Mapping multi-contrast microstructural MRI of the placenta

Paddy Slator, Centre for Medical Image Computing, UCL (p.slator@ucl.ac.uk)

If you find any mistakes or typos don't hesitate to email me!

Background

In Coursework 1, you analysed brain diffusion MRI (dMRI) data with a variety of microstructural models. In this project, you will explore *multi-contrast* dMRI scans of the placenta. These have a couple of important differences:

1. This is multi-contrast dMRI data; as well as diffusion properties the MRI sequence also probes T2* relaxation (more on that later).
2. These are scans of the placenta acquired during pregnancy. There are some important differences between placenta and brain dMRI data. For one, in the placenta flowing blood has a much bigger volume than the brain, and hence a bigger effect on the dMRI signal. This means that we need to use different microstructural models with different assumptions about tissue.

In this project, you will use a variety of approaches to analyse multi-contrast placental diffusion MRI scans acquired during pregnancy. In the earlier tasks you will replicate some previous results. Later tasks are more open ended.

Data

MRI volumes

This comprises two multi-contrast diffusion MRI scans. So far you have only looked at diffusion MRI data, where b-value and gradient directions are varied to yield image contrast. In this data an additional MR scanner parameter, the echo time (TE), is also varied. There are two scans stored as nifti files:

- one healthy control: **'pip0101_20_20_1401_T2MEdiff_abs.alle.nii'**
- one participant who went on to be diagnosed with pre-eclampsia (a common pregnancy complication): **'pip0120_20_20_2501_T2MEdiff_abs.alle.nii'**

Masks

Each dataset has two corresponding binary masks, with each specifying a region of interest (ROI). The masks have the same spatial dimensions as the MRI volumes, and each voxel in the mask is either a one (if the voxel is inside the ROI) or a zero (if outside the ROI). There are two masks for each scan: a placenta ROI, and an ROI comprising the placenta and an adjacent section of uterine wall. Like the MRI volumes, these are nifti files:

- **'pip0101_placenta_and_uterine_wall_mask.nii.gz'**
- **'pip0120_placenta_and_uterine_wall_mask.nii.gz'**
- **'pip0101_placenta_mask.nii.gz'**
- **'pip0120_placenta_mask.nii.gz'**

MRI acquisition parameters

As you learnt previously, to analyse a diffusion MRI (dMRI) scan requires knowledge of the diffusion weighting for each volume, encoded by the b-value (bvals) and gradient directions (bvecs). Since this is multi-contrast data, each acquired volume also has a corresponding echo time (TE), which gives us information on T2* relaxation. Similarly to diffusion MRI, T2*

relaxation causes the signal to decay exponentially, although the relationship is reversed – *higher* T2* relaxation time equals *slower* decay. For this data, the acquisition parameters are contained in a gradient table called **grad_echo.txt**: a tab-separated .txt file where each row corresponds to a single multi-contrast dMRI volume. The first three columns of grad_echo.txt contains the bvecs – gradient strengths in the x, y and z directions; the fourth column contains the b-values (in s/mm^2); and the fifth column contains the echo times (in ms).

Models

The microstructural models we fit to the data need to reflect the tissue composition of the placenta, and also account for the additional TE dependence of the data. These models allow us to estimate diffusion-derived parameters related to tissue microstructure, as well as T2* relaxation times.

T2*-ADC

As you have seen, we can analyse dMRI data using a wide variety of microstructural models. The simplest and most well-known is the apparent diffusion coefficient (ADC) model which relates the observed signal (S) to the b-values with a simple exponential decay function. We can extend this model to also account for the T2* decay in this data as follows:

$$\mathrm{S(b, TE)} = \mathrm{S0}\exp(-TE/\,T2^{*})\exp(-\mathrm{b\ D})$$

where b is the b-value, TE is the echo time, S0 is the signal at b=0 and the lowest TE (TE = 78ms for this data), D is the apparent diffusion coefficient, and T2* is the T2* relaxation time. We call this model the T2*-ADC model.

T2*-IVIM

However, the ADC has many flaws. For one it doesn't account for the contribution to the signal from different tissue compartments with vastly different diffusivities. For example, blood perfusing in capillaries and vessels "diffuses" (technically it's not true diffusion – we call it pseudo-diffusion) much faster than water within tissue. We can build multi-compartment models that account for this. The intravoxel incoherent motion (IVIM) model is a two-compartment model, where one compartment accounts for diffusion (e.g. water in tissue), and one accounts for perfusion (e.g. water in flowing blood). The combined T2*-IVIM model is given by

$$\mathrm{S(b, TE)} = \mathrm{S0}\exp(-TE/\,T2^{*})\,[\mathrm{f}\exp(-\mathrm{bD_p}) + (1-\mathrm{f})\exp(-\mathrm{bD})]$$

where f is the perfusion fraction, D_p is the blood diffusivity, and D is the non-blood diffusivity. We can think of f as the fraction of a voxel that comprises perfusing blood, D_p as the rate at which this blood is perfusing, and D as the diffusivity of the "non-flowing blood". The fitted parameter values should be constrained so that D_p is larger than D, and f is between 0 and 1.

Continuum modelling

A continuum model assumes that a voxel (or ROI) contains water with a spectrum of MR properties. For a general n-dimensional multi-contrast MRI experiment the voxel signal is

$$\mathrm{S(b,TE)} = \int\int \mathrm{F}(T2^*, \mathrm{D})\ \exp(-TE/\,T2^*)\exp(-\mathrm{bD})\ dT2^*\ dD$$

Where $\mathrm{F}(T2^*, \mathrm{D})$ is the T2*-D spectrum, i.e. the 2D distribution of T2* and diffusivity values within the voxel or ROI, and $\exp(-TE/\,T2^*)\exp(-\mathrm{bD})$ is known as the kernel.

The T2*-D spectrum spectrum can be estimated from multi-contrast diffusion MRI data as follows. The signal equation above is first discretised onto a defined 2D grid of T2* and D values of size N_{T2^*} by N_D; the values covered by this grid should reflect the expected T2*, D values. This gives the following discretized signal expression

$$\mathrm{S(b,TE)} = \sum_{i=1}^{N_{T2^*}} \sum_{j=1}^{N_D} \mathrm{F}(T2_i^*, \mathrm{D_j})\ \exp(-TE/T2_i^*)\exp\left(-\mathrm{bD_j}\right)$$

Where $\mathrm{F}(T2_i^*, \mathrm{D_j})$ is the value of the spectrum at position (i, j) in the 2D grid of T2*, D values. By choosing an ordering of the elements of the 2D grid coordinates, the signal for the whole dataset can hence be written in matrix form as

$$\mathrm{S} = \mathrm{KF}$$

Where S is a column vector (length $\mathrm{N_S}$, the number of acquired volumes) of the signals, K is a matrix, size N_S by $N_{T2^*}N_D$, of kernel values at the 2D grid coordinates, and F is an $N_{T2^*}N_D$ length column vector of spectrum values. This matrix equation can be solved with non-negative least squares (lsqnonneg in matlab) to estimate the T2*-D spectrum.

CORE TASKS

These tasks are more structured, whereas the advanced tasks are more open ended.

Task 1 – Load and plot the MRI volumes and masks

Load the MRI volumes (e.g. using matlab niftiread function). Make sure the images have been loaded as double-precision arrays (if not, convert them). What is the dimensionality of the data? Plot some image slices in the first, second and third spatial dimensions. Load the mask nifti files and plot some representative image slices of the placenta and uterine wall masks to familiarize yourself with the position of these structures. The supplied schematic drawing (placenta_schematic.pdf) may be helpful.

Task 2 – Load and plot the MRI acquisition parameters

Load the gradient table (**gradecho.txt**) into a matlab array. How many rows are there in the gradient table, and how does this correspond to the dimension of the loaded MRI volumes? How many unique b-values does the gradient table have? How many unique echo times? Make a 2D scatter plot of the b-values and echo times (echo times on the x-axis, b-values on y-axis).

Task 3 – Fit the combined T2*-ADC model

Fit the T2*-ADC model to the data in a single voxel (make sure the voxel is within one of the ROIs). Assume Gaussian noise and put sensible constraints on S0, D, and T2*; you can look

at the maps in Figures 4 and 5 of reference [1] to help you choose constraints. Check that the fit is good by plotting a voxel's raw signal and the model predicted signal on the same axis in a few example voxels. Fit the T2*-ADC model to all voxels within the placenta and uterine wall mask, and hence make voxelwise maps of the fitted model parameters. (If fitting to all voxels in the mask is taking too long, you can try fitting only to voxels in slice 7 of both scans.)

Task 4 – Compare maps for control and pre-eclampsia participants

Make a figure that visualises the differences between voxelwise maps for the control and pre-eclampsia scans. You could plot the parameter maps side by side (make sure you use the same color scaling), perhaps with some arrows to point out differences, plot boxplots that show how the parameter values within ROIs differ, or think of something else…

Task 5 – Fit the combined T2*-Intravoxel incoherent motion (IVIM) model

Now fit the T2*-IVIM model, which explicitly accounts for the effect of perfusing blood on the signal. Enforce the condition that D_p>D when fitting. Plot maps of the fitted parameters (S0, D, D_p, f, T2*) for control and pre-eclampsia scans, and compare them to the T2*-ADC maps.

Task 6 – Model selection with BIC

Calculate the Bayesian information criterion (BIC) model selection statistic, for the T2*-ADC and T2*-IVIM models. Calculate the BIC in every voxel and plot maps of which model explains the data best (i.e. has the lowest BIC value) in each voxel – see reference [2] for some examples of these maps for diffusion MRI (i.e. not including T2*) models. Describe which model best explains the data in different areas and participants.

ADVANCED TASKS

Now you will fit some more complex models to the data. These tasks are more open ended than the core tasks.

Task 7 – Continuum modelling

So far, we have always assumed the number of model compartments before fitting to the data. Data-driven methods, as used in [1], make less assumptions and try to learn directly from the data. Your task is to implement continuum model fitting to estimate the T2*-D spectrum for the ROIs. First calculate the average signal in each of the ROIs by averaging across the 4^{th} dimension (i.e. the multi-contrast volumes). Then follow the instructions above to calculate the spectra, and display them in contour plots; see reference [1] for examples of placental T2*-D spectra.

Task 8 – Extended compartment models

Try adding another compartment (or compartments) to the T2*-IVIM model, and fit your new model to the data. Study the T2*-D spectra from Task 7 and read up on placental structure in references [1–3], and hence justify your choice of additional compartment(s) in the report. What aspects of placental microstructure and/or perfusion do you anticipate your new model will capture? Plot maps and calculate the BIC for your new multi-compartment models. (Note that as you add more parameters to the models there comes a point where the data will no longer support the fitting, so don't be discouraged if some of

your plots and maps don't look very good – I would be very surprised if they all looked perfect! Just report what model you fitted, explain the reasons behind your choice, and plot some simple parameter maps.)

References

1. Slator PJ, Hutter J, Palombo M, Jackson LH, Ho A, Panagiotaki E, et al. Combined Diffusion-Relaxometry MRI to Identify Dysfunction in the Human Placenta. Magn Reson Med. John Wiley & Sons, Ltd; 2019; 1–22. doi:10.1002/mrm.27733
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3. Melbourne A, Aughwane R, Sokolska M, Owen D, Kendall G, Flouri D, et al. Separating fetal and maternal placenta circulations using multiparametric MRI. Magnetic Resonance in Medicine. John Wiley & Sons, Ltd; 1 Jan 2018: 350–361. doi:10.1002/mrm.27406