Verbena documentation

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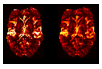
Contents:



Verbena is a Bayesian Inference tool for quantification of perfusion and other haemodynamic parameters from Dynamic Susceptibility Contrast perfusion MRI of the brain.

VERBENA complements the OXASL pipeline for the quantification of perfusion using Arterial Spin Labelling MRI and is built on the same core inference algorithm (FABBER). VERBENA uses a specific physiological model for capillary transit of contrast within the blood generally termed the 'vascular model' that was first described by Ostergaard (see below). In VERBENA the model has been extended to explicitly infer the mean transit time and also to optionally include correction for macro vascular contamination - contrast agent within arterial vessels - more information on the model can be found in the theory section.

VERBENA takes a model-based approach to the analysis of DSC-MRI data in contrast to alternative 'non-parametric' approaches, that often use a Singular Value based Deconvolution to quantify perfusion. An alternative Bayesian Deconvolution approach is also available, but not currently distributed as part of FSL. For more information see the reference below and contact the senior author.

VERBENA is included in FSL v6.0.1.

CHAPTER 1

Running verbena

For the full usage of VERBENA type `verbena` at the command line. A typical usage of VERBENA would be:

```
verbena -i data.nii.gz -a aif.nii.gz -o output_directory -m mask.nii.gz
```

This would process the 4D DSC data in `data.nii.gz` using the AIFs supplied in `aif.nii.gz` and using the modified Vascular Model to estimate (relative) perfusion, commonly referred to as cerebral blood flow (`rCBF`), along with the mean transit time (`MTT`) and the transit time distribution parameter `lambda`.

Maps of these are placed in the output directory. Analysis is only performed within the mask supplied (`mask.nii.gz`) which will normally have been derived from a brain extraction using BET or other equivalent tool.

1.1 AIFs

VERBENA takes as an input a 4D Nifti file containing the Arterial Input Functions (AIFs) this should have identical dimensions to the data and thus should have a single AIF time course for every single voxel (within the mask).

If the AIF is taken directly from the DSC data it will be in the form of a DSC signal. However if the AIF has been preprocessed using some other tool, or a predefined 'population AIF' is being used, it may take the form of a *concentration* time curve. In this case the option `-aifconc` should be given to indicate this. Verbena will perform conversions between signal and concentration curves as required.

Often this will be a single global AIF replicated for every single voxel. However, VERBENA allows for different AIFs to be specified for individual brain regions should a local AIF be available.

We do not currently include a tool for the selection or identification of the AIF. Often the AIF time course will be manually selected from the DSC data by the identification of a major artery, various automated methods have been developed in the literature and it may be possible to find tools that implement them online.

1.2 Acquisition parameters

The `-tr=TR` option is used to specify the time resolution of the data in seconds, i.e. the time spacing between volumes. The `-te=TE` option specifies the assumed TE of tissue, used for conversion of concentration to signal

1.3 Macro vascular contamination

By adding the `-mv` option an additional component will be added to the model (based on the AIF) to account for macro vascular contamination contrast in large arteries, see Theory. When this option is included a further image will be produced in the output directory that maps the Arterial Blood Volume (`rABV`) in relative units.

By default the additional macro vascular component is added when the concentration time course of the voxel is calculated, optionally addition of the tissue and macro vascular component can be done as signal time courses using the `-sigadd` option.

1.4 'Model-Free' Analysis

VERBENA takes a model-based approach to perfusion quantification. It is possible to use a more conventional Singular Value Decomposition deconvolution method by choosing the `-modelfree` option.

This 'model-free' quantification can also be used to create initial estimates for the main model-based VERBENA analysis using the `-modelfreeinit` option, which may lead to more robust results in some cases.

CHAPTER 2

Theory

2.1 The Vascular Model

The Vascular Model was originally proposed by Ostergaard et al[1]. and was used for the analysis of DSC data (within a Bayesian like algorithm) by Mouridsen et al.[2]. The basic principle follows all tracer kinetic studies and treats the concentration of contrast agent in the tissue as the convolution of an arterial input function (AIF) and a residue function.

$$C(t) = CBF \int_0^t C_a(\tau) R(t-\tau) d\tau$$

Where C_a is the arterial concentration as a function of time (AIF) which describes the supply of tracer by the blood and $R(t)$ is the *residue function* which describes the dissipation of the tracer once it has arrived - for example how long a unit of contrast agent remains before it is removed to the venous vasculature. . CBF is the cerebral blood flow which scales the concentration.

In the context of DSC-MRI the convolution model is applied to each voxel in turn and the residue function represents the residence of the agent within the tissue volume described by the voxel. In the healthy brain the Gadolinium tracer that is used in DSC-MRI does not leave the vasculature and thus the residue function encapsulates the transit of the contrast agent through the capillary bed. In fact the residue function is the integral of the distribution of transit times for blood passing through the voxel - a key parameter of which is the mean transit time (MTT), which is routinely used in DSC perfusion as a surrogate measure of perfusion (although it is often calculated without finding the transit distribution itself).

The Vascular Model assumes that the transit time distribution can be modelled as series of parallel pathways of differing lengths that can be summered by a gamma distribution of transit times.

$$R(t) = \int_t^\infty \frac{1}{\beta^\alpha \Gamma(\alpha)} t^{\alpha-1} e^{\frac{-t}{\alpha}}$$

[1] *Ostergaard L, Chesler D, Weisskoff R, Sorensen A, Rosen B. Modeling Cerebral Blood Flow and Flow Heterogeneity From Magnetic Resonance Residue Data. J Cereb Blood Flow Metab 1999;19:690–699.*

[2] *Mouridsen K, Friston K, Hjort N, Gyldensted L, Østergaard L, Kiebel S. Bayesian estimation of cerebral perfusion using a physiological model of microvasculature. NeuroImage 2006;33:570–579. doi: 10.1016/j.neuroimage.2006.06.015*

Here $\alpha > 0$ and $\beta > 0$ describe the shape and scale of the transport distribution. $\alpha\beta$ is the mean of the distribution which can be identified as the mean transit time (MTT) of the tracer.

In practice DSC measures the effect that this concentration of contrast agent has on the T2* of the voxel which is described by a non-linear transformation.

$$S(t) = S_0 e^{r_2 C(t) TE}$$

Where S_0 is the baseline signal before the bolus arrives and r_2 is the T2 relaxivity of the contrast agent.

In VERBENA it is this final estimated signal that is compared to the data and used to find the optimal parameters using a Bayesian inference algorithm. Additionally the potential for a time delay between the supplied AIF (often measured at a remote location from the tissue) and the tissue signal is included in the model.

2.2 The Modified Vascular Model

VERBENA implements a modified version of the Vascular Model whereby the MTT is not pre-calculated from the data, but instead is a further parameter to be estimated as part of the inference applied to the data. This removes the risk of bias from the separate MTT calculation and also allows for a separate macro vascular component to be implemented within the model.

The other model parameter used by Verbena is named lambda and is identified with α. in the residue function model. Hence in it's basic form the Verbena model contains three parameters: `CBF`, `MTT` and `lambda`. An additional parameter `delta` can be used to model a delay in the arrival of the arterial input.

2.3 Macro Vascular Contamination

VERBENA has the option to include a macro vascular component to the model. This combines the estimated concentration time curve from the (modified) vascular model with a scaled version of the AIF, where the AIF is representative of contrast that is still within the large arteries during imaging and the scaling is a (relative) measure of arterial blood volume.

The component is subject to a 'shrinkage prior' that aims to provide a conservative estimate - so that this component is only included in voxels where the data supports its inclusion, recognising that macro vascular contamination will be be universally present within the brain, but only occur in voxels that contain large arteries.

The combination of tissue and macro vascular contributions could be done in terms of the concentrations of contrast in the voxel. However, since in DSC it is the T2* effect of the concentration that is measured, the summation might be better done with the signals once their effect on T2* has been accounted for. VERBENA offers the option to do either, there is currently no clear evidence as to which is most physically accurate and it is likely that both are an incomplete representation of the reality, see Chappell et al[3].

2.4 The CPI model

The CPI model (Control Point Interpolation) is an alternative model for the residue function $R(t)$. Rather than base this function on physical assumptions, the CPI model simply defines a finite number of 'control points' C_n whose residue function values $R(C_n)$ are allowed to vary as model parameters. The full residue function is determined by fitting a natural spline curve to these points with the constraint that $R(0) = 1$ (no loss of contrast agent at time zero).

[3] *Chappell, M.A., Mehndiratta, A., Calamante F., "Correcting for large vessel contamination in DSC perfusion MRI by extension to a physiological model of the vasculature", e-print ahead of publication. doi: 10.1002/mrm.25390*

In addition we expect $R(t)$ to be a decreasing function, hence the C_n are modelled by multiplicative factors each in the range $[0, 1]$ with $R(C_{n+1}) = P_{n+1}R(C_n)$.

The CPI method allows great flexibility in the shape of the $R(t)$ however this is at the cost of larger numbers of model parameters.

2.5 References

CHAPTER 3

Referencing

If you use VERBENA in your research, please make sure that you reference Chappell et al[1].

The following articles provide more background on the original vascular model from which the VERBENA model is derived:

An alternative Bayesian 'non-parametric' deconvolution approach has been published in:

[1] *Chappell, M.A., Mehndiratta, A., Calamante F., "Correcting for large vessel contamination in DSC perfusion MRI by extension to a physiological model of the vasculature", e-print ahead of publication. doi: 10.1002/mrm.25390*