In-situ characterization of SABRE catalyst activation via T_1 measurements in the Earth's Magnetic field

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1. Introduction

Efficient Signal Amplification By Reversible Exchange (SABRE)[1] hyperpolarisation for a given analyte requires the optimisation of a wide range of experimental conditions. In the standard approach, experiments are achieved using a two-stage method, where hyperpolarisation and detection are separated in time and space. Integration of a liquid nitrogen-based *para*-hydrogen generator with Earth's Field NMR (EFNMR) detection enables SABRE experiments to be performed *in situ*[2]. By combining this instrument with an active field correction device, complex experiments may be performed in a simple and reproducible manner, including time-resolved, multi-step experiments, such as the monitoring the formation of the SABRE-active catalyst.[2]

2. *In situ* SABRE at the Earth's field

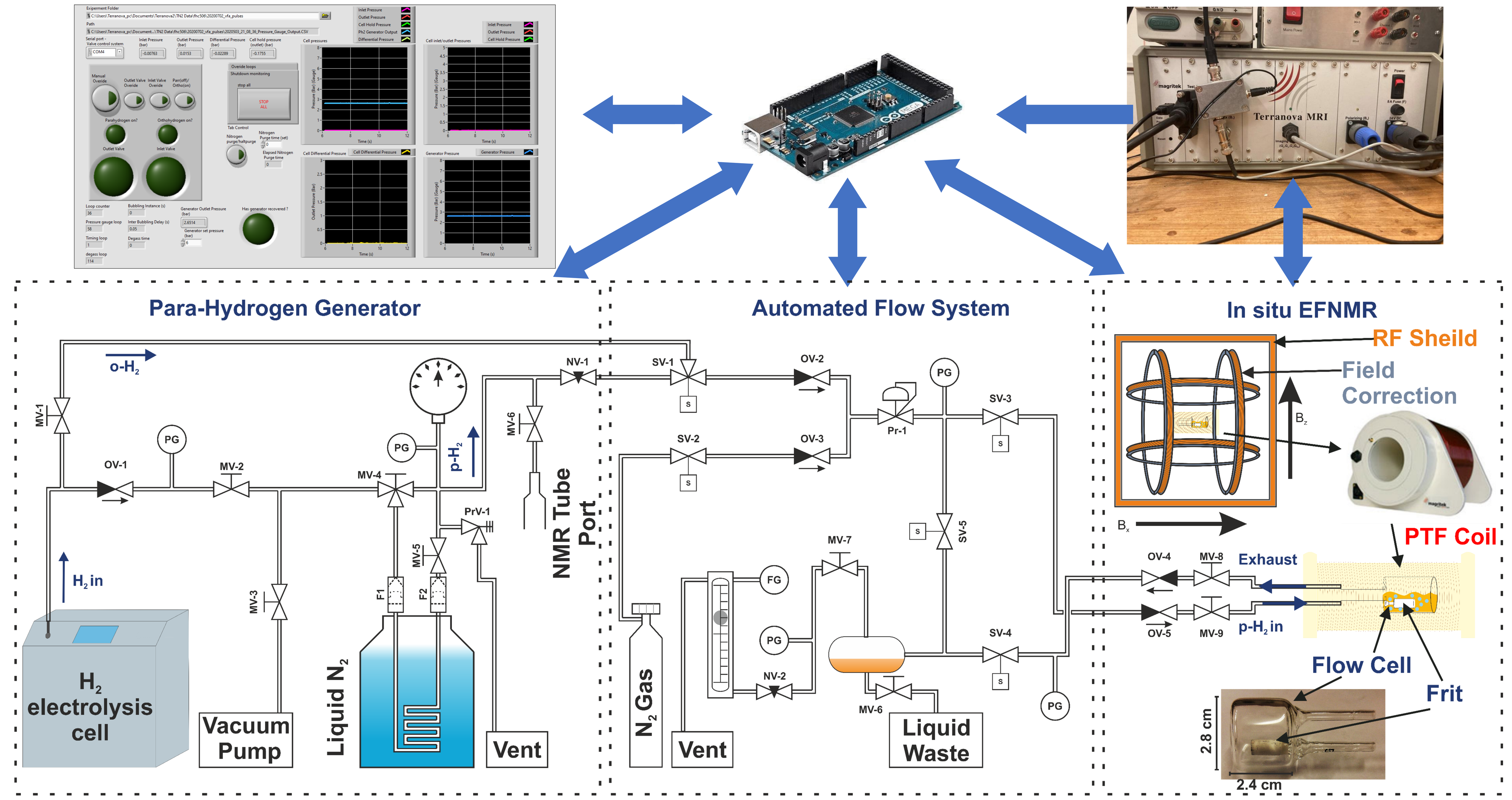

Figure 1: Simplified manifold diagram and schematic of the *in situ* SABRE system with EFNMR detection. The modular system is controlled by an Arduino MEGA via a LabVIEW front end. H_2 is produced via an electrolysis cell and enriched by a liquid N_2 generator to produce ~52 % pH_2. This is bubbled through the solution inside the EFNMR probe. The NMR detector includes a flow cell, RF shield and field correction coils. The Magritek Terranova electromagnet generates the required PTF = 65 G before NMR is performed in the Earth's field ~0.5 G.

3. Variable flip angle, single shot T_1 measurements

- A major challenge of the EFNMR is calibration of NMR parameters such as RF flip angle due to the low Larmor frequency and the variable orientation of B_E relative to B_1.
- Careful optimisation of RF parameters and EFNMR probe orientation allow for accurate pulse calibration and the implementation of a **Single Shot Variable Flip Angle hyperpolarisation** lifetime (T_1) measurement[3].

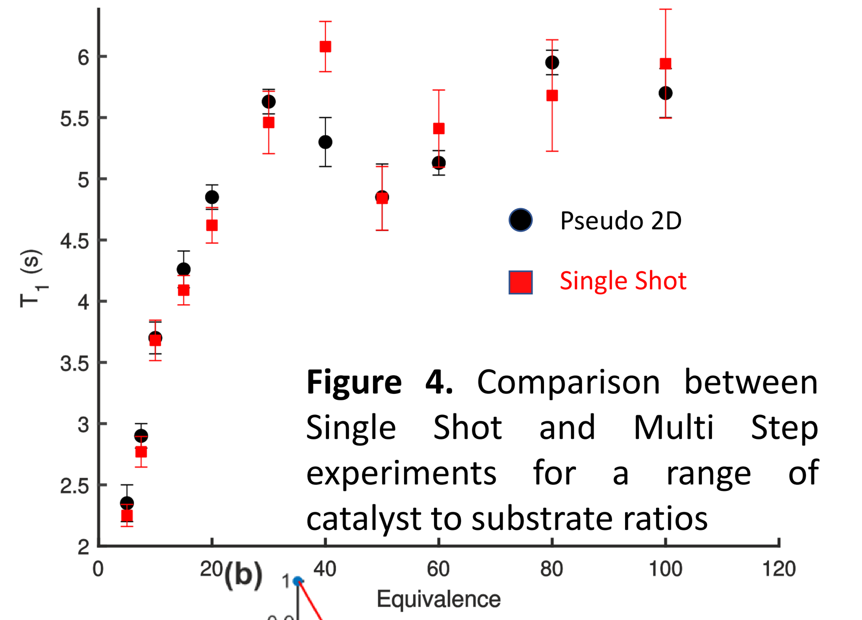

Figure 4. Comparison between Single Shot and Multi Step experiments for a range of catalyst to substrate ratios

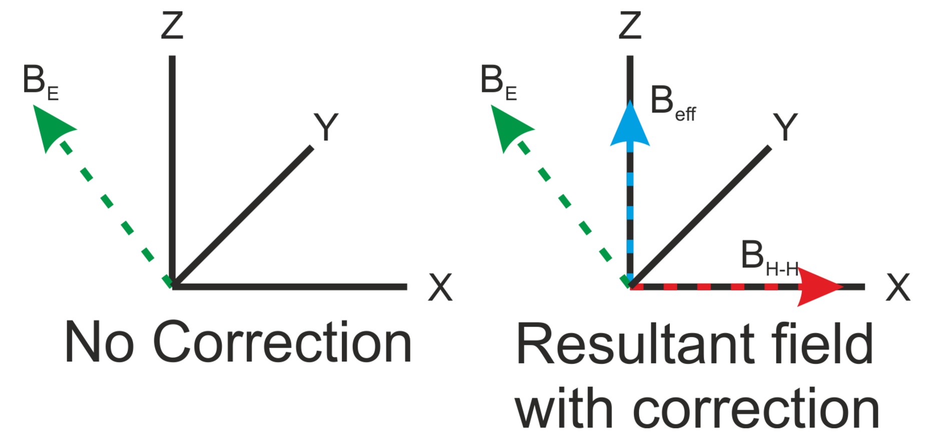

Figure 2. Cartoon of field correction where B_e the bulk Earth's field, $B_{h\text{-}h}$ the field correction produced by a Helmholtz pair, B_{eff} the resultant field.

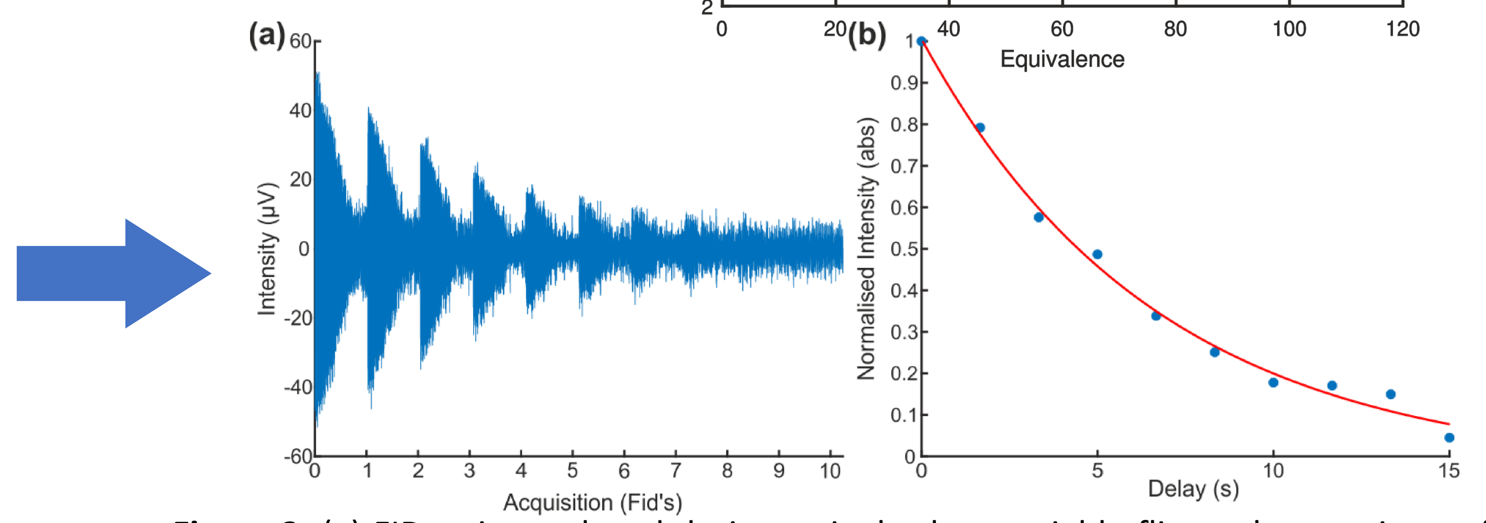

Figure 3. (a) FID train produced during a single shot, variable flip angle experiment for 50 mM Pyridine and 5 mM pre-catalyst in 4 ml CH_3OH. (b) Example T_1 decay curve.

4. Monitoring SABRE catalyst activation

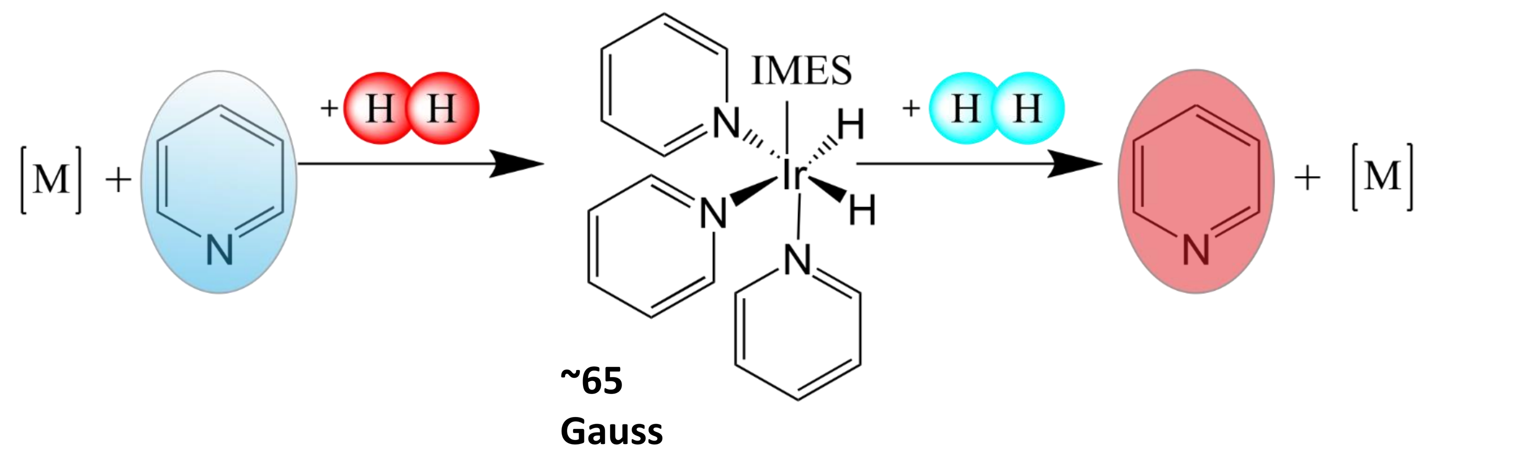

Figure 5. Schematic of the catalytic transfer of polarisation from *p*-H_2 to a substrate using a reversible exchange reaction. The spin order of the *p*-H_2-derived hydrides of the active catalyst is transferred to the substrate via the *J* coupling network. Exchange leads to a build-up of hyperpolarised substrate in solution.

- The active SABRE catalyst mediates polarisation transfer between *p*-H_2 and substrate in a polarisation transfer field (PTF) of 10's of G.
- Polarisation transfer is catalytic and the exchange process is reversible, therefore continuous polarisation is possible.[2]

- As the SABRE catalyst is air sensitive, the typical experiments begins with a pre-catalyst which in turn must be activated before efficient SABRE may be performed.
- The *activation* of the catalyst can be monitored in situ by measuring the change in hyperpolarisation lifetime as a function of *p*-H_2 bubbling time.

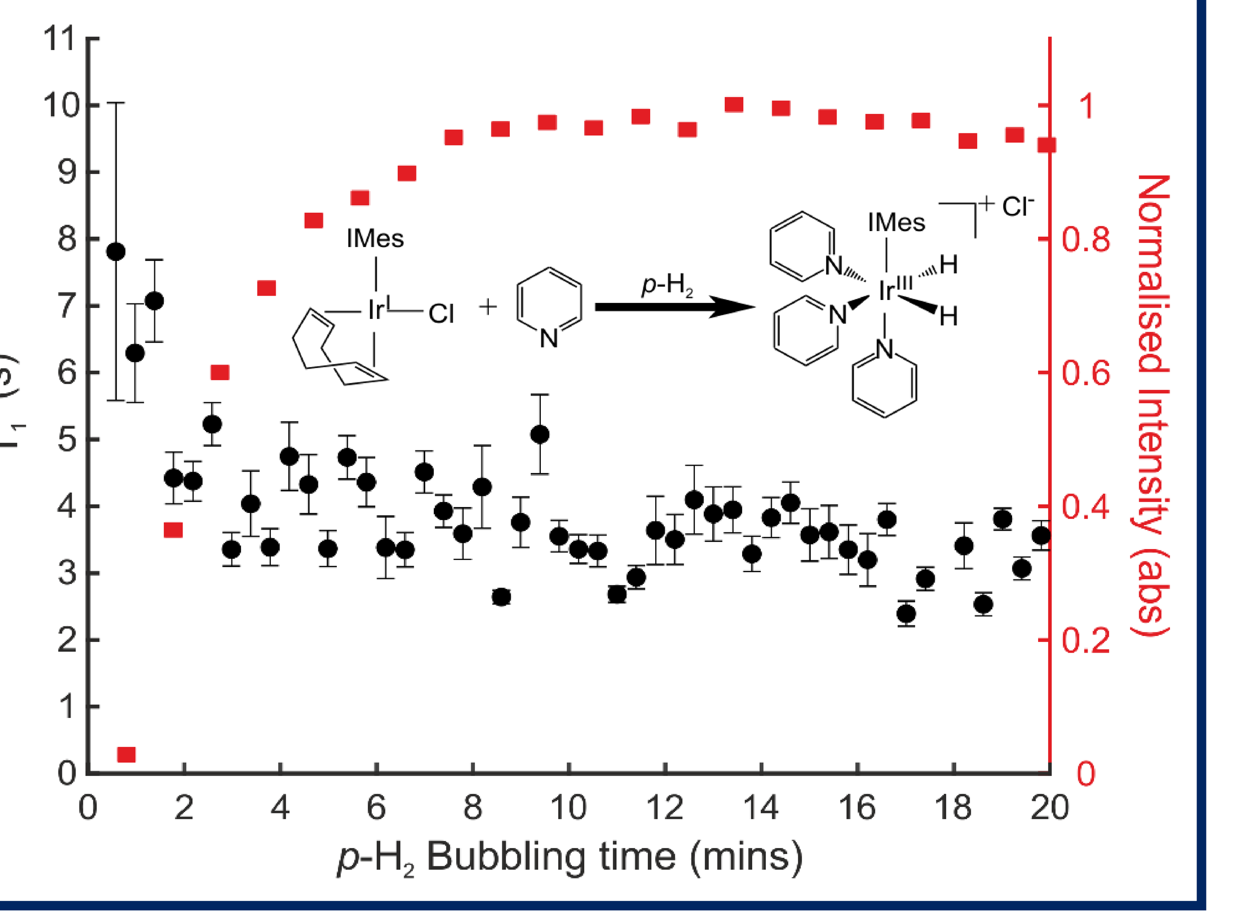

Figure 6. *insert* Simplified activation scheme of the sabre catalyst. Activation curve for 50 mM of pyridine with 5 mM SABRE pre-catalyst in 4 mL of CH_3OH, monitored by single shot T_1 measurements (Black Circles), and SABRE signal intensity (red squares)

5. Conclusions

- A flexible instrumentation and detection scheme for SABRE-enhanced Earth's field NMR is presented, which enables a wide range of experimental parameters such as p-H_2 Flow rates, pressures and polarisation transfer fields, to be probed with *in situ* NMR detection.
- Accurate pulse calibration enables sophisticated NMR pulse sequences to be achieved using EFNMR detection.
- SABRE catalyst activation has been monitored using single shot lifetime measurements.

6. References and Acknowledgements

1. Adams R.W. et al., Science, 323, 1708-11 (2009). 2. Hill-Casey, F. et al,, *Molecules*, *24*(22), 4126 (2019). 3. Semenova, O. et al., Anal. Chem. *91*(10), 6695–6701 2019.

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