Evolution and basic properties of the cell

Cells as the basic unit of life

- Living organisms are single cells or composed of cells
- Atypical occurrence: striated muscle, giant algae
History of Cell Biology

1595 – (Jansen): first light microscope

1655 – Hooke: ‘cells’ in cork

1674 – Leuwenhoek: observed protista (animalcules)

1833 – Brown: described the cell’s nucleus from the orchid

1839 – Schleiden & Schwann: proposed cell theory (all organisms are comprised of cells)

1857 – Pasteur: discovery of lactobacillus (bacteria are also cells)

1858 – Rudolf Virchow: omnis cellula e cellula - cells develop only from pre-existing cells by a process called cell division

1859 – Darwin: The origin of species (1839!) – evolution theory

1866 – Mendel: Father of Genetics

1874 – Flemming: described chromosome behaviour during mitosis.

1882 – Koch: discovers mycobacterium tuberculosis, establish pathogenic role of bacteria

1894 – Altmann: first described mitochondria.

1898 – Golgi: described the Golgi apparatus.

…

…

Cell culturing, Biophysical and Molecular biology tools for observation and manipulation

...............
„The 8th day of creation”

1951, HeLa

*The Immortal Life of Henrietta Lacks* by Hilary Mantel

*Science* 2010:329 52-56
Creation of a Bacterial Cell Controlled by a Chemically Synthesized Genome
Origins and main features of life

** compartmentalisation **

- info coded in DNA (genotype)
- (main) flow of information: DNA→RNA→protein
- universal genetic code
- ribosomes
- “phenotype” determined primarily by proteins

Miller experiment

RNA-based systems

EVLUTION OF RNAs THAT CAN DIRECT PROTEIN SYNTHESIS

RNA and protein-based systems

EVOLUTION OF NEW ENZYMES THAT CREATE DNA AND MAKE RNA COPIES FROM IT

present-day cells
In most general terms life involves a system of enzyme catalyzed anabolic and catabolic processes with the ability of self-reproduction.

RNA molecules can function as enzymes (ribozymes): RNA polymerase, splicing, polypeptide synthesis, even reverse transcriptase – thus the RNA world probably preceded the protein world.

By coupling the systems of RNA and protein synthesis – via the aminoacyl-tRNA synthetases – the universal genetic code evolved.

Science 2007; 318. 62 – 64. Life with Oxygen
September 2009 Scientific American; The Origin of Life on Earth
eLife. 2017; 6: e32330. Transitioning to DNA genomes in an RNA world
Evolution of life forms

mutations + selection + endosymbiosis

Changes in leaps

Earth: 4.5 billion* yrs
Life arises on Earth: 3.5-4 billion yrs
Pro/eukaryotes: 3 billion yrs
Plants, animals, yeasts: 1.5 billion yrs

* billion=$10^9$ (short scale!)
Main features of the evolution of life on Earth:

• prebiological evolution → “organic soup”; RNA → DNA
• catalyzed chemical reactions, trigger principle, cascade principle, feed-back regulation, linked reactions
• mutability and selection
• propagation of traits: self-reproductive capacity
  E. coli divides every 20-40 mins
  Regulated mutation rate
  mutations are buffered by other proteins
• compartmentalization
• changes in leaps: phagocytic capacity, splicing, sex
• metabolism: anaerobic > aerobic, ATP
Prokaryotes (arche- and eubacteria)

- nucleoid

DNA:
- circular, 0.75–5 Mbp
- usually no introns
- 1 chromosome, membrane-attached

Eukaryotes

- unicellular: protists, yeast
- multicellular: plants, animals

-nucleus
  (RNA and protein synthesis separated*)
- nucleolus
- histons

DNA:
- linear, 15 Mbp-
- introns in genes*
- several chromosomes, nucleoskeleton-anchored
Prokaryotes

- no inner compartmentalization.
- no cytoskeleton
- no endocytosis, exocytosis

metabolism: aerob/anaerob
usually unicellular

Eukaryotes

- mitochondrion, chloroplasts, ER, Golgi, lysosomes, peroxisomes
- microtubules, microfilaments, intermediate filaments
- endocytosis, exocytosis
- usually aerobic
- usually multicellular → differentiation
### Characteristic cell biological differences between prokaryotes and eukaryotes

<table>
<thead>
<tr>
<th></th>
<th>Prokaryotes</th>
<th>Eukaryotes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Nucleus</strong></td>
<td>only nucleoid</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Introns</strong></td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Transcription, translation</strong></td>
<td>In one compartment</td>
<td>In separate compartments</td>
</tr>
<tr>
<td><strong>Intracellular membrane systems (ER, Golgi)</strong></td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Mitochondria</strong></td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Phagocytosis</strong></td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Linear (rather than circular) chromosomes, with telomers</strong></td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Centrioles/centrosome or PCM</strong></td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Regulation of cell division</strong></td>
<td>Based on the domino principle</td>
<td>Based on a clockwork machinery</td>
</tr>
</tbody>
</table>
Mesosome: membrane invagination, where the circular DNA is anchored. Parallel, rather than sequential processes. Evolution of membrane systems led to endosymbiotic events, crucial for the origin of the eukaryotic cell.
Mitochondria are thought to have descended from close relatives of typhus-causing bacteria.

(cilia? – spirochetes???)

http://evolution.berkeley.edu/evo library/article/history_24
Entangle–engulf–endogenize (also known as E³) model

Fig. 5 | Proposed hypothetical model for eukaryogenesis. a, The syntrophic/fermentative host archaeon is suggested to degrade amino acids to short-chain fatty acids and H₂, possibly by interacting with H₂-scavenging (and indirectly O₂-scavenging) SRB (orange; see Supplementary Note 6). b, The host may have further interacted with a facultatively aerobic organotrophic partner that could scavenge toxic O₂ (the future mitochondrion; red). Continued interaction with SRB could have been beneficial but not necessarily essential; dotted arrows indicate the interaction; see Supplementary Note 7. c, Host external structures could have interacted (for example, mechanical or biological fusion⁵⁰) with the aerobic partner to enhance physical interaction and further engulf the partner for simultaneous development of endosymbiosis and a primitive nucleoid-bounding membrane. d, After engulfment, the host and symbiont could have continued the interaction shown in b as a primitive type of endosymbiosis. e, Development of ADP/ATP carrier (AAC) by the endosymbiont (initial direction of ATP transport remains unclear; see Supplementary Note 9). f, Endogenization of partner symbiosis by the host through delegation of catabolism and ATP generation to the endosymbiont and establishment of a symbiont-to-host ATP channel.

https://www.nature.com/articles/s41586-019-1916-6
Phylogenetics: based on genetic similarities (genotype), rather than phenotype

- other bacteria
- photosynthetic bacteria
- plants
- animals
- fungi

- archaebacteria
- eubacteria
- anaerobic ancestral eucaryote

- ancestral procaryote

- chloroplasts
- mitochondria
- O₂

- nucleus: yes
- i.c. membranes: yes
- cytoskeleton: yes
- phagocytosis: yes
- mitochondria: no
Endosymbiosis

**Classical definition:**
During evolution, a eukaryotic organism, already equipped with adequate cytoskeleton and internal membrane systems for this purpose, engulfed/phagocytosed a prokaryotic organism and they started to live together for their mutual benefit. Mitochondria came about when an aerobic prokaryote performing oxidative phosphorylation was internalized, chloroplasts derived from prokaryotes performing photosynthesis. The origin of peroxysomes is probably similar.

**Definition which allows more for recent research insights:**
During evolution, an organism, already equipped with adequate cytoskeletal and membrane elements for this purpose (probably an archea), engulfed a prokaryotic organism and they started to live together for their mutual benefit. Mitochondria came about when an aerobic prokaryote performing oxidative phosphorylation was internalized, chloroplasts derived from prokaryotes performing photosynthesis. The origin of peroxysomes is probably similar.
Modern Cell Theory

• All known living things are made up of cells that are their structural & functional units.
• All cells come from pre-existing cells by division (spontaneous generation does not occur).
• Cells contain hereditary information which is passed from cell to cell during cell division.
• Cells are similar in chemical composition.
• Cells maintain their organized structure by investing energy. Energy producing and energy draining catabolic and anabolic processes happen inside cells.
How cells gain energy

**anabolic**

CO₂, H₂O, N₂ → organic compounds →

**catabolic** (reactions)

glycolysis,
if there is O₂: oxydative phosphorylation

**Autotrophic:**

*Photosynthesis* (hv)

*Chemosynthesis* (ΔG)

**Heterotrophic:** organic compounds of other organisms „minimum medium“:
glucose, H₂O, salts

---

ATP

e⁻ D → e⁻ A

---

…..S, Fe-, organic compounds…. anaerobic

H₂O ......................... O₂ aerobic
**Important dimensions in cell biology**

### Size (Linear)

<table>
<thead>
<tr>
<th>Component</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water molecule</td>
<td>0.3 nm</td>
</tr>
<tr>
<td>DNS diameter</td>
<td>2 nm</td>
</tr>
<tr>
<td>Average protein</td>
<td>3-6 nm</td>
</tr>
<tr>
<td>Cell membrane</td>
<td>7 nm</td>
</tr>
<tr>
<td>Virus (HIV)</td>
<td>100 nm</td>
</tr>
<tr>
<td>Bacteriophage (T4)</td>
<td>225 nm</td>
</tr>
<tr>
<td>Mitochondrion</td>
<td>1-5 μm</td>
</tr>
<tr>
<td>Bacterium (E. coli)</td>
<td>1-5 μm</td>
</tr>
<tr>
<td>Green algae</td>
<td>5-6 μm</td>
</tr>
<tr>
<td>Chloroplast</td>
<td>2-10 μm</td>
</tr>
<tr>
<td>Yeast</td>
<td>3-6 μm</td>
</tr>
<tr>
<td>Red blood cell</td>
<td>7.2 μm</td>
</tr>
<tr>
<td>Average cell</td>
<td>10-20 μm</td>
</tr>
<tr>
<td>Neuron cell body (spread out)</td>
<td>70 μm</td>
</tr>
<tr>
<td>Neurite (axon)</td>
<td>&lt;1.5 m</td>
</tr>
</tbody>
</table>

### Concentration

<table>
<thead>
<tr>
<th>Component</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 molecule in E. coli ban</td>
<td>1 nM</td>
</tr>
<tr>
<td>1 molecule in a HeLa cell</td>
<td>1 pM</td>
</tr>
<tr>
<td>Average water content</td>
<td>70 %</td>
</tr>
<tr>
<td>Proteins in a cell</td>
<td>3 mM</td>
</tr>
<tr>
<td>Small metabolites in a cell</td>
<td>300 mM</td>
</tr>
</tbody>
</table>

### Time

<table>
<thead>
<tr>
<th>Event</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prot. diffusion across bacterium</td>
<td>10 ms</td>
</tr>
<tr>
<td>Molecular motor covers 1 μm</td>
<td>1 s</td>
</tr>
<tr>
<td>Prot. diffusion across HeLa cell</td>
<td>10 s</td>
</tr>
<tr>
<td>E. coli division cycle</td>
<td>20-40 min</td>
</tr>
<tr>
<td>Yeast division cycle</td>
<td>70-140 min</td>
</tr>
<tr>
<td>HeLa cell cycle</td>
<td>15-30 h</td>
</tr>
</tbody>
</table>

### Speed

<table>
<thead>
<tr>
<th>Component</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>DNS polymerase (E. coli)</td>
<td>200-1000 bases/s</td>
</tr>
<tr>
<td>DNS polymerase (humán)</td>
<td>40 bases/s</td>
</tr>
<tr>
<td>RNS polymerase</td>
<td>10-100 bases/s</td>
</tr>
<tr>
<td>Ribosome</td>
<td>10-20 AA/s</td>
</tr>
</tbody>
</table>

cell membrane: 4-10nm, average protein: 3-6nm, water molecule: 0.3 nm
Basic quantitative features of cell biological relevance
(A) 

- 0.2 mm (200 μm) — minimum resolvable by unaided eye
- 20 μm
- 2 μm
- 200 nm
- 20 nm
- 2 nm
- 0.2 nm

1 m = 10^3 mm = 10^6 μm = 10^9 nm

(B)
Cells Need to Have Large Surface Area-to-Volume Ratio (limits size)

<table>
<thead>
<tr>
<th></th>
<th>(a)</th>
<th>(b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of cells</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>Total surface area</td>
<td>24 cm$^2$</td>
<td>48 cm$^2$</td>
</tr>
<tr>
<td>Total volume</td>
<td>8 cm$^3$</td>
<td>8 cm$^3$</td>
</tr>
<tr>
<td>Surface area/volume</td>
<td>24/8 = 3:1</td>
<td>48/8 = 6:1</td>
</tr>
</tbody>
</table>

![Diagram showing surface area and volume comparison for cells with different dimensions.](image)
Cell functions:

- self-maintenance, housekeeping
- motility
- growth, proliferation
- cell-cell communication
- differentiation, morphogenesis

\[
\text{determined by } \text{gene expression}
\]
Main features:

- Information is coded in DNA (genotype)
- (main) flow of information: DNA→RNA→protein
- universal genetic code
- ribosomes (25,000/E. coli)
- “phenotype” determined primarily by proteins
Gene expression

Prokaryotes

DNA

mRNA

protein

transcription

translation

Eukaryotes

DNA

intron

exon

primary RNA*

processing

5’ Cap

3’ polyA tail

Splicing

export

mRNA

translation

*primary RNA transcript: pre-RNA, hnRNA
How many genes code a cell:

<table>
<thead>
<tr>
<th>Organism</th>
<th>Number of Genes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mycoplasma</td>
<td>~300</td>
</tr>
<tr>
<td>E. coli</td>
<td>~4000</td>
</tr>
<tr>
<td>Yeast</td>
<td>~6000</td>
</tr>
<tr>
<td>C. elegans</td>
<td>~20000</td>
</tr>
<tr>
<td>Human</td>
<td>≥20000</td>
</tr>
</tbody>
</table>

Genome size (bp):

<table>
<thead>
<tr>
<th>Organism</th>
<th>Genome Size (bp)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mycoplasma</td>
<td>~5 million</td>
</tr>
<tr>
<td>E. coli</td>
<td>~12 million</td>
</tr>
<tr>
<td>Yeast</td>
<td>~100 million</td>
</tr>
<tr>
<td>Human</td>
<td>~3000 million</td>
</tr>
</tbody>
</table>
How can we have more proteins than genes? – Alternative splicing!

Gene: 1 2 3 4

mRNA: 1 2 3 4

Alternative Splicing:

mRNA: 1 2 3
Protein A

mRNA: 1 2 4
Protein B
Why do humans have 30x more DNA and about the same number of genes as C. elegans?

Levels of gene expression regulation in eukaryotes: protein factors and miRNAs, circular RNAs

- **IncRNAs** (long non-coding RNA)
- **miRNAs** (micro RNA)
<table>
<thead>
<tr>
<th>Keywords</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>arche- and eubacteria</td>
<td></td>
</tr>
<tr>
<td>prokaryotes, eukaryotes</td>
<td></td>
</tr>
<tr>
<td>Escherichia coli</td>
<td></td>
</tr>
<tr>
<td>Caenorhabditis elegans</td>
<td></td>
</tr>
<tr>
<td>protist (protozoa)</td>
<td></td>
</tr>
<tr>
<td>yeast</td>
<td></td>
</tr>
<tr>
<td>cell culture</td>
<td></td>
</tr>
<tr>
<td>Phagocytosis</td>
<td></td>
</tr>
<tr>
<td>endosymbiosis (in evolution)</td>
<td></td>
</tr>
<tr>
<td>exon, intron, splicing</td>
<td></td>
</tr>
<tr>
<td>transcription, translation</td>
<td></td>
</tr>
<tr>
<td>ribosomes</td>
<td></td>
</tr>
<tr>
<td>genotype</td>
<td></td>
</tr>
<tr>
<td>phenotype</td>
<td></td>
</tr>
<tr>
<td>metabolism</td>
<td></td>
</tr>
<tr>
<td>anabolic, catabolic</td>
<td></td>
</tr>
<tr>
<td>heterotrophic</td>
<td></td>
</tr>
<tr>
<td>autotrophic</td>
<td></td>
</tr>
<tr>
<td>anaerobic, aerobic</td>
<td></td>
</tr>
<tr>
<td>photosynthesis</td>
<td></td>
</tr>
<tr>
<td>chemosynthesis</td>
<td></td>
</tr>
<tr>
<td>glycolysis</td>
<td></td>
</tr>
<tr>
<td>oxidative phosphorylation</td>
<td></td>
</tr>
</tbody>
</table>
Questions you should be able to answer

• Do plants have mitochondria?
• Which organelle(s) had originated by endosymbiosis?
• Do bacteria have ribosomes?
• How many genes code for an E. coli bacterium?
• What are introns and exons?
• What are leading and lagging strand syntheses?