# PIPAc

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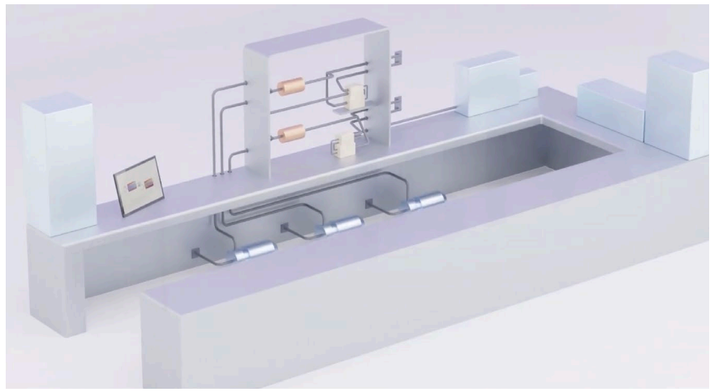


*Autonomous factory powered by AI and flow chemistry*

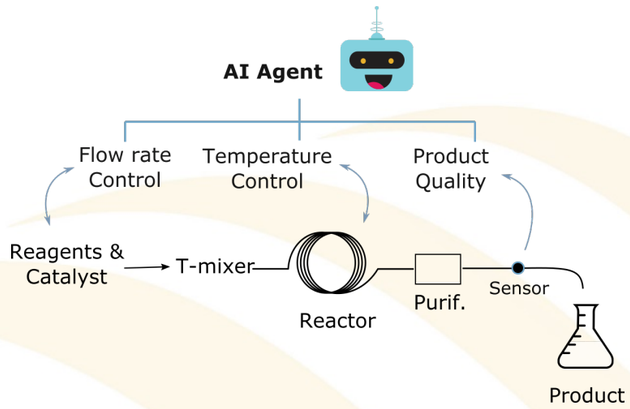
**PIPAc (*Production Intelligente de Principes Actifs*)** will bring the first AI-powered autonomous industrial demonstrator for active pharmaceutical ingredients (APIs) manufacturing. The outcome is high-quality API production, safer by design. The innovation relies on several key ingredients: continuous flow chemistry, artificial intelligence, and additive manufacturing.

In *flow chemistry*, chemical reactions are performed in a continuous flow, rather than in batch mode. This allows for better control and optimization of the reaction conditions, leading to **higher yields** and better product **purity**. Continuous flow chemistry approach can also reduce the amount of produced waste and reduce energy use. A small amount of any intermediate reaction products guarantees a **safer process** at all times. Additionally, this approach is easier and faster to scale-up, **reducing time to market**, and is compact. Therefore, it allows for mobile production on-demand, which is highly relevant for this application.

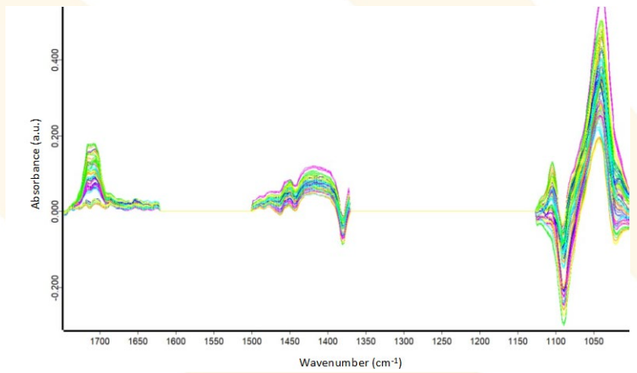
*Artificial intelligence* (AI) takes the advantages of flow chemistry one step further by adapting synthesis parameters in real-time to an ever-changing environment. For example, the flow rate is adapted to any fluctuations of the reactor temperature to guarantee the **best yield**. Available 24/7, AI will **reduce operator's stress** and thus reduce the risk of making a mistake. Another feature enabled by AI will be **predictive maintenance** of the installation.

Finally, *additive manufacturing* (3D printing) is changing the way we design the process. We manufacture chemical reactors tailored specifically to the reaction. By using customized design and materials, we improve mixing properties, heat transfer, chemical resistance, and other characteristics. This enhances **reaction performance**, while further reducing **energy** consumption.

## Real-Time In-Flow Reaction Monitoring



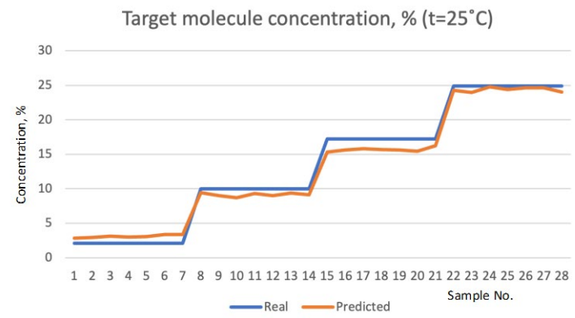

Autonomously piloted systems require a sensing apparatus for the state estimation. Our goal is to analyze data captured in real-time to distinguish and quantify reaction products directly in-flow. This is essential for reaction monitoring and control. Spectroscopy methods for chemical products detection are attractive because of their relatively low cost and ease of use.




*Preprocessed IR spectral data are analysed to determine the progress of the reaction*

Infrared (IR) spectroscopy is a valuable technique for real-time in-line reaction monitoring, providing a fast and non-invasive method for analyzing chemical reactions. By measuring the absorption of IR light by a sample, it is possible to determine the unique "fingerprint" of a chemical compound and identify its presence and concentration in a mixture. This allows for continuous monitoring of reactions, enabling better control and optimization of the process.

First, a calibration procedure is performed on known synthetic mixtures of reactants and reaction products. Those mixtures are then measured in-flow by IR spectroscopy. The IR data are then preprocessed to determine spectral regions containing the most relevant information. Finally, a model is built to estimate target molecule concentration. This model is then validated in the lab using previously unknown mixtures as seen below. The target molecule concentration estimate will be used by the AI agent to autonomously pilot the reaction.




*Analyzed spectral data provide an estimate for target molecule concentrations*

A key advantage of using IR for in-line reaction monitoring is its ability to provide fast results. Because the technique is non-invasive and does not require contact with the sample, it is used to monitor reactions in real-time without disrupting the process. In addition, IR spectroscopy can be used to analyze a wide range of compounds, including both organic and inorganic substances.

## Perspectives

Real-time in-flow reaction monitoring is a technique that allows us to monitor chemical reactions as they occur, in real-time. This allows us to control the reaction more accurately and effectively, by using an AI agent to adjust the reaction conditions on-the-fly. By doing this, we can optimize the reaction to produce the desired outcome more efficiently and with fewer waste products. This is particularly useful for reactions that are difficult to control or that require precise conditions to be successful. In addition, we are planning to integrate an NMR instrument for reaction monitoring. The NMR technique will give us more structural information and the capacity to quantify without the need to have references standards.

In our demonstration, we will show how the AI agent can be used to pilot a continuous flow process, adjusting the reaction conditions (such as flow rate) in real-time to achieve the best possible outcome. These lab-scale demonstrations will open the door towards the first industrial chemical production demonstrator autonomously piloted by AI.

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