Press Release

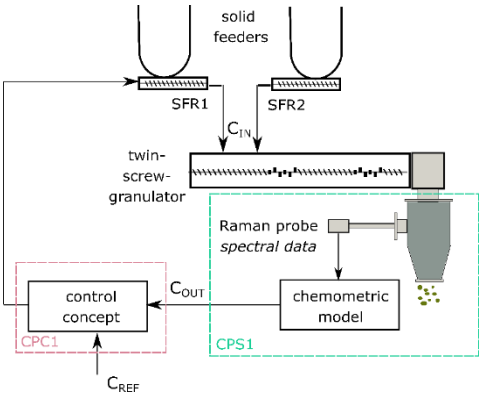
April 2022

CAPRI Cognitive Sensor and Control Concept for Blend Uniformity

Hardly any other industry is currently undergoing such significant changes as the pharmaceutical industry, as digital transformation has merely begun to disrupt and change the way we manufacture medicines. Often considered notoriously slow and somewhat impervious to change, regulatory authorities and pharmaceutical companies have recently started to embrace the possibilities that digitalisation and increased connectivity offer. Strategically leveraging new (analytical) technologies and innovative approaches in manufacturing, such as digital twins, machine learning algorithms and modern sensors shorten product development cycles, automate labour-intensive tasks to decrease overheads and reduce the potential of human error significantly. Therefore, understanding the impact and successful deployment of these novel techniques in compliance with strict regulations is essential to respond to accelerated market dynamics, ensure patient safety, and improve drug production sustainability.

The Research Center Pharmaceutical Engineering (RCPE) within CAPRI develops cognitive sensors and control concepts for continuous pharmaceutical production settings in close collaboration with fellow partners. As most process analytical technologies (PAT) have been developed for traditional batch processing, the use in more modern continuous manufacturing routes requires modifications and newly developed solutions. All testing and experimental validations are performed with RCPE's ConsiGma™ CTL 25 (GEA), one of the industry's most frequently used continuous tableting lines. Prototypes can be evaluated under conditions that closely resemble industrial reality, and these learnings can be used to avoid costly trial-and-error engineering.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 870062.



The therapeutic effect of any medicine depends on the targeted delivery of an active pharmaceutical ingredient (API). Therefore, the concentration of an API within any drug product is considered a critical quality attribute that ensures efficacy. Developing a cognitive control concept that monitors and automatically modifies the manufacturing conditions based on sensor data in real-time has been the focal point of our project work (Figure 1).

Figure 1: Two-step approach combining a cognitive sensor for API concentration measurement (CPS1) and cognitive control concept (CPC1) applied to a ConsiGmaTM-25 production plant.

Raman Spectroscopy is a standard technique used for quantifying the API concentration after twin-screw granulation (TSG), particularly suitable for low API concentrations due to its high sensitivity. To implement existing PAT solutions, such as the Kaiser Optical Systems RamanRxn2™ Hybrid, we have developed a sampling device that automatically draws representative samples from the product stream and allows in-line monitoring of the API concentration in real-time. The 3D-printed prototype consists of a rotating chamber of two cups, periodically presenting a fixed amount of material to the sensor, while excluding the interference effect with e.g. ambient light (Figure 2).

Figure 2: CPS1 - mechanical interface with 3D-printed prototype.

The sample holder is rotated 180° by an electric drive, emptying one cup while simultaneously filling the other. During rotation, a sealing lip cleans the probe window of residual granules to prevent fouling. Additionally, a pneumatic cleaning mechanism removes granules from the 3D-printed sample chamber. A stainless-steel cylinder was constructed with an opening on the side to insert the system, easy to clean, and with Tri-clamp flanges attached and ready to be placed on the ConsiGma TM-CTL 25 TSG outlet.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 870062.

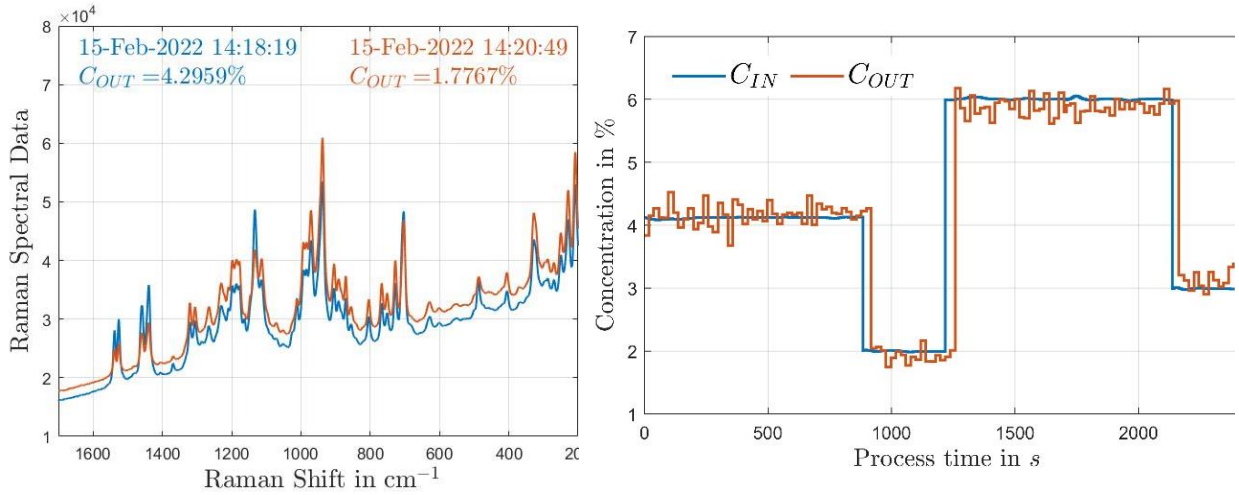


Figure 3: CPS1 is used to continuously monitor API concentration: A chemometric model converts the Raman spectra to the API concentration (left). A good agreement between the known inlet concentration and via the CPS1 estimated outlet API concentration is achieved (right).

We have developed a chemometric model based on principal component analysis to extract the API outlet concentration from Raman spectral data. The data required for model identification purposes have been collected via pilot-plant experiments involving stepwise variations of solid feed rates (SFR), resulting in variations of API concentration at the TSG inlet. The quality of the developed model has been validated on the new set of data.

The cognitive sensor is embedded in the line's control concept in the final step. As the sampling device and Raman system exchange information over the industry-standard OPC-UA, maximum compatibility is assured. The implemented chemometric prediction engine converts the Raman spectral data to the API outlet concentration (Figure 3). This real-time information is fed to a feedback control concept. The control concept keeps the API concentration close to its reference value by adjusting the TSG inlet concentration via SFR changes. In such a way, the effect of material- and equipment disturbances can be compensated. Furthermore, the CPS1 information can be used to discard out-of-specification material based on reliable knowledge of API concentration.

The introduced two-step approach combining cognitive sensor and control concept ultimately improves product quality and reduces waste material.

About the project

Project Full Name: **C**ognitive **A**utomation Platform for European **PR**ocess **I**ndustry digital transformation

Project ID: 870062

Start Date: 01/04/2020

CAPRI (www.capri-project.com) is a 42-month H2020 project that brings cognitive solutions to the Process Industry by developing, testing, and experimenting an innovative Cognitive Automation Platform (CAP) towards the Digital Transformation. To achieve that, CAPRI enables cognitive tools that provide existing process industries flexibility of operation, improving the performance across different indicators (KPIs) and state of the art quality control of its products and intermediate flows.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 870062.

Three main technical objectives enabled by the development, testing and experimentation of an innovative Cognitive Automation Platform (CAP) for three use cases from process industry (asphalt, pharmaceutical tablets and steel billets and bars manufacturing), are being pursued:

- **Process Industry Digital Transformation & Automation** through digital technologies like data collection, storage, and knowledge extraction to provide detailed insights into process control and resource availability.
- **Improved performance and flexibility in the process industry** via digitalisation of process industries to dramatically accelerate change in resource management, improve their performance and flexibility and in the design and the deployment of disruptive new business models.
- **Next generation process industry plans** for their autonomous operation of plants based on embedded cognitive reasoning, while relying on high-level supervisory control as well as providing support for optimised human-driven decision-making.

Follow us

For additional information please contact

Project Coordinator: CARTIF
Cristina Vega Martínez criveg@cartif.es

Dissemination & Exploitation Manager: Core-Innovation
Nikos Kyriakoulis nkyriakoulis@core-innovation.com

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 870062.