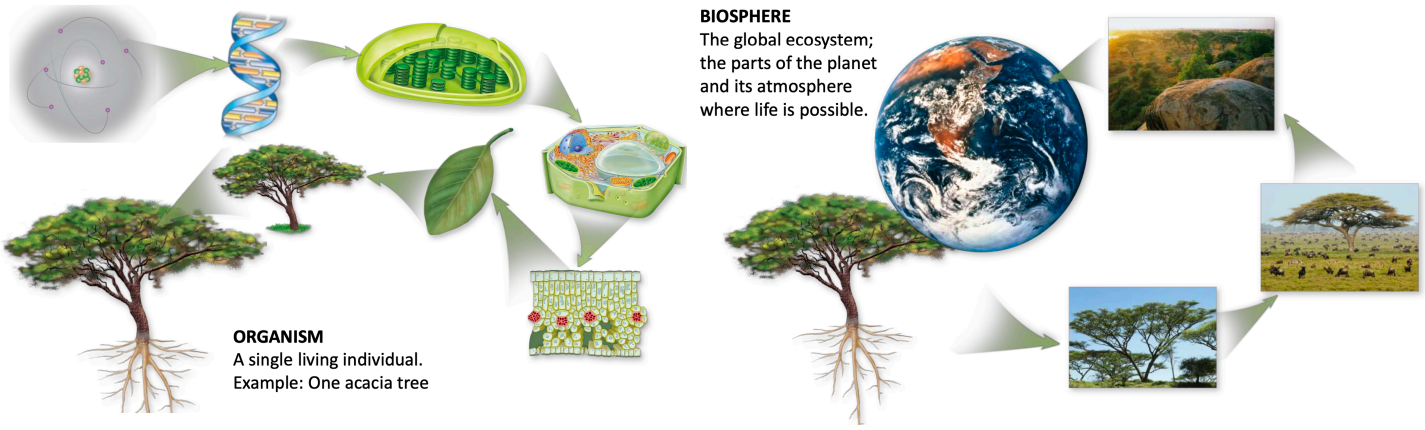
LIFS 1901 Notes

by Frank Chen

All living things generally share these 7 characteristics
Cell – Organisms are made up of **cells** and are organized into levels
Metabolism – acquire and use energy
Reproduce – makes more of itself
Respond to stimuli – able to sense the surroundings
Homeostasis – to maintain your internal state
Growth and Development – increase in size or number of cells vs changes that take place from conception to maturity
Adaptation – Have the capacity to adapt to the environment through evolution

Parasites are considered **living**, but **viruses** are considered **non-living**.

Living things are organized in a hierarchy of 12 levels.
atom<molecule<organelle<**cell**(50–200μm)
<tissue<organ<organ system<**organism**
<population<community<ecosystem<**biosphere**



Chemical cycling & energy flow (one-way, through the food chain)

The 8-level Classification of Living Things (Taxonomy)
Domain域 > Kingdom界 > Phylum门 > Class纲 > Order目 > Family科 > Genus属 > Species种
DKPCOFGS

3 Domains
Bacteria 细菌域: Single cells. Bacteria are found nearly everywhere.
Archaea 古菌域: Single cells. Many live in extreme environments, e.g. salty, acidic, lack oxygen conditions.
Bacteria(Eubacteria) + Archaea(Archaebacteria) = **Prokaryotes 原核生物**

Eukarya 真核生物域: Eukaryotic cells. Single-celled and multi-celled species of protists, fungi, plants and animals.

Kingdom Protista 原生生物
Kingdom Plantae 动物界
Kingdom Animalia 植物界
Kingdom Fungi 真菌界

Archaea and Eukarya are more close to each other.

The Linnaean system – Binomial in Latin
Species = genus, specific epithet
Genus capitalized, both words in italics
e.g. Species: *Homo sapiens* (Genus: Homo)

A species: One or more groups of individuals that potentially interbreed, produce fertile offspring, and do not interbreed with other groups.

The Process of Science
Observation → Question → Research topic area → Hypothesis → Prediction → Test with experiment → Analyze data → Conclusion → Communication

Inductive reasoning (Bottom-up logic) & **Deductive reasoning** (Top-down logic)
Inductive: specific observations → general conclusions
Deductive: general principles → specific conclusions
Inductive reasoning is not always reliable, while deductive reasoning is generally considered more reliable.

Animal models
Chimpanzee
Mouse (>90%)
Zebrafish (84%)
Fruit fly (77%)
Roundworm (65%)

Control Group/Experimental Group
Data must be repeatable

Cation 阳离子
Anion 阴离子

3 Types of bonding
Ionic bonds / Covalent bonds / Hydrogen bonds

Electronegativity is the measure of an atom's ability to attract electrons in a chemical bond.
Cohesive forces / Adhesive forces
Polar/Nonpolar Covalent bonds

due to the polarity of water molecules, allows them to surround and separate ions and polar molecules
NaCl in water: Ionized and polar molecules form hydrogen bonds and are hydrophilic
solute溶质 + solvent溶剂 = solution溶液
Cohesion causes water to have a high surface tension
Ionization of water
pH = −log [H+]
pH of blood ~ 7.4
Bicarbonate Buffer in Blood: HCO3−
Acid: H+ + HCO3− = H2O + CO2
Base: OH− + HCO3− = H2O + CO3^2−

Macromolecules are made from monomers
Triglyceride(甘油三酯) = 3 Fatty Acid(脂肪酸) + Glycerol(丙三醇)
H2CO−CO−[CH2]n−CH3
HCO−CO−[CH2]n−CH3
H2CO−CO−[CH2]n−CH3

Carbohydrate
C:H:O=1:2:1

simple	monosaccharide	glucose/fructose/galactose	
	单糖	葡萄糖/果糖/半乳糖	
	disaccharide	maltose/sucrose/lactose	
	二糖	麦芽糖/蔗糖/乳糖	
complex	polysaccharide	starch/glycogen/cellulose/fiber	(insoluble)
	多糖	淀粉/糖原/纤维素	

Starch stored in plants, glycogen stored in animals
Cellulose in cell walls

Lipid
Triglyceride/phospholipid/steroid/wax (hydrophobic, insoluble)
Saturated (solid) / monounsaturated / polyunsaturated (liquid) fat
Margarine 人造黄油
Steroid 类固醇
All have a backbone of four fused carbon rings
cholesterol 胆固醇 → steroids like sex hormone
Phospholipid
Hydrophilic head Hydrophobic tail
{N(CH3)3−CH2−CH2}−{PO4}−CH2−HCO−CO−[CH2]n−CH3
−H2CO−CO−[CH2]n−CH3

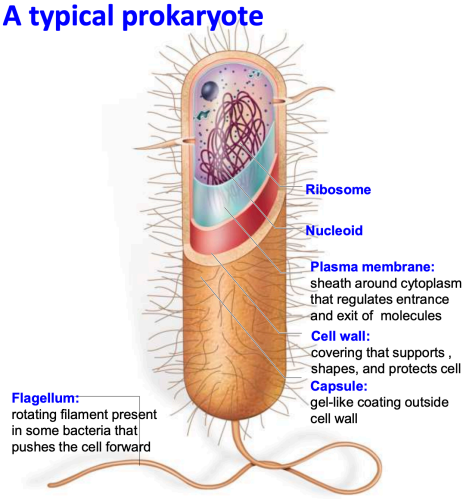
Protein
Composed of amino acid(氨基酸) monomers
NH2−CH2−COOH + NH2−CH(CH3)−COOH → NH2−CH2−CO−NH−CH(CH3)−COOH + H2O
O=C−N−H: peptide bond(肽键)

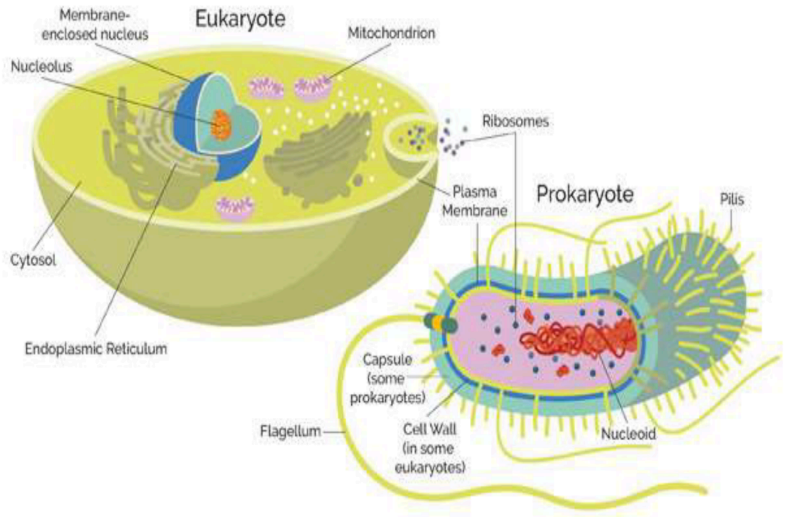
Amino group
H2N–CHR–COOH (side chain R)
20 amino acids, 11 are non–essential (–ine)
4 levels of protein structure
Primary structure: sequence of amino acids
Secondary structure: helix/pleated sheet, H bonds
Tertiary structure: 3D, polypeptide chain, S bonds, H bonds, hydrophobic interactions
Quaternary structure: two or more polypeptides join to form a single protein
Prion – misfolded protein – mad cow disease

Nucleic Acid
DNA → mRNA → protein
Nucleotide 核苷酸
triphosphate + 5–carbon sugar + nitrogenous base
PO4–[C5]–Base
Base: DNA: A/C/G/T, RNA: A/C/G/U, A=T, C≡G
Purine 嘌呤: A/G
Pyrimidine 嘧啶: C/T/U
Adenine 腺嘌呤, Thymine 胸腺嘧啶, Guanine 鸟嘌呤, Cytosine 胞嘧啶, Uracil 尿嘧啶
P group in 5', –OH group in 3'
5' 3'
S–T=A–S
P P
S–C≡G–S
P P
S–A=T–S
3' 5'
mRNA, tRNA, rRNA
Found by James Watson and Francis Crick
Adenosine Triphosphate 腺苷三磷酸
Base–[C5]–P–P~P

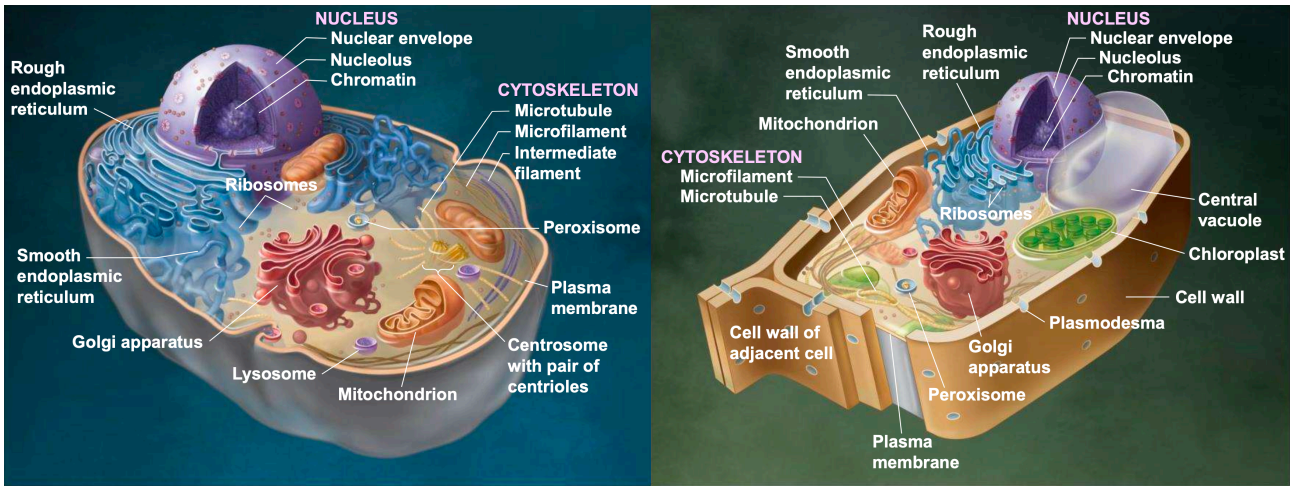
Small cells have a higher surface–volume ratio
microvilli 微绒毛
alveoli 肺泡
Electron microscope: SEM, TEM
More than 1000x
Scanning/transmission Electron microscope
Eukaryote 真核细胞
process membrane–enclosed structures including the nucleus
All cells except bacteria and archaea
Prokaryote 原核细胞
Lack membrane–enclosed structures, lack the nucleus 细胞核
Contain a nucleoid 类核

A typical prokaryote





Prokaryote: nucleoid, circular DNA
Eukaryote: nucleus, organelles, linear DNA
Both: cells, cell membrane, ribosomes 核糖体



Cytoplasm 细胞质
Nucleus 细胞核
- nucleolus 核仁 (inside nucleus)
- nuclear envelope 核膜 (double plasma membrane)
- nuclear pores 核孔 allowing RNA and proteins to move in and out
- chromatin 染色质

Ribosome 核糖体
Peroxisome
Centrosome 中心体
- Centriole 中心粒

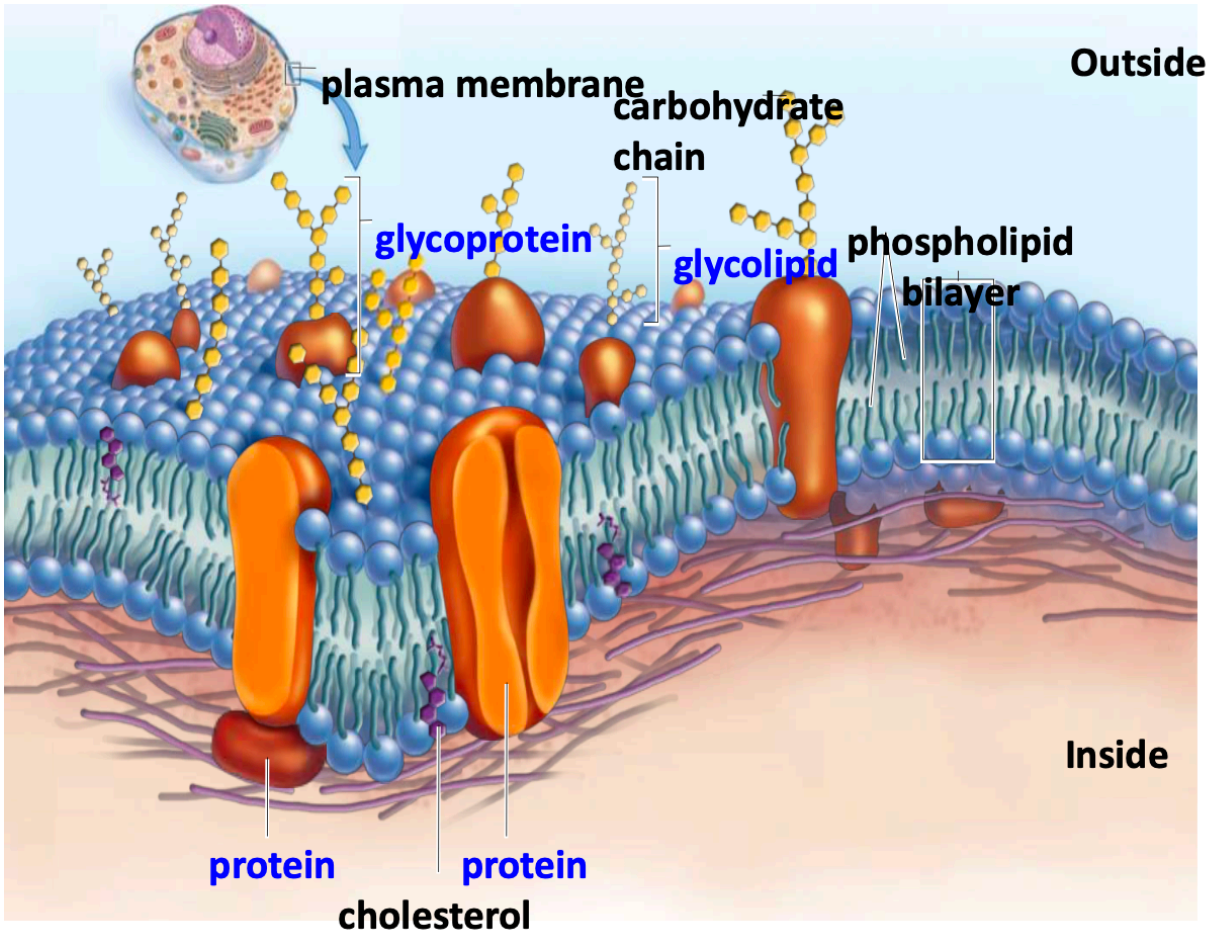
Lysosome 溶酶体
Mitochondrion 线粒体
    double-membrane
    matrix 基体
    cristae 嵴
Golgi Apparatus 高尔基体
Smooth Endoplasmic Reticulum 滑面内质网
Rough Endoplasmic Reticulum 粗面内质网 (ribosomes attached)
Chloroplast 叶绿体（植物）
    stroma 基质
    granum 基粒
    thylakoid 类囊体
Central Vacuole 中央液泡（植物）
Cytoskeleton 细胞骨架
Ribosomes use mRNA as a template to make proteins – the protein factories

Endomembrane System 内质膜系统
Protein synthesis → modification → packaging
Ribosome: make proteins
    no membrane, not an organelle
RER: synthesizes proteins
SER: synthesizes lipids and also performs various other functions
Golgi Apparatus: modify and tag proteins to 3 destinations: cell membrane / secreted out / makes lysosome
Lysosome: containing digestive enzymes – recycling plant
chloroplast & mitochondria: double membrane

Chloroplast: Sun + CO_2 + H_2O → [C] + O_2 (photosynthesis)
Chlorophyll 叶绿素
[C] + O_2 → CO_2 + H_2O + ATP

Cytoskeleton
    shaper/mover/cell division
Motor protein
Myosin – interacts with actin (muscles)
Kinesin (move to plus end), **Dynein** (move to minus end) – walk along microtubules to transport vesicles and organelles
Flagella – using dynein to bend: dynein side arms reach to their neighbors

Microtubule 微管 – shaper/cell division, constantly (de)polymerize to change the cell's shape, position cell organelles
    made of tubulin 微管蛋白
Actin Filament (Microfilament) 微丝
    two actin chains twisted in helix
    dense web under plasma membrane / found in microvilli to provide support



Actin subunits allow cells to change shape quickly to form pseudopods

Intermediate Filament 中间丝（动物）– shaper, surrounding nucleus

high strength, permanent, made from **keratin** (角蛋白) – in hair and fingernails

Plasma membrane = cell membrane = cytoplasmic membrane

Phospholipid bilayer

glycoprotein

glycolipid

cholesterol

integral protein

peripheral proteins: Located on the inner or outer surface of the membrane.

Fluid–mosaic model

Diffusion and Osmosis

Isotonic, hypotonic, and hypertonic solution

Simple diffusion – selectively permeable

can:

hydrophobic molecules: O2, CO2, N2, steroid

small uncharged molecules: H2O, glycerol, urea

cannot:

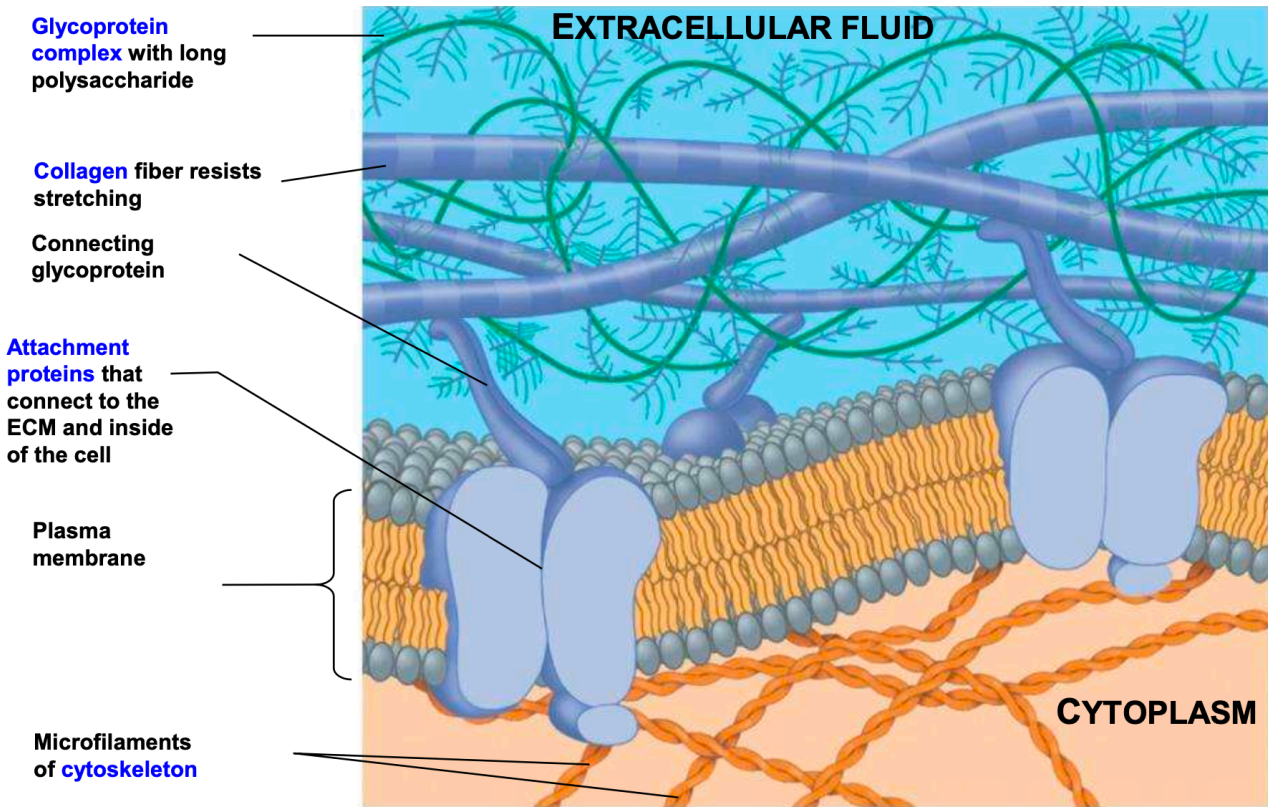
large uncharged polar molecules

ions

Bulk transport
endocytosis 胞吞
exocytosis 胞吐
phagocytosis 吞噬
pinocytosis 胞饮
Receptor–mediated endocytosis
Channel protein – specific molecule/ion (e.g. aquaporin) passive transport
Carrier protein: passive/active transport (e.g. Sodium–Potassium pump, 3Na+, 2K+)

Junction proteins
Extracellular matrix
collagen fibre

Adheren junction
found in tissues that require stretching: skin
Desmosome – provides strong adhesion between cells
Tight junction – tight junction proteins so that no liquid leaks out
found in kidneys/intestines
Gap junction – communication channels – small molecules and ions, electricity
Plasmodesmata (plant cells)

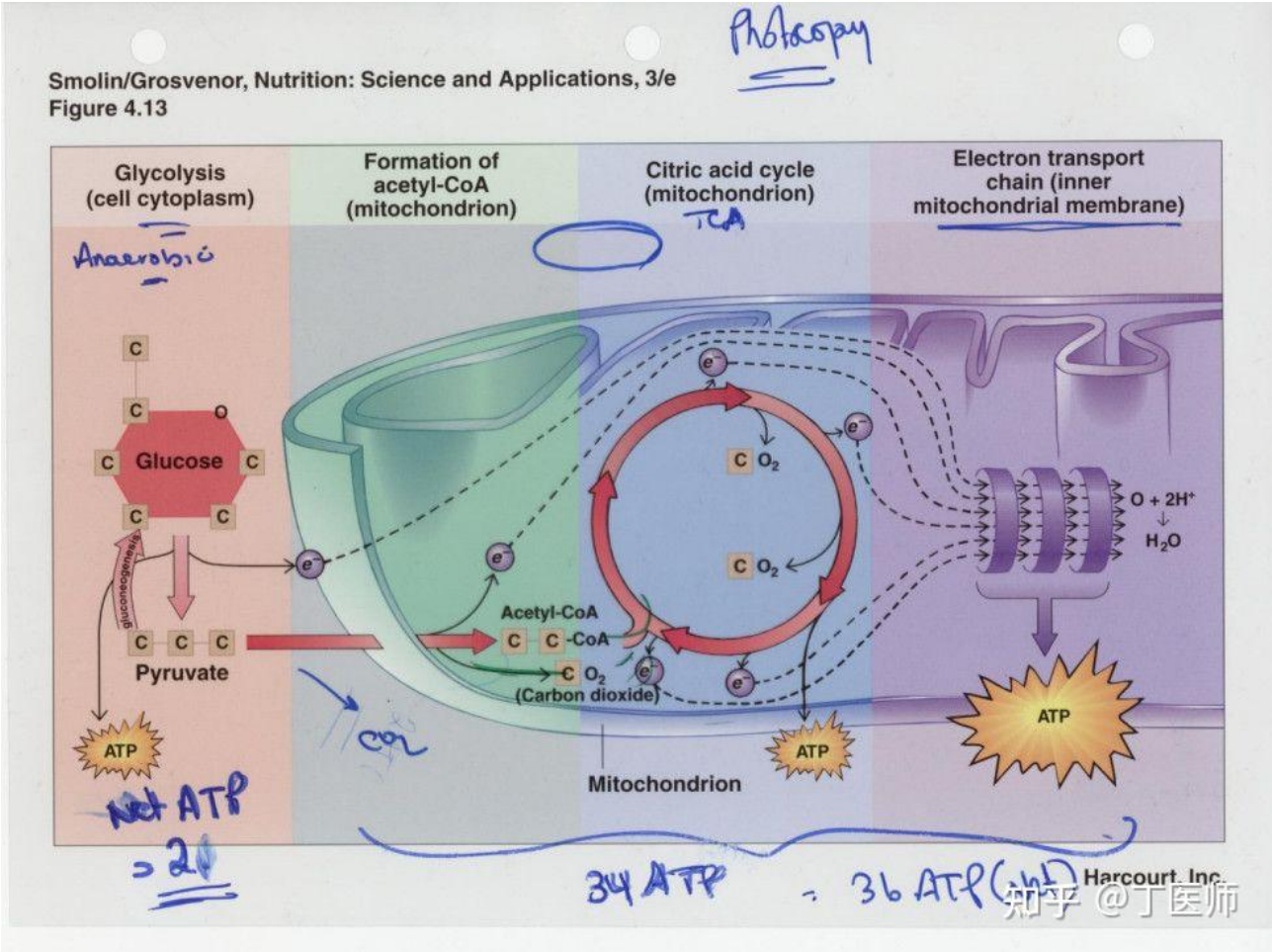


Metabolism: all reactions that take place in order for things to live
Catabolism: the breakdown of molecules (usually release energy)

Anabolism: the synthesis of all compounds needed by the cell (requires energy)

Phosphorylation: ADP + Pi → ATP
ATP: Adenosine triphosphate

Enzymes can denature
Enzymes named [substrate] + –ase
Cofactors – non–protein helpers
Coenzyme – organic cofactors
Biochemical pathways are regulated by feedback inhibition



2 ways: Competitive/noncompetitive inhibitor
Poisons and drugs are often enzyme inhibitors

NAD+ + 2H+ + 2e– → NADH + H+
FAD + 2H+ + 2e– → FADH2
Aerobic respiration
Glucose (6C)
↓ **Glycolysis** (cytoplasm) [2NAD+ → 2NADH] [– 2ATP + 4ATP → 2ATP]
2 **Pyruvate**(丙酮酸) (3C) + 2ATP + 2e–
↓ **Pyruvate Oxidation** (mitochondrial matrix) [2NAD+ → 2NADH]
2 **Acetyl** (2C) CoA + 2CO2 + 2e–

↓ **Citric Acid Cycle (Tricarboxylic Acid Cycle/Kreb's Cycle)** (cristae)

[6NAD+ + 2FAD → 6NADH + 6H+ + 2FADH2]

4CO2 + 8e− + 2ATP

↓ **Oxidative Phosphorylation** = **Electron Transport Chain** + **Chemiosmosis** (inner membrane)

Pumping H+ into intermembrane space to create a proton gradient

A membrane protein that acts as a molecular rotary motor

½O2 + 2H+ + 2e− = H2O

ADP + Pi + H+ = ATP

Total: C6H12O6 + 6O2 → 6CO2 + 6H2O + 38ATP

CO2: step2, 3

ATP: step1, 3, 4(many)

NADH: step1, 2, 3(many)

Anaerobic respiration – fermentation(发酵)

Pyruvate + 2e− → 2 Ethanol(乙醇) or 2 Lactate(乳酸) + 2ATP + 2CO2

Lactate fermentation (animal, certain bacteria)

Alcoholic fermentation (yeast and other fungi)

After Midterm

Recap:

Protein
Composed of amino acid(氨基酸) monomers
NH2–CH2–COOH + NH2–CH(CH3)–COOH → NH2–CH2–CO–NH–CH(CH3)–COOH + H2O
O=C–N–H: peptide bond(肽键)
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Nucleic Acid
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triphosphate + 5–carbon sugar + nitrogenous base
PO4–[C5]–Base
Base: DNA: A/C/G/T, RNA: A/C/G/U, A=T, C≡G
Purine 嘌呤: A/G
Pyrimidine 嘧啶: C/T/U
Adenine 腺嘌呤, Thymine 胸腺嘧啶, Guanine 鸟嘌呤, Cytosine 胞嘧啶, Uracil 尿嘧啶
P group in 5', –OH group in 3'
5' 3'
S–T=A–S
P P
S–C≡G–S
P P
S–A=T–S
3' 5'
mRNA, tRNA, rRNA
Found by James Watson and Francis Crick
Adenosine Triphosphate 腺苷三磷酸
Base–[C5]–P–P~P

Protein are the direct determinants of life

1 polypeptide ~ 360 amino acids (avg.)
DNA is the ultimate determinant of life

Chromosome
DNA associated with proteins is packed into a **chromosome**
1 chromosome = 1 double–stranded DNA
1 prokaryotic cell has **1 circular** chromosome = 1 circular DNA
1 eukaryotic cell has **n linear** chromosomes = n linear DNA
Regularly – chromosomes extended & spreading in nucleus, indistinguishable
Cell dividing – no nucleus, chromosomes condensed, distinguishable
DNA/chromosome length and number in 1 cell

	Basepairs per chromosome	Chromosomes per cell
E. Coli (大肠杆菌)	10^6	1
Brewer's yeast	10^5	16
Fruit fly	10^7	8
Human	10^8	46
Loblolly pine	10^9	24

3–nucleotide unit = codon = triplet code
The genetic code table of **coding strand**

	T	C	A	G	
T	TTT Phe	TCT Ser	TAT Tyr	TGT Cys	T
	TTC Phe	TCC Ser	TAC Tyr	TGC Cys	C
	TTA Leu	TCA Ser	TAA stop	TGA stop	A
	TTG Leu	TCG Ser	TAG stop	TGG Trp	G
C	CTT Leu	CCT Pro	CAT His	CGT Arg	T
	CTC Leu	CCC Pro	CAC His	CGC Arg	C
	CTA Leu	CCA Pro	CAA Gln	CGA Arg	A
	CTG Leu	CCG Pro	CAG Gln	CGG Arg	G
A	ATT Ile	ACT Thr	AAT Asn	AGT Ser	T
	ATC Ile	ACC Thr	AAC Asn	AGC Ser	C
	ATA Ile	ACA Thr	AAA Lys	AGA Arg	A
	ATG Met	ACG Thr	AAG Lys	AGG Arg	G
G	GTT Val	GCT Ala	GAT Asp	GGT Gly	T
	GTC Val	GCC Ala	GAC Asp	GGC Gly	C
	GTA Val	GCA Ala	GAA Glu	GGA Gly	A
	GTG Val	GCG Ala	GAG Glu	GGG Gly	G

DNA
5'–ATGGAC…CAGTGA–3' (non–template strand = coding strand)
3'–TACCTG…GTCACT–5' (template strand = non–coding strand)
↓**Transcription** (5'→3')
RNA
5'–UACCUG…GUCACU–3' (RNA strand)
↓**Translation** (5'→3')
Protein
NH3+–Met–Asp…–Gln–CO2– (polypeptide)

Gene = Heritable section of DNA that determines the character of living organisms = Instructions for protein production

Gene Expressed = Gene's instructions used by the cell = Synthesis of its encoded polypeptides

Transcription
Each gene can be transcribed many times
1. Promoter sequence attracts RNA polymerase **(Initiation)**
2. RNA polymerase unwinds DNA from 5' to 3' **(Elongation)**
3. Produce RNA
4. DNA rewound after RNA polymerase left
5. RNA polymerase comes across a terminator and falls off the DNA **(Termination)**
6. RNA product transported out of the nucleus if involved in protein synthesis (eukaryotes)

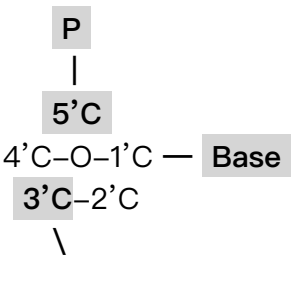
Terminator sequence = inverted complementary sequences, making RNA stick to itself to escape from RNA polymerase

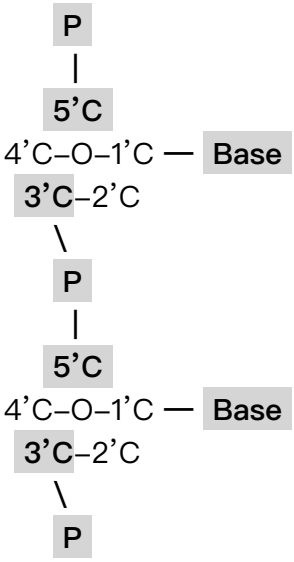
RNA
Messenger RNA (mRNA)
Coding for proteins, template for translation
Ribosomal RNA (rRNA)
Forming ribosomes together with ribosomal proteins
Transfer RNA (tRNA)
Transferring amino acids for translation
Nucleotide of rRNA and tRNA do not form codons

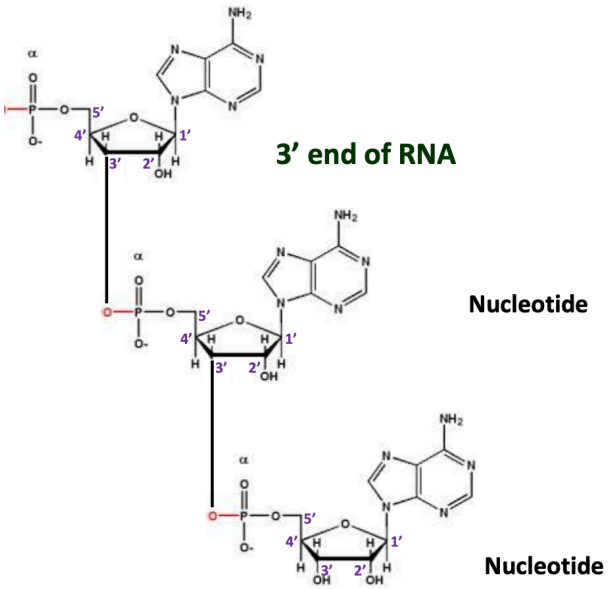
Backbone Sugars
Deoxyribose (DNA)
C4O–2'C–H, less reactive, more stable → master copy, permanent
Ribose (RNA)
C4O–2'C–OH, more reactive, less stable → working copy, disposable

Nucleoside triphosphate (activated nucleotide)
P3–[C5]–A/C/G/U (P2 removed during transcription)
P3 = **Triphosphate**
[C5] = **Ribose**
A/C/G/U = **Nitrogenous Base**
PO3––[C5]–A/C/G/U = **Nucleotide**

5' position







3' position

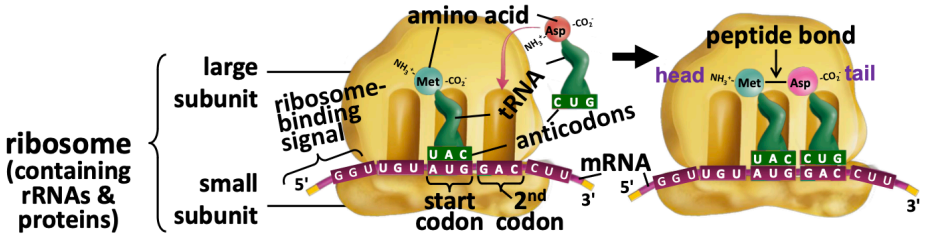
Transfer RNA (tRNA)

Mediator between mRNA and amino acid

Having a specific anticodon to basepair with a specific codon on the mRNA

Carrying the corresponding amino acid on the other side

Translation



1. Ribosome recognizes ribosome–binding sequence and the start codon (AUG) on mRNA
2. A tRNA with anticodon (UAC) for the start codon carrying amino acid (Met) is recruited to the ribosome–mRNA complex
3. A tRNA with anticodon for the 2nd codon carrying the corresponding amino acid is recruited to the ribosome–mRNA complex
4. A peptide bond is formed between the first and the 2nd amino acid
5. The ribosome shifts downstream along the mRNA to locate the 3rd codon
6. Repeat 3, 4, 5
7. Ribosome arrives at a stop codon and releases the mRNA

Polypeptide product

(Head = amino) NH3+–Met–Val–…–Asp–CO2– (Tail = carboxyl)

Ribosome = 3 rRNA + >50 Protein Molecules

Regulatory Elements of a Non–protein–coding Gene

Transcription promoter

Transcription start site (TSS)

Transcription terminator
Transcription termination site (TTS)
Transcribed region = from TSS to TTS
Product = RNA

Regulatory Elements of a Protein-coding Gene (10^2 bp in prok., 10^3-5 in euk.)
Transcription promoter (TP, determine the rate of transcription = number of mRNAs)
Transcription start site (TSS)
Ribosome binding site (RBS, determine the rate of translation = number of proteins per mRNA)
Start codon (ATG)
Stop codon (TAA/TAG/TGA)
Transcription terminator
Transcription termination site (TTS)
Protein coding region = from start codon to stop codon (inclusive)

In a multicellular organism, every cell contains all the genes of that organism.

	Genes in one set	Total length of DNA per set of genes (bp)	Avg. distance between two genes (bp)
E. Coli (大肠杆菌)	4300	~10^6	1100
Brewer's yeast	6600	~10^7	1800
Fruit fly	15600	~10^8	8300
Human	**21000**	**~10^9**	**140000**
Loblolly pine	50000	~10^10	440000

There are high proportions of repeat sequences (junk DNA) in eukaryotic genomes

Regulation of gene expression in response to external signals
Eg1: No lactose → lacZ gene not expressed
LacI repressor protein binds between the promoter and TSS
Lactose binds to the repressor to change its shape so that it cannot bind to lacZ DNA
Eg2: UV → production of pigment

Regulation of gene expression
RNA/Protein production (transcription) (usual)
RNA/Protein sequence modification (RNA splicing)
RNA/Protein transportation
RNA/Protein degradation

During embryonic development of an organism:
Different parts receive different signals, expressing different subsets of genes, thus differentiating.
Stem cell = Undifferentiated cells

Cell division

Binary fission
G1 phase = growth
S phase = DNA replication and growth
G2 phase = growth
M phase = mitosis = cell division
Diploid = having 2 sets of chromosomes
Human body cell contains:
23 different chromosomes, 2 copies of each chromosome

1 chromosome = 2 chromatids(染色单体) + centromere(着丝粒)

Mitosis(有丝分裂)
1. Chromosomes replicated
2. Chromosomes condense
3. Centrosomes move to poles and send out spindle-like microtubule fibers
4. Nuclear envelope disintegrates
5. Spindle fibers attach to the centromere, aligning chromosomes at the equatorial area
6. Centromere protein degrades, chromosomes pulled toward opposite poles
7. Nuclear envelope re-forms around each collection of chromosomes to form 2 nuclei
8. Chromosomes de-condense
9. Plasma membrane constricts and separates the cell into 2 portions

Programmed cell death
Damaged beyond repair
Dividing out of control
Infected by virus

Fertilized egg
↓ **DNA replication**
↓ **Cell division**
↓ **Cell differentiation**
↓ **Cell death**
Adult organisms (10^14 cells)

Some cells stop dividing in adult organisms, e.g. neurons, heart muscle cells

Asexual reproduction = … from one existing individual (favorable condition)
Sexual reproduction = fusion of cells produced by 2 separate individuals (unfavorable condition)
Almost all **multicellular eukaryotes** – Sexual reproduction
Most **unicellular eukaryotes** – Both asexual and sexual reproduction, depending on the environmental conditions
All **prokaryotes** – Asexual reproduction

All prokaryotes are unicellular

Sex cells are haploid = containing 1 set of chromosomes

Meiosis(减数分裂) = Reductive cell division
Chromosomes already replicated
1. Chromosomes condense
2. Centrosomes move to poles and send out spindle-like microtubule fibers
3. Homologous chromosomes pair up
4. Exchange of chromosome segment
5. Nuclear envelope disintegrates
6. Spindle fibers attach to the centromere, aligning **paired** chromosomes at the equatorial area
7. **Paired chromosomes lose bonding**, pulled toward opposite poles
8. Nuclear envelope re-forms around each collection of chromosomes to form 2 nuclei
9. Chromosomes de-condense
10. Plasma membrane constricts and separates the cell into 2 portions
11. A further division similar to mitosis

Overall outcome of meiosis
1 germline cell(生殖细胞) → 4 sex cells
Each sex cell is haploid = has 1 set of chromosomes
Contain recombinant chromosomes

Difference among living individuals
Regular individuals of the same species have
Same assemblage of genes
Same assemblage of chromosomes
Small differences in DNA sequences
Allele(等位基因) = same locus with different DNA sequences
Difference of DNA sequences between 2 unrelated humans = 0.1% = 3x10^6 bp, most of which are outside genes
Difference of DNA sequences between humans and chimps = 1.25%

Mutation
Mutation in a somatic cell is inherited by all tissue cells that it generates
Mutation in a germline cell is inherited by its descendants

Point mutation = small mutation involving 1 or a few bp
In protein-coding region
Base substitution
ATGCAAAGTCAC…
Met-Gln-Ser-His-…
Missense mutation = 1 amino acid change
ATGCAA**C**GTCAC…

Met–Gln–**Arg**–His–…

Silent mutation = no amino acid change

ATGCAAAG**C**CAC…

Met–Gln–Ser–His–…

Nonsense mutation = protein truncation

ATG**T**AAAGCCAC…

Met

Base deletion/insertion

Frameshift mutation = deletion/insertion of a non–3n of bp

Insertion

ATGCAA**G**AGTCAC…

Met–Gln–**Glu–Ser–…**

Deletion

ATGCAAGTCAC…

Met–Gln–**Val–…**

In regulatory region

Promoter mutation

stronger/weaker binding to RNA polymerase

higher/lower transcription level

increase decrease in gene expression level

Ribosome binding site mutation

Change in a large chromosome segment

Gene loss (deletion) or gain (duplication)

non–viability or inferiority

e.g. Cri du chat syndrome

DNA rearrangement

Translocation/Inversion/…

reduced fertility

Change in chromosome number

Euploid(整倍体) = Diploid

Aneuploid(非整倍体)

e.g. Trisomic (21) = Down syndrome

Polyploid(多倍体)

non–viability or inferiority

reduced fertility e.g. seedless watermelon

bigger than diploid

reproducing asexually only

Internal mutation mechanisms

Point mutations

1. Spontaneous changes in nitrogenous bases

C≡G → A=T

2. Reaction with water

C≡G → A=T

3. Reactive oxygen species

C≡G → A=T

4. Mistakes made by DNA polymerase

misincorporation of nucleotide (1 in 10^6–9)

slipping/jumping along DNA (causing small DNA deletion or duplication)

Large chromosome mutations

5. Unequal exchanges of chromosomal segments = unequal crossovers

Gene disruptions and large chromosome mutations

6. Transposition of transposon

Chromosome number mutations

7. Failure of spindle function during cell division

Aneuploidy/Polyploidy

8. Failure of cell division after DNA replication

Polyploidy

9. Cell fusion

Polyploidy

External mutation mechanism

Chemical mutagens

1. DNA adduct formation (point mutations)

chemicals react with nitrogenous bases

e.g. PAHs(多环芳香烃)/Nitrosamines(亚硝胺)

2. Spindle disruption (chromosome number mutations)

e.g. vinblastine & vincristine from periwinkle

Physical mutagens

3. Ionizing radiations (point mutations & large chromosome mutations)

γ–, X–radiations, breaking bonds wherever they hit

4. UV radiations (CC/CT/TC→TT point mutations)

dimerization of adjacent pyrimidines

Biological mutagens

5. viruses (gene disruptions & large chromosome mutations)

insert their DNA into the host cell genome randomly, causing disruption

Viruses = small particles made up of biological molecules

Size = 0.03–0.2 μm

Virus = genome + protein coat (+ envelope) (+ spikes)

Genome = DNA or RNA, 10^3–5 b(p), 2–300 genes

Viruses multiply only when they are inside host cells

DNA virus

replicated by host–cell DNA polymerase

multiple copies of viral DNA genome

Retrovirus(逆转录病毒)

turn into DNA by virus–encoded reverse–transcriptase

inserted into host–cell genome by virus–encoded integrase
transcribed by host–cell RNA polymerase
multiple copies of viral RNA genome

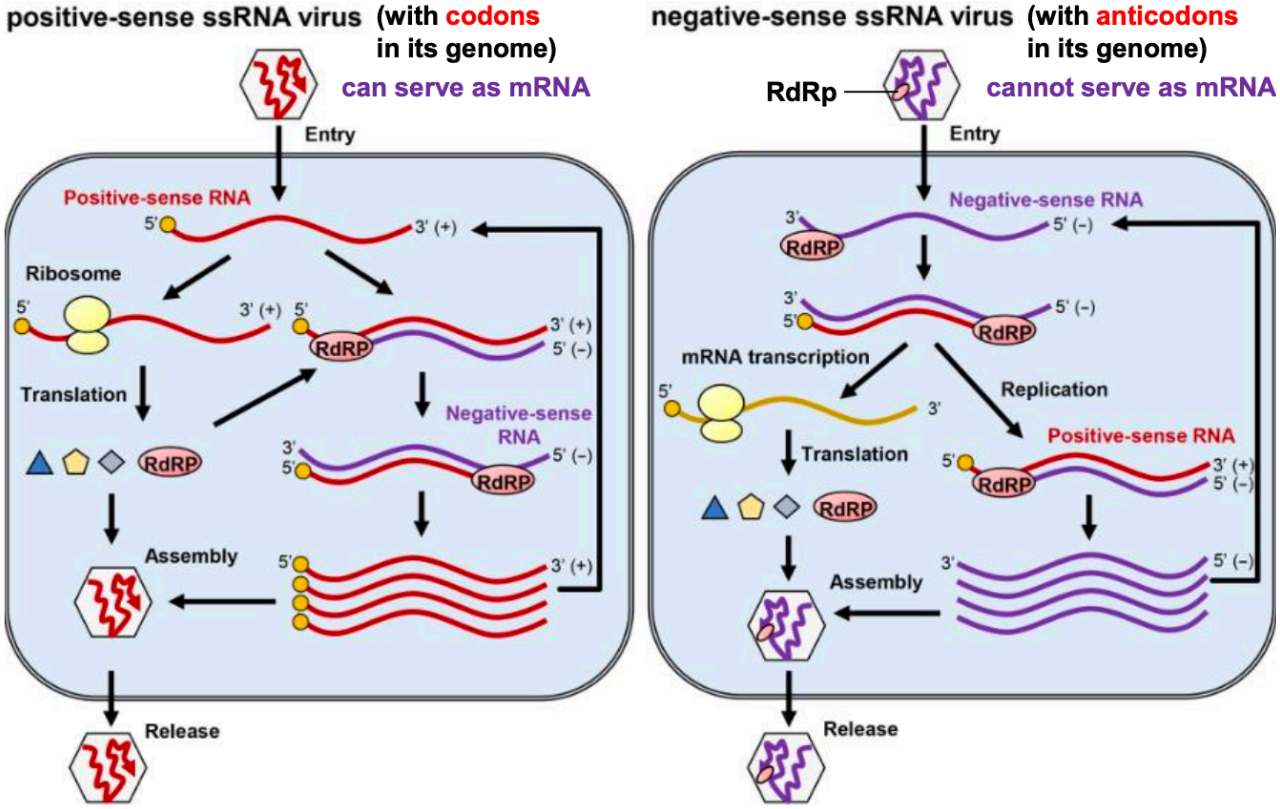
Other RNA virus

virus–encoded RNA polymerase which synthesizes RNA using RNA as the template (RNA–dependent RNA polymerases, aka RdRP)

Immune response of the host

Eliminate viral particles and virus–infected cells

Antibodies & killer T cells



B cells & antibody

1. Have receptors that can bind different foreign molecules
2. Continuously circulate in the body and check for foreign molecules
3. Once bound, B cells divide repeatedly to produce many clones
4. B cell clones produce and release antibodies that can bind the particular foreign molecules
5. These antibodies coat the foreign molecules
6. Scavenger cells swallow and destroy foreign items
7. Some B cell clones differentiate into long–life memory B cells that when they encounter the same foreign molecules, they can divide and release antibodies rapidly.

Killer T cells

1. All cells present the peptides degraded from proteins on their surfaces using **presenter protein MHC–I**
2. Killer T cells with different receptors are constantly made
3. Circulate in the body and check with MHC–I–presented peptide
4. Once bound, the killer T cell kills the cell

5. Divide repeatedly to produce many clones
6. Circulate in the body, looking for cells with the same peptides
7. Some Killer T cell clones differentiate into long-life memory killer T cells that when they encounter the same foreign peptides, they can divide rapidly.

Protein vaccine (sp, B)
- spike proteins on the surface of the virus
- generating memory B cells having receptors that can bind the virus surface
- not including killer T cell response
- have relatively mild side effects

Inactivated vaccine (mp, B)
- virus particles inactivated by chemicals
- multiple protein targets
- have relatively mild side effects

mRNA vaccine (sp, B+T)
- mRNA of gene coding for a virus surface protein, packaged in a liposome
- Inducing memory B cells & memory killer T cells
- only one protein target

DNA vaccine
- DNA of gene coding for a virus surface protein, packaged in a liposome
- unable to enter the cell nucleus

Virus vectored DNA vaccine (sp, B+T)
- DNA of gene coding for a virus surface protein, packaged in a virus vector
- Inducing memory B cells & memory killer T cells
- only one protein target

Attenuated vaccine
- viral particles with changes in genome
- still able to infect cells, producing less progeny virus
- Inducing memory B cells & memory killer T cells
- most effective, but dangerous

Antivirals = anti-virus drugs
Chemicals inhibiting virus-specific biological activities
- Reverse transcriptase(逆转录酶) & integrase of retroviruses(逆转录病毒整合酶)
- RdRp of RNA viruses other than retroviruses
- Viral proteases(病毒蛋白酶)

Virus-specific antibodies
Stimulators of anti-virus immune responses
- e.g. interferons