

# Mathematical and Statistical Tools for Online NMR Spectroscopy in Chemical Processes

Simon Kern, Svetlana Guhl, Klas Meyer, Andrea Paul, Wolfram Bremser, and Michael Maiwald

Bundesanstalt für Materialforschung und -prüfung (BAM), Richard-Willstätter-Str. 11, D-12489 Berlin, Germany

## Motivation

- New "plug and produce" concept
  - Modular and standardized chemical production elements
  - Novel online sensors
  - Closed-loop control methods
- More efficient and flexible low to medium scale production for specialty chemicals.
- Specific challenges are
- Higher quality levels: more accurate sensors
  - Innovative products: fast design, engineering and optimization
  - short set-up times



Fig. 1: Containerized modular plant (source: INVITE GmbH)

## Plug and Produce Concept for a Lithiation Reaction

The laboratory set-up at BAM exhibits same reactor residence times as plant using controlled syringe pumps and NMR analyzers.

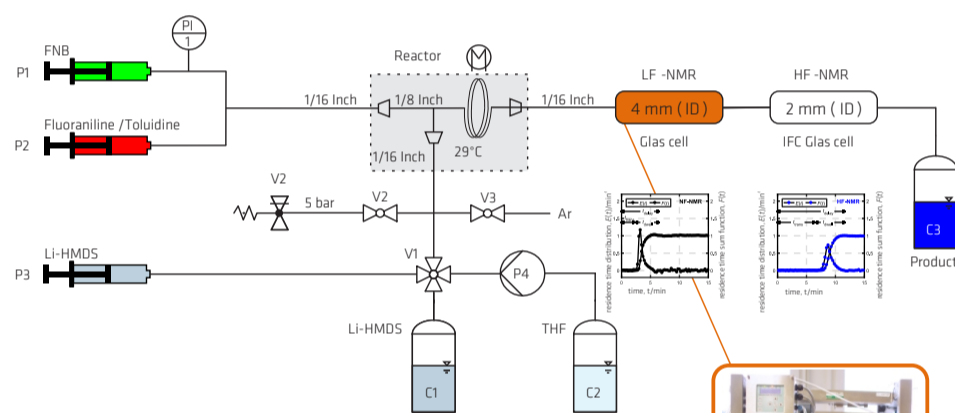


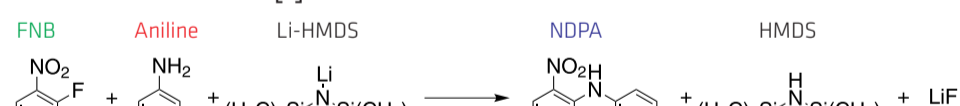
Fig. 2 (top): Concept and flow scheme of the lithiation reaction in continuous mode at BAM as a scale-down of the real modular plant

Fig. 3 (right): Field demonstrator featuring ATEX housing for spectrometer and electronics, embedded PC for automated data preparation and analysis, programmable logic controller (PLC) connected to plant process control system (PLS)



## Model Reaction and Specific Challenge

In CONSENS, two aromatic substances (Eq. 1) are coupled by a lithiation reaction [1]:



Eq. 1: Reaction scheme, FNB: 1-Fluoro-2-nitrobenzene, Li-HMDS: Lithium bis(trimethylsilyl)amide, NDPA: 2-Nitrodiphenylamine

## Online Spectra of Lab Experiments

In a first step the reaction was performed in batch mode. The Li-HMDS was dosed stepwise. Spectra were acquired with a high field and a benchtop instrument (Fig. 4) in order to produce first spectral data.

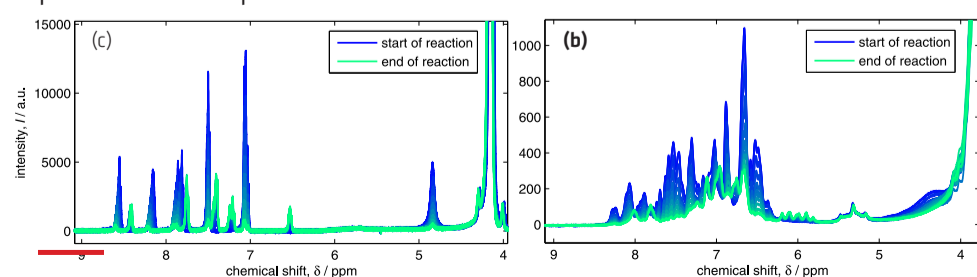
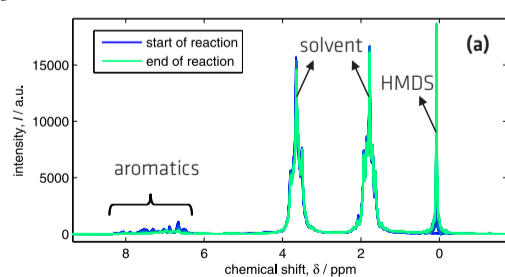


Fig. 4: (a) Complete spectrum (43 MHz) and aromatic region of shift corrected <sup>1</sup>H spectra at (b) 500 MHz and (c) 43 MHz for the lithiation reaction

## Physically Motivated Spectral Models

When it comes to NMR data evaluation under industrial process conditions, the shape of signals can change drastically due to nonlinear effects. Additionally, the multiplet structure becomes more dominant because of the comparably low-field strengths which results in overlapping of multiple higher order NMR signals. For this reason, Indirect Hard Modeling (IHM) was chosen for NMR data analysis, which is depicted in Fig. 5. Pure components models can be derived from first principles information, e.g., NMR predictors.

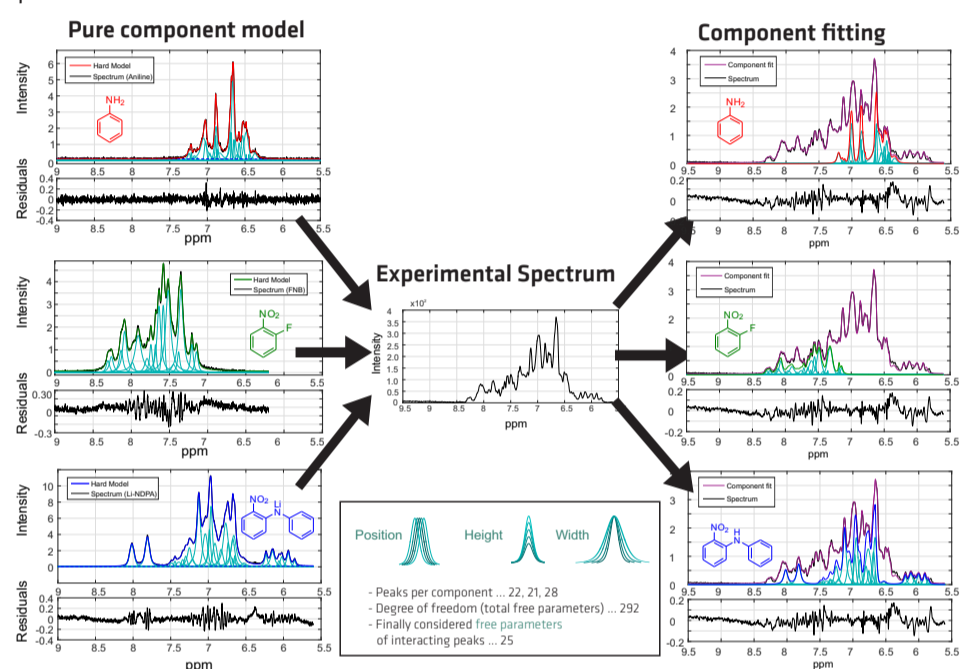


Fig. 5: Data analysis scheme for Indirect Hard Modeling (IHM) of the aromatic region (see Fig. 4b) of the NMR spectrum: left: pure component models are built upon NMR spectra of the reactands and products; middle: experimental spectrum; right: representation of the experimental spectrum by adjustment of the three pure component models. Selected parameters of Lorentzian-Gaussian functions such as position, height, or width can be optimized to account for line shifts or other non-linear effects along the course of the reaction (see frame).

## Validation Runs according to Design of Experiments

A considerable number of continuous experiments were performed for validation according to a DoE (Fig. 6b) taking account for various reaction conditions by individually adjusting the flow rates of the reagents aniline, FNB, and Li-HMDS. Figure 6a depicts amount of substance fractions observed with the NMR sensor and the IHM methods over an observation period of six hours.

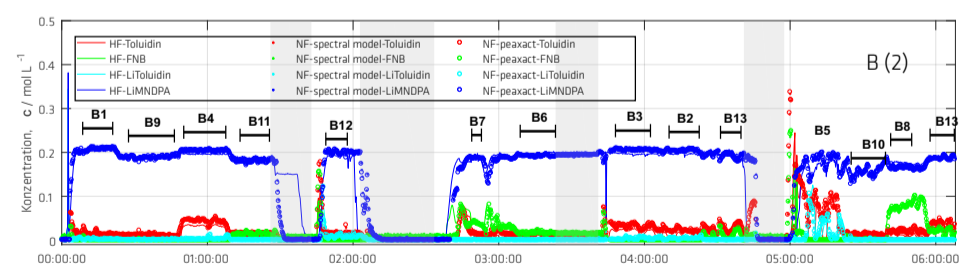
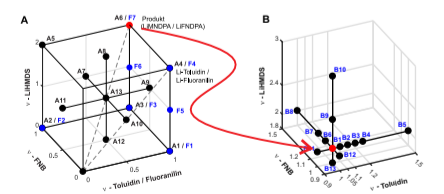


Fig. 6a (top): The largest prediction uncertainties in mole fractions were found for aniline to be 5-7% relative, i.e., 0.25-0.35% absolute. Fig. 6a (right): Design of Experiments for validation run.



## References and Acknowledgements

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