An introduction to concepts for the Cell Biology course (How does life work) RL150523

Life is made up of cells. A cell is the basic unit of life. Cells can live independently (single celled life), or together (multicellular life). The Science that studies how cells function, and function together, is called cell biology.

There are hundreds of sorts of cells, but there is one major division. Prokaryotes are relatively simple cells, which tend to live by themselves. Eukaryotes are more complex cells and the sort of cell that can easily cooperate with other cells. Which they tend to do, as multicellular life forms. Humans are made up of billions of eukaryotic cells that work together.

Cells are small. A cell is so small you can't see it except with a microscope. Most cells are one hundredth of a millimetre (10^{-5}m) across. You can see exactly how small cells (and DNA and atoms) are in this video: https://www.youtube.com/watch?reload=9&v=uaGEjrADGPA

Most life on Earth consists of one cell, which means that these cells must do all the stuff necessary to live by themselves. Which is a lot. Because they have to perform all kinds of functions in a small volume their potential to evolve is limited. Multicellular life like humans consists of billions of cells. This has the advantage that cells can specialize, for example to eye and brain cells. That is why you can read this now, and a bacterium cannot. Cooperation and specialization are key to complex life. In this way, multicellular life can form something that transcends the sum of its parts (https://en.wikipedia.org/wiki/Emergence).

Life is cooperative. A single cell is limited in size because it must take care of his own energy supply. If a cell becomes bigger it will start to suffer from an unfavourable surface/content ratio. As soon as a cell becomes twice as large (its diameter increases by a factor of 2), the surface increases by a factor of 4, but the volume increases by a factor of 8. This has the unfortunate effect that there is relatively less surface area to provide the larger inside of the cell of the necessary energy and building materials via diffusion. Diffusion does not require any energy, because it relies on gradients found in nature. On the small scale of normal single-celled life, diffusion is very efficient. https://en.wikipedia.org/wiki/Diffusion). Therefore, single-celled organisms have always remained small. The only solution to creating larger, more complex life-forms is to have cells cooperate. The physics of diffusion is why you are not one big cell but a collection of cells that work together.

Total surface area (height × width × sides × number of boxes)	6	150	750
Total volume (height × width × length × number of boxes)	1	125	125
SA:Vol ratio (surface area ÷ volume)	6	1.2	6

Source. https://ib.bioninja.com.au/standard-level/topic-1-cell-biology/11-introduction-to-cells/sa--vol-ratio.html

Note: While the above is physically correct, the recent discovery of relatively large bacteria (and viruses) shows there is more to this story. And shows how biology can find ways around what seems absolute limitations.

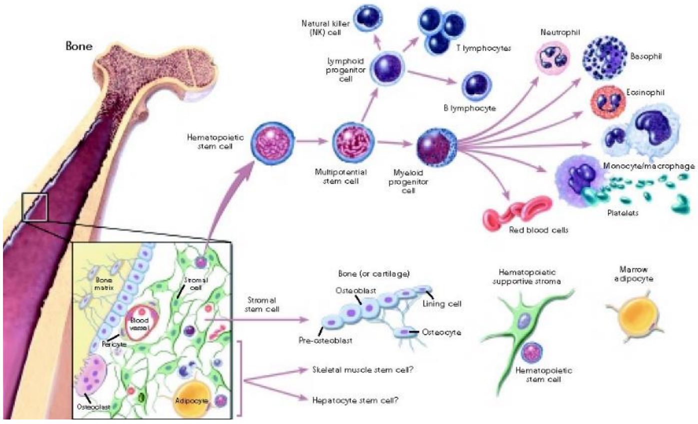
Not every type of cells is capable of efficiently working together. Only so-called Eukaryotes can become specialized. Eukaryotes (Latin for "real nucleus") are not only specialized as cells but are actually so-named for their specialized components, such as the cell nucleus. How eukaryotic cells are build is shown in this video: https://youtu.be/URUJD5NEXC8

Note that eukaryotic cells have specialized energy generators, the mitochondria. Mitochondria are remnants of bacteria (prokaryotes) that started a collaboration with the first eukaryotic cells, hundreds of millions of years ago. (https://en.wikipedia.org/wiki/Mitochondrion). The mitochondria specialized in energy generation and in return got a safe place to live and all the material they needed. Meanwhile the rest of the eukaryotic cell was free to specialize in other tasks. So, in eukaryotes (which includes humans), cells work together in many and deep ways.

Energetic Life depends on mitochondria. Mitochondria are also useful to solve the surface/content problem. If the eukaryotic cell ensures that there are sufficient sugars and other materials in the vicinity of these mitochondria they can, by diffusion, efficiently absorb all these substances and provide the energy that the whole cell needs. Now, when cells acquire many mitochondria (the average cell has dozens), cells can become much larger than bacteria (prokaryotes) and therefore readily specialize, for example to brain cells up to a meter long. Or, to lung and blood cells that efficiently shuttle sugars, building materials and oxygen to the mitochondria everywhere in the body.

Because of mitochondria, life can also function at a much higher energy level, get warm-blooded and develop large energy-intensive brains. Essential to this whole story is the use of Oxygen, which ensures that much more energy can be generated in the mitochondria from a single molecule of sugar (glucose) then is possible without it. However, Oxygen also causes damage by Oxygen Radicals which contributes to ageing. So, ageing is, in part, a consequence of our energetic life-style. Much more on mitochondria, Oxygen and energy can be found in the work of Nick Lane: (https://nick-lane.net/)

Multicellular life has stem cells. A multicellular organism like a human consists of billions of cells that work together. In addition to specialization, this has another major advantage. If a part of the body gets damaged, those cells are removed and the body simply creates a few new cells. In this way, the larger partnership of the organism can continue to function. The creation of new cells is done by stem cells. These are cells that can still divide rapidly, where normal cells hardly divide at all (https://en.wikipedia.org/wiki/Stem_cell).



Source. https://stemcells.nih.gov/info/Regenerative_Medicine/2006Chapter2.htm

Cells actually are continuously damaged, by Oxygen Radicals and UV-radiation, for example. But the root cause of all damage is a physical phenomenon called Entropy, whereby Order always lapses into Disorder, in the long run (https://en.wikipedia.org/wiki/Entropy).

Stem cells can, partly, reverse this decay by replacing the cells that have fallen to entropy. But it is important to realize that in a fully developed individual, replacement can never be 100% complete. In the first place, adult tissues do not always have stem cells (e.g., cartilage), and stem cell capacity is also diminishing with age. More importantly, cellular repair is limited by a necessarily strict control of cell division. Cells that divide uncontrollably are known as cancers. https://en.wikipedia.org/wiki/Cancer. Cumulative damage (original damage minus what can be repaired) is called ageing. Full repair is only possible by rebuilding an individual from scratch, which happens with new generations.

Note: The evidence that life is cooperative is overwhelming. However, there also is evidence that in any individual organism cells compete, for resources and space. Both aspects might be at work at the same time. Therefore, cooperation seems a necessity, not a choice (a phenomenon that also seems applicable to human behaviour). The role of competition is most apparent in cancer. Some cells which are better at dividing will simply outgrow the tissue. This is why cell division needs to be well controlled, and full repair of damage is not possible. Repair and control of cancer have to strike a balance to allow for longer lifetimes. But, as a consequence, indefinite lifetimes are not possible.

Life is modular. Replacing damaged material is not only done at the cellular level. The individual proteins and DNA building blocks inside cells can also be replaced after damage. And only when that is no longer sufficient (this also is never 100% efficient) will the entire cell be replaced. In fact, in a cell, everything is constantly replaced. At the atomic and/or cellular level, after a few years you are formed from completely new parts. This also applies to the brain, and to your DNA. Especially a long living organism like a human is therefore a collection of cells and atoms that constantly changes.

Of note is that incomplete repair of damaged DNA is actually essential for evolution to take place. The need for mutations (https://en.wikipedia.org/wiki/Mutation) might be another reason repair (at least for DNA) is never 100%.

Over sufficient amounts of time (years), an organism such as a human will consist of completely new cells/atoms. You may then wonder whether a person is still the same once all parts have been replaced. This paradox is known as the “Ship of Theseus” (https://en.wikipedia.org/wiki/Ship_of_Theseus). A way around this paradox would be to assume that life is an emergent property of material stuff working together.

Important to realize is that the individual is also a replacement level, as are cells and atoms. Individuals who are damaged (aged) beyond repair are replaced by new ones. This is called generational change (https://en.wikipedia.org/wiki/Biological_life_cycle). This level of replacement is essential for a well-functioning system of life. Also, because small adjustments can be made with each new generation that help us deal with changing circumstances, through evolution (https://en.wikipedia.org/wiki/Introduction_to_evolution). So, you are necessarily a <u>temporary</u> collection of atoms and cells.

Life is information. To know where new atoms and cells should end up in your body, information is needed. The information determines which physical components go were. The information system of life consists mainly of DNA (https://en.wikipedia.org/wiki/DNA).

The transmission of information to future generations is done through a single cell; a really special one. An egg or sperm cell is the ultimate stem cell that can give rise to a whole new organism. The DNA in these cells is handled in such a way that it only carries very limited amounts of the damage (Entropy) that the parent was subjected to, to the next generation. Therefore, the next generation can largely start over.

Note: Most of the protection of information is performed in the egg cell, which is one of the reasons these cells cannot become too old and women generally cannot conceive beyond 40 years of age.

The little bit of Entropy that is passed on, are a few mutations and epigenetic modifications. These are necessary for adaptation to new circumstances. Epigenetics works through changes in how DNA is used, not through changes of the DNA itself (https://en.wikipedia.org/wiki/Epigenetics).

Epigenetics works via RNA, especially microRNAs. In addition to DNA, there is therefore another important information system. RNA is more than just an intermediate form of DNA to convert information into proteins. Many life forms, including some viruses (like Corona), do not even have DNA at all, but they do have RNA. https://en.wikipedia.org/wiki/RNA).

Mutations provide for evolution in the longer term. Epigenetic modifications provide for shorter-term evolution. And through epigenetic modifications, limited information about the parent's experiences can also be passed on. Entropy is thus used by life to amass just the right amount of damage. Also, Entropy is key to efficient energy generation and a host of other basic biological functions. Therefore, the very physical restrains that work against life, make it possible at the same time.

Of note is that because of the importance of information to life, there is much potential in using information technology to manipulate life. Also, information does not seem to be subject to decay by entropy. This might be one of the reasons it is so useful for a system that can endure the ages.

Life acts through proteins. DNA and RNA (information) does not do much in your body. The structures that eventually do the work in a cell and beyond, are proteins. They build and maintain a body. Proteins (https://en.wikipedia.org/wiki/Protein) give a physical structure to life forms, but these are therefore subject to Entropy. Information (probably) is not. This is why each form of life has two systems side by side, information and proteins.

Requiring two separate systems makes it difficult to imagine how life could have arisen. Both systems are complex and must have developed at the same time because they depend on each other. And both systems are organized in a completely different way. Here, RNA might have played a key role. RNA can contain both information and do work. https://en.wikipedia.org/wiki/RNA_world However, the role of RNA in life as we know it now is mainly to carry information.

Anyway, a human (and every other life form) is a double system. And by transferring (almost) only information from one generation to the next, physical degradation (Entropy) is suddenly no longer a hindrance. Generational change is therefore essential for keeping the system of life going, in the longer term. Mostly information is passed on so that every new generation can start fresh in the fight against Entropy. The fact that life is partly information is the escape clause that life has found in order to be able to continue to exist in "deep time" (4 billion years and counting) (https://en.wikipedia.org/wiki/Deep_time).

Life wants to endure. Life depends on new generations. But those generations first have to be produced. For any organism, this means it must first survive a certain amount of time before it is able to reproduce. Anything without a strong survival instinct will not be able to pass on its information. Because this behaviour is hard-wired (through relentless selection over the ages) evolution makes us all want to keep on living, even after we have already reproduced. This causes social and psychological problems. Replacement is essential but we do not want to be replaced, because we are necessarily afraid of death.

But, eventually, all physical components are replaced, including individuals. A human being is necessarily a temporary collection of cells and atoms. Individual life is by definition temporary. Only in this way the system of life can endure. Even if we value (our) individual life, it is important to realize that biology works as a system where individual atoms, cells and humans are eventually replaced.

Much more (technical) information about cells, energy and DNA can be found in the book: Molecular & cell biology for Dummies (author: Rene Fester Kratz). This is also recommended for the course.

This introduction is a primer for the course “Cell Biology” (How does life work?) which consists of eight classes:

Information (DNA/RNA)

Energy (mitochondria)

Communication (cooperation of cells)

Biochemistry (how atoms and charge make proteins)

Immunology (how do we stay healthy)

Stem cells (resilience and ageing)

The nervous system (emergence and consciousness)

The future of cell biology (new therapies, and new ethical issues)

R. Licht PhD., Goirle, 2023