Physical Biology of the Cell

PBoC@MOLPIT

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- Rob Phillips Group: Physical Biology of the Cell
  - http://www.rpgroup.caltech.edu/


http://microsite.garlandscience.com/pboc2/

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  - PowerPoints® 263M - Physical Biology of the Cell
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  - Nice & Useful video edu!
SnapShot: key numbers in biology

**Cell size**

<table>
<thead>
<tr>
<th>Bacteria (E. coli)</th>
<th>0.7-1.4 μm diameter, 2-4 μm length, 0.5-5 μm³ in volume; 10⁸-10¹⁰ cell/ml for culture with OD₆₀₀≈1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yeast (S. cerevisiae)</td>
<td>3-6 μm diameter, 20-160 μm³ in volume</td>
</tr>
<tr>
<td>Mammalian cell volume</td>
<td>100-10,000 μm³; HeLa cell: 500-5000 μm³ (adhering to slide: 15-30 μm diameter)</td>
</tr>
</tbody>
</table>

**Concentration**

- **Concentration of 1 nM:**
  - in E. coli: 1 molecule/cell;
  - in HeLa cells: 1000 molecules/cell

- **Characteristic concentration for a signaling protein:** 10 nM-1 µM

- **Water content:** 70% by mass; general elemental composition (dry weight) of E. coli: C₆H₁₀O₅N₃; Yeast: C₆H₁₂O₆N₁

- **Composition of E. coli (dry weight):** 55% protein, 20% RNA, 10% lipid, 15% other

- **Protein concentration:** 100 mg/ml = 3 mM; 10⁻¹⁰⁷ per E. coli (depending on growth rate);

**Diffusion and catalysis rate**

- **Diffusion coefficient for an “average” protein:** in cytoplasm D=5-15 μm²/s → 10 ms to traverse an E. coli, 10 s to traverse a mammalian HeLa cell; small metabolite in water D=500 μm²/s

- **Diffusion-limited on-rate for a protein:** 10⁸-10³ s⁻¹M⁻¹ → for a protein substrate of concentration 1 µM the diffusion-limited on-rate is 100-1000 s⁻¹ thus limiting the catalytic rate k_cat

**Genome sizes and error rates**

- **Genome size:**
  - E. coli (enterobacteria) = 5 Mbp
  - S. cerevisiae (budding yeast) = 12 Mbp
  - C. elegans (nematode) = 100 Mbp
  - D. melanogaster (fruit fly) = 120 Mbp
  - A. thaliana (plant) = 120 Mbp
  - M. musculus (mouse) = 2.5 Gbp
  - H. sapiens (human) = 2.9 Gbp
  - T. aestivum (wheat) = 16 Gbp

- **Number of protein-coding genes:**
  - E. coli = 4000; S. cerevisiae = 6000; C. elegans, A. thaliana, M. musculus, H. sapiens = 20,000

- **Mutation rate in DNA replication:** 10⁻⁸-10⁻¹⁰ per bp

- **Misincorporation rate:**
  - Transcription: 10⁻⁴-10⁻³ per nucleotide
  - Translation: 10⁻³-10⁻⁴ per amino acid

**Energetics**

- **Membrane potential:** 70-200 mV → 2-6 k_BT per electron (k_BT = thermal energy)

- **Free energy (∆G) of ATP hydrolysis under physiological conditions:**
  - 40-60 kJ/mol → 20 k_BT/molecule ATP
  - ATP molecules required during an E. coli cell cycle: 10⁵-10⁸

- **∆G^0** resulting in order of magnitude ratio between product and reactant concentrations:
  - 6 kJ/mol → 60 meV → 2 k_BT

**Length scales inside cells**

- **Nucleus volume:** 10% of cell volume
- **Cell membrane thickness:** ≈ 4-10 nm
- **“Average” protein diameter:** ≈ 3-6 nm
- **Base pair:** 2 nm (D) × 0.34 nm (H)
- **Water molecule diameter:** 0.3 nm

**Division, replication, transcription, translation, and degradation rates**

- **Cell cycle time** (exponential growth in rich media): E. coli = 20-40 min; budding yeast = 70-140 min; HeLa human cell line: 15-30 hr
- **Rate of replication by DNA polymerase:**
  - E. coli = 200-1000 bases/s
  - Human = 40 bases/s. Transcription by RNA polymerase 10-100 bases/s
- **Translation rate by ribosome:** 10-20 aa/s

**Degradation rates (proliferating cells):**

- mRNA half life < cell cycle time
- Protein half life ≥ cell cycle time
Key Numbers for Cell Biologists

- http://www.bionumbers.org/ =>
  - http://bionumbers.hms.harvard.edu/KeyNumbers.aspx
- Cell size (1-3)
- Length Scales Inside Cells (4-8)
- Division, Replication, Transcription, Translation & Degradation Rates (9-12)
- Concentration (13-17)
- Energetics (18-20)
- Diffusion and Catalysis Rate (21, 22)
- Genome sizes & Error Rates (23-26)
**Cell size**

1. Bacteria (E. coli): \(\approx 0.7-1.4 \, \mu\text{m} \) diameter, \(\approx 2-4 \, \mu\text{m} \) length, \(\approx 0.5-5 \, \mu\text{m}^3 \) in volume; \(10^8-10^9 \, \text{cell/ml} \) for culture with \(\text{OD}_{600}=1\).
2. Yeast (S. cerevisiae): \(\approx 3-6 \, \mu\text{m} \) diameter, \(\approx 20-160 \, \mu\text{m}^3 \) in volume.
3. Mammalian cell volume: \(100-10000 \, \mu\text{m}^3\); Hela: \(500-5000 \, \mu\text{m}^3 \) (adherent on slide \(\approx 15-30 \, \mu\text{m} \) diameter).

**Concentration**

13. Concentration of 1 nM in:
   - E. coli: \(\approx 1 \) molecule/cell;
   - Hela: \(\approx 1000 \) molecules/cell
14. Characteristic concentration for a signaling protein: \(10 \, \text{nM-1} \mu\text{M} \)
15. Water content: \(\approx 70\% \) by mass; General elemental composition (dry weight) of E. coli: \(\approx C_4H_7O_2N_1\); Yeast: \(\approx C_9H_{10}O_3N_1\)
16. Composition of E. coli (dry weight):
   - \(55\% \) protein,
   - 20\% RNA,
   - 10\% lipids,
   - 15\% others
17. Protein conc. \(\approx 100 \, \text{mg/ml} = 3 \, \text{mM} \). \(10^6-10^7 \) per E. coli (depending on growth rate); Total metabolites (MW<1kD) \(\approx 300\text{mM}\)

**Energetics**

18. Membrane potential \(\approx 70-200 \, \text{mV} \) \(\rightarrow 2-6 \, k_B T \) per electron (\(k_B T = \) thermal energy)
19. Free energy (\(\Delta G\)) of ATP hydrolysis under physiological conditions:
   - \(\approx 40-60 \, \text{kJ/mol} \) \(\rightarrow 20k_B T/\text{molecule ATP}\);
   - ATP molecules required to make an E. coli cell: \(\approx 10-50 \times 10^9\)
20. \(\Delta G^0\) resulting in order of magnitude ratio between products and reactants concentrations:
   - \(\approx 6 \, \text{kJ/mol} = 60 \, \text{meV} = 2 \, k_B T\)

**Diffusion and Catalysis Rate**

21. Diffusion coefficient for an “average” protein in cytoplasm \(D = 5-15 \, \mu\text{m}^2/\text{s} \) \(\rightarrow 10 \, \text{millisecond} \) to traverse an E. coli \(\approx 10 \, \text{s} \) to traverse a mammalian (Hela) cell; small metabolite in water \(D = 500 \, \mu\text{m}^2/\text{s}\)
22. Diffusion limited on-rate for characteristic protein \(10^8-10^9 \, \text{s}^{-1} \text{M}^{-1} \) \(\rightarrow \) for a protein substrate of concentration \(\approx 1 \mu\text{M} \) the diffusion limited on-rate is \(\approx 100-1000 \, \text{s}^{-1} \) thus limiting the catalytic rate \(k_{\text{cat}}\)

**Genome sizes & Error Rates**

23. Genome size:
   - E. coli: \(\approx 5 \, \text{Mbp}\);
   - S. cerevisiae (yeast): \(\approx 12 \, \text{Mbp}\);
   - C. elegans (nematode): \(\approx 100 \, \text{Mbp}\);
   - D. melanogaster (fruit fly): \(\approx 120 \, \text{Mbp}\);
   - A. thaliana (arabidopsis): \(\approx 120 \, \text{Mbp}\);
   - M. musculus (mouse): \(\approx 2.5 \, \text{Gbp}\);
   - H. sapiens (human): \(\approx 2.9 \, \text{Gbp}\);
   - T. aestivum (wheat): \(\approx 16 \, \text{Gbp}\)
24. Number of protein-coding genes:
   - E. coli: \(\approx 4000\):
   - S. cerevisiae: \(\approx 6000\);
   - C. elegans, A. thaliana, M. musculus, H. sapiens: \(\approx 20000\)
25. Mutation rate in DNA replication:
   - \(\approx 10^{-8}-10^{-10} \) per bp
26. Misincorporation rate:
   - Transcription: \(\approx 10^{-4}\) per nucleotide;
   - Translation: \(\approx 10^{-3-10^{-4}}\) per amino-acid

**Length Scales Inside Cells**

4. Nucleus volume \(\approx 10\% \) of cell volume
5. Cell membrane thickness \(\approx 4-10 \, \text{nm}\)
6. “Average” protein diameter \(\approx 3-6 \, \text{nm}\)
7. Base pair: \(2 \, \text{nm} \) (D) \(\times 0.34 \, \text{nm} \) (H)
8. Water molecule diameter \(\approx 0.3 \, \text{nm}\)

**Division, Replication, Transcription, Translation & Degradation Rates**

at 37°C with a temperature dependence Q10 of \(\approx 2-3\)
9. Cell cycle time (exponential growth in rich media): E. coli: \(\approx 20-40 \, \text{min}\); yeast: 70-140 min; human cell line (Hela): \(15-30 \, \text{hours}\)
10. Rate of replication by DNA polymerase
    - E. coli: \(\approx 200-1000 \) bases/s;
    - Human: \(\approx 40 \) bases/s. Transcription by RNA polymerase \(10-100 \) bases/s
11. Translation rate by ribosome: \(10-20 \, \text{aa/s}\)
12. Degradation rates (proliferating cells):
    - mRNA half life < cell cycle time;
    - Protein half life \(\approx cell \) cycle time

Useful biological numbers extracted from the literature. Numbers and ranges should only serve as “rule of thumb” values. References are in the online annotated version at the BioNumbers website. Consult website and original references to learn about the details of the system under study including growth conditions, method of measurement, etc.

Current (2013) SI System:
Dependence of base unit definitions on other base units
Proposed «Quantum SI» System (2014)
Biological measures & gauges

• From Key Numbers for Cell Biologists
• Towards BioMeasures & BioGauges
  • ? who, where, when
• To make «Biological SI» System
• With Fundamental Biological Constant
  • Based on «Quantum SI» System

• Let's act together