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NMR Planar Micro coils for micro spectroscopy: Design and characterisation

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Abstract- The goal of this study is to determine the concentration sensitivity and the limit of detection of a SNMR receiver planar micro coil with ellipsoidal geometry 1000 x 500µm, fabricated using an electroplating technique and used as SNMR receiver coil at 200 MHz. The maximum signal intensity on the NMR images and simulation of RF field distribution allows defining an active volume of 0.8 µL. The localised spectroscopy based on a PRESS sequence shows that the concentration sensitivity is closed to S_C=2.33M^{-1} and the limit of detection LOD = 0.8M. This micro-system offers the possibility of new investigation techniques based on implantable micro coils used for in vivo study of local cerebral metabolites occupying a small volume (µL to nL order).

I. INTRODUCTION

Nuclear magnetic resonance spectroscopy is one of the most often used techniques to study the metabolism changes in different biological and chemical samples. The field of NMR has developed a large array of experimental capabilities but NMR sensitivity still lags significantly behind most other analytical methods by a factor of 100-1000 especially for many important mass-limited and concentration-limited situations. Actual studies are concentrated on the analysis of limited samples volume (orders of µL) [1].

According to Hoult and Richards [2], the reduction of the diameter and length of the coil increases the sensitivity. On the other hand, for a fixed coil size and line width the concentration and mass sensitivity is directly proportional to the fraction of volume within the coil which is occupied by sample. This parameter, called the filling factor, depends of the inner diameter of the sample container and the NMR coil diameter. Conventional NMR instruments used for small volume analysis give a low signal to noise ratio (SNR) because of their large dimensions compared to the sample size. Adapting the coils dimensions to the samples dimensions, the filling factor will be ameliorate and also the signal to noise ratio and the coil sensitivity (B_1/i), where B_1 is the RF field and i is the unit current [3]. These considerations establish both the mass-sensitivity, $S_m = \mathrm{SNR}/\mathrm{mol}, ([S_m] = \mathrm{mol}^{-1})$, and the concentration-sensitivity, $S_C = \mathrm{SNR}/\mathrm{C}, ([S_C] = \mathrm{M}^{-1})$, C being the sample concentration, as useful figures of merit in NMR probe evaluation [4]. From NMR literature is well known the fact that the signal strength and detection depends of the several factors like: the field uniformity in the excitation process, the sensitivity, size and geometry of the RF receiver coil, the sample concentration and volume, the number of magnetically equivalent nuclei which give rise to a particular resonance, the line width of the resonance. At this point, it is necessary to determinate the sample observation efficiency, which is the ratio between the total sample volume and the volume of sample observed by the RF coil. Because of magnetic susceptibility discontinuities at air-container interfaces, the sample usually extends beyond the coil region to provide quality data; a limit of detection (LOD) in terms of mass of sample, $\mathrm{LOD}_m = 3/S_m$, and concentration of sample, $\mathrm{LOD}_C = 3/S_C$ which yields an S/N of 3, for the entire sampling system can be significant and has to be determined. So far, the micro coil-based NMR experiments were focused on the micro coils of solenoid geometry [1, 4, and 5]. The planar micro coils investigations starts with Massin et al [6-9] who have focused on the performances of 500µm and 1mm inner diameter planar micro coils fabricated by photolithographic techniques. Eroglu et al [10-11] investigated a method for monitoring activity of pancreatic β-cells using a 2mm diameter planar coil at 500MHz. Grant et al [12-14] have focused on the MRI experiments on single neuron investigation. Our approach consists in the use of implantable planar micro coils with ellipsoid geometry fabricated using an electroplating technique in order to determinate the active volume and its NMR spectroscopic performances. In this paper we present the electrical characterisation, the B_1 radiofrequency (RF) field distribution and the micro coil concentration sensitivity and limit of detection for our micro coil.

II. MATERIALS

The presented micro coil is a planar coil with ellipsoidal geometry 1000µm x 500µm with 4 turns (fig. 1), fabricated using an electroplating technique [15]. In our simulation model the four turns micro coil is approximated as four concentric loops with trace width of 22µm, trace thickness 46µm. We also consider spiral coils having conductor traces estimated as 2 segments and 2 circle arcs for each turn with a thickness of 46µm, width 22µm and spacing between turns of 20µm. The spacing between the traces is kept constant all along the loop surface and it is equal to 20µm.

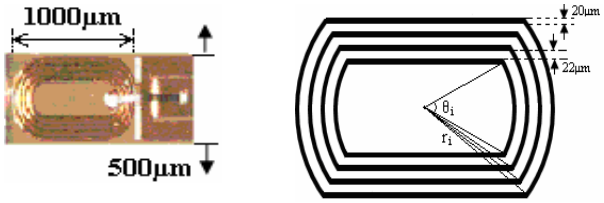


Fig.1: SEM view of the planar micro coil (a) and the concentric loop model used for the Matlab simulations (b).

The electric characterisation of the micro coil was performed using a HP 4195A network analizer and have these values: L= 7,5nH, R = 0, 62Ω, Q=24.

The decoupling problem: For a micro coil used in the emission-receive mode the field of view obtained is a relatively small part of the active coil volume because of the non-uniformity of the excitation. Using two separate coils, one for emission, a Rapid Biomed birth-cage (inner diameter 6.9cm) which offers field uniformity, and our micro coil as receiver we are able to increase the sensitivity and RF field uniformity. When the planar micro coil is used for detection only and another coil for excitation there is a strong electromagnetic coupling caused by mutual inductance since both coils operate at the same resonance frequency. We can eliminate the mutual induction by detuning the micro coil during the excitation phase and quenching the emission coil during the detection phase [16]. This problem can easily be solved using a PIN diode as we can see in figure 2.

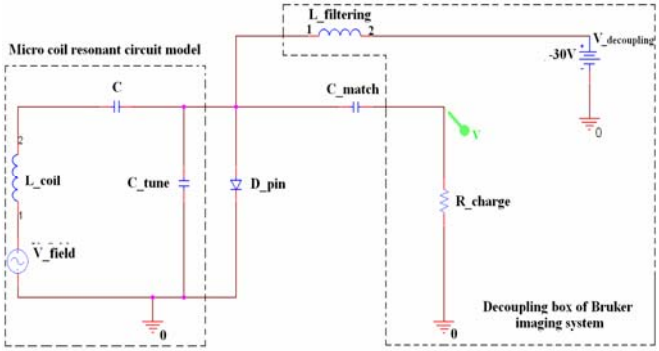


Figure 2: The model for the receiver NMR micro coil and its decoupling circuit.

The circuit in figure 2 is the micro coil resonant circuit model. The third capacity, C, is imposed by the presence of the PIN decoupling diode in order to avoid the short circuit of the command tension ($V_{\_decoupling}$) by the micro coil. In the decoupling mode, the PIN diode is in conduction, commanded with a tension of +3.8V. The tuning capacity will be short circuited by the PIN diode, the frequency of resonance of the micro coil becomes: $f_{res} = 1/\left(2\pi\sqrt{L_{coil} \cdot C}\right)$; the decoupling mode is activated when the NMR sequence generates the RF pulses .

In the reception mode the PIN diode is commanded with a command tension ($V_{\_decoupling}$) of -30V. The resonance frequency becomes $f_{res} = 1/\left(2\pi\sqrt{L_{coil} \cdot C_{eq}}\right)$ and it is equal to 200.3MHz, the proton resonance at 4.7T, where $C_{eq} = \left(C \cdot C_{tune}\right)/\left(C + C_{tune}\right)$. The presence of the filtering inductance $L_{\_filtering}$ is used to avoid the possible looses of the NMR signal on the command way and also to block the noise induced by the command way.

III. METHODS

The knowledge of the coil RF field cartography in terms of uniformity and amplitude and the knowledge of the corresponding sensitivity distribution make possible a precise localisation of voxel selection for NMR imaging and spectroscopy investigations. The field map of the presented micro coil was computed using the Matlab software with the concentric loop model [8] showed in figure 1 using the Biot-Savart Law.

The amplitude of field distribution strictly depends of the geometrical parameters of the coil (width, trace height and trace spacing) and each conductive part contributes in the field generation. So, all conductive parts of the micro-coil may be decomposed in elementary segments carrying currents. The principle of superposition permit to add together the corresponding elementary magnetic vectors and thus the global magnetic field of the micro-coil can be calculated using the Biot-Savart law. The sensitivity for the modulus image is obtained by projecting B_1 into the plane perpendicular to the main magnetic field B_0 and numerically generating the variation of the magnetic field in the other two axes.

In NMR experiments only the perpendicular component of the magnetic field gives the NMR signal detection. In order to correlate the MRI images with the Matlab simulations it is necessary to numerically generate the distribution of the magnetic field in a plane perpendicular to the coil surface. The distance from the micro coil surface is d = 1.25mm (figure 3 a, b).

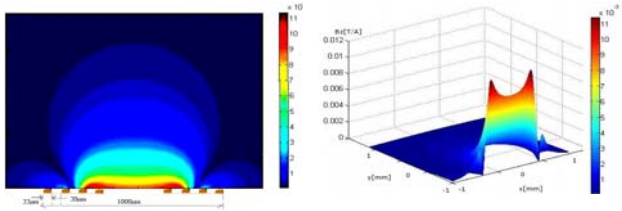
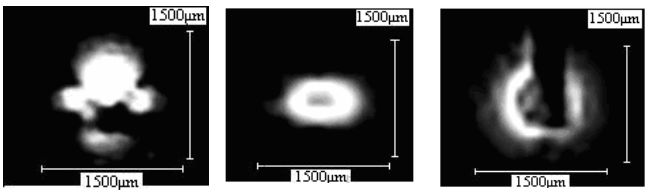


Figure 3: 2D sensitivity map (a) and the spatial distribution (b) of the Bz magnetic field component of the planar micro coil at d = 1.25mm.

RF field map by NMR imaging

NMR experiments were performed using a BRUKER 4.7T Biospec System with 270 mT/m gradient set. The planar micro coil is used for signal detection only. It was immersed in a water sample and NMR images showing the signal distribution were acquired using a FLASH sequence with: FOV =1.19cm, TR/TE=100/6ms, 30° flip angle, 1mm thick slice, coronal plane, 100µm spatial resolution, 2 averages.



(a) (b) (c)

Figure 4: MRI images obtained at 4.7T: coronal plane (a) and transversal plane (b) are obtained and enable to evaluate the active volume of the planar micro coil.

The active volume of the planar micro coil will be determined by estimating the volume in which the signal is distributed. In that case the signal to noise ratio is SNR = 80. The MRI results will be correlated with the simulations showed above.

IV. RESULTS

The MRI results show that the maximal signal intensity covers a zone of 600µm in length and approximately 350µm in height. These dimensions make possible to estimate the voxel size at 0.8 mm^3 and the active volume of the micro coil at 0.8µL.

To determine the concentration sensitivity (S_C) and the limit of detection (LOD) we used an ethanol sample of 5M concentration and a volume of 0.6ml. The water signal was suppressed by variable power RF pulses with optimized relaxation decays (VAPOR). Outer volume suppression (OVS) combined with a short echo time PRESS sequence was used for localisation. The sequence parameters are: TR/TE = 2500/20ms, voxel size = 2 mm, 64 accumulations, acquisition time 2min45s. Eddy current compensation and static magnetic field drift correction were applied during the acquisition. We have obtained all the three characteristic groups of ethanol (CH_3-CH_2-OH). From left to right the proton signals of the –OH group, -CH_2 and –CH_3 can be identified. The hyperfine structure resonance of the methylene and methyl groups clearly appears in spectrum in figure 5.

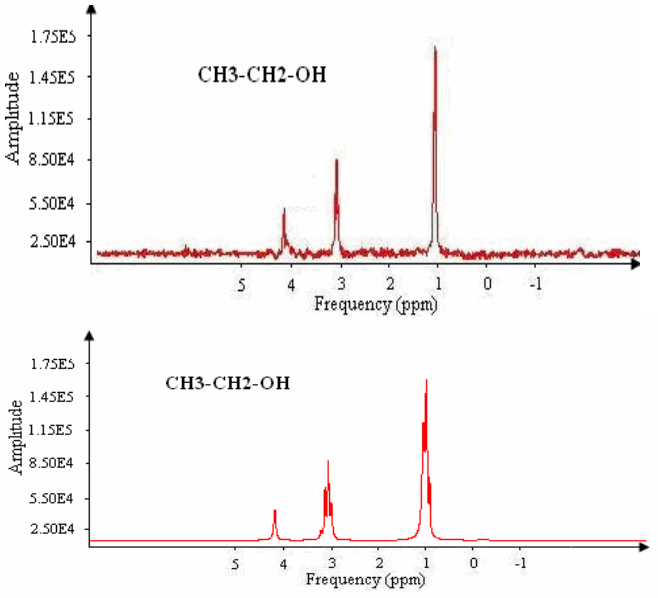


Figure 5: Ethanol spectre obtained with a PRESS sequence (a) and the AMARES quantification (b).

The MRS data processing are performed using the jMRUI software, the quantification is performed using AMARES method [17] (figure 5). The removal of residual water components was performed in a pre-processing step using the Hankel-Lanczos Singular Value Decomposition algorithm – HLSVD.

The concentration sensibility is closed to S_c = 4.46 M^{-1} (for the biggest peak of CH_3 group) and the limit of detection of LOD = $3/S_c$ ~700mM.

IV. CONCLUSIONS

The MRI results are in good concordance with the simulation, the active volume found at 0.8µL makes possible a précised voxel selection in the localised spectroscopic experiments. At this scale the knowledge of the maximal signal distribution is essential in all the NMR investigations. The values of sensitivity concentration and the limit of detection of 700mM show great promise for in vivo study of local cerebral metabolites occupying a small volume in living tissues. The micro coils will be implanted in the rat skull and used to determine by NMR spectroscopy the variation of proton and phosphorus cerebral metabolites.

V. REFERENCES

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