



Groupe Français de
Photochimie,
Photophysique et
Photosciences (GFP2P)



Gruppo Italiano di Fotochimica
(GIF)



Société Française de
Photobiologie (SFPb)



Società Italiana di Fotobiologia
(SIFB)

First Joint Congress of the French and Italian Photochemists and Photobiologists



Bari, Ex-Palazzo delle Poste
September 19 – 22, 2016

Booklet of Abstracts

First Joint Congress of the French and Italian Photochemists and Photobiologists

Joint Meeting of the



Groupe Français de Photochimie,
Photophysique et Photosciences (GFP2P)



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Société Française de Photobiologie (SFPb)



Società Italiana di Fotobiologia (SIFB)

**Bari, Ex-Palazzo delle Poste
September 19-23, 2016**

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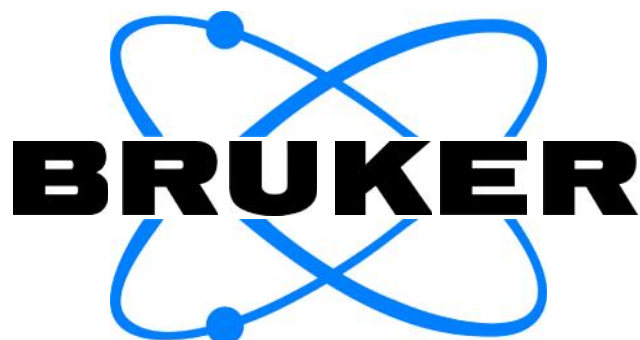
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Conference Program

Monday 19th September

14.00 Opening Ceremony

Chairperson: E. Sage

14.45 **Plenary: J. Piette** (Liège, BE) *RIP3 antagonizes a TSC 2-mediated pro-survival pathway in Photodynamic therapy-induced glioblastoma cell death*

15.30 **P. Arnoux** (Nancy, FR) *New trends in photodynamic therapy*

15.45 **A. Mazzaglia** (Messina, IT) *Folate-decorated amphiphilic cyclodextrin/pheophorbide nanoassemblies for targeted PDT*

15.45 **É. Ishow** (Nantes, FR) *Hybrid multimodal nanoparticles as nano swiss-knives for diagnostics*

16.15 **M. Bocé** (città) *Efficient NO release by trans- and cis-(Cl,Cl)-[Ru^{II}(FT)Cl₂(NO)](PF₆) under excitation in the NIR region*

16.30 **D. Vione** (Torino, IT) *Photochemical reactions in sunlit lake waters*

16.45 **COFFEE BREAK**

Photochemistry

Chairperson: S. Sortino

17.15 **Keynote (PhD Prize): R. Mazzarro** (Bologna, IT) *Solar energy conversion performed by solution-processed silicon nanocrystals*

17.45 **F. Loiseau** (Grenoble, FR) *A Ruthenium(ii)–Copper(ii) dyad for the photocatalytic oxygenation of organic substrates mediated by dioxygen*

18.00 **E. La Mazza** (Messina, IT) *Ultrafast energy transfer in a new dendritic antenna based on a new 1,3,5-triazine ligand*

18.15 **M. Marchini** (Bologna, IT) *Pimerization drives supramolecular polymerization of a shape-persistent tetrahedral molecule bearing four bipyridinium units*

18.30 **P. Changenet-Barret** (Palaiseau, FR) *Conformational relaxation of 1,1'-Bi(2-naphthol) derivatives probed by subpicosecond circular dichroism*

18.45 **M. Natali** (Ferrara, IT) *Photoinduced Charge Separation in Porphyrin Ion-Pairs*

Photobiology

Chairperson: M. Sliwa

Keynote: D. Kirilovsky (Gif-sur-Yvette, FR) *The Photoactive Orange Carotenoid Protein and Photoprotection in Cyanobacteria*

C. Brunet (Napoli, IT) *Photodefence responses of coastal diatoms: role of light spectrum*

M. Landi (Pisa, IT) *Physiological response of red versus green morphs of sweet basil to high solar irradiances: what type of photoprotection?*

D. Piano (Cagliari, IT) *The S-layer as a UV-radiation shield: the case of Deinococcus radiodurans and its S-layer Deinoxanthin Binding Complex*

M. Jaubert (Paris, FR) *Diatom phytochromes reveal the existence of far-red light based sensing in the ocean*

S. la Gatta (Bari, IT) *Heptamethine cyanine dyes working as light harvesting antennas in biohybrid photosynthetic assemblies*

Tuesday 20th September

Photochemistry

Chairperson: S. Campagna

- 09.00 **Keynote (GIF YIA): F. Monti** (Bologna, IT) *Luminescent transition-metal complexes for lighting*
- 09.30 **Keynote (GIF YIA): D. Ravelli** (Pavia, IT) *Photocatalytic Hydrogen Atom Transfer (HAT) reactions in synthesis*
- 9.45
- 10.00 **M. La Rosa** (Bologna, IT) *Photoactive Nanohybrids Based on Chemically Functionalized Semiconductor Quantum Dots*
- 10.15 **C. Raviola** (Pavia, IT) *Photochemistry of 2-halothiophenes: a journey from heteroaryl radical to heteroaryl cation*
- 10.30 **T. M. G. Salerno** (Messina, IT) *Localization-controlled two-colour luminescence imaging via environmental modulation of energy transfer in a BODIPY dyad*

10.45 COFFEE BREAK

Chairperson: E. Sage

- 11.15 **Keynote: P. Pallavicini** (Pavia, IT) *Gold nanostars: versatile nanoparticles for photothermal action and two-photon luminescence tracking*
- 10.30 **N. D. McClenaghan** (Talence, FR) *Message in a Bubble: Phototriggered Events in Microdomains*
- 10.30 **H.-P. Lassalle** (Nancy, FR) *Characterization of PAMAM-Ce6 dendrimeric nanoparticles for photodynamic treatment*
- 10.30 **R. Méallet-Renault** (Orsay, FR) *Luminescent Superhydrophobic surfaces for anti-microbial adhesion and anti-biofilm applications*
- 10.30 **M. Erard** (Orsay, FR) *Quantitative analysis of protein-protein interactions in live cell using the new generation of cyan fluorescent proteins. Application to the NADPH oxidase complex*

Photobiology

Chairperson: G. Miolo

- Keynote: M. D. Galibert** (Rennes, FR) *Ultraviolet Radiation: "Dr. Jekyll or Mr Hyde"?*
- A. Ferino** (Udine, IT) *Role of the NF- κ B/Snail/RKIP loop in the response to PDT treatment in pancreatic carcinoma cells*
- P. Marchesani** (San Giovanni Rotondo, IT) *Laser therapies for treating chronic pain and for increasing wellbeing*
- J. Bertrand** (Orsay, FR) *UVB represses melanocytes cell migration through S-catenin*
- J.-P. Souchard** (Toulouse, FR) *Synthesis, physico-chemical properties, cellular penetration and photodynamic antiproliferative activity on MCF7 breast cancer cell line of new rose bengal-estradiol conjugates*
- A. Bour** (Paris, FR) *Photo-induced oxidation of bio-mimetic membranes*

12.45 **LUNCH**

Chairperson: D. Bassani

- 14.15 **Keynote: M. Sliwa** (Villeneuve d'Ascq, FR) *Ultrafast photodynamics of photo-switchable fluorescent proteins: ultrafast absorption spectroscopy and serial femtosecond crystallography*
- 14.45 **C. Mastrodonato** (Talence, FR) *New quadrupolar dyes as sensitive pH probes for two-photon imaging*
- 15.00 **J. Manzi** (Bologna, IT) *Real-time pH measurements in growing inorganic structures by fluorescence imaging*
- 15.15 **A. Espagne** (Paris, FR) *Ultrafast Dynamics of a GFP Chromophore Analogue: Competition between Excited-State Proton Transfer and Torsional Relaxation*

15.30 **COFFEE BREAK**

- 16.00 **R. Chahboune** (Aubière, FR) *Hydrogen Peroxide as an efficient photo-inducer for the complete degradation of organic pollutants: kinetics and analytical studies*
- 16.15 **M. Liberi** - *Bruker Sponsored presentation*

16.30 **POSTER FLASH PRESENTATION**

17.15 **POSTER SESSION**

18.30 **GENERAL ASSEMBLY OF SOCIETIES**

Wednesday 21st September

Chairperson: A. Credi

- 09.00 **Plenary: L. De Cola** (Strasbourg, FR) *Seeing, understanding and controlling self-assembly of luminescent species*
- 09.45 **V. Peings** (Pau, FR) *Coupling photocatalysts and ferrate oxidation: towards an innovative solution for wastewater treatment*
- 10.00 **I. Grigioni** (Milano, IT) *The exchange of photogenerated charge carriers between WO_3 and $BiVO_4$ in coupled $WO_3/BiVO_4$ systems*
- 10.15 **F. Milano** (Bari, IT) *The photoelectrochemical domain of bacterial photosynthesis*
- 10.30 **M. Baroncini** (Bologna, IT) *An artificial molecular pump powered by light energy*

10.45 **COFFEE BREAK**

- 11.15 **Keynote: T. Douki** (Grenoble, FR) *Recent advances in the formation of DNA damage by UV radiation: from test tube experiments to human skin*
- 11.45 **E. Bignon** (Villeurbanne, FR) *Modelling the structure and triplet-triplet energy transfer of the 6-4 photoproduct*
- 12.00 **Lara Martinez-Fernandez** (Napoli, IT) *Photophysical and photochemical processes in AT-DNA: insights from Quantum Mechanical calculations*
- 12.15 **H. Gattuso** (Vandoeuvre-les-Nancy, FR) *Two-photon-absorption DNA photosensitization, modeling the production of solvated electrons*
- 12.30 **T. Gustavsson** (Gif-sur-Yvette, FR) *Effect of methylation on cytosine*

12.45 **LUNCH**

Photochemistry

Chairperson: C. Vevvert-Bizet

- 14.15 **Marta Penconi** (Milano, IT) *Degradation mechanism in Flrpic: blue phosphorescent OLED emitter*
- 14.30 **C. Remy** (Cachan, FR) *Synthesis and spectroscopic studies of fluorescent molecular receptors for the detection of atrazine and melamine derivatives*
- 14.45 **L. Ravotto** (Bologna, IT) *Shining light on benzodipyrrens: from NIR-emissive complexes to hydroperoxide sensing and “dial-a-color” fluorescence*
- 15.00 **F. Romano** (Bologna, IT) *Water-Soluble Photoluminescent Silicon Quantum Dots*
- 15.15 **S. Lazzaroni** (Pavia, IT) *Vegetable oils-derived resins for stereolithography*

Photobiology

Chairperson: P. Vicendo

- F. Barra** (Napoli, IT) *Photodynamic Therapy with 5-Aminolaevulinic Acid and Nuclear Injury: Role of ABCG2 in Preventing DNA damage*
- G. Rea** (Roma, IT) *Photochemical characterization of Chlamydomonas mutants for biotechnological applications*
- G. Sed** (Roma, IT) *Study and development of photobioreactors (PBRs) analyzing geometry effects on microalgal biomass growth in residual light*
- F. Palomba** (Bologna, IT) *Mastering Surface Interaction of New Theranostic Nanomaterials*
- S. Ruscigno** (Bari, IT) *Mucus-penetrating lipid nanovesicles for pulmonary drug delivery*

15.30 **COFFEE BREAK**

Photochemistry

Chairperson: G. Bourg-Heckley

- 1600 **Keynote: M. Brigante** (Clermont-Ferrand, FR) *Understanding the role of chemistry in atmospheric water: the key role of photochemists*
- 16.30 **V. Rizzi** (Bari, IT) *Photoactive chitosan films*
- 16.45 **A. Bianco** (Clermont-Ferrand, FR) *Photochemistry in cloud waters: reactivity and fate of organic compounds*
- 17.00 **J. Chauvin** (Grenoble, FR) *Photocatalytic reduction of CO₂ mediated by [Os(diimine)(CO)₂Cl₂] precursor catalyst*

Photobiology

Chairperson: T. Gustavsson

- Keynote: G. Romano** (Firenze, IT) *Ingestible device for intragastric PDT against Helicobacter pylori*
- S. Manfredini** (Ferrara, IT) *Oxisol: a new dualistic molecule endowed with very potent antioxidant and uv-booster properties for skin photo-oxidative protection*
- R. Boudjemaa** (Orsay, FR) *Micro to nanometric optical imaging resolution to better understand bacterial biofilms persistence: in vitro and in vivo visualization and characterization of antibiotics action*
- S. Lembo** (Salerno, IT) *Light-independent pro-inflammatory and pro-oxidant effects of purified human hair melanins on keratinocyte cell cultures*

- 17.15 **G. Ragazzon** (Bologna, IT) *Fluorescence lifetime measurements and pH titrations as tools to expand the knowledge on a switchable [2]rotaxane*
- 17.15 **H. Azaari** (Rabat, MA) *Influence of parameters in photocatalytic degradation of chloridazon herbicide in aqueous solution*
- 17.15 **M. Venturini** (Brescia, IT) *Daylight Photodynamic Therapy in the treatment of mild and/or moderate Actinic Keratosis of the face and/or the scalp*
- 17.15 **A. Zanca** (Brescia, IT) *Reflectance confocal microscopy allows in vivo real-time noninvasive assessment of the outcome of methyl aminolaevulinate photodynamic therapy of basal cell carcinoma*
- 18.00 **SOCIAL EVENT AND DINNER**

Thursday 22nd September

Photochemistry

Chairperson: R. Méallet-Renault

- 09.00 **Keynote: R. Métivier** (Cachan, FR) *Enhanced fluorescence photoswitching in multichromophoric molecules and nanosystems*
- 09.30 **O. Soppera** (Mulhouse, FR) *Molecularly imprinted polymers for sensor applications by photopolymerization*
- 09.45 **D. Vona** (Bari, IT) *Photonic platforms and fluorescent mesoporous scaffold: diatoms as a new tool for materials*
- 10.00 **B. Storti** (Pisa, IT) *Interlacing biophysical methods to unveil morphology and dynamical interactions with microtubules of transient receptor potential vanilloid 1 (TRPV1) at nanoscale in living cells*
- 10.15 **G. Longobucco** (Ferrara, IT) *Emerging Pollutants Photo-Oxidation by WO₃*
- 10.30 **M. Louis** (Cachan, FR) *Bistable mechanofluorochromic materials based on difluoroboron S-diketone dyes*

Photobiology

Chairperson: E. Reddi

- Keynote: F. Quaglia** (Napoli, IT) *Polymeric nanoparticles for combined photo/chemo-therapy*
- S. Bonneau** (Paris, FR) *Berberine as a Photosensitizing Agent for Antitumoral Photodynamic Therapy: Insights into its Association to Low Density Lipoproteins*
- E. Caruso** (Varese, IT) *Photodynamic activity of a diarylic-porphyrin linked to a biocompatible polymeric nanostructure*
- S. Mariano** (Lecce, IT) *In vivo and in vitro comparative study of uptake of silver and gold nanoparticles exploitable in the context of photodynamic therapy*
- F. Mammano** (Padova, IT) *Effects of focal photodynamic therapy on cancer cells in vitro and in mouse models in vivo*
- G. Zampini** (Perugia, IT) *Nanomodulation of singlet oxygen and bacterial inactivation efficiency by silica-PpIX nanocomposites*

10.45 **COFFEE BREAK**

Chairperson: F. Fusi

11.15 **Keynote: R. Pini** (Sesto Fiorentino, IT) *Photo-active plasmonic nanoparticles for biomedical applications*

11.45 **S. Fery-Forgues** (Toulouse, FR) *Conjugates of benzoxazole and GFP chromophores with AIE behavior: polymorphism, rigidochromism, nanoparticles and cell uptake*

12.00 **R. Grasso** (Catania, IT) *Delayed luminescence spectroscopy from human glioblastoma cells to monitor the effects of drug-loaded nanostructured lipid carrier*

12.15 **J. Boucard** (Nantes, FR) *Photo- and magneto-activity tuning of bimodal hybrid nanoassemblies as contrast agents*

12.30 **F. Petronella** (Bari, IT) *Novel multifunctional nanocrystalline UV and Visible light active photocatalysts for environmental applications*

12.45 **CLOSING REMARKS**

PLENARY LECTURES

RIP3 antagonizes a TSC 2-mediated pro-survival pathway in Photodynamic therapy-induced glioblastoma cell death

Gregory Fettweis, Emmanuel Di Valentin, Laurent L'homme, Cédric Lassence,
Franck Dequiedt, Marianne Fillet, Isabelle Coupienne and Jacques Piette

Laboratory of Virology & Immunology, GIGA-Research, B34, University of Liège, B-4000 Liège, Belgium

Glioblastoma are the deadliest type of brain cancer and are frequently associated with poor prognosis and a high degree of recurrence despite removal by surgical resection and treatment by chemo- and radio-therapy. Photodynamic therapy (PDT) is a treatment well known to induce mainly necrotic and apoptotic cell death in solid tumors. 5-aminolevulinic acid (5-ALA)-based PDT was recently shown to sensitize human glioblastoma cells (LN-18) to a RIP3 (Receptor Interacting Protein 3)-dependent cell death which is countered by activation of autophagy. These promising results led us to investigate the pathways involved in cell death and survival mechanisms occurring in glioblastoma following PDT. In the present study, we describe a new TSC2 (Tuberous Sclerosis 2)-dependent survival pathway implicating the p38 and MK2 (MAPKAPK2) kinases. Moreover, we characterized a new RIP3/TSC2 complex whose formation is under the control of 14-3-3 proteins. In this complex, RIP3 promotes cell death by targeting the TSC2 survival pathway. These results highlight (i) a new role of TSC2 to protect glioblastoma against PDT-induced cell death and (ii) TSC2 and 14-3-3 as new RIP3 partners.

Seeing, understanding and controlling self-assembly of luminescent species

Luisa De Cola

Institute de Science et d'Ingénierie Supramoléculaires (I.S.I.S.),
Université de Strasbourg and KIT, Germany (decola@unistra.fr)

Luminescent molecules that can undergo self-assembly are of great interest for the development of new materials, sensors, biolabels.... The talk will illustrate some of the recent results on soft structures based on metal complexes able to aggregate in fibers, gels and soft mechanochromic materials [1]. The use of platinum complexes as building block for luminescent reversible piezochromic and mechanochromic materials will be illustrated. The emission of the compounds can be tuned by an appropriate choice of the coordinated ligands as well as of their aggregation in different structures. The formation of soft assemblies allows the tuning of the emission color, by pressure and temperature leading to a new class of materials possessing reversible properties. We demonstrate how even small changes in molecular design can completely inhibit or enhance the formation of organized supramolecular architectures, leading to a deep understanding of the key factor affecting the whole self-assembly process.

For some of the compounds we have indeed unraveled a highly complex supramolecular landscape comprising two kinetic assemblies and the thermodynamic isoform. We have not only characterized all the assemblies, but also the full chemical management is successfully achieved by the proper use of supramolecular and photochemical approaches. The monitoring of the different emission properties, used as fingerprint for each of the assembled species, allowed an unprecedented real-time visualization of the evolving self-assemblies [2]. We have been able to control the assemblies and obtain uniform size of the aggregate that can even be converted in a thermodynamic unstable species by light. The full control of multiple pathways opens the way to design complex systems in and out of their thermodynamic equilibrium.

The assembly processes can also be studied in confined spaces. The use of zeolites and mesoporous silica able to entrap precursor for the formation of metal cluster or the isolation of desired polymorphs with defined properties is also shortly illustrated [3].

References

- [1] C. A. Strassert, L. De Cola et al. *Angew. Chem. Int. Ed.*, **2011**, *50*, 946; M. Mauro, L. De Cola et al. *Chem. Commun.* **2014**, *50*, 7269
- [2] A. Aliprandi, M. Mauro, L. De Cola *Nature Chemistry*, **2016**, *8*, 10-15
- [3] L. Donato, E.A. Prasetyanto, C. Rosticher, L. De Cola submitted

KEYNOTE LECTURES

Solar energy conversion performed by solution-processed silicon nanocrystals

Raffaello Mazzaro^{1,2*}, Antonino Arrigo¹, Marica Canino²,
Francesco Romano¹, Giacomo Bergamini¹, Paola Ceroni¹

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Silicon nanocrystals (SiNCs) in the quantum size range (2-12 nm) are attracting an increasing interest: on the contrary of bulk silicon, they display a bright emission, which can be tuned from the visible to the near-infrared spectral region by increasing their size. Compared to more traditional quantum dots, such as CdSe, SiNCs offer the following advantages: silicon is abundant, easily available and essentially non toxic, it can form covalent bonds with carbon, thereby offering the possibility of integrating inorganic and organic components in a robust structure¹. Moreover, being Si an indirect band gap semiconductor, the photophysical properties of SiNCs are characterized by an extremely large Stokes shift, long phosphorescence lifetimes and photoluminescence quantum yield as high as 45%. These properties, together with the interest in materials compatible with the Si-based technology, promote SiNCs as ideal candidates for sensing and photovoltaic applications. In particular for the conversion of sunlight to electrical energy, the energy provided by the UV component of the solar spectrum can be down-converted by SiNCs to visible light, matching the typical high responsivity region of conventional Si-based or dye sensitized solar cells.

In this contribution, the implementation of SiNCs in cutting-edge photovoltaic technologies will be discussed. Specifically, the embedding of these nanocrystals in polymer matrix was exploited to prepare semi-transparent polymer waveguides and the photophysical properties of embedded SiNCs were deeply investigated². In addition to this, the photovoltaic performance of the prepared plates as solar concentrators will be reported, demonstrating the feasibility and the promising features of SiNCs based integrated photovoltaics.

This research is supported by the European Commission ERC Starting Grant (PhotoSi, 278912).

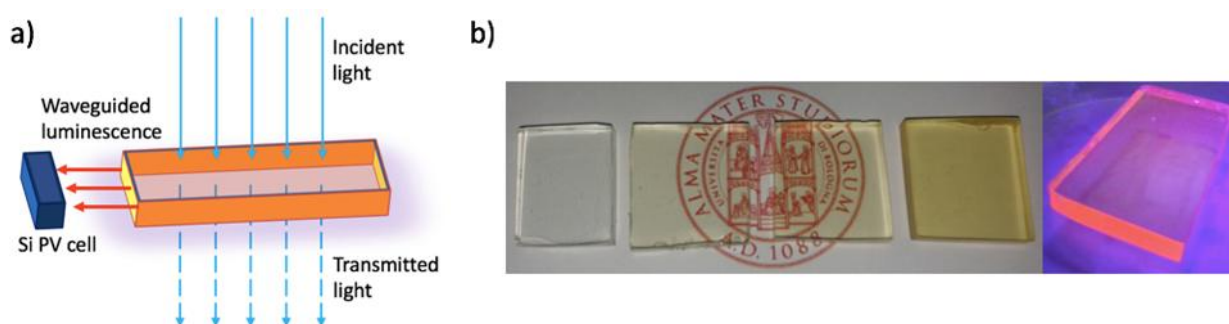


Fig. 1 a) Schematic representation of a the proposed photovoltaic device; b) Picture of polymer plates embedding SiNCs under visible and UV light.

References

1. Mazzaro, R. *et al.* Photoinduced Processes between Pyrene-Functionalized Silicon Nanocrystals and Carbon Allotropes - *St. Chem. Mater.* **27**, 4390–4397 (2015).
2. Coropceanu, I. & Bawendi, M. G. Core/Shell Quantum Dot Based Luminescent Solar Concentrators with Reduced Reabsorption and Enhanced Efficiency. *Nano Lett.* **14**, 4097–4101 (2014).

The Photoactive Orange Carotenoid Protein and Photoprotection in Cyanobacteria

Diana Kirilovsky

Institute for Integrative Biology of the Cell (I2BC), CEA, CNRS, Université Paris-Sud, Université Paris-Saclay, 91198 Gif sur Yvette, France and Institut de Biologie et Technologies de Saclay (iBiTec-S), CEA, 91191 Gif-sur-Yvette, France.

The photoactive Orange Carotenoid Protein (OCP) photoprotects cyanobacteria cells by quenching excess energy absorbed by phycobilisomes (PBSs), the cyanobacterial antenna, and by directly interacting with singlet oxygen. Both, the dark orange form (OCPo) and the photoactivated red light form (OCPr) quench singlet oxygen. In contrast, only OCPr is able to bind PBSs and to quench excess energy. Light absorption by the carotenoid provokes a break of the hydrogen bonds between its keto group and the protein inducing a reorganization of the protein, its opening and the translocation of the carotenoid. In the opening of the OCP, the amino acid interactions in the central interface between the C-terminal (CTD) and the N-terminal domains (NTD) and those between the N-terminal arm and the CTD are broken. The carotenoid-protein interactions are completely different in the orange and red forms. The NTD of OCPr binds to the core of PBS between two allophycocyanin trimers. The Fluorescence Recovery Protein (FRP) by binding to the CTD of the bound OCPr helps the detachment of the OCP from the PBS and then accelerates the dark reversion OCPr to OCPo. In many cyanobacteria, multiple copies encoding homologues to OCP-NTD and one homologue to the CTD-OCP are dispersed in their genomes. All the NTD homologues named Helical Carotenoid Proteins (HCP) attach a carotenoid but have distinct functions. Only one is able to bind PBS and to quench energy, two are very good singlet oxygen scavengers and the fourth one is involved in an unknown mechanism. The interaction between HCPs and the CTD homologous and the construction of a photoactive OCP-like including these proteins are studied.

Luminescent transition-metal complexes for lighting

Filippo Monti and Nicola Armaroli

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The European Union set the ambitious target of reducing the final energy consumption by 20% within 2020. This goal demands a remarkable change in how we generate and consume energy and urgently calls for an aggressive policy on energy efficiency. Since almost 20% of the European electrical energy is used for lighting, considerable savings can be achieved with the development of novel and more efficient lighting concepts [1].

In the last decades, several outstanding goals have been achieved in this area, for instance with the invention of blue Light-Emitting Diodes (LED), which was awarded the Nobel Prize in Physics in 2014, and the commercialization of the first displays based on Organic Light-Emitting Diodes (OLEDs), allowing the fabrication of flexible and ultrathin luminescent surfaces.

Within this framework, our research group has been involved in the development of a new concept for flat and flexible electroluminescent devices, i.e. the Light-Emitting Electrochemical Cells (LECs) [2a]. Such devices rely on a much simpler architecture compared to OLEDs and they are therefore expected to be a viable low-cost alternative to the technologies already on the market [2].

In this talk, some of the objectives we accomplished in the development and characterization of emitting materials for LECs will be presented. The first part of the presentation will be focused on cationic cyclometalated iridium(III) complexes, with a particular emphasis on deep-blue emitting materials since they turned out to be rather challenging due to emission red-shift in the solid state and instability under operative conditions [3].

In the second part, cationic copper(I) complexes as a potential alternative to iridium(III) counterparts will be discussed [4]. Iridium, in fact, is one of the rarest elements on the Earth crust and, therefore basing a large-scale lighting industry on this metal might be unrealistic. Copper, on the other hand, is much more abundant and cheaper, but exhibits several drawbacks if used as metal center for luminescent complexes, such as limited color tunability and low stability in the devices.

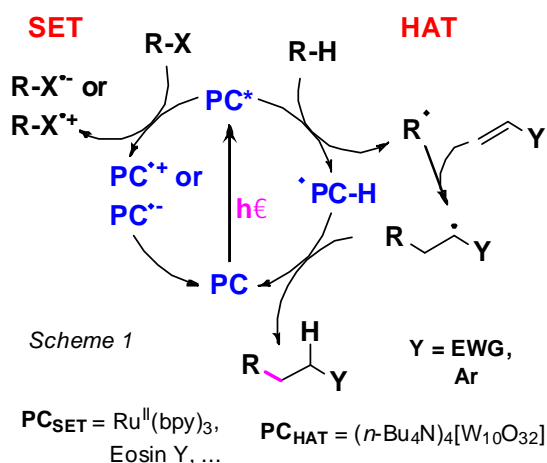
1. (a) L. S. Brown, Plan B. Mobilizing to save the civilization, W. W. Norton & Company, New York, 2009. (b) Light's Labour's Lost - Policies for Energy-efficient Lighting, tech. rep., International Energy Agency, 2006.
2. (a) <https://www.cello-project.eu/> (b) R. D. Costa et al., *Angew. Chem., Int. Ed.*, 2012, 51, 8178.
3. (a) N. M. Shavaleev et al., *Inorg. Chem.*, 2012, 51, 2263; (b) F. Monti et al., *Inorg. Chem.*, 2013, 52, 10292; (c) F. Monti et al., *Inorg. Chem.*, 2014, 53, 7709; (d) F. Monti et al., *Inorg. Chem.*, 2015, 54, 3031; (e) F. Monti et al., *Faraday Discuss.*, 2015, 185, 233.
4. (a) A. Kaeser et al., *Inorg. Chem.*, 2013, 52, 12140; (b) M. Mohankumar et al., *Chem. Eur. J.*, 2014, 20, 12083; (c) J.-J. Cid et al., *Polyhedron*, 2014, 82, 158.

Photocatalytic Hydrogen Atom Transfer (HAT) reactions in synthesis

Luca Capaldo, Stefano Protti, Angelo Albini, Maurizio Fagnoni and Davide Ravelli

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Photocatalytic reactions applied to organic synthesis have recently gained increasing attention, thanks to the unconventional pathways that become accessible in this way and the mild conditions involved, often in strict agreement with the general principles of Green Chemistry. These reactions are based on the use of a photocatalyst (PC, Scheme 1), a species that is responsible for light absorption and, once in the excited state, for the activation of the actual substrate of the reaction through a *chemical* step. [1] Among the peculiar activation modes of PC, two main fields can be recognized, viz. Single Electron Transfer (SET) and Hydrogen Atom Transfer (HAT) processes. The former approach is undoubtedly the most investigated one, where visible light absorbing Ru- and Ir-polypyridyl complexes, as well as organic dyes, led to the development of a hot topic, tagged as "photoredox catalysis with visible light". [1] These reactions involve the transfer of one electron between PC* and the substrate R-X, leading to the formation of the corresponding radical ion R-X^{•+} or R-X^{•-} (Scheme 1, left part). However, the main drawback of this strategy consists in the use of redox active reagents, matching the redox potentials of PC. By contrast, HAT processes offer the possibility of activating directly a C-H bond in the substrate (Scheme 1, right part). The main limitation to the development of this topic is represented by the number of PCs able to promote HAT steps, currently limited to the families of polyoxometalates and (aromatic) ketones. [2]



In recent years, we have developed a number of photocatalytic methods for the photogeneration of C-centered radicals and the ensuing addition onto C=C double bonds, including electron-poor olefins and vinyl aromatics. This strategy is based on the use of UV-light absorbing tetrabutylammonium decatungstate (TBADT, $(nBu_4N)_4[W_{10}O_{32}]$) as the photocatalyst. [3] Upon absorption of a photon, this compound cleaves homolytically (often with high chemo- and regioselectivity) C-H bonds in a variety of organic derivatives. [2,3] In this way, the smooth C(sp³)-H and C(sp²)-H functionalization of aldehydes, amides, ethers and acetals, as well as alkanes was achieved (see R-H in Scheme 1). Interestingly, this approach was demonstrated to work also under solar light irradiation [4] and could be optimized under flow conditions. [5]

Recent developments in the field of photocatalytic HAT processes involve the design and optimization of visible light absorbing photocatalysts, including porphyrin complexes and related derivatives.

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Ultraviolet Radiation: "Dr. Jekyll or Mr Hyde"?

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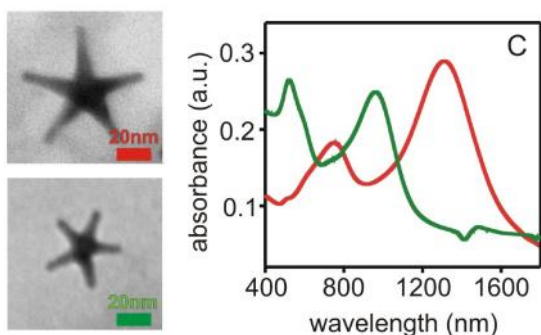
Ultraviolet (UV) radiation is essential for life but the most prominent skin threat. The effects of sun exposure are wide from pigmentation disorders to skin cancers, the latter being life threatening. Pigmentation is the most powerful protection towards the carcinogenic effect of UV exposure. Well-pigmented skins are clearly better protected from skin cancer than white Caucasian skin. The level of direct UV-induced DNA damage being lowered in pigmented skin. However it is now clear that the repertoire of effects mediated by the exposure to UV is not limited to direct DNA damage. Deciphering the role of UV exposure on gene expression as identifying the signaling pathways that are activated is thus essential. This will help to propose adapted tools to prevent and neutralize the adverse effects of solar exposure.

Gold nanostars: versatile nanoparticles for photothermal action and two-photon luminescence tracking

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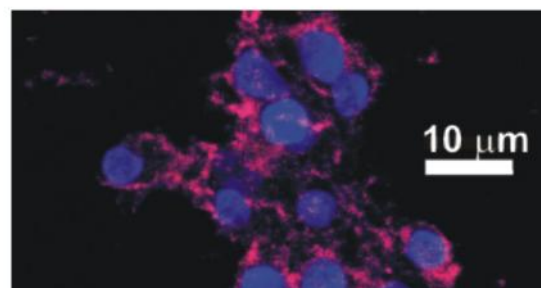
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Gold nanostars (GNS) are gold nanoparticles with a variable number of branches protruding from a core. We have developed synthetic approaches leading to the aqueous synthesis of GNS with controlled morphology, and in particular with a limited number of branches (2-6) protruding from the core and presenting an overall flat shape.[1,2] Such GNS are synthesized with a seed-growth approach, using weakly interacting surfactants as protecting/directing agents. The latter can be easily displaced from the gold surface by any molecule bearing groups with high Au affinity, such as thiols and disulphides. By this, complete surfactant elimination is obtained and stabilizing, biocompatible, multifunctional coatings can be easily grafted on the GNS surface, allowing interactions with cells and tissue. On the optical point of view,



these GNS display intense LSPRs (localized surface plasmon resonances), in the near IR, whose positions are tunable during the synthesis and fall in the 750-1800 nm range, that includes the bio-transparent window (750-950 nm). Irradiating the LSPRs of GNS results both in a photothermal response with intense local temperature increase[3] and in an intense luminescence, when two-photon excitation with pulsed laser is used.

In this lecture the possibilities offered by TPL (two-photon luminescence) for cell imaging and for investigating the GNS interactions with cells will be illustrated when using near-IR excitation in the bio-transparent window, and giving hints about the GNS internalization (depending on their shape and surface charge) and about their intracellular dynamic behaviour.[4] The use of near-IR laser sources to induce a local hyperthermia on bulk materials coated by GNS monolayers will also be illustrated, as it leads to responsive antibacterial surfaces, capable of inducing the death both of plactonic bacteria and of biofilms.



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Ultrafast photodynamics of photo-switchable fluorescent proteins: ultrafast absorption spectroscopy and serial femtosecond crystallography.

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Reversibly photo-switchable fluorescent proteins find growing applications in cell biology, yet mechanistic details, in particular on the ultra-fast photochemical time scale, remain unclear. We employed time-resolved pump-probe absorption spectroscopy on two different reversibly photoswitchable fluorescent proteins IrisFP [1] and rsEGFP2 [2] in solution to study photo-switching from the non-fluorescent (off) to the fluorescent (on) state. As reported for another photo-switchable fluorescent protein (Dronpa) [3, 4] evidence is also provided here for the existence of several intermediate states on the pico- and microsecond time scales that are attributed to chromophore isomerization and proton transfer, respectively. For both proteins different kinetic modelling is in favor of a sequential mechanism with the existence of a main excited state intermediate with a lifetime of about few picoseconds, which controls the switching quantum yield (Figure 1) [5]. Time-resolved serial femtosecond crystallography (SFX) on the ps timescale has now the potential to structurally resolve details of ultrafast reaction [6]. In view of future experiments aiming at a structural characterization of the crucial intermediate state, we will also discuss here the use of serial femtosecond crystallography (SFX) at an X-ray free electron laser to solve the structure of photo-switchable protein. This research is carried out in collaboration with the Institut de Biologie Structurale in Grenoble (Adam, Bourgeois, Byrdin, Colletier, Coquelle, Feliks, Field, Fieschi, Guillon, Schirò, Thepaut, Weik, Woodhouse), Max-Planck-Institut für medizinische Forschung in Heidelberg (Barends, Doak, Foucar, Hilpert, Kovacsova, Nass, Roome, Schlichting, Shoeman), Department of Physics in Rennes (Cammarata), and the SLAC National Accelerator Laboratory in Menlo Park (Aquila, Boutet, Hunter, Koglin, Liang, Robinson).

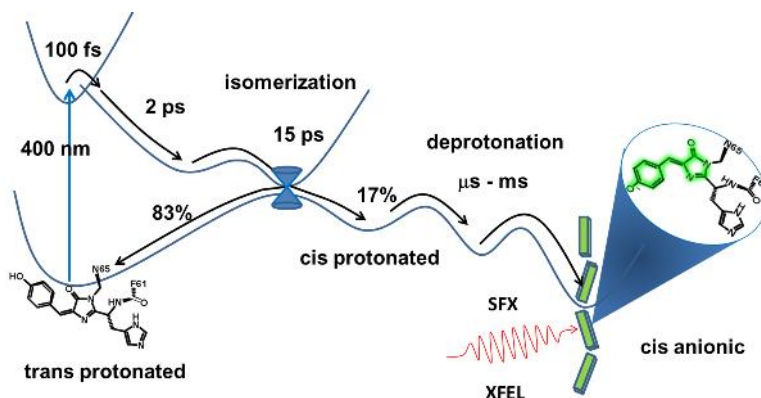


Figure 1: General photo-mechanism of off-to-on switching for green IrisFP in solution.

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Recent advances in the formation of DNA damage by UV radiation: from test tube experiments to human skin

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Modifications of the chemical structure of DNA by UV radiation plays a key role in numerous deleterious processes such as induction of skin cancer and phototoxicity of drugs and xenobiotics. The most frequent types of DNA photoproducts are pyrimidine (6-4) pyrimidone photoproducts (64PPs) and cyclobutane pyrimidine dimers (CPDs), both resulting from photoaddition reactions between adjacent bases. 64PPs and CPDs are produced by direct absorption of UVB and UVC photons by DNA. Evidence have been obtained recently that exposure of isolated DNA to UVC leads also to its photoionization. Damage are found in particular on guanine with formation of 8-oxo-7,8-dihydroguanine (8-oxoGua) and adducts with polyamines when the latter molecules are added to the reaction medium.

CPDs, but not 64PPs, were also found in isolated and cellular DNA exposed to UVA, showing that DNA can absorb photons in this wavelength range. CPDs have been found to be the most frequent UVA-induced DNA lesions, more than oxidative damage, in cultured cells and human skin. UVA plays also a role in dimerization of pyrimidine bases in the photoconversion of 64PPs into their Dewar valence isomers, a process observed in nucleosides, isolated DNA and cells.

UVA can also trigger the formation of CPDs by photosensitization. In this reaction a photosensitizer, such as aromatic ketones or fluoroquinolones, reaches a triplet excited states and transfers its energy toward thymine which is the DNA base with the lowest excited triplet state energy. Recent results show that thymines are much more reactive when the adjacent base is another thymine than when it is a cytosine. This suggests that, like in the formation of pyrimidine dimers by direct absorption of UV photons, delocalized states made possible by the stacking in DNA play a key role in triplet energy transfer.

A last phenomenon leads to the formation of CPDs: the formation in the dark in melanocytes after exposure to UVA. This unexpected reaction is likely to result from the formation of oxidation products of melanin upon irradiation that then decompose in the dark into excited carbonyls. The latter excited species would then transfer their energy to DNA and induce the formation of CPDs. Melanocytes exhibit other specificities in terms of UVA-induced damage. First, the yield of CPDs and 8-oxoGua, the main UVA-induced oxidation product, are similar while in other cells CPDs are present in a 3 to 5-fold excess. This increased sensitivity of melanocytes to oxidative stress is possibly explained by the pro-oxidant properties of melanin. This *in vitro* observation may explain why albino mice develop melanoma mostly as a response to UVB and pigmented ones as the result of UVA irradiation.

All these recent findings confirm the relevance of DNA damage, and in particular of pyrimidine dimers, to the biological effects of UV. More sophisticated tools in both the analysis of final products and the identification of the very early events following initial excitation keep on showing the complexity of the photochemistry in double-stranded DNA compared to more simple models such as isolated bases or dinucleotides.

Understanding the role of chemistry in atmospheric water: the key role of photochemists

Marcello Brigante^{1,2}, Angelica Bianco^{1,2}, and Gilles Mailhot^{1,2}

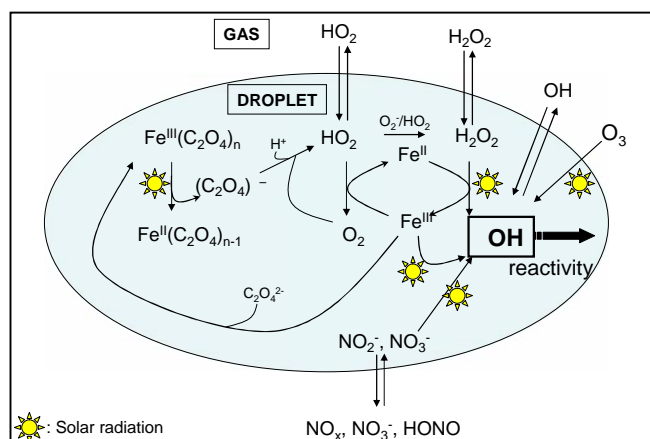
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Organic and inorganic composition of atmospheric waters can be modified by a multitude of chemical reactions. Nevertheless, main transformations are attributed to the strong reactivity of photogenerated hydroxyl radical (HO^\bullet) so called the “detergent of the atmosphere”. An important source of HO^\bullet is represented by *in-situ* generation: direct formation on the surface or in the bulk phases of atmospheric droplets can be attributed to the naturally occurring constituents such as hydrogen peroxide (H_2O_2), nitrates (NO_3^-), nitrites (NO_2^-) and Fe(III) aquacomplexes or organic complexes. Moreover, it is known that the generation of HO^\bullet can be obtained in the dark (Fenton reaction) or under sun-radiation (photolysis of precursors).

The HO^\bullet -mediated oxidation of organic compounds in the aqueous phase leads to the formation of shorter and multifunctional organic species up to their complete mineralization. Moreover, as recently reported, complex chemical reactions catalyzed by HO^\bullet can also lead to the formation of accretion products such as

oligomers. Actually, main investigations focus on the fate of short chain carboxylic acids that are always found in cloud water. However, less than 12 % of organic matter is attributed to the carboxylic acids and so more than 80 % remains uncharacterized. The main goal, for a better understanding of cloud aqueous phase chemistry, is a deep characterization of this medium in order to investigate new transformation pathways occurring under solar irradiation.



In this talk, spectroscopic and photochemical approaches (*i.e.* continuous irradiation and

nanosecond transient spectroscopy) that can be used to estimate the oxidant capacity of the cloud aqueous phase chemistry will be introduced. Moreover, main results on the photochemistry of cloud aqueous phase will be presented. These results highlight the relevance of the complementary approach (*i.e.*, characterization and reactivity assessment) in improving the understanding of photochemical and radical-driven transformations in this complex medium.

Ingestible device for intragastric PDT against *Helicobacter pylori*

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In the framework of bacterial infections, those associated with *Helicobacter pylori* (Hp) are among those raising greatest concern, as they show a high worldwide prevalence combined with high failure of pharmacologic solutions due to antibiotic resistance. To overcome this limitation, endoscopic PDT devices have been tested, e.g. in the form of modified gastroscopes, also taking advantage from the endogenous production of photoactive porphyrins by the bacterium itself. In scientific literature, the proof-of-principle of Hp killing by visible light has been demonstrated in *in vitro* models¹ and in one case also *in vivo*². However, all the illumination techniques realized up-to-date exhibit clear disadvantages, namely great invasivity, poor patient compliance and adverse effects.

In this context, we propose the use of an innovative device to perform intragastric PDT against Hp in a minimally-invasive and efficient way³. By combining photonics and robotics, we have patented and designed an ingestible luminous capsule whose geometrical, mechanical and light-emission properties were compatible with an efficient bacterial photo-killing and the necessary safety requirements. During its permanence in the gastric antrum, where Hp is mostly found, the capsule illuminates the gastric wall thanks to Light Emitting Diode (LED) sources, powered by a built-in battery. Once in the intestine, the device will be turned off thanks to appropriate sensors.



In this communication, the state of the art of PDT against Hp will be briefly presented, and the characteristics of the capsule prototype realized up to now will be described, including the illustration of its light-emitting properties. Preliminary results in terms of *in vivo* photo-killing efficacy and safety studies will be presented. In addition, a semi-theoretical approach for the study of the action spectrum for *in vivo* photo-killing against Hp will be shown; here, the gastric wall light-filtering and diffusing effects are explicitly taken into account, besides the photo-physical properties of Hp porphyrins. This study has led to the definition of the best illumination wavelengths needed to optimize the PDT efficacy during the capsule permanence time in the stomach.

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Enhanced fluorescence photoswitching in multichromophoric molecules and nanosystems

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The field of advanced photoactive supramolecular systems and nanomaterials, with unconventional photoswitching capabilities, is extremely active and has been attracting ever-growing interest in recent years in many research fields for their potential applications in biological sensors, targeted medicine, high-resolution imaging, and innovative materials science. We report here on the design, fabrication and spectroscopy of photoswitchable emissive molecules and nanosystems, advantageously combining a large number of photochromic and fluorescent moieties.[1]

Three different strategies to achieve enhanced photoswitchable fluorescent supramolecular nano-architectures are presented, gathering a number of fluorescent and photochromic molecular species (see Figure 1): (1) multiphotochromic β -cyclodextrins with fluorescence properties; (2) photoswitchable multi-emissive silica nanoparticles containing multiple photochromes and fluorophores; (3) ultra-bright and sensitive nanoparticles obtained by the reprecipitation method of a photochromic-fluorescent dyad molecule;[2]

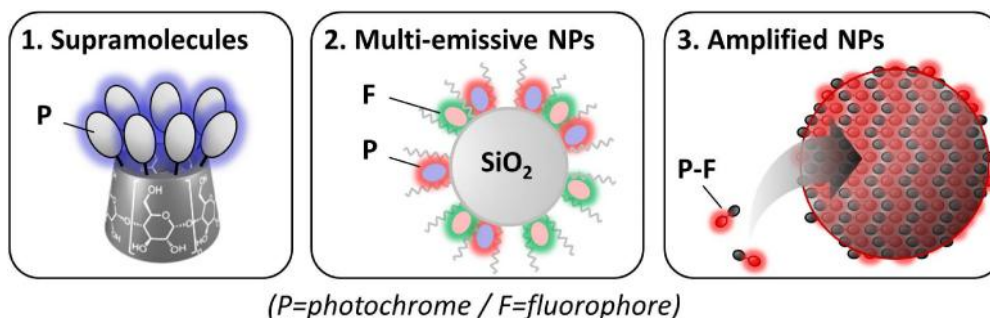


Figure 1. Design of photochromic-fluorescent molecules and nanosystems for enhanced fluorescence photoswitching.

In these various systems, the emission signal could be successfully and reversibly switched by light, either on an “ON-OFF” basis, or with an “emission color switch” mode. A thorough study involving structural characterizations, modeling and spectroscopy measurements, from the ensemble level down to the single nanoparticle level, allowed us to quantify the switching efficiency, demonstrate nonlinear photoswitchable fluorescent properties, and decipher the processes driven at the nanoscale (intra- and intermolecular energy transfer) leading to amplification effects resulting from the large number of chromophoric species involved.

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Polymeric nanoparticles for combined photo/chemo-therapy

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Combination chemotherapy is becoming increasingly relevant to attain long-term prognosis and better quality of life in cancer patients. The basic concept in this strategy is to attack tumor on different sides by acting on a single oncogenic pathway through different mechanisms or across parallel pathways, without amplification of side effects. Coupling conventional chemotherapy with photodynamic therapy (PDT) represents an intriguing option to address tumor heterogeneity and drug resistance issues. In this context, delivery of cocktail therapies through nanocarriers offers an unprecedented opportunity to control not only the level of bioactive species in the body at organ, cellular and subcellular level but also timing of release.

Polymeric nanoparticles (NPs) are at limelight in the burgeoning field of nanomedicine since their properties can be suitably manipulated by tuning polymer structure and mode of carrier assembly in view of selective targeting to tumor tissue. Furthermore, NPs can be designed to incorporate drugs that have different physical-chemical properties such as size, hydrophilicity and stability. To this end, NPs with core-shell architectures have great potential in delivering therapeutic combinations since they allow to change easily the ratio between transported drugs which can be crucial to attain desired therapeutic effect.

When developing NPs for photo/chemo-therapy, a rational design should be planned taking into account specific needs dictated by i) disease features (tissue, stage, vascularization extent, presence of metastases); ii) the strategy selected to accumulate the highest dose fraction at tumor level and to deliver the drug at correct location (intracellular/tumor interstitium, sustained or pulsed release); iii) physical-chemical properties of the drug (solubility profile, stability); iv) achievement of a product with satisfactory shelf-life.

After a short overview of polymer NPs for cancer therapy, including some biological design guidelines, the basic principles to design NPs able to overcome PDT shortcomings will be illustrated. Finally, some examples of polymeric NPs developed by us in the past 5 years for the above bimodal therapeutic treatments will be described, highlighting the logical design and their potential in cancer therapy.

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Photo-active plasmonic nanoparticles for biomedical applications

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We review our experimental activities on the exploitation of a light stimulation produced by a laser source to “activate” suitable photothermal transducers like plasmonic nanoparticles for applications in bonding and repair of biotissues, in cancer diagnostics and therapy and for drug release.

Laser-assisted tissue repair or laser welding has been proposed to close chronic accidental and surgical wounds. An exemplary application is in micro-vascular surgery for the repair of arterial wounds. To this aim, we have engineered a hybrid bioadhesive consisting in a chitosan film doped with gold nanorods (GNRs) that can be activated by NIR laser light to induce a well-localized photothermal effect leading to the adhesion of the film with the arterial wall. The effectiveness of the patches to close arterial wounds has been tested in vivo in preclinical studies in rabbits.

Moreover, the combination of pulsed and CW near-infrared laser light with plasmonic particles is gaining relevance for the photoacoustic imaging and photothermal ablation of cancer. Selective targeting of malignant cells with these contrast agents may rely on complementary biochemical and biological strategies, including the use of specific probes or the exploitation of cellular vehicles. Here we moved from a platform of PEGylated GNRs with plasmonic NIR bands and we implemented different approaches for active delivery by functionalization with (i) antibodies against cancer antigen 125 (CA125), which is a common biomarker for ovarian lesions; (ii) inhibitors of carbonic anhydrase 9 (CAIX), which are expressed by hypoxic cells such as those found in solid tumors; and (iii) by introducing macrophages as a versatile model of cellular vehicles that would phagocytose the particles and home to inflammatory lesions. In vitro studies on cell cultures on those different approaches will be presented and discussed.

For drug release, nano-gold and other light-responsive nanomaterials can be employed for the development of an implantable device for on demand chemical release in the form of a light-activated sponge-like scaffold. The photothermal response of the gold nanoparticles contained inside the sponge triggers a contraction in proximal drug-loaded thermosensitive micelles, thus promoting the expulsion of the drug from the sponge. An advanced version of this device consists in a dispersion of graphene nano-sheets in a biopolymer matrix, which is activated by millisecond-long light pulses for confined and precisely dosed drug release.

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ORAL CONTRIBUTIONS

New trends in photodynamic therapy

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Photodynamic therapy (PDT) is a treatment option of cancers and other diseases involving light, a photosensitizer and molecular oxygen leading to cell death (phototoxicity). These three elements together lead to the production of reactive oxygen species, especially singlet oxygen, in the target tissue. The selectivity of PDT comes from both the localization of the photosensitizer in the tumor and the illumination of the cancerous region. This performs damages in the tumor area without affecting the normal tissue, a major goal in cancer therapy. However, there are also some shortcomings of PDT: poor selectivity of photosensitizers for the tumor tissues, low penetration of light in the cancerous area, measurement of the effect of the treatment.

To take up these challenges, successive generations of photosensitizers have been designed and accepted in clinical treatments. The first and still widely used is *Photofrin*, a mixture of haematoporphyrin derivatives. The second generation of PS consists of pure molecules with higher absorption in the therapeutic window. The third generation of PS are targeted compounds, photosensitizers linked to a targeting moiety such as sugars or peptides or encapsulated into nano particles. The fourth generation are theranostic platforms that perform both diagnosis and therapy.

Many strategies have been developed to enhance efficiency of photodynamic therapy. For overcoming problems with light penetration in the tissues, the two-photon or up-conversion excitation allow the absorption of two photons of lower energy in therapeutic window. The use of scintillators able to absorb X-rays radiations and convert it in visible (or NIR) photons is of great interest.

The development of multifunctional nanoparticles which can get together a magnetic core as contrast agent for magnetic resonance imaging, a photosensitizer, a PEG coating and a targeting unit is another mean to experiment theranostic.

The aim of my talk is to present different strategies that have been developed to take up the challenges of photodynamic therapy in the research field (red or NIR absorption, targeting, nanoparticles...) and to develop particular cases emerging from our lab work.

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Folate-decorated amphiphilic cyclodextrin/pheophorbide nanoassemblies for targeted PDT

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Nowadays, active targeting of a drug in tumor sites is generally accomplished by tailoring a nanosystem with receptor targeting groups such as folate, antibodies, saccharides and peptides. Targeted PDT treatment relies on the selective accommodation of a photosensitizer (PS) in tumor sites following irradiation, thus generating the cytotoxic singlet oxygen (1O_2).¹ Here we report a nanoassembly based on amphiphilic cyclodextrin carrier (aCD, SC6OH), entrapping pheophorbide (Pheo) as PS and tailored with folate–adamantanyl (Ada-Fol) as folate receptor (FOLR1) targeting group. SC6OH@Ada-Fol /Pheo nanoassemblies (1) (see Figure 1), prepared by hydration of organic film and sonication, were studied by complementary techniques such as UV-Vis, steady-state and time-resolved fluorescence. The nanosystem 1 showed an hydrodynamic radius of ~ 300 nm, Z-potential of ~ -45 mV, Pheo loading and entrapment efficiency of $\sim 4\%$ and $\sim 66\%$, respectively. Pheo was retained for ~ 2 weeks from 1 in PBS (pH=7.4) at 37°C. In order to verify the targeting properties, we evaluated in vitro the effectiveness of 1 on cell growth for different cancer cell lines over-expressing FOLR1 (MCF-7, MD-MBA and A549) and very low expressing FOLR1 (PC3). Our data indicate that the nanoassembly 1, upon red-light irradiation, inhibits cell proliferation depending on FOLR1 expression.

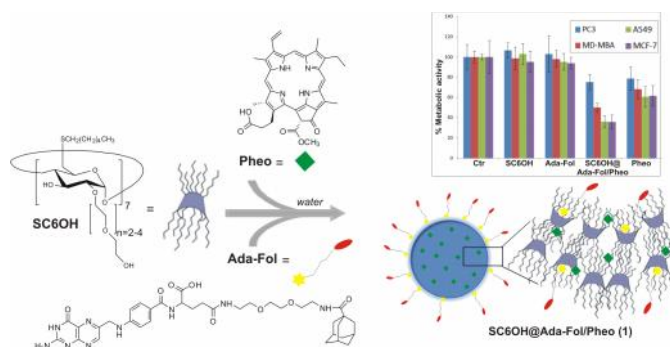


Figure 1. Sketched depiction of 1 formation. In the inset: metabolic activity on MCF-7, MD-MB A549 and PC3 treated with 1 ([Pheo] = 500 nM, 3 h, Resazurin assay) ad upon red-light irradiation.

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Hybrid multimodal nanoparticles as nano swiss-knives for diagnostics

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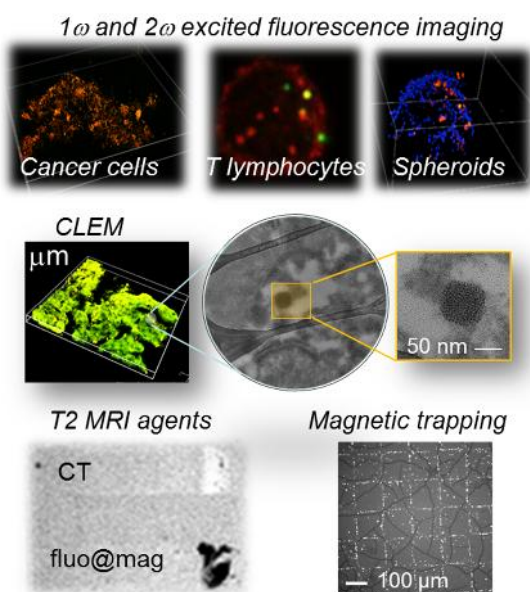
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Hybrid nanoassemblies combining multimodal properties stir nowadays considerable interest to take advantage of complementary features (spatial resolution, sensitivity, penetration depth, functional vs structural imaging) issued from using distinct imaging techniques.



To this aim, we have designed core-shell hybrid nanoobjects, comprising a non-doped photoactive core (photochromic, fluorescent) coated with a shell of superparamagnetic iron oxide nanoparticles.¹ The versatile fabrication process allowed us to easily generate a range of nanoassemblies differing by the nature of their photoactive core, the size of the magnetic units, or the nature of the outer stabilizing ligands opening perspectives for *in vivo* imaging and targeting.²

In this way, proper surface functionalization led to significant accumulation in tumors after intravenous injection or enabled specific *in vitro* and *in cellulo* protein recognition with high selectivity.

Through several examples, we want to report on the various modalities of the developed *fluo@mag*

nanoassemblies, spanning a large range of potential applications: magnetic guidance and extraction, correlative light electron microscopy, T2 contrast agents for MRI at low doses, protein targeting, and finally one- and two-photon excitation fluorescence microscopies of cancer cells and strongly autofluorescent tissues.³

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Efficient NO release by *trans*- and *cis*-(Cl,Cl)-[Ru^{II}(FT)Cl₂(NO)](PF₆) under excitation in the NIR region

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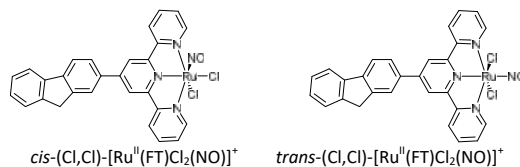
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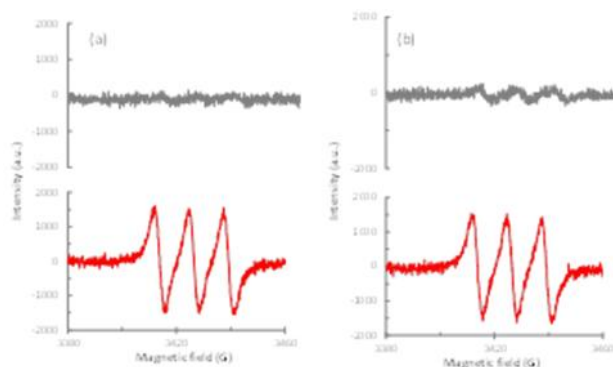
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Nitric oxide NO[•] has long been considered only as a pollutant gas from combustion engines. However in 1992, it was named as "Molecule of the Year" by *Science* review after the discovery of its physiological function and its involvement in different cellular processes. It was recognized that the biological effect is dependent on its concentration in the cell media. Hence the photodynamic therapy combined with systems that provide a fixed concentration of NO[•] under irradiation is a very challenging topic. The ruthenium complexes based on nitrosyl ligand are potentially photoreactive systems. Our study is devoted to the development of ruthenium nitrosyl complexes able to release NO[•] by one or two photon excitation. Indeed, the photo-release by a two-photon process allows selective treatment of tumors installed in deeper layers, for excitement in the therapeutic window.



We will present the synthesis and characterization of two *cis* isomers (Cl, Cl)- and *trans* (Cl, Cl)-[Ru^{II}FTCl₂(NO)](PF₆).ruthenium complexes¹ where FT denotes the 4'-X-2,2':6',2''-terpyridine ligand with X = fluorene. The study of NO photorelease by one photon excitation and the corresponding quantum yield (Φ_{NO}) will be discussed as well as the two-photon excitation study. Finally, we will show preliminary study on toxicological study (cytotoxicity and photocytotoxicity) for *trans* (Cl, Cl) - [Ru^{II}(FT)Cl₂(NO)](PF₆) complex.



Triplet electron paramagnetic resonance signals from NO trapping by [Fe(MGD)₂] for *trans*-(Cl,Cl)-[Ru(FT)Cl₂(NO)]PF₆ (a) and *cis*-(Cl,Cl)-[Ru(FT)Cl₂(NO)]PF₆ (b) upon two-photon excitation at $\lambda = 810$ nm. Control (black line) before irradiation.

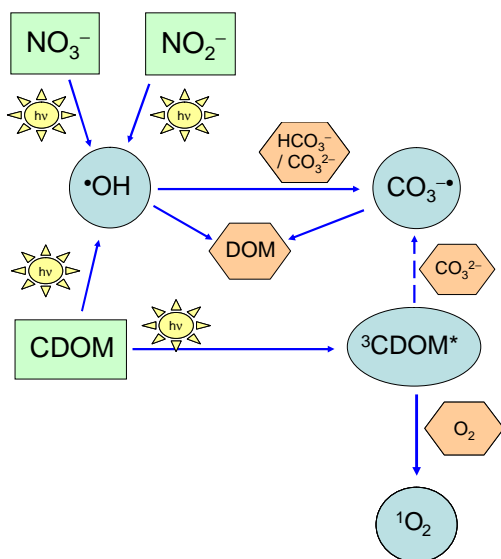
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Photochemical reactions in sunlit lake waters

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Photochemical reactions are important in the processing of natural dissolved organic matter (DOM) and of organic xenobiotics in sunlit surface waters [1,2]. They consist of direct photolysis, where sunlight absorption by the compound itself triggers transformation, and indirect photochemistry. In the latter, sunlight is absorbed by photoactive compounds called photosensitisers, such as the chromophoric fraction of DOM (CDOM), nitrate and nitrite.



Irradiated photosensitisers produce reactive transient species such as the hydroxyl radical ($\cdot\text{OH}$), singlet oxygen ($^1\text{O}_2$) and CDOM triplet states ($^3\text{CDOM}^*$). Moreover, the oxidation of carbonate and bicarbonate by $\cdot\text{OH}$ and of carbonate by $^3\text{CDOM}^*$ yields the carbonate radical ($\text{CO}_3^{\cdot-}$). The mentioned transients reach steady-state concentrations in surface waters due to very fast deactivation. The radicals $\cdot\text{OH}$ and $\text{CO}_3^{\cdot-}$ are mainly scavenged by DOM [3], $^1\text{O}_2$ is deactivated by collision with water, while $^3\text{CDOM}^*$ mainly reacts with O_2 to produce $^1\text{O}_2$. We have developed a photochemical model that predicts the steady-state concentration of the transients and the transformation kinetics of dissolved compounds as a function of sunlight spectrum and irradiance, water chemistry and depth [4]. The model can be used to determine the steady-state levels of $\cdot\text{OH}$, $\text{CO}_3^{\cdot-}$, $^1\text{O}_2$ and $^3\text{CDOM}^*$ from dissolved organic carbon (DOC), nitrate, nitrite, inorganic carbon/alkalinity and pH. These water chemistry data

are available for a number of lake ecosystems, allowing the study of the seasonal and long-term evolution of photochemistry. The key seasonal issue is the irradiance of sunlight, which is higher in spring and summer compared to autumn or winter. Due to photosynthetic activity or CaCO_3 precipitation, other important factors are the winter maxima of nitrate and alkalinity and the summer maxima of DOC. Long-term modifications can be caused by climate change or direct human disturbance [5], such as an increase or a decrease in the input of nutrients from wastewater. Variations in alkalinity and pH are the most reliable parameters for assessing the effects of climate on water chemistry (mostly affecting small lakes [6]), while the DOC often increases in nordic environments and decreases in sub-tropical areas that undergo desertification. In arid environments the seasonal fluctuations in the water level may affect photochemical processes, largely depending on the prevailing water loss process (outflow/seepage vs. evaporation).

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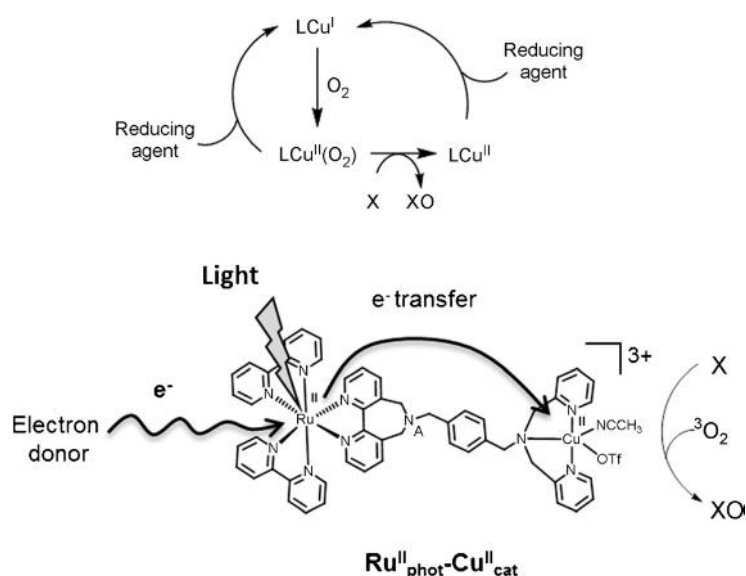
A Ruthenium(ii)–Copper(ii) dyad for the photocatalytic oxygenation of organic substrates mediated by dioxygen

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Dioxygen activation by copper complexes is a valuable method to achieve oxidation reactions for sustainable chemistry. The development of a catalytic system requires regeneration of the Cu^I active redox state from Cu^{II}. This is usually achieved using extra reducers that can compete with the Cu^{II}(O₂) oxidizing species, causing a loss of efficiency. An alternative consists of using a photosensitizer to control the reduction process. Association of a Ru^{II} photosensitizing subunit with a Cu^{II} pre-catalytic moiety assembled within a unique entity (see Figure) is shown to fulfill these requirements.



In the presence of a sacrificial electron donor and light, electron transfer occurs from the Ru^{II} center to Cu^{II}. In the presence of dioxygen, this dyad proved to be efficient for sulfide, phosphine, and alkene catalytic oxygenation.¹ Mechanistic investigations gave evidence about a predominant ³O₂ activation pathway by the Cu^I moiety.

In order to avoid the use of a sacrificial reducing agent, two catalytic subunits will now be connected on the same photosensitizer, allowing the occurrence of two catalytic reactions on the same supramolecular array without waste of product.

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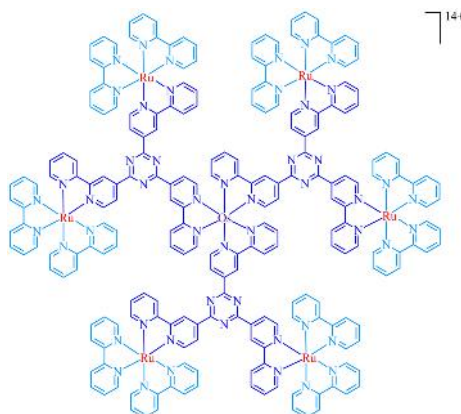
Ultrafast energy transfer in a new dendritic antenna based on a new 1,3,5-triazine ligand

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The 1,3,5-triazine motif has become an important molecular component for organic, supramolecular and coordination chemistry due to its diverse reactivity, electronic and structural influences.[1] Catalysis,[2] medicinal chemistry [3] and polymer chemistry [4] are examples of several application focused on triazine-containing compounds. Moreover, Ru(II) and Os(II)-polypyridine complexes are of high interest due to their possibility to easily tune their photophysical and electrochemical properties. Such complexes have already found uses in a wide variety of photosensitization applications, for instance switches,[5] molecular engines,[6] dye-sensitized solar cells[8] and light harvesting antenna.[7]



Scheme 1.

Herein, we report the synthesis and the photophysical and redox properties of a new Ru₆L₃Os antenna system whose bridging ligand “L” (in dark blue in Scheme 1) was designed in order to enhance the electronic delocalization of the acceptor orbital for the MLCT and therefore to lower the absorption energy in the system. Ultrafast *pump-probe* spectroscopy experiments have been performed to demonstrate efficient energy transfer processes from the Ru(II) subunits to the Os(II) core, that happens in the tens of ps.

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Pimerization drives supramolecular polymerization of a shape-persistent tetrahedral molecule bearing four bipyridinium units

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The formation of π -bonded dimers from the spontaneous and reversible association of π -radicals has been named pimerization.^{1,2} The first reported example is that of monoreduced methylviologen in de-aerated aqueous solution:³ the pimerization process is evidenced by a change in colour from blue (typical of the monoreduced monomeric form) to violet, typical of the pimer species. The pimerization constant of methylviologen in aqueous solution is quite low (385 M^{-1}),³ so that highly concentrated solution are necessary ($>0.1 \text{ M}$) to form a significant amount of pimer. The equilibrium between monomeric and pimeric species of viologens have been investigated not only to build up supramolecular structures, but also in view of applications in light-attenuation in electrochromic devices, as well as spintronics and data storage devices: the monoreduced monomer is paramagnetic and the pimer is diamagnetic.¹

The presence of N-benzyl or N-phenyl units enhance the pimerization constant in aqueous solution because of a more favourable stacking of the aromatic rings and a more hydrophobic character that prevents a good solubility of the monoreduced bipyridinium unit.

In this contest we synthesized a shape-persistent molecule featuring four bipyridinium units (1^{8+}), following the synthetic procedure already reported,⁴ with a rigid architecture that prevents intramolecular pimerization. The investigation is thus focused on the possibility to form a supramolecular polymer by intermolecular pimerization of bipyridinium units, as schematically represented in figure follow. As

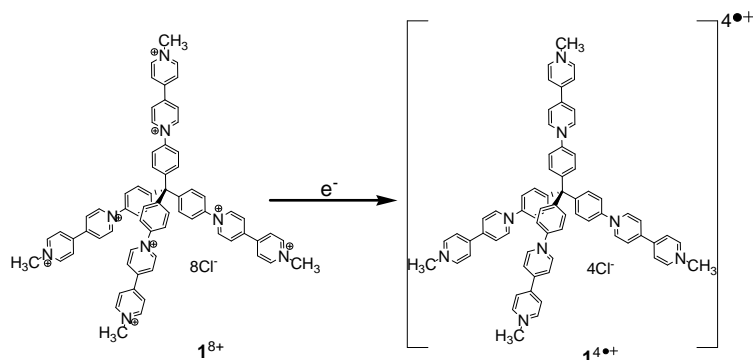


Figure Scheme of pimerization reaction of 1^{8+}

expected, the tetramer is able to form the pimer species at lower concentration (μM), compared to methylviologen.

The present study reports a detailed characterization of 1^{8+} including photophysical, electrochemical, and EPR properties and quantum-chemical calculations. The reduction and subsequent pimerization has been driven by chemical, electrochemical methods or by γ -radiation. The kinetics of reduction has been studied by pulse-

radiolysis, to obtain the kinetic of the monoreduced and pimer formation with high energy electron beam. Finally, we were also able to estimate the pimerization constant from spectrophotometric measurements of monoreduced specie: we found that the equilibrium constant increase with the amount of monoreduced subunits, due to cooperative effect.

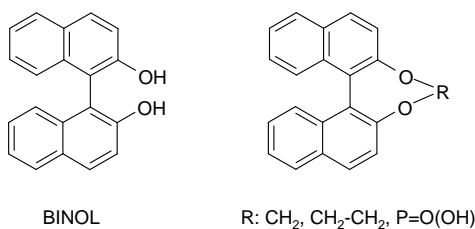
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Conformational relaxation of 1,1'-Bi(2-naphthol) derivatives probed by subpicosecond circular dichroism

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Binaphthols (BINOLs) is class of molecule widely used as elementary chiral building blocks for the design of new materials with chiroptical properties.¹ Origin of BINOL chirality arises from the coupling between the electric dipole moments of the two naphthol moieties. It is known that in their excited state, BINOLs have different chiral properties than in their ground state, due to the reorientation of the two naphthol groups. While ground state absorption properties of BINOLs have been carefully studied, information about the spectral properties of their excited states remains scarce. In this context, we undertook a comparative study of the excited state dynamics of several BINOL derivatives, by subpicosecond transient absorption (TRABS) and circular dichroism (TRCD) spectroscopy in the middle UV. In contrast to TRABS, TRCD provides a direct measurement of the conformational changes of BINOLs.² Conformational dynamics of BINOLs are found to depend strongly on the solvent hydrogen-bonding and viscosity. In addition, a significant increase of the CD signals has been observed for the bridged compounds, in stark contrast to BINOL.



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Photoinduced Charge Separation in Porphyrin Ion-Pairs

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Ion pairs between porphyrin-type compounds have been successfully employed for spectral sensitization of semiconductor surfaces¹ and for the preparation of collective binary ionic materials for photonic and (photo)catalytic applications.² The understanding of the photophysical processes occurring within ion-paired porphyrin dimers is thus of remarkable importance for the optimization and improvement of such systems. Herein we describe the formation of ion-pair species between tetracationic ZnTMePyP⁴⁺ or H₂TMePyP⁴⁺ and tetraanionic ZnTPPS⁴⁻ or H₂TPPS⁴⁻ porphyrins, their characterization in a variety of solvent mixtures and the thorough investigation of their photophysical behavior by time-resolved techniques.³ In all the systems studied, very fast and efficient photoinduced charge separation is observed, with the cationic porphyrin being reduced and the anionic one oxidized. Interestingly, despite the very short charge separation distance, the lifetime for charge recombination, depending on the energy gap, can extend into the nanosecond time domain, showing great potential for the utilization of this molecular design within energy conversion schemes.

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Photodefence responses of coastal diatoms: role of light spectrum

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Light is a driving force behind the synthesis of biomass in photoautotrophs. In pelagic ecosystems, highly variable light strongly affects microalgae at an ecological (success and succession), molecular (acclimation, carbon allocation), photosynthetic and growth levels. Therefore, manipulation of light appears to be an attractive tool for enhancing growth of microalgae in order to extend the use of these organisms in biotechnological field. Diatoms are responsible for 40% of the marine primary production strongly contributing to the biogeochemical cycling of nutrients. The diatom's extraordinary ecological success relies to their biological peculiarities and refined mechanisms to cope with environmental changes. Their high degree of flexibility capability to acclimate very fast to the changing environment and rapid growth rate make them key species for application in biotechnological field. In this work, we investigated the photoprotection-antioxidant network system, as well as growth rate, carotenoids and xanthophylls profile, antioxidant- and carotenogenesis-relied gene activation, photosynthetic rate and regulation in the diatom *Skeletonema marinoi* under different light regimes. The responses to different growth light regimes induced composite acclimative patterns manifesting in strong alterations in the cell biology. Our study demonstrates, the dual effects of spectral composition and intensity of light in driving differential mechanisms involved in the defence photoprotection-antioxidant network system. We show for the first time the modulation of photodefence mechanisms, observing complementary and/or alternative tuning processes developed by diatoms to cope with variable light they may experience in the water column. The pivotal role of the spectral composition of light, mainly by the presence or absence of red, selects the defence strategy of the cells. This study increases our knowledge on the photophysiological processes activated by microalgae and selected by the natural environmental forcing, as well as provides valuable insights for the light manipulation of diatom's cultivation to maximize bioactive molecules production.

Physiological response of red versus green morphs of sweet basil to high solar irradiances: what type of photoprotection?

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After more than three decades of extensive research conducted at different scale levels, whether anthocyanins effectively help plants to cope with an excess of solar radiation remains a highly debated matter. Epidermal anthocyanins have also been shown to greatly affect the suite of morpho-anatomical, physiological and biochemical traits responsible for carbon assimilation in some species, including sweet basil, and this poses the serious question whether or not cyanic plants are inherently less efficient in terms of CO₂ assimilation when compared to green morphs. In this study, analyses of daily photosynthetic performances through gas exchanges and chlorophyll fluorescence kinetics, as well as the daily variations of individual products of the methylerythritol phosphate and the phenylpropanoid pathway were conducted in green (Tigulio, TG) and purple-leafed (Red Rubin, RR) basil to unveil their differential responses under high solar irradiance. Expression of genes encoding for isoprenoid and phenylpropanoid by-products were also monitored by RNA-seq analyses. Leaves of TIG and RR did not differ in terms of daily CO₂ gain. RR displayed a higher photosynthetic rate during the central hours of the day, while TIG was more performant in early morning and late afternoon. Saturation of photosynthesis occurred at 880 and 1250 $\mu\text{mol m}^{-2}\text{s}^{-1}$ photosynthetic active radiation in TIG and RR, respectively. Maximal photosystem II efficiency, F_v/F_m , declined more in TIG than in RR from 12:00 to 14:30 pm, while in both genotypes recovered fast in late afternoon. Mechanisms involved in thermal energy dissipation (estimated by non-photochemical quenching, NPQ) were scarcely activated in RR (from 1.26 at 8:30 up to 1.39 at 14:30), whilst NPQ was markedly higher in TIG, especially in sunny hours (+46% on average in central hours as compared to early morning). Consistently, xanthophyll content (VAZ) as well as de-epoxidation state of VAZ (DES) increased strongly in TIG especially under high irradiances, while sunlight irradiance had a very minor effect on DES in RR. The greater stomatal closure found in TIG than in RR, especially under high irradiances, paralleled with higher level of foliar free abscisic acid (free-ABA). Albeit a stimulation of carotenoid metabolism, a *de-novo* synthesis of ABA unlikely contributed to the higher concentration of foliar ABA found in TIG than that of RR as the expression of zeaxanthin epoxidase was lower in TIG, whereas the expression level of neoxanthin synthase and 9-*cis*-epoxycarotenoid oxygenase did not differ between TIG and RR. Conversely, the strong over-expression of β -glucosidase1, supports the idea that de-conjugation of the glycosylated form of ABA (ABA-GE) may have contributed to enhance the level of foliar free-ABA of TIG. In this study we offer clear evidences of an effective photo-protective role of epidermal anthocyanins in leaves of sweet basil. We also demonstrate that red and green basil displayed similar capacities to assimilate carbon on daily bases, even though cyanic leaves had severe limitations as compared to the acyanic counterpart at relative low solar irradiances, while the purple genotype performed better under high irradiances. Our results lead also to hypothesize that ABA-GE de-conjugation may have particular significance (in complementing *de-novo* ABA biosynthesis) in green leaves suffering from severe light excess, in which de-epoxidation largely overcomes epoxidation of VAZ and violaxanthin is preferentially utilized to sustain zeaxanthin biosynthesis rather than ABA and neoxanthin, thereby offering photoprotection to chloroplast.

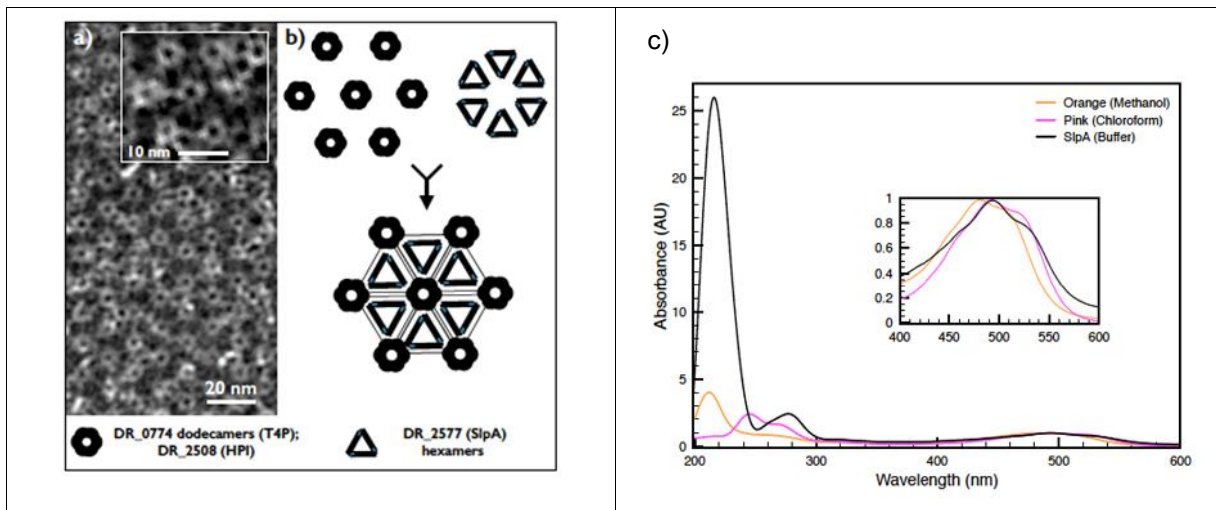
The S-layer as a UV-radiation shield: the case of *Deinococcus radiodurans* and its S-layer Deinoxanthin Binding Complex

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Deinococcus radiodurans has the puzzling ability to withstand over a broad range of extreme conditions including high doses of ultraviolet radiation and deep desiccation. This bacterium is surrounded by a surface layer (S-layer) built of a regular repetition of several proteins [1], assembled to form a paracrystalline structure. We have reported that the protein DR_2577 is a major Surface layer component of the radio-resistant bacterium *D. radiodurans* and that it appears to be organised into three hierarchical orders characterised by monomers, stable dimers formed by the occurrence of disulphide bonds, and hexamers resulting from a combination of dimers (Figure 1a,b) [2]. Recently, we have described a novel complex named S-layer Deinoxanthin Binding Complex (SDBC – Figure 1c) [3]. The complex is composed by deinoxanthin, a strong protective antioxidant specific of this bacterium, folded in the major S-layer protein DR_2577. The spectroscopical and genetical characterisation of the SDBC revealed features which could suggest a protective role in a way in which the S-layer shields the bacterium from incident ultraviolet light and behaves as a first lane of defence against UV radiation.



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Diatom phytochromes reveal the existence of far-red light based sensing in the ocean

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Phytochromes are a Red/Far-Red light photoreceptor family broadly distributed throughout plants, fungi, and photosynthetic and non-photosynthetic bacteria. Phytochrome genes are also found in photosynthetic marine organisms. Considering the fast attenuation of the red and far-red light in the water column, the role of a Red/Far-Red sensor in the aquatic environment is enigmatic. It has been recently shown some eukaryotic algal phytochromes can span their absorption spectrum over the visible spectrum, from far-red to blue light [1].

We have extended analysis of the phytochrome photoreceptor class to marine diatoms, one of the major groups of phytoplankton [2]. We provided the first evidence that phytochromes from the 2 model diatom species, *Phaeodactylum tricornutum* (Pt-DPH) and *Thalassiosira pseudonana* (Tp-DPH), are red/far-red light sensitive photoreversible proteins, using biliverdin as chromophore. Interestingly, the red/far-red absorbance peaks of both diatom phytochrome Pr and Pfr forms are red-shifted as compared to other known marine unicellulars. We established that the diatom Pt-DPH acts as a far-red light activated kinase *in vitro*, suggesting that it could transduce a signal through a phosphorylation cascade. Furthermore, exposure to both red and far-red light leads to changes in gene expression in *P. tricornutum*. The specific disappearance of gene expression responses to far-red light in *dph* knockout cells demonstrates that Pt-DPH mediates far-red light signaling. Digging into the increasing number of sequenced genomes and metagenomic information, we have identified *DPH* genes in diverse diatom species, widely distributed along the water column. This emphasized the ecological significance of far-red light sensing and raised questions about the sources of far-red light underwater. Our analyses indicate that, although far-red wavelengths from sunlight are only detectable at the ocean surface, chlorophyll fluorescence and Raman scattering can generate red/far-red photons in deeper layers, opening up novel perspectives on phytochrome-mediated far-red light signaling in the ocean, as well as, on the light sensing and adaptive capabilities of marine phototrophs.

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[2] Fortunato et al, Plant Cell 2016

Heptamethine cyanine dyes working as light harvesting antennas in biohybrid photosynthetic assemblies

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Over billions of years, extremely efficient molecular machines have evolved to perform very specific tasks^[1]. In recent years, the idea of extending the physiological activity of biological macromolecules, through modifications designed *ad hoc* to carry out specific purposes, began to emerge within the scientific community. We wish to functionalize proteins and enzymes to extend their chemical and physical properties for applicative purposes. It intends to synthesize organic-biological hybrid system through bioconjugation techniques, able to form selective and covalent bonds between the biological part and its organic counterpart^[2]. These hybrid systems are potentially interesting as active materials in next-generation devices in different technological areas using as biosensors, photocatalysts and photovoltaic materials. The natural candidates capable of performing these tasks are the photosynthetic systems, in particular the photosynthetic reaction center (RC) from the purple bacterium *Rhodospirillum rubrum* strain R26, whose unique photoconversion capability generates a stable charge separated state with an efficiency close to unity. On the other hand, to employ efficiently RC in hybrid devices, the light harvesting ability of the isolated protein must be refurbished to increase its absorption cross-section. About that, an organic fluorophore HCy-1 (Figure 2) belonging to the class of heptamethine cyanines^[3], suitably covalently bioconjugated to the residues of the RC lysine, has recently been employed as a molecular antenna in order to improve the properties of absorption and photoconversion of the RC. It is properly tailored to absorb light in the visible spectral range (400-700 nm), where the RC absorbance is very low, and efficiently emit in the near infrared region (750-900 nm), in correspondence of the highest RC absorption peaks with a high Stokes shift (Figure 2). Our results confirm that the hybrid works better than the natural pristine protein and is capable of extending the photoactivity in the visible range wavelengths useful for energy photoconversion.

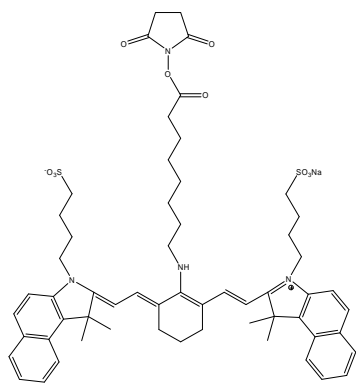


Figure 2. Structure of heptamethine cyanine dyes HCy-1

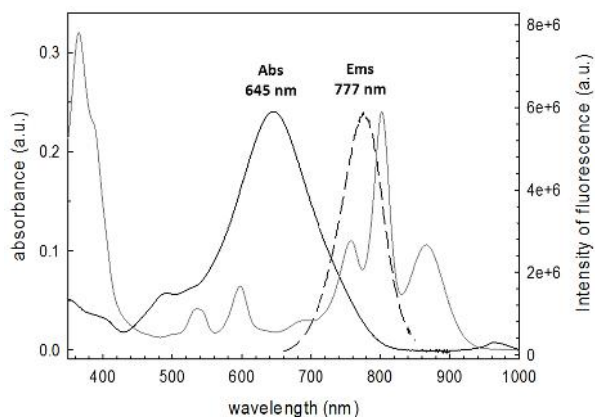


Figure 1. Comparison between absorption spectrum (black line) and emission spectrum (dashed line) of Hcy-1 with the absorption of RC (grey line)

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Photoactive Nanohybrids Based on Chemically Functionalized Semiconductor Quantum Dots

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Quantum dots are semiconductor nanocrystals endowed with unique size-dependent optical and electronic properties that arise from quantum confinement effects [1]. These properties, combined with an excellent photostability and the possibility of surface functionalization, make them interesting scaffolds for the development of multicomponent photoactive systems. Hence, their utilization for different applications within the field of supramolecular chemistry – particularly, for the construction of luminescent switches and chemosensors – is the objective of intensive investigations in several laboratories [2].

With the aim of developing new generations of photoactive nanoscale devices, we have synthesized and investigated conjugates composed of inorganic nanocrystals whose surface is covered with functional organic ligands. Luminescent nanocrystals (e.g., CdSe or CdSe/ZnS) of different diameters have been obtained with an accurate control on size by means of solution-based methodologies [3,4]. We have developed efficient procedures to modify the quantum dot surface with molecular ligands in order to implement solubility of the nanohybrids in desired solvents [5] and/or introduce chemical functionalities [6]. We have also shown that quantum dot-molecule conjugates can be obtained by in situ ligand modification [7] or by self-assembly under appropriate conditions [8]. The interplay between the inorganic nanocrystal and the attached molecular units gives rise to photoinduced energy- and electron-transfer processes that may be exploited for luminescence sensing and switching purposes [2].

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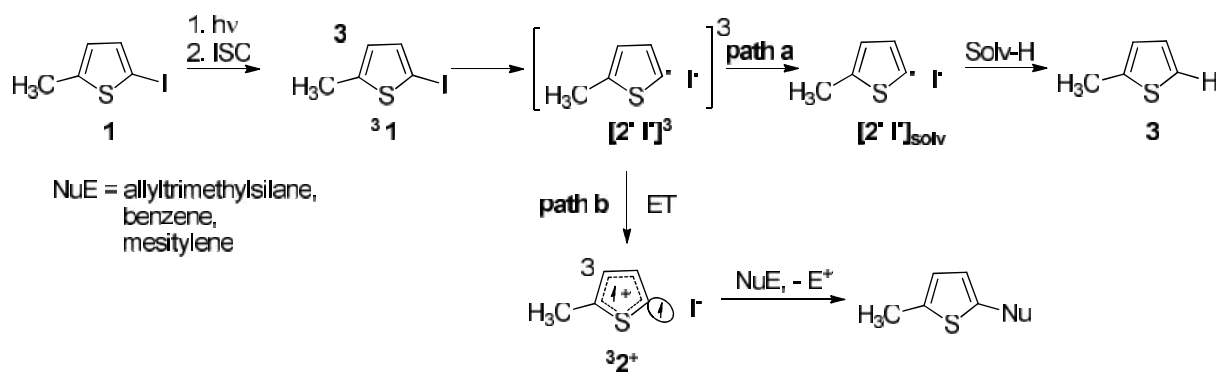
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Photochemistry of 2-halothiophenes: a journey from heteroaryl radical to heteroaryl cation

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Formation of (hetero)aryl-carbon bond is one of the main issue of organic chemistry. Photochemistry is a useful tool to reach this goal under mild conditions.¹ Indeed, my research group have recently demonstrated that irradiation in polar protic solvents (MeCN, alcohols, alcohols/water) of easy available aryl halides and esters gives access to the corresponding first triplet excited state which undergoes heterolysis of the Ar-X (or Ar-O) bond forming the corresponding triplet aryl cation.² This intermediate reacts selectively with π bond nucleophiles ((hetero)aromatics, alkenes, alkynes, vinyl ethers) affording a wide range of substituted benzenes (biphenyls, γ -benzyl lactones, arylalkynes, arylacetals). In order to enlarge the scope of this reaction we investigated the possibility to generate an heteroaryl cation. For this purpose we studied the photochemistry of (2-substituted) halothiophenes. While the arylation is inefficient with 2-chloro(bromo)thiophenes, iododerivatives give satisfactory results. Irradiation of 2-iodo-5-methylthiophene (**1**) (analytically more expedient respect to 2-iodothiophene) in the presence of π bond nucleophiles (benzene, mesitylene and allyltrimethylsilane) afforded arylated products in good yields (40-70%) along with a modest amount (up to 35%) of 2-methylthiophene (**3**). A deep combined experimental and computational study suggests that the first step is the homolysis from the triplet state of the thienyl-iodine bond leading to a triplet radical pair [**2**[•] I[•]].³ Diffusional separation generates a solvated radical pair [**2**[•] I[•]]_{solv} (path a)³ and then the 2-thienyl radical (**2**[•]) may abstract hydrogen from the solvent to give **3**. An intramolecular electron transfer (ET) in [**2**[•] I[•]]³ (path b),³ however, strongly competes to give a triplet thienyl cation (**3**²⁺) which is trapped by π bond nucleophiles (NuE).³



Scheme 1 Photo-arylations via heteroaryl cation.

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Localization-controlled two-colour luminescence imaging via environmental modulation of energy transfer in a BODIPY dyad

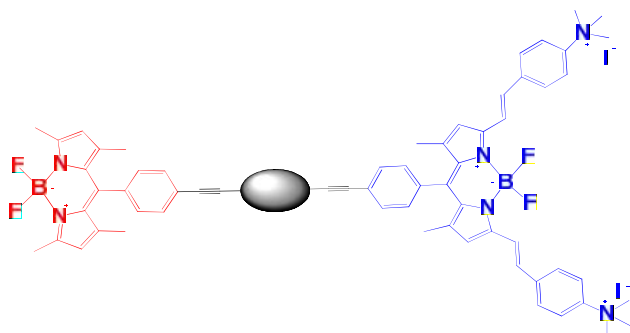
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The search for new highly luminescent molecules is a very attractive field for various reasons, including the development of new dyes for fluorescent imaging. Among the chromophores, 4,4'-difluoro-4-bora-3a,4a-diaza-s-indacene (Bodipy) and derivatives are intensively studied because of their high chemical and photo stability, high absorption coefficients and high fluorescence quantum yields, combined with relative simple strategies for their syntheses.¹ Moreover, Bodipy luminescence properties can be easily tuned by small modification of their skeleton, so spectral shifts in the absorption and emission bands, can be generated by introducing the appropriate substituent pattern.²

Finally, thanks to their stability to the physiological conditions, Bodipy dyes have found a large application in the biomedical field, as labelling reagents for biological molecules such as proteins, DNA, carbohydrates. For all these reasons, although known since 40 years, the number of papers regarding these chromophores

still increases exponentially every year. In this communication, we will describe the synthesis, the spectroscopic properties and the cellular uptakes of a new bi-chromophoric bodipy-based dyes, such as the one shown in the figure. This compound, can give multicolor emission, and it is capable to localize in different sites of the cell, with one color emission dominating on depending of the localization site. Thanks to this unprecedented characteristics this new



Bodipy based dye could be used as luminophores for imaging purpose and could provide cellular mapping, without requiring the use of several different compounds simultaneously.

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Role of the NF- κ B/Snail/RKIP *loop* in the response to PDT treatment in pancreatic carcinoma cells

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Photodynamic therapy (PDT) is a treatment modality of different tumours based on a systemic or topical administration of a photosensitizer, which is then activated by light. In the activated state, the photosensitizer reacts with molecular oxygen and generates reactive oxygen species including singlet oxygen that cause cell damage. Cell death occurs by apoptosis and/or necrosis and the outcome of the treatment depends on the PDT dose. It is also known that the apoptotic signalling pathway is commonly dysregulated in cancer. Several transcription factors have been identified as mediators of cell survival after PDT, one of this is NF- κ B (Nuclear factor κ B).

We have been studying a particular pathway, related to PDT, where NF- κ B modulates the expression of downstream genes involved in tumor progression. In tumor cells, NF- κ B is a key element of a loop that upregulates the pro-survival YY1 and Snail genes and inhibits the pro-apoptotic RKIP gene. We have investigated how the NF- κ B/Snail/RKIP loop responds to PDT in two pancreatic cancer cell lines, PANC-1 and BXPC-3. Our aim was to find out a strategy to sensitize tumor cells to the photodynamic treatment. As photosensitizer we used the cationic porphyrin TMPyP4 (tetra-meso(N-methyl-4-pyridyl) porphine; P4) that can be irradiated with white light (fluence of 7.2 J/cm²).

First, we examined in the two cancer cell lines the phototoxicity of TMPyP4 at different concentrations and observed a clear dose-response inhibition of cell growth. When we focused on low doses (<IC50) we found that after an initial partial damage, the cells activated a protective response. In fact, scratch-wound and clonogenic assays showed that low doses P4/PDT led to cellular recover. To know if this cell recovery is mediated by changes of the NF- κ B/Snail/RKIP loop, we performed Western blot assays to evaluate the expression of the genes involved in the loop. We found that a low-dose P4/PDT increased both pro-survival NF- κ B and downstream Snail, while decreased pro-apoptotic RKIP. In contrast, with a high dose P4/PDT (\geq IC50) we observed a decrease of NF- κ B and Snail and an increase of RKIP. These results are in keeping with the observed tumor cell growth arrest.

To sum up, our study indicates that pancreatic cancer cells respond to P4/PDT through the modulation of the NF- κ B/Snail/RKIP loop. To potentiate the photodynamic treatment we focused on Nrf2 as it is overexpressed in pancreatic cancer cells. The nuclear factor Nrf2 behaves as a redox sensor that stimulate the expression of detoxifying enzymes, antioxidant proteins and drug transporters (e.g.ABCG2) when the oxidative stress in the cell increases. Considering that PDT stimulates the expression of Nrf2, we hypothesize that the inhibition of Nrf2 should make the cells more sensitive to the treatment. In addition, we want to investigate if there is a link between KRAS, Nrf2 and the NF- κ B/Snail/RKIP loop.

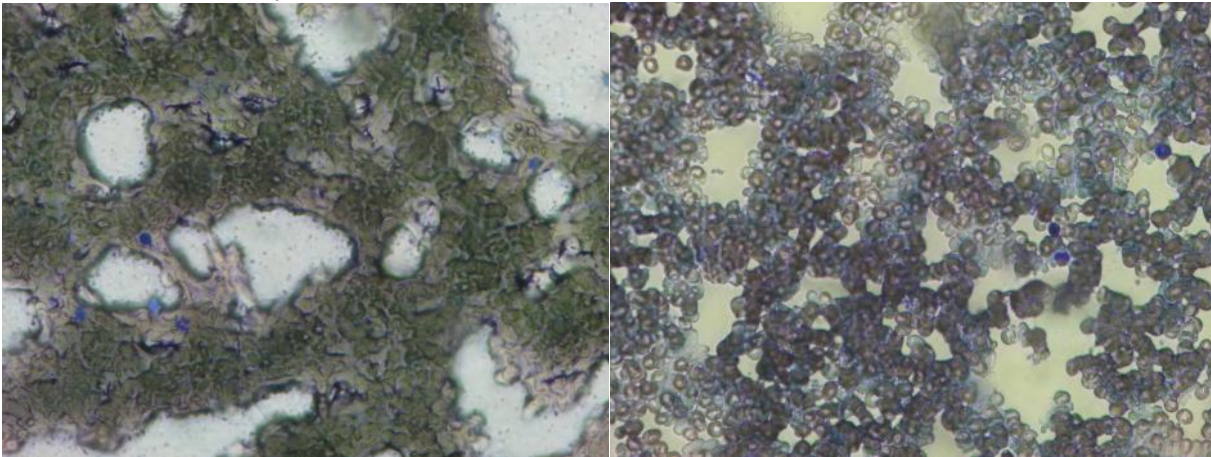
Laser therapies for treating chronic pain and for increasing wellbeing

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Introduction:

The method of intravenous laser blood irradiation (ILLT) has demonstrated to have an analgesic, antiinflammatory and biostimulating effects. The ILLT is a minimal invasive, quick and safe, non-pharmaceutical intervention that may be beneficial for patients with alteration of rheologic properties of the blood as well as improvement of microcirculation.



Before treatment

After treatment

Image of the peripheral blood. May Grunwald-Giemsa

Objectives:

Aim of the study was to assess the efficiency of Intravenous low-level laser therapy (ILLT) in maintaining good health.

Material and methods:

A total of 15 adults enrolled in a quasi-experimental clinical study. The technical execution is simple and uncomplicated. All patients underwent 10 sessions of intravascular laser blood irradiation; the application location was performed on cubital vein with a sequence of 3 treatments per week. We started with one wavelength (usually 658 nm) for 20 minutes and a power of 15 mW. If the patient tolerated the treatment, in a second session different wavelength were available at 632 nm, 532 nm, 405 nm, 432 nm. Usually, each laser is applied for 10-15 minutes. The data survey on patient's quality of life was carried out using the « SF12 questionnaire on general health conditions ».

Results:

We obtained successful treatments in skin diseases, oncology, vascular, diabetes, rheumatoid arthritis. Intravenous laser blood irradiation leads to an improvement in the quality of life of patients.

Discussion and conclusions:

We obtained on 9/15 patient, after the first treatment, general well-being and no adverse effects. Thus, ILLT is essential additional therapy in microcirculation pathology.

UVB represses melanocytes cell migration through β -catenin

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The exposure of skin to ultraviolet (UV) radiation can have both beneficial and deleterious effects by leading, for instance, to increased pigmentation and vitamin D synthesis but also to inflammation and skin cancer. UVB may induce some genetic and epigenetic alterations, and reversible changes associated with post-translational and gene regulation modifications. β -catenin is a main driver in melanocyte development, infrequently mutated in melanoma, but its cellular localization and activity is frequently altered. Here, we evaluated the consequence of UVB on β -catenin in the melanocyte lineage. We find that *in vivo*, UVB induces cytoplasmic/nuclear relocalization of β -catenin in melanocytes of newborn mice and adult human skin; and that *in vitro*, UVB increases β -catenin stability, accumulation in the nucleus, and co-transcriptional activity in mouse melanocyte and human melanoma cell lines, leading to the repression of cell motility and velocity. The activation of β -catenin by UVB can be induced by BIO or CHIR, two inhibitors of GSK3 β . In conclusion, UVB represses melanocyte migration through the GSK3- β -catenin axis.

Synthesis, physico-chemical properties, cellular penetration and photodynamic antiproliferative activity on MCF7 breast cancer cell line of new rose bengal-estradiol conjugates.

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Photodynamic therapy (PDT) is an anti-cancer therapeutic treatment based on the release of reactive oxygenated species by a photosensitizer in the presence of light and oxygen. To increase the photocytotoxic activity of the photosensitizer, the active vectorization of rose Bengal by targeting the nuclear receptor of oestradiol was carried out. To achieve this objective, the derivatisation of estradiol in position 17 β using succinic anhydride was optimized in the first time according to solvents and temperature. In the second time, the fixing of rose Bengal to the 17 oestradiol hémisuccinate via an arm spacer, the dioxadodécanodiamine, using bonds amides formation, was carried out by comparing the effectiveness of the activators of acid function benzotriazolyl-N-oxytris- (diméthylamino) phosphonium (BOP), dicyclocarbodiimide (DCC), N(3-diméthylaminopropyl) éthylocarbodiimide (EDC) and 1-hydroxybenzotriazole (HOBT). In the third time the arm spacer, dioxadodécanodiamine which measures 16 Å was substituted by four different arms length, 7.4; 30; 38 and 76 Å. The physico-chemical properties (UV-visible absorption, fluorescence, generation of singulet oxygen) of the 5 conjugates were characterized. The photocytotoxic activity, as well as the cellular penetration towards human breast cancer cells (MCF-7) of the different conjugates were studied. The length and lipophilicity of the arm spacer are limiting factors to the photocytotoxic activity. The E-RB (16 Å) conjugate showed a photocytotoxic activity 13 times superior to that of the rose Bengal, the E-RB (7,4 Å) conjugate was 6 times superior to the rose Bengal in term of photocytotoxic activity, the E-RB (30 Å) and E-RB (38 Å) conjugates were 2.5 times superior to the rose Bengal, the E-RB (70 Å) conjugates had a photocytotoxic activity similar to rose bengal. The images carried out with confocal microscopy revealed that the E-RB (16 Å) conjugate targeted the nucleus of the human breast cancer cells (MCF-7). The others conjugates, like RB, are excluded very quickly from the cancer cells.

Photo-induced oxidation of bio-mimetic membranes

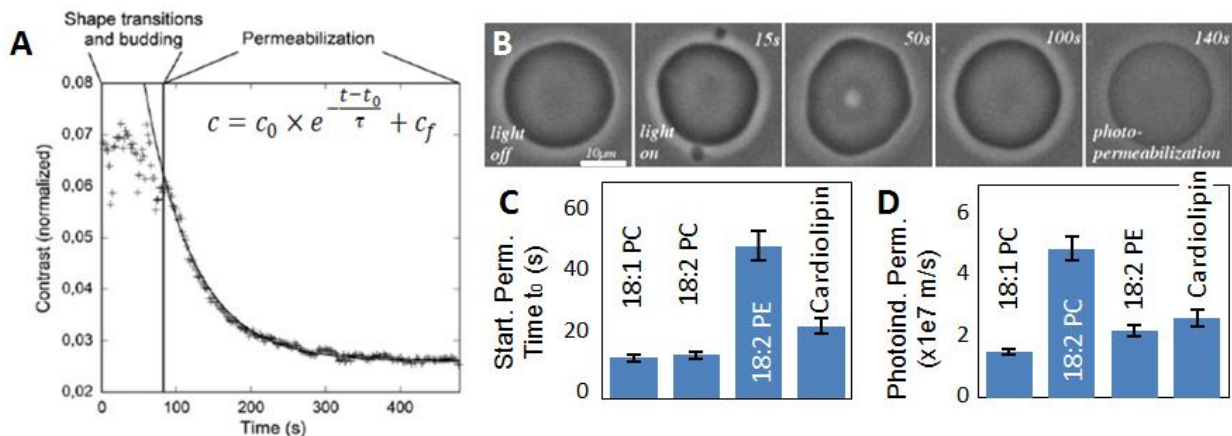
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Mitochondrial membrane oxidation is an important phenomenon involved in aging, degenerative diseases, cell apoptosis and mitochondrial functioning. Here we study lipid oxidation effects depending on the number of insaturations along the aliphatic chains and the lipid polar headgroups.

Our study consists in following photo-induced oxidation of model membranes (Unilamellar Vesicles) of different compositions by two experimental set-ups. The first setup enables us to characterize the ability of vesicles to resist oxidation [1-2]. Changes in phase contrast of giant vesicles allow to determine the membrane permeation caused by oxidation. Typically when oxidation starts, contrast first fluctuates for a time called starting permeation time, then decreases exponentially with a characteristic time used to define a photo-induced permeability (see fig.). The second setup gives us access to the chemical scenario corresponding to oxidation. Optical tweezers are coupled to a non-resonant Raman spectroscope [3].



(a-b) Typical exponential decrease of a being-oxidized vesicle contrast. (c-d) Starting permeation time and photo-induced permeability for different membrane composition.

In most cases, our results evidence a good accordance between the number of chemical targets and the mechanical modifications of the membranes. Two points have to be highlighted. First, the number of insaturations does not influence the starting permeabilization time of the membrane. Second, a small amount of cardiolipin postpones membrane oxidation effects. Raman experiments show that a one-insaturation-per-chain lipid oxidation corresponds to a cis-trans isomerism.

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Message in a Bubble: Phototriggered Events in Microdomains

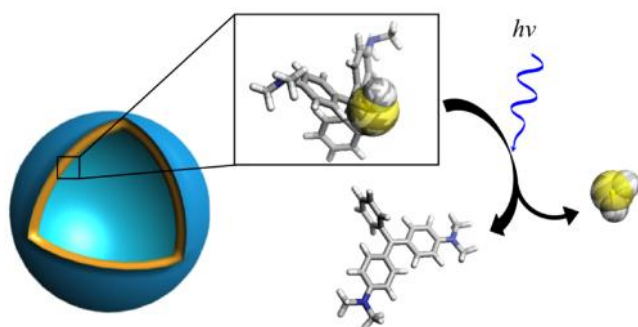
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One goal of our work is to establish a strategy whereby functional molecules can communicate with one another in solution and in organized, self-assembled media (biotic and abiotic). Natural systems use chemical communication with small molecules and ions to promote transfer of information in different processes. Here we consider rudimentary artificial biomimetic systems integrating photonic and ionic processes, where remote control of ion release from synthetic molecular receptors, and thus chemical information transfer, is governed by a photonic stimulus in a bottom-up strategy. Fast processes of photoejection and migration of ions are particularly well-suited to studies in real-time via fluorescence. As well as studies in solution, communication between distant sites / molecules considers the use of photoejected ions in nanocapsules and organized media including micron-sized polymersome hosts. Proof-of-principle of compartmental effects for chemical transfer in dynamic and non-dynamic nano-/microdomains has recently been demonstrated.[1,2]



A prototype polymersome host system for reversible H₂S release (or hydroxide ion release) in pseudophysiological conditions will also be described, see figure.[3] H₂S has been recently identified as one of three endogenous gasotransmitters.

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Characterization of PAMAM-Ce6 dendrimeric nanoparticles for photodynamic treatment.

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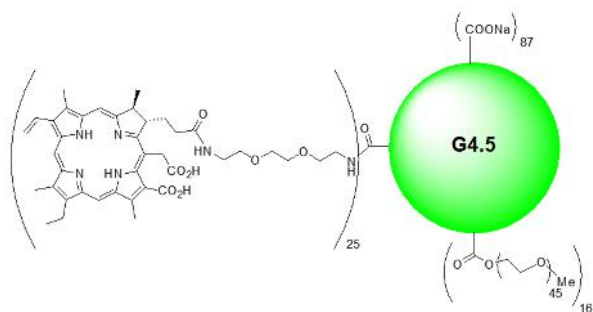
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A key principle of nanomedicine is to use nanoparticles (NPs) to improve the transport of active and/or contrast agents to a target tissue and to strengthen intra-tissue accumulation. Several nanoconstructions have been investigated regarding anticancer drug delivery, most of them based on lipid or polymer structures (Marchal et al. 2015).

Similar to chemotherapeutic agents, the use of biocompatible nanoscale systems for photosensitizers (PSs) delivery in photodynamic therapy (PDT) of cancer demonstrated a significant improvement in PSs bio-availability, -distribution and efficacy of the treatment (Marchal et al., 2015; Abrahamse et al. 2016). PDT is based on the combined action of PS, light and molecular oxygen, leading to the generation of toxic reactive oxygen species (ROS) with the resulting damage of malignant and nonmalignant cells alike, depending on PS distribution (Agostinis et al. 2011; Castano et al., 2004).

Vectors allowing both to avoid the fast release of relevant molecules and their high local concentration have emerged in recent years, these are dendrimers.

Dendrimers are regular hyperbranched macromolecules a few nanometers in diameter (2-10 nm) and which may have on their surface different functional groups. Because of their low cytotoxicity and their solubility in water polyamidoamines or "PAMAM"-dendrimers appear as a very attractive class of biocompatible nanovectors for drug targeting in cells and tissues (Lee et al. 2005). Thanks to the many functional groups on the periphery of the dendrimer, it is easy to graft therapeutic molecules such as photosensitizers, stealth elements (polyethylene glycol), or targeting moieties (aptamers, antibodies, etc...) while controlling the size and lipophilicity of the carrier. All this will allow monitoring and optimizing cellular uptake, biodistribution and pharmacokinetics of the molecule of interest.



The present study investigates generation 4.5 PAMAM dendrimer, covalently functionalized with the PS Chlorin e6 (Ce6). The singlet oxygen generation efficiency and fluorescence emission were moderately affected by the covalent binding of the Ce6 to the dendrimer. This construction allows the vectorization of 32 Ce6 molecules per dendrimer. In vitro, PAMAM dendrimers improve the PDT efficiency of Ce6 by promoting their cellular internalization via an active endocytosis mechanism. However, the PDT efficiency of NPs is limited by the high local concentration of Ce6 at the periphery of dendrimers decreasing production

of singlet oxygen. Ce6 release could restore Ce6 photophysical properties and as such improve the PDT efficiency of NP.

Thus, the next step of this work was to design a cleavable NP able to release the Ce6 under esterase activity. In solution the NP characterization demonstrated that the photophysical properties of Ce6 were recovered after their release from the NP. This cleavable construction displays promising perspectives for future PDT applications.

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Luminescent Superhydrophobic surfaces for anti-microbial adhesion and anti-biofilm applications

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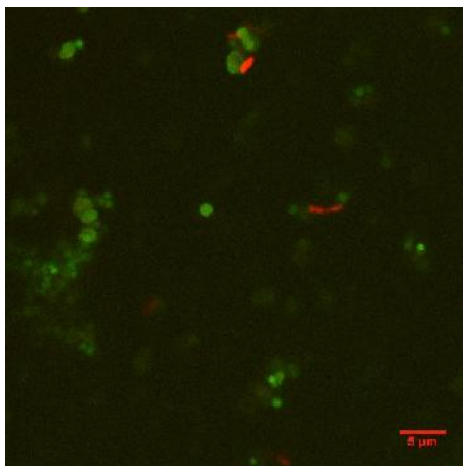
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The control in surface hydrophobicity and water adhesion is extremely important for anti-microbial adhesion or anti-biofilms properties. For the first time we will show that the use of fluorescent monomers such as Pyrene with various substituents differing by their hydrophobicity, size or rigidity/flexibility can lead to surfaces with tunable hydrophobicity, water adhesion and fluorescence properties by a direct electropolymerization process[1].

Seven original monomers with fluoroalkyl, alkyl, phenyl, adamantly and triethyleneglycol substituents were synthesized and studied. The surface roughness is highly dependent on the substituent and it seems that the fluorescence signal correlates well with the surface roughness. Superhydrophobic properties and highly oleophobic properties are obtained using fluoroalkyl chains due to the presence of nanostructured microparticles. In comparison to the structured absorption and emission bands of Pyrene monomers, the Pyrene polymers exhibit a broad structureless spectral shape, where the loss of vibronic structure arises from the Pyrene oligomerization and loss of aromatic Pyrene core structure.

This work is a first tentative to combine superhydrophobic and fluorescent properties using an innovative strategy.

In order to investigate and demonstrate that such superhydrophobic and oleophobic surfaces have anti-microbial adhesion and anti-biofilms properties, preliminary results on *E. coli* and two pathogenic bacteria (*S. Aureus*, *P. Aeruginosa*) will be presented.



Superhydrophobic surface (green - Exc488nm) and *Pseudomonas Aeruginosa* after 2h incubation (Red - exc633 syto9 tagging)

1. «Electrodeposition of Polypyrenes with Tunable Hydrophobicity, Water Adhesion, and Fluorescence Properties» G. Ramos Chagas, X. Xie, T. Darmanin, K. Steenkeste, A. Gaucher, D. Prim, R. Méallet-Renault, G. Godeau, S. Amigoni, F. Guittard, *J. Phys. Chem. C* 2016, 120 (13), 7077–7087

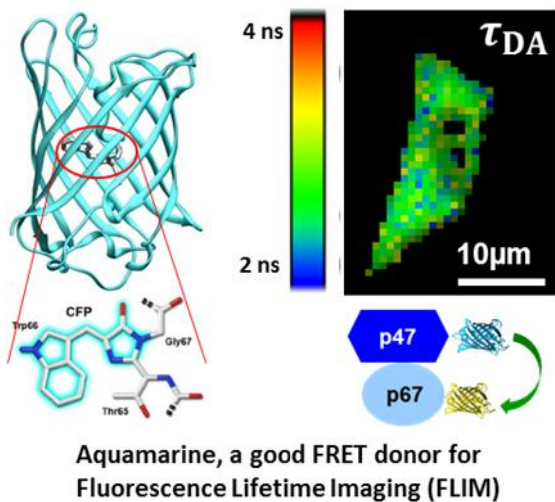
Quantitative analysis of protein-protein interactions in live cell using the new generation of cyan fluorescent proteins. Application to the NADPH oxidase complex.

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Fabienne M erola¹, Marc Tramier², Oliver N usse¹, Marie Erard¹

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Cyan fluorescent proteins (CFPs) derived from *Aequorea victoria* green fluorescent protein are the most widely used F rster resonant energy transfer (FRET) donors used to design genetically encoded biosensors and analyze protein-protein interactions in live-cell. Until very recently, the weak and complex fluorescence emission of cyan variants, such as enhanced cyan fluorescent protein (ECFP) or Cerulean, has remained a



**Aquamarine, a good FRET donor for
Fluorescence Lifetime Imaging (FLIM)**

major bottleneck in these FRET techniques [1]. We showed that the introduction of only two mutations, T65S and H148G, in ECFP leads to a new variant, Aquamarine, equivalent to the best CFPs now available. Besides an impressive pH stability ($pK_{1/2} = 3.3$), Aquamarine shows a very low general sensitivity to its environment, undetectable photoswitching reactions and a good photostability. Its fluorescence quantum yields is close to 90%, and its long, near-single fluorescence lifetime is about 4 ns [2]. Aquamarine was used to probe the interactions between the subunits of the phagocyte NADPH oxidase, a key enzyme of the immune system, generating superoxide anions, which are precursors for other reactive oxygen species. This oxidase is composed of six subunits, the membrane-bound gp91 and p22, a small GTPase Rac and the cytosolic p47, p67, and p40 [3].

We analyzed the interactions between the cytosolic subunits of the NADPH oxidase in their resting state by quantitative F rster Resonance Energy Transfer (FRET) combined with Fluorescence Lifetime Imaging (FLIM) and Fluorescent Cross Correlation Spectroscopy (FCCS). We were able to distinguish between specific and unspecific protein-protein interaction and quantify the fraction of proteins in interaction. In addition, we got structural information about the organization of the interacting proteins and proposed for the first time a 3D-model of the cytosolic complex of the NADPH oxidase covering the *in vitro* as well as the live cell situation.

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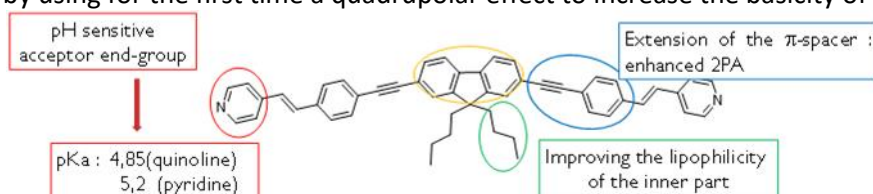
New quadrupolar dyes as sensitive pH probes for two-photon imaging

Cristiano Mazzagonato¹, Jonathan Daniel¹, Guillaume Clermont¹, Bertrand Goudeau¹, Hannah Voldoire¹, Stéphane Arbault¹, Olivier Mongin², Michel Vaultier¹ and Mireille Blanchard-Desce¹.

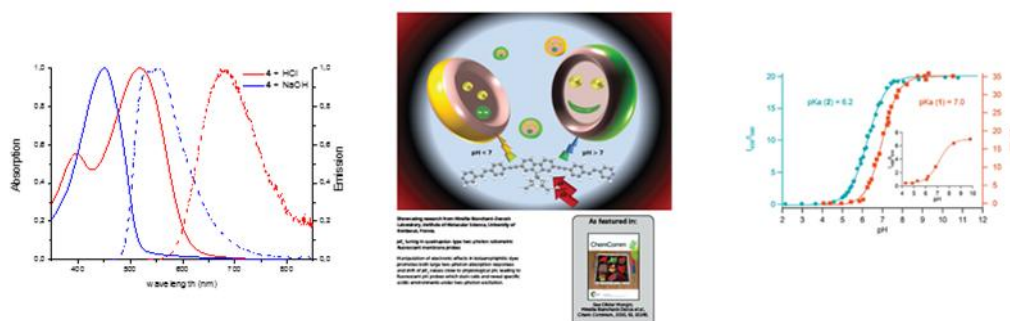
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Two-photon (2P) excitation techniques offer distinct advantages for bio imaging [1]. This has prompted many efforts towards the development of suitable two-photon fluorescent probes (2PFP). In particular, pH probes play a key role due to the relations between pH variation and several important processes in living cells. Key criteria for the design efficient and exploitable 2PFP pH probes are high sensitivity at specific pH range and large 2PA cross sections (σ_2) in the biological spectral window (typically 700-1000 nm). With this aim in mind, we here introduce a new family of 2PFP pH probes which combine large 2PA response, ratiometric (absorption and emission) behavior and high sensitivity close to physiological pH. Their multipurpose molecular design relies on a quadrupolar structure (D- π -A- π -A) based on a fluorene core acting as electron-donor (D) and pyridine or quinoline end-groups as electron-acceptors (A). This design was meant to both (i) enhance the 2PA response in the NIR region and (ii) tune their pKa values close to physiological pH by using for the first time a quadrupolar effect to increase the basicity of the end-groups.



Following this route, a series of novel 2PFP probes have been synthesized and their photophysical properties have been investigated. All new 2PFP show large 2PA responses (up to 4000 GM) as well as strong modulation of their 2PA response with pH. In addition, all new 2PFP show a unique ratiometric behavior, of major interest for use as 2PFP in various media (including biological environments). Furthermore, the molecular engineering strategy was found to be valid as the quadrupolar effect was found to be effective in inducing a marked shift of the pKa values close to physiological pH (from 4.8-5.2 to 6.2-7.0). As such, these probes offer major potentialities for *in vivo* monitoring of slight pH variations close to physiological pH. In particular, these 2PEF probes could be used for two-photon imaging of COS7 cells revealing acidic environments of intracellular organelles [2].



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Real-time pH measurements in growing inorganic structures by fluorescence imaging

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Self-assembled structures formed in alkaline solutions of sodium silicate and water, in the presence of carbonate, are widely studied. Special interest has been devoted to understanding the growth's mechanism and, in particular, pH has been hypothesized to play an important role in these processes. According to a recent models, a local decrease and an oscillatory behaviour of the pH^[1] are expected to occur on the growing front of the crystals, as a result of the alternate precipitation of silicate and carbonate.^[2] In order to experimentally demonstrate this mechanism, we used OFF-ON fluorescent chemosensors that allowed us to monitor the pH changes in real time during the growth of these structures. The fluorescent probes were specifically with the aim to monitor different values of local pH changes, depending on the kind of studied systems. Using wide field fluorescence imaging microscopy and ImageJ software, indeed, we succeed in correlating the detected fluorescence with the local pH changes.

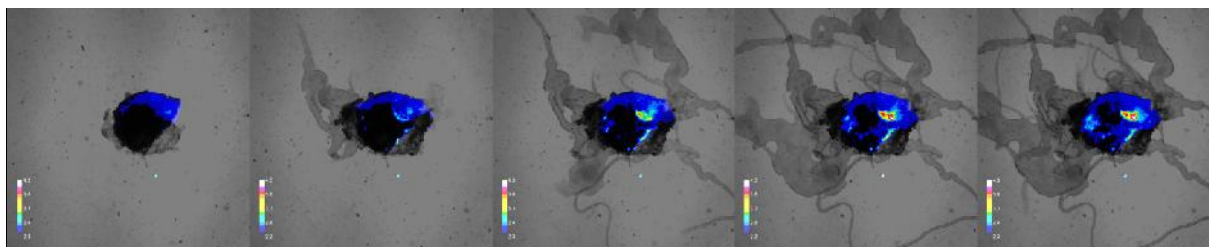


Fig. 1. Superimposition of a transmission image of a silica garden and its pH changes (in false colours) at different times during its growth.^[3]

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Ultrafast Dynamics of a GFP Chromophore Analogue: Competition between Excited-State Proton Transfer and Torsional Relaxation

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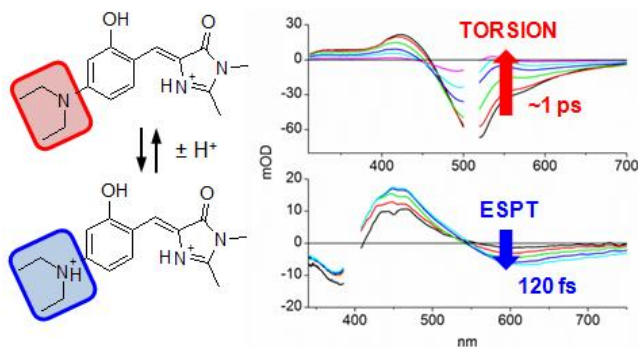
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The photophysics of GFP-related fluorescent proteins and their chromophores relies on a competition between excited-state proton transfer (ESPT) and torsion. In solution, the light-induced dynamics of the p-hydroxybenzylideneimidazolinone (p-HBDI) chromophore of GFP is dominated by ultrafast torsional motions at the ethylene bridge.¹ In contrast, inside the GFP β -barrel, torsions are hindered and neutral p-HBDI undergoes fast excited-state deprotonation to form anionic p-HBDI, the species responsible for the strong green fluorescence of GFP.² Chromophore torsion is nevertheless observed in some fluorescent proteins other than GFP, due to different protein-chromophore interactions. ON-OFF photoswitching in photochromic proteins such as Dronpa is for instance based on chromophore cis/trans photoisomerization.³

Mimicking these processes using simple molecular systems derived from the GFP chromophore is



currently attracting much interest. The excited-state dynamics of o-hydroxy derivatives of HBDI in solution were reported to be governed by ESPT, offering the opportunity to study this reaction in solution.⁴ It is also known that electron donating amino substituents in para position promote torsional relaxation.⁵ The molecules studied until now however do not allow direct investigation of the competition between ESPT and torsion since they exhibit only one of the two processes.

In the present work, we studied OHIM, a GFP chromophore analogue bearing o-hydroxy and p-diethylamino substituents. The high interest of OHIM is that the above-mentioned competition may be investigated in a single molecule, under pH control. We studied the light-induced dynamics of OHIM by femtosecond transient absorption spectroscopy, at different pH, and found that it is determined by the electron donating character of the diethylamino group. Torsional relaxation dominates when the diethylamino group is neutral, while ultrafast ESPT followed by cis/trans isomerization and ground-state reprotonation are observed when the diethylamino group is protonated and therefore inactive as an electron donor.

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Hydrogen Peroxide as an efficient photo-inducer for the complete degradation of organic pollutants: kinetics and analytical studies

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Due to increased regulations about the drinking water quality and better understanding of the benefits of UV processes in water treatment, a growing number of techniques largely consider the use of UV oxidation processes. Thus, our present research work was devoted to the state of the art in the investigations of the kinetics and the mechanism of photo-induced oxidative degradation of organic compounds of various classes by hydrogen peroxide in aqueous solutions. We have deeply analysed the impact of several physical and chemical parameters (substrate structure, pH of the solution, hydrogen peroxide concentration, oxygen concentration and presence of various inorganic ions) and the rate of the photo-oxidative process.

The UV/H₂O₂ process is accomplished through the efficient generation highly oxidative species. The UV light catalyses the dissociation of hydrogen peroxide into hydroxyl radicals through chain reactions. These oxidant species efficiently react with the organic compounds of interest that is present in the medium of interest. This process has been shown to be effective in destroying many micro-pollutants present in the groundwater as well as in surface water through direct chemical oxidation. The key design and operating parameters for UV/H₂O₂ systems include: peroxide dose, UV lamp type and intensity, reactor contact time, and control system (pH and temperature). The hydroxyl radical generated in the UV/H₂O₂ process is non selective and thus can be trapped by organic as well as inorganic compounds. Water quality parameters, such as organic matter, alkalinity, and nitrite play an important role for the UV/H₂O₂ system because they are considered hydroxyl radical traps, which reduce system effectiveness during the oxidation of the contaminants. Another parameter that is critical is the use of hydrogen peroxide in excess since it can act as a scavenger, leading to a limit of effectiveness.

In the present work, we used the system UV/H₂O₂ as a preliminary process for the degradation of two types of pollutants: sulfonyleureas and nitroso compounds. This allowed a complete and fast removal of these pollutants. The complete degradation clearly involves hydroxyl radicals that were identified and also quantified by nanosecond laser photolysis measurements. The process highly depends on the initial substrate concentration, pH and the concentration of the photoinductor H₂O₂. The presence of inorganic ions (chloride, nitrate, carbonate...) that could be present in waters was shown to inhibit the pollutants degradations. Within this present work, a special attention was also devoted to the elucidation of products formed during the above photo-oxidative process. This was performed by using liquid chromatography coupled to tandem mass (LC/ESI/MS²) and GC/MS. The deep investigation of the fragmentation processes of the generated products permitted the establishment of precise chemical structures. The complete overview of the kinetic results as well as the nature of the products permitted us to propose a full mechanistic scheme for the photo-oxidative degradation of the studied pollutants.

Coupling photocatalysts and ferrate oxidation: towards an innovative solution for wastewater treatment

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A limiting factor in the photocatalytic oxidation using UV irradiation of TiO₂ is the recombination of conduction band electron (e⁻_{cb}) with electron holes (h⁺_{vb}) on TiO₂ surface. Coupling ferrate(VI), known as an “environmentally friendly” oxidant, with UV/TiO₂ photocatalysis may involve an oxidation synergism arising from the Fe(VI) scavenging of e⁻_{cb} and the corresponding beneficial formation of highly reactive Fe(V). This study describes the results of coupling P25 TiO₂ (suspension or supported on three-dimensional foams) and Fe(VI) (pure or Fe(VI) matter synthesized in our laboratory) to remove model pollutants.

Kinetics of disappearance of rhodamine 6G ([R6G]₀=10⁻⁵M; pH=8.25±0.05), in presence of TiO₂ ([P25]=0.1g/L) illuminated under an UV source (365nm, 4.5×10¹⁷photons/s), Fe(VI) ([Fe(VI)]₀=10⁻⁴M) or both, are followed by spectrophotometry. Total organic carbon and OH⁻ radicals measurements are conducted. A synergism is highlighted during the treatment of R6G with UV/TiO₂ associated to pure Fe(VI), while this abatement is not reached when coupling Fe(VI) matter with UV/TiO₂ (Figure). A study of the impact of the inorganic salts presents in the Fe(VI) matter (10⁻⁴M of SO₄²⁻, Fe³⁺, Cl⁻, CO₃²⁻) on the oxidative activities is presented. A competition of adsorption between salts and R6G at the catalyst surface and a trapping of OH⁻ radicals are highlighted for each salt, particularly with SO₄²⁻: the adsorption of R6G on TiO₂ is reduced from 0.25mg/g to 0.03mg/g and the kinetic of production of OH⁻ is divided by 3.

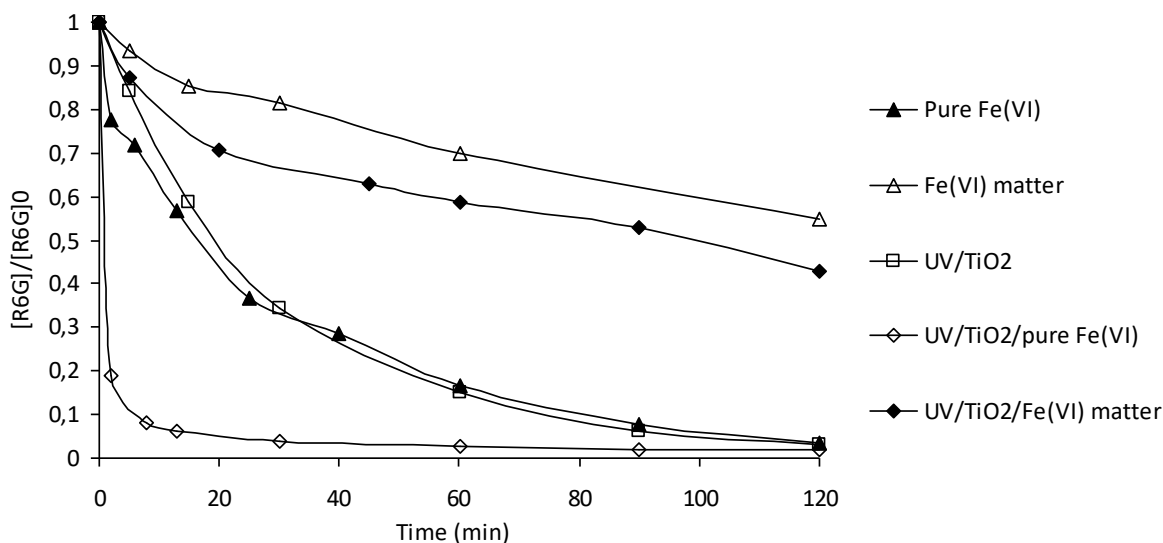


Figure: R6G removal according to time

A procedure for the use of Fe(VI) matter is proposed to avoid the inhibition of the photocatalytic activity after studying some factors as elimination of inhibitors ions, optimization of the concentrations... It results a greater oxidation and the synergetic effect is observed for the treatment of other pollutants (dyes, phenol...), providing an environmentally and economically sustainable technology for water treatment.

The exchange of photogenerated charge carriers between WO_3 and BiVO_4 in coupled $\text{WO}_3/\text{BiVO}_4$ systems

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Conversion and storage of solar energy in the form of fuels, such as photocatalytic splitting of water to generate hydrogen, have attracted increasing interest during the last two decades. Semiconducting materials that are active under visible light have been extensively studied as possible photocatalysts. Among these, BiVO_4 has rapidly emerged as one of the most promising photocatalytic materials that can absorb light up to 520 nm [1]. The electron/hole pairs that are generated following BiVO_4 band gap excitation are effective for water splitting, especially when BiVO_4 is combined with other metal oxides, such as WO_3 .

In the $\text{WO}_3/\text{BiVO}_4$ heterojunction the excellent visible light harvesting properties of BiVO_4 are combined with the superior conductivity of the photogenerated charge carriers, typical of WO_3 [2]. Due to the favorable band alignment between the two oxides, photopromoted electrons in BiVO_4 migrate into the

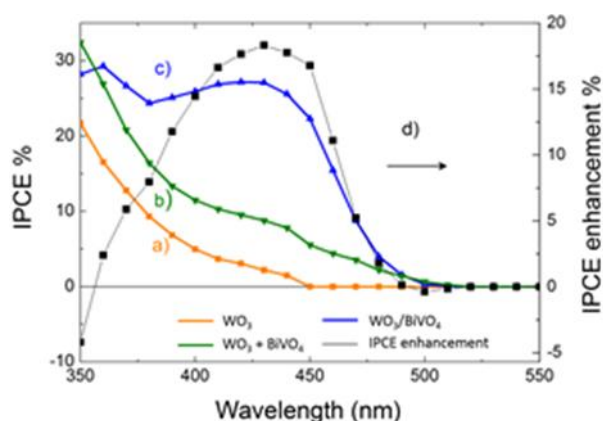


Figure 1. a) IPCE measurements of the WO_3 photoanode, b) sum of the IPCEs measured with the WO_3 and the BiVO_4 films c) IPCE recorded with the $\text{WO}_3/\text{BiVO}_4$ film and d) IPCE enhancement (i.e. the difference between trace c and b). The IPCEs were carried out in Na_2SO_4 0.5 M aqueous solution and with an applied bias of 1.23 V vs RHE and the BiVO_4 layer was 75 nm thick.

WO_3 conduction band (CB) and rapidly diffuse at the external circuit, exploiting the better charge mobility of the latter material. Thus, in this semiconductor oxide sensitized photoanode, better spatial charge separation is achieved by decreasing the electron-hole pairs recombination in photoexcited BiVO_4 . While band alignment and the enhanced performance of the heterojunction photoanode clearly suggest this charge transfer interaction, a direct and complete evidence of the fast dynamics occurring after photon absorption is still missing.

In our previous study, by using femtosecond transient absorption spectroscopy, the excited state dynamics in BiVO_4 alone were compared to that of the $\text{WO}_3/\text{BiVO}_4$ coupled system and we found that in the latter system trapped holes recombine faster with photoexcited electrons [3]. Such faster transient absorption signal decay suggests that a new electron-hole recombination path is at work when BiVO_4 is in contact with WO_3 .

We present here the results of our recent investigation on the wavelength-dependent photoactivity of individual WO_3 , BiVO_4 and $\text{WO}_3/\text{BiVO}_4$ heterojunction photoanodes and on the dynamics of the photoproduced charge carriers detected by transient absorption spectroscopy. The implications of this study allow to explain the photoactivity of the studied system as a function of the excitation wavelength (see Figure 1) in correlation with the lifetime of trapped holes detected in photoexcited BiVO_4 through femtosecond transient absorption measurements.

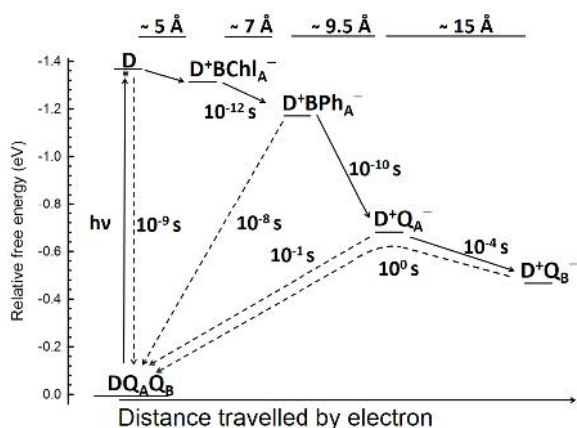
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The photoelectrochemical domain of bacterial photosynthesis

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Plants, algae and some kinds of photosynthetic bacteria, widespread on both land and water, play a crucial role in the biosphere, as they use sunlight to generate biomass. An estimated energy value of about 4.0×10^{21} J is converted in one year by these organisms into valuable biomolecules and molecular oxygen. All life forms on Earth, as well as modern energy sources, strictly depend on photosynthesis and today we have a quite deep knowledge of this natural process at a molecular level. Photosynthesis inspires many research efforts aiming to develop artificial machineries for efficient energy conversion¹. In bacterial photosynthesis, the pivotal enzyme is the photosynthetic reaction center (RC), possibly the transmembrane protein most studied at structural and functional level and used as model for the construction of biohybrid devices. In this contribution, I will focus on the thermodynamic aspects of the photoinduced electron transfer cascade, how it works in vivo and how it can be exploited in photoelectrochemical cells. As sketched in the figure, the energy of a photon is used by the cofactors embedded within the RC to promote a redox reaction between a specialized pair of bacteriochlorophylls (the primary donor D, with $E_m = 450$ mV) and the quinone acceptor Q_B (with $E_m = +100$ mV). This non-spontaneous process is made possible by the energy hc/λ gained by D at 860 nm which generates a new redox couple D^*/D^+ with a very reducing $E_m = -980$ mV. It will be shown that under normal daylight illumination $[D^*]$ is several order of magnitudes less than $[D]$, so that the actual yield of conversion of photonic energy in excitation energy is 59%. Moreover, the largest part of the excitation energy gained by D^* is wasted during the charge transfer chain along the intermediate acceptors. However, the final charge separated state $D^+Q_B^-$ is higher in energy than the initial ground state, and, remarkably, it is obtained with a unitary quantum efficiency and has a lifetime in the order of seconds. Such extremely efficient photoconverter can be isolated from its host organism and it is stable enough to be used for



building photoelectrochemical cells that are presently at the proof-of-concept stage. In fact, in the presence of exogenous electron donors (the physiological cytochrome c_2 or artificial ferrocenes) and a quinone pool, the light triggers a photocycle having as final products the reduced quinol and the oxidized exogenous donor. In a classical three-electrode cell, if the potential of the working electrode is set to the appropriate value, it will be able to give electrons to the photo-oxidized exogenous donor and the relevant signal is detected as photocurrent. The efficiency of this process depends on the nature and concentration of the involved species, the material of the working electrode and the interface between the RC and the electrode. All these aspects will be presented and discussed

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An artificial molecular pump powered by light energy

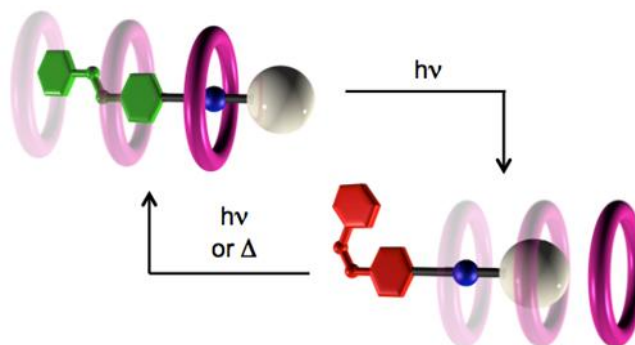
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The bottom-up design, preparation and characterization of chemical systems that behave as molecular-scale machines and motors is a stimulating challenge of nanoscience.¹ The interest on this kind of systems arises from their ability to perform a (useful) function in response to chemical and/or physical signals. In this context, the use of light stimulation has several advantages, primarily because photons can be used to supply energy to the system (i.e., write) as well as to gain information about its state (i.e., read).²

Here we will describe investigations undertaken in our laboratories aimed at photo-inducing and -controlling large-amplitude molecular motions, both under thermodynamic and kinetic viewpoints, in multicomponent (supramolecular) species that comprise photoreactive units.³ This work has recently culminated with the design, construction and operation of a system in which light irradiation causes the relative unidirectional transit of a nonsymmetric molecular axle through a macrocycle (see Figure).⁴

The device rectifies Brownian fluctuations by energy and information ratchet mechanisms and can repeat its working cycle under photostationary conditions (i.e., it shows autonomous energy dissipation). The conceptual and practical elements forming the basis of autonomous light-powered directed motion are implemented with a minimalist molecular design. As a matter of fact, this is the first example of a photochemically driven artificial molecular pump.⁵ Systems of this kind can not only lead to radically new approaches in catalysis, materials science and medicine, but also disclose unconventional routes for the conversion of light energy into chemical energy.



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Modelling the structure and triplet-triplet energy transfer of the 6-4 photoproduct.

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It is well known that DNA is a target for UV-induced damage, generating two main photolesions: cyclobutane pyrimidine dimers (CPD), (6-4) photoproducts (6-4PP) and their Dewar isomers [1]. These lesions are highly cytotoxic and genotoxic if they are not repaired by enzymes. 6-4PP can be even more harmful for DNA, this lesion may act as sensititizer by its 5-methyl-2-pyrimidone (Pyo) moiety, inducing Triplet Triplet Energy Transfer (TTET) toward an adjacent thymine [2]. We studied 6-4PP structure in B-DNA along 1 μ s classical Molecular Dynamics simulation (MD) and we investigated its spectroscopic properties using hybrid quantum-mechanics/molecular-mechanics (QM/MM) techniques rooted in TD-DFT. First, investigations were performed on Pyo as an artificial nucleobase in double-stranded DNA [3]. MD simulations shown that Pyo disturbs nor the overall B-DNA helicity neither the Watson-Crick pairing, and exhibits a strong stacking with adjacent thymine, which is needed for the Dexter type TTET. Our QM/MM calculations revealed that this energy transfer is facile, with a barrier of 0.4 eV (see Figure 1).

However, these results may differ for 6-4PP, which can trigger a strong distortion strongly the double helix to accomodate the cross-link. Along our dynamics for a 16-bp duplex, we probe the rearrangement of the structure which is bent in order to restore a π -stacking with a proximal thymine.

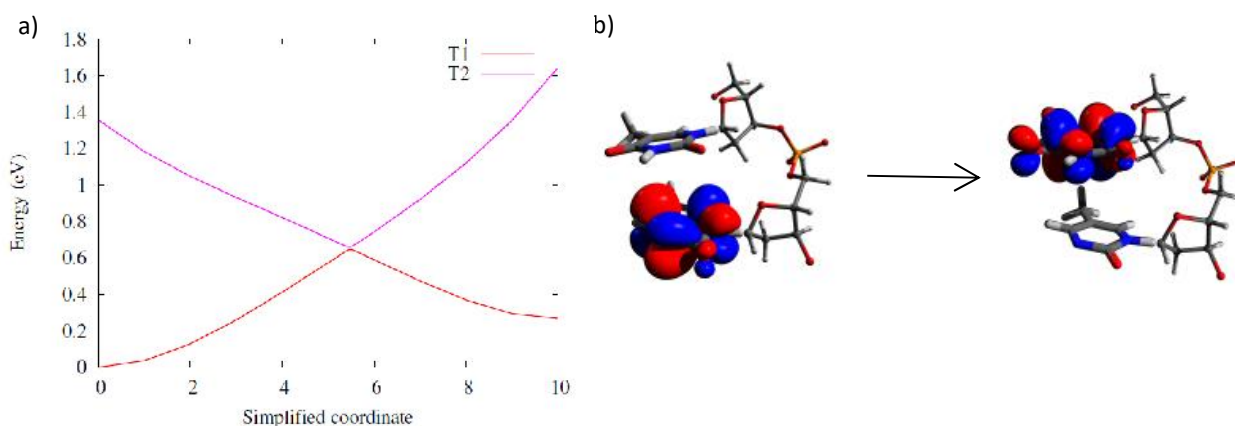


Figure 3. a) TTET energy path along the simplified coordinate. b) Natural-transition Orbitals (NTOs) show the TTET between pyo (up) and the adjacent thymine (bottom).

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Photophysical and photochemical processes in AT-DNA: insights from Quantum Mechanical calculations

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The study of the photo-activated processes in AT based oligonucleotides allows appreciating the richness of the processes triggered in DNA by UV absorption. We shall discuss the computational and experimental evidences that photo-excitation of single-stranded AT DNA can transfer an electron between stacked bases, as it happens in other sequences.¹⁻² An important methodological advance, as the excited state IR calculated spectra, together with its comparison with time resolved IR spectra allow to show that the signature of the Charge Transfer Excited States survives for long time scales.³ In alternated d(AT) d(AT) duplex this process also occurs, whereas in (dA) (dT) homoduplexes ET can trigger interstrand proton transfer reaction.⁴ Furthermore, we study how long-living excitons between stacked bases can be connected to photodimerization reactions between AA, AT and TT and what is the role of the charge transfer states.⁵⁻⁷

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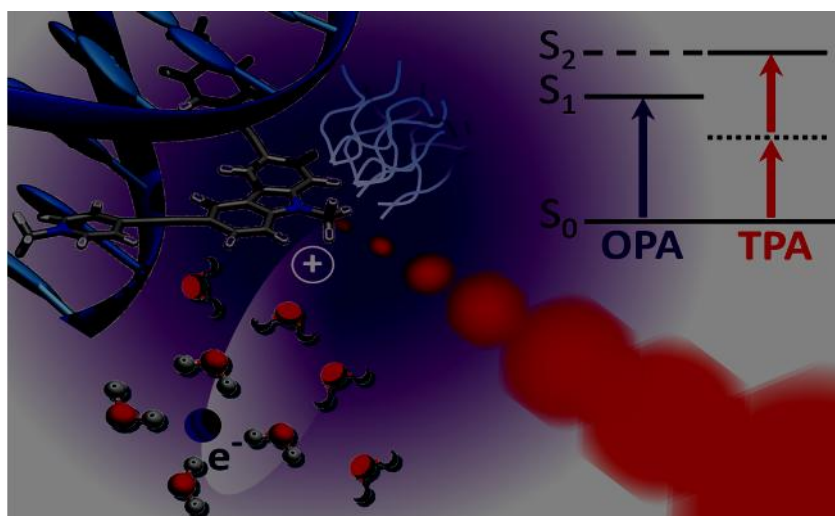
Two-photon-absorption DNA photosensitization, modeling the production of solvated electrons.

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Photodynamic therapy relies on the photosensitization of DNA by photoactive drugs able to trigger processes that will induce damages upon excitation. Within these phenomenon one can find electron transfer, hydrogen abstraction, triplet energy transfer all resulting on the photoexcitation of the drug. Nowadays, tetrapyrrolic photosensitisers are widely used for this purpose notably due to the efficient population of the triplet manifold. Two-photon-absorption (TPA) further improves photodynamic therapy efficiency, allowing to exploit the phototherapeutic wavelength window (infrared). A novel carbazole moiety (BMEMC) presents the ability to interact with DNA and induce damages upon TPA. Its action mechanism has been rationalized using computational chemistry technics such as molecular dynamics and quantum chemistry, in particular concerning its efficiency in hypoxic conditions enabling the treatment of solid tumor.



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Effect of methylation on cytosine

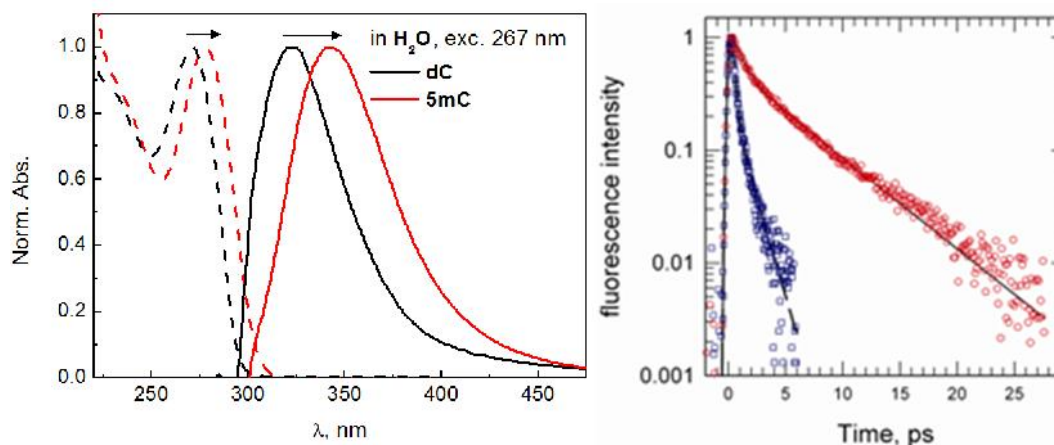
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Absorption of UV radiation by DNA may result in damage to the genetic code and provoke skin cancer. Although 5-methylcytosine (5mC) represents less than 5% of the bases in the human genome, it is associated with 30% of mutational hotspots, which correlates with the increased quantum yield of cyclopyrimidine dimers (CPDs) at T5mCG sites. To understand the origin of this increased reactivity, we have undertaken a study of relevant methylated and non-methylated DNA sequences combining time-resolved spectroscopy and theoretical calculations (molecular dynamics and DFT/TD-DFT).

Here we report the results on the monomeric bases cytosine and 5-methylcytosine. The steady-state absorption and emission spectra (left figure) are strongly red-shifted in the methylated compound, showing the highly stabilizing role of the methyl group. The femtosecond fluorescence results show that methylation of cytidine strongly increases its fluorescence lifetime (right figure). Moreover, the nature of the solvent (polarity, hydrogen bonding and viscosity) has been investigated.



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Degradation mechanism in Firpic: blue phosphorescent OLED emitter

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One of the main issue in organic light emitting diode technology (OLED) is related to the stability of the emissive organic materials. OLED degradation occurs because of the accumulation of non-radiative recombination centers and luminescence quenchers at morphological and chemical defects. In this contest, the study of degradation pathways, ultimately leading to OLED failure, is essential to meet the device lifetime and efficiency requirements.¹

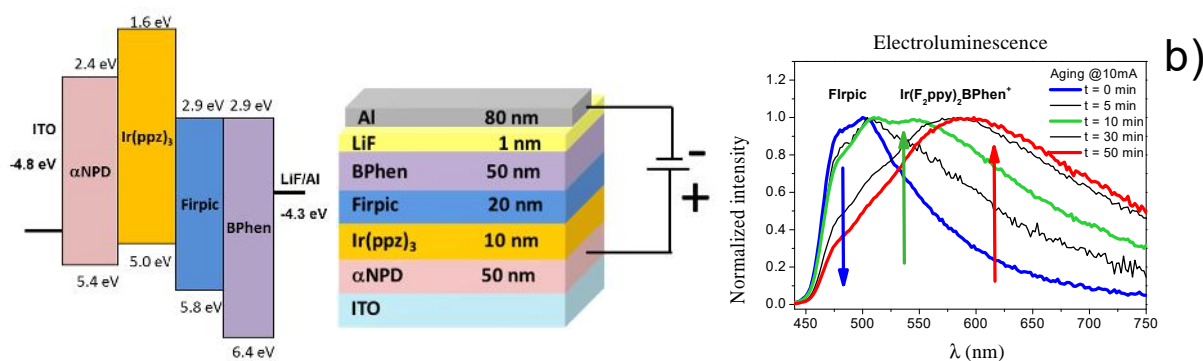


Figure 1: a) Proposed chemical degradation of Firpic emitter; b) OLED structure (α NPD: hole transport material; Ir(ppz)₃: electron blocking layer) and material energy levels; electroluminescence spectral change during OLED aging.

Firpic (figure 1) is one of the most used blue emitter used in OLEDs. Its degradation, involving the loss of fluorine and/or the loss of picolinate ligand, have been observed, while yet unclear.^{2,3} In our study we designed and realized a model, fully vacuum processed, OLED where Firpic is used as neat emitting material and BPhen both as the electron transport one and probe for evidencing Firpic degradation. First, we investigated the Firpic reactivity towards thermal ligand metathesis with BPhen (Figure 1a). The chemical evidence of the picolinate instability in Firpic is proved through combined photoluminescence and mass spectroscopy experiments, trapping the coordinative-unsaturated chromophore with BPhen to yield Ir(F₂ppy)₂(BPhen)⁺. Second, we performed DFT ab-initio molecular dynamics and TDDFT calculations to elucidate the microscopic mechanisms of the degradation of Firpic and its derivatives. Finally, we realized and aged an OLED with the structure depicted in figure 1b, and studied the degradation occurring at the interface Firpic/BPhen. Upon aging of the device, the bluish electroluminescence spectrum evolves into the green and red one clearly indicating the formation of low energy emissive species compatible with the emission of the Ir(F₂ppy)₂(BPhen)⁺.

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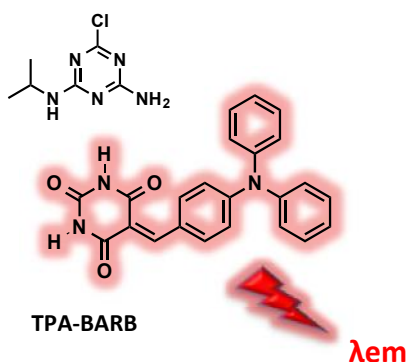
Synthesis and spectroscopic studies of fluorescent molecular receptors for the detection of atrazine and melamine derivatives

Charlotte Remy¹, Clemence Allain¹, Isabelle Leray¹

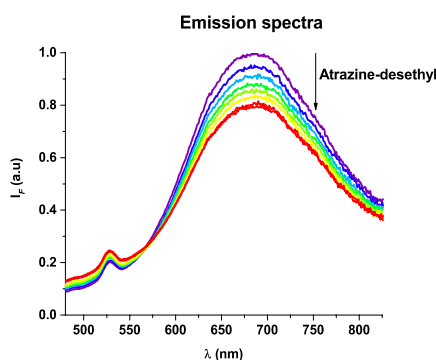
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The detection of polluting species such melamine, atrazine and its by-products is nowadays a social and environmental issue. Indeed, atrazine has been a widely used pesticide since 1960 but this molecule and its degradation product were found to be highly poisonous to the environment and human health.¹ Melamine was illegally added to food products to artificially increase the apparent protein content but excessive ingestion could lead to urinary system damage, kidney stone and ultimately death.²

Atrazine-desethyl



Titration of atrazine-desethyl with TPA-BARB probe



It is a real challenge to develop fluorescent probes for the detection of neutral molecules. Indeed, these fluorophores must combine two properties: they should selectively recognize the analytes and they should display significant changes in fluorescence emission upon binding. That is why we developed new charge-transfer type fluorophores with an acceptor–donor–acceptor (ADA) hydrogen bond motif in order to detect the analytes by hydrogen bonding. Barbituric acid derivatives and naphthalimide probes were synthesized and their photophysical properties were determined. Interaction and detection of the analytes were followed by UV-Vis and fluorescence spectroscopy.

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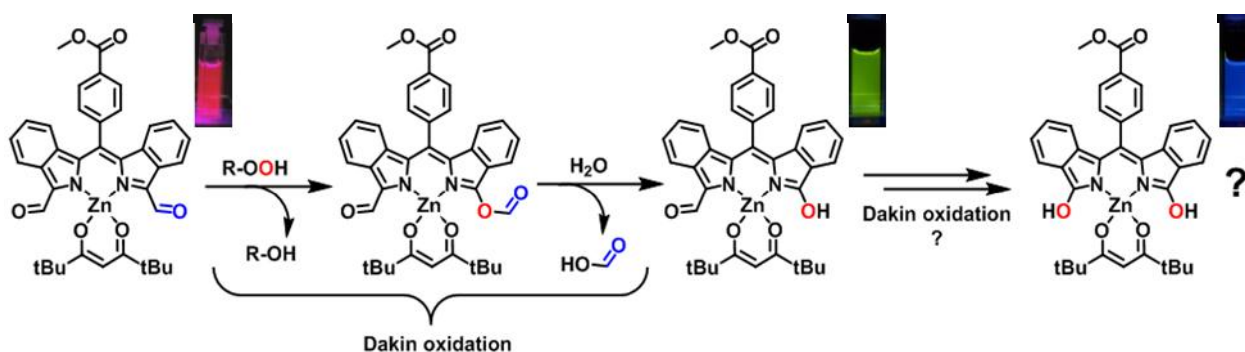
Shining light on benzodipyrins: from NIR-emissive complexes to hydroperoxide sensing and “dial-a-color” fluorescence

Luca Ravotto¹, Dr. Tatiana Esipova², Dr. Massimo Baroncini¹,
Dr. Giacomo Bergamini¹, Prof. Paola Ceroni¹, Prof. Sergei Vinogradov².

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Benzodipyrins, the benzofused analogues of dipyrins, are a strongly colored class of molecules, recently made much more accessible through an easy and versatile synthetic strategy¹. As ligands, they readily form stable complexes with a variety of metal ions. Some of these complexes, like the Zn²⁺ ones, have already been identified as strongly fluorescent in preliminary studies². However, benzodipyrins and their metal complexes remain a still largely unexplored class of compounds. To address this issue, we synthesized and spectroscopically investigated a family of benzodipyrins with different carbonyl substituents, focusing on the tuning of the photophysical properties.



During the investigation we discovered that one of the complexes, containing formyl groups, undergoes an unexpected reaction in THF, associated with a change of the emission color of the solution from red to green to blue. A combined spectroscopic and synthetic study allowed to elucidate the mechanism, which involves hydroperoxide species formed upon reaction of the solvent with oxygen and leads to the formation of at least one new class of fluorescent complexes. Interestingly, the reaction can be induced and controlled by UV light irradiation of the solvent, constituting an unusual way to perform it and allowing the precise control of the emission color within an RGB scheme (with the possibility to generate white light emission). Moreover, the ratiometric fluorescent response of the system may lead, upon optimization of the reaction conditions, to sensing applications in the field of food quality analysis and explosives detection.

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Water-Soluble Photoluminescent Silicon Quantum Dots

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Luminescent quantum dots (QDs) have been proposed as an alternative material to fluorescent organic dyes for bio-imaging applications.[1] Photobleaching and solubility are among the most important challenges associated with organic dyes and limit long-term in vitro and in vivo bioimaging. QDs are more stable against photo-bleaching, exhibit tunable optical properties, and possess versatile surface chemistry.[2] Unfortunately, traditional quantum dots are composed of Group II–VI, IV–VI, and III–V type semiconductors, these include toxic heavy metals, such as cadmium, lead, mercury, and arsenic as well as elements whose reserves are depleting, such as indium and selenium and hence are of limited practical utility for applications involving biological systems. Silicon quantum dots (**SiQDs**) have attracted a great attention due to the great abundance of Si and its low toxicity. Several applications ranging from medicine to electronic and optoelectronic devices have been realized based on SiQDs.[3] Synthetic methods form SiQDs with either a hydride- or halogen terminated surface; these reactive surfaces render SiQDs prone to oxidation under ambient conditions and they agglomerate in solution. To address these stability issues, the SiQDs need to be further functionalized.

Different synthetic strategies are reported to deliver water soluble silicon nanoparticles for biological applications, which, to the best of our knowledge, often suffer of high polydispersity of the nanoparticles, low quantum yields (when reported), or scarcely tunable photoluminescence. Within the framework of the ERC Starting Grant project "**PhotoSi**" we are developing water-dispersible silicon nanoparticles coated with a suited PEG polymer. Silanol-ended PEG polymers were synthesized and grafted onto silicon nanoparticles functionalized with chlorosilane moieties. Here we report synthesis and photophysical characterization of 3 nm and 5 nm SiQDs.

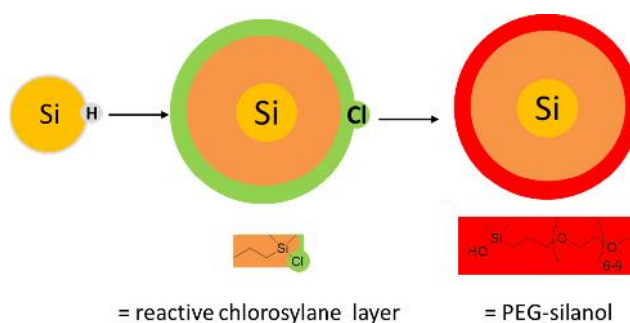


Fig. 1. General synthetic scheme for water soluble SiQDs.

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Vegetable oils-derived resins for stereolithography

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Stereolithography is a 3D printing technique in which a liquid monomer is photo-polymerized to give a solid object. The widely used materials usually belong to acrylate monomers and the (photo) polymerization occurs through radical pathway. Photoinitiators can absorb UV or (less often) visible light giving radicals for direct decomposition or hydrogen abstraction. Due to the toxicity of acrylates vegetable oils derived monomers were proposed in this study. In fact, vegetable oils contains unsaturations and thus they can be exploited as monomers. As an example, linseed oil, tung oil or edible oils (soybean, sunflower or mais) could be used as raw materials. Unlikely, the photoinduced radical polymerization of these oils does not occur or it's too slow for 3D printing applications. Thus oils were modified as epoxides. Epoxides are more reactive monomers with respect to natural oils and they can be polymerized through cationic mechanism. The aim of this work is to use visible light simply generated by a normal digital projector like those used in classrooms. For this reason only few photoacid generators (PAG) are commercially available but they are ineffective for the polymerization of epoxidized oils. Therefore, a multicomponent photoinitiated mixture was used [1]. The system is composed by a radical photoinitiator (phenylbis (2,4,6-trimethylbenzoyl)-phosphine oxide (BAPO)) that gives a high efficient photocleavage (fig. 1 step a,b). The radicals produced abstract efficiently hydrogen from a silane (fig. 1 step c) giving a silyl radical easily oxidized by a iodonium salt (fig.1, step d). Finally, the silyl cation can start the polymerization (fig. 1 step e).

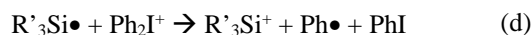
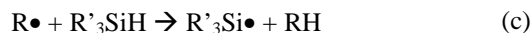
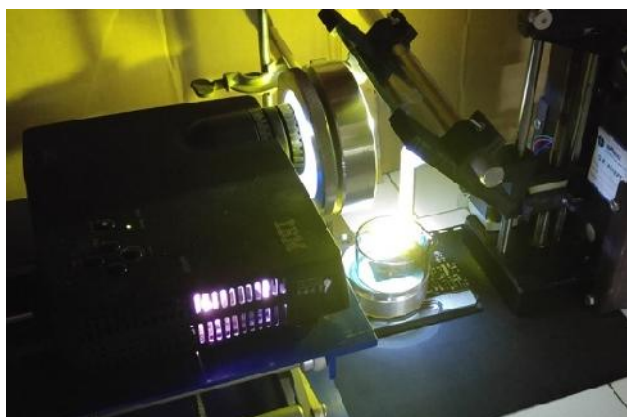


Figure 1. Apparatus used for 3D printing (left) and photoinduced polymerization mechanism (right)

In this way several objects were printed giving a polymer showing elastomeric properties and high temperature resistance (300 °C under nitrogen). Furthermore the polymer should have a good biodegradability and a lower environmental impact with respect to acrylic resins.

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Photodynamic Therapy with 5-Aminolaevulinic Acid and Nuclear Injury: Role of ABCG2 in Preventing DNA damage

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Despite several advantages, Photodynamic therapy remains a marginal approach to cure specific types of cancers mainly because the low penetration of light into human tissues. This limited penetration into

targeted tissue restricts the usefulness of the photoactivation process.

The ability of Photodynamic therapy with 5-aminolaevulinic acid (5-ALA/PDT) to induce nuclear DNA damage following photoactivation of Protoporphyrin IX (PpIX), the photosensitizer generated from the endogenous metabolism of 5-ALA, is still scarcely investigated.

We tried to dissect the molecular effectors involved in the DNA damage to identify the conditions by which the photodynamic treatment may acquire cytotoxic properties by irreversibly damaging the nuclear compartment.

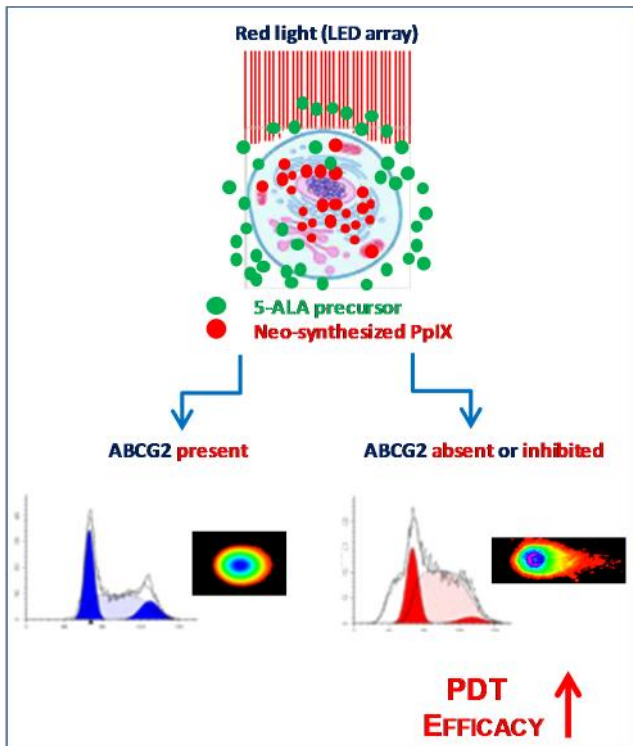
We selected five human cell lines expressing or not the main genome guardian p53, and the cellular efflux regulator ATP binding cassette G2, ABCG2. The cell lines were: 1. two lung adenocarcinoma cell lines, namely H1299 (p53^{-/-}) and A549 wild type (p53^{+/+}); 2. two sub-clones of the same cell line HCT-116, that differ for p53 expression (p53^{+/+} and p53^{-/-}) and 3. a prostate adenocarcinoma cell line, PC3 (p53^{-/-}). Cell cycle

profiles, DNA damage (phosphorylated γ -H2AX and Comet assay) and ABCG2 expression in these cells were measured before or after irradiation. We find that all cell lines, except A549 and PC3, underwent extensive DNA damage. A549 and PC3 cells, although different for p53 expression, displayed high levels of ABCG2 and no DNA damage upon irradiation. We hypothesize that constitutional absence of ABCG2 or its pharmacological inhibition is necessary to observe a measurable PDT mediated DNA damage. In fact, in the presence of an ABCG2 inhibitor, both A549 and PC3 cells subjected to 5-ALA/PDT, presented unequivocal signs of DNA damage.

Overall, the data show that the level of expression of ABCG2 determines the cell aptitude to defend its DNA from PDT-induced injury.

Currently we are investigating the regulation of the transcription of ABCG2 under the various conditions in all 5 cell lines.

Taken together all these findings provide new information on the effectiveness of 5-ALA/PDT and indicate a potential way to shift PDT from a palliative to a more effective approach in cancer therapy.



Photochemical characterization of *Chlamydomonas* mutants for biotechnological applications

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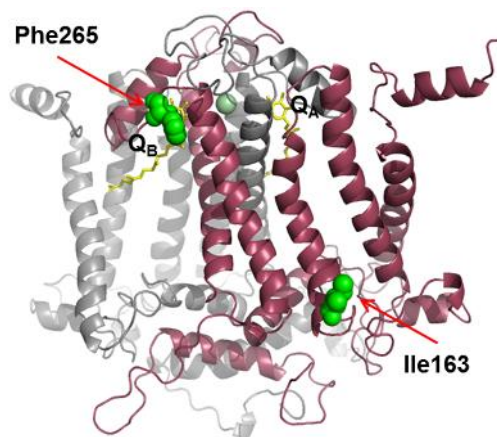
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Large scale cultivation of microalgae holds the demanding promise to support a biomass-based economy dealing with the production of renewable biological resources and their conversion into food, feed, bioenergy and bio-based products¹. Intense research efforts are hence focused on selection of highly productive strains, and/or engineering of well-known genotypes to introduce competitive traits enabling their adaptation to the industrial cultivation conditions. Indeed, photosynthesis is one of the main target of this research field, being tightly linked to the sustainable production of biomass and added-value compounds^{2,3}. The photosynthetic machinery is a smart assembly of *ad hoc* light collectors, protein-metal clusters, and redox biocatalysts enabling the conversion of solar energy into



chemical energy. The process relays on the transduction of photo-excitation events into transmembrane charge-separated states that occurs with very high quantum efficiency, and a series of electron transfer reactions leading to the production of all the goods that fuels our daily life. In addition, photosynthesis gains renewed interest due to the possibility to integrate whole plant cells or their photosynthetic sub-components into optoelectronic devices such as biosensors for environmental monitoring, and/or bio-photoelectrochemical cells for clean energy production². In the quest to identify parameters correlated with a more efficient photosynthetic performance or biotechnologically useful phenotypes, we studied the structure/function relationships occurring in *Chlamydomonas reinhardtii* strains hosting single amino acid substitutions in the photosystem II D1 (PSII-D1) protein. The mutants were produced by combining *in silico* studies with an *in vitro* directed evolution

approach followed by site-directed mutagenesis experiments^{4,5}. Selected mutants were characterized determining the growth rate, pigment content, electron transport efficiency of PSII and rate of oxygen evolution. The performed studies enabled the identification of phenotypes having enhanced stability and photosynthetic performance under stressful conditions⁶, and improved sensitivity to triazines and urea type herbicides⁷. Furthermore, PSII structure was analyzed by molecular dynamics simulations providing insights into the mechanisms of plastoquinol-plastoquinone exchange^{8,9}.

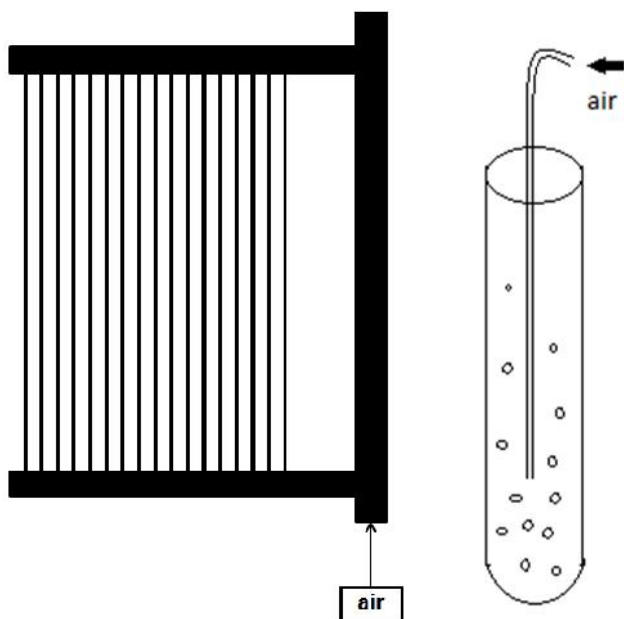
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Study and development of photobioreactors (PBRs) analyzing geometry effects on microalgal biomass growth in residual light

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The primary goal of photobioreactor design is achieving the maximum conversion of light energy into chemical energy that is the maximum photosynthetic efficiency, while keeping biomass production cost at a compatible level



for the range of specified applications. Culturing microalgae in media formulated from wastewaters fits this purpose by reducing the nutrient cost and providing bioremediation if the growth effects of nutrients restriction, toxicity and, above all, light limitation, are taken into account.

Aim of this study is investigating the influence of dark media on raw biomass, carbohydrates, proteins, chlorophylls and lipids accumulation in photosynthetic organisms cultured in photobioreactors with different light path lengths.

Two different types of closed photobioreactor geometries were adopted. The former type is aimed at carrying out parallel small-scale experimental runs in a (possibly large) array of experimental conditions in a practical and space- and time-saving way; a small-volume bubble column photobioreactor was adopted

in this role. The second type is aimed at reducing light limitation effects, in order to enhance phototrophic growth in spite of medium and culture absorbance. A short-light path flat panel photobioreactor was taken to represent the target photobioreactor. Semi-continuous culture systems of the microalga *Scenedesmus dimorphus* strain 1237 were realized in synthetic culture media, where all nutrients are present and toxic compounds are absent, with the addition of a nontoxic dark dye at different dilution rates, in order to introduce a purely radiative growth rate limitation.

In different geometries the significance of the growth rate reduction changes. Flat Panel PBR ensures the same growth rate even though the culture media has a great absorption in the visible spectra. Biomass composition was determined for every culture in diluted dark colored synthetic medium to understand physiological effects: carbohydrates, proteins, chlorophylls and lipids accumulation effects are discussed.

Mastering Surface Interaction of New Theranostic Nanomaterials

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We developed a class of nanoparticles composed of a silica core surrounded by PEG shell, where many different properties can be implemented in a single nanostructure. They can therefore exhibit multimodal functions, which we tailor, because of their negligible toxicity, for application in nanomedicine, in particular in medical diagnostics and therapy, i.e. in "Theranostic". [1]

The synthesis of these nanoparticles is made via a robust Micellar-Assisted method. We can selectively label with efficient fluorophores different the compartments of the nanoparticle, for gathering information on the interactions of the nanostructure with drugs, (bio)polymers and biological cells. This information is then used to develop the potential of the nanoparticles for *in vitro* and *in vivo* applications. In addition, these systems can be advantageously loaded with additional species, such as drugs, photoswitches, and chemosensors, in many cases increasing their chemical and photochemical stability.

The versatility of this synthetic strategy has been exploited by us in several fields spanning from sensors [4], imaging [1-3], fluorescent-photoswitchable nanoparticles [5], and ECL [6]. Progress in the engineering of these nanostructures represents, to our opinion, a very interesting challenge toward the development of theranostic nanomedicine, improving early diagnosis but also the safety and efficacy of therapy.

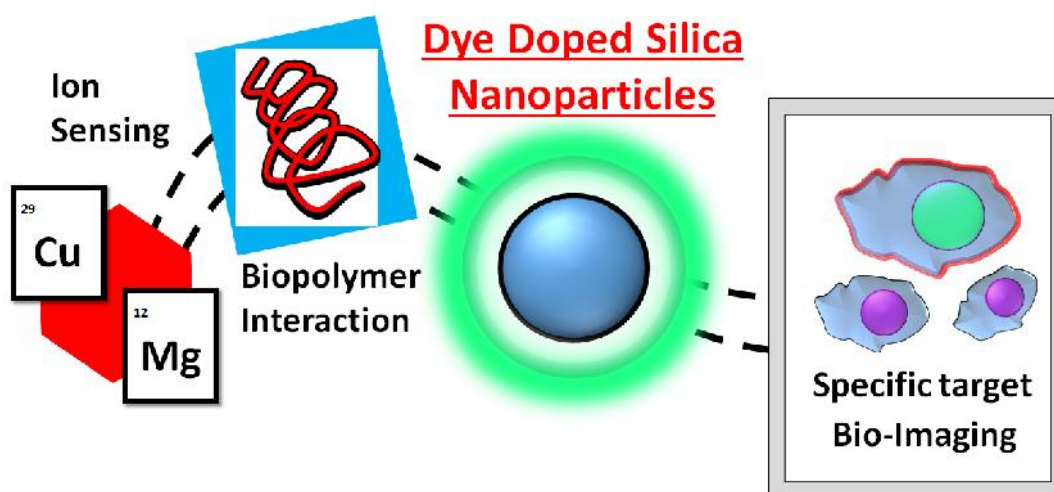


Fig. 1. Schematic representation of the Dye Doped Silica Nanoparticles features.

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Mucus-penetrating lipid nanovesicles for pulmonary drug delivery

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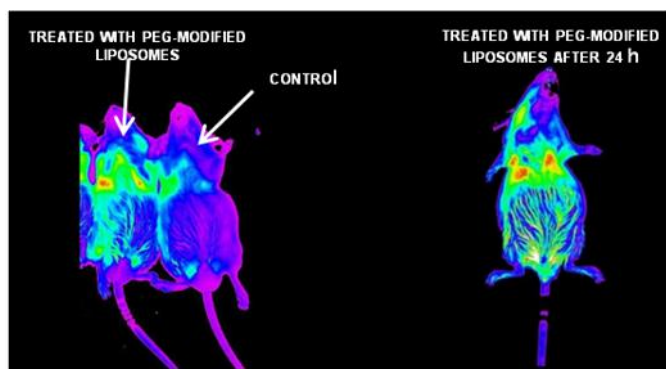
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The aim of this study was the development of a lipid nanosystem for the pulmonary delivery of Beclomethasone Dipropionate (BDP), a steroid anti-inflammatory drug, which is able to have an important role in the prevention and cure of most of respiratory diseases. To this end, the composition of the nanovesicles was specifically chosen in order to obtain a good yield of drug's encapsulation in the bilayer and an adequate distribution of vesicles' size and stability. Natural and biologically safe phospholipids were used in order to assure the maximum biocompatibility. In addition, specific hydrophilic polymers, such as PEG and PLURONIC F127, were used to test if they were able to improve the steric stabilization and the vesicles' mucus penetrability. Indeed, enhancing mucus-penetrating properties is considered to be of great importance in pulmonary drug delivery, in order to more efficiently penetrate into the mucus layer that covers lungs in several pathological conditions, such as cystic fibrosis (CF), chronic obstructive pulmonary disease (COPD), and lung cancer. The Micelle-to-Vesicle Transition (MVT) method was used to prepare vesicles including BDP. This method permitted to obtain small unilamellar vesicles (SUVs), with a small diameter (≈ 100 nm) particularly suitable for in vivo aerosol administration of drugs. Vesicles were characterized in size, morphology and zeta potential and the entrapment efficiency of BDP into lipid nanovesicles was determined. The nanovesicles' toxicity was evaluated on NCI-H441 (human lung adenocarcinoma epithelial) cells by MTT cytotoxicity assay. In addition, bronchoalveolar lavage was carried out in murine models. The fluorescence images of mice treated with liposomal formulations showed that liposomes modified with a hydrophilic coat were able to reach the deeper part of lungs (see figure above). Finally, mucus-penetration tests were carried out on the expectorate of CF afflicted patients, as well as the uptake capability was evaluated on NCI-H441 cells by cytofluorimetry. This study highlights that this SUVs are very promising in pulmonary drug delivery.



murine models. The fluorescence images of mice treated with liposomal formulations showed that liposomes modified with a hydrophilic coat were able to reach the deeper part of lungs (see figure above). Finally, mucus-penetration tests were carried out on the expectorate of CF afflicted patients, as well as the uptake capability was evaluated on NCI-H441 cells by cytofluorimetry. This study highlights that this SUVs are very promising in pulmonary drug delivery.

Photoactive chitosan films

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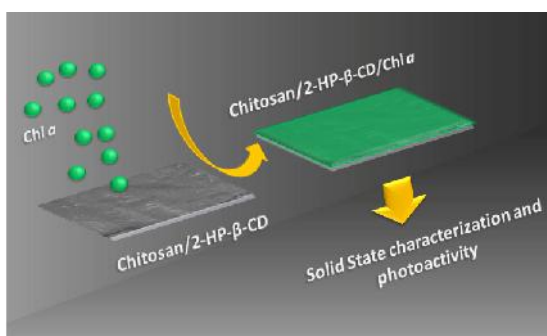
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Novel photosensitizing film based on the natural hybrid polymer Chitosan/2-hydroxy-propyl- β -Cyclodextrin (CH/CD) is synthesized introducing Chlorophyll *a* (CH/CD/Chl*a*) as a photoactive agent for possible application in antimicrobial photodynamic therapy (PDT).¹ The polymer absorbs visible light, in turn able to generate reactive oxygen species (ROS) and, therefore it can be used as environmental friendly and



biodegradable polymeric photosensitizer (PS).² The modified film is characterized by means of different spectroscopic, calorimetric, diffraction techniques and microscopic imaging methods including time-resolved absorption spectroscopy. UV-Vis, FTIR-ATR and X-ray Photoelectron Spectroscopy (XPS) analyses suggest that Chl*a* shows a strong affinity toward

Chitosan introducing interactions with amino groups present on the polymer chains. Nanosecond laser flash photolysis technique provides evidence for the population

of the excited triplet state of Chl*a*. Photogeneration of singlet oxygen is demonstrated by both direct detection by using infrared luminescence spectroscopy and chemical methods based on the use of suitable traps. Scanning Electron Microscopy (SEM), Atomic Force Microscopy (AFM) and Differential Scanning Calorimetry (DSC) analyses confirm also the occurrence of structural changes both on the film surface and within the film layer induced by the insertion of the pigment. Moreover, X-ray Diffraction data (XRD) shows the existence of an amorphous phase for the chitosan films in all the compared conditions.^{1,2}

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Photochemistry in cloud waters: reactivity and fate of organic compounds

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The physico-chemical composition of cloud aqueous phase collected at the Puy de Dome (pdD) station (1465 m a.s.l.) in France was studied during three campaigns in 2013 and 2014. Total Organic Carbon (TOC), four carboxylic acids, hydrogen peroxide as well as main inorganic anions and cations concentrations were determined.

This work was focused on the quantification of oxidative capacity through production rate of hydroxyl radical (HO•) using terephthalic acid probe technique [1]. The main aim is to correlate the contributions of nitrate, nitrite and hydrogen peroxide to the formation rate of hydroxyl radical in synthetic and real cloud water samples. This work shows that hydroxyl radical formation rate is mainly due to the hydrogen peroxide photolysis (90%) while contribution of nitrate, nitrite, complexed iron (via Fenton and photo-Fenton processes) and dissolved organic matter is negligible (lower than 10%).

In a second step experimental data were compared to those obtained using a dynamic air parcel model that was developed to simulate tropospheric cloud events (M2C2) [2] as a function of different air masses origins.

Photogenerated HO• reacts in cloud water with dissolved organic matter (DOC). Unfortunately, little is known about DOC composition but it was estimated that carboxylic acids contribute for the 11 % of the TOC [3]. In this work we investigate the oxidation of carboxylic acids and amino acids by hydroxyl radical in real and synthetic cloud water under solar simulated irradiation.

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Photocatalytic reduction of CO₂ mediated by [Os(diimine)(CO)₂Cl₂] precursor catalyst

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A series of four trans-(Cl)-[OsII(NN)(CO)₂Cl₂] complexes (**C1-C4**, figure 1) has been synthesized for application as electro and photocatalyst towards the two-electrons coupled two-protons CO₂ reduction. Electrocatalysis performed in CH₃CN shows that the selectivity of the reaction can be switch toward the production of CO by a substitution with electron donating group (**C2**, **C3**) and toward HCOO⁻ with electron withdrawing substitution (**C4**). The electrocatalytic process is due to the formation of an Os(0)-bond polymer species after the loss of 2 Cl⁻ per metal center.¹ Under UV-visible irradiation, the excited states of the complexes are efficiency quenched by a reductive electron transfer reaction in presence of tertiary amine (TEOA). The photoreduction leads under argon to the formation the corresponding Os(0)-bond polymer species.² We show that photolysis of the complexes under CO₂ in DMF + TEOA induced the CO₂ reduction. The photocatalysis produces CO as a major product with a remarkable stable turn over frequency during 14 h of irradiation. Electron donating substitution on the diimine ligand increases the CO production turnover number. Transient absorption measurements show that the one electron reduced Os(I) complex (obtained after quenching with TEOA) dimerize under argon, whereas under CO₂, the species reacts directly with a first order kinetics and a rate constant of 1.5 10³ s⁻¹.³ The results suggest that the electrocatalysis and photocatalysis follow two distinct processes, starting mainly from an Os(I) dimer precatalyst when the reduction is performed by an electrode and a Os(I) mononuclear species in case of a photoreduction process.

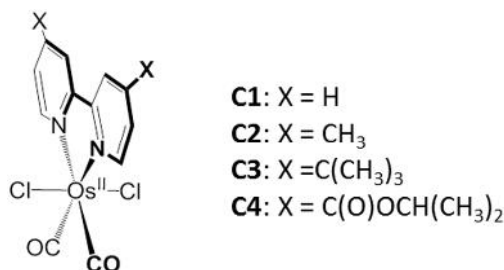


Figure 1. Molecular structures of the osmium precatalyst studied in this presentation.

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Fluorescence lifetime measurements and pH titrations as tools to expand the knowledge on a switchable [2]rotaxane

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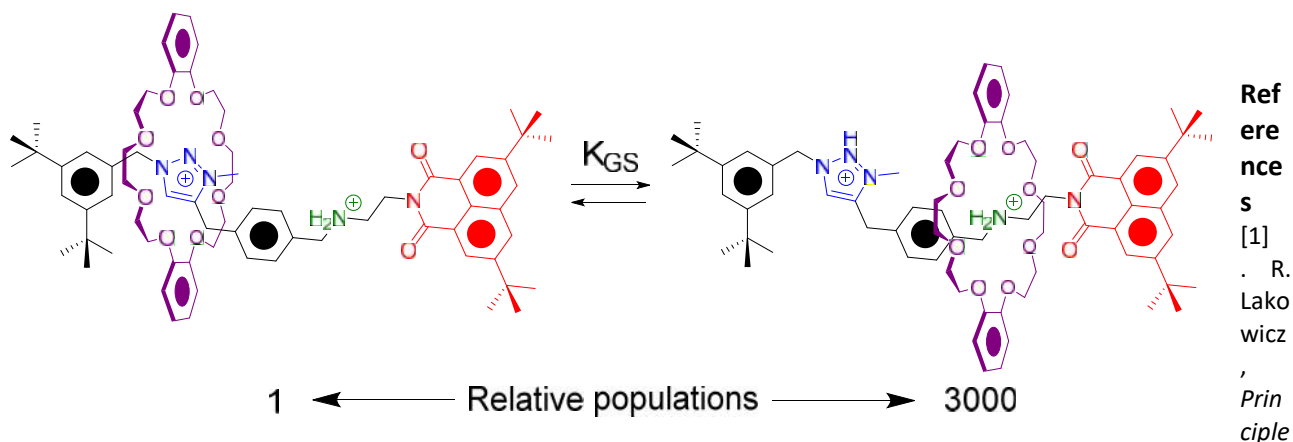
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Luminescence lifetime measurement is an established tool in the study of proteins. Indeed this time-resolved measurement can be used to characterize static and dynamic conformational properties, disclosing information about the fluorophore environment within the protein¹.

We successfully extended this strategy to the study of interlocked molecules: in particular the previously inaccessible² ground-state conformational equilibrium of a [2]rotaxane (see figure) has been disclosed, thanks to the high sensitivity of this method.

A second assay based on simple acid-base titrations was also implemented and gave identical results, thus (i) confirming the reliability of lifetime measurements to probe the conformational distribution and (ii) highlighting the inherent dependence between the conformational characteristics³ of the system and the apparent ammonium pKa⁴, that is the key property on which the switching capability of such systems relies. These two convergent methods are new and sensitive, and expand the toolbox for the characterization of the ground-state thermodynamics of bistable interlocked systems to luminescent or pH dependent systems.



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- [2] For a discussion on the methods to characterize the ground state distribution of interlocked molecules see: a) A. C. Fahrenbach, J. F. Stoddart *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **2011**, *108*, 20416-20421; b) A. C. Fahrenbach, J. F. Stoddart *et al.*, *Acc. Chem. Res.* **2012**, *45*, 1581-1592;
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Influence of parameters in photocatalytic degradation of chloridazon herbicide in aqueous solution

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Nowadays, the chemical compounds such as pesticides, pharmaceuticals, veterinary, drugs, cosmetics, dyes... have been extensively used and their amount has been increased drastically. Owing to their potential persistence, toxicity, carcinogenicity, their presence in the various environment compartments such as soils, atmosphere and surface waters have raised increasing concerns and interest. Therefore, their environmental fate, namely their degradation processes, transfer and the elucidation of the transformation metabolites are of great interest. A large number of studies are available regarding their degradation, fate and behavior in different compartments such as water, soil and food with the aim to reduce their potential negative effect. Moreover, it has been found that some of the xenobiotics are highly persistent and their complete elimination is difficult to achieve using many of the existing water treatment facilities.

Currently Heterogeneous photocatalysis is a process that is growing rapidly in environmental engineering and for removing organic pollutants such as pesticides from water. In this present work, we are interested in the degradation of chloridazon, herbicide family pyridazinones that present high water solubility by heterogeneous photocatalysis by the use of titanium dioxide TiO₂ under excitation at 365 nm.

The main objective is to optimize the conditions for total degradation or mineralization of the solution in order to decontaminate the water. The aim of this work was to for Assessment of impact parameters on photodegradation of chloridazon. TiO₂ P25 degussa was used as catalyst and photodegradation Occurred in aqueous solution under excitation at 365nm. The effect of different TiO₂ concentrations, the herbicide concentration and irradiation time were Investigated. The analyzes were performed by (HPLC). Similarly, it has been shown that the ions Cl⁻, SO₄²⁻, NO₃⁻, CO₃²⁻ has an effect on the photocatalytic degradation on the basis of the results, we concluded that this pollutant disappears completely after 20 minutes of irradiation. The structure elucidation was obtained by using HPLC/ESI/MS and HPLC/ESI/MS² techniques in positive mode and through the complete study of the various fragmentation pathways.

Oxisol: a new dualistic molecule endowed with very potent antioxidant and uv-booster properties for skin photo-oxidative protection

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The cutaneous tissue is the first barrier against environmental insults such as UV radiation, cigarette smoke (CS), diesel fuel exhaust, halogenated hydrocarbons, heavy metals and ozone. It is possible to substantially reduce the incidence of skin cancer in humans by photo-protective strategies; one of these is the application of sunscreen preparations which, when applied to the surface of the skin, attenuate the transmission of the solar radiation, however even when correctly applied a part of the radiation can reach the skin and induce ROS related depletion of antioxidant defence and induce important damages. Furthermore, several skin diseases such as melanoma, psoriasis and dermatitis have now been associated with CS exposure as a model of pollution damages.

In the present study an innovative approach to skin protection was based on the development of a new class of molecules in the aim to develop dualistic molecules able to quench UV-induced ROS and concomitantly improve capability of UV filter to block rays.

To reach the goal, a research project has been started, taking as a model natural polyphenols, that resulted, over 5 years of investigation, in the discovery and application of a new heterocyclic polyphenol (OXISOL) that work both as UV booster for filters and very potent antioxidant. Antioxidant properties were assessed with different complementary methods (i.e. DPPH; FRAP; PCL; ORAC). UVA and UVB filtering properties were assessed in several kind of sunscreen model formulations (i.e. O/W, W/O, Emulgel, S/W, W/S, Oil) alone and in combination with chemical and physical filters by both in vitro (Diffey and Robson Protocol) and in vivo measurements (ISO 24444: 2010). Moreover, OXISOL was tested on a Reconstructed Human Epidermal (RHE) model employing normal human-derived epidermal keratinocytes, which have been cultured to form a multilayered highly differentiated model of the human epidermis. The cells were pre-treated and exposed to chemical smoke (CS), and oxidative stress and inflammation markers evaluated in order to verify the efficacy of the dermo-cosmetic formula against the oxidative effects of CS. Phototoxicity tests were conducted on an immortalized, non-tumorigenic cell line of human keratinocytes (NCTC-2544). Photostability studies were carried out with a solar simulator device (Suntest CPS+; Atlas, Linsengericht, Germany) equipped with a Xenon lamp, an optical filter to cut off wavelengths shorter than 290 nm and an IR-block filter to avoid thermal effects

OXISOL, resulted endowed with unprecedented antioxidant activity (expressed as units of micromol trolox/millimol: DPPH (4225,00); FRAP (9.004,00); PCL (48.750,00); ORAC (28.315,00). Moreover, very surprisingly, although it was not endowed of any UV filtering capability, when evaluated in combination with the most frequently employed physical and chemical UV filters it increased SPF-A and SPF-B up to 37% in both in vitro and in vivo measurements. Finally, OXISOL significantly decreased, in in vitro and in vivo tests, DNA and protein photo-degradation and protected RHE cells against oxidative damages related to chemical pollution (i.e. CS). Taken all together, these data points to a significant role of OXISOL in sunscreens and anti-ageing preparations, which remain so far unprecedented.

Micro to nanometric optical imaging resolution to better understand bacterial biofilms persistence: *in vitro* and *in vivo* visualization and characterization of antibiotics action

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The extensive research devoted to understand biofilms resistance/tolerance to antimicrobials has been oriented on mechanisms involving specific genetic or physiological cell properties but also on antibiotic sorption and/or reaction with biofilm components that may lessen the antimicrobial bioavailability, decreasing its efficiency. This latter hypothesis can be now explored *in vitro* using a set of advanced fluorescence imaging devices with microscopic (time-lapse imaging and Fluorescence Recovery After Photobleaching (FRAP)) and nanoscopic (Single Molecule Localization Microscopy (SMLM)) resolutions. We employed these techniques to characterize the dynamics of fluorescently-labeled antibiotics in biofilms formed by *Staphylococcus aureus* (*S. aureus*) clinical isolates. This correlative dynamic fluorescence microscopy approach has allowed discarding a lack of antibiotic bioavailability and specific interaction with its bacterial target to explain exposed biofilms persistence.

However, *in vitro* biofilms may greatly differ from the *in vivo* ones not only from a structural point of view but also because of the presence of the host immune system that is difficult to mimic *in vitro*. In order to better understand biofilms persistence phenomenon *in vivo*, we have developed an original mouse model allowing to assess the antibiotics efficacy against vascular prosthesis-related *S. aureus* infections using the performance of 3D-fluorescence imaging: removed infected prosthesis implants, treated or not with antibiotics, were observed by fluorescence confocal microscopy to characterize their structure, control cellular viability and identify immune cells.

Conclusions from the *in vivo* study are consistent with data from the *in vitro* model using the same strains, indicating the relevance of the joined approach to examine drugs activities on infectious biofilms. Taken together, these results reveal that antibiotic resistance/tolerance phenomena is essentially related to the specific physiology of adhered bacteria, and that infection persistence may be explained by the remaining viable bacteria inside immune system cells.

Light-independent pro-inflammatory and pro-oxidant effects of purified human hair melanins on keratinocyte cell cultures.

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The purpose of this study was to test the ability of red human hair pheomelanin (RHP) to induce oxidative damage and/or direct inflammatory response on cultured keratinocytes, independently from light exposure.

Spontaneous immortalized keratinocytes (HaCaT cells) were incubated, in the dark, for 24 hours with RHP or black human hair eumelanin (BHE) (0.5 mg/ml; 0.05 mg/ml; 0.005 mg/ml), previously purified from red and black hair. Proteins from white human hair (WHP) were used as negative control. Toxicity of RHP, BHE and WHP was assessed through cell viability; thereafter the possible pro-inflammatory effect was explored analyzing IL-1 β , IL-6 and TNF- α expressed (qRT-PCR) or secreted (ELISA) by stimulated cells. In addition, determination of cellular antioxidants (GSH and NADPH) and lipid peroxidation markers (thiobarbituric acid reactive substances: TBARS) was performed, respectively through HPLC and spectrophotometer.

Exposure to RHP or BHE, but not to WHP, moderately decreased keratinocyte viability ($p < 0.05$). RHP, and to a minor extent BHE, promoted expression of pro-inflammatory interleukins and oxidative damage in the dark. In detail, gene expression increase was dose related and highly significant for TNF- α and IL-1 β ($p < 0.001$), whereas protein secretion of IL-6 resulted more enhanced ($p < 0.001$) than TNF- α or IL-1 β ($p < 0.01$). Cellular depletion of GSH and NADPH was registered, as well as TBARS increase, after exposure to RHP ($p < 0.01$) and BHE ($p < 0.05$).

The results of our study indicate that RHP works as a direct pro-inflammatory and pro-oxidant agent in keratinocyte cultures, independently from light exposure. Hence, the role of RHP in melanomagenesis is reinforced, as well as its potential ability in worsening inflammatory skin conditions could be hypothesized.

Daylight Photodynamic Therapy in the treatment of mild and/or moderate Actinic Keratosis of the face and/or the scalp

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Actinic Keratosis (AK) is a common epithelial non-infiltrative lesion caused by chronic exposure to ultraviolet (UV) radiation damaging cell cycle regulators and leading to proliferation of cytologically abnormal epidermal keratinocytes. They are characteristically found on sun-exposed areas such as the face, bald scalp, neck, chest, back of the hands and forearms.

Various treatment options are available for AK lesions, including destructive therapies (e.g. cryosurgery or excisional surgery) and topical therapies (e.g. 5-fluorouracil, imiquimod, diclofenac, ingenol mebutate). Photodynamic therapy (PDT) is a highly effective treatment for AK, offering the advantage of excellent cosmesis. As large areas can be treated, multiple AKs may be treated at the same time. It is recommended as a first-line treatment for individual, or multiple and/or confluent AKs.

A cream formulation containing Methyl Aminolevulinate (MAL), has been approved with a red LED light via a suitable lamp (conventional PDT, cPDT) for the treatment of AK, Bowen's Disease and Basal Cell Carcinoma in several countries worldwide. MAL is not a photosensitizer itself but topical application results in the formation of photoactive protoporphyrin IX (PpIX). Light activation of accumulated porphyrins leads to a photochemical reaction and thereby phototoxicity to the light-exposed target cells. The effectiveness and safety of MAL cPDT have been demonstrated in several clinical trials for the treatment of AK.

Several clinical studies have shown that MAL can also be activated by natural daylight. Most recently, two phase III clinical studies performed in Australia and Europe have confirmed that MAL with daylight photodynamic therapy (DL-PDT) treatment regimen was non-inferior to cPDT in terms of efficacy, with the advantage of being almost painless and leading to less treatment-related adverse events.

Daylight-PDT (DL-PDT) treatment regimen for Methyl Aminolevulinate (MAL) is an alternative to the MAL conventional PDT (cPDT) and is currently approved for the treatment of AK, Bowen's Disease and Basal Cell Carcinoma in several countries. MAL Daylight-PDT is an effective, safe and alternative treatment for both mild and moderate AK lesions and is associated with high subject satisfaction and good cosmetic results.

We reported our experience about DL-PDT in the treatment of mild and/or moderate AK of the face and/or the scalp.

Reflectance confocal microscopy allows *in vivo* real-time noninvasive assessment of the outcome of methyl aminolaevulinate photodynamic therapy of basal cell carcinoma

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Photodynamic therapy (PDT) with methyl aminolaevulinate (MAL) is an approved noninvasive treatment option for basal cell carcinoma (BCC). *In vivo* reflectance confocal microscopy (RCM) is a noninvasive imaging technique that has proved useful for *in vivo* real-time cytomorphological analysis of BCC cells infiltrating the epidermis.

The aim of this study was to investigate the use of *in vivo* RCM to assess the persistence of BCC cells surviving MAL-PDT.

In vivo RCM images of 20 biopsy-proven BCCs were taken before patients underwent a treatment cycle with MAL-PDT. Follow-up after 3 months was performed using clinical examination, RCM and conventional dermoscopy. Treated areas also underwent a targeted 3-mm punch biopsy for standard haematoxylin and eosin histology stain to establish the clinical and instrumental correlation of the treatment outcome.

Three months after PDT, clinical examination established that two out of 20 BCCs were persistent; dermoscopy found three out of 20 residual BCCs, but RCM showed that one of these lesions was a false positive, and showed persistent BCC foci in five out of 20 lesions. Histological analysis of targeted biopsies confirmed these results.

RCM provided noninvasive, early detection of incipient recurrences of BCC after MAL-PDT. RCM findings steered targeted biopsies and surgical removal, or a new MAL-PDT, of these subclinical recurrences with minimal invasiveness.

Molecularly imprinted polymers for sensor applications by photopolymerization

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In the context of chemical microsensors or microbiosensors, Molecularly Imprinted Polymers (MIPs) are particularly well adapted as synthetic biomimetic recognition materials, because of their greater chemical and physical stability compared to their biological counterparts like enzymes or antibodies, and easier processing and engineering.

Recent examples of MIP have demonstrated their interest for chemical sensors associated to a wide range of chemicals for which these materials exhibit both specificity and sensitivity. However, their development in devices has been confronted to the difficulty to interface the functional material with the transducer or with a microchip. The photochemical route that we proposed significantly simplifies the integration of the functional material into the sensor device. Specific MIP precursors formulations were prepared to fulfill the requirements for micropatterning and molecular imprinting.

Molecularly Imprinted Polymers (MIP) were prepared by photochemical route. Photoinduced polymerization was used to achieve the preparation of the MIP and at the same time spatially controlled irradiation allowed shaping the material to confer it an optical function useful for interrogation. Such route significantly simplifies the integration of MIP in sensors¹. Advanced methods of photopatterning were used including interference (holography)^{3,4}, optical near-field², lithography on optical fibers⁵ and two-photon stereolithography⁶. Photopatterning appears thereby as one of the most suitable methods for patterning MIP at the micro and nano scale, directly on the transducer surface. Demonstration of use of these strategies for sensor application is presented. Such route opens new opportunities for low cost, highly sensitive and highly specific sensors.

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Photonic platforms and fluorescent mesoporous scaffold: diatoms as a new tool for materials

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Diatoms are single cell photosynthetic algae with microscopic 3D silica shells (frustules), which exhibit highly porous, nanopatterned surfaces with excellent mechanical properties. After removal of the organic matrices by acidic/oxidative cleaning, the resulting nanostructured biosilica shells become useful for applications including photonics, molecular biosensing, separation and also as drug delivery microsystems.[1] Recently biosilica was studied as a silica-layer forming system for tissue engineering.[2] The periodic and hierarchical nanostructure of frustules exhibits evolutive properties, like optimization of harvesting capability and photosynthetic activity of diatom cells.[3] Pores in diatoms are "hot-spots" in the formation of frustules and act as "defects" which modulate natural directionality of light propagating inside the frustule. A diatom cell is so a "photonic box" in which the ordered periodic patterns give rise to variations of high and low refractive index areas. Morphology, average dimension and the periodic pattern of pores in frustules are strictly dependent on the algal species. Literature presents examples of diatoms-based single-cell photonic crystals, alone or in combination with dyes.[4] Here we report methodological approaches for making diatoms frustules be *photonic platforms*, starting from biosilica extraction methods from living *Thalassiosira weissflogii* specie for device application.[5] For the case we exploited in vivo and in vitro approaches to chemically conjugate biosilica with fluorescent dyes (III generation dyes, via APTES chemistry) and a phosphorescent complex (I generation dye, via electrostatic interaction), to combine these organic optically active moieties to the biosilica properties. As III generation dyes, we studied the chemical addressing of a new synthesis blue-fluorescent bis-phenyleneethynylene dye (BPE, with silane tail) in the biosilica, for photonic application, and a new-synthesis fluorene-based moiety for singlet oxygen generation (molecule A, with silane tail). After in vivo incorporation of these dyes into *Thalassiosira weissflogii* diatom frustules, the resulting luminescent micro/nano- structures have been characterized by fluorescence microscopy and optical spectroscopy. We demonstrated that these dyes selectively convey in vivo into the nanostructured biosilica, they are resistant to an acidic oxidative treatment and various spectroscopies demonstrate that frustules act as waveguide selectors and as photonic combinatorial matrices, in the case of BPE, and as biosilica-based singlet oxygen producers for Photo-Dynamic Therapy (PDT) applications, in the case of molecule A. Here we also report the covalent functionalization of extracted biosilica with new synthesis red emitting T-BTZ-T-B-based dye (tiophene-benzothiadiazole-tiophene-benzoil, redDV) via APTES chemistry (III generation dye) [6], to produce *fluorescent biosilica scaffold* for bone tissue regeneration. We finally exploited in vivo doping of *Thalassiosira weissflogii* frustules to make a positively charged Iridium Complex (MLP10, I generation dye) address biosilica shells and obtain phosphorescent biosilica μ pixels, useful in photonics, PDT and in luminescent devices.



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Interlacing biophysical methods to unveil morphology and dynamical interactions with microtubules of transient receptor potential vanilloid 1 (TRPV1) at nanoscale in living cells

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Transient Receptor Potential Vanilloid 1 (TRPV1) is a nonselective cation channel involved in the transmission and modulation of nociception, as well as in the integration of several painful stimuli.¹ Recent evidences suggest a peculiar interaction between TRPV1 and microtubules for transmission of pain at the cellular level.² By means of a high-sensitivity multiplex imaging approach, we monitored the nanoscale interactions of TRPV1 with microtubules. In more details, we first combined Temporal Image Correlation Spectroscopy (tICS) measurements with FRET, in order to unveil the dynamic properties of TRPV1-microtubule complex. Next, we used the combination of FRET with *i*MSD³ analysis based on Spatio-Temporal Image Correlation Spectroscopy (STICS) in order to demonstrate the presence of a directional diffusion of TRPV1 complexes with microtubules structures. Changes in TRPV1 aggregation upon receptor stimulation and/or microtubule depolymerization were investigated by fluorescence anisotropy associated to homo-FRET.⁴ The latter experiments highlighted that microtubule depolymerization induces the formation of large, non-functional aggregates. Finally, we applied single molecule localization techniques in order to improve the spatial resolution of TRPV1 detection. We demonstrated that TRPV1 is organized heterogeneously on plasma membrane in sub-micron membrane domains with different sizes by both super-resolution optical fluctuation imaging (SOFI) and photo-activated localization microscopy (PALM) by using the genetically-encoded photochromic reporter EYQ1.⁵ Our work clarified the membrane organization of TRPV1 at nanoscale in living cells, as well as the role of microtubule in preserving the receptor's functionality. In this context, future experiments will target specifically the nanoscale morphology of TRPV1-microtubules complexes on plasma membrane.

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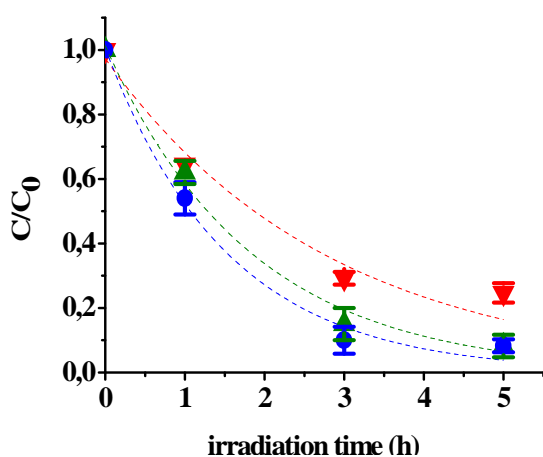
Emerging Pollutants Photo-Oxidation by WO₃

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Pharmaceuticals are not completely removed by wastewater treatment plants and are discharged into the environment. Therefore, they may have adverse impact on aquatic organisms and on human health.

We recently demonstrated that a photo-electrochemical method based on the use of WO₃ can be applied for the efficient removal of this contaminants¹. WO₃ is a semiconductor that once photoexcited (up to 450 nm) generates charge carriers. Holes are very oxidant and produce OH[•] radicals by the oxidation of water. The formation of these radicals that we pointed out by EPR spin trapping experiments, is fundamental because they start the oxidation of the drug molecule. At the same time, electrons promoted to the conduction band are pushed to a cathode, where a reduction reaction can take place, by a positive applied bias.



Herein, we discuss the results about the ability of this semiconductor to decompose organic pollutants. We have considered suspensions of WO₃ powder, WO₃ colloid sintered on conductive glass and WO₃ grown on metallic tungsten. We perform photocatalytic and comparatively photo-electrocatalytic experiments on atenolol and carbamazepine, chosen as representative compounds for environmental contamination. It is observed that when a positive bias is applied, the highest decomposition rates are obtained. At the same time we verified from HPLC-MS that prolonging the irradiation period, the starting drug is degraded and the same fate occurred also to all the degradation intermediates allowing complete mineralization.

In view of the scale up of the device, other experiments have been carried out that show the possibility to work at natural pH values (around 6), to use innocuous Na₂SO₄ as supporting electrolyte in concentrations similar to that of natural waters, to use wavelengths up to 450 nm.

Moreover, the electrons pushed to the dark cathode by the applied bias can be responsible of a reductive reaction, such as the reduction of protons to molecular hydrogen. For this, our photo-electrochemical device allows the conversion of solar light (that excites WO₃) into a clean energy form through the simultaneous decontamination of wastewater contaminants, otherwise not easily removed.

¹ G. Longobucco, L. Pasti, A. Molinari, N. Marchetti, S. Caramori, V. Cristino, C. A. Bignozzi, *submitted*

Bistable mechanofluorochromic materials based on difluoroboron β -diketone dyes

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The development of mechanofluorochromic materials is a modern and innovative research field ^[1], at the frontier between organic synthesis, photophysics and mechanics. Mechanofluorochromic materials (MFC) are a class of smart materials characterized by a significant change of their emission wavelength, in the solid-state, when subjected to mechanical strains (pressure, shearing, stretching...). There is a growing interest in MFC compounds, particularly for their possible application as sensors ^[2] in building materials or aeronautics, for example.

The boron diketone derivatives, already known to show promising MFC properties as well as significant solid-state fluorescence quantum yield, are particularly interesting ^[3]. We synthesized new compounds, modifying the substituents allowing, or not, the formation of hydrogen-bonds, to analyze their impact on observed MFC properties.

This new series of compounds undergo a MFC behaviour. The synthesis as well as the photophysical, spectroscopic, theoretical and mechanical properties of the compounds in solution, in the solid state as well as in nanoparticles will be displayed analyzed and discussed in detail. A combined atomic force microscopy and fluorescence microscopy study (steady-state and time-resolved) will notably be presented.

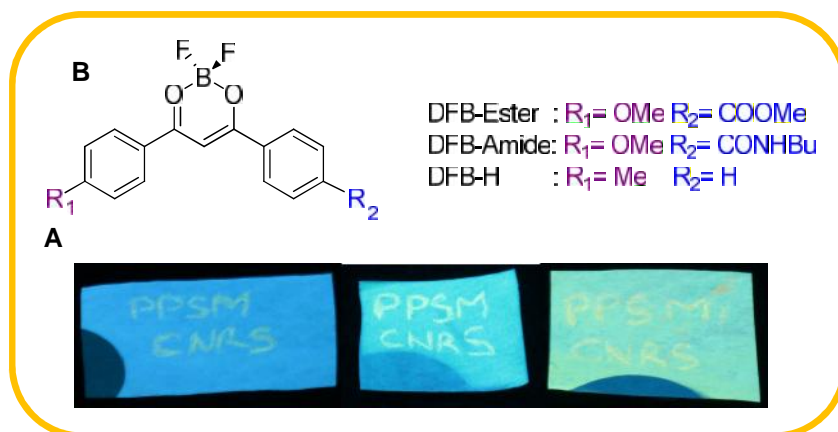


Figure 1. A. Target compounds. B. Photographic pictures of the fluorescent thermally annealed thin films of DFB-H (left), DFB-ester (center), DFB-amide (right) compounds. PPSM CNRS was written with a spatula using the MFC properties of the films.

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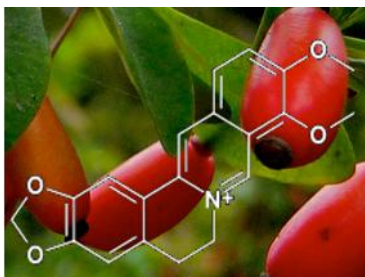
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Berberine as a Photosensitizing Agent for Antitumoral Photodynamic Therapy: Insights into its Association to Low Density Lipoproteins

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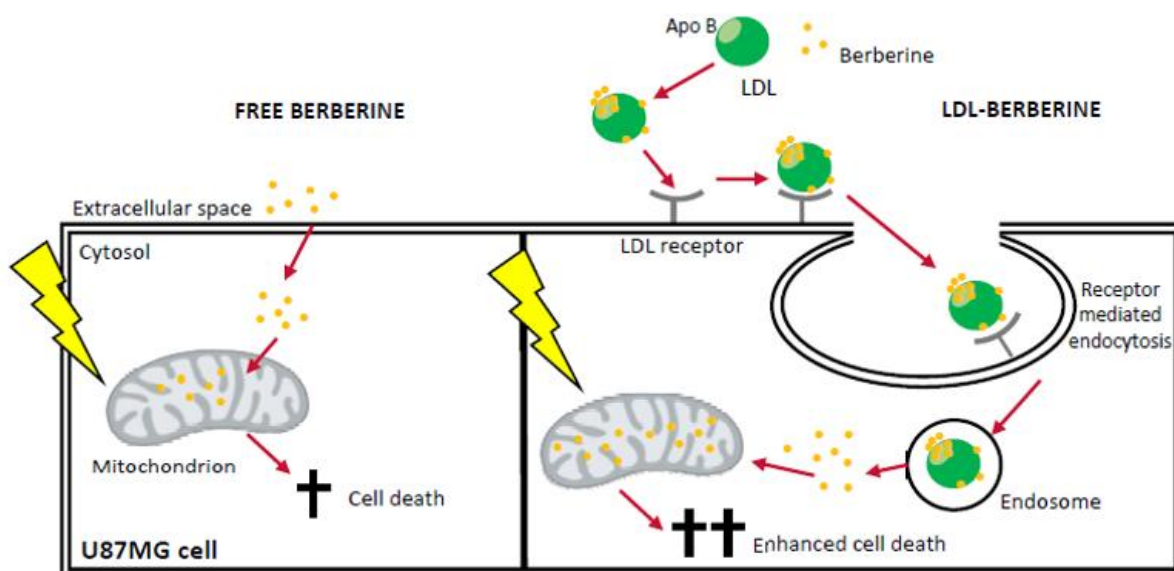
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Recent years have seen a growing interest in Berberine, a phytochemical with multispectrum therapeutic activities, as anti-tumoral agent for photodynamic therapy (PDT). In this context, low density lipoproteins (LDL) play a key role in the delivery of the photosensitizer in tumor cells. We correlate the physicochemical parameters of the berberine association to LDL with the influence of LDL-delivery on its accumulation in a glioma cell line and on its photo-induced activity in view of antitumor PDT. Our results evidence an important binding of 400 berberine molecules per LDL. Changes in berberine and apoprotein

fluorescence suggest different fixation types, involving various LDL compartments including the vicinity of the apoprotein. The berberine association to LDL does not affect their recognition by the specific B/E receptors, of which over-expression increases the cellular uptake of LDL-preloaded berberine. Fluorescence microscopy evidences the mitochondrial labeling of the glioma model cells, with no significant modification upon LDL-delivery. Moreover, the cellular delivery of berberine by LDL increases its photocytotoxic effects on such cells. So, this research illustrates the potential of berberine as a photosensitizing agent for PDT, in particular due to their behavior towards LDL as plasma vehicles, and gives insights into its mechanisms of cell uptake.



Photodynamic activity of a diarylic-porphyrin linked to a biocompatible polymeric nanostructure

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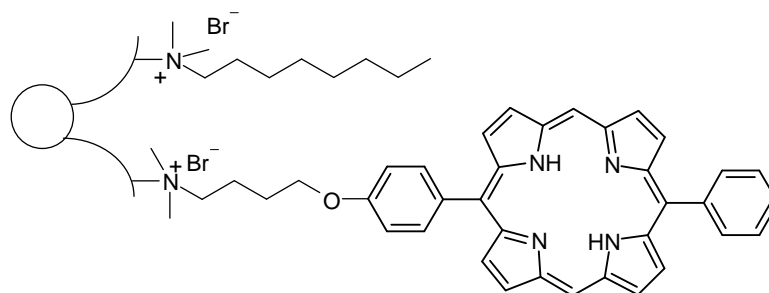
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Photodynamic therapy (PDT) is based on the systemic or topical administration of a non toxic compound, called photosensitizer (PS), followed by an incubation period. The diseased area is then irradiated with light of a specific wavelength to activate the PS. Upon activation, the PS switches from its ground state to an excited singlet state, initiating a chain of electronic transitions that results in the production of death-inducing reactive oxygen species (ROS), mainly singlet oxygen (¹O₂). This treatment can be used as an alternative to the most common tumour therapies or in the treatment of localized bacterial infections (aPDT).

A small number of PSs have been approved for clinical PDT applications on different cancer types, but more are currently undergoing clinical trials. Most of these novel PSs retain the cyclic tetrapyrrole structure typical of porphyrins, and of their derivatives (chlorins and bacteriochlorins), or belong to the class of the phthalocyanines.

In this work it is reported the synthesis of one new asymmetric diarylic porphyrin, characterized by the presence of one phenyl ring and one 4-bromobutoxyphenyl substituent in order to covalently embed the porphyrin structure in a biocompatible polymeric nanostructure, here reported.



The new porphyrin, the monomeric precursor, the polymer and the resulting nanoparticles, were fully characterized by UV-spectroscopy, fluorescent analysis, NMR, photon correlation spectroscopy, polydispersity index and zeta-potential.

As first experimental data we check the resistance to photobleaching of the porphyrin alone and when loaded onto the nanoparticles. The results confirm that the nanostructure does not alter the porphyrin resistance to photobleaching.

The porphyrin and the porphyrin loaded onto the nanoparticles were then tested *in vitro* on the adenocarcinoma tumour cell lines, HCT116. The conditions for the *in vitro* tumour cells treatment require 24h of incubation and 2h of irradiation with 500 Watt white halogen lamp. Overall, both free porphyrin and the one loaded onto the nanoparticles showed comparable results, with IC₅₀ values ranging between 1-10 nM. The cell death mechanism was investigated more deeply by determining the ROS production, the apoptosis percentage and the intracellular localization of the PS.

In vivo and *in vitro* comparative study of uptake of silver and gold nanoparticles exploitable in the context of photodynamic therapy

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Photodynamic therapy (PDT) is a promising anti-tumor modality used in clinic for the treatment of both cancer and non cancer pathologies. It consists in the applying of molecules called photosensitizers (PSs) subsequently activated by irradiation with visible light. This process in the presence of tissue molecular oxygen leads to generation of reactive oxygen species (ROS) *via* a photodynamic reaction, that kill ill cells both directly through triggering cancer cells death and indirectly by disrupting blood vessels leading to hypoxic condition. The greatest advantages of PDT are the minimal systemic toxicity and high selectivity of PS to cancer cells. Recently, the combination of PDT with other strategies has emerged as a fascinating opportunity in cancer therapy due to the ignition of synergistic effects. In this context, nanotechnology is emerging as an active research area in PDT field. In PDT, engineered nanomaterials (NMs) can be exploited mainly as nanocarriers because they can transport hydrophobic drugs, have large surface area modifiable to improve selective targeting, are efficiently taken up by cells, can allow a controlled drug release. An alternative exploitation of NMs in PDT is their use as PSs, being able to absorb light and switch to an excited state leading to photochemical generation of ROS, or as agents by improving photodynamic reaction *via* enhancing singlet oxygen production. Among the NMs used as PSs delivery, metallic NPs, such as gold (Au) and silver (Ag) NPs, represent a valuable tool in PDT protocols. In fact, they can be used to enhance singlet oxygen production from PSs by exploiting surface plasmon resonance phenomenon based on the interaction of the conduction electrons of metal nanostructures with incoming light.¹ The current work presents preliminary data about the internalization of Ag and AuNPs in, *in vitro*, HeLa cells, and *in vivo* biodistribution after intravenous injection in mouse caudal vein. Literature data concord that AuNPs are highly stable and biocompatible; conversely, AgNPs could release Ag⁺ ions. To avoid this, we use glycans, *i.e.*, glucose and glucose/sucrose, as capping agents to prevent Ag⁺ ions release. The shape, size, subcellular localization and the absorption properties of NPs were determined by using transmission electron microscopy and ultraviolet-visible spectroscopy respectively. In addition, ICP-MS was used to quantify the NPs into HeLa cells. Light microscope, MTT assay and flow cytometry were used to investigate cellular effects of the NPs. Finally, ROS generation was evaluated *via* NBT assay. The average size of AgNPs and AuNPs was 30±5 nm and 15±5 and the maximum absorption peak at 420 and 530 respectively. These peaks coincide with light wavelength used by us in previous works in PDT to excite Rose Bengal PS in HeLa cells.²⁻⁵ Both NPs enter HeLa cells and elicit different responses: AuNPs do not induce toxic effects; at contrary, AgNPs induce HeLa cells responses like viability and proliferation decrement, and ROS generation. TEM analysis on mice organ samples shows that Au and AgNPs reach brain, kidneys, liver, intestine, spleen and hearth. Moreover, the subcellular localization of NPs is inside cytoplasm, endoplasmic reticulum, lysosomes, nearby and inside mitochondria, and in the nucleus. This study highlights the potentiality to use such nanostructures in PDT: data *in vivo* suggest their ability to pass biological barriers, reach different organs and localize in intracellular organelles very pivotal for photodynamic toxic effects. Moreover, the possibility to conjugate the AgNPs with photosensitizers can synergize the PS toxic effects against cancer cells by exploiting the metal enhanced singlet oxygen generation. In fact, it has been demonstrated⁶ that the PS Rose Bengal in close proximity to silver thin films generates more singlet oxygen by enhancing the light absorption due to coupling to silver surface plasmons.

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Effects of focal photodynamic therapy on cancer cells *in vitro* and in mouse models *in vivo*

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Ionizing and nonionizing radiation affect not only directly targeted cells but also surrounding “bystander” cells. The underlying mechanisms and therapeutic role of bystander responses remain incompletely defined. Here we show that activation of the photosensitizer aluminum phthalocyanine chloride (Sigma-Aldrich, Cat. N. 362530) *in a single cell* triggers apoptosis in bystander cancer cells, which are electrically coupled by gap junction channels and support the propagation of a Ca²⁺ wave initiated in the irradiated cell. The latter also acts as source of nitric oxide (NO) that diffuses to bystander cells, in which NO levels are further increased by a mechanism compatible with Ca²⁺-dependent enzymatic production (1). We detected similar signals in tumors grown in dorsal skinfold chambers (2) applied to live mice (1, 3). Pharmacological blockade of connexin channels significantly reduced the extent of apoptosis in bystander cells, consistent with a critical role played by intercellular communication, Ca²⁺ and NO in the bystander effects triggered by photodynamic therapy. Recent evidence points to a critical involvement of IP₃R-linked Ca²⁺ signals for the spreading of cytochrome-c induced apoptosis in cellular systems coupled by gap junction channels (4, 5). Consistent with this tenet, we found that 2-APB, a well known blocker of IP₃R-dependent calcium release (6) that also inhibits gap junction channels (7), reduced significantly Ca²⁺ wave speed and caused the most pronounced reduction in both ΔCa²⁺ and ΔNO bystander response amplitudes. The importance of connexins as defense from tumorigenesis and their beneficial role in primary tumors is well supported by several *in vitro* and *in vivo* models (8, 9). Our results suggest that potentiating bystander effects upregulating connexins by either targeted drug treatments or viral transduction in primary tumors might enhance the therapeutic potential of photodynamic therapy. They also suggest that temporarily inhibiting gap junction communication might reduce unwanted side effects produced by photodynamic treatment of vascular disorders in the retina (10).

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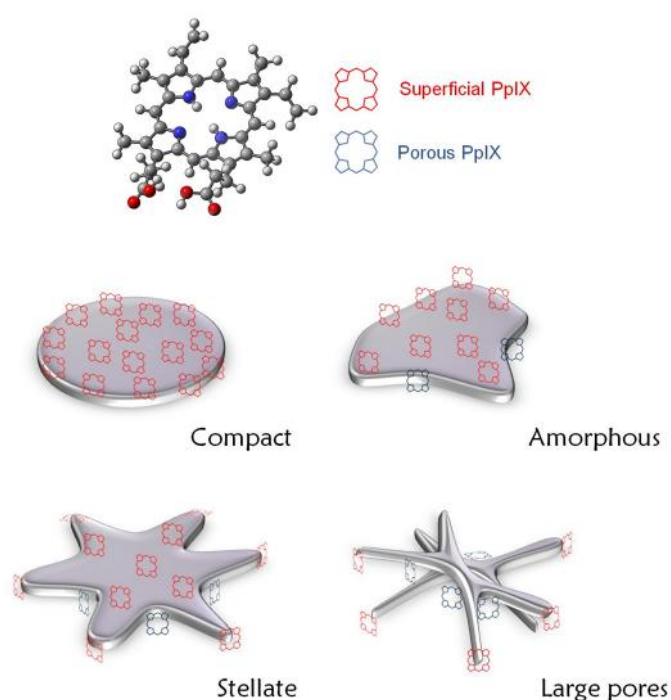
Nanomodulation of singlet oxygen and bacterial inactivation efficiency by silica-PpIX nanocomposites

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Different silica-PpIX nanocomposites have been synthesized to evaluate the dependence of singlet oxygen production and bacterial inactivation efficiency on the morphology of the nanomaterials. Modulation of the synthetic procedure allowed to obtain silica nanoparticles with different porosity which were characterized by TEM and spectroscopic analysis after PpIX adsorption. Time-resolved phosphorescence measurements on the different nanoporous samples revealed that the porosity of the nanoparticles plays a pivotal role on the singlet oxygen deactivation mechanism.



Thus, apart from the expected deactivation of singlet oxygen outside the silica matrix, a second component has been observed for the porous materials, attributed to the deactivation of singlet oxygen inside the pores. The relative efficiency of singlet oxygen production resulted to be higher for the sample with the greatest pores volume. The capability of the nanocomposites to inactivate bacteria was tested *in vitro* on *Staphylococcus aureus* strain. Interestingly, the efficiency for singlet oxygen production of the nanocomposites and their bacterial inactivation efficiency followed an opposite trend, indicating that the relative position of the photosensitizer and the superficial properties of the particles affect the antibacterial activity of the overall system.

Conjugates of benzoxazole and GFP chromophores with AIE behavior: polymorphism, rigidochromism, nanoparticles and cell uptake

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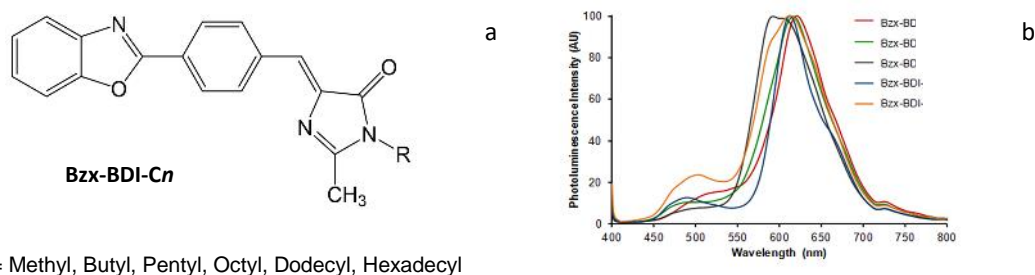
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The fluorescence quenching due to the formation of aggregates has long been a formidable barrier to the development of fluorescent organic materials. Fifteen years ago, the discovery of compounds whose emissions are induced by aggregate formation has opened new perspectives of applications.¹ More specifically, in the field of biological and *in vivo* imaging, these compounds have led to a new generation of fluorogenic sensors and luminescent organic nanoparticles for long-term cellular tracing, angiography and cancer diagnosis.

Recently, we reported a new set of chromophores that exhibit aggregation-induced emission (AIE). They consist of a benzoxazole derivative incorporated in a synthetic chromophore of the Green Fluorescent Protein (GFP) (Figure 1a).² They merged the excellent photoluminescence efficiency of benzoxazoles³ with the AIE behavior of GFP chromophores.⁴ The photophysical study revealed that emission in the orange-red (Figure 1b) originates from a long-distance excimer. The compounds also displayed interesting effects of rigidofluorochromism, polymorphism and mechanofluorochromism.

The compounds showed no cytotoxicity. Particles were prepared using a method based on solvent exchange. Microfibers, platelets and rounded microparticles were obtained depending on the compound. The same method was used to prepare homogeneous populations of nanoparticles (NPs) that measured around 70 nm for the analogs of moderate chain length (C4 to C8) and more than 100 nm for the long-chain analogs. The two types of NPs were used extemporaneously for cell biology observations.⁵ The influence of the length of the alkyl chain upon the spectroscopic properties, the self-association properties and the behavior with respect to living cells will be discussed.



R = Methyl, Butyl, Pentyl, Octyl, Dodecyl, Hexadecyl

Figure 1. a) Chemical structure of the studied benzoxazole-benzylideneimidazolinone conjugates (Bzx-BDI-Cn)
b) Solid-state emission spectra ($\lambda_{\text{ex}} = 384 \text{ nm}$)

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Delayed luminescence spectroscopy from human glioblastoma cells to monitor the effects of drug-loaded nanostructured lipid carrier

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Recent studies have shown the possibility to use in cancer research the Delayed Luminescence (DL)¹. Features of such ultraweak luminescence, emitted in the visible wavelength range after photo stimulation, with lifetimes from 10⁻⁷ to 10 s, have been correlated to apoptosis and oxidative stress, pointing to a relation between DL and cell status, and mitochondrial status in particular.

In this work, we investigated the DL emission of human glioblastoma multiforme (GBM) U-87MG cells, the most common and lethal type of brain cancer, treated with ferulic acid (FA)² carried by nanostructured lipid carrier (NLC)³.

FA is considered a natural antioxidant and anti-inflammatory agent. However, on increasing the concentration or in presence of metal ions, FA shows pro-oxidant behaviour inducing, as for instance, mitochondrial permeability transition, release of cytochrome c and caspase-3 activation. NLC, a new generation of carriers, is good candidate to penetrate the blood-brain barrier, showing more efficiency in encapsulating and releasing drugs than solid lipid carriers.

With the aim to correlate DL emission to the effects induced on U-87MG cells by different treatments, that is free FA, unloaded NLC, and ferulic acid-loaded nanostructured lipid carrier (NLC-FA), we measured the DL emission in three different wavelength ranges: 425-475 nm (the blue region where the reduced nicotinamide adenine dinucleotide, NADH, emits), 525-575 nm (the green/yellow region where flavins contribution is foreseen) and 625-675 nm (the red region, where protoporphyrin IV and singlet oxygen emit). DL time trends showed a multimodal behaviour. To compare data, DL spectral yields in three different time intervals were evaluated: 10-100 μ s (DL-I), 100 μ s – 1 ms (DL-II) and 1-10 ms (DL-III).

Cytotoxic effects were evaluated by MTT test. The effects on activation of the apoptotic pathway and cell cycle regulation were evaluated by testing caspase-3 cleavage and p53 protein overexpression. Data were statistically analysed using one-way analysis of variance (one-way ANOVA). Differences between groups were considered statistically significant for *p < 0.05.

Preliminary but surprising results showed that even if unloaded NLC does not affect cells vitality and affect to a minor extend the number of positive cells for caspase-3, it was able to down-regulate p53 expression levels. In parallel relevant changes, with respect control, were registered in DL emission, especially for the red component at longer time intervals. These results supported the idea that the lipid concentration in NLC influences within certain limits the functionality of mitochondrial respiratory chain and the production of ROS, so confirming the potentiality of delayed luminescence spectroscopy as tool to investigate the alterations of the complex I functionality of mitochondrial respiratory chain.

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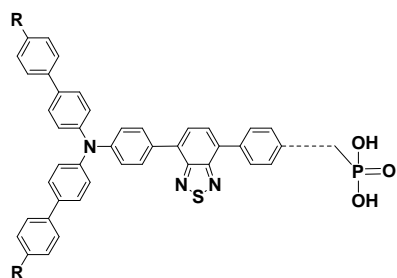
Photo- and magneto-activity tuning of bimodal hybrid nanoassemblies as contrast agents

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Bimodal hybrid nanoassemblies, combining fluorescence and magnetism, represent promising tools for bioimaging. The search for high-contrast bioimaging agents prompted us to build original raspberry-like nanoarchitectures comprising fluorescent organic nanospheres (FONs) coated by superparamagnetic iron oxide nanoparticles¹. Such a combination enables cross-correlated *in cellulo* and *in vivo* imaging investigations.

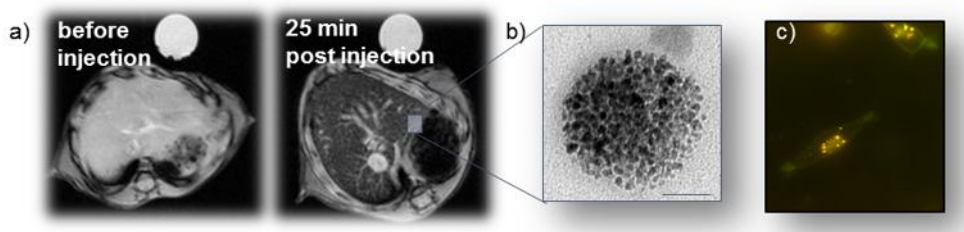


Structure of organic fluorophores

We have developed a variety of FONs (hydrodynamic diameter ~ 100 nm) by reprecipitating hydrophobic organic fluorophores in water. The latter provide a red-emission signal that can be tuned as a function of the charge transfer magnitude involved in the fluorophore excited state. Hence a fluorescence signal in the 610-675 nm spectral window and a large Stokes shift (>5000 cm⁻¹) can be obtained, which limits autofluorescence from living organisms.

In addition, the fluorophores contain phosphonic acid moieties amenable to chelate iron oxide superparamagnetic nanoparticles, regarded as attractive contrast agents for *in vivo* MRI². First MRI investigations were successfully conducted with 7 nm-large iron oxide nanoparticles³. Currently, we are tuning the nanoparticle diameter up to 10 nm to yield even darker imaging contrast.

Such raspberry-like nanoassemblies could be coated with appropriate pegylated polyelectrolytes and showed preferential accumulation in mouse tumors after intravenous injection. All these combined properties pave the way toward theranostic potentialities by improving the target localization and anticipating the related toxicity side-effects⁴.



a) MRI of mouse liver before and 25 min post injection of the nanoassemblies; b) TEM imaging of a raspberry-like nanoassembly (scale bar: 50 nm); c) Fluorescence microscopy of cancer cells incubated with nanoassemblies

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Novel multifunctional nanocrystalline UV and Visible light active photocatalysts for environmental applications

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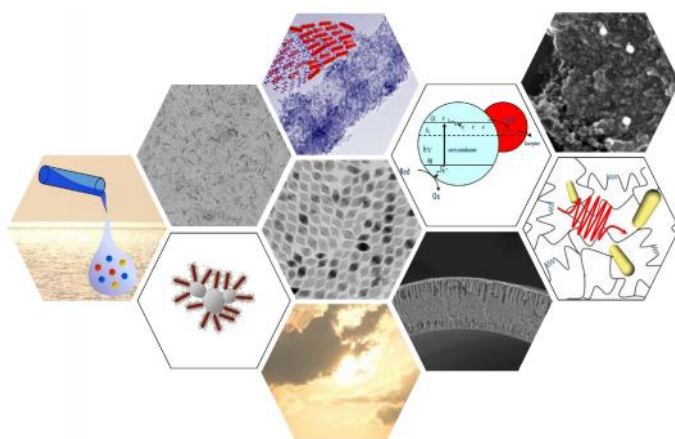
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Nanostructured materials thanks to their size/shape dependent physical-chemical properties and to their high surface-to-volume ratio, provide the opportunity to develop innovative materials for heterogeneous photocatalysis.

The degradation of organic pollutants in water is one of the most appealing application of photocatalysts. It occurs by generating oxidant species ($\bullet\text{OH}$ radicals) under proper irradiation, exploiting wide band gap semiconductors (TiO_2 , ZnO) photogenerated electron-hole (e^-/h^+) pairs.

Nonetheless, wide band gap semiconductors can be activated only by UV light, thus limiting the fraction of solar spectrum able to generate $\bullet\text{OH}$ to $\sim 4\%$. Current efforts in the field of designing and synthesis of photocatalysts aim at improving charge separation, inhibiting charge carrier recombination and enhancing

the catalytic activity in the visible region. To achieve such goals we have investigated synthesis and characterization of several nanostructured photocatalysts, consisting of TiO_2 nanocrystalst of different size and shape, rationally modified with noble metals, semiconductor or carbon nanotubes. In particular, multifunctional catalysts have been prepared, namely TiO_2/Ag , TiO_2/Au , $\text{TiO}_2/\text{Fe}_x\text{O}_x/\text{Ag}$, TiO_2/CNTs . The photocatalytic properties of the obtained nanomaterials have been tested in the photocatalytic degradation of several organic pollutants in comparison with their commercial counterpart. The



obtained results point out the higher photoactivity of nanosized catalysts, the possibility to shift their photoactivity in the visible range and their viability for several environmental related applications.

POSTER CONTRIBUTIONS

Morphology effects in all iron oxide-based photoanodes

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The exploitation of renewable energy sources (such as sunlight), strived to produce alternative fuels, is one of the most pursued strategies to relieve the global energy thirst. With this aim, a viable but challenging approach consists in the development of photoelectrochemical cells.[1] These devices mimic the natural photosynthesis by storing solar energy as chemical energy in value-added compounds produced at two separated electrodes.

In this contribution, we will report recent results obtained with all iron oxide-based photoanodes, able to efficiently perform the semireaction of water oxidation.[2]

In particular, crystalline hematite ($\alpha\text{-Fe}_2\text{O}_3$) was coupled with pulsed-laser deposited amorphous iron oxides, thus combining the sunlight absorption and charge carrier generation properties of the former [3] with the catalytic activity of the latter.

Insights on the morphology effects of the nanosized amorphous catalyst on the performances of the photoanodes will be also discussed, evidencing the importance of a porous versus a compact catalytic layer. The choice of iron oxide clearly fulfils the requirements associated with a large scale application of this kind of devices, *i.e.* the cheapness due to earth abundance and the non-toxicity, along with the good performances of the final photoanodes.

Acknowledgments: The project leading to this application has received funding from the PAT (Provincia Autonoma di Trento) project “ENAM” (in cooperation with MCB-CNR Institute), the FIRB-MIUR “Nanosolar” project and the European Union’s Horizon 2020 Research and Innovation Programme under the Marie Skłodowska-Curie Grant Agreement No. 705723.

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Luminescent heterobimetallic supramolecular systems: Europium sensitization by Iridium complexes

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Lanthanides ions exhibit the ability to emit light in narrow bands which result in very pure color, but they have very low molar absorption coefficient. In order to overcome this problem, and increase the efficiency of emission, they are normally sensitized by organic molecules, building complexes and taking advantage from the so called 'antenna effect'.¹ Transition metal complexes may be an interesting alternative to sensitize lanthanide ions pushing further the efficiency of the system.

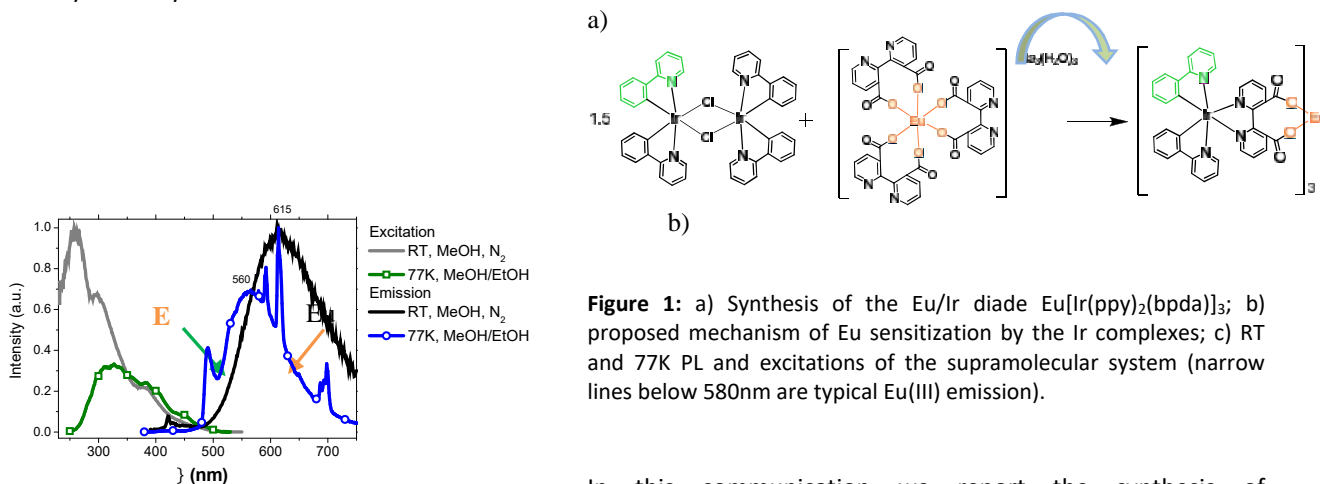


Figure 1: a) Synthesis of the Eu/Ir diade $\text{Eu}[\text{Ir}(\text{ppy})_2(\text{bpda})]_3$; b) proposed mechanism of Eu sensitization by the Ir complexes; c) RT and 77K PL and excitations of the supramolecular system (narrow lines below 580nm are typical Eu(III) emission).

Ir In this communication we report the synthesis of $\text{Eu}[\text{Ir}(\text{ppy})_2(\text{bpda})]_3$, the first prototype heterobimetallic supramolecular system made of three cyclometalated iridium sensitizers ($\text{Ir}(\text{ppy})_2$, ppy = 2-phenylpyridinate) arranged around a central europium acceptor atom (Figure 1a). The Ir sensitizers and the Eu ion are joined through the bifunctional *bpda* ligand (3,3'-dicarboxy-2,2'-bipyridine) which can strongly bond the Ir center at the bipyridine core and the Eu one with the carboxylic functions. The bipyridine ligand also serves as π -conjugated bridge to support the energy and/or charge transfer sensitization process (Figure 1b). The synthesis of the supramolecular system is carried out in one-pot from the corresponding precursors; the product can be easily recovered and purified through multiple precipitation. The optical absorption (excitation) spectra of the product (Figure. 1c) accounts, in the visible region between 390-500nm, for the presence of the MLCT transitions of the cyclometalated Ir centers. Exciting into the MLCT bands of the Ir complexes, the room temperature photoluminescence emission is mainly originated by the broad emission of the Ir system itself (which obscure any emission from the Eu ion). On the contrary, at low temperature, the strong rigidochromic blue-shift of the Ir emission allows the system to emit from both the Ir center and the Eu one. This implies the effective, even though non-complete, sensitization of the Eu ion.

Further experiments are in progress by varying both, the cyclometalating sensitizer (*ppy*) and the metal center (Ir); the ease of the synthetic protocol seems to be promising for the extension of the methodology to other lanthanide ions, in particular those emitting in the NIR region.

The authors greatly acknowledge the "Short Term Mobility" program of the CNR for supporting the exchange program with Prof. Lima

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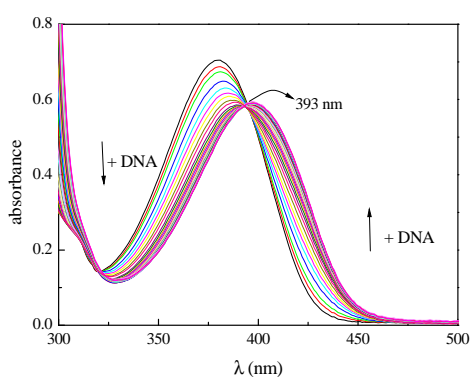
Photobehaviour of styryl-azinium iodides and their interaction with nucleic acids

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Previous studies on methyl-pyridinium and methyl-quinolinium salts have shown that they are capable of crossing biological membranes and interacting with nucleic acids, features typical of potential anticancer drugs. This work consists in verifying the properties of some new derivatives to exhibit enhanced binding efficiency and selectivity towards biological targets. Thus, the interaction between these compounds and DNA and RNA was quantified by spectrophotometric and fluorimetric titrations, measuring their binding constants (K in the 10^4 - 10^6 M^{-1} range). Their mechanism of binding was defined by linear dichroic measurements that allowed to detect the angle of interaction between ligand and DNA, revealing



that these molecules act as intercalators or groove binders. Interaction between some azinium salts and non-ionic surfactants was studied in order to find agents for drug solubilization and drug delivery: the studied intercalators were found to insert in the non-ionic micelles core, establishing hydrophobic interactions, and to be released in the presence of DNA, due to their higher affinity to the latter. Since intercalators are not selective towards cancer cells, but indiscriminately attack all cell clusters in replication, causing the wanted shutdown of the tumor mass growth as well as serious side effects, it can be pivotal to focus their action in a localized area. An interesting strategy

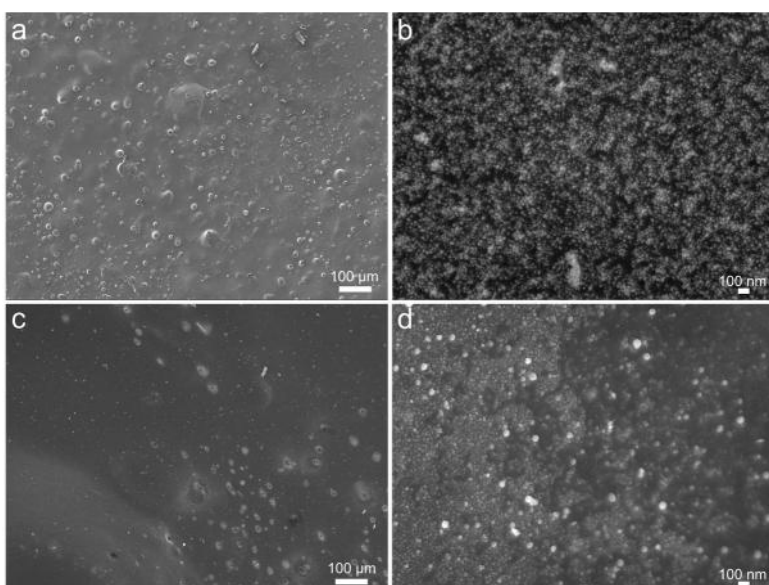
relies on photoswitchable processes, such as photoinduced intercalation or local production of ROS (reactive oxygen species, cytotoxic for their high oxidizing power), since the use of optical fibers allows to convey the activating light beam to a specific region. In order to test whether such mechanisms were effectively competitive deactivation pathways for these molecules, their photobehaviour was investigated in both buffered water and in organized media, before and after complexation with salmon DNA. Steady-state techniques were used to determine the quantum yields for the relaxation processes, pulsed spectroscopies with ns-time resolution were used to evidence possible formation of radical species, and fs-time resolved methods (transient absorption and emission) allowed the dynamics of drug-DNA interaction and the evolution of the precursors to the photoactive species to be evaluated. Analysis of the non-linear optical properties, by determining the "cross section" for the two-photon absorption (TPA), was carried out with a home-made instrument for two-photon induced fluorescence detection (TPIF) with ns resolution. Quantum mechanical calculations were performed to study the conformational disorder and the properties of the excited electronic states of the ligands, aiming to check and improve our understanding of the structure-properties relations. Once identified the most promising molecules, it was possible, in collaboration with the group of Molecular Biology of our University, to probe their cytotoxic activity on actual cell lines, performing MTT viability assay and in vitro measurements of confocal fluorescence microscopy to spot the localization of drugs within cellular compartments. Preliminary results carried out on the breast cancer cell line (MCF7) indicated accumulation of drugs in punctate structures located in the nucleoli, confirming their affinity towards both DNA and RNA.

Hybrid nanocomposite formation of SnO₂/PMMA through pulsed laser irradiation

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In recent years, the field of organic-inorganic nanocomposites has attracted great consideration due to the possibility to combine some characteristic features of both organic polymers and inorganic materials exploitable for various applications such as gas sensing and environmental protection.¹ However, one of the most important drawbacks associated with the nanocomposite formation is related to the filler dispersion inside the polymeric matrix to achieve homogeneous materials. In order to circumvent this issue, a possible strategy can be represented by the so-called “*in situ synthesis*” of nanoparticles in solid polymeric films in



which the desired material is directly synthesized in a polymeric structure avoiding particles aggregation.² This innovative and unconventional approach allows at the same time to form metal and metal oxide nanoparticles and to embed them into the polymer matrix, eventually leading to the final nanocomposite material.^{3,4}

In this contribution, the localized *in situ* formation of tin dioxide (SnO₂) nanoparticles embedded in polymethyl methacrylate (PMMA) films will be presented. This is achieved by the photo-induced reduction of the metal oxide precursor included in the polymeric films, through controlled

UV and Visible pulsed laser irradiation. Interestingly, SnO₂ particle formation follows the same formation pathways with both laser wavelengths.

By using a combination of structural, morphological and spectroscopic techniques (XRD, TEM, SEM, UV-Vis), we will demonstrate that the pulsed laser irradiation at 355 and 532 nm generates the reduction of the metal oxide precursor leading to SnO₂ particle formation homogeneously distributed in the polymeric film, as displayed in the representative SEM images.

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Photophysical Study of Cobalt Based Mediators for Dye Sensitized Solar Cells with a Focus on Electrostatic Interactions

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The importance of molecular charge in electron transfer processes that take place in photoelectrochemical regenerative solar cells is not well understood.

In this regard a series of three cobalt (II) complexes, previously studied as redox mediators in dye sensitized solar cells, were characterized in combination with two ruthenium (II) dyes, [Ru(dcb)(dnb)(NCS)₂] (where dcb = 2,2'-bipyridyl-4,4'-dicarboxylic acid; dnb = 4,4'-dinonyl-2,2'-bipyridine) and the highly cationic [Ru(deeb)(tmam)₂]⁶⁺ (where deeb = 4,4'-diethyl ester-2,2'-bipyridine; tmam = 4,4'-bis[(trimethylamino)methyl]-2,2'-bipyridine)¹.

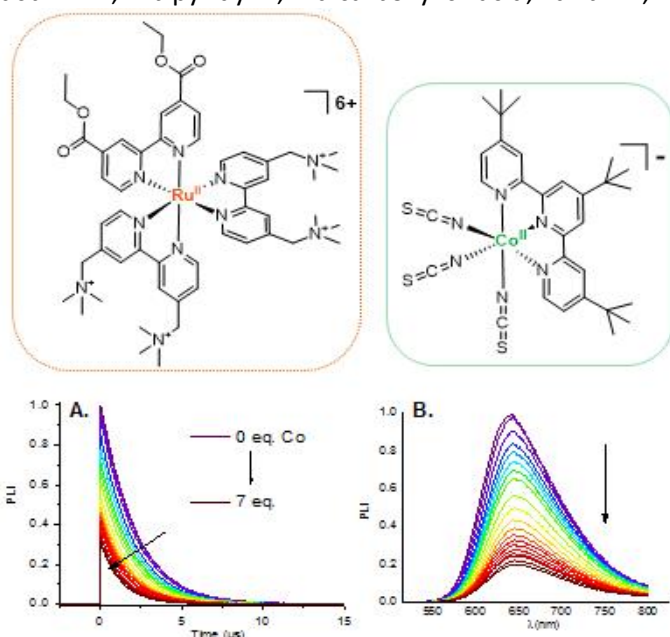


Figure. Time-resolved (A) and steady-state (B) PL spectral changes of Ru(deeb)(tmam)₂ with increasing [Co]

[Ru(deeb)(tmam)₂]⁶⁺ (where deeb = 4,4'-diethyl ester-2,2'-bipyridine; tmam = 4,4'-bis[(trimethylamino)methyl]-2,2'-bipyridine)¹.

The cobalt based electron donors used were [Co(bpy)₃]²⁺ and [Co(dtb)₃]²⁺, and the negatively charged complex [Co(ttt)(NCS)₃]⁻¹ (where bpy = 2,2'-bipyridine; dtb = 4,4'-Di-tert-butyl-2,2'-bipyridine; ttt = 4,4',4''-Tri-tert-Butyl-2,2':6',2''-terpyridine).

A regeneration study of the [Ru(dcb)(dnb)(NCS)₂] dye anchored to the mesoporous nanocrystalline TiO₂ semiconductor surface was conducted by transient absorption spectroscopy. It was observed that the dye regeneration was more efficient for [Co(bpy)₃]²⁺ and [Co(dtb)₃]²⁺ than for [Co(ttt)(NCS)₃]⁻¹, despite its larger driving force. This could be rationalized based on the electrostatic properties of the molecules involved, indeed their global and localized charges could give rise to electrostatic repulsions.

To further investigate the electrostatics, quenching studies with the cobalt mediators and the positively charged dye [Ru(deeb)(tmam)₂]⁶⁺ in acetonitrile solution were performed. Steady-state and time-resolved photoluminescence spectroscopy showed that [Co(ttt)(NCS)₃]⁻¹ quenches the excited dye emission more efficiently than both [Co(bpy)₃]²⁺ and [Co(dtb)₃]²⁺. Also, a static component consistent with the formation of an ion-pair adduct with the ruthenium complex was observed.

These results encourage future studies at the TiO₂ interface of the interactions observed in solution between then [Ru(deeb)(tmam)₂]⁶⁺ dye and the three cobalt complexes, to provide a deeper understanding of the electron transfer dynamics involved in photoelectrochemical systems containing such molecular species.

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CAPSULIGHT: Photokilling of *Helicobacter pylori* by endogenous pigments

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The gram-negative bacterium *Helicobacter pylori* colonizes the mucus layer of stomach and duodenum ; up to 50% of the world population is thought to be infected by this microaerophilic bacterium, with infection rates nearing 90% in some countries. *H. pylori* has been shown more effective in infecting the host when in presence of inflammation and chronic gastritis and is usually eradicated only by antimicrobial therapy. Unfortunately, eradication is a complex process with heavy side effects; moreover *H. pylori* strains are beginning to show antibiotic resistance and patients are found to be unresponsive to treatment. For these reasons alternative ways to treat and eradicate this bacterium are sought.

Among the strategies alternative to antibiotic treatment, antimicrobial PhotoDynamic Therapy (PDT) presents encouraging features for the treatment of infections originated by microbial pathogens because of a broad spectrum of action and low mutagenic potential. Antimicrobial PDT is particularly effective when the target microorganism presents endogenous pigments.

In the case of *H. pylori*, it has been shown that the photosensitizers Protoporphyrin IX and Coproporphyrin are endogenously produced and accumulated in the body of the bacterium, therefore *H. pylori* might be a suitable target of antimicrobial PDT. For this purpose, small capsules bearing a LED source of an appropriate wavelength are engineered, so that irradiation can be performed *in situ* without the use of invasive endoscopic light.

Within a research project funded by Regione Toscana («CAPSULIGHT : Design of an ingestible robotic pill based on LED sources for the treatment of gastrointestinal disorders - BANDO FAS SALUTE 2014, CUP B52I14005760002) for the development of light capsules suitable for ingestion, we are testing the effect of irradiation on the photophysical and photochemical properties of Protoporphyrin IX and Coproporphyrin, the endogenous photosensitizers of *H. pylori*.



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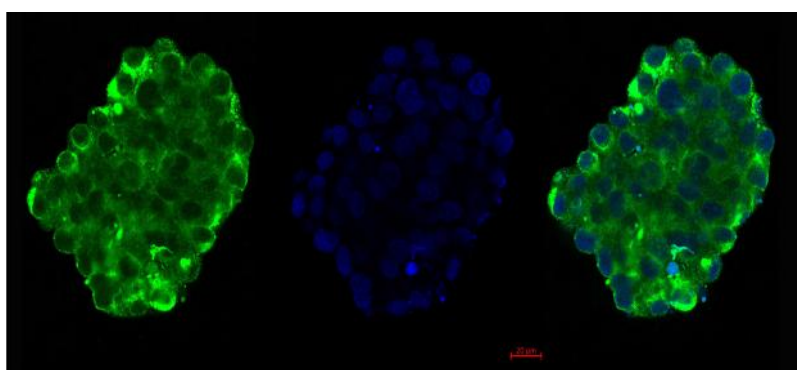
Progetto sviluppato con il determinante contributo della Regione Toscana a valere sul Programma Attuativo Regionale cofinanziato dal FAS (FSC)

Effectiveness of photoactivatable drugs on prostate cancer stem cells: a pilot study

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Currently available treatment modalities in prostate cancer (PCa) target mature and proliferating tumor cells without affecting the tumor-initiating PCa stem cells (SCs) Many patients initially experience a positive treatment response but some develop progressive disease, including tumor recurrence, metastasis, and therapy resistance. Various focal treatments, such as phototherapy, cryotherapy, interstitial thermotherapy and dynamic high-frequency ultrasound (HIFU), are being evaluated for PCa treatment. Among photoactivatable compounds, furocoumarins possess the interesting property to be highly effective when



Confocal microscopy of DU145 spheres treated with anti-CD44 antibody (green). Nuclei were counterstained with DAPI (blue).

UVA irradiated, whereas are inert in the dark, thus lacking toxicity. Furthermore, it has been suggested a potential role of the bioactive compounds isolated from the medicinal plant *Psoralea corylifolia* (neobavaisoflavone and psoralidin) in prostate cancer chemoprevention through enhancement of TRAIL-mediated apoptosis. In this context, this work was aimed at verifying whether photoactivation of a linear furocoumarin, 8-methoxy psoralen (8-MOP), and an angular one, trimethyl angelicin (TMA) could

target PCaSCs. Other than UVA light, longer wavelengths, such as 420 nm (Vis), were investigated in order to minimize surrounding tissue damage induced by light, reduce the mutagenicity of the DNA lesions induced by furocoumarins (monoadducts over cross-links), increase light penetration into the target tissue, thus allowing the use of more convenient light sources for in vivo application. While 8-MOP was able to form both crosslinks and monoadducts under the two wavelengths, TMA demonstrated to induce only the less mutagenic monoadducts in the DNA under Vis light. Production of singlet oxygen was detected only under UVA light for the two furocoumarins, while Vis light was ineffective. Superoxide anion formed as a minor component of the ROS under both lights. Biological assays were carried out on DU145 cells, a prostate cancer cell line and sphere formation was used as a model for cancer cell stemness (see figure). After irradiation with 2 J/cm² UVA, both 1 μM 8-MOP and TMA completely abrogated sphere formation. On the contrary, upon activation with 2 J/cm² of VIS light, TMA was more effective than 8-MOP. Indeed, sphere formation was totally inhibited by 10 μM TMA, whereas 10 μM 8-MOP had no effect. Collectively, our data suggest that TMA plus VIS may be a potential focal treatment towards PCaSCs. It will be noteworthy to ascertain whether, other than DNA lesions, other molecular targets, such signaling pathways involved in the induction and maintenance of stemness in cancer cells, could be affected.

Towards Photochemically Driven Artificial Molecular Pumps: a Rational Approach

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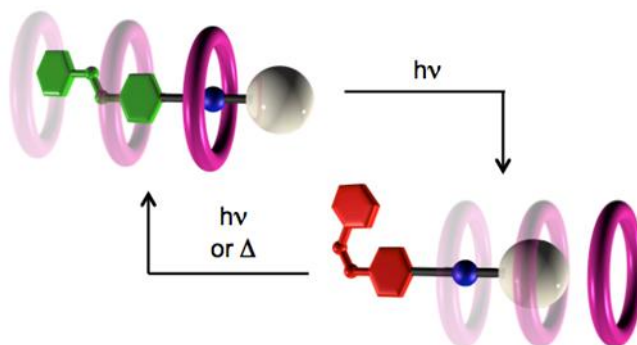
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The bottom-up design, preparation and characterization of chemical systems that behave as molecular-scale machines and motors is a stimulating challenge of nanoscience.¹ The interest on this kind of systems arises from their ability to perform a (useful) function in response to chemical and/or physical signals. In this context, the use of light stimulation has several advantages, primarily because photons can be used to supply energy to the system (i.e., write) and to gain information about its state (i.e., read).²

Here we will describe investigations undertaken in our laboratories aimed at photo-inducing and -controlling large-amplitude molecular motions, both under thermodynamic and kinetic viewpoints, in multicomponent (supramolecular) species that comprise photoreactive units.³ This work has recently culminated with the design, construction and operation of a system in which light irradiation causes the relative unidirectional transit of a nonsymmetric molecular axle through a macrocycle (see Figure).⁴



As a matter of fact, this is the first example of a photochemically driven artificial molecular pump.⁵ Systems of this kind can not only lead to radically new approaches in catalysis, materials science and medicine, but also disclose unconventional routes for the conversion of light energy into chemical energy.

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Investigation of the hydroxyl directing effect on the Paternò-Büchi reaction on 5-(2-triisopropylsilyloxazolyl)methanol derivatives.

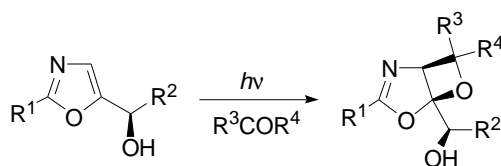
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The synthesis of oxetanes through the use of the Paternò-Büchi reaction has been extensively studied during the last century. Several attempts to obtain stereoselective reactions have been performed mainly when the olefinic reagents were furan, silyl enol ethers or enamines. Stereoselectivity can be obtained when a stereogenic center is present in this type of reagent, as reported for some silyl enol ethers and enamine.¹ Furthermore, high stereoselectivity has been obtained by introducing a chiral auxiliary in the carbonyl compounds,² or by using a chiral carbonyl compounds.³

Another approach used already to obtain a stereoselective Paternò-Büchi reaction has been to use olefins bearing a hydroxyl group near the reaction centre. This approach has been used successfully on allylic alcohols⁶ and on 2- and 3-furylmethanol derivatives.⁴ In these cases, a possible interaction between the hydroxyl group and the triplet state of the carbonyl compound could account for the observed high stereoselectivity. If oxazolymethanol derivatives are used as substrates in this reaction, a possible competing effect due to the presence of the lone pair on the nitrogen atom on the oxazole ring could be present, if the second above reported hypothesis is the effective one. In order to investigate this hypothesis we synthesized some 5-oxazolymethanol derivatives and tested their reactivity towards benzaldehyde and benzophenone in a Paternò-Büchi reaction.

The photochemical coupling of 5-oxazolymethanol derivatives with benzophenone and benzaldehyde showed that the hydroxyl directing effect in the Paternò-Büchi reaction described in the case of allylic alcohols and furylmethanol derivatives can also be present in the case of 5-oxazolymethanol derivatives. The results show that the hydroxyl directing effect in the Paternò-Büchi reaction described in the case of allylic alcohols and furylmethanol derivatives can be present also in the case of 5-oxazolyl methanol derivatives. The attack of the excited carbonyl compound occurs only on the same side where the hydroxyl group is present. On the basis of the obtained results we can exclude the possible competing role of the lone pair of nitrogen in the formation of a complex between the excited triplet state of the carbonyl compound and the substrate. The results are in agreement with the formation of a hydrogen bond between the reagents. In this case, the reaction with aromatic aldehydes showed an unusual *endo* stereoselectivity. The observed stereoselectivity can be predicted on the basis of the interaction between HSOMO and LSOMO in the biradical intermediate.



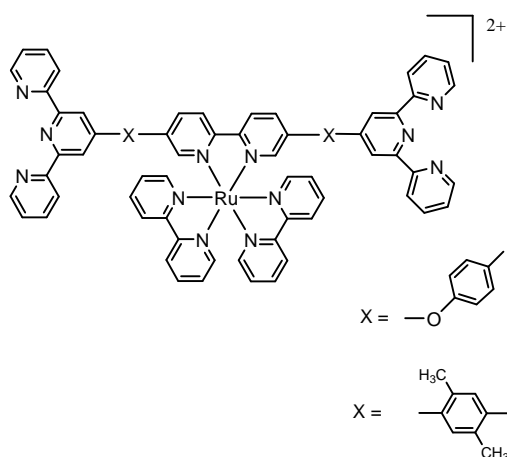
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Photoinduced charge separation within metallo-supramolecular wires made with a $[\text{Ru}(\text{bpy})_3]^{2+}$ -bis terpyridine building block

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Assemblies of transition metal complexes with photochemical properties are often investigated with the goal to mimic the functions performed by natural system such as solar energy conversion and storage.¹ For that purpose, $[\text{Ru}(\text{bpy})_3]^{2+}$ (bpy= 2,2'-bipyridine) has been widely studied as photosensitizing subunit, owing to its relatively long lived $^3\text{MLCT}$ state, which is appropriate energy to split water, its stability, synthetic accessibility and ability to be derivatised.² On the other hand, metallic complexes built with tpy (tpy=2,2';6',2''-terpyridine) ligands having axial symmetry are expected to be useful for linear construction of multinuclear assemblies.³ In that context $[\text{Ru}(\text{bpy})_3]^{2+}$ like complex bearing two free terpyridines groups on the same bipyridine, have been synthesized (scheme 1) and used to construct inorganic triad on electrode, in a stepwise process.⁴ In this communication we will report on the synthesis and characterization of the $[\text{Co}^{\text{III}}\text{-Ru}^{\text{II}}\text{-Fe}^{\text{II}}]^{7+}$ triad, where $[\text{Co}(\text{tpy})_2]^{3+}$ subunit acts as an electron acceptor and $[\text{Fe}(\text{tpy})_2]^{2+}$ as an electron donor. Visible irradiation of the modified electrode in the presence of triethanolamine in CH_3CN induces the generation of an anodic photocurrent. The magnitude of the photocurrent will be compared to that obtained with related $[\text{Co}^{\text{III}}\text{-Ru}^{\text{II}}]$ diade.⁵ The influence of the structure of the $[\text{Ru}(\text{bpy})_3]^{2+}$ -bis terpyridine building block on the photocurrent generation will also be discussed.



Scheme 1. Molecular structure of the $[\text{Ru}(\text{bpy})_3]^{2+}$ -bis terpyridine building blocks.

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Ultrafast relaxation dynamics of monomer and aggregate forms of a Zn-phtalocyanine

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The molecule 9(19),16(17),23(24)-tri-*tert*-butyl-2-[ethynyl-(4-carboxymethyl)phenyl] zinc(II)-phtalocyanin (ZnPc) is a push-pull phtalocyanine able to inject electrons into the conduction band of TiO₂, and function as photosensitizer for DSSC applications.¹ We have characterized its photophysics in solution, by analyzing the time evolution of its excited states in a time interval spanning from tens of femtoseconds up to 1.5 nanoseconds. It has been found that depending on the solvent in which the sample is dissolved, ZnPc can exist as monomer or aggregate form. In particular, the sample is in the monomeric form if dissolved in ethanol, while in chloroform the increasing intensity of a blue shifted absorption band in the Q-band absorption region around 630 nm indicated the formation of H-aggregates. We have characterized the spectroscopic properties of monomer and aggregate solutions by recording absorption and fluorescence spectra in different conditions. The comparison of time resolved data recorded for the monomer and aggregate solutions allows us to identify different relaxation pathways. By comparing the kinetics recorded upon S1 and S2 excitation it has been possible to estimate a very fast internal conversion dynamics in the monomer solution, occurring on a sub-picosecond time scale. The formation of H-aggregates further complicate the relaxation dynamics, by introducing a further non radiative decay channel, and inducing an overall faster relaxation.

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The S-layer as a UV-radiation shield: the case of *Deinococcus radiodurans* and its S-layer Deinoxanthin Binding Complex

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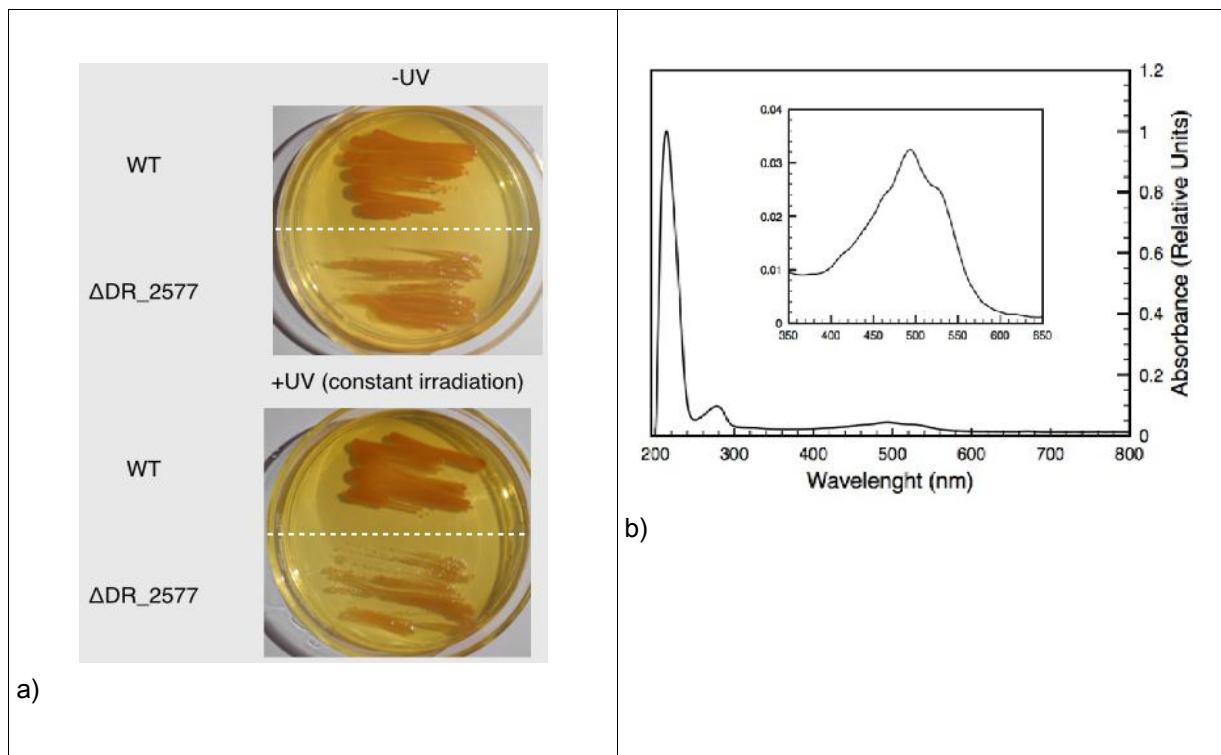
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Deinococcus radiodurans is a poly-extremophile bacterium able to overcome high doses of ionizing and ultraviolet radiations, as well as environmental stresses. One of the exquisite characteristic of this bacterium is its surface layer (S-layer), a paracrystalline structure built of a regular repetition of several proteins [1] in which the protein DR_2577 is the main component. Being organised into hexamers resulting from a combination of dimers [2], DR_2577 is building a novel complex named S-layer Deinoxanthin Binding Complex (SDBC) [3] by the binding of the carotenoid deinoxanthin, a strong protective antioxidant specific of this bacterium. Recently, we have reported that deletion mutants for DR_2577 show a decrease in the UVC resistance (Figure 1a) and that deinoxanthin possesses specific spectroscopical features consistent with a protective role of the SDBC (Figure 1b). We proposed a model in which *D. radiodurans* S-layer is behaving as a first shield against UV radiation and having an essential role for the survival and development of this bacterium in extreme conditions.



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IUPAC Project measurement of photoluminescence quantum yields

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The photoluminescence quantum yield (QY) is one of the most important quantitative properties of a luminescent sample, and robust ways to measure it are essential in the application of luminescence techniques^{1,2}. In this project, sponsored by IUPAC (#2013-040-1-300), we perform an inter-laboratory comparison of QY measurements, with a focus on the classical method based on standards. Ten laboratories participate in this project. In addition to the authors, the principal investigators involved are B. Albinsson (Gothenburg, Sweden), K. Ghiggino (Melbourne, Australia), G. Orellana (Madrid, Spain), A. Patra (Bhopal, India), R. Méallet-Renault (Orsay, France), W. Qin (Lanzhou, China), and W.W. Yam (Hong Kong, China).

The project will deliver:

1. an insight into the reproducibility and inter-laboratory variability of “routine” QY measurements.
2. an extended set of standards for QY measurement.

Preliminary results from the project will be presented. Absorption, excitation and corrected emission spectra of 22 commonly used dyes as obtained in the ten laboratories are compared. QYs were measured of 15 samples against 7 well-established standards^{3,4,5}.

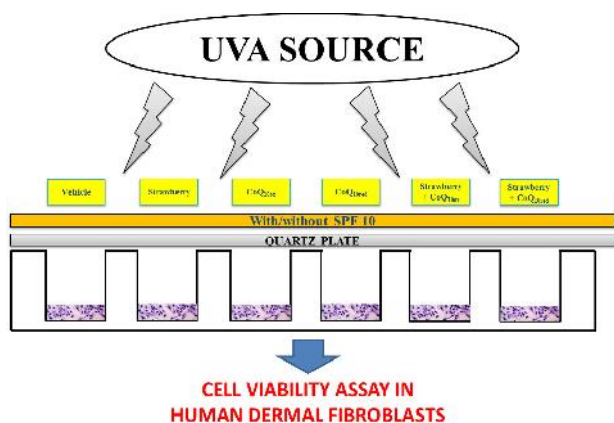
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The possible use of strawberry in cosmetic formulation

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A growing number of studies suggest a strong association between a diet rich in fruits and vegetables and a lower incidence of different chronic pathologies (1). Focusing on fruits, it is quite complex to explain their potential health benefits, given the wide variety of fruits available for consumption and their complex composition. For these reasons, in recent decades, individual subgroups of fruits have been taken into account, to facilitate the observation and promote their specific health benefits. In this context berries, and in particular strawberries, have been extensively studied over the last two decades for their beneficial properties (2). Recently, their possible use in ameliorating skin conditions has been proposed; however, their role in preventing UVA-induced damage in cosmetic formulation has not yet been investigated. Skin is constantly exposed to environmental stressors, such as UVA radiation, that induce oxidative stress, inflammation and cell death via the production of ROS. For these reasons the creation of a new cosmetic product enriched with strawberry polyphenols could represent an innovative tool to provide photoprotection. First of all, the nutritional and phytochemical quality of strawberry fruit extracts was



evaluated: the total antioxidant capacity, the radical scavenging activity, the content of total phenolics, flavonoids, anthocyanins, vitamin C and folates were measured in the different extracts. An UV filter combination often used in sunscreen products was chosen for the realization of the final product. Different formulations with diverse combination of strawberry extract were realized. Biological *in vitro* assay on human dermal fibroblast cells showed a photoprotective role of these formulations on cell viability, alone or in association with nanoparticles of Coenzyme Q₁₀ (reduced and oxidized form) and with sun protection factor 10. These results should be

validated on *in vivo* models, testing the efficacy of the new product on animals. The future results will demonstrate the protective effect of strawberry on skin cells against UVA induced damage, suggesting, for the first time, the use of a natural source of antioxidants against skin damage.

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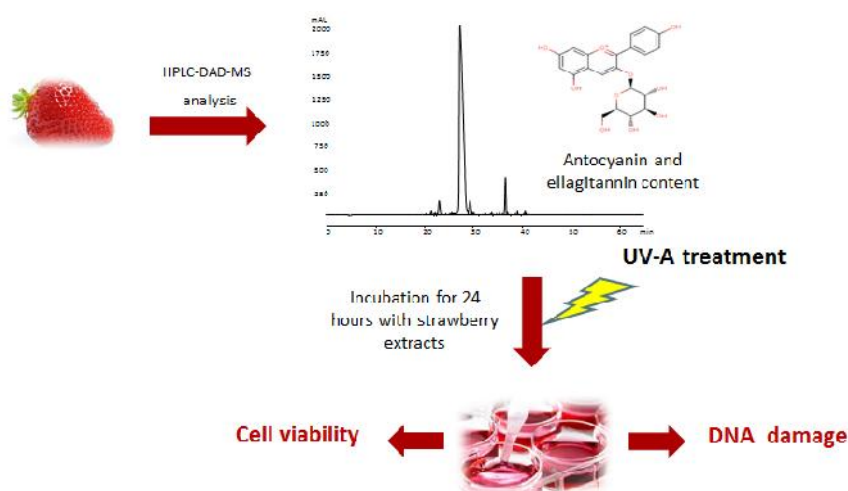
Photoprotective activity of natural dietary compounds: the case of strawberry polyphenols

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It is known that exposure to UVA radiation causes many adverse biological effects which may lead to a wide array of skin diseases. Basically, the skin possesses extremely efficient defence mechanisms in form of antioxidant enzymes (i.e., superoxide dismutase, catalase, glutathione peroxidase) and nonenzymatic antioxidant molecules (i.e., vitamin C, vitamin E, ubiquinone), but, because of constant environmental exposure to physical and chemical agents, an oxidant/antioxidant imbalance results, which greatly influences its well-being. Strawberry (*Fragaria x ananassa*) is a rich source of polyphenols with strong antioxidant and anti-inflammatory properties. In the present study the phenolic contents and total antioxidant capacities of strawberry extracts were evaluated, as well as their capacity to protect human dermal fibroblasts against UVA irradiation. Methanolic extract from *Sveva* cultivar was analyzed for anthocyanin content and for its ability to protect human dermal fibroblast against UVA radiation (Fig. 1).



Different anthocyanin and ellagitannin pigments were identified and quantified by using HPLC-DAD-ESI/MS, while high antioxidant capacity values were measured by both FRAP and TEAC assays. After 24 hours of incubation with strawberry extract at different concentrations (0.05, 0.25, 0.50 mg/ml of extract), a photoprotective activity in fibroblasts exposed to UVA radiation was observed, with an increase in cellular viability of about 24% and a concomitant decrease in DNA damage for 86%, compared to control cells. Our preliminary data show that strawberry extracts are able to protect skin cells against the adverse effects of UVA radiation and that this photoprotective capacity might be due to the antioxidant activity of strawberry constituents.

Intragastric PDT against *H pylori*: a stomach wall illumination model

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In the field of illumination sources to perform PDT endoscopically, innovative solutions have been defined and studied in many applications, e.g. in the case of catheter infections, lung and pancreas tumours, stomach infections by *H. pylori* (Hp). To perform intra-gastric PDT against Hp, we have recently designed an illuminating ingestible device equipped with LED sources. In order to optimize the photo-killing efficacy, the analysis of the light action spectrum is paramount. This depends on multiple factors among which (i) the photosensitizer absorption spectrum; (ii) the tissue optical properties (i.e. absorption and scattering); (iii) the tissue geometry and (iv) the illumination geometry.

In this poster, we concentrate on the definition of a model for the gastric wall structure and illumination. Our approach is based on the knowledge of the stomach mucosa optical properties that have been used to perform Monte Carlo simulations of the light transmitted and reflected by simple plane parallel layer models of the stomach *plicae*. Then, to obtain an estimate of the light action spectrum for the PDT against Hp, we merged this results with the absorption spectrum of the bacterium endogenous photosensitizers. However, this does not take into account neither the illumination geometry, nor the stomach wall surface geometry.

To explicitly consider these important factors, we adopted a simple 3D geometrical model of the stomach corpus and pyloric antrum inner surface and evaluated the light intensity impinging on each surface point and the angle of incidence of the light rays. The illuminator was modelled as an isotropic point source with a specific position inside the stomach. Then we merged this illumination geometry model with the Monte Carlo simulations of the action spectrum by taking into account the effect of the particular value of the light intensity and angle of incidence, to obtain an average action spectrum and also to evaluate its variations on the stomach inner surface.



Regione Toscana



Progetto sviluppato con il determinante contributo della Regione Toscana a valere sul Programma Attuativo Regionale cofinanziato dal FAS (FSC)

Chalcogenide-based photoanodes for photoelectrochemical water splitting applications

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Efficient solar light conversion into fuels, such as H₂ or hydrocarbons, requires the use of photoactive materials combining good visible light absorption properties, suitable band gap energy position, durability under harsh operation conditions and slow electron-hole pair recombination. In photoelectrochemical water splitting the overall reaction is divided in the two half reactions of oxygen and hydrogen evolution occurring at the photoanode and at the photocathode, respectively.

Transition metal oxides have been widely employed as photoanode materials because of their suitable band gap energy position and high stability. TiO₂, WO₃, BiVO₄ and Fe₂O₃ are by far the most extensively studied semiconductors for such application, but suffer from lower than optimal band-gap energy (> 2.2 eV) and from fast charge carrier recombination. Other narrower band gap semiconductors should be used as photoanodes. Chalcogenide nanomaterials such as those based on CdS and CdSe possess promising properties which have attracted great interest in solar energy conversion applications, particularly in quantum dot sensitized solar cells and in photocatalytic water splitting [1,2]. CdS and CdSe can be combined in the CdS_xSe solid solution having a band gap energy tunable from 2.6 to 1.8 eV; its high conduction band energy allows photoexcited electrons to be injected in the lower lying conduction band of TiO₂ (in quantum dot sensitized solar cells) or directly drive proton reduction to H₂.

However, CdS and CdSe are unstable under irradiation in water environments and undergo photocorrosion or photopassivation if used as a photoanode. On the other hand, in the last few years, many protection techniques have been investigated in order to stabilize narrow band gap materials [3, 4].

Here we report our preliminary results on the use of chalcogenide-based photoanodes in water oxidation and their stabilization by the deposition of protective overlayers. The electrodes were prepared through the successive ionic layer adsorption and reaction (SILAR) process on a TiO₂ mesoporous host scaffold. Based on our initial investigations, CdS/TiO₂ photoanodes show promising properties, including high quantum yields under low intensity monochromatic irradiation and extremely low overpotentials required to attain a stable photoresponse. Figure 1 reports the incident photon to current efficiency (IPCE) curves recorded with the same CdS/TiO₂ photoanode at several applied potentials.

While oxide semiconductors such as WO₃, BiVO₄ and Fe₂O₃ need large positive overpotentials to generate measurable photocurrents, the here studied CdS/TiO₂ photoanodes are active at applied biases as low as 0.0 V vs. RHE due to the high energy conduction band of these two materials. On the other hand, stability under high intensity irradiation remains an issue and photoanodes undergo deactivation under simulated solar light conditions. Therefore further studies are underway to protect the photoelectrodes with recently developed strategies which should potentially offer a way to overcome such instability limitations.

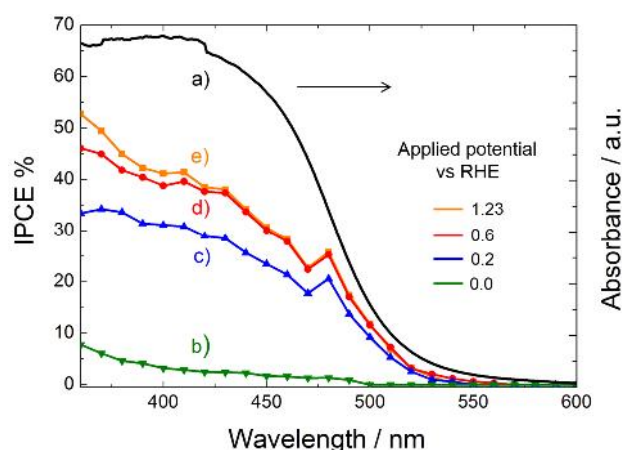


Figure 1. a) UV-Vis absorption spectra and IPCE measurements of a CdS/TiO₂ photoanode carried out in NaOH 1.0 M aqueous solution, with an applied bias of b) 0, c) 0.2, d) 0.6 and e) 1.23 V vs RHE.

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Genetically Engineering Light-Harvesting Antennas to Maximize Quantum Energy Transport

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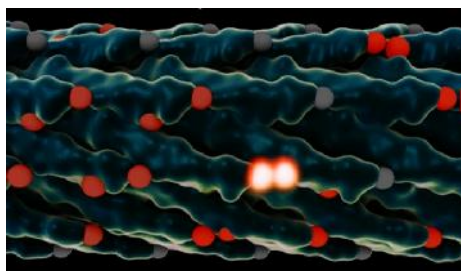
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One of the challenges for achieving efficient exciton transport in solar energy conversion systems is precise structural control of the light-harvesting building blocks. Here, we create a tunable light-harvesting material consisting of a connected chromophore network on an ordered biological virus template. Using genetic engineering, we establish a link between the inter-chromophoric distances and emerging transport properties. The combination of spectroscopy measurements and dynamic modelling enables us to

elucidate quantum coherent and classical incoherent Förster exciton transport at room temperature.

We have created an intermediate configuration showing improved exciton transport compared to an incoherent transport configuration. This improvement arises from a regime of stronger coupling between the chromophores, where usually quantum coherence effects accompany the enhancement of transfer. We thus have provided evidence for an important energy-transfer design concept: beyond-Förster transport boosts the transfer efficiency.

This system may prove especially useful for investigating higher-level energy transport mechanisms; for example, exciton relaxation effects and directing the exciton transport towards specific sites. In addition, we lay the fundamentals for a wide range of applications relying on efficient energy transfer, such as organic photovoltaics and light-driven catalysis.

pH-driven nano-assembly of a new Bodipy based sensor

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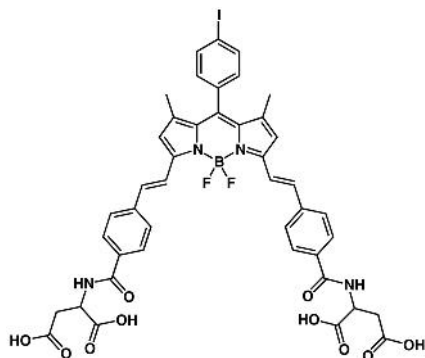
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4,4-Difluoro-4-bora-3a,4a-diaza-s-indacene (BODIPY) dyes are an important class of highly luminescent materials that have been found in widespread applications for biochemical labeling, photonic molecular systems, laser dyes, organogelators, and light-emitting devices because they tend to be strongly UV-absorbing molecules that emit relatively sharp fluorescence peaks with high quantum yields.¹

The absorption spectrum of BODIPY exhibits an intense $S_0 \rightarrow S_1$ transition with its maximum at 505 nm due to a large transition dipole on the line which links 2-position with 6-position of the BODIPY core.^{2,3}

They are relatively insensitive to small changes of polarity and pH of their environment and are reasonably stable under physiological conditions. Actually, the presence of substituent groups able to modulate

hydrophilic and hydrophobic interactions are important to drive self-assembly enhancing their tendency to form aggregates and modulating their solubility in polar solvents. The self-assembly results in highly organized aggregates with various morphologies such as spheres, rods, planar bilayers, vesicles, and others. The formation of these morphologies depends on solvent environments, molecular structure, and shapes, as well as the relative fraction of hydrophilic and hydrophobic parts.



Here we report the photophysical study of a Bodipy aggregates, based on a new dye in which the hydrophilic moiety consists of a chelating (able to coordinate Zn, Ca and Cu cations) and pH sensitive subunit.

The aggregation can be modulated by small pH changes and the disassembly by protein interactions.

In particular the aggregates, 80 nm in dimension, does not exhibit luminescence but, changes in pH or interactions with BSA and HSA can switch-on their intense emission in the red.

This behaviour could allow to localize themselves in some cell compartments and for selective imaging of different compartments in cells.

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Cationic poly(ϵ -caprolactone) nanoparticles as versatile scaffolds for combining photo/chemotherapy in cancer

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Coupling chemotherapy with photodynamic therapy (PDT) is nowadays opening intriguing horizons towards new and still underexplored multimodal therapies of cancer. In this context, engineered polymer nanoparticles (NPs) offer great potential since they permit to locate therapeutic species at disease site and to control the release of therapeutics in the same region of space [1]. It is expected that an enhanced therapeutic benefit of the treatment and a simultaneous reduction of side effects occur.

Cationic nanoparticles (NPs) are at limelight in the field of cancer nanotechnology due to their unique ability to penetrate deeply inside tumor tissue [2]. To this purpose, here we have developed an array of polymeric NPs based on an amino-terminated poly(ϵ -caprolactone) (PCL+) mixed with poly(ethylene glycol)-poly(ϵ -caprolactone) (PEG-PCL) or poly(ϵ -caprolactone) diol (PCL-OH) to attain cationic scaffolds with different charge density and surface hydrophilicity. As active drug cargo, the lipophilic anticancer drug Docetaxel (DTX) was entrapped in the NP core whereas anionic tetrasulfonate photosensitizers, i.e. porphyrin (TPPS₄) or phthalocyanine (ZnPcS₄), were adsorbed on the surface.

NPs were prepared by nanoprecipitation of PCL+ and different PCL+/PEG-PCL or PCL+/PCL-OH mixtures with yields around 80%. The size of unloaded nanoscaffolds was below 200 nm with PI<0.2, while zeta potential could be tuned depending on the percent amount of PEG-PCL or PCL-OH employed. DTX entrapment did not alter size and zeta potential of the nanoscaffold. On the other hand, the adsorption of the photosensitizer could reverse zeta potential depending on the amount loaded onto NPs. Adsorption extent of the negatively-charged photosensitizers was in line with the different density of cationic charge on the nanoscaffold surface. TPPS₄ and ZnPcS₄ were partly monomerized when adsorbed onto cationic NPs depending on the composition of the polymeric scaffolds.

Cationic NPs were stable in DMEM FBS+ while becoming negatively charged due to ion and protein interaction. Extensive aggregation of PCL+/PCL-OH NPs was instead observed in phosphate buffer. To further engineer NP surface, a top coat of Hyaluronan (HA) was applied to neutralize positive charge and to encourage NP accumulation in cancer cells overexpressing CD44 receptors. HA adsorption on the different nanoscaffolds reversed surface charge from positive values to negative values and increased colloidal stability of NPs especially in phosphate buffer.

The optimized NPs carrying DTX and the photosensitizer were finally tested on cancer cells to assess the impact of surface modification on trafficking and photoactivity.

Acknowledgments

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Photodegradation of the antibiotics Sulfamethoxazole, Hydrochlorothiazide under Simulated Sunlight

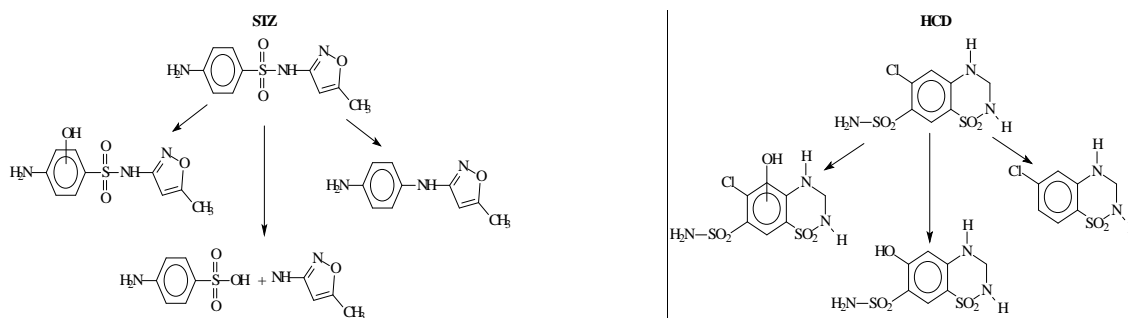
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Nowaday the emergence of pharmaceuticals in the aquatic and terrestrial environment have been a major concern. They have been detected in sewage-treatment plants, sediments, and soils as well as at surface and drinking water. So far, there is limited information in the literature on the fate of these compounds when they are exposed to solar light in the various environmental compartments. The objective of the present study is to investigate the degradation process of two different antibiotics Sulfamethoxazole (**STZ**), Hydrochlorothiazide (**HCD**) in aqueous solutions when exposed to simulated solar light. We mainly concentrate our effort on the kinetic studies by evaluating the degradation quantum yield as well as the effect of various parameters such as oxygen concentration, pH and the presence of inorganic ions. The main effect was observed by molecular oxygen parameter. We also make an important effort in the elucidation of the main intermediate and stable by-products. A lot of information is available on the stability and fate of parent compounds and not so many on their transformation products. These may present a toxicity level higher than the precursor substrate and should be identified and analysed. The structure elucidation was obtained by using the HPLC/ESI/MS and HPLC/ESI/MS² techniques in negative as well as positive modes and through the complete study of the various fragmentation pathways. The main involved photochemical processes were i) the scission of the bridge through a photohydrolysis process, ii) selective hydroxylation of the aromatic moiety iii) Desulfonation process and iiiii) in the case of HCD to dechlorination reaction. A mechanism was then proposed in the light of the kinetic and analytical studies.

Keywords : antibiotics, sunlight, photolysis, Sulfamethoxazole, Hydrochlorothiazide



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Influence of mTHPC liposomal distribution in multicellular spheroid on the photodynamic therapy efficacy

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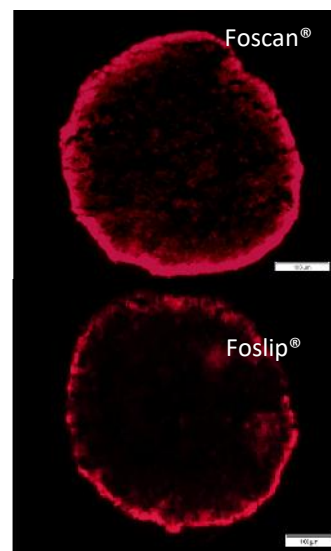
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Meta-tetra(hydroxyphenylchlorin) (mTHPC, Foscan®) is a clinically approved photosensitizer (PS) for the photodynamic therapy (PDT) of cancer and is characterized by high absorption in the deep red and high ¹O₂ quantum yield⁽¹⁾. Various studies demonstrated that PDT efficacy is tightly related to intracellular and intratissular localization of mTHPC⁽²⁾. However, Foscan® is a highly hydrophobic compound, it is partially aggregated even in the bloodstream thus resulting to unfavorable biodistribution and important side effects. Poor tumor selectivity and pharmacokinetics of Foscan® led to the development of mTHPC liposomal formulation, Foslip®⁽¹⁾. *In vivo*, Foslip® has showed a rapid biodistribution and clearance from the bloodstream⁽³⁾. This formulation is interesting for PDT due to the decreased accumulation in skin compared to Foscan® and reduced pain upon intravenous administration⁽⁴⁾.

Multicellular spheroid is a non-vascularized micro-tumor tridimensional model of cells, similar to micro-metastases. Compared to monolayer cells, multicellular spheroid shows micro-environment similar to *in vivo* situation. Heterogeneous population of cells is the consequence of the oxygen gradient, naturally found in multicellular spheroid making it a suitable model to study PDT parameters⁽⁵⁾. Thus, importance of irradiation fluence rate and nonuniform distribution of mTHPC has been demonstrated earlier^(6, 2).

The aim of this study was to determine whether mTHPC nanovectorization could induce a different spatiotemporal distribution of Foscan® and its impact on PDT efficacy. After 3, 6 and 24 h incubation, mTHPC uptake in HT29 multicellular spheroids was assessed by fluorescence measurements while the time-related diffusion of Foscan® and Foslip® was studied with fluorescence microscopy. After irradiation with various fluences administrated at the fluence rate of 30 mW.cm⁻², cell survival was estimated using clonogenic assays.

Already 3 h after incubation, a better accumulation in multicellular spheroids is observed with Foscan®. The maximum of mTHPC uptake is found after 24 hours. Foslip® displays less intracellular accumulation irrespective to incubation time along with a shorter diffusion distance. Unexpectedly, Foslip® demonstrated higher photocytotoxicity compared to liposome-free mTHPC. For instance, the 50% Foslip-mediated cells photoinactivation was observed at 30 J.cm⁻², while much less photokilling was noted with Foscan®. This result can be partially linked to the difference of diffusion observed between Foscan® and Foslip® (see the figures here enclosed) and Foslip® monomer state. Further investigations are in progress to unravel these results. In conclusion, integration of mTHPC in liposomes improves photocytotoxicity in HT29 multicellular spheroids.



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Charge injection into nanostructured TiO₂ electrodes from the photogenerated reduced form of a new Ru(II) polypyridine compound: the "anti-biomimetic" mechanism at work

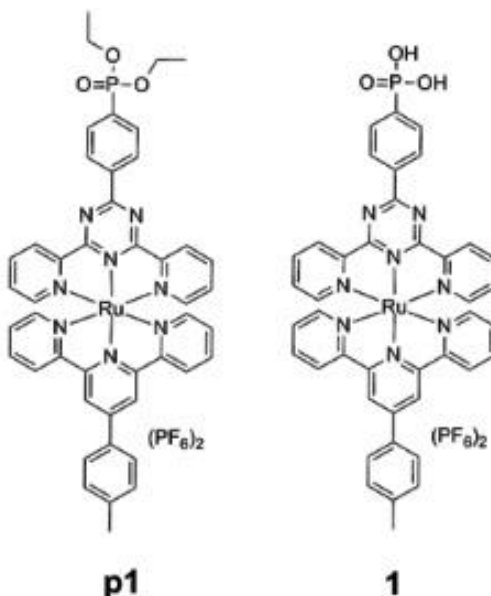
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Visible light sensitization of semiconductor electrodes by molecular dyes (photosensitizers) is an attractive approach to solar energy conversion. Indeed, this approach is well-explored in dye-sensitized solar cells (DSSC) for conversion of solar energy into electrical energy.

In DSSC based on n-type semiconductor electrodes, in principle the injection process can be generated and sustained by two different interfacial electron-transfer mechanisms: biomimetic and anti-biomimetic. In a biomimetic mechanism, the excited dye transfers an electron to the conduction band of the semiconductor electrode. The oxidized form of the dye is then reduced by the electrolyte that is present in the solution of DSSC. In an anti-biomimetic mechanism, it assumes that the excited photosensitizer does not inject an electron into the semiconductor, instead it is quenched according to a reductive electron transfer pathway by an electrolyte in solution. Successively, the reduced form of the photosensitizer transfers the electron to the conduction band of the semiconductor.



Figure

Here we report on the synthesis and investigation of their photophysical and redox properties in solution, of the new Ru(II) polypyridine compounds, **p1** and **1** (see **Figure**). Once **p1** is turned into **1** by substituting the ethyl groups with protons it is activated for the TiO₂ coupling. Whereas the excited state of the TiO₂-anchored species **1** is unable to inject electrons into the TiO₂ conduction band - therefore to produce sustained photocurrent in DSSC - the reduced form of the TiO₂-anchored **1**, produced via reductive photoinduced electron transfer quenching by ascorbate salts, efficiently injects electrons into TiO₂. To the best of our knowledge, this result represents the long-time searched experimental proof that the "anti-biomimetic" mechanism can be operative for DSSCs

Response of *Pseudomonas aeruginosa* transposon mutants to photo-oxidative stress

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The human opportunistic pathogen *Pseudomonas aeruginosa* is ubiquitously present in a widespread of environments. It often colonizes immune-compromised patients such as cystic fibrosis (CF), burnt or HIV-infected patients, producing damages in their tissues and interfering with the host's immune system by means of many virulence factors.

An important issue in the management of this bacterium is its resistance to antimicrobial treatments. Thus, scientists are searching for new drugs and alternative therapeutic strategies to combine to traditional chemotherapy; among these, antimicrobial photodynamic therapy (aPDT) is considered a promising tool. Photodynamic therapy (PDT) exploits the photo-oxidative stress elicited by exogenously administered photosensitizers (PSs) that absorb visible light and cause the production of reactive oxygen species (ROS), which in turn cause oxidative damage to bacterial cells. However the bacterial response to photo-oxidative stress induced photodynamically has not been deeply investigated.

At the aim of identifying *P. aeruginosa* PAO1 genetic determinants involved in response to photo-oxidative stress, a transposon insertion library was constructed. The attention was focused on Pseudomonas Quorum System (PQS), one of the Quorum Sensing (QS) intracellular signalling systems. PQS through Pseudomonas quinolone signal, 2-heptyl-3-hydroxy-4-quinolone (PQS), plays an important role in the expression of several virulence factors as well as in inducing a protective stress response. It was investigated if PQS mutants could cope with photo-oxidative stress in a different manner respect with PAO1 wild type strain.

Photoinactivation experiments were performed on two PQS overproducing mutants and on two PQS deficient mutants. PQS overproducer mutants displayed a statistically significant tolerance towards PDT treatment respect with PQS deficient mutants and PAO1 strain.

Further investigations should be focused on elucidating the indirect and/or direct role of PQS in response to PDT. PQS could play a defence role regulating the expression of genes involved in the response to photo-oxidative stress or PQS itself could quench singlet oxygen or scavenge radicals.

Synthesis and photochromism of N-methyl-carbazole benzopyrans

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One of the interests of our research groups is currently addressed to the synthesis and photophysical and photochemical characterization of some photochromic compounds showing possible P-type photochromism [1]. Benzo- and naphthopyrans derivatives possessing a high conversion percentage into the transoid-trans coloured isomer (TT), along with a long-lasting thermal stability of the latter, may represent an interesting goal for researchers looking for photoswitchable devices and have been object of investigation in our laboratories [2,3].

In this work, we report the synthesis and an investigation of the photochromic behaviour of some benzopyran derivatives bearing a N-methyl carbazole unit in the molecular structure [4]:

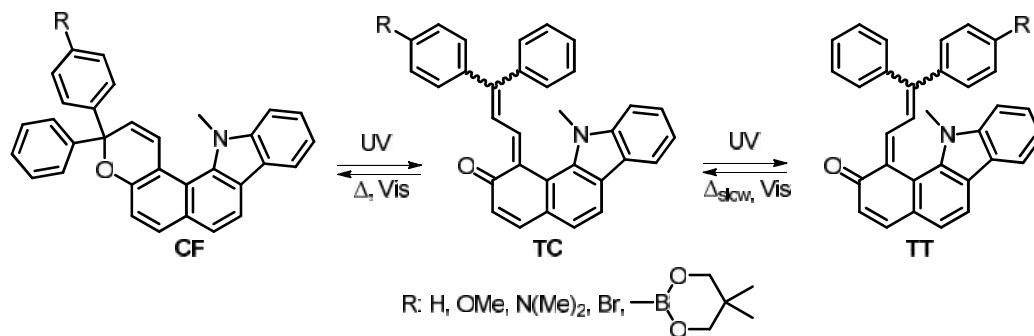


Fig. 1. Simplified photochromic interconversion of N-methyl-carbazole benzopyrans.

The unsubstituted parent molecule (CF) shows a high conversion percentage into the transoid-trans (TT) isomer upon UV irradiation and can be completely bleached back to the starting material by visible light. The stability in the dark of the TT isomer produced upon UV irradiation is remarkably high, and its colouration persists through weeks. Quantitative absorption spectra of both the colourless starting material and the TT coloured isomers have been measured, along with the quantum yields for the UV photocoloration and visible photobleaching processes. The thermal stability of the TT isomer and the photochromism of these benzopyrans can be tuned by the donor strength of the substituent located on the phenyl ring linked to the sp³ carbon atom of the pyran ring.

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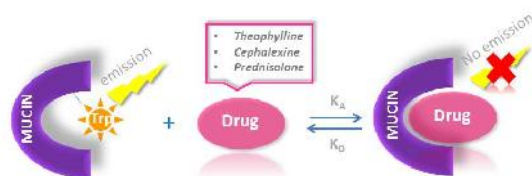
Mucin–drugs interaction: The case of theophylline, prednisolone and cephalexin

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Cystic fibrosis is characterized by progressive airway obstruction; in physiological conditions, the airways are protected by a layer of mucus, mainly composed of water, ions, lipids, and approximately 2% of protein: the protein mainly expressed is mucin, a large extracellular glycoprotein with an high molecular weight (0.5 and 20 MDa). The protein core, making up the 20% of the molecular mass, is characterized by a central glycosylated region, composed of a large number of tandem repeats that are rich in serine, threonine and proline, that linked many carbohydrates primarily N-acetylgalactosamine, N-acetylglucosamine, fucose, galactose, and sialic acid (N-acetylneuraminic acid) and traces of mannose and sulfate, and a second region



located at the amino and carboxy terminals, with an amino acid composition more representative of globular proteins, relatively little O-glycosylation and a few N-glycosylation sites [4] and a high proportion of cysteine (>10%)¹. Mucins are involved in many pathological processes: pre-neoplastic and neoplastic lesions of gastrointestinal tract and

respiratory tract. They are overexpressed and ipoglycosilated and for this reason, in recent years, they have been identified as important prognosis markers and as many important therapeutic targets. Qualitative and quantitative abnormalities of mucins also characterize the pathogenesis of chronic diseases such as asthma, BPCO and cystic fibrosis. The primary defect in cystic fibrosis is caused by abnormal function of epithelial chloride channel protein encoded by the transmembrane conductance regulator in cystic fibrosis (CFTR), whose gene is located on chromosome 7q31.2. This defect leads to the inability of a normal secretion of Cl⁻ in the mucus, causing the formation of thick secretions and difficult to remove, that can cause a high risk of bacterial infections. Therefore, the thickness and the composition of the layer of mucus may prevent the crossing of the drugs and the drug interacts with the therapeutic target. The binding of mucin with three commercially available drugs (theophylline, cephalexin and prednisolone) belonging to different pharmaceutical classes was investigated. The studied drugs are normally used to treat the symptomatology of cystic fibrosis. The binding has been studied by spectroscopic approaches, as UV-Vis and fluorescence, to obtain thermodynamic constant of dissociation (K_D) and association (K_A), binding sites and thermodynamic parameters of the drug-protein binding. At last, following the theory of the Energy Transfer Fluorescence Resonance (FRET)² we have been calculated the efficiency of energy transfer and the bond length between gastric mucin and drugs.

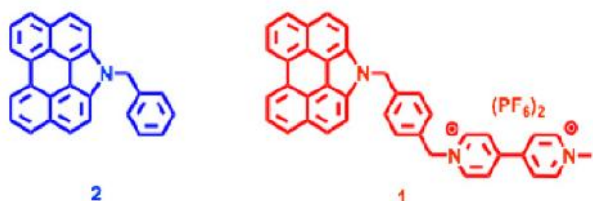
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Energy- and Electron- transfer processes in nanofibers made of *N*-annulated Perylene and MV²⁺ subunits

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Energy and Electron Transfer processes play a crucial role in natural phenomena such as photosynthesis.[1] In the natural photosynthetic unit in plants, carotenoids, acting as antennas, absorb solar radiation in the spectral region and transfer the resulting excitation energy to chlorophyll through singlet–singlet energy transfer.[2] The energy then migrates from one chlorophyll molecule to another, unidirectionally in an array, and ultimately reaches the “special pair” in the reaction center where charge separation occurs. The non covalent approach observed in the nature, has been widely established as a strategy to construct artificial antenna moieties such as self-assembled multiporphyrin systems.[3] In recent years, long-range ordering in well-defined aggregates of *p*-conjugated components has been considered as a new type of light-harvesting antenna. Various approaches have been taken, with dendrimers,[4] mesoporous silica,[5] and porphyrin arrays connected by covalent bonds[6] or by noncovalent selfassembly [7] being used to mimic this natural energy and or electron transfer process.



Recently we reported about the first donor-acceptor species (**1** in Figure) in which a strongly emissive *N*-annulated perylene dye (**2**) have been connected to a methyl- electron acceptor unit via its macrocyclic nitrogen atom, by a stepwise modular procedure.[8] In this species photoinduced oxidative electron transfer from the excited state of the dyad, centered on the *N*-annulated perylene subunit, to the appended methyl viologen electron acceptor takes place in a few ps.

The charge-separated species recombines in 19 ps. Taking advantage of the nature of this species we prepared well-defined aggregates, by mixing the *N*-annulated perylene subunit (**2**) in different ratio with the dyad (**1**). In this work we demonstrate that one appended methyl viologen *N*-Perylene subunits (**1**) it is able to quench up to six strongly emissive **2** species if aggregate in ordered fibers.

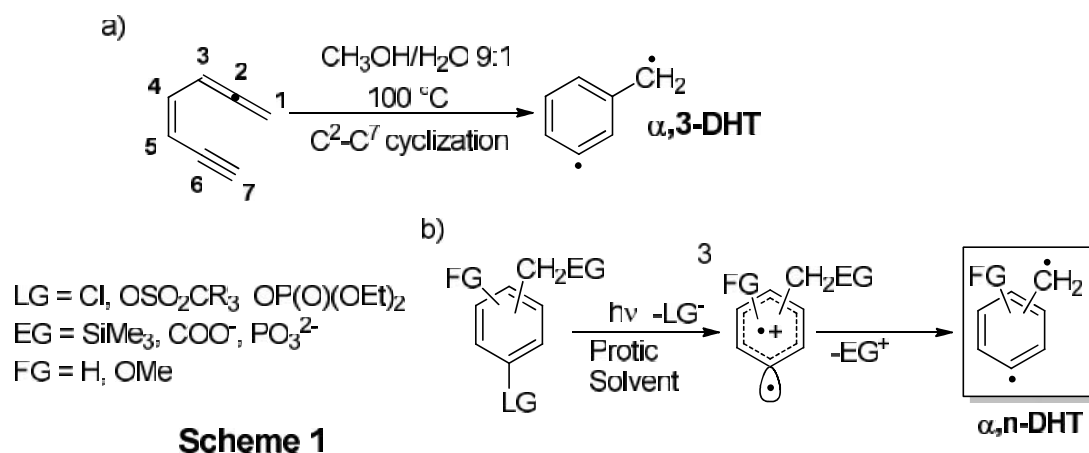
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From aromatics to α,n -didehydrotoluenes: a one-photon journey

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Attention to didehydroaromatic intermediates is growing because of their important role in organic synthesis, [1] theoretical chemistry [2] and biological [3] applications. These biradicals are usually generated from highly unsaturated polyenes, such as enediynes and enyne-allenes. In particular, the latter compounds undergo a C^2-C^7 cyclization (the so called Myers-Saito reaction) upon thermal activation, to afford a $\alpha,3$ -didehydrotoluene ($\alpha,3$ -DHT, the only isomer accessible by this approach; Scheme 1, part a). [4]



Recently, we developed a photochemical route to all of the α,n -DHT isomers ($n = 2-4$) starting from substituted benzyl derivatives. This involves the irradiation of compounds having both a leaving group (LG) on the aromatic ring and an electrofugal group (EG) in benzylic position. Thus, in protic solvents (alcohol or aqueous buffer) the generation of a phenyl cation via one-photon induced heterolytic cleavage of the Aryl-LG bond is followed by loss of EG⁺ (see Scheme 1, part b), to afford the desired α,n -DHT. [5] Several suitable precursors of the desired α,n -DHT have been investigated by means of a combined experimental and computational approach. Some generalizations emerged on the generation and on the chemical reactivity of such biradicals are presented herein.

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Molecular Dynamics simulations of Ru-based dendrimers for light harvesting

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The natural photosynthesis, optimized through millennia of evolution, provides a highly efficient way to store and convert the solar radiation into chemical energy. Due to the increase in global energy demand, the search on artificial photosynthesis has been extremely appealing in the last decades. The solar-powered water oxidation can be exploited for hydrogen generation by direct photocatalytic water splitting.

To mimic the natural photosynthetic systems, a synthetic one, capable of performing artificial photosynthesis, should contain the following basic components: light-harvesting antennae, charge separation units and multielectron transfer catalysts. The design of synthetic catalysts able to efficiently drive light-induced multielectron transfer processes, together with its adequate understanding, is considered one of the most important aspects to achieve.

Recently, it has been shown that decanuclear Ru(II) dendrimers, based on 2,3-bis(2'-pyridyl) pyrazine (dpp) bridging ligands, can be ideal photosensitizers for photoinduced water oxidation. Indeed, they have three advantages: they absorb a good amount of visible light, they have a fast and efficient photoinduced electron transfer, and the oxidized sensitizer has a suitable potential [1].

In the present work, we investigate the structure of the photosensitizer by quantum mechanics calculations and molecular dynamics simulations.

To identify the more stable isomeric structures of these complexes in the experimental conditions, we compared the relative stability of all stereoisomer mixtures. Molecular dynamics calculations reveal the details of the tridimensional structure of the dendrimer aggregates.

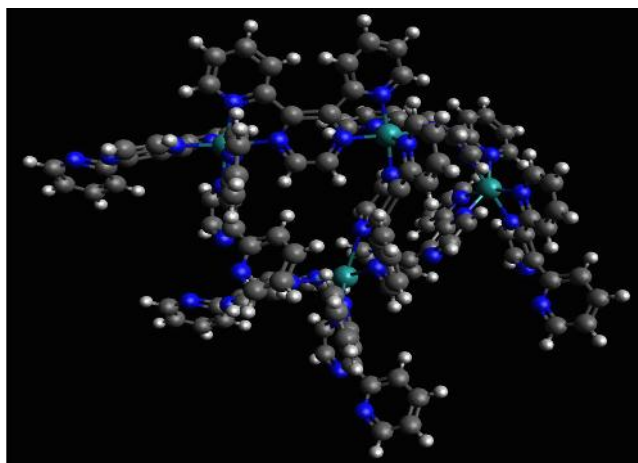


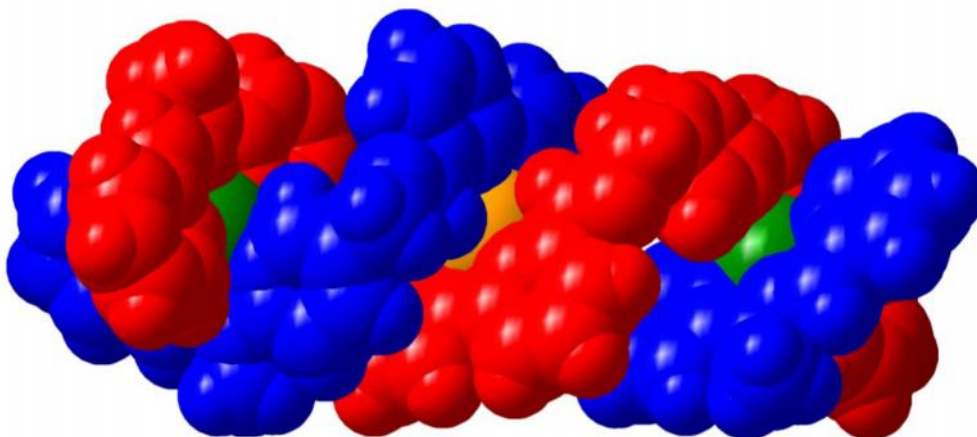
Fig. 1st central portion (4 Ru nuclei) of one decanuclear Ru(II) dendrimer, based on 2,3-bis(2'-pyridyl) pyrazine (dpp) bridging ligands

- [1] F. Puntoniero, A. Sartore, M. Orlandi, G. La Ganga, S. Serronia, M. Bonchio, F. Scandola, and S. Campagna : *Photoinduced water oxidation using dendrimeric Ru(II) complexes as photosensitizers*, Coord. Chem. Rev, Vol 255, November 2011, doi:10.1016/j.ccr.2011.01.026

Self-Assembly of photochemically-active helicate compound

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A helicate can be defined as a discrete helical supramolecular complex, constituted by one or more organic strands, which are wrapped around a series of metal ions. These complexes are known for their possible use as storage information systems and for the possibility of mimicking biological behaviors. It is interesting to incorporate within these systems, suitably modified, photoactive subunits. In particular, we mean to take advantage of the properties of suitable molecular strands in order to self-assemble species capable to lead to photoinduced intramolecular charge separated states.

To achieve this goal we built two ligands, each of them composed by two different moieties, with different behaviors and functions. In one of the two moieties of the ligand, the needed information to allow self-assembly is stored. The other part of the ligand is the photoactive subunit. In this system the photoactive subunit contains a perylene derivative, which will be involved in a photoinduced electron transfer with an appended methyl viologen electron acceptor. Perylene and methyl viologen derivatives are linked to different helicate strands.

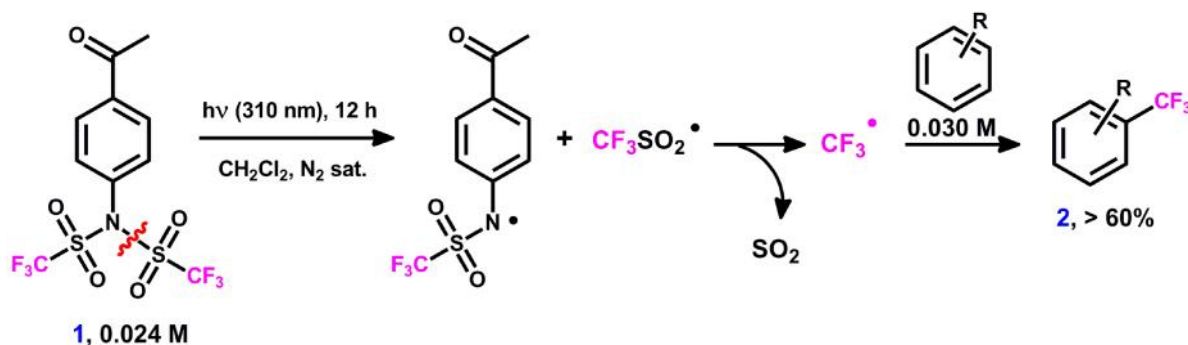
Photochemical trifluoromethylation of aromatics by *N*-aryltrifluoromethanesulfonimides

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Fluorine is a very popular element in lead optimization for drug discovery. Indeed its presence in the structure of drug candidates can improve their metabolic stability, membrane permeability and bioactivity, thus enhancing their pharmacological properties.¹ Noteworthy, among fluorinated drugs, a great number is given by aromatics bearing a trifluoromethyl group (e.g. Fluoxetine, Leflunomide, Nilutamide, etc.). For this reason much efforts are done to find synthetic ways to insert the trifluoromethyl group onto aromatic rings and researchers mainly focus their research on the formation of the Ar-CF₃ bond employing transition metal catalysis.² A greener and more convenient strategy relies on radical trifluoromethylation by photoredox catalysis³ but even in this case expensive catalysts and reagents are usually employed. Herein we present a simple and clean photochemical trifluoromethylation of aromatic compounds using cheap *N*-aryltrifluoromethanesulfonimides as trifluoromethylating reagents.

As an example, *N*-(4-acetylphenyl)-1,1,1-trifluoro-*N*-[(trifluoromethyl)sulfonyl]methanesulfonamide **1** was irradiated (310 nm) in deaerated dichloromethane in the presence of an aromatic compound until total conversion of **1** is reached, giving trifluoromethylated derivative **2**. A reasonable mechanism for the reaction consists of a photoinduced homolysis of a N-S bond of compound **1** to afford a trifluoromethanesulfonyl radical readily prone to release SO₂ thus releasing a trifluoromethyl radical. The latter then reacts with aromatic rings to give eventually compound **2**. Noteworthy, each of the two N-S bond may be sequentially broken during irradiation, thus improving the performance of the trifluoromethylating agent. In selected cases, the reaction can be likewise repeated with similar results by using sunlight irradiation of **1**. This feature can open the way for green “window-ledge” trifluoromethylations based on the presented strategy.



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2. O. A. Tomashenko, V. V. Grushin, *Chem. Rev.*, **2011**, *111*, 4475-4521.
3. S. Barata-Vallejo, S. M. Bonesi, A. Postigo, *Org. Biomol. Chem.*, **2015**, *13*, 11153-11183.

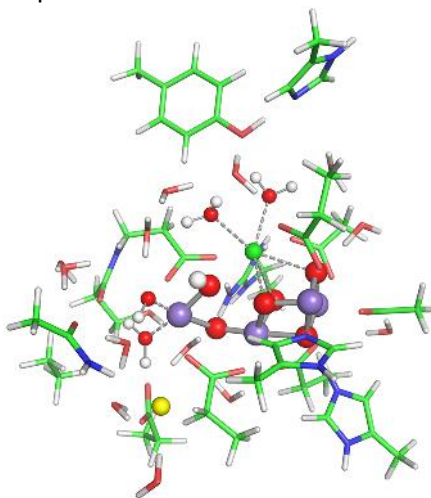
Vibrational spectroscopic study of intermediate states along the S₂ to S₃ transition of the Kok-Joliot's cycle

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A crucial step in the mechanism for oxygen evolution in the Photosystem II complex resides in the transition from the S₂ to the S₃ state of the Kok-Joliot's cycle. Using QM/MM dynamics and gas phase models we have built a comprehensive pathways of intermediate steps which involves interconversions between open and closed cubane isomers and the binding of a water molecule to Mn₄, upon its oxidation.



In order to better interpret the experimental infrared data available for S₂ and S₃ states we have extracted from QM/MM dynamics vibrational properties through dipole-dipole autocorrelation function and vibrational density of states.

Our results allowed us to assign specific vibrational bands to molecular motions in different regions of the catalytic pocket and in different parts of the vibrational spectra.

In particular to help the interpretation of the computational and experimental data in the COO stretching frequency region (1300-1700 cm⁻¹), we perform vibrational analysis of the Tyr and Asp amino acids in the gas phase to use these data as reference frequencies for further band shift interpretation.

The spectral signatures arising by this analysis can be easier interpreted to assign experimentally known bands to specific molecular motions.

1. Oxygen-evolving complex; Photosystem II; Water oxidation; S-state cycle; Vibrational spectroscopy; NMA; FTIR.

Autofluorescence spectro-endomicroscopy of alveoli: comparative spectral analysis of healthy smoker volunteers and amiodarone-induced pneumonitis patients

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Using autofluorescence (AF) endomicroscopy with spectroscopic analysis capability, we showed in previous studies^{1,2} that, under 488 nm excitation, the technique images the elastin network of the proximal and distal respiratory system. Due to tobacco tar fluorescence, the method also allows to image alveolar macrophages in healthy smokers. Amiodarone is an anti-arrhythmic agent, the most severe side effect of which is pulmonary toxicity³, referred as amiodarone-induced pneumonitis (AIP). Spectro-endomicroscopy was performed in amiodarone treated non-smoker patients (ATNS) suffering from AIP and healthy smokers (HS). Alveolar fluorescent cellular infiltration is observed in both patient groups with similar images. Our objective was to assess the possibility for discriminating these two groups by an analysis of their alveoli fluorescence emission spectra.

The spectro-endomicroscope, based on the technology developed by Mauna Kea Technologies (Paris, France), allows real time simultaneous recording of the spectrum and the microscopic images of the observed field of view (600 μm) under 488nm excitation. Reference spectra of elastin powder from human lung, flavins (FAD) in bidistilled water and tobacco tar from smoked cigarette filter-tips were acquired with the instrument under the same experimental conditions as those used for endoscopic measurements. The subjects included in this study were selected from the cohort enrolled in the ALVEOLE controlled clinical trial (gov.identifier: NCT00213603): seven ATNS patients (41 spectra) and five HS volunteers (21 spectra). Data acquisition was performed during conventional white-light endoscopy according to a protocol described in reference 2. Each normalized spectrum was modeled as a linear combination of several components: cellular flavins (FAD) and another cellular component, namely lipopigments, modelled by a Voigt profile, extracellular matrix (ECM) elastin and tobacco tar; HbO₂ absorption was also taken into account. Besides the FAD and elastin contributions, the addition of a tobacco tar component is necessary to account for HS group spectral shape.

As expected, the results of this fitting procedure show the presence of elastin and FAD in both groups: elastin is a major component of the distal lung interstitial network, present in the axial backbone of the alveolar ducts and alveolar entrances and FAD coenzymes, related to cell metabolism, are present in all cell types. Regarding the HS group, the major component of the global modeled spectrum corresponds to the smoked cigarette filter-tip spectral contribution originating from macrophages containing highly fluorescent tobacco tar; the relative contribution of elastin is weak compared to the highly fluorescent cell contribution. For the ATNS group, tobacco tar contribution is found to be zero, while the Voigt-shape spectrum component attributed to lipopigments is specific to this group. This spectral analysis suggests a different origin of the cellular fluorescent signal in ATNS patients compared to smokers and allows to clearly differentiate between similar cellular infiltrated images from these two groups.

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[2] Thiberville L, *et al.*. "Human in vivo fluorescence microimaging of the alveolar ducts and sacs during bronchoscopy" Eur. Respir. J. 33, 974-985 (2009).

[3] Rakita L., Sobol S., Mostow N. and Vrobel T. "Amiodarone pulmonary toxicity" Am. Heart. J. 106, 906-916 (1983).

Polycarboxylic Acid-Cyclodextrin/Porphyrin Finished Fabrics as Photosensitiser Releasers for Photodynamic Antimicrobial Therapy

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Nowadays, since the developing of multidrug-resistant bacteria, due to the overstated use of antibiotics, research effort is focused on new antibacterial therapeutic approaches. Photodynamic antimicrobial therapy (PAT) is a well-known alternative way to treat local infection caused by different microorganisms such as Gram (+) and Gram (-) bacteria, viruses, fungi and protozoa.¹ PAT plays a crucial role in the treatment of surface wounds, burns, abscesses, oral sites and the middle ear infections. Native and hydroxypropylated cyclodextrins (HP β -CD) have been successfully fixed to textiles based on natural and synthetic fibers by using polycarboxylic acids (PCA) as crosslinking agents.² The concept is based on reversible host-guest complexation of different typology of drug molecules in the cavities of CDs immobilized on the graft, followed by its sustained and controlled delivery in release medium. A relevant advantage of this concept is its versatility, as it is compatible with a wide range of antibiotics offering good potential for PAT. Here we present a polypropylene (Poly) fabric finished with citrate-hydroxypropyl- β -CD polymer (CTR-CD) entrapping the tetraanionic 5,10,15,20-tetrakis(4-sulfonatophenyl)-21H,23H-porphine (TPPS) as photosensitizer. To the best of our knowledge, this CD/TPPS finished fabric represents a novel eluting device to efficiently deliver TPPS to bacterial cells, which can be photo-inactivated upon irradiation. Morphology of fabric was characterized by optical (OM) and scanning electron microscopy (SEM). Optical properties were investigated by UV-vis absorption, and steady- and time-resolved fluorescence emission spectroscopy. XPS and FT-IR revealed the chemical composition and the distribution map of the molecular components on the fabric, respectively. Direct ¹O₂ determination allowed evaluating the potential photodynamic activity of fabric. Release kinetics of TPPS in PBS (pH=7.4) pointed out to the role of the CD cavity to control the charge elution from fabric. Transfer of TPPS from PolyCTR-CD/TPPS to colonies of Gram (+) *S. aureus* ATCC 29213 was carried out and the presence of TPPS in the bacterial cells was confirmed by UV-Vis extinction and fluorescence emission spectra. Finally, photodynamic antimicrobial properties were assessed upon transfer on the colonies and following irradiation.

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