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Automated microfluidic platform for on field high sensitivity quantification of cardiac troponin I

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HAL Authorization

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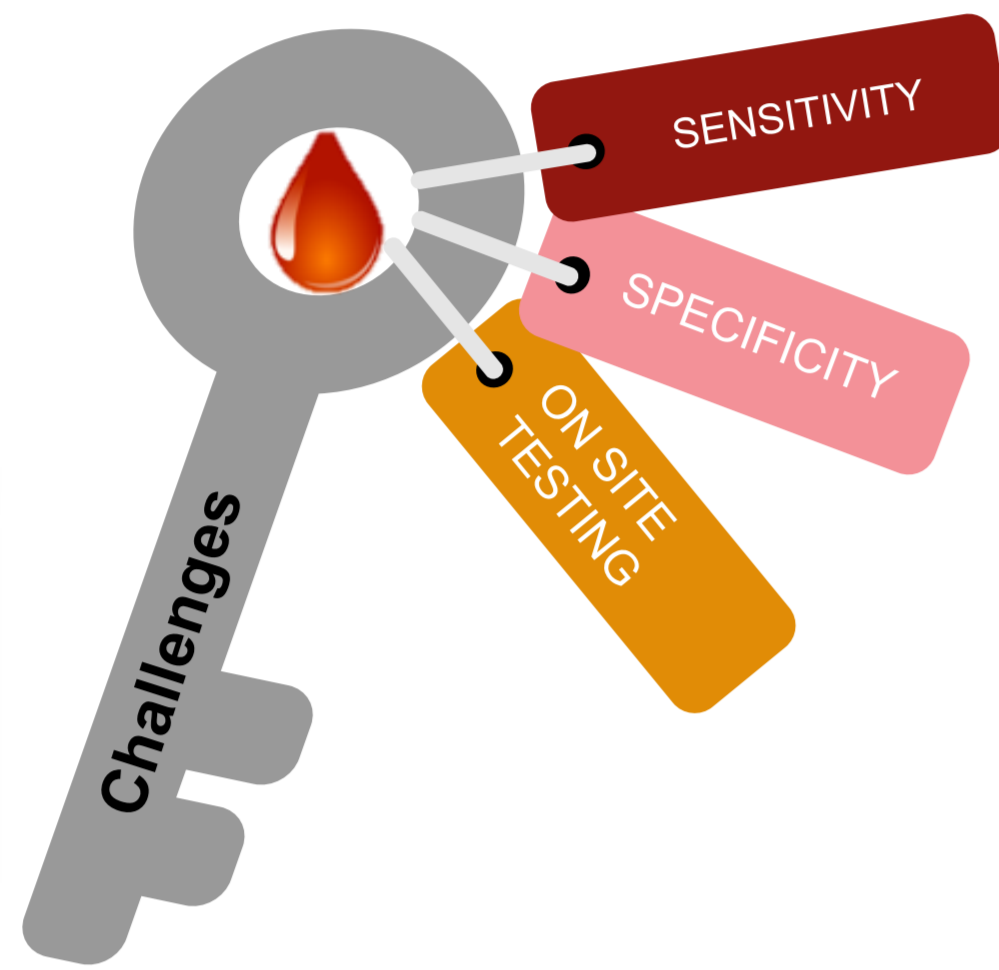
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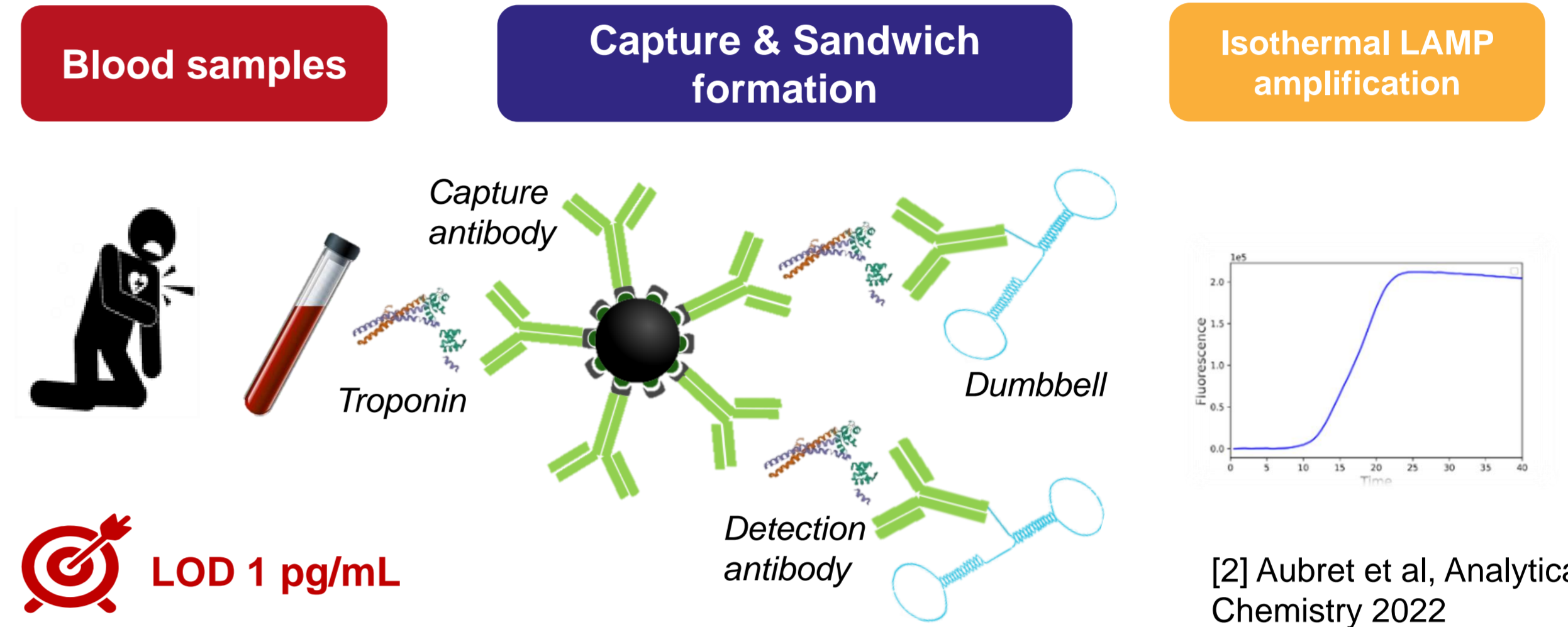
Context

How to improve cardiac diseases diagnosis?



- Cardiovascular diseases leading cause of death in the world
- Myocardial infarction requires quick diagnosis
- Troponin I gold standard biomarker
- Delocalised assays: high medical need
- Current Point of Care devices : not enough sensitive

[1] Savonnet et al., J Pharm Biomed Anal. 2021



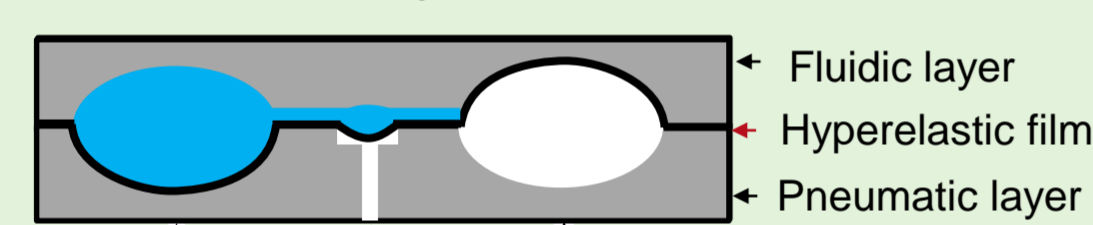
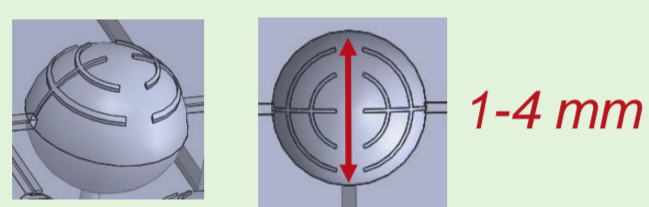
[2] Aubret et al, Analytical Chemistry 2022

Automated microfluidic platform

Figure 1 : Flow Stretch technology

Network of channels and collapsible chambers

- Mixing
- Washing
- Capture
- Heating
- Optical reading



[3] Parent et al, Lab on Chip 2022

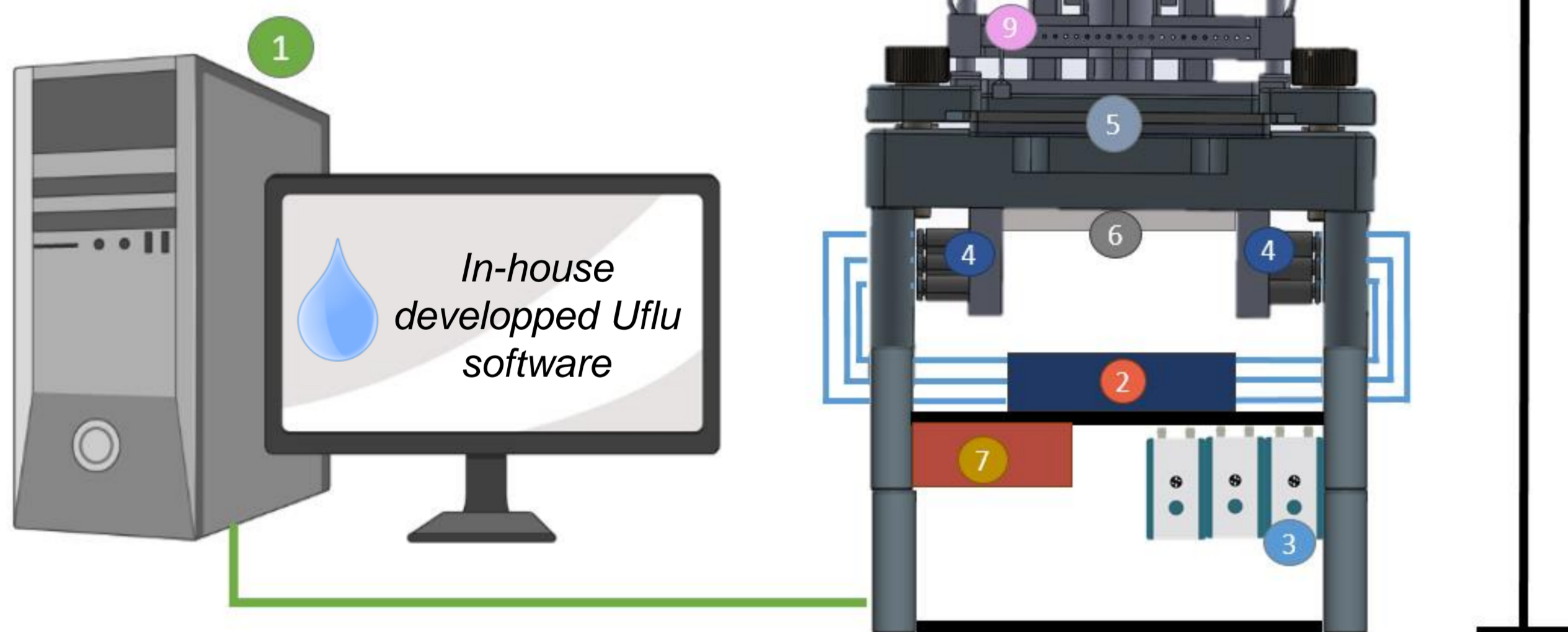


Figure 2 : Microfluidic instrument and its main functions

- 1 Computer and software interface
- 2 Controller for solenoid valves
- 3 Pressure controller
- 4 Solenoid valves
- 5 Microfluidic cartridge
- 6 Peltier module, ventilation and heat dissipator
- 7 Thermoelectric controller
- 8 LED and camera
- 9 Magnetic arm

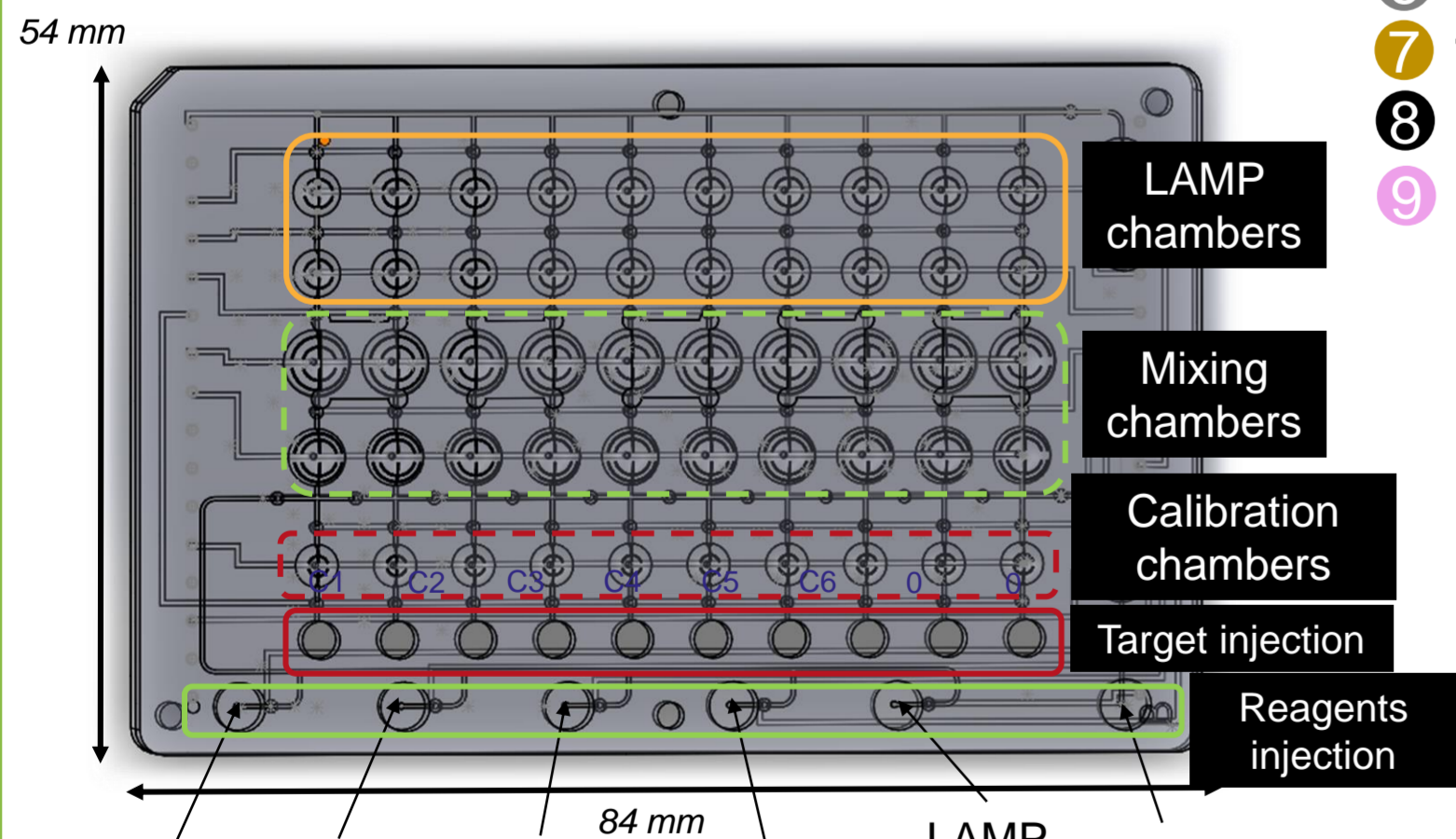


Figure 3 : Microfluidic cartridge

Troponin quantification

Each steps of the protocol are achieved either on microplate or on chip except for the LAMP amplification achieved on a commercial instrument

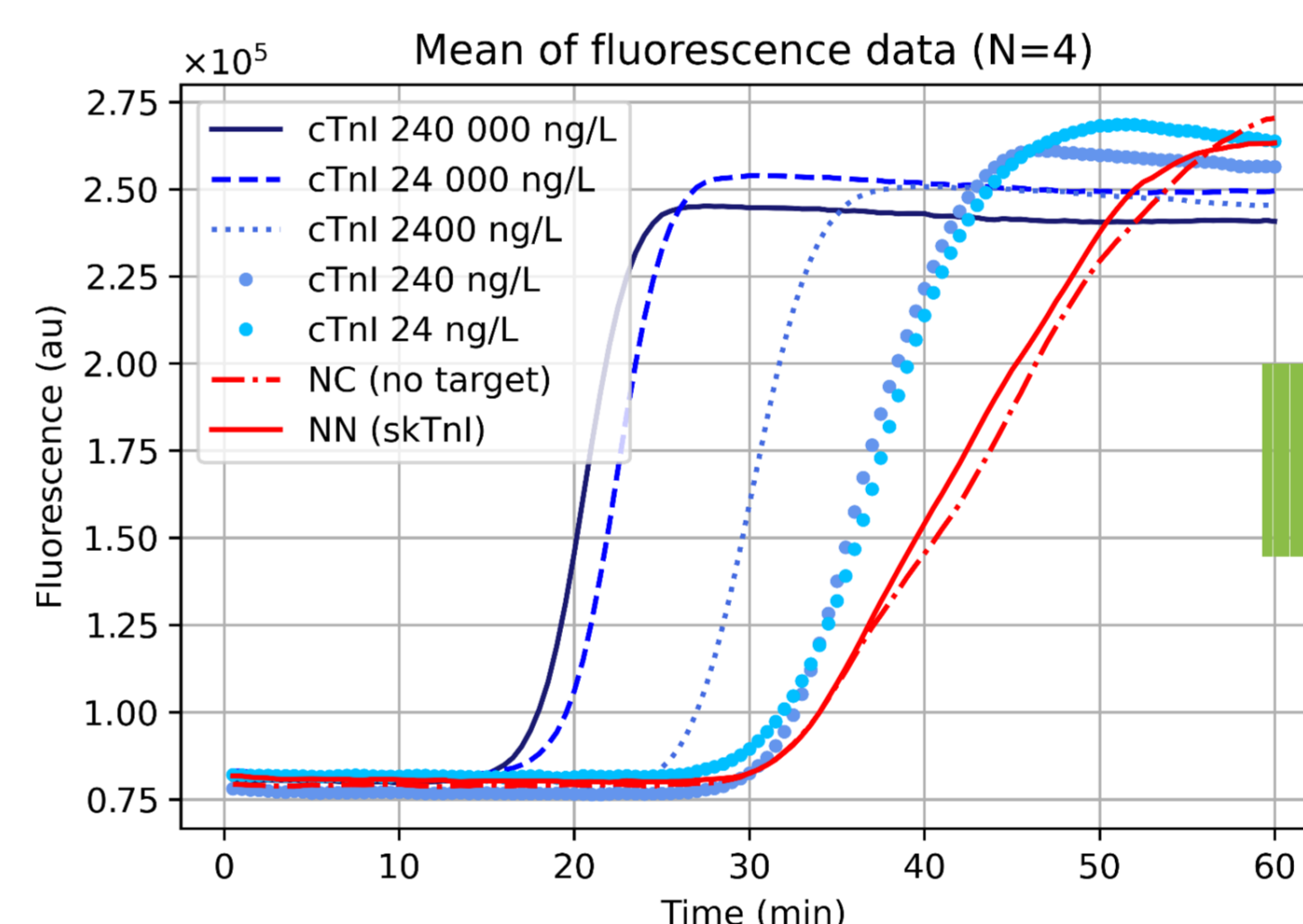


Figure 4 : Fluorescence data over time for different troponin concentrations in buffer medium on microplate

- ImmunoLAMP : combination of antibody recognition and LAMP amplification for troponin sensing
- LOD 240 ng/L ~ 240 pg/mL

LAMP on chip



Figure 6 : (A) Chip observed fluorescence (B) Chip thermal profile for a set temperature of 75°C

- System thermal characterization using Comsol Multiphysics
- Fluorescent measurement over time in FlowStretch chambers
- FlowStretch membrane porosity & bubbles apparition

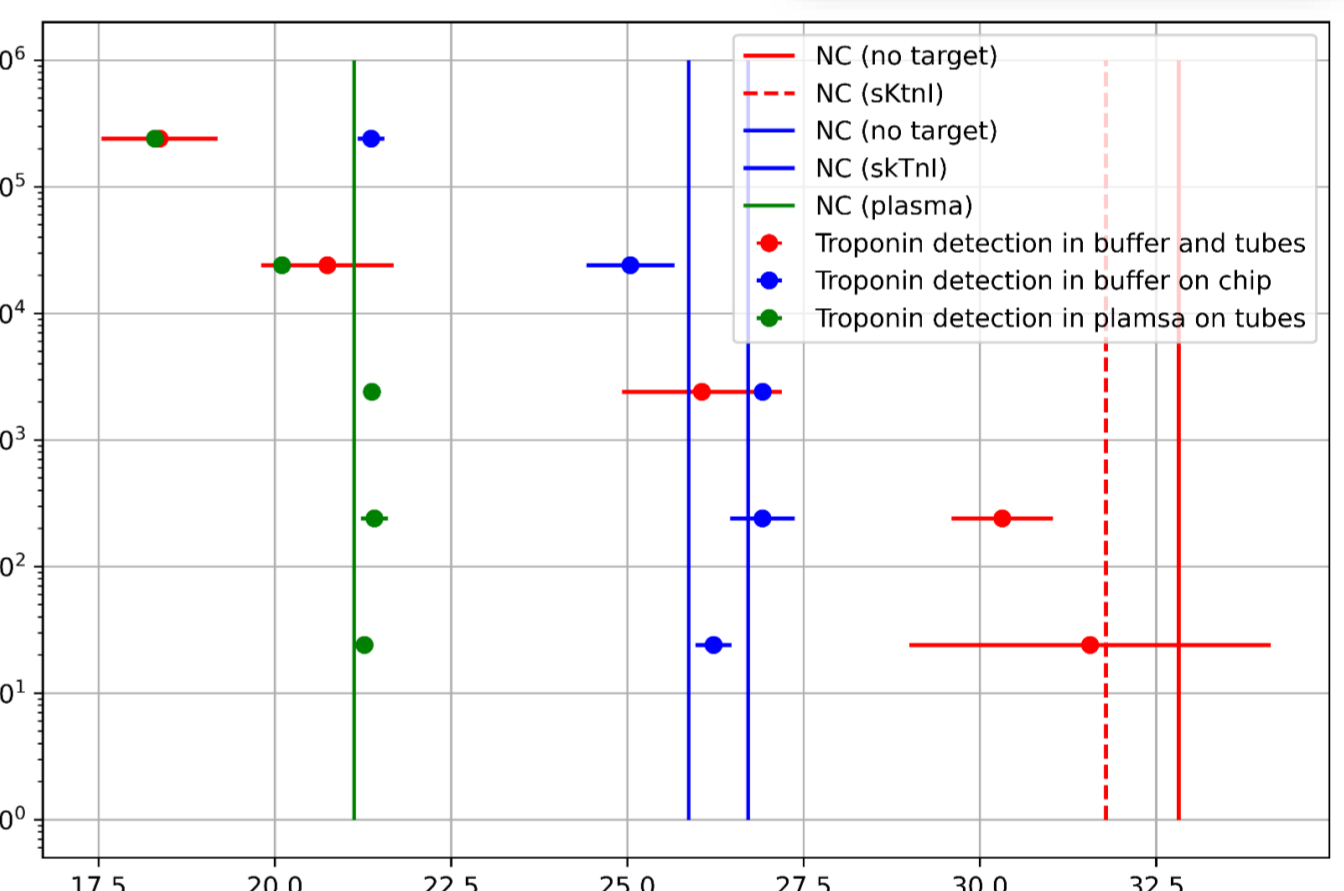
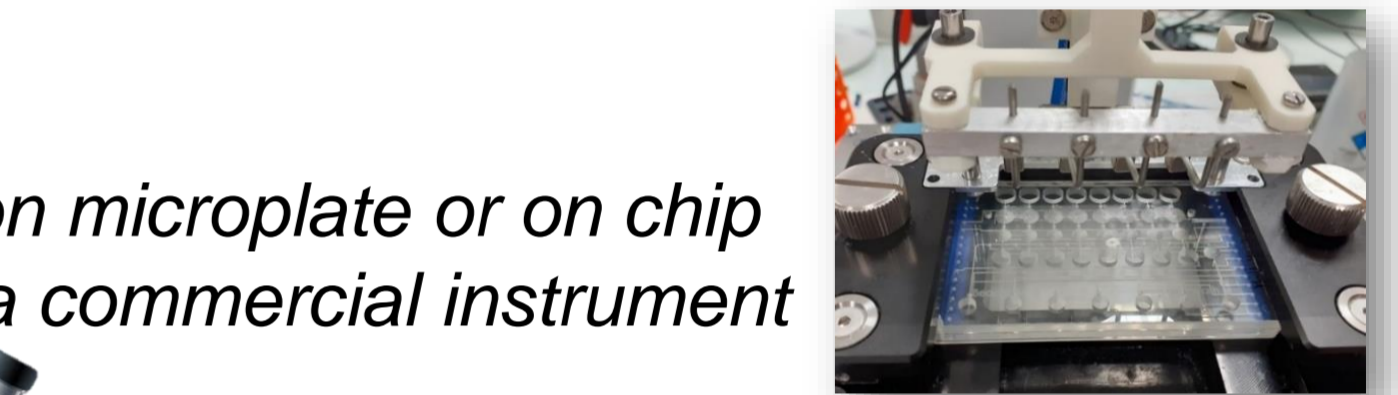


Figure 5 : Troponin quantification on microplate in buffer (red) and in plasma (green), and on chip in buffer (blue)

- Non specific signal in complex medium (human plasma) due to non specific binding on magnetic beads
- Higher LOD for on chip sensing

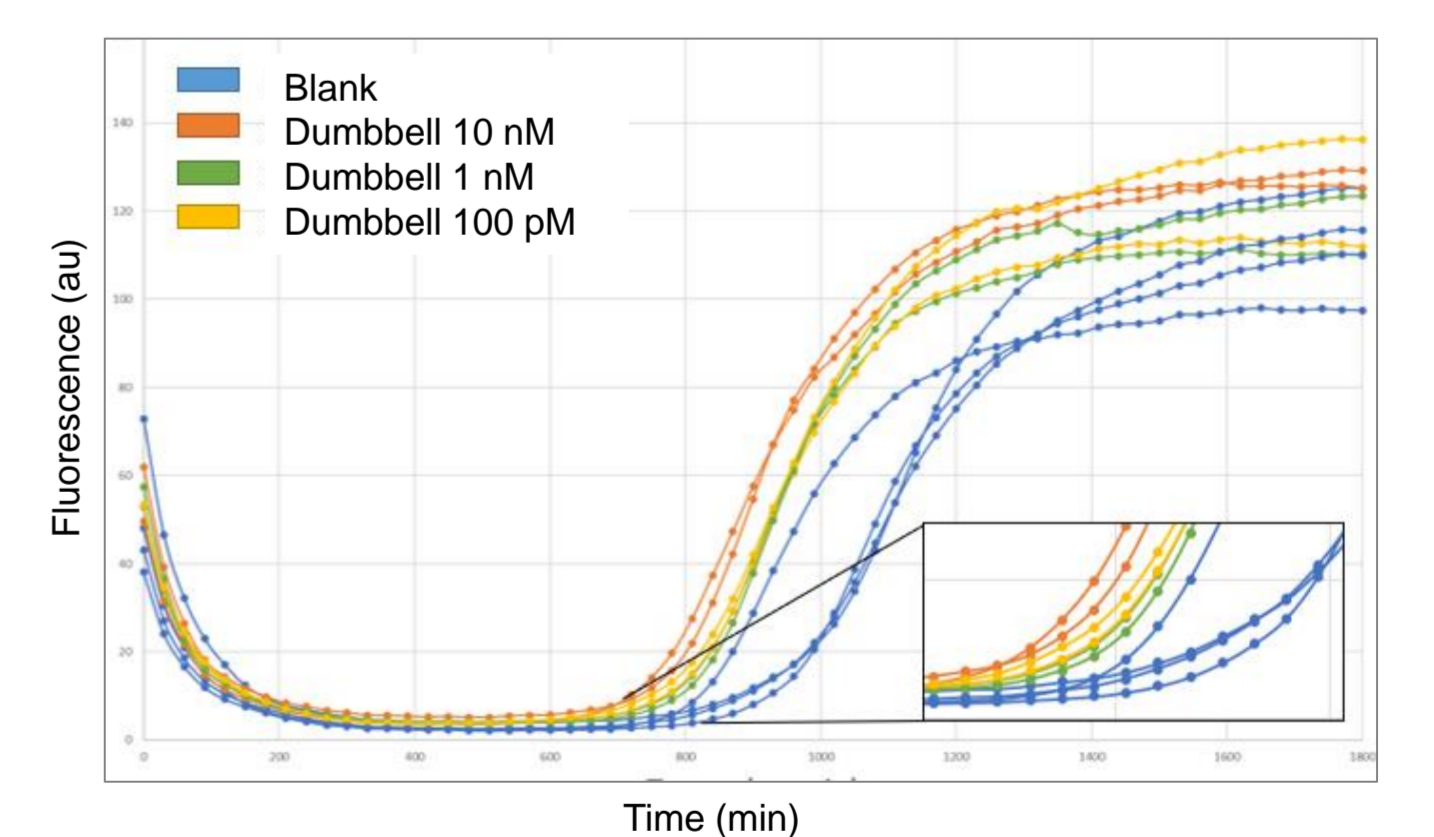


Figure 7 : Fluorescence over time during isothermal amplification on chip

Conclusions & perspectives

- Design of a new sensing method for high sensitivity troponin quantification relying on antibody sandwich and isothermal exponential dumbbell amplification : **Immuno-LAMP**
- On going research in complex medium (plasma) and on chip integration
- Development of an **automated instrument** for protocol integration
- Microfluidic technology compatible with magnetic bead based protocols and nucleic acid amplification on a single chip for **Point-of-Care Diagnostics**

Sensitivity



Portability



Automated platform for high sensitivity troponin sensing