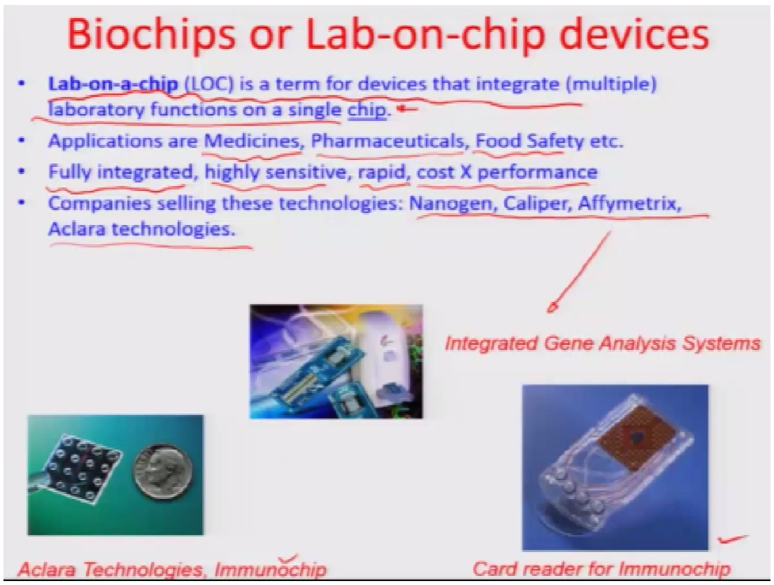
Design Practice - 2
Prof. Shantanu Bhattacharya
Department of Mechanical Engineering
Indian Institute of Technology-Kanpur

Lecture - 12
Lab-on-Chip

Hello and welcome to this Design Practice 2 module 12. We will be continuing on the topic of micro-electro mechanical systems or MEMS.

(Refer Slide Time: 00:21)

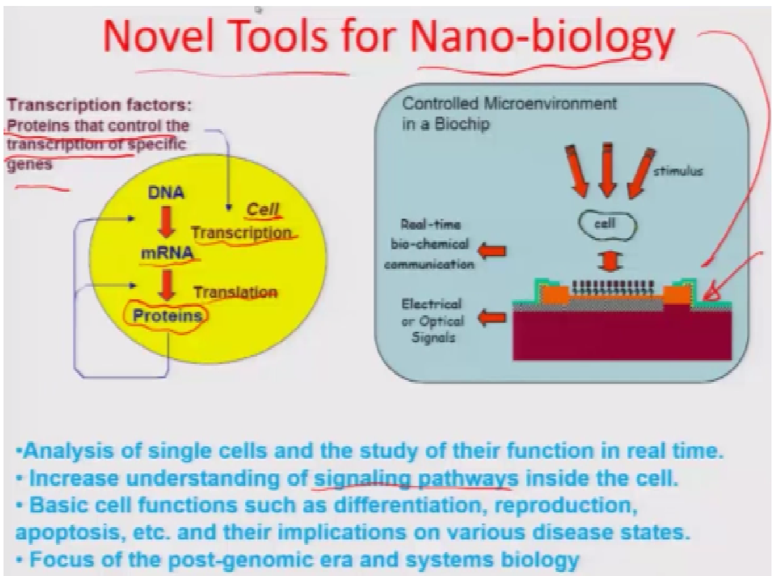


So we were discussing about biochips or lab-on-chip devices and basically if you may recall lab-on-chip is a term for devices that would integrate multiple laboratory functions on a single chip with extremely small minuscule fluid volumes. There are applications in the area of research related to medicines for example pharmaceutical research deploys quite a bit of this lab-on-chip for studying issues related to protein chemistry or protein fouling or you know associated technology, associated technology models.

A lot of these chips are off and on used in food safety particularly food and water safety which are considered to be the borders which would be agents of carrying infection into the human systems and somehow need to be detected. The advantages that lab-on-chip have to offer are many. For example they are away from human intervention fully integrated in nature, highly automated, highly sensitive, very rapid to work in and then you can you talk about the cost performance product of this chip so they are low cost and high performance so they are also one of the object of you know central theme or attention of lot of companies.

So some companies which sell these technologies are for example Nanogen, Caliper, Affymetrix, Aclara so on so forth and by and large a major portion of the lab-on-chips are still dedicated to the area of integrated gene analysis. Although there are technologies which have evolved which are considered to be immunochips where Elisa and some other assays are carried out okay.

(Refer Slide Time: 02:02)



When we talk about a step further and hit upon the domain of independent cells and their behavior, so we are all aware that the human cell or let us say any million cell is a fantastic piece of machinery because it does compress information which is stored somewhere in the chromatin region in form of chromosomes or DNA into sequences which can then or mRNA sequences which can then lead to the production of proteins at the, the produced proteins in the otherwise well-known protein warehouses which are present in the perinuclear region of a cell.

And this mRNA molecules typically take the information which you know is generated by a signal which is carried into the nuclear region you know by a sigma factor okay which typically associates with the RNA polymerase and otherwise very well-known enzyme and tries to compress information from the DNA to the RNA. So it is a very complex process of transcriptizing the sequence information which is there on the DNA of a cell.

Probably some of you are also aware of the fact that once the mRNA is made and then the mRNA goes into the you know perinuclear region in those protein warehouses which are floating around otherwise known as endoplasmic reticulum. There is a you know there is a change of the language from the normal sequences on RNA to sequence of amino acids which are otherwise well known as proteins and these proteins are what determines the functionality and behavior the physiological aspects related to a living cell.

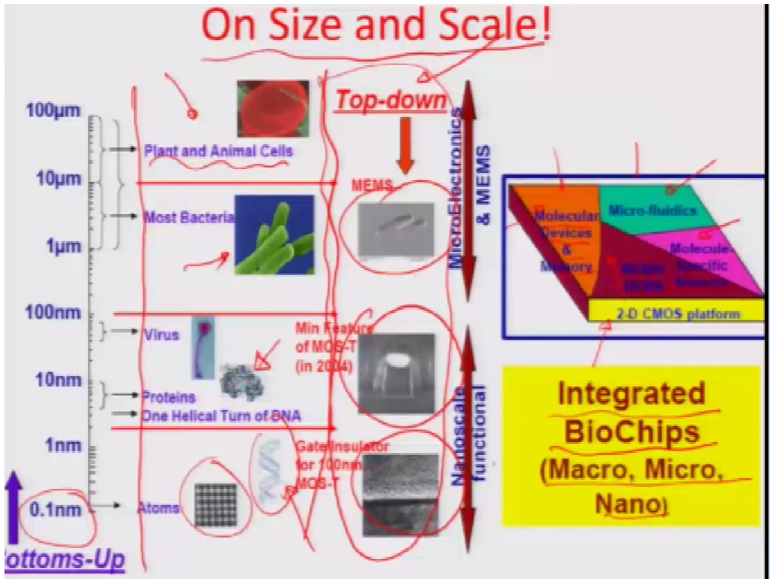
So proteins control quite a bit of transcription or specific genes and you know such movements of DNA to RNA and then to proteins are being controlled okay in a real time through you know in a very closed paced way because whatever expression changes happen in the surface of a cell can be monitored on a real-time basis through again using MEMS platform okay.

And so some of these tools maybe an array of MOSFET devices which are going to measure the change in current on the basis of surface potential changes across the surface you know of a cell as it expresses proteins etc. They are all in place to tell about this road map and analyze how single cells would behave and understand the various signaling pathways within the cells which would lead to such a transcription and translation mechanism okay.

So it is a women’s utility to self-physiology particularly to understand how they behave with stimuli under different conditions and so this whole area of nano-biology in a way uses such microstructures created and printed in a very array like manner to understand more about how much expression is happening on surface of the cells etc. So this are one of the novel tools for nano technology.

Also better known as nano-biology there are dedicated centers to studying of how cells would you know change expressions etc. based on either electronic responses or fluorescence responses and it is worthwhile to use MEMS in these kind of sensing mechanisms.

(Refer Slide Time: 05:25)



So today you know talking on the size and scale obviously when we talk about merging these two world's together there are different biological moieties for example on the left side of the scale here varying from even the you know atomic level of TENS of Armstrongs all the way to 1 Armstrong all the way to about plant and animal cells which are quite high in size maybe 20 micron plus.

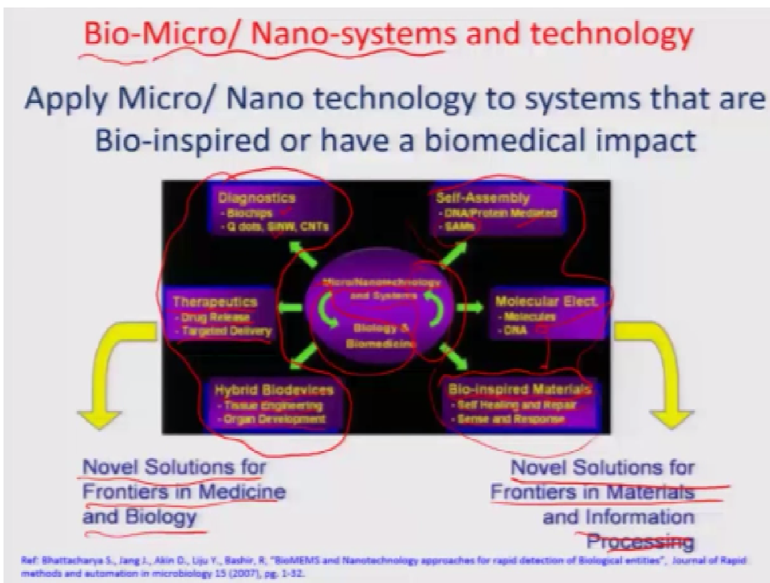
And on the left the world that relates to how microstructure can result in some of the features and structures of a size parity with some of these biological features and structures. This for example is a double helical structure of a DNA. This is a virus molecule a few hundred nanometers in size. This right here is an assumed image of an E-coli bacteria.

And so therefore when we talk about such a merger between the you know fabricated structures and the naturally available structures one thing which is very clear is because of the very miniscule contribution of its own mass or weight related to such structures it is always a very nice merger you know and it is always a very sensitive detection okay.

So therefore technologies have evolved on 2D CMOS platforms which have all these different devices integrated including microfluidic MEMS, molecular specific sensors MEMS and MEMS you know which are the structural nature and then of course molecular devices and memory together to give you some idea of how these entities do behave in different environments and what are the kind of stimuli that they are able to generate.

So these typically form the area of what you know as integrated biochips okay; so both the macro, micro, and nano area. There is a huge amount of demand of you know such technologies they are rapidly emerging around the world. Part of it also is reflected under the overall broad stream of bio design and so therefore it is of quite a bit of significance to a product design engineer as well as a bio design engineer okay who can take these technologies further for very simple easy to use you know products which would serve the diagnostic needs you know for the human society.

(Refer Slide Time: 07:44)



So when we look in a nutshell this whole area of micro and nano systems and how it has evolved, a lot of to and fro inspirational learning has happened in both areas. For example there has been devices which are made through biological entities look at DNA based nano wires or molecular nano wires which are inspired for some of the next generation molecular electronic devices that are highly inspired from what happens in biology and bio medicine.

And it gives something which is of significance to the area of micro and nano systems. Then we talk about self-assemblies both DNA and protein mediated or self assembled monolayers or if you talk about inspirational learning borrowed from the skin, look at the skin for example. It is such a wonderful thing, it can sense you know it can respond, it can heal and so if you look at the skin from a perspective of an engineering object it is a dense array of sensors integrated together you know into a small area.

And so therefore it can of course inspire a lot of learning experiences from micro nano technology where you can have bio inspired materials or skin like materials okay which can serve the humanity better in general. On the left side here are some of the tools that we have taken up from the micro nano systems technology and it helps in really the bi inspired world and for example we talk about hybrid bio devices where structuring at the micro nano scale are used heavily for doing tissue engineering applications.

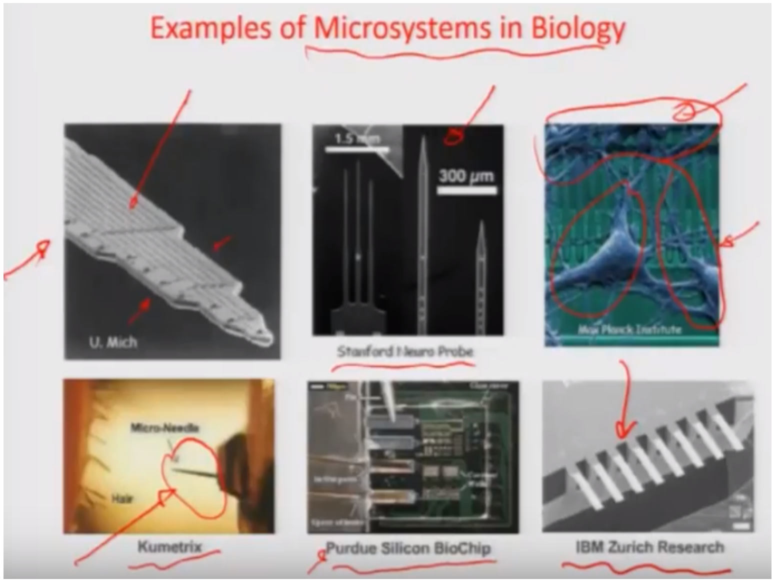
There are scaffolds which are grown which are of sacrificial material and they are biocompatible and there is cell growth promoted within such scaffolds and then later on the scaffolds are edged out or pulled out so that you have a hollow structure in between. Similarly, you know there are the therapeutics associated with drug release target delivery.

Today we can actually make a carbon nano tube with functionalization both internally and externally and you know you can flow this through intravenous means to a certain site which is affected with some tumorous growth or maybe cancerous growth something like this and then that is where drug delivery can targetedly happen for therapeutic purposes again borrowed inspiration from the micro nano technology.

You can you can also borrow a lot of inspiration from bio chips and what quantum dots or silicon nano wires can do in terms of recognition which can directly help the bio world. So there is a lot of learning from micro nano technology which can even translate into biology and biomedicine. So on the right side here which is learning borrowed from biology into micro nano technology would produce some novel solutions for some frontiers in materials and information processing systems.

Whereas when the learning is reversed that means you are learning from the micro nano technology systems and applying to biology and biomedicine. There can be some novel solutions and frontiers in medicine and biology. So that is how we can actually look at it as a synergistic system and all these are based on or rotating around that fundamental micro and nano systems.

(Refer Slide Time: 10:28)



So there are some other examples i would like to look at very closely which are found abundantly in the you know areas of microsystems for biology. For example look at this Neuro Probe which has been developed by Dr. Weiss group at the University of Michigan. It is about you know it is a probe which would have a lot of printed electronics and would be able to monitor the electrical activity of the brain tissue particularly in rat brain.

And for using this probe the incision that is needed to insert this probe into the brain is very small because the overall dimensions of this probe is also quite small. It is again borrowed as an inspiration from the area of micro nano systems. But it can do something like painless monitoring okay of the electrical activity of brain tissue for example. This again is a another very nice example, this is a Neuro Probe developed at Stanford.

Which typically was supposed to do deep electrical stimulation which is a you know again a therapeutic strategy given to particularly Parkinson disease patients and the idea is that if you can make this experience painless for them it is going to be of immense value okay to the society. These are a set of neuron cells growing on bunch of moss transistors which are micro padded on a surface.

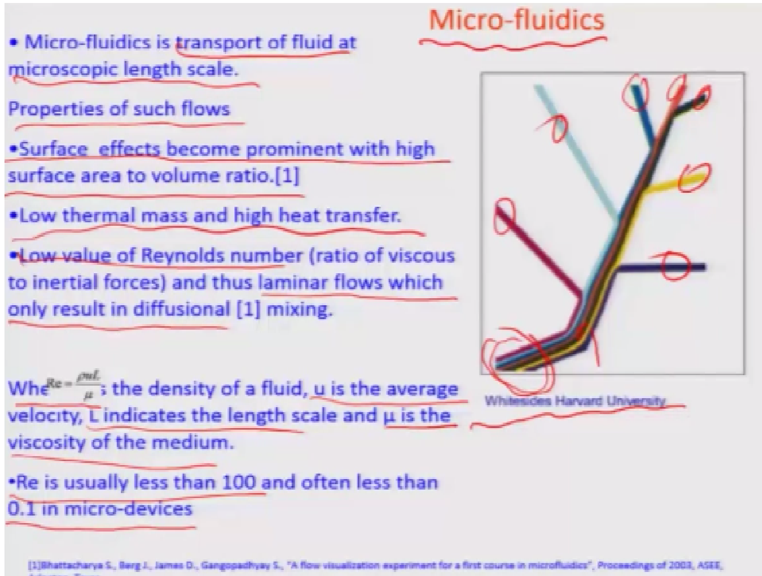
And this is the area of nano biology I have described in the last step where whatever happens on the surface of the cells and the understanding that you develop here is physiologically how the cells would respond in proximity of each other or while they are spread apart on a surface and how they cross talk with each other. So this is again another beautiful example of how micro nano technology can be inspired for something directly translating to the biology or biomedicine.

This right here is the micro needle. It is again another example which can be you know how micro and nano systems go into helping the humanity through interaction with the human side. We all know how painful it is to inject something intravenously into babies for example or even into you know old age people or normal human beings. Some of the people are very afraid of painful injections.

So this injection right here is rhythming very well with the you know with the injector on a mosquito and therefore just as a mosquito bite when the mosquito bites you, you do not feel the pain because the needle which goes, the mosquito needle which goes into your body typically goes in a region which is just above the vasculature where there are pain receptors and is not able to damage deform those pain receptors which otherwise would be the case when you try a bigger needle.

So this right here is another example of a silicone biochip which has been developed at Purdue for detection of food microorganisms. There is another example right here about a series of micro cantilevers which have been developed by IBM Zurich Research which talks about how cantilevers and bending in cantilevers can be mapped to physical reactions sorry chemical reactions which happen on the surface of these cantilevers. So these are various examples of how microsystems can be manifested within the field of biology and biomedicine.

(Refer Slide Time: 14:50)

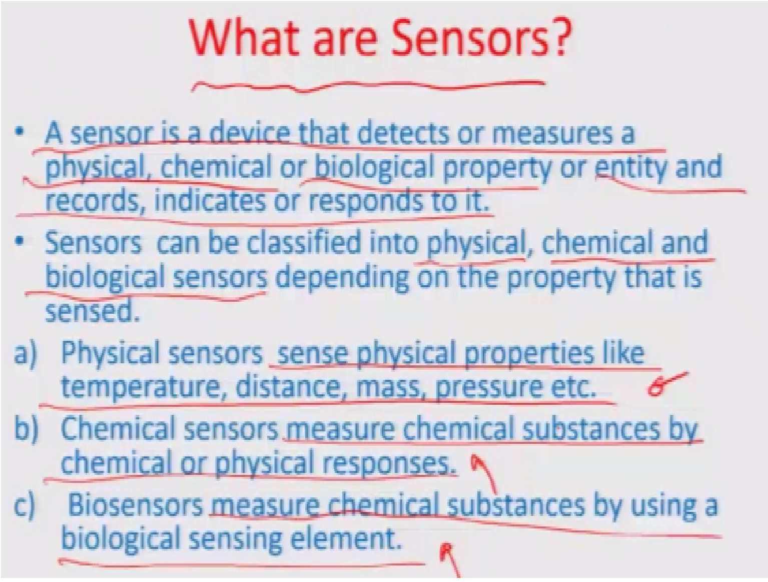


A small you know take on further applications is this domain of microfluidics which have come up because of the advent of the biochips and the diagnostic assays. So if you look at the area of microfluidics it is a transport of fluids at the microscopic length scale and there are many properties of such flows. For example there are surface effects which become prominent with high surface area to volume, low thermal mass and high heat transfer capability within these channels, low value of Reynolds number.

Okay, so these are some of the associated aspects of this field of microfluidics where laminar flows you know because of the low Reynold number values lead to mixing which is only diffusional in nature. There are hardly any eddies or vortices which are generated within the floors. This simulation right here is 5 dyes going n to n parallelly in a micro channel. So the Reynolds number which is actually the ratio between the inertial and viscous forces is usually dependent on the average velocity, the length scale factor.

And you know the viscosity of the medium Re is usually less than 100, very often it is less than 0.1 when we talk about microfluidic devices and so these colors here as you are seeing they are although they are flowing past each other they can be extracted as is without much mixing because most of them are having almost you know 0 concentration difference. So such experiments are even possible at you know the microscopic length scale where we can talk about such you know microfluidic devices with peculiar properties which can be used for many applications.

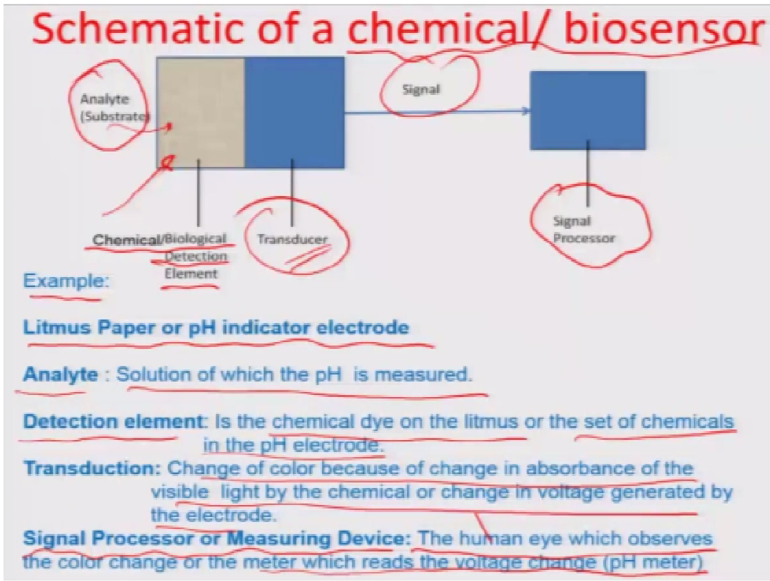
(Refer Slide Time: 16:39)



So we will now try to look at a slightly different aspect which is about how to design sensors and what really are sensors and so definition wise if you look at sensors it is really a device that detects or measures a physical any chemical or a biological property of entity and records indicates or responds to it. Sensors can be classified into all different physical, chemical and biological sensors depending on the property that is sensed.

Physical sensors for example sense physical properties like temperature, distance, mass, pressure, etc. chemical sensors measure chemical substances by chemical or physical responses. Biosensors of course measure chemical substances by using a biological sensing elements and so it is all about what exactly is that element and how there is a change in the signal. How there is a transduction for the sensor to start detecting various responses.

(Refer Slide Time: 17:36)



So when we talk about a schematic of how a sensor should look like and this is more prominent towards when we talk about chemical and biosensors particularly. So there are very many components of such a sensor. For example let us say there is an analyte of interest which you want to detect for a certain specific chemical and let us say the sensor which is built here has a chembio detection element which is specific to a certain chemical which if we would bind to the analyte and thereby produce a response which converts or transduces into something which is machine readable.

Now chemical signal converting into an electrical or an optical signal is a very common place affair which happens in almost all of molecular identifications which are carried out. So such a change in response for example let us we are talking about a gas sensor. So if there is an element which takes up a certain gas from a set of gases within the environment and changes some property okay the property could be let us say you know it starts releasing electrons thereby you know making positive ions and changing the conductivity because of such release of electrons into the environment because of the reducing gas that comes in okay.

So it can detect reducing gas by change of resistivity. So this transduction that is happening at the interface is because of a phenomena of reduction which is happening because of a electron getting donated and change in conductivity owing to this donation of the electron in the presence of a certain gas. So the gas creates a physical change which creates a signal further, an electrical signal in this particular case which can tell you about how much gas was present.

Okay, so they are quantifying the signal, the electrical signal in terms of the concentration of the gas that was present. So this is the whole modality or scheme of how sensing can be carried out. So you are transducing from chemical to let us say electrical in that particular case and this signal is now recorded somewhere. It could be a computer which records the signal. Or maybe it could be some kind of a storage device which records the signal.

And it gives you an idea about what is the concentration of the analyte gas which was there in the system because of which this particular signal was generated. There are many example of this like which are continuously you know seen for example the simplest case would be that of a litmus paper or a pH indicator electrode. So here what is happening is there is an analyte which is a solution of which the pH is to be measured. There is a detection element.

It is a chemical dye on the litmus or a set of chemicals in the pH electrodes. There is a transduction which is a change of color now because the pH paper changes in red color, becomes red color or blue color. So change of color because of the change in absorbance of the visible light by the chemical or change in voltage generated by an electrode. Either way this is caused by the presence of hydrogen ions okay which can detect whether how acidic or how basic a solution is.

And then the signal processor for example in the case of a color changes your brain which records the color change, you are able to see the color change through your eyes okay and if I looked at how my eye functions is also a sensor or how my nose functions that is also a sensor. I am going to come to that level probably in the next lecture, not in this lecture. But this is how you record the simple litmus paper.

The dye on the litmus paper being the recognition element and the dye changing color which is again made visible to the eyes and eye being the recording device makes the whole sensory system sense the hydrogen ion concentration. So there are numerous such examples in how a chemical and biosensor can be defined. But what I am going to do is probably in the next lecture I am going to start giving some description about how our basic senses like the sense of smell or let us say the sense of you know visualization is basically outlaid as a sensorial model.

So I will close this particular module here and meet you in the next module. Thank you very much.