CfffF 2021

CHEMISTRY FOR THE FUTURE 2021

Pisa, June 30 - July 2, 2021

Dipartimento di Chimica
e Chimica Industriale

Via G. Moruzzi 13
Pisa (IT)

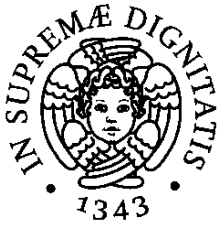
Organised by

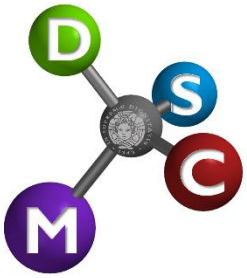
Doctoral School in Chemistry and Material Science

Dipartimento di Chimica e Chimica Industriale
Università di Pisa

With the contribution of Società Chimica Italiana - Sezione Toscana

Società Chimica Italiana





Organising Committee

Alberto Gobbo

Alessandra Recchimurzo

Carlotta Pieroni

Cosimo Micheletti

Eduarda Sangiogo Gil

Elena Pulidori

Francesca Binacchi

Öyküm Naz Avci

Simona Braccini

Thantip Roongcharoen

SCIENTIFIC PROGRAM

Chemistry for the Future 2021

Wednesday – June 30th

9:20 - 9:45	Welcome and Opening
9:45 - 10:30	**Prof. Wolfgang Kroutil** - University of Graz - Biocatalysts as alternative tool for organic synthesis
10:30 - 11:00	**Elisabetta Parodi** - University of Pisa - Biocatalysis: a green approach to high added value chemicals
11:00 - 11:15	*Break*
11:15 - 12:00	**Prof. Peter Dubruel** - Ghent University - AUP as versatile hydrogels for biomedical applications
12:00 - 12:30	**Silvia Pizzimenti** - University of Pisa - The curing process of historical and contemporary oil paints
12:30 - 14:00	*Lunch Break*
14:00 - 14:45	**Prof. Mario Barbatti** - Aix-Marseille University - Perspectives in Mixed Quantum-Classical Dynamics for Modeling Molecular Photoprocesses
14:45 - 15:15	**Mattia Bondanza** - University of Pisa - A Multiscale Perspective for Investigating Protein Photoactivation Mechanisms: The Case of OCP
15:15 - 15:30	*Break*
15:30 - 16:00	**Michele Nottoli** - University of Pisa - Development of new methods for quantum/classical molecular dynamics simulations
16:00 - 17:00	***Flash poster presentation***

Thursday – July 1st

9:30 - 10:15	**Prof. Paolo Melchiorre** - ICIQ Tarragona - Expanding the Potential of Asymmetric Catalysis with Light
10:15 - 10:45	**Valerio Zullo** - University of Pisa - Exploiting chirality of isohexide scaffolds: synthesis, characterization and applications of new chiral auxiliaries from isomannide and isosorbide
10:45 - 11:00	*Break*
11:00 - 11:45	**Prof. Robert Pal** - University of Durham - Light-driven molecular nanomachines as targeted photodynamic therapy agents
11:45 - 12:15	**Delio Santalucia** - University of Pisa - Study of new synthetic approaches to the production of isoprostanoic derivatives

12:15 - 14:00 *Lunch Break*

14:00 - 14:45 **Prof. Peter Sadler** - University of Warwick - Medicines for the Future: Mendeleev, COVID-19 and Beyond

14:45 - 15:15 **Silvia Schoch** - University of Pisa - The anticancer Potential of Versatile Diiron Vinyliminium Complexes

15:15 - 15:30 *Break*

15:30 - 16:00 **Dalila Iacopini** - University of Pisa - Stereoselective synthesis of glycoconjugates for diagnostic applications

16:00 - 17:00 ***Flash poster presentation***

Friday – July 2nd

9:30 - 10:15 **Dr. Giulia Mollica** - Aix-Marseille University - Solid-state DNP NMR strategies for the investigation of nucleation and crystallisation of polymorphic molecular solids

10:15 - 10:45 **Federica Nardella** - University of Pisa - Advanced analytical pyrolysis techniques for studying complex mixtures of natural and synthetic polymers

10:45 - 11:00 *Break*

11:00 - 11:45 **Prof. Concetta Giancola** - Università di Napoli Federico II - Physical chemistry in cancer research: the case of DNA G-quadruplexes as targets for anticancer therapeutics

11:45 - 12:15 **Roberto Francischello** - University of Pisa - Development of new experimental and data processing methods at critical signal-to-noise conditions in nuclear magnetic resonance

12:15 - 14:00 *Lunch Break*

14:00 - 14:30 **Andrea Bonini** - University of Pisa - A Label-free impedance biosensing assay based on CRISPR/Cas12a collateral activity for bacterial DNA detection

14:30 - 15:00 **Federico Maria Vivaldi** - University of Pisa - Development of a wearable sensor array for body fluid analysis

15:00 - 16:00 ***Flash poster presentation***

16:00 - 16:15 Closing

ABSTRACTS

ORAL COMMUNICATIONS

Biocatalysts as alternative tool for organic synthesis

W. KROUTIL[1], S. POMPEI[1], C. GRIMM[1], W. B. BREUKELAAR[1], J. H. SCHRITTWIESER[1], A. SWOBODA[1], I. OROZ-GUINEA[1], V. JURKAS[1], C. K. WINKLER[1], S. GANDOMKAR[1], F. A. SORGENFREI[1]

[1] *Institute of Chemistry, University of Graz, NAWI Graz, Heinrichstrasse 28, 8010 Graz, Austria*
Wolfgang.Kroutil@uni-graz.at

Using biocatalysts in organic synthesis is a continuously increasing field [1]. We contributed to the field by developing e.g. a formal reductive amination of ketones, enabling e.g. regio- and stereoselective amination of di-ketones and improved the reaction sequence by substituting chemical reactions with biocatalytic ones [2,3].
The biocatalytic reaction toolbox was further extended e.g. by a biocatalytic Friedel-Crafts like reaction [4,5], giving for the acylation of catechols alternative protocols. Furthermore, the biocatalytic Pictet-Spengler reaction of tryptamine and aldehyde enables a C-C bond formation leading to chiral amines, namely beta-carbolines allowing the shortest synthesis of (*R*)-harmicine [6,7]. Oximes have not been reported at all to reduced by a defined single enzyme. We were just recently able to identify en-reductases as suitable catalyst for the asymmetric reduction of activated oximes.Recently we combined a chromoelective oxidation with biocatalytic reactions to furnish either the (*R*)- or (*S*)-configured product (Figure 1) [8].

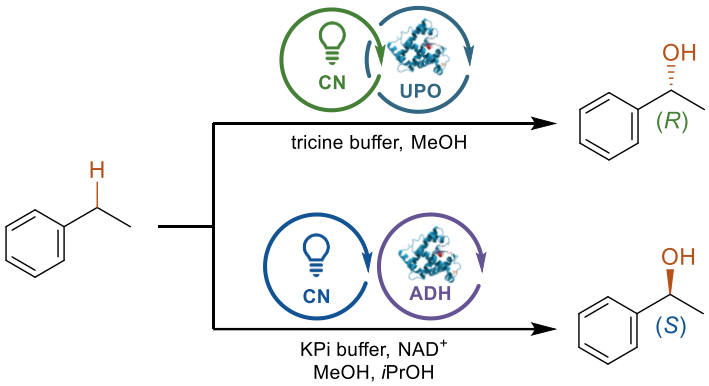


Figure 1. Combining chromoselective oxidation with biocatalytic reactions.

References:

[1] C. K. Winkler, J. H. Schrittwieser, W. Kroutil, *ACS Cent. Sci. 7*, 1, 55-71 (2021).

[2] R. C. Simon, B. Grischek, F. Zepeck, A. Steinreiber, F. Belaj, W. Kroutil, *Angew. Chem. Int. Ed.* 51, 6713-6716 (2021).

[3] N. Alvarenga, S. E. Payer, P. Petermeier, C. Kohlfuerst, A. L. Meleiro Porto, J. H. Schrittwieser, W. Kroutil, *ACS Catal.* 10, 1607-1620 (2020).

[4] N. G. Schmidt, T. Pavkov-Keller, N. Richter, B. Wiltschi, K. Gruber, W. Kroutil, *Angew. Chem. Int. Ed.* 56, 7615 (2017).

[5] A. Żądło-Dobrowolska, L. Hammerer, T. Pavkov-Keller, K. Gruber, W. Kroutil, *ACS Catal*. 10, 1094 (2020).

[6] D. Pressnitz, E.-M. Fischereder, J. Pletz, C. Kofler, L. Hammerer, K. Hiebler, H. Lechner, N. Richter, E. Eger, W. Kroutil, *Angew. Chem. Int. Ed*. 57, 10683-10687 (2018).

[7] E. Eger, A. Simon, M. Sharma, S. Yang, W. B. Breukelaar, G. Grogan, K. N. Houk, W. Kroutil, *J. Am. Chem. Soc*. 142, 792 (2020).

[8] L. Schmermund, S. Reischauer, S. Bierbaumer, C. K. Winkler, A. Diaz-Rodriguez, L. J. Edwards, S. Kara, T. Mielke, J. Cartwright, G. Grogan, B. Pieber, W. Kroutil, *Angew. Chem. Int. Ed*. 60, 6965-6969 (2021).

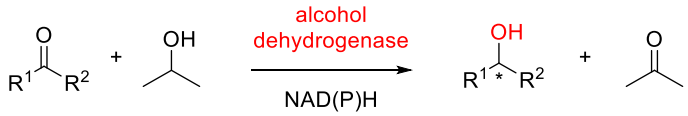
Biocatalysis as a green approach to high added value chemicals

E. PARODI[1], O. PICCOLO[2], A. PETRI[1]

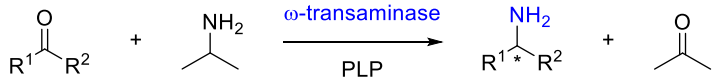
[1] *Dipartimento di Chimica e Chimica Industriale, Università di Pisa, Via G.Moruzzi 13,56124 Pisa, Italia*
[2] *Studio di Consulenza Scientifica (SCOP), Via Bornò 5, Sirtori (LC), Italia*
elisabetta.parodi@phd.unipi.it

Biocatalysis, during the last decades, has emerged as a powerful alternative to traditional chemical processes. Enzymes are biological catalyst that, due to their origin, are designed to catalyse chemical transformation with high activity and selectivity in mild conditions. Furthermore, isolated enzymes or enzyme preparations are nowadays available in large number from different commercial sources, and they can be handled like a common chemical catalyst.[1] Nowadays, biocatalytic processes are exploited in the industry for the enantioselective synthesis of fine chemicals and pharmaceuticals. In this context, we studied two interesting classes of enzymes: alcohol dehydrogenases and ω-transaminases.
Alcohol dehydrogenases catalyse the enantioselective reduction of prochiral ketones and thus are valuable catalysts for the synthesis of enantiopure building blocks. Nevertheless, free enzymes have some drawbacks such as the lack of stability in organic solvent and at high temperatures, difficult work-up and high cost. In order to obtain stable and recyclable catalysts, we studied two different immobilization strategies: the covalent bonding to solid carriers and the formation of cross-linked enzyme aggregates.

Figure 1. Synthesis of enantiopure alcohol with alcohol dehydrogenases



ω-Transaminases catalyse the transamination of prochiral carbonyl compound to enantiopure amines



which are important precursors of biologically active compounds with different industrial applications.[3]

Figure 2. ω-Transaminases for the synthesis of enantiopure primary amines

We optimized the synthesis of some industrially valuable enantiopure amines, exploiting both immobilized and free biocatalysts. The possibility of performing this biocatalytic process in non-conventional co-solvents, such as deep eutectic solvents (DESs), was also investigated.

References:
[1] K. Faber, *Biotransformation in Organic Chemistry*, Springer, (2018)
[2] B.S. Chen, F.Z.R de Souza, *RSC. Adv.*, 9, 2102-2115, (2019)
[3] S.A. Kelly, S. Phole, S. Wharry *et al.*, *Chemical Reviews*, 118, 349-367, (2018)

AUP as versatile hydrogels for biomedical applications

PETER DUBRUEL[1] and (inter)national collaborators

[1] *Ghent University, Department of Organic Chemistry and Macromolecular Chemistry, Polymer Chemistry and Biomaterials Research (PBM) Group*
Peter.Dubruel@ugent.be, https://pbmugent.eu/

Hydrogels have found widespread application in the biomedical field as they mimic some of the properties of the extra-cellular matrix in which cells reside.
In the PBM group, we have developed and patented a novel type of photo-cross-linkable polyethylene oxide (PEO) containing hydrogel building blocks (so-called "AUP") that combine some unique features like very high water-solubility (9 g AUP per ml water) and solid-state photo-reactivity.[1] The general chemical structure is shown in the below figure.

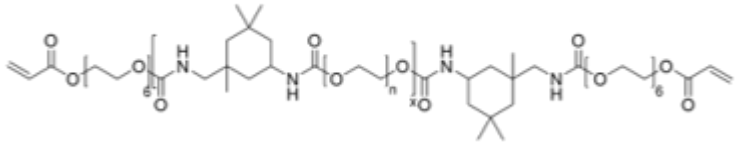
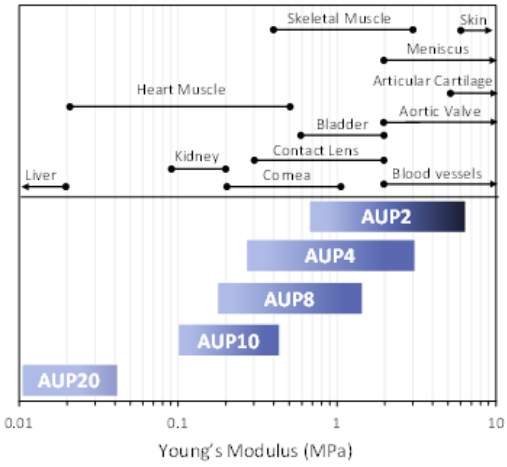
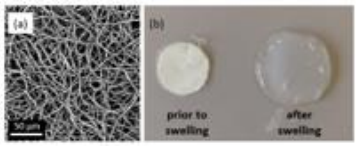
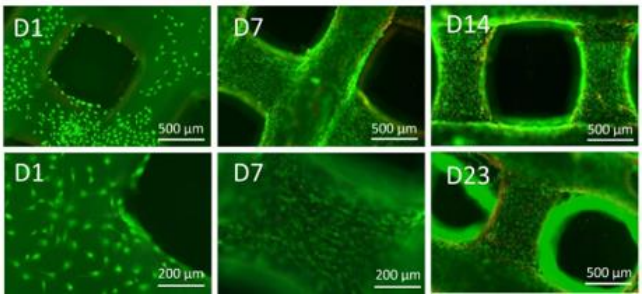


Figure 1. Chemical structure of AUP hydrogel building blocks.

By varying the molar mass of the central PEO block, the swelling properties and the mechanical properties (see below figure, left panel) of hydrogel discs could be varied, indicating that the polymers might find application in various soft tissue applications.







Next, the obtained AUP were applied for developing scaffolds through electrospinning (shown in the above figure, top right panel) and 3D printing opening various application fields.
In a final stage of our work, we also showed that the biocompatible AUP, lacking cell-interactivity, can be converted in cell-interactive materials through addition of Laponite as additive (above figure bottom right panel).

References:
[1] WO2017005613A1, Novel urethane-based materials, derivatives, methods of their preparation and uses.

The curing process of historical and contemporary oil paints

S. PIZZIMENTI[1], G. CAROTI[1], L. BERNAZZANI[1], M. R. TINÈ[1], M. HINTZ[2], C. DUCE[1], I. BONADUCE[1]

[1]Department of Chemistry and Industrial Chemistry, University of Pisa. Via Giuseppe Moruzzi 13, Pisa, Italy
[2]Golden Artist Colors, Inc., 188 Bell Road, New Berlin, NY, USA
silvia.pizzimenti@phd.unipi.it

Paint consists of pigment particles dispersed in an organic fluid binder. When a drying oil - a plant oil rich in triglycerides of polyunsaturated fatty acids - is used as a binder, the paint is an oil paint. The air-curing process, during which a liquid oil paint layer converts to a durable film, is known as autoxidation [1]. The autoxidation of oil paints entiles the formation of peroxide species which evolve according to two main competitive phenomena - cross-linking and oxidation, of which cross-linking is fundamental for obtaining a durable film [2]. The latter aspect has a direct impact on the lifetime of paintings [2]. The extent of cross-linking and oxidation phenomena, and hence the durability of paintings, strictly depends on the oil and on the other component mixed to oil (e.g., pigments and additives) [2].
Autoxidation of oil paints is a very slow process and the understanding the effect of the type of oil, pigments and additives from the quantitative point of view is not straightforward. A useful approach is to follow the mass change under a controlled and constant air flow by a thermogravimetric measurement, the so-called “oxygen uptake” [3]. The mass change is due to two competitive phenomena: the peroxides formation with consequent mass increase, and the evolution of low molecular weight compounds (as a consequence of oxidative degradation) that leads to the mass decrease, respectively. We implemented a semi-empiric equation to fit the experimental oxygen uptake profiles were in order to comparatively studying the kinetics of the oil oxidation, estimate oxygen addition and oxidative degradation [4].
This approach was successfully applied on different model paints composed of relevant oils and pigments in art history: linseed oil, safflower oil, lead white, ultramarine blue and carbon black. Lead white catalyses the oxygen uptake of both oils and it speeds up the decomposition of hydroperoxides, favouring the fast formation of a stable polymeric network [4].
Ultramarine blue paints oil reacts more slowly and for a longer time with oxygen, incorporates more oxygen and it is more prone to oxidative degradation, especially when safflower oil is concerned [4]. Carbon has an antioxidant effect and inhibits the radical chain propagation of linseed oil.
Currently, our effort has been focused on another problematic pigment: cadmium red (CdSSe). When cadmium red is admixed with oil, the paint shows a very slow drying. For this reason, paint manufacturer companies are forced to use metal-based driers to reduce the drying time. No scientific studies reported systematic research on the curing process of cadmium red paint, and how this is affected by the paint formulation. Our study was carried out by fitted oxygen uptake profiles in combination with other analytical techniques (DSC and SPME-GC-MS) to gain complementary information.
This work is part of a wider research project aimed at understanding the chemistry of oil paint film formation and ageing. This information is valuable to support the design and implementation of conservation strategies, but can also be used to improve artists' paint manufacturing.

References:

[1] J. Honzíček, Ind. Eng. Chem. Res. 58, 12485-12505 (2019).
[2] I.Bonaduce, C. Duce, A. Lluveras-Tenorio, J. Lee, B. Ormsby, A. Burnstock and K. J. van den Berg. Acc. Chem. Res. 52, 3397-3405 (2019).
[3] M. Lazzari and O. Chiantore. Pol. Degrad. Stab. 65, 303-313 (1999)
[4] S. Pizzimenti, L. Bernazzani, M.R. Tinè, V. Treil, C. Duce and I. Bonaduce I. ACS Appl. Polym. Mater. 3, 1912-1922 (2021).

Perspectives in Mixed Quantum-Classical Dynamics for Modeling Molecular Photoprocesses

MARIO BARBATTI

Aix Marseille University, CNRS, ICR, Marseille – France
The Light and Molecules Group
mario.barbatti@univ-amu.fr - www.barbatti.org

Electronically-excited molecular and supramolecular systems are central to diverse fields, including biology (photosynthesis, vision), health (phototherapy, imaging), and technology (photonics, photovoltaics, photocatalysis).

Upon photoexcitation, these molecules and molecular assemblies become unequilibrated systems, with multiple competing reaction pathways and time evolution spanning from few picoseconds to microseconds, depending on the processes involved. Moreover, they present highly complex electronic densities and often visit geometric conformations with multireference character. Such features make their analysis challenging for both experimentalists and theoreticians, and the synergy between these fields has been the key to characterize these systems successfully.

Mixed quantum-classical nonadiabatic dynamics (MQCD)[1] helps by providing insights into the physical-chemical phenomenon, delivering information for the deconvolution of experimental time-resolved data, and predicting properties before and after synthesis. However, using MQCD methods faces different challenges, such as developing new functionalities, reliable research protocols, efficient computational methods, tools for integration with experimental analysis, and a balanced description of the electronic correlation between different diabatic states.

In this lecture, I will present applications showing how MQCD methods can be used to investigate electronically excited molecular systems. I will also discuss recent methodological advances.[2,3] Finally, I will critically appraise the field and examine new perspectives, including the advent of machine learning.[4]

References:

[1] Crespo-Otero, R.; Barbatti, M. Recent Advances and Perspectives on Nonadiabatic Mixed Quantum-Classical Dynamics. Chem. Rev. 2018, 118, 7026-7068.

[2] Kossoski, F.; Barbatti, M. Nonadiabatic dynamics in multidimensional complex potential energy surfaces. Chem. Sci. 2020, 11, 9827-9835.

[3] Barbatti, M. Simulation of Excitation by Sunlight in Mixed Quantum-Classical Dynamics. J. Chem. Theory Comput. 2020, 16, 4849-4856.

[4] Dral, P. O.; Barbatti, M. Molecular Excited States Through a Machine Learning Lens. Nat. Rev. Chem. 2021, accepted.

A Multiscale Perspective for Investigating Protein Photoactivation Mechanisms: The Case of OCP

MATTIA BONDANZA[1]

[1] *Dipartimento di Chimica e Chimica Industriale, University of Pisa, 56124 Pisa, Italy*
mattia.bondanza@phd.unipi.it

Orange Carotenoid Protein (OCP) is a carotenoid-protein complex involved in photoprotective mechanisms of cyanobacteria. It works as a molecular light switch, that under high light conditions undergoes to a structural rearrangement that initiates the biological response. Due to its unique features, OCP has been intensely studied both from a biochemical point of view and in a bioengineering perspective. Despite this wide interest, today, the details of the photochemical mechanism that leads from the photoexcitation of the chromophore to the structural rearrangement of the complex and finally to the biological function are still not fully elucidated. Here we present an in-depth computational study to provide answers to the relevant questions about the photoactivated mechanism and propose a new interpretation of experimental data. To reach these goals we have exploited a computational toolbox which integrates advanced computational techniques coming from biophysics (enhanced sampling, accurate force-fields...) and theoretical chemistry (modern electronic structure methods, polarizable QM/MM embedding...).

References:

[1] M. Bondanza, L. Cupellini, P. Faccioli, and B. Mennucci, *JACS*, **2020**, 142, 21829-21841
[2] M. Bondanza, L. Cupellini, F. Lipparini, and B. Mennucci, Chem, **2020**, 6, 187-203
[3] L. Cupellini, M. Bondanza, M. Nottoli and B. Mennucci, BBA - Bioenergetics **2020**, 1861, 148049.

Development of new methods for quantum/classical molecular dynamics simulations

MICHELE NOTTOLI[1]

[1] *Dipartimento di Chimica e Chimica Industriale, Università di Pisa, Via G. Moruzzi 13, 56124 Pisa, Italy*
michele.nottoli@phd.unipi.it

The accurate computational modeling of molecules embedded in complex (bio)matrices, and of their properties, requires the use of molecular dynamics simulations coupled with a hybrid quantum/classical description of the system. Molecular dynamics is required both to perform statistical sampling over the accessible configurations of the system and to follow non equilibrium phenomena. Hybrid quantum/classical methods are used to describe accurately the interesting region of the system through quantum mechanics (QM), while accounting for the surrounding environment in a computationally affordable way through molecular mechanics (MM) [1] or polarizable continuum models (PCMs) [2].

In this contribution, we start by addressing the theoretical and computational problems involved in these kind of simulations. The mathematical aspects are dealt by introducing a Langrangian formalism for the description of polarizable embedding models, and of multiple polarizable embedding models coupled together [3]. Whereas the theoretical and computational problems are addressed by the introduction of new implementations. In this context, we discuss the newly developed PCMs based on the domain decomposition [4] and an interface between a QM code (Gaussian) and a molecular dynamics code (Tinker), to perform multiscale MD simulations in the ground and excited states [5].

This interface is applied to the study of the excited state proton transfer in 3-hydroxyflavone in two different solvents: methanol and methylcyclohexane [6]. By using a combination of molecular dynamics and umbrella sampling, we find an ultrafast component of the transfer, which is common to the two solvents, and a much slower component, which is active in the protic solvent only.

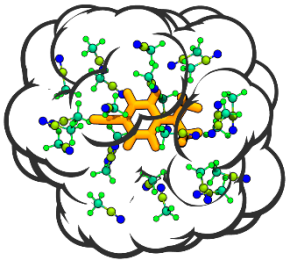


Figure 1. System described using the 3-layer QM/MM/continuum model.

Finally we discuss a multi-layer QM/MM/continuum model, that takes advantage from both state-of-art polarizable QM/MM and QM/continuum models. The new QM/MM/continuum model (Figure 1) is benchmarked against other models, on structures of varying size derived from mutants of the green fluorescent protein.

References:

[1] A. Warshel, *Annu. Rev. Biophys. Biomol.*, 32, 425-443 (2003).
[2] J. Tomasi, B. Mennucci, R. Cammi, *Chem. Rev.*, 105, 2999-3093 (2005).
[3] M. Nottoli, F. Lipparini, *J. Chem. Phys.*, 153, 224108 (2020).
[4] M. Nottoli, B. Stamm, G. Scalmani, F. Lipparini, *J. Chem. Theory Comput.*, 15, 6061-6073 (2019).
[5] M. Nottoli, B. Mennucci, F. Lipparini, *Phys. Chem. Chem. Phys.*, 22, 19532-19541 (2020).

Expanding the Potential of Asymmetric Catalysis with Light

P. MELCHIORRE[1,2]

[1] *ICIQ - Avinguda Països Catalans, 16 43007 - Tarragona, Spain*
[2] *ICREA - Pg. Lluís Companys 23, 08010 - Barcelona, Spain*
pmelchiorre@iciq.es

The chemical reactivity of electronically excited molecules differs fundamentally from that in the ground state. This is the underlying reactivity concept of photochemistry,[1] which has traditionally allowed the development of unique chemical transformations not achievable via conventional ground-state pathways.[2] For example, an excited-state molecule is both a better electron-donor (i.e. a better reductant) and electron-acceptor (i.e. a better oxidant) than in the ground state. This explains why the light excitation of organic molecules can unlock unconventional reactivity manifolds.

In this context, our laboratory has been exploring the potential of some organocatalytic and organometallic intermediates, with a well-established thermal reactivity, to directly reach an electronically excited state upon visible-light absorption to then switch on novel catalytic functions.[3] Studying the mechanism[4] of these photochemical approaches allowed us to expand the synthetic possibilities offered by the excited-state reactivity of organocatalytic and organometallic chiral intermediates and to develop enantioselective radical processes.[5]

References:

[1] V. Balzani, P. Ceroni, A. Juris, Eds. in *Photochemistry and Photophysics*, Wiley-VCH, 2014.
[2] A. Albini, M. Fagnoni, Eds. in *Handbook of Synthetic Photochemis*try, Wiley-VCH, 2010.
[3] (a) E. Arceo, I. D. Jurberg, A. Álvarez-Fernández, P. Melchiorre, *Nat. Chem. 5*, 750–756 (2013). (b) J. J. Murphy, D. Bastida, S. Paria, M. Fagnoni, P. Melchiorre, *Nature, 532*, 218–222 (2016). (c) M. Silvi, C. Verrier, Y. Rey, L. Buzzetti, P. Melchiorre, *Nat. Chem.*, *9*, 868–873 (2017). (d) B. Schweitzer-Chaput, M. A. Horwitz, E. de Pedro Beato, P. Melchiorre, *Nat. Chem.*, *11*, 129–135 (2019).
[4] L. Buzzetti, G. E. M. Crisenza, P. Melchiorre, *Angew. Chem. Int. Ed.*, 58, 3730–3747 (2019).
[5] M. Silvi, P. Melchiorre, *Nature*, *554*, 41–49 (2018).

Exploiting chirality of isohexide scaffolds: synthesis, characterization and applications of new chiral auxiliaries from isomannide and isosorbide

VALERIO ZULLO[1], ANNA IULIANO[1] AND LORENZO GUAZZELLI[2].

[1] *University of Pisa, Department of Chemistry and Industrial Chemistry, via Moruzzi 13, 56124 Pisa, Italy*
[2] *University of Pisa, Department of Pharmacy, via Bonanno 33, 56126 Pisa, Italy*
valerio.zullo@phd.unipi.it

In the last few years, valorization of biomasses and use of renewable compounds became one of the focuses of *green chemistry* with the aim of developing future *sustainable* processes.
Organic chemistry has been largely influenced by this *green* turn, with a consequent higher interest towards the use of biomass-derived molecules and *greener* synthetic protocols.
Following this trend, in the area of enantiodiscrimination and molecular recognition *chiral pool*-derived selectors have been widely employed.
These compounds possess intriguing features, such as the enantiopure and renewable nature, large availability and low cost. Furthermore, in several cases they are even easy to functionalize.
Among these molecules, isomannide and isosorbide, two sugar-derived molecules obtainable from starch industry and processing of corn oil, and endowed with the above mentioned features, have been widely employed in asymmetric synthesis and enantiomeric recognition.[1-3]
Indeed, isomannide and isosorbide possess a chiral vaulted structure with two easy-to-functionalize hydroxyl groups which are one *endo* and one *exo* in isosorbide or both *endo* and pointing towards the inner of the cavity in isomannide. (**Figure 1**)

Isomannide **1** Isosorbide **2**

Figure 1. Isomannide and isosorbide.

In the present work, starting from these sugar-derived compounds, we developed straightforward and reliable synthetic protocols to functionalize either one or both hydroxyl groups with the goal of enhancing intermolecular enantioselective interactions with target compounds.
Following these procedures, we synthesized families of new structurally-related chiral selectors, such as *chiral ionic liquids* [2] and neutral mono- and di-carbamates, through cheap protocols, simple reactions and with a particular attention towards minimizing time consuming and solvent demanding purification steps.
The new compounds were fully characterized by means of thermal and spectroscopic techniques, the retention of the chiral information was tested and their enantiodiscrimination capability was inquired, leading to promising results.

References:

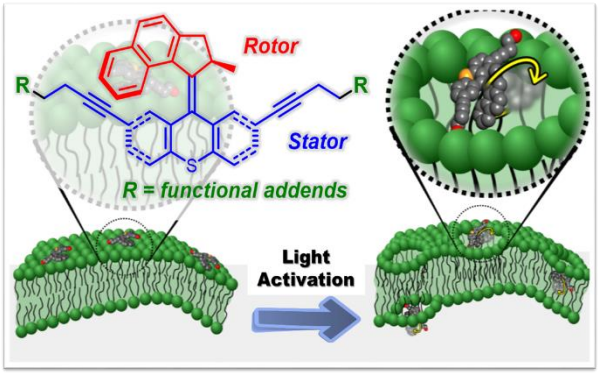
[1] "Isomannide and isosorbide", *e-EROS Encyclopedia of Reagents for Organic Synthesis*, Wiley, 1-5 (2012).
[2] M. Kadraoui, T. Maunoury, Z. Derriche, S. Guillarme, C. Saluzzo, *Eur. J. Org. Chem.*, 441–457 (2015).
[3] V. Zullo, A. Iuliano, L. Guazzelli, *Molecules*, 26, 2052 (2021).
[4] V. Zullo, M. Górecki, L. Guazzelli, A. Mezzetta, G. Pescitelli, A. Iuliano, *Journal of Molecular Liquids*, 322, 114528 (2021).

Light-driven molecular nanomachines as targeted photodynamic therapy agents

THOMAS BRADFORD,[1] LIU DONGDONG,[2] RICHARD S. GUNASEKERA,[2] VÍCTOR GARCÍA-LÓPEZ,[2] LIZANNE G. NILEWSKI,[2] JAMES M. TOUR[2] AND ROBERT PAL,[1,*]

[1]Department of Chemistry, Durham University, South Road, DH1 3LE Durham, UK
[1]Department of Chemistry, Rice University, Houston, Texas 77005, USA
robert.pal@dur.ac.uk; Tel No. +44(0)1913342102

Keywords: nanomachines, light activation, multi-photon, PDT, anti-bacterial



An important need for personalised therapeutics is the effective targeted in vivo destruction of selected cells and cell types, that are currently being highlighted by emergence of powerful optogenetic strategies. Using a new generation of light activated uni-directional molecular nanomachines (MNM) we have demonstrated their application to expedite necrotic cell death using single photon excitation in the UV domain. [1,2]
Recently we have embarked to promote our "proof of principle" technology into in vivo biomedical applications using two photon (2PE) activation, as UV light activation in vivo has significant limitations associated with shallow tissue penetration and non-uniform excitation/activation, limiting the 3D precision required for therapeutics.
This direction in activation not only allow deeper tissue penetration to realise in vivo photodynamic therapy (PDT) development, but also remove UV radiation as a confounder of biomedical efficacy. Since with 2PE MNM activation will only occur in a small truly diffraction limited 3D voxel it allows the next phase of targeted photodynamic therapy protocols and methods to be designed, as with careful chemical engineering of the MNMs cell type and target receptor specific binding can be facilitated with experimental therapeutic precision as small as a single cell. We demonstrated that by scanning a safe dose of NIR light in a 3D raster pattern for a predetermined period of time and repetition, only the surface bound MNM bearing cancerous cells are lysed, whereas all 'healthy' neighbouring cells remain intact and unaffected.[3] Once fully developed and validated 2PE activation of cell type and condition specific MNMs could be potentially adopted as a new form of extremely high optical precision, facile and non-invasive Type IV PDT for cancer treatment via selectively induced apoptosis. This alongside their emerging application as 'mild-UV' activated antibacterial agents[4] renders light driven molecular nanomachines to be one of the most promising candidates for nano-biomedical applications.

References:

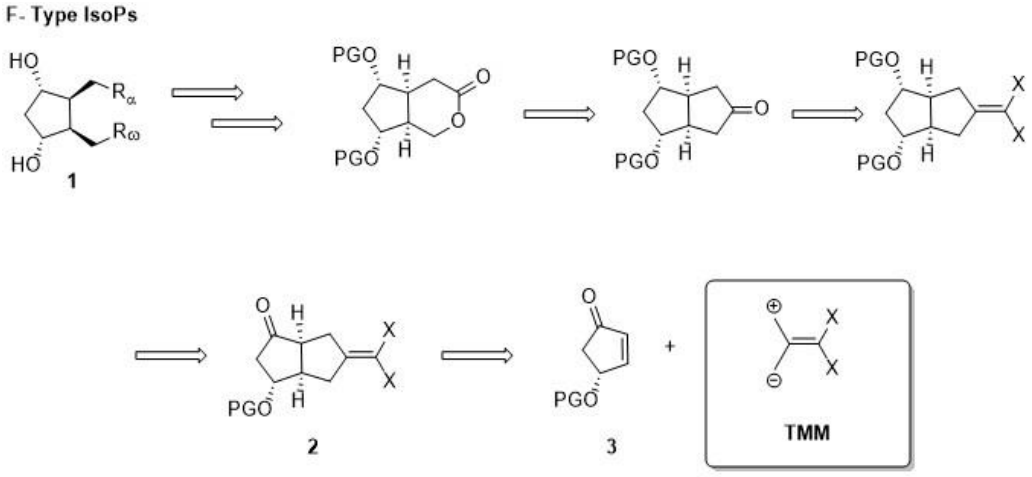
[1] C. Ayala Orozco, D. Liu, Y. Li, L.B. Alemany, R. Pal, S. Krishnan, J.M. Tour, Visible-Light-Activated Molecular Nanomachines Kill Pancreatic Cancer Cells, ACS Applied Materials & Interfaces. 12 (2020) 410–417.
[2] V. García-López, F. Chen, L.G. Nilewski, G. Duret, A. Aliyan, A.B. Kolomeisky, J.T. Robinson, G. Wang, R. Pal, J.M. Tour, Molecular machines open cell membranes, Nature. 548 (2017) 567–572.
[3] D. Liu, V. García-López, R.S. Gunasekera, L. Greer Nilewski, L.B. Alemany, A. Aliyan, T. Jin, G. Wang, J.M. Tour, R. Pal, Near-Infrared Light Activates Molecular Nanomachines to Drill into and Kill Cells, ACS Nano. 13 (2019) 6813–6823.
[4] T. Galbadage, D. Liu, L.B. Alemany, R. Pal, J.M. Tour, R.S. Gunasekera, J.D. Cirillo, Molecular Nanomachines Disrupt Bacterial Cell Wall, Increasing Sensitivity of Extensively Drug-Resistant Klebsiella pneumoniae to Meropenem, ACS Nano. 13 (2019) 14377–14387.

Study of new synthetic approaches to the production of isoprostanoic derivatives

D. SANTALUCIA[1], A. MANDOLI[1]

[1] *Dipartimento di Chimica e Chimica Industriale – Università di Pisa*
delio.santalucia@phd.unipi.it

Isoprostanes (IsoPs) [1], together with their stereoisomers, the prostaglandins, are important members of the large family of metabolites produced *in vivo* by the oxidation of polyunsaturated fatty acids. The biosynthesis of IsoPs follows a non-enzymatic pathway, due to the action of reactive oxygen species. Since their discovery in the '90s, IsoPs have attracted interest in medical applications as important biomarkers of oxidative stress. Structurally, IsoPs (like **1** in **Scheme 1**) show a cyclopentane ring with two functionalized side chains. Given the very large number of possible isomers, a lot of them are still uncharacterized compounds. The challenge represented by their preparation has stirred up the interest of organic chemists for decades [2, 3]. Our work is focused on finding a new, concise, flexible, and stereoselective synthetic route, based on strategies (**Scheme 1**) where the key step is a cyclopentanulation reaction (**4** to **3**) that makes use of trimethylenemethane (**TMM**) synthetic equivalents. The results of different approaches towards this goal will be presented.



Scheme 1. Retrosynthetic strategy for the preparation of IsoPs derivatives.

References:
[1] Galano, J.-M. et al. *Prog. Lipid Res.* 68, 83–108 (2017).
[2] Jahn, U., Galano, J.-M., Durand, T. *Angew. Chemie Int. Ed.* 47, 5894–5955 (2008).
[3] Oger, C. et al. *Synthesis* 50, 3257–3280 (2018).

Medicines for the Future: Mendeleev, COVID-19 and Beyond

PETER J. SADLER

Department of Chemistry, University of Warwick, Coventry CV4 7AL, UK

Mendeleev's periodic table created 152 years ago, contained 63 elements. Today, 118 elements are known, 81 of which are stable and might support life. About 19 elements appear to be essential for human life, possibly up to 7 more, but as yet we cannot assign genetic codes to all essential elements. Equally interesting are the requirements of microbes for elements, especially since there are 10x as many microbes as human cells in the body. Nowadays, about 76 elements, both stable and radioactive, are used in various therapeutic and diagnostic applications [1, 2].

It is not only the element itself which is important for biological activity, but its speciation. For metals, the oxidation state, types and numbers of coordinated ligands, and the coordination geometry are all important. A major challenge is to determine metal speciation in complicated biological (e.g. cellular) environments. Moreover, metal speciation can change through redox and ligand substitution reactions, on timescales from nanoseconds to years. Also cellular media are heterogeneous and constantly changing.

I will illustrate these points with examples for the essential elements iron, copper and zinc in the context of biogenic metals in the brain [3], and roles in COVID-19 [4], as well as for non-essential metals bismuth, ruthenium, osmium, iridium and platinum as anticancer and antimicrobial/antiviral agents, and organometallic, photoactivatable, and catalytic metallodrugs [5-10].

Medicinal inorganic chemistry is exciting because it offers potential for discovery of unique drugs with novel mechanisms of action which might combat resistance to current therapies [11]. Future progress depends on the application of a wide range of state-of-the-art bio-analytical techniques and methods, including synchrotron x-ray imaging, high resolution mass spectrometry, and metallomics.

References:

[1] R.J. Needham, P.J., Sadler In: Mingos D. (ed) The Periodic Table II. Structure and Bonding, Springer, Cham 182. pp 175-201 (2019),
[2] C. Imberti, P.J. Sadler, *Adv. Inorg. Chem*. *75*, 3-56 (2020).
[3] J. Everett, F. Lermyte, J. Brooks, V. Tjendana-Tjhin, G. Plascencia-Villa, I. Hands-Portman, J. Donnelly, K. Billimoria, G. Perry, X. Zhu, P.J. Sadler, P.B. O'Connor, J.F. Collingwood, N,D. Telling,
Science Adv. (2021), in press.
[4] O.W.L. Carter, Y. Xu, P.J. Sadler, *RSC Advances*, 11, 1939-1951 (2021).
[5] J.M. Hearn, I. Romero-Canelón, A.F. Munro, Y. Fu, A.M. Pizarro, M.J. Garnett, Ultan McDermott, N.O. Carragher, P.J. Sadler, *Proc. Natl. Acad. Sci. USA 112*, E3800-5 (2015).
[6] A. Frei, J. Zuegg, A.G. Eliott, M. Baker, S. Braese, C. Brown, F. Chen, C. Dowson, G. Dujardin, N. Jung, A.P. King, A.M. Mansour, M. Massi, J. Moat, H.A. Mohamed, A.K. Renfrew, P.J. Rutledge, P.J. Sadler, M.H. Todd, C.E. Willans, J.J. Wilson, M.A. Cooper, M.A.T. Blaskovich *Chem. Sci*. *11*, 2627-2639 (2020).
[7] H. Huang, S. Banerjee, K. Qiu, P. Zhang, O. Blacque, T. Malcomson, M.J. Paterson, G.J. Clarkson, M. Staniforth, V.G. Stavros, G. Gasser, H. Chao, P.J. Sadler, *Nature Chem. 11*, 1041–1048
[8] H. Shi, C. Imberti, G.J. Clarkson, P.J. Sadler, *Inorg. Chem. Front.*, *7*, 3533-3540 (2020).
[9] J.P.C. Coverdale, I. Romero-Canelón, C. Sanchez-Cano, G.J. Clarkson, A. Habtemariam, M. Wills, P.J. Sadler, *Nature Chem.*, 10, 347-354 (2018).
[10] E.M. Bolitho, J.P.C. Coverdale, H.E. Bridgewater, G.J. Clarkson, P.D. Quinn, C. Sanchez-Cano, P.J. Sadler, *Angew. Chem. Int. Ed.* 133, 6536-6546 (2021),
[11] E.J. Anthony, E.M. Bolitho, H.E. Bridgewater, O.W.L. Carter, J.M. Donnelly, C. Imberti, E.C. Lant, F. Lermyte, R.J. Needham, M. Palau, P.J. Sadler, H. Shi, F.-X. Wang, W.-Y. Zhang, Z. Zhang,
Chem. Sci. 11, 12888–12917 (2020).

The anticancer Potential of Versatile Diiron Vinyliminium Complexes

S. SCHOCH[1]

Dipartimento di Chimica e Chimica Industriale – Università di Pisa
silvia.schoch@phd.unipi.it

The involvement of iron in several important biochemical pathways and its essential nontoxicity in many forms make iron complexes appealing candidates for drug development.[1] Besides, diiron complexes offer the opportunity of cooperative effects between the two metal centres, especially if directly bound, allowing reactivity patterns not available on analogous mononuclear species and to stabilise uncommon ligands by means of multisite coordination modes.[2] In this setting, cationic FeII -FeII compounds containing a vinyliminium bridging ligand have recently shown a promising cytotoxicity profile associated to a multitargeted action and a significant selectivity. These complexes are easily obtained by gram-scale procedures from the commercial [Fe2Cp2(CO)4] (Cp = η 5 -C5H5), via the stepwise assembly of isocyanide and alkyne units on the diiron frame. In general, they are appreciably soluble and substantially stable in aqueous media, and the broad scope of the synthesis reaction allows to tune their properties on varying the R, R' and R'' substituents (Figure 1).[3] The optimisation of the anticancer activity has been pursued by following two main strategies. First, the incorporation of a bioactive organic molecule (i.e. aspirin, chlorambucil, monosaccharides) has been achieved, since a similar approach has been previously demonstrated to provide a favourable synergic effect on the biological activity of various transition metal compounds.[4-6] Second, trimetallic structures have been obtained by tethering another metal fragment with a document anticancer activity (i.e. ferrocenyl, organo-iridium) to the vinyliminium ligand. The synthetic design, the preparation and the biological evaluation of the resulting functionalised complexes will be presented, including several experiments aimed at elucidating the mechanism of action.

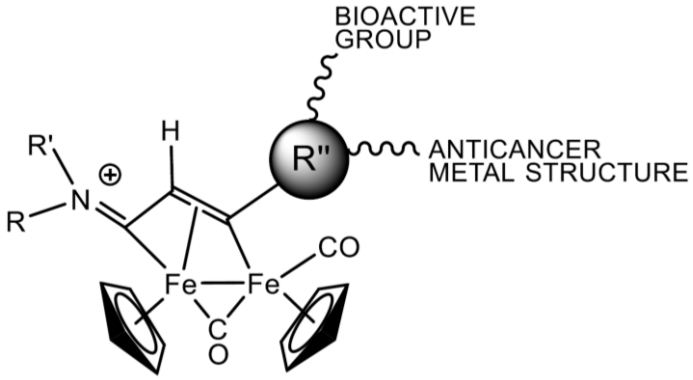


Figure 1. Generic structure of cationic diiron complexes with a bridging vinyliminium ligand, and possible strategies for functionalisation. R, R' = alkyl or aryl; R'' = alkyl, aryl, pyridyl.

References:
[1] U. Basu, M. Roy, A. R. Chakravarty; Coord. Chem. Rev., 417, 213339 (2020).
[2] F. Marchetti, *Eur. J. Inorg. Chem.*, 2018, 3987-4003 (2018).
[3] D. Rocco, L. K. Batchelor, G. Agonigi, S. Braccini, F. Chiellini, S. Schoch, T. Biver, T. Funaioli, S. Zacchini, L. Biancalana, M. Ruggeri, G. Pampaloni, P. J. Dyson, F. Marchetti, *Chem. - Eur. J.*, 25, 14801- 14816 (2019).
[4] Q. Cheng, H. Shi, H. Wang, Y. Min, J. Wang, Y. Liu, *Chem. Commun.*, 50, 7427-7430 (2014).
[5] A. A. Nazarov, S. M. Meier, O. Zava, Y. N. Nosova, E. R. Milaeva, C. G. Hartinger, P. J. Dyson, *Dalton Trans.*, 44, 3614-3623 (2015).
[6] M. Patra, T. C. Johnstone, K. Suntharalingam, S. J. Lippard, *Angew. Chem. Int. Ed.*, 55, 2550-2554 (2016).

Stereoselective synthesis of glycoconjugates for diagnostic applications

DALILA IACOPINI[1], SEBASTIANO DI PIETRO[2], GIOVANNI SIGNORE[3], VALERIA DI BUSSOLO[2]

[1] *Dipartimento di Chimica e Chimica Industriale, Università di Pisa, Via G. Moruzzi 3, 56124 Pisa, Italy*
[2] *Dipartimento di Farmacia, Università di Pisa, Via Bonanno 33, 56126 Pisa, Italy*
[3] *Fondazione Pisana per la Scienza, Via F. Giovannini 13, 56017 San Giuliano Terme (PI), Italy*
dalila.iacopini@phd.unipi.it

Enzymes play a fundamental role in the regulation of cellular metabolism. Many pathologies are closely related to an enzyme pool malfunction: Lysosomal Storage Diseases (LSDs) are caused by the reduced or absent activity of specific enzymes, while many tumoral processes sustain their dysregulated growth from the increased activity of some enzymes.[1] In particular, both in the area of lysosomal disorders and in the tumoral field of considerable interest are α- and β-glucosidase enzymes, hydrolases having a good specificity for a large variety of sugary residues.[2] However, most of the fluorescence-based analytical methods are limited at cuvette use and they can't be adapted *in vitro*: many of these assays use coumarin-based scaffolds as fluorophore unit, but the protocols often require a basification step as the emitted fluorescence comes mainly from the fluorophore anionic form at pH values (up to 10) which are not compatible with living cells (neutral/acidic pH).[3] In order to overcome this limitation, we developed a ratiometric fluorescent pH biosensor based on a conjugated coumarin-triazine scaffold that is excitable in the visible range with a pseudo-linear ratiometric response over more than 6 pH units with a single fluorogenic unit, which allowed us to map the whole *endo*-lysosomal pH landscape of living cells with a single acquisition. The probe can discriminate, based on intracellular acidity, between physiologic and tumor cells, being potentially suitable in perspective as diagnostic tool.[4] Subsequently we proceeded with the stereoselective glycoconjugation of these systems, exploiting both innovative and more traditional glycosyl donors[5a-b], in order to obtain manno-, gulo- and gluco-conjugated coumarin-based fluorophores. The purpose was to improve the cellular uptake of the probe into the tumor cells and quantify the cellular glycolytic activity by the observation of the fluorescence change upon cleavage of the glycosidic bond (Fig. 1).

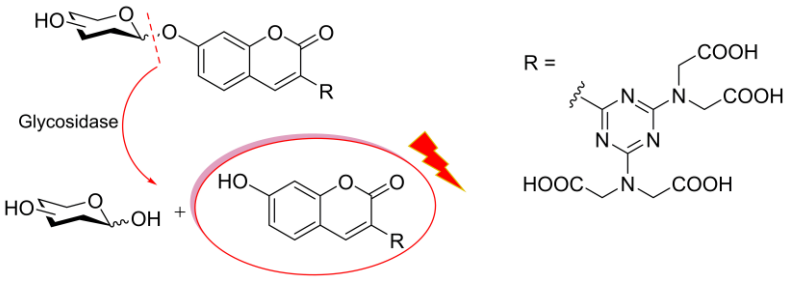


Figure 1. enzymatic cleavage of the coumarin-based glycoconjugate.

References:
[1] F. Begarani, F. D'Autilia, G. Signore, A. Del Grosso, M. Cecchini, E. Gratton, F. Beltram, F. Cardarelli, *ACS Nano.*, 13, 1670-1682 (2019).
[2] P. Vaupel, F. Kallinowski, P. Okunieff, *Cancer Res.,* 23, 6449-6465 (1989).
[3] P. Cui, X. Jiang, J. Sun, Q. Zhang, F. Gao, *Methods Appl. Fluoresc.*, 5, 1-8 (2017).
[4] D. Iacopini, A. Moscardini, F. Lessi, V. Di Bussolo, S. Di Pietro, G. Signore, *Bioorg. Chem.,* 105, 1-7 (2020).
[5] a) V. Di Bussolo, M. Caselli, M. R. Romano, M. Pineschi, P. Crotti, *J. Org. Chem.,* 69, 7383-7386 (2004). b) V. Di Bussolo, L. Checchia, M. R. Romano, M. Pineschi, P. Crotti, *Org. Lett.,* 10, 2493–2496 (2008).

Solid-state DNP NMR strategies for the investigation of nucleation and crystallisation of polymorphic molecular solids

G. MOLLICA[1], M. JURAMY[1], R. CHÈVRE[1], F. ZIARELLI[2], E. BESSON[1], S. GASTALDI[1], S. VIEL[1], K. D. M. HARRIS[3], P. THUREAU[1]

[1]Aix Marseille Univ, CNRS, ICR UMR 7273, Marseille, France
[2]Aix Marseille Univ, CNRS, Centrale Marseille, FSCM, Marseille, France
[3]School of Chemistry, Cardiff University, Cardiff, Wales, United Kingdom
giulia.mollica@univ-amu.fr

Crystallization plays an important role in many areas of biology, chemistry, and materials science, but the underlying mechanisms that govern crystallization are still poorly understood because of experimental limitations in the analysis of such complex, evolving systems. To derive a fundamental understanding of crystallization processes, it is essential to access the sequence of solid phases produced as a function of time, with atomic-level resolution. Rationalization of crystallization processes is particularly relevant for polymorphic functional materials, for which manufacture or storage-induced, unexpected, polymorph transitions can compromise the end-use of the solid product. Interestingly, these transformations often imply the formation of metastable forms. Today, detection and accurate structural analysis of these – generally transient – forms remain challenging, essentially because of the present limitations in temporal and spatial resolution of the analysis, preventing the rationalization (and hence the control) of crystallization processes.

In our laboratory, we develop dynamic nuclear polarization (DNP) solid-state NMR approaches to overcome these limitations [1]. In this contribution, I will present some of our latest results showing that cryogenic MAS NMR [2] combined with the sensitivity enhancement provided by DNP [3] can be an efficient way of monitoring the structural evolution of crystallizing solutions with atomic-scale resolution on a time scale of a few minutes. I will discuss current approaches and recent developments allowing to detect and characterize transient, metastable phases formed at the early stages of crystallization through the use of tailored DNP polarizing agents [4].

References:

[1] *This project has received funding from the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation programme (grant agreement No 758498)*.

[2] P. Cerreia-Vioglio, G. Mollica, M. Juramy, C.E. Hughes, P.A. Williams, F. Ziarelli, S. Viel, P. Thureau, K.D.M. Harris, *Angew. Chem. Int. Ed*. 57, 6619 (2018).

[3] P. Cerreia-Vioglio, P. Thureau, M. Juramy, F. Ziarelli, S. Viel, P.A. Williams, C.E. Hughes, K.D.M. Harris, G. Mollica *J. Phys. Chem. Lett.* 10, 1505 (2019).

[4] M. Juramy, R. Chèvre, P. Cerreia-Vioglio, F. Ziarelli, E. Besson, S. Gastaldi, S. Viel, P. Thureau, K.D.M. Harris, G. Mollica *J. Am. Chem. Soc.* (2021), DOI: 10.1021/jacs.0c12982

Advanced analytical pyrolysis techniques for studying complex mixtures of natural and synthetic polymers

F. NARDELLA[1], S. BELLAVIA[1], M. MATTONAI[1], E. RIBECHINI[1]

[1] *Department of Chemistry and Industrial Chemistry, University of Pisa, Via G. Moruzzi 13, 56124 Pisa, Italy*
federica.nardella@phd.unipi.it

In recent years, the co-pyrolysis of lignocellulose and plastics has been widely investigated as a potential way to upgrade the pyrolysis oil produced (bio-oil) [1]. The use of synthetic polymers as co-reactant produces synergistic effects, which could lead to an improvement of the quality of the bio-oil and enhance liquefaction and gasification [2]. However, the complexity of the process is such that a sufficiently deep knowledge on the matter has not yet been obtained. In this frame, analytical pyrolysis has become a tool of choice to describe the composition of the pyrolysates and to obtain insights into the reaction mechanisms and kinetics [3].
In present work, the co-pyrolysis of lignocellulosic biomass and plastic, such as polyethylene and polystyrene, was studied by analytical pyrolysis-based techniques starting by the investigation of the single natural and synthetic polymers. Products distribution and kinetic of several plant species pyrolysis and their components (cellulose, hemicellulose and lignin) were determined by Py-GC/MS (pyrolysis-gas chromatography mass spectrometry) and EGA-MS (evolved gas analysis-mass spectrometry). The effects of both mechanical and irradiation-based pre-treatments on biomass components pyrolytic behaviour were also investigated.
Synergistic effects produced by the addition of plastics, in different blending ratios, were then evaluated. Py-GC/MS provided information on the chemical composition of the pyrolysates allowing the estimation of experimental values of H/C and O/C. Differences between these values and theoretical ones calculated by the weighted average of the value of the single co-reactants in the mixture were shown. In addition, to emphasize the influence of one co-reactant on the other, EGA-MS results were compared with theoretical degradation curves built by hypothesizing that no synergistic effect is occurring during co-pyrolysis. EGA-MS data were also used to estimate the apparent activation energies for the pyrolysis reaction of each fraction by isoconversional methods.
Finally, the same methodology was used to investigate the co-pyrolysis of polyethylene and polystyrene wastes mixed with wastes from biomass processing such as pulp and paper residues.

References:

[1] Z. Wang, K. G. Burra, T. Lei, A. K. Gupta, *Prog. Energy Combust. Sci.,* 84 (2021)
[2] S. Kumagai, A. Matsukami, F. Kabashima, M. Sakurai, M. Kanai, T. Kameda, Y. Saito, T. Yoshioka, *Process Saf. Environ.*, 143, 91-100 (2020).
[3] A. C. Johansson, L. Sandström, O. G. Öhrman, H. Jilvero, *JAAP*, 134, 102-113 (2018).

Physical chemistry in cancer research: the case of DNA G-quadruplexes as targets for anticancer therapeutics

C. GIANCOLA

Department of Pharmacy, University of Naples Federico II
giancola@unina.it

In the last decades, progresses on cancer research have led to significant improvements in people's time and quality of life, especially for the advancement of the comprehension of basic molecular mechanisms involved in neoplastic transformation and tumorigenesis. In the field of the development of new strategies for cancer treatment through therapies that target specific molecular targets, chemistry can make significant contributions. Specifically, physical chemistry helps in the understanding of the energetics of molecular target/drug interaction and addresses the choice of the best drug candidates.
The discovery of G-quadruplex (G4) arrangements in G-rich DNA sequences has shed light on a new role for DNA in biology [1]. G-quadruplexes are nucleic acid structures formed in relevant genomic region, as telomeres and oncogene promoters. The information acquired on telomere biology and the improvement of biophysical methodology have greatly contributed to understand G-quadruplex structures stability and dynamics giving substantial insight into the biological implications of their occurrence in cell systems [2]. G-quadruplexes in oncogene promoters have been considered as potential new targets for anticancer therapies, relying on the idea that the overexpression of oncogenes containing potential G-quadruplex structures can be deactivated by G-quadruplex-binding ligands *in vivo* [3]. In addition, G4-unwinding helicases counter telomere/gene modulation by G4s and are sensibly overexpressed in several cancers. The helicase role in cancer onset is complex and their inhibition tout-court is not a viable option. Besides, several G4-stabilizing small organic molecules inhibit tumour cells growth and, although there is information on the impact of G4-binders on helicase-G4 recognition/interaction, little is known on the interaction modes and energetics. Here, physicochemical methodologies in combination with biological assays are applied and discussed to gain information on the G4/drug [4,5] and G4/helicase interaction *in vitro* and *in-cell*.

References:

[1] Sen D., Gilbert W., *Nature*, 334, 364–366 (1988).
[2] Zahler A.M., Williamson J.R., Cech T.R., Prescott D.M., *Nature*, 1991 Apr 25; 350(6320):718-20.
[3] Balasubramanian, S., Hurley, L. H. & Neidle, S. *Nat. Rev. Drug Discov.* 10, 261–275 (2011).
[4] D'Aria F, Pagano B, Petraccone L, Giancola C. *Int J Mol Sci.* 22, 448-460 (2021).
[5] D'Aria F, D'Amore VM, Di Leva FS, Amato J, Caterino M, Russomanno P, Salerno S, Barresi E, De Leo M, Marini AM, Taliani S, Da Settimo F, Salgado GF, Pompili L, Zizza P, Shirasawa S, Novellino E, Biroccio A, Marinelli L, Giancola C., *Eur J Pharm Sci.*, 149, 105337-105350 (2020)

Development of new experimental and data processing methods at critical signal-to-noise conditions in nuclear magnetic resonance

ROBERTO FRANCISCHELLO[1,2], ALESSANDRA FLORI[2], LUCA MENICHETTI[3], MARCO GEPPI[1]

[1] *Dipartimento di Chimica e Chimica Industriale, Università di Pisa, Pisa, Italia*
[2] *Fondazione Toscana Gabriele Monasterio, Pisa, Italia*
[3]*Istituto di Fisiologia Clinica, CNR, Pisa, Italia*
roberto.francischello@phd.unipi.it

Nuclear magnetic resonance (NMR) is a powerful and flexible technique for investigating materials: NMR can investigate material composition, molecular conformations and dynamics, and also intermolecular interaction. All those kinds of information can be obtained without damaging or altering the sample in different physical states (liquid, soft, amorphous, crystalline, etc.) thanks to different spectroscopic methods, which belong to the two big branches of solution-state and solid-state NMR. A third crucially important branch of NMR allows the obtainment of localized information and images, and it is called Magnetic Resonance Imaging (MRI). The major downside of NMR is its low intrinsic sensitivity, commonly dealt with by accumulating many experiments ("scans") under the same conditions, in order to increase the Signal-to-Noise Ratio (SNR) of spectra or images. This low sensitivity usually implies long experimental times.

While these long times, although undesired, can be somehow bearable for some applications, like in material science, they are completely unsuited for biological application or reaction monitoring. Therefore, great attention is paid in scientific and technical research in developing methods to increase the SNR or to reduce single scan times with the common aim to reduce the whole experimental time in several NMR applications.

Here I will to present both experimental and signal processing methods to reduce the acquisition time, enhance the SNR, and characterize the signal properties. Whenever possible I will show the benefits of combining both experimental and signal processing methods to increase the SNR.

First, I will show the use of dissolution dynamic nuclear polarization (d-DNP) to greatly enhance, up to three orders of magnitude, the polarization level, which is directly proportional to the signal intensity, of small molecules for MRI experiment. The aim is to produce a biocompatible perfusion tracer using 13C-labelled urea and water. I will also discuss the technical challenges involved in the conversion of a 13C hyperpolarization system into a 1H system.

Then, I will describe the use of the low-rank approximation method to noise reduction in several NMR dataset, showing examples from different NMR fields: spectroscopy, relaxometry, and imaging. I will also highlight the synergy between d-DNP and the low-rank approximation method due to the d-DNP signal characteristic.

Finally, I will conclude my presentation by discussing improved estimated model parameters thanks to low-rank approximation denoise, preliminary results from Monte Carlo simulations, and the use of Neural Networks for analyzing multi-exponential relaxations.

A Label-free impedance biosensing assay based on CRISPR/Cas12a collateral activity for bacterial DNA detection

A. BONINI[1], N.POMA[1], F. VIVALDI[1], D. BOTTAI[2], A. TAVANTI[2], F. DI FRANCESCO[2]

[1] Department of Chemistry and Industrial Chemistry – University of Pisa, Via G. Moruzzi 13, Pisa, Italy
[2] Department of Biology – University of Pisa, Via San Zeno 35-39, Pisa, Italy.
andrea.bonini@phd.unipi.it

The rapid and selective identification in the clinical setting of pathogenic bacteria causing healthcare associated infections (HAIs) and in particular blood stream infections (BSIs) is a major challenge, as the number of people affected worldwide and the associated mortality are on the rise. In fact, traditional laboratory techniques such culture and polymerase chain reaction (PCR)-based methodologies are often associated to high turnaround times, which justify the pressing need for the development of rapid, specific and portable point of care devices [1]. Recently, a new class of programmable endonuclease enzymes called Cas proteins associated to clustered regularly interspaced short palindromic repeat loci (CRISPR) has revolutionised molecular diagnostics. The use of Cas proteins in optical and electrochemical biosensing devices has significantly improved the detection of nucleic acids in clinical samples [2]. In this study, a CRISPR/Cas12a system was coupled with electrochemical impedance spectroscopy (EIS) measurements to develop a label-free biosensing assay for the detection of *Escherichia coli* and *Staphylococcus aureus,* two bacterial species commonly associated to BSI infections. The programmable Cas12a endonuclease activity, induced by a specific guide RNA (gRNA), and the triggered collateral activity were assessed in *in vitro* restriction analyses, and evaluated thanks to impedance measurements using a modified electrode [3].

References:

[1] D.R. Jenkins, Nosocomial infections and infection control, Med. (United Kingdom). 45 (2017) 629–633
[2] A. Bonini, N. Poma, F. Vivaldi, A. Kirchhain, P. Salvo, D. Bottai, A. Tavanti, F. Di Francesco, Advances in biosensing: The CRISPR/Cas system as a new powerful tool for the detection of nucleic acids, J. Pharm. Biomed. Anal. 192(2021) 113645.
[3] A. Bonini, N. Poma, F. Vivaldi, D. Biagini, D. Bottai, A. Tavanti, F. Di Francesco, A Label-free impedance biosensing assay based on CRISPR/Cas12a collateral activity for bacterial DNA detection, J. Pharm. Biomed. Anal. (Under review).

Development of a wearable sensor array for body fluid analysis

F. VIVALDI[1], A. BONINI[1], N. POMA[1], E. EREEMEVA[1], B. MELAI[1], P. SALVO[2], AND F. DI FRANCESCO[1]

[1] Department of Chemistry and Industrial Chemistry, University of Pisa, Via Giuseppe Moruzzi 13, 56124, Italy
[2] Institute of Clinical Physiology of National Research Council, Via Moruzzi 1, 56124, Pisa, Italy.
federicomaria.vivaldi@phd.unipi.it

The increasing popularity of sports practice is producing a rising demand for smart wearable devices to track athlete performance and conditions both during training and competition. The actual method for everyday monitoring is based on the measurement of physiological parameters such as heart rate, breathing rate, heart rate variability, posture, and position [1]. However, these physiological parameters alone do not cover that information coming from metabolic such as the production of lactate or the electrolyte loss. (Bio)chemical sensors may represent a powerful tool for the next generation of smart monitoring, due to low cost, easy use, and potential for miniaturization.
Furthermore, the increasing knowledge regarding the analysis of non-invasive matrix such as sweat is unfolding new possibilities for personalized health monitoring, without resorting to blood, whose sampling make such matrix barely compatible with automatized remote systems for continuous or frequent analysis.
In this work, a wearable sensor array for body fluids analysis will be presented. The development of sensors for pH [2], conductivity, uric acid and lactic acid will be outlined. Practical examples will be given to highlight the pros and cons necessary to define a fluid sampler, and how graphene-based materials such as laser induced graphene may allow the development of electrodes and electronics of wearable smart systems for body fluids analysis.

References:
[1] Weakley, J., Morrison, M., García-Ramos, A., Johnston, R., James, L.,Cole, M. H.. The Validity and Reliability of Commercially Available Resistance Training Monitoring Devices: A Systematic Review. Sports Medicine, 1-60. 2021
[2] Vivaldi, F., Santalucia, D., Poma, N., Bonini, A., Salvo, P., Del Noce, L., Melai, B., Kirchhain, A., Kolivoška, V.,Sokolová, R., Romadová M. Di Francesco F.. A voltammetric pH sensor for food and biological matrices. Sens. Actuators B Chem. 2020

POSTER COMMUNICATIONS

P1: Ö. N. AVCI, L, SEMENTA, A. FORTUNELLI, “Modelling of Oxygen Evolution Reaction (OER) Mechanism on Spinel Oxide-type (AB2O4) Catalysts”

P2: I. BARGAGLI, G. SOTTILE, F. SABATINI, F. MODUGNO, J.J. LUCEJKO, “HPLC-DAD-FD analysis of carbohydrates labelled by reductive amination”

P3: D. BARIK, K. KUNDU, M. DASH, “Montmorillonite stabilized Chitosan-co-Mucin hydrogel for tissue engineering”

P4: R. BASSAM, A. EL HALLAOUI, N. JARMOUNI, M. TRIDANE, T. AINANE, S. BELAAOUAD, “Removal of cadmium ions on naturals clays from aqueous solution by adsorption process: kinetic and isotherm studies”

P5: S. BELLAVIA, F. NARDELLA, M. MATTONAI, E. RIBECHINI, “Co-pyrolysis of biomass and plastic: evaluation of synergistic effects and kinetics by analytical pyrolysis”

P6: D. BIAGINI, S. GHIMENTI, T. LOMONACO, S. MRAKIC-SPOSTA, A. VEZZOLI, D. BONDI, T. PIETRANGELO, V. VERRATTI, F. DI FRANCESCO, “Oxidant status and inflammatory response of high-altitude trekkers in the Nepal Himalaya”

P7: F. BINACCHI, CASSANDRA ELIA, TARITA BIVER, S. BONNET, L. MESSORI, A. PRATESI, “Pd(II) complexes with tetradentate aromatic ligands: a study of ligand dependent interaction with relevant biosubstrates”

P8: A. BOTTO, F. ANASTASI, I. BONADUCE, M. CAPULA, E. GIOVANNETTI, L.A. MCDONNELL, “Bio-orthogonal non-canonical amino-acid tagging (BONCAT) of pancreatic ductal adenocarcinoma”

P9: S. BRACCINI, G. PECORINI, C. TACCHINI, F. CHIELLINI, D. PUPPI, “Chitosan-Alginate Polyelectrolyte Complex Scaffolds by Additive Manufacturing for 3D In Vitro Modelling of Ovarian Cancer”

P10: A. CAPUTO, A. BONINI, F. VIVALDI, B. MELAI, N. POMA, E. EMEREEVA, F. DI FRANCESCO, “Functionalization of gold surfaces by NHCs: a valid alternative to thiols”

P11: G. CAROTI, S. PIZZIMENTI, C. DUCE, I. BONADUCE, “A study on the curing of cadmium red model - oil paints using mass spectrometry techniques”

P12: E. CIGNONI, M. LAPILLO, L. CUPELLINI, S. ACOSTA GUTIERREZ, F. GERVASIO, B. MENNUCCI, “Another perspective for nonphotochemical quenching in plant antenna complexes”

P13: F. CORDELLA, G. ANGELICI, F. BELLINA, A. CUZZOLA, N. DRAGONE, M. LESSI, D. VERGARA, “A structure-activity relation study of amino acid derivatives of pterostilbene analogues”

P14: F. DAUS, A. MOHAN, A. GABBANI, F. PINEIDER, “Plasmonic oxide nanoparticles for photothermal therapy”

P15: N. DI FIDIO, C. ANTONETTI, A. M. RASPOLLI GALLETTI, “Biological and electrochemical valorisation of lignocellulosic wastes from pulp & paper industry to give new generation biodiesel and aromatic compounds”

P16: E. EREMEEVA, F. VIVALDI, A. BONINI, N. POMA, B. MELAI, F. DI FRANCESCO, “Spray coated graphenic electrodes for potentiometric measurements of pH”

P17: S. GALATI, D. YONCHEV, R. RODRÍGUEZ-PÉREZ, M. VOGT, T. TUCCINARDI, AND J. BAJORATH, “Use and rationalization of machine learning approach for predicting isoform-selective inhibitors of carbonic anhydrase enzyme”

P18: E. GIORGI, A. PRATESI, C. GABBIANI, “Gold-based cytotoxic complexes for targeted anticancer treatments”

P19: A. GOBBO, L. BIANCALANA, M. GUELFI, F. MARCHETTI, G. PAMPALONI, “Straightforward Synthesis of a New Family of Robust and Easily Functionalizable Ruthenium(II)-Tris(pyrazolyl)methane complexes”

P20: E. GUAZZELLI, E. MASOTTI, F. DOMENICI, S. GABRIELLI, G. PARADOSSI, M.T.F. TELLING, N. MAHMOUDI, F. UHLIG, M. KRIECHABAUM, G. GALLI, E. MARTINELLI “Understanding the single-chain folding and temperature-responsive self-assembly of amphiphilic random copolymers in solution”

P21: C. GUERRINI, J. LA NASA, I. DEGANO, F. MODUGNO, E. RIBECHINI, M. P. COLOMBINI, “A real-time, non-destructive and in situ technique for characterizing archaeological artifacts by VOC profiling: Selected Ion Flow Tube-Mass Spectrometry (SIFT-MS)”

P22: N. JARMOUNI, M. TOMAIUOLO, F. PINEIDER, “Synthesis, optical and structucal properties of lead bromide perovskite nanocubes (NCs) APbBr3 (A: Cs+, MA+, FA+)”

P23: N. LANDI, E. MAURINA, E. CARIGNANI, S. BORSACCHI, L. CALUCCI, D. MARONGIU, M. SABA, M. GEPPI, “Solid-State NMR study of a multiple-cation lead mixed-halide perovskite with high efficiency”

P24: A. LENZI, D. BIAGINI, S. GHIMENTI, F. VIVALDI, A. BONINI, P. SALVO, R. FUOCO, F. DI FRANCESCO AND T. LOMONACO, “Determination of salivary short chain fatty acids and hydroxy acids in heart failure patients by in-situ derivatization and HiSorb-probe sorptive extraction coupled to thermal desorption and gas chromatography-tandem mass spectrometry”

P25: R. LORÈ, C. ANTONETTI, D. LICURSI, M. MARTINELLI, A. M. RASPOLLI GALLETTI, “Sustainable n-butyl levulinate production from raw and waste biomass”

P26: C. MAROTTA, D. CIRRI, A. PRATESI, C. GABBIANI, “Activatable Pt(IV) compounds as potential anticancer prodrugs”

P27: M. MATTONAI, F. NARDELLA, E. RIBECHINI, “Modelling and optimization of an extraction procedure for lignin using deep eutectic solvents and microwave heating”

P28: E. MAURINA, N. LANDI, E. CARIGNANI, S. BORSACCHI, L. CALUCCI, D. MARONGIU, M. SABA, M. GEPPI, “2D Ruddlesden-Popper Perovskites BA2MAn-1PbnI3n+1 as studied by Solid-State NMR Spectroscopy”

P29: G. MELANI, A. M. VALENCIA, C. COCCHI, M. IANNUZZI, “Donors, acceptors and a bit of aromatic: A computational study of molecule-surface interactions onto 2D hexagonal boron nitride towards photo-active interfaces”

P30: C. MICHELETTI, V. A. DINI, D. GENOVESE, N. ZACCHERONI, C. GUALANDI, A. PUCCI, “Mechanochromic thermoplastic elastomers doped with pyrene”

P31: A. MOHAN, A. GABBANI, F. PINEIDER, “Indium Tin Oxide nanocrystals – factors altering the geometry”

P32: T. NACCI, F. SABATINI, I. DEGANO, F. MODUGNO, “Validation of Py-GC/MS to investigate synthetic fibers”

P33: T. NOTTOLI, J. GAUSS, F. LIPPARINI, “A Second-Order CASSCF Algorithm with the Cholesky Decomposition of the Two-Electron Integrals”

P34: G. PECORINI, S. BRACCINI, S. SIMONI, E. MARTINELLI, L. CARMASSI, D. LI VECCHI, F. CHIELLINI and D. PUPPI, “Additive Manufacturing of Biotechnological Polymers and Relevant Composites for Biomedical Applications”

P35: C. PELOSI F. WURM, C. DUCE, M. R. TINÉ, “Thermal and biophysical stability of protein-polymer conjugates in solution”

P36: C. PIERONI, E. MARSILI, D. LAUVERGNAT, and G. GRANUCCI, F. AGOSTINI, M. PERSICO, “Relaxation dynamics through a conical intersection: Quantum and quantum-classical studies”

P37: E. PULIDORI, S. MICALIZZI, E. BRAMANTI, L. BERNAZZANI, C. DUCE, C. DE MARIA, F. MONTEMURRO, C. PELOSI, A. DE ACUTIS, G. VOZZI AND M. R. TINÉ, “Eco-friendly keratin extraction from poultry feathers and production of keratin-based biomaterials”

P38: A. RECCHIMURZO, C. MICHELETTI, F. BALZANO, G. UCCELLO BARRETTA, “An efficient bis-thiourea CSA for the enantiodiscrimination of amino acid derivatives by NMR spectroscopy”

P39: A. ROGGI, I. FIASCHI, E. MARTINELLI, “SBS functionalized anion exchange membranes for water electrolysis”

P40: T. ROONGCHAROEN, L. SEMENTA, A. FORTUNELLI, “Catalysts design by predictive Modelling of Aqueous Phase Reforming of Liquid Renewable Feedstocks”

P41: E. ROSADONI, M. BIAGETTI, M. FAUSTI, G. GRANUCCI, S. GUARIENTO, M. LESSI, C. MICHELETTI, A. PUCCI, P. RONCHI, F. BELLINA, “C-2 dehydrogenative alkynylation of imidazoles”

P42: C. ROSELLINI, M. CORSI, S. BRACCINI, D. PUPPI, F. CHIELLINI, G. BARILLARO, “Fabrication of liver-lobule-like hexagonal chamber-on-chip scaffold based on biodegradable polymers by replica molding process”

P43: G. SALVADORI, G. GRANUCCI, B. MENNUCCI, “On the photoactivation of a bacteriophytochrome through a QM/MM Surface Hopping approach”

P44: S. SAMAL, M. DASH, “Polymer Scaffolds encapsulated with exosomes as a potential biomaterial for bone regeneration”

P45: E. SANGIOGO GIL, M. PERSICO, G. GRANUCCI, “Surface hopping dynamics with Frenkel exciton model and semi-empirical FOMO-CI method for the study of excited states in systems containing two or more chromophores”

P46: A. TADDEUCCI, F. ZINNA, G. PESCITELLI, G. SILIGARDI, L. DI BARI, “Imaging spectroscopies on thin films of chiral π-conjugated materials”

P47: M. TOMAIUOLO, G. BICCHIERAI, N. JARMOUNI, F. PINEIDER, “Quantum size effects in Cadmium Selenium (CdSe) quantum dots”

P48: O.G. WILLIS, F. ZINNA, L. DI BARI, “Structure based effects on near-infrared chiroptical properties of lanthanide complexes”

P49: M. YAGHOUBI JOUYBARI, J. GREEN, H. ASHA, R. IMPROTA, F. SANTORO, “A Fragment Diabatization Linear Vibronic Coupling Model for Quantum Dynamics of Photoexcited DNA BasePairs”

Modelling of Oxygen Evolution Reaction (OER) Mechanism on Spinel Oxide-type (AB_2O_4) Catalysts

ÖYKÜM NAZ AVCI[1,2], LUCA SEMENTA[1], ALESSANDRO FORTUNELLI[1]

[1]CNR-ICCOM, Consiglio Nazionale delle Ricerche, via G. Moruzzi 1, 56124, Pisa, Italy
[2]Department of Chemistry and Industrial Chemistry, University of Pisa, Via G. Moruzzi 13, Pisa, Italy
oykum.avci@pi.iccom.cnr.it

Water electrolysis is a well-established method to produce hydrogen from the renewable energy sources. The oxygen evolution reaction (OER) and hydrogen evolution reaction (HER) are the two important processes that are involved in electrochemical water splitting process that, in case of large-scale, is greatly hindered by the sluggish anodic OER. Even with state-of-the-art precious catalysts (i.e. RuO_2 and IrO_2) a substantial over-potential is required to drive the OER. Anion Exchange Membrane Water Electrolysis (AEMWE) has several advantages such as the use of non-noble metals as catalysts, low ohmic resistance, and good gas separation characteristics of membrane electrolyte.[1] Ni, Fe, Co based oxides are chemically stable in alkaline media and they show a OER performance relatively comparable to the Ru and Ir oxides.[2] Furthermore, combinations of these metals to obtain bimetallic catalysts, such as spinel oxides (AB_2O_4), have demonstrated to be highly active and stable for this electrochemical reaction.[3] In order to design promising electrocatalysts that enhance OER activity and selectivity, atomistic understanding of target reaction mechanism is essential. Throughout this study, selected inverse-spinel oxide catalysts, $NiFe_2O_4$, $CoFe_2O_4$, will be investigated to map out complete free-energy landscape considering experimental overpotentials for OER reaction by employing Density Functional Theory (DFT). The O-O bond formation barrier with Transition-State-like structures on selected spinel systems for OER is also illustrated/modeled, which correspondingly predict OER kinetics for this systems.

References:
[1] I. Vincent, D. Bessarabov., *Renewable and Sustainable Energy Reviews.*, 81*,* 1690–1704 (2018).
[2] M. Gong, H. Dai, *Nano Res.,* 8**,** 23–39 (2015).
[3] J.S. Kim, B. Kim, H. Kim, K. Kang, *Adv. Energy Mater.,* 8**,** 1702774 (2018).

HPLC-DAD-FD analysis of carbohydrates labelled by reductive amination

I. BARGAGLI[1], G. SOTTILE[1], F. SABATINI[1], F. MODUGNO[1], J.J. LUCEJKO[1]

[1]*Department of Chemistry and Industrial Chemistry, University of Pisa*
i.bargagli@studenti.unipi.it

Carbohydrates play a vital role in the control of biological processes and are constituent of biomaterials used by men since ancient history in a variety of everyday and technological activities. The determination of molecular composition of carbohydrates (polysaccharides, oligosaccharides and sugars) is essential in many research and industrial fields such as food chemistry, biochemistry, material science and heritage science. The analysis of monosaccharides, released by hydrolysis of oligosaccharides and polysaccharides, allows to achieve fundamental information for the characterization of carbohydrates. Given the vast interest in determining the molecular composition of saccharidic materials, it is of high interest to develop simple, fast, and robust analytical methods able not only to qualitatively characterise them but also to quantify sugars in saccharidic hydrolizates. The analysis of monosaccharides can be performed directly [1] or after derivatization. The reductive amination is a widely used derivatization reaction, for carbohydrates analysis in liquid chromatography, especially towards glycans from plasma [2]. However in literature, there are very few applications for monosaccharides and even less for uronic acids [3]. We developed and optimized a method for the quantitative analysis of monosaccharides and uronic acids by high performance liquid chromatography coupled with diode array and fluorescence detector (HPLC-DAD-FD) by means of reductive amination, using 2-aminobenzamide and 2-picoline borane as reducing agent. The one-pot reaction (Figure 1) proceeds through the formation of a Schiff base after reaction of the carbonyl of monosaccharide in its linear form with 2-aminobenzamide. The iminium ion is then reduced to form an amine. To optimise reagents ratio, temperature and time of the labelling reaction and the chromatographic separation, we focused on the analysis of 7 monosaccharides (xylose, glucose, rhamnose, arabinose, galactose, mannose, fucose) and 2 uronic acids (glucuronic acid and galacturonic acid) which are the main constituents of wood polysaccharides (hemicelluloses and cellulose). Labelling by reductive amination allows fluorescence detection of monosaccharides: the use of a FD guarantees a higher sensitivity than UV-absorbance methods.

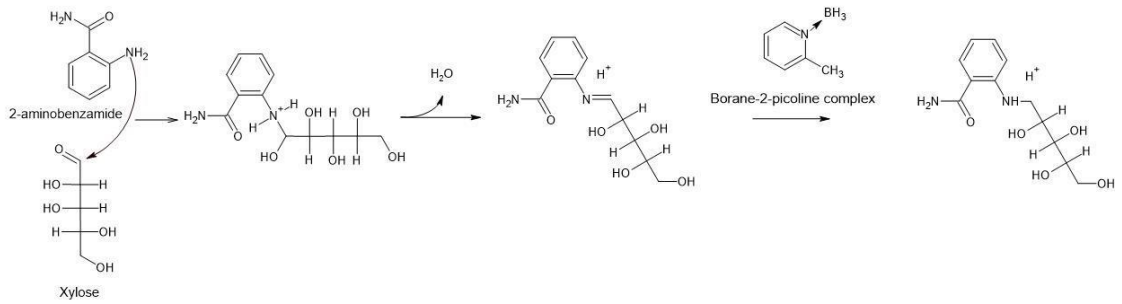


Figure 1. Reductive amination reaction for xylose

References:
[1] T. R. I. Cataldi and C. Campa, “Carbohydrate analysis by high-performance anion-exchange chromatography with pulsed amperometric detection : The potential is still growing,” no. September 2015, 2000.
[2] E. S. L. R. Ruhaak, “2-Picoline-borane A non-toxic reducing agent for oligosaccharide labeling by reductive amination.pdf.” pp. 2330–2336, vol. 10, 2010.
[3] J. Fang, G. Qin, J. Ma, and Y. She, “Quantification of plant cell wall monosaccharides by reversed-phase liquid chromatography with 2-aminobenzamide pre-column derivatization and a non-toxic reducing reagent 2-picoline borane,” vol. 1414, pp. 122–128, 2015.

Montmorillonite stabilized Chitosan-co-Mucin hydrogel for tissue Engineering

D.BARIK[1,2], K.KUNDU1, MAMONI DASH[1]

[1]*Institute of Life Sciences, Nalco Square, Odisha, India.*
[2]*School of Biotechnology, Kalinga Institute of Industrial Technology (KIIT) University, Bhubaneswar, Odisha, 751024 India*
debyashreeta.b@ils.res.in

Tissue engineering is an interdisciplinary field that applies the principles of engineering and life sciences to restore, maintain or improving tissue function or an entire organ. [1]. The concept of tissue engineering involves combining living cells with a natural/synthetic support or scaffold to build a three dimensional (3D) living construct that is able to functionally, structurally and mechanically replace the intended tissue [2]. Polymers have played a crucial role in developing such templates that promote mineralization leading to bone regeneration. In this study, we developed a hybrid scaffold comprising of a polysaccharide chitosan chemically conjugated to a protein mucin and encapsulated with Montmorillonite (nanoclay). Poly-HEMA is grafted onto the backbone of chitosan and the presence of nanoclay provides the needed stability for gel formation. Our aim is to validate the cell viability and cell-cell interaction on these nanoclay scaffolds with different composition of mucin and chitosan in it. Scaffolds with different ratios of the polysaccharide and protein were prepared to evaluate their biocompatibility. The prepared scaffolds showed appreciable material properties such as swelling and porosity. Two cell lines were used for evaluating the biocompatibility of the developed scaffolds. The scaffolds were biocompatible both with MC3T3 and C2C12 cell lines indicating their potential for tissue engineering applications in general.

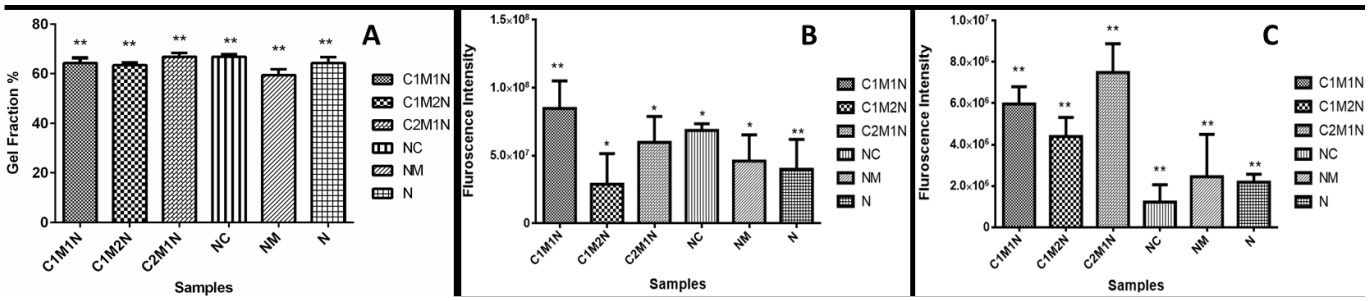


Figure 1. A) Gel fraction ratio %, B) Biocompatibility analysis of scaffold by MTT assay on MC3T3-E1 cell line, C) Biocompatibility analysis of scaffold by MTT assay on C2C12 cell line

References:
[1] D. Howard, L.D. Buttery, K.M. Shakesheff, S.J. Roberts, Tissue engineering: strategies, stem cells and scaffolds, J Anat 213(1) (2008) 66-72.
[2] M.R. Iaquinta, E. Mazzoni, M. Manfrini, A. D'Agostino, L. Trevisiol, R. Nocini, L. Trombelli, G. Barbanti-Brodano,F. Martini, M. Tognon, Innovative Biomaterials for Bone Regrowth, Int J Mol Sci 20(3) (2019) 618.

Removal of cadmium ions on naturals clays from aqueous solution by adsorption process: kinetic and isotherm studies

RAJAA BASSAM[1], ACHRAF EL HALLAOUI[2], NABILA JARMOUNI[1], MALIKA TRIDANE[1,3], TARIK AINANE[4], AND SAID BELAAOUAD[1]

[1]Laboratory of physical chemistry of materials LCPM, Faculty of Siences Ben M'Sik, Hassan II University of Casablanca, B.P.7955, Bd CdtDriss El Harti, Morocco.
[2]Laboratory of Organic, Organometallic and Theoretical Chemistry, University Ibn Tofail, Faculty of Science, B.P. 133, 14000, Kenitra, Morocco
[3]Regional Center for Education and Training Occupations. Casablanca Anfa, Bd BirAnzarane Casablanca, Morocco.
[4]University of Sultan Moulay Slimane, Higher School of Technology Khenifra, PB 170, Khenifra, Morocco
bassam.rajaa@gmail.com

Water is a component of the mineral and organic worlds, and it is an essential element in human life and its activity, including domestic, industrial and agricultural activities, making it a receiving element exposed to all types of pollution[1]. Heavy metals are the most dangerous and toxic pollutants of water and wastewater[2], [3]. Generally, heavy metals are described as a group of trace elements metals and metalloids including manganese, nickel, chromium, lead, arsenic, mercury and cadmium[4].
The objective of this work is to study the adsorption of cadmium on naturals clays (collected from the middle Atlas, Morocco) in order to highlight their potential as a low-cost adsorbent for the treatment of polluted water in a physico-chemical adsorption process. A batch test was conducted to investigate Cd (II) adsorption, the influence of serval experimental parameters was investigated. The isotherm study showed that results were well presented by Freundlich model. Furthermore, the adsorption of Cd2+ on naturals clays is described perfectly by a pseudo-second order kinetics. The use of these natural clays may offer a low-cost adsorption material which may possibly contribute as a low-cost alternative and ecofriendly adsorbent for removal of cadmium in industrials wastewater.

References

[1] B. A. Fowler, 'Monitoring of human populations for early markers of cadmium toxicity: A review☆', *Toxicology and Applied Pharmacology*, vol. 238, no. 3, pp. 294–300, Aug. 2009, doi: 10.1016/j.taap.2009.05.004.
[2] O. B. Akpor, G. O. Ohiobor, and D. T. Olaolu, 'Heavy metal pollutants in wastewater effluents: Sources, effects and remediation', *Advances in Bioscience and Bioengineering*, vol. 2, pp. 37–43, Nov. 2014.
[3] N.- Amin, A. Hussain, S. Alamzeb, and S. Begum, 'Accumulation of heavy metals in edible parts of vegetables irrigated with waste water and their daily intake to adults and children, District Mardan, Pakistan', *Food Chemistry*, vol. 136, no. 3–4, pp. 1515–1523, Feb. 2013, doi: 10.1016/j.foodchem.2012.09.058.
[4] N. S. Bolan *et al.*, 'Cadmium Contamination and Its Risk Management in Rice Ecosystems', in *Advances in Agronomy*, vol. 119, Elsevier, 2013, pp. 183–273.

Co-pyrolysis of biomass and plastic: evaluation of synergistic effects and kinetics by analytical pyrolysis

SIMONA BELLAVIA[1] , FEDERICA NARDELLA[1] , MARCO MATTONAI[1] , ERIKA RIBECHINI[1]

[1]*Department of Chemistry and Industrial Chemistry, University of Pisa, Via G. Moruzzi 13, 56124, Pisa (Italy)*
s.bellavia4@studenti.unipi.it

Biomass represents an abundant energy resource, which can provide second generation fuels and value-added chemicals. The biomass sources for conversion derive generally both from the forest and the agriculture sector and from waste generated by industrial and domestic uses [1].
At the same time, the amount of plastics produced has increased sharply in the past few years and only 10% can be recycled. Thermochemical processes such as pyrolysis have drawn attention as interesting options for the utilization and valorisation of these waste materials [2].
The co-pyrolysis of biomass-plastic wastes mixtures offers a potential way to upgrade these wastes since it produces synergistic effects arising from the interaction of the two components [3].
Analytical pyrolysis techniques are the most used approaches to investigate products distribution and thermal decomposition of biomass and plastic co-pyrolysis [4].
In present work, we exploited pyrolysis gas chromatography/mass spectrometry (Py-GC/MS) to investigate the co-pyrolysis of biomass and plastic wastes. Several waste materials were characterized to select the best feedstocks for co-pyrolysis experiments.
The selected materials were mixed in different blending ratios and studied by Py-GC/MS to obtain information on the chemical composition of the pyrolyzate. Synergistic effects were evaluated by estimating experimental values of H/C and O/C on the basis of the compounds identified.
Principal components analysis (PCA) was used to evaluate complex data sets derived from Py-GC/MS and to highlight the differences in products composition between the samples investigated and mixtures of virgin plastic and untreated biomass.

References

[1] V. Kumar, P. Pathak, and N. K. Bhardwaj, *Waste Manag.*, 102, 281–303 (2020)
[2] Z. Wang, K. G. Burra, T. Lei, and A. K. Gupta, *Prog. Energy Combust. Sci.*, 84, 100899 (2021)
[3] G. Özsin and A. E. Pütün, *Energy Convers. Manag.*, 149, 675–685 (2017)
[4] F. Nardella, S.Bellavia, M. Mattonai, and E. Ribechini, submitted to *Bioresource Technology*

Oxidant status and inflammatory response of high-altitude trekkers in the Nepal Himalaya

D. BIAGINI[1], S. GHIMENTI[1], T. LOMONACO[1], S. MRAKIC-SPOSTA[2], A. VEZZOLI[2], D. BONDI[3], T. PIETRANGELO[3], V. VERRATTI[4], F. DI FRANCESCO[1]

[1]Department of Chemistry and Industrial Chemistry, University of Pisa, Via Giuseppe Moruzzi 13, Pisa, Italy
[2]Institute of Clinical Physiology, National Council of Research (IFC-CNR), ASST Grande Ospedale Metropolitano Niguarda, 20162 Milan, Italy
Department of Neuroscience, Imaging and Clinical Sciences, University "G. d'Annunzio" of Chieti – Pescara, Chieti, Italy;
[4] Department of Psychological, Health and Territorial Sciences, University "G. d'Annunzio" of Chieti – Pescara, Italy
denisebiagini@virgilio.it

Oxylipins are powerful bioactive lipid mediators generated from both ω-3 and ω-6 polyunsaturated fatty acids (PUFAs) through enzymatic (e.g. prostanoids, epoxy and hydroxy fatty acids) and non-enzymatic (e.g. isoprostanes) oxidation reactions. The production of these lipid mediators is considerably increased during inflammation and oxidative stress, which play a key role in body adaptation when challenged with any physical task. In particular, high-altitude training leads to multiple physiological challenges because of physical activity and altitude-induced hypoxia. The adaptation of human body to reduced oxygen availability and oxygen reactive species overproduction is a complex phenomenon affecting physical performances and endurance. The aim of this work was to evaluate changes in oxidative and inflammatory status, before and after an altitude trek during an expedition in the Himalayas, Nepal. Participants (n=6) completed a combined circuit of 300 km distance in 19 days with over 16,000 m of difference in altitude and average daily walk of 6 hrs. The determination of plasmatic oxylipins was performed through a powerful analytical platform combining micro-extraction by packed sorbent technique (MEPS) and ultra-high performance liquid chromatography coupled to electrospray ionization-tandem mass spectrometry (UHPLC-ESI-MS/MS). The proposed analytical method was fully validated and guaranteed excellent analytical performances, i.e. precision (RSD ≤ 10%), recovery (90-110 %) and LODs in the range of 10-100 pg mL-1. The straightforward application of the present method for the monitoring of Italian trekkers on Himalaya is widely displayed, thus furnishing a comprehensive description of lipid mediator rearrangement upon high-altitude exercise, e.g. the significant overexpression of both pro-inflammatory prostaglandins and the well-recognized marker of oxidative stress, F_2-isoprostane, after altitude trek.

Pd(II) complexes with tetradentate aromatic ligands: a study of ligand dependent interaction with relevant biosubstrates

F. BINACCHI[1], CASSANDRA ELIA[1], TARITA BIVER[2,1], SYLVESTRE BONNET[3], L. MESSORI[4], ALESSANDRO PRATESI[1]

[1]Department of Chemistry and Industrial Chemistry, University of Pisa, Via G. Moruzzi 13, 56124 Pisa, Italy
[2]Department of Pharmacy, University of Pisa, Via Bonanno 6, 56126 Pisa, Italy
[3]Leiden Institute of Chemistry, University of Leiden, Einsteinweg 55, 2333 Leiden, Netherlands
[4]Laboratory of Metals in Medicine (MetMed), Department of Chemistry "U. Schiff", University of Florence, Via della Lastruccia 3, 50019 Sesto Fiorentino, Italy
francesca.binacchi@phd.unipi.it

Platinum complexes are studied since the discovery of cisplatin, which is known to produce DNA damages and cell apoptosis [1]. Due to the many similarities between Pt(II) and Pd(II), there is interest in studying Pd(II) complexes as potential anticancer drugs. Given the much faster hydrolysis of Pd(II) complexes with respect to the Pt(II) analogues, there is the need for a very strong nitrogen ligand, able to ensure the reaching of its biological target. Compounds with tetradentate ligands obviate this rapid hydrolysis reaction [2,3].

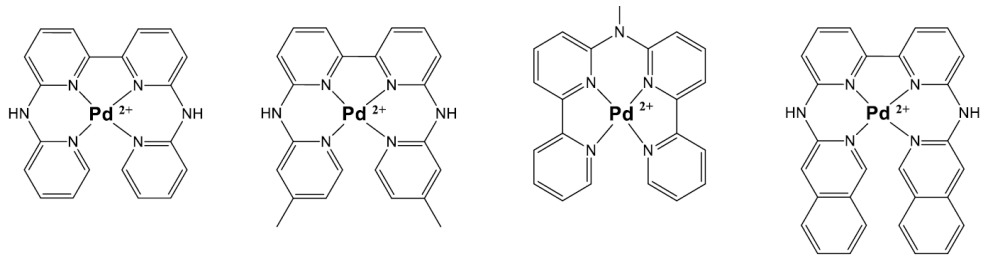


Figure 1. Chemical structure of the studied Pd(II) metal complexes

Here, we present a series of stable four-coordinated complexes of Pd(II) comparing their interaction with poly and oligonucleotides. Natural double-stranded DNA, poly(rA)poly(rU) and poly(rA)2poly(rU) RNAs, DNA G-quadruplexes and a RNA four-way junction are all considered in our studies. These systems are analysed using different techniques and approaches (spectrophotometric and fluorometric titrations, melting assays, viscosity tests and mass spectrometry). In this contribution, we will present our results, which enlighten that little changes in the ligand produce significant differences in the mode of interaction.

References:
[1] B.H. Harper, F. Li, R. Beard, K.B. Garbutcheon-Singh, N.S. Ng, J.R. Aldrich-Wright, *Supramolecular Systems in Biomedical Fields*, H.J. Schneider, Royal Society of Chemistry, 260-299 (2013)
[2] A.S. Abu-Surrah, H.H. Al-Sa'doni, M.Y. Abdalla, *Cancer Therapy*, 6, 1-10 (2008)
[3] M. Heydari, M.E. Moghadam, A.A. Tarlani, H. Farhangian, *Applied Biochemistry and Biotechnology*, 182, 110-127 (2017)

Bio-orthogonal non-canonical amino-acid tagging (BONCAT) of pancreatic ductal adenocarcinoma

A. BOTTO[1,2], F. ANASTASI[2,3], I. BONADUCE[1], M. CAPULA[2,4], E. GIOVANNETTI[2,5], L.A. MCDONNELL[2]

[1] *Department of Chemistry and Industrial Chemistry, University of Pisa, 56124 Pisa, Italy*
[2] *Fondazione Pisana per la Scienza ONLUS, 56107 San Giuliano Terme, PI, Italy*
[3] *NEST Laboratories, Scuola Normale Superiore, 56127 Pisa*
[4] *Scuola Superiore Sant'Anna, 56127 Pisa*
[5]*Vrij Universiteit Amsterdam, 1081 HV Amsterdam, Netherlands*
a.botto@fpscience.it

Pancreatic ductal adenocarcinoma (PDAC) has a very poor prognosis, with less than 10% of patients alive 5 years after diagnosis. The prognosis of cancer patients is much improved is through earlier detection. A recent study reported 5- and 10-year survival rates of 49% and 31%, respectively, for T1-2, N0 and R0 tumors.[1] Earlier diagnosis would enable treatment to begin when the tumour is in its earlier stages, and so improve patient prognosis. This aim would be achieved by developing a method able to isolate and identify characteristic markers of PDAC.

PDAC is characterized by a robust fibroinflammatory response, widespread vascular collapse, and hypoperfusion that make the tumor highly hypoxic and nutrient deprived. This microenvironment promotes tumor invasion, progression, leads to chemotherapy or radiotherapy resistance and eventual mortality. Within the nutrient deprived environment autophagy is central to PDAC metabolism. It has been demonstrated that autophagy shares molecular machinery with exosome biogenesis.[2,3] Exosomes are extracellular vesicles that are secreted from all cells and are present in all body fluids. These vesicles contain molecules characteristic of their cell of origin. Accordingly, the altered autophagy in the highly hypoxic/nutrient-deprived regions of PDAC are expected to be mirrored by altered exosomal molecular signatures, and importantly exosomal surface markers that would enable the specific isolation of PDAC exosomes from patient serum/plasma.

To isolate exosomes from hypoxic cells I will develop a protein labelling approach that is cell type/phenotype specific, and will enable exosome isolation through the labelled exosome-surface proteins. Bio-orthogonal non-canonical amino-acid tagging (BONCAT) is a technique that labels proteins with an azido moiety; this moiety is introduced during protein synthesis using methionine surrogates, then with a simple click chemistry reaction only the proteins that contain the azido moiety will be enriched.[4]

Cell-specific BONCAT labelling can be achieved using azidonorleucine (Anl) as the Met surrogate. Anl is only incorporated into proteins by a specific mutant form of the protein methionyl-tRNA synthetase (MetRS*). Accordingly, Anl labelling can be restricted to cells equipped with this mutant form. The DNA of MetRS* is introduced into cells by transfection, using specific promoters to target specific cell phenotype (e.g. HIF1α for hypoxia). Once Anl is added to the media all methionines in the newly synthesized proteins from MetRS* transfected cells will be substituted for Anl, importantly this also includes exosome surface proteins.

Here we will show progress in method development, including preliminary results showing incorporation of BONCAT labels into PDAC tumor cells (SUIT2 028) and their enrichment.

References:

[1] Seppänen, H. *et al.* The Results of Pancreatic Resections and Long-Term Survival for Pancreatic Ductal Adenocarcinoma: A Single-Institution Experience. *Scand. J. Surg.* **106**, 54–61 (2017).
[2] Seo, J.-W. *et al.* Autophagy is required for PDAC glutamine metabolism. *Sci. Rep.* **6**, 37594 (2016).
[3] Sousa, C. M. *et al.* Pancreatic stellate cells support tumour metabolism through autophagic alanine secretion. *Nature* **536**, 479–483 (2016).
[4] Alvarez-Castelao, B. *et al.* Cell-type-specific metabolic labeling of nascent proteomes in vivo. *Nat. Biotechnol.* **35**, 1196–1201 (2017).

Chitosan-Alginate Polyelectrolyte Complex Scaffolds by Additive Manufacturing for 3D *In Vitro* Modelling of Ovarian Cancer

S. BRACCINI[1], G. PECORINI[1], C. TACCHINI[1], F. CHIELLINI[1], D. PUPPI[1]

[1]*BIOLab Research Group, Department of Chemistry and Industrial Chemistry, University of Pisa, Udr INSTM-Pisa, Via G. Moruzzi 13, 56124, PISA, Italy.*
simona.braccini@phd.unipi.it

Hydrogels have been used over the past two decades as one of the most common types of tissue engineering scaffold thanks to their ability to maintain a distinct 3D structure in physiological environment, offer structural support for cells in the engineered tissues, and simulate the native extracellular matrix functions. The high-water content absorbed by hydrogels can provide an ideal environment for cell survival mimicking that in many native tissues [1]. One of the most common methods for hydrogel preparation is through physical crosslinking of hydrophilic macromolecular chains. Polyelectrolyte complexes (PECs) are formed by electrostatic interactions between oppositely charged groups present along the backbones of two polyions. PECs between polymers from natural sources have been widely investigated in tissue engineering to exploit their biocompatibility, controlled biodegradability, and tuneable mechanical properties, as well as cost-effective, environment-friendly, and energy-efficient production [2].
In this contribution different ratios of chitosan and alginate, polyions of natural origin with established biocompatibility, were used to fabricate 3D PEC hydrogels with a predefined porous structure by means of *Computer-Aided Wet Spinning* (CAWS). Indeed, this Additive Manufacturing technique allows the fabrication of scaffolds with advanced control over external geometry, internal pore size and distribution, determined by the deposition path of a polymeric fibre in a coagulation bath [3] (Figure 1).
Experimental investigations showed that the designed chitosan-alginate PEC hydrogels were stable in cell culture medium at 37 °C for a period of 90 days, demonstrating their suitability for long-term 3D cell culture applications. Moreover, biological characterization carried out with A2780 ovarian cancer cell line highlighted interesting differences in cell adhesion and colonization among investigated hydrogels with different composition (Figure 1) that could be correlated to the different scaffold's mechanical properties.

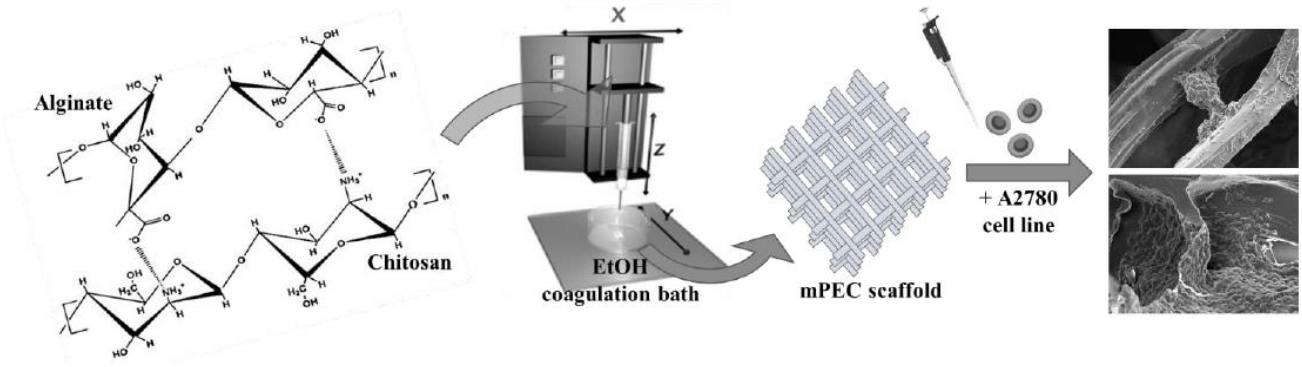


Figure 1. Schematic illustration of the production of PEC scaffolds by means of Computer-Aided Wet Spinning (CAWS) technique and their combination with A2780 ovarian cancer cell line.

References:
[1] S. Mantha, S. Pillai, P. Khayambashi, A. Upadhyay, Y. Zhang, O. Tao, H.M. Pham, S.D. *Materials (Basel)*., 12(20):3323 (2019).
[2] A.D. Kulkarni, Y.H. Vanjari, K.H. Sancheti, H.M. Patel, V.S. Belgamwar, S.J. Surana, C.V. Pardeshi. Artif. *Cells Nanomed. Biotechnol.*, 44, 1615-1625.
[3] D. Puppi, F. Chiellini. *Polym. Int.*, 66, 1690-1696 (2017).

Functionalization of gold surfaces by NHCs: a valid alternative to thiols

A. CAPUTO, A. BONINI, F. VIVALDI, B. MELAI, N. POMA, E. EMEREEVA, F. DI FRANCESCO

Department of Chemistry, University of Pisa, Via Moruzzi 13, 56124, Pisa, Italy
a.caputo11@studenti.unipi.it

The formation of self-assembled monolayers (SAM) on gold plays a crucial role in abroad range of applications ranging from chemical sensing and electrochemistry to catalysis and drug delivery. The most used and important functionalization approach in the last 30 years is based on the organosulfur-gold interaction. However, the chemistry of interaction of sulphur with gold is still partially controversial, and the oxidative and thermal sensibility of the Au-S bond does not allow a widespread commercial use. To overcome this issue, a new way to modify and functionalize gold surfaces based on N-heterocyclic carbenes (NHC) has been developed in the last decade[1,2]. NHCs ligands have attracted attention in the surface chemistry field thanks to the higher stability of the Au-NHC bond compared toAu-S, and due to their tuneable proprieties[3]. Indeed, the binding energy of the NHC-Au bond is 90 kJ/mol^{-1}stronger than the corresponding Au-S[4].In this scenario, the present workshows a new NCH based gold functionalization approach for bio/sensing applications. A dimethyl imidazolium salt (*dmim*) was synthesized as NHC precursor, following *green chemistry* and *click chemistry* principles, and used to functionalize the surface of a gold disk electrode. The changes in electrochemical properties and stability overtime were evaluated and compared with C-15 and C-16 alkylthiols by electrochemical impedance spectroscopy (EIS) and cyclic voltammetry (CV). The NHC-based approach for the formation of SAM showed good electrochemical properties, an increased stability overtime and better reproducibility compared to the classic thiol-gold functionalization.Based on these results, we believe that this strategy could open new ways for the functionalization of gold electrodes.

References:

[1]Crudden, C. M.; Horton, J. H.; Ebralidze, I. I.; Zenkina, O. V.; McLean, A. B.; Drevniok, B.; She, Z.; Kraatz, H.-B.; Mosey, N. J.; Seki, T.; Keske, E. C.; Leake, J. D.; Rousina-Webb, A.; Wu, G. Ultra Stable Self- Assembled Monolayers of N-Heterocyclic Carbenes on Gold. *Nat. Chem.***2014**, *6* (5), 409‑414. https://doi.org/10.1038/nchem.1891

[2]Zhukhovitskiy, A. V.; MacLeod, M. J.; Johnson, J. A. Carbene Ligands in Surface Chemistry: From Stabilization of Discrete Elemental Allotropes to Modification of Nanoscale and Bulk Substrates. *Chem. Rev.***2015**, *115* (20), 11503‑11532. https://doi.org/10.1021/acs.chemrev.5b00220

[3]Engel, S.; Fritz, E.-C.; Ravoo, B. J. New Trends in the Functionalization of Metallic Gold: From Organosulfur Ligands to N-Heterocyclic Carbenes. *Chem. Soc. Rev.***2017**, *46* (8), 2057‑2075. https://doi.org/10.1039/

[4]C7CS00023ETrujillo, M. J.; Strausser, S. L.; Becca, J. C.; DeJesus, J. F.; Jensen, L.; Jenkins, D. M.; Camden, J. P. Using SERS To Understand the Binding of N-Heterocyclic Carbenes to Gold Surfaces. *J. Phys. Chem. Lett.***2018**, *9* (23), 6779‑6785. https://doi.org/10.1021/acs.jpclett.8b02764.

A study on the curing of cadmium red model - oil paints using mass spectrometry techniques

G. CAROTI[1], S. PIZZIMENTI[1], C.DUCE[1], I. BONADUCE[1]

[1]*Department of Chemistry and Industrial Chemistry, University of Pisa. Via Giuseppe Moruzzi 13, Pisa, Italy.*
g.caroti4@studenti.unipi.it

The curing of an oil paint is a very complex process based on two competitive phenomena: cross-linking and oxidation.[1] These phenomena proceed by a free radical chain mechanism, which can be described in terms of initiation (extraction of hydrogen atoms thanks to light and heat to form initio radical R·), propagation (formation of peroxyl radical ROO·, extraction of hydrogen atom from nearby molecules by ROO · to form hydroperoxide ROOH and new R·, decomposition of ROOH and so on) and termination (recombination of radicals to form non-radical products).[2] Some of the oxidation products are low molecular weight and may remain liquid inside the network or even volatilise. Cross-linking reaction result in formation of oligomers and cross-linked structures, causing the formation of the polymeric network.[1,3] The rate at which the oil dries depends on the type of oil (drying, semi-drying,…), but also the nature of pigment plays a crucial role.[4] In this study the behaviour of cadmium red has been investigate in comparison of the already known behaviour of lead white and ultramarine blue.[5]

Cadmium red is a cadmium sulfoselenide, a solid solution of CdS and CdSe, whose color tunes from orange to red by increasing the amount of selenium. Cadmium red is a semiconductor and the band gap of CdSSe depends on the amount of sulphur and selenium. When excited with a photon with energy higher than the band gap (λ<596 nm), cadmium sulfoselenide generates electron-hole pairs which migrate to the surface of particles.[6]

To simplify the complex process of curing, methyl esters have been used as model paint binders in place of a vegetable oil. Methyl esters, such as methyl linoleate and methyl linolenate, are easier systems to study rather than mixtures of triacylglycerols, and have been extensively used as model lipids in the context of food.[2]

In this study, the curing of cadmium red model paints has been investigated by mass spectrometry techniques, in particular SPME-GC-MS (Solid Phase Micro Extraction – Gas Chromatography Mass Spectrometry), GC-MS (Gas Chromatography - Mass Spectrometry), EGA-MS (Evolved Gas Analysis – Mass Spectrometry) and FIA-ESI-MS (Flow Injection Analysis – Electrospray Ionization – Mass Spectrometry). The model paint were prepared by mixing the methyl esters with the pigment, applied onto a gas slide and were analyzed systematically over a period of two months (Figure 1).

SPME-GC/MS was used to investigate the volatile components formed upon curing, GC-MS to study the oxidised monomers, FIA-ESI-MS to study the oligomeric components and EGA-MS to understand the molecular structure of the components with different thermal stability, up to the polymeric network.

References:

[1] Bonaduce I, Duce C, Lluveras-Tenorio A, *Acc Chem Res*. 2019;52(12):3397-3406.
[2] *Lipid Oxidation Also in the Oily Press Lipid Library :*; 2014.
[3] Lazzari M, Chiantore O, *Polym Degrad Stab*. 1999;65(2):303-313.
[4] Bonaduce I, Carlyle L, Colombini MP, *PLoS One*. 2012;7(11).
[5] Pizzimenti S, Bernazzani L, Tinè MR, Treil V, Duce C, Bonaduce I, *ACS Appl Polym Mater*. Published online 2021.
[6.] Liu H, Gao H, Long M, *Environ Sci Technol*. 2017;51(12):6877-6886.

Another perspective for nonphotochemical quenching in plant antenna complexes

E. CIGNONI[1], M. LAPILLO[1], L. CUPELLINI[1], S. ACOSTA GUTIERREZ, F. GERVASIO[2,3,4], B. MENNUCCI[1]

[1]Dipartimento di Chimica e Chimica Industriale, University of Pisa, via G. Moruzzi 13, 56124, Pisa, Italy
[2]Department of Chemistry, University College London, WC1E 6BT London, UK
[3]Pharmaceutical Sciences, University of Geneva, CH-1211 Geneva, Switzerland
[4]ISPSO, University of Geneva, CH-1211 Geneva, Switzerland
edoardo.cignoni@phd.unipi.it

Light-harvesting complexes (LHCs) of plants exert a dual function of light-harvesting and photoprotection [1]. By changing their conformation, they can switch from an active, light-harvesting state to a quenched state where excess energy is dissipated into heat [2]. Both the mechanism of quenching and the identity of the quenched/active states are still subject to debate, despite the experimental efforts [3]. The main mechanisms proposed for the chlorophyll de-excitation involve a nearby carotenoid, which quenches the excitation via an excitation energy transfer (EET) and/or a CT mechanism. We characterize the conformational space and the quenching mechanisms of CP29, a minor LHC of plants, through enhanced-sampling techniques, validation with CryoEM data, dimensionality reduction schemes and electronic calculations. We show that different apoprotein conformations are reflected in changes of carotenoid geometries and carotenoid-chlorophyll interactions. Our results suggest a quenching mechanism mediated by either short-range effects and/or the tuning of the carotenoid site energy in response to protein movements.

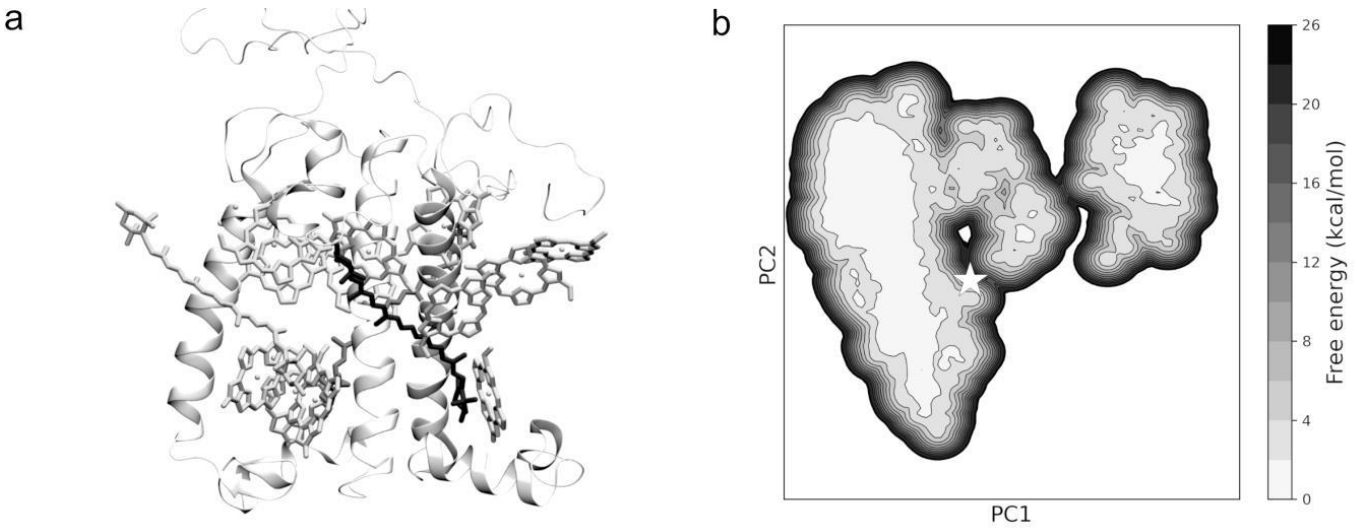


Figure 1. (a) The CP29 system, showing three embedded carotenoids and thirteen chlorophylls. (b) Exploration of the parallel-tempering in the well-tempered ensemble (PT-WTE) simulation shown in a reduced PCA space. The star indicates the starting point of the simulation.

References:

[1] Croce, R., van Amerongen, H. *Nat Chem Biol* **10,** 492–501 (2014).
[2] Pinnola A., Bassi R. *Biochem Soc Trans* **46**, 467–482 (2018).
[3] Ruban, A. V. *FEBS letters* **592**, 3030-3039 (2018).

A structure-activity relation study of amino acid derivatives of pterostilbene analogues

F. CORDELLA[1], G. ANGELICI[1], F. BELLINA[1], A. CUZZOLA[1], N. DRAGONE[1], M. LESSIA, D. VERGARA[2]

[1]Department of Chemistry and Industrial Chemistry, University of Pisa, 56124 Pisa, Italy
[2]Department of Biological and Environmental Sciences and Technologies, University of Salento, 73100 Lecce, Italy
fabianacordella@gmail.com

Breast cancer is the most common cancer in women worldwide. It is characterized by several subtypes, including triple negative breast cancer. Cell line MDA-231 is the most studied as template of triple negative breast cancer and it was demonstrated that long-terms outcomes are poor for this subtype of breast cancer because it develops resistance to therapy over time [1]. This makes it necessary to develop new treatment strategies, by development of innovative therapeutic compounds and new pharmacological approaches. Recent studies show that Pterostilbene is able to trigger a mechanism that led to growth inhibition of breast cancer. Pterostilbene is a naturally dimethylated analog of the less bioavailable resveratrol which shows, as well, cardioprotective, chemopreventive, antioxidant and anti-inflammatory properties [2]. Considering the interesting anticancer activity of pterostilbene we proposed the synthesis of amino acid derivatives of pterostilbene analogues, through peptide coupling reaction. The insertion of different amino acids in the main scaffold could indeed increase the chemical diversity and the bioavailability [3]. The synthesised products have been tested at the University of Salento on cell line MDA-231. The results showed better activity for derivatives obtained from the coupling between amino analog of pterostilbene and amino acids, so further studies were based on the modification of the positive hits through a structure-activity relation study. [Fig. 1 a]

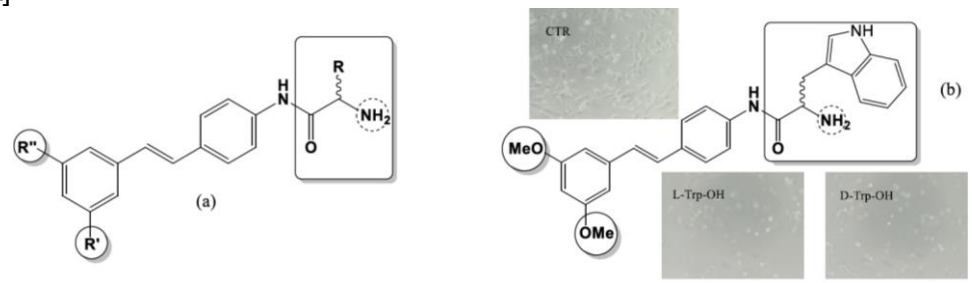


Figure 1: a) Summary structure of modified groups; b) Comparison between MTT test (24 h, 10 μM) of CTR and MTT test of L-Trp-OH and D-Trp-OH derivatives that inhibit proliferation of MDA-231.

The synthesis of 3',5'-dimethoxy-4-amino stilbene was carried out with two different reactions: Heck reaction, a Pd-catalyzed reaction between 3,5-dimethoxystyrene and 4-iodoaniline and Horner-Wadsworth-Emmons (HWE) reaction, between diethyl(4-nitrobenzyl)phosphonate and 3,5-dimethoxybenzaldehyde, followed by the reduction of nitro group. Peptide coupling reaction was carried out with optimized literature procedure.

The MTT test performed on all the synthetic products gave promising preliminary results for two of the synthesized molecules [Fig.1 b], for which complete cellular mortality is recorded after 24 h. Further studies are underway on these two molecules in order to understand their mechanism of action and to study possible toxicity on healthy cells.

References

[1] A. M. Gonzalez-Angulo, F. Morales-Vasquez, and G. N. Hortobagyi, "Overview of resistance to systemic therapy in patients with breast cancer," *Adv. Exp. Med. Biol.*, vol. 608, pp. 1–22, 2007.

[2] J. A. Alosi, D. E. McDonald, J. S. Schneider, A. R. Privette, and D. W. McFadden, "Pterostilbene Inhibits Breast Cancer In Vitro Through Mitochondrial Depolarization and Induction of Caspase- Dependent Apoptosis1," *J. Surg. Res.*, vol. 161, no. 2, pp. 195–201, 2010.

[3] M. Azzolini *et al.*, "New natural amino acid-bearing prodrugs boost pterostilbene's oral pharmacokinetic and distribution profile," *Eur. J. Pharm. Biopharm.*, vol. 115, pp. 149–158, 2017.

Plasmonic oxide nanoparticles for photothermal therapy

F. DAUS[1], A. MOHAN[1], A. GABBANI[1,2], F. PINEIDER[2]

[1]*Department of Chemistry and Industrial Chemistry, University of Pisa, Italy*
[2]*CNR-ICCOM, Sesto Fiorentino (FI), Italy*
f.daus@studenti.unipi.it

Hyperthermia is a kind of treatment in which human tissues are exposed to high temperatures in order to damage and kill the cancer cells or to make them more sensitive to radiations or anti-cancer drugs. There are different kinds of hyperthermia, but this project is focused on photothermal hyperthermia: plasmonic nanoparticles (NPs) are administered to the patient and then a radiation of a proper wavelength is applied to interact with them and causing their heating, leading to the death of the tumor cells, while the healthy ones are left unaltered. However, when aiming for deep-tissue penetration, the ability of the light to penetrate the healthy tissues without causing any damage to them is the key parameter[1]. For this reason, it is of fundamental importance that the employed radiation has a wavelength that falls within one of the so-called "biological windows". Three windows have been identified: the first window between 700 and 950 nm, the second one between 1000 and 1350 nm and the third one between 1550 and 1870 nm[2]. So far metal NPs have been mainly used for this purpose, especially Au NPs, since they are unique in being able to keep their optical properties in cells for a long time under certain conditions, although peculiar shapes are necessary in order to obtain an absorption peak in one of the wavelength regions mentioned above. Doped semiconductors rapresent a valid alternative to metal nanostructures. In particular, the main benefit in using these kinds of material is the NPs' small size, which results in a negligible scattering contribution, in addition to the fact that no specific shape is required (spherical NPs are sufficient)[3]. In this regard, ITO (Indium Tin Oxide) NPs have been synthesized using a procedure developed by our laboratory as a modification of previously developed methods[4,5]. The synthesis is carried out in 1-Octadecene using $In(acac)_3$ and $Sn(acac)_2Cl_2$ as precursors and oleic acid and oleylamine as surfactants. The absorption spectra of ITO NPs in C_2Cl_4 show a peak around 1800 nm (Fig. 1), which is in the range of the third biological window. Hyperthermia measurements were carried out with a 1650 nm LED (13mW) and the temperature variations were collected using a thermocouple. An ITO dispersion with high optical density (A=10 cm^{-1}) showed a temperature increase of 2.5°C in 30 minutes under irradiation, which is an interesting result considering the source's low power (Fig.2). Another promising doped semiconductor is FICO (Fluorine-Indium Cadmium Oxide), FICO NPs' synthesis was performed in Octadecene using $Cd(aca)_2$ and InF_3 as precursors and oleic acid as surfactant. In this case the main benefit comes from the narrow LSPR peak (Fig. 1), which can be tuned across a significant wavelength range as a result of the cooperative effects of the mixed cationanion doping, making them good candidates as well for the hyperthermia treatment[6].

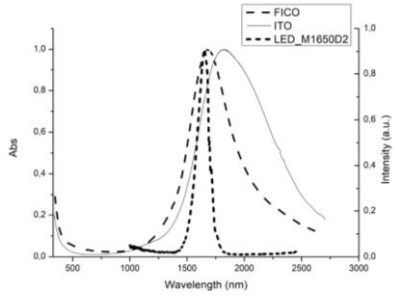


Figure 1. Absorption spectra of ITO, FICO NPs spectrum.

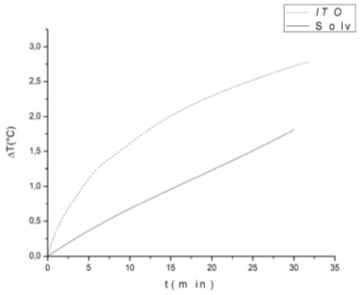


Figure 2. ΔT observed vs. LED emissions irradiation time of ITO NPs and the solvent.

References:
[1] L. Jauffred et al., Chem. Rev. 2019, 119, 8087-8130
[2] E. Hemmer et al, Nanoscale Horiz., 2016, 1, 168
[3] A. Agrawal et al., Chem. Rev. 2018, 118 (6), 3121-3207
[4] M. Kanehara et al., J. Am Chem. Soc., 2009, 131, 17736-17737
[5] S. I. Choi et al., Chem Mater. 2008, 20, 2609-2611
[6] Y. Xingchen et al., J. Am. Chem. Soc. 2014, 136, 11680-11686

Biological and electrochemical valorisation of lignocellulosic wastes from pulp & paper industry to give new generation biodiesel and aromatic compounds

N. DI FIDIO[1], C. ANTONETTI[1], A. M. RASPOLLI GALLETTI

[1]*Department of Chemistry and Industrial Chemistry, University of Pisa, Via G. Moruzzi 13, 56124 Pisa, Italy;*
n.difidio@studenti.unipi.it

Technical lignin and cellulosic wastepaper represent the main side-streams of the existing industrial-scale biorefineries and paper industry. The valorisation of these renewable and low- or negative-value feedstocks is a strategic approach to enhance the biorefinery and paper industry sustainability. Lignin represents a promising source of aromatic compounds, while cellulosic wastepaper is a high-quality source of sugars which can be converted into several added-value bioproducts, such as biofuels, biochemicals and biomaterials. In this perspective, in the present work, the electrochemical valorisation of lignin to give aromatics was performed [1], whereas in the case of wastepaper, a direct enzymatic hydrolysis was optimised to simultaneously produce glucose and xylose which were then fermented by oleaginous yeasts to produce new generation biodiesel [2]. In particular, the soda technical lignin Protobind™ 1000 (P1000) was adopted as starting material. It is produced on an industrial scale by the company GreenValue (Switzerland), starting from a mix of wheat straw and sarkanda grass, after an alkaline extraction with sodium hydroxide.

In order to improve the lignin exploitation to added-value aromatic compounds, a mild chemical conversion route based on electrochemistry was investigated [1]. Under the optimal reaction conditions (NiOOH electrode, pH 14, lignin 20 g/L, 0.4 V), the electro-oxidative depolymerisation of lignin by electrolysis was performed in a divided cell. The main products were sinapic acid, vanillin, vanillic acid, and acetovanillone. The obtained preliminary results demonstrated the potential feasibility of this innovative electrochemical route for lignin valorisation for the production of bio-aromatic chemicals.

The wastepaper derived from the converting process for the production of tissue paper products by different local companies in Lucca (Italy). The waste cellulosic powder is produced in the converting section, where the paper coil is unrolled and the sheet is subjected to mechanical operations to give the final commercial product. This cellulosic waste is not suitable to be recycled within the same papermaking process. For this reason, it is typically recovered by aspiration and sent to the landfill. Regarding the exploitation of wastepaper, an innovative two-step process for the conversion of waste tissue paper to single cell oil (SCO) was optimised. SCO represents an outstanding alternative to both fossil sources and vegetable oils for the production of biodiesel. Hydrolysates containing glucose and xylose were produced by enzymatic hydrolysis of the untreated waste. Under the optimised reaction conditions (Cellic® CTec2 25 FPU/g glucan, 48 h, biomass loading 20 g/L), the yield of 95 mol% was reached for both glucose and xylose. The undetoxified hydrolysate was adopted as substrate for a batch-mode fermentation by the oleaginous yeast *Lipomyces starkeyi*. Lipid yield, lipid content for single cell, oil production and maximum oil productivity were 20.2 wt%, 37 wt%, 3.7 g/L and 2.0 g/L/d, respectively. This new generation oil, obtained from a negative value industrial waste, represents a promising platform chemical for the production of biodiesel, biosurfactants, animal feed and biobased plastics.

References:

[1] N. Di Fidio, J. Timmermans, C. Antonetti, A.M. Raspolli Galletti, R.J.A. Gosselink, R. Bisselink, T. Slaghek, *New J. Chem*., in press, (2021), https://doi.org/10.1039/D1NJ01037A.

[2] N. Di Fidio, F. Dragoni, C. Antonetti, I. De Bari, A.M. Raspolli Galletti, G. Ragaglini, *Bioresour. Technol.,* 315, 123790-123798 (2020).

Spray coated graphenic electrodes for potentiometric measurements of Ph

E. EREMEEVA, F. VIVALDI, A. BONINI, N. POMA, B. MELAI, F. DI FRANCESCO

Department of Chemistry and Industrial Chemistry, University of Pisa, Via Giuseppe Moruzzi 13, 56124, Italy
e.eremeeva@phd.unipi.it

The measurement of pH is carried out daily in many laboratories, but knowledge of the pH level is also important in health monitoring systems, which require small and wearable pH sensors very different from the fragile and bulky glass electrodes. The fabrication of many pH sensors on plastic, silicon or ceramic substrate has been reported [1]. Here we present a fabrication procedure for spray-coated graphenic working electrodes for pH sensing. Spraying parameters were optimized for inks based on graphene oxide (GO), reduced graphene oxide (rGO) and functionalized reduced graphene oxide (rGOf). The resulting pH sensors were calibrated in saline buffers (pH 2-7) by open circuit potentiometry thanks to a Palmsens 4 potentiostat (control software Pstrace 5.8) and an Ag/AgCl reference electrode. The highest sensitivity (-53 mV/pH) and reproducibility was obtained with the rGOf working electrode (Figure 1). Future work will aim at improving the production process for voltammetric analyses and wearable applications.

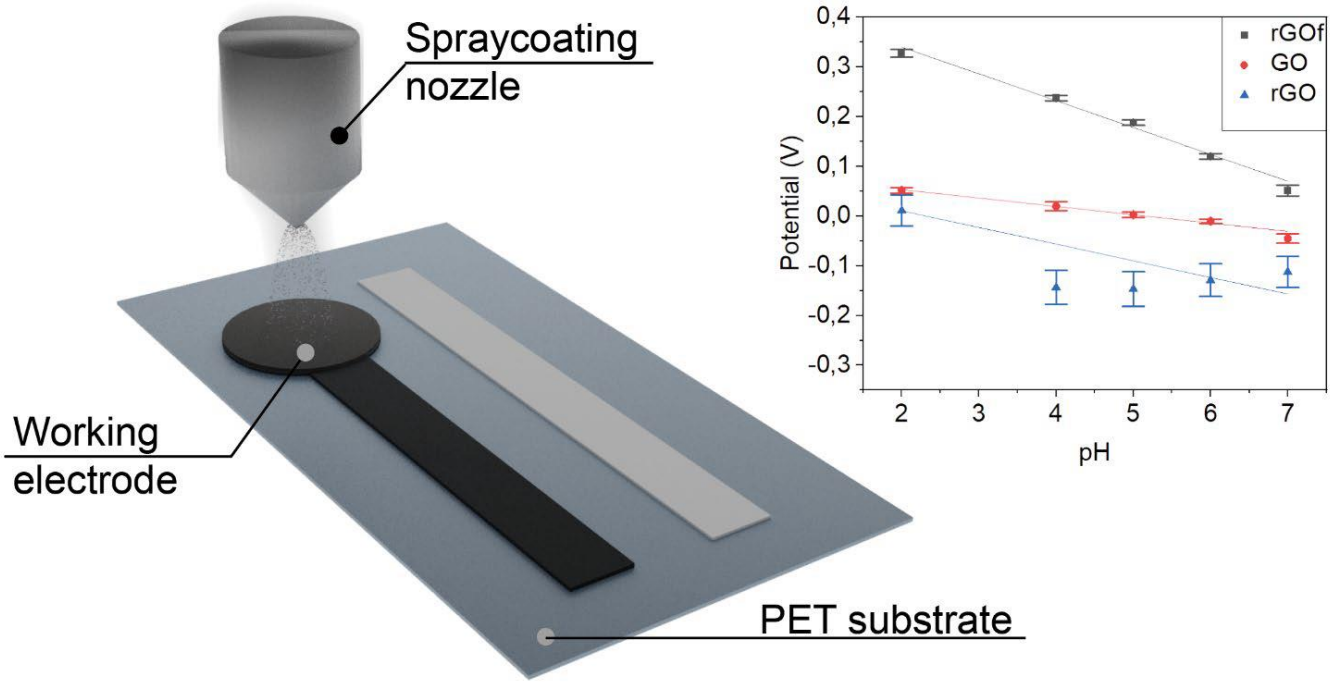


Figure 1. 3D model of spray-coated electrodes system and calibration curves of three working electrodes: rGOf, GO, rGO.

References:
[1] P. Salvo, B. Melai, N. Calisi, C. Paoletti, F. Bellagambi, A. Kirchhain, M.G. Trivella, R. Fuoco, F. Di Francesco, Sensor. Actuat. B-Chem. (2017).

Use and rationalization of machine learning approach for predicting isoform-selective inhibitors of carbonic anhydrase enzyme

SALVATORE GALATI[1,2], DIMITAR YONCHEV[1], RAQUEL RODRÍGUEZ-PÉREZ[1,3], MARTIN VOGT1, TIZIANO TUCCINARDI[2], AND JÜRGEN BAJORATH[1]

[1]Department of Life Science Informatics, B-IT, LIMES Program Unit Chemical Biology and Medicinal Chemistry, Rheinische Friedrich-Wilhelms-Universität, Endenicher Allee 19c, D-53115 Bonn, Germany.
[2]Department of Pharmacy, University of Pisa, 56126 Pisa, Italy.
[3]Present address: Novartis Institutes for Biomedical Research, Novartis Campus, CH-4002
salvatore.galati@phd.unipi.it

The metalloenzyme carbonic anhydrase (CAs) catalyzes a very simple but essential physiological reaction, carbon dioxide hydration to bicarbonate and protons and are among the most intensely studied enzymes as pharmaceutical targets. Many of human (h) CA isoforms involved in these processes are important therapeutic targets with the potential to be inhibited to treat a wide range of diseases. A peculiarity of carbonic anhydrase inhibition is the interaction of the ligands with the zinc cation present in the catalytic pocket of the enzyme. Given the conserved catalytic mechanisms and the high structural similarity shared by many hCA isoforms, a major challenge for allowing a CA-targeted therapy is the discovery of selective inhibitors. Of particular interest are inhibitors endowed with selectivity for hCA isoforms involved in specific pathologies over widely distributed isoforms, such as hCAI or hCAII, that are essential for many physiological processes.
To address this challenge, we have attempted to predict compounds that are selective for isoform hCAIX (a tumor-associated protein) over hCAII (ubiquitously expressed), on the basis of a carefully curated data set of selective and non-selective inhibitors. Using a machine learning approach, we obtained very high accurate predictions for hCAIX-selective inhibitors. The results were further investigated leading to the identification of structural features crucial for the accurate predictions.
These features were then studied based on the available X-ray structures of hCAs-inhibitor complexes to identify substructures responsive to the isoforms-selectivity of the predicted inhibitors. Our results confirmed the reliability of selectivity predictions and allowed interpretation of black box character results provided by machine learning approaches. Furthermore, the machine learning models developed here have considerable potential to aid in the identification of novel hCAIX-selective compounds.

References:
[1] A. Angeli, F. Carta, C. T. Supuran. Carbonic Anhydrases: Versatile and Useful Biocatalysts in Chemistry and Biochemistry. *Catalysts*, 10, 1008 (2020).
[2] C. B. Mishra, M. Tiwari, C. T. Supuran. Progress in the Development of Human Carbonic Anhydrase Inhibitors and Their Pharmacological Applications: Where Are We Today? *Med. Res. Rev.*, 40, 2485–2565 (2020).
[3] A. Nocentini, C. T. Supuran. Carbonic Anhydrase Inhibitors as Antitumor/Antimetastatic Agents: A Patent Review (2008-2018). *Expert Opin. Ther. Pat.*, 28, 729–740 (2018).

Gold-based cytotoxic complexes for targeted anticancer Treatments

E. GIORGI[1], A. PRATESI[1], C. GABBIANI[1]

[1]*Department of Chemistry and Industrial Chemistry (DCCI), University of Pisa, Via Giuseppe Moruzzi 13, 56124 Pisa, Italy*
ester.giorgi@phd.unipi.it

Although chrysotherapy has ancient origins, gold compounds have had limited clinical use in modern medicine, especially confined to the treatment of severe rheumatoid arthritis. The most known gold-based antarthritic compound is Auranofin which, in the last two decades, has attracted much interest for its promising antiproliferative properties, becoming an attractive candidate to be "repurposed" as a potential anticancer drug.[1] Auranofin causes induction of apoptosis in cancer cells mainly through the inhibition of mitochondrial thioredoxin reductase TrxR, a flavoenzyme involved in cellular redox homeostasis. In cancer cells, TrxR overexpression plays a key role in mitochondrial metabolism deregulation and apoptosis evasion, thus representing an interesting druggable target for new gold-based anticancer compounds.[2] As a result, the studies on the antiproliferative properties of Auranofin opened a new interesting research field on Au(I) complexes as prospective anticancer compounds.[3] In this project, we propose the synthesis of new cytotoxic gold-based complexes with cytotoxic properties, investigating also their biological activity on selected cancer cell lines. The gold complexes will be constituted by several elements: a Nheterocyclic carbene moiety, that provides stable gold-carbene coordination, an anthracenyl residue, as a fluorescent label, and eventually an amino-linker for the anchorage of the metal complex on other bioactive molecules. In fact, the new Au-complexes will be functionalized and delivered according to two different targeting strategies. The first approach consists of a mitochondrial-targeting strategy, through an appropriate functionalization of Au-compounds with peptoids[4] (**Figure 1a**), that can be easily accumulated inside mitochondria. Among mitochondria specific targeting molecules that could be linked to the Au complexes, peptoids present several advantages: resistance to proteolysis and consequently higher bioavailability, non-immunogenicit and simple synthetic route. The second approach concerns functionalization with peptides,[5] according to a cancer cell targeting strategy. In fact, it would be interesting to consider the use of a specific peptide[5] (**Figure 1b**) able to specifically recognize integrin receptors, usually overexpressed on the ovarian cancer cell surface. The selective interaction between the peptide and the integrin receptors may lead to selective uptake of gold compounds, with potentially higher anticancer efficacy and fewer side effects.

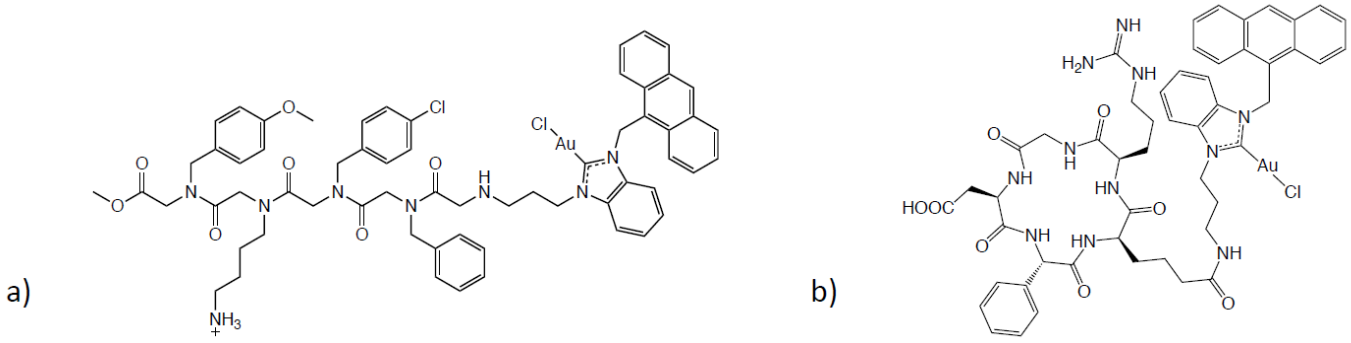


Figure 1. Examples of a gold complex coupled with peptoid (a) and peptide (b) as selective carriers.

References:
[1] C. Roder, M.J.Thomson, *Drug in R&D,* 15, 13-20 (2015).
[2] V. Scalcon, et al., *Free Radic. Biol. Med.,* 127, 62-79 (2018).
[3] S.J. Berners-Price, A. Filiposka, *Metallomics,*3, 863-873 (2011).
[4] D. K. Kolmel et al., *Pharmaceuticals*, 5, 1265-1281, (2012).
[5] A. Dal Pozzo et al., *Bioorg. Med. Chem.*, 18, 64-72 (2010).

Straightforward Synthesis of a New Family of Robust and Easily Functionalizable Ruthenium(II)-Tris(pyrazolyl)methane Complexes

A. GOBBO[1], L. BIANCALANA[1], M. GUELFI[1], F. MARCHETTI[1], G. PAMPALONI[1]

[1]Dipartimento di Chimica e Chimica Industriale, Università di Pisa, Via Moruzzi 13, 56124 Pisa (Italy)
alberto.gobbo@phd.unipi.it

Ruthenium(II) complexes containing a η^6-arene ligand have aroused a huge interest for their medicinal and catalytic potential.[1] On the other hand, the chemistry of analogous compounds with tris(pyrazolyl)methane (tpm), i.e. a tridentate ligand which is expected to provide considerable stability to the structure, has been limitedly investigated heretofore.[2] The available synthetic routes to this type of compounds present important limitations in terms of yield, products purity, challenging work-up and limited number of accessible structures.

In this work, a straightforward method to access a variety of novel ruthenium(II)-tpm complexes was developed. The synthesis of the key precursor $[RuCl(tpm)(PPh_3)_2]Cl$ was improved with respect to the literature, and then optimized for gram-scale preparations. Using this complex as starting material, a variety of neutral ligands such as pyridines, phosphines/phosphites, nitriles and isocyanides can be easily incorporated within the Ru-tpm scaffold with hight yields (Figure 1).

Moreover, facile esterification of coordinated 4-pyridinemethanol allowed to tether different bioactive fragments to the complexes, in view of possible biological applications. Using this approach, complexes were obtained functionalized with ethacrynic acid (a glutathione S-transferase inhibitor), chlorambucil (chemotherapy medication) and NSAIDs (cyclooxygenase inhibitors).

Most of the metal products display an appreciable water solubility. The stability was investigated by NMR in aqueous and cell culture solutions, revealing a substantial robustness of the structure except for slow, reversible chloride/water substitution. The octanol/H_2O partition coefficients were assessed by UV-Vis technique. Catalytic and biological studies on the new complexes are in course.

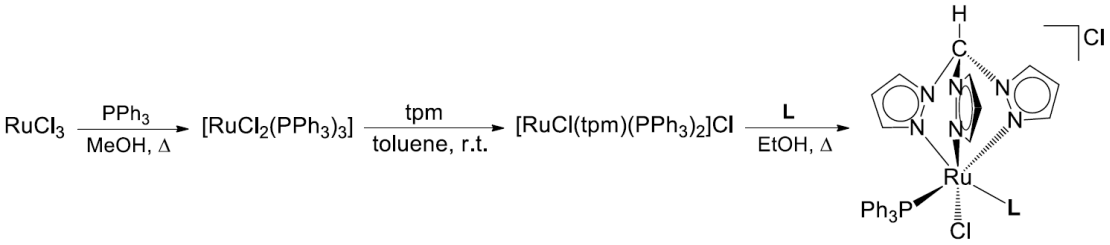


Figure 1. Ruthenium(II)-tpm complexes accessible from optimized synthetic strategies (**L** = pyridines, phosphines/phosphites, nitriles, isocyanides and functionalized 4-pyridinemethanol ligands).

References:

[1] See for instance: (a) A. A. Nazarov, C. G. Hartinger, P. J. J. Dyson, *Organomet. Chem.*, 751, 251 (2014). (b) B. Li, P. H. Dixneuf, *Ruthenium in Catalysis*, 48 (2014).

[2] (a) A. Llobet, P. Doppelt, T. J. Meyer, *Inorg. Chem.*, 27, 514 (1988). (b) M. Fajardo, A. de la Hoz, E. Diez- Barra, F. A. Jalón, A. Otero, A. Rodriguez, J. Tejeda, D. Belletti, M. Lanfranchi, M. A. J. Pellinghelli, *Chem. Soc. Dalton Trans.*, 1, 1935 (1993).

Understanding the single-chain folding and temperature-responsive self-assembly of amphiphilic random copolymers in solution

E. GUAZZELLI[1], E. MASOTTI[1], F. DOMENICI[2], S. GABRIELLI[2], G. PARADOSSI[2], M.T.F. TELLING[3], N. MAHMOUDI[3], F. UHLIG[4], M. KRIECHABAUM[4], G. GALLI[1], E. MARTINELLI[1]

[1]*DCCI, University of Pisa, IT*
[2]*DCST, University of Rome Tor Vergata, IT*
[3]*STFC Rutherford Appleton Laboratory, Chilton, UK,*
[4]*IIC,Graz University of Technology, AT*
elisa.guazzelli@dcci.unipi.it

The concept behind the fast developing field of single-chain nanoparticles (SCNPs) is inspired by the precise and efficient folding of natural macromolecules, that can provide complex functions related to their three-dimensional arrangement.[1] The self-assembly of neutral amphiphilic random copolymers consisting of hydrophilic poly(ethylene glycol) methacrylate and hydrophobic (meth)acrylates is considered one straightforward approach to generate dynamic, stimulus-responsive SCNPs in water, via hydrophobic intramolecular interactions.[2,3] These special SCNPs are generally referred to as unimer micelles, in analogy with the intermolecular micelles formed by common amphiphiles.
The self-assembling behaviour of amphiphilic methacrylic random copolymers with perfluorohexyl and oligo(oxyethylene) side chains was investigated. Dynamic light scattering (DLS), small-angle neutron scattering (SANS) and small-angle x-ray scattering (SAXS) techniques all served to characterize the self-folded nanostructures and to deepen our understanding of the morphology and size adopted by the copolymers as a result of the self-assembling process. In particular, SAXS analysis proved that the fluorinated copolymers formed small and compact intrachain globular unimers in water. By complete contrast, all samples showed a random coil conformation in organic solution. SANS results allow to clarify the effect of temperature on the self-assembling features and the structural morphology of both unimer single-chain entities and larger multi-chain aggregates. The existence of three distinct phases of self-assembled structures was pointed out as a function of increasing temperature: 1) globular unimers; 2) coexistence of extended unimers and aggregates; and 3) aggregates, which overall showed full reversibility in a wide range of copolymer concentrations (Figure 1).

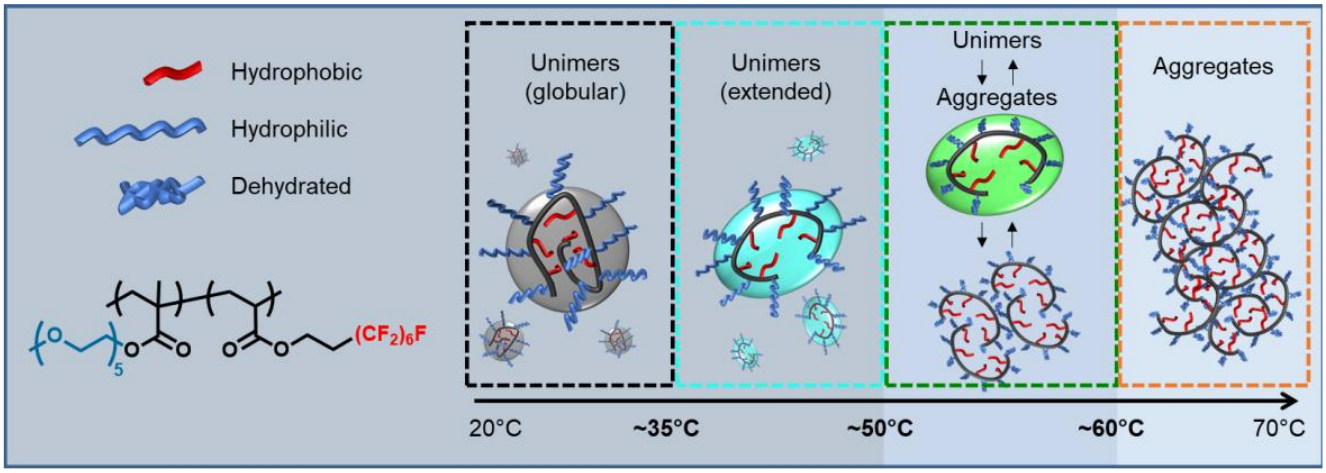


Figure 1. Schematic representation of the self-assembly of amphiphilic fluorinated random copolymers

References:
[1] J.A. Pomposo (Ed.), Single-chain Polymer Nanoparticles: Synthesis, Characterization, Simulations, and Applications, Wiley-VCH, Weinheim, 2017.
[2] F Domenici *et al*., *Macromol Chem Phys* 222 (5), 2000447 (2021)
[3] E Martinelli *et al*., *Macromol Chem Phys* 219 (15), 1800210 (2018)

A real-time, non-destructive and in situ technique for characterizing archaeological artifacts by VOC profiling: Selected Ion Flow Tube-Mass Spectrometry (SIFT-MS)

CAMILLA GUERRINI, JACOPO LA NASA, ILARIA DEGANO, FRANCESCA MODUGNO, ERIKA RIBECHINI, MARIA PERLA COLOMBINI

Department of Chemistry and Industrial Chemistry, University of Pisa, Via G. Moruzzi 13, 56124, Pisa (Italy)
c.guerrini5@studenti.unipi.it

Archaeological artifacts or remains are direct evidence of cultures and practices of the past. Therefore, the chemical investigation of these objects can improve the knowledge of ancient civilizations and their life styles, provide insights into the materials originally used and information beyond the written records. From the chemical point of view, organic residues present in association with cultural heritage objects are complex mixtures of organic natural materials as well as transformation products due both to natural ageing and human interventions.
Because of their intricate composition, the study of organic archaeological residues at a molecular level usually requires sampling and micro-destructive protocols based on separation techniques such as gas-chromatography coupled with mass spectrometry (GC/MS), analytical pyrolysis coupled with GC/MS and liquid chromatography coupled with mass spectrometry (HPLC/MS).
A different approach consists in analysing volatile organic compounds (VOCs), commonly sampled by means of solid phase micro extraction followed by gas chromatography mass spectrometry analysis (SPME-GC/MS).
This work presents a non-destructive approach based on transportable selected ion flow tube-mass spectrometry (SIFT-MS) to profile VOCs in situ. SIFT-MS was applied to characterize and investigate the composition of organic residues by analysing the VOCs released by ancient Egyptian findings belonging to the collection of the Egyptian Museum of Turin (Italy). In particular, the Egyptian Museum gave us the opportunity to analyse *in situ* some objects, as sarcophagi containing animal mummies (fishes and birds), jars and amphorae recovered in the famous tomb of Kha (New Kingdom, XVIII dynasty, 1425– 1353 BC). In this way it has been possible to take advantage of the significant potentialities of SIFT-MS as a fast, non-destructive and non-invasive sensitive technique, applicable *in situ*.
The collected data were elaborated by principal component analysis (PCA) allowing us to highlight differences or similarities among the samples. In the scatter plot there are two distinct groups: one for the mummies and the other for the jars. These promising results prove the suitability of the approach for *in situ* screening of VOCs to guide a theoretical sampling.

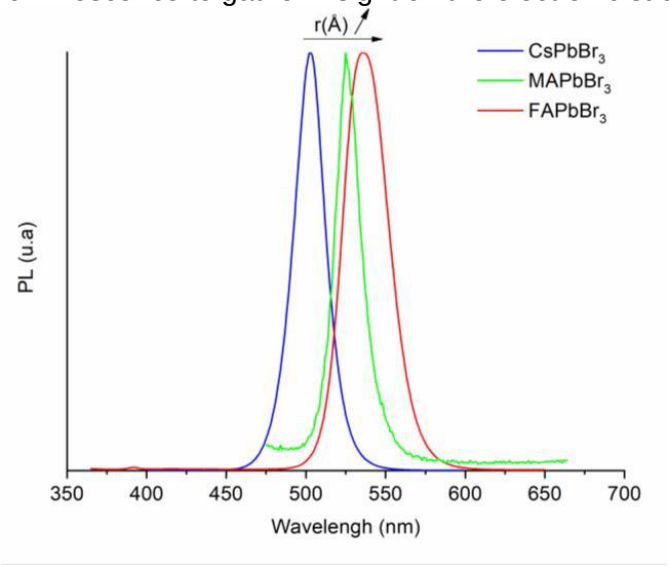
Acknowledgements
The Egyptian Museum is acknowledged for involving us in analysing objects from their collection and the authors are particularly grateful to Valentina Turina, Dr. Federica Facchetti and Dr. Enrico Ferraris for their contribution to the analytical campaign and in the interpretation of the results. SRA Instruments (Italy), and in particular Andrea Carretta, is acknowledged for providing the SIFT-MS instruments in the frame of the POR FSE 2014-2020 Regional Project MS-MOMus “Spettrometria di Massa SIFT portatile e identificazione di Materiali Organici in ambiente Museale”.

Synthesis, optical and structucal properties of lead bromide perovskite nanocubes (NCs) $APbBr_3$ (A: Cs^+, MA^+, FA^+)

N. JARMOUNI[1], M. TOMAIUOLO[2], F. PINEIDER[2]

[1]*LPCM, Faculty of Sciences Ben M'sik, University Hassan II of Casablanca, Morocco*
[2]*Department of Chemistry and Industrial Chemistry, University of Pisa, Italy*
nabilajarmouni@gmail.com

All-inorganic and organic-inorganic lead halide perovskite nanocrystals based on bromide are very promising high-color purity light emitter semiconductors due to their pure green emission and excellent optical properties [1]. In this work, Cesium, methylammonium, and formamidinium lead bromide ($CsPbBr_3$, $CH_3NH_3PbBr_3$, and $CH(NH_2)_2PbBr_3$) perovskite nanocrystals have been synthesized by the hot injection method according to. Imran et al [2] synthesis approach in which the benzoyl bromide was used as halide precursor which was swiftly injected into a solution of desired cations (Cs^+, FA^+, MA^+) with proper ligands at the desired temperature, to provoke the nucleation and the growth of Lead bromide perovskite NCs. By investigating the radius of the A cation (Cs^+= 1.67 Å, MA^+=2.17 Å, FA^+=2.53 Å) in the A-site of the perovskite structure. The resultant inorganic and organic-inorganic lead bromide perovskite $APbBr_3$ colloidal nanocubes with excellent control over the size distribution exhibited very high phase purity, and excellent optical properties such as a high green photoluminescence emission redshift efficiency, and narrow full width at half-maximum. These synthesis $APbBr_3$ perovskite NCs will be incorporated in solar concentrator devices and studied with magnetic circular dichroism and magnetic circularly polarized luminescence to gather insight on the electronic structure of their ground and excited states.



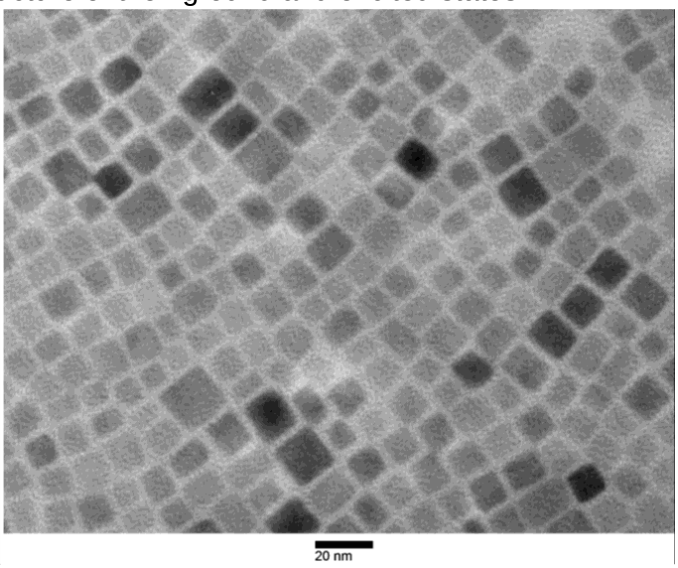


Figure 1. PL spectra for $FAPbBr_3$ NCs showing the red-shift of the emission peak with increasing the radius of the A cation, and TEM images of $CsPbBr_3$ NCs with an average size of ~ 12 nm.

References:
[1] Kulkarni, Sneha A., et al. Small Methods 3.1 (2019): 1800231.
[2] Imran, Muhammad, et al. Journal of the American Chemical Society 140.7 (2018): 2656-2664.

Solid-State NMR study of a multiple-cation lead mixed-halide perovskite with high efficiency

N. LANDI[1], E. MAURINA[1], E. CARIGNANI[2], S. BORSACCHI[2,3], L. CALUCCI[2,3], D. MARONGIU[4], M. SABA[4], M. GEPPI1,[2,3]

[1]Department of Chemistry and Industrial Chemistry, University of Pisa, via G. Moruzzi 13, 56124 Pisa, Italy;
[2]Institute for the Chemistry of OrganoMetallic Compounds, Italian National Council for Research, CNR/ICCOM, via G. Moruzzi 1, 56124 Pisa, Italy;
[3]Center for Instrument Sharing, University of Pisa (CISUP), 56126 Pisa, Italy;
[4]Department of Physics, University of Cagliari, S.P. Monserrato-Sestu Km. 0700, Monserrato, 09042 CA, Italy.
noemi.landi@phd.unipi.it

Hybrid organic-inorganic metal-halide perovskites have emerged as highly interesting materials for various applications, such as thin-film photovoltaics or light-emitting devices, due to their outstanding optoelectronics properties. A main advantage of these materials is their tunability. Their macroscopic properties are intrinsically related to their microscopic features (*i.e.* atomic and molecular organization and dynamics), so mixtures of different cations and anions can be used to tune the optoelectronic properties and to enhance efficiencies and stabilities.
Their promising properties have brought about an increased effort in the research of these materials. Starting from methylammonium lead iodide ($MAPbI_3$), the archetypical hybrid halide perovskite material, several variations to the hybrid perovskite structure have been tested. In particular, the use of mixed-ion structures, in which the compositional complexity is increased by introducing dopants into the perovskite structure, has resulted in a remarkable improvement in perovskite solar cell performance. Thus, since their first use as sensitizers for solar cells in 2009 [1], perovskite solar cells have developed rapidly, achieving high power conversion efficiencies (well above 20%) and improved stability. Some of the latest top efficiencies have been reached by multiple-cation lead mixed-halide perovskites (Cs,FA,MA)Pb(I,Br)3 [2][3][4].
However, the role of the dopants and additives in the high performance of the perovskite solar cells has not been fully understood yet, and its transferability to other perovskites is not straightforward.
For this reason, it is important to be able to gain atomic-level understanding of these materials.
Solid-State NMR (SSNMR) spectroscopy is strongly sensitive to the local chemical environment, and as such, it proved to be a perfectly suited technique to investigate mixed perovskites.
In this study, we focused on the perovskite with formula $Cs_{0.05}FA_{0.81}MA_{0.14}PbI_{2.55}Br_{0.45}$ because of its high performance. We investigated it by means of SSNMR for the first time, with MAPbI3 being used a reference compound. ^{207}Pb, ^{13}C and ^{1}H high-resolution SSNMR experiments allowed us to characterize the structure and composition of the samples, highlighting phase homogeneity and/or segregation, and to investigate ion dynamics by exploiting both spectral and relaxation properties.

References:

[1] A. Kojima, K. Teshima, Y. Shirai, T. Miyasaka, *J. Am. Chem. Soc*., 131, 6050-6051 (2009).
[2] M. Saliba, T. Matsui, J.-Y. Seo, K. Domanski, J.-P. Correa-Baena, M. K. Nazeeruddin, S. M. Zakeeruddin, W. Tress, A. Abate, A. Hagfeldtd, M. Grätzel, *Energy Environ. Sci*., 9, 1989–1997 (2016).
[3] Y. Sun, J. Peng, Y. Chen, Y. Yao, Z. Liang, *Sci. Rep.*, 7, 46193 (2017).
[4] T. J. Jacobsson, S. Svanström, V. Andrei, J. P. H. Rivett, N. Kornienko, B. Philippe, U. B. Cappel, H. Rensmo, F. Deschler, G. Boschloo1, *J. Phys. Chem. C*., 122, 25, 13548–13557 (2018).

Determination of salivary short chain fatty acids and hydroxy acids in heart failure patients by in-situ derivatization and HiSorb-probe sorptive extraction coupled to thermal desorption and gas chromatography-tandem mass spectrometry

A. LENZI[1], D. BIAGINI[1], S. GHIMENTI[1], F. VIVALDI[1], A. BONINI[1], P. SALVO[2], R. FUOCO[1], F. DI FRANCESCO[1] AND T. LOMONACO[1]

[1]*Department of Chemistry and Industrial Chemistry, University of Pisa, Via G. Moruzzi 13, Pisa, Italy*
[2]*Institute of Clinical Physiology, CNR, Via G. Moruzzi 3, Pisa, Italy*
alessio.lenzi@phd.unipi.it

Short chain fatty acids (SCFAs) are the predominant products of dietary fiber fermentation operated by gut microbiota. Their variation in human can emphasize the predisposition to metabolic diseases. Studies have also highlighted their implication in the regulation of blood pressure, and in the increased risk of Heart Failure (HF) [1]. On the other hand, compounds unrelated to microbiota activity, such as 3-hydroxybutyric acid and lactic acid, are used as energy sources during acute energies crisis. In the last few years, a link between oral and gut microbiomes was underlined. Differences in the oral metabolome, as for example in the SCFAs family of compounds, are known to be correlated to the health of salivary microbiome, which is also related to the development of a low-grade inflammation in the host, and consequently to potential increasing risks of cardiovascular diseases [2].

The aim of this work was to develop and validate an analytical procedure based on an innovative single step in-situ derivatization with pentafluorobenzyl bromide (PFB-Br) and HiSorb-probe sorptive extraction for the determination of a panel of low-molecular weight salivary metabolites (SCFAs, 3-hydroxybutyric acid, and lactic acid). Reaction's derivatives released from HiSorb probe by thermal desorption were analyzed by gas chromatography-tandem mass spectrometry. A Central Composite Face-Centered experimental design was used for the optimization of the molar ratio between PFB-Br and target analytes, the derivatization temperature and time which resulted respectively 100, 60 °C and 180 min. A sample volume of 20 µL of saliva guaranteed limits of detection between 0.1-100 µM. Intra- and inter-day precision and recovery were in the range of 10-15% and 70-98%, respectively, thus highlighting the reliability of the method.

The validated method was employed as a proof-of-concept method to monitor and compare SCFAs and hydroxy acids collected from saliva of 13 HF patients during hospitalization, with the aim to preliminary evaluate the role of these compounds as potential salivary indicators of the course/progression of the disease.

References:

[1] L.B. Richards, M. Li, B.C.A.M. van Esch, J. Garssen, G. Folkerts, *PharmaNutrition*, 4, 68-111 (2016).
[2] M. Pietiäinen, J.M. Liljestrand, E. Kopra, P.J. Pussinen, *Eur. J. Oral Sci.*, 126, 26-36 (2018).

Sustainable *n*-butyl levulinate production from raw and waste biomass

R. LORÈ, C. ANTONETTI, D. LICURSI, M. MARTINELLI, A. M. RASPOLLI GALLETTI

Dipartimento di Chimica e Chimica Industriale, Università di Pisa
r.lore@studenti.unipi.it

Alkyl levulinates (ALs) are biobased chemicals having a strong potential to be used in various applications[1], in place of traditional petrochemicals. The choice of this class of levulinic acid derivatives as starting feedstocks to further up-grade is very attractive, due to the moderate reactivity of their ester groups, leading to remarkable advantages in selectivity towards the final desired product(s), as occurs for ketals[2], alkoxypentanoates, γ-valerolactone, 2-methyltetrahydrofuran, valeric acid/alkyl valerates,1,4-pentanediol, and N-substituted pyrrolidinones, which are preferably produced from ALs, rather than free levulinic acid.
As an additional noteworthy advantage, esters have lower boiling points than the corresponding carboxylic acids, thus allowing an easier and cheaper separation/purification by distillation[3].
The use of these bio-products as bio-fuels has been proposed in the past, but low-chain ALs suffer from some limitations, including high oxygen content, good water solubility, and low energy density. Longer-chain ALs are certainly more appropriate for diesel-fuel blends and the real development of high-volume fuel applications and, in this context, BL has recently aroused greater interest when blended with diesel or biodiesel[4], allowing for cleaner combustion, mainly in terms of low CO and soot emissions.
Regarding the possible ALs synthetic strategies, the direct one-pot alcoholysis[5] of real biomasses represents a promising greener and sustainable approach for the industrial production of ALs. To promote the market for these bio-products and, concurrently, the immediate development of new applications, it is necessary to speed up the intensification of their production processes. In this perspective, the choice of the appropriate starting feedstock is fundamental and strategic for improving the growth of the alcoholysis process.
The present investigation represents a concrete valorization of various feedstocks having low or negative value (such as defatted cardoon, giant reed, pomace, and paper mill wastes), employing *n*-butanol as the green reagent/reaction medium, very dilute sulfuric acid as the homogeneous catalyst, and different heating systems. Optimization of the reaction conditions has been carried out on different raw materials and compared with the results obtained on a model microcrystalline cellulose (MCC). Under the optimized reaction conditions, starting from the above raw or waste biomasses, maximum yields of about 40 mol %, evaluated respect to the units of glucose in the starting materials, were reached. Remarkably, these results were analogous to those obtained under the same reaction conditions in the butanolysis of a pure valuable substrate as MCC. Lastly, a characterization of the recovered residues has been realized, to propose their exploitation in the context of a more sustainable and integrated process, in agreement with the principles of the circular bio-economy.

References:

[1] A. Démolis, N. Essayem, F. Rataboul, *ACS Sustainable Chem. Eng*., 2, 1338−1352 (2014).
[2] F. A. Freitas, D. Licursi, E. R. Lachter, A. M. Raspolli Galletti, C. Antonetti, T. C. Brito, R. S. V.Nascimento, *Catal. Commun*., 73, 84–87 (2016).
[3] J. C. van der Waal, E. de Jong, *Industrial Biorenewables: A Practital Viewpoint*; de María, P.D., Ed.; John Wiley & Sons: Hoboken, NJ, USA, pp. 97–120 (2006).
[4] S. Frigo, G. Pasini, G. Caposciutti, M. Antonelli, A. M. Raspolli Galletti, S. Gori, R. Costi, L. Arnone, *Fuel,* 297, art. no. 120742 (2021)
[5] A. M. Raspolli Galletti, C. Antonetti, S. Fulignati, D. Licursi, *Catalysts*,10, 1221 (2020).

Activatable Pt(IV) compounds as potential anticancer prodrugs

C. MAROTTA[1], D. CIRRI[1], A. PRATESI[1], C. GABBIANI[1]

[1]*Department of Chemistry and Industrial Chemistry, University of Pisa, via Moruzzi 13, 56124 Pisa, Italy*
carlo.marotta@phd.unipi.it

Cisplatin and its derivatives are anticancer drugs currently used in therapy whose commonly accepted mechanism of action mainly consists in the binding to the DNA. However, despite their efficacy, they show several side effects. On the other hand, Pt(IV) complexes are kinetically more inert than their Pt(II) counterparts, and thus less toxic.[1] These complexes act as prodrugs that can be activated inside the cancer cells through reduction, thus releasing the Pt(II) drug and the two axial ligands.[2] The Pt(II) species are responsible for the cytotoxicity but the introduction of bioactive axial ligands might further improve the pharmacological properties of these molecules.[3]
In this frame, we proposed new promising Pt(IV) complexes bearing Doxycycline and α-tocopherol succinate (α-TOS) as axial ligands. α-TOS is an analogue of Vitamin E which was proved to be cytotoxic in many different cancer cell lines by targeting mitochondria.[4] Doxycycline is an antibiotic that showed the ability to decrease the content of cancer stem cells (CSCs) in breast cancer patients and to inhibit their propagation in several other cancer cell lines (ovarian, prostate, pancreatic, and lung carcinoma, melanoma and glioblastoma). Since CSCs promote tumour initiation, recurrence, metastatic spread and poor survival in many different tumour types, their targeting could lead to beneficial therapeutic effects. Moreover, a complex bearing both Doxycycline and α-TOS as axial ligands could show a synergistic effect, since both these drugs are able to target mitochondria.

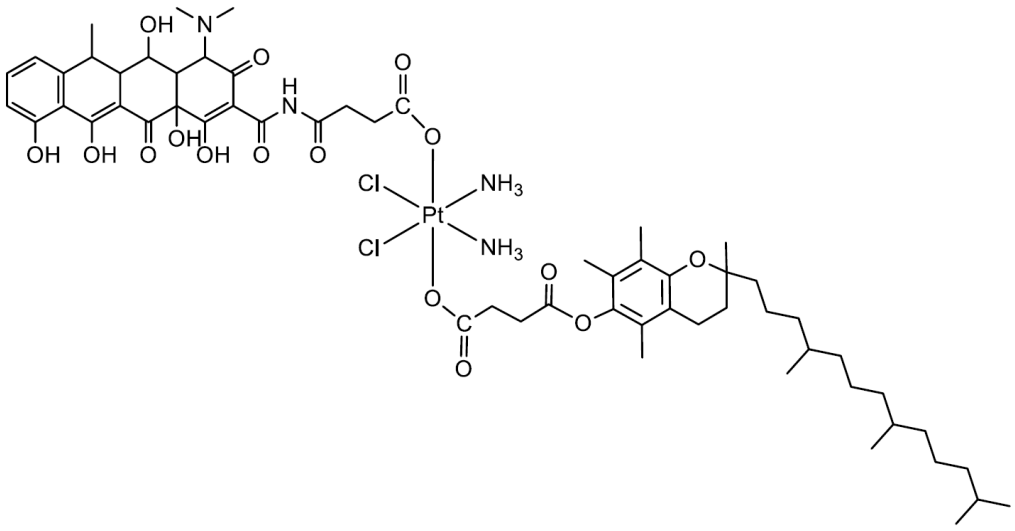


Figure 1. Pt(IV) complex based on Cisplatin with Doxycycline and α-TOS as axial ligands

References:
[1] W. Roy Mason, *Coord. Chem. Rev.*, 7, 241 (1972).
[2] E. Petruzzella et al., *Chem. Sci.*, 9, 4299–4307 (2018).
[3] T.C. Johnstone et al., *Inorg. Chem.*, 52, 21 (2013).
[4] K. Suntharalingam, Y. Song, S. J. Lippard, *Chem. Commun.*, 50, 2465–2468 (2014).

Modelling and optimization of an extraction procedure for lignin using deep eutectic solvents and microwave heating

M. MATTONAI[1], F. NARDELLA[1], E. RIBECHINI[1]

[1]*Department of Chemistry and Industrial Chemistry, University of Pisa*
Via G. Moruzzi 13, 56124 Pisa (IT)
marco.mattonai@dcci.unipi.it

Deep eutectic solvents (DES) are innovative solvents with promising lignin solvation capability. DESs have a low environmental impact, and their physico-chemical properties can be finely tuned by changing their composition [1,2]. Optimization of lignin extraction procedures using DESs is still an open challenge, and additional research is required to assess how the different experimental parameters can influence the extraction yield.

Here, we prepared four different DESs using choline chloride and light carboxylic acids (formic, lactic, acetic, propionic) and tested their suitability to extract lignin from a softwood (fir) under different conditions. A microwave oven was used to ensure an efficient and fast heating of the sample. The extracts were characterized by evolved gas analysis-mass spectrometry (EGA-MS) and analytical pyrolysis-gas chromatography coupled to mass spectrometry (Py-GC/MS) to evaluate their thermal behaviour and the presence of impurities.

Py-GC/MS analysis showed that the mixture of choline chloride and formic acid provided the highest purity of extracted lignin (Figure 1). We optimized the extraction yield of this DES using a Box-Behnken experimental design with three factors: microwave temperature, DES/wood mass ratio, and formic acid/choline chloride molar ratio. The extraction yield increased steadily when both temperature and DES/wood mass ratio increased, and when the amount of formic acid in the DES decreased. EGA-MS analyses showed slight variations in the thermal stability of extracted lignins as a function of the experimental conditions. Once optimized, the method was also tested on a hardwood (oak) and an herbaceous plant (elephant grass).

The results of this work show the interesting potential of microwave-assisted DES extraction of lignin, and how EGA-MS and Py-GC/MS can provide fundamental information on the properties of the extracts.

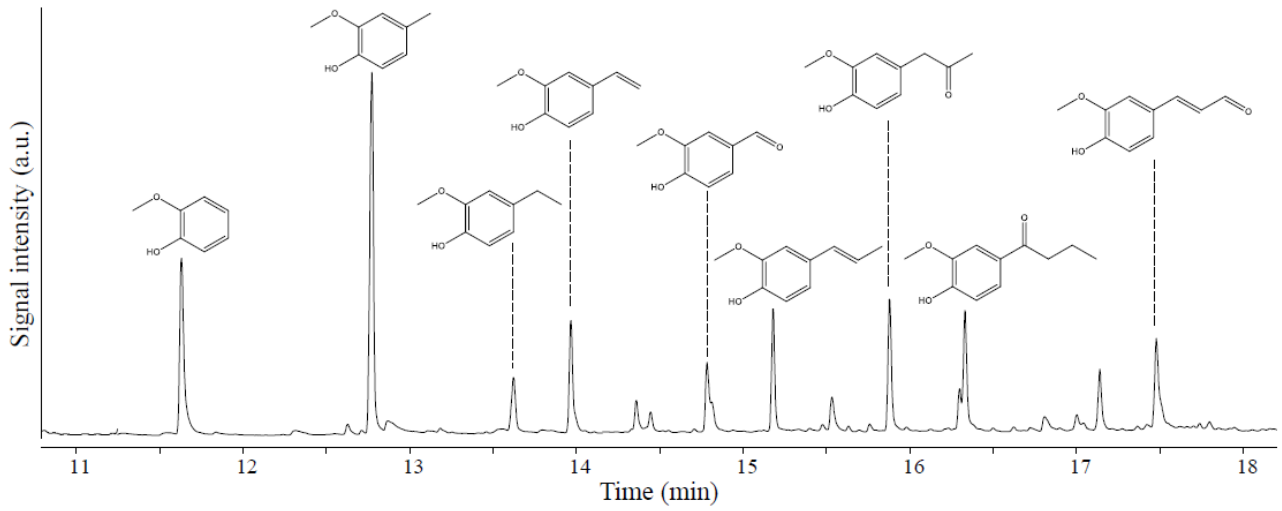


Figure 1. Py-GC/MS profile of lignin extracted using choline chloride and formic acid.

References:
[1] Z. Chen, A. Ragauskas, C. Wan, *Industrial Crops & Products*, 147, 112241-112248 (2020).
[2] H. Xu, J. Peng, Y. Kong, Y. Liu, Z. Su, B. Li, X. Song, S. Liu, W. Tian, *Bioresource Technology*, 310, 123416-123429 (2020).

P28

2D Ruddlesden-Popper Perovskites $BA_2MA_{n-1}Pb_nI_{3n+1}$ as studied by Solid-State NMR Spectroscopy

ELENA MAURINA [1,2], NOEMI LANDI [1], ELISA CARIGNANI [3], SILVIA BORSACCHI [3,4], LUCIA CALUCCI, [3,4] DANIELA MARONGIU [5], MICHELE SABA[5], MARCO GEPPI [1,3,4]

[1]Department of Chemistry and Industrial Chemistry, University of Pisa, via G. Moruzzi 13, 56124 Pisa, Italy;
[2]Scuola Normale Superiore, Piazza dei Cavalieri, 7, 56126 Pisa, Italy
[3] Institute for the Chemistry of OrganoMetallic Compounds, Italian National Council for Research, CNR/ICCOM, via G. Moruzzi 1, 56124 Pisa, Italy;
[4]Center for Instrument Sharing, University of Pisa (CISUP), 56126 Pisa, Italy
[5]Department of Physics, University of Cagliari, S.P. Monserrato-Sestu Km. 0700, Monserrato, 09042 CA, Italy
e.maurina@studenti.unipi.it

Lead Halide Perovskites are interesting semiconductors used in different optoelectronic devices (e.g. sensitizers for solar cells, photodetectors, LEDs). Recently, 2D analogues of Hybrid Lead Halide Perovskites (HLHP) have attracted considerable attention because they offer the possibility of tunable band gap and enhanced environmental stability with respect to the corresponding 3D systems. 2D Ruddlesden–Popper (RP) perovskites can be prepared by adding a large organic mono ammonium cation L^+ in the precursor solution. In this way the 3D structure of corner-sharing octahedra (ABX_3) is disrupted and a structure with a bilayer of spacer cations between metal halide sheets is formed ($L_2A_{n-1}B_nX_{3n+1}$). For example, butylammonium (BA) is a suitable organic cation to force the archetypical perovskite $MAPbI_3$ into 2D RP perovskites $BA_2MA_{n-1}Pb_nI_{3n+1}$ (Figure 1), which are the object of the present study. The layer thickness of metal halide sheets is specified by n and can be adjusted by tuning precursor stoichiometry. Solid-State NMR stands out as characterization technique for HLHP for its ability to study ion dynamics, compositional variations and ion incorporation, chemical interactions and degradation mechanisms [1,2]. In this work, the 2D RP perovskites $BA_2MA_{n-1}Pb_nI_{3n+1}$ with n=1, 2, 3 have been characterized by Solid-State NMR and compared with 3D $MAPbI_3$ as a reference compound. The structural features of these systems have been investigated by ^{207}Pb, ^{1}H, and ^{13}C spectra recorded under Magic Angle Spinning and static conditions; the obtained results have been discussed also by comparison with very recent literature [3]. In addition, the variable temperature measurement of ^{13}C and ^{1}H spin-lattice relaxation times (T_1) allowed dynamic properties of the organic cations in the series of samples to be investigated.

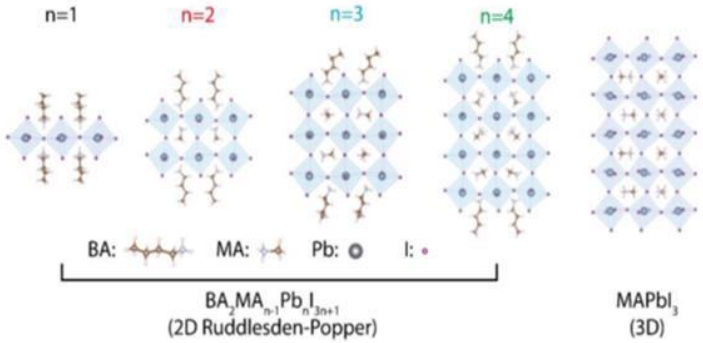


Figure 1. Schematic structure of 2D RP perovskites $BA_2MA_{n-1}Pb_nI_{3n+1}$ for n=1, 2, 3, 4, and of the corresponding 3D perovskites $MAPbI_3$.

References:

[1] W. M. J. Franssen, A. P. M. Kentgens, *Solid State Nucl. Magn. Reson*. **2019**, 100, 36-44.
[2] L. Piveteau, V. Morad, M. V. Kovalenko, J. Am. Chem. Soc.. **2020**, *142* (46), 19413-19437
[3] J. Lee, W. Lee, K. Kang, T. Lee, S. K. Lee, *Chem. Mater*. **2021**, *33*, 370-377.

Donors, acceptors and a bit of aromatic: A computational study of molecule-surface interactions onto 2D hexagonal boron nitride towards photo-active interfaces

GIACOMO MELANI[1], ANA M. VALENCIA[2], CATERINA COCCHI[2], MARCELLA IANNUZZI[1]

[1]*Department of Chemistry, Universität Zürich, CH*
[2]*Institute of Physics, Carl-von-Ossietzky Universität Oldenburg, DE*
giacomo.melani@chem.uzh.ch

Light-induced processes at the nanoscale have rapidly become of fundamental importance for many technological applications in the field of photonics, opto-electronics, and materials science. Moreover, in the past few years, the quest for innovative photochromic and opto-electronic devices has been further advanced thanks to the discovery of two-dimensional materials, among all graphene [1]. The potential employment of 2D materials in hybrid interfaces is extremely promising not only for their relatively easy preparation but also for their intriguing surface specific physical properties [2]. Furthermore, recently complex, hierarchical structures, also referred to as “hybrid organic / inorganic materials” have been engineered, which reveals a multitude of diverse physical features emerging from this complexity [3]. Due to their intrinsic structural and electronic characteristics, 2D materials like graphene or hexagonal boron nitride (hBN) nanosheets can be stacked on top of each other, held together mainly by van der Waals dispersion forces [4]. In this study we investigate using periodic Density Functional Theory calculations the electronic properties of hybrid interfaces composed by a free-standing monolayer of hBN and prototypical organic chromophores. These compounds are adsorbed onto the BN-surface through non-covalent interactions due to the known inertness of this 2D material [5, 6]. Nonetheless, the adsorption of donor-like molecules (bithiophene and tetrathiofulvene, or TTF), acceptor-like (tetracyanoquinodimethane, or TCNQ, and its fluorinated derivative, F4-TCNQ) as well as of a polycyclic aromatic (pyrene) can introduce features of charge transfer and hybridization of electronic levels at the Fermi surface. This study will constitute the basis for further investigations using non-adiabatic molecular simulations (i.e. Real-Time Time-Dependent DFT + Ehrenfest Dynamics and Surface Hopping) to unravel features such as excited-state charge transfer and vibronic coupling at the interface within a time-resolved picture. Such methodology has been already successfully employed to describe the laser induced dynamics of F4-TCNQ onto a semiconducting (silicon) substrate [7].

References:

[1] “Recent advanced in two-dimensional materials beyond graphene”, G. R. Bhimanapati et al., ACS Nano, 9, 11509 (2015).
[2] “Heterostructures based on inorganic and organic van der Waals systems”, G.-H. Lee et al., APL Mater., 2, 092511 (2014).
[3] “When 2D materials meet molecules: Opportunities and challenges of hybrid organic/inorganic van der Waals heterostructures”, M. Gobbi et al., Adv. Mater., 30, 1706103 (2018).
[4] “Synthesis of hexagonal boron nitride heterostructures for 2D van der Waals electronics”, K. K. Kim et al., Chem. Soc. Rev., 47, 6342 (2018).
[5] “Two dimensional hexagonal boron nitride (2D-hBN): Synthesis, properties and applications”, K. Zhang et al., J. Mater. Chem. C, 5, 11992 (2019).
[6] “Functionalized hexagonal boron nitride nanomaterials: Emerging properties and applications”, Q. Weng et al., Chem. Soc. Rev., 45, 3989 (2016).
[7] “Ultrafast charge transfer and vibronic coupling in a laser-excited hybrid inorganic/organic interface”, M. Jacobs et al., Advances in Physics X, 5, 1, 174988 (2020).

P30

Mechanochromic thermoplastic elastomers doped with pyrene

C. MICHELETTI[1], V. A. DINI[2], D. GENOVESE[2], N. ZACCHERONI[2], C. GUALANDI[2], A. PUCCI[1]

[1]Department of Chemistry and Industrial Chemistry University of Pisa
[2]Department of Chemistry "G. Ciamician", University of Bologna
cosimo.micheletti@phd.unipi.it

Mechanical forces applied to polymeric materials cause the cleavage of covalent bonds and dissociation of non-covalent interactions, leading to the deterioration of the material properties. This degradation could lead to irreparable failure of the material and catastrophic damage. Force and damage detection is essential for either the replacement or reparation of the materials before these bad luck scenarios may occur.
Mechanochromic polymers,1 which change their optical properties (in emission and/or absorption) under mechanical force, have attracted large interest over the last years. Mechanical stimuli applied to polymeric chains are transferred to the covalently attached or physically dispersed mechanophores, thus potentially causing structural variations and triggering photophysical changes clearly visible also without using complex apparatus.
Pyrene chromophore is one of the most exploited aggregachromic probe of external solicitations being capable to form excited state dimers (excimers) in a rigid matrix upon aggregation, that are characterized by clearly different emission features with respect to the monomer.2 Such aggregates can be easily broken by temperature or mechanical stresses. This feature allowed the use of pyrene in combination with polymer matrices for the development of smart chromogenic materials sensitive to mechanical solicitations.3
In this work, the emission properties of pyrene have been investigated when physically dispersed at different contents or covalently linked to a thermoplastic elastomer based on the poly(b-styrene-b-(ethylene-co-butylene)-b-styrene) (SEBS). For the covalent approach, a SEBS copolymer grafted with 0.2 wt.% of succinic anhydride moieties has been employed. The study has initially addressed the characterization of the pyrene-doped matrices in terms of morphology and emission properties of the derived films, to determine the occurrence of the characteristic pyrene excimer band. Then, fluorescence studies (steady-state and time-resolved) under films deformations have been performed to study the mechanochromic response and its reversibility under successive deformation-relaxation cycles, highlighting very relevant differences between the covalent and the physical dispersion approaches.

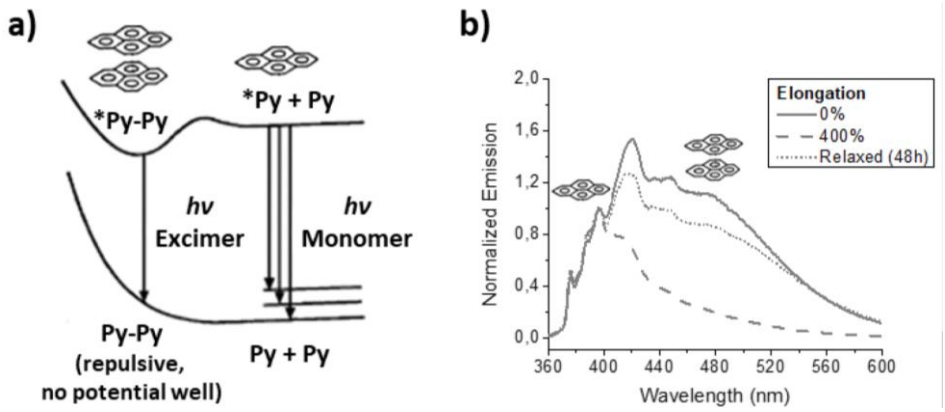


Figure 1. (a) Potential surfaces of the ground and the luminescent excited electronic state of pyrene. (b) Emission of SEBS grafted with pyrene units at different draw ratio.

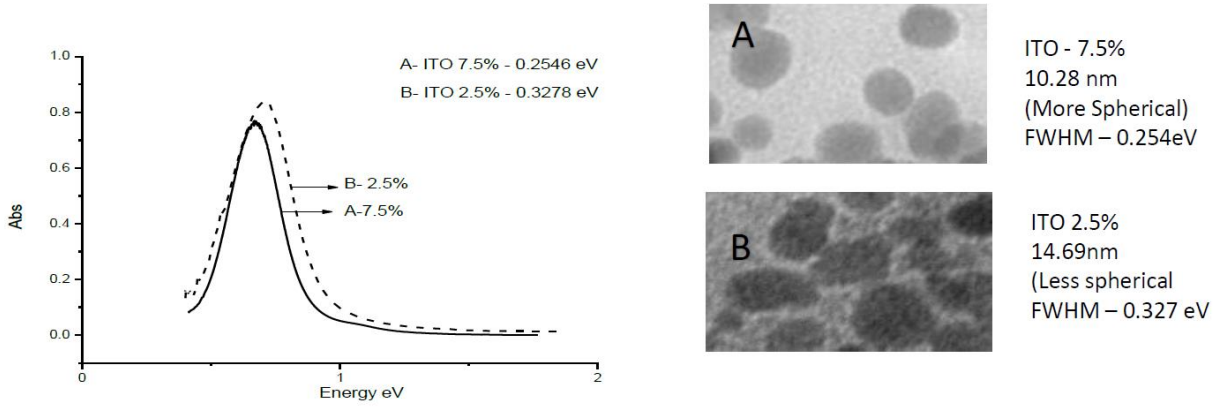
References:
[1] a) A. Pucci, *Sensors*, 19, 4969, (2019); b) F. Ciardelli et al., *Chem. Soc. Rev.*, 42, 857 (2013).
[2] a) C. WU et al., *J. Biomed. Nanotechnol.*, 5, 495, (2009); b) F. M. Winnik, *Chem. Rev.*, 93, 587 (1993).
[3] T. Wang et al., *Macromol. Chem. Phys.*, 221, 1900463, (2020).

Indium Tin Oxide nanocrystals – factors altering the geometry

ANANTHAKRISHNAN MOHAN[1], ALESSIO GABBANI[1,2], FRANCESCO PINEIDER[1]

[1]*University of Pisa, Pisa, Italy*
[2]*CNR-ICCOM, Sesto Fiorentino (FI), Italy*
ananthakrishnan.mohan@phd.unipi.it

Electrical conductivity and optical transparency enable nanocrystals of Indium Tin Oxide (ITO Ncs) to be significant technological materials. They have applications in touch screens and light emitting diodes as a transparent electrode, in smart windows and in solar cells. In nanoscale ITO, the plasmon resonance is confined (Localised surface Plasmon Resonance – LSPR). This property increases the scope of ITO in LSPR-based techniques like refractometric sensing. The ITO NCs are found to be superior in terms of LSPR quality to the conventional plasmonic nanoparticles of Gold and Silver. In magnetoplasmonics, ITO NCs have more significance as they exhibit a much sharper and stronger LSPR in the Infra-Red region, greater magnetic modulation, potential magnetic co-doping, control over the geometry etc. The reported results suggest that the control over geometry of ITO NCs is very important in obtaining a higher quality LSPR response. The sphericity of shape, particle size and crystallinity can alter the LSPR quality which essentially affects the utility of the material in mentioned applications. A broadening of the LSPR absorption signal is observed when the ITO NCs deviate from spherical shape, which is expected to be controlled by altering some parameters. The synthesis used in this preliminary investigation is thermal decomposition of organometallic precursors of Sn and In in a medium of Octadecene with surfactants. The process was developed in our laboratory as a refinement of previously reported synthetic procedures. The factors that alter the particle geometry are nucleation temperature, dopant concentration etc. Dopant percentage and growth temperature are the parameters studied here. The NCs were analysed using powder X-ray diffraction, UV-Vis-IR spectrophotometry (for LSPR), Transmission Electron microscope, and the effectiveness of doping was studied using Inductively coupled plasma -atomic emission spectroscopy.
The size decreases when the doping percentage is larger. The shape appears to be more spherical in doping level 7.5%. The spherical nature is dependent on the doping percentage. The higher temperature tends to lower the particle size slightly. The samples with intermediate intended doping (7.5% - 10%) appear to be having highest achieved doping and sphercity. The results of these analyses can be quite helpful to predict and design an optimized ITO nanocrystal that can produce good LSPR response.



F**igure 1**. The relation between shape (spherical) and the quality of LSPR (FWHM) of two samples of ITO (2.5% &7.5%)

References:

[1] Kanehara, M., Koike, H., Yoshinaga, T., & Teranishi, T. (2009). Indium Tin Oxide Nanoparticles with Compositionally Tunable Surface Plasmon Resonance Frequencies in the Near-IR Region. *Journal of the American Chemical Society*, *131*(49), 17736–17737.
[2] Bühler, G., Thölmann, D., & Feldmann, C. (2007). One-Pot Synthesis of Highly Conductive Indium Tin Oxide Nanocrystals. *Advanced Materials*, *19*(17), 2224–2227

Validation of Py-GC/MS to investigate synthetic fibers

T. NACCI[1], F. SABATINI[1], I. DEGANO[1], F. MODUGNO[1]

[1]*Department of Chemistry and Industrial Chemistry, University of Pisa, Pisa, Italy*
tommaso.nacci@phd.unipi.it

The intensive everyday usage of synthetic materials causes the release of a large amount of microplastics (MPs) in all environmental compartments. In particular, textile microfibers (MFs) are generated during the washing of synthetic textiles and then discharged along with degradation products in the oceans through sewage water [1, 2]. So, it is important to develop new analytical protocols for the quali- quantitative characterization of MFs in environmental samples, and to study the degradation processes that can occur. Polymer identification often relies on non-invasive and non-destructive analytical tools, such as Raman and Attenuated Total Reflectance Fourier Transform Infrared (ATR-FTIR) spectroscopies [3, 4]. However, these techniques are limited to a surface evaluation of the samples, preventing information on the bulk to be obtained.

Recently, Evolved Gas Analysis coupled to Mass Spectrometry (EGA-MS) and multi-shot Pyrolysis coupled to Gas-Chromatography and Mass Spectrometry (Py-GC/MS) are emerging analytical methods for the characterization and quantification of MPs in environmental samples [5], but their application on MFs is still limited [6, 7].

The main advantages of these techniques are related to their capability to discriminate and characterize different fractions of composite samples, and to the small amount of textile fibers required for the analysis. During EGA-MS analysis, the sample is subjected to a programmed heating and the gases evolved are analysed by the mass spectrometer. This technique provides useful compositional information by correlating specific thermal regions with the corresponding average mass spectra. Instead, in Py-GC/MS the sample is introduced in a micro-furnace and flash pyrolyzed at a certain temperature. The produced pyrolysis products are then separated on a gas-chromatographic column and revealed by the mass spectrometer. It is also possible to pyrolyze the same sample multiple times at different temperatures in order to characterize different fractions.

The present work aims at characterizing synthetic textile samples by EGA-MS and Py-GC/MS in order to investigate the effects induced by the photo-oxidation of the fibers. In particular, two different artificial ageing methods will be compared: UV irradiation in ageing chamber, and online micro UV irradiation-Py-GC-MS. The results allowed us to better understand the processes that take place during the first steps of photo-oxidation of synthetic fibers.

References:

[1] M.A. Browne, P. Crump, S.J. Niven, E. Teuten, A. Tonkin, T. Galloway, R. Thompson, *Environ. Sci. Technol.*, 45, 9175-9179 (2011).
[2] L. Sørensen, A.S. Groven, I.A. Hovsbakken, O. Del Puerto, D.F. Krause, A. Salvo, A.M. Booth, *Sci. Total Environ.*, 755, 143170 (2021).
[3] J. Miller, E. Bartick, *Appl. Spectroscop.*, 55, 1729-1732 (2001).
[4] P. Peets, I. Leito, J. Pelt, S. Vahur, *Spectrochimic. Acta A.*, 173, 175-181 (2017).
[5] J. La Nasa, G. Biale, D. Fabbri, F. Modugno, *J. Anal. Appl. Pyrol.*, 149, 104841 (2020).
[6] F. Sabatini, T. Nacci, I. Degano, M.P. Colombini, *J. Anal. Appl. Pyrol.*, 135, 111-121 (2018).
[7] S. O'Brien, E. Okoffo, J. O'Brien, F. Ribeiro, X. Wang, S. Wright, S. Samanipour, C. Rauert, T. Toapanta, R. Albarracin, K. Thomas, *Sci. Total Environ.*, 747, 141175 (2020).

A Second-Order CASSCF Algorithm with the Cholesky Decomposition of the Two-Electron Integrals

TOMMASO NOTTOLI[1], JÜRGEN GAUSS[2], FILIPPO LIPPARINI[1]

[1]Dipartimento di Chimica e Chimica Industriale, Università di Pisa. Via G. Moruzzi 13, I-56124 Pisa, Italy
[2]Department Chemie, Johannes Gutenberg-Universität Mainz, Duesbergweg 10-14, D-55128 Mainz, Germany
tommaso.nottoli@phd.unipi.it

We present the implementation of a second-order CASSCF algorithm in conjunction with the Cholesky decomposition of the two-electron repulsion integrals.[1,2] The algorithm, called Norm-Extended Optimization,[3,4] guarantees convergence of the optimization, but it involves the full Hessian of the wavefunction and is therefore computationally expensive. Coupling the second-order procedure with the Cholesky decomposition leads to a significant reduction in the computational cost, reduced memory requirements, and an improved parallel performance. As a result, CASSCF calculations of larger molecular systems become possible as a routine task. The performance of the new implementation is illustrated by means of benchmark calculations on molecules of increasing size, with up to about 3000 basis functions and 14 active orbitals.

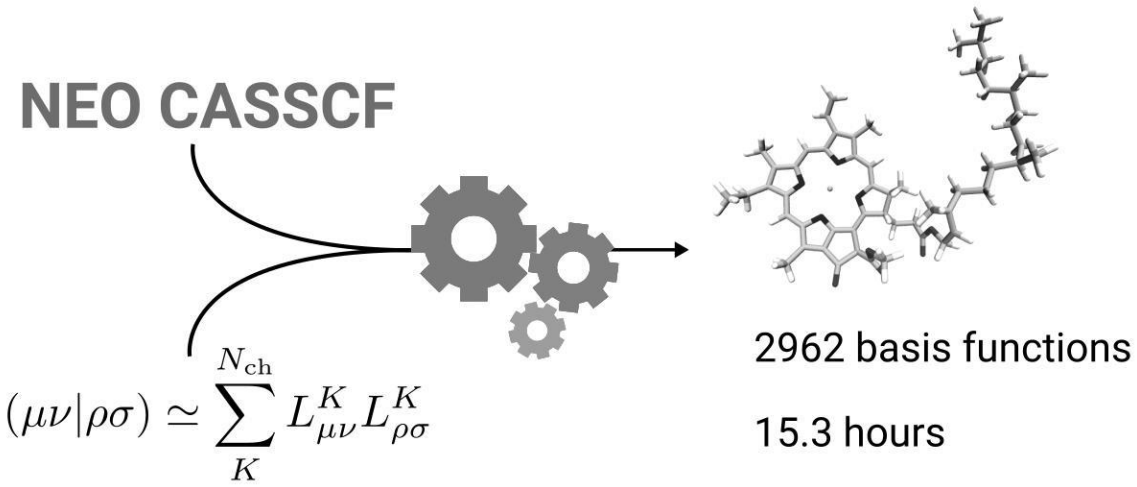


Figure 1. The Cholesky Decomposition is exploited in the second-order CASSCF optimization algorithm. The combined machinery is used to compute the ground state energy of a large system namely, the chlorophyll a molecule with 2962 basis functions in about 15 hours.

References:
[1] H. Koch, A. Sánchez de Merás, T. B. Pedersen, *J. Chem. Phys.*, 118, 9481-9484 (2003).
[2] I. Røeggen, T. Johansen, *J. Chem. Phys.*, 128, 194107 (2008).
[3] H. J. Aa. Jensen, P. Jørgensen, *J. Chem. Phys.*, 80, 1204-1214 (1984).
[4] H. J. Aa. Jensen, H. Agren, *Chem. Phys.*, 104, 229-250 (1986).

Additive Manufacturing of Biotechnological Polymers and Relevant Composites for Biomedical Applications

G. PECORINI[1], S. BRACCINI[1], S. SIMONI[1], E. MARTINELLI[1], L. CARMASSI[1], D. LI VECCHI[1], F. CHIELLINI[1] and D. PUPPI[1]

[1]*BIOLab Research Group, Department ofChemistry and Industrial Chemistry,University of Pisa, UdR INSTM Pisa, Via Moruzzi 13, 56124, Pisa, Italy*
gianni.pecorini@phd.unipi.it

Bio-based polymers possess several peculiar features, e.g., unique chemical structure, bioactivity, non-toxicity, and biocompatibility, that position them at the forefront of modern biomedical materials sector [1]. Biotechnological polymers can be obtained through extraction from natural sources, polymerization through fermentative processes, or through the synthesis of bio-based monomers and their further chemical polymerization [2]. In this contribution scaffolds designed for tissue engineering and made of different biotechnological polymers have been fabricated employing Fused Deposition Modelling (FDM) or Computer-Aided Wet-Spinning (CAWS). FDM and CAWS are additive manufacturing (AM) techniques which involve the computer-controlled deposition of respectively a melt polymer filament on a heated plate or a polymer solution extruded directly into a coagulation bath. Polyhydroxyalkanoates (PHAs) are a class of bio-polyesters produced by many bacteria. Thanks to their biocompatibility, biodegradability, superior mechanical properties and processing versatility, in comparison with other biopolymers, PHAs have become unique polymer candidates for advanced research in regenerative medicine [3]. Poly(3-hydroxybutyrate-*co*-3-hydroxyvalerate) (PHBV) is one of the most studied polymers belonging to PHAs family. Forming a blend between PHBV and other thermoplastic polymers, such as poly(D,L-lactide) (PDLLA) or poly(lactide-*co*-glycolide) (PLGA) resulted to be a valuable way to increase its processing properties by melt- and solution-based AM techniques. In particular, scaffolds constituted by PHBV/PDLLA (figure 1a) or PHBV/PLGA blends were fabricated by employing FDM and CAWS, respectively. Loading PHBV and PHBV/PLGA with osteoinductive ceramics, such as nanohydroxyapatite (nHA) and β-tricalcium phosphate (β-TCP), resulted in bioactive nano/microcomposite scaffolds designed for bone regeneration (figures 1b-1e). PLLA and PLGA are linear aliphatic polyesters approved by FDA for biomedical applications, whose monomer precursors can be obtained through fermentative processes. Nanocomposite scaffolds based on PLLA/nHA or PLGA/nHA were fabricated by CAWS, figure 1f)-1g). In addition, nHA was functionalized through a PDLLA or PLGA chain grafting strategy based on a transesterification reaction, in order to increase its interaction with the polymeric matrix and its stability when suspended in organic solvents. In this way scaffolds with enhanced mechanical properties could be obtained. Chitin is a linear polysaccharide extracted from the exoskeleton of crustaceans and produced by some fungi and bacteria, applied in the development of materials approved for use in the biomedical field [4]. Chitin dissolved in ethyl methylimidazolium acetate was successfully processed by CAWS to obtain 3D scaffolds with different shapes (figure 1h).

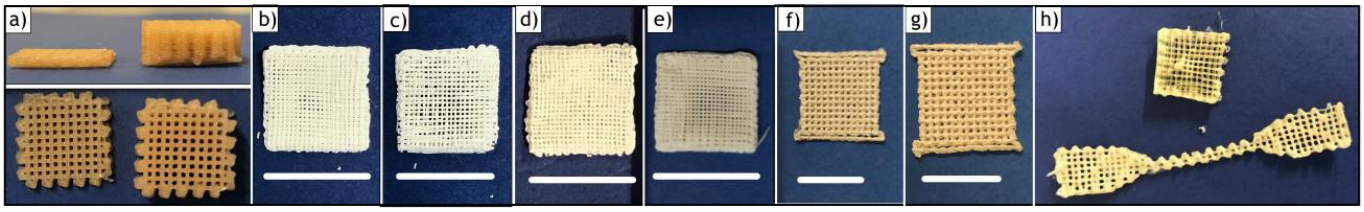


Figure 1. Representative pictures of scaffold prototypes: a) PHBV/PDLA scaffolds; b) PHBV/nHA scaffolds; c) PHBV/PLGA/nHA scaffolds; d) PHBV/β-TCP scaffolds; e) PHBV/PLGA/β-TCP scaffolds; f) PLLA/nHA scaffolds; g) PLGA/nHA scaffolds; h) chitin scaffolds (size bars length: 1 cm).

References:

[1] Bedian, L., A.M. Villalba-Rodriguez, G. Hernandez-Vargas, R. Parra-Saldivar, and H.M. Iqbal, Int J Biol Macromol, 2017. **98**: p. 837-846.
[2] Berezina N. and Martelli S. M., in *Renewable Resources for Biorefineries*, 2014, 1-28.
[3] Puppi, D., G. Pecorini, and F. Chiellini, Bioeng., 2019. **6**(4).
[4] Yang, T.L., Int J Mol Sci, 2011. **12**(3): p. 1936-63.

P35

Thermal and biophysical stability of protein-polymer conjugates in solution

CHIARA PELOSI[1] FREDERIK WURM[2], CELIA DUCE[1], MARIA ROSARIA TINE'[1]

[1]Dipartimento di Chimica e Chimica Industriale, Università di Pisa, Via Moruzzi, Pisa 56124, Italy
[2]Sustainable Polymer Chemistry Group, MESA+ Institute for Nanotechnology, Faculty of Science and Technology, Universiteit Twente, PO Box 217, 7500 AE Enschede, The Netherlands.
chiara.pelosi@dcci.unipi.it

Protein-polymer conjugates are a new class of biohybrids materials with high potentialities for biomedical applications [1]. Most of the works reported in the literature are focused on their synthesis and their characterization, either *in vitro* or *in vivo*. Beyond these aspects, their biophysical evaluation is an important point to deeper understand their microscopic behaviour and to orientate the design of future candidates.
In this frame, we evaluated the physical and thermal stability of the protein in solution, using model conjugates made by the protein myoglobin, and the polymers polyphosphoesters (a novel class of biocompatible and biodegradable polymers [2]). We focus our attention on the observation of the protein unfolding (by using Circular Dichroism, UV-Vis spectroscopy, nano-Differential Scanning Calorimetry and Fluorimetry) and the protein degradation rate induced by proteolytic enzymes (by using UV-Vis absorbance).
Overall, we observed decreasing protein stability with increasing the hydrophobicity of the attached polymers [3]. Calorimetry showed that in the conjugates the protein unfolding enthalpy and temperature decrease, but the more hydrophilic polymers enhance the protein thermal reversibility, reducing thermally induced aggregation phenomena. This behaviour was confirmed by CD measurements, used also to evaluate protein denaturation at different pHs or urea concentrations. The measurements made by UV-Vis absorbance confirmed the protective action of hydrophilic polymers toward the action of proteolytic enzymes, while the more hydrophobic polymers enhance the protein degradation rate.

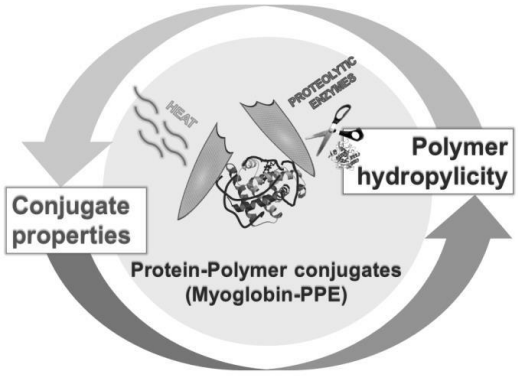


Figure 1. Scheme of protein-polymer conjugates, and the influence of the polymer hydrophilicity of the protein properties.

[1] S. N. S. Alconcel, A. S. Baas, and H. D. Maynard, *Polym. Chem.*, 2 (7), 1442, (2011).
[2] C. Pelosi, M. R. Tinè, M. R. and F. R. Wurm, *Eur. Polym. J.*, 141, 110079, (2020).
[3] C. Pelosi, C. Duce, M. R. Tinè, M. R. and F. R. Wurm, *Biomacromolecules,* (2021).

P36

Relaxation dynamics through a conical intersection: Quantum and quantum-classical studies

CARLOTTA PIERONI[1,2], EMANUELE MARSILI[3], DAVID LAUVERGNAT[2], and GIOVANNI GRANUCCI[1], FEDERICA AGOSTINI[2], MAURIZIO PERSICO[1]

[1]Università di Pisa, Dipartimento di Chimica e Chimica Industriale, via G. Moruzzi 13, 56124 Pisa, Italy
[2]Université Paris-Saclay, CNRS, Institut de Chimie Physique UMR8000, 91405 Orsay, France
[3]Department of Chemistry, Durham University, South Road, Durham DH1 3LE, United Kingdom
carlotta.pieroni@phd.unipi.it

Trajectory-based approaches to nonadiabatic dynamics are powerful tools for predicting the fate of a molecule after photo-excitation [1] or the products of a collision reaction. The approximations, in the treatment of nuclear dynamics and in the description of electron-nuclear coupling, make them computationally efficient, at least compared to a numerically-exact solution of the time-dependent Schrodinger equation. Clearly, the computational efficiency comes at the price of losing accuracy or missing critical features, such as tunnelling and zero-point energy, interferences, quantum decoherence, to name a few. Related to this point we study the relaxation process through a conical intersection of a photo-excited retinal chromophore model. The analysis is based on a two-electronic-state two dimensional Hamiltonian developed by Hahn and Stock [2] to reproduce, with a minimal model, the main features of the 11-cis to all-trans isomerization of the retinal of rhodopsin. In particular, we focus on the performance of various trajectory-based schemes to nonadiabatic dynamics: trajectory surface hopping (TSH) [3], trajectory surface hopping including energy decoherence corrections (TSH-EDC) [4], Ehrenfest dynamics (EH) [5], and the coupled-trajectory mixed quantum-classical (CT-MQC) [6] scheme derived from the exact factorization of the time-dependent electron-nuclear wavefunction. We compare quantum-classical results to numerically-exact quantum vibronic wavepacket dynamics. The purpose of the work is to investigate, by analyzing electronic and nuclear observables, how the sampling of initial conditions for the trajectories affects the subsequent dynamics [7].

References:

[1] S. K. Min, F. Agostini, I. Tavernelli, and E. K. U. Gross, “Ab initio nonadiabatic dynamics with coupled trajectories: A rigorous approach to quantum (de)coherence,” J. Phys. Chem. Lett. 8, 3048–3055 (2017).
[2] S. Hahn and G. Stock, “Quantum-mechanical modeling of the femtosecond isomerization in rhodopsin,” J. Phys. Chem. B 104, 1146–1149 (2000).
[3] J. C. Tully, “Molecular dynamics with electronic transitions,” J. Chem. Phys. 93, 1061 (1990).
[4] G. Granucci and M. Persico, “Critical appraisal of the fewest switches algorithm for surface hopping,” J. Chem. Phys. 126, 134114 (2007).
[5] J. C. Tully, “Mixed quantum-classical dynamics,” Faraday Discuss.110, 407 (1998)
[6] F. Agostini, S. K. Min, A. Abedi, and E. K. U. Gross, “Quantum-classical non-adiabatic dynamics: Coupled- vs. independent-trajectory methods,” J. Chem. Theory Comput.12, 2127–2143 (2016)
[7] C. Pieroni, E. Marsili, D. Lauvergnat, and F. Agostini, “Relaxation dynamics through a conical intersection: Quantum and quantum-classical studies” J. Chem. Phys. 154**,** 2021

Eco-friendly keratin extraction from poultry feathers and production of keratin-based biomaterials

E. PULIDORI[1], S. MICALIZZI[2], E. BRAMANTI[3], L. BERNAZZANI[1], C. DUCE[1], C. DE MARIA[2], F. MONTEMURRO[2], C. PELOSI[1], A. DE ACUTIS[2], G. VOZZI[2] AND M. R. TINÉ[1]

[1]Department of Chemistry and Industrial Chemistry, University of Pisa, Via G. Moruzzi 13, 56124 Pisa, Italy
[2]Research Centre E. Piaggio and Department of Information Engineering, University of Pisa, Largo L. Lazzarino 1, 56126 Pisa, Italy
[3]Institute of Chemistry of Organometallic Compounds, National Research Council, via G. Moruzzi 1, 56124 Pisa, Italy
elena.pulidori@unipi.it

Poultry slaughterhouses produce tons of poultry feathers waste which are buried in landfills or incinerated, contributing to environmental pollution [1]. This biomass waste is composed by 90% of keratin [2], biodegradable and biocompatible protein with high sulphur content and peculiar properties (e.g., high tensile strength, mechanical stability, and rigidity) [3] that make it suitable to produce useful materials in various application fields [4-6]. Therefore, the poultry feathers can be exploited and used as a natural source of this protein.
In this study, we developed eco-friendly keratin extraction process which allows to obtain keratin with different molecular weights suitable for different applications. Using directly the raw extracted soluble keratin with low molecular weight (about 10 kDa), mixed with porcine gelatine and 3-(Glycidyloxypropyl)trimethoxysilane (GPTMS) as cross-linker, it is possible obtain keratin-based electrospun mats by electrospinning process. Instead, the insoluble keratin was used as filler of polylactic acid (PLA) matrix to obtain bioplastic material for 3D printing applications.
Thermal, mechanical, morphological and barrier properties of these different keratin-based bioplastics were investigated. Results highlighted that the properties can be modulated by changing keratin and GPTMS concentration. These materials could be used in the packaging field and as filtering/purifying membranes.

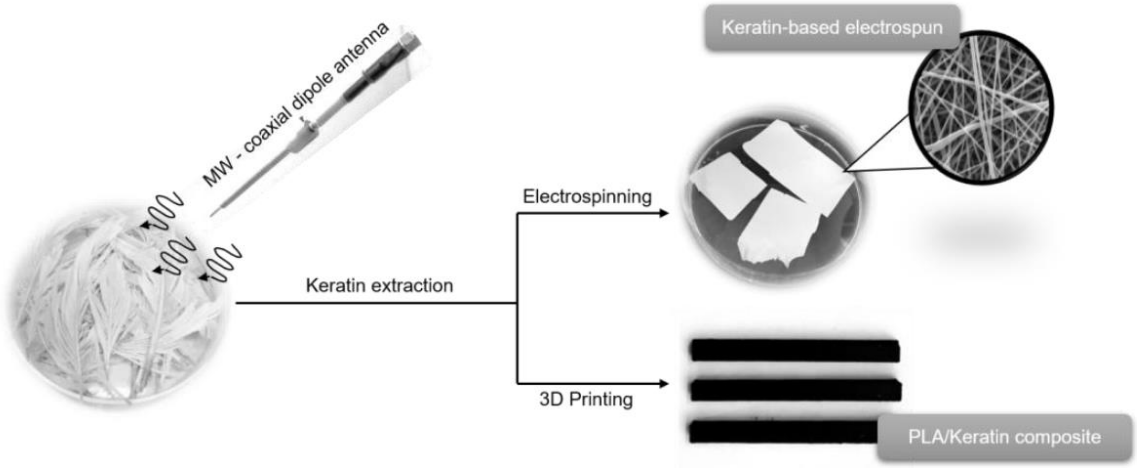


Figure 1. Schematized process which summarizes the main steps to obtain keratin-based materials from poultry feathers**.**

References:
[1] S. Sharma, A. Gupta, Braz. Arch. Biol. Technol., 59 (0), 1-14 (2016*).*
[2] T. Korniłowicz-Kowalska, J. Bohacz, Waste Manage., 1, 1689–1701 (2011).
[3] J. Mckittrick, P. -Y. Chen, S. G. Bodde, W. Yang, E. E. Novitskaya, M. A Meyers, JOM, 64, 449-468 (2012)
[4] J. Rouse, M. Van Dyke, Mater., 3, 999-1014 (2010)
[5] H. Xu, S. Cai, L. Xu, Y. Yang, Langmuir, 30, 8461-8470 (2014)
[6] N. Ramakrishnan, S. Sharma, A. Gupta, B. Y. Alashwal, Int. J. Biol.Macromol., 111, 352-358 (2018)

An efficient bis-thiourea CSA for the enantiodiscrimination of amino acid derivatives by NMR spectroscopy

A. RECCHIMURZO, C. MICHELETTI, F. BALZANO, G. UCCELLO BARRETTA

Department of Chemistry and Industrial Chemistry, University of Pisa, Pisa, Italy
alessandra.recchimurzo@phd.unipi.it

Different response of biological systems depending on the divergent pharmacological activity exhibited by enantiomers of an active ingredient has urged several research areas[1] to develop increasingly reliable methods for monitoring and quantifying stereoisomers.[2] On this issue, NMR spectroscopy plays a leading role based on the possibility to differentiate enantiomers by use of suitable chiral auxiliaries, which transfer the substrates in a diastereoisomeric environment. In particular, chiral solvating agents (CSAs) are very popular due to the fact that their use does not require any derivatization process since the CSA and the enantiomeric substrates are simply mixed into the NMR tube before the measurement.[3-5]
We report here the use of the bis-thiourea CSA **BTDA (**Figure 1A) for the NMR enantiodiscrimination of *N*-(3,5)-dinitrobenzoyl α-amino acid derivatives (Figure 1A).[6] The cooperativity between the two thiourea arms of the dimer in the interaction with the substrates led to remarkably higher nonequivalences compared to those obtained in the presence of monomer parent (**TMA**, Figure 1A).[7] As a matter of fact, **BTDA** assumes a cleft conformation (Figure 1B) and by means of an extended hydrogen bonding network interacts with enantiomeric substrates, which bisect the major grooves of CSA structure. An achiral base additive (DABCO) is required not only for the solubilization of the enantiomeric compounds but also to mediate the interaction between them and the CSA, thus enhancing the enantiodifferentiation in the NMR spectra. Chiral discrimination mechanism was carefully investigated by NMR, through the determination of the complexation stoichiometries, association constants and stereochemistry of the diastereomeric solvates.

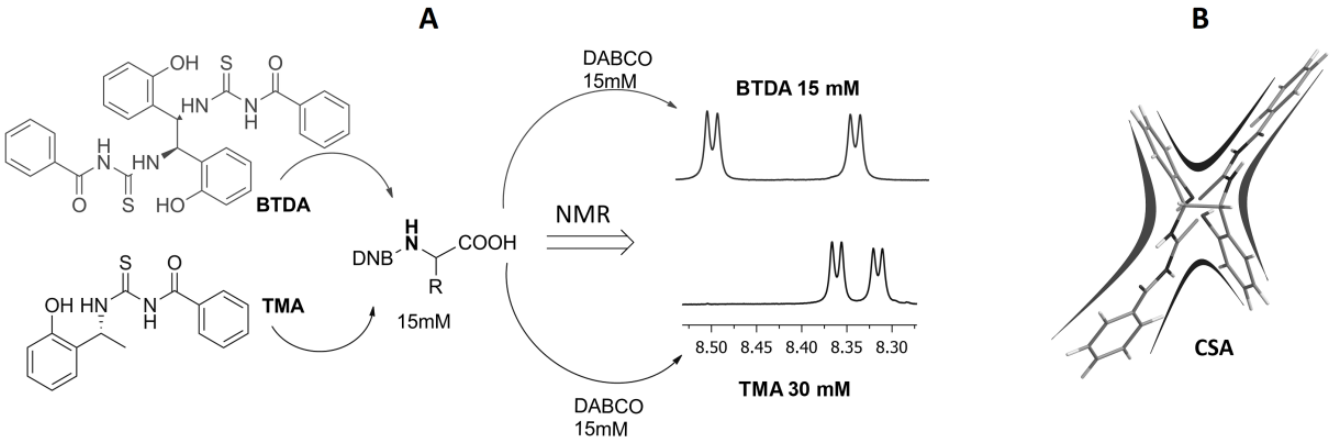


Figure 1. Comparison of nonequivalences of *NH* proton of amino acid derivatives in the presence of DABCO and **BTDA** or **TMA** (A). CSA cleft conformation (B).

References:
[1] T. H. Webb, C. S. Wilcox, *Chem. Soc. Rev.* 22, 383–395 (1993).
[2] J. D. Morrison, *Asymmetric Synthesis*, 1, (1983).
[3] F. Balzano, G. Uccello-Barretta, F. Aiello, In Chiral Analysis: Advances in Spectroscopy, Chromatography and Emerging Methods; *Elsevier*. Ch. 9, 367–427 (2018).
[4] G. Uccello-Barretta, F. Balzano, *Top. Curr. Chem.* 341, 69–131 (2013).
[5] T. J. Wenzel, Differentiation of Chiral Compounds Using NMR Spectroscopy; Wiley & Sons (2018).
[6] A. Recchimurzo, C. Micheletti, G. Uccello-Barretta, F. Balzano, *J. Org. Chem.* (2021), https://doi.org/10.1021/acs.joc.1c00340
[7] A. Recchimurzo, C. Micheletti, G. Uccello-Barretta, F. Balzano, *J. Org. Chem.* 85, 5342–5350 (2020).

SBS functionalized anion exchange membranes for water electrolysis

A. ROGGI[1], I. FIASCHI[1], E. MARTINELLI[1]

[1]*Department of Chemistry and Industrial Chemistry. University of Pisa, 56124 Pisa (Italy)*
andrea.roggi@phd.unipi.it

Among the different types of electrolysis cells, anion exchange membrane (AEM) water electrolysis is a promising technology for hydrogen production from renewable energies.[1,2] In recent years, various polymeric systems have been studied for the development of anionic exchange membranes (AEM) with the main purpose of preparing innovative membranes, possibly at low cost, which are characterized by high ionic conductivity, chemical stability in an alkaline environment, low hydrogen permeability to limit the hydrogen crossover, good mechanical properties and low swelling in operating conditions. The goal of developing a membrane, in which all these requirements are combined and optimized in a synergistic way, represents a challenging task that nowadays limits the large-scale application of AEM technology. The present work was, therefore, aimed at addressing several unique features of AEM for implementation in an industrially scalable, cost-effective and sustainable energy- production process through a suitable synthetic strategy that involved the post-modification of a commercially available poly(styrene)-*b*-poly(butadiene)-*b*-poly(styrene) triblock copolymer (SBS) matrix by grafting side chains of vinylbenzyl chloride (VBC), capable of providing functional groups easily convertible into quaternary ammonium cationic groups. In particular, by taking advantage of the controlled nature of the TEMPO-mediated radical polymerization, it was possible to evaluate the average number of grafted chains per SBS polymer backbone as well as to modulate the graft length and the VBC content in the copolymer. Moreover, chains composed of styrene/VBC random copolymers were also grafted onto SBS in order to increase the styrene mole fraction and improve the mechanical properties of the membrane. The obtained SBS-based graft copolymers were, therefore, used for the fabrication of anion exchange membrane by solution casting, that were mechanically and electrochemically characterized. Control over ionic exchange and conductivity, water uptake and mechanical properties demonstrated how it was feasible to tune the ultimate behaviour of membranes by varying the molecular parameters of the graft copolymers in general, and the VBC functionalization degree in particular. Several key properties were found to be comparable or even better than those of the state-of-the-art commercial membranes.

References:

[1] H. A. Miller, K. Bouzek, J. Hnat, S. Loos, C. I. Bernäcker, T. Weißgärber, L.Röntzsch, J. Meier-Haack, Sustain. Energy Fuels 2020, 4, 2114–2133.
[2] D. Henkensmeier, M. Najibah, C. Harms, J. Žitka, J. Hnát, K. Bouzek, J. Electrochem. Energy Convers. Storage 2021, 18, DOI 10.1115/1.4047963.

Catalysts design by predictive Modelling of Aqueous Phase Reforming of Liquid Renewable Feedstocks

THANTIP ROONGCHAROEN[1,2], LUCA SEMENTA[3], ALESSANDRO FORTUNELLI[2]

[1]Department of Chemistry and Industrial Chemistry, DSCM, University of Pisa, Via G. Moruzzi 13, Pisa, Italy
[2]CNR-Istituto di Chimica dei Composti Organometallici, Via G. Moruzzi 1, 56124, Pisa, Italy
[3]CNR-Istituto per i Processi Chimico-Fisici, Via G. Moruzzi 1, 56124, Pisa, Italy
Thantip.roongcharoen@pi.iccom.cnr.it

Aqueous Phase Reforming (APR) can be considered as a process similar but alternative to the traditional steam reforming since it can be used to convert streams of low value mixed polyols (generated by a range of sustainable biomass conversion processes such as pyrolysis) to H_2/CO/CO_2.[1-2] The APR reaction can be performed under relatively mild conditions (200−250 °C, 20−50 bar), with considerable economic and technical advantages over existing reforming techniques.[3-4] Conversion of these compounds can be achieved using Pt based catalysts but the selectivity to higher value hydrocarbon has also been demonstrated using bi-metallic catalysts such as Pt-Re, Pt-Mn, and Pt-Ru.[5] This study focuses on investigating bimetallic catalysts under intermediate conditions, i.e. low temperatures (200-300°C) and correlating their properties with the catalytic activity and selectivity in order to develop a cheaper and efficient APR catalyst. Various computational methods (based on DFT and systematic sampling techniques) have been used to simulate and predict the geometric (shape, faceting) and electronic structure of bimetallic clusters. The most preferable adsorption positions of key species will be explored and the reaction mechanisms of APR with specific attention to the determination of the rate-determining-step will be investigated. Moreover, producing a catalytic model and prediction of conversion and selectivity ratios will be compared with the outcome of experimental catalytic tests.

References:
[1] Sá, S.; Silva, H.; Brandão, L.; Sousa, J. M.; Mendes, A., Applied Catalysis B: Environmental 2010, 99 (1), 43-57.
[2] Davda, R. R.; Shabaker, J. W.; Huber, G. W.; Cortright, R. D.; Dumesic, J. A., Applied Catalysis B: Environmental 2005, 56 (1), 171-186.
[3] Cortright, R. D.; Davda, R. R.; Dumesic, J. A., In Materials for Sustainable Energy, pp 289-292.
[4] Davda, R. R.; Shabaker, J. W.; Huber, G. W.; Cortright, R. D.; Dumesic, J. A., Applied Catalysis B: Environmental 2003, 43 (1), 13-26.
[5] Kim,H.-D.; Park, H. J.; Kim, T.-W.; Jeong, K.-E.; Chae, H.-J.; Jeong, S.-Y.; Lee, C.-H.; Kim, C.-U., International Journal of Hydrogen Energy 2012, 37 (10), 8310-8317.

C-2 dehydrogenative alkynylation of imidazoles

E. ROSADONI[1], M. BIAGETTI[2], M. FAUSTI[1], G. GRANUCCI[1], S. GUARIENTO[2], M. LESSI[1], C. MICHELETTI[1], A. PUCCI[1], P. RONCHI[2], F. BELLINA[1]

[1]Dipartimento di Chimica e Chimica Industriale, Università di Pisa, Pisa, Italy
[2]Chiesi Farmaceutici, Parma, Italy
e.rosadoni@studenti.unipi.it

Imidazole scaffolds are frequently found in bioactive compounds,[1] and organic functional materials such as liquid crystals and fluorescent dyes.[2] Considering their wide range of possible applications, the development of simple functional group-tolerant synthetic methods that allow direct and selective heterocycle elaboration under mild conditions aroused considerable attention.[3] Recently, the transition metal-catalyzed dehydrogenative cross-coupling reactions involving aromatic Csp2-H bonds of azoles emerged as an attractive strategy for the direct functionalization of their heteroaromatic cores, due to the fact that a pre-activation of both the coupling partners isn't required, in contrast with the traditional cross-coupling reactions.[4] Over the last years this research group has been interested in studies aimed to broaden the substrate scope of the direct functionalization of azoles and, in particular, to develop efficient synthetic protocols for the carbon-carbon bond forming reaction by regioselective palladium-catalyzed C-H bond activation of imidazole derivatives. In this contest, the development of an efficient procedure for the regioselective C-2 dehydrogenative alkynylation of *N*-substituted imidazoles with terminal alkynes will be the main topic of this communication.[5]

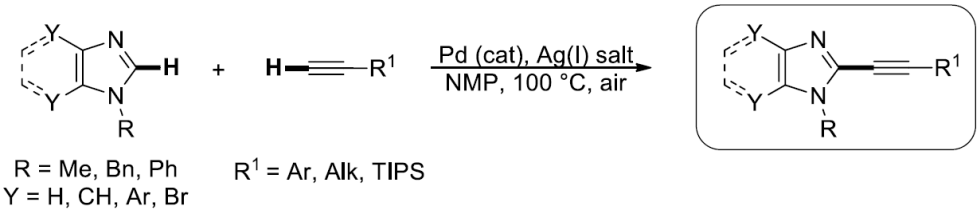


Figure 1. General procedure for the synthesis of 2-alkynylimidazoles

When appropriate, the chemical behavior of azoles other than imidazole will be compared and discussed, along with the results obtained when the dehydrogenative alkynylation was applied to the preparation of new synthetic push-pull heteroaromatic dyes.

References:

[1] For selected recent reviews on the biological activity of imidazole derivatives, see: (a) L. Zhang, X. Peng, G. L. V. Damu, R. Geng, C. Zhou, *Med. Res. Rev.* **2014**, *34*, 340; (b) R. Rossi, M. Lessi, C. Manzini, G. Marianetti, F. Bellina, *Synthesis* **2016**, *48*, 3821.

[2] (a) J. Kulkánek, F. Burês, *Beilstein J. Org. Chem*. **2012**, *8*, 25; (b) H. Liu, Y. Chen, *Tetrahedron* **2013**, *69*, 1872.

[3] For selected reviews on the synthesis of azoles, see: (a) A. V. Gulevich, A. S. Dudnik, N. Chernyak, V. Gevorgyan, *Chem. Rev.* **2013**, 113, 3084; (b) J. Hassan, M. Sévignon, C. Gozzi, E. Schulz, M. Lemaire, *Chem. Rev.* **2002**, *102*, 1359.

[4] For recent references on cross-dehydrogenative coupling of heteroarenes, including azoles, see: (a) Y. Yang, J. Lan, J You, *Chem. Rev.* **2017**, *117*, 8787; (b) *Heterocycles via Cross Dehydrogenative Coupling*, A. Srivastava and C. K. Jana Eds., Springer Nature, Singapore, **2019**.

[5] For recent reviews on the cross-dehydrogenative alkynylation of heteroarenes, see: (a) B. Panda, *Asian J. Org. Chem.* **2020**, *9*, 492; (b) F. Bellina, M. La Manna, E. Rosadoni *Curr. Org. Chem.* **2021**, accepted for publication.

Fabrication of liver-lobule-like hexagonal chamber-on-chip scaffold based on biodegradable polymers by replica molding process

C. ROSELLINI[1], M. CORSI[2], S. BRACCINI[3], D. PUPPI[3], F. CHIELLINI[3], G. BARILLARO[2]

[1]*Department of Biology, University of Pisa*
[2]*Department of Information Engineering, University of Pisa*
[3]*Department of Chemistry and Industrial Chemistry, University of Pisa*
c.rosellini3@studenti.unipi.it

Two-dimensional (2D) monolayer cultures have been used since the early 20th century as *in vitro* models for the study of human diseases and therapies. Although 2D cell cultures have been an important tool in clinical research, they fail to provide a realistic representation of the *in vivo* environment in terms of topological, mechanics, and fluidic cues. For instance, they lack a threedimensional environment, cell-cell and cell-matrix interactions and they are cultured under static conditions [1]. Organs-on-chips (OoCs) are one of the alternatives to 2D cultures. The basic idea of these devices is to reproduce the environment of a physiological or pathological organ *in vitro* [2]. The development of this microfluidics based technology could fill the gap between *in vitro* and *in vivo* models by offering new strategies for pharmacological research and beyond. Organ-on-chip devices that reproduce various organs and tissues have been developed over the past decade, among which lung, liver, gut, kidney, heart and even body-on-chip, containing the functions of multiple organs and tissues [3]. In particular, different types of Liver-on-chip (LoC) have been designed because the liver is an important organ that plays several key functions in the body, including detoxification, glycogen storage, plasma protein synthesis and especially metabolism. Due to its role, the liver is the main organ involved in drug metabolism and these devices could be used to predict drug toxicity profiles [4].

In this work, we target the design, fabrication and characterization of a biodegradable liver-lobule-on-chip (Figure 1), providing a microphysiological niche for hepatocyte cultures. The use of biodegradable polymers for the lobule-like scaffold allows the latter to dissolve once cells have arranged into hepatic cords, thus achieving a fully-biological lobular structure. A polymer-based replication technology, namely replica molding, is used to create reusable PDMS masters from a microstructured lobule-like SU-8 master fabricated by standard UV photolithography; then, the bioerodible scaffolds for hepatocyte culture are achieved through replica molding of the PDMS masters using suitable polymers by solvent casting. Different types of polymers have been considered for the preparation of the bioerodible scaffolds, namely, hydrogel-forming natural polymers (Chitosan and Gelatin) and natural (PHBV) or synthetic (PLGA, PDLLA, PCL) aliphatic polyesters. Adhesion and proliferation of human hepatocellular carcinoma cells (HepG2) will be assessed in static conditions. In addition, preliminary microfluidic studies for cell culture in dynamic conditions will be carried out.

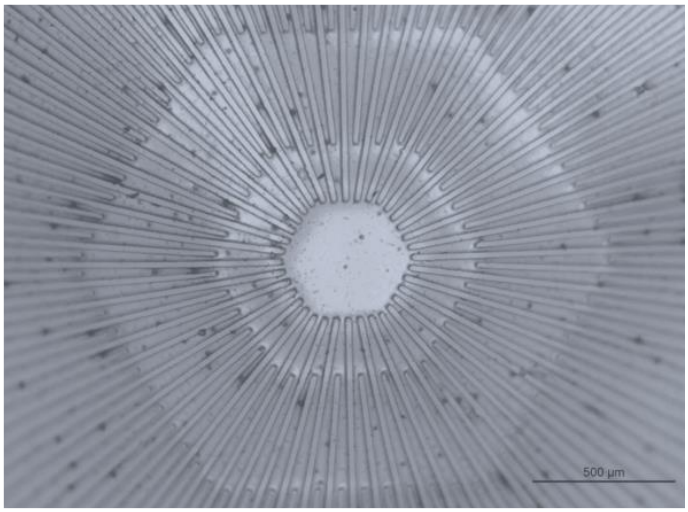


Figure 1. Bright-field micrograph of PDLLA scaffold (magnification 5X)

References:

[1] R. Mittal, F. W. Woo, C. S. Castro, M. A. Cohen, J. Karanxha, J. Mittal, T. Chhibber, V. M. Jhaveri, *J Cell Physiol.*, 234, 8352-8380 (2019).
[2] Q. Wu, J. Liu, X. Wang, L. Feng, J. Wu, X. Zhu, W. Wen, X. Gong, *BioMed. Eng*., 19,9 (2020).
[3] H. Kimura, Y. Sakai, T. Fujii, *Drug Metabolism and Pharmacokinetics*., 33, 43-48 (2018)
[4] B. Delalat, C. Cozzi, S. R. Ghaemi, G. Polito, F. H. Kriel, T. D. Michl, F. J. Harding, C. Priest, G. Barillaro, N. H. Voelcker, *Adv. Funct. Mater.*, 28, 1801825 (2018).

On the photoactivation of a bacteriophytochrome through a QM/MM Surface Hopping approach

GIACOMO SALVADORI[1], GIOVANNI GRANUCCI[1], BENEDETTA MENNUCCI[1]

[1]*Department of Chemistry and Industrial Chemistry, University of Pisa, 56124 Pisa, Italy*
giacomo.salvadori@phd.unipi.it

Phytochromes are multi-domain red-light photoreceptor proteins, which can be switched between metastable red absorbing (Pr) and far-red absorbing (Pfr) states, allowing them to regulate cellular processes in plants, bacteria, and fungi[1]. They are homo-dimeric complexes in which each monomer consists of the protein and a chromophore, a linear tetrapyrrole known as bilin. The ability to act as light switches in these organisms depends on the key interactions between the bilin chromophore and the apoprotein, that determine the structure of the bilin and the conversion between Pr and Pfr[2]. The whole process begins with light absorption by the bilin, rapidly followed by the isomerization of a double bond (Figure 1). The protein, therefore, on a different timescale, undergoes a structural change[3]. Here, we investigate the photochemical process by combining classical Molecular Dynamics simulations with a trajectory surface hopping approach[4]. For non-adiabatic dynamics, we used a QM/MM scheme, where the QM subsystem is the bilin chromophore and the MM subsystem is the rest of the single monomer, in the Pr state, with a water shell around the QM subsystem.

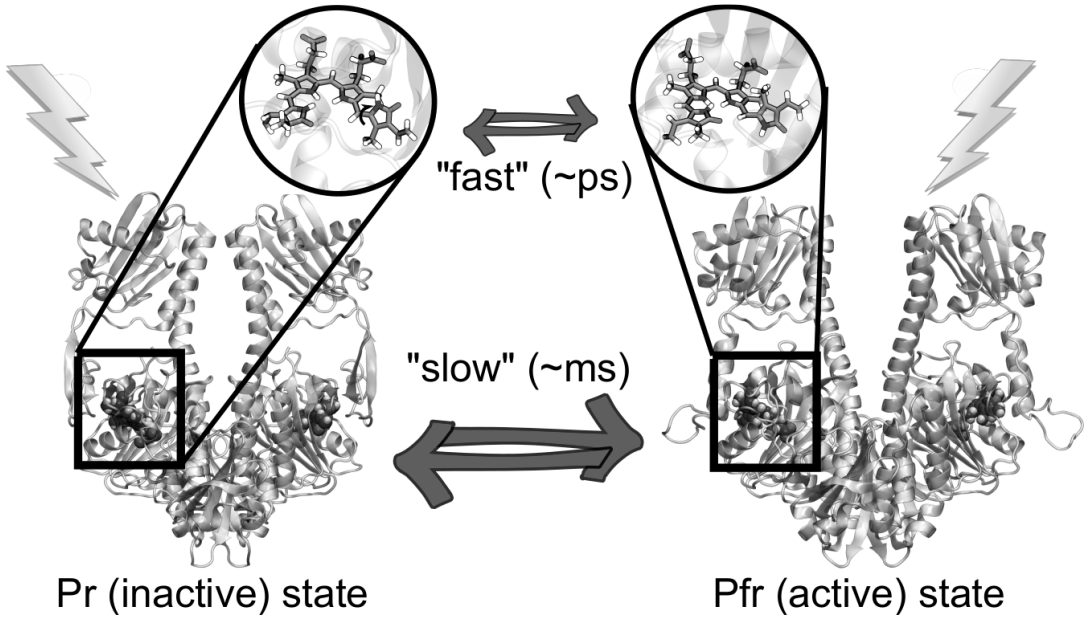


Figure 1. Representation of the two photo-products: Pr and Pfr, together with the respective chromophores.

References:
[1] M.E Auldridge, K.T Forest, *Crit Rev Biochem Mol Biol.*, 46(1), 67-88 (2011).
[2] H. Takala, H. K. Lehtivuori, O. Berntsson, A. Hughes, R. Nanekar, S. Niebling, M. Panman, L. Henry, A. Menzel, S. Westenhoff and J. A. Ihalainen, *J. Biol. Chem.*, 293, 8161–8172 (2018).
[3] J.Kubel, M. Chenchiliyan, S.A. Ooi, E. Gustavsson, L. Isaksson, V. Kuznetsova, J.A. Ihalainen, S. Westenhoff and M.Maj, *Phys. Chem. Chem. Phys.*, 22, 9195-9203 (2020).
[4] G. Granucci, M. Persico and A. Toniolo, *J. Chem. Phys.*, 114(24):10608-10615 (2001).

Polymer Scaffolds encapsulated with exosomes as a potential biomaterial for bone regeneration

S. SAMAL[1, 2], M.DASH[1]

[1]*Therapeutic Biomaterials Team, Institute of Life Sciences, Bhubaneswar- 751023, Odisha, India*
[2]*School of Biotechnology, Kalinga Institute of Industrial Technology, Bhubaneswar- 751024, Odisha, India*
sasmita.s@ils.res.in

Healthy bone possesses a balanced remodeling sequence; where osteoclasts resorb bone (osteoclastogenesis), and then osteoblasts form bone at the same site (osteogenesis)[1]. During sequential events in a tissue, intracellular communication is an important phenomenon. In this respect, exosomes (30-200nm) are gaining much attention due to their ability to transfer vital information such as specific proteins, mRNA, and miRNA to target cells which allow cell-to-cell communication. Exosomes released from osteoblasts tend to stimulate osteogenesis via RANKL-RANK mediated pathway, thereby promoting bone regeneration[2]. In this work, we have attempted to explore the osteogenic enhancenment potential of isolated exosomes from mouse pre-osteoblst cells (MC3T3-E1). The SEM image revealing the morphology of isolated exosomes has been shown in figure 1A. Treated exosomes showed enhanced cell proliferation in a time and concentration dependent manner as compared to the control (figure 1B). Thereafter, these exosomes wereare encapsulated in polymer scaffolds that are being developed using different chemistries. The scaffolds are aimed at resembling the native extracellular matrix (ECM)[3], and upon appropriate encapsulation-strategy enhance osteogenesis.This startegy will eventually lead to a biometarial which enable to achieve the therapeutic target in a much more efficient way than native exosomes.

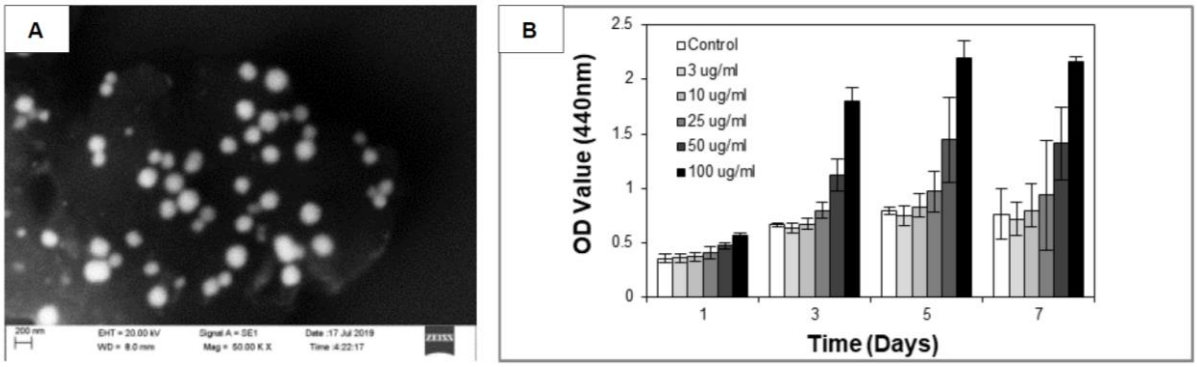


Figure 1. (A) Representative scanning electron micrograph of isolated exosomes. (B) Cell proliferation by exosomes at different time points evaluated by WST-1 assay.

References:
[1] Dimitriou, R.; Jones, E.; McGonagle, D.; Giannoudis, P. V. J. B. m., Bone regeneration: current concepts and future directions. **2011,** *9* (1), 1-10.
[2] Gao, M.; Gao, W.; Papadimitriou, J. M.; Zhang, C.; Gao, J.; Zheng, M., Exosomes-the enigmatic regulators of bone homeostasis. *Bone Res* **2018,** *6*, 36-36.
[3] Whang, K.; Goldstick, T. K.; Healy, K. E. J. B., A biodegradable polymer scaffold for delivery of osteotropic factors. **2000,** *21* (24), 2545-2551.

Surface hopping dynamics with Frenkel exciton model and semi-empirical FOMO-CI method for the study of excited states in systems containing two or more chromophores

EDUARDA SANGIOGO GIL[1], MAURIZIO PERSICO[1], GIOVANNI GRANUCCI[1]

[1]*Department of Chemistry and Industrial Chemistry, University of Pisa, Via G. Moruzzi 13, 56124 Pisa, Italy*
eduarda.sangiogogil@phd.unipi.it

In the mixed quantum-classical, trajectory-based, approaches for nonadiabatic dynamics simulations in molecules, the electronic energies and couplings are usually obtained with multiconfigurational approaches like CASSCF/CASPT2, which are needed to describe appropriately conical intersections and near degeneracy regions, bond breaking, etc. However, these multiconfigurational methods present both high complexity and high computational cost, which restrict their applicability to the study of only small systems. Semiempirical models for excited states, such as the FOMO-CI method, are much faster and already proved to be useful for many classes of compounds. [1,2] When considering multichromophoric systems, the combination between an inexpensive electronic structure method, such as the FOMO-CI, with the excitonic scheme where only excited states localized on a single chromophore are considered, may allow to perform nonadiabatic dynamics studies of large and complex systems.
We have then formulated and implemented a "divide and conquer" procedure, based on the exciton model approximation and on the semiempirical FOMO-CI electronic structure method, to describe excitation energy transfer in multichromophoric systems. We proposed two different implementations for the Frenkel exciton model, that differ in the way the excitonic couplings are computed. The validation of the proposed methodologies was carried out by comparing the results obtained with our exciton model with the ones obtained using a “supermolecule” approach. The *trans*-azobenzeno-2S-phane (2S-TTABP), formed by two azobenzene units held together by sulfur bridges, was chosen system to perform our validation. The results obtained with the exciton model (in terms of excitation transfer, excited states lifetimes, and photoisomerization quantum yields) compares well with the ones obtained by treating the system with the full quantum approach for the electronic structure.

References:

[1] G. Granucci, A. Toniolo and M. Persico, *J. Phys. Chem.*, 114, 10608-10615 (2001).
[2] M. Persico and G. Granucci, *Theor. Chem. Acc.*, 133, 1526 (2014).

Imaging spectroscopies on thin films of chiral π-conjugated materials

ANDREA TADDEUCCI,[1,2] FRANCESCO ZINNA,[1] GENNARO PESCITELLI,[1] GIULIANO SILIGARDI,[2] LORENZO DI BARI[1]

[1]Dipartimento di Chimica e Chimica Industriale, Università di Pisa, Pisa, Italy
[2]Diamond Light Source, Didcot, United Kingdom
andrea.taddeucci@phd.unipi.it

Thin films of π-conjugated systems are nowadays used as active layers in various kinds of new generation organic optoelectronic devices (OFET, OLED, OPV). Introducing chirality can guide their aggregation in the solid state,[1] leading to a wide range of optoelectronic properties; furthermore, chirality is able to promote detection,[2] absorption or emission[3] of circularly polarised light in devices and the selection of electrons' spin.[4] Manifold π-conjugated chiral materials have been prepared to achieve solid state optoelectronic properties in the visible spectrum. Imaging spectroscopies, possible only using highly collimated synchrotron radiation, are important tools to characterise and try to predict the optoelectronic features of these systems. In particular, dealing with chiral materials, Circular Dichroism imaging[5] (CDi) can furnish information about helically organized domains and possible localized polymorphisms.[6] Mueller Matrix Polarimeter imaging (MMPi) is another more powerful pioneering spectroscopy that can give spatially resolved information about all the transmission related optical contributions of the material (Absorbance, Circular Dichroism, Circular Birefingence, Linear Dichroism and Linear Birefringence).

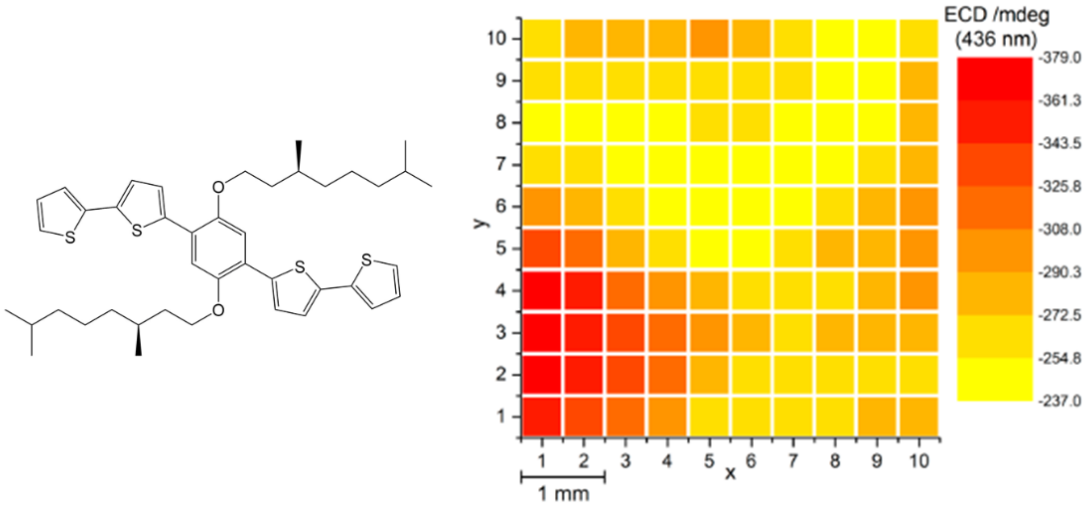


Figure 1. Single wavelength Circular Dichroism imaging (CDi) map of a spin-coated film made by a π-conjugated chiral small organic molecule

References:
[1] G. Albano, G. Pescitelli, L. Di Bari, *Chem. Rev.*, 120, 10145−10243 (2020).
[2] Y. Yang, R. C. da Costa, M. Fuchter, A. J. Campbell, *Nat. Photonics.*, 7, 634-638 (2013).
[3] G. Albano, L. A. Aronica, A. Minotto, F. Cacialli, L. Di Bari, *Chem. Eur. J.*, 26, 16622-16627 (2020).
[4] R. Naaman, D. H. Waldeck, *J. Phys, Chem. Lett.*, 3, 2178-2187 (2012).
[5] R. Hussain ,T. Javorfi, G. Siligardi, *Front. Chem.*, 9, 616928 (2021).
[6] G. Albano, M. Górecki, G. Pescitelli, L. Di Bari, T. Javorfi, R. Hussain, G. Siligardi, *New J. Chem.*, 43, 14584-14593 (2019).

Quantum size effects in Cadmium Selenium (CdSe) quantum dots

M. TOMAIUOLO[1], G. BICCHIERAI[1], N. JARMOUNI[2], F. PINEIDER[1]

[1]*Department of Chemistry and Industrial Chemistry, University of Pisa, Italy*
[2]*LPCM, Faculty of Sciences, Ben M'sik University Hassan II of Casablanca, Morocco*
m.tomaiuolo1@studenti.unipi.it

CdSe quantum dots (QDs) are semiconductor nanocrystals that exhibit excellent optical and electronic properties, including their bright luminescence, a broad excitation profile, narrow emission peaks, and exceptional photostability [1]. In addition, their optical and electrical properties are highly size-dependent. In this present work, we investigate the quantum size effect in CdSe quantum dots. By tuning the growth process time of CdSe quantum dots, we can tune the size and consequently the absorption and the photoluminescence emission of the quantum dots. The synthesis of cadmium selenide quantum dots was performed via hot injection method, using the oleic acid as the primary ligand and octadecene as the noncoordinating solvent with the addition of trioctylphosphine oxide like a secondary ligand following Quanqin Dai et al synthetic approach [2], this approach leads to improve the size distribution of CdSe quantum dots. The obtained CdSe QDs at different growth times from 60 s to 3000 s exhibited a emission wavelength ranging from 516 to 595 nm and an average diameter from 1.5 nm to 4 nm.
Another phenomenon that depends critically on CdSe particle size is the photoinduced electron transfer to an appropriate molecule bound to the nanoparticle surface, such as buckminsterfullerene derivatives. [3] The electronic transfer occurs through the migration of the excitons, promoted by light, starting from the nanoparticles (donor) towards an adsorbed C_{60} derivative (acceptor). This photo-induced process is highly dependent on the size of the NPs.

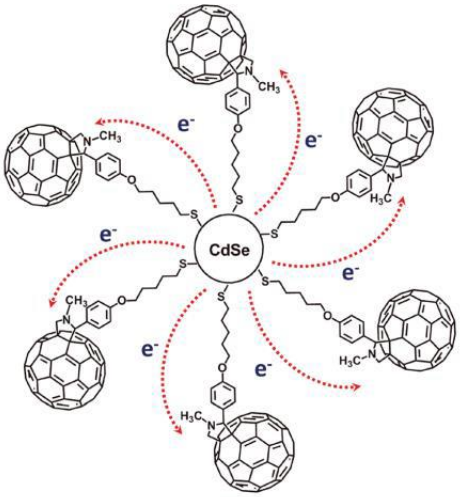


Figure 1. schematization of electron transfer

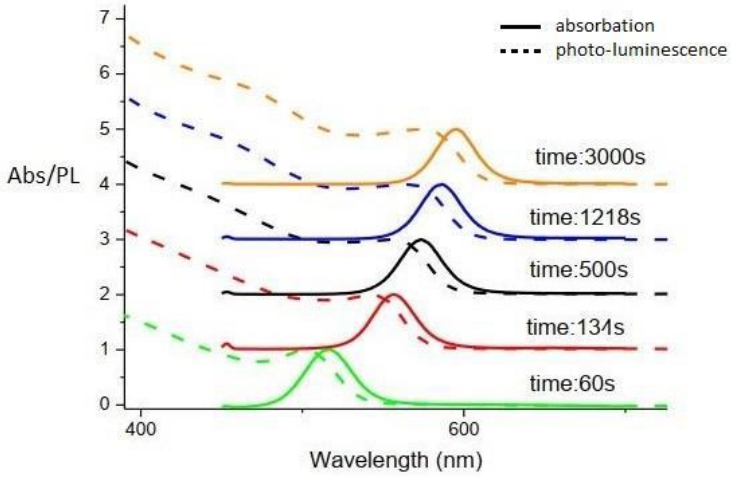


Figure 2. Abs and PL spectra of CdSe QDs at different times of growth process.different times of growth process

References:
[1] Resch-Genger, U.; Grabolle, M.; Cavaliere-Jaricot, S.; Nitschke, R.; Nann, T. Quantum Dots versus Organic Dyes as Fluorescent Labels Nat. Methods 2008, 5, 763– 775
[2] Quanqin D. et al., Colloidal CdSe Nanocrystals Synthesized in Noncoordinating Solvents with the Addition of a Secondary Ligand: Exceptional Growth Kinetic, J. Phys. Chem. B 2006, 110, 16508-16513.
[3] Jin Ho Bang and Prashant V. Kamat; ACS, CdSe Quantum Dot-Fullerene Hybrid Nanocomposite for Solar Energy Conversion: Electron Transfer and Photoelectrochemistry, vol. 5, no. 12, 9421–9427, 2011

Structure based effects on near-infrared chiroptical properties of lanthanide complexes

OLIVER G. WILLIS,[1] FRANCESCO ZINNA,[1] LORENZO DI BARI[1]

[1]*Dipartimento si Chimica e Chimica Industriale, Università* di Pisa, Pisa, Italy
oliver.willis@phd.unipi.it

Circularly polarized light (CPL) is paramount to many current and future technologies. Devices which emit polarized light have great importance for emerging technologies. Various ytterbium and other lanthanide complexes with different organic ligands and a defined stereochemistry have been prepared which show chiroptical activity within the near-infrared (NIR) region. Chiroptical properties in the NIR region can be investigated to gain insight into structure-property relationships. Greater understanding of how the scaffolds of lanthanide complexes influence the chiroptical response will help future rational design of complexes with strong CPL activity. Developing NIR-CPL emitters may have applications ranging from CPL-based (bio)-assays to chiral optoelectronics and telecommunications.

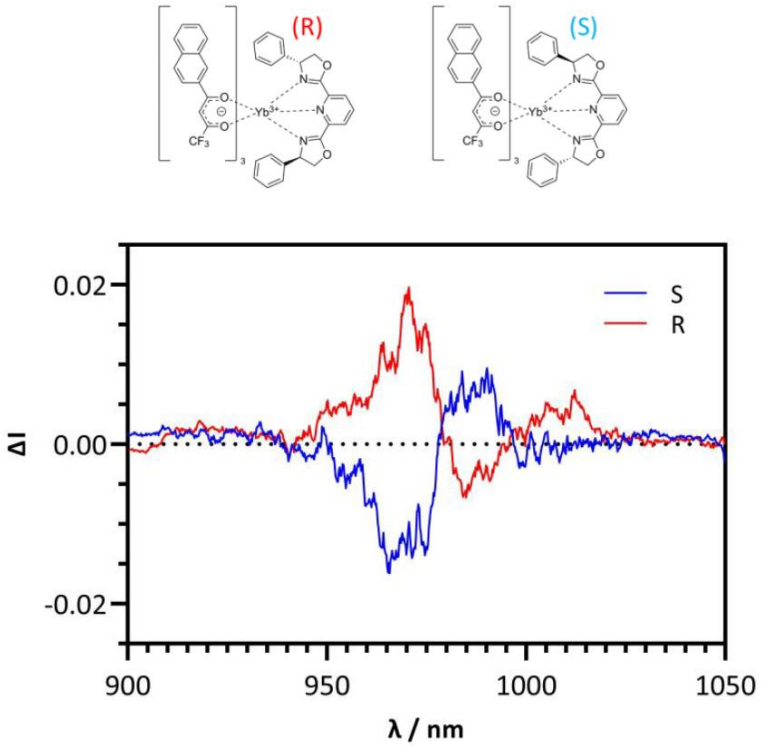


Figure 1. NIR-CPL spectrum of two enantiomers of a novel ytterbium complex.

References:
[1] F. Zinna, U. Giovanella and L. Di Bari, *Adv. Mater.*, 27, 1791–1795 (2015).
[2] S. Di Pietro and L. Di Bari, *Inorg. Chem.*, 51, 12007–12014 (2012).
[3] D. Shirotani, H. Sato, K. Yamanari and S. Kaizaki, *Dalt. Trans.*, 41, 10557–10567.(2012).
[4] J. R. Robinson, X. Fan, J. Yadav, P. J. Carroll, A. J. Wooten, M. A. Pericàs, E. J. Schelter and P. J. Walsh, *J. Am. Chem. Soc.*, 136, 8034–8041 (2014).
[5] L. Di Bari, M. Lelli, G. Pintacuda, G. Pescitelli, F. Marchetti and P. Salvadori, *J. Am. Chem. Soc.*, 125, 5549–5558 (2003).
[6] F. Zinna, L. Arrico and L. Di Bari, *Chem. Commun.*, 55, 6607–6609 (2019).

A Fragment Diabatization Linear Vibronic Coupling Model for Quantum Dynamics of Photoexcited DNA BasePairs

M. YAGHOUBI JOUYBARI[1], J. GREEN2, H. ASHA[2], R. IMPROTA[2], F. SANTORO[1]

[1]CNR-ICCOM, Area della Ricerca, via G. Moruzzi 1, I-56124, Pisa, Italy
[2]CNR-IBB, via Mezzocannone 16, 80134, Naples, Italy.
martha.yaghoubi@pi.iccom.cnr.it

Multichromophoric systems (MS) contain a broad family ranging from light-harvesting systems to nucleic acides, with a wide range of applications and novel properties[1]. Unique optoelectronic properties of MS, highly efficient excitation energy transfer and electron transfer, made them an appealing target to study in detail their excited-state dynamics. The population of delocalized (over multiple chromophores) and localized (on a single chromophore) excited states and the formation of Charge Transfer states are the main photoactivated processes in MS and they are usually described by excitonic Hamiltonians which focus on inter-molecular (from one chromophore to another) processes. On the other side, in excitonic Hamiltonians, the internal conversion or intersystem crossing between local excitations in individual chromophores are ignored. However, in many MS such as DNA, the timescale of intra-system processes on individual chromophores is similar to those of inter-molecular ones, and therefore, the competition between these two decay processes needs to explicitly investigated. In DNA, an example of MS, base-pairs, i.e. complementary purine and pyrimidine bases interacting through hydrogen bonds, are stacked in a double-helix arrangement.

In this contribution, we aim to study the competion of energy and charge transfer and internal conversions in MS with a fully quantum dynamical approach. To that end, we introduce an effective fragment-based diabatization (FrD)[2,3]. The FrD-LVC Hamiltonian is parameterized with TD-DFT calculations. For the quantum dynamics calculation, we adopted ML-MCTDH method using Quantics package. In this framework, we define diabatic states based on reference states as local excitations on individual fragments and orbital transitions between fragments to describe charge transfer (CT) states. In this study, we apply this method to investigate the excited-state dynamics of guanine-cytosine and adenine-thymine Watson-Crick DNA base pairs as an archetypal example of MS with intra and inter-molecular decay pathways. Here, we consider several diabatic electronic states that are potentially involved in the dynamics and all vibrational modes of the two base-pairs. The calculations predict that for initial photo-excitation on the first two bright states, $\pi\pi^* \rightarrow$ CT is the main decay pathway for deactivation of GC, whereas in AT, internal conversion of $\pi\pi^*$ to $n\pi^*$ plays a fundamental role in the decay process.

References:
[1]Teo, Y. N., Kool, E. T. *Chemical reviews*, *112*(7), 4221-4245 (2012)..
[2]Green, J.A., Asha, H., Santoro, F. and Improta, R., 17,405-415 *(2020).*
[3]Green, J.A., Jouybari, M.Y., Aranda, D., Improta, R. and Santoro, F., *Molecules*, *26*(6), 1743 (2021).

Invited Speakers

Mario Barbatti – Institut de Chimie Radicalaire of the Aix-Marseille University (FR)

Peter Dubruel – Ghent University (BE)

Concetta Giancola – Università di Napoli Federico II (IT)

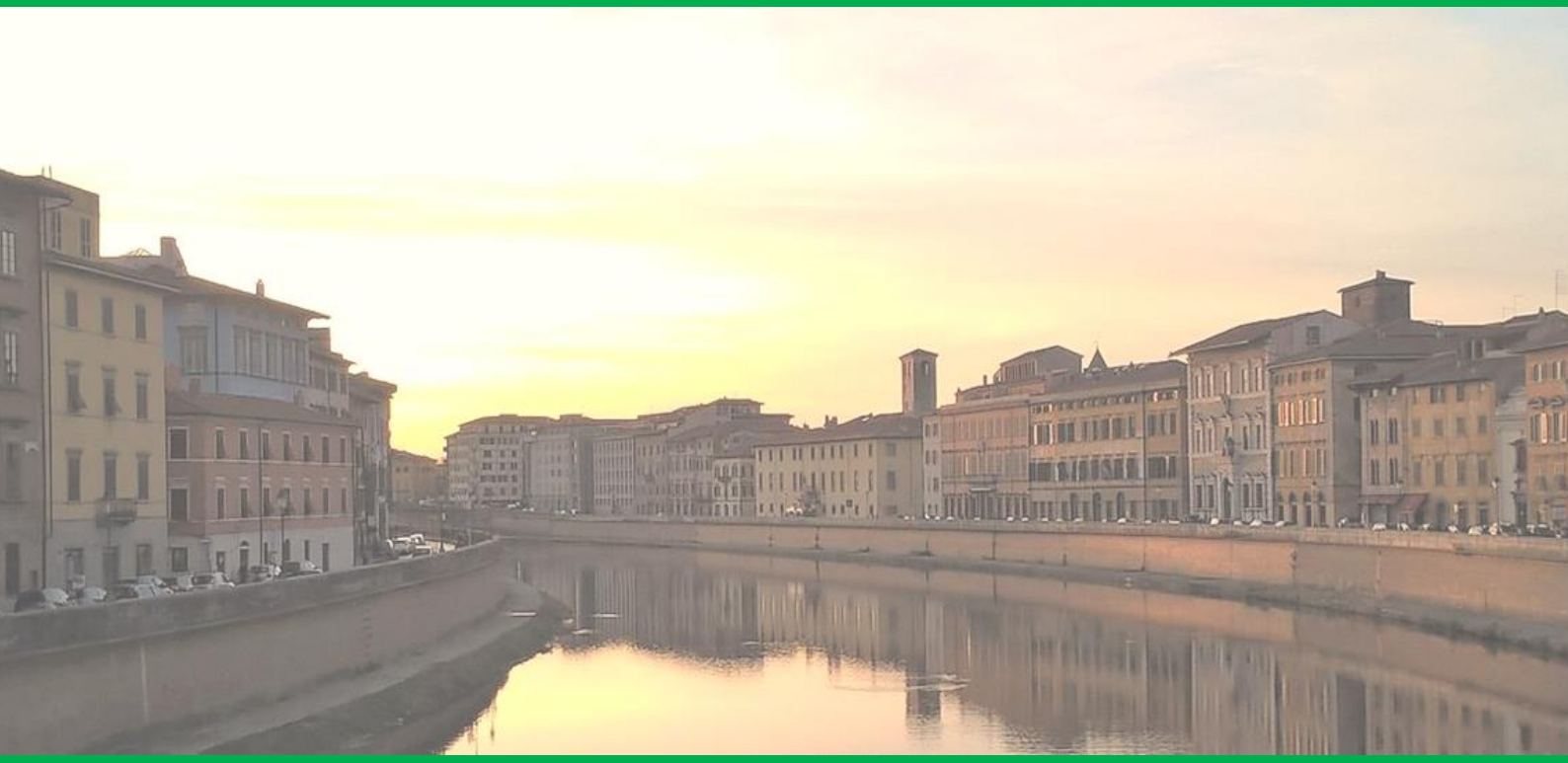
Wolfgang Kroutil – University of Graz (AT)

Paolo Melchiorre – ICIQ Tarragona (ES)

Giulia Mollica – Institut de Chimie Radicalaire of the Aix-Marseille University (FR)

Robert Pal – University of Durham (UK)

Peter J. Sadler – University of Warwick (UK)



The Organizing Committee – 2nd year PhD Students of DSCM