Cellular Biophysics
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Energy and Thermodynamics of Life - Part- 01

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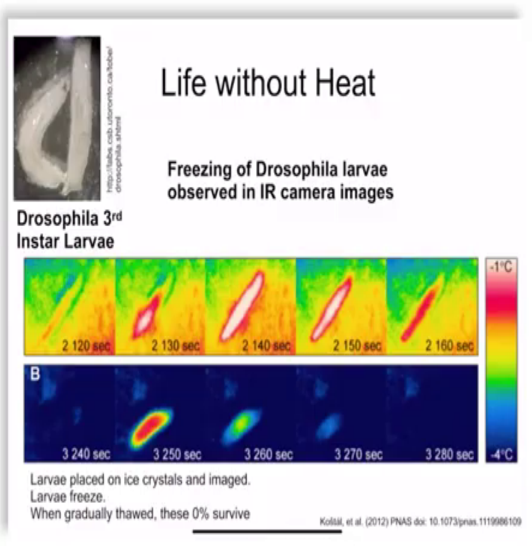

When we talk about life it is impossible to imagine life without heat by which I mean that if larvae of drosophila some of you may have had the privilege of working in the drosophila biology labs in IISER Pune of which we have a lot in biology. And if you place them at minus 4 degrees Celsius then over time after thawing they lose viability such that 0 percent survive. Now, what happened here was that they went through freezing.

Now, what I am not telling you is that of course there are methods of cryopreservation which involve tissue permeabilization or cell permeabilization and anybody who has worked in a cell culture lab and this is a cellular biophysics course so I think some of us, I think some of you must have, know that there are cryo-protectants which can avoid this fate.

But as the cell becomes more than one cell, 5 cells, 10 cells, organoids, organs, whole animals, the ability of these cryo-protectants to penetrate all the tissue protect it, keep viability and at the same time prevent poisoning reduces to almost none.

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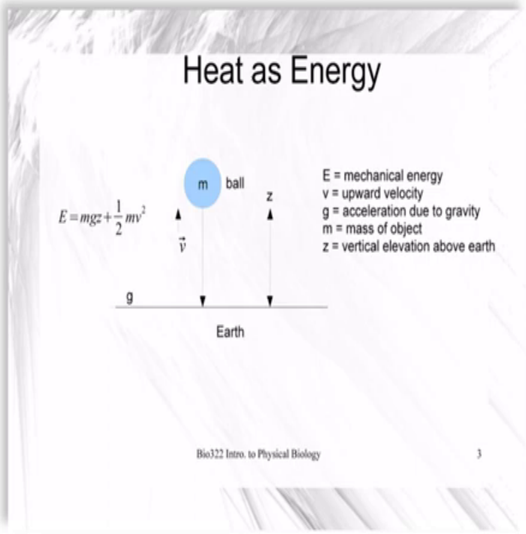

So, where is this heat coming from and what is it? So, we go back to our high school physics and ask the question can we understand heat in terms of energy. And so for that example what I have taken here is your classic ball falling experiment. You drop a ball of mass m, it has a potential energy before it starts which is mg z, and when you drop it, it starts increasing in velocity until it reaches some terminal velocity and hits the ground.

It has crossed through some height z. Now, this movement is because earth has gravitation and the kinetic energy at the point where it is falling is given by $1/2mv^2$. But the real question arises which is now that the ball fell we said energy is the summation of the potential and kinetic energy, it is a fair assumption I think, fair statement. But where did the energy go?

And most of you probably remember that we say that not just is the energy not zero and it did not just disappear but in fact energy is conserved, this was a proposition made by Leibniz in 1693, Physics is an old subject, yes. And just Δt very small fraction of time before the ball lands or at the time that the ball has hit the kinetic energy is still non-zero it is still moving. After it lands kinetic energy is 0, potential energy is also 0, so where did the energy go, it went into friction.

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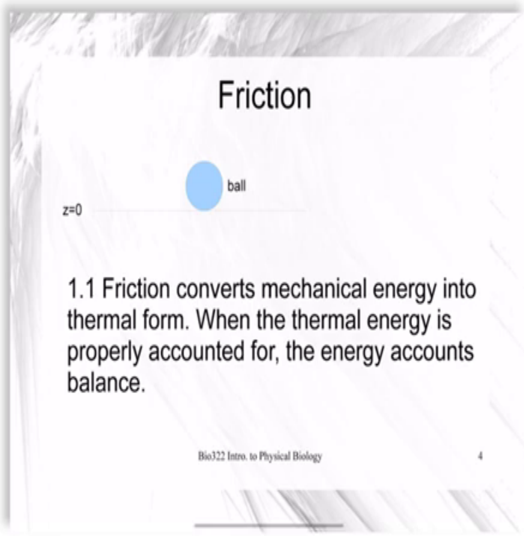

Friction which converts this mechanical energy, this mechanical energy that drove the movement into thermal energy, thermal energy is nothing but heat. When the thermal energy is properly accounted for then we get a complete energy balance.

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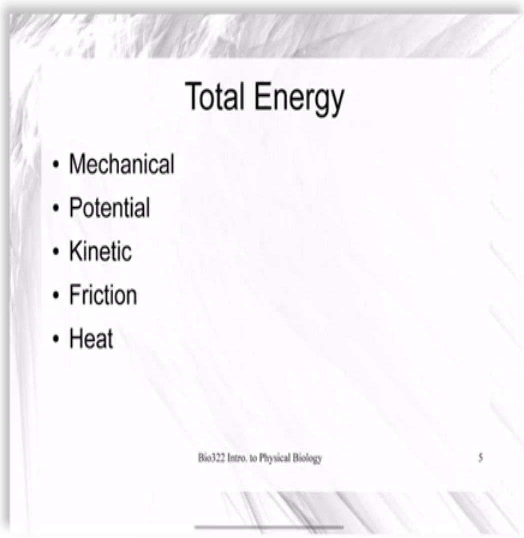

So, in some senses for our true calculus of total energy we need to include not just potential and kinetic energy but mechanical, friction and heat energy.

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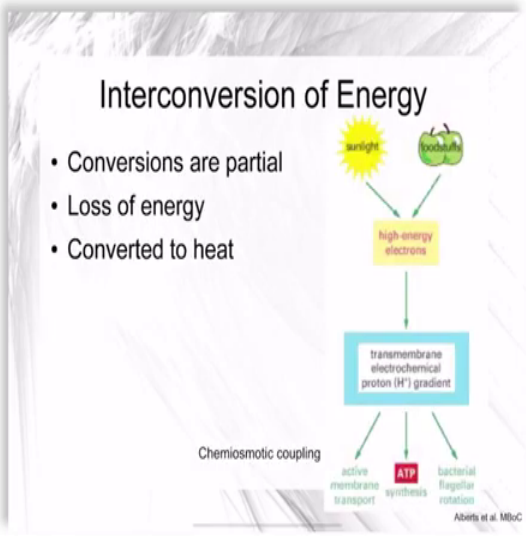

In fact this interconversion of energy even shows up in a cell biology textbook quite exciting in some sense in my view. In terms of this idea that the biosphere takes radiation energy from the sunlight, converts it to high energy electrons which are photosynthetically then captured into chemical energy through transmembrane proton gradients resulting in ADP synthesis and active membrane transport and in cases of lower organisms even flagella rotations.

And this Chemiosmotic coupling is critical for the process of life to even work on earth. However, all conversions as we know are partial, there is always a loss of energy, where does this energy get lost is it is converted to heat.

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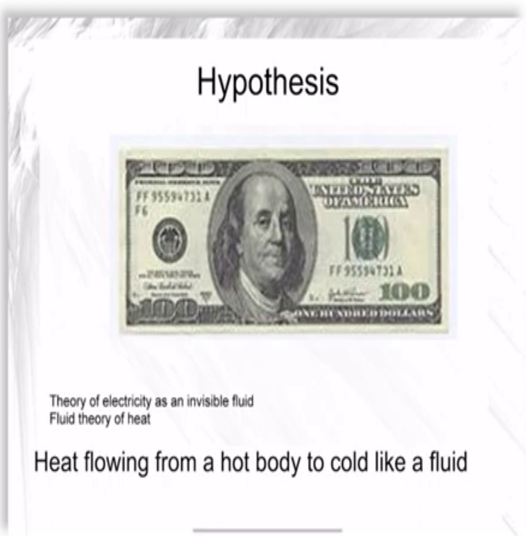

So, in a sense heat is everywhere, it is ubiquitous and it seems to go from one system to another. So, in order to account for this one of the early thinkers on this whose ideas are written down, therefore, we have some trace of it, was a hypothesis made by amongst other people Benjamin Franklin who is one of the few politicians who also did some science, so he is a politician so his name is on the currency bill but he is also a researcher.

So I do not know why he is he there for his politics or is he there for science but he is definitely there on a bill. The theory of electricity as an invisible fluid also led to the idea of theory of heat as a fluid. And the idea was amongst other things other people proposed by Benjamin Franklin as heat flowing as a fluid from a hot body to cold body.

Now, one of the nice things about making such statements, some such clear hypotheses is that they can be tested and rejected. So, I urge all of you who are in a research seminar to listen very carefully to experts in the field of theoretical modeling or biophysics or even biology whether when they state they have a hypothesis whether they went around trying to prove it or to test it, and usually you will find good scientists are usually trying to test it.

Because often the most deep insights are obtained by rejecting a hypothesis. In fact it turns out evidence was found to reject this hypothesis. So, even if his name is on a Dollar bill, he was wrong.

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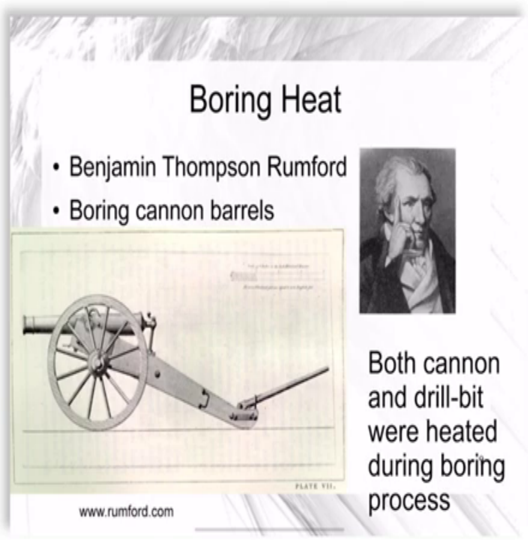

And some of the evidence was found by work done by another Benjamin this one was Thompson Rumford during the process of boring of cannon barrels, meaning to say making cavities for the barrels of a cannon to allow the cannon ball to go. So, when they, when they had a metal cylinder and they ran the drill bit you know the part that makes the hole, during the boring process both were heated.

So, both the bit was heated and the cannon metal was heated. But when they stopped when they stopped the heat also stopped. So, it was kind of strange because it contradicted this idea of flow, there was no flow where was it flowing from, if it was a liquid it should have flowed from the bit to the cannon or the cannon to the bit and they should have both then either one should have been cold, one should have been hot or they should have continued to be so even when the movement stopped.

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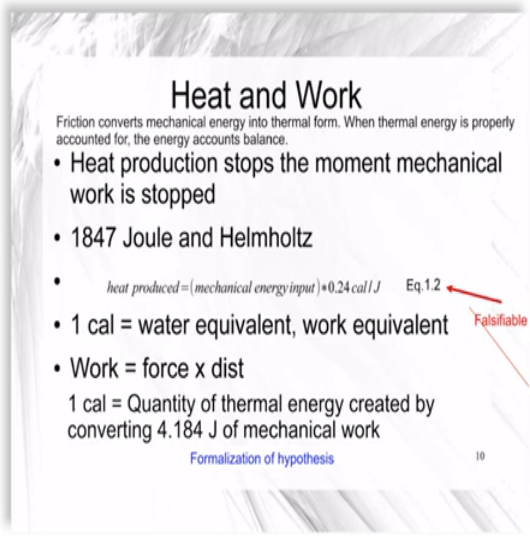

So, obviously it meant that this process of boring was itself generating heat. And in that sense there is an interconnection between heat and work which now we know since 1847 attributable to both Joule and Helmholtz, is that heat production stops the moment the mechanical work is stopped and so in that sense we can define heat produced to be the mechanical energy input into 0.24 calories per joule.

This is also called the work equivalent of heat and one calorie was defined as water equivalent or work equivalent, work at the same time can also be defined in terms of force times distance. So, one calorie today in our modern definitions is defined as the quantity of thermal energy created by converting 4.184 joules of mechanical work into thermal.

So, to summarize one a bad hypothesis or an incorrect hypothesis, this was useful because it formalized the process of thinking about how heat is generated and transferred. The second thing is that by doing experiments and by measuring this hypothesis could be tested, rejected, an alternative formulated and found to be a more precise statement of nature.

So, this concept of modelling is an ancient one, 200, 300 years old concept in physics, it is a little new in biology but let us see how far we can get with this. And that is partly what I meant earlier when I said about testing versus proving a hypothesis, this equation heat produced is equal to mechanical energy input into 0.24 calories per joule makes our theory falsifiable.

Meaning to say if a monkey does the experiment and monkeys know how to measure, I mean if you can teach a monkey to measure or a PhD student or a BSMS student performs the same experiment whether they are sitting in Pune, in Patna or Pataliputra or wherever it does not matter, you should get the same answer. And if you do not then there is something falsifiable if the experiment is done under the same conditions.

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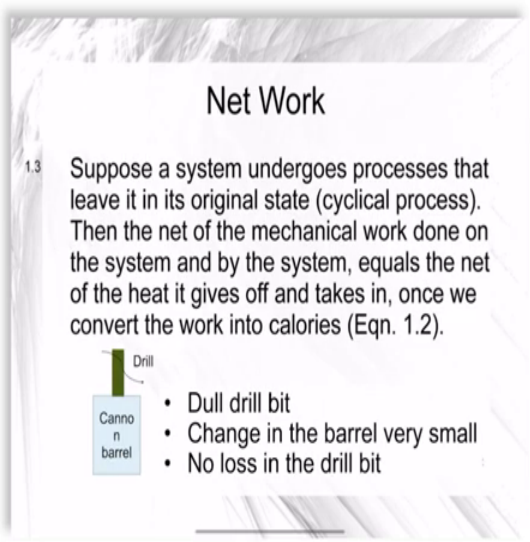

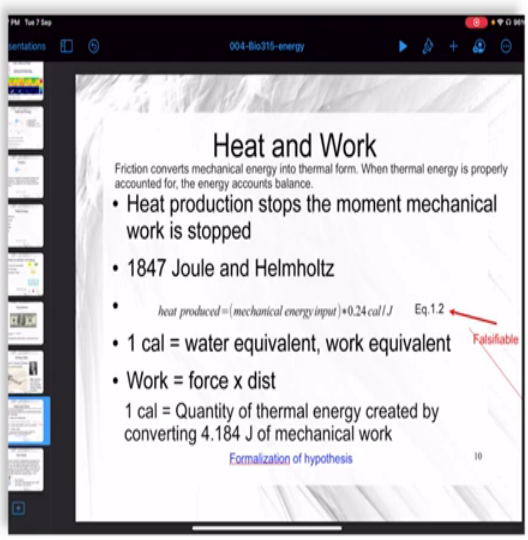

Now, this allows us to of course state that if an energy, if the system undergoes a cyclical process meaning to say it is modified in a way that it goes from state A to B to C to A again and it leaves it unmodified then the net mechanical, net mechanical work done on the system by the system equals the net of the heat it gives off and takes in once we convert the work into calories.

So, an example would be if you had a dull drill bit, you know that the drill if you want to make a hole in a wall and you are trying to drill when I was a child we used to have a hand driven drill now of course you get a nice Bosch drill which is motorized and so on, the bit has to be sharp. If you have a dull drill bit firstly you will have a hard time going in even if you have a very fast motor but on top of that you will generate a lot of heat. So, the change in the barrel is very small there is no loss in the drill bit so this is what your cyclical system is.

And in such a case so this was an example of such a cyclical process then the mechanical work done on the system and by the system equals the net of the heat it gives off and takes in once we convert the work into calories. That is verbose statement of the previous equation 1.2 which was heat produces equal to mechanical energy input into 0.24 calories per joule you understand that.

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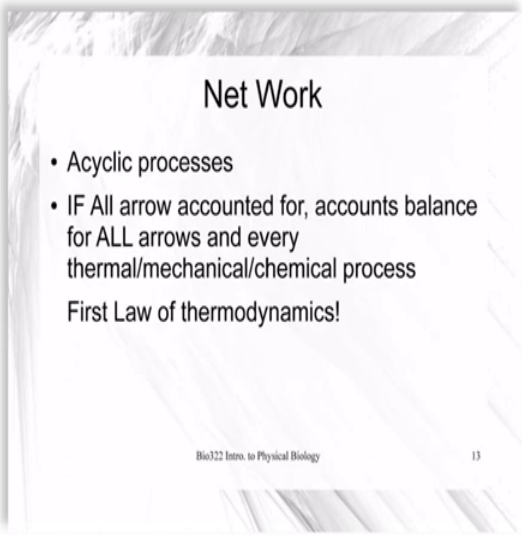

However, there are also acyclic processes if all the arrows in such a case are accounted for and all accounts balance for all arrows and every thermal mechanical chemical process then the energy is conserved and this is nothing but the first law of thermodynamics.

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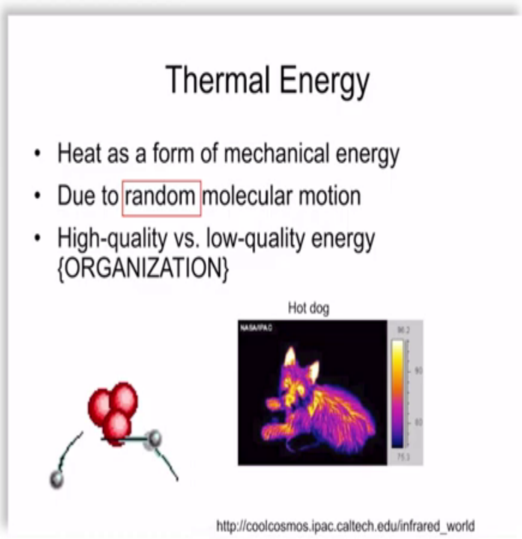

Now, going back to what is heat I mean we said what is the relationship between heat and mechanical energy but what is it I mean we are saying it has an equation and it has equivalent to mechanical work to do mechanical work you get some heat but where does it, what is the molecular basis of it, how does it arise?

In that sense we can say that while heat is a form of mechanical energy it is due mechanistically it is due at a molecular level due to random molecular motion. In that sense, we talk at a molecular level of high quality versus low quality energy which relates to the level of organization, you understand that when something is random it is less organized than when something is non-random. And this illustration is only to tell you about what, any living organism imaged in a thermal camera will show you that it is giving of some heat.

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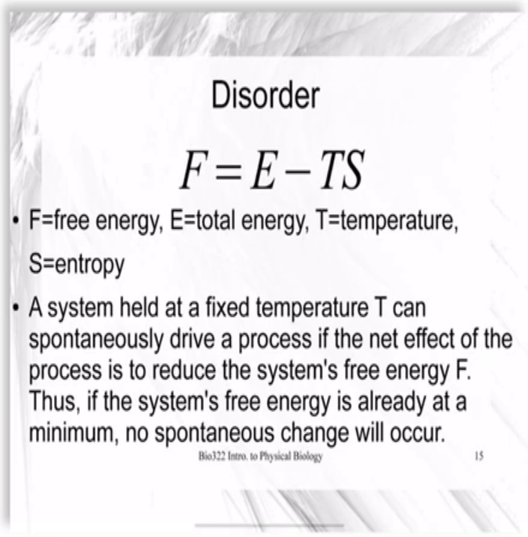

The flip side of heat is also that it is a measure of disorder and that measure of disorder comes from entropy. So, the free energy plus the temperature times the entropy gives you the total energy of the system or in other words the free energy is the difference between the total energy and the loss due to entropy at a given temperature.

A system therefore held at some fixed temperature can spontaneously drive a process if the net effect of the process will reduce the system's free energy. This means that entropy itself can drive something but if the system's free energy is already at a minimum no spontaneous change will occur, it talks about spontaneity.

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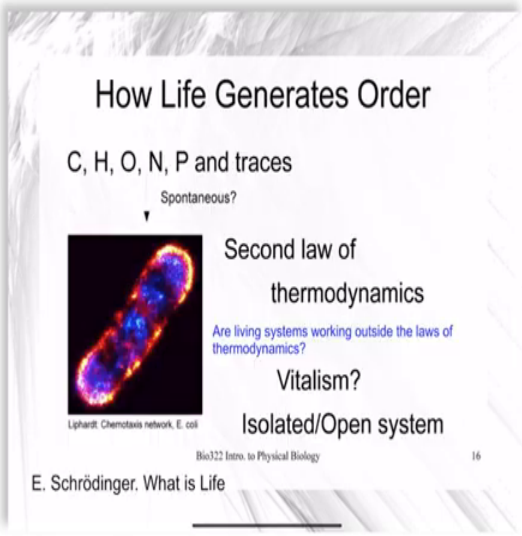

Now, this is kind of funny because if we go back and ask the question about the origin of life and we know that living systems consist of carbon, hydrogen, oxygen, nitrogen and phosphorus and traces on earth at least carbon based life. Then can we take a test tube mix these elemental components, let us say a long chain carbohydrate, some water to get H, N, O, some nitrates and some phosphates and maybe add a little bit of magnesium and some ions and shake it.

Will it spontaneously give rise to the kind of complex shape and structure that we expect from living cells? Can we get it? And the answer is sort of obvious to all of us that no I mean you do not get origin of life every two days in your tea cup, I mean you have more or less everything, you have sugar which are the carbohydrates, you have water, you have probably dissolve some oxygen, you have some nitrates, phosphates, traces.

You have everything I mean there is some pesticide in your tea so it is also there, you put milk you get all sorts of other things. So, you have even lipids in fact. So if your tea cup does not form life then something is going on something universal and that we say is partly attributable to all systems living or non-living following the second law of thermodynamics.

But for a very long time this was an open question, this was a question which was framed in the following way life preserves order, living systems cells divide they form cells that look like themselves, rabbits multiply by making more rabbits that look like themselves by sexual reproduction of course and order is preserved, but the second law of thermodynamics tells us that all disorder of the universe keeps increasing.

So, the question then arose are living systems working outside the laws of thermodynamics, I mean is there a contradiction? In other words life on earth or at least as far as people were thinking about at that time must therefore be violation and this was called vitalism. But the answer to that question was that this is a badly framed question, it was this idea that living systems are not isolated closed systems, but in fact they are taking, they are creating order in themselves at the cost of disorder in their environment.

And in that sense living systems must by definition be open systems and then we are back in consonance or in agreement with the second law of thermodynamics and this is the real crux of the essay by Erwin Schrodinger on what is life. I urge you to read it, it is not part of the course material in the sense that you are encouraged to at least understand the concept but beyond that it is up to you. Suffice to say Schrodinger came at this problem as a physicist.

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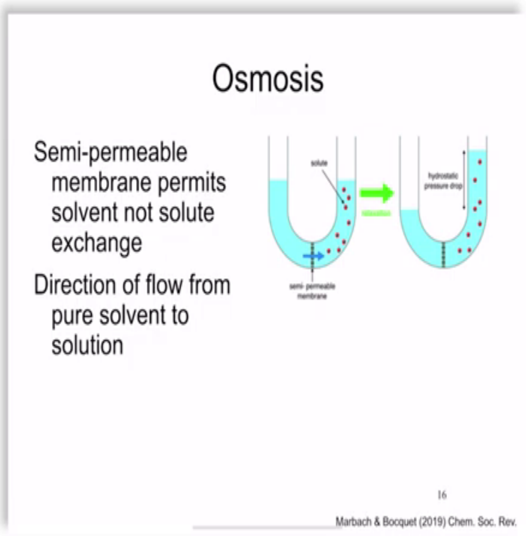

But we are going to go back and ask this in terms of some more general questions about the spontaneity of life and next week when we meet we are going to discuss this a little bit, can life spontaneously arise when it did once why did it do so, what could it be that may be the driving force.