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Mobile NMR: applications to materials and biomedicine

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Mobile nuclear magnetic resonance deals with unilateral sensors like the NMR-MOUSE® to investigate materials non-destructively. The tested samples cover a great range of applications: from elastomers of great importance in materials science to the most complicated biological structures, the essence of the biomedicine. The investigation can be simple NMR relaxometry with a bar or "U" shaped magnet NMR-MOUSE®, profile imaging, and 2D or 3D imaging using an unilateral NMR tomograph. The relaxation times obtained from an exponential fit to echo decay envelopes describe the physical states of elastomers: fatigue, aging, strain, etc. An NMR experiment on a stress-strain device showed a good correlation of a plot of the transverse relaxation times versus strain with the stress-strain diagram. As a new imaging device in biomedicine, the unilateral NMR tomograph was tested. It enables acquisitions of 2D profiles with a planar resolution of 0.8 mm^2 and a field of view of 4x4 cm.

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1. Introduction

Nuclear Magnetic Resonance (NMR) is an established powerful analytical tool widely used for structural and conformational analysis in chemistry, biology, medicine and material science [1,2]. Material characterization is mainly carried out by measuring NMR parameters like the chemical shift, the nuclear spin relaxation times, the dipolar coupling, and the self-diffusion coefficient. Furthermore, images can be produced by NMR in which the contrast is determined by these parameters, and NMR is employed to characterize diffusive and coherent molecular motion in a non-invasive fashion. NMR methods have been initially developed to work in the homogeneous fields of the strong magnets, but the limited working volume of these devices restricts the applications of NMR, in particular for *in situ* studies of large objects. In addition to conventional NMR, where the sample is adapted to fit into the probe, there is inside-out NMR, which uses open magnet geometries. Such sensors are low cost and portable. They provide excellent versatility in accessing a large number of applications which are inaccessible to closed magnet geometries. Historically the inside-out concept was developed for examining geological formations by lowering a full NMR spectrometer into a borehole to record signals from different formations. Different tool geometries have been designed for well-logging, and water reservoir studies. Later on the concept of single-sided NMR was extended to moisture detection in composites, medical diagnostics, material analysis, and quality control.

A hand held single-sided NMR sensor that has extensively been used for non-destructive material testing is the NMR-MOUSE® (mobile universal surface explorer) [3]. Its original construction combines two permanent magnets with opposite polarization placed on an iron yoke to form a U-shaped magnet (Fig. 1) with the radio-frequency coil situated in the magnet gap following earlier concepts of unilateral sensors with electromagnets for moisture detection in soil and road decks [4].

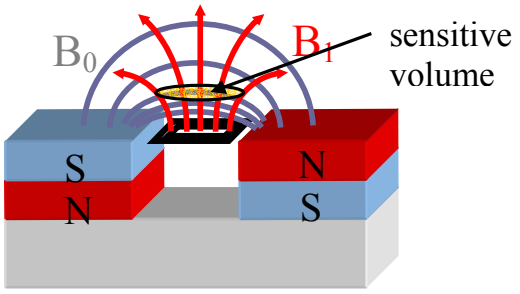

Fig. 1. The U-shaped magnet NMR-MOUSE.

The NMR-MOUSE® is a registered trademark of RWTH Aachen

The open magnet defines a sensitive spot above its surface, from where the NMR signal is measured. This type of NMR offers interesting applications especially for solid materials [2,6-8], where translational molecular diffusion is absent and higher field gradients can be tolerated. Because of the low and highly inhomogeneous fields the chemical shifts cannot be observed at this level, but relaxation times can be measured by echo-detection techniques. The main characterization procedure requires that a correlation between the relaxation times measured with the MOUSE and the material property of interest exists.

Another design is the bar-magnet NMR-MOUSE that consists of a Fig. 8 type surface coil mounted on one of the pole faces of a bar magnet [8]. The main difference between the two devices is the direction of the magnetic

field which in the first case is horizontal and in the case of the bar magnet is vertical with respect to the sensor surface. The coils may have different shapes according to the magnet geometry and the type of sample.

By fitting the NMR-MOUSE with surface gradient coils, an open tomograph is obtained [9]. The one shown in Fig. 2 has been developed at RWTH Aachen in a DFG supported collaborative project FOR 333 "Surface NMR of Elastomers and Biological Tissues". It weighs only 36 kg and has been applied in this study. On account of the inhomogeneous magnetic fields of the device, special phase encoding methods were developed for imaging [9]. The novel open tomograph is able to produce 3D images of small volumes near the surface of arbitrarily large objects. Depending on the sample and the spatial resolution, the acquisition time for one image ranges between one minute and two hours.

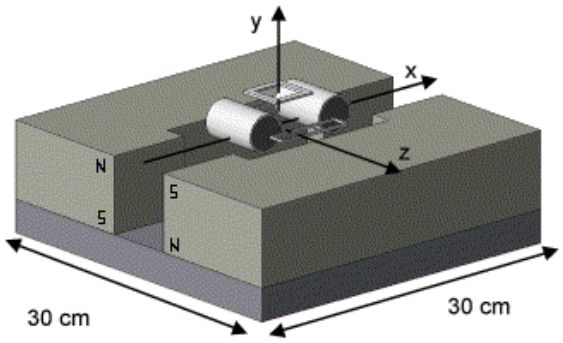

Fig. 2. Drawing of an open tomograph provided as a single-sided sensor (magnet geometry and gradient coil system position).

2. Experimental data

2.1. In situ NMR at a Stress-Strain Device

Elastomers are polymeric materials with a broad range of applications. Due to this technical importance, elastomers are continuously improved and analysed mostly by destructive methods in terms of test samples. There are stretching methods for elasticity tests, torque measurements for mechanical resistance tests, etc.

To determine the mechanical properties, for example a cross-linked natural rubber (NR), the sample is tested with a stress-strain device to observe the fatigue with the number of strain cycles, or the stress-strain diagram of a single experiment is recorded until the sample breaks. The changes induced by stretching cross-linked NR samples have also been characterized by mobile NMR on-line. Our mobile probe (Fig 3) was operating at a resonance frequency of 22.5 MHz.

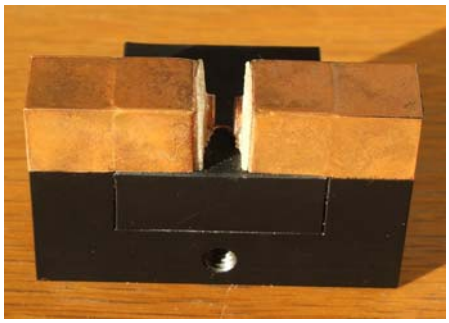

Fig. 3. The NMR-MOUSE used for in situ measurements at a stress-strain device.

In the 4mm wide gap between the two permanent magnets, the radio frequency coil is placed. It consists of two opposite windings positioned on the surfaces of the two permanent magnets. During the experiment, the sample is located in this gap, and between the two windings of the rf coil. The sensitive volume of the probe is a function of the coil diameter, the field gradient inside the gap and the pulse length used in the excitation sequence. As Hahn echo experiments are very time consuming, and the Carr-Purcell-Meiboom-Gill (CPMG) sequence uses a train of refocusing pulses which due to the high power released in the material require a long repetition time, the solid-echo sequence was found to be the most suitable experimental method. The experimental set-up (Fig. 4) consists of a programmable stress-strain device which is able to stretch the sample up to a given percentage of its initial length and to hold it at that elongation the desired period of time. The sample can then be further stretched. The stress-strain device was interfaced with the NMR-MOUSE connected to a mobile preamplifier and NMR spectrometer and controlled by a computer.

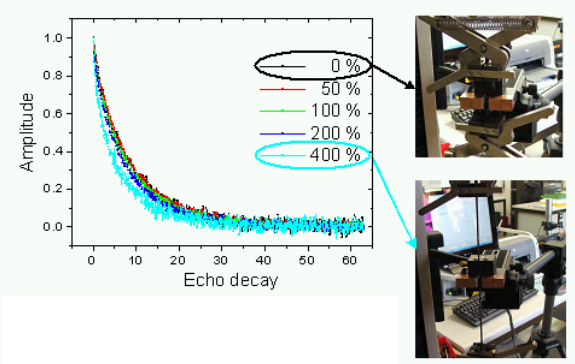

Fig. 4. Normalized solid echo decays measured on a NR sample relaxed and stretched, and the experimental setup for the relaxed state and at maximum elongation.

The experimental time was only seven minutes for each elongation step using 1500 scans. By fitting the solid echo decays with an exponential function, one can get a value of the effective transverse relaxation time ($T_{2\text{eff}}$) of the sample. This value is in fact a mixture of T_1 and T_2

because of the imperfection of the excitation pulses due to the field inhomogeneities. As any of the exponentials showed a fitting error above the desired precision limits, another approach for the pure T_2 weighting was necessary. The first step was to neglect in every decay the first echo. The next step was to normalize every decay to 1 by dividing each echo in the train by the second echo. By this computation, the errors due to the spin density variations with the strain are eliminated and fitting errors are avoided. The so-obtained decays which contain the pure $T_{2\text{eff}}$ information can then be compared with good reproducibility. Fig. 4 depicts the six normalized decays: for no stretch and for 50%, 100%, 200%, and 400% elongations. The NMR-MOUSE was always displaced in the middle of the elongated sample. The two photos show the set-ups for no elongation and maximum elongation. The experimental data show a faster signal decay when the sample is stretched compared to the relaxed or less stretched states. By forming the sum of the echo amplitudes for each decay, one can quantify this variation. Fig 5. represents the results of this computation.

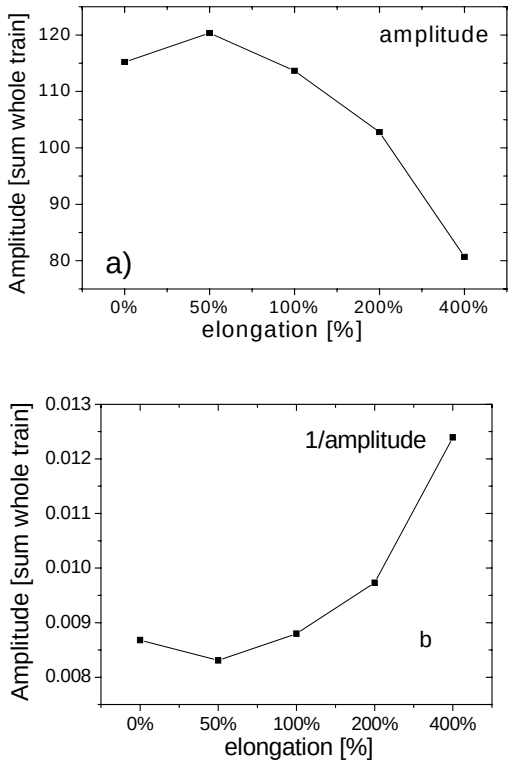

Fig. 5. a) The sum of the echo amplitudes in the solid echo trains (after normalization) for each elongation. b) The inverse values of the echo sums as a functions of the elongation.

The amplitudes drop with the elongation. As the effects of the field inhomogeneities and the variations in the amount of sample inside the sensitive volume due to the elongation are eliminated, the observed effect is a pure $T_{2\text{eff}}$ effect. $T_{2\text{eff}}$ decreases with the elongation, the sample becomes more rigid, and the polymer chains become more oriented while the force necessary to elongate it increases.

To check the reproducibility of the experiment and the importance of the probe position the experiment was repeated. Another sample with the same formulation was measured. In this case, the NMR-MOUSE was kept in the same position during the whole experiment. This sample was elongated until it broke. The decays, and the inverses of the signal amplitudes as functions of the elongation, are depicted in Fig. 6.

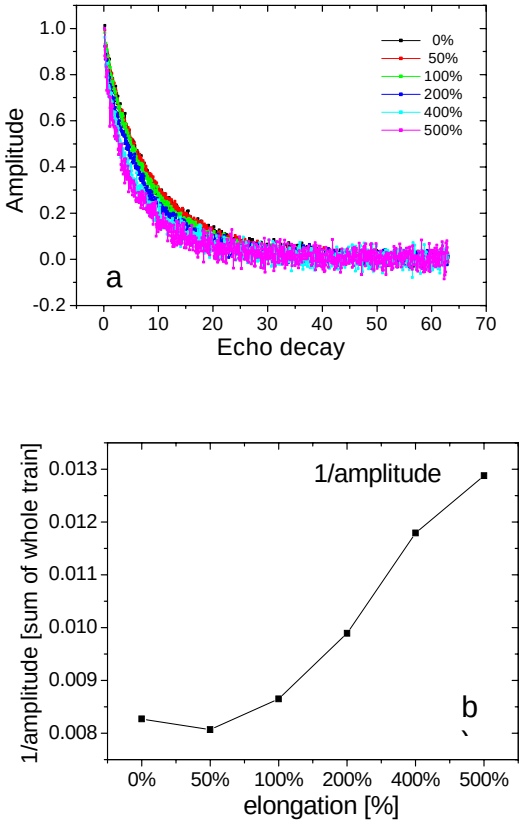

Fig. 6. Another sample, the same formulation (the NMR-MOUSE is kept in the same position, at one edge of the sample during the whole experiment for all elongations). a) The solid echo decays for the six states (five elongations). b) The inverse values of the echo sums as functions of the elongation.

The inverse proportionality between the strain measured for a given deformation of an elastomer, and the transverse relaxation time T_2 of the deformed elastomer is well known [11,12] and was used to calibrate our device. The diagram recorded by the stress-strain device was compared with the NMR diagram representing the inverse values of the echo amplitude sums as function of the elongation (Fig. 7).

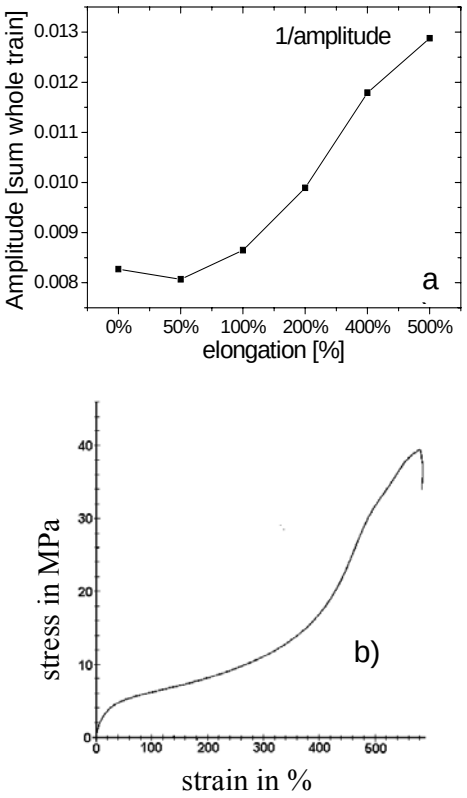

Fig. 7. a) The inverse values of the echo amplitudes sums as functions of the elongation; b) The stress-strain diagram.

The two diagrams are very similar. This shows the excellent concordance between the results from mechanical testing and the NMR results obtained with the NMR-MOUSE.

2.2. Mobile NMR imaging applications in biomedicine

Unlike conventional NMR, unilateral NMR imaging with the NMR-MOUSE can be used in materials science to visualize large objects nondestructively. It can image volume regions near the surface of samples with a three-dimensional (3D) spatial resolution by combining the radio-frequency slice selection with planar phase encoding achieved by the application of two perpendicular gradient fields. The almost linear gradient field close to the permanent magnet surface, can be exploited to measure NMR parameters in planes at well defined penetration depths just by retuning the resonance circuit to different frequencies. By changing the resonance frequency, it is possible to select the position of a slice with a precision of about 0.3 mm for a pulse length of 3 μs. Thinner slices can be selected with longer pulse widths on the expense of sensitivity. The definition of thin slices, however, will be limited by the homogeneity of the polarization field, i. e. by the quality of the magnet material, the geometries of the coil and the magnet, and the bandwidth of the spectrometer.

The unilateral tomograph has been used previously [13] to image elastomer products for quality control. Biomedical applications of single-side imaging are still a challenging topic. To assist in maxilo-facial surgery, a fast non-destructive portable imaging device would be of great use. According to this request, the unilateral NMR tomograph was tested as a new imaging device in biomedicine. The subject was a head of a rat *in vitro* (Fig. 8).

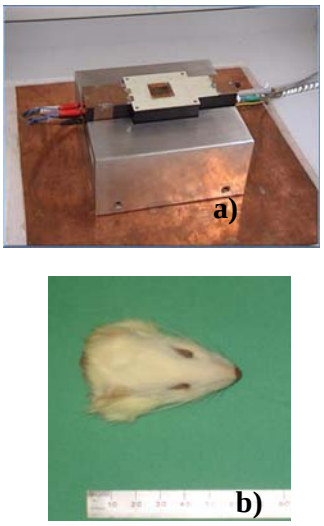

Fig. 8. a) The unilateral mobile NMR tomograph used to image the mandibula of a rat in vitro. b) The sample.

The pulse sequence consists of an encoding period where the radio-frequency pulses and the gradient pulses for planar position encoding are applied and a detection period where the sensitivity is improved by detecting a CPMG. Depending on how many echoes are added in the train, different sensitivities and T_2 weighting effects are achieved. For data analysis, the entire echo trains were evaluated, so that a voxel with the tissue having long relaxation time and a high proton density appears bright in the image, while the hard structures like the bone and teeth appear dark. A set of 2D profiles of the mandibula was acquired at different positions by changing the relative position of the sample with respect to the probe. The images (Fig. 9) reveal the mandibula morphology at each position of the slice with a T_2-weighted spin density contrast. The maximum planar resolution was 0.8 x 0.8 mm^2. The measurement time was ca. 30 minutes for a field of view of 4 × 4 cm^2. The teeth as well as the bone structures can be easily discriminated in the images. The spatial resolution still cannot compete with other microscopic methods, but the great advantages like the portability of the device, and the low costs of the method

can be good reasons for a potential use of the unilateral NMR imaging for biomedical analysis.

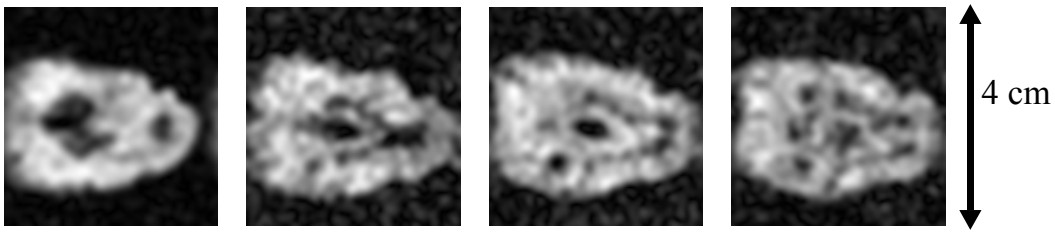

Fig. 9. 2D profiles trough the rat mandibula. The acquisition time of one image is ca. 30 minutes for a field of view of 4 × 4 cm. The planar resolution is 0.8 mm^2.

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3. Conclusions

The NMR- MOUSE is able to detect and quantify different elongations of cross-linked NR; the stress-strain results correlate well with the NMR-MOUSE results (NMR echo amplitude).

The 2D profiles of the rat mandibula obtained with the unilateral tomograph were one of the first applications of the NMR-MOUSE in biomedicine. Although the contrast between the soft and hard tissues is good and the image quality is acceptable, the method needs to be improved for a clinical use, to shorten the experimental time and increase the sensitivity.

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