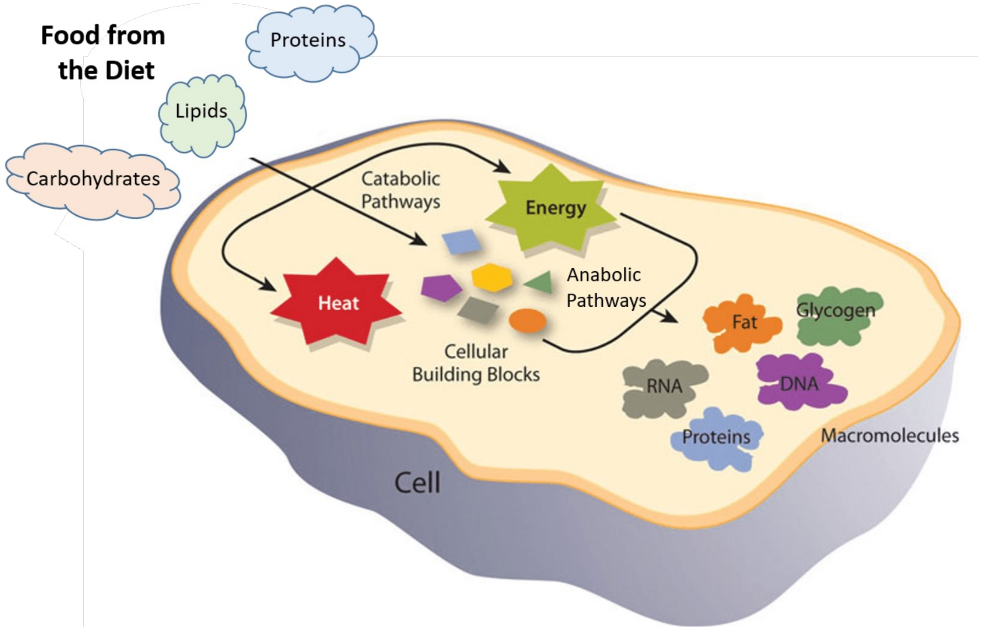
Lesson 5
Cellular Chemistry, Reaction Thermodynamics and Enzymes



Metabolism

- The cell is an ideal continuous chemical reactor
- The ensemble of cellular chemical reactions = **metabolism**
- **Anabolic reactions** = build up molecules (*e.g.*, condensation)

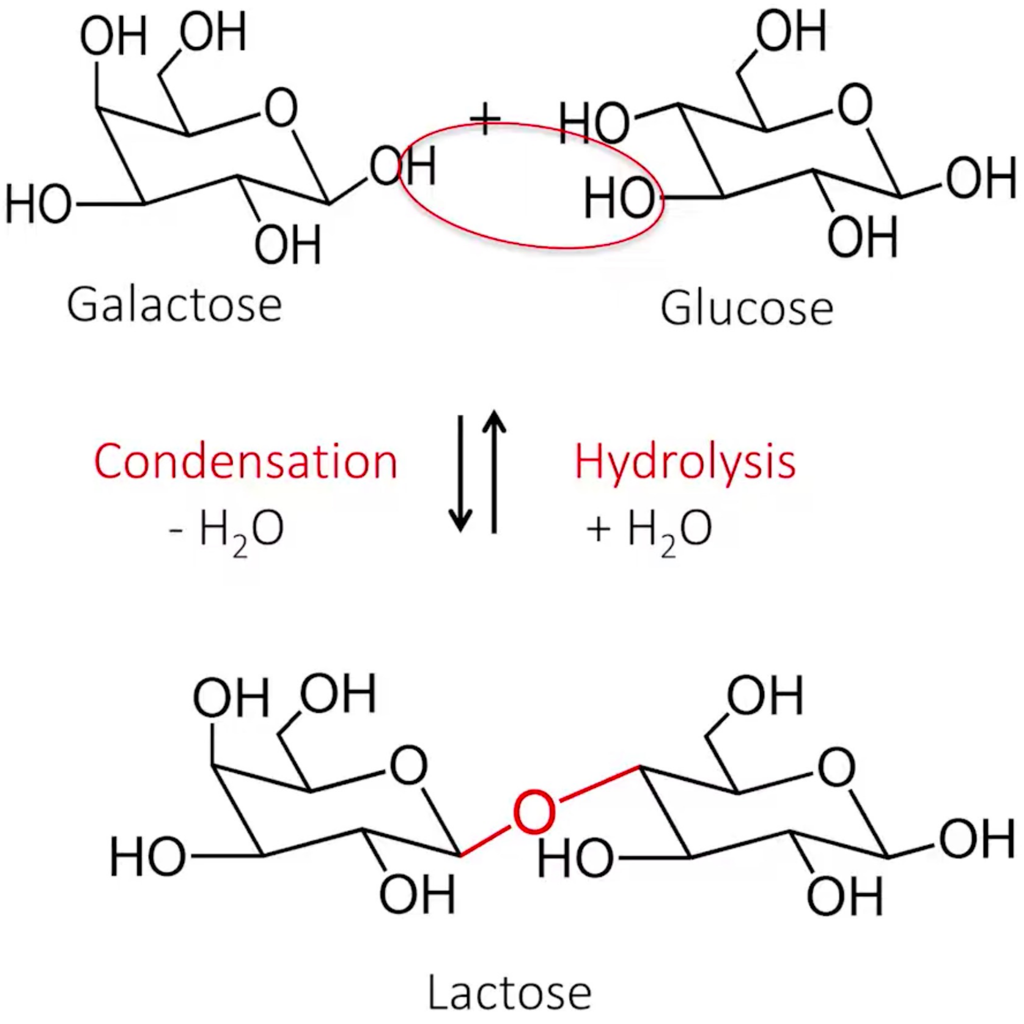
$$M\text{-}OH + M\text{-}OH \rightarrow M\text{-}O\text{-}M + H_2O$$

- **Catabolic reactions** = break down molecules (*e.g.*, hydrolysis)

$$M\text{-}O\text{-}M + H_2O \rightarrow 2\ M\text{-}OH$$

Factory, Maurice Utrillo, 1923

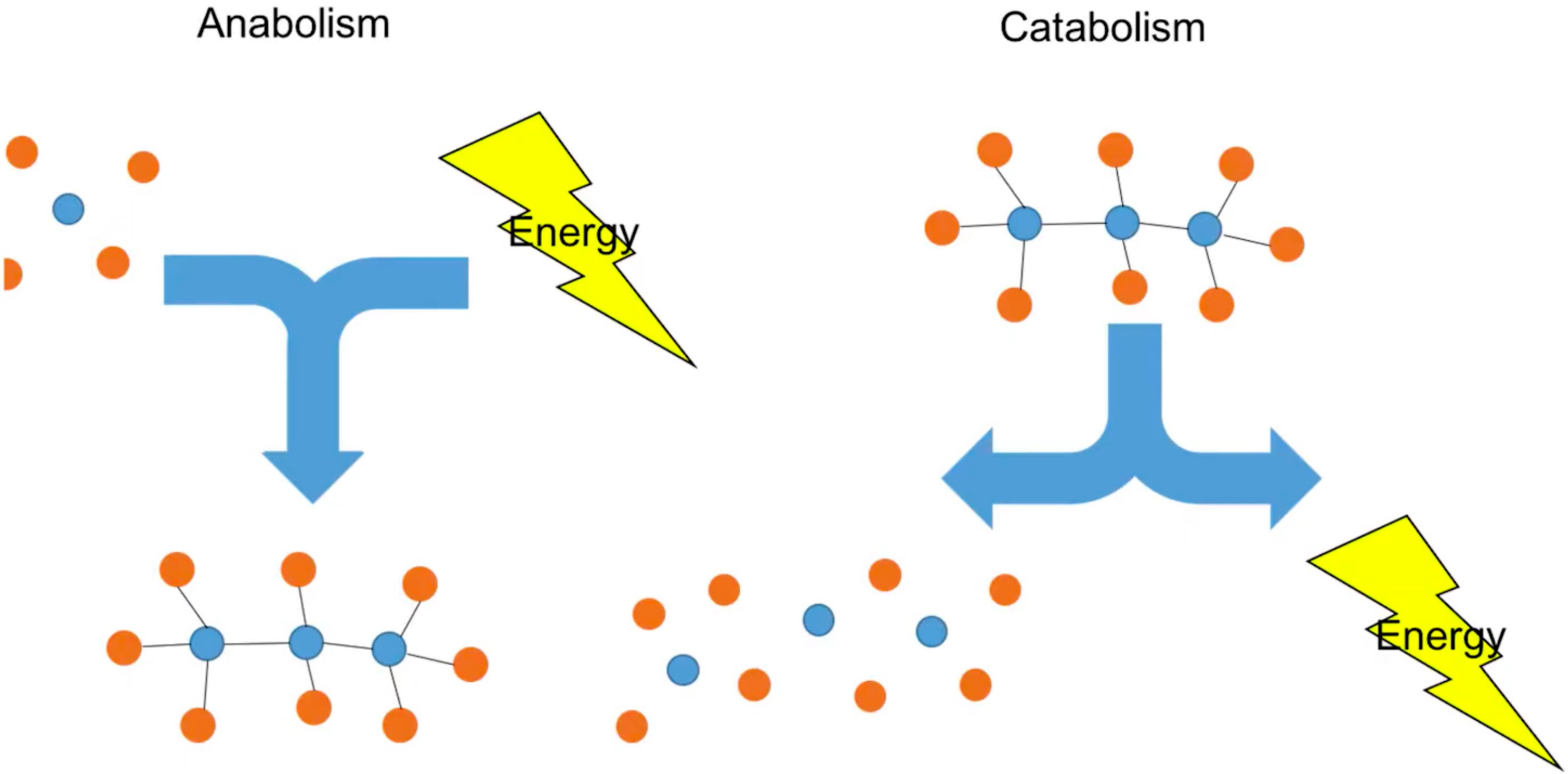
Condensation & hydrolysis



Condensation:
Covalent bonds form with loss of water
Build molecules
Anabolic

Hydrolysis:
Covalent bonds break with addition of water
Break down molecules
Catabolic

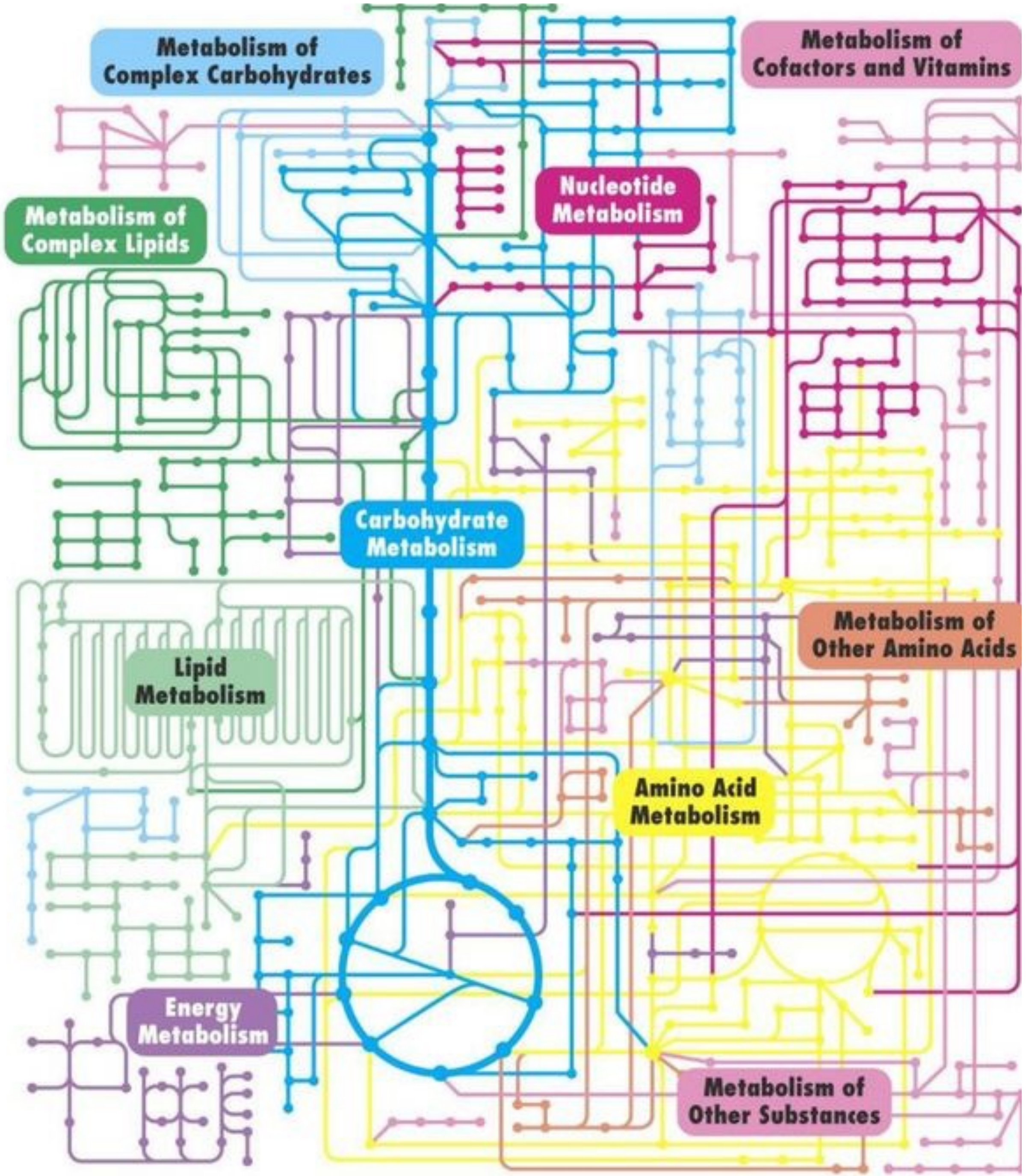
Metabolism & Energy



The metabolic map

Dots = molecules

Lines = chemical reactions making up the metabolism of the cell



Free energy difference

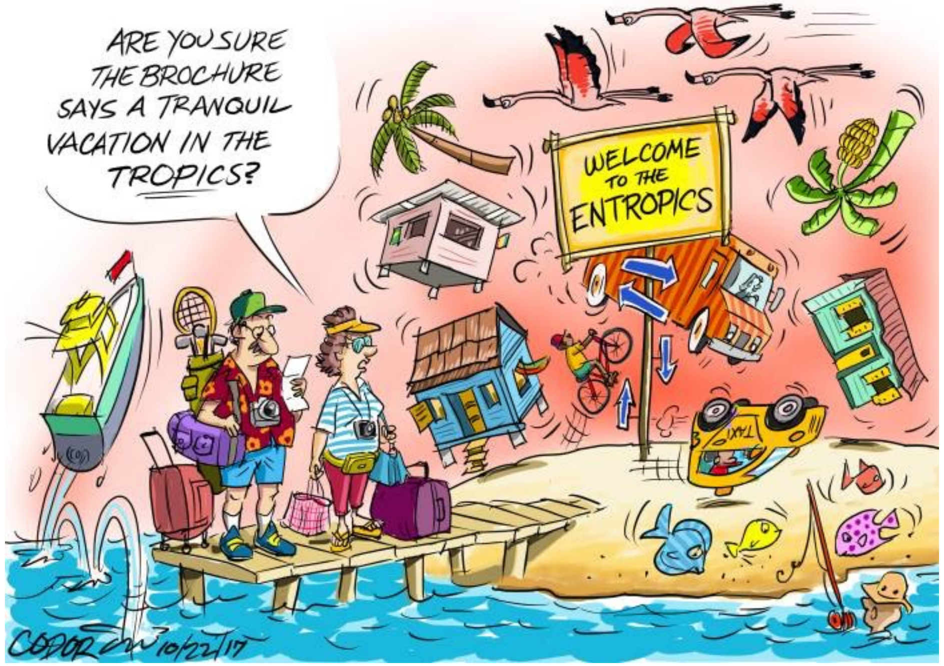
- Reactions are governed by **free energy** (*usable energy*) **G**

  Reagents ⇄ Products

- What really matters is the **free energy difference $\Delta G = \Sigma G_P - \Sigma G_R$**
- ΔG stems from a fundamental law of thermodynamics

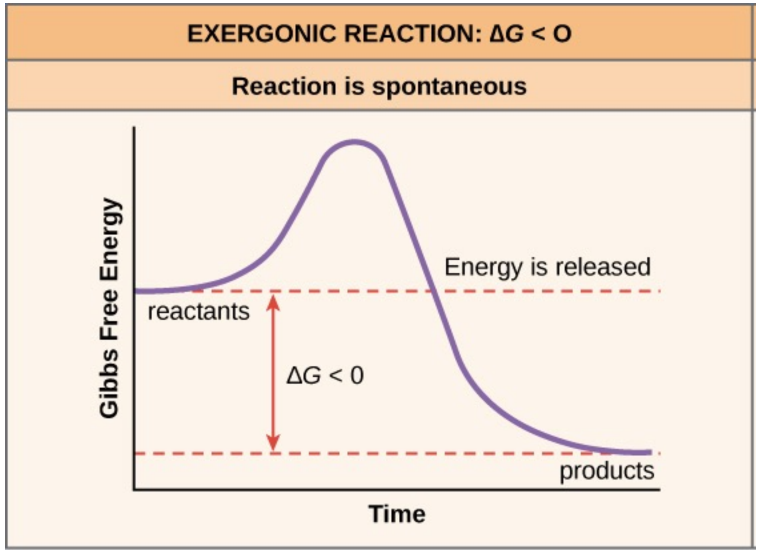
  $$\Delta G = \Delta H - T\Delta S$$

- **H** = **Enthalpy** = *total energy*
- **T** = **Temperature**
- **S** = **Entropy** = *useless energy*



Free energy difference

- $\Delta G < 0$ ($G_P < G_R$) → Energy released, reaction proceeds (thermodynamically spontaneous, exergonic)



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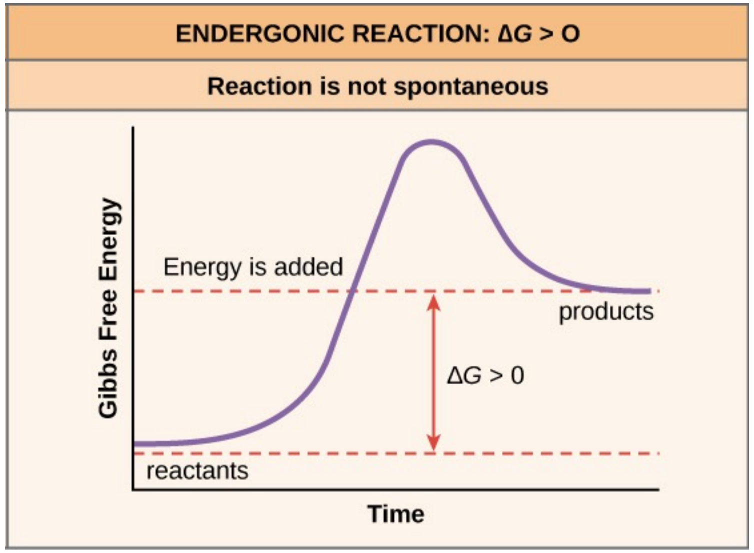

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- $\Delta G = 0$ ($G_P = G_R$) → Chemical equilibrium ($R \rightarrow P = P \rightarrow R$)

$$A \leftrightarrow B$$

$$K_{eq} = [B]/[A]$$

$$\Delta G = -RT \ln [B]/[A]$$

$$\Downarrow$$

$$\Delta G = -RT \ln K_{eq}$$

R= 8.314 J/(mol K) = 1.987 cal/(mol K)

Going to work in the cell factory

- Cells transfer energy from food molecules to run their processes
  - Synthesis
    - Complex molecules (DNA, proteins)
    - Organized structures (organelles)
  - Organization
    - Generation of specialized compartments to store and organize materials for specific tasks

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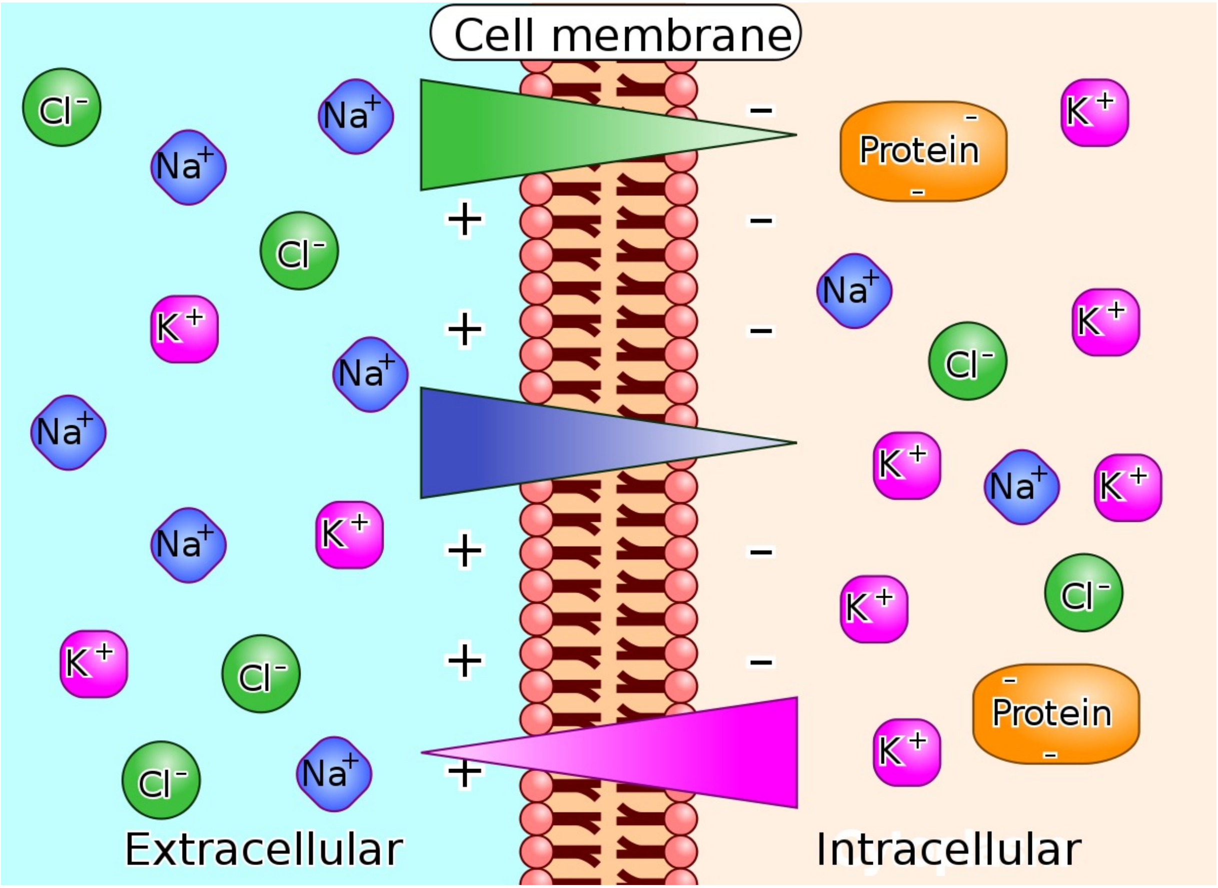
        - Cells organize ions on either cell membrane sides to create electrochemical potentials
            - Mechanism that controls signaling and transfer of materials across the membranes



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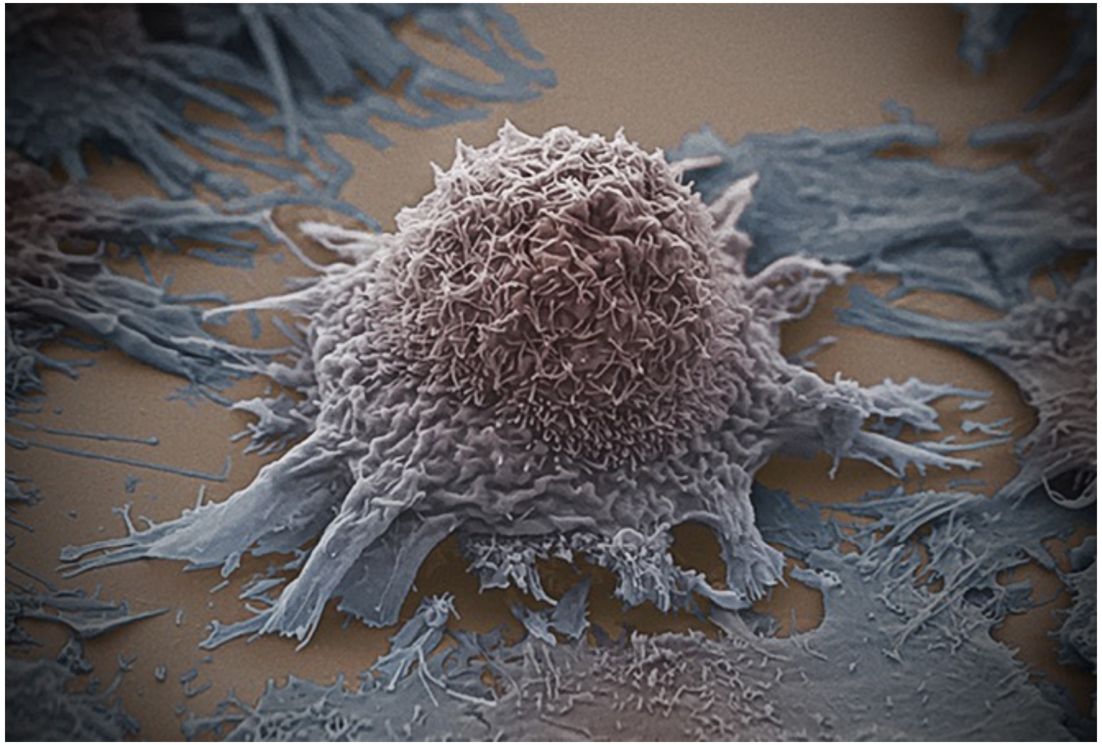
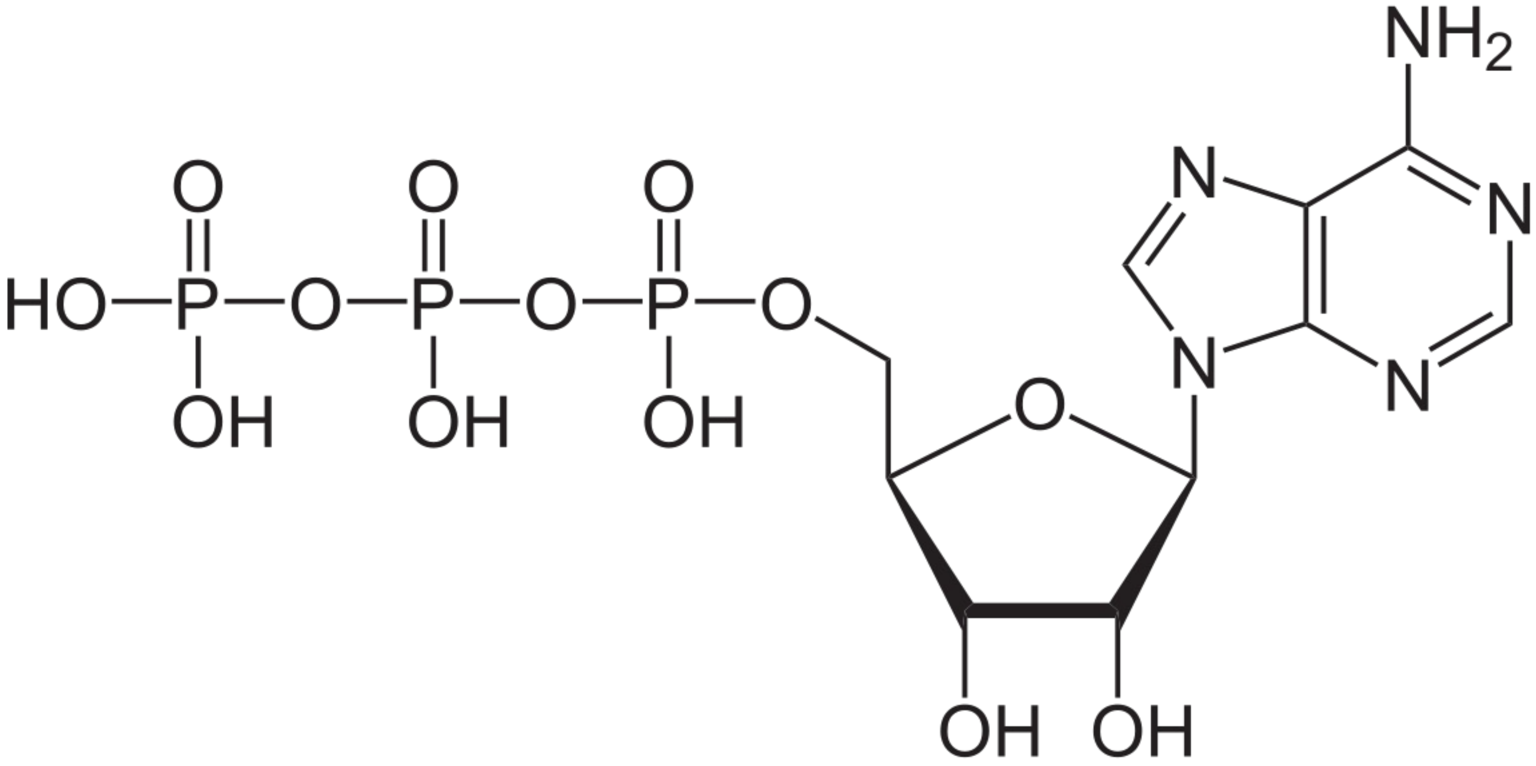
  - Creation of electrochemical gradients
    - Cells organize ions on either cell membrane sides to create electrochemical potentials
      - Mechanism that controls signaling and transfer of materials across the membranes
  - Transport and movement
    - Cells transport molecules from one side of the cell to another
    - Some cells swim or crawl using special motility proteins



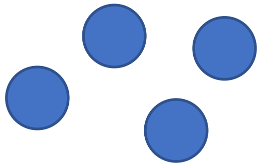
Where does cell energy really come from?

- Cells do not use the energy from food directly
- Adenosine triphosphate, the energy middleman

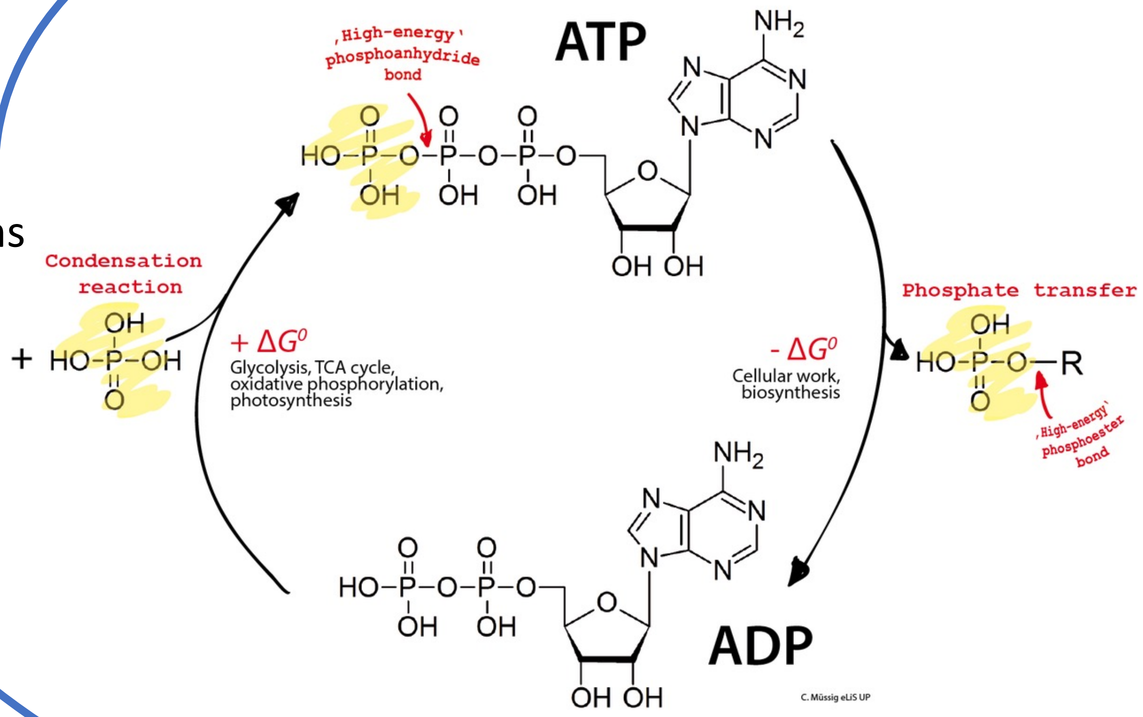


The ATP/ADP cycle

Simple molecules
glucose, amino acids, fatty acids

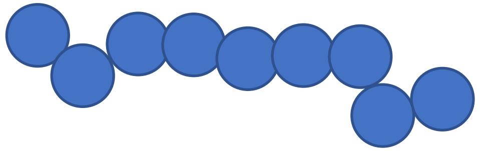


Catabolism – Exergonic reactions transfer energy from complex molecules to ATP



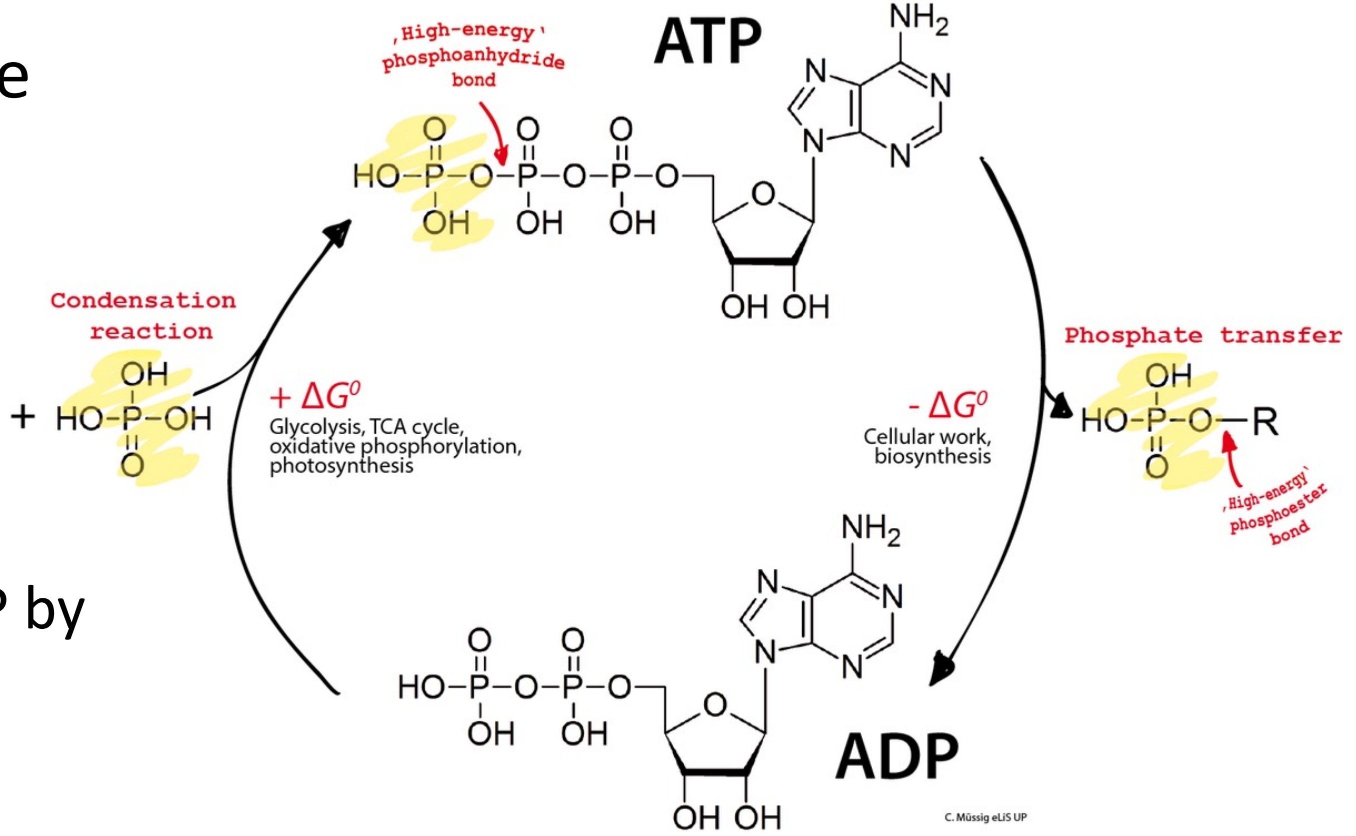
Anabolism – Endergonic reactions transfer energy from ATP to complex molecules

Complex molecules
polycarbs, proteins, lipids

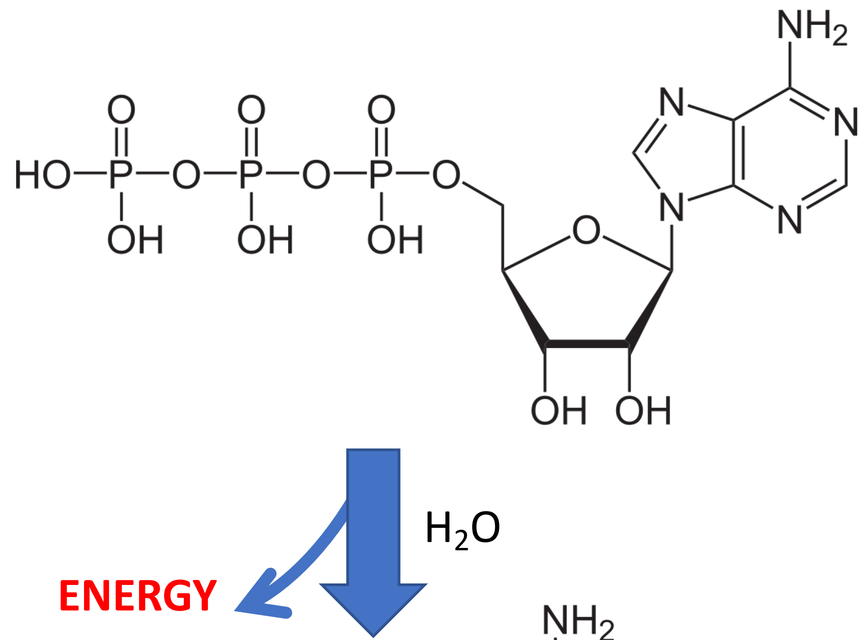


The ATP/ADP cycle – energy coupling

- Cells make and break ATP all the time
- In endergonic reactions
  - Energy is provided by ATP hydrolysis to ADP and P_i
- In exergonic reactions
  - Energy is captured to restore ATP by ADP and P_i condensation



As easy as 1,2,3 – ATP, ADP and AMP

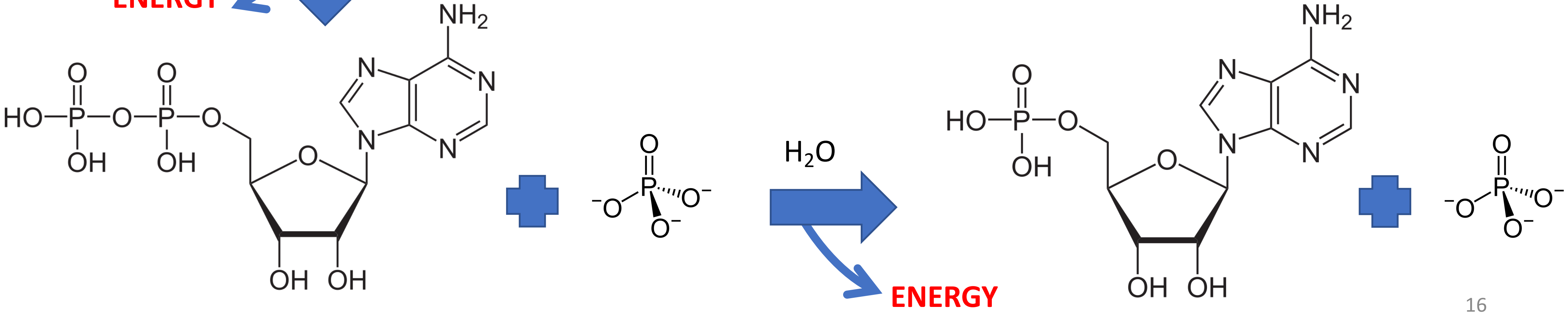


$ATP \rightarrow ADP + P_i$

$\Delta G = -\ 30.5\ kJ/mol = 7.29\ kcal/mol$

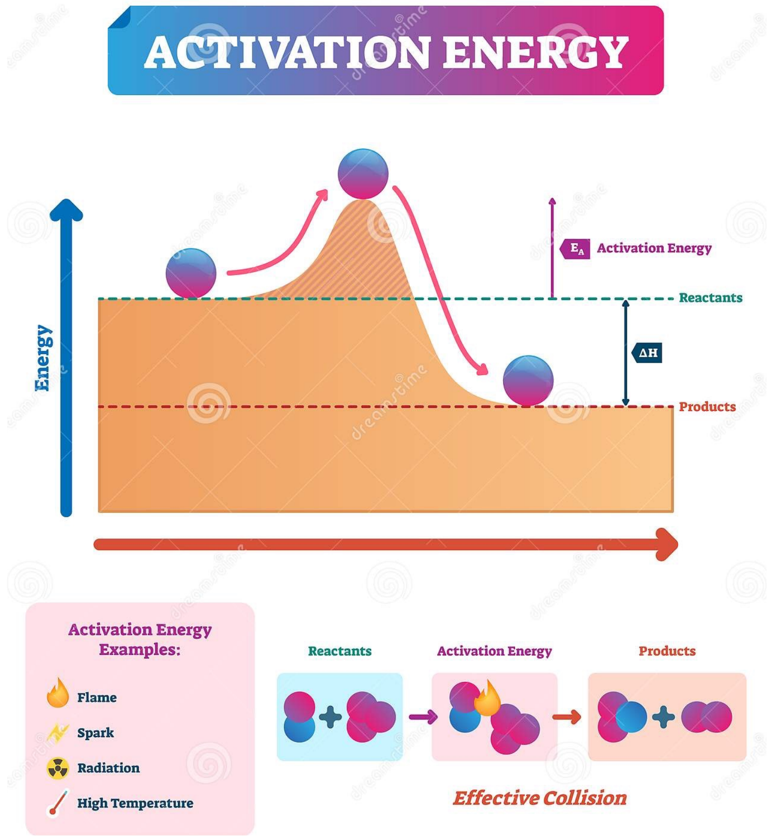
$ADP \rightarrow AMP + P_i$

$\Delta G = -\ 30.5\ kJ/mol = 7.29\ kcal/mol$



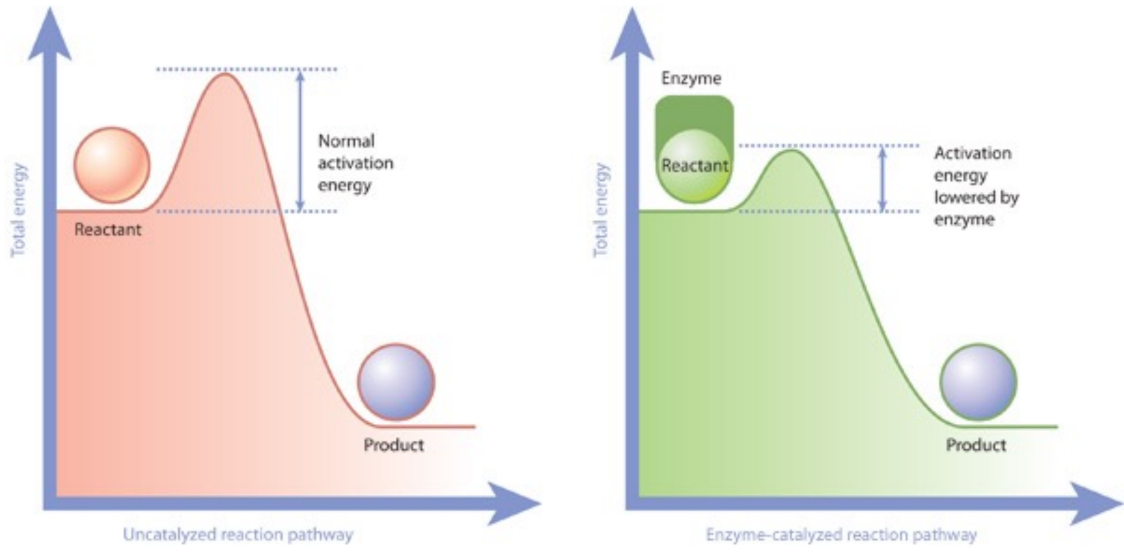
Free energy difference

- Even if a reaction is thermodynamically spontaneous ($\Delta G < 0$), it may not occur
  - It needs an “energetical push”
- **Activation energy E_a = energy barrier**



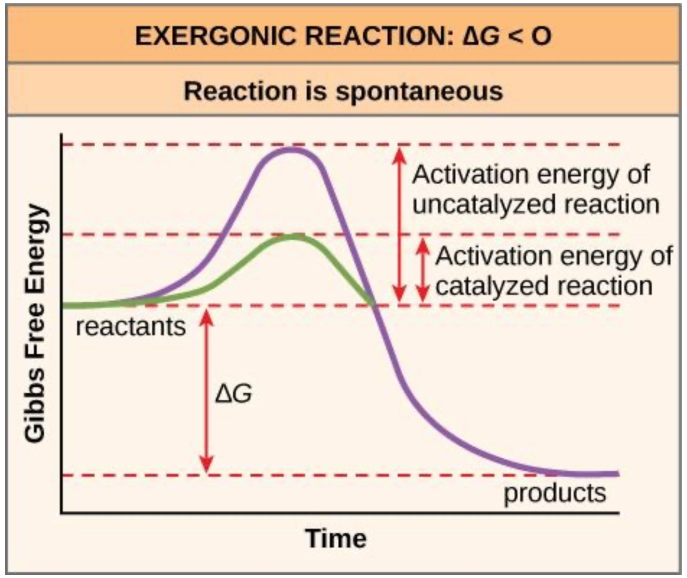
Enzymes

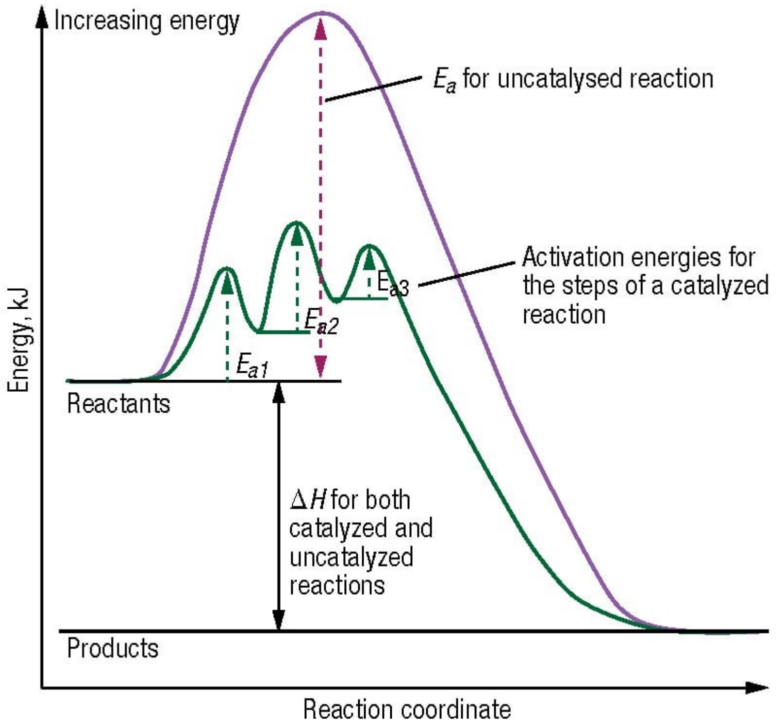
- Even if a reaction is thermodynamically spontaneous ($\Delta G < 0$), it may not occur
  - It needs an "energetical push"
- **Activation energy E_a = energy barrier**
- **Catalysts** = particular class of chemical substances that lower E_a and promote reactions
- **Enzymes** = biological catalysts (mostly proteins)



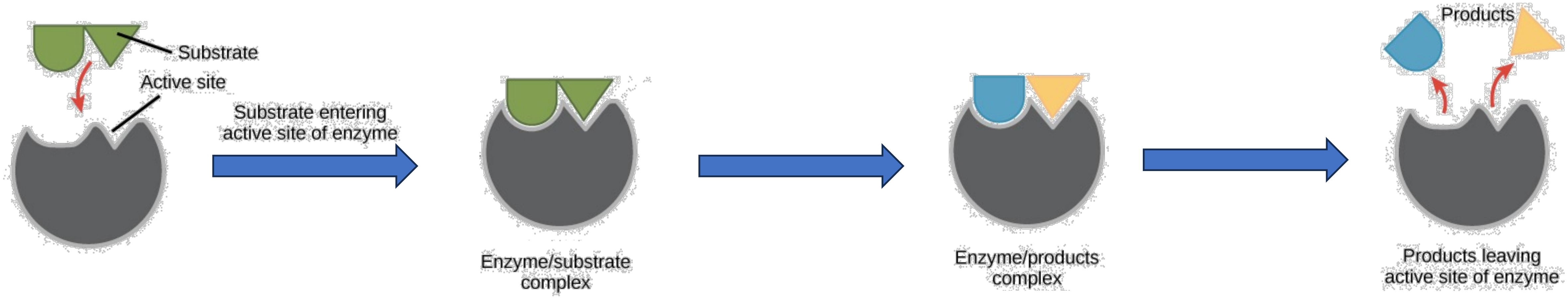
Enzymes

- There are approximately 1300 different enzymes found in the human cell
- Each enzyme catalyzes a specific chemical reaction
- **ENZYMES DO NOT CHANGE THE ΔG OF A REACTION BUT JUST SPEED UP THE REACTION RATE**
  - By breaking down the reaction into different steps, each of which has a low E_a





Enzymes



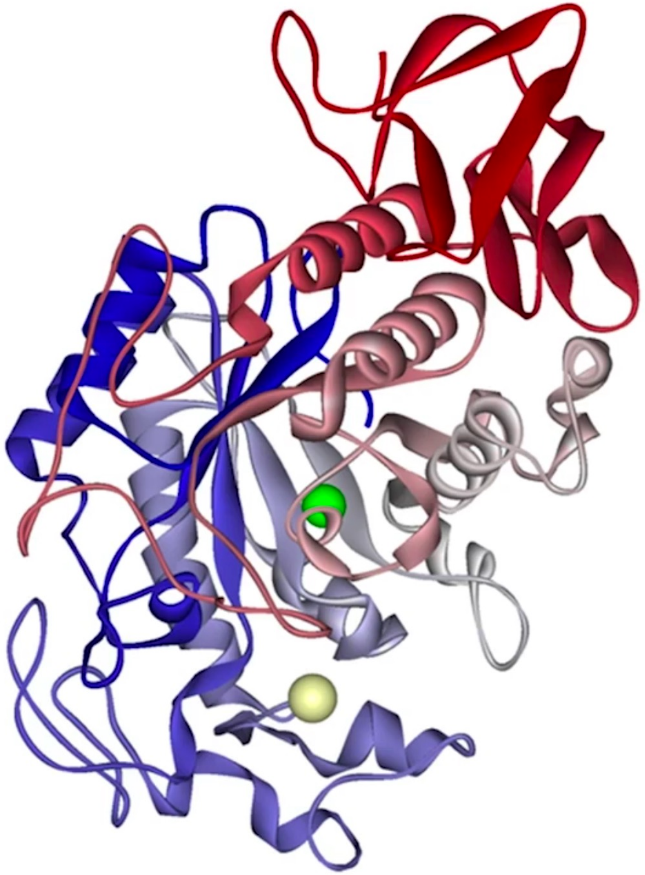
ENZYME CYCLE
(reversible)

Enzyme specificity

Cellulose and starch are both glucose polymers

Cellulase
breaks β-1,4 bonds in cellulose
People do not have this enzyme so we cannot digest grass!

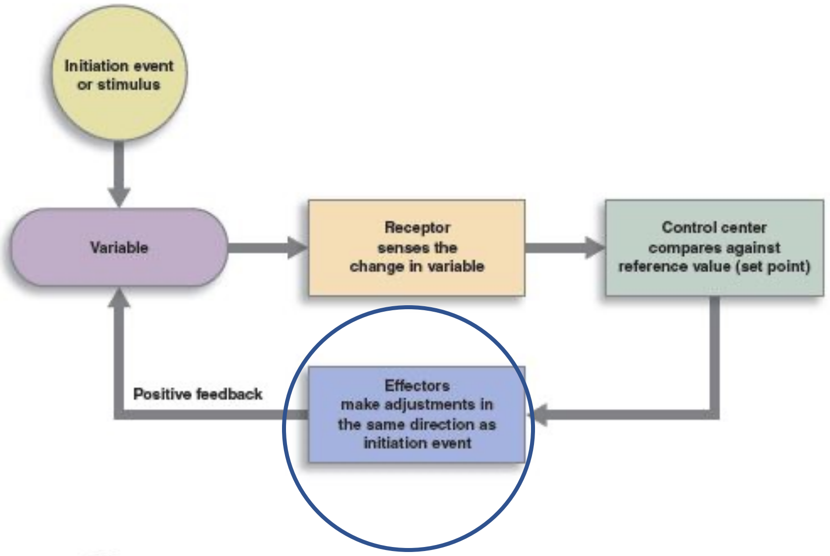
Amylase
breaks α-1,4 bonds in starch
People have this enzyme!

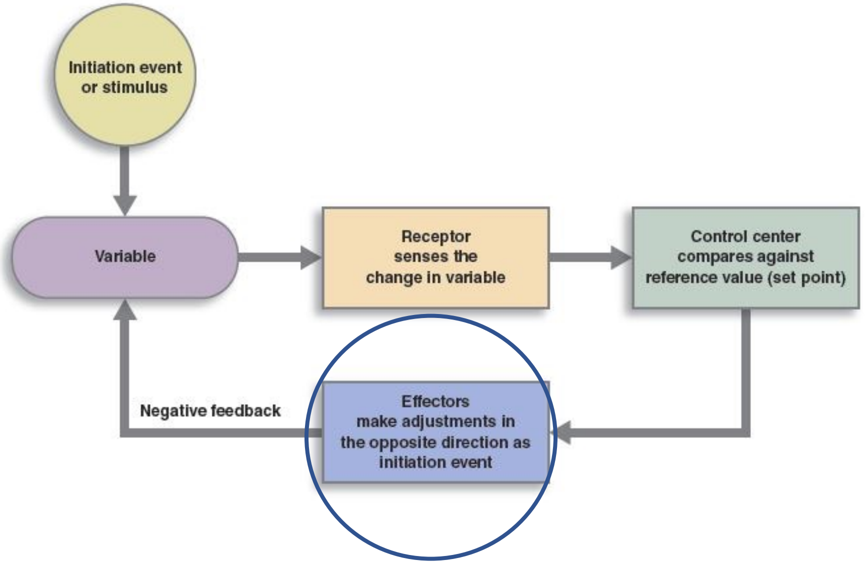


ENZYME SPECIFICITY

Metabolic pathways

- Cellular chemical reactions all catalyzed by enzymes
- Cellular chemical reactions are often linked into **pathways**
  - Ordered sequence of chemical reactions
- Pathways = the "cell production line"
  - Starting from point A → land up with a particular product that the cell really needs
- Reactions are organized into multistep pathways
- Cellular pathways are governed by internal feedback mechanisms
  - **Positive feedback** = make more product(s) along that particular pathway
  - **Negative feedback** = make less and/or stop producing product(s) along that particular pathways
- Cellular pathways can also be mastered by external control signals





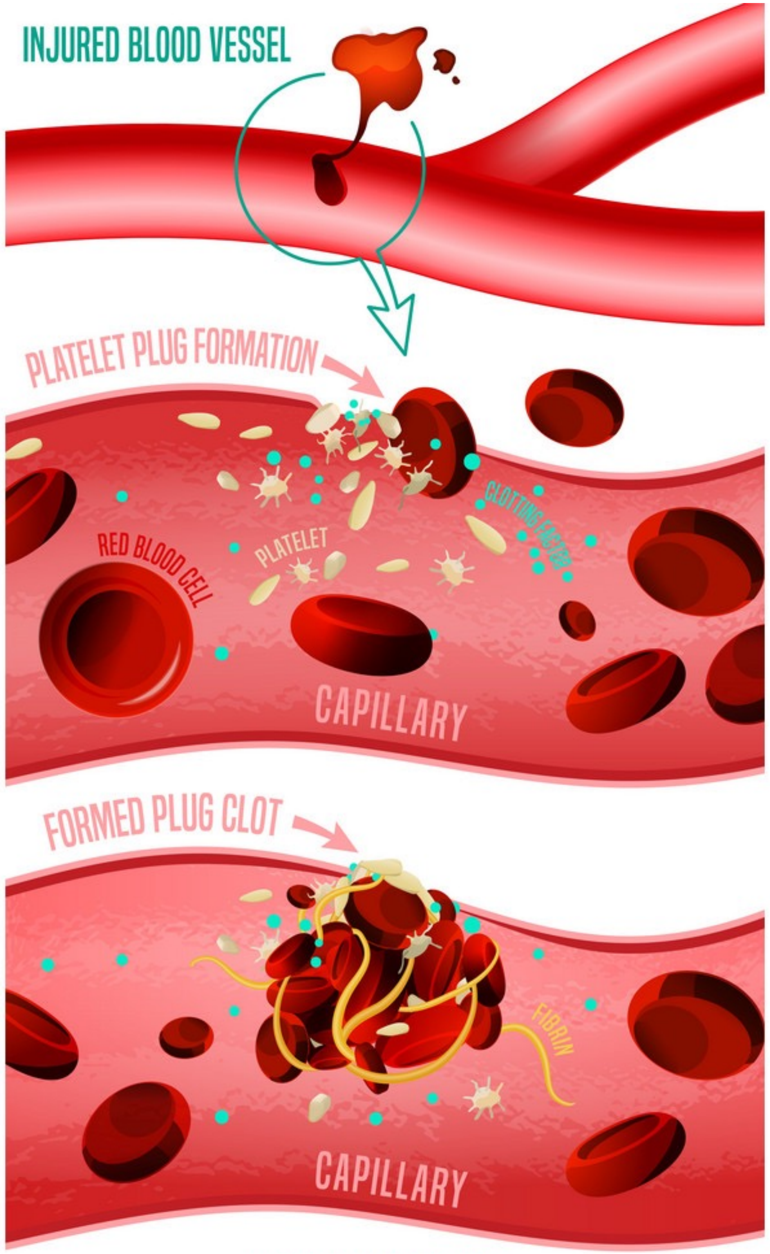
Positive feedback loops

Blood clot formation

DAMAGED TISSUE RELEASES CHEMICALS → CHEMICALS INITIATE PLATELET ACTIVATION → PLATELETS RELEASE MORE CHEMICALS → CLOT FORMS OVER WOUNDED TISSUE

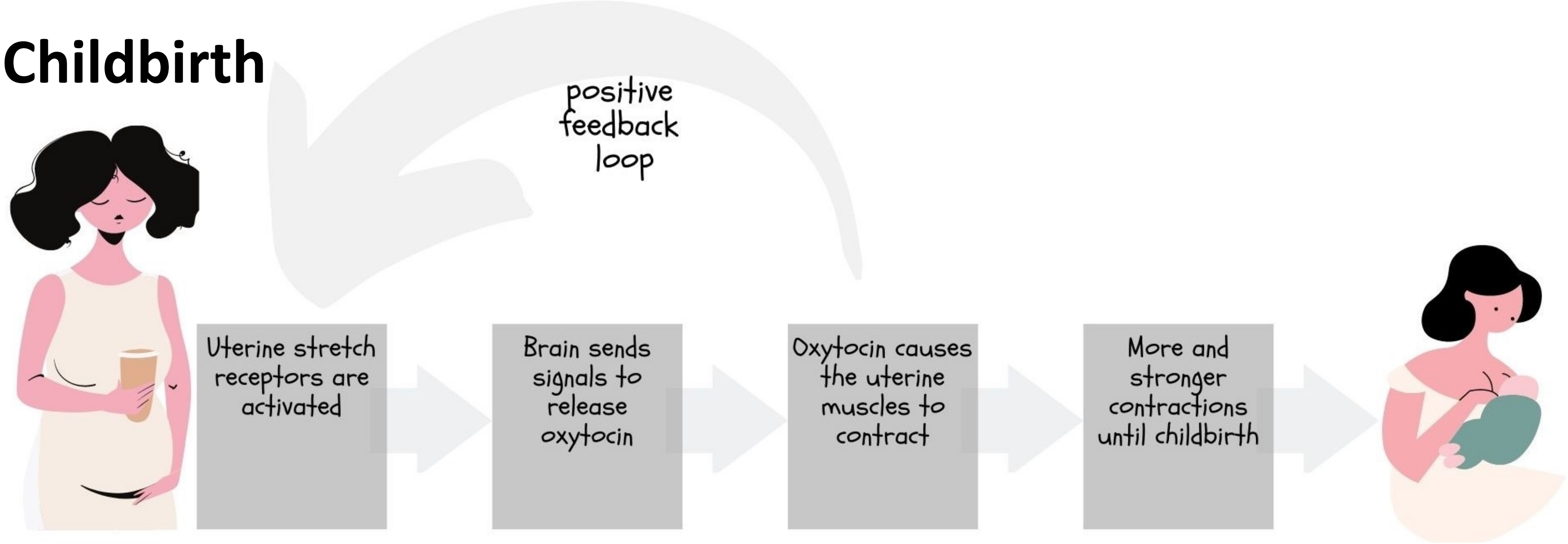
feedback loop

- When the body gets injured the major threat to life is excessive loss of blood
- Blood pressure and blood flow at the site of injury are reduced
- At the site of the injury, blood clotting factors are released to initiate blood clotting
  - Clotting factors are responsible for the formation of a clot in the injured or wounded area
- Once the process begins it promotes the clotting process further → overall, the process of sealing the injured site is speeded up
- This is one of the life-saving examples of positive feedback



Positive feedback loops

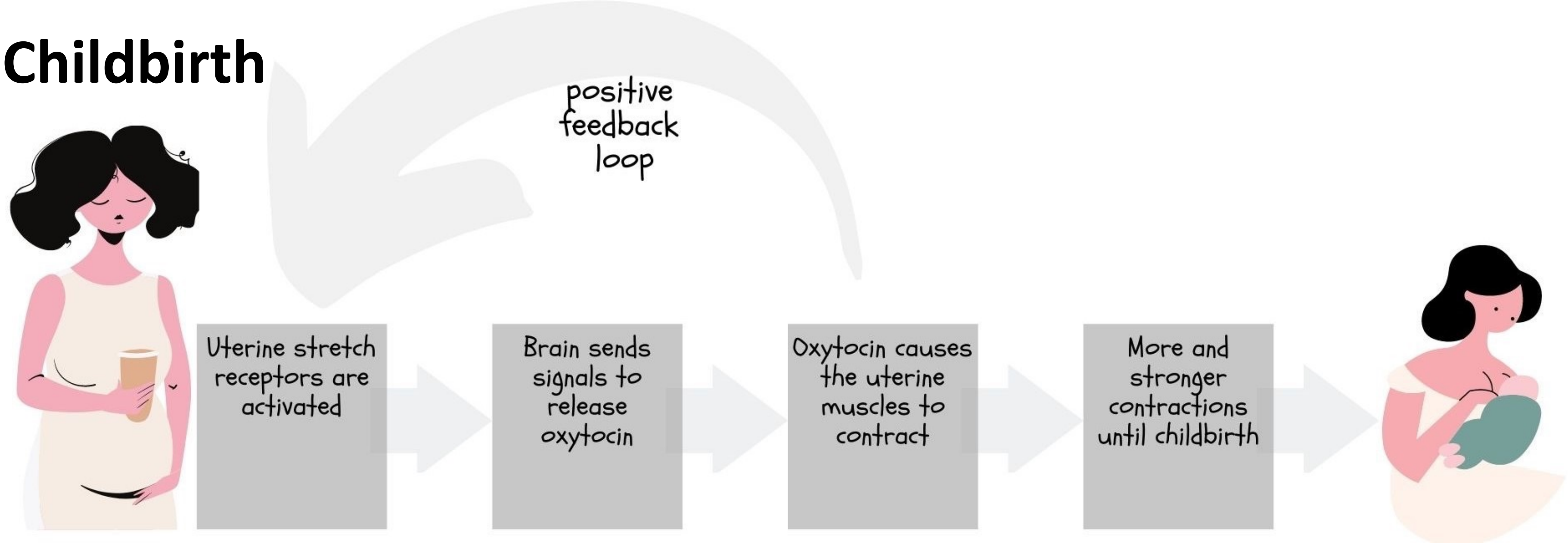
Childbirth



- The onset of contractions in childbirth is also known as the *Ferguson reflex*
- The baby pushes against cervix, causing it to stretch
- Stretching of cervix causes nerve impulses to be sent to the brain
- Brains stimulates the posterior pituitary gland to to release oxytocin
- Oxytocin stimulates the uterine muscle to contract, initiating the birth process
- The fetus responds to uterine contractions by releasing prostaglandins, which triggers further uterine contractions

Negative feedback loops

Childbirth



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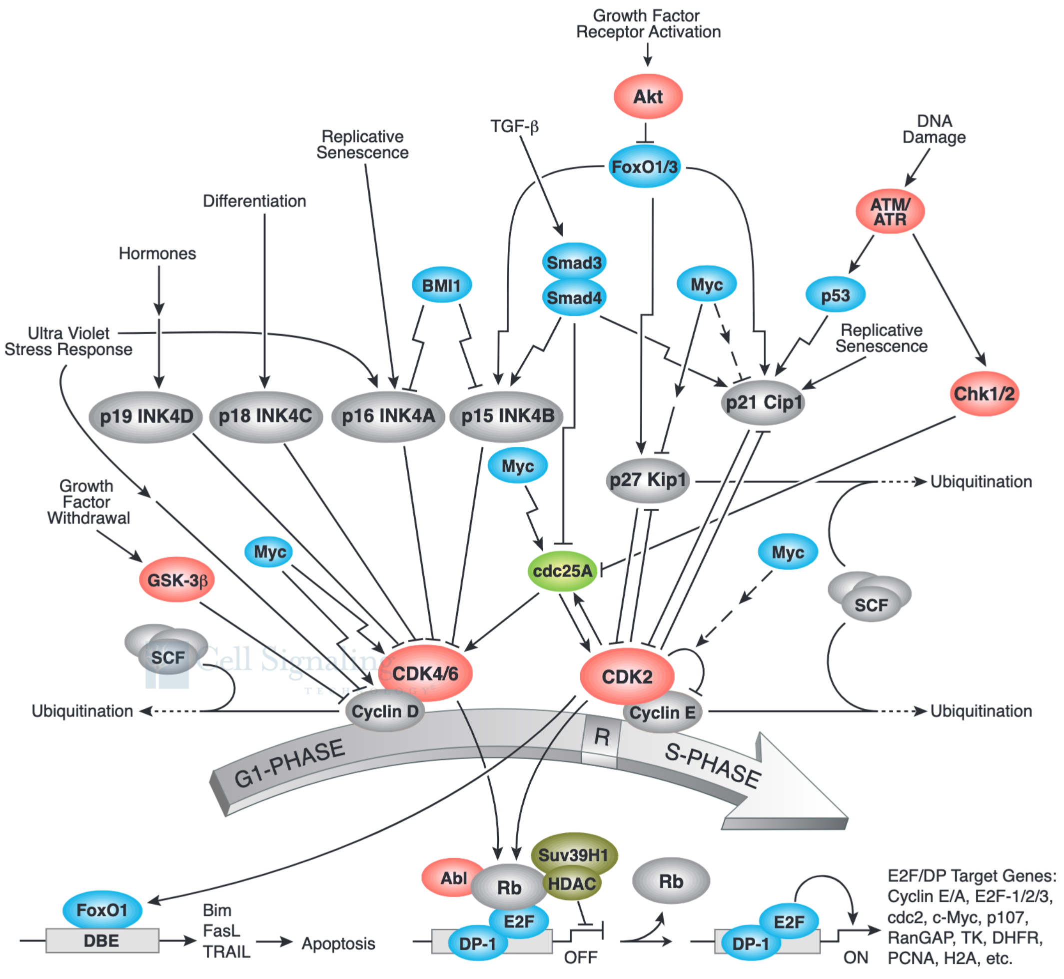
Cellular pathways (examples)

Production (positive)

Inhibition (negative)

Cell Cycle Control: G1/S Checkpoint



Cell Cycle Control: G2/M DNA Damage Checkpoint