



**DEPArray™: Progettazione, prototipazione e
fabbricazione di un sistema per l'individuazione, la
manipolazione ed il sorting di singole cellule**

**Ing. Gianni Medoro (Silicon Biosystems)
Dott. Davide Ramanand (Skytechnology)**

NI Medical Innovation Summit Modena 8th June 2010

Silicon Biosystems Spa – Bologna ITALY

www.siliconbiosystems.com

Agenda

- Company Introduction
- DEPArray™ Technology
 - Cell Manipulation by Dielectrophoresis
 - Uniqueness of Performances
- DEPArray™ Applications
 - Oncology: Personalized Therapy
 - Prenatal Diagnosis: Non Invasive Approach
- Partnership Network
 - Synergy with National Instruments and Sky Technology

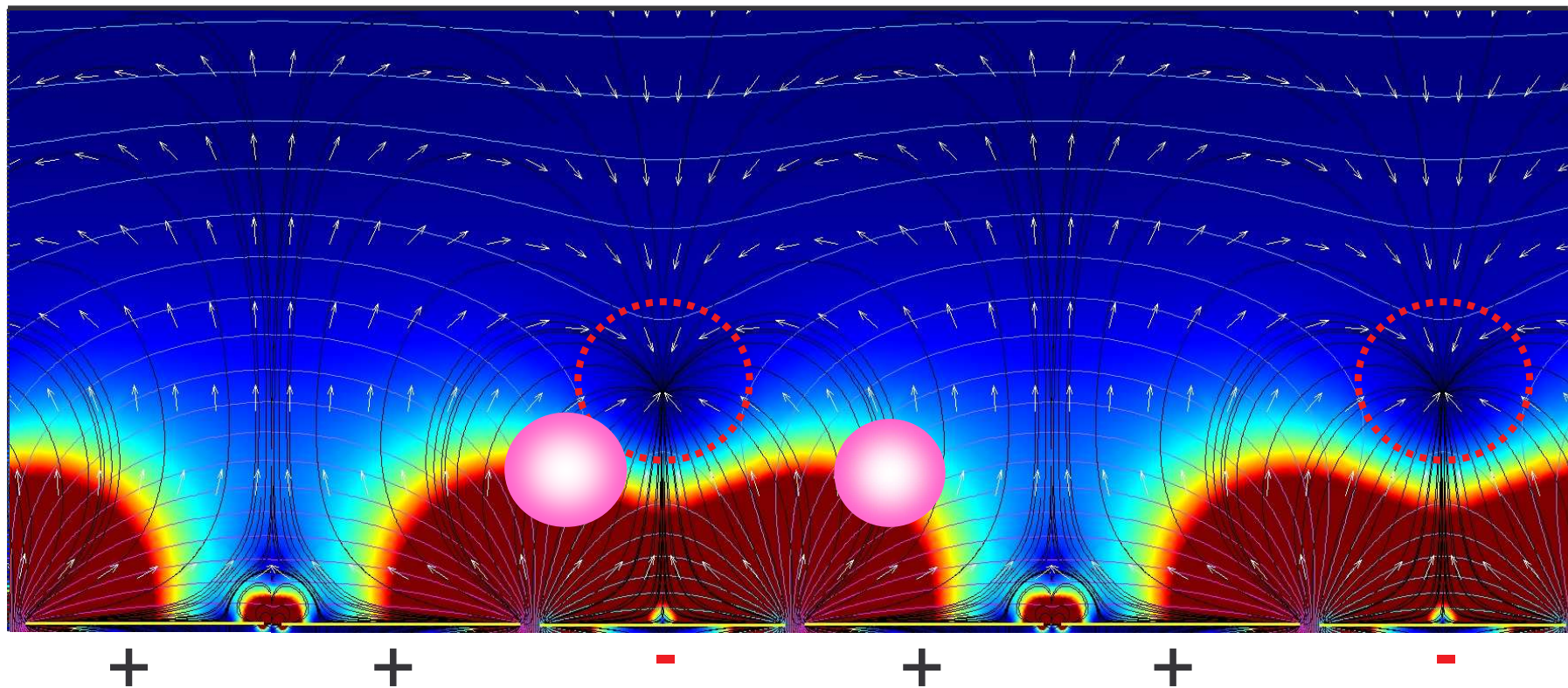
10 Years from Technology Concept to Mature Product with Applications

- 1999** Company founded by 4 scientists at Bologna University
Core patent on Moving DEP Cages filed
- 2000-2005** DEPArray™ technology Proof-of-concept developed under EU, Government and Regional funding (> 5M€ total)
- 2006** 1st fund raising round (1.5M€)
DEPArray™ technology and NIPD application development
- 2007** 2nd fund raising round (5.5M€)
Direct & Indirect Gov funding: (~ 2.5 M€)
- 2008** 3rd fund raising round (3.5M€)
Oncology application development started
- 2009** CE Mark for DEPArray™
Start of marketing activities
- 2010** 4th fund raising round (5M€)
Head count ~24 FTE, 27 patents filed
NIPD and Oncology Applications close to Pilot Trial

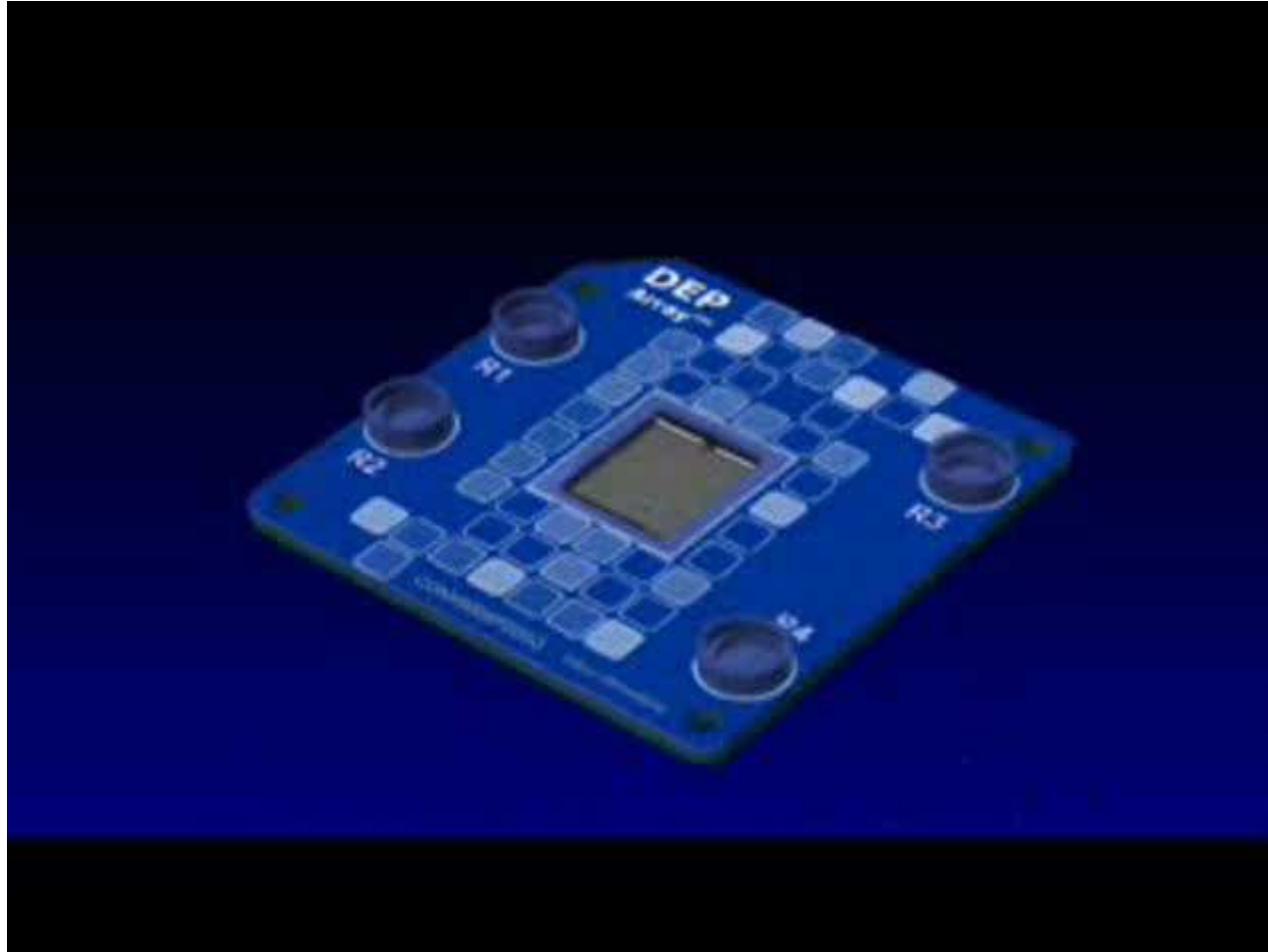
DEPArray™ Cell Sorting

Silicon Biosystems Patented Technology: Moving DEP Cages

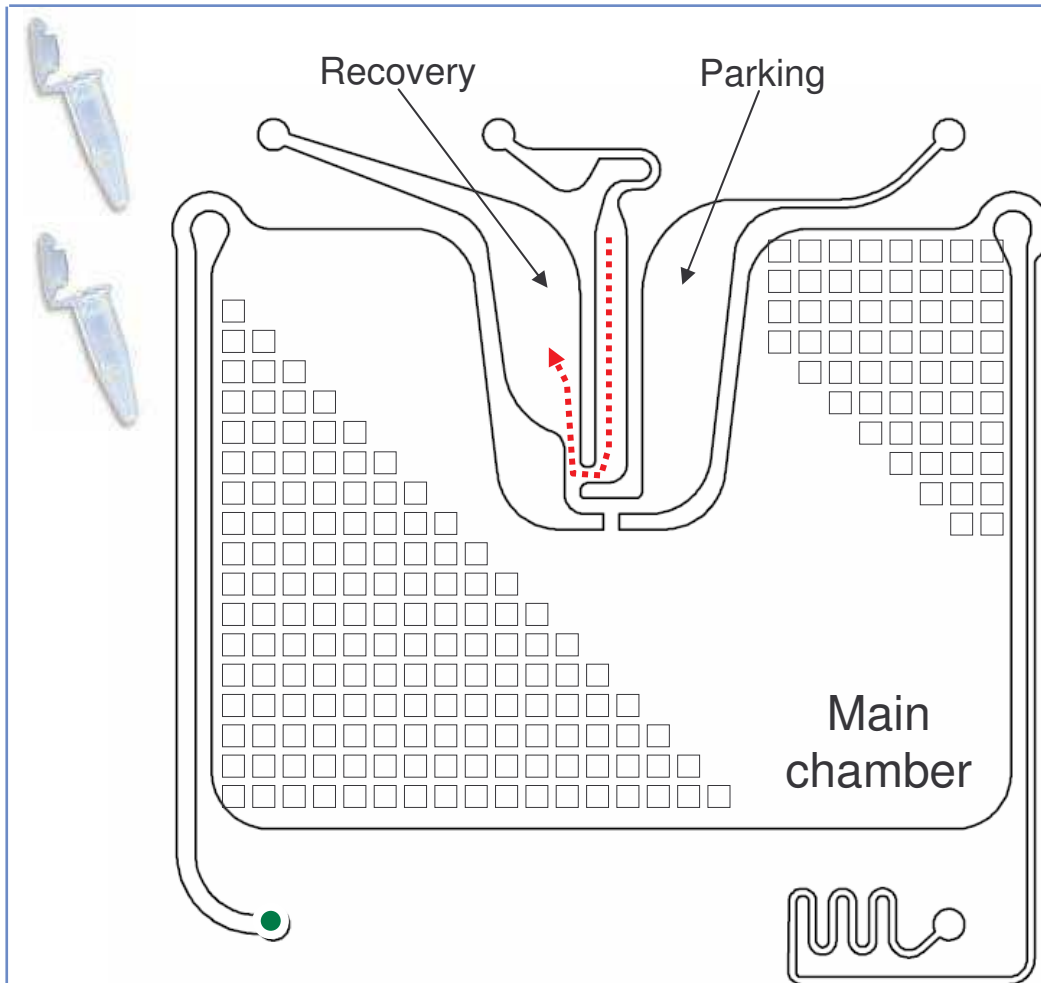
Cell trapping by DEP cages
Non-uniform electric field generated by the chip
electrodes (cross section)
cage-move



Sorting of Fluorescent Cells with DEPArray™



Moving DEP Cages Enables Outstanding Performance in Single-Cell Sorting

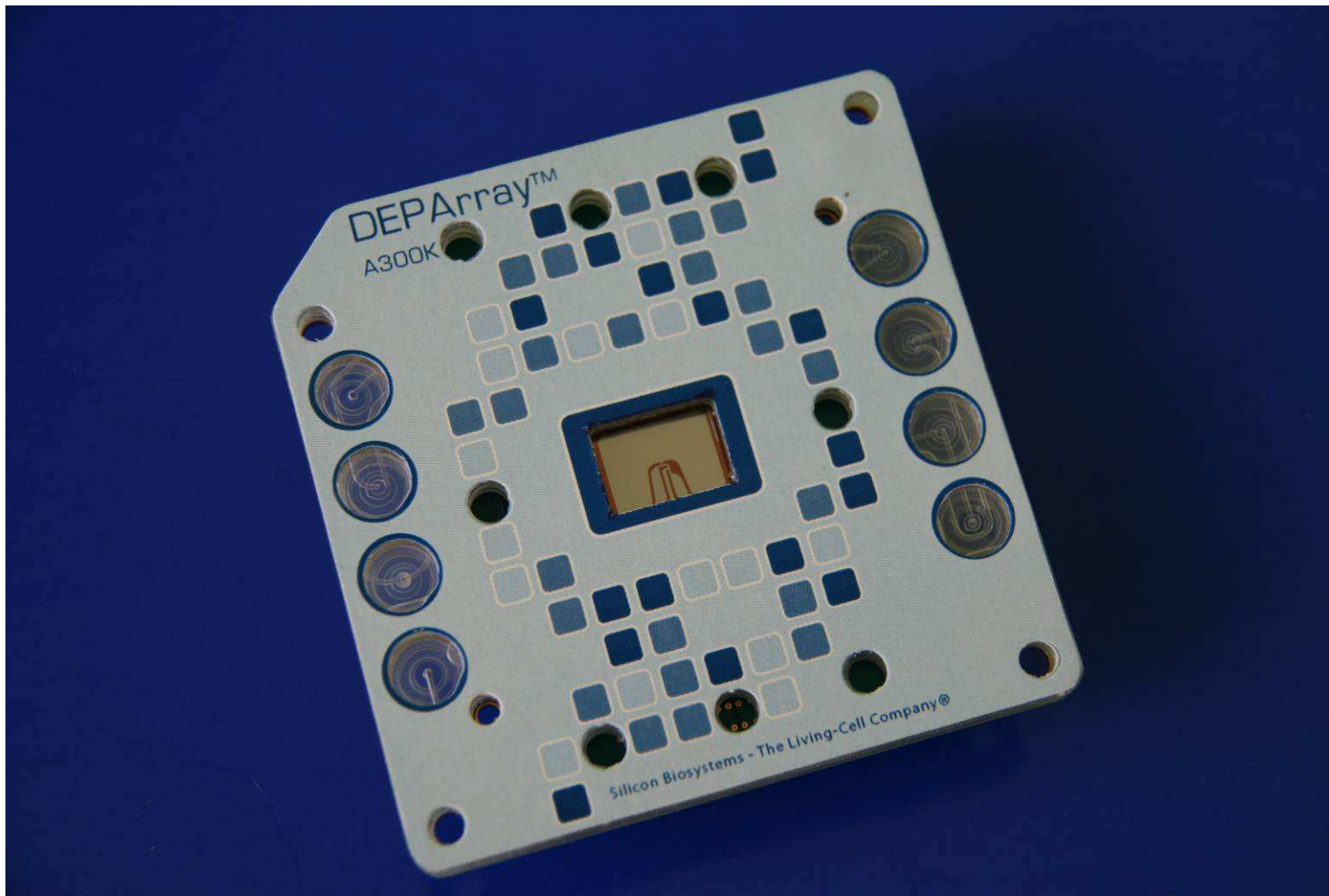


1. Inject, trap and image all cells
2. Move all cells of interest into Parking chamber
3. Move separately to Recovery chamber and flush

Features

- Multiparametric image-based sorting
- Single cell resolution
- Small cell loads
- Gentle on cells
- No a priori thresholds → choose *best* cells
- Sorting based on slow kinetics (10-100s minutes) possible

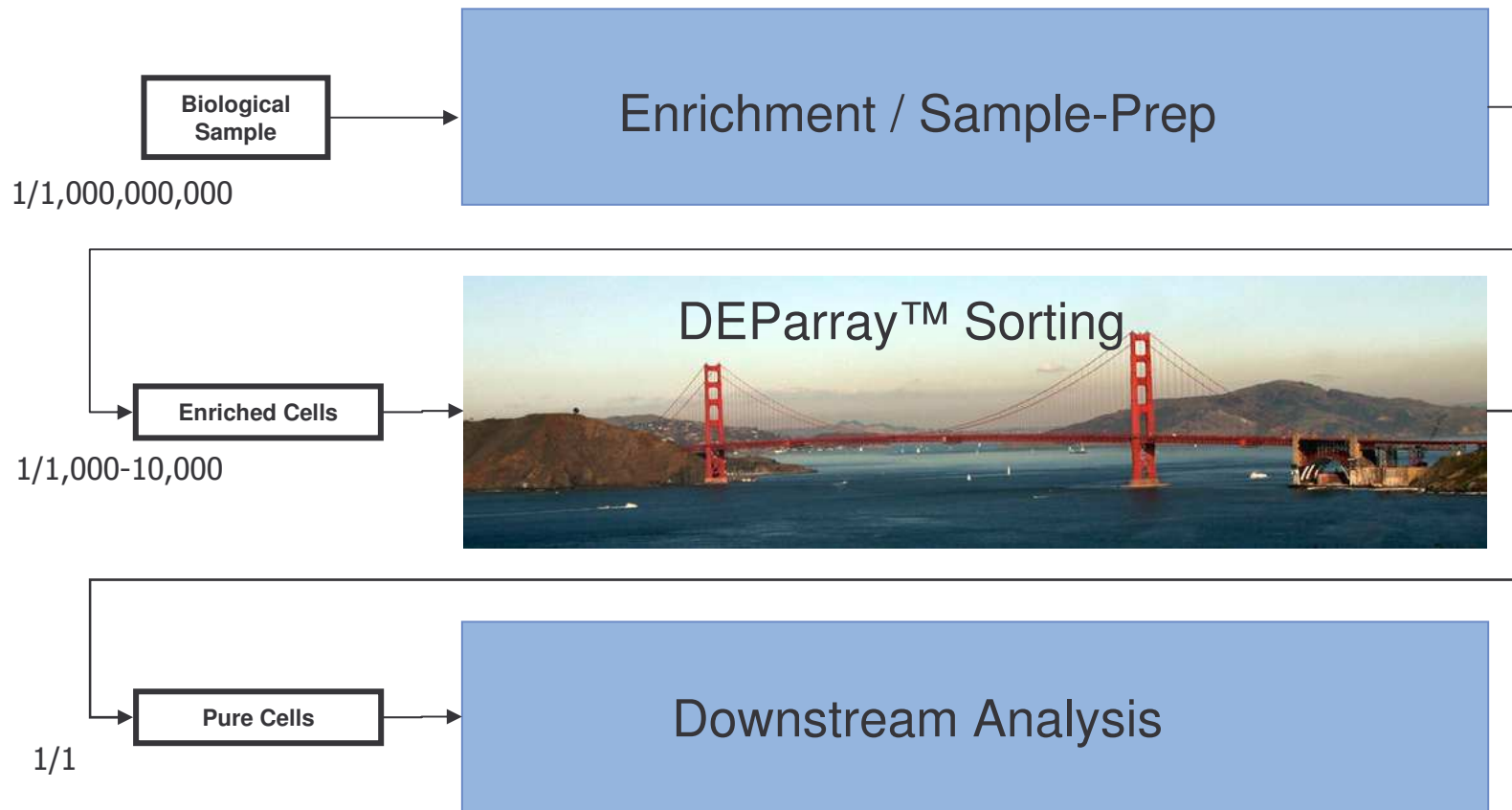
Individual Cell Sorting with DEPArray™ A300K



Click on image to start movie

DEPArray™ is the *Last Mile* for Automatic Rare-Cells Sorting in High-Value Applications

We bridge the gap between enrichment and single-cell analysis



Targeting Unmet Medical Needs with DEPArray™

- Oncology: Circulating Tumor Cells Isolation
 - From prognosis (based on enumeration of CTC) to personalized therapy (based on isolation of CTC)

- Prenatal Diagnosis: Circulating Fetal Cells Isolation
 - From Amniocentesis and Villocentesis to Non-Invasive Prenatal Diagnosis (based on Circulating Fetal Cells)

- Life-Science Research
 - Stem-cells
 - Immunology
 - Single-cell biology

Cancer Personalized Therapy

with DEPArray™

Rare, but Important: The Role of CTC in the Creation of Metastasis

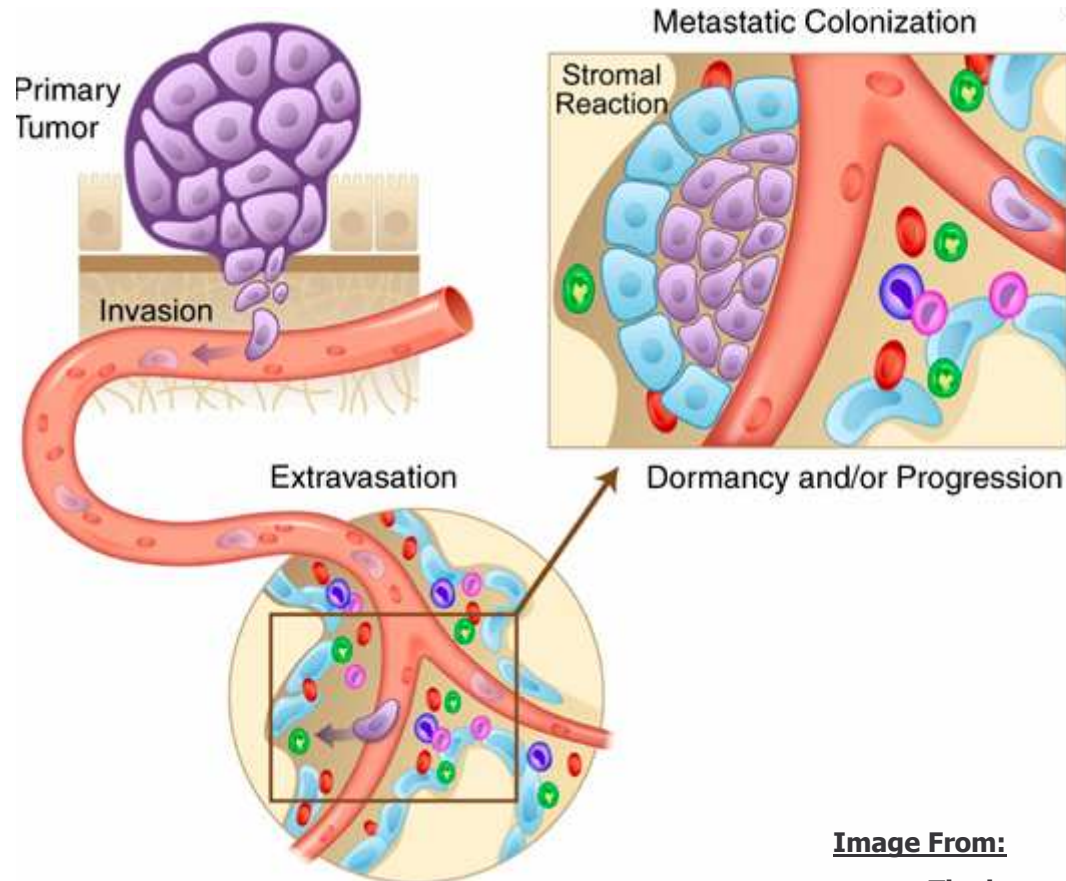


Image From:

The bone marrow niche: habitat to hematopoietic and mesenchymal stem cells, and unwitting host to molecular parasites

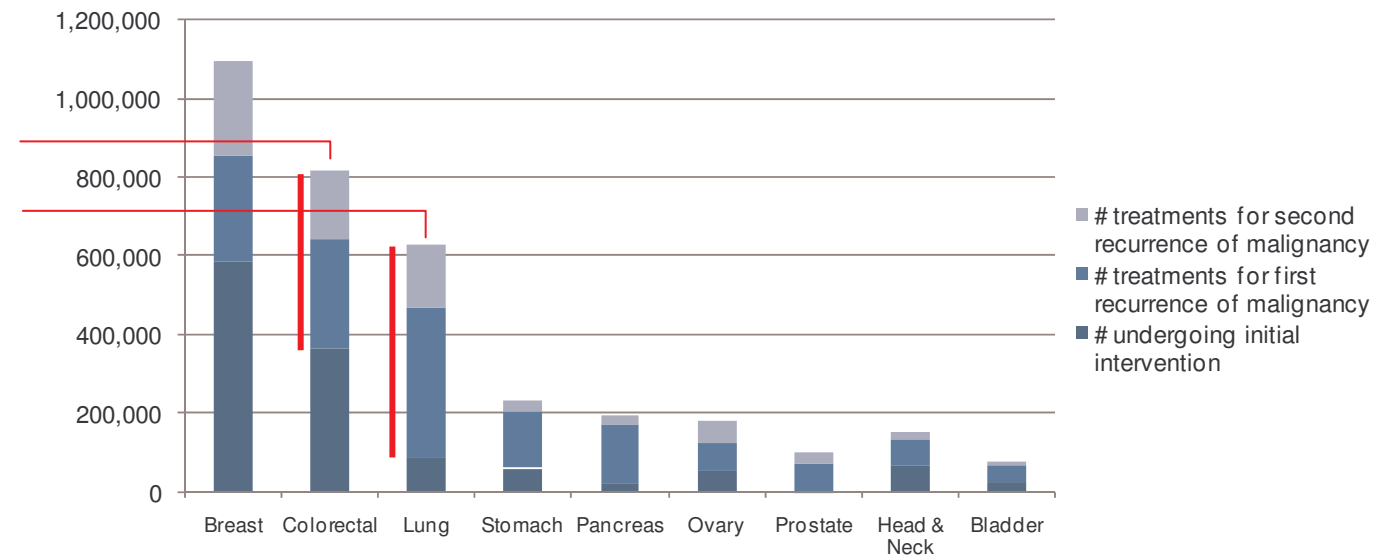
Y Shiozawa, A M Havens, K J Pienta and R S Taichman

Personalized Oncology Treatment: genetic detection to identify addressable patients

- Silicon Biosystems tests for genetic profiling enables to determine effectiveness and allows targeting of treatment
 - Cell growth inhibitor treatment is fastest growing class of cancer drugs from \$9.5bn in 2005 to \$22bn in 2010 at a CAGR of 18%
 - Cell growth inhibitor treatment is expensive (monthly cost ranging from \$3,000 to \$10,000), with significant side-effects

Annual courses of treatment EU, US, Japan by type of cancer

Colorectal and Lung represent ca 1m courses of treatment requiring monitoring each year



CTC genetic profiling: dramatic improvement in patient life



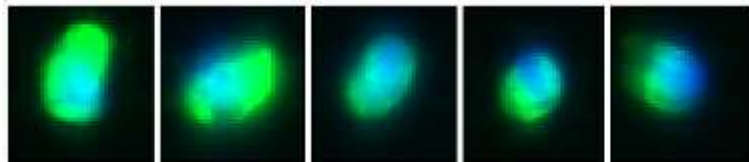
A market paradigm switch:
from prognosis
to personalized therapy

CTC molecular analysis allows
selection of most effective
drugs

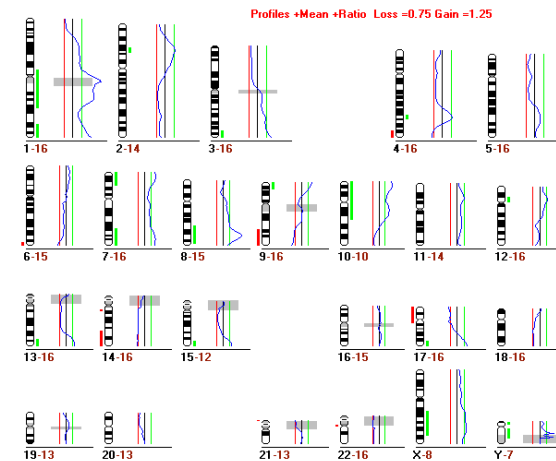
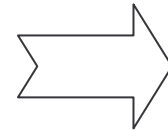
- Longer & Better life for patient
- Cost saving for healthcare system

DEPArray™ Enables the Isolation of Circulating Tumor Cells and their Molecular Analysis

- Genome-wide detection of chromosomal unbalances

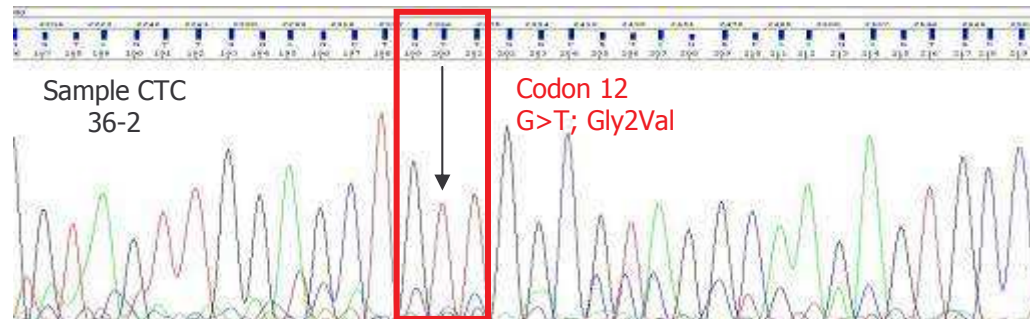


CTCs (CK-green/DAPI-blue) isolated with DEPArray™ from a metastatic breast cancer patient



- Detection of point mutations (e.g. KRAS)

CTCs isolated with DEPArray™ from a metastatic colorectal cancer patient



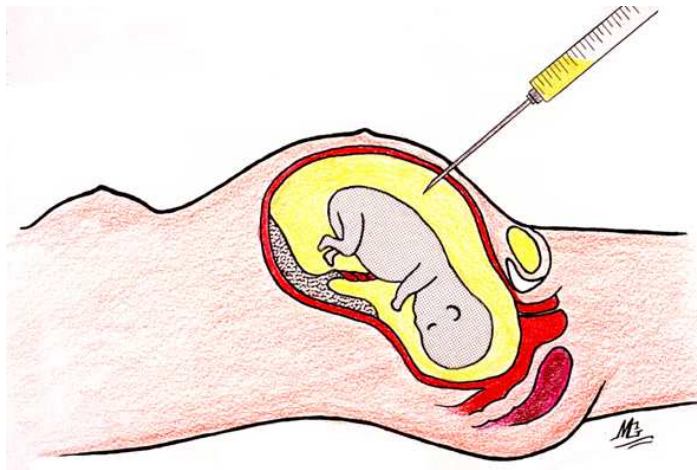
e.g. KRAS mutation testing is required to predict efficacy of treatment with Ceutximab or Panitumumab

Non Invasive Prenatal

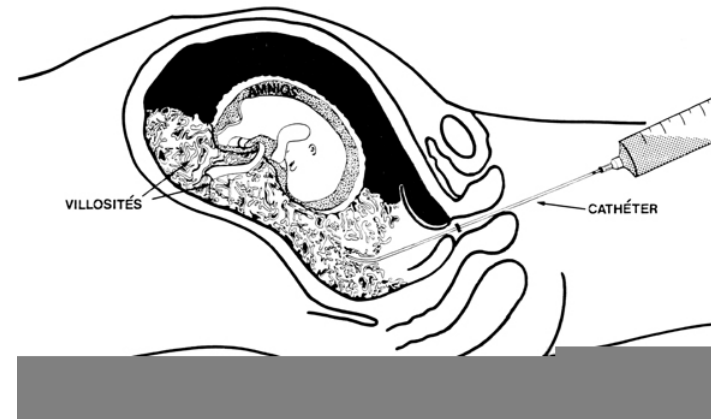
Diagnosis with DEPAarray™

Amniocentesis and chorionic villus sampling: high-risk of miscarriages and unpleasant procedures

Amniocentesis



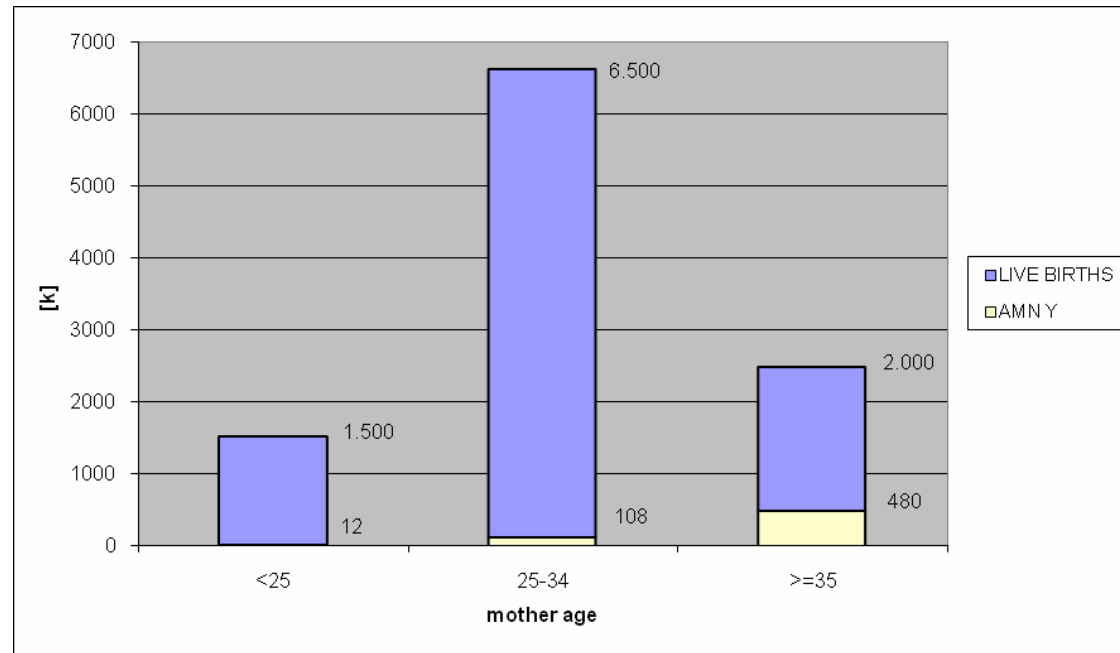
Chorionic Villus Sampling



Risk of fetal loss 0.5-1.5%

Mother's age	Risk	Need
20 years	1 in 1,600	Low
25 years	1 in 1,300	Medium
30 years	1 in 1,000	
35 years	1 in 365	High
40 years	1 in 90	
45 years	1 in 30	

Sizeable and highly predictable market for NIPD



2.0m high-risk pregnancies in EU, US and Japan, but only 24% adoption of amniocentesis test which has a risk of miscarriage

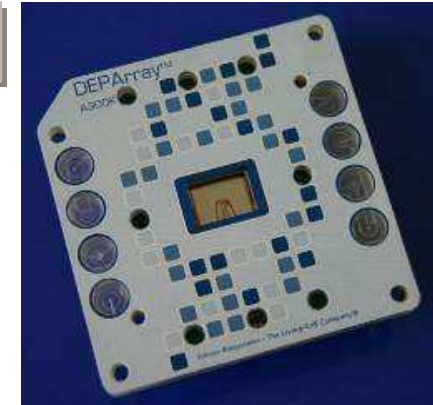
Partnership Network

DEPArray™ System

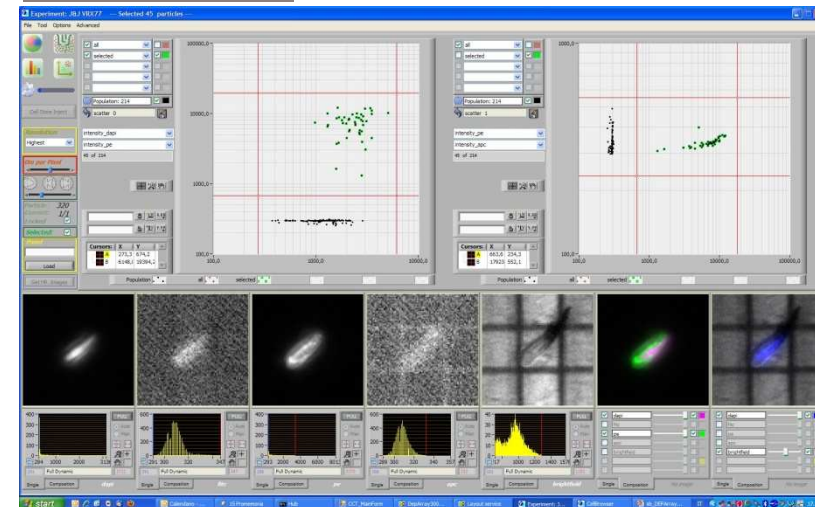
Equipment



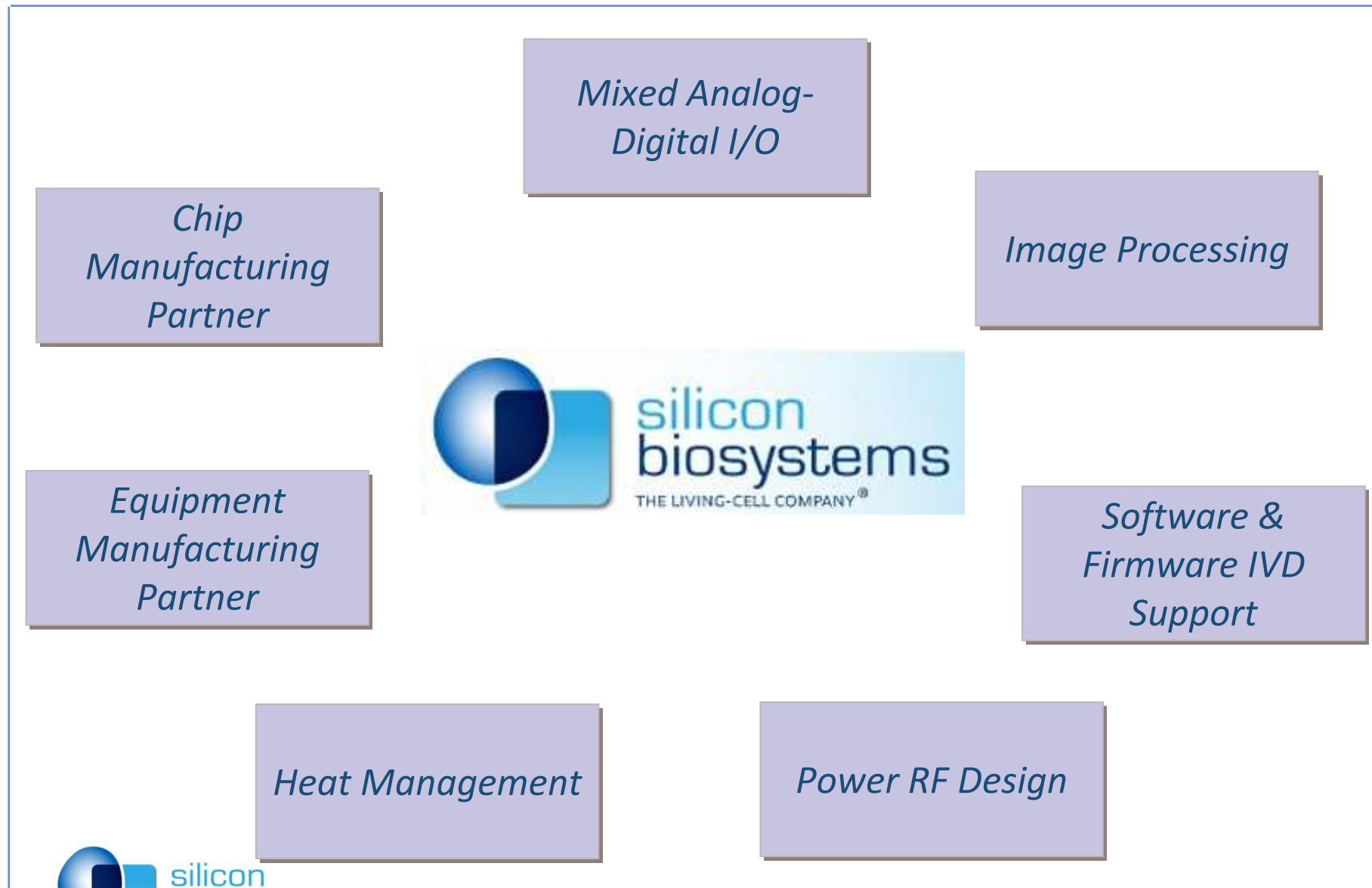
Lab-on-a-Chip



Software



Network of Competences



Network of Competences



*Chip
Manufacturing
Partner*



*Equipment
Manufacturing
Partner*

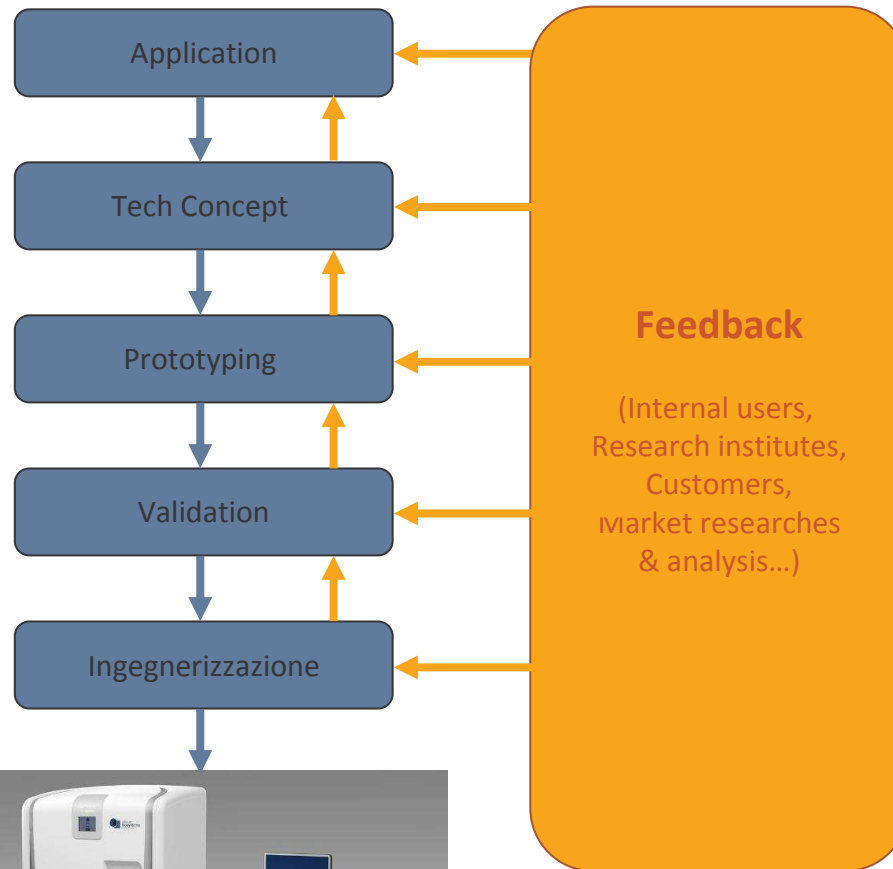


Heat Management

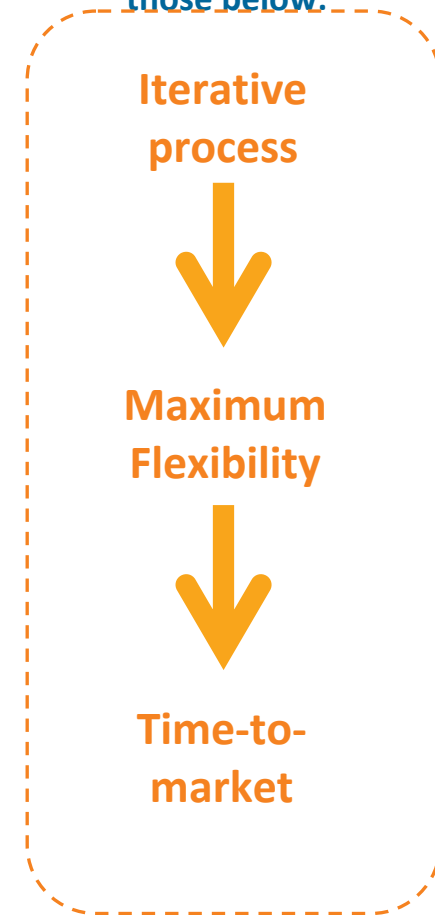
Power RF Design



Partnership goals



Partnership had to address all arisen necessities, especially those below:



Needs

- Flexibility
- Time-to-market
- Proven success (on specific items)
- Qualified support
- Future development support
- Robustness
- Maintainability

Why NI - 1

- Worldwide player
 - Products wide choice ('Time-to-market', 'Support')
 - Ease of integration (HW with SW) ('Time-to-Market', 'Flexibility')
 - Local & central branches ('Support')

- Corporate support
 - R&D - upon agreement ('Support')
 - Product Development ('Future development')

- Alliance Partner Network
 - Services Firm ('Support', 'Robustness')
 - Integrators ('Support', 'Robustness')

- Large Libraries Collection ('Time-to-market', 'Support', 'Robustness')

- Long-Term Support ('Maintenability' (& Evolution as well))

- LabVIEW real-time ('Robustness')

Why NI - 2

- Try-'n'-buy operation ('Time-to-Market', 'Support' (NI Italy+corporate))

- Openness
 - Integration with Silicon Biosystems proprietary service infrastructure ('Time-to-Market', 'Robustness')
 - Integration with third-parties instrumentation drivers ('Time-to-Market')
 - Integration with third-parties imaging algorithmics ('Time-to-Market', 'Robustness')

- Wide COTS offering
 - Cost optimization path support ((near!) 'Future development') (FlexRIO?)
 - Runtime changes can be easily managed ('Flexibility', 'Time-to-market')

- Certified/Supported COTS
 - Widely used COTS as a facilitating element in regulated markets certification achievement ('Support', 'Robustness')

In our experience, NI is a dynamic reality putting much attention on market evolutions, interested in supporting strategic partnerships.

Conclusions

- Technically: an outstanding exercise!
 - The machine involves knowledge and requirements necessitating many different aspects and corresponding knowledge
- Ethically: biomedical devices are of undiscussed ethic value
 - Thinking in terms of machine intended use is a great motivational point
- But overall: great team work!
 - All involved parties have really pushed far beyond 'the usual'
 - Integration issues couldn't be surpassed without all actors strong involvement

...So, looking forward to next meeting to share with you future evolutions!

www.siliconbiosystems.com

www.ni.com/it

www.skytechnology.it
