Modelling Biochemical Reaction Networks

Lecture 1: Overview of cell biology

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Types of cells

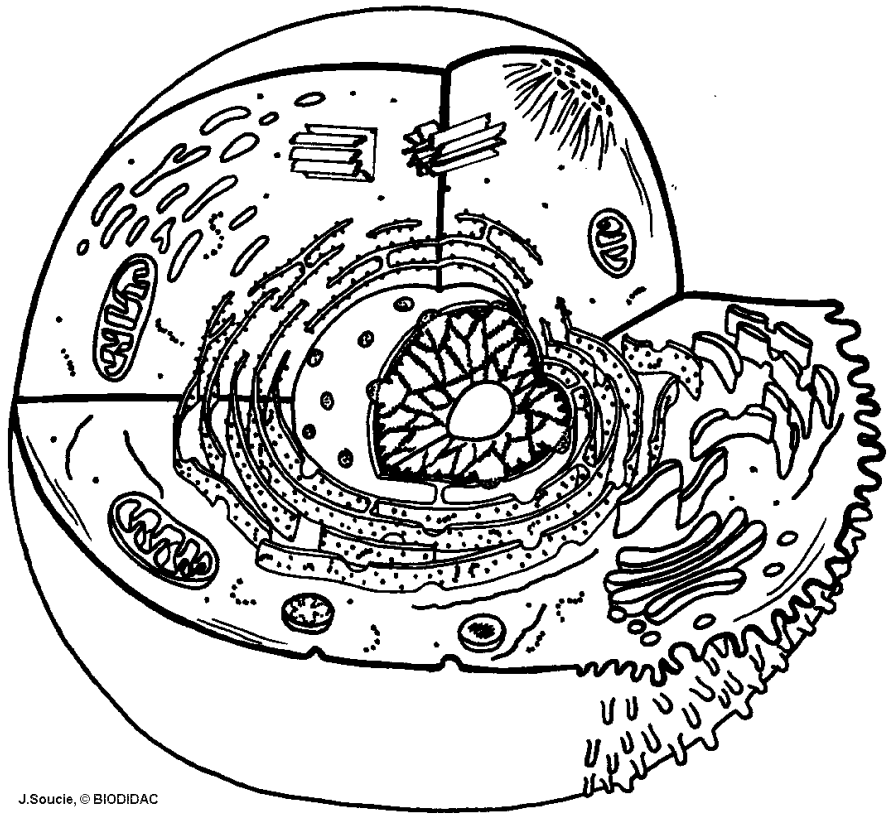
Prokaryotes: Cells without nuclei ("bacteria")

- Very little internal compartmentalization, e.g. no mitochondria
- Typically very small, 1–2 μm long
- Prokaryotes are not monophylletic: the archaea are more closely related to eukaryotes than to the eubacteria (true bacteria)

Eukaryotes: Cells with a nucleus, which contains their DNA

- Have many other compartments, including (but not limited to) mitochondria, peroxisomes, lysosomes, Golgi complex, endoplasmic reticulum
- Plant cells have additional compartments, including chloroplasts and glyoxysomes
- Relatively large, with diameters of 5–100 μm

Eukaryotic cells



Source: BIODIDAC database
(`http://biodidac.bio.uottawa.ca`)

Membranes

- While the nucleus is the defining feature of eukaryotes, perhaps their most important feature is the very large membrane area within the cell.
- Some reactions can occur in solution, but many reactions have to be carried out on membranes, or in compartments isolated from the rest of the cell.
- Transport across membranes is therefore also critical to eukaryotic function.

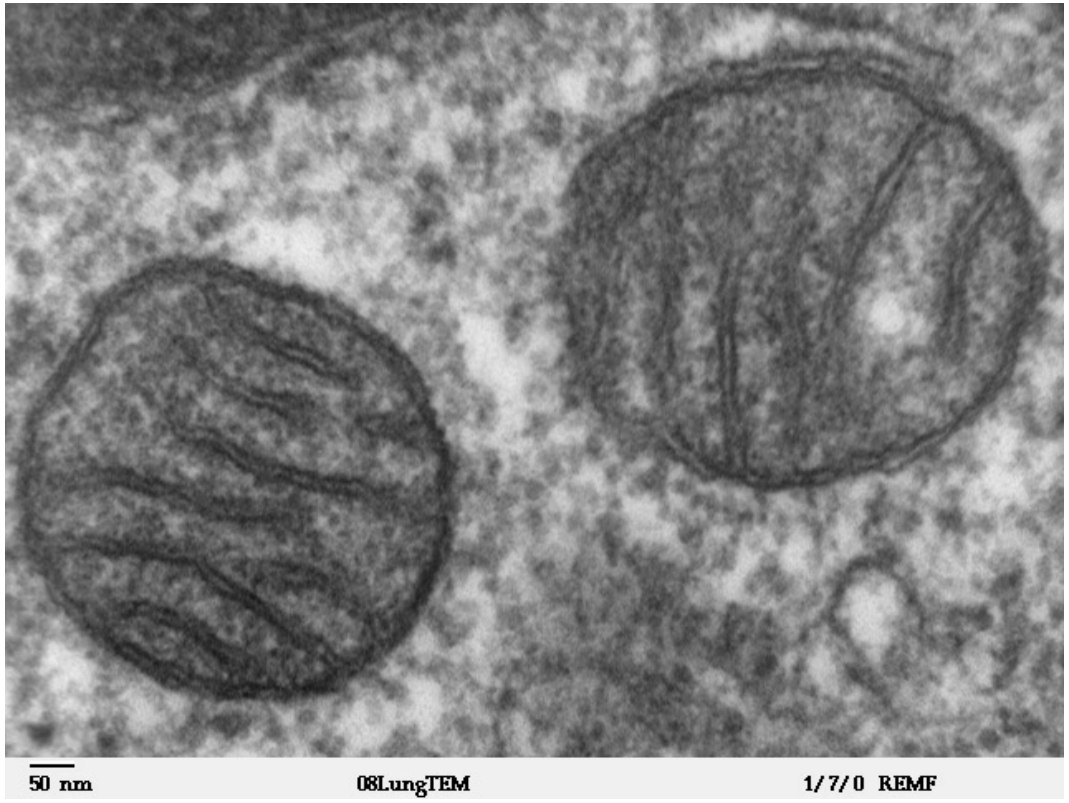
The cytoplasm

- Everything outside the nucleus and inside the cell membrane
- Includes all the organelles except the nucleus
- The fluid phase outside the organelles is called the cytosol, although the words cytoplasm and cytosol are often used interchangeably.
- The cytosol is the site of a great variety of biochemical reactions, including protein synthesis (translation).
- The cytosol is sometimes described as an aqueous phase, although it is extremely viscous (about six times the viscosity of water, similar to the viscosity of vegetable oil) due to the high concentration of macromolecular solutes.

The nucleus

- Separated from the main compartment of the cell (cytoplasm) by a nuclear envelope which contains some pores
- Contains most of the cell's DNA
- Site of transcription: the mirror-image "copying" of DNA into RNA
- Site of post-transcriptional modification of RNA, including splicing
  - A eukaryotic gene is typically made up of an alternation of expressed sequences (exons) and intervening sequences (introns).
  - The introns are cut out and the exons reassembled by the splicing machinery, yielding a mature transcript or messenger RNA (mRNA).

Mitochondria



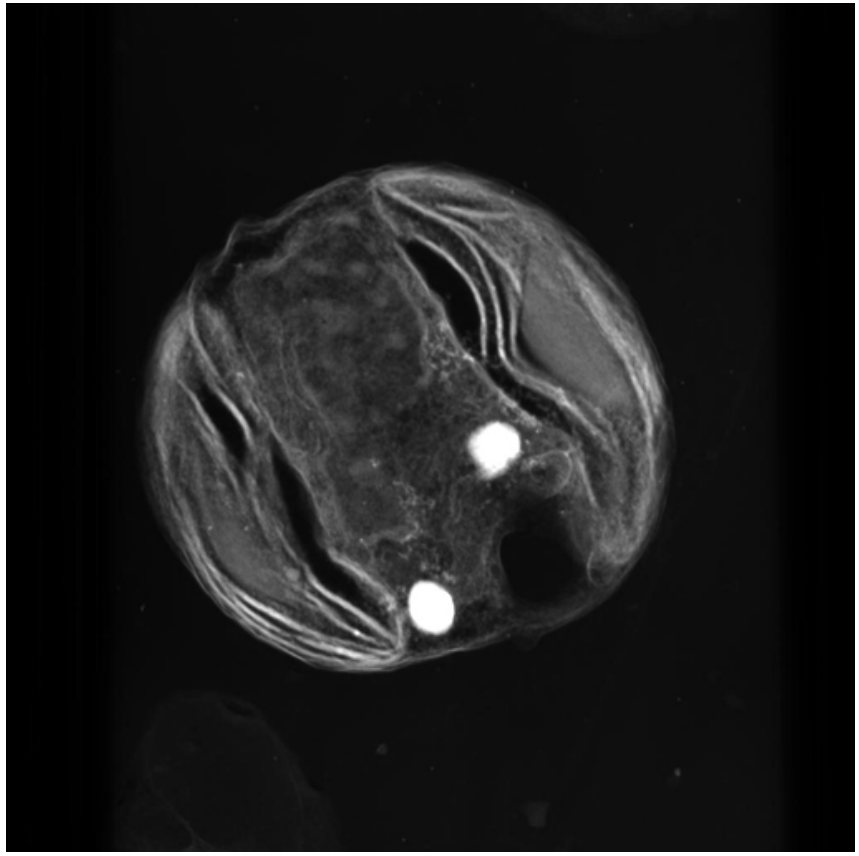
Mammalian lung mitochondria

Source: Louisa Howard, public domain image (`http://en.wikipedia.org/wiki/File:Mitochondria,_mammalian_lung_-_TEM.jpg`)

Mitochondria

- Singular: mitochondrion
- Major energy-production sites of cell
  - Produce ATP from glucose by oxidation
- Most cells have many mitochondria;
  exact number very variable from one type of cell to another, even within the same organism
- Have some of their own DNA, along with the machinery to transcribe and translate the mitochondrial genes

Chloroplasts



Source: Cell Centered Database `http://ccdb.ucsd.edu/sand/main?mpid=3411&event=displayRaw`

Chloroplasts

- Contains a light-harvesting pigment (chlorophyll)
- Energy used to generate ATP
- ATP used to power synthesis of carbohydrates (sugars and starch)
- Photosynthetic tissues (e.g. leaves) generally have many chloroplasts
- Have some of their own DNA, along with the machinery to transcribe and translate these genes

The cytoskeleton

- Eukaryotes also have rigid but dynamic structures mainly made of actin and of microtubules, collectively known as the cytoskeleton.
- Cytoskeletal elements are continually created (by polymerization) and destroyed (by depolymerization); the balance between these two processes at any point in the cell determines whether the cytoskeleton grows in a certain direction or retracts from it.
- Functions:
  - Gives the cell its shape
  - Cell locomotion
  - Positioning of organelles in the cell
  - Cytokinesis (final stage of mitosis)
  - Tracks for transport of cargos around cell

Diffusion

- Stokes-Einstein formula:

$$D = \frac{k_B T}{6\pi R\eta}$$

where k_B is Boltzmann's constant, T is the temperature, R is an effective radius of the solute, and η is the viscosity of the solvent.

$$\therefore D \propto \frac{1}{\eta}$$

- For small molecules in water, $D \sim 10^{-9}\,\mathrm{m}^2/\mathrm{s}$
  $\therefore$ in cytoplasm, $D \sim 10^{-10}\,\mathrm{m}^2/\mathrm{s}$.
- For macromolecules in water, D can be as small as $10^{-11}\,\mathrm{m}^2/\mathrm{s}$.
  $\therefore$ D for (free) macromolecules in cytoplasm may be as small as $10^{-12}\,\mathrm{m}^2/\mathrm{s}$.

Diffusion

- Consider the Einstein formula for the mean squared displacement of a diffusing particle along a particular direction:

$$x_{\text{rms}} = \sqrt{2Dt}$$

  where D is the diffusion coefficient of a substance in a particular medium and t is the time.
- If L is a characteristic length scale for a compartment, then

$$t_{\text{mix}} = \frac{L^2}{2D}$$

  defines a characteristic mixing time by diffusion.

Characteristic mixing times in cytoplasm

		$t_{\mathrm{mix}}/\mathrm{s}$	
Cell type	L/m	Small molecule	Macromolecule
Prokaryote	10^{-6}	10^{-2}	1
Eukaryote	10^{-5}	1	100

Implications for modeling

- Can treat bacteria as well mixed provided we are interested in processes on time scales $\gg 1\,\mathrm{s}$
- Important to consider compartmentation in eukaryotes
- Can treat cytosol as well mixed by diffusion provided we are interested in processes on time scales $\gg 100\,\mathrm{s}$
- Active transport of cargos by cytoskeleton may make diffusion less relevant to some processes in eukaryotes

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