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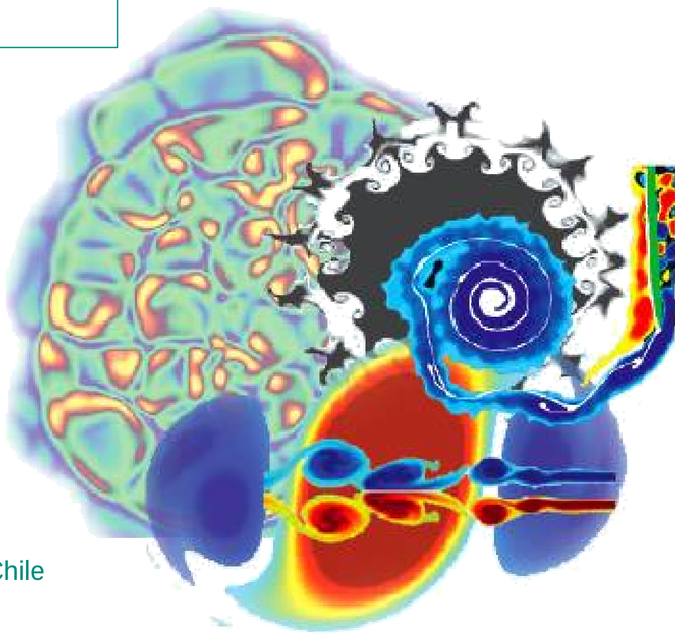
# First Latin American SCAT Workshop:
## *Advanced Scientific Computing and Applications*

# ***Microfluidics***


Prof David Emerson

CCLRC Daresbury Laboratory

University of Strathclyde

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# Outline of presentation

- Introduction to the field of microfluidics and MEMS
- The view from the top
  - microfluidics from a macroscopic perspective
- The view from the bottom
  - microfluidics from a microscopic perspective
- Manufacture of MEMS
  - important materials used
- Final remarks

## MEMS - Science Fiction or Science Fact?

- In 1966, Gene Roddenberry introduced the world to Star Trek
- The television series made use of the *tri-corder* – a fictional device that was portable and could analyse several different quantities
- In the “23rd century” we have:
  - essentially an advanced gas chromatograph!

Image showing Spock using his tri-corder

# MEMS - Science Fiction or Science Fact?

- In 1966, Gene Roddenberry introduced the world to Star Trek
- The television series made use of the *tri-corder* – a fictional device that was portable and could analyse several different quantities
- In the "24th century" we have the updated version!
  - Both devices have "sensors" and "displays"

It is claimed that the tri-corder has inspired many novel devices e.g. PDA, mobile phones

Specialised device used in Deep Space 9

# MEMS - Science Fiction or Science Fact?

In the Fantastic Voyage, a submarine and crew are reduced in size to travel through the blood stream to perform laser surgery on a blood clot in the brain. Innerspace (1987) was an updated version.

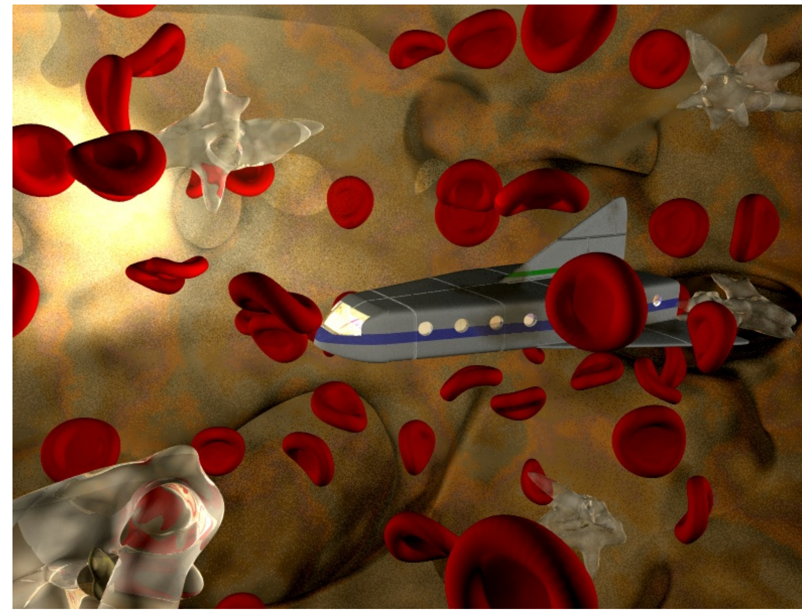



Image from the Fantastic Voyage (1966)

This has inspired people to think of unmanned "submarines" that can perform modest operations.

# MEMS - Science Fact – the Mobile Phone

The Nokia 3250

A 2MP video camera

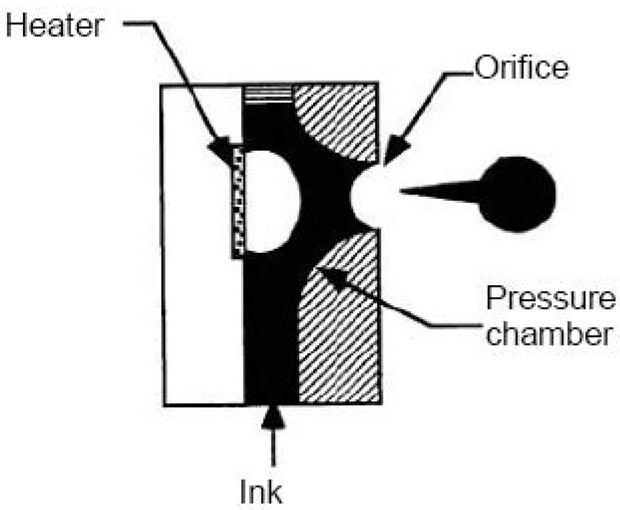
MP3 player

GPRS, internet access

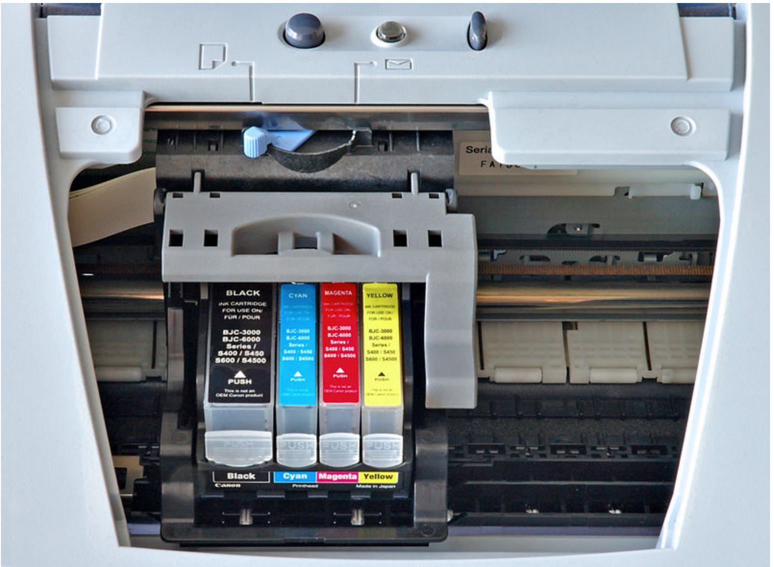
Developments rely on $\mu$ Technology

# MEMS - Science Fact – the Ink-Jet Printer

- The ink-jet printer - a perfect example of $\mu$ fluidics in action

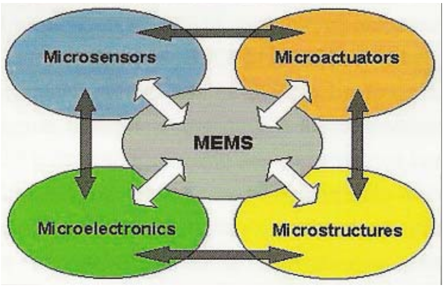



Thermal ink-jet operation



# Introduction to MEMS

- What is MEMS all about?
- MEMS (Micro-Electro-Mechanical Systems) refers to small devices that combine mechanical and electrical components with feature sizes ranging from 0.1 microns (0.000 000 1 metres) to 1 millimetre
- MEMS are not restricted to any specific application or device and can be deployed in conventional macroscopic systems to perform a particular function (e.g. flow control). They are not defined by any specific fabrication process and can be made from a diverse range of materials (silicon, glass, plastic,…..)
- MEMS are used for sensing (accelerometers), control, detection,……
- MEMS can also incorporate optics (MOEMS) and are the primary route for the use of nanotechnology



# Introduction to microfluidics

- What is microfluidics

- Microfluidics is a *new* branch of fluid mechanics that is destined to have a major impact on many aspects of science and technology – it is anticipated that microfluidics will be particularly successful in the chemical, medical, biological and environmental fields.

- Microfluidics has emerged with the development and manufacture of micro-scale devices, commonly referred to as MEMS (Micro-Electro-Mechanical Systems).

- Microfluidics requires the design, fabrication and implementation of suitable pumps, valves, mixing and separation elements for precise control of *small volumes* of gases or liquids ($\mu$L$\rightarrow$fL) in *micron-scale channels* (1 mm $\rightarrow$ 1 $\mu$m).

- Other terms:

- Micro Total Analysis Systems ($\mu$TAS) – (Swiss, early 90's).

- Lab-on-a-chip (US, mid 90's ; UK, late 90's).

- Micromachines (Japan)

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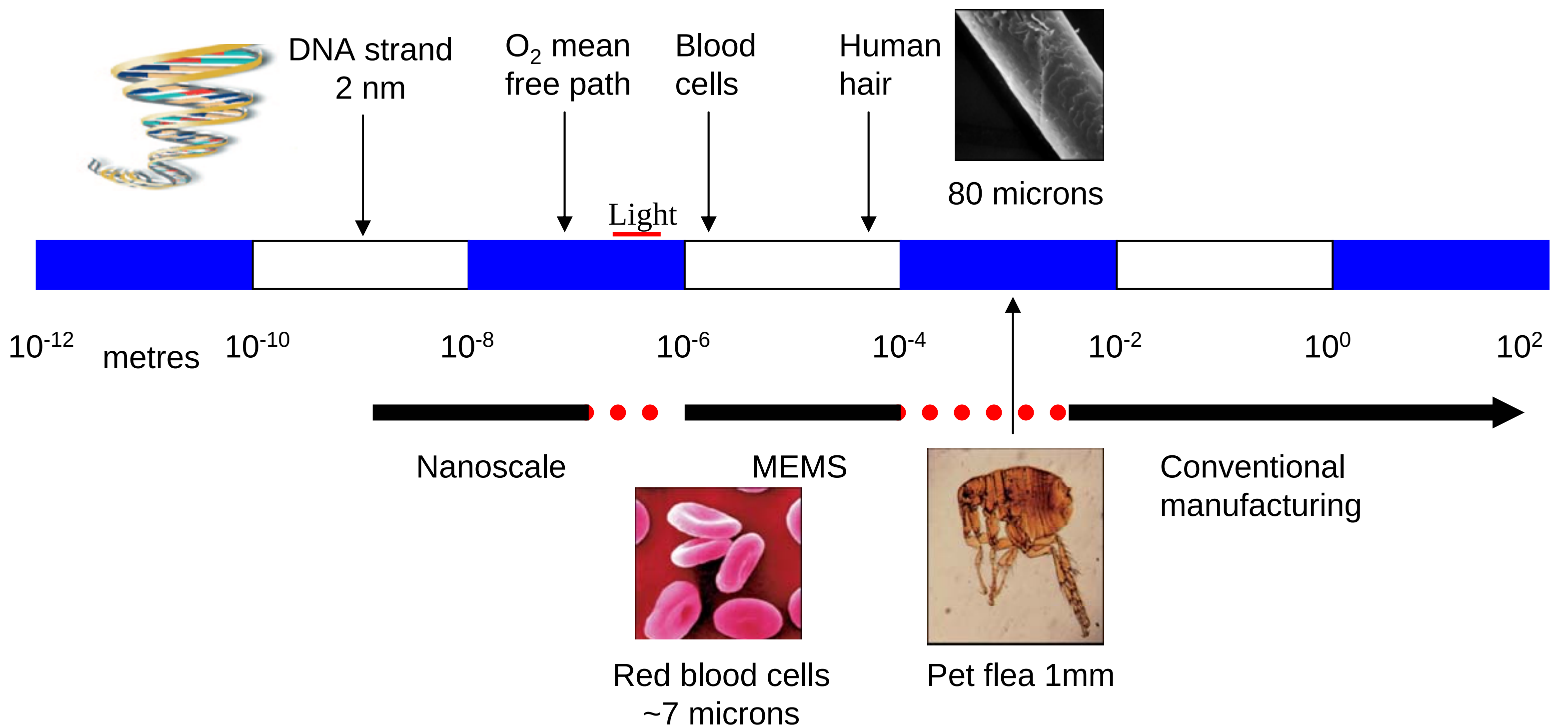
# Typical length scales related to MEMS




MEMS can combine electrical, mechanical and fluidic components down to a characteristic length scale of 1 micron i.e. *three orders of magnitude* smaller than conventionally machined components.

# Advantages in scaling down

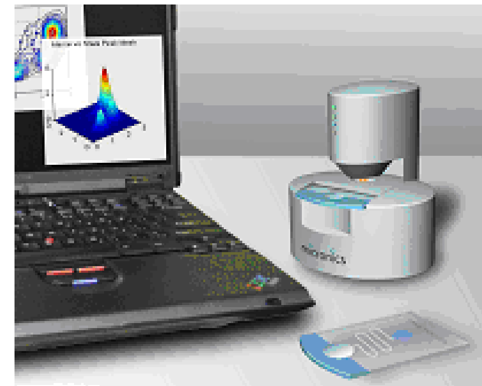
- There are sound commercial reasons for miniaturisation:
- Very small fluid volumes:
  - (a) reduced consumption of samples and chemical reagents
  - (b) excellent control of ultra small volumes
  - (c) vastly increased surface-to-volume ratios
    - improved heat transfer and better chemical control
- Enhanced performance:
  - (a) faster mixing times
  - (b) increased chemical yields
  - (c) faster throughput rates for chemical assays
  - (d) higher frequency responses for pressure/chemical sensors
- Reduced manufacturing costs
- Portability: e.g. “point-of-care” medical applications
- Lower power and chemical consumption (reduced operating costs)
- Automation: synthesis, sample preparation and analysis can be performed on a single chip
- Parallel systems: high throughput “scale-out” applications

# Application areas

- Medical diagnostics
- Portable/disposable testing kits
- Environmental monitoring
- DNA sequencing and assays
- Drug discovery – combinatorial chemistry (synthesis) and screening
- PCR - polymerase chain reaction
- Molecular biology applications – cell manipulation, miniaturised flow cytometers, blood plasma separations, etc.
- Chemical engineering – process development, hazardous exothermic reactions, highly-efficient heat exchangers
- Engine management systems
- Power MEMS: micro-fuel-cells, micro-generators
- Portable devices for detection of trace concentrations of air-borne pollutants – NOx, SOx, particulates, etc.
- Battlefield detection of anthrax spores and nerve agents

# Microfluidics also uses less laboratory space!


Conventional flow cytometer



The Microcytometer™ System (developed by Micronics) is the first portable flow cytometer that works directly using a whole blood sample without any preparatory steps. It greatly minimizes reagent use and contains the sample, reagents and waste on-card.

The system uses a droplet of whole blood to provide a complete blood count ("CBC") analysis. Sample to result is achieved in less than 5 minutes.

# A brief history of MEMS development

- 1961 – first silicon pressure sensor demonstrated
- 1970s – first silicon accelerometer demonstrated
- 1979 – first micromachined inkjet nozzle
- 1982 – LIGA process introduced
- 1988 – first MEMS conference
- 1992 – first micromachined hinge
- 1993 – first surface micromachined accelerometer sold
- 1994 – Deep Reactive Ion Etching (DRIE) patented

- TAS - early 1980s
- MicroTAS - 1989

## Microfluidics: the view from the top

# Fluid Dynamics: Some Key Parameters

| Parameter | Symbol | Definition | Scale |
|---|---|---|---|
| Reynolds Number | Re | $\rho uL/\mu$ | L |
| Knudsen Number | Kn | $\ell/L$ | 1/L |
| Weber Number | We | $\rho u^2L/\sigma$ | L |
| Capillary Number | Ca | $\mu u/\sigma$ | - |
| Mach Number | M | u/c | - |
| Grashof Number | Gr | $g\rho^2\beta(T_2 - T_1)L^3/\mu^2$ | $L^3$ |

List not exhaustive!

# Reynolds Number

$$\mathrm{Re} = \frac{\rho u L}{\mu}$$

### Re < 2000

- Laminar flow
- Flow remains as distinct layers
- Physics relatively simple
- Mixing by diffusion
- Flow speed usually low

### 2000 < Re < 4000

- Flow changing from laminar to turbulent
- Distinct layers are gone
- Physics quite complex
- Mixing by turbulence and diffusion
- Modest flow speeds

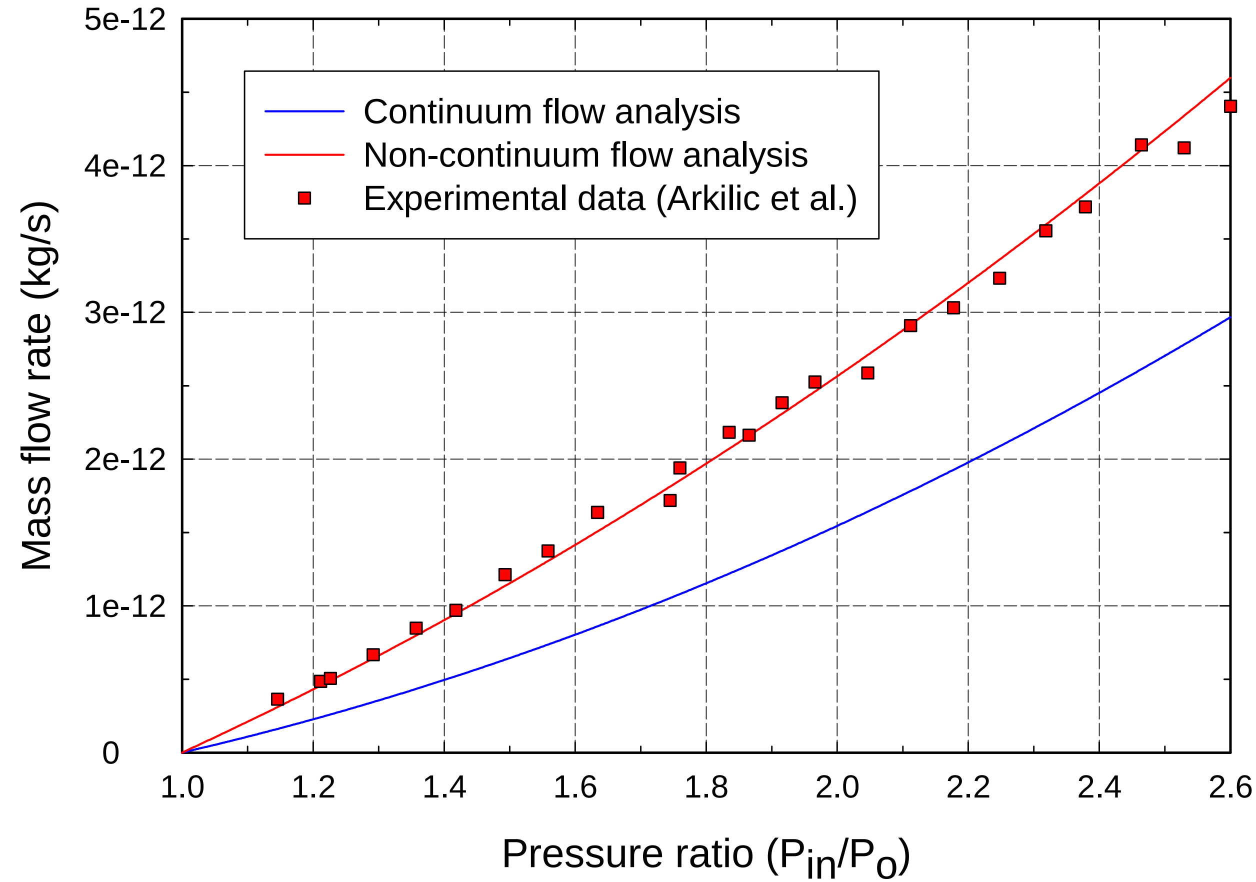
### Re > 4000

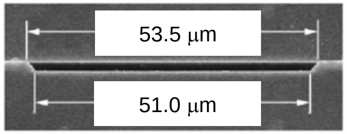
- Turbulent flow
- Flow chaotic: no distinct layers
- Physics very complex
- Mixing by turbulence
- Flow speed usually high

# The Knudsen number Kn

- $Kn = \lambda / L$
  - Air at S.A.T.P: mean free path, $\lambda \sim 10^{-7}$ m
    device length $L \sim 10^{-6}$ m
  - Hence Kn ~ 0.1
  - Rarefaction effects can be appreciable
- What does this imply?
  - Navier Stokes equations in conjunction with no-slip boundary conditions not valid for many gas flows in MEMS
  - Slip-flow boundary conditions are needed
  - Mass flow rates, velocity gradients, wall shear stresses and hydrodynamic drag forces will be affected

# Helium mass flow rate through a silicon micro-channel



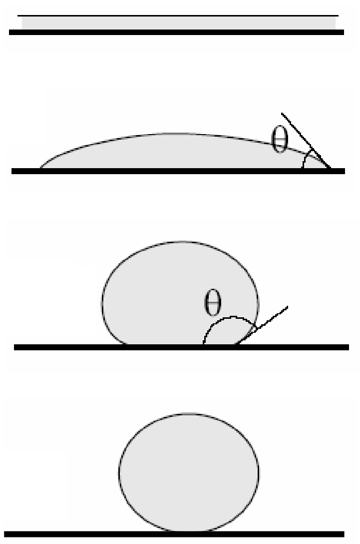



# Weber number

Weber number represents ratio of

inertial force to surface tension

$$We = \frac{\rho u^2 L}{\sigma}$$




cos θ = 1

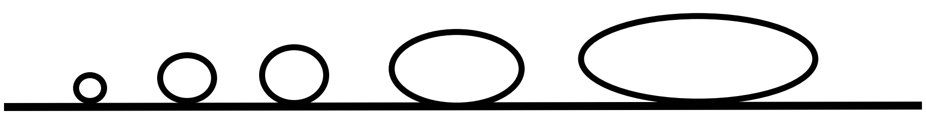
0 < cos θ < 1

-1 < cos θ < 0

cos θ = -1

Gravity not important for “small” drops.

Drop shape “flattens” as drop size increases



# Surfaces are all important!

In conventional (macroscopic) fluid modelling, surface properties can usually be ignored i.e. for liquids and gases the famous no-slip condition can be applied in most cases.

This is **NOT** true at the micro-scale: the surface can have a profound effect of flow behaviour.

Some simple examples of how surfaces & near-wall layers affect the flow:

For gases, the Navier-Stokes equations begin to break down at ~10 $\mu$m

For liquids, hydrophobic surfaces significantly alter flow rates

For electroosmotic flow (EOF), the Debye layer plays a crucial role

# Microfluidics: laminar flow dominates!

Laminar flow – very little mixing of the three coloured dyes.

An absorption-driven integrated microfluidic channel. The fluid is initially transported by surface tension and then flow is controlled by the absorption pad.

# Are quantum effects important?

- We know that Newton's second law breaks down under certain conditions which means that the Navier-Stokes equations are no longer appropriate. For gases, the Knudsen number guides us. There are two other areas where Newton's laws are no longer appropriate: one case concerns special relativity which is not an issue for MEMS. The other case is quantum theory.
- Quantum effects are important when a particle's *de Broglie* wavelength is comparable to a typical length scale of the system:

$$\lambda = \frac{h}{p} = \frac{h}{mv}$$

where $h$ is Planck's constant, $p$ is the particle's momentum, which for nonrelativistic gases moving at ~500 m/s, gives $\lambda$ = 0.2Å.

# Microfluidics: the view from the bottom

# Nanotechnology

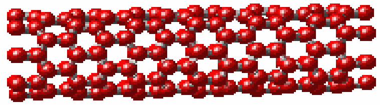
- Nanotechnology and the underpinning nanoscience is REAL. It is already out there in coatings, paints, sun lotions, and also materials such as fabric for trousers and shirts!
- Some definitions:
  - Nanoscience is the study of phenomena and manipulation of materials at the molecular scale
  - Nanotechnology involves the design, characterisation, production and application of structures and devices
- It is all about objects with nano-scale dimensions or manipulating properties at the molecular level.
- Unlike MEMS, nanotechnology has raised many questions and concerns about potential societal implications.

# At the nano-scale . . . . .

The sample volumes at the nano-scale are **extremely** small . . .

For example: a 1 $\mu$m long carbon nanotube with a 10nm diameter would hold around 0.1 aL i.e. $0.1 \times 10^{-18}$ litres

Figure of a SWNT courtesy of NASA



Today, scientists can build 20cm long carbon nanotubes. However, for the carbon nanotube to occupy the same volume as a human hair (~80 $\mu$m diameter), the tube would be long enough to go around the earth!

# How do liquids behave at the nanoscale

Q: How can we model liquids at the nano-scale?

It is highly unlikely that the Navier-Stokes equations are valid at the nanoscale. However, there is no clear length scale at which this breakdown occurs.

Q: When is Brownian motion important?

Experimentally, we know this starts becoming important between 1-10 $\mu$m

Q: Does the no-slip condition hold?

We'll look at this in the next couple of slides.

# Density at the nanoscale

Water is generally considered to be incompressible. This means that the density is constant. Is this assumption valid at the nanoscale?

Consider a carbon nanotube with diameter 2.712nm filled with water. As the wall is approached, a distinct layering of the oxygen (+) and hydrogen (x) molecules is observed. Only “far” from the wall is the bulk density constant.

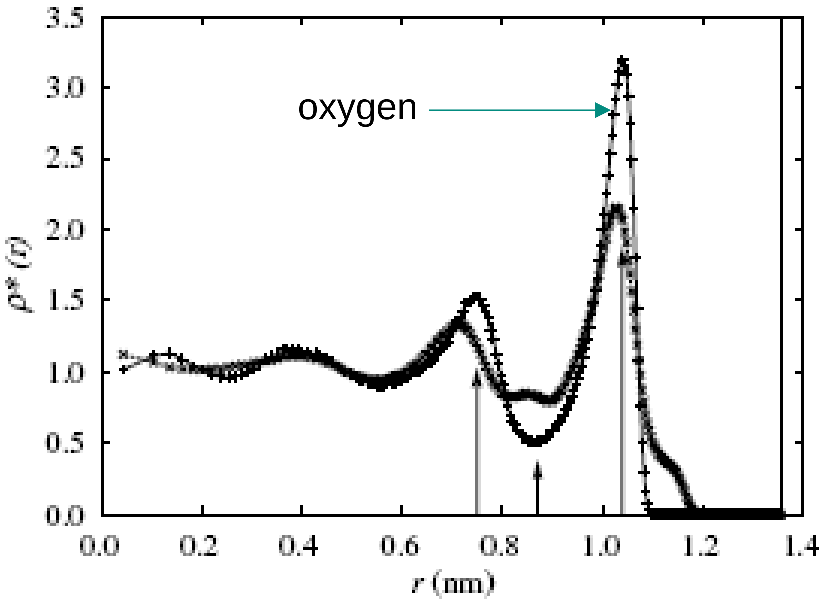



Figure by E.M. Kotsalis et al.

Int. J. of Multiphase Flow (2004) V30 pp. 995-1010.

# Velocity at the nanoscale

Q: Is the flow parabolic?

Q: What happens at the wall?

Several carbon nanotubes with diameters ranging from 2.712nm to 5.424nm are filled with water. There is strong evidence of slip at the wall.

All calculations are done using nonequilibrium molecular dynamics.

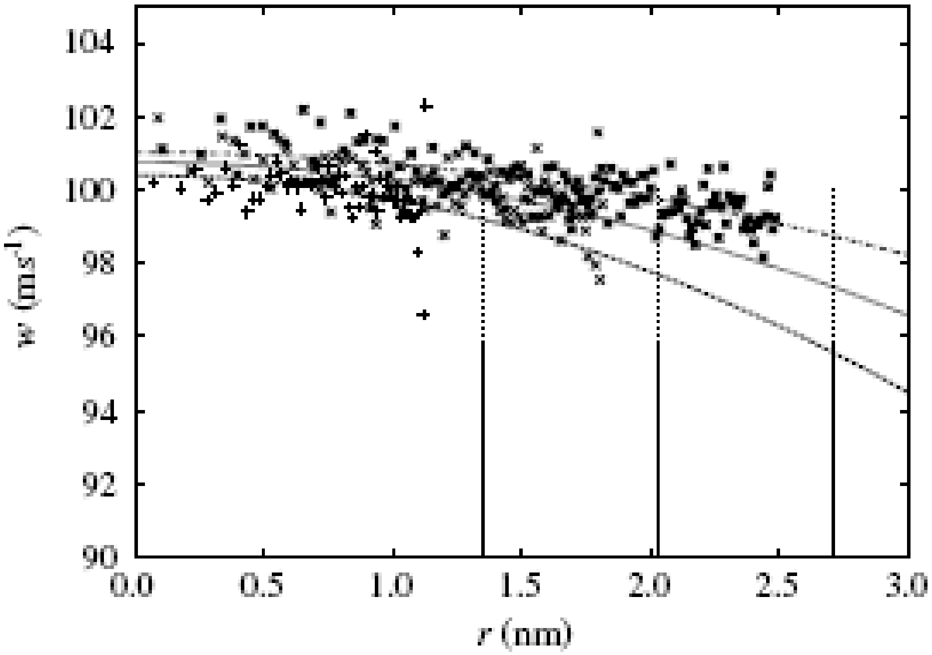



Figure by E.M. Kotsalis et al.

Int. J. of Multiphase Flow (2004) V30 pp. 995-1010.

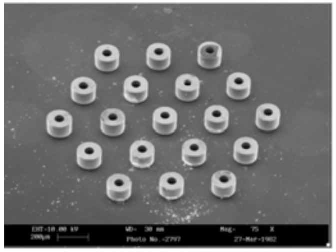
# Nanotechnology – societal issues

- Unlike any other area of science, nanotechnology raises major concerns in society e.g. self-replicating nanobots, grey goo!
- Nano-scale particles readily cross cell membranes – raises concerns about terrorism using nanotechnology, inhaling manufactured particles, potential for particles to have increased toxicity/eco-toxicity, can it be controlled?
- On the positive side, clothing material manipulated at the molecular level can already resist most stains but could be designed to change colour with mood, designer sun-tans and cosmetics, self-cleaning windows (already developed by Pilkington) and seats,…………
- Experience with GM food has shown that having public support is vital if this science is to be accepted

# Manufacture of MEMS

# Available materials (1)

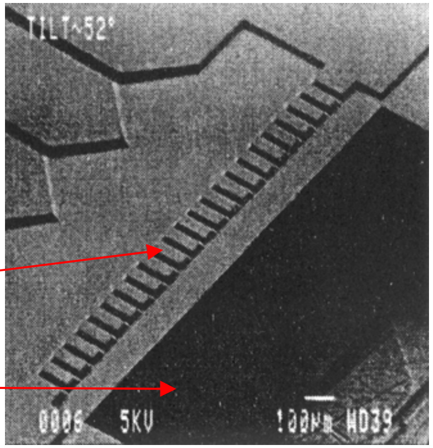
- Silicon
- crystalline
- semi-conductor
- transparent at $\lambda > 1.1\ \mu m$
- high mechanical strength
- technology well developed (integrated circuits, early 60's)
- surface micro-machining (2D structures)
- bulk etching (3D structures)
- dry or wet processing



Array of nineteen 178 $\mu$m diameter silicon nozzles for a micro-thruster
[CMF, Rutherford Appleton Laboratory]

Filter channels
(30 $\mu$m wide x 25 $\mu$m deep x 140 $\mu$m long)

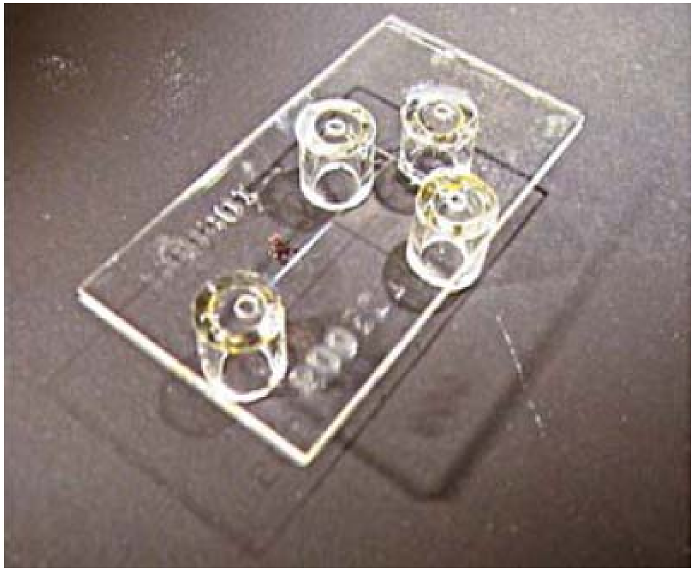
Syringe insertion well




SEM image of micro-manifold
[Harper et al. (BNFL) 1995]

# Available materials (2)

- Glass
- amorphous
- electrical insulator
- transparent
- good chemical and biochemical compatibility
- bulk etching (similar to silicon)
- wealth of experience in research laboratories
- little commercial technology base

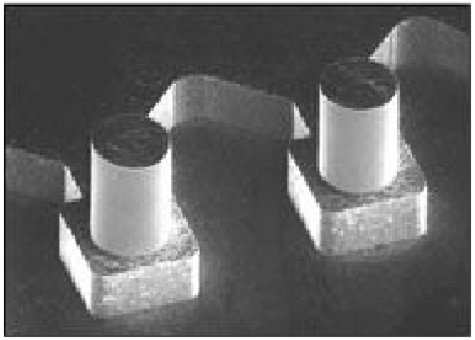


Electrophoresis microchip developed at the Institute of Microelectronics and Microsystems (IMM), Switzerland.

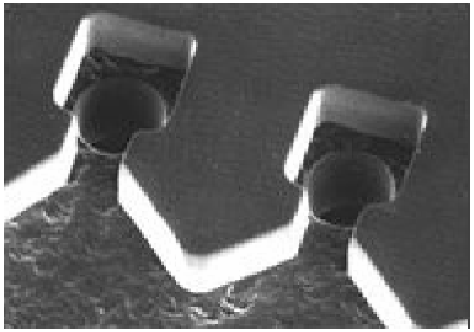
# Available materials (3)

- Polymers
- wide variety (PMMA, PC, etc.)
- choice of optical/chemical properties
- replication techniques include:
  - hot embossing
  - micro injection moulding
  - casting
- resolution: µm to nm

**Micro-injection moulding**



Mould insert for a micro-nozzle [FSRM, Switzerland]



Plastic replication of the mould insert

# Moving and manipulating fluids in micro-channels

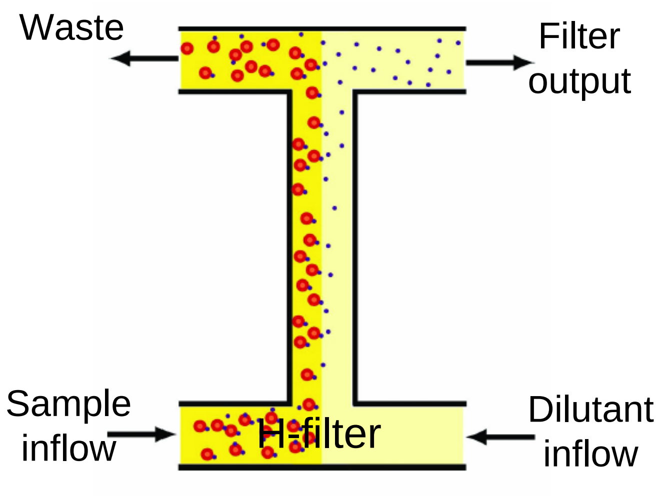
# Fluid manipulation techniques

| *Mechanism* | *Liquids pumped* | *Comments* |
|---|---|---|
| Pressure | Aqueous and non-aqueous | • Independent of solution composition<br>• Dependent on density, viscosity, channel geometry |
| Electroosmosis | Mostly aqueous | • Very dependent on buffer composition (e.g. ionic strength, pH)<br>• Requires high electric fields |
| Centrifugal | Aqueous and non-aqueous | • Independent of solution composition<br>• Dependent on viscosity, density, channel geometry |
| Ultrasonic | Aqueous and non-aqueous | • Requires complex integrated structure |
| Electrohydrodynamic | Non-conductive liquids (non-aqueous) | • Requires high electric fields |
| Surface tension | Aqueous and non-aqueous | • Passive, requires no external applied force<br>• Once channel filled, liquid movement stops |

# Diffusion-based separations

•The different diffusion rates of molecules and particles can be used to separate them according to their size:

- An example of a practical microfluidic device making use of diffusion-based separation is the H-filter, developed at the University of Washington.
- The H-filter allows a continuous extraction of molecular analytes from fluids containing larger particles (e.g. blood cells, bacteria, viruses etc.) *without the need for a filter membrane*.
- The filter output is preferentially enriched with smaller (faster diffusing) molecules.



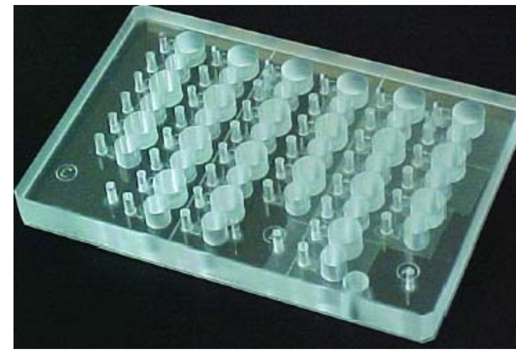
# Microfabricated H-filter


Packaged H-filter

# Diffusion-based separations

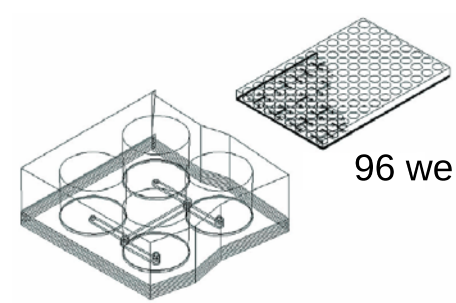
Applications:

- blood plasma separations
- PCR product clean-up
- drug discovery
- artificial kidneys?



Hydrostatic pressure-driven H-filter cartridge in a 96-well plate format developed by Micronics Inc.

A disposable H-filter for separating flourescein from labelled dextrane molecules.



96 well card

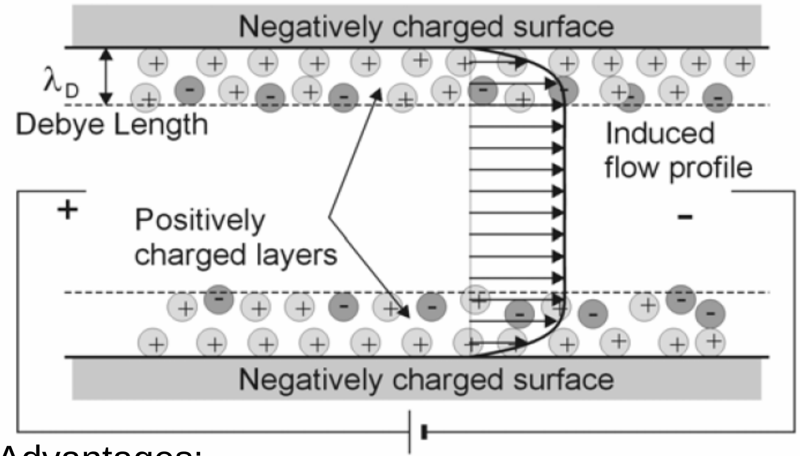
Unit cell

- Electroosmotic flow

# Electroosmotic flow (EOF)

• Aqueous fluids can be transported by applying an electric field to produce an electroosmotic flow (EOF):

- Electroosmosis requires a material with a surface charge
- Glass/many polymers have permanent negative surface charge
- Diffuse layer of positive charges assemble near the channel wall forming a thin (1-10 nm) *"double layer"*
- Applying a voltage across the ends of the channel induces motion of the positive ions
- Motion propagates to the interior of the fluid by viscous drag



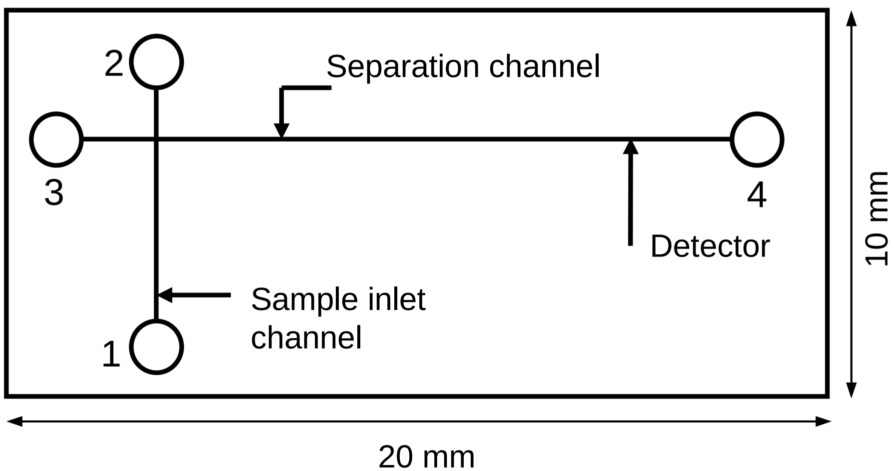

Advantages:

- No pumps or valves required
- Uniform velocity profile across channel
- Minimal sample dispersion

Disadvantage:

- Low fluid velocity ( < 10 mm/s)

# Capillary electrophoresis

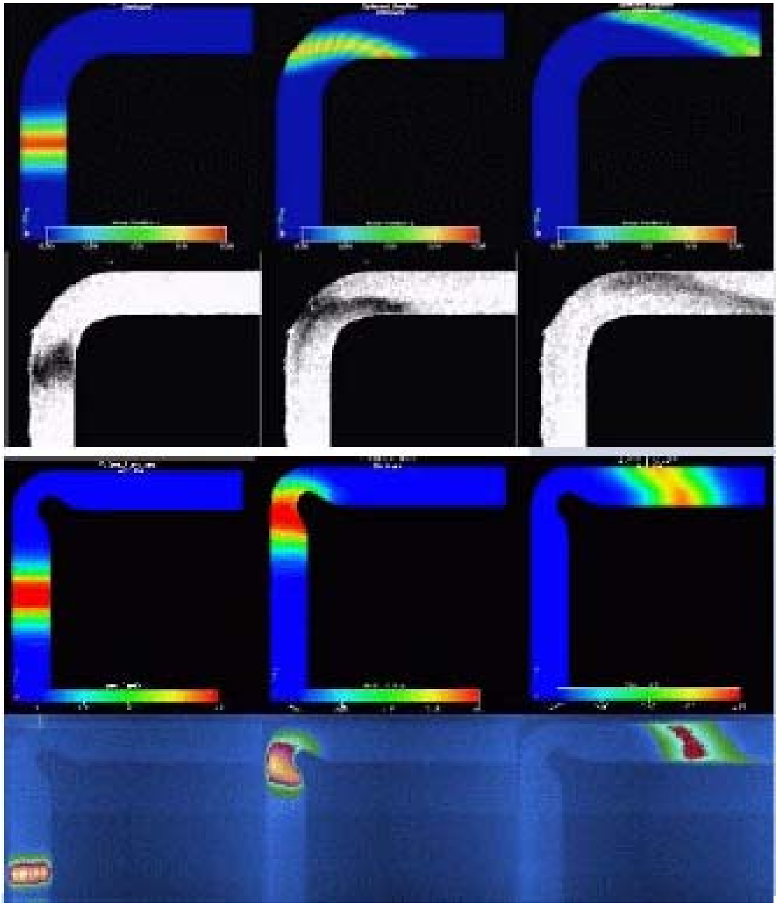



Schematic of capillary electrophoresis chip developed by J. Harrison

Operating sequence:

- Channels filled with a buffer solution.
- Sample solution then transported by electroosmotic flow from sample inlet to sample outlet – electrical field applied between (1) and (2).
- Sample flow switched off and electrical field applied between (3) and (4) to transport the fluid down the separation channel.
- The flow pushes the sample volume or plug defined by the intersection of the two channels.
- Electrophoretic separation occurs as the sample travels along the separation channel.

# Electroosmotic flow – the 'race track' effect



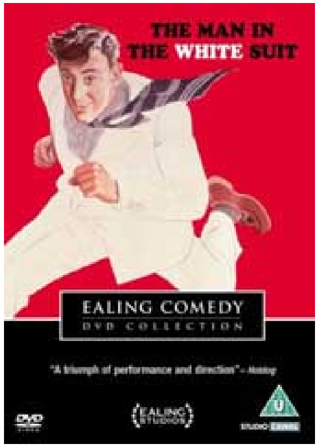
Geometry of channel bends is critical to reducing broadening of transported samples.

*Ref*: J.I.Molho *et al*., "Optimization of turn geometries for microchip electrophoresis", Analytical Chemistry, Vol. 73(6), 2001, pp. 1350-60.

# Concluding remarks - the "disruptive" technology

Micro- and nano-technology can revolutionise many areas

However, this can cause problems for companies – they can be put out of business overnight!




*The Man in the White Suit* (1951)

Sidney Stratton, a humble inventor, develops a fabric which never gets dirty or wears out. Once someone buys one of his suits they won't ever have to fix them or buy another one, and the clothing industry will collapse overnight.

# Acknowledgements

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