Based at ULiège, the Center for Integrated Technology and Organic Synthesis (CiTOS) and the FloW4all platform (Flow Technology Resource Center) combine fundamental academic research with services for industry. Their specialty: performing organic synthesis using continuous flow reactors.

It all began in 2013 with the creation of CiTOS by Prof. Jean-Christophe M. Monbaliu. On his return from the United States, he was determined to develop his own research using micro- and mesofluidic reactors to enable new chemical transformations. In less than ten years, the laboratory has acquired an international reputation and has brought together a team of 25 researchers.



© CiTOS - FloW4all's team, from the left to the right: Dr. Diana Silva-Brenes, Platform Manager; Prof. Dr. Jean-Christophe Monbaliu, Platform Director; Mrs. Elyse Macors, Platform Chemist



© CiTOS - Lithiation platform at pilot scale © Courtesy of Corning

The research performed at CiTOS has resulted in new methods for the efficient, safe, cost-effective, and versatile production of high value-added organic compounds. The use of bio-sourced starting materials plays an important role in many of the projects. For example, procedures to use CO2 and glycerol, both of which are industrial waste products, to prepare green solvents or fuel additives have been developed. Another project, funded by the US FDA, aims to manufacture medicines produced entirely from biosourced materials (i.e., derived from biomass) using a small, flow production unit.

The laboratory favors quantum chemistry and artificial intelligence approaches to accelerate the development of new micro and mesofluidic processes, while reducing the waste associated to trial-and-error optimisation. The use of computer simulation tools to suggest optimal conditions for new reactions is a trademark of the research developed in

the group.

From research to industrial application

Since its inception, CiTOS has aspired to conduct fundamental research with extremely practical applications, therefore placing a strong importance on the scalability and potential industrialization of its results. Two milestones have contributed to make this aspiration a reality.

The Corning partnership

First, in 2017, CiTOS became the first European Corning Qualified Laboratory, associating itself with one of the most important manufacturers of micro- and mesofluidic reactors for industrial applications. This partnership reinforced the laboratory’s access to industrial equipment and strengthened its range of services for industry.

The FloW4all platform

Secondly, in 2022, the FloW4all Resource Centre was established, made possible by funding from the Walloon Region (Belgium). The FloW4all platform specializes in the use of fluidic reactors to solve challenges in the field of industrial chemical synthesis, integrating the fundamental research knowledge developed at CiTOS with practical knowledge of the industrial sector. The platform relies on dedicated personnel, highly qualified in continuous flow reactors and pilot-scale equipment.

FloW4all has a large inventory of chemical synthesis and flow chemistry equipment to address a large variety of applications. Not only does the platform continue to provide services as a Corning Qualified Laboratory, but it also includes reactors from other leaders in industrial flow equipment. Another major advantage is the presence of dedicated in-house analytical facilities, including both in-line and offline equipment, which allows to immediately assess results.



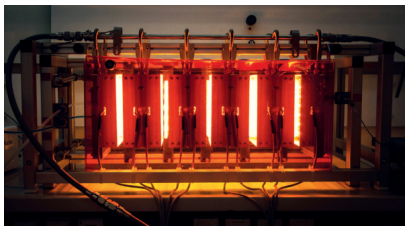
© CiTOS - CiTOS-FloW4all’s analytical platform

Its wide variety of equipment makes FloW4all an excellent partner to develop processes under continuous flow from lab scale up to pilot scale conditions. Partnerships with the most important manufacturers of industrial flow reactors expedite the transposition of the processes to industrial scale. In addition, the platform benefits from several licences from the Federal Medicines Agency, enabling it to legally produce psychoactive pharmaceutical compounds, hormonal compounds, and narcotics precursor compounds.

Training, collaboration, and future perspectives

FloW4all is active in flow chemistry training, providing both theoretical and practical sessions on the use of flow chemistry. This training has enabled various companies to initiate their own explorations of flow chemistry. However, most of the activities of the platform focus on the development of protocols for chemical synthesis under flow conditions. Over the past 7 years, around twenty industrial collaborations have been established. Examples of projects include being part of the development of the contraceptive active ingredient estetrol (E4). The collaboration resulted in a new continuous flow protocol for the preparation of a critical intermediate as a cost-reducing alternative to the original methodology.

For another partner working in the field of polymers and catalysts, the goal is to increase the efficiency of the catalyst preparation, as well as on-demand customization of the product. Another important collaboration involving an American company aimed at developing high value-added molecules derived from glycerol.



© CiTOS - Pilot photoreactor for singlet oxygen oxidations © Courtesy of Corning

The exploration of flow reactors for industrial applications is of particular interest when promoting the repatriation of production facilities to Europe. The advantage of continuous reactors in terms of safety and environmental friendliness may provide a way to re-design chemical processes to make them compatible with current European regulations. Perhaps the most pressing challenge remaining, however, lies in raising awareness of the potential of flow chemistry. Chemical manufacturers and reglementary

agencies benefit from familiarity with this new field to accelerate the widespread incorporation of flow reactors in chemical processes.

With the support of collaborations and partnerships, and through ongoing research efforts, CiTOS and FloW4all ultimately aim to support this goal and make the advantages of flow chemistry available to the chemical manufacturing world.



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