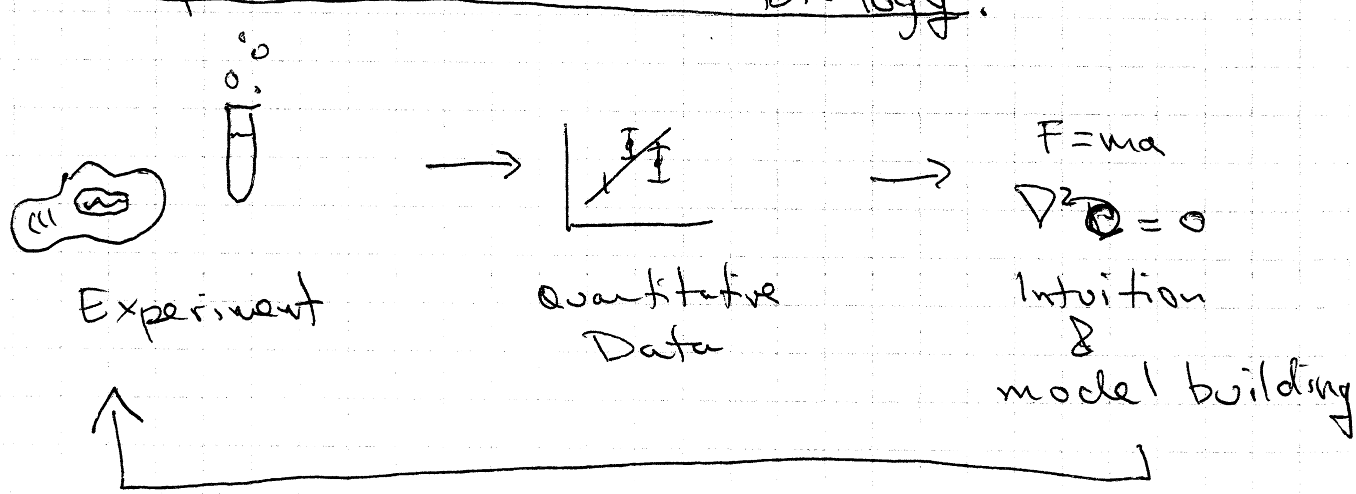
A Molecular Census:

- Biological systems span a range of spatial sizes, from the atomic up to many meters. Their dynamics ranges over many timescales.
- Biological systems are composed of 1000's of self organizing molecular components
- Given the vast range of scales and the large variety of parts, its important to have a sense of the numbers of things.
- **Why?** ① being able to estimate numbers of parts etc builds intuition.

  ② allows one to assess what aspects of a given biological process will be important quantitatively

  - in complex systems, the things one ignores are as important as the things that are considered.
  - models are *always* incomplete

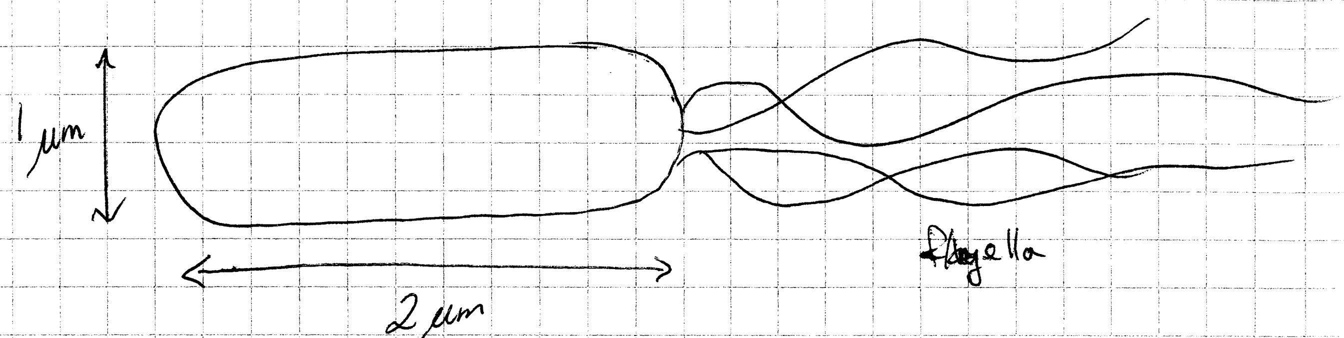
Roadmap to Quantitative Biology:



Quantity of interest	Symbol	Rule of thumb
E. coli		
Cell volume	$V_{E.coli}$	$\approx 1\ \mu m^3$
Cell mass	$m_{E.coli}$	$\approx$ 1pg
Cell cycle	$t_{E.coli}$	$\approx$ 3000 s
Cell area	$A_{E.coli}$	$\approx 6\ \mu m^2$
Genome Length	$N_{bp}^{E.coli}$	$\approx 5 \times 10^6$ bp
Swimming speed	$v_{E.coli}$	$\approx 20\ \mu m/s$
Yeast		
volume of cell	V_{yeast}	$\approx 60 \mu m^3$
Mass of cell	m_{yeast}	$\approx$ 60 pg
diameter of cell	d_{yeast}	$\approx 5\ \mu m$
Cell cycle time	t_{yeast}	$\approx$ 200 min
Genome Length	N_{bp}^{yeast}	$\approx 10^7$ bp
Organelles		
Diameter of nucleus	$d_{nucleus}$	$\approx 5\ \mu m$
Length of mitochondrion	l_{mito}	$\approx 2\ \mu m$
Diameter of transport vesicles	$d_{vesicle}$	$\approx$ 50 nm
Water		
Volume of molecule	V_{H_2O}	$\approx 10^{-2}\ nm^3$
Density of water	ρ	1 g/cm^3
Viscosity of water	η	$\approx$ 1 centipoise (10^{-2} g/cm s)
Hydrophobic embedding energy	$\approx E_{hydr}$	25 cal/mol A^2
DNA		
Length per base pair	$l_{\rm bp}$	$\approx$ 1/3 nm
Volume per base pair	$V_{\rm bp}$	$\approx 1\ nm^3$
charge density	λ_{DNA}	2 e/0.34 nm
Persistence length	$\xi_{\rm P}$	50 nm
Amino acids and Proteins		
Radius of "Average" Protein	$r_{protein}$	$\approx$ 2 nm
Volume of "Average" Protein	$V_{protein}$	$\approx 25\ nm^3$
Mass of "Average" Amino Acid	M_{aa}	$\approx$ 100 Da
Mass of "Average" Protein	$M_{protein}$	$\approx$ 30,000 Da

Bacteria as the standard ruler:

- E. coli is an excellent model organism – many complex behaviours and has a long history of quantitative experiments



- Volume: $V_{cell} \approx 1\ \mu m^3 = 1 fL$
- Area: $A_{cell} \approx 6\ \mu m^2$

Cells are crowded:

Mass: $\text{Mass} = \text{density} \times \text{volume}$

$$\approx \text{density}_{H_2O} \times V_{cell}$$

$$\approx 1 g/mL \times 1 fL = 1 pg$$

Dry mass: Experiment $\rightarrow$ $M_{Dry} \approx 0.3\ pg = 30\%$ Mass

Protein mass: avg protein = 300 amino acids (AA)

$1\ AA = 100\ Da$ & $\underline{1\ Da = m_{proton}} = 1.6 \times 10^{-24}\ kg$

so average protein mass,

$$m_{protein} = (300) \times (100\ Da) \times (1.6 \times 10^{-24} g) \approx 5 \times 10^{-20} g$$

Number of proteins in E. coli:

50% of dry mass is protein from experiment

$$N_{protein} = \frac{\text{protein mass}}{\text{mass per protein}} = \frac{0.15\ pg}{5 \times 10^{-20} g} \approx 3 \times 10^6$$

Number of Ribosomes:

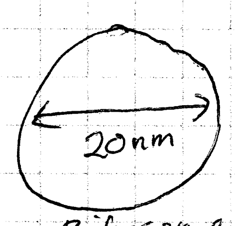
Expt: 20% of protein mass is contributed by ribosomes

$$M_{ribosome} = 2.5\ MDa$$

but 1/3 Ribosome is protein & 2/3 is rRNA

$$N_{Ribosome} = \frac{(0.2)(0.15\ pg)}{830{,}000\ Da} = 20{,}000$$

How much volume do ribosomes occupy?



$$V_{ribosome} = \frac{4}{3}\pi (10\ nm)^3$$

$$V_{tot} = (20{,}000)\frac{4}{3}\pi (10\ nm)^3 \approx 10^8\ nm^3$$

$$\approx 10\%\ V_{cell}$$

Number of H_2O molecules

70% of mass is H_2O

$$N_{H_2O} = \frac{0.7 \times 10^{-12} g}{18\ g/mol} \times 6 \times 10^{23}\ \text{molecules/mol} \approx 2 \times 10^{10}\ H_2O$$

Substance	% of total dry weight	Number of molecules
Macromolecule		
Protein	55.0	2.4×10^6
RNA	20.4	
23S RNA	10.6	19,000
16S RNA	5.5	19,000
5S RNA	0.4	19,000
Transfer RNA (4S)	2.9	200,000
Messenger RNA	0.8	1,400
Phospholipid	9.1	22×10^6
Lipopolysaccharide	3.4	1.2×10^6
DNA	3.1	2
Murein	2.5	1
Glycogen	2.5	4,360
Total macromolecules	**96.1**	
Small molecules		
Metabolites, building blocks, etc.	2.9	
Inorganic ions	1.0	
Total small molecules	**3.9**	

Table 2.1: Observed macromolecular census of an *E. coli* cell. (Data from F. C. Neidhardt *et al.*, Physiology of the Bacterial Cell, Sunderland, Sinauer Associates Inc., 1990 and M. Schaechter *et al.*, Microbe, Washington DC, ASM Press, Washington, 2006.

Concentrations and #'s of molecules

$$\text{concentration} = \frac{\#}{\text{volume}}$$

units: molar $= [M] = \dfrac{1 \text{ mol}}{1 \text{ liter}} = \dfrac{6.02 \times 10^{23}}{1 \text{ L}}$

Cellular concentrations range from $1\,nM \rightarrow 1\,\mu M$

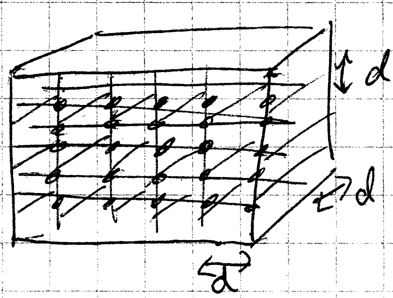
What is concentration of 1 molecule in E. coli?

$$c_1 = \frac{1}{1\,fL} = \frac{1 \text{ molecule}}{1 \times 10^{-15} L} \cdot \frac{1 \text{ mol}}{6 \times 10^{23} \text{ molecule}} \approx 2\,nM$$

so a concentration of $2\,\mu M \approx 1000$ molecules in the cell

Distance between molecules:

- Assume molecules sit on a square lattice in a square cell of volume V



spacing between molecules is d.

$$c = \frac{N}{V} = \frac{N}{(N \cdot d^3)} = d^{-3}$$

so spacing $= d = c^{-1/3}$

for $c = 2\,\mu M \rightarrow d \sim 150\,nm$

for $c = (1 \times 10^6)\, 1\,nM \Rightarrow d \sim 1\,nm \leftarrow$ hardly any space between proteins

(1×10^6 = # of proteins)