Introduction and Part I finished

3 weeks down; 7 to go

Where you should be

- Comfortable with
  - P. Chem/Kinetics
  - Biochemistry as defined by the recommended reading materials
- Become familiar with
  - The simulation workflow, the MASSpy, computation
- Getting ready for
  - Visualization or results, pooling of variables, interpretation
  - Dealing with metabolic pathways and enzyme functions
  - Thinking about networks

On to Part II

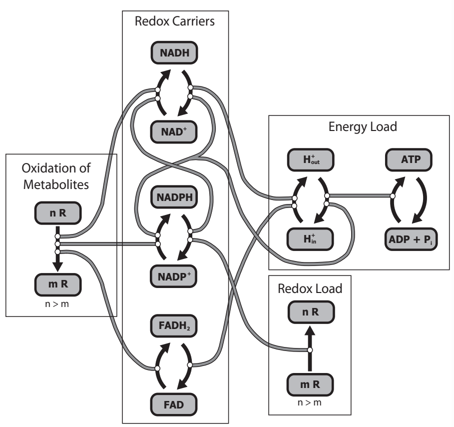
Part I

$$x_1 \underset{}{\overset{v_1}{\rightleftharpoons}} x_2 \overset{v_2}{\rightleftharpoons} x_3 \overset{v_3}{\rightarrow} x_4$$

$$\mathbf{S} = \begin{pmatrix} -1 & 0 & 0 \\ 1 & -1 & 0 \\ 0 & 1 & -1 \\ 0 & 0 & 1 \end{pmatrix} \qquad \frac{d\mathbf{x}}{dt} = \mathbf{Sv}(\mathbf{x})$$

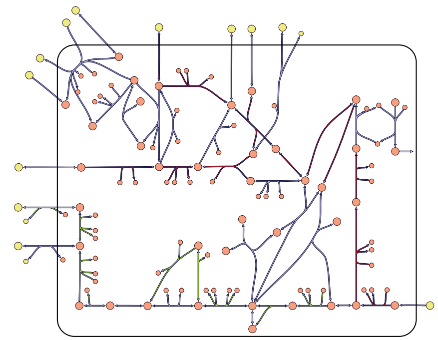
--Basics--

Part II



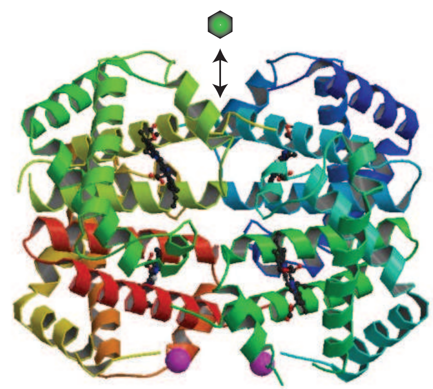
--Biological features--

Part III



--Metabolic networks--

Part IV

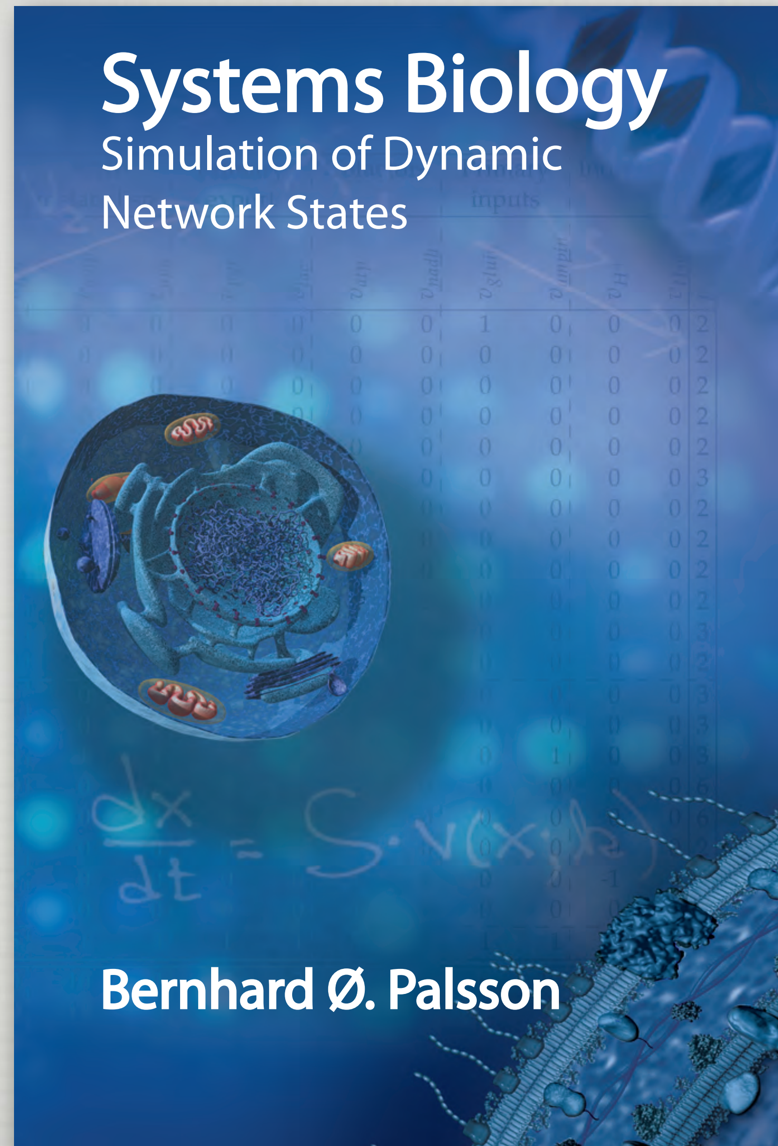


--Macromolecular systems--

Parameterization

$$\frac{d\mathbf{x}}{dt} = \mathbf{S}\mathbf{v}(\mathbf{x};\mathbf{k})$$

where do these numbers come from?

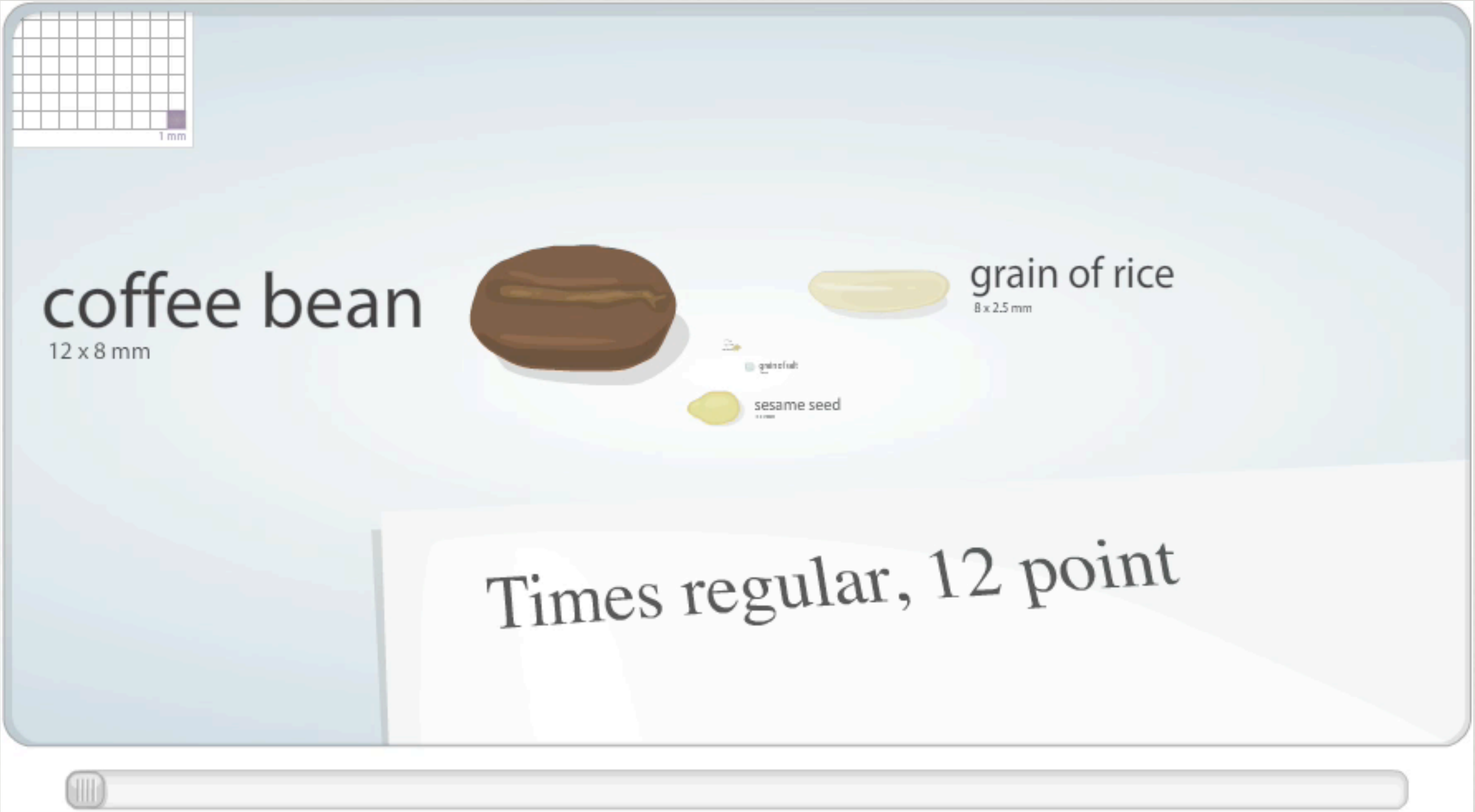


Lecture #7

Estimation and Orders of Magnitude

Content

- Orders-of-magnitude
- Estimation
- Observations about Cells
- Examples from Metabolism
  - What are Typical Concentrations?
  - What are Typical Turnover Times?
- Kinetic Parameter Estimation
  - What to look for and where to search?
- Orders-of-magnitude example
- Summary



Meter (m)	Centimeter (cm)	Millimeter (mm)	Micrometer (μm) (aka micron)	Nanometer (nm)	Angstrom (Å)	Picometer (pm)
10^{0} m	10^{-2} m	10^{-3} m	10^{-6} m	10^{-9} m	10^{-10} m	10^{-12} m
1 m	0.01 m	0.001 m	0.000001 m	0.000000001 m	0.0000000001 m	0.000000000001 m
	1/100 m	1/1,000 m	1/1,000,000 m	1/1,000,000,000 m	1/10,000,000,000 m	1/1,000,000,000,000 m
	hundredth of a meter	thousandth of a meter	millionth of a meter	billionth of a meter	ten billionth of a meter	trillionth of a meter

http://learn.genetics.utah.edu/content/begin/cells/scale/

Estimation:

How many beans are in the jar?

Enrico Fermi (1901 - 1954) was an Italian physicist, particularly remembered for his work on the development of the first nuclear reactor, and for his contributions to the development of quantum theory, nuclear and particle physics, and statistical mechanics.

Famous for quick answers through back-of-the-envelope calculations

Introduction to Fermi problems

The classic Fermi problem is:

"How many piano tuners are there in Chicago?"

Estimation proceedure…

- ***Assumptions***
  - There are approximately 5,000,000 people living in Chicago.
  - On average, there are two people in each household in Chicago.
  - Roughly one household in 20 has a piano that is tuned regularly.
  - Pianos that are tuned regularly are tuned on average about once per year.
  - It takes a piano tuner about 2 hours to tune a piano, including travel time.
  - Each piano tuner works 8 hours in a day, 5 days in a week, and 50 weeks in a year.
- ***From these assumptions we can compute that the number of piano tunings in a single year in Chicago is***

$$\frac{5*10^6 \text{ people}}{\left(\frac{2 \text{ people}}{1 \text{ household}}\right)} * \frac{1 \text{ piano}}{20 \text{ households}} * \frac{1 \text{ piano tuning}}{1 \text{ piano} * 1 \text{ year}} = \boxed{\frac{125000 \text{ piano tunings}}{1 \text{ year}}}$$

$$\frac{50 \text{ weeks}}{1 \text{ year}} * \frac{5 \text{ days}}{1 \text{ week}} * \frac{8 \text{ hrs}}{1 \text{ day}} * \frac{1 \text{ piano tuning}}{2 \text{ hrs} * 1 \text{ piano tuner}} = \boxed{\frac{1000 \text{ piano tunings}}{1 \text{ year} * 1 \text{ piano tuner}}}$$

$$\frac{125000 \text{ piano tunings}}{1 \text{ year}} * \frac{1 \text{ year} * 1 \text{ piano tuner}}{1000 \text{ piano tunings}} = \boxed{125 \text{ piano tuners in Chicago}}$$

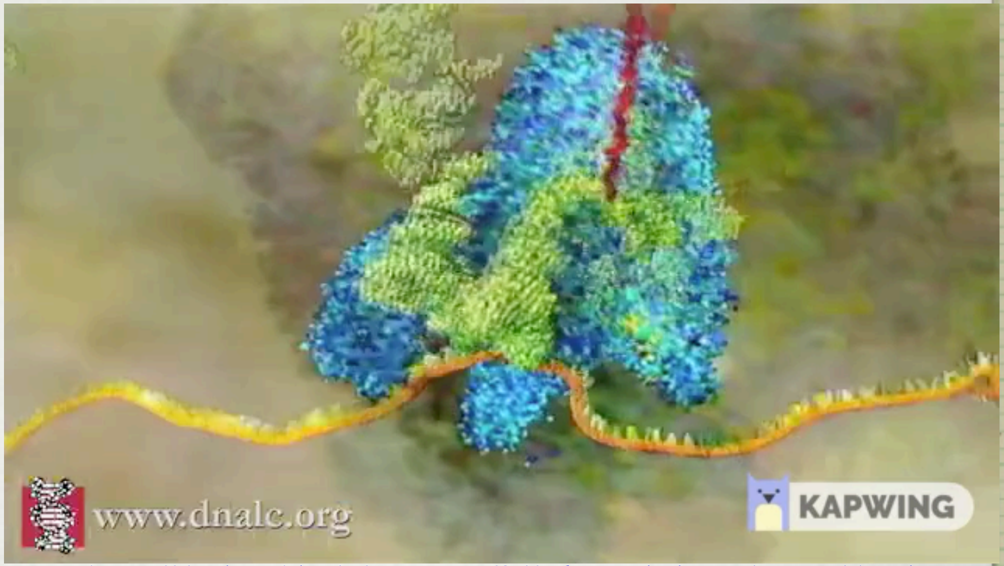
Real significance …

- Possible to estimate key biological quantities on the basis of a few foundational facts and simple ideas from physics and chemistry.
- Numbers collected by the scientific community that initially appear unrelated are brought together as a tool of inference to shed light on biological mechanisms.

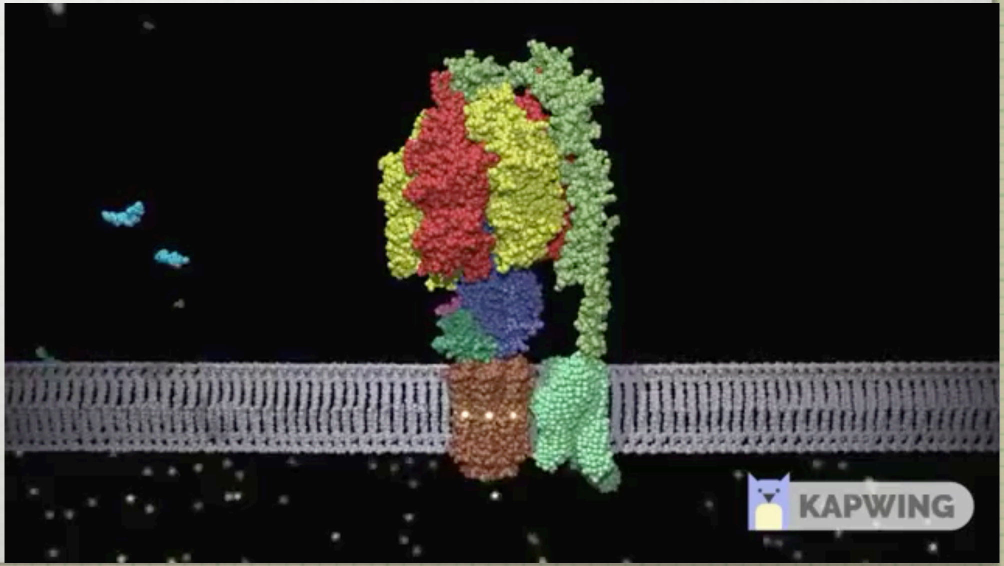
Biological examples

- How many proteins can be produced from a single mRNA in *E. coli*?

- How many ATP synthase complexes are required for optimal growth on glucose in *E. coli*?



https://dnalc.cshl.edu/resources/3d/16-translation-advanced.html



Stock Lab (The Victor Chang Cardiac Research Institute) https://www.youtube.com/watch?v=b_cp8MsnZFA

Proteins/mRNA

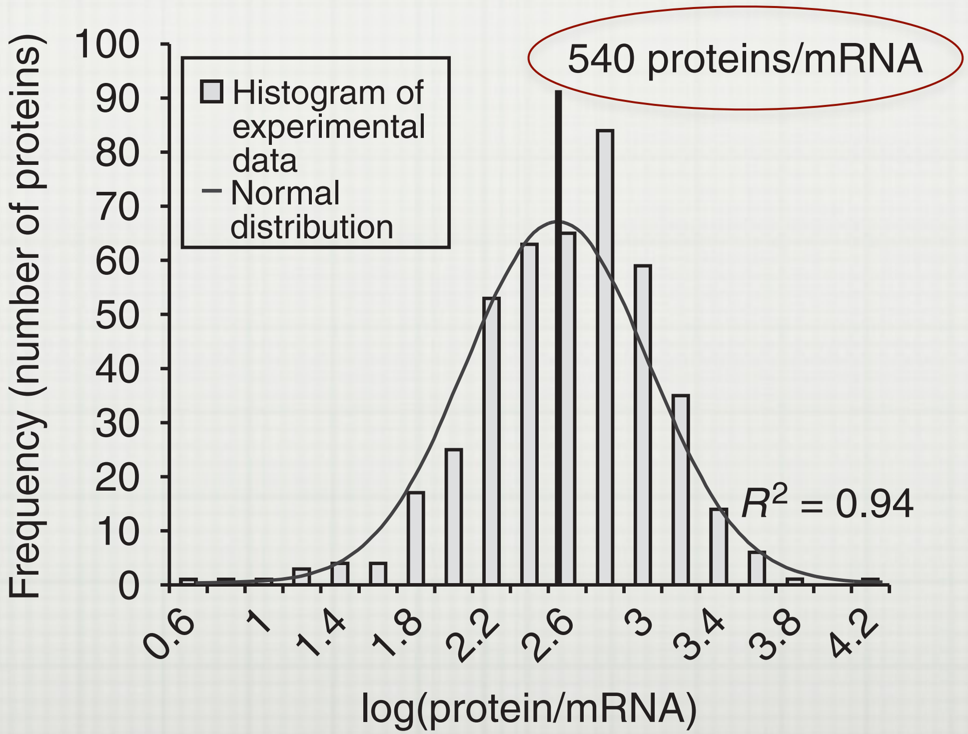
- ***Assumptions***
  - The average length of mRNA is 1100 nt.
  - A ribosome can bind to mRNA every 50 nt due to structural considerations.
  - The rate of translation for one ribosome is 16 amino acids per second.
  - The average length of a protein is 367 amino acids.
  - The average half-life of mRNA is 6 minutes (360 seconds).
- ***From these assumptions we can compute that the number of proteins translated over the lifetime of an mRNA transcript is***

$$\frac{1100\ \text{nt}}{1\ \text{mRNA transcript}} * \frac{1\ \text{ribosome}}{50\ \text{nt}} = \boxed{\frac{22\ \text{ribosomes}}{1\ \text{mRNA transcript}}\ \left(\text{Maximum ribosome loading}\right)}$$

$$\frac{16\ \text{AA}}{1\ \text{sec} * 1\ \text{ribosome}} * \frac{22\ \text{ribosomes}}{1\ \text{mRNA transcript}} = \boxed{\frac{352\ \text{AA}}{1\ \text{sec}}\ \left(\begin{array}{c}\text{Translation rate w/}\\ \text{maximum ribosome load}\end{array}\right)}$$

$$\frac{1\ \text{protein}}{367\ \text{AA}} * \frac{352\ \text{AA}}{1\ \text{sec}} \approx \frac{1\ \text{protein}}{1\ \text{sec}} \longrightarrow \frac{1\ \text{protein}}{1\ \text{sec}} * \frac{(360\ \text{sec}/\ln 2)}{1\ \text{mRNA}} \approx \frac{519\ \text{proteins}}{1\ \text{mRNA}}$$

Let's see how we did…



Lu et al., *Nat Biotech* 2007

Another example: ATP synthase

- ***Assumptions***
  - Max velocity of ATP synthase: 230 revolutions/sec (828000 rev/ hr) [PMID 15668386]
  - Three ATP produced each revolution of ATP synthase.
  - For aerobic growth at an uptake rate of 10 mmol glucose $gDw^{-1}\ hr^{-1}$, growth computations show that required flux through ATP synthase is 52 mmol $gDw^{-1}\ hr^{-1}$
  - The optimal growth rate is 0.7367 doublings/hr (approx. 1 doubling/hour).
  - There is approximately 200,000 inner membrane proteins
  - Each ATP synthase complex has 22 proteins.
- ***From these assumptions, we can compute how many inner membrane proteins are***

$$\frac{0.052\ \text{mol}}{1\ \text{gDW}\ \text{hr}} * \frac{2.8 * 10^{-13}\text{gDW}}{1\ \text{cell}} * \frac{6.022 * 10^{23}\ \text{ATP}}{1\ \text{mol}} = \boxed{\frac{8{,}768{,}032{,}000\ \text{ATP}}{1\ \text{hr}} \quad \left(\begin{matrix}\text{ATP required per hour} \\ \text{for optimal growth}\end{matrix}\right)}$$

$$\frac{230\ \text{revs}}{1\ \text{sec}} * \frac{3600\ \text{secs}}{1\ \text{hr}} * \frac{3\ \text{ATP}}{1\ \text{rev}} \approx \boxed{\frac{2.5 * 10^{6}\ \text{ATP}}{1\ \text{hr} * 1\ \text{ATP synthase}} \quad \left(\begin{matrix}\text{ATP produced per hour} \\ \text{by 1 ATP synthase}\end{matrix}\right)}$$

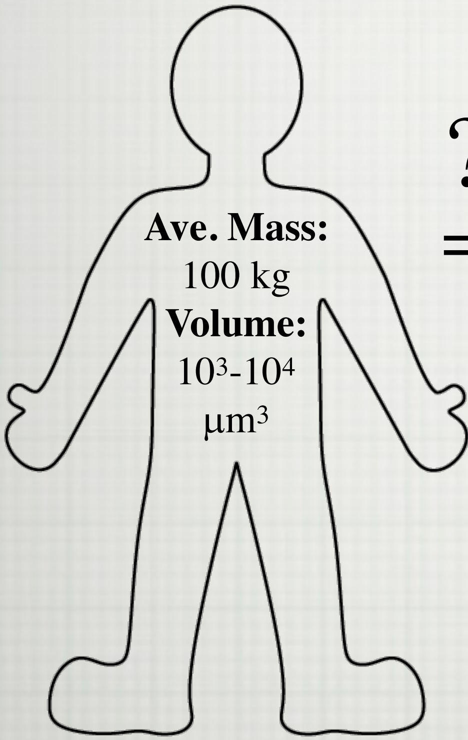
$$\frac{8{,}768{,}032{,}000\ \text{ATP}}{1\ \text{hr}} * \frac{1\ \text{hr} * 1\ \text{ATP synthase}}{2.5 * 10^{6}\ \text{ATP}} \approx 3510\ \text{ATP synthase complexes} \quad (\text{working at } V_{max})$$

$$\frac{3510\ \text{ATP synthase} * 22\ \text{proteins}/1\ \text{ATP synthase}}{200{,}000\ \text{total proteins}} \approx 0.4$$

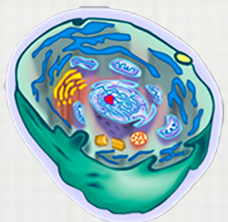
ATP synthase accounts for approximately 40% of inner membrane proteins

Cells in a Human

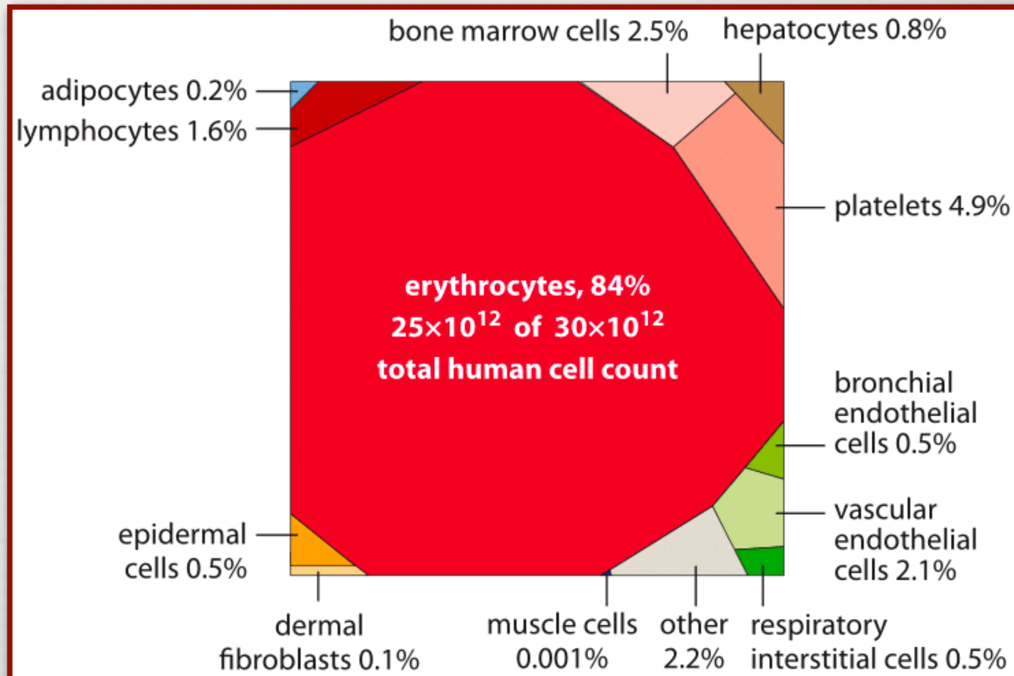
How many cells are there in the human body?



? =



Ave. Mass:
10^{-12}-10^{-11} kg



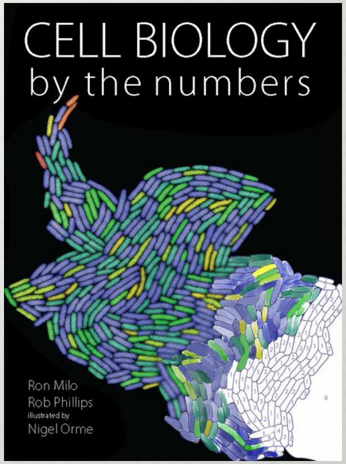
$$N \approx \frac{100 \text{ kg human}}{10^{-12} - 10^{-11} \text{ kg per cell}} = \mathbf{10^{13} - 10^{14}} \textit{ cells in the human body}$$

Resource: BioNumbers database

Property	Organism	Value	Units	ID	Details
Average duration of a single eye blink	Human Homo sapiens	0.1-0.4	sec	100706	http://faculty.washi...
Size of glucose molecule (open chain form)	Generic	1.5	nm	106979	Daniel Minoli, Nanotechnology...
One unit of OD600 corresponds to a cell wet weight and a cell dry weight of	Bacteria Escherichia coli	Cell wet weight 1.7g/L: cell dry weight 0.39g/L		109836	Glazyrina J, Materne EM...
Identification of total proteins in A. baumannii DU202 cultured in LB medium supplemented with imipenem	Bacteria Acinetobacter baumannii	Table - link	N/A	111523	Yun SH et al., Quantitative...
Estimations of periplasmic volume from distributions of different solutes in suspensions of Salmonella typhimurium LT2	Bacteria Salmonella typhimurium	Table - link	N/A	108473	Stock JB, Rauch B, Roseman...
Number of hairs on human head	Human Homo sapiens	90,000-150,000	unitless	101509	Amazing numbers in biology...
Number of cells in colony	Bacteria Escherichia coli	3.3e+9 (Table - link)	Cells/colony	104458	Mashimo K, Nagata Y, Kawata M...
Diameter of neutrophil	Human Homo sapiens	8.4 (7.3-9.7 Table - link)	µm	100510	Downey GP, Doherty DE...
Density and mass of each organ/tissue	Human Homo sapiens	Table - link	N/A	110245	International commission...
Diameter of HEK-293 cell	Human Homo sapiens	13	µm	108893	http://www.invitroge...

+3,000 monthly visitors

+50 countries



http://book.bionumbers.org/

Source: http://bionumbers.hms.harvard.edu/

BioNumbers is coordinated and developed by Ron Milo at the Weizmann Institute in Israel.

Key Concepts

- Characteristic order of magnitude for key quantities that characterize cellular functions can be estimated
- Data on cell size, mass, composition, metabolic complexity, and genetic makeup are available
- Numerous databases now available on the web
- Useful estimates of fluxes, concentrations, kinetics, and power densities in the intracellular environment can be made based on this data

Key Numbers for Cell Biologists

Cell size

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

Length Scales Inside Cells

4. Nucleus volume ≈10% of cell volume
5. Cell membrane thickness ≈4-10 nm
6. "Average" protein diameter ≈3-6 nm
7. Base pair: 2 nm (D) x 0.34 nm (H)
8. Water molecule diameter ≈0.3 nm

Division, Replication, Transcription, Translation & Degradation Rates
at 37°C with a temperature dependence Q10 of ≈2-3

9. Cell cycle time (exponential growth in rich media): *E. coli* ≈20-40 min; yeast 70-140 min; human cell line (Hela): 15-30 hours
10. Rate of replication by DNA polymerase *E. coli* ≈200-1000 bases/s; human ≈40 bases/s. Transcription by RNA polymerase 10-100 bases/s
11. Translation rate by ribosome 10-20 aa/s
12. Degradation rates (proliferating cells): mRNA half life < cell cycle time; protein half life ≥ cell cycle time

Concentration

13. Concentration of 1 nM in: *E. coli* is ≈1 molecule/cell; Hela ≈1,000 molecules/cell
14. Characteristic concentration for a signaling protein ≈10 nM-1μM
15. Water content: ≈70% by mass; General elemental composition (dry weight) of *E. coli*: ≈$C_4H_7O_2N_1$; Yeast ≈$C_6H_{10}O_3N_1$
16. Composition of *E. coli* (dry weight): ≈55% protein, 20% RNA, 10% lipids, 15% others
17. Protein conc. ≈100 mg/ml=3 mM. 10^6-10^7 per *E. coli* (depending on growth rate); Total metabolites (MW<1kD) ≈300mM

Energetics

18. Membrane potential ≈70-200 mV → 2-6 k_BT per electron (k_BT≡thermal energy)
19. Free energy (ΔG) of ATP hydrolysis under physiological conditions ≈40-60 kJ/mole → ≈20k_BT/molecule ATP; ATP molecules required to make an *E. coli* cell ≈10-50×10^9
20. ΔG^0 resulting in order of magnitude ratio between products and reactants concentrations: ≈6 kJ/mol ≈60 meV ≈2 k_BT

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.

Diffusion and Catalysis Rate

21. Diffusion coefficient for an "average" protein: in cytoplasm D≈5-15 $\mu m^2/s$ → ≈10 millisec to traverse an *E. coli* →≈10 s to traverse a mammalian (Hela) cell; small metabolite in water D≈500 $\mu m^2/s$
22. Diffusion limited on-rate for characteristic protein ≈10^8-10^9 $s^{-1}M^{-1}$ → for a protein substrate of concentration ≈1μM the diffusion limited on-rate is ≈100-1000 s^{-1} thus limiting the catalytic rate k_{cat}

Genome sizes & Error Rates

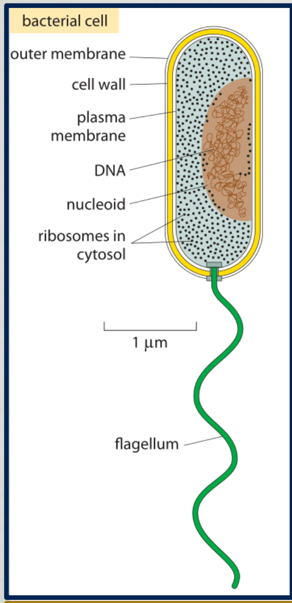
23. Genome size: *E. coli* ≈5 Mbp; *S. cerevisiae* (yeast) ≈12 Mbp; *C. elegans* (nematode) ≈100 Mbp; *D. melanogaster* (fruit fly) ≈120 Mbp; *A. thaliana* (arabidopsis) ≈120 Mbp; *M. musculus* (mouse) ≈2.5 Gbp; *H. sapiens* (human) ≈2.9 Gbp; *T. aestivum* (wheat) ≈16 Gbp
24. Number of protein-coding genes: E. coli ≈4,000; S. cerevisiae ≈6,000; C. elegans, A. thaliana, M. musculus, H. sapiens ≈20,000
25. Mutation rate in DNA replication ≈10^{-8}-10^{-10} per bp
26. Misincorporation rate: transcription ≈10^{-4} per nucleotide; translation ≈10^{-3}-10^{-4} per amino-acid

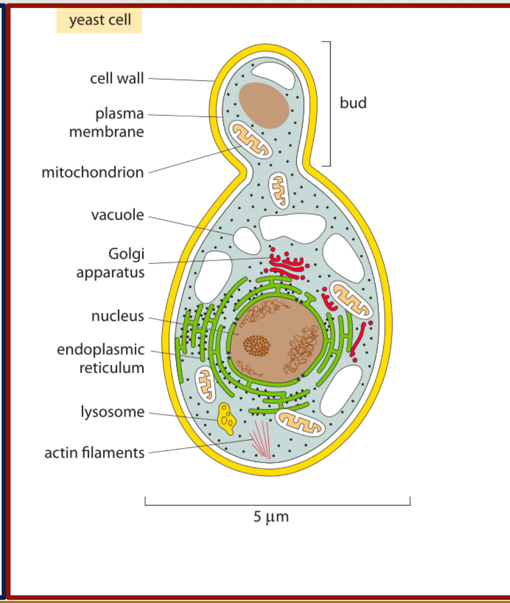
Click on a number to see full description and reference
www.BioNumbers.org

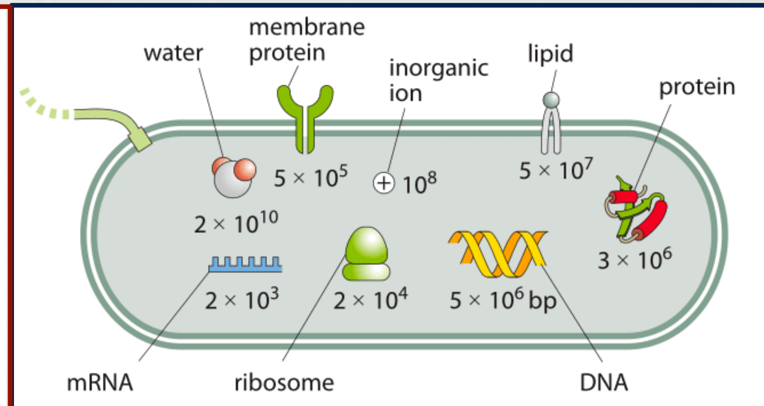
Orders of Magnitude

SOME OVERALL OBSERVATIONS ABOUT CELLS

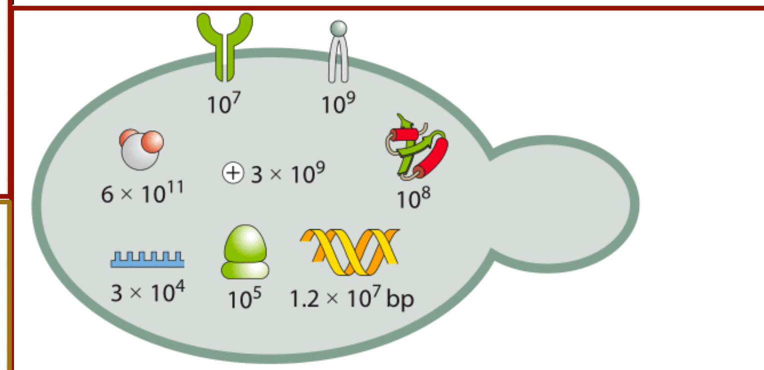
Cell Sizes and Interiors



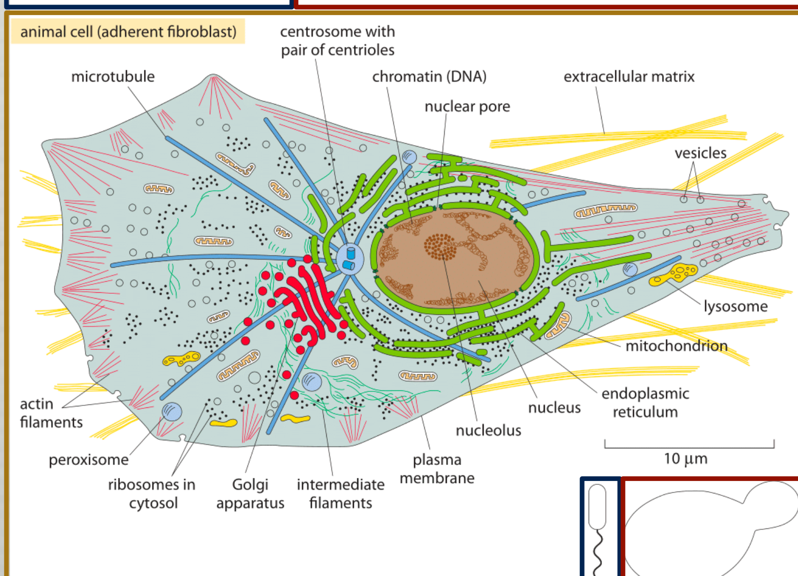


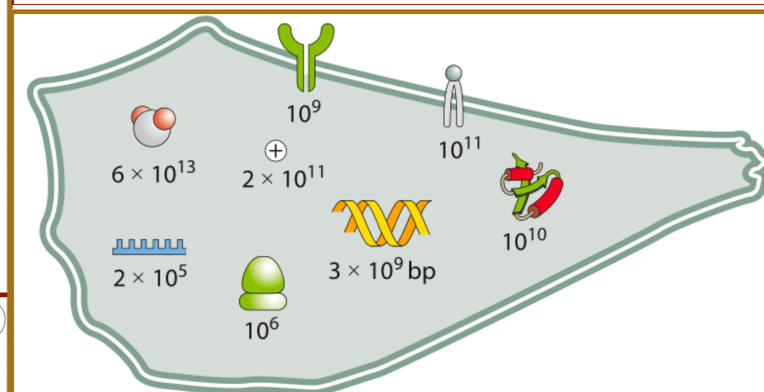


E. coli
Bacterial
$V \approx 1\ \mu m^3$
$L \approx 1\ \mu m$
$\tau \approx 1$ hour



S. cerevisae
Yeast
$V \approx 30\ \mu m^3$
$L \approx 5\ \mu m$
$\tau \approx 3\ hour$





HeLa
Mammalian
$V \approx 3000\ \mu m^3$
$L \approx 20\ \mu m$
$\tau \approx 1\ day$

Cell Biology By The Numbers: Figures 0-1, 1-1

Range of Cell Sizes and Shapes

- Relative to *E. Coli*

1 micron

(A) Giardia lamblia

(B) Plant cell

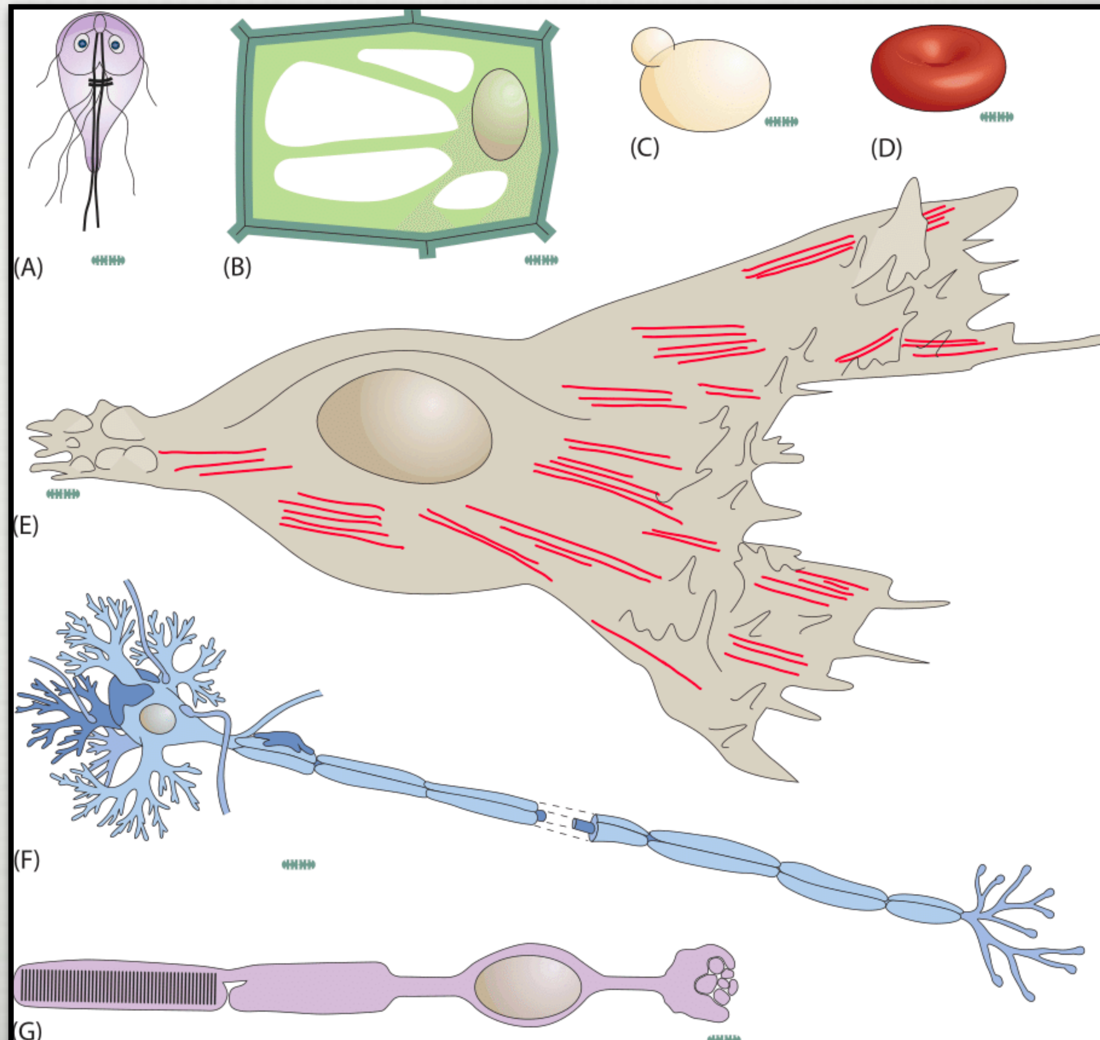
(C) Budding yeast cell

(D) Red blood cell

(E) Fibroblast cell

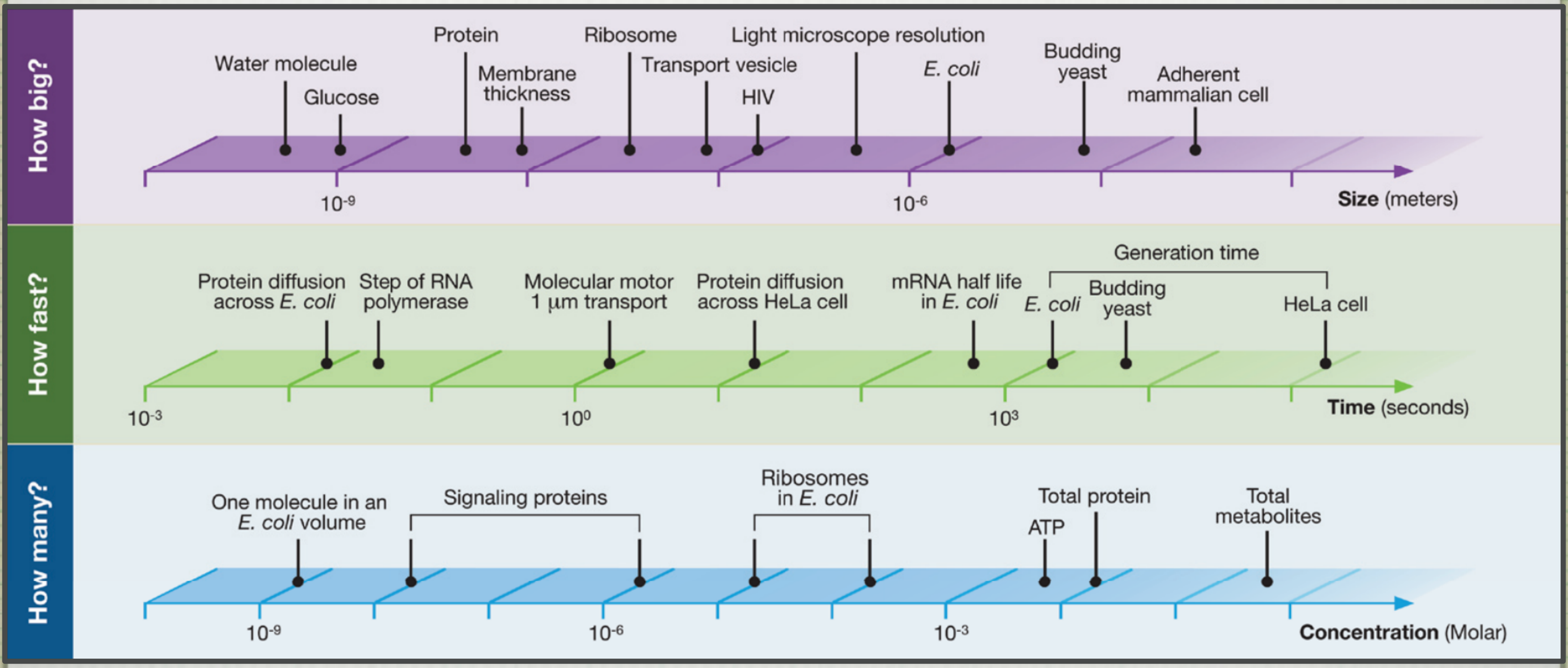
(F) Eukaryotic nerve cell

(G) Rod cell from retina



Cell Biology By The Numbers: Figure 1-17

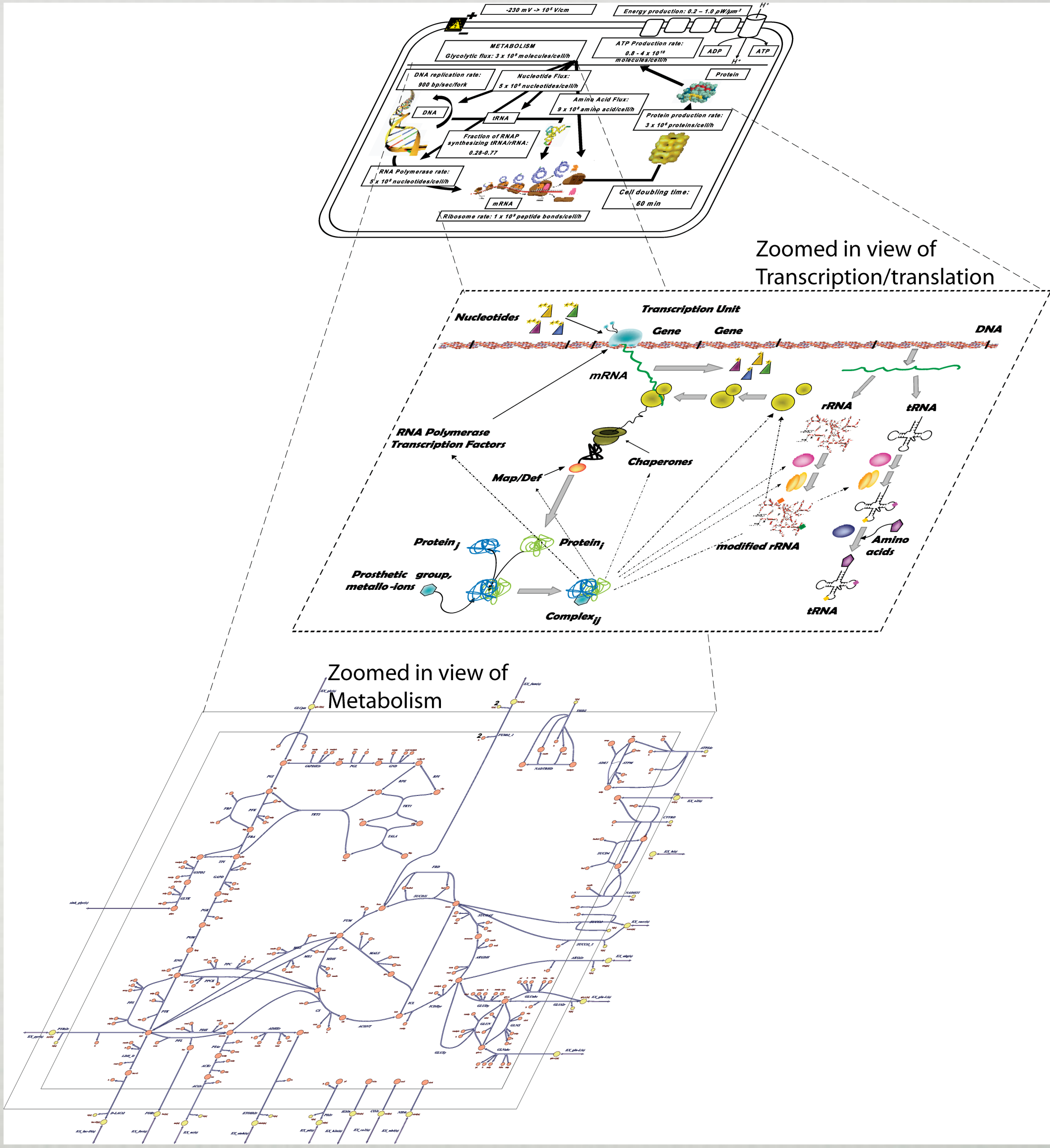
The Multi-Scale Nature of Biology



Multi-scale relationships

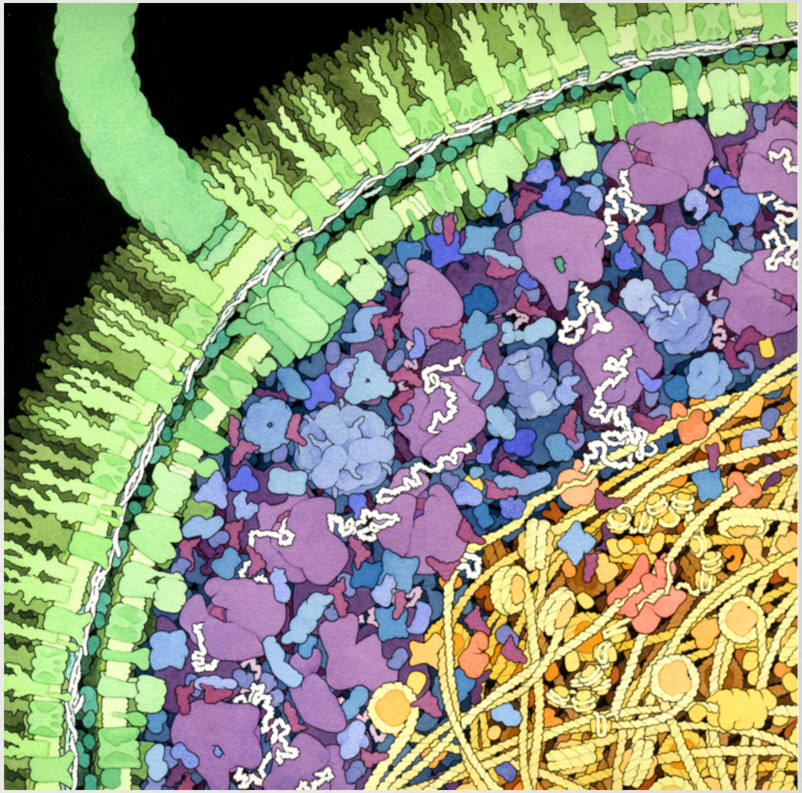
(many processes to consider):

metabolism, transcription, translation, phenotypes



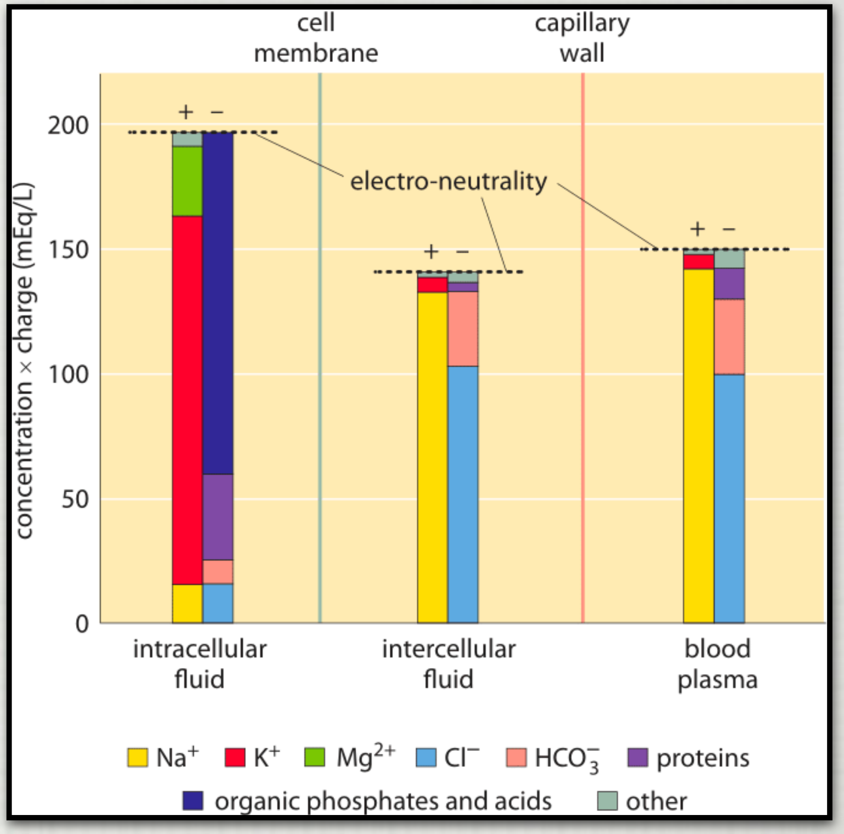
Small molecule scale

METABOLISM



Concentrations of Ions

- Census of ionic charges in a mammalian tissue cell
  - Law of electro-neutrality
  - Osmotic balance between compartments
- Intracellular Fluid
  - Many metabolites & proteins are negatively charged
  - K^+, Mg^{2+}, Cl^- are most abundant ions
- Concentrations can change by more than an order of magnitude depending on…
  - Cell type
  - Physiological conditions
  - Environmental conditions



ion conc. (mM)	sea water	*E. coli*	*S. cerevisiae*	mammalian cell (heart or RBC)	blood plasma
K^+	≈10	30-300	300	100	4
Na^+	≈500	10	30	10	100-200
Mg^{2+}	≈50	30-100 (bound); 0.01-1 (free)	50	10 (bound) 0.5 (free)	1
Ca^{2+}	≈10	3 (bound);100 nM (free)	2 (bound)	10-100 nM (free)	2
Cl^-	≈500	10–200 media dependent		5-100	100

Cell Biology By The Numbers: Figure 2-12, Table 2-3

Typical Metabolite Concentration

1. The number of different metabolites present in *E. coli* is on the order of 1000.
2. An average metabolite has a median molecular weight of about 312 gram/mol.
3. We estimate the typical metabolite concentration:

$$C_m \approx \frac{1 \text{ gm/ cm}^3 \cdot 0.01}{1000 \cdot 312 \text{ gm/ mole}} \approx 32 \ \mu\text{M}$$

and:

$$1\mu\text{M} \quad = \quad \frac{10^{-6} \text{ moles}}{(10 \text{ cm})^3} \cdot \frac{\text{cm}^3}{(10^4 \mu\text{m})^3} \cdot \frac{6 \cdot 10^{23} \text{ molecules}}{\text{mole}}$$

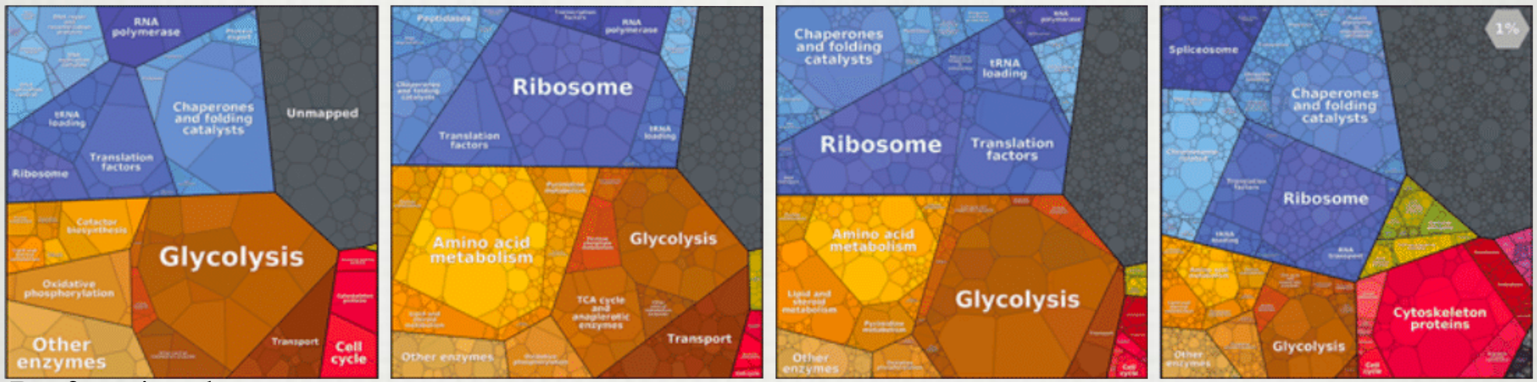
$$= \quad 600 \text{ molecules}/\mu\text{m}^3$$

A typical metabolite concentration translates into about:

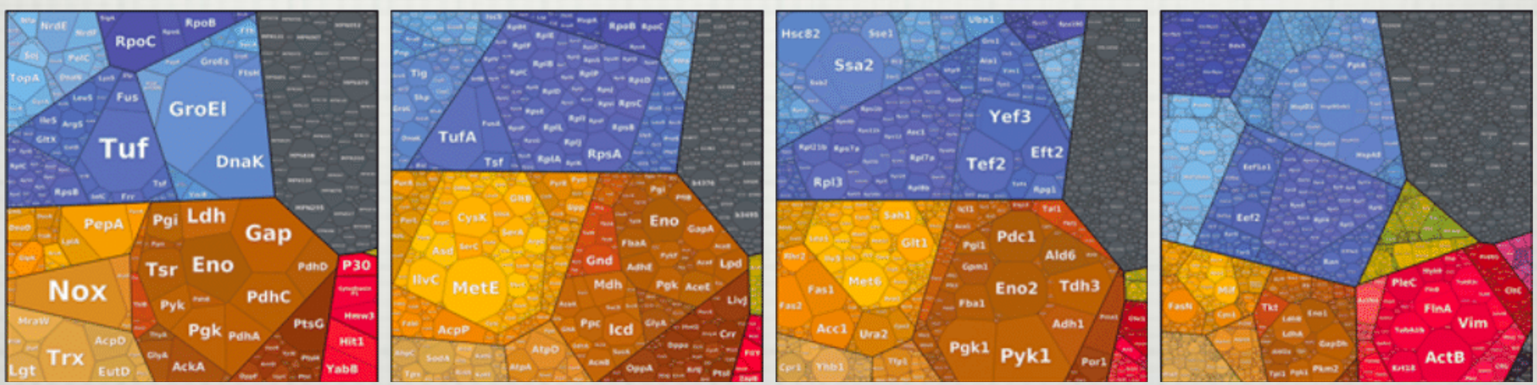
19,000 molecules per cubic micron!

Proteomaps

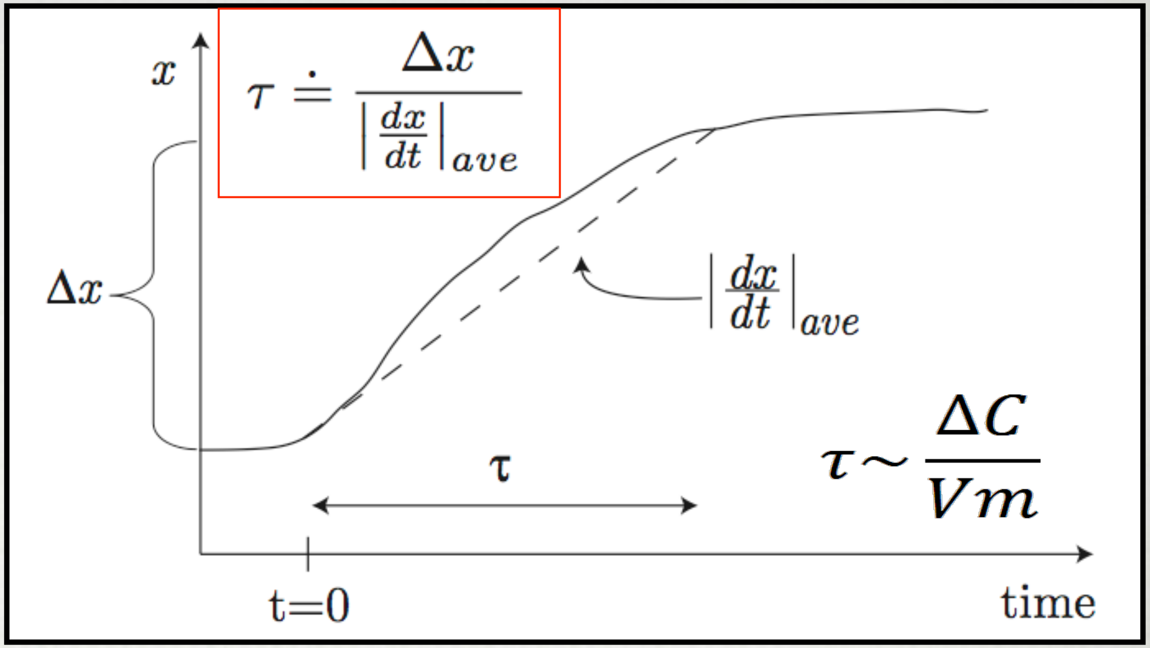
M. pneumoniae — *E. coli* — *S. cerevisae* — *H. Sapiens* (HeLa)



By functional category



By protein name

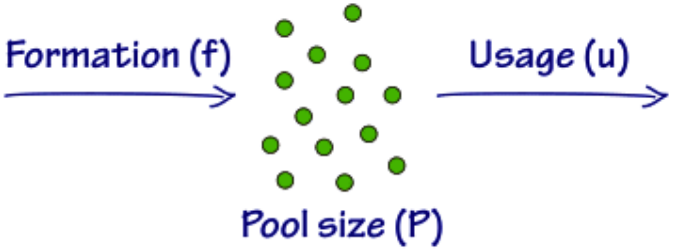


Timescales

TURNOVER TIMES

Defining the Turnover Time

defining the turnover time



metabolite	turnover time (s)		
	Arabidopsis	*S. cerevisiae*	*E. coli*
NADP	0.01	-	-
ADP	0.07	0.3	0.8
Calvin-Benson cycle intermediates (R5P, S6P, X5P, Ru5P, SBP, RuBP)	0.1-1	-	-
DHAP/G3P	0.2	-	-
ATP	0.3	1.4	2
3PGA	0.7	7	3
inorganic C	0.8	-	-
FBP	0.8	7	1.2
pyruvate	-	1.7	1.5
F6P	3	7	1.2
AMP	-	3	9
UDPG	40	-	-
G6P	40	17	4
glycerol-3-phosphate	-	60	13
TCA cycle (Suc, Fum, Mal)	-	4-30	0.7-9

Cell Biology By The Numbers: Estimate 4-8, Table 4-3

Turnover Times of Glucose in *E. coli*

Estimating a glycolytic flux

1. The total stoichiometric amount of glucose that is needed to generate one *E. coli* cell is about 3 billion molecules per cell.
2. Doubling time for *E. coli* is 60 min.
3. Volume of the *E. coli* cell is 1-2μm^3

$$Glycolytic\ flux = \frac{3.0\ x10^9 molecules}{cell\ x\ 60min}$$

$$= \frac{3.0x10^9 molecules}{cell\ x\ hr}$$

$$= 4.2\ x\ 10^5 - \ 8.4\ x10^5\ \frac{molecules}{\mu m^3\ x\ sec}$$

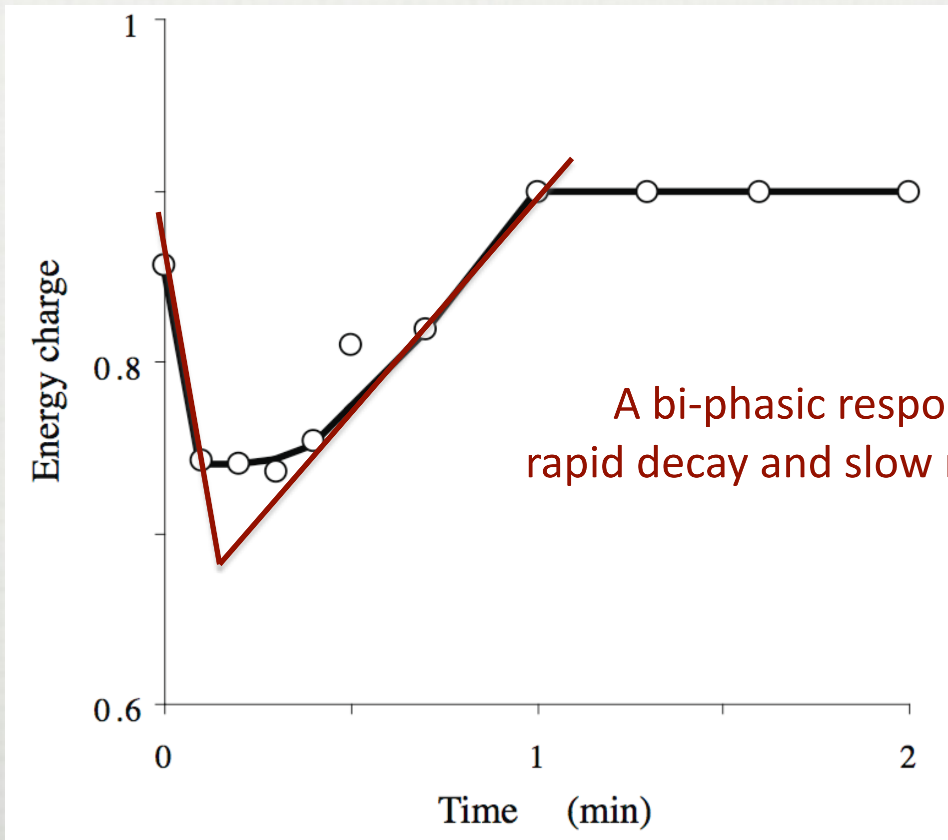
Glucose turnover in rapidly growing *E. coli:*

- Extracellular Glucose concentration: 1-5 mM (*6-30 x 10^5 molecules/cell*)
- Turnover time is on the order of sec

$$\tau_{glu} = \frac{6 - 30\ x\ 10^5\ molecules/cell}{4.2 - 8.4\ x\ 10^5\ \frac{molecules}{\mu m3}/cell} = 1.5 - 4\ sec$$

The Measured Time Response of the Energy Charge

$$\frac{(2ATP+ADP)}{2(ATP+ADP+AMP)}$$



A bi-phasic response:
rapid decay and slow recovery

Turnover times in RBC glycolysis

$$\tau_R = \frac{C_m}{1.25mM/hr}$$

Compound	Concentration (mM)	Turnover time (sec)
G6P	0.038 ± 0.012	109
F6P	0.016 ± 0.03	46
FDP	0.0076 ± 0.004	21
DHAP	0.140 ± 0.08	7 (min)
GA3P	0.0067 ± 0.001	19
1,3DPG	0.0004	1.1
3PG	0.045	2 (min)
2PG	0.014 ± 0.005	40
PEP	0.017 ± 0.002	50
PYR	0.077 ± 0.05	4 (min)
LAC	1.10 ± 0.50	52 (min)

Fast and slow:

Distributed time constants

NUMERICAL VALUES OF KINETIC CONSTANTS

Sources of Information

- BRENDA: Enzyme Database
- KEGG: Kyoto Encyclopedia of Genes and Genomes
- BioCyc: Pathway/Genome Databases (PGDBs)
- EXPASY: Bioinformatics resource portal
- UniProtKB: Universal protein knowledge
- KDBI: Kinetic Data of Bio-molecular Interactions
- NCBI
  - Entrez Gene, PubMed, PubChem, etc.

What to look for?

- Association rate ($k^+/k_{on}/k_{forward}$)
- Dissociation rate ($k^-/k_{off}/k_{reverse}$)
- Catalytic (k_{cat})
- Equilibrium/Dissociation (K_{eq}/K_D)
- Inhibition (K_I)
- Michaelis Menten (K_M)
- Inhibitor Conc. at 50% response (IC50)
- Maximum reaction velocity (V_{max})
- Experimental Conditions
  - pH value/Temperature conditions (Standard?)

BRENDA

1987 2019

The Comprehensive Enzyme Information System

Text-based queries

- Full-text Search
- Advanced Search
- Enzyme & Disease

Structure-based queries

- Ligand Structure Search
- Metabolic Pathways
- Enzyme Structures

Explorer

- Enzyme Classification
- TaxTree
- Protein folding: CATH / SCOPe
- Ontologies

Visualization

- Word Maps
- Genomes
- Functional Parameter Statistics
- Metabolic Pathways

Prediction

- Membrane Helices
- Localization Prediction
- EnzymeDetector

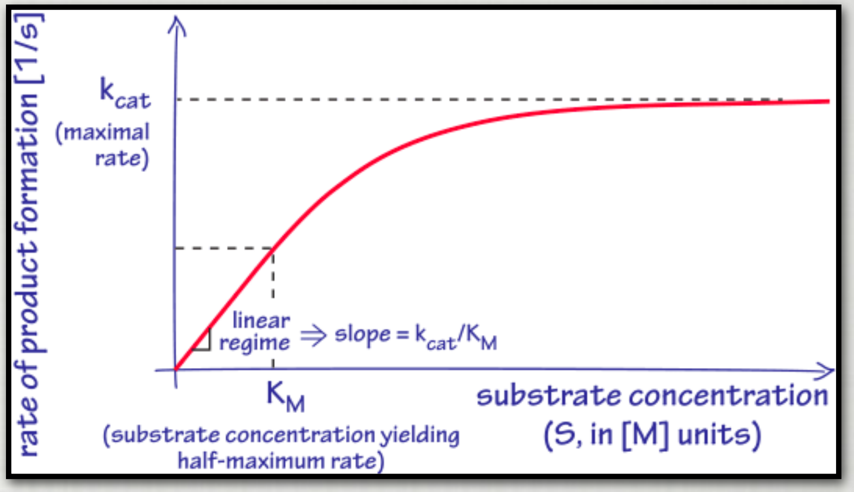
Supporting

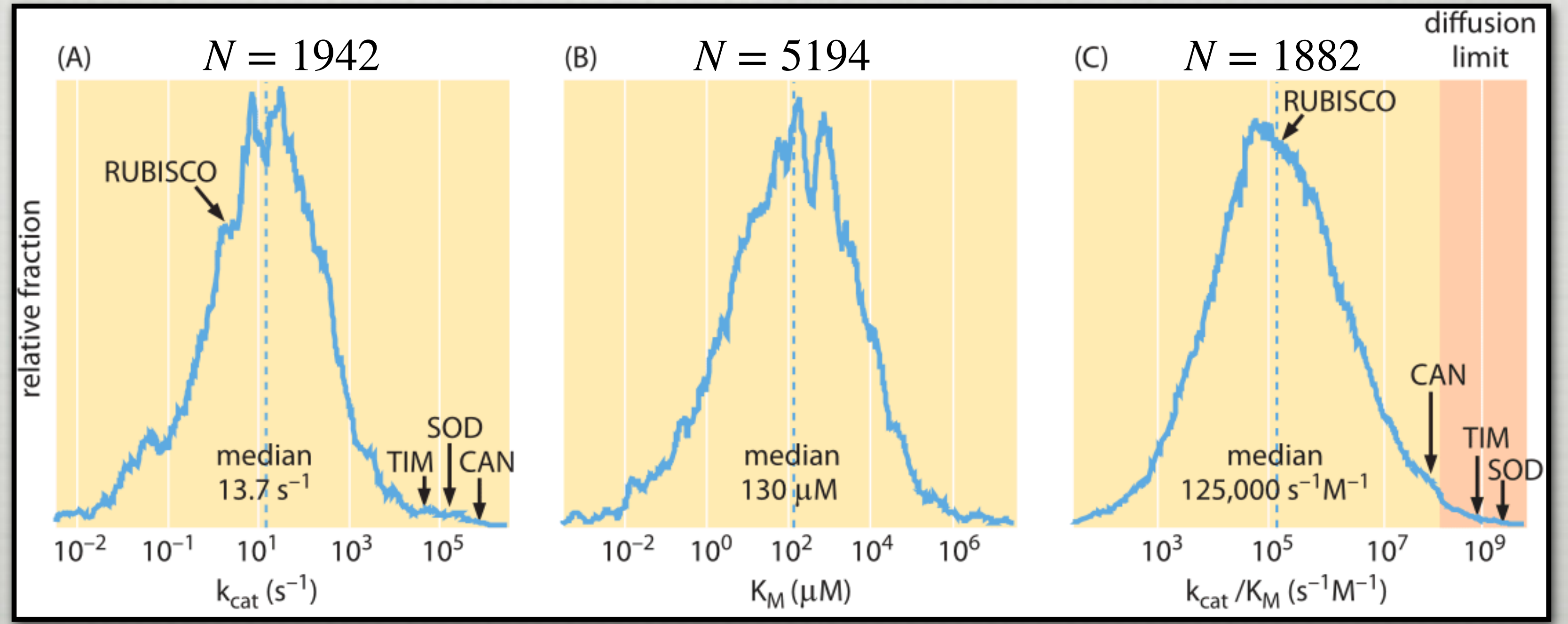
- BRENDA Tissue Ontology
- Biochemical Reactions

http://www.brenda-enzymes.org

Distribution of Enzyme Kinetic Parameters

$$V = \frac{k_{cat}[E]_T[S]}{K_m + [S]}$$

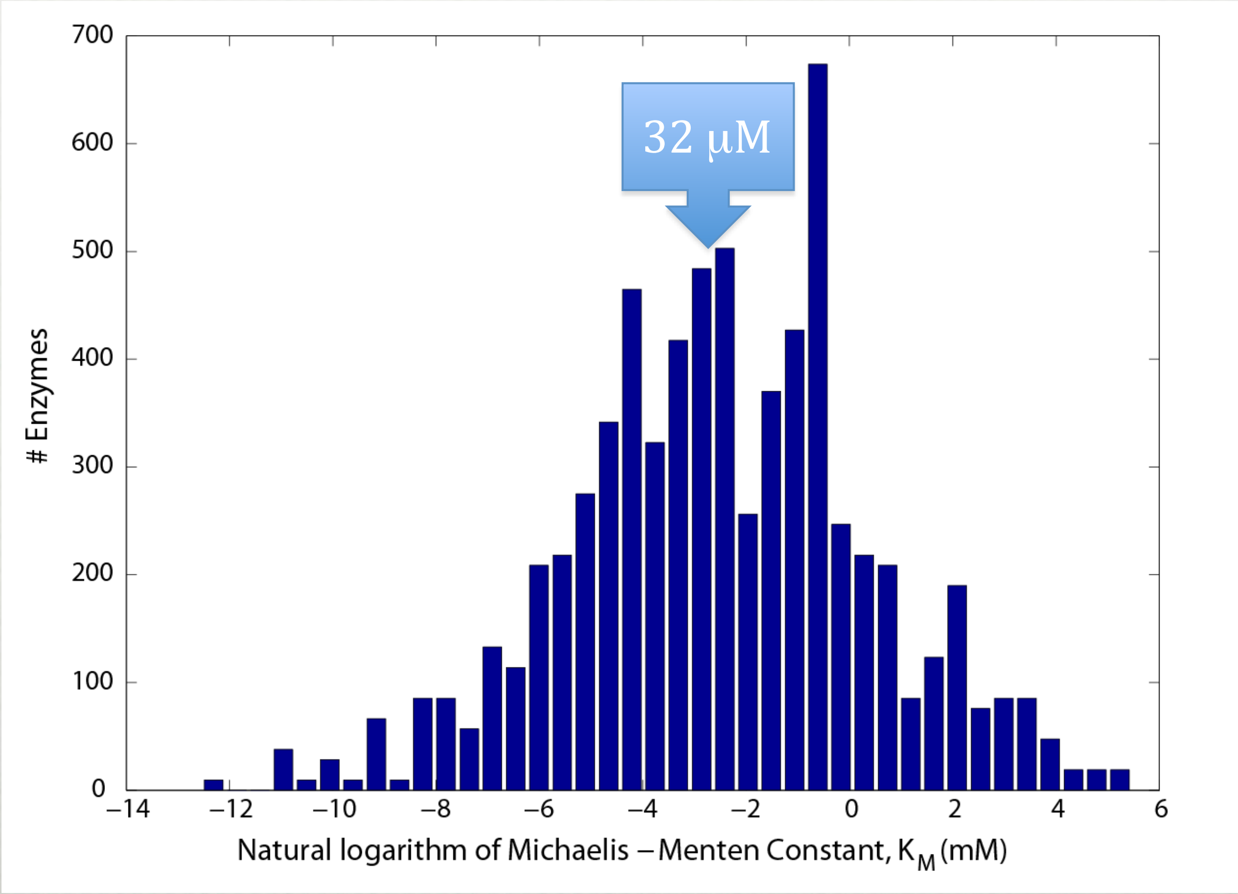




Cell Biology By The Numbers: Figure 4-5, 4-6

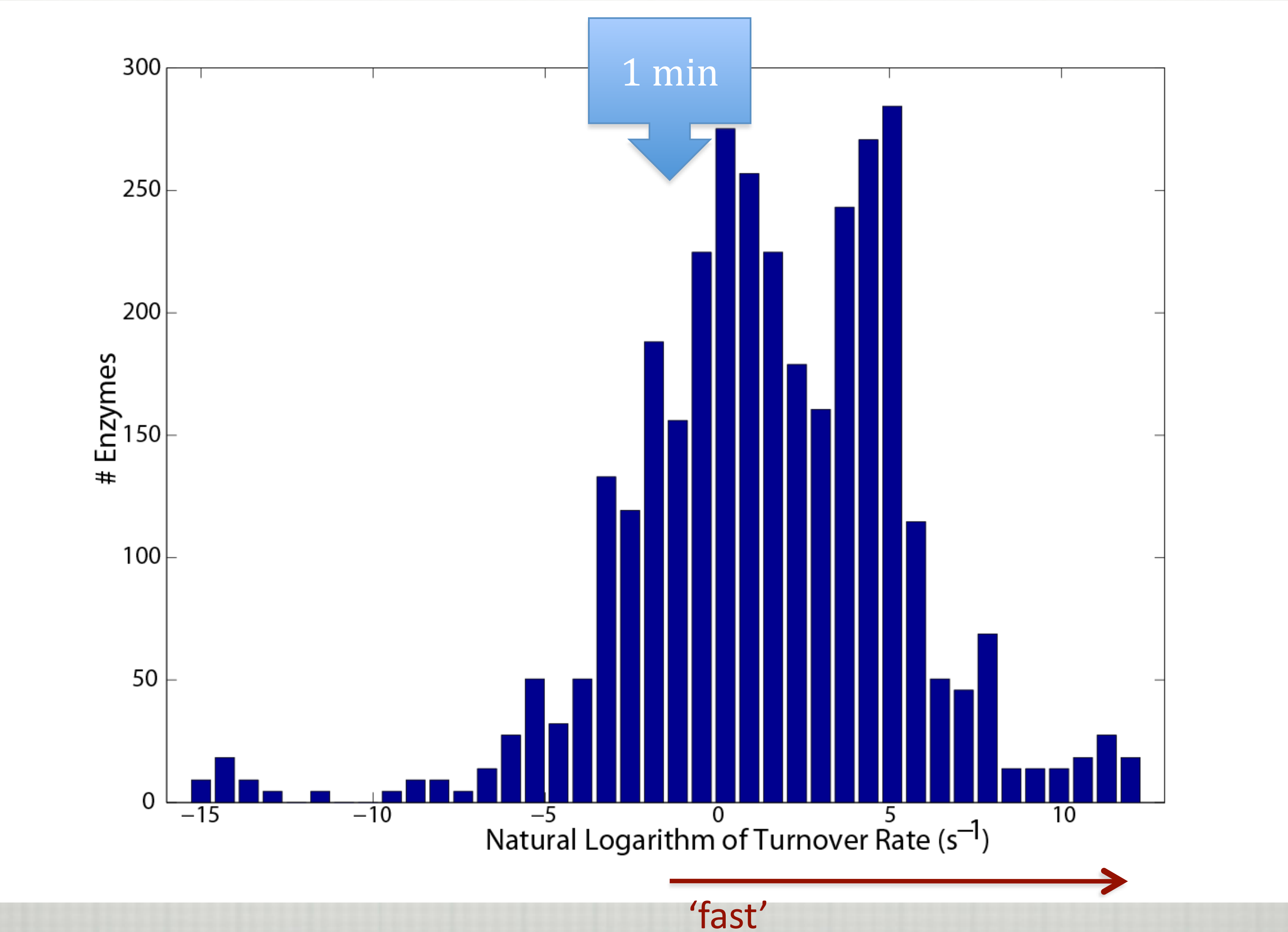
Kinetic Constants of *E. coli* Enzymes

- Average enzyme concentration is on the order of an average kinetic constant ($[E] \sim K_m$)



http://www.brenda-enzymes.info/

Typical Enzyme Turnover Times



http://www.brenda-enzymes.info/

eQuilibrator

- Thermodynamic analysis
  - Can account for different pHs and ionic strengths
- Estimation of
  - Gibbs Free Energy:
    - 1M at standard: ΔG^{o}
    - 1mM at standard: ΔG^{m}
    - Nonstandard: $\Delta G'$
  - Reduction Potential
  - Equilibrium Constants

eQuilibrator

How much is a trillion dollars?

ORDER-OF-MAGNITUDE: AN EXAMPLE

$1 Trillion & US Debt in Physical $100 Bills

$100 Dollars

DEMON • OCRACY.INFO
ECONOMIC INFOGRAPHICS

What does this mean for you and me?

The San Diego Mid-Coast Trolley Project

- Project Duration
  - Late 2016- Late 2021 (~5 years)
- Total Estimated Cost of Project:
  - $2.1 billion
- Extension of Blue Line by
  - 11 miles

$$\frac{\$2.1 \text{ billion}}{11 \text{ miles}} \approx \$200 \text{ million per mile}$$

https://www.keepsandiegomoving.com/Mid-coast/midcoast-FAQ.aspx
http://worldpopulationreview.com/us-cities/san-diego-population/
https://www.sandag.org/uploads/publicationid/publicationid_2052_20893.pdf

The End