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Thematic Workshop

FUNCTIONAL MATERIALS for HEALTHCARE

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Workshop proceedings

Organizing Committee

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Scientific Program

List of presentations:

- 9.00** **Introduction**
Sebastiano Andò, Francesco Puoci, Maria Stefania Sinicropi
(*University of Calabria*)
- 9.30** **Session 1** (Chair: Maria Stefania Sinicropi)
Organic Cell Stimulating and Sensing transistor architecture for neural cells investigation
Michele Muccini (*Institute for the Study of Nanostructured Materials*)
- 10.00** **Molecularly imprinted polymers for therapeutic use in metabolic disorders: the case of phenylketonuria**
Francesco Puoci (*University of Calabria*)
- 10.30** **Microfluidic procedures for fabrication of hyaluronic acid based biomaterials**
Fabio Salvatore Palumbo (*University of Palermo*)
- 11.00** **Coffee break & Poster Session**
- 11.45** **Session 2** (Chair: Maria Rosaria Plutino)
Wearing active principles: technologies for controlled release from textiles
Ada Ferri (*Polytechnic University of Torino*)
- 12.15** **Sol-gel technology: new opportunities for medical textiles functionalization**
Giuseppe Rosace (*University of Bergamo*)
- 12.45** **Concluding remarks**
Maria Rosaria Plutino (ISMN-CNR), Maria Stefania Sinicropi
(*University of Calabria*)

Lectures

Organic Cell Stimulating and Sensing transistor architecture for neural cells investigation

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The development of innovative bioelectronic devices for monitoring nerve cells activity with improved biocompatibility, sensitivity and spatiotemporal resolution is a stringent condition to understand brain physiology and pathophysiology. We have already demonstrated that primary neurons can adhere, grow and differentiate on a suitably engineered perylene-based thin-film transistor platform, while maintaining their firing properties even after a prolonged time of cell-culturing [1]. Moreover, we implemented the platform called organic cell stimulating and sensing transistor device (O-CST) for stimulating the neuronal cells and recording the bioelectrical activity [2]. Here, our recent activity concerning the validation of O-CST for the study and manipulation of ion channels and calcium signaling in non excitable (glial) cells and on the study of sensing and transduction mechanisms of O-CST will be presented.

O-CST is biocompatible with astrocytes and its operation lead to an exclusive increase in the astroglial inward whole-cell conductance that we could attribute to specific ion channel. We also found that O-CST stimulation evokes an intracellular calcium increase, which can be monitored by calcium imaging due to the O-CST's transparency. Notably, by a combination of patch-clamp, calcium imaging and computational analyses, we show that the evoked current and calcium response are dependent on the O-CST device architecture.

Furthermore, by performing Electrical Impedance Spectroscopy (EIS), we propose the working principles of the sensing mechanism of the O-CST architecture by introducing a suitable equivalent circuit. We succeeded in validating a macroscopic model by achieving surface potential maps of the organic layer surface after the device biasing in wet conditions [3]. Collectively, our results confirm the potential of O-CST for selective manipulation of bioelectrical activity of neural cells and describe a model that is straightforward to discriminate the different processes occurring at the interphase between the electrolyte and the organic layer which rule the ions-electrical transduction mechanism in the device.

[1] Toffanin S., Benfenati V., Muccini M. et al., *J Mater Chem*, 2013, 1, 3850-3859.

[2] Benfenati V., Toffanin S., Muccini M. et al., *Nature Materials*, 2013, 12, 672-680.

[3] Lago N., Muccini M., Toffanin S., et al., *Organic Electronics*, 2016, 35, 176–185.

Molecularly Imprinted Polymers and metabolic disorders

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Molecular Imprinting represents a very promising and attractive technology for the synthesis of Molecularly Imprinted Polymers (MIPs) characterized by specific recognition capabilities for a desired template molecule in preference to other closely related compounds. MIPs are synthesized by polymerizing functional and cross-linking monomers around a template molecule to obtain a highly cross-linked three-dimensional network polymer. Once polymerization has taken place, the template is extracted to give a porous material containing binding sites that are complementary to the target molecule in terms of size, shape and functionalities. MIPs can find application in several fields as chromatographic stationary phases, solid-phase extraction (SPE), receptors, affinity and sensing materials, drug delivery systems.

When a critical enzyme for a metabolic pathway is disabled and/or when a control mechanism is affected, a metabolic disorder occurs. Many of these metabolic diseases are inborn errors of metabolism due to a mutation in a metabolic enzyme or in regulatory proteins and in transport mechanisms. Among them, phenylketonuria (PKU) is caused by variants on the gene for phenylalanine hydroxylase (PAH), which result in a phenylalanine (Phe) accumulation to neurotoxic levels. Therefore, MIPs able to selectively recognize and bind Phe could find application in the treatment of PKU attenuating the absorption of this amino acid.

Microfluidic procedures for fabrication of hyaluronic acid based biomaterials

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Microfluidics has emerged as an innovative approach to manipulate small amounts of reagents in order to provide an accurate control of mixing and physical processes at microscales. The advantages of microfluidics include reduced reagent and drugs consumption, efficient heat and mass transfer and enhanced process accuracy and efficiency¹. Microfluidic technology can allow manufacturing improvements in the fields of drug and cell therapies; products obtained can be polymeric nanoparticles, nanofibrils, nanoemulsions, microparticles and fibers². In comparison to conventional preparation methods, microfluidic offers superior control over biomaterials yield and physicochemical properties³. As example, nanoparticle size can be readily tuned by adjusting the flow rate, solvent polarity, concentration, and composition of polymers. In addition, nanoparticles manufactured by microfluidics can be parallelized and scaled up in the pharmaceutical industry to enable large-scale production⁴. Microfluidics has been recognized also to be an efficient method to produce fibers. It is possible use these microfibers for many applications in regenerative medicine or for drug delivery purposes. Native hyaluronic acid has been slightly employed for microfluidic fabrication procedures because lacks of stimulus sensible self-assembling properties. Hyaluronic acid can represent a convenient choice for the production of micrometric bioactive materials due to the ability of stimulate specific cellular responses and in consideration of its targeting properties, for the production of nanoparticles. Recently we have proposed a hyaluronic acid derivative functionalized with pendant octadecylamine (C₁₈) and ethylenediamine (EDA) groups having ionic strength sensitive properties that can be exploited for controlled physical crosslinking into buffers having physiologic ionic strength⁵⁻⁸. In this work, the possibility to control the shape and dimension of biomaterials via microfluidic fabrication technique has been investigated by regulating HAEDAC₁₈ molecular weight and the viscosity of polymeric dispersion using as solubilizing agent hydroxypropyl- β -cyclodextrin (HPCD). Two HAEDAC₁₈ derivatives having different molecular weight have been assayed for production on nanogels and micrometric fibers that have been assayed for potential drug delivery and regenerative medicine applications.

- [1] Top. Curr. Chem. 2011; 304: 27–68.
- [2] ACS Nano2010; 4:1671–1679.
- [3] J. Controll. Rel. 219 (2015) 536–547.
- [4] Pharm. Res. 2015 32:2727–2735.
- [5] Macromol. Biosci., 2016, 16, 1485-1496.
- [6] Mater. Letters, 2016, 182, 309–313.

Wearing active principles: technologies for controlled release from textiles

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Biofunctional textiles are new functional materials recently proposed to deliver active principles through an extremely comfortable delivery system: a piece of garment. A number of functionalized garments are now reaching the market under the classification of cosmeto-textiles. This definition was coined by the European Committee for Standardization CEN in the Test Report 15917:2009, which established the following major issues to be addressed by cosmeto-textiles: safety, claimed effect, care resistance and labelling. In between market enthusiasm and regulatory bodies prudence, textile research centres are working to develop and validate biofunctional fibres, fabrics or garments which are expected to release active principles in a reliable fashion.

The speech will present state-of-the-art technologies for the production of biofunctional textiles through two main technologies: microencapsulation and host-guest systems. Besides the literature review, the experience of the authors in this field will be presented. Cyclodextrin-based nanosponges, able to form stable complexes with active principles, and microcapsules of biodegradable polymers have been used for the functionalization of natural and synthetic fibres. A number of different applications have been envisaged, such as mosquito-repellence, sleep-wake regulation, refreshing comfort and slimming effect.

The research covered the entire functionalization and validation process: from the synthesis of the delivery systems to fabric functionalization. from quantification of the active principles on the fabric before and after fabric care cycles to in-vitro release kinetics. In one case, in-vivo tests were carried out to check safety and exclude any adverse effect on the skin.

The aim of the speech is drawing attention to a potential niche-market for added-value textiles. At the end of the speech, the audience will have a clear idea of advantages and disadvantages of cosmeto- and biofunctional garments.

Sol-gel technology: new opportunities for medical textiles functionalization

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Chemical finishing has always been an important component of textile processing, but in recent years the trend to “high-tech” products has increased their interest and use. As the use of high-performance textiles has grown, the need for chemical finishes to provide the fabric properties required in these special applications has grown accordingly [1]. Textile materials (woven, nonwoven, knitted, and composites) have found different end-uses in medical and healthcare applications. Depending on the specific end-use, different products have to meet the demands for the specific end-use performances [2]. Irrespective of their applications, internal (surgical threads and various implants) or external (gauzes, bandages, surgical masks, gowns and apparel, nappies, tampons, and so on), medical textiles have to be comprised of basic bioactive properties, especially antimicrobial [3]. In the last few years, sol-gel technology, as a chemical finishing technique for fabric, has shown interesting application for the textile industry. This is mainly due to the versatility of this technique and the ease with which its properties may be tailored to fit a particular application. The unique and new properties of sol-gel materials have attracted not only scientists and researchers but also businesses, due to their huge economical potential. The type of solvent is an important parameter in technical processes. Organic solvents have the advantage of low times of dry treatment and can in this way lead to a reduction in working time and energy costs but due to environmental and safety aspects water containing systems are usually favoured [4]. For these reasons, for the most common textile applications the sol has to contain a high content of water and the amount of organic solvent should be as small as possible. A thermal treatment of the coating should not exceed a maximum of 180°C, because of the limited thermal stability of textile fabrics. Textiles should have also a homogeneous coloration which is stable under the conditions of a common sterilisation procedure (121°C and 1.5 bar). The goal of this presentation is to demonstrate the potentiality of sol-gel based halochromic dyestuff coatings in the development of wearable optical sensor device for pH real-time measurements [5,6]. In fact, pH sensors are nowadays important due to the wide range of information that they may provide about the wearer’s health (i.e. body hydration level or potential pathogenesis of skin disease) and so for their impact on daily life and in several fields such as medical, diagnostic and environmental.

- [1] Schindler WD, Hauser PJ, Chemical Finishing of Textiles, WoodheadPublishing, Cambridge, 2004.
- [2] White WC, Bellfield R, Ellis J, Vandendaele IP. Controlling the spread of infections in hospital wards by the use of antimicrobials on medical tetxtiles and surafaces. In: Medical and Healthcare textiles, Woodhead Publishing Limited, 2010.
- [3] Harrison PW. Developments in Medical Textiles. The Textile Institute, Textile Progress, 32, 4, Manchester, 2002.
- [4] Mahltig B, Audenaert F, Böttcher H (2005) J Sol-Gel Sci Technol 34:103.
- [5] Caldara M, Colleoni C, Guido E, Re V, Rosace G (2012) Sens. Actuators B 171–172: 1013–1021.
- [6] Caldara M, Colleoni C, Guido E, Re V, Rosace G (2016) Sens. Actuators B 222:213-220.

Poster presentations

In vitro antioxidant, anti-inflammatory and mucolytic activities of methylsulfonylmethane

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Design, synthesis and anti-proliferative activity evaluation of new N-tioalchilcarbazole derivatives

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Gold-based nanoconjugates of antiretroviral agents: exploring multivalency in anti-HIV drugs

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Carbazole Functionalization of Gold Nanoparticles: Synthesis and Physical-Chemical Characterization

Sinicropi M.S.,^a Iacopetta D.,^a Ceramella J.,^a Caruso A.,^a Muià N.,^a Puoci F.,^a Saturnino C.,^b Longo, P.,^c Galletta, M.,^d De Luca, G.,^{d,e} Plutino M.R.^f

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Titanium dioxide nanoparticles: metabolic profiling on human keratinocytes

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Stabilization strategies for photosensitive drugs

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New Quercetin Derivatives: evaluation of antiproliferative activity and inhibition of human Topoisomerase I and II

Iacopetta Domenico^a, Caruso Anna^a, Ceramella Jessica^a, Muià Noemi^a, Puoci Francesco^a, Scrivano Luca^a, Grande Fedora^a, Rosano Camillo^b, Plutino Maria Rosaria^c, Sinicropi Maria Stefania^a

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Interconnected PolymerS TeChnology: an effective approach for the treatment of hair loss

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Synthesis and in vitro anti-cancer evaluation of cross-linked poly(ethyl cyanoacrylate) nanoparticles loaded with quercetin

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Doxorubicin adsorption on novel pure and hybrid Zeolite Membranes

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Self-supported nanozeolite membranes for cell cultures

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Calixarene-capped gold nanoparticles for sensing of bioactive molecules

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Wearable sensors based on hybrid sol-gel for the monitoring of sweat pH

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