

2016-01-12

ONLINE-NIEDERFELD-NMR-SPEKTROSKOPIE IN MODULAREN ANLAGEN DER PROZESSINDUSTRIE

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Andrea Paul, and Michael Maiwald

Division 1.4: Process Analytical Technology

Our Key Areas

Gas Analysis

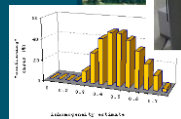
- Primary Reference Gas Mixtures
- Gas Analysis, Gas Metrology
- Certification of Sec. Gas Mixtures



Located in Berlin, Germany

Process Spectroscopy

- Online NMR Spectroscopy, qNMR
- Raman Spectroscopy and Microscopy
- NIR, MIR, FIR spectr., IR Microscopy
- Data Treatment: Statistics, Numerics
- Measurement Uncertainty Evaluation



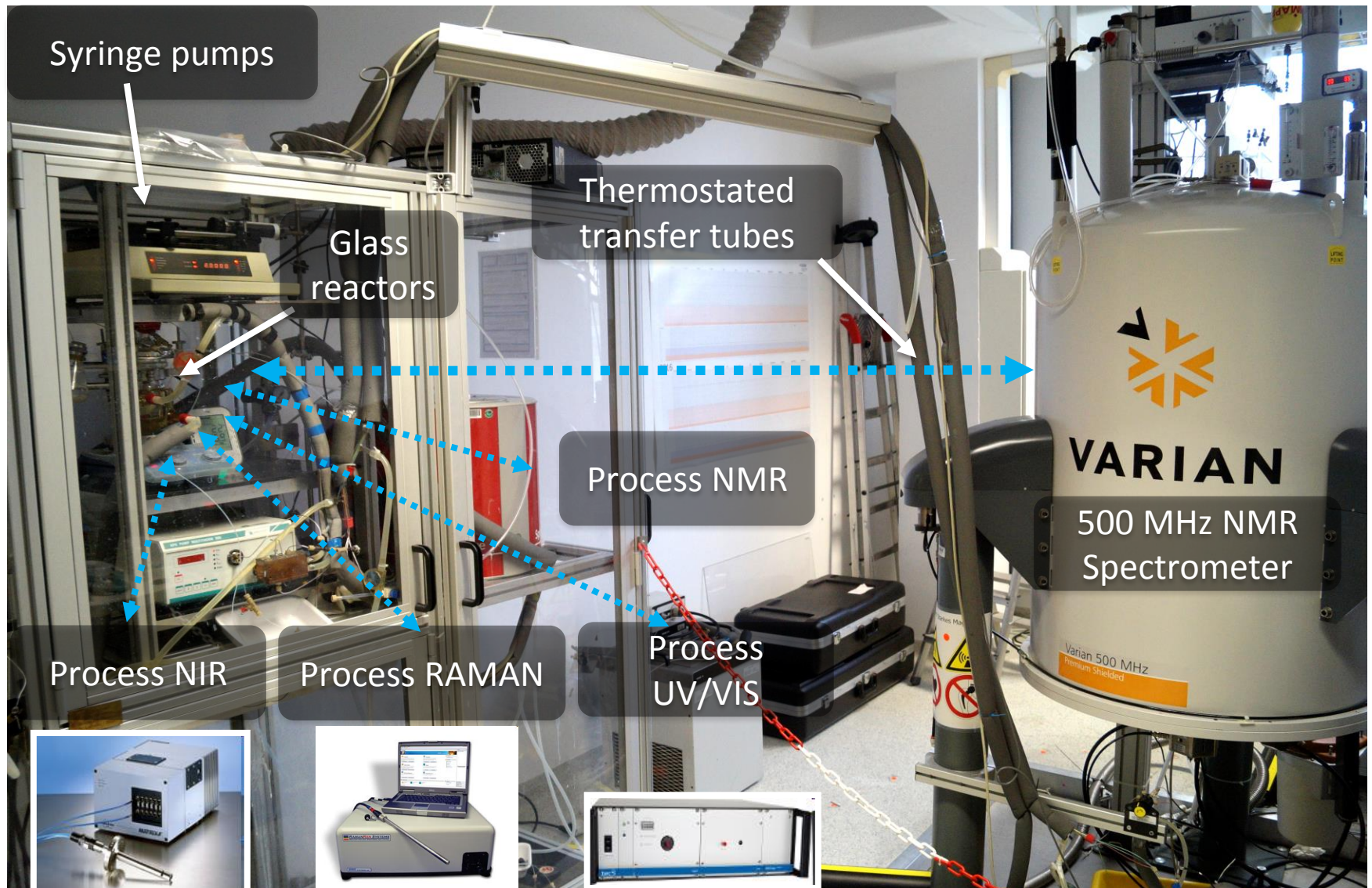
Inorganic Process Anal. Technol., XRF

- X-ray fluorescence Analysis (XRF)
- Laser-induced Breakdown (LIBS)
- Total Reflectance XRF (T-XRF)



07.2016

Online NMR Spectroscopy as Reference Hyphenation to reactors and devices



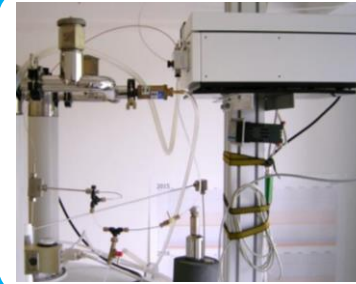
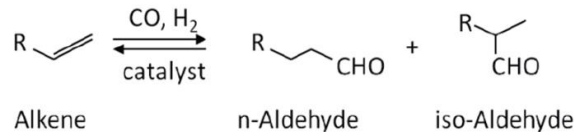
Process analytical technology for intensified processes



Examples from BAM

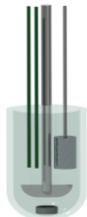
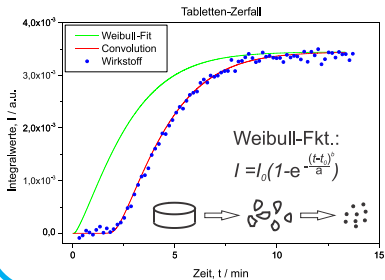


Catalysis:
Hydroformylations of C12-alkenes
in micro emulsions

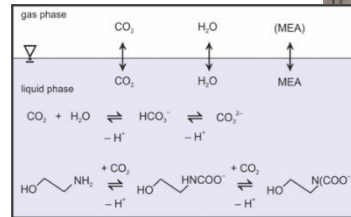


qNMR (Metrology):
Gases and
condensed phases
up to 1000 bar

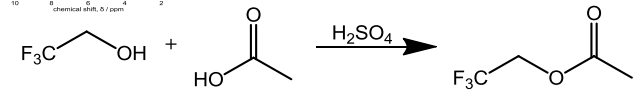
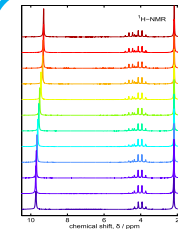
Pharmaceuticals:
Liberation kinetics



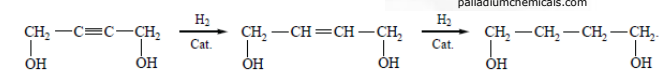
CO₂ scrubbing



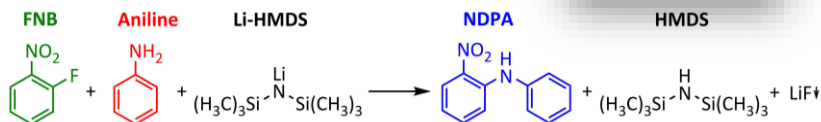
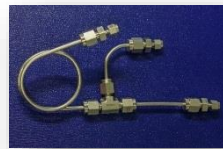
Method development:
Esterifications
(model reactions)



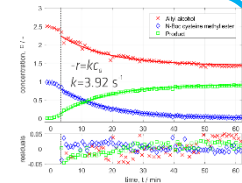
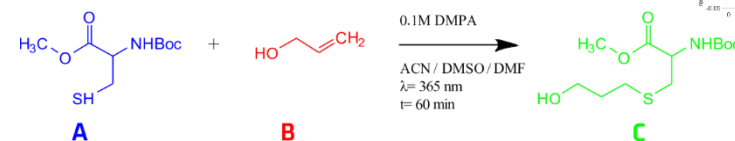
Catalysis:
Hydrogenations



Reaction Engineering:
Lithiation reactions



Reaction Engineering:
Photo reactions („click chemistry“)



CONSENS: fast online sensors and advanced process control

Flexible intensified continuous plant

Characteristics

Miniaturized equipment

Intensified heat & mass transfer

Possibly modular setup



Benefits

Product uniformity

Sustainability

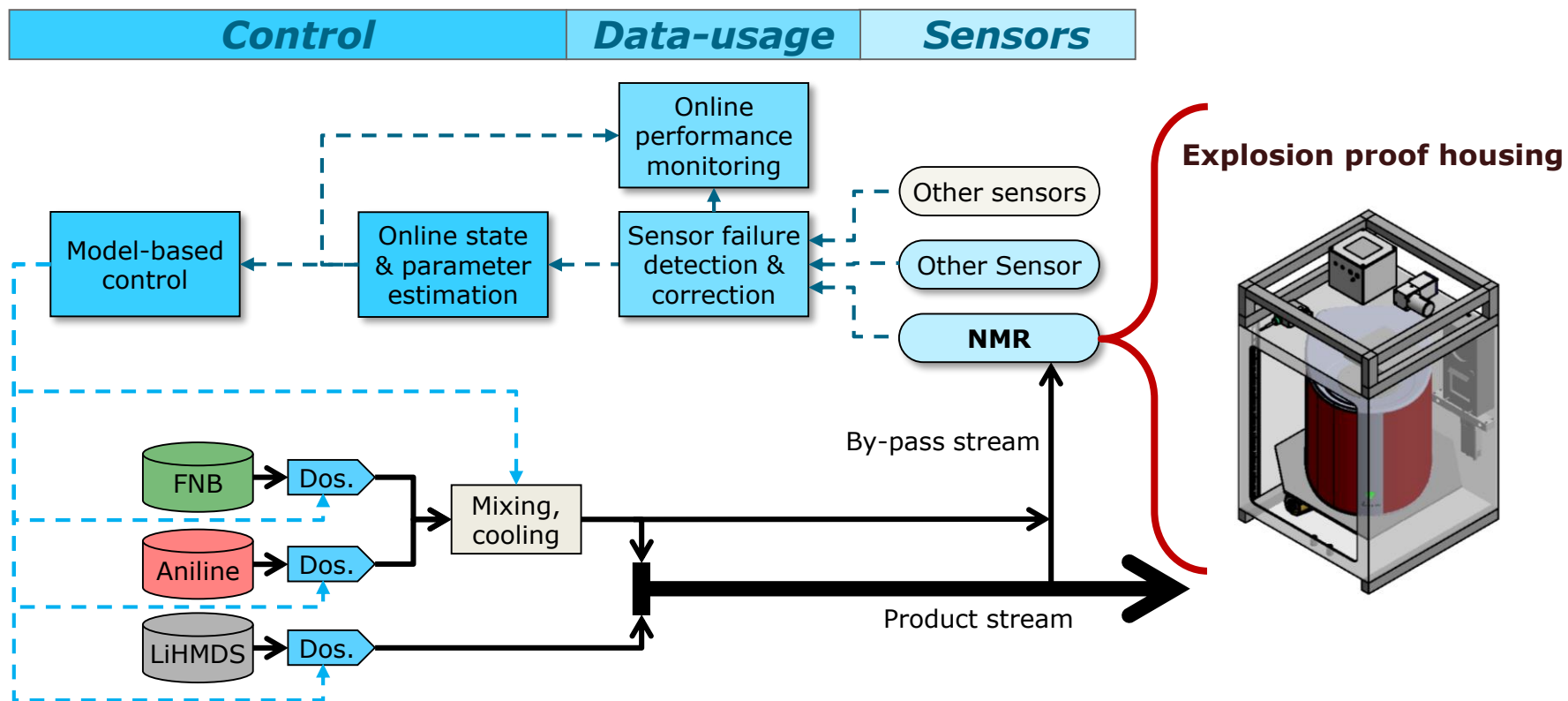
Fast adaption to market demand

Innovative products

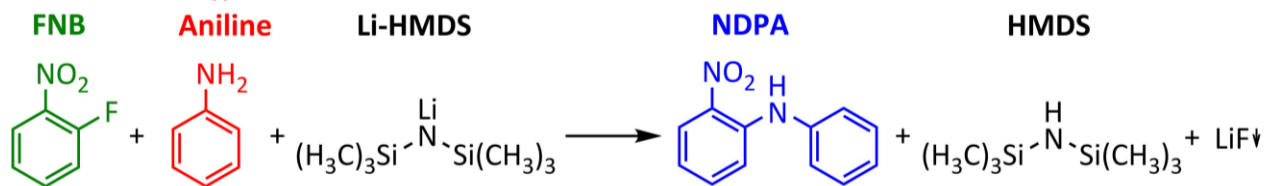
Containerized modular plant from F³ Factory project

CONSENS: Case study 1

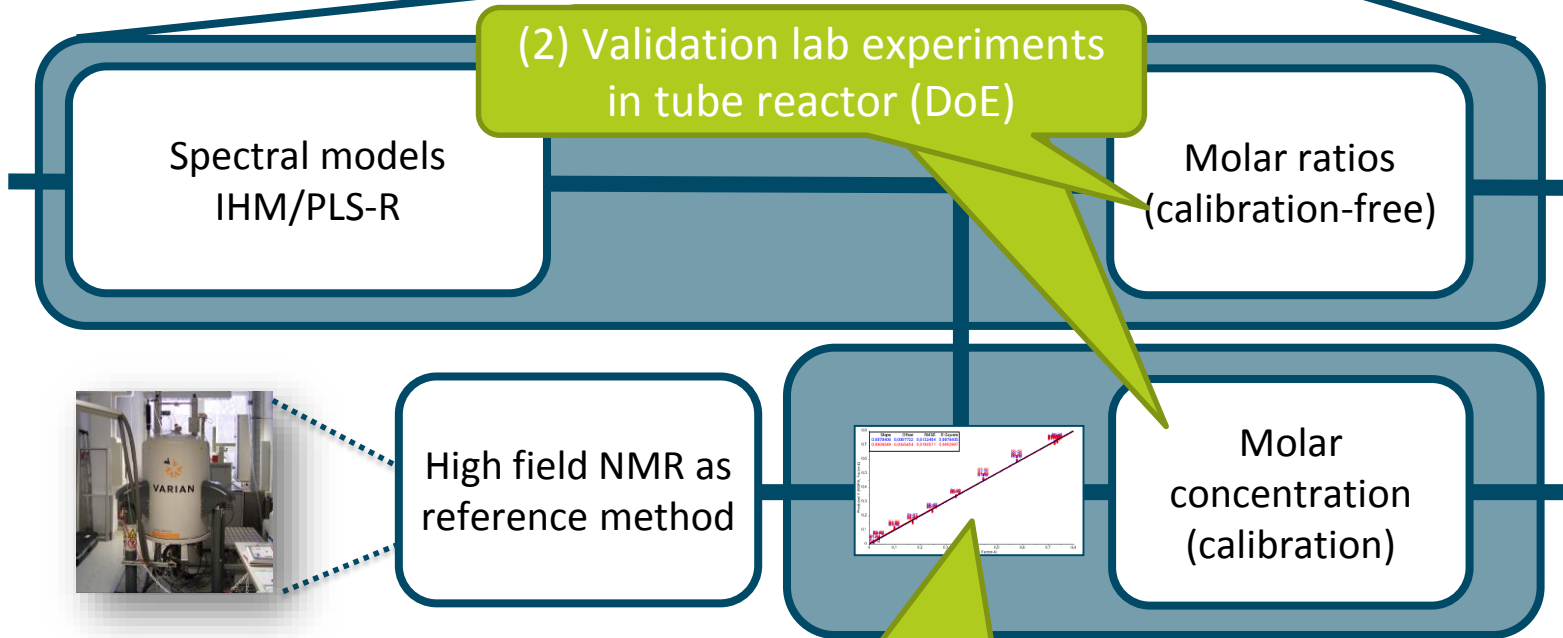
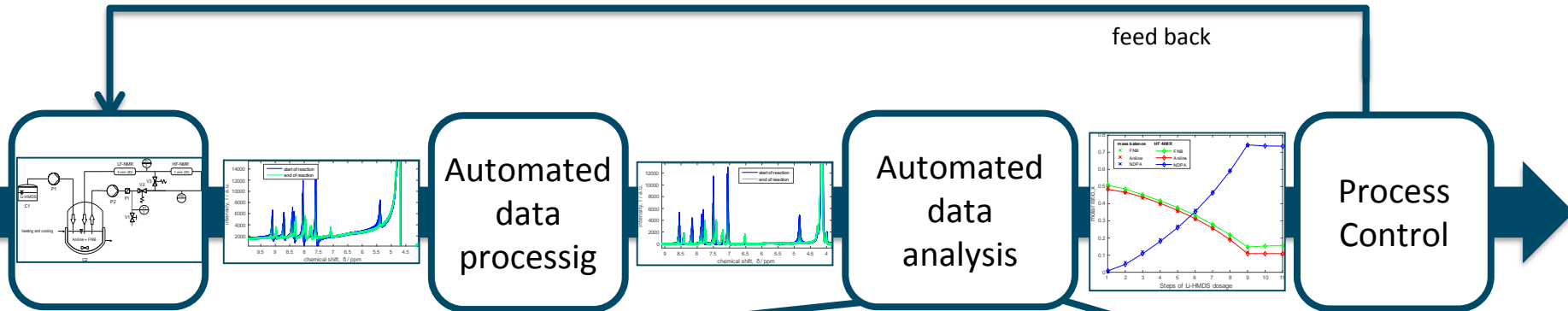
Intensified synthesis of organic compounds



Reaction Scheme:



Low Field NMR Automation Scheme



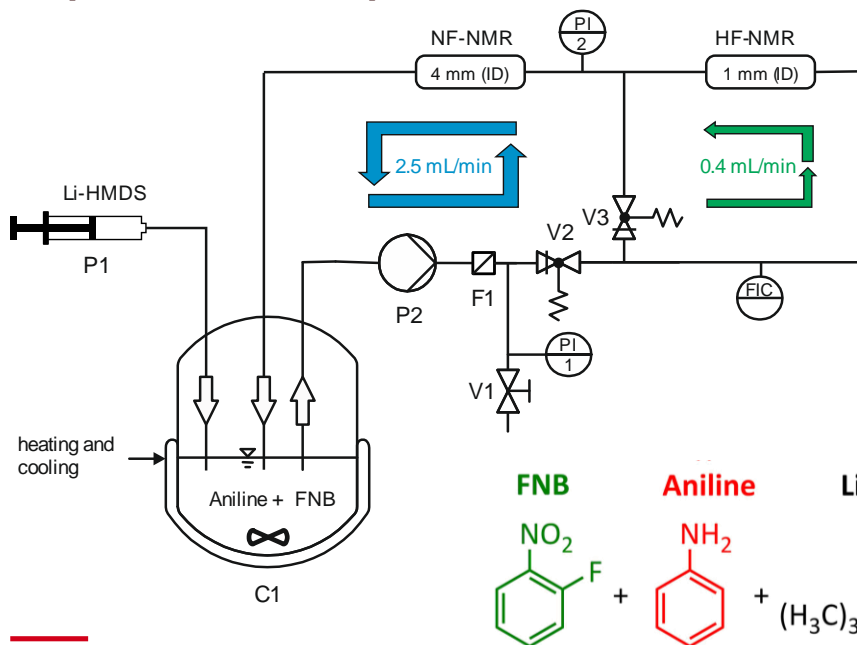
(1) Calibration

Lab experiments in batch along reaction co-ordinate

- Data in parallel acquired with high-field and low-field spectrometer
- „Fast“ and „slow loop“
- Li-HMDS was dosed stepwise

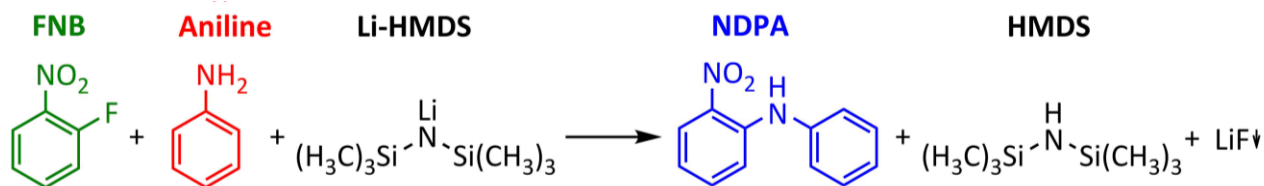


Experimental set-up

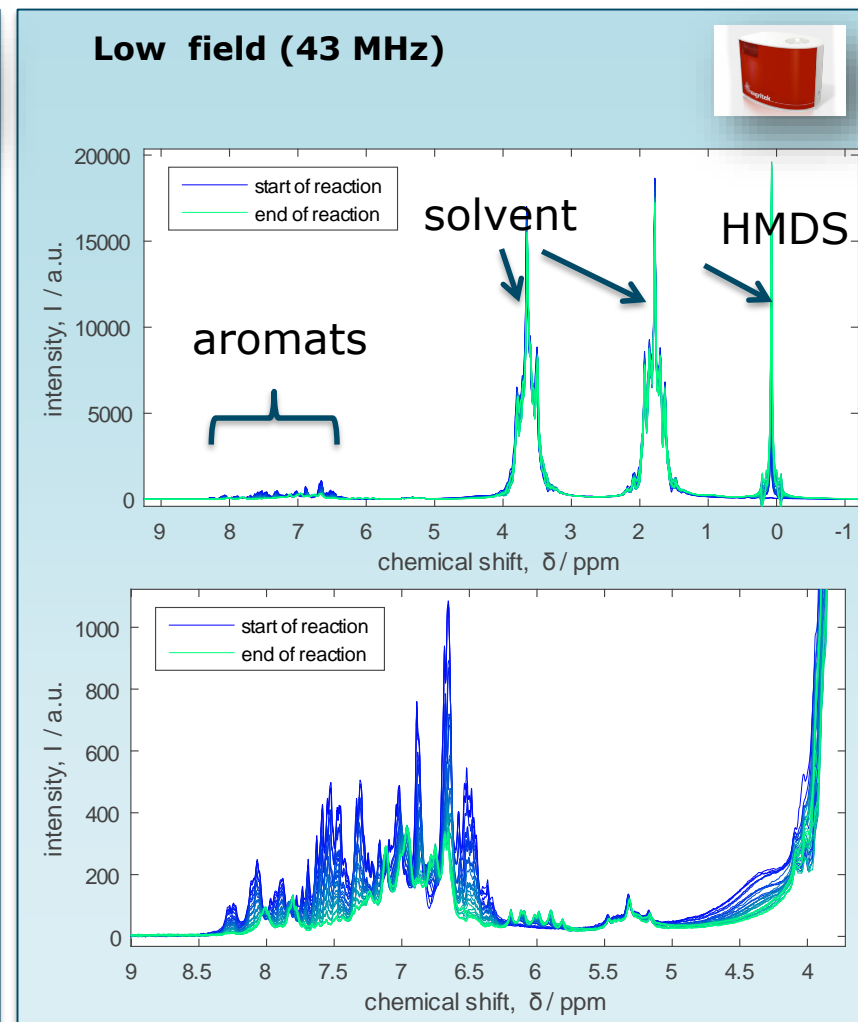
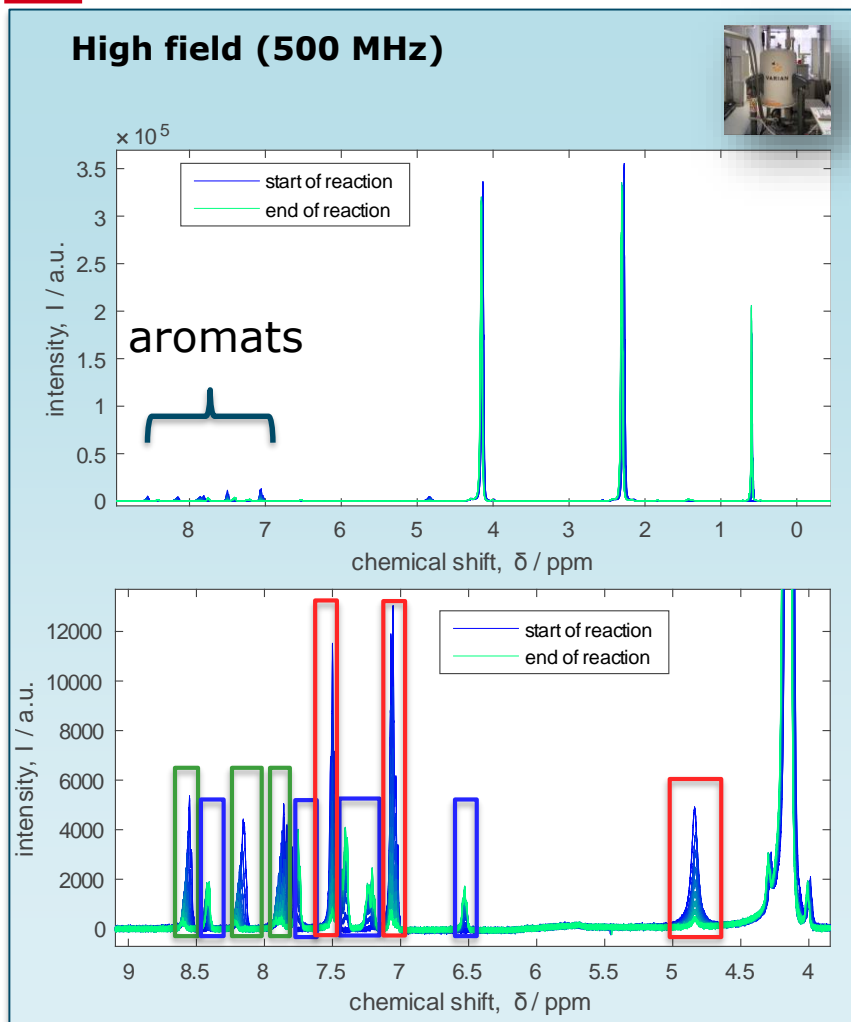


- Exothermic reaction
➔ required cooling (28.5 °C)
- Li-HMDS in two-fold excess

Reaction Scheme:



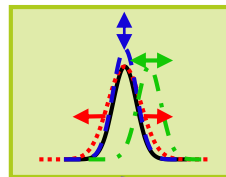
Online Proton Spectra of lithiation reaction step



Modeling → peak fitting of pure component spectra → mixture model

Analysis → "component fitting" → calculation of component area

- » Group of peaks represent pure component spectra

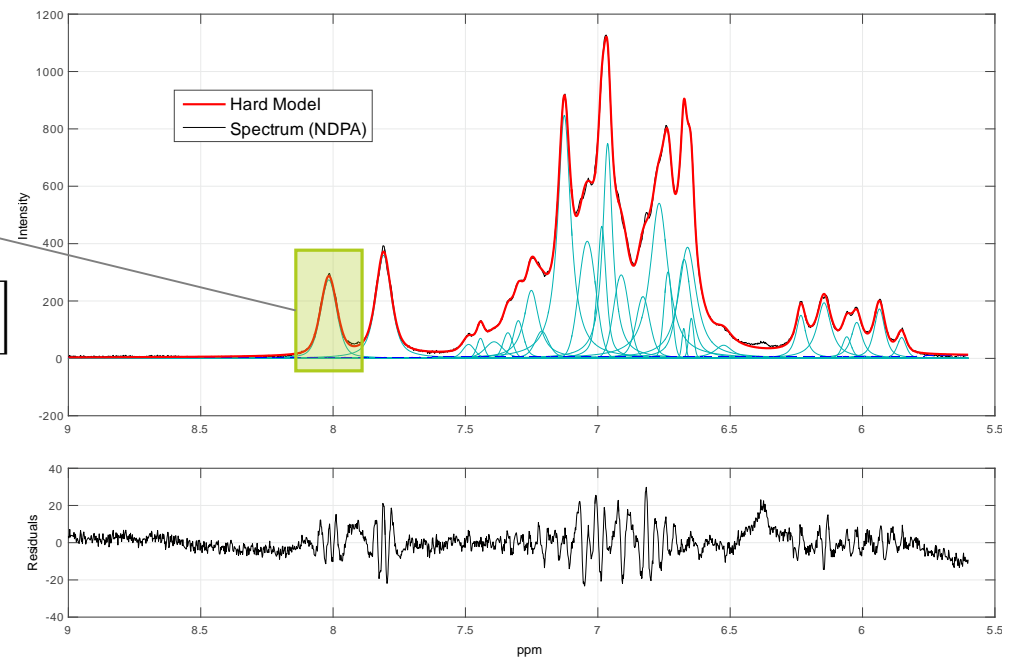


- » Pseudo-Voigt function

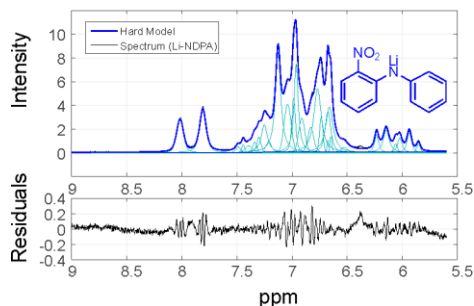
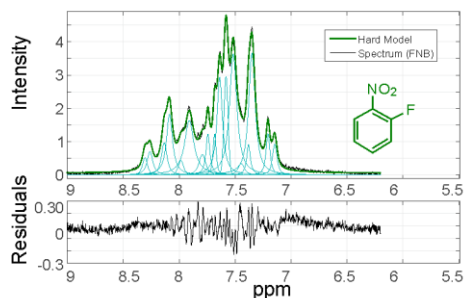
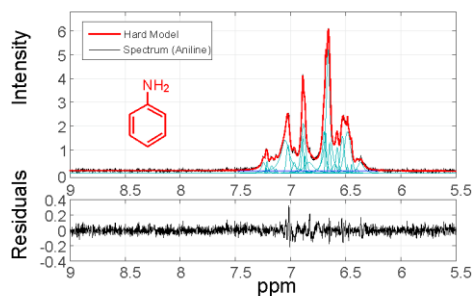
$$V = \alpha \left[\beta \cdot \exp\left(-\ln(2) \frac{(x - \delta)^2}{\gamma^2}\right) + (1 - \beta) \frac{\gamma^2}{(x - \delta)^2 - \gamma^2} \right]$$

α = peak maximum
 β = Gaussian-Lorentzian-ratio
 γ = half width
 δ = center position

Hard model for pure components



Pure component models

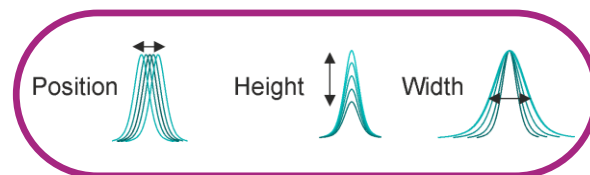


Mixture model



Modeling → Mixture model

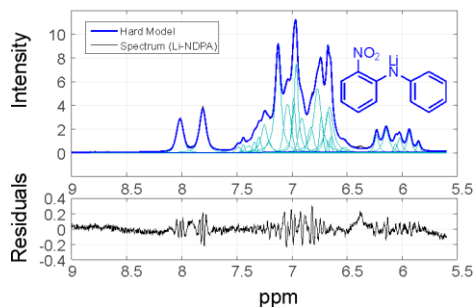
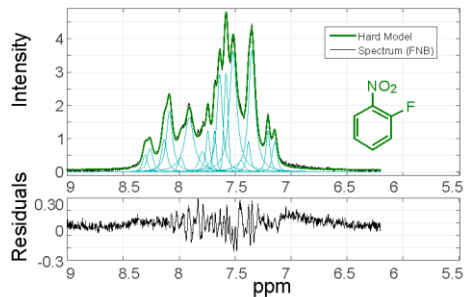
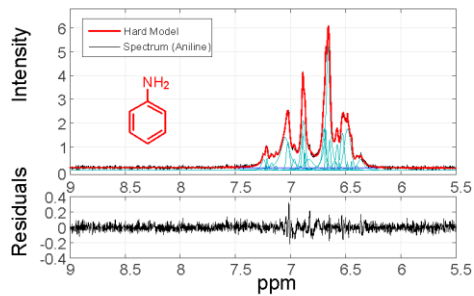
No. components	3
Peaks per component	22, 21, 28
Degree of freedom (total free parameters)	292
Considered interacting peaks	25
Max. peak shift	0.01 ppm
...	...



Peak area ratio for each pure component model is kept constant!

IHM – „component fitting“

Pure component models

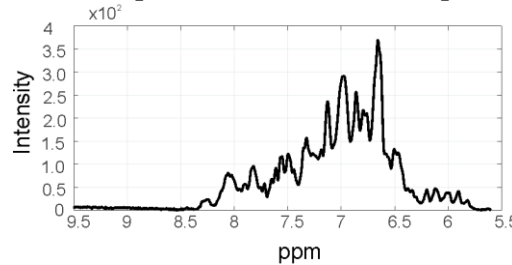


Analysis "component fitting"

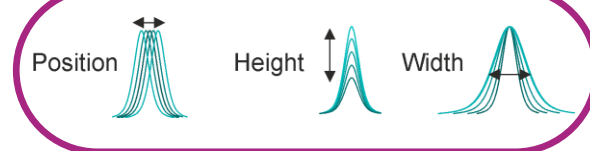
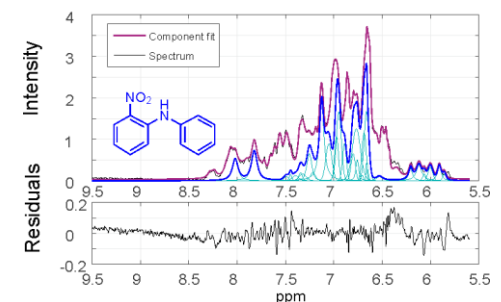
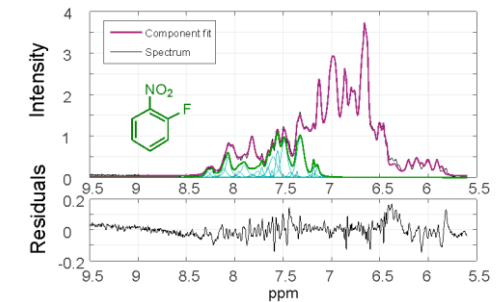
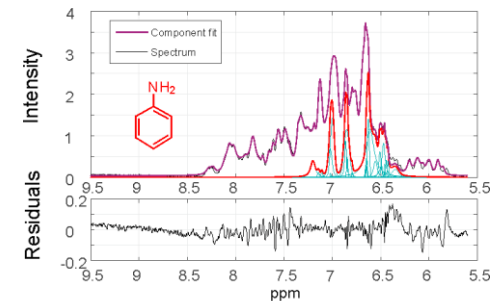
Mixture model

Component fitting

Experimental Spectrum



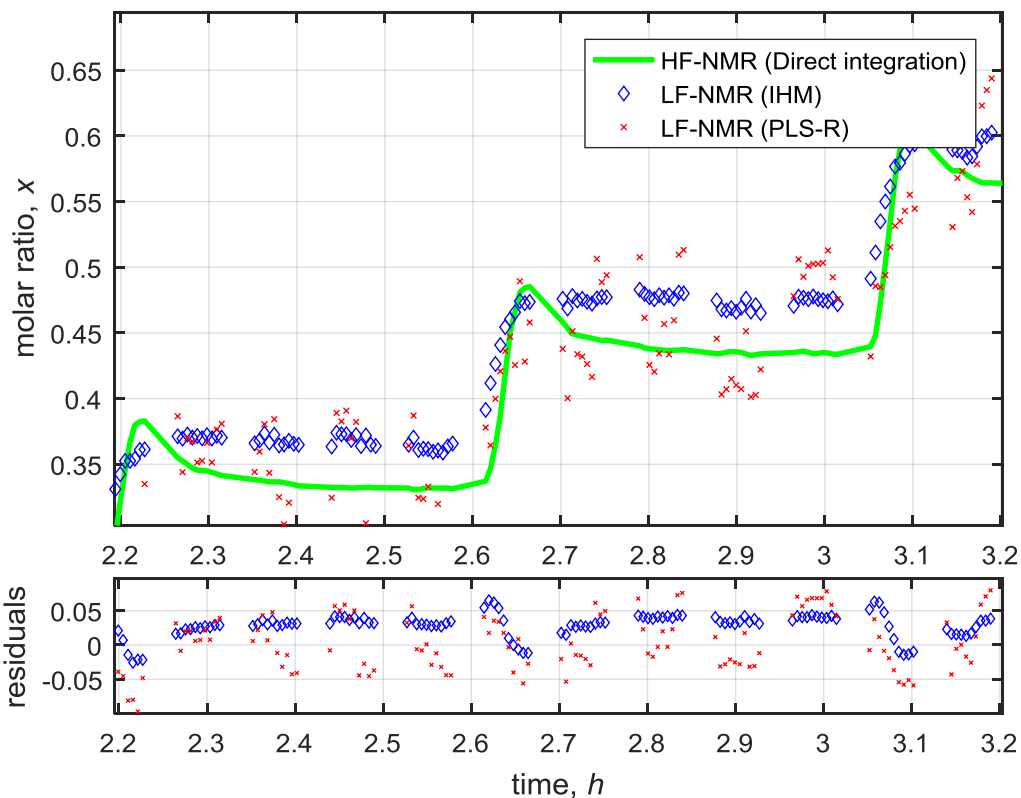
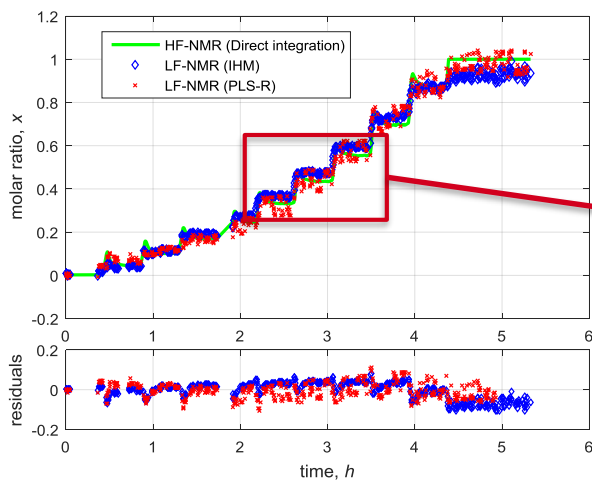
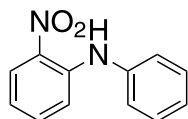
Deconvoluted spectrum



(1) Calibration: Results for Product NDPA BAM

Lab experiments in batch along reaction co-ordinate

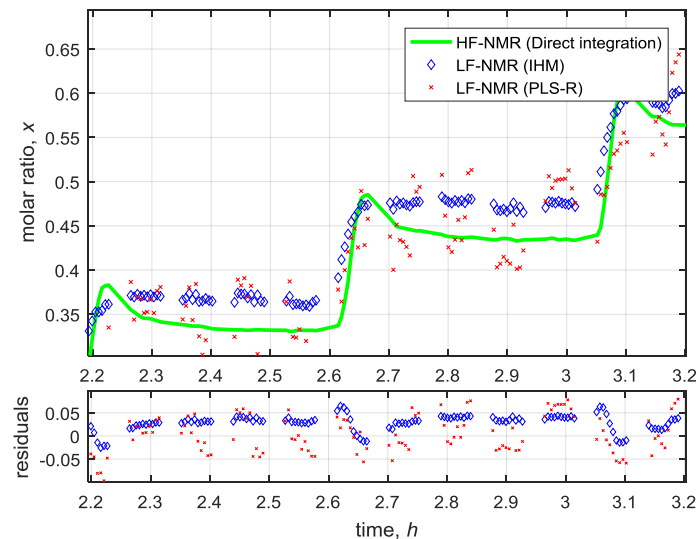
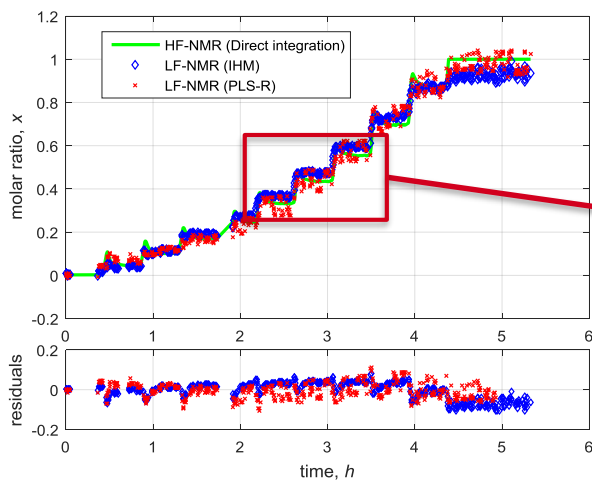
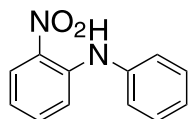
NDPA



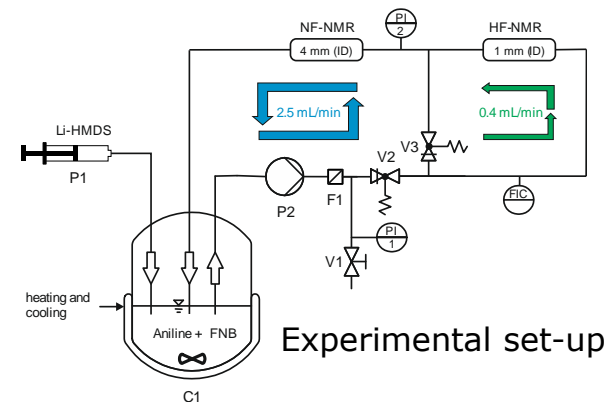
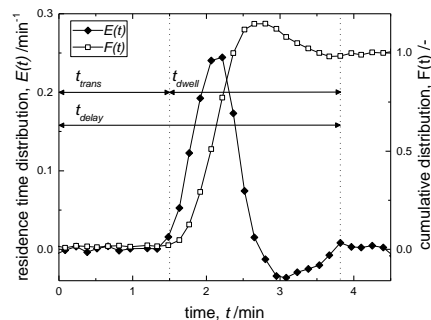
(1) Calibration: Results for Product NDPA

Lab experiments in batch along reaction co-ordinate

NDPA



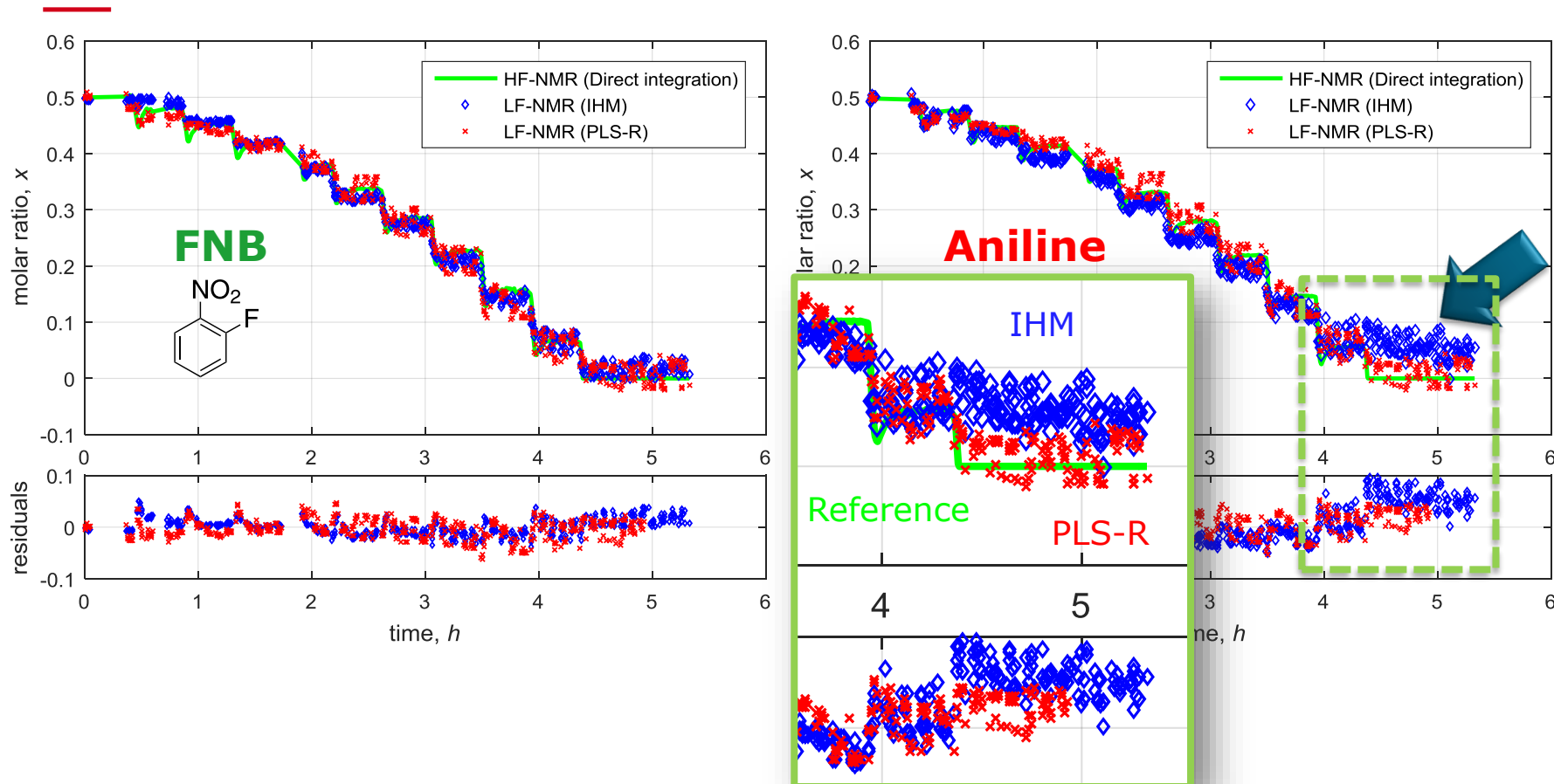
Residence time distribution (RTD) for HF-NMR and NF-NMR varies



Experimental set-up

(1) Calibration: Results for Substrates

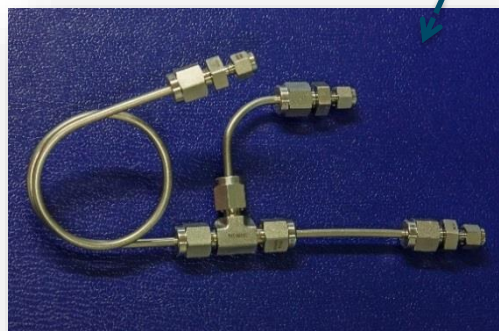
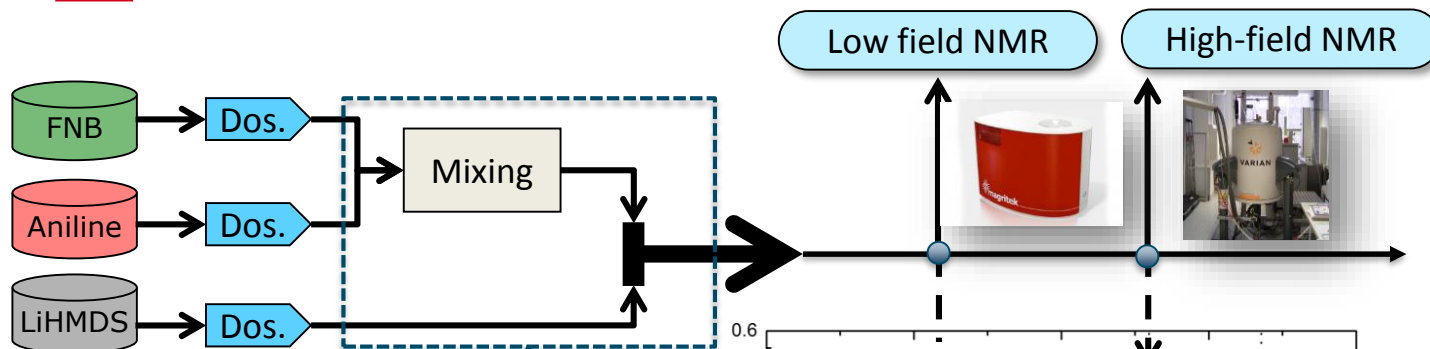
Lab experiments in batch along reaction co-ordinate



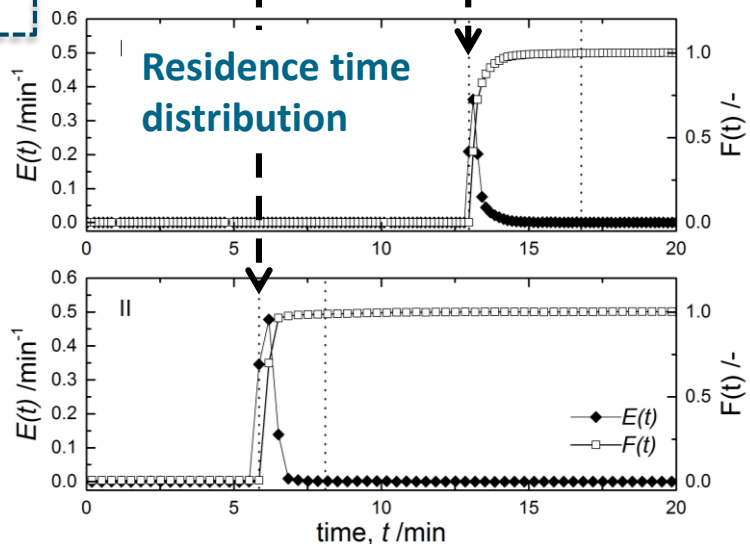
- Low concentration of Aniline difficult
- prediction uncertainty 5-7 % relative, i.e., 0.25-0.35 % absolute

(2) Validation lab experiments in tube reactor

Continuous Lithiation Reaction Set-up at BAM



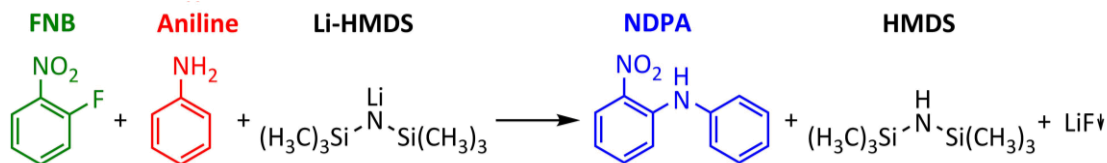
» same residence time as pilot plant



» Experimental design for validation of spectral models

» Full conversion was achieved

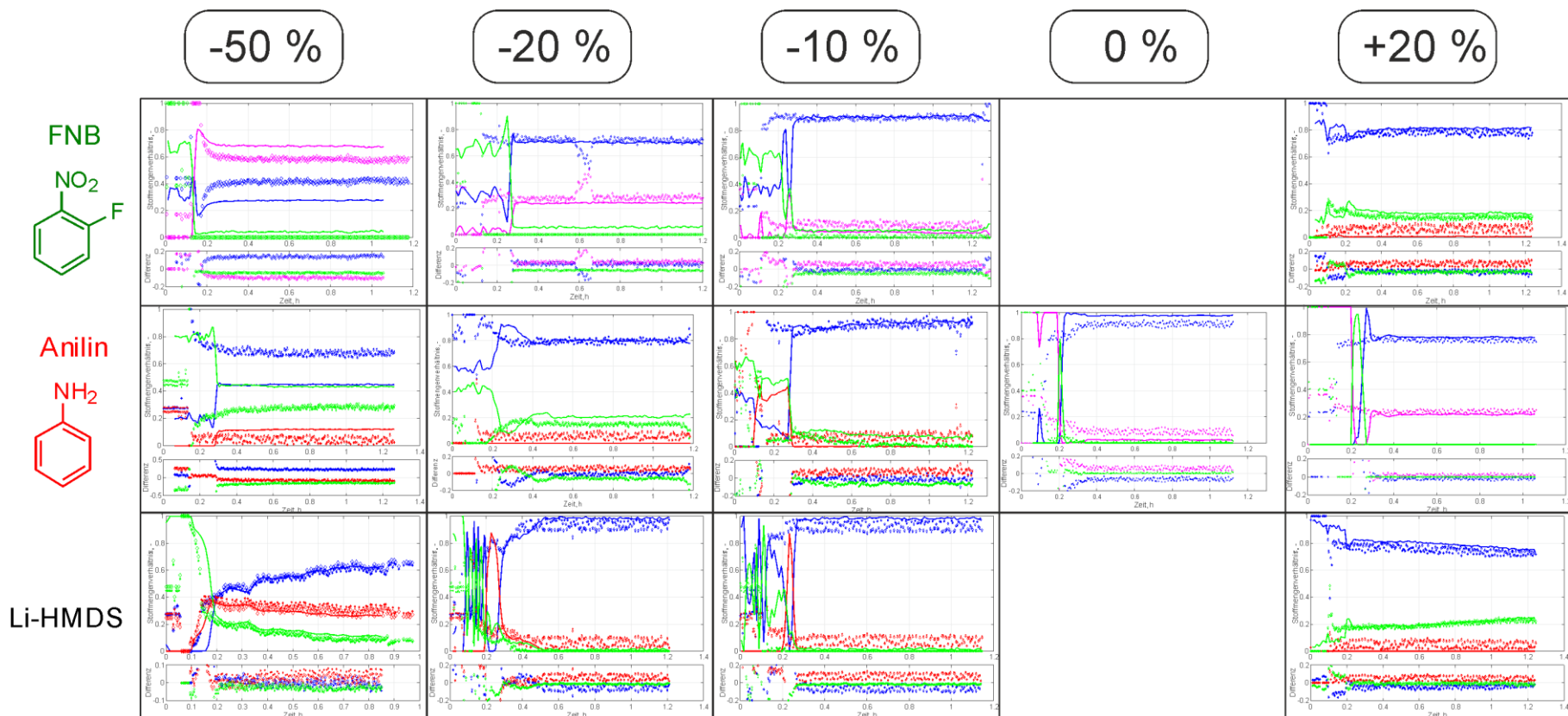
Reaction Scheme:



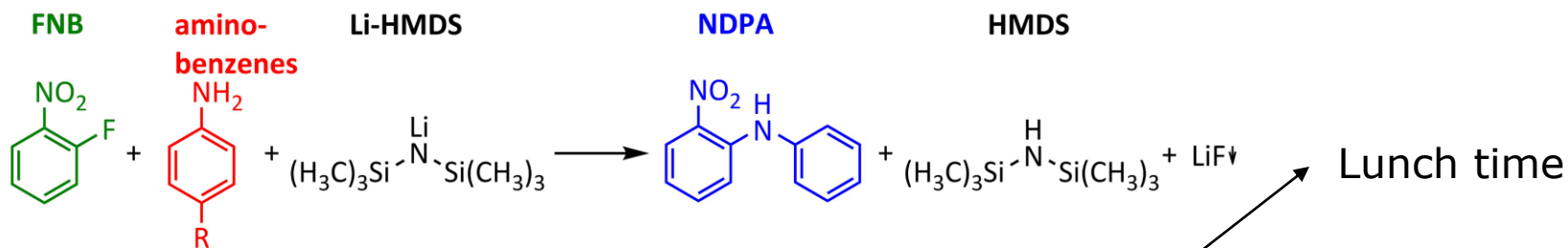
(2) Validation lab experiments in tube reactor

Continuous Lithiation Reaction Set-up at BAM

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

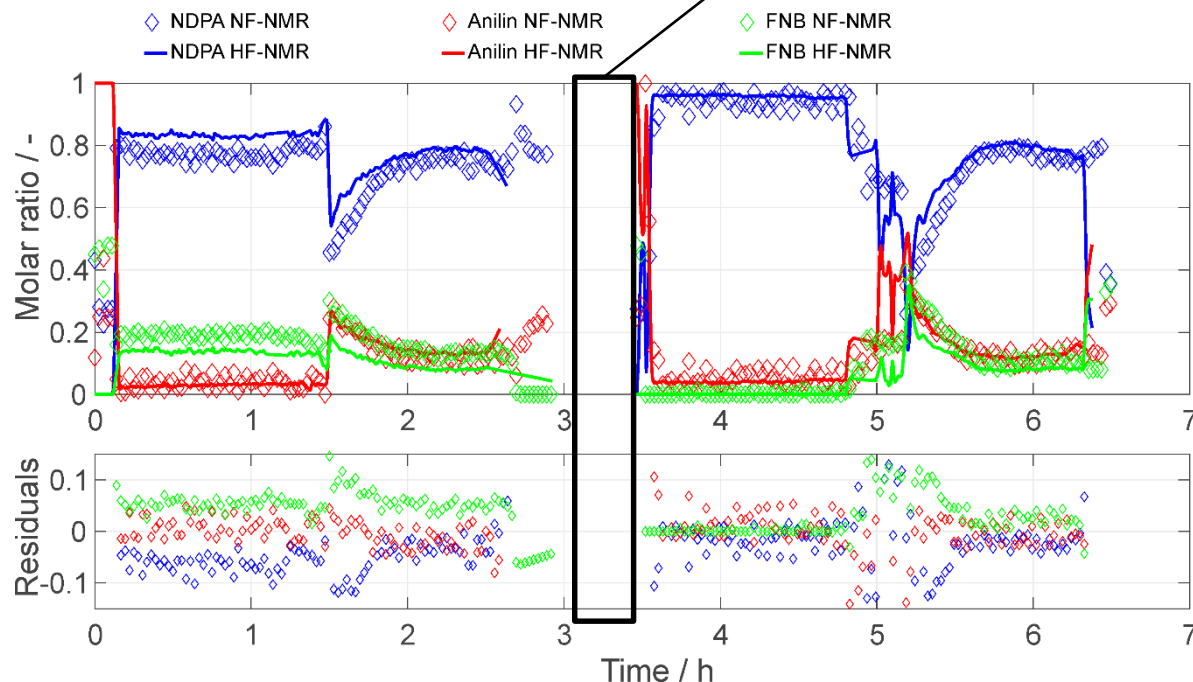


Monitoring of continuous aromatic substitution reaction by low field NMR



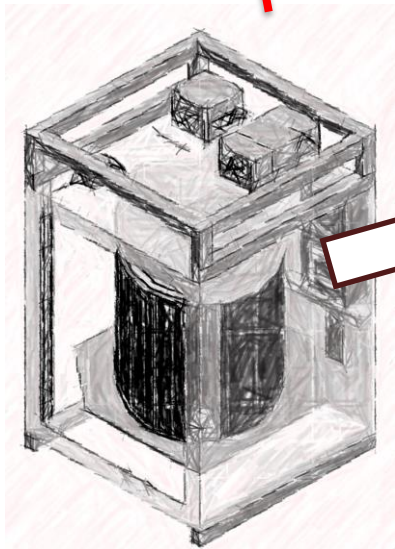
R = H, CH₃, F

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



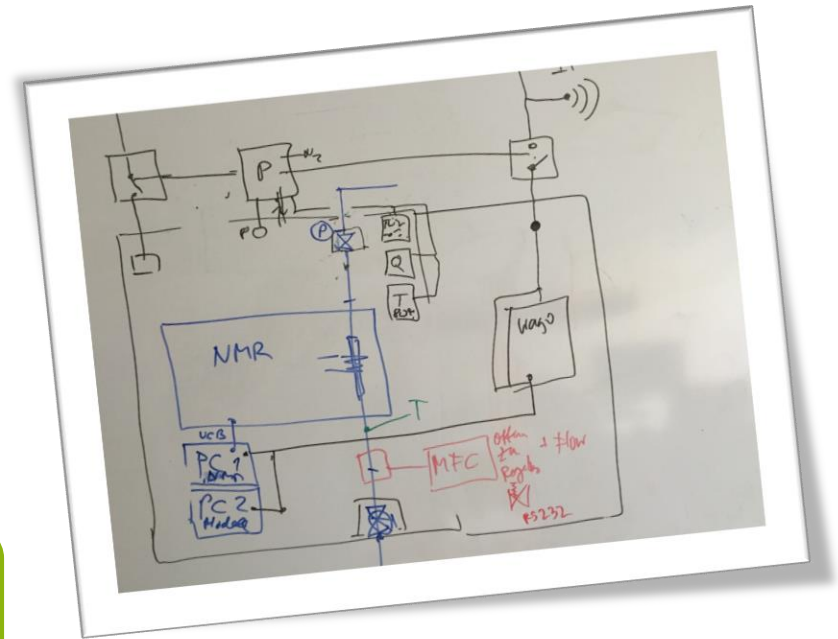
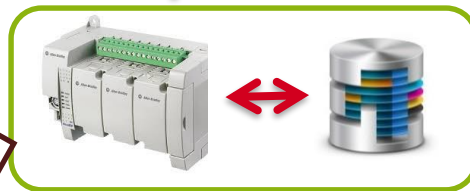
Communication concept and automation

Safety Information
- Leakage, T , p



NAMUR
status signals

Conventional
4-20 mA



OPC-UA
Client

ATEX-proof

Fast field bus



Closing the gap...

Key Attributes of NMR Spectroscopy for Industrial Online Applications

Laboratory research

Sensitivity/sufficient S/N ✓

Long term stability ✓

Validation in lab scale ✓

Spectral assignments ✓

Dispersions and Emulsions ✗

Chemical industry

ATEX/Explosion proof ✓

PLC interfaces (✓)

Automated data analysis ✓

Validation in industrial environment ✗

Thermostated and optimised flow probes ✗

Smart Field Bus ✗



qNMR SUMMIT 2017

March, 16th–17th 2017

Berlin, Germany



- Discussion of the current status of qNMR
- Scientific exchange concerning, ISO17025, validation, ring tests, quantification capabilities, and statistical methods
- Enhanced cooperation of all qNMR groups at international level
- Public discussion platform to promote know-how transfer
- Support of co-operation for harmonization

Please submit your paper and register using the submission form until
February, 17th 2017

Proposed Schedule

March, 16th 2017	09:00–12:00	Workshop
	12:00–14:00	Lunch/Finger food – Registration
	14:00–18:30	qNMR-Summit (lectures + open space discussion)
March, 17th 2017	20:00	Social Program
	08:30–13:00	qNMR-Summit (lectures + open space discussion)
	13:00–14:00	Lunch/Finger food
	14:00	End of event

Location

Bundesanstalt für Materialforschung und -prüfung (BAM)
Branch Adlershof
Richard-Willstätter-Str. 11
12489 Berlin
Germany
Building 8.05 / Lecture Hall 201 + 202

Contact and paper submission

Dr. Michael Maiwald
Bundesanstalt für Materialforschung und -prüfung (BAM)
e-mail michael.maiwald@bam.de
phone +49 30 81 04 – 11 40

Conference Website

<http://nmrvalidation.org>

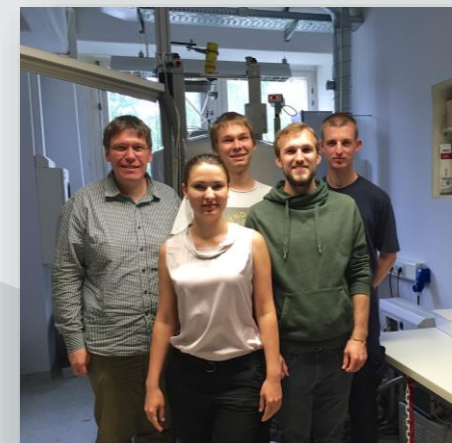
→ Upcoming events

THANK YOU!

Jürgen Kolz	Magritek
Ullrich Koch	Magritek
Juan Perlo	Magritek
Mike Bernstein	MestreLabs


Harald Pape	PTB
Clemens Minnich	S-Pact
Dirk Engel	S-Pact

NMR Group at BAM:

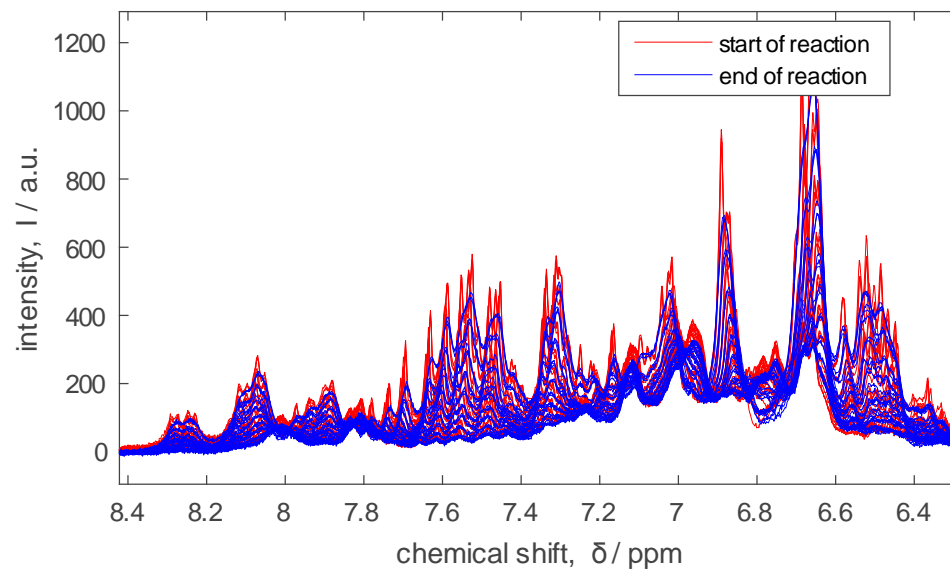


CONSENS – Integrated Control and Sensing for Sustainable Operation of Flexible Intensified Processes, funded by the European Union's Horizon 2020 research and innovation programme under grant agreement N° 636942.
www.consens-spire.eu

-
- Spectra for repeated batches vary, e.g., due to the quality of the respective shim
 - fundamental acceptance criteria for online NMR spectroscopy:

 robust data pretreatment and evaluation strategy with the potential for automation

Comparison of proton spectra of different runs



Sample Temperature and Signal-to-Noise-Ratio

5 mm PTFE tube

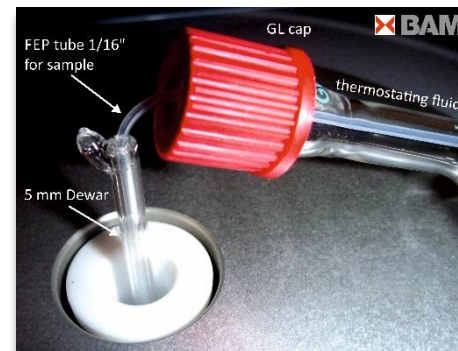
» Sample temperature: 28.5 °C

» SNR: 333

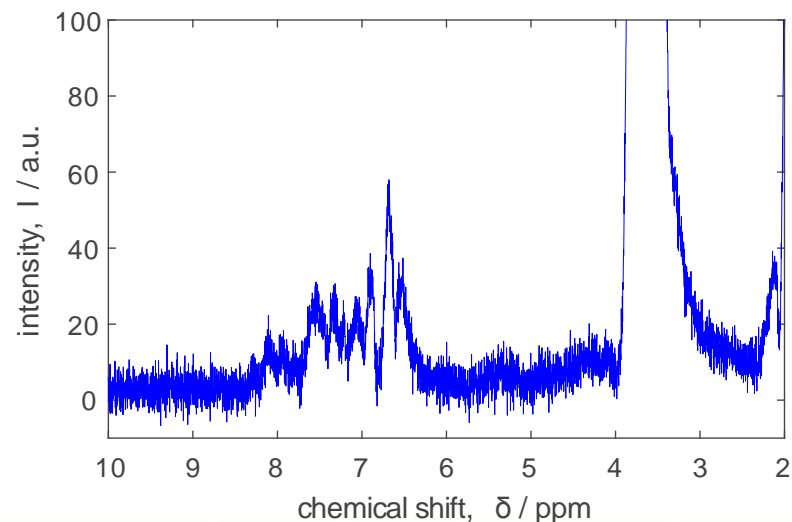
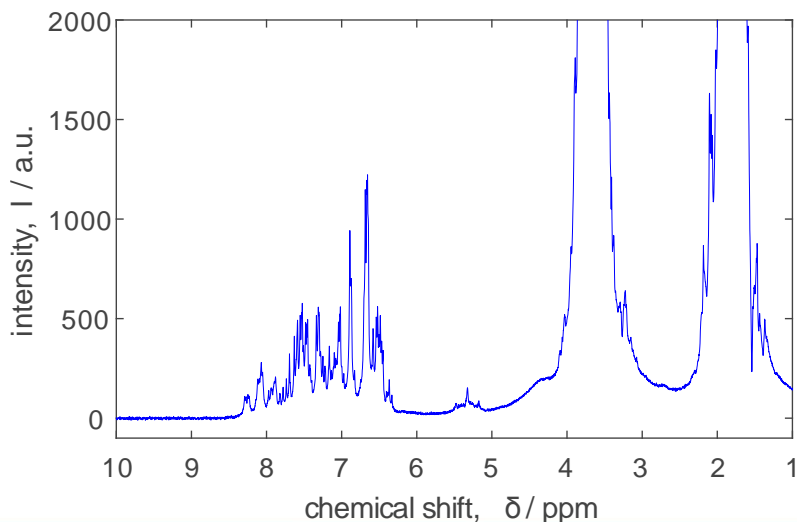
1/16 inch dewar cell

» Sample temperature: 20 – 60°C

» SNR: 8



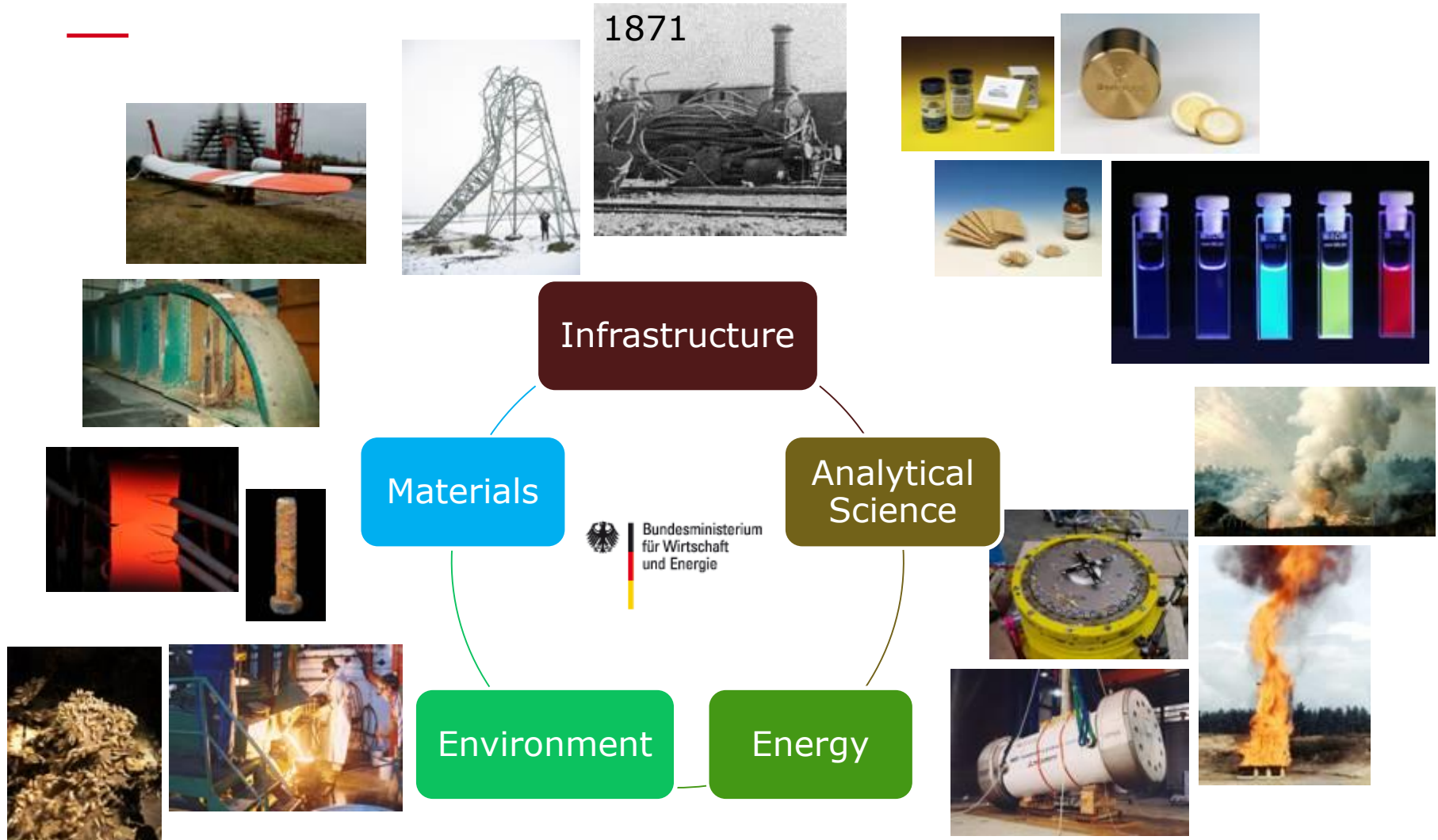
Aniline/FNB Mixture (10 w%)



Safety in Technology and Chemistry



Our Key Areas



BAM is a senior scientific and technical Federal institute with responsibility to Federal Ministry for Economic Affairs and Energy