This research program aims at the development of integrated photocatalytic micro-structured devices for the continuous synthesis of high value-added organic molecules, such as active pharmaceutical ingredients, through the efficient in situ generation and handling of singlet oxygen. The conception of such devices implies a multidisciplinary expertise in (a) design and preparation of photocatalytic porphyrin-metal nanoparticle couples, (b) coating techniques, (c) photocatalytic transformations, and (d) design of micro-scale continuous organic processes.

1. **Background and philosophy of the project**

   Continuous-flow micro- and mesostructured reactors (MRs) offer a wide range of advantages for performing organic transformations: fine control of the reaction conditions, inherent safety and homogeneity of the production. They also enable faster, cleaner and intensified organic transformations. Another important aspect of MR technology is the acceleration of the transfer between R&D (optimization on microscale) and production (scaling-out or numbering-up). Their small footprint reduces operating costs and enables mobile chemical facilities. Due to these intrinsic properties, MRs have been proven to drastically improve process efficiency while handling unstable or rapidly decaying molecules.

   Singlet oxygen ($^{1}O_{2}$) is a short-lived excited species with a high intrinsic reactivity and has a broad range of applications ranging from the detoxification of industrial effluents to the manufacturing of valuable organic molecules. High $^{1}O_{2}$ concentration is required to ensure high oxygenation rates. Although there are many ways to produce $^{1}O_{2}$, a simple, controllable and energetically convenient method consists of photo-induced electronic energy transfer from an excited state of a catalytic photosensitizer (PS) to ground state triplet oxygen ($^{3}O_{2}$). Typically, $^{1}O_{2}$ is generated from light (LEDs, lasers or sunlight) and air or oxygen in the presence of a PS such as porphyrins. However, the industrial application of photocatalytic transformations is often hampered by low light penetration in large batch reactors, resulting in poor selectivity and low reaction rates. Moreover, common strategies for the generation of $^{1}O_{2}$ employ homogeneous photosensitizers that remain dissolved in the crude effluent, therefore requiring extensive purifications. By contrast, the use of MRs with internal walls coated with photosensitizers would suppress both the poor light penetration encountered in large reactors as well as the contamination of the final product.

   A number of physicochemical properties are required for a PS to be efficient for $^{1}O_{2}$ production: (a) high absorption coefficient in the spectral region of the exciting light; (b) an excited state of appropriate energy; (c) high quantum yield (> 0.4) and lifetime (> 1 μs); and (d) high photo-stability. Among PSs that satisfy these properties, porphyrins have drawn attention because of their ability to absorb several wavelengths in the UV-vis spectrum. Moreover, the immobilization of PSs on the internal walls of a MR would avoid deactivation issues as often encountered when used as homogeneous catalysts.

   A promising way to ensure high $^{1}O_{2}$ concentration consists in combining the PS with noble metal nanoparticles (NPs, e.g. silver or gold) that exhibit a strong localized surface plasmon resonance (LSPR) under light illumination. The excited NPs plasmon enhances the electromagnetic field surrounding the PS, thus increasing its electronic population in the excited...
state and enhancing PS fluorescence emission and/or the PS triplet state (3PS) quantum yield. In an oxygen-saturated environment, the increased 3PS yield is expected to go with an increase in 1O2 concentration. These LSPR processes and their efficiency are known to be dependent on several important parameters. Among others, (a) the NPs size, (b) the PS-NPs spacing distance, (c) the intrinsic PS nature, (d) the PS orientation and (e) the nature of the PS-NP linkage are the most notorious.

2. Objectives
This project aims at the development of integrated MRs containing immobilized sensitizers for the generation, handling and use of high concentrations of singlet oxygen in a convenient, highly efficient and up-scalable way with a view to develop large scale oxygenation processes. The narrow reaction channels in MRs will be coated with a thin film containing PS-NP couples. Such a design will allow complete light penetration in the reaction medium. Due to the very large surface-to-volume ratio which ensures excellent contact between supported PS-NP photocatalysts and the oxygen inside the micro-channels, the production of singlet oxygen will be maximized, resulting in high oxygenation rates of the substrate. Moreover, the continuous mode will suppress overexposure and photodecomposition of the substrates and/or the oxygenation products. The development of such microstructured photocatalytic reactors could therefore offer a solution for large-scale photocatalytic oxygenation reactions for numerous applications.

3. Strategy
To achieve the general objectives of the project, the research program has been divided into the three following work packages (WPs):

- **WP1 - Development and optimization of efficient PS-NP couples for the photoinduced production of 1O2**
This work package involves the development of new porphyrin-based PSs, their coupling with metallic nanoparticles and the study of the resulting LSPR. A library of porphyrin-metal NP (Ag and Au) couples will be synthesized and characterized in order to quantify their ability to generate 1O2 from air under visible light irradiation. To stabilize the porphyrin and allow the further production of a coating in WP2, a sol-gel method will be used to anchor the porphyrin on the surface of an oxide matrix (e.g. SiO2, ZrO2, Al2O3 or TiO2) that will encapsulate the metal NPs. Various critical parameters will be investigated in order to optimize the production of 1O2, such as (a) the nature of the porphyrin, of the supporting oxide and of the metal NPs, (b) the size of NPs, (c) the porphyrin-NP distance, and (d) the orientation of the porphyrin on its support.

- **WP2 - Coating of PS-NP couples on various materials**
The system composed of porphyrin, oxide matrix and nanoparticles developed in WP1 will be coated on different supports that are commonly used for machining MRs (glass, fused silica, perfluorinated polymers and various metals). Two strategies will be tested: (a) a two-step method consisting in depositing the encapsulated NPs first and then grafting the porphyrin on the oxide surface; (b) a one-step method consisting in the direct deposition of the porphyrin-oxide-NP. Several coating technologies will be investigated such as (a) dip-coating, (b) spray-coating, and (c) electrodeposition. The resulting coated materials will be used to carry out the 1O2 oxygenation of α-terpinene as a model reaction and to quantify the production efficiency of 1O2 in a pseudo-continuous setup.
WP3 - Design and development of a continuous-flow photo microreactor

A photocatalytic MR will be developed from the results gathered in WPs 1&2, and tested with model reactions (e.g. the $^{1}O_2$ oxygenation of $\alpha$-terpinene). The MR will be machined using standard microfabrication techniques by an external specialist, using a standard design. The photocatalytic coating will be achieved either by dip- or spray-coating or electrodeposition on the MR internal walls. Regarding the photochemical process, the operating parameters, such as the nature of the light source, the flow rate, the irradiation time and the source of oxygen, will be optimized. The kinetics will be modelled in order to validate the concept (high kinetic constants) and to derive a kinetic equation for upscaling purposes.

A summary of the strategy is presented in Figure 1. The project regroups three research teams, CiTOS, NCE and GRASP-Biophotonics, with complementary areas of expertise in continuous-flow organic synthesis, the design of nanostructured catalysts and the study of the interactions of molecules and nanostructures with light. It aims at combining these areas of expertise to (a) develop highly efficient porphyrin photosensitizer - metallic nanoparticle couples for a maximized generation of $^{1}O_2$, (b) implement coating techniques to produce active thin films containing photosensitizers on specific microstructured surfaces and (c) develop continuous-flow synthetic oxygenation routes towards industrially relevant molecules. Besides, this research proposal will trigger a long term, multidisciplinary collaboration between the partners.

![Figure 1](image1.png)

**Figure 1.** Flow philosophy and complementarity of the various teams.

4. References

6. Some of these parameters have been briefly addressed during M. Lismont’s PhD thesis in the GRASP-Biophotonics Laboratory. The preliminary results will be important starting points for the project.
7. C. A Páez, D. Liquet, C. Calberg, D. Eskenazi, J.-P. Pirard, B. Heinrichs, WO2013171297; BE2012000326 A.