Project Number: 257401

A highly integrated and sensitive POrous SIlicon based lab on a chip for multiple quantitaTIVE monitoring of food allergies at point of care.

Specific Targeted Research Project

Information Society Technologies

Deliverable D11.17: Final Positive dissemination-kit with all promotional material / publications/presentations made by the project in raising public participation and awareness as well as involving actors other than the research community.

Due date of deliverable: **February 28th 2014**

Actual submission date: **May 21st 2014**

Start date of project: 2010-09-01 Duration: 3 ½ Years

Organisation name of lead contractor for this deliverable: **UVEG**

Revision **[1.0]**

Project co-funded by the European Commission within the Seventh Framework Programme		
Dissemination Level		
PU	Public	X
PP	Restricted to other programme participants (including the Commission Services)	
RE	Restricted to a group specified by the consortium (including the Commission Services)	
CO	Confidential, only for members of the consortium (including the Commission Services)	

1. About this deliverable

1.1. Introduction

This document reports on the final Positive dissemination kit which consists of an account of all dissemination activities that have taken place throughout the project along with examples of the promotional material used to do so.

1.2. Scope of the deliverable

The deliverable really just contains scans of all promotional material such as POSITIVE project leaflets/flyers/brochures, posters, videos, 2/3 slide presentation, newsletter created and used/distributed throughout the project as well as a list of the events where this occurred.

1.3. Structure of this deliverable

The report is laid out according to the tasks defined in WP11 as follows:

T11.2: Creation and distribution of promotional material such as POSITIVE project leaflets/flyers/brochures, posters, videos, 2/3 slide presentation, newsletter, etc., available for broader distribution at key events and through a regularly updated database of contacts (including newcomers registering through the web-site). Months: 1-42. (D11.2, D11.7, D11.12, D11.14, D11.17) (All partners)

Contents

2. Description of work performed

2.1. T11.2: Creation and distribution of promotional material such as POSITIVE project leaflets/flyers/brochures, posters, videos, 2/3 slide presentation, newsletter, etc., available for broader distribution at key events and through a regularly updated database of contacts (including newcomers registering through the web-site).

2.1.1. Dissemination activities

Key to content:

FY – Flyer	PO-Poster	PT- Presentation
NL – Newsletter	PR – Press release	OR - Other

2.1.1.1. Positive web-site

At the start of the project an interactive webpage, www.fp7positive.eu, was designed and published to allow world-wide knowledge of the activities and results of the project. From it promotional material could also be downloaded.

2.1.1.2. Dissemination events to other FP7 RTD projects

Table: Dissemination events to other FP7 RTD projects

Date	Event	Format
M4, 14, 27, 45	Positive Interest Group including The Europrevall, Ga2LEN and Nanospad consortia	NL
M3	Biophotonics cluster meeting presentation	PT, FY
M3	Photonics Open Day	PT, FY
M5	Interchange with coordinator of FP7 Mash project	OR
M8	EC MNBS Concertation meeting	PT, FY
M11	Silicon Photonics summer school organized by FP7 HELIOS and UKSP.	PO, FY
M18	CFBI organized meeting for Microfluidics Group	UVEG
M20	Interchange with FP7 FoodMicrosystems project	OR
M21	MNBS Concertation meeting	PO, FY
M25	ICT Proposers Day	FY, PO
M25	COWIN Market Place, Paris.	OR
M27	EC MNBS Concertation meeting	PT, PO
M37	EC MNBS Concertation meeting	PT, PO, FY
M39	EC-WS on Cross Key enabling technologies for Healthcare with presentation topics	FY

2.1.1.3. Press releases

Table: planned press releases.

Date	Press release content	Format
M4	Project start: http://www.kth.se/en/aktuellt/supersnabba-allergitest-snart-har-1.74636 http://www.kth.se/en/ees/omskolan/organisation/avdelningar/mst/news/quick-food-allergy-test-just-a-drop-of-blood-1.73580	PR
M4	Project start in the Farfield Periodical NewsLetter, Illuminations 14: http://www.farfield-group.com/pdfs/Newsletter_Issue_14.pdf	PR
M5	Farfield Group Press release:	PR

	Farfield Join Forces to Detect Hypersensitivity of Allergens http://www.farfield-group.com/readstory.asp?sid=113	
M7	Press release done through Euromediag diffusion list (http://www.eurobiomed.org/en/euromediag/) in which Phylogene is involved. Euromediag is a group of diagnostics actors inside Eurobiomed competitivity pole. Euromediag also initiated a EU meta-cluster which includes Euromediag (Eurobiomed-France), Wal-DX (Biowin-Belgium), Biocat (Barcelona, Spain), Kakow life Sciences cluster (Poland), Nexxus (Scotland- UK), OBN (Oxford, UK), Uppsala Bio (Uppsala - Sweden) and ZMDB (Berlin-Brandebourg - Germany).	PR
M7	Press-release through Almanacco della Scienza (http://www.almanacco.rm.cnr.it/reader/?MIval=cw_usr_view_articolo.html&id_articolo= 1753&id_rub=13&giornale=1760)	PR
M29	A press-release in M29 highlights the major technical achievements since the project began.	PR
M45	A press release announcing innovation developed within the whole project will be released at the end of M45.	PR

2.1.1.4. "Student days" and "Open days"

Table: Public events targeted for Positive dissemination

Date	Event	Format
M20	Positive open day at KTH in connection with the bi-annual Course Fair for the students	FY, PO
M21	Expociencia 2012	FY
M39	Medica 2013	PO
M19	Positive Students day	PO, FY
M7	Open day at UNITN. NL group disseminated POSITIVE related activities to undergraduate students that visited the Nanoscience research group laboratories	PO, FY
M18	Public dissemination event “Realizzazione di un sensore point-of-care in silicio poroso per analisi quantitative delle allergie alimentari”, 10 February 2012, City Hall of Levico Terme (Italy).	PT
M15	Nationaler Zukunftstag 2011, open day for students to visit CSEM’s facilities in Alpnach	FY
M18	Information day at CSEM for Executive MBA course from HSLU	PT, FY

2.1.1.5. Other dissemination events

Table: Other dissemination events

Date	Event	Format
M1	PECs IX	PO
M9	CLEO (Poster)	PO
M9	Therapeutics for personalized medicine	PT, FY
M9	26th International Symposium on MicroScale Bioseparations	PT
M9-10	EuroNanoForum	PO
M10-11	pHEALTH 2011	PT, FY
M10	Advances in microarray technology	PT
M11	UK FP7 ICT meeting	PT, FY
M12	Nanophotonics for sensing & nonlinear optics workshop	PO
M13	Swedish Medical Technology Days	PO
M14	Medica 2011	PO, FY
M14	NanoTech Italy 2011	PO, FY
M14	MicroTAS2011	PO, FY
M14	SSI-2012	PT
M17-18	MEMs 2012	PO
M18	CFBI organised meeting for Microfluidics Group	PT

M18	SPIE Photonics West	PT, FY
M19	European Lab-on-a-Chip Congress	PO
M19	Swedish MEMS conference (http://www.msw2012.org/),	PT
M19	PSST	PT
M20	Europtrode,	PO
M21	MNBS	PO, FY
M21	Euromediag Convention	PO
M21	Fotonica2012	PO
M25	Information on optical packaging technology for MCCS (Micro Center Central Switzerland, organization with 17 shareholders)	PT
M27	Medica 2012	PO, FY
M34	DPI User Meeting	FY
M30	Italian national conference	PT
M34	WaferBond '13	PO, FY
M37	Italian national conference	PT
M39	ASME	PT
M25	28th International Symposium on MicroScale Bioseparations and Analyses.	PT, FY
M26	IEEE Sensors 2012	PT
M31	AMT2013	PT
M33	Nanotech 2013	PO, FY
M32	SPIE Microtechnologies	PT
M34	IEEE Transducers	PT
M42	Swedish national conference MSW 2014	PO
M42	SPIE Photonics West	PT, FY

2.1.2. Promotional materials

2.1.2.1. Newsletters

POSITIVE NEWSLETTER 1: NEW PHOTONIC BIOSENSORS FOR THE FAST AND SAFE DETERMINATION OF SENSITIZATION TO MULTIPLE FOOD ALLERGENS

Six European research centres and two industry partners have joined in a new European research consortium called POSITIVE. The goal of POSITIVE is to develop new rapid and multi-assay diagnostics for determining sensitization to food allergens. The European Union supports the consortium during a three-year period with 2.9 MEuro through its Seventh Framework Programme.

Food allergies can provoke clinical reactions whose most severe is anaphylaxis, with respiratory and/or cardiovascular problems that might result in death. They are common in 1-2% of adults and up to 8% of children, corresponding to a serious public health problem that affects over **15 million people in Europe** from infants to the elderly and its prevalence is increasing.

POSITIVE will develop a diagnostic platform that can quickly and safely identify the sensitization of a patient to multiple food allergens so as to be able to proscribe a suitable diet and lifestyle. Ideally it will be a rapid system with little hands-on time, so as to be used at point of care (PoC) in an intensive care unit by paramedics.

The consortium will develop a state-of-the-art diagnostics Lab-on-a-Chip platform via an integrated microfluidic sample preparation technique capable of serum preparation from whole blood of volumes, <100µl. The detection will be based on ultrasensitive photonic biosensors that are integrated into the lab-on-chip device. A final prototype consisting of a packaged biochip and reader will be used on clinical samples in order to determine sensitization to allergens such as that for hen's eggs, cow's milk, peanuts, wheat, tree nuts, fish, sesame, and shrimp ingestion.

More information about POSITIVE and its partners can be found on the POSITIVE website http://www.positive.eu or in the attached project flyer.

ABOUT THE POSITIVE CONSORTIUM:

Positive project manager and main contact person:

Dr. Daniel Hill, UVEG – Universitat de Valencia (http://www.uv.es/umdo)

Other partners:

Royal Institute of Technology - Microsystem Technology Lab (http://www.ee.kth.se/mst)

Centre Suisse d'Electronique et de Microtechnique (http://www.csem.ch)

Farfield Group Ltd (http://www.farfield-scientific.com/)

Charite Universitaetsmedizin Berlin (http://www.charite.de)

Phylogene SA (http://www.phylogene.com)

Università degli Studi Di Trento (http://science.unitn.it/~semicon/)

Consiglio Nazionale Delle Ricerche (http://www.icrm.cnr.it)

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Highlights of technology developed in first 12 months:

The project is proceeding according to plan with all deliverables and milestones having been reached timely, these report on the following developed technology –

- We have defined the specifications of the final product, sample and sample treatment and project prototype. We have studied and written what could be the risks and defined specifications of some alternative solutions
- Construction and testing of temperature control unit and integration with fluidic cell enclosure from CSEM and software modification.
- Development of off-stoichiometry thiolene based sensor chip encapsulation
- Development of process for low temperature "click" wafer bonding of off-stoichiometry thiol-ene (OSTE) polymers to silicon
- Module developed for blood filtering
- Various microfluidic flow cells have been developed for device cartridges
- Development of models for birefringence in porous silicon membranes etched from (100) and (110) silicon for polarimeter and interferometer schemes
- Identification of depolarization causes in porous silicon membranes
- Bulk refractive index experiments have successfully been performed for porous silicon membranes

Partner feature:

Nanoscience Laboratory

Nanoscience Lab (NL) is a well-established research group with a strong focus on Silicon Photonics. The head of the lab, Prof. L. Pavesi, has provided a strong contribution to the development of the Si Photonics field, obtaining remarkable results in demonstrating the use of Si nanostructures in active photonic devices. The group is internationally renowned and actively collaborates in different research projects all centered in the core field of Silicon Photonics. NL has a number of activities focused in integrated photonics for ICT applications (integrated optical network, optical switching and routing) and optical sensing. Moreover NL has mastered the PS etching mechanism to experimentally demonstrate important phenomena such as optical analog of Bloch oscillations and Anderson light localization in extremely complex 1D photonic crystals composed of up to hundreds of layers. From its strong involvement in integrated photonic research, NL posseses advanced capabilities for modeling photonic structures modeling (in house developed codes, FDTD and PWE engines) and a dedicated cluster facility. NL has also demonstrated the use of advanced PS structures in sensing applications and fabricates highly sensitivity, multi-parametric gas sensors. More recently the group acquired a substantial background in PS surface functionalization and optimized different strategies to effectively stabilize PS surfaces.

Primary contact person

Dr. Paolo Bettotti
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Participants

Dr. Paolo Bettotti works as researcher at NL and has developed an electrochemical etching procedure to obtain high aspect ratio macroporous silicon from p-type substrates. His research interests are shared between integrated photonics for ICT and optical sensing application. The two fields share the common background of the integrated optical structures. He possesses an in depth knowledge of porous silicon (PS) fabrication that spans both nano and macroporous structures. Concerning PS he has focused his work on material applications: worked on PS functionalization techniques with rare earth and solgel material, demonstrated the use of PS as high sensitivity gas sensors and as a positronium source. He also possesses expertise about photonic structure modeling and material characterization with spectroscopic and microscopic (optical, electronical and scanning probe) techniques.

Porous Silicon membrane development feature:

In Positive the group provides its strong knowledge on the fabrication of complex porous silicon (PS) multilayers. Porous silicon (PS) membranes with different pore size and porosities have been fabricated on both p- and n-type substrates and particular attention given to microfluidics requirements. Different substrates have been investigated to optimize the porous structures so as to respect both optical and fluidics membranes properties. Porous free standing membranes are essential to achieve the ultimate goals in POSITIVE. They are fabricated from specifically chosen substrates and then distributed amongst the other project partners for their processing and/or analysis. A method to control the partial membrane detachment from the bulk supporting silicon substrate has been developed to permit the transport of the delicate membranes to other partners for their mounting on suitable supports. In order to achieve a stable device operation it has been necessary to reduce the high surface energy possessed by PS. Various passivation methods to stabilize PS surface have been developed: thermal treatment (to create a thin oxide layer over PS surface), and chemical reactions (such as silanization and hydrocarbonization) have been considered. All of these methods have demonstrated their usefulness in avoiding uncontrolled surface oxidation and a stable PS surface state and optical properties.

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POSITIVE NEWSLETTER 3: NOVEL SURFACE FUNCTIONALISATION CHEMISTRIES – SPECIFIC BIOSENSING FOR THE FAST AND SAFE DETERMINATION OF SENSITIZATION TO MULTIPLE FOOD ALLERGENS

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Highlights of technology developed in the second 12 months of Positive:

During the past 12 months many innovative technologies have been developed whilst we have been working towards the novel Positive platform. Through the ingenious use of a substitute membrane for biosensing the project has ended the year proceeding to plan if not slightly behind schedule which is not unusual in these types of projects. From protocols developed in the project state of art porous silicon for polarimetric biosensor purposes is being produced, independently of all other tasks for its later inclusion in the final device. We note:

- **Functionalised porous silicon membrane based sensor**
  - Protocols have been developed for high yield and reproducibility production of stable high quality free standing porous silicon membranes with tunable pore sizes (40-100 nm), controllable homogenous thickness (>3µm) and <15mm diameter.
  - Successful coating of porous membranes surfaces with a functional polymer.
  - Pores roughness has been greatly reduced increasing the optical birefringence by a factor of 50% and easing liquid flux.
  - Lowest limit of detection at 1500nm for detection of alcohols with different refractive indices was 6.25×10^{-6} RIU for porSi membranes prepared from (100) Si.
- **Polarimetric readout platform**
  - Real-time sensing volumetric and biosensing results with a throughput of one data point per second.
  - Study of the wavelength influence over the detection limit by using three different wavelengths: 808 nm, 980 nm and 1500 nm.
  - Detection limit for volumetric sensing the same order of magnitude for the three wavelengths studied but 980 nm is preferred for low cost detectors.
  - Salt injection experiments for porous alumina demonstrated a limit of detection of 2.7×10^{-6} RIU (@980 nm).
- **Biosensing**
  - Protein spotted and blocked functionalised alumina stored at 4ºC without desiccant shown to maintain protein activity for at least 4 months.
  - Protein physisorption of BSA on porous alumina demonstrated responses are proportional to concentrations.
  - Biosensing has been reproducibly seen when running a bioassay of primary IgG at different concentrations to porous alumina membranes with various surface chemistries followed by a secondary IgG.
- **Cartridge**
  - Components successfully designed and realized in Y1 (sensor chip, microfluidic flow cells, blood filter) have been implemented within a prototype semi-disposable cartridge.
  - The cartridge has been tested fluidically showing the basic functionality. Optimization of the design is ongoing.
- **Platform**
  - Components successfully designed and realized in Y1 (temperature control unit, flow control, vacuum pump, software control have been implemented within a breadboard instrument.
  - The platform has been tested fluidically with the cartridge showing the basic functionality of the platform with the cartridge. The cartridge has all fluids on-board and is actuated pneumatically through the instrument.
  - Based upon experimental results the optical instrumentation has recently undergone further optimization. Optical functionality tests have shown the general suitability for multispot phase change measurements.

Partner feature:

The Institute of Molecular Recognition Chemistry (ICRM), based in Milan, is one of the several research institutes of Italian National Research Council (CNR). ICRM employs 75 scientists and technicians. The Institute has been actively involved in research activities in Biomolecules (natural bioactive substances & synthesis of compounds of biological interest); Chemical biotechnologies (bioconversions & analytical methodologies); Mechanisms of bioregulation (molecular basis of biological regulation & experimental & theoretical studies of molecular recognition). Research facilities: CNR is equipped to carry out monomer and polymer synthesis; IR, circular dicroism, viscometer, spectrophotometer and different chromatographic systems are available to characterize and purify polymers. CNR possess the following instruments: 1) Microarray platform including: spotting station, automated hybridization station and LIF scanners 2) Various capillary electrophoresis units 3) MegaBACE Capillary Array DNA Sequencer 4) Microchip electrophoresis units.

The Analytical Microsystem group, led by Dr. Marcella Chiari, carries out research activities aimed at developing micro-analytical techniques for genomics and proteomics. It is active in different projects, organized around the following themes: 1) Chemical aspects of microarray technology 2) Automated systems for the analysis of gene and protein expression, 3) Miniaturized analytical systems for microchip electrophoresis, CNR has an internationally recognized know-how in the production of polymeric coatings for analytical devices microchip electrophoresis and microarrays on different materials including glass, silicon oxide and nitride, polydimethylsiloxane, COC, ITO and gold. The team, comprising organic, bio-organic and computational chemists, biochemists and biotechnologists, is equipped to carry out monomer and polymer synthesis; IR, circular dicroism, and different chromatographic systems are available to test and purify polymers; DPI (Dual Polarization Interferometry) is available to characterize coatings.

Primary person contact Dr. Marcella Chiari
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Participants

Marcella Chiari (F) Principal investigator; World-wide recognized experience in development of hydrophilic linear polymers. She has developed a number of new hydrophilic acrylic monomers and polymers to be used in capillary electrophoresis as DNA sieving matrices and as capillary coatings. She is active in the area of protein and DNA microarray. Her activity is documented by over 130 publications and several patents. She has been a contractor of the EC several times and is responsible for several national research programs.

Marina CRETICH (F), Research scientist at National research council of Italy at the Institute of Chemistry of Molecular Recognition (ICRM) in Milano. Laurea degree in Biological Sciences, specialty Molecular Biology, at Università degli Studi di Milano (1998). Her research interests, documented by more than 40 JCR publications, cover the field of analytical microsystems: microarrays, lab on chip, microchip electrophoresis and microfluidics. She is actively involved in several national and international projects on the development of microsystems for diagnosis and monitoring.

Laura Sola (F), Ph.D at ICRM, has a consolidate knowledge in polymer science and associated organic chemistry. Her main activity is coating and coating chemistry. She has experience in different analytical techniques for polymer characterization (GPC, NMR, IR), as well as in micro- and nanosystems for measurement and testing of coatings (AFM, XRR).

Surface functionalization of porous membranes

The surface functionalization is one of the most important components of a sensor platform. The surface chemistry greatly affects the specificity of the target and background binding as the local environmental conditions that exist following immobilization of the probe to the sensor surface strongly influence protein interactions. Additionally, the orientation and crowding effects are critical for the functionality of bound proteins.

The widely used approach of surface functionalization through monodimensional (1-D) coatings implies modification of the support by various types of organosilanes such as aldehyde, epoxy, mercapto or amino silanes. The 1-D surface chemistries however often suffer from drawbacks, such as spot smearing, poor spot morphology and protein denaturation due to hyrophobicity. They also suffer from loss in probe functionality that results from the close proximity of the probe to the sensor surface.

The proximity of probes to a solid surface, generally leads to reduced specificity of target binding and loss of probe functionality. One of the main sources of protein denaturation is the strong interaction between the proteins and the surface. The surface proximity can also result in interactions between the target and the surface, which may further hinder specific probe-target binding. A related effect is the orientation of immobilized probes; for randomly oriented probe proteins a large portion of the active sites may be inaccessible to targets in solution. This is especially likely for probe proteins that are randomly oriented on a solid, as the active binding site will be obstructed by the solid surface for a majority of the probes. These effects are significantly reduced for the so called 2D surface coatings, which describe surface chemistries consisting of functionalized polymers that are bound to solid surfaces in a brush type configuration. For probes immobilized on a polymeric scaffold, the effects of orientation are mitigated because binding sites can remain accessible if the polymer permits diffusion of the target protein to the probe binding site.

The focus of the activity at CNR in Positive is the design of 2D polymeric coatings with optimal features (thickness and probe density) specifically tailored to the characteristics of the sensor.

CNR has experience in the synthesis of functional polymers and in the development of coating procedures that are characterized by i) robustness, ii) high compatibility with sensor structure iii) precise control of coating thickness. The unit has completed the development and characterization of a three components polymer: DMA (dimethylacrylamide), MAPS (3-(trimethoxysilyl)propyl methacrylate), and NAS (acryloyloxysuccinimide) (Figure 1). [1]

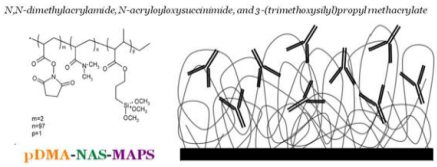

Figure 1 (a) The three major components of the polymer are DMA, NAS and MAPS in ratio 97:2:1. NAS provides the active groups, which specifically bind amine functional groups on the probe, the MAPS covalently binds to the oxide surface and DMA adsorbs to the oxide surface and provides the backbone of the polymer. (b) The polymer swells upon hydration to provide a near liquid environment for the probes. [2]

This polymer forms a film on the surface of various materials by dip and rinse coating. The coating procedure is fast and highly compatible with the characteristics of different sensors. DMA provides the majority of the polymeric structure and also adsorbs to the oxide surface, MAPS covalently binds to the oxide and NAS is the active groups that covalently binds the functional amine groups on the DNA probes.

This polymer has been used by the CNR unit to functionalize the surface of porous silicon. The coating process devised for porous silicon was not applicable to alumina, the alternative porous material considered in Positive. With this latter material a two-step procedure was devised. In the first step, a monolayer of MAPS was grafted to the surface followed by a radical polymerization of DMA and NAS monomers. The process was carried out in dimethylformamide and the polymer was covalently grafted to the surface through the incorporation of MAPS allyl moieties. Alternatively 1-D coatings have also been considered. Research is ongoing to determine whether polymer swelling is an obstacle to liquid flow in nanochannels.

1. G. Pirri, F. Damin, M. Chiari, E. Bontempi, and L.E. Depero, "Characterization of a polymeric adsorbed coating for DNA microarray glass slides," Analytical Chemistry, vol. 76, 2004, pp. 1352–1358.

2. A. Yalçın, F. Damin, E. Özkumur, G. di Carlo, B.B. Goldberg, M. Chiari, and M.S. Ünlü, "Direct observation of conformation of a polymeric coating with implications in microarray applications," Analytical Chemistry, vol. 81, 2008, pp. 625–630.

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Positive will send out a newsletter once per year for the next three years. You received this email because you were identified by one of the Intopsens partners as a potential interessee in the technology we develop. If you do not want to receive more annual newsletters, please reply to this email and write UNSUBSCRIBE in the Subject field.

POSITIVE NEWSLETTER 4: MULTIPLE SPOT PHASE CHANGE MEASUREMENTS IN A FLOW THROUGH MEMBRANE – REAL TIME MULTIPLEXED BIOSENSING FOR THE FAST AND SAFE DETERMINATION OF SENSITIZATION TO MULTIPLE FOOD ALLERGENS

Six European research centres and two industry partners have joined in a new European research consortium called POSITIVE. The goal of POSITIVE is to develop new rapid and multi-assay diagnostics for determining sensitization to food allergens. The European Union supports the consortium during a three-year period with 2.9 MEuro through its Seventh Framework Programme.

Food allergies can provoke clinical reactions whose most severe is anaphylaxis, with respiratory and/or cardiovascular problems that might result in death. They are common in 1-2% of adults and up to 8% of children, corresponding to a serious public health problem that affects over **15 million people in Europe** from infants to the elderly and its prevalence is increasing.

POSITIVE will develop a diagnostic platform that can quickly and safely identify the sensitization of a patient to multiple food allergens so as to be able to proscribe a suitable diet and lifestyle. Ideally it will be a rapid system with little hands-on time, so as to be used at point of care (PoC) in an intensive care unit by paramedics.

The consortium will develop a state-of-the-art diagnostics Lab-on-a-Chip platform via an integrated microfluidic sample preparation technique capable of serum preparation from whole blood of volumes, <100µl. The detection will be based on ultrasensitive photonic biosensors that are integrated into the lab-on-chip device. A final prototype consisting of a packaged biochip and reader will be used on clinical samples in order to determine sensitization to allergens such as that for hen's eggs, cow's milk, peanuts, wheat, tree nuts, fish, sesame, and shrimp ingestion.

More information about POSITIVE and its partners can be found in the attached project flyer or on the POSITIVE website http://www.fp7positive.eu ,

ABOUT THE POSITIVE CONSORTIUM:

Positive project manager and main contact person:

Dr. Daniel Hill, UVEG – Universitat de Valencia (http://www.uv.es/umdo)

Other partners:

Centre Suisse d'Electronique et de Microtechnique (http://www.csem.ch)

Farfield Group Ltd (www.farfield-group.com)

Charite Universitaetsmedizin Berlin (http://www.charite.de)

Phylogene SA (http://www.phylogene.com)

Università degli Studi Di Trento (http://science.unitn.it/~semicon/)

Consiglio Nazionale Delle Ricerche (http://www.icrm.cnr.it)

Royal Institute of Technology - Microsystem Technology Lab (http://www.ee.kth.se/mst)

Highlights of technology developed in Positive:

After switching to porous alumina membranes the project progressed rapidly and following a 6 month extension in its final 18 months we have been able to demonstrate:

- Real time measurements for concentrations of IgG down to 33.7ng/ml (225pM), with a noise floor of 3.7ng/ml (25pM) and a good reproducibility, bound to Anti β-LG which is attached to the β-lactoglobulin immobilized on the functionalized porous alumina membrane for a total assay time below one hour for sample volumes (Anti β-LG) < 100 µl. Capture efficiency was <70%.
- Serum flow through the mounted membranes with a very large binding response through physisoprtion and also flow through functionalized and β-LG spotted porous alumina chips for which a new mounting chip with a smaller spot size was developed.
- Chips can be multiply spotted with allergen and these multiple allergens are active on planar devices, both in array format as a fluorescent assay and in sequential experiments on a Refractive index sensitive device. One allergen has also been spotted and shown to be active on the porous POSITIVE device and used for a full concentration dependent assay.
- The multiplexed instrument showed very well its suitability for simultaneous multi-spot phase change measurements with linear response to different saline concentrations, so far down to a 4% solution or 10mrad.

Although resources have not permitted us develop an instrument that meets all of the required end-user specifications within the time frame of the project whilst endeavoring to do so several interesting technologies or technological applications have been developed and/or demonstrated including:

(1) Combination of OSTE(+)[1] with copolymer. The method aims at improving and simplifying the batch back-end processing of microarrays and create microfluidic cells. The Biosticker is aimed to be a plug-in for existing microarray platforms to enable faster protein assays and DNA hybridizations through mass transport optimization. (KTH, CNR)

(2) A micro-well platform enabling simultaneous flow through and optical inspection. This unique technology has applications in single cell studies, where the response of individual cells trapped in the micro-wells to stimulants supplied in the flow stream can be followed by microscopy in real-time. (KTH, CSEM, UVEG)

(3) A high performance sensor chip thermal control system that has already been implemented in optical instrumentation in over a dozen international University and industrial research laboratories. (Farfield)

(4) A module developed for blood filtering that enables several 100 µl of whole blood to be filtered and plasma to be generated for subsequent analysis. This will find uses in lab on chip applications which require alternatives for plasma extraction from whole blood samples which is currently done in dedicated laboratories by centrifugation. (CSEM)

(5) A module for sequential actuation of a set of fluids through a microfluidic cartridge, which also enables priming of the cartridge with CO_2 and avoids the introduction of air plugs between the different fluids[2] (CSEM).

(6) A fluorescence based milk and egg allergen microarray for detection of specific IgE and IgG with sensitivity and reproducibility comparable to the commercially available ImmunoCAP ISAC from Thermo Fisher. (C-UB, CNR)

[1] Mercene Labs AB is a spin-off Company from KTH commericializing OSTE, which was developed during FP7 InTopSens and FP7 Positive, for device fabrication by customers.

[2] CSEM is working on a demonstrator of a compact, stand-alone pressure driven fluid handling module anditt is intended to have this ready for SLAS 2015 in Washington DC to present to the lab automation and instrumentation community. CSEM is also implementing such a module in two currently running projects, one for food quality monitoring and one for 3D cell tissue generation for pharma research.

Partner feature:

csem

CSEM SA, founded 1984, is a private applied research and development center specializing in micro- and nanotechnology, systems engineering, photovoltaics, microelectronics, and communications technologies. CSEM's mission is to develop applied technology platforms in these domains and transferring them to the industrial sector, thereby enhancing the competitiveness of industry. The development of such highly innovative platforms is supported by the Swiss Confederation and by several cantons including Neuchâtel, Basel Land, Graubünden and the cantons of central Switzerland Switzerland (Obwalden, Nidwalden, Luzern, Schwyz, Zug and Uri).

The emphasis of technology platforms in the field of life sciences is on (lab) automation & instrumentation, diagnostics, and quality & process control. CSEM is thus an ideal partner for the realization of integrated solutions for the field of life sciences instrumentation by enabling new approaches and more reliable process flows. The following technologies in this field are currently covered.

Miniaturization and automation for the preparation and handling of samples and reagents

Integration of miniaturized sensors and actuators for process monitoring or control, signal processing, (micro)fluidic systems (design, modelling, fabrication), automation, combining microfluidics & robotics

Links: Integration & Packaging, Automation,

Methods & tools for handling of cells, cell clusters, tissue samples or small model organisms

Development of methods and modules for picking, sorting, manipulating, dosing of cells, microtissues, small model organisms etc. using microfluidic systems, MEMS, robotics or a combination thereof

Links: Integration & Packaging, Biosurface Engineering

Biosensor development

Development of (label-free) optical biosensors, fluorescence-based biosensors, electrochemical sensors

Links: Nanosurface Engineering, Biosurface Engineering

In-vitro platform for monitoring (3D) cell cultures for assessing the effect of compounds or toxicological studies of compounds in the life sciences

Development of microsystems for the integration of cells or cell clusters, support membranes as artificial biological barriers, modified surfaces for controlled or structured growth of cells, chip-based 3D cell cultures, sensors for measuring metabolic products of cells

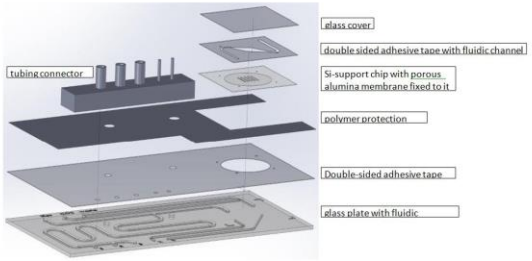
Links: Nanosurface Engineering, Biosurface Engineering

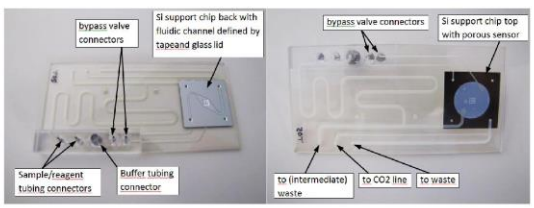
Contact: microfluidics@csem.ch

YouTube Channel: www.youtube.com/user/CSEMmicrofluidics

Activity within POSITIVE

Within POSITIVE the partner CSEM is responsible for the development of the measurement platform providing the fluidic actuation and optical readout for the multispot measurements. To this end, CSEM has developed a fluidic module for sequential actuation of three fluids, stored in tubing reservoirs, through a microfluidic cartridge. The fluidic module employs CO_2 priming of the microfluidic cartridge containing the nanoporous membrane. Only through this feature can a dry nanoporous structure be filled with aqueous solutions at pressures in the few 100 mbar range. The optical module of the multispot measurement platform uses a diode laser modulated with a photo elastic modulator to illuminate a 16 spot sample. The transmitted light is then measured using a phasecam camera with lock-in functionality. The customized software enables to automatically locate the 16 light spots in the camera image and to measure changes in the retardance of each spot. Changes in retardance are caused by changes of the refractive index within the well aligned pores of the nanoporous membrane. CSEM is also responsible for the development of the microfluidic cartridge incorporating the nanoporous sensor membrane. The assembly of this cartridge and the two sides of an assembled cartridge are shown below.





ABOUT THIS NEWSLETTER - SUBSCRIBE/UNSUBSCRIBE

You received this email because you were identified by one of the Positive partners as a potential interessee in the technology we develop. This is the fourth and final newsletter.

2.1.2.2. Flyers

The POSITIVE consortium...

- will develop a label-free biosensor for the point of care evaluation of food allergy risks
- will create disposable lab-on-chip cartridges with integrated microfluidic sample preparation and ultrasensitive photonic transducers, as well as a bench-top readout system
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SEVENTH FRAMEWORK PROGRAMME

POSITIVE

POSITIVE

A highly integrated and sensitive POrous multiple quantitaTIVE monitoring of Food

Food allergy as a condition and current diagnostic methods

Food allergies can provoke clinical reactions whose most severe is anaphylaxis, with respiratory and/or cardiovascular problems that might result in death. They are common in 1-2% of adults and up to 8% of children, corresponding to a serious public health problem that affects over **15 million people in Europe** from infants to the elderly and its prevalence is increasing.

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Therefore, blood based tests, mostly using the FEIA, RAST and ELISA techniques are often used. These tests are normally performed as a laboratory test using sent-in blood samples. On the other hand point-of-care (PoC) devices exist; however, they are currently able to assay only few allergens at a time. Other immunological blood tests, using enzymes, are now superseding the original methodology. Moreover, the existing market PoC products provide at best semi-quantitative determination of allergy sensitization.

Lab-on-chip technology for rapid and low cost quantative determination of hundreds of food allergies

POSITIVE is developing a state-of-the-art diagnostics Lab-on-a-Chip platform via an integrated microfluidic sample preparation technique capable of serum preparation from whole blood of volumes, <100µl. A final prototype consisting of a packaged biochip and reader will be used on clinical samples in order to determine sensitization to allergens such as that for hen's eggs, cow's milk, peanuts, wheat, tree nuts, fish, sesame, and shrimp ingestion.

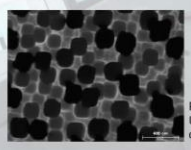
POSITIVE

SIlicon based lab on a chip for allergies at point of care.

Porous silicon transducers provide optical readout

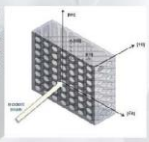
Porous silicon (porSi) is an almost ideal material as a signal transducer for *label free optical biological sensing* with many advantages, which include:

(1) ease of fabrication (by the electrochemical etching of a silicon wafer in hydrofluoric acid) of high-quality optical elements with a nanoporous sponge-like structure,
(2) the possibility of integration with wafer level IC processing (porSi is widely exploited as a sacrificial material in micromachining technology and as a buffer layer in realization of microsensors and microsystems),
(3) an extremely large internal surface (~500 m^2/cm^3) that can in principle be leveraged to enhance device sensitivity many orders of magnitude over a planar device of comparable transducer diameter,
(4) pore sizes tunable across biologically relevant length scales,
(5) convenient covalent and non-covalent surface chemistry.



Porous silicon sample made at UNITN, electron microscope image courtesy of University of Valencia

Polarimetry schematic, courtesy of University of Valencia



Recently, sufficiently high optical quality porSi for inexpensive multiple optical biosensors compatible with a present-day on-chip microelectronics and nanophotonics productions has become available. This has permitted us to propose two different types of biosensing optical elements in this project with predetermined porous layer morphology. Due to their small size, many sensors can be put next to each other on a single photonic chip. Their limit of detection and selectivity will approach the state of the art for highly integrated label-free lab on a chip devices. Technology is also being developed to couple in and read out light from the entire biosensor array at once with a low cost reader.

POSITIVE

The POSITIVE Consortium

KTH – the Royal Institute of Technology The **Microsystem Technology Lab** is a leading MEMS and microfluidics group. It coordinates the project and leads the intgeration of the biochip.
Contact: Prof. Wouter van der Wijngaart, wouter@ee.kth.se, URL: www.ee.kth.se/mst

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POSITIVE contact point

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www.fp7positive.eu

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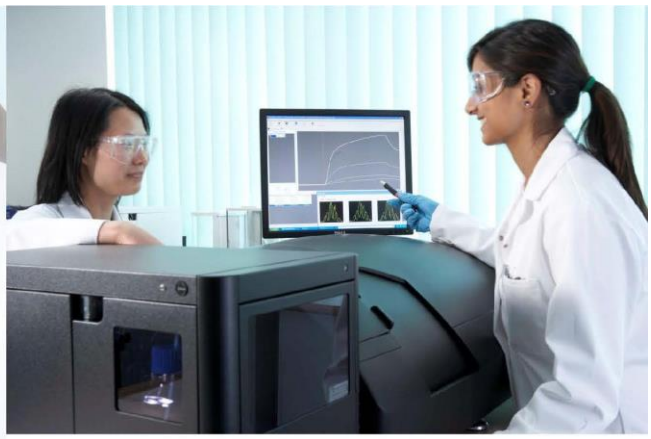

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SEVENTH FRAMEWORK PROGRAMME

POSITIVE

A highly integrated and sensitive POrous multiple quantitaTIVE monitoring of Food allergies at point of care

Food allergy as a condition and current diagnostic methods

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Project Innovation to date

The project has just completed its second year and it has made some great advances against very difficult challenges, proof of that coming recently in the form of successful bio-sensing experiments. In working towards the readiness of technologies necessary for realizing the Positive instrument we have developed technologies that not only offer functionality that the machine requires but will also have numerous applications across many areas of life. Such advances include:

- Development of a reliable and reproducible process to obtain porous membrane with highly tailored structural properties (thickness, porosity and pore size) and that shows a fluidic-friendly behavior.

- The development of OSTE materials. OSTE is the first polymeric material developed specifically for the needs of microfluidic devices. We envision that OSTEs will be a very strong alternative for rapid prototyping of microfluidic devices thanks to rapid turnaround, high yield and properties very close to those found in the final commercial products.

- Development of a proprietary robust polymer coating that makes the surface functionalization of sensors easier, faster and reproducible, enables a high probe density and has a good stability. The area of potential applications is very diverse and large.

Lab-on-chip technology for rapid and low cost quantative determination of hundreds of food allergies

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- A module developed for blood filtering that enables several 100 ul of whole blood to be filtered and plasma to be generated for subsequent analysis. This will find uses in lab on chip applications which require alternatives for plasma extraction from whole blood samples which is currently done in dedicated laboratories by centrifugation.

- The development of an instrument based on multiple spot phase change measurements on a flow through membrane. This overcomes limitations found in solid surface, planar assay systems which have to be incubated for long periods of time for the molecules of interest to be captured at the sensing surface.

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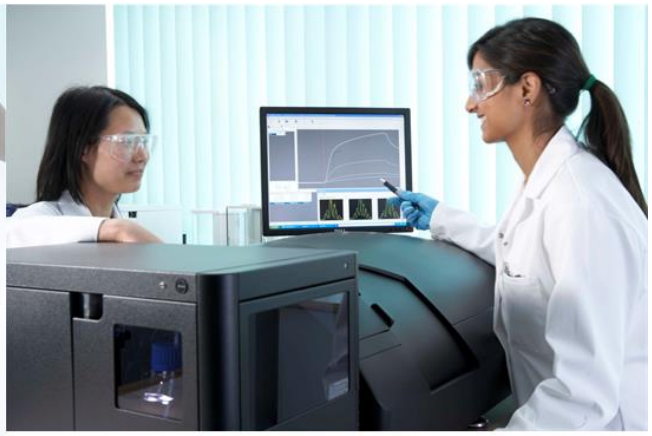

The POSITIVE consortium between 2010-2014 had aimed...

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POSITIVE

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Project Innovation from Start to End

The project has just come to completion after 42 months of significant advance towards our initial high risk-high gain target of developing a Lab-on-Chip fiagnositc platform for multiple food allergies. On our way we faced to very difficult challenges that led us to develop some very interesting individual component technologies or novel applications of existing technologies including the below:

- Combination of OSTE(+)[1] with copolymer. The method aims at improving and simplifying the batch back-end processing of microarrays and create microfluidic cells. The Biosticker is aimed to be a plug-in for existing microarray platforms to enable faster protein assays and DNA hybridizations through mass transport optimization. (KTH, CNR)

- A micro-well platform enabling simultaneous flow through and optical inspection. This unique technology has applications in single cell studies, where the response of individual cells trapped in the micro-wells to stimulants supplied in the flow stream can be followed by microscopy in real-time. (KTH, CSEM, UVEG)

- A high performance sensor chip thermal control system that has already been implemented in optical instrumentation in over a dozen international University and industrial research laboratories. (Farfield)
- A module developed for blood filtering that enables several 100 µl of whole blood to be filtered and plasma to be generated for subsequent analysis. This will find uses in lab on chip applications which require alternatives for plasma extraction from whole blood samples which is currently done in dedicated laboratories by centrifugation. (CSEM)

- A module[2] for sequential actuation of a set of fluids through a microfluidic cartridge, which also enables priming of the cartridge with CO_2 and avoids the introduction of air plugs between the different fluids (CSEM).

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2.1.2.3. **Posters**

POSITIVE

Photonic sensing of food allergens

Food allergens

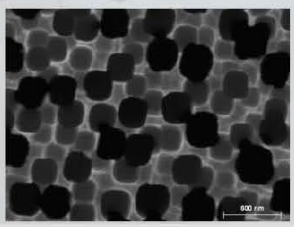
Food allergies can provoke clinical reactions whose most severe is anaphylaxis, with respiratory and/or cardiovascular problems that might result in death. They are common in 1-2% of adults and up to 8% of children, corresponding to a serious public health problem that affects over **15 million people in Europe** from infants to the elderly and its prevalence is increasing.

Lab on a chip

POSITIVE is developing a state-of-the-art diagnostics Lab-on-a-Chip platform via an integrated microfluidic sample preparation technique capable of serum preparation from whole blood of volumes, <100µl. A final prototype consisting of a packaged biochip and reader will be used on clinical samples in order to determine sensitization to allergens such as that for hen's eggs, cow's milk, peanuts, wheat, tree nuts, fish, sesame, and shrimp ingestion.

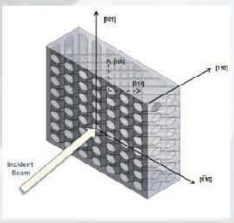
Photonic sensing

Recently, high optical quality porous silicon, an almost ideal material as a signal transducer for *label free optical biological sensing*, has become available. This has permitted us to propose two different types of biosensing optical elements in this project for inexpensive multiple optical biosensors compatible with a present-day on-chip microelectronics and nanophotonics production. Due to their small size, many sensors can be put next to each other on a single photonic chip. Their limit of detection and selectivity will approach the state of the art for highly integrated label-free lab on a chip devices.



Porous silicon sample made at UNITN, electron microscope image courtesy of University of Valencia

Polarimetry schematic, courtesy of University of Valencia



ICMUV Institut de Ciència dels Materials de la Universitat de València

KTH Vetenskap och Konst

Consiglio Nazionale delle Ricerche

Farfield Group

The POSITIVE Consortium
www.fp7positive.eu

PHYLOGENE

csem

CHARITÉ 300

University of Trento – Italy, Department of Physics, Nanoscience Laboratory

POSITIVE is financially supported by the EU through the 7th Framework Programme.

POSITIVE

Photonic sensing of food allergens

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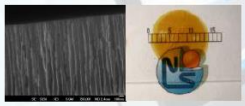
Innovation

The project has just completed its second year and it has made some great advances against very difficult challenges, proof of that coming recently in the form of successful bio-sensing experiments. In working towards the readiness of technologies necessary for realizing the Positive instrument we have developed technologies that not only offer functionality that the machine requires but will also have numerous applications across many areas of life. Such advances include:



- Development of a reliable and reproducible process to obtain porous membrane with highly tailored structural properties (thickness, porosity and pore size) and that shows a fluidic-friendly behavior.
- The development of OSTE materials. OSTE is the first polymeric material developed specifically for the needs of microfluidic devices. We envision that OSTEs will be a very strong alternative for rapid prototyping of microfluidic devices thanks to rapid turnaround, high yield and properties very close to those found in the final commercial products.
- A module developed for blood filtering that enables several 100 ul of whole blood to be filtered and plasma to be generated for subsequent analysis. This will find uses in lab on chip applications which require alternatives for plasma extraction from whole blood samples which is currently done in dedicated laboratories by centrifugation.

The POSITIVE Consortium
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POSITIVE

Project Innovation from start to end

Food allergens

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Lab on a chip

POSITIVE aimed to develop a state-of-the-art diagnostics Lab-on-a-Chip platform via an integrated microfluidic sample preparation technique capable of serum preparation from whole blood of volumes, <100µl. A final prototype was to consist of a packaged biochip and reader to be used on clinical samples in order to determine sensitization to allergens such as that for hen's eggs, cow's milk, peanuts, wheat, tree nuts, fish, sesame, and shrimp ingestion.

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The project has just come to completion after 42 months of significant advance towards our initial high risk-high gain target of developing a Lab-on-Chip diagnostic platform for multiple food allergies. On our way we faced to very difficult challenges that led us to develop some very interesting individual component technologies or novel applications of existing technologies including:

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- A high performance sensor chip thermal control system that has already been implemented in optical instrumentation in over a dozen international University and industrial research laboratories. (Farfield)
- A module developed for blood filtering that enables several 100 µl of whole blood to be filtered and plasma to be generated for subsequent analysis. This will find uses in lab on chip applications which require alternatives for plasma extraction from whole blood samples which is currently done in dedicated laboratories by centrifugation. (CSEM)
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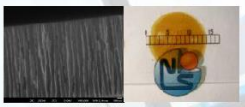

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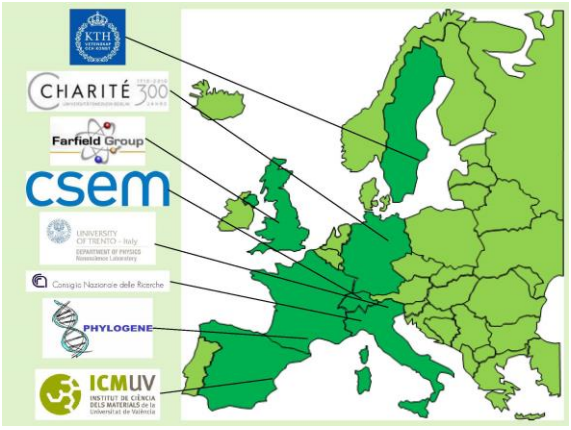
2.1.2.4. **Presentations**

POSITIVE

A highly integrated and sensitive POrous SIlicon based lab on a chip for multiple quantitaTIVE monitoring of Food allergies at point of care.

Keywords:
Lab on a chip
Rapid cost-effective multiplexed biochip
integrated sample preparation
Microfluidic
Porous silicon
portable label-free multiallergy diagnostic
biomolecular recognition optical sensor

Contact information: www.fp7positive.eu



About food allergies

Food allergies – sensitization to food products
Life threatening:
Can provoke clinical reactions whose most severe is anaphylaxis, with respiratory and/or cardiovascular problems that might result in death.
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Current diagnostic technology:
Skin prick test - has its limitation.
Alternatives are blood based tests, mostly using the FEIA, RAST and ELISA techniques, usually lab-based.
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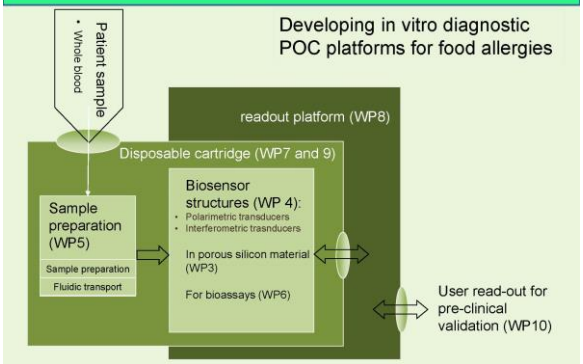
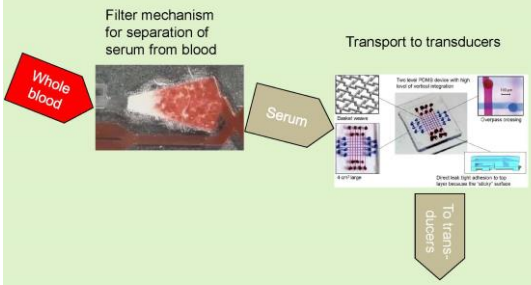
POSITIVE technology:
100µL whole blood sample
Sensitization determination to 10 food allergies in 15'

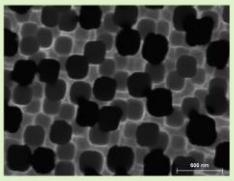
Positive diagnostic procedure



Sample preparation and transport



Porous silicon transducer material and mechanisms

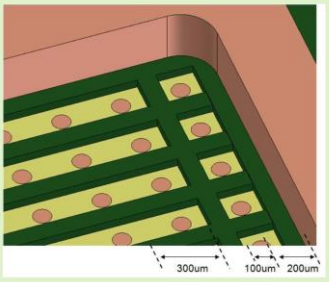


Porous silicon sample made at UNITN, electron microscope image courtesy of University of Valencia

Polarimetry schematic, courtesy of University of Valencia

Functionalized porous silicon with surface based immunoassays with sensing by two different transducer mechanisms

Porous silicon transducer arrays



Arrays of optical transducers with surface based immunoassays

POSITIVE

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Keywords:
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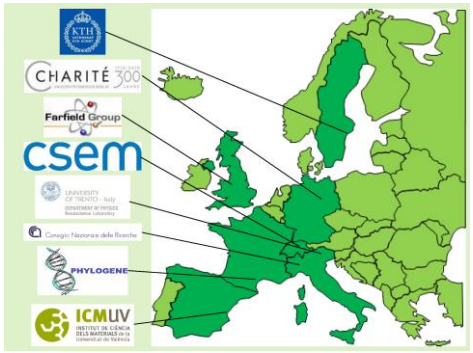

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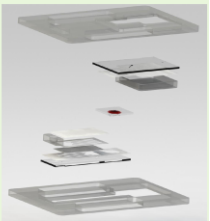
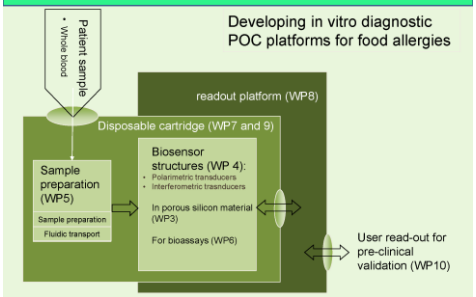
100µL whole blood sample
Sensitization determination to 10 food allergies in 15'

Our Goal

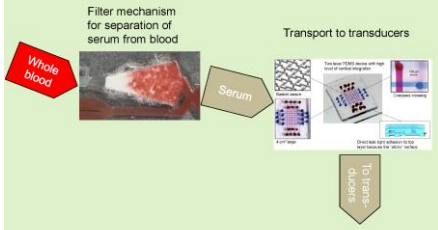
- A commercial product within two years of project conclusion.
- Innovative and commercially relevant research is ensured by the consortium's two technological companies' clear vision of what the market is and what is needed of the product if it is to be successful.
- All pediatricians should have this machine on their desk, whether they work in a hospital or in general practice.
- The companies' knowledge of the market really provides us with an excellent road map for innovation, making sure that we will able to exploit our results fully.



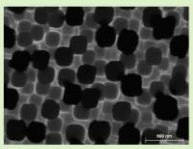
Positive diagnostic procedure



Sample preparation and transport



Porous silicon transducer material and mechanisms



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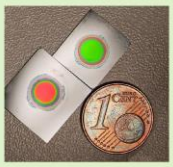
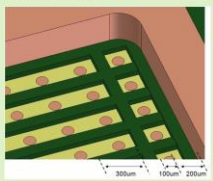


Porous silicon membranes

Arrays of optical transducers defined within a membrane



Positive Innovation

- **Entering Y3** - great advances made against very difficult challenges.
- Technologies developed offering functionality for Positive and beyond.
  - **Reliable/reproducible process to obtain porous membrane** with highly tailored structural properties (thickness, porosity and pore size) and fluidic-friendly. *Filtering applications.*
  - **OSTE materials** - the first polymeric material developed specifically for microfluidic devices. *Competition with commodity and engineering plastics in commercial devices.*
  - **Blood filter module** that enables several 100 ul of whole blood to be filtered and plasma to be generated for subsequent analysis. *Lab on Chip applications.*
  - **Multiple spot phase change measurement**s. Overcomes the instability limitations found in phase change measurement systems. *Interferometry applications.*
  - Proprietary robust polymer coating for improved surface functionalization of sensors. ***The area of potential applications is very diverse and large.***
  - Disposable cartridge including a low-cost module for sequentially flowing liquids from individual reservoirs. ***Lab on Chip applications.***

Positive Progress

- *Integrating these technologies* into a prototype machine since Y1.5 for delivery to the clinical partner, Charité Hospital Berlin.
- Charité will carry out *trials with the instrument* and pre-validate it up until the end of the project.
- Sensors will be able to get up to *ten different measurements of food allergies at a time* in our eventual prototype, which will tell us to what degree the person is allergic.
- Sensors can then be *scaled up to hundreds of food allergies* in order to be able to test all the food allergies at the same time.

Read more about the project on Positive's homepage

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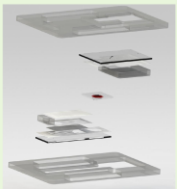
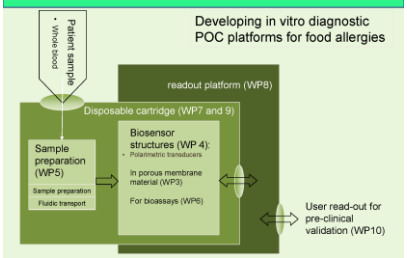
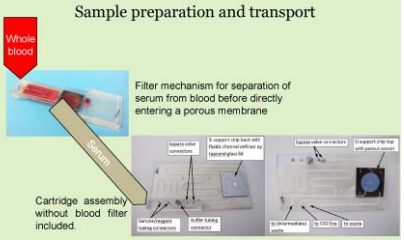


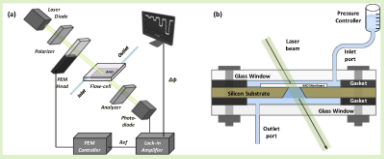
Positive diagnostic procedure



Sample preparation and transport

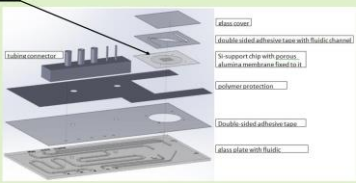


Layout of the optical polarimetric readout platform



Porous alumina sensor within the cartridge

Functionalised porous alumina membranes in a micromachined silicon chip support structure



Positive Progress

Highlights of technology developed in Positive:

- After switching to porous alumina membranes the project progressed rapidly and following a 6 month extension in its final 18 months we have been able to demonstrate:
- Real time measurements for concentrations of IgG down to 33.7ng/ml (225pM), with a noise floor of 3.7ng/ml (25pM) and a good reproducibility, bound to Anti β-LG which is attached to the β-lactoglobulin immobilized on the functionalized porous alumina membrane for a total assay time below one hour for sample volumes (Anti β-LG) < 100 µl. Capture efficiency was <70%.
- Serum flow through the mounted membranes with a very large binding response through physisorption and also flow through functionalized and β-LG spotted porous alumina chips for which a new mounting chip with a smaller spot size was developed.
- Chips can be multiply spotted with allergen and these multiple allergens are active on planar devices, both in array format as a fluorescent assay and in sequential experiments on a Refractive index sensitive device. One allergen has also been spotted and shown to be active on the porous POSITIVE device and used for a full concentration dependent assay.
- The multiplexed instrument showed very well its suitability for simultaneous multi-spot phase change measurements with linear response to different saline concentrations, so far down to a 4% solution or 10mrad.

Positive Innovation From Start to End

Although resources have not permitted us develop an instrument that meets all of the required end-user specifications within the time frame of the project whilst endeavoring to do so several interesting technologies or novel application of existing technologies have been developed and/or demonstrated including:

1. Combination of OSTE(+)[1] with copolymer. The method aims at improving and simplifying the batch back-end processing of microarrays and create microfluidic cells. The Biosticker is aimed to be a plug-in for existing microarray platforms to enable faster protein assays and DNA hybridizations through mass transport optimization. (KTH, CNR)
2. A micro-well platform enabling simultaneous flow through and optical inspection. This unique technology has applications in single cell studies, where the response of individual cells trapped in the micro-wells to stimulants supplied in the flow stream can be followed by microscopy in real-time. (KTH, CSEM, UVEG)
3. A high performance sensor chip thermal control system that has already been implemented in optical instrumentation in over a dozen international University and industrial research laboratories. (Farfield)

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Positive Innovation From Start to End

4. A module developed for blood filtering that enables several 100 µl of whole blood to be filtered and plasma to be generated for subsequent analysis. This will find uses in lab on chip applications which require alternatives for plasma extraction from whole blood samples which is currently done in dedicated laboratories by centrifugation. (CSEM)
5. A module[2] for sequential actuation of a set of fluids through a microfluidic cartridge, which also enables priming of the cartridge with CO_2 and avoids the introduction of air plugs between the different fluids (CSEM).
6. A fluorescence based milk and egg allergen microarray for detection of specific IgE and IgG with sensitivity and reproducibility comparable to the commercially available ImmunoCAP ISAC from Thermo Fisher. (C-UB, CNR)

[2] CSEM is working on a demonstrator of a compact, stand-alone pressure driven fluid handling module and it is intended to have this ready for SLAS 2015 in Washington DC to present to the lab automation and instrumentation community. CSEM is also implementing such a module in two currently running projects, one for food quality monitoring and one for 3D cell tissue generation for pharma research.

Read more about the project at www.fp7positive.eu

2.1.2.5. **Press-releases**

Quick food allergy test - just a drop of blood

Over 15 million people in Europe – including eight percent of all children - suffer from food allergies, and this number is growing steadily. Currently, children who portray mild symptoms may undergo a skin prick test that is not only lengthy but particularly painful and usually very traumatic. Researchers from the Positive consortium are about to change all that by putting a food allergy machine on every pediatrician's desk, a machine that produces test results in 15 minutes from a miniscule drop of blood.

Today's food allergy tests can be very expensive, take a long time, as well as being both difficult to administer and quite painful. This is especially true for the common skin prick test on young children whose arms are not large enough to take the regular test made on adults. Instead they have to be held face down for long periods of time while the pediatrician scratches food extracts into different marked patches on the skin of the child's back.

Daniel Hill, Project Coordinator of Positive and researcher at UMDO in the University of Valencia

"For a one-year-old child this could be a very traumatic experience, and even more so for the parents. They are held face down and typically cry throughout the whole frightening experience. What if the pediatrician suspects a severe allergy to certain foods? Then they have to undergo blood tests which require a sizeable extraction which is not only difficult to undertake is also very traumatic. Then, the tests can take several days at considerable cost." says Daniel Hill, Project Coordinator of Positive and senior researcher at the Unit of Optoelectronic Materials and Devices (UMDO) in the University of Valencia, Spain.

The Positive consortium is opening the door to a new scenario. Together with industrial partners, researchers from six universities and research institutes, and with a SEK 29 million grant from the EU, they are aiming to put a diagnostic platform, using a biosensor, on every pediatrician's desk. This machine will be able to test for multiple food allergies very quickly, safely and painlessly from a tiny drop of blood.

"This will be a convenient test, made right there in your pediatrician's office, that will give test results within 15 minutes at low cost levels as no samples have to be sent to a laboratory. The doctor places the tiny drop of blood on a cartridge containing several sensors containing food extracts, and places the cartridge inside a machine the size of a shoe box on the desk," explains Daniel.

So far, alternatives to the skin prick and blood-based lab tests have not been able satisfy all three desired parameters: to test all food allergies at the same time, to do it quickly and to do it painlessly. Current alternatives that can cover hundreds of food allergies are very expensive and take more than five hours to produce the test results necessitating another scheduled visit to the pediatrician with all the inconvenience, additional cost and cramming of the busy practitioners' agenda this entails. Even then the test only says whether there is an allergy or not without saying how severe it might be.

"We have tested the material the sensors will be made of and we have determined that it will be able to get up to ten different measurements of food allergies at a time in our eventual prototype, which will tell us to what degree the person is allergic. The first step afterwards will be to scale it up for hundreds of food allergies in order to be able to test all the food allergies at the same time."

With time Daniel Hill is hoping for a change of attitude towards the routine testing of food allergies in children.

"Today at birth all children immediately undergo several tests including Apgar and the heel test and as they grow parents take them to be weighed, measured and vaccinated. Instead of only testing children when they are showing symptoms, sometimes of life-threatening reactions, the screening of food allergies might be included within these general checkups. This way not only will all children be able to avoid potentially fatal reactions to certain foods but also not have to undergo the slow, painful, difficult, somewhat limited and sometimes costly current diagnostic tests – potentially substantial socio-economic savings! Ultimately of course this is dependent on the willingness of countries' public health systems and authorities to include this in their general battery of tests."

The consortium is pushing to present a commercial product within two years of project conclusion. Innovative and commercially relevant research is ensured by the consortium's two technological companies' clear vision of what the market is and what is needed of the product if it is to be successful.

"Our vision is that all pediatricians should have this machine on their desk, whether they work in a hospital or in general practice. The companies' knowledge of the market really provides us with an excellent road map for innovation, making sure that we will able to exploit our results fully."

- Read more about the project on Positive's homepage

For more information, contact Daniel Hill, daniel.hill@uv.es

Technology from the University of Valencia for better diagnosis of food allergies

Researchers at the Institute of Materials Science of the University of Valencia, in consortium with various European companies and institutions, are developing a system based on photonic biosensors for rapid diagnosis of food allergies. The objective of this project funded by the EC is to make a low-cost instrument that in fifteen minutes, and from a single drop of blood, perform effective allergy tests potentially for hundreds of foods, simultaneously and without risk to patients.

Undiagnosed food allergies and unsuitable diets are, according to the experts, factors that can significantly reduce the quality of life of people, and even cause death. More than 15 million people in Europe suffer from food allergies, including 6% of children, and this number grows progressively with great social and economic costs.

"Currently, the most common allergy tests are expensive tests and especially traumatic for children, as well as pose a risk of adverse reactions," said Daniel Hill, coordinator of POSITIVE- as the project is called - and researcher of the UMDO (Unit Optoelectronic Materials and Devices) group in the Institute of Materials Science at the University of Valencia. "Beyond the project, the idea is to be able to put a food allergy diagnostic instrument that is fast, effective and safe in the office of every pediatrician, so that they can test during the first few years of life. The incorporated technology will on one hand allow the analysis from just one drop of blood, overcoming the frequently troublesome blood sampling issue, and on the other provide much greater information for a more precise diagnosis.

POSITIVE is a multidisciplinary project focused on the development of a system of high-tech biosensors oriented to the recognition of biomolecules symptomatic of allergic reactions to food from patients. The system combines different technology components, some of which are reported in various scientific journals (IEEE Photonics, 4, 3, 986, Lab on Chip: 2012.12, 3032-3035, etc.), that demonstrate multiple applications in different fields such as, for example, analysis of blood markers or filter laboratories. From the developed fluidically compatible porous membrane with biosensor functions, the first polymeric material developed especially for microfluidic devices, or a new module for filtering blood that solves certain problems and improves on previous systems, to a more stable instrument, a patent on polymer coatings and a disposable cartridge for the detection of biomolecules responsible for allergic reactions the first functional instrument will be built in February 2013.

According to Daniel Hill, the instrument will be ready to begin clinical trials with patients from June, and testing will take place at the Hospital of the Universitaetsmedizin Berlin (Germany). "According to our calculations, from the bioassays using non-human molecule samples, the final prototype will be able to detect up to ten different food allergy measurements," says Hill. "The objective, once the project has ended, is to build a commercial instrument capable of detecting all food allergies at the same time, quickly, safely and at a very low cost."

Furthermore UMDO team of the University of Valencia, form the research group POSITIVE European companies and institutions such as the Centre Suisse d'Electronique et microtechnique, SA-CSEM (Switzerland) - Farfield Group Limited (UK), PHYLOGENE (France), Charité - Universitaetsmedizin Berlin (Germany), Universita Degli Studi di Trento (Italy), Consiglio Nazionale delle Ricerche, Milan (Italy) and Kungliga Tekniska Hoegskolan (Sweden).

The POSITIVE project is being followed by the world leader in this sector. This is the Phadia, a division of the multinational Thermo-Fischer, who from the beginning has shown interest in the development of the technology.

"Innovative technologies for a rapid food allergy test"

Over 15 million people in Europe – including eight percent of all children - suffer from food allergies, and this number is growing steadily. Currently, children who portray mild symptoms may undergo a skin prick test that is not only lengthy but particularly painful and usually very traumatic. Researchers from the Positive consortium of industrial partners, 6 universities and research institutes after 3 ½ years in a 2.9M€ funded EC project have taken a large step forward to the realization of putting a food allergy machine on every pediatrician's desk, an instrument that can produce test results in 15 minutes from a miniscule drop of blood.

Today's food allergy tests can be very expensive, take a long time, as well as being both difficult to administer and quite painful. This is especially true for the common skin prick test on young children whose arms are not large enough to take the regular test made on adults. Instead they have to be held face down for long periods of time while the pediatrician scratches food extracts into different marked patches on the skin of the child's back.

"Positive, which has just recently finished, was a high risk but high gain project, with many known challenges at the time of its conception as a proposal 5 years ago, but since then it has also provided us with plenty more along the way. Although with the time and resources available we were not able to fully develop all of the technologies necessary to realize the aforementioned food allergy machine we made great progress and in doing so developed some very innovative technologies. In fact those technologies themselves could find a way into commercial products for food allergy diagnostics or other applications." Says Daniel Hill Project Coordinator of Positive and researcher in the UMDO group at the University of Valencia.

Those technologies or technological applications that have been developed and/or demonstrated include:

(1) Combination of OSTE(+)[1] with copolymer. The method aims at improving and simplifying the batch back-end processing of microarrays and create microfluidic cells. The Biosticker is aimed to be a plug-in for existing microarray platforms to enable faster protein assays and DNA hybridizations through mass transport optimization. (KTH, CNR)
(2) A micro-well platform enabling simultaneous flow through and optical inspection. This unique technology has applications in single cell studies, where the response of individual cells trapped in the micro-wells to stimulants supplied in the flow stream can be followed by microscopy in real-time. (KTH, CSEM, UVEG)
(3) A high performance sensor chip thermal control system that has already been implemented in optical instrumentation in over a dozen international University and industrial research laboratories. (Farfield)
(4) A module developed for blood filtering that enables several 100 µl of whole blood to be filtered and plasma to be generated for subsequent analysis. This will find uses in lab on chip applications which require alternatives for plasma extraction from whole blood samples which is currently done in dedicated laboratories by centrifugation. (CSEM)

[1] Mercene Labs AB is a spin-off Company from KTH commericializing OSTE, which was developed during FP7 InTopSens and FP7 Positive, for device fabrication by customers.

(5) A module for sequential actuation of a set of fluids through a microfluidic cartridge, which also enables priming of the cartridge with CO_2 and avoids the introduction of air plugs between the different fluids[2] (CSEM).
(6) A fluorescence based milk and egg allergen microarray for detection of specific IgE and IgG with sensitivity and reproducibility comparable to the commercially available ImmunoCAP ISAC from Thermo Fisher. (C-UB, CNR)

"From the advances made in biosensing and the development of a working automated instrument over the past 18 months the consortium remains convinced that with some further development a prototype could be realised that could give up to ten different measurements of food allergies at a time which would tell us to what degree the person is allergic. From there it would be fairly straight forward step to scale it up for hundreds of food allergies in order to be able to test all the food allergies at the same time."

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[2] CSEM is working on a demonstrator of a compact, stand-alone pressure driven fluid handling module anditt is intended to have this ready for SLAS 2015 in Washington DC to present to the lab automation and instrumentation community. CSEM is also implementing such a module in two currently running projects, one for food quality monitoring and one for 3D cell tissue generation for pharma research.

3. Conclusions

The project Positive has been promoted on numerous occasion at various different audiences and these events have been recorded within this document and the material presented too as a testimony to a successful series of dissemination of the project.