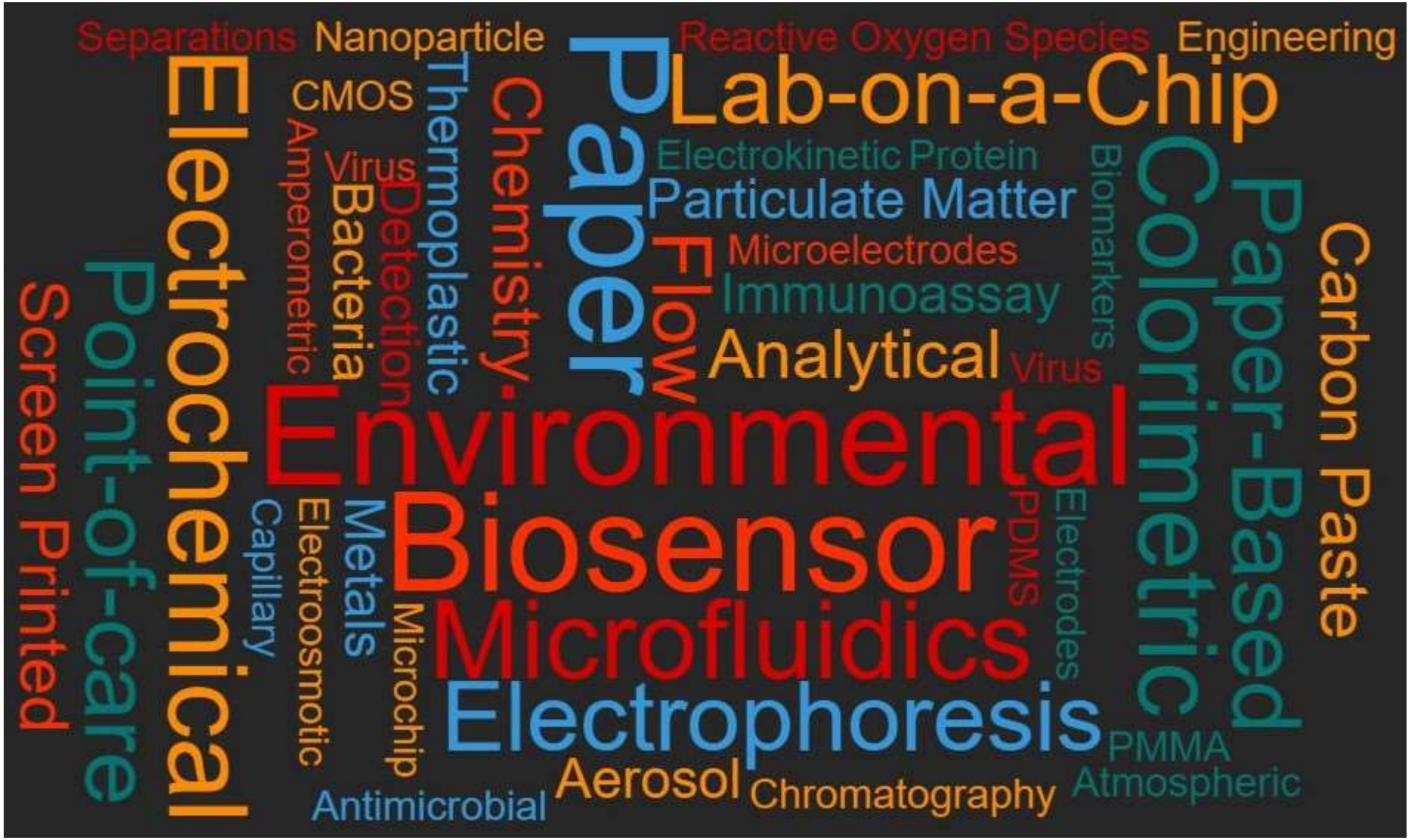
LAB-ON-A CHIP DEVICES FOR QUICK MEDICAL DIAGNOSTICS



COMPILED BY HOWIE BAUM

POINT OF CARE (POCT) TESTING

POCT consists of FAST medical diagnostic testing performed close to the patient, instead of a traditional centralized hospital lab or offsite laboratory .

It includes Lab-on-a- Chip devices and many other types.

In clinical diagnostics, it is the fastest-growing segment.

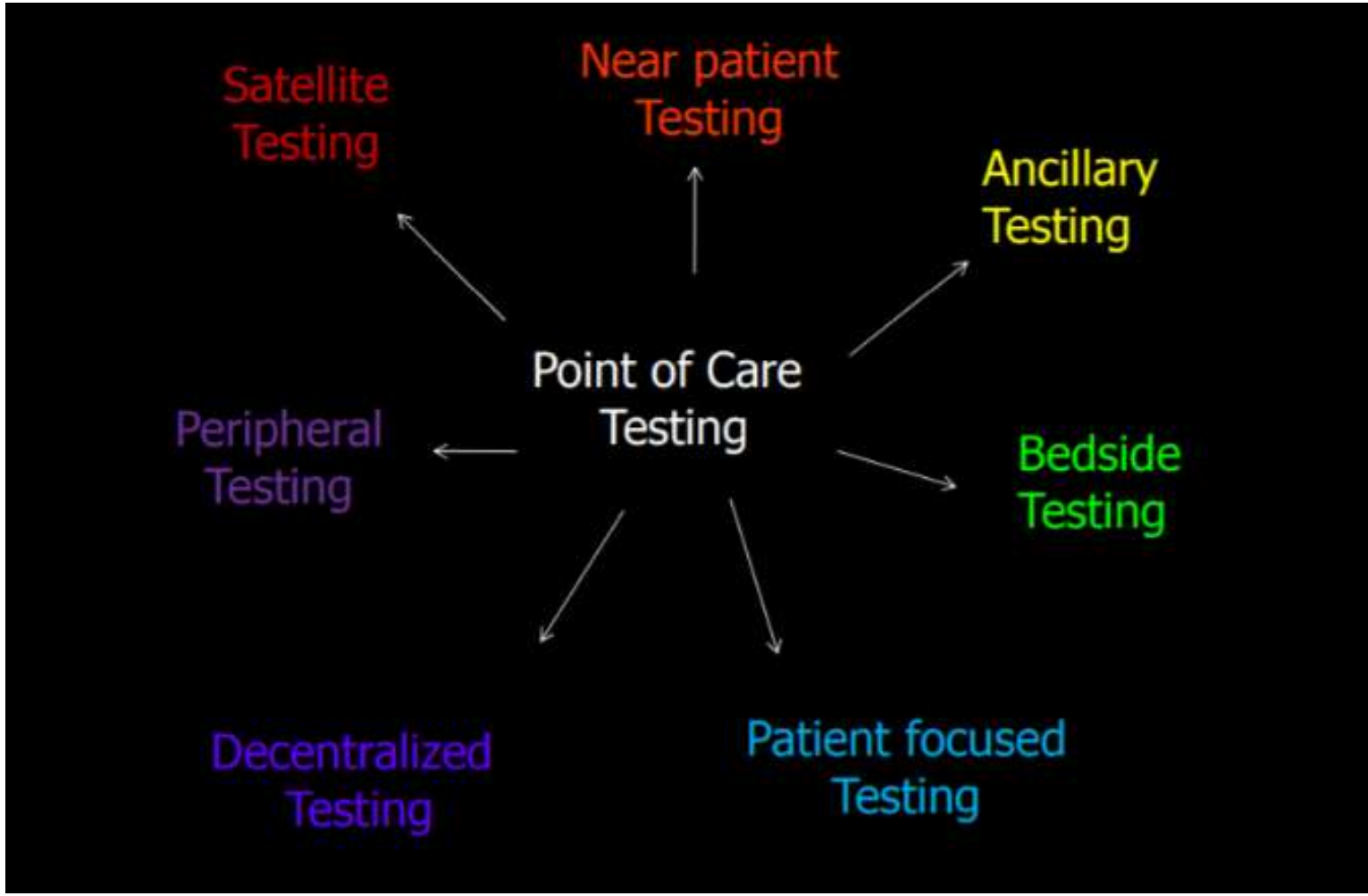
It enables improved patient outcomes, increased patient access, lower total cost of care, and a shorter time for a diagnosis.

POINT-OF-CARE TESTING (POCT)

It is also known as remote testing, rapid diagnostics, near-patient testing, bedside testing, or satellite testing.

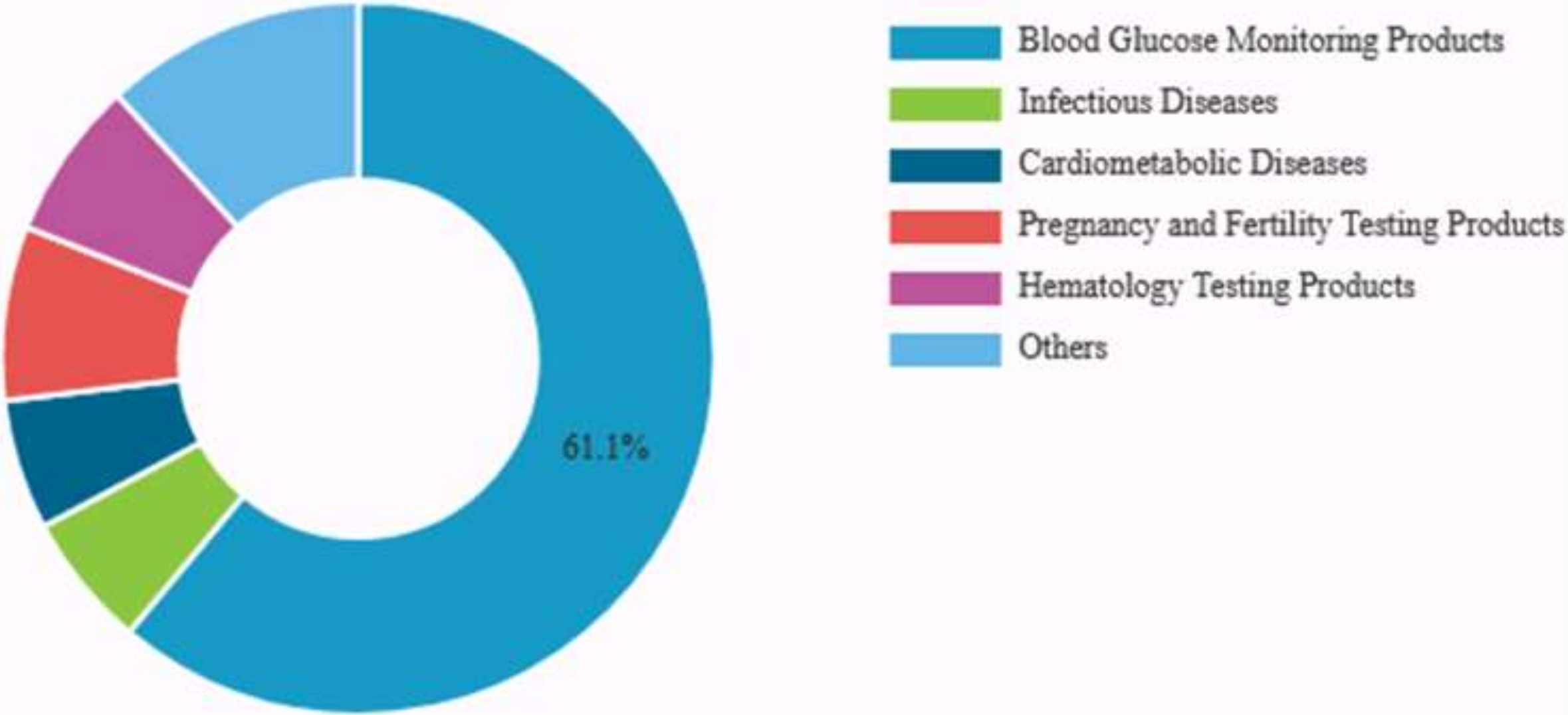
It could be done at a health clinic, at home, in an ER room, in an ambulance, at an accident scene, on an airplane - essentially anywhere.

Many point-of-care tests can give a patient results (and in some cases diagnoses) quickly so that treatment or a consultation with a Doctor can be provided quickly.



- **POCT is currently routine in all hospitals and for some home use applications.**
- **POC tests can potentially empower patients to self-test in the privacy of their homes, especially for stigmatized diseases such as HIV.**
- **The global point of care diagnostics market size was valued at $18.8 billion dollars in 2019.**
- The integration of **Electronic Health Records (EHR**) and **Picture Archiving and Communication System (PACS)** has revolutionized the market for point of care diagnostics or testing.

Global Point of Care (POC) Diagnostics Market Share, By Product, 2018



THE VALUE OF QUICK MEDICAL DIAGNOSTIC TESTING

1) Medical diagnostics testing influences approximately 70% of health care decisions.

2) Non-communicable diseases (NCDs) kill more than **36 million** people each year, such as Alzheimer's disease, amyotrophic lateral sclerosis (ALS), arthritis, etc.

3) **Some 80% of all NCD deaths occur in low- and middle-income countries so** it is important to create devices with low costs, low power consumption, and robustness.

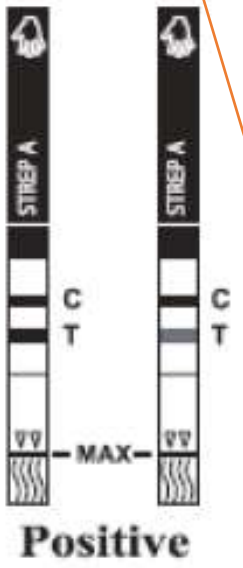
4) Many of these devices should also be usable in places where there are few trained health care workers, and where parts, supplies and maintenance are very difficult to obtain.

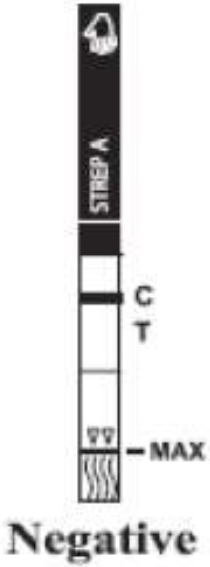
THE INTERESTING ASPECTS OF POINT OF CARE MEDICAL TESTING

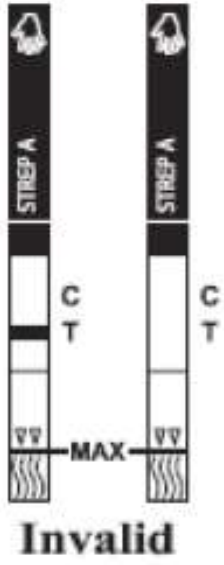
1) **They are usually small devices like a bio-chip or a paper strip that can quickly detect one or a wide range of medical conditions at one time.**

2) They give a quick indication of a possible problem so a person can go to their doctor to get it diagnosed for early treatment.

3) **It allows physicians and medical staff to accurately achieve real-time, lab-quality diagnostic results within minutes rather than hours.**



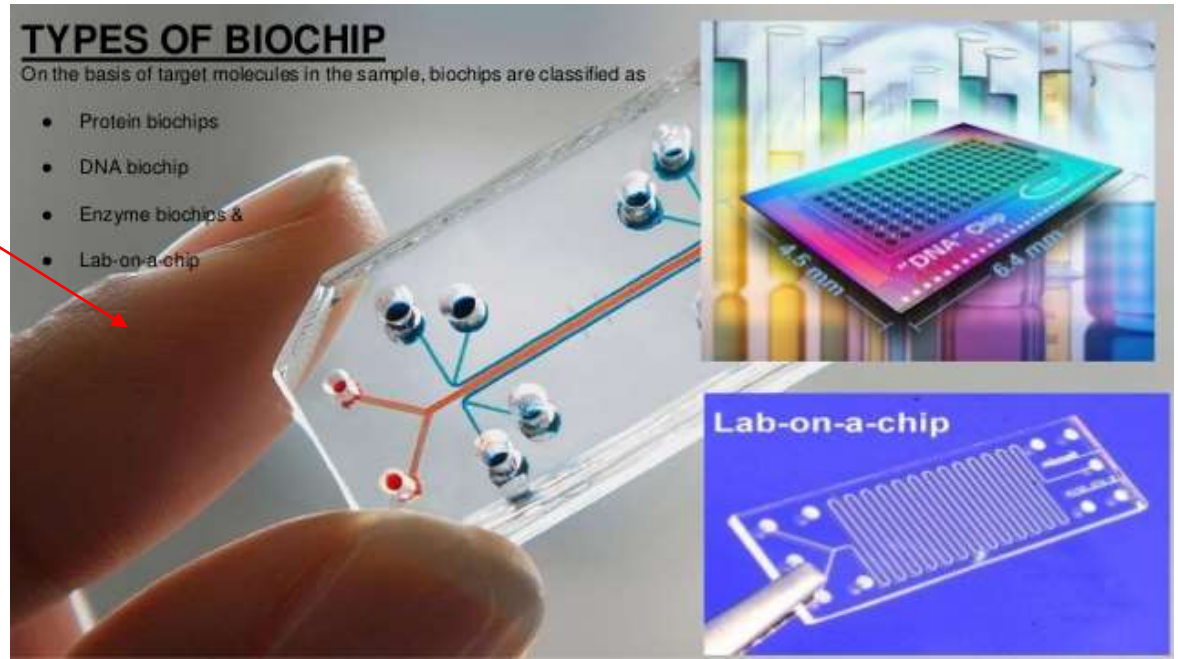




TWO BROAD TYPES OF DEVICES FOR POINT OF CARE (POC) TESTING

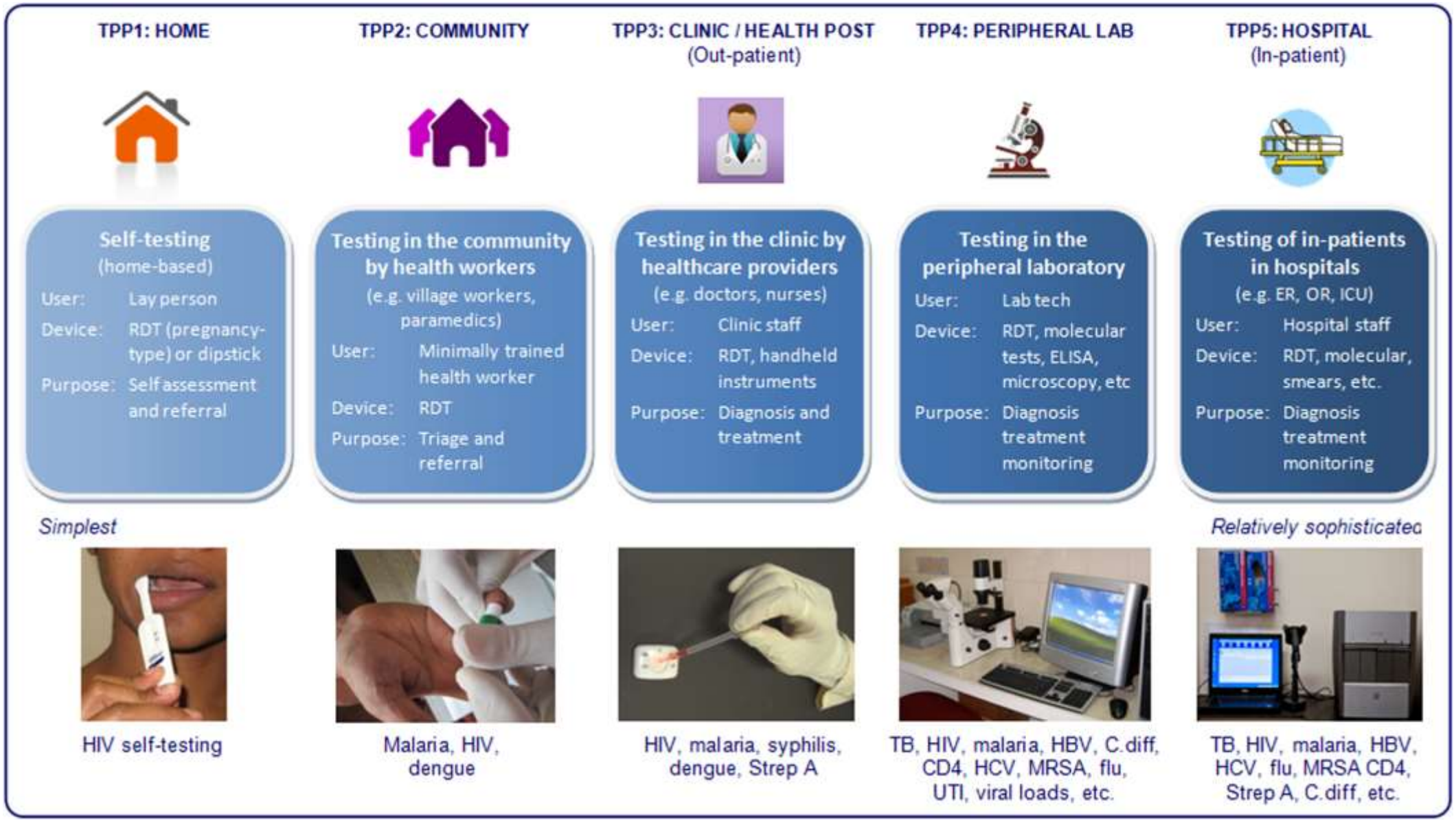
1) **Small bench top analyzers** (for example, blood gas and electrolyte systems)

2) **Hand held, single use chip or paper devices** (for urine albumin, blood glucose, blood coagulation and many other types of tests)



THIS PRESENTATION FOCUSES ON THESE TYPES OF DEVICES

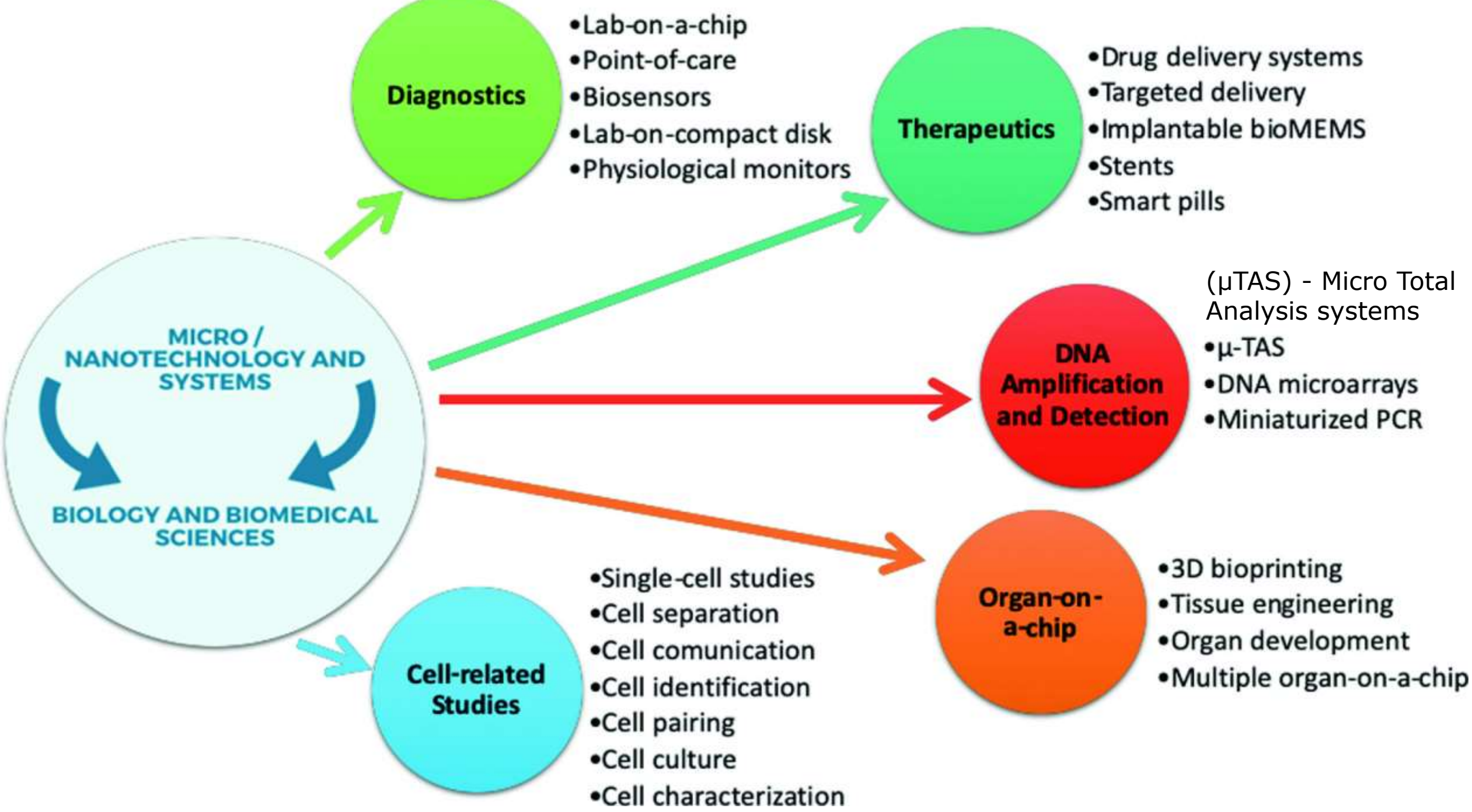
DIVERSITY OF TARGET PRODUCT PROFILES, USERS, AND SETTINGS WITHIN THE SPECTRUM OF POC TESTING



RDT – Rapid Diagnostic Test

WHAT KIND OF MEDICAL CONDITIONS CAN BE CHECKED ?

- Infectious diseases
- Blood Glucose (for persons with diabetes)
- Cholesterol
- Cancer (tumor marker testing)
- Pregnancy
- Strep–Group A streptococcus bacteria
- Flu (Influenza) virus
- **Covid-19 virus**
- Urinary Tract Infection (UTI)
- Anemia
- Cardiac marker
- MRSA
- Electrolytes analysis
- Drug abuse
- Malaria
- HIV
- Dengue Fever
- Hepatitis
- DNA analysis
- RNA analysis
- Tumor Marker
- Blood Coagulation
- Animal or person tracking
- Ph of body fluid (acidic or basic)
- Enzyme analysis
- Blood gases
- Food pathogens screening
- Hemoglobin diagnostics


MICRO / NANOTECHNOLOGY AND SYSTEMS
BIOLOGY AND BIOMEDICAL SCIENCES
Diagnostics
•Lab-on-a-chip
•Point-of-care
•Biosensors
•Lab-on-compact disk
•Physiological monitors
Therapeutics
•Drug delivery systems
•Targeted delivery
•Implantable bioMEMS
•Stents
•Smart pills
(µTAS) - Micro Total Analysis systems
DNA Amplification and Detection
•µ-TAS
•DNA microarrays
•Miniaturized PCR
Cell-related Studies
•Single-cell studies
•Cell separation
•Cell comunication
•Cell identification
•Cell pairing
•Cell culture
•Cell characterization
Organ-on-a-chip
•3D bioprinting
•Tissue engineering
•Organ development
•Multiple organ-on-a-chip

Advantages

Reduced tum around time

Improved patient morbidity & mortality
Reduction in hospital admission

Improved interaction between patient and carer

Reduction in clinical visits

Improved cost of care

Reduction in administrative work associated With test requesting & reporting

Disadvantages

Increase in administrative work associated with training and Certification of operators

Caregivers required to perform test

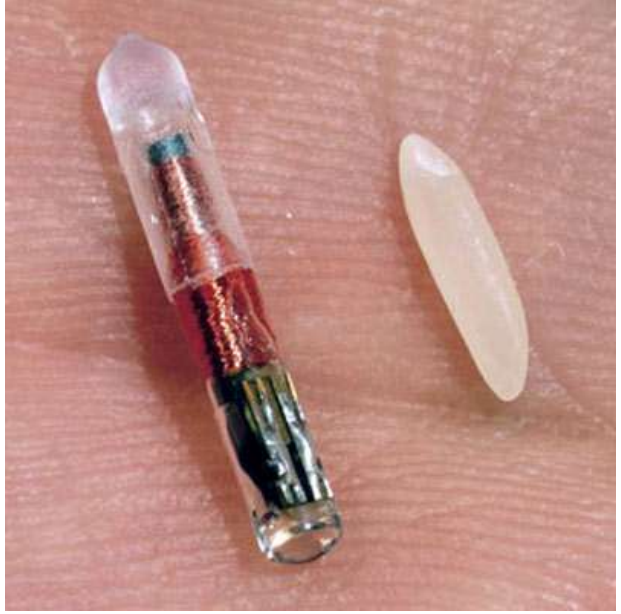
Increased risk of errors

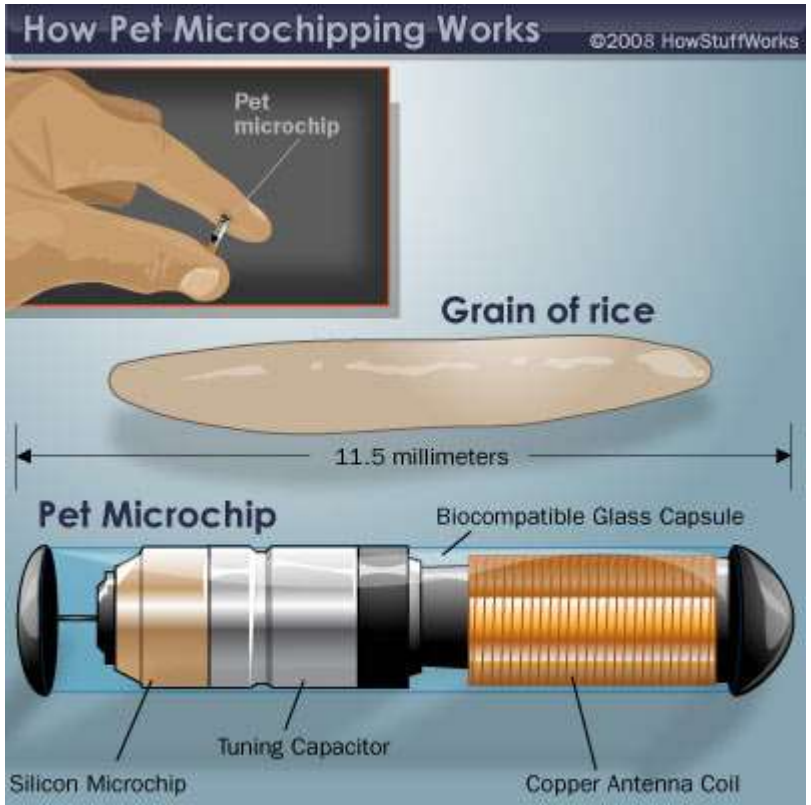
THESE ARE NOT THE KIND OF BIO-CHIPS WE ARE TALKING ABOUT !! 😊

WHAT COMES TO MIND WHEN YOU HEAR THE WORD MICROCHIP ?

1) If you have a dog or cat, you may have had a microchip implanted under the animal's skin, which is a little longer than a grain of rice. It identifies them in case they get lost.

2) Sometimes, one may be put into a human's hand, in case they have Alzheimer's disease or another form of Dementia, and may wander at times.





KEVIN WARWICK – THE FIRST PERSON TO GET A MICROCHIP IMPLANT

In 1998, Kevin Warwick, a British scientist known as "Captain Cyborg," became the first human to receive a microchip implant.

On August 24, 1998, he had a simple Radio Frequency Identification Device (RFID) implanted beneath his skin which he uses to control doors, lights, heaters, and other computer-controlled devices where he works, lives, and he can also use it to pay for things at stores and some kiosks.

BLOOD GLUCOSE LEVEL TESTING FOR DIABETICS

Blood glucose (blood sugar) monitoring is the primary tool people have to find out if their blood glucose levels are within a healthy range.

HOW DO DIABETES TEST STRIPS WORK?

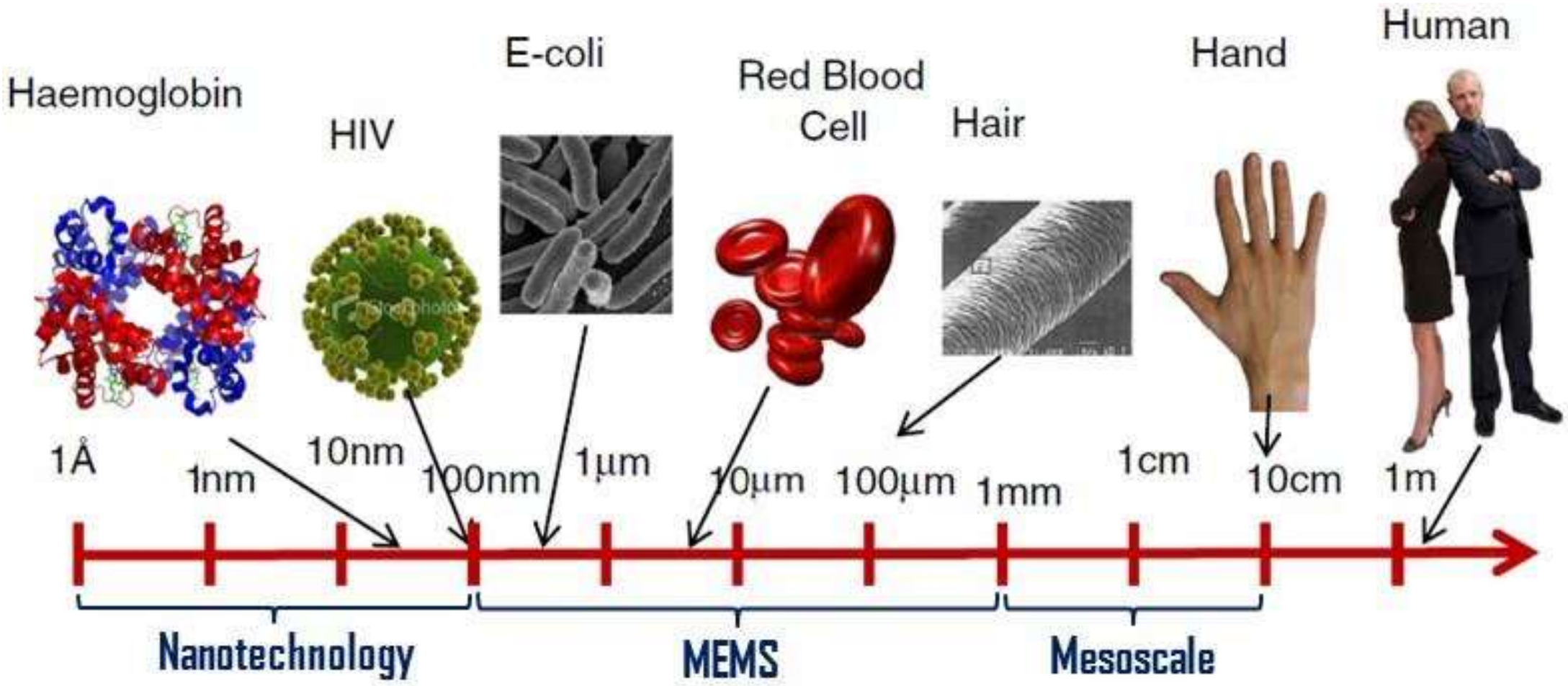
When blood is placed onto the special paper test strip, it reacts with a chemical called glucose oxidase producing gluconic acid from the glucose in the blood.

At the other end of the test strip, the meter transfers a current to it. The test strip has electric terminals which allow the meter to measure the current between the terminals.

The current between the terminals changes depending on the level of gluconic acid that has been produced.

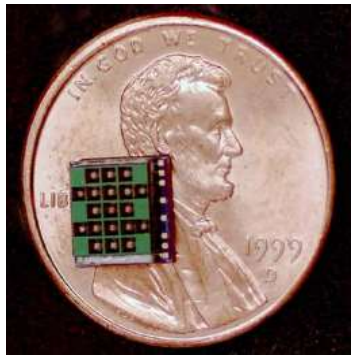
The blood glucose meter then uses an algorithm to work out the blood glucose level based upon the difference in current.

MICRO ELECTROMECHANICAL SYSTEMS (MEMS)

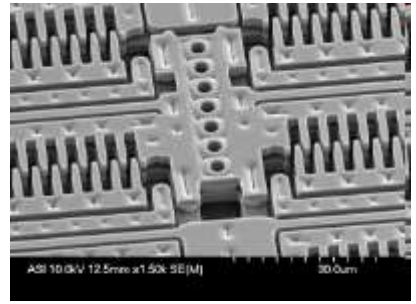


What are MEMS?

- **M**icro(small)



- **E**lectro(electric components/functionality)



http://www.memx.com/

- **M**echanical(mechanical components/functionality)

http://www.memx.com/

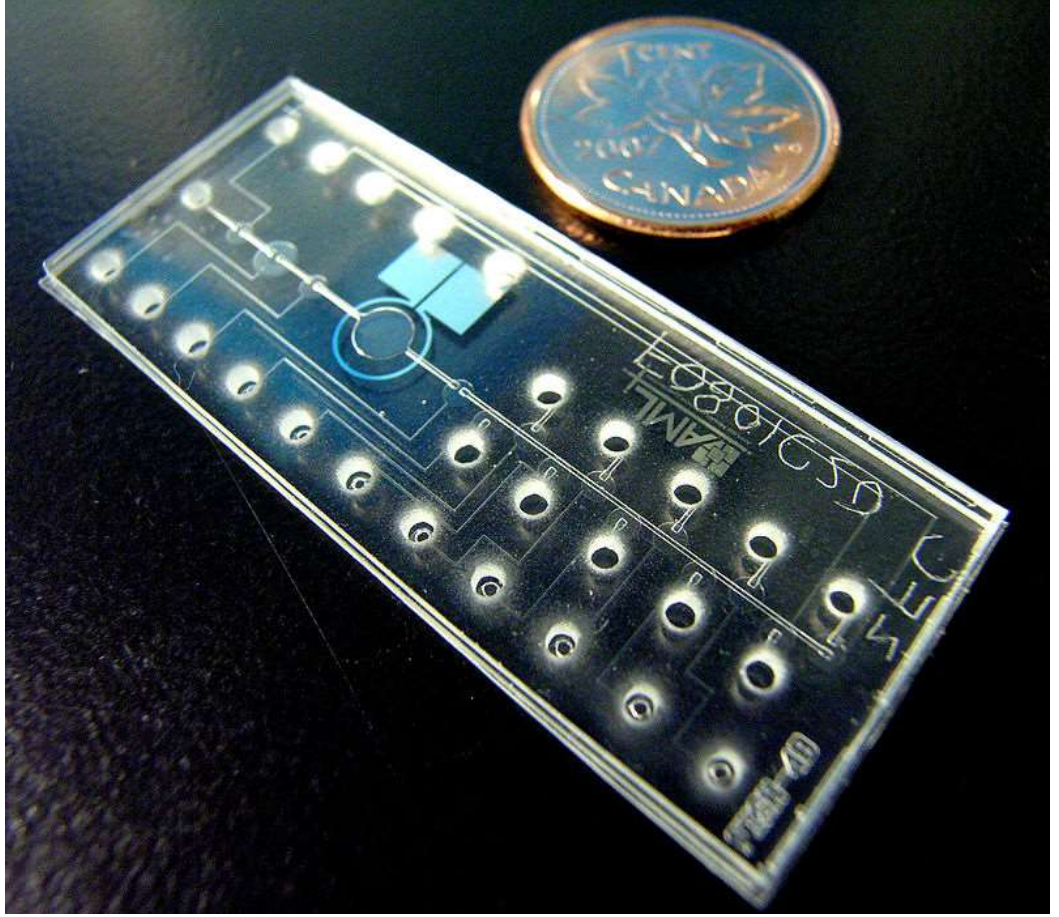
- **S**ystems(integrated, system-like functionality)

Bio-MEMS is an abbreviation for biomedical (or biological) micro-electro-mechanical systems.

Bio-MEMS have considerable overlap, and is sometimes considered synonymous, with lab-on-a-chip (LOC) and micro total analysis systems (μTAS).

Bio-MEMS is typically more focused on mechanical parts and microfabrication technologies made suitable for biological applications.

On the other hand, lab-on-a-chip is concerned with miniaturization and integration of laboratory processes and experiments into single (often microfluidic) chips.



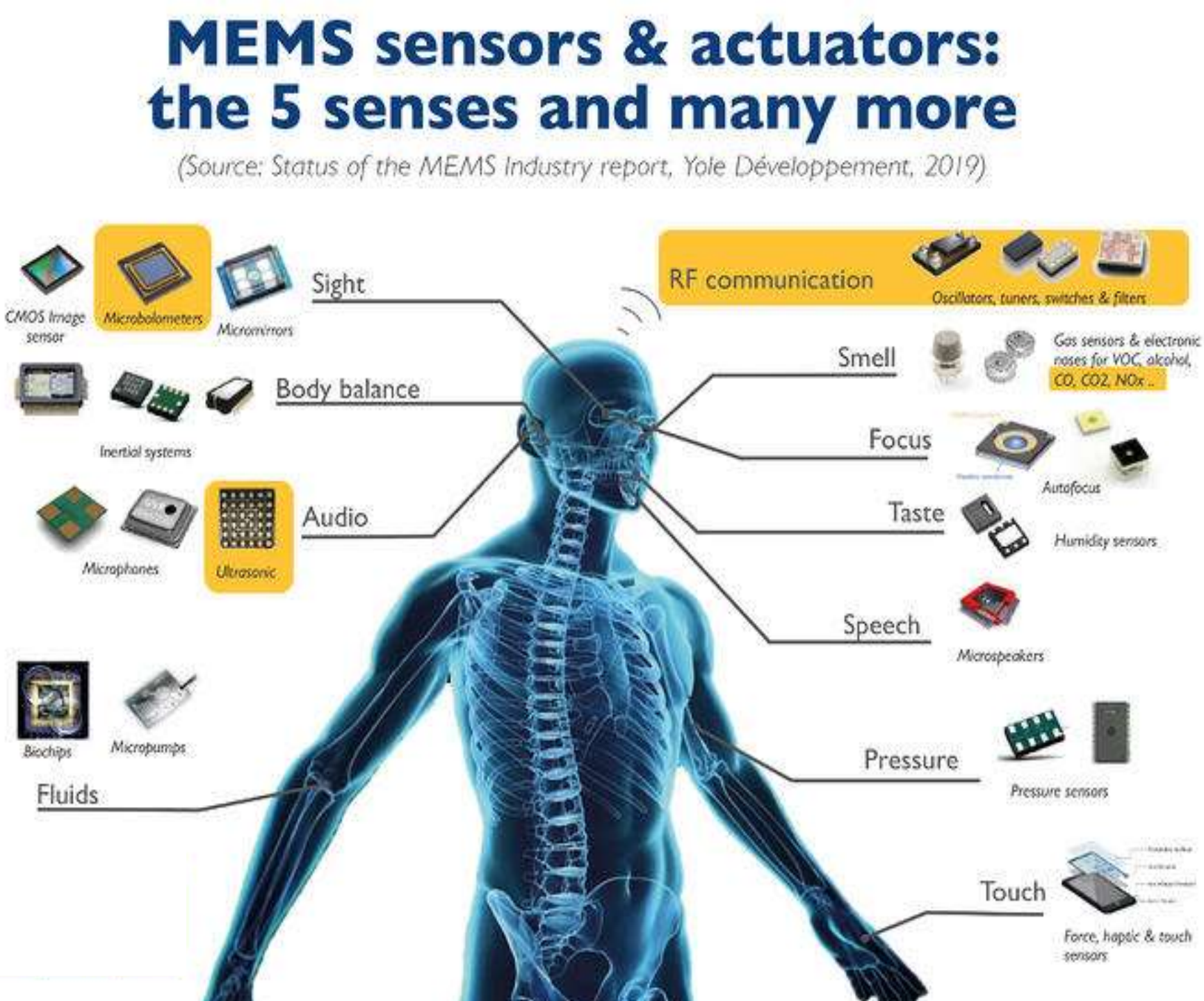
An example of a bio-MEMS device is this automated FISH microchip, which integrates reagent multiplexer, a cell chamber with a thin-film heater layer, and a peristaltic pump.

FISH stands for Fluorescence *in situ* hybridization and is a molecular technique that uses fluorescent probes.

BIO-MEMS MARKET VALUE

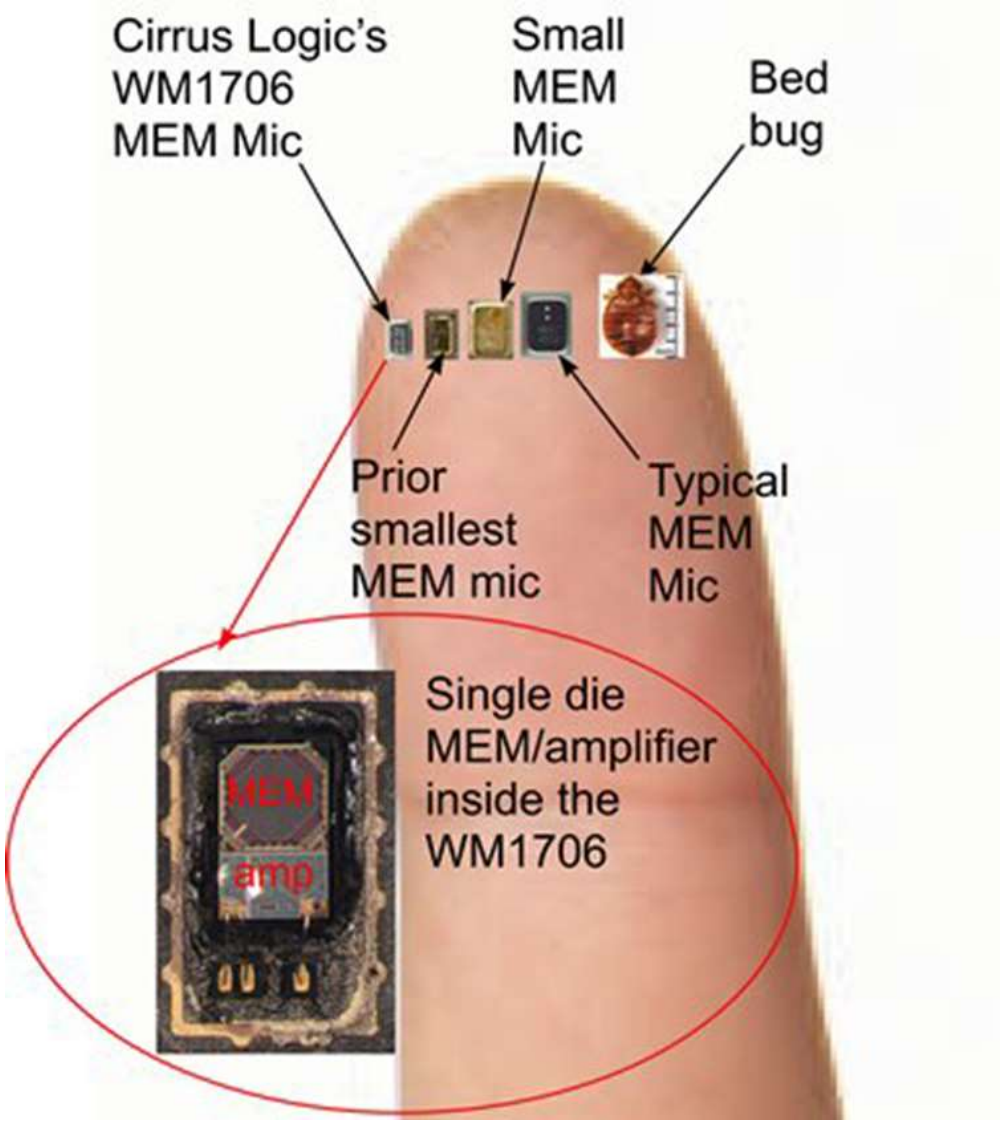
The value of the BIO-MEMS-only market reached $11.6 billion in 2018, with consumer applications accounting for more than 60% of the total market.

https://www.youtube.com/watch?v=tOg1ClLF2Gk
10 minutes



COMMERCIAL APPLICATIONS OF BIO-MEMS INCLUDE:

- **Disposable pressure sensors for use in healthcare.**
- **Pedometer**
- **Blood pressure monitoring**
- **Early diagnosis of Glaucoma**
- **Used in hearing aid microphones**
- **Very small pumps for insulin infusion devices for diabetics**
- **Complex procedures such as DNA analysis**
- **Biomedical transducers medical implants**
- **Microsurgical tools**



Capsule Endoscopy

Devices used to perform endoscopy operations

				
Capsule	PillCam® SB 3 Given Imaging	EndoCapsule® Olympus America	MiroCam® IntroMedic Company	OMOM® Jinshan Science and Technology
Size *	Length: 26.2 mm Diameter: 11.4 mm	Length: 26 mm Diameter: 1 1mm	Length: 24.5 mm Diameter: 10.8 mm	Length: 27.9 mm Diameter: 13 mm
Weight	3.00g	3.50g	3.25-4.70g	6.00g
Battery life	8 hours or longer	8 hours or longer	11 hours or longer	6-8 hours or longer
Resolution	340x340	512x512	320x320	640x480
Frames per second	2 fps or 2-6 fps	2 fps	3 fps	2 fps
Field of view	156°	145 °	170°	140°
Communication	Radio frequency communication	Radio frequency communication	Human body communication	Radio frequency communication
FDA approval	Yes	Yes	Yes	No
Price per capsule	$500	$500	$500	$250

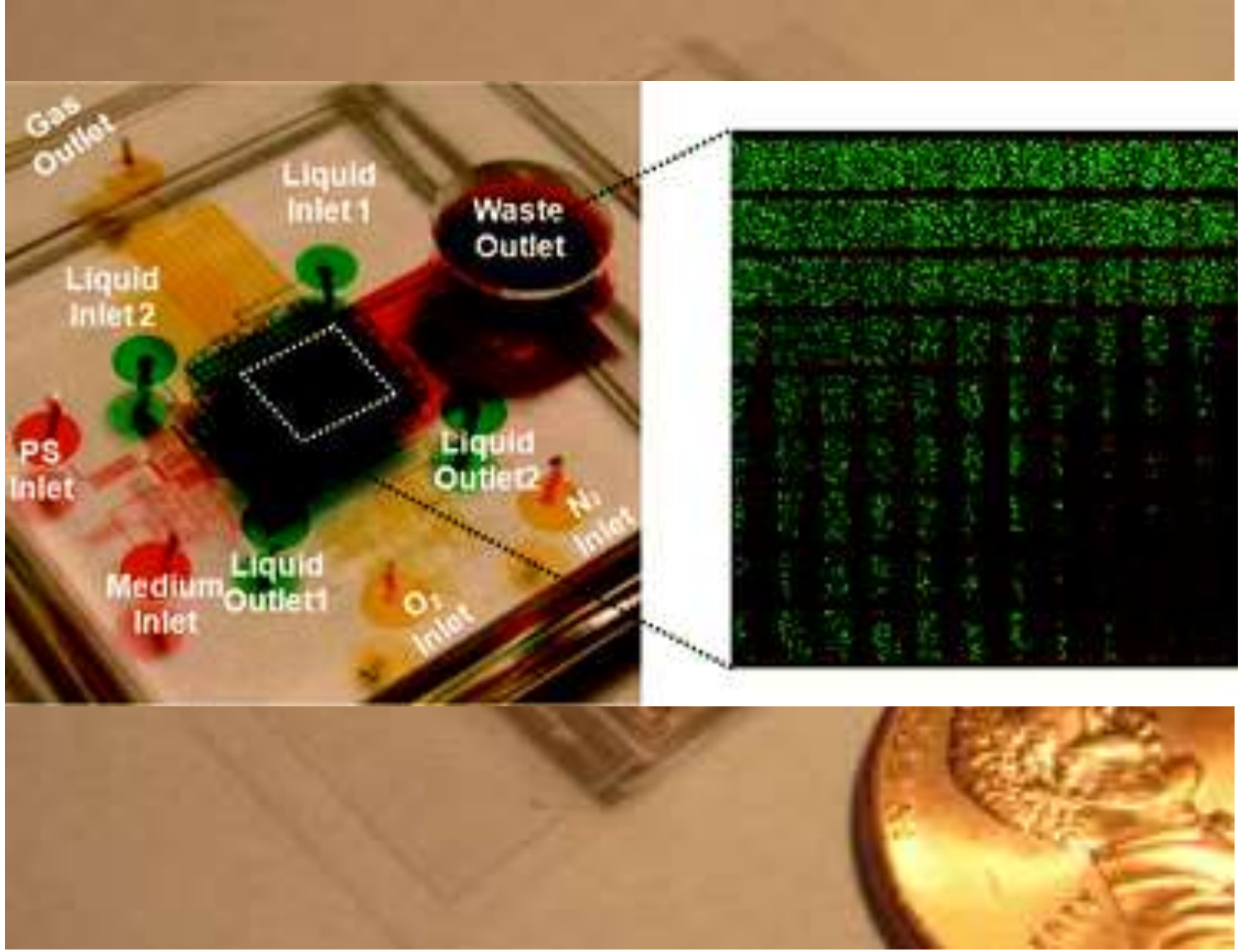
* 25 mm (**millimeters**) = 1 inch

PHOTODYNAMIC THERAPY FOR CANCER

One promising area of skin cancer treatment is photodynamic therapy (PDT), which combines the agents of a photosensitive drug, light, and oxygen to attack cancerous tumors and lesions on or just below the skin, by selective optical illumination.

The Biochip shown is for testing photodynamic therapy which uses a unique type of drug, called a photosensitizer, that generates high energy oxygen when activated by light, in this case an LED laser.

The oxygen reaction destroys cells locally only in the immediate surrounding area, which in this case is the tumor, without damaging other healthy cells.



The central testing area of this biochip is 5 square millimeters. The inside structure is comprised of 3 layers, each testing a key element of the therapy: drug, oxygen, and light.

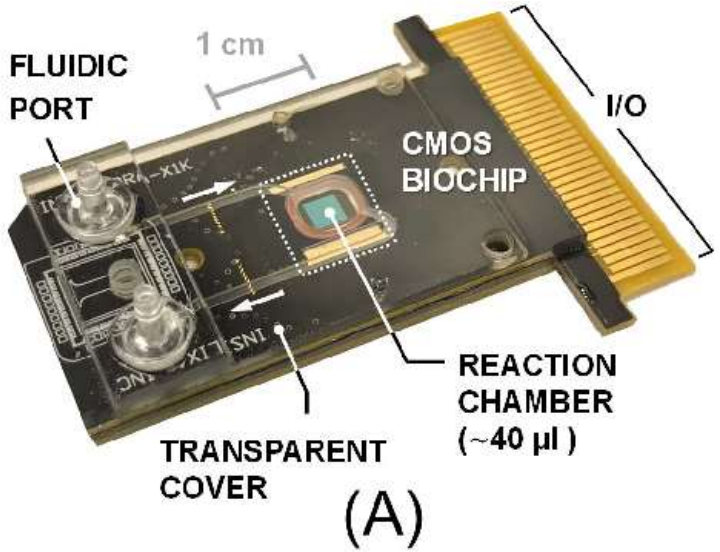
CMOS FLUORESCENCE BIOCHIP FOR DNA AND RNA TESTING

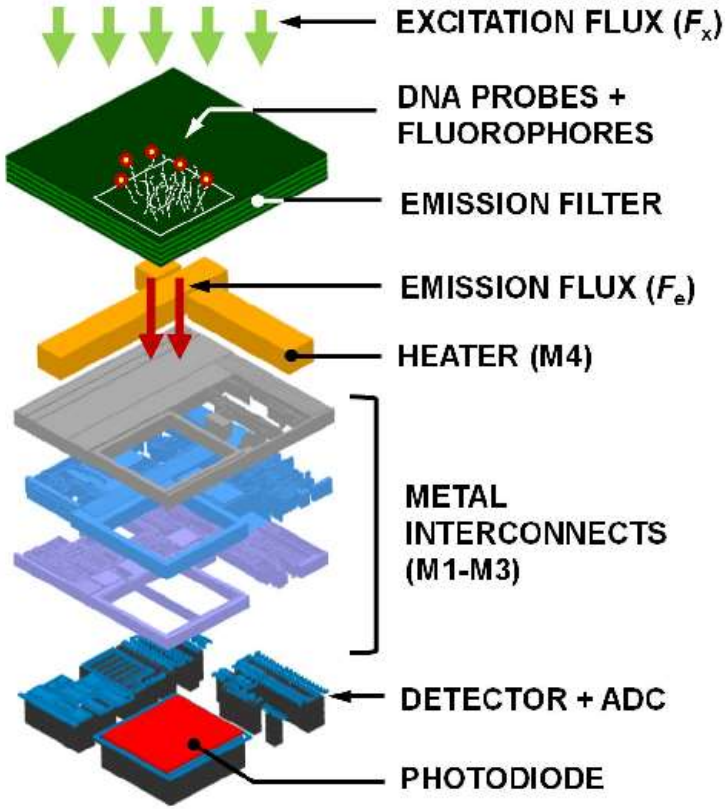
Design and successful implementation of a fully integrated **CMOS** fluorescence biochip for DNA and RNA.

The biochip includes a 32 × 32 array of fluorescence detection biosensing elements.

Each biosensing element is capable of having unique DNA probe sequences, an emission filter, a heater for thermal cycling, and a high performance and programmable photodetector.

CMOS – Complementary Metal Oxide Semiconductor

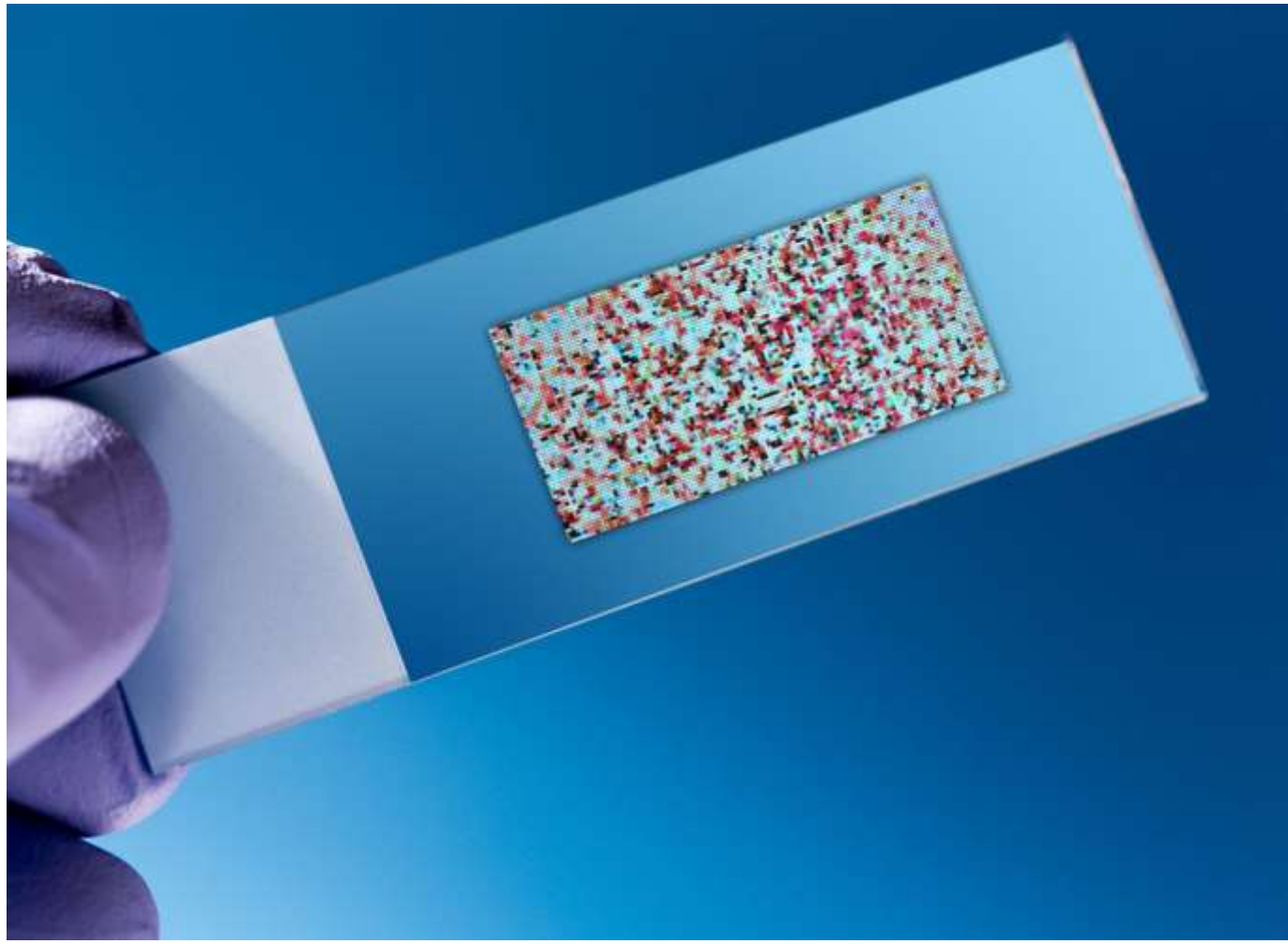




3D AND MULTI-DIMENSIONAL PRINTING OF BIOCHIPS

A new, potentially more efficient and cost-effective method for preparing biochips (also known as microarrays)

Researchers with the ASRC's Nanoscience Initiative detail how they have combined microfluidic techniques with beam-pen lithography and photochemical surface reactions to devise a new biochip printing technique.



Biological probes are patterned into biochips using nanoscopic light-pens (show in the highly magnified image at the right), allowing researchers to increase the number of probes that can be put onto a single chip.

The method involves exposing a biochip’s surface to specific organic reagents, and then using a tightly focused beam of light to adhere the immobilized reagents to the chip’s surface

Advanced Science Research Center at the Graduate Center, CUNY

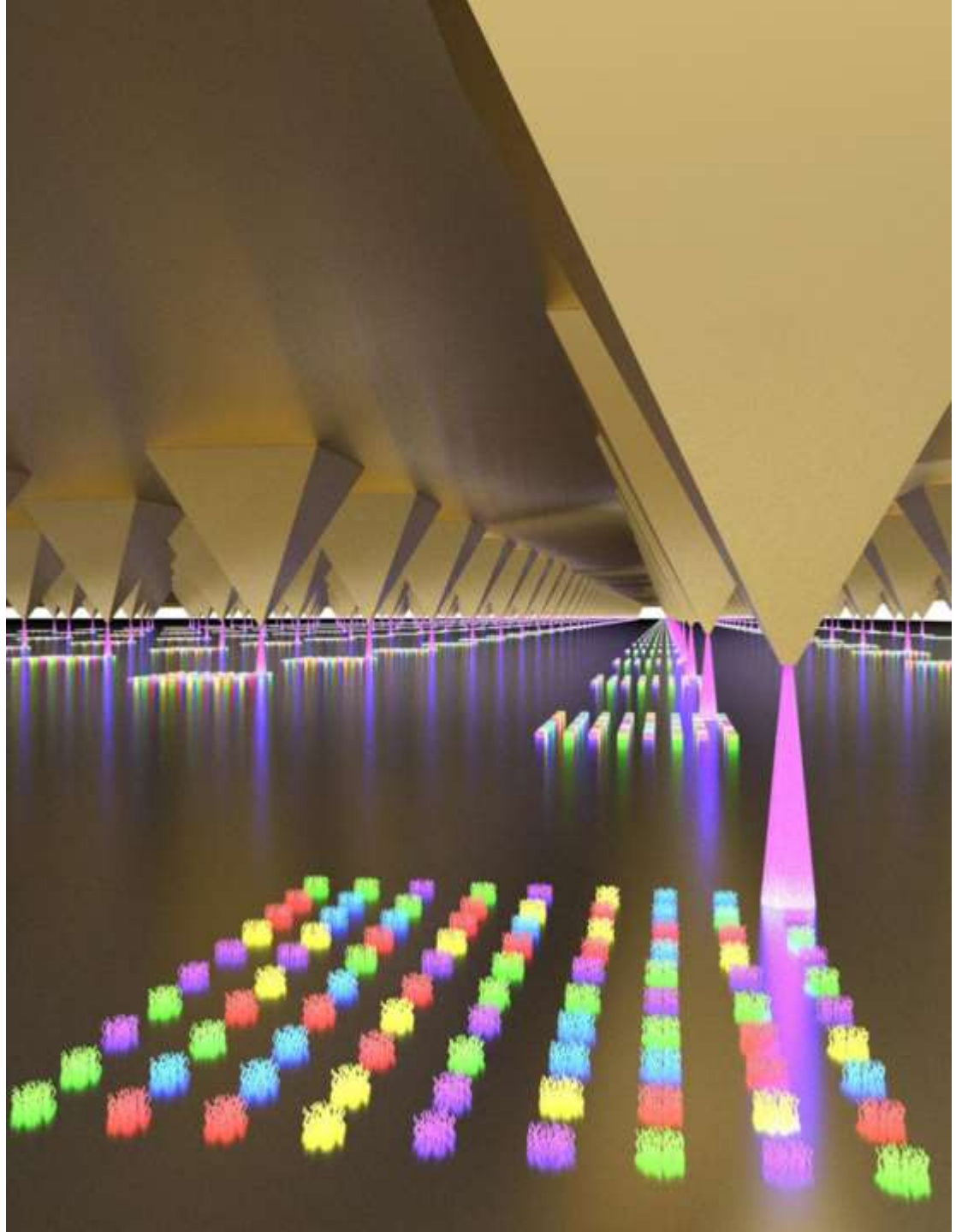
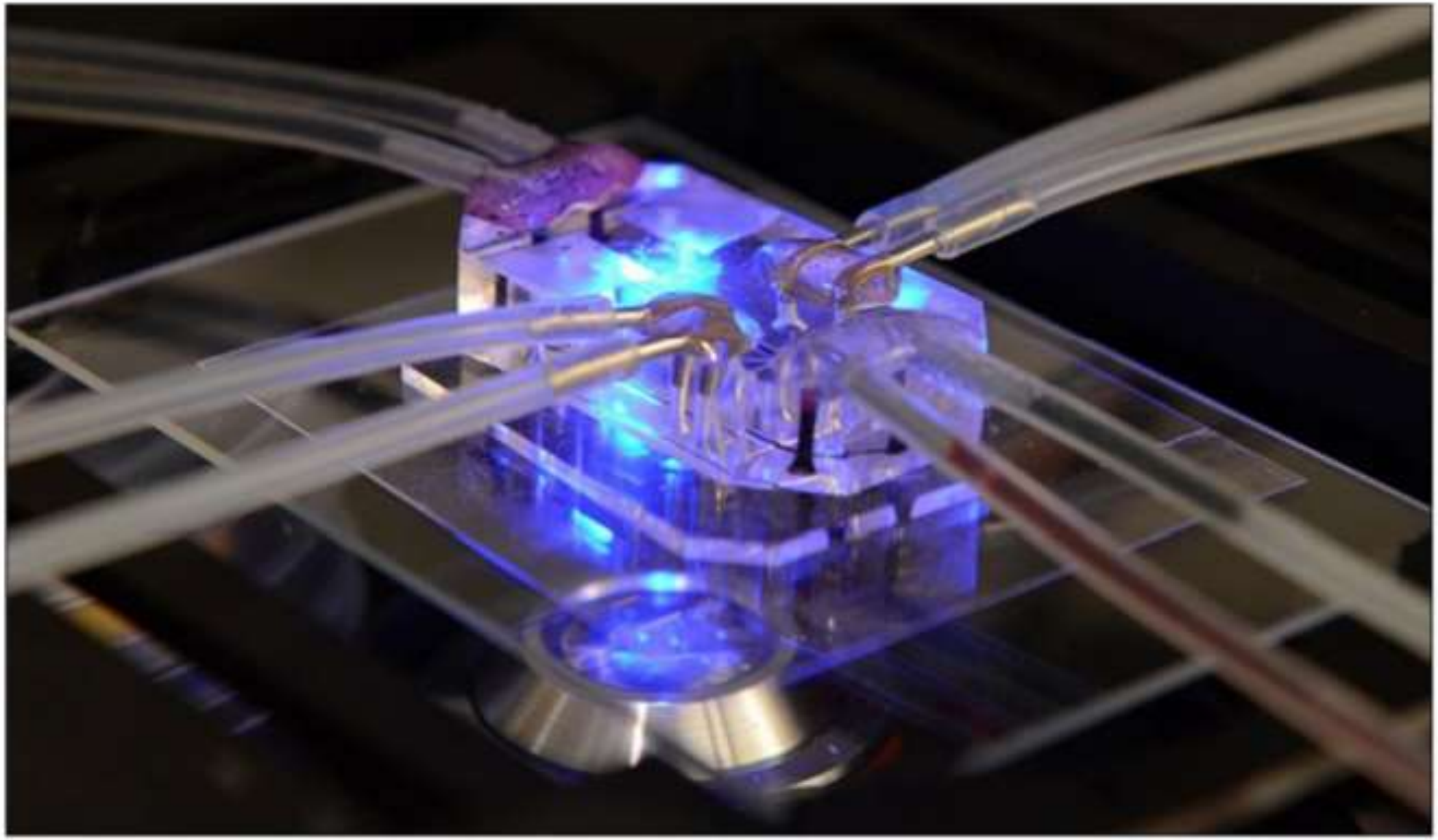


Figure 1: Example of a Tissue Chip



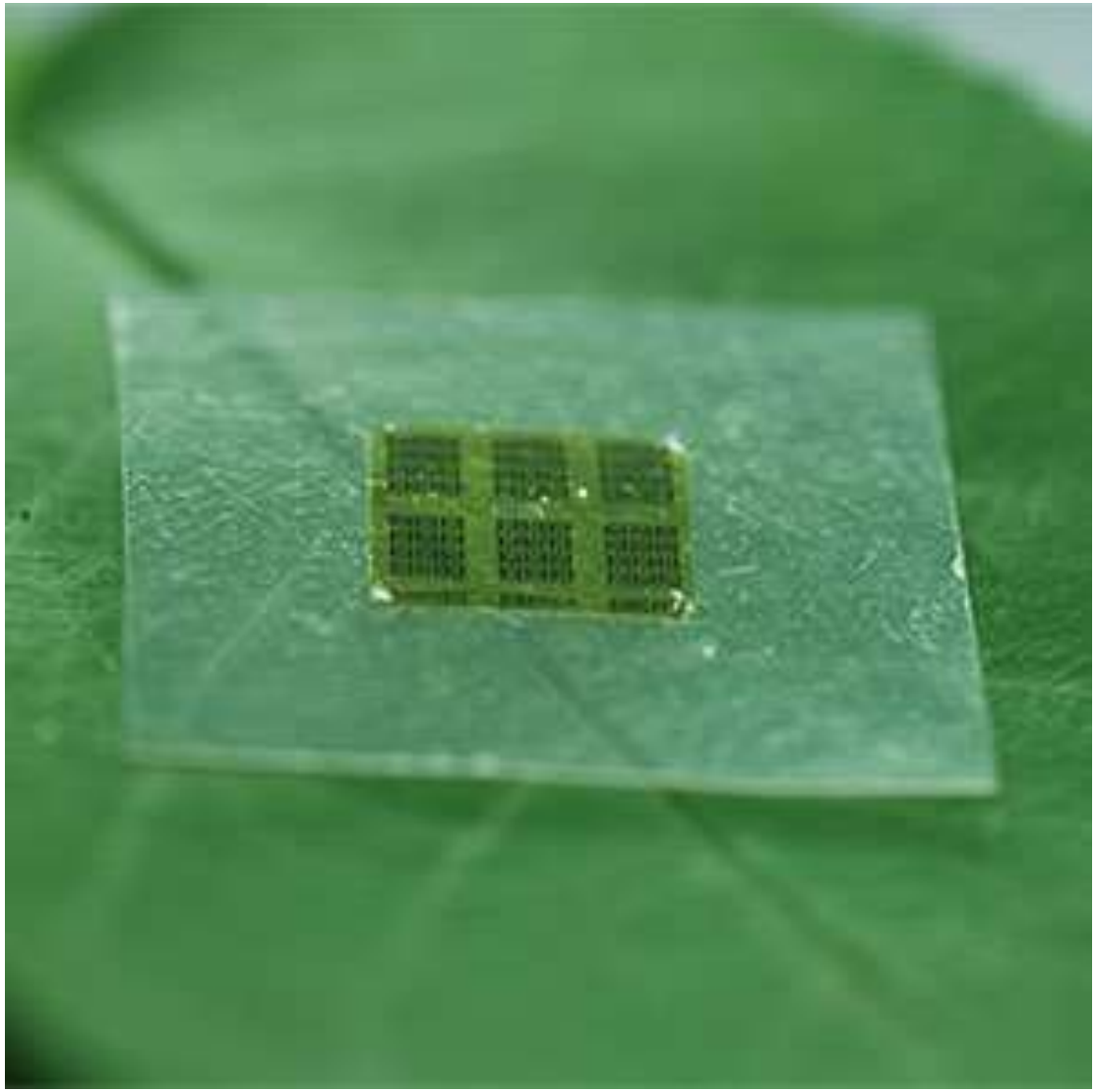
Tissue chips contain features designed to replicate the complex biological functions of specific organs.

Source: Wyss Institute for Biologically Inspired Engineering, Harvard University. | GAO-19-629

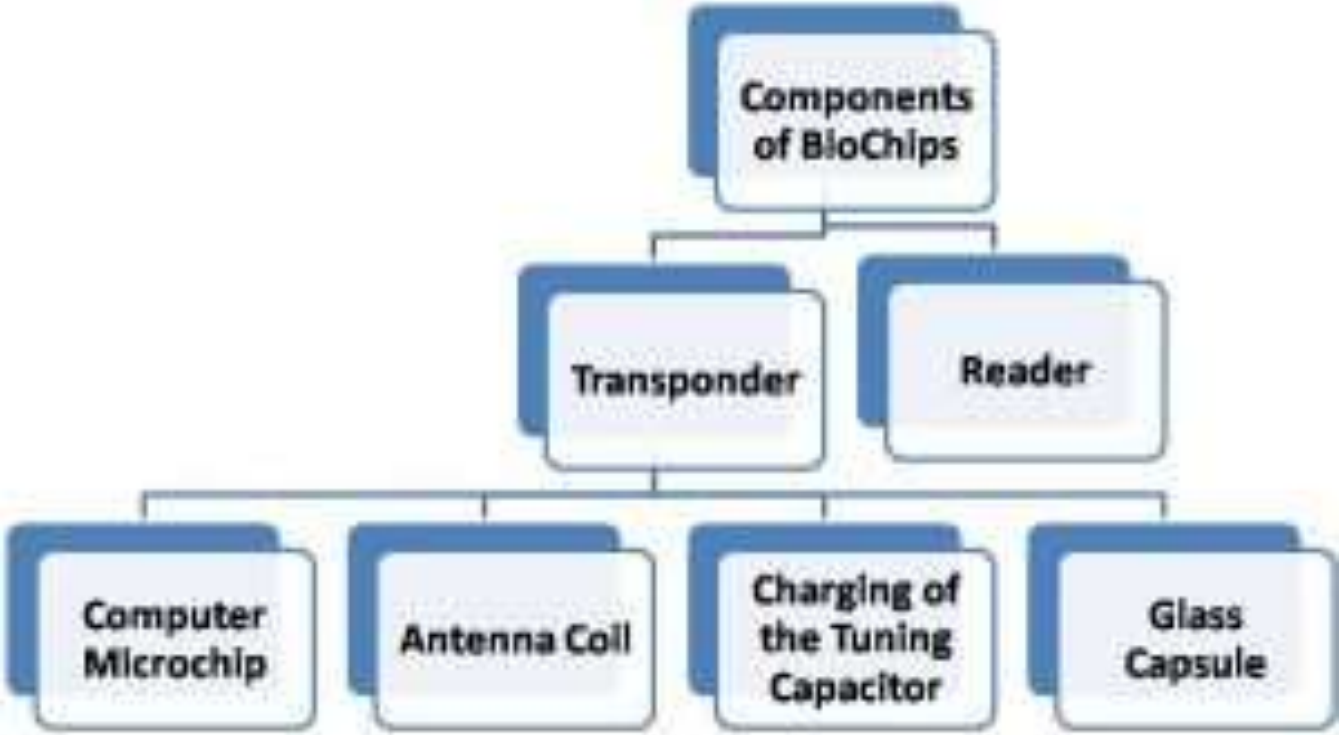
Biodegradable, wood-based computer chips can perform just as well as chips commonly used for wireless communication, according to new research.

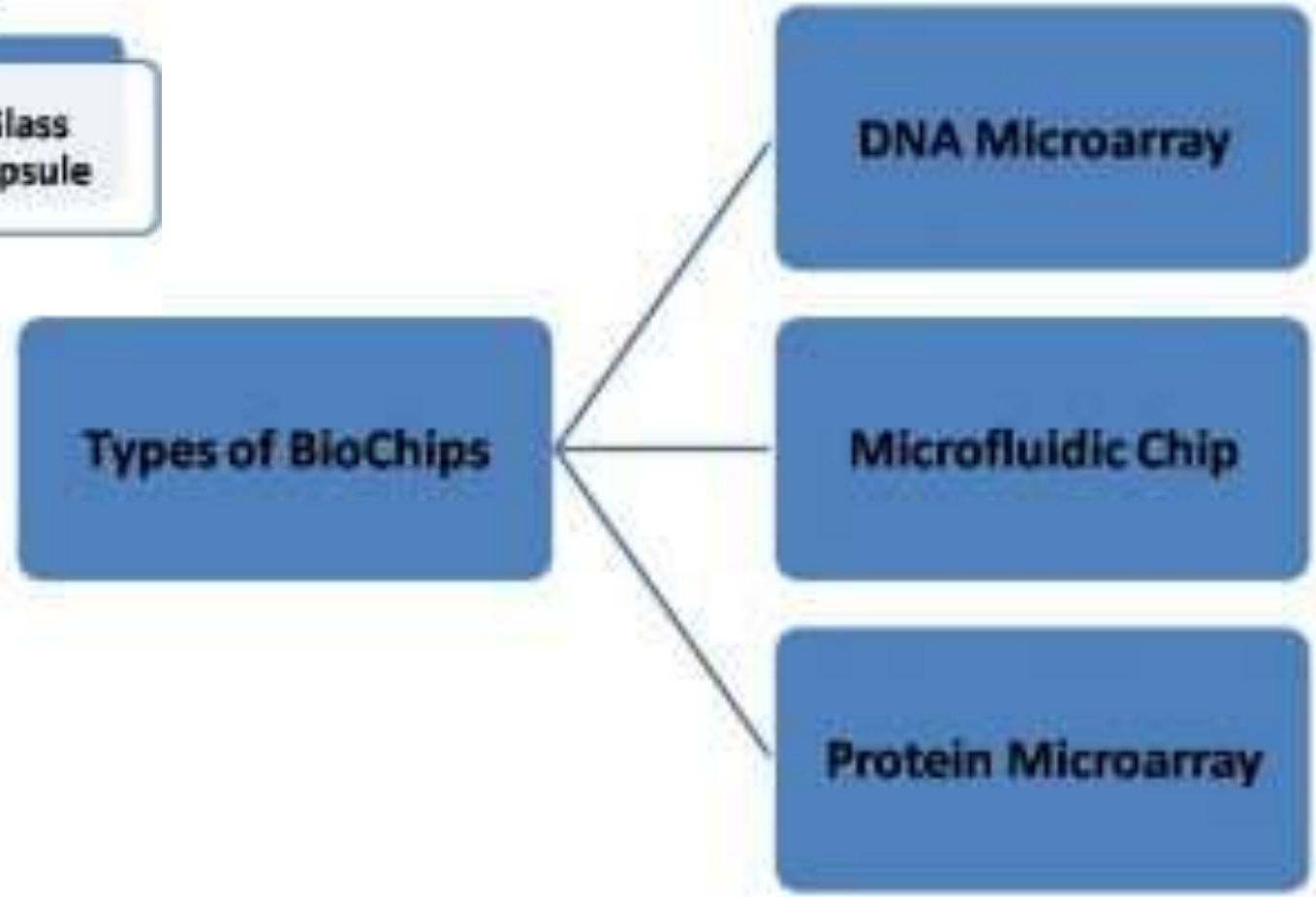
The inventors feel that the new chips could help address the global problem of rapidly accumulating electronic waste, some of which contains potentially toxic materials.

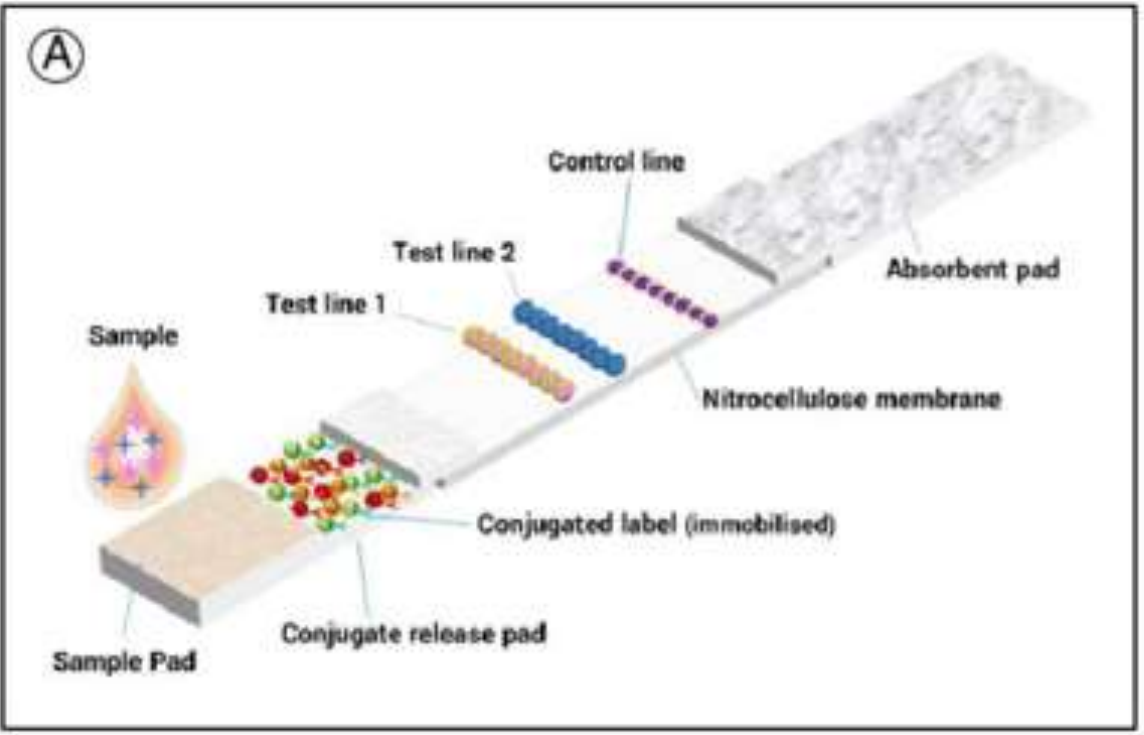
The results also show that a transparent, wood-derived material called nano-cellulose paper is an attractive alternative to plastic as a surface for flexible electronics.

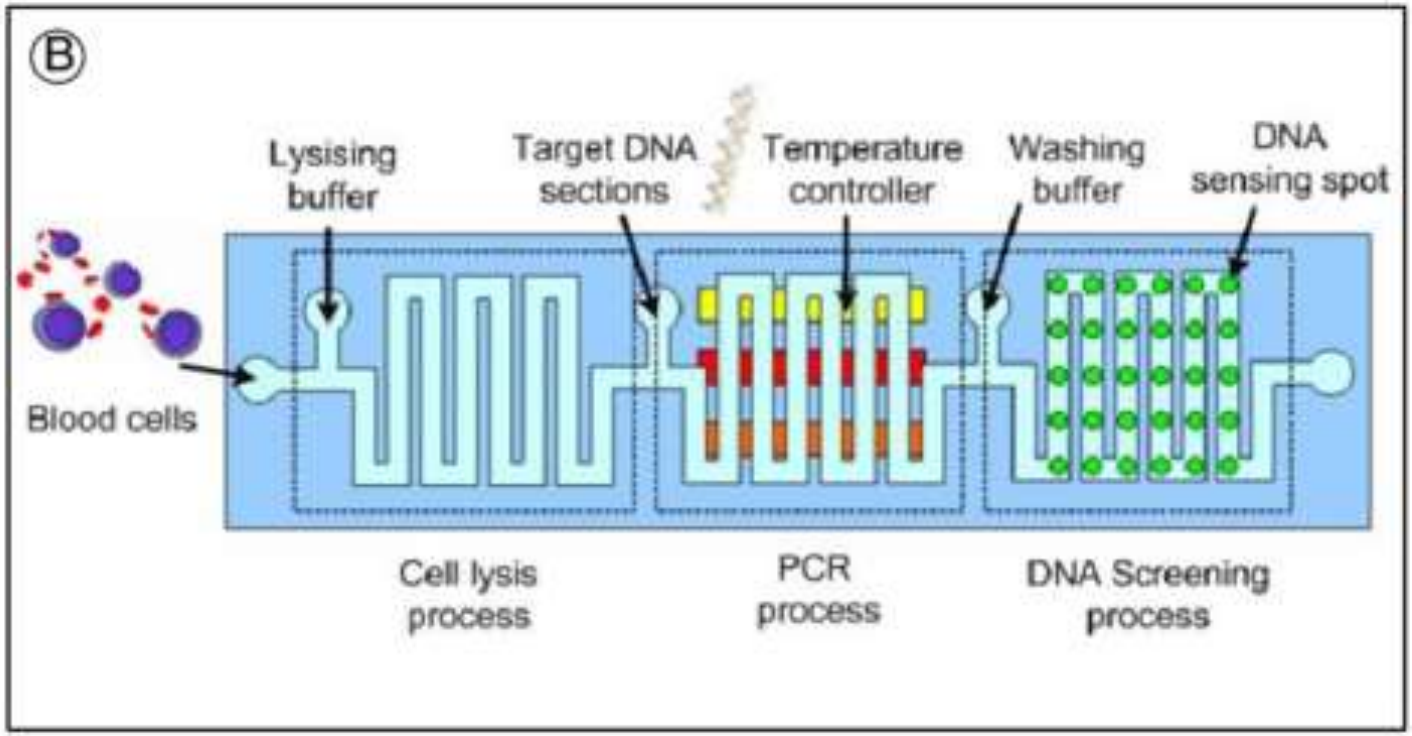


Electronic components made of gallium arsenide sit on top of a surface made of nano-cellulose, which is made from wood.


Components of BioChips
Transponder
Reader
Computer Microchip
Antenna Coil
Charging of the Tuning Capacitor
Glass Capsule


Types of BioChips
DNA Microarray
Microfluidic Chip
Protein Microarray

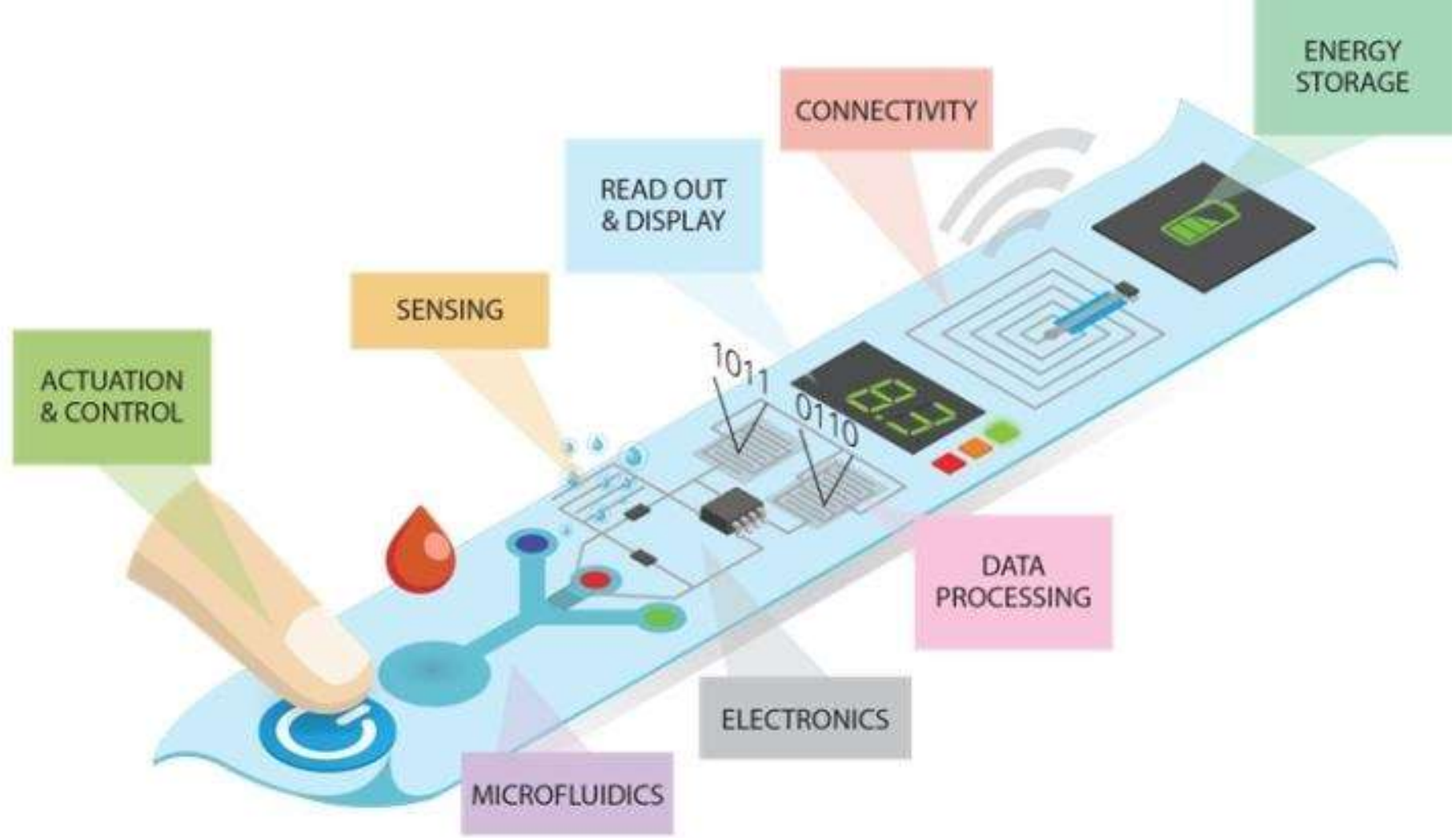




Schematic diagram of two common point-of-care techniques: lateral flow immunoassay (A) and microfluidics (B). **Polymerase chain reaction (PCR).**

https://www.youtube.com/watch?v=2KoLnIwoZKU&t=1s 1.5 minutes

These figures are adapted from the homepages of (A) ABINGDON HEALTH (https://www.abingdonhealth.com/articles/competitive-inhibition-sandwich-immunoassay-formats-lateral-flow/) and (B) Research in Bio-Optofluidic System Lab (http://homepage.ntu.edu. tw/~nthuang/research.html).



Envisaged integrated point-of-care diagnostic device, published by The Royal Society of Chemistry.

Screen-printed radio frequency identification (RFID) tags on flexible substrates. The purpose of these RFID tags is to enable low-cost and integrated point-of-care diagnostic solutions

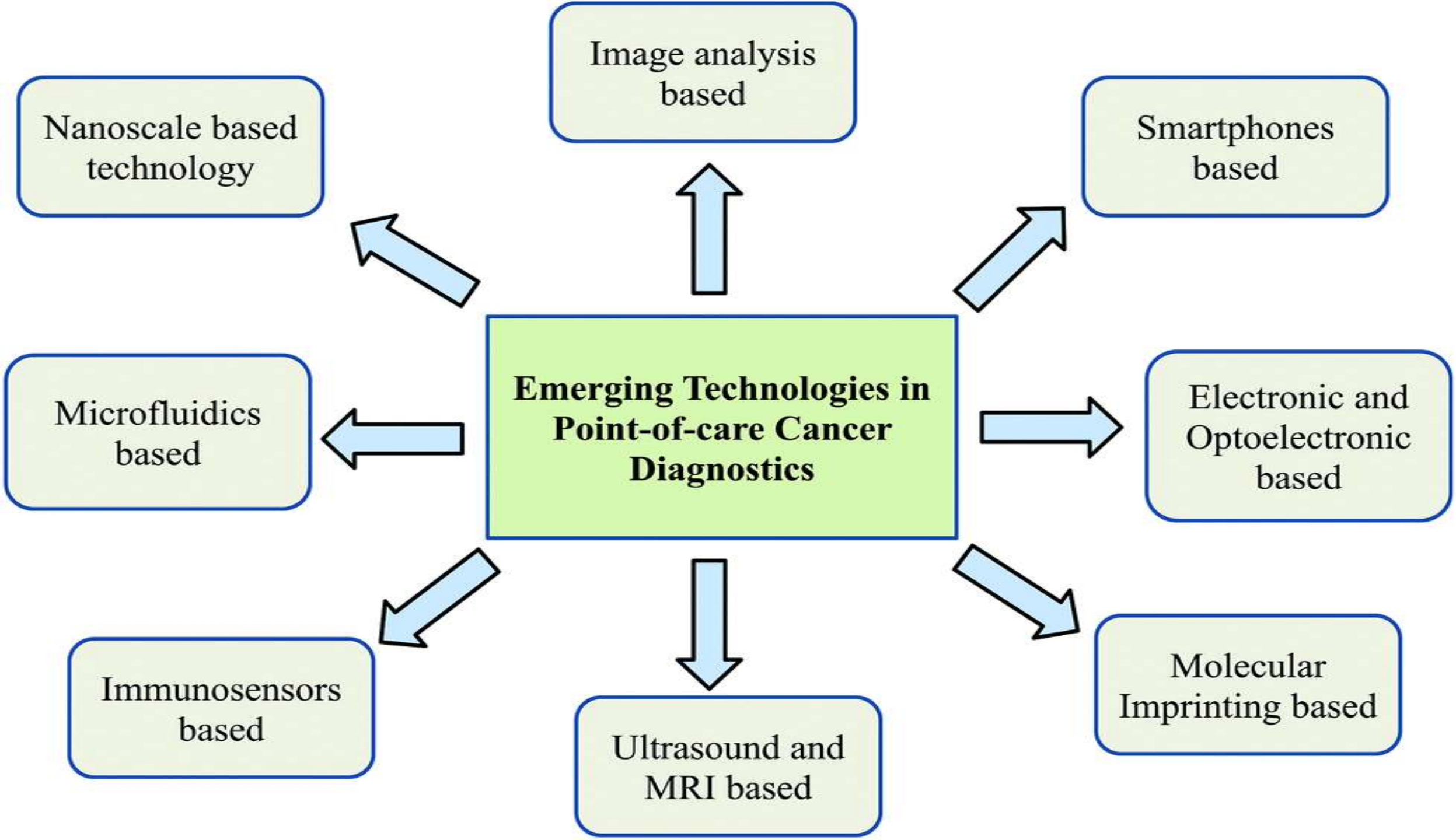


Image analysis based
Nanoscale based technology
Smartphones based
Emerging Technologies in Point-of-care Cancer Diagnostics
Microfluidics based
Electronic and Optoelectronic based
Immunosensors based
Ultrasound and MRI based
Molecular Imprinting based

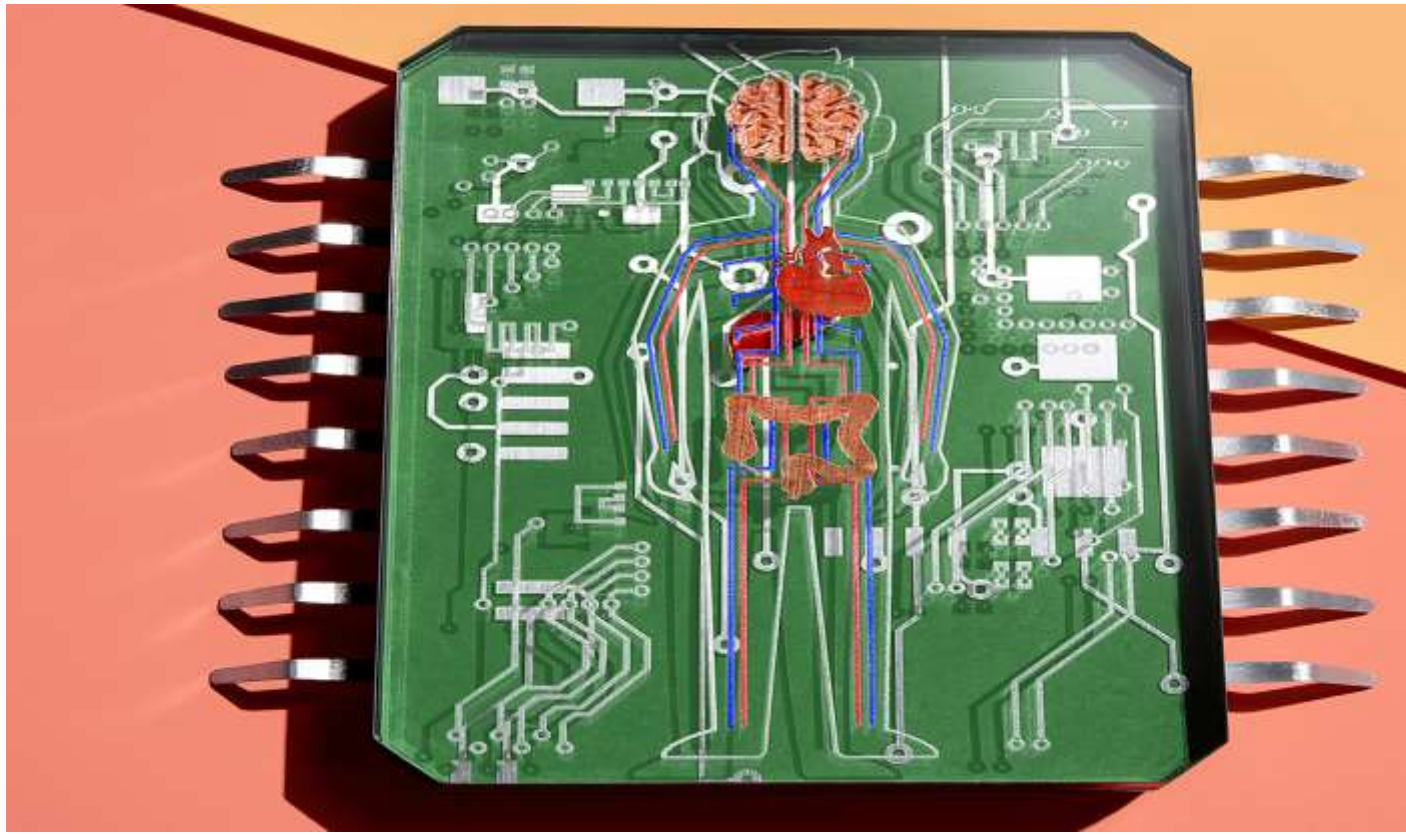
THE ULTIMATE IN PERSONALIZED MEDICINE: YOUR BODY ON A CHIP

ONE DAY YOUR DOCTOR COULD PRESCRIBE DRUGS BASED ON HOW A BIOCHIP VERSION OF YOU REACTS TO THEM

These organ-on-a-chip devices—usually made on substrates of plastic or rubber, not silicon—contain living cells.

The cells are organized to form a 3D bit of artificially grown tissue, often called an organoid, that operates like a human organ but on a scale of cubic millimeters.

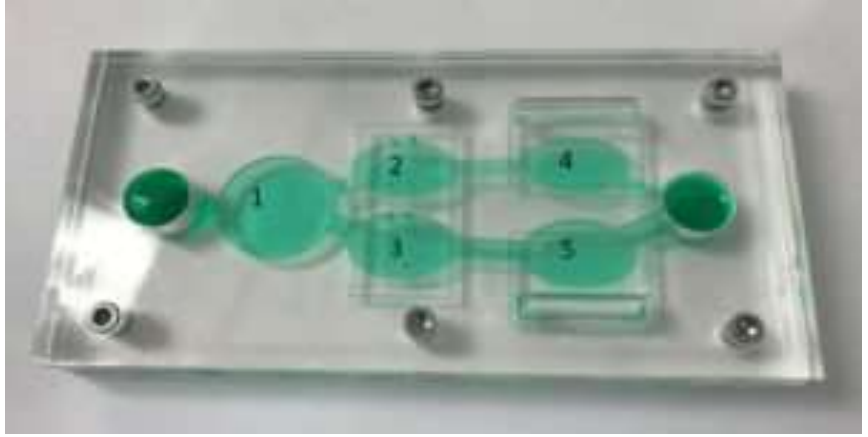
A liver organoid might be functional enough to metabolize the painkiller paracetamol. A lung organoid could simulate breathing.



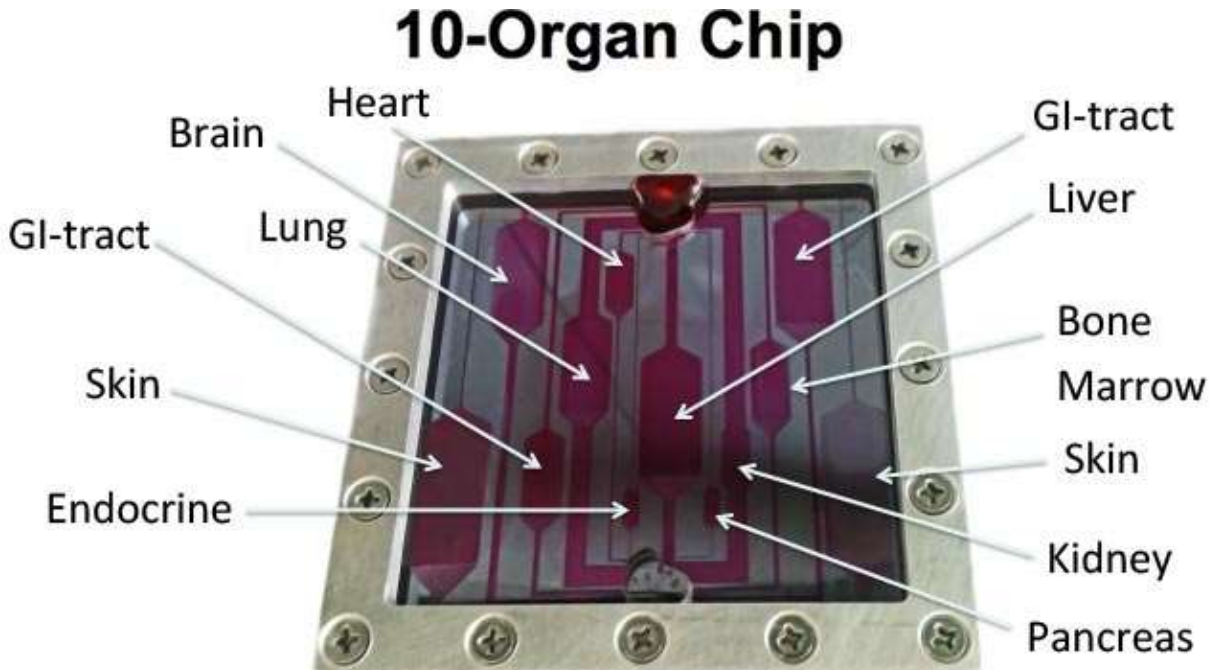
PHYSIOLOGICALLY ACCURATE MODEL OF THE HUMAN BODY INCORPORATING 5 AND 10 ORGAN SYSTEMS INTERCONNECTED USING A MICROFLUIDIC PLATFORM.

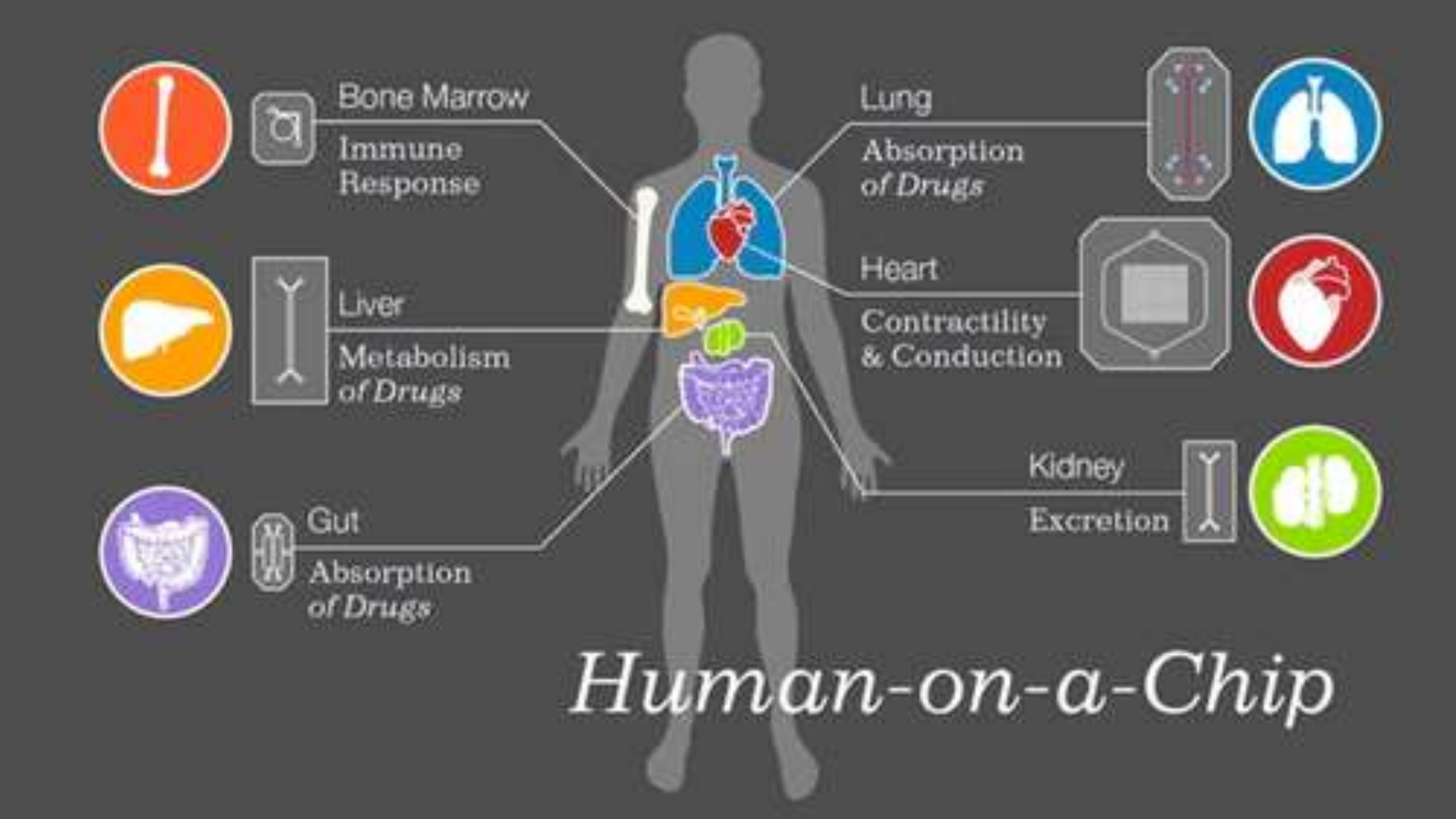
It is hoped that this “Body-On-A-Chip” model will provide the means to generate highly predictive and in- depth analyses of novel therapeutic methods.

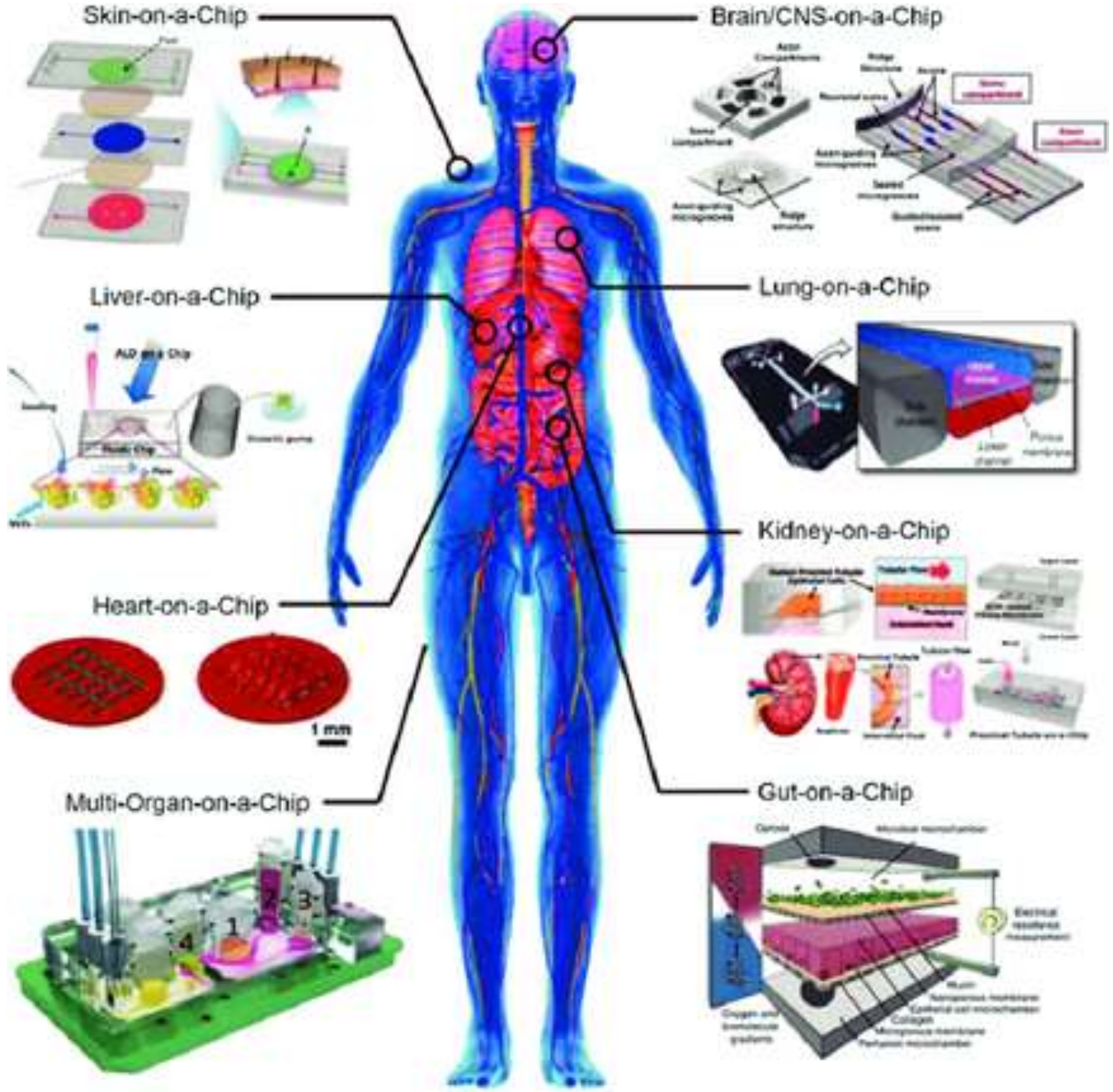
The successful development of such advanced human models may also pave the way for the reduction and eventual replacement of animals in preclinical drug development which are costly, time-consuming and often poor predictors of human responses to drugs.



Hesperos, a US Orlando based company, has been able to create a microfluidic lab that can manage up to 5 organs which makes it possible to observe the dynamics in the interaction among the 5 different organs.




Bone Marrow
Immune Response
Liver
Metabolism of Drugs
Gut
Absorption of Drugs
Lung
Absorption of Drugs
Heart
Contractility & Conduction
Kidney
Excretion
Human-on-a-Chip

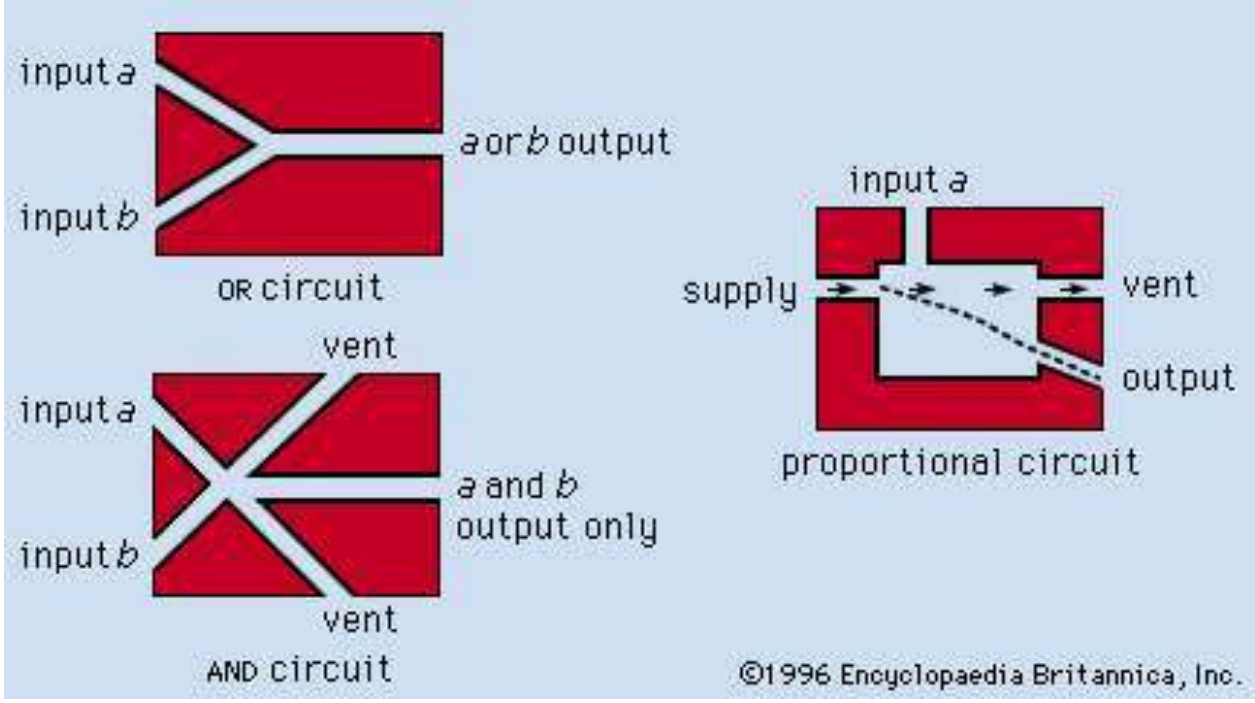

Skin-on-a-Chip
Brain/CNS-on-a-Chip
Liver-on-a-Chip
Lung-on-a-Chip
Kidney-on-a-Chip
Heart-on-a-Chip
1 mm
Multi-Organ-on-a-Chip
Gut-on-a-Chip

FLUIDICS

Fluidics, or fluidic logic, is the use of a fluid to move within very thin channels to operate a control system, similar to those performed with electronics.

The technology use the flow characteristics of liquid or gas to operate a control system. One of the newest of the control technologies, fluidics has in recent years come to compete with mechanical and electrical systems.

Fluidic devices operate on either the digital principle (they are either "on" or "off") or the analog principle (the output of the device is continuously proportional to the input).



CHIP-BASED SYSTEMS USING MICRO FLUIDICS

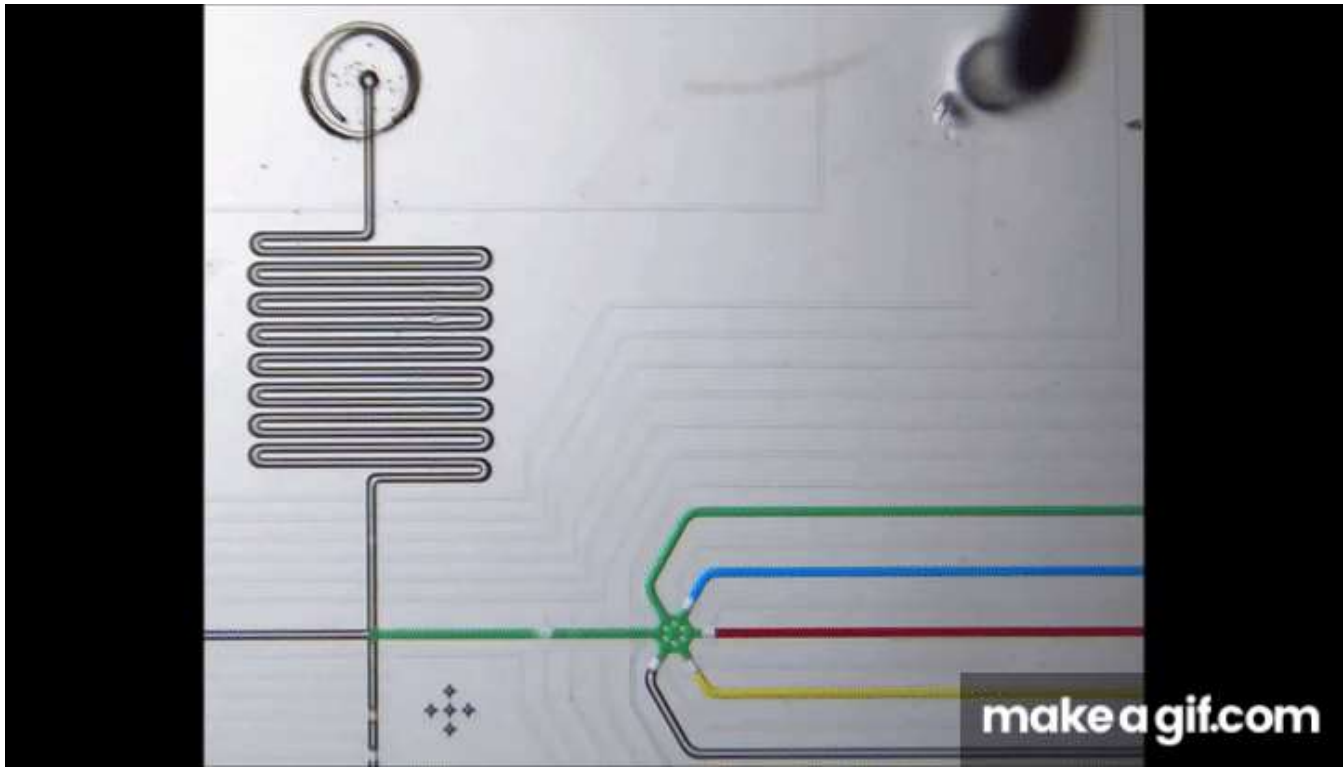
The main type of micro fluidic device is the chip-based system. **This is made of a chip having micro channels by which fluids are driven and in where reactions take place.**

Channels can have a square or round shape and their dimension range from few micrometers (millionths of a meter) to 800-900 μm (billionths of a meter).

Pumps are required to conduct fluids inside channels. They supply solutions in a continuous manner or are used for dosing.

Also, micro valves are used to determine the flow direction and/or the mode of movement.

The principal advantage of micro fluidics is that miniaturization on chips permits enhancing efficiency and mobility as well as reducing sample and reagent volumes.



Microfluidics relates to design and study of devices which move or analyze the tiny amount of liquid, smaller than a droplet.

Microfluidic devices have microchannels ranging from sub-micron (millionths of a meter) to few millimeters (thousandths of a meter).

To compare, a human hair is about 100 microns (millionths of a meter) thick.

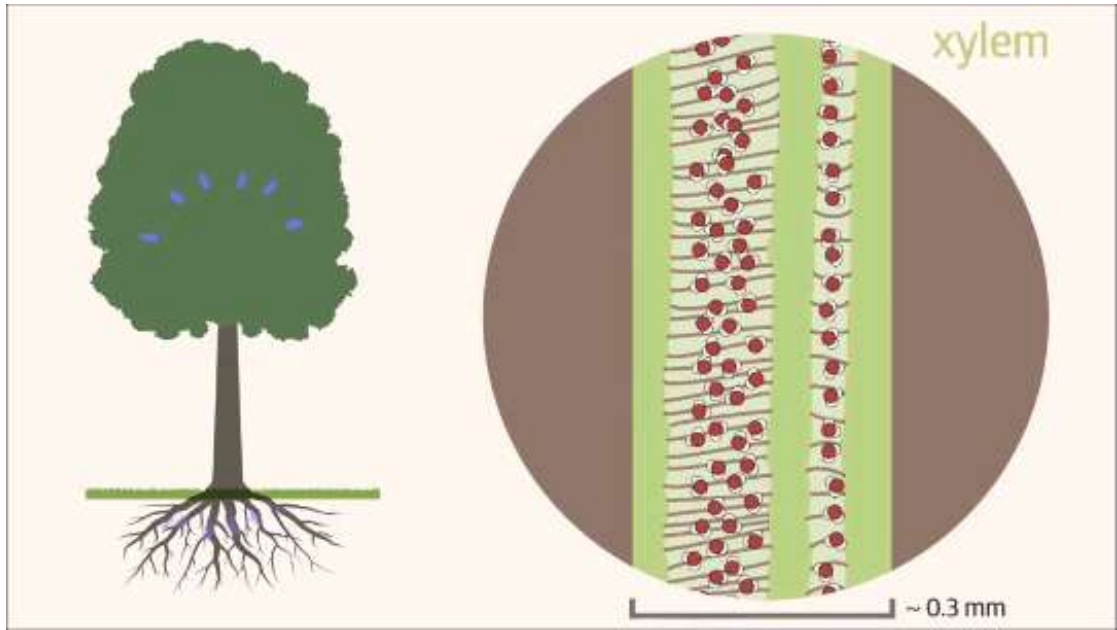
Microfluidics has been increasingly used in the biological sciences because precise and controlled experiments can be conducted at a lower cost and faster pace.

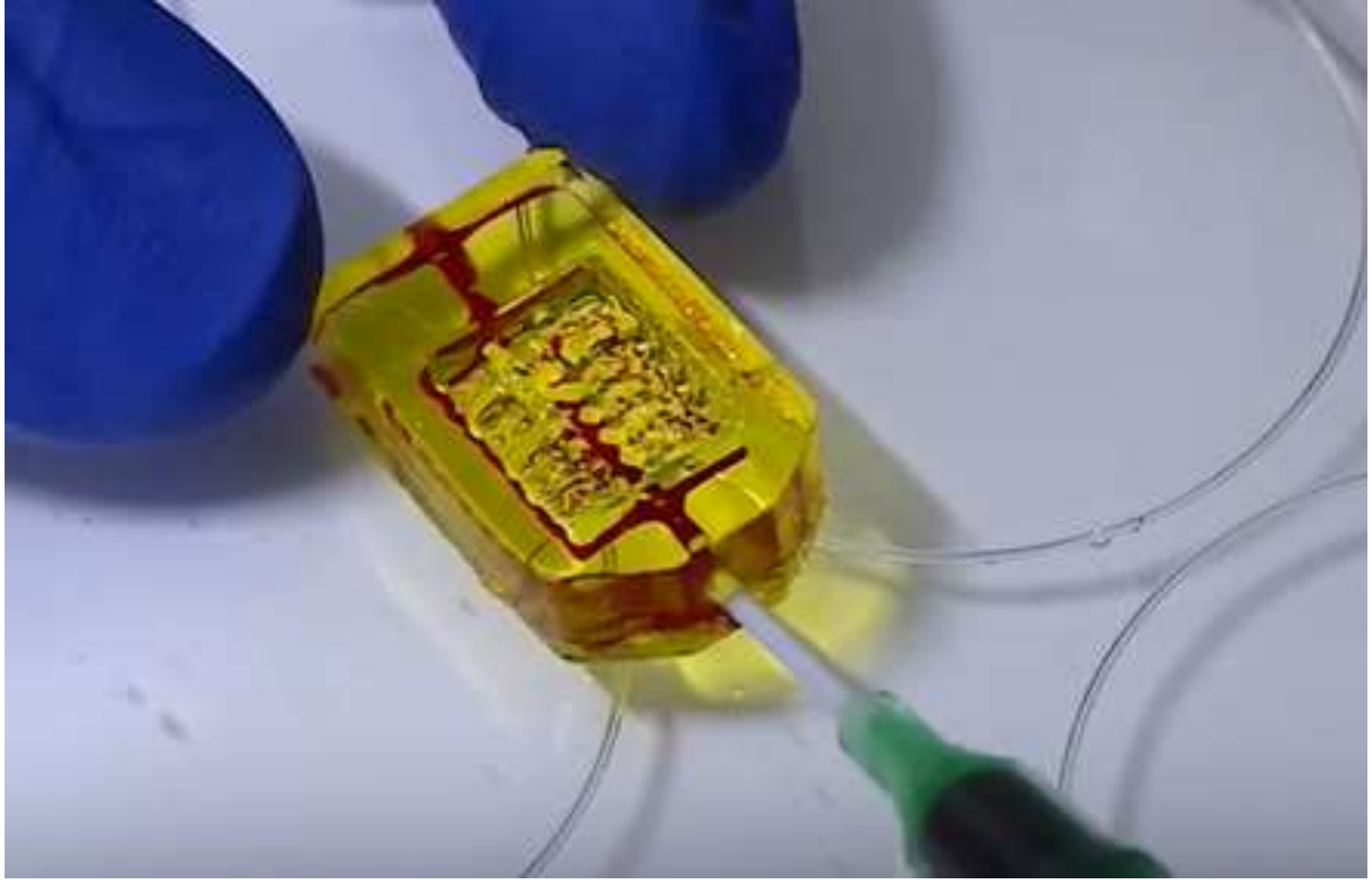
Lab on a Chip devices use microfluidics for applications such as Point of Care testing of diseases, or Organ on a Chip studies.

CAPILLARY BASED - Capillary microfluidic devices use capillary action to manipulate liquids.

Capillary action is a physical process that pulls a liquid into a thin tube. The thinner the tube, the more the fluid is pulled in.

Its effect is found in both Chip-Based and Paper-Based devices.





Bioengineers have cleared a major hurdle on the path to 3D printing replacement organs.

It's a breakthrough technique for bioprinting tissues with exquisitely entangled vascular networks that mimic the body's natural passageways for blood, air, lymph and other vital fluids.

THE PREPARATION OF PC MICROFLUIDIC CHIP BY INKJET PRINTING.

(a) A hydrophobic (water-hating) substrate was prepared by coating a pre-cleaned glass slide with

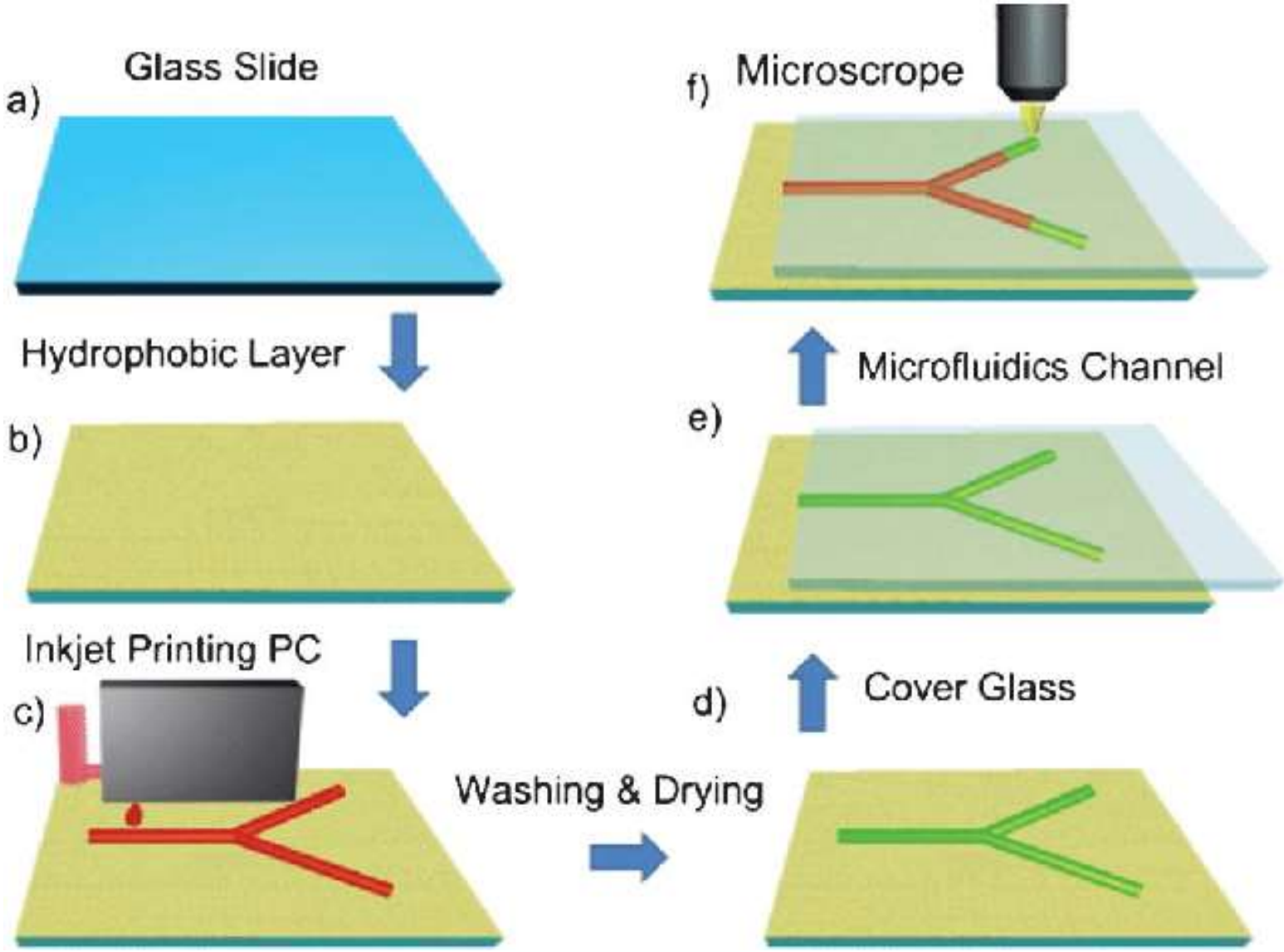
(b) a hydrophobic layer composed of polystyrene and hydrophobic Silicon oxide nanoparticles.

(c) Y-shape PC channel was inkjet printed on the substrate by using colloidal spheres dispersion as the ink.

(d) The assembled PC pattern was washed to remove the residual ink solvents

(e) Encapsulated with a cover glass.

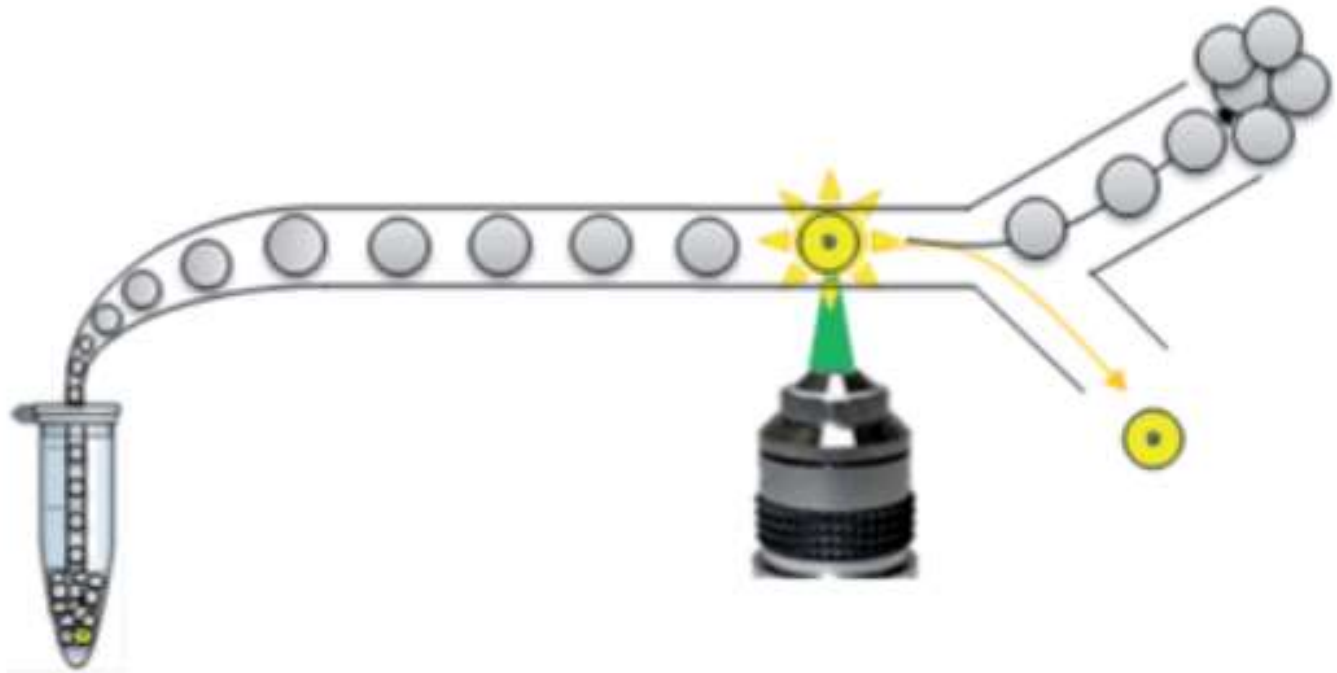
(f) The surface-tension confined microfluidic chip was used for detection.



Droplet microfluidics for high-throughput biological assays

Mira T. Guo, Assaf Rotem, John A. Heyman and David A. Weitz

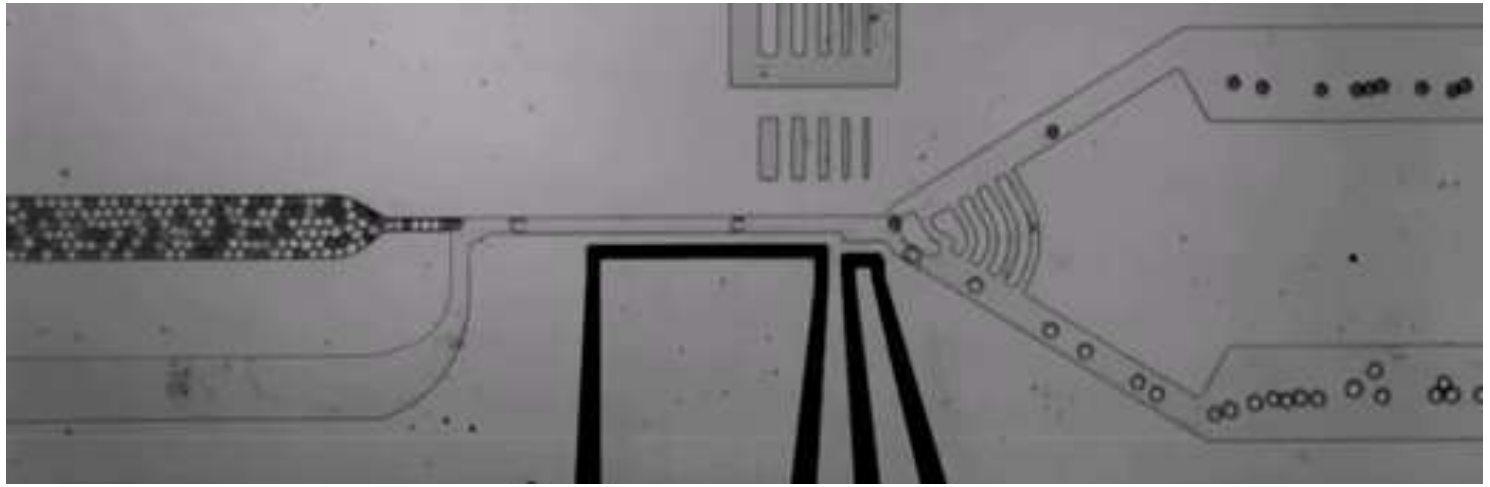
Droplet microfluidics enables new high-throughput screening applications by using picolitre volumes, kilohertz manipulation and measurement speeds, and high effective concentrations.

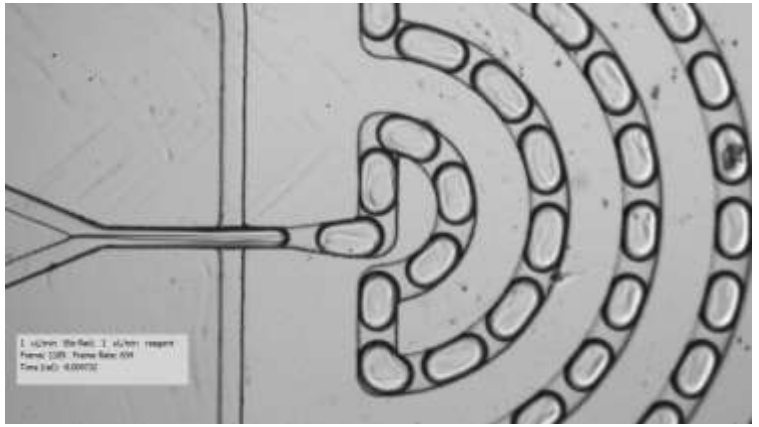


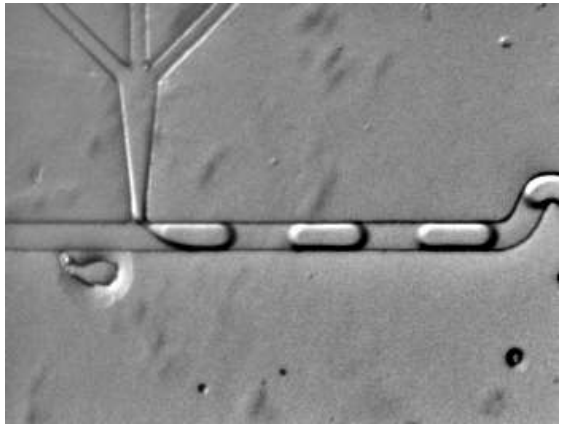
Producing liquid droplets of controlled size and composition is vital for making bio-pharmaceuticals, advanced materials, cosmetics, food, and human tissue manufacturing.

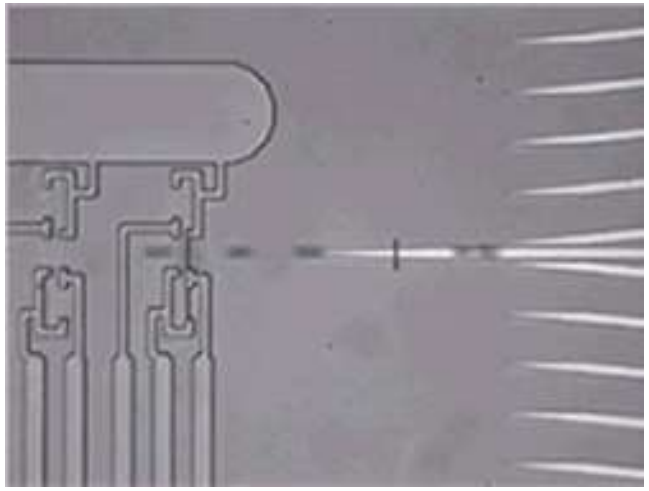
Digital microfluidics (DMF) is another platform for lab-on-a-chip systems that is based upon the manipulation of microdroplets.

Droplets are dispensed, moved, stored, mixed, reacted, or analyzed on a platform with a set of insulated electrodes.







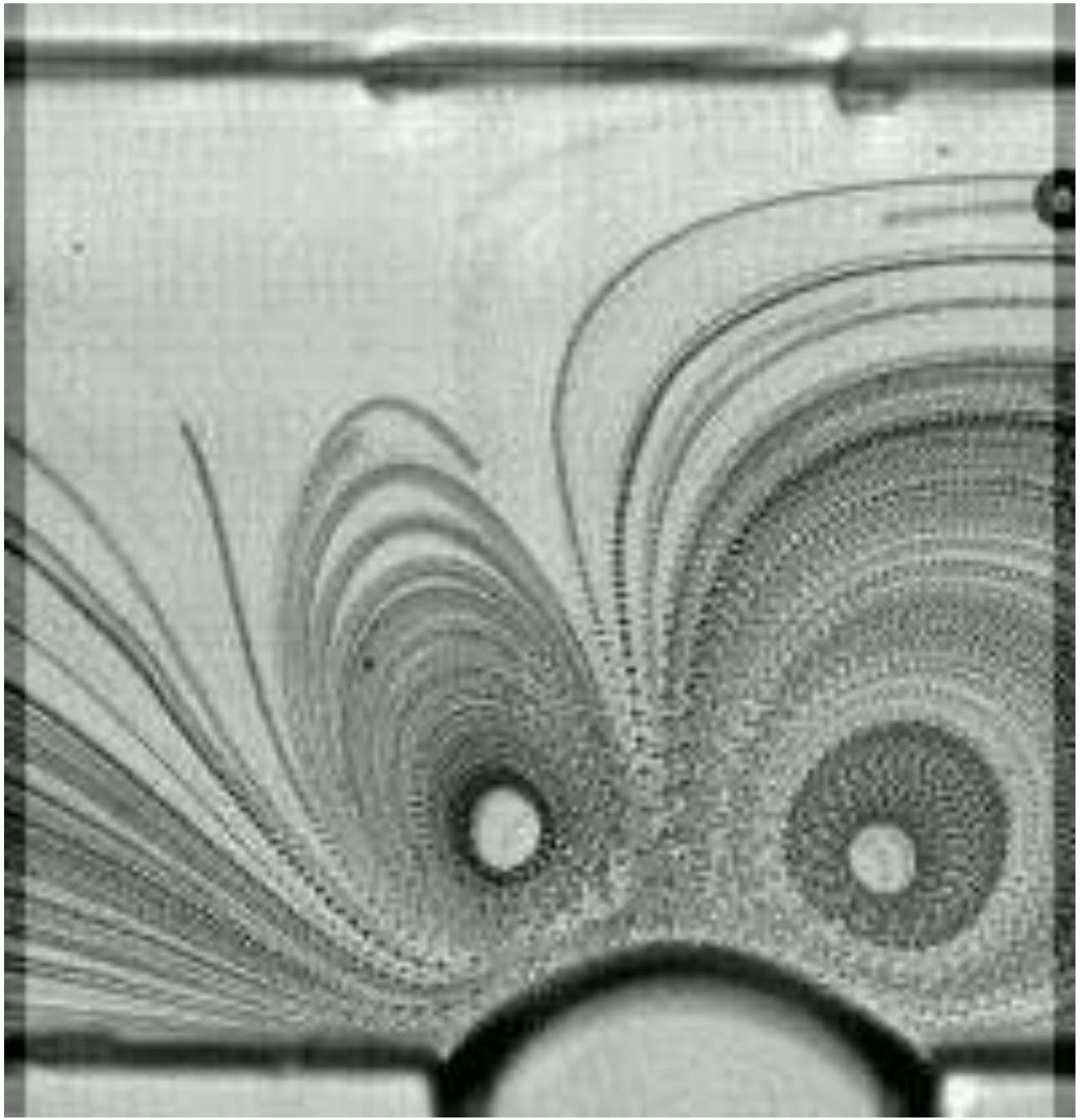


Microfluidic devices, also known as labs-on-a-chip, require clever techniques for processes like sorting particles by size.

One such technique uses an oscillating bubble to sort particles.

When the bubble vibrates back and forth, it creates what's known as a streaming flow – large regions of recirculation (shown as gray ellipses in the right image).

If the bubble is placed inside a channel, we say that two flows have been superposed; the device combines both the left-to-right flow.

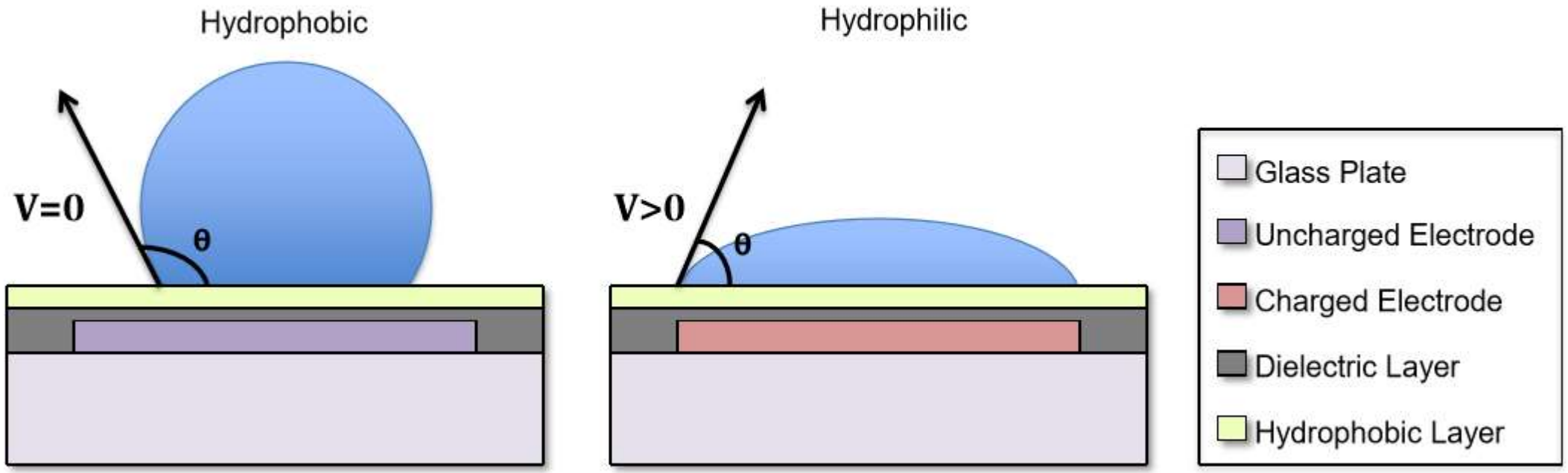


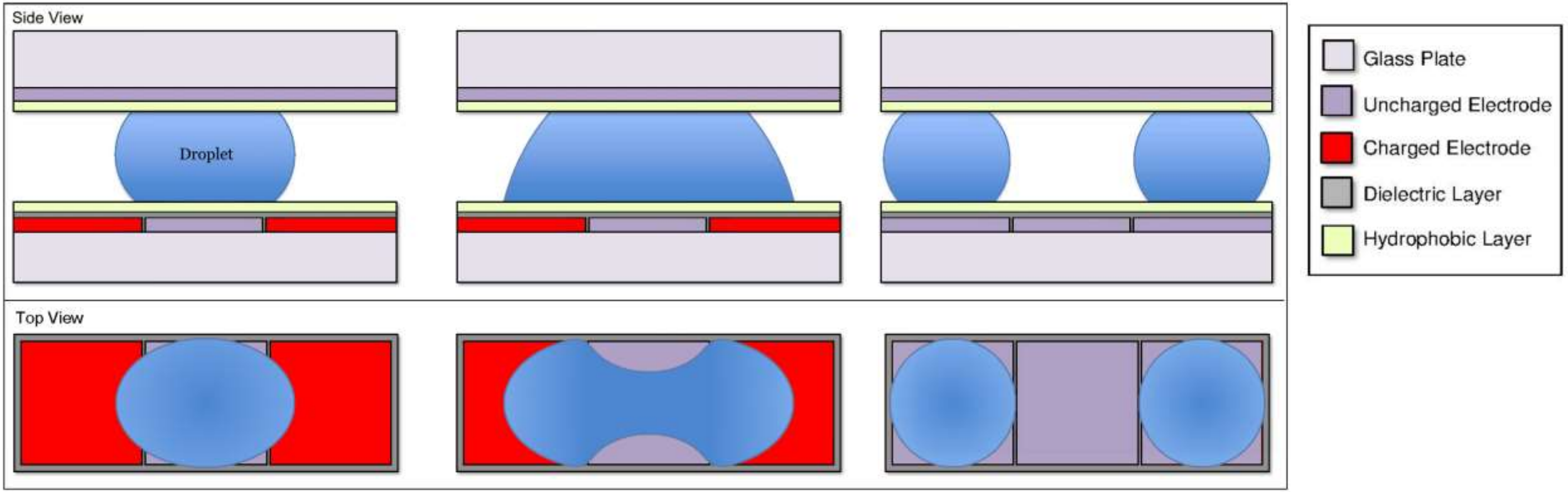
APPLYING A VOLTAGE TO AN ELECTRODE LETS A DROP WET OUT A SURFACE

When no voltage (V) is applied to an electrode, the surface maintains its hydrophobicity.

The addition of voltage (V>0) to an electrode creates a temporary hydrophilic (water-loving) surface and induces the aqueous droplet to wet the surface.

(2) The contact angle (θ) is formed by the tangential line of the droplet to the surface.

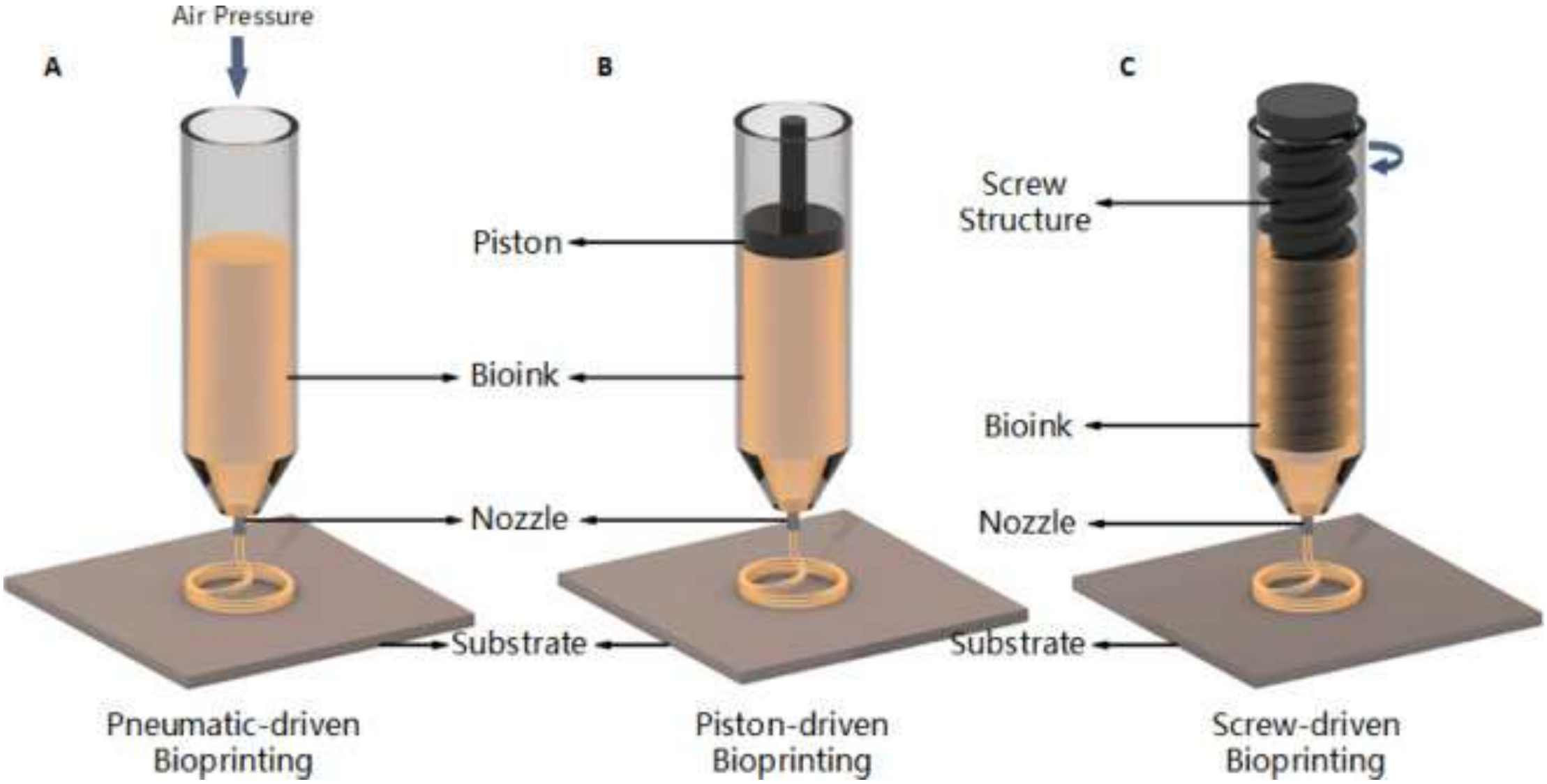




A droplet can be split by charging two electrodes on opposite sides of a droplet on an uncharged electrode.

In the same way a droplet on an uncharged electrode will move towards an adjacent, charged electrode, this droplet will move towards both active electrodes.

Liquid moves to either side, which causes the middle of the droplet to neck and then separate into 2 drops.



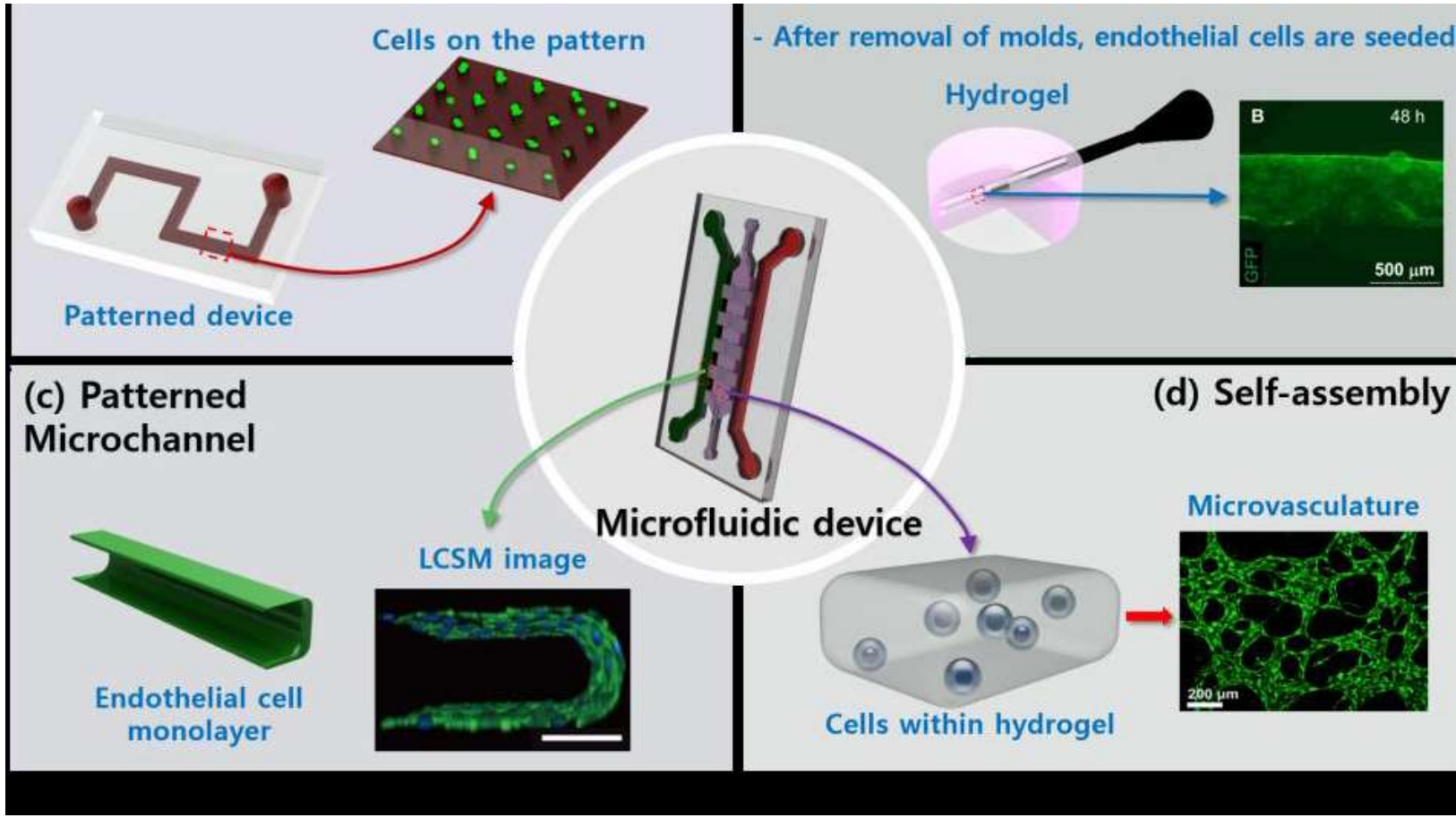
. Principles of extrusion-based bioprinting.

BLOOD VESSEL ON A CHIP

This is a 3D blood vessel-on-a-chip model that can be used to understand what happens to vessels during injury on a molecular scale.

We hope to use these devices to learn more about how to keep vessels healthy, and about what goes awry in disease settings.

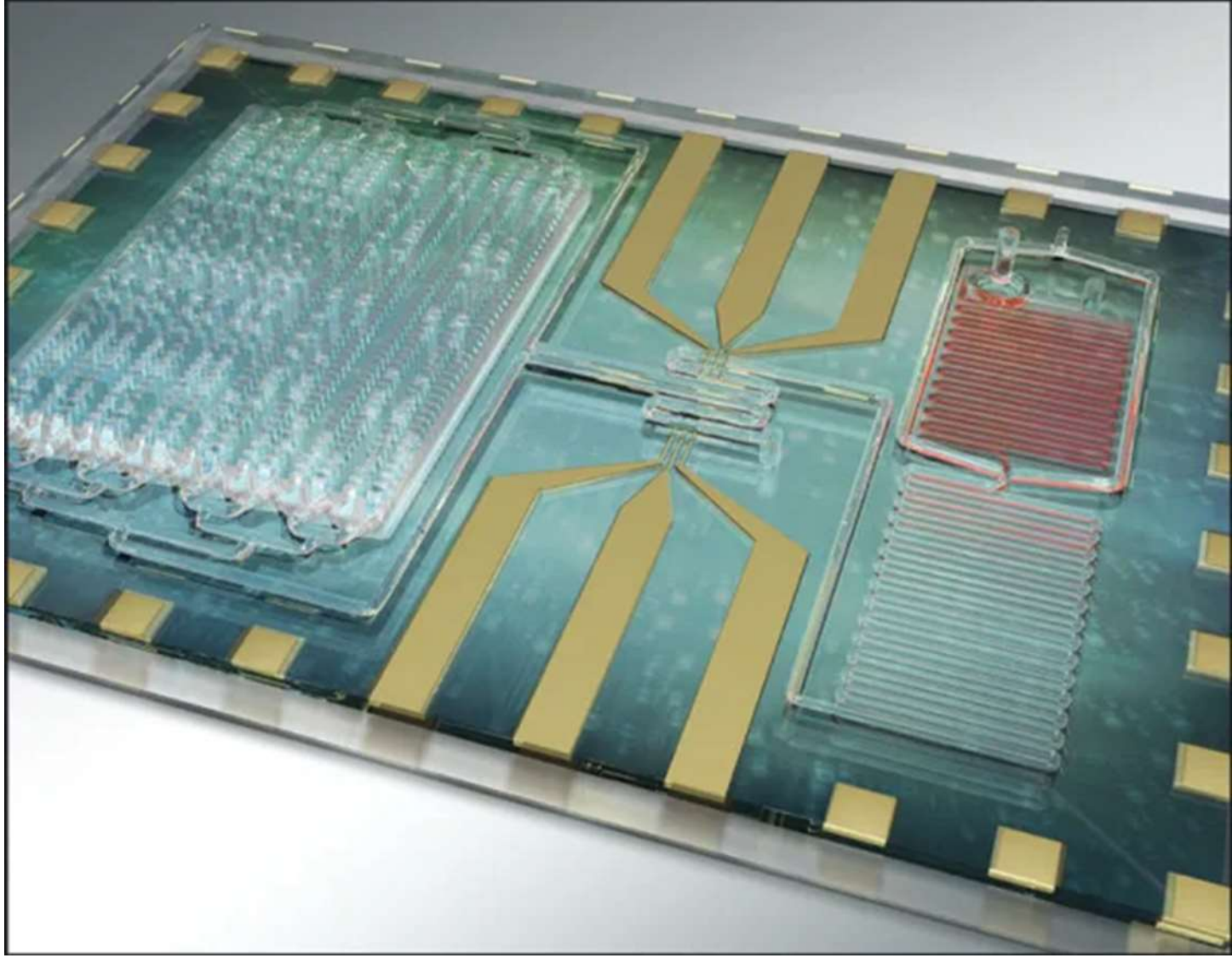
The 3D blood vessel-on-a-chip has allowed a research team to identify specific proteins that regulate vascular barrier function.



This is a rapid test using a single drop of blood for early detection of the deadly blood infection, sepsis.

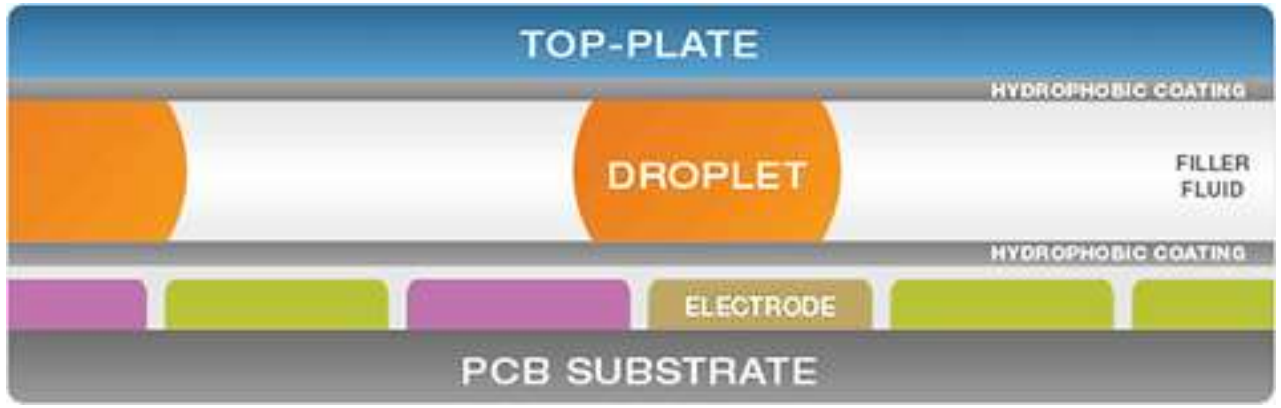
The microfluidic chip could enable early intervention for this life-threatening complication, which accounts for the most deaths and highest medical expenses in hospitals worldwide.

The Sepsis biochip showing microfluidic channels that remove red blood cells on the right and the larger chamber of microchip posts on the left that capture the CD64 positive immune cells that are markers for sepsis.



(Credit: Rashid Bashir, U. Illinois at Urbana-Champaign.)

MICROFLUIDIC CHIP RAPIDLY IDS DEADLY BLOOD INFECTIONS

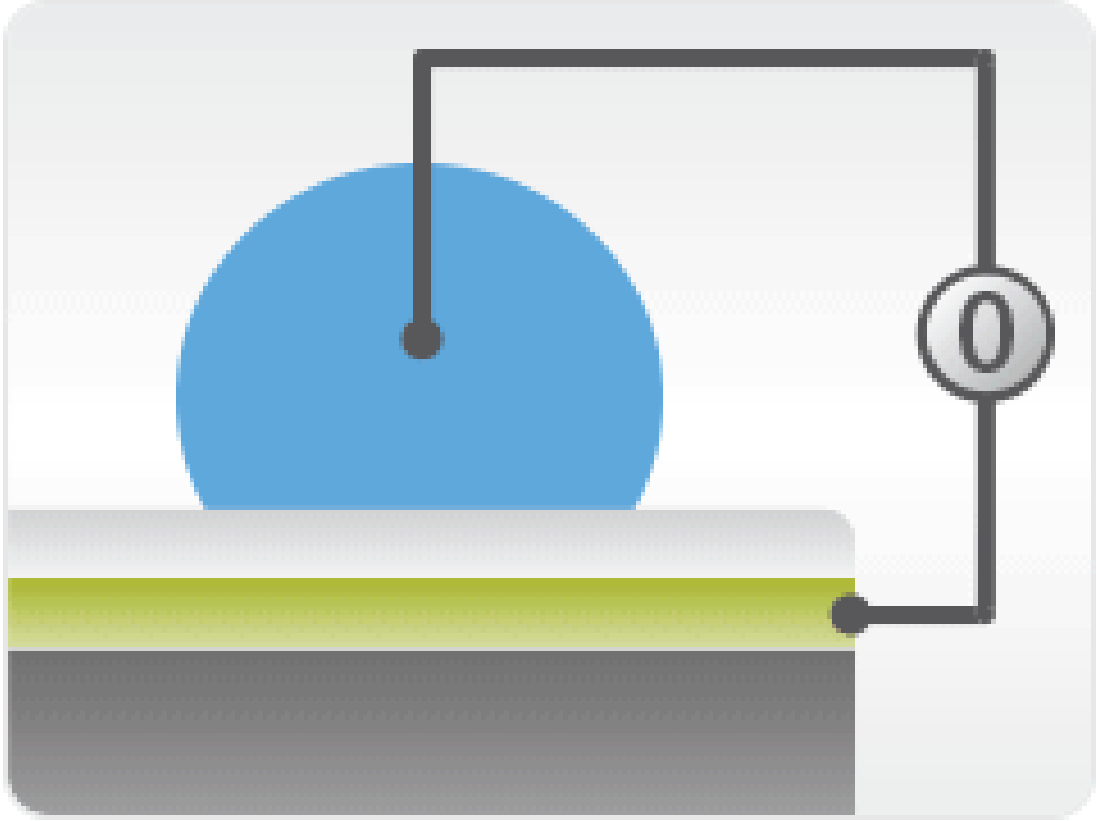


DIGITALLY CONTROLLED DROPLETS

Digital microfluidics harnesses electrowetting to control droplets.

Electrical signals are applied to an array of electrodes to define the size and position of each droplet.

Droplets are moved by turning the voltage on and off in succession across adjacent electrodes.



TECHNOLOGY BASICS: "ELECTROWETTING"

Digital microfluidics is based on the use of "electrowetting," which refers to the ability of an applied voltage to modulate the "wettability" of a surface.

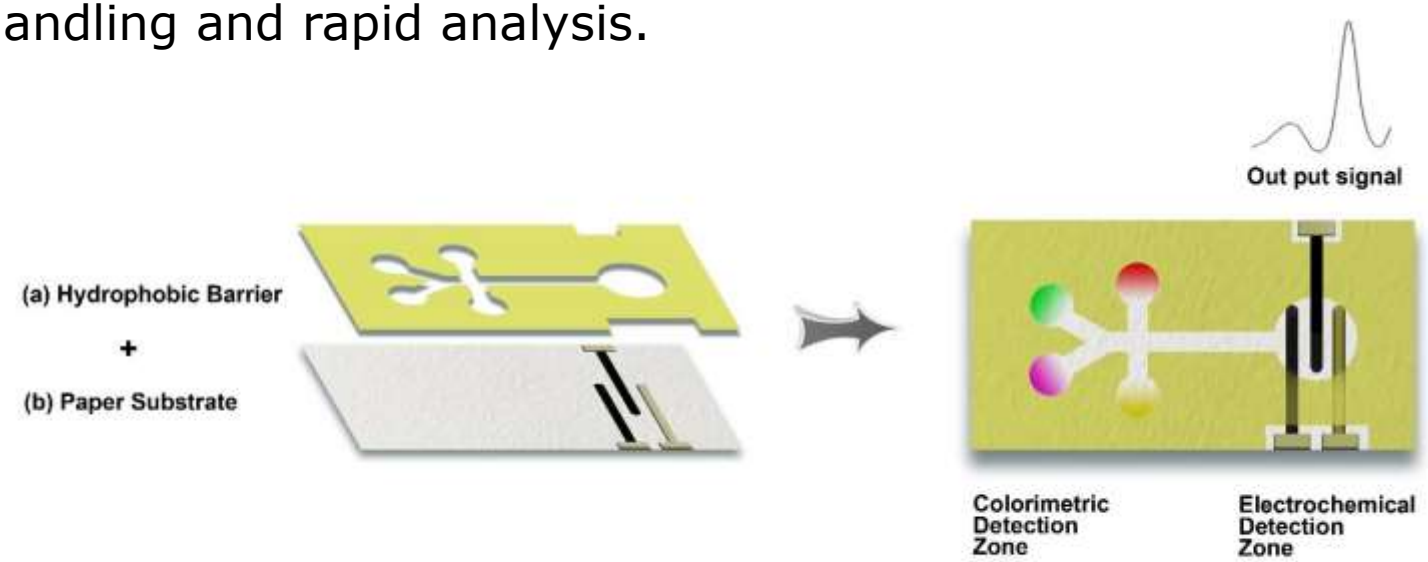
Watery droplets naturally "bead-up" on a hydrophobic surface, but a voltage applied between a droplet and an insulated electrode can cause the droplet to spread on the surface.

PAPERTRONICS

The field of paper electronics or "papertronics" has recently emerged as a game-changing platform for next-generation applications in healthcare, environment monitoring, display, flexible electronics, and energy storage devices.

It uses both fluidic and electronic components for new functions, minimizing the design complexity of the systems, and provide efficient manufacturing using existing printing technologies.

Fluidic components, patterned in paper, allow for instrument-free liquid transport via capillary wicking and storages of biological and/or chemical reagents within their 3D fiber network of paper; thereby, enabling power-free fluid handling and rapid analysis.



Schematic presentation for the construction of a dual-detection potential microfluidics paper-based analytical devices (μPADs). (a) The patterning of appropriate wax on the paper. (b) The paper substrate. (c) The completed μPAD with dual color and electrochemical detection methods.

FIRST INTRODUCED IN 2007, PAPER MICROFLUIDIC DEVICES CAN BE CATEGORIZED INTO THESE 3 AREAS:

A. Biochemical

B. Immunological

C. Molecular detections

They are mainly designed for:

1) The detection of various types of substances and compounds

2) Medical and forensic diagnostics

3) Urine analysis by measuring glucose and protein concentration

4) Pathogen and toxin detection

Microfluidic Paper-based Analytical Devices (μPAD)

Low Volume

Low Cost

Portable

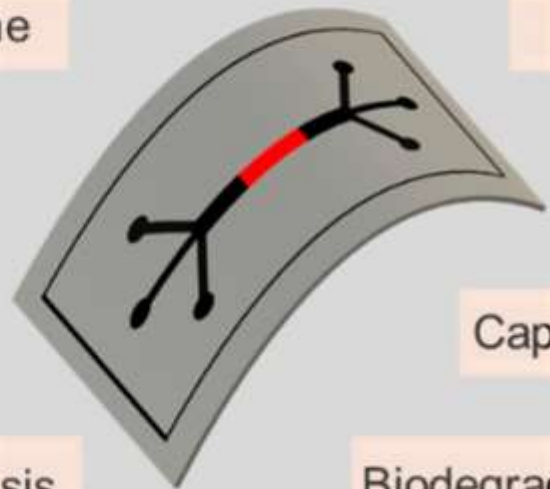
Flexible

Fast Reaction

Capillary Flow

Multianalysis

Biodegradable



2D & 3D Fabrication Techniques

Flow Control Methods

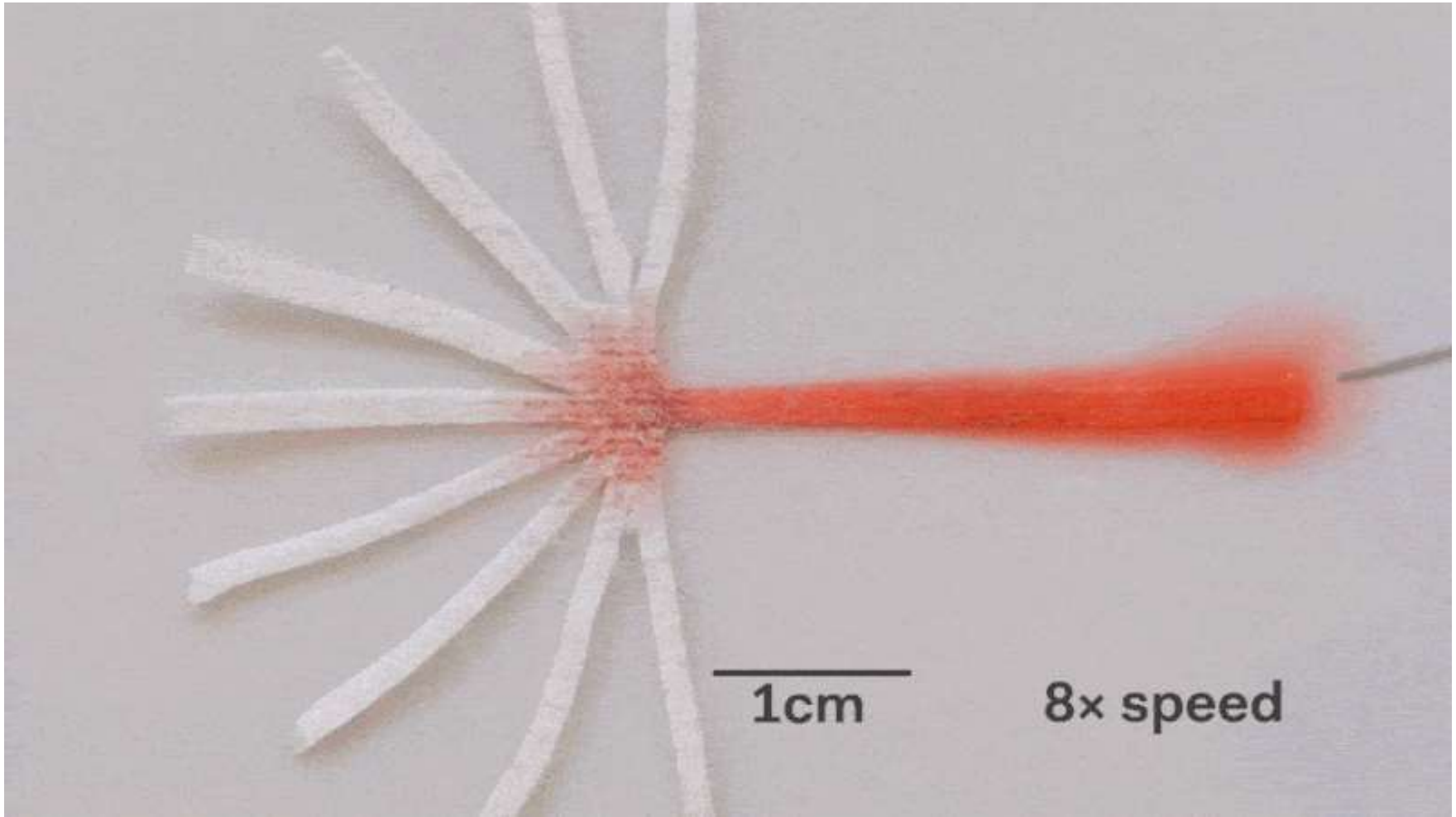
- Health Diagnostics
- Environmental Monitoring
- Food Quality Control
- Drug Analysis
- Cell Assays

Paper is a hydrophilic (water loving) material meaning that its affinity with water allows solutions to flow through the porous structure. This simple capillary action does not require added mechanical constructions for pumping.

Paper-based analytical devices are being utilized as biosensors and immunoassays for detecting biological analytes associated with disease. The technology is also being employed for testing contaminated food in order to reduce rates of infections caused by foodborne pathogens.

The speed of fluid flow in paper microfluidic channels can be controlled by cutting paper at different angles to the paper grain.

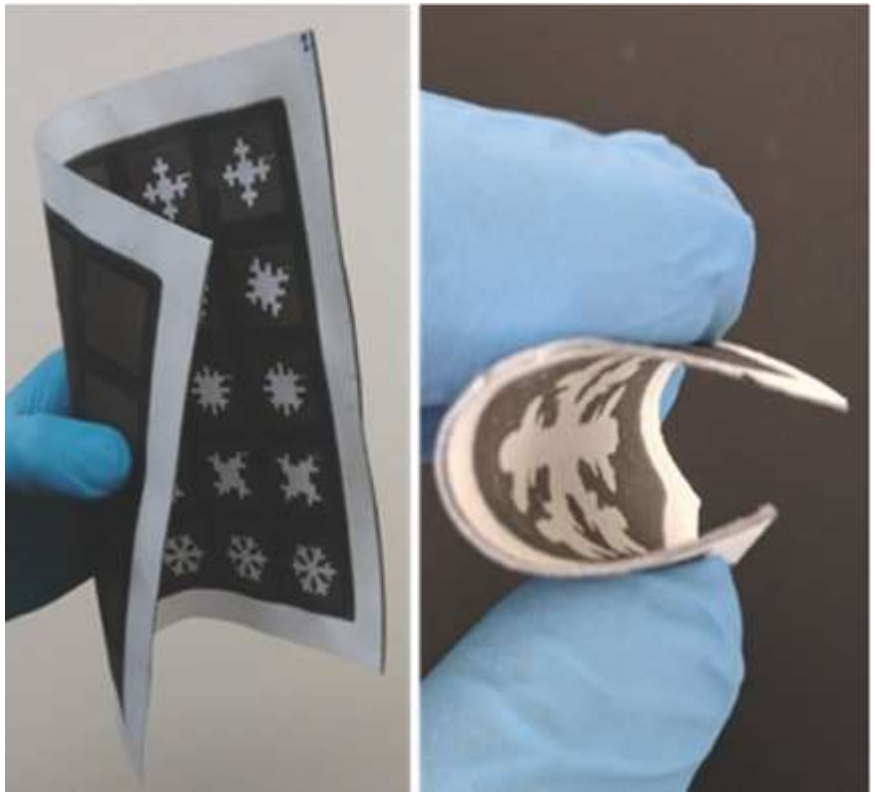
Here the central branch has the fastest flow as it is cut parallel to the grain. This animation is sped up 8 times.



PAPERTRONICS

A stackable and 3D manufactured bacteria-powered battery is constructed within a single sheet of paper for on-chip, disposable paper-based electronics or “papertronics.”

The manufacturing technique on paper greatly reduces fabrication time and cost of the bio-batteries and revolutionizes their potential use as a disposable power source in remote and resource-limited regions for self-powered devices.

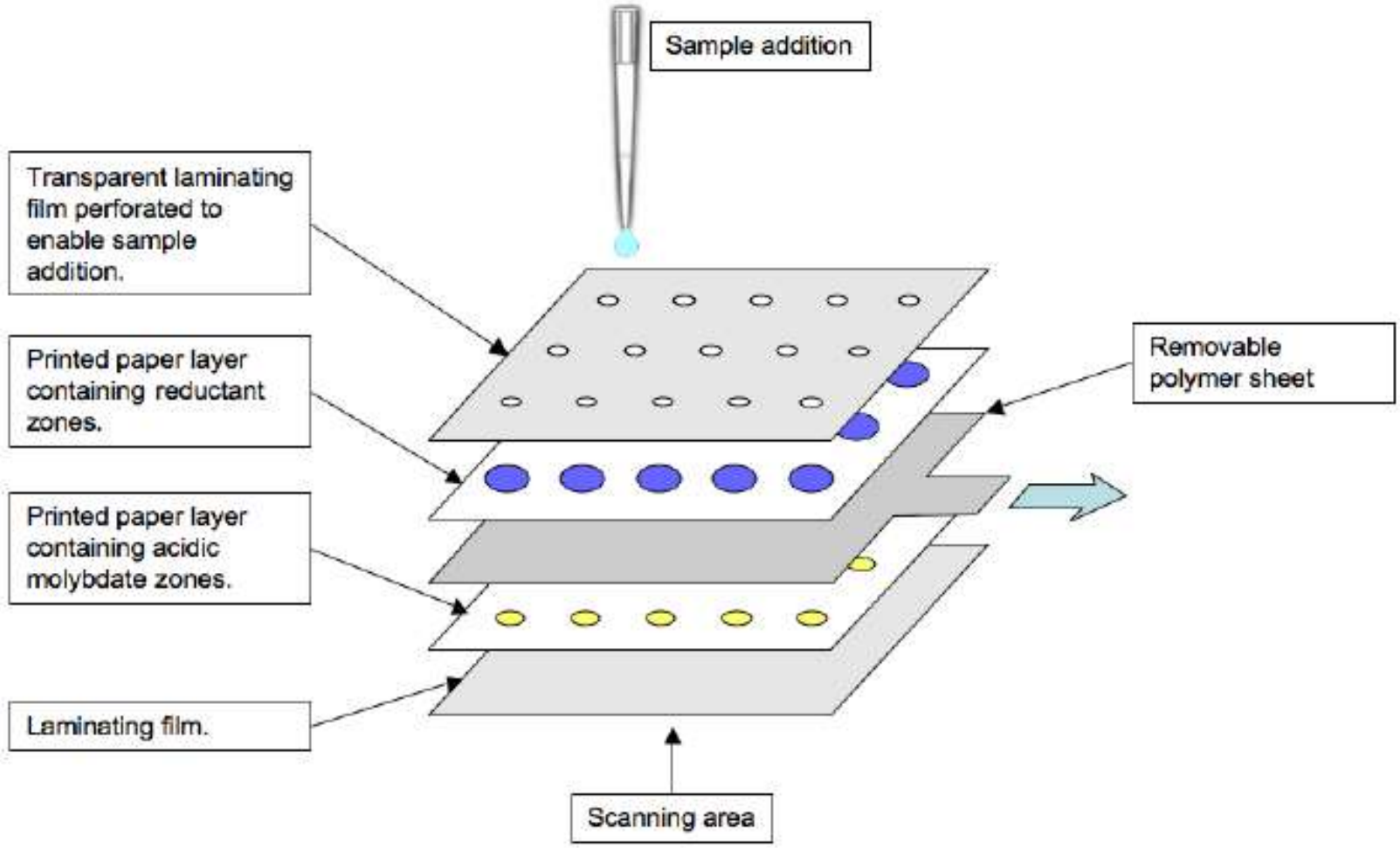


MICROFLUIDIC PAPER ANALYTICAL DEVICES

In the last decade, a new generation of analytical devices has emerged based on cellulose materials – so-called **microfluidic paper-based analytical devices (μPADs)** – a field that will change the face of the diagnosis of different diseases and sensing of a wide range of biological/chemical/ biochemical phenomena.

This example is of a low-cost microfluidic paper-based analytical device (μPAD) for the determination of reactive phosphate in soil.

This device allows up to 15 places for measuring phosphate levels on one credit card-sized device and requires only a desktop or hand scanner for signal detection and measuring.



Drugs of Abuse Test
McKesson 14-Drug Panel with Adulterants - Urine Sample cup

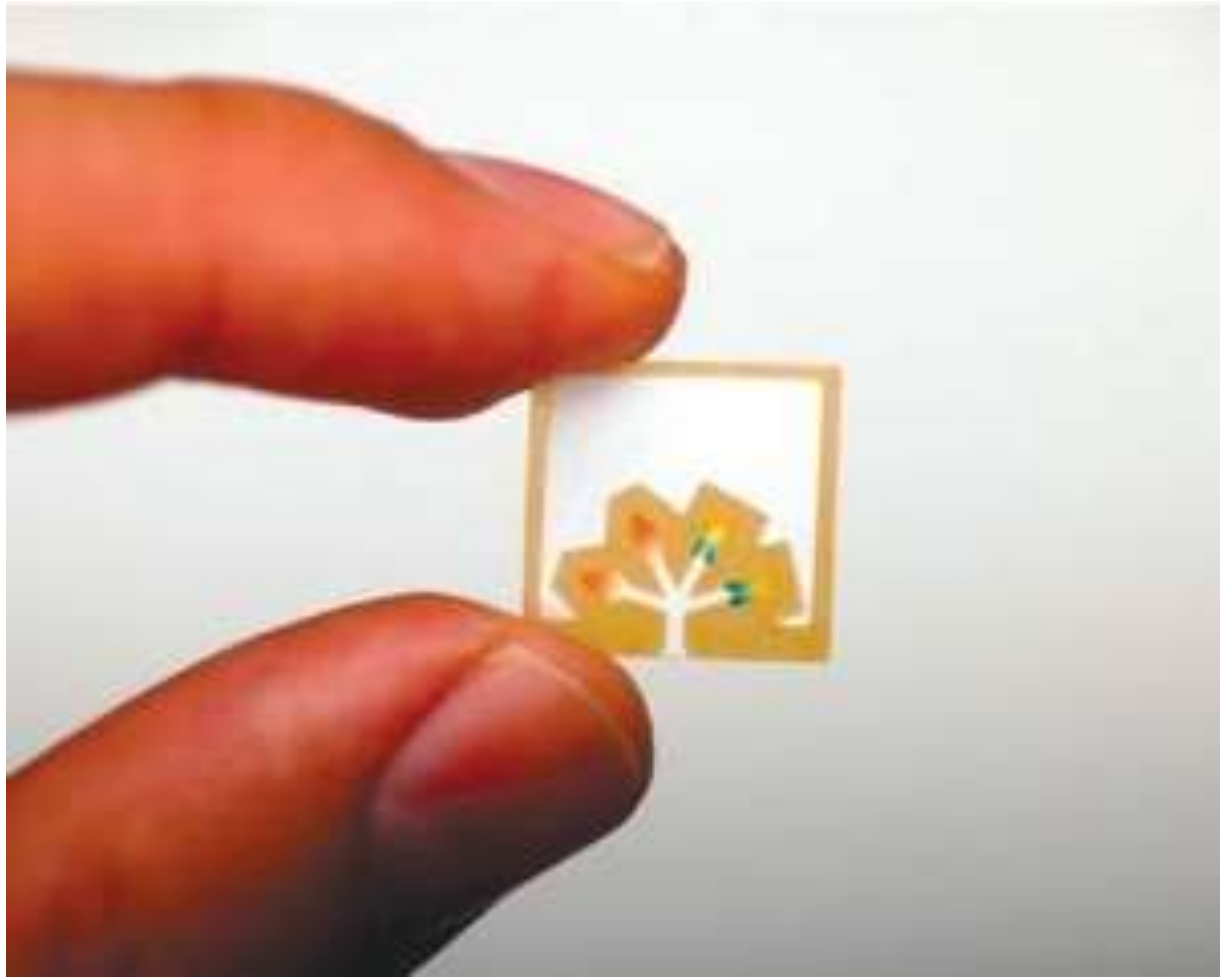
AMP - Amphetamine
BAR – Xanax “Bars”
BUP - Buprenorphine
BZO - Benzodiazepine
COC - Cocaine
mAMP/MET - Methamphetamine
MDMA - 3,4-methylene-dioxy-meth-amphetamine
(Ecstasy/Molly)

MOP300 – an opiate
MTD - Methadone
OXY - Oxycodone
PCP – Phencyclidine
PPX - Propoxyphene
TCA - Tricyclic Antidepressant
THC (OX, pH, SG) – Cannabis - Marijuana

Paper microfluidic devices were developed to not only make diagnosis devices environmentally friendly and affordable (above all in in the developing world) but also to be able to instantly conduct tests in urgent situations or remote areas, cut out from technology

These diagnostic systems, often called **paper microfluidic analytical devices (µPDAs),** are made of patterned paper on which a small volume of fluid placed over will move by capillary action.

To top it all, paper is not only an inexpensive and handy material but it also constitutes a very light substrate that can be stored and transported easily and at low cost.



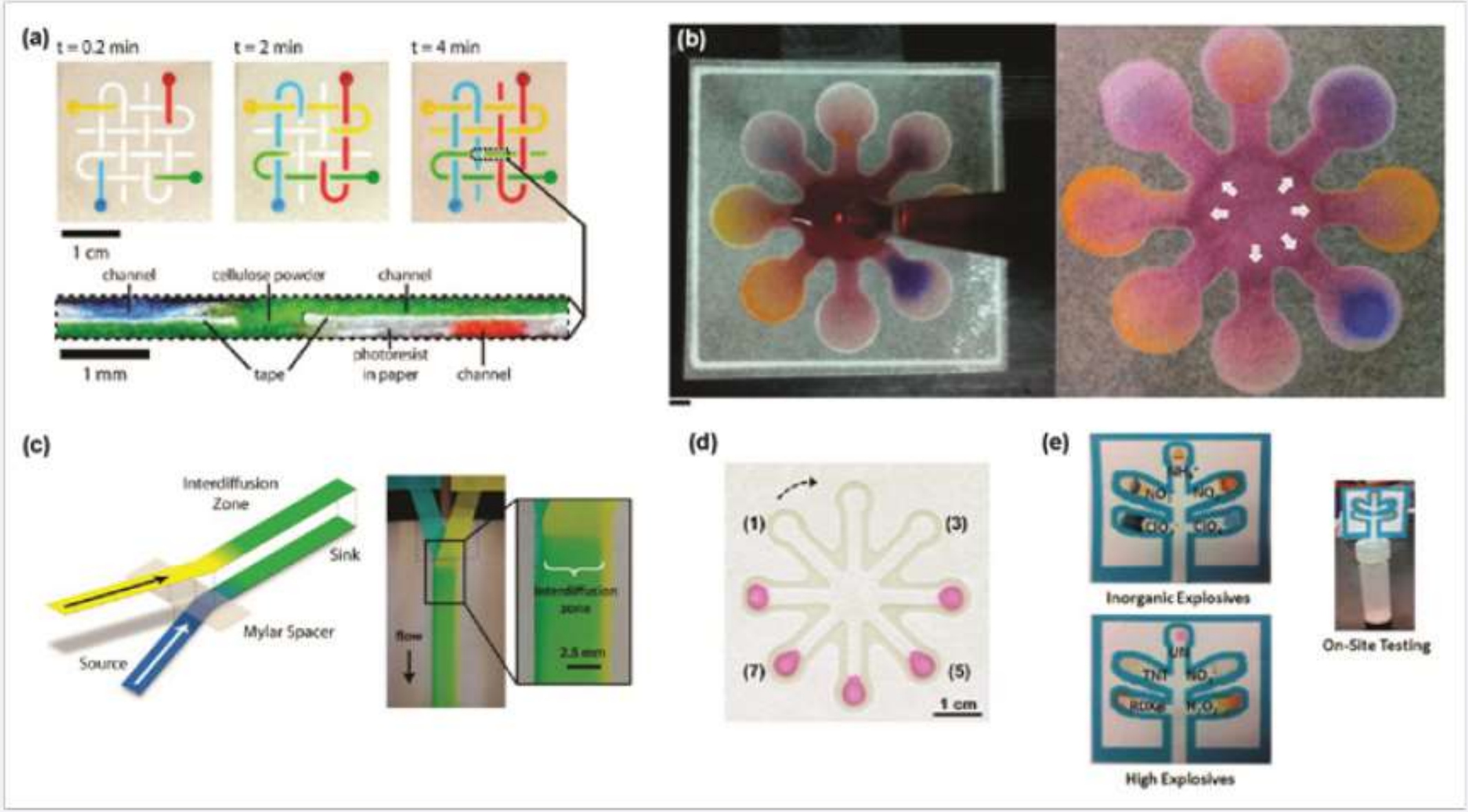
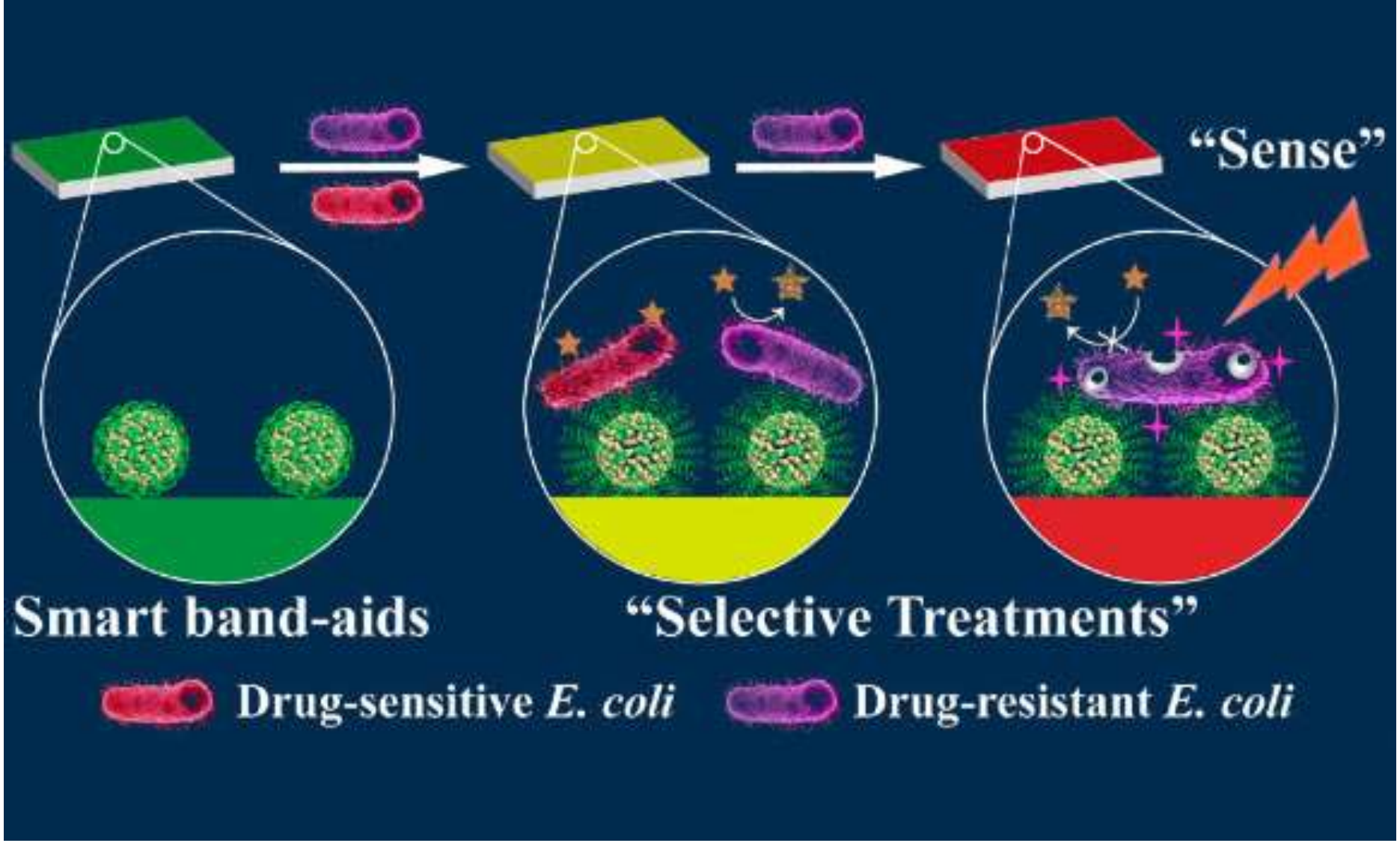


Figure 3: Examples of paper-based system: (a) Three-dimensional patterns system [66]. (b) Red wine analyzer system [67]. (c) Mixing system [68]. (d) Nitrite determination system [69]. (e) Explosives detection system [70].



These are paper-based bandages that can sense drug-resistant and drug-sensitive bacteria in wounds and implement a selective antibacterial strategy; the colors of bandages indicate bacterial infection (yellow) and drug resistance (red), just like a bacterial resistance colorimetric card.

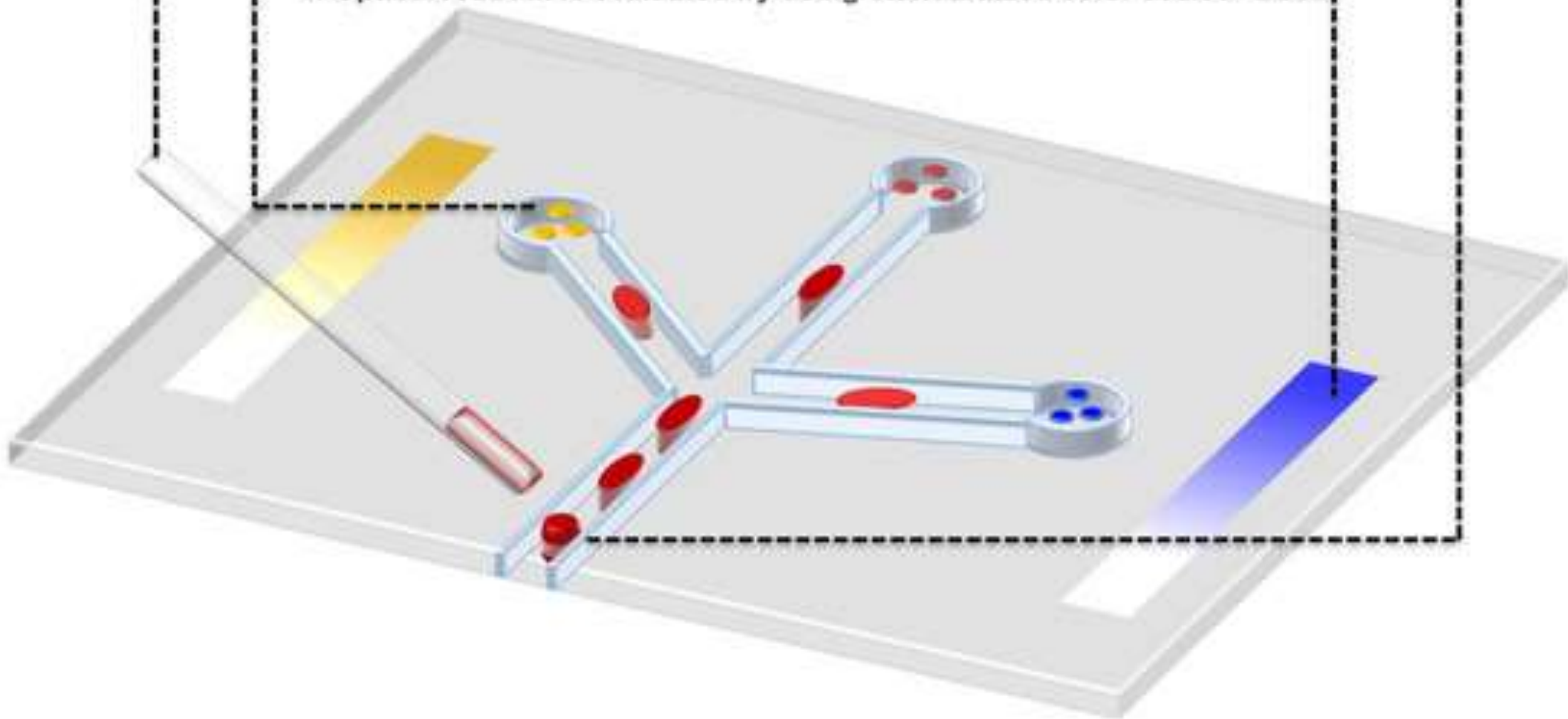
Image credit: Sun *et al*, doi: 10.1021/acscentsci.9b01104

1: Blood samples can be dropped onto the sensor without pre-processing

2: Wax channels printed on paper drive the sample by capillarity

3: Specific reagents are embedded in dedicated chambers in which a dye is formed as end-product of biochemical reactions

4: Optical readout is evaluated by using standardized color scales



A FLUIDIC OSCILLATOR IS A DEVICE WITH NO MOVING PARTS THAT SPRAYS A FLUID FROM SIDE TO SIDE.

A nozzle funnels a fluid jet through a chamber with two feedback channels.

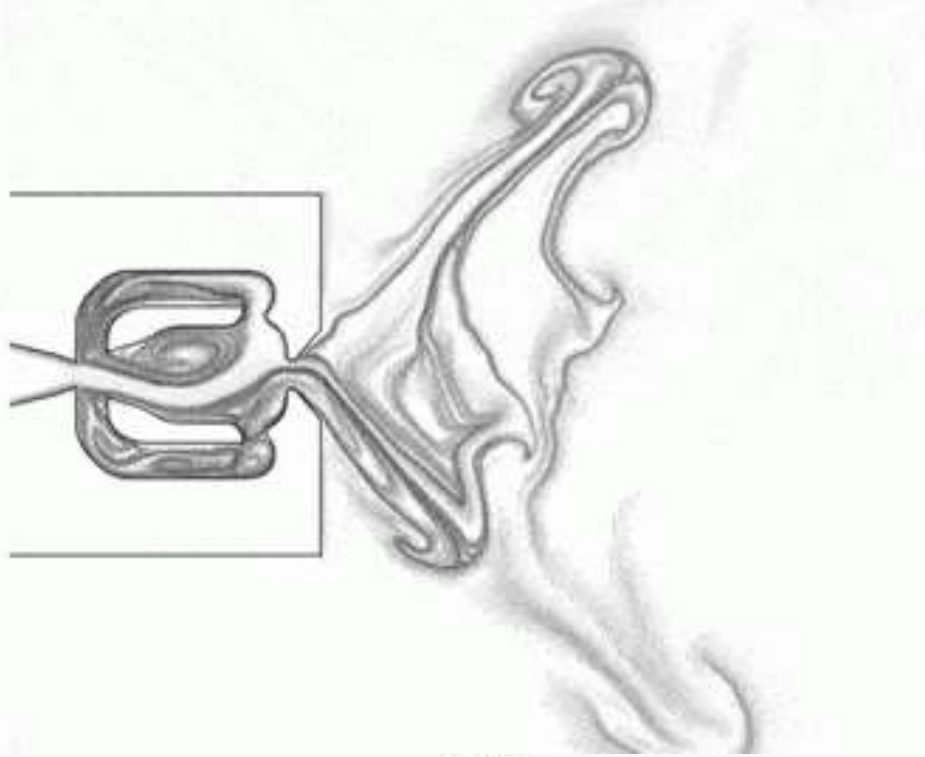
When the jet sweeps close to one side of the chamber, part of the fluid is directed along the feedback channel and back toward the inlet.

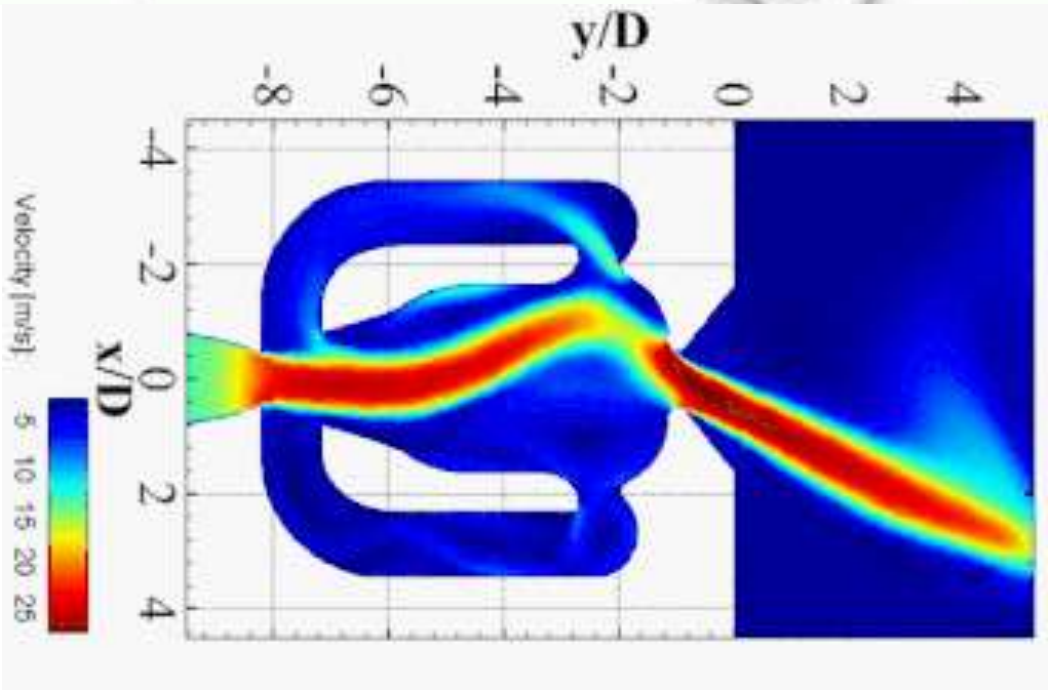
That flow feeds into a recirculating separation bubble in the middle of the chamber.

As that bubble grows, it pushes the jet back toward the other feedback channel, continuing the cycle.

Many automobiles use fluidic oscillators in their windshield washer sprays.

(Image credit: M. Sieber et al., source)

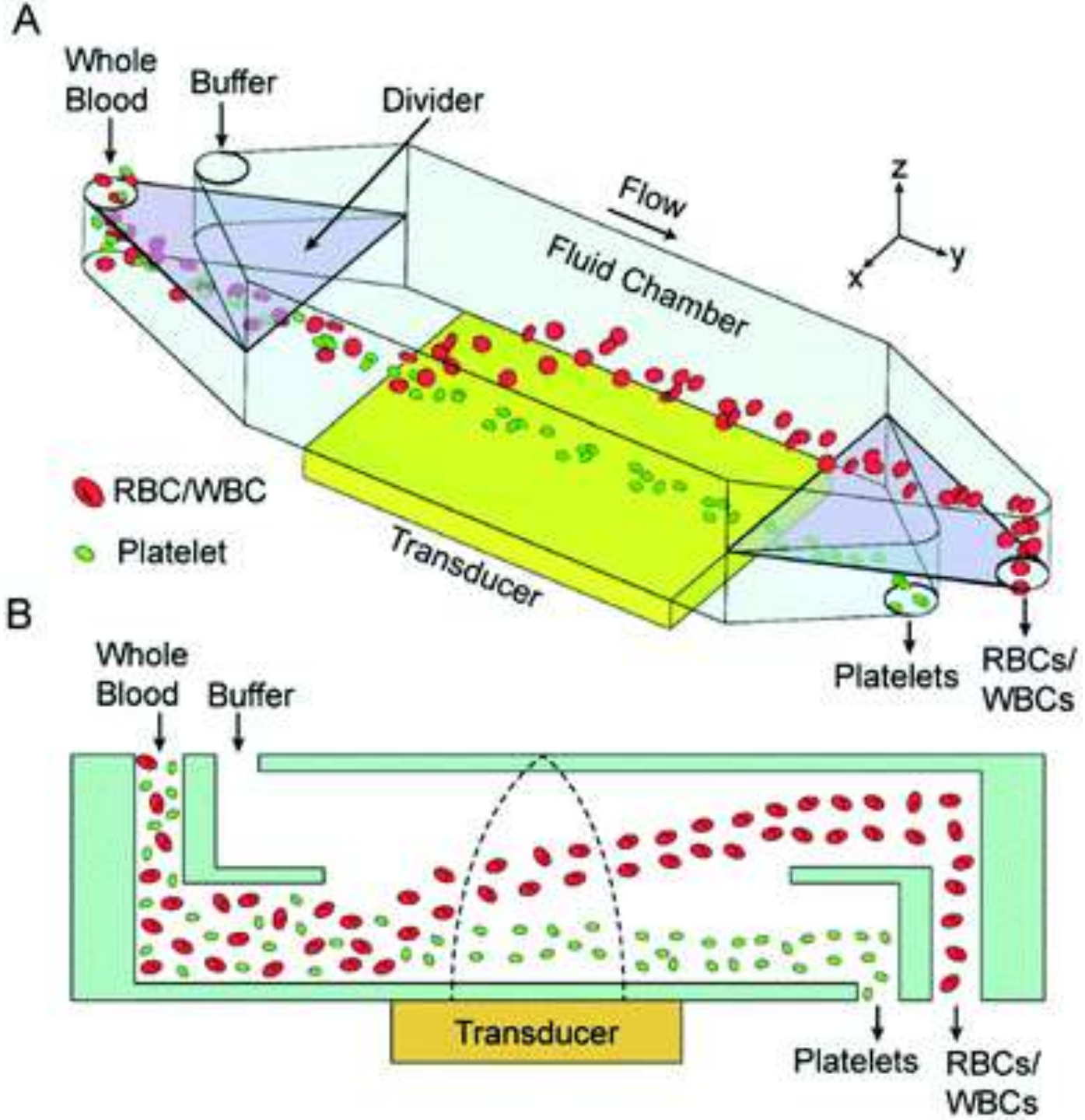




SCHEMATIC OF AN ACOUSTIC-BASED SEPARATION DEVICE THAT CAN BE USED TO SEPARATE PLATELETS FROM WHOLE BLOOD.

(B) The side view of this device, which shows how RBCs are pushed up by the acoustic waves.

(Reproduced from ref. 139 with permission of The Royal Society of Chemistry, copyright 2016.)

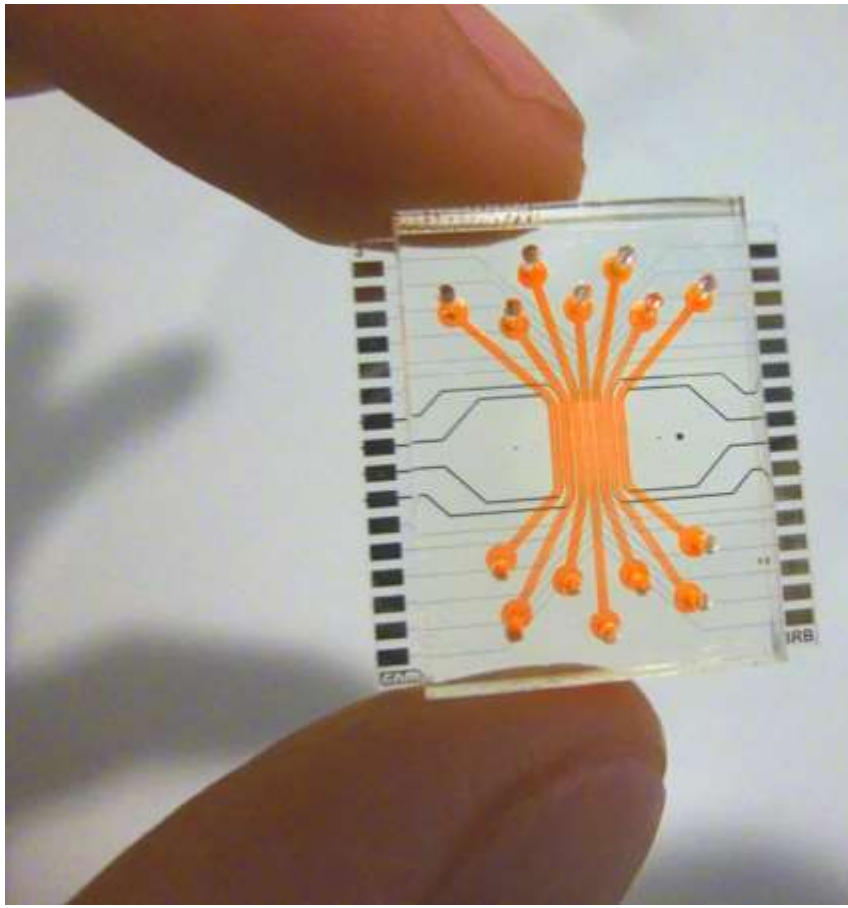


SCIENTISTS EMULATE THE HUMAN BLOOD–RETINAL BARRIER ON A MICRO-FLUIDIC CHIP

The device contains living cells and mimics the structure and physiological conditions of the blood–retinal barrier. It can be use for testing molecules in a real tissue and studying diseases such as diabetic retinopathy.

The methods helps to find ways of reducing animal testing and accelerating clinical trials by mimicking tissues and organ functions, very close to reality.

It is called an Organ-on-a-chip” and is made of several parallel compartments, arranged to emulate the retinal layer structure.



In every compartment a type of cell has been cultured:

- Endothelial cells (which constitute capillary vessels which carry oxygen and nutrients)
- Neuronal cells (which form the neuroretina)
- Retinal pigmented epithelial cells, which form the outer layer of the blood-retinal barrier.

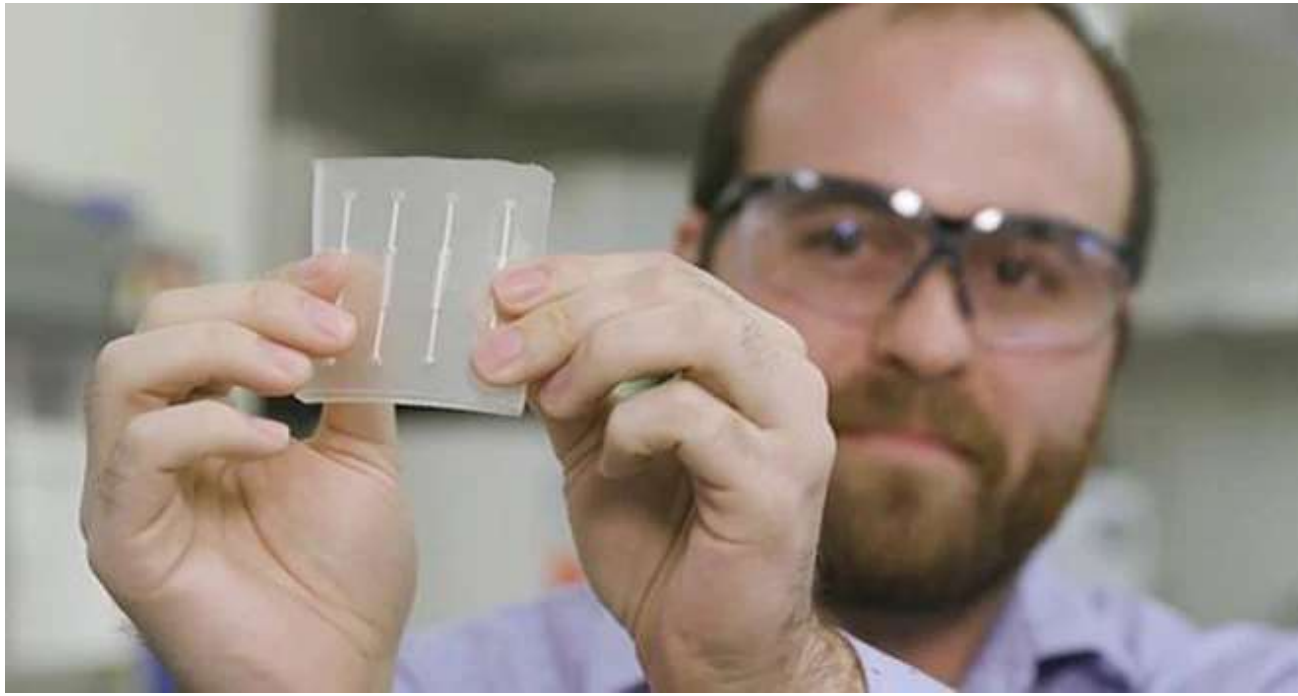
RESEARCHERS ONE STEP CLOSER TO MIMICKING THE BLOOD BRAIN BARRIER ON A CHIP

The blood brain barrier (BBB) in humans consists of blood vessels and tissues that regulate the passage of chemicals and other substances going from the bloodstream into the brain.

It does a good job of keeping potentially harmful molecules from crossing over and affecting the central nervous system.

The downside is that if clinicians need to treat a brain problem, such as toxic chemical exposure or a tumor, it's difficult to get therapeutic drugs across that barrier to do their jobs.

Engineers and biologists at Lawrence Livermore National Laboratory (LLNL) recently made significant strides in modeling the BBB in 2D and 3D by combining fluidics with cell seeding.

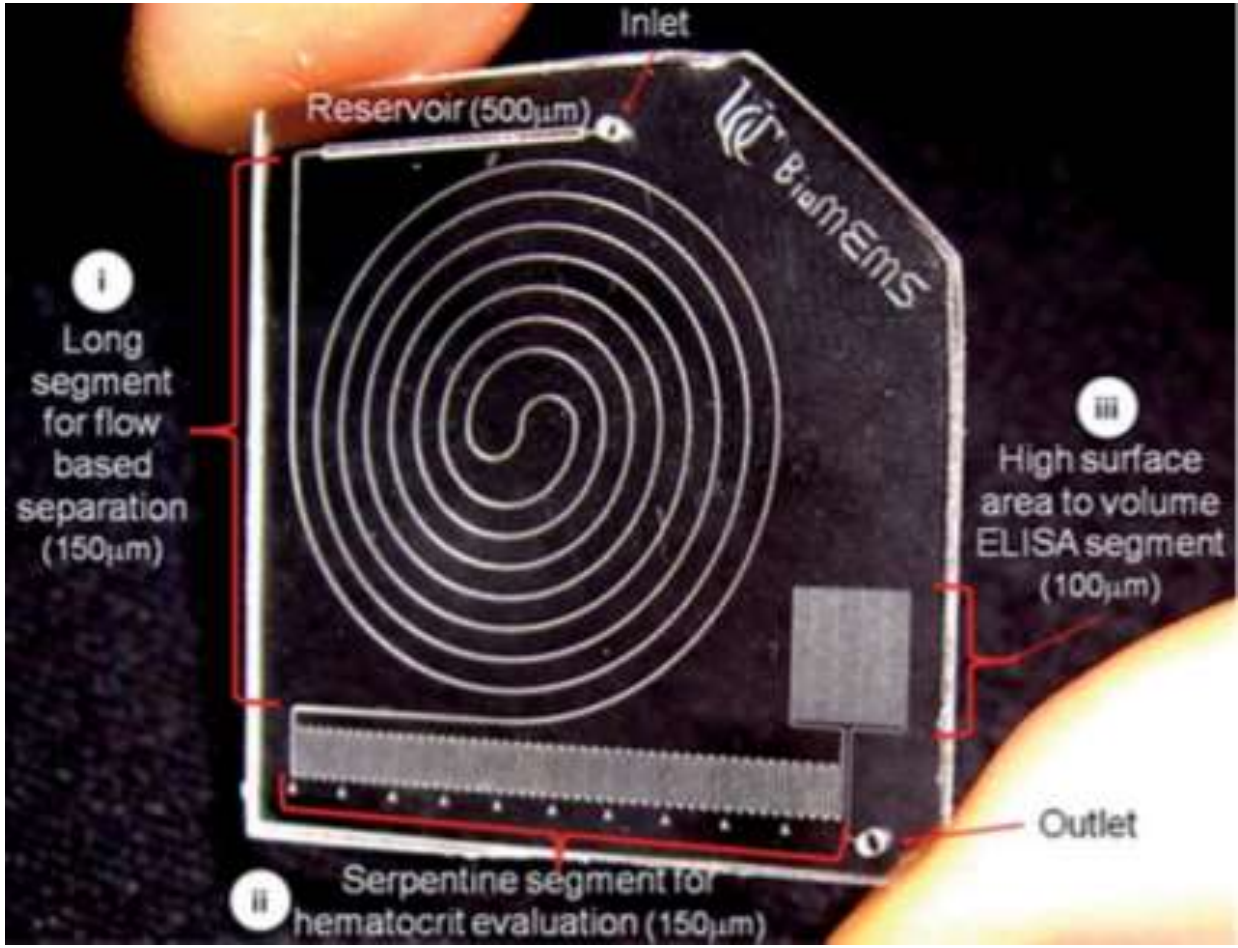


CHIP DESIGN FROM THE UNIVERSITY OF CINCINNATI

This is an integrated blood analysis chip design fabricated in a clear plastic like Polyethylene. It is very small with dimensions of .107 inch X .107 inch.

At the top inlet, a blood sample is injected into to a long spiral flow-based separation channel.

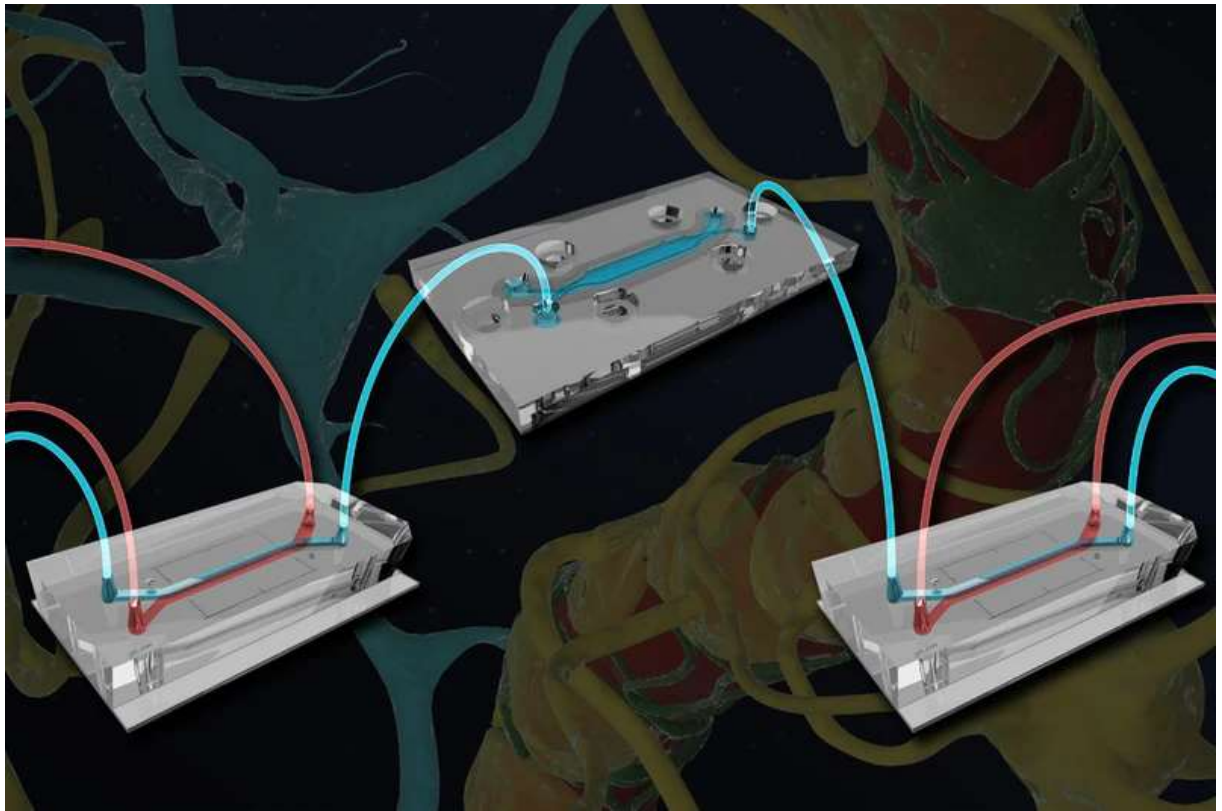
When the blood sample reaches and flows into the long serpentine segment, (ii) the hematocrit (% of red blood cells in the blood sample) is evaluated based on the number of serpentine switchbacks that are filled with packed erythrocytes, which are red blood cells that contain hemoglobin)



ANOTHER USE OF FLUIDIC CHIPS TO ANALYZE WHAT MATERIALS CAN PASS THE BLOOD-BRAIN BARRIER

One Brain Chip (top) containing neurons and astrocytes is connected via microfluidic channels to two blood-brain barrier (BBB) chips containing endothelial cells and their supporting astrocytes and pericytes.

The researchers were able to trace the flow of molecules from the blood capillaries across the BBB and into the brain and found that substances produced by the endothelial cells help maintain nerve function. Credit: Wyss Institute at Harvard University



EACH CHIP IS MADE BY STANDARD INKJET PRINTING, REQUIRES JUST 20 MINUTES TO ASSEMBLE, AND THE COST? A SINGLE PENNY

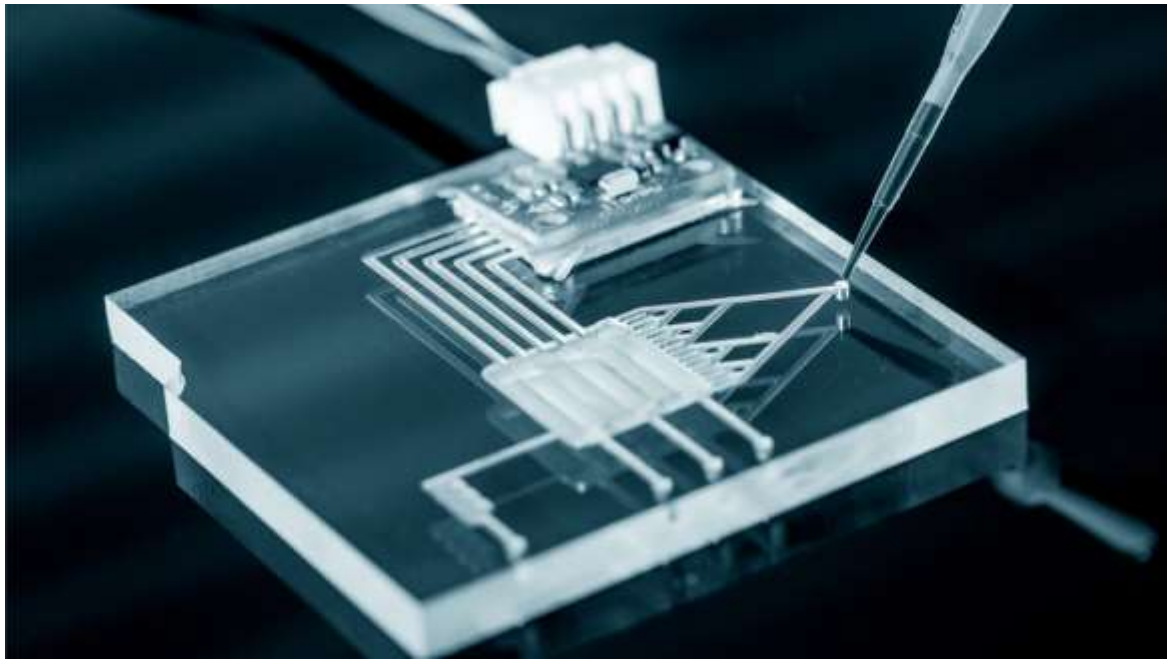
The flexible inkjet-nanoparticle-printed biochip (FINP). It can diagnose cancer and infections.

The printing of a special coating was done with an ink-jet printer.

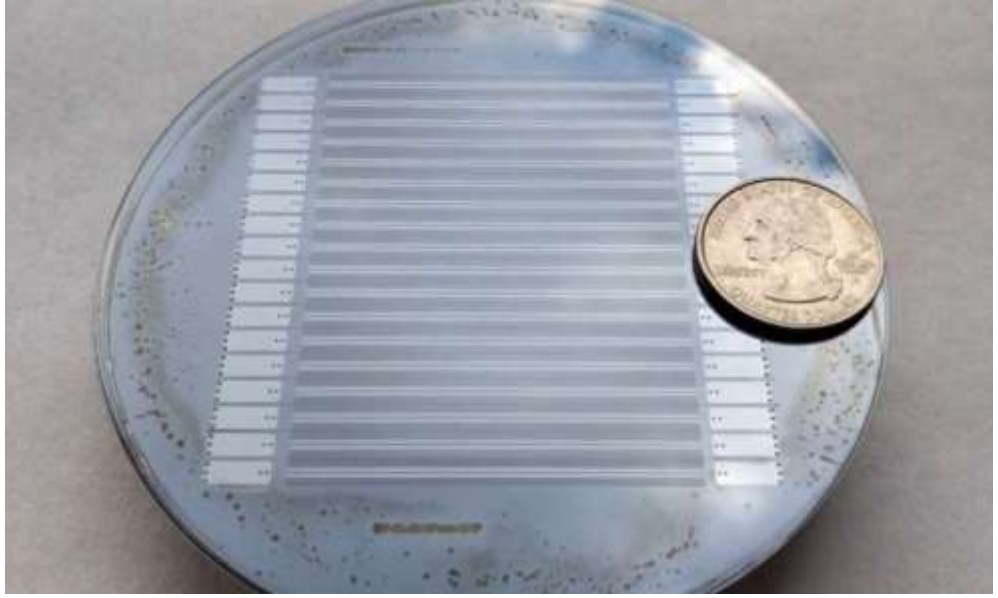
The new chip, dubbed FINP chip, is a modular, three-layered sandwich: the top reusable layer is made of commercially available conductive particles directly printed onto a flexible polyethylene sheet.

The bottom layer is a disposable silicone chamber designed to hold biological fluids.

A thin insulating barrier separates the top electronics from the chamber.



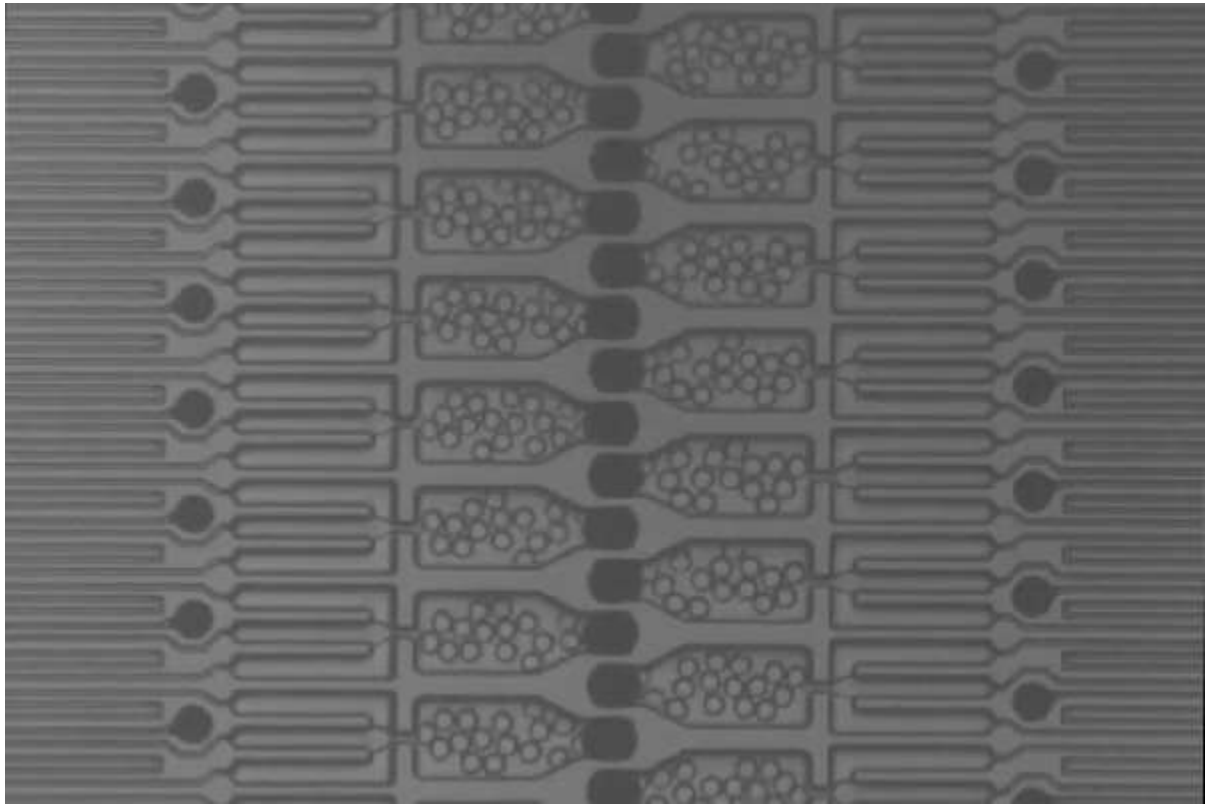
MAKING MORE THAN 300 BILLION DRUG MICROPARTICLES AN HOUR, ALL ON A SILICON-AND-GLASS CHIP THAT CAN FIT INTO A SHIRT POCKET



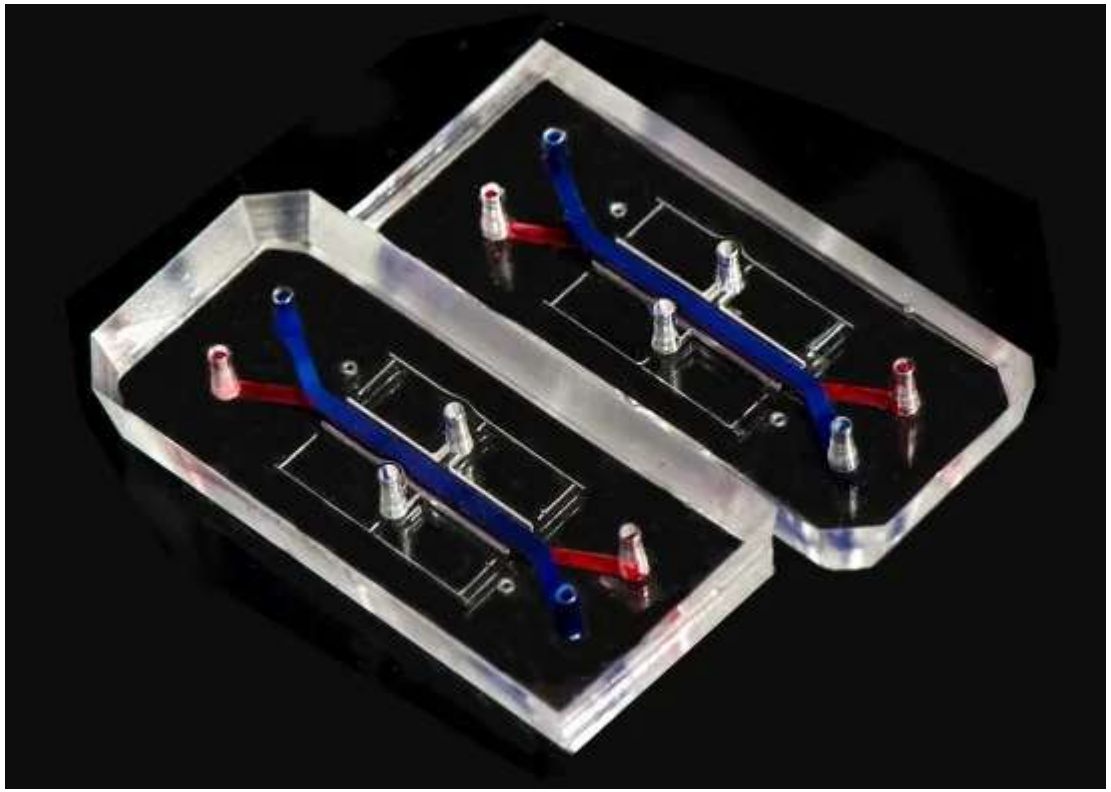
The Penn Engineering team fit 10,260 of these microparticle-generating devices onto a four-inch silicon wafer.

The innovation is a new fluidic device resulting in a system that can manufacture these drug particles a thousand times faster than ever before.

Many drugs are encapsulated in solid micro-particles, the size and shape of which determine the timing of the drug's release and its delivery to specific parts of the body.



CHIPS THAT MIMIC ORGANS COULD BE MORE POWERFUL THAN ANIMAL TESTING



Scientists at Lawrence Livermore National Laboratory have made a system called iCHIP that connects four organs: the brain, the peripheral nervous system, the blood-brain barrier, and the heart.

Immunotherapy drugs are tricky to study in animals because they consist of molecules that target specific proteins on *human* immune cells, fitting like a key in a lock.

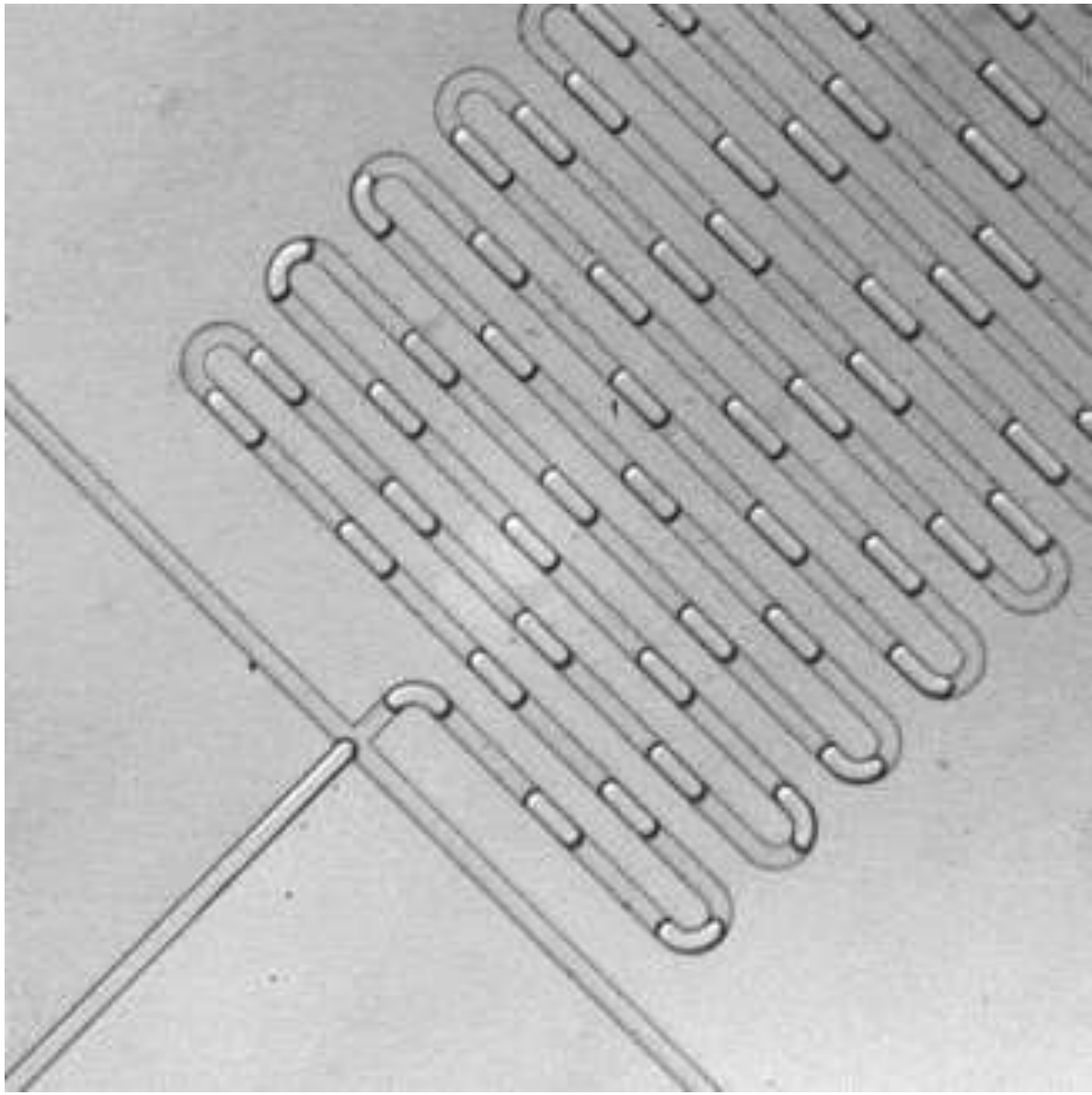
MICROFLUIDIC TECHNOLOGIES FOR FAST TESTS IN BIOCHEMISTRY

This process can perform biological assays in water-in-oil microemulsions.

Each picoliter-sized droplet (a millionth of a liter) can contain reactions containing different cells, biomolecules, or combinations of chemicals.

Various microfluidic modules enable droplets to be loaded with single cells, incubated over a range of times and temperatures, injected with additional reagents, and sorted based on their optical properties.

These droplet operations can be performed with full automation at 1,000 per second, providing a general platform for fast procedures in biochemistry.

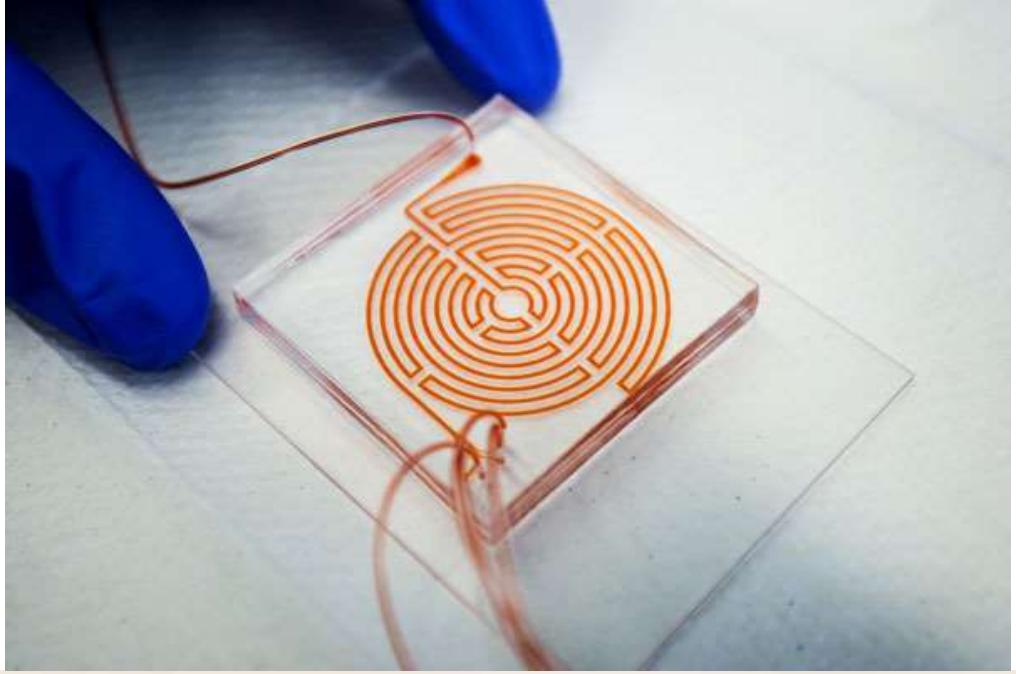


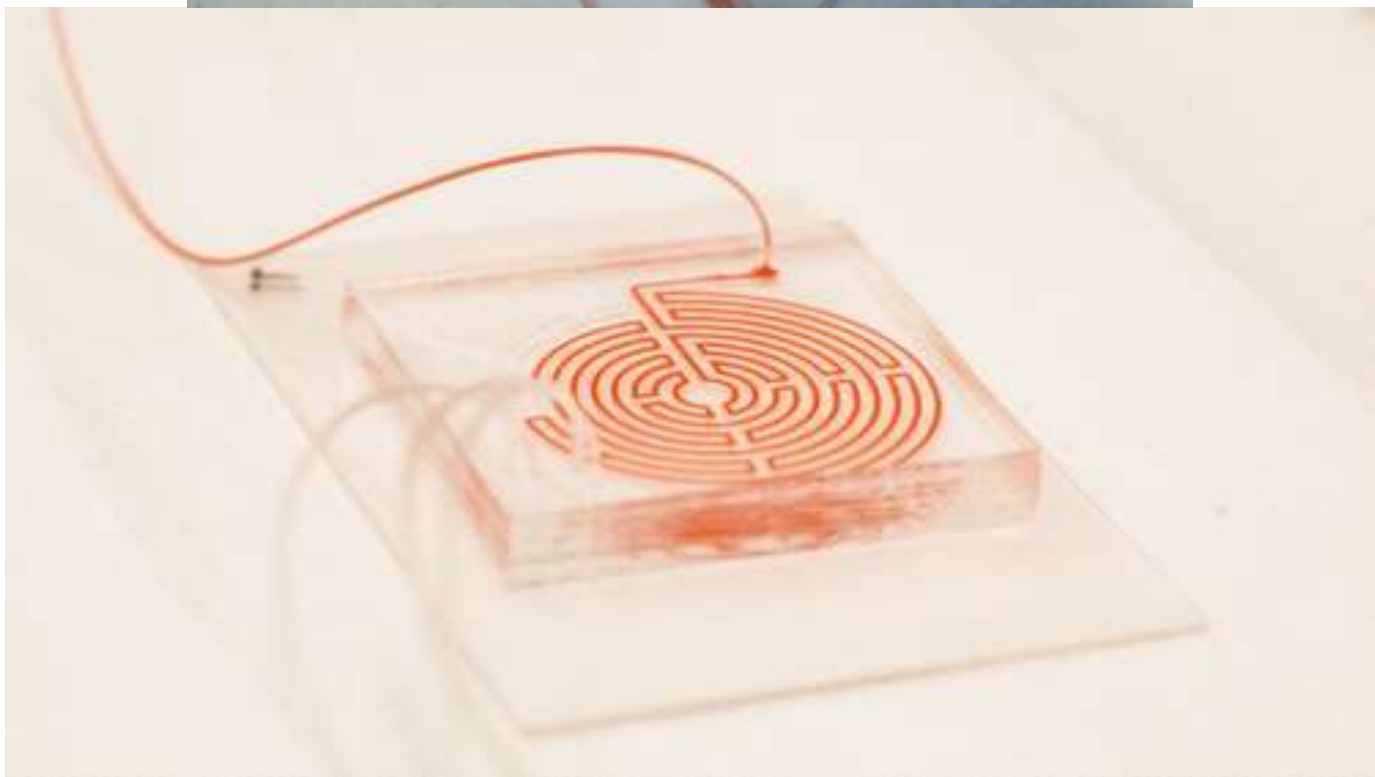
LABYRINTH' CHIP COULD HELP MONITOR AGGRESSIVE CANCER STEM CELLS

Blood runs through the labyrinth chip, quickly separating cancer cells from white and red blood cells.

Inspired by the Labyrinth of Greek mythology, a new chip etched with fluid channels sends blood samples through a hydrodynamic maze to separate out rare circulating cancer cells into a relatively clean stream for analysis. It is already in use in a breast cancer clinical trial.

Credit: Joseph Xu, Michigan Engineering Communications & Marketing.



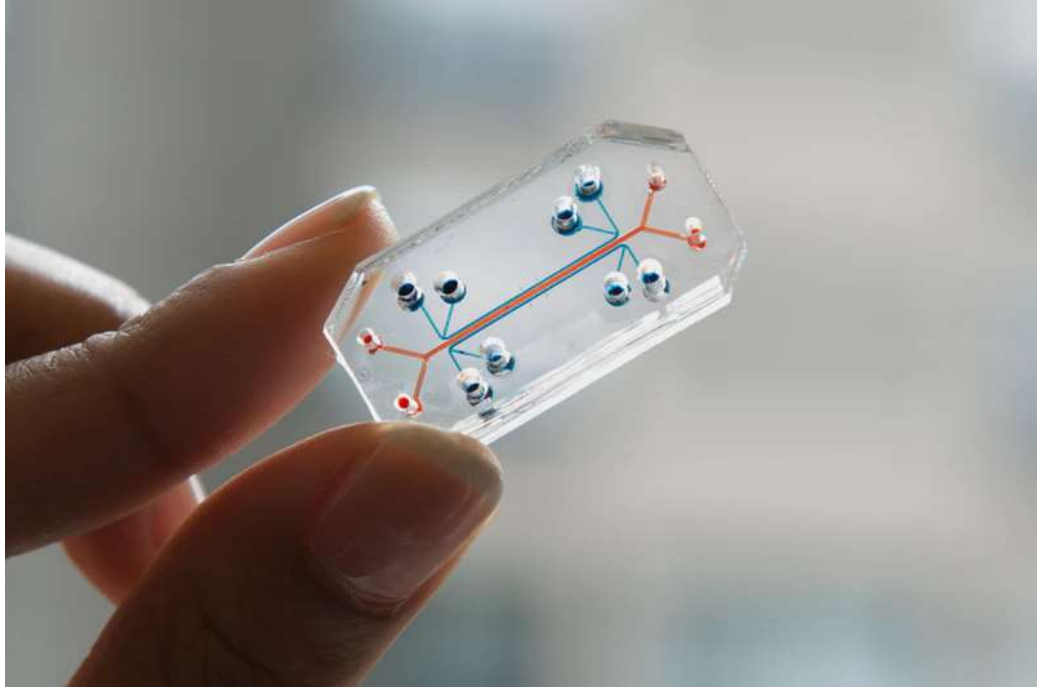


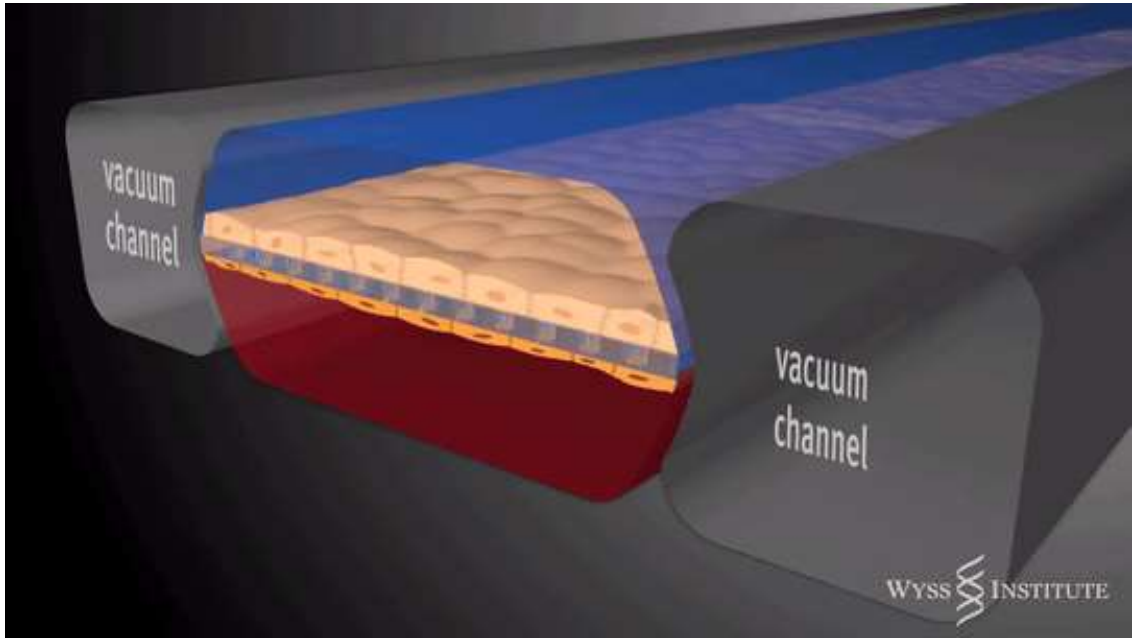
"LUNG-ON-A-CHIP" SETS STAGE FOR NEXT WAVE OF RESEARCH TO REPLACE ANIMAL TESTING

The lung-on-a-chip device is a crystal clear, flexible polymer about the size of a memory stick that contains hollow channels fabricated using computer microchip manufacturing techniques.

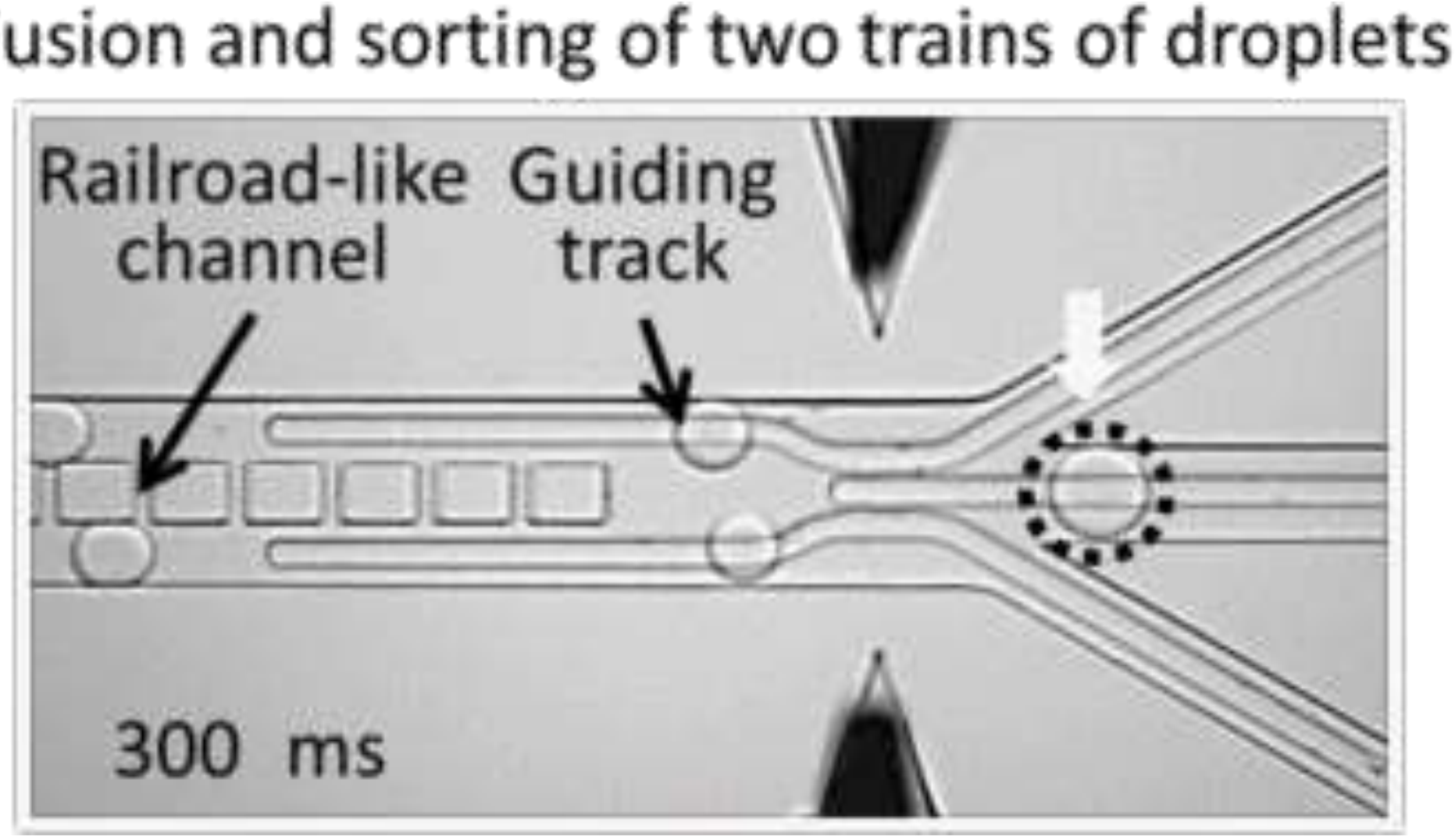
Two of the channels are separated by a thin, flexible, porous membrane that on one side is lined with human lung cells from the air sac and exposed to air; human capillary blood cells are placed on the other side with medium flowing over their surface.

A vacuum applied to side channels deforms this tissue-tissue interface to re-create the way human lung tissues physically expand and retract when breathing.
https://www.youtube.com/watch?v=Mg2fJ0UBj_0&t=9s





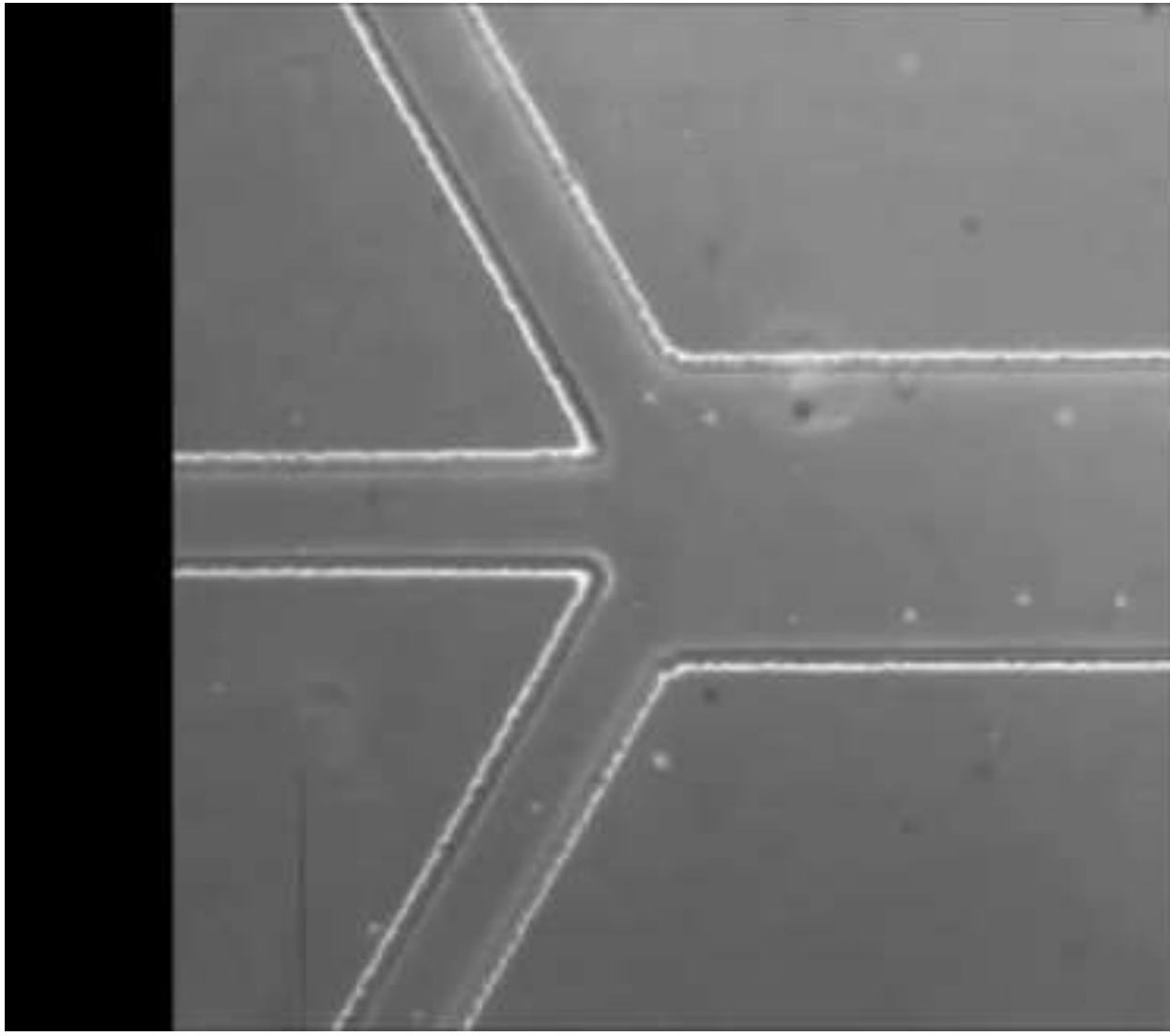
FUSION AND SORTING OF TWO PARALLEL TRAINS OF DROPLETS USING A RAILROAD-LIKE CHANNEL NETWORK AND GUIDING TRACKS



MALARIA DETECTION USING INERTIAL MICROFLUIDICS

Diagnosis of malaria at the early stage of infection is challenging due to the difficulty in detecting low abundance parasites from blood

A method has been developed that uses pinched flow dynamics to isolate malaria parasites from blood containing white blood cells (WBCs) by keeping the flow of the blood cells to the sides of the walls of the main section so they can be separated from the Malaria cells.



MEET EVATAR: THE LAB MODEL THAT MIMICS THE FEMALE REPRODUCTIVE SYSTEM

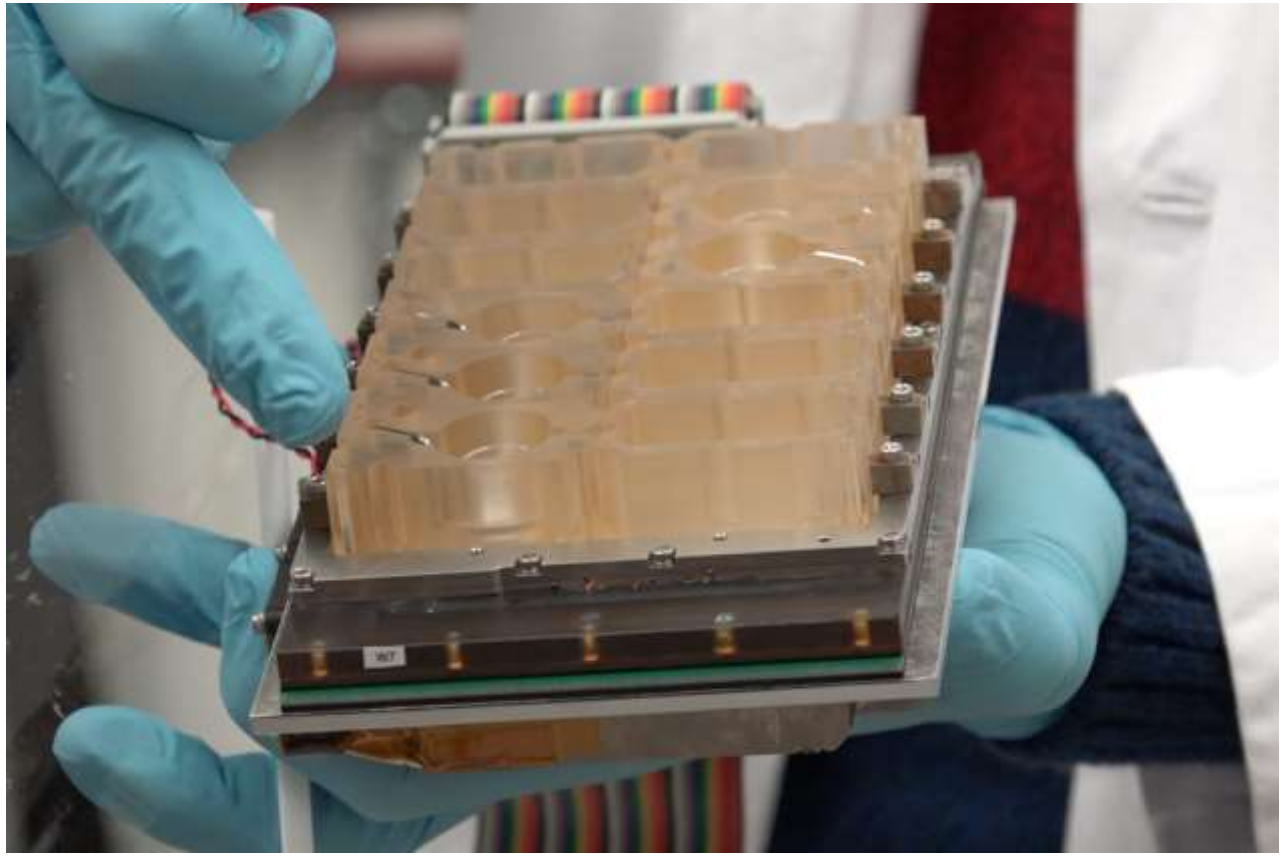
A three-dimensional model has all the parts of the female reproductive system — ovaries, fallopian tubes, a uterus and a cervix.

A liver, while not a reproductive organ, is included in the system because it metabolizes drugs.

It is so close to the real thing it even simulates a menstrual cycle and pregnancy hormones.

The model, fabricated with human and mouse tissue and named Evatar, can be used to test drugs, with implications for women dealing with painful periods, infertility and other conditions.

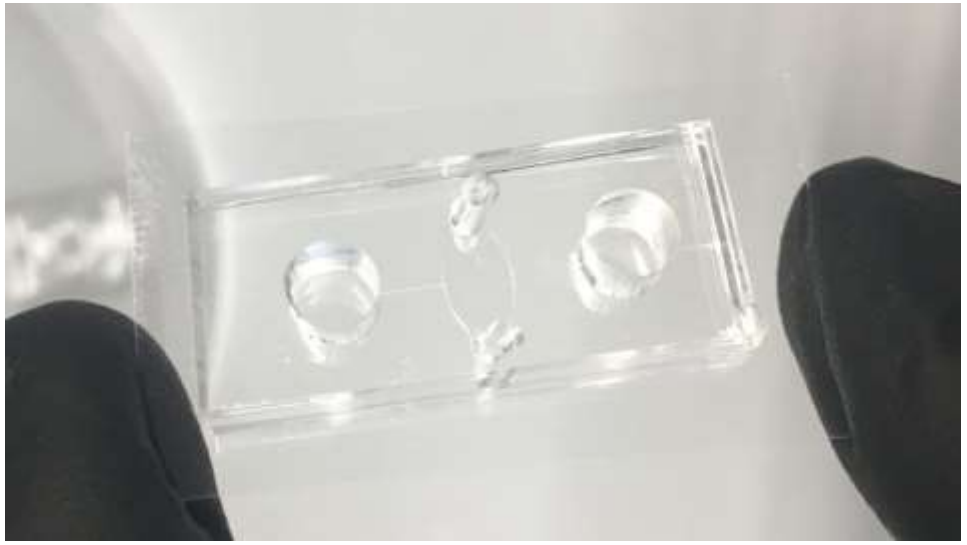
https://www.youtube.com/watch?time_continue=5&v=z9lvA70DoPs&feature=emb_logo



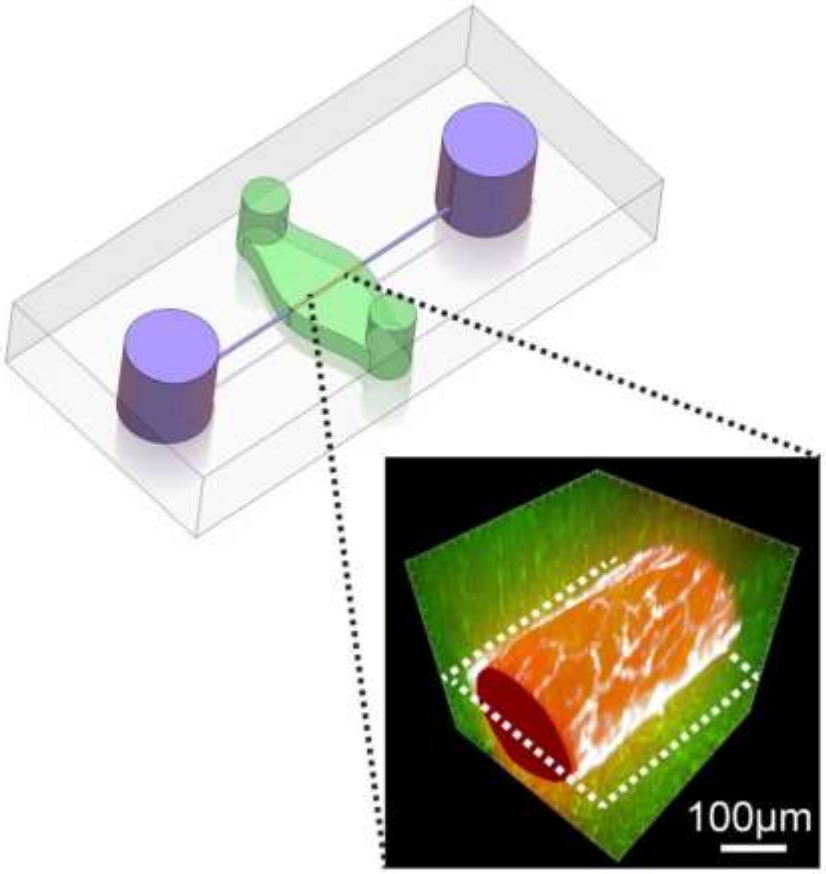
Credit...Northwestern University

NEW DEVICE LEADS TO DISCOVERY THAT MAY BENEFIT CANCER PATIENTS

Two medical researchers were excited to use a new 3D blood vessel-on-a-chip that they developed in Professor Christopher Chen's lab because it provided a perfect platform for studying the effects of mechanical forces of blood flow on vessels in life-like conditions.



This is the blood vessel-on-a-chip that was developed to study how blood flow affects vessel integrity



A graphic representation of the chip shows where the manufactured blood vessel sits.

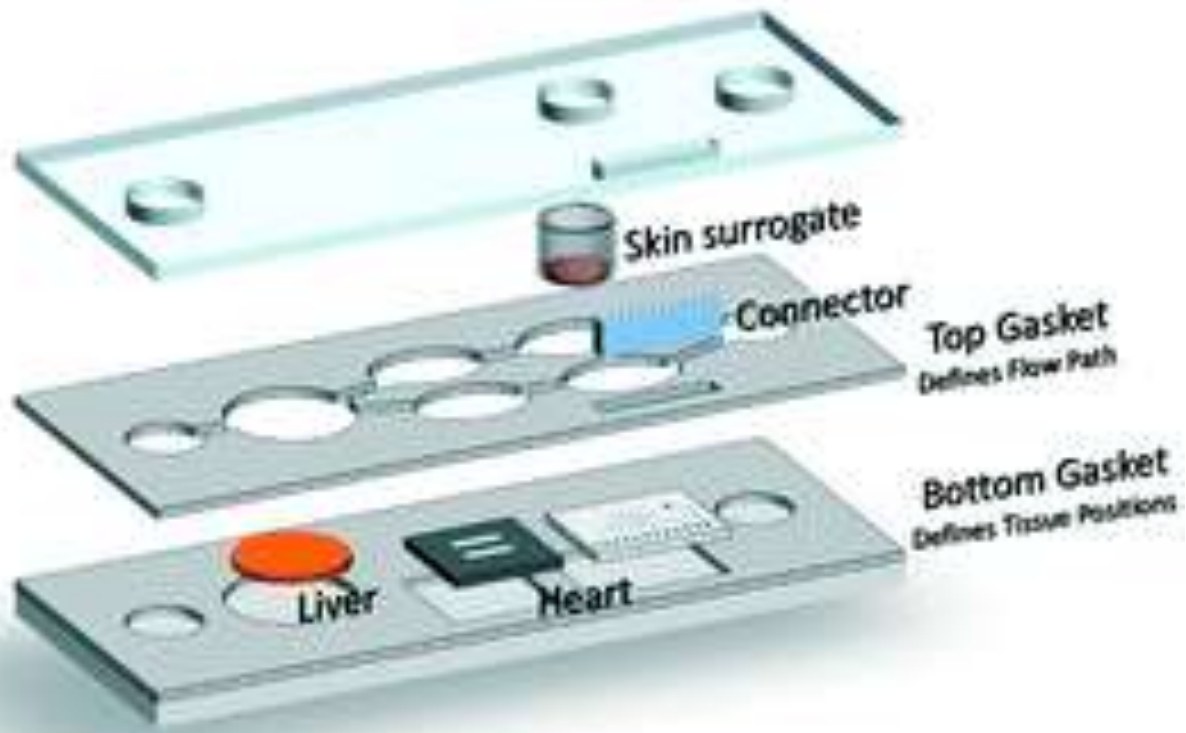
The two surrounding blue cylinders are where the researchers hooked up the simulated blood flow

Body-on-a-chip in vitro systems are a promising technology that aims to increase the predictive power of drug efficacy and toxicity in humans when compared to traditional animal models.

Here is a new heart–liver body-on-a-chip system with a skin surrogate to assess the toxicity of drugs that are topically administered.

The heart–liver system was successful in predicting the effects for both cardiac and liver functions changes due to the compounds.

The difference in the concentrations of drugs applied topically compared to systemically indicates that the barrier properties of the skin surrogate were efficient



ORGAN ON A CHIP

Ultimately, scientists want to start linking these organs-on-a-chip together, to be able to see how a drug, chemical, or other substance acts all over the human body.

For the time being, the breakthroughs in the Huh lab are models of the:

Eye
Lung
Placenta
Pancreas
Cervix
Fat

They will open the door to new studies on conditions ranging from pre-term birth to diabetes.

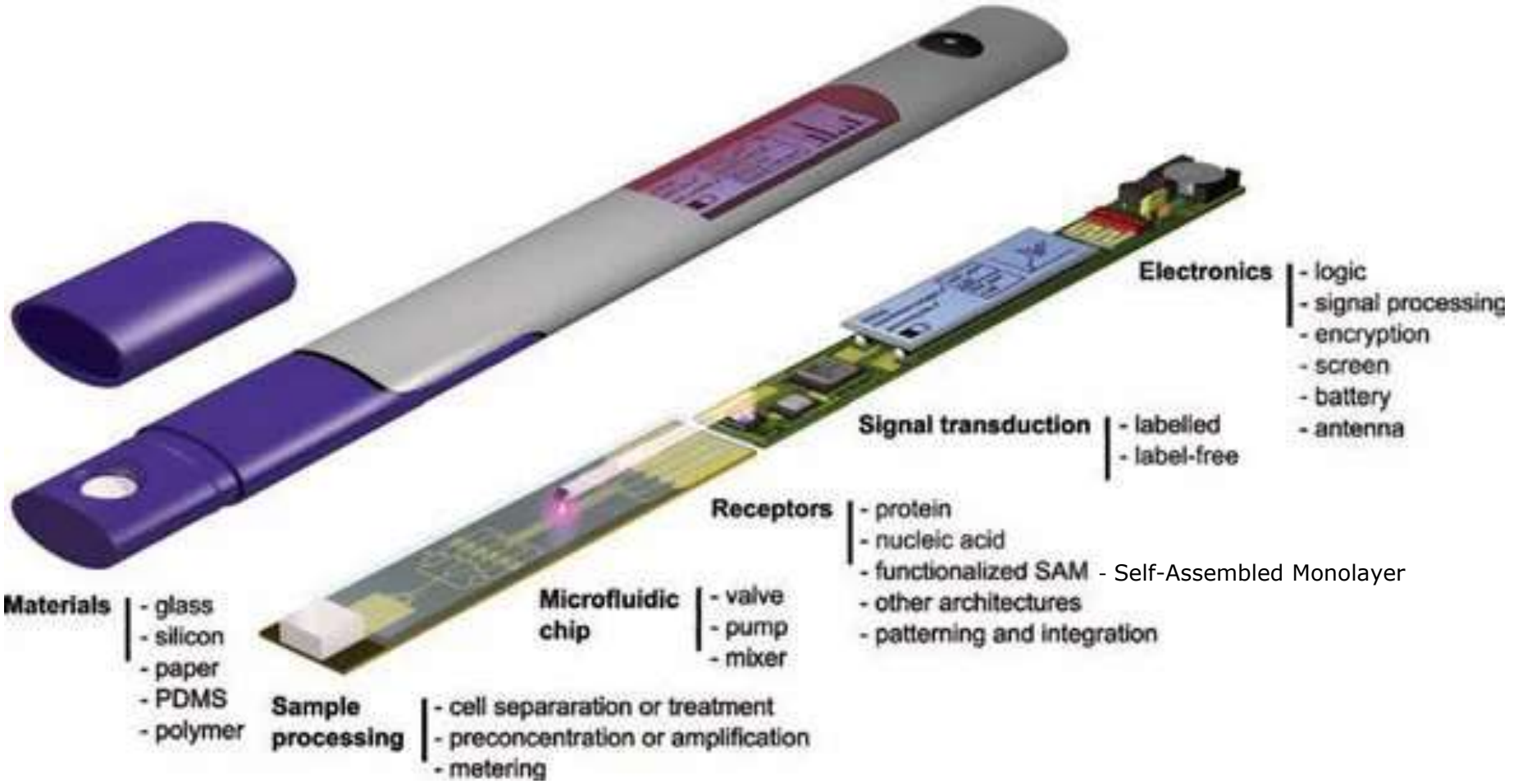
https://penntoday.upenn.edu/news/organs-chip-hurtle-toward-final-frontier

https://www.emulatebio.com/blog/national-geographic-further

THE IDEAL POC DIAGNOSTIC DEVICE IN THE FUTURE

It will detect several body fluids within minutes from a very small sample and report the encrypted results to an electronic health record.

The microfluidic chip, shown here encapsulated in purple plastic, is disposable and the mass manufacturing material cost would be less than $1.



Self-Assembled Monolayer

(PDMS – Poly dimethyl siloxane)

Key Summary:

- POCT is a modern variant of laboratory medicine. Its technical development has been largely determined by the miniaturization of instruments and procedures, as well as the use of modern information technologies.

- Aside from the determinations of blood sugar and blood gases, a wide variety of clinical chemical, immunological, hematological and hemo-staseo-logical procedures are now available.

- POCT is of considerable medical significance in providing emergency analyses in potentially fatal situations. In intensive medical care, not only purely medical, but also organizational aspects are important. The organizational aspects are clearly more important in outpatient clinics and patient admission.

- The aim of POCT is to accelerate diagnostic and therapeutic processes and thus to reduce the time spent by the patient in the hospital, intensive care ward or operating theater, as well as reducing treatment costs by adequate structure of the therapy, optimal patient monitoring and avoiding complications.

The above information is from the article “Point-of-Care Testing in Hospitals and Primary Care” https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2936038/

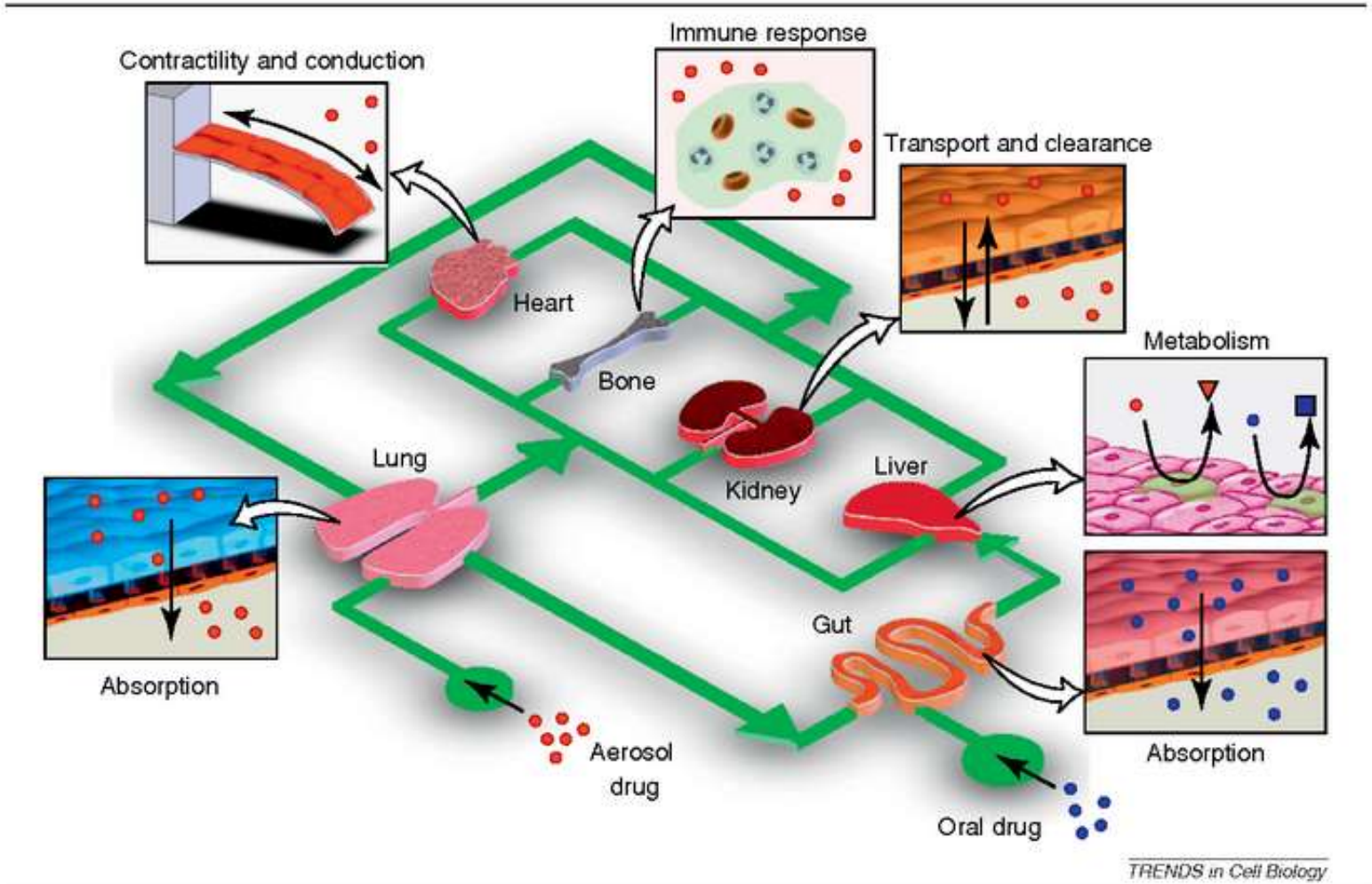


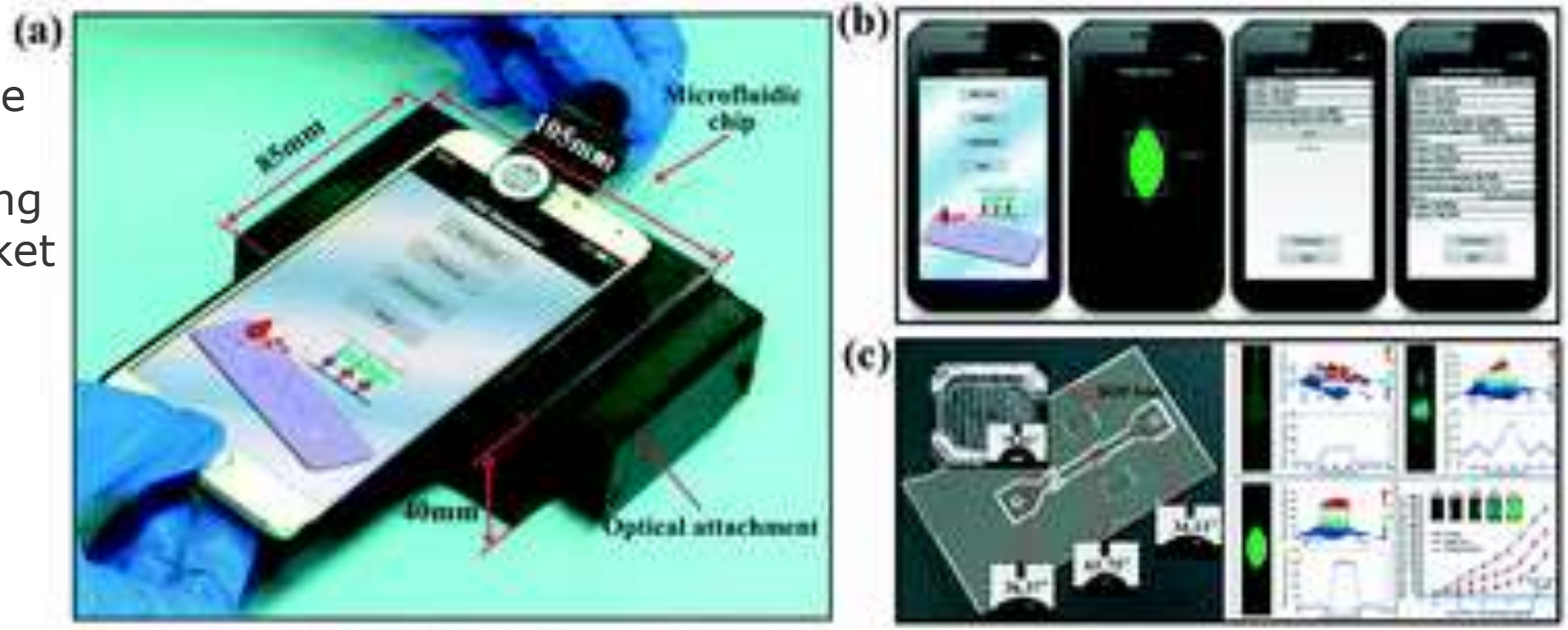
Figure 4. The human-on-a-chip concept. Biomimetic microsystems representing differe circulatory system in a physiologically relevant manner to model a complex, dynamic reliably evaluate drug efficacy and toxicity. As shown in this example, an integrated sys be used to study the absorption of inhaled aerosol drugs (red) from the lung to microcirc or conduction), transport and clearance in the kidney, metabolism in the liver, and im introduced into the gut compartment to investigate interplay between orally administe various organs. Less

POINT OF CARE DEVICES SHOWING TEST RESULTS WITH SMART PHONES

Several smart phone-based devices and associated tools have emerged as a next-generation point of care diagnostics or testing devices, contributing to the market revenue throughout the forecast period.

For instance, **the smartphone-app combined with an autonomous Bio-chip is used for rapid testing to see if a person had a heart attack.**

This platform is easily applicable in resource-limited settings where it provides test results within 12 minutes.



The Luminostics company has developed a diagnostic platform with smartphone readout for rapid home testing, point-of-care testing and global health applications.

The diagnostics platform is compatible with most smartphone models, can detect or measure bacteria, viruses, proteins, and hormones from swabs, saliva, urine, and blood.

French drugmaker Sanofi is collaborating with US start-up company Luminostics to develop a smartphone-based self-diagnosis test for COVID-19 that could give a result within 30 minutes.

SMART PHONE USAGE FOR POC TESTING

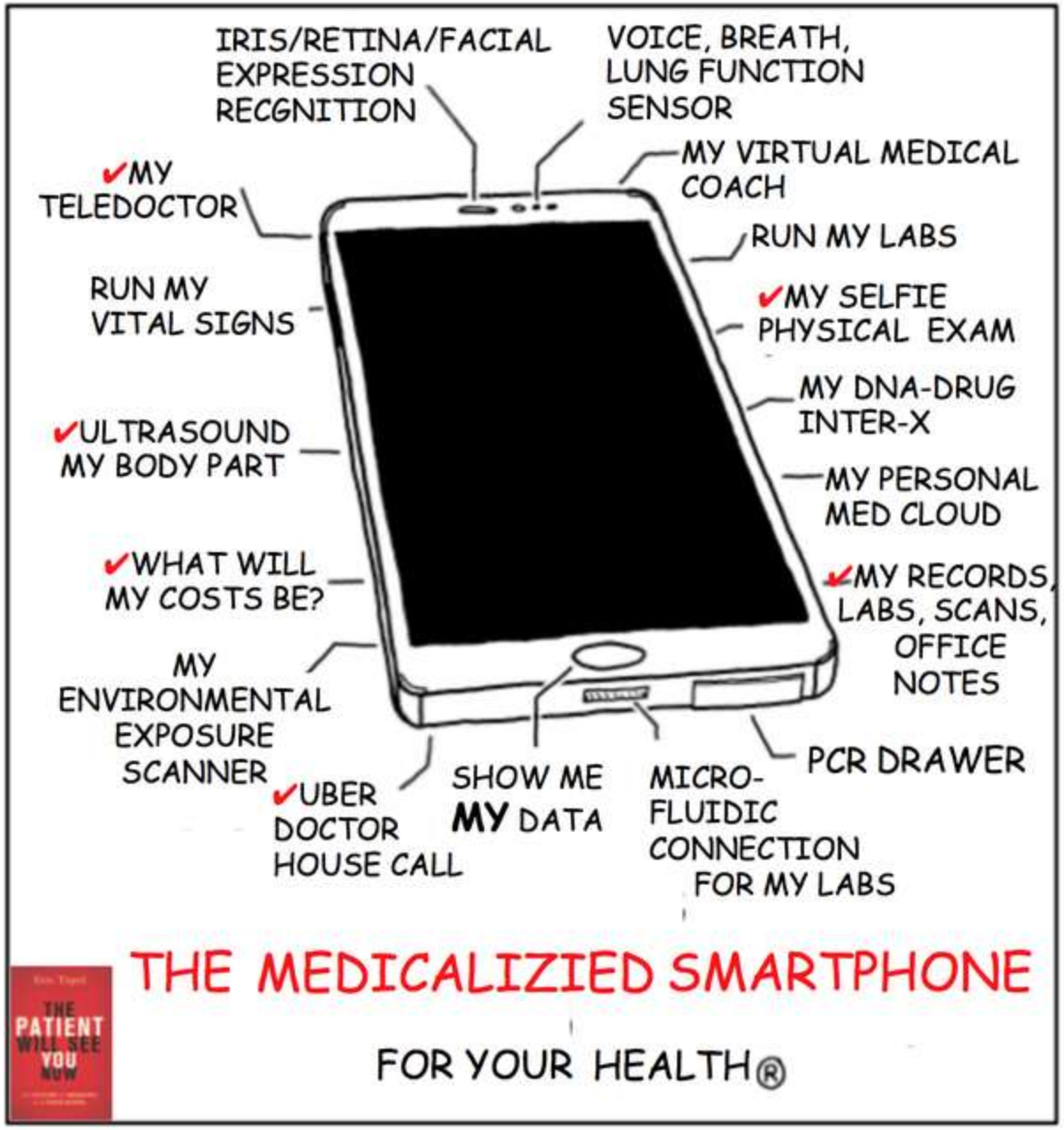
The number of current worldwide smartphone users is around 3.5 billion - 45% of the world's population owns a smartphone.

It is predicted that by 2023, the number of mobile device users will increase to 7.3 billion.

ADVANTAGES OF SMART PHONES:

- Can be held in one hand and are lightweight so they can be carried for long periods of time.
- Have very responsive touch screens
- Some models are water resistant
- Compact and long-lasting batteries with 1 to 3 days of usage without charging.
- Made to use multiple connectivity standards - GSM, 4G, LTE and 5G.

- Can connect to other systems using wireless technology that allows monitoring devices to talk to each other (ANT+)
- Capable of connecting with a USB connection, WIFI, Bluetooth and near-field communication (NFC)
- Precision camera lenses can be added to capture images with resolutions up to 64 Megapixels (MP) and with multiple aperture settings.
- Use auto focus features with hybrid optical zoom and some models can record high quality videos.
- Embedded sensors such as accelerometers and gyro sensors can be used to monitor the movement of patients (i.e. walking, movement while sleeping, or even in the event of a fall).
- Temperature and RGB light sensors are used for monitoring patients' vital signs such as monitoring pulse, breathing and oxygen saturation levels.



SURGICAL DIAGNOSIS APPLICATIONS OF A SMARTPHONE ADAPTER

(A) Phone-based otoscopy and laptop-based wireless endoscopic otoscopy

(B) A polarized dermoscope mounted on a cellular telephone enables accurate comedone manipulation

(C) Smartphone-endoscope adapter to capture video

(D) Smartphone attached to a microscope through a 3D printed adapter,

(E) Smartphone microscope adapter

(F) Smartphone attached to a microscope through an adapter

University of Cincinnati Smartphone Lab delivers test results in 'split' second

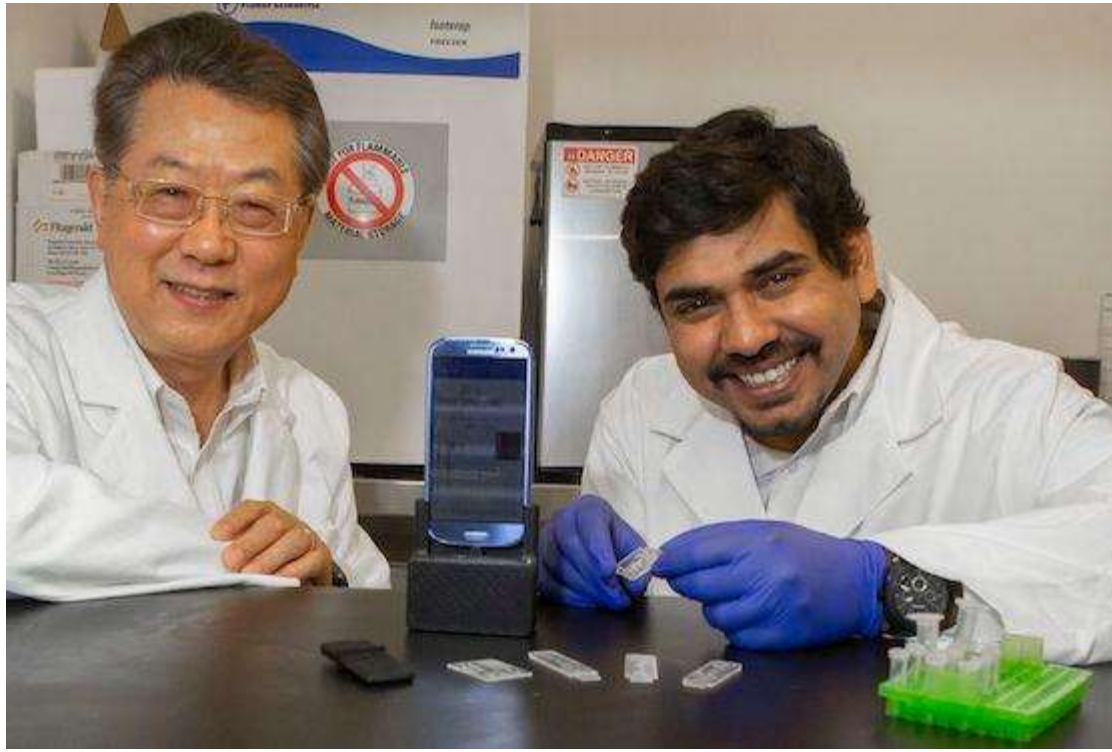
Using your phone to diagnose disease or track your medical condition is the holy grail for remote health monitoring, but so far, it's been impractical to combine the two in a single device.

Tech companies don't want the regulatory headaches that would come from labeling phones medical devices.

University of Cincinnati engineers have come up with the next best thing.

Professor Chong Ahn led a lab team that designed a tiny portable device that plugs into a phone, connecting it automatically to a doctor's office through a custom app UC also developed.

With a single drop of blood or saliva on the UC-designed custom plastic lab chip, the device smaller than a credit card can diagnose infectious diseases such as coronavirus, malaria, HIV or Lyme disease or countless other health conditions like depression and anxiety.



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