Custom Micro / Nano System Development and Production
for Telecom, Process Control, Life Sciences and Space

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The advanced microfluidics and integrated optics technology forming the micro system analysis core to be integrated in the ExoMars Life Marker Chip instrument

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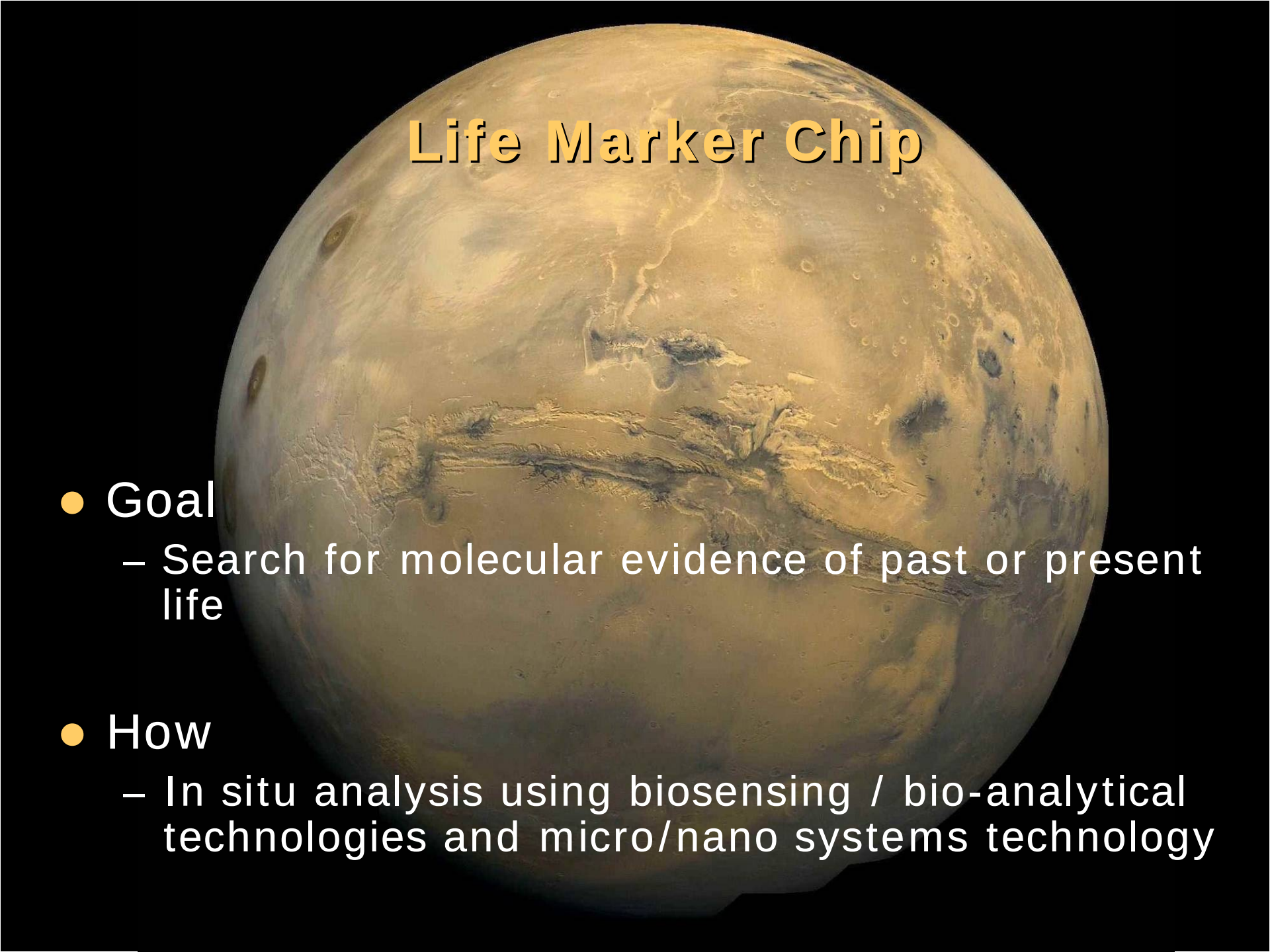
Dave Cullen, Cranfield Univ. (UK)

7th ESA Round-Table on MNT for Space Applications
September 13-17, 2010
ESTEC Conference Center, Noordwijk, The Netherlands



Life Marker Chip

- Goal
  - Search for molecular evidence of past or present life
- How
  - In situ analysis using biosensing / bio-analytical technologies and micro/nano systems technology

Overview

- Introduction LioniX
- Life Marker Chip on ExoMars rover
- LMC instrument
- LMC microfluidics
- LMC integrated optics
- Spin-off and commercialisation
- Future developments
- Concluding remarks

Mission Statement

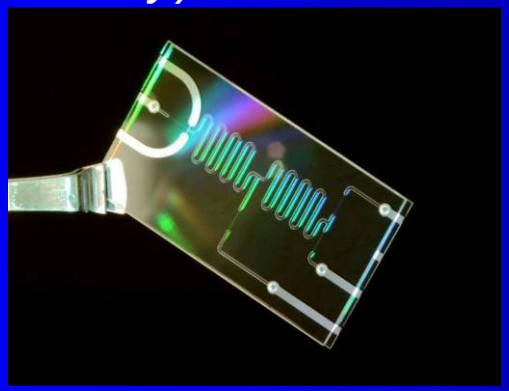
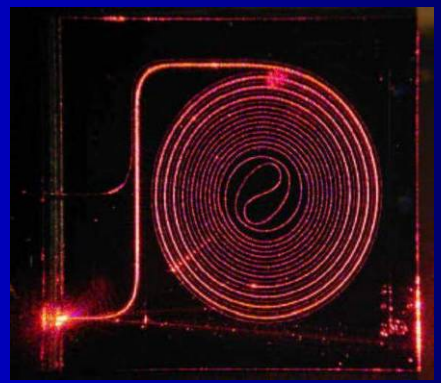
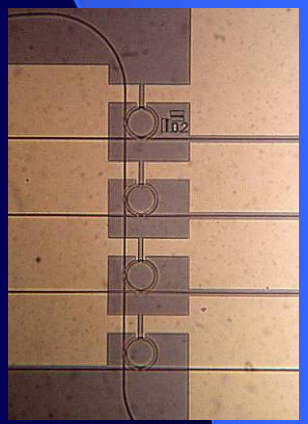
LioniX is a leading provider in development and production of leveraging products based on micro/nano technology for its (OEM) customers in Telecom, Industrial Process Control, Life Sciences and Space.

The core technologies are integrated optics and microfluidics, including surface functionalization.

LioniX offers ‘design for manufacturing’ and ‘horizontal integration’ by partnering with foundries and suppliers of complementary technologies

Overview LioniX

- Located at the Science Park University of Twente
- Sister company iX-factory at MST.factory Dortmund
- 25 people, mainly highly educated
- Private company (BV), profitable
- Shareholder Panthera Group BV (70 people)
  - Product spin-outs / sister companies
- Core technologies/activities
  - Lab-on-a-Chip / (bio)chemical sensor systems
  - Micro-photonic signal/data processing (communications, spectrometry)

In-house facilities

Low-volume production at:

- State-of-the-art micro/nano facilities of the MESA+ NanoLab (facility sharing)
- Private facilities for core technologies
- iX-factory GmbH (Dortmund, Germany)
- High volume production at contracted foundries



Customers

- Established national and worldwide customer network
- Representatives in UK, Scandinavia, Israel, USA, Asia
- Telecom:
  - Fiber-to-the Home, satellites, mobile communication
- Process Control:
  - chemistry/pharma, bioprocessing, water
- Life sciences:
  - food, biotech, medical
- Space:
  - bioanalytical systems, optical data/signal processing
- OEM's, VC start-up companies
- Innovative end-users
  - multinationals, research institutions

Vescent Photonics

CoreCom lightwave processing

SIEMENS

Unilever

Bronkhorst® HIGH-TECH

esa

NIVR

Confidential

Universiteit Twente

Life Marker Chip on Mars

ExoMars elements and planning

ESA

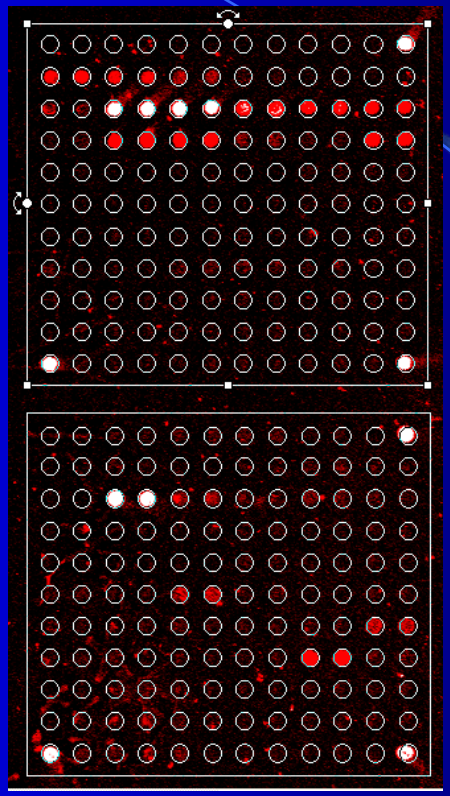
Life Marker Chip on Mars

Antibody microarray technology

allows the attachment of thousands of probes in a few square centimetres on a solid support. Smaller reaction volumes and higher reaction kinetics, together to its great potential for miniaturization and robotization, make microarray technology a good system for *in situ* analysis of biomarkers in astrobiology.

Features

1. Capable to detect extant and extinct life
2. Multiple molecular detection in parallel
3. No special external calibration
4. Allows detection of broad molecular size range
5. Sensitivity: From ppb to ppt
6. Results are very easy to analyze
7. Biotechnology industry supports this technology.



Typical image with one hundred different antibodies as well as positive and negative control

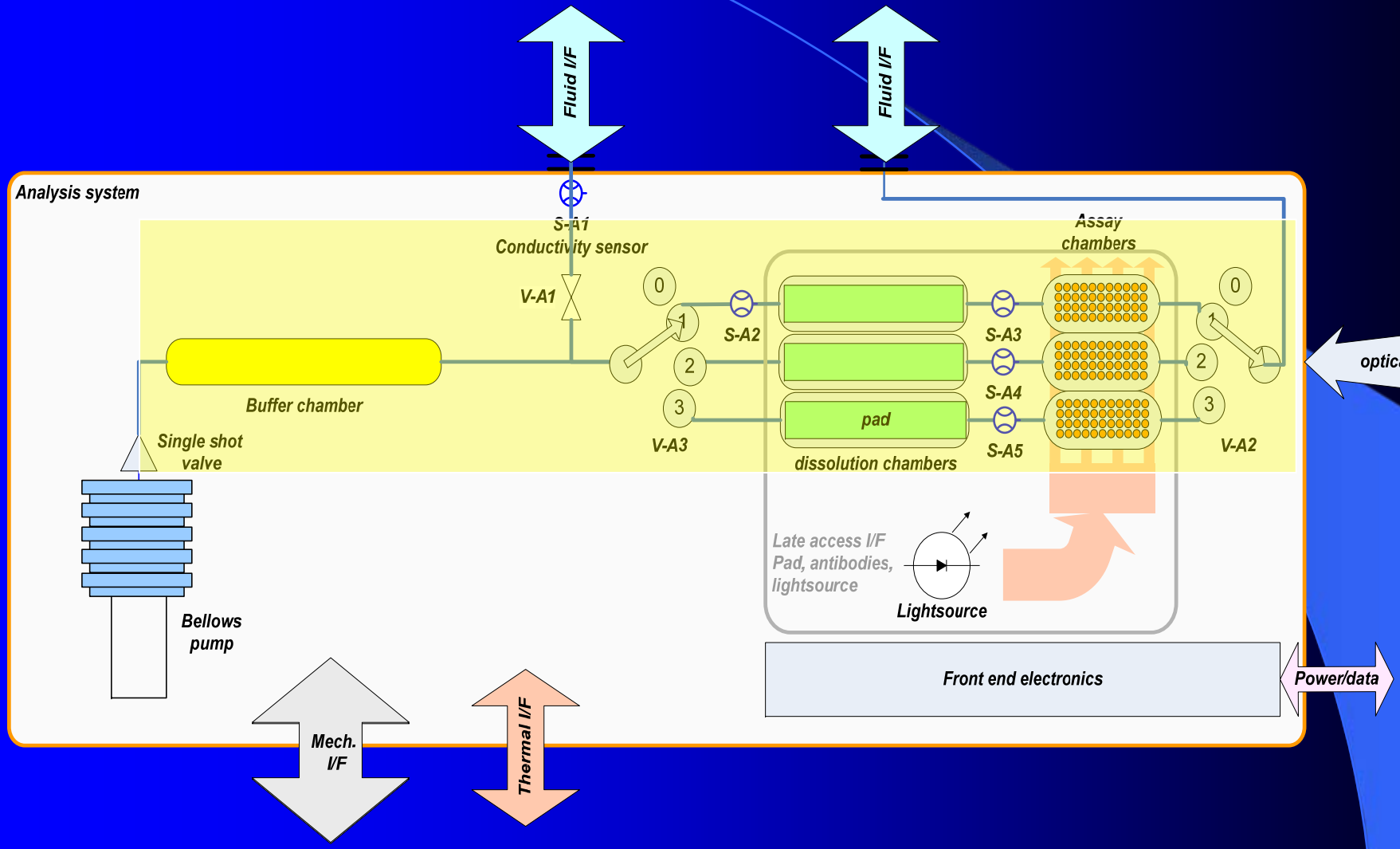
Present life biomarkers

1. **Whole cells,**
2. **Cellular debris, biofilms**
3. **Biopolymers**

Past life biomarkers

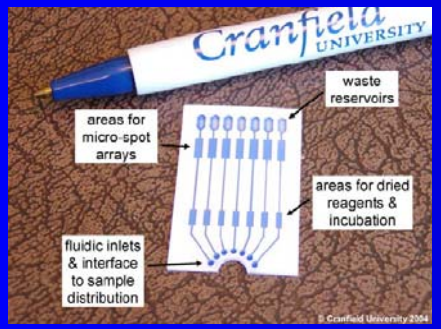
1. **Aliphatic Hydrocarbons.**
2. **Monocyclic hydrocarbons.**
3. **Tricyclic hydrocarbons.**
4. **Aromatic carotenoids.**
5. **Hopanoids and other pentacycic triterpanes.**
6. **PAHs.**
7. **Lipids – Steroids.**
8. **Porphyrins and maleimides.**
9. **Aminoacids (aa) and nucleotides.**
10. **Nucleotides and other metabolites**
11. **Polymers**

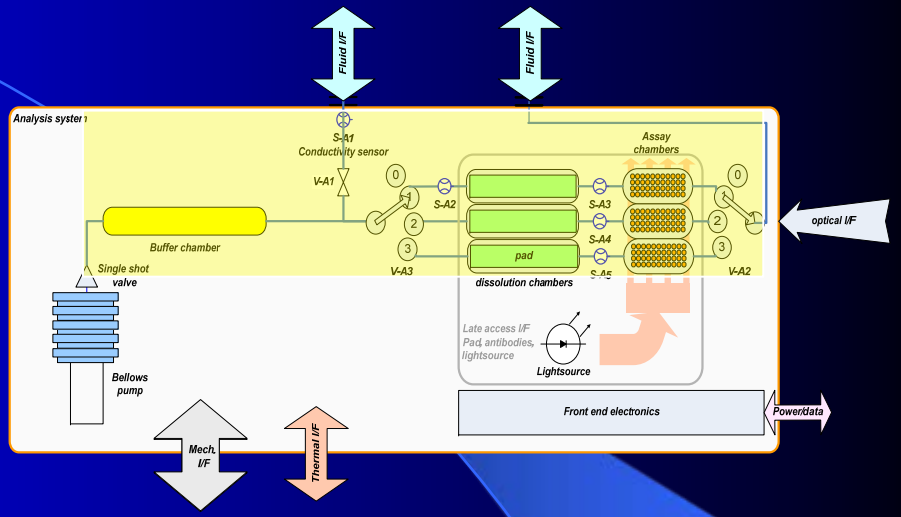
Analysis subsystem fluidics



Micro / Nano / Bio Tech in LMC

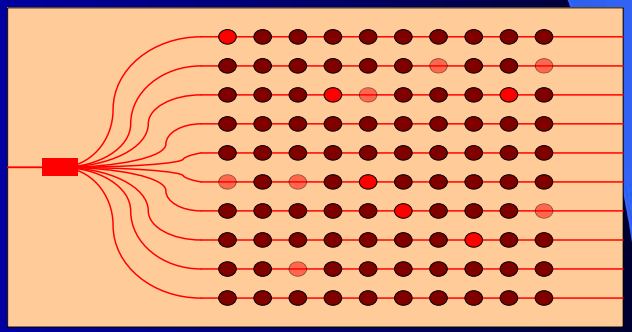
- **Antibody microarray**
- competition assay format (3 chemistries)
- predosed dried chemicals
- single-use
- 4 arrays of 10x10 spots





- **Microfluidics based core system**
- based on micro/nano technologies
- micro channels: fluidic connections
- micro chambers: reagents, array, buffer
- micro sensors: electricial conductivity
- planar optical waveguides: excitation of dyes
- micro system integration: compact subsystem
- hybrid selector valve

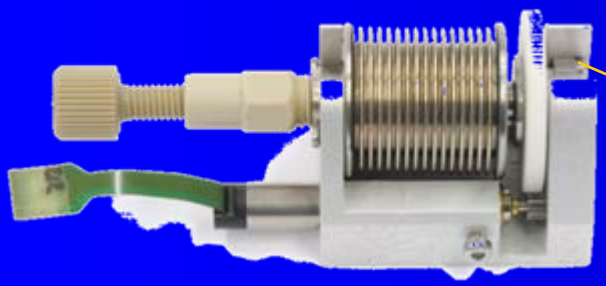
- **Integrated planar waveguides**
- Laser Induced Fluorescence (LIF)
- excitation by 'manifold' substrate



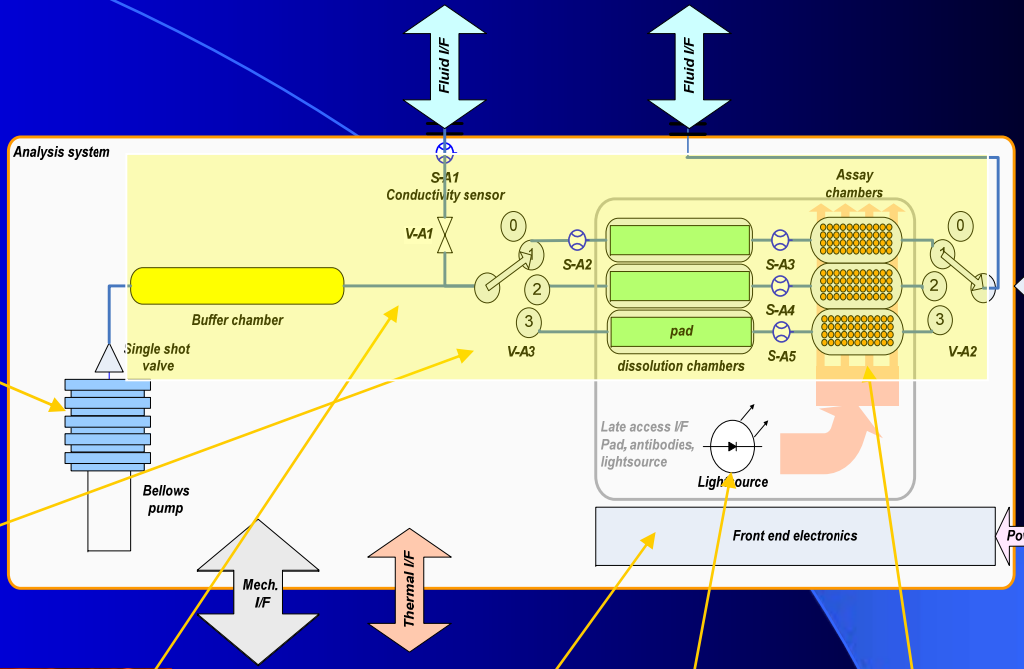
Chips system integration

Courtesy of Guus Borst
Dutch Space

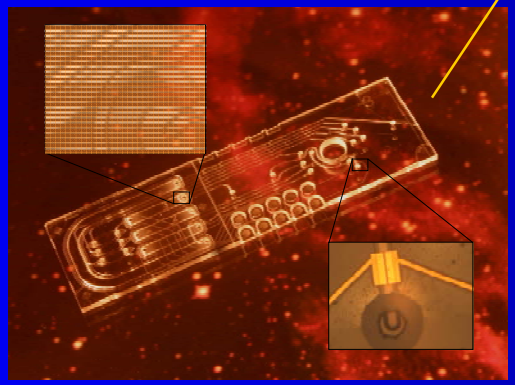
LMC Analysis Subsystem Elements



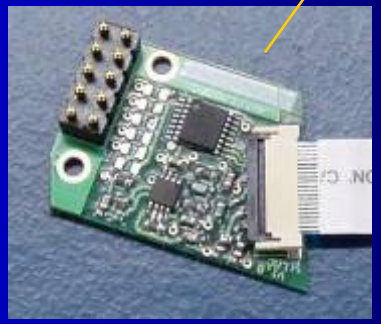
Fluid storage, valve and pump



Rotary valve to control the fluid over the chip



Glass chip with integrated fluid channels, chambers and sensors



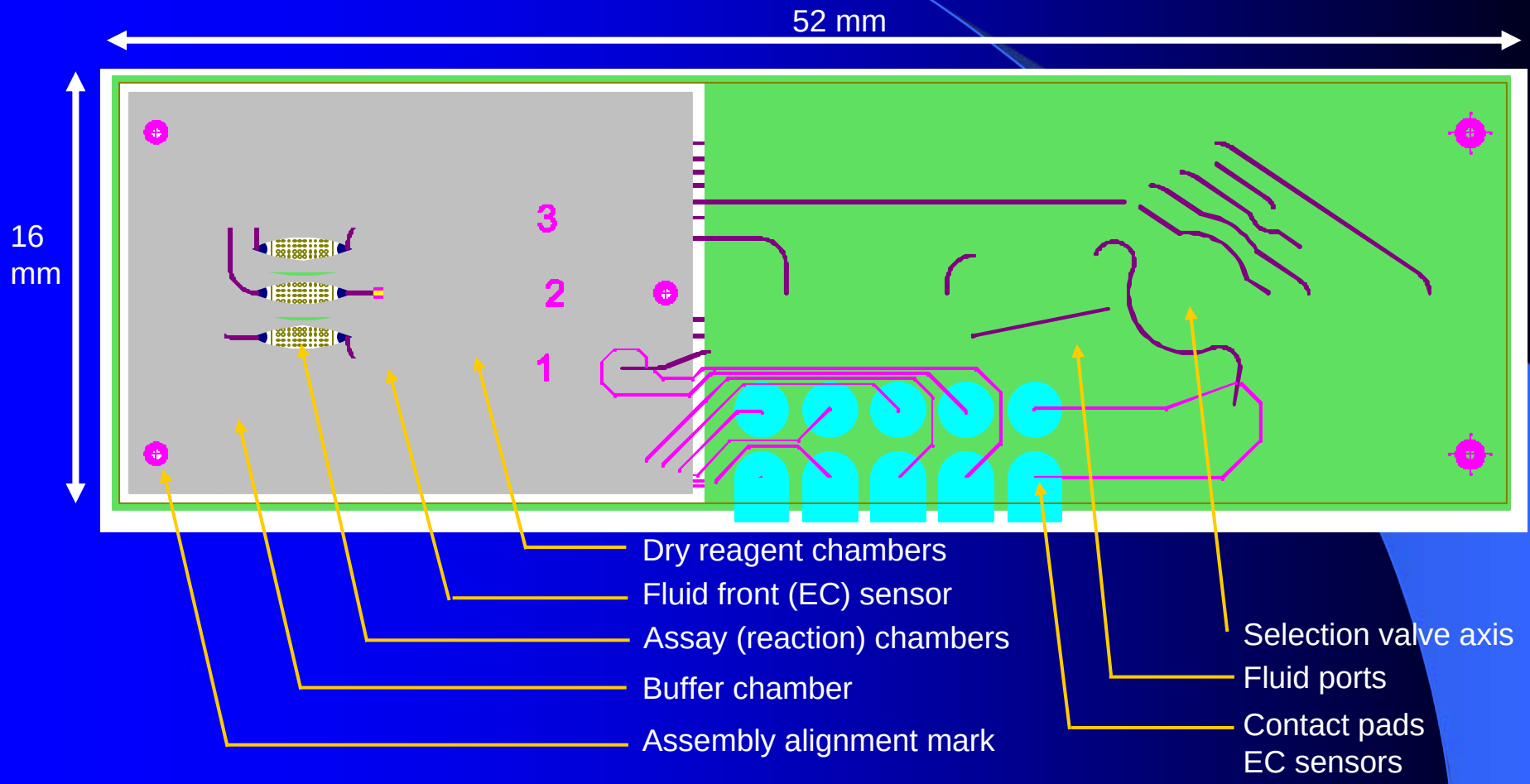
Electronics to read out the sensors

Laser

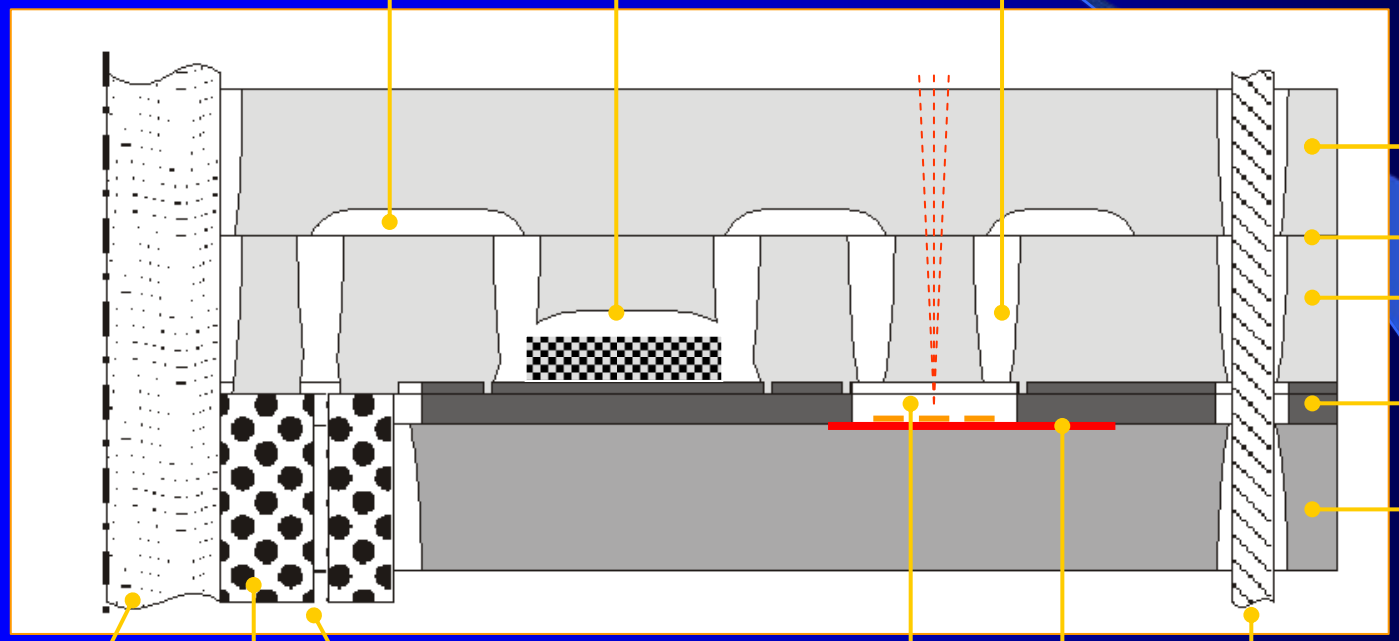
Waveguides to excite the attached antibodies

Microfluidic chip
(view from above)

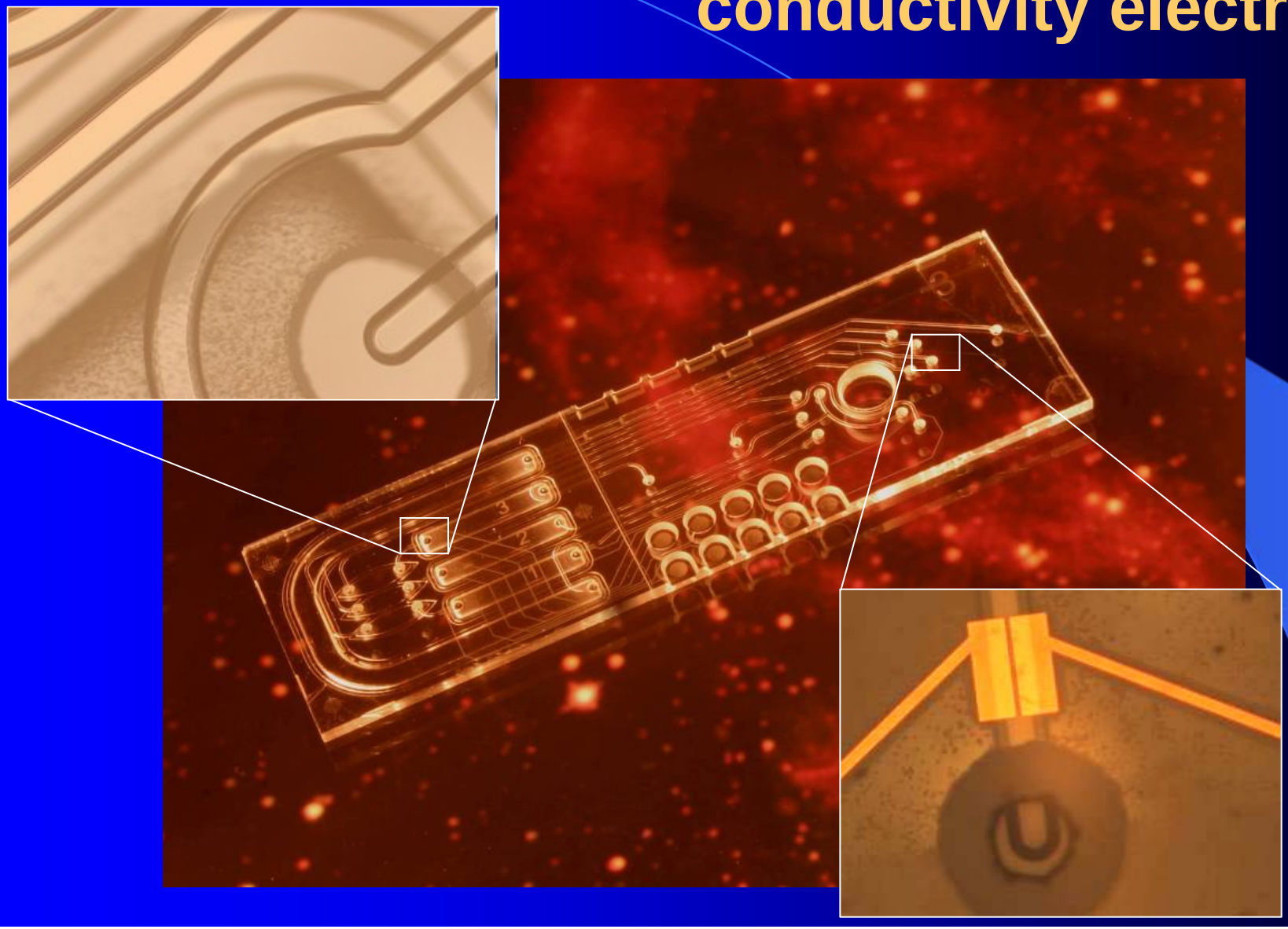
1G-prototype



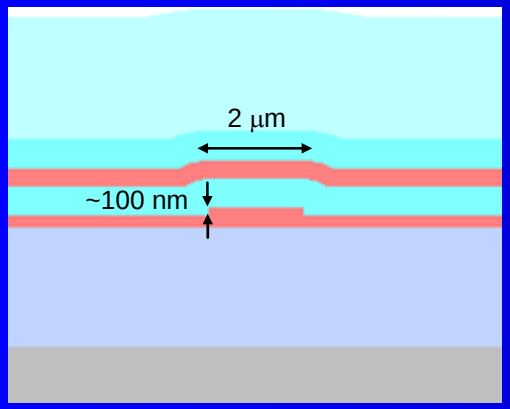
Microfluidics chip (cross-section)



Fluidic chip with conductivity electrodes

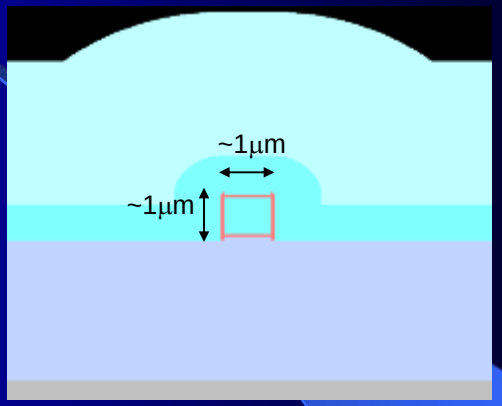


Planar waveguide technology TriPleX™

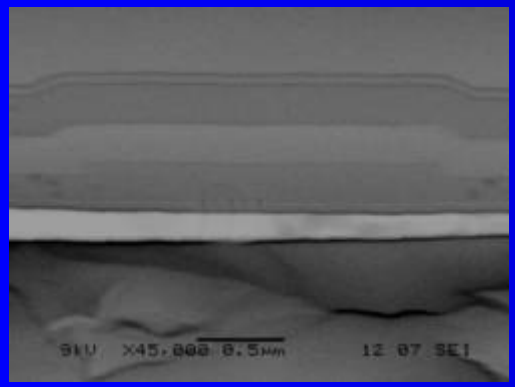


'sensing' geometry for Lab-on-a-Chip

Si_3N_4: red layer
SiO_2: red layer

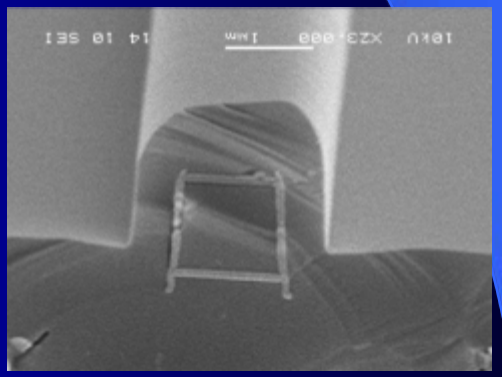


'fiber-like' geometry for data/telecom



Core of TriPleX™: Si_3N_4 / SiO_2 / Si_3N_4

'Design by geometry'

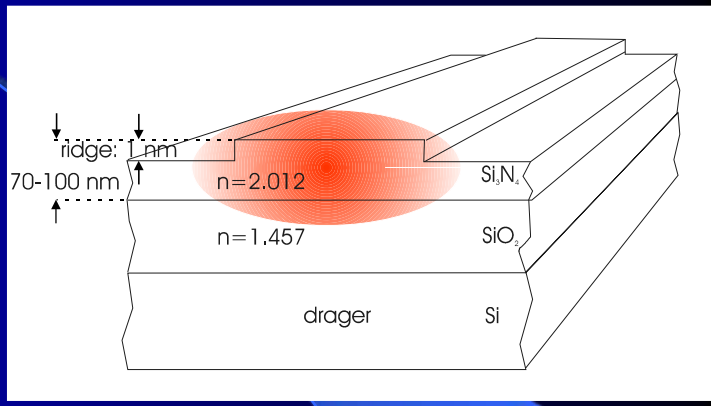


Features of TriPleX™

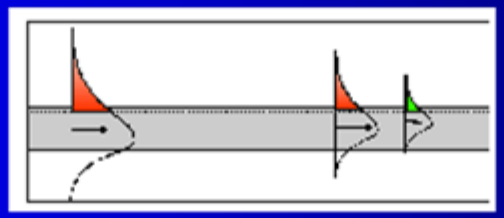
- based on standard, reproducible and stable thin films
  - SiO_2 and Si_3N_4
  - compatible with CMOS
  - transparant 400nm – 2500nm (VIS-(N)IR)
- high index contrast
  - small bending radius
  - large scale integration (LSI)
- low propagation loss and birefringance
- monolithical integration in Lab-on-a-Chip
  - compatible with fused silica
  - compatible with fused silica bonding
- unique platform for optical data/signal processing
  - design by geometry (not constrained by material properties)
  - RF photonics: filtering, routing, beamforming
  - spectrometry: Earth Observation

Features of TriPleX™

- unique platform for optical detection
  - excitation and sensing of fluorescence in functionalised layer
  - absorption in VIS-(N)IR
  - refractive index sensing (interferometry, selective layer)



Absorption
(VIS – (N)IR)

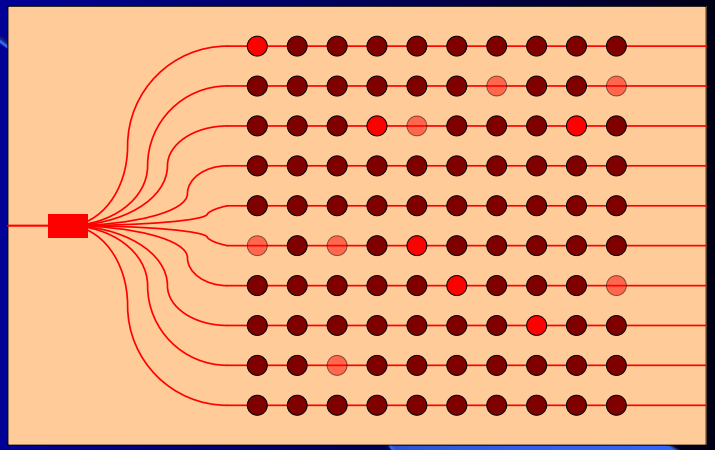


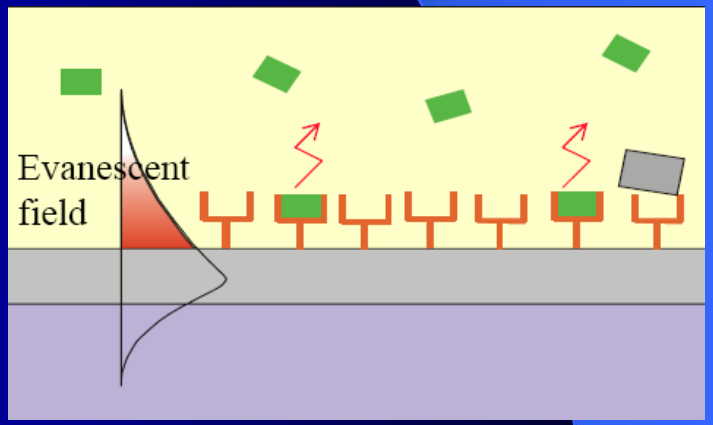
Excitation
(Fluorescence)

Refractive index
(interferometry)

Detection in LMC

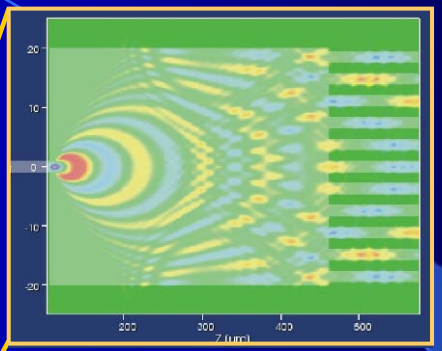
- Each reaction chamber contains an array of 10x10 spots; each spot is functionalised to sense a specific target; spots for self-test included
- Integrated waveguides on silicon substrates using TriPleX™
- Excitation of the (*hopefully!*) bound fluorophores by the evanescent field of the waveguide
- Detection by a camara imaging system

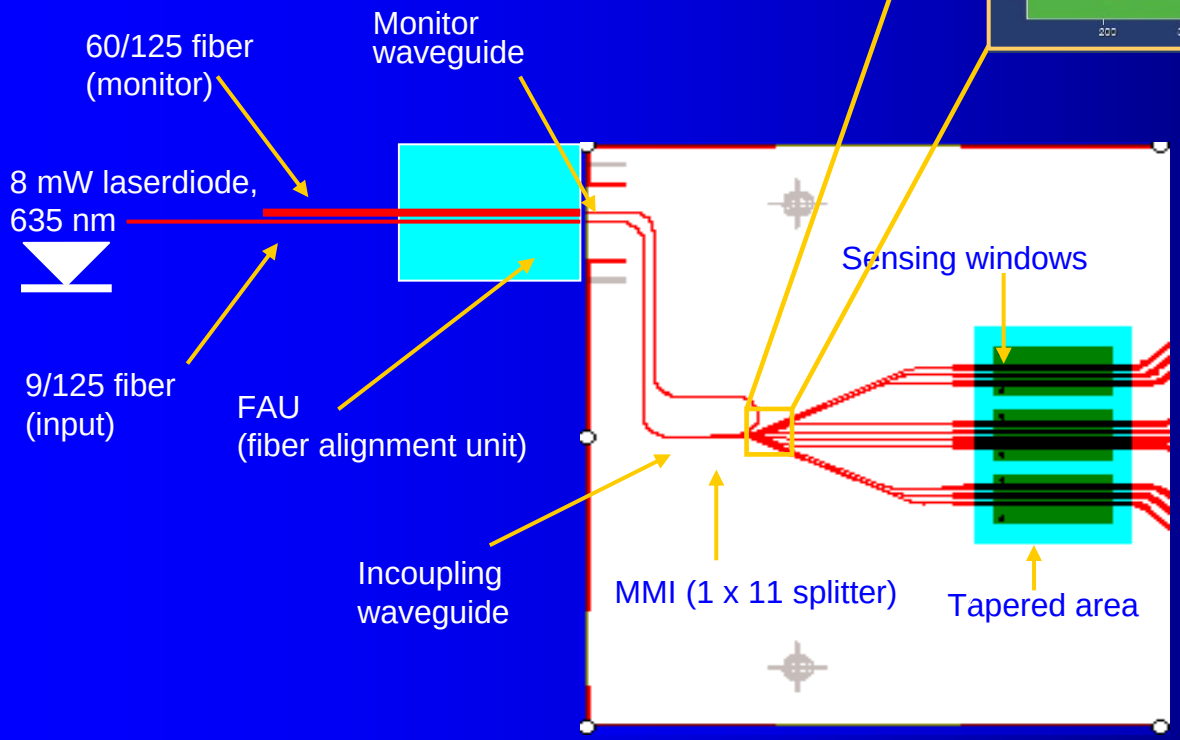




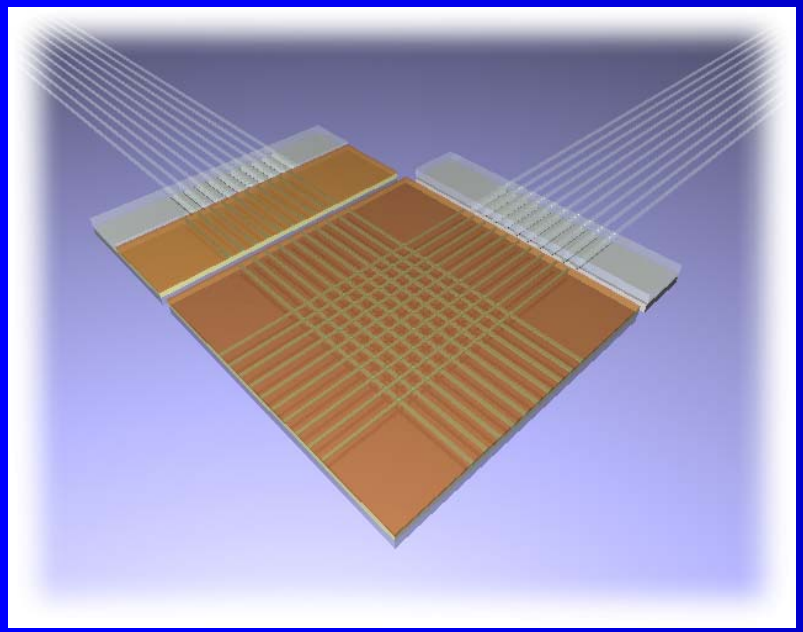
Optical chip and fiber connections

Multimode Interferometer





Planar waveguides in microarrays



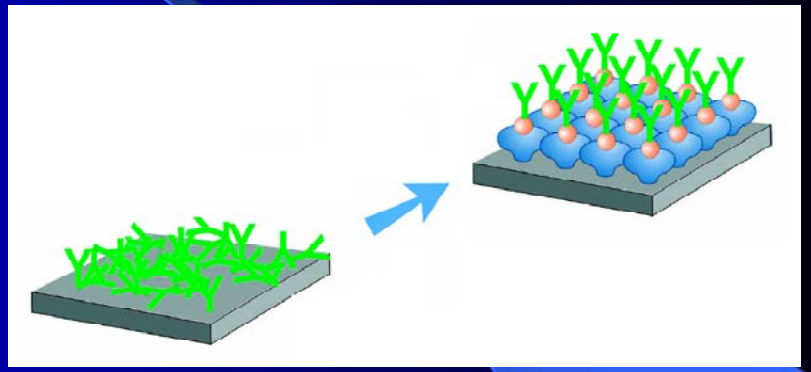
- functionalised spots of:
  - oligo strands for DNA array
  - antibody/protein array
- planar waveguides for:
  - excitation fluorescent dyes
  - sensing of fluorescence

Spin-out applications

- LMC: *based on bulky R&D/lab equipment*
  - high-throughput screening
  - genomics (DNA) and proteomics (proteins)
  - micro-arrays, capillary electrophoresis, sequencers
  - Commercial: Affymetrix, Agilent, Illumina, Roche, …
- LMC: *complete miniaturized system*
  - including sample pre-processing!
  - ‘flow through’, ‘closed’ systems
  - dedicated applications
  - compact and user-friendly
- LMC: *enabling technologies for ‘**field**’ analysis*
  - analysis in space (micro-gravity, life support systems)
  - medical (point-of-care)
  - food quality and safety
  - industrial process control
  - environmental and water
  - safety & security

Innovative surface functionalisation

- State-of-the-art technology
  - transfer of 3D/titer plate assays to 2D/surface in microfluidics/LoaC
  - 'Trial-and-error' / 'fingerspitzengefühl'
  - Low stability, reproducibility
  - Low homogeneity, efficiency
  - Qualitative detection
  - *Single-use*
- Future technology
  - 'rational design' by convergence of:
    - surface and supramolecular (nano) chemistry
    - biochemistry
    - multiscale modelling & simulation tools
  - better performance
    - stability, reproducibility
    - higher sensitivity ➡ smaller spots ➡ higher density
    - quantitive detection and analysis
  - ***regenerable arrays***
    - ***more applications technically and economically feasible***



Concluding remarks

- Innovative micro/nano technologies in Life Marker Chip instrument
- LMC as enabler for terrestrial applications
- Future developments in functionalisation of micro-arrays will enable more application opportunities