

# Assessment and Validation of Various Flow Cell Designs for Quantitative Online NMR Spectroscopy

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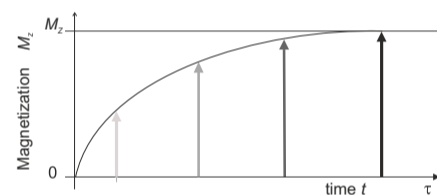
## Motivation

Online NMR reaction monitoring is usually performed in bypass systems either in continuous or stopped flow mode. Both operation procedures rely on flow-through cells instead of standard NMR tubes. In order to receive high quality spectra it is essential to choose an optimal flow cell design. This includes the cell geometry as well as the material used. The specific conditions of the chemical reaction under investigation and external factors such as safety requirements should be considered as well. For the reaction monitoring with low field (LF) NMR spectroscopy such flow-through cells for high temperature and pressure are not yet readily available.

## Flow-through Cells - Things to Consider

### Geometry

- A small bypass volume and high flow rates reduce the transfer time between the reactor and the NMR instrument.
- In order to achieve a high signal-to-noise ratio a large sample volume in the active region is beneficial.
- Full magnetization is a prerequisite for quantitative measurements limiting the usable flow rate



**Fig. 1:** Magnetization build-up is related to the longitudinal relaxation  $T_1$ . It is specific to every nucleus as well as dependent on other factors such as temperature.

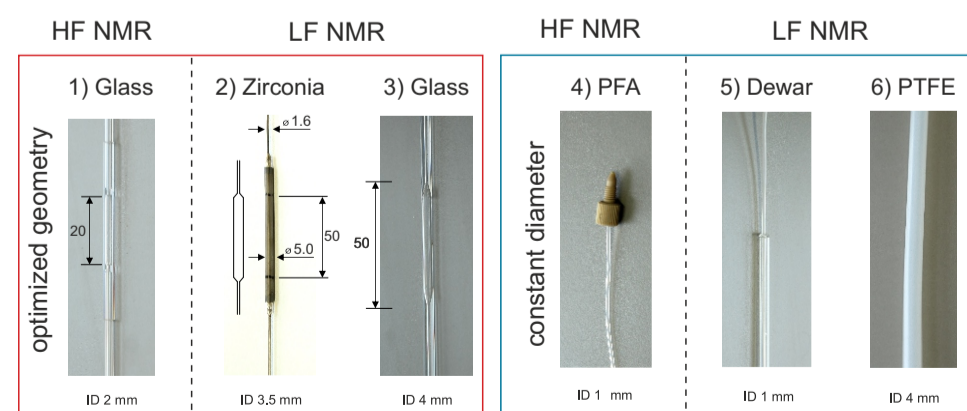
- Both, in plug and laminar flow [1, 2] the magnetization  $M$  depends on the polarization length  $L_{pol}$ , the average flow velocity  $\bar{v}$  and the longitudinal relaxation  $T_1$ .

plug flow: 
$$\frac{M}{M_0} = 1 - \exp\left(-\frac{L_{pol}}{\bar{v}T_1}\right) \quad (1)$$

### Materials

- Industrial applications demand for high pressure, temperature and chemical resistance of the flow cell material
- Only NMR-compatible materials can be used (no steel)
- Last but not least: The prices of cells differ significantly

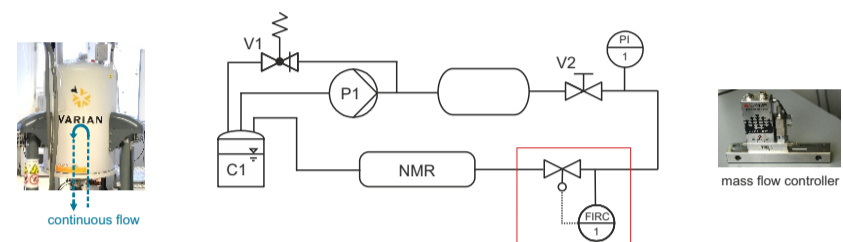
## Comparing Several HF and LF NMR Flow-through Cells



**Fig. 2:** NMR-flow-through cells made of a variety of materials: Glass, zirconia, perfluoroalkoxy alkane (PFA) and polytetrafluoroethylene (PTFE) with two different geometric designs.

## Setup for the Determination of Maximal Flow Rates

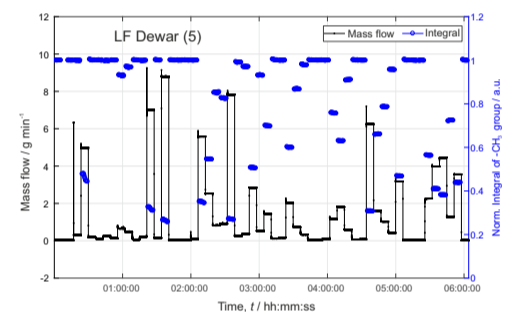
- Pump (P1) supplies a constant Ethanol pressure of 9.5 bar
- Reservoir to reduce pressure oscillations
- Random computer controlled changes of the mass flow via a mass flow controller to avoid temperature effects
- Automated acquisition of NMR spectra



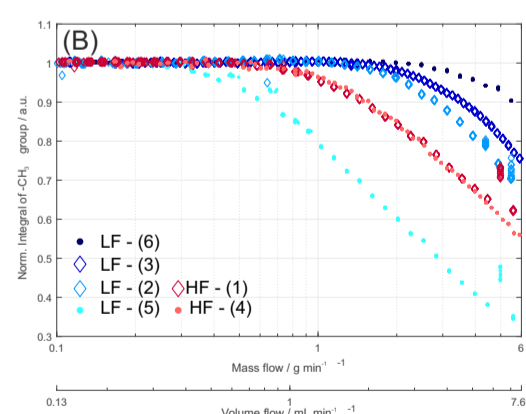
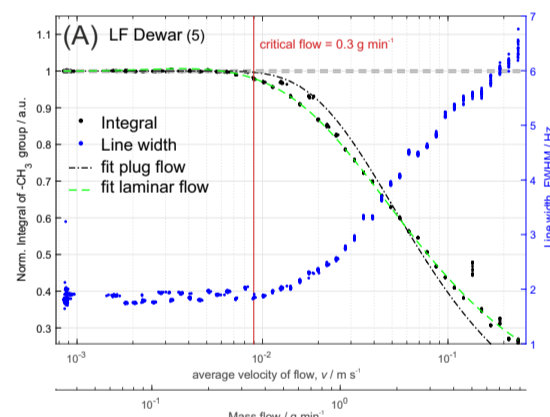
**Fig. 3:** Schematic representation of the test setup consisting of a reservoir C1, pump P1, pressure indicator PI, two valves V1 and V2, a mass flow controller and the NMR.

## Results

- More than 50 different flow rates, 15 spectra each, acquired over a period of 6 hours [3].
- At elevated flow rates the peak area decreases, the linewidth increases



**Fig. 4:** Random variation of the Ethanol flow rates and integrals recorded.



**Fig. 5:**  $\text{CH}_3$  Integrals and line widths ordered according to flow (A). Comparison of the various flow cells concerning their critical flow through rate (B).

### Optimized Geometry

- Higher flow rates and thus shorter transfer times
- More efficient premagnetization in LF NMR, not in HF NMR
- Larger volume in the active region results in a higher signal-to-noise ratio
- Experimental data fit well to a laminar flow profile model

## References

- [1] N. Zientek et al., J. Magn. Reson. 2014, 249, 53-62.
- [2] D. W. Arnod et al., J. Appl. Phys. 1965, 36, 870-871.
- [3] L. Wander, master's thesis, Humboldt Universität zu Berlin 2017.



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