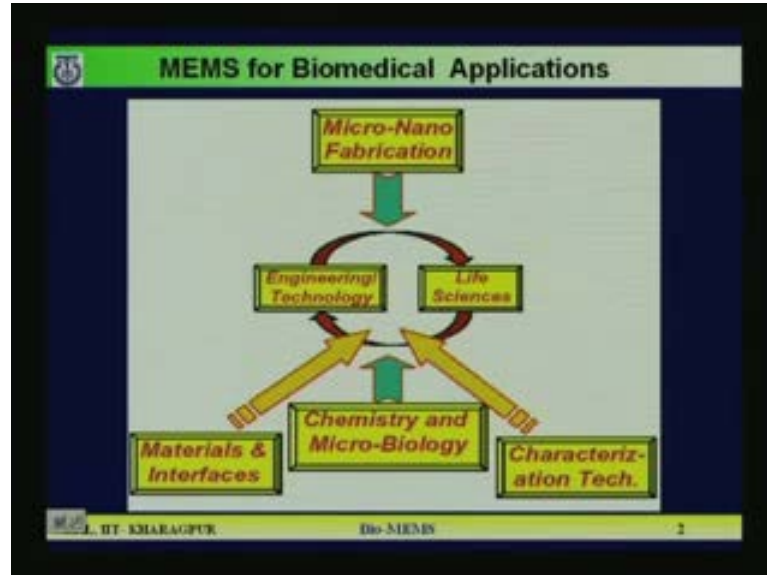


MEMS and Microsystems
Prof. Santiram Kal
Department of Electronics and Electrical Communication Engineering
Indian Institute of Technology, Kharagpur
Lecture No. # 32
MEMS for Biomedical Applications (Bio-MEMS)

I will now discuss on a very interesting topic and fascinating topic. That is MEMS for biomedical applications and you know if something is used for human body for biological application. So you have to take 100 percent precaution before using it in any of the animals or any of the biological system. Because you cannot make harm to the system. For your devices which you are intending to use for certain application, they may not deteriorate the functioning of the existing living beings. At the same time you should not do something which will create some problem in the environment also. So that is why like other sensors which are being used in case of appendix, in case of automobiles, in case of say space or in case of industrial control or entertainment or IT, whatever it is. So those sensors are I agree that those sensors are high precision and good quality. But those are not dealing with directly the biological system or any of the living being organism.

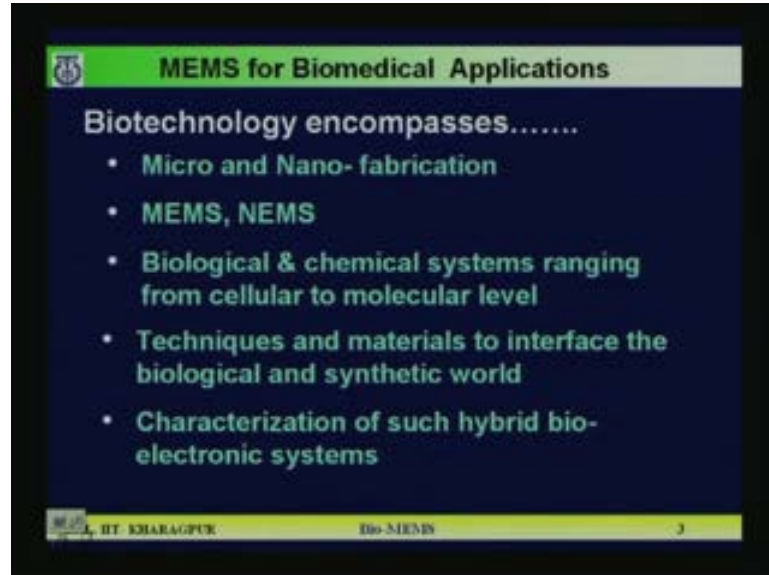
But if you go for using a particular sensors and actuators for living beings, so it has to qualify other aspects also. Those aspects are mainly it has to be biocompatible. But what is that? That is if you are going to reduce certain diseases or remove certain diseases in a living body or human being, so the methods you are going to adopt, they cannot call for other problems in the human body. So that is the point you have to take care. So that is why in case of biological system the MEMS which are coming up for biological application, the real life practical testing is becoming more and more difficult until unless you get permission from different government bodies or authorities who control the biological medicines or any kind of the biological interaction. So there clearance is too required before you go for testing of those devices. So we will just see now in this lecture how the MEMS device is going to play a major role in different biological functioning and how it can be used for diagnostic purpose in a fascinating way, in a very challenging way.

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Now if you look into the Bio-MEMS, biological MEMS application is sometimes called is a Bio-MEMS. So in Bio-MEMS what are the different things coming into the picture? Here you can see first is the micro-nano fabrication and in the middle is that engineering technology and life science circle is there in the life science and engineering technology we are adopting and now lot of promotion combinations are going on, lot of evaluations are taking place and what is the input to this evaluation to this research? One is materials and interface; another is chemistry and microbiology and characterization technology. So these are the various inputs micro and nano fabrication is the basic thing because of which are getting the MEMS sensors and then evolution is possible. That means improvement evolution means in positive direction for that you need thoroughly the knowledge or understanding of materials which we are going to use for biological application and their interfacing with the biological system. Chemistry you have to know particularly microbiology, biochemistry. You have a good knowledge on that and characterization technology this characterization technology in many cases should be noninvasive. So those kinds of thing you have to keep in mind. So all these things makes the Bio-MEMS area more challenging.

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Now biotechnology encompasses what is, one is micro and nano-fabrication. As I showed you, MEMS and NEMS micro electromechanical systems and NEMS is Nano Electromechanical Systems. Biological and chemical systems ranging from cellular to molecular level you have to go to the cell level. What chemistry is going, on molecular level you have to see something if you go for DNA research or a gene research, then you have to understand the microbiology fully. Techniques and materials to interface the biological and synthetic world. So interface is another point because some ultimately diagnostic and controlling part will be electronic but which you are going to implant the device is into the human or any living body. So they are mostly, they are synthetic or polymeric in nature. Many of the metallic structure you cannot use inside the body which will detonate which will react with lot of systems and characterization of such hybrid bio-electronic system. Bio-electronic system characterization. How do you get output of that and how would you modify those sensors, for that you need the characterization of the complete system.

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MEMS for Biomedical Applications

Bio-MEMS can be defined as....

"Devices or systems, constructed using techniques inspired from micro/nano scale fabrication, that are used for processing, delivery, manipulation, analysis, or construction of biological and chemical entities"

– Bashir, Purdue Univ., 2004

Bio-Sensors can be defined as.....

"Analytical devices that combine a biologically sensitive element with a physical or chemical transducer to selectively and quantitatively detect the presence of specific compounds in a given external environment"

– Vo-Dinh and Cullum, 2000

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Now what is the definition of Bio-MEMS? Lot of scientist in that area they put forward lots of definitions I had coated some of the definitions here. One is from Bashir from Purdue University. According to him the devices or systems constructed using techniques inspired from micro nano scale fabrication that are used for processing, delivery, manipulation, analysis or construction of biological and chemical entities, these are Bio-MEMS. On the other hand some other scientist in 2000 they defined biosensors as they are analytical devices that combine a biologically sensitive element with a physical or chemical transducer to selectively and quantitatively detect the presence of specific compounds in a given external environment, this is another definition.

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MEMS for Biomedical Applications

Bio-Chips can detect...

- Cells, microorganisms, viruses, proteins, DNA and small molecules of biomedical importance and interest.

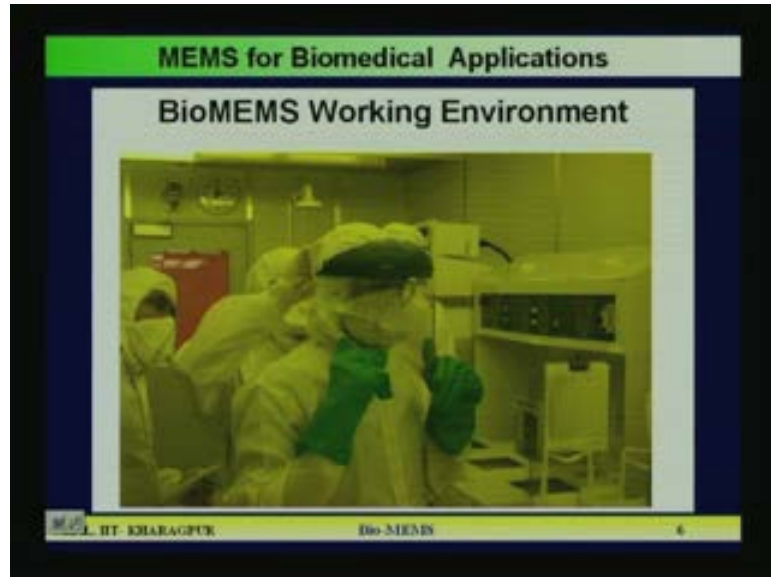
Bio-MEMS application ranges.....

- Diagnostics such as DNA and protein microarrays, microfluidics, tissue engineering, drug delivery systems, implantable BioMEMs etc...

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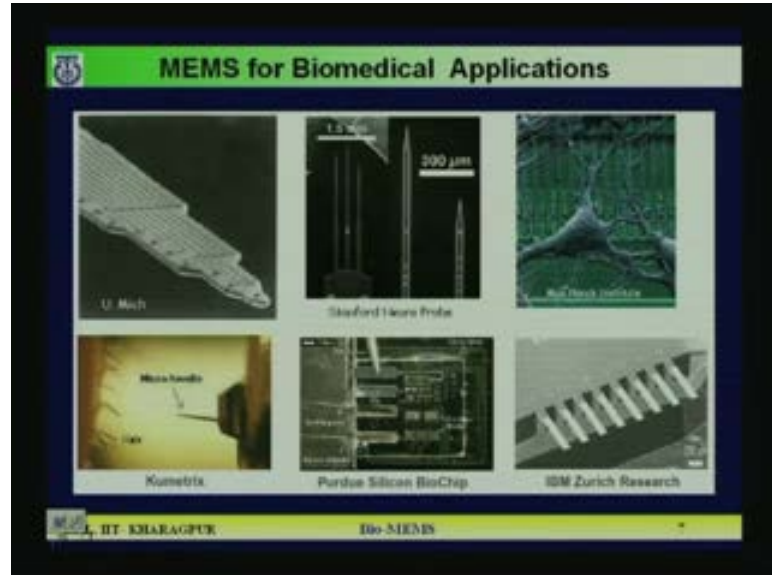
So ultimately what Bio-chips can do? Bio-chips can detect cells, microorganisms, viruses, proteins, DNA and small molecules of biomedical importance and interest. So your system should be such that the microsystem or micro sensor, they can detect all those kinds of things. What are the applicants ranges of Bio-MEMS? In case of diagnostic such as DNA and protein microarrays, microfluidics, tissue engineering, drug delivery systems, implantable BioMEMS, these are different application ranges of bio-sensors.

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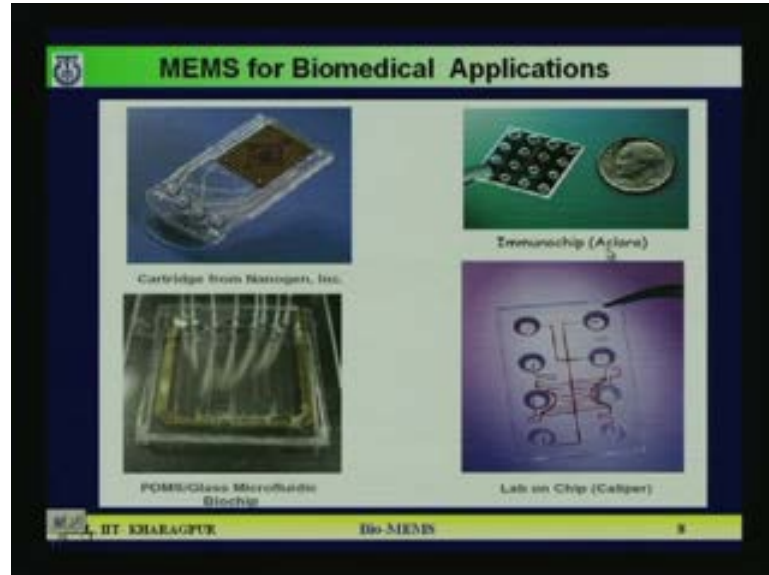
The working environment of the BioMEMS is shown in this particular picture where you can see some extra precautions has been taken to protect the workers or researchers because you are dealing with some of the chemicals, some of the viruses, which may be dangers to mankind. So if you are dealing with those viruses or the chemicals or proteins, whatever it is which may be harmful to human body, you have to take that precaution. Those who are working with on the gene therapy or the genomics and proteinomics, gene transfection, so they have to take care a lot before handling those kind of the elements for characterization and testing.

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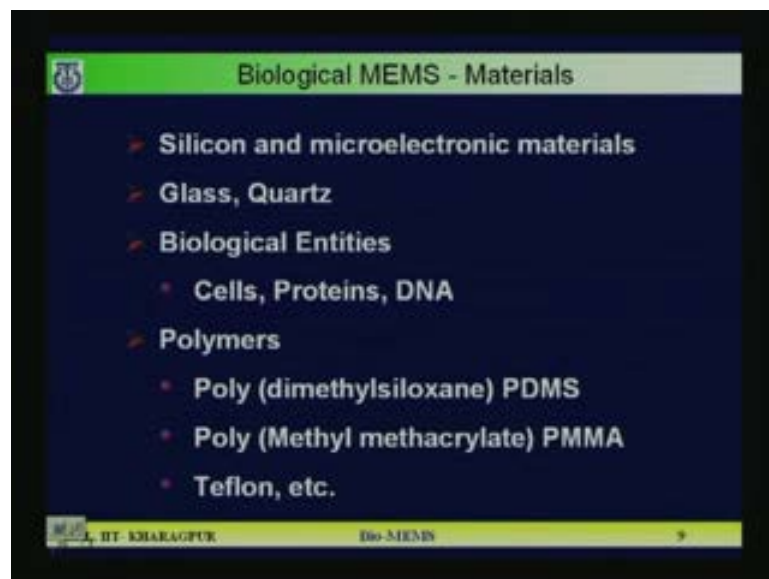
Now before going to little bit in detail of the sensors here some of the Bio-MEMS devices which are marketed, those are shown in this slide. First one is from University of Michigan; second one is from University of Stanford. This is a neuro probes for neurological application and third one is Max plug Institute. These are some of the cells for testing certain diagnostic purpose. Here some kuimetrix some player in the Bio-MEMS area you can see they have devised a micro needle and this micro needle and in the other side is the hair. Those dimension if the tip of the micro needle is small as much smaller than the tip than that of the hair dimension. So that micro needle has been fabricated using silicon micro machining technology. Some silicon Bio-Chips have been reported from Purdue University that is also shown here and for IBM Zurich research lab, you can see some of the cantilever structures which are used for biomechanics also. So these are some of the research results from various laboratories around the globe who are working since last 5 to 10years on various areas of the biosensors.

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Some other finished products from companies are shown here. One is the cartridge, biomedical cartridge from Nanogen, some is Immunochip, and this one is Immunochip from Aclera. Here is PDMS glass microfluidic biochip and this is lab on chip from Caliper. So these are some finished products from the companies.

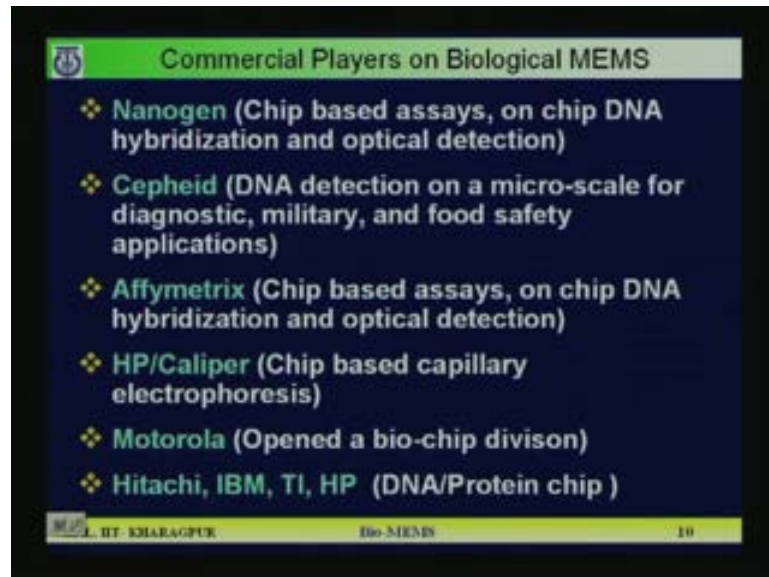
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Now what are the different aspects of Bio-MEMS? One is material so obviously and in biological application, silicon although it is used, but it is not a good choice of material which can be implanted into the human body. Some other microelectronic materials people are looking for, those are glass and quartz. Some of the MEMS or bio-chips which are used

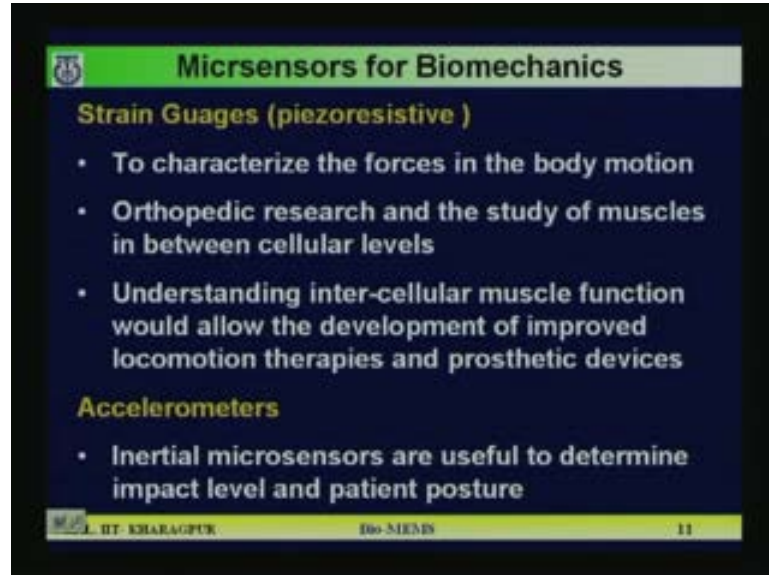
for external diagnostic purpose or reaction purpose, those you can make use of quartz or glass or silicon etcetera. But the problem comes if you want to implant some of the chips into the living body or living animals or the human being, human body, whatever it is. Now biological entities, those are cells proteins and DNA. Polymer is most favorable material for bio-MEMS application. Some of are poly dimethylsiloxane, that is PDMS another is Methyl methacrylate which is PMMA, Teflon. These are some of the common polymers which are used in biological MEMS.

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The commercial players on biological MEMS are Nanogen who are producing chip based assays, on chip DNA hybridization and optical detection. Cepheid, DNA detection on a micro-scale for diagnostic, military and food safety application. Affymetrix chip based assays, on chip DNA hybridization and optical detection. HP and Caliper chip based capillary, electrophoresis. Motorola opened a bio-chip division separately. Hitachi, IBM, TI, HP, they are in the line and they are concentrating on DNA and protein chip.

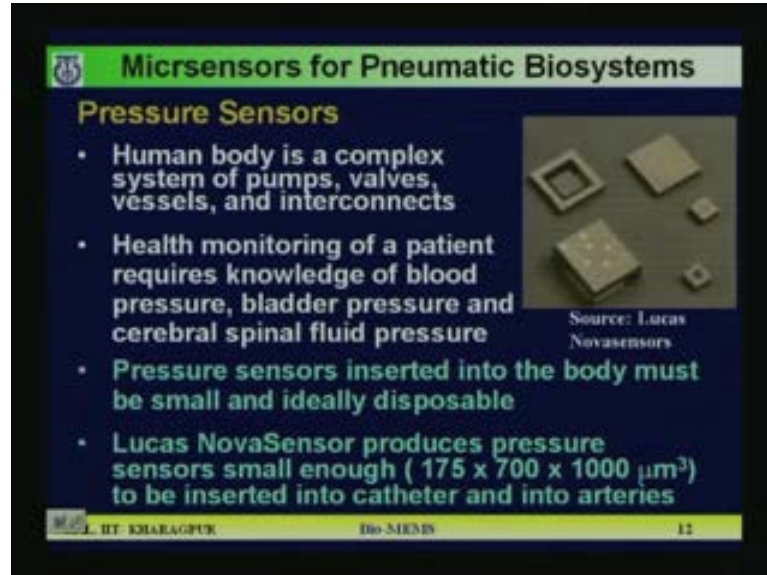
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Now I will discuss the few applications of Bio-MEMS. First I will attack on biomechanics. Microsensors for biomechanics. So for biomechanics one sensor is very much used. That is a strain gauge. Strain gauge is basically made using piezoresistive mechanism of the silicon. Since silicon is piezoresistive material you know. That is basically used to characterize the forces in the body motion. In the body in muscle there are lots of mechanical movement of the muscles and if you want to monitor the movements of the muscle, so you need this strain gauges. So strain gauge if you attached on any muscle and then because of the forces in the muscle, so the strain will be developed and that if it is the piezoresistive, so that can give certain output. Another application of the strain gauges are in orthopedic research and the study of muscles in between cellular level particularly muscles which are in between cell, those characterization is very important in many cases and in between cell muscle movement and there characterization is possible with microminiaturized strain gauges which can be implanted in the particular location.

So MEMS miniaturization has made it possible to make the micro strain gauge which can be implanted in different locations. Even in the muscles which are in between cellular cells. Third application understands inter-cellular muscle function which would allow the development of improved locomotion therapies and prosthetic devices. Locomotion therapy and prosthetic devices for that you need that this strain gauges accelerometers. That is also used in biological application accelerometer how it is made already I discussed in detail. These sensors are useful to determine impact level and patient posture. Impact level suddenly you are hitting on a practical muscle. What is the impact? There is sudden impact and that can be sensed by inertial sensors and what is the attitude of the posture of the patient. If you give an impulse on a particular muscle or particular section of any of your body, so that can be properly diagnosed with the help of the accelerometers or any gyros, both the sensors are used in case of the biological application.

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Microsensors for Pneumatic Biosystems

Pressure Sensors

- Human body is a complex system of pumps, valves, vessels, and interconnects
- Health monitoring of a patient requires knowledge of blood pressure, bladder pressure and cerebral spinal fluid pressure
- Pressure sensors inserted into the body must be small and ideally disposable
- Lucas NovaSensor produces pressure sensors small enough ($175 \times 700 \times 1000 \mu\text{m}^3$) to be inserted into catheter and into arteries

Source: Lucas NovaSensors

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Now micro sensors for pneumatic bio systems. They use pressure sensors. We know that human body is a complex system of pumps, valves, vessels and interconnects. Heart is a example of pumps valves are there lot of valves are there. You know during passage of your fluids which may be blood also in the human body. Interconnect and vessels with tubes the arteries and veins lot of those are interconnect of the fluids. Even in urology there are lots of interconnections vessels are there for culturing urine and for disperse the urine. Not only that the water is also extracted in some cases, those cases they require the pressure sensors. Wherever is a valve pump where is that valve what is the pressure generated from the pump or valve that has to be monitored for that you need pressure sensor. Health monitoring of a patient require knowledge of blood pressure, bladder pressure and cerebral spinal fluid pressure. These are the three important aspects blood pressure, bladder pressure and cerebral spinal fluid pressure. Those can be precisely monitored with the help of high precision pressure sensor. Pressure sensors are inserted into the body that must be very small and is to be disposable.

Because once you used a certain section to measure the pressure of a bladder the same sensor cannot be used in other place which you say. For example for measuring the cerebral spinal fluid pressure. So those kinds of sensors must be disposable kind of thing. In this aspect in a pneumatic biosystems Lucas NovaSensors are going far ahead for marketing devices and in this picture you can see the pressure sensors of different sizes and some of the sensors are highly miniaturized. So that easily you can implant those sensors even in cerebral spinal fluid as spinal fluid channel location. So the sensor of smallest size of the order of 175 micrometer by 700 micrometer by 1000 micrometer is reported from the Lucas NovaSensors and those kinds of sensors can be inserted into catheter and into arteries. So in the tip of the catheter you can put those miniaturized pressure sensors and you can push the whole thing into the arteries. Because its dimension is negligible in comparison to the channel inside the arteries. So those are some of the application of the pressure sensors in pneumatic biosystems.

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Microsensors for Chemical Biosystems

- Living organisms are extremely sophisticated chemical processing systems
- Application includes medical diagnostic instruments, drug screening, implantable sensors for prostheses and environment monitoring
- Challenges are – delivery, reaction control and waste disposal

Impedance Sensors

- Gases or vapors and their relative conc. changes conductivity of some materials e.g., conductive polymers and metal oxides

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Now coming microsensors for chemical biosystem. Living organisms are extremely sophisticated and they are extremely high sensing molecules, living organism and if you want to make some reaction with some chemicals, so you have to do it with lot of precautions and care. Lot of applications in medical diagnostic instruments is there for the chemical biosystems. They are drug screening, implantable sensors for prostheses and environment monitoring. Challenge lies here the delivery reaction control and waste disposal. For example if you want to diagnose something and you want to implant something into the body. So major problem is delivery because how the chemicals should be delivered into that particular location. Then after delivering these chemicals into the living organism, then the how can you control the reaction.

If the reaction is not favorable to the patient, then you have to control, you will have to stop. How can do it? That is other challenge and third one is waste disposal. Since it is a chemical reaction with the living organism, some byproduct will be there. If that byproduct is not friendly to the human body, how can you remove that byproduct? That is waste disposal that is other problem. In this direction for chemical biosystem, some sensors are used which has a resistance type impedance sensors. And what is impedance sensor? Those are basically the impedance or rather the resistances will change with absorption of certain chemicals into the living organism. Gases or vapors and their relative concentration can change the conductivity of some materials for example conductive polymers and metal oxide.

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Polymer Based Gas Sensors

Many polymers will geometrically swell reversibly when exposed to certain gases. Swelling to a greater or lesser extent depends on variety of gases.

- Polypyrrole – a conductive polymer used directly as chemiresistor
- Insulating polymers are doped with conductive particles (e.g., carbon black) to reduce their conductivity
- Resistance of doped polymer will change as a function of chemically specific and concentration dependent swelling

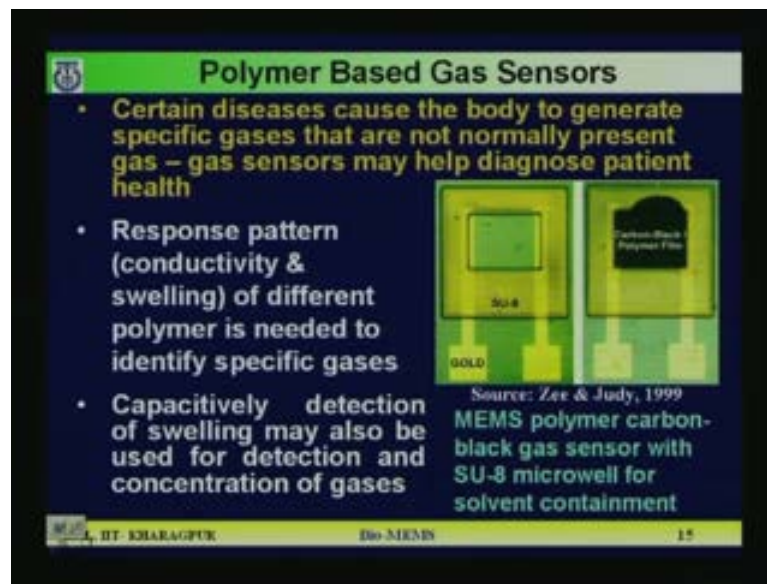
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There are certain polymers I can name one polymer also which is Polypyrrole. That polymer is a conductive polymer and it is directly used as chemiresistor. There are two things happening in case of polymer if gas is observed. One is the conductive polymer its conductivity changes if gas is absorbed and the second is if some gas is absorbed by a polymer it swells. Its swelling means its volume changes. Now you see there are two kinds of the mechanisms you can get from here. Once you can from the conductive change or resistance change of the polymer directly you can reflect in to your voltage signal and by absorption of certain chemicals or gases or vapors if it swells, then you can make a capacitance also and then you have to not conductive. But insulating polymer as a dielectric and if you have conducting polymer on both side as a electrode, then on absorption of gas if it swells, then the capacitance will change. So in both directions people are working and they are making lot of sensors which are used as a gas sensor.

One because lot of gases are they evolved in your human body in system also. So you have to sense that gases. But the problem there are two problem one is the type of gases which gas is revolving and another is the concentration of gas molecules, two things are important. In some cases the concentration can be directly measured with the swelling, how much swelling capacitive type of sensors, how much it swells with concentration and the second because if you want the selectivity. That means which gas is revolving then you need the knowledge of polymers which reacts which gases. In those cases single polymer sensor may not be useful. You have you have an array of sensors for different kind of polymer and you have to know before hand which polymer can react with which kind of gases. So accordingly both the things are available, which kind of gas and how much concentration of gas is available with this kind of polymer, gas polymer based gas sensors. Now many polymers will geometrically swell reversibly. When exposed to a certain gases swelling to a greater or lesser extend depends on variety of gases.

Now one important point is mentioned here, swell reversible it is not that. Once is swelled expand it cannot contract, both should be possible. When the gas concentration is more, it swells; when it is less, it may contract. Swells mean it may expand or it can reduce the volume. So both are required. A conducting polymer as I mentioned Polypyrrole is used for this purpose. Insulating polymers are doped with conducting particles like carbon black to reduce their conductivity. Basically you can start with the insulating polymer and by adding or implanting many of conductive particles like carbon black you can reduce their conductivity also. Resistance of doped polymers will change as a function of chemically specific and concentration dependent swelling. One is chemical specific, another is concentration dependent swelling. You see both things are important. One should be chemically specific polymer, another is concentration dependent swelling. So that you can know type as well as concentration both.

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Now some of the sensors which have been reported by Judy Etel in 1999 are shown in this diagram. Certain diseases causes the body to generate specific gases that are not normally present gas normally those gases are not present. But certain disease can generate those gases and gas sensors of this kind may help diagnose particular patient's health. A response pattern, what is the response pattern? One is conductivity change, another is swelling. These are the response pattern of different polymer is needed to identify specific gases. So if you want to identify specific gas you have to have the response pattern before-hand. Otherwise you cannot identify the type of gases. Capacitively detection of swelling may also be used for detection and concentration of gases and that I just told you can see it first photo resist you see here you can make a group and in that group you can make this solvent which is the basically the polymer solvent and if you want to change its conductivity, you can put some carbon black polymer field on top of the oil which contains the solvent. So these oils are micro oils are created to have to contain the solvent and to react with the gases. So these are some of the gas sensors.

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Electrochemical Sensors

Oxidation / reduction of chemical species on a conducting electrode can be observed by measuring the movement of charge – potentiometric (potential dependent on chemistry) and amperometric (current generated by reaction) sensing

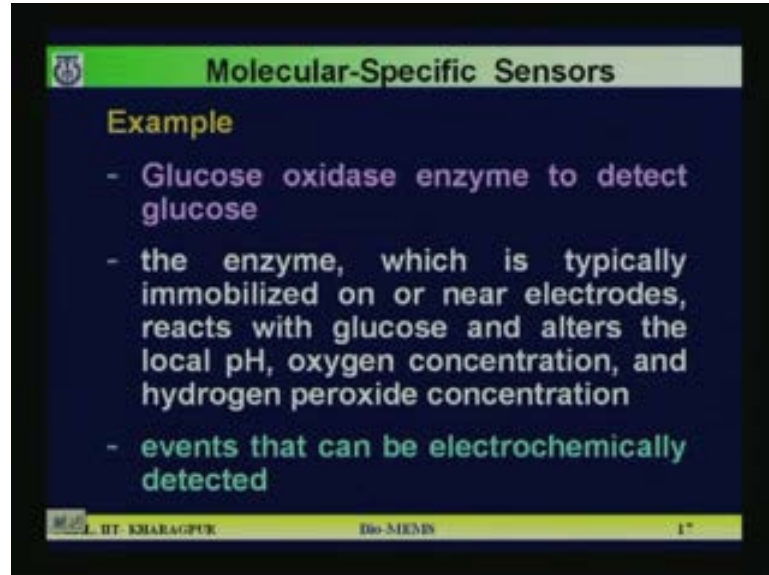
- Micromachining processes can be used to accurately and reliably define the area, number, and relative position of electrodes that are exposed to the solution

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Now I'll talk little bit on electrochemical sensor. An electrochemical sensor basically oxidation reduction of chemical species on a conducting electrode is done there that is detective and there the oxidation reduction of the chemical species. What will happen due to that? Charge will be generated and the movement of the charge and if the charge moves they can be sensed by two ways. One is known a potentiometric way which basically potential difference, potential dependent on chemistry and the another is amperometric way. Current generated by reaction there are two kinds of sensing. One kind is known as potentiometric sensing and the other kind is known as amperometric sensing. Micromachining processes can be used to accurately and reliably define the area number and relative position of electrodes that are exposed to the solution.

So here comes you micromachining technology with specific because here you are going to have electrodes and those electrodes are inserted in a chemical where reaction with the chemicals. Those reactions are oxidation reduction reactions and there charges will move from one electrode to other electrode and the movement of the charge will either reflected to the voltage change which is known as potentiometric sensing and also it can be reflected to current change which is known as the amperometric sensing. So these are the basic principle of the electrochemical sensors and here requirement is to accurately designed and fabricate the electrodes, microelectrodes.

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Molecular-Specific Sensors

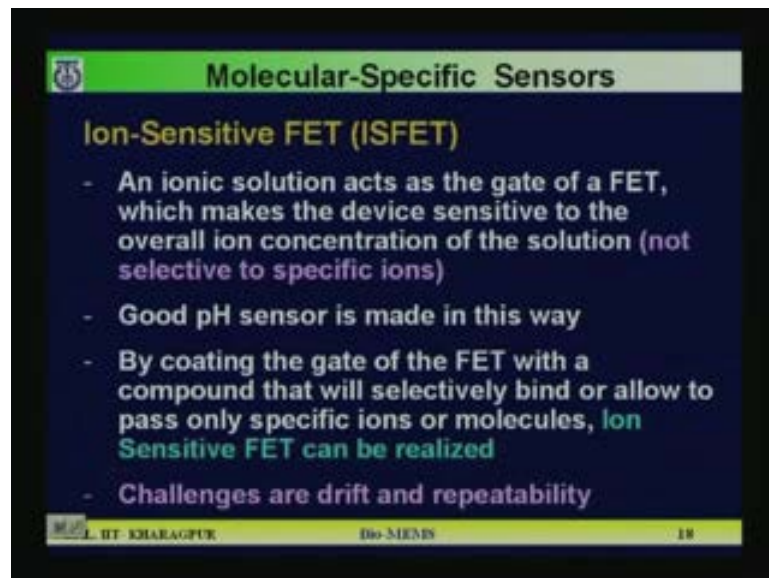
Example

- Glucose oxidase enzyme to detect glucose
- the enzyme, which is typically immobilized on or near electrodes, reacts with glucose and alters the local pH, oxygen concentration, and hydrogen peroxide concentration
- events that can be electrochemically detected

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And some of the examples in this direction are glucose oxidase enzyme to detect glucose. In a blood, how much glucose is there, that can be easily detected by this technique. Using oxidation reaction, using some enzyme. So this is known as glucose oxidase enzyme to detect glucose. Here the enzyme which is typically immobilized. That is immobilized on or near electrodes. It reacts with glucose and alters the local pH value, oxygen concentration and hydrogen peroxide concentration. So this can be used for glucose sensor. Those events can be electrochemically detected. That is glucose oxidase enzyme reaction.

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Molecular-Specific Sensors

Ion-Sensitive FET (ISFET)

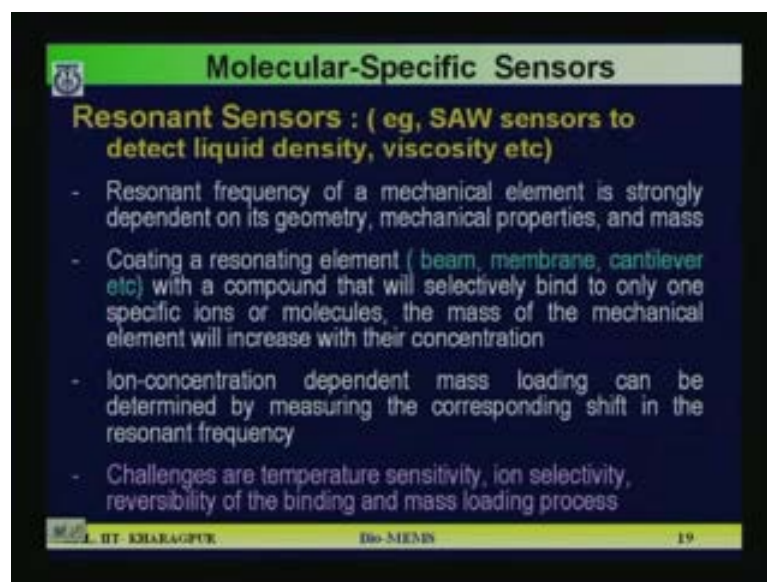
- An ionic solution acts as the gate of a FET, which makes the device sensitive to the overall ion concentration of the solution (not selective to specific ions)
- Good pH sensor is made in this way
- By coating the gate of the FET with a compound that will selectively bind or allow to pass only specific ions or molecules, **Ion Sensitive FET can be realized**
- Challenges are drift and repeatability

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Next kind of sensor I would like to discuss is molecular specific sensor. One example is ISFET. What is that ion sensitive FET? Field effect transistor, you know source drain and gate these three are the electrodes. So now the performance of the most devices depends greatly on the gate electrode is voltage on the gate electrode. Now in this kind of the ISFET what is being done? The gate is not normal, the silicon gate or polysilicon metal gate, gate is ionic gate. Basically an ionic solution they act as a gate. Ionic solution means it will have lot of ions. If the ions changes, their concentration changes. Automatically it will have great influence on the performance of the MOSFET. In earlier we used to apply some voltage on the gate electrode instead of that we are using a chamber which contain some ionic solution. So that ion means some charges will be there on the gate and that is going to influence the source to ring and then to source currents in the MOSFET. So that ionic solution acts as a gate of an FET which makes the device sensitive to the overall ion concentration of the solution.

Not selective to specific ions in that case. Because depending on the concentration of the ionic concentration in the solution you can get the drain currents and other things. It can be used a good pH sensor and already pH sensor is made using this technology, ISFET technology. But we are interested not only the concentration of ion we are interested also to detect the specific ions. How can we do that? That is also possible which is known ion selective FET. For that what you have to do? You have to coat the gate of the FET with certain compound and that compound will attract selectively or bind some of the molecules or ions from the solution. Then it will be ion selective. That means if you can make the gate with an electrode which is coated with certain compound and those compound selectively bind the ions from the ionic solution. Then if these ions are not bind to the gate electrode, so then that is not going to influence the ISFET current. So in that way you can make this ISFET ion selective also. But the main challenges here are drift and repeatability in this kind of ISFET sensors. So ISFET is a very popular device in molecular specific sensor.

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Molecular-Specific Sensors

Resonant Sensors : (eg, SAW sensors to detect liquid density, viscosity etc)

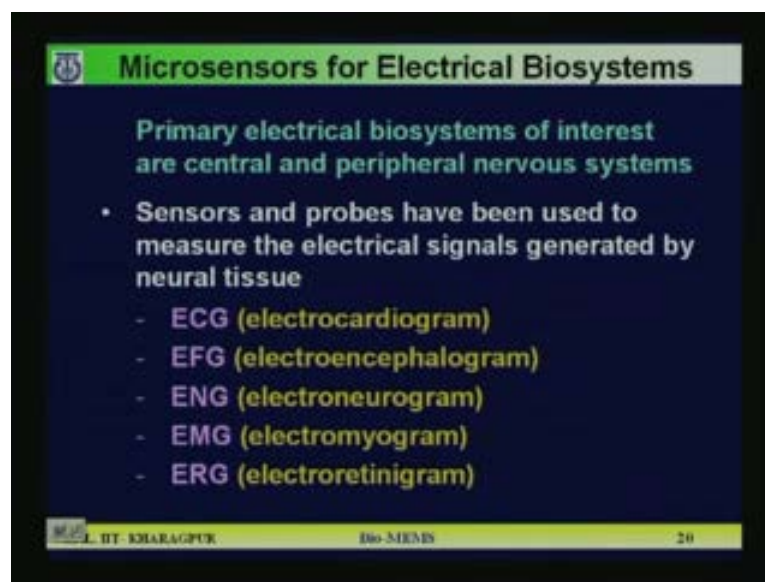
- Resonant frequency of a mechanical element is strongly dependent on its geometry, mechanical properties, and mass
- Coating a resonating element (beam, membrane, cantilever etc) with a compound that will selectively bind to only one specific ions or molecules, the mass of the mechanical element will increase with their concentration
- Ion-concentration dependent mass loading can be determined by measuring the corresponding shift in the resonant frequency
- Challenges are temperature sensitivity, ion selectivity, reversibility of the binding and mass loading process

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Now another molecular-specific sensor is a resonant sensor. Examples are SAW surfaced acoustic wave sensors to detect liquid density and viscosity of the fluid. The resonant sensors are also used as it is made by compatible. So that it can be directly used with the microorganism and ionic solutions. This bio fluids it can be directly used and what are the resonant structure? The resonant structure will have certain mass also. Some flexures or those flexures may be membrane or it may be cantilever or it may be beam. These are the resonating element. Those resonating elements what you can do, you can miniaturize those elements and those elements can be used to selectively react with certain ions. You can coat those resonating element with certain compound and that compound will selectively bind to only one specific ions or molecule. Then what will happen? If those resonators will attract some specific ions and molecules, then the mass of that resonator will increase and because of the change of mass, its resonant frequency also will change.

So that is the principle used in this kind of resonant sensors where we can fabricate accurately. Some resonating structures and those structures may be membrane, may be cantilever, and may be beams. Now those beams or cantilevers are coated with certain compound, those compounds will attract certain specific ions or molecules and when these are attached or bind on the surface of those micromechanical structures. Then automatically its mass will increase and as a result of which the resonant frequency will change. So that is the mechanism which is used in this kind of the resonant sensors which are used in biomedical application. Ion concentration dependent mass loading can be determined by measuring the corresponding shift in the resonant frequency. That is the basic principle. Here the challenges are temperature sensitivity, ion selectivity, reversibility of the binding and mass loading process. Reversibility of the binding is a major problem. Because once it is attached to a particular electrode, how can you detach it? So that is the problem. So those challenges you have to sought it before practically use of those sensors in biological or biomedical application.

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Microsensors for Electrical Biosystems

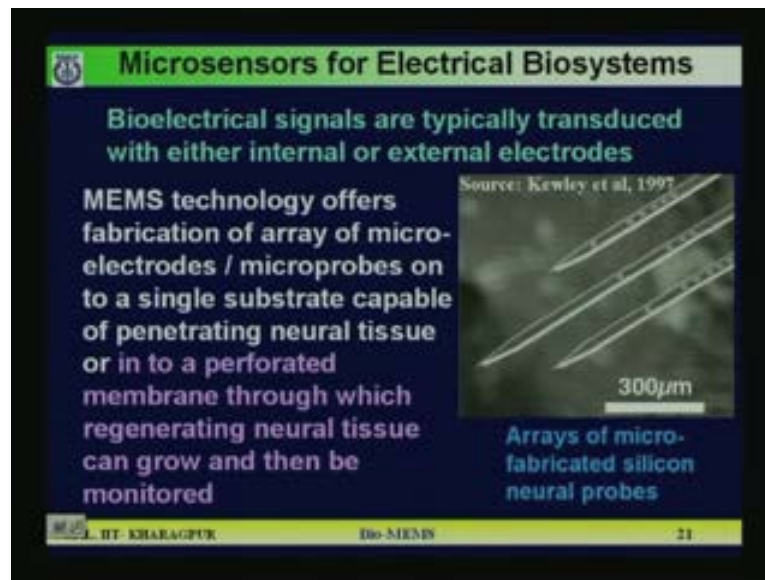
Primary electrical biosystems of interest are central and peripheral nervous systems

- Sensors and probes have been used to measure the electrical signals generated by neural tissue
 - ECG (electrocardiogram)
 - EFG (electroencephalogram)
 - ENG (electroneurogram)
 - EMG (electromyogram)
 - ERG (electroretinogram)

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Now microsensors for electrical biosystems. Primary electrical biosystems of interest are central and peripheral nervous systems. These are of primary interest. Sensor and probes have been used to measure the electrical signals generated by neural tissues. Neural tissues they generate electrical signal and those signals are sensed or probes using certain microprobes and here the examples in this direction are electrocardiogram which is known as ECG, electroencephalogram which is known as EFG, electroneurogram which is known as ENG, electromyogram that is know as EMG and electrorentinigram that is known as ERG. So these various kinds of sensors which are based on electrical biosystems. They are ECG, EFG, ENG, EMG and ERG.

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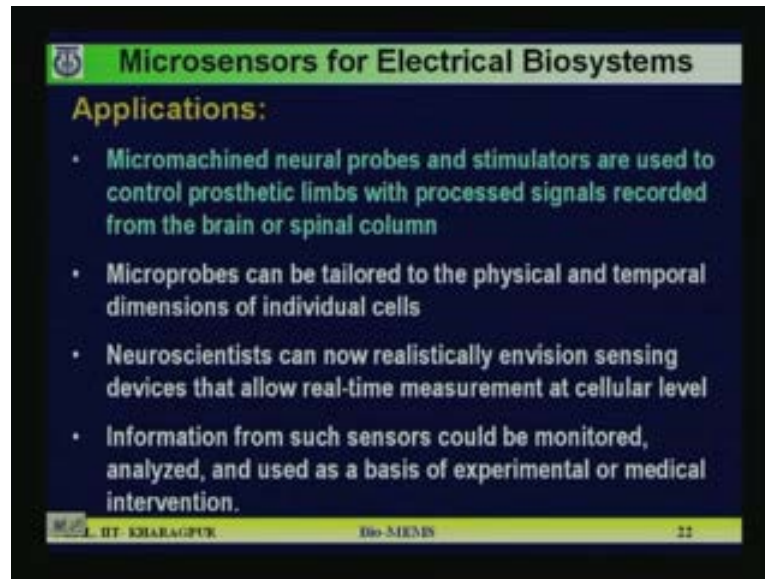


Now some of the examples are shown here. Bioelectrical signals are typically transduced with either internal or external electrodes. In what way MEMS are coming in to the picture? MEMS are coming in to the picture, in this particular case in fabrication of microprobes. Microprobe or microelectrodes on a single substrate which can penetrate the tissue without disturbing the tissue. So here you can see some of the pictures, the array of micro-fabricated silicon neural probes. So these tips are you can imagine is of the order of few micron may be 5 to 10 micron. This length is 300 micron and if you compare the tip with this length, so easily you can see it is of the order of say 5 to 10 micrometer only. So this small tip, this basically electrode and its tip is micro needly kind of thing that can be easily be penetrated into the probe in into the neurons without damaging it and you can collect the electrical signals from the neuron for diagnostic purposes.

Whether it is a retina or it is a heart or it is other body in all those cases, the electrical signals can be tapped with the help of these neural probes and after that you can process the signal for diagnostic purposes. Another technique which is used sometimes, they use perforated membrane and those perforated membranes are implanted into that, into the areas whose or in which place you want to make certain monitoring of you want to make some or you want to monitor the neuron behavior or its growth. In that case if you implant those membrane

they in those membranes, they regenerated neural tissue will be formed and they can grow and they can come across through the membranes, small membranes and which you can easily monitor for your diagnostic purposes.

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The slide is titled "Microsensors for Electrical Biosystems" and lists four applications of microsensors. The text is as follows:

- Micromachined neural probes and stimulators are used to control prosthetic limbs with processed signals recorded from the brain or spinal column
- Microprobes can be tailored to the physical and temporal dimensions of individual cells
- Neuroscientists can now realistically envision sensing devices that allow real-time measurement at cellular level
- Information from such sensors could be monitored, analyzed, and used as a basis of experimental or medical intervention.

At the bottom of the slide, there is a footer with the text "IIT KHARAGPUR" on the left, "Bio-MEMS" in the center, and "22" on the right.

In that area lot of application are there. What are the applications are mentioned here? Micromachined neural probes and stimulators are used to control prosthetic limbs with processed signals recorded from the brain or spinal column. Microprobes can be tailored to the physical and temporal dimensions of individual cells. That means depending on your application you can tailor the size of the probes also. Neuroscientist can now realistically envision sensing devices that allow a real time measurement at cellular level. At a cell level these probes can get the signal. So you can get the real time measurements at the cell level easily using these microprobes which are made using micromachining technology. Information from such sensors could be monitored. It could be analyzed and used as a basis of experimental or biomedical intervention. So these are the applications of microprobes.

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MEMS Biomedical Microactuators

Biomedical actuators are used to control the biological objects or their environment on microscopic scale

Micromanipulators:


- Micromanipulators are driven by a micro-actuation mechanism capable of operating in a conductive solution.
- Good candidates include magnetic, pneumatic, thermal, and shape memory alloy actuation


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Now I will discuss on microactuators. Some of the sensors which are used in biomedical application I told you. Now let us see how the microactuators are formed and how they are used in biomedical scenario. Biomedical actuators are used to control the biological objects or their environment on microscopic scale. First example is micromanipulator. What are the jobs of the micromanipulators? Micromanipulators are driven by a microactuation mechanism capable of operating in a conductive solution. So that means microactuation mechanism. How this microactuation mechanism can be achieved? For them good candidates are magnetic pneumatic thermal and shape memory alloy. These are good candidates for microactuation in micromanipulator.

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MEMS Biomedical Microactuators


(Source: Judy et al, 1995)
Magnetic micro-actuator manipulating a single-cell protozoa in saline


(Source: Lee et al, 1995)
Surgical microgripper actuated by shape-memory-alloy forces – it is capable of grasping tissues during endoscopic surgical procedures

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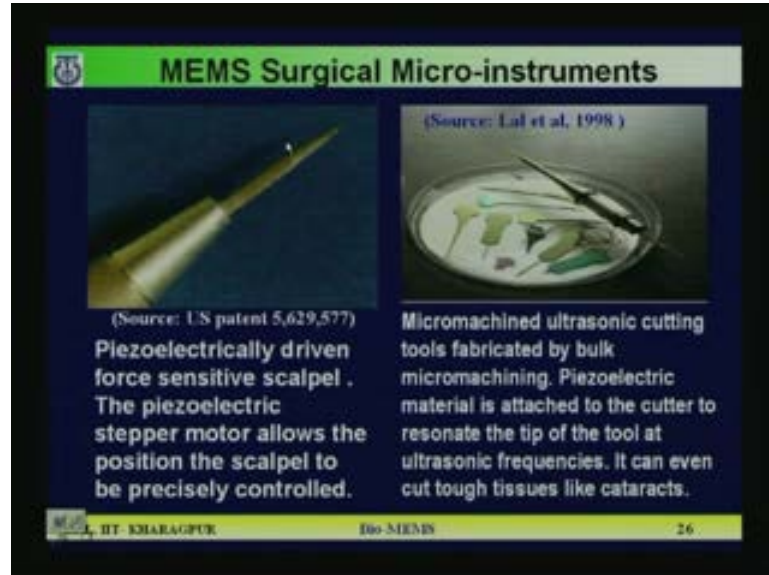
And now some pictures are shown in this viewgraph which are microactuators. First one is basically is a magnetic microactuator which is used for manipulating a single cell protozoa in saline water is a magnetic microactuator is again taken from Judy in 1995. He is from university of California and they are pioneering in this particular magnetic micro actuator research and other is microgripper which is used for surgical application. Microsurgery and any kind of surgical application grippers are important tools and they are used or they are made using shape memory alloy, shape memory forces. This particular micro-actuator is capable of grasping tissues during endoscopic surgical procedures. So endoscopic surgical operation, this kind of microactuator which is based on shape memory, alloy principle is nowadays used in operation theaters also.

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Some other surgical micro instruments are also discussed. The capability of most microactuators to surgically interact with biological tissues is hindered by their inability to withstand forces on the scale of 1 milli newton. Because those microactuators are manipulator, they are not capable of higher forces. If you have some gripper or some tweezer, so they should be there they should be capable of holding something grip, something with more force. But most of the cases at the beginning we found that the problem is the generation or withstanding more forces. That is not more than 1 milli newton. Recently high force small displacement stepper motors are used or resonant microactuators are used for microactuation in surgical devices. One is small size stepper motors or resonant microactuators. So there you can have larger force if you work in the resonant mode. That is one of the solution people are looking for. MEMS technology offers a variety of capabilities to surgical micro instruments. For example micro heaters, micro sensors, fluid delivery, fluid extraction, feedback and control system. In those cases basically the MEMS devices are coming into the picture in surgical environment.

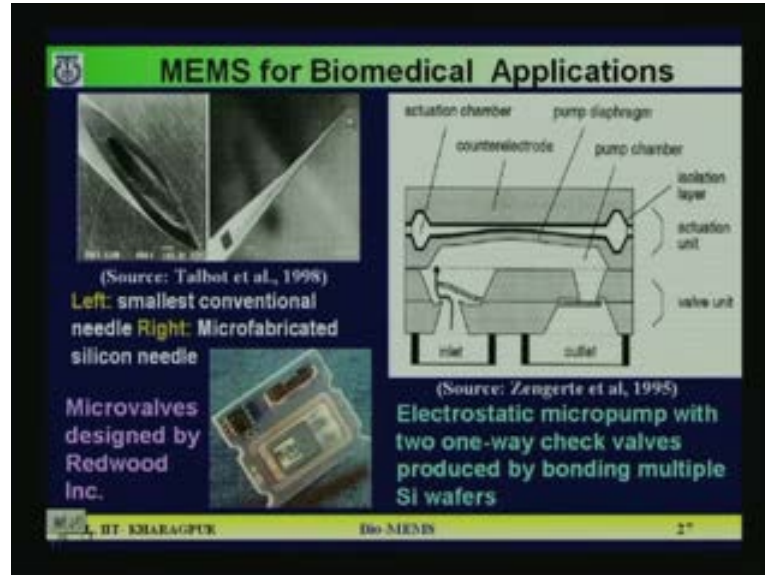
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Now here again some of the pictures which shows the some of the micro instruments, in the left side you can see one scalpel. That scalpel is basically driven with the piezoelectric forces and the piezoelectric stepper motor allows the position, the scalpel to precisely control. This is one of scalpel used in microsurgery and other picture shows some of the cutting tools which are used in microsurgery and those are based on ultrasonic vibration. The micromachined ultrasonic cutting tools they are fabricated from bulk micromachining. Piezoelectric material is attached to the cutter to resonate the tip of the tool. Because for resonance here you have to have some piezoelectric material which will be resonating by application with certain electric field.

So those piezoelectric materials are coated at the tip of this cutting tool and they are forced to vibrate in with the help of ultrasonic source or ultrasonic energy is given to those tools. So that it can vibrate with ultrasonic frequencies and nowadays the cutting tools are available using this technique, made using this technique. They can even cut tough tissues like cataract in the optical or in ophthalmology they can. They are highly used for removing any cataract. They are basically hard lens, they are lens. Basically this is made of hard tissues. Those tissues can be cut using those ultrasonic cutting tools. So these are some of the applications towards the surgical and micro actuators I just mentioned here.

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Others are again some kind of valves are shown here. Some kinds of needles are also shown here. You can see the diagram in the left side. These are the conventional needle which is nearly 30 gauge needle. You can see here in centre there is a hole and through that hole some fluid can come and this is the tip of the needle and in the right side itself the silicon needles are there. You can see the tip in silicon needle and if you compare this tip along with the conventional tip you can imagine how nice needles can be made using silicon micromachining. These are the micro needles. On the right side you can see the micropump. This is driven by electrostatic energy electrostatic micropump with 2 one-way check valves. This is inlet, this is outlet. What is the principle of operation here and that is electrically driven. That mean you have to have the 2 electrodes here and those electrodes either depending on the supply they can attract. This is basically a diaphragm.

By electrostatic energy this diaphragm middle diaphragm can be attracted towards the upper diaphragm. As a result of which this chamber, the pump chamber will be at the low pressure. So automatically due to the outside pressure the value will open and the fluid will flow into the chamber. Now if you release the diaphragm, by again the electrostatic actuation, by then this diaphragm will go down and it will put pressure on the fluid into the chamber. So as a result of which this valve will close and this valve will open. So if you pressure from inside this valve will open and the fluid can flow here. So that means in one valve you are sucking the fluid and other valve you are ejecting the fluid. So just by using some the electrostatic actuation, it is made using 3 pieces. Top piece, middle piece and bottom there are four pieces; one, two, three, four and they are combined together by the wafer bonding technology and this kind of the valve, micro valve or micropump is used for sucking fluids during the surgical operation and some other cases.

Here some of the micro valves are shown which is designed by Redwood incorporated. This is commercially available, some of the micro valves which is used in biological application, biomedical application. So here I can just conclude that the biomedical application is a really

fascinating in case of MEMS and microsystem. I have not covered here the DNA synthesis and gene sequencing that required a thorough knowledge of the microorganism as well as the molecular chemistry, biochemistry and without the adequate knowledge of the biochemistry or cell biology you cannot go for that. Anyway some of the idea I gave you in different areas where the biosensors are made using micromachining technology. It may be inertial sensor, it may be chemical sensor, it may be gas sensor, it may be some neuron sensor, for microprobes microneedles and also I mentioned some of the microactuators which are used in case of microsurgery. So with this let me stop today.