Lecture 2: Cells and What They are Made of

Quantitative Models of Biological Function

Sizing up Cells

APh/BE161: Physical Biology of the Cell
Cell Theory: Cells as the Indivisible Units of Life

Microscopical Researches into the Accordance in the Structure and Growth of Animals and Plants.

Translated from the German of Dr. Th. Schwann, Professor in the University of Louvain, Spec. Med.

By Henry Smith, Fellow of the Royal College of Surgeons of England, Surgeon to the Royal General Dispensary, Aldersgate Street.

London printed for the Sydenham Society 1857.
Louis Pasteur revealed unequivocally that microorganisms are cells.

Many of the important domestic uses of microbes reflect their metabolism.

Unity of biochemistry (unifying theme of biology)
Pasteur demonstrated convincingly that microbes (other than yeast) were present in improperly fermenting solutions.

Pasteur reasoned that putrefaction was the result of microbes and hence, disease (itself a kind of putrefaction) was the consequence of microbes.

Pasteur thought each type of fermentation caused by a different microorganism (hence, bad fermentation the result of contaminating microorganism).

``Memoire sur la fermentation appelée lactique’’, Memoire sur la fermentation alcoolique’’

``The obvious is that which is never seen until someone expresses it simply.” - Christian Morgenstern
The Standard Eukaryote: S. cerevisiae

Figure 1-32  Essential Cell Biology, 2/e. (© 2004 Garland Science)
Koch formulated rules for proof that a particular microorganism is the pathogen of interest (i.e. the "smoking gun"). These are:

- Found in all cases of the disease examined
- Can be prepared and maintained in a pure culture
- Capable of producing the original infection, even after several generations in culture
- Can be retrieved from an inoculated animal and cultured again.
- Koch used this kind of thinking in determining the causative agents of anthrax and tuberculosis.
Shapes, sizes and contents of different types of cells.
**The Standard Cell:** “Not everyone is mindful of it, but cell biologists have two cells of interest; the one they are studying and *Escherichia coli.*” – Schaechter et al.

**Cells:** There is nothing smaller that is alive, nothing bigger is more alive – paraphrasing J. Theriot.
Other Hall of Fame Cells: Prokaryotes
- *Listeria monocytogenes*

Theriot Lab - Stanford University, see their amazing movies
Other Hall of Fame Pathogens: *Treponema pallidum*

- Otherwise known as the cause of Syphilis.
- Note that prokaryotes come in a dazzling variety of shapes.
Other Hall of Fame Pathogens: Giardia
Other Hall of Fame Cells: Eukaryotes

http://www.utah.edu/unews/news_images/070101_nerv

Structure and function intimately related

Annoying feature: no scale bars!

http://www.cimaging.net/Examples/D1_Cells/FAC1_Protein/Fibroblast/fibroblast.html
Muscle Organization
Nueromuscular Junction
Other Hall of Fame Cells: Eukaryotes


Emiliana huxleyi - coccolithophore
Other Hall of Fame Cells: Archaea
What Are Cells Made Of?

(Frey et al.)

(McIntosh et al.)

(Medalia et al.)
Main macromolecular constituents of *E. coli* and HeLa cells

<table>
<thead>
<tr>
<th>Component</th>
<th>Amount per HeLa cell</th>
<th>Amount per <em>E. coli</em> cell</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total dry weight</td>
<td>400 pg</td>
<td>0.4 pg</td>
</tr>
<tr>
<td>Total DNA</td>
<td>15 pg</td>
<td>0.017 pg</td>
</tr>
<tr>
<td>Total RNA</td>
<td>30 pg</td>
<td>0.10 pg</td>
</tr>
<tr>
<td>Total protein</td>
<td>300 pg</td>
<td>0.2 pg</td>
</tr>
<tr>
<td>Cytoplasmic ribosomes</td>
<td>$4 \times 10^6$</td>
<td>$3 \times 10^4$</td>
</tr>
<tr>
<td>Cytoplasmic tRNAs</td>
<td>$6 \times 10^7$</td>
<td>$4 \times 10^5$</td>
</tr>
<tr>
<td>Cytoplasmic mRNAs</td>
<td>$7 \times 10^5$</td>
<td>$4 \times 10^3$</td>
</tr>
</tbody>
</table>

source: Lodish et al., Molecular Cell Biology 3rd ed.

Composition of an *E. coli* cell

<table>
<thead>
<tr>
<th>Component</th>
<th>Molecules per cell</th>
<th>Kinds of molecules</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein</td>
<td>2,360,000</td>
<td>1050</td>
</tr>
<tr>
<td>RNA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>rRNA</td>
<td>56,100</td>
<td>3</td>
</tr>
<tr>
<td>tRNA</td>
<td>205,000</td>
<td>60</td>
</tr>
<tr>
<td>mRNA</td>
<td>1,380</td>
<td>400</td>
</tr>
<tr>
<td>Lipid</td>
<td>22,000,000</td>
<td>4 major</td>
</tr>
<tr>
<td>Lipopolysaccharide</td>
<td>1,200,000</td>
<td>1</td>
</tr>
<tr>
<td>Metabolites, cofactors, ions</td>
<td>&gt; 400,000,000</td>
<td>800+</td>
</tr>
</tbody>
</table>

source: Moran et al., Biochemistry 2nd ed.
DNA Structure
Genome Sizes: How DNA Is Used
A Tour of Some of the Macromolecules of Life: Goodsell’s Cartoons
A Single Molecule Census of the Cell: The Parts List

(A) Glucose molecule
(B) Glycerol molecule
(C) Carbon dioxide molecule
(D) Dodecane molecule

Figure 2-20: Essential Cell Biology, 2/e. © 2004 Garland Science
A Single Molecule Census of the Cell

Envelope
- Flagella: 6 proteins (~2 x 10^4 molecules/cell)
- Pili: 1 protein (~2 x 10^4 molecules/cell)

Outer membrane
- 50 proteins (~4 abundant, 10^4 molecules/cell)
- 5 p-lipids (~5 x 10^4 molecules/cell)
- 1 LPS (9 x 10^4 molecules/cell)

Capsule
- 1 complex polysaccharide

Wall
- Peptidoglycan (1 molecule/cell)

Periplasm
- 50 proteins (~10^4 molecules/cell)

Cell membrane
- 200 proteins (~2 x 10^4 molecules/cell)
- 7 p-lipids (~1.5 x 10^4 molecules/cell)

Nucleoid
- DNA (haploid chromosome, ~1 molecule)

Cytosol
- 1,000 proteins (~10^6 molecules/cell)
- 60 tRNAs (~2 x 10^4 molecules/cell)
- Glycogen (variable)

Polysomes
- ~18,000 ribosomes/cell in 1,000 polysomes
- 55 proteins (~10^6 molecules, 1 of each per 70S ribosome)
- 3 rRNAs (16S, 16S, 23S, 56,000 molecules, 1 of each per 70S ribosome)
- 1,000 mRNAs (~1,400 molecules, 1 per polysome)
### Table 1. Overall macromolecular composition of an average *E. coli* B/r cell

<table>
<thead>
<tr>
<th>Macromolecule</th>
<th>Percentage of total dry weight</th>
<th>Weight per cell (10^{15} x weight, grams)</th>
<th>Molecular weight</th>
<th>Number of molecules per cell</th>
<th>Dry weight (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein</td>
<td>55.0</td>
<td>155.0</td>
<td>4.0 x 10^4</td>
<td>2,360,000</td>
<td>1,860</td>
</tr>
<tr>
<td>RNA</td>
<td>20.5</td>
<td>59.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>23S rRNA</td>
<td></td>
<td>31.0</td>
<td>1.0 x 10^6</td>
<td>18,700</td>
<td></td>
</tr>
<tr>
<td>16S rRNA</td>
<td></td>
<td>16.0</td>
<td>5.0 x 10^6</td>
<td>18,700</td>
<td></td>
</tr>
<tr>
<td>5S rRNA transfer</td>
<td>1.0</td>
<td>3.9 x 10^4</td>
<td>1.0 x 10^4</td>
<td>18,700</td>
<td></td>
</tr>
<tr>
<td>messenger</td>
<td>8.6</td>
<td>2.5 x 10^4</td>
<td></td>
<td>205,000</td>
<td></td>
</tr>
<tr>
<td>DNA</td>
<td>3.1</td>
<td>9.0</td>
<td>2.5 x 10^9</td>
<td>2.13</td>
<td></td>
</tr>
<tr>
<td>Lipid</td>
<td>9.1</td>
<td>26.0</td>
<td>705</td>
<td>22,000,000</td>
<td></td>
</tr>
<tr>
<td>Lipopolysaccharide</td>
<td>3.4</td>
<td>10.0</td>
<td>4346</td>
<td>1,200,000</td>
<td></td>
</tr>
<tr>
<td>Murein</td>
<td>2.5</td>
<td>7.0</td>
<td>[904]_i</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Glycogen</td>
<td>2.5</td>
<td>7.0</td>
<td>1.0 x 10^6</td>
<td>4,360</td>
<td></td>
</tr>
<tr>
<td>Total macromolecules</td>
<td>96.1</td>
<td>273.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Soluble pool</td>
<td>2.9</td>
<td>8.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>building blocks</td>
<td></td>
<td></td>
<td>7.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>metabolites, vitamins</td>
<td></td>
<td></td>
<td>1.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inorganic ions</td>
<td>1.0</td>
<td>3.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total dry weight</td>
<td>100.0</td>
<td>284.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total dry weight/cell</td>
<td></td>
<td>2.8 x 10^{-13} g</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Water (at 70% of cell)</td>
<td></td>
<td>6.7 x 10^{-13} g</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total weight of one cell</td>
<td></td>
<td>9.5 x 10^{-13} g</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

In balanced growth at 37°C in glucose minimal medium, mass doubling time, g, of 40 minutes. The data assembled from Dennis and Bremer (1974), Maaloe (1979), F. C. Neidhardt (unpublished), Roberts et al. and Umbarger (1977).

There are four classes of phospholipids, each of which exists in many varieties as a result of variable residues.
The Outcome from Structural Biology: Boat loads of atomic coordinates.

“A science is built up of facts as a house is built up of bricks, but a mere accumulation of facts is no more a science than a pile of bricks is a house.” – Poincare

See http://www.rcsb.org/pdb/

All cartoons due to David Goodsell, Scripps
Physicists characterize collective excitations as ONS (phonons, magnons, excitons, etc...) Biologists also consider collective phenomena in the form of interacting macromolecular complexes.
Ribosomes and the Tree of Life

One of the great themes of all of biology: the unity of biochemistry. Evident especially with the processes of the central dogma, but also as concerns metabolism.

A beautiful use of this idea by Carl Woese - molecular analysis of the tree of life.

Only figure in Darwin’s “Origin”

after Woese CR, THE ORIGIN OF LIFE
CAROLINA BIOLOGY READERS, Copyright 1984
Filopodia in motile cells

(Medalia et al.)

Mitochondria

(Frey et al.)
Experimental Transformation of Biology: X-Ray Crystallography of Proteins

(a) 

(b) 

(c) 

(d)