Data Science in Bioinformatics

WS 22/23

From strands to strings

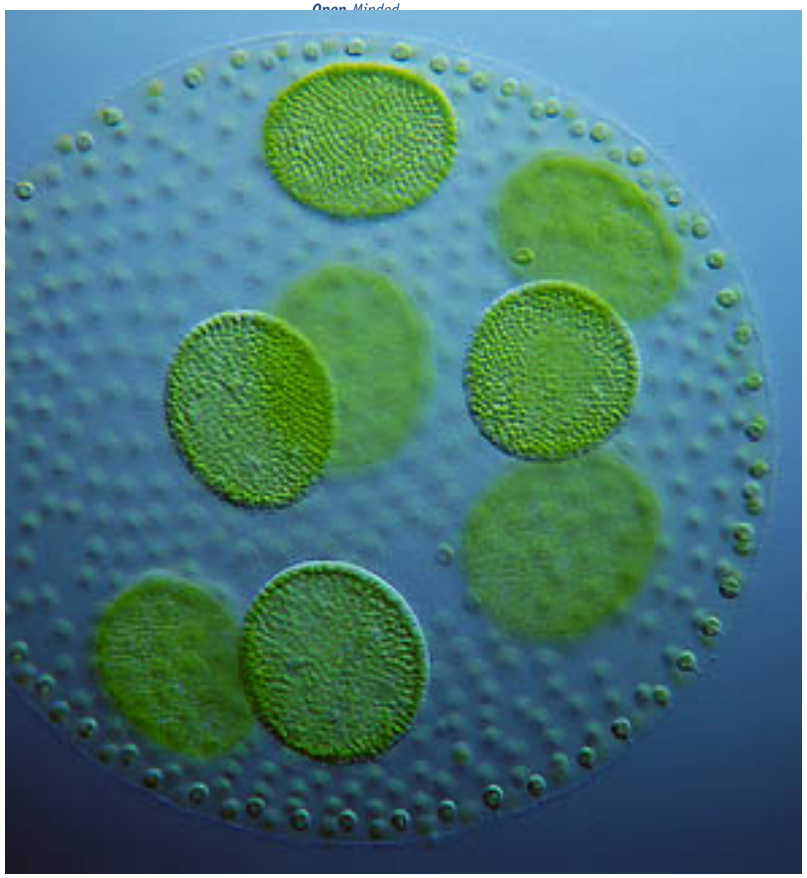
Life, DNA and sequences: biological basics for bioinformaticians

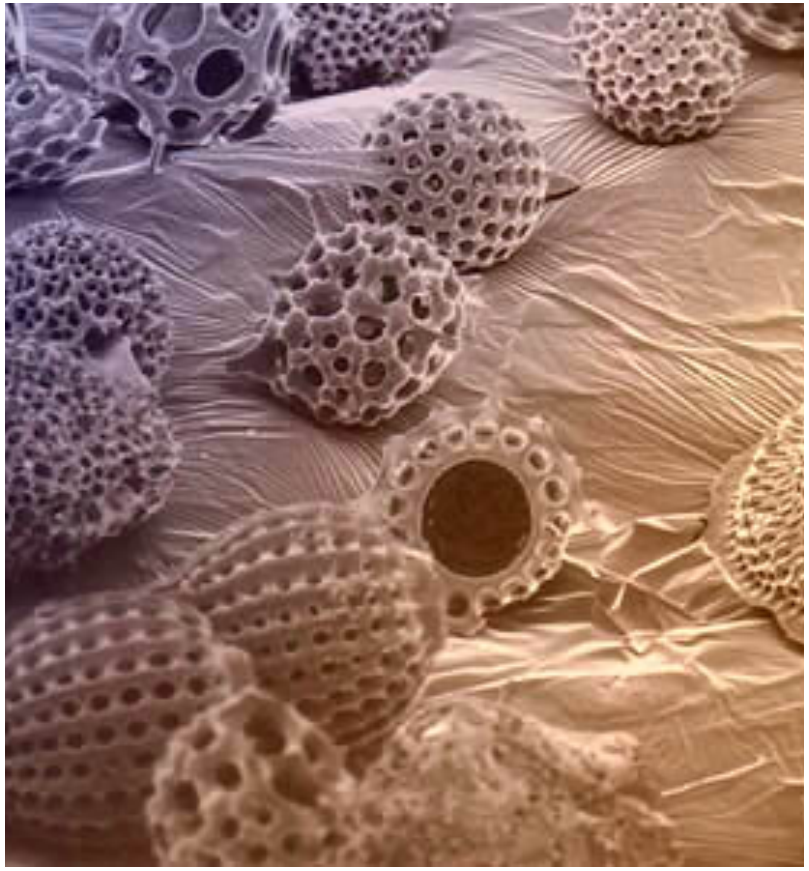
Lecturer: Dr. Simon Magin

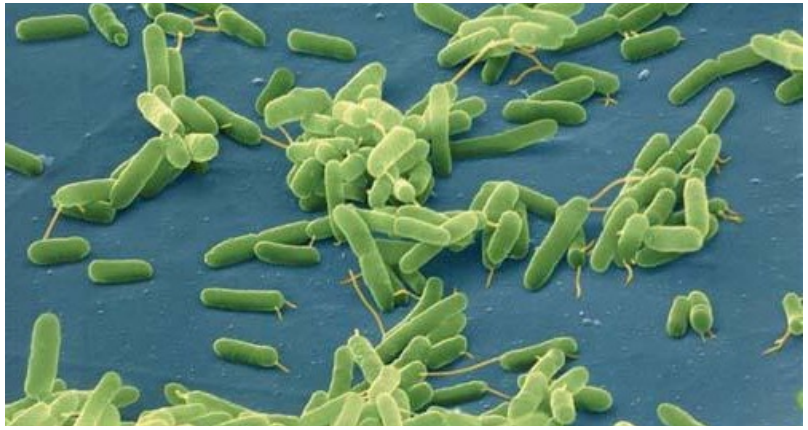
Course Date: 17.10.2022

Todays Topics

- **Life on earth: Diversity on common ground**
- **Chemistry of life: Biological Macromolecules (DNA, RNA, Proteins) and their structure**
- **Fundamental cellular processes: Replication, Transcription, Translation**
- **Bioinformatics: Fasta format and excercise**
- **Classification: Cellular Blueprints and Domains of Life**
- **Finally: What about Viruses?**

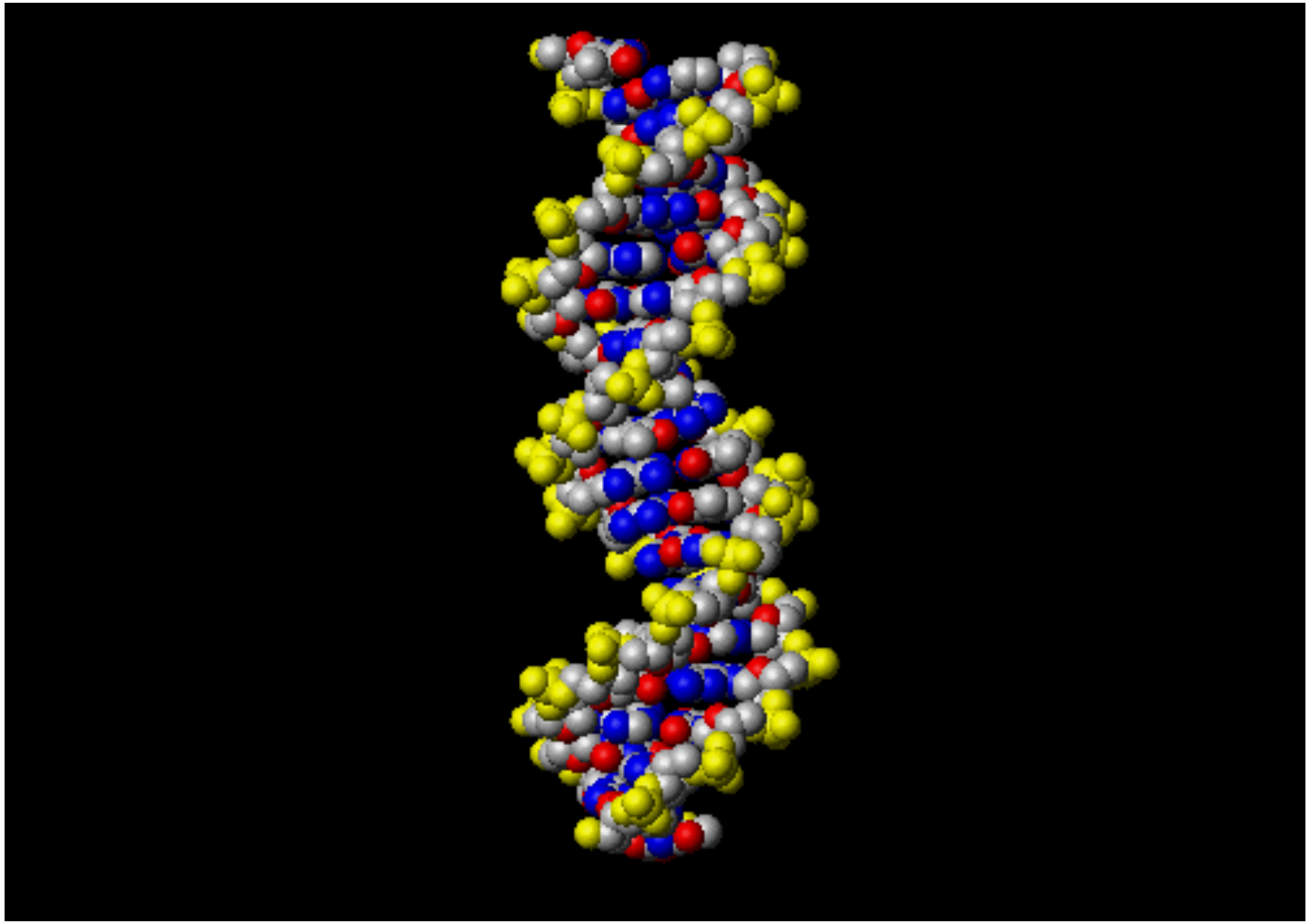






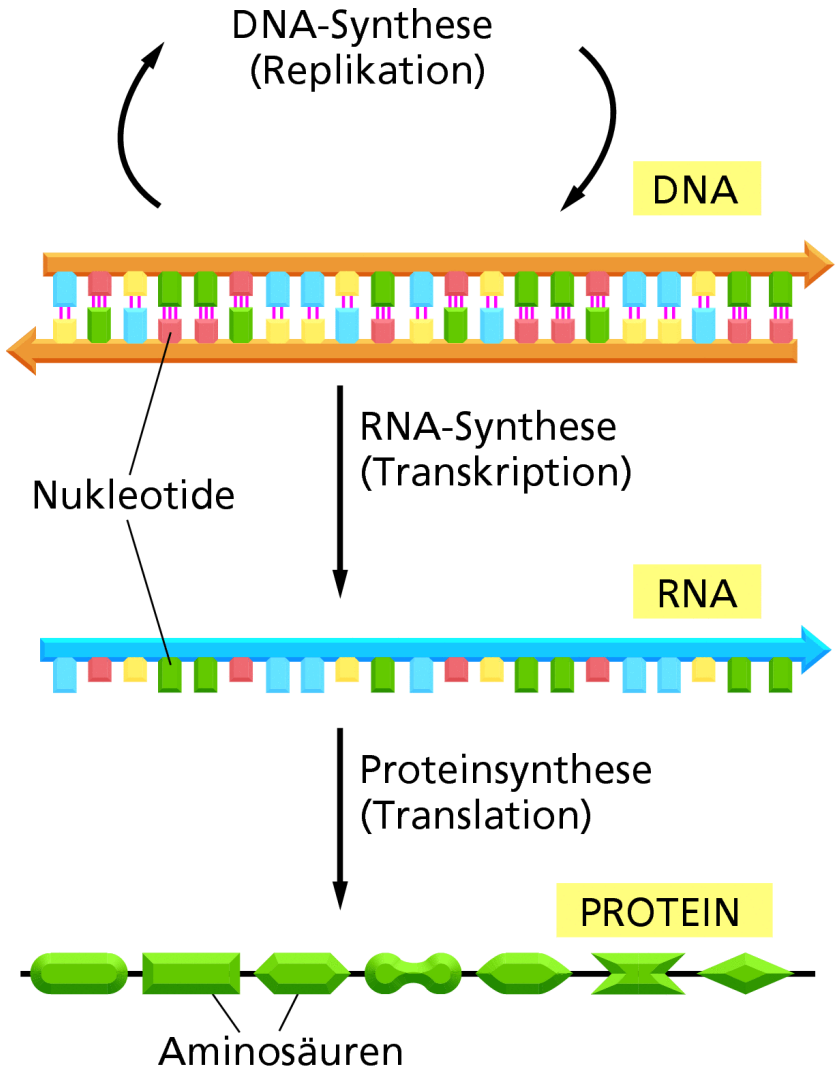
Life on earth

Double-stranded DNA (deoxyribonucleic acid)



Chemistry of Life

All the macromolecules which are central for the workings of a cell, be it for storage of information or to carry out work, are polymers (strings) of basic building blocks.



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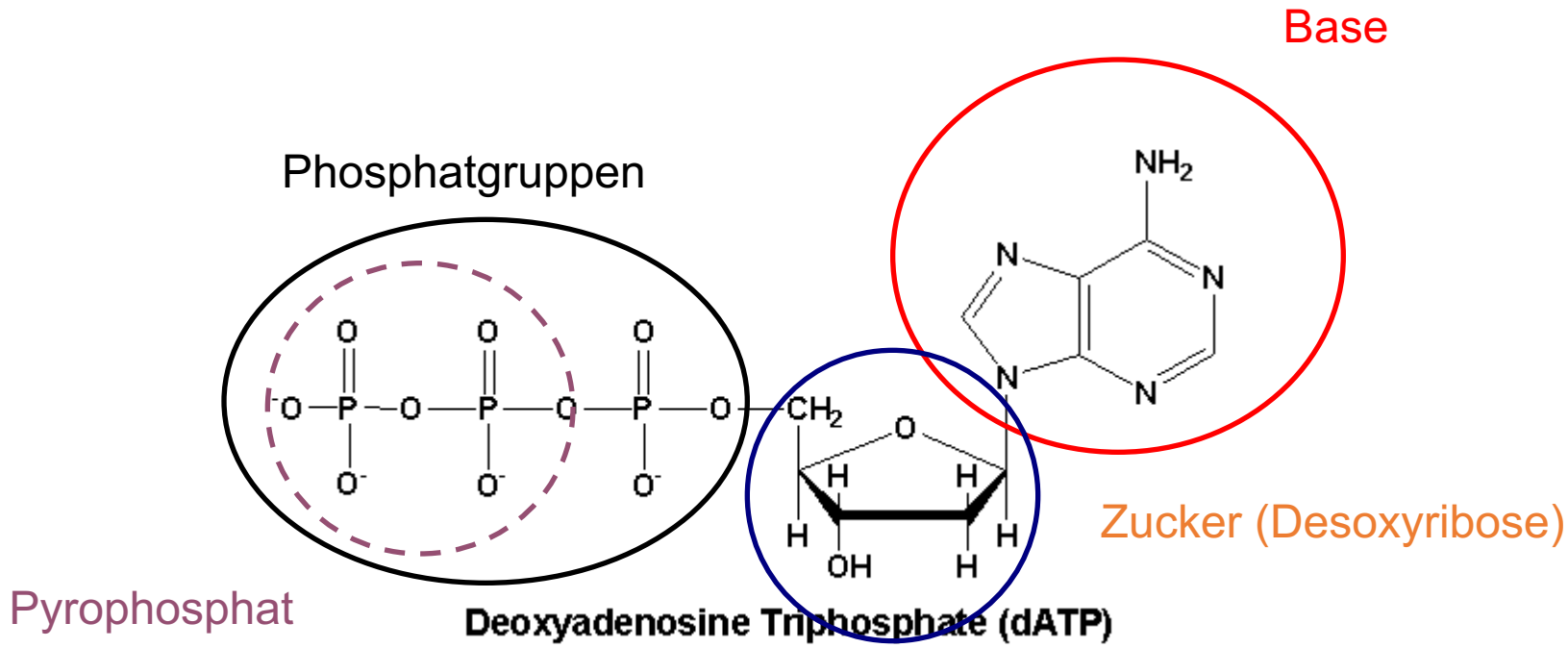
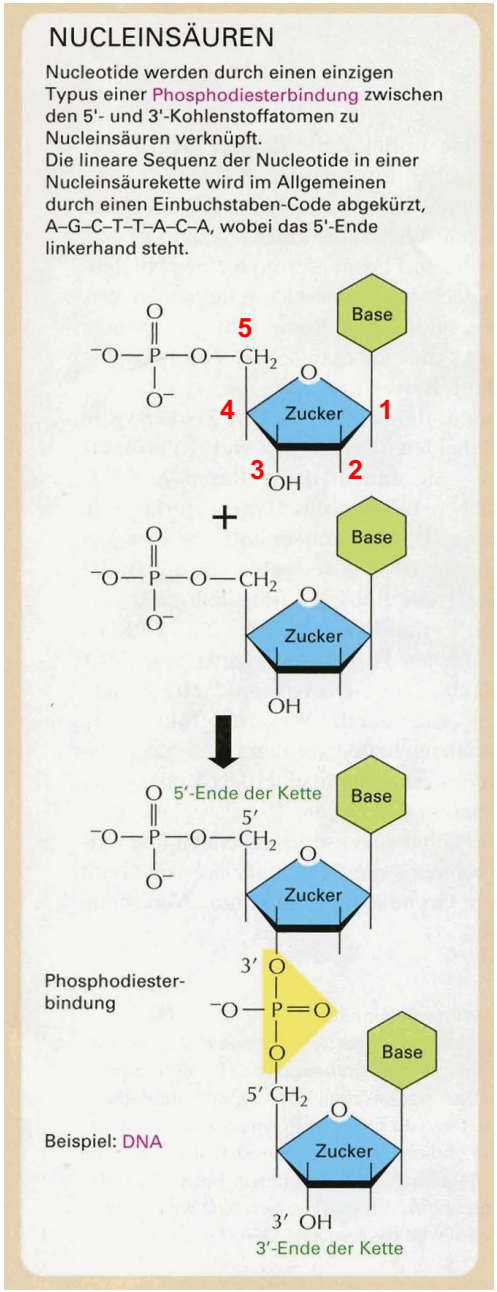
ISBN: 978-3-527-32824-6 Fig. 01-002

deoxynucleotide triphosphates dNTPs



DNA synthesis

Chaining nucleotides into a DNA strand through polymerization



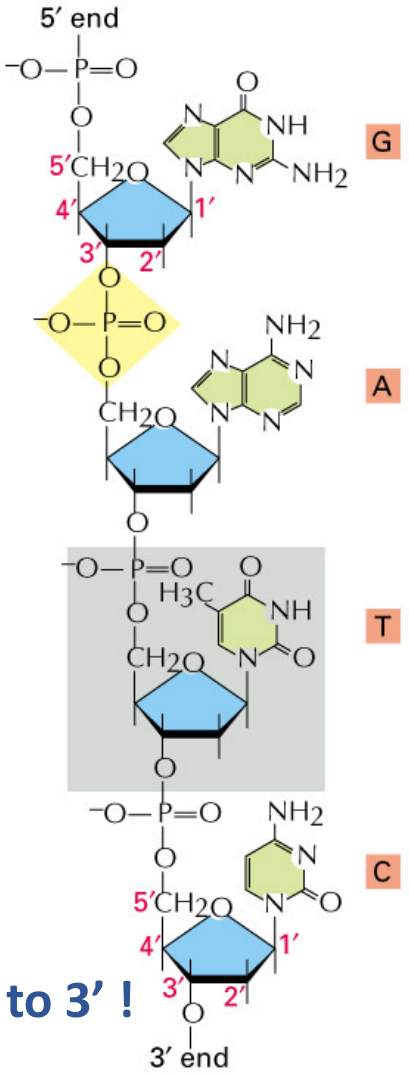
DNA-Polymerase

Sugar

Phosphate

Sugar

Phosphate

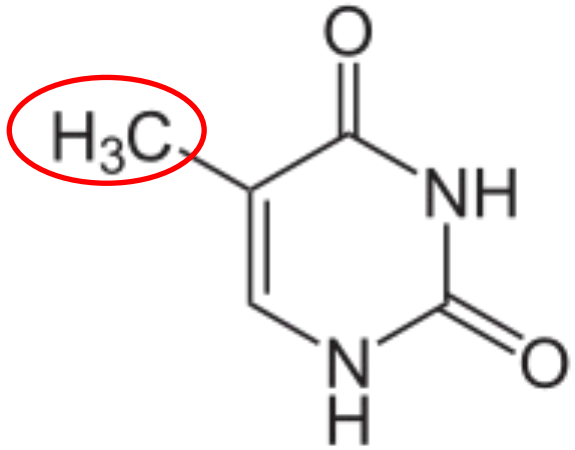


Purines

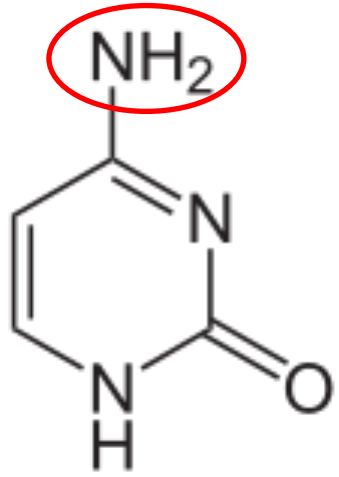
Pyrimidines

DNA synthesis always proceeds from 5’ to 3’ !

Pyrimidines

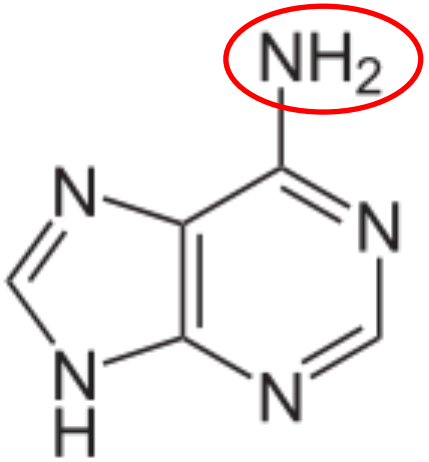


Thymine

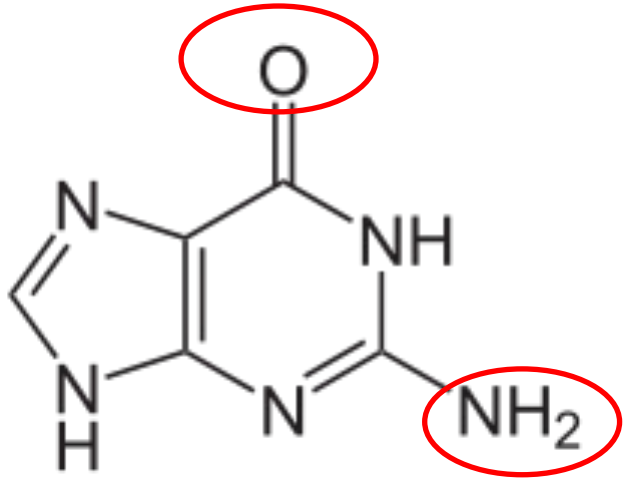


Cytosine

Purines

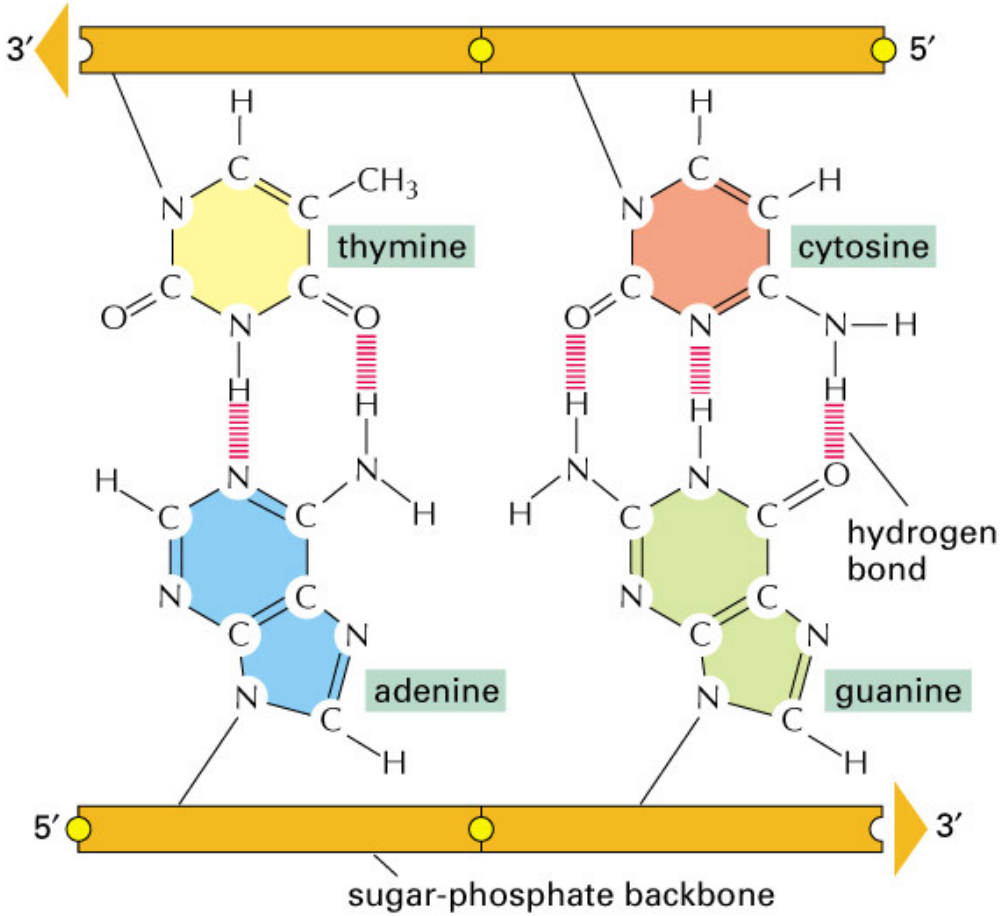


Adenine



Guanine

Complementary base pairing in the DNA double helix

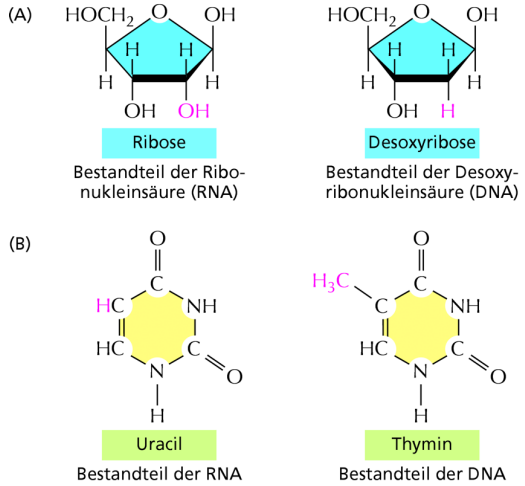


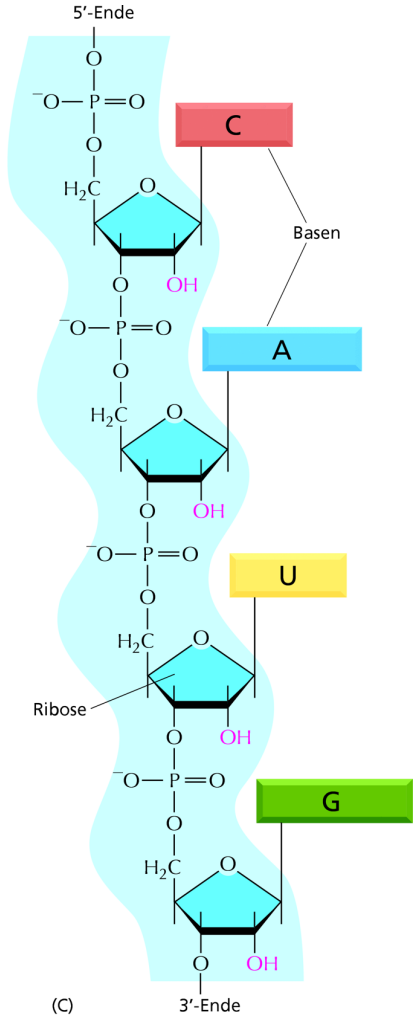
Pyrimidine

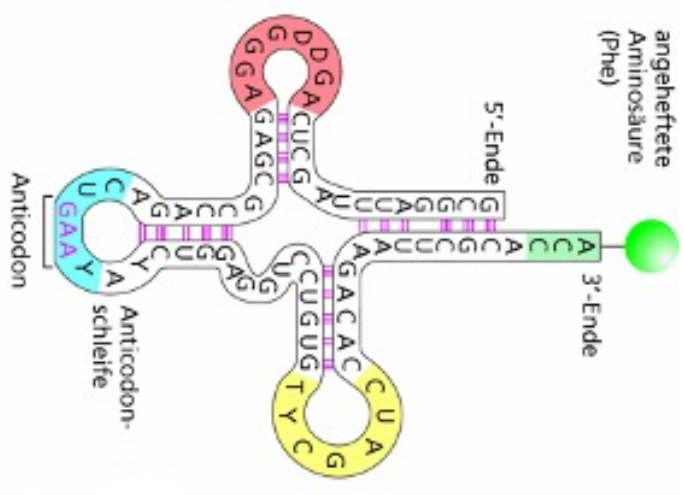
Purine

- Two strands of DNA form a double helix through base-pairing
- The 5’-3’ directionality of the strands is opposing
- Genes can be located on each of the two complementary, antiparallel strands
- Genes can be overlapping and interleaved

RNA

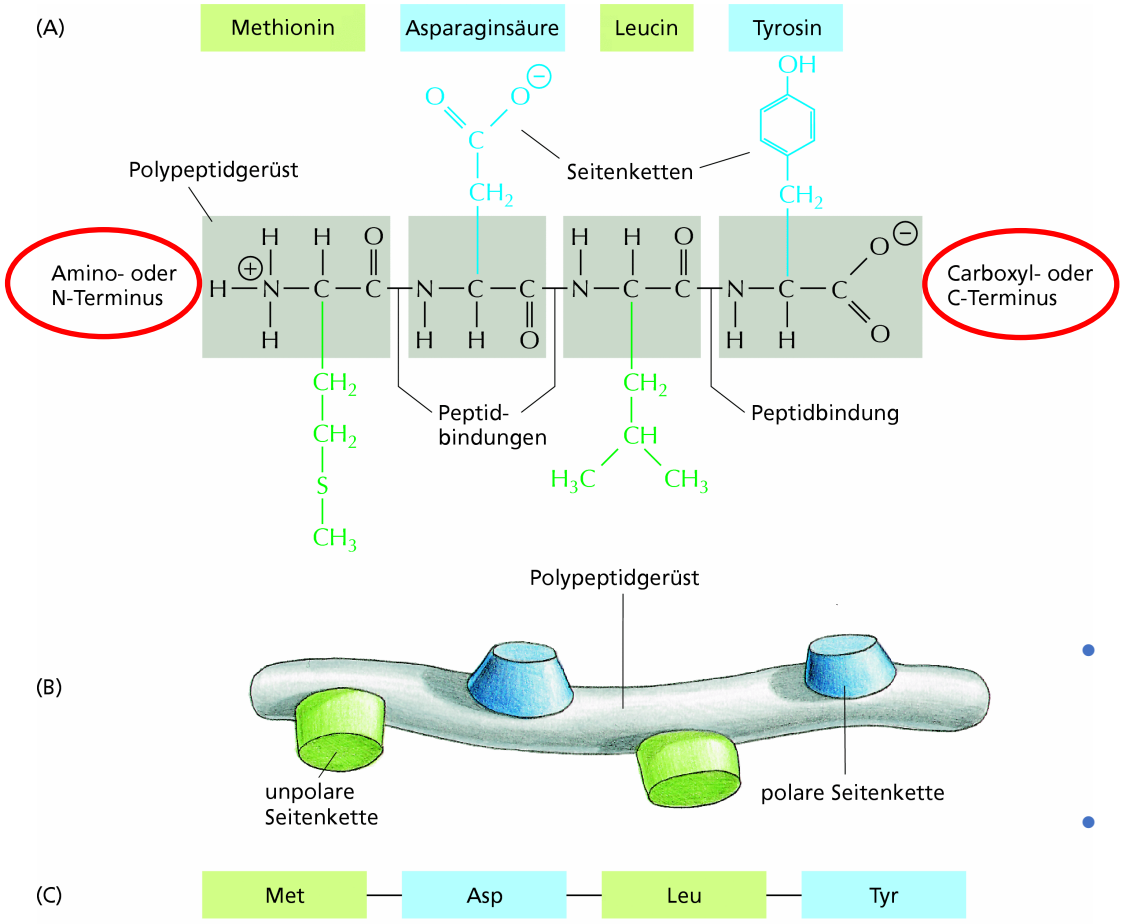


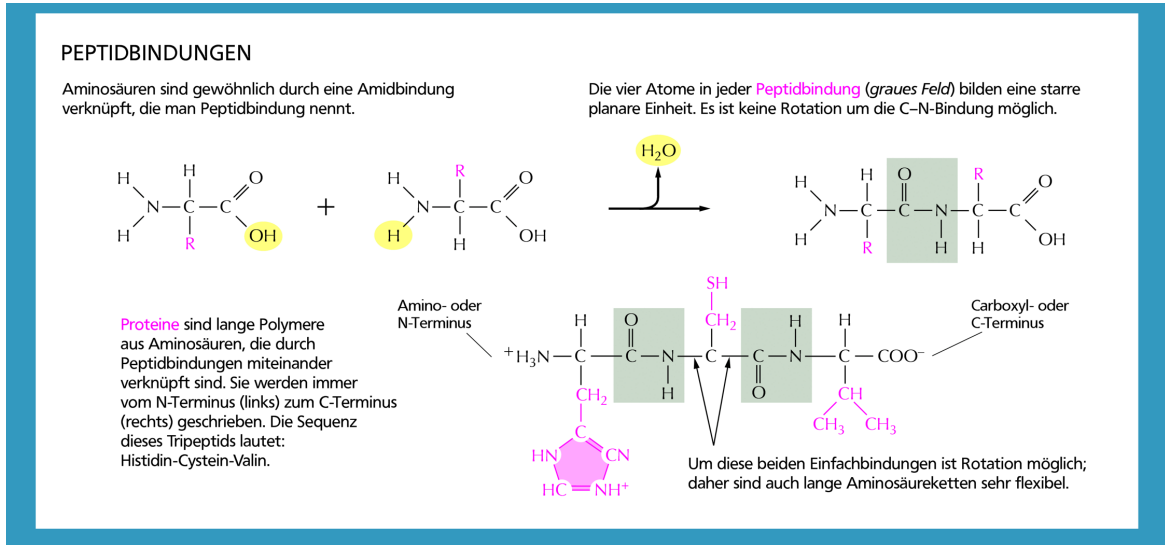




- Sugar is Ribose (as opposed to Deoxyribose)
- In RNA the base Uracil is used in place of Thymine
- Responsible for transport and translation of information
- Also structural and enzymatic functions (rRNA, rybozymes)
- Typically single stranded (except secondary structures)

Proteins





- **Proteins are chains of amino acids linked by peptide-bonds, which can fold into highly complex three dimensional structures**
- **Proteins catalyze reactions, form structures, interact, connect, move, modify, sense, signal …**

Proteins

There are 20 Amino acids of which proteins are composed

AMINOSÄURE			SEITENKETTE
Asparaginsäure	Asp	D	negativ
Glutaminsäure	Glu	E	negativ
Arginin	Arg	R	positiv
Lysin	Lys	K	positiv
Histidin	His	H	positiv
Asparagin	Asn	N	ungeladen polar
Glutamin	Gln	Q	ungeladen polar
Serin	Ser	S	ungeladen polar
Threonin	Thr	T	ungeladen polar
Tyrosin	Tyr	Y	ungeladen polar

polare Aminosäuren (hydrophil)

AMINOSÄURE			SEITENKETTE
Alanin	Ala	A	unpolar
Glycin	Gly	G	unpolar
Valin	Val	V	unpolar
Leucin	Leu	L	unpolar
Isoleucin	Ile	I	unpolar
Prolin	Pro	P	unpolar
Phenylalanin	Phe	F	unpolar
Methionin	Met	M	unpolar
Tryptophan	Trp	W	unpolar
Cystein	Cys	C	unpolar

unpolare Aminosäuren (hydrophob)

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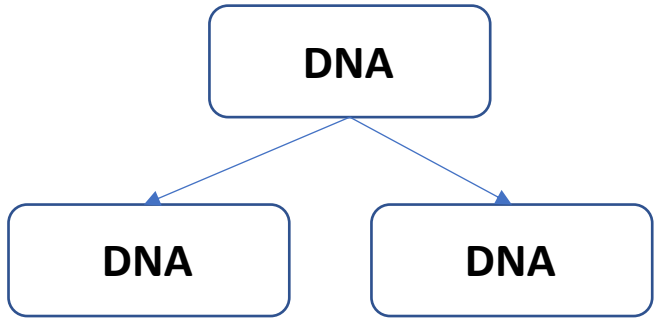
Three fundamental cellular processes to remember

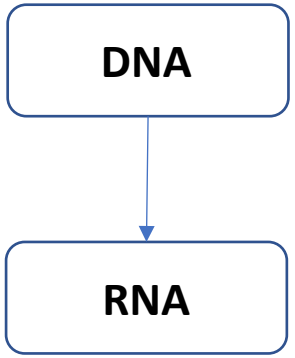
DNA replication
DNA Polymerase



Duplicates nucleic acid

Prerequisite for cell division

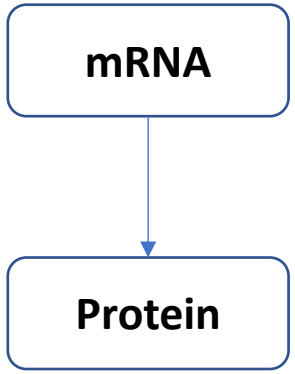
Transcription
RNA Polymerases



Transcribes one type of nucleic acid into another

generation of mRNA, rRNA, tRNA …..

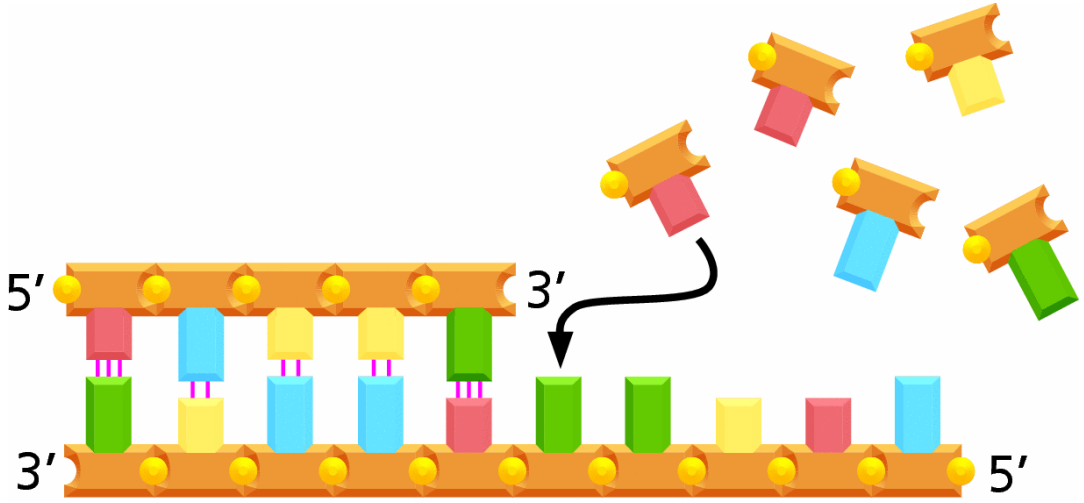
Translation
Ribosomes, tRNA

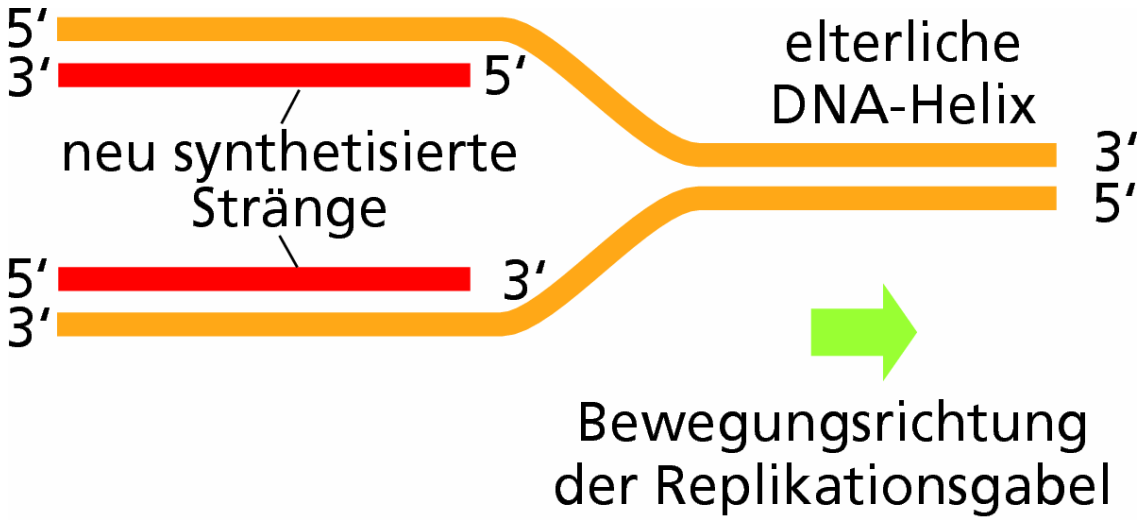


Translates nucleic acid to amino acid sequence

Proteinbiosynthesis

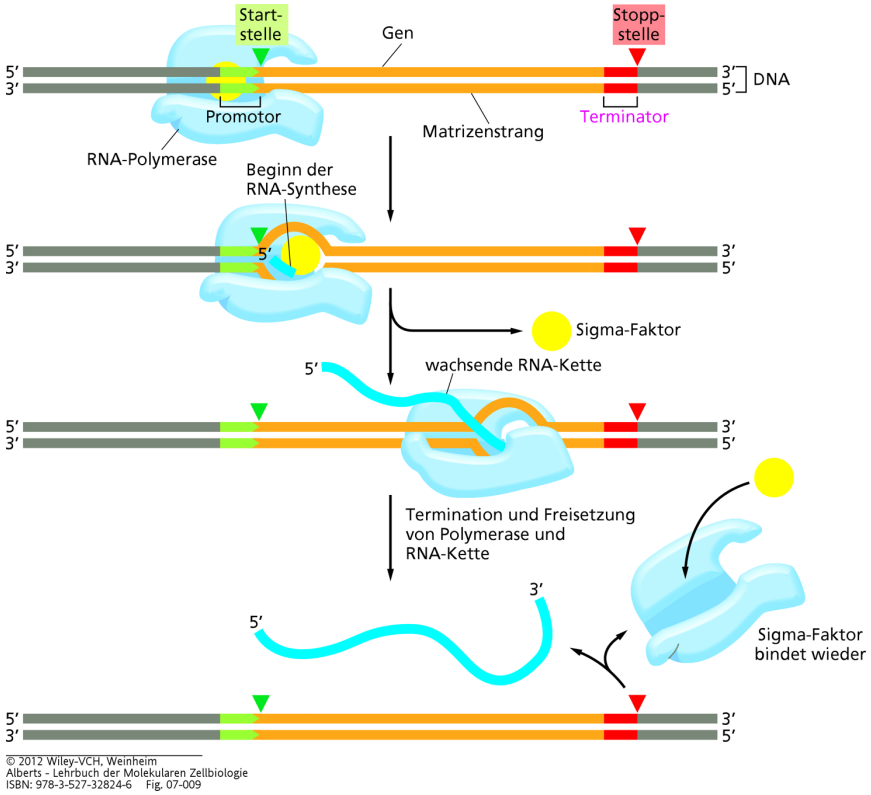
DNA Replication

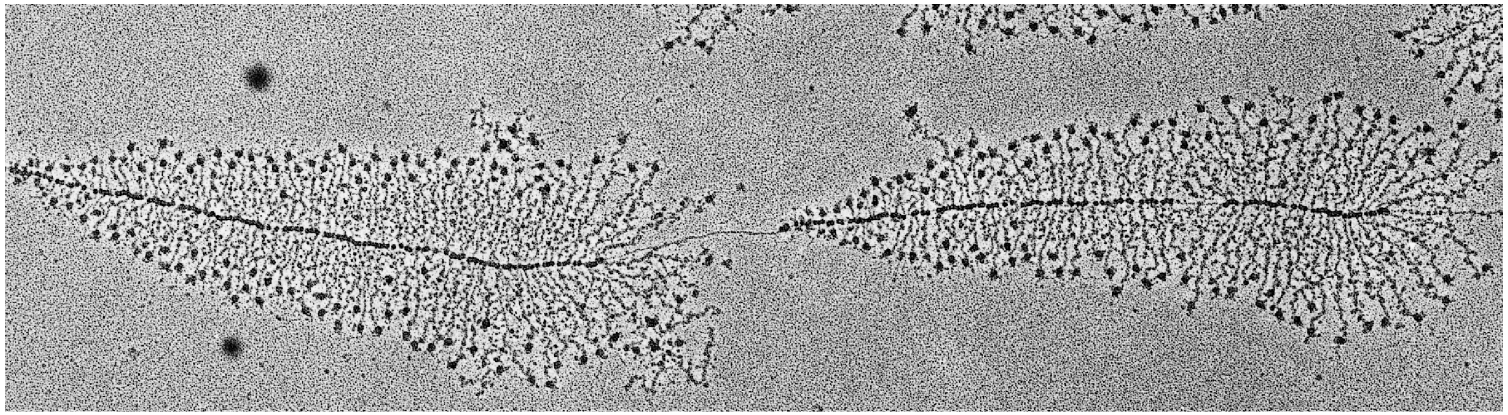




- **Principle of complementarity underlies DNA replication**
- **replication mode is semi-conservative**
- **DNA de-novo synthesis has to go from 5’ -> 3’ direction on the leading and lagging strand**

Transcription





- Transcription is initiated at regulatory elements in the DNA called promoters
- Many RNA copies can be produced simultaneously
- The DNA Template remains unchanged
- Amount of RNA copies in the cell depends on rate of transcription (gene regulation, strength of Promoter) and half-live of RNA

Translation

Translation
Ribosomes, tRNA

mRNA

Protein

Translates nucleic acid to amino acid sequence

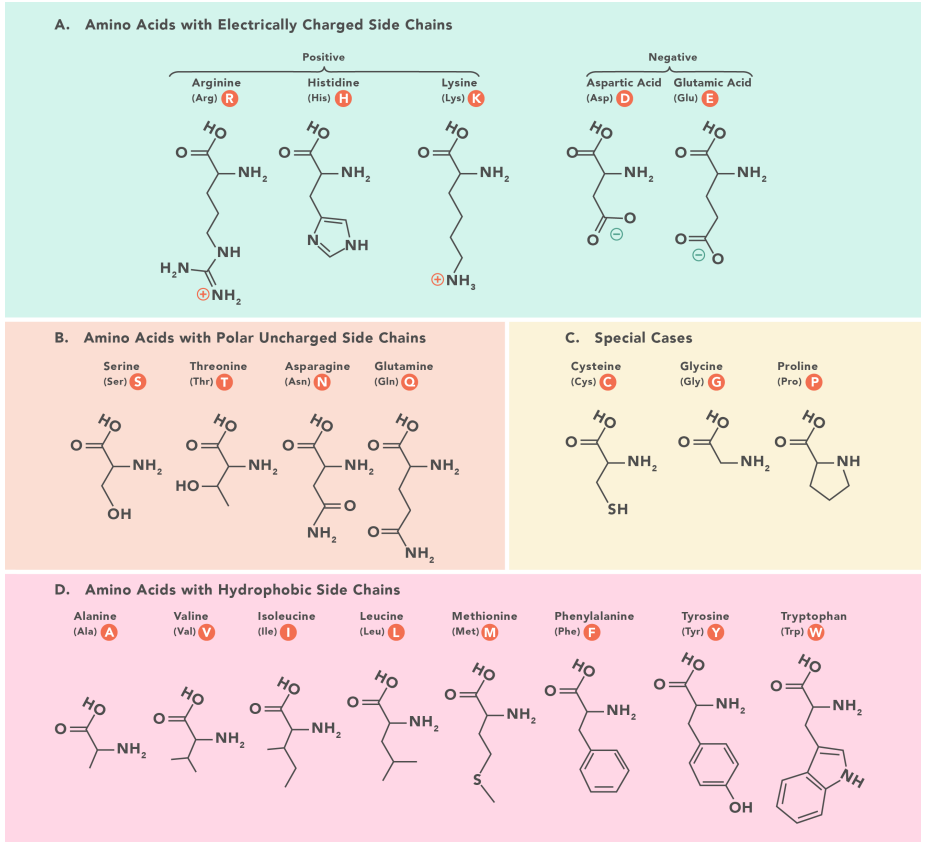
Proteinbiosynthesis

Four-letter RNA ”alphabet”
(4 bases)

A
U
G
C

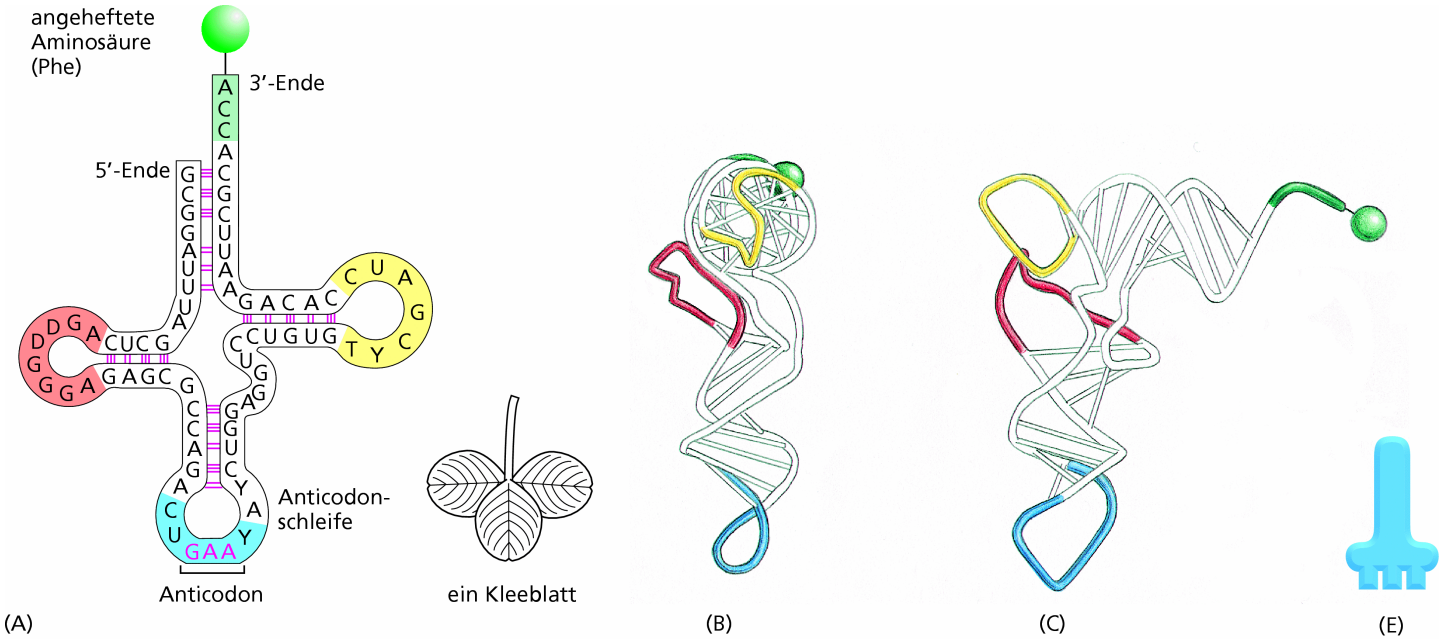
?

Twenty-letter Protein alphabet
(20 amino acids)



Translation

tRNAs act as adaptors to connect nucleic-acid sequences to amino-acids

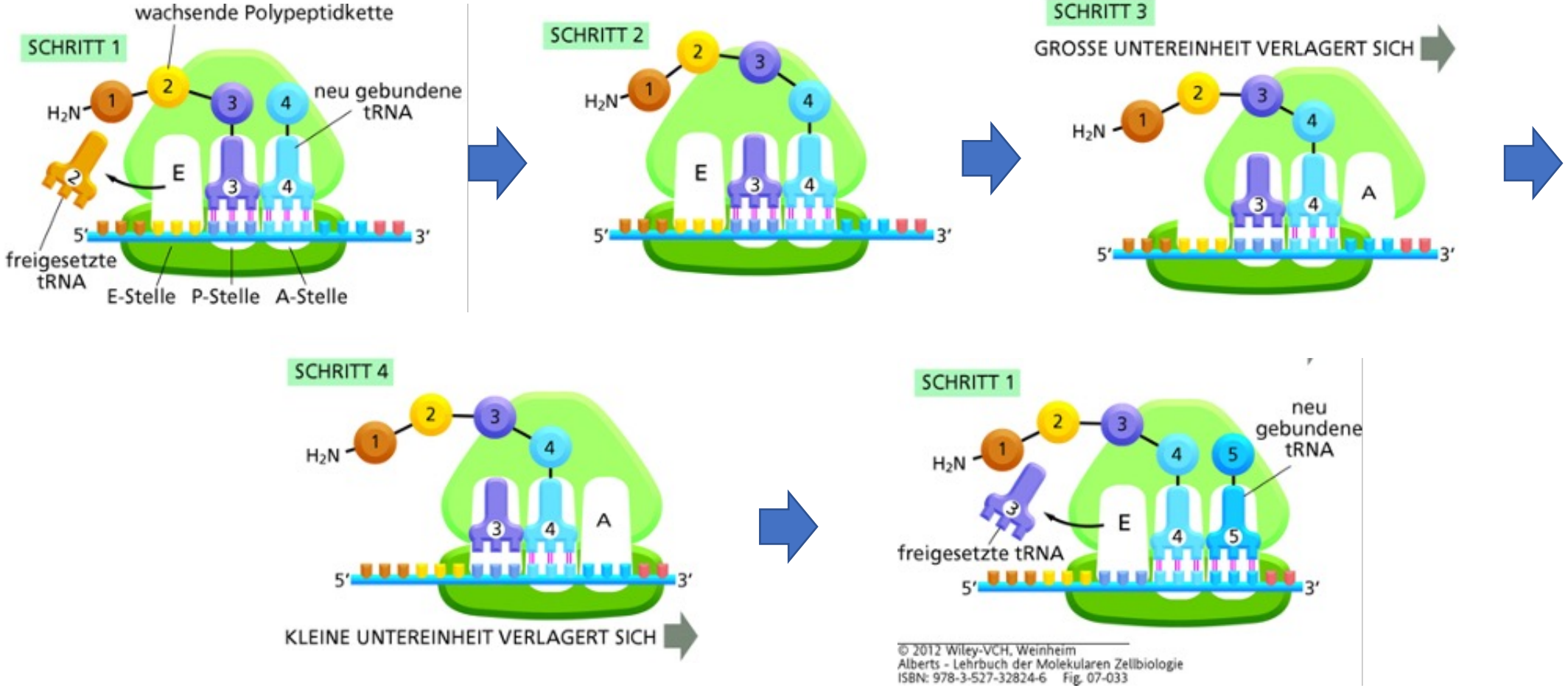


5′ GCGGAUUUAGCUCAGDDGGGAGAGCGCCAGACUGAAYAYCUGGAGGUCCUGUGTYCGAUCCACAGAAUUCGCACCA 3′

(D) Anticodon

Translation

takes place at Ribosomes



Translation

The genetic code

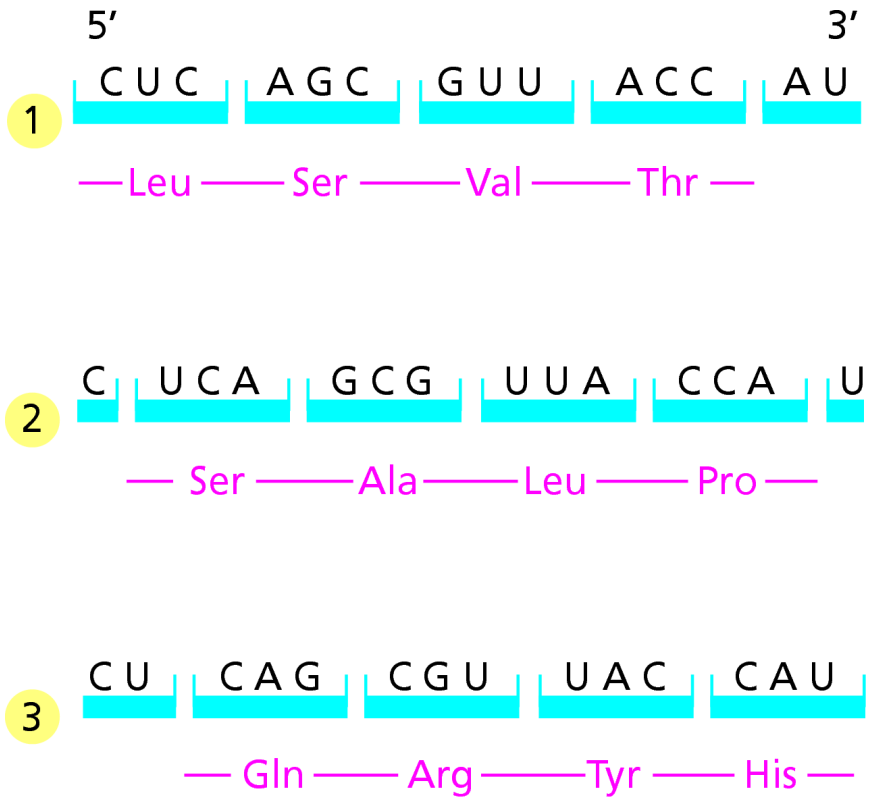
GCA GCC GCG GCU	AGA AGG CGA CGC CGG CGU	GAC GAU	AAC AAU	UGC UGU	GAA GAG	CAA CAG	GGA GGC GGG GGU	CAC CAU	AUA AUC AUU	UUA UUG CUA CUC CUG CUU	AAA AAG	Start AUG	UUC UUU	CCA CCC CCG CCU	AGC AGU UCA UCC UCG UCU	ACA ACC ACG ACU	UGG	UAC UAU	GUA GUC GUG GUU	UAA UAG UGA
Ala	Arg	Asp	Asn	Cys	Glu	Gln	Gly	His	Ile	Leu	Lys	Met	Phe	Pro	Ser	Thr	Trp	Tyr	Val	Stopp
A	R	D	N	C	E	Q	G	H	I	L	K	M	F	P	S	T	W	Y	V	

Alberts - Lehrbuch der Molekularen Zellbiologie
ISBN: 978-3-527-32824-6 Fig. 07-024

- **The Genetic code is like a dictionary used to translate nucleic acid sequence into amino acid sequence**
- **The RNA is read in triplets of bases (corresponding to the anticodons of the tRNAs) called codons**
- **Since RNA is a linear Polymer consisting of 4 different bases, there are 4 X 4 X 4 = 64 possible combinations of bases**
- **Since there are only 20 different amino acids, the code has evolved to be redundant (degenerate code)**
- **There are two special types of codons signaling the start and stop of a protein: Start & Stop codons**
- **This genetic code is used by all life forms on earth**

Translation

Open Reading Frame (ORFs)



Alberts - Lehrbuch der Molekularen Zellbiologie
ISBN: 978-3-527-32824-6 Fig. 07-025

- **The partitioning of the genetic code into triplets gives rise to 3 potential “reading frames” on any give stretch of DNA/RNA**
- **The presence of a Start codon not only signals the onset of translation, but at the same time defines the reading frame**
- **An ORF is opened by a start-codon and closed by a subsequent stop-codon lying within the same reading frame**
- **Deletions or insertion within a coding sequence shift the reading frame and therefore disrupt the information that follows them**

From strands to strings

- Fasta (.fasta, .fa, .fna) is a text-based format for biological sequences
- Headers/deflines are preceded by ">" and contain a name or description of the following sequence
- The monomers (nuleotides or amino acids) are represented by single letters in the sequence
- Nucleic acid sequence always depicted as single strand and from 5'-3' direction
- Protein sequence typically starting from the N-Terminal end
- Sequence can either be contained in one line (sequential) or in multiple lines (interleaved)

```
1  >Example_DNA_seq_1
2  ATGCGTGGGTGTCCATGCGTGATGTCGTATGCTATGTGATGCTTGTCGTAGTTTTTTCCCACTCTATCTTAAGCGGACTTGCGTGATGTCGTATGCTATGTGATGGC
3  >Example_DNA_seq_2
4  GCCATCACATAGCATACGACATCACGCAAGTCCGCTTAAGATAGAGTGGGAAAAAACTACGACAAGCATCACATAGCATACGACATCACGCATGGACACCCACGCAT
5
```

```
1  >Example_Protein_seq_1
2  MFVFLVLLPLVSSQCVNLTTRTQLPPAYTNSFTRGVYYPDKVFRSSVLHSTQDLFLPFFSNVTWFHAIHVSGTNGTKRFD
3  NPVLPFNDGVYFASTEKSNIIRGWIFGTTLDSKTQSLLIVNNATNVVIKVCEFQFCNDPFLGVYYHKNNKSWMESEFRVY
4  GWIFGTTLDSKTQSLLIVNNATNVVIKVCEFQFCNDPFLGVYYHKNNKSWMESEFRVYSSANNCTFEYVSQPFLMDLEGK
5  >Example_Protein_seq_2
6  SSANNCTFEYVSQPFLMDLEGKQGNFKNLREFVFKNIDGYFKIYSKHTPINLVRDLPQGFSALEPLVDLPIGINITRFQT
7  LLALHRSYLTPGDSSSGWTAGAAAYYVGYLQPRTFLLKYNENGTITDAVDCALDPLSETKCTLKSFTVEKGIYQTSNFRV
8  QPTESIVRFPNITNLCPFGEVFNATRFASVYAWNRKRISNCVADYSVLYNSASFSTFKCYGVSPTKLNDLCFTNVYADSF
9
```

Excercise

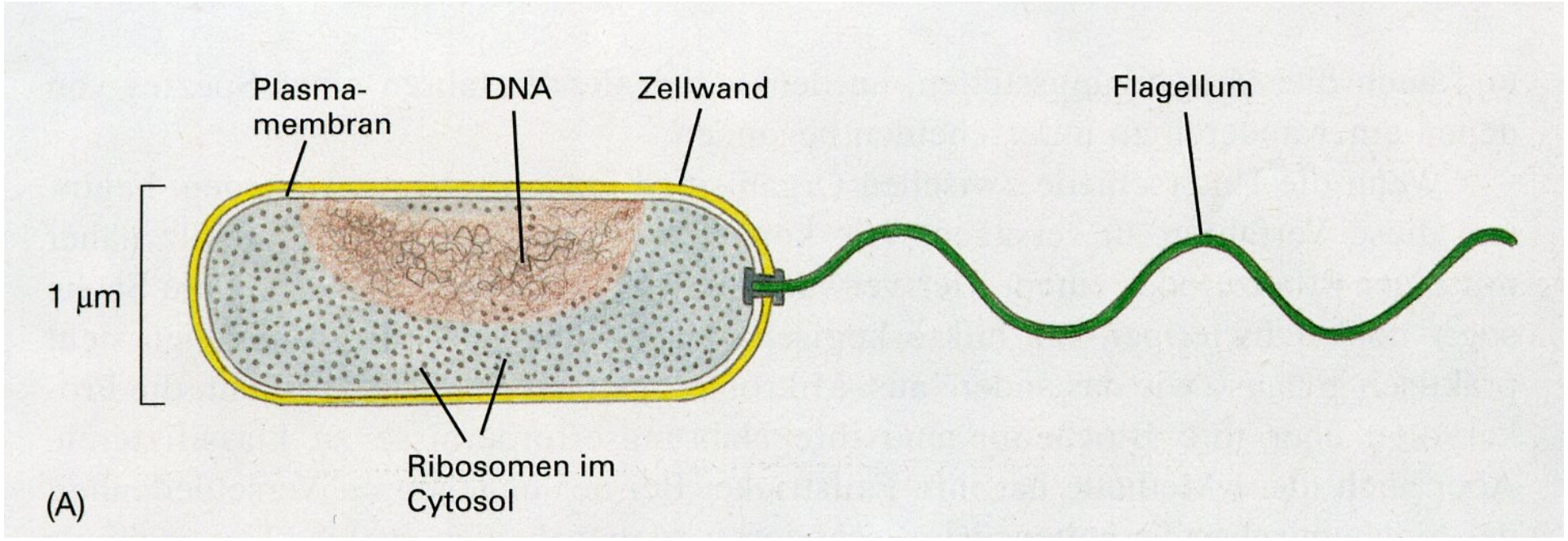
Write a python script that:

1. **finds all ORFs in the provided DNA sequence**
2. **Selects the ORFs that code for proteins >40 amino acids**
3. **Selects the ORFs that do not lie within a larger ORF**
4. **translates the selected ORFs into an amino acid sequence**

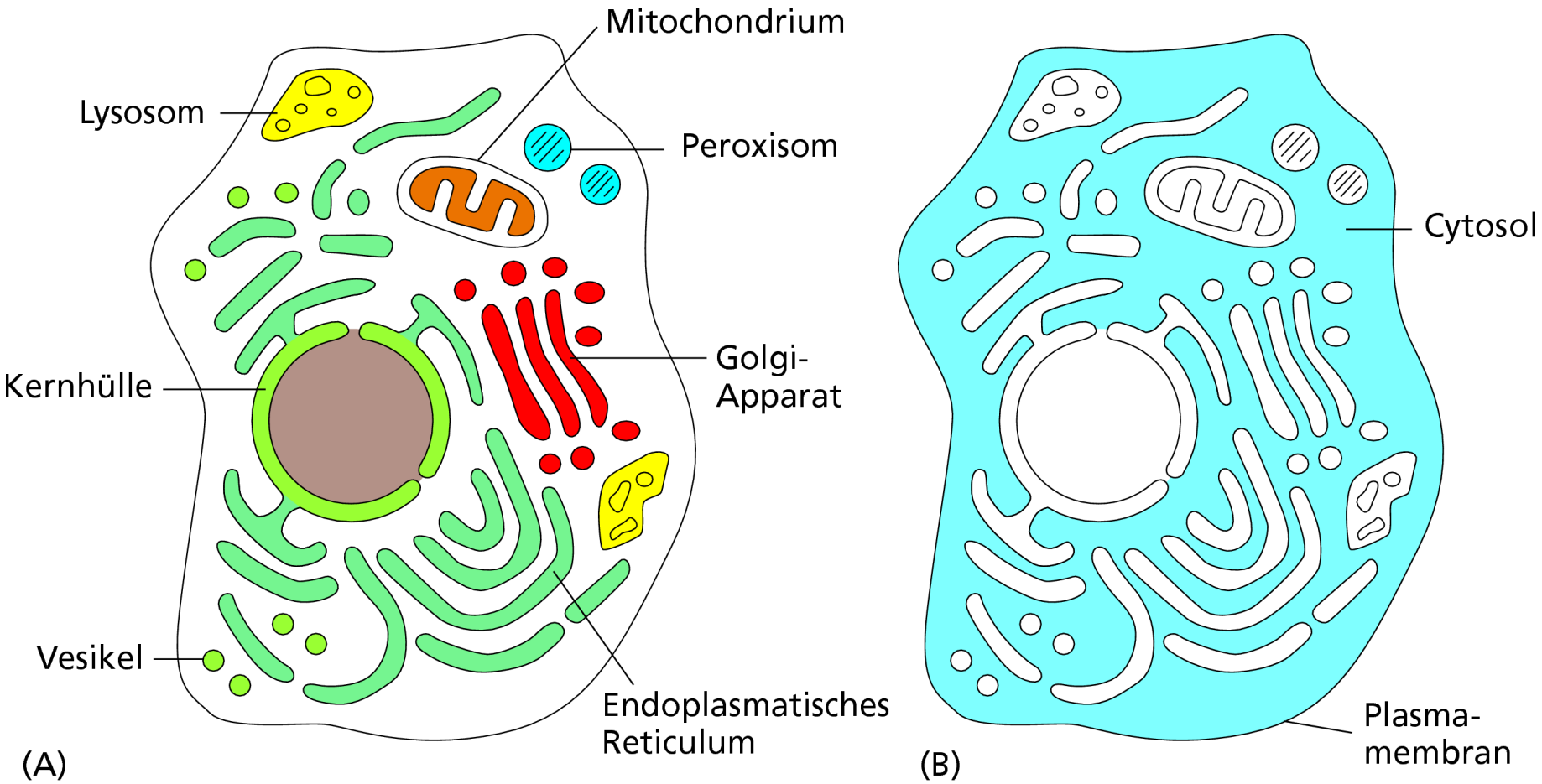
Classification of life

- How are those fundamental processes connected and organized in order to actually bring forth life?
- The most elementary unit of live is a cell
- A cell is an enclosed space in which the reactions of life can take place and that contains the hereditary material through which the information necessary to maintain those reactions can be passed on
- Basically there are two blueprints for cells

Prokaryotic cells



Eukaryotic cells



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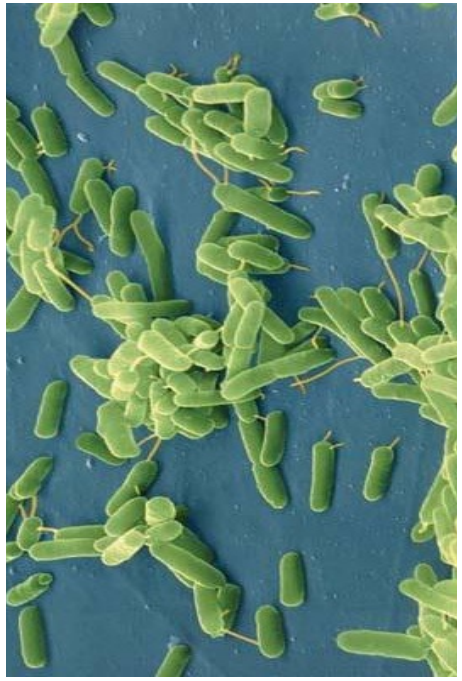
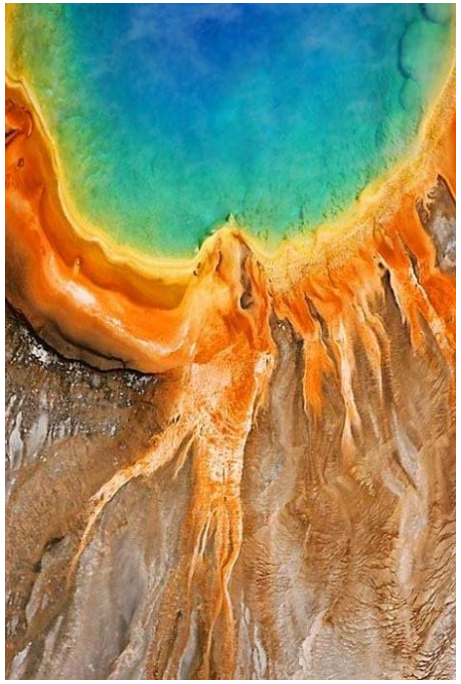
Domains

based on molecular criteria (rDNA sequence)

Bacteria



Archea



Eukaryota

What about Viruses?

- Viruses are evolutionary very old (may date back to the last universal common ancestor)
- Viruses infecting all types of life exist: from bacteria over yeast to humans
- Through their ubiquitous interactions with life forms on all branches of the evolutionary tree they have been affecting and shaping life on this planet throughout its existence
- However: Virus aren’t capable of replicating themselves independently of their hosts
- Next: A spotlight on human pathogenic viruses

Data Science in Bioinformatics

WS 22/23

Next: Viruses

Lecturer: PD Dr. Ricarda Schmithausen

Course Date: 17.10.2022