

TWINFUSYON

Twinning for Improving Capacity of Research in Multifunctional Nanosystems for Optronic Biosensing

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D2.2 Report on a First Analysis of Organisations/Individuals/Industry in Optronics Biosensing

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1 SUMMARY

There are new opportunities in biosensing offered by the dramatically increased synergy between photonics, optoelectronics (optronics) and biology, fostered by rapid advances in technologies at the atomic scale and in system, cell, and molecular biology.

Realizing the promise of optronic biosensing requires research that crosses disciplines, such as electrical engineering, photonics, biology, chemistry, physics, and materials science, to address research areas and identified challenges of

- 1. Understanding biomolecule/cell-electron/photon interfaces;
- 2. Understanding bio responses—and their variabilities—to stimulation (electrical, photonic, mechanical, chemical, thermal, etc);
- 3. Ability to collect and analyze essential data on the state of biomolecules and cells (chemical, physical, structural, functional);
- 4. Ability to monitor, in real-time, the bioevents, which requires comprehension of interaction between molecules;
- 5. Ability to detect, identify, and quantify thousands of different biomarkers simultaneously.

Transitioning the results of this multidisciplinary research to commercial products can be expedited through collaboration at early stages between the optoelectronic/photonic industry and the biomedical device industry, along with the academic and government research communities. Government, industry, and academic leaders from different sectors and disciplines who do not necessarily speak the same 'language' must be willing to commit to joint efforts where interdisciplinary contributions are necessary for success.

This is the spirit inspiring and guiding also the TWINFUSYON project.

This deliverable analyses the international state-of-the-art of the research landscape, patents, organisations and individuals of optoelecronic/optronic biosensing, with a look also at graphene, other 2D crystals and plasmonics biosensing.

In this report, we define a biosensing system as a compact analytical device incorporating a biological or biologically derived sensing element (the bio receptor) either integrated within or intimately associated with a physicochemical transducer. Typical bio receptors are enzymes, microorganisms, antibodies, tissue, organelles and chemoreceptors. Typical transducer types are amperometric, potentiometric, semiconductors, thermometric, photometric and piezoelectric

METHOD

The terms "optoelectronic biosensor", "optronic biosensor/biosensing", "plasmonic biosensor", "graphene and 2D biosensor" and "biosensors" were searched in Isi Web of Knowledge, Pubmed, Sciencedirect, and google, and all related articles and patents were analysed.

Market reports on Biosensing from Yole Development, IDTech, Strategyr, were also selected.

The analysis is based on three types of indicators: scientific publications reflecting research activities, EU funded projects reflecting the cooperative EU funded initiatives and patents referring to technological and market-oriented activities.

The analysis shows that the optronic sensing field is growing, exhibiting very strong international dynamics. The international research landscape is increasingly influenced by activities in China. Europe is playing an important role internationally at a similar level as the US.

A large part of research in biosensing is still focussed on more conventional devices.

The landscape of potential applications of optronic sensing is dominated by military applications, but is expanding to the biosensing.

Overall data clearly indicate that optoelectronic biosensing is getting increasingly interesting for highthroughput sensing technologies that can enable simultaneous detection of a wide range of

proteins/biomolcules with innovative solutions toward cost-effective and handheld wireless biosensor devices with a desired list of performance metrics.

2 AT A GLANCE

Technologically, a biosensor is an integrated miniaturized device that has a biosensitive layer, connected to a transducing system for signal detection. The biosensitive layer is created by immobilization of the biological recognition element (enzyme, antibody, oligonucleotide, receptor protein, microorganism or the whole cell) on the surface of the biosensor (Figure 1). The biosensitive layer should be bioselective and sensitive to capture the appropriate analyte (enzyme, antigen, DNA/RNA, toxin, virus, heavy metal, pesticide, *etc.*) and interpret accurately the bio-recognition event. Biosensors integrate the selectivity of biomolecules and the processing power of modern microelectronics and optoelectronics [1].





Solid-state optronic biosensors are based on concepts of integrating on a CMOS platform several components of steady-state (SS) and time-resolved measurements (TRM) in a miniature multi-spectral filterless design, capable of detection and quantification of several important analytes, is presented. Light-emitting diodes (LED) and wavelength-selective photodiodes (PD) covering the entire range of wavelengths from UV to near-IR are used for excitation and detection, respectively. Figure 2 shows an example of a recently developed integrated biosensing prototype platform based on the Au-nanoprobe biodetection and the optoelectronic sensor towards a low-cost portable system [2]



Figure 2. Example of a optoelectronic biosensing platform presentation. Prototype incorporating all the components and suitable for USB connection to a PC: PCB, photodetector, LED and cuvette; the detection schematic with the PCB developed for data acquisition is highlighted. The light allowed through the solution reaches the sensor that generates a photocurrent, which is then converted to a voltage. This analog signal is filtered, amplified and then converted to a digital signal by the analog to digital converter (ADC). Finally, the signal is transmitted to the computer via a serial communication protocol. [*Source: L.B. Silva et al. / Biosensors and Bioelectronics 26 (2011) 2012–2017*]

Although most of the basic principles of optoelectronic(optronic) sensors have been known for more than forty years, and optoelectronic sensor technology emerged over the past 10–20 years, the industrial applications are relatively new.

The global biosensors market is segmented as follows:

Biosensors Market, by Technologies

- Electrochemical
- Optical
- Thermal
- Piezoelectric

Based on technology, the market is categorized into electrochemical, optical, piezoelectric, and thermal. Electrochemical technology segment held maximum portion and accounted for more than 65% of the overall market share in 2016. However, optical emerged as the fastest growing technology segment over the next few years, especially merging electronic and photonics platforms giving rise to optoelectronic (optronic) sensors, accompanied by a drop in the market share of piezoelectric and thermal biosensors.

Security and biodefense is the fastest growing category in the optronic biosensors market.

With specific reference to the segment of optoelectronic optronic label free biosensing:

Label-free technologies are increasingly used in drug discovery for the detection and characterization of molecular interactions. The inherent advantages of label-free technology over alternative technologies like ELISA and flow cytometry are a significant factor driving its adoption. The label-free detection is a highly sensitive method used for detection of endogenous targets in cell assays, and eliminates the need for reporter

labels like dyes, tags, or specialized reagents. Use of labels may confound data due to steric hindrance, and quenching. Conventional label-based technologies are usually labour intensive, cumbersome and time consuming. Label-free technologies offer the ability to analyse molecular interactions without use of labels, in small reaction volumes and are much more rapid than conventional techniques. Furthermore, increasing drug discovery programs by pharmaceutical companies and academic institutes, increase in pharmaceutical outsourcing, and increasing molecular interaction analysis in drug discovery are the important growth drivers for this market during the forecast period between 2015 and 2020.

In this field, major technologies are as reported in Figure 3:

- Bio-layer Interferometry (BLI)
- Cellular Dielectric Spectroscopy
- Optical Waveguide Grating Technology (OWG)
- Surface Plasmon Resonance (SPR)
- Other Technologies



Figure 3: [Source: http://www.marketsandmarkets.com/Market-Reports/label-free-detection-market-32435593.html]

Biosensors Market, by Applications

- Medical
- Environment
- Food Toxicity Detection
- Agriculture
- Industrial Process Control
- Forensics
- Others (Bio-defense, drug abuse prevention etc.)



By application, the medical sensor industry dominates the demand from the global biosensors market by a valuation of more than US\$11bn at the end of 2016. Other leading applications of biosensors include food toxicity detection, agriculture, industrial process control, and environmental applications. The range of markets of interest reported is shown in Figure 4 [3].



Figure 4. Target markets for companies involved in biosensors and biosensing

Biosensors Market, by End Users

- Point of Care Testing
- Home Healthcare Diagnostics
- Research Laboratories
- Security and Bio-defence
- Food Industry

A growing number of industrial applications is also being demonstrated, which run from a better process control to safety and security improvement, with particular care devoted to transportation, environment, structural health monitoring and food quality

Healthcare applications hold 66% of biosensor market revenue share. However, the application of biosensors in agriculture is set to register highest CAGR of 11% from 2016 to 2024. The share is shown in Figure 5.



Figure 5: Biosensors Market, by End Users [https://www.gminsights.com/industry-analysis/biosensors-market]



The specific optronic biosensor technology breakdown by sector in 2016 is shown in Fig. 6

Figure 6. World optronic biosensor technology breakdown by sector in 2016 (adapted from Ref. http://www.sensorsmag.com/specialty-markets/medical/strong-growth-predicted-biosensors-market-7640)

Biosensors Market, by Region

Based on region, the market is classified into North America, Europe, Asia Pacific, Latin America and Middle East & Africa. North America and Europe collectively accounted for more than 50% of the overall revenue in 2016 primarily owing to strict health regulations paired with rising health expenditure in these regions, as shown in Fig. 7.



Figure 7. Global Biosensors Market, by Region, 2014-2020 (in BN USD)

3 OPTRONIC BIOSENSING: A TAXONOMY

Various technical strategies are adopted for developing optoelectronic biosensors in order to provide fundamental knowledge and develop technological scenarios. Integrated strategies using multiple technologies ranging from electrochemical, electromechanical, electronic, optical-based biosensors and genetically engineered microbes are modern methods for biosensor discoveries. With the emphasis on the research tools that demonstrate how the performance of biosensors evolved from the classical electrochemical to optical/visual, polymers, silica, glass, and nanomaterials to improve the detection limit, sensitivity, and selectivity to label-free biosensors involved usage of transistor or capacitor-based devices and nanomaterials, the scheme in Fig. 8 summarises disciplines, technologies and challenges involved in developing optronic biosensing technologies, from which a taxonomy can be derived.

COMPONENTS				
Sensors: - Physical:	Wireless Networks Autonomous Systems	Analytical	Defence/Security Aerospace	Profitable Manufacturing
- Electronic - Photonic - Chemical	& Robotics Vacuum	Scientific Test & Measurement	Space Scientific (inc Research Facilities)	Resource Efficiency Quality of Life
- Biological Optics/Photonics	Cryogenics	Metrology	Healthcare Life Science Built Environment	Leading Edge Science
	Displays	Process	Environmental Automotive	Improved Transport Secure Information
	Distributed Computing	Control	Semiconductor Industrial Arts & Heritage	Technology
	Power Systems	Lindedded Systems	Food	
Packaging	TIES	Skills/Training		
Fabrication (inc MNT) Materials	Electronics Systems Engineeri	Signal I ng Modelli	Processing/Analysis ng & Simulation	Measurement Standards Certification
	Electrical Engineer	ing		

Figure 8: Sensing and instrumentation supply chain [source: http://www.npl.co.uk/upload/pdf/hill.pdf]

Considering the variety and complexity of the previous topics involved, the taxonomy based on the identified publications was organized into several topical areas, as shown in Figure 9.

"Photonic Biosensor"

"Optoelectronic Biosensor"

Field: Research Areas	Record Count	% of 1468	Bar Chart	Field: Research Areas	Field: Research Areas Record Count	Field: Research Areas Record Count % of 234
ENGINEERING	1066	72 616 %	_			
INSTRUMENTS INSTRUMENTATION	989	67.371 %		CHEMISTRY	CHEMISTRY 99	CHEMISTRY 99 42.308 %
OPTICS	970	66.076 %		ENGINEERING	ENGINEERING 97	ENGINEERING 97 41.453 %
PHYSICS	848	57 766 %	_	INSTRUMENTS INSTRUMENTATION	INSTRUMENTS INSTRUMENTATION 91	INSTRUMENTS INSTRUMENTATION 91 38.889 %
MATERIALS SCIENCE	793	54 019 %	_	PHYSICS	PHYSICS 74	PHYSICS 74 31.624 %
CHEMISTRY	746	50.817 %	_	MATERIALS SCIENCE	MATERIALS SCIENCE 68	MATERIALS SCIENCE 68 29.060 %
SCIENCE TECHNOLOGY OTHER TOPICS	646	44 005 %	_	OPTICS	OPTICS 67	OPTICS 67 28.632 %
BIOPHYSICS	378	25 749 %	-	SCIENCE TECHNOLOGY OTHER TOPICS	SCIENCE TECHNOLOGY OTHER TOPICS 67	SCIENCE TECHNOLOGY OTHER TOPICS 67 28.632 %
SPECTROSCOPY	269	18 324 %	-	BIOCHEMISTRY MOLECULAR BIOLOGY	BIOCHEMISTRY MOLECULAR BIOLOGY 46	BIOCHEMISTRY MOLECULAR BIOLOGY 46 19.658 %
RADIOLOGY NUCLEAR MEDICINE MEDICAL IMAGING	268	18 256 %	-	SPECTROSCOPY	SPECTROSCOPY 44	SPECTROSCOPY 44 18.803 %
MEDICAL LABORATORY TECHNOLOGY	250	17 302 %	-	BIOPHYSICS	BIOPHYSICS 37	BIOPHYSICS 37 15.812 %
MEDICAL ENDORATORY TECHNOLOGY	2.14	16 757 %	-	ELECTROCHEMISTRY	ELECTROCHEMISTRY 26	ELECTROCHEMISTRY 26 11.111 %
BIOCHEMISTRY MOLECULAR BIOLOGY	240	16 /85 %	-	MEDICAL LABORATORY TECHNOLOGY	MEDICAL LABORATORY TECHNOLOGY 26	MEDICAL LABORATORY TECHNOLOGY 26 11.111 %
BIOCHEMISTRY MOLECULAR BIOLOGY	242	10.405 %	-	MATHEMATICS	MATHEMATICS 25	MATHEMATICS 25 10.684 %
ACOUSTICS	100	12.070 %	-	BIOTECHNOLOGY APPLIED MICROBIOLOGY	BIOTECHNOLOGY APPLIED MICROBIOLOGY 22	BIOTECHNOLOGY APPLIED MICROBIOLOGY 22 9.402 %
ELECTROCHEMISTRY	169	11.512 %		RADIOLOGY NUCLEAR MEDICINE MEDICAL IMAGING	RADIOLOGY NUCLEAR MEDICINE MEDICAL IMAGING 22	RADIOLOGY NUCLEAR MEDICINE MEDICAL IMAGING 22 9.402 %
POLYMER SCIENCE	89	6.063 %	-	POLYMER SCIENCE	POLYMER SCIENCE 16	POLYMER SCIENCE 16 6.838 %
CELL BIOLOGY	86	5.858 %		CELL BIOLOGY	CELL BIOLOGY 12	CELL BIOLOGY 12 5.128 %
BIOTECHNOLOGY APPLIED MICROBIOLOGY	81	5.518 %		MECHANICS	MECHANICS 12	MECHANICS 12 5.128 %
MICROSCOPY	75	5.109 %	1 C C	COMPUTER SCIENCE	COMPUTER SCIENCE 10	COMPUTER SCIENCE 10 4.274 %
CRYSTALLOGRAPHY	70	4.768 %	1	ENVIRONMENTAL SCIENCES ECOLOGY	ENVIRONMENTAL SCIENCES ECOLOGY 10	ENVIRONMENTAL SCIENCES ECOLOGY 10 4.274 %
GENETICS HEREDITY	59	4.019 %	1.0	CRYSTALLOGRAPHY	CRYSTALLOGRAPHY 9	CRYSTALLOGRAPHY 9 3.846 %
COMPUTER SCIENCE	57	3.883 %	1.	ACOUSTICS	ACOUSTICS 8	ACOUSTICS 8 3.419 %
TELECOMMUNICATIONS	55	3.747 %	1.0	ENERGY FUELS	ENERGY FUELS 7	ENERGY FUELS 7 2.991 %
IMMUNOLOGY	53	3.610 %	1.00	MATHEMATICAL COMPUTATIONAL BIOLOGY	MATHEMATICAL COMPUTATIONAL BIOLOGY 7	MATHEMATICAL COMPUTATIONAL BIOLOGY 7 2.991 %
REMOTE SENSING	39	2.657 %	1.	TOXICOLOGY	TOXICOLOGY 5	TOXICOLOGY 5 2.137 %



Figure 9: Taxonomy and main disciplines resulting from the analysis of optronic biosensing (including photonic biosensing)

Engineering (15%) – Electronic and optical components of bio-sensing systems and integration issues. Topics include: On-chip integration of sensors, real-time processing of multi-parametric bioelectronic signals, CMOS IC/microfluidic hybrid systems for cell manipulation and electrochemical analysis, Micro-photodiodes arrays for imaging bio-events, 3D chip integration and packaging, field-Effect-Transistor-like, CMOS, MEMS devices for bio-sensing; design of portable, miniaturised, implantable devices

Instruments (14%) - Works on sensors, monitoring systems and metrology, bio-electronic instrumentation and practical (e.g. clinical) application of bio-electronic devices

Optics (14%) - Several distinct categories were identified of fabrication and optical functioning and properties of biosensors, application of biosensors

Physics (12%) - Fundamentals, concepts models, simulation, and new concepts related to biosensing

Materials Science (12%) - Materials and fabrication techniques for bio-sensing devices, 3D assembly, self-assembly, nano-particles, nano-tubes, nano-wires, emerging 2D materials nd graphene-related materials, e.g. graphene oxide, etc.

Chemistry (11%) – Efforts focused on the chemical modelling of the biorecognition events responsible of the functioning of the device

Science Technology (9%) covers a wide range of aspects and issues related to biosensor technology, health and biosecurity.

Biophysics (6%) - focus on understanding fluid dynamics or on understanding biological function from molecules to cells. Both experimental and theoretical methods are applied. Topics include instabilities in fluid flows, micro fluidics, biosensing and cell handling, mechanics of cell division and cell motility, mechanics of single DNA molecules, the use of statistical physics to describe single molecule biophysics experiments, or suggestion of biomimetic systems that solve specific problems.

Spectroscopy (4%) - Focus on surface plasmon resonance (SPR) biosensing

Bio-chemistry/Molecular biology (3%) - Research focused on the interaction between bio-molecules and solid surfaces. Examples include bio-molecule immobilization, electron transfer in biochemical reactions and between bio-objects and the solid surface. The latter is often referred as "bio-electronic interface". This definition is narrower than broader concept of bio-electronic interface as interaction between electronic devices and bio-objects

From the involvement of all those research disciplines and area it can be inferred a very broad distribution of groups/individuals/companies active in optronic biosensing.

4 RESEARCH ACTIVITIES

A proxy for activity, especially in academia, is publications. In order to assess optronic biosensing research activity, an analysis of publications was made using the Science Citation Index ExpandedTM (SCIE), available through the Web of Science[®].

Publications that contained the words specified below in their title or abstract were identified.

The total number of papers with "**Optoelectronic biosensor"** is 234, with the following figures. Figure 10 shows the number of publications by year. The availability of a large variety of new or advanced materials has also contributed to the improvement of the general performance of optoelectronic sensors and of their design flexibility. Looking at the scientific literature, it clearly appears that in the recent years there has been an increasing number of journals and magazines dealing with the subject of sensors, with large room dedicated to optical and optoelectronic devices. Every year, published papers propose a large number of novel configurations and applications. The number of papers per year increased markedly in 2014 and large has continued to grow. Moreover, the number of citations to the papers identified has increased exponentially (Figure 10b). Because many papers related to optronic biosensing do not use the term in the title or abstract, the absolute number of papers underestimates the actual level of activity; however, it is clearly increasing over time, indicative of an area of expanding activity.



Figure 10 Publications per year with the keyword "optronic biosensor"

Authors are very spread with a share < 5%.

The geographical distribution of the location of the authors' research institutions is as indicated in the below, which suggests that, although U.S. authors have published more papers than authors from any other, the centre of activity is in Europe (50% of publications), followed by the United States (\sim 21%) and Asia (\sim 20%).

USA	27	21.260 %	
PEOPLES R CHINA	25	19.685 %	
GREECE	12	9.449 %	
GERMANY	10	7.874 %	
INDIA	8	6.299 %	
SPAIN	8	6.299 %	
BRAZIL	7	5.512 %	1 (A)
NETHERLANDS	7	5.512 %	10 A
POLAND	6	4.724 %	1.00
SOUTH KOREA	6	4.724 %	1.
FRANCE	5	3.937 %	1.00
ISRAEL	5	3.937 %	1.
ITALY	5	3.937 %	1.00
TAIWAN	5	3.937 %	1.00
UKRAINE	4	3.150 %	1.00
DENMARK	2	1.575 %	1
JAPAN	2	1.575 %	1
MALAYSIA	2	1.575 %	1.
MEXICO	2	1.575 %	1
NORTH IRELAND	2	1.575 %	1.
PORTUGAL	2	1.575 %	1
SAUDI ARABIA	2	1.575 %	1
SINGAPORE	2	1.575 %	1.00
SWITZERLAND	2	1.575 %	1

The top 25 Institutions in Optoelectronic (Optronic) biosenors are identified as follow:

NCSR DEMOKRITOS	11	4.701 %	1.00
JOBST TECHNOL GMBH	6	2.564 %	1
NATIONAL ACADEMY OF SCIENCES UKRAINE	6	2.564 %	1
CONSEJO SUPERIOR DE INVESTIGACIONES CIENTIFICAS CSIC	5	2.137 %	1
WAGENINGEN UNIVERSITY RESEARCH CENTER	5	2.137 %	1
CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE CNRS	4	1.709 %	- E
CONSIGLIO NAZIONALE DELLE RICERCHE CNR	4	1.709 %	1
FRAUNHOFER GESELLSCHAFT	4	1.709 %	1
HEBREW UNIVERSITY OF JERUSALEM	4	1.709 %	1
TEXAS A M UNIVERSITY COLLEGE STATION	4	1.709 %	1
TEXAS A M UNIVERSITY SYSTEM	4	1.709 %	1
UNIVERSITY OF CALIFORNIA SYSTEM	4	1.709 %	1
CSIC	3	1.282 %	1
HEBREW UNIV JERUSALEM	3	1.282 %	- E
LASHKARYOV INSTITUTE OF SEMICONDUCTOR PHYSICS	3	1.282 %	1
NATIONAL TSING HUA UNIVERSITY	3	1.282 %	1
NATL TSING HUA UNIV	3	1.282 %	1
RIKILT WAGENINGEN UR	3	1.282 %	1
STATE UNIVERSITY SYSTEM OF FLORIDA	3	1.282 %	1
THETAMETRISIS SA	3	1.282 %	1
UNITED STATES DEPARTMENT OF DEFENSE	3	1.282 %	1
UNIV WARSAW	3	1.282 %	1
UNIVERSIDADE NOVA DE LISBOA	3	1.282 %	1
UNIVERSITY OF ATHENS	3	1.282 %	1
UNIVERSITY OF WARSAW	3	1.282 %	1

Among the highest cited paper in optronic sensing in the last 10 years with a citation number >30 we have the following papers, showing a broad variety of topics, mainly materials-oriented and not predominance of a particular Country and/or group.

TITLE	AUTHORS	JOURNAL	COUNTRY
Lanthanide-Doped Nanocrystals:	Wang, Guofeng; Peng,	ACCOUNTS OF CHEMICAL	China
Synthesis, Optical-Magnetic Properties,	Qing; Li, Yadong	RESEARCH, 4, 322-332 (2011)	
and Applications			
Towards integrated and sensitive surface	Hoa, X. D.; Kirk, A.	BIOSENSORS &	Canada
plasmon resonance biosensors: A review of	G.; Tabrizian, M.	BIOELECTRONICS, 23, 151-160	
recent progress		(2007)	
Biomolecule-nanoparticle hybrid systems	Willner, Itamar;	BIOELECTROCHEMISTRY, 70, 2-11	Israel
for bioelectronic applications	Willner, Bilha; Katz,	(2007)	
	Eugenii		
Narrow bandgap colloidal metal	Kershaw, Stephen V.;	CHEMICAL SOCIETY REVIEWS	China
chalcogenide quantum dots: synthetic	Susha, Andrei S.;	42, 3033-3087 (2013)	
methods, heterostructures, assemblies,	Rogach, Andrey L.		
electronic and infrared optical properties			
Handheld high-throughput plasmonic	Cetin, Arif E.; Coskun,	LIGHT-SCIENCE &	USA
biosensor using computational on-chip	Ahmet F.; Galarreta,	APPLICATIONS, 3, e122 (2014)	
imaging	Betty C.; et al.		
A plasmonic biosensor array by block	Shin, Dong Ok; Jeong,	JOURNAL OF MATERIALS	South Korea
copolymer lithography	Jong-Ryul; Han, Tae	CHEMISTRY, 20, 7241-7247 (2010)	
	Hee; et al		
Optoelectronic properties of	Pita, Marcos; Kraemer,	ACS NANO, 2 2160-2166 (2008)	Germany
Nanostructured Ensembles Controlled by	Melina; Zhou, Jian; et		Spain
Biomolecular Logic Systems	al.		USA

The programs supporting fundamental science and engineering research on devices and methods for measurement and quantification of biological analytes are distributed as shown in Fig. 11



Figure 11: Main funding agencies supporting research and engineering in optoelectronic biosensing

5 OPTRONIC SENSORS MAINLY FOR DEFENCE and SECURITY SECTOR

The challenges related specifically to sensor technologies and proposed technologies are shown below and have been compiled using various references [4,5]: ISTAR (intelligence, surveillance, target acquisition and reconnaissance) is a hugely relevant technology strategy for sensors in the defence and security industry, these will involve technologies such as THz, CCD, CMOS, IR and microwave imaging. The inclusion of intelligence into the ISTAR strategy requires more than simply sensing something, it requires turning the data into information for better decision-making and strategy formation. This will require develop ING its skills in backend processing - ICT, statistical and mathematical approaches such as machine vision, risk and uncertainty quantification and management.

Overview of current challenges and technologies in the defence and security market

CHALLENGE	SENSOR TECHNOLOGY
Significant increase in effective range for target detection and identification – whilst operating in difficult environments with scene clutter and noise	CCD / CMOS Spectroscopy
Increase sensitivity of threat detection – trace amount of substances or detection of low profile/camouflaged UAVs etc.	 Biosensors Radiation detectors Spectroscopy
Deliver significant increase in field of view – whilst retaining high resolution	CCD / CMOS
Provide stand-off detection and recognition of targets – through obsourants and materials, debris, fog, adverse weather, day or night	IR sensors X-ray detectors
Sensing technologies to meet the trends of a busier battlefield	IR sensors
Increase the variety of detectable threats, with multiple sensors on one platform	 Biosensors Spectroscopy Lab-on-a-ohip
The importance of on-site processing for real-time intelligence, increasing the generation of information not just data	Integrated processing technology
Imaging round corners	IR sensors X-ray detectors
Non-contact sensors for the evaluation of defence materials	Ultrasound
Advanced EM systems for passenger and baggage screening	 THz imaging X-ray tomography γ-ray soreening
Smart sensors (where am I, what am I looking at? Automated ID) Detection, recognition and identification. Situation awareness Pattern of life generation 	 GPS RF Digital Compasses
 SWAP challenges. Unique challenges for ADS sensors Size: for covert operations, sensor sywstems should be discrete. Weight: may need deployment anywhere, must be easily transported. Power: minimizing communication, could be remote locations and must reduce burden on SATCOM 	 MEMS Energy harvesting technologies Disruptive technologies in material science.
Due to the potentially dangerous situation these systems will be in, ease of use is essential.	
As terrorists exploit military hardware and commercially-sourced technology, we require disruptive technologies to regain the advantages	 RF Quasi optical EO

6 RESEARCH PLAYERS in GRAPHENE and 2D MATERIALS BIOSENSORS

TWINFUSYON aims at exploring the potential of graphene and other 2D materials in optronic biosensing; therefore, we have extended the analysis to graphene and other 2D materials biosensors. Being in fact the extreme case of surface science, 2D materials possess the highest surface-to-volume ratio. This feature makes them extremely prospective for sensors applications, where the interface occurring phenomena define the device performance [6].

Therefore, the number of reports as papers devoted to biosensors using 2D materials as a transducer has been constantly growing since the graphene discovery, as is evidenced by a search on ISI Web of Science as shown Figure 12.



Figure 12. Dynamics of the reports on 2D materials application as a transducer material for biosensors during 2005–2015. [Source: Isi Web of Science]

Such progress is due to extensive graphene development as a material, with graphene biosensors", resulting in 3664 items in Isi Web of Science and only a small number of 412 reports is devoted to biosensors based on non-graphene 2D materials, which includes mainly US and China Universities and Institutes. The tables below report the top 25 Countries active in "graphene and 2D materials biosensors", which have at least 10 records in the field.

PEOPLES R CHINA	2098	60.270 %	
USA	278	7.986 %	
INDIA	254	7.297 %	
SOUTH KOREA	226	6.492 %	
IRAN	193	5.544 %	1
TAIWAN	128	3.677 %	1
MALAYSIA	78	2.241 %	1
AUSTRALIA	70	2.011 %	1
TURKEY	70	2.011 %	1
SINGAPORE	68	1.953 %	1
SPAIN	68	1.953 %	1
ENGLAND	47	1.350 %	1
JAPAN	40	1.149 %	1
CANADA	39	1.120 %	1
SAUDI ARABIA	37	1.063 %	1
FRANCE	36	1.034 %	1
GERMANY	36	1.034 %	1
ITALY	36	1.034 %	1
THAILAND	24	0.689 %	1
BRAZIL	22	0.632 %	1
ROMANIA	22	0.632 %	1
GREECE	19	0.546 %	1
PORTUGAL	19	0.546 %	1
POLAND	17	0.488 %	1
SWEDEN	15	0.431 %	1
CZECH REPUBLIC	13	0.373 %	

Making a ranking by Institutions/Universities, no EU universities are in the top 100 Institutions with a number of items > 10, indicating that this field is clearly dominated by China, US and Korea.

NA

The situation changes in the emerging "other 2D materials biosenors" as shown by the following list, listing in the top 10, the CNRS (France) as 4th and CNR (Italy) as 10th.

Field: Institutions	Record Count	% of 412	Bar Chart
NANYANG TECHNOL UNIV	13	3.155 %	1
NANYANG TECHNOLOGICAL UNIVERSITY	13	3.155 %	1.00
VYANG TECHNOLOGICAL UNIVERSITY NATIONAL INSTITUTE OF EDUCATION NIE SINGAPORE	13	3.155 %	1.00
CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE CNRS	12	2.913 %	1.
STATE UNIVERSITY SYSTEM OF FLORIDA	10	2.427 %	1
CHINESE ACADEMY OF SCIENCES	9	2.184 %	1
UNIVERSITY OF CALIFORNIA SYSTEM	9	2.184 %	1
STATE UNIVERSITY OF NEW YORK SUNY SYSTEM	8	1.942 %	1
CHINESE ACAD SCI	7	1.699 %	1
UNIVERSITE PARIS SACLAY COMUE	7	1.699 %	1
CHINESE UNIVERSITY OF HONG KONG	6	1.456 %	1
HELMHOLTZ ASSOCIATION	6	1.456 %	1
NATIONAL UNIVERSITY OF SINGAPORE	6	1.456 %	1
NATL UNIV SINGAPORE	6	1.456 %	1
CONSIGLIO NAZIONALE DELLE RICERCHE CNR	5	1.214 %	1
COUNCIL OF SCIENTIFIC INDUSTRIAL RESEARCH CSIR INDIA	5	1.214 %	1
HARVARD UNIVERSITY	5	1.214 %	1
OSAKA PREFECTURE UNIVERSITY	5	1.214 %	1
SUNGKYUNKWAN UNIVERSITY	5	1.214 %	1
TSINGHUA UNIVERSITY	5	1.214 %	1
UNITED STATES DEPARTMENT OF DEFENSE	5	1.214 %	1
UNIV PARIS 11	5	1.214 %	1
UNIVERSITY OF PARIS SUD PARIS XI	5	1.214 %	1
AGENCY FOR SCIENCE TECHNOLOGY RESEARCH ASTAR	4	0.971 %	1
HARVARD UNIV	4	0.971 %	1
ISLAMIC AZAD UNIVERSITY	4	0.971 %	1
JILIN UNIVERSITY	4	0.971 %	1
AGENCY FOR SCIENCE TECHNOLOGY RESEARCH ASTAR	4	0.971 %	1
HARVARD UNIV	4	0.971 %	1
ISLAMIC AZAD UNIVERSITY	4	0.971 %	1
JILIN UNIVERSITY	4	0.971 %	1
LUND UNIVERSITY	4	0.971 %	1
MAX DELBRUCK CENTER FOR MOLECULAR MEDICINE	4	0.971 %	1
STANFORD UNIVERSITY	4	0.971 %	1
SUNGKYUNKWAN UNIV	4	0.971 %	1
UNIVERSITY OF FLORIDA	4	0 971 %	1
UNIVERSITY OF ILLINOIS SYSTEM	4	0.971 %	1
UNIVERSITY OF ROCHESTER	4	0.971 %	i.
UNIVERSITY OF SCIENCE TECHNOLOGY UST	4	0.971 %	1
UNIVITTINOIS	3	0 728 %	
UNIVERSIDADE FEDERAL DE SAO CARLOS	3	0.728 %	1
UNIVERSITE CONSTANTINE	3	0.728 %	1
	3	0 728 %	1
UNIVERSITY OF CALIFORNIA BERKELEY	3	0 728 %	1
UNIVERSITY OF CHINESE ACADEMY OF SCIENCES	3	0 728 %	
UNIVERSITY OF CRETE	3	0 728 %	1
UNIVERSITY OF ILLINOIS UPBANA CHAMPAIGN	3	0.728 %	1
	3	0.728 %	1
	3	0.720 %	1
	3	0.728 %	1
	3	0.720 %	1
	3	0.728 %	1
UNIVERSITY OF WASHINGTON SEATTLE	3	0.720 %	1
UNIVERSITE SYSTEM OF GEORGIA	2	0.720 %	1
AINYANG NORMAL UNIV	3	0.720 %	1

7 DESCRIPTION OF PLAYERS IN "PLASMON BIOSENSOR"

TWINFUSYON aims at exploring the potential of the surface plasmon resonance of plasmonic nanosystems in optronic biosensing; therefore, we have extended the analysis to "plasmon biosensor".

Surface plasmon resonance (SPR) biosensing [7,8] has been demonstrated in the past decade to be an exceedingly powerful and quantitative probe of the interactions of a variety of biopolymers with various ligands, biopolymers, and membranes, including protein:ligand, protein:protein, protein:DNA and protein: membrane binding. It provides a means not only for identifying these interactions and quantifying their equilibrium constants, kinetic constants and underlying energetics, but also for employing them in very sensitive, label-free biochemical assays [9-11], which is the topic and goal of the TWINFUSYON project.

In its high throughput SPR biosensing measurements can be made in array format with 120 interactions measured simultaneously. That is, 120 SPR binding and sensing curves can be measured simultaneously using SPR microscopy and a computer-interfaced video camera to probe the interactions of a protein with all 120 elements in a 10x12 array of spots on a sensor surface. [12]

"PLASMON BIOSENSOR" resulted in 6296 RESULTS, with the following distribution by Countries, showing that EU, with the various contributing Countries, is leading the field

USA	1338	21.252 %	
PEOPLES R CHINA	1078	17.122 %	
JAPAN	491	7.799 %	
SOUTH KOREA	380	6.036 %	
GERMANY	352	5.591 %	
ENGLAND	299	4.749 %	1.00
FRANCE	293	4.654 %	1.0
CANADA	276	4.384 %	1.00
TAIWAN	275	4.368 %	1.0
SWEDEN	272	4.320 %	1.00
ITALY	248	3.939 %	1.00
INDIA	247	3.923 %	1.00
SPAIN	221	3.510 %	1.00
AUSTRALIA	181	2.875 %	1.00
CZECH REPUBLIC	133	2.112 %	1.00
SWITZERLAND	120	1.906 %	1.
SINGAPORE	115	1.827 %	1
BELGIUM	104	1.652 %	1.
NETHERLANDS	100	1.588 %	1.00
IRELAND	74	1.175 %	1.00
TURKEY	71	1.128 %	1.000
AUSTRIA	69	1.096 %	1.
IRAN	67	1.064 %	1.
NORTH IRELAND	65	1.032 %	1
ISRAEL	64	1.017 %	1.00

In terms of Funding Agencies, the European Commission is after the National Science Foundation of China and of US.



Figure 13: Distribution of main funding agencies in plasmon (SPR) biosensors

It is a very positive result that analysing the 50 top Organisations, the statistics show that there are 9 European Institutes/Universities among the first 25, with a very good placing of CNRS and CNR in the top 10 Organisations active in the field.

CHINESE ACAD SCI	168	2.668 %	1
UNIV WASHINGTON	91	1.445 %	1
JILIN UNIV	82	1.302 %	1
NANYANG TECHNOL UNIV	71	1.128 %	1
UNIV UTAH	70	1.112 %	1
NORTHWESTERN UNIV	57	0.905 %	1
CNRS	56	0.889 %	1
NATL TAIWAN UNIV	56	0.889 %	1
SEOUL NATL UNIV	56	0.889 %	1
ZHEJIANG UNIV	55	0.874 %	1
CSIC	54	0.858 %	1
CNR	53	0.842 %	1
KYUSHU UNIV	53	0.842 %	1
UNIV FLORENCE	51	0.810 %	1
BIACORE AB	48	0.762 %	1
QUEENS UNIV BELFAST	48	0.762 %	1
TSINGHUA UNIV	47	0.747 %	1
UNIV TORONTO	45	0.715 %	1
OSAKA UNIV	44	0.699 %	1
CITY UNIV HONG KONG	43	0.683 %	1
UPPSALA UNIV	43	0.683 %	1
ACAD SCI CZECH REPUBLIC	42	0.667 %	1
DUBLIN CITY UNIV	42	0.667 %	1
GEORGIA STATE UNIV	42	0.667 %	1
NATL INST ADV IND SCI TECHNOL	41	0.651 %	1
UNIV TOKYO	41	0.651 %	1
LINKOPING UNIV	40	0.635 %	1
UNIV ILLINOIS	40	0.635 %	1
YONSEI UNIV	40	0.635 %	1
ODANELELD UNIV	20	0.040.0/	

Jiri Homola, (<u>http://www.ufe.cz/cs/jiri-homola</u>) Professor of Physics, at the Institute of Photonics and Electronics, Academy of Sciences of the Czech Republic – Prague is the author with the highest number of records in this field and the most cited papers and reviews on the topic.

He has been contributing to SPR Core biosensing together with Prof Charles T. Campbell, from Chemistry Department of Washington University (<u>https://depts.washington.edu/chem/people/faculty/campbell.html</u>) and has developed widely-used data-analysis techniques for SPR sensing.

The SPR microscope follows in many ways the design by Prof. W. Knoll (Director of Director, Max-Planck-Institut für Polymerforschung, Mainz first and then Managing director of the Austrian Institute of Technolog https://www.ait.ac.at/fileadmin/cmc/downloads/New_Ueber_das_AIT/CV_Knoll.pdf) [13].

As for the SPR (surface plasmon resonance) –biosensors market analysis, global surface plasmon resonance devices market is estimated to account for US\$1,110.4mn by the end of 2025, owing to increasing application in drug discovery segment for drug-cell interaction analysis [14].

Increasing adoption of label-free detection techniques over labelled detection techniques due to costeffectiveness, availability of versatile products in the SPR market for refined outcomes and coupling of complementary techniques with SPR to enhance specificity of the test are major factors leading to increased demand for surface plasmon resonance. This in turn is fuelling growth of the global surface plasmon resonance market. Emergence of alternative techniques for detection of protein and high prices of products are few factors expected to hamper growth of the global surface plasmon resonance market to a certain extent. Major trends in the surface plasmon resonance market include increased adoption of microfluidics technique to lower consumption of reagent, introduction of advanced imaging software for analysis of surface plasmon resonance and consistent investment in research and development by various companies.

Key Market Players

Although the most popular commercial instruments for SPR biosensing are those with trademark Biacore [15], other key market players are GE Healthcare, Bio-Rad Laboratories, Inc., Biosensing Instruments, Horiba Ltd. and Reichert Technologies (acquired by Ametek, Inc.). Major players in surface plasmon resonance market focus on enhancing their global and regional presence through introduction of novel products and strategic operational expansion. GE Healthcare was the market leader in 2014, owing to a broad product portfolio. Bio-Rad Laboratories has discontinued manufacture of ProteOn XPR-36 - an imaging system used for analysis of biomolecular interactions.

A full list of the main SPR biosensors suppliers can be found at <u>https://www.sprpages.nl/suppliers</u>. Therefore, it is not repeated here.

A round-up of the SPR instruments currently available can be found at <u>https://www.sprpages.nl/instruments</u>. The instruments differ in their way of using the technology and design of bringing the interactants in contact which each other.

Overall, an interesting website providing several tools and information about SPR biosensors is <u>https://www.sprpages.nl</u>.

8 RESEARCH PLAYERS in SPR GRAPHENE and other 2D-MATERIALS BASED BIOSENSORS

There is interest within TWINFUSYON in assessing the potential of and increasing the knowledge and capacity in novel biosensors coupling the concept of graphene and other 2D materials with surface plasmon resonance concept. Therefore, we have analysed the merged field of "SPR graphene biosensors".

The Isi Web of science database provided only 224 entries, with the activity started in 2010.

The field is dominated by China (50%) followed by India and US, with a few EU Countries with a share between 6% (France) and 1% as shown in the following table.

Among the top 50 Institutions, only University of Lille appears as EU representative as shown below COUNTRIES INTITUTES/UNIVERSITIES

Countries/Territories	Record Count	% of 224	Bar Chart				
PEOPLES R CHINA	79	35.268 %					
CHINA	33	14.732 %					
INDIA	32	14.286 %					
USA	20	8 929 %					
FRANCE	12	5 357 %		JILIN UNIV	15	6.608 %	1.1
	12	5.357 %	1	JILIN UNIVERSITY	14	6.167 %	
SOUTHKORLA	12	5.557 %		CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE CNRS	10	4.405 %	1.1
AUSTRALIA	10	4.464 %	- 10 C	IIT BHUBANESWAR	9	3.965 %	1.0
TAIWAN	10	4.464 %	- 10 C	UNIVERSITE DE VALENCIENNES ET DU HAINAUT CAMBRESIS	9	3.965 %	1.0
MALAYSIA	9	4.018 %	1.00	UNIVERSITE LILLE NORD DE FRANCE COMUE	9	3.965 %	1.0
SINGAPORE	8	3.571 %	1.00	UNIVERSITY OF LILLE I	9	3.965 %	1.0
ΙΤΑΙ Υ	7	3 125 %	1	CHINESE ACADEMY OF SCIENCES	8	3.524 %	1.0
SDAIN	6	2,670,9%	1	DEAKIN UNIVERSITY	7	3.084 %	1.0
SPAIN	0	2.079 %	1	INDIAN INST TECHNOL BHUBANESWAR	7	3.084 %	1.0
IRAN	5	2.232 %	1	MOTILAL NEHRU NATIONAL INSTITUTE OF TECHNOLOGY	7	3.084 %	1.0
CANADA	4	1.786 %	1	NANYANG TECHNOLOGICAL UNIVERSITY	7	3.084 %	1
EGYPT	4	1.786 %	1	UNIVERSITY NATIONAL INSTITUTE OF EDUCATION NIE SINGAPORE	7	3.084 %	
ENGLAND	4	1.786 %	1	NATIONAL TAIWAN NORMAL UNIVERSITY	1	3.084 %	
GERMANY	4	1 786 %	1		6	2.643 %	
	4	1.700 %		INDIAN INSTITUTE OF TECHNOLOCY IIT	5	2.203 %	
ISRAEL	4	1.700 %	1		5	2.203 %	1.1
SWITZERLAND	4	1.786 %	1		5	2.203 %	1.1
UK	4	1.786 %	1	NATI TAIWAN NORMAL UNIV	5	2 203 %	i.
BANGLADESH	3	1.339 %	1	SHENZHEN UNIV	5	2.203 %	1
CZECH REPUBLIC	3	1.339 %	1	SHENZHEN UNIVERSITY	5	2.203 %	1
GREECE	3	1 339 %	1	COUNCIL OF SCIENTIFIC INDUSTRIAL RESEARCH CSIR INDIA	4	1.762 %	1.00
ROMANIA	3	1 339 %	1	ECOLE POLYTECHNIQUE FEDERALE DE LAUSANNE	4	1.762 %	1
ROWANIA	5	1.533 %		NANKAI UNIVERSITY	4	1.762 %	1
BRAZIL	2	0.893 %	1	NANYANG TECHNOL UNIV	4	1.762 %	1.00
INDONESIA	2	0.893 %	1	SHANDONG UNIVERSITY	4	1.762 %	1

Overall, the research efforts in Plasmon Graphene (and other 2D –materials) biosensors, in terms of technology are distributed as shown in Figure 14 compared to the other technologies



Figure 14: Distribution of "graphene and other 2D-materials biosensor" technologies

9 DESCRIPTION OF MARKET PLAYERS/MARKET SHARE

KEY INDUSTRIAL PLAYERS

Internationally, the biosensor market is dominated by medical and healthcare sectors, comprising most of its estimated total market value of \$23 billion by 2020 while the present market is around \$12.8. The key players in this market are international giants such as:

Roche Diagnostics	Abbott Diagnostics	Bayer Diagnostics	Biacore	
Hoffmann-La Roche	Abbott Point Of Care Inc	Lifesensors Inc	M-Biotech	
Biosensors	Dupont, Lifesensors	Siemens Healthcare	Nova Biomedical	
International Pte. Ltd	Inc			
Medtronic Diabetes	ACON Laboratories	Medtronic Inc	Agamatrix Inc	
	Inc			
Bio-Rad Laboratories	Ercon Inc			
Inc				

which account for more than 60% of global sales [16]. These companies have grown by company acquisition or licencing of technology, which is largely generated by SMEs. The remaining sectors include food toxicity, environmental, industrial, agriculture and others.

With specificity of optronic/optical label-free biosensing, the major players in the market are

U.S.					
Ametek, Inc.	Bio-Rad Laboratories, Inc.	BiOptix	General Electric Corporation Healthcare and Life Sciences	Danaher Corporation	
Corning, Inc	Pall Corporation	PerkinElmer			
EU					
Attana AB (Sweden)	La Roche (Switzerland)	Cambridge LifeSciences Ltd UK	Innovative Biosensors Inc	Sigma Aldrich Corporation	
THALES Group					

A full list of companies active in optoelectronic sensing can be found at:

 $\underline{http://www.sens2b-sensors.com/directory/sensor-technologies-measurement-principles/optoelectronic-sensors/}$

Internationally, the optronic sensors market is dominated by multinational companies, and the largest defence spenders: North America and Europe have well developed domestic CBRNe industries, which makes them self-reliant. Companies of note are: Thales Group (France) Argon Electronics, FLIR Systems, Blucher GmbH, Federal Resources and Smiths Detection [17].

The size of the companies involved in the aerospace, defence and security sensor/biosensor market are predominantly medium or large (approximately 2/3) companies (Figure 15 (a)) this dominance of the larger players is confirmed with reference to the top 10 companies (in terms of revenue): QinetiQ, Selex, Ultra Electronics PMES, Astrium Ltd, TT Electronics Plc., BAE Systems, Honeywell, Goodrich, e2v Technologies and Meggit who possess 77% of the sensor market.



Figure 15. (a) Size of the companies in the defence and security sensor market and (b) Shape of the supply chain in the defence and security sensor sector

10 PATENTING

A quantitative analysis of innovation in the optronic biosensors community can be inferred through the IPO patent landscape analysis of sensor systems. Total global patents for the sensors in bio science sector are shown in Figure 16 and indicate the main European Countries behind the USA and Japan.





A total of 248 patents with the word "optronic" in the title and/or abstract resulted from the search. However, those patents, where THALES Group (France), is one of the major applicants refers to generally sense for the military, defence and biodefence (see paragraph 5). The full list of patents is available on Isi Web of Science; here in the Annex 2, a selection is reported of thoe more of relevance for this context.

Noteworthy a relevant patent has been applied from Prof. R. Martins <u>of CENIMAT - Universidade NOVA</u> <u>de Lisboa</u> [http://www.cenimat.fct.unl.pt/people/rodrigo-ferrao-paiva-martins], who proposed the integration of this biodetection method into a sensing platform comprising a broad band color sensitive amorphous/nanocrystalline silicon photodetector and a laser (high intensity light source) (Portugal Patent no. 103561; South Africa Patent no. 2009/01612, Ref.: PTI-ZA 40004/09; Europe: PCT/IB2007/053614.

Another relevant patent worthy to be mentioned in this context is:

Integrated optoelectronic silicon biosensor for the detection of biomolecules labeled with chromophore groups or nanoparticles

US 20050003520 A1

ESTRATTO

An integrated optoelectronic silicon biosensor that can detect biomolecules by the change of the optical coupling between the integrated light source and the integrated detector that is caused by the binding of the appropriately labeled analytes onto the recognition molecules, that have been previously immobilized onto the integrated optical fiber that connects the optical source with the detector. The device contains the optoelectronic silicon chip and its biological activation. The optoelectronic chip is realized following integrated circuits fabrication methods so as the light source, the detector and the optical fiber, that optically couples the light source with the detector, to be monolithically integrated on the same silicon substrate. The biological activation of the chip is performed through physicochemical modification of the chip surface in order to permit immobilization of the recognition biomolecules onto the optical fiber surface. The biomolecules to be determined (proteins or oligonucleotides) are labeled with chromophore groups or nanoparticles or enzymes and after their coupling by the recognition biomolecules reduce the optical coupling between the light source and the detector providing a measure of their concentration.

11 CONCLUSIONS

Optronic biosensing is gaining attention. Integration and demonstration gaps exist and are blocking the value chain through academia, SMEs, systems integrators and instrumentation companies to endusers. The EU has significant presence at each stage of the value chain but has not been able to overcome the skills shortages and risk aversion that is preventing the component and sub-system level technology becoming sensor system solutions, positioning the EU groups behind China and US

As diagnostic optronic biosensing devices continue to be kept smaller, more portable, more energy efficient, and cheaper, their use in bio-medical applications will continue to grow. We can also expect that optronic biosensors will significantly contribute to intelligent information systems in stationary and mobile applications.

The advances of novel materials like graphene and other 2D-materials are also having an effect on optronic biosensors, and it is likely that integrated nanoscale sensors will revolutionize health care, climate control, and detection of toxic substances

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NOTE: All the information and list of groups are publically available on the web. No confidential information is disclosed in this report

ANNEX 1: LIST OF MAJOR BIOSENSORS & BIOELECTRONICS COMPANIES/LABS IN EUROPE

- Biocrates
- Janssen Diagnostics (J&J)
- Anagnostics
- ViennaLab Diagnostics
- Aposcience
- Euro Diagnostica
- Immunodiagnostic Systems
- Biocartis
- Dako (Agilent)
- Genclis
- Orion
- Trinity Biotech
- Novartis Diagnostics
- Abbott
- AbbVie
- CenterVue
- DiaSorin
- Ferrer
- Grifols
- ProteoMediX
- Igen Biotech
- Roche
- Immunovia
- InDex Pharmaceuticals
- Caris Life Sciences
- Randox Laboratories
- Abcodia
- vantix DIAGNOSTICS
- Axis-Shield
- BioReliance (SAFC)
- Oxford Biodynamics
- Quotient
- BioReliance (SAFC)
- Atlas Genetics
- Epigenomics.
- Seegene
- Immunodiagnostic Systems
- Altona Diagnostics
- Qiagen
- HUMAN Diagnostics
- Curetis
- DiaSys Diagnostic Systems
- Exosome Diagnostics
- EKF Diagnostics
- BioNTech
- Orgentec Diagnostics
- Aesku Diagnostics
- Oncolead
- WILEX
- Biosensor Srl (Italy)

ANNEX 2: LIST OF MAJOR BIOSENSORS & BIOELECTRONICS LABORATORIES WORLDWIDE

- Universal Biosensors
- Oncocyte (BioTime)
- US Diagnostics
- Atomo Diagnostics
- Nodexus
- Avant Diagnostics
- Celera (Quest Diagnostics)
- Genoptix (Novartis)
- Exogen Biotechnology
- **BioGenex**
- GenMark Diagnostics
- Teco Diagnostics
- Agena Bioscience
- bioTheranostics (bioMerieux)
- Hycor Biomedical
- Biomerica
- Vortex Biosciences
- Target Discovery
- ImmunoScience
- **GRAIL**
- Nanomedical Diagnostics
- Eurogentec
- GenBio
- Inova Diagnostics (Werfen)
- Helix
- Crescendo Bioscience (Myriad Genetics)
- Miroculus
- Scantibodies Laboratory
- GeneMed Biotechnologies
- Cellular Engineering Technologies (CET)
- Olympia Diagnostics
- Almen Laboratories
- Medix Biochemica
- Matrix-Bio
- PDx Biotech
- **BioGenex**
- o Nippon Kayaku
- Enterome Biosciences
- Alper Biotechnology
- Nuclea Biotechnologies
- vantix DIAGNOSTICS
- MP Biomedicals
- Progenika
- **Bionique Testing Laboratories**
- **Biomed Diagnostics**
- EDP Biotech
- **RJS Biologics**
- Vitruvian Biomedical
- Shine Medical Technologies

Universities Associated with Biosensors Research in Europe

- Departamento de Ciência dos Materiais, Faculdade de Ciências e Tecnologia, Universidade Nova de Lisboa and CEMOP-UNINOVA
- Lehrstuhl für Photonik und Optoelektronik Department für Physik und CeNS Ludwig-Maximilians-Universität München
- Organic Semiconductor Centre, SUPA School of Physics & Astronomy University of St Andrews
- Centre for Advanced Sensor Technologies, Bath University, UK
- Humboldt Universität zu Berlin, Germany
- University of Twente, Netherlands
- Nanobioelectronics & Biosensors at *Institut Català de Nanociencia i Nanotecnologia* (<u>ICN</u>), situated at Autonomous University of Barcelona
- EPFL Valais Walli, Switzerland
- Friedrich Schiller University Jena, Germany
- Institute of Health Care Engineering with European Testing Center of Medical Devices at Graz University of Technology, Austria.
- Swansea University, UK
- University of Glasgow, The Advanced Medical Diagnostics and Lab-on-aChip
- Imperial College London
- Institute of Analytical Chemistry, Chemo & Biosensors, University of Regensburg
- Optical Biosensors & Biophotonics, University of Southampton
- University of Cambridge
- Leibniz Institute of Photonic Technology, Germany
- Technishe Universitat Brunschweig, Germany
- ANSES-Laboratory of Fougeres, France
- Center for Pharmaceutical Engineering (PVZ)-Institute of Micro-technology (Germany)
- Universite Catholique de Louvain, Belgium
- Austrian Institute of Technology, Austria
- University of Technology of Troyes, France
- Centro de Investigación Cooperativa en Biomateriales CIC biomaGUNE, Spain
- University Potsdam and Fraunhofer Branch, Bioanalysis and Bioprocesses, IZI-BB, Potsdam, Germany
- Institute of Bio-Sensing Technology (IBST)

Note: The list is not comprehensive and is not intended to include all major groups involved in biosensing. It includes Institutions and groups that have been identified on the basis of KeyNotes, and Plenary talks at biosensing international conferences with topics related to optoelectronic biosensors.

ANNEX 3: LIST OF MAJOR COMPANIES ASSOCIATED WITH BIOSENSORS RESEARCH WORLDWIDE

- Abaxis
- Abbott Point of Care (i-STAT)
- ACAMP (canada)
- ACEA Bioscience
- Achira Labs
- Adhesives Research
- Advanced Liquid Logic
- Advion
- Affymetrix
- AgilentArcxis Biotechnologies
- Biodetection instruments
- BioMicro Systems
- Biosurfit
- Boston Microfluidics
- Cambridge Biomagnetics
- CEA Laboratory of Electronics and Information Technologies (LETI)
- Debiotech
- DEOS Labs
- DNA Electronics
- Fluidmedix
- Fluidware Technologies
- Fluxion Biosciences
- GE Healthcare
- GeneWave
- Grace Bio-Labs
- Habsel
- Helicos Bioscences
- IMT (Innovative Micro Technology)
- Incept BioSystems
- Kryoz Technologies
- LC Sciences
- Maxwell Sensors
- MBio Diagnostics
- MEMSCAP
- MicroCHIPS
- Microflexis
- Microflow Laboratory
- Microfluidic Imaging
- Microfluidic ChipShop
- MicroLab Devices
- Nanion Technologies
- Nanobiosym
- Nanopoint Imaging
- Optotrack
- Pathogenetix
- Proteus Biomedical
- Rheonix
- Rogue Valley Microdevices
- Samsung
- SensLab
- Shrink Nanotechnologies

- Silicon Biosystems •
- Spectrafluidics •
- Stanford Microfluidics Foundry
- T2 Biosystems
- Technobiochip
- Tronics Microsystems
- Wasatch Microfluidics
- Weidmann Plastics
- Xennia
- YMC
- Z-microsystems

ANNEX 4: LIST OF "OPTRONIC" PATENTS

<u>Movement detection device for use in</u> optronic system, has masks partially obscuring sensitive areas of mega-pixels of photodiode, respectively, where each mask includes opaque zone and transparent zone that are alternatively arranged

Patent Number: FR3023957-A1; WO2016008959-A1; FR3023957-B1; CA2954908-A1; EP3170205-A1 Patent Assignee: SAGEM DEFENSE SECURITE; SAFRAN ELECTRONICS & DEFENSE Inventor(s): BOUSQUET M.

<u>Method for processing movements of high frequencies in e.g. camera, involves transmitting values</u> representative of movement of images to movement compensation device so that device implements feedback to compensate for movement of images

Patent Number: FR3023956-A1; WO2016008911-A1; CA2955368-A1; EP3170303-A1 Patent Assignee: SAGEM DEFENSE SECURITE; SAFRAN ELECTRONICS & DEFENSE Inventor(s): REYMOND G.

<u>Vertical cavity surface emitting laser module, has set of exit reflectors that is common to set of laser</u> <u>diodes of module and is formed by photonic crystal membrane, and coupling discontinuity provided</u> <u>between set of laser diodes</u>

Patent Number: FR3036004-A1 Patent Assignee: CENT NAT RECH SCI; ECOLE CENT LYON; UNIV LYON 1 BERNARD CLAUDE; INSA INST NAT SCI APPLIQUEES LYON Inventor(s): LETARTRE X; VIKTOROVITCH P.

Method for assembling single-mode polymer waveguide connector for ribbon cables for optical interconnects in e.g. fiber-optic communication application, involves removing lid after bonding alignment features of waveguide to ferrule features Patent Number: US9417404-B1 Patent Assignee: INT BUSINESS MACHINES CORP Inventor(s): BARWICZ T; NUMATA H; TAIRA Y.

<u>Method for detection of surface contamination by particles moving in open air in control area in</u> <u>industrial sector, involves carrying out image processing of analysis surface at points to detect</u> <u>particles on collection surface</u>

Patent Number: FR3032036-A1; WO2016120276-A1 Patent Assignee: CEA COMMISARIAT LENERGIE ATOMIQUE & ENER; CNRS CENT NAT RECH SCI; UNIV AIX-MARSEILLE; WINLIGHT SYSTEM; UNIV AIX MARSEILLE AMU Inventor(s): ESCOUBAS L; GODEFROY P; PALAIS O; et al.

Elongate shape workpiece for use in field of portable optronic equipment, has embossed mesh that is integrally formed with internal face of side walls of workpiece and is configured to support side walls Patent Number: FR3030321-A1 Patent Assignee: SAGEM DEFENSE SECURITE Inventor(s): YANTIO G; RIOU J; CAILLIE J; et al.

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Method for detecting defective pixels as part of image-processing procedure in e.g. optronicsystem, involves associating pixel with classification value representing defective pixel when threshold is reached for number of detections Patent Number: FR3028376-A1; WO2016071461-A1 Patent Assignee: SAGEM DEFENSE SECURITE

Inventor(s): MALTESE D; OUDINOT M; PERDRIAU Q; et al.

<u>Coating a surface comprises depositing at least two populations of nanoparticles of different sizes on a surface to be treated, and crosslinking the surface coated nanoparticles with an alkoxide of transition metal in an acid solution</u>

Patent Number: WO2015177229-A2; WO2015177229-A3; CA2949412-A1; EP3145642-A2; US2017120294-A1 Patent Assignee: CNRS CENT NAT RECH SCI; SURFACTIS TECHNOLOGIES

Inventor(s): PORTET D; LEFEVRE N; BEJANIN S; et al.

<u>Method for maintenance of e.g.</u> optronic <u>equipment</u>, involves determining optimal date of maintenance <u>based on state of equipment and aggregate time of use of equipment by minimizing mathematical</u> expectation of time cost function

Patent Number: WO2015091752-A1; FR3015734-A1; EP3084692-A1; US2016314405-A1; FR3015734-B1 Patent Assignee: THALES; INST NAT RECH INFORMATIQUE & AUTOMATIQUE; THALES SA Inventor(s): BIHANNIC D; BAYSSE C; DE SAPORTA B; et al.

<u>Method for generating software code for parallelization of associative function in e.g.</u> optronic field, involves repeatedly applying associative function from input datum using software program, and synchronizing tasks of same group

Patent Number: FR3014221-A1; FR3014221-B1 Patent Assignee: THALES; THALES SA Inventor(s): DENEL S; HEYMAN J.

<u>Spectral-encoded polarization microscope for use in optronic laboratories for visualizing moving living specimen, has polarizer coupled to retarder, and capture device coupled to polarizer and capturing light passing through polarizer</u>

Patent Number: WO2014200928-A1; DE112014002748-T5; US2016154229-A1; JP2016521866-W Patent Assignee: UNIV TEXAS SYSTEM Inventor(s): POENIE M; MILNER T; YIN B; et al.

<u>Spectral separation component for multi-spectral single pupil</u> optronic system, has rear face convex along generatrix defined by cylindrical surface in fixed direction, where generatrix of cylindrical surface is parallel to edge of dihedral

Patent Number: FR2998977-A1; WO2014086649-A1; FR2998977-B1; EP2929379-A1; US2016216525-A1; EP2929379-B1

Patent Assignee: THALES; THALES SA Inventor(s): FORESTIER B.

Power laser device i.e. fiber laser device for use in e.g. industrial applications, has spatial phase modulator i.e. LCD modulator, supplied with digital hologram to diffract signal beam in order of one at input of amplifying fibers Patent Number: EP2688158-A2; FR2993717-A1; FR2993717-B1; EP2688158-A3 Patent Assignee: THALES; THALES SA Inventor(s): LALLIER E.

Laser device for e.g. scientific applications, has spatial phase modulator supplied with hologram to diffract signal beam at input of fibers, where modulator comprises refresh rate phase law characteristics Patent Number: EP2688159-A2; FR2993718-A1; FR2993718-B1; EP2688159-A3 Patent Assignee: THALES; THALES SA

Inventor(s): LALLIER E.

<u>Coupling unit for attaching housing of optronic sensor arrangement at partially radiation-transparent</u> <u>carrier element, such as vehicle window, has border strip formed of plastic material and is filled with</u> high viscosity silicone material

Patent Number: DE202014001524-U1 Patent Assignee: OECHSLER AG

Optical system for use in optical test bench used to test optical/optronic observation system, has deviating device to deviate collimated light wave to provide test light wave, and with focal length adjustable to infinity or preset value

Patent Number: FR2985811-A1; WO2013104851-A1; EP2802854-A1; US2014347653-A1; FR2985811-B1; CN104136902-A; RU2014133181-A

Patent Assignee: CASSIDIAN TEST & SERVICES; CASSIDIAN TEST & SERVICES INC; CASSIDIAN TEST SERVICES

Inventor(s): PITTE E; PETIT V; LECOQ P; et al.

<u>Video</u> optronic system for realizing supra-hemispherical vision of scene to protect e.g. terrestrial vehicle, has captured image processing unit, and adaptation unit adapting dynamics of image to dynamics of image display device and/or eye

Patent Number: FR2964818-A1; WO2012034963-A1; FR2964818-B1; CA2811231-A1; US2013176386-A1; EP2616864-A1; CN103097935-A; JP2013542637-W; HK1184861-A0; US9025004-B2; RU2013116986-A; CN103097935-B; RU2574324-C2; IL225141-A; EP2616864-B1; JP6132767-B2 Patent Assignee: THALES; THALES SA Inventor(s): MIDAVAINE T.

Thermally engineered substrate used for electronic, optronic or optoelectronic device comprises multiphase material including polycrystalline aluminum nitride as first phase Patent Number: US2012146023-A1; WO2012082729-A1; KR2014017515-A; JP2014507363-W; US8766274-B2 Patent Assignee: HEXATECH INC Inventor(s): CRAFT S; MOODY B; DALMAU R; et al.

Optronic system for identifying e.g. jeep in e.g. micro-electronics field to observe components, has optical or radiofrequency communication units transmitting images by computer processing unit to reconstruct object in three dimensions Patent Number: FR2953313-A1; EP2333481-A1; JP2011123060-A; CA2721891-A1; US2011254924-A1; FR2953313-B1; US8836762-B2; EP2333481-B1; ES2525011-T3; JP5891560-B2 Patent Assignee: THALES SA Inventor(s): BERGINC G; JOUFFROY M.

Tunable diode laser spectrometry (TDLS) gas sensor for measuring carbon dioxide concentration in incubator used in biological applications, has window that is provided to separate absorption pick-up unit and measuring pick-up unit

Patent Number: US2011304844-A1; EP2397838-A1; US8330107-B2 Patent Assignee: WILLING B; KOHLI M; SEIFERT A; LEISTER PROCESS TECHNOLOGIES; AXETRIS AG Inventor(s): WILLING B; KOHLI M; SEIFERT A.

Microscope has microscope base, microscope column and support arm positioned at microscope column in different heights over microscope base for optical or optronic observation system Patent Number: EP2309303-A1 Patent Assignee: PHOTONIC OPTISCHE GERAETE GMBH&CO KG Inventor(s): FEGER D. Optronic device manufacturing method, involves providing substrate and forming nitride buffer film on substrate by atomic layer deposition

Patent Number: TW201005986-A Patent Assignee: TEKCORE CO LTD Inventor(s): FU J; LIU Y; WANG T; et al.

<u>Nanocomposite, useful in device for optical limitation and protection, for protecting optical</u> <u>and/oroptronic device against electromagnetic waves, comprises one-dimensional nanomaterials and</u> <u>nano-oxide of transition metal</u>

Patent Number: FR2942350-A1; WO2010092264-A1; FR2942350-B1; EP2396277-A1; US2012092758-A1; IL214673-A

Patent Assignee: COMMISSARIAT ENERGIE ATOMIQUE; INST FRANCO ALLEMAND RECH SAINT LOUIS; CNRS CENT NAT RECH SCI; SAINT LOUIS INST Inventor(s): KELLER S V; TEISSIER A; LUTZ Y; et al.

<u>Infrared detector i.e. short wavelength infrared detector, for use in optronic system, has lower electric contact comprising layer of n-doped III-V materials comprising mesh parameter compatible with that of substrate</u>

Patent Number: FR2939967-A1; WO2010066735-A2; FR2939967-B1; WO2010066735-A3; EP2359414-A2; US2011248316-A1; US8610171-B2; EP2359414-B1

Patent Assignee: THALES SA; SOFRADIR SOC FR DETECTEURS INFRAROUGES Inventor(s): BOIS P; MARCADET X; PAPUCHON M; et al.

<u>Passive optical limiter useful in an active</u> optronic system, comprises a nonlinear material for switching in a predetermined optical band from a transparent state to an opaque state as a function of the power, and an optical structure

Patent Number: US2010213356-A1; US8228584-B2 Patent Assignee: THALES; CENT NAT RECH SCI; ECOLE NORMALE SUPERIEURE DE LYON Inventor(s): BERGINC G; FENEYROU P; BOUIT P; et al.

<u>Single-mode power laser device for single-mode power amplification system in e.g. lidar, has</u> <u>conversion section comprising optical fiber, and middle section including free end that constitutes</u> <u>output for outputting optical power beam</u>

Patent Number: FR2931309-A1; WO2009138309-A1; FR2931309-B1 Patent Assignee: THALES SA Inventor(s): BRIGNON A; HUIGNARD J P; POCHOLLE J P; et al.

<u>Object or fixed aerial target detecting method for</u> optronic <u>monitoring system, involves repeating</u> application of temporal confirmation criterion for selected pixels in measurement where pixels are taken into account in number calculation

Patent Number: FR2932278-A1; WO2010003742-A1; FR2932278-B1; EP2294441-A1; US2011080480-A1; EP2294441-B1; US8558891-B2; IL209788-A Patent Assignee: THALES SA Inventor(s): DUFOUR J Y; LEMPERIERE N; PRENAT M.

Optronic system i.e. thermal camera, has data storage unit storing data used by calculation unit, where data are cumulative data and not measurements of temperatures and cool-down time in order to limit size of storage unit Patent Number: FR2930678-A1; WO2009130136-A1; FR2930678-B1; EP2269016-A1; US2011037856-A1; US8857196-B2; IL208897-A

Patent Assignee: THALES SA Inventor(s): BIHANNIC D.

Microscope stand

Patent Number: AT506565-A1; EP2128679-A2; EP2128679-A3; AT506565-B1; US2011085234-A1

Patent Assignee: PHOTONIC OPTISCHE GERAETE GMBH&CO KG; PHOTONIC OPTISCHE GERAETE GMBH & CO KG; FEGER D Inventor(s): FEGER D.

<u>Laser device for e.g.</u> optronic application, has structure that is mobile in translation in plane perpendicular to axis of beams such that structure's translation drives deflection of sub beams with angle added to another angle of sub beams

Patent Number: FR2923092-A1; WO2009056588-A1; WO2009056588-A4; EP2206011-A1; FR2923092-B1; EP2206011-B1; DE602008006246-E

Patent Assignee: THALES SA

Inventor(s): BELLANGER C; BOURDERIONNET J; BRIGNON A; et al.

<u>Optical switch for switching optical signal between optical paths, has bending mechanism for</u> <u>electrostatically bending movable portion of first guide to optically couple first guide to adjacent</u> <u>second guide</u>

Patent Number: WO2008154071-A1; EP2162801-A1; US2010183302-A1; JP2010529504-W Patent Assignee: RES TRIANGLE INST Inventor(s): MCGUIRE G E; LAMVIK M; GOODWIN S.

Dual-field infrared imaging system for e.g. camera, has combination including lenses made of germanium, zinc sulfide and calcium fluoride, and inlet pupils respectively provided near and upstream head lens of convergent head group

Patent Number: FR2910133-A1; WO2008071579-A1; EP2092386-A1; CA2672624-A1; US2010033578-A1; EP2092386-B1; DE602007007514-E; US8369008-B2; CA2672624-C Patent Assignee: THALES SA Inventor(s): FORESTIER B; JOUGLA P.

Formation of metal-containing nanoparticle e.g. on or in optical memories substrate (e.g. hydrogel), by applying directional radiation source to substrate solution mixture, causing second agent (e.g. reducing agent) to dissociate

Patent Number: US2007134902-A1 Patent Assignee: UNIV MISSOURI Inventor(s): BERTINO M; LEVENTIS N; TOKUHIRO A; et al.

Film producing method for e.g. optic application, involves selectively implanting atomic species via face of wafer for forming implanted zone at predefined depth, and forming protective layer in horizontal walls of step

Patent Number: FR2888400-A1; US2007023867-A1; WO2007017763-A2; EP1911085-A2; CN101213651-A; KR2008022213-A; JP2009500839-W; TW200721263-A; US7572714-B2; TW311776-B1; KR1015158-B1; EP1911085-B1; WO2007017763-A3; JP4943426-B2; SG138993-A1; SG138993-B Patent Assignee: SOITEC SILICON ON INSULATOR TECHNOLOGIES; AULNETTE C; CAYREFOURCQ I; MAZURE C Inventor(s): AULNETTE C; CAYREFOURCQ I; MAZURE C.

Laser source for e.g. optronic countermeasure application, has neodymium-doped crystal pumped by pumping unit and emitting radiation at specific wavelength, where radiation reacts with methane to generate another radiation

Patent Number: FR2888409-A1; US2007019688-A1; DE102006031183-A1; DE102006031183-B4; US7974318-B2 Patent Assignee: INST FRANCO ALLEMAND RECH SAINT LOUIS; DEUT FRANZOESISCHES

FORSCH INST Inventor(s): HIRTH A; KIELECK C. <u>Semiconductor material structure formation for, e.g., opto-electronics, involves thermally oxidizing</u> <u>oxidizable layer such that combination of oxidizable layer and insulating layer forms insulating layer</u> of structure with desired thickness

Patent Number: FR2886457-A1; US2006270244-A1 Patent Assignee: SOITEC SILICON ON INSULATOR TECHNOLOGIES; DAVAL N; LE VAILLANT Y Inventor(s): DAVAL N; LE VAILLANT Y M.

<u>Optical triangulation measuring device for measuring distance and inclination of substrate`s flat</u> surface, has processing unit to process signals provided by sensors for supplying information relating to position and inclination of surface

Patent Number: WO2006097645-A2; FR2883369-A1; EP1859321-A2; CN101142535-A; JP2008533483-W; EP1859321-B1; DE602006004715-E; US2009141290-A1; US7616327-B2; CN100524042-C; JP4885942-B2; WO2006097645-A3; WO2006097645-A8 Patent Assignee: SAGEM DEFENCE SECURITE; SAGEM SA; SAGEM DEFENSE SECURITE; MICHELIN J Inventor(s): MICHELIN J; MICHELIN J L.

Optronic multiplex interface state indicating device and method and its interface

Patent Number: CN1777086-A; CN100531025-C Patent Assignee: HANGZHOU H3C TECHNOLOGIES CO LTD Inventor(s): LI X; DEGN X; ZHOU Z.

High voltage temperature on-line monitoring optronic switching contact box structure

Patent Number: CN1776764-A; CN100369070-C Patent Assignee: CHEN J Inventor(s): CHEN J.

Diamond particle production for chemical mechanical polishing, used in manufacturing microelectromechanical system device, involves processing feed material at specific energy intensity using multicarbide spheres

Patent Number: US2006157603-A1 Patent Assignee: DOBBS R Inventor(s): DOBBS R.

<u>Fabrication of a multi-layer structure from semiconductor materials with reduced electrical losses,</u> <u>notably applicable for silicon on insulator structures</u>

Patent Number: FR2860341-A1; WO2005031853-A1; WO2005031842-A2; EP1665368-A1; EP1665367-A2; US2006166451-A1; KR2006069496-A; US2007032040-A1; CN1856873-A; CN1860603-A; JP2007507093-W; JP2007507100-W; KR2006118437-A; KR789527-B1; US7585748-B2; CN100477152-C; WO2005031842-A3; JP2012104855-A; SG120692-A1; SG120698-A1; SG120698-B; JP5518911-B2 Patent Assignee: SOITEC SILICON ON INSULATOR TECHNOLOGIES; UNIV CATHOLIQUE LOUVAIN; RASKIN J; LEDERER D; BRUNIER F; UNIVERSITY LOUVAIN Inventor(s): RASKIN J P; LEDERER D; BRUNIER F; et al.

<u>Preparation of oxidized surface of first wafer for bonding with second wafer used in, e.g.</u> <u>microelectronics, involves treating the oxidized surface of the surface with solution of ammonium</u> hydroxide/hydrogen peroxide

Patent Number: US2005218111-A1; FR2868599-A1; WO2005096369-A1; EP1730772-A1; KR2007005660-A; CN1954422-A; JP2007533123-W; KR881682-B1; JP2010268001-A; JP4653862-B2; SG126273-A1; SG126273-B Patent Assignee: MALEVILLE C; MAUNAND T C; SOITEC SILICON ON INSULATOR TECHNOLOGIES; COMMISSARIAT ENERGIE ATOMIQUE Inventor(s): MALEVILLE C; MAUNAND T C; MALLEVILLE C; et al. <u>Treatment of an electrical conducting service layer of a multi-layer semiconductor structure to</u> produce several insulated conducting islets, for micro-electronic, optical and optronic applications

Patent Number: FR2867606-A1; WO2005088716-A2; US2006201907-A1; EP1723671-A2; KR2006118604-A; CN1947248-A; JP2007528597-W; KR828113-B1; JP4510876-B2; US7790048-B2; CN1947248-B; WO2005088716-A3; SG125507-A1; SG125507-B

Patent Assignee: SOITEC SILICON ON INSULATOR TECHNOLOGIES; ALLIBERT F; BRUNIER F Inventor(s): BRUNIER F; ALLIBERT F.

<u>Fabrication of a number of chips, incorporating electronic</u>, optronic and/or opto-electronic circuits, in <u>a single three stage operation</u>

Patent Number: FR2869455-A1; US2005236700-A1; WO2005106948-A1; EP1756864-A1; KR2007004056-A; CN1947240-A; JP2007535158-W; KR836289-B1; US7544586-B2; JP4782107-B2; EP1756864-B1; EP1756864-B9; SG126648-A1; SG126648-B Patent Assignee: SOITEC SILICON ON INSULATOR TECHNOLOGIES; GHYSELEN B; RAYSSAC O Inventor(s): GHYSELEN B; RAYSSAC O.

Device for detecting pathological states of internal organs by measuring biopotentials at early stage

Patent Number: RU2240720-C2 Patent Assignee: YUDAKOV S I Inventor(s): YUDAKOV S I; PARUSHIN E B; BONDARENKO V A.

<u>Microelectro-mechanical-system (MEMS)-based optical image switch for e.g.</u> optronic/photonic device has symbols formed on optical surfaces of pulse laser diode array so that array emits laser pulses corresponding to images of symbols

Patent Number: US2005157162-A1; US7800639-B2 Patent Assignee: UDY J D Inventor(s): UDY J D.

<u>Computerized device for determining electromammographic potential in carrying out mass screening</u> <u>of mammary glands</u>

Patent Number: RU2255650-C1 Patent Assignee: VASILEVSKII I A; ZHURAVLEV V L; YUDAKOV S I Inventor(s): VASILEVSKII I A; ZHURAVLEV V L; YUDAKOV S I.

Optronic <u>component for spectral separation uses diffraction element between input and output fibres</u> with variable index end portions

Patent Number: FR2830334-A1; WO2003029862-A2; EP1433006-A2; AU2002362522-A1; JP2005504353-W; US2005031257-A1; EP1433006-B1; DE60209153-E; DE60209153-T2; US7336868-B2; WO2003029862-A3 Patent Assignee: HIGHWAVE OPTICAL TECHNOLOGIES SA; FOUCHEL J; YENISTA OPTICS SA Inventor(s): FOUCHE J B; FOUCHEL J.

Device for drying substrate comprises a processing container to which cleaning fluid after cleaning substrates is drained and a nozzle for injecting drying fluid into container

Patent Number: WO2003054930-A; FR2833753-A1; WO2003054930-A2; AU2002364824-A1; EP1456869-A2; US2005016680-A1; JP2005513798-W; TW200303578-A; WO2003054930-A3 Patent Assignee: VACO MICROTECHNOLOGIES SA; RACCURT O Inventor(s): RACCURT O.

Minuscule image creation method for optronic/photonic devices, involves forming image of alphanumeric symbol by reflection of laser light pulse from marked mirror Patent Number: US2002110349-A1 Patent Assignee: UDY J D Inventor(s): UDY J D.

Portable device for detecting pathological states of mammary glands

Patent Number: RU2176474-C1 Patent Assignee: DZHMUKHADZE R L Inventor(s): DZHMUKHADZE R L; YUDAKOV S I.

<u>Flow meter has narrowing device, differential manometer, as well as secondary instrument including</u> <u>generator, logical circuit, binary and binary-decade counters, first and second digital-and-analog</u> <u>converters</u>

Patent Number: RU2152003-C1 Patent Assignee: AZERB NEFTEGAZAVTOMAT RES P[RODN ASSOC Inventor(s): AMIROV A M O; GUSEINOV M S O; ALIEV N A O; et al.

Integrally packed optronic integrated circuit device

Patent Number: WO9940624-A1; AU9922981-A; EP1051746-A1; KR2001040740-A; JP2002512436-W; US2003080398-A1; US2003151124-A1; US6624505-B2; TW526568-A; US6646289-B1; US7157742-B2; US2007040180-A1; US2007042562-A1; KR657117-B1; US7781240-B2; US2010323475-A1; EP2381478-A2; EP2381478-A3; EP2381478-B1; US8592831-B2; US2014077395-A1; US9530945-B2 Patent Assignee: SHELLCASE LTD; BADEHI A; TESSERA TECHNOLOGIES HUNGARY KFT; ENG & IP ADVANCED TECHNOLOGIES LTD; INVENSAS CORP Inventor(s): BADEHI A.

Optical receiver for input to optronic device

Patent Number: FR2771814-A1 Patent Assignee: THOMSON CSF SA Inventor(s): ILLIAQUER G; THIBOUT P; FORESTIER B.

<u>Passive response device for optronic friend or foe identification|has triple modulatable reflector made</u> up of combination of prisms or mirrors, as reflectors

Patent Number: DE19652920-A1; DE19652920-C2 Patent Assignee: DIEHL GMBH & CO; DIEHL STIFTUNG & CO Inventor(s): WARM B.

Micrometer designator laser alignment system|includes optical and infrared units in scanning head having two appropriately transparent windows

Patent Number: EP489649-A; FR2670019-A; EP489649-A1; FR2670019-A1; US5200622-A; EP489649-B1; DE69111032-E Patent Assignee: THOMSON CSF Inventor(s): ROUCHON J M; RICCI J L; RICCI L.

Opto-electronic flip=flop|has luminophore crystal and output LED and uses photoresistors as photodetectors in photon-coupled pairs Patent Number: SU1651356-A Patent Assignee: RADAEV N N Inventor(s): RADAEV N N; NOVOSELOV Y U N; LOTYSHEV E V.

New isotropic acrylic! polymers and copolymer|having nonlinear response, used as transparent optical component in optical light switch and light modulator devices Patent Number: EP328268-A; JP2003403-A; US4913844-A; CA1337450-C Patent Assignee: HOECHST AG; HOECHST CELANESE CORP Inventor(s): DEMARTINO R N; DE MARTINO R N.

<u>Controlling photochromic reaction|by applying magnetic field so as to control recombination reaction</u> of cleaved photochromic cpd. dispersed in viscous medium Patent Number: JP1004687-A Patent Assignee: SUMITOMO ELECTRIC IND CO

Prepn. of semiconductor structure with pn-transition|involves using manganese as alloying acceptor impurity to improve photoelectric properties Patent Number: SU928942-A Patent Assignee: IOFFE PHYS TECH INST Inventor(s): ESINA N P; ZOTOVA N V; MATVEEV B A.

Ternary alloy semiconductor substrate/with ternary alloy epitaxial layer, useful for optronic detectors with high shunt impedance and low leakage Patent Number: FR2556134-A1 Patent Assignee: SA DE TELECOMMUNICATION Inventor(s): DURAND A R: ROYER M: TRIBOULET R G.

Hot steel strand quality assessment|by scanning surface with opto-electronic sensor after descaling Patent Number: DE3236416-A; EP105401-A; JP59082150-A; BR8305413-A; ZA8307209-A Patent Assignee: LICENTIA PATENT-VERW GMBH; MANNESMANN AG Inventor(s): SCHONE G; AURIN I; EHLERT K P; et al.

Induction motor speed regulator has rotor energising shunt thyristor via bridge rectifier with optoelectronic thyristor, with LED energised by bridge Patent Number: SU838993-B Patent Assignee: SYZRAN KUIB POLY Inventor(s): GULUBKOV N E; GOLUBKOV V N.

<u>Protection circuit for secondary power sources</u> with opto-electronic decoupling unit and galvanic <u>decoupling of output from sources</u>

Patent Number: SU860036-B Patent Assignee: KROVOPUSKOV V I Inventor(s): KROVOPUSKO V I; LEBEDINSKI I I; SOROKIN E A.