LAB ON A CHIP: A MINIATURIZATION OF LABORATORY TECHNIQUES

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OUTLINE

- History
- Main components of a chip and types of chips
- Applications
- Current developments
WHAT IS LAB ON A CHIP?

- Miniturization and integration of laboratory techniques.

- Usually done on a device involving a microplate no greater than a few centimetres square that allow the use of laboratory techniques on the microscale.


A LITTLE BIT OF HISTORY

- Started around the 1950s with semiconductors being miniaturized and lithography based technology used in pressure sensors
- Development of chips able to handle fluids with capillary connections allowing mixers, valves, pumps, dosing devices…
- 1975: S.C. Terry developed the first Micro Total Analysis System (μTAS)

Three major components:

1- actuator
   - mechanical or electrical force on fluid or object via electromagnetic interactions
2- pumps
3- readout device
   - sensors will measure thermal, optical, electrical or magnetic signals
WHAT TECHNIQUES CAN BE USED FOR LAB ON A CHIP?

- ESI/ESI-MS
- Microfluidics
- Centrifuge
- HPLC
- Selection and analysis of single 3D cell structure
- Dielectrophoresis
- Flow cytometry
- PCR
- Proteomics
- Chromatography
- Imaging

WHAT IS MICROFLUIDICS?

Liquid chemistry at a microscopic level

- Mixing
- pH
- Acid-base equilibria
- Flow physics
- Capillarity
- Electrokinetics
- Electrolyte chemistry
- Separation
- Detection


2) HOW TO CHOOSE A MICROFLUIDIC CHIP? https://www.fluigent.com/microfluidic-expertise/what-is-microfluidic/how-to-choose-a-microfluidic-chip/?gclid=Cj0KCQiA4sjyBRC5ARIsAEHsELcEo7xRN-6A3x0_iMmHfZShWG1Ca0xd5mkjoB0SCZ7Y29pDVzF7ynFBgaAtWyEALw_wcB (accessed Feb 23, 2020).
WHY ARE WE DEVELOPING THESE CHIPS?

Medical advancements
- Point of care
- Accessibility
- Cost reduction
- Better detection
- Prevention
- Personalized care

Pharmaceutical advancements
- Pharmacokinetics
- Shorter approval wait time
- Reliability of results
- Reduce cost
- Waste reduction
- Drug discovery
- Personalized care
BASICS OF A CHIP

PDMS: polydimethylsiloxane (rubberlike medical grade silicon)

- Photolithography
- Thin film deposition
- Etching
- Substrate bonding

Glass-PDMS

Paper

BASICS OF A CHIP

Thermoplastics

- Polymethyl methacrylate (acrylic glass / plexi glass)
- Polycarbonate
- Polystyrene
- Cyclic olefin

Polymers/copolymers

- Soft microfabrication
- Micromoulding
- Microcontact printing
- Substrate bonding
BASICS OF A CHIP

Photolithography

BASICS OF A CHIP

Microcontact printing

Step 1: PDMS stamp is wetted with the material
Step 2: The material is put on the raised part of the stamp
Step 3: The stamp is pressed physically on the substrate
Step 4: The material is printed on the substrate

Substrate bonding

A Fabricate master by rapid prototyping
B Place posts to define reservoirs
C Cast prepolymer and cure
D Remove PDMS replica from master
E Oxidize PDMS replica and flat in plasma and seal

PHOTOLITHOGRAPHY

Step 1: Wafer cleaning
Step 2: Photoresist application
Step 3: UV exposure
Step 4: Development
Step 5: Thin film metal deposition
Step 6: Lift-off
ADVANTAGES

- Reduces wastes and cost by using very small amounts of reagents and sample
- Good control over the interactions and concentrations
- Faster response time
- Allows the analysis to be done at the point of care rather than a centralized laboratory
- Reduction of human error
- Ease of use
DISADVANTAGES

- Interactions between surface and chemicals are greater (capillary force, surface roughness, chemical interaction, etc.)
- Low signal to noise ratio if the detection needs more than microscales dynamics
- We aren’t at a point yet where they can be commercialized.
- Some still depend on external systems to control flow and volumes, etc.
APPLICATION OF LAB ON A CHIP – CENTRIFUGE
LAB ON A DISC V. CONVENTIONAL METHOD OF PLATELET ISOLATION


LAB ON A DISC: RESULTS

A-D – method based platelets purity

E – platelet yield based on method used

F - reproducibility of method and error margin

G – white blood cell present in samples with platelets

H-J – activation of platelets based on method

WHY IS IT HARD TO UPSCALE? AND WHY SHOULD WE CARE?

Why haven’t we commercialized?
- Cost
- Standardization of the design
- User-friendly interface with macroscopic world
- Many chips could change our lives but cannot be adopted into the mainstream and we need to adapt them

Can we commercialize?
- PCB microfluidic chips are more cost effective
- Already established
- Have the manufacturing capabilities
- The standardization already exists

THANK YOU!
REFERENCES

Microfluidics cell culture that emulates the physico-chemical microenvironment of tissue and organ-level.

Done by controlling the dynamic conditions on the chip.

Done for specific individuals representing that individual’s genetics, physiology, etc,... This is called precision medicine and is increasingly becoming important for groups that are non-responders to standard practice medicine. Many people are hospitalized due to adverse effects to their treatments or medicine = 100 000 + deaths per year. Precise medicine would reduce harm, increase quality of life and potentially reduce cost of the healthcare system. We want to recapitulate a patient's complexity in a controlled system (as we would in any organ grown culture) but this time we want to be able to go from the prep to analysis to results on one chip.

Human cells are cultured, and in engineered microenvironments mimic the tissue geometry, actuation dynamics, flow and gradients just like the human body. Eg: lung-on-a-chip breathing, vessels on a chip (tumour cells in perfused blood vessels), gut on a chip (peristaltic actuation and flowing microbes), multi-organ chips (pancreas and liver to maintain glucose liver)

Organ on a chip = high level of control of biological, physical and chemical cell culture in a single microsystem. You only need a small sample of the primary organs and fluid sample. Personalization = using patients' samples (primary tissue by biopsy or other, blood, stool)

OTHER SUBJECTS OF INTEREST:


- **And** Gac Séverine Le; Berg, A. van den. Miniaturization and mass spectrometry; A Silicon-Based ESI Chip with Integrated Counter Electrode and Its Applications Combined with Mass Spectrometry; RSC Publishing: Cambridge, UK, 2009, 47-66.
