

**E·MRS**  
European Materials Research Society

**Spring Meeting 2021**  
May 31 | June 4 | Virtual Conference

**SYMPOSIUM 0**  
Bioinspired and biointegrated materials as new frontiers  
nanomaterials 10<sup>th</sup> edition

*Nature Inspirations Powering Life*  
Raphael (1480-1520) An Allegory (Detail)  
National Gallery London, UK

Thursday June 3.2021  
**Stimuli - Responsive Materials, Surfaces/Interfaces and Systems**  
Multi-Functionality **SESSION** Invited Presenters

*The E-MRS INVITED Organizer/Chair Dr. Donata Iandolo (Ecole des Mines de Saint-Etienne, University of Lyon, Universite Jean Monnet, INSERM, France)*



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*The E-MRS INVITED Chair*

*Full Professor BEATRICE FRABONI (University of Bologna, Italy)*



**Beatrice FRABONI**

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Dr. **Donata IANDOLO** is Senior postdoc at the Ecole des Mines de Saint-Etienne (France). She has recently completed a Marie-Sklodowska Curie postdoctoral fellowship at the Department of Chemical Engineering and Biotechnology of the University of Cambridge. She received her master's degree in Industrial Biotechnologies at the University of Naples "Federico II" (Italy) and a PhD thesis in Industrial Biotechnologies. She then joined the Soft Matter Nanotechnology Group at the National Nanotechnology Laboratory (CNR-NANO) (Lecce, Italy) and subsequently worked with Prof. Magnus Berggren at the Laboratory of Organic Electronics. She carried out her Marie-Sklodowska Curie fellowship in Roisin Owens' laboratory. Her research focus is on the use for bioelectronics materials and devices for bone tissue engineering and sensing.

**The activity in the E-MRS:** Dr. Donata IANDOLO contributed to the E-MRS 2014 - 2019 editions with a special invited Presentations and common presentation with Graduate Student (Young Investigator FORUM 2017) and Keynote Presentation at The Young Scientists Forum (2019) at the E-MRS Symposia "Bioinspired and Biointegrated Materials as New Frontiers Nanomaterials" VI, VII th editions.

Dr. IANDOLO is now the Invited Organizer/Chair and Key Presenter at Special Session the Symposium X th edition.

**Recent Publications:**

- Sheard, J., Bicer, M., Meng, Y., Frigo, A., Martinez Aguilar, R., Vallance, T., **Iandolo, D.** and Widera, D. (2019) Optically transparent anionic nanofibrillar cellulose is cytocompatible with human adipose tissue-derived stem cells and allows simple imaging in 3D. *Stem Cells International*. **2020**.
- Decataldo, F., Druet, V., Pappa, A.M., Pitsalidis, C., Tan, E., Savva, A., Inal, S., Kim, J.K., Owens, R., Fraboni B., **Iandolo, D.**, BMP-2 functionalized PEDOT:PSS-based OECTs for stem cell osteogenic differentiation monitoring. *Flexible and Printed Electronics*. Accepted Manuscript online 26 November **2019**. doi: [10.1088/2058-8585/ab5bfc](https://doi.org/10.1088/2058-8585/ab5bfc).
- **Iandolo, D.**, Pennacchio, F. A., Mollo, V., Rossi, D., Dannhauser, D., Cui, B., Owens, R. M., Santoro, F., 3D Biointerfaces: Electron Microscopy for 3D Scaffolds–Cell Biointerface Characterization. *Advanced Biosystems*. **3**, 2, 1970024, **2019**. doi: [10.1002/adbi.201800103](https://doi.org/10.1002/adbi.201800103)
- D. Sheard, J., Bicer, M., Meng, Y., Frigo, A., Martinez Aguilar, R., Vallance, T., **Iandolo, D.** and Widera, D. Optically Transparent Anionic Nanofibrillar Cellulose Is Cytocompatible with Human Adipose TissueDerived Stem Cells and Allows Simple Imaging in 3D. *Stem cells international* **19**, 12, **2019**. doi:[10.1155/2019/3106929](https://doi.org/10.1155/2019/3106929).
- Brooke, R., Edberg, J., **Iandolo, D.**, Berggren, M., Crispin, X., Engquist, I., Controlling the electrochromic properties of conductive polymers using UV-light. *Journal of Materials Chemistry C*, **6**, 17, 4663-4670, **2018**. doi:[10.1039/C7TC05833K](https://doi.org/10.1039/C7TC05833K).

**Abstract Control ID number PIDWZ**

**Key Presentation**

**(key presentation) Bone tissue engineering: a bioelectronics approach**

Donata Iandolo,<sup>a,b</sup> Jonathan Sheard,<sup>c</sup> Charalampos Pitsalidis,<sup>b</sup>  
F. Santoro,<sup>d</sup> Bianxiao Cui,<sup>e</sup> Darius Widera,<sup>c</sup> Roisín M. Owens<sup>b</sup>

<sup>a</sup>*École des Mines de Saint-Étienne, INSERM U1059, France;* <sup>b</sup>*Department of Chemical Engineering and Biotechnology, University of Cambridge, United Kingdom;* <sup>c</sup>*School of Pharmacy, University of Reading, United Kingdom;* <sup>d</sup>*Center for Advanced Biomaterials for Healthcare (Italy);* <sup>e</sup>*Department of Chemistry, Stanford University (US).* e-mail: [donata.iandolo@emse.fr](mailto:donata.iandolo@emse.fr)

Osteoporosis is a skeletal disease characterized by bone loss and bone microarchitectural deterioration. The increasing life expectancy calls for innovative and effective approaches to compensate for bone loss. Due to their well-documented regenerative and anti-inflammatory potential, stem cells represent a promising option. The knowledge of bone piezoelectricity and of bioelectricity as a further cue to influence cell fate, in addition to biochemical and mechanical ones, has elicited for the use of physical stimulation together with electroactive materials as smart alternatives for bone tissue engineering. The combination of smart substrates, stem cells and physical stimulation to induce cell differentiation is therefore a new avenue in the field. Biomimetic scaffolds were prepared by combining the conducting polymer PEDOT:PSS with collagen type I, the most abundant protein in bone. Pores sizes, mechanical and impedance properties were measured as a function of scaffolds composition. Two populations of stem cells were used to understand the impact of scaffold composition on cell behavior. Recent results on devices developed to assess stem cell differentiation will be presented.



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Beatrice FRABONI is a Full Professor of Physics, holds a Ph.D. in Physics from the University of Bologna, a Master in Microelectronics from the University of Cambridge (United Kingdom) and a Master in Science and Technology of Semiconductors from the University of Parma. In 2000 she joined the Faculty of Physics at the University of Bologna. Since 2019 serves as the Director of the Collegio Superiore of the University of Bologna. Her research activity focuses on the analysis and characterization of the electrical transport properties of organic and inorganic semiconducting materials and of advanced (bio)electronic devices. She coordinates national and international research projects, published over 150 papers in international refereed journals and holds 10 patents.

Co-author of over 150 publications in internationally refereed journals and various invited contributions in international conferences and workshops. Co-author of 15 patents. Founding member of the academic Spin-off "LabTrek", targeting the development and production of educational apparatuses for teaching physics at an advanced level. Award IITWIN (Associazione Italiana Donne Inventrici e Innovatrici): Best Woman Inventor of the year (2016). Award OA-LOPEC (Large-area, Organic & Printed Electronics Convention) Competition: Best publicly funded demo for the i-FLEXIS Project (2017).

The activity at The E-MRS: Professor Beatrice FRABONI - The E-MRS Executive Committee Member. The Executive Committee is in charge of all aspects relative to the life and work of the Society.

*Abstract Control ID number IRD9P*

*Key Presentation*

### **(key presentation) Textile organic biosensors for advanced wearable healthcare**

L. Possanzini (1), I. Gualandi (2), M. Tessarolo (1), F. Mariani (2), F. Decataldo (1), E. Scavetta (2), B. Fraboni (1)

(1) *Dipartimento di Fisica e Astronomia, Università di Bologna, Italy*

(2) *Dipartimento di Chimica Industriale, Università di Bologna, Italy.*

The development of portable and wearable sensors is of high importance in several fields, such as point-of-care medical applications and environmental monitoring. To this end, Organic Electrochemical Transistors (OECTs) offer consistent advantages such as easy and cheap readout electronics, low supply voltage (usually  $< 1$  V), low power operation ( $< 100$  nW), bio-compatibility, ease of integration. Moreover, the transistor configuration provides intrinsic amplification of the output signal and gives design freedom in terms of device geometries and substrates (flat/flexible). Here we report a new biosensing platform inspired by the organic electrochemical transistor (OECT), based on a composite material of PEDOT:PSS (poly(3,4-ethylenedioxythiophene) poly(styrene sulfonate)) and Ag/AgX nanoparticles, where X refers to the ion to be detected in the fluid of interest (e.g. Cl<sup>-</sup>, Br<sup>-</sup>, I<sup>-</sup> and S<sup>2-</sup>). The Ag/AgX NPs act as a gate electrode embedded into the conductive polymer channel, thus combining an intrinsically amplified response with a simple two terminal electrical connection. Electrostatic Force Microscopy and Electrochemical Impedance Spectroscopy analyses demonstrate the electronic coupling between the electrochemically active NPs and the semiconducting polymer, which allows to explain the sensor amplified transduction. The analytical signal is the current that flows in the composite polymer and its variation is directly proportional to the logarithm of Cl<sup>-</sup> concentration in the range  $10^{-4}$  to 1 M. The simple, two terminal configuration of the here proposed biosensors has relevant positive implications on the read-out electronics, on the adaptability to unconventional geometries and on the response time, faster than for a conventional OECT endowed with a standard Ag/AgCl gate electrode [1]. Moreover, its ability to operate by sampling only a few microliters of fluid is ideal for wearable, non-invasive bio-fluid sampling. The analysis of concentrations of ions in biofluids, such as sweat, is crucial for several health conditions. In particular, the evaluation of Chloride concentration in sweat for infants and children is a method for diagnosing Cystic Fibrosis. Moreover, the presence of different ion concentrations in sweat can be directly related to dehydration and its real-time monitoring while training can help athletes' control and improve their performance. The main bottlenecks for developing such non-invasive biosensors are the relatively large amount of biofluid needed for such analyses and the sensitivity and portability of the sensing system, issues that are fully overcome by the here proposed biosensors. We demonstrate their operation and performance in artificial sweat and we validate the implementation of our biosensors in a fully textile electronic device, fabricated directly onto a cotton yarn for real-time sweat monitoring. [1] I. Gualandi, M. Tessarolo, F. Mariani, T. Cramer, D. Tonelli, E. Scavetta and B. Fraboni, *Sensors & Actuators: B.* 273, 834 (2018)





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Dr. **Mark Schwartzman** is an Assistant Professor in the Department of Materials Engineering and in the Isle Katz Institute for Nanoscale Science & Technology that is part of the Ben-Gurion University of the Negev, Israel. He received his PhD in Columbia University, NY in 2009, and did his postdoc training in Weizmann Institute of Science, Rehovot, Israel. He has over 10 years of research experience on nanoimprint lithography and nanostructured materials. Over the years, he has publications in various prestigious international journals including Science and PNAS and presented his work at various national and international conferences. He is a reviewer for the Journal of Vacuum Science and Technology since 2008 and affiliated with the Israel Vacuum Society since 2009.

### **Selected Publications**

1. G. Le Saux\*, N. Bar Hanin\*, A. Edri, U. Hadad, A. Porgador, and M. Schwartzman, "Nanoscale Mechanosensing of Natural Killer Cells is Revealed by Antigen-Functionalized Nanowires", *Adv. Mater.* **2019**, 31,1805954.
2. D. Tsivion, M. Schwartzman, R. Popovitz-Biro, P. von Huth, and E. Joselevich, "Guided Growth of Millimeter-Long Horizontal Nanowires with Controlled Orientations" *Science* **2011**, 333 (6045), 1003.
3. M. Schwartzman, D. Tsivion, D. Mahalu, O. Raslin, and E. Joselevich, "Self-Integration of Nanowires into Circuits by Guided Growth" *Proc. Nat. Acad. Sci. USA* **2013**, 100 (38), 15195.

*INVITED Author/Article for SPECIAL ISSUE of the Journal*

*Abstract Control ID number N7TKI*

*Key Presentation*

## **Molecular Scale Spatio Chemical Control of the Activating-Inhibitory Signal Integration in NK Cells**

**Mark Schwartzman**

*Department of Materials Engineering, Ben-Gurion University of the Negev, Beer-Sheva, Israel*

The role of the spatial juxtaposition between activating and inhibitory receptors in cytotoxic lymphocytes has been strongly debated in the context of the inhibition of immune signaling. The challenge in addressing this problem was so far a lack of experimental tools which can simultaneously manipulate different signaling molecules. Here, we circumvented this challenge by introducing a nanoengineered multifunctional cell niche, in which activating and inhibitory ligands are positioned with molecular-scale variability and control, and applied it to elucidate the role of the spatial juxtaposition between ligands for NKG2D and KIR2DL1 activating and inhibitory receptors in Natural Killer (NK) cells in KIR2DL1-mediated inhibition of NKG2D signaling. We realized the niche by a nanopatterning of nanodots of different metals with molecular scale registry in one lithographic step, followed by a novel ternary functionalization of the fabricated bi-metallic pattern and its background with three distinct biochemical moieties. We found, that within the probed range, the 40 nm gap between the activating and inhibitory ligands provided an optimal inhibition condition. Supported by theoretical modeling and simulations, we interpret these findings as a consequence of the size and conformational flexibility of the ligands in their spatial interaction. Our findings provide an important insight into the spatial mechanism of the inhibitory immune checkpoints, whose understanding is both fundamentally important, and essential for the rational design of future immunotherapies. Furthermore,

our approach is highly versatile and paves the way to numerous complex molecular platforms aimed at revealing molecular mechanisms through which receptors integrate their signals.

*INVITED Author/Article for SPECIAL ISSUE of the Journal*

*Abstract Control ID number R4UAJ*

*Invited Presentation*

## **Nanoscale spatio-mechanical regulation of the immune signaling in cytotoxic lymphocytes**

**Mark Schwartzman**

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It has been long known that cytotoxic lymphocytes the sentinels of our immune system differentiate between pathogens and healthy cells by sensing environmental chemical cues, which are delivered by the ligands expressed on the surface target cells. Yet, it is becoming progressively clear that lymphocytes sense also physical environmental cues, such as ligand arrangement, mechanical stiffness, and topography. In the first part of my talk, I will review our recent study of the role of the ligand arrangement in the immune function of Natural Killer (NK) cells, using nanoengineered stimulating platforms based on patterned arrays of ligands. The first generation of such platforms was based on arrays of nanoimprinted metallic nanodots functionalized with activating ligands, which allowed us to discover the minimal spatial requirement of  $\sim 1$  ligand per sq. micron needed for the activation of NK cells. The next, more advanced generation of arrays came to examine how the segregation between activating and inhibitory ligands affects the inhibition of activating signaling in NK cells. The platform was based on ordered arrays of nanodots of two metals selectively functionalized with activating and inhibitory ligands, whose segregation was systematically tuned between 0 nm to 40 nm. Surprisingly, we found that inhibition efficiency increased with the spacing between the ligands within the probed range, and rationalized this finding by physical modeling of the ligand-receptor binding kinetics. In the second part of my talk, I will review our recent study of the role of environmental elasticity and topography in the function of cytotoxic lymphocytes. Stimulation of NK cells on planar elastomers functionalized with activating ligands revealed a bell-shape trend of activation vs. elastic modulus<sup>3</sup>. A more complex stimulating platform was based on ligand functionalized nanowires aimed at delivering the chemical, nano-topographical, and mechanical cues, whose combination produced an enhanced immune response of NK cells. To separately reveal the effect of each cue, we recently stimulated NK cells and CD8<sup>+</sup> T cells on nanowires with varied length and bending moduli and found that these physical parameters of nanowires greatly affects the signaling and the immune function of the lymphocytes. Overall, our work provides an important insight into the way the physical cues regulate the function of NK cells and T cells.



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Dr. **Katalin Balázsi**, material scientist, graduated in 2002 (Slovak Technical University, Bratislava). She got her PhD in 2005 from the Slovak Technical University, Bratislava. She is leading the team with 40 researchers, engineers and technicians of Thin Film Physics Department of Institute for Technical Physics and Materials Science, Centre for Energy Research (MTA EK). She has a long-time expertise on field of transmission electron microscopy. She is author/co-author of 100 scientific papers with 800 independent citations. She was a visiting professor at Institute of Materials Science, Slovak Academy of Sciences Visits in 2012.

She is a president of Association of Hungarian Woman in Science (2018-2021), secretary of the Hungarian Society for Material Sciences (2013-2020), secretary and treasurer of the Hungarian Microscopic Society (2018-2022), council member of European Ceramic Society (2018-2020), Delegate in Nanometer Structure Division of IUVESTA (2013-2019). Dr. Balázsi is working as PI in several national and EU FP7, M-ERANET projects.

Publications: <https://www.mendeley.com/profiles/katalin-balazsi/publications/>

Dr. **Csaba Balázsi** is a Scientific Advisor in Centre for Energy Research, Centre of Excellence, Hungarian Academy of Sciences. He is metallurgical engineer with 25+ years of practice in various physical and chemical technologies of nanocomposite manufacturing, including ceramic processing, nano-milling, hydrothermal, powder metallurgy, sintering, electrospinning. His research area is covering R&D of high-performance materials for medical, sensor and high temperature applications. He was involved in the development of nanoporous hexagonal tungsten oxide materials for gas sensorics, carbon nanotube/graphene nano-platelet added silicon nitride ceramic composites for tribological applications and several other nanocomposites, including nanoceramic dispersion strengthened steels for nuclear/HT applications and biogenic calcium-phosphate based biocompatible composites for orthopedics. He is co-author in 200 publications, 9 patents and is principal investigator in several national (OTKA, NKFIH, Tét, Eötvös, Bolyai) and international (FP7, NATO, NSF, ESA, H2020, EIT KIC RAW, Flag-ERA, NKFIH-TÜBITAK, COST-EXTREME) research grants. He is President of Fine Ceramics section of the Hungarian Scientific Society of Silicate Industry (SZTE) and Representative of SZTE in International Ceramic Federation (ICF), Fellow of the European Ceramic Society, Member of Council Board and Permanent Executive Committee (ECERS), Board Member of the Hungarian Society of Materials Science (MAE), Member of the American Ceramic Society (ACERS), Executive Committee Member of Federation of European Materials Societies (FEMS) and Steering Committee Member of Energy Materials Industry Research Initiative (EMIRI).

Publications: <https://m2.mtmt.hu/gui2/?type=authors&mode=browse&sel=10002487&view=dataSheet>

**The activity in E-MRS:** Prof. Dr. Csaba Balázsi was Symposium Chair in EMRS 2009 Fall Meeting “Novel bio &c hemosensing materials for Health, Safety and Security Applications” and in EMRS Fall Meeting 2012, „Ceramics and Ceramics Based Nanocomposites”.

## **Novel ceramic biomaterials: design and applications**

Katalin Balázs and Csaba Balázs

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The 400 000 artificial hip joint operations made every year in the world and there are 25 000 000 people with a total hip replacement. The wear and risk of the implant loosening increases so that after 10 years 10-20% of the implants have to be renewed. Biomaterials used for implant should possess some important properties in order to long-term usage in the body without rejection. The biocompatibility, mechanical, chemical and surface properties play a key role in the creation of sufficient and long-term functional replacements. New fundamental research outcomes with industrial perspectives are given for understanding the applications of ceramics in load-bearing and low-load-bearing bioimplants with directions for future developments. Nowadays,  $\text{Si}_3\text{N}_4$  is a new bioceramic with extremely good mechanical properties. Hydroxyapatite (HA) is a widely used bioceramic in implantology considering its high bioactivity. A bioactive coating (HA) on the bioinert ceramic implant's surface ( $\text{Si}_3\text{N}_4$ ) could help avoid the rejection from the body in the critical early few days after the operation. The preparation and characterization of bioceramics will be showed from traditional technologies to novel applications. The main trends and fundamental scientific problems will be discussed.

*INVITED Author/Article for SPECIAL ISSUE of the Journal*

*Abstract Control ID number WM5H1*

*Invited Speech for Discussion*

## **Electrosprayed bioactive calcium phosphate layers starting from biogenic raw materials**

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Ceramic structures at the nanometre range have been proven to have improved properties and characteristics that differ from their bulk, allowing for opportunities in novel technological applications. Ceramic layers with some advantages, including a very high surface-to-volume and aspect ratio can be processed by cheap and quick method, that is electrospraying. This presentation reviews results on the electrospinning and electrospraying of various bioceramic layers starting from biogenic raw materials and their potential applications in the biomedical field.



## Patrick van Rijn

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**Patrick van Rijn** his research interests are developing new biointerfaces in order to understand the relationship between material properties and cellular behavior. For this purpose, his group developed high-throughput technologies to investigate surface parameter dependent biological phenomena but also created novel coating approaches and delivery strategies using nanohydrogels. The research that is conducted in his group is both of fundamental and applied character with strong connections to the clinic and industry.

Patrick is chair of the Netherlands Society for Biomaterials and Tissue Engineering (NBTE), program leader for the research program “Nanobiotechnology and advanced therapeutic materials”, topical editor biomedical polymer for the open access journal *Polymers* (MPDI), and was Symposium Organizer” Functional Materials and Interfaces” at the E-MRS and at the German Materials Science Society conference. For full research interests, education, and group composition and collaborators, visit [vanrijn-lab.nl](https://vanrijn-lab.nl).

### Selected Recent Publications

1. S. Brosel-Oliu, *et al.*, “3D impedimetric sensors as a tool for monitoring bacterial response to antibiotics”, *Lab on a Chip*, **2019**, doi:10.1039/C8LC01220B.
2. G. Zu, *et al.*, “Development of an Aptamer-Conjugated Polyrotaxane-Based Biodegradable Magnetic Resonance Contrast Agent for Tumor Targeted Imaging”, *ACS Appl. Bio Mater.*, **2019**, DOI: 10.1021/acsabm.8b00639.
3. D. keskin, *et al.*, “Inhibiting Bacterial Adhesion by Mechanically Modulated Microgel Coatings”, *Biomacromolecules*, 2019, doi:10.1021/acs.biomac.8b01378.
4. O. Mergel, *et al.*, “Cargo shuttling by electrochemical switching of core-shell microgels obtained by a facile one-shot polymerization”, *Chem. Sci.*, **2019**, doi: 10.1039/c8sc04369h
5. D. Gehlen, *et al.*, “Rapid and Robust Coating Method to Render Polydimethylsiloxane Surfaces Celladhesive”, *ACS Appl. Mater. Interfaces* **2019**, *11*, 44, 41091.

*Abstract Control ID number CCBGL*

*Key Presentation*

## Nanogels as a versatile multi-modal biomedical nanomaterial

**Dr. Patrick van Rijn**

*University of Groningen/ University Medical Center Groningen  
Department of BioMedical Engineering-FB40*

Nanogels are hydrogel-based nanoparticles that are highly tunable in chemical composition and physicochemical properties. These nanoparticles are highly versatile in their uses and allow for several functions to be combined including antimicrobial properties, fluorescence and MRI tracking and imaging, anti-adhesive, controlled release, and responsiveness to various stimuli. Because of this variety of functions and properties, the particles are used in controlled delivery, imaging, theragnostic approaches and functional biomedical multi-modal coatings. The studies presented provide insights in the capabilities of such nanogels, the preparation, modification, and the use of them together with biological systems ranging from in vitro studies to in vivo uses. The ease of scaling, the diversity, and ease of applicability make these particles very powerful and tremendously complement the existing nanotoolbox of liposomes, polymersomes, protein-based nanostructures, and inorganic nanoparticles.





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Dr **Albena Daskalova** has an expertise on ultra-fast laser material processing for diverse applications in medicine and tissue engineering. She is an associate professor at laboratory of Micro and Nano Photonics, Institute of Electronics-BAS, since 2019. Currently she is a head of newly formed Femtoscience application group at IE-BAS (<http://www.femtosciencegroup.eu/>). She has obtained her PhD degree at Institute of Applied Physics in Vienna University of Technology in 2003 and have received a Marie Curie individual grant in 2009 at Institute of Electronic Structures and Lasers- Foundation of Research and Technology (IESL-FORTH), Heraklion, Crete. Her current interests are directed towards application of laser methods for treatment of diverse biomaterials and producing matrices with enhanced surface properties for application in tissue engineering. She is a project leader and participant in numerous National and International projects funded by Bulgarian National Science Fund, Horizon 2020, Laserlab Europe and COST. She has co-authored more than 25 publications in international peer reviewed scientific journals

1. Albena Daskalova, Irina Bliznakova, Liliya Angelova, Anton Trifonov, Heidi Declercq, Ivan Buchvarov, " Femtosecond Laser Fabrication of Engineered Functional Surfaces Based on Biodegradable Polymer and Biopolymer/Ceramic Composite Thin Films", *Polymers*, Vol. 11(2), pages 378, 2019, IF -3.164
2. A. Carvalho, L. Grenho, M. H.Fernandes, A. Daskalova, A. Trifonov, I. Buchvarov, F. J.Monteiro, "Femtosecond laser microstructuring of alumina toughened zirconia for surface functionalization of dental implants", *Ceramics International*, Volume 46, Issue 2, 1 February 2020, Pages 1383-1389, IF- 3.450
3. A. Daskalova, B. Ostrowska, A. Zhelyazkova, W. Świążkowski, A. Trifonov, H. Declercq, C. Nathala, K. Szlazak, M. Lojkowski, W. Husinsky, I. Buchvarov, „Improving osteoblasts cells proliferation via femtosecond laser surface modification of 3D-printed poly-ε-caprolactone scaffolds for bone tissue engineering applications”, *Applied Physics A*, Vol 124:413, IF-1.455, 2018

*INVITED Author/Article for SPECIAL ISSUE of the Journal*

*Abstract Control ID number CBZIO*

*Invited Presentation*

### **High intensity laser induced poly-lactic acid (PLA) surface modification for enhancement of biocompatibility properties of biology**

Albena Daskalova<sup>1</sup>, L. Angelova<sup>1</sup>, D. Aceti<sup>1</sup>, E. Filipov<sup>1</sup>, Rosica Mincheva<sup>2</sup>,  
Xavier Carrete<sup>2</sup>, Anton Trifonov<sup>3</sup>, Ivan Buchvarov<sup>3</sup>

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Ultrashort pulse laser interaction has been extensively studied for the modification of material properties in various materials. Femtosecond laser applications to microprocessing have received great attention in recent years. This is due to the characteristics of ultra-short laser-material interaction expressed in extremely high-peak power and femtosecond pulse duration which is less than material thermal relaxation time. Moreover, the effects of temperature distribution during material processing can be strongly minimized with ultrashort pulses leading to non-thermal and spatially localized effects that can facilitate volume ablation without collateral thermal damage. Using femtosecond processing laser-induced surface structures provide a response by the formation of micro/nano scale structures, which are acquired with respect to laser processing parameters. Such surface feedback can be applied to finely tune and control diverse properties like wettability, reflectivity and biomimetics. By simply controlling the laser parameters, diverse surface roughness can be achieved, thus influencing cellular dynamics like adhesion, migration, and differentiation which can be tuned via altering topographical properties and chemical composition of the surface. In the current study poly(lactic acid) (PLA) polymer surfaces were modified by Ti:sapphire femtosecond laser at different laser energies and number of applied laser pulses. Thus, implant surface modifications have been examined, and different laser-based surface treatments were applied to obtain

structures with hierarchical geometries. The results demonstrate that the control of the laser parameters can obtain bioactive surfaces by the nondestructive laser modification process.



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*Invited Presentation*

**Nanofibrous scaffolds and wound dressings prepared by electrospinning of biodegradable polymers and plasma processing**

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Regenerative medicine stands before the problem to replace non-functional tissues or improve the wound healing. Therefore, many laboratories try to develop resorbable tissue scaffolds that could support the patient's cells or breathable wound dressings that could immobilize biocide particles. The scaffold material should be biocompatible, biodegradable, and easy to manufacture, thus economically viable. A possible answer is to produce a structure made of a biodegradable polymer that mimics extracellular matrix (ECM), which would be peacefully received and gradually degraded when the new tissue has formed. The solution for wound dressings can also benefit from the nanofibrous structures that have bioactive surface able to immobilize biomolecules and particles. One of the promising polymers is FDA-approved polycaprolactone (PCL) due to its relatively low cost, excellent processability and mechanical properties, non-toxicity and low immunogenicity. However, the pristine form of PCL has a bioinert and hydrophobic surface causing problems with protein adsorption resulting in reduced cell adhesion. Our previous publications showed that PCL nanofibrous mats could be efficiently modified by plasma polymerization, which leads to the formation of bioactive surface exhibiting increased cell attachment and proliferation, offering also a possibility to attach proteins [1,2,3]. We have also shown the filamentary substructure of electrospun PCL/poly(ethylene oxide) (PEO) mixtures and changes of their functional properties for varying PCL:PEO ratio and plasma processing [4]. In this conference contribution, we will discuss processing aspects of the plasma-polymer-coated nanofibrous mats, the penetration depth of plasma polymerization and bioactivity of functional plasma polymer surfaces. [1] P. Cernochová et al., Cell type specific adhesion to surfaces functionalised by amine plasma polymers, *Scientific Reports* 10 (2020) 9357 [2] I. Nemcakova et al., Behaviour of Vascular Smooth Muscle Cells on Amine Plasma-Coated Materials with Various Chemical Structures and Morphologies, *International Journal of Molecular Sciences* 21 (2020) 9467 [3] E. Makhneva et al., Cyclopropylamine plasma polymer surfaces for label-free SPR and QCM immunosensing of Salmonella, *Sens. Actuator B-Chem.* 276 (2018) 447-455 [4] V. Kupka et al., Well-Blended PCL/PEO Electrospun Nanofibers with Functional Properties Enhanced by Plasma Processing, *Polymers* 12(1403) (2020) 16



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*INVITED Author/Article for SPECIAL ISSUE of the Journal*

*Abstract Control ID number OANC2*

*Invited Presentation*

### **Hyaluronic acid and polypeptides assemblies: smart designs, from thin coatings to hydrogels with antimicrobial properties**

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All implantable biomedical systems face several risks once in contact with the host tissue: excessive immune response to the implant and development of bacterial biofilms. A multifunctional surface coating that can address all these two issues concomitantly would significantly improve clinical outcomes. Polyarginine (PAR), a synthetic highly cationic polypeptide, can act on macrophages to control innate immune response and also as an antimicrobial agent due to its positive charges. We developed a new polyelectrolyte multilayer film based on PAR and hyaluronic acid (HA). The layer-by-layer PAR/HA films have a strong inhibitory effect on the production of inflammatory cytokines released by human primary macrophages subpopulations [1]. Next, we show that PAR/HA films were very effective to inhibit pathogenic bacteria associated with infections of medical devices [2] [3]. We demonstrate that exclusively films constructed with poly(arginine) composed of 30 residues (PAR30) acquire a strong antimicrobial activity. This system can also be fabricated in the form of hydrogel [4], useful to provide antibacterial properties to porous implants like surgical meshes. Recent developments to render these systems smart and responsive have also been made to obtain a release and activity only when bacteria are closed to the implants. [1] Özçelik, H. et al. Adv. Healthc. Mater. 2015; 4, 2026-36. [2] Mutschler, A. et al. Chem. Mater. 2016; 28, 8700-09. [3] Mutschler A. et al. Chem. Matter., 2017; 29, 3195-01. [4] Knopf-Marques H. et al. Mat. Sci. Engineer., 2019, C, 104, 109898-07.



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*INVITED Author/Article for SPECIAL ISSUE of the Journal*

*Abstract Control ID number EBXZW*

*Invited Presentation*

### **Albumin-based biomaterials produced by salt-assisted compaction**

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Albumin membranes formulated by evaporation in the presence of salt represent a new class of materials (EU patent submitted). In the present study, solutions of bovine serum albumin (BSA) and various salts are evaporated at 37 °C and pH 6 in order to prepare albumin-based material. Among others, NaBr allows the formation of stable and water-insoluble albumin membranes, thus providing a solid material exclusively composed of albumin after thorough washing. The conditions for obtaining BSA/NaBr membranes are assessed, and the molar ratio salt/albumin proves to be a key parameter for their formation. The Young modulus (E) of the materials lies around  $0.86 \pm 0.13$  MPa. Biological assays show that these albumin membranes are not cytotoxic, do not induce an inflammatory response and allow cell adhesion. Therefore, due to their interesting properties, these materials are suitable candidates for the development of scaffolds for tissue engineering and biodegradable implantable devices.





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*INVITED Author/Article for SPECIAL ISSUE of the Journal*

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*Invited  
Presentation*

### **Bisphosphonates adsorption on oxide nanoparticles through an experimental and theoretical approach**

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Bisphosphonates are known for its attested properties to positively influent on bone remodeling, mainly decreasing the osteoclast activity leading to an increased osteoblast growth and activity. Although exhibiting beneficial properties, these compounds are also related to jaw osteonecrosis from intravenous and oral administration in patients. Having that in mind, surface modification of implants using bisphosphonates is a suitable alternative to overcome this collateral effect. Different studies have reported that BP's when immobilized on surface can promote bone growth through local release and/or coordinating the calcium on hydroxyapatite crystals. Despite BP's strong bind to HA, implants' surfaces are currently made of titanium alloys, which surface is mainly composed of titanium dioxide. In this way, a detailed study of adsorption of BP's is necessary in order to advance and explore its potential use. Aiming to elucidate aspects of bisphosphonates adsorption on titanium dioxide the purpose of this work is to functionalize titanium dioxide in two different phases using etidronate, alendronate and risedronate. As a first step, the adsorption of bisphosphonates will be evaluated using FTIR and measuring the solution concentration after adsorption through UV-Vis. Then, the desorption will be evaluated using simulated body fluid in order to mimic the body condition. Again, the concentration will be evaluated through UV-Vis. In order to provide deeper understanding from the obtained results, some molecular simulations will be performed. Simulations of the electronic structure using methods as DFT (density functional theory) will take place, once techniques like Condensed to Atoms Fukui Indexes (CAFI) can provide a good understanding of the reactivity of the molecules. The Condensed to Atoms Fukui Indexes uses the electronic population of each atom in order to calculate the Fukui Indexes, parameters that can be used to analyze the system reactivity and determine the most probable adsorption way of each molecule. Some vibrational calculations will also be made, aiming to compare the theoretical and experimental results from the FTIR experiments. In this way, it is expected that this work helps to establish the optimum procedure to functionalize oxide surfaces using bisphosphonates keeping its osteogenic properties.



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Dr. Ashwini B. Salunkhe currently working as a Assistant Professor in Department of Physics, Rajaram College, Kolhapur. She has completed her M.Sc. with specialization in Solid state Physics from Shivaji University Kolhapur in 2009 and Ph.D. in Physics in 2012 from Centre for Interdisciplinary Research, D.Y. Patil Education Society, Kolhapur. Her research is focused on the Development of magnetic nanoparticles for cancer theragnostic. Based on her research work she has received gold medal with certificate of Excellence in research by D.Y. Patil University, Kolhapur. She is 2 times recipient of a PEIN fellowship by University of Santiago de Compostela, Spain (2012 & 2014) and European Union's EUPHARATES postdoctoral fellowship in 2015. She is also recipient of Government of INDIA's Dr. D.S. Kothari postdoctoral fellowship for 2014-2016 to develop magnetic nanoparticles for stem stell labelling in University of Pune, Pune. She has published 28 research articles with 2 review articles.

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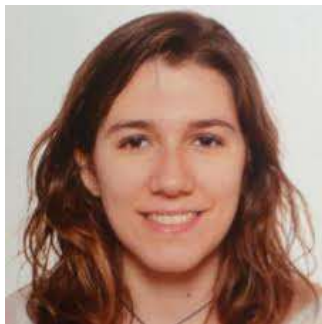
*Invited  
Presentation*

### **Magneto-Chemotherapy with high magnetic moment iron oxide nanoparticles for cancer theragnostic**

Ashwini Salunkhe

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High magnetic moment Fe<sub>3</sub>O<sub>4</sub> nanoparticles (NPs) are synthesized through simple co precipitation method by using new generation base Diisopropylamino (DIPA) which plays dual role as reducing agent and surface stabilizer. Spherical NPs with ~ 15 nm size and high magnetization value of about 92 emug<sup>-1</sup> at room temperature are obtained by this novel method. High specific absorption rate value of ~717 wg<sup>-1</sup> is obtained for Fe<sub>3</sub>O<sub>4</sub> NPs in water at an alternating magnetic field of 20 kAm<sup>-1</sup> and frequency of 267 KHz, which is attributed to high magnetization value. Magneto-polymeric micelle structure is formed by using Pluronic F127, anticancer drug Doxorubicin is conjugated in micelle by covalent linking with ligand molecules for magneto-chemotherapy. Finally, the magnetic resonance imaging (MRI) guided magneto-chemotherapy is achieved on breast cancer (MCF7) cells with ~ 96 % killing of cancer cells.



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I am currently working in this search. I am a predoctoral student in the Magnetic Nanomaterials Group at the University of Barcelona. I was trained as a Chemist, but during the Master in Nanoscience and Nanotechnology I discovered the transversality and the possibilities that nanoparticles offer us.

In 2016 I started my doctorate at the Magnetic Nanomaterials Group (UB). And currently my research is focused on the synthesis by chemical routes and the characterization of nanoparticles. I am working to make hybrid nanomaterials using nanoparticles of different materials to obtain combinations of plasmonic and magnetic properties, as well as a good response as X-ray contrast agents.

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Abstract Control ID number GIJ19*

*Invited Presentation*

### **Picking out iron oxide nanoparticles with custom-made morphology, oxidation state and magnetic response through the selective re**

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Iron oxide nanoparticles (NPs) are versatile building blocks in a variety of biomedical and environmental applications due to their good magnetic performance, ease of production and functionalization by chemical routes, and low toxicity. However, controlling the electronic and magnetic properties of iron oxide NPs remain a challenge because of their crucial dependence on composition, structure, surface chemistry, and interparticle interactions. [1, 2]. In this framework, we studied the effect of the amount of both 1,2-hexadecanediol and the solvent 1-octadecene on the thermal decomposition method with iron (III) acetylacetonate. On the one hand, low amounts of either of the two reagents result in large NPs containing both Fe<sub>3</sub>O<sub>4</sub> and FeO phases but with high values of the reaction yield. On the other hand, above certain threshold of the reagents the NPs are single-phase, single-crystal Fe<sub>3</sub>O<sub>4</sub> NPs with diameters below 10 nm and narrow size distributions, however the reaction yield suffers a slight decrease. Consequently, the samples exhibited two distinct magnetic behaviors depending on the amount of these two reagents. The hysteresis loops at room temperature for the small NPs showed the typical features of superparamagnetism: values of the saturation magnetization close to the bulk one for magnetite with no coercive field. On the contrary, larger NPs showed ferrimagnetic behavior with reduced values of the saturation magnetization, as well as shifted hysteresis loops at 5 K after field cooling the sample at 1 T. The Zero-field cooling-field cooling (ZFC-FC) curves below 200 K for the small NPs showed a peak below room temperature corresponding to the blocking temperature, while those curves for the larger particles displayed two peaks at higher temperatures which can be associated with the Verwey and Neel transitions of magnetite and wüstite phases, respectively. The latter is correlated with the biphasic nature of the large NPs. With this accurate monitoring of the reaction conditions, we have added an extra level of optimization to the synthesis of these NPs. In fact, we have found that, for 1 mmol of iron (III) acetylacetonate, the minimum amounts of 1,2-hexadecanediol and 1-octadecene for the preparation of monophasic, single-crystal Fe<sub>3</sub>O<sub>4</sub> NPs are 2.5 mmol and 5 mL, respectively. This allows us to tune the properties of each sample of iron oxide NPs to its specific application. [3] Acknowledgements The work was supported by Spanish MCIU and AEI (MAT2015-68772-P; PGC2018-097789-B-I00) and European Union FEDER funds. M.E-T. acknowledge Spanish MCIU for BES-2016-077527. References [1] A. Fraile Rodríguez, C. Moya, M. Escoda-Torroella, A. Romero, A. Labarta and X. Batlle. J. Mater. Chem. C, 6, 4, 875-882 (2018). [2] C. Moya, M. P. Morales, X. Batlle and A. Labarta. Phys. Chem. Chem. Phys., 17, 19, 13143-13149 (2015). [3] M. Escoda-Torroella, C. Moya, A. Fraile Rodríguez, X. Batlle and A. Labarta. Langmuir, 37, 1, 35-45 (2021)



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*Invited Presentation*

### **Natural 3D scaffolds for cultivation of adult stem cells and generation of clinically compliant stem cell secretome fractions**

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Since its early days, ex vivo mammalian cell culture has been conducted on flat two-dimensional (2D) glass or polystyrene surfaces. Although 2D cell culture is still widely used, it is known to result in unnatural cell polarity and morphology in addition to lacking the three-dimensional extracellular matrix. These drawbacks are especially evident if the cultivated cells are clinically relevant cell types including but not limited to stem cells. In this context, 2D cultivation is known to interfere with stem cell proliferation and to alter the cell phenotype. In this talk, different approaches to stem cell cultivation, differentiation, and assessment of migration in 3D will be discussed. In particular, biocompatible natural scaffolds for the cultivation of adult human neural crest-derived stem cells and human mesenchymal stem cells of different origins will be presented. Moreover, the impact of 3D cell culture on the regenerative potential of stem cell secretome will be discussed.





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Dr. Federico Cerrone obtained a M.Sc. in Biological Sciences (2005) by Polytechnic University of Marche-Italy. PhD (2007-2011) in Environmental Microbiology by the Institute of Water Research-University of Granada-Spain. Postdoctorate Researcher at University College of Dublin-Ireland (School of Biomolecular and Biomedical Science) under the supervision of Prof. Kevin O'Connor. Current senior Research Scientist in Biorbic-UCD (Bioeconomy Research Centre). The core of his research is on chemical modification and application of biomaterials manufactured by microbial metabolism *via* fermentation technology. Throughout his postdoctorate period, he has been funded by Science Foundation Ireland (SFI) for research in the circular economy and application of biobased chemicals as novel materials; in particular, two consecutive SFI-TIDA (Technology Innovation Development Award) grants (13/TIDA/B2588 and 14/TIDA/2377) have been funded for the application of biopolymers as novel materials for translational medicine. His main focus is on electrospinning and modification of microbial aromatic polyhydroxyalkanoates into nanofibers. These novel materials proved particularly efficient in the increase of the *in vitro* lifespan of human iPSC derived cortical neurons and increased their neurite elaboration. These results hold hope for a more efficient neuroregeneration and also opened further collaborations in the field of translational medicine and neurobiology. In fact he established a multilateral collaboration with the Neurobiology group of the Department of Stem cell Biology of the Friedrich-Alexander University of Erlangen-Germany and with the Department of Biochemistry and Molecular Biology, University of Southern Denmark. This cluster coordinated by Dr. Cerrone includes material scientists, neurobiologists and molecular biologists. Dr. Cerrone has a H-index of 11, having published 14 papers in the interdisciplinary area of microbial biotechnology, biomimicry and material science. He also published a chapter book and has an international patent.

*Abstract Control ID number ZX62L*

*Invited Presentation*

### **Polyhydroxyphenylvalerate/polycaprolactone nanofibers improve the life-span and mechanoreponse of human iPSC-derived cortical neuronal cells.**

Federico Cerrone<sup>\*(1)</sup>, Tatyana Pozner<sup>(2)</sup>, Paolo Ceppi<sup>(3)</sup>, Murugan Rajendiran<sup>(4)</sup>,  
Shu Wenting<sup>(5)</sup>, Eoin O'Cearbhaill<sup>(5)</sup> Brian J. Rodriguez<sup>(6)</sup> Kevin O'Connor<sup>(7)</sup>.

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Efficient neurite outgrowth, mechanoreponse and the increasing of the survival rates are critical for the successful cultivation of cortical neurons *in vitro*[1] and the potential of central nervous system regeneration *in vivo*, after maturation of these cells[2]. Polyhydroxyphenylvalerate (PHPV), an aromatic polyester of bacterial origin[3], was electrospun into nanofibers and blended with polycaprolactone (PCL) and electrospun in nanofibers for use in a 3D (CellCrown™) configuration and in a 2D coverslip

coated configuration. Contact angle and nanoindentation tests by atomic force microscopy (AFM) showed that PHPV has a higher hydrophilicity and adhesion when compared to pure PCL. Height images derived by AFM scan identify a mixed roughness/smoothness ratio of the PHPV/PCL blend, where PHPV is responsible for the smoother component while PCL gives the roughness component of the blend. Nanoindentation tests of the electrospun fibers, done by AFM, exhibit correlated force-map curves that can identify the Young's modulus of the materials[4]. PHPV, other than increased adhesion, has a more viscoplastic behaviour in the stress/strain response (where the plastic modification of the material is evident at an earlier stage than PCL) but is too soft and show poor mechano-response for cell cultivation. PCL has a strain hardening behaviour under stress [5] and higher elasticity, but it is hydrophobic and too tough and stiff, hindering cell survival. PHPV/PCL shows a superior behaviour compared both to PCL and PHPV. The same rheological results have been confirmed by stress/strain tests at macroscale by Universal Tensile Machine (UTM); PHPV/PCL has a measured stiffness and an elastic modulus 2.3 and 2.4-fold lower than PCL, respectively. The PHPV/PCL blend maintains the mechanical solidity but having a higher hydrophilicity, softness and a relatively low stiffness can sustain for longer the attachment of neuronal cells, and improves their adhesion and their neurite elaboration, facilitating synaptic contacts. In facts, electrospun PHPV/PCL allow a 2.3-fold increase in the life-span of human induced pluripotent stem derived cortical neuronal cells (hiPS) compared to pure PCL fibers. HiPS-derived cortical neuronal cells grown on PHPV/PCL fibers show a 3.8-fold higher cumulative neurite elaboration compared to neurites grown on PCL fibers only. 96% of cortical neuronal cells die after 8 days of growth when plated on PCL fibers alone while more than 83% and 55% are alive on PHPV/PCL fibers on day 8 and day 17, respectively [6]. An increased migration rate of cortical neuronal cells is also promoted by the blend compared to the PCL fibers alone. The critical survival rate improvement of hiPS derived cortical neuronal cells on PHPV/PCL blend holds promise in using these biocompatible nanofibers as implantable materials for regenerative purposes of an active cortical neuronal population after full maturation *in vitro* [6].

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## **Anna LAROMAINE SAGUE**

Dr.

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My scientific work is interdisciplinary encompassing chemistry, materials science and biology and inspired by my work experience at world leading institutions in three different continents. My research steps are intrepid, innovative and solid from synthesis of materials to cell cultures pushing the state of the art while blending disciplines. I strongly believe on the power of scientists to speed the translation of materials to a final product and its potential to run the world-economies. Since May 2011 I joined the ICMAB-CSIC as Researcher within the Group of Nanoparticles and Nanocomposites.

Currently my research is divided in two parts: 1) the production of bacterial cellulose materials and their nanocomposites and 2) the evaluation of nanoparticles using different approaches such as cell cultures and the nematode *Caenorhabditis elegans*. Research interest - cellulose, nanoparticles, biomaterials, nanocomposites and *Caenorhabditis elegans*

*Abstract Control ID number 38GNO*

*Invited Presentation*

### **Exploiting Cellulose as wound healing material in plants**

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Montserrat Capellades<sup>2</sup>, Núria S. Coll<sup>2</sup>, Anna Laromaine<sup>1\*</sup>

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Food security and the need to increase sustainably crop yields for a rapidly growing world population are among the greatest social and economic challenges of our century. The most extended agricultural practice to enhance crop yield is to increase host plant density, which in turn tends to increase the severity of plant diseases.<sup>1</sup> Furthermore, globalization has contributed to the spreading of new pests into regions in which plants were not adapted, causing unaffordable agronomic losses. Most plant diseases occurring in agriculture are caused by fungal pathogens.<sup>2</sup> Plant diseases caused by pathogenic bacteria are less prevalent; but their effects on agriculture are also devastating.<sup>3</sup> In this work, we present an anti-bacterial and anti-fungal patch, which exploits the potential of smart-based nanomaterials as pesticides and silver nanoparticles (AgNPs) as anti-bacterial active component, improving the efficiency and environmental sustainability of pesticides application. In order to prevent the release of the NPs to the environment and their runoff loss during application, we attached the active silver nanoparticles to a bacterial cellulose (BC) matrix to obtain BC-AgNPs hybrid films. The bacterial cellulose matrix has similar chemical composition to the plant cellulose present in leaves but shows higher purity, crystallinity and water absorbance.<sup>4-5</sup> We take advantage of the gel-like nature of the bacterial cellulose matrix to in situ synthesize and embed AgNPs. We evaluated the release and attachment of silver nanoparticles to a bacterial cellulose matrix and their in vitro anti-pathogenic properties against an array of plant pathogens with high agro-economical impact, such as the bacterium *Pseudomonas syringae* and the fungus *Botrytis cinerea*. These anti-bacterial and anti-fungal capacities were also assessed in vivo using the plant species *Nicotiana benthamiana* a close relative of tobacco and tomato; both widely used as a model organism in plant biology.<sup>6</sup> Insights of other applications on wound healing also will be provided. References (1) Sundström, J. F. et al. Future threats to agricultural food production posed by environmental degradation, climate change, and animal and plant diseases - a risk analysis in three economic and climate settings. *Food Secur.* 6, 201?215 (2014). (2) Agrios, G. N. *Plant Pathology*. Quinta edición. Academic Press. Nueva York. (2005). (3) V. Rajesh Kannan, K. K. B. Sustainable Approaches to controlling plant pathogenic bacteria. (2015). (4) Klemm, D. et al. Nanocelluloses: A new family of nature-based materials. *Angew. Chemie - Int. Ed.* 50, 5438?5466 (2011). (5) Zeng, M., Laromaine, A. & Roig, A. Bacterial cellulose films: influence of bacterial strain and drying route on film properties. *Cellulose* 21, 4455?4469 (2014). (6) Enhancing Localized Pesticide Action through Plant Foliage by Silver-Cellulose Hybrid Patches A. Alonso-Díaz, J. Floriach-Clark, J. Fuentes, M. Capellades, N. S. Coll, A. Laromaine; *ACS Biomater. Sci. Eng.*, (2019), 5 (2), pp 413?419.



### **Antonina P. Naumenko**

PhD, Senior researcher

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Graduated from the Faculty of Physics, Kyiv State University. TG Shevchenko majoring in General Physics (specialty Solid State Optics) in 1974. He has been working at the University since 1974: Art. laboratory assistant, engineer, graduate student, junior researcher, researcher, senior researcher. She defended her PhD thesis "Dynamics of crystal lattices and symmetry of energy states in non-metallic crystals containing pyramidal structural elements" in 1999. In 2007, she received the title of senior researcher. For many years, she was a responsible contractor, a scientific secretary of the SCNTP programs of Ukraine. Main directions of scientific work: investigation of features of structure of ceramics, semiconductor and layered materials by the methods of oscillatory spectroscopy. Author of 80 scientific papers and 1 invention.

*INVITED Author/Article for the SPECIAL ISSUE of the Journal*

*Abstract Control ID number XSBE0*

*Invited Presentation*

## **Capability of Spectroscopic Characterization for Fast Screening Multicomponent Polymer-based Nanocomposites for Antitumor Therapy**

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Cisplatin (cis-Pt) is a complex of platinum which widely used as an anticancer drug. Transplatin (trans-Pt) has the same chemical formula, but different positions of atoms. Cisplatin connects to DNA in cancer cells and stops DNA replication, namely making cross-links between guanine bases. Transplatin is less reactive to DNA but also demonstrate cytotoxicity effect.

In this work we make an attempt to connect the differences in the biological activity of mentioned structures with the data obtained by optical spectroscopy methods. The UV-vis spectra as well as fluorescence and phosphorescence spectra of water solutions of cis-Pt and trans-Pt were investigated at temperatures 300 and 77 K. Quantum chemical calculations were used for correct interpretation of obtained results. We also characterized these compounds using such powerful method as Raman spectroscopy. Cisplatin (cis-Pt) is a complex of platinum which widely used as an anticancer drug. Transplatin (trans-Pt) has the same chemical formula, but different positions of atoms. Cisplatin connects to DNA in cancer cells and stops DNA replication, namely making cross-links between guanine bases. Transplatin is less reactive to DNA but also demonstrate cytotoxicity effect. In this work we make an attempt to connect the differences in the biological activity of mentioned structures with the data obtained by optical spectroscopy methods. The UV-vis spectra as well as fluorescence and phosphorescence spectra of water solutions of cis-Pt and trans-Pt were investigated at temperatures 300 and 77 K. Quantum chemical calculations were used for correct interpretation of obtained results. We also characterized these compounds using such powerful method as Raman spectroscopy.



The E-MRS Symposium O Scientific Committee Board Invited to held this event  
Professor, Research Fellow PEILIN CHEN, Academia Sinica, Taiwan.



### Peilin Chen

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KEY PRESENTATION  
Abstract CONTROL ID number M9ZHY

## Integrated PEDOT Based Microfluidic Platform for the Isolation and Detection of Circulating Tumor Cells

In this study, we employed a novel one step electrospinning process to fabricate poly(ethylene oxide) (PEO)/poly(3,4-ethylenedioxythiophene): polystyrenesulfonate (PEDOT:PSS) core/shell nanofiber structures with improved water resistance and good electrochemical properties. We then integrated a biocompatible polymer coating with three-dimensional (3D) PEDOT-based nanofiber devices for dynamic control over the capture/release performance of rare circulating tumor cells (CTCs), as well as the label-free detection by using organic electrochemical transistors (OECTs). The detailed capture/release behavior of the circulating tumor cells was studied using an organic bioelectronic platform comprising PEO/PEDOT:PSS nanofiber mats with 3 wt % (3-glycidyloxypropyl) trimethoxysilane as an additive. We have demonstrated that these nanofiber mats deposited on five-patterned indium tin oxide finger electrodes are excellent candidates for use as functional bioelectronic interfaces for the isolation, detection, sequential collection, and enrichment of rare CTCs through electrical activation of each single electrode. This combination behaved as an ideal model system displaying a high cell-capture yield for antibody-positive cells while resisting the adhesion of antibody-negative cells. Taking advantage of the electrochemical doping/dedoping characteristics of PEDOT:PSS materials, the captured rare cells could be electrically triggered release through the desorption phenomena of PLL-g-PEG-biotin on device surface. More than 90% of the targeted cancer cells were captured on the 3D PEDOT-based nanofiber microfluidic device; over 87% of captured cancer cells were subsequently released for collection; approximately 80% of spiked cancer cells could be collected in a 96-well plate. For the OECT design, it was demonstrated for monitoring CTC-capture performance and identifying cancer cell phenotypes. This 3D PEDOT-based bioelectronic device approach appears to be an economical route for the large-scale preparation and detection of systems for enhancing the downstream characterization of rare CTCs.

### Biography:

Peilin Chen received his Bachelor degree in Chemistry from National Taiwan University in 1990 and obtained his Ph.D. degree in Chemistry from University of California, Irvine in 1998. He worked as a postdoctoral fellow in the Chemistry department of University of California, Berkeley between 1999 and 2001. Prof. Chen joined Research Center for Applied Sciences, Academia Sinica, Taiwan as an Assistant Research Fellow in 2001. He was promoted to Associate Research Fellow and Research Fellow in 2005 and 2010, respectively. He served as the deputy director of the Research Center for Applied Sciences between 2010 and 2012 and the Chief Executive Officer of the thematic center of Optoelectronic in 2012. Prof. Chen was a visiting Professor in RIKEN and Kyoto University. Prof. Chen received several prestigious awards in Taiwan including Research Award for Junior Research Investigators in Academia Sinica, Ta-You Wu Memorial Award of National Research Council and Career Development Award in Academia Sinica. Prof. Chen has authored or co-authored more than 130 papers in refereed journals and conference proceedings, he has delivered more than 70 invited talks in international meetings and conferences. He organized more than 10 international symposia.

2. Professor Fuyuhiko Tamanoi, Kyoto University, Kyoto, Japan

## A new radiation therapy by combining gadolinium-loaded nanoparticles and monochromatic X-ray



### Fuyuhiko Tamanoi

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KEY PRESENTATION

Abstract CONTROL ID number E7IYP

In this talk, I will discuss our recent attempt to develop a new type of radiation therapy that combines synchrotron-generated monochromatic X-ray with mesoporous silica nanoparticles (MSNs). In this approach, we deliver high Z elements such as gadolinium, gold or silver to the tumor by the use of nanoparticles that result in distributing the element throughout tumor mass (tumor spheroid). Then the spheroid is irradiated with monochromatic X-ray generated at SPring-8, a synchrotron in Harima, Japan. When we used monochromatic X-ray harboring an energy level that corresponds to the K-edge energy of the element, we observed dramatic destruction of the tumor spheroid. Our analysis suggests that the effect is due to the Auger effect releasing electrons that will damage DNA and cause cell death. Our approach will provide a solution to the problem with current radiation therapy regarding adverse effect on normal tissues. In addition, effect of X-ray at the tumor can be amplified by the absorbance of the X-ray energy with high Z elements. This work was carried out in collaboration with Drs. Saitoh and Shiro at SPring-8 (QST).

### Biography:

Fuyuhiko Tamanoi received his PhD in Molecular Biology from Nagoya University in 1977. After completing postdoctoral training at Harvard University, he worked at Cold Spring Harbor Laboratory as a staff scientist (1980-1985). He was appointed as an Assistant Professor at the University of Chicago. He was appointed as an Associate Professor at University of California, Los Angeles and promoted to Professor in 1997. In 2017, he received an appointment at Kyoto University. He has recently established Quantum Nano Medicine Center at Kyoto University. He has worked on various aspects of Cancer research that include signal transduction, anticancer drugs and nanoparticle-based therapy.



## **Organosilica Nanoparticles for Biomedical Applications toward Nano-Theranostics**

### **Michihiro Nakamura**

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INVITED Author/Article for SPECIAL ISSUE of the Journal

KEY PRESENTATION

Abstract CONTROL ID number DXKZS

Medical applications of multifunctional nanoparticles are expected to be one of the most important possibilities in innovative medicine. Organosilica nanoparticles are novel nanomaterials that are prepared from a single organosilicate coupling agent (organotrialkoxysilane) such as 3-mercaptopropyltrimethoxysilane. Organosilica nanoparticles are both structurally and functionally different from typical silica nanoparticles (inorganosilica nanoparticles) prepared from tetraalkoxysilane. The organosilica nanoparticles contain both interior and exterior functionalities such as mercaptopropyl residue as prepared. The organosilica nanoparticles allow for facile surface and internal functionalization, offering new opportunities to create multifunctionalized nanoparticles. Over the last two decades, research on the internal functionalization of organosilica nanoparticles has evolved. Various sizes of fluorescent organosilica nanoparticle containing various types of fluorescent dye including near infrared (NIR) dye can be prepared using a one-pot synthesis. In addition, functional fusions of organosilica nanoparticles and other functional nanoparticles such as quantum dots, gold nanoparticles, and iron oxides are possible based on organosilica particles technology. These multifunctionalized organosilica nanoparticles are useful for various imaging techniques such as in vivo imaging, cell labeling, time-lapse fluorescent imaging, and multimodal imaging. Multifunctionalized organosilica nanoparticles have high potential to create novel imaging systems and provide novel information of cell characteristics and functions. In recent year, we have launched additional research on surface functionalization of organosilica nanoparticles using biomolecules and polymers. Surface-functionalized organosilica nanoparticles revealed various alterations of the interaction with cells including tumor cells and macrophages. We applied multifunctionalized NIR organosilica nanoparticles to tumor-bearing mouse. The particles showed an accumulation on tumor tissue on NIR in vivo imaging, and damaged tumor cells by using photodynamic effect. Imaging and therapy using multifunctionalized organosilica nanoparticles allow for nano-theranostics.

### **Biography:**

Michihiro Nakamura is a Professor and Chairman of Department of Organ Anatomy and Nanomedicine in Yamaguchi university Graduate School of Medicine since 2016. Recently he is the leader of International Nano-Theranostic Center (iNTC) for center formation project of Yamaguchi University. He was awarded his M.D. degree from the Tokushima University School of Medicine, and obtained medical license in 1992. He studied enzymology and protein engineering, and was awarded his Ph.D. degree in 1997 from the Graduate School of Medicine at Tokushima University. After 3 years of clinical training as a clinical resident in rheumatology and hematology at Kyushu University, he joined the medicine faculty of the Tokushima University as an assistant professor in 1999. From 2002 to 2004 he studied immunotoxin and molecular interaction as a visiting fellow in Laboratory of Molecular Biology, National Cancer Institute, NIH in USA. His research interests include the creation and applications of multifunctional nanoparticles in biomedical research since 1999. He has developed a novel type of silica nanoparticles, organosilica nanoparticles made from a single organosilicate. He demonstrated that multifunctional nanoparticles provide novel imaging approaches such as single cell imaging and multimodal imaging providing seamless and sequential findings of tumor tissue from macro to micro. His current research activities include multifunctional nanoparticles enable to create novel imaging system and therapeutic applications toward cancer theranostics.

4. Principal Research Scientist **Yongdoo Choi** National Cancer Center, Goyang, Republic of Korea



## **Activatable theranostic agents for targeted near-infrared fluorescence imaging and photodynamic therapy**

### **Yongdoo Choi**

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INVITED PRESENTATION

Abstract CONTROL ID number 6EVAF

My laboratory has been developing various types of activatable and dual-targeted photosensitizing agents as smart theranostics for selective near-infrared fluorescence imaging and photodynamic therapy (PDT) of cancers and inflammatory diseases. Recently a fucoidan-based theranostic nanogel (CFN-gel) consisting of a fucoidan backbone, redox-responsive cleavable linker, and photosensitizer was developed to achieve activatable near-infrared fluorescence imaging of tumor sites and an enhanced PDT to induce the complete death of cancer cells. A CFN-gel has nanomolar affinity for P-selectin and VEGF. Moreover, a CFN-gel is non-fluorescent and non-phototoxic upon its systemic administration due to the aggregation induced self-quenching in its fluorescence and singlet oxygen generation. After internalization into cancer cells and tumor neovascular endothelial cells, its photoactivity is recovered in response to the intracellular redox potential, thereby enabling selective near-infrared fluorescence imaging and an enhanced PDT of tumors. It also provides a significant antitumor effect in the absence of light treatment *in vivo*. Our study indicates that a fucoidan-based theranostic nanogel is a new theranostic material for imaging and treating cancer with high efficacy and specificity.

### **Biography:**

Dr. Yongdoo Choi received his Bachelor degree in Polymer Engineering from Chonnam National University in 1996 and obtained his Ph.D. degree in Material Science from Gwangju Institute of Science and Technology, Korea in 2003. He worked as a postdoctoral fellow in the Radiology department of Massachusetts General Hospital, Boston between 2003 and 2006. He joined National Cancer Center (NCC), Korea as a Senior Research Scientist in 2007. He is now a principal research scientist and chief of Nanochemistry Laboratory at NCC Korea. He is serving as a deputy editor of *Quantitative Imaging in Medicine and surgery*, Associate editor of *Frontiers in Bioengineering and Biotechnology*, *Frontiers in Materials*, *Frontiers in Molecular Biosciences*, Editorial Advisory Board of *Bioconjugate Chemistry*, etc. His laboratory focuses on the development of novel molecular imaging agents for image-guided surgery, activatable photodynamic therapy agents, and theranostic nanomedicines.



5. **Hideaki Yamamoto**, Associate Professor Tohoku University, Japan



## **Ultrasoft silicone elastomer as a biomimetic scaffold for neuronal cultures**

**Hideaki Yamamoto<sup>1</sup>, Takuma Sumi<sup>1</sup>, Shigeo Sato<sup>1</sup>, Ayumi Hirano-Iwata<sup>1,2</sup>**

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KEY PRESENTATION  
CONTROL ID number ZS4SQ

Nerve-cell culture takes an irreplaceable role in molecular and cellular neuroscience. However, its use in studies at the systems level has been limited due to the substantial difference between in vivo in vitro network dynamics. The dynamics is affected by the difference in the intercellular connectivity (Yamamoto et al., *Sci. Adv.* 4, eaau4914 (2018)), as well as by the excessively strong excitatory synapses in cultured neurons. Recently, a study was reported that stiff scaffolds enhance the strengths of excitatory synapses in cultured hippocampal neurons (Zhang et al., *Sci. Rep.* 4, 6215 (2014)). As neuronal cultures are generally performed on polystyrene or glass, which is approximately  $10^6$  to  $10^7$  times stiffer than the brain tissue, we hypothesized that the in vitro artifact in excitatory synaptic strength can be reduced by using a scaffold that mimics the elasticity of the brain tissue. Here we employed an ultrasoft silicone elastomer, whose elastic modulus resembles that of the brain tissue ( $\sim 0.5$  kPa), as a scaffold for culturing rat cortical neurons. We investigated the effect of the biomimetic elasticity on the strength of excitatory synapses and the spontaneous network activity (Sumi et al., arXiv 1912.05050 (2019)). We found that the amplitude of excitatory postsynaptic currents was smaller on softer scaffolds. Although globally synchronized bursting activity in cortical cultures were still observed when the cells were grown on the ultrasoft substrate, neuronal correlation was significantly reduced as compared to the cultures on stiffer ( $>14$  kPa) substrates. In the latter half of the talk, we will show how the multielectrode array devices with the ultrasoft cell-device interface can be fabricated by taking advantage of additive manufacturing technologies, such as inkjet printing (Yamamoto et al., *Adv. Biosys.* 3, 1900130 (2019)). Our device employs 3D micropillar electrodes, which can be fabricated relatively easily by inkjet printing. Such devices facilitate the stimulation and recording of cultured neuronal networks grown on biomimetic scaffolds, for both basic research and pharmacological studies.

### **Biography:**

Hideaki Yamamoto received his bachelor's degree in Electrical Engineering from Waseda University in 2005 and obtained his PhD in 2009 from the same university. He then conducted postdoctoral research at Waseda University and at Tokyo University of Agriculture and Technology, before joining Tohoku University in 2014. He is currently an Associate Professor and a JST-PRESTO Researcher at Research Institute of Electrical Communications. He is interested in how a complex network of excitable cells realize robust computation in the brain. To this end, he develops microfabrication and surface modification technologies to engineer the structure and function of cultured neuronal networks in culture. He is currently a member of the Japan Society of Applied Physics, the Japan Society of Vacuum and Surface Science, and the Japan Nanomedicine Society.

6. Professor **Jiashing Yu**, National Taiwan University, Taiwan



## Naturally derived biomaterials for 3D stem cells loaded bio-ink

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INVITED Author/Article for SPECIAL ISSUE of the Journal

KEY PRESENTATION

Abstract CONTROL ID number OPNBT

The native tissues are complex structures consisting of different cell types, extracellular matrix materials, and biomolecules. Traditional tissue engineering strategies have not been able to fully reproduce biomimetic and heterogeneous tissue constructs because of the lack of appropriate biomaterials and technologies. However, recently developed three-dimensional bioprinting techniques can be leveraged to produce biomimetic and complex tissue structures. To achieve this, multicomponent bioinks composed of multiple biomaterials (natural, synthetic, or hybrid biomaterials), different types of cells, and soluble factors have been developed. In addition, advanced bioprinting technologies have enabled us to print multimaterial bioinks with spatial and microscale resolution in a rapid and continuous manner, aiming to reproduce the complex architecture of the native tissues. In this study, we developed a new formulation of bio-ink which is based on methacrylated keratin and methacrylated glycol chitosan. The feasibility of this bioink was tested with human adipose-derived stem cell toward specific differentiation conditions.

### Biography:

Dr. Yu received her B.S. in Chemical Engineering in 2003 from National Taiwan University, Taiwan, R.O.C and Ph.D. in 2008 from UC Berkeley/UC San Francisco Joint Graduate Group in Bioengineering. Dr. Yu worked as a postdoctoral researcher at UCSF Medical School and Cardiovascular Research Institute from 2008-2010. She relocated back to her alma mater in 2010 and was an Assistant Professor from 2010-2015 and Associate Professor from 2015-2019. Dr Yu is promoted to full Professor from Aug, 2019

Dr. Yu's group focus on customized and functional modification of biomaterials including surface modification of biomaterials to enhance cell and extracellular matrix (ECM) interaction. Antibody and peptides conjugated nanoparticles as biosensors and drug delivery vehicles for cancer therapy, cell encapsulation and 3D culture of hASCs (human adipose-derived stem cell) in alginate-based microspheres and various porous scaffold and hydrogel for stem cells differentiation. The group has representative publications in *Biomaterials*, *Tissue Engineering*, *ACS Applied Materials and Interfaces*, *Journal of Materials Chemistry B* and *Biomaterials Sciences* etc.

Selected Awards and Fellowships of Dr. Yu include: Young Investigator Award 2012. ISOMRM International Symposium of Materials on Regenerative Medicine. Young Investigator Award, Certificate of Excellence, 2014 World Congress on Preventive and Regenerative Medicine (WCPRM). Recipient, Best Advisor Award (2016), National Taiwan University. Recipient, International Lectureship of the 97th Annual Meeting of The Chemical Society of Japan (March 2017). Recipient, Outstanding Achievement and Contribution. Asia Pacific Society for Materials Research 2017 (July 2017). Young Investigator Award 2017. 3th ISOMRM International Symposium of Materials on Regenerative Medicine

Dr. Yu is the editorial board members of *Physics and Chemistry of Stem Cells* (Walter de Gruyter, German) and *Am J Tissue Eng & Stem Cell* (Columbia International Publishing, USA). She is the Associate Editor of *Acta Cardiologica Sinica*.

7. Professor **Daisuke Miyoshi**, Konan University, Japan



## **Phase separation of G-quadruplex nucleic acids and arginine-rich peptides**

### **Daisuke Miyoshi**

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INVITED Author/Article for SPECIAL ISSUE of the Journal

KEY PRESENTATION  
Abstract CONTROL ID number

Molecular environments inside cells are surprisingly crowded with numerous number of biomolecules. About 40 percent of the cell volume is occupied by biomolecules. Biochemical reactions are subject to be temporally, spatially, and specifically controlled. From biochemical and biophysical point of views, it is incredible that selective interactions and specific functionalization of biomolecules in the temporal and spatial-specific manner can be achieved under the complex molecular crowding environments. One of the key futures to achieve the specific interaction of biomolecules is collective biomolecular behavior. In recent years, biomolecular localization and compartmentation systems using droplets via liquidliquid phase separation (LLPS) inside cells, become one of the most hot research topics in biology. Droplets are temporarily formed, and their formation is reversible and responsive to various external signals, which are in contrast with aggregation of biomolecules which is generally irreversible. In this presentation, we will show a model system of a droplet in a test tube, in which we use nucleic acids (RNA and DNA) which forms G-quadruplexes and arginine-rich peptides which do not have any stable structure. By mixing these two components, a rapid LLPS was observed. It was suggested that the Gquadruplex structure is critical for undergoing LLPS. In the talk, we would like to discuss property of the droplet as a biomaterial.

### **Biography:**

Daisuke Miyoshi received his Bachelor degree in Chemistry from Konan University, Japan in 1995 and obtained his Ph.D. degree in Science from the same University in 2003. He worked as a postdoctoral fellow in the chemistry department of University of Illinois at Urbana-Champaign between 2003 and 2004. He joined Frontier Institute for Biomolecular Engineering Research (FIBER), Konan University, Japan as an Assistant Professor in 2004. He was promoted to an Associate Professor and a Professor in 2009 and 2014, respectively in the current department. His research interests include non-canonical nucleic acid structures (G-quadruplex, I-motif, triplex, junction, hairpin loop, etc.), small molecules targeting nucleic acids and their applications especially molecularly-targeted photodynamic therapy, molecular crowding, and liquid-liquid phase separation. He has authored or co-authored more than 130 papers, reviews, and book chapters, and delivered more than 50 invited talks in international and domestic meetings and conferences.

8. Professor **Dehui Wan**, National Tsing Hua University, Taiwan



## **Light-mediated Multifunctional Nanocomposite Hydrogels for Cancer Therapy**

### **Dehui Wan**

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INVITED Author/Article for SPECIAL ISSUE of the Journal  
KEY PRESENTATION

Abstract CONTROL ID number KQNO5

Nowadays, problems of energy crises and climate change pose a threat to human living. Therefore, developing eco-friendly cooling systems is an utmost issue to work on. Most of current cooling methods require energy to carry heat away. By means of passive radiative cooling, the system can radiate heat to outer space through the atmospheric transmission window between 8-13  $\mu\text{m}$ , thus lowering the temperature without any energy consumption. Some photonic solar reflector and thermal emitter, like  $\text{HfO}_2$ ,  $\text{SiO}_2$  and metamaterial film, can reflect incident sunlight while emitting radiation in the atmosphere windows. However, with its complicated fabrication and high cost, nanophotonic approach is hard to scale up to meet the requirements of commercial applications. Meanwhile, we focus on natural materials of great potential which are still not well-studied. Compared to the typically narrow Infrared (IR) emissivity peaks of artificial daytime cooling materials, the extremely broadband emissivity peak of the natural materials could cover two atmospheric windows (8-13  $\mu\text{m}$  and 1625  $\mu\text{m}$ ). Here, we present a study on silk cocoon, which is characterized by its 90% absorption at IR wavelengths and simple, well-studied fabrication process for different morphologies. We fabricated silk fibroin thin film with thickness ranging from 6 to 88  $\mu\text{m}$  by adjusting the concentration of silk fibroin solution. We observed the broadening of thickness leads to an increase in emissivity over IR wavelength regions, indicating thickness is the key factor to optical and radiative control. In addition to simulated spectra, the optical constants of silk film are calculated for further analysis. We also investigated the broadband absorption and extinction coefficients at NIR wavelength. Throughout the MIR wavelengths (4-25  $\mu\text{m}$ ), silk films exhibit a maximum absorbance of 92% at the thickness of 100  $\mu\text{m}$ . However, the absorbance of silk film has positive correlation with thickness in solar spectrum region, resulting in high  $P_{\text{sun}}$  performance. Therefore, thermal simulation is applied to find the lowest  $T_{\text{equ}}$ , at which the optimal thickness of silk film is located. Finally, we conducted temperature measurements on the optimal silk films practically to verify its daytime radiation cooling ability. With silk covering, the surface temperature of a smartphone decrease by 3.5 K, while the average absorbance of mobile phone is significantly enhanced to 94 % in atmospheric window.

### **Biography:**

Dr. Dehui Wan received his B.S. (2003) in Chemistry and Ph.D. (2010) in Material Science and Engineering at the National Taiwan University. He completed his doctoral thesis under the supervision of Dr. Hsuen-Li Chen and developed various novel nanoparticle-based optical systems for light-harvesting devices and optical data storage. He later worked with Dr. Younan Xia as a postdoctoral research fellow of Department of Biomedical Engineering, Georgia Institute of Technology. He joined the faculty of National Tsing Hua University as a tenure-track Assistant Professor in 2013 and was promoted to Associate Professor in 2017. His work integrates shape-controlled synthesis, surface chemistry and optical engineering of nanostructures to develop novel bio/chemical sensors, energy efficient devices, and photothermal cancer therapy. Dr. Wan has published 27 journal papers with nearly 1300 citations and an h-index of 15, and he also published 6 international patents. He received National Tsing Hua University Young Investigator Award (2016) and Dr. Zhao-ren Li Biomedical Engineering Young Investigator Award (2016).





## **Acid-Triggered dePEGylation for Efficient Delivery of Stealthy Mesoporous Silica Nanoparticles from Circulation to Tumor**

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INVITED PRESENTATION  
Abstract CONTROL ID number 3IISC

Mesoporous silica nanoparticles (MSNs) is a promising nanocarrier for delivering anti-tumor drugs to cancer. Polyethylene glycol (PEG) has been linked to many nanocarriers to increase the dispersity, bioavailability and circulation time of nanoparticles. However, on the other hand, PEGylation could limit the cellular uptake and endosomal escape of MSN, resulted in significant loss of activity of the delivery system.

In this study, to overcome the “PEG dilemma”, we synthesized pHR-MSN-PEG/DA@EPIs, in which pHresponsive (pHR) core-shell MSNs were utilized as nanocarriers, the anti-tumor drug epirubicin (EPI) was encapsulated by electrostatic interaction, and the amine-containing (DA) functional groups were introduced to control the loading and release of EPI. In vitro studies showed that the plain pHR-MSN-PEG/DA is non-toxic and the cleavage of PEG from carriers was achieved in response to acidic environment, result in high efficiency of cellular uptake. In addition, pHR-MSN-PEG/DA@EPIs showed considerable cytotoxicity towards 4T1 tumor cells. For in vivo studies, pHR-MSN-PEG/DA showed excellent passive targeting behavior due to the enhanced permeability and retention (EPR) effect, and strong tumor inhibition effects in a chicken embryo chorioallantoic membrane (CAM) tumor model.

### **Biography:**

Si-Han Wu received his Master's and Ph. D. in Chemistry from National Taiwan University in 2008 and 2013, respectively. After a post-doc at Research Center for Applied Sciences of Academia Sinica, he joined Taipei Medical University as an assistant professor. His research interests are in the field of hybrid nanomaterials, focusing on the build-up of mesoporous, hollow and multiple-compartmentalized silica nanomedicine. His current research is aimed to clarify the relationship between synthetic identity and physiological responses, with a focus on (I) developing clinically translatable silica-based nanomedicine to eradicate hypoxic tumor cells, and (II) constructing bacteriatargeting porous silica nanohybrids as antibacterial, antioxidant and anti-inflammatory carriers for sepsis management.



## **Tensed actin cap fibers are required to stabilize $\beta 1$ integrin adhesions and direct cell migration along spatially patterned extracellular matrix**

### **Jau-Ye Shiu**

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INVITED PRESENTATION

Abstract CONTROL ID number QD501

Our ability to control cell behavior by properly engineered materials and microenvironments is tightly coupled to understanding the mechanisms of cell-matrix interactions. Anisotropy of extracellular matrix (ECM) drives cell alignment and directional migration during processes like development and wound healing, but also in cancer cell migration and invasion. So far, migrational persistence whether on flat isotropic or anisotropic surface patterns and fibers was mostly studied as local phenomenon asking how specific integrins are responsible for the recognition of the spatial ECM cues. Yet, cell alignment and directional migration in response to external ECM cues requires signal integration across length scales. By producing patterned 2  $\mu\text{m}$  ECM stripes, which lead to cell alignment, and testing the previously described pan-integrin null fibroblast cells, we indeed observed that cell alignment and directional migration on patterned stripes were lost when  $\beta 1$  integrin was absent. By combining nanopillar arrays with printed celladhesive fibronectin (FN) stripes, we could probe subcellular force distributions at submicron resolution. While it was previously recognized that the  $\alpha v$ - and  $\beta 1$ -class integrin signaling pathways are coupled, via myosin II contractility, we discover here that myosin III coupling of these integrin signaling pathways requires a stiff cell nucleus. Importantly, directional migration along adhesive patterned stripes was also impaired for lamin A/C knockout cells, incapable of forming an actin cap and restored upon lamin A/C rescue. Together, our data suggest that  $\beta 1$  integrin is required for the recognition of spatial ECM cues and that force transmission to the nucleus via lamin A/C is essential for subsequent directional migration.

### **Biography:**

Jau-Ye Shiu received his Bachelor degree in Physics from Chinese culture University in 2002 and obtained his Ph.D. degree in Material Science and engineering from National Chiao Tung University, Taiwan in 2009. He worked as a postdoctoral fellow in the in the Laboratory of Applied Mechanobiology at ETH Zurich between 2010 and 2015. Dr. Shiu is a Junior Group Leader / Oberassistent in the Laboratory of Applied Mechanobiology at the Department of Health Sciences and Technology.

## **Development of fluorometric reagent for detection of sodium ion in living cell**



### **Shigeori Takenaka**

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KEY PRESENTATION  
Abstract CONTROL ID number 382D8

Potassium (K<sup>+</sup>) and sodium (Na<sup>+</sup>) ions existed under inter- and extra-cells and regulates membrane potential. They have an integral role in nerve and brain action and their aberrance encompasses severe disease such as a cardiac arrest. It is very important to analyze K<sup>+</sup> and Na<sup>+</sup> concentration in of blood and this analysis is one of health checking item. Until now, K<sup>+</sup> and Na<sup>+</sup> concentrations were detected with ion-selective electrode and high performance ion-selective electrode has been developing. However, imaging reagents of K<sup>+</sup> and/or Na<sup>+</sup> under homogenous aqueous medium are delayed. The K<sup>+</sup> sensing reagent under aqueous medium has been reported as a basic skeleton of the crown ether coupled with chromophore and is not discriminated between K<sup>+</sup> and Na<sup>+</sup> because of their similar diameter as 266 pm and 190 pm, respectively. On the other hand, G4 DNA structure has the stacked G-quartet planes and has the created space in the center between G-quartet planes incorporates K<sup>+</sup> with the stabilization. Use of this characteristics lead to K<sup>+</sup> sensing system. We were firstly reported the fluorometric K<sup>+</sup> sensing system. They synthesized oligonucleotide carrying human telomere sequence and fluorescent resonance energy transfer (FRET) chromophore pairs of FAM and TAMRA. This molecule folds to G4 structure in the presence of K<sup>+</sup> and two chromophores closes each other to observe FRET signal. Since the amount of G4 formation is correlated with K<sup>+</sup> concentration, K<sup>+</sup> is quantified FRET signal change under homogeneous aqueous medium. The high selectivity of K<sup>+</sup> over Na<sup>+</sup> was realized in this system whereas azacrown ether or troazacrown ether shows only 30-times preference of K<sup>+</sup>/Na<sup>+</sup>. This reagent was named as potassium sensing oligonucleotide (PSO). Fluorometric Na<sup>+</sup> imaging was also reported azacrown type chromophore, SBFI, where its selectivity of Na<sup>+</sup>/K<sup>+</sup> was 2.6-times. We developed oligonucleotide carrying FRET pair enhanced in the presence of Na<sup>+</sup> by noticing the difference of G4 structures in the presence of K<sup>+</sup> or Na<sup>+</sup>: Basket and hybrid types were formed for Na<sup>+</sup> and K<sup>+</sup>, respectively. Use of human telomere sequence, they constructed the oligonucleotide giving enhanced FERT signal in the presence of Na<sup>+</sup>. They named as sodium sensing oligonucleotide, SSO. PSO or SSO developed by our group was stabilized in the presence of K<sup>+</sup> or Na<sup>+</sup> and this stabilization effect was monitored as melting temperature, T<sub>m</sub>, in a melting curve plotted FRET signal change against temperature: the temperature in the presence of 1:1 of G4 and single stranded DNA is T<sub>m</sub>. Here, we tried to improve selectivity of SSO based on systematic sequence change of G4 sequence and we found the sequence of G4 carrying higher preference for Na<sup>+</sup> than for K<sup>+</sup>. Introduction of FRET dyes for this G4 sequence give fluorometric detection of Na<sup>+</sup> in living cell.

### **Biography:**

Shigeori Takenaka was born in 1959 in Fukuoka. He received his PhD in 1988 at Kyushu University. He worked at Kyushu University as Research Associate (1987-1989) and as Associate Professor (1989-1991, 1996-2005). He also worked at Kyushu Institute of Technology (KIT) as Associate Professor (1991-1996) and as Professor (2005-). He was a visiting scientist for Prof. W. David Wilson, Georgia State University (1994-1995). He was Director of Research Center for Bio-microsensing Technology (RCBT). Prof. Takenaka received several prestigious awards in Award such as 2019 Award of the Japan Society for Analytical Chemistry, 2015 SPSJ Mitsubishi Chemical Award (The Society of Polymer Science, Japan), 2003 Award of new product (Asahi Foundation, Japan), and 2001 Nanotechnology Award (International Nanotechnology Conference, Japan). Prof. Takenaka has authored more than 245 papers in refereed journals, 40 reviews and 25 contributing book.

12. Dr. Associate Professor in chemistry **Shinobu Sato**



## DNA bundling using supramolecular interaction

### Shinobu Sato

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INVITED Author/Article for SPECIAL ISSUE of the Journal

INVITED PRESENTATION  
Abstract CONTROL ID number 2FTTM

Shinobu Sato, Kensuke Hiraki, Shigeori Takenaka  
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Regulation of higher-order DNA structures is interesting from the viewpoint of the development of nano-materials and drugs. Here, supramolecular interaction was applied to the regulation of higher-order DNA structures by DNA interacting molecules. Naphthalene diimide is known to bind to double stranded (ds) DNA by threading intercalation. We tried to establish a double-stranded DNA bundling method using host-guest complex formation between  $\beta$ -cyclodextrin ( $\beta$ -CD) and adamantane (Ad). This method also makes it possible to easily assemble nanostructures regardless of DNA complementarity. Naphthalene diimide having two adamantanes (NDI-Ada2) and benzene derivatives carrying two  $\beta$ -CDs (bis- $\beta$ -CD derivative) were synthesized. When NDI-Nme-Ad2 was added to 12 meric double-stranded DNA in 100 mM AcOK-AcOH, a large hypochromic effect was observed by UV/vis spectra. The binding constant ( $K$ ) of NDI-Ada2 with double stranded DNA was determined by UV/vis spectral titration to be  $9.1 \times 10^5 \text{ M}^{-1}$ . This suggested that NDI-Ad2 binds to double-stranded DNA in threading intercalated mode. As a second step, we tried to bundle duplex DNAs bound to NDI-Ada2 through bis- $\beta$ -CD derivative. Gel electrophoretogram of the linear duplex DNA fragments of pBR322 (4361 bp) in the absence or presence of NDI-Ada2 and the bis- $\beta$ -CD derivative showed the retarded DNA bands only in the presence of NDI-Ada2 and the bis- $\beta$ -CD derivative. When NDI-Ada2 was added to pUC19, an extended DNA structure was observed at 0.75  $\mu\text{M}$  NDI-Ada2, 0.75  $\mu\text{M}$  pUC19 by AFM measurement. However, the DNA form changed spherically at 0.75  $\mu\text{M}$  NDI-Ada2, 0.75  $\mu\text{M}$  pUC19, and 0.75  $\mu\text{M}$  bis- $\beta$ -CD derivative. Since a random coil was observed in the case of DNA alone, this shape change is considered to be due to DNA bundling. This result is consistent with the result of gel electrophoresis, indicating that duplex DNAs are bundled each other through the host-guest interaction between adamantane and  $\beta$ -CD.

### Biography:

Shinobu Sato was born in 1981 in Fukuoka. He received his PhD in 2005 at Kyushu University. He worked at Kyushu University as Research Associate (2005-2011) and as Associate Professor (2012-Now). He collaborated with the Research Center for Bio-microsensing Technology (RCBT). Together with Prof. Takenaka, he received several prestigious awards such as 2019 Award of the Japan Society for Analytical Chemistry, 2015 SPSJ Mitsubishi Chemical Award (The Society of Polymer Science, Japan). Associate Professor Shinobu Sato has authored more than 86 papers in refereed journals, 12 reviews and 6 contributing books.





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INVITED Author/Article for SPECIAL ISSUE of the Journal:

INVITED COMMUNICATION

Abstract CONTROL ID number 78R7Q

**Electrochemically active ligand targeting for G-tetraplex in a living cell**

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Various anti-cancer drugs have been developing for chemotherapy for cancer. Recently, tetraplex DNA ligands targeting for tetraplex structure of telomere DNA with low side effects. This comes from the selective inhibition of telomerase activity with the stabilization of tetraplex structure of telomere DNA and subsequently inducement of apoptosis in the cancer cell. We have been developing the cyclic naphthalene diimide (cNDI) derivative as tetraplex DNA selective ligand: cNDIs stacked with G-quadruplex plane of tetraplex DNA whereas they didn't bind to double stranded DNA with steric hindrance under intercalation process [1]. On the other hand, ferrocene is known to generate hydro radical (OH $\cdot$ ) from Fenton reaction with hydro peroxide in our body and this leads to cell damage of our body. Combination between ferrocene and cNDI should lead to more effective anti-cancer drug. We successfully synthesized cyclic ferrocenylnaphthalene diimide derivatives (cFND) and showed high binding constant for tetraplex DNA with  $10^6$  M $^{-1}$  order than that for DNA duplex. Circular dichroism (CD) spectra of tetraplex DNA with or without cFND showed induced CD, which suggested the effective stacking interaction between naphthalene chromophore and G-quartet plane of tetraplex DNA [2]. Furthermore, cFND also led to apoptosis of HeLa cell with several micro molar of IC $_{50}$ . [1] Y. Esaki, Md. M. Islam, S. Fujii, S. Sato, S. Takenaka, *Chem. Commun.*, 2014, **50**, 5967-5969. [2] S. Kaneyoshi, T. Zou, S. Ozaki, R. Takeuchi, A. Udou, T. Nakahara, K. Fujimoto, S. Fujii, S. Sato, S. Takenaka, *Chem. A Eur. J.*, 2020, **26**, 139-142.

