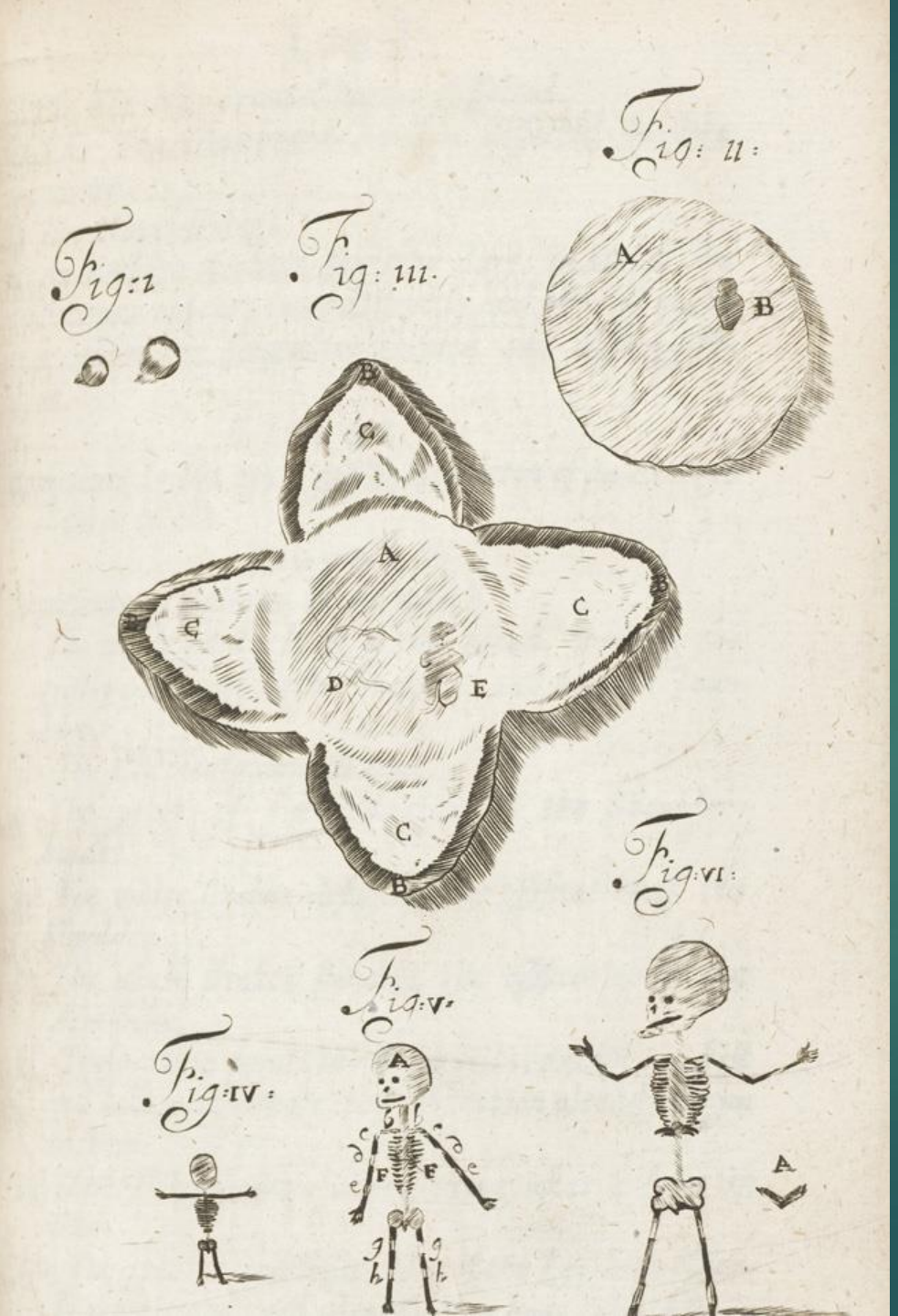
HPS208 – How we think about life

Key Terms

- The Machine Conception of the Cell
- Inheritance
- Paley's Argument from Design

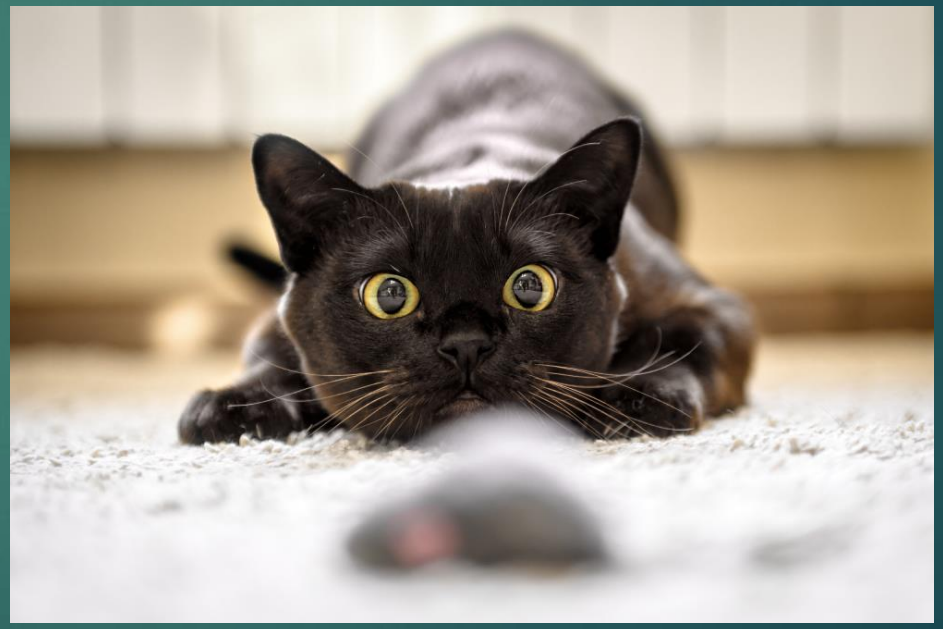


Review

- Last time we talked about preformationism, as a response to the difficulty of reconciling mechanism with embryonic development
- I doubt many people were swayed to become committed preformationists

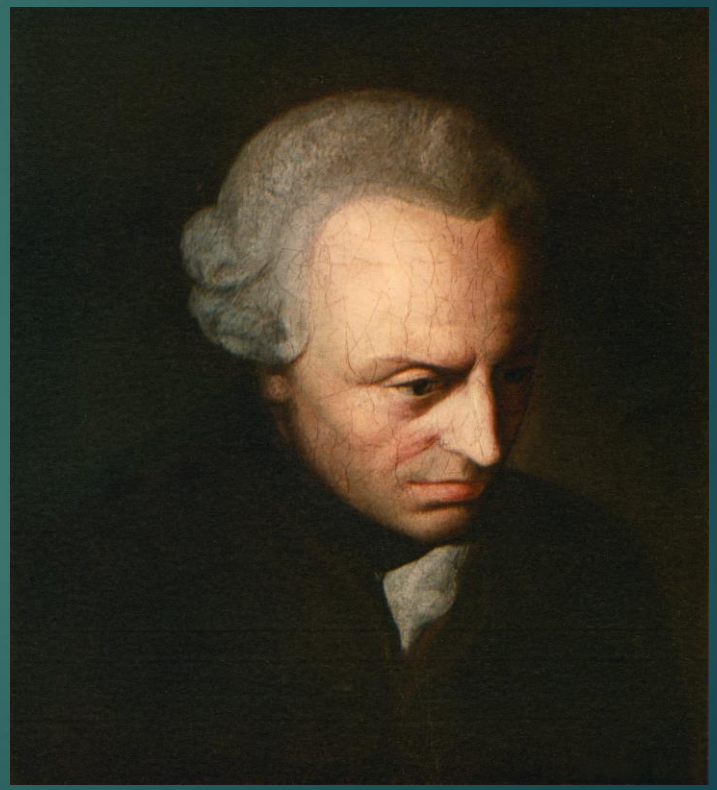
Organic Unity and Purposiveness

- One of the central arguments used by Malebranche (1638-1715) for preformationism was the fact that living things look designed
- And further, that each of their parts depends on the whole organisms for its function
- E.g., just a heart doesn't do you much good without a circulatory system, lungs, nerves, etc.



Kant's Critique of Mechanism

- Immanuel Kant (1724-1804) made a very similar argument, though not for preformationism
- Kant was on board with the idea that scientific explanations of material things should be mechanical
- But he also thought living things posed a particular problem

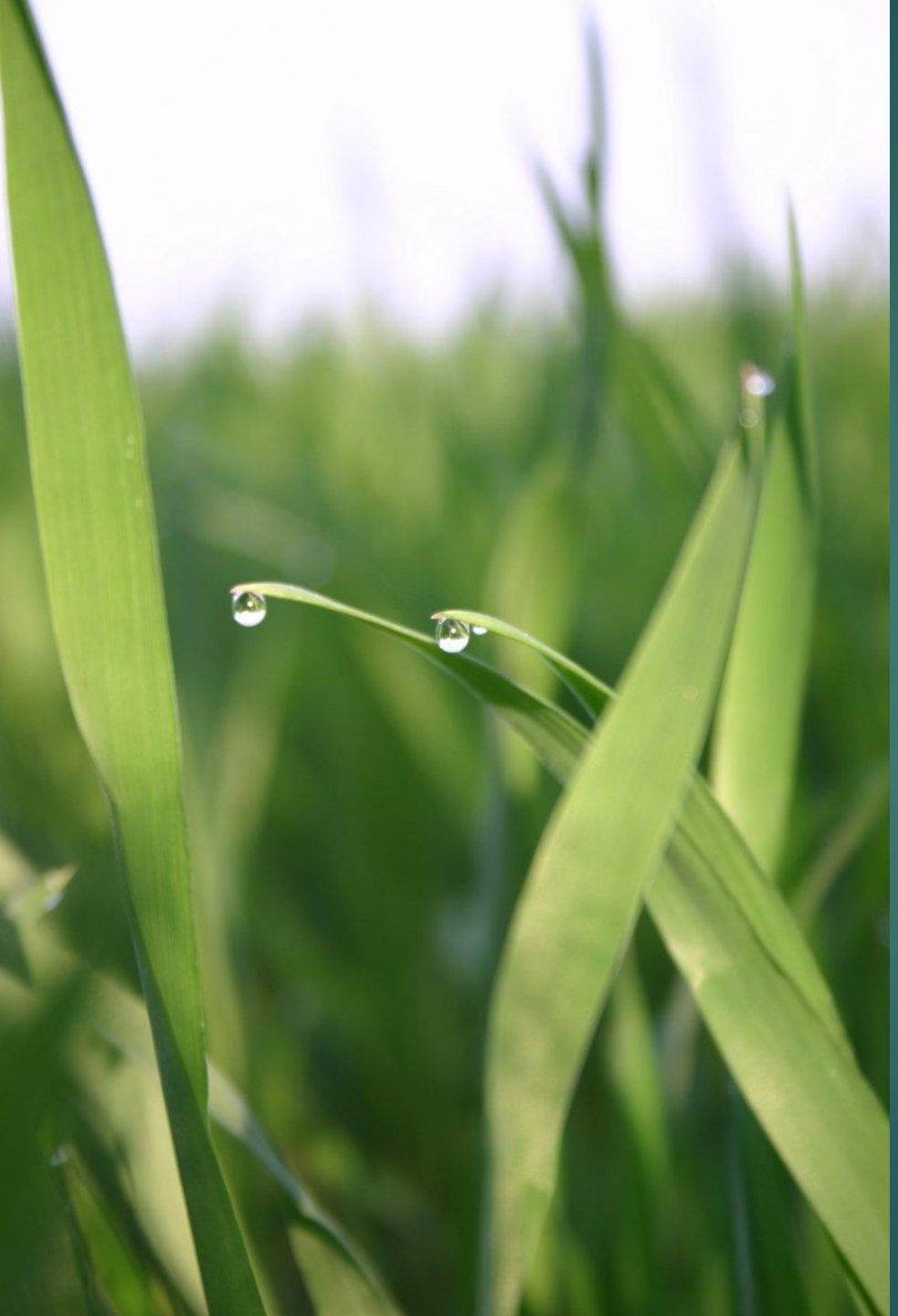


The unity of organisms

- In all living things, he observed, the parts seem to serve the survival of the whole, and the whole produces the parts
- "nature, considered as a mere mechanism, could have formed itself in a thousand different ways without hitting precisely upon the unity in accordance with such a rule" (Kant, 1790/2000, 5:360)

Hollow bones

- The bones of (most) birds are much less dense than terrestrial animals, practically hollow
- Why would that be the case?
- It looks mechanically contingent (it could have been otherwise)

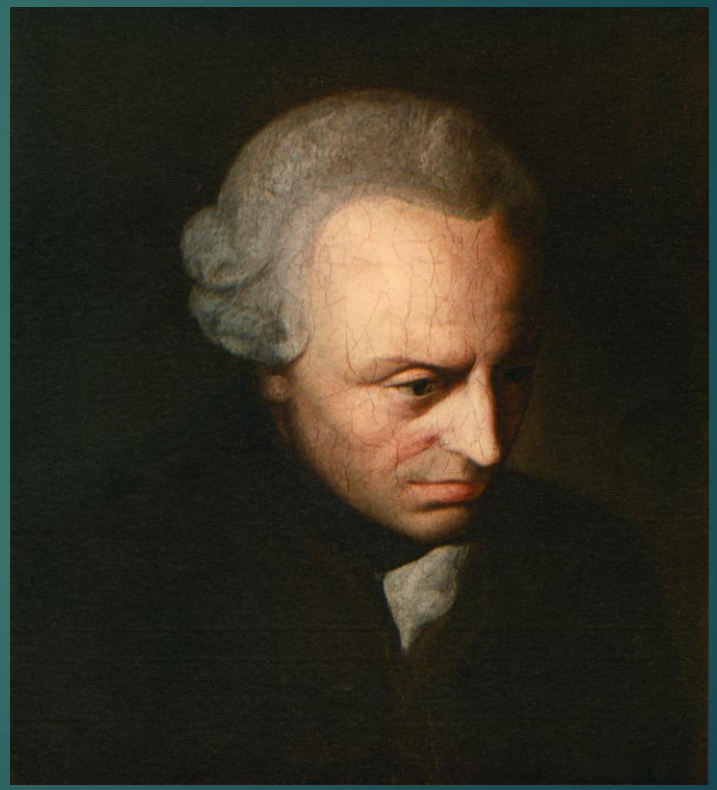


Newton of a blade of grass

- Kant believes only mechanical explanations are scientifically valid
- But he also thinks living things can't be explained without teleology
- Therefore, he says, there cannot ever be a science of living things – no Newton of even a blade of grass

Kant's Critique of Mechanism

- We don't need to go too deep into what Kant thought this demonstrates
- (For the curious, he uses it as one of his antinomies, arguments that are meant to show that we must conceptually distinguish the phenomena of experience from the noumena of reality itself)
- The point for us is just that this argument was still current a generation after Malebranche



The Watchmaker

- Possibly the most famous use of this style of argument was by William Paley, in a 1802 book arguing for the existence of God
- Paley asks us to imagine walking along a beach and finding a watch, perfectly constructed such that it keeps good time
- One would naturally conclude that it had a designer, wouldn't one?

Paley's Argument from Design

(1) Living things appear to have been designed.

(2) The only reasonable explanation of the appearance of design is a designer.

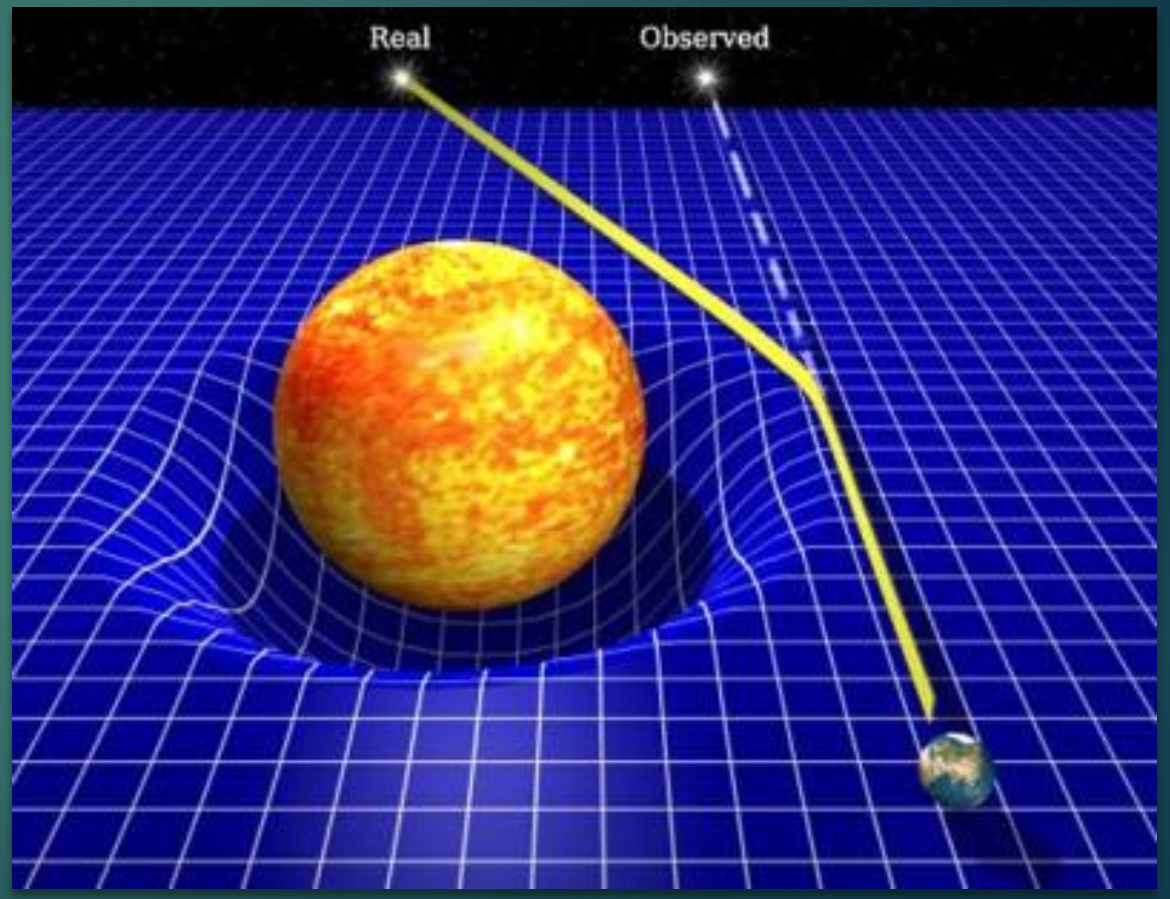
(C) Living things were intelligently designed.

(1) Living things appear to have been designed.

- Paley gives us a brief description of when things ‘appear to have been designed’
- First, the parts seem to *serve a purpose*
- Second, if the parts were just a little different, they would not serve that purpose

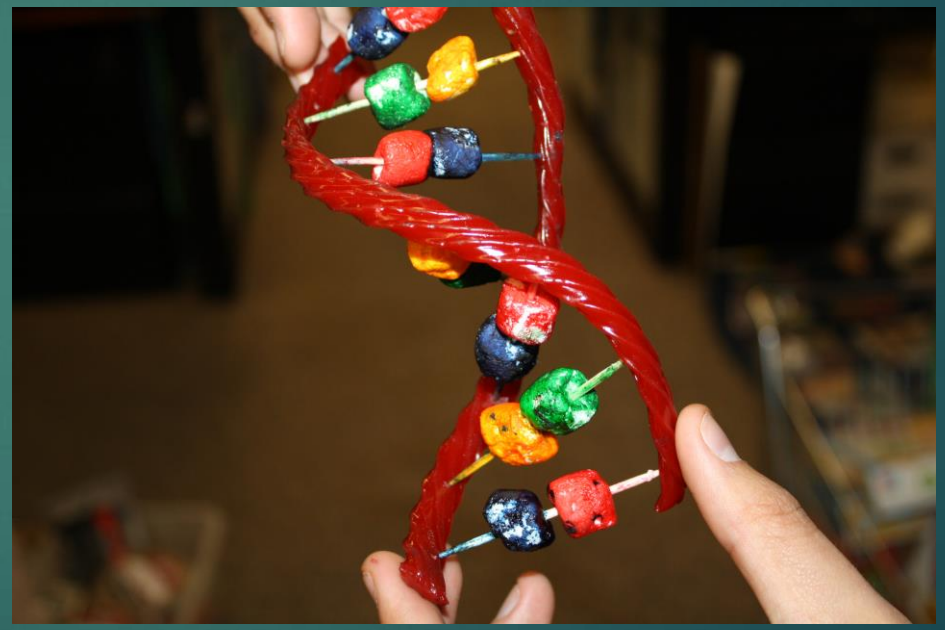
(2) The only reasonable explanation of the appearance of design is a designer.

- This is an inference to the best explanation
- We observe some phenomenon
- Some hypothesis is the best explanation we can give of it
- Therefore, that hypothesis is likely to be true



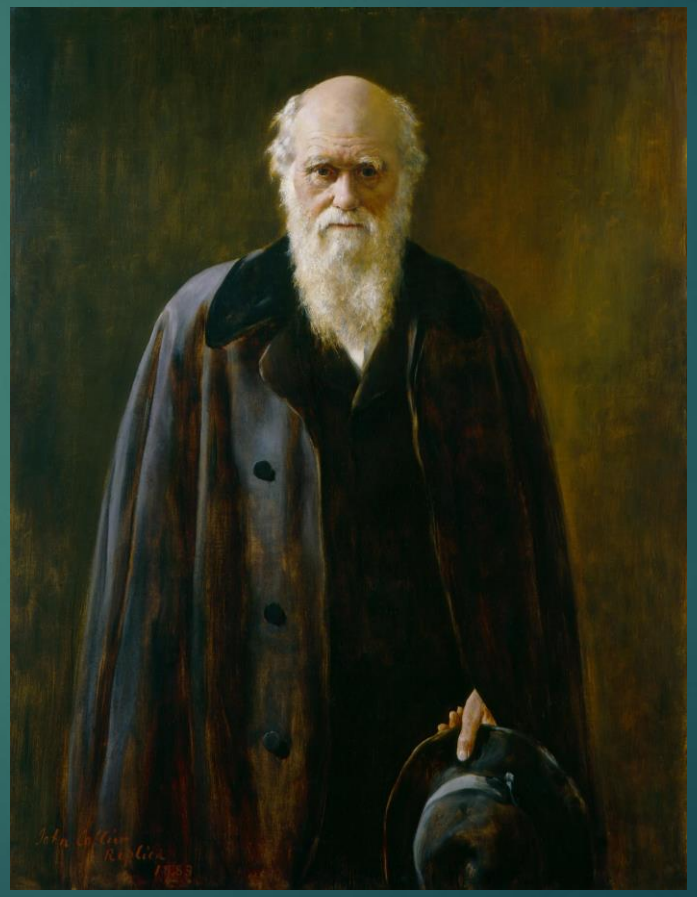
(C) Living things were intelligently designed.

- If the first two premises are granted, it's hard to see how to deny the conclusion
- Most people think (2) is wrong, since Paley was writing shortly before Darwin's theory of evolution was published



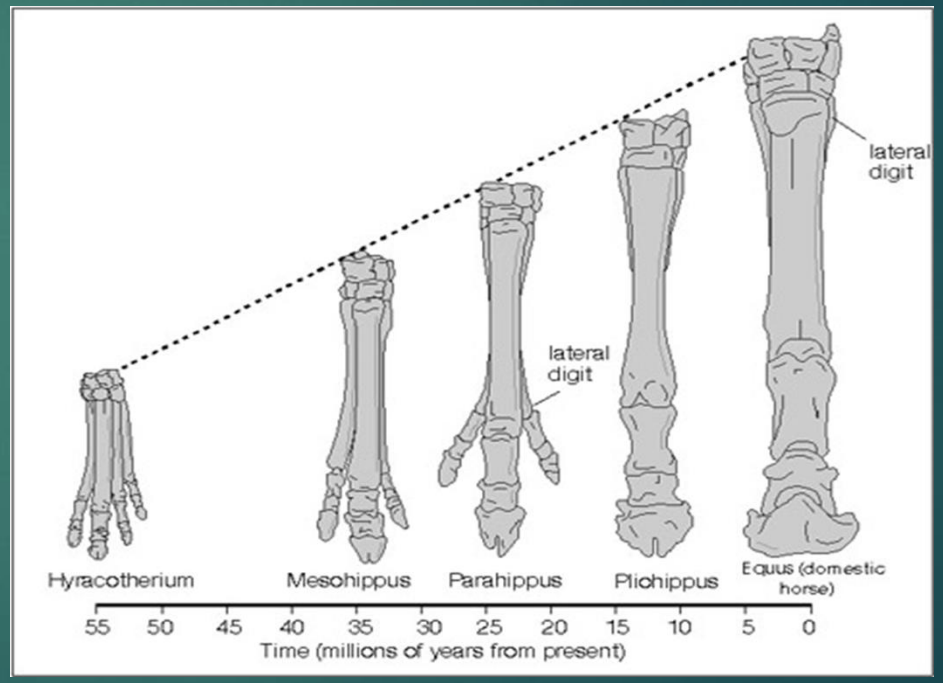
The Origin of Species

- This style of argument lost steam after 1859, when Darwin published *On the Origin of Species by Means of Natural Selection*
- But it's worth noting, people did not leap on board with Darwin's ideas right away
- In fact, a vigorous scientific debate persisted for another 100 years

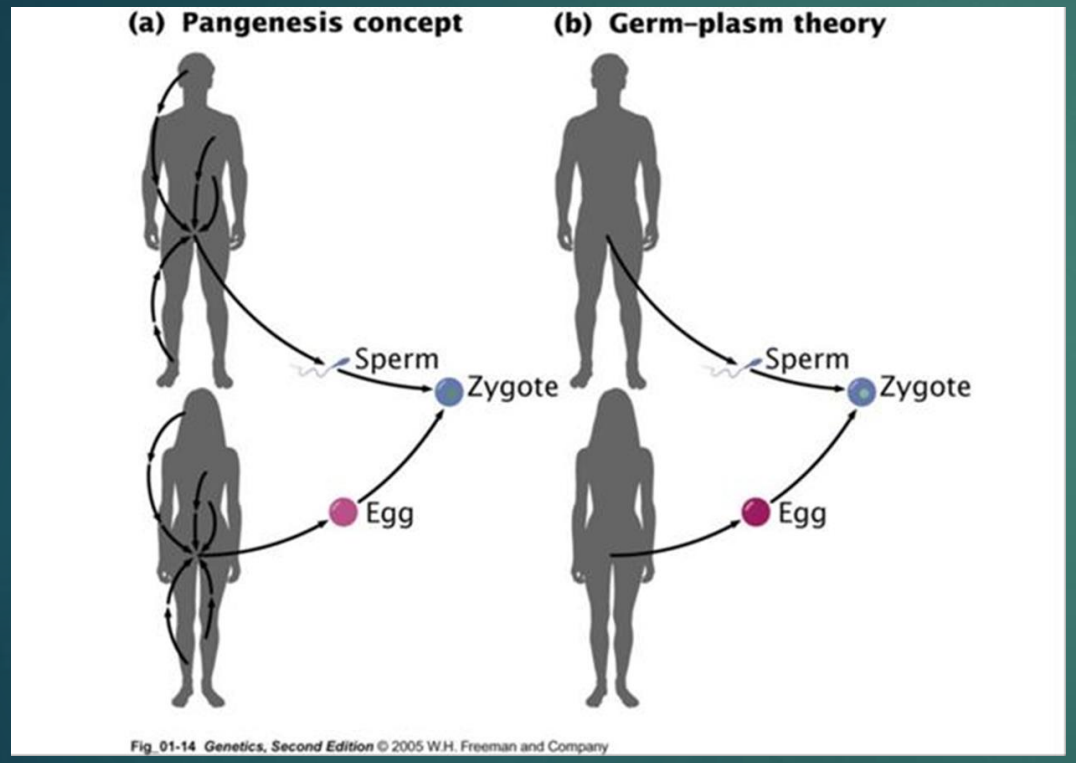


Orthogenesis

- Some early paleontologists for example, didn't find Darwin's picture convincing
- They saw fossils which seemed to show smooth, linear development across massive time-spans
- Some preferred the idea of orthogenesis, which is that species change over time according to internal principles
- People differed on which principles they thought those were, from an inner "perfecting principle" to just small mechanical changes across generations

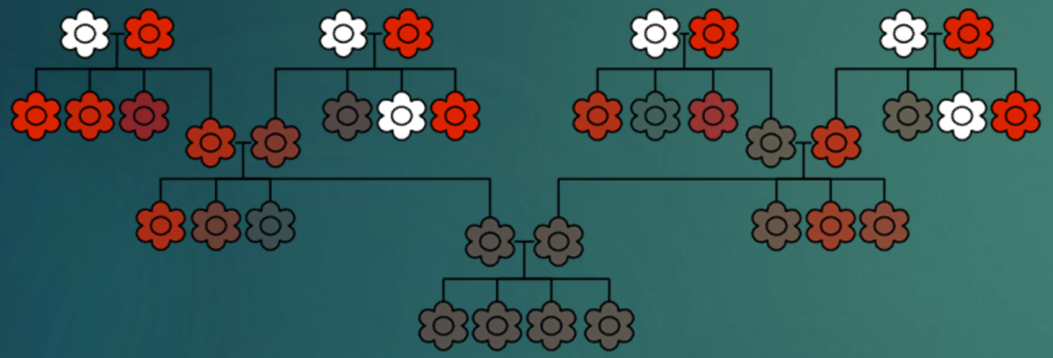


Inheritance



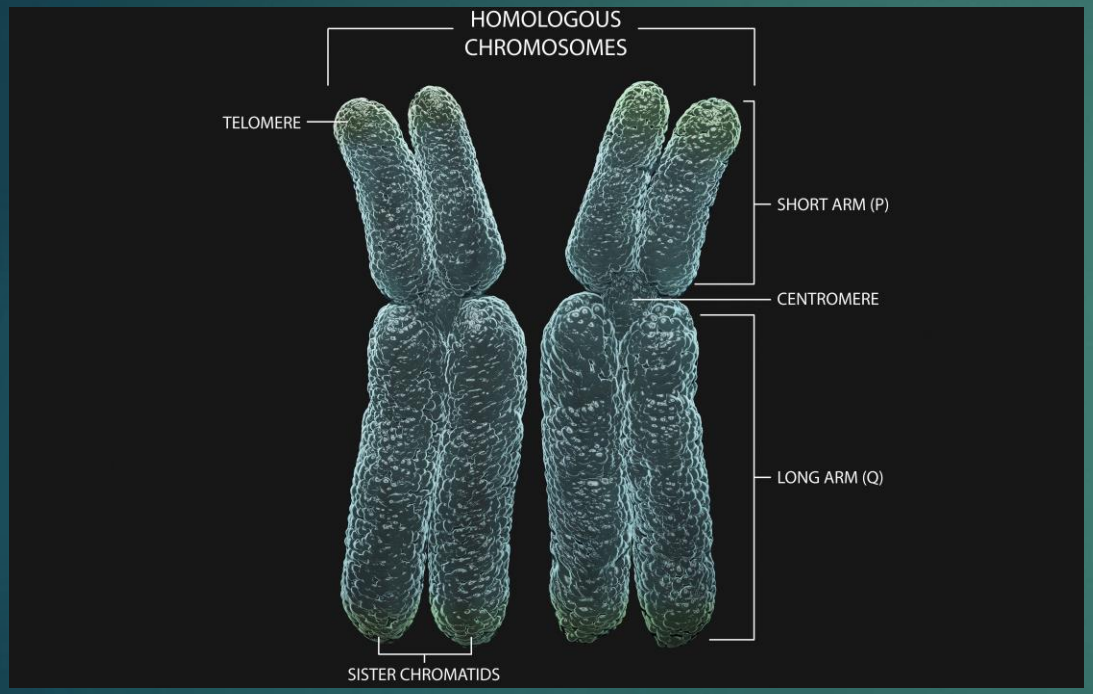
- Darwin's theory of inheritance was also a bit of a problem
- Darwin was a pangenesist, who thought that tiny "gemmules" were collected from all over the body to transmit form to the next generation
- In an 1889 publication, August Weismann described testing this by cutting the tails off of five generations of mice
- Unsurprisingly, each new generation of mouse had perfectly formed tails

Blending Inheritance



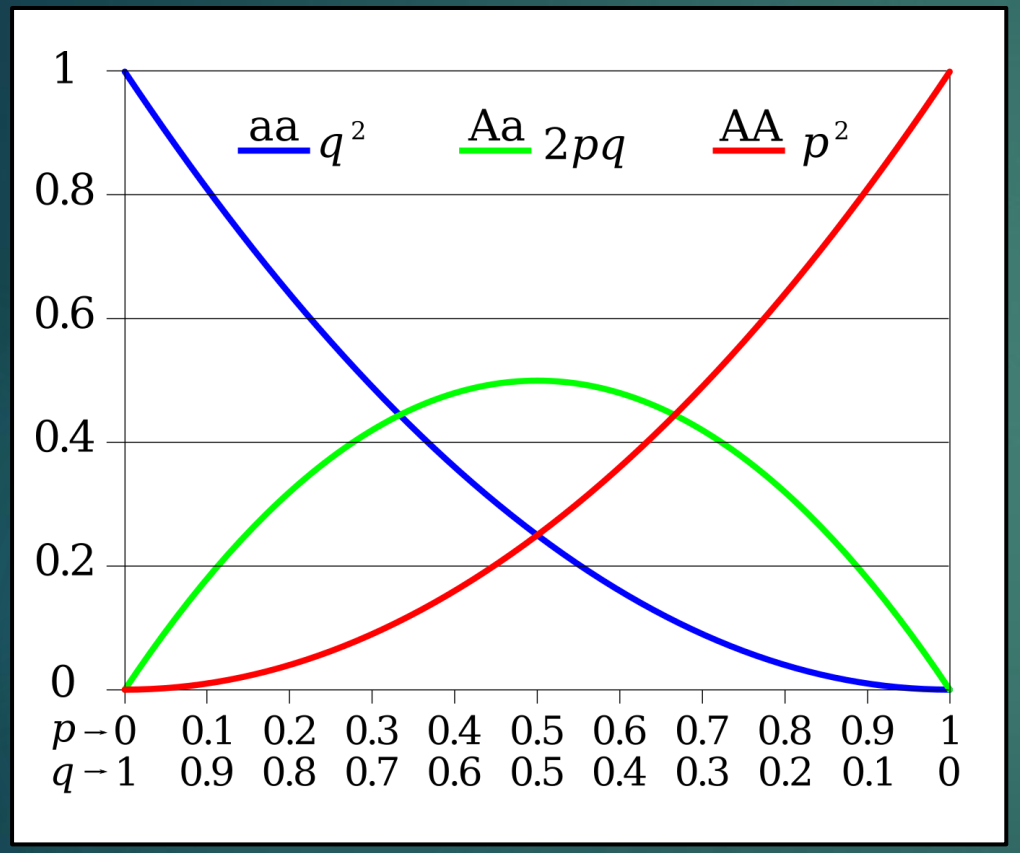
- Darwin also subscribed to ‘blending inheritance’
- This is the idea that for any given trait, children will be (on average) a blend between their two biological parents
- But there’s a problem here, for a theory that says natural selection actions on variation in a population…

Inheritance



- In the late 1800s and early 1900s, the chromosomes were first observed and identified as a possible location for hereditary material
- In the 1920s and 30s experiments on drosophila flies allowed the very first rough mapping of where on a chromosome a given trait could be coded

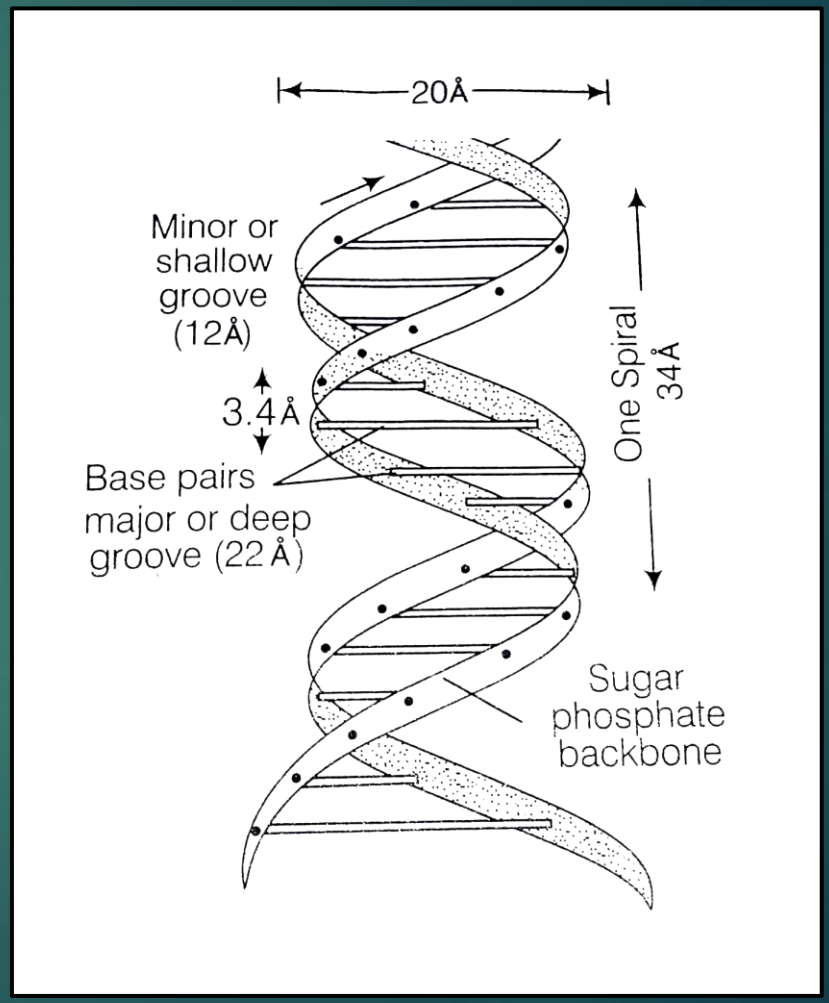
The Modern Synthesis

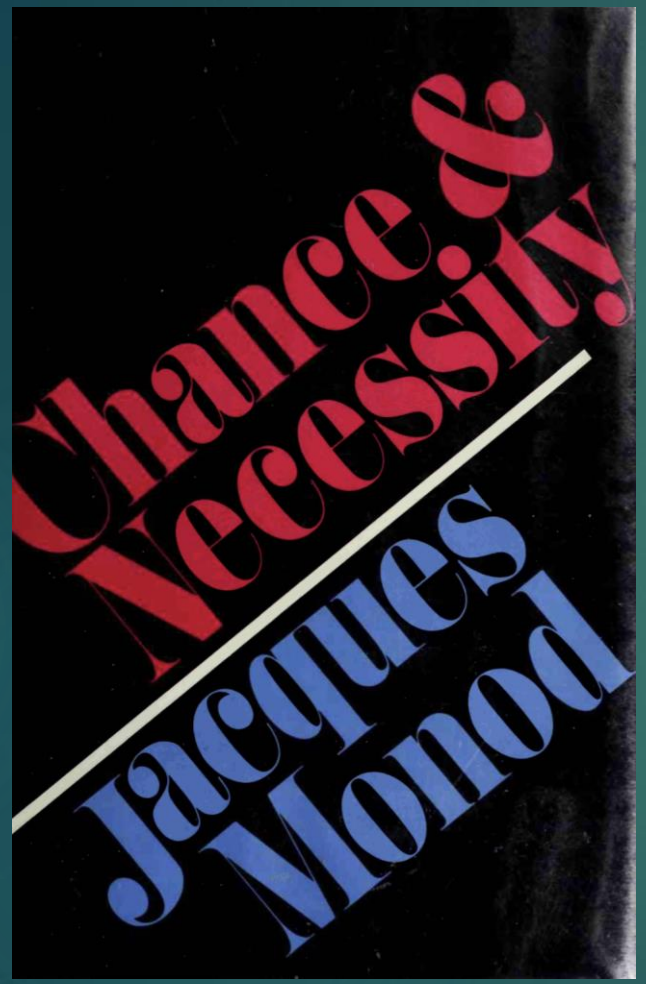


- In the 1930s and 40s, a picture of evolution which incorporated mendelian genetics with some mathematical models borrowed from physics emerged
- It showed how you could get something that looked like blending inheritance by assuming a large number of separate, randomly assorted genes

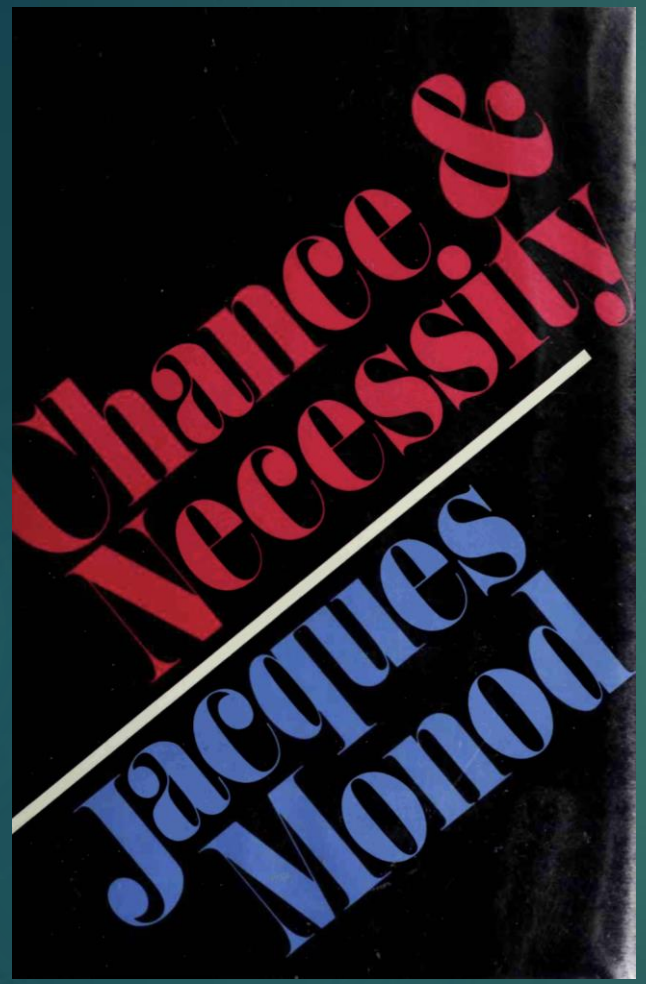
DNA

- Then in 1953, using some x-ray crystallography data they stole from Rosalin Franklin, Watson and Crick published the model of the structure of DNA
- It's exactly the sort of thing assumed by the Modern Synthesis view





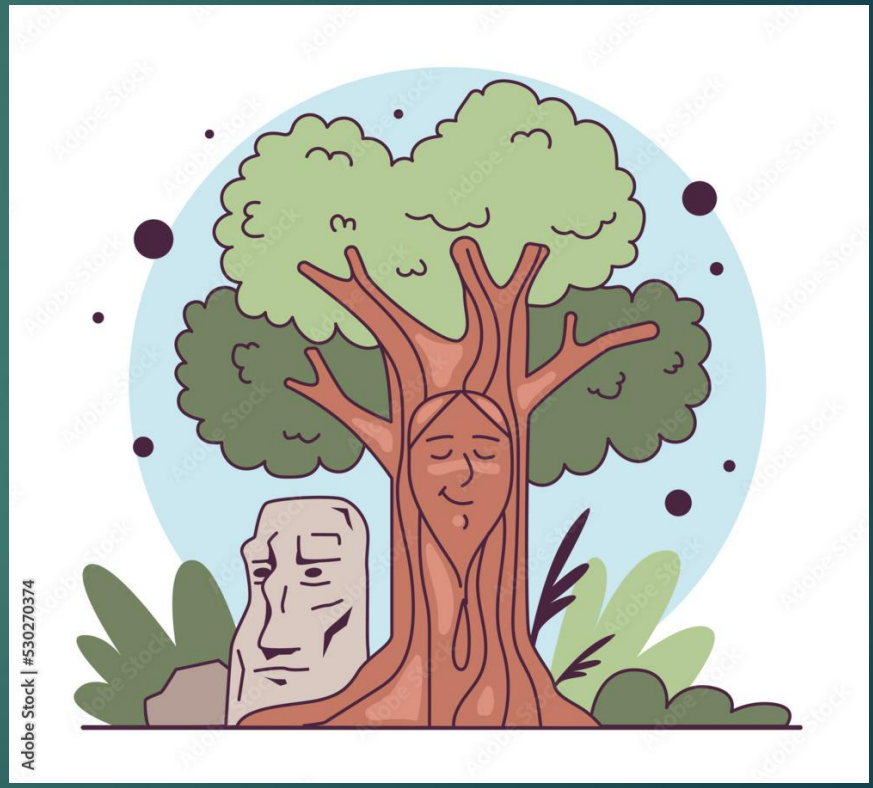
- Nobel prize winning biologist Jacques Monod's 1970 *Chance and Necessity* was a bestseller (by the standards of popular science books)
- He tried to translate for a popular audience what he thought the new science of molecular biology meant for people and our relationship with nature

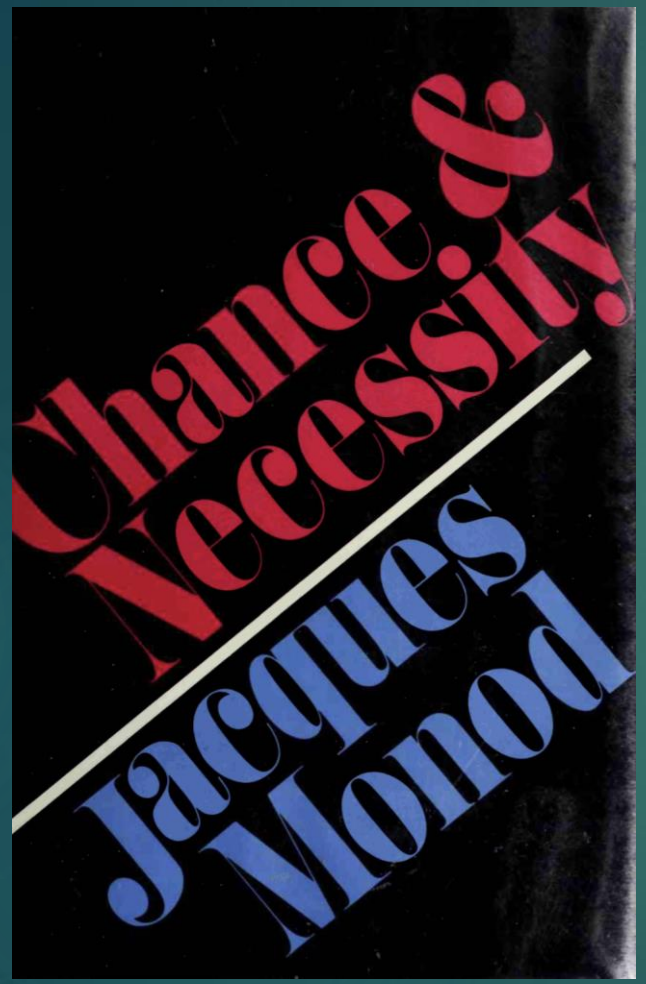


- Monod argued that we are basically programmed by our genes
- And our genes are the product of natural selection working relentlessly on random variation
- In this sense, he argues, we are accidental creatures who appear designed only because of the certainty of death for any creature that happens to vary in the wrong ways

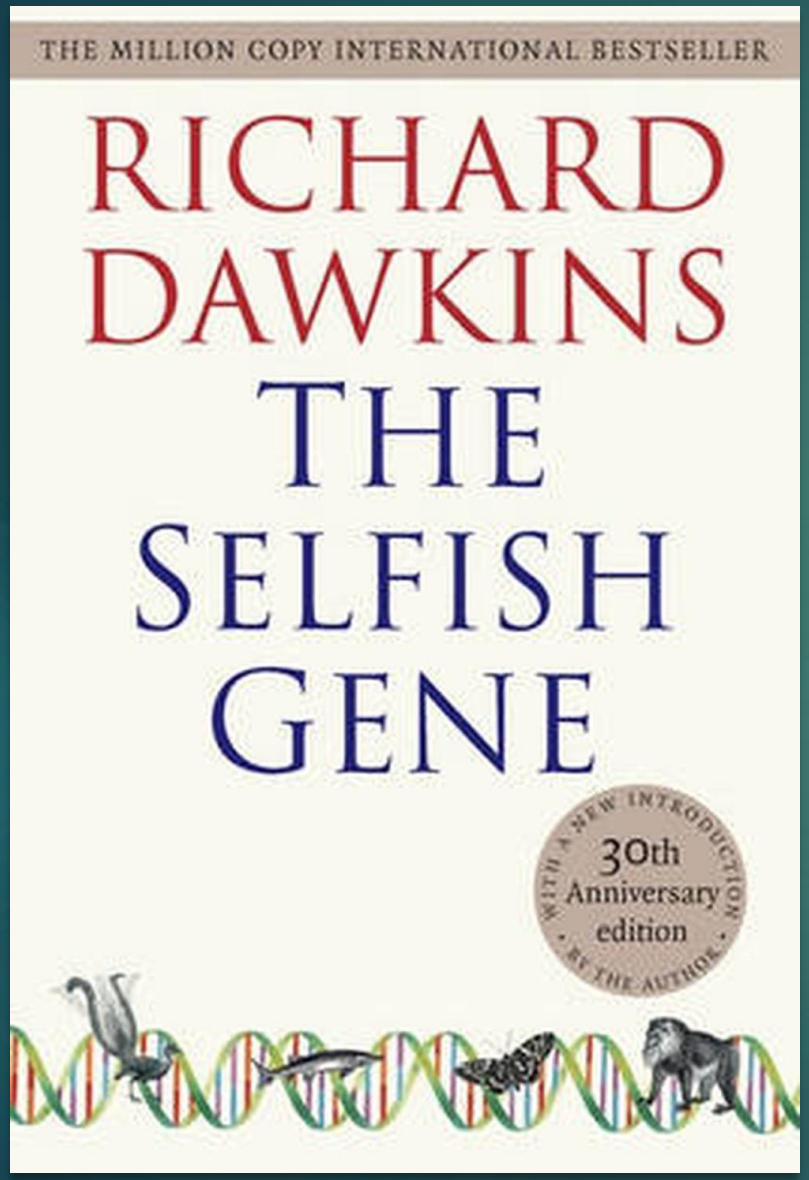
The ancient covenant

- “Man must at last finally awake from his millenary dream ; and in doing so, awake to his total solitude, his fundamental isolation. Now does he at last realize that […] he lives on the boundary of an alien world. A world that is deaf to his music, just as indifferent to his hopes as it is to his suffering or his crimes.”
- (Monod, quoted in Prigogine and Toffler p. 3)



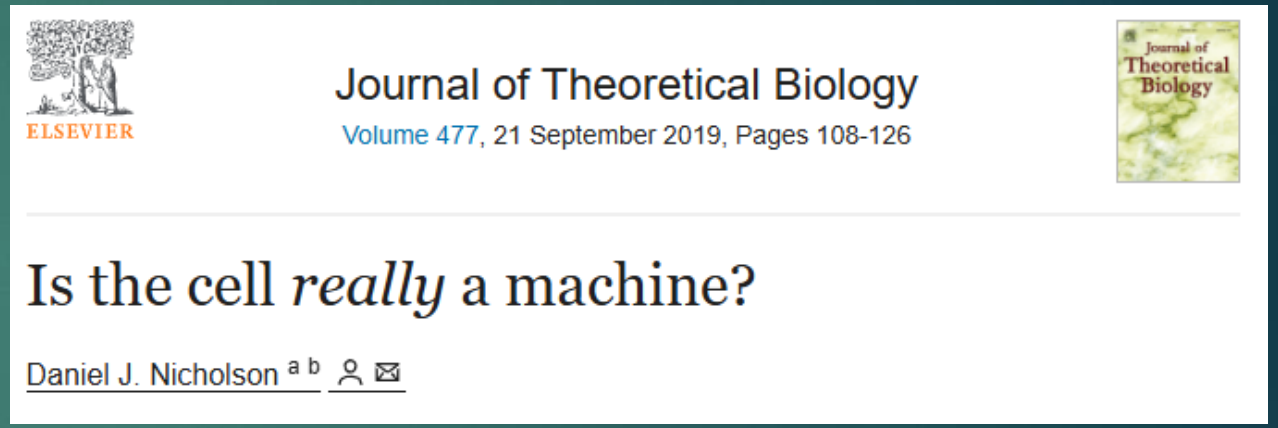


- "Through its properties, by the microscopic function that establishes between DNA and protein, as between organism and medium, an entirely one-way relationship, this system obviously defies any 'dialectical' description. It is not Hegelian at all, but thoroughly Cartesian: the cell is indeed a machine." (Monod, pp.110-111)



- "We are survival machines—robot vehicles blindly programmed to preserve the selfish molecules known as genes. This is a truth which still fills me with astonishment."
- - Dawkins

- Nicholson argues that despite being a pervasive metaphor across biology, the equation of cells with machines is misleading
- He labels this treatment of cells as little machines The Machine Conception of the Cell (MCC), *aka* mechanicism
- Let's keep mechanism and MCC separate in our minds

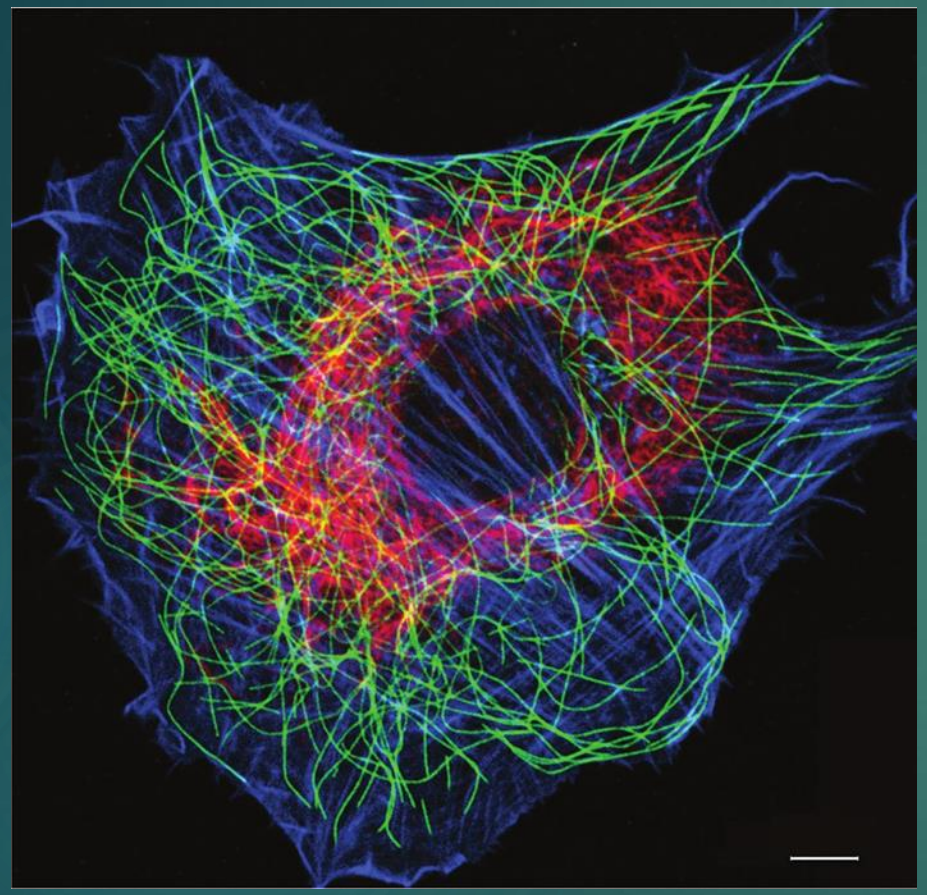


What is a machine?

"…a machine can be characterized in very general terms as **a device with fixed interacting parts that operate in a coordinated fashion to produce a predetermined outcome**. More specifically, one can identify four distinctive properties of machines that are particularly relevant in contemporary formulations of the MCC." (p.109, emphasis added)

What is a machine?

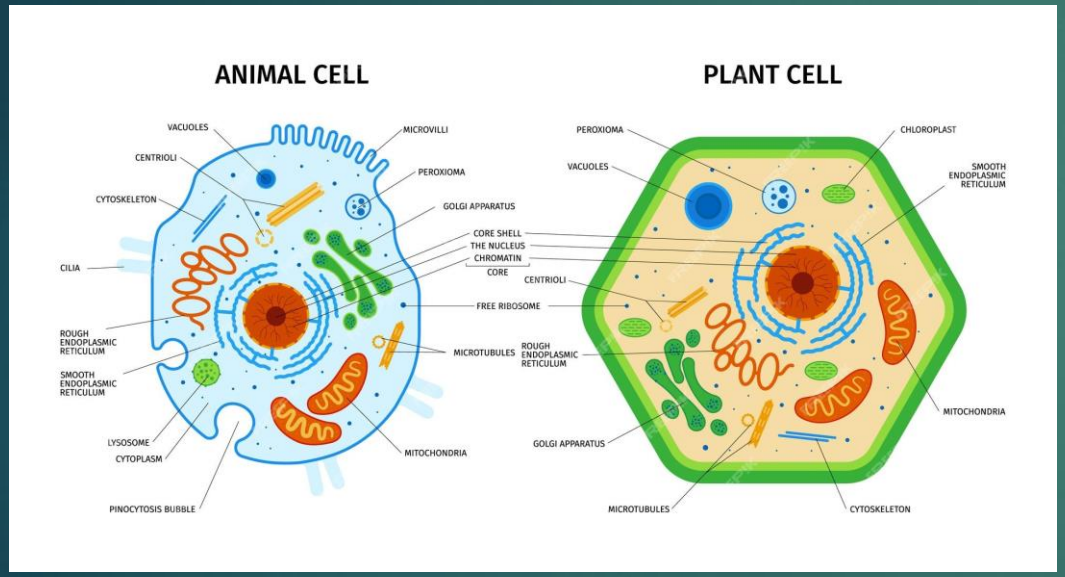
1. Describable by blueprints – a list of parts and how they fit together
2. Designed to efficiently perform a specific function
3. Follow the same sequence of steps every time to achieve that function
4. You can start and stop the machine without it falling apart



Describable by blueprints – a list of parts and how they fit together

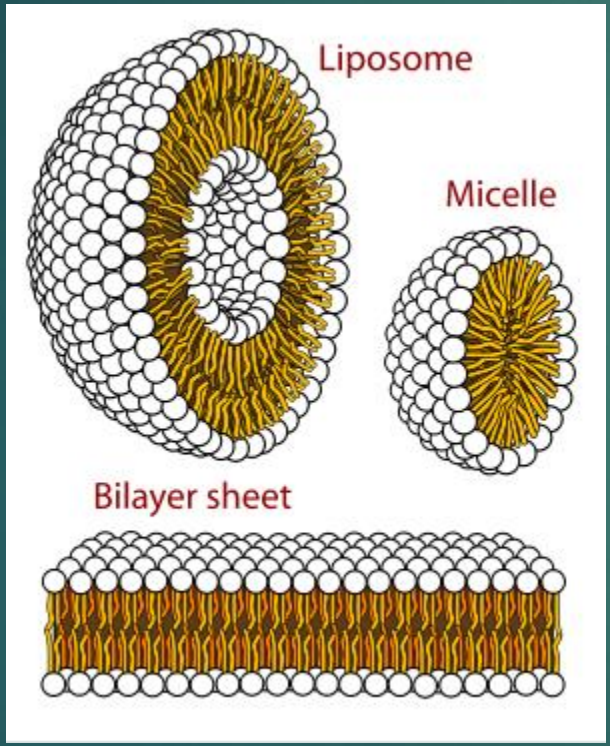
Vs. Self-Organized

Cellular Architecture



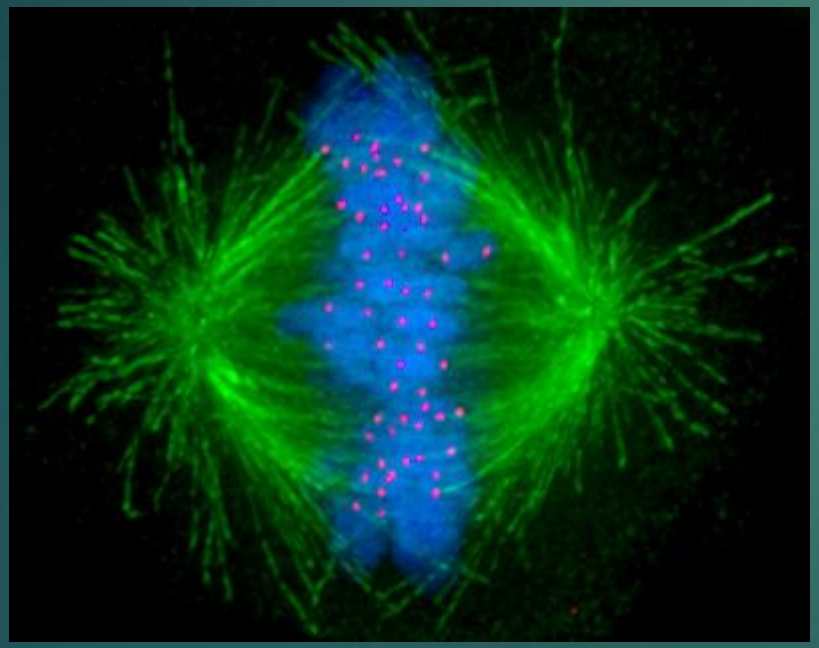
- Prior to the 20th century, studying cellular architecture involved killing the cell, immobilizing the parts
- But 21st century labelling techniques allows cell biologists to follow individual molecules, proteins, enzymes, etc
- What they found, Nicholson argues, is that a living cell involves much less self-assembly than believed, and a lot more self-organization

Self Assembly



- Self-assembly is when molecules clump together into a shape naturally
- The lipid bilayers that form our cell walls, for example, are the result of basic chemistry
- One end is attracted to water, and the other is repelled by it, causing the molecules to arrange themselves neatly
- It takes no work to maintain these shapes

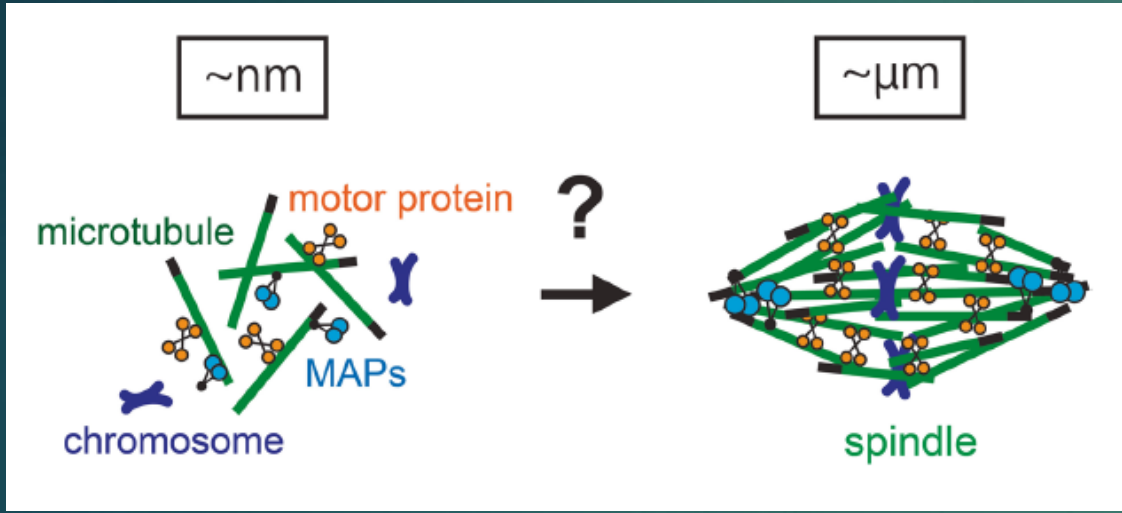
Mitotic Spindle



"The traditional view of the mitotic spindle apparatus as a molecular machine which is built through a defined irreversible set of instructions is gradually being replaced. It can instead be envisaged as a self-regulating dynamic structure where multiple pathways of MT [microtubule] generation are spatially and temporally controlled and integrated, constantly 'talking' to one another and modifying the behaviour of their MTs in order to maintain a flexible yet robust steady-state spindle. (Duncan and Wakefield, 2011, p. 330)"

(quoted in Nicholson, p. 111)

Mitotic Spindle



"During cell division, the network of microtubules undergoes massive rearrangement to self-organize into the spindle, a bipolar structure essential for accurate chromosome segregation. This structure ensures the stable transmission of the genome from the mother cell to two daughter cells, yet the process by which the ordered architecture emerges from a collection of protein "parts" remains a mystery." (p.613)

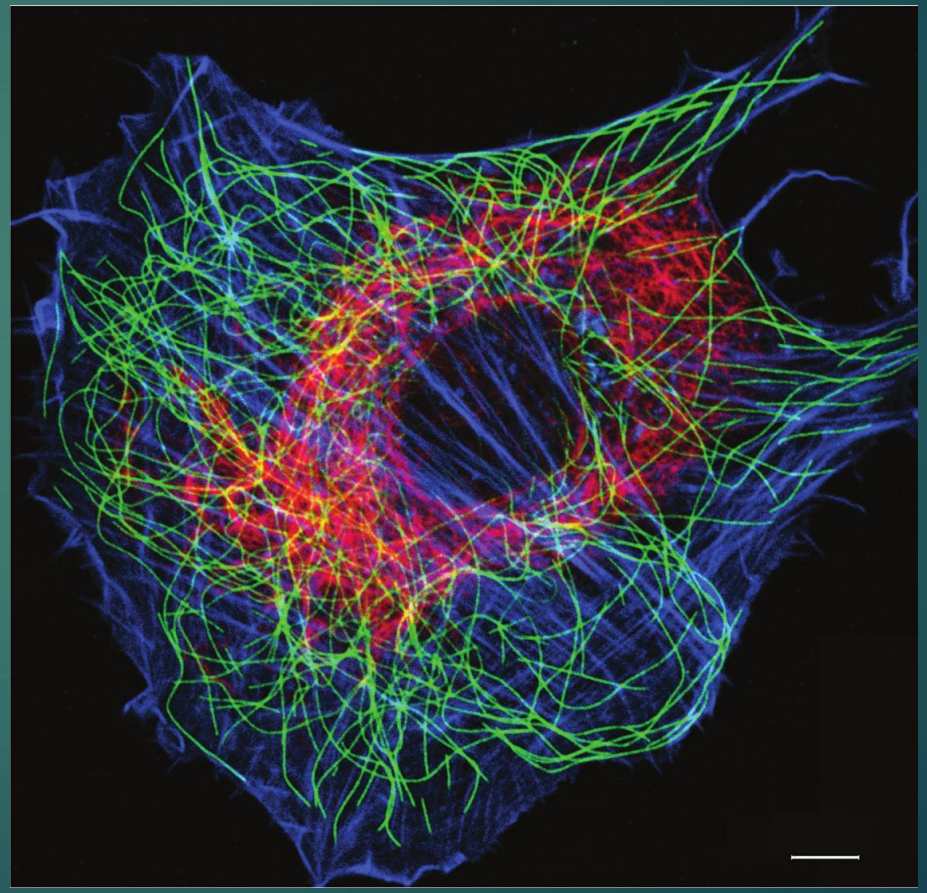
Sridhara, A., & Shimamoto, Y. (2024). Microtubule choreography: Spindle self-organization during cell division. Biophysical Reviews, 16(5), 613-624.

Self-Organization

- In self-organization, the system is not at thermodynamic equilibrium
- Energy (and usually matter) flow through the system
- Without any central authority planning it out, the system spontaneously becomes orderly in some way

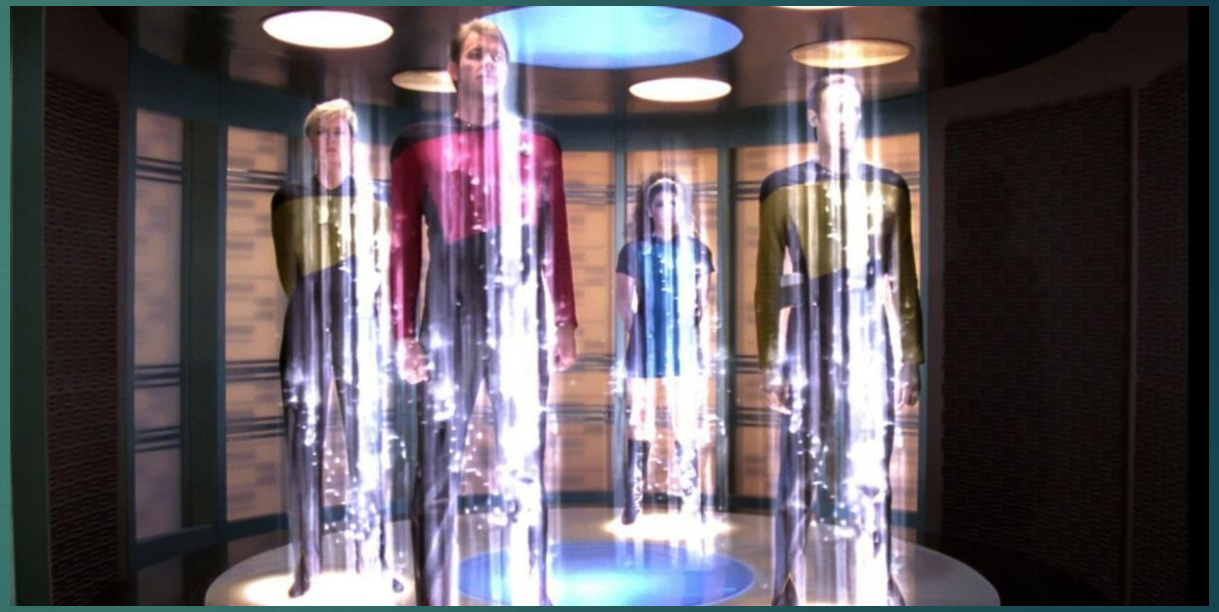
A self-organizing cytoskeleton

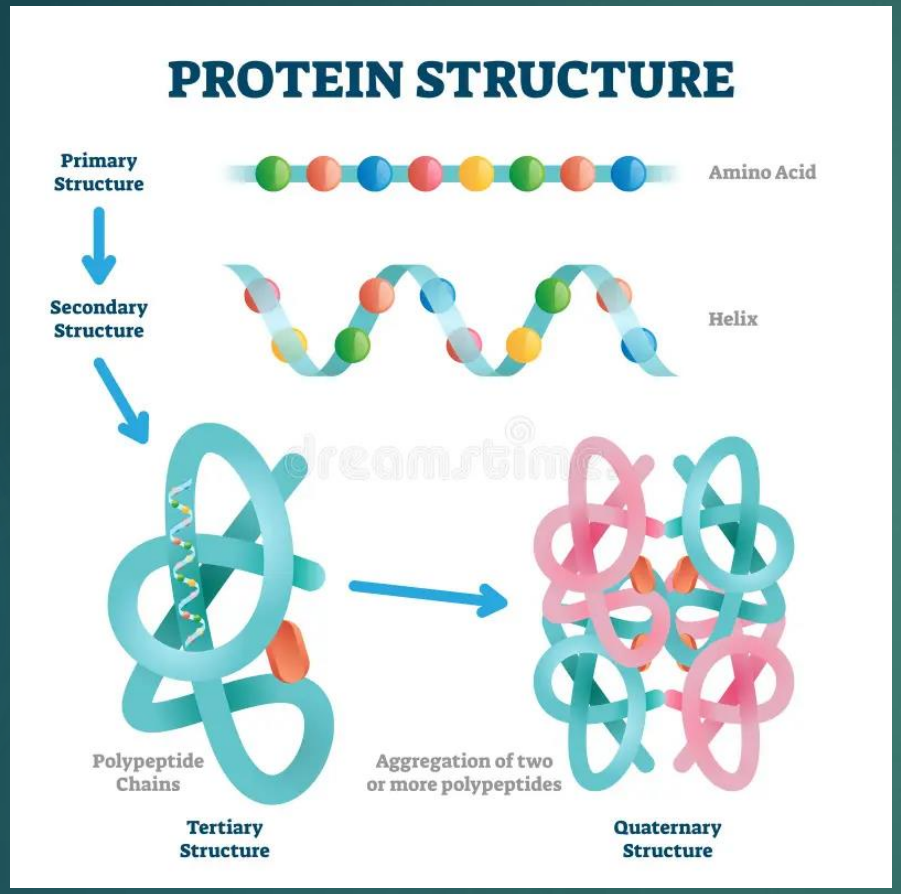
- Nicholson argues that while some parts of the cell are self-assembled, many are self-organized
- E.g., the cytoskeleton, the set of microtubes that give the cell structure
- When parts of this are labelled, it turns out that there is a constant turn-over of matter, which requires energy
- Only the form is preserved, and even that varies dynamically



Form and Matter

- Nicholson talks about how the cell preserves form by cycling through matter
- "More broadly, the transition from a structural to a processual conception of the cellular architecture implies shifting our attention from matter to form. Due to its dynamic nature, what persists in a cell over time is its form, not its matter: the individual molecules that make up a cell come and go, but its over-arching organization remains." (p. 112)





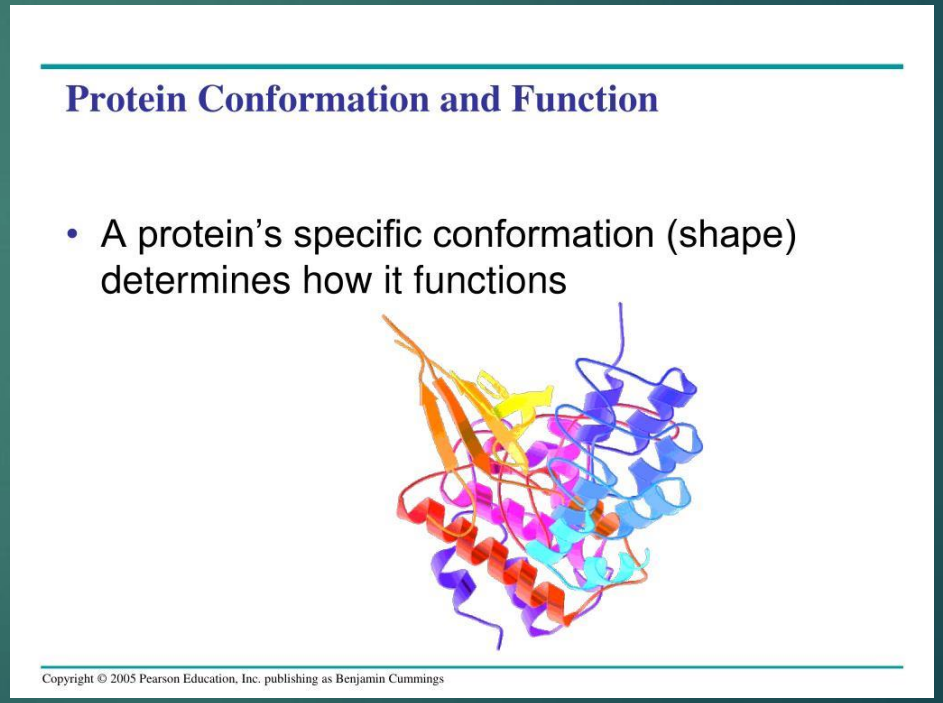
Designed to efficiently perform a specific function

Vs. A balance of efficiency and adaptability

Form and Function

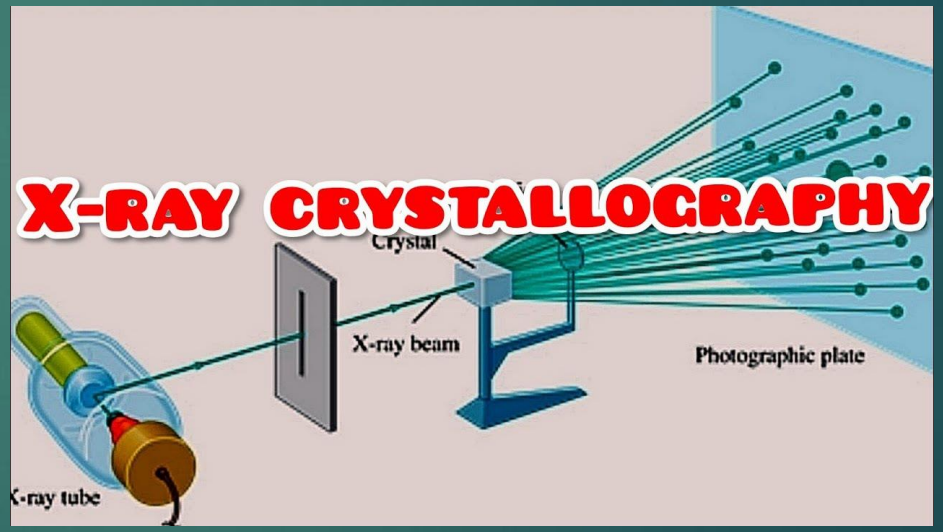
"Why do we call the large protein assemblies that underlie cell function protein machines? Precisely because, like the machines invented by humans to deal efficiently with the macroscopic world, these protein assemblies contain highly coordinated moving parts. Within each protein assembly, intermolecular collisions are not only restricted to a small set of possibilities, but reaction C depends on reaction B, which in turn depends on reaction A—just as it would in a machine of our common experience. (Alberts, 1998 , p. 291)"

Quoted in Nicholson, p. 113

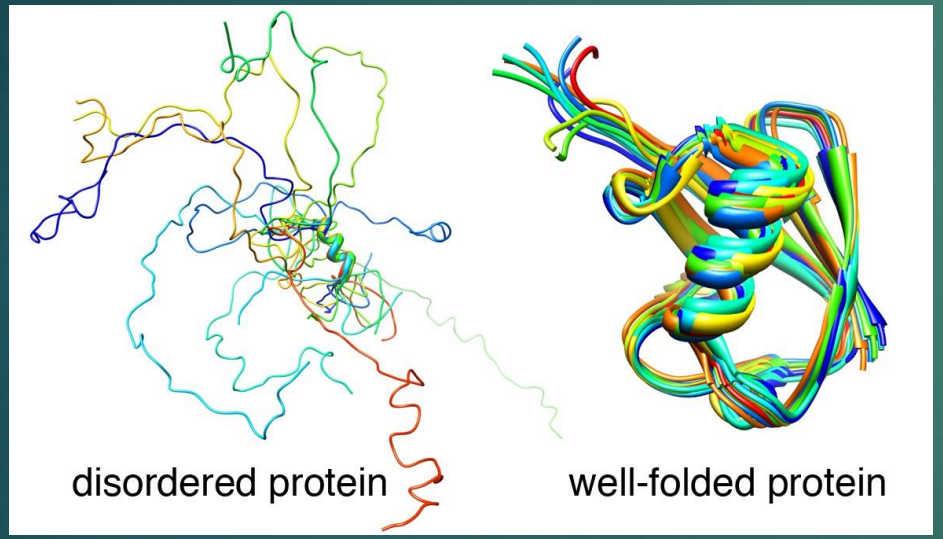


Studying protein structure

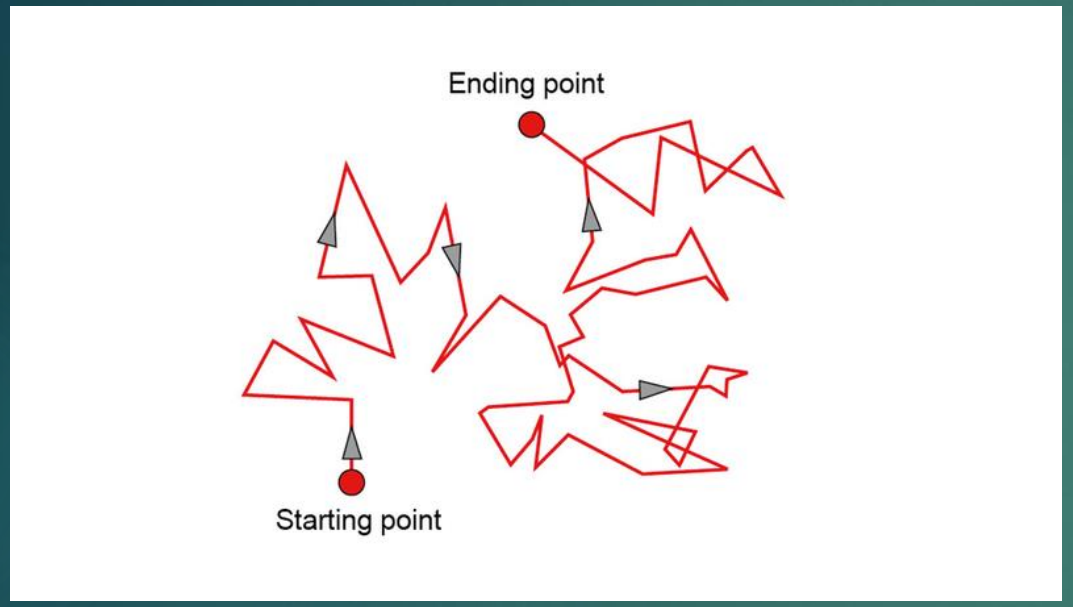
- The technique Rosalin Franklin used to observe the structure of DNA was x-ray crystallography
- You take some DNA, crystallize it into a solid, then shoot x-rays through it
- The way the x-rays scatter tells you about the structure



Intrinsically Disordered Proteins



- But studying proteins using nuclear magnetic resonance spectroscopy has shown that many proteins are partly or completely disordered
- That is, they change shape
- "In mammals, it has been estimated that approximately 75% of signalling proteins and about 50% of all proteins contain at least one disordered region of more than 30 amino acids, and as many as 25% of all proteins are completely disordered" (p. 114)



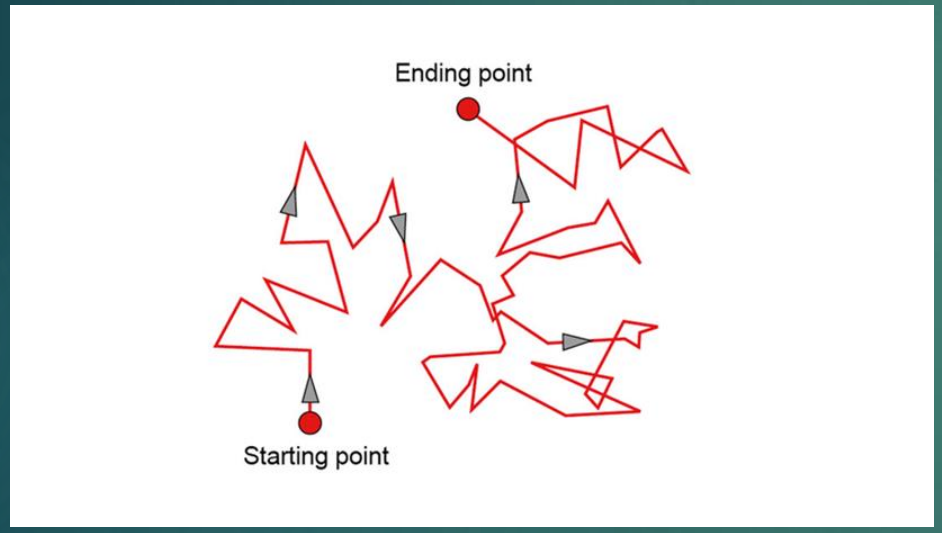
Follow the same sequence of steps every time to achieve that function

Vs. Stochastic and Probabilistic

Scale and Physical Forces

- Nicholson argues that our intuitions, based on medium-sized objects, mislead us about the cellular level
- Scale matters a lot in terms of which forces dominate
- E.g., a whale experiences water as though it were much thinner than us
- Whereas a paramecium experiences it as a thick soup

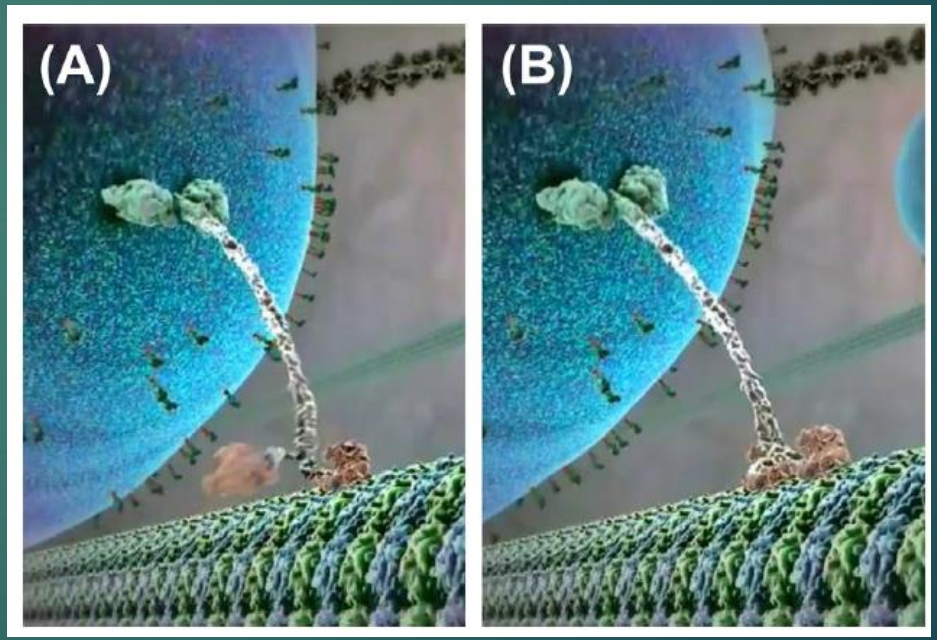
Brownian Motion



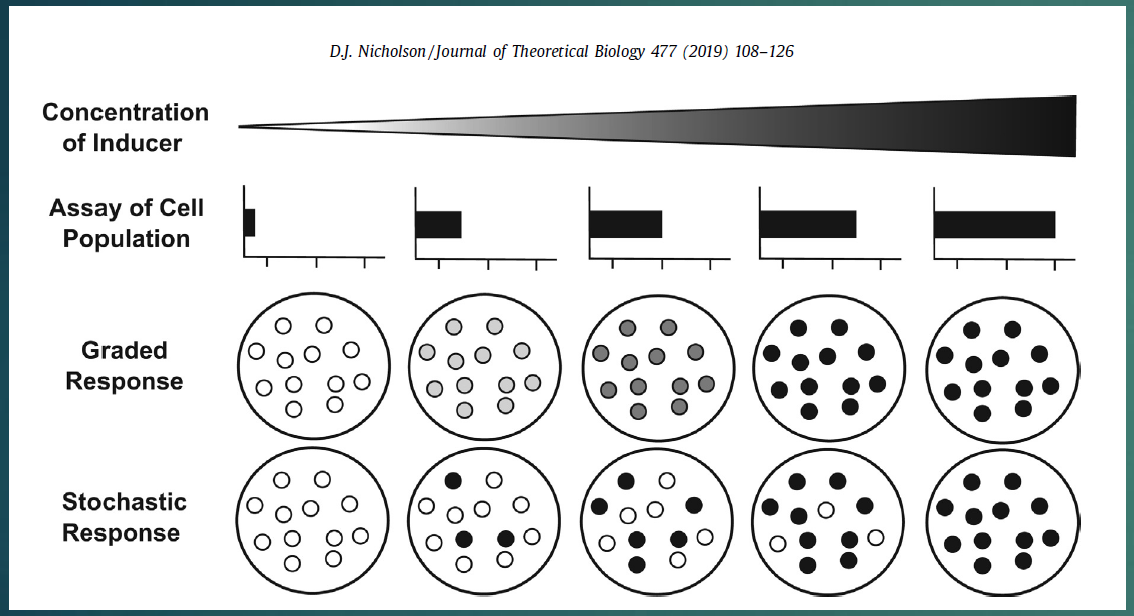
- At the cellular level, Brownian motion is a major determinant of how things move
- Brownian motion is just the movement caused by being jostled at a molecular level
- Randomness plays a huge role in determining how things will move in the cell!

Kinesin ‘walks’

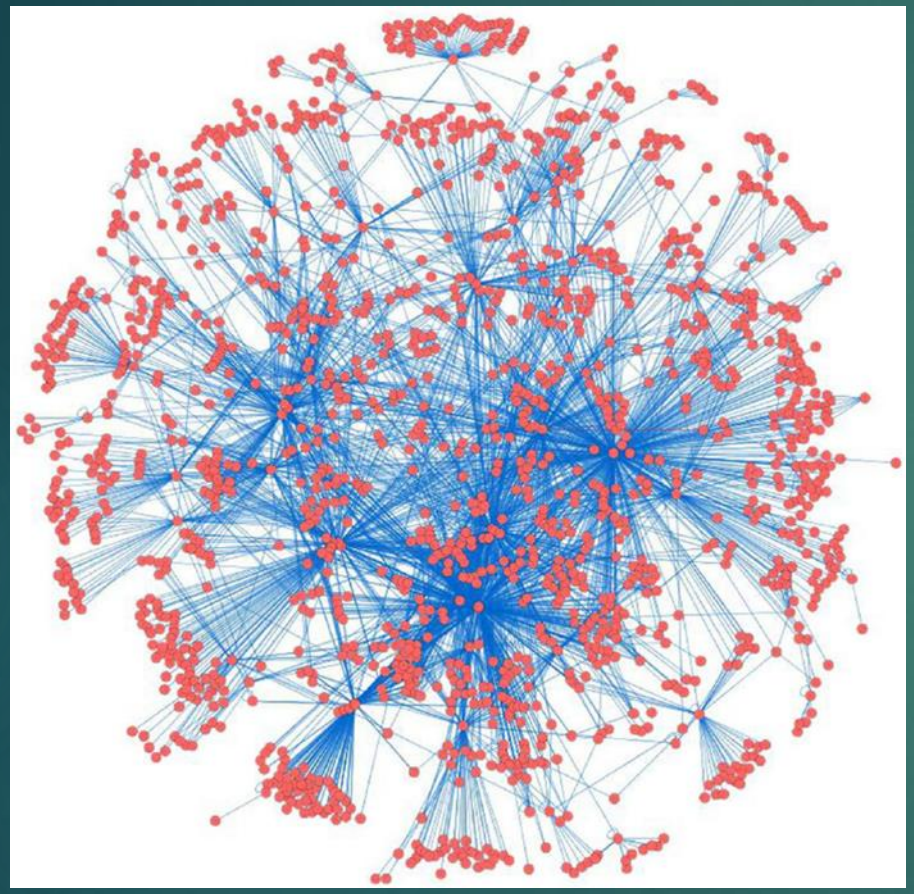
- You may have seen video of little machines “walking” along microtubules
- Nicholson argues this (may be) misleading
- This apparently driven behaviour is one model of how this works
- Another is a kind of ratchet system, where random jiggling is biased in one direction by burning ATP
- http://www.artofthecell.com/the-inner-life-of-the-cell



Stochastic Gene Expression



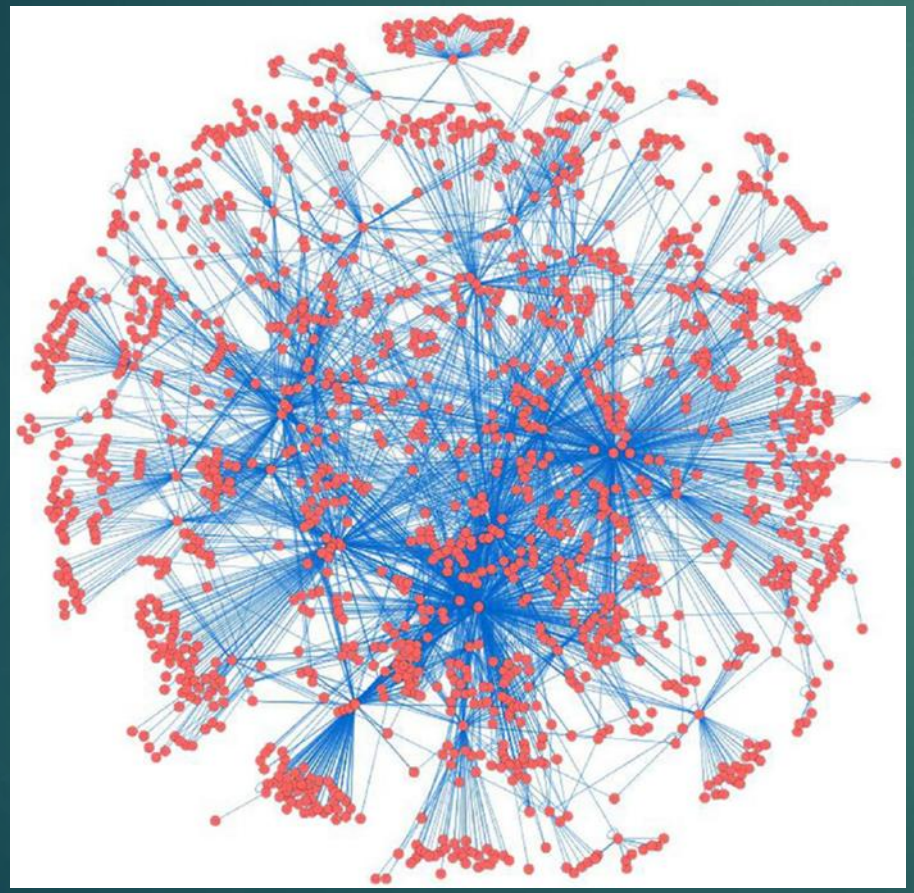
- Genes can be more or less expressed (transcribed into RNA which ribosomes use as a pattern for proteins)
- Inducers help determine their level of expression
- Researchers believed that this was a simple linear relationship, as in the 'graded response'
- But now that they can study individual cells, it turns out gene expression happens in stochastic bursts



You can start and stop the machine without it falling apart

Vs. Dense interactive causal networks

Gene Regulatory Networks



- This is a map of the gene regulatory network for e. coli
- Genes can increase or decrease the activity of other genes
- Knowing how active a gene will be in an environment requires (at minimum) knowing what all the other genes are doing
- Allen, J. D., Xie, Y., Chen, M., Girard, L., & Xiao, G. (2012). Comparing statistical methods for constructing large scale gene networks. PloS one, 7(1), e29348.

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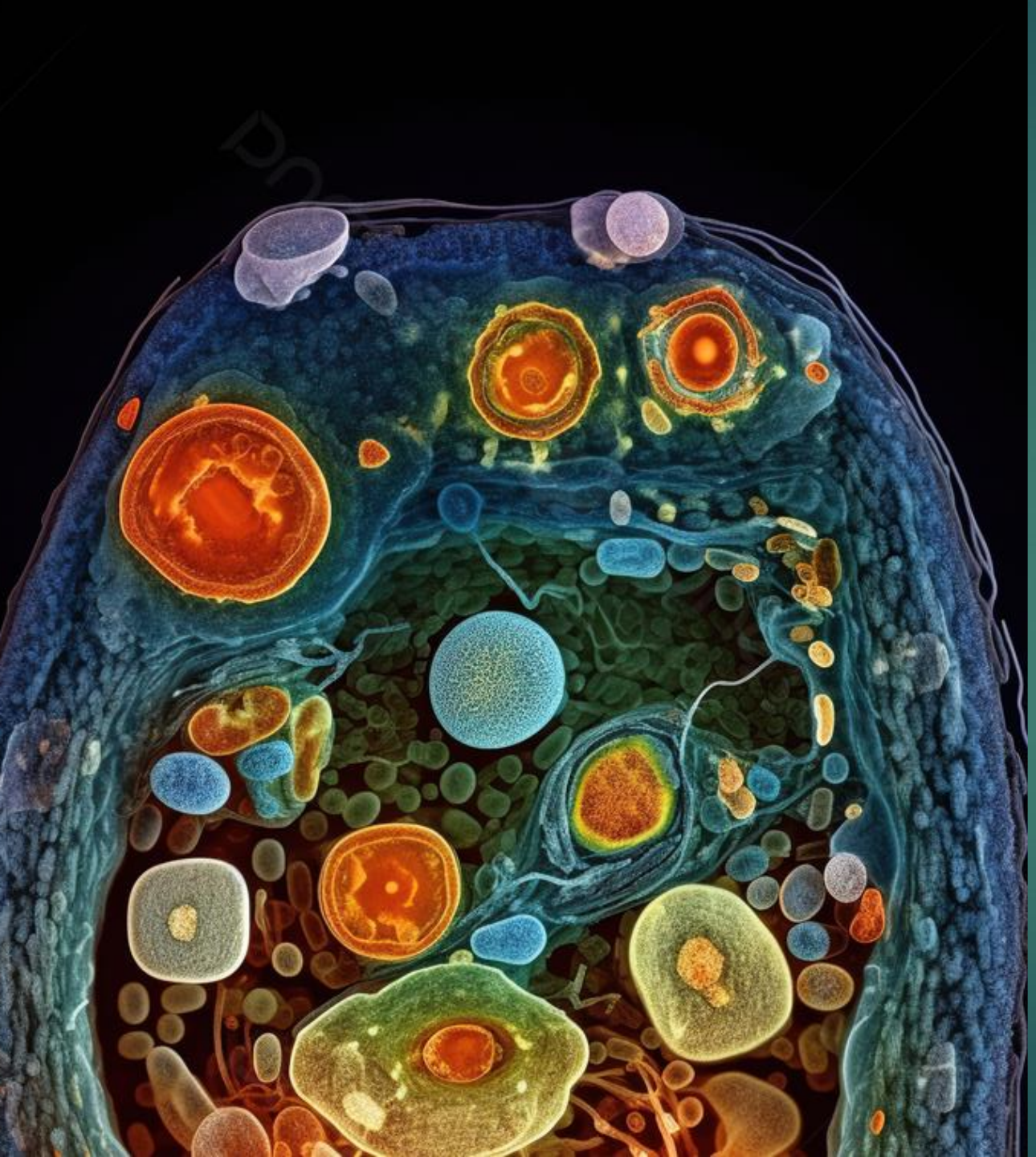
1. Describable by blueprints – a list of parts and how they fit together
2. Designed to efficiently perform a specific function
3. Follow the same sequence of steps every time to achieve that function
4. You can start and stop the machine without it falling apart



"Monod was wrong. The cell is not a machine, but something altogether different—something more interesting yet also more unruly. It is a bounded, self-maintaining, steady-state organization of interconnected and interdependent processes; an integrated, dynamically stable, multi-scale system of conjugated fluxes collectively displaced from thermodynamic equilibrium." p.123

Next time: Self-Organization