BioMEMS and Microfluidics
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Lecture – 4
Review of Lecture – 1, 2 &3

So, this is actually the last lecture of this week which is actually a review lecture for what has been whatever has been whatever material has been covered so far in the first three lectures. So, we introduced in the first lecture the subject of bio mems and micro fluids, we talked about the various definitions bio mems is defined as biological or biomedical application of mems or micro electro mechanical systems technology. We also talked about bio nano technology which is actually the biological applications of nano technology better known as science of as object, which are smaller than about 100 nano meters are so. We briefly described micro fluidics as a study of fluid transport at the microscopic length scale, and we also talked about the various utilities that such systems would have.

We started with scale and size concept which would give you an idea of emergence of the field, and why it is need wherein we discussed various size issues related to the biological species. We talked about bacterial cells which are about close to more than a micron size we have also described viruses which are a few 100 nano meters starting up from molecules describe the one helical turn of a DNA to be about 3 to nano meters 20, 30 Armstrong. And we further merged into the highest cell, highest size cell which is most plant and animal cells which are more than 10 micron sizes. While comparing them with the objects and systems, which are possibly fabricated using mems technology which could size very well or rhyme very well with the sizes of these biological activities.

We talked about these scale issues as a basic reason for the emergence of these two fields where one field would concerned the top down approach of fabrication from higher size wafer to various smaller elements of the sizes of these entities. And the other side would be a bottom up approach that Mother Nature typically has from this smallest elementary atom or molecules all the way to the most of complex from. And then we said that because of these two areas are synergistic, there is a scope of match of dimensions between both the areas. Therefore, automatically the a field of study called biomems emerges, where the detection of the entities biological entities can be very easily done with some of the sizes that miniaturization has to offer mass or of sizes equal to that of the biological entities. We further

define micro fluidic transport and talked about Reynolds number, we also discussed about the implication of Reynolds number on the Laminarity of the floor, the example that was given was the mixing or the parallel flow of seven different dice in a small channel, where the rice would emerge as such without any mixing if there would be no diffusive transport.

Also discussed was the benefits that micro fluidics would provide by giving a small volume of fluid, which needs to be thermally which needs to be in various applications thermally cycled, and the advantage that micro scale would provide is a very high heat transfer coefficient in such small volumes. Also we discussed about various aspects of mixing and how Reynolds number, low Reynolds number promotes this concept of band like flows, which would not promote by enlarged mixing. And then we also discuss some problem examples from the actual mems to name, where we would describe the application of micro needle or even the applications of mass transistors towards single cell, and the way that the cells would behave with respect to each other you listen while sitting over an array of MOSFETS.

We also described the micro cantilever array, and how it could be used for biological detection, and also talked about the concept of lab on chip where a series of bio molecular reactions from the laboratory would carried out in a small chip level of less than an inch by inch size. We further analyzed different real life mems applications more concerned with physical mems, where we would talk about things like single chip accelerometer or single chip micro phone. And also describe about the digital micro mirror device, we also mentioned about how the mems technology is useful for fabrication of micro cantilevers, and then we started with sensors.

We actually related to develop a sensor model which would comprised typically of a recognition element a transduction mechanism, and generate a signal which would be more machine readable. In fact, the sensor was laid out as something which would analyze from variety of analtytes selectively one particular analyte that would happen with respect to a recognition element which would be able to recognize that particular analyte, this recognize element would typically be mobilized on the surface of the transduction assembly or the transducer which would convert the chemical signal or whatever signal comes from the analyte into a machine determined signal which could be an optical signal or electrical signal.

The signal would be transmitted to the processer which would case of a fully automated system would be the brain of the computer. And in case you talk about human systems or biological system it could be the brain of a human being or a living being. We described a sensors and classified them in to three categories; physical sensor which would typically look into all physical parameters like measurement of properties like temperature, distance, pH temperature, pressure, mass, so on so forth.

We also talked about chemical sensors which would measure at typically chemical substances or chemical responses selectively, we further describe bio sensors which typically would use a biological recognition element that would be responsible for detecting a biological or a biological species. Further senses were the sensor model was outlaid for a variety of different situations like one was litmus paper. We described the litmus paper having a content which would be the die of the litmus paper which would change the coloration to be the recognition element , which would be sensitive to the pH a hydrogen ions in the in the solution.

Then, further the transduction that would take place would be in terms of a change in the absorption spectrum or a color change of that particular di molecule. Finally, resulting in giving a visual display of such pH change in terms of a color change, we further also explore different organs that human beings have the sense organs a sensor models. For example, we talked about the human nose and we mentioned that how series of chemical reactions which would lead to a sort of electron release would take place at the cilia of the factory cells, which is also in the region of the mucous membrane, it is the part of mucous membrane.

Basically, the what we could do is it would try to synthesize a series of proteins at very high rate, which would interact with different constituents of the filtered air which would go into the human nose system, and thus result in some electro chemical changes and this would eventually lead to a read out of smells readout and classification of smells like sweaty, penchant, sweet, rotten, so on so forth, by means different rates of electron release.

This finally, would go up into the brain through the olfactory route. So, that you can distinguish between these smells, and the defense mechanism of the body can then generate some actions which would avoid those smells which are particularly pungent or sweaty, etcetera. We also described about the human eye, and we talked about the retinal the retina which is actually at the back of the eye, and it comprises of these Rhodopsin molecule which is an opsin protein, and typically it is linked covalently to a compound called retinal. And

there are two isomers of retinal; one is cis and Trans isomer. And one typically light would do is to fall on this part of Rhodopsin molecule and change the cis to the Trans state as resulting in a again a electron realize. And therefore, different intensities of light like bright light or dim light would categorized suitably by means of such electron realizes, which would then flow through the optical nerve all the way to the brain.

So, that is how we categorize the various sense of models in the biological systems. We further described the various aspects of the sensor design like recognition elements, transaction types, method of immobilization, performance factors of the sensors, so on so forth. And finally, studied this independent domains 1 by 1; for example, we mentioned about iron selective electrodes in the recognition element, and their typically the selectivity of recognition element would really introduce the sensor to respond to one analyte from a group of different analytes.

It would also try to avoid interference from the other analyte, which are present in the sensing modality in that contest we discussed bio senses particularly, which would be using recognition elements like antibodies or enzymes or even nucleic acids and receptors which would typically identify one particular species here. And the example was given was that of glucose sensor where the enzyme GOD or glucose oxides would be able to analyze only or catalyze only the glucose molecule into gluconic acid NH_2O_2 thereby increasing the pH of the medium.

So, basically the selectivity components sometimes comes from the recognition elements sometimes, it comes from the design of the electrode which is sensing at the particular analyte of interest in this context. We described enzyme linked immune absorbent assay ELISA which talks about the detection of HIV species within the infected patients, and the idea which is projected here is that there is a glass plate in which the coat in the antigens of the HIV antigens particularly, and the logic that is used is that if this HIV species are present within the human system is causes defense mechanism is generate into the anti body, and this anti body is so called anti HIV antibody, which would be binding nature of HIV antigens. If there is a coating of the HIV antigens of the plate, a glass plate essentially which in vitro, and the patient samples the blood samples of the infected patient or otherwise healthy patient is put separately on this coated plates requirement of the anti body be in the blood sample would allow the body of an infection patient's blood sample bind with HIV coating top of the glass surface, and for the otherwise healthy patient, because the anti bodies or generally not

produce in the body in presence of any HIV antigen to the body those they would not and binding there.

So, what it practice at the third stage is that there is another antibody secondary anti body, which as in enzyme typically which would create is change in color of a chromo gene or a color die. So, this anti body is capable of binding to the anti HIV, antibody is basically blood in the plate that plate as a stag. Now there is a antigenic layer the human anti HIV, anti body generated from the human system, we wash of everything in else which is there, and then there is a secondary anti body which is coming in the bundle as a stag layer on the top of this primary anti body binding to it, and the secondary anti body has the enzyme. So, if the patients sample patient blood had the anti body corresponding to HIV, then the sole binding even to this three layer would generate.

That would to be the presence of the enzymes and when there is a forth steps, where the chrome gene or which color die which is put inside this is system immediately there would be a change of color change of absorption spectrum. So, the contestation of the change of inspector also define the mount of anti bodies, which present in the patient sample, which is very good integrate of the extent to HIV are invented the patient in other case. Of course, for the healthy patient, because not even in the primary of anti bodies for corresponding anti HIV, they are in the blood sample there would not be any such as binding, and there would not be the presence of enzymes, because we wash the steps in every event, and there is no covalent link in whatever would be on in plate typically care able.

So, you not have in any color change in that particular case, we also describe about various other modality to the sensor design transfusion development, we specifically mention the most of transduction which is most available. Today particularly on a commercial scale in electro chemical, and the reasons that were indicated that were electro chemical transistor is always more unable to reading out devices that produce electron as result of there, sensing modality and thus this is more integratable with microelectronic more integrate able with process, which make this mode of sensing in very useful, because it process the data come out such as sensing method or sensing modality. We also describe about the new thirst area of protons devices, where there is change in terms of number of protons generate neutron transistor is final signal in terms of light signal in photons, and there is a increasing term, because of the rapidly of the photon generated, you know the process of transmitting the photons the over rapidly of the sensing system should also increase.

Therefore, tendency of increasing now shifted to the photons, devices although they faraway from commercialization as one day. We also talk about mass based sensing small change in mass of the micro are even some times, the nano level is very sensitively detect by means of cantilever device, sometime piezoelectric pastels. We talked about different transducers, which produce, which change in the electron floor here, we mention of course, different electro chemicals sensing modality, and potentiometric and voltammetry. And also describe conductometry impedimentary and some of the futuristic modality of sensing.

We also talk about the various method of mobilization mentioning here, there the recognition element which we need to… Finally, immobilize on the surface transduce for the sensor needs to be put in place, and there is a various ways of the doing mobilization there would be a covalent attachment of species to the surface could be a attachment through ligand, in there be a ligand chemistry a linker molecule between the sensor surface on other side, and the recognize molecule in other side that would also be a method of micro in capsulation where typically trap this analyte, which between two or more membrane there would be physically entrap using something like a gel or a paste on the surface. And trying to marbleize recognition element within that gel at various levels each of them have their own limitation some of them also in terms of advantages in terms of fabrication process can be classified into various types.

We describe the performance factor where, we look into the different yard sticks available for a sensor engineer distinguish the efficacy of the sensing device. For example, one such parameter would be selectively able to distinguish between life be interested, and other would be in range of sensitivity of what milli molar level or micro molar level of

the change of concentration of distinguish there would also be a question of accuracy what is the percentage, which in the sensing domain operate accurately giving replicable read out every time. And then we talked about various other performance yard stick lights response time recovery time and life time, so on. So, then we shifted on to description on bio chips, and lab on chips we briefly talk about the very wide presence of lab on chip devices in the area integrated gene analyze and detection. And we also describe come nobel tools nanobiology, where again you know how single cell behave in terms of molecules - 1000 of molecules on its surface could be very useful information to know about collective or individual behavior of the cell, and this data would be used immense used to the physiologist, and this whole new area of nano biology.

Suppose to generate those tools particularly integration with micro domain or nano domain integration with electronics, such tools give very rapidly sensing mechanism for understanding, how the molecules start producing on the surface of the cell. For example, or how they start disappear and individual cell to cell communication would them to the cyber in terms of electrical impulses, and responses here. We also mention about the process of transcription and translation, where DNA would typically decoded to messenger RNA much shorter transcript of the DNA, and then it would eventually translate related to all different together language from the sequence of nuclei type sequence of amino acids. So, the final goal to produce the sequence of amino acid, and other wise and this mechanism is happens with in the whole cell.

We further started with some introductory topic in the area of micro fabrication. We describe about the surface and bulk micro machining, and we also talked about various material which is used for the proposes of devices there is three different generation of materials like silicon glasses of course, because most of the mems process are borrowed from the micro electronics industry. They would also be a polymers, we should able to typically rhyme very well behave very well in presence biological spices. And then of course, there will be a completely new class of mems devices, which have made of the biological entity themselves like, let us do for the example DNA printers or cell base devices, so on so forth. We described different process where serious of steps selectively lithography steps, we could be small vias, and with thin membrane standalone top of them.

Describe how to make briefly in such a membrane either it is a beam like orientation or a cantilever like orientation. We started off with some description of concepts like what etching would be selectively, and then of course we just started introducing the photolithography process and photoresis. So, this sort of concludes, what we learnt in the first week of our lectures, I eventually also like to provide an assignment, and in end of this lecture which you have to submit back to us.

Thank you.