BioMEMS and Microfluidics
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Lecture – 03

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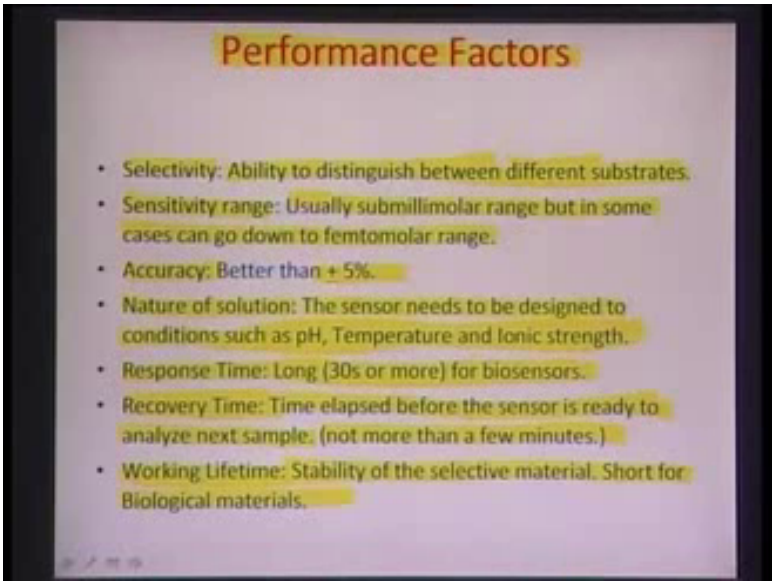

So, you know the after the sensitivity range in the performance factors another very important aspects is the accuracy. The sensor accuracy has to be in most of the cases better than plus minus 5 percent. So, accuracy also reflects repeatability or you know the kind of parity between the measurements that sense makes with time if you have multiple reading. Another very important aspect of performance, you know which has to be kept in mind it is a kind of intangible aspect is the nature of solution of the variety of solution that the sensual can scan.

So, when design the sensor very important aspect to take care of is, whether the sensor can which scan various condition of pH temperature and ionic strength, etcetera. And essentially the sensor when you talk about designing the sensor, it has to be designed for you know its operability you know, its ability to get operated in varied conditions or different pH temperature, ionic strength, etcetera.

So, that is another aspect - performance factor aspect of a particular sensor. Another very important aspect which makes the sensor really gives a commercial angle, its performance time or you know response time. So for bio sensors typically the response have been found out to be little longer, it takes about 30 seconds or more. In the context I would like to say

that you know in electro chemical sensing operations this sensor time becomes very you know high, because of the fact that you have to recondition the electrodes the sense of electrodes and that is the very time consuming process.

So, that essentially although it is not the part of the actual response time comes in the overall time of the sensing of such an electrode. So, if you are having a real time process where there is the continuous monitoring of the analytic of interest with time, it is a very critical aspect that what is the response time of the sensor, how soon can it process a chemical information into an electrical or otherwise optically readable signal a very important. And other important aspect, it is also the part of performance factor is the recovery time of a particular sensor.

So, I would like to define this as the time elapsed before the sensor is ready to analyze next sample. So, essentially it is the time between the ready outs, if you have two or more certain you know readings that you want to take out the same sensor how much amount of reconditioning time is need. So, that you can get the sensor have an issue. So, that the sensing can start very accurate bases. So, that that is an important aspect of the performance factor of the sensor.

So, if you have a recovery time of more than a minute more than a few minutes. Then really it does not make sense in real time operations anymore, and very important aspect - another very important aspect, it is the working life time of a sensor like things like stability of selective material, you know it defines this kind of issues in case of glucose sensors as I was illustrating in my last lecture this enzyme the glucose oxidase it is very affinity enzyme it can only have defined shelf life. So, if these kinds of moieties which are essentially reorganization elements they change their behavior with time what good, it is to the sensing aspect. So, the working life time is a very important factor that needs to be considered, if you want to design good sensor.

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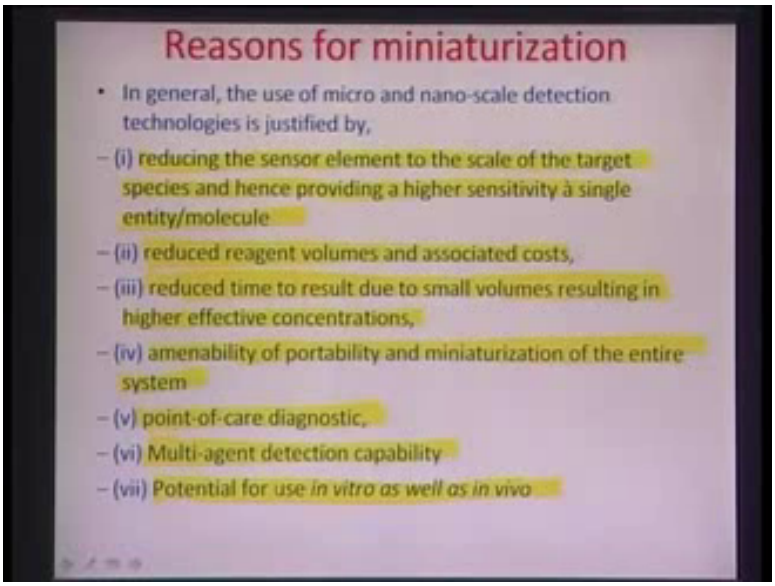

Let us actually now go to the next level, and try to find out that this whole kind of rays to miniaturize you know starting from… Let say the microchips why really it is important, what are the some of the reasons for miniaturizing, let say sensors. So, the justification can be provided by looking at several aspects own aspect could be that you know that we would be talk the scale, and sizes the reduction the sensor element to the scale of the target species that would actually give a higher sensitivity for detecting a single entity or a molecule. So, it is very important aspect. So, you are talking about you know the particular detecting element to be of the size of a single molecule or a single moiety of interest.

So, when the size compression is there is a automatically a higher sensitivity of detection of such a process, another very interesting aspects is you know reduced reagent volumes and cost of operations in you know some time back. I was mentioning about this process of polymerized chain reaction where you artificially trying to amplify small segment of DNA, and you know it is a fascinating process, but unfortunately, it is a very expensive process, because it uses some of these chemically isolated base pairs some enzymes. You know some ironic buffers etcetera, which gives the whole reaction cost, you know a different dimension all together.

So, therefore more number of PCR runs essentially is as a cost is at a more money spending you know issue. So, therefore it is important that the if we can design a sensor in a manner which can do a micro PCR; that means, you take a small volume where let say the overall

volume is about one micro liter in nature. And then you have these different components which go in to the reaction probably of the order of Pico liters. So, in that case the cost the overall associated cost reduces.

So, one of the reasons why miniaturization is important is that the region volumes used for chemical analysis automatically reduce, because of the size factor reduce time to result due to small volumes, you know is a very important aspect. And as we know that when we talk about concentrations of different moieties within a solution; there is an aspect of diffusion, which comes in to picture automatically. And if you have a gradient of concentration there is always a tendency of molecules to diffuse a homogenize the particular medium. So, if this overall volume over which we are talking is very small, then the diffusion mechanics is much more rapidly taking place, and as a result of which the homogenization from which the sensing activity would start really is much quicker.

So, this has is effects in terms of response time of the sensor also the miniaturization a sensor or miniaturization the volume of fluid, which is to be sensed essentially reduces the time to homogenize. So, that you have an accurate read out much faster of course, supportability is a major issue these days, there is a concept of bed side monitoring of a patient where in a we also know this whole area as point of care diagnostics, where we take a small sensor to where the patient is, and really the sensor does a job its job in the real time bases just by you know just the continuously monitoring the patient health, and such sensors have to miniaturize. Otherwise if you move the whole laboratory how is it possible really. So, the concept of lab on chip really emerged, because of the need to make things more portable, so that they can be more delivered at the point, where it is needed essentially. So, amenability to portability is very important aspect why the sensor should be miniaturized.

So, point of care diagnostic essentially which we talked about I would just like to share with you that, now a days in advanced health care schemes, there are small ring like sensors which they would just put around your finger, and they can monitor your things like you know blood glucose level very easily on an optical bases. So, any patient who goes into an emergency care essentially is given such a ring to wear, and the ring has perfectly wirelessly communicating system which would give information about a you know the content or the hemoglobin the glucose content of the patient from the time to time.

So, this is point of care this comes very close to where the patient is placed actually, and does its job on a continuous basis miniaturization is also helpful for multi agent detection capabilities. What essentially it means is that, if you have more than one agents that you want to detect, and if you really want to detect each agent on a very small bases. You could densely integrate several such detection protocols on a small particular chip, and that sense of microchip technology essentially that you can on a very dense networked bases do multi agent detection on a very small area and the very important last, but not the least why miniaturization is needed at least in some of the reasons which appear to be the most prominent ones is the potential for use in vitro as well as in vivo so far, those of you who were new in this area in vitro essentially means outside the human body.

So, the sensor can do it sharp outside the human body in vivo. On the other hand is inside the human body. So, all these real time sensors that we have been illustrating from time to time are essentially in vivo sensors implant the sensor on to the human body, and it keeps on monitoring the health rapidly and it keeps on giving data rapidly, so that in vivo sensor. So, miniaturization is very helpful for in vitro as well as in vivo sensing. So, one of the reasons is that if you are talking about an implantable sensor, and the sensor is of the size of pen, can you imagine the amount of pain that the patient is inflicted upon, if you want to locate this sensor somewhere within his body. So the smaller the sensor is the better in that case, because it can cause a pain less delivery of the sensor to the target where it can detect or it can start detecting.

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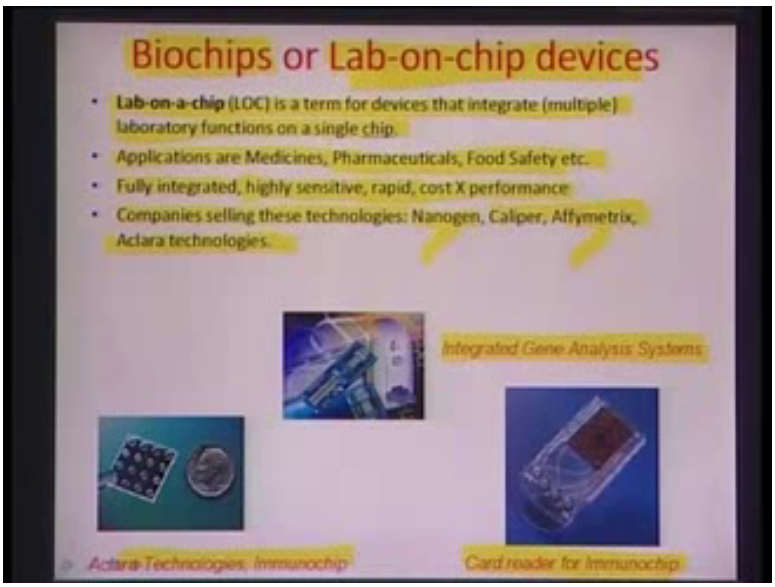

So, again you have been talking about lab on chip devices, I guess you have a fairly good idea about what bio chips are... So, let me just definitionally you know kind of out lay what this technologies all about. So, Lab-on shape is a term for devices that integrate multiple laboratory functions on a single chip. So, very obvious the definition that have several function in a laboratory, which are kind of integrated together to do some detection this lab on chip is something that brings all this functions to a very small single chip. There are enormous applications of lab on chip as on date, there are commercially available protocols to their applications in medicines pharmaceuticology for food safety, so on so forth. And some of the advantages that such devices offer on a commercial bases is that they are fully integrated and essentially without or may be with very less, I should say human intervention.

So it is a very clean process, you do not have a chance of contamination, just because of multiple handling has happens very often in the laboratory, they are highly sensitive in nature, because of the miniaturized form of this chips. As we have been often on talking about before there are extremely rapid the time of response is less, because of all these homogeneous aspects of the analyte, and you know being a small volume the diffusion restriction are automatically minimized so on so forth, And then this other aspect of cost performance product. So, essentially these are low cost high performance devices. So, that is why they are really high utility, the lab on chips are really a high utility, a h kind of devices. So, some of the companies selling these technologies across the globe to name a few Nanogen, caliper technologies, isometric, clara technologies, so on so forth.

Essentially these two companies Nanogen and isometric, are selling auto catering to the whole diagnostics industry by selling, you know gene identification platforms. And we will be discussing in details about these as we go along our lectures as too some of the strategies and mechanisms that these manufactures use to identify these chemical this sequence of base pairs single DNA molecule. So, in general this is a known fact that you know if you look at all the commercial applications, all these lab on chip systems more or less majority, I would say almost eight ninety percentage of products which are currently available are in this integrated gene analysis area.

There are some products which have developed in the anthology like aclara; aclara has a product or this caliper technologies has product, where in immunochemistry is used for identification of cells or biological moieties. So, that is in a nutshell what the status of lab on

chips technique are, I would now like to illustrate a very important area which has come of off lead, because of the development of these tools and this is also known as a nano biology.

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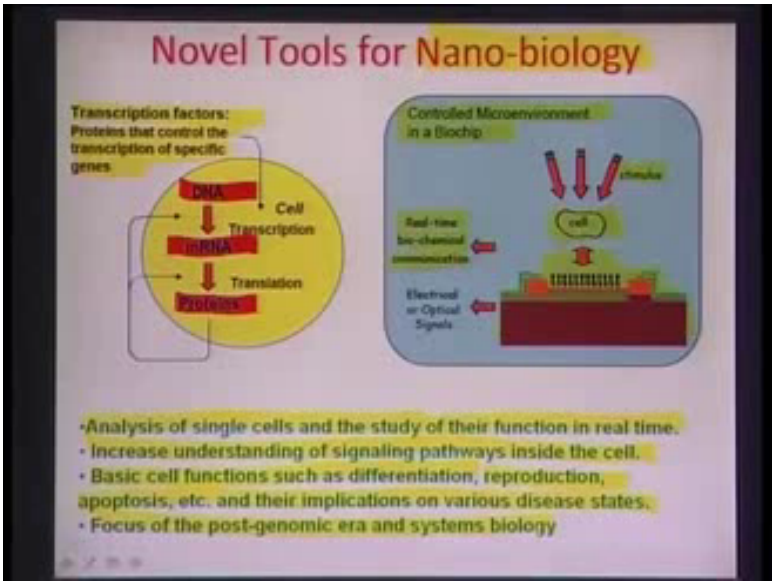

So, the MEMS technology… In fact, the miniaturization technology is very useful for studying certain aspects of single cells. So, here in this particular case as you have seen this is the controlled microenvironment in a biochip, where you have you know have kind of its like something like, let us see a nano wire. Between two posts and you have a silicon platform here it is like a MOSFET device. So, essentially whatever is going on in terms of chemical changes in top of this, this region gets converted in terms of a surface potential. And if there is a charge transfer process which is happening in this particular region, the surface potential change would result in a variation in the range source current in the MOSFET device.

So, therefore, it can be a very good identification bases or you know what is going on in a single cell which is immobilized in to this area. So, you give stimulus to the cell and see how the cell performs. Now how is it important these, you know this is very, very interesting that actually, there is an increased requirement of understanding of the physiology of a single cell in the presence or absence of it's, you know identical other cells and. So, there is a lot of signaling mechanism between let us say more than one cells growing on a certain area which results in a totally different behavioral change of cell of interest.

So, self in biology is essentially now a day's focuses on to these molecular events, which take place in the presence or absence of a group of other cells one more interesting factor is that

you know the way that proteins are produced, and I am to actually introduce this topic a little, doing a basic biology that what happens in a cell. So, there is a certain programming aspect of particular cell, which we have to really read, if we come to you know such a mechanism.

So, as we know that there is there is this molecular information stored within the in the DNA of a particular cell. So, this information is a base of giving what kind of proteins the cell produces this area. Now a day's is increasingly going because proteins essentially are a very important bases of the state of health of a certain cell. So, there is a there is a process called transcription, and translation within single cells, and it is a huge nano machinery, which is at work there is a tendency of this messenger RNA, which is the compressed code essentially code encoding a certain area or region of the gene that we are taking about, and the RNA actually comes all the way from the nucleus into the cytoplasm through the cytoplasm, it goes to something called an endoplasmic reticulum which also the protein warehouse of the cell, where these is a coding which happens on this mRNA, and the base pairs of mRNA's are converges rapidly on to a sequence of amino acids which is essentially the protein which is being produced.

So, this is this is the fantastic process which is going on. So, Nano biology again study is very closely these signaling effects within the cells, which asks the cell to code a certain region of the gene based on the impulse of the response that is has from an environment, and such studies can only be possible when you make the sensing system doing these studies on very, very highly miniaturized bases.

So, in a nut shell what I would like to say is you know the increase in this concepts of miniaturization has resulted into, you know this fantastic field of Nano biology to get developed, where analysis of single cells and study of their function in real time can be accomplished, there can be an increased understanding of the signaling pathways inside this cell some of them. We have been mentioning often on basic cell functions such as how the cells differentiate in the presence of absence presence or absence of its own types around it the way they reproduce that the way the apoptosis are die after certain time, and their implications on various disease states. They can be understood on a very molecular level and essentially the focus of the post genomic area and systems biology some of these newly emerging fields are in this area more often cut.

So, Nano biology definitely is you know probably one of the areas of interest which automatically get cropped up, because of this micro system technology. So, this pretty much brings us to the end of this lecture, and next time we will be seeing how micro fabrication tools can be used to realize things which are small and miniaturized which could do some of these jobs that I have been mentioning over the last two lectures. So, probably we will discuss a little bit of micro fabrication related process in our next lecture.

Thank you.