Physics of Biological Systems
Prof. Mithun Mitra
Department of Physics
Indian Institute of Technology, Bombay

Lecture - 41
Introduction to Biological Dynamics

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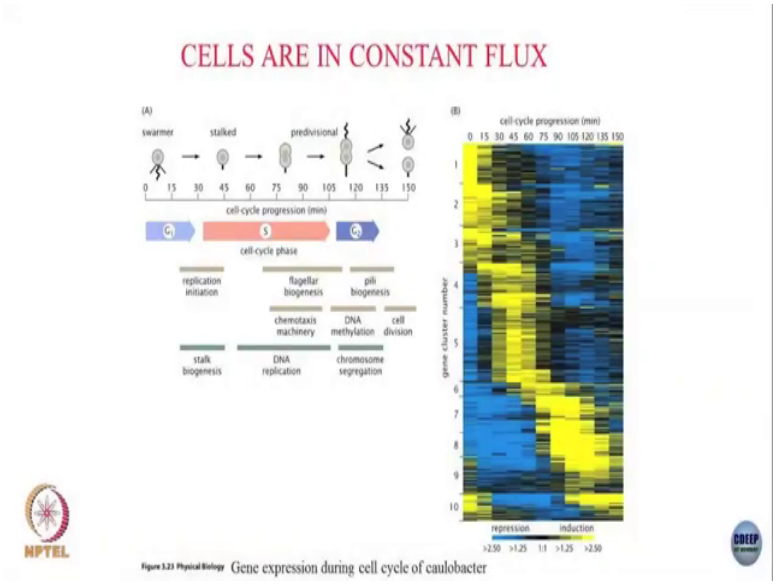

Figure 3.23 Physical Biology Gene expression during cell cycle of caulobacter

By taking the case of an E.coli with estimated numbers of various proteins that are to be found inside the cell, right? Some millions of proteins and billions of water molecules and small ions and so on and so forth and; however, the thing to realize of course, is that these numbers are sort of whatever we found.

Let us say there are some 10 to the power of 6 protein proteins and so on. Whatever numbers these numbers that we estimated these are sort of an average order of magnitude numbers. In reality the numbers of proteins, but if I think of a particular protein the number of copies of

that protein inside the cell is sort of continuously changing, right. And this is one such there is a figure that sort of tries to estimate that.

So, this is Caulobacter, this is a bacteria, this is the cell cycle of that. So, it is this total cell cycle from birth till cell division is around 150 minutes, it is 2 and a half hours and these are the various phases of the cell cycle G 1 S phase and G 2 phase, ok. So, what these people have done is that they have looked at clusters of proteins or clusters of MRNA, rather corresponding to various proteins that are active at different at that are active. And then see when these MRN as or these DNA segments, these are these genes basically they are active as a function of the cell cycle time, ok. So, this curve over here is your cell cycle time from 0 to 150 minutes. Over here are these are different gene clusters and different gene clusters are responsible for different tasks.

So for example, cluster 1 might be replication; cluster 2 might be biogenesis, then there are clusters for chromosome segregation, DNA replication and so on and so forth. And these colors represent 2 is when they are up regulated; sorry, this yellow is when they are up regulated blue is when they are down regulated.

So, what you can see is that not all of these are sort of up regulated or active at the same time of the cell cycle. For example, this cluster over here clusters 8 and 9. These are sort of active towards the end of the cell cycle, not so much towards the beginning; whereas, these clusters are sort of active towards the initial phase of the cell cycle, not so much towards the end. And depending you can then say that which clusters are active.

When? So, for example, this one is active towards the initial part of the cell cycle, this chromosome segregation which happens when the cell is dividing that is active towards the end of the cell cycle when the cell division of course, is the absolutely at the end and so on. So, if you basically if you, classify genes according to their function; so, cluster genes or RNA or proteins whatever you classify them according to their function.

They are not always on they are not always produced then numbers fluctuate as the cell goes through its cycle depending on the function of that particular protein. And this is something

that one must keep in mind that if I say that there are 1000 copies, it does not mean that the cell has 1000 copies of that protein throughout that cell cycle.

In some, in some during some time of the cell cycle it might during some time of the cell cycle' it might be completely absent. So, that is one sort of thing to show that the cell is in constant flux; things are constantly changing inside the cell. Therefore, one must look at kinetics of these things protein concentrations and so on in order to see what effects these have one cells out. So, that is number 1 proteins or MRN as another thing for example, is this cytoskeleton.

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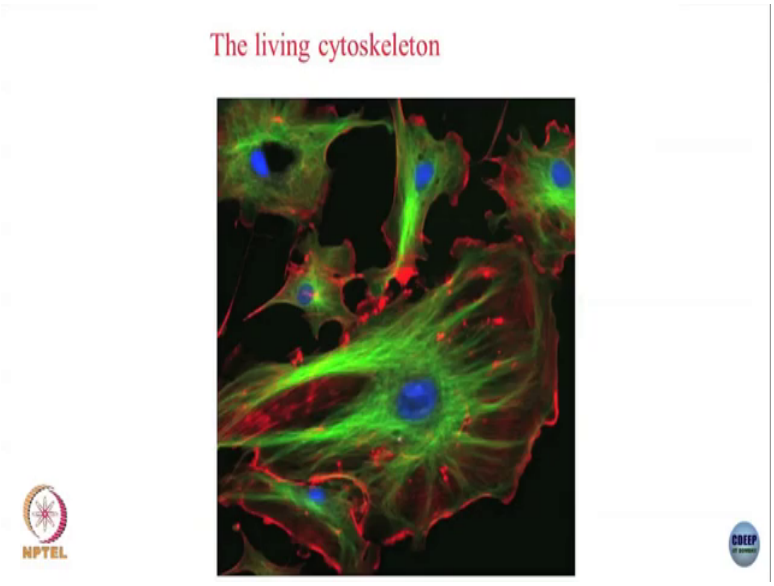

So, again we have talked about microtubules and actins, this is again an electron micrograph showing that the green filaments over here are the microtubules, the red spots are these actin filaments, the blue is the nucleus that is not worried about, but these actin this cytoskeletal filament actins and the microtubules are extremely dynamic. They polymerize and they

depolymerize the rate of polymerization of the rate of depolymerization may depend again on the state of the cell cycle itself.

For example, microtubules when the cell is dividing it assembles to form the spindle pole and pulls apart the chromosomes and so on. So, again we look at these how to deal with this dynamic instability of the cytoskeleton filaments, the fact that they are constantly in a state of flux their polymerizing depolymerizing over the next few lectures. So, just to remind this was the structure of the microtubules.

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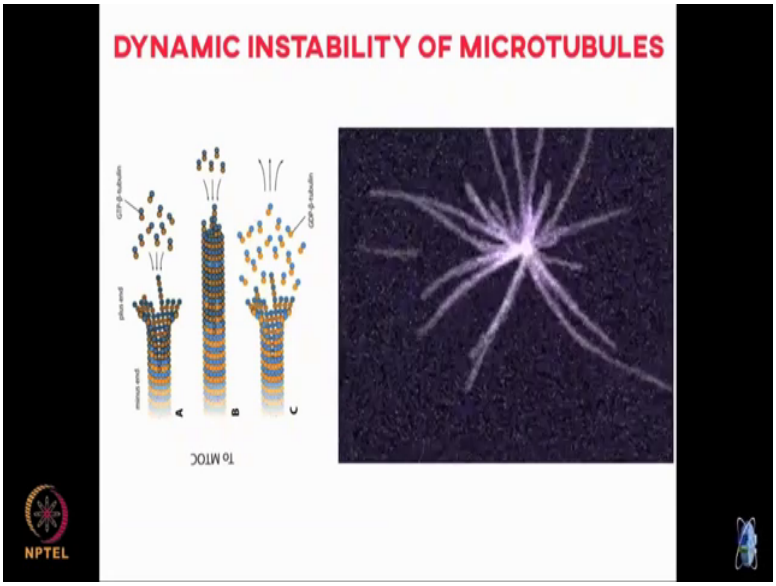

If you remember, my good the basic subunit are these tubulin dynamics alpha tubulin and a beta tubulin, because there is a structurally symmetry we can assign a plus end and the minus end. So, this is the one where it nucleates from this microtubule organizing center; microtubule organizing center that is the minus end generally.

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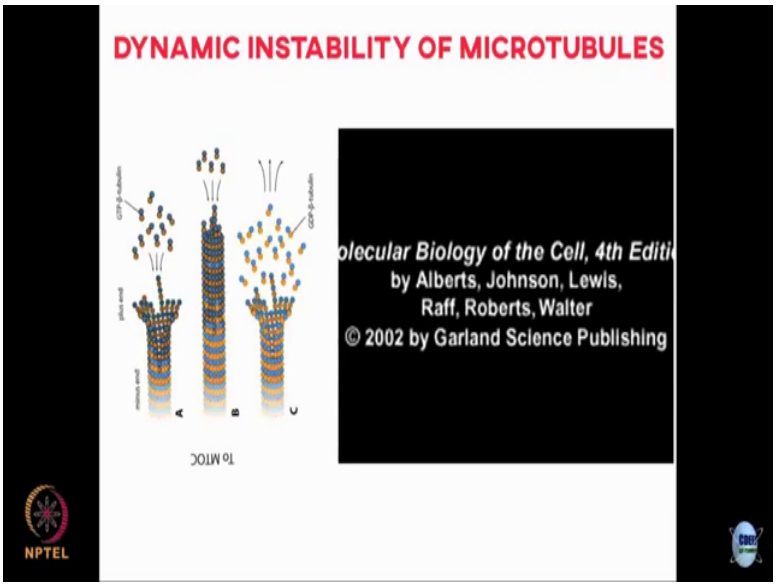

And then you have this microtubule going out of there.

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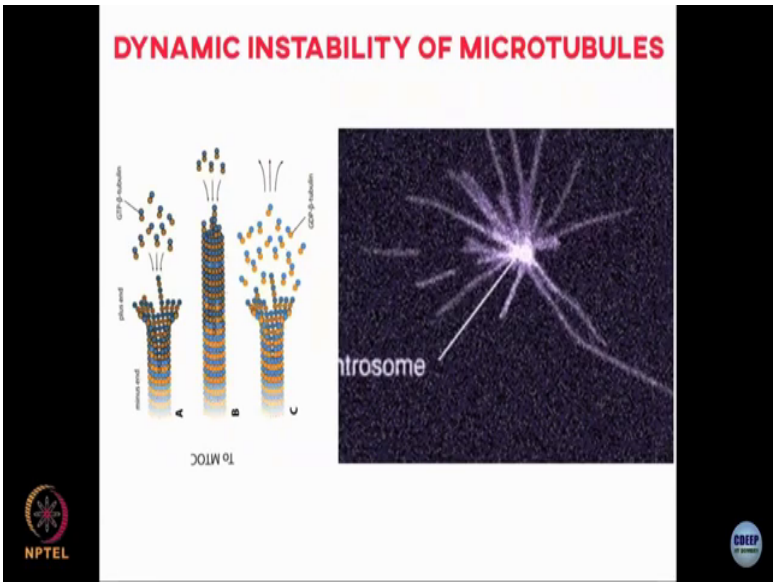

So, the microtubule consists of 13 filaments like this called protofilaments. Each protofilament is made up of these alpha beta tubulin subunits.

And when they polymerize, they polymerize like this. When they depolymerize, they look slightly different the structure is slightly different; it is sort of splayed out.

And you can see this hopefully this will play again. So, if you look at these microtubules, they are going to some are going to be growing; some are going to be shrinking and they are going constantly going to switch from a growth phase to a shrinking phase. And like I said this is very important in the case of the spindle formation, I am sorry the picture is not very clear not even over there.

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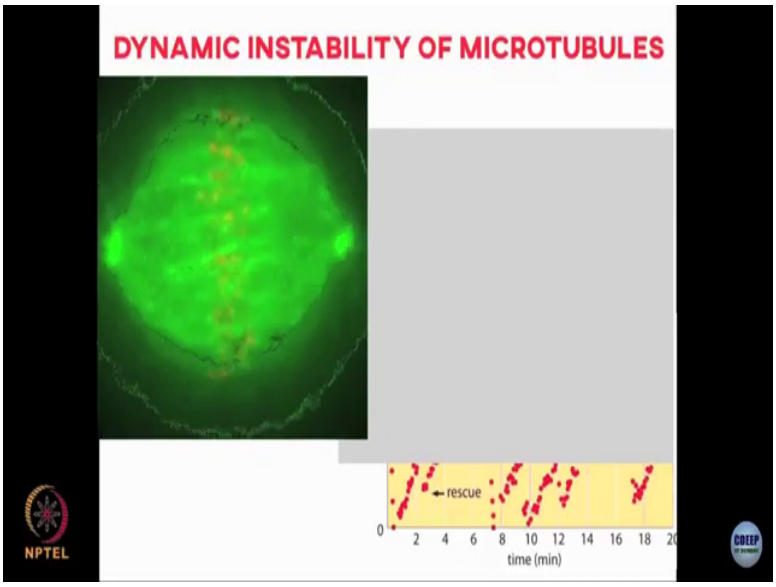

So, these yellow things are your chromosomes which are going to be pulled apart. These green lines are the microtubules which originate from the spindle poles, the structure is like this. Here you have your two spindle poles your microtubules are originate like this.

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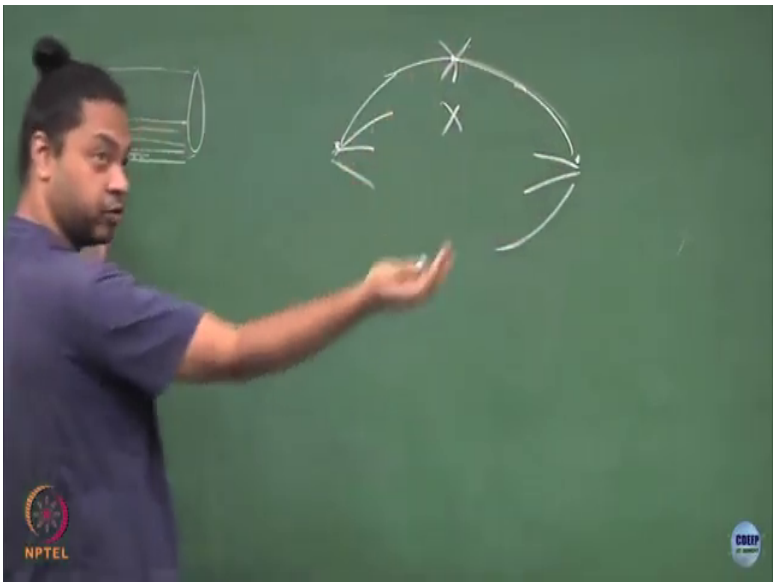

And here are your chromosomes, the microtubules come and attach and then they pull the two copies of the chromosomes towards the two poles. If you look at the lengths as a function of time coming; so, if you look at the microtubule length as a function of time, you can see that it grows for some time.

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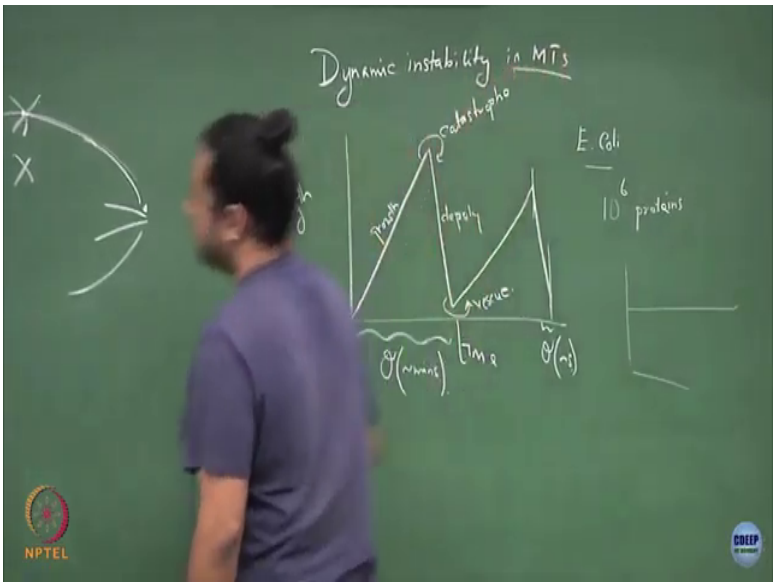

So, the length grows and then suddenly it undergoes depolymerization. So, if the length sort of drops very close to 0 and again it will grow and again, it will drop at some time; so, this process of switching from growth.

So, this is the growth phase, the growth of the polymerization, this is the depolymerization, this switching is called the catastrophe, is called catastrophe. And this switching from the depolymerization back to the growth phase is called a rescue, is called a rescue.

If you look at this curve which I; so, the length scales of these are very different. So, for example, growth typically happens over time period of the order of minutes, a time period of the order of minutes. So, if you look at this curve these lines, if they continue they would be the growth phase roughly 2 minutes, 3 minutes is what the growth phase corresponds to.

Whereas this fall this de polymerization that happens very quickly over them order of a few seconds.

So, if you look at this length of this microtubule as a function of time, this is definitely not something that I would call in equilibrium. The length as a function of time is not something that is sort of roughly constant, it is constantly undergoing this sort of a flux between a growth in it a catastrophe phrase.

And again, we will try to look at how to sort of model this sort of dynamics where you have this polymerization, de polymerization and switching between them the same thing happens also for actins; so, the same thing happens.

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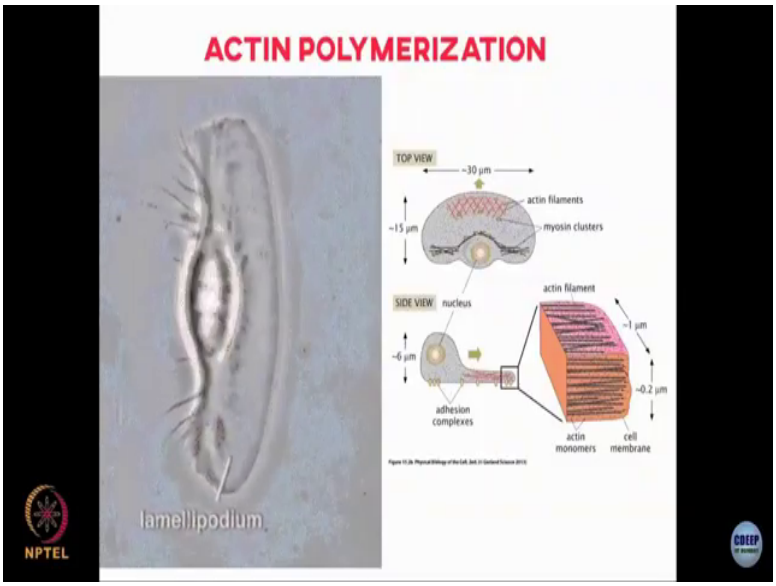

So, this is an actin polymer.

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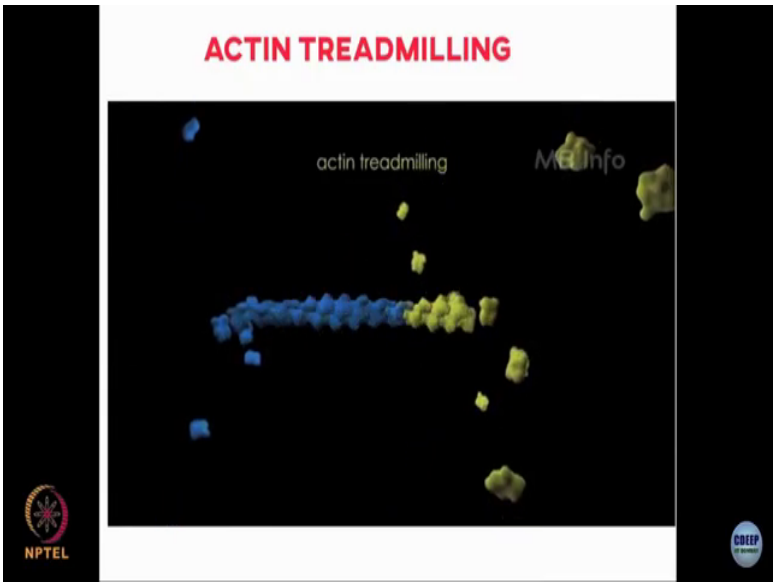

So, the actin again has these subunits which are called the G actin the globular actin, they come and bind to this actin filament. And again the actin has a structural asymmetry; it has a plus end and a minus end. And on average polymers will most sorry, monomers will act with the plus end and they will fall off the minus end.

So, this acts this process in micro tubule is called dynamic instability, this process of growth and shrinkage, it is called dynamic instability in microtubules, in microtubules. Whereas, in actins where you have this actin filament and you have addition at one end and from the other end the minus end it sort of falls off.

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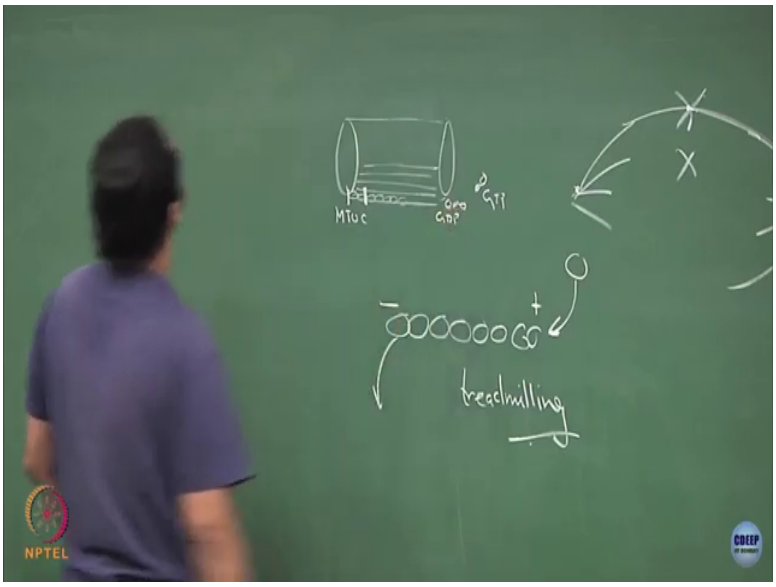

So, this is called thread milling. So, this is called actin thread milling, the monomers add at one end and it falls off the other end. And this has various consequences so for example, if you looked at this slide it does; it means what is so, these are actin processes in that they require energy. So, it refers to the state of whether it is an ATP s whether the subunits have an ATP attached to them; so, whether they are hydrolyzed or not. so whether it is an ATP state or ADP state.

So, that is true actually even in microtubules, there you have GTP and GDP. So, if you will see so, these are microtubules, right. So, when its subunits are being added, they have they are this in this GTP state, the triphosphate. And then once they are added, they actually the GTP converts to GDP. So, when they are being added, they are being added in the GTP state, then

once they are added they convert to this GDP state. And that is why if when it falls off actually the thing that comes out is GDP beta tubulin, ok.

So, there is an internal state, because this is an active process, there is an internal state. And it is true also in the case of actin, there is this ATP to ADP conversion which is why you see those as different colors over there.

I am trying to avoid that slide for the time being; here this curve has now come. So, this was the catastrophe and the rescue. So, these are experimental plots of this microtubule length as a function of time, ok.

So, just to shows how what effect does this polymerization de polymerization have. So, this is actually a cell, It's skin cell from a fish if I remember correctly and this is moving,. So, if you zoom in and if you look at this so, what happens in this leading edge is that there are these actin filaments and then there are molecular motives that move on these actin filaments. These actin filaments push against the cell membrane making the cell membrane sort of extend in this way in sort of. So, this is the top view of this cell, this is a side view of this cell. So, they extend these, what I call these lamellipodia and then they sort of crawl up along the cell surface.

So, in this leading edge of this cell, there are these highly dense networks of actin monomers. So, these are; so, this is again of active process to an interplay of these myosin motors and these actin filaments in the polymerization of these actin filaments. A same phenomenon, ok; since, we are on this slide anyway let me just show you that. So, this is what comes over here is yellow.

And then slowly as the ATP becomes ADP, you will see that it becomes blue over here so, the states changes. And now let me figure out how this is another example of how actin polymerization can help things move.

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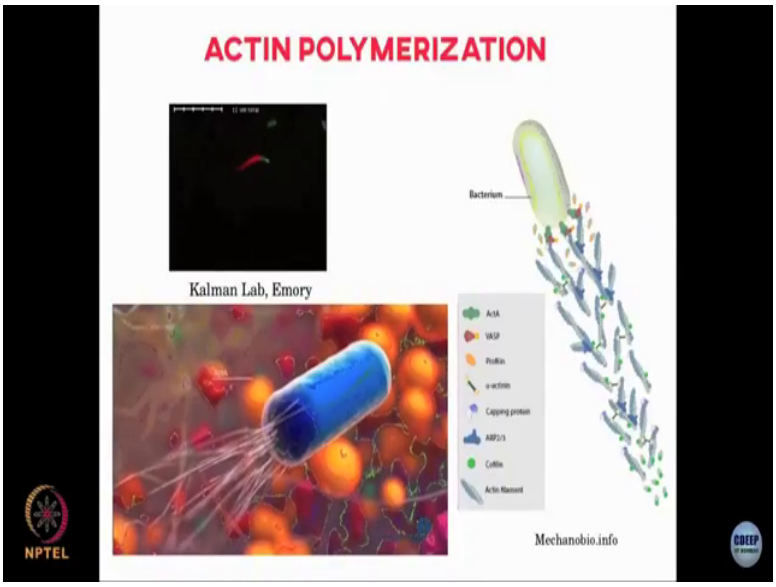

So, this is an illustration of a bacteria listeria which has invaded a cell. So, it is a infectious bacteria so, which has invaded a cell. What it does is that it takes over the actin polymerization machinery of the cell and it uses that machinery to sort of move around inside the cell.

So, let me try to see. So, here is the bacteria, these blue things that you see are these actin filaments and as these actin filaments polymerize, they sort of produce a force that pushes the bacterium like this, ok. And what you are seeing over here are the in this red is marked as these actin, this green is marked as this bacterium cell. So, this actin polymerization provides a force that should sort of pushes this bacteria along and this is what is known as an actin permit.

And again, we will look at this in a little more detail when we look at actin and microtubules in the subsequent classes. So, you have subunits being added over here that provides the force

that sort of propels this bacteria forward. So, this is the same thing; these are just snapshots of that movie.

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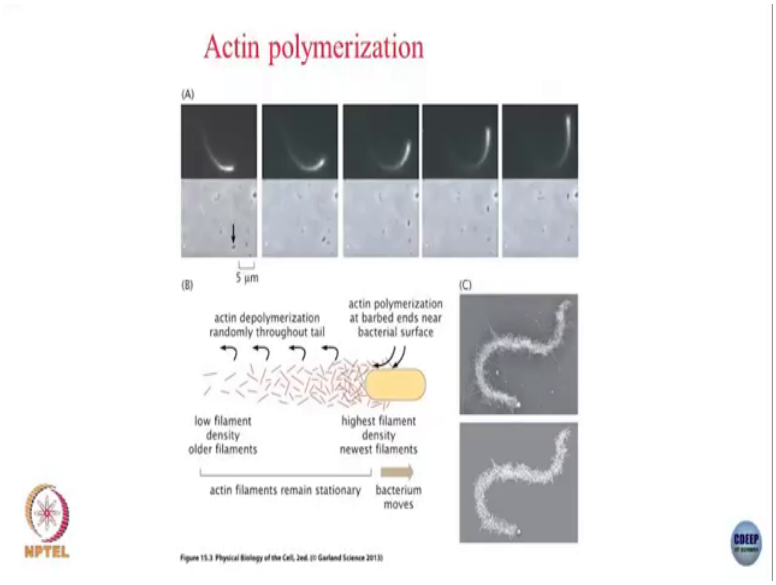

If you look at these actin filaments, there is a high density of filaments near the bacteria there is a low density of filaments which are these longer leaf filaments as you move further and further away from the bacteria filaments. So, which are these longer leaf filaments, as you move further and further away from the bacteria.