NANOPIPETTES

1. INTRODUCTION:-

Pipettes and capillaries are the most fundamental instruments used for material transport in laboratory. They work on the principle of pressure difference and surface tension and are widely used in titration, surface tension measurements and a host of other supplementary functions. These pipettes and capillaries that seem to be trivial at macroscopic levels become literally magic wands at micro and nano levels. Even at these levels it is only the pressure difference and the surface tension that is working but their application seems to have far reaching consequences. The most versatile and widely studied element that is capable of forming itself into such structures is Carbon.

Carbon is the most dynamic element in the periodic table. Apart from having a whole branch of Chemistry namely Organic Chemistry, to its credit, in its elemental form also, it manifests its beauty. Its multidimensional morphologies have been studied for a long time and the arrival of bucky ball has kick started a whole new area of research, namely nanotechnology. The work started with the synthesis of nanotubes and then went on to synthesis of helix-shaped nanotubes, nanocones, horns and trees. One such fall out of this research is "Nanopipette".

At first sight, it appears very similar to nanocones. This deception is common because its morphology does bear the appearance of a cone. But on closer observation, a thin hole running through the length of the structure and this made the structure interesting from an engineering point of view. Since these structures have a narrow top part and a broad bottom part, just like a macroscopic glass pipette, they came to be called as "nanopipette" and the nomenclature was only justified when they were actually put into practical use. (Fig 1. carbon nanopipettes[1])

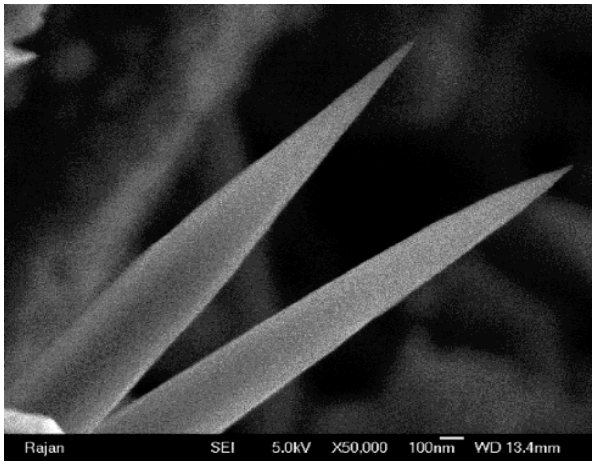


Fig 1. Carbon Nanopipettes

The most significant or remarkable aspect of this structure is that though the outer surface is found to be tapering from bottom to top, the core seems to be of constant width through the length of the structure. The base was found to have a diameter of about 6 μm while the tip had nano dimensions. The length on the other hand was substantially large with dimensions of a few tens of a micron. The most important part i.e. the core had a dimension of about 3-4 nm.

The structure was studied under a TEM in the dark field imaging mode with special focus on the tip. In dark field imaging, the aperture is shifted laterally to allow only diffracted beams to pass through and not the transmitted beam. Thus a dark spot on the image means a region that is transparent to electrons and a bright area meant an electron opaque area. In this case, the tip was of sufficient thickness to be subjected to TEM and the image obtained had a dark inner core of uniform width indicating a hole and a bright outer wall indicating presence of a definite structure. (See Image[1])

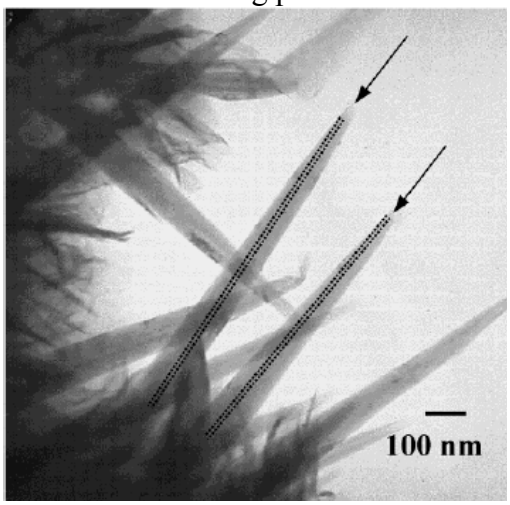


Fig. 2 Central Hole running through the structure

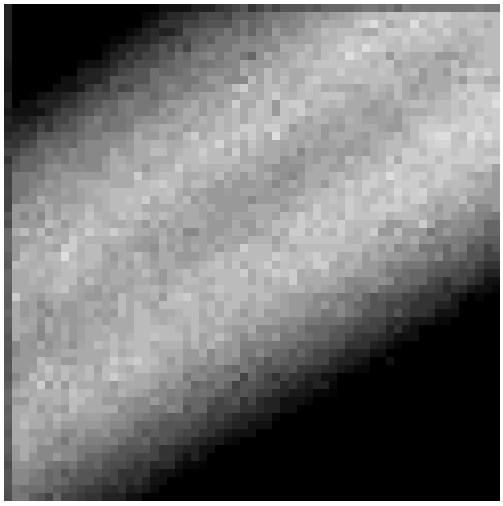


Fig. 3 TEM image.

The diffraction pattern confirmed that the wall was made of graphite although the exact way in which graphite has formed leading to the formation of such a unique structure could not be ascertained unless the area in the vicinity of the base was studied. When this was done, graphite was found to have wound itself in a helical fashion. Also another observation was that each individual structure had its own pitch angle thereby giving rise to a complex overall morphology. The pipettes thus owes its shape to this coiling of overlapping graphite planes so as to leave a constant diameter hole in the middle.(See image for individual pitch angle[1].)

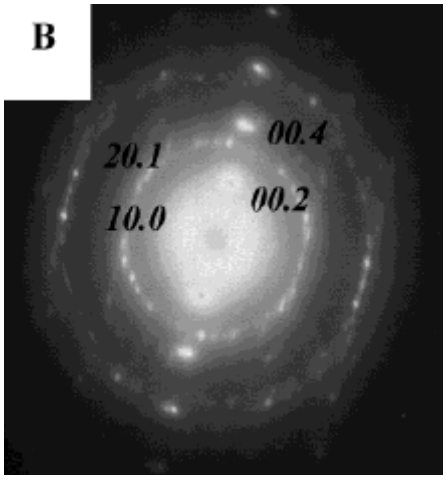


Fig. 4 Diffraction Pattern

2. SYNTHESIS OF CARBON NANOPIPETTES:

The circumstances were propitious for the formation of nanopipettes when Platinum and Molybdenum substrates were in the form of wires or sheets. Apart from these, microcrystalline diamond coated substrates of above elements were also found to be appropriate.

The substrates were immersed in Microwave plasma that had 1-2 % CH_4/H_2 maintained at a pressure of .066 atm. And a power of 1100W. These conditions are the same ones that favour the growth of nanotubes. After the deposition was complete, some regions were found to be coated with a diamond film and apart from these films several whiskers were also found. Solid Boron was used to ensure that the diamond film mentioned above was conducting.

The type of substrate largely determines the deposition time. Plain Platinum and Molybdenum substrates had a growth time of 24 hrs. while those substrates which had diamond films took 1-2 hrs. The temperature at the centre of plasma was found to be around 2000°C. The vertical orientation of the platinum wire resulted in plasma discharge at the melting point of Platinum[2].

The experiment can also be done with slightly modified substrate. Platinum wires that were already coated with microcrystalline diamond films were taken and electrodeposited with Platinum so as to attain a thin film of about 50 nm. The growth was allowed to continue for about 1 hr. The modified substrate served as a method to study the exact growth mechanism.

3. OBSERVATION AND RESULTS:-

Carbon nanotubes weren't first examples of conical structures. Graphite also showed this formation and to explain this a model was devised. It proposed that the graphite sheet overlaps itself and instead of joining the ends, wound itself around the whisker thereby resulting in thickening along the length and not concentric tubes[3]. These helical structures were also observed while heating Silicon Carbides though the reason given for this phenomenon was due to nucleation along a screw dislocation that is perpendicular to the surface and that the time dependent adsorption of impurity prevented the graphite prevented it from spreading and forming a surface[4].

However in this case, the formation mechanism was slightly different. Plain Platinum substrates that were subjected to long term experiments had a dense deposit of Carbon at the tip and regions away from the tip had diamond crystals and whisker like structures while the same experiment on Molybdenum resulted in dense deposits over a

large area, diamond micro crystals in some regions and nanopipettes observed all over the dense deposit. (1.Pt-plated Mo 2.Diamond coated Mo) [2]

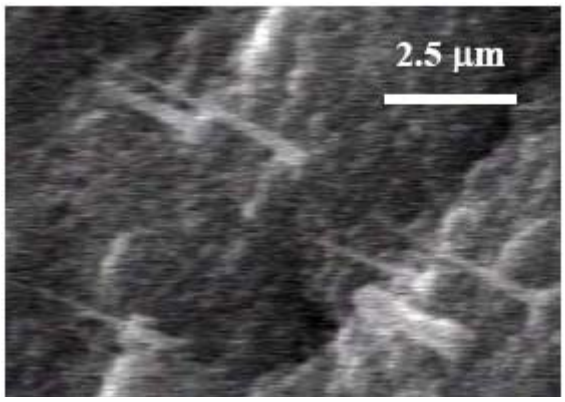


Fig. 5 Nanopipettes on plain Pt

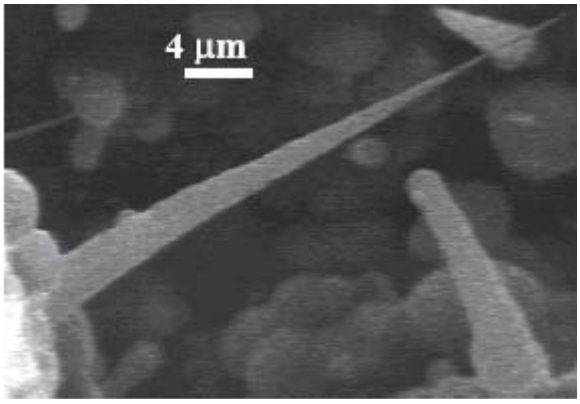


Fig. 6 Nanopipettes on Diamond coated Mo

The short term experiments had something else to show. The Molybdenum and diamond substrates though had resulted in nanopipettes; they were in arrays, unlike the previous case. Another striking aspect was the continuously changing aspect ratio (ratio of the width of the base to that of height) right from the tip to the end of the substrate. As mentioned earlier, the plasma has a temperature of about 2000°C and the discharge rises the temperature still further, sufficient enough to melt and even evaporate Platinum. These high temperatures and conical shape gives us sufficient ground and evidence for assuming that its growth can be explained using "Evaporating catalyst" model[1]. According to this model, it is the Platinum catalyst particle that acts as an initiator for the growth of a tube, especially Multiwalled carbon nanotubes, in our case the tube being the pipette. The outer diameter seems to reduce as the catalyst evaporates as was observed during a sequential step experiment.

The "Evaporating catalyst" model met with a death blow when the modified substrate experiment was performed (electrodeposited Platinum film on Molybdenum substrate). The continuously changing morphology was what served the contradiction or anomaly. The tip of the wire had a cone shaped deposit whose core was made up of a carbon nanotube which in turn had a graphite periphery. The competitive process of etching and growth of crystalline Carbon was clearly seen at some distance from the conical structures. Though the nanotube continued to make up the cores, the peripheral graphite manifested a radical change by fast growth. The end result of all these changes being the increasing in aspect ratio. The pattern continued even at far away regions finally ending up in nanopipettes. (See figure for continuously changing morphology)[1]

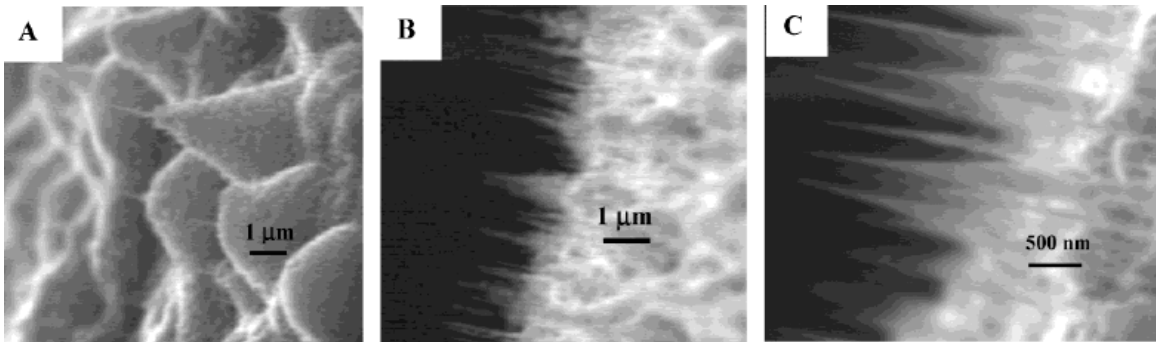


Fig.7 (A)Conical structures with central tube(B)Aspect ratio decreases, giving rise to(C) nanopipettes

When we try to explain the morphology formation with evaporating catalyst model, a paradoxical conclusion of abrupt evaporation rate changes arising along the length is arrived at, thereby making "Evaporating Catalyst" model inconsistent and making "Selective etching and growth mechanism" to be the sole reason for the formation of conical nanopipettes with varying aspect ratios. It is possible to vary the thickness of the peripheral graphite by adjusting the position of the substrate immersed in the plasma. The selective etching and growth mechanism mentioned, is highly dependent on the temperature, radical and ion density variation within the plasma. For example, the tip of the substrate experiences very high temperature and has a high tendency to favour the growth of graphite, a competing phase. Another important factor that governs the growth process is the substrate and its coating[2].

Coated or uncoated Molybdenum sheet substrates which promote carbon phase deposition when subjected to a deposition time of 4 or more hours gave both graphite and carbon nanopipettes. While short term experiments on same Molybdenum substrate gave multi walled carbon nanotubes, Platinum coating favoured the growth of nanopipettes. However this again was accompanied by graphite deposition. The only substrate that gave a uniform array of carbon nanopipettes was that of diamond as its stability prevented any sort of etching action in the plasma. This uniformity of structure with enhanced length of the pipettes is indispensable for engineering and medical applications.

Thus to sum it up, we start with a nanotube that gets coiled around in a helical fashion by graphite to which the conical shape is attributed to. This coiling keeps the primary tube intact. The dominance of etching mechanism at the tip of the substrate gives rise to low aspect ratio whiskers while the dominance of growth mechanism gave rise to high aspect ratio whiskers in regions away from the tip. (See figure for tip region and far region topography. Note the distinct change in aspect ratios)[2]

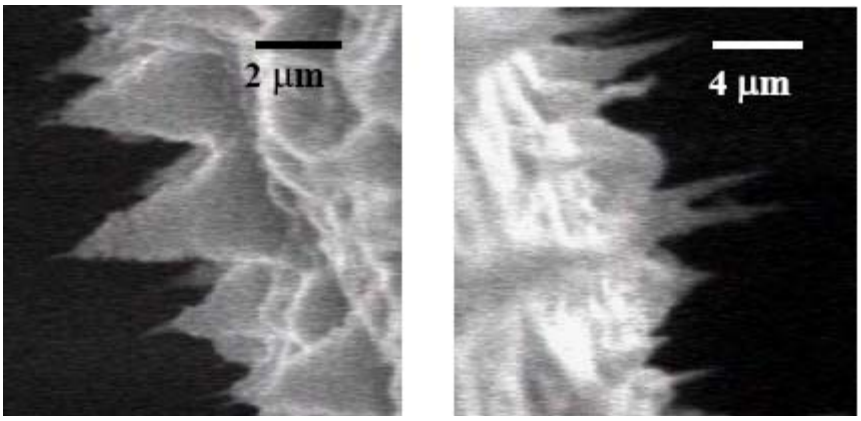


Fig.8 Tip of the Pt substrate, has cones while the far away region has nanopipettes

4. ELECTROCHEMICAL STUDIES ON NANOPIPETTES:-

The necessity of studying electrochemical properties arises due to the fact that material transfer in medical applications is carried out through chemisorption of electrons[5].

4.1. ELECTROCHEMICAL SET UP:-

The electrolytic bath had only one compartment with Ag/AgCl(3 M NaCl) as reference electrode. Samples were taken and those regions which do not contain an array of nanopipettes were coated with an insulating and inert epoxy to avoid substrate interference. To study the morphological impact on properties, one sample with haphazard arrangement of nanopipettes and another with regular arrangement of nanopipettes with 2 μm inter-pipette distance were taken. The platinum wire served as an electrical contact.

The solution used for studying their response was 1 mM Potassium Ferricyanide with .1 M KCl and 1 mM Dopamine (3-hydroxy tyramine hydrochloride) with .1 M KCl. Potassium Ferricyanide serves as a calibration analyte while dopamine is important from the electrochemical detection point of view[7]. The first substrate, namely the one with haphazardly grown nanopipettes had only limited area exposed to the electrolyte and a major part of it covered by epoxy coating. Due to this dopamine response was governed by diffusion and though peaks were observed in limiting current vs. scan rate graphs, they were drowned in the background current. The electrochemical area, as calculated by Randles-Selvick equation was in close agreement with the actual exposed area. (See figure for nanopipettes on electrode.)

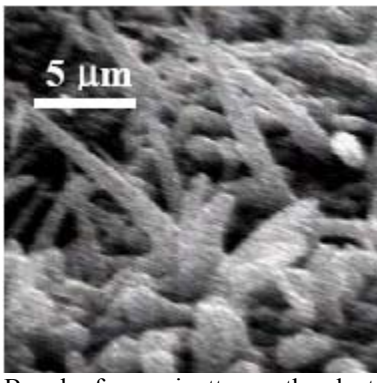
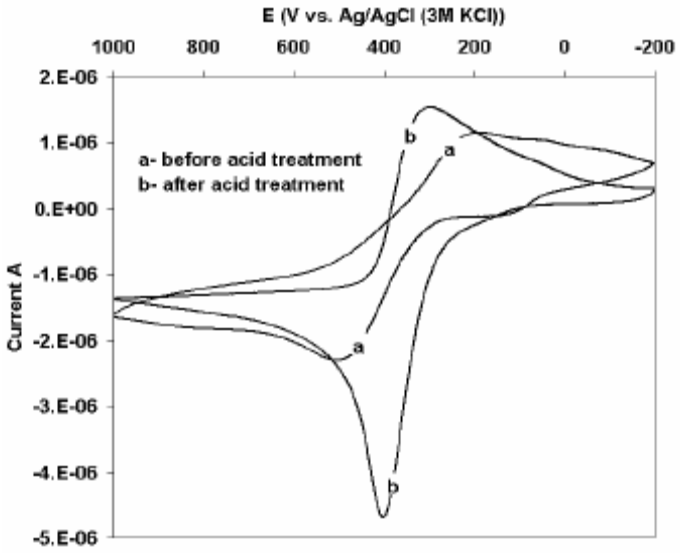


Fig. 9 Bunch of nanopipettes on the electrode

Though single walled nanotubes exhibited similar results, smaller dimensions and faster kinetics of nanopipettes greatly decreased the time required for such studies. This also helps in studying unstable intermediate analysis of complex reactions which otherwise may go unnoticed. The second substrate i.e. the one with array of nanopipettes was more suited for the above mentioned application. The inter-pipette distance was greater than two overlapping diffusion boundary layer. It was also found that the pipettes were highly stable and treatment with acid made many reactions reversible.

For substrates with a regular array of pipettes, the currents observed were higher due to greater amount of exposed area. The area calculated from Randles-Selvick equation tallied with the actual geometric area here also. The major advantage of carbon nanopipettes over carbon nanotubes is that nanotubes require surface preparation before they can be used as electrodes and during this treatment, only basal graphite planes are exposed which causes slowness in electron transfer kinetics. Nanopipettes don't need any sort of preparation; a single electrochemical acid-treatment would suffice. Peak responses to electrochemical tests provide for easy detection. (See figure for peaks observed in electrochemical studies.)



5. APPLICATION OF NANOPIPETTES:

5.1. AS A SENSOR FOR THE RAPID DETECTION OF NEUROLOGICAL SOLUTES:

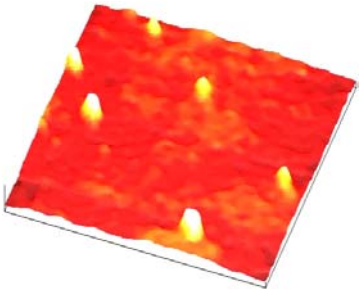
They are the most simplistic and cheapest nanoarray electrochemical sensor that has an additional advantage of behaving like single nanoelectrode. The conical shape of nanopipette is fully exploited for its dimensions are just sufficient to serve as nanoelectrode and since their fabrication involves chemical vapour deposition on platinum substrate, the substrate itself serves as electrical contacts.

The most important aspect to be kept in mind while using a nanopipette array is that the spatial distribution of tips should be atleast 2 μm. This necessity arises form the fact that too dense distribution results in overlapping of diffusion boundary layers which can slow down the diffusion rate and restrict it to only to one dimension. Highly efficient nanoelectrode behaviour can be obtained only when the individual pipettes are sufficiently separated. At the bases, these pipettes are very close and this may cause some problems. To avoid this, a simplistic approach is that of applying an insulating film by dip-coat method followed by UV curing. When this is done, the base area is completely covered with polymer leaving only the top most tips exposed. The polymer coating serves another purpose of reducing background current that are normally encountered during electrochemical studies.

The strenuous methods of micro fabrication are easily overcome by this technique. These pipette arrays are now being used for spontaneous detection of multiple compounds, determination of fouling resistances and in detection of neuro transmitters.

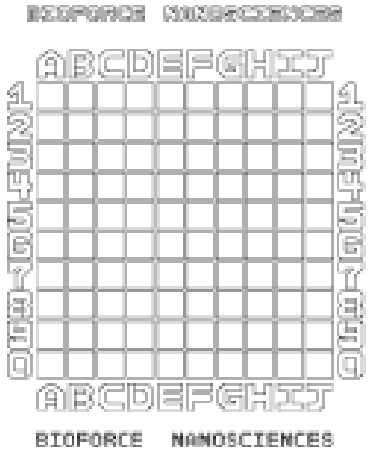
5.2. PROTEIN PRINTING WITH AN ATOMIC FORCE SENSING NANO PIPETTE / NANO FOUNTAIN PEN

One of the most recent developments is the direct printing of proteins on a surface using a cantilevered nano pipette as the probe of a scanned probe microscope. Protein features as small as 200 nm were directly delivered through the 100nm aperture of the nano pipette by simply contacting the probe with any surface. This actually would allow for direct connection of the methodology to standard separation technique so that multiple proteins can be printed through one pipette at different locations under ambient conditions. The figure shows the protein molecules that are arranged over a biochip. The deposition and confinement of molecules in nano metric domains is a problem of considerable current interest. It is of particular importance when molecules are of a biological nature such as deoxyribonucleic acid (DNA) or proteins. The age of genomics and proteomics has triggered the development of the next generation chip or the so called “biochip”.



The biochip consists of an array of dots each consisting of a small volume of molecules or dots consisting of fragments of deoxyribonucleic acid (DNA) in a protein chips, the spot consists of various proteins[7]. The biochip would allow the researchers to study interactions of very large number of molecules at once on a single platform. This is a very vital requirement for processing vast amount of information involved with the field of genomics and proteomics.

The size of the biochip is about 150-200μm. For the deposition of protein molecules we should use the "fountain pen chemistry" based on the development of cantilevered nanopipettes as AFM sensors and use of flow molecules to the substrate. This technique can e readily connected to standard separation methods like high performance liquid chromatography (HPLC) and can be used in ambient conditions. The connection of nanopipettes to the high performance liquid chromatographer would allow the writing of dots of many different proteins with one cantilevered nanopipettes connected to HPLC or in an air environment on standard substrates that are used for protein printing.

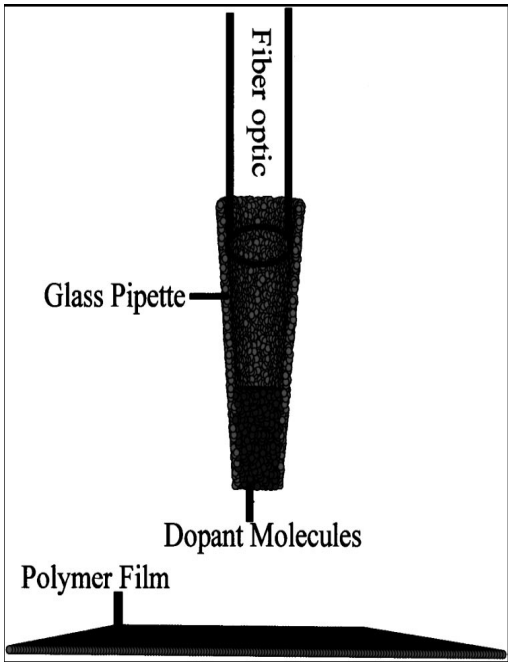


The figure shows a biochip array where different protein molecules can be stored inside each of the individual squares. The solutions of both the proteins used to print in biochip are loaded in the large end of the pipette. The loading of the solution is carried out with the help of a vacuum inserter and due to the capillary action the solution containing the required proteins would be sucked to the pipette tip. The flow of different proteins inside the nanopipette would depend upon the densities of the individual protein molecules. The protein pattern formed on the surfaces was strongly bonded. The main bonding force that binds the protein to the substrate is the van der walls force of attraction coming into play due to the presence of covalent bonds in the protein molecule. These patterns are not removed upon washing them with acetone and the imaging of the dots can be done with the help of tapping mode in atomic force microscopy. In the tapping mode of motion of the cantilever with oscillate the stylus to high frequency which would provide fine imaging of the surface. The protein printing is to be performed at RT though under special techniques the writing can be performed under high temperature suing laser implantation. The scan rate of the pipette was performed at a frequency at 2Hz[7]. However humidity tends to affect the protein on to the surface. This because water or moisture would tend to increase the cohesive force as compared to the adhesive force due to which the force of binding or protein molecule on to the substrate material would tend to decrease. So the humidity level should be made minimum. The best protein printing can however be obtained only under vacuum conditions.

5.3. LASER EXPULSION OF AN ORGANIC MOLECULAR NANOJET FROM A SPATIALLY CONFINED DOMAIN:-

Functional organic molecule can be manipulated into a fluorescent features as small as 450 nm on a polymer substrate or film using a method derived from laser ablation and laser implantation. This technique utilizes a piezo electric driver to position a pipette having an aperture and doped at the tip with organic molecules. The pipette would be held at a height of a few tens of nanometres above a polymeric film. The pipette is subsequently irradiated using 3ns (full width at half maximum) laser pulses are guided down to the tip by a fiber optic. This method of ablation confinement gives fine spatial control for placing the organic molecules in a designated regions and it has a very great application in the field of opto-electronics.

Laser ablation has proven to be a key player in many fields of engineering. Laser ablation and implantation have been used to produce features in polymer films and surface limits by wavelength. This involves mechanical confinement of the ablation process using glass nanopipette and having a fine tapered aperture of 100nm. The laser ablation and implantation have advantage and a method developed to create implanted features on the surface of the substrate and formation of clusters of nanoparticles.

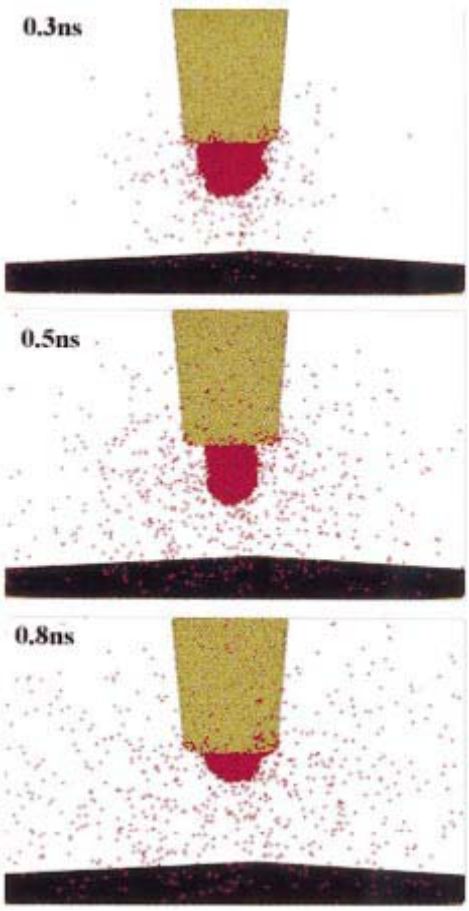


The laser ablation method of experimentation is as shown in the figure. The nanopipette consists of 100nm opening and it is positioned at 30nm-50nm above a polymer film using a shear force feed back controlled piezo- driver. A fiber optic tube guides laser light of suitable wavelength selected by an optical parametric oscillator into the pipette to irradiate the molecules inside the pipette. The irradiated molecules are then photo-thermally expelled from the nanopipette tip as a jet of gaseous and molten material that are then quenched on the surface of a polymer film where they form aggregate in the form of nano-clusters. However one of the main disadvantages of this method is that we cannot know the state or condition of polymer initially as they are inside the pipette[8].

To study the manner in which laser light propagates in doped and undoped nanopipette having a tip dimension of 100nm, the photograph shows the interference pattern formed by the 488nm light from an Ar^+ laser that had travelled inside the pipette and excited the pipette forming an image on the transparent plate. The undoped pipettes give a coaxial series of interference fringes starting from the very end region of the nanopipette tip. This would mean that light propagates to the end of the tip via partial internal reflections in the walls of pipette with leaked light from the interference fringes. For the doped pipette tips the interference fringes stop short of the end of the tip. This would mean that light has been absorbed by

the dopant molecules. The dopant molecules would be having a higher refractive index than the glass material of the nanopipette. The most common dopant material that have been used for this purpose are C545 (coumarin) and DCNA (Di-cyano anthracene) [8]

In order to gain qualitative understanding of the processes leading to the nanojet formation, implantation, and cluster deposition and to explain the strong flow dependence and thresholds of transfer process a series of simulations of molecular ejection from a doped nanopipette was performed. (Here we do not use undoped pipette because then there is a possibility that the laser from the optical parametric oscillator may damage the substrate.)



There are actually 3 distinct regimes of laser flow that is present.

Sub-ejection threshold where the laser flow was insufficient for molecular transfer to the polymer target surface. This mainly due to the surface tension forces would tend to dominate more.

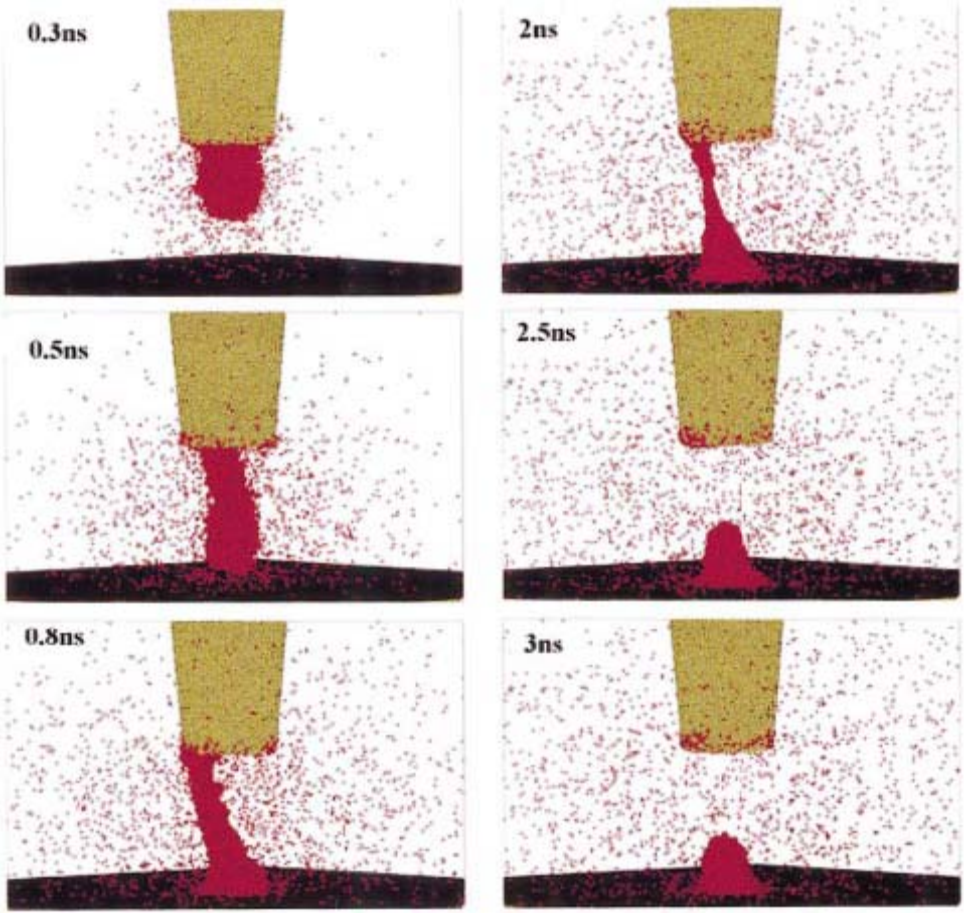
The figure of simulation under the time of a time sequence less than 1 nano-second. The expulsion force which is provided by the gas phase is not sufficient for the ejection of liquid droplet. The liquid droplet formation primarily occurs at time between 03ns to 0.5 ns.

This liquid drop formation is followed up by the retraction of the liquid drop back into the tip of the nanopipette. This is because the surface tension forces would tend to overcome the gravity forces of the liquid droplet. This is followed up by retraction of the droplet back to the nanopipette.

After the sub ejection threshold regime of laser flow we have the cluster formation and the implantation regime. In the cluster formation regime the laser flow was sufficient to eject the material. But the materials are not sufficiently hot to become thermally dispersed. They would tend to get adhered to the polymer substrate. There is a tendency of the material to get mixed up with the polymer substrate.

The third regime is known as implantation regime. Here the laser flow is sufficiently high enough to be in a thermally activated state. The material inside the pipette would be ejected with very high velocity. This is because the laser heating would tend to induce

tremendous amounts of thermo elastic stress into the material which would tend to get relieved by expansion force. This force would be sufficient to overcome the surface tension very easily. Since the velocity of the ejected materials is very high it would get implanted into the surface region.



At higher flow rates the laser induced heating is stronger and the resulting number of gas phase molecules becomes larger. As a result a nanojet of molecular liquid and gas are ejected from the tip from the tip. This would result in the formation of nano clusters on the surface of the substrate. In the above figure we see that the bulk part of the ejected material forms a compact liquid bridge all the way from the tip of the pipette to the substrate. The bridge would break after 2ns forming a drop to the surface. Fast cooling of the droplet due to evaporation and heat conduction to the surface would lead to the formation of compact non dispersed nano cluster[8].

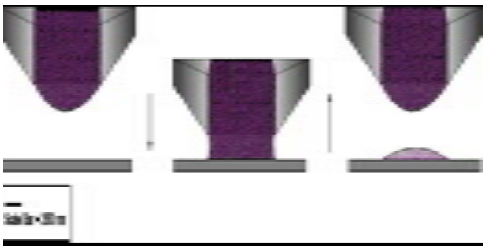
A further increase of laser flow leads to stronger heating and explosive boiling of the molecular material in the pipette tip. A hot mixture of gas phase molecules and small cluster is ejected from tip at higher flow rates. The substrate is represented by a rigid monolayer. The temperature that would be obtained using this process would be about 1500k and the ejection velocity would be of the order of 1000m/s. This would result in fast transient melting of the exposed polymer surface region and would result in the formation of an efficient implantation of the molecule.

In the above cases that are mentioned here are in non-biological systems where the material is transferred through an air or purge gas system environment to the target surface. But in case of a biological sample and a biocompatible polymer surface the region in between would have to be covered with an aqueous solution. This medium would act as a quenching medium and would help in reducing the thermal damage to the substrate.

5.4. FEMTO (FLUID ENHANCED MOLECULAR TRANSFER OPERATION) PROCESS: -

The FEMTO process enables the direct deposition of any molecules on virtually any surface. Small molecules, bio molecules, reactive solutions and even nano particles in the form of clusters or particles can be deposited on the surface. In fact because there is a fluid transfer the size or molecular weight of the material has no effect on the process.

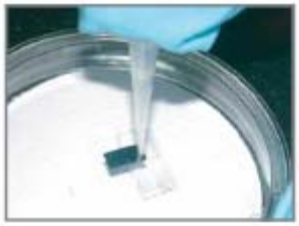
The femto continuous fluid flow can be used to rapidly print thousands of spots with atto-liters to femto litre volumes and in the entire diameters ranging from 1 to 20μm. The key to femto process is the surface patterning tool with its micro fluidic channels constantly delivers a fresh supply of liquid to be transferred on to the surface. Multiple surface patterning tool can be loaded to allow printing of a single compound or multiplexed printing of several different molecules[9].



As shown in the figure the fluid flow from the reservoir down the channel to the end of a cantilever where a narrow tiny gap is present. Upon contact with the surface a small volume of liquid held in the gap by surface tension is directly transferred to the surface in an event typically requiring less than 10 m sec. The liquid inside the pipette is immediately replenished. The nano pipette would be very difficult to load them with liquid solution and their closed design makes them prone to blockage. The femto process of open channels ensures that the liquid would always have a path to the surface for maximum reliability. The surface patterning tool or the nano pipette can be used for creating an array of molecules on to the surface.

The loading of liquid into the pipette can be either done by back loading or front loading.

5.4.1. BACK LOADING PROCESS:-



Back loading involves pipetting small volumes of the liquid sample about 0.1μL into one of the etched wells of the section. The sample would fill the well and flood the channel that runs down the length of the cantilever. The

back loading method is generally favourable when there are large numbers of substrate molecules present[9].

FRONT LOADING PROCESS: - front loading of the surface patterning treatment is often convenient for arraying compounds in a relatively small number of domains. A small vacuum would be created through which the liquid would be sucked in.

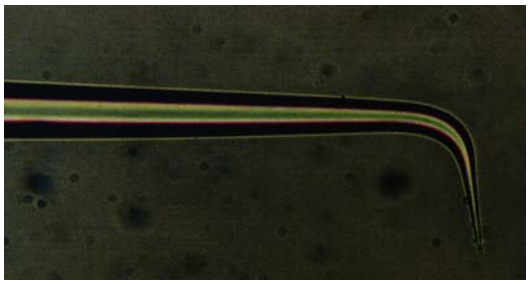
5.5. SINGLE MOLECULE NUCLEIC ACID DETECTION WITH NANO PIPETTES

The main idea is to develop a new method or technology that will enable the single molecule detection and identification of DNA sequences present in the biological sample. The main idea would be to focus on detecting nucleic acid labelled with varying size of nano particles by recording the changes in the ionic currents through a small nano meter scale channel inside the nanopipette.

By this we can have the labelled oligo nucleotides to be hybridized to test samples and the un-hybridized labelled molecules removed by additional nanopipette. The remaining labelled DNA molecules can be rapidly detected on a single molecule basis through the nanopipette[10]. This will result in an ultra sensitive rapid gene-typing technology that can be used for diagnostic studies. The diagnostic part would include the detection of pathogens or determination of a human gene type in a clinical sample. This nanopipette DNA detection technology would also pave way fro second generation devices which allow higher resolution detection and would be used for rapid single molecule DNA sequencing and the entire DNA code can be obtained in a few micro seconds.

5.6. MODIFICATION OF NANOPIPETTE AS PROBES:-

5.6.1. CANTILEVERED NANOPIPETTES:-

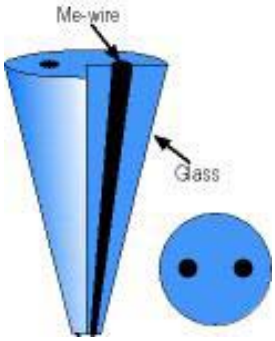


The cantilevered nanopipettes can be used as nano-pens for controlled delivery or removal of molecules from regions as small as 100nm. They can also be used as a vessel for containing molecules whose optical properties changes in response to their chemical environment. By exciting these molecules with external illumination one can overcome many

of the limitations of propagating light through near field apertures. Nanopipettes extend their domains into transmission of high powered light pulses for the use in micro and nano-lithography and optical photo mask repairs. With the help of cantilevered nanopipettes we can obtain controlled chemical etching of atomic force microscopy. These AFM nanopipettes can be used for chemical imaging of the surface of the materials by a suitable mode of vibration. By the use of these pipettes we can also perform embedding chemical sensitive dyes into the polymer matrix. The fig shows a typical nanopipette by which the delivery of chemicals can be performed at right angles. They can also be made to act as a minute selector of different ions like H , Na , Cl.

5.6.2. DOUBLE WIRED PROBE:-

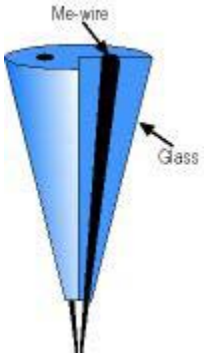
In the Double-Wire Electrode probe, two platinum wires are tapered inside a dual-channel nanopipette and kept electrically uncoupled. They can be used to perform electrical measurements, such as resistance and capacitance measurements, on Submicron-scale devices. Because the probes use normal-force feedback to stay in contact with the surface, these electrical measurements can be correlated with the surface topography obtained through the simultaneously obtained AFM image. In addition, inducing a voltage between the wires heats the liquid medium, creating micro-bubbles which can make fine incisions in tissues as they break apart. The major applications are to perform electrical measurements such as resistive and capacitive measurements on sub micro level scales.



5.6.3. HOLLOW NANO AFM PROBE:-

These probes are useful for high peak power laser pulses and can be used in IR and very deep UV regions where regular optical fibers do not transmit (For example 10μm IR wavelengths). These probes have a high threshold for damage making them especially useful for nano-lithography and for highly localized metal removal using femto second laser pulses. The femto second laser pulses are generated through Fourier transformation technique instruments. These probes are generally immobile in nature. So these probes are not recommended for general transverse imaging in AFM. These probes use normal force feed back to stay in contact with the surface. The electrical measurements can be correlated to the surface topography.

5.6.4. NANO TWEEZERS:-Another modification of the nanopipette double probe is use of nano tweezer. The nano tweezer probe consists of two platinum wires tapered inside a nano pipette. They are kept electrically uncoupled i.e. there is no connection or internal circuit existing between the two Pt wires. By the application of potential the two wires are made to flex. So in the application the probe can be made to get over on top of a



molecule and then by the application of potential they would be made to close around the molecule. This molecule can now be easily displaced.

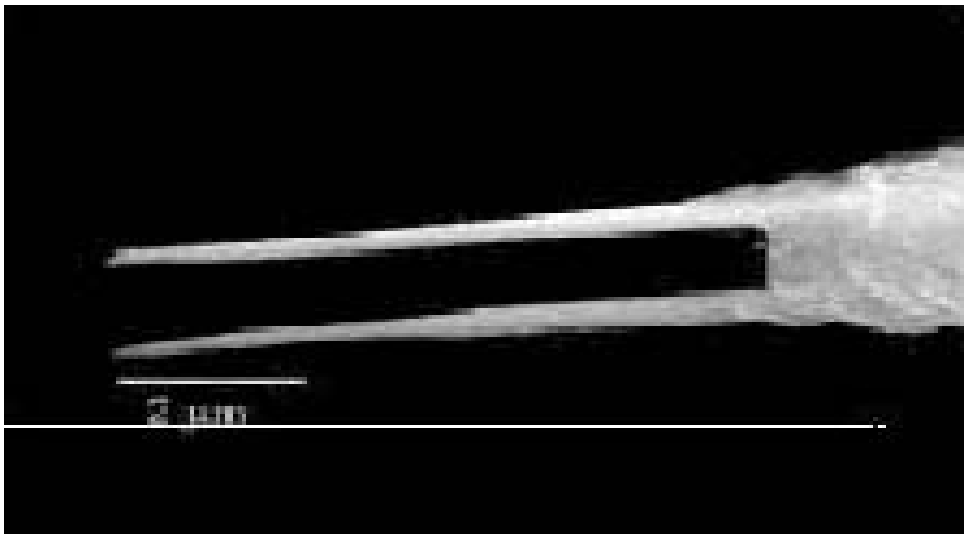


Fig.10 The figure shows a typical nano tweezer with Pt wires.

5.6.5. NANO IR SOURCE:-

In this probe the two uncoupled metal wires that run separately through the carbon or glass nanopipette are fused together at their tip. Running a current through them would tend to heat then at the fused junction. This heating up of the fused junction would act as a source for infrared radiation to heat a small region of the surface. In case of biological samples this would result in the formation of micro bubbles that make fine incisions on the biological tissue. The typical wire is about 25 or 50 nm and the sensing region is about 100nm.

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