Cellular Biophysics
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Cell-Biology by Numbers

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Hi! In the upcoming segment we are going to continue with quantitative biology and sometimes referred to as biology by numbers to discuss a little bit the senses of biomolecules at a cellular scale. The numbers that I am going to give you I will discuss a bit about whether we need to remember, why, what sense it makes and which ones are more important than others.

But as I said at the beginning of the segment any number has to be against or for such for some hypothesis or model. One of the important aspects of getting numbers is how we measure them. So, techniques, experimental techniques become very important. We will also speak after this about time scales in terms of movement, growth and transport.

And discuss a little bit about some very fascinating questions about how cells manage to keep regularity in times, they are almost like clocks they work in fact in many senses like clocks, but they are not clocks obviously they do not have the wheels, they do not have the digital machinery, so how does that function, we will talk about it.

And finally we will end this order of magnitude and biology by numbers segment by discussing energy scales. Because no matter how we see it energy rules and this is sort of going to be our next segment anyway. So, let us get to it.

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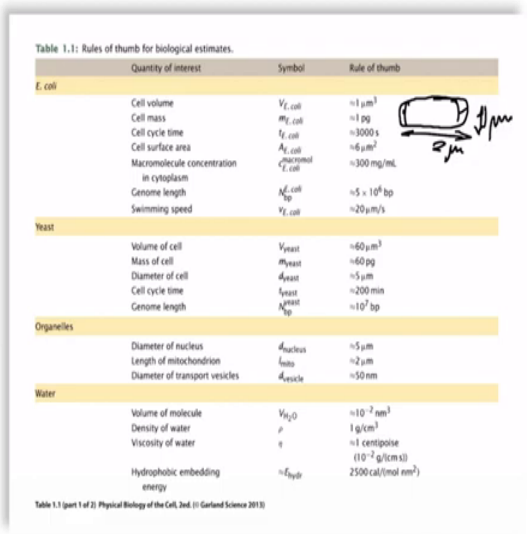
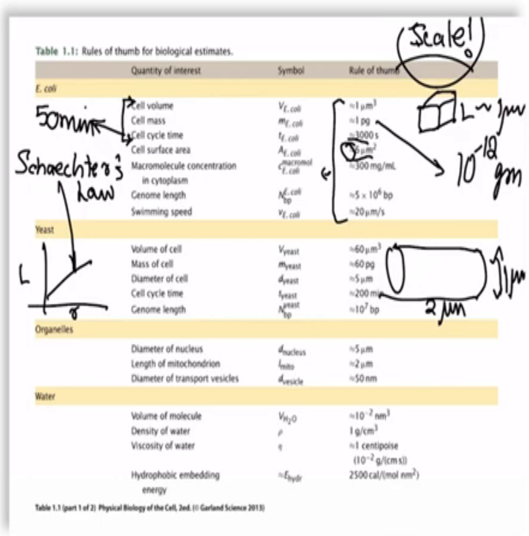


Table 1.1: Rules of thumb for biological estimates.

	Quantity of interest	Symbol	Rule of thumb
E. coli			
	Cell volume	$V_{E. coli}$	≈1 μm³
	Cell mass	$m_{E. coli}$	≈1 pg
	Cell cycle time	$t_{E. coli}$	≈3000 s
	Cell surface area	$A_{E. coli}$	≈6 μm²
	Macromolecule concentration in cytoplasm	$c_{E. coli}^{macromol}$	≈300 mg/mL
	Genome length	$N_{bp}^{E. coli}$	≈5 × 10⁶ bp
	Swimming speed	$v_{E. coli}$	≈20 μm/s
Yeast			
	Volume of cell	V_{yeast}	≈60 μm³
	Mass of cell	m_{yeast}	≈60 pg
	Diameter of cell	d_{yeast}	≈5 μm
	Cell cycle time	t_{yeast}	≈200 min
	Genome length	N_{bp}^{yeast}	≈10⁷ bp
Organelles			
	Diameter of nucleus	$d_{nucleus}$	≈5 μm
	Length of mitochondrion	l_{mito}	≈2 μm
	Diameter of transport vesicles	$d_{vesicle}$	≈50 nm
Water			
	Volume of molecule	V_{H_2O}	≈10^{-2} nm³
	Density of water	ρ	1 g/cm³
	Viscosity of water	η	≈1 centipoise (10^{-2} g/(cm s))
	Hydrophobic embedding energy	$\approx E_{hydr}$	2500 cal/(mol nm²)

Table 1.1 (part 1 of 2) Physical Biology of the Cell, 2ed. (© Garland Science 2013)



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You are looking at a table taken from a textbook physical biology of the cell and perhaps those of you who studied chemistry or physics are aware that typically physical or chemical constants are mentioned at the beginning of the textbook. I challenge you to show me a textbook in biology that does this.

And if you are a biologist you should argue that this is not easy because if I show you a microbiology textbook versus a biochemistry textbook versus an animal physiology textbook, the numbers, the variables that are used as well as the values that are found will differ. And it is for exactly this reason that we spent some time thinking about *E. coli* as a model cell.

Because what it tells us is that at least for one cell type can we get some numbers that allow us to get a relative sense of magnitude? So, for example, if I look at the first of these variables which is with regard to *E. coli* and we take the numbers for volume then if you recall we described *E. coli* as a cylinder, spherocylinder with some ends of 2 micron by 1 micron. But if we decide to ignore all this detail, then we can perfectly well assume that it is a cube with the length of approximately one micron.

This is what we are referring to when we talk about scale. In other words relatively how big is it, and therefore one micron cube. The mass of an *E. coli* cell comes out to be one Picogram approximately. We say approximately because amongst other things it may depend what cell cycle stage we take, what growth conditions we use, what bacteria, bacterial metabolic state we are looking at and so on.

So, also to remind ourselves what is 1 picogram, 10^{-3} grams is 1 milligram, 10^{-6} grams is 1 microgram, 10^{-9} grams is 1 nanogram, 10^{-12} grams is 1 picogram. So, this is nothing but 10^{-12} grams. Cell cycle time is about 33000 seconds.

Those of you who studied microbiology maybe know that we typically state that the so-called doubling time of *E. coli* at fast growth is 20 minutes, this 3000 is nothing but 50 minutes, 3000 seconds 50 minutes. We are again trying to consider average times. It becomes an interesting problem which is to ask. In terms of the cell cycle time of *E. coli*, how long does it actually take to divide?

But there is a law which goes by the name of the person who came up with it Schaechter, Moselio Schaechter, he writes a very beautiful blog on American Society Microbiology's website, which states that the growth rate and cell length scale linearly, this is called Schaechter’s law and there is a precise relation for this.

So, in a way these are not independent variables, they are interdependent you could say. So, by changing one you can change the other. And the causal links you see once we put a number to it the causal links become interesting. What about cell surface area? We can come up with 6 micron square which is considering the spherocylinder.

For the cylindrical part we have $\pi r^2 h$ which if I take my calculator is π into 0.5 r^2 micron square, π into 0.5 micron square into 2 microns which is 1.57 about 1.6 micron square. And the cylinder has cells on top so we can add that volume and we are referring to the volume of, I am sorry the surface area of where this is 1.5 microns square.

We are referring to the area, the area of the caps is two caps we can argue they are hemispheres, so two caps make one complete sphere with radius 0.5. So, we are talking 4/3πr, I am sorry $2\pi r^2$, 2 π into 0.5^2 it is 1.5 + 1.5 it is 6 microns square. I want you to find out how the cell surface of an *E. coli* cell can become 6 micron square.

It is important at this point to question these numbers because they are approximations as I keep highlighting over here, but these approximations are obtained from certain assumptions, whatever macromolecular concentration in cytoplasm it is about 300 mg per ml, genome length is 4.8 into 10^6 base pairs which is approximately 5 x 10^6, 5 billion, 5 million base pairs.

Swimming speeds is about 20 micrometers per second we discussed this in the earlier section on fluids. So, should you remember these numbers absolutely? Why should you remember these numbers, because as I was discussing these are telling us about the scale and relative size of things at a cellular level which in fact for almost no other organism do we have with such detail and such reproducibility.

Which is another way of saying that we would love to have these measurements for other cell types too, but until we have them we are better off with the numbers we have, so yes, you do need. What about bigger cells? Yeast is a eukaryotic, eukaryote this is a *Saccharomyces cerevisiae* you see the brewer's yeast or baker's yeast has a volume of 60 x 10^3 micrometer cube.

The mass of the cell is 60 picograms, remember it is about 60 times that of the *E. coli* cell, the diameter of the cell is 5 microns as opposed to 1 and 2 micron for *E. coli* and cell cycle time is 200 minutes as opposed to 50 minutes for *E. coli*. Everything is bigger, everything is slower and the genome is 10 times longer, which is 10^7 base pairs.

Organelles on the other hand like the nucleus, cell nucleus are of size typically 5 micron diameter but they may vary, the length of the mitochondrion is about 2 microns, the damage of transport vesicles is 15 nanometers, so these are nanometer, nano vesicles, nanoparticles you could say.

Vesicles by the way are the ones that we find very interesting in terms of transport of viruses. So, coronavirus internalization does not take the vesicle transport but other viruses usually take the vesicle root, certainly bacteria, intracellular bacteria take vesicle the endocytic vesicles, in animal cells this pathway is very important and we may have some opportunity to discuss it and talk about water.

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Table 1.1: Rules of thumb for biological estimates.

	Quantity of interest	Symbol	Rule of thumb
E. coli			
	Cell volume	$V_{E. coli}$	$\approx 1\ \mu m^3$
	Cell mass	$m_{E. coli}$	≈ 1 pg
	Cell cycle time	$t_{E. coli}$	≈ 3000 s
	Cell surface area	$A_{E. coli}$	$\approx 6\ \mu m^2$
	Macromolecule concentration in cytoplasm	$c^{macromol}_{E. coli}$	≈ 300 mg/mL
	Genome length	$N^{E. coli}_{bp}$	$\approx 5 \times 10^6$ 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}	≈ 60 pg
	Diameter of cell	d_{yeast}	$\approx 5\ \mu m$
	Cell cycle time	t_{yeast}	≈ 200 min
	Genome length	N^{yeast}_{bp}	$\approx 10^7$ bp
Organelles			
	Diameter of nucleus	$d_{nucleus}$	$\approx 5\ \mu m$
	Length of mitochondrion	l_{mito}	$\approx 2\ \mu m$
	Diameter of transport vesicles	$d_{vesicle}$	≈ 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	≈ 1 centipoise (10^{-2} g/(cm s))
	Hydrophobic embedding energy	$\approx E_{hydr}$	2500 cal/(mol nm^2)

Table 1.1 (part 1 of 2) Physical Biology of the Cell, 2ed. (© Garland Science 2013)

What about water? Since everything is made up of water in biology. The volume of water is 10^{-2} nanometer cube, density is 1 gram per centimeter cube, viscosity is one centipoise and the hydrophobic embedding energy we talked about this in the hydrophobicity part is 2500 calories per mole per nanometer square.

Now, with some of these parameters I do not mind if you do not remember them but the cellular scales you must and the organelles scales.

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Table 1.1: Rules of thumb for biological estimates.

	Quantity of interest	Symbol	Rule of thumb
DNA			
	Length per base pair	l_{bp}	$\approx 1/3$ nm
	Volume per base pair	V_{bp}	≈ 1 nm^3
	Charge density	λ_{DNA}	$2e/0.34$ nm
	Persistence length	ℓ_p	50 nm
Amino acids and proteins			
	Radius of "average" protein	$r_{protein}$	≈ 2 nm
	Volume of "average" protein	$V_{protein}$	≈ 25 nm^3
	Mass of "average" amino acid	M_{aa}	≈ 100 Da
	Mass of "average" protein	$M_{protein}$	$\approx 30{,}000$ Da
	Protein concentration in cytoplasm	$c_{protein}$	≈ 150 mg/mL
	Characteristic force of protein motor	F_{motor}	≈ 5 pN
	Characteristic speed of protein motor	v_{motor}	≈ 200 nm/s
	Diffusion constant of "average" protein in cytoplasm	$D_{protein}$	$\approx 10\ \mu m^2/s$
Lipid bilayers			
	Thickness of lipid bilayer	d	≈ 5 nm
	Area per molecule	A_{lipid}	$\approx \frac{1}{2}$ nm^2
	Mass of lipid molecule	m_{lipid}	≈ 800 Da

Table 1.1 (part 2 of 2) Physical Biology of the Cell, 2ed. (© Garland Science 2013)

DNA, now we come to molecules, DNA has a length of base pair of 0.3 nanometers 0.34, volume per base pair is 1 nanometer cube this is the volume which is made up by the base pair height combined with the diameter of the DNA which is 2 nanometers. Charge density is 2 electrons per 0.34 nanometers and persistence length something we will talk about later 50 nanometers.

50 nanometers translates to around 150 base pairs in terms of persistence law. What about proteins? So, we spoken about cells, organelles, water molecules, DNA. What about proteins? So, the average radius of protein is 2 nanometers. Now, this is again an average value, as you saw everything has a distribution, everything is widely distributed at times in biology, but the average number is twos.

So, when someone asks you what is the size of a protein 2 nanometers is a good number, this radius that means the diameter is 4, using $4/3\pi r^3$ you can calculate the volume of such a protein it is about 25 nanometer cube, while the mass of an average amino acid is 100 Daltons and the number of amino acids making up a protein result in typical average number result in 30 kilo Dalton as the average mass of a whole protein.

These numbers I do expect you to at least have some inkling and not be lost when I ask you these because these are giving us a relative sense of what is the size and shape of the basic molecular building blocks of life that is DNA, protein RNA and lipids. The characteristic force of a protein we will come about to talk about later by pico newton, the speed of motor proteins is 200 nanometers per second.

The diffusion constant of average protein cytoplasm is 10 micron square per second and can be up to 100. The thickness of a bilayer is 5 nanometers, 2.5 nanometers or 2 nanometers approximately the height of a single lipid. The area of the lipid is half nanometer square and the mass full of molecule is 800 Daltons.

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	Quantity of interest	Symbol	Rule of thumb
E. coli	Cell volume	$V_{E. coli}$	≈1 μm³
	Cell mass	$m_{E. coli}$	≈1 pg
	Cell cycle time	$t_{E. coli}$	≈3000 s
	Cell surface area	$A_{E. coli}$	≈6 μm²
	Genome length	$N_{bp}^{E. coli}$	≈5 × 10⁶ bp
	Swimming speed	$v_{E. coli}$	≈20 μm/s
Yeast	Volume of cell	V_{yeast}	≈60 μm³
	Mass of cell	m_{yeast}	≈60 pg
	Diameter of cell	d_{yeast}	≈5 μm
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Organelles	Diameter of nucleus	$d_{nucleus}$	≈5 μm
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Water	Volume of molecule	V_{H_2O}	≈10⁻² nm³
	Density of water	ρ	1 g/cm³
	Viscosity of water	η	≈1 centipoise (10⁻² g/(cm s))
	Hydrophobic embedding energy	$\approx \varepsilon_{hydr}$	25 cal/(mol Å²)
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	Volume per base pair	V_{bp}	≈1 nm³
	Charge density	λ_{DNA}	2e/0.34 nm
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Amino acids and proteins	Radius of "average" protein	$r_{protein}$	≈2 nm
	Volume of "average" protein	$V_{protein}$	≈25 nm³
	Mass of "average" amino acid	M_{aa}	≈100 Da
	Mass of "average" protein	$M_{protein}$	≈30,000 Da
	Protein concentration in cytoplasm	$c_{protein}$	≈300 mg/mL
	Characteristic force of protein motor	F_{motor}	≈5 pN
	Characteristic speed of protein motor	v_{motor}	≈200 nm/s
	Diffusion constant of "average" protein	$D_{protein}$	≈100 μm²/s
Lipid bilayers	Thickness of lipid bilayer	d	≈5 nm
	Area per molecule	A_{lipid}	≈ ½ nm²
	Mass of lipid molecule	m_{lipid}	≈800 Da

So, these key facts are nice to keep by you and you may want to refer to them.

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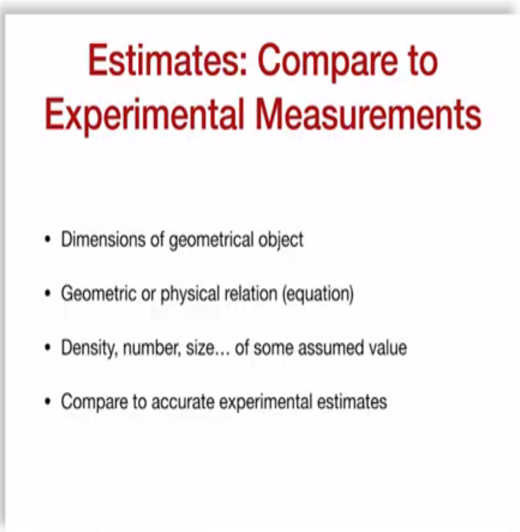

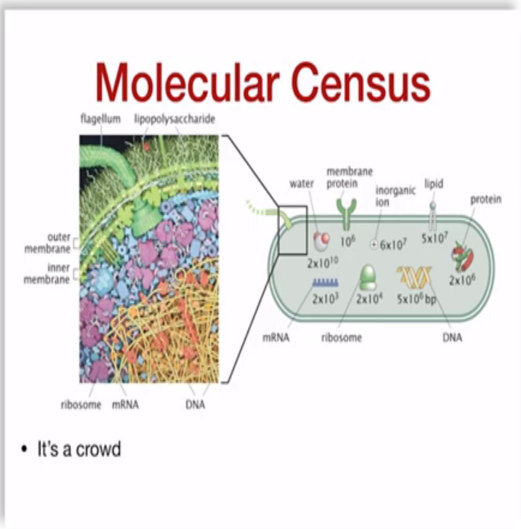

In terms of estimates we compare experimental measures to our estimates and we check whether our estimates, you know we made these estimates of cows and of cells and a number of proteins. Two accurate experimental measurements, so the molecular sensors suggests that a cell is a crowded place. But how do you get this molecular census, what method can we use to obtain numbers that we can compare our rough estimates to.

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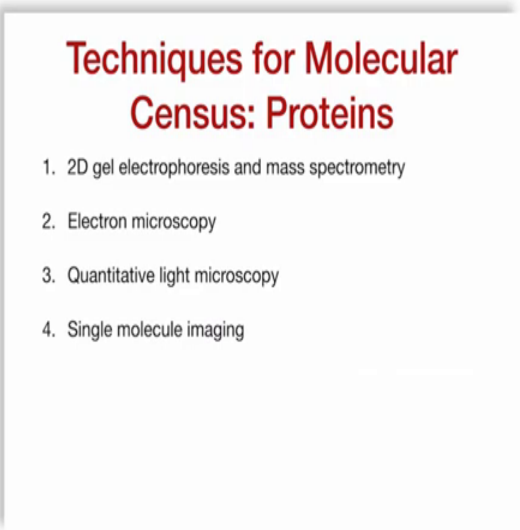

And this is the crux of the next section.