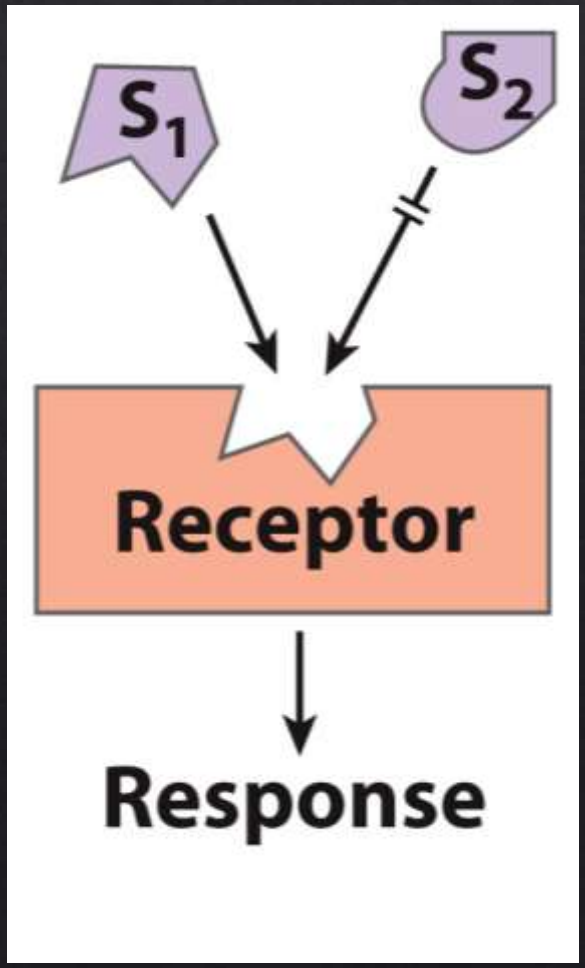
Biosignaling & metabolism

Signal transduction

Information (signal) is detected by a specific receptor and transformed into a cellular response. It is always a chemical process.

Types of signals include:

- antigens
- hormones
- neurotransmitters
- light
- touch
- pheromones



Picture from Nelson&Cox

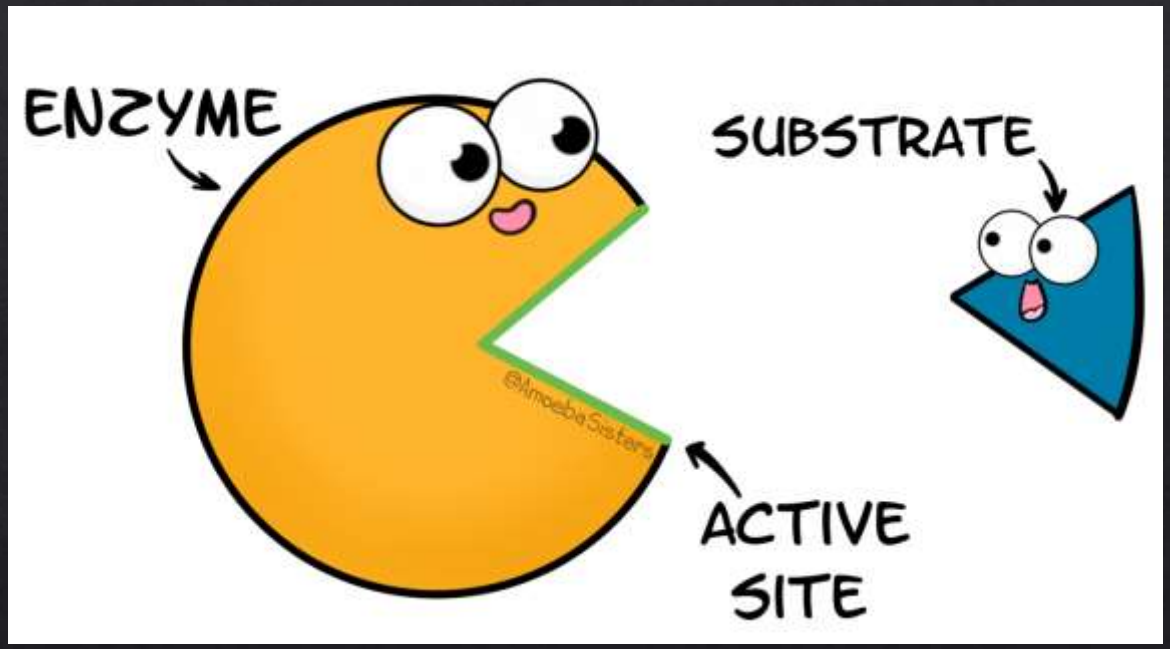
Specificity in signal transduction

3 factors:

- High affinity receptor-signal
- Cooperativity in the ligand – receptor interaction
- Enzyme cascades

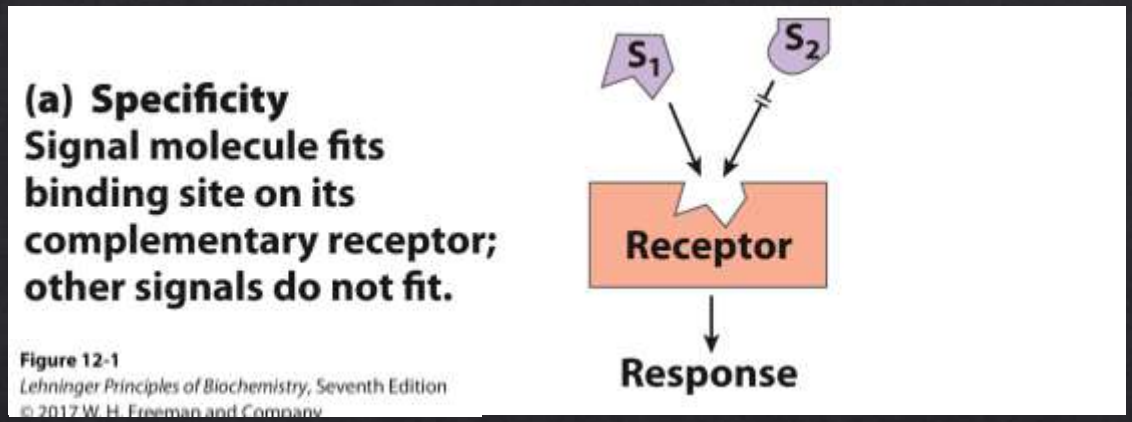
6 features

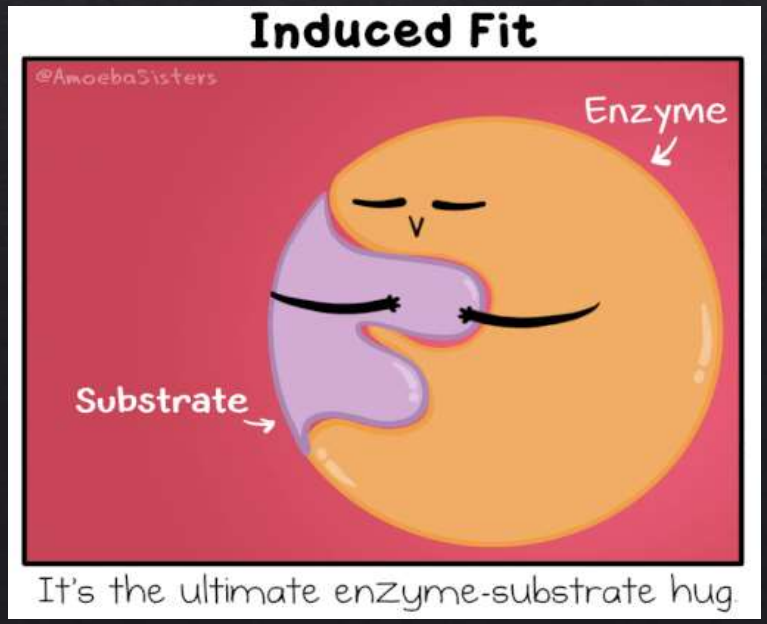
10 basic types of protein components



Specificity in signal transduction

Affinity receptor-signal

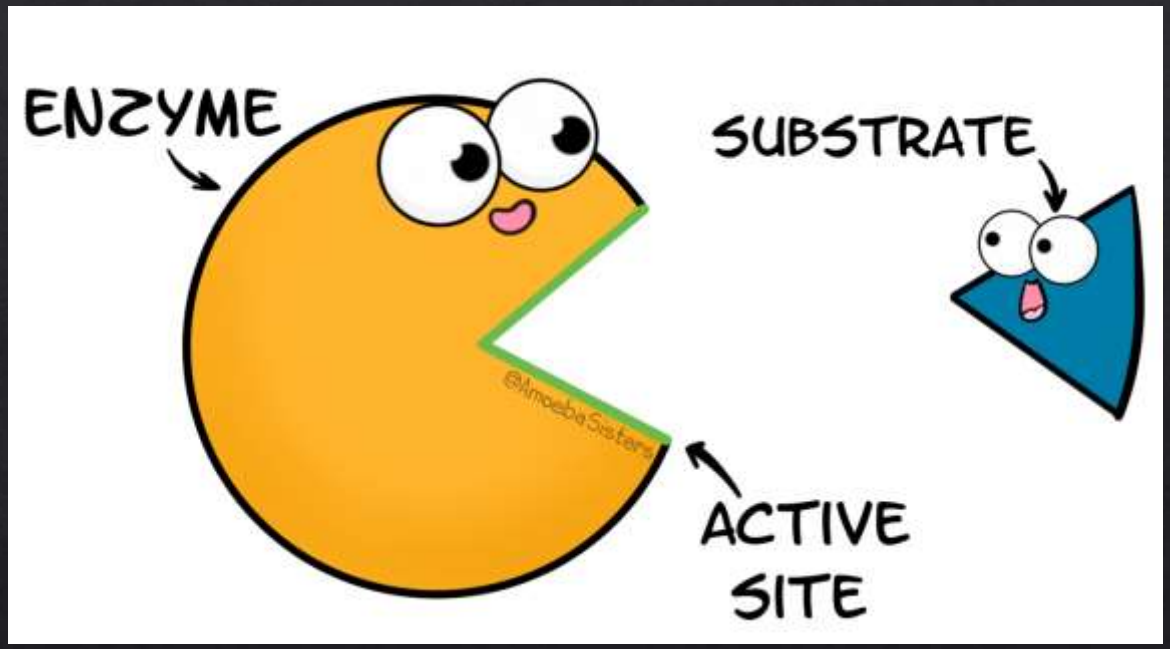




Specificity in signal transduction

Cooperativity:

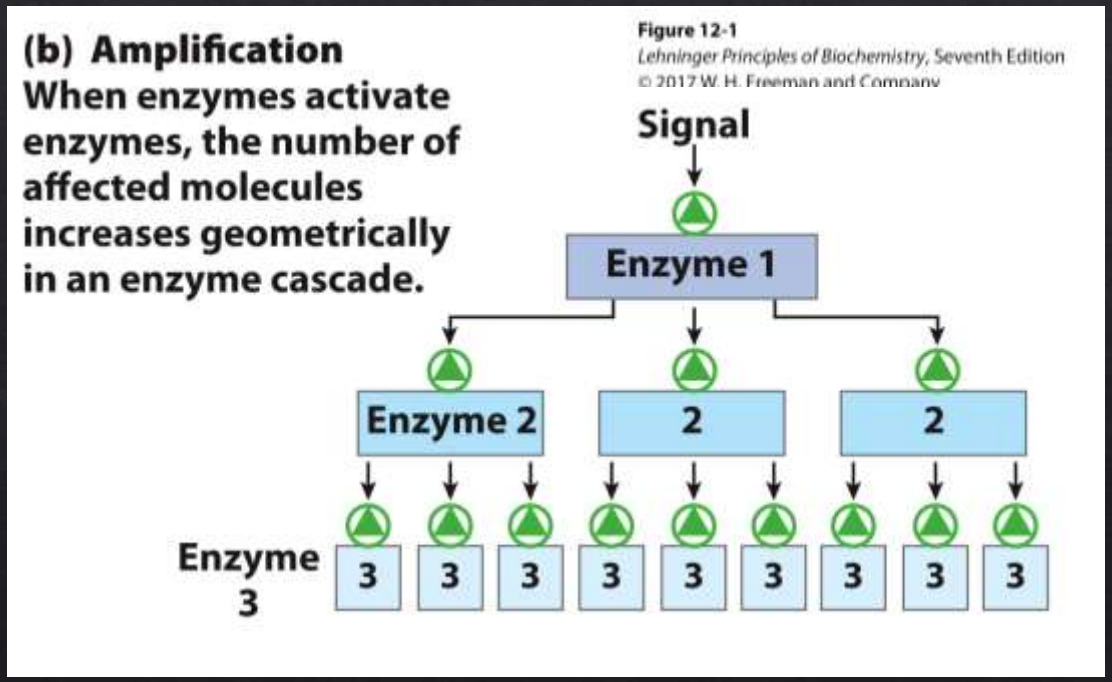
- Large changes in receptor activation with small changes in ligand concentration



Specificity in signal transduction

Enzyme cascade:

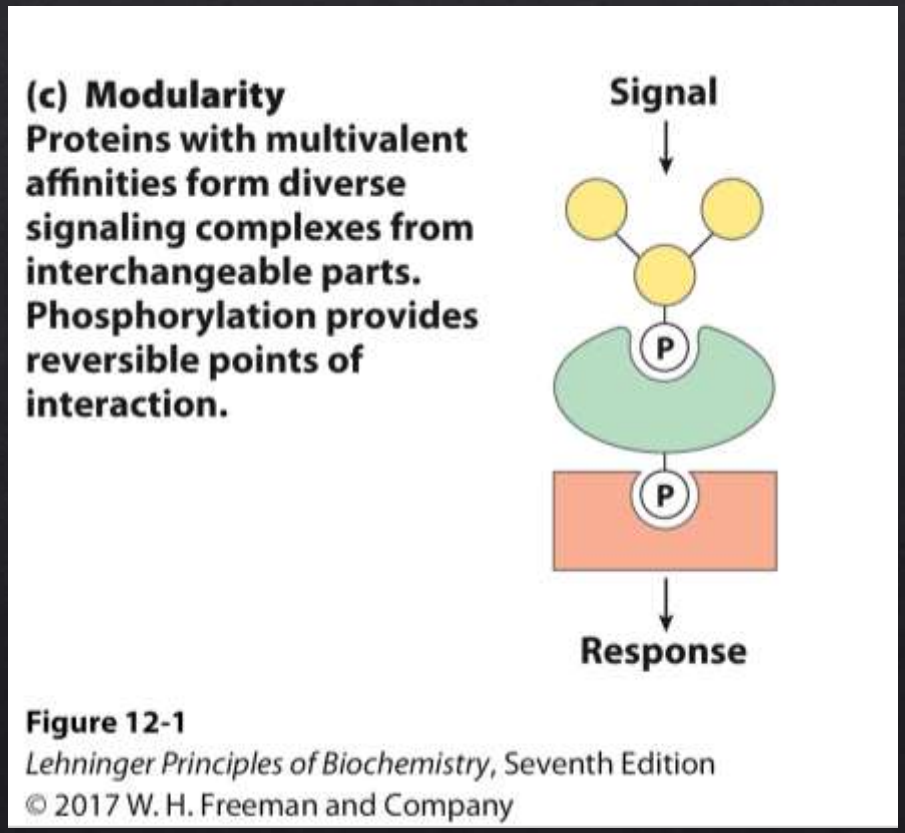
- Enzyme activated by a signal receptor
- Activated enzyme catalyzes the activation of another enzyme, etc.
- Can produce amplification of several orders of magnitude in millisec
- Response to signal should be terminated, effects proportional to stimulus



Specificity in signal transduction

Modular response:

- Signaling proteins can recognize multiple other proteins
- Signaling proteins can be "combined"
- Many of the protein-protein interactions sites are disordered
- Scaffold proteins can bring several enzymes together



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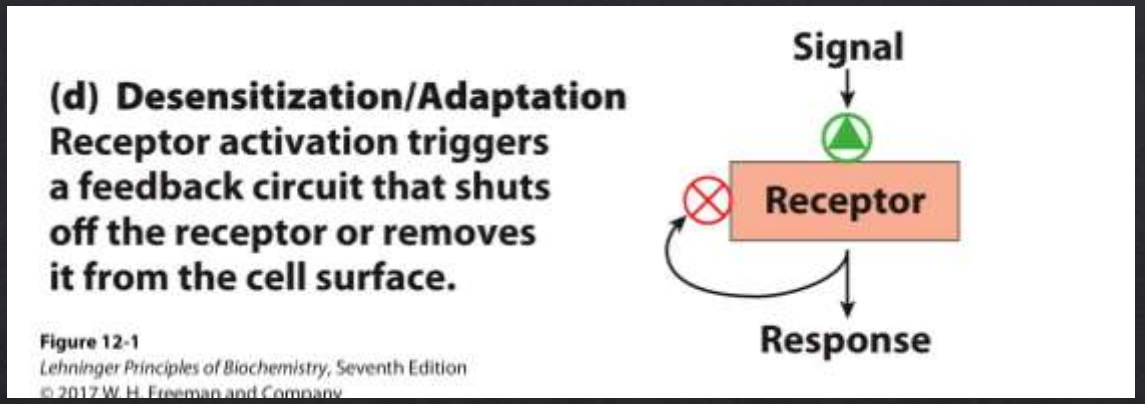
Specificity in signal transduction

Desensitization:

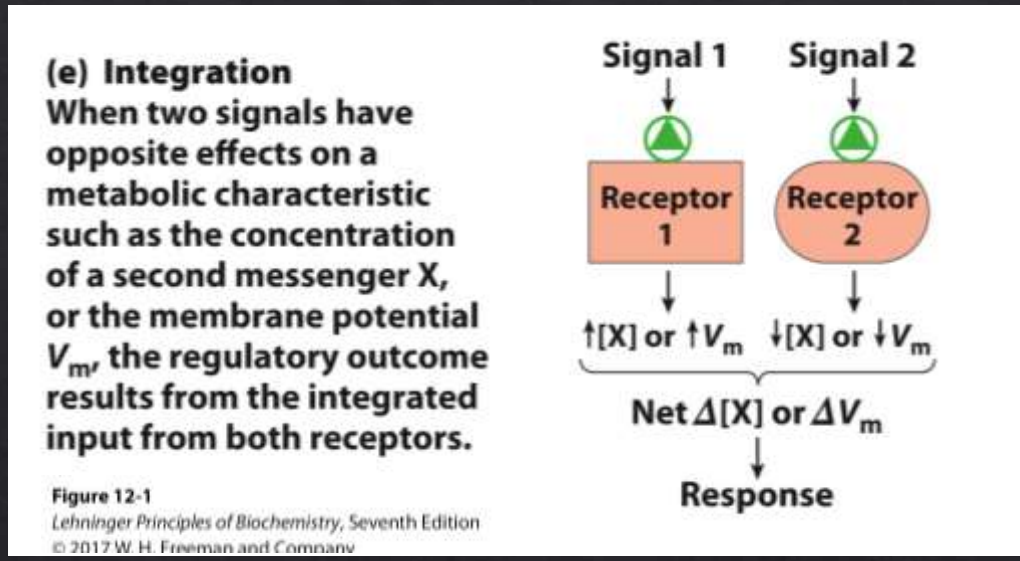
- Prolonged presence of the signal inactivates the response
- Can be reactivated by decreased concentrations



Specificity in signal transduction

Integration:

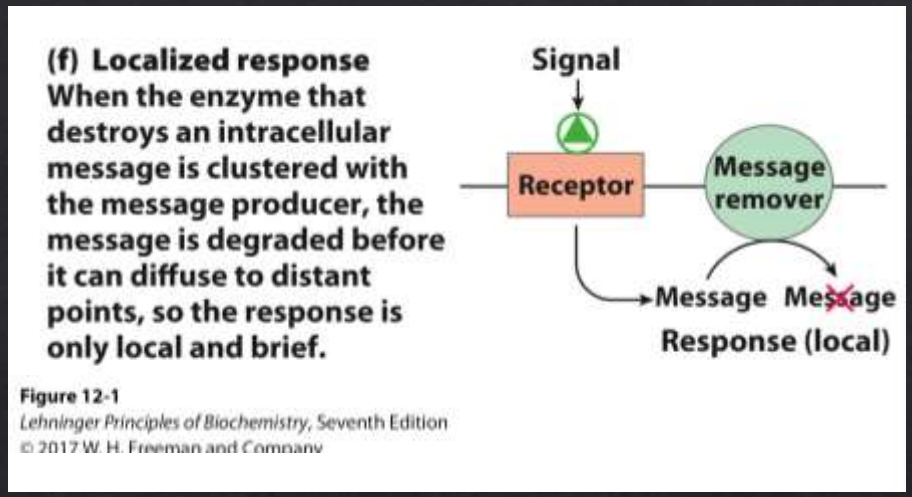
- Unified response to multiple stimuli
- Fundamental to maintain complex equilibria within the cell and the organism



Specificity in signal transduction

Localization:

- All components of the signaling system are confined to specific structures
- No effect on other cell regions



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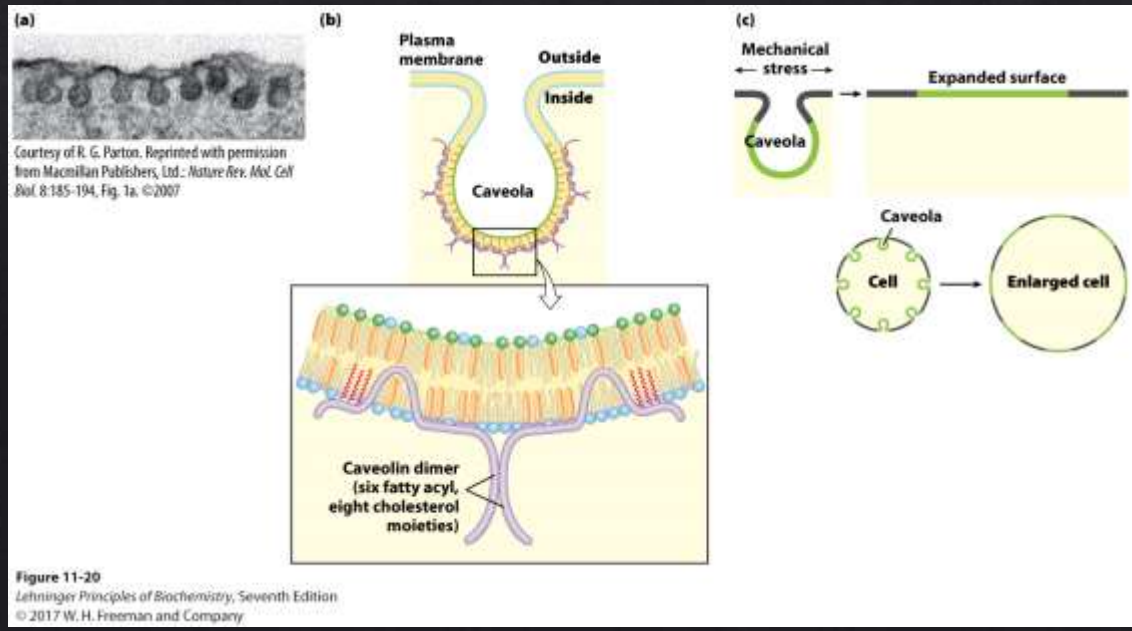

Courtesy of R. G. Parton. Reprinted with permission from Macmillan Publishers, Ltd.: *Nature Rev. Mol. Cell Biol.* 8:185-194, Fig. 1a. ©2007

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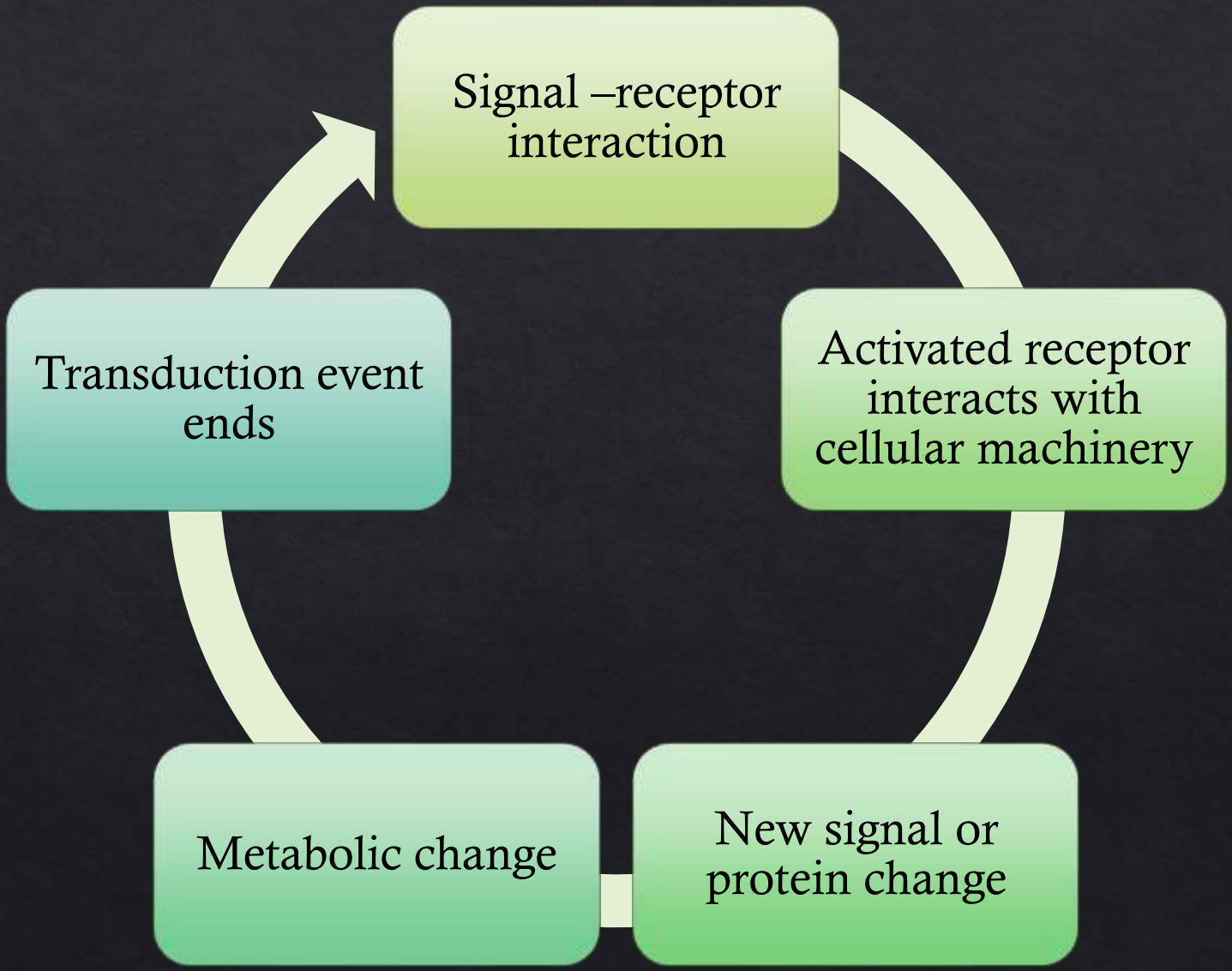
Signal trasduction



Common membrane receptors

1. **G protein–coupled receptor**
External ligand (L) binding to receptor (R) activates an intracellular GTP-binding protein (G), which regulates an enzyme (Enz) that generates an intracellular second messenger (X).

2a. **Receptor enzyme (tyrosine kinase)**
Ligand binding activates tyrosine kinase activity by autophosphorylation.

3. **Gated ion channel**
Channel opens or closes in response to concentration of signal ligand or membrane potential.

Plasma membrane

L R G Enz X

L L

L Ion L

2b. Kinase activates transcription factor (T), altering gene expression.

Kinase cascade

T

4. **Nuclear receptor**
Hormone binding allows the receptor to regulate the expression of specific genes.

T Protein mRNA DNA

L Protein mRNA DNA

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Common membrane receptors

1. **G protein–coupled receptor**
External ligand (L) binding to receptor (R) activates an intracellular GTP-binding protein (G), which regulates an enzyme (Enz) that generates an intracellular second messenger (X).

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T Protein mRNA DNA

L Protein mRNA DNA

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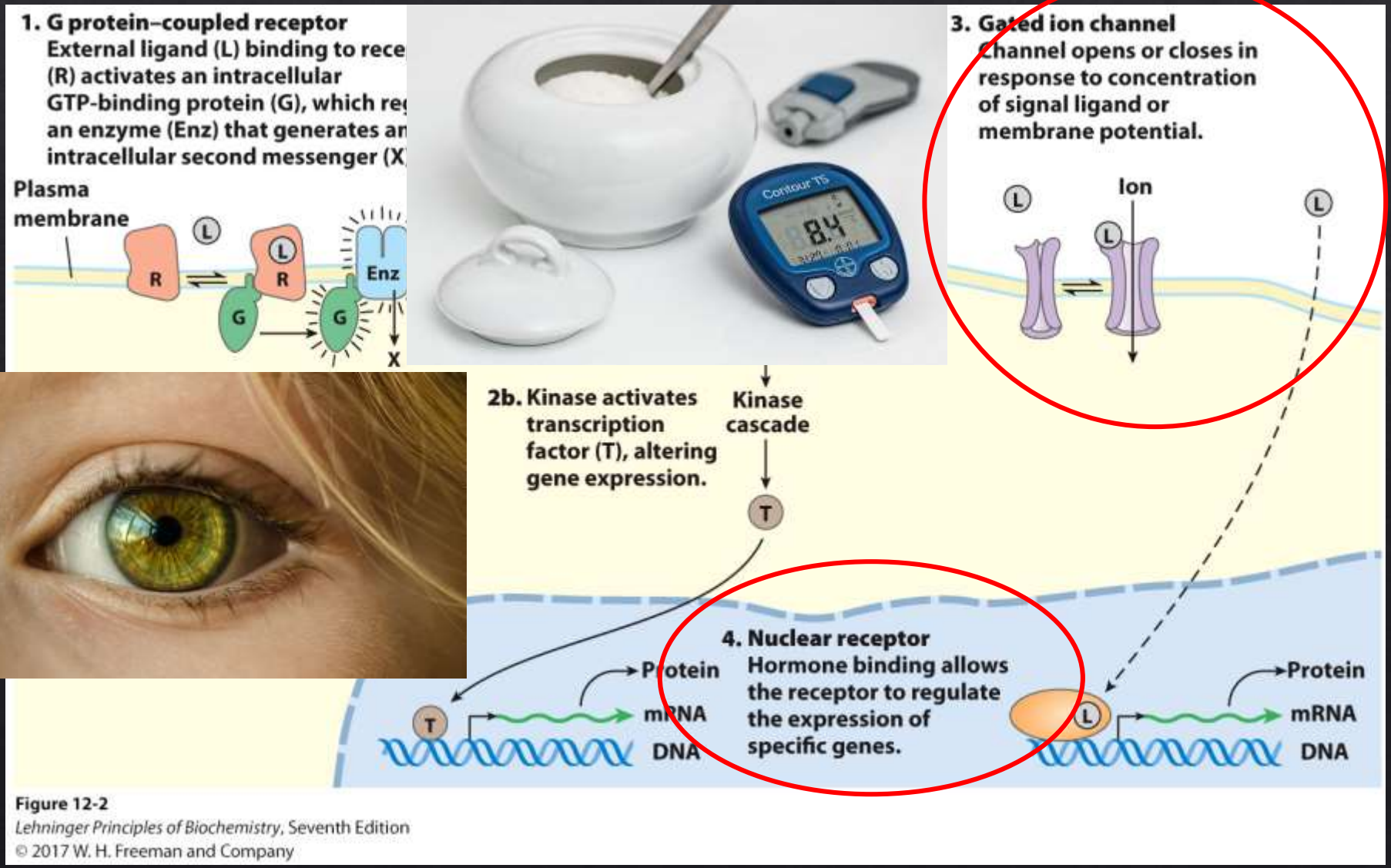
Common membrane receptors



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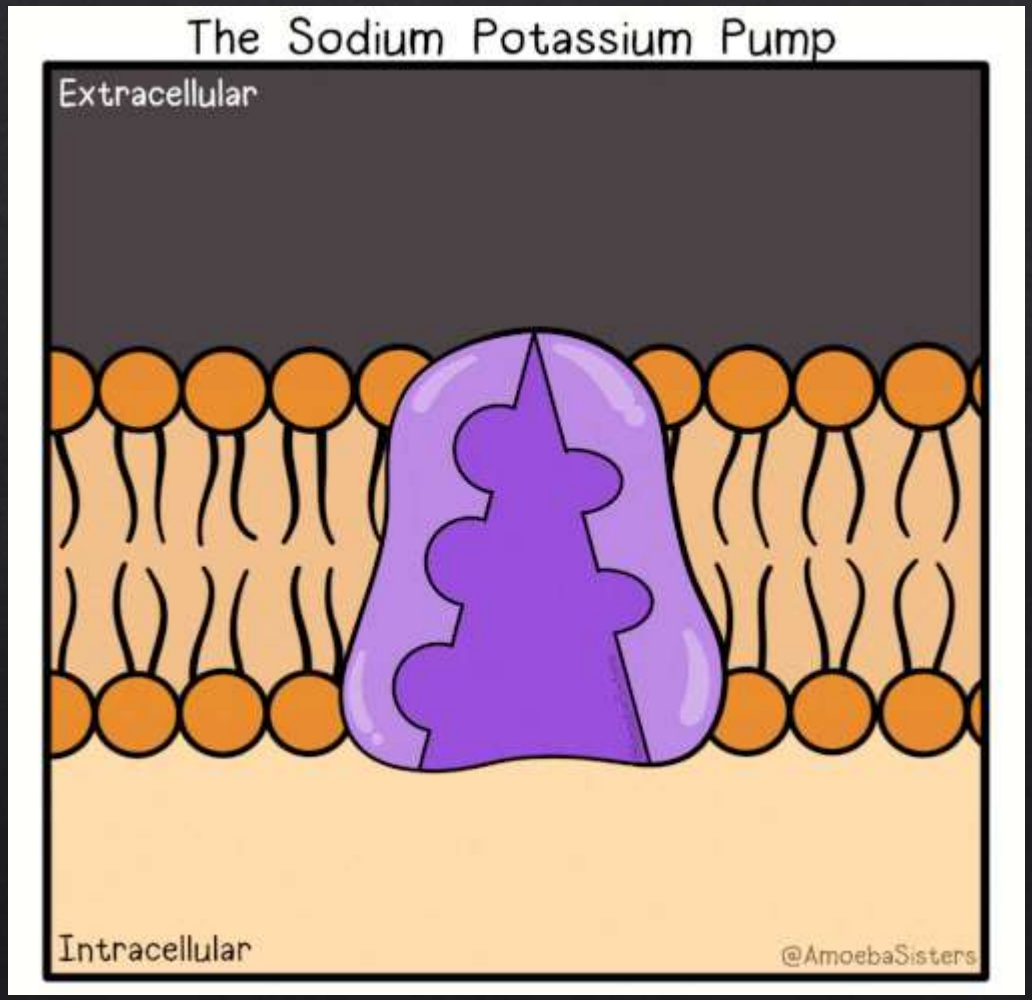
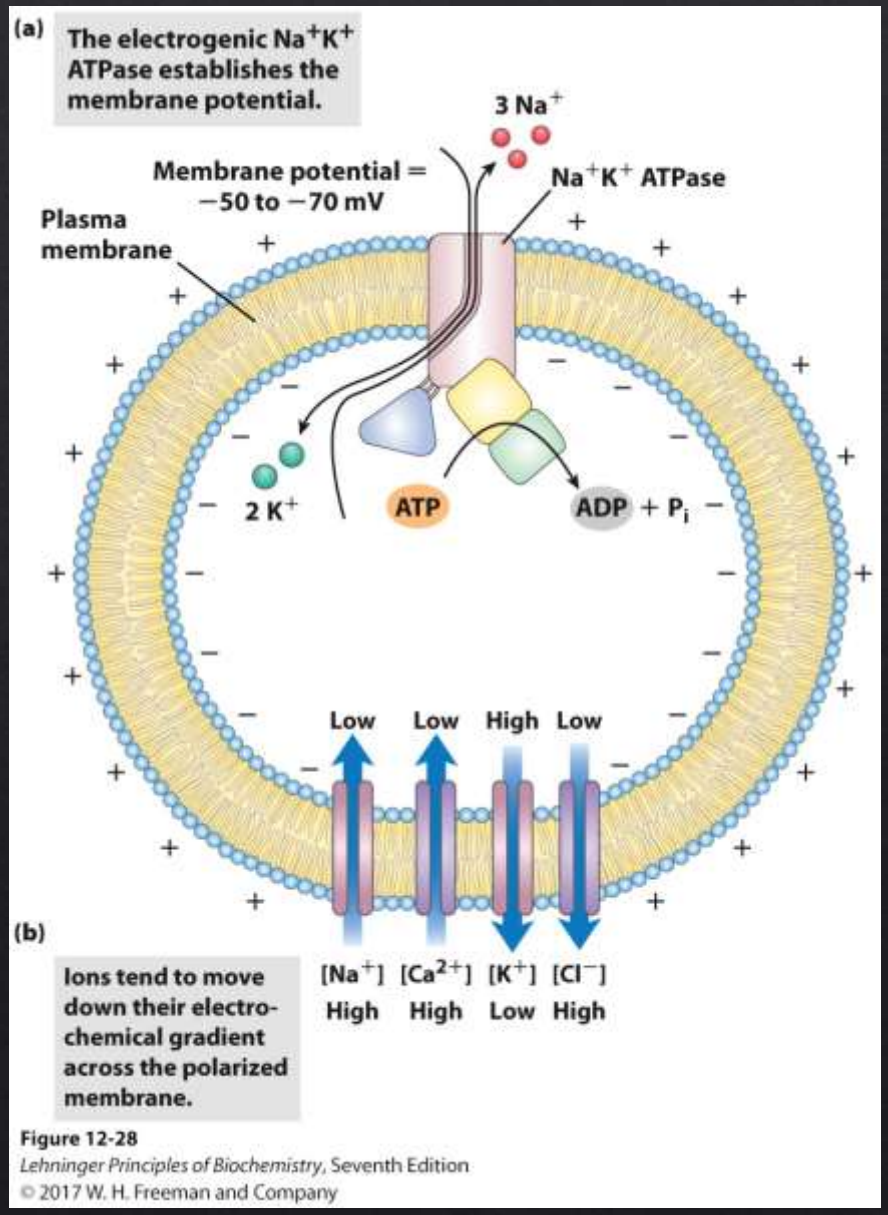
Gated ion channels

- Fundamental for transmission of electrical signal (muscle contraction, nerve conduction, etc.)
- The gate is opened/closed through a ligand
- The Na/K pump keeps the charge imbalance needed by the cell



Gated ion channels

- The membrane potential is the result of the types and N° of ion channels open in that moment
- Opening/closing of these channels regulates from muscle contraction to nervous transmission to hormone release



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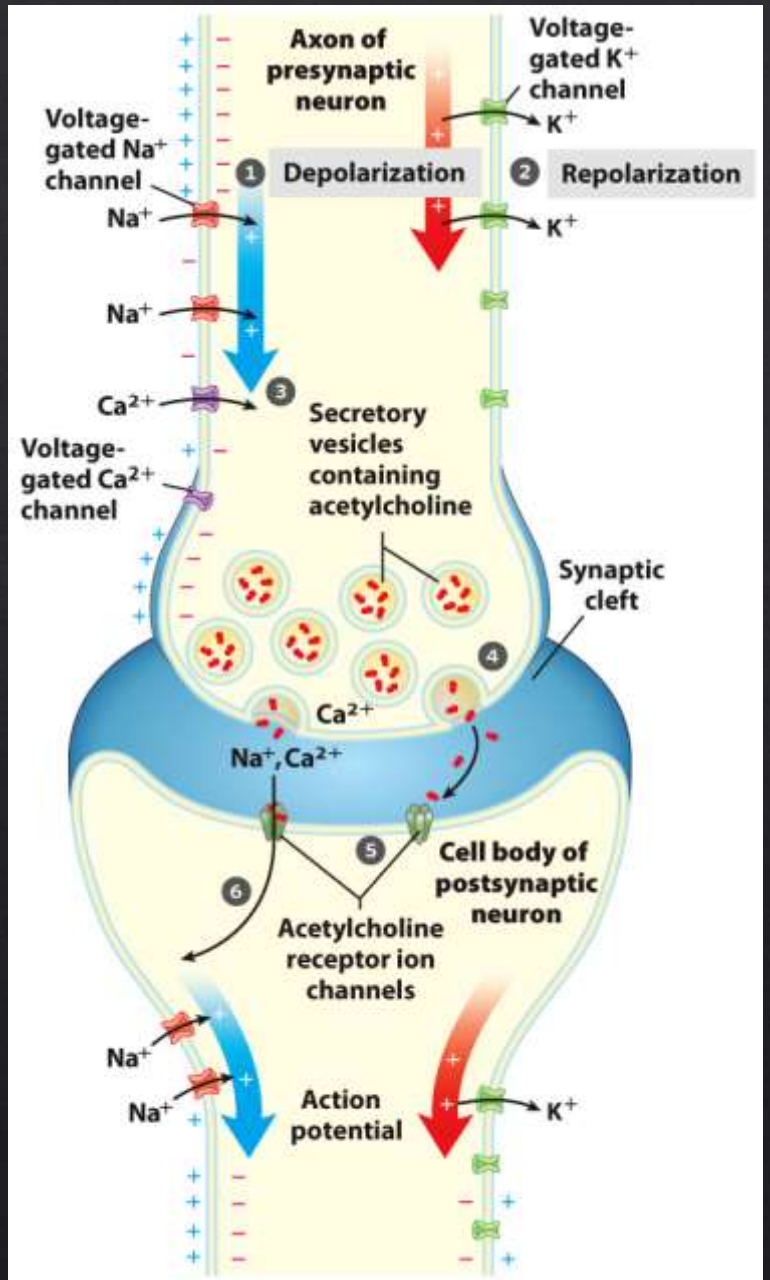
Gated ion channels

- Neurons carry electrical impulse from the cell body through the axon, triggering the release of neurotransmitters at the synapse
- Voltage gated Na^+, K^+ and Ca_2^+ channels essential for this. Na opens in response to neurotransmitter, K in response to Na restoring the equilibrium, Ca open when reached by this wave and release the neurotransmitter that will start the process in the adjacent cell



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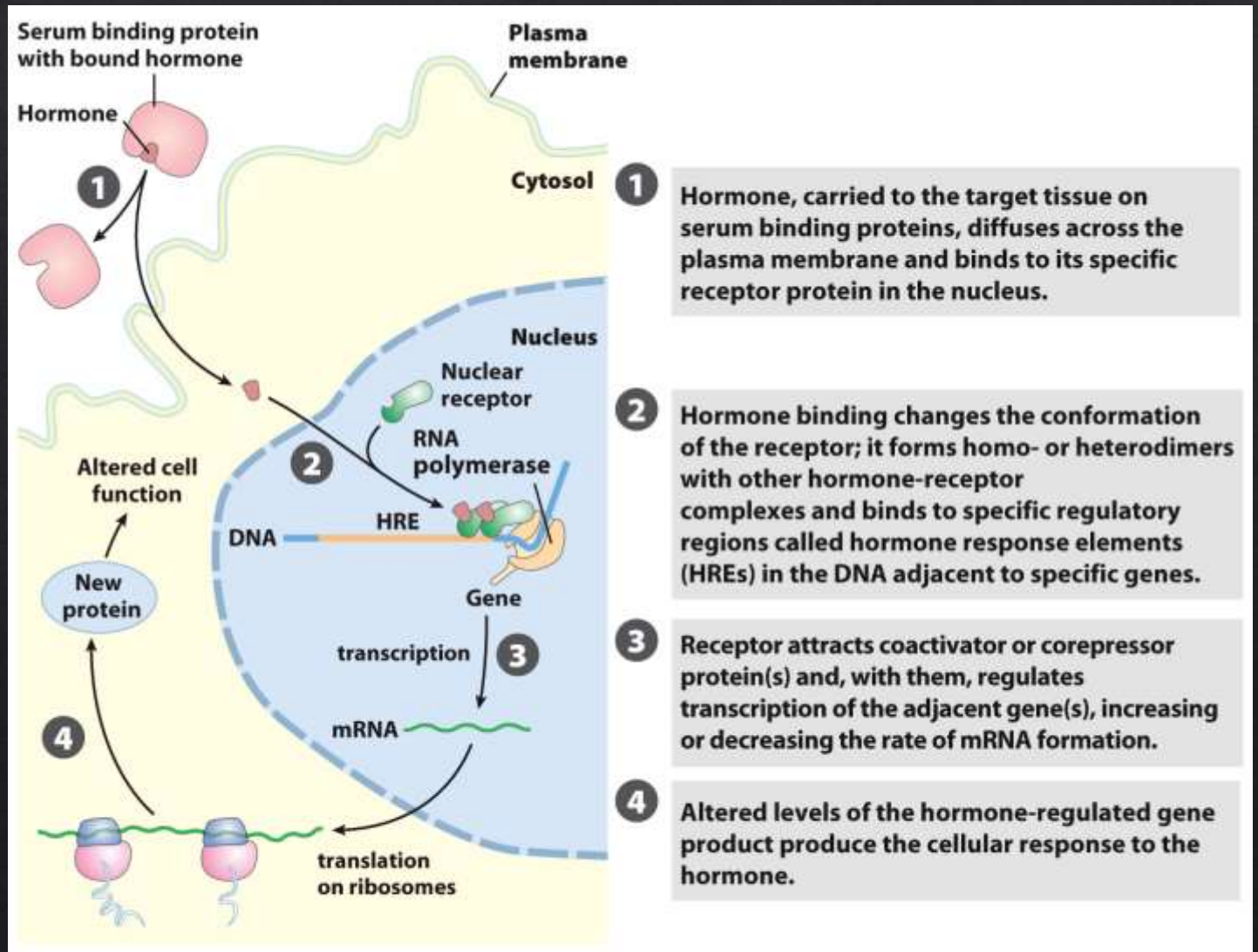
Nuclear hormone receptors



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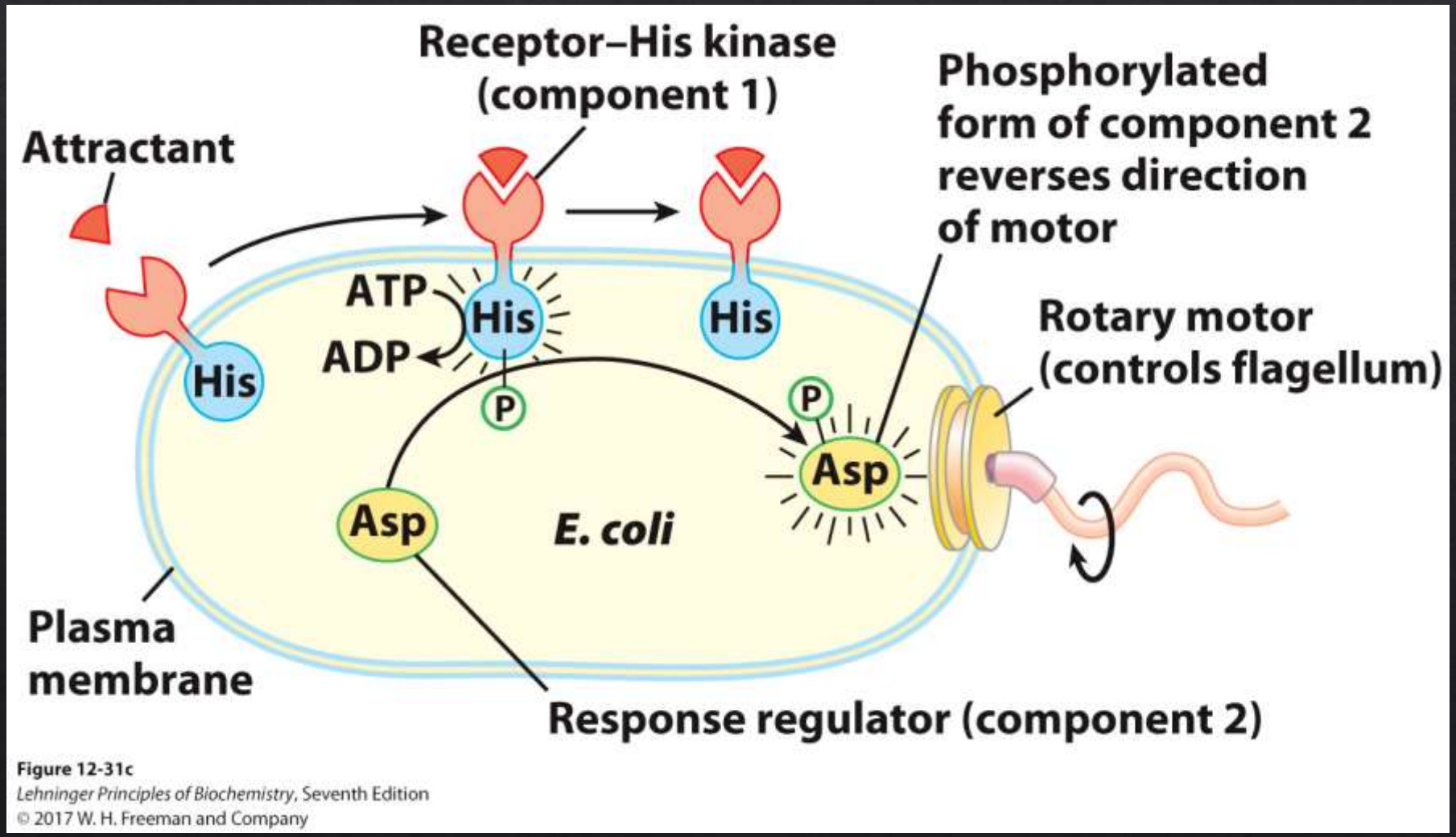
Bacterial chemotaxis



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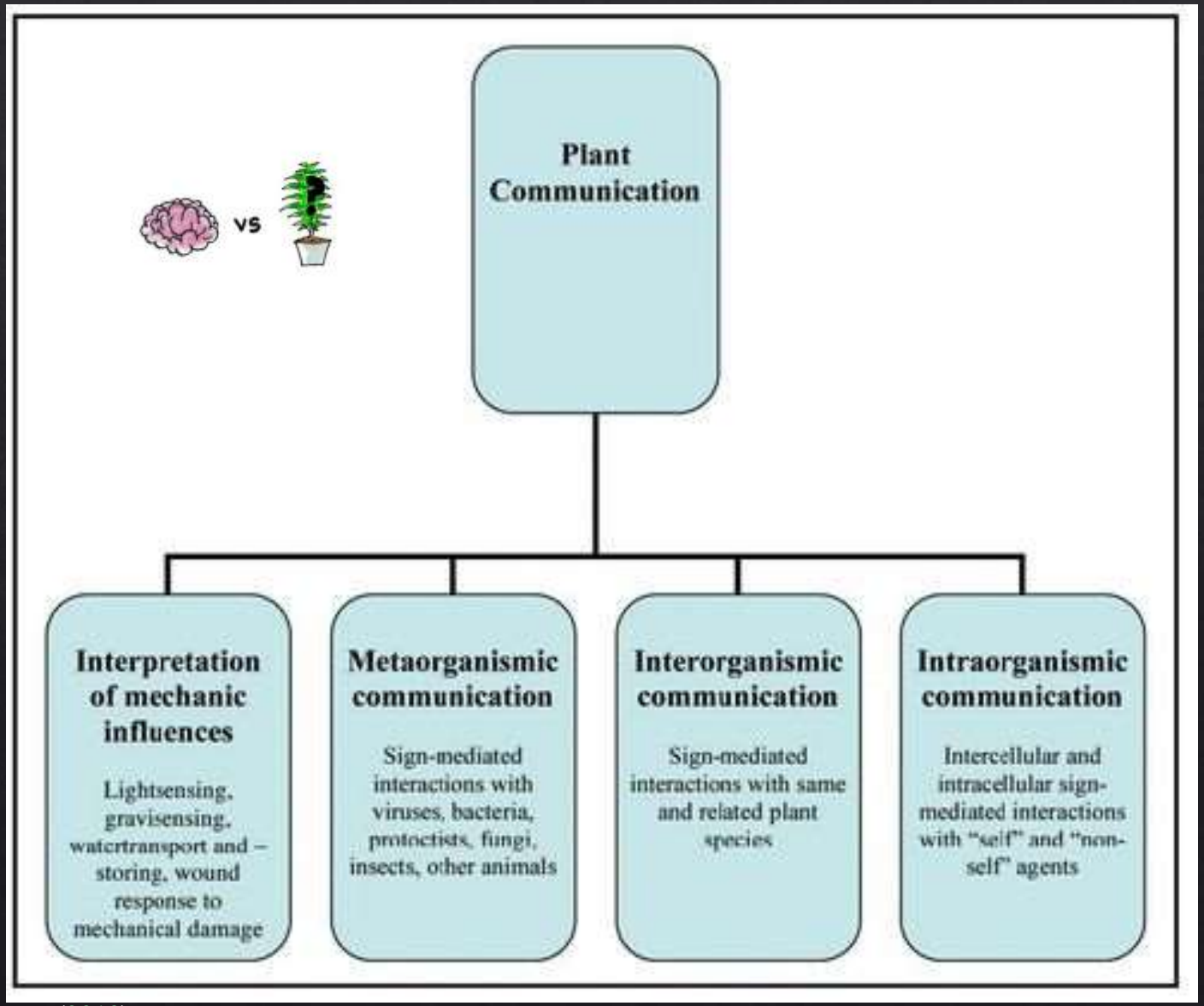
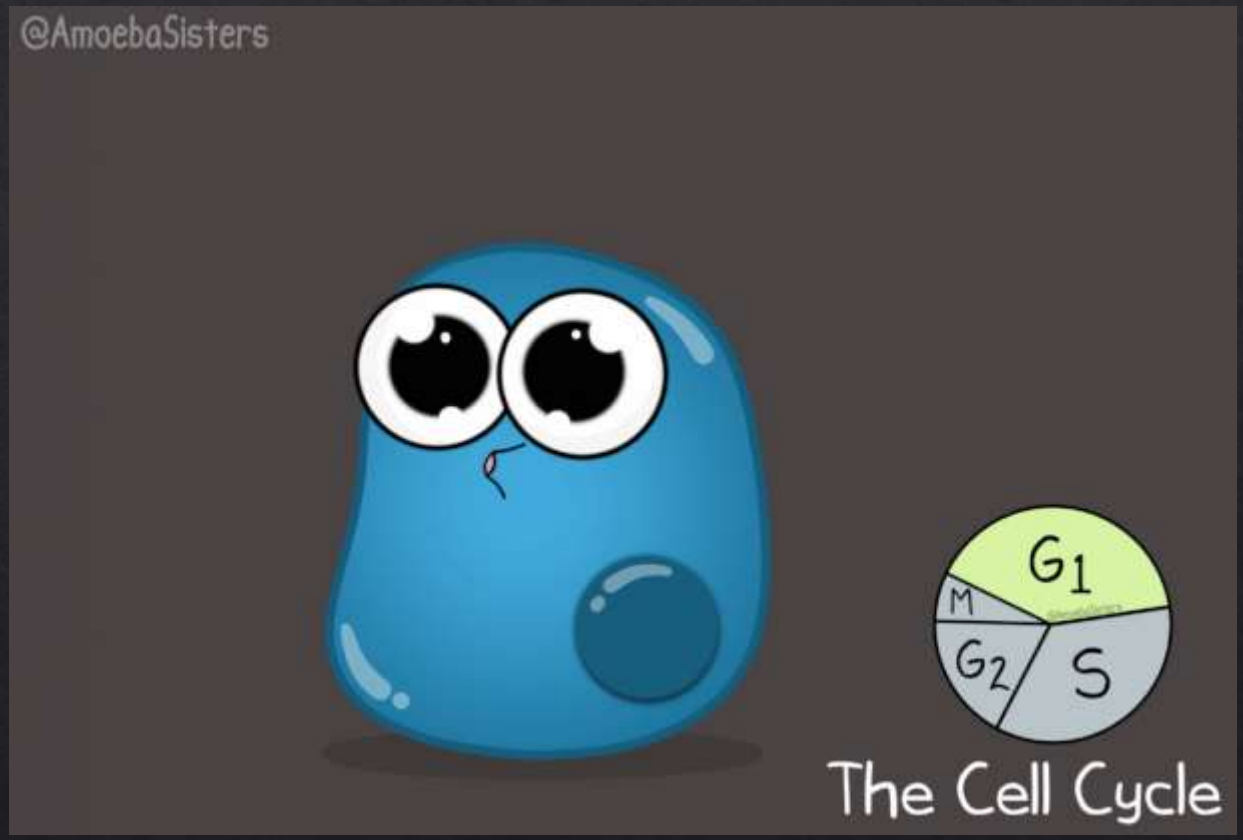
Biosignaling in plants

Plant biosignalling

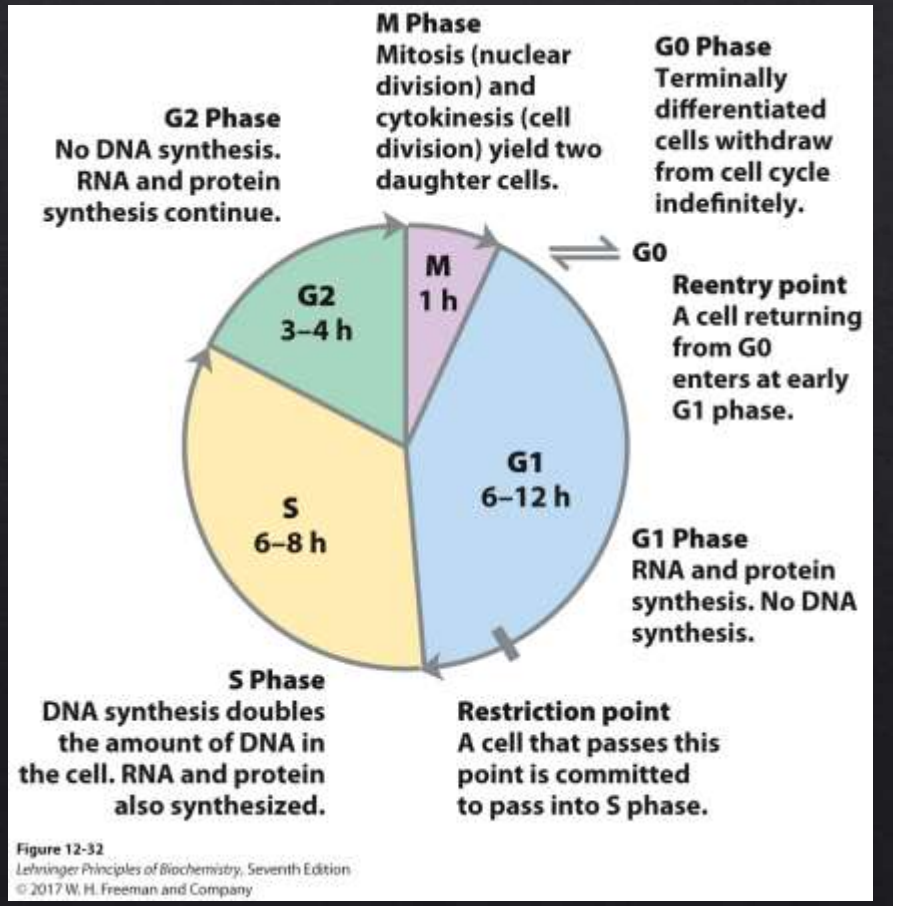


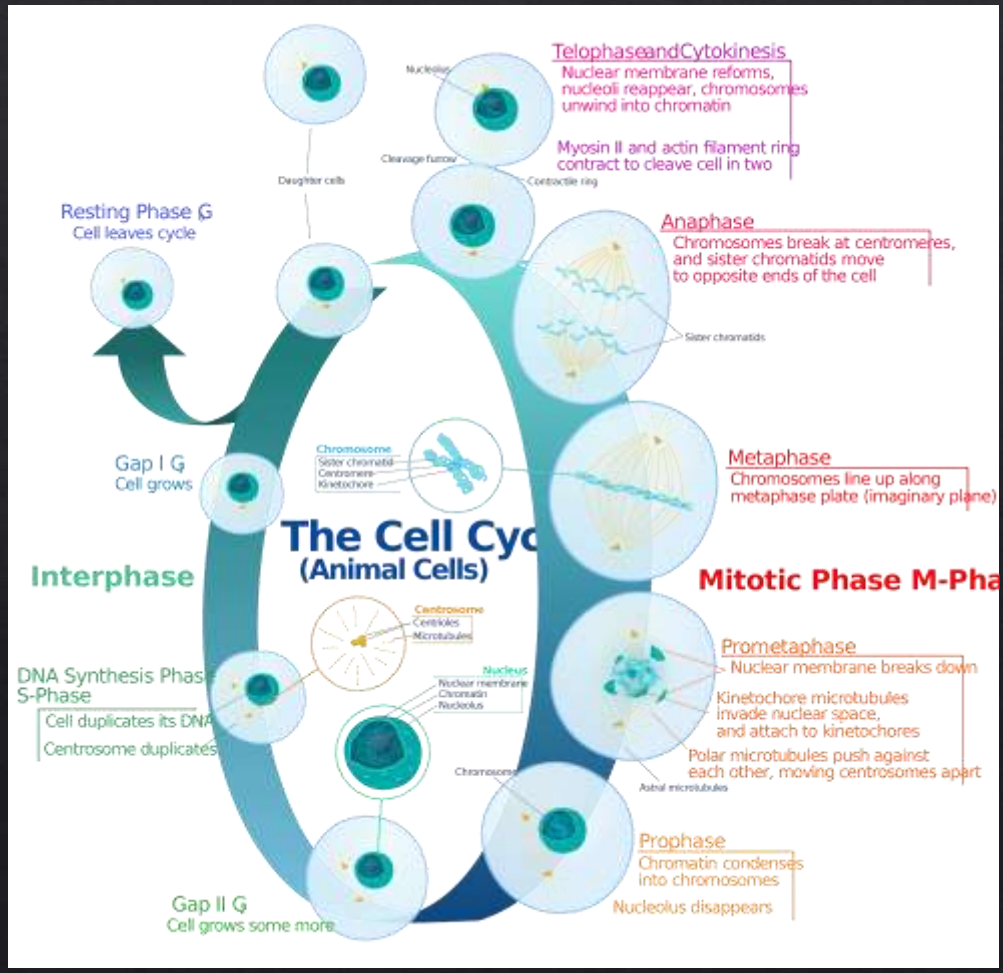
Picture from Witzany (2010)

Cell cycle is signal regulated



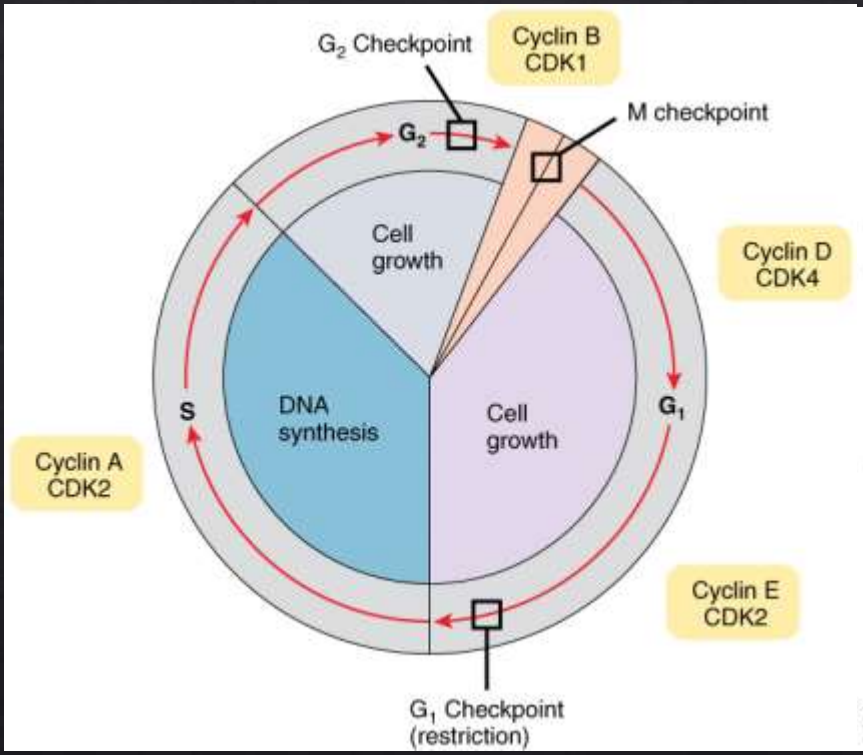
Cell cycle is signal regulated

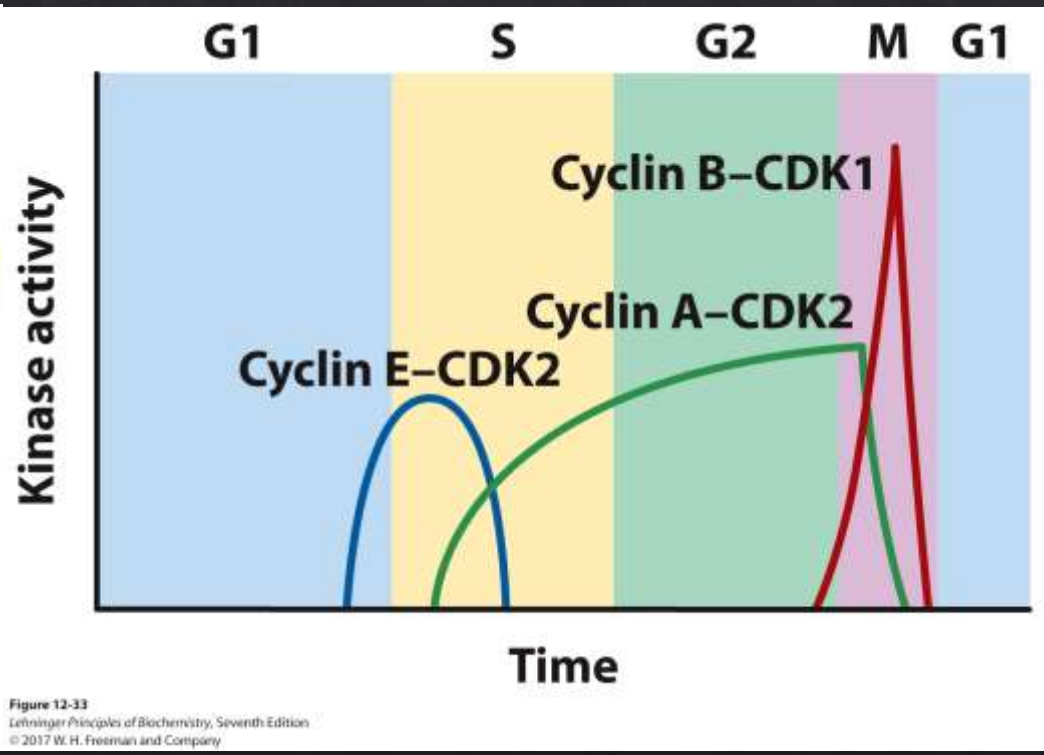




Picture by Kelvinsong on Wikimedia

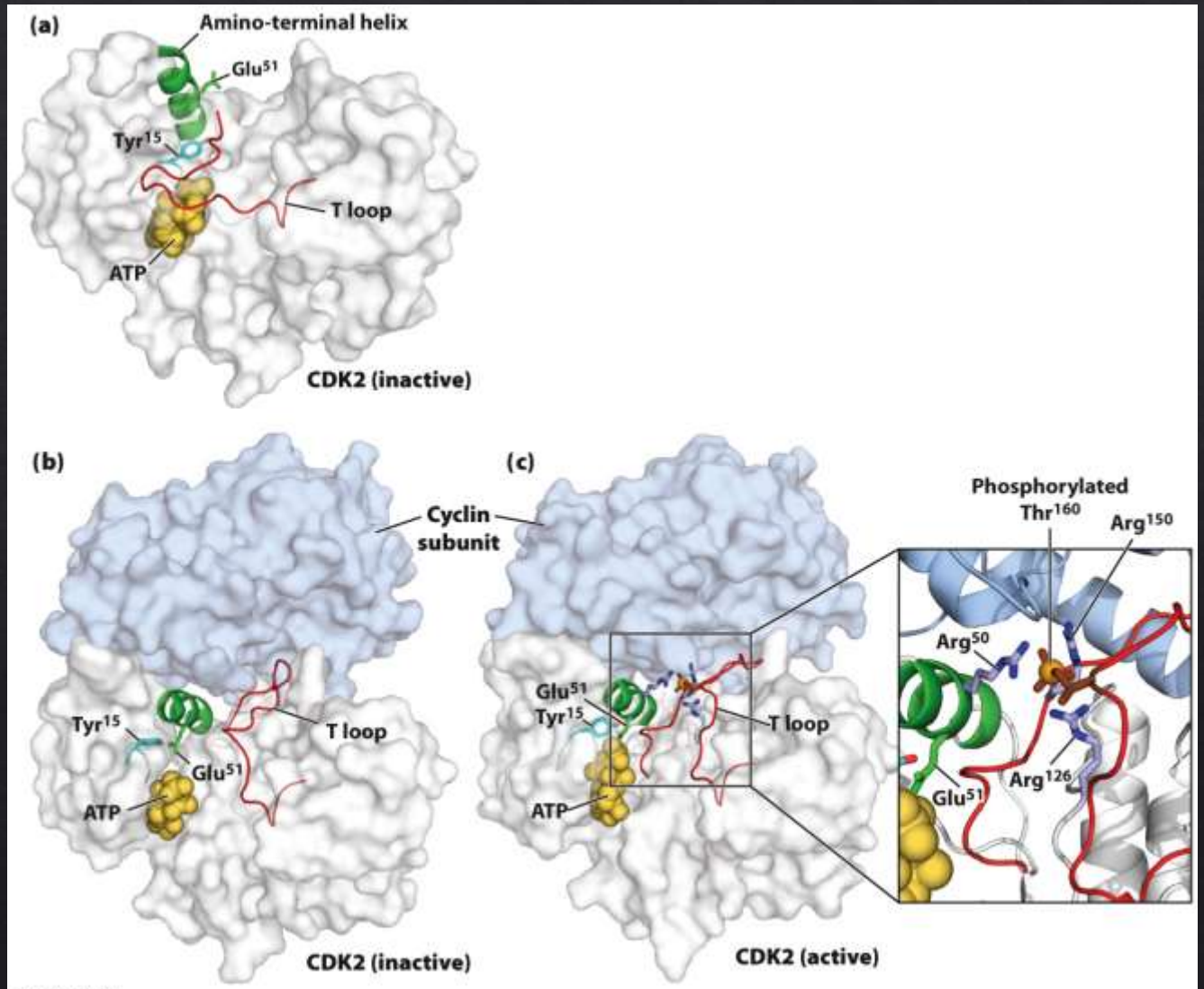
Cell cycle is signal regulated by cyclin-dependent kinases





Picture by OpenStax on Wikimedia

Cell cycle is signal regulated



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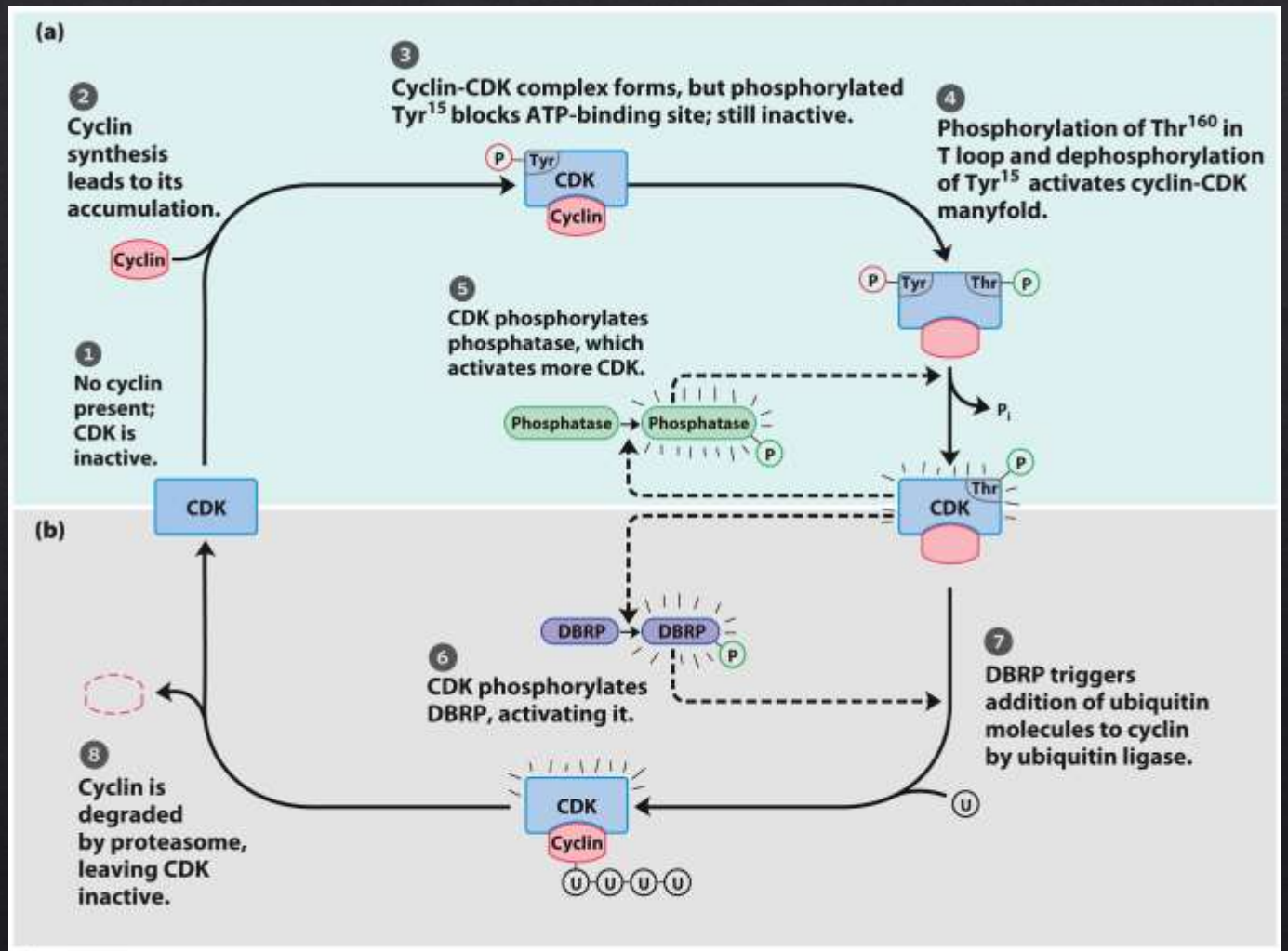
Cell cycle is signal regulated



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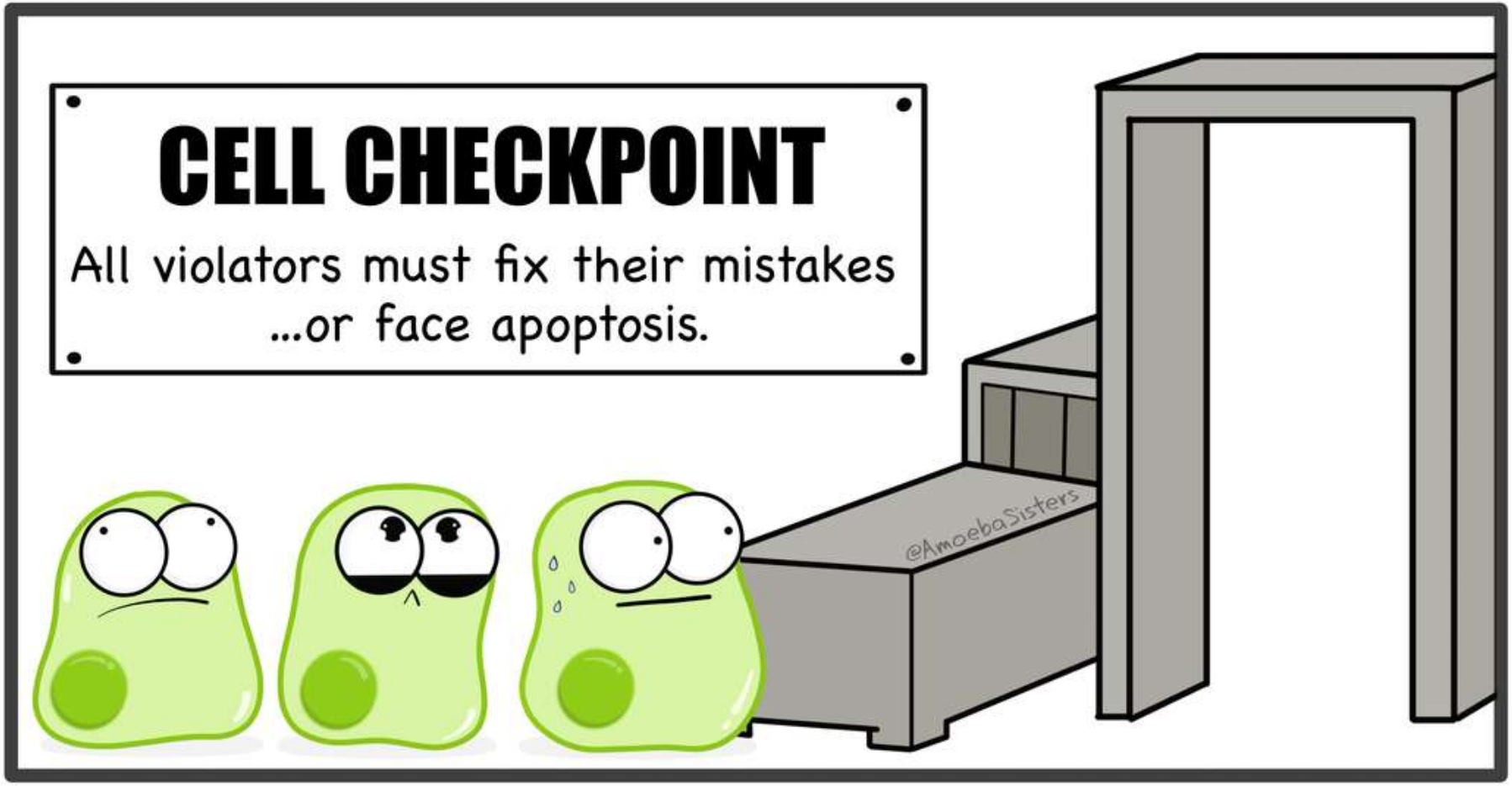
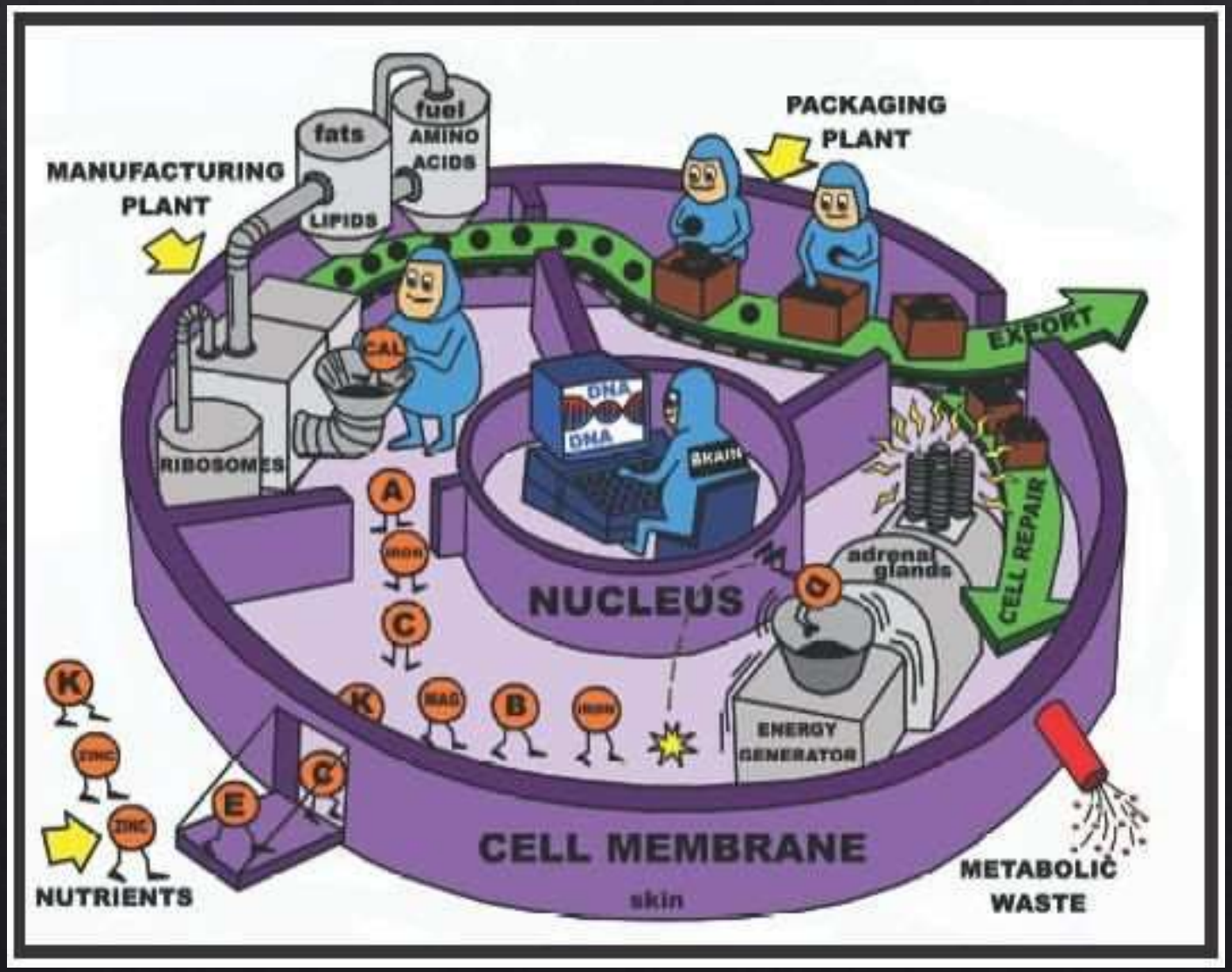
Paramecium Parlor



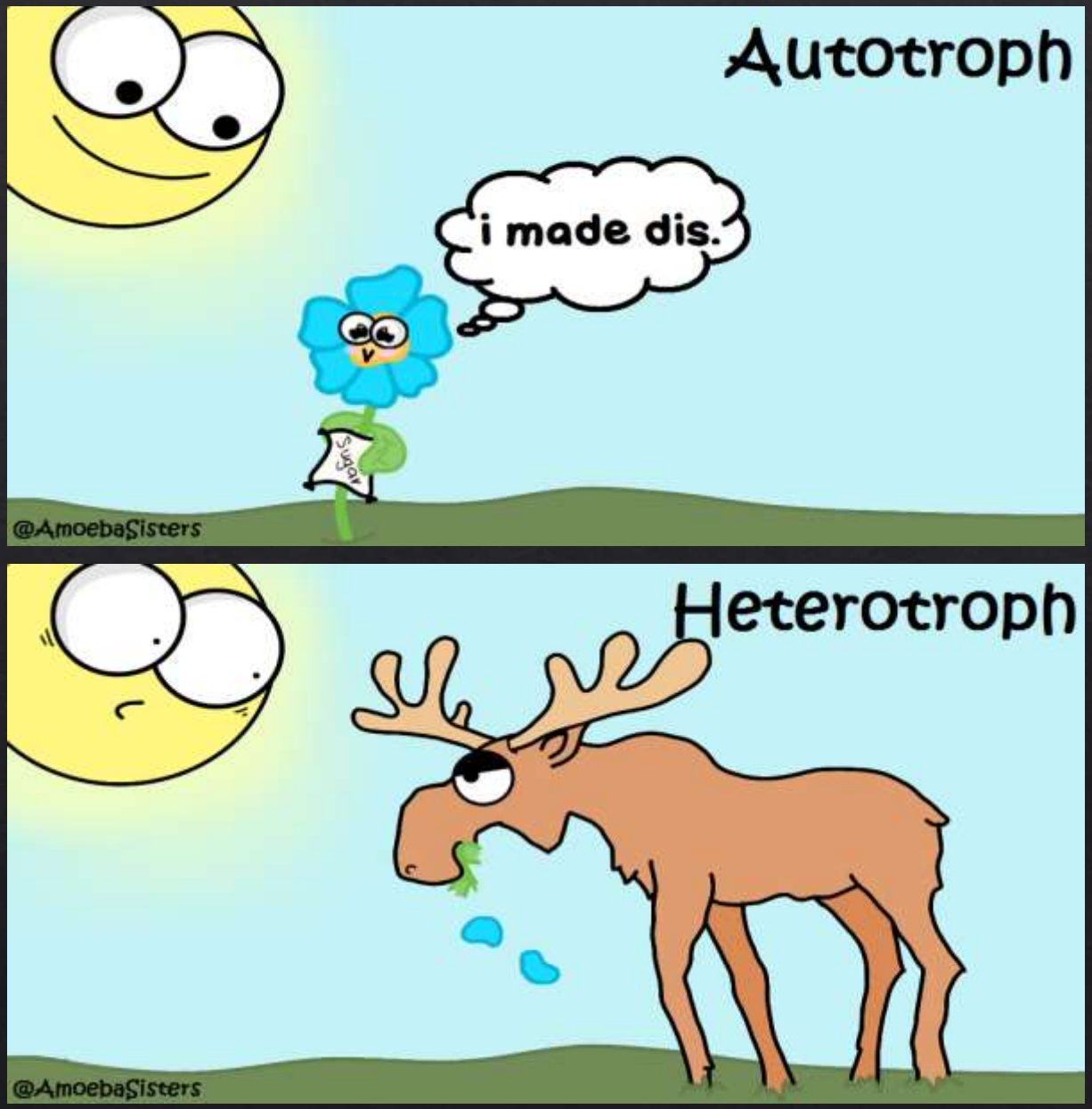
The cell checkpoints were always a site of intense scrutiny.


15 minutes

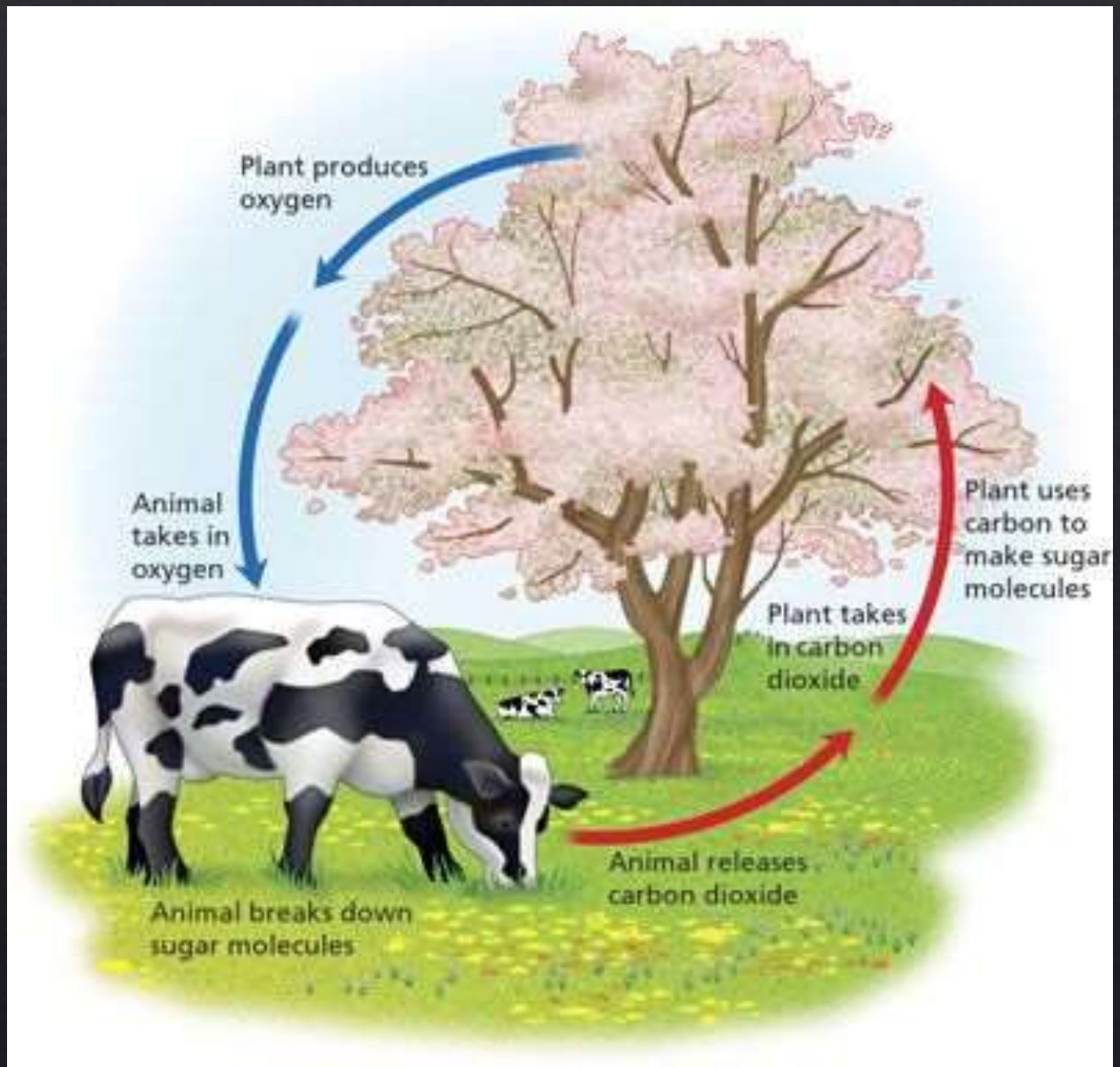
Metabolism


fuel
fats
AMINO ACIDS
LIPIDS
MANUFACTURING PLANT
PACKAGING PLANT
EXPORT
CELL REPAIR
RIBOSOMES
DNA
DNA
BRAIN
NUCLEUS
adrenal glands
ENERGY GENERATOR
CELL MEMBRANE
skin
NUTRIENTS
METABOLIC WASTE

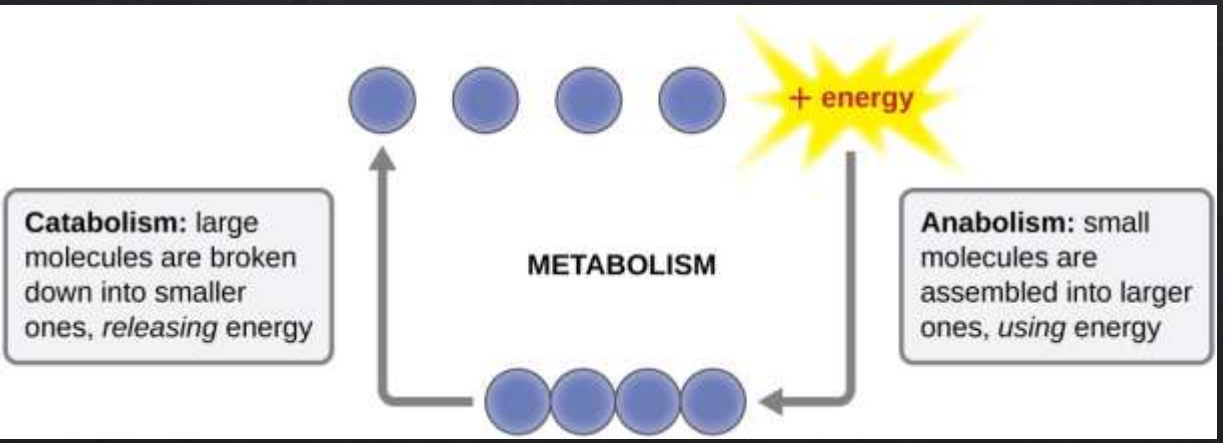
Autotrophs vs. Heterotrophs



Autotrophs vs. Heterotrophs



Catabolism vs. Anabolism



Picture from LumenLearning

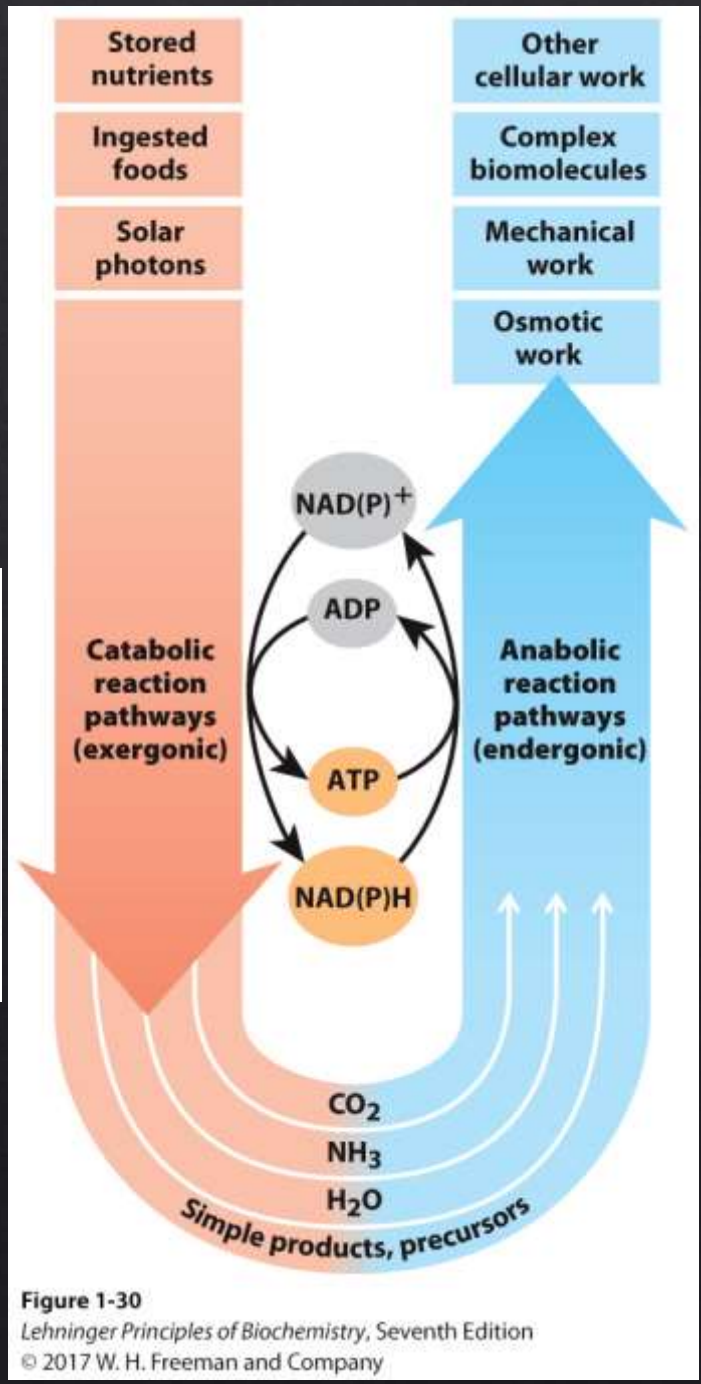


Figure 1-30
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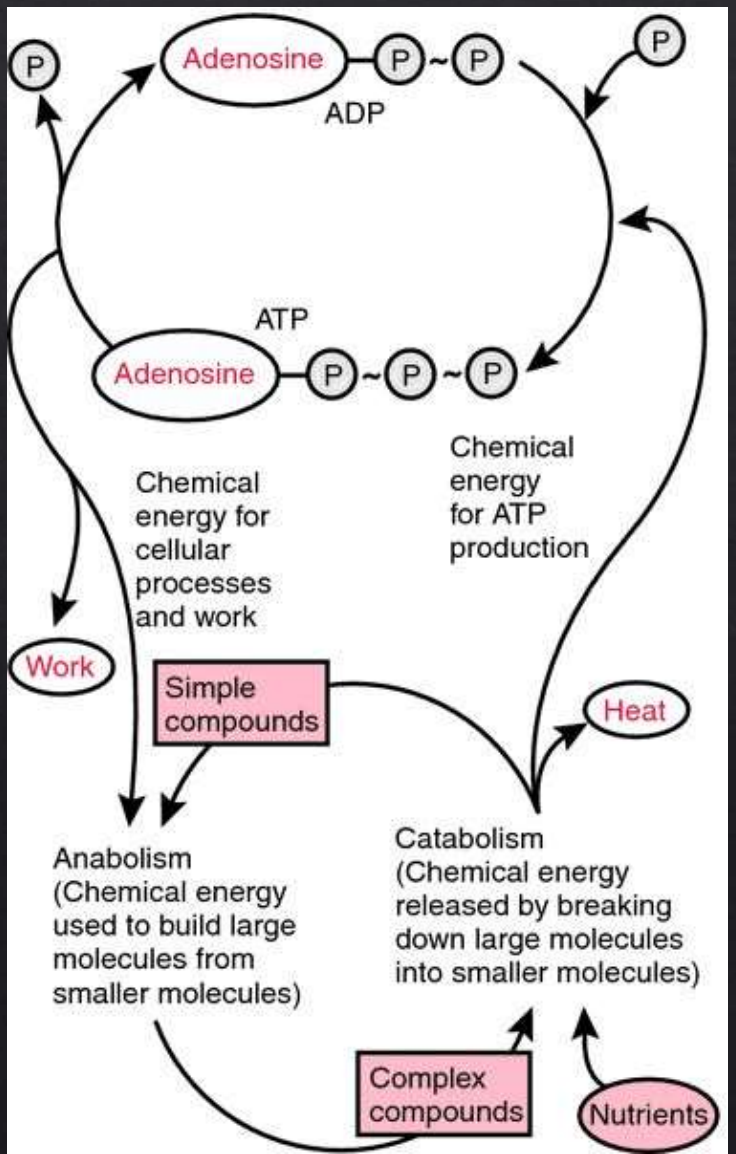
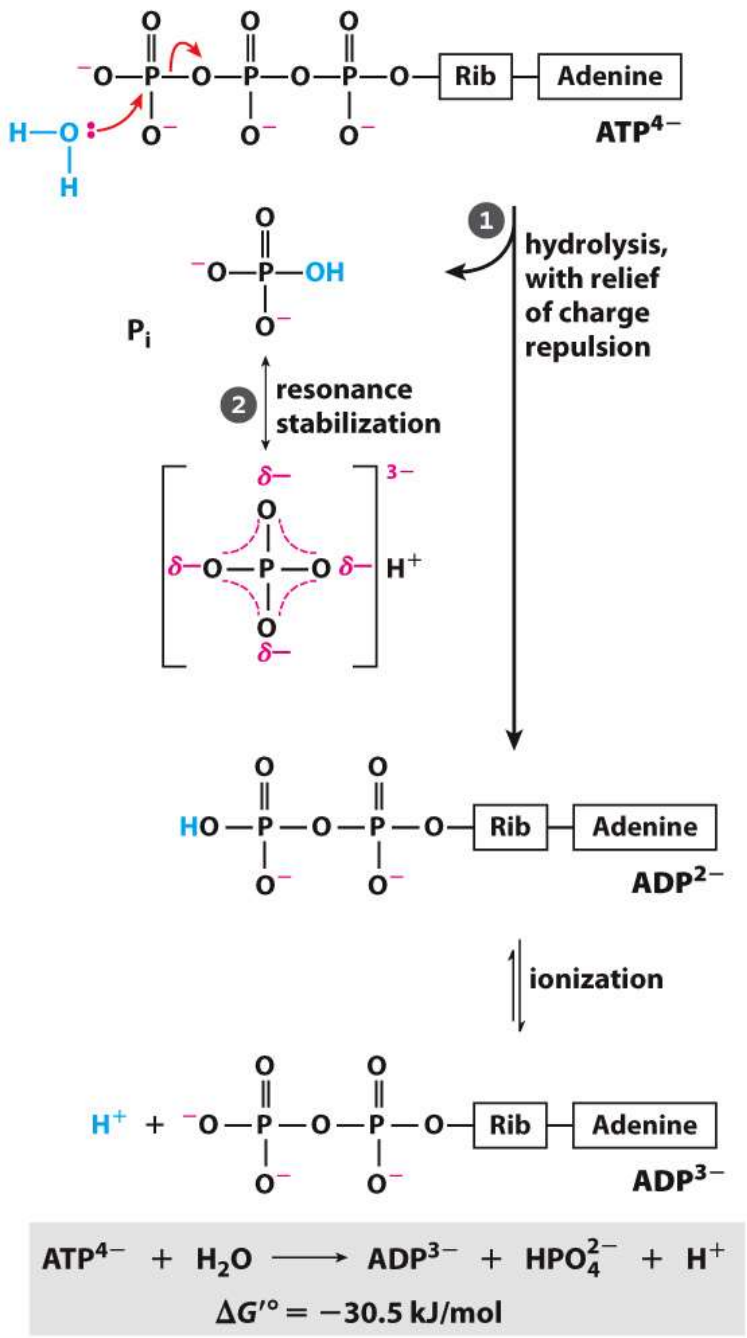
Paramecium Parlor
And can I get a name for this order?
Sure! It's Adenosine Triphosphate.
Ade...adeno...uh,
Adenosine... triphosphate.
@AmoebaSisters
triphosphate... so, uh, t-r-i-f
Oh, it's a 'ph.'
You know what... just put ATP.

ATP





$$ATP^{4-} + H_2O \longrightarrow ADP^{3-} + HPO_4^{2-} + H^+$$

$$\Delta G'^{\circ} = -30.5 \text{ kJ/mol}$$

Figure 13-11

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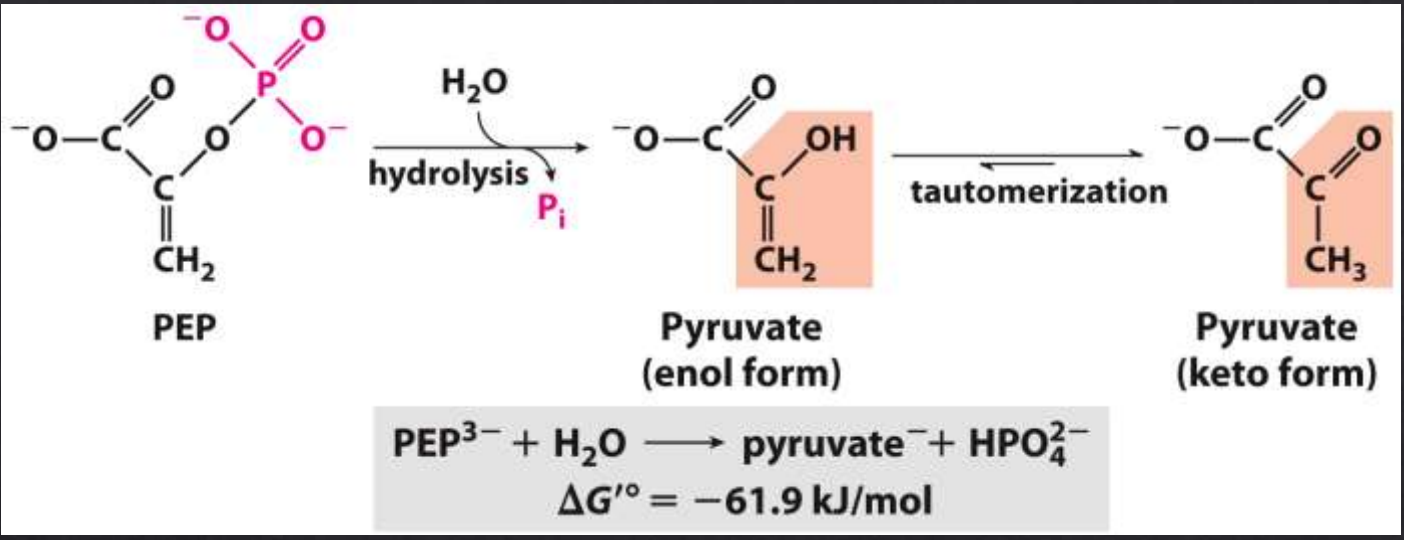
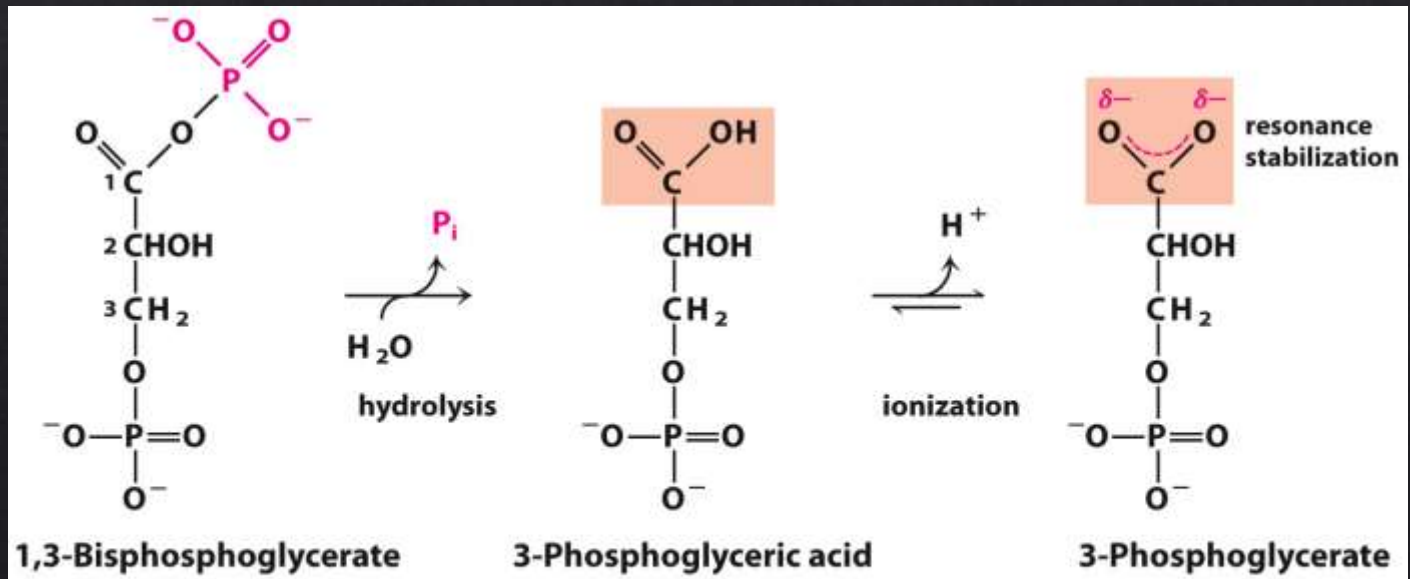
Other phosphate releasing molecules



$$PEP^{3-} + H_2O \longrightarrow pyruvate^{-} + HPO_4^{2-}$$
$$\Delta G'^{\circ} = -61.9\ kJ/mol$$



$$1,3\text{-Bisphosphoglycerate}^{4-} + H_2O \longrightarrow 3\text{-phosphoglycerate}^{3-} + HPO_4^{2-} + H^+$$
$$\Delta G'^{\circ} = -49.3\ kJ/mol$$

Pictures from Nelson&Cox

Energy transfer

- Generally summarised as hydrolysis, it's a 2-steps group transfer covalent reaction (S_N2 enzyme mediated)
- Products more stable than reactants
  - Bond strain relieved by charge separation
  - Stabilised by ionization
  - Stabilised by isomerization
  - Stabilised by resonance

TABLE 13-6 Standard Free Energies of Hydrolysis of Some Phosphorylated Compounds and Acetyl-CoA (a Thioester)

	$\Delta G'^{\circ}$ (kJ/mol)	$\Delta G'^{\circ}$ (kcal/mol)
Phosphoenolpyruvate	−61.9	−14.8
1,3-Bisphosphoglycerate (→ 3-phosphoglycerate + P_i)	−49.3	−11.8
Phosphocreatine	−43.0	−10.3
ADP (→ AMP + P_i)	−32.8	−7.8
ATP (→ ADP + P_i)	−30.5	−7.3
ATP (→ AMP + PP_i)	−45.6	−10.9
AMP (→ adenosine + P_i)	−14.2	−3.4
PP_i (→ 2P_i)	−19.2	−4.0
Glucose 3-phosphate	−20.9	−5.0
Fructose 6-phosphate	−15.9	−3.8
Glucose 6-phosphate	−13.8	−3.3
Glycerol 3-phosphate	−9.2	−2.2
Acetyl-CoA	−31.4	−7.5

Sources: Data mostly from W. P. Jencks, in *Handbook of Biochemistry and Molecular Biology*, 3rd edn (G. D. Fasman, ed.), *Physical and Chemical Data*, Vol. 1, p. 296, CRC Press, 1976. Value for the free energy of hydrolysis of PP_i from P. A. Frey and A. Arabshahi, *Biochemistry* 34:11,307, 1995.

Table 13-6
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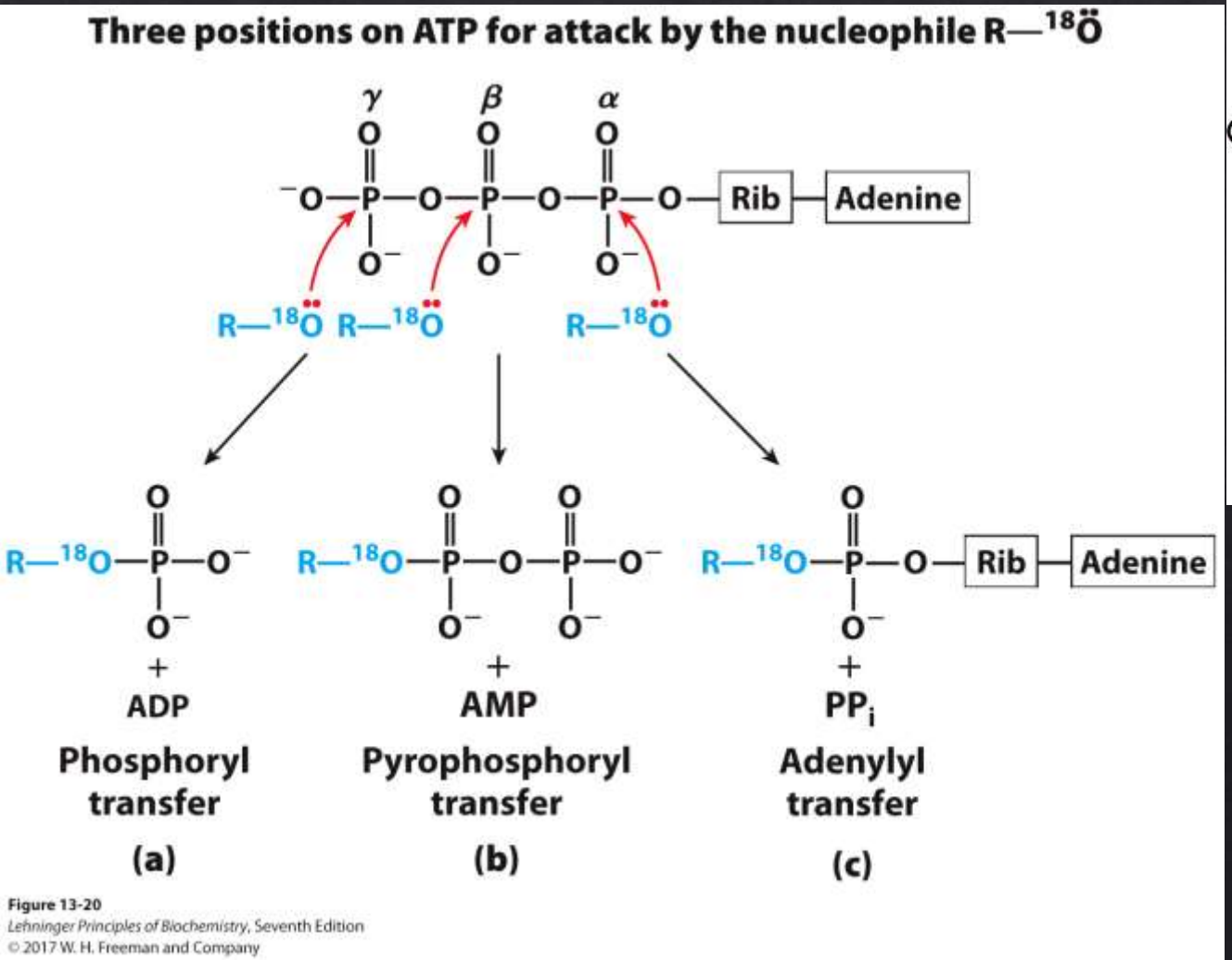
ATP



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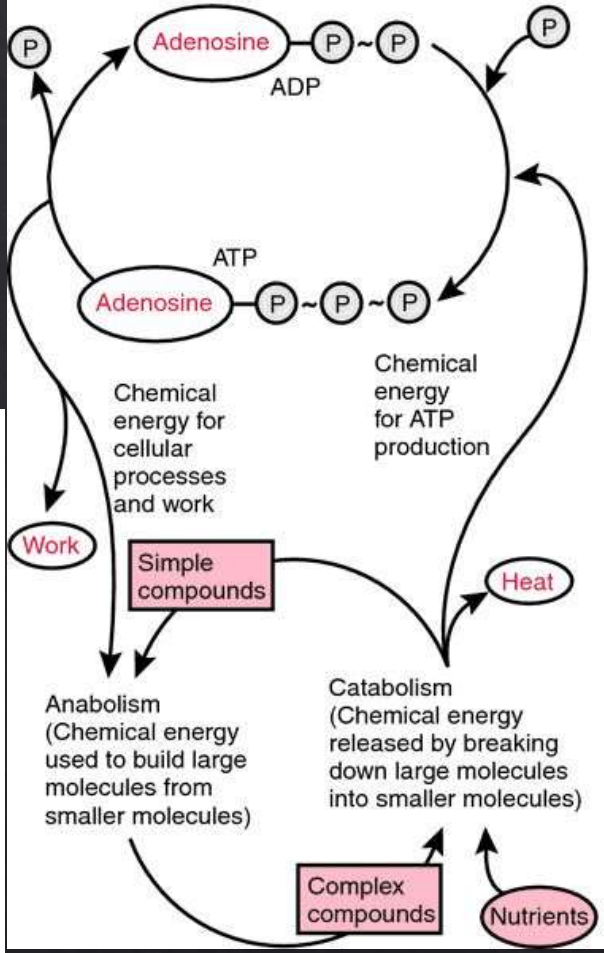
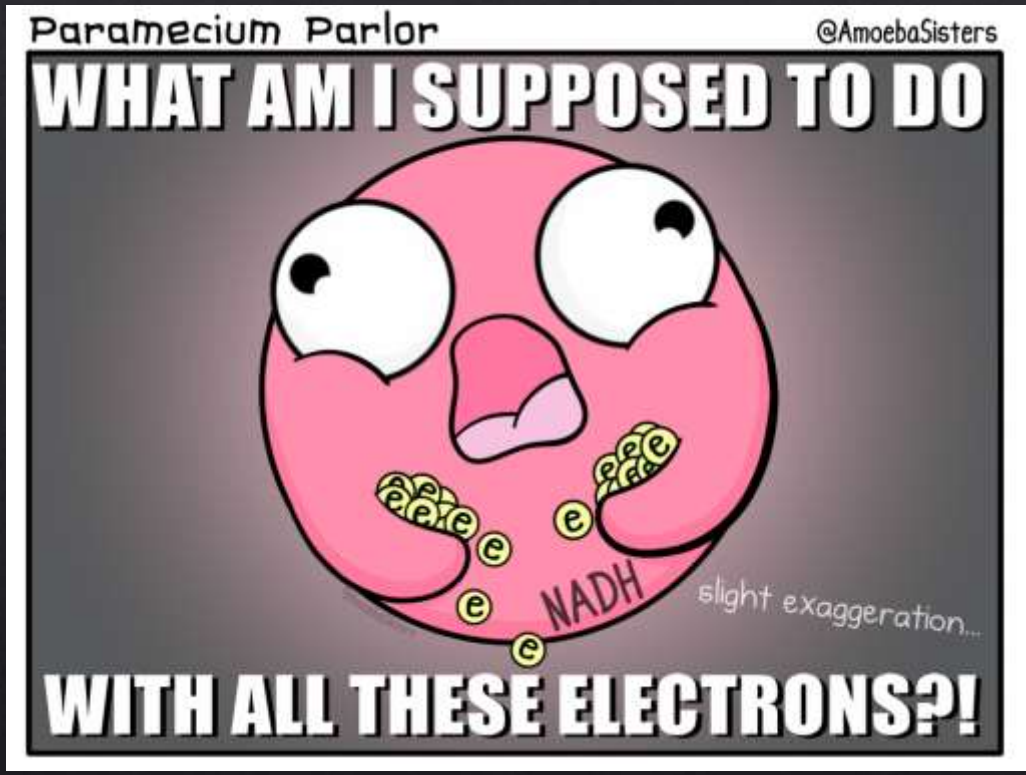


Redox reactions

- Electron transfer in redox reactions is as important as phosphoryl groups
- Electron flow is responsible for all work done by organisms
- Electron sources are food (heterotroph) or a chemical species excited by light (autotroph)



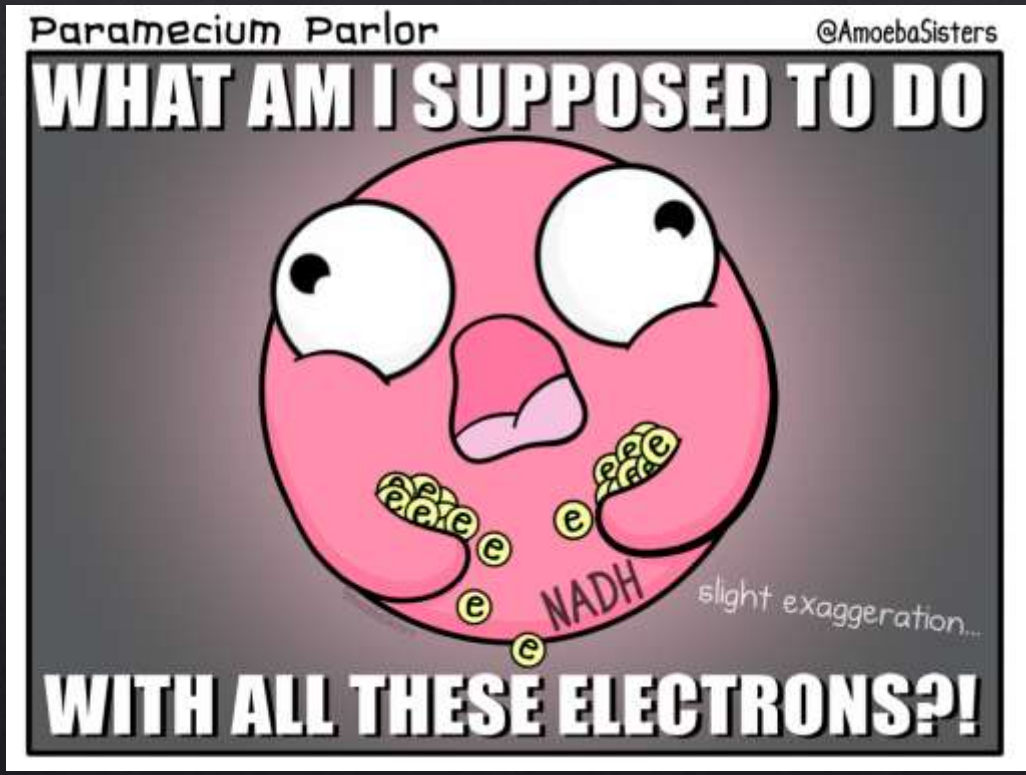
Redox reactions

- Electron flow in cells goes from glucose to O_2
- The intermediate steps of this process are what makes biological work possible
- Often oxidation synonymous of dehydrogenation. Dehydrogenases enzymes as catalists

Redox reactions

Electrons are transfered from an electron donor to an electron acceptor

- Directly as electrons
- As hydrogen atoms
- As hydride ion ($:H^-$)
- Through combination with oxygen (e.g. alchool formation)



Redox reactions

In cellular metabolism electrons are often transferred through electron carriers (coenzymes)

- NAD
- NADP
- FMN
- FAD

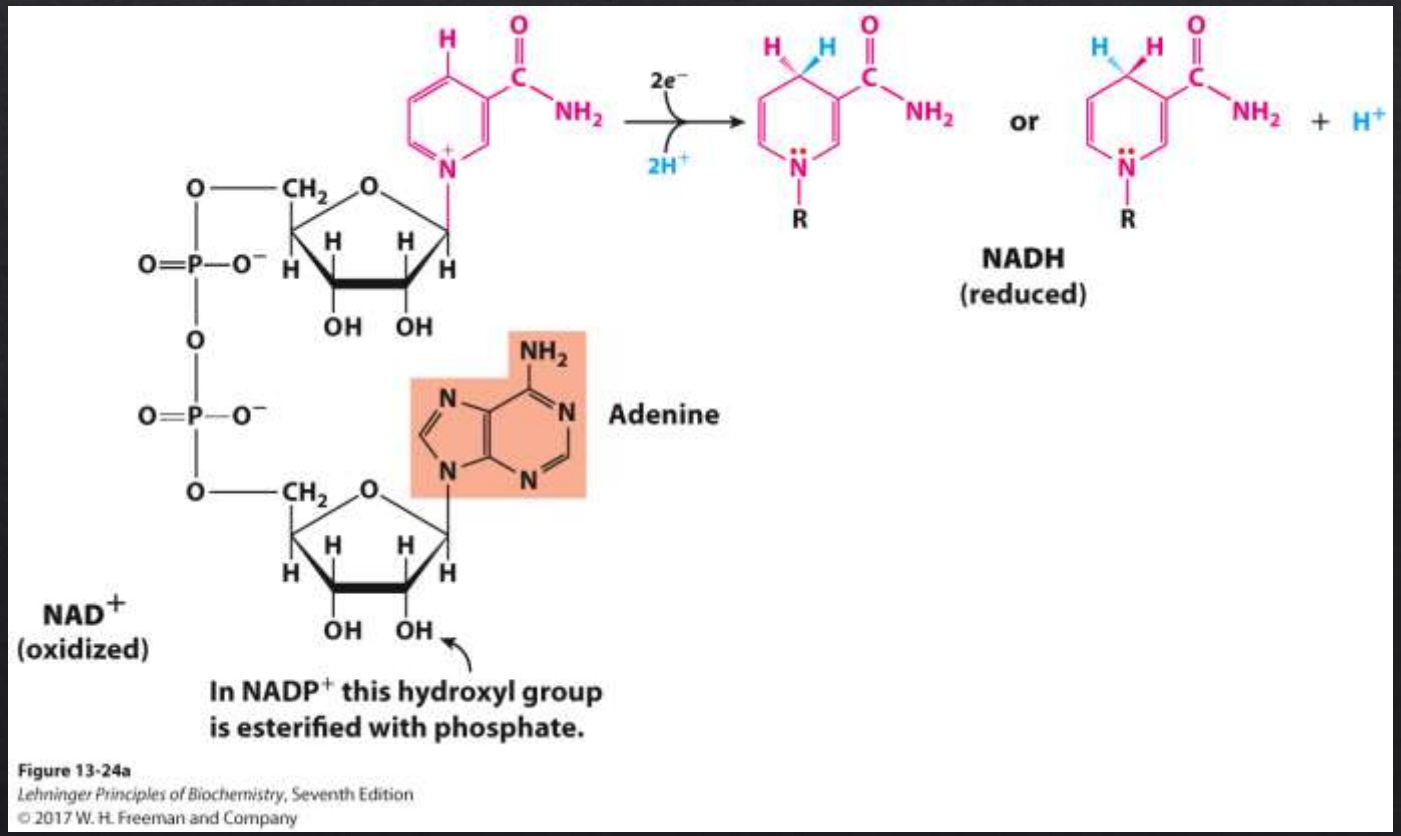


Figure 13-24a
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