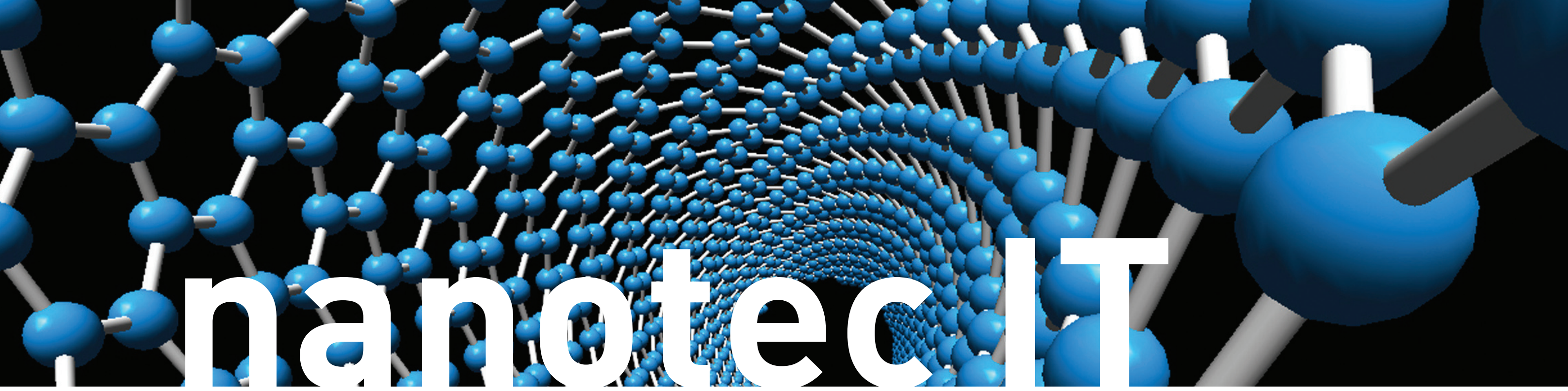

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Editoriale

In Italia l'attività nel campo delle nanotecnologie è negli anni passati costantemente aumentata e, come messo in evidenza dal 3° Censimento AIRI/Nanotec IT delle Nanotecnologie in Italia (in corso di pubblicazione), il Paese può vantare, accanto ad una ricerca accademica competitiva, sovente con posizioni di eccellenza, anche una presenza crescente di imprese private, grandi e PMI.

Il Convegno Internazionale NanotechItaly2010, tenutosi a Venezia il 20–22 ottobre 2010, che è diventato ormai un appuntamento di riferimento per quanti in Italia sono attivi in questo campo, anche quest'anno ha visto nei tre giorni una partecipazione notevole, con interventi da parte di rappresentanti del mondo della ricerca pubblica e di quello delle imprese che hanno fornito una panoramica ampia di questo attività. Gli articoli di questa Newsletter ne sono un esempio significativo.

Nel sottolineare questi aspetti positivi, tuttavia, non si possono però nascondere alcune criticità che penalizzano l'azione in questo campo. Se consideriamo, infatti, l'entità dell'impegno economico, esso risulta sensibilmente inferiore non solo a quello dei paesi più avanzati ma anche a quello dei paesi emergenti piu' attivi, il che, se non corretto a tempo, rischia di non far cogliere appieno al Paese le opportunità offerte dalle nanotecnologie, con implicazioni negative sul suo posizionamento competitivo, visto il ruolo chiave che tutti attribuiscono alle nanotecnologie nel processo di innovazione.

Complessivamente, a livello globale, la spesa (pubblica e privata) per la attività di R&S nelle nanotecnologie ha raggiunto, infatti ormai una somma di più di 13 miliardi di Dollari. Gli Stati Uniti, con circa 1500 milioni di dollari, ed il Giappone, con 600 milioni di dollari rimangono i Paesi maggiormente impegnati, seguiti dalla Germania, che in Europa è di gran lunga la piu attiva, mentre anche Paesi come Cina, Russia e India negli ultimi 2-3 anni hanno fortemente incrementato le risorse dedicate a questo settore andandosi a collocare, in particolare i primi due, tra i Paesi di punta, almeno in termini di entità dello sforzo economico. L'Unione Europea a sua volta, che già nel 7° Programma Quadro (2007-2013) ha dedicato a questo settore più di 3500 milioni di Euro, è intenzionata a rafforzare ed ottimizzare questo impegno ed è in corso un'azione volta a definire una Piattaforma Europea per le Nanotecnologie alla quale faranno riferimento i finanziamenti in questo settore nell'ambito dell'8° Programma Quadro, il quale dovrà indirizzare e sostenere l'azione di R&S dell'Unione Europea per il raggiungimento degli obiettivi indicati dall'Agenda Europa 2020.

In Italia la spesa per la attività di R&S nelle nanotecnologie è, come detto, lontano da quella dei Paesi suddetti, ma la limitatezza delle risorse finanziarie (pubbliche), peraltro generalizzata, non è tuttavia il solo fattore che penalizza l'azione nelle nanotecnologie in Italia. Un altro aspetto critico è il fatto che l'attività, pur avendo prodotto in molti casi risultati notevoli, è andata avanti, almeno fino a poco tempo, fa senza un disegno strategico definito che ottimizzasse gli sforzi. Molti dei Paesi leader del settore, a partire da Stati Uniti e Germania, hanno attivato da tempo iniziative nazionali specifiche per le nanotecnologie, con obiettivi e linee strategiche precise e fondi (consistenti) dedicati. Esse si sono rivelate fondamentali per indirizzare e rendere piu' efficace l'azione di quei Paesi, contribuendo al raggiungimento della attuale posizione di forza.

AIRI/Nanotec IT ha più volte sollecitato l'attivazione anche in Italia di una Iniziativa Nazionale per le Nanotecnologie (INN) con fondi dedicati adeguati ed un disegno strategico definito, per perseguire proprio tali obiettivi. Purtroppo ciò fin'ora non è avvenuto nonostante quanti sono impegnati in questo campo, in particolare le imprese, ne abbiano riconosciuto l'utilità e ne lamentino apertamente la mancanza.

Ultimamente sono state avviate, nell'ambito della ricerca pubblica, varie iniziative di tipo organizzativo e programmatico, che possono contribuire a limitare questa carenza, ma questo da solo non è certamente sufficiente.

Nel contesto della iniziativa in corso per la realizzazione di una Piattaforma Europea per Nanotecnologie, è stata avviata anche un'azione volta a definire una Piattaforma Italiana. Questa attività, alla quale AIRI/Nanotec IT partecipa e contribuisce attivamente, dovrebbe consentire di focalizzare obiettivi ed esigenze delle nanotecnologie in Italia in relazione a quelli messi in evidenza nell'ambito della Piattaforme Europea e puo' costituire un ulteriore passo avanti per ottimizzare l'impegno in questo campo.

L'attivazione di una iniziativa specifica di sostegno e di indirizzo (anche l'Iran ne ha una..) rimarrebbe comunque un obiettivo da perseguire. Essa, infatti, contribuirebbe ad ottimizzazione l'attività promossa sulla base degli obiettivi indicati dalla Piattaforma inquadrandola in un disegno strategico Nazionale complessivo e, inoltre, consentirebbe di cavalcare meglio l'evoluzione dello sviluppo delle nanotecnologie (ancora in una fase iniziale) facilitando al contempo una azione volta a far si esso avvenga in maniera responsabile. AIRI/Nanotec IT, facendosi portavoce dei propri iscritti, è convinta dell'importanza strategica di una Iniziativa Nazionale per le Nanotecnologie e seguiterà ad adoperarsi perché questo possa realizzarsi.

Elvio Mantovani
Direttore AIRI/Nanotec IT

The Avidin-Nucleic Acids Nano Assemblies (ANANAS), as powerful molecular amplifiers in in vitro diagnostics

Margherita Morpurgo
ANANAS Nanotech S.r.l. in collaboration with the University of Padova and Istituti ZooProfilattici delle Venezie (IZV) e della Lombardia ed Emilia Romagna (IZSLER), Italy.

ANANAS Nanotech

ANANAS Nanotech is an Italian University spin-off that was founded in 2007 with the mission to transform into commercial products the patented polyavidin nanoparticle platform developed within the University benches.
The ANANAS nanoparticles are a novel kind of stable, fully biocompatible poly-avidin nanoassemblies, with controllable and application-adaptable size, obtainable by means of a highly reproducible and economic self-assembly-guided preparation method [1] These patented particles extend the potentialities of worldwide used avidin-biotin-based technologies in in vitro diagnostics and drug-delivery applications. In diagnostics about 200-fold higher sensitivity is obtained without the need for the operator to change his technological platform. High drug payloads can be targeted to localized body sites using a straightforward nanoparticle loading strategy. Winner of the 2007 nanochallenge international prize, the company has launched its first high sensitivity IVD kit for research use in July 2010. The IVD products pipeline has been growing since then. ANANAS Nanotech products are currently dedicated to research labs. The company also addresses IVD kit producers that can increase the performance of their products with minimal impact on the final analytical protocol (no need for the operator to change his/her hardware or mode of operating). In addition, the higher sensitivity allows reducing the amount of the primary antibody necessary for analysis with the end result of reducing analysis costs.

Technology

Avidin is a protein from egg white that is capable of binding with high affinity (K_d~10^{-15}M) four biotin molecules. This property represents the basis for its exploitation as a molecular tool in many biotechnological applications among which immunodiagnostics and drug delivery [2]. The protein in fact is used as a universal tool capable of bringing together different chemical and biochemical function, provided that have been previously covalently linked to a biotin moiety (an easy procedure). In diagnostics, avidin is used to bring together an analyte recognizing molecules (eg. An antibody) and a signal generating element, so that the signal can be localized where the analyte is present (Figure 1)
However, classic avidin-biotin technology potentials are limited by the maximum number (4) of ligands that can be brought together by the individual avidin unit.
The ANANAS particles are nanosystems (about 100 nm in diameter) potentially capable of overcoming such limits since they have a "core" composed of several avidin units and, consequently, they are characterized by higher and precisely defined biotin loading capacity (**Figure 1**).

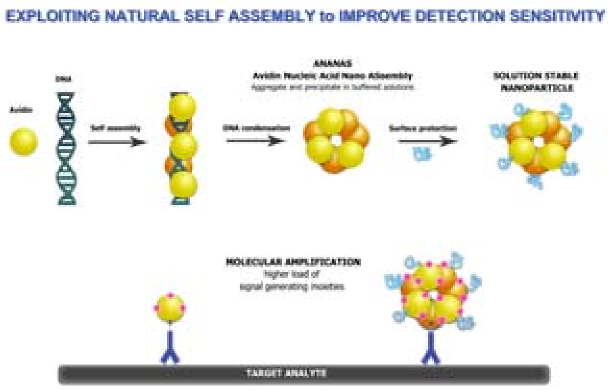

Figure 1. The ANANAS concept vs monomerica avidin.

The performance of the ANANAS particles, has been assessed in several *in vitro* diagnostics configurations and compared to that of benchmark reagents currently in the market in three analytical set-ups.
Figure 2 shows the results of an Enzyme-Linked ImmunoSorbent Assay (ELISA) experiment in which detection of a biotinylated antibody was achieved with either a commercial avidin-HRP conjugate or the ANANAS integrated system. The latter gives rise to a positive response (characterized by signal/standard deviation > 2) at all points tested. This corresponds to a detection limit of less

than 0.023 pg/well. In the same analytical set-up, the positive signal onset for the commercial competitor avidin-HRP was at 6.17 pg/well. The ANANAS enhanced sensitivity is due to both lower noise and higher signal intensities. The enhancement factor in this analytical set-up (calculated from the ratio of the two onset values) was of about 240 fold.

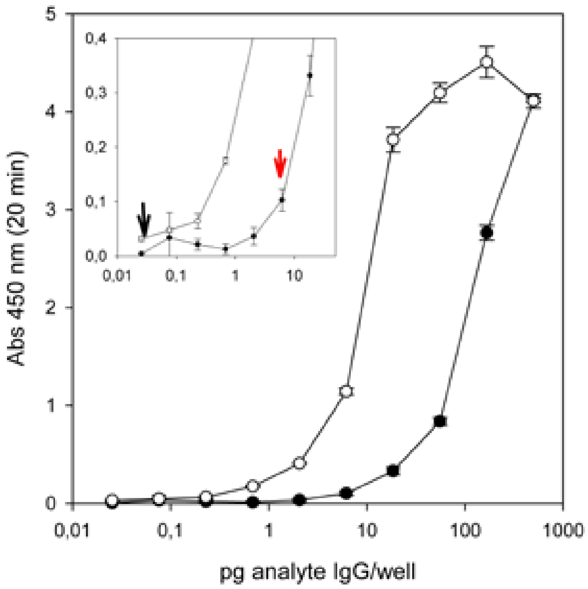

Figure 2 ANANAS (o) vs commercial avidin-HRP (•) in a model ELISA assay. Arrows indicate the positive signal onsets (signal/stdv >2).

Figure 3 *shows the analytical performance of the ANANAS system in a blot assay where the analyte was mouse IgG from serum, which was diluted serially into PBS/BSA. In this case, the ANANAS performance was compared to that of the commercial competitor Vectastain ABC from Vector Labs, which relies on a patented avidin-based amplifying technology. The results of this assay can be used to predict the efficacy of detection in Western or Southern blots.*

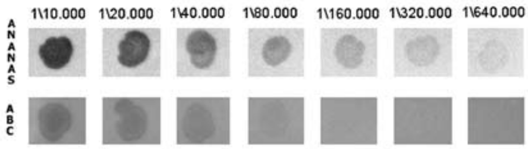

Figure 3. Detection of mouse IgGs from serum in a dot blot experiment using the ANANAS system and commercial enhanced Vectatstain ABC system. Spots (1µl) were made with mouse serum serially diluted from 1:10000 to 1:640000 in PBS/BSA.

As in ELISA, the ANANAS system shows significantly higher sensitivity than the commercial competitor, due to both reduced noise and higher signal. In this experimental set-up the ABC system positive onset was at mouse serum dilution of 1/80.000, which corresponds to about 125 pg of IgG/spot, whereas positive signal with the ANANAS system was observed also at the higher dilution tested (1/640000), which corresponds to about 16 pg of IgG. Therefore, the enhancement factor is > 8 fold. This result is of particular interest, since the ABC system itself already relies on a signal amplifying technology.

Figure 4 shows preliminary data obtained in a real analytical context, namely in the detection of anti-BHV1 (Bovine herpes virus type 1) IgGs in cow milk. The presence of these antibodies in milk is due to either infection or immunization with BHV1**.**

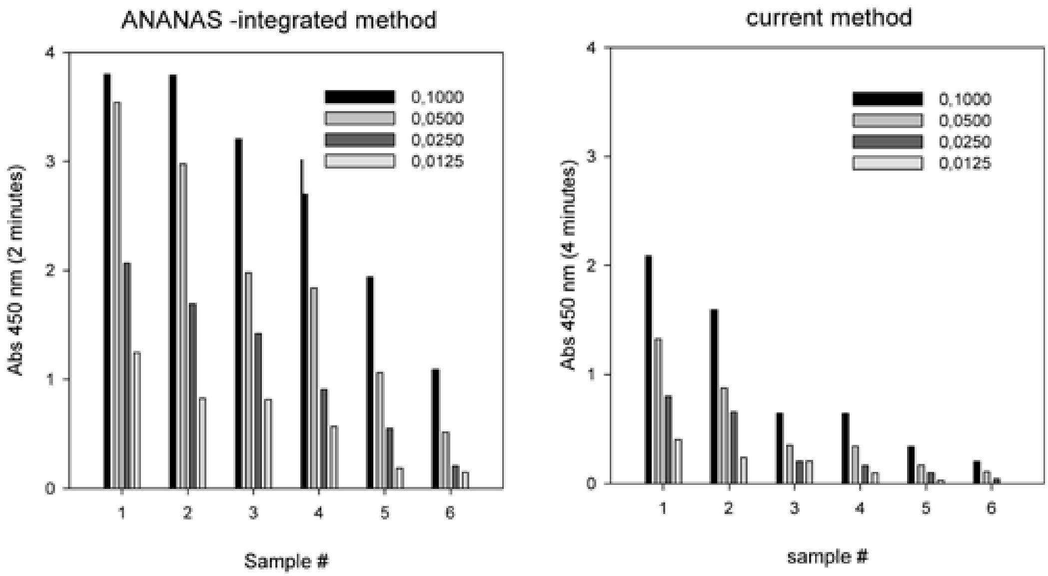

Figure 4. Detection of anti-BHV1 IgGs in six positive cow milk samples, each diluted with negative milk. The dilutions tested are 1 to 10; 1 to 20, 1 to 50 and 1 to 125.

Known positive milk samples were diluted in negative milk to simulate a real stable situation, in which bulk milk is obtained upon pooling together the product of several cows. In this situation the presence of an infected animal (and thus the early diagnosis of an infected stable) may be masked by diluting seropositive milk with that of healthy animals. The results show that the ANANAS integrated detection system yields to significantly higher reading values than the competitor system, despite the shorter development time used. In all milk tested, a clear positive response was observed in all of the dilutions investigated (up to 1 to 125). Experiments with a larger pool of samples, aimed at estimating the actual sensitivity and specificity of the integrated system are currently underway.

Conclusions

The novel Nanoassembled ANANAS system improves the performance of present *in vitro* diagnostics technologies within classic assay platforms. The system can be easily integrated in the majority of the immunodiagnostics set-ups, where it allows improving the sensitivity without the need for the user to invest in novel instrumentation. The sensitivity reached with colour-based developments is on the same scale as the one obtained with ECL integrated with classic avidin-based or HRP-antibody conjugates. The ANANAS technology then represents an easy and low cost alternative to improve research and diagnostic laboratories sensitivity.

The ANANAS Team

The ANANAS team comprises technical and Industrial skills. ***Margherita Morpurgo*** is ANANAS CSO, is assistant professor at the School of Pharmacy at the University of Padova. She has more than 15 years of experience in chemistry, biochemistry, avidin-biotin technology and drug delivery, with a training record that includes long term collaborations with major international research Institutions and current international network of collaborations. Her research interests focus on the development of organic and inorganic assemblies for drug delivery and diagnostic use. Key personnel in the R&D team include ***Mauro Pignatto*** and ***Sonia Facchin***, a pharmaceutical chemist and biologist who joined the ANANAS project since its early stage. ***Davide Merlin,*** ANANAS CFO has a long professional experience in business planning, market analysis, and start-up strategy developed by an international consulting firm. ***Paolo Gubitta,*** has more than 10 years of experience in research and consulting in the field of organizational development, strategy of small and medium size company, recruitment and selection of highly qualified people. ***Nicola Realdon***, associate professor at the School of Pharmacy at Padova University is expert in Pharmaceutical technology and legislation. Before starting his academic career he worked several years in pharma industry. He has extensive experience in production, quality assurance and regulatory affairs acquired in pharmaceutical industries. The institutional partners of ANANAS are The ***University of Padova*** and ***Veneto Nanotech***.

Additional information: Experimentals

Goat-IgGs, rabbit-anti-Goat IgGs were purchased from KPL. Horseradish Peroxidase (HRP), Avidin-HRP conjugate and TMB were from Sigma Aldrich. ANANAS particles containing about 300 avidin units/particle were prepared and provided by ANANAS Nanotech. Detection antibodies and horseradish peroxidase (HRP) were biotinylated according to standard protocols. Anti-mouse IgG ABC Vectatstain detection reagents were purchased from Vector Labs (USA); Anti-bovine IgG1 monoclonal antibody (MAb) and BHV1-antigen coated microwell plates were kindly provided by IZSLER (Brescia, Italy); IBR Positive and negative cow milk samples were provided by IZV (Legnaro, Padova, Italy).

Performance on a generic ELISA platform

96 well polystyrene plates (Nunc Maxisorp) were conditioned with rabbit anti-goat IgG. After washing, serial (1/4) dilutions of biotinylated goat IgGs (from 55 to 0.023 pg/well) were incubated for 1 h. After well washing, detection was performed using commercial avidin-HRP conjugate or the ANANAS particles followed by biotin-HRP. After the final wash, detection was achieved using TMB as the HRP substrate and reading the plate at 450 nm after 2-20 minutes incubation.

Performance on a blot platform

Serial amounts of biotinylated goat IgG were spotted on a PVDF membrane. After quenching, detection was achieved with the Vectastain-ABC system or ANANAS particles + biotin-HRP, followed by colour development with the diaminobenzidine (DAB) substrate.

Detection of IBR positive cows from milk samples

BHV1 antigen was trapped onto Nunc Maxisorp plates by a virus specific MAb coated to the solid phase. Positive cow milk samples were serially diluted into negative milk and incubated for 1h at 37°C. After washing, an anti-bovine IgG1 MAb, HRP conjugated (IZSLER) or biotinylated and, followed by ANANAS and biotin-HRP, were delivered; colour development was finally achieved with TMB.

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Thermotherapy with Magnetic Nanoparticles

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The therapeutic effectiveness of heat in the treatment of cancer has been known for decades and many of the corresponding molecular mechanisms are understood [1]. Although various successful clinical trials have been conducted [2-4], due to complicated technical setup and heat distribution problems, hyperthermia is not yet well established as a therapeutic method.

Thermotherapy using magnetic nanoparticles is a new approach for the local treatment of solid tumors and one of the first clinical applications of nanotechnology in cancer therapy. The principle of the NanoTherm therapy, developed by MagForce Nanotechnologies AG, is the introduction of an aqueous magnetic fluid containing nanoparticles into a tumor. The particles are activated by a magnetic field that changes its polarity 100,000 times per second, and thus heat is produced. Depending on the duration of treatment and the achieved intratumoral temperatures, the tumor cells are either directly destroyed (thermal ablation) or sensitized for concomitant chemo- or radiotherapy (hyperthermia).

With this new procedure, it is possible to combat the tumor from inside, thereby sparing surrounding healthy tissue. The nanoparticles remain in place at the treatment area, allowing for repeated treatments and the integration into multimodal therapy concepts.

The first component of the NanoTherm therapy is NanoTherm, a so called ferrofluid, meaning a liquid that reacts to the presence of a magnetic field. The liquid's magnetic characteristic stems from its iron-oxide nanoparticles. Despite an average diameter of approximately only 15 nanometers, the nanoparticles possess a strong magnetic character (referred to as superparamagnetism). Due to their special aminosilane coating, these small magnets can be finely dispersed in water, forming a colloidal solution that is dispensable with a syringe. Once inside the alternating magnetic field applicator (NanoActivator), these specifically designed nanoparticles are responsible for the production of warmth. As a "transducer" the nanoparticles can very efficiently change magnetic field energy into heat and, due to their coating structure, remain in the tumor tissue as a stable deposit. The unique characteristics of NanoTherm nanoparticles are the basis for the NanoTherm therapy.

Fig 1: The NanoTherm magnetic fluid

Fig. 2 Screenshot of the NanoPlan therapy planning software

The next component of the NanoTherm therapy is the NanoPlan therapy software, which supports the treating physician in the development of a treatment planning. Based on the distribution of the nanoparticles as shown in a post-operative CT scan, NanoPlan uses the Bioheat-Transfer equation to estimate the treatment temperatures as a function of the magnetic field strength. The intuitive workflow guides the user through a series of treatment parameters questions. As a result, the software creates a three-dimensional image of the tumor, the nanoparticle depots, and the thermometry catheter for direct temperature measurements. In addition, an estimation of the temperature distribution can be shown in correlation with the field strength. By changing the given parameters, it is possible to simulate different scenarios and the optimal treatment field strength can be determined. The final step of the NanoTherm therapy is carried out in the magnetic field applicator NanoActivator, which was developed specifically for the therapy. The machine's 100 kHz oscillating coil current can be continuously adjusted between 100 and 500 amperes, resulting in a magnetic field strength of approximately 2 to 15 kA/m. The resulting magnetic field activates the iron oxide nanoparticles in the NanoTherm magnetic fluid, by which therapeutic treatment temperatures within the tumor are achieved. The NanoActivator can be used for tumors in all areas of the body.

In more than 15 years of basic research and numerous preclinical studies, the advantages of NanoTherm therapy have been demonstrated, e.g. in prostate carcinoma [5, 6] and glioblastoma animal models [7]. Since 2003, various clinical studies (phase I and II) have been performed in collaboration with different clinical partners, demonstrating the safety and efficacy of the new method in humans for different tumour entities, i.e. glioblastoma multiforme [8, 9], prostate cancer [10, 11], and residual tumours (ovarian and cervical carcinoma, sarcoma) [12]. Thermotherapy was thereby applied in combination with radio or chemotherapy, exploiting the well known synergistic effects between the different therapies.

In the phase II glioblastoma multiforme trial completed in 2009 [8], a combined treatment of fractionated stereotactic radiotherapy and NanoTherm therapy was applied to 66 patients (59 with recurrent glioblastoma). In the single-arm two-centre study, the patients received neuronavigationally-controlled intratumoral injection of the nanoparticles, followed by 6 thermotherapy sessions in the alternating magnetic field applicator. Treatment was combined with fractionated stereotactic radiotherapy with a median dose of 30 Gy in a median fractionation of 5x2 Gy/week. Median time between primary diagnosis and first tumour recurrence was 8.0 months.

Median overall survival after diagnosis of the first tumour recurrence was 13.4 months, side effects were mild to moderate and no serious complications were observed. Survival in the historical control was 6.2 months after conventional treatments [13]. Due to this positive outcome, MagForce received European regulatory approval for its medical products NanoTherm and NanoActivator for the treatment of brain tumours.

Fig. 3 The NanoActivator causes the particles to oscillate in an alternating magnetic field and generates heat in the tumour.

For future applications, MagForce is working on a new generation of nanoparticles that can offer even greater therapeutic potential to its NanoTherm therapy. Through modification of the nanoparticle surface with functional drug delivery systems that can be triggered by the heat generated by the particles, it is possible to combine hyperthermia with chemotherapy in an optimal timeframe. Additionally, in order to develop multifunctional nanocarriers with multiple therapeutic applications, MagForce is also exploring the use of targeting ligands with tumour localizing properties along with stealth coatings for a future systemic administration.

The Berlin based company MagForce Nanotechnologies AG focuses on the use of nanotechnology for the treatment of solid tumors. The company's proprietary NanoTherm® therapy consists of three components: NanoTherm® (a magnetic fluid), NanoPlan® (a therapy planning software), and NanoActivator™ (an alternating magnetic field applicator).

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Disordered optical materials: from fundamental research to applications in solar energy

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European Laboratory for Non-linear Spectroscopy (LENS), National Institute of Opics (CNR-INO).

Photonic nano structures

The transport of light in complex dielectric materials is a rich and fascinating topic of research. With complex dielectrics we intend dielectric structures with an index of refraction that has variations on a length scales that is very roughly comparable to the wavelength. Such structures strongly scatter light. A possible building block for constructing a complex dielectric is a micro sphere of diameter comparable to the wavelength and of a certain refractive index that is different from its surrounding medium. The single scattering from such a sphere has a rich structure due to internal resonances in the sphere, but its behaviour is well-understood and can be calculated using the formalism of Mie-scattering. A complex dielectric material can then be realized by micro-assembly of several micro spheres. The spheres can be assembled in various ways with as two opposite possibilities a completely disordered packing and a fully ordered assembly. (See Fig.1.)

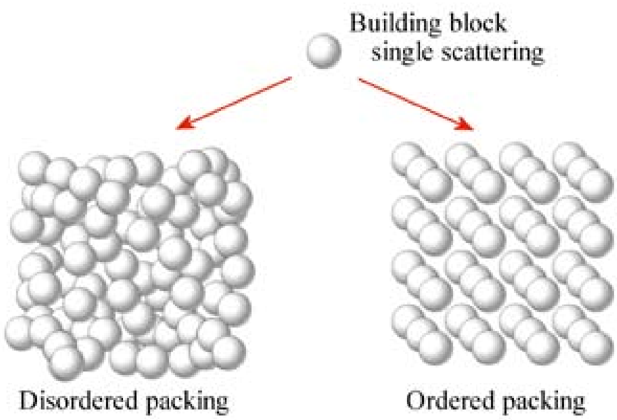

Figure 1 Micro assembly of a complex photonic system. The two extremes are fully disordered assembly (left) leading to random multiple light scattering and ordered assembly (right) resulting in a photonic crystal or possibly a photonic band gap material.

Even though the same spheres with the same single scattering properties are used, their cumulative behaviour after assembly will depend heavily on the way the spheres as packed together. This is due to the interference between the scattered waves and the way the waves are multiply scattered from one sphere to another. If the spheres are packed according to a crystal-like structure then the interference will be constructive only in certain well defined directions, giving rise to Bragg refraction and reflection. In the disordered case the light waves will perform a random walk from one sphere to the other. The occurrence of interference effects is now less obvious to understand, however also in random systems interference effects turn out to be very important [1].

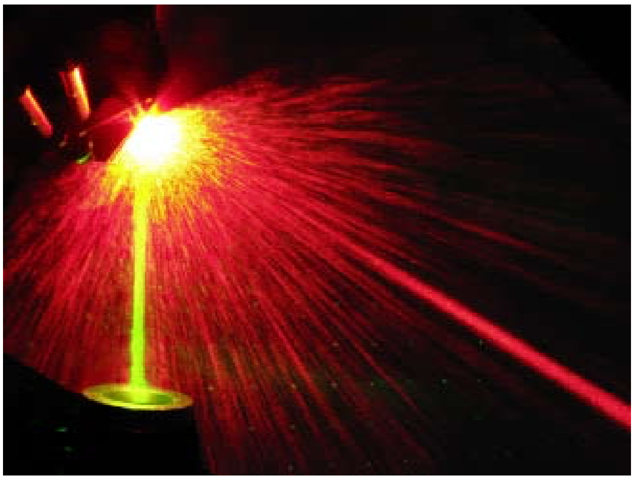

Figure 2 Output of a random laser made by grinding a laser crystal into a powder and exciting it optically. The random series of lines is due to the speckle generated by the random structure and corresponds to the modes of the random laser. [From: Stefano Gottardo, Riccardo Sapienza, Pedro D. García, Alvaro Blanco, Diederik S. Wiersma, and Cefe López, Resonance-driven random lasing, Nature Photonics 2, 429 (2008).]

Interference of light in random dielectric systems influences the transport of light in a way that is similar to the interference that occurs for electrons when they propagate in disordered conducting materials. As a result, several interference phenomena that are known to occur for electrons appear to have their counterpart in optics as well. Interesting examples are correlations and memory effects in laser speckle, universal conductance fluctuations of light, weak localization, and Anderson localization [2]. In the case of Anderson localization the interference effects are so strong that the transport comes to a halt and the light becomes localized in randomly distributed modes inside the system. Interference effects in multiple scattering can furthermore be used to study the dynamics of optically dense colloidal systems.

Also in ordered systems interference can give rise to dramatic effects. If the scattering of the spheres that constitute a photonic crystal is strong enough (that is the refractive index contrast between the spheres and their surrounding medium is large and their diameter is resonant with the wavelength) the interference can become destructive in all direction, for a certain range of frequencies. In analogy with the behaviour of electrons in semiconductors this range of optical frequencies is referred to as a photonic band gap. Inside a photonic band gap the density of light modes becomes zero, which means that even vacuum fluctuations are suppressed. A small impurity inside such a photonic band gap material will give rise to a localized mode around this impurity.

The micro assembly of complex photonic materials as depicted in Fig.1 is concerned with three dimensional structures. The same principle can be applied to lower dimensional systems. In the case of 2D structures one uses a planar waveguide in which a pattern can be created, e.g. simply by inserting sub-micron sized holes. The behaviour of light in three dimensional systems is often difficult to describe theoretically. The advantage of lower dimensional structures is that an analytical theoretical description is often available, facilitating the interpretation of experimental results. 2D structures in particular, turn out to be extremely interesting for applications in the field of solar energy and lighting [3].

How interference effects occur in disordered structures

Interference often determines the optical properties of materials and leads, in the case of photonic crystals, to a coloured appearance that depends on viewing angle. More suppristing, maybe, is the fact that interference also is important in disordered structures. If we shine a laser beam on a white material like a piece of paper we see a grainy pattern of intensity maxima and minima. This is due to interference between waves that have been scattered randomly inside the paper and is called laser speckle. (See Fig. 2, in which the speckle pattern created by a random laser is shown.) Speckle is present also inside a random system in the form of local maxima and minima. Speckle occurs in any disordered material, no matter what its specific microscopic structure or level of disorder.

Anderson localization and solar cells

In very strongly scattering materials interference effects can lead to a strong version of localization, also called Anderson localization, being the optical counterpart of localization of electrons in strongly disordered conductors. Anderson localization inhibits the free propagation of waves and the optical diffusion process thereby comes practically to a halt. Although the detailed mechanism behind localization is quite complex, one can visualize the effect as being due to the formation of randomly shaped but closed modes with an overall exponentially decaying amplitude. (See Figure 3.) The average spatial extend of these localized modes defines a length scale called the localization length. The connection between weak and strong localization is then also immediately clear. While in the case of weak localization the interference occurs outside the sample between light waves that have travelled along half-closed loops, in strong localization the same interference occurs inside the sample along closed-loop paths [2].

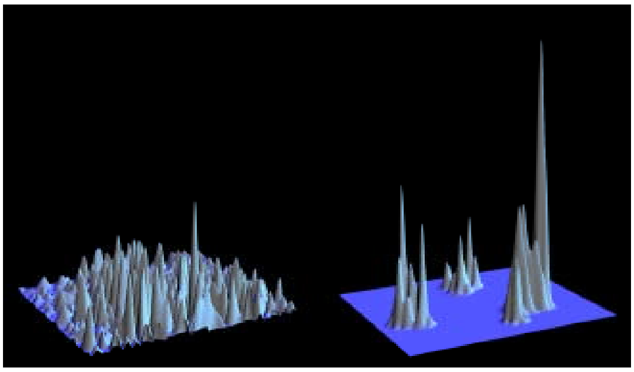

Figure 3 Spatial distribution of the light inside a random sample. In a regular disordered structure the distribution is dominated by speckle (left) while in the case of Anderson localization the light is highly localized in space and hence trapped in random modes (right). [From: D.S. Wiersma, P. Bartolini, A. Lagendijk, and R. Righini, Localization of Light in a disordered medium, Nature 390, 671 (1997).]

Localization is expected to occur when the disorder is so strong that the mean free path ζ becomes smaller then the reciprocal wavevector, so that: $k \zeta <= 1$. The product $k \zeta$ is therefore often used as parameter to characterize the amount of optical disorder, with the disorder increasing for decreasing $k \zeta$. Most optical materials in daily life have $k \zeta$ values that are much bigger than one and are therefore only weakly to modestly scattering. Even for very dense clouds we have $k \zeta$ values that are bigger than 10^6, so that light is diffusively transported instead of trapped. This is also the reason that sunlight can penetrate clouds diffusively. If clouds were to Anderson localize light, the incident sun would

be mostly reflected back leaving the earth completely dark on a cloudy day.
Anderson localization is a phenomenon that is very interesting from a fundamental point of view, while at the same time could be used in applications, for instance, to trap and thereby efficiently absorb light in solar cells [4,3]. A spin-off company of the CNR, called Lambda Energy (www.lambdaenergy.com), is planning to target this type of application, as well as that of using Anderson localization, and nanostructured photonic materials in general, to create efficient light sources and diffusers.

Beyond diffusion: optical Levy flights
In our understanding of transport processes we usually assume that the distance covered at every step of the random walker is not varying very much. This simplification seems reasonable at first sight, since it allows to consider only the average value of this step length, the so called mean free path. Physicists use this simplification, which is based on the central limit theorem, very often. In a Lévy flight the step length of the random walk is far from constant and this means that in some occasions very large steps can occur. These large steps not only mean that the random walker can cover a much vaster area, but they also lead to the counter-intuitive property that the average step length diverges [5-7].

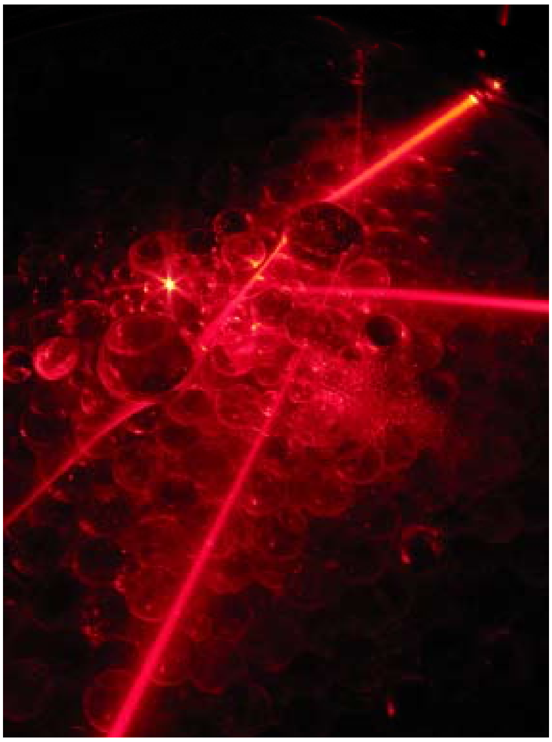

Figure 4 Flights of fancy: an inhomogeneous disordered photonic material can be used to create optical Lévy flights. This new material is also termed Lévy glass and behaves as a superdiffuser for light. [From: Pierre Barthelemy, Jacopo Bertolotti, and Diederik S. Wiersma, A Lévy flight for light, Nature 453, 427 (2008).]

Many processes in nature are actually based on Lévy flights. An important example is that of the search pattern that animals follow in search for food. Honey bees that are placed in a new environment will perform a Lévy flight to scan the area. By performing a Lévy flight they can cover a much vaster region then by performing a normal random walk. At the same time they manage to gather detailed local information in their search. Other examples of Lévy processes can be found, for instance, in the trend of the stock market, the distribution of human travel, and the diffusion of liquids in the earth's crust.

Given the vast amount of literature on optical random walks and light diffusion one might wonder if it is possible to find or realize an optical material in which light waves perform a Lévy flight. In such a Lévy glass the photons would perform a random walk with a step length distribution given by Lévy statistics. The result would be an optical super diffuser. A relatively easy, but so far unexplored possibility to do this, using high refractive index scattering particles (Titanium Dioxide in our case) in a glass matrix. The local density of scattering particles is modified by including glass microspheres of a well-chosen size distribution. These glass microspheres do not scatter since they are incorporated in a glass host with the same refractive index. Their purpose is to modify locally the density of scattering elements. In Figure 4 the concept of an optical Lévy flight is visualized.

The power-law step size distribution of a Lévy flight is expected to give rise to strong fluctuations in the transport properties of individual samples. In the total transmission profile one should therefore observe large differences from one disorder realization to another. In comparison, a common diffusive sample would show nearly no fluctuations. The characteristics of the Lévy flight also survive if we perform an average over a large number of samples. In that case we observe that the Lévy flight spreads the light much more efficiently than the regular Gaussian system. This is a direct consequence of the superdiffusive transport in Lévy systems. It is very interesting to examine interference effects like Anderson localization in such optical super diffusers, with many open questions left to address [8].

Applications
The research on light diffusion and disordered photonic structures in general has seen an enormous boost in recent years. One of the reasons is that most photonic materials, and especially photonic crystals, intrinsically suffer from structural order [9]. It is simply impossible to make a perfect photonic crystal without some level of randomness. This made it ever so important to understand how disorder affects the propagation of light and what the physics is behind disorder related optical phenomena. It also became clear, however, that disorder is not necessarily a disadvantage. It was found, for instance, that disorder in photonic crystals can

lead to a very efficient trapping mechanism for optical waves. This is very promising for optical memory applications, slow light devices and even quantum optical devices, where the disorder can be actually used as an advantage [10].

Another fascinating application of diffusive materials is that of random lasing [11,12]. The multiple scattering process is capable of trapping light very efficiently and, combined with an appropriate gain medium, this can be used to create a laser source. Such a random laser uses multiple scattering as confinement mechanism and requires no mirrors or other form of cavity. (See Figure 2.) The output of such a disordered amplifying material is, of course, spread out over a broad angular range, but has otherwise several properties that are similar to the emission from a regular laser. Apart from having a narrow spectrum, the output of a random laser can have a surprisingly high level of coherence, in the sense that the photon statistics have the typical characteristics of the coherent state as produced by a laser. A random laser is capable of generating such output with an optical cavity.

Coming back to Lévy glass, one would like to use this material first of all to study the physics of Lévy transport processes in an easy and controlled way in the laboratory. In addition, this material has a very new optical appearance which could make it interesting for jewelry or art objects. Another property which can make it interesting for applications is its very efficient diffusive power. This can help the distribution of environmental light in lighting applications. It would also be interesting to try to implement optical gain in these Lévy glasses to obtain a random laser based on superdiffusion.

The LENS laboratory

LENS is a European center of excellence of the University of Florence that focusses on basic research and applications in various fields of physics and chemistry, including atomic physics, photonics, chemical physics, and life sciences (www.lens.unifi.it). LENS is the largest laser facility in Italy and part of the Italian roadmap of large scale infrastructures. The institute is also closely linked to the Italian research council CNR and thereby has a bridge function between university and CNR. The institute provides access to its equipment and knowledge to all members of the European Community via European research and training programs and currently organizes an international PhD school.

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Nanostructured cathodes and anodes for lithium ion batteries for automotive applications

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Introduction

It is well known that the main efforts in the development of Li-ion systems go towards a lower cost, lower pollution but high specific performance and arise from huge market applications like portable electronic devices, like portable phones, camcorders and lap-top computers and the huge market of electric vehicles (EVs) and hybrid-electric vehicles (HEVs) [1-3]. In particular, the investigation on new materials for the positive and negative electrodes is one of the basic lines of research. For automotive application, where very big amounts of materials are used, some important characteristics must be taken into particular account: low environmental impact, safety, high performance and low costs. High performance can be achieved by using suitable cathodic materials that also highly influence the battery cost and the environmental impact. Safe Li-ion cells can be assembled by using polymeric instead of liquid electrolytes or by changing the anodic material. In Politecnico di Torino, the electrochemistry group is studying new materials to be applied as electrodes and electrolyte in lithium ion batteries. In Politecnico labs such materials are synthesized and characterized in little cells (about 1 cm^2) and in coffee bags. Actual researches are supported by regional, national and European funding and also by international companies. Here are reported some of the results obtained thanks to a fruitful collaboration between IRCELYON, leader on the synthesis of nano and mesostructured materials, and Politecnico of Torino, well known research centre on the materials for electrochemical generators. Researches on cathodic materials [4] are at the present very advanced and posed the basis of a patent and next future industrial application. The results presented here on anodic materials, although promising, are actually only preliminary. During the presentation, it will be pointed out as a deep study of nanostructured materials, starting from the synthesis to the electrode production, is fundamental for practical application in the automotive field.

Experimental

The lithium iron phosphate samples were prepared by direct mild hydrothermal synthesis following [4]. Starting materials were $FeSO_4 \cdot 7H_2O$, H_3PO_4, LiOH in the stoichiometric ratio 1:1:3 and hexadecyl-trimethylammonium bromide ($C_{19}H_{42}BrN$, CTAB). The receipt was bettered adding a co-solvent during the synthesis [5]. The BET surface area of calcined sample is 60 m²/g. XRD data show that the sample is highly crystalline and very pure. Different preparation methods were used to synthesize TiO_2. In particular samples were synthesized starting from P123 and $Ti(OEt)_4$ or $Ti(OBu)_4$, from TBAB (Tetrabutyl ammonium bromide) and $Ti(OPr)_4$ and from CTAB or $C_{18}TAB$ (Octadecyl Trimethyl Ammonium Bromide) and $TiOSO_4$. The data here reported are relative to the preparation of TiO_2 starting from TBAB (defined just above) and $Ti(OPr)_4$. The components were mixed in a solution of TABT and at the boiling point is added $Ti(OPr)_4$. The mixture was stirred for 3 h, washed with water and ethanol and then calcined in air in the temperature range 250° C – 550° C. The final sample presented a BET surface area of 122 m²/g .
Fe_2O_3 was prepared as a replica of SBA15 mesoporous sample. SBA15 was impregnated woth $FeNO_3$ $9H_2O$ and calcined in air at 300 and 600 °C. Silica was removed with NaOH solution. Voltammetric and galvanostatic tests were carried out using liquid electrolyte (1M LiPF6 in a 1:1 mixture of ethylene carbonate (EC) and diethyl carbonate (DEC).

Results and discussion

Cathodic material

$LiFePO_4$ was chosen as cathodic material as it is intrinsically safe and it has a low environmental impact. The reported synthesis is low cost and very simple. A patent is pending on the presented process.
The addition of the template together with the co-solvent during the synthesis of $LiFePO_4$ leads to the formation of a very pure sample covered by a thin carbon layer, as shown by HRTEM image in Fig.1.

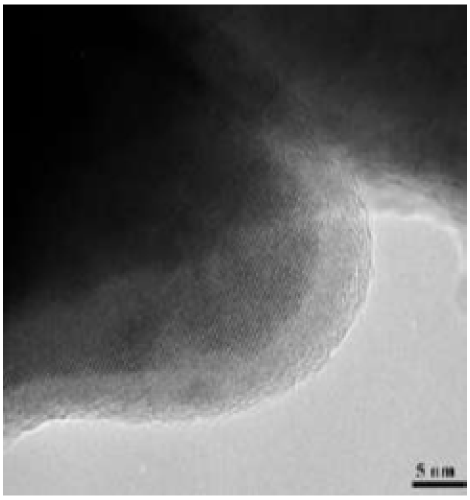

Fig.1 HRTEM image of $LiFePO_4$/C composite

Electrochemical tests (Fig.2), at room temperature, show the very good performance of the $LiFePO_4$ samples: the plot puts in evidence the good cycling stability of this sample, which shows a high rate capability and even a slight progressive improvement of the charge coefficient at high discharge regimes. The capacity at C/20 is very close to the theoretical value (170 $mAhg^{-1}$). A very low decrease in capacity is present at high Crates (e.g. 20C). This makes this sample particularly attractive for automotive applications as it can be fast charged and discharged.

This C layer is thick enough to assure a good electronic conductivity, but it is also permeable to Li^+ ions, to assure the ionic conductivity. Cathodic particles are nanostructured: its average size is about 40 nm. These two characteristics, nanosize and carbon coating, permits the complete charge and discharge of the active material contained in the sample.

Anodic material

The substitution of graphite, commonly used as anodic material, with oxides at higher voltage, makes the complete cell more stable and therefore more safe, but with lower voltage. The use of a template assisted synthesis makes possible to obtain nanostructured particles also in the case of anodic materials. In particular here is presented a TiO_2 sample whose particles size is lower of 10 nm, (Fig.3). TiO_2 particles are very well crystallized.

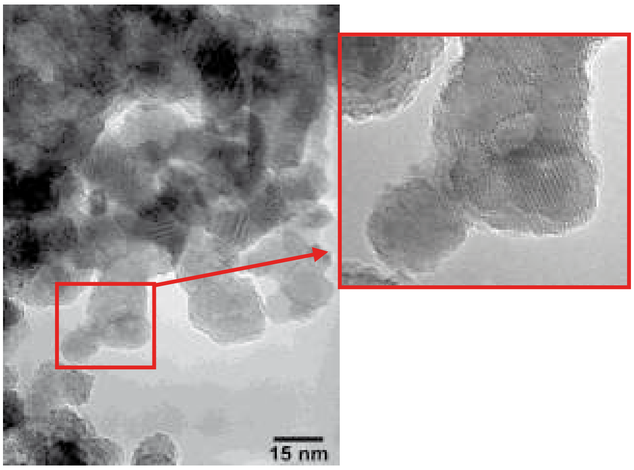

Fig. 3 HRTEM image of TiO_2 sample.

Preliminary data of charge and discharge of one of the prepared samples show a good cyclability of TiO_2 (Fig.4). The specific capacity is not far from the theoretical one. The studied sample shows an important loss of capacity after the first cycles, but after these, the electrochemical performance are promising as there is a very slow fading during cycling even at higher C rates.

Electrochemical experiments on the complete cell are still running

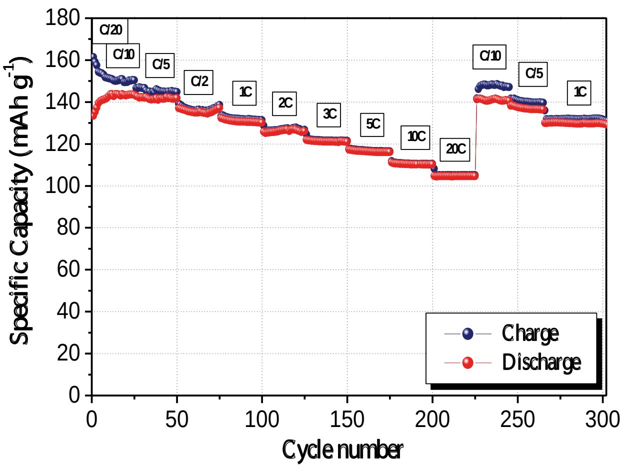

Fig.2 Charge–discharge cycling test of $LiFePO_4$/C sample at different C-rate (from C/20 to 20C) EC/DEC mixture.

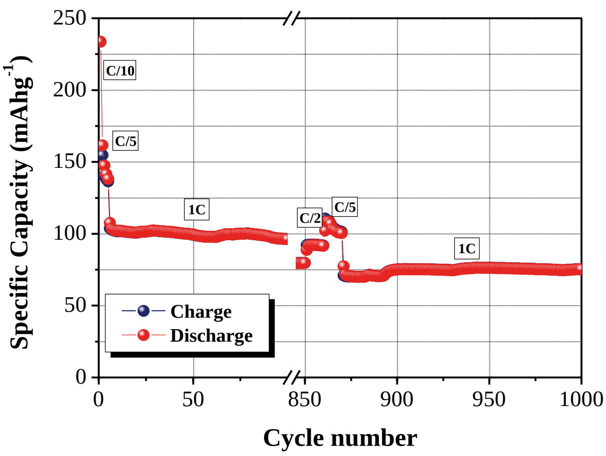

Fig. 4 Charge–discharge cycling test of TiO_2 sample at different C-rate (from C/20 to 1C)

Fe_2O_3 was also synthesized ad it is an interesting material to be used as anode for Liion cells. It is a very low cost and highly environmental friendly materials. Moreover its theoretical capacity is higher than 1000 $mAhg^{-1}$, making it very attractive for the automotive application. The TEM micrograph (Fig. 5) shows a well crystallized, nanosized and ordered sample.

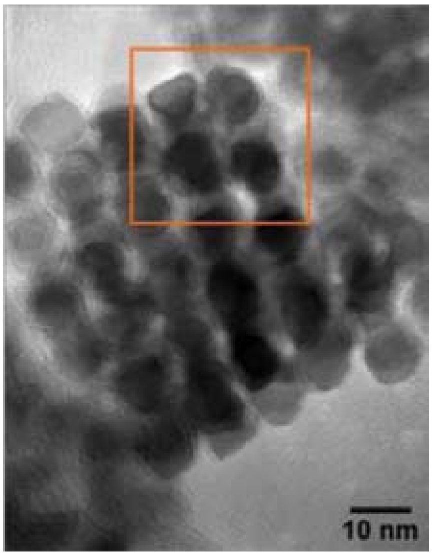

Fig. 5 HRTEM image of Fe_2O_3 sample.

Nevertheless, though the structural characteristics are very interesting by the nanotechnological viewpoint, the electrochemical performance are quite unsatisfying, as shown in Fig. 6.
The electrochemical activity falls after few cycles.

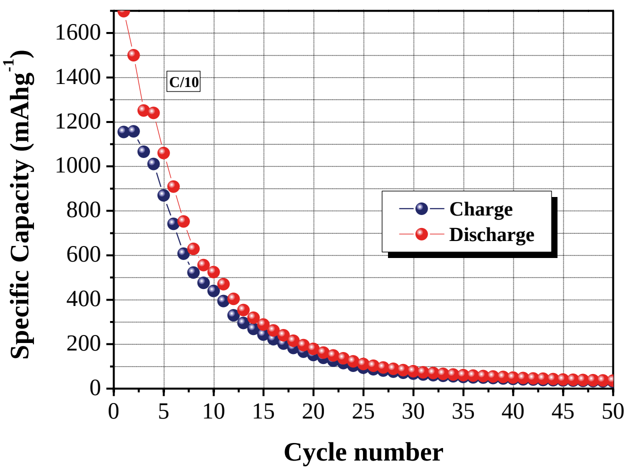

Fig. 6 Charge–discharge cycling test of Fe_2O_3 sample at different C-rate (from C/20 to 1C)

To understand this behaviour, it must be taken into consideration the electrochemical mechanism of charge and discharge of Fe_2O_3. As reported in [7] during reduction, metallic iron is formed, causing the mesoporous structure to collapse and making the following charge reaction very difficult.

$$Fe_2O_3 + 6Li^+ + 6e \leftrightarrow 3Li_2O + 2Fe$$

This reaction can be reversible, but the mesoporous structure cannot be obtained again during cycling.
To increase the electrochemical performance, new nanostructured sample have been prepared at lower temperature and nanorods have been obtained which show higher electrochemical activity [8]. Other synthetic ways will be carried out to get nanospheres.

Conclusion

Nanostructured materials are very important for electrochemical cells in particular for automotive applications. As for Li-ion cells high surface area is needed, the synthesis of nanosized particles is a milestone.
$LiFePO_4$, here presented, shows all characteristics necessary to be a very interesting cathode as it is intrinsically safe, environmental friendly and low cost as starting materials and preparation method. The coverage with a thin C layer makes it ready for use.
TiO_2 produced as nanoparticles looks to be a very interesting material for the application as anodic material. Unfortunately TiO_2 presents a too high voltage to be coupled with $LiFePO_4$ for automotive application, but, being more safe than the common carbonaceous materials, it can lead to interesting performance if coupled with high voltage cathodes. Moreover the use of nanotechnology has to be tailored according to both the application and the reaction mechanism occurring during the practical application (in the presented cases charge and discharge of the electrochemical cells) in order to assure high performance.

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Bio-sketch

Dr Silvia Bodoardo is assistant professor at Politecnico di Torino. Her research activity is carried out in the electrochemistry group and it is mainly centred on materials for electrochemical applications.

The electrochemistry group is composed by prof. Nerino Penazzi, prof. Paolo Spinelli, Dr Carlotta Francia, Dr Giuseppina Meligrana, Dr Claudio Gerbaldi and other 10 young researchers and Phd students.

Present research activity of the electrochemistry group in Politecnico follows these main lines:

- Electrochemical characterization nano- and mesoporous materials containing redox active metal species.
- Synthesis and characterization of electrodic materials for Li-ion cells, mainly focused on Li(Fe,Mn)PO4 cathodic materials.
- Synthesis and characterization of new polymeric electrolytes for Li-ion cells.
- Synthesis and characterization electrochromic materials
- Studies on Li-air systems

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A new anti-counterfeiting marking system

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Introduction

Counterfeiting is a global problem that can have major social and economic consequences. The spread, number and kind of counterfeit goods has greatly increased in recent years: according to the study of Counterfeiting Intelligence Bureau (CIB) of the International Chamber of Commerce (ICC), counterfeit Goods make up 5 to 7% of World Trade. In a recent update [1] OECD has estimated in $250 billion in 2007 the worldwide value of international trade in counterfeit and pirated goods.

As a consequence, there is a urge in developing and adopting innovative anti-counterfeiting technologies able to ensure a real protection and/or traceability of a number of items, including, e.g., forensic documents, dangerous waste, strategic components (like microprocessors in automotive/aerospace fields, both civilian and military), pharmaceutical products, currency notes, identity/credit/debit cards, quality control, commercial/artistic objects.

Our Laboratory in ENEA has recently developed a new method to fight counterfeiting and to trace critical goods, based on our know-how in the fields of optics, laser, plasma and radiation-matter interaction. Our technology allows to vary the protection level in relation to the desired extent by properly increasing the complexity of the marking procedure. On the other side, the specific reading technique is straightforward using a dedicated apparatus.

1. Background

In the last years at the ENEA Research Centre in Frascati expertise has grown in the generation of ionizing radiation and on its applications. [2, 3]. A plasma source driven by two different XeCl excimer lasers is operative and the produced radiation is used in different fields, ranging from X-ray microscopy to radiobiology, from micro-radiography to contact lithography and atomic spectroscopy. Based on this plasma source, we developed an apparatus for EUV projection lithography obtaining a sub-100-nm-resolution pattern on polymethylmethacrylate (PMMA) resist [4, 5].

Besides affecting the chain bonds of polymers like PMMA, the plasma produced ionizing radiation also may alter the atomic structure of a class of crystalline luminescent materials, thanks to its high-energy photons. In particular conditions, the radiation can "print" on the material an invisible trace corresponding to a pre-determined image, patterned, e.g., on a mask. Since most luminescent materials can be grown in form of thin films on flexible and transparent substrates, they can be used as adhesive tags to be put on every items to be protected and traced.

2. Marking features

The writing process is free from any pigment deposit on the luminescent material. This allows, when needed, the achievement of an extremely high resolution in writing, down to the sub-micrometer scale (not attainable with e.g., the current ink-jet printer technology). The image generated on the film (symbol, code, number, matrix, and so on) is invisible and can also be encoded using the state-of-the-art cryptography techniques. The ENEA system is based on a "physical" reading of the hidden image, performed by means of a dedicated optical device.

Also, our technology enables to vary the security degree depending on the requirements: the writing system complexity can be increased up to a virtually inimitable marking. In fact, the image can be transferred on the film by a simple contact mask or by projection optics, scaling in this way the invisible mark details from millimeter down to micrometer size and below, so that these details cannot be distinguished using a conventional optical microscope.

It is worth to underline that the proposed system is based on absolutely novel principles, materials and methods, which are distinct from the invisible marks made using fluorescent inks, whose application does not permit to reach our high resolutions. ENEA has developed both the writing radiation source and the reading/decoding system, has tested the results and assembled a complete system to make prototype tags.

3. Experimental results

Figure 1 shows two pictures of the same region of the luminescent material, in the form of a thin film coating on a glass substrate, after exposure behind a contact mask (grid with hexagonal symmetry). The two images are taken through an optical microscope with conventional illumination and using the specific ENEA patented reading technique. The mask pattern is visible only with the appropriate reading system.

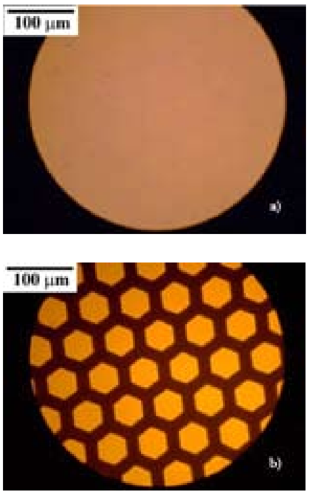

Figure 1: – Luminescent pattern obtained by contact lithography and observed at an optical microscope by visible light (a) and by using the ENEA reading technique (b).

In another prototype, we deposited a thin film of luminescent material on a plastic badge commonly used for credit or identity cards. We exposed the film to ionizing radiation trough a contact mask, thus transferring an invisible image on it, and then we put a standard plastic-coating to protect the badge. Figure 2 shows a comparison between the picture of the badge taken under natural light illumination and the image observed using the specific reading system in conjunction with an optical microscope at low magnification (2.5x). It is evident that the pattern becomes visible only in the second case.

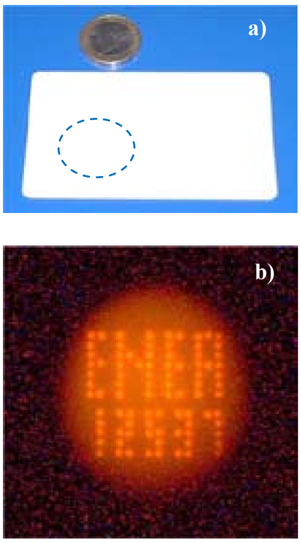

Figure 2 – a) Picture taken under natural light illumination of a standard badge (85 mm×54 mm) with an invisible mark within the dashed area; b) Picture taken at the optical microscope (magnification 2.5×) showing the same dashed area as in a), but using the ENEA reading system.

More complex patterns can be obtained by projection EUV lithography tools, using reflective masks and de-magnifying optics, which allow the reduction of the details size down to the 100-nm range. This means that our technique can be tailored on the customer demand, up to tags that are virtually impossible to counterfeit.

The security level of our technology can be further increased by digital encoding of the image, applying the current state-of-the-art cryptography techniques. In this case the control would rely not only on the physical reading of the image, but also on its decoding with the appropriate digital key/algorithm.

A prototype of a portable device able to read the invisible marks is shown in figure 3. In this case an encoding technique has been applied to crypt the hidden pattern. The PC screen shows the raw data matrix (an array of tiny squares as a 2-D barcodes) written on the film as read by the device, and the corresponding pattern "WATER MARKING" decoded by a dedicated software.

Figure 3: – Prototype of the portable reading device able to read the invisible images. On the PC screen there is the coded data matrix (a 2-D binary array) read by the ENEA device on the film, and below, the corresponding sign "WATERMARKING" as decoded by a specific software.

An additional way to further increase the security level of our technology consists in structuring the fluorescent film as a series of thin layers separated each other by non-luminescent materials, with a variable thickness. In this way, after irradiation by ionizing radiation, the spectral energy of the used ionising radiation affects the luminescence ratio of the different layers, and therefore a mark imprinted with a ionising radiation having a spectral energy different from a pre-determined original one can be easily identified.

ENEA has filed a patents about the invisible marking system [6].

4. Application to radioactive waste

A critical field of marking application is related to the traceability of radioactive waste, from both civilian (power plants, hospitals) and military uses, in order to fight their illegal disposal.

We made irradiation experiments to check if the high-energy photons emitted by radioactive substances were able to alter the structure and optical properties of the proposed materials. A lu-