Phase Modeling in Arterial Spin Labeling FMRI

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Introduction

Phase information is routinely discarded from FMRI data analysis.

Complex-valued image analysis boosts the sensitivity and specificity of BOLD contrast FMRI time series (Rowe, 2005).

While one can intuitively see that the sensitivity of statistical analyses is greater just by virtue of having more data available (real and imaginary components), there are biophysical reasons to predict changes in the MR signal's phase in the presence of BOLD activation. (Menon, 2002; Nencka and Rowe, 2007)

Typical ASL FMRI analysis (OLS analysis of the subtracted magnitude data) "wastes" information by using only the magnitude of the signals, as potentially valuable phase information is routinely discarded.

The presence of the inversion labeled ASL data can also induce changes in the phase of the labeled images, also called tagged imaged, relative to the control images, as we discuss below in greater detail.

We examine the biophysical basis for phase changes in the ASL signal (independent of the BOLD effect related phase changes), and develop an analysis approach for ASL time series that includes least-squares analysis of the complex undifferenced ASL data as has been done for magnitude data (Mumford et al., 2006).

Our analysis scheme models the changes in perfusion and BOLD contrast as complex quantities.

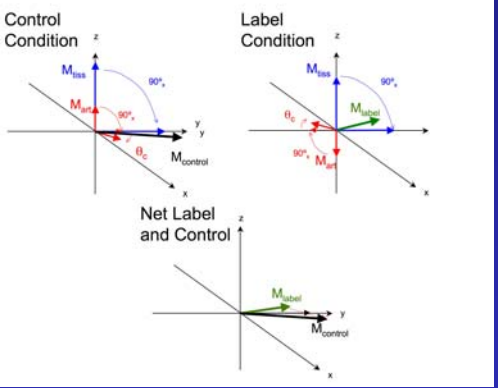


Figure 1 – Vector Model of ASL experiment

Simple cartoon (not drawn to scale) illustrating the sources of magnetization and their phase gain during the acquisition segment of an ASL experiment.

Blue arrows indicate the magnetization due to the tissue spins, and red arrows indicate the magnetization from the arterial sources.

The net magnetization vectors under control and labeled conditions are shown in black and green, respectively.

Note that the tissue magnetization vector is shortened as the tagged blood exchanges into the tissue.

ASL Activation study

Stimulation: Visual stimulation paradigm (8 Hz flashing checkerboard: six cycles of 50 s rest – 50 s active).

Five slices were prescribed encompassing the visual cortex and 150 time frames were collected.
Experiment repeated using two different methods of arterial signal suppression and compared to no suppression at all:

1. Pair of flow crusher gradients (VENC = 3.3 cm/s),
2. Post inversion delay of 1200 ms.

Experiments

Human Studies: Scanning protocols were performed using a 3.0 T Signa LX Excite scanner (General Electric, Waukesha, WI) in accordance to the University of Michigan's IRB regulations.

ASL resting state study: arterial suppression

Anatomy

A high resolution T1-weighted GRE image (TR = 200, TE = 3.4, flip = 90, FOV = 24, matrix size = 256 × 256) was collected in the same location as the ASL images described above for anatomical reference.

Angiographically weighted image was also collected using a multi-shot spiral sequence in order to localize the major arteries within the slice (GRE, TR=100, TE = 11, flip = 90, N. interleaves = 8).

Binary masks for the arteries and for brain tissue were constructed by thresholding the arterially weighted images by visual inspection of the image intensity histogram.

ASL

ASL imaging was done using the pseudo-CASL sequence (spin-echo spiral acquisition with TR /TE = 4000 /15 ms., slice thickness = 7 mm, FOV = 24 cm, 1 slice, 96 time frames).

Labeling pulses : train of Hanning window shaped pulses (pulse width = 500 μs, pulse spacing = 290 μs, flip angle 22.5 degrees, net gradient moment = 3×10^{-5} G/cm/s) applied for 3600 ms.

Experiment 1: Post inversion delays of 0, 1200 and 1800 ms without any flow crushers.

Experiment 2: no post-inversion delay, but in the presence of a pair of flow crushers (pulse width = 2 ms, separation = 8.8 ms, amplitude= 0, 1, 2 and 4 G/cm). The VENC values of this pair were *Inf* (i.e., no crushers), 6.6 and 3.3 cm/s along the Y gradient axis.

Processing:

1. Complex reconstruction
2. Realignment (MCFLIRT): magnitude and phase
3. Calculate mean magnitude and phase differences
4. Maps of Correlation between magnitude and phase time courses

Complex Analysis

Three general linear models for the **unsubtracted** activation data.

1. Linear regression model (linear x with linear y) applied to the magnitude-only (MO) data
2. Angular regression model (linear x with angular y) applied to the phase-only (PO) data
3. Nonlinear regression model that fully utilizes the complex magnitude and phase (MP) data .

The design matrix utilized for these analyses included represent a baseline, the BOLD response, an ASL control regressor, and an ASL tag regressor. Together, they make up the columns of the design matrix. A contrast C=(0,0,-1,1) was utilized to test hypotheses H_0: Cβ=0 versus H_1: Cβ≠0 for a difference between tag and control images.

Arterial Volume Imaging by Saturation (AVIS)

Another activation study was performed using an ASL method that produces arterial volume images - described in detail in the following reference (Vazquez et al., 2006),

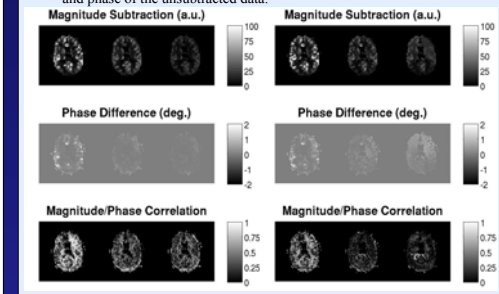
Experiment 1: Visual stimulation used was the same as above but the activation and rest blocks were each 60 s in duration.

Experiment 2: Hypercapnia was induced by administration of 5% CO2 in 95% oxygen for 30 seconds. Baseline breathing mixture was 100% O2.

Baseline (Rest) ASL Results

The images below show ASL images acquired with different techniques and degrees of arterial suppression. The left panel shows data using post inversion delays (PID) while the right panel shows data collected using crushers.

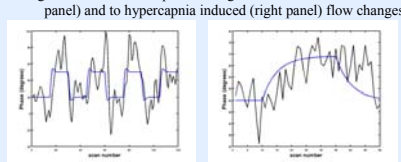
The top row of images shows the mean magnitude subtraction of the time course, the middle row shows the mean phase difference, while the bottom row shows the correlation between magnitude and phase of the unsubtracted data.



Magnitude and phase time courses were correlated in arterial regions. This correlation was significantly reduced by the use of post inversion delays and flow crusher gradients (bottom row), supporting an arterial origin for the correlation. The reduction in correlation was much stronger in the case with diffusion crushers because diffusion crushers introduce a lot of phase noise in the images.

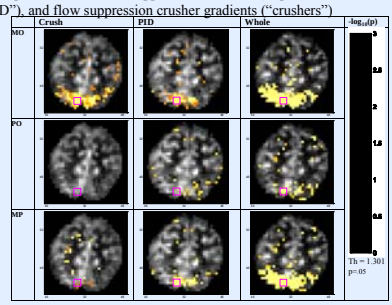
AVIS Results

The figures below indicate phase changes due to activation induced (left panel) and to hypercapnia induced (right panel) flow changes



Complex Analysis Results

The figure below is one slice of the resulting statistical maps ($-\log_{10}(p)$) obtained using the three models: First row: Magnitude-Only ("MO"), second row: Phase-Only ("PO"), third row: Magnitude-and-Phase ("MP"). Each column shows data acquired with different arterial suppression technique: No arterial suppression ("whole"), post inversion delays ("PID"), and flow suppression crusher gradients ("crushers")



Discussion

- Arterial Spin Labeling (ASL) has the potential of being a very powerful tool for functional neuroimaging but it is plagued by inherently low SNR. It is therefore imperative that ASL image analyses utilize the greatest amount of information possible in the signal.
- There is a significant phase difference (up to 7 degrees) between control and tagged images when the arterial component of the signals is preserved.
- The phase difference is greatly reduced as the arterial contribution is suppressed by post inversion delays and flow crushing gradients.
- The phase difference between control and tagged images increases with increasing blood flow, and thus changes in the phase of the ASL signal are indicative of neuronal activation.
- Increase in blood flow alone produces a change in the phase of arterial volume images collected using the AVIS (arterial volume imaging by saturation) technique.
- Complex ordinary least-squares analysis techniques for estimation and detection are adapted and demonstrated on ASL data. Complex Analysis reduces false positive rate.

References

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