Dispositivi biomedicali in medicina personalizzata

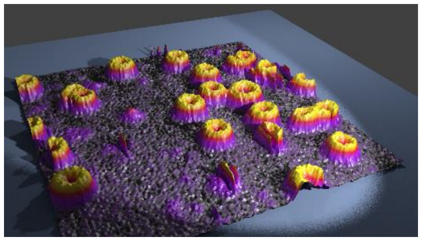
Cecilia Pederzolli
Fondazione Bruno Kessler
LaBSSAH Laboratory
cecilia.pederzolli@fbk.eu

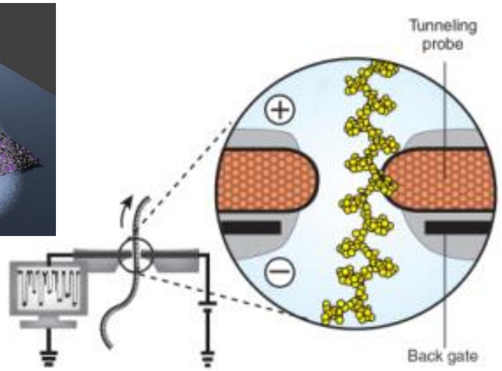
Laboratorio di sequenziamento e di analisi strutturale di biomolecole per la salute

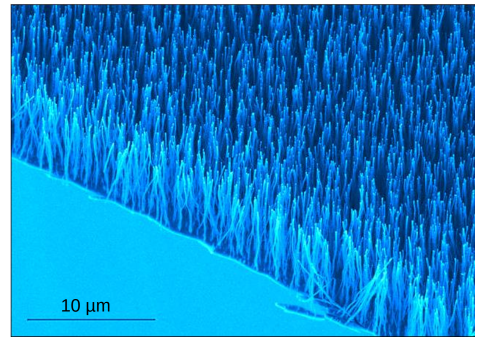
Tecnologie convergenti per la medicina del futuro (1)

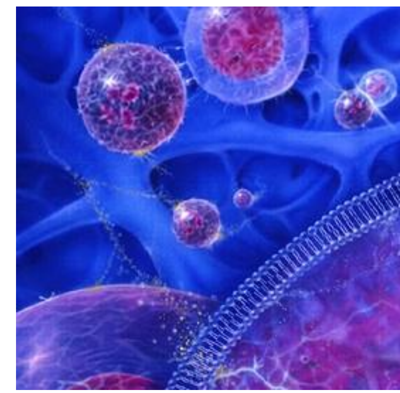
Approccio interdisciplinare

L'integrazione dei progressi scientifici e tecnologici di settori quali la biologia, la chimica, la fisica, l'ingegneria, l'informatica e la medicina.









Aumento della *<u>capacità di manipolazione della materia a livello molecolare</u>* alla base degli sviluppi nei settori della diagnostica, dell'analitica, della terapeutica e della strumentazione medica.

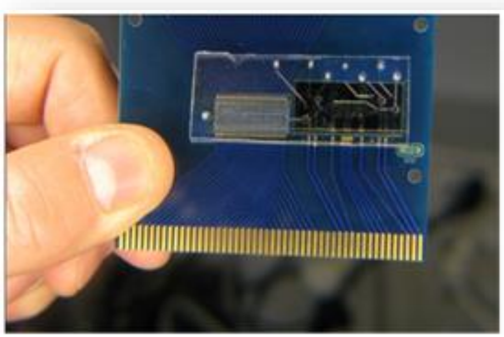
La rivoluzione della medicina del terzo millennio, che sarà caratterizzata da una più accurata prevenzione, diagnosi e terapia delle malattie.

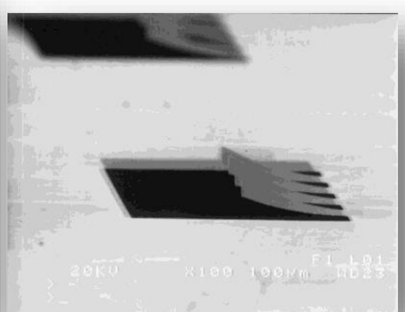
Tecnologie convergenti per la medicina del futuro (2)

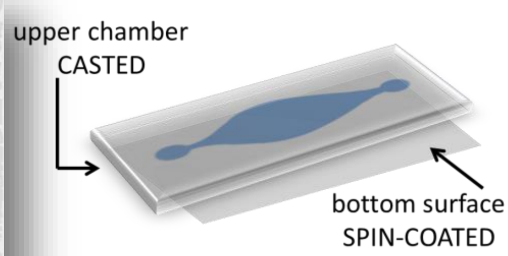
Approccio sistematico per progettare una medicina personalizzata

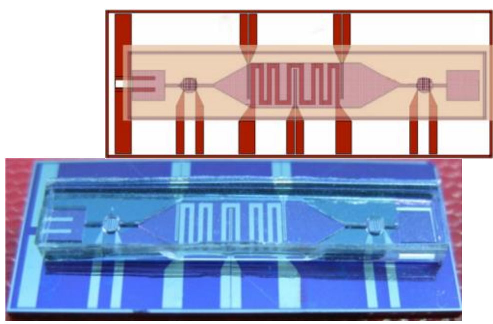
Ampio settore scientifico:
dalla diagnostica in vitro ed in vivo alla tecniche terapeutiche includendo targeted drug delivery e medicina rigenerativa, interfacciando nanomateriali (strutture, superfici, particelle, etc.) o strumenti analitici con sistemi umani (cellule, tessuti, etc.) all’imaging molecolare, al drug discovery su basi molecolari.

Grazie agli strumenti messi a disposizione è possibile da un lato, mettere a punto terapie che vadano ad agire a livello molecolare e dall’altro incrementare sempre di più la sensibilità e precisione dei metodi diagnostici per un’individuazione precoce delle malattie.









Micro e nanotecnologie per applicazioni biologiche e biomediche

Vantaggi rispetto alla macro-scala:

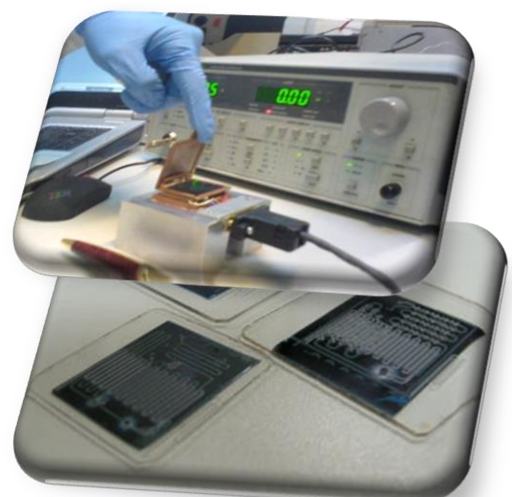
- minime quantità di campione e reagenti
- rapporto superficie/volume favorevole
- tempi di processamento ed analisi più veloci
- elevata sensibilità e riproducibilità
- elevata parallelizzazione (*high-throughput*)
- ridotti rischi di contaminazione
- possibilità di realizzare sistemi portatili

Nanotecnologie (nanomateriali, biointerfacce)

Microtecnologie microfluidica, fotonica e sensoristica

Microdispositivi per la diagnostica molecolare e la ricerca in **campo biomedicale**

Sistemi altamente integrati per la quantificazione di marcatori in fluidi biologici



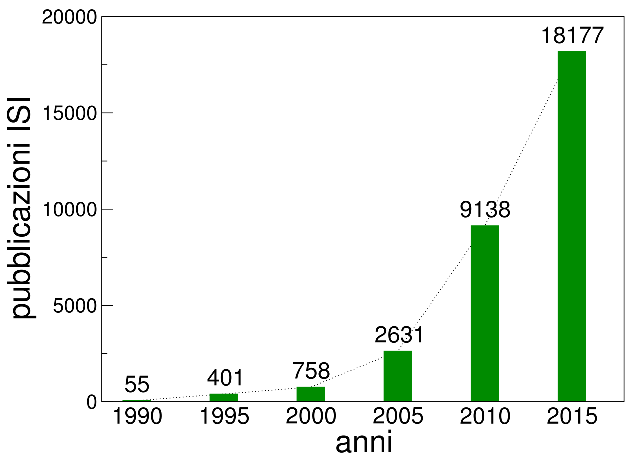
Sviluppo di materiali, dispositivi e sistemi per la comprensione della biologia cellulare e molecolare come anche per la rilevazione e la diagnosi di malattie.

Micro e nanotecnologie per applicazioni biologiche e biomediche

articoli su biomarcatori

dal 1990 - ora: 126401

WEB OF SCIENCE



a) enormi potenzialità per lo sviluppo di test efficienti su array di biomarcatori

ma

b) barriere da superare

1) **Integrating** lab-on-a-chip (LOC) systems into point-of-care (POC) structures that completely replicate the full functionality provided in remote laboratory settings;

2) Failure of current LOC systems to **compete with remote testing**, both from cost as well as performance perspectives;

3) LOC systems' need to **develop new conten**t that is unavailable at remote labs; and

4) Insights into multiple phases of **regulatory approva**l that has traditionally taken decades to complete.

McDevitt et al., J Biosens Bioelectron 2015, 6:2

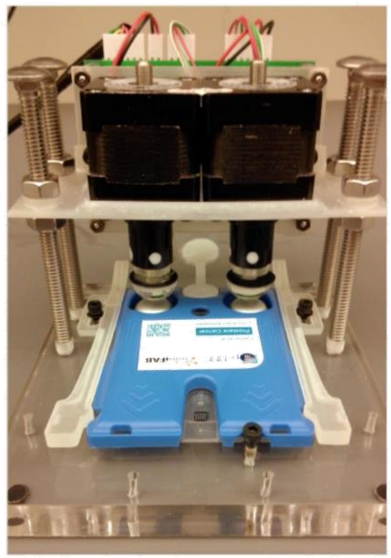
Sviluppo di un Sistema Completo

Esempio: lo sviluppo di un sistema (1)

Prof. John McDevitt
Rice University – NY University USA

PATHWAY TO ANALYZER

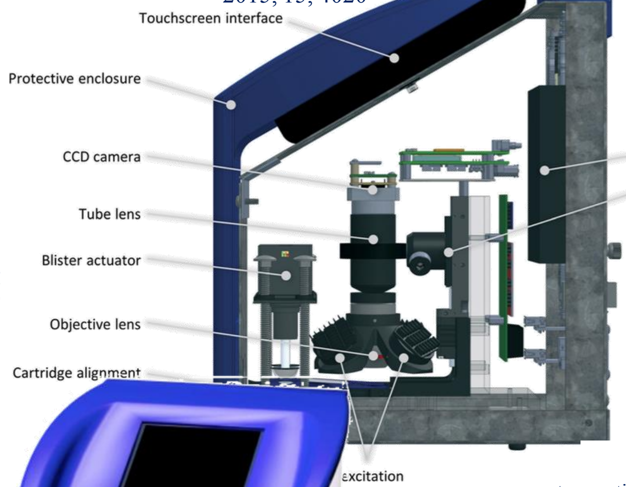
Syringe pumps + Microscope
- External fluid source
- Inefficient use of space
- Semi-automated
- “Chips-in-a-lab” 1



Blister + Mechanical Actuation
- Integrated concept

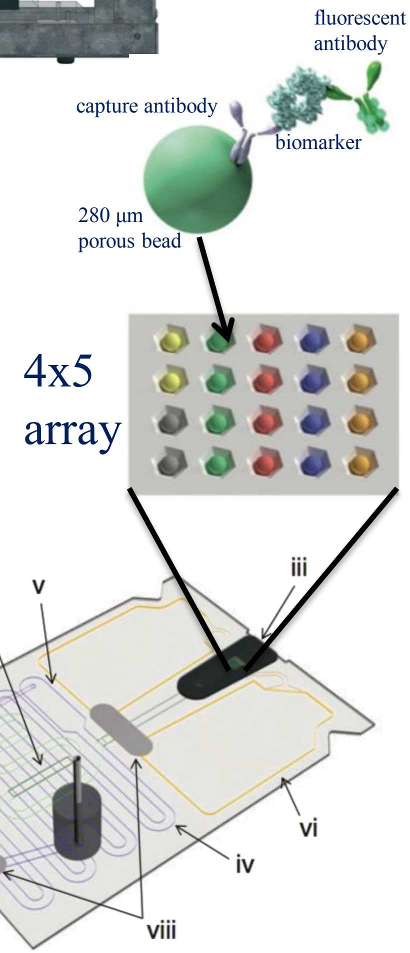
2

McRae et al., Lab Chip, 2015, 15, 4020



Analyzer
- Full solution

3



Shadfan et al., Cancer Prev Res 2015;8:37-48

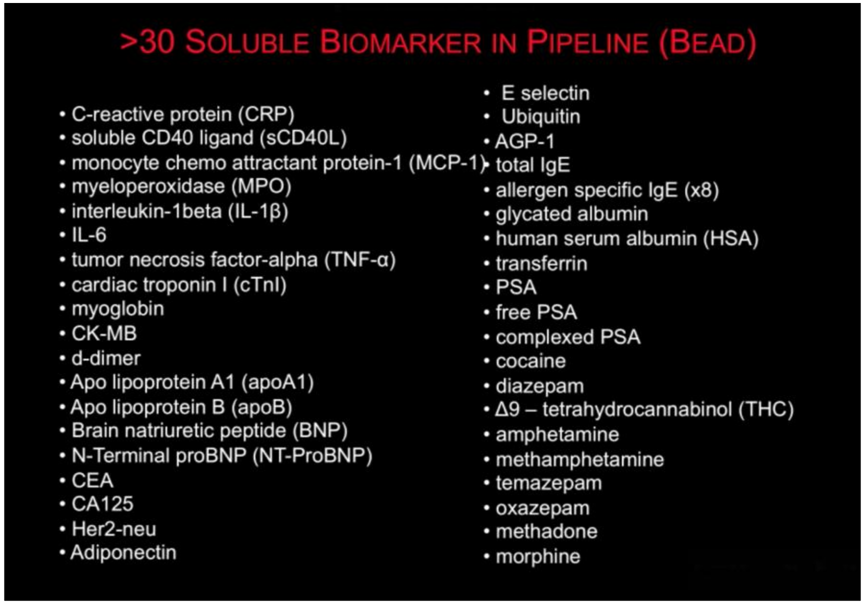
adattato da McDevitt

Esempio: lo sviluppo di un sistema (2)

Trials clinici

Study	Sponsor	Area	# of subjects	Clinical Site	Bio-markers
Development of A Lab-on-a-Chip System for Saliva-Based Diagnostics	National Institute of Dental and Craniofacial Research (NIDCR)	Cardiac Disease	1,000 patients	Baylor College of Medicine	15 proteins
Advanced Bio-Nano-Chips for Saliva-Based Drug Tests at the Point of Arrest	Home Office-Center of Applied Science and Technology (HO-CAST)	Drugs of Abuse	240 participants	Baylor College of Medicine	12 drugs
Texas Cancer Diagnostics Pipeline Consortium	Cancer Prevention Research Institute of Texas (CPRIT)	Ovarian Cancer	1,250 patients	MD Anderson Cancer Center	4 proteins
	Cancer Prevention Research Institute of Texas (CPRIT)	Prostate Cancer	400 patients	UT Health Science Center-San Antonio	3 proteins
Pilot and Prospective Studies for the Development of the Trauma Chip	Texas Emerging Technology Fund	Acute Kidney Failure	120 patients	UT Health Science Center-Houston	3 proteins
Development of p-BNCs for the Monitoring of Anti-Epilepsy Drugs Levels in Saliva	John S. Dunn Foundation	Epilepsy	100 patients	UT Health Science Center-Houston	3 proteins

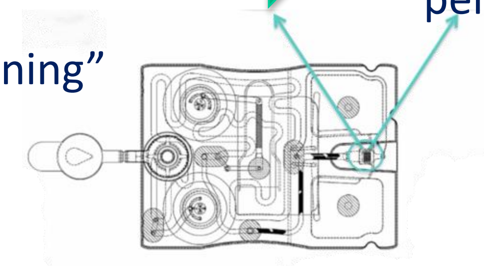
McDevitt et al., J Biosens Bioelectron 2015, 6:2



Esempio: lo sviluppo di un sistema (3)

Combinazione di:
- ✓ nanomateriali
- ✓ microelettronica
- ✓ algoritmi di "machine-learning"

1 singolo indice per ogni malattia



McDevitt et al., J Biosens Bioelectron 2015, 6:2

McRae et al., Lab Chip, 2015, 15, 4020

migliorativo rispetto a un test ELISA di laboratorio in termini di: tempo, limite di rivelazione, facilità nell'uso

Fasi principali dello sviluppo

- 10.7 M$ — Ricerca Clinica e di Base
- 22.0 M$ — Trials Clinici
- 1.4 M$ — Strumentazione

2000 — 2005 — 2010 — 2015

Una via alternativa: Sistemi a basso costo di realizzazione

Dispositivi analitici basati su carta – alcuni esempi

LaBSAH

Realizzazione di dispositivi semplici, portatili, monouso e convenienti

analytical chemistry

Article

pubs.acs.org/ac

Paper Electrochemical Device for Detection of DNA and Thrombin by Target-Induced Conformational Switching

Josephine C. Cunningham, Nicholas J. Brenes, and Richard M. Crooks*

Contents lists available at ScienceDirect

Biosensors and Bioelectronics

journal homepage: www.elsevier.com/locate/bios

ELSEVIER

Short communication

A paper strip based non-invasive glucose biosensor for salivary analysis

CrossMark

Anuradha Soni, Sandeep Kumar Jha*

Lab on a Chip

ROYAL SOCIETY OF CHEMISTRY

PAPER

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Cite this: *Lab Chip*, 2016, **16**, 112

Electroanalytical devices with pins and thread†

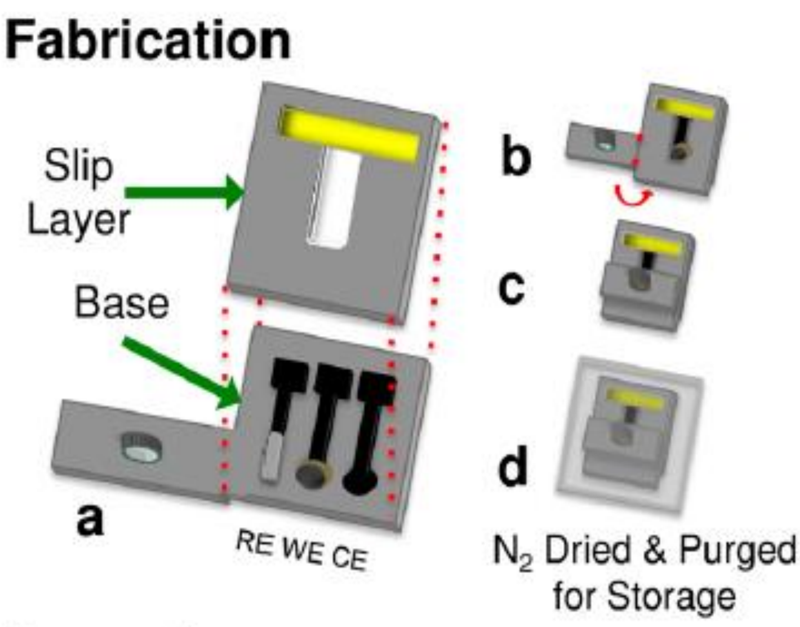
Ana C. Glavan,[a] Alar Ainla,[a] Mahiar M. Hamedi,[a] M. Teresa Fernández-Abedul*[ac] and George M. Whitesides*[ab]

Dispositivi analitici basati su carta (1): trombina, DNA

Cunningham et al.
Analitical Chemistry **86** (2014) 6166–6170

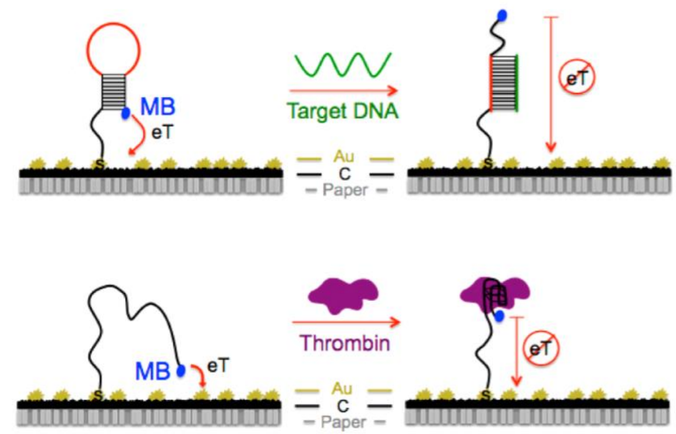
Biosensore per DNA e Trombina – rivelazione elettrochimica
Substrato in carta contiene molecole che cambiano di conformazione in seguito all'interazione con le molecole bersaglio – il sensore passa dallo stato attivo a quello inattivo

Limite rivelazione: trombina 16 nM, DNA 30 nM



Principio funzionamento

Aptamero legato a marcatore elettrochimico



sensore attivo
blu di metilene vicino alla superficie

sensore inattivo
blu di metilene lontano dalla superficie

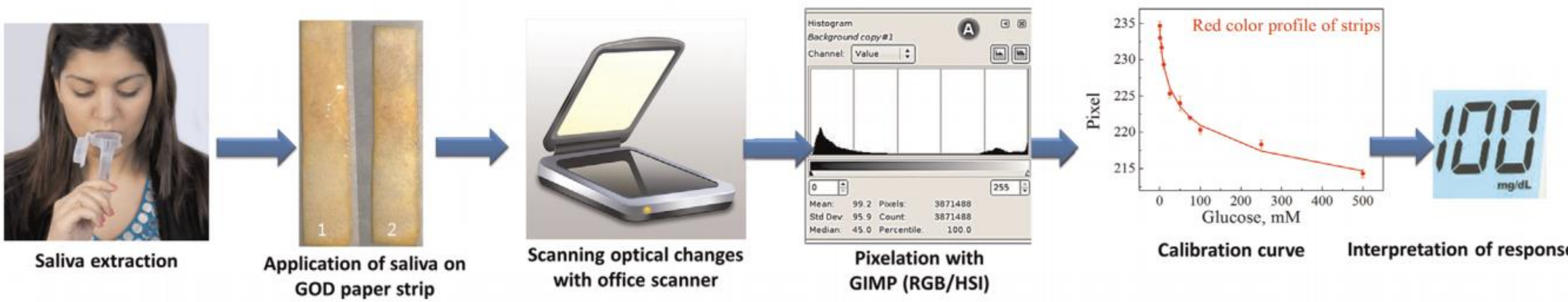
Dispositivi analitici basati su carta (2): glucosio

Anuradha Soni, Sandeep Kumar Jha
Biosensors and Bioelectronics **67** (2015) 763–768

Biosensore per glucosio nella saliva – rivelazione ottica

Un colorante sensibile al pH cambia colore in seguito ad una reazione enzimatica

La striscia di carta contiene l'enzima glucosio ossidasi – il risultato è acquisito con un normale scanner



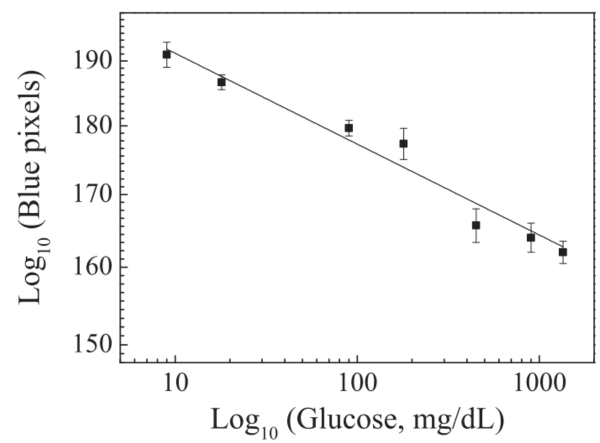
Sensore semplificato per diabetici

Basso costo

Semplice utilizzo

Tempo processamento 45 sec.

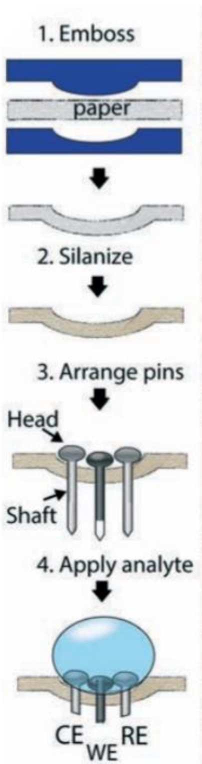
Volume campione 50µl



Dispositivi analitici basati su carta (3): lattato

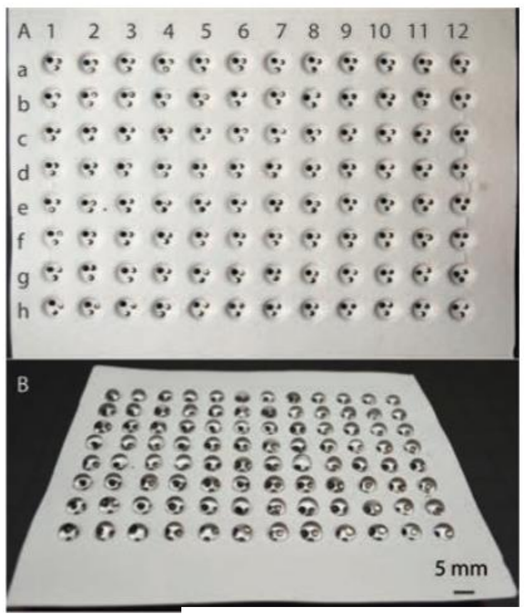
Ana C. Glavan et al.
Lab Chip **16** (2016), 112- 119

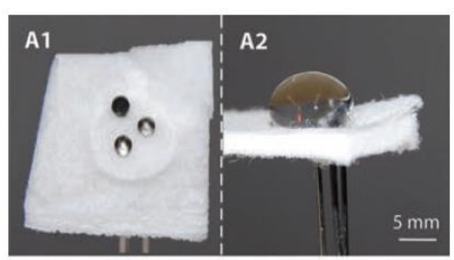
Biosensore elettrochimico – basato su carta trattata (idrofobica e oleofobica) e su spilli (3 per sensore, uno ricoperto di carbonio)

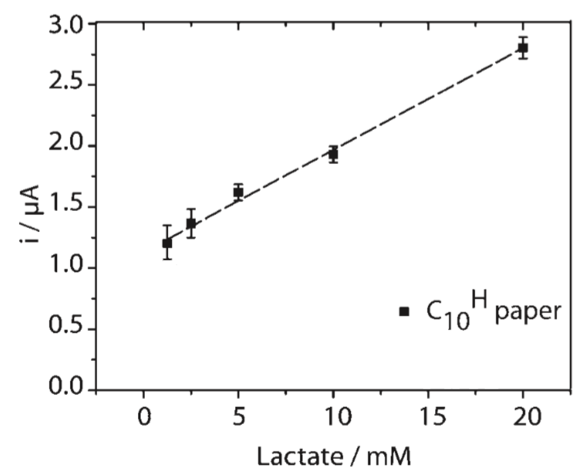


schema di un elettrodo su carta

array di 96 elettrodi







dimostrazione di funzionamento: rivelazione dell'l-lattato in siero umano

Micro e nanotecnologie per applicazioni biologiche e biomediche: l'esperienza del LaBSSAH

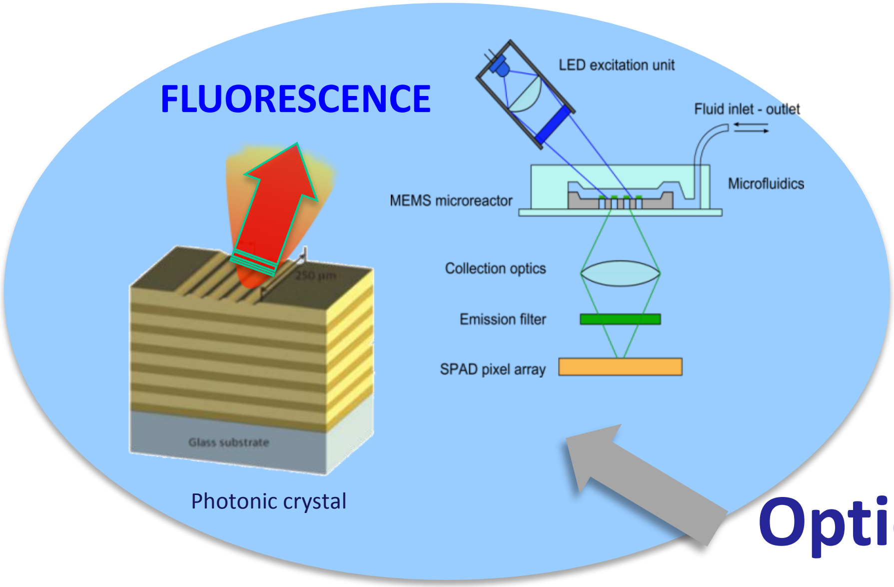
Employment of new methods for the functional analysis of patient samples

- DNA sequencing
- Nanobiotechnologies
- Cell biology
- Bioinformatics
- Start-up accelerator

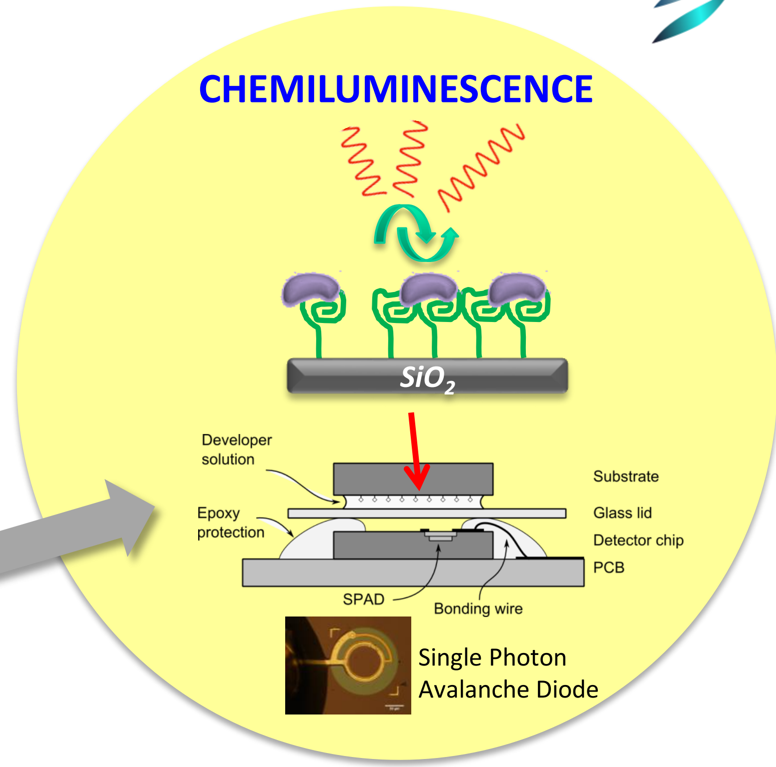
Personalised medicine

Fields of application: oncology, neurodegenerative diseases

Diagnosis through micro-nanotechnology (*optical sensors*)



Optical sensors

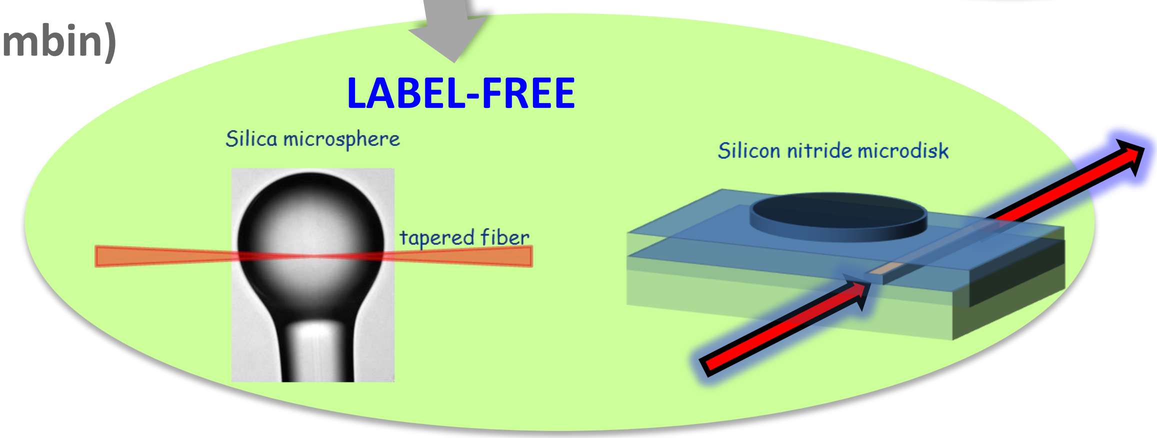


DETECTION OF:

Small molecules (aflatoxin)

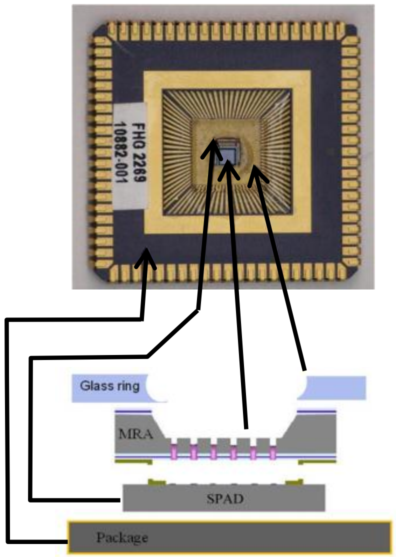
Proteins (VEGF, thrombin)

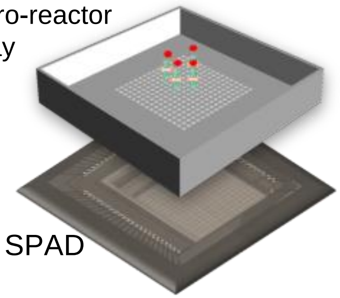
miRNAs



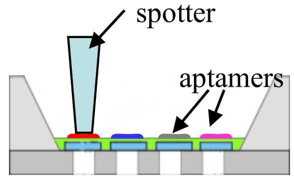
collaborazione con UNITN-Dip. Fisica, FBK-Centro Materiali e Microsistemi, CNR-IFAC Firenze , PoliTO

Protein Detection using a fluorescence approach based on SPAD detector

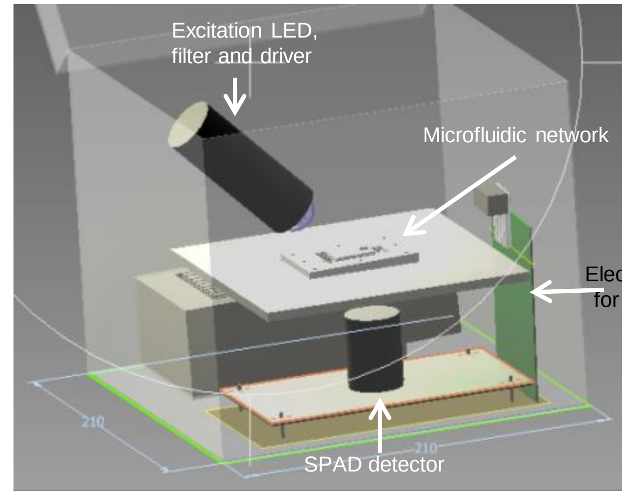




Specific DNA-aptamers are immobilized on functionalized micro-reactor array

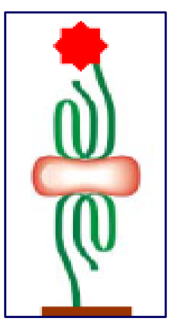


Integrated system



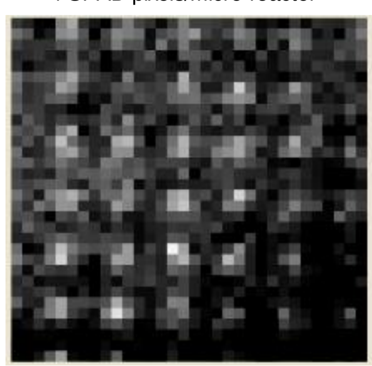
Two blood proteins are tested: Human Thrombin and Vascular Endothelial Growth Factor (VEGF)

A secondary fluorescent-labelled aptamers is used to detect the protein

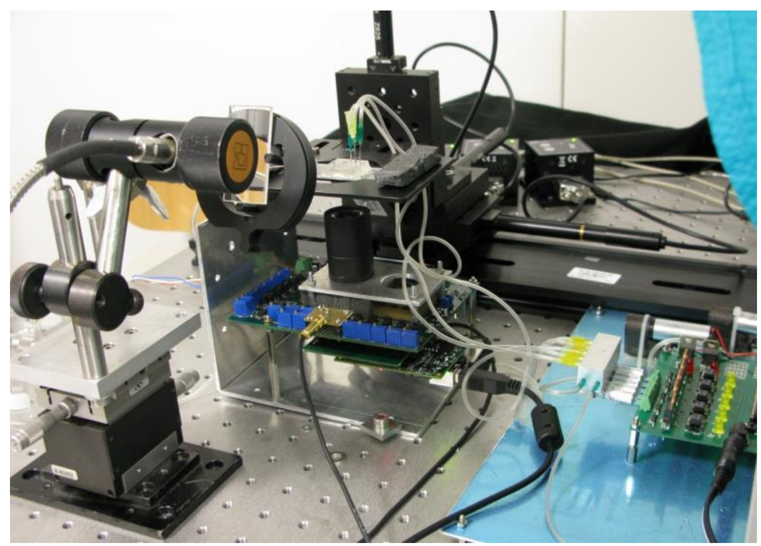


Thrombin analysis

256 micro-reactor array
4 SPAD pixels/micro-reactor



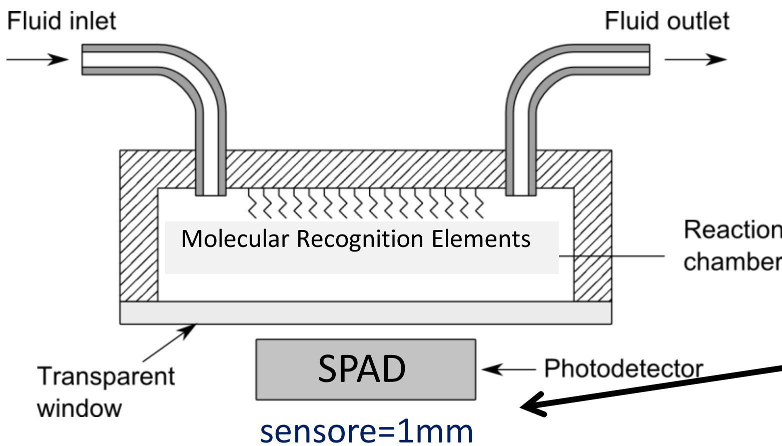
Thrombin concentration: 300nM
Total measurement time: 2.5 min

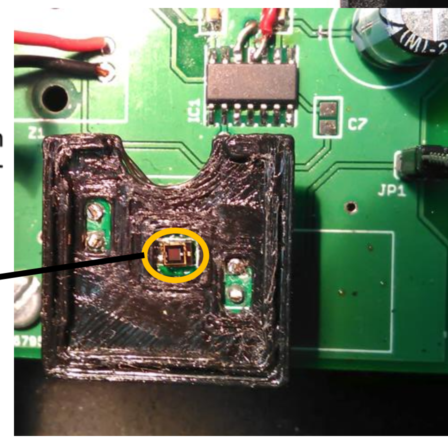


On bench fluorescence system setup

Chemiluminescence SPAD–based sensor for biomolecules detection

Schematic cross-section of the system





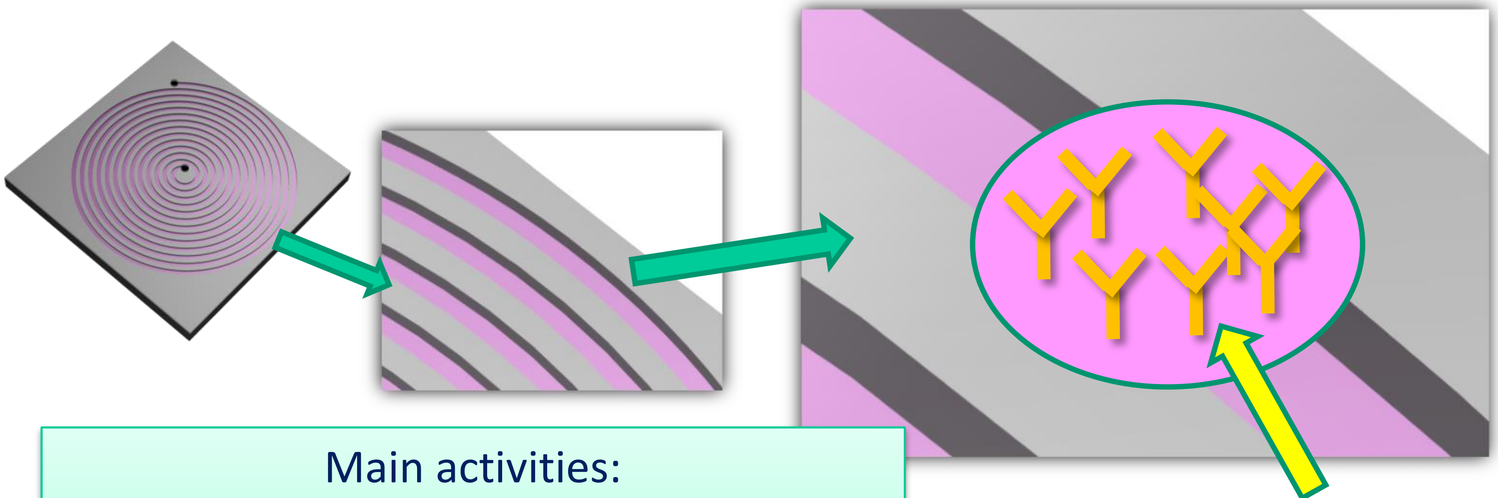
11 cm

- ✓ **High-performance, Single Photon Avalanche Diodes** (SPADs) developed by CMM-FBK in combination with a **chemiluminescence reaction** → **high sensitivity (pM)**.
- ✓ **No** external light source.
- ✓ SPAD detectors are **directly coupled** with the biorecognition layer → **no optical components** in the detection path.
- ✓ The biorecognition elements could be DNA-aptamers or antibodies, for an **increased flexibility** of the platform.

Miniaturized diagnostic assay for the specific detection of biomarkers physiologically present in minute quantity in a patient’s bloodstream or body fluid

Pasquardini et al. Biosensors and Bioelectronics (2015)
Patent pending n. 102016000031665 (25/03/2016)

Diagnosis through micro-nanotechnology (*molecular diagnostic*)

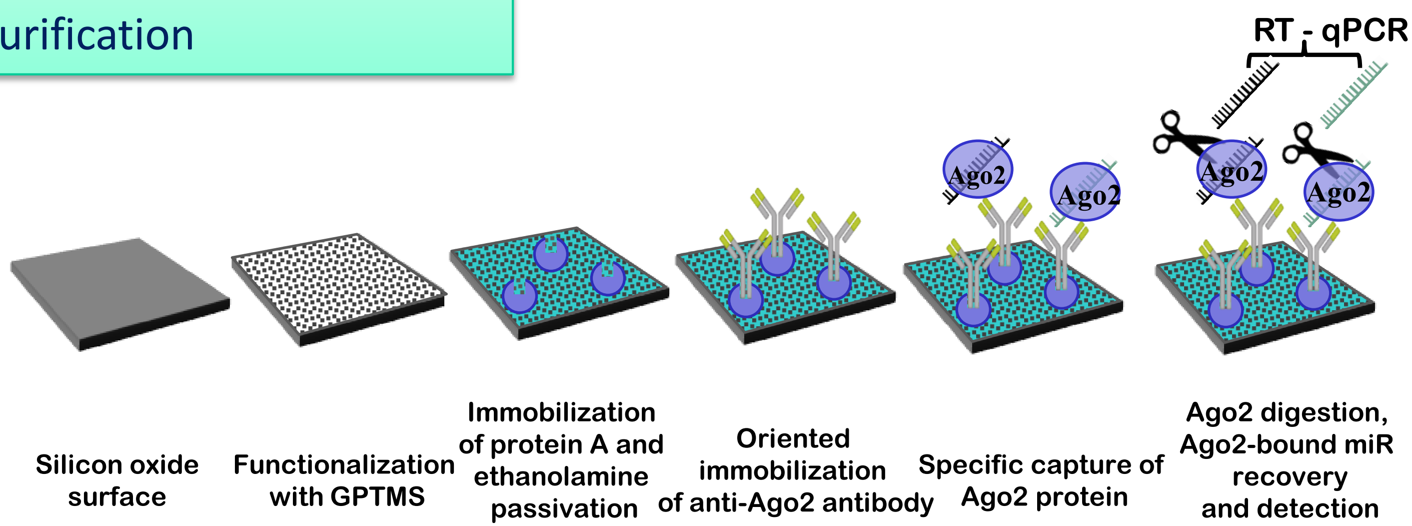


Faster and cheaper system, simple use, smaller samples, decentralized and non-invasive analysis

Main activities:

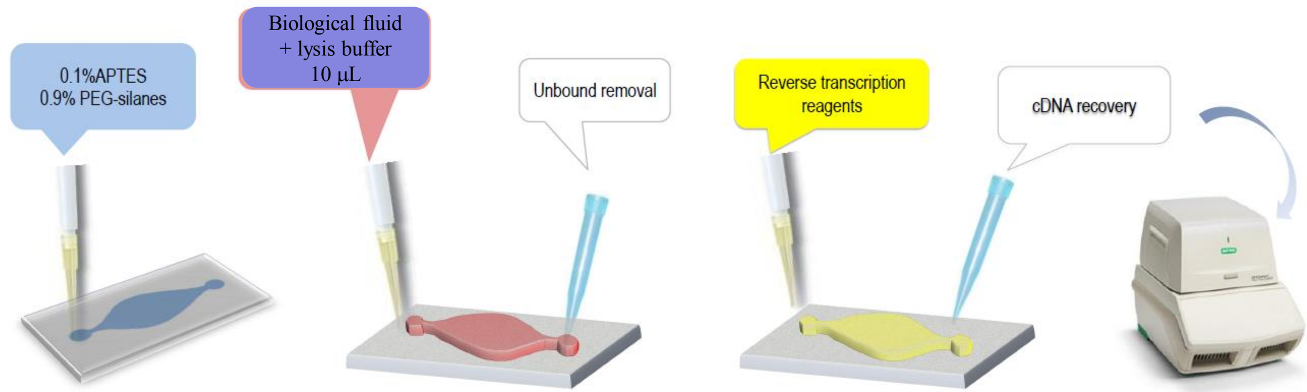
- On-chip nucleic acids purification from biological samples
- Cell vesicles purification

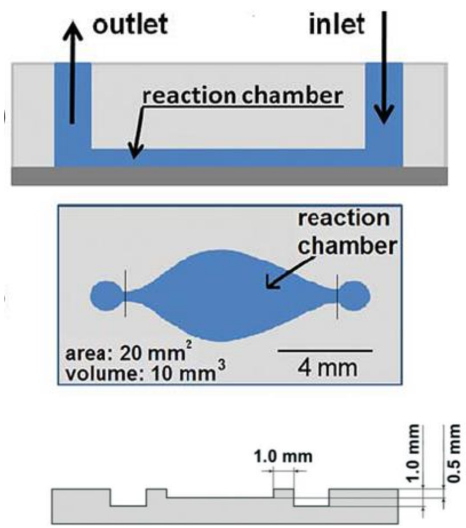
microliters– bioactive surfaces- detection



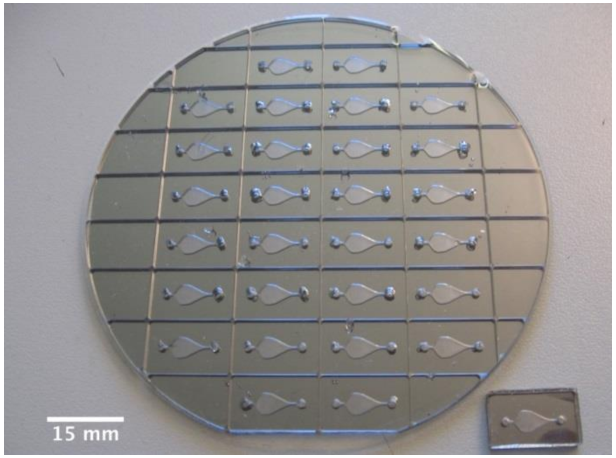
On-chip RNA purification and analysis

blood | 0 | | time scale (minutes) <120 | diagnose

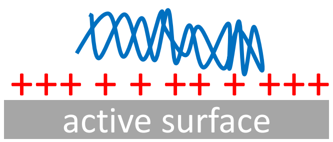




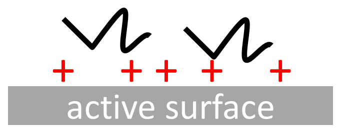
- ✓ selective extraction of circulating miRNAs starting from cell supernatants or plasma
- ✓ direct on-chip reverse transcription no detachment step required
- ✓ compatibility with real-time quantitative PCR and digital droplet PCR



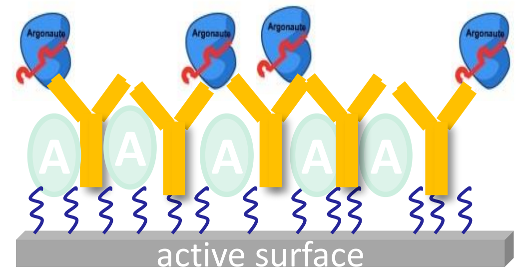
On-chip biomolecules purification from biological samples



DNA purification



RNA purification

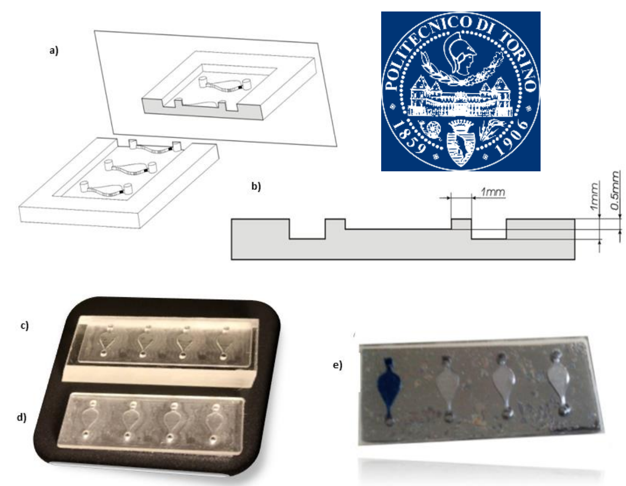


PROTEIN purification (e.g. AGO2)

applications

- Inherited diseases identification (hemochromatosis, deafness, taste markers, SNPs…)
- Pathogens identification (respiratory infections, *Salmonella*)
- meat contaminations (pork/beef/horse)

- Cancer biomarkers (specific microRNAs, e.g. miR-21) detection from cellular supernatant, human plasma and serum, cardiac biopsy
- Pathogens identification (Hepatitis C Virus)



Pasquardini et al. Appl Surf Sci. (2011); Pasquardini et al. Lab on a chip (2011); Potrich et al. Biomed Microdev. (2012); Potrich et al. BioNanoSci. (2013); Potrich et al., Lab on a chip (2014); Santini et al., Coll Surf B: Biointerfaces (2014); Vaghi et al., Biophys Chem. (2015); Frascella et al., Analyst (2015)

Povo, 24-09-2016

Ringraziamenti

FONDAZIONE BRUNO KESSLER
CMM
Center for Materials and Microsystems

Leandro Lorenzelli
Georg Pucker
David Stoppa

FONDAZIONE BRUNO KESSLER LaBSAH

Lorenzo Lunelli
Cristina Potrich
Gaia C. Santini
Valentina Vaghi
Lia Vanzetti

http://naomi.science.unitn.it/
NAoMI Project
Province of Trento "Great Projects 2006"

NEWTON project
www.nanonewton.it
MIUR FIRB 2010

UNIVERSITY OF TRENTO

Lorenzo Pavesi
Laura Pasquardini
Lucio Pancheri

Fabrizio C. Pirri
Matteo Cocuzza

Fondazione IRCCS Istituto Nazionale dei Tumori
via Venezian, 1 20133 Milano

Paola Tiberio
Maria Grazia Daidone

IFAC

Silvia Soria

UNIFE

Manuela Ferracin
Massimo Negrini

ISTITUTO DI CANDIOLO-IRCCS

Federico Bussolino