

# Reading Between the Lines – Automated Data Analysis for Low Field NMR Spectra

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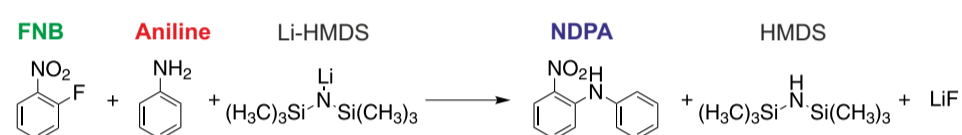
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## Motivation

For reaction monitoring using NMR instruments, in particular, after acquisition of the FID the data needs to be corrected in real-time for common effects using automated methods. When it comes to NMR data evaluation under industrial process conditions, the shape of signals can change drastically due to nonlinear effects. However, the structural and quantitative information is still present but needs to be extracted by applying predictive models.

## Model Reaction

In the studied model reaction two aromatic substances (Eq. 1) are coupled initiated by a lithiation step:



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

## Online NMR Spectra

- Reaction was investigated in semi-batch mode
- Two spectrometers (43 MHz and 500 MHz) were connected to process in by-pass via flow cells

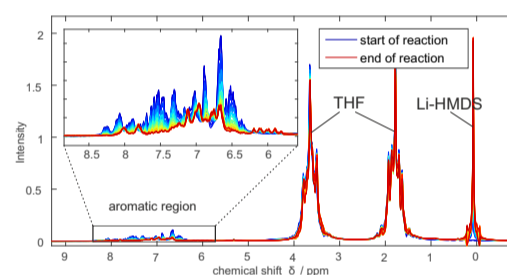
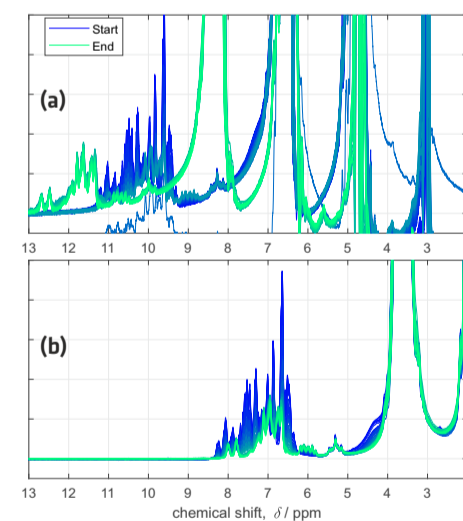


Fig. 1: Online low-field NMR spectra (43 MHz), single scan each 15s

## Automated Data Processing



Acquired raw spectra were processed with the following tools:

- Phase correction (Entropy minimization method, [1])
- Baseline correction (Low-order Polynomial fit, [2])
- Alignment (icoshift [3])

Fig. 2: Online low-field NMR spectra (43 MHz), (a) raw spectra, (b) processed spectra

## Quantitative Results and Online Validation

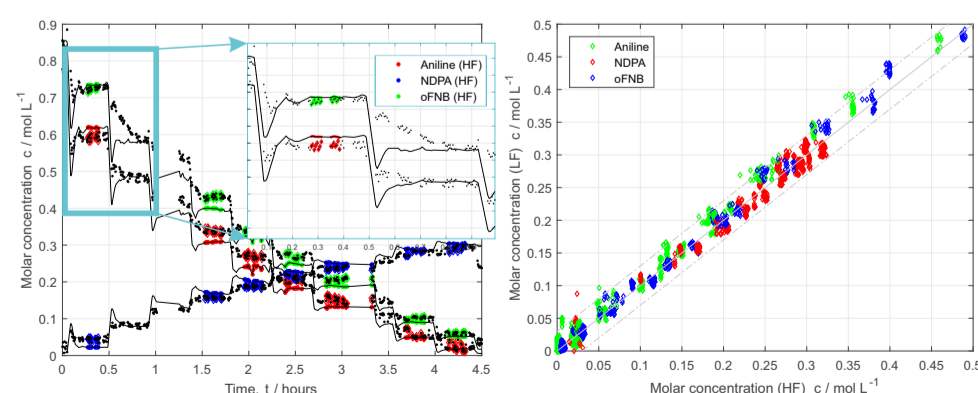


Fig. 3: Concentration during semi-batch measured via high-field NMR (lines) and low-field NMR (dots) with steady state classification

Fig. 4: Comparison of high-field and low field NMR results during steady state condition

## Spectral Modeling

Pure component models based on Pseudo-Voigt functions (Eq. 2) can be derived via peak fitting of measured pure components ( $\mathbf{a}_1$ ) or by the use of spin calculations ( $\mathbf{a}_2$ ).

$$V = \alpha \left[ \beta e^{-4 \ln 2 \frac{(x - \delta)^2}{\gamma^2}} + (1 - \beta) \frac{\gamma^2}{(x - \delta)^2 + \gamma^2} \right]$$

Eq. 2: Pseudo-Voigt Function

### (a) Empirical Generation of Pure Component Models

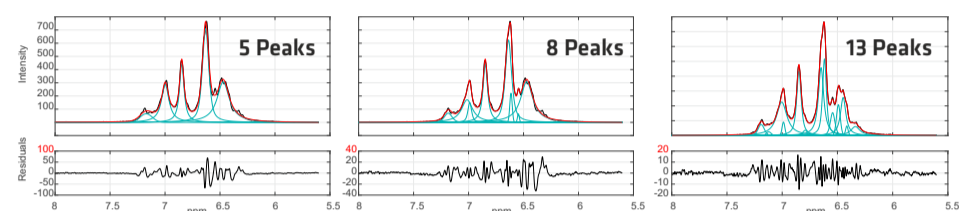


Fig. 5: Residuals during peak fitting of pure components (aniline) increase with number of peaks

### (a) Physically Derived Pure Component Models

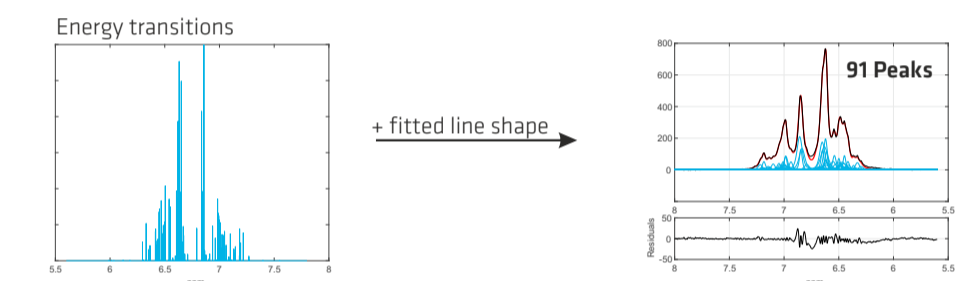


Fig. 6: Calculation of pure component model based on spin calculations (NMR Solutions, Kuopio)

### (b) Model Fitting to Mixture Spectrum

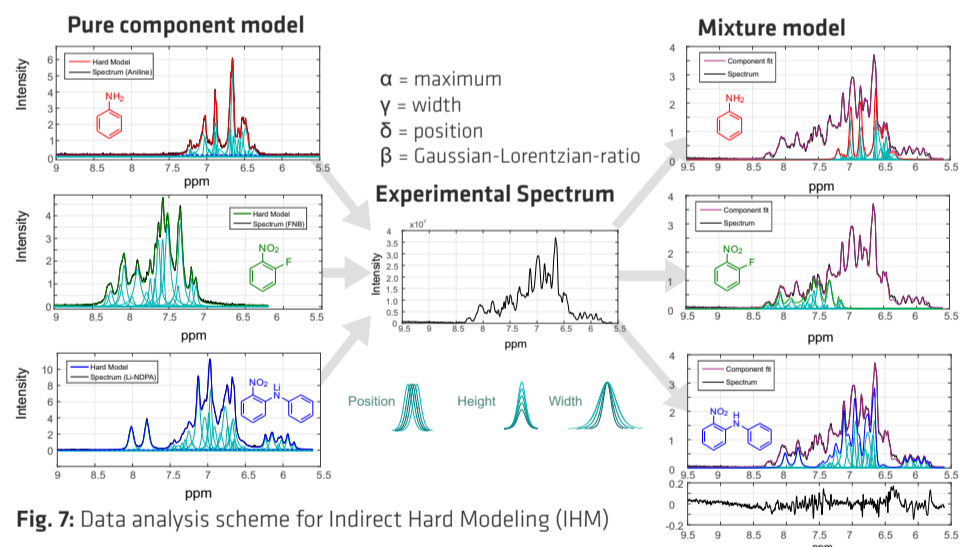


Fig. 7: Data analysis scheme for Indirect Hard Modeling (IHM)

## Discussion

- Good agreement between LF and HF NMR spectrometers
- Suitable method for monitoring the model reaction
- Challenging at low substrate concentration

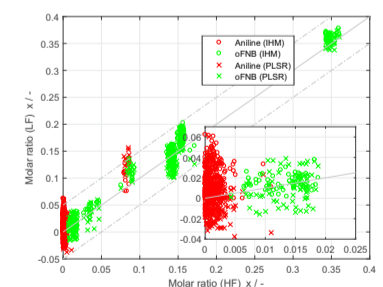


Fig. 7: Validation of data evaluation for continuous lithiation process

## References

- Chen et al., J Magn Reson. 2002, 158, 164-168.
- Mazet et al., Chemometrics Intell. Lab. Sys. 2005, 76, 121-133.
- Savorani et al., J Magn Reson. 2010, 2, 190-202.