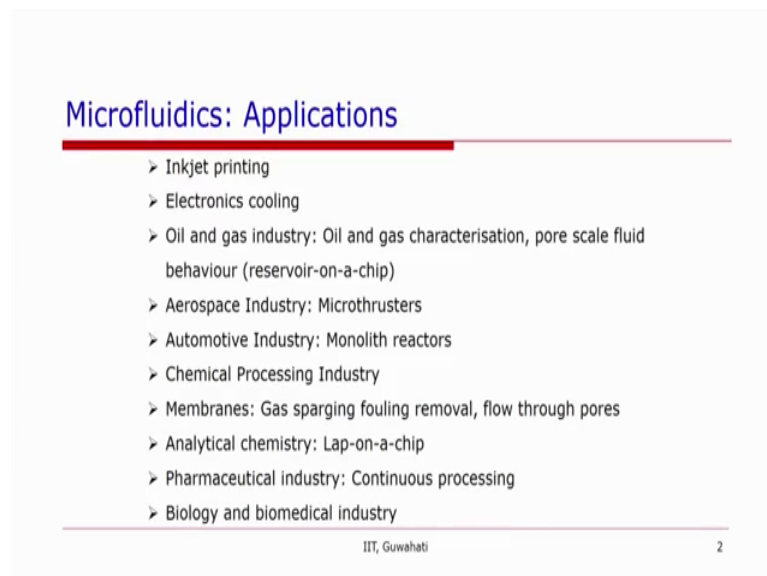


Multiphase Microfluidics
Dr. Raghvendra Gupta
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Lecture – 23
Microfluidics: Applications

So in this lecture, we will continue the discussion of different Applications of Microfluidic technology and in different areas. So, here is the list that we have seen or some of the applications that we have listed of Microfluidics.

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Microfluidics: Applications

- Inkjet printing
- Electronics cooling
- Oil and gas industry: Oil and gas characterisation, pore scale fluid behaviour (reservoir-on-a-chip)
- Aerospace Industry: Microthrusters
- Automotive Industry: Monolith reactors
- Chemical Processing Industry
- Membranes: Gas sparging fouling removal, flow through pores
- Analytical chemistry: Lap-on-a-chip
- Pharmaceutical industry: Continuous processing
- Biology and biomedical industry

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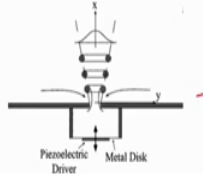
By no means this list is exhaustive actually while preparing for this lecture as I look upon the applications of micro fluidics, I get to see more and more applications.

And then, I realized that if I would like to give a comprehensive overview of the fields that Microfluidics can have an impact upon probably I would need a another course to discuss the application, all the applications of micro fluidics. If I will be able to compile all the applications in one lecture that will be humongous tasks in itself ok.

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Aerospace Industry

- Aerodynamic flow control of aerospace vehicles
 - MEMS based flow control systems
 - Synthetic jets for thrust vectoring
 - Supersonic microjets
 - Fluidic Oscillators
 - Turbulent boundary layer control



Synthetic jet: Image from Smith and Glezer et al., Pof, 1998

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So, let us look at some more applications and in this, we will look at the some applications in Aerospace Industry. So, in the Aerospace Industry, there can be different applications of micro fluidics. One of them is in flow control of Aerodynamic flow control of the aerospace vehicles.

These aerospace vehicles can be Aeronautical applications. For example, aeroplanes etcetera or it can be for space applications for rockets. So, these involve sensors actuators or thrusting devices. And these applications are generally based on MEMS. MEMS as you would know that Micro Electro Mechanical Systems. So, the Mechanical electrical Mechanical and electronic systems which are working at the micron size, they are called MEMS and. So, some of those devices are say Synthetic jet for thrust vectoring.

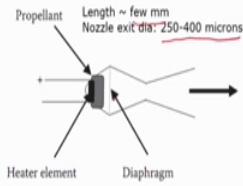
So, here is a image of a Synthetic jet or it can be Supersonic micro jets, Oscillator, Fluidic Oscillators or Turbulent boundary layer control. So, where these different jets or oscillators, they can affect the overall flow and change the thrust vectoring for a over the aerofoils etcetera.

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Aerospace Industry

Micropropulsion devices:

- Microsatellite (100 kg), nano (10 kg), pico (1kg), femto (<100 gm)
- MEMS-based cold gas, plasma and combustion based thrusters being developed
- Criteria of impulse bit size: smallest impulse that can be given
- 10^{-4} - 10^{-6} N.s for 1 kg mass



Schematic of a microthruster
Image from Microfluidics and Nanofluidics
Handbook, Mitra et al., 2011

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Another application is in Micropropulsion devices. So, with the application of satellite in a number of areas, there have been a thrust towards developing smaller and smaller satellites; so based on that the different names for satellites have also been standardized.

So, a satellite which raise about 100 kg is named as Micro satellite. A satellite which is about 10 kg is a nano satellite. Pico satellite is 1 kg and femto satellite is less than 100 grams.

These this classification I have taken from the micro fluidics and nanofludics handbook and each satellites they will have the names based thrusters and these thrusters based on maybe cold gas thruster or plasma thruster or combustion based thrusters.

Now, one of the challenges in this is that the impulse bit sizes or the small amount of impulse that is required to control these small satellites a. So, it is very important to have that one can or one should be able to produce the amount of impulse accurately so that the accurate or the desired control direction can be given to the satellite.

And so, the kind of impulse the kind of numbers that are required you can see from here that for 1 kg mass the impulse required is about 10^{-4} to 10^{-6} Newton's second. So, this requires.

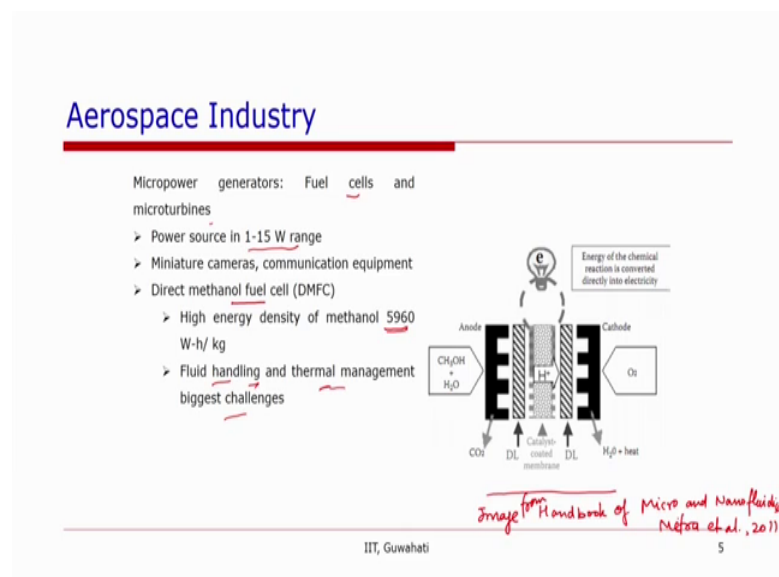
That one should be able to have the smallest bit of impulse. So, that one can have increments over it, but if the minimum amount of impulse is required that can be given

that is the impulse bit size discussed here. So, that is a typical micro thrusters or a schematic of a micro thrusters where there is a propellant and the heater element attached to it.

This micro thrusters is only few mm in diameter and the exit diameter of the nozzle which can be supersonic nozzle or subsonic nozzle. It is about 250 to 400 microns and as the when this thruster is to be used and the element is heated.

And the propellant converts into gas, the pressure builds up and this diaphragm and the gases come out and the desired thrust stage giving.

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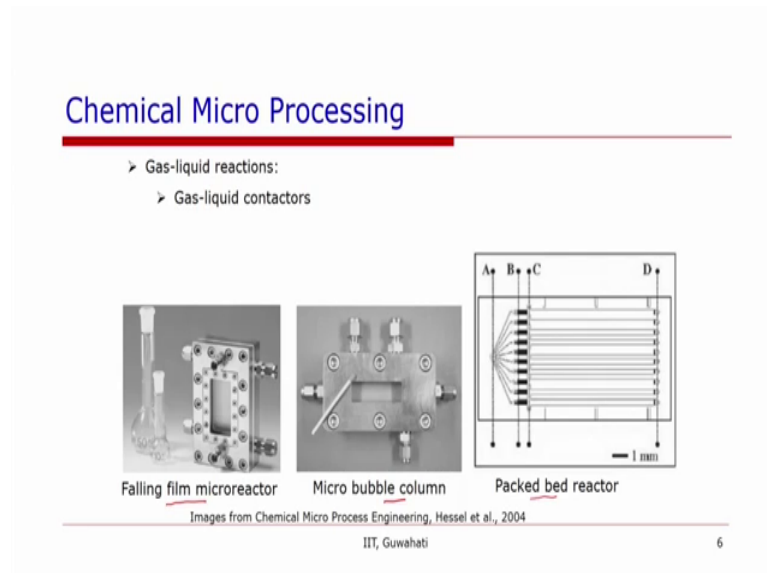
Another application in aerospace industry is in Micro power generators, in the in terms of for example, fuel cells and micro turbines. So, these generators are expected to provide power in the range of 1 to 15 Watt and this power might be required for miniature cameras or mobile applications and other applications where power is required.

So, among the different fuel cells Direct methanol fuel cell is the preferred method. Here is a schematic of the Direct methanol fuel cell and this Image is again taken from Handbook of Micro and Nanofluidics ok. So, these direct methanol fuel cells, they have very high energy density of about 5960 Watt hour per kg.

In these, whatever we have learnt in this course, the gas liquid flow in micro channels. So, some of these works in micro channels have been motivated by the fluid handling and thermal management challenges in PMF fuel cell or direct methanol fuel cell. So, these are the 2 biggest challenges in the in these fuel cells. So, in the aerospace industry we will looked at 3 applications here.

The Aerodynamic flow control of aerospace devices so as to control the lift and drag on the vehicles and then, micro thrusters for micro propulsion devices or for micro satellites; then, micro power generators; for example, fuel cells and micro turbines ok.

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Now coming to Chemical process industries which is the main area of this course because this course has been offered under the Chemical Engineering discipline, so because this is a multi phase flow course. So, what I have listed here is some of the Gas-liquid reactions and in this image what you see is some of the micro reactors for Gas-liquid applications.

The first one is Falling film micro reactor, where the liquid film falls on the wall of the channel and the gas comes between the 2 plates and the interface between the 2 gas and liquid provide the contact area for the mass transfer between the gas and liquid phase.

Another application is Micro bubble column; you can guess or estimate the size of the channel by looking at the majestic. So, the size of the channel window and we see here is less than is smaller than a majestic.

Another one is a Packed bed reactor. So, where there are different channels and in which it has been packed. So, these are different type of contactors and we have just I have just listed or shown three contractors here.

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Chemical Micro Processing

Gas-liquid reactions:

- Direct halogenation: Fluorination
 - Wide applications as pharmaceuticals, dyes, liquid crystals and crop-protection agents: every third drug contains fluorine moiety
 - Complex synthesis routes: low selectivity and high waste generation
 - Direct route requires precise temperature control
 - Overheating causes radical formation
 - Extremely fast fluorination reaction, mass transfer limited
 - High interfacial area density
 - Precise residence time
 - Extremely fast reaction, too long exposure results in secondary reactions

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So, one of the most investigated reaction in micro channels has been Halogenations and in particular Fluorination. So, this is for example, Fluorination of toluene because this has wide applications in a number of industries, pharmaceuticals, dyes, liquid crystals crop protection agents.

Actually every third drug contains fluorine moiety. The general in general the synthesis route of these fluorine compounds are complex synthetic root there is no direct synthesis root and these results in the selectivity of these routes is low and the amount of material that is wasted is quite high.

So, the direct route it might be cheaper, but it requires precise temperature control because reactions are fast and exothermic and if the overheating or the hot spot formation happens, then, the undesired reaction may take place and one will again get poor selectivity, so as these fluorine as we know that is a very reactive compound. So,

the fluorination reactions are very fast and so, they are often limited by the mass transfer between the gas and liquid phases.

So, one will need high interfacial area density which is what we can easily get in micro channels. So, it becomes a good candidate to perform gas liquid reactions in micro channels. One also need because it is exothermic reaction. So, one need to have good heat transfer and try to maintain the isothermal conditions in the reactor which is very difficult in a large reactor. But it or a stirred tank reactor for example,

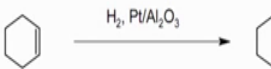
But it can be done in micro channels. One also need to have precise control over the things, precise control over the residence time, precise control over the pressure and temperature over which the reactor will be operating because the residence time need to be precise. Because if it is too long; then, secondary reaction may take place and the selectivity will again be poor.

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Chemical Micro Processing

Gas-liquid reactions:

- Addition to carbon-carbon multiple bonds e.g. cycloalkene hydrogenation



The diagram shows a chemical reaction where cyclohexene (a six-membered ring with one double bond) reacts with hydrogen gas (H₂) in the presence of a platinum/alumina (Pt/Al₂O₃) catalyst. The product is cyclohexane (a saturated six-membered ring).

- Performed in trickle bed reactors
- Fast process
- Exothermic reactions: Avoidance of hot spots

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So, by selectivity I mean the yield of the desired product or divided by the yield of the undesired product which is only term generally at selectivity in chemical reaction engineering. Another gas liquid reaction which has been studied it carbon-carbon multiple multiple bond addition for example, cycloalkane hydrogenation.

So, here is an example of this. This reaction has been performed and trickle bed reactor and it is well studied. So, actually this reaction has been used as benchmarking for micro reactors.

It is again a fast reaction and exothermic. So, it can be performed in micro reactions. So, that hot spots do not form and large interfacial area is provided for the reaction to happen. There are number of other reactions that have been performed in a micro (Refer Time: 14:04).

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Pharmaceutical Industry

- Transition from batch to continuous mode
 - IndusMagic (www.indusmagic.org) project at NCL, Pune
 - Novartis-MIT centre for continuous manufacturing

DSM Pharma implements microreactor technology
28 January 2009 01:25 Source: KGS News
SAN FRANCISCO (KGS) News: Netherlands-based DSM Pharmaceutical Products has begun integrating and running micro-reactor process technology to produce current good manufacturing practices (cGMP) quality pharmaceutical chemicals, said a company official Tuesday.

Swiss firm Lonza turns to microreactors to develop drugs
08 June 2009 22:40 Source: KGS News
NEW YORK (KGS) News: Swiss fine chemicals major Lonza has used its microreactor technology (MRT) to scale up the synthesis of multiple developmental drugs for a major pharmaceutical company, a Lonza official said on Monday.

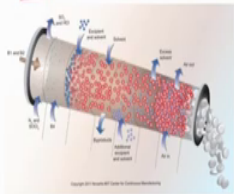


Image from <https://novartis-mit.mit.edu/> accessed on 12 March 2018

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Now, one of the applications of chemical micro processing is in the Pharmaceutical Industry; where, in general the trend is to have batch reactor. So, what I mean by batch reactor that the 2 reactants or all the reactants are mixed in a vessel or in the reactor and then, the reaction happens. After the reaction, the product is taken out and then, again the vessel is cleaned and it can be used for another reaction or if the same reaction is to be carried out.

So, same product is to be manufactured. Then, this without cleaning one can have the reactions. Now, when one does this then it is highly likely that the product quality from one batch to another batch may differ.

So, there might be a non uniformity in the product. But the use of batch reactors in pharmaceutical industry is preferred because of the low quality or not quality, but the low

quantity of the reactants and products that are involved. One does not need very large scale reactors in pharmaceutical industry and the chemicals that are dealt with are generally of high cost.

So, they need to be used judiciously to reduce the production cost. Moreover, the same reactor after cleaning can be used for another reaction. So, these problems can be circumvented or can be addressed by using continuous micro reactors. Micro reactors will of course, offer the advantage of the continuous flow reactors at the larger scale.

But at the same time it will also give one the freedom to perform reactions with low volume of fluids. So, one can have this and then, one can number up the process by or one can scale up the process by having number of micro channel or micro reactors in parallel.

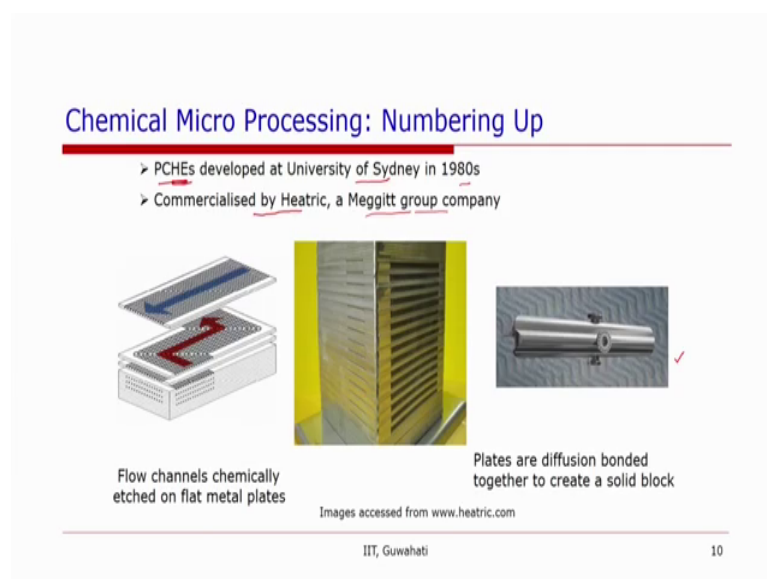
So, that the reaction can be scaled up and it can be performed in the micro reactors. So, in recent years, in last 2 decades at least there have been a drive to for the to persuade the pharmaceutical industry looking at the options changing from the Batch reactor mode to the Continuous flow reactor mode at home as well as internationally.

So, for example, there has been about 15 or 20 years ago, there has been a Novartis and MIT centre for continuous manufacturing where, they looked at different research problems that are required to be addressed for continuous manufacturing of pharmaceutical products.

There are some other news items and that there have been investment from Swiss firm Lonza and DSM Pharma to convert to micro reactor process technology to produce pharmaceutical chemicals.

Back home, there is a project running at National Chemical Laboratory, The NCL lab in Pune where they have the project is called IndusMagic, in which the goal is to develop novel reactors for process intensification and one of the reactors that they are looking at actively is Micro reactors for speciality and fine and speciality chemicals. Mostly, these chemicals are used in pharmaceutical industry.

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So, one of the issues that often comes up when one is looking at using micro reactors and chemical processing that how to scale up. So, as I have discussed in quite a few times during the course that this is scaling up is achieved by numbering up.

So, one example is Printed Circuit Heat Exchangers which were developed at the University of Sydney in 1980s and then, it was commercialized by Heatric which is now a group of a part of a Meggitt aerospace company.

So, in these micro reactors on the metal plates the flow, Flow channels are chemically etched, as you can see here that on a metal plate the channels are etched and the these channels can be straight channel or channels like this or they can be tortuous passage.

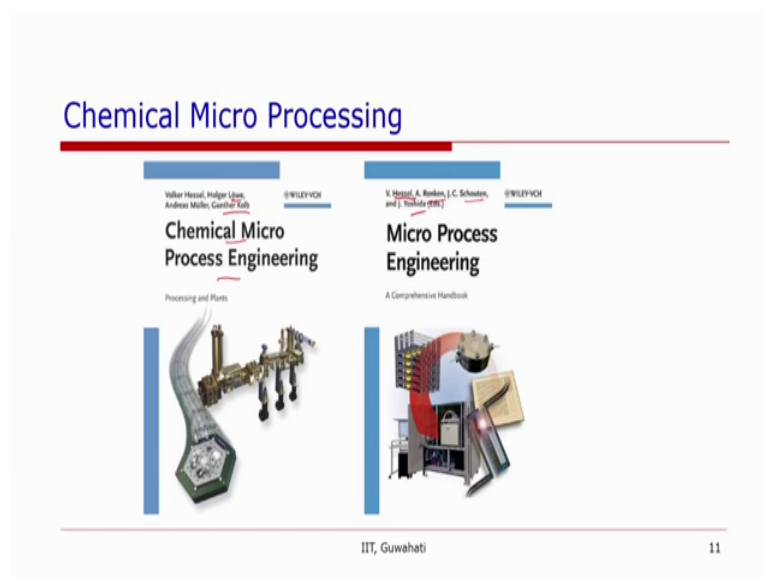
So, as to enhance the mixing and then these plates are diffusion bonded together and one they will look like this and then form with the inlet and outlet manifolds one can create a reactor of this form which will be very compact reactor. Now, this the technology which they use has been used for developing heat exchangers and it is commercialized successfully.

In recent decade they have been looking at and Heatric as well as other companies and researchers have been looking at using the same concept for a scaling up the micro reactors. So, this is because in this we are not changing the scale of the reactor rather

than the number of the reactors that are being used for the application is being increased. So, for example, in this one can have thousands of micro reactors are running parallel.

So, one of the problems or one of the challenges in addressing this or in numbering up is that the uniform distribution of the reactant in the channels because when one have the fluid coming from the manifolds, it is very difficult to distribute the liquid or gas equally in the channels and this becomes even more challenging when one is dealing with multi phase flow systems. So, this is an active area of research that how one can have the equal distribution or the control distribution of the fluid in number of reactors like this.

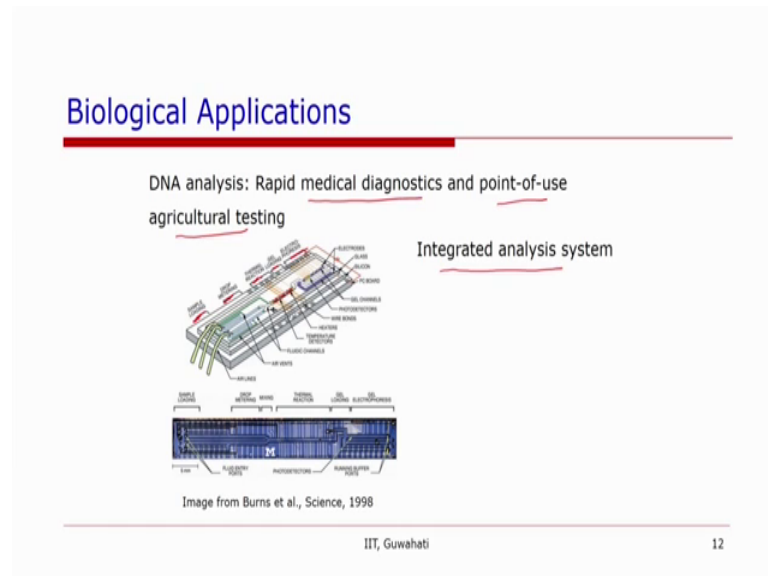
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So, here are 2 sources of information for the students who want to further know about the Chemical Micro processing in. So, so the chemical engineering or reactions in micro reactors one can look at these 2 volumes by professor hassle Professor Schouten and Rankin Sheila and others, Professor Kohl, Professor Lowe.

So, they are all who have been working on the micro reactor technology in its commercialization for last few decades and this is these books having the several volumes are a good source of information about the Fundamentals of Transport processes in micro reactors, Computational and experimental techniques as well as the different Experimental Protocols for different reactions and applications in for reactions in micro channels.

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Now, let us look at some of the biological applications by no means the application that I Show. Cover all the applications, but I just showing few applications; one of this is DNA analysis. So, DNA analysis involves a number of processes and it will be useful for medical diagnostics as well as for point of use testing in agricultural.

So, here is a integrated analysis system in which all the steps of the DNA analysis, sample loading, drop metering, thermal reaction, gel loading and electrophoresis to be changed for separation and the exists particles. So, this all have been integrated on a single chip and such a compact and small scale device can be very useful for analysis of DNA and in these applications.

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Biological Applications

Cell encapsulation: Treatment of hormone or protein deficient diseases, cancer therapy, microcarriers, scaffold for cell cultures and tissue engineering

Image from Sugiura et al., Biomaterials, 2005

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Then, another application is encapsulation of the Cells which is required for say example drug delivery for treatment of hormone or protein deficient diseases or cancer therapy for micro carriers or scaffold for cell cultures and tissue engineering.

So, this is a system for developing the 300 micron size the 300 micron size bits which can encapsulate cells. Then, there is another application.

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Biological Applications

- Hemorheology $\tau = f(\dot{\gamma}), \mu$
- Microvascular network
- Interaction between blood flow and surrounding tissues
- Leukocyte transport and adhesion

Image from Applied Biofluid Mechanics, Lee and Jerry, 2007

Roleaux Formation: Image from Microfluidics and Nanofluidics Hnadbook, Mitra et al., 2011

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In understanding the Hemorheology. So, the Hemorheology or the Hemodynamics refers to the study of flow of blood and Rheology as you might know that Rheology is the

science of looking at the relationship between a stress and rate of strain or the viscosity of the complex fluids.

So, as we know that blood is a suspension of red blood cells, white blood cells and platelets in plasma. So, it is complex fluid consisting of plasma which have properties of water, but it also have some proteins associated with it, so which makes it slightly complex.

But most of the time it can have the density and viscosity that of water. It has slightly visco elastic nature as the recent research has shown. Now, when there are small deformable particles most of them are red blood cells.

So, the suspended particles in the blood the 99 percent of the suspended particles are red blood cells and in the total volume of the blood the volume of these red blood cells will be 45 around 45 percent in a healthy human being.

And this blood which flows in the vascular network which is the network of arteries capillaries and veins in the body. Now, the size of the capillaries in the smaller arteries which are called artery also and smaller veins which are called venues, it can be as small as few microns about 8 to 10 microns.

The size of a red blood cells which is a disc shaped cell; it is about 8 micron in diameter of the disk and 2 micron in thickness. So, as one moves in the smaller veins or the smaller arteries of the capillaries, the size of the blood cells and the capillaries are almost same. And the capillaries when these blood cells are moving through the capillaries, they need to deform and flow through one by one.

Even in larger arteries where the diameter is 300 micron or smaller, as you can see here there is an interesting effect that is observed in capillaries probably a micro channel effect this effect is known as Fahreus which suggests that the viscosity of the blood; this is relative viscosity of the blood is it decreases when the channel size decrease below 300 mm. So, understanding the processes that is happening at these smaller sizes is very important for a number of biomedical applications.

For example, the techniques are being developed to estimate the viscosity of blood inside the blood vessels and identify or diagnose the diseases from those for such application

one need to have very detailed understanding from the fluid mechanic as well as other transport processes that is happening in these micro devices or in these micro channels.

So, one need to study first these things in the in the laboratory environment and gain confidence over it for example, recently there has been a nano machine developed at Indian Institute of Science in Bangalore; where, the plan to measure the viscosity of the blood using a helical coil or nano helical coil using the magnetic field. Another interesting phenomena that happens in micro or at low shear rates in blood that the red blood cells they stack together.

So, as you can see here that at low shear rates which will often be the case in at low velocities and low channel sizes because the velocities are very high when the blood comes out from the heart say in our tiny large arteries. When it goes to capillaries the viscose at the velocity of the blood will be smaller.

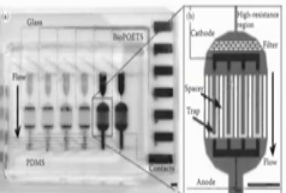
So, the shear rates will be smaller and red blood cells they tend to aggregate and this formation is called Roleaux Formation and when this formation happens? The viscosity of blood is known to be or (Refer Time: 31:27) is known to be a newtonian fluid above a certain shear rate. But at lower shear rate, it is it behaves as a complex fluid.

So, it shows the shear thinning behaviour. So, all these investigation of the flow of a foreign material in the blood or flow of red blood cells their movement or the movement of sick and healthy red blood cells; all this needs to be investigated in Microfluidic devices. So, of course, there is lot of scope for micro fluidics in Hemodynamics and Hemorheology.

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Micro Total Analytical Systems

- A single and fully automated incorporating sample preparation, liquid handling, detection and readout electronics
- Also known as ~~PTAS~~ TAS, lab-on-a-chip, miniaturised analysis systems
- Applications in medicine, drug discovery, forensic science, bio warfare defense, environment monitoring



Integrated microfluidic cell culture and lysis on a chip
Image from Nevill et al., Lab Chip, 2007

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Similarly, it is also the language as we know that where the exchange of oxygen happens in at a membrane exchanges of oxygen and carbon dioxide carbon dioxide happens between the air and blood and this happens in smaller spherical kind of cells which is which are called Alveolis.

So, there have been devices which are developed to understand the mass transfer processes that happens at the lung and then, T device had been known named as lung on a chip devices another application which we just saw an example in a for DNA analysis is called micro total analytical system.

So, in analytical chemistry one need to go through a different stage is sample preparation, liquid handling, detection and the reading out the electronics. It will be wonderful if one can combine and integrate all these steps in a single platform and that is what these micro total analytical systems are supposed to provide. So, these are also known as micro total and system work mu TAS or lab-on-a-chip devices.

So, you have all the functions that you need to do in a chemistry lab integrated over a chip. So, that is why the name and miniaturized analysis system and they have of course, applications anywhere where you want to analyze chemically or biologically a particular sample.

So, in medicine, drug discovery, forensic science, biowarfare defense, environmental monitoring, oil and gas industry and so on and so forth. So, this is another example of integrated Microfluidic cell culture analysis on a chip. We have already seen an example for DNA.

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Microfluidic Bubble Logic

- Can encode on-chip process control for microfluidic devices
- Presence of a bubble a "1" and absence a "0"
 - A bubble is a single bit of information
 - This bit of information can also carry a material or chemical
 - Computation also results in physical material processing at the same time

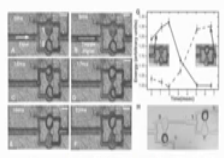


Image from Prakash and Gershenfeld, Science, 2007

microfluidic devices can carry their own process control information without the need for an external microprocessor.

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So, a related application of this micro total analysis is has come from Professor Gershenfeld lab in at MIT, where they have suggested that in micro fluidics one can use bubble logic.

So, one can encode on chip process controlled using bubbles for Microfluidic devices; where, the presence of bubble is 1 and the absence of bubble and 0. So, this bubble is a single bit of information using this 1 and 0 and this bit of information it can also carry a material or a chemical in these bubbles or droplets. So, the computation that happens in these chips can also result in physical material processing at the same time.

So, one do not need electronics separately as they suggest that the micro fluidic devices can carry their own process control information without the need for an external microprocessor. So, that will be this is just a conceptualization stage, but if it can be done and commercialized and this will be a wonderful thing having a lab-on-a-chip device which has its own logic.

So, these are some of the applications that we have discussed and as I said at the start of this lecture, there are a number of applications in a number of works of in our day to day life as well as industry Biomedical applications, Aerospace applications, Automotive applications, Cosmic industry applications, Pharmaceutical industry applications where these micro fluidics are required and as micro fluidics depends on the control of the process one need to have precise control of the systems. Most of the systems that we have discussed are developed in micro channels, because they offer the advantage of precise control over the processes.

So, whether one needs the precise control, one need to understand the processes that are happening and one need to know the fluid mechanics, heat transfer, mass transfer reactions that are happening in these systems. One also need to because most of the fluids that we handle are multiphase fluids. So, one need to have a very good understanding of the Multi-phase Microfluidics that happen in these systems.

Thank you.