Functional MRI and the Lagrangian description of flow

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Abstract. To investigate local neuronal activity changes and functional connectivity during cognitive and sensory stimuli, functional magnetic resonance imaging (fMRI) relies mainly on the hemodynamic response to brain activation and on measuring small fluctuations in the blood oxygenation levels. Since the basal amount of glucose and oxygen consumptions of the brain are much higher than the activity evoked by cognitive stimuli, the effect of spontaneous cerebral activity must be deduced to evaluate the fMRI responses to given cognitive tasks. We report that in our experiments with water flowing in pipes at an oblique angle with respect to the scan slice a diffuse response can be observed besides other flow artefacts, which can undermine fMRI interpretations. We point out that those artefacts are considered as such because hydrodynamic models disregard the appearance of flow in the images, and more generally the differences between mechanical representations and images.

1. Introduction

Magnetic resonance imaging (MRI) scanners obtain pictures across living organisms that look much like anatomical sections without any need to resort to invasive techniques and exogenous contrast agents. The images are elicited mainly from tissue water, and are formed by sampling spatially encoded free induction decay (FID) responses to radio-frequency (RF) pulses. The contrast originating from the interconnected tissues with distinctive features is epitomized in a few macroscopic parameters. Among them the best known are the relaxation time of the magnetization $T_1$, its dephasing time $T_2$, and the water proton density $\rho$. Moreover, for clinical imaging purposes pulse sequences were devised, that are most sensitive to a single parameter, and accordingly the images obtained were called $T_1$-, $T_2$- and $\rho$-weighted.

Alongside with use in clinical diagnostics, MRI is applied to probe the organization of cerebral cortical areas since 1992 with the aim of linking together functional specializations and anatomical locations. Since the neuron action potentials known to occur from electrophysiology studies cannot be directly monitored with the MRI technique, the direct study of functional activation at neuron scale by functional MRI (fMRI) is precluded. The direct study of neuronal activity is ruled out for yet another reason. Although highly contrasted MR images across the human brain can be obtained, the achieved image resolution of about $0.2\, mm^3$ isn’t enough to address the morphology of the nervous tissue – neurons and glia – at the cellular level. In fact, while under the light microscope stained anatomical preparations revealed the existence of a complex neuronal cytoarchitecture, and accordingly immunohistochemical and autoradiographic markers of cell lineages started to be combined with stereological methods in animal studies, there is yet scant evidence of how to relate MRI images of living human brains with the segregation of the...
physiological functions. This gap should be covered by MRI registrations of functional data. The current aim of fMRI is to uncover neural correlates of cognitive processes on a local basis, and explain them with the help of cytoarchitectonic maps. Our purpose is to draw attention via a simple flow phantom to the fact that a RF image across a living being doesn’t coincide with the cut of its cellular structure model derived from an anatomy atlas.

2. MRI of flow

In 1950 Hahn showed that the $T_2$ relaxation parameter also depends on diffusion [1]. In 1951 Suryan confirmed that the signal intensity in nuclear magnetic resonance (NMR) is affected by flow conditions, and decreases with increased flow velocity along the main field under steady conditions, once signal saturation is avoided. In 1959 Singer applied the NMR technique to living beings, and later he showed that motion of water protons in a homogeneous magnetic field $B_0$ can be accurately measured by time-of-flight methods and by phase encoding. On the threshold of the amazing MRI developments the design of pulse sequences apt to quantitatively evaluate blood flow in major blood vessels were taken up again [2].

In brain physiology liquid motion enters in two ways: first the diffusion of liquids between brain regions is an aspect of functional specialization, it being a clue for interconnectivity, and second hemodynamics supplies oxygen and glucose to an organ lacking any substantial capacity of energy storage. In fMRI, contrast is deemed to rely mainly on changes in the regional blood flow and blood oxygenation levels. As far back as 1881 an Italian physiologist hypothesized that the neural activity is tightly intertwined with precisely controlled changes in blood flow [3]. This insight is interpreted to mean that neural activation is coupled to the microcirculation that provides tissue perfusion.

In MRI, flow is a source of image contrast that allows extracting information on blood already from conventional spin echo (SE) and from gradient echo (GRE) sequences. Both sequences have drawbacks. Thus the former, SE, allows measurements in a restricted velocity range only, while the latter, GRE, is too sensible to field inhomogeneities $B_1$ due to different tissue susceptibilities. The relationship between the two time constants is $\frac{1}{T_2^*} = \frac{1}{T_2} + \gamma B_1$, with $\gamma = 42.58 MHz/T$. When deploying GRE pulse sequences to obtain $T_2^*$-weighted images, contrast regions appear around veins and in regions densely packed with venous capillaries that cannot be evidenced just as well while using a spin echo (SE) sequence. The supplemental contrast was ascribed to local susceptibility changes due to high deoxy-hemoglobin levels in blood. During oxygen uptake by red cells, hemoglobin switches from the paramagnetic to the diamagnetic state, and contrast disappears. The Lagrangian description of flow is assumed to be valid in numerical simulations, because the labeled water protons are precisely the particles displaced by motion [4, 5]. The link between local blood contrast and brain activation also depends on whether the course of the veins and capillaries correspond in the images and anatomically.

3. Materials and methods

Experiments were performed on a Tomikon MRI system using a $B_0 = 4.7 T$ superconducting magnet with an inner bore diameter of 40 cm. Since $\omega_0 = \frac{2\pi}{\tau} \times B_0$, the operating frequency was $\approx 200 MHz$. The bore diameter of the inner probe head was 25 cm. The echo time $TE = 34.06 ms$, by definition the time between the 90° pulse and the maximum of the echo, was factory set, while we put the pulse sequence repetition time $TR = 2 s$. Sixteen sequential copies of a single slice were acquired by applying a 90° sinc shaped pulse envelope followed by sixteen 180° rephasing pulses (Carr-Purcel-Meiboom-Gill sequence - CPMG).

With reference to figure 1, a slice in a plane perpendicular to the magnet axis ($z$-axis) is frequency encoded by applying a slice-gradient $G_s$ during the 90°-excitation. That FID is refocused sixteen times and its echo is acquired with read-gradient $G_r$ on. Application of the latter gradient encodes a phase $\varphi \propto \gamma \int G_r(t) dt$ on the frequency response projected onto the $x$
-axis, that is responsible for the shape of the profile in the transformed signal. The R-preload gradient compensates in advance for the FID dephasing introduced by the read-gradient. The R-trim aims at rephasing the FID within the loop by trial and error. In the method of image reconstruction from projections used here the section is reconstructed from data obtained by increasing the angle that the read-gradient axis forms in the $xy$ plane before each new acquisition. As an alternative, the phase encoding method implemented as 2D-Fourier transform technique would change the dephasing of the preload gradient in the $y$-direction. Our acquisition matrices were $256 \times 256$, and the field of view (FOV) was $12\text{cm}$. Constant, laminar flow rates through a $3.5\text{m}$ long silicon tube of $0.9\text{cm}$ gauge passing four times through a rigid $9 \times 9 \times 5\text{cm}^3$ stand were obtained exploiting a Mariotte bottle as a tank. Nominal slice thicknesses were 4, 8 and $12\text{mm}$, and the measured flow rates $Q$ were in the range $0.36 - 5.7\text{cm}^3/\text{s}$. Consequently, mean flow velocities $Q/F \ (F = \pi 0.45^2)$ ranged from $0.57\text{cm/s}$ to $9.7\text{cm/s}$. Data for flow perpendicular to the slice, and inclined rearwards by $45^\circ$ from the vertical ($y$-direction) were collected at the Fraunhofer Institut directed by prof. K. Gersonde. We refer to [6, 7] for further experimental details. For comparison, the lumen of cerebral vessels is seldom larger than a few millimeters, and the flow is always pulsed. Mean flow in large vessels is reported to be about a dozen centimeters per second.

4. Results and discussion
Since the $45^\circ$ tilt has no component along the $x$-direction, flow doesn’t affect the phase-encoding along it, and the imaged $x$-position of the tubing doesn’t suffer any speed dependent overall displacements even without flow-compensating gradients [8]. As the velocity increases, though, the boundary layer of relatively stagnant flow near the wall is distorted along the $y$-direction, and so is the parabolic Poiseuille profile. The flow lines are cut, which is why the velocity component perpendicular to the slice is estimated with a higher error, and also depends on the slice thickness.

The $12\text{mm}$ slice is too large for our $9\text{mm}$ inner gauge tubing. In passing, with increasing slice size flow-induced field inhomogeneities contribute additional distortions to the image. The intensity of the odd echoes for the remaining slice thicknesses roughly satisfies an exponential curve $M(t) = M(0) \exp(-t/T_{2,eff})$ with an effective time constant $T_{2,eff} = T_2 + \frac{v}{d}$, where $T_2$ refers to immovable water, and $v/d$ accounts for the component of velocity perpendicular to the slice $d$ of flowing water. The factory set $TE$ value is too high, limiting the range of measurable velocities. Above $4\text{cm/s}$ the signal intensity for the $4\text{mm}$ slice at once reduces to $1/e \approx 0.368$, and prevents from estimating the value of $v$. Again, our repetition time $TR = 2s$ is too short for the magnetization of water protons to return to the unexcited condition, because water has a $T1$ relaxation time in excess of $4s$. For this reason the SE pulse sequence keeps a steady state magnetization different from the fully relaxed one, and acquisitions occur under dynamic saturation conditions.
Figure 2: Images of water flowing at 4 cm³/s in a tubing oriented at 45° wrt. the slice. Top: 4mm slice, echoes 1 and 5. Bottom: 8mm slice, echoes 1, 5, and 7. Insert: the stand.

Figure 3: Water flowing in the 4mm slice at 45° wrt. it. Rising flow rates, 0.36, 2.6, and 5.7 cm³/s. Top: 1st echoes. Bottom: echoes 15, 9, and 3.

In figure 2 the 4mm and 8mm slices are shown for \( v \approx 6.4 \text{ cm/s} \). The small bright spots appearing nearby are water filled reference vials parallel to the stand. With the stand at 45° the 8mm slice isn’t entirely contained within it, but in no case the course of the real tubing just outside it can run parallelly to the slice. Yet, the first echoes show partially excited liquid flowing within the tubing, which is washed out in subsequent echoes. The residual excitation belongs to the response to the 90° sinc pulses other than the actual one. It hasn’t yet decayed after \( TR \), and is correctly refocused. The effect is further highlighted in figure 3. At low velocity stagnancy supports formation of refocused spots along the tubing, and contributes to the image at late times. On the opposite, rapid flow smears the course of the tubing already in the first image, affecting a wider range as the velocity rises.

5. Conclusions

Inflow and outflow from an imaging section is known to affect the intensity of a blood vessels’ lumen. It is also known that flow oblique to the read-out direction causes a speed dependent displacement of the lumen from the vessel wall. Since our flow phantom with adjustable constant flow is simple, and we use a standard spin-echo sequence, we can show how the signal echoed from water flowing into sloped pipes, whose course lies manifestly outside of the imaged slice, is projected onto it. Velocity dependent smeared patterns appear on the image. When using MRI for demanding applications, like image-guided surgery, geometric and flow artefacts, that also depend on the chosen acquisition sequence, ought to be noticed and corrected as far as possible on each patient. Perhaps such smeared patterns also matter in connection with diffusion and capillary flow in functional MRI (fMRI). Anyway, MRI images look more like an electromagnetic field than an idealized mechanical cut, and cannot be forced to correspond point by point with anatomical sections. In particular, due to the above flow and diffusion effects on the images, the Lagrangian specification of spin flow may be apt to lead to misinterpretation if one is looking after small signal differences.

6. References

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