Biomicrofluidcs: Why Research in Biomedical Field Should Change

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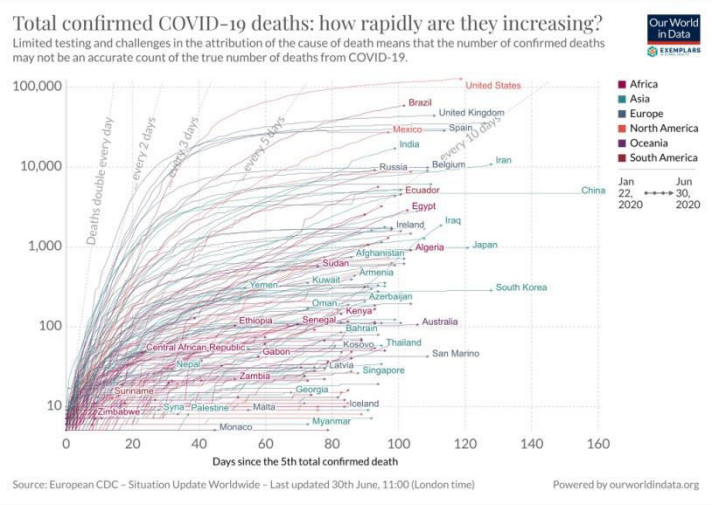
Learnings from the Current Pandemic

- Extra focus should be given to healthcare.
- Vulnerability to a pandemic doesn't depend on a country's wealth.
- Long term infrastructure can not be replaced by make shift arrangement.
- **Research should be major component in healthcare infrastructure.**
- For critical situations, the traditional trends of research such as waiting for decades to bring new drug/vaccine to the market may not be appropriate.

Image Source: TIMESOFINDIA.COM / Feb 14, 2022, 17:12 IST

Source: Google images

Source: Google images



India – What We Need in Healthcare

- Focus on India specific bacterial\viral infection based diseases such as tuberculosis, malaria, COVID-19, encephalitis, etc.
- Promoting an affordable healthcare system.
- Research in affordable healthcare system both at high end and preventive level.
- Proper delivery system including production supply chain and delivery personnel.
- Developing "ASSURED" point-of-care disease diagnostic devices.

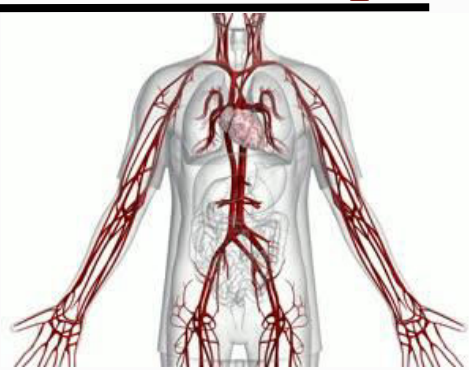
- **Not possible only with medical practitioners and healthcare workers.**
- **Role of technology, management, entrepreneurship, business, government efforts and policies are extremely critical.**

"ASSURED" (affordable, sensitive, specific, user-friendly, rapid, equipment-free, and deliverable to those in need)

Conventional Bio-Methods

Why the conventional methods should be replaced?

- Failed to mimic human physiological conditions such as space, temperature gradients, chemical gradients, pressure, oxygen gradients, stress, micro-flow conditions, etc.
- Sample and reagent consumption – More
- Time consuming
- Requires specialized equipment
- Non-affordable
- Occupies more space
- Can be hazardous



shutterstock.com

micromyx.com

https://www.happi.com/contents/view_breaking-news/2016-06-07/employment-woes-for-us-chemical-industry

http://www.joinnparks.com/biospace.html

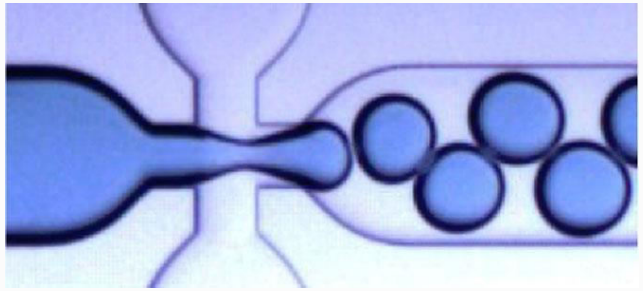
https://www.aegenviro.com/blog/handling-hazardous-materials-safety-top-priority/

http://www.wisegeek.com/what-is-centrifugal-force.htm

A New Technology to the Aid

Microfluidics

Precise control and manipulation of very small volumes of liquid flow.

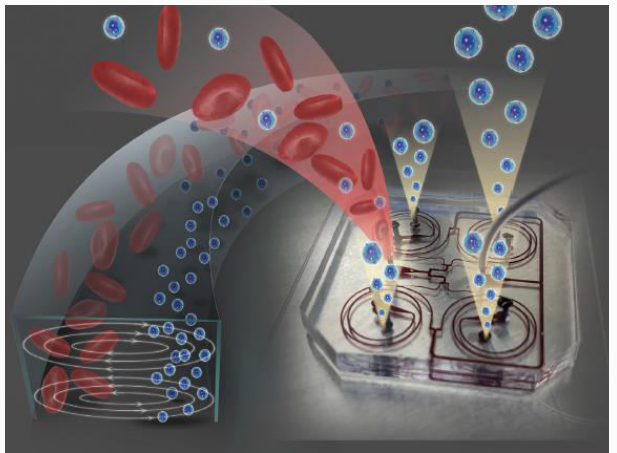


http://www.lboro.ac.uk/research/amr/therapeutics_diagnostics/fp3/

- Possibility of mimicking human physiology.
- Thermal, chemical and **bio-physical gradients** of interest can be created and maintained.
- Future technology for complete health monitoring, drug delivery and bio-analysis.
- Rapid and efficient diagnostics for all.
- Replaces expensive equipments.

www.kinergetics.com

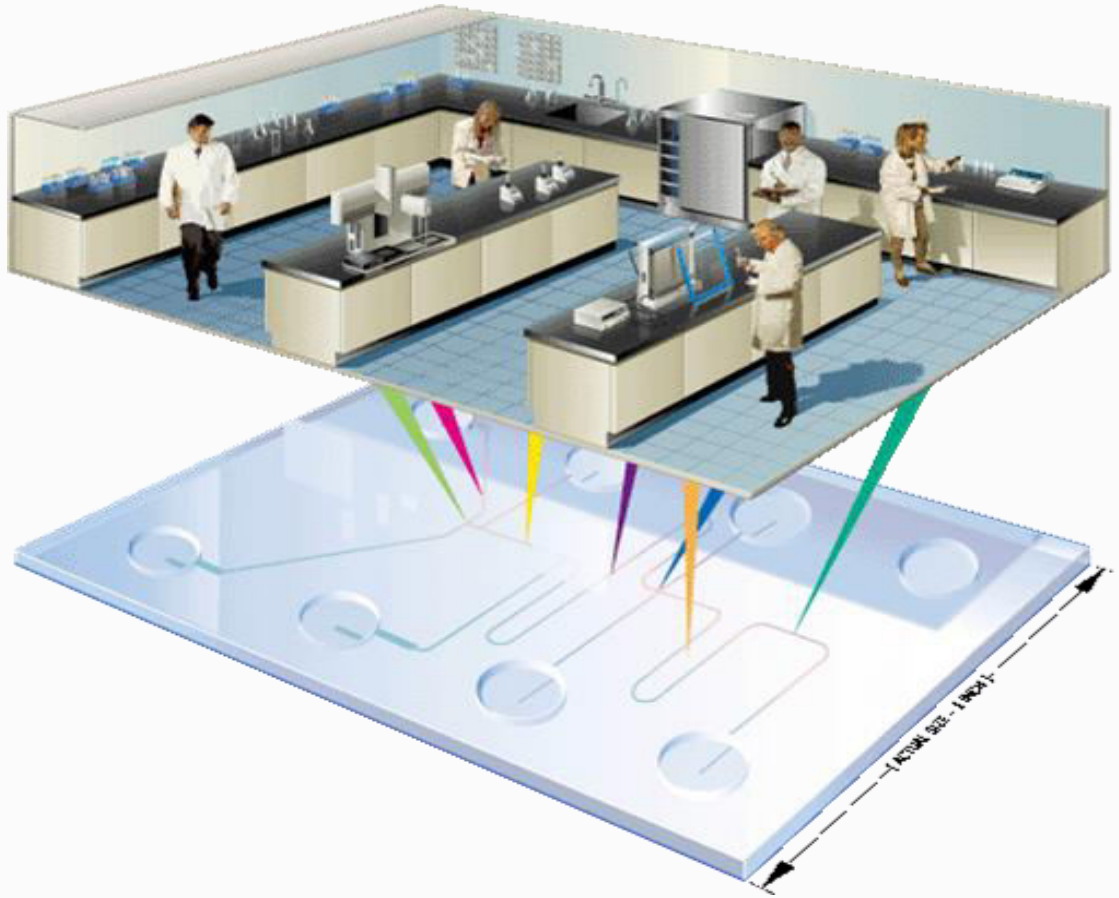
Vascular risk profiling in type 2 diabetes mellitus (Prof. Subra Suresh's group)



	Traditional Laboratory	Microfluidic "Lab-on-a-chip"
Cost	Often very high	Inexpensive
Equipment	Specialized equipment	Everything on chip
Time to get results	Significant time	Quick

What is “Lab-on-a-chip (LOC)”?

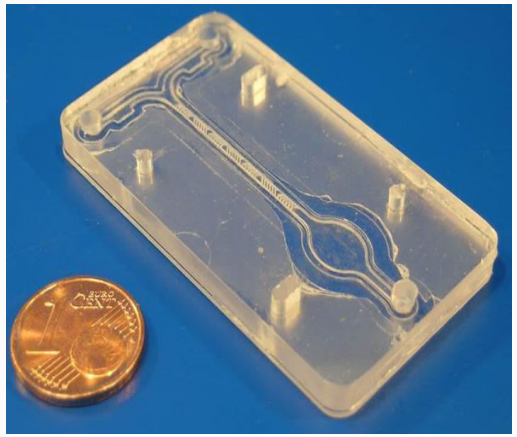
Device that integrates one or several laboratory functions on a single chip of only millimeters to a few square centimeters in size.



http://www.gene-quantification.de/lab-on-chip.html

What “Lab-on-a-chip” can do?

- Mimic the human physiology
- Disease diagnosis
- Drug discovery, screening and testing
- DNA amplification
- ELISA, etc.,



http://www.kemikro.rwthaachen.de/cms/KEmikro/Forschung/Ultraschallschweissen/~hnnr/Lab-on-a-chip/?lidx=1

Microfluidic Technology in Fight Against COVID-19

- **Microfluidic based RT-PCR and ELISA for detection of corona virus**

In News: Microfluidics Lab @ iitkgp

IIT Kharagpur develops portable rapid device to detect virus

PIONEER NEWS SERVICE
NEW DELHI

Indian Institute of Technology (IIT) Kharagpur researchers have developed a cost-effective portable diagnostic device that can detect Covid-19 infection within an hour and estimated to cost just ₹400.

This entire test can be conducted in an ultra-low-cost portable enclosure as an alternative to specialised laboratory equipment. The same portable unit can be used for a large number of tests, on mere replacement of the paper cartridge after each test.

The device has been proven to produce no false result with remarkable accura-

the Mechanical Engineering Department, and Dr. Arindam Mondal from the School of Bio Science, both from IIT Kharagpur. The technology essentially deploys a disposable simple paper-strip for chemical analysis and visualization of results.

"The new device has been designed to be usable at locations with extremely poor resources in an uncontrolled environment, catering the needs of the underserved population. Moreover, it can be operated by minimally trained personnel, precluding the needs for skilled technicians," said Dr Chakraborty.

While the Institute can produce the testing kit up to a

technology companies.

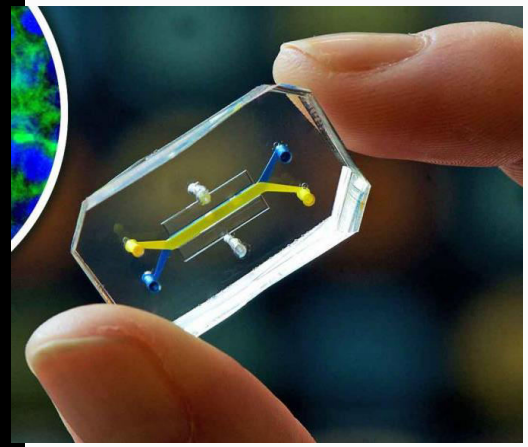
Dr Mondal added, "The unique portable device developed by the IIT Kharagpur researchers has not only been validated for the diagnostics of

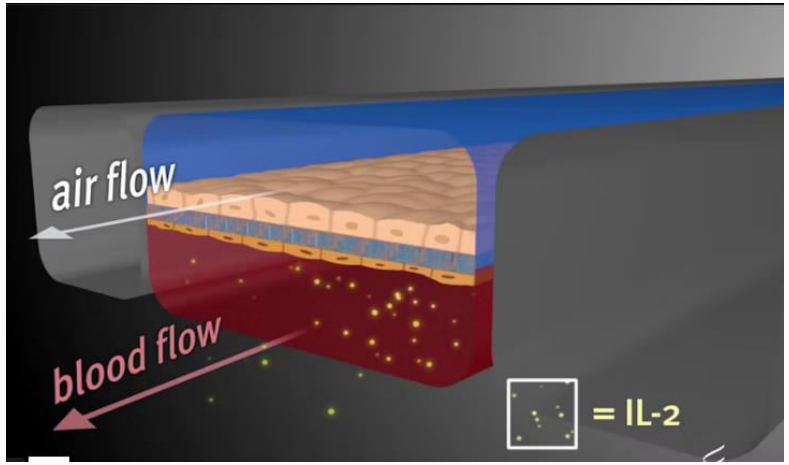
RNA virus by following the same generic procedure. The impact of this, therefore, is long lasting, empowered by the capability of detecting unforeseen viral pandemics in the coming years that may potentially endanger human lives time and again."

The project received financial support from the Institute in late April after Professor V K Tewari, Director, IIT Kharagpur, decided to set up a fund to support Covid-19 related research and product development.

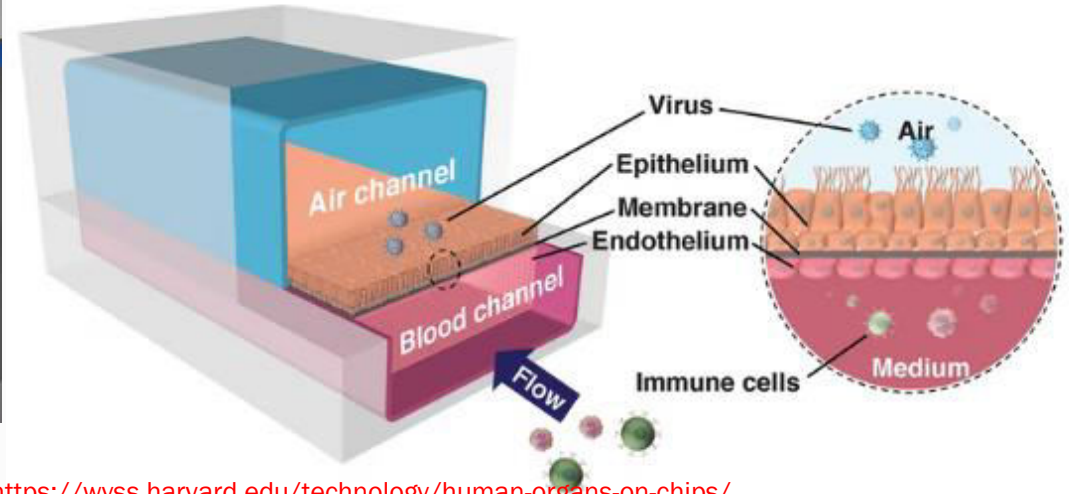
"We are ready for commercialization of the product. Any corporate or start-up can approach the Institute for technology licensing and commer-

- **Corona virus disease modelling with microfluidic technology – Wyss Institute**



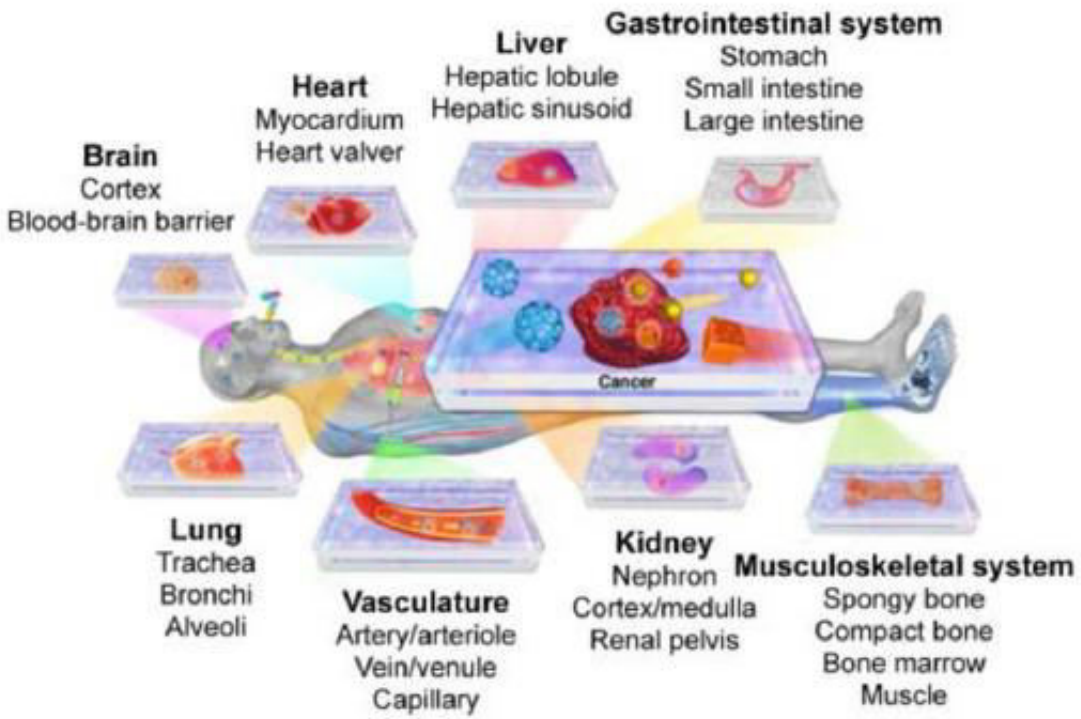


https://www.youtube.com/watch?v=52IL9gemyDw



https://wyss.harvard.edu/technology/human-organs-on-chips/

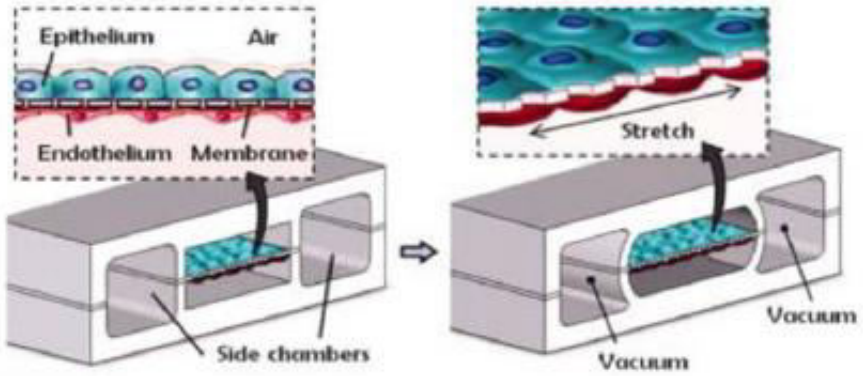
A



B

	Animal	Lung-on-Chip	Organoid	Air Exposed Primary Cells	2D Cell line
3D tissue architecture	●●●	●●○	●●○	●○○	○○○
Full cell differentiation	●●●	●●○	●●○	●●○	●○○
Hemodynamic	●●●	●●●	○○○	○○○	○○○
Circulating immune cells	●●●	●●○	○○○	●○○	○○○
Physiological biomechanics	●●●	●●○	●○○	●○○	○○○
Long-term viability	●●●	●○○	●●○	●●○	●●●
Familiarity	●●●	●○○	●●○	●●●	●●●
Access to luminal space	●●○	●●●	●○○	●●●	○○○
Patient-specific cells	●○○	●●●	●●●	●●●	●●●
Conserved disease phenotype	○○○	●●○	●●○	●○○	●○○
Throughput	○○○	●○○	●●○	●●○	●●●

C



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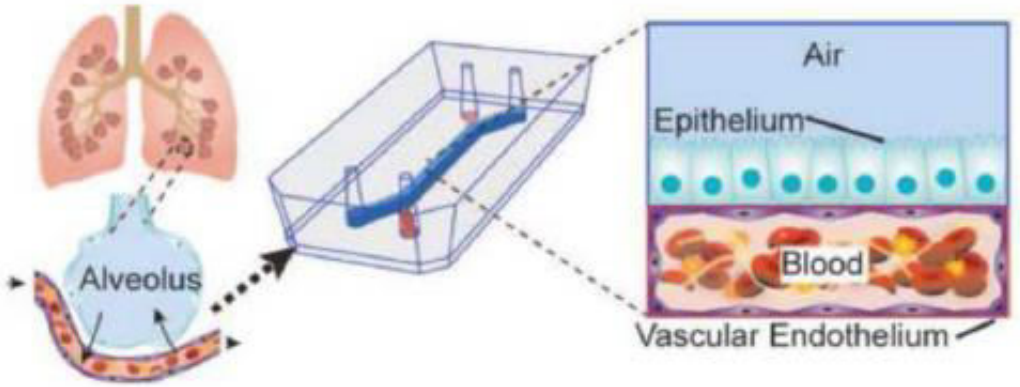


Why healthcare should shift to microfluidic devices for diagnostic purpose?

Medical Diagnostics in remote places

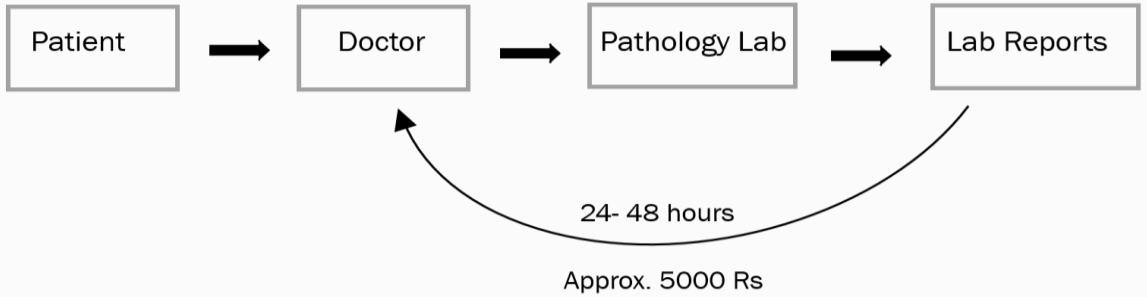
- Medical diagnostics are not easily accessible.
- Giant diagnostic equipment's are not portable.
- Timely detection of infection impossible.
- Physicians has to follow trial and error treatment.
- Medical facilities are often sparse or temporary.
- Power limitation

https://pakistaniat.com/2007/01/19/bicycle-ambulance-health-pakistan-development/

http://phlessons.com/345/2014/03/26/mobile-medicine-clinics-in-the-developing-world/

Solution with Microfluidic Devices

How routine pathological tests are done?

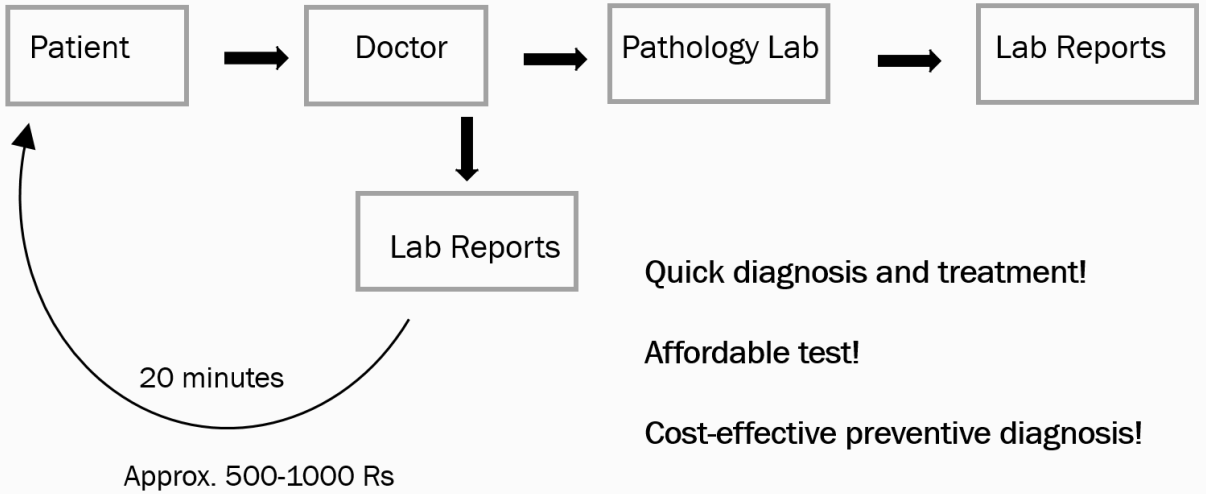


DELAY in diagnosis and treatment!

Tests are EXPENSIVE!

NO PREVENTIVE diagnosis due to lack of health awareness and high cost .

Solution with Microfluidic Devices



Quick diagnosis and treatment!

Affordable test!

Cost-effective preventive diagnosis!

With microfluidics

Healthcare is portable: can travel to patients

In-expensive

Low power requirements

Faster results

Can perform complex diagnostics

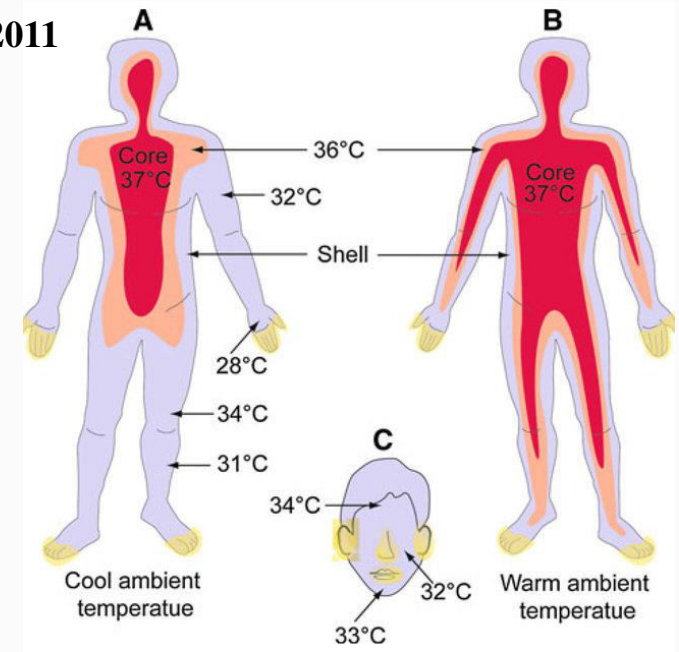
High throughput, precision and sensitivity

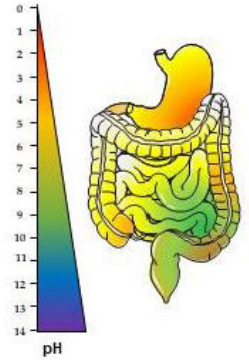
Less consumption of samples and reagents

Parallelization

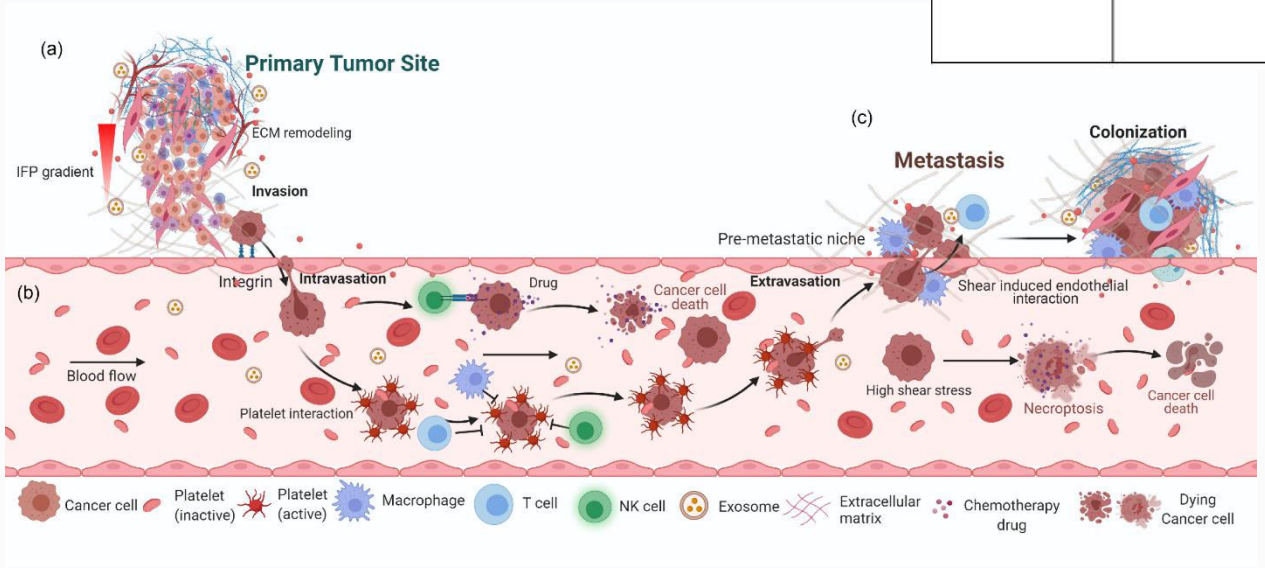
Bio-Microfluidic Research at Our Lab, IIT Madras

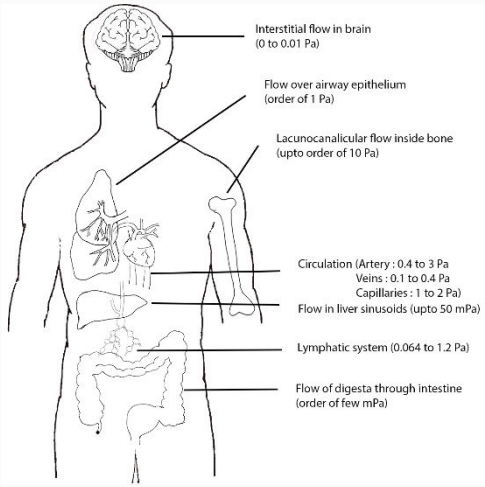
White, 2011



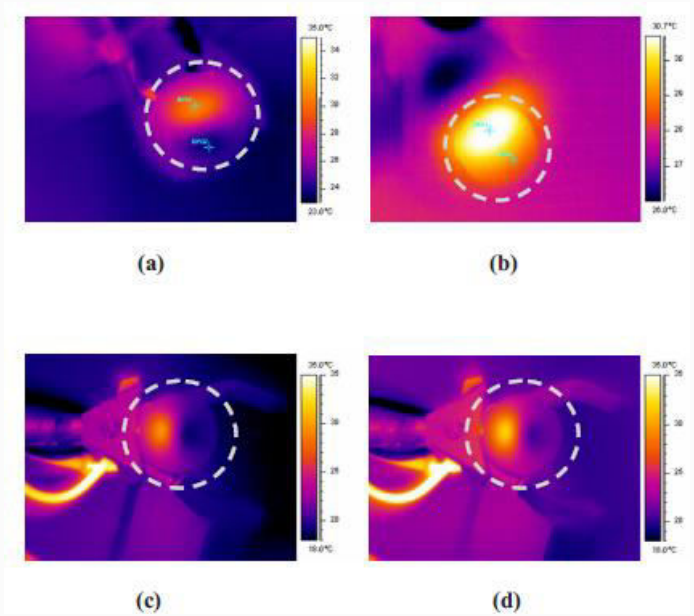
Organs	pH	Oxygen level	Microbial loads (CFU/ml)	Transit time	Digestive processes
Stomach			10^1-10^3	15-150 min	• Mechanical digestion *Peristaltic mixing* *Food breakdown* • Chemical digestion of proteins and lipids
Small intestine - Duodenum - Jejunum - Ileum			10^3-10^4 10^4-10^6 10^6-10^8	3-5 h	• Mechanical digestion *Peristaltic mixing and propulsion* *Segmentation* • Chemical digestion of carbohydrates, lipids, nucleic acids, polypeptides • Absorption of di-tripeptides, amino acids, glucose, fructose, vitamins, minerals and water
Colon			10^{10}-10^{12}	24-96 h	• Mechanical digestion *Segmental mixing and propulsion* • Fermentation (short chain fatty acids production) • Absorption of ions, minerals, vitamins, water and organic molecules

Jubelin *et al;* 2018





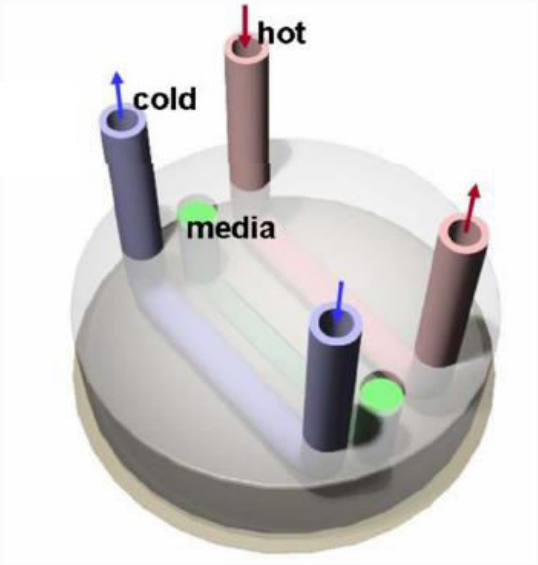
Thermotaxis of Breast Cancer Cells

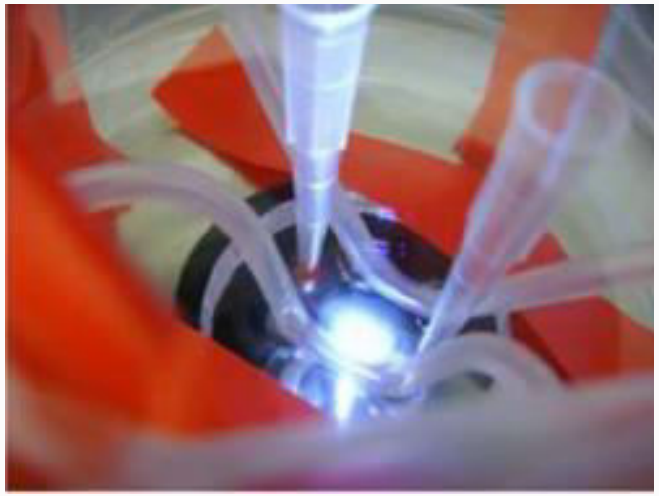


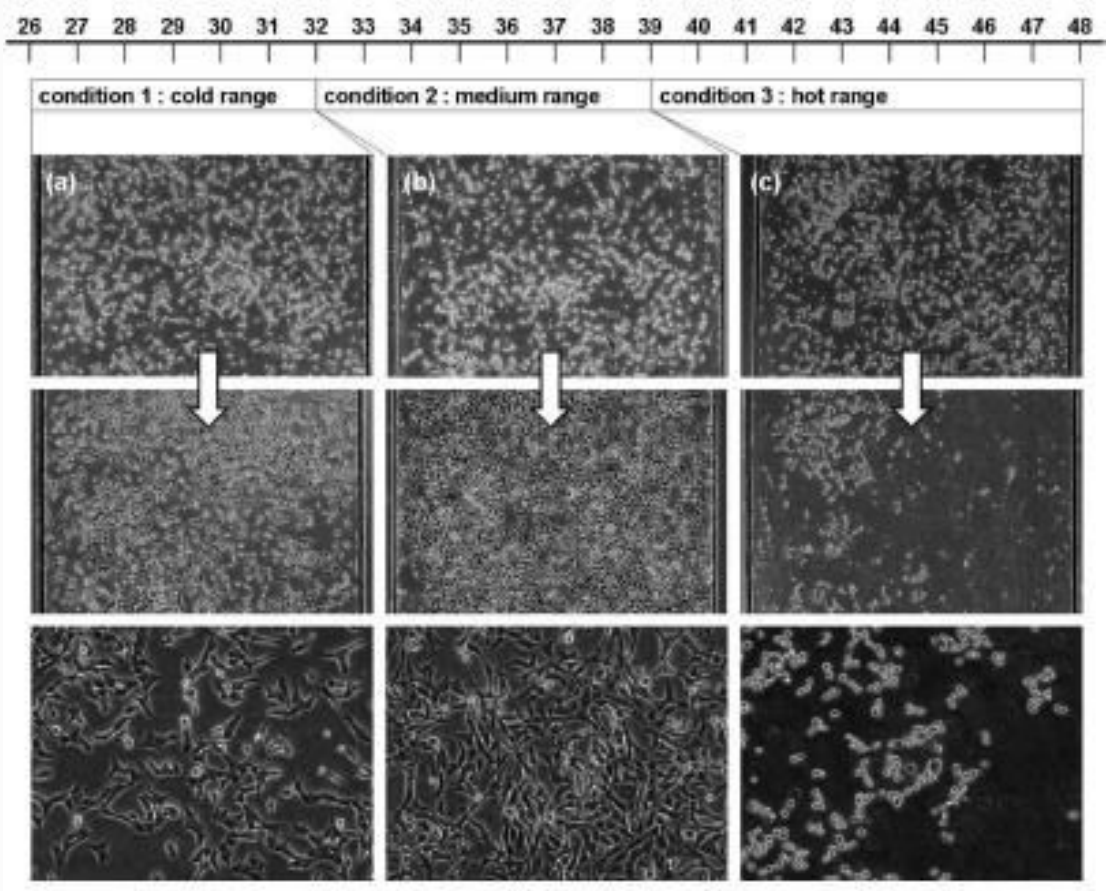
Journal: Biomicrofluidics, 2, 034106, 2008

Title : A microfluidic platform for studying the effects of small temperature gradients in an incubator environment

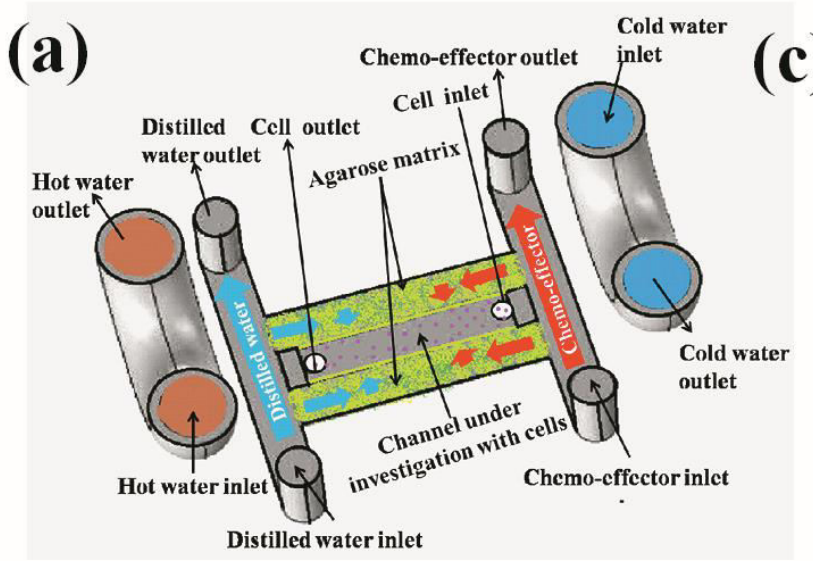
Authors: **Sarit K. Das,** Seok Chung, Ioannis Zervantonakis, Joseph Atnafu and Roger D. Kamm

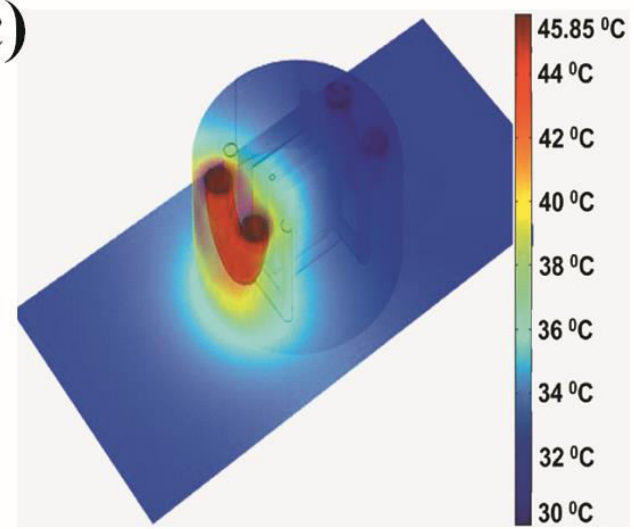


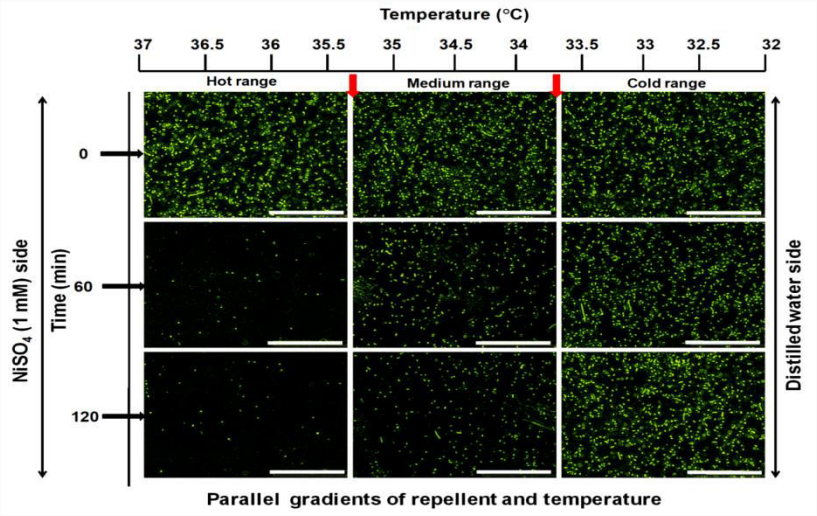




Chemical and Temperature - Parallel and Opposing Gradients

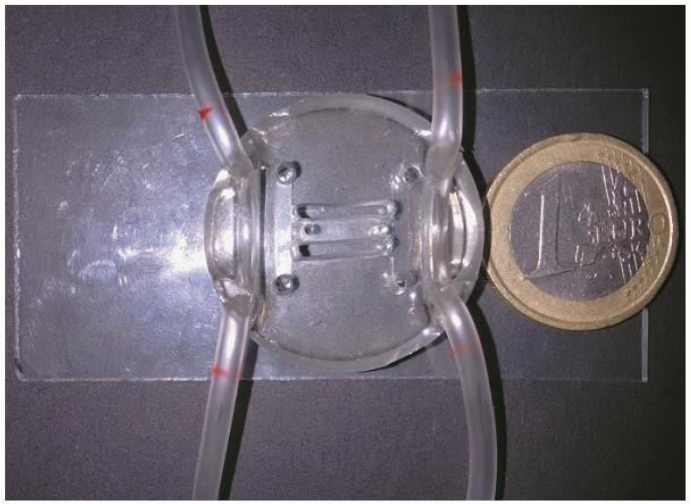




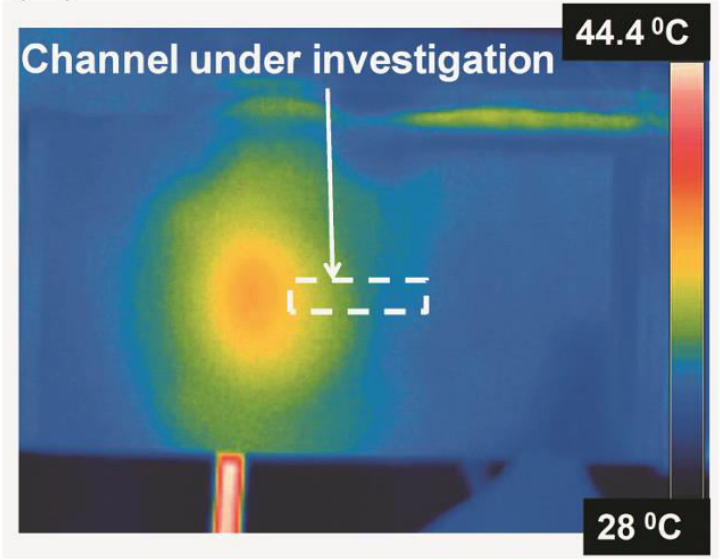


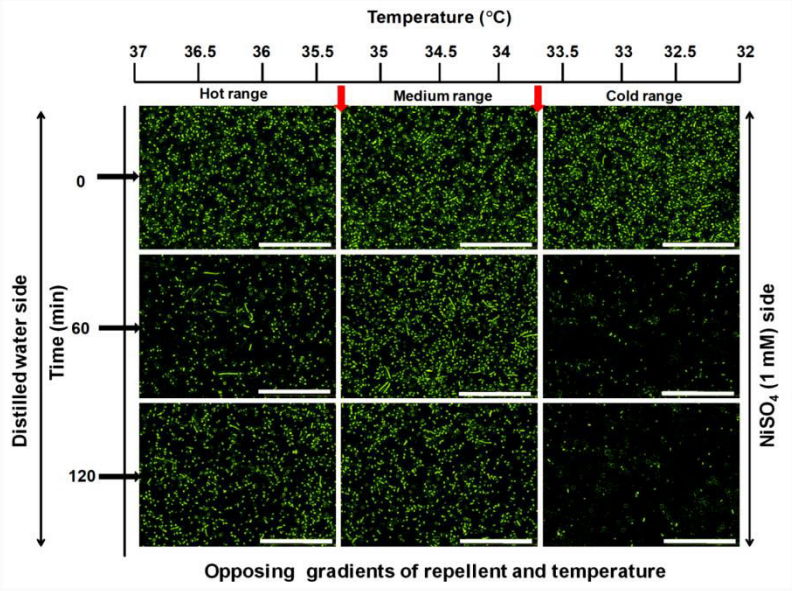
Scale bar: 100 µm

(b)



(d)

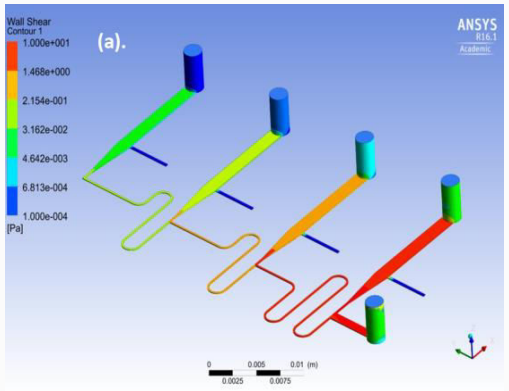


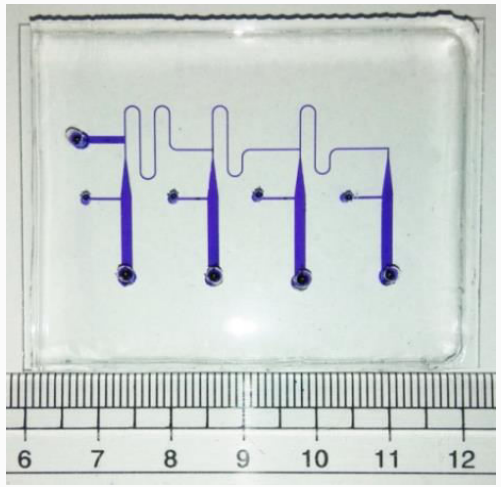


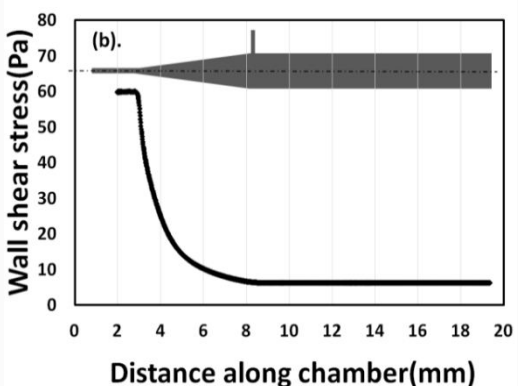
Scale bar: 100 µm

Murugesan et al. 2016 and 2017

Influence of Flow Induced Shear Stress (FSS) in Human body

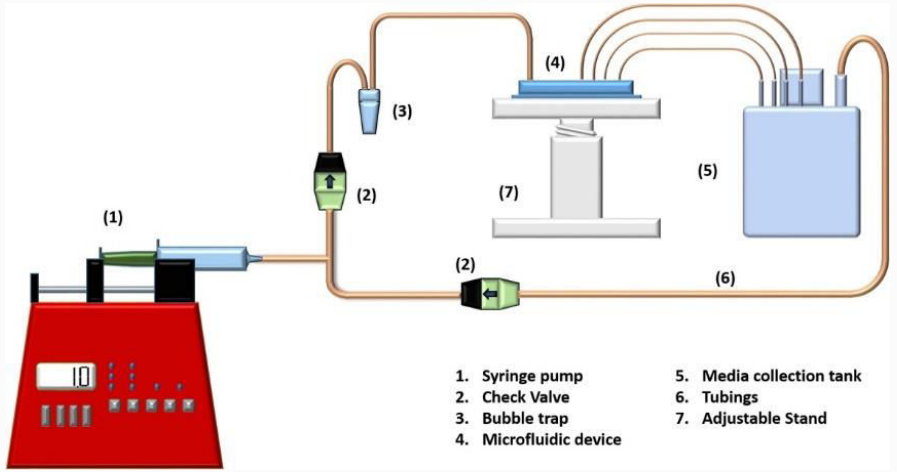




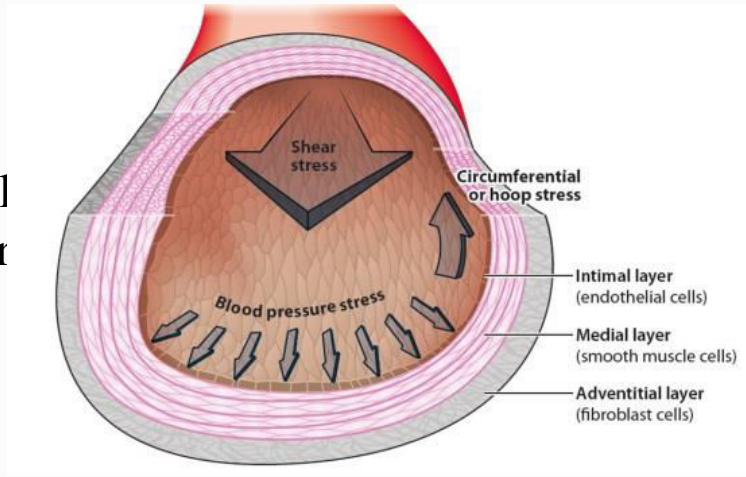


Mechanotransduction:

Mechanism by which cells convert mechanical stimulus (tension, compression, pressure, fluid shear stress etc.) into chemical activity.

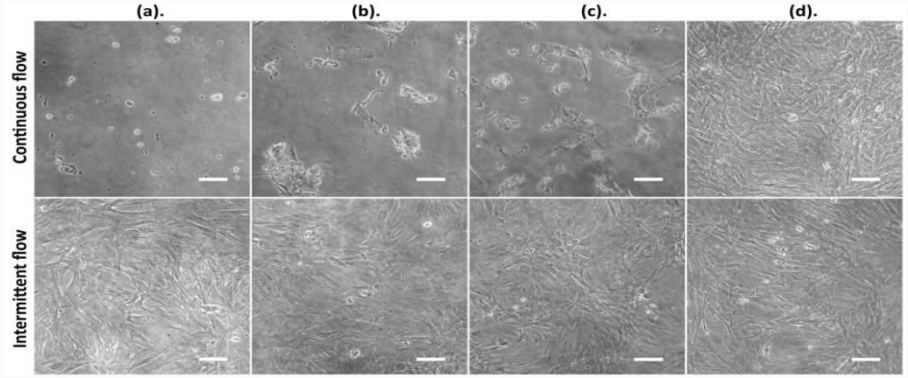


Bubble trap



Courtesy: Google images

Flow rate -160 µl/min (to get shear stresses of 1.03 Pa, 101.9 mPa, 10 mPa and 1.09 mPa in champers 1,2, 3 and 4 respectively)



(1.03 Pa) (101.9 mPa) (10 mPa) (1.09 mPa)

4 days of flow with silane coating (scale bar =100 µm)

- Cell detachment in continuous flow even after silane coating
- Healthy and proliferating cells in all intermittent flow chambers
- No noticeable cell alignment

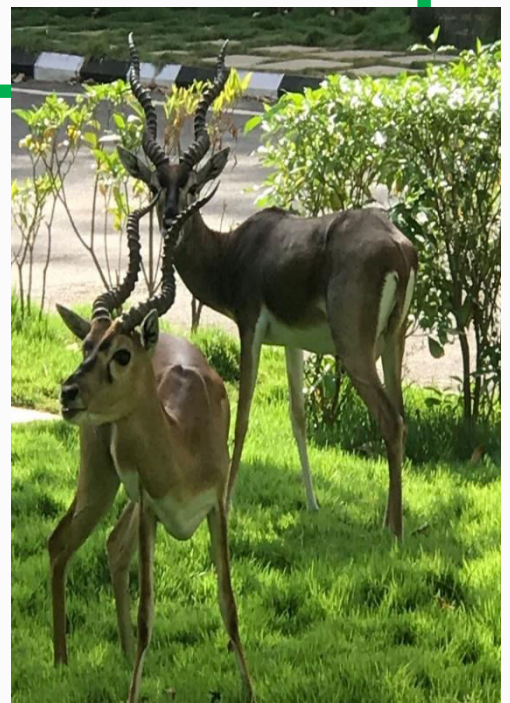
Dash et al., 2020

1. **Lab-on-a-chip - may one day commonly be used as a rapid risk assessment tool in medical practitioner's offices and as personal risk assessment tool at home.**

2. **With the advent of Organ-on-a-chip / Body-on-a-chip, drug screening, development and validation can be carried out without sacrificing the lives of animals and terminally ill humans.**

The engineers, chemists, biologists, mathematicians, entrepreneurs, business people, government, medical practitioners and healthcare workers should work together to bring healthcare solutions in the future.

Thank you



SKD Group, IIT Madras

Questions?