ON-CHIP MICRO-INCUBATOR WITH INTEGRATED SENSORS AND ACTUATORS

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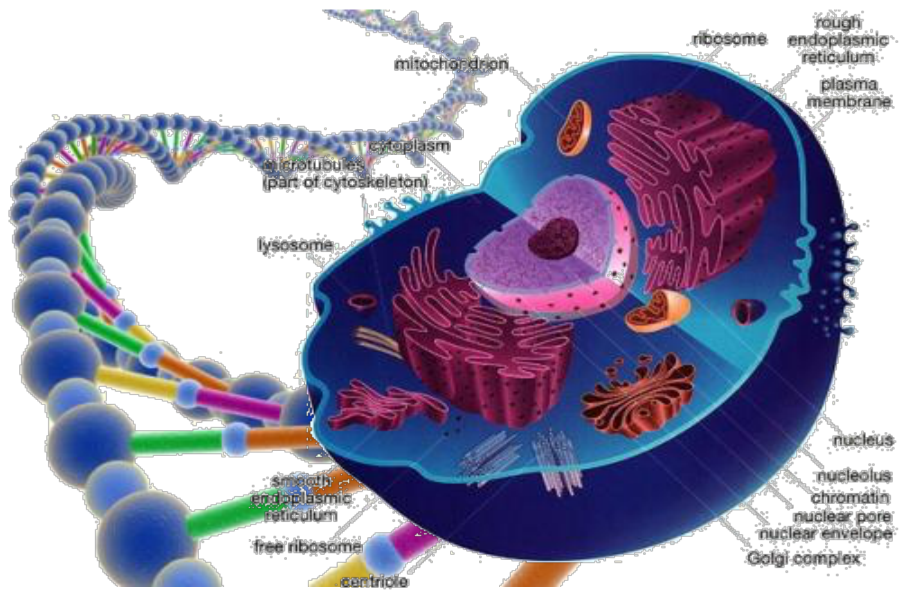
Outline

- Background and motivation
- Technology overview
- Cell incubator system design
- Device fabrication
- Preliminary results
- Conclusions

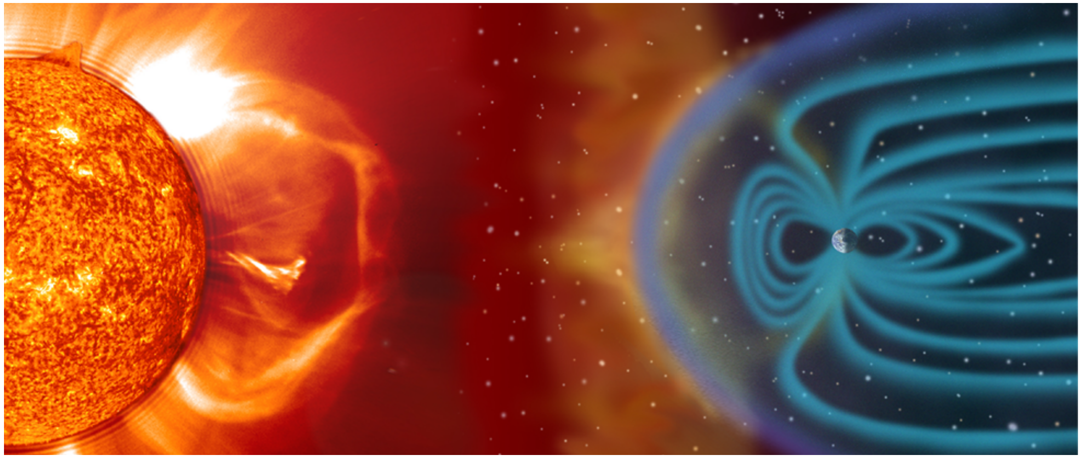


Background

- **Degenerative pathologies** are among the greatest long-term risk for astronauts exposed to **space environment** during deep space mission
- A breakthrough goal, to improve risk modeling, is to **provide biological in-situ analysis** of those effects

Space biolabs

- On-ground simulation of deep space radiation environment is unsatisfactory
- Space biolabs allow:
  - to study combined effect of microgravity and radiations on living cells and on cell components from DNA to mitochondria
  - to perform metabolic studies
  - to develop and test drugs for mitigation of the effects



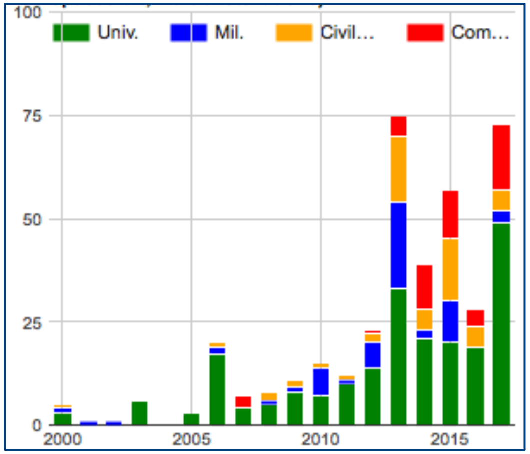
Space biology research

- The goal of space biology is to answer the question about **how spaceflight affects biological processes**
- Space biology research began to expand as a field of practical interest shortly after the end of World War II
  - 17 December 1946 on V-2 rocket: exposure of fungus spores to cosmic radiation in upper atmosphere
- Space Biology is part of NASA's Life Sciences Program since the 1960's
  - Sounding rockets in 1965 (150 km),
  - Gemini 9 and 12 missions in 1966 (300 km)
  - Apollo 16 mission
- First exposure of microorganisms to space radiation, proved that **life could survive the extremely harsh conditions of open space**

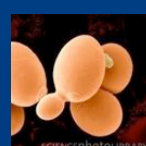
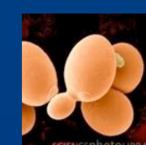
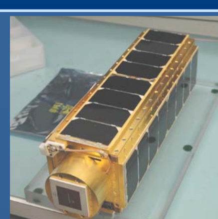
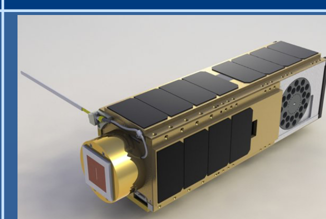
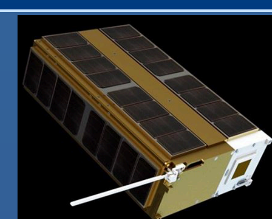
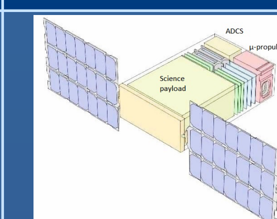
Image source: nasa

Cubesats for space biology

- Fast development time
  - 18 – 36 months from concept to operations
- Educational value
  - Mission life-cycle comparable to student’s career
- Access to space environment
  - Various orbits
- Autonomous operation
  - Reduced need for astronauts time
  - Less constraints with respect to ISS
- Low cost
  - Launched as secondary payload
  - Low-cost of failure
  - Experiment re-iteration (test, learn, iterate)
  - **Compatible to ‘short-duration’ biological experiments**

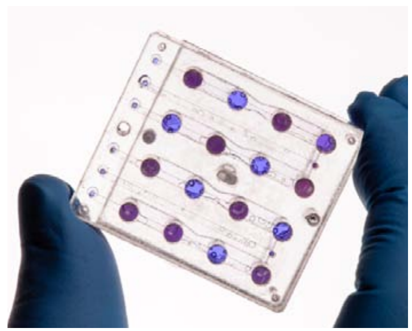


Biological cubesat missions

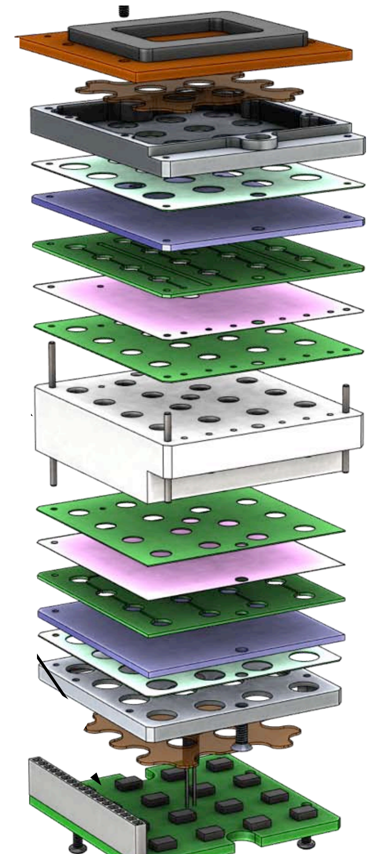
GeneSat-1	PharmaSat	O/OREOS	ECAMSat	NASA BioSentinel
2006 (Minotaur I)	2009 (Minotaur I)	2010 (Minotaur IV)	2017 (ISS)	Planned 2018 (Orion mission)
3U cubesat (2U payload, 1U bus)	3U cubesat (2U payload, 1U bus)	3U cubesat (2U payload, 1U bus)	6U cubesat	6U cubesat
Gene expression experiment	Antifungal dose response	Microbe survival and activity UV-induced organic degradation	Space effects on antibiotic resistance	Biological response to space radiation beyond LEO
E. coli 	S. cerevisiae 	B. subtilis, H. chaoviatoris (SESLO experiment) PAH, a.a., porphyrin, quinone (SEVO experiment)	E. coli 	S. cerevisiae 
				

State-of-the-art

- Current and coming 'bio'-cubesat mostly rely on 'conventional' technologies and instrumentation
- Lab-on-chip devices are also used



Biosentinel fluidic card
(source: nasa)

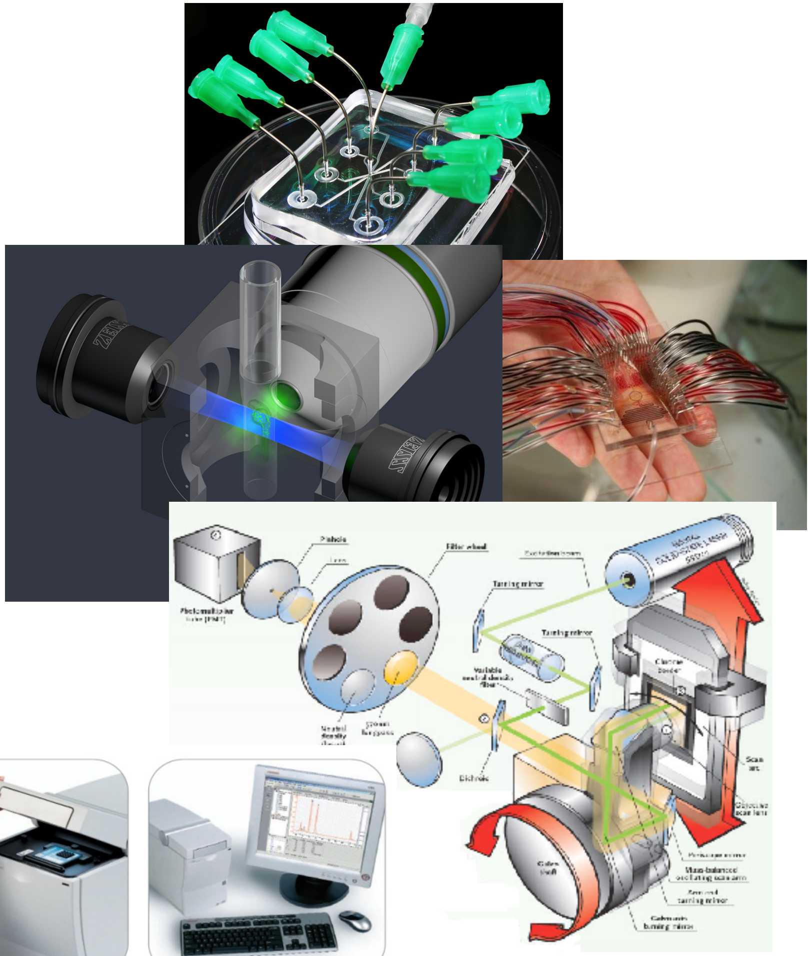


Biosentinel arrangement
(source: nasa)

- However these are 'just' microfluidic devices which still require significant external hardware for operation
- **Need for new paradigm for more efficient integration**

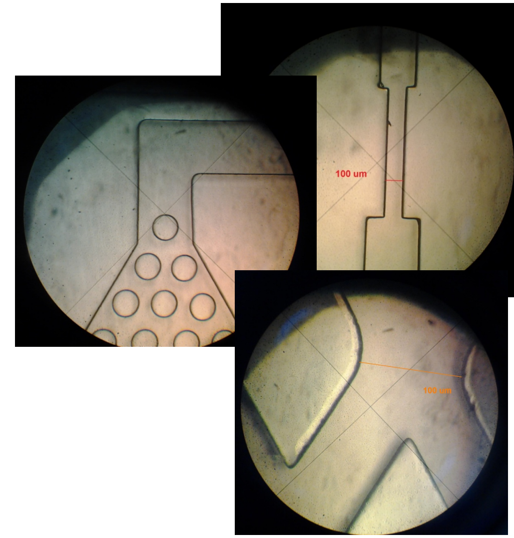
‘True’ lab-on-chip technology

- Three main action areas
  - Microfluidics
  - Analytical detection
  - Sensors and actuators

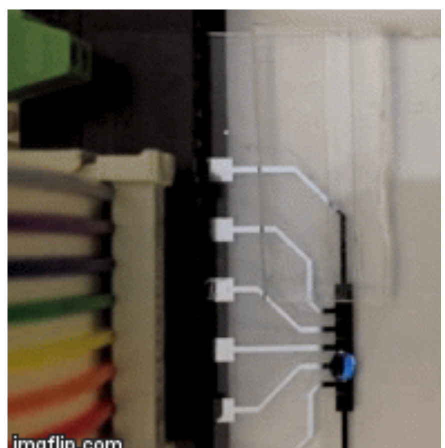


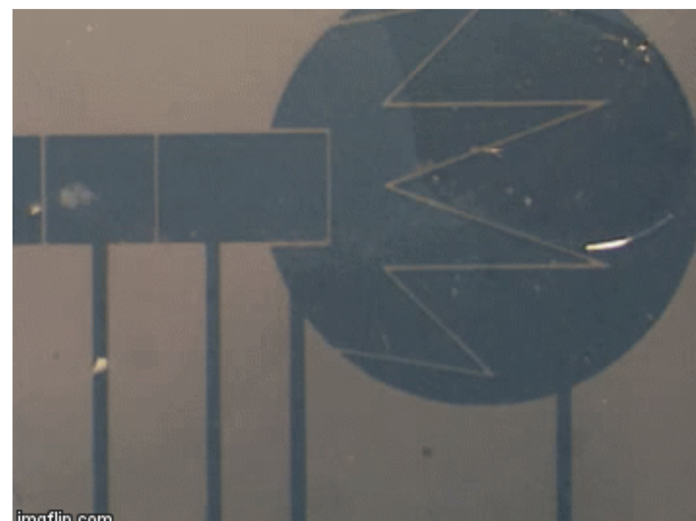
On-chip microfluidics

- Autonomous capillary flow
- On-chip flow control by Electro Wetting On Dielectrics



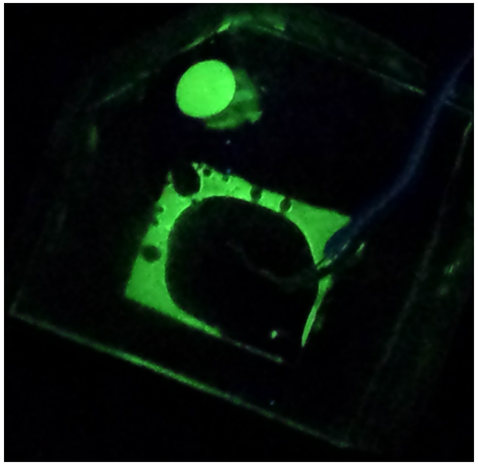
No need for pumps





Analytical detection

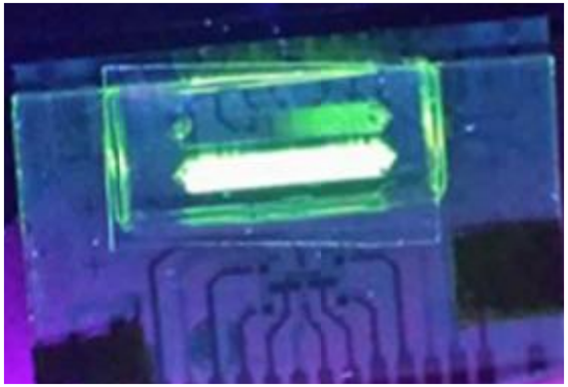
- Chemiluminescence
- Bioluminescence



No need for excitation sources

No need for optical filters

High specificity and selectivity

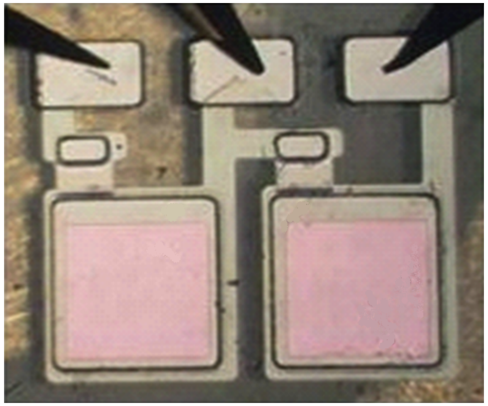


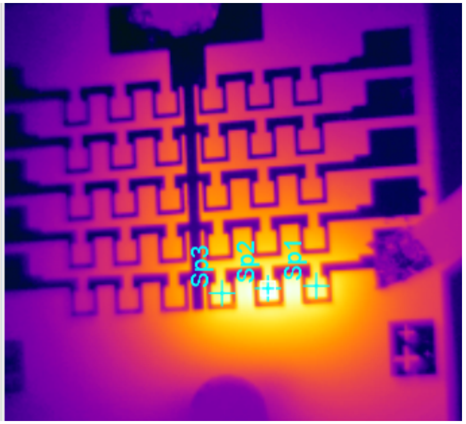
On-chip sensors and actuators

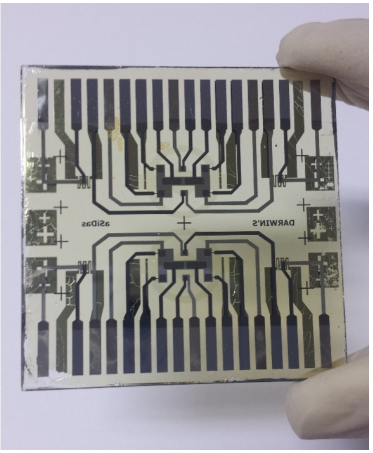
- a-Si:H optical and temperature sensors
- Thin-film resistive heaters

No need for external sensing devices

Optimal thermal and optical coupling



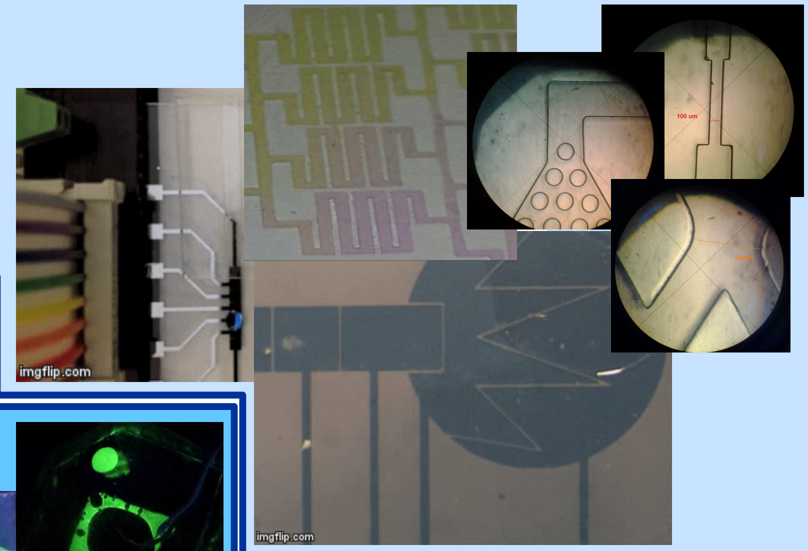




Fully integrated lab-on-chip

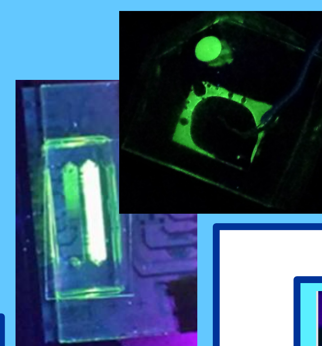
- On-chip microfluidics
  - autonomous capillary flow
  - active flow control by EWOD

  No need for pumps



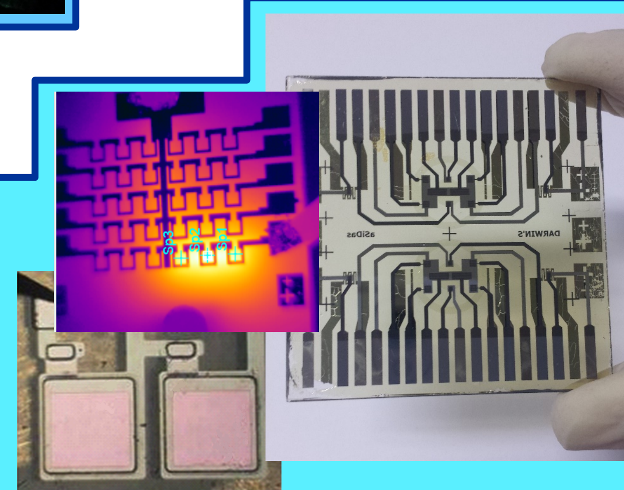
- Analytical detection
  - chemiluminescence
  - bioluminescence

  No need for excitation sources
  No need for optical filters
  High specificity and selectivity



- Integrated sensors and actuators
  - a-Si:H optical and temperature sensors
  - thin-film resistive heaters

  No need for external sensing devices
  Optimal thermal and optical coupling



Fully-integrated lab-on-chip advantages

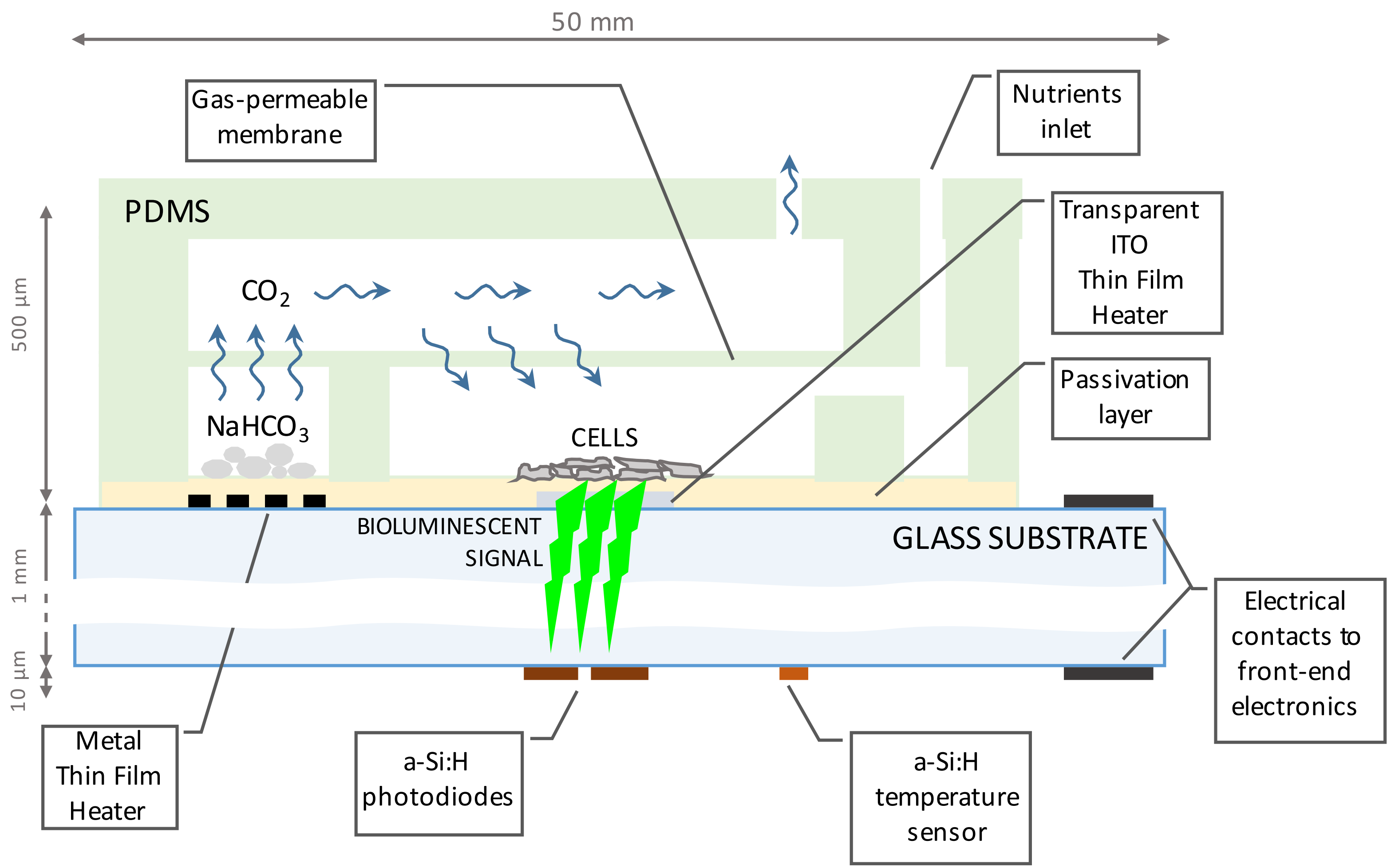
- Extreme compactness
- Low power consumption
- High assay specificity due to CL approach
- High sensitivity provided by a-Si:H photosensors
- Large analytical dynamic range
- Intrinsic mechanical stability (monolithic integration, no alignment issues)
- The combination of capillarity and EWOD opens the possibility to implement a wide variety of microfluidic configurations

MICRO INCUBATOR

Cell incubator system design

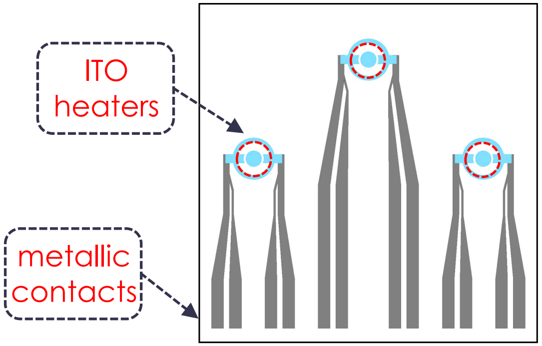
- Main requirements
  - shall host the cell culture
  - shall refresh the culture medium
  - shall regulate culture temperature
  - shall ensure right CO_2 concentration
  - shall provide cell culture monitoring capabilities
- Additional features
  - low-power consumption
  - multiple cultures on the same chip with different needs (e.g. different temperature)

Cell incubator idea

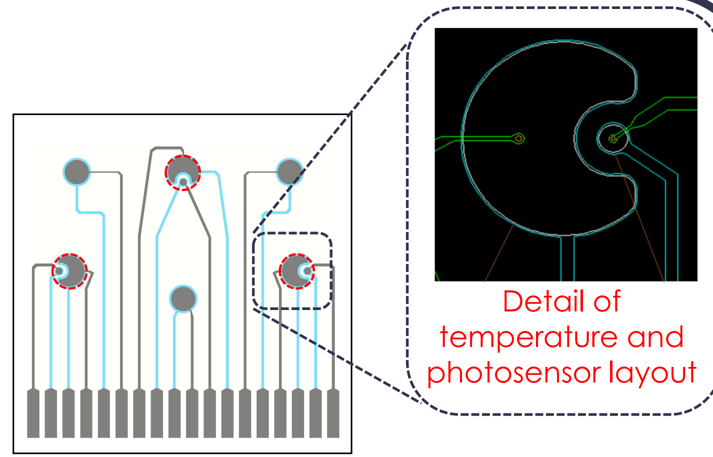


Incubator prototype layout

SMART GLASS

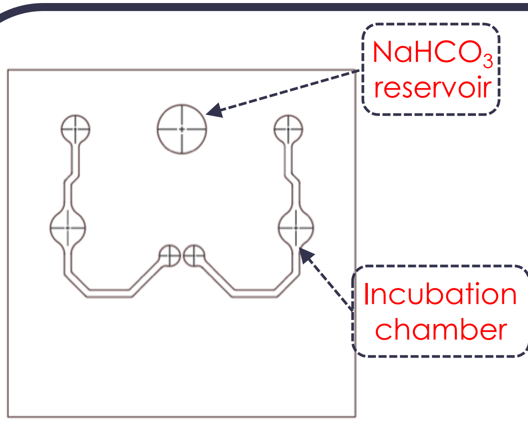


Top-side
thin-film transparent heaters

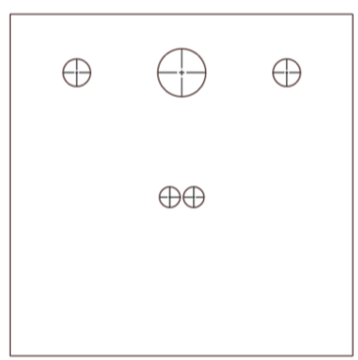


Bottom-side
a-Si:H optical and temperature sensors

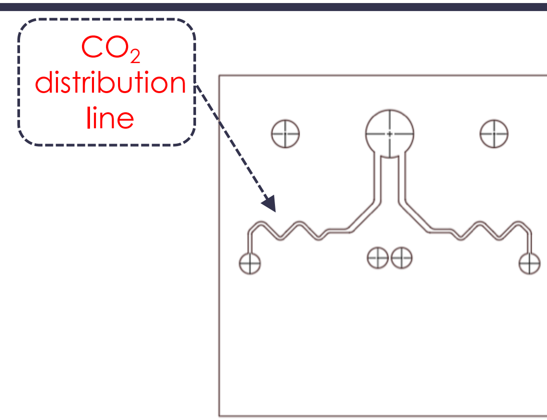
MICROFLUIDICS



First layer
incubation chambers and
CO_2 source reservoir



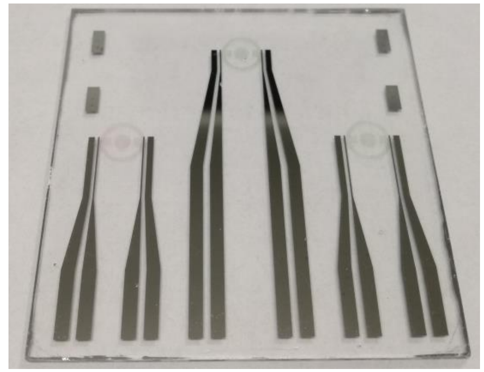
Second layer
gas-permeable
membrane



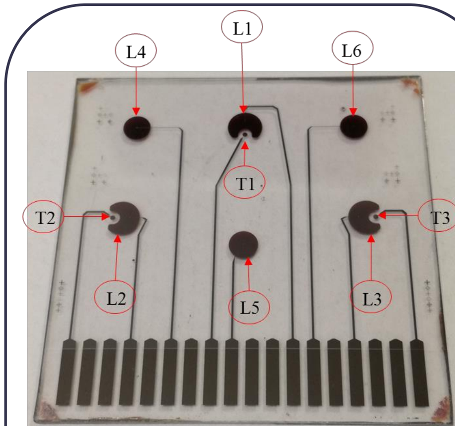
Third layer
CO_2 distribution line

Smart-glass fabrication and test

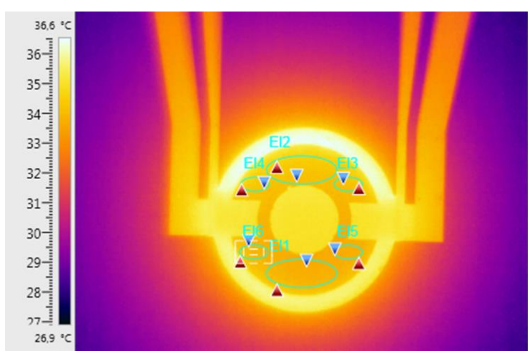
- Thin-film technology (PECVD, RF sputtering, thermal evaporation)
- Photolithographic process
- Wet and dry etching
- Both glass sides process
- **Need for careful process design and material selection**

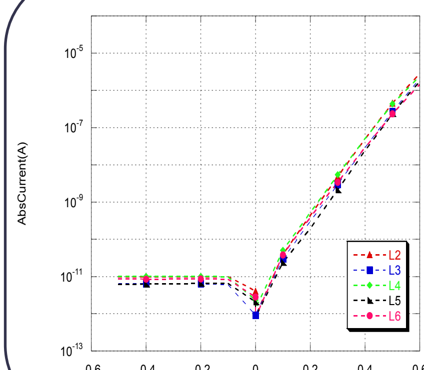


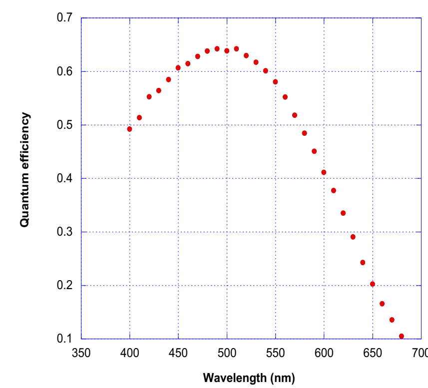
Top-side thin-film transparent heaters with metallic contacts



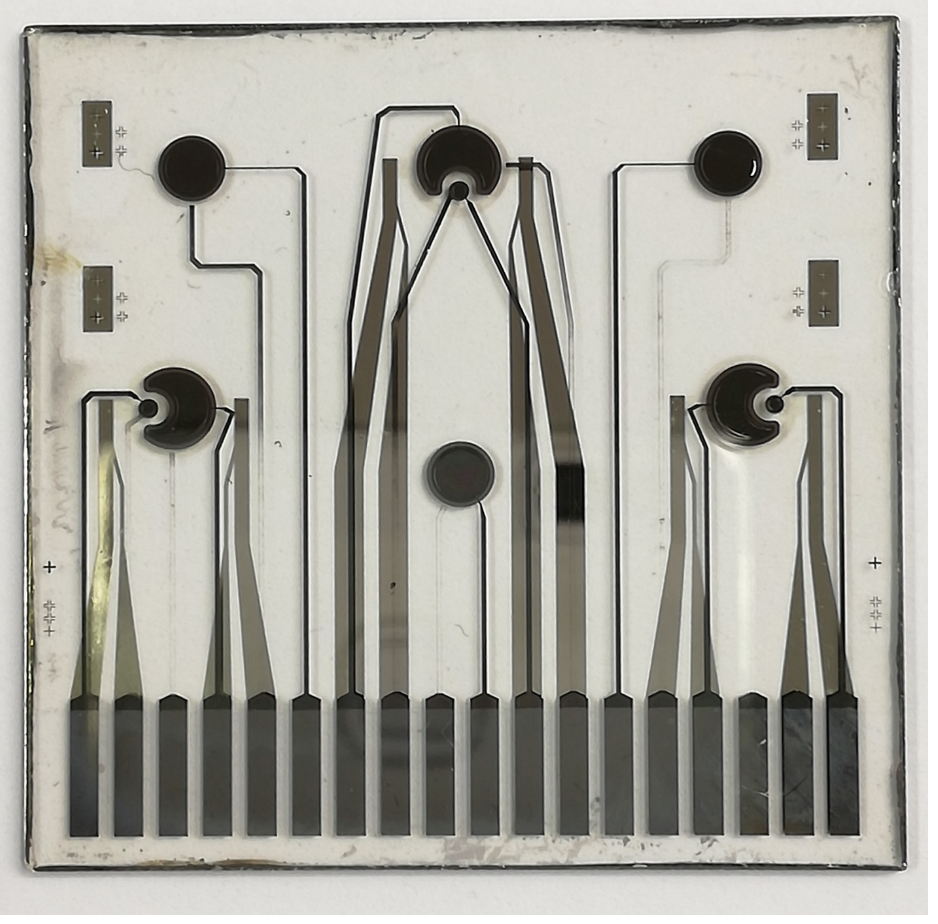
Bottom-side a-Si:H optical and temperature sensors







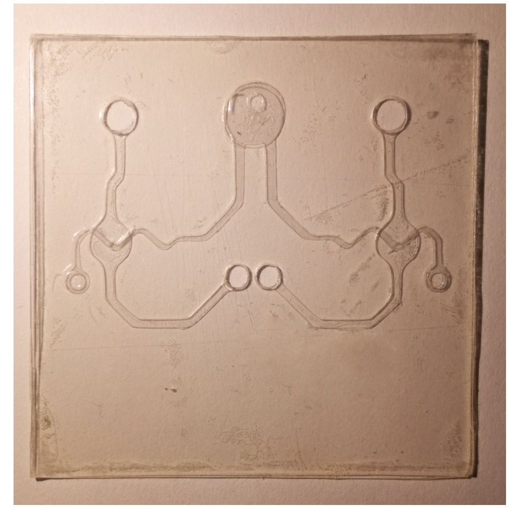
Smart-glass

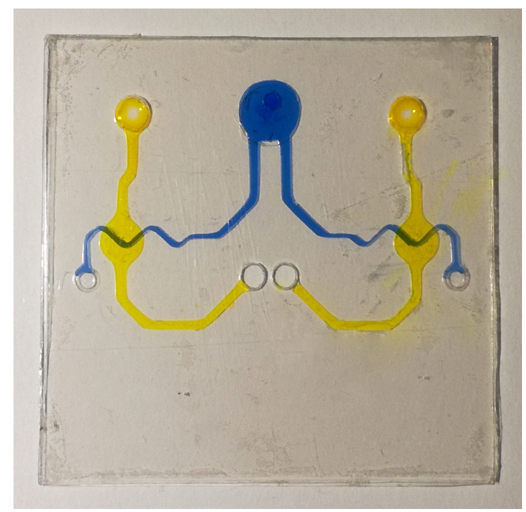


View from sensor's side

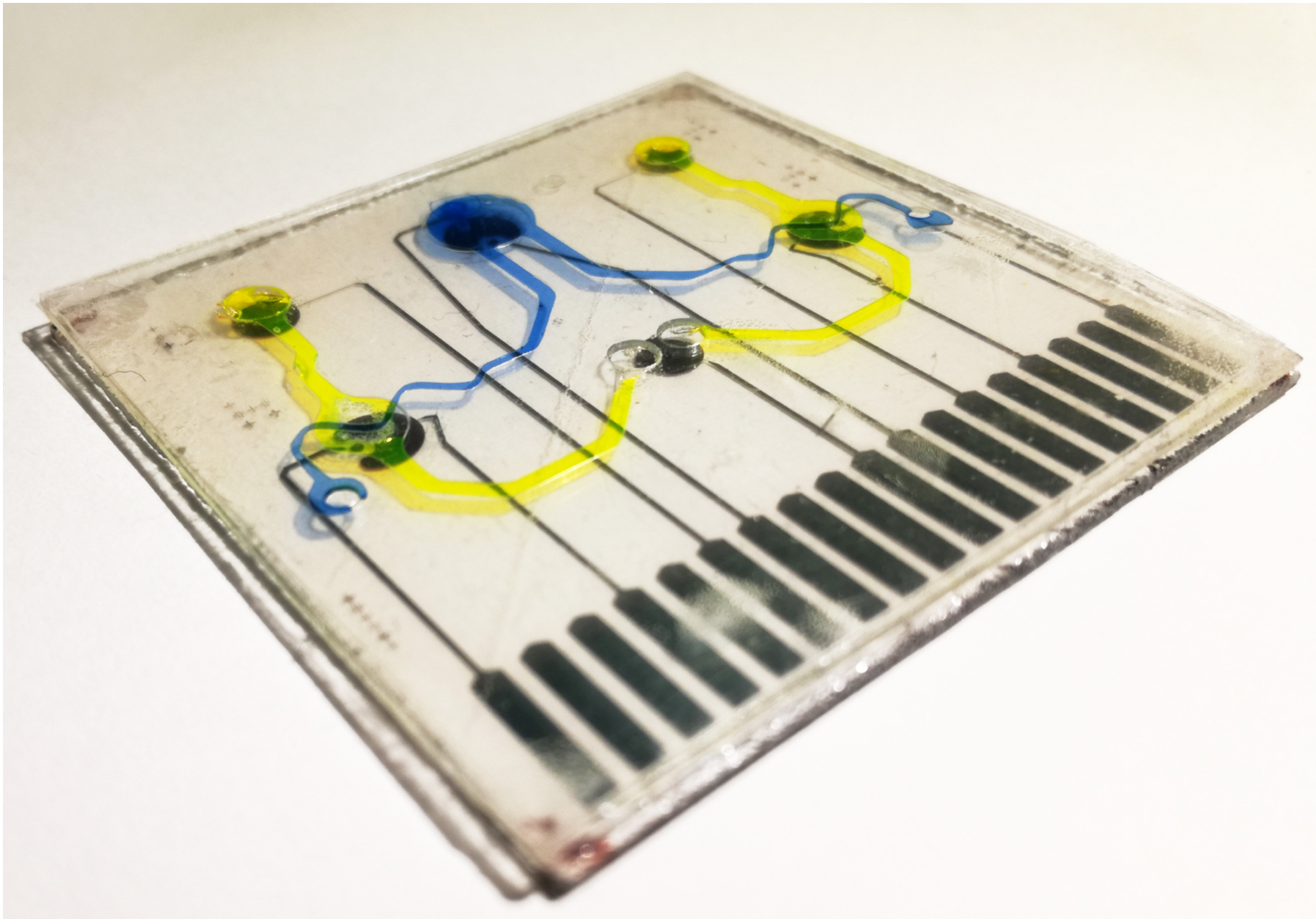
Microfuidics fabrication and test

- Several technological options available
  - photolithography (SU-8)
    - fine details but expensive
  - soft lithography (PDMS)
    - gas-permeable but hydrophobic
  - xurography (PSA)
    - rapid but coarse details
- Combinations of the three technologies is possible



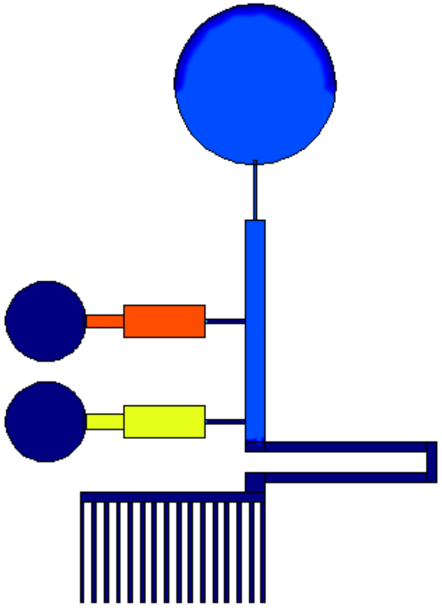


Micro-incubator assembly

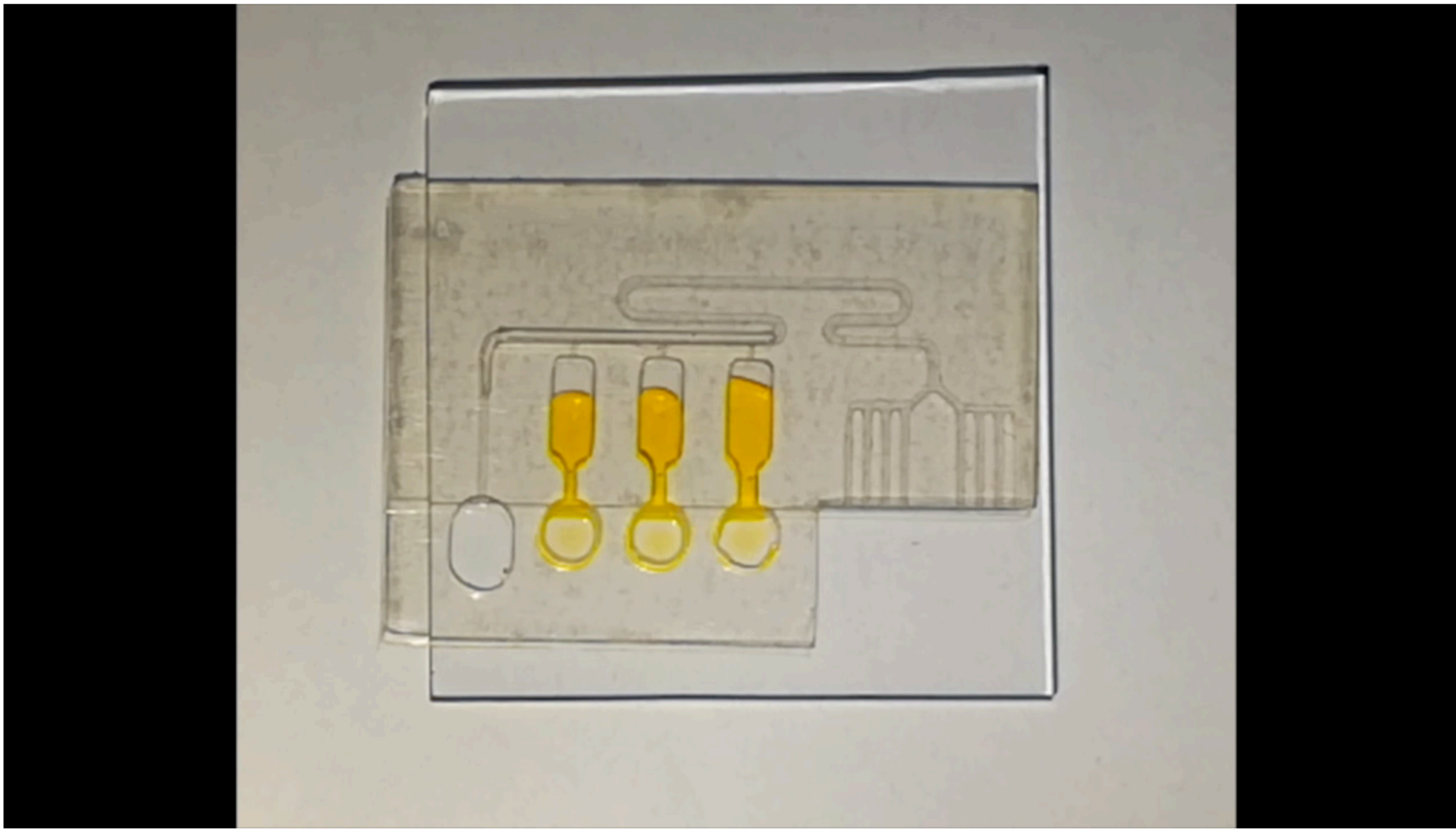


Next steps

- Design of autonomous capillary structures for autonomous delivery of fluids (e.g. fresh culture medium, drugs, reagents)
- Use of capillary structure as:
  - trigger valves
  - retention burst valves
  - flow resistors
  - capillary pumps



Preliminary tests of autonomous capillary systems



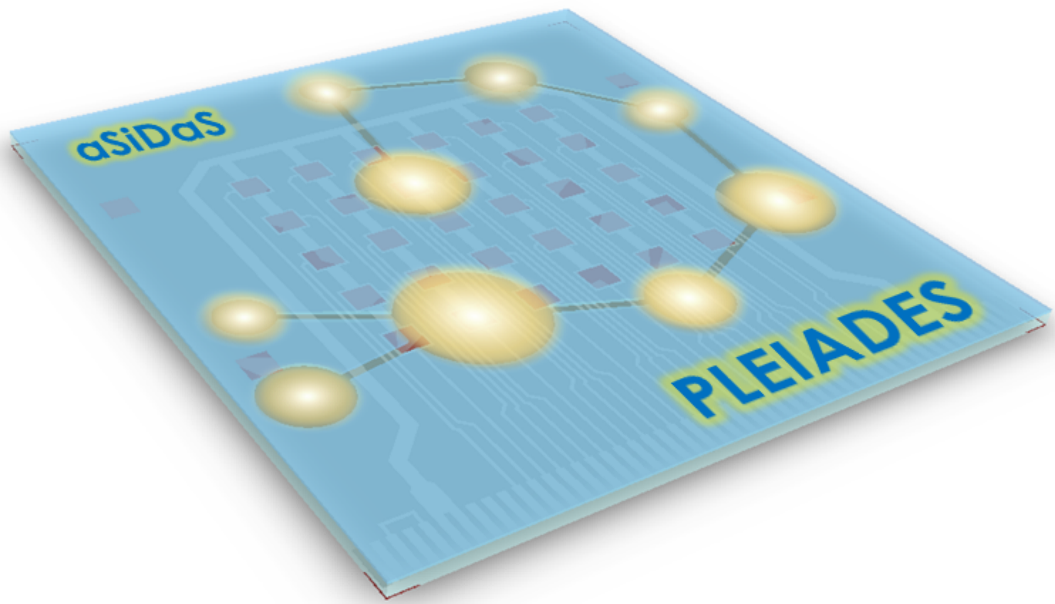
Conclusions

- **Fully-integrated lab-on-chip technology** enables more compact autonomous devices suitable for 'bio'-experiments on cubesat platforms
- **Micro-incubator** with on-chip environmental control and sensors for cell culture monitoring
- **On-chip production of CO_2** from solid phase
- **Modular design** that can be adapted to different cell culture requirements
- **Autonomous microfluidics** enables chip operation without external pumps

Acknowledgements

PLEIADES

Planetary
Life
Explorer with
Integrated
Analytical
Detection and
Embedded
Sensors



Thank you for your attention!