

20.01.2017

2. NMRPM (NMR Process Monitoring)
 Kaiserslautern, Germany

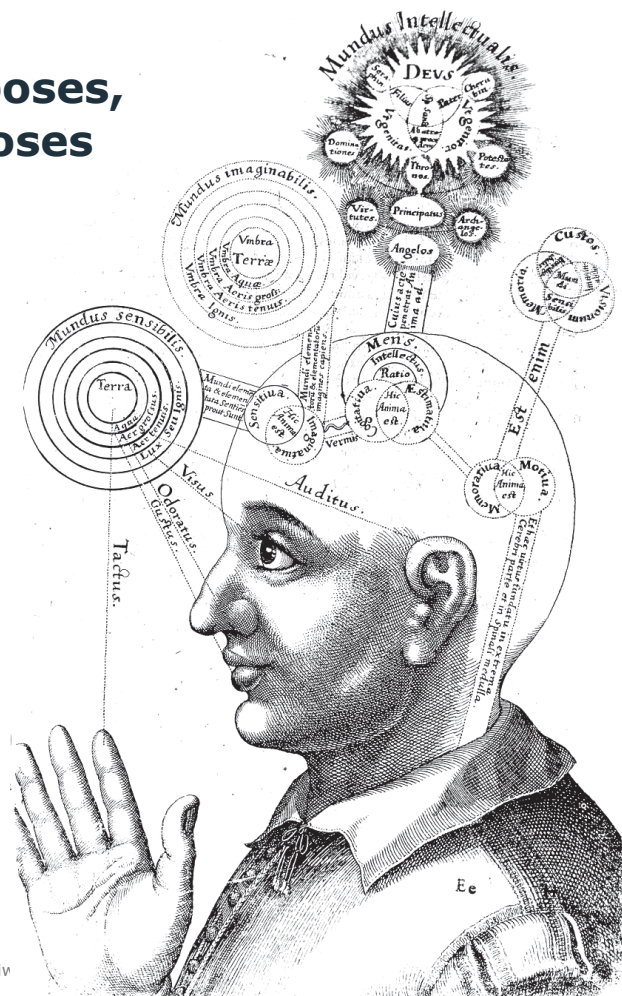
MAN PROPOSES, GOD DISPOSES – THE WAY FROM REACTION MONITORING TO INDUSTRIAL AUTOMATION

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 Patrick Gräßer, Lukas Wander, Andrea Paul

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Man proposes, God disposes

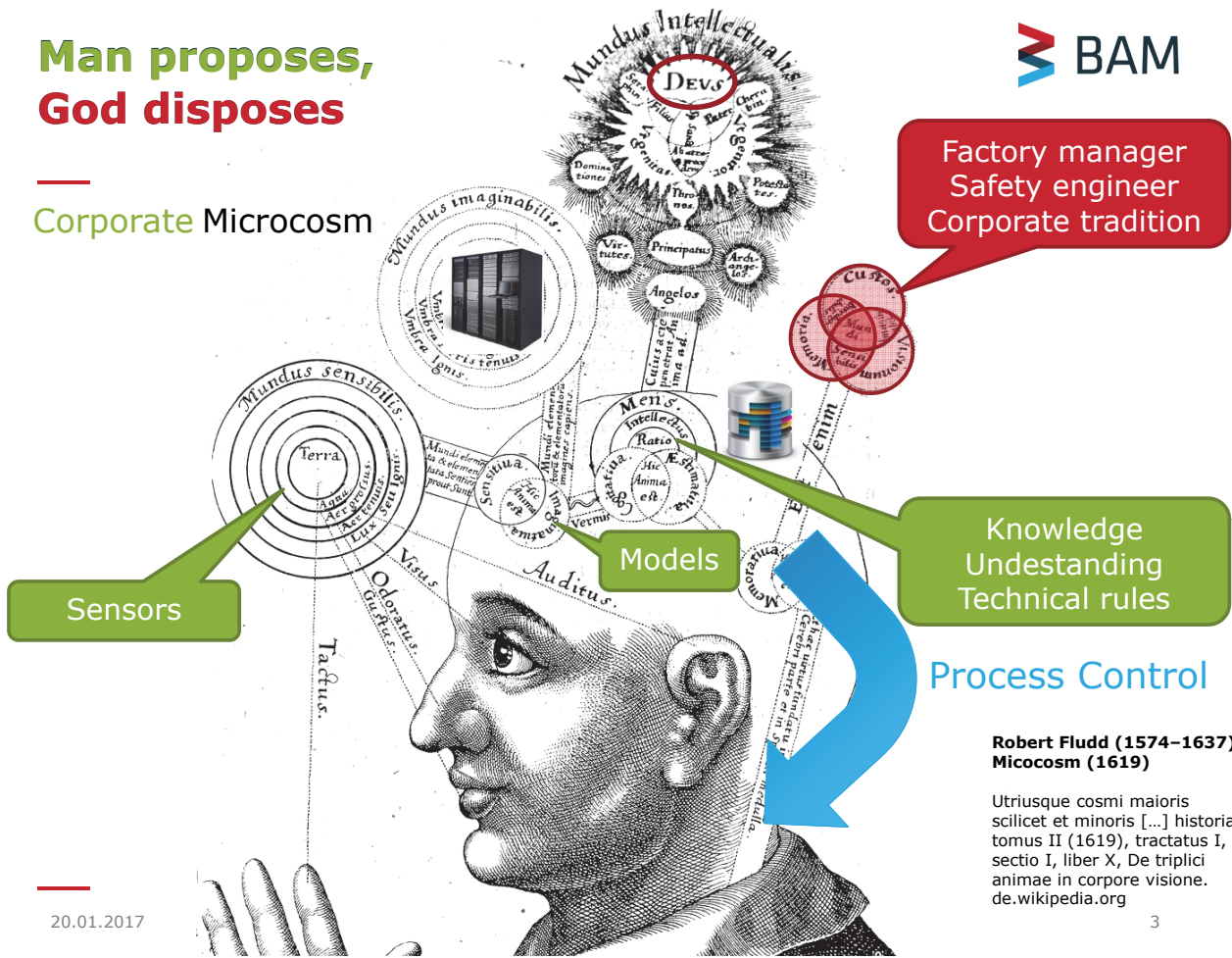


Robert Fludd (1574–1637)
Micocosm (1619)

Utriusque cosmi maioris
 scilicet et minoris [...] historia,
 tomus II (1619), tractatus I,
 sectio I, liber X, De triplici
 animae in corpore visione.
de.wikipedia.org

Man proposes, God disposes

Corporate Microcosm



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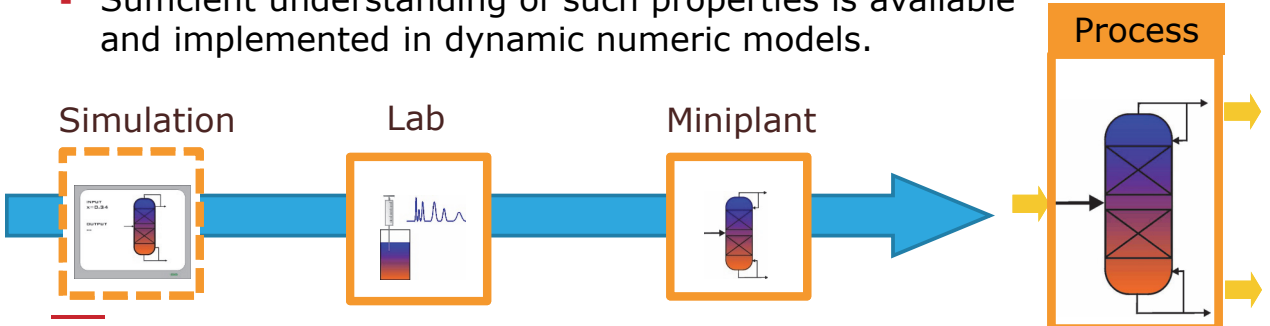
Robert Fludd (1574–1637)
Microcosm (1619)
Utriusque cosmi maioris scilicet et minoris [...] historia, tomus II (1619), tractatus I, sectio I, liber X, De triplici animae in corpore visione. de.wikipedia.org

Contemporary process engineering Towards Cyber-Physical Production Systems (CPPS)



Process engineering focuses on the design, operation, control, and optimization of chemical, physical, or biological processes.

- Involves creating production facilities that translate raw materials into value-added products along the supply chain
- Conversions typically take place in repeated reaction and separation steps – either in batch or continuous processes.
- Computer aided tools: mass transfer, thermodynamic, kinetic, and other physical properties of treated materials
- Sufficient understanding of such properties is available and implemented in dynamic numeric models.



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M. Maiwald Man Proposes - God Disposes

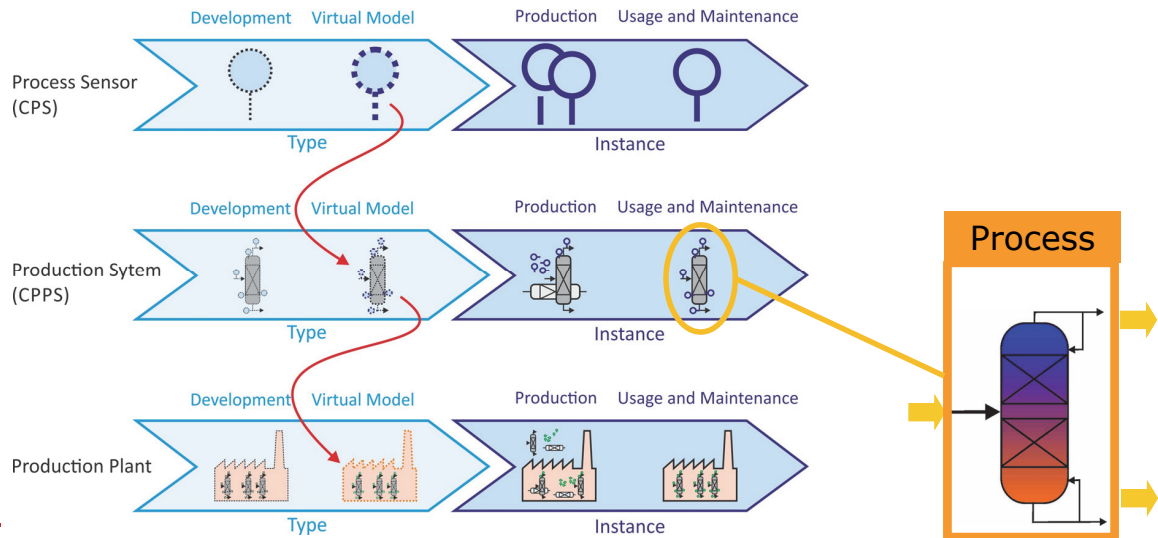
2. NMRPM, Kaiserslautern

Contemporary process engineering

Towards Cyber-Physical Production Systems (CPPS)

"Cyber-Physical Systems (CPS) are integrations of computation with physical processes. Embedded computers and networks monitor and control the physical processes, usually with feedback loops where physical processes affect computations and vice versa".

E.A. Lee, Cyber Physical Systems: Design Challenges, EECS Department, University of California, Berkeley, 2008.



Integrated process design and intensified processes

- Intensified continuous processes

Motivation

- Continuous Processing
- Standardized modular equipment
- Numbering-up on demand
- Fast response to marked change

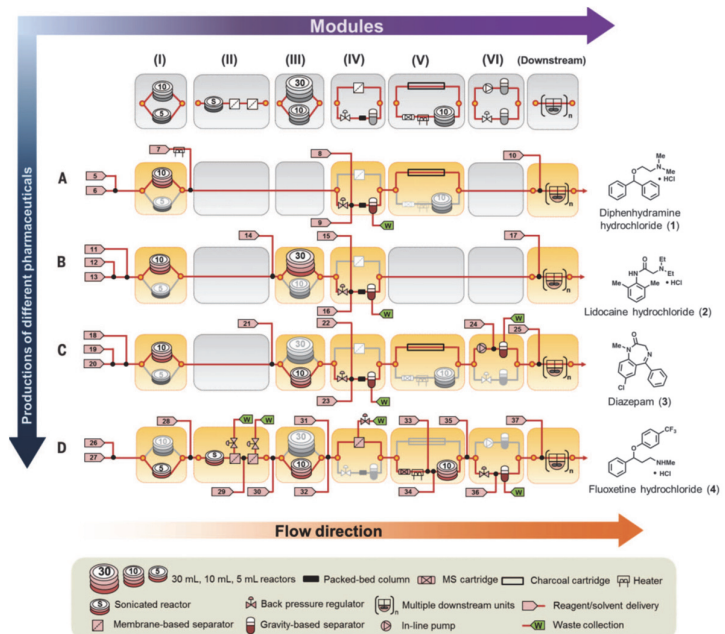
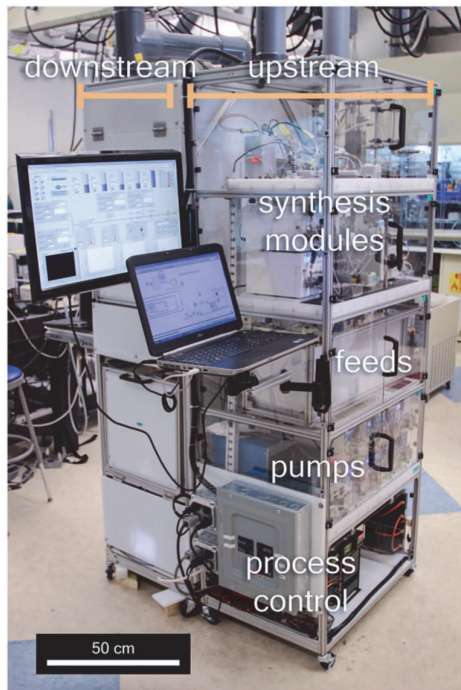
More efficient and flexible low to medium scale production of specialty chemicals

Intensified production concepts require for adaptive sensor and process control technology

- Short set-up times
- Modular control strategies

Integrated process design and intensified processes

Example: Flow Chemistry



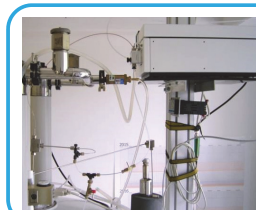
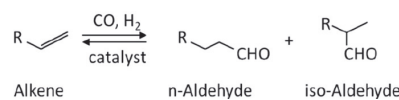
A. Adamo, R. L. Beingsner, M. Behnam et al., On-demand continuous-flow production of pharmaceuticals in a compact, reconfigurable system, Science Science 352(6281), 2016, 61-67

Process analytical technology for intensified processes

Examples from BAM

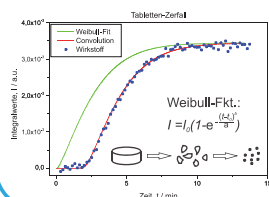


Catalysis:
Hydroformylations of C12-alkenes in micro emulsions

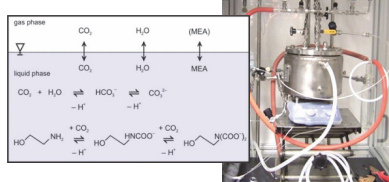


qNMR (Metrology):
Gases and condensed phases up to 1000 bar

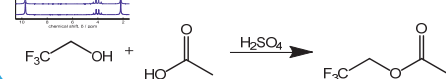
Pharmaceuticals:
Liberation kinetics



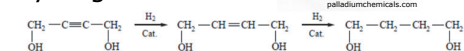
CO₂ scrubbing



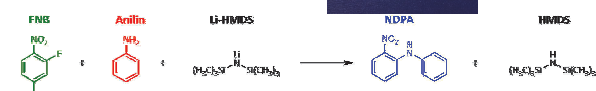
Method development:
Esterifications (model reactions)



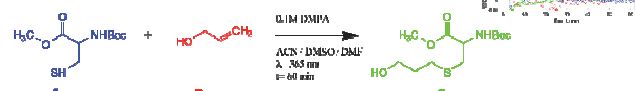
Catalysis:
Hydrogenations



Reaction Engineering:
Lithiation reactions

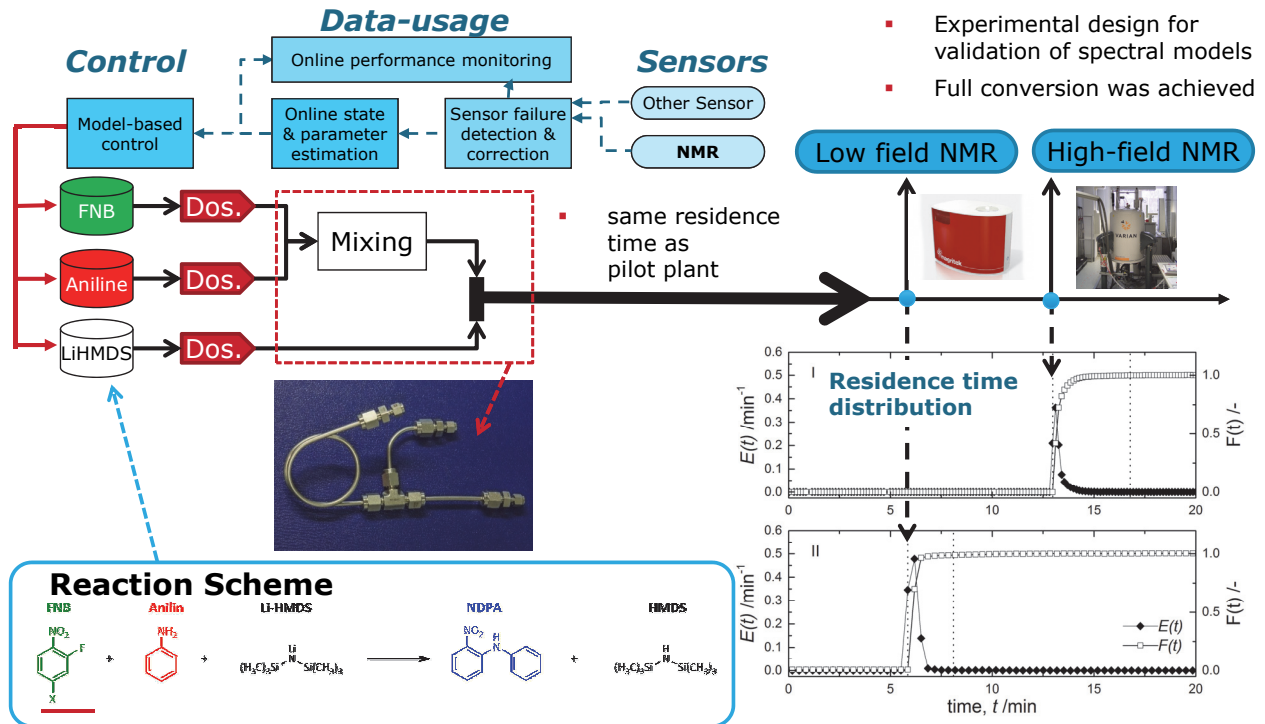


Reaction Engineering:
Photo reactions („click chemistry“)



Validation lab experiments in tube reactor

Continuous Lithiation Reaction Set-up at BAM



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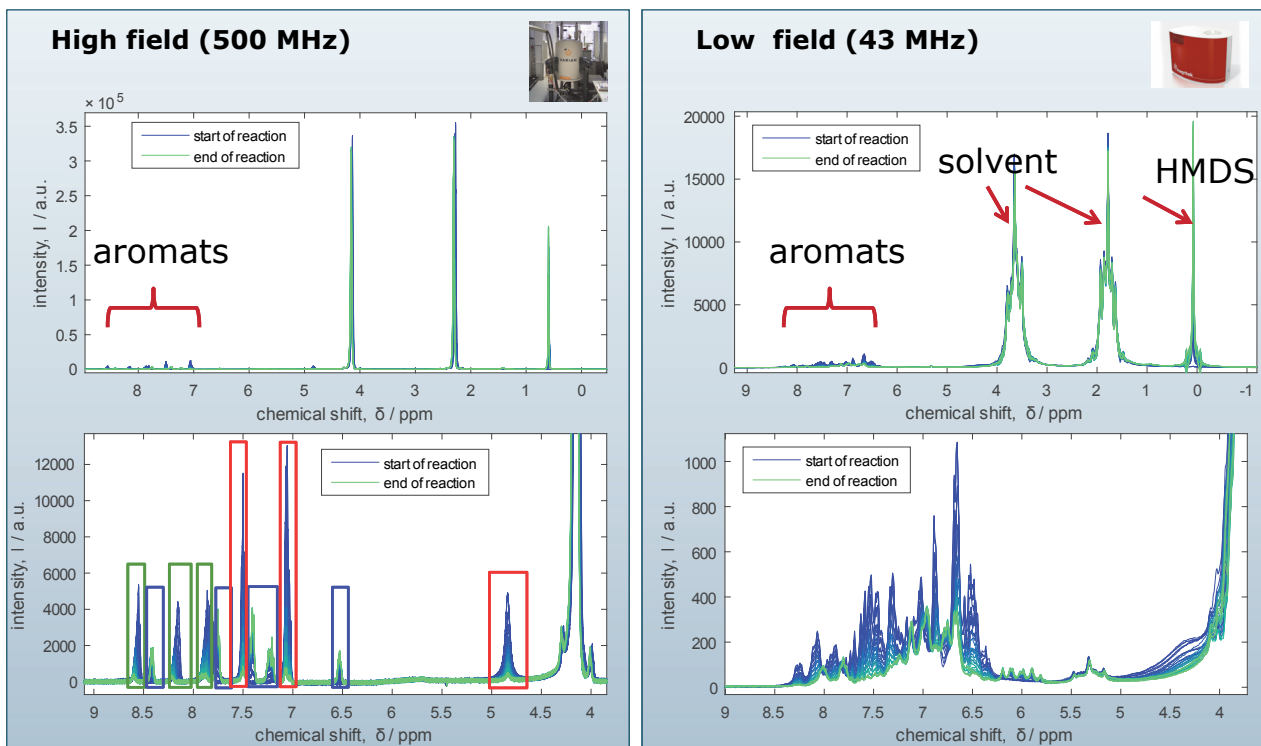
Man Proposes - God Disposes

2. NMRPM, Kaiserslautern

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Proton NMR Spectra 500 MHz vs 43 MHz

Lab experiments in batch along reaction co-ordinate



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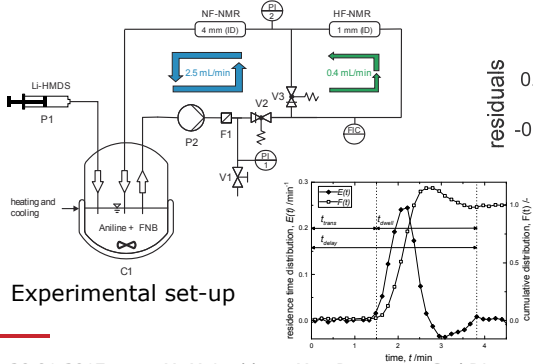
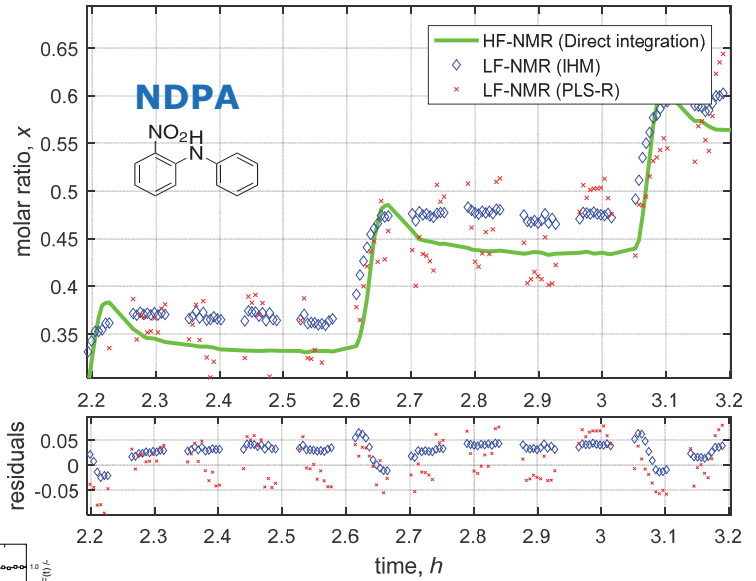
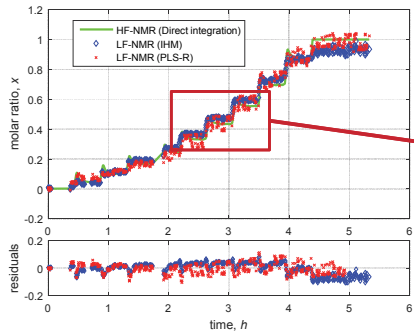
2. NMRPM, Kaiserslautern

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Model Building: IHM and PLS-R

Lab experiments in Batch Along Reaction Co-ordinate

Validation with HF-NMR

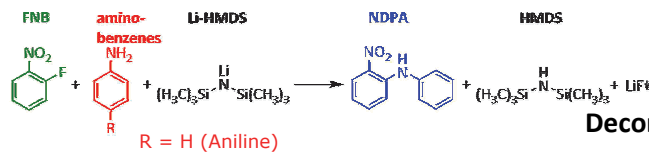
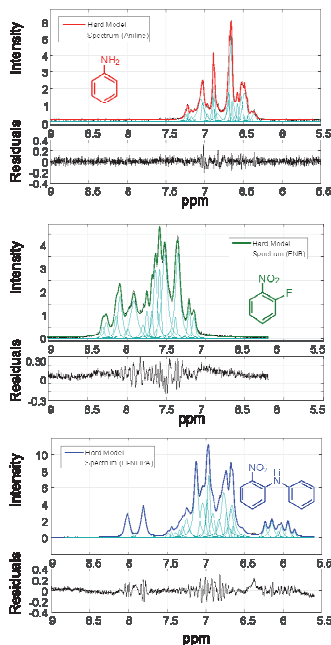


RTD of high field NMR
(Back-mixing)

Indirect Hard Modeling (IHM)

How it works

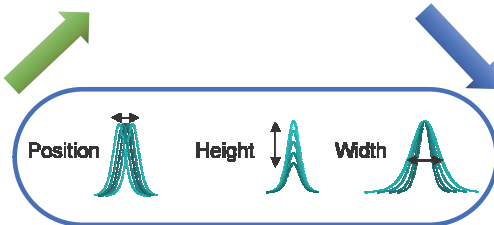
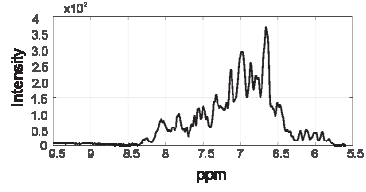
Pure component models



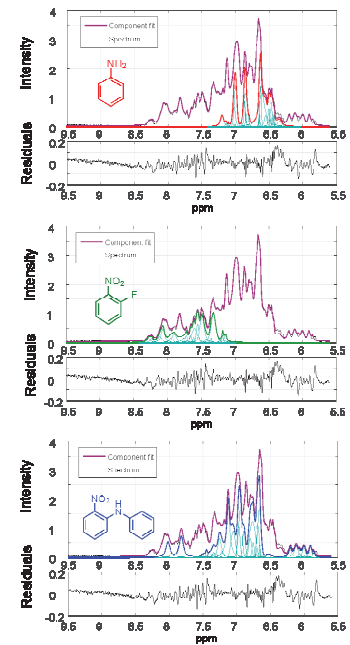
Mixture model

Component fitting

Experimental Spectrum



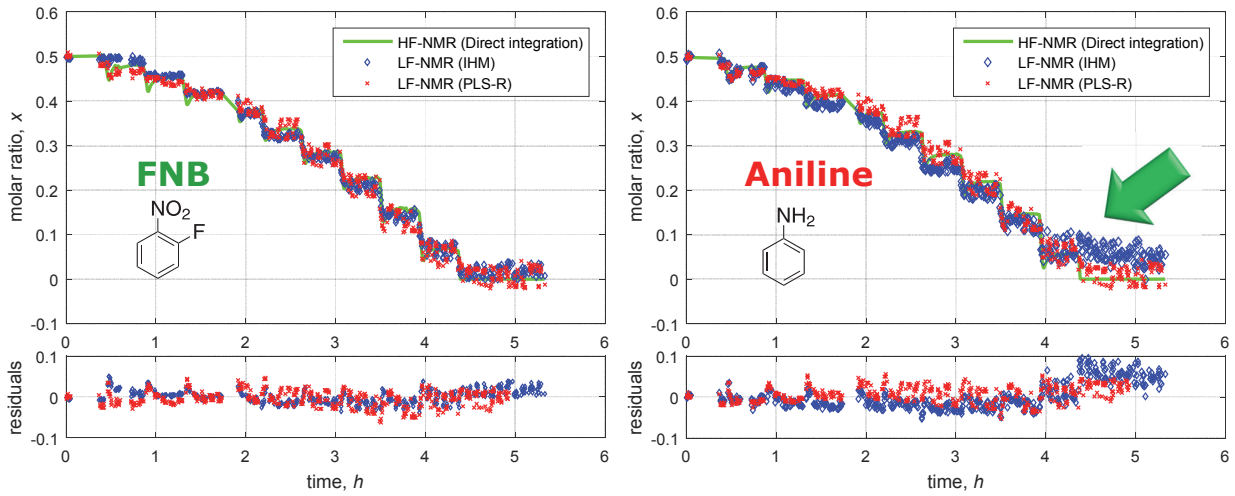
Deconvoluted spectrum



Model Building: IHM and PLS-R

Lab experiments in Batch Along Reaction Co-ordinate

Current Limitations

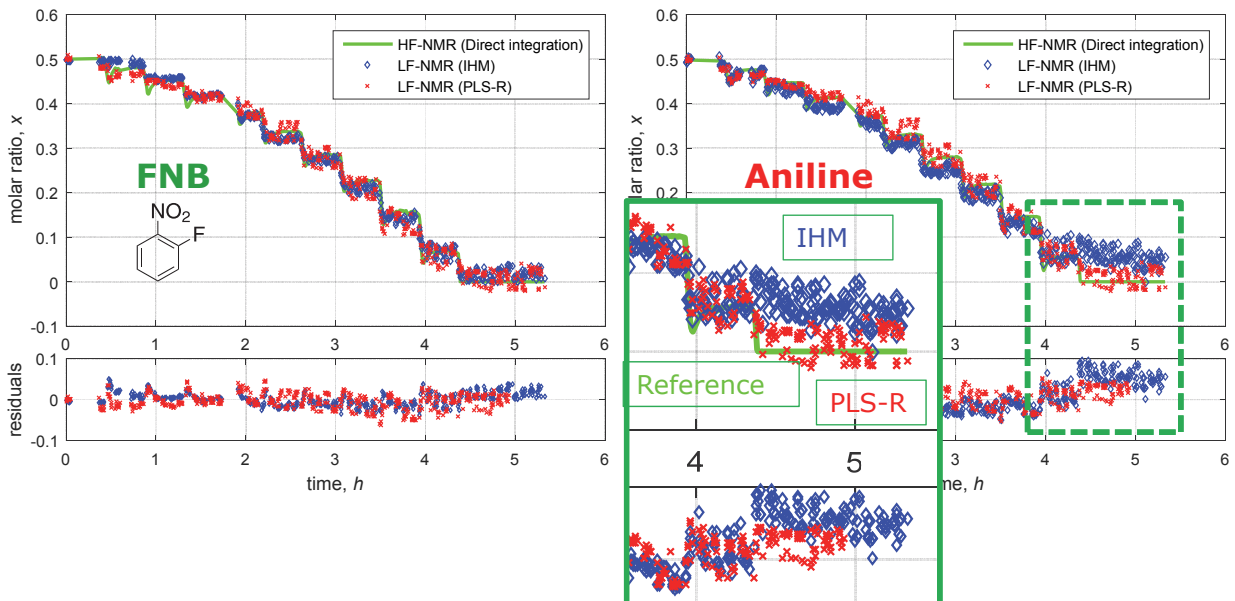


- Model limitations for low concentration of Aniline
- Prediction uncertainty 5–7 % relative, i.e., 0.25–0.35 % absolute

Model Building: IHM and PLS-R

Lab experiments in Batch Along Reaction Co-ordinate

Current Limitations

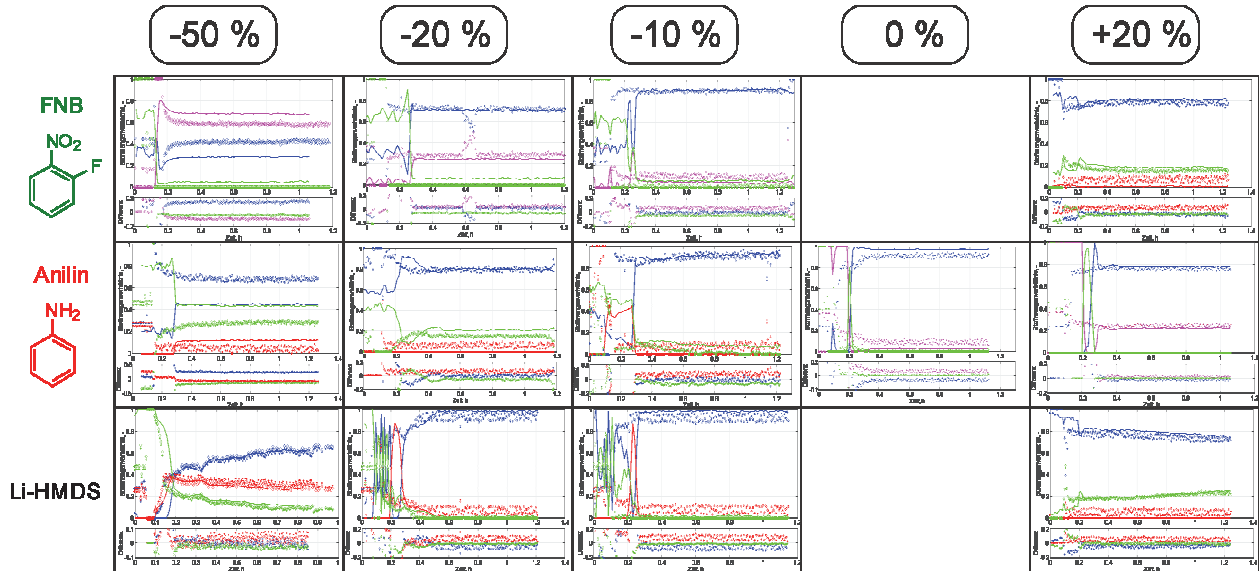


- Model limitations for low concentration of Aniline
- Prediction uncertainty 5–7 % relative, i.e., 0.25–0.35 % absolute

Model Validation

Lab Experiments (DoE) in Continuous Tube Reactor

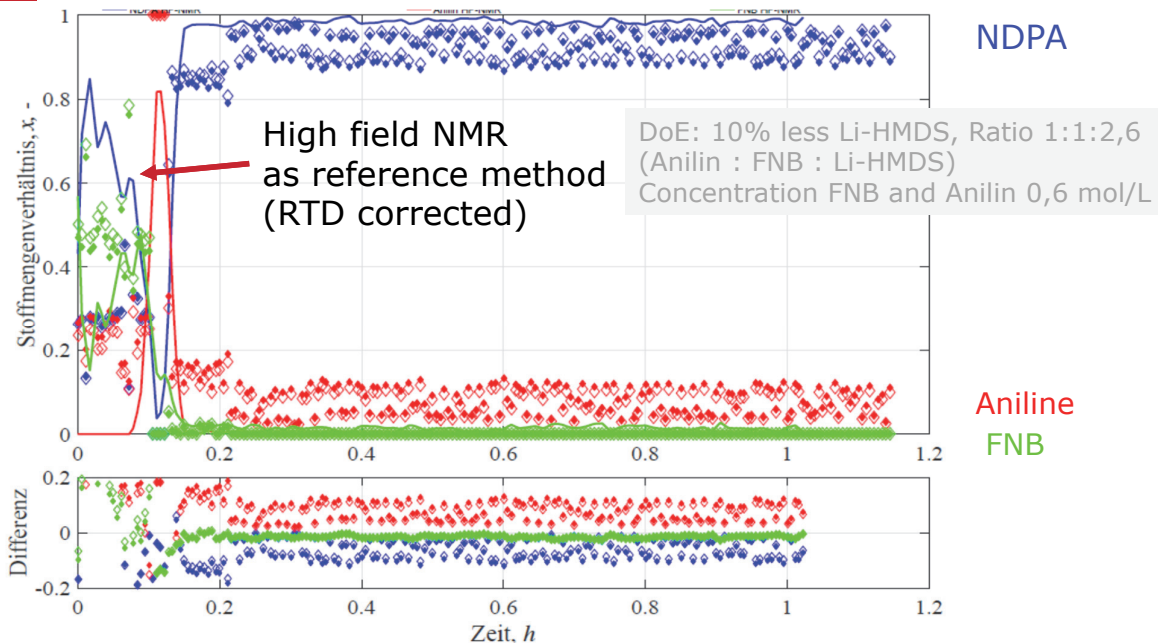
- Two series covering 1 : 1 : 2.3 (FNB : Aniline : Li-HMDS)
- Additional experiments, e.g., concentration variation in THF etc.



Model Building: IHM and PLS-R

Lab experiments in Batch Along Reaction Co-ordinate

Current Limitations

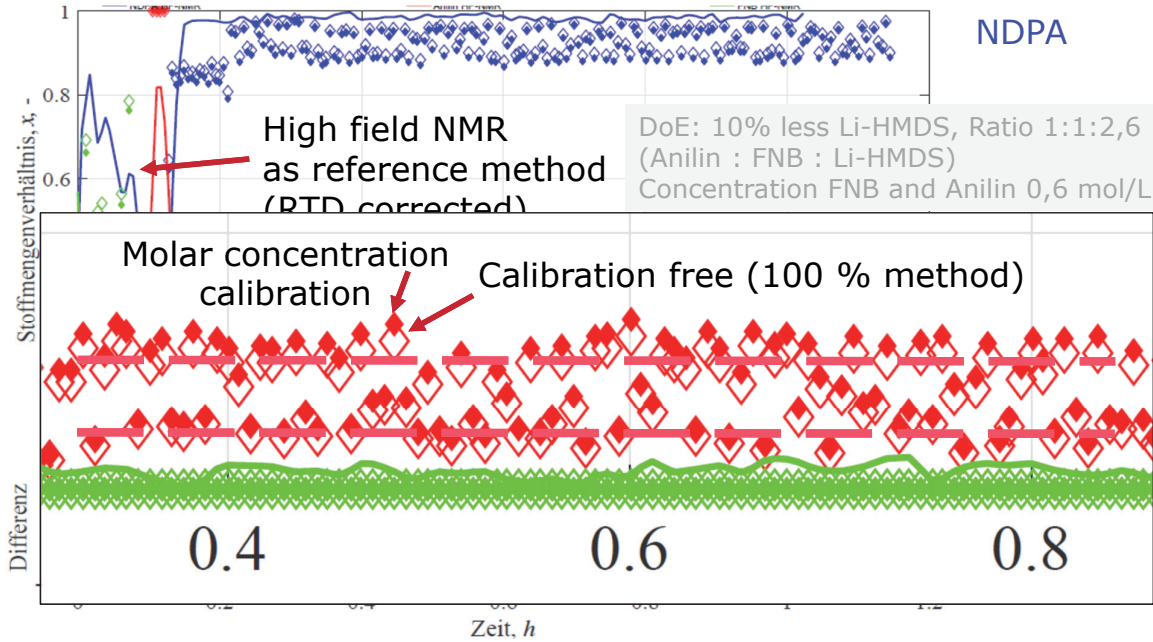


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Model Building: IHM and PLS-R

Lab experiments in Batch Along Reaction Co-ordinate

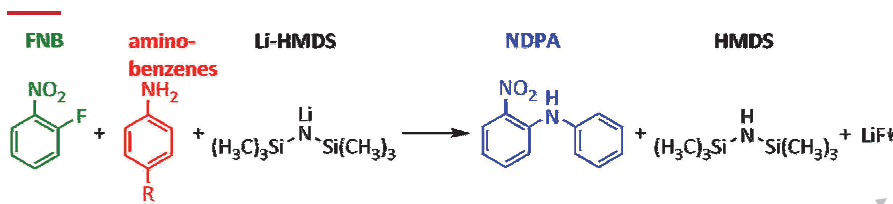
Current Limitations



- Model limitations for low concentrations of Aniline
- Prediction uncertainty 5–7 % relative, i.e., 0.25–0.35 % absolute

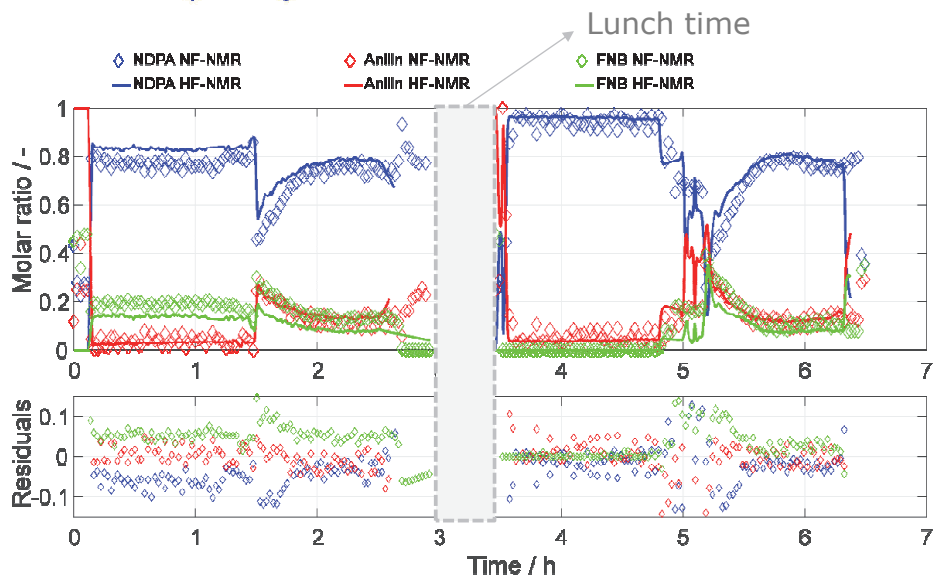
Model Validation

Variation of Substituents in Continuous Tube Reactor



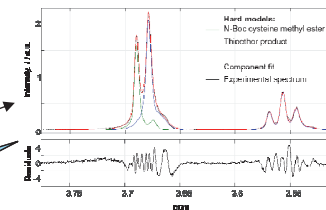
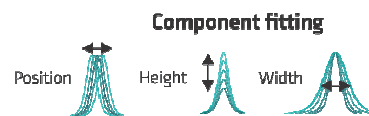
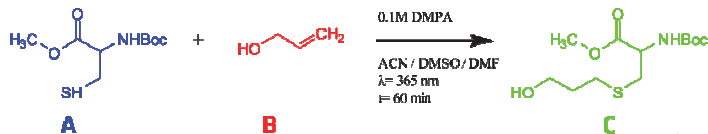
R = H, CH₃, F

- Various substituents
- Fast adaption of spectral models to various substituents
- Calibration-free

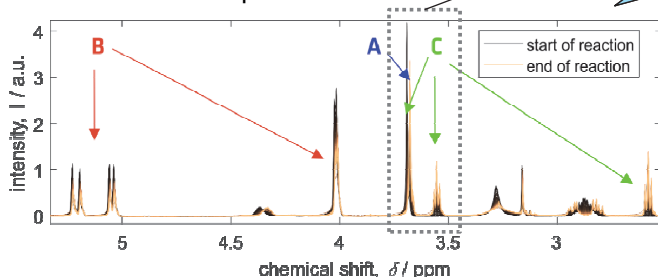


"Click" analytics for "click" chemistry – a simple method for calibration-free evaluation of online NMR spectra

Reaction mechanism of the thio-ene coupling monitored with online NMR spectroscopy:



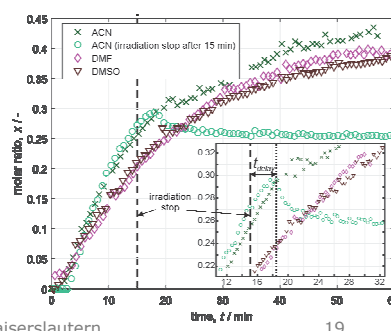
Recorded online spectra:



Spectral modeling



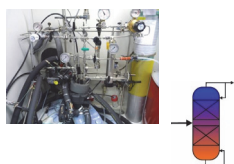
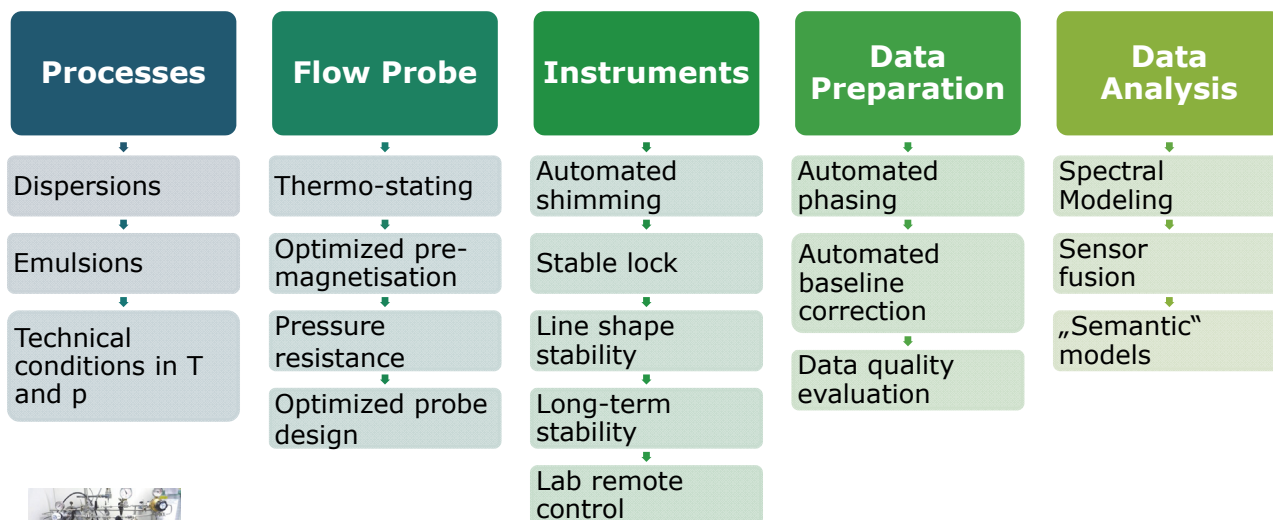
Kinetic information for various solvents:



S. Kern, A. Onichimowska, et al., J. Magn. Reson. submitted 2016

Summary: Low Field Reaction Monitoring And it's Way to Industrial Automation

ToDoS



Current and future requirements to process sensors

Sensors go smart

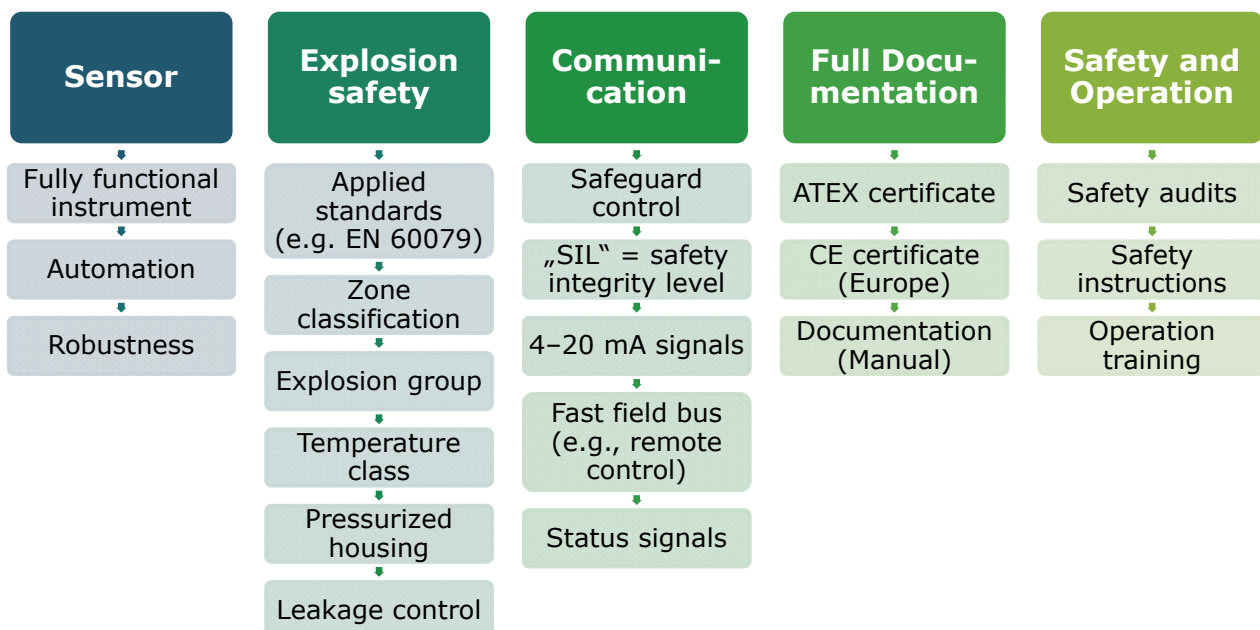
- Smart process sensors are important parts of cyber-physical production systems and generate new business cases for users, instrument manufacturers, and service providers.
- „Smart“ sensors provide services within networks and use information out of the network.



- Use of „complicated“ sensors has to be simplified towards „plug and play“

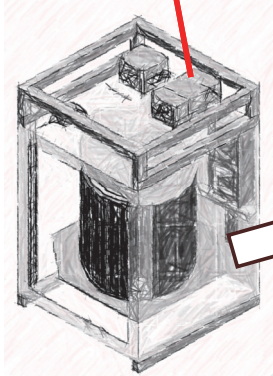
Industrial Automation

Current Technical and Cultural Requirements to Process Sensors



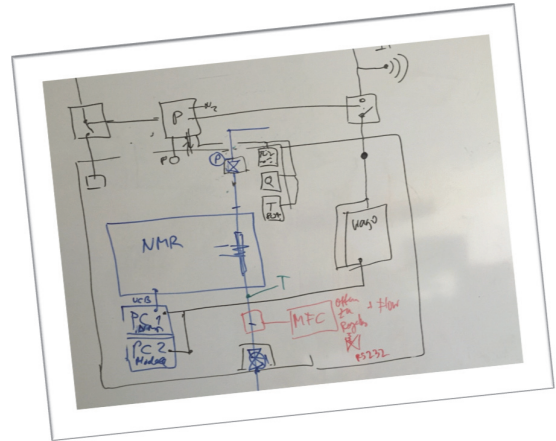
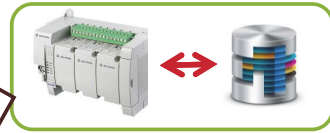
Communication Concept

Safety Information
- Leakage, T, p



NAMUR status signals

Conventional 4-20 mA



OPC-UA Client

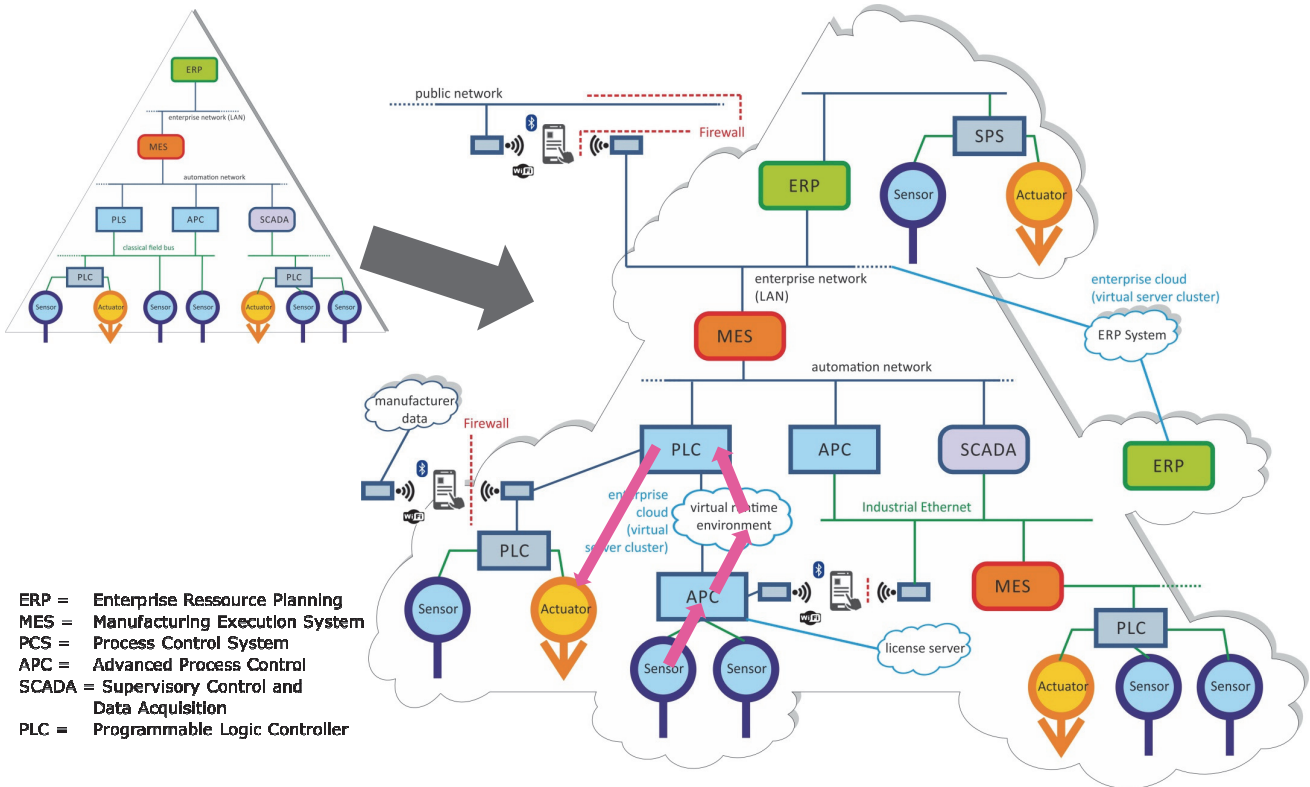
ATEX-proof WiFi



Fast field bus

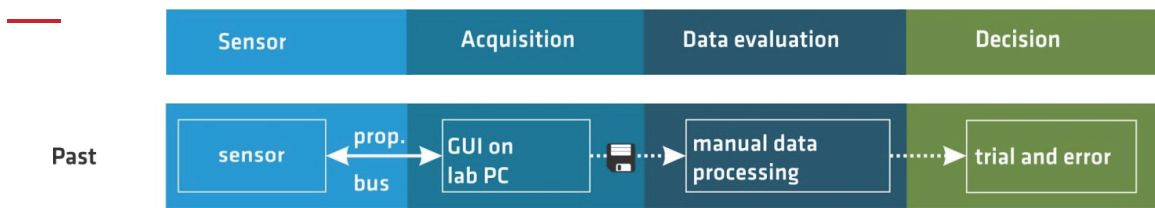


Smart Sensors



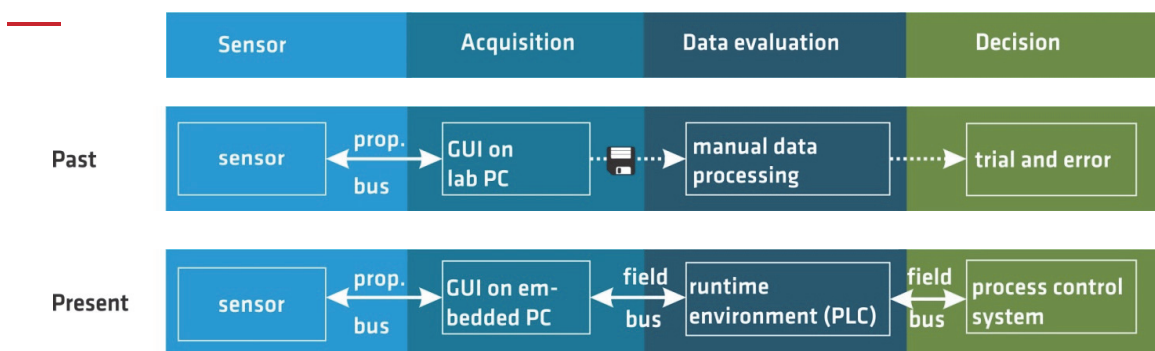
From Lousy Interfaces to "Industrie 4.0" BAM

Use of Runtime Environments



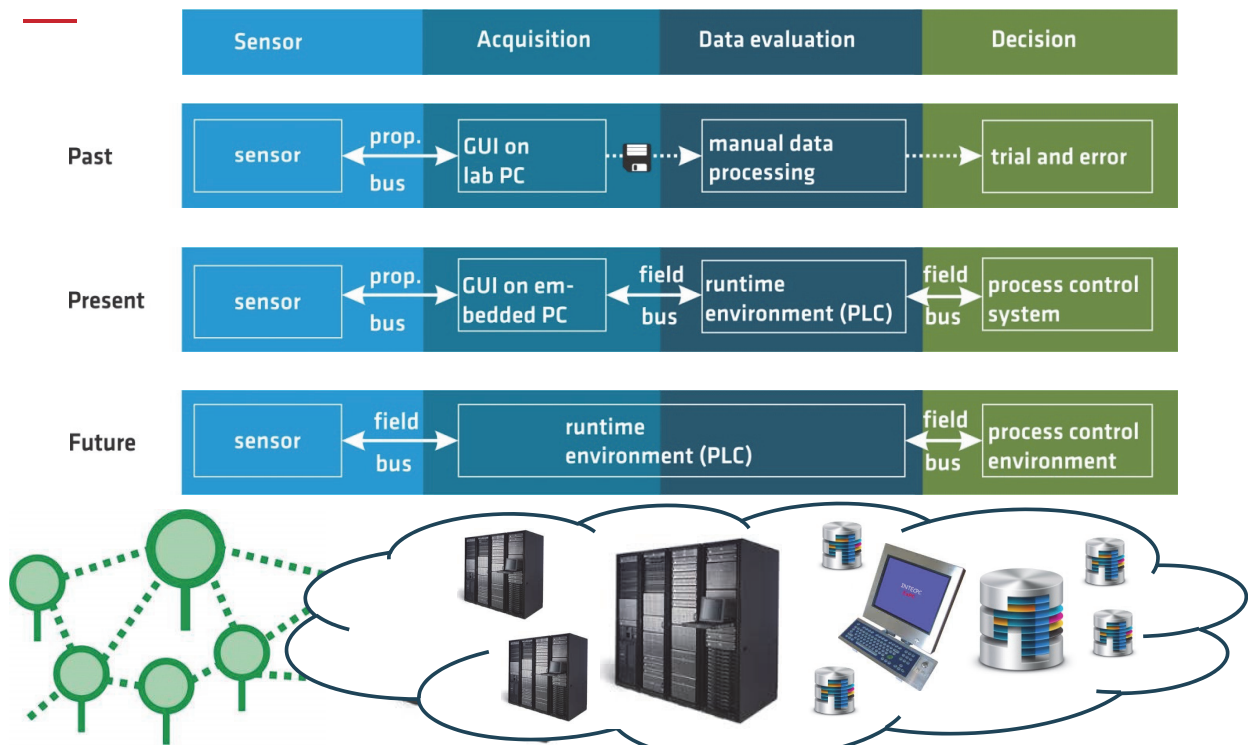
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Use of Runtime Environments



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2. NMRPM, Kaiserslautern

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Acknowledgements



Thank You!

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Clemens Minnich
Dirk Engel

PTB
S-Pact
S-Pact



CONSENS – Integrated Control and Sensing for Sustainable Operation of Flexible Intensified Processes, funded by the European Union's Horizon 2020 research and innovation programme under grant agreement N° 636942; www.consens-spire.eu

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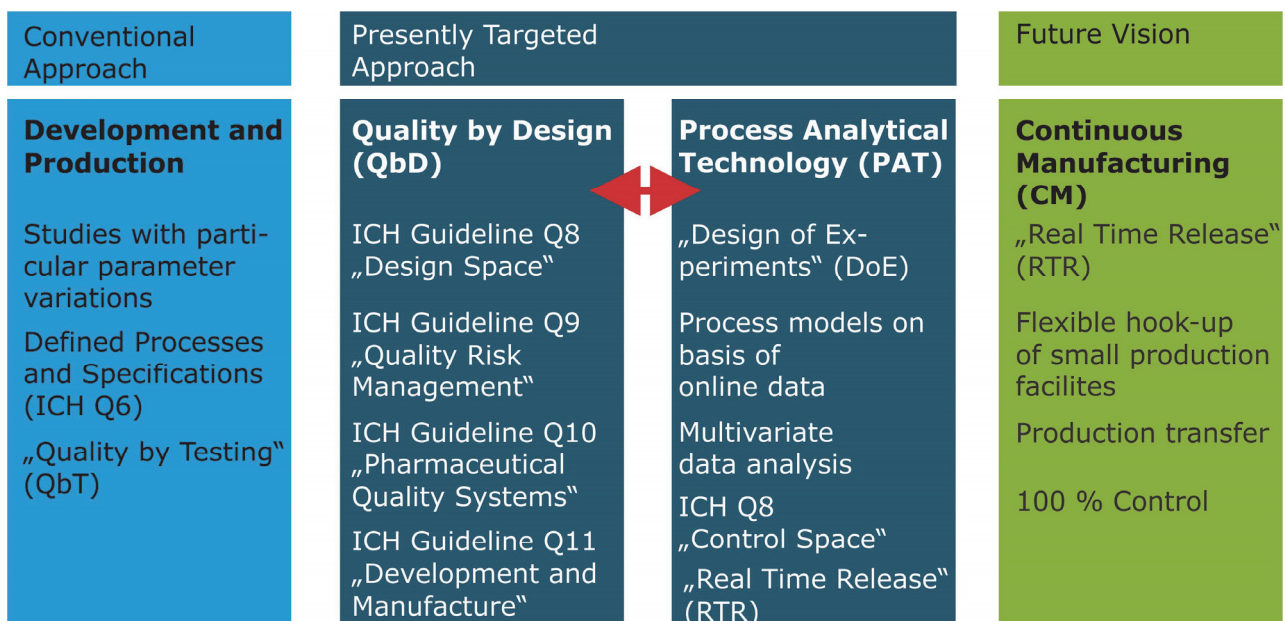
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- Contemporary process engineering
- Integrated process design and intensified processes
 - Intensified continuous processes
 - Integrated processes
 - Towards continuous pharmaceutical manufacturing
 - Flow chemistry
- Contemporary automation and process control
- Current and future requirements to process sensors

Integrated process design and intensified processes

Towards continuous pharmaceutical manufacturing



- Current focuses of research are closed-loop adaptive control concepts for plant-wide process control, which make use of specific or non-specific sensors along with conventional plant instruments.
- Such advanced control solutions could give more information than only control information, such as
 - sensor failure detection
 - control performance monitoring
 and improve simulation-based engineering.

Motivation

- processes can automatically be driven much closer to the optimal operating limit
- adaptation during the life cycle of the process
- potential to automatically cope with changes of the raw-materials as well as process conditions

Model Building: IHM and PLS-R

Lab experiments in Batch Along Reaction Co-ordinate

Current Limitations

