



European  
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## HOLISTIC APPROACH OF MICROFLUIDIC SYSTEM PROTOTYPING AND PRODUCTION

Nicolas LAFITTE (Fluigent on behalf of HoliFAB consortium)

EuroNanoForum 2019, June 13<sup>th</sup>

# SUMMARY

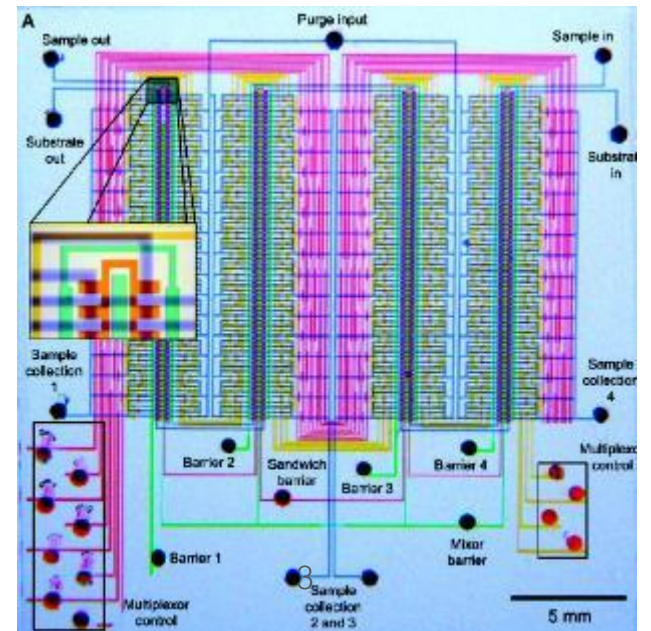
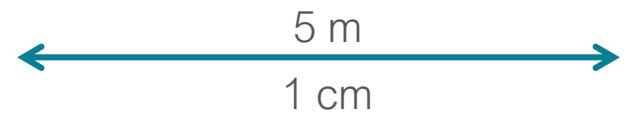
1. Holistic approach of microfluidic
2. Pilot lines for microfluidic system production
  - Microfluidic chips by 3D printing
  - Microfluidic chips by injection moulding
  - Instruments integration and production
3. Demonstrators of HoliFAB
  - Clinical applications
  - Biology research applications
  - Environmental applications
4. Conclusions and perspectives towards November 2020

## › Microfluidics: XXI<sup>th</sup> century technological breakthrough

- Manipulation of fluids on the micrometre scale
- “fluidic microprocessor”

## › Advantages

- Reduce (dramatically) sample/reagents per test: nanoliter and picoliter
- Parallelisation
- Automation (fluidic microprocessor)
- Control of physical/biological parameters at  $\mu\text{m}$  scale



# THE “CHIP-IN-THE-LAB” PROBLEM

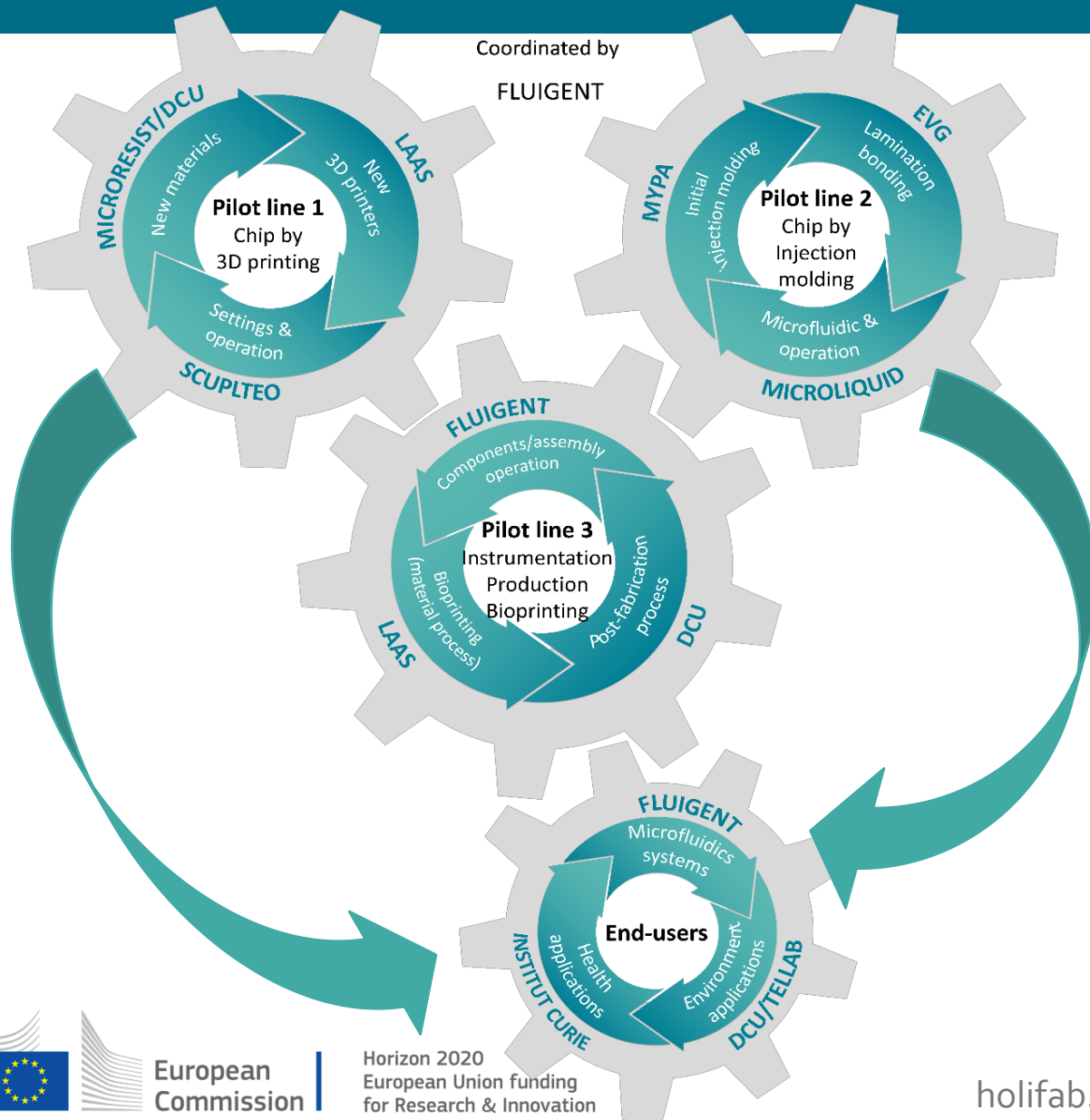
A typical research lab instrument



Towards end-users



- Long and tedious process
- Final instrument expensive  
Cost: 50~200 k€

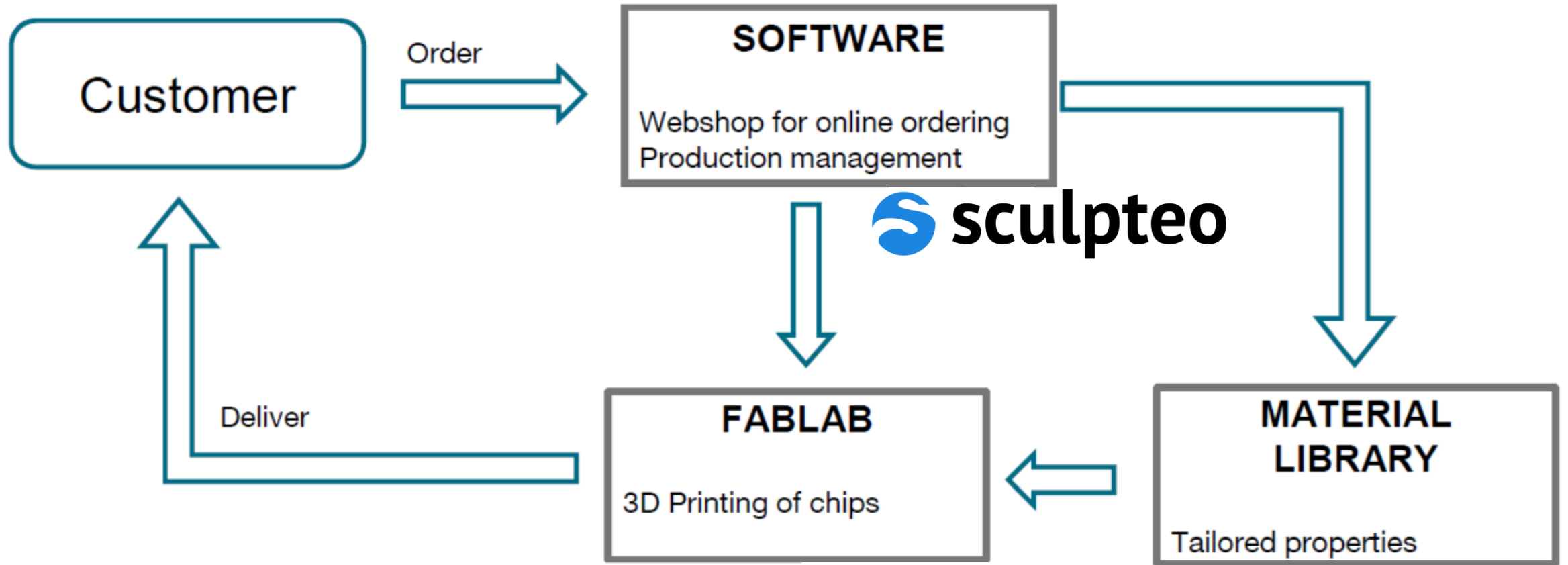


- Holistic approach = Global networked workflow outlook for improving
  - Design (time and cost),
  - Fabrication (time and cost)
  - Performances (customer requirements)
- Independent but complementary pilot lines
- Answer to market requests :
  - Different market sizes: prototypes, small and large productions
  - Large variety of applications
  - Address new markets

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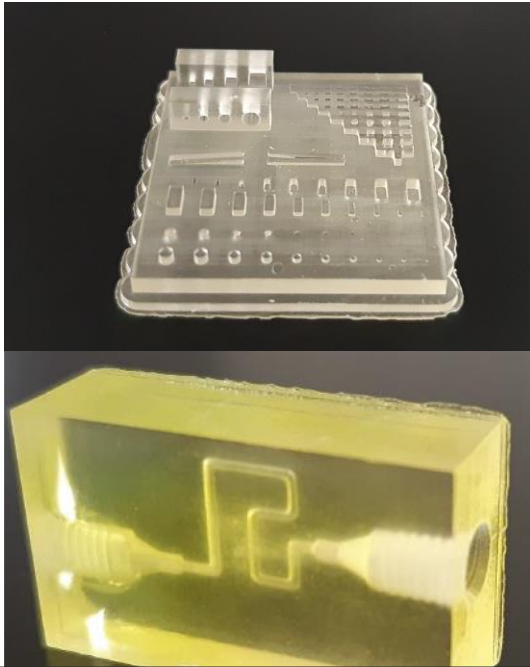
# PILOT LINE : CHIP BY 3D PRINTING



# PILOT LINE CHIP BY 3D PRINTING

## ACHIEVEMENTS : HARDWARE

### Very high resolution 3D printing

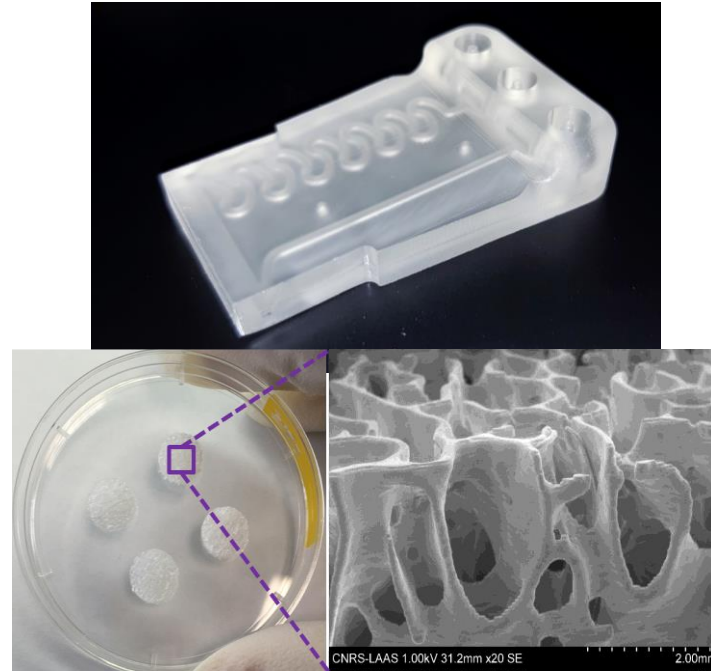


Targeted Resolution X,Y : 1-3  $\mu\text{m}$

Targeted Resolution Z : 5-100  $\mu\text{m}$

Estimated Throughput : >20 chips/day  
(Dimensions : 2 x 10 x 20 mm)

### High resolution 3D printing

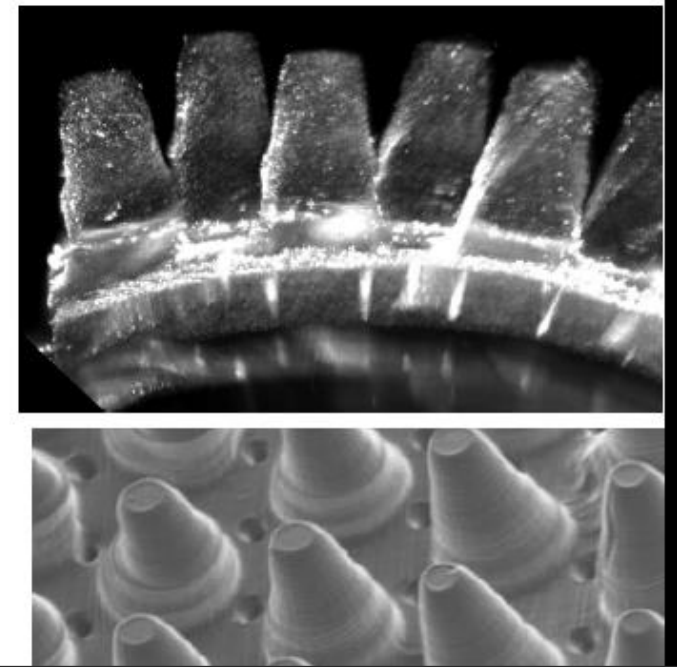


Targeted Resolution X,Y : 30-40  $\mu\text{m}$

Targeted Resolution Z : 10-100  $\mu\text{m}$

Estimated Throughput : 10 chips/hour  
(Dimensions : 2 x 10 x 20 mm)

### LAAS-technology bioprinting (LAMP)



Bioprinting for organ-on-chip application :

- Bioprinting of bio-compatible and soft hydrogel for 3D tissue engineering
- 3D printed microenvironment models
- Multimaterial

Targeted Resolution X,Y : 20  $\mu\text{m}$

Targeted Resolution Z : 5-500  $\mu\text{m}$



- › Challenges and requirements
  - › Customer-oriented project management
    - › Webshop layout
  - › 3D printing tools dedicated to high resolution printer
    - › Resolution vs speed optimization



Log in with your local account to  
holifab.fabpilot.com

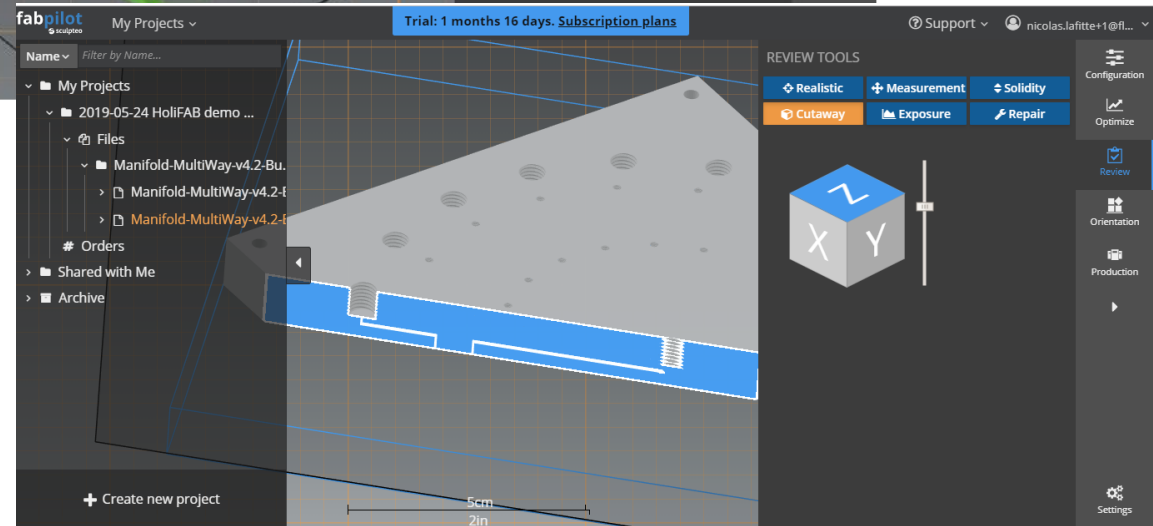
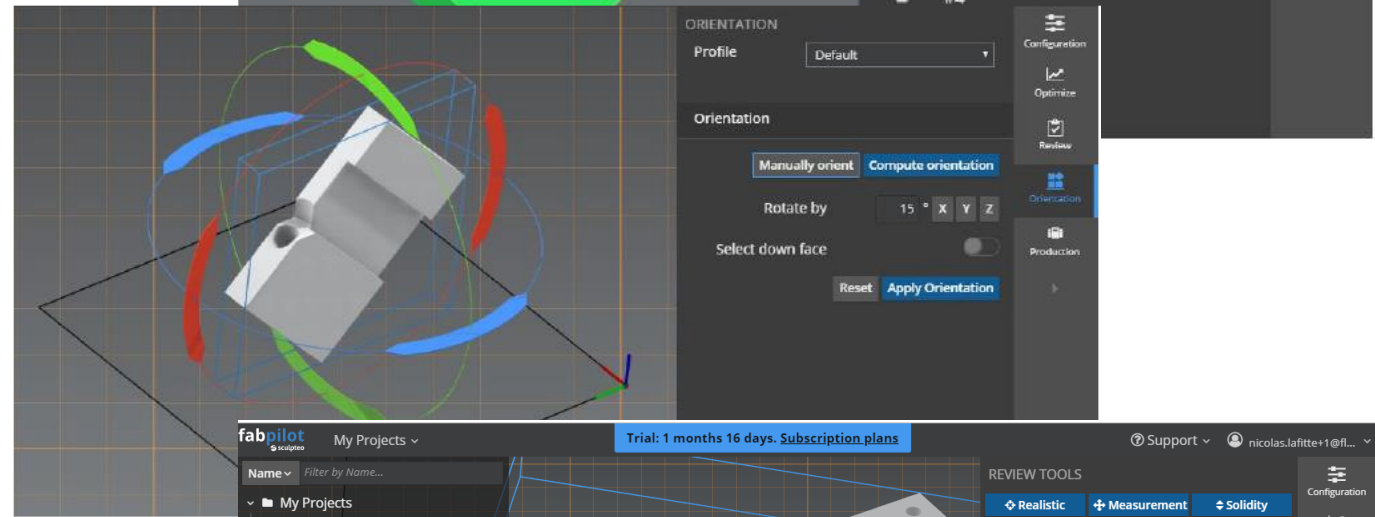
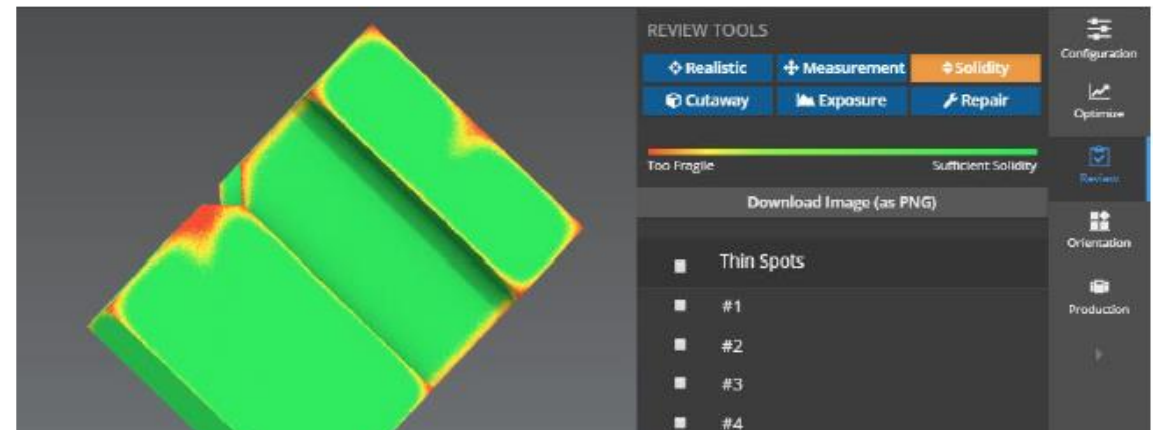
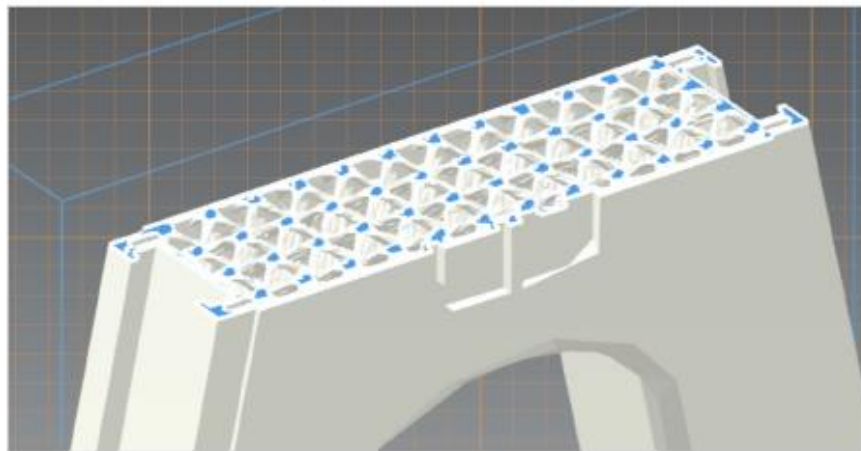
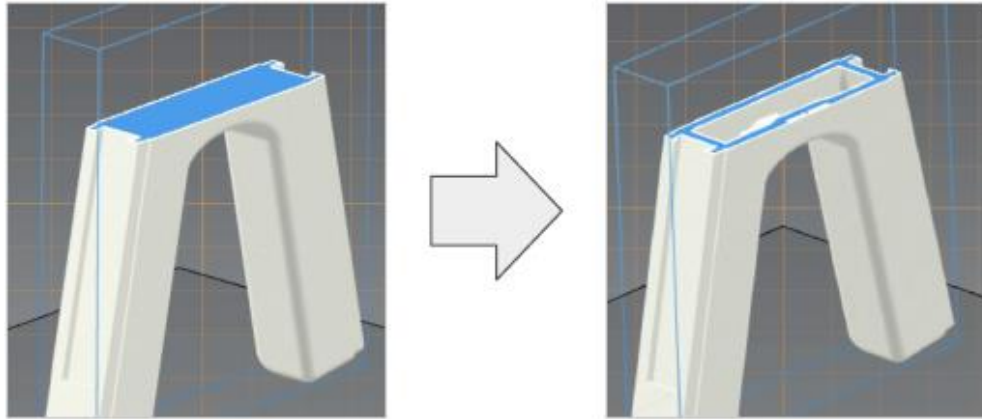
[Forgot your password?](#)

# Online Additive Manufacturing Software

Upload, Repair, Analyze, Optimize,  
Price, Prepare and 3D Print on your  
own machines from anywhere



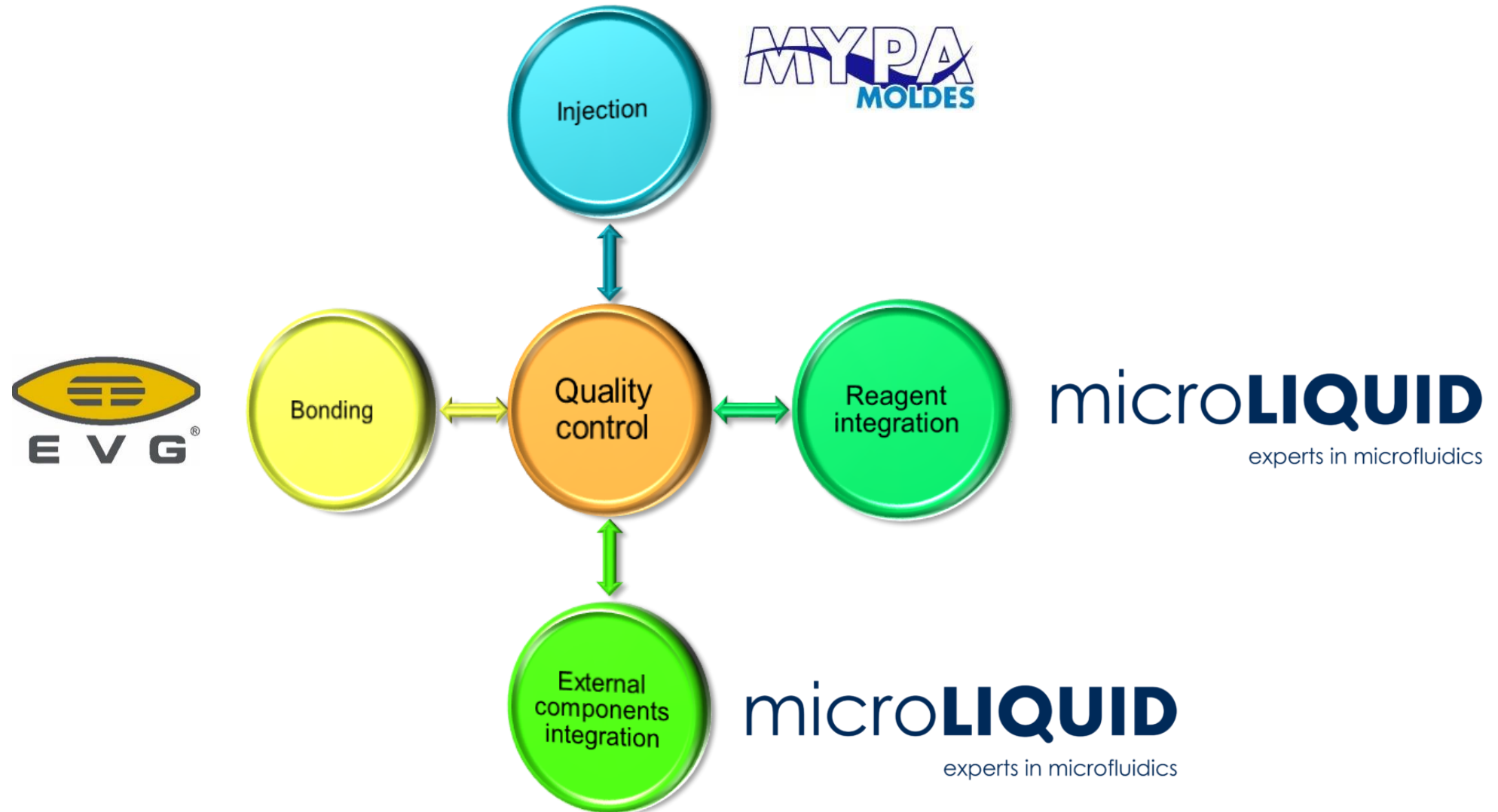
# ONLINE 3D FEATURE TOOLS



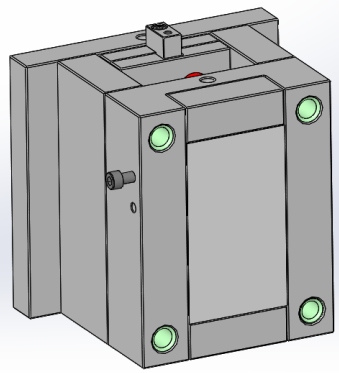
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# PILOT LINE : CHIP BY INJECTION MOULDING



# PILOT LINE CHIP BY INJECTION MOULDING ACHIEVEMENTS



and  
bonding machine

Special strategy for the mold in order to achieve the chip micrometer dimensions challenges

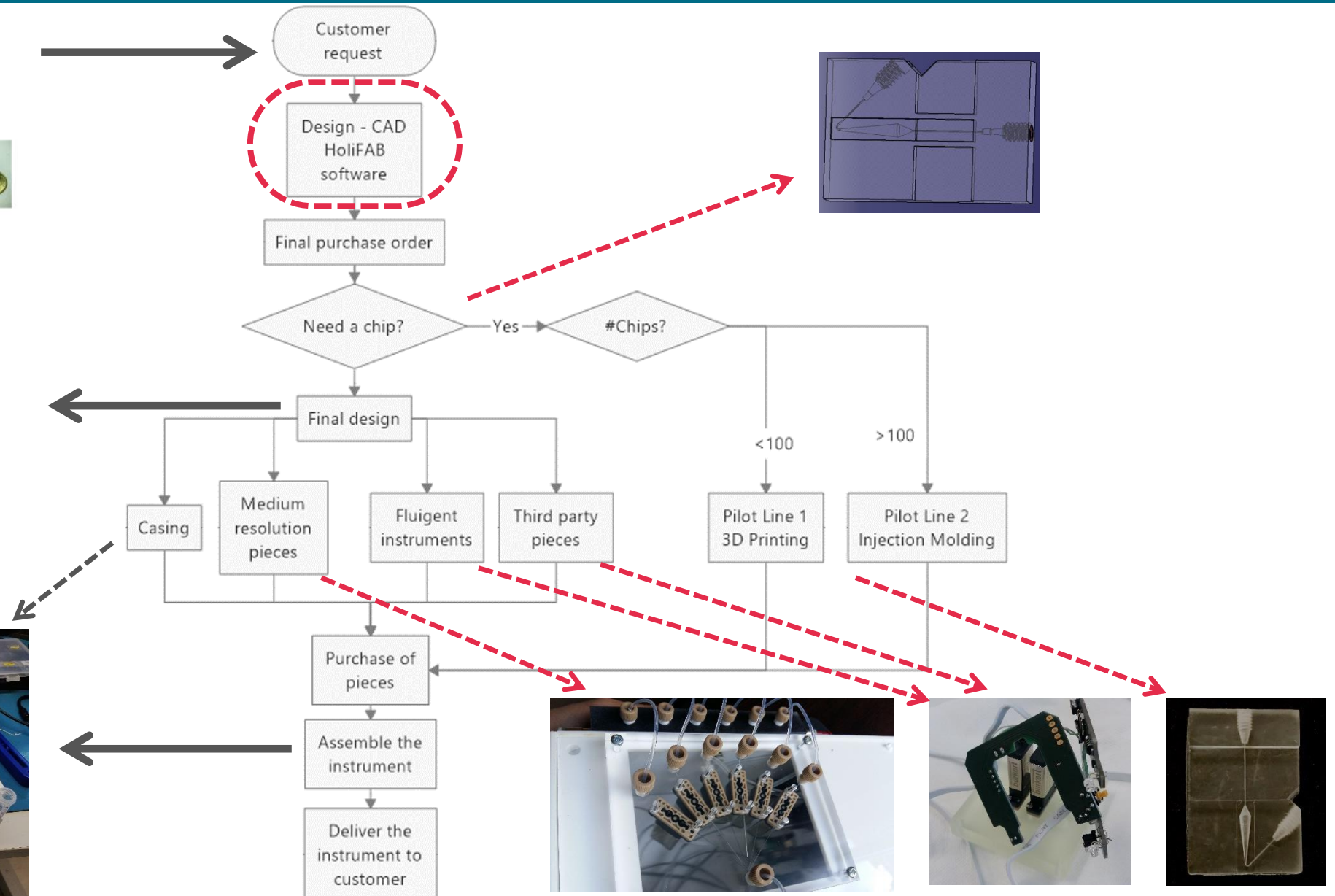
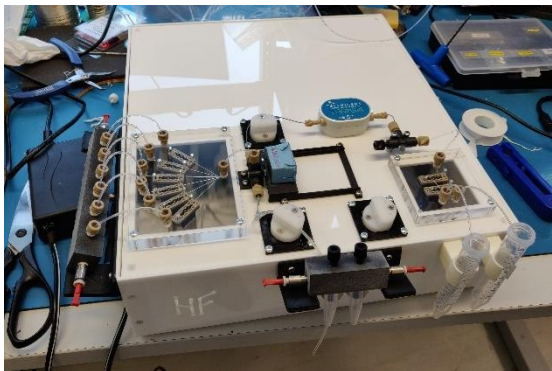
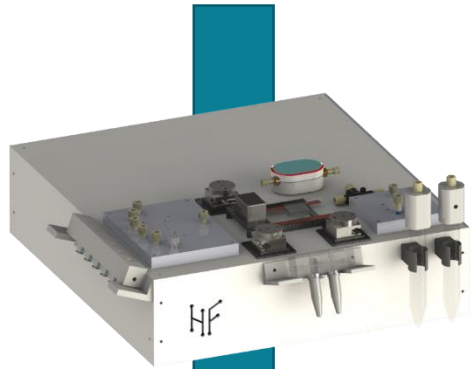
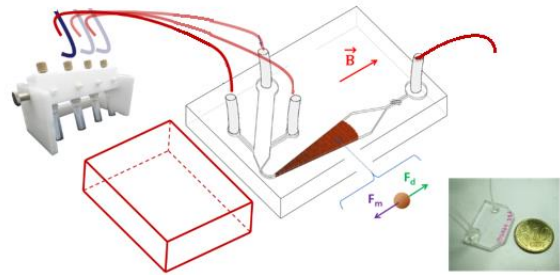


Dispensing robot

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# OPERATION OF THE PILOT LINE





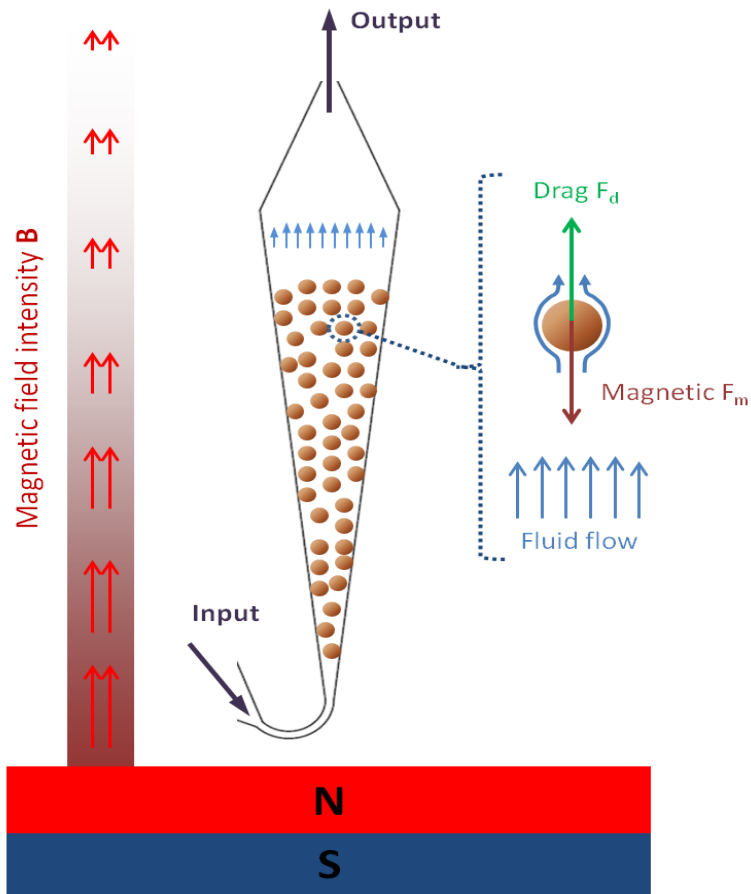
- › Develop a **Computer-Aided-Design (CAD) software** dedicated to the design and assembly of microfluidic systems
  - Assist R&D engineers and researchers in their design
  - Check for design and assembly errors
  - Implement (mathematical) routines for **automatization and optimization of the design**

	Actual pilot line	Future pilot line
BOM		Around 20% less
R&D engineer time	> 100 hours	< 20 hours
Production technician time	~ 60 hours	~ 40 hours
Production cost		Up to 60% less
Instrument development time	Several weeks	Several days

# SUMMARY

1. Project presentation
2. Pilot lines
3. Demonstrators of HoliFAB
  - Clinical application by CNRS-Curie
  - Organ-on-chip application by CNRS-Curie and CNRS-LAAS
  - Environmental application by DCU and TelLab
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## Fluidized bed for ctDNA concentration and detection

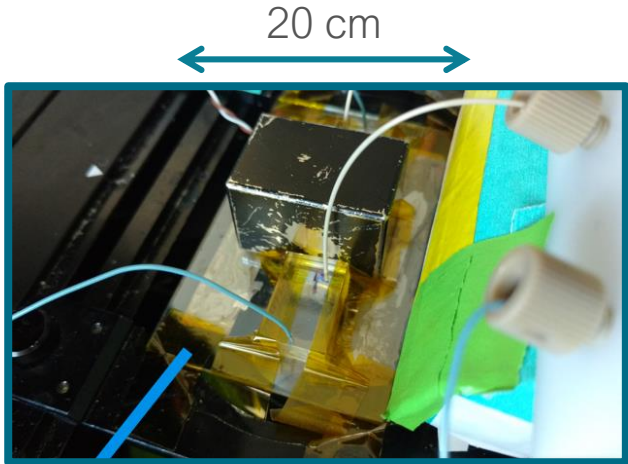


### Principle

- › Original technology:
  - › Circulatory tumor DNA captured on magnetic beads in flow-through mode

### Societal relevance

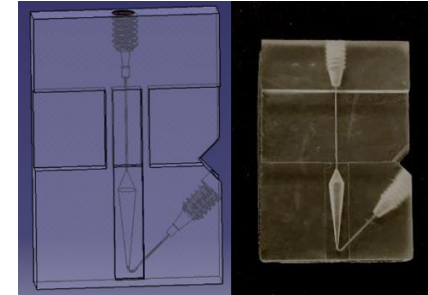
- › Clinical biomarker of current interest:
  - › Strong societal/economic impact
- › Versatile technology
  - › Protein biomarkers, infection detection, etc...



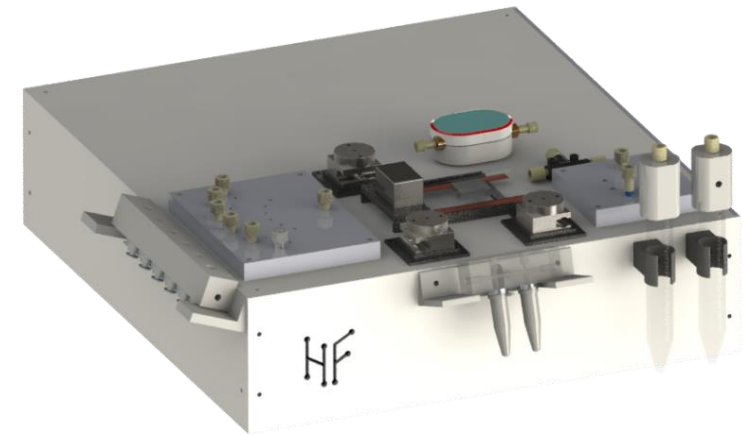
- › Microfluidic chip
  - › Lab-made in PDMS or COC
- › Experimental setup
  - › Researcher-assembled with end-user products



- › **Pilot line 1** : Microfluidic chip production



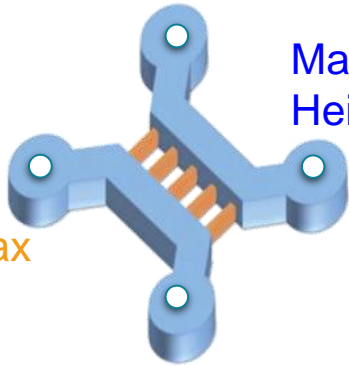
- › **Pilot line 3** : Microfluidic system integration



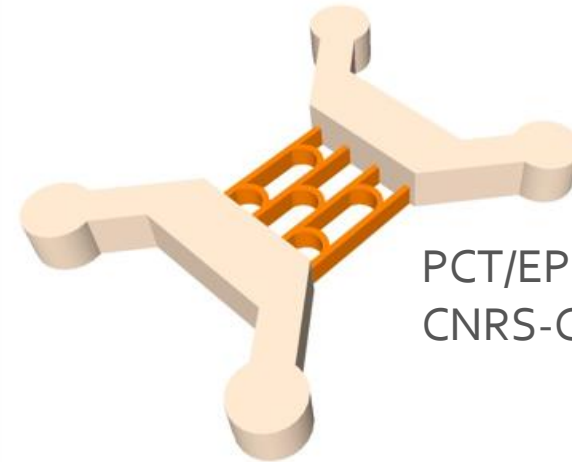
> **Neurons-on-Chip** : *in vitro* neural networks in microfluidic culture chambers

Main issue: Somas / axons compartmentalization

Micro-channels  
Height: 3-5 $\mu\text{m}$  max  
Width: 10 $\mu\text{m}$

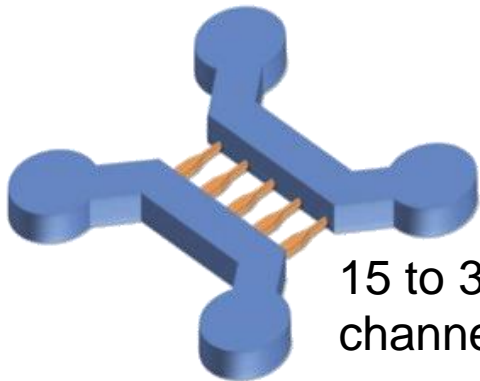


Macro-chambers  
Height: 30-50 $\mu\text{m}$

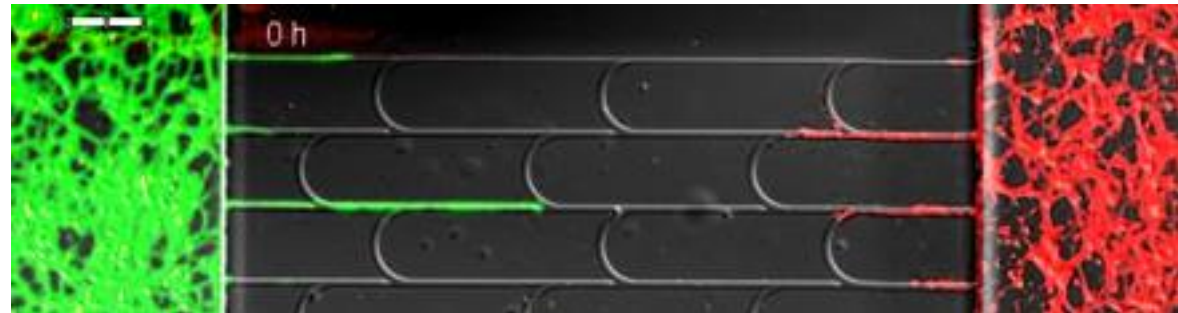


PCT/EP2016/075469 2016  
CNRS-Curie

Additional issue: directionality



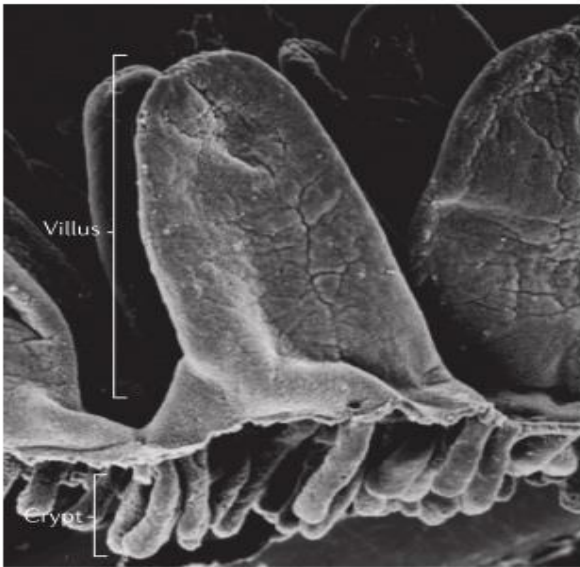
15 to 3 $\mu\text{m}$  wide  
channels



→  
Axonal growth direction

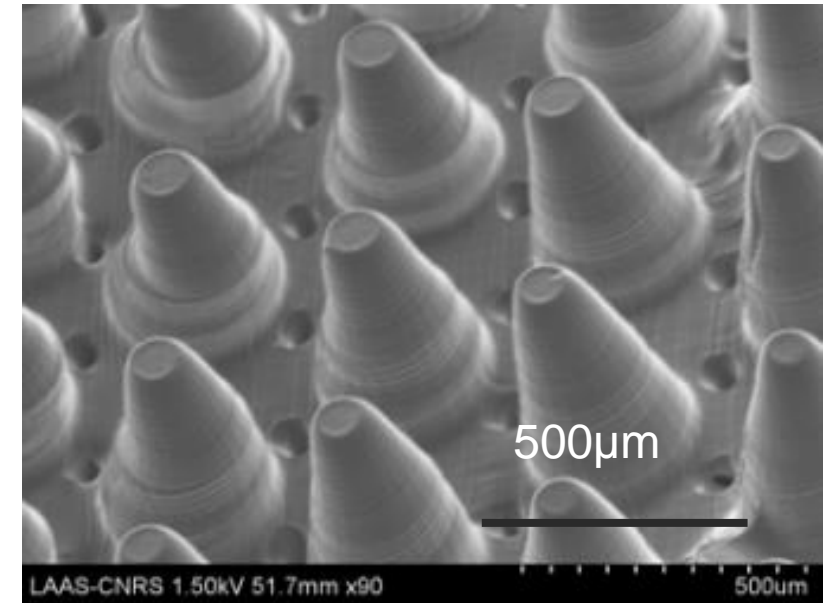
## > Gut-on-Chip : *in vitro* 3D cellular architectures

**a** Small intestine

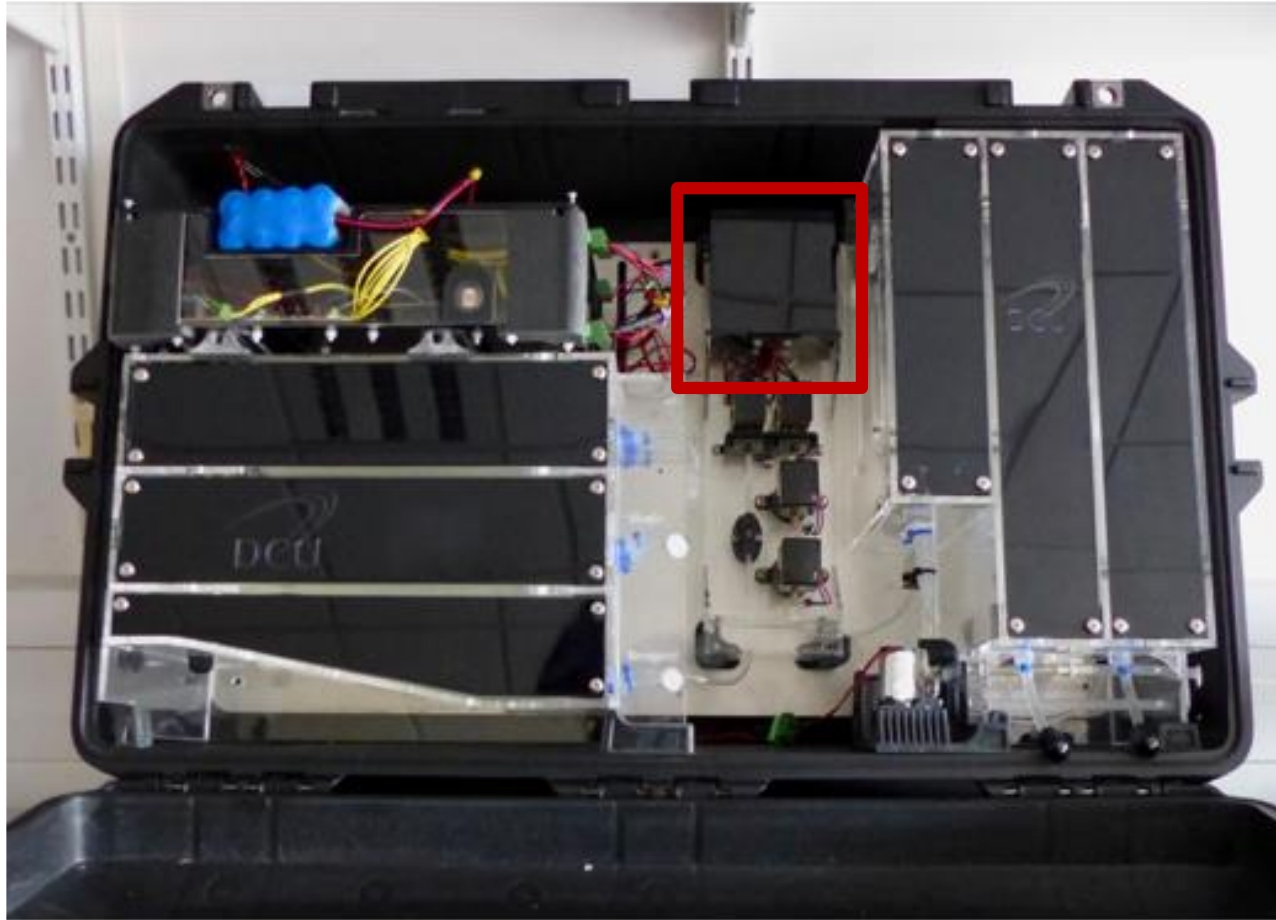


## > Relevance to HoliFAB

- 3D architecture (DILASE 3D)
- Role of Stiffness / Topography
- Microfluidic addressing
- Biochemical heterogeneity



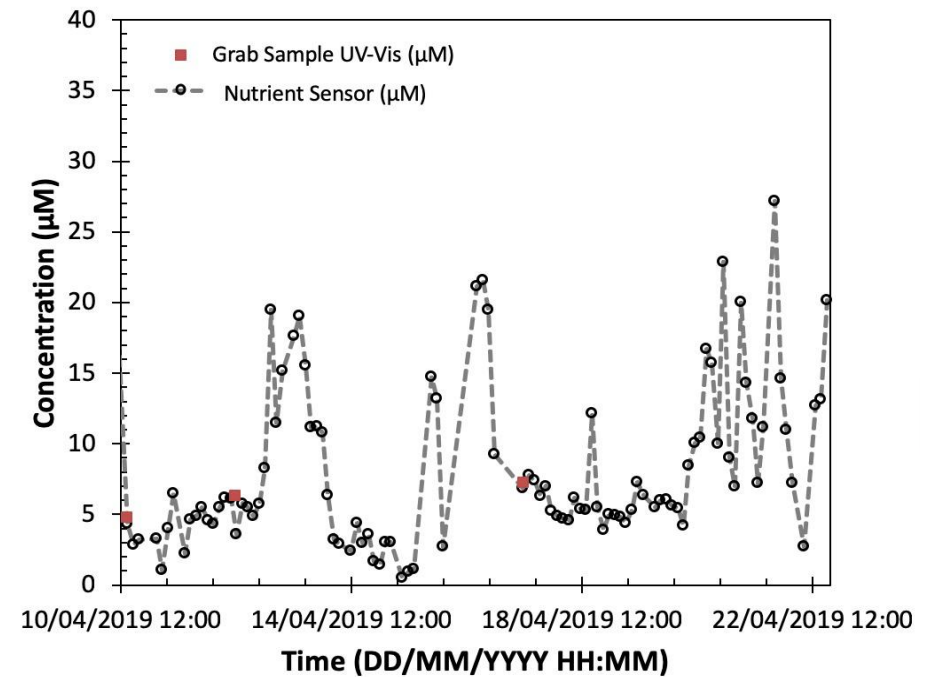
# ENVIRONMENTAL APPLICATION : WATER MONITORING



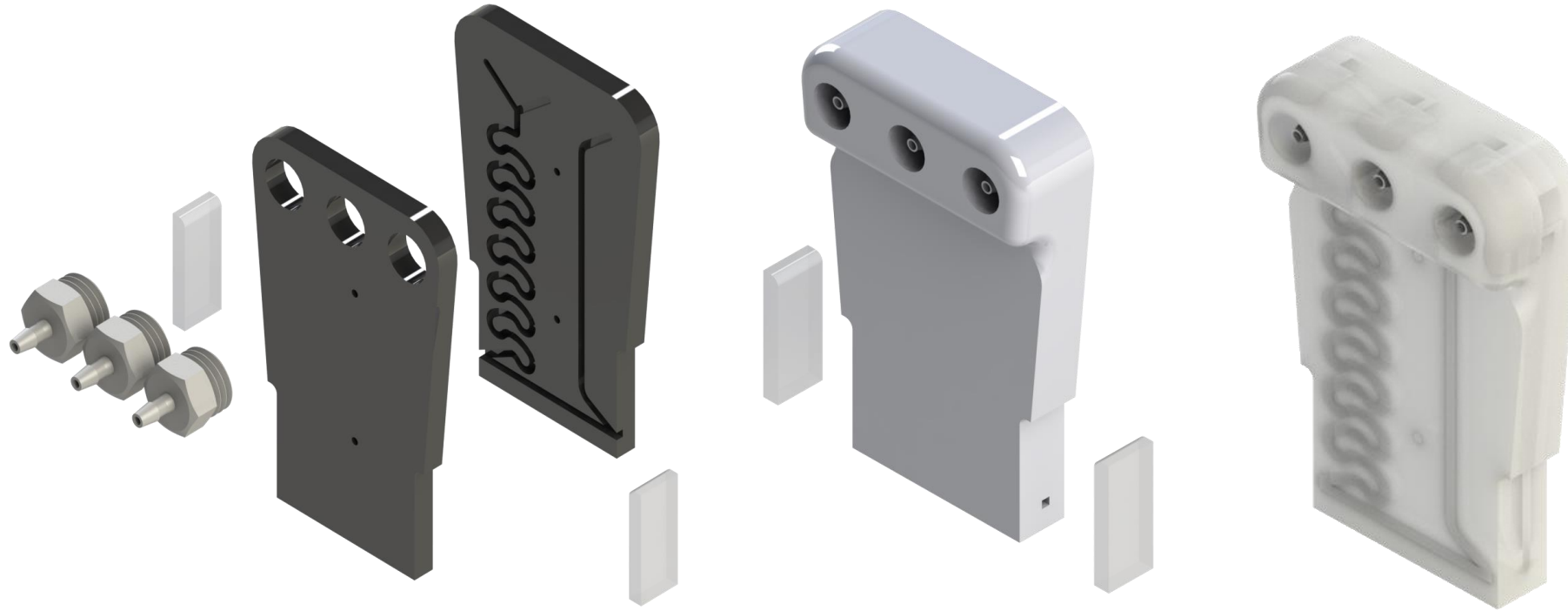
**112 Phosphate ( $\text{PO}_4^{3-}$ ) measurements from 10 April 2019 to 22 April 2019**



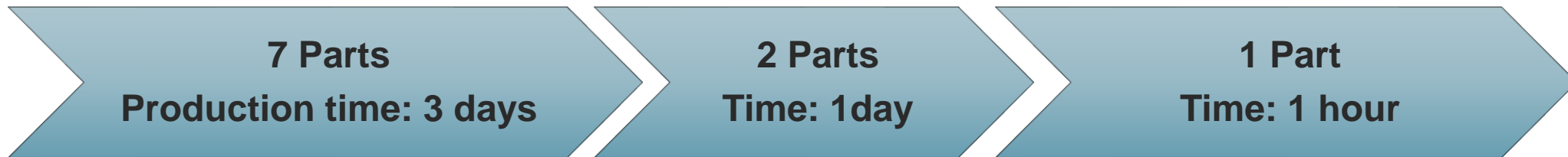
**Sampling rate every 2.5 hours**







> **Pilot line 1** : Microfluidic chip with 3D features by 3D printing



# SUMMARY

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2. Pilot lines
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- › We are preparing towards November 2020 the technologies required to microfluidics for its industrialization and the benefit of everyone and any applications

Thank you for your attention

Website: <http://holifab.eu>

Twitter: @HoliFAB



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