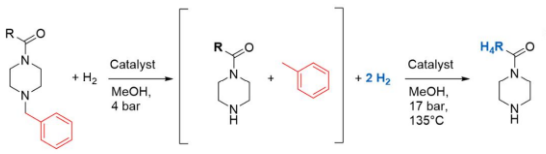
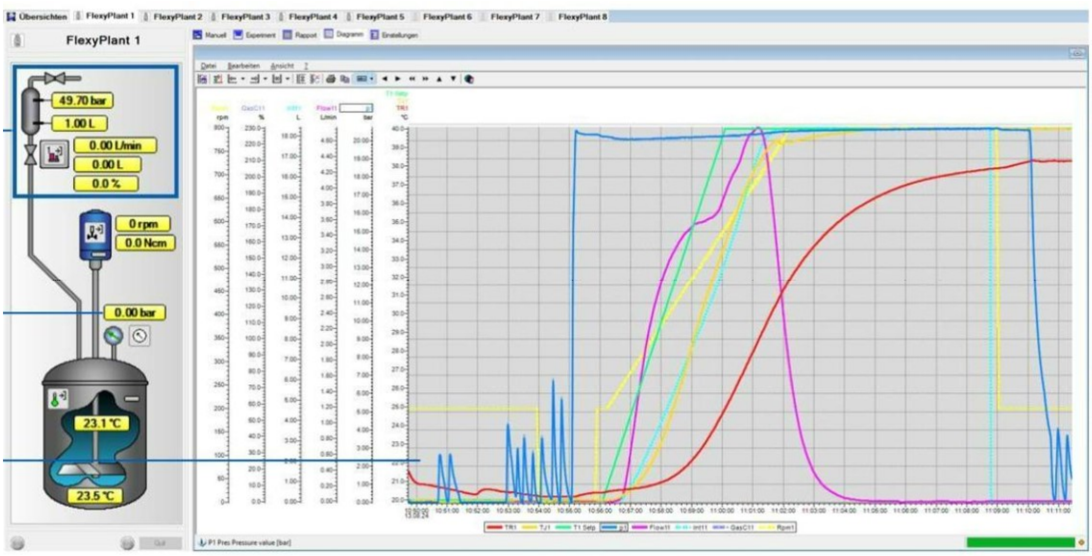
Application note

Fast and precise investigation of high-pressure reactions using SYSTAG's FlexySys



FlexySys

FlexySys is a powerful tool to manage multiple reactors in the process research and development lab. Together with the specialists of DOTTIKON, SYSTAG enlarged FlexySys to the field of high-pressure chemistry. FlexySys enables to program and control reaction parameters. Reproducibility and increased productivity are further value-added parameters thanks to the integrated recipe control. The reaction can be followed online by data analysis, allowing the user to get a deep insight into the high-pressure chemistry.



Introduction

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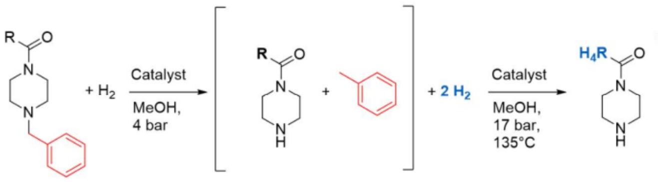
High-pressure reactions (mainly catalytic hydrogenations) are of undeniable interest in the chemical industry. A deep know-how in this chemistry improves the manufacture of e.g. APIs, commodities, and performance chemicals. Profound knowledge of the reaction conditions is therefore mandatory to deliver a robust and safe high-pressure process.

The following example shows the advantage of a SYSTAG FlexySys data acquisition and analysis tool:



Pic 1: Reaction formula

The reaction runs in two steps, whereas the first (debenzylation) can be run under mild conditions (low temperature, low pressure). The second step needs a higher temperature and pressure to be applied. Hence, 4 bar were decided for the first reaction step, while 17 bar and IT = 135°C for the second one was designed. As the same catalyst can be used for both reactions, the development goal was to run both steps in a telescoped way in the same autoclave. However, the reaction always failed due to incomplete overall conversion.

Pic 2: Parallel Pressure Reactor

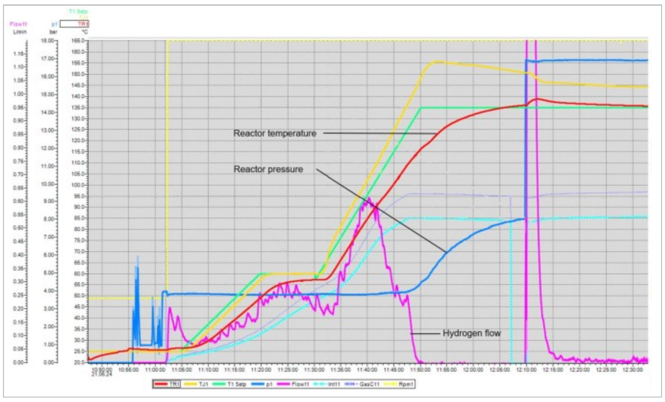
Process Investigation

Scope

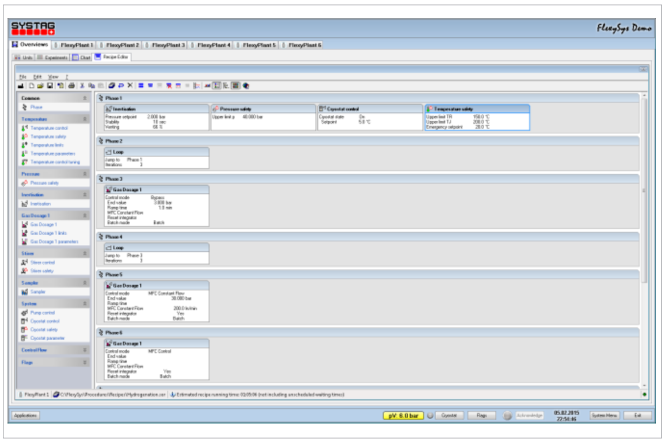
The objective was to understand the reaction, to find the root cause for the incomplete reaction course as well as to provide improved reaction conditions for a full conversion within a short hydrogenation time and a good quality of the resulting product solution.

Process Investigation using FlexySys

The hydrogenation was held for over 24h and still showed incomplete conversion. To save energy, the exothermic temperature release of the hydrogenation was used for heating to IT = 135°C. The graph from FlexySys shows that the hydrogen flow (pink curve) suddenly stops once the temperature (red line) achieves IT = 105–110°C (at daytime 11:50).



Pic 3: On-line chart with temperature and H2 flow



Pic 4: Recipe User Interface

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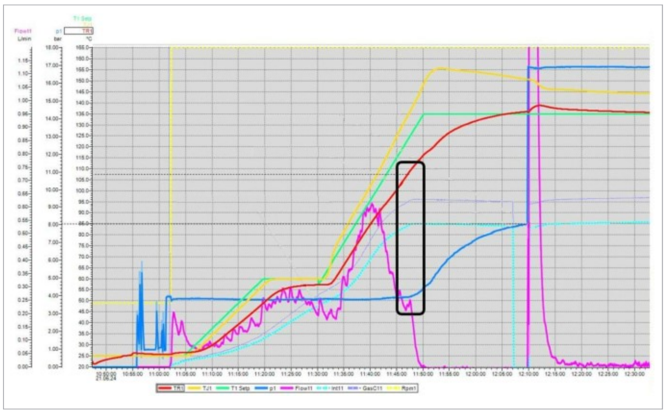
Process Investigation

Understanding of each reaction part is key

Even the manual adjustment of the hydrogen pressure (blue line) to 17 bar (at daytime 12:10) did not reactivate the hydrogenation. This can be seen from the hydrogen flow (pink curve) which is still at zero (from daytime 12:15). If that situation occurs on production scale, the costs of a failure batch could be in the multiple CHF 100'000 range. Therefore, a thorough understanding of each reaction part is key.



Pic 5: Chart with adjusted Hydrogen pressure (blue)

In the range, where the hydrogen flow (pink curve) stops, the reactor pressure (blue line) starts to increase from 4 bar to 8 bar. This is just caused by the vapor pressure of the solvent (methanol), which "overtakes" the hydrogen pressure (4 bar) at temperatures above 105–110°C. The pressure adjusting valve then closes the hydrogen flow – which leads to a lack of hydrogen. The hydrogenation "starves" and so shows incomplete conversion.

This demonstrates that only by additional data evaluation (in this case the hydrogen flow, pink curve) the root cause of a reaction failure can be elucidated. FlexySys does that job excellent.

Improved Lab Procedure

Problem solving

There are two possibilities to solve this problem: Either the reaction temperature should be held below IT = 105–110°C or a higher hydrogen pressure must be applied earlier in the reaction course. Lowering the temperature results in a longer reaction time – and was therefore ruled out. An experiment was performed, where a hydrogen pressure of 20 bar was applied from the beginning and the temperature was allowed to achieve 150°C.

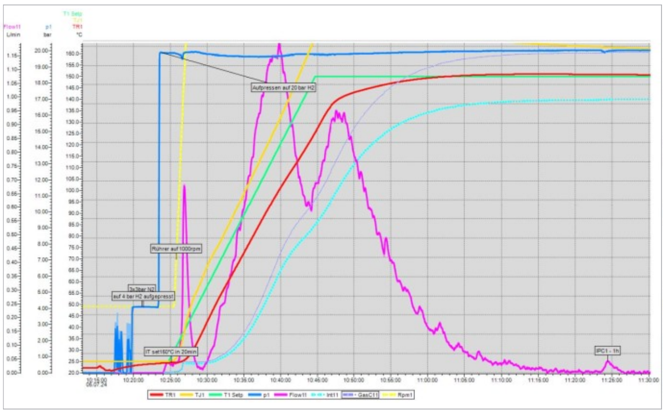


Chart 6: Optimized procedure

The hydrogenation was running without any problems and just after 1 hour a conversion of 99.9% is obtained with an excellent purity profile. On the diagram, one can even see the two broad peaks in the hydrogen flow (pink line) elucidating the two reaction steps. Note: The first thin peak signalizes the saturation of the solution and catalyst with hydrogen at the start of the stirrer (yellow line) – before the reaction starts. Some essential operations can be linked from the protocol to the graph (black subtitles), helping to understand the process even more profoundly.

More added value thanks to FlexySys:

- Enables detailed process analysis and understanding by multiple data acquisition
- Detection of optimization potentials and fast root cause analysis
- Prevention of quality issues in production (avoidance of additional costs and troubleshooting)
- Powerful tool for process development, even in the high-pressure field
- Standardized and easy handling of the system
- Parameters can be adjusted from the office as well (RemoteX)

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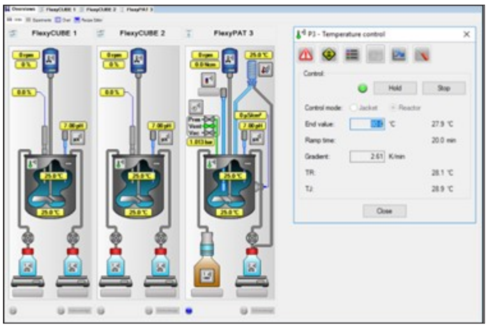
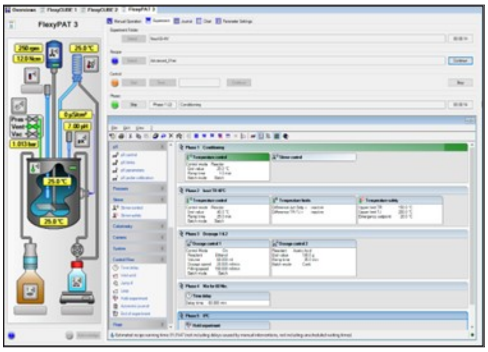
FlexySys - modular software platform for laboratory application



FlexySys — simplicity and flexibility through structured functions

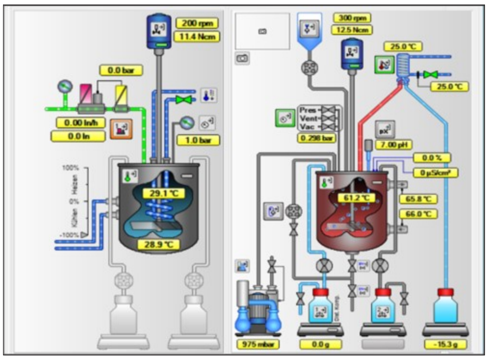
Simplicity: Thanks to intuitive functions, experiments can be carried out safely and without extensive training.

Flexibility: Thanks to a wide range of standardized functions, we can offer you a solution tailored to your own process, so that you can conduct your work as efficiently as possible. Existing equipment can also be integrated into the software. This way, you not only save money, but also increase the system's availability.



Efficiency, safety and reproducibility thanks to recipe control

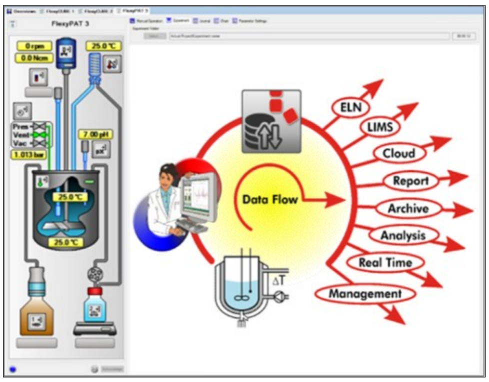
Using recipes, sub-processes such as inerting or even complete experiments can be carried out reproducibly and efficiently, even without supervision. Maximum flexibility is guaranteed by the combination of manual interventions, fully automatic recipe operation and the "edit on the fly" function. Alongside all the necessary safety limits, which the system immediately regulates into the previously defined safety state, a variety of process limits can also be defined. These include, for example, the maximum permissible temperature rise during dosing.



Customer-specific adjustments

The software can be tailored to a large number of different processes. For example, distillations, filtrations or pressure controls can be automated via the software using standardized functions, while reaction energies can be measured (calorimetry) or analysis devices such as turbidity measurements and particle size analyzers can be implemented.

Customer-specific turnkey solutions, combined with services in the field of plant design and plant qualification in the GMP environment (IQ/OQ), pro-



Data management and eJournal

During an experiment, all the events and data are recorded automatically. This also applies for any integrated analytical instrument. In addition, all the data along the workflow, such as the numbers of manual weighings of solids or the batch numbers of educts, can be managed via the software. All the data and information is compiled in Word format in an automatically generated e-journal, which can then be centrally archived in higher-level data management programs (ELN or LIMS) using the "CollectX" add-on. This way, the traceability of all the experiment related data is ensured and data analysis is also guaranteed across departments.

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