Cell and Molecular Biology
Prof. Vishal Trivedi
Department of Biosciences and Bioengineering
Indian Institute of Technology, Guwahati
Week 04
Cellular Transport
Lecture - 15
Transport in Prokaryotic Cells

Hello, everyone. This is Dr. Vishal Trivedi from the Department of Biosciences and Bioengineering, IIT Guwahati. And what we were discussing was the different aspects of the cells as well as how the molecules within the cells regulate the different activities. So, in this context, so far, what we have discussed is the basic structures of the cells. We have discussed the cell division.

We have discussed the fate of cell division and how cell division is being controlled. And if you recall from the previous lecture, we also discussed the different control mechanisms, how the cell cycle is regulated, and what will happen if the cell cycles do not go through these control mechanisms. In the previous lecture or module, we also discussed how you can study the cell cycle, how you can study mitosis and meiosis, and all those kinds of events. If you recall from the previous lecture, we also discussed that nutrition, as well as the uptake of molecules, is very important for a cell to survive and respond to different types of functions.

So in today's lecture and in this particular module, we are actually going to discuss how the cells are taking up the different types of molecules, what the different types of mechanisms are, and so on. So let's start today's lecture. And so the first thing is that we have to understand the transport mechanisms, right? So, the transport mechanism is where the simple biomolecule is going to be transported from one place to another. It could happen inside the cell as well as outside the cell. So what we have done is elaborate on the discussion about how transport occurs outside the cell so that the cell can take up different types of molecules, and then it will respond accordingly to the signals received from those molecules and how transport occurs inside the cell as well.

So when we talk about transport, it is a very, very important phenomenon within the biological system, right? Because the transport allows the absorption of nutrients, right? Because you know that different types of nutrients come from the different ways in which organisms absorb the nutrients, for example, when you are eating pizza or when you are eating bread, the bread goes through a very systematic way of different processes by which the multiple constituents of the pizza or the bread are digested, and that's how it is actually going to. Produce the biomolecules, and these biomolecules are then going to be taken up by the cell through a process called transport. Apart from that, it is also going to be used to remove the waste, right? By using a similar kind of mechanism in reverse order, as seen in the nutrient, you are actually taking the molecule inside. In the waste, you are actually putting the reactions in exactly the opposite direction, and that's how

you're removing the waste. Then the transport phenomena are also important for regulating cell signaling and communication.

This is the way we are going to discuss in our next module. So that time you will understand much better how the transport is actually controlling the signaling as well as the communications. Then, because of the transport, the cell is also responding to the external stimuli. This is also a part of the signaling and communications. And then it will also be a very, very important part of the defense mechanism.

So that is what you are also going to understand much more in detail when we discuss the immune system. And at the end, these transport mechanisms are also being used to maintain homeostasis. So what we have seen is that transport in cells or transport in organisms is very, very important because it regulates and maintains the different types of processes. Let's take an example of a process. So I have taken an example of digestion.

For example, when you are taking the pizza and you know that the pizza has all the biomolecules, it's going to have proteins in the form of cheese, it is going to have fat in terms of butter, and it is also going to have carbohydrates in terms of the dough we are using to make the pizza. So when you take the pizza, the food is going to be broken down into small molecules: protein will be broken down into amino acids, carbohydrates will be broken down into simple sugars, and fat will be broken down into fatty acids and glycerol. And then they are actually going to be absorbed by the epithelial lining within the intestine; this epithelial lining is going to be called the villi, which are present in the small intestine. Right, so that's how it is within the small intestine. You really are actually going to absorb these materials, right? How are they going to absorb? They are actually going to be absorbed by a phenomenon of transport because these biomolecules have to be transported and have to cross the cell, right? Then only will they enter into the body, right? So these molecules are then transported across the cell to enter the nearby capillaries and the bloodstream.

The molecules are then transported to cells where they are required to process like growth, repair, and energy production. Remember that this transport phenomenon is not going to happen only once. It is going to happen on multiple occasions, isn't it? From the epithelial lining of the elementary canal, it is going to enter the bloodstream. From the bloodstream, it will enter the different organs. For example, it goes to the liver.

For example, if there are carbohydrates, they will go into the liver. Then the liver is going to process these carbohydrates to produce, you know, glycogen and stored fat, and fat is going to go to the fatty cells, right? And that's how it's going to be converted into storage fat and other kinds of material, right? So, at the end, the waste material, the waste products of this digestion, are also going to be removed by the alimentary canal as well as by the organs. In this phenomenon, you are also actually going to have the transport phenomena. The transport is not only for the biomolecules; it can also be for inorganic molecules, including gases. For example, there will be a transport of oxygen at the lung surface, then it will enter the bloodstream and go to different parts of the blood and different parts of the body.

And then it is going to be distributed, and from the different parts of the body, the carbon dioxide is going to be taken up. Then it will reach the lungs, and it will be going out right. This is actually very, very essential, and that's why the transport phenomena are very, very essential for an organism to survive. And it also helps in maintaining the pH balance. So all this, I think you will understand when you discuss or when you would like to study human physiology.

So if you study human physiology, you will see that there are many processes within human or animal physiology where, without transport, it is not possible to run those mechanisms. For example, for the excretions, the kidney has to transport the different types of waste material, but it also has to transport the material back into the bloodstream, which is good for the body. For example, it has to transport back glucose and other kinds of essential biomolecules, but it has to take up urea and other kinds of toxicants from the blood, right? And that's how it is; actually, this transport phenomenon is also helping in maintaining the homeostasis of the body, right? So it actually maintains the natural environment of the body, and that's how it is very, very essential for the survival of the organisms. Now when we talk about the transport phenomena, all of this has already been discussed. So I have divided this into two processes.

One is how the transport phenomena are happening in the prokaryotic system and how the transport phenomena are happening in the eukaryotic system. Although there are no exclusive phenomena for the prokaryotic system or the eukaryotic system, the cellular machinery could be different in the prokaryotic system versus the eukaryotic system. So let's first talk about the, you know, the prokaryotic systems. So when you want to understand a transport phenomenon, what you have to understand is that if there is a molecule, for example, if this is a glucose molecule, right? If this is a glucose molecule, what is present in the environment? And if this is a bacterium, right, this glucose has to enter and get into the cytosol, right? But in this particular journey, it has to pass through this specific barrier, right? It has to pass through this particular cellular barrier. And this information about the cellular barrier is very important because, accordingly, you or the organism are going to devise the transport phenomena, right? So for the transport phenomena, two things are very important: one, the chemical nature of the molecule that needs to be transported; and then, the cellular barrier, right? The decomposition, as well as the stoichiometry of this particular barrier.

So there are various surfaces in bacterial cells, primarily the capsule, slime layers, cell wall, cytoplasmic membrane, and outer membrane. And these are the barriers. These could vary among different bacteria, and this could be variable in terms of the compositions and all those kinds of things. So these structures form a barrier by controlling the movement of a molecule across the membrane. For example, the cytoplasmic membrane is semipermeable.

Most biological molecules cannot pass through it and require specific transport proteins to facilitate movement across the membrane. The outer membrane is selectively permeable and allows the movement of nutrients while blocking antibiotics. So this is just

a simple example to explain that these barriers have the job of maintaining the internal environment of the organisms intact. So they will actually be going to oppose the entry of these molecules and they will oppose the cell. If the cell is looking for or is interested in taking up these molecules, then it will actually devise the mechanisms by utilizing different types of proteins, carriers, transporters, and so on.

So these are the things which we are going to discuss in this particular module. So now when you talk about the barriers in the bacteria, you can actually have the barriers in terms of decomposition variations and all that. So you can actually have either the gram-positive bacteria or the gram-negative bacteria. So in the gram-positive bacteria, you are going to have the thick peptidoglycan cell wall, right? Which is located outside the cytoplasmic membrane? So basically, you are actually going to have three or four barriers, right? You are going to have a barrier in terms of the cell wall. You are going to have a barrier in terms of the cytoplasmic membranes.

And then you are also going to have a barrier in terms of the other kinds of surfaces, depending on the different types of prokaryotic organisms. Whereas in gram-negative bacteria, you are going to have a thin cell wall, and you are going to have the periplasmic space between the inner membrane and the outer membrane; and then within this, you are actually going to have the cytoplasmic membrane, right? So, collectively these surface layers not only provide structural protection but also play a crucial role in regulating the movement of molecules into and out of the cell. So, this is what it shows here. So, this is for the Gram-positive bacteria, and this is for the Gram-negative bacteria. And all these we have discussed in detail when we were discussing the cellular structure.

Gram-positive bacteria cell walls and gram-negative cell walls are not going to be discussed in detail; as for the barrier, you are going to have these four barriers: first, the cytoplasmic membrane, which is semi-permeable. Or selectively permeable, actually, then you are going to have the cell wall, then you are going to have the outer membrane, and you are going to have the inner membrane, and all these structures we have discussed in detail when we were talking about them in modules two and three, when we were discussing the cellular structures, right? Now let's talk about the different transport processes in the prokaryotic systems. When you talk about the transport processes in the prokaryotic system, I will tell you that these are not exclusive mechanisms of the prokaryotic system. The similar kind of mechanism could also exist in the eukaryotic system. So don't we get confused that, okay, these are the things that are going to happen only in the prokaryotic system? It could happen in the eukaryotic system as well, right? So there are four different ways in which the transport is going to happen.

One is that you're going to have passive diffusion. The second, you are going to have the primary active transport. So you're going to have passive diffusion. You are going to have active diffusion or active transport. Within active transport, you'll have primary active transport, secondary active transport, and a specialized class of transporters that will only present the bacteria.

Okay, so these are called PTS. Now let's first talk about primary diffusion or passive

diffusion. So it is one of the simplest mechanisms by which a molecule can cross the cell membrane. Remember that the passive means it will happen spontaneously. So passive means it will happen spontaneously and automatically.

Right. So there is no extra effort required for this particular type of process. Right. So, in this process, the molecule dissolves into the phospholipid bilayer, right? And it diffuses through it and dissolves into the aqueous environment on the other side of the membrane, right? And this is what is called passive diffusion, which means it can actually enter the cell and come out of the cell without any extra effort. The driving force in the process is the concentration gradient, right? So, it can go from higher concentrations to lower concentrations. The direction of the transport depends on the relative concentration of the molecule inside and outside the cell.

The net movement of the molecule occurs from an area of higher concentration to an area of lower concentration. The majority of the drug molecules are actually following passive diffusion. There are drugs that are actually also following active transport. But the majority of the drugs that are hydrophobic in nature can directly dissolve into the lipid bilayer, and that's how they get into the cell. And because the concentration of the drug is going to be higher outside and lower inside, that's why it is actually going to be transported without any problem.

Now, it is a non-selective process where any molecule that can dissolve in the phospholipid bilayer can be transported across the membrane and reach equal concentrations on both sides. So, how long is this transport going to happen? This is going to happen until C1 is equal to C2, which means C1 is the outside concentration and C2 is the inside concentration. So, this means if this is a bacterium, you have the C2 inside and C1 outside, right? And suppose you added molecule X, correct? So if molecule X has a C1 concentration outside and a C2 concentration inside, and if C1 is bigger than C2, then it will start transporting inside. And this molecule is actually hydrophobic in nature. It can dissolve into the transport bilayer.

So, it will keep going, keep going, keep going until C1 is not equal to C2. And you understand why the transport is, you know, going to be stopped when we discuss the thermodynamics of this process in our subsequent lectures. So a small, relatively hydrophobic molecule can efficiently diffuse across the membrane. Examples of molecules that can transport across the membrane by passive diffusion include gases like carbon monoxide, carbon dioxide, hydrophobic molecules like benzene, and small uncharged polar molecules like water and ethanol.

So these are some of the places. Remember that this could happen in the prokaryotic system as well as in the eukaryotic system. So you can actually have the transport of gases like carbon dioxide and CO_2. So you can actually put the oxygen inside and CO_2 you can take up. That is going to happen at the surface of the lungs, right? And then you can also have the hydrophobic molecules; an example is given as benzene, but it could be any drug that is hydrophobic in nature. That's why many people actually try to generate hydrophobicity within the molecule so that the uptake is going to be better and the cell is

going to take up these molecules.

Then the other molecule is like ethanol and water, right? Many people say that water is not a hydrophobic molecule, but water is also transported through passive diffusion. Now, in contrast, most other biomolecules cannot cross the membrane by passive diffusion because they can't dissolve in the hydrophobic bilayer. So, for example, you can have glucose, and you can have charged molecules like sodium, potassium, hydrogen, and so on. The transport of these molecules across the membrane requires the transporter and the channel protein. So remember that for glucose and all these kinds of charged molecules, you require a transporter as well as channel proteins.

Now let's talk about the other class, which is called primary active transport. So, as the name suggests, the primary active transport means that this is going to be active. This is for that. You are supposed to do something right, or you are going to work for it.

Right. So active transport is a process that requires energy to move molecules across the membrane with the help of transport proteins. And because it requires energy, you are supposed to work for this particular task. Right. It is mainly divided into primary and secondary types based on the source of energy that is going to be used. In primary active transport, the energy from chemical reactions like ATP hydrolysis is directly used to transport molecules.

This energy is used to move the molecule across the concentration gradient in an energetically unfavorable manner. So remember that energetically favorable means that you go from the higher concentration of the molecule to the lower concentration of the molecule. And then, basically, you are going to follow the passive diffusion mechanism. But when you want the molecule and the concentration of that molecule is low in the environment, then you are supposed to spend energy so that you will get that molecule, right? One example of family active transport is the ABC transporters, right? So ABC transporters, that is what is shown here, right? So, ABC transporters are membrane transporters that have a highly conserved ATP binding cassette. They use energy derived from ATP hydrolysis for transporting the molecules.

ABC exporters are a type of AV transporters. They consist of two nucleotide binding domains, NBDs, and two transmembrane domains, which are called BMDs, right? So what it's showing here is the nucleotide binding domain, and then you have the transmembrane domains. Some transporters are termed half-size transporters with one NVD and one TMD fused together into a single polypeptide chain. So you can actually have two different types of variations. In one, you are going to have two NVD domains and two transmembrane domains.

In the other cases, it's going to be half. The other exporters that have NBD are separate polypeptide chains. Then we have a general mechanism for every transporter suggesting is the alternate access model. Two confrontations with the transporters are observed. You are going to have both the outward-facing and the inward-facing. So in the outward-facing or the OX, the NBDs form a closed dimer, each with one ATP or ATP analog

bound in its active site, while the TMDs adopt an extracellular-facing V shape, right? And then in an inward direction, the NVDs are widely separated, and both the TMDs and MVDs form an inverted V shape facing the inside of the cell.

When the two ATP molecules and a substrate bind to the IF conformation, it triggers a transition to the OF state during which the substrate is released to the extracellular side. ATP hydrolysis then induces the switch back to the IF conformation and completes the export cycle. So in primary active transport, you are actively going to use ATP to induce the conformational changes. See, this energy is not being used for anything else. This energy is being used so that you can create a gap or make a passage for the molecule to come, right? So, that is why you are actually going from outward-facing to inward-facing conformations, and because of these switchings you are actually making, you know, the V shape like this or this, right? So, when you do it like this, the molecule will enter here, and when you do it like this, the molecule will get inside, right? So basically what happened is that when you make a space like this, the molecule will enter here when you make this molecule.

So it is actually going to be that the energy is required for flipping your two domains, the NBD domain and the transmembrane domain. Right. And it can happen in both directions, from inside to outside or outside to inside, right? Depending on where you want the entry, do you want it this way or that way, right? Then the second is secondary active transport. So this is just a derivative of the primary active transport where the alternative energy is going to be used. So in secondary active transport, the transport of a molecule is linked to the electrochemical potential of a solute.

The solute gradient, which is initially established by a primary active transport system using ATP dehydrolysis, provides the driving force to move the other molecules against their concentration gradient. So this is one of the places where the secondary active transport occurs. It does not use ATP directly but rather relies on the energy stored in the coupled transport of another molecule moving down its gradient. Many molecules are transported across the concentration gradient by an electrochemical H plus gradient. One of the classical examples is the proton gradient that is generated within the mitochondria or the chloroplast, and that is how this particular proton gradient is used for deriving energy.

So, if you do it in the reverse selection, you can. So, if you see in this case, you are spending the energy to generate the gradient, right? You can do the reverse, right? You can use the gradient to generate the energy correctly. One example of secondary transport is the lactose permease of E. coli, or lacY, which is a galactoside H_2O trans importer, right? So it is composed of the 12 transmembrane helices. So these are the 12 transport helices: 1, 2, 4, 5, 6, and 12. With two domains having six transmembrane helices each connected by a long loop, this is what it's going to show: this will have 1 to 6, and this will be 7 to 12, with all these connected by a long loop.

In the N-terminal, there are six helices, and in the C-terminal, there are six helices, which are connected through a long loop present in the center. And likewise, does coupled

translocation of the galactoside with H+ and use the free energy released by the H+ translocation for the galactose transport across the concentration gradient. So, what it is going to do is actually transport the H plus, and when the H plus is transported, it is going to generate the electrochemical gradient, and that gradient is going to be utilized for producing energy, which will be utilized for the transport of another molecule known as galactoside. So according to the alternating access mechanism, the transport protein in outward-facing conformation first gets protonated and then binds the substrate. Substrate binding potentially induces conformational changes leading to the inward-facing conformation.

Finally, the substrate and the protons are released from the transport protein into the cytoplasm. The transport protein returns to the outward-facing conformation. So this is what I was talking about, right? So initially, I was saying it like this, like this, and like this, right? So this is the actually outward-facing conformation. So where you are actually going to have the two domains, you know, coming together, and then what will happen is the H plus is going to bind, and it is actually going to induce the conformation, and then you are actually going to have the inward-facing conformation, and that's how you're going to deliver.

The substrate and you are also going to deliver the H^+ ions. So, this is the way in which secondary active transport is going to transport the H plus and galactoside inside the cell, right? So, H plus will come and bind; it is going to induce conformational changes, and the substrate is going to bind. This is the outward conformation, this is the inward conformation, and that is how it is actually going to release the molecule, resulting in inward conformations. Now let's talk about this specific class of transporters, right? So, the transport mechanism processes, where you are going to have this specific class of molecules, which is called pts. So the PEP sugar phosphotransferase system, or the phosphoenolpyruvate (PEP) sugar transport system, is found only in bacteria.

So remember, this is exclusive to bacteria. It may not be found in the eukaryotic systems. The system catalyzes the transport and phosphorylation of sugar derivatives such as monosaccharides, disaccharides, and amino acid sugars. Polyphenols use the PEP or phosphoenol pyruvate as an energy source and phosphoryl donor. So PEP is going to serve two functions. It is actually going to transfer the phosphate group, and it is also going to provide the energy.

Thus, it phosphorylates its external carbohydrate substrate, and their transport in cells leads to the accumulation of the sugar phosphate esters. The uptake of sugar coupled with its phosphorylation involving substrate modification is termed the grouped translocations. Many phosphoryl transferase proteins participate in the system and form a phosphoryl transferase chain where PEP is the phosphoryl donor, while sugar is the final phosphoryl acceptor. PTS consists of two cytoplasmic proteins, which are generally components of PTS enzyme 1 and the histidine-containing phosphocarrier protein HPR. The enzyme E2 or the E2 complex is specific to each PTS system, and it provides carbohydrate density.

It is made up of either a distinct protein or a single multi-domain protein. It consists of

E2A and E2B, which are hydrophilic domains, along with two transmembrane domains called E2C and E2D. Now the general mechanism includes the transfer of the phosphoryl group from the PEP to PE1, which then transfers it to the HPR, which transfers it to the E2A, and then transfers it to the E2B. E2B transfers the phosphate to the sugar while E2C binds the excess cellular sugar and transports it across the membrane so it enters the cytoplasm as a single protein. So this is what is going to happen, right? So you're going to have phosphoenolpyruvate, which is PEP, right? So, this is going to be PEP, right? And that is going to transfer the phosphate group onto the E1, right? So this is going to transfer the phosphate group onto E1.

And then the E1 is going to get phosphorylated. PEP is going to be converted into pyruvate. And then from here, it is going to be taken up by the HPR, or an HPR is going to be phosphorylated. Once the HPR is phosphorylated, this phosphate is going to be taken up by the E2A, right? And E2A is being phosphorylated. And then the A2A is taking up this phosphate to phosphorylate the sugar molecules, as well as the E2B, E2C, and E2D.

And that's how it is actually going to catalyze the transport mechanism. This is a major transport mechanism that is classified based on its mode of transport. So there are many mechanisms through which the cells are actually transporting molecules, right? And these mechanisms are being classified based on their mode of transport, how they couple with energy sources, subsets, and the phylogenetic grouping of the proteins. So which correlates to their structure, function, and mechanism of action. So you are actually going to have four or five different ways in which you can classify the transport mechanisms, right? You can actually have them based on the mode of transport, right? So, for mode of transport, you're going to have whether the transport is associated with energy or not. And then it is whether it is specific for a particular substrate or whether it is specific for a particular class, and then how these proteins are related to each other.

Based on this, the transport mechanisms or transport mechanisms across the membrane can be classified into two different classes: one is transporter-independent, which means you don't require any proteins, so in this, you are actually going to have passive diffusion. Then we have the transporter-independent process, so this is going to be second class, where you actually require a transporter. These are going to be active transports; this is going to be passive transport. This is going to be active transport, and both of these processes we have already discussed, right? Then you are going to have a transporter-dependent process.

So, within the transporter-dependent process, you can either have the channels. This is going to be 2A, right? Or you can actually have the carriers, right? And don't worry about it. We'll discuss all of this, right? And within the channels, you can actually have things based on the structures. What are the structural components that are present? So you can have the alpha-helix protein channels.

You can have a beta-barrel. You can have toxin channels. You can have peptide channels. Similarly, for the carriers, it can be either the primary active carriers, you can

have uniportals, you can have secondary active transporters, and then you have group translocations. And within the primary active transporters, you can have the phosphate bond hydrolysis-driven transporters, you can have the decarboxylation-driven transporter, you can have the oxygen reduction transporter, you can have a methyl transference transporter, you can have light absorption-dependent transporters, and then you can have the mechanical transporters. Within the mechanical transporters, you can have symporters or antiporters. Similarly, for the beta-barrel protein, you can have the porins or the gated active channels.

So these are the different classes of proteins that are actually going to participate in the transport phenomena. So basically, you are going to have two different types of phenomena: transporter-independent phenomena or transporter-dependent phenomena. Let's talk about this. So you can have the transporter-independent phenomena or diffusion.

So this is anyway that we have already discussed. Then you talk about the transporter-dependent phenomena. Right. So this is going to be a channel. So transporter-independent phenomena occur when you have diffusion. So, as I said, you know, diffusion is passive, right? So it's going to go from high concentrations to low concentrations.

It requires no energy, and the driving force for the momentum of the molecule is the concentration gradient. Examples of the molecules include gases, hydrophobic molecules, small and charged molecules, water, ethanol, and so on. And we have discussed a few examples in a couple of previous slides. Then we have the transporter-dependent diffusions. So you're going to have the carriers? You can have uniportals, secondary active transporters, and group translocators.

So let's first talk about the transporter-dependent diffusions, right? So it allows the transport of molecules that are polar and charged, such as carbohydrates, nucleotides, ions, and amino acids, across the plasma membrane. The mechanism includes the channels or the carriers. Now, talking about the channels, right? So channel proteins form the pores in the plasma membrane that lead to the free diffusion of any molecule of suitable charge and size. So, for example, in this case, you have the porins, right? The porins actually have a cavity or tunnel, and then they will be assembled onto the plasma membrane, creating a pipe-like structure.

Within this pipe, you can have specificity in terms of which molecules will pass through. One example of a channel protein is porins, which are present in the outer membrane of gram-negative bacteria, some gram-positive bacteria, mitochondria, and chloroplasts. Porins span the membrane in the form of beta-barrel structures, and that's how they actually create a tunnel through which molecules can pass. Then the porins allow the passive diffusion of small polar molecules and certain ions across the outer membrane by forming the aqueous water-filled channels. They mostly form a homotrimer in the outer membrane.

The moment does not require energy and follows the concentration gradients. General porins lack strict subjectivity, although some display a mild preference for anions or cations. Then selectively, porins are small and allow the passage of specific channel compounds. They selectively depend on both sides of the size limit of the channel and the properties of the amino acid residues that line the pores. So, basically, porins could be non-selective.

So they will actually allow any molecule that is smaller than this to pass through. Then the porins can be of the specific type. So that specific type of porin could be specific because the surface is coated in such a way that it only allows the moment of specific molecules. Or it could be because of the pore size. So it will not allow any molecule that is above this pore size, right? The other examples of channel proteins are the ion channels.

So they facilitate the movement of ions across the plasma membrane. The transport across this channel is very rapid and is approximately a thousand times the portal rate of the carrier proteins. These channels are very selective by nature. Only ions of appropriate charge and size can move through them due to the restriction by the narrow pores; therefore, the specific channel protein permits the movement of sodium, potassium, calcium, and chloride across the membrane. Remember, all these ion channels are actually very essential because they regulate the transport phenomena, and that's why these molecules are also excellent targets for drug development. Most ion channels are not always open, and their opening is controlled by a gate that temporarily opens in response to a particular signal or stimulus, right? So there are many examples where you have voltage-gated channels and ion gradient channels, and so on.

So opening allows the ion to flow through the channels, and then ligand-gated channels open upon binding of the signaling molecule, while voltage-gated channels open when there are changes in the membrane's electrical potential. So there are several mechanisms through which these channels could be opened or could be closed.

Right. So one of the mechanisms is that you're going to have a ligand that will go and bind here. Right. And then when the ligand is going to bind, there will be conformational changes, and because of that, the outer channel is going to be opened. Right, so earlier the channel is going to be constricted; then it is going to be relaxed. Similarly, you can have the voltage-gated channels. Voltage-gated channels are mostly present in the neurons and other places, right, and they will actually also do the same thing.

So ligand-gated ion channels open in response to the binding of specific molecules. Examples are LIC, which are homopentameric ion channels. It is a cation-specific ion channel, and then we have LIC, which can be activated by primary amines like propylamine. Then we have voltage-gated channels. So voltage-gated channels are opening in response to a change in the membrane potential. Examples are sodium-CH-bac consisting of four tantra members with identical subunits, each with six transmembrane helices S1 to S4.

And from the voltage-sensing domain, S5 and S6 form the common pore domain connected by the P-loop and are involved in ion translocation. The levas motive found in the p-loop of each subunit is some type of channel and plays a role in ion selectivity. So this is what the voltage-gated ion channels are, where you have the S1 to S6, and these are actually going to be responsive to the membrane potential across the membrane. So when a potential difference arises across the membrane, the resulting electric field induces a conformational change in the voltage-gated ion channels, right? So this is what it's going to have, right? So when there are conformational changes, when there are ion voltage-gated channels or voltage across the membrane, it is going to induce the conformational changes, and that's how you are going to have the ion channels that are going to be open. This structural shift opens the channel pore, allowing the specific ions to flow through their concentration gradient.

The resulting ion movement generates an electrical current that alters the membrane potential, often leading to the depolarization of the membranes. This is what you might have studied when there is neural conduction within the neuron, right? So it happens exactly the same way that sodium is entering, potassium is going out, and that's how it is actually going to be produced. A layer or a wave of the plus and minus, plus and minus, and that is how the current goes from one part of the cell to the other part of the cell. And then we have the carriers. So you can have the primary active transporters, within which you have the uniporters, secondary active transporters, and group translocators.

So carrier proteins actually bind the molecule that has to be transported and undergo conformational changes, which allow the molecule to move across the membrane. Within this, you will have the primary active transporters. It includes the transport of molecules across the membrane, using the concentration gradient and the chemical energy, such as ATP hydrolysis. Then we have the unipodters. So unipoters, as the name suggests, are going to allow only the movement, right? So unipoter is a transmembrane protein that facilitates the transport of a single type of molecule or ion across the membrane without requiring ATP hydrolysis or the simultaneous movement of another substance.

It facilitates the diffusion of the substrate down the concentration gradient, doesn't it? So, basically, it allows the movement of a single molecule, right? That's why the name is the unit transporters, and they will actually allow the molecule to move according to the concentration gradient. These transporters do not require any active energy, and molecules are transported by the conformational changes upon ligand binding. So, examples of the unit transporter are the semi-suites, right? This is a topology of the semi-suites, right? The structure is made up of three transmembrane helices, like 1, 3, and 2, and they function in their active form as a dimer. The general mechanism is that the outward open state binds sugar on the outside, the occluded state traps sugar inside the proteins, and the inward open state releases the sugar into the cytoplasm.

Then we have the secondary-active transporters. So they utilize the energy stored in the electrochemical gradient, which is often established by primary active transport, to move the molecule across the concentration gradient without directly using ATP. Some examples are coupled transporters, where the movement of one molecule is entirely

dependent on the transport of others. And the coupled transporter can occur in two ways. Either the symporters move the second solute in the same direction, while the antiporters transfer the second solute in the opposite direction. So basically, when are you actually going to have the coupled transport, right? So transporters could be three types: uniporters, symporters, or antiporters.

Symporters are only transferring one molecule, right? But the symporters transfer the two molecules simultaneously. So, molecule number one and molecule number two will both enter simultaneously, right? Then the antiporters are actually transporting molecule number one and molecule number two. So molecule number one will be outside, and molecule number two will be inside, which means they are in opposite directions. So molecule one will enter, and molecule two will go out, right? So molecule two will go out, and molecule one will enter. So that's how it is going to have the movement of the molecules in the opposite direction. The solute sodium transporters are integral membrane proteins that utilize the existing sodium gradient to transport molecules such as sugars, amino acids, ions, etc.

Examples of the bacteria include the sodium proline transporters and VOTP, right? And the sodium sialic acid transporter, which is called a CRT, is present. Put-P transporters contain possibly 13 transmembrane domains connected by hydrophilic loops. They usually have a core of 10 transmembrane domains arranged in a 5-inverted repeat with an antiparallel orientation. The sodium gradient provides energy for the transporter to move proline across its concentration gradient.

The proposed mechanism is alternating access mechanism. So the sodium is going to bind to the symporter in an outward open fashion state, which induces conformational changes allowing the substrate to bind. It goes through further conformational changes, first leading to the offloaded state, and then reopening the substrate and the ion binding site towards the cytoplasm. Both ions and substrates are released in the cell. The transport returns to the original outward open state for the next transport cycles.

Then for the antiporters, the main function of the antiporter is to maintain pH homeostasis and sodium efflux. The efflux is important for sodium circulation in and out of the cell. As many as bacteria rely on both proton motive forces and the protomotive forces. Some of the sodium-potassium antiportals have the NHA fold.

They have the inverted topology repeating, forming the two domains. One is the core domain responsible for ion transport. The other is the dimerization domain. The core domain contains the two partially unwound transmembrane helices with sodium inside, right? So, antiporters are putting A into this side and B into that side. So, they will actually be moving the molecules in different directions. For example, sodium-potassium antiporters put sodium inside and potassium outside. And as far as the mechanism is concerned according to the pH sensor model, the acidic cytoplasm makes the transport inactive and the pH sensor is protonated, which blocks the sodium binding.

In alkaline pH, the sensor gets deprotonated, and the sodium binds, leading to the

translocation across the membrane. Before the translocation of the sodium, a proton has to be released. And then we have the group translocators, right? So these are another class of molecules, right? So, group translocator, the transport of the molecule coupled with the chemical modification of the molecule is termed the group translocator. An example of this transport is the phosphoenolpyruvate:carbohydrate phosphotransferase system. This system we have already discussed in detail when we were discussing, and this is the exclusive system that is present in the bacterial system, right? So this is all about the transport phenomenon within the prokaryotic system. What we have discussed is that cellular transport is a critical process that ensures the proper cellular function by regulating the movement of molecules across the membrane.

Different membranes and the surface layer form a barrier and regulate the movement of molecules across them. Various transport processes and mechanisms are present in bacteria for processing, such as picking up essential nutrients, eliminating waste products, and regulating ion levels. Transport proteins play a crucial role in these processes, facilitating the selective movement of molecules across the membrane. So, with this, I would like to conclude my lecture here. In our subsequent lecture, we are going to discuss some more aspects related to cellular transport. Thank you.