

Bioengineering

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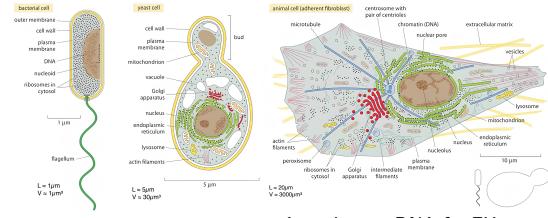
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Giga	G	10^9	Milli	m	10^{-3}	Pico	p	10^{-12}
Mega	M	10^6	Mikro	μ	10^{-6}	Femto	f	10^{-15}

Orientation of the cell

Central Dogma of Molecular Biology



Cells:



nucleus: houses DNA for EK
nucleolus: produces ribosomes/rRNA
mitochondria: cellular respiration (prod. ATP)
ribosome: produces proteins from mRNA transcripts

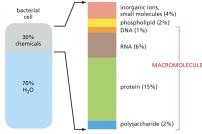
RER, SER and Golgi: involved in protein/lipid synthesis/processing

cytoskeleton: structure to cell, transport mol. in the cell or to enable the cell to move (cell migration)

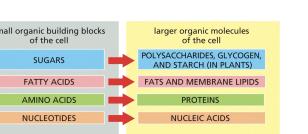
centrosome: organizes microtubules during cell division allows the mother cell to split into 2 cells

Building Blocks

Cell composition:



Main building blocks:



- Lipids (fatty acids):** long-term energy storage, cell membrane structure, signaling molecules.
- Proteins (amino acids):** perform most of the cell's functions, including catalyzing reactions, signaling, and structural support. amino group NH_2 , carboxyl group COOH
- Nucleic acids (nucleotides):** store and transmit genetic information (DNA, RNA), carry energy
- Carbohydrates (Sugars):** short-term energy storages and for structural support.

Bounds

$$\text{Covalent} \longleftrightarrow 100k_B T$$

$$\text{Ionic} \longleftrightarrow 1 - 10k_B T$$

$$\text{Hydrogen} \longleftrightarrow 1k_B T$$

$$\text{Van der Waals} \longleftrightarrow 0.1k_B T$$

$$\text{Electrostatic} \longleftrightarrow 0.1k_B T$$

K_D : Equilibrium const.; indicates the ratio of free & bound units

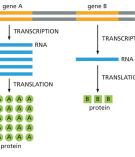
k_{off} : Dissociation rate constant; inverse of time protein dissociates from the ligand

k_{on} : Association rate constant, speed of the reaction

Enzymes (aka catalysts)

- Accelerate reaction by lowering the activation energy
- Are not consumed in the reaction
- Are specific to the reaction they catalyze
- Do not change the equilibrium point of the reaction.

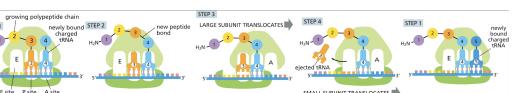
Biosynthesis



Genes are not always on and do not always produce the same number of transcripts or proteins.

Synthesis of proteins is a complicated and tightly regulated process.

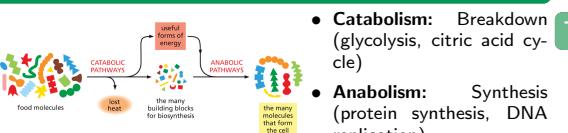
Translation by Ribosomes



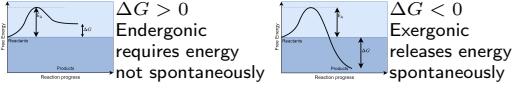
- On the mRNA, every three bases (= nucleotides) form one codon (needs ATP).
- A tRNA brings a matching amino acid. It has an anticodon that is complementary to the mRNA codon.
- The tRNA binds to the mRNA in the ribosome (at the A site).
- The amino acid is added to the growing polypeptide chain.
- The tRNA is ejected (from the E site), and the ribosome shifts forward by one codon.
- The process repeats until a stop codon is reached.

Multiple ribosomes can translate the same mRNA at the same time (making multiple proteins at the time), forming a polyribosome (or polysome).

Energy and Metabolism

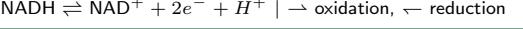


Free Energy

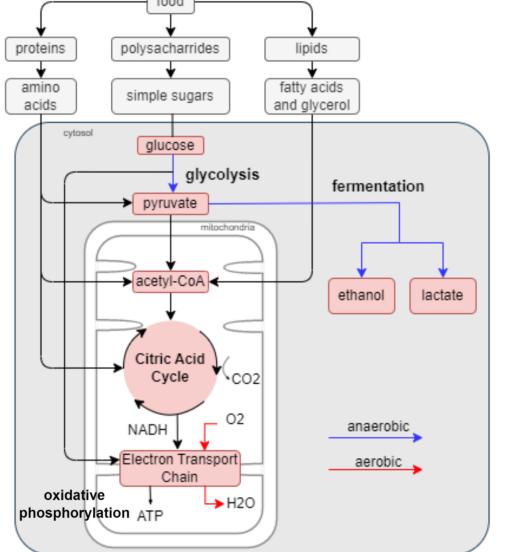


Redox

Oxidation loss of e^- ($H^+ + e^-$) | Oxidation of glucose
 Reduction gain of e^- ($H^+ + e^-$) | Reduction of pyruvate



Glucose Metabolism



Stage Molecules Glycolysis

Invest 2 ATP, 2 NAD^+ , 1 glucose
 Payoff 4 ATP (2 net), 2 NADH , 2 H^+ , 2 pyruvate
 Net gain 2 ATP, 2 NADH , 2 pyruvate

Stage Molecules Citric Acid Cycle

Invest 2 Acetyl-CoA, 6 NAD^+ , 2 FAD, 2 GDP (ADP)
 Payoff 6 NADH , 2 FADH_2 , 2 GTP (ATP), 4 CO_2
 Net gain 2 ATP (GTP), 6 NADH , 2 FADH_2 , 4 CO_2

Stage Molecules Oxidative Phosphorylation

Invest 10 NADH , 2 FADH_2 , 6 O_2
 Payoff 34 ATP, 6 H_2O
 Net gain 34 ATP, 6 H_2O

Transcription

- Small region of DNA opens and unwinds.
- RNA polymerase (catalytic enzyme) interacts with one strand in the open region of DNA and adds ribonucleotides to grow an RNA polymer.
- RNA polymerase further unwinds the DNA in the forward direction.

types of RNA

Type	Function
messenger RNA mRNA	code for proteins
ribosomal RNA rRNA	form core of ribosomal structure and catalyze protein synthesis
micro RNA miRNA	regulate gene expression
transfer RNA tRNA	serve as adaptors between mRNA and amino acids during protein synthesis
other non-coding RNA	RNA splicing, gene regulation, telomere maintenance, etc.

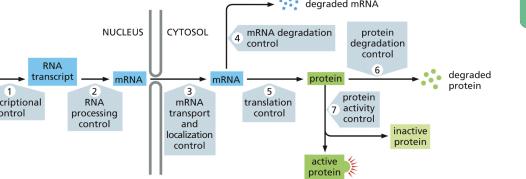
Eukaryotes vs Prokaryotes

- Multiple types of RNA polymerases transcribe different classes of RNA.
- Transcription initiation is more complex.
- mRNA molecules undergo splicing, where introns (non-coding regions) are removed and exons (coding regions) are joined together to form the final RNA.
- 1 type of RNA polymerase transcribes all types of RNA.
- Transcription initiation is a simpler process.
- mRNA molecules are translated immediately after transcription

Both use gene regulatory proteins that bind to specific sequences of DNA:

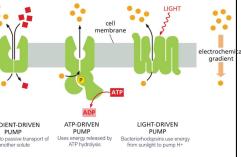
- Repressors: Bind to sequences to turn genes off. Make it more difficult for RNA polymerase to bind to DNA.
- Activators: Bind to sequences to turn genes on. Make it more favorable for RNA polymerase to bind to DNA.

Gene Regulation



Active Transport

Pumps:



Vesicular Transport

- Endocytosis: into cell
- Exocytosis: out of cell
- Pinocytosis: cell drinking
- Phagocytosis: cell eating
- Receptor-mediated endocytosis: specific uptake of molecules

Passive Transport

Diffusion:

Along concentration gradient, from high to low concentration.

$$\tau_D = \frac{l^2}{D} \quad D = \frac{k_B T}{6\pi\eta a}$$

Osmosis:



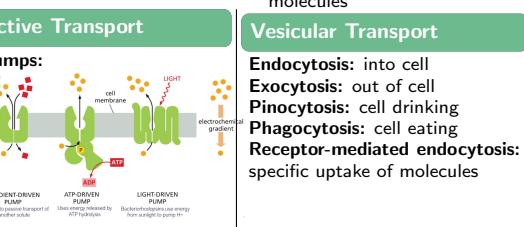
Hypertonic: high solute concentration

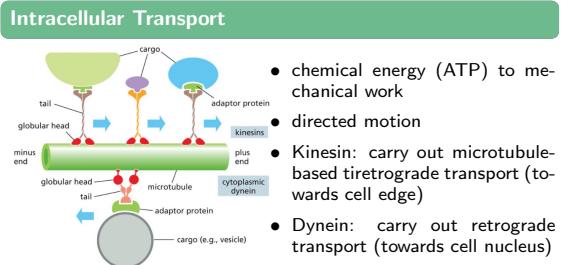
Hypotonic: low solute concentration.

Membrane is selectively permeable, allowing some molecules to pass through while blocking others.

Facilitated Diffusion:

- selective to size and charge of solute
- bidirectional
- gated by external inputs
- Transporter good for large molecules





Cell Sensing and Signaling

Cellular Communication

Long Range:

Endocrine

- into blood stream
- affect whole organism
- in neurons (electric)
- at synapses (chemical)

Short Range:

Paracrine

- affect local tissue
- Contact Dependent
- direct binding

Signaling

Cell Surface Receptors:

Extracellular signal molecule (hydrophilic or charged) causes receptor to release intracellular signal molecule.

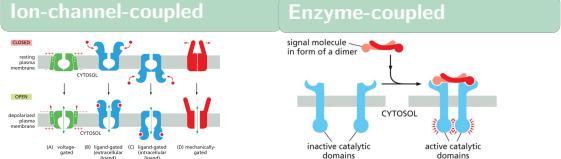
Intracellular Receptors:

Signal molecule (hydrophobic) cross the membrane and act inside the cell.

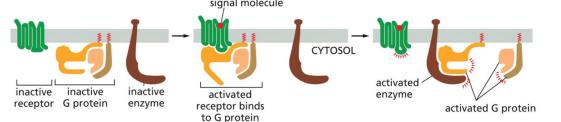
Signal is:

- Amplified
- Integrated
- Distributed
- Modulated (feedback loop)

Receptors



G-protein-coupled receptors



- Ligands (ex.: hormones, neurotransmitters) bind to GPCR (G-protein coupled receptor) which changes conformation
- Activated receptor causes G-protein to exchange its GDP for GTP gets activated
- G-protein modulates the activity of effector molecules generate intracellular second messenger