A METHOD FOR DETERMINING THE DETECTION LIMITS AND SENSITIVITY IN A ^{19}F MR EXPERIMENT

Alexander John Taylor[1], Josef Granwehr[2], James Lee Krupa[3], Clémentine Lesbats[4], Joseph S Six[4], Galina Pavlovskaya[4], Thomas Meersmann[4], Neil R Thomas[3], Dorothee P Auer[1], and Henryk M Faas[1]

[1]Division of Clinical Neurosciences, School of Medicine, University of Nottingham, Nottingham, Nottinghamshire, United Kingdom, [2]Sir Peter Mansfield Centre, School of Physics and Astronomy, University of Nottingham, Nottingham, United Kingdom, [3]Centre for Biomolecular Sciences, School of Chemistry, University of Nottingham, Nottingham, United Kingdom, [4]Sir Peter Mansfield Magnetic Resonance Centre, University of Nottingham, Nottingham, United Kingdom

Introduction:
Fluorine (^{19}F) MR methods benefit from excellent specificity due to the lack of biologically endogenous fluorine, yet suffer from low sensitivity since only small concentrations of fluorinated compounds can be administered *in vivo*. Detection limits are crucially important for techniques such as cell labelling with a fluorinated contrast agent, but these limits must be experimentally derived. Here, we detail a method that which can predict the minimum sensitivity achievable for any fluorinated compound, prior to performing an experiment, provided a setup specific parameter (a gauge factor) has been determined once.

Theory and methods:
Adapted from an expression for the theoretical signal to noise ratio (SNR) in an NMR experiment, we derive a formula for the SNR, Ψ, of a fluorine compound resulting from a single 90° pulse (Eq. 1), where n_e is the number of fluorine spins per molecule, β is the pulse flip angle, Q is the quality factor, F is the pre-amp noise figure, V_s is the sample volume, T is the temperature and all other symbols have their standard meanings. We then derive an expression for the minimum detectable concentration, c_{min}, for a minimum detectable SNR, Ψ_{min}, (Eq. 2), where Λ is a constant, and K is the gauge factor. The gauge factor is an experimental parameter which, once determined, acts to align experimental and theoretical values in Eqn. 2 and is specific to the coil/scanner setup used. Using a Bruker 9.4T imaging system and ^{19}F volume coil, single pulse NMR spectra were acquired (TR = 120s; NA = 10). The SNR values were measured for two fluorinated compounds, ne = {6,9}, and for varying concentrations of trifluoroacetic acid (C3). Using Eq. 1, theoretical SNRs were calculated using an experimentally determined gauge factor, shown in Table. 1.

$$\Psi = \frac{cN_A n_e \gamma \hbar^2 V_s}{16}\sqrt{\frac{\mu_0 Q \omega_0^3 \pi T_2^*}{F k_B^3 T^3}}\sin(\beta) \qquad [1]$$

$$c_{min} = \frac{\Lambda}{K}\frac{\Psi_{min}}{n_e V_s \sqrt{T_2^*}\sin(\beta)} \qquad [2]$$

Results:
The ratio of experimental SNR and theoretical SNR divided by the gauge factor was calculated for C1 and C2, establishing an average value of K = 2550. This gauge factor was applied to the theoretical model predicting the SNR of TFA (Fig. 2A), such that the theory agreed well with experiment. To determine ^{19}F sensitivity, TFA concentrations for a minimum target SNR of 3.5 were determined by best fit extrapolation of the model (Fig. 2C); a value of 16 mM was determined as a minimum detectable concentration for both theory and experiment.

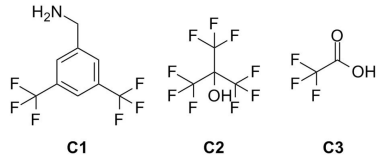

Figure 1: Chemical structures of three fluorinated compounds containing different number of fluorine atoms in each molecule.

Sample	n_e	T_1 [s]	T_2^* [ms]	SNR_e	SNR_t/K [$m^{1.5}$]	K [$m^{-1.5}$]
C1	6	1.591 ±0.008	78	41.0±3.8	$(1.5\pm0.2)\times10^{-2}$	$(2.7\pm0.4)\times10^{2}$
C2	9	3.121 ±0.005	112	67.0±6.2	$(2.8\pm0.3)\times10^{-2}$	$(2.4\pm0.3)\times10^{2}$

Table 1: Relaxation values, SNRs and gauge factors for compounds C1 and C2. SNR_e and SNR_t are the experimental and theoretical SNRs respectively. The far right column is the calculated gauge factor for each compound.

Discussion:
The theoretical model provides a method with which one can estimate the expected sensitivity of a compound, prior to performing an experiment. This was achieved by using a gauge factor which is proved valid for fluorine compounds with different structures. Combining this method with optimised ^{19}F imaging techniques would allow *a priori* sensitivity estimates of new contrast agents and detection limits for *in vivo* biomarkers.

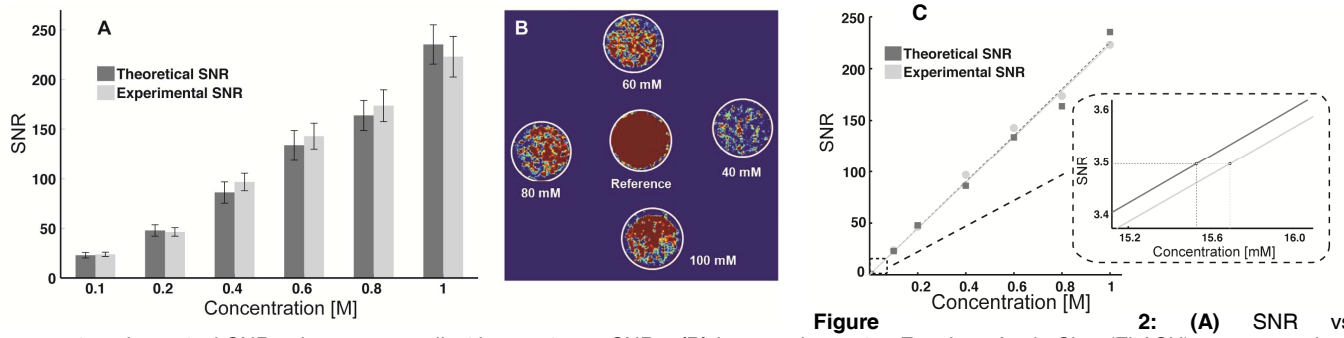

Figure 2: **(A)** SNR vs. C3 concentration; theoretical SNR values agree well with experiment SNRs. **(B)** Image taken using Fast Low Angle Shot (FLASH) sequence, showing the relation between intensity and concentration, can be used to determine SNRs, instead of NMR spectra, when applying this method to MR imaging. **(C)** Extrapolation of C3 SNR data gives minimum detectable concentrations for both theoretical and experimental values using lines of best fit.