ESE 680-003
Special topics in electrical and systems engineering:
Systems Biology
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Basics of molecular cell biology

Topics

- Evolution and the origin of life
- Atoms and molecules
- Carbohydrates, proteins and lipids
- Parts and functions of the cell
- DNA and gene expression

Origin of life

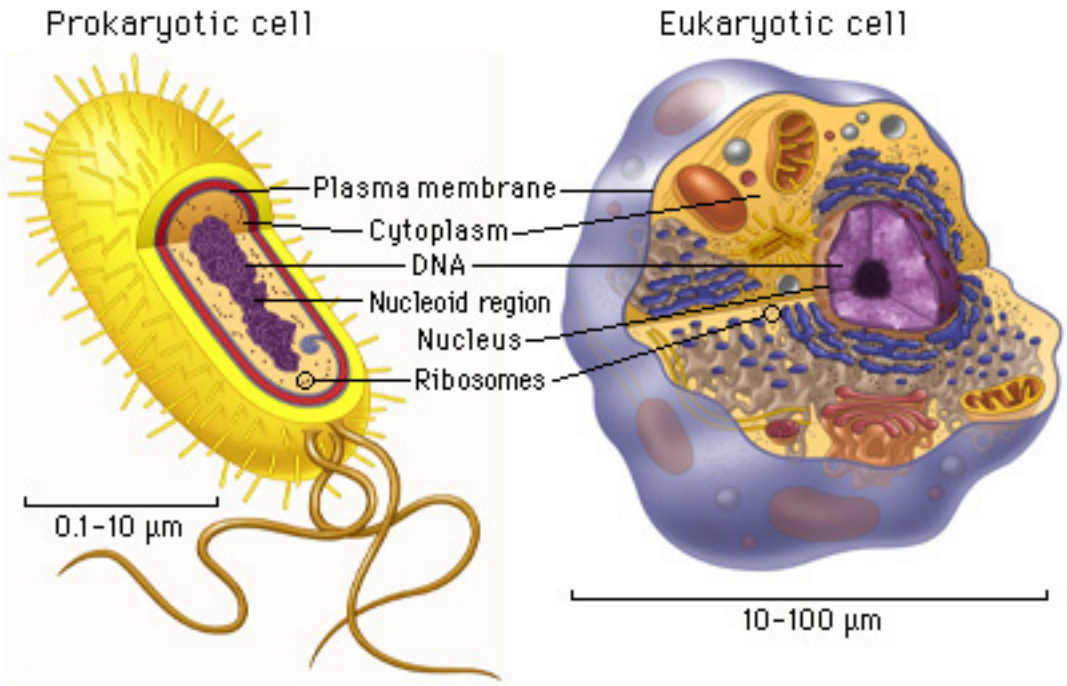
- Started on Earth 4.5 billion years ago
- Volcanism: H_2O, CH_4, NH_3, H_2S
  - Reducing atmosphere
  - Early ocean
- Loss of hydrogen: N_2, CO, CO_2, H_2O
  - Energy (Sun, UV, electrical discharges)
  - Catalytic effect of solid state surfaces
  - Enrichment of organic molecules in the ocean

Origin of life

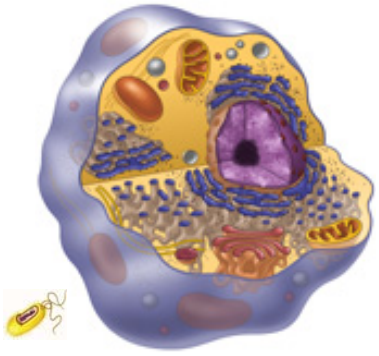
- Prebiotic broth hypothesis
  - Macromolecules
  - Molecular aggregates
  - Simple compartmented pathways
  - Enzymes (low temperature reactions)
  - Directed synthesis and reproduction
- First cells – end of abiotic evolution

Evolution

- Prokaryotes
  - simple organisms
  - 1-10 microns in length
  - Single cell
  - No compartments
  - Simple cell division



- Eukaryotes
  - higher organisms
  - 10-100 microns
  - multicellular
  - mucleus, cytosol, organelles
  - mitosis and meiosis



Evolution

- Prokaryotes have sexual reproduction
  - Genetic material comes from two non-symmetric sources (fertilized egg)
- Parasites do not have their own metabolism
  - E.g. viruses – rely on other organisms
- Aerobic vs. anaerobic
- Multicellular organisms have differentiated cells
  - Same genotype, different phenotype

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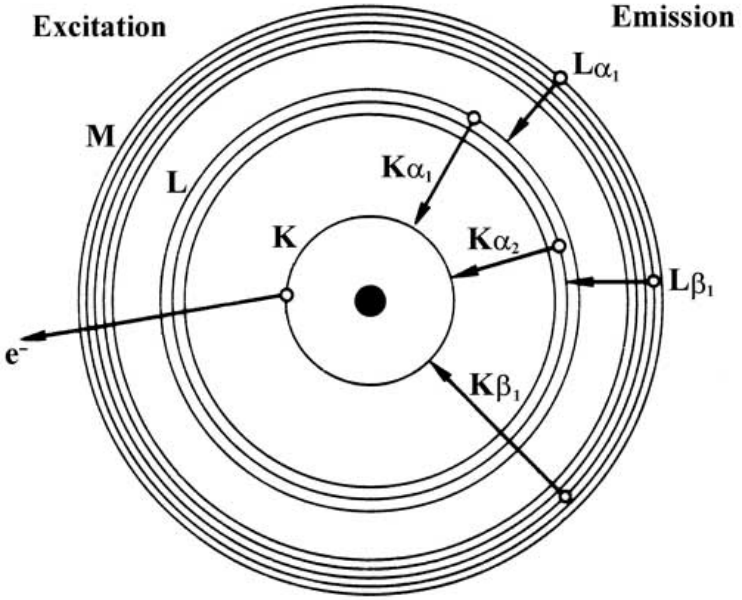
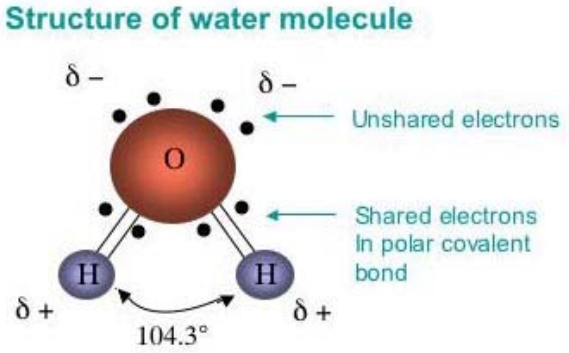
Chemical bonds and forces

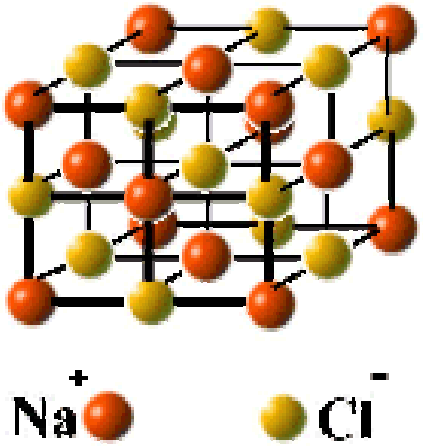
- Shell model of atoms
  - Nucleus: positively charged heavy
  - Electrons on shells
  - Electrostatics and quantum mechanics
- Molecules
  - Atoms linked by bonds
  - Bonds are formed by the interaction of the electrons of different atoms

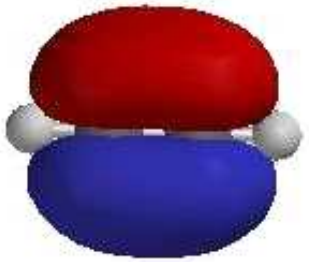


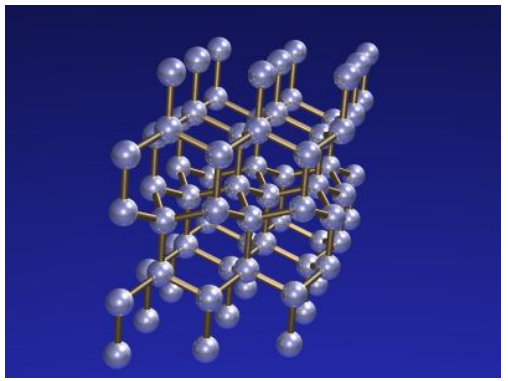


Chemical bonds and forces

- Several types of bonds
  - Big differences in strength
- Electrostatic
  - Very strong, e.g. Na^+Cl^- (salt, a crystal)
  - Atoms exchange electrons to achieve complete shell
  - Remain bound due to electrostatic attraction
- Covalent
  - Very strong, e.g. C (diamond, a crystal)
  - Electrons are shared between several atoms
  - Molecular orbitals
  - Forms (backbone of) molecules

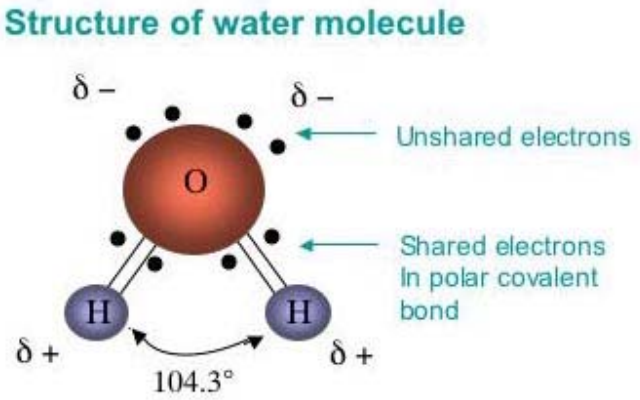






Chemical bonds and forces

- Weaker types of bonds
- Polar molecules
  - H_2O: electrons are more attracted to the oxygen atom
  - Hydrogen atoms become positively charged
- Hydrogen bonds
  - Polarized hydrogen attracted to negatively charged parts of other molecules
  - 4.0 kJ/mol
- Van der Walls forces
  - Induced polarization of electron clouds
  - 0.4 kJ/mol
  - Of both signs: optimal distance



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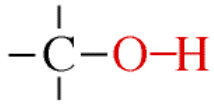
Organic molecules

- Typically have a carbon chain
- Certain groupings of atoms tend to be conserved within many different molecules
  - Functional groups
  - Stability due to special configuration, electron orbits
  - Some are polar
- Classified by functional groups, structure

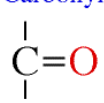
Functional groups

Hydroxyl



- Hydroxil:
  - Linked to absorbtion and release of water (condensation, hydrolysis)
  - Alcohols

Carbonyl

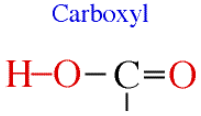


Ketone, located in a carbon chain

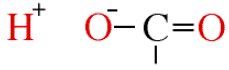
Aldehyde, located at the end of a chain

- Carbonyl:
  - Aldehydes
  - Ketones
  - Important in carbohydrates

Carboxyl

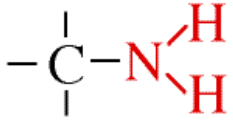


often dissociates



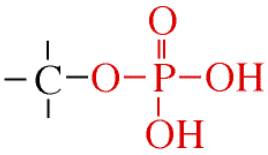
- Carboxyl
  - Organic acids

Amino



- Amino
  - Amino acids have an amino and a carboxyl group
  - Crucial role as part of the catalytic domain of enzymes

Phosphate



- Phosphate
  - Bridging ligand in large molecules
  - Di- and tri-phosphates act as energy unit
  - Regulation of enzyme activities (MAP kinases)

Classes of molecules: Carbohydrates

- Energy storage
- General formula: $C_n(H_2O)_n$
- Monosaccharides: 3-7 carbon atoms
- Polysaccharides

Classes of molecules: Lipids

- Non-polar therefore hydrophobic (not soluble in water)
- Tend to form nonpolar associations or membranes
- Three types of lipids
  - Neutral lipids (storage fat)
  - Phospolipids (membranes)
  - Steroids (four condensed carbon rings, hormones)

Classes of molecules: Proteins

- Roles:
  - Cytoskeletal framework
  - Catalytic enzymes for highly specific biochemical reactions -> control of metabolism
- Polypeptide chain
  - 20 types of amino acids covalently linked
- Primary structure given by the element on the chain
- Secondary & tertiary structures
  - α-helix and β-strand
  - folding

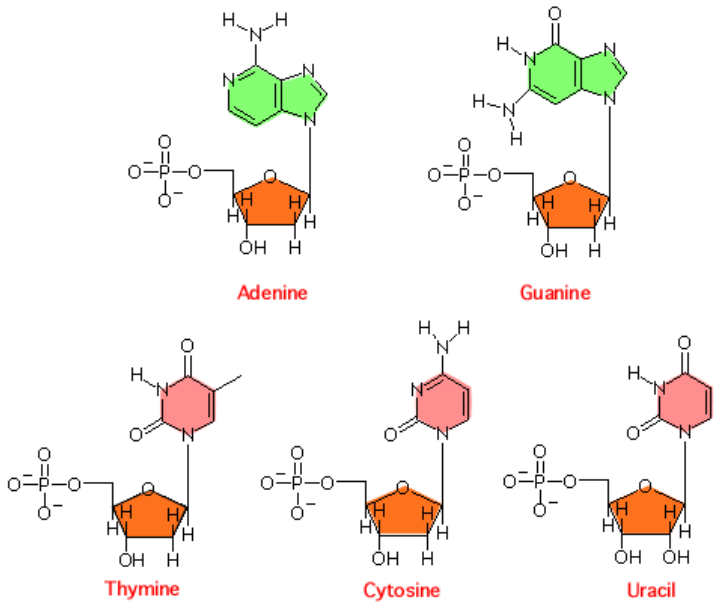
Classes of molecules: Nucleic acids

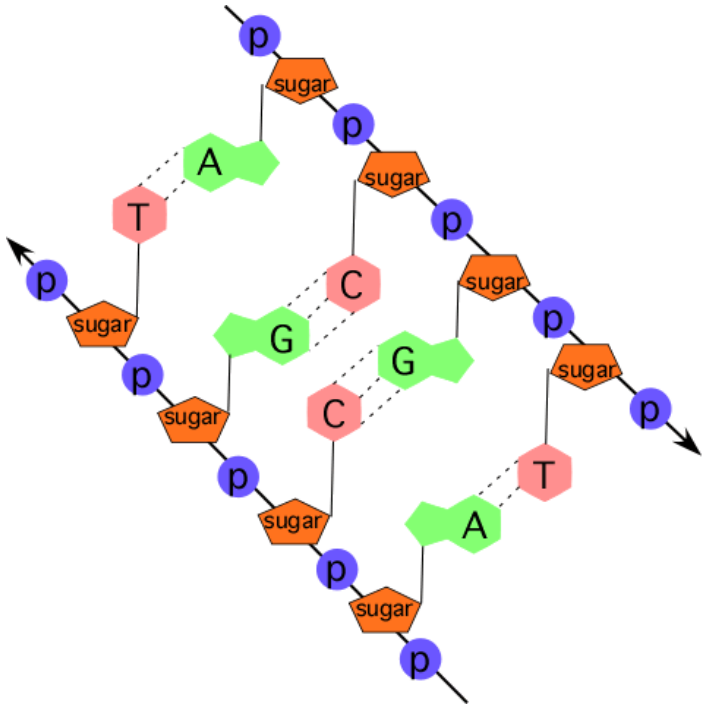
- DNA, RNA
- Polymers built up of covalently bound **mononucleotides**
- Mononucleotides
  - Nitrogen-containing base
  - Pentose
  - One or more phosphate groups
- Four (five) different bases:
  - Cytosine, Thymine, Adenine, Guanine, Uracyl

Classes of molecules: Nucleic acids

- DNA: ATGC; RNA: AUGC
- Phosphate groups link nucleotides together forming the backbone of one strand
- DNA consists of two antiparallel strands, linked together by hydrogen bonds between pairs of complementary bases
  - A-T, G-C
- RNA occurs as a single strand

Nucleic acids





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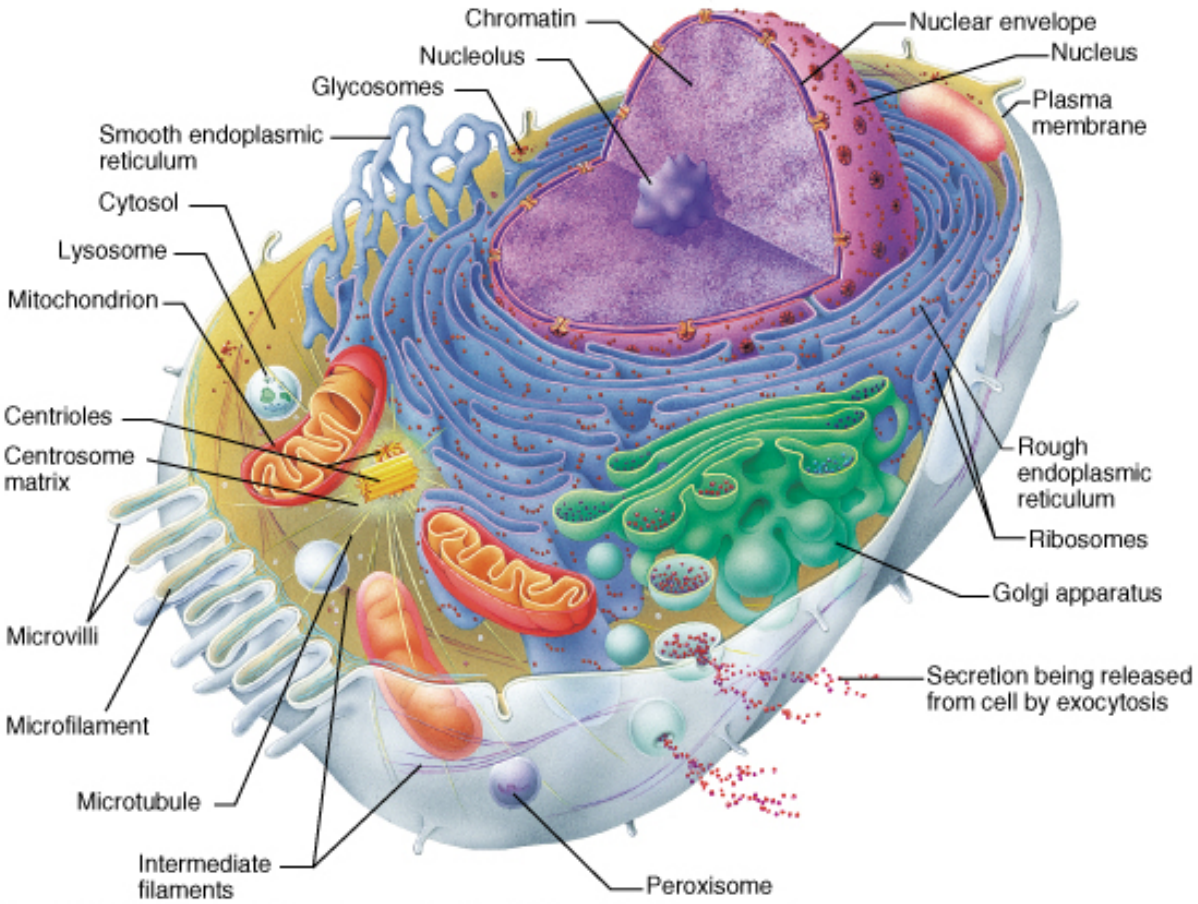
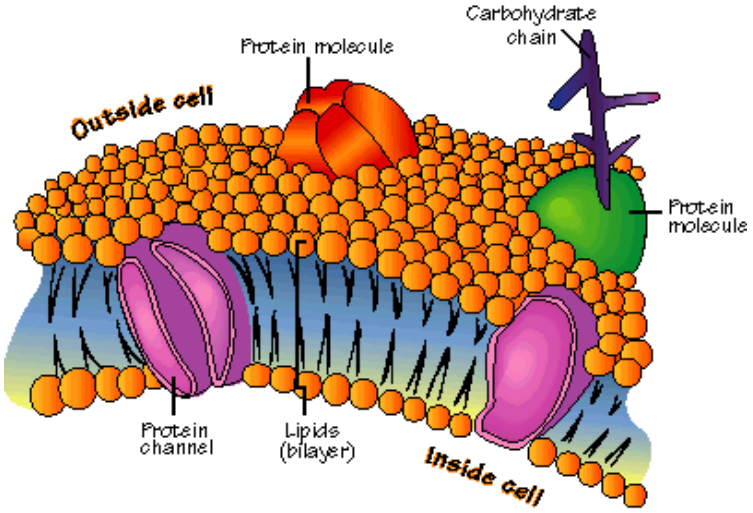
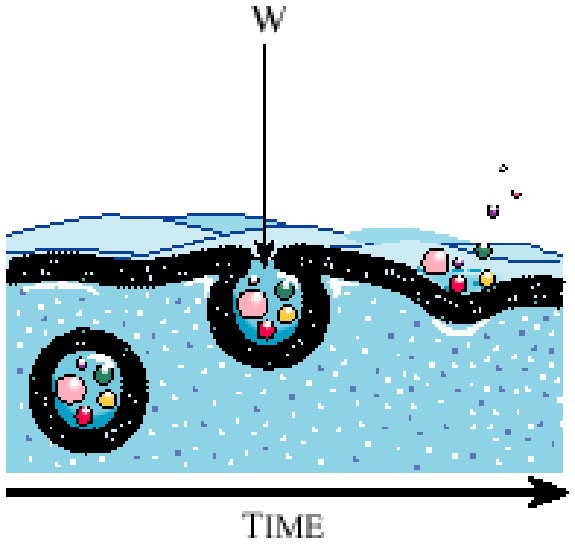
Structure of the cell



Cell membrane

- Lipid bilayer, with membrane proteins inserted
- Fluid mosaic model
- Also acts as a selective filter for nutrients and byproducts
- Ability to form a cavity that pinches off as a vesicle
  - transport





Nucleus

- Prokaryotes store genetic information in a single, circular, double stranded DNA, and sometimes smaller plasmids
- Eukaryotes have a nucleus which occupies about 10% of cell volume
- Nuclear envelope, with regulated traffic between the nucleus and the cytosol
- Genetic material forms the chromatin
- Chromosomes consist of two identical chromatids
  - each is a double stranded DNA
  - wound around histones (protein complexes)

Cytosol

- Fills the space between the organelles of the cytoplasm
- About 50% of cell volume
- Contains the cytoskeletal framework
  - Protein filaments
  - Responsible for coordination of cytoplasmatic movements
  - Three types: actin, microtubules, intermediate
- Actin
  - cell shape, muscle contraction
- Microtubules
  - rapid motions, e.g. flagella
- Intermediate
  - fibrous proteins; mechanical resistance

Organelles

- Mitochondria (“power plants”)
  - Only in eukaryotes
  - Size of a bacterium
  - Partially autonomous; have their own DNA
  - Produce the bulk of ATP in the cell
- Endoplasmatic reticulum (ER)
  - Biosynthesis of membrane lipids
- Golgi complex, lysosomes, peroxisomes, veiscles

Cell cycle

- Interphase and M-phase
- M-phase division itself
  - Nuclear division
  - Cytokinesis (division of cytoplasm)
- Eukaryotic cells have two copies of each chromosome (diploid)
  - Mitosis
  - Meiosis

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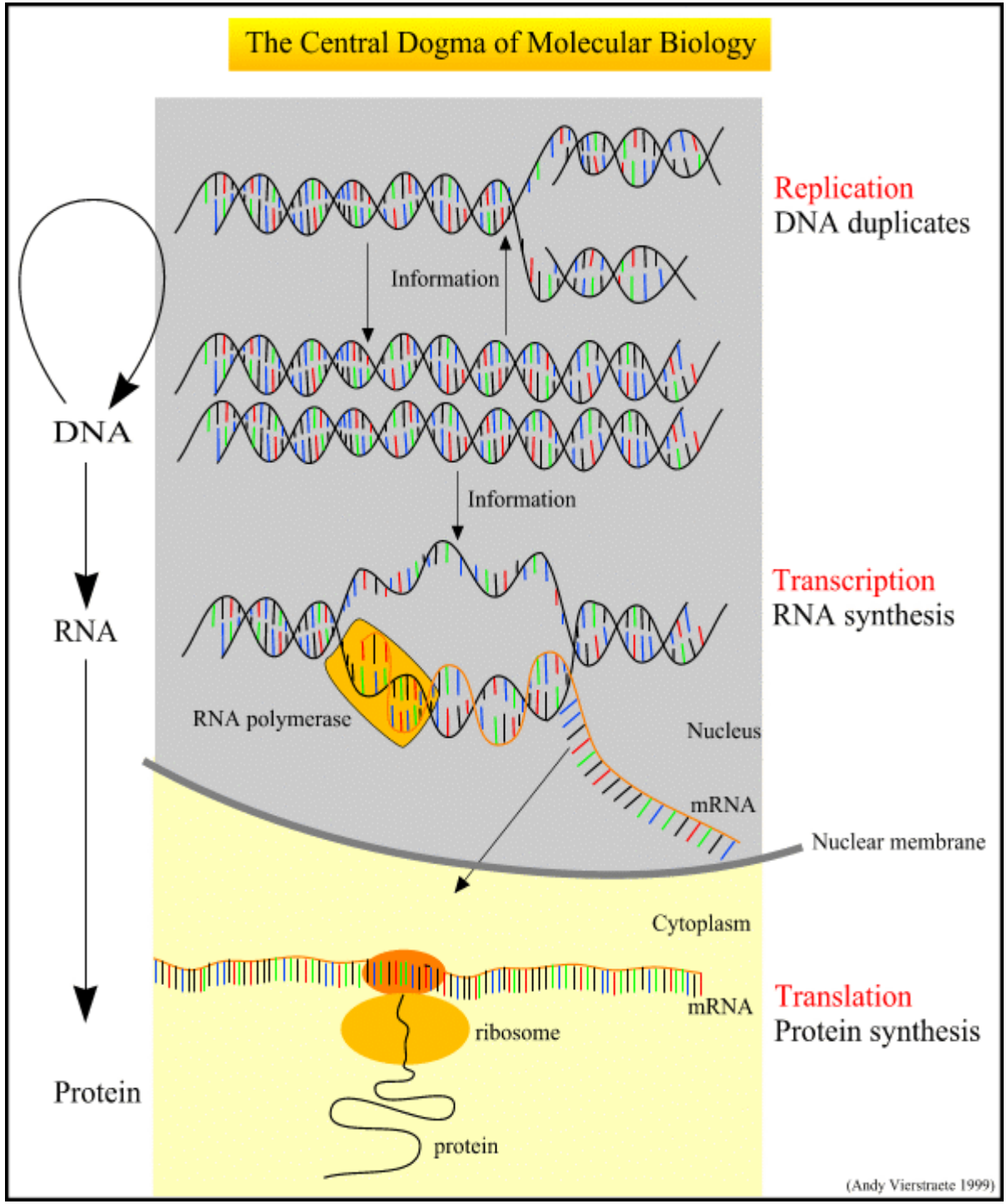
Gene expression

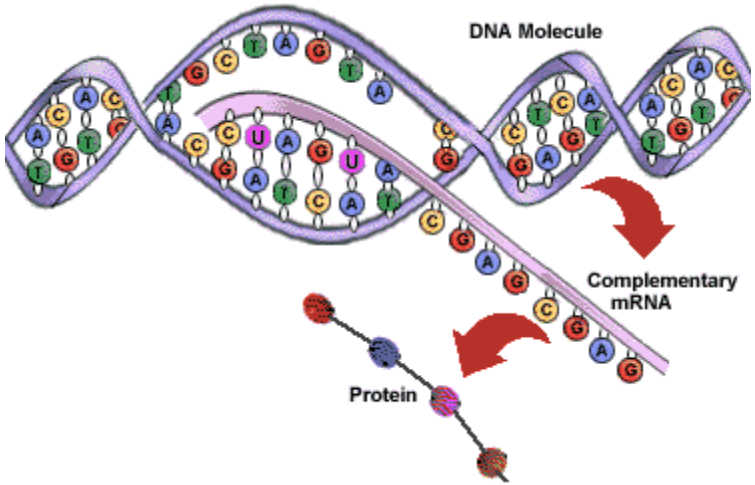
- Genes are regions of DNA which are transcribed separately into mRNA
- mRNA is further processed (spliced)
- mRNA is transferred outside the nucleus
- mRNA binds to ribosomes which transcribes its sequence into a polypeptide chain
- Newly formed chain folds into the protein


The Central Dogma of Molecular Biology
Replication
DNA duplicates
Information
DNA
Information
Transcription
RNA synthesis
RNA
RNA polymerase
Nucleus
mRNA
Nuclear membrane
Cytoplasm
mRNA
Translation
Protein synthesis
ribosome
Protein
protein
(Andy Vierstraete 1999)

Transcription

- Performed by RNA polymerase (RNAP)
- Promoter site
  - Initially binds RNAP (initiation complex)
  - Its affinity to RNAP, activity state determine transcription of the gene
- Elongation phase
  - RNAP moves along the DNA and synthesizes complementary RNA
  - DNA unwinds and rewinds as RNAP advances
- Termination
  - Rho-independent (GC-rich hairpin structure)
  - Rho factor binds to newly formed RNA

Transcription



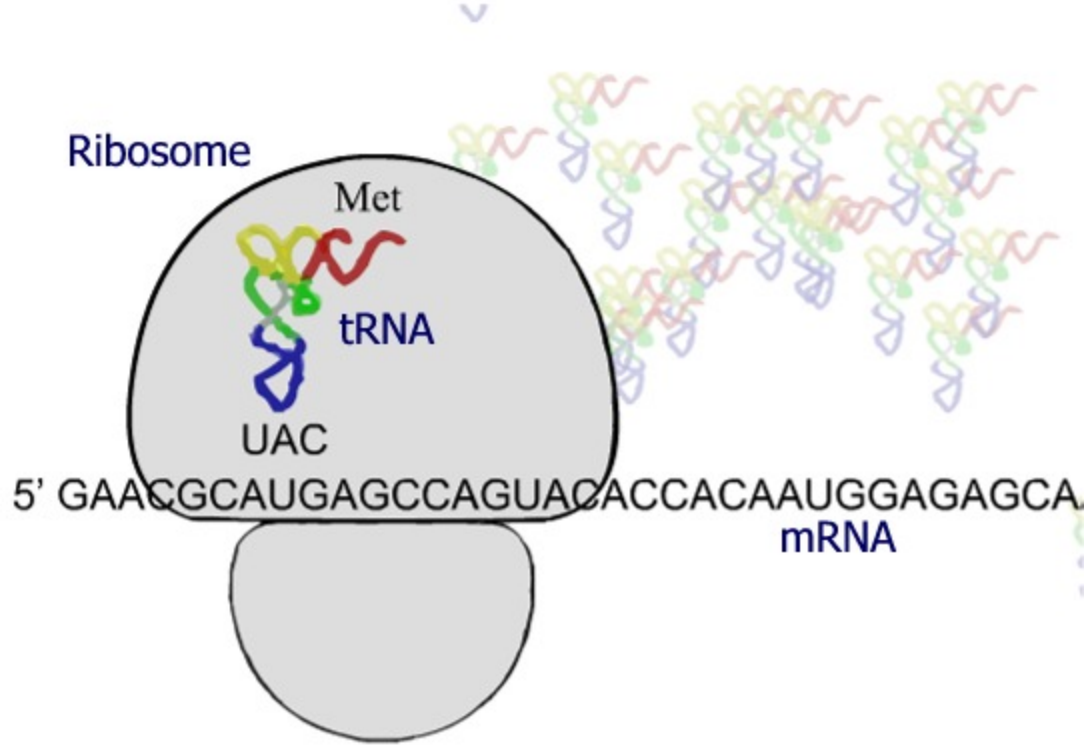
mRNA processing

- Prokaryotes
- Introns (nontranslating regions)
- Exons bound together after splicing out the introns
- Transport of mature mRNA into cytosol
- Transport to specific locations

Translation

- Coding mRNA is processed by ribosomes
- mRNA is the “message”, serves as a blueprint
- The final product is the protein that is synthesized using elementary amino-acids
- tRNA is used to bring in the matching (cognate) amino-acid to the translating ribosome

Translation



Regulation of gene expression

- Multiple modalities
- Transcriptional
  - Repression
  - Activation
- Post-translational

Organizational issues

- Schedule: MW 9:30 – 11:00
- Room: Towne 303
- Instructors:
  - **George Pappas**: pappasg@seas.upenn.edu (TBA)
  - Vijay Kumar: kumar@me.upenn.edu
  - Harvey Rubin: rubinh@mail.med.upenn.edu
  - *Agung Julius*: agung@seas.upenn.edu (Tue 3-4)
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