

Cellular Biophysics
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Physical Basis of Life

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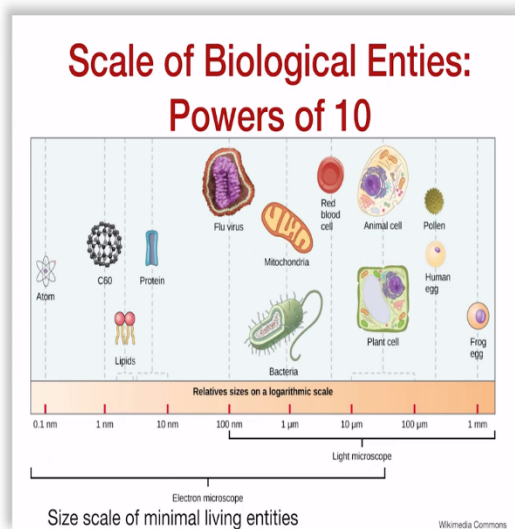
Defining Life

Properties of living organisms

- Replication
- Division
- Metabolism
- Stimulus-response
- ...
- More?

What are the most important questions in biology? And yet, the hardest to answer is to define life. Because biology is the logic of life. And yet, for centuries, biologists have struggled to define it.

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In fact, if we look at the definitions from the Greek philosophers and businesses they almost seem like definitions made by children to us today. On the other hand, religious explanations require that some higher power creates and so there is no material explanation or definition there, so you have no explanation.

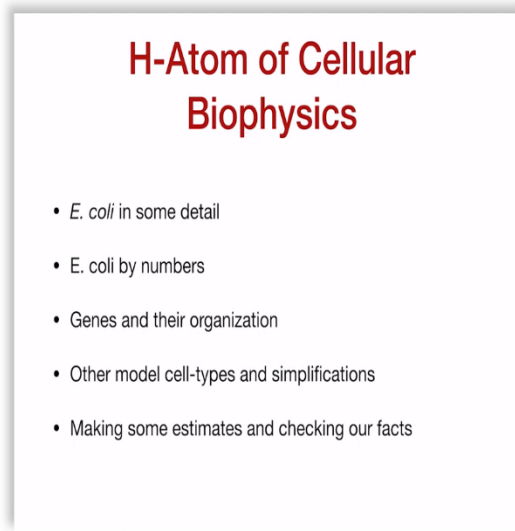
But if we are to use our knowledge of chemistry, physics, mathematics, and to try to define living organisms in a physical sense, then we can come up with a list of features that they must have, they probably must replicate, it is kind of obvious, life is that which gives rise to more life. The fact that they can make more of themselves can be either division or reproduction. But we can always argue that giving rise to itself can also be a feature of crystals.

So, if you put salt crystal, salt crystal in our mouth saturating solution of salt you will see growth. So, growth alone cannot be a definition of life. What about metabolism? What about the fact that living systems are able to take in substances, modify them chemically, use their material for energy generation and excrete something or we would normally call metabolism at a cellular scale. Well, that might work.

You can maybe build a reactor of course, that takes in feedstock and some enzymes and produce some output and you can throw away the waste product. What about stimulus response, they should be capable of doing all of these things replicate, divide, reproduce, to metabolism, respond to the external environment, react in a certain way, many of our computer control devices like the air conditioning in home which is auto set to a certain temperature does that when the room gets very hot it turned on when the room gets cooled it switches off.

So, there are more definitions, but all these definitions are a featureless outcome. The problem is that a universal definition of life is very hard. And one of the leading physicists of the 1900s Erwin Schrodinger came up with one such definition and we are going to talk a little bit about it.

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So, we know that biological properties are over a vast, we on the one hand can look at trees and whales and biofilms and fungal colonies as very large-scale structures ecosystem level. Or we can go down to a single egg cell or human cell or a pollen grain or animal cell and about 10s of micrometers, 10 to 30 microns, red blood cell at about 7 microns, mitochondrion 1 micron, flu virus 100 nanometers, protein at 2 to 3 nanometers, lipids at a few nanometers, carbon complexes at 1 nanometers, 360 in this case, and single atoms at about 1 angstrom.

So, when we look at the size scale, and the scale as you notice is a logarithmic base 10 scale, .1, 1, 10, 100, 1 micron is 100 nanometers etcetera. This tells us that somewhere between an atom and a whole human being there is a size at which we can call it a life. We asked what is a life, what is the definition of life. And the interesting part is that a cell is probably the smallest unit of life below which organelles themselves do not do all the things that we consider essential for life.

Many cells do what is essential for life and more. So, at the smallest simplest form of life is a cell. That is amazing. That is also telling us that if we want to understand the physical basis, the biophysics, the foundations of life, then we should focus on ourselves. Remember, I asked you at the beginning, why do we bother with cellular biology, why studying quantitative biology at the level of cell, that is because they are the foundation of life.

When we ask the question, is a virus alive, we are always given the answer maybe, sometimes it is sometimes it is not. You have all heard of the Coronavirus, I think many of you have been

affected by it, our entire lives were put out of order. But you cannot kill the virus because the virus when it is outside the body is not alive, it is only when it is inside a host cell and it has parasitized it. Can it actually be considered to be alive?

Mitochondrion cannot exist on its own. A bacterium can and a bacterium is what we consider to be a basic cell unit. That is easy to study. But it is not like a eukaryotic, so maybe we need to go bigger to plant cell and animal cell. But cell, certainly, we can agree is a basic unit of life. You remember your high school chemistry, in that you were taught a lot of things about hydrogen atom. I am sure some of you must have wondered why are we learning hydrogen, why not nitrogen, why not beryllium, why not lithium, why not gold, Au.

Well, the simplest, simplest answer to that question and the series of questions is not because we favor one atom or another but because hydrogen is the simplest atom. If we at least understand something simple, then we can understand something complex. If you do not even understand the simple thing, then how can we understand the complex.

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Why numbers?

- Physical laws expressed in mathematical language
- **Concepts** and **generalities**
- Connect apparently unrelated properties

Geometry $\pi = C/2r$ Statistics $PDF_{\mu,\sigma}(x) = \frac{1}{\sigma\sqrt{2\pi}} e^{-\frac{(x-\mu)^2}{2\sigma^2}}$

The slide includes a diagram of a circle with radius 'r' and circumference 'C', and a graph of a normal distribution curve with mean 'μ' and standard deviation 'σ'. A vertical text on the right side reads: 'E. Wigner - "The unreasonable effectiveness of mathematics in the natural sciences".'

So, in a similar way, Escherichia coli serves as a hydrogen atom of cellular biophysics, which means that the E coli cells represent the simplest form of a cell that we can understand thoroughly because we know so much or almost 100 years, we have been studying it as biologists. I am not 100 years old. We know the genes, their organization.

We know other cell types that are complications of the same cell. And we can make number estimates. guesses about the numbers, ideas about the quantitative nature. And you can check out facts because there is data out there. So, this is why not just are we studying, focusing on cells we are also studying one kind of focusing on one kind of cell namely E coli.

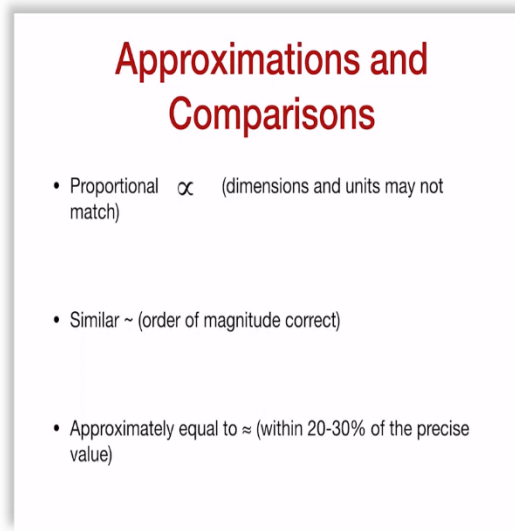
So, second question you can ask is, of course, why should we bother with numbers, why is quantitative biology is so important. And the simple answer is that physical laws are expressed in mathematical language, mathematical language is nothing but a relationship between numbers. We need concepts and generalities because otherwise every time we look at a new bacteria, we will always ask what is the name, where do we find it, we do not know anything else about it, etcetera, etcetera.

So, quantitation or numbers allow us to connect what may be otherwise unrelated properties supervision. The most obvious two ways by which numbers apply to biological systems are geometry and statistics. We will also come to some more complicated and more specific way of looking at it. But biostatistics is one of the most impressive tools in the field of biology, because none of Mendel's laws could be possible without the use of statistics.

And none of the theory, the beautiful and very useful theory in physics, because of which we have our cell phones, satellites, rockets, automobiles, aero planes, all of these would not be possible without maths. Eugene Wigner, who is a well-known theorist in mathematics, wrote an article on the unreasonable effectiveness of mathematics in the natural sciences, I recommend those if you are interested in reading it further, this is not compulsory. So, it is not surprising that maths is important.

And therefore, if we want to bring biology closer into the natural sciences, we need to think of it in terms of numbers also. So, the geometric idea was π is equal to C by $2r$, this is what you get from quantifying a circle. And this is the Gaussian curve, and it is a probability distribution function with σ μ , so that is the σ the standard deviation, μ is the mean is given as $\frac{1}{\sigma \sqrt{2\pi}}$ into exponential minus x minus μ whole square upon two σ square.

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Approximations and Comparisons

- Proportional \propto (dimensions and units may not match)

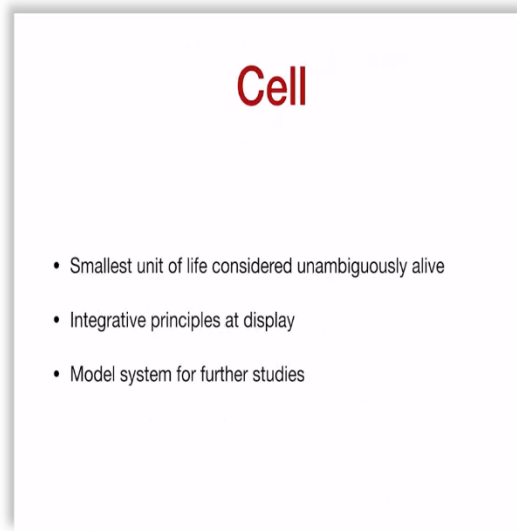
- Similar \sim (order of magnitude correct)

- Approximately equal to \approx (within 20-30% of the precise value)

I keep referring to approximations, and I want to state three rules here. The three rules are, you can use the proportional sign between two variables when the dimensions and units may not match, meaning to say, volume is proportional to length, the units do not match the dimensions do not match, dimensions does not match, if there a cube actually. Similar means they are order of magnitude correct.

When I say that the acceleration due to gravity is similar to 10 meters per second square, meaning to say it is not 100 and it is not 1, it is 9.8 meters per second square, so order of magnitude I am correct. Approximately equal to means with the two-tilde sign and within 20 to 30 percent of the precise value. Please remember these three rules of approximation and comparison is important.

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For a cell, which is the smallest unit of life that we can unambiguously, meaning without debate without discussion say that it is alive. Many integrated principles are displayed and it serves as a model system for further studies. So, in the next sections, we are going to try to enumerate a cell, meaning quantify a cell. Give us a feeling for numbers. Get some sense of time, energies and sizes, and get at concepts of cellular organization.