BioMEMS and Microfluidics
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Lecture - 01
Introduction to BioMEMS and Microsystem

Good afternoon, I am Shantanu Bhattacharya and I will be your instructor for this course on the introduction to BioMEMS and Microsystems. Let me introduce a little bit of, what BioMEMS really is BioMEMS is also in other words called bio micro-electromechanical systems. It is really about things, which I do very useful and important things that a scale which is micro or sub macro in the regime. So, I would like to discuss today a few basic source of introductory concept, which are important for understanding this course more properly.

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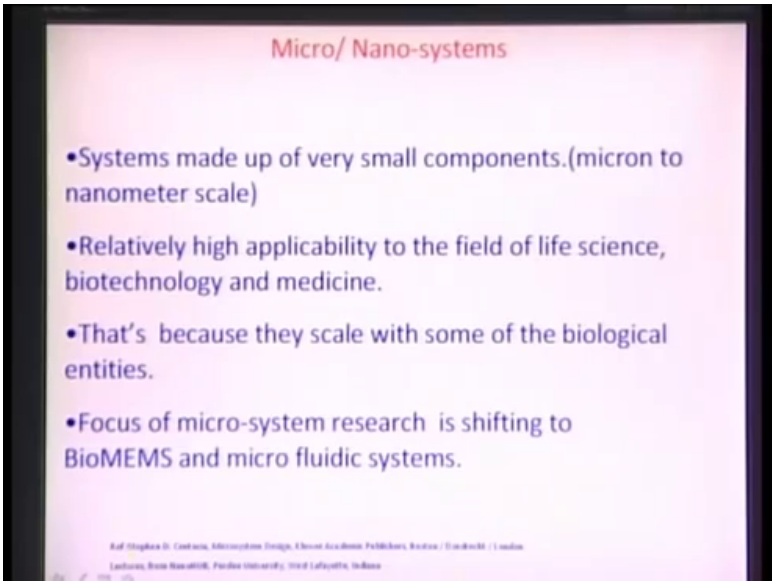

So, let's go to have a look at what definitional micro nano-systems can do they are really system is made up of very small components micron nanometer in scale they have a relative high applicability to the field of life sciences biotechnology and medicine, which as really started more with you know the advent of things called lab on chip technology as I will be describing later throughout the course.

And essentially one of the reasons, why these components rime so well with life sciences based detection and diagnostics and biotechnology and medicine applications is, because they

really size with similarly to some of the biological entities and as of late the focus of such micro system research is gradually shifting to micro fluidic systems.

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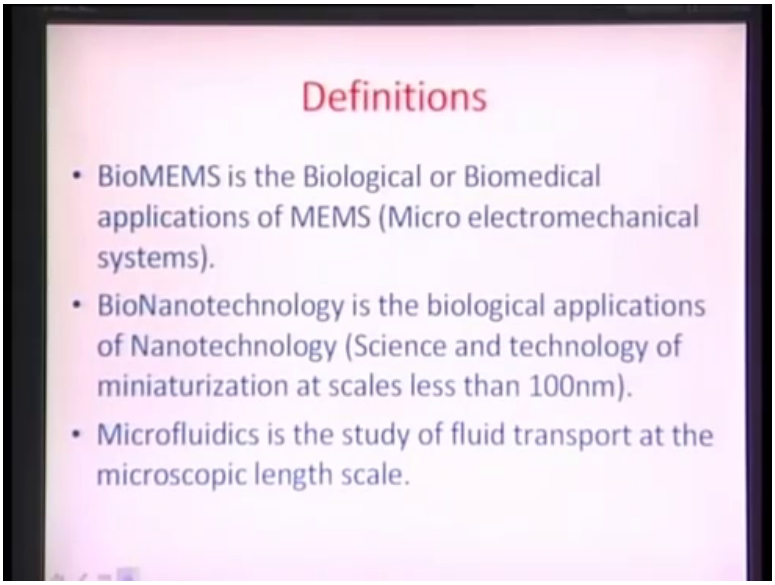

So, let us understand little more of what definitionally BioMEMS can be laid out as, so BioMEMS really is the biological or biomedical application of MEMS technology. And there are few more important terms and I would like to discuss before starting one is Bionanotechnology, which is the, the Biological applications of Nanotechnology science and technology at the scale you known at the scale less than 100 Nano meter is really, what nanotechnology is and if you combine that to Biological concepts, then it is also known as Bionanotechnology.

Microfluidics is will be seeing later on throughout modules is the study of fluid transport at microscopic length scale and this concept are really all very integrated important to understand the utility are the essence of BioMEMS.

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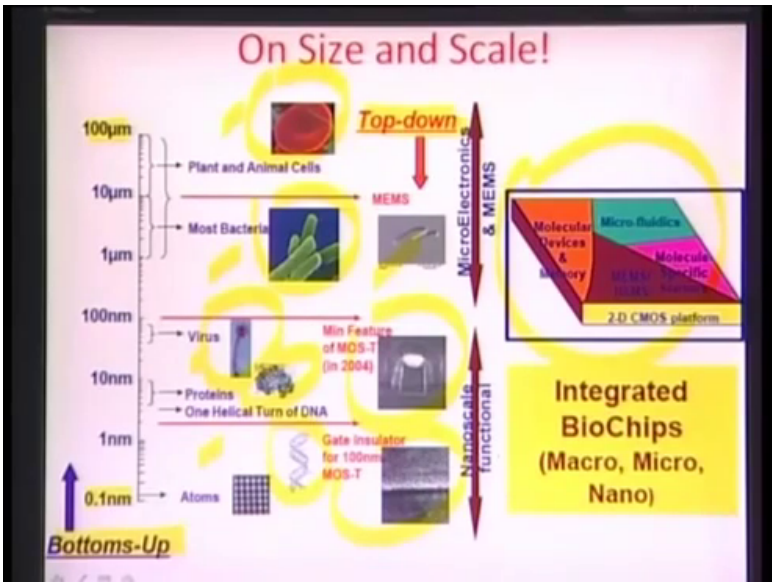

So, let us have a little more diagrammatic representation on what are the sizes and scales that I have been talking about. So, if you really look at this is scale here the scale here on the left on your left here start from 0.1 Nano meters all the weight about 100 microns. And let me be a little more specific on, what 100 microns would really look like human hair diameter typically is that of about 100 micro meters, so that's how small it is and 0.1 Nano meter is several 1000 of that dimension actually.

So, you are dividing that as speeding that in to almost about 10000 times in order to achieve something like 0.1 Nano meters. Now, if you look at some of these entities here as can be represented on the just very next to this scale most of the plant and animal cells and this right here is actually red blood cell there are millions of such cells within the human body this is shaped like something like a button and they rim in the range of about 100 to 10 microns.

In fact, red blood cell the assume images of which is represented here is about 20 microns also. If you go a little bit down this cell for example, this here is E Coli.. this is equalize of E Coli. Bacteria most bacteria cells rim in the range about 1 to 10 microns. So, they are at least a tenth smaller or at least a tenth smaller, then million as the plant and animals cells.

Let us go a little bit down further here this right here is actually a virus, which is the essentially nothing but, a cote of a capside made up proteins an enclosing sum genomic information. And is the typically the sizes of this viruses are of the order few 100 Nano meters. If you go a little bit further down we have molecules like let say proteins are DNA

and here something very interesting DNA it is nothing but, it twisted ladder. So, you take a laded and kind of twisted and one helical turn of a DNA is something like about 2 to 3 Nano meters about 20, 30 Armstrong . And, if you go a little bit down further you have atoms and molecules and this really is an approach, which is also known as the bottom up approach are bottom up means of manufacturing somehow we can illustrated this as a mother nature's has been making this higher form this lower ones which are principally atoms by using concepts of self-assembly and energy driven mechanics and so on so forth..

So, if you look at the figures some from the right here really they are things, which are actually made using the top down approach, which means that we have a bigger much bigger size wafer are plot form. And you are trying to reduces at through micro machining are technologies, which we together known as micro technologies and trying to make smaller and smaller sizes in the way. So, if you look at this figure here this illustrates actually nothing but, a micro cantilever.

So, I call it something like diving board in a swimming pool as a there is a pool and there is a kind of you know board, which is striking out and the only different here is that board is about nothing but, 200 to 300 Nano meters is thick and the projected about 10 to 50 microns ahead and, so the scale is simply 2 to 2 very small he go down a bit further this right here is a very interesting example It is a poly silicon gate with nitrate spacing in fact it is the commercially available device.

So, if you, look at the ITRS road map the international semiconductor technologies road map. It mentions that by the year 2004 actually, which was about 3 to 4 years back the transistors the minimum features size on a transistor was close to about 100 Nano meters and it has even reduce, now further. For such a device the gate insulator, which is actually something like you know packing between the it is like a dielectric material between the metal contact and the actual device that insulator about 2 to 3 Nano meters.

So, why I am showing you all this is that if you really compare this features and objects on a size scale they very well rim with each other. Like for example, as I told you viruses about few hundred microns few hundred Nano meters and you can really with micro and Nano technologies produce features like a polysilicon gate, which is of the same range molecules are even little bit further down and that rimes very well with this gate insulator. So, this size compressive kind of allows as the luxury of bringing these two words close together. So, that

they can be they are accurate sensing deduction diagnostic so, on, so forth. So, that is why Bio MEMS

If you look at some of these kind of modules are you know figures here this represents the basics schematic of how this MEMS can be laid out on simple let say to this simple plot form. So, it is a combination of different concepts like molecular devices on memoir you know MEMS and MEMS technologies micro fluidics systems and then, microelectronic and you combine everything together to form something, which you can senses and diagnose these life size entities very sensitive and accurately in this area Bio MEMS it is becomes that if you can develop these kind of approaches and call them integrated Biochips at the micro macro Nano scale and this could be very useful as will see throughout the lecture and letter how they can various applications of such architectures of such technologies.

So, one thing very important to mention here is that, because these life type of entities tends to be happy with in fluid environments therefore for their accurate t diagnostics are deduction it is very important for the entities to be in actually fluids and we should prepare fluidics in a manner, which can again rim very well with their sizes, so that we can have concepts like you know single cell by single cells transfer are trying to isolate the molecules on a plate of surface. So, therefore, the concept of micro nano fluidic emerges from there. So, these are really integrated together and it is very important for understanding is simple in intuitive engineering design I would say for doing something with more precision rapidity accuracy so on so forth..

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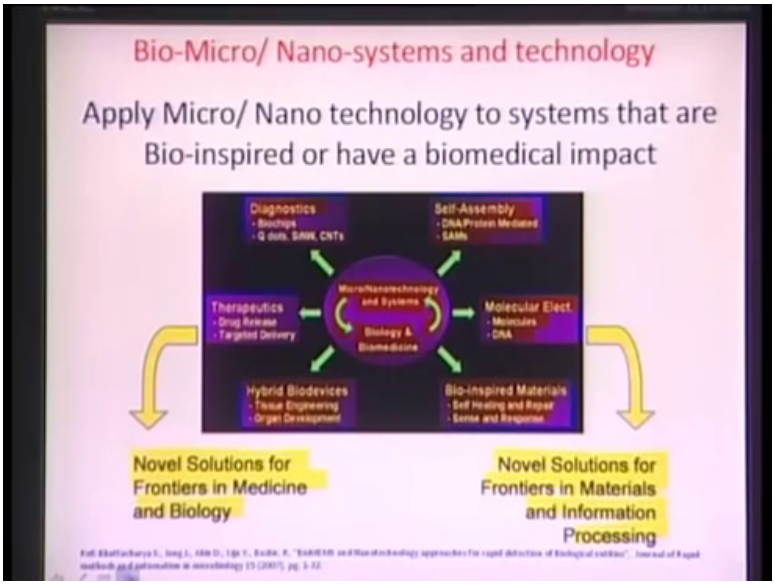

So, I really put this whole field as it is as synergistic learning experience between the areas of micro Nano technology and systems and Biology Bio medicine. And you know really these technologies are the systems are Bio inspired in a sense that there is too inflow learning between biology and this technique. And, so if you look at this figure here more clearly left sides this idea.

So, here if you see the circle in the center here represents these tow area micro nanotechnology and systems and biology and bio medicine and if you see there are these tow arrows and both sides well they are showing that what can be learn from, what. So, if you look at the boxes on the left like diagnostics biochips quantum dots silicon Nano wires carbon Nano tubes these are really some of the technologies that we can applied to biology and Bio medicine and we can learn from the micro nanotechnology and systems.

Similarly, you have area like as therapeutics really target delivery nowadays there is huge impacted of how microscopic quantities are mites quantities of tracks can be injected, how do you do that. So, you have very good learning experience from micro Nano technology and systems and try to relies dimensions and features in a manner that this is doable another very interesting area is this hybrid bio devices and nowadays there are this whole initiative of issue engineering you can develop something artificial heart or artificial kidney and artificial liver.

So, essentially is the nothing but, an approach, we are used tried to utilize some of the learning experiences from micro nanotechnology and system and apply directly to make artificial organs maybe. The boxes here on the right are actually reveres process of learning; that means, there are based on concepts where learning borrowed from biology and Bio medicine and applied on to micro nanotechnology and systems. And you can see these some of the examples as self-assembly are DNA are protein mediators.

So, I will be describing little bit details latter what DNA structure looks like are how it actually self assembles. But, the DNA unique kind of entity, which is able to you know it is able to kind of a pack togather in a certain shape or features or pattern and it really gives as a lot of inspiration a lot of learning. So, from the diesel and wiger with which the two strands of DNA, which are complementary each other and a self-assemble and stitch an each other the base pairs we could have a lot of a learning which we can apply to really micro and nanotechnology.

So, self-assemble mono layer as matter of factor another area where you know from just from basic elemental chemistry we could make micro Nano patterns are features of this molecule over the different parts of surface and that could realize micron Nano domain are micro Nano features from learning borrowed biology and Bio medicine. Similarly, another very fascinating area is molecular electronics where we talk about single molecule being able to conduct current between to poles which are placed one molecule path are may be a single DNA and there are a lot of interesting work in this area we says that you know if you have it is DNA is as a wire which is connecting between two poles and just simple use it as a just a .you know the resistive circuit it just follow the v=yr relationship I own this case as you know the GC content are the one side to design content of the DNA is increase you see that there is change in conductivity so on so forth. So there is a huge effort of using the some of the entities to words transferring charges very sensitively at a very small scale. And this could be immensely contribute to the field of micro nano technology. Similarly human skin its very interesting example having we called it balance bio inspired material just think about how important the human skin is and what kind of properties does it have it can self-feel it can response it can do all of you know repairing self-repairing kind of things automatically. And if you really what want to replicate something like human skin that would be a fascinating ease micro nanotechnology, where probably millions of sensor are pack on to a surface and each these sensor has a different job.

So, I really call this areas that the inspiration learning from micro nanotechnology to biology and bio medicine would be able to develop novel solutions for some of the frontiers in materials and information process medicine biology. And, similarly the learning experience that we have from biology and bio medicine would be able to develop some novel solutions frontiers materials and information process. So, it is really a synergism, which is exits between the two areas and therefore, it is also the best impress to integrate the area of bio with is micro Nano system and thus the terminology as we have been describing like bio memes bio Nano technology etcetera automatically self immerge, because of this mechanisms.

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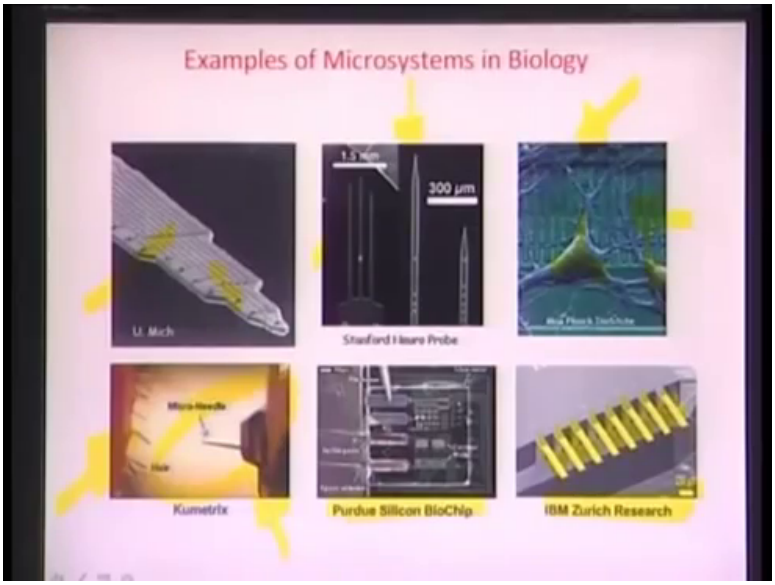

Let see, what can these kind of micro systems really do in biology and this is a slide which I really keep on illustrating time and again. It gives in a sense of what kind of applications are really available and some of them mind you work really commercially available applications as well be illustrating. So, this here as you see is nothing but, and neuro probe it is develop by doctor wise is group at the, university of Michigan Ann arbor. And essentially if you see this is again a very fine example of micro nanotechnology where in this particular features is probably of the size of just of few microns there are these small, small as you see here the small wires, which are printer by just lithographic processes on to such a probe and this prop is use for electrical monitoring the electrical activate of brain cells or brain tissues .

Now, the why micro technologies required in that is that is you think out neurosurgeon who is actually just operating on some bodies you know the cranium portion and he wants to inject big tool we can just to electrical response monitor it is not a very feasible option you know the patient would suffer a lot of pain there would be general, general tendency of the unnecessary damage, which may of have along consequence in terms of the patient's post-surgical health. And lot of other issues are considered.

Now, if instead of that replace of whole electrical sensing tap its very small micro needle, which can just go in to a very small area of the cranium and do the same job as a big tip would be doing that kips really the utility are a sense of such a technology. This again is a very fine example it is basically very long cylindrical like probe neuroprobe developed at stem probe and essentially use for giving deep electrical stimulation specially patient suffering from Parkinson's disease.

This area again as a very fashioning area and I call it probably the future in the area of bio memes bio technology this is essentially a set of neuron cells, which are growing on an array of mass fate you can see these here are the cells they are growing on set of mass transistors this area as also known as by the by nanobiology. Now, think about that the signaling between these cells and I would going to be little bit details biology later as we go along these area. Essentially this cells grow in a very unique manner with there is a lot of signaling path way between the two, which would certified are which signified the behavior of such cells.

So, if we can study uniquely on a single cell bases what are those signaling path ways is terms of may be exchange of iron or chemicals between the these two cell this of humans utility to in general you know understanding life process as such. So, there is huge initiated, now how to study these cells on single cell bases and trying to illustrate what kind of chemical reactions on the surface of within the cells as going on and what kind of communications is going on between such cells which would relate to their behavior in general. Again this a very good example that you know I almost always keep on mentioning this micro needle and this comes for very common life experience.

So, the needle of the mosquito is essentially when a mosquito bites you, you do not really feel the pain, what happens is that as the needles goes into your skin the needle of mosquito go into a skin there is a post injection swelling, which comes up, that swelling is not, because of any you know pain effects or any effects, because of the needle picking in that essentially,

because when the mosquito actually tries to drop blood it release some enzymes, which kind of tries to blood sample and it becomes very easy for to draw a blood sample in this manner.

But, again the fact that when the needle goes in to the skin it hardly makes in a difference to do this can you do not feel any pain. And the reason why pain is really felt in the human skin it is because that there are if you look at the skin really beyond you know about, let say 100 microns of layer of dead cells, which we also know epithelium they starts set of set of receptors called pain receptors which are nerve ending essentially and the mosquito needle is.

So, thin that goes into the 100 microns and goes very close to that region of pain receptors, but it is hardly able to deflect or damage some of these receptors. So, there is no pain sensation and mosquito does his job it goes into another vasculature pick the blood samples. And then, you know it kind of feeds itself on that bases. So, the same principal has been used using this borrow in this inspiration from micro nano from the biology and bio medicine to make what you called micro needles.

This write here a illustration what a micro needle really means if you look at this needle it is something close in the dimension to that, that of mosquito and there is a in fact commercial company called kumetrix which cells 1000 of needles on something like a patch which you really wind around the patients hands and it can do things like you know parallel processing including monitoring of analyze inside the blood sample drawing of sample from time to time extra.

So, it is fascinating example of what micro Nano technology can do by replicating biology or getting bio inspire and do something use full and important. This again is a very interesting and fascinating example of what we called bio chip or lab on chip and I am going to come to it this in just about a minute in more details about for what bio chips really are. So, essentially these are you know protocols, where whatever is possible with in a laboratory is all miniaturize down to a single chip scale. And in terms of handling very small droplets or micro fluids of micro volume you quickly and rapidly do whatever laboratory does on a much bigger scale.

So, this is also known as lab on a chip or bio chip and lot of research, where in integration on electronic optics lot of different transition techniques or taking place into densely integrated platform also known as bio chip or known as lab on chip kind of mechanism. This is again a

very fantastic example of what can micro technology do in biology and these here are those diving boat kind of swimming fool structure this are micro cantilevers.

Essentially the scale here if you see is only 250 microns, which means that they are projected about, let say about three times that size about 750 microns. But, look at that thickness really they are about the tenth, which about lat say about 300 Nano meters are. And interestingly there are several of these uniquely position and spaced small, small cantilever devices available to this edge of this particular, let say piece material, which can be silicon and what it did essentially does it is nothing but, a mass detector. So, if you are able to somehow you marbleize some cells are some molecules on the top of this particular structure of cantilevers due to the weight that is somehow you marbleize on the top.

There is a deflection in bending and the deflection and bending you would back calculate by using the equation called as Stoney's equation and I will be doing detail of this little bit later. The mass of the particular entity; however, the advantages of small size of the cantilever the there is solution of to which you really pick up masses go up o the order of about femto grams you know Pico to femto grams and that was give to you a unique of applications of micro systems in biology.

So, we have been discussing earlier about micro fluids we have been really learning it as important, because you talking about biology entities and typically all biological entities are happy when they are in fluidic environments. But, it is very interesting that you know the behavior of fluid at this particular scale microns scale really very very countering to any person, who trained to microscopic fluid behavior in any engineering curriculum.

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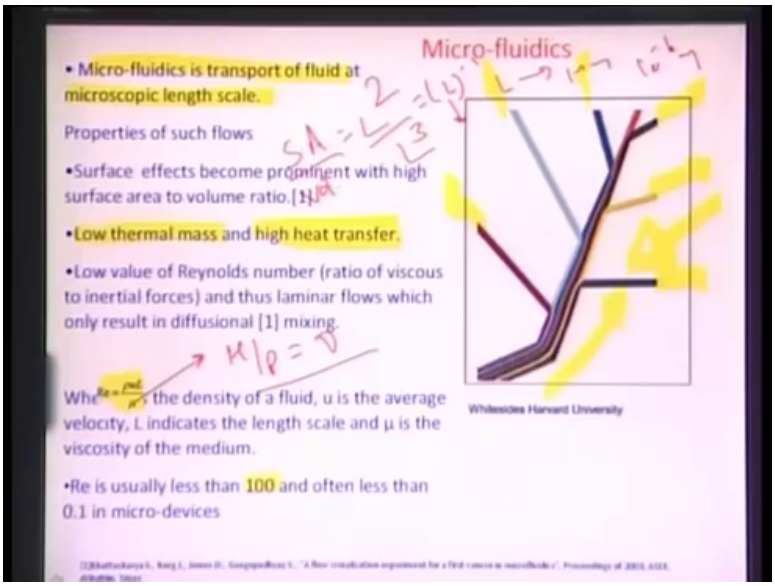

As I earlier indicated that the definition of micro fluid is really is the transport of fluid at the microscopic length scale. And there are some unique properties and changes, which happen, because of the scale change while the properties is very, very important to be mention is of the surface effects become prominent with high surface area to volume ratio. And, if you look at, if you just dimensionally compare surface area to the volume it can be represented as L square by L cube, which is about L to the power of minus 1 .

So, if this L is going to the micron level micrometer level which is nothing about 10 to the power minus 6 meters you can just think about that the you know the surface area become, so more most some much more prominent with respect to the volume it become about 10 to the power of 6 times more prominent with respect to the volume. So, you have some forces are some effects, which are related more towards the surface they gain much more in prominent in comparison to the volume force. In case of fluid volume forces could be something like you know inertia could be something just acceleration due do gravity of a small fluid mass. And these are also packed together is intertidal effects essentially you know the pressure driven aspects of flow, which is consent with the mass of the fluid flow. And surface area on other hand something, where there could be forces of surfaces tension, which is just related to what is the length you known of interface of fluid with respect to some other particular boundary or may be viscous forces, where surface area becomes more prominent.

So, has surface area related activity are events become prominent in this case therefore, you know the viscous forces of surface tension related forces are much more into question. And these are critical parameters for designing such devices over the general macroscopic idea of designing devices on the bases of volume based flows. And other very interesting effects here is, because of the low thermal mass and high heat transfer we talking about miniaturize droplet size. In terms few micro liters of volume and therefore, it is very easy to probably conclude that it has very low thermal mass that is number one and essentially, because of this low thermal mass there would be high heat transfer they are initiated inside micro fluid device where in some of the fluids are tried to make into a thin layer on the surface. So, if you look that instead of making that thick layer more volume based your making more surface base and thinner layer.

How you make that is again what BioMEMS tells you BioMEMS technology Bio MEMS fabrication technology tells you. So, essentially you're taking the whole fluid surface and therefore, trying to increase the heat transfer way. And other very interesting factor is a low Reynolds's number Reynolds's numbers all we know as the ration of inertial forces. And essentially you can also represent it as rho u l by mu as you can see here rho is the density of the fluid, which is flowing u is the velocity l is the corresponding length scale and mu is the essentially the viscosity of the medium.

So, also you can actually make this in by rho and make this the dynamic viscosity of the material. Now, no reynolds number really is typically asset an domain micro fluids you know there is lot of changes, because of this low Reynolds number value number one change, which happens is we can consider this as let say a pack of cars. So, you have about 100 of cars, which is moving in a very small street, which is you know may be peak traffic hour in our city here and what would happen, what you think would happen in a such situation happens. The cars would try to move in aligned manner in more like steam line fashion without really much cris-cross.

Because, you were packing lots of car together number one the velocity of the car would also go down. And then, even if we assume that the high velocity there is always the tendency of cars to move one beneath one behind another there would be hardly any people who would be trying to acts smart and change their lanes, because that essentially means collision or crayons or an accident.

So, therefore, if we just compare similar analogy in terms of molecules, which we are compress to the very small street or a very thin area this molecule also tend moving something called steam lines wherein they would move parallel to each other without that many of them really adventure really going to each other stand and colliding with each other. So, therefore, very unfortunate or may be in some situation fortunate I will be illustration later these with examples fact is that this molecules tend to remain in their own path without really going across parallel tracks or paths the situation, where is mixing hardly it becomes almost.

Next to important until and unless as we see later they are diffuse the forces which the molecule crisscross on the bases of concentration radiance between to flows. Just to illustrate this fact that kind of browed an example from wide size group here as you see the essentially this is a simulation, which talks about they are a set of this 1 2 3 4 5 6 around 6 dies of different colors, which are flowing, which are flow in a microscopic dimension.

They go in this manner and there are several of these track, which are emanating from different areas and as you see this fluids kind of go by together there is a unique tendency of the colors to get separated without getting mixed. So, this red color which was injected here as it retreat after a while and this blue color as treat as while, Similarly, this drake blue color as treat some while and the color cell them mix and it is really a real time simulation and this is what happen in the micro scale also, where you can see that the fluids also though flowing parallel hardly tend to mix because of the low Reynolds number value. So, just for illustration array in bio MEMS devices Reynolds numbers in bio MEMS devices is usually less than 100 are often or and as most often less than 0.1 are also.

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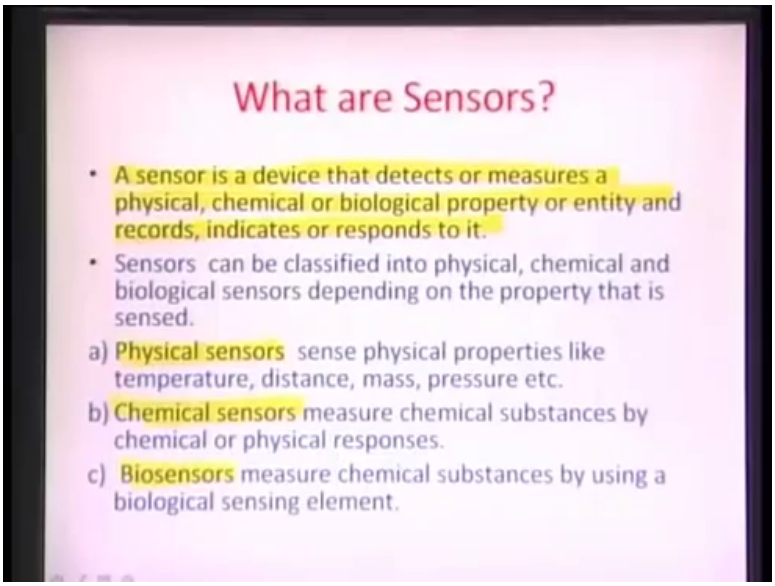

So, let we talk about little bit of sensor, now because this would be important for understanding say essentially the purpose of a bio MEMS devices is to really sense something sense a detecting something with some degree of accuracy. So, definitional we look at what sensors is sensors really is a device that detects or measure a physical chemical or biological property or entity and records are indicates or respond to it. So, essentially it would use for some kind of measurement could be a physical property, physical property could be something like temperature distance mass of an object the pressure in a particular channel is are all physical property.

So therefore, sensor can be something which detects of physical property and those sensor are known as physical sensors as it illustrate here. It could detect chemical properties and chemical substances, where in things like may be the chemical nature of analytic are you known the chemical and physical responses of substance to an environment is recorded. So, these type of sensors are also known as chemical sensor.

Then, finally, we have biological sensors which monitor or measures the chemical substances using a biological sensing elements. So, essentially there is always an integration between what chemistry to offer and what biology has to do, but the idea is that you classify some of those chemical sensors or bio sensors if the detection element is actually, more like a biological sensing element. So, that was bio sensors would do.

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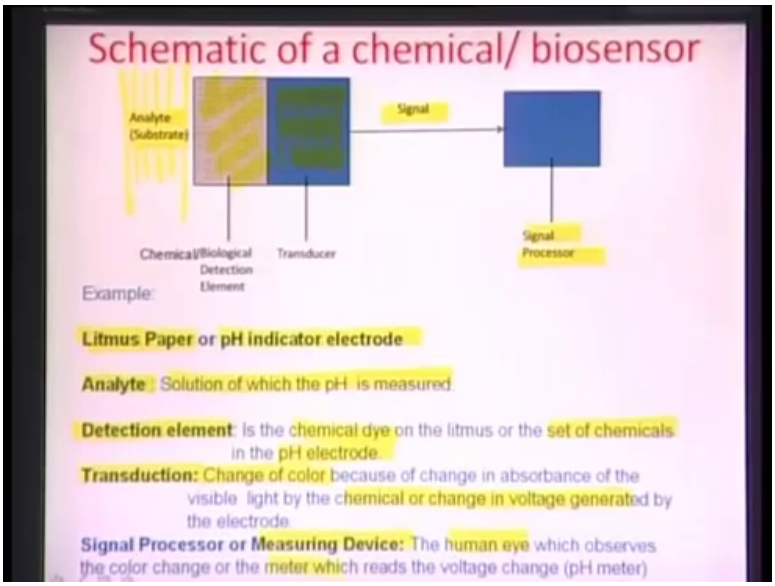

So, essentially schematically we can really in a very organize manner represent the sensor as something, which is going to detect this analyze or substrate which is present in this region and for detecting it you have something called a detection element which can be either the chemical in nature or biological in nature and then the detection element has a change in property. So, it may be a change in chemical property it may be a change in optical property and may be change in electrical property. And essentially this, this element, which there for the detection proposes has a change in property in the presence of the analyte or the substrate of interest.

It generates something called a signal and the signal can be further transfused by this particular element here, which is also an integrate part of the sensor and what does transaction really mean transaction is essentially is nothing but, a change of signal from one form to another. So, if you have a chemical agent there it is going to change in to a electrical signal or an optical signal, so this is called transduction. Transduction is a change in signal of one kind to another. So, you have an element here on the bio sensor as you see here which does this transduction.

So, whatever signal is generated from the biological detection element of the chemical detection in the presence of the analyte or substrate is transuded into a signal some form and this signal is essentially fade into a processor, which would be trying to read analyze interpret

the signal and trying to conclude whether there is an analyte of interest present or absence are in what quantity is this analyte of interest are present.

So, to gather this thing is can be define as an organized this schematic of what a chemical are a biosensor would do. Let me give an example the laboratory level litmus paper is something that probably all of you have used in your school days. And what essentially happen is that you if you expose this paper to a variety of pH; that means, variety of acidic or basic fluids it is changes it is coloration. So, there is a change in the absorption wave length of light, because of, which you can find a different color appearing based on different pH. So, there are now, commercial available litmus papers, where there are range of colorations, which are illustrate for the even having a resolution almost 1.0 pH change. So, you can at all different pH get a different absorption spectrum on the color. So, this is the finest example of a sensor are may be something like a pH indicator electrode, where you deep an electrode in a material and that electrode has a change in electrical property, which is signify what is the hydrogen ion concentration of a particular medium. So, these are examples of sensor chemical sensors.

So, let as try to illustrate this simple litmus paper or pH indicator electrode as a sensor module. So, you have an analyte which is the solution in which the pH is to be measured it can be a basic or acidic pH you have a detection element an in case of litmus paper it is the chemical die and in case of pH electrode this is the set of chemical of course. And this chemical die what it does it the transduction; that means, when the expose to an acid or pH of certain you know kind it is rapidly changes it is absorbance spectrum. So, therefore, as you know the absorbance spectrum is change that is the change in coloration of a particular material, so it change color.

The change in color because of chemical die getting expose to a certain level of hydrogen irons and can calibrate in a manner that if you have a x concentration you will have a different color if your y concentration you will have a different color. And, so there is certain scale on which is this can be mention in terms of color scale. So, that is what the transduction element is and in case of litmus paper with the human eye which observes this coloration changes is nothing but, the signal processor.

So, it is essentially the measuring device, which tells you that what color corresponds to what pH looking at a calibrate scale, which has been done before by somebody and which is

mentioned in all these packs of litmus papers and you just comparing the color through your eye to the color that is on the scale so that is essentially the signal processor.

Similarly, if you look at the pH electrode the set of chemicals in the pH electrode is the deduction element and the change in voltage which is generated by the electrode is essentially ways and means of chemical to electrical transduction. So, whatever solutions you are trying to gage that solution is essentially measure by putting the electrode inside and there is a change in voltage or potential because of that. So, the transduction is from chemical; that means, generated by hydrogen irons in a particular solutions of a pH to a voltage, so it is essentially a potentiometric sensor study in little bit detail later on..

Then, the signal processor in the devices really a meter, which can read what is a change in the voltage. So, that can be electronic meter which can do that really and therefore, you can also illustrate the electrode as analyte, which is the acid or the chemical of whose pH to be measured set of chemicals inside the pH electrode as the detection element. And then, the chemical to voltage change is a transaction process and the measuring device as meter, which reads the voltage change, so, that is how…

. So, as we were talking about sensors let as actually looking at some the interest sensors that human body has human nose is the one of the most important sensor at the human body has or in fact, our eyes can be illustrate as a sensor model. So, I would like look little bit into how human nose functions, because it is the you known the bio MEMS area and there is amount of life science aspect in it one should know really how our body can be adjust or how can our body can be lead out in different sense of our body can lead out sensor.

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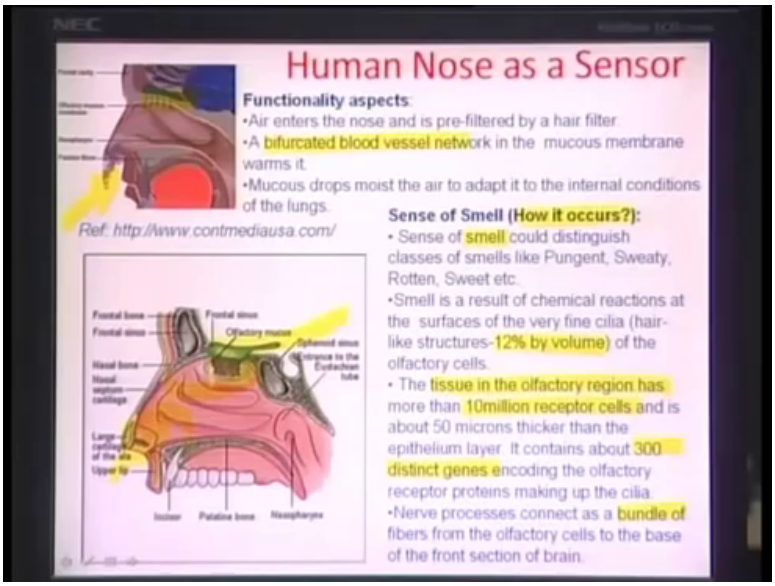

So, this essentially is what the internal view of the nasal tract would look like in a human body and let first illustrate the functionality aspects. So, what would you really need the nose for, so there is air, which has oxygen, which is essentially an oxygen rich components and we have to take this in take this air for our survival and the first thing that this air has to do is to get pre filter. So, as it enters the nasal track here there are set of this you see in this region there are this hair like entities which are able to kind of pre filter whatever particulate the air has if for just cleaning it before entering the human body.

Once the air goes inside it actually touches the bifurcated blood vessels network in this region also known as the olfactory mucous region where there is a membrane which does two fold objectives one is that it warms up the air, which you have a taken in and then, it makes little bit moisten. So, that it adjust to the internal condition of the lungs, in to which the air is directly sent in after passing through it. So, it becomes warm and become a little moisture, so that is how the nose operate.

Now, every interesting factor in the nose is what we know in the sense of smell, how does really sense of occur look at is nothing but, the signal transduction process. And as we know we can really classify something called smell into different classes like pungent, sweaty, rotten, sweet, so on, so forth. depending on whatever the ambient is and really, if you look at what is going on the smell is result of thousands of millions of chemical reactions, which

takes the surfaces of very fine hair like moiety called cilia essentially in the olfactory cells, which are in this particular area, so are in this area as a matter of air.

So, there a fine hair like cilia kind of moiety of the cell surface, where 1000 of chemical reaction taking place by the input the air comes in, which classify the smells as pungent, sweaty, rotten, sweet so on so forth. So, essentially the hair like structure 12 percent volume the whole olfactory membrane, so that is how small it is and this is the kind of illustration of this smaller it is the better it is which is the a driving lesson of micro Nano technology.

So, just to give you some facts and figure the tissue in the all factory region has more than 10 million receptor cells, which have this hair like moiety and is about 50 microns, thick in the normal about epithelium layer. So, the epithelium layer that we have in our body is about 100 microns, so the total thickness of this particular you known the olfactory region about 150 y microns also. And it contain about 300 distinct genes, which encode the olfactory region which make up the cilia.

So, the cilia what we talking above 1000 of chemical reaction are going on are made up of some protein molecule and they are coded by about 300 different genes inside this olfactory cells and it is a self-emerging process. So, as there is a some transduction of let say some kind of reaction chemical reaction into an electronic impulse, which goes through your bundle of nerves which are connected add the back end of the olfactory cells like this you know to your brain. So, essentially the electronic impulse, which is going because of this electro chemical process which is happening on the surface of the cilia..

And those, basically the protein that is changing it is classification is continuously being updated or typed by the distinguish gene, which are available in inside t this cell, so it is a continuous process. So, there are new moiety of every time were new reaction would take place and, because of that new electrons would generate and the electron flows the continuous process which goes to the brain and that classify that based on that some that to pungent too sweet or rotten or sweaty kind of sensation, so this are some category.

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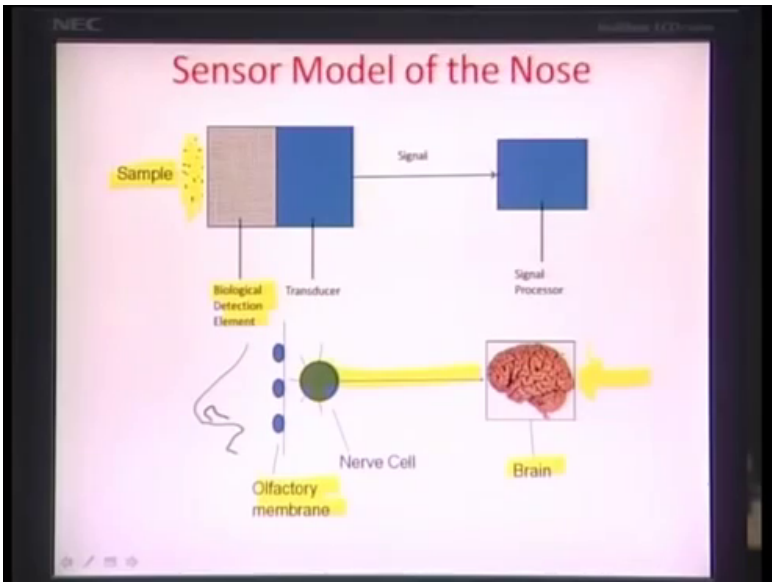

So, therefore if I am really like to look at human sense the human nose as the sensor model it as containing the biological detection element, which is working on a sample of interest here which is nothing but, the air sample and the biological detection in our cases olfactory membrane this uniquely made or you know crafted tissues, which gives you a transduction from chemical to electrical and the electrical impulse is taken by nerve inform an electrical signal all the way to the microprocessor in our body the signal processor, which is the brain in this case. So, really human nose can be categories an artificial sensor..

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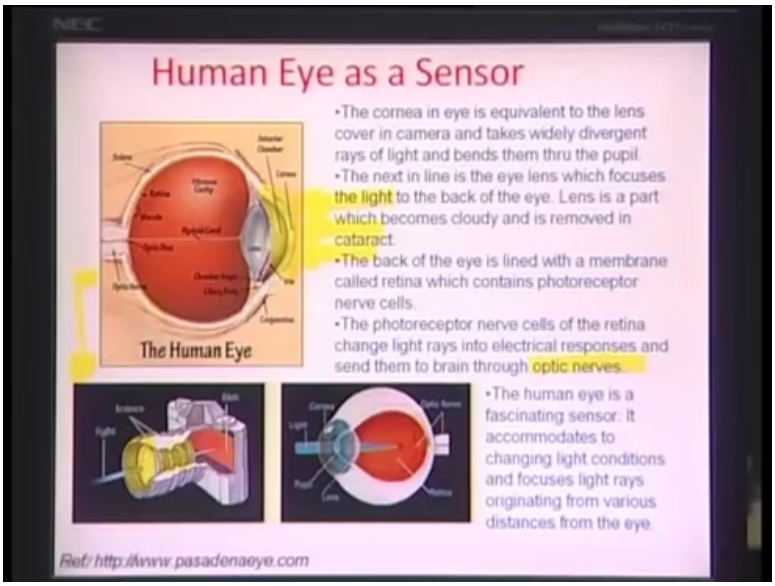

Let us look at eyes, eyes are typically very important consequent of the human body, which takes applied would able take a distinguish and identify between objects and this is how it works, so the cornea in the eye as can be illustrate in this particular figure here is the equivalent to the lens cover of camera. So, let us kind of try to analog provide analogy between the cornea or the lens of the whole eye structure and mechanical as simple camera you know an optical device essentially.

So, the lens cover here may be in this region is equivalent to something, which we called the cornea and rays, which come and strikes the cornea kind of get bend through this region called the pupil region, which is just immediately behind cornea and focus on into the lens the eye lens. The eye lens further focus these rays into the back end of the eye, which is this particular membrane here, which is also known as the retina.

So, it is pretty much same as you have these lens here as you seen the camera you have a lens cover, which is in the cornea and this lens is focus the light ray into something called the film into, which the responses recorded in terms of an optical signal. So, the back end of the eye is really a the center where responses can be converted from optical into electrical and will learn little bit how that happens essentially the photoreceptor nerve cells of the retina changes light rate into electrical response and send them into brain through optic nerves and there is a chemical electro chemical transduction process, which happens there is compound called retinal, which changes into it is transform giving and electron, which goes into the brain and causes the sensation because of that. So, the human eye is a fascinating sensor it accommodate to changing light conditions automatically there is a contraction and expansion in this receiving part of the eye due to which the light can focus on to you know retina for light emanating from various distances place close or far away from the eye you have a different focusing aspect of the length, which can accurately focus it every time on to the retina respective of how far or how near in the object. So, it is essentially again and interesting sensor model.

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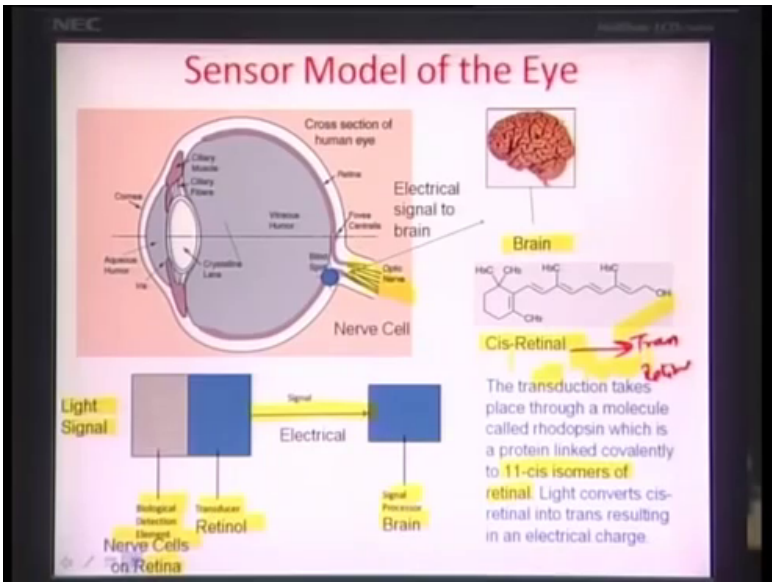

So, if you put this whole thing together as the sensor device. So, the analyte of interest here really is the light signal, which we are trying to detected the biological detection element here of the nerve cell on the retina as we have been talking about and the transduction here is a retinol just coming in a little bit and. So, there is conversion of the light really passing through this biological detection element in to an electrical signal, which goes through these optic eye nerves into the brain and thus the brain here essentially is a signal processor. And it detects and changes according to the responses gets.

So, what happens essentially in the transduction, let us look at the molecular structure here called cis retinal is illustrate here the transduction takes place again through a molecule called rhodopsin, which is essentially an opsin protein and covalently linked to this component called 11 cis isomers of retinal and whenever light falls on at this retinal is converted in to transform and this cis covert into trans retinal form, which slight change in orientation there is essentially a the change over a part of a molecule and what is generate extra electron.

And that electron is what causes sensation, so the whole retina is split up into millions of cells each of which is essentially works in a work center, where there is a change in these compound retinal from cis to trans and that generates and impulse or signal which is also known as light Now this light can into various intensity it based on how many electrons are really generated and goes into the optic nerve. So, human eye again is a fascinating sensor on which one can really think of.

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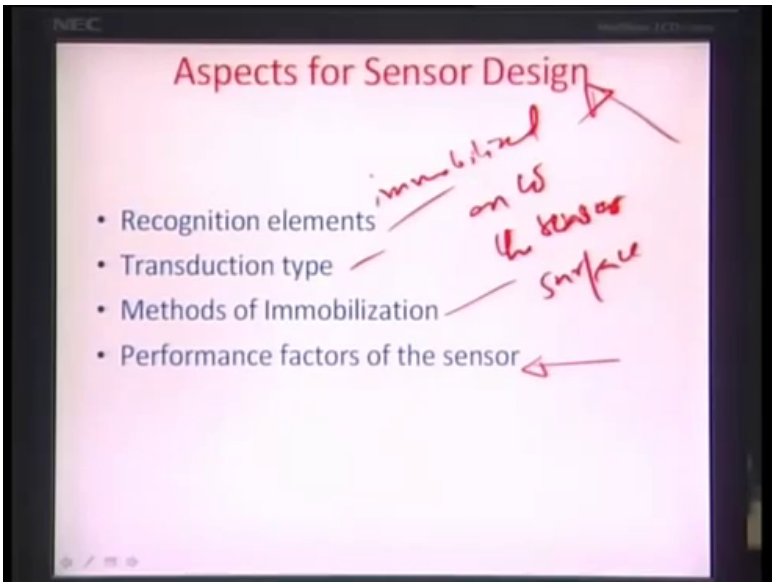

So, when we look at the various aspect for sensor design and I would like to illustrate this point very well, because again the purpose of bio MEMS devices is really sensor or diagnosing some of the things or some of the analyte of interest So, what are aspects goes into sensor design there are four different broad areas in to which categories one are what is the recognition element really is at a is at a biological element it is a physical element, what exactly recognize the analyte of interest or the object of interest, which has to be sense, what is the transduction type, what exactly the transduction type is the chemical to electrical is at a chemical to optical is at a electro chemical process. And then, we have very important issues called method of immobilization, which means that this recognize element has to be immobilized on to the sensor surface .So, there are different ways and means of doing that. So, that is another aspect when we consider sensor design and then finally, we are left with the performance factors of the sensor, where in we gage how effective the sensor would be is it really doing is job in the manner that is supposed are this design is, do far.

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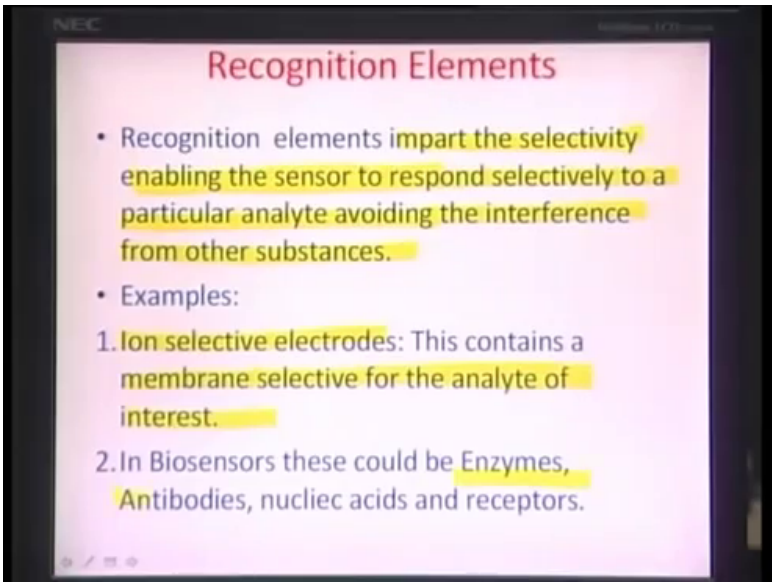

So, we will study this aspect one by one and go a little bit more into recognition elements. So, what really recognition element are so, recognition element as I told you before are elements, which would impart of the selectivity enabling the sensor to respond selectively to a particular analyte avoiding the interference from other substances. So, if there are more than one analytes in a solution and you want to investigate a certain analyte over the other. The recognize element, which would give this selectivity of measuring, what you want to measure has supposed to other five components may be or six components which are just presented there.

So, therefore, some examples of this recognition element could be things like let say ion selective electrode you have a membrane which is selective for the analyte of interest. So, essentially there is a membrane which would pick and choose the particular ion of interest in to picture, so that is what the recognition element would be probably in bio sensor these could be biological moieties like enzymes antibodies, nucleic acids and receptors etcetera. So, e will be studying it off and on detail later that, Let say for a example the glucose bio sensor the enzyme called gluco oxidase.

In short form we called god, which converts glucose into gluconic acid in NHO2, if you have a pH sensor monitor and increase in hydrogen concentration to keep see in there is keep increase, because of NHO2 god catalyst into gluconic acid. So, but recognition element is that in enzyme and so, there is a very important aspect, that what that element would, which

can select the specific chemical of interest over the others. So, therefore, you know this the recognition element is very important for any sensor essentially.

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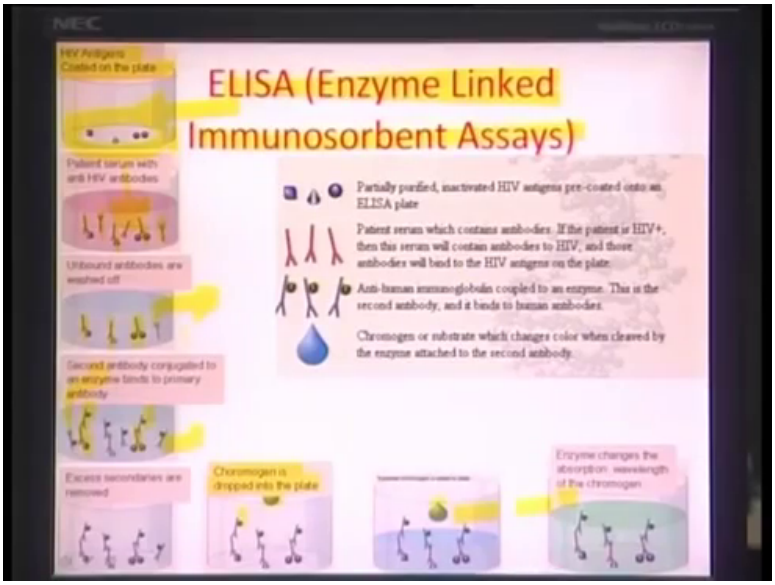

So, let be give a illustration of what some of these element look like this is diagnostic or detection process known as Elisa which you also know as enzyme linked immunosorbent assays. So, let us look at step by step, what happens in such mechanism such a such a diagnostic protocol. Here, it is essentially the play of enzyme it is play of enzyme which causes a change in color are change in absorption spectrum of the particular media, which let us you know whether there is a presence and absence of the antigen of interest enzyme or the analyte of interest enzyme the blood of the particular patient. So, f, you look at the various steps here, so you take something called a plate in which antigens and I just in a minute come to what antigens are HIV antigens are immobilize you see this particular you know this moieties which are present here there are HIV antigens.

So, antigens are set of chemicals which come as the response of pathetic attack with in the human body, which are chemicals which are generated inside the body I nothing these antigens. Which show are signify the presence or absence of particular you know taking species, which may be to healthy over all physiological set up of particular be. So, there are this antigen, which is coated on it particular plated here and we essentially take the serum patient who is probably we diagnosis for HIV as positive or negative. And as we know the first line of defense within the human body is our human immune system and whenever there

is a some kind of you know antigen attack first line defense generate chemical are moiety antibodies, which is try to bind or leave are some of these attack and they do very well with antigen and they bond do very well with antigen.

So, we drop the blood into this particular coated antigens and assuming that they are the patient is positive, which is immune response happen there is tendency of some of anti-bodies get bonded on to this immobilized antigens the unbounded wash out later on and so you have only this bonded on to the antigens the antigen are immobilized that means they chemically somehow attached to the surface of interest in this case which is actually reaped. And here the antigen was getting bonded and unbounded typically washed of this surface then want a then, we secondary anti body which bind to the primary anti body on particular to secondary anti body that you have an enzyme of a certain conjugate on secondary enzyme.

So, essentially to this element as you seeing by a blue arrow or this blue feature and this red feature they are conjugate of each other. So, they are bind together to this secondary anti body this is primary anti body which is this immobilized antigen and the secondary anti body which enzyme, which is actually conjugate to the antibody Now, this kind of orientation wash out those and you have bound specimen here on to the surface of the plate. And then, you put something called which can change color on coming in the contact this enzyme in interest.

So, this is called a chromogen, so in the case you dropping a material chromogen into the plane as soon as the chromogen come into the here the color of the chromogen consider the change in coloration from blue to green assuming that there where known antibodies in the patient serum very beginning here, so there would be any bound antibodies surface due to which he enzymes will not bind into the immobilized antigen, because the secondary anti body only bind to the primary anti body the red anti body, so the absence of red would mean all free they would be washed off and there would be hardly change color of the chromogen.

So, if there a change in chromogen it kind of reflects the concentration secondary anti body in the patient blood and the sorry the primary anti body in the patient blood it also indicate that how badly or how worst mean effected or inflected. So, with this I would like to round of the first lecture and in the next section we would discuss little bit detail on how the other aspect on sensor design in can be you know illustrate or study in details.

Thank you.