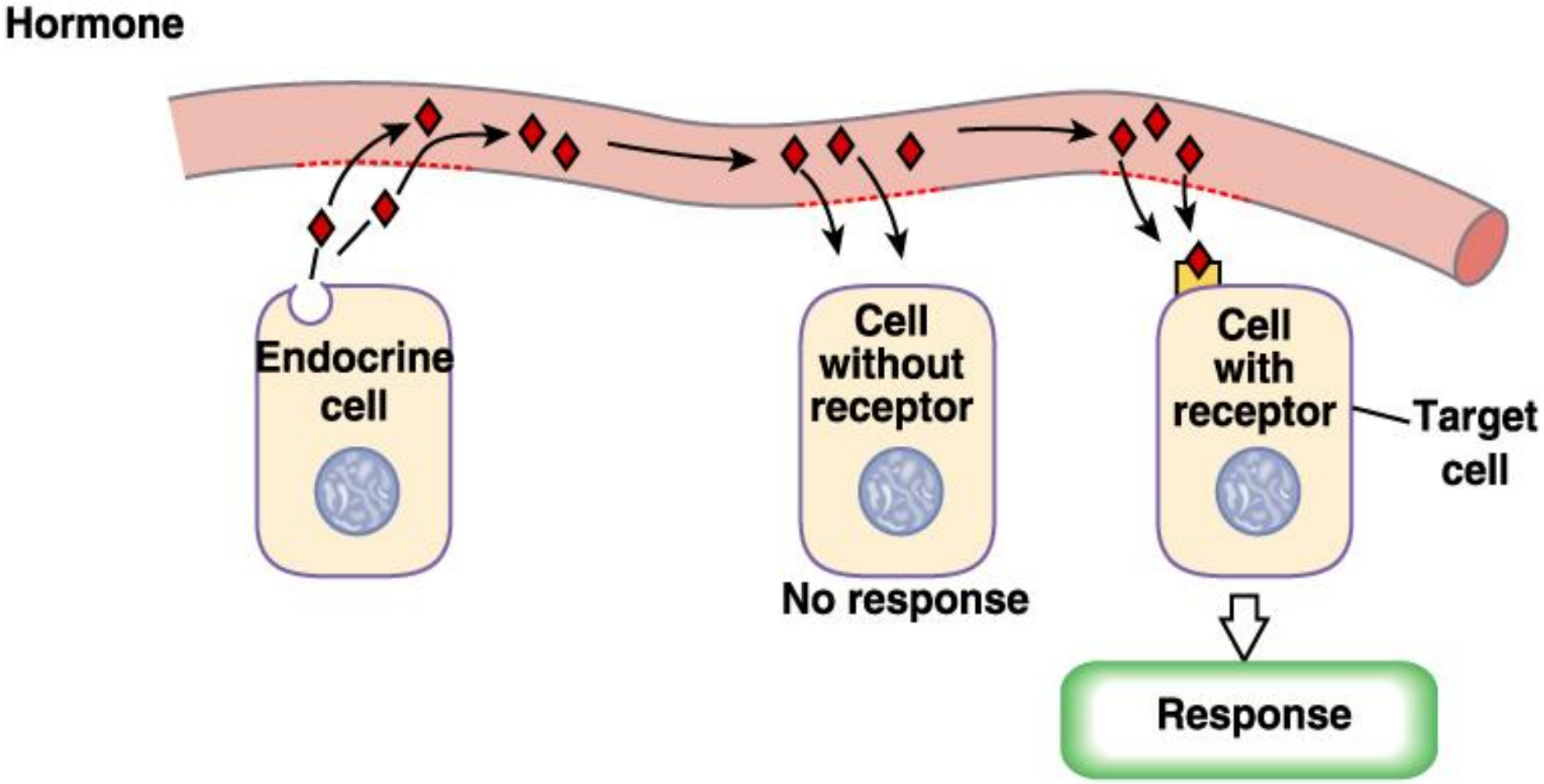
Gated Channels

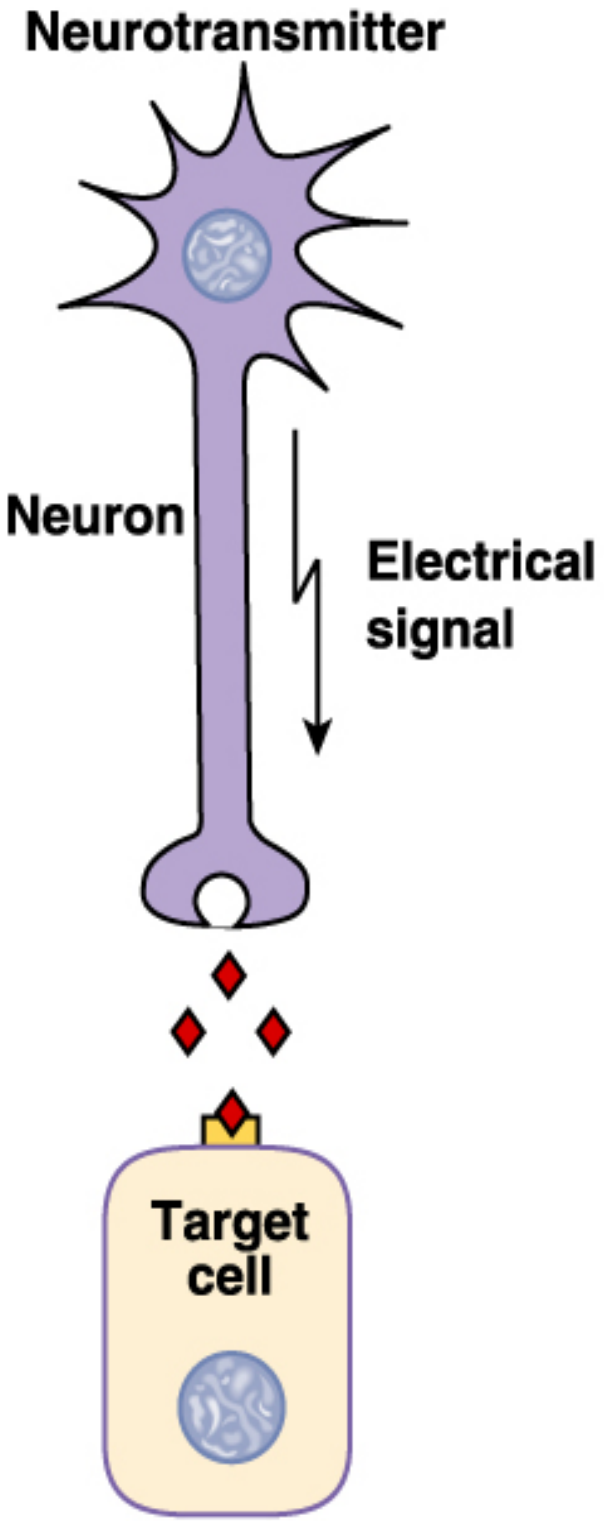


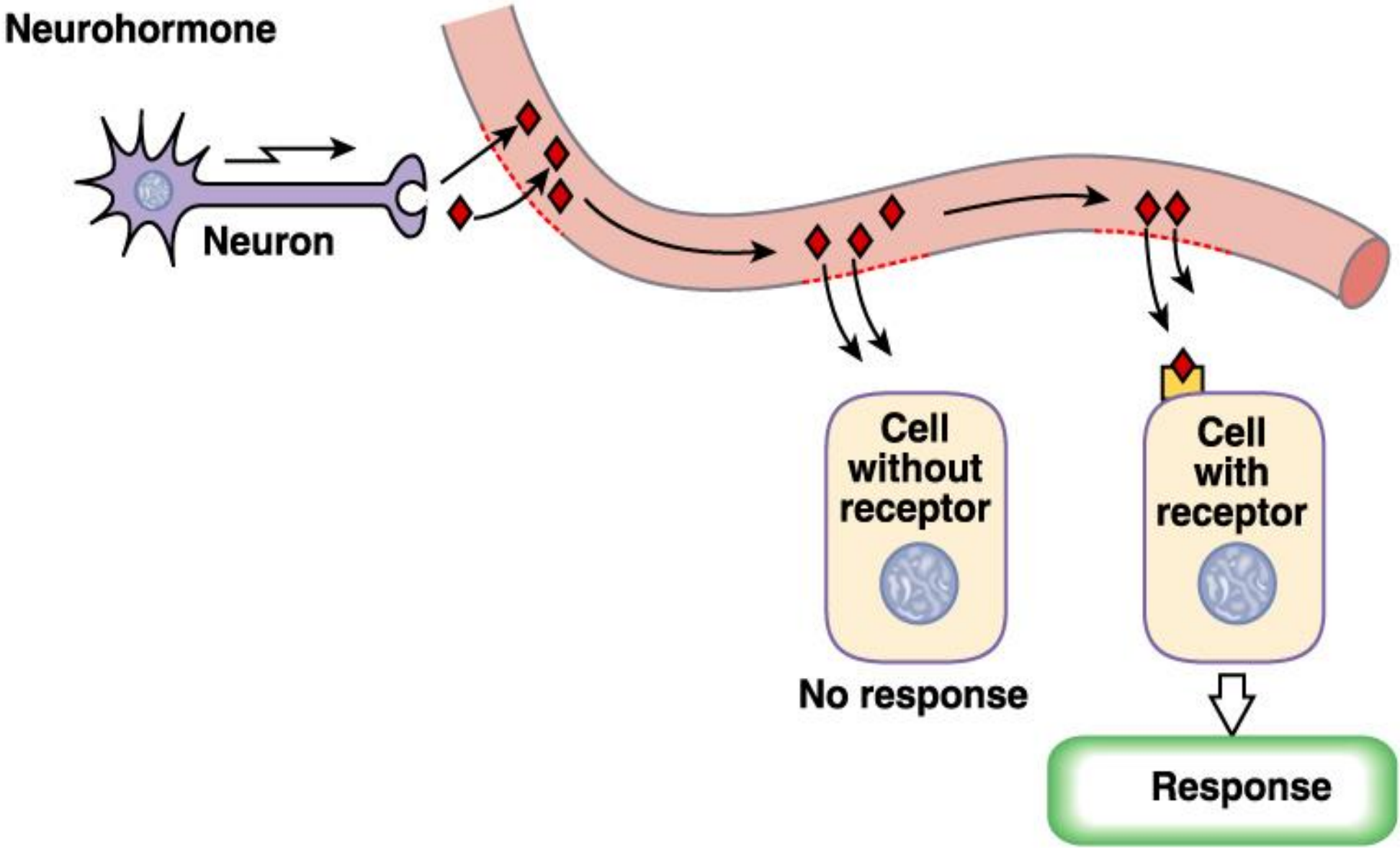
Gap junctions




Autocrine and paracrine signals
Receptor

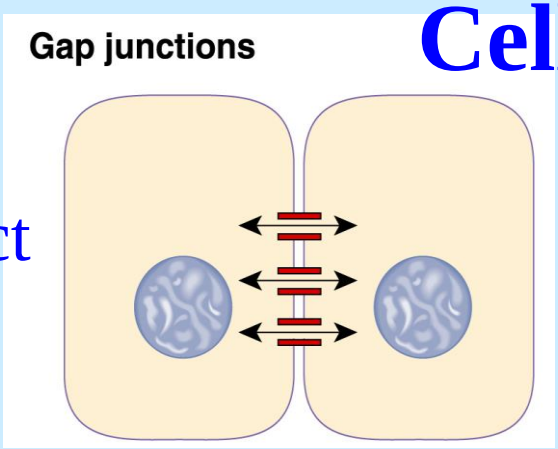

Hormone
Endocrine cell
Cell without receptor
No response
Cell with receptor
Target cell
Response


Neurotransmitter
Neuron
Electrical signal
Target cell

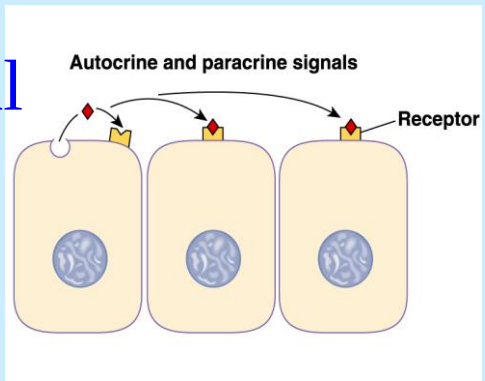

Neurohormone
Neuron
Cell without receptor
Cell with receptor
No response
Response

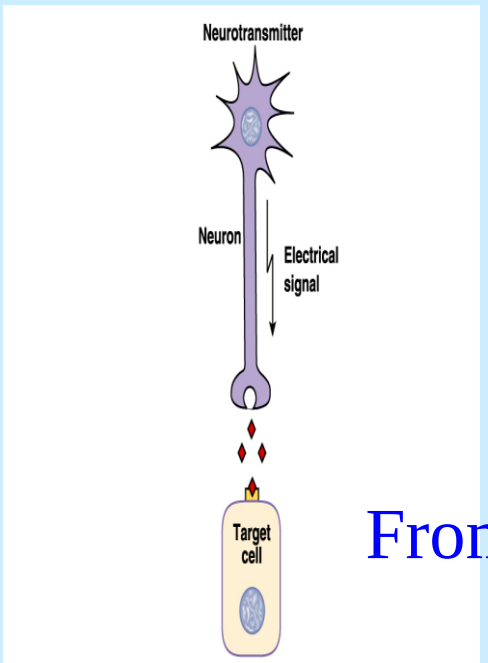
Cell-to-Cell communication

direct

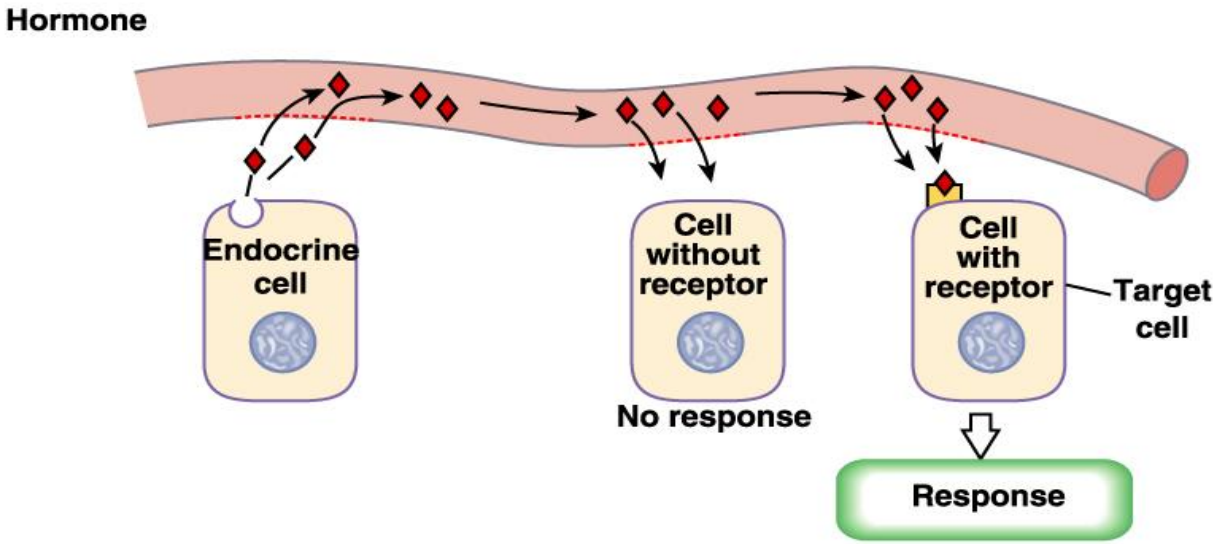


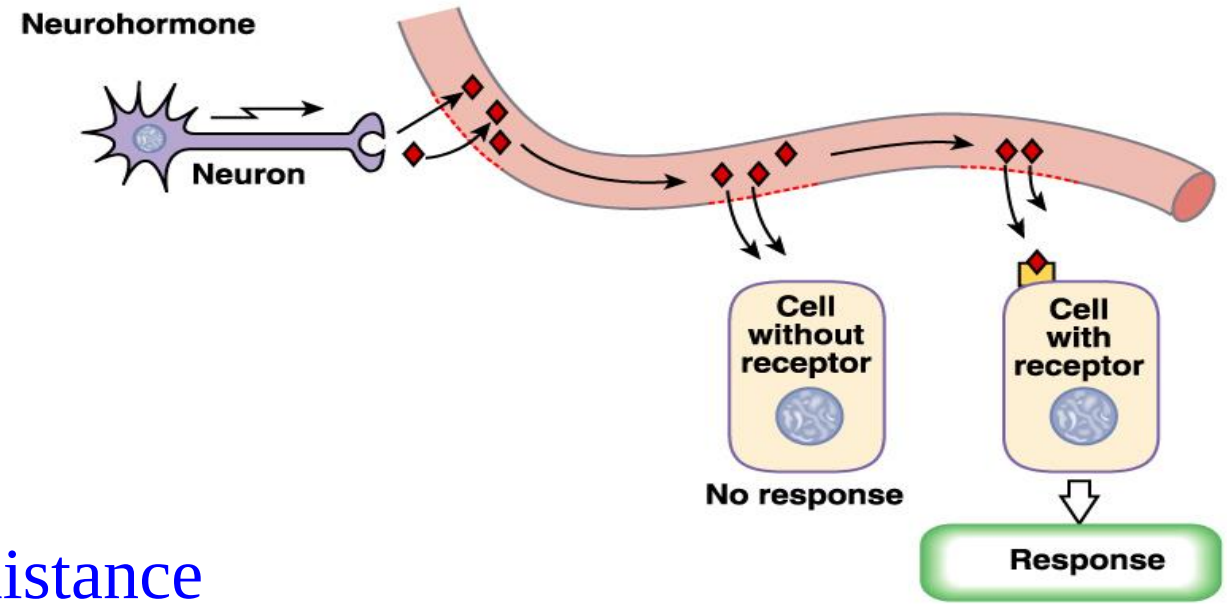
local





From distance





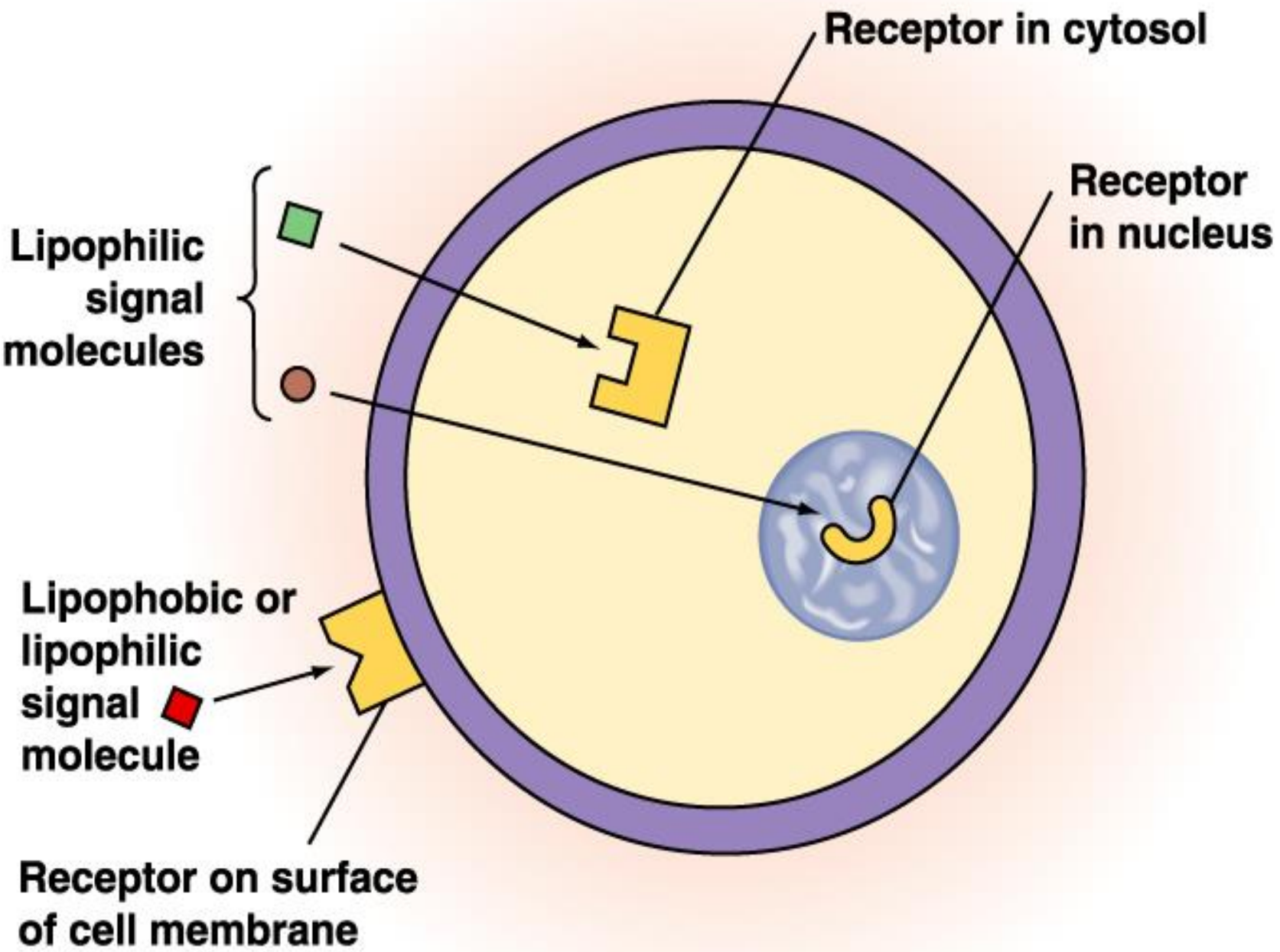
There are two basic types of physiological signals:

- **electrical**
- **chemical**

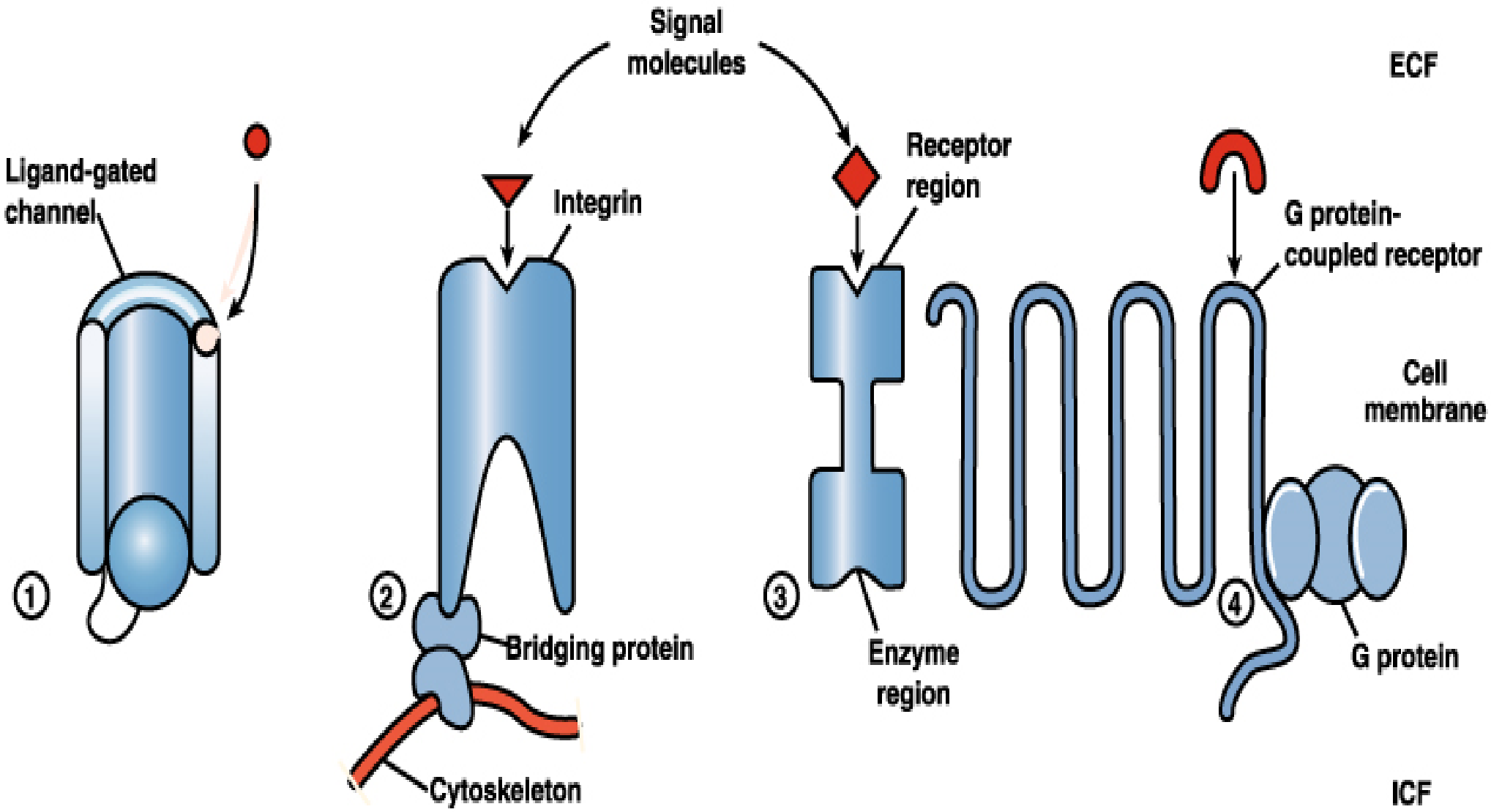
There are three ways of inter-cellular communication:

1. **Direct** transfer through gap junctions
2. **Local** chemical communication (paracrine messages from neuromodulators, cytocines, ecosanoids etc.)
3. Communication **from distance**

Target cell receptors



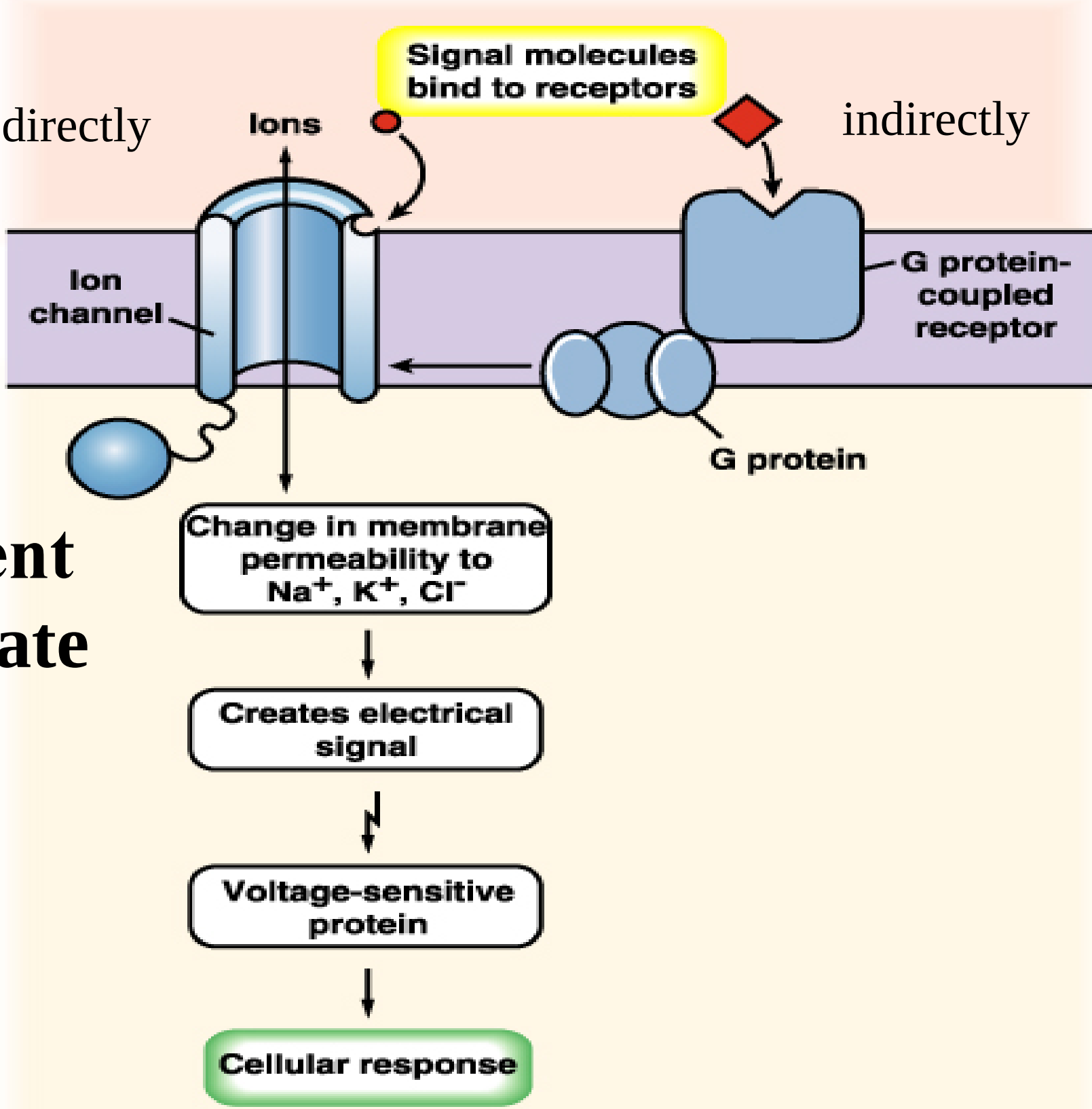
Four classes of membrane receptors



Through channel opening…

directly

indirectly



…movement of ions create electrical signals

External signal

Radio waves

Receptor

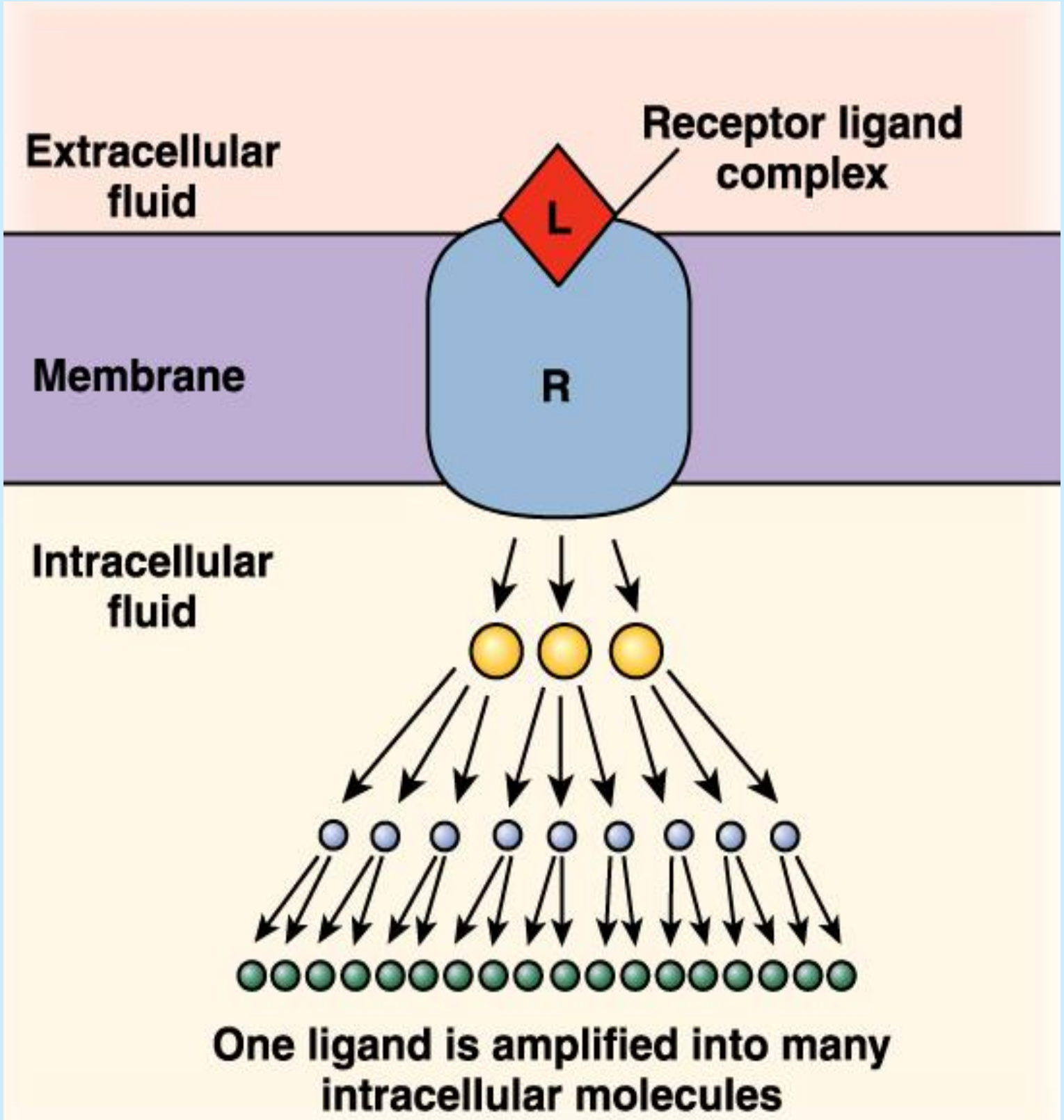
Transducer

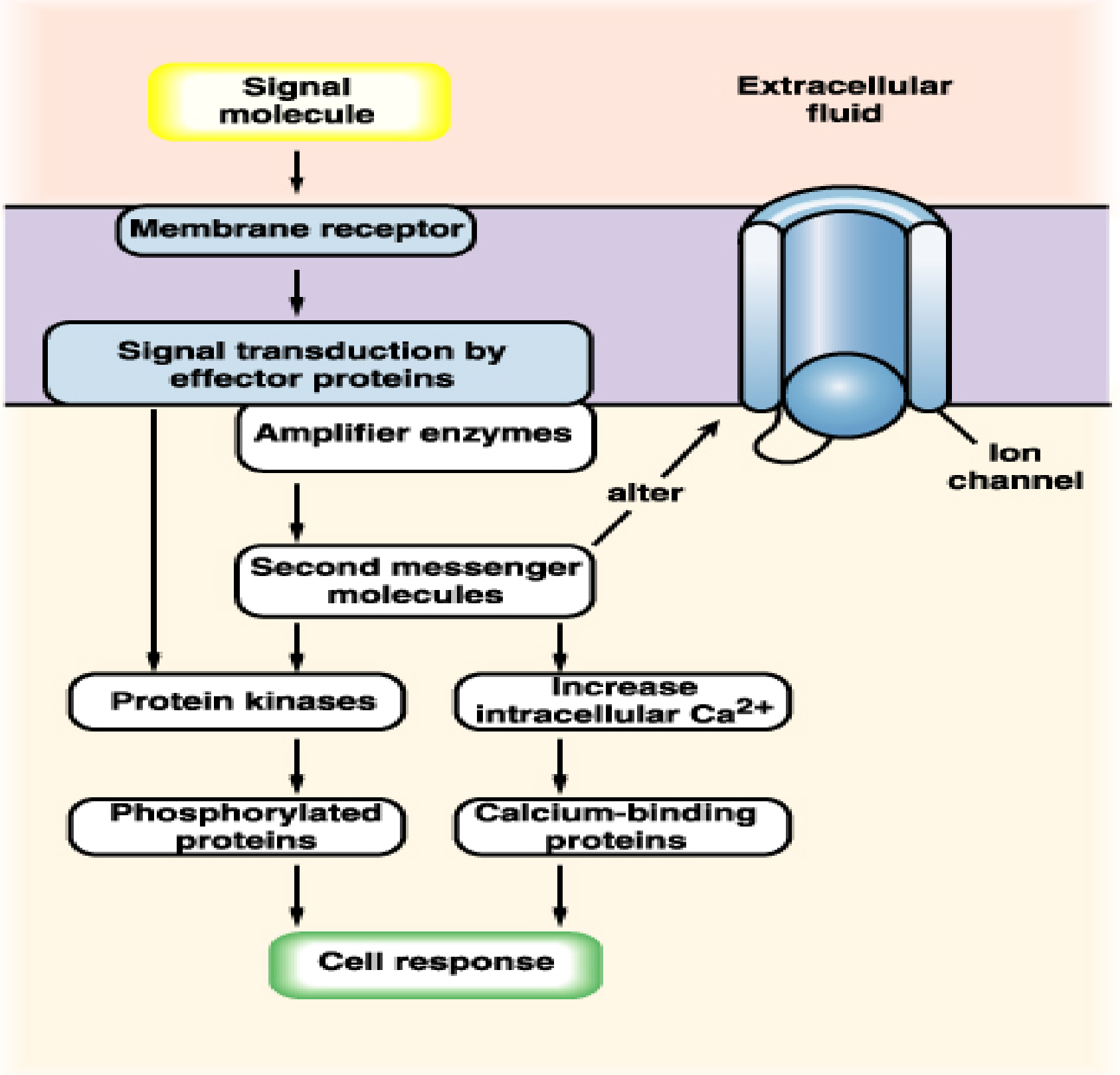
Amplifier

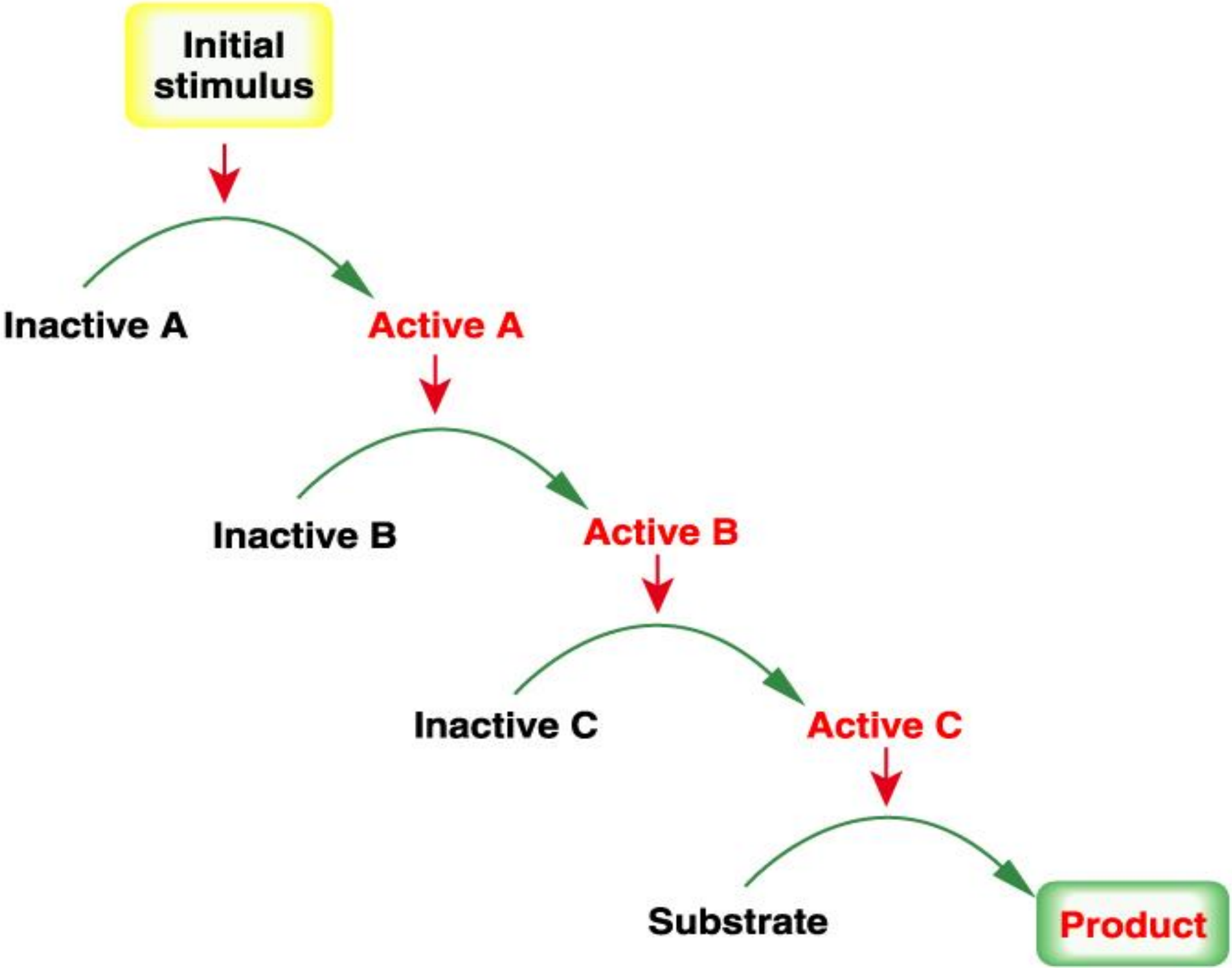
Radio

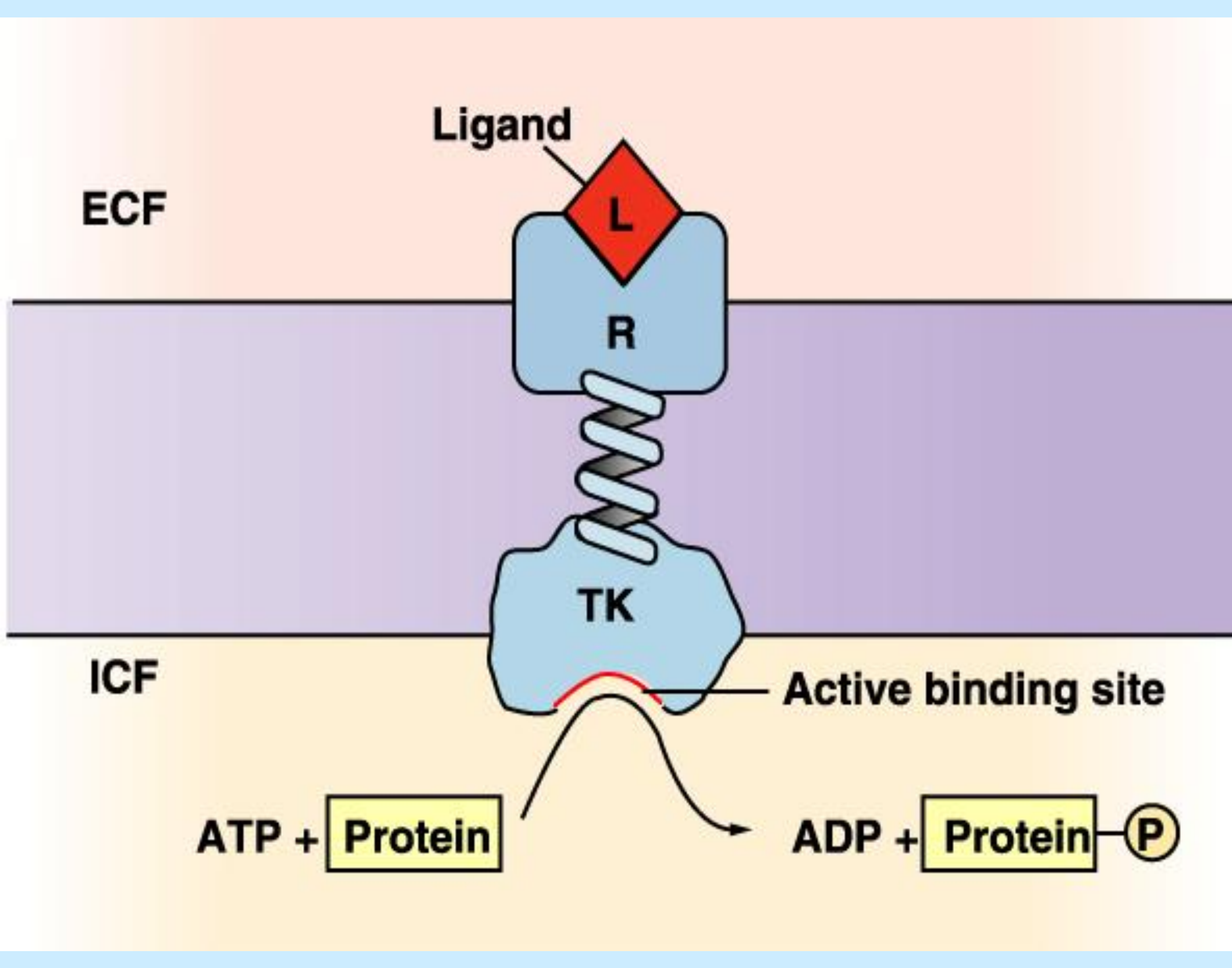
Response

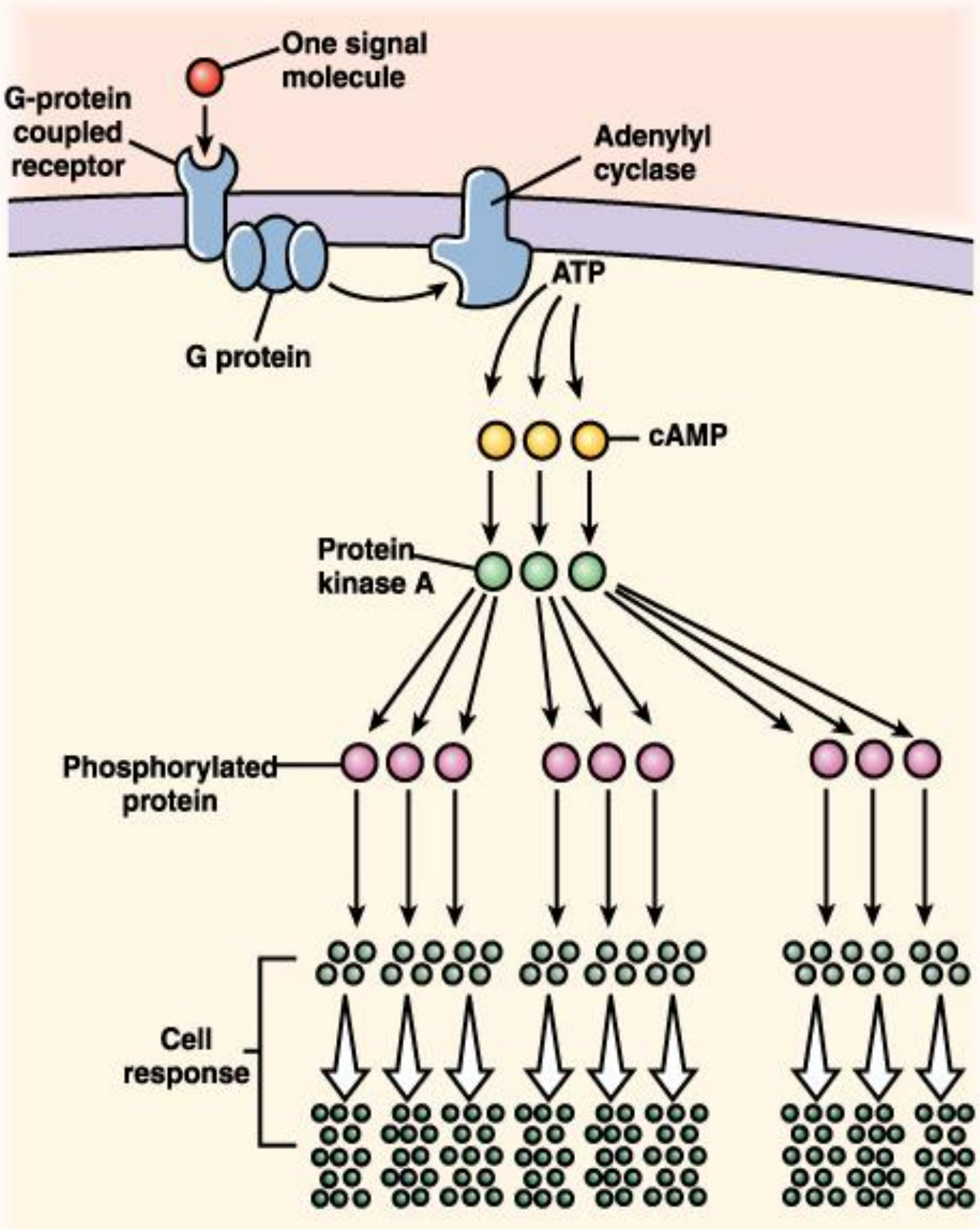
Sound waves

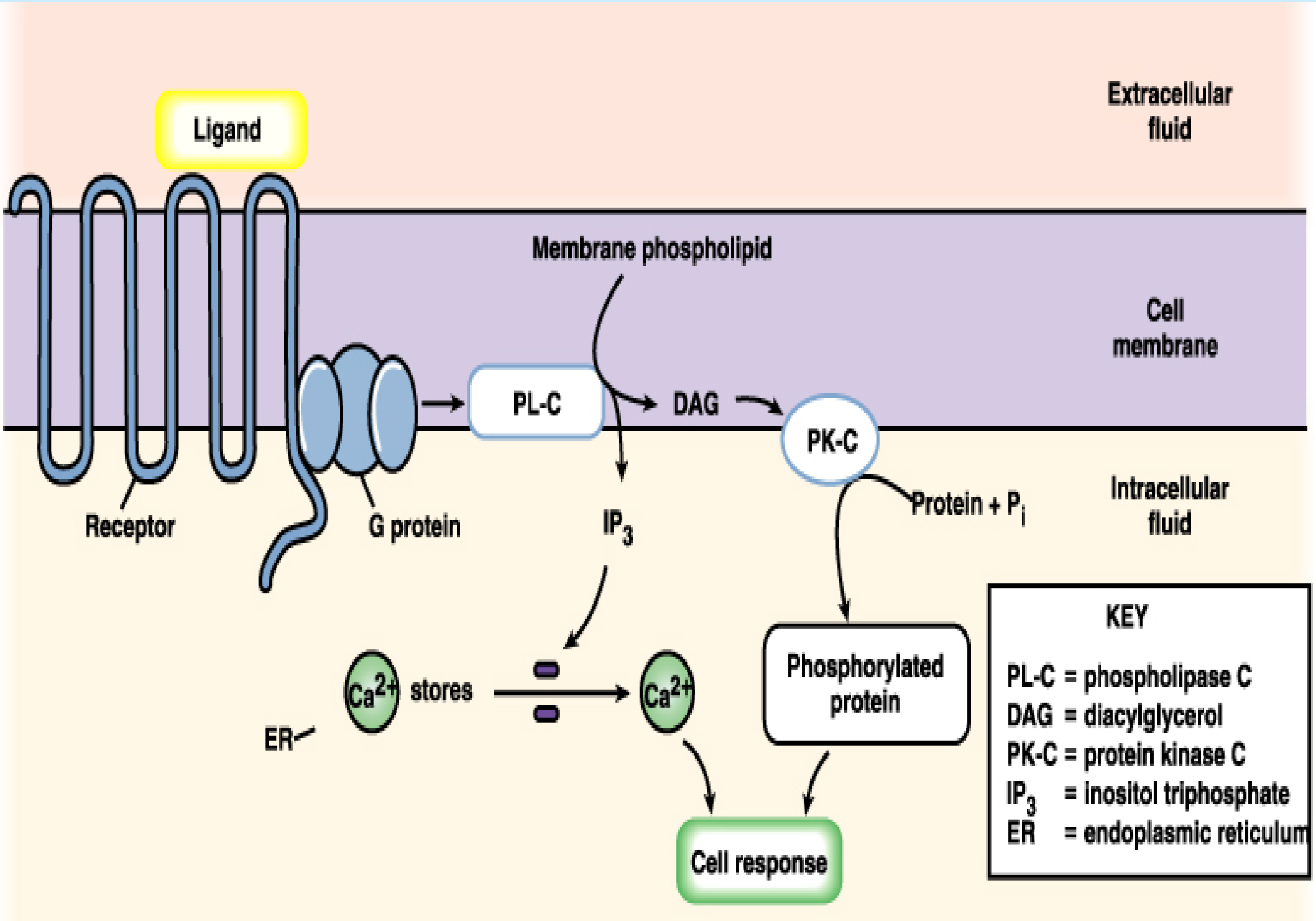

Extracellular fluid
Receptor ligand complex
L
Membrane
R
Intracellular fluid
One ligand is amplified into many intracellular molecules

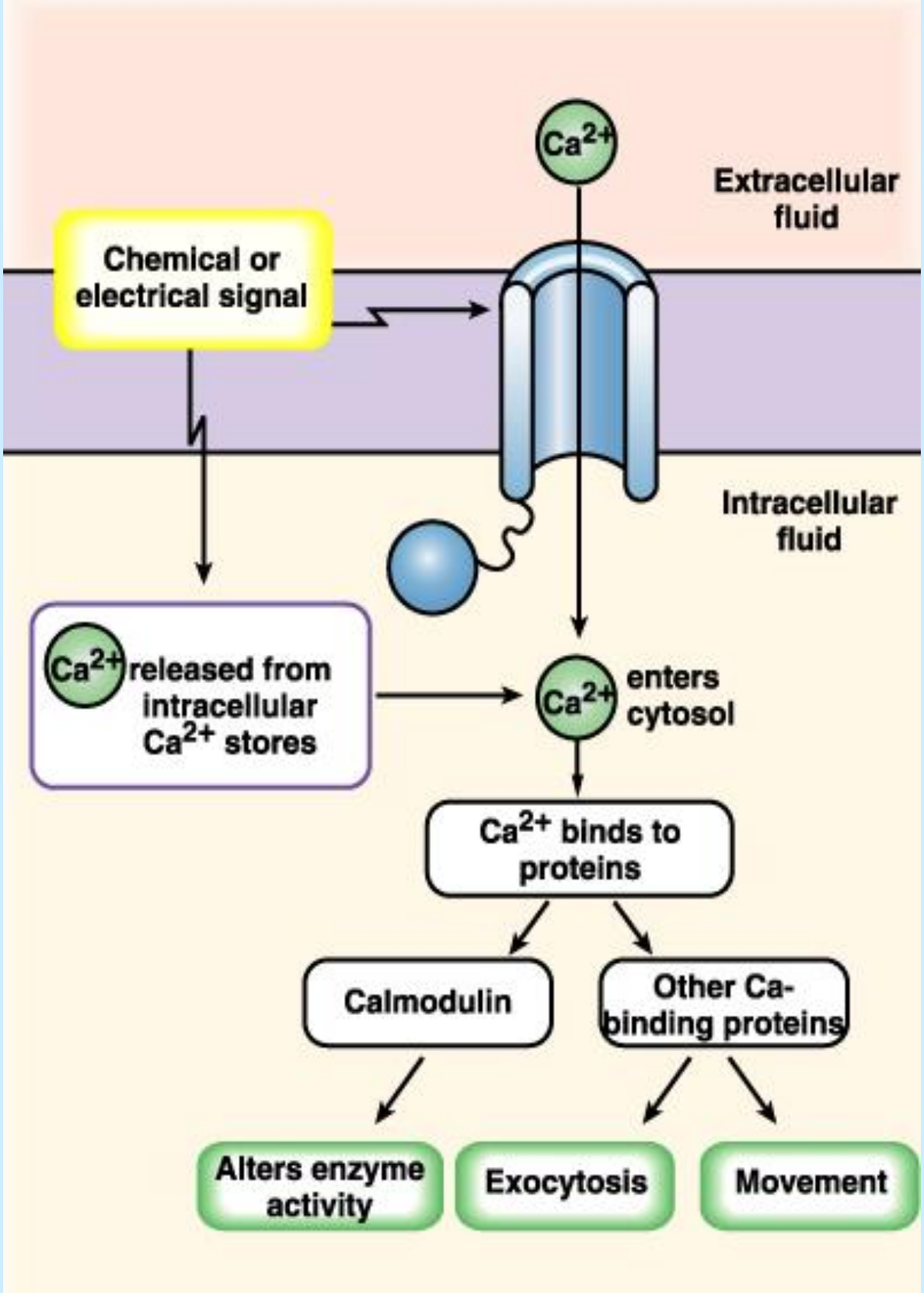

Signal molecule
Extracellular fluid
Membrane receptor
Signal transduction by effector proteins
Amplifier enzymes
alter
Ion channel
Second messenger molecules
Protein kinases
Increase intracellular Ca^{2+}
Phosphorylated proteins
Calcium-binding proteins
Cell response

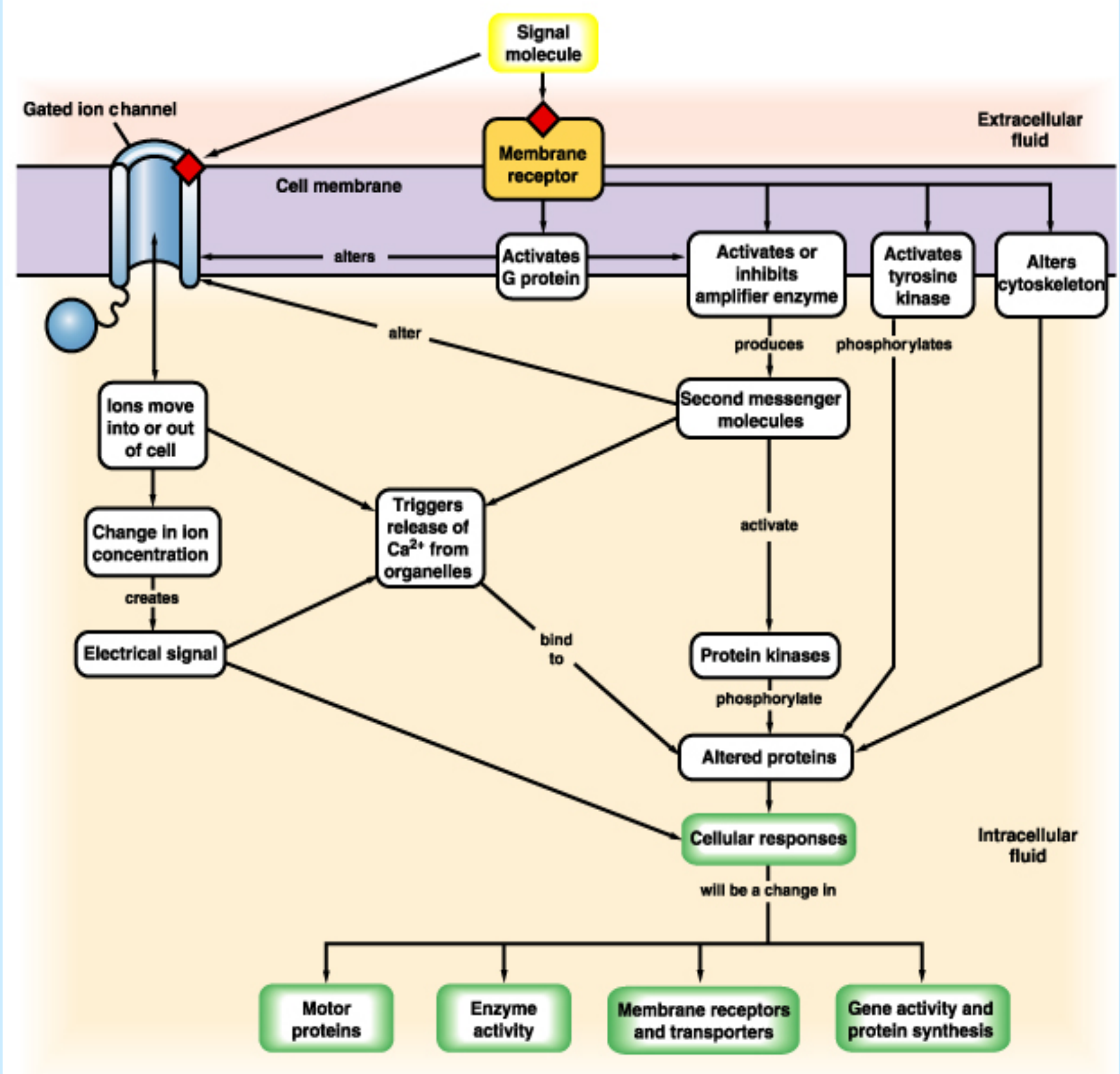

Initial stimulus
Inactive A
Active A
Inactive B
Active B
Inactive C
Active C
Substrate
Product

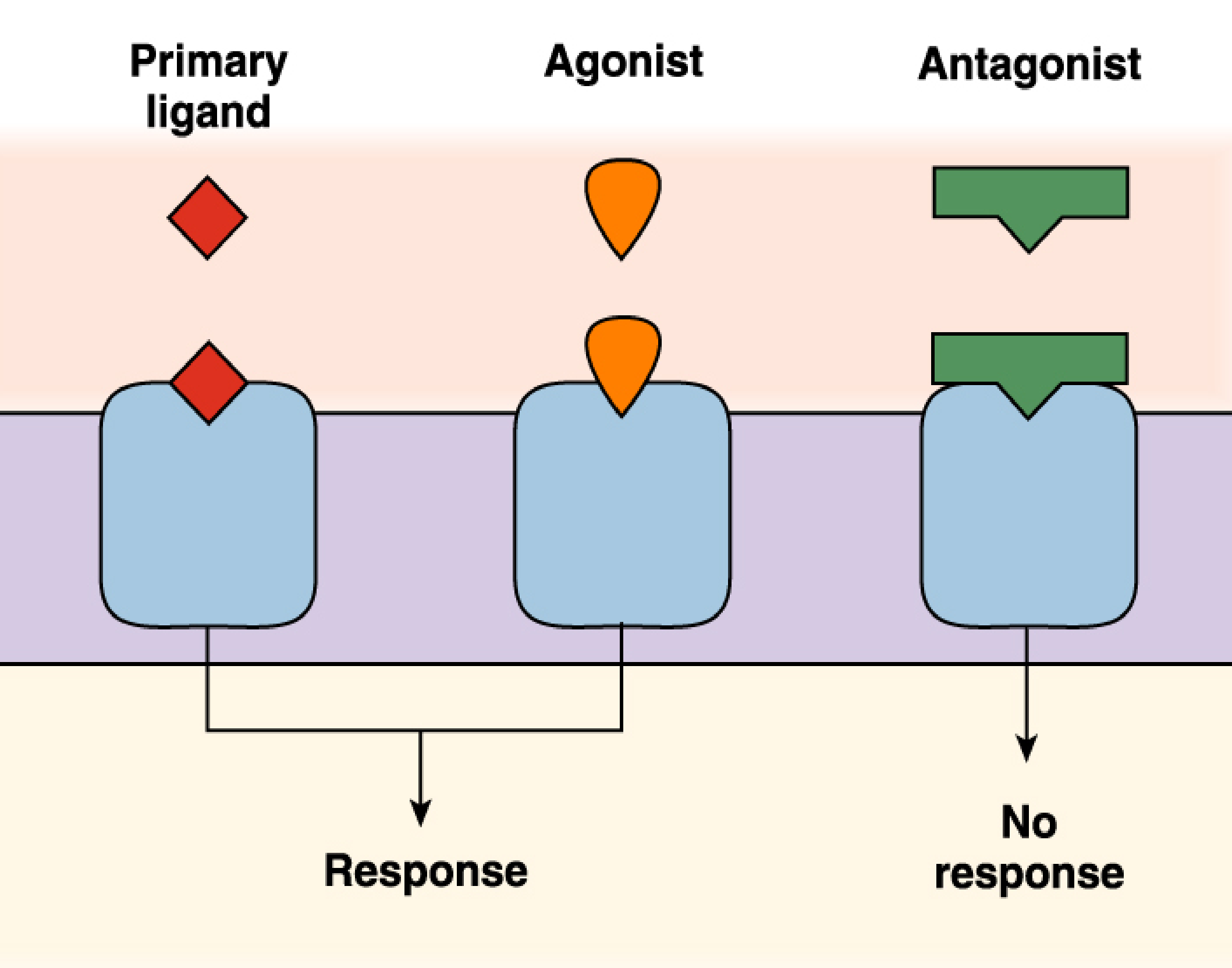

Ligand
ECF
L
R
TK
ICF
Active binding site
ATP + Protein
ADP + Protein P


One signal molecule
G-protein coupled receptor
Adenylyl cyclase
ATP
G protein
cAMP
Protein kinase A
Phosphorylated protein
Cell response

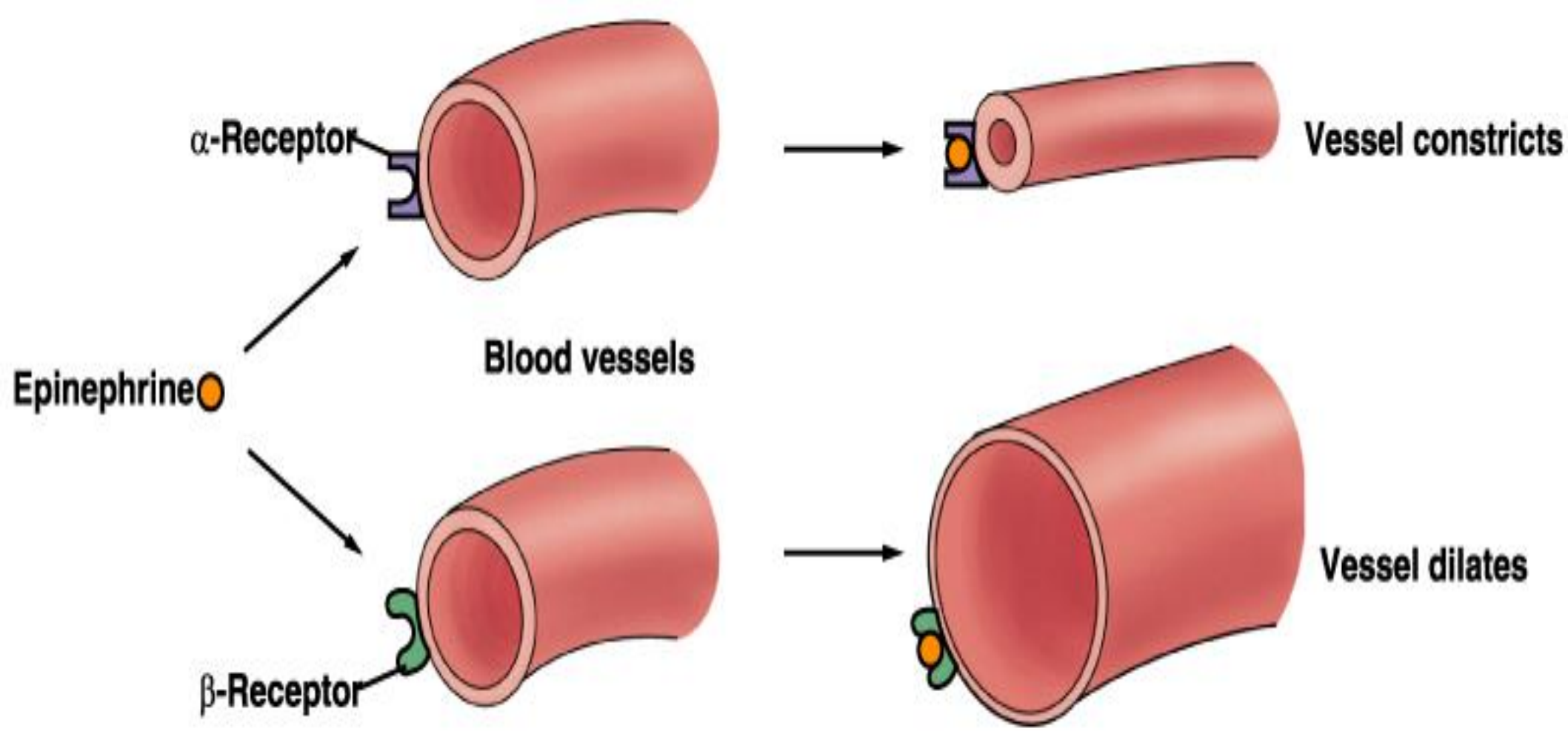

Extracellular fluid
Ligand
Membrane phospholipid
Cell membrane
PL-C
DAG
PK-C
Receptor
G protein
IP_3
Protein + P_i
Intracellular fluid
Ca^{2+} stores
ER
Ca^{2+}
Phosphorylated protein
Cell response
KEY
PL-C = phospholipase C
DAG = diacylglycerol
PK-C = protein kinase C
IP_3 = inositol triphosphate
ER = endoplasmic reticulum

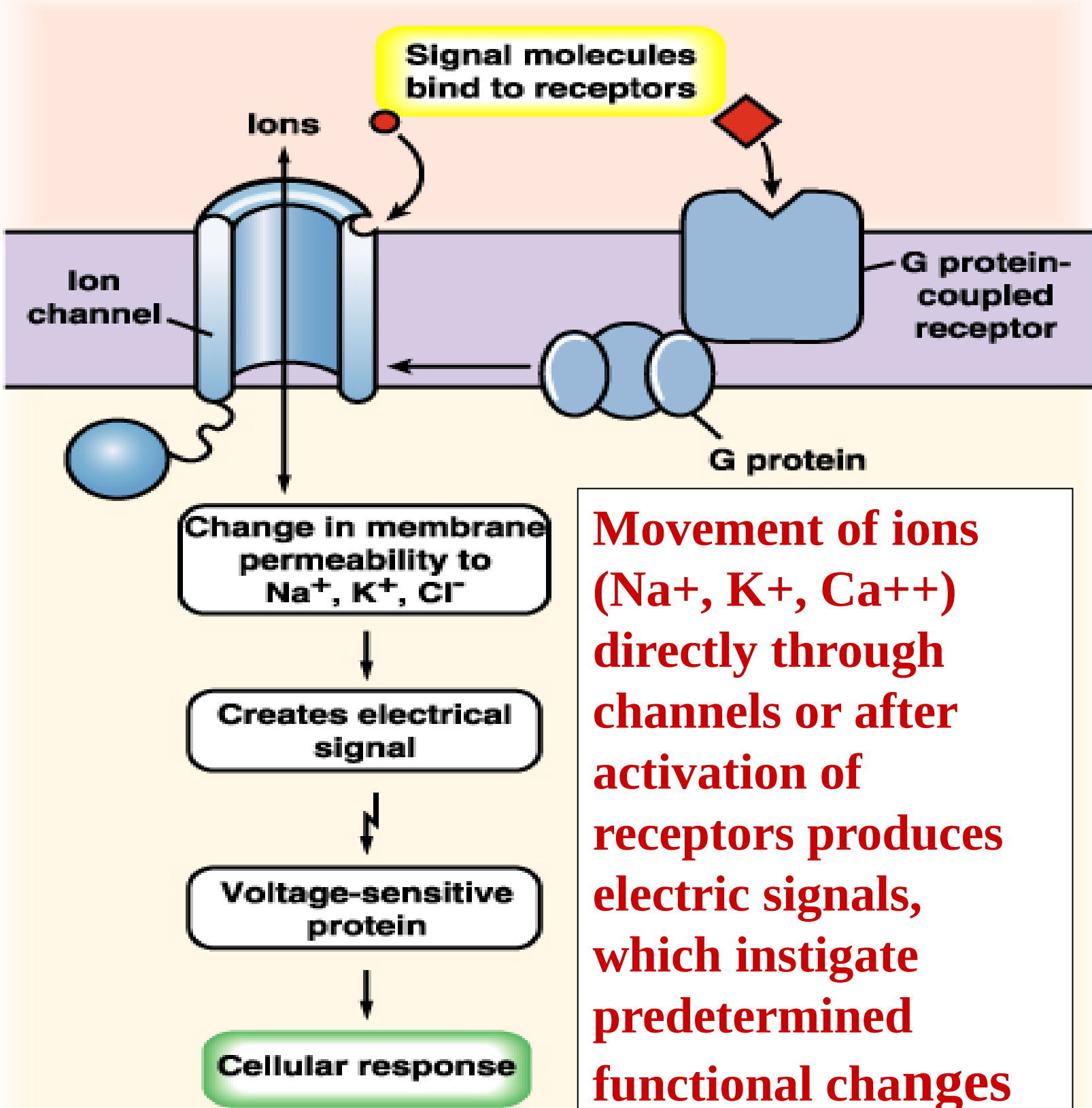

Ca^{2+}
Extracellular fluid
Chemical or electrical signal
Intracellular fluid
Ca^{2+} released from intracellular Ca^{2+} stores
Ca^{2+} enters cytosol
Ca^{2+} binds to proteins
Calmodulin
Other Ca-binding proteins
Alters enzyme activity
Exocytosis
Movement


Signal molecule
Gated ion channel
Extracellular fluid
Membrane receptor
Cell membrane
alters
Activates G protein
Activates or inhibits amplifier enzyme
Activates tyrosine kinase
Alters cytoskeleton
alter
produces
phosphorylates
Second messenger molecules
Ions move into or out of cell
Triggers release of Ca^{2+} from organelles
Change in ion concentration
activate
creates
Electrical signal
bind to
Protein kinases
phosphorylate
Altered proteins
Cellular responses
Intracellular fluid
will be a change in
Motor proteins
Enzyme activity
Membrane receptors and transporters
Gene activity and protein synthesis


Primary ligand
Agonist
Antagonist
Response
No response

An agonist may activate two types of receptors with two different actions





Movement of ions (Na+, K+, Ca++) directly through channels or after activation of receptors produces electric signals, which instigate predetermined functional changes

1.4. Methods

Scientific Methods in Physiology

- What are the steps?

- Observation
- Hypothesis
- Experimentation
- Replication of results
- Theory

Method (⇐ μετά + οδός)

= follow someone on the road,

= examining a subject with some principles and rules of procedure

= the scientific way of research = the proper and logical way of achieving a goal

e.g. EEG, MEG, ECG

A method includes various

Techniques (⇐ τέχνη ⇐ τίκτω)

= a particular set of processes with which we face a specific problem in the framework of a general methodology and under specific circumstances

e.g. epidermal, epicortical, intracranial, extra- or intracellular recording of brain generated electrical potentials – evoked potentials, 3D visualization of EEG current sources in the framework of EEG METHOD

Experimentation

Independent variable – controlled by experimenter.

Dependent variable – responds to independent variable, i.e. gives experimental results.

Control group – same as experimental group except that manipulated variable is not manipulated. Purpose?

Experimental Design

Crossover study – each subject acts as both experimental and control group.

Blind study – subjects are not informed.

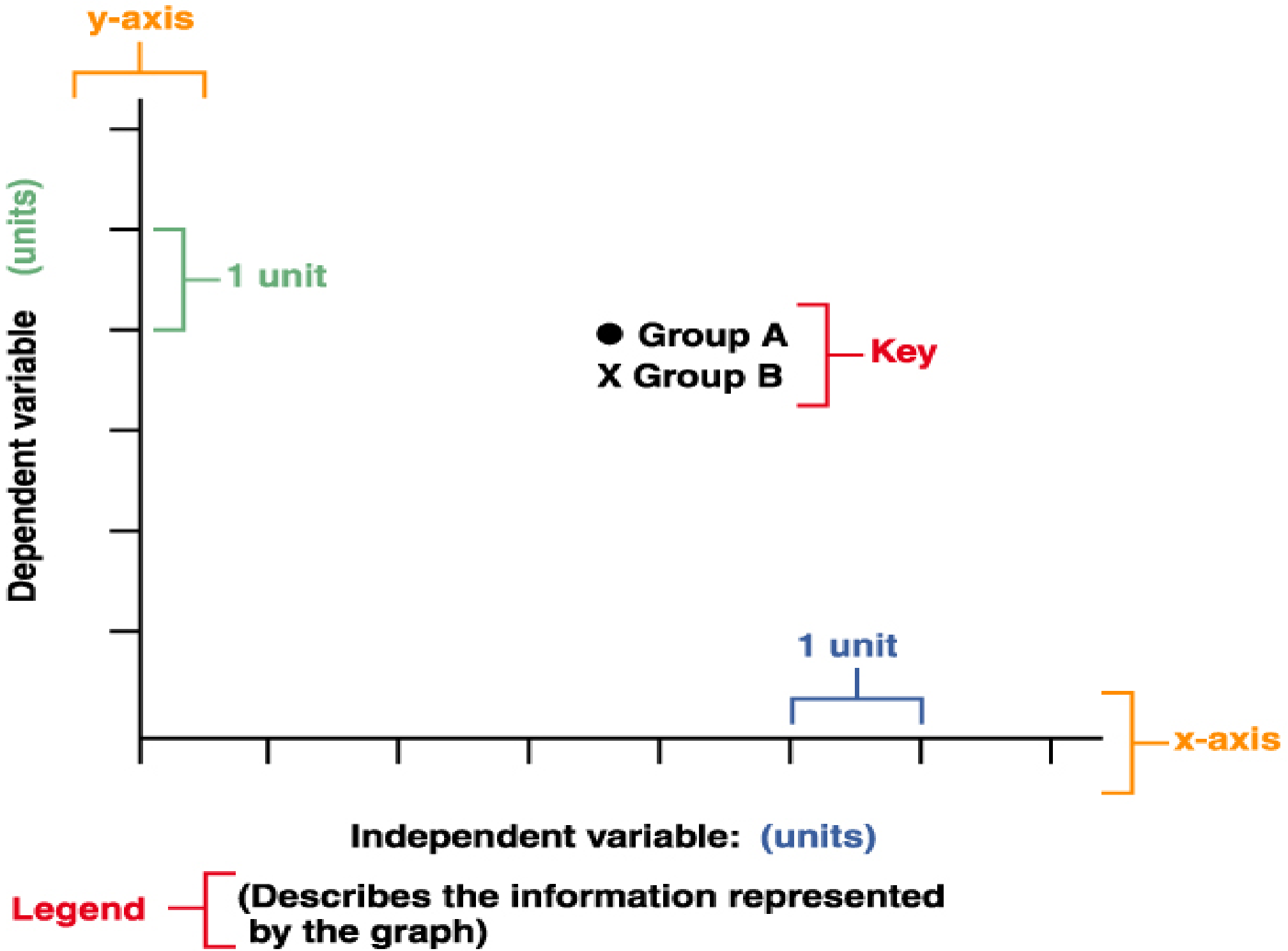
Double-blind study – subjects and experimenter are not informed.

Double-blind crossover study – same group for experiment and control, but double-blind.

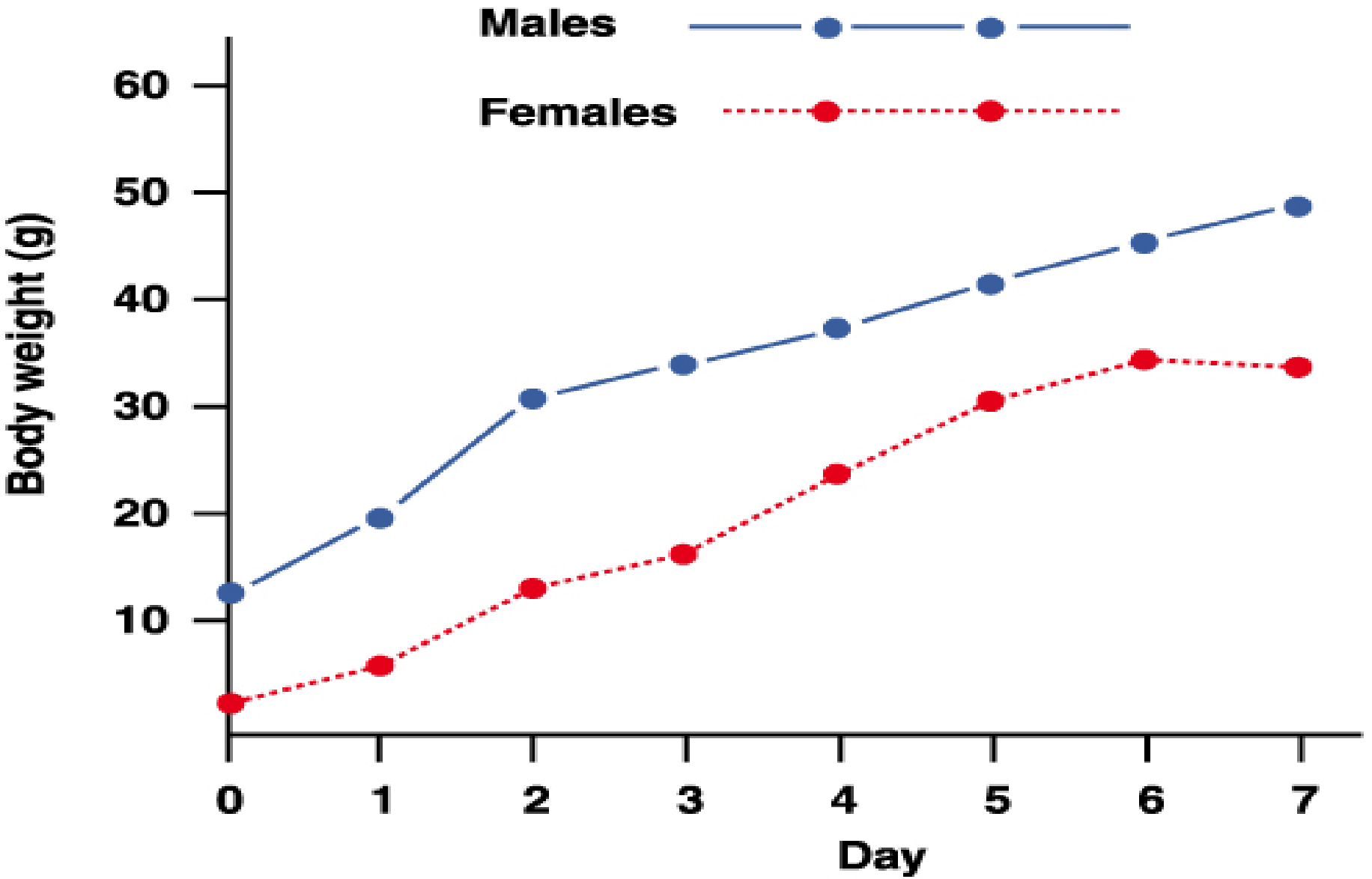
Placebo effect – changes that occur because subjects are participating in the experiment.

Ethical Issues. i.e. when humans are used as experimental subjects

The standard features of a graph include units and labels on the axes, a key, and a figure legend.

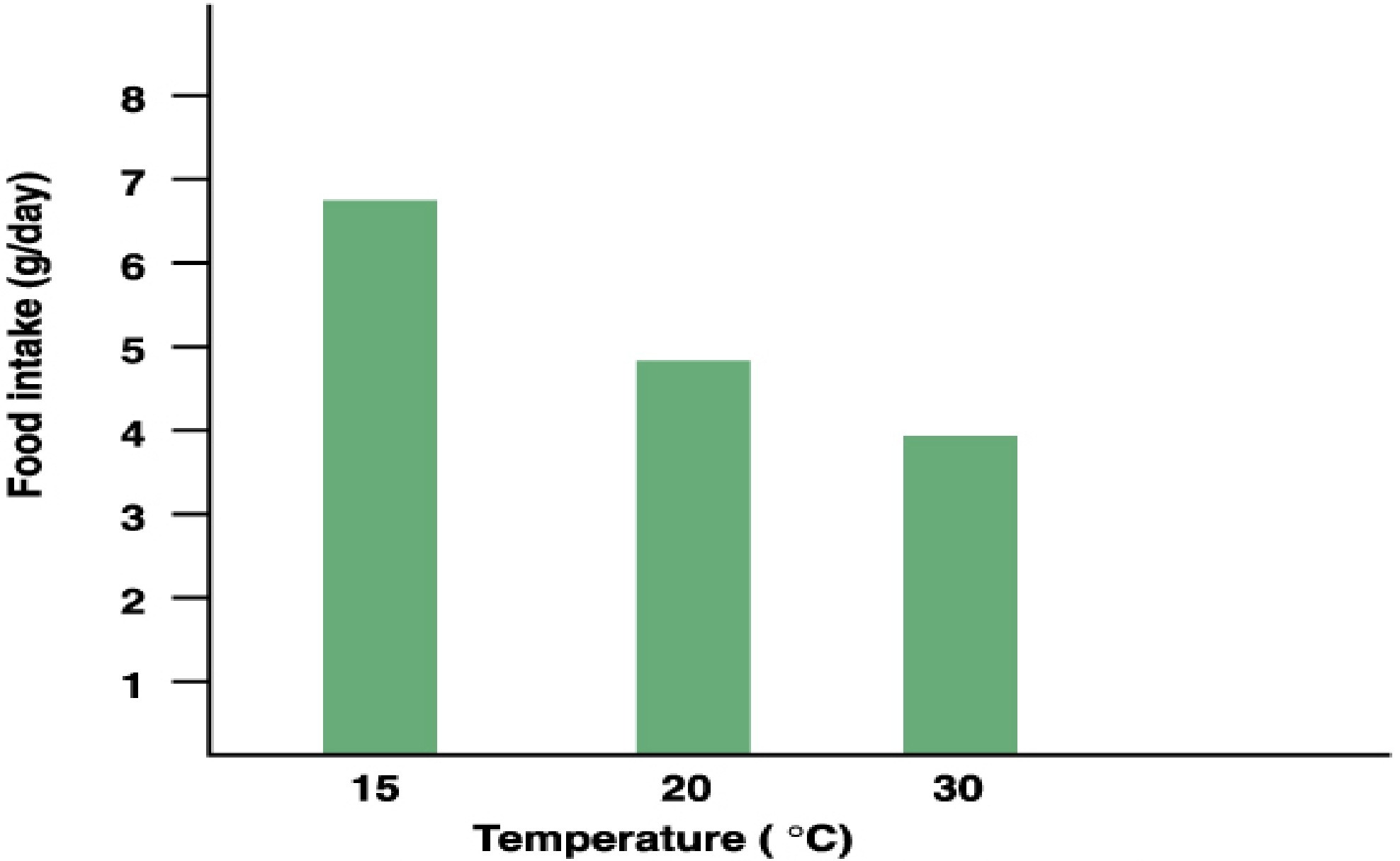


Line graph.The x-axis frequently represents time; the points represent individual observations. The points may be connected by lines, in which case the slope of the line between two points shows the rate at which the variable changed.



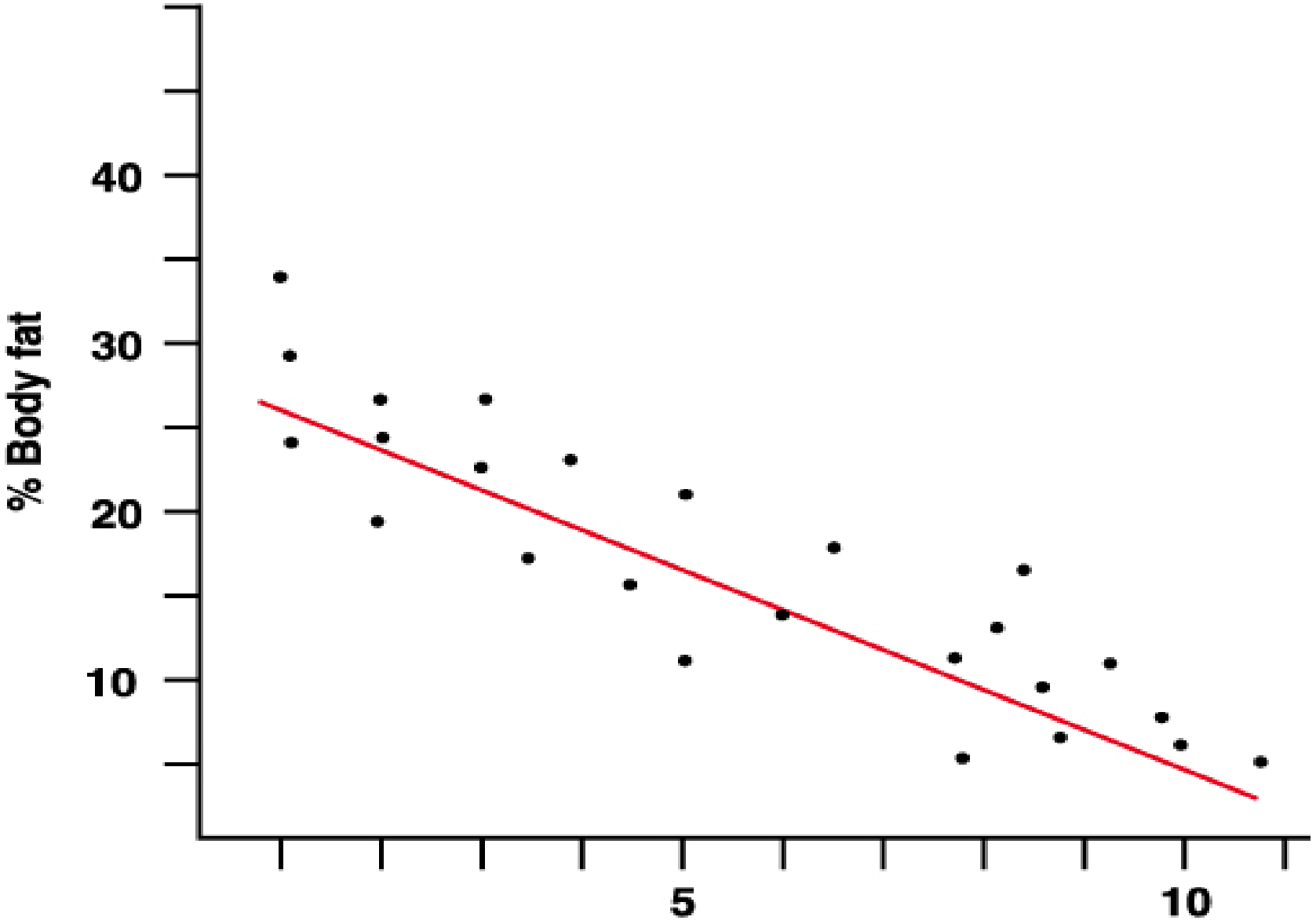
Male and female mice were fed a standard diet and weighed daily.

Bar graph.Each bar shows a fixed number or amount of a variable. The bars are lined up side by side along one axis so that they can be easily compared with one another. Scientific bar graphs traditionally have the bars running vertically.



Canaries were acclimated to the temperatures shown, and their food intake was monitored for three weeks.

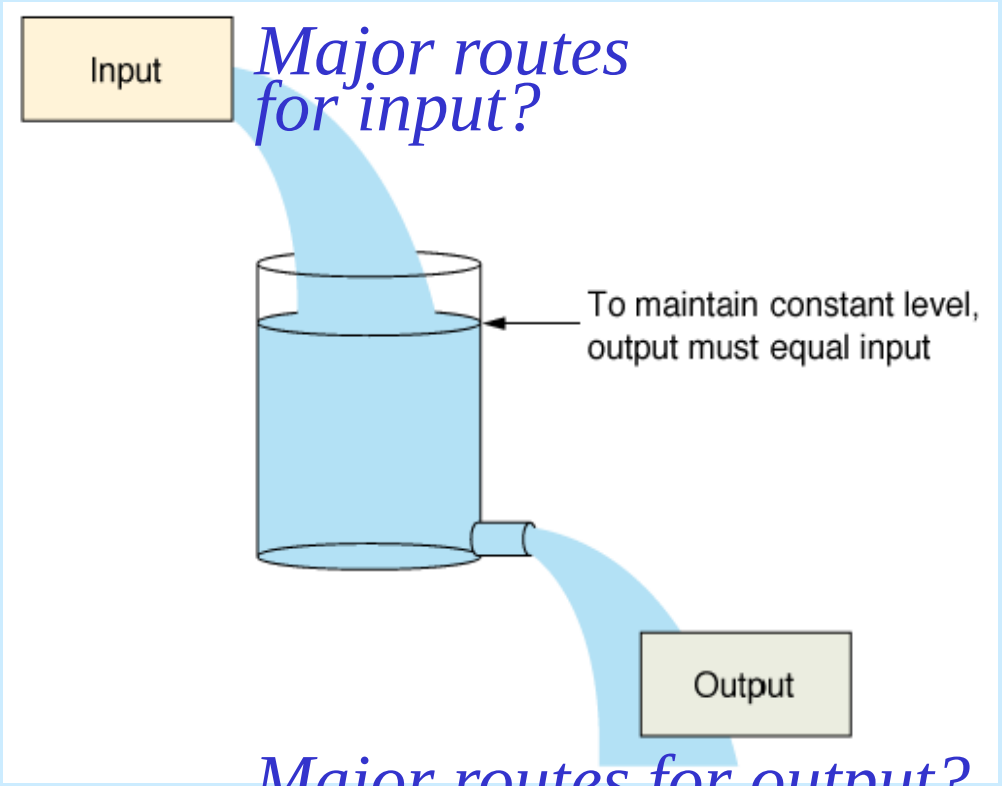
Scatter plot.Each point represents one member of a test population. The individual points of a scatter plot are never connected by lines, but a best fit line may be estimated to show a trend in the data, or better yet, the line may be calculated by a mathematical equation.



Male college students participated in a ten-week weight training class.

❸ *Energy Flow and Law of Mass Balance*

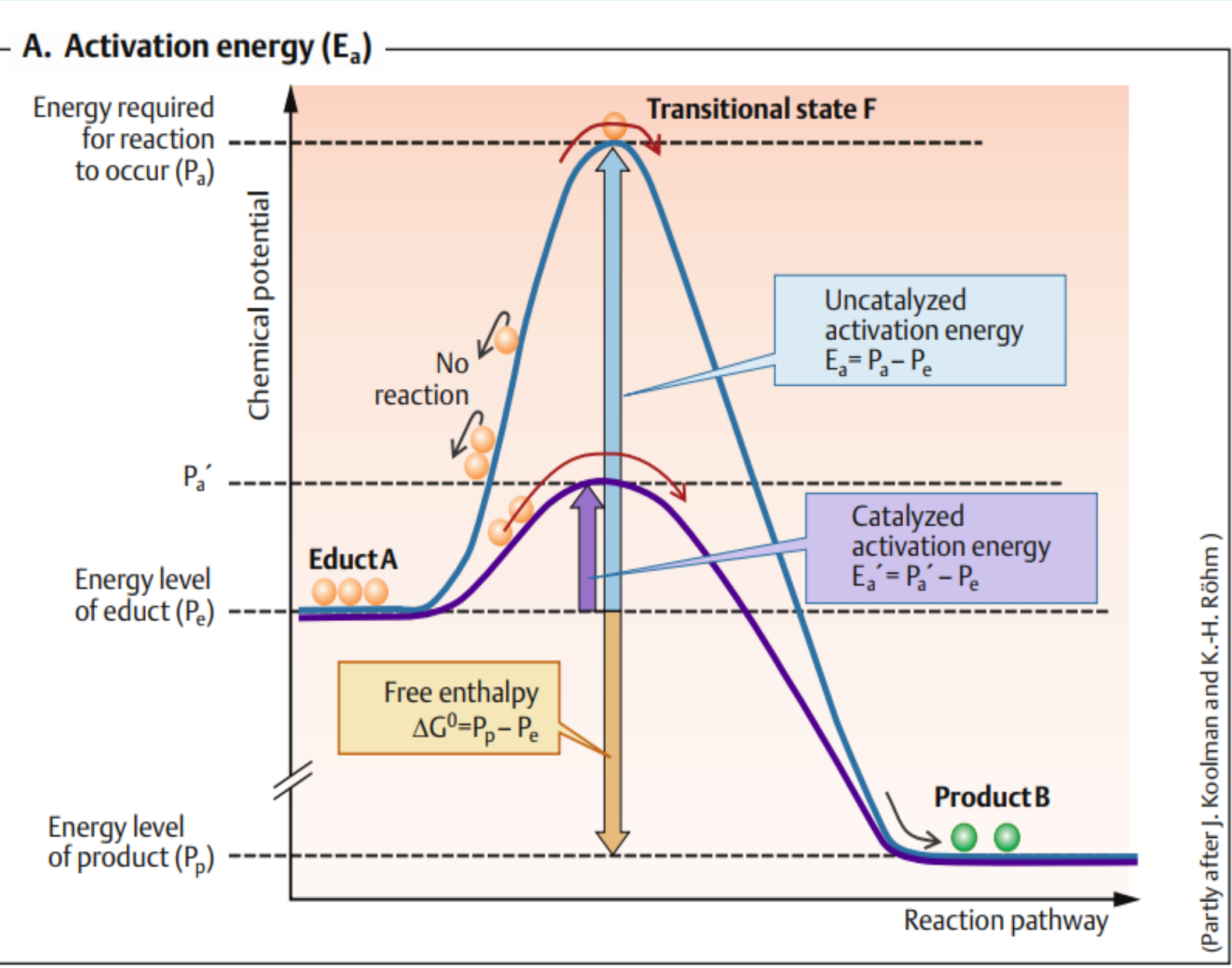
All living processes require constant input of energy
Where from? –
How is it stored?
How is it used to do work?

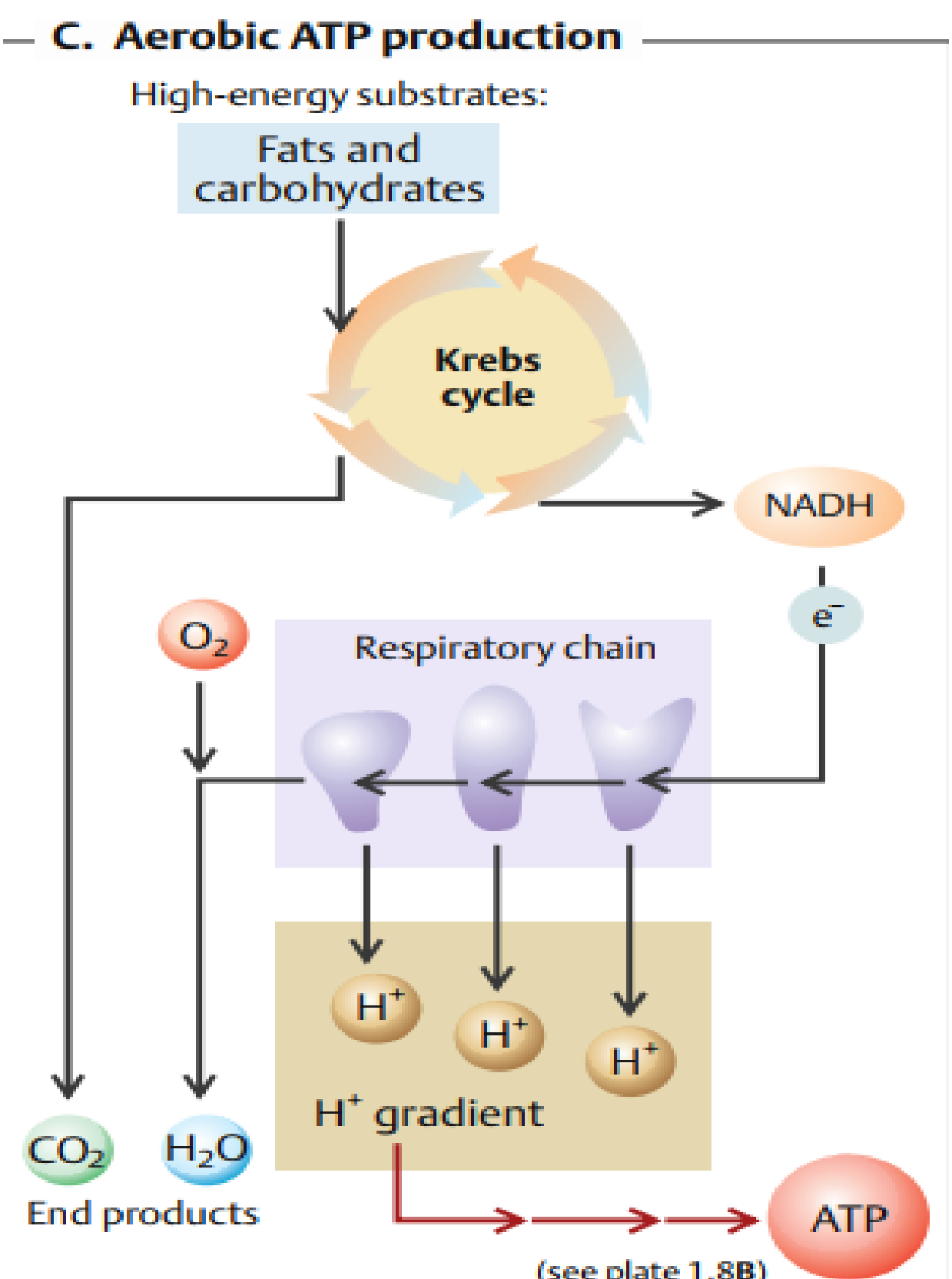


1.5. Energy

Total amount of substance in body = intake + production - output

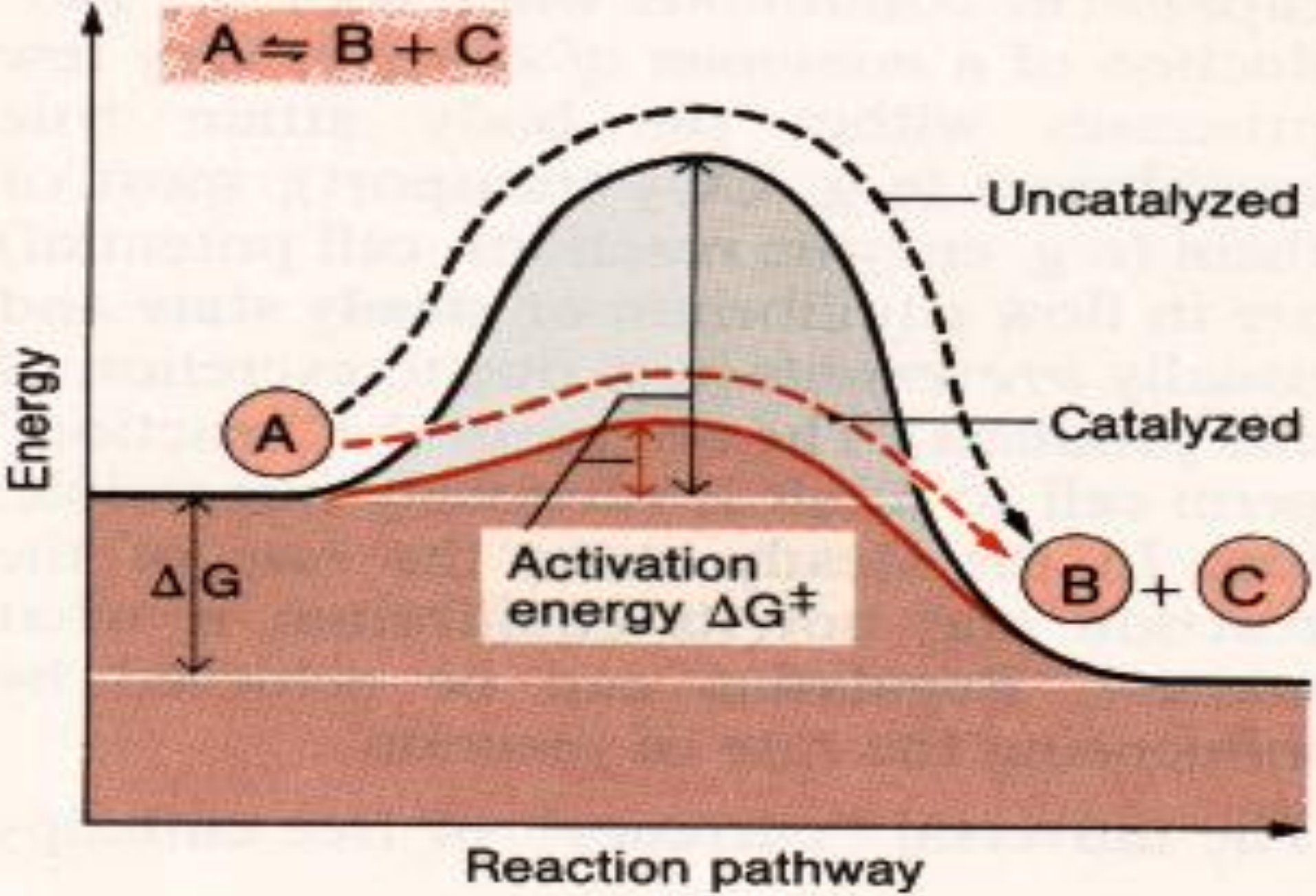
What substances are maintained through law of mass balance?

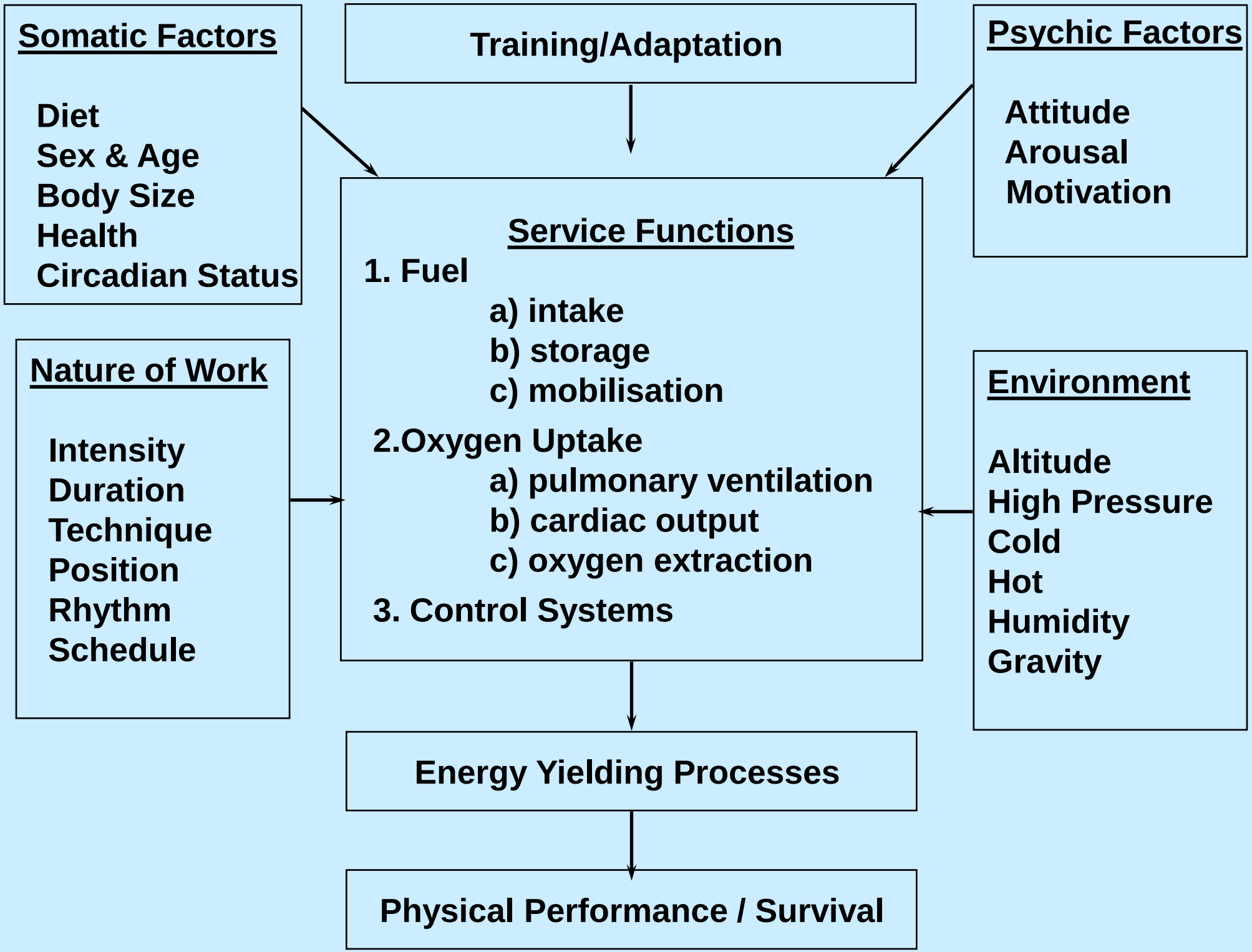

A. Activation energy (E_a)
Energy required for reaction to occur (P_a)
Chemical potential
Transitional state F
Uncatalyzed activation energy
$E_a = P_a - P_e$
No reaction
P_a'
Catalyzed activation energy
$E_a' = P_a' - P_e$
Educt A
Energy level of educt (P_e)
Free enthalpy
$\Delta G^0 = P_p - P_e$
Product B
Energy level of product (P_p)
Reaction pathway
(Partly after J. Koolman and K.-H. Röhm)



The free energy liberated upon hydrolysis of ATP is used to drive hundreds of reactions within the body, including the active transmembrane transport of various substances, protein synthesis, and muscle contraction. According to the laws of thermodynamics, the expenditure of energy in all of these reactions leads to increased order in living cells and, thus, in the organism as a whole. **Life is therefore characterized by the continuous reduction of entropy associated with a corresponding increase in entropy in the immediate environment and, ultimately, in the universe.**

Biochemical reactions are dependent on energy




Somatic Factors
Diet
Sex & Age
Body Size
Health
Circadian Status
Training/Adaptation
Psychic Factors
Attitude
Arousal
Motivation
Service Functions
1. Fuel
a) intake
b) storage
c) mobilisation
2.Oxygen Uptake
a) pulmonary ventilation
b) cardiac output
c) oxygen extraction
3. Control Systems
Nature of Work
Intensity
Duration
Technique
Position
Rhythm
Schedule
Environment
Altitude
High Pressure
Cold
Hot
Humidity
Gravity
Energy Yielding Processes
Physical Performance / Survival

Energy Yielding Processes

1. Fuel

- **a) intake**
- **b) storage**
- **c) mobilisation**

2.Oxygen Uptake

- **a) pulmonary ventilation**
- **b) cardiac output**
- **c) oxygen extraction**

The ability of muscles to transform chemical energy to mechanical energy depends on the capacity of integrative physiological systems to deliver fuel and oxygen to the muscle cells.

Energy Metabolism in Cells

Carbohydrate ⇒ Sugars
Fat ⇒ Fatty acids
Protein ⇒ Amino acids
} ⇒ ATP

$$ATP + H_2O \leftrightarrow ADP + P_i + H^+ + 7\ kcal/mole$$

Anaerobic metabolism

Glycolysis

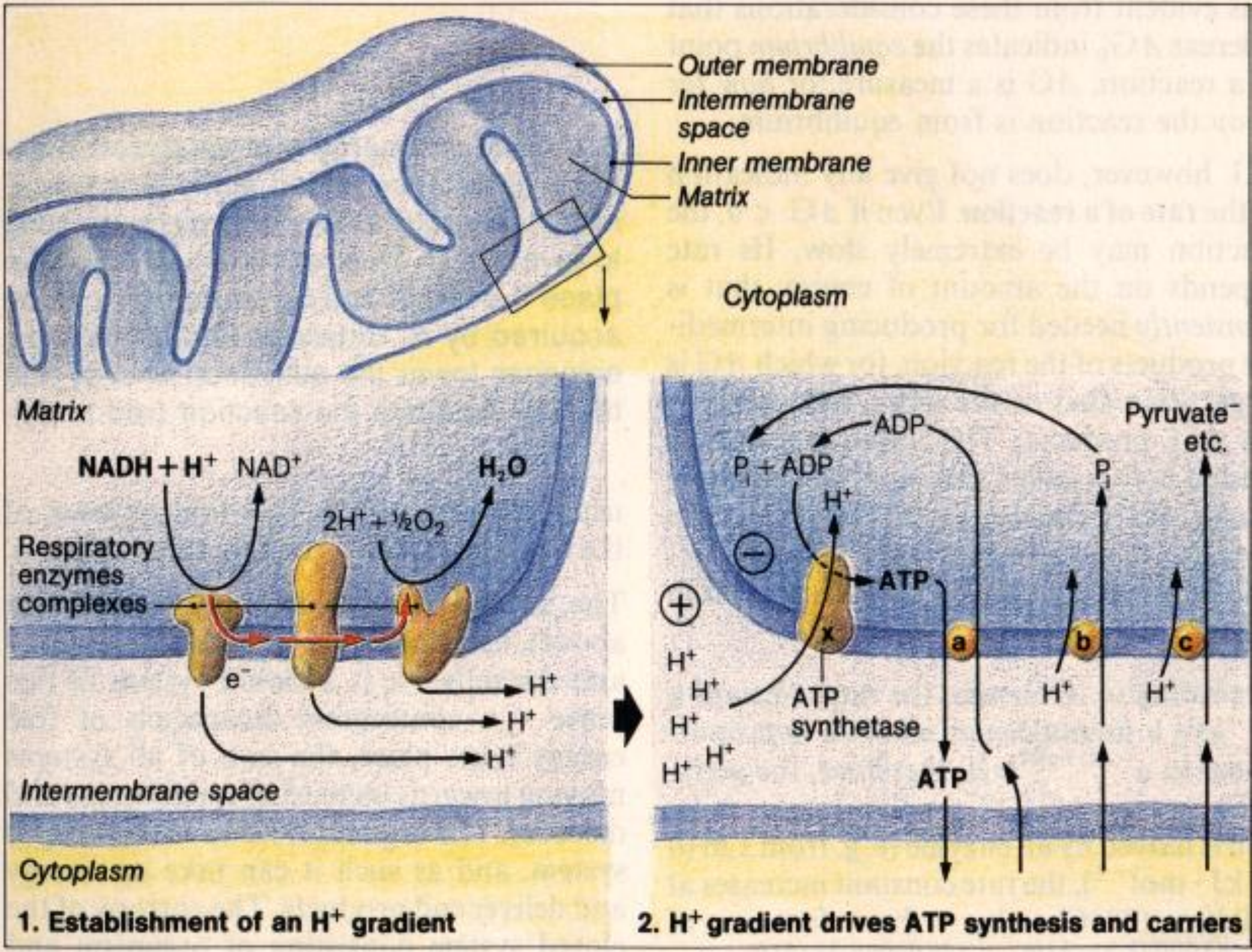
glucose ⇒ glucose-6-phosphate ⇒ 2 pyruvate + 2 ATP

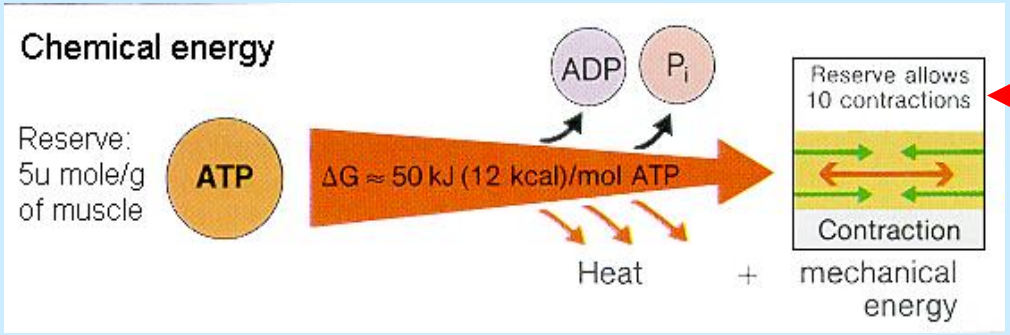
- Reactions take place in cytoplasm
- In absence of O_2 yields 2 ATP molecules/glucose

Aerobic metabolism

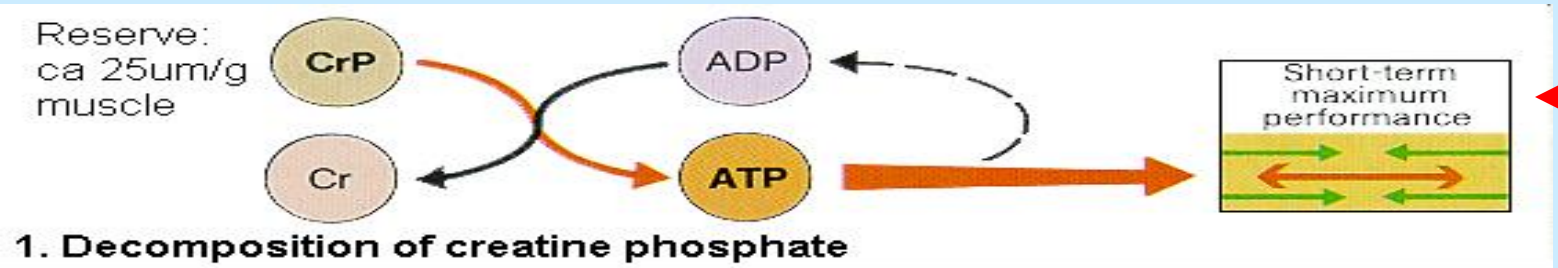
Oxidative phosphorylation

- Reactions take place in mitochondria in presence of O_2
- Formation of H_2O from H^+ (Krebs cycle) and O_2 ⇒ ATP
- Yields 38 ATP molecules/glucose

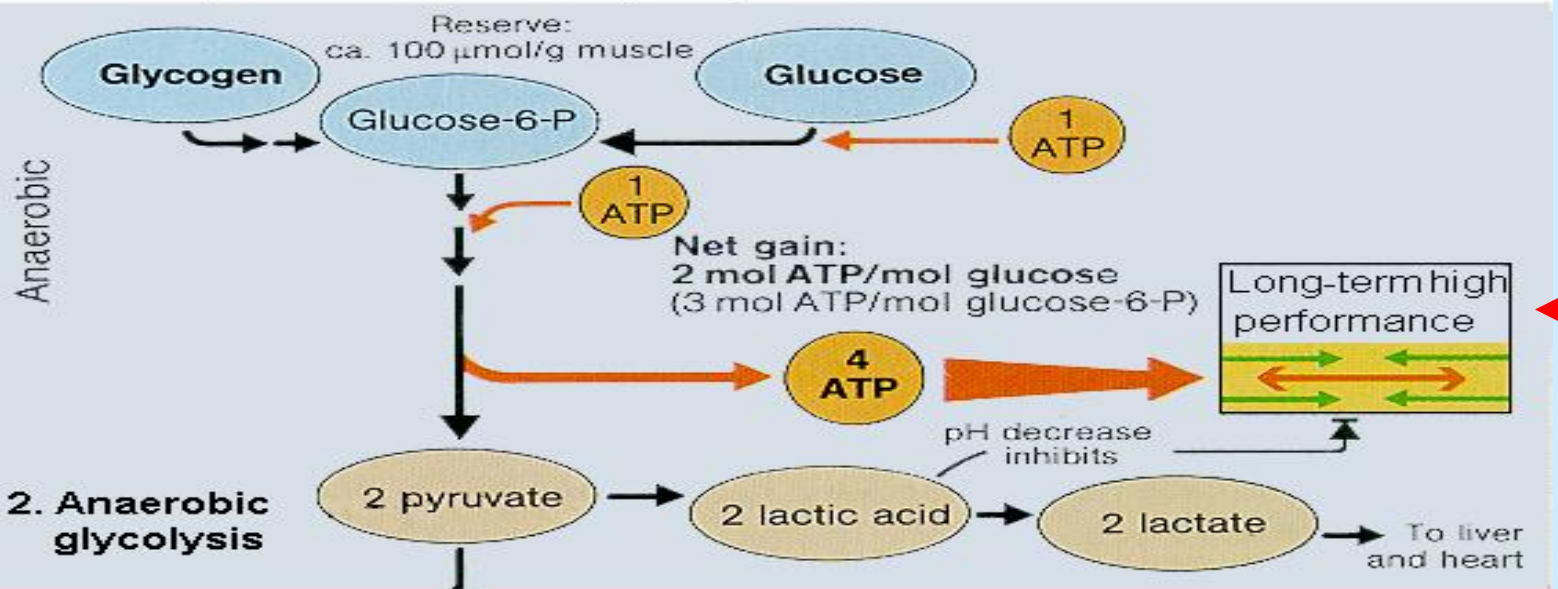

Outer membrane
Intermembrane space
Inner membrane
Matrix
Cytoplasm
Matrix
NADH + H+
NAD+
H2O
2H+ + ½O2
Respiratory enzymes complexes
e−
H+
H+
H+
Intermembrane space
Cytoplasm
1. Establishment of an H+ gradient
ADP
Pyruvate− etc.
Pi + ADP
Pi
H+
ATP
x
a
b
c
H+
H+
H+
H+
H+
H+
ATP synthetase
ATP
2. H+ gradient drives ATP synthesis and carriers



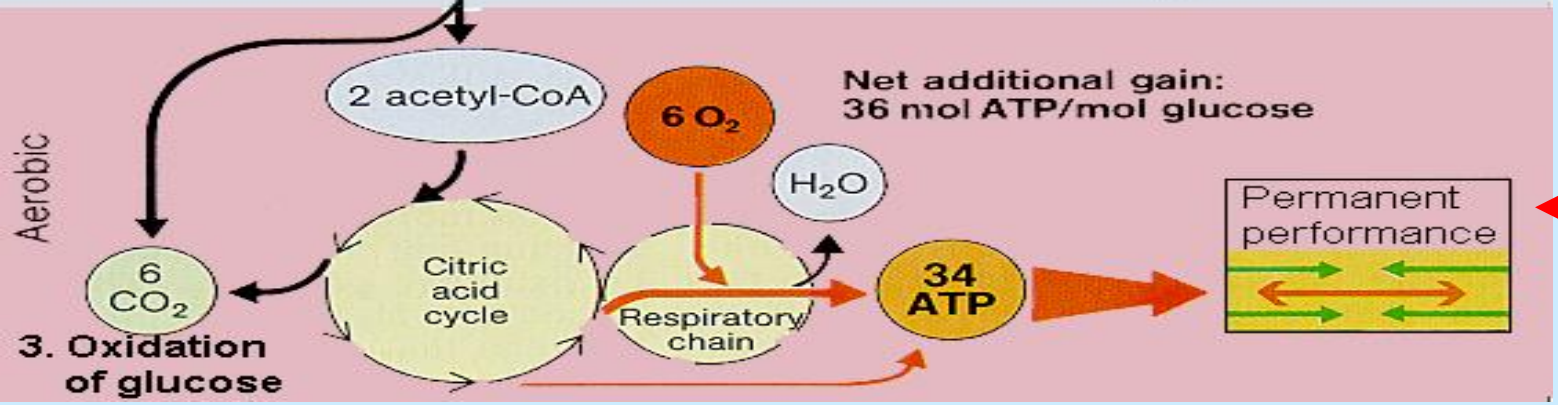
10 contractions



50 contractions



400 contractions



Unlimited

Having studied the mechanisms of survival … let us **define life**

At the beach you spot a starfish.
How would you discover whether it is dead or alive?

- **Responsiveness –** alive organisms respond to changes in their environment
- **Adaptability –** Alive organisms have the ability to undergo long term changes in order to adapt to their environment.
- …

What is life?

LIFE is the property or capacity distinguishing alive organisms from dead ones and from inert matter and which is expressed with endogenous functions, like…

- metabolism
- reproduction
- development
- responsiveness to stimuli
- adaptation to the environment
- …

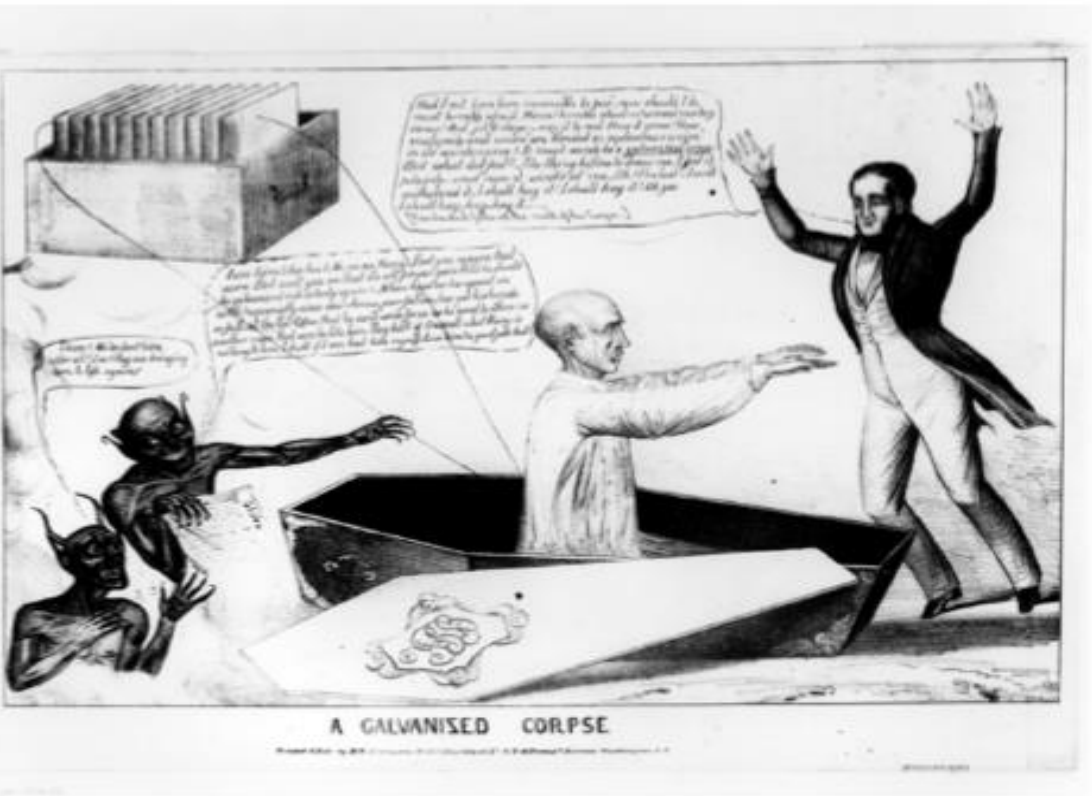
But … it is not always so easy to define life

i.e. a car fulfills many of these requirements …

- It responds to orders from the wheel and the brake
- it moves
- it consumes gasoline and transforms it to energy.

Is a virus alive?

The discovery of electrical excitability of tissues from a dead animal, produced the wrong impression than a live human can be created by assembling together all dead body parts and subjecting them to a strong electric shock. It was a fake news which lead to great social concerns , **What was the moral issue?**



Look, it's moving. It's alive, it's alive, it's alive. It's moving
It's alive, it's alive, it's alive, it's alive, it's alive!