MICROFLUIDIC MAGNETIC RESONANCE CHIP WITH INTEGRATED SOLENOIDAL MICROCOIL FOR DISPOSABLE USE IN A MODULAR PROBE

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ABSTRACT

We report a Magnetic Resonance (MR) probe consisting of a microfluidic chip with integrated solenoidal microcoil and the resonant circuit electronics on a modular basis. The MEMS fabricated microfluidic chip is connected to the electronics using a non-permanent clamping mechanism with vertical interconnect stripes. Thus, the fluidic chip can be easily replaced after usage with a new one, whereas the electronics remains in the MR probe. The filling of the microcoil is achieved using only capillary force without external fluidic tools. The integrated solenoidal microcoil is demonstrated at 400 MHz (^{1}H Larmor-frequency at 9.4 Tesla) at a minimum imaging resolution of 33 µm × 33 µm (x-y) and a signal to noise ratio (SNR) of 31 in a single scan (51 seconds).

KEYWORDS: micro-droplet nuclear magnetic resonance, microcoil, on-chip magnetic resonance imaging

INTRODUCTION

The MR technique offers structural and chemical insight in biological samples in a non-destructive manner. At the microscale, optimum sensitivity is achieved when microcoils are used [1]. For the analysis of small sample volumes in the nanoliter range, miniaturized coil detectors for nuclear magnetic resonance spectroscopy (NMR) [2] and imaging (MRI) [3] have been presented. Following the trend of Lab-on-a-Chip devices, microcoils were combined with microfluidics in order to carry out on-chip nuclear magnetic resonance analysis of e.g. cells [4,5] or to monitor chemical reactions [6]. In this paper, the presented device demonstrates the concept of a micro-droplet based magnetic resonance probe for the handling and analysis of small analyte quantities in an efficient and straighforward manner.

CONCEPT

With microcoils the practical difficulty is the analyte loading without external pumps and tubes. The presented microfluidic chip simplifies the analyte loading procedure by integrating the microcoil in a hydrophilic channel (Fig. 1a-d). A micro-droplet of the analyte is directly dispensed onto the inlet of the microfluidic chip and the microcoil below is filled due to capillary force (Fig. 1b). An analyte volume of less than 1 µL is needed to fill the fluidic chip completely.

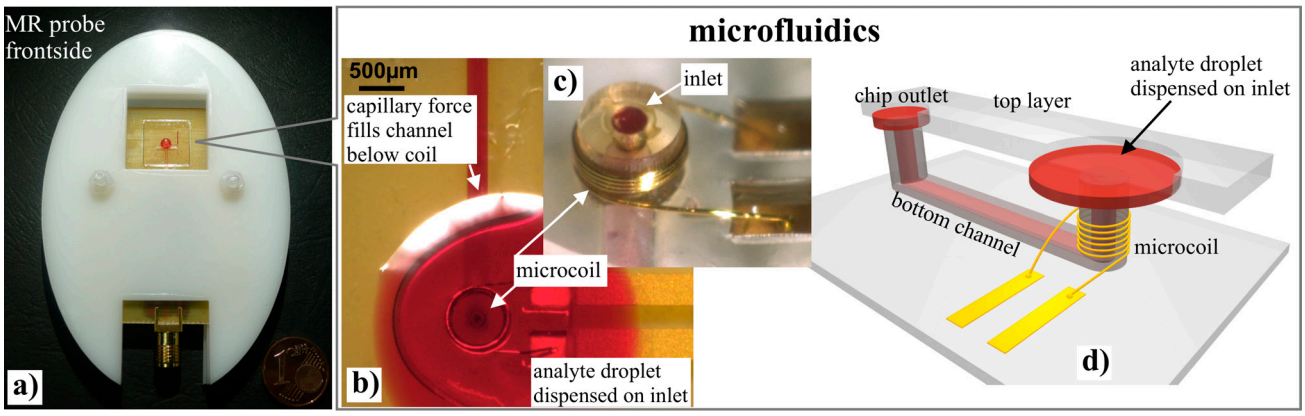

Figure 1: a) Frontside of the whole MR probe showing the microfluidic chip with integrated microcoil b) Enlarged view of fluidic chip which was filled by placing an 1 µL droplet on top of the microcoil (coloured water for better visibility). Capillary force fills the channel below the microcoil automatically. Hydrophilic character of the channel was generated using O_2 plasma treatment c) Microcoil at intermediate fabrication step prior to lamination of top layer. d) Schematic cross-section of fluidic chip. Bottom channel connects inlet and outlet through microcoil.

FABRICATION

The fabrication process of the microfluidic chip is similar to the process presented in Ref. [7]. The fabrication of the microfluidic chip is based on a combination of UV-photolithography, automatic wirebonding and high-precision UV-lasering. First, a Pyrex substrate sputtered with a Cr/Au layer is patterend with UV-photolithography in order to obtain the mold for the following electroplating step. The target thickness of the electroplating step takes into account the increased resistivity of the gold metal pads due to the skin effect. In a next step, the microfluidic bottom channel is

formed using the lamination of PerMX 3050 dry-resist (DuPont). In total, three dry-resist layers are transferred onto the substrate in order to define the bottom channel (Fig. 2a-c). The post which acts as a mechanical support for the microcoil is fabricated in the follwing step (Fig. 2d). A 400 µm thick layer of SU-8 2150 (MicroChem) photoresist is spun onto the substrate and subsequently softbaked on a leveled hotplate. During the softbake, thickness variations of the resist due to the bottom channel structures are minimized. The softbaked resist is patterend using UV-photolithography, cured in a following post exposure bake and developed in PGMEA. In Figure 2e), the windings of the microcoil around the SU-8 post is done [8]. The final step of the process flow is the lamination of the top layer (Fig. 2f). In order to access the bottom fluidic channel below the microcoil, the dry-resist membrane which still seperates the bottom fluidic channel from the inlet and the outlet is removed using a high-precision UV-laser step (Fig. 2g).

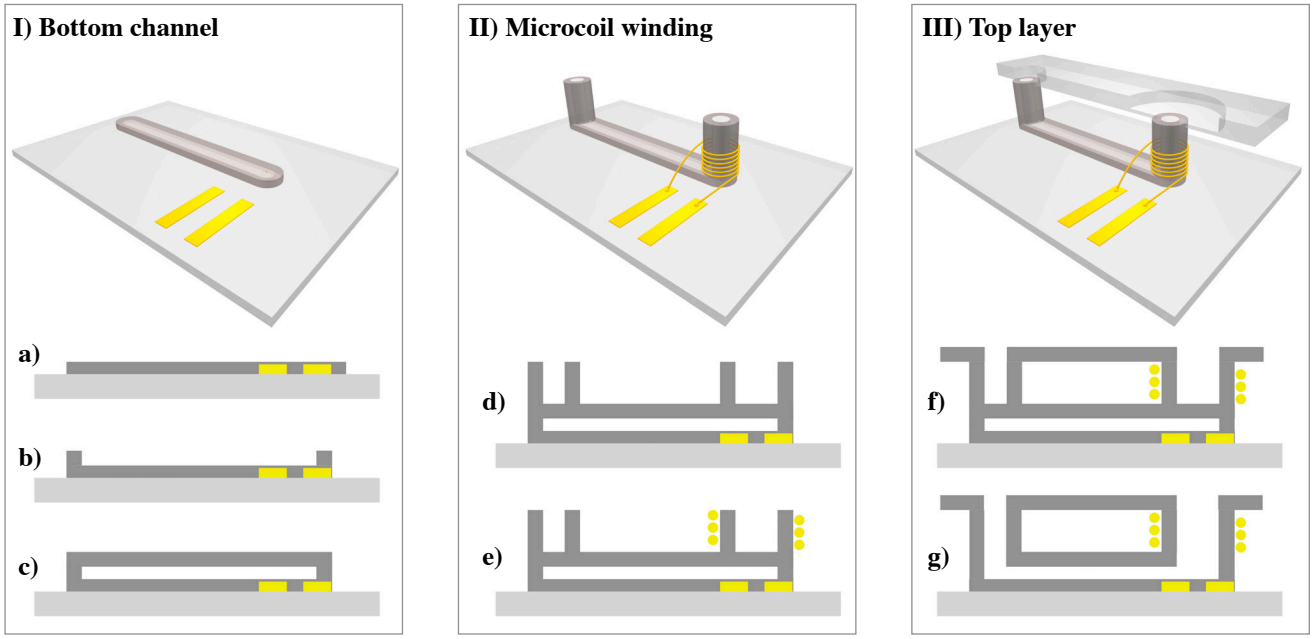

*Figure 2: Process flow of the microfluidic chip with integrated microcoil. **I** a) to c) bottom channel is made in a sequential dry-resist lamination step with UV-lithography of PerMX 3050 **II** d) thick SU-8 2150 spincoating and UV-photolithography in order to define the mechanical support for the microcoil and the outlet of the fluidic chip e) coil winding using a commercial automatic wirebonder machine **III** f) lamination of dry-resist to define the top layer g) UV-high-precision lasering to achieve fluidic access to the bottom fluidic channel by removing the dry-resist membrane.*

MODULAR MR PROBE DESIGN

The rear of the modular MR probe (Fig. 3a) shows the capacitive tuning and matching electronic network which is connected to the solenoidal microcoil on the fluidic chip (Fig. 3b). The microcoil itself is 450 µm in diameter and 200 µm in height (Fig. 3b). The quality-factor of the solenoidal microcoil is measured to be 41 at at a frequency of 400 MHz (Inductance = 23 nH, Resistance = 1.4 Ω). Using the capacitive network, the microcoil is matched to 50 Ω and tuned to the Larmor frequency of 400 MHz. The measured S_{11} power reflection value is better than -45 dB for both the unloaded and loaded state of the microcoil (Fig. 3c). This value represents negligible power losses due to the impedance interface between the MR probe and the electronic input of the 9.4 Tesla Bruker BioSpec 94/21 system.

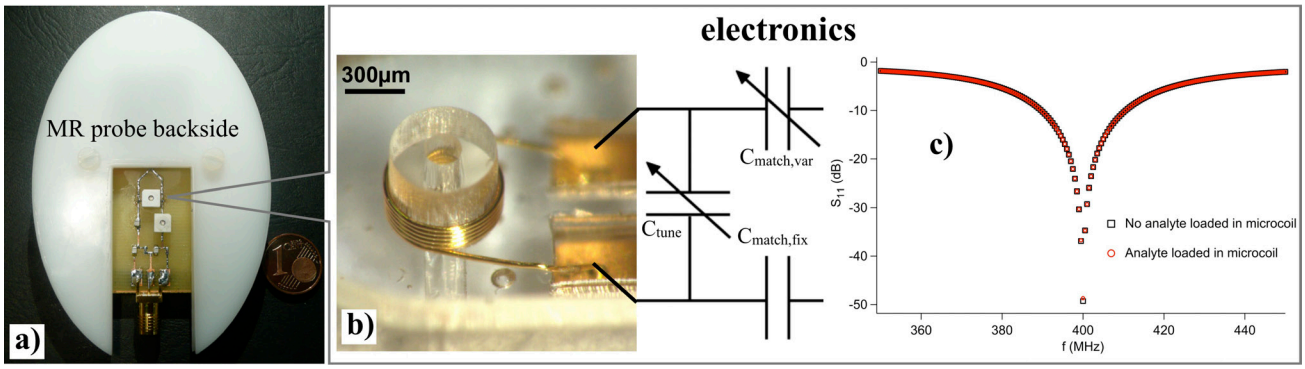

Figure 3: a) Backside of the whole MR probe showing the tuning&matching electronics for for the microcoil b) Schematic of tuning & matching resonance circuit (C_{tune}=0.6-2.5 pF, $C_{match,fix}$=2.4 pF, $C_{match,var}$=0.6-2.5 pF) c) S_{11} power reflexion coefficient measured for the unloaded (-49 dB) and loaded (-48 dB) microcoil.

A polymer frame houses both the microfluidic and the electronics module (Fig. 4a). Both modules are electronically connected to each other using a clamping mechanism with vertical interconnects, as shown in Figure 4b). These interconnects consist of alternating conductive (metal) and non-conductive (polymer) layers with a pitch of 100 µm. Another advantage of this non-permanent interconnect type is a convenient replacement of the microfluidic chip after usage without soldering. Also, the electronic module can be exchanged to adjust the MR-probe to different Larmor-frequencies.

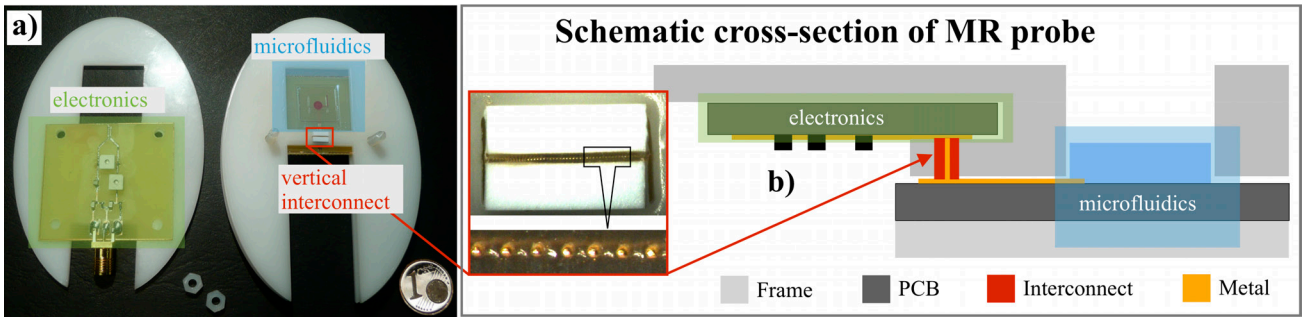

Figure 4: a) Two halves of the MR probe before assembling them together. The microfluidics (blue) and the electronics (green) part are connected using the vertical interconnect stripe (red frame). b) Schematic cross-section of the MR probe also showing the microfluidics (blue shading) and electronics (green shading) part.

PROOF OF CONCEPT

The tuned and matched microcoil was tested by imaging in a 9.4 Tesla Bruker BioSpec 94/21 system with a gradient strength of 0.675 Tesla/meter. In the x-y direction, a minimum spatial resolution of 33 µm × 33 µm was achieved with a slice thickness of less than 200 µm (Fig. 5a). The obtained image in Figure 5b) indicates both complete filling of the microchannel through the coil and an homogeneous signal intensity within the sensitive volume of the microcoil. With a total acquisition time of 51 seconds the image data was obtained with a calculated SNR of 31. For images with improved resolution, the concept of the MR probe will be tested at a higher magnetic gradient strength.

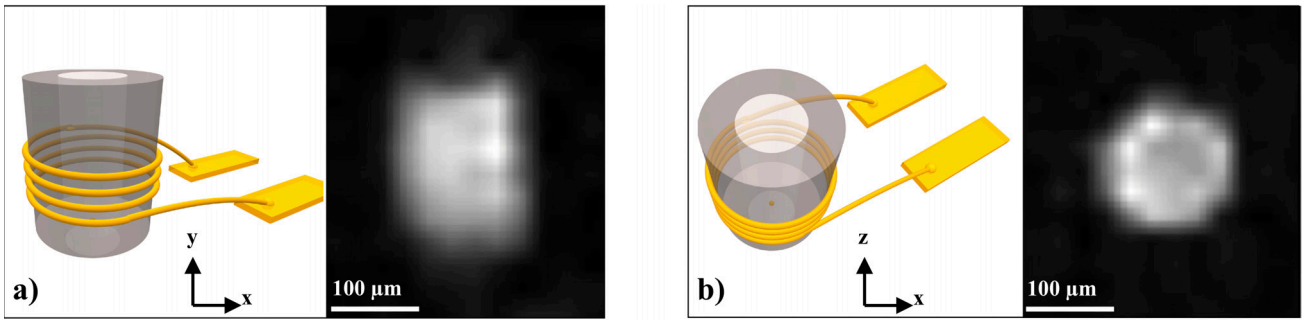

Figure 5: Demonstration of microcoil completely filled with 3.5 nL water sample. a) MR-image with 33 µm × 33 µm resolution in the x-y direction b) MR-image of microcoil from the top showing the cross-section of the microchannel.

CONCLUSION

For nuclear magnetic resonance applications in Lab-on-a-Chip devices, it is essential to minimize the amount of sample which is required for high-resolution spectroscopy or imaging. A smart integration concept of microcoil detectors in a microfluidic networks is therefore a strong requirement. The presented concept to only use micro-droplets for the filling of a solenoidal microcoil therefore may offer new methods for NMR based Lab-on-a-Chip tools.

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