Image Analysis and Statistical Inference in Neuroimaging with R

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Abstract

R is a free software environment for statistical computing and graphics. It compiles and runs on almost every UNIX platform, Windows, and Mac OS.

In this paper, we report on several R packages built for the analysis of neuroimaging data in the context of functional Magnetic Resonance Imaging, Diffusion Tensor Imaging, and Dynamic Contrast-Enhanced Magnetic Resonance Imaging. We will review their methodology and give an overview over their capabilities for neuroimaging. Finally, we summarize some of the current activities in the area of neuroimaging software in R in general.

Introduction

The rapid progress of research in the neuroscience and neuroimaging fields has been accompanied by the development of many excellent analysis software tools. These are implemented in a variety of computer languages and programming environments, such as Matlab, IDL, Python, C/C++ and others. This diversity has developed over time through a combination of user preferences and the strengths/weaknesses of the computing environments. Many of these software tools are freely available, like SPM (Ashburner et al., 2008), AFNI (Cox, 1996), FSL (Smith et al., 2004), Freesurfer, or BrainVISA, some are commercial like BrainVoyager, and Analyze. Typically, the software tools can be extended by the user to fit their needs in the data analysis. The NIPY (Millman and Brett, 2007) project e.g. is written in Python and a explicitely allows for the integration, modification and extension of code.

R is a free software environment for statistical computing and graphics (R Development Core Team, 2010). It compiles and runs on almost every UNIX platform, Windows, and Mac OS. Access to R is provided via the Comprehensive R Archive Network (CRAN, `http://cran.r-project.org`) and R-Forge (`http://r-forge.r-project.org`). R provides a wide range of statistical (linear and nonlinear regression modelling, classical statistical tests, time-series analysis, classification, clustering, etc...) and graphical techniques, and is highly extensible. As of November 2010, the CRAN package repository features over 2600 separate packages contributed by R users. A recent community website (`http://crantastic.org`) provides the facilities to search for, review and tag CRAN packages. Several mailing lists are maintained in order to provide updates and access to literally thousands of R users. This is in addition to a complete set of open-access manuals about the R language.

Why is it worthwhile to consider just another programming environment for neuroimaging? R is the free and platform-independent quasi-standard computational environment within the statistics community. R grants access to many well-developed statistical tools needed for the analysis of neuroimaging data. R easily integrates, other software can be used from within R and R can be used within a more general workflow. Finally, special R packages for neuroimaging provide enhanced functionality which is not available elsewhere.

In this paper, we report on several R packages built for the analysis of neuroimaging data in various context. We will shortly review the methodology of each package to give an impression of their capabilities for neuroimaging. The paper is organized by the type of data which is to be analyzed and covers functional Magnetic Resonance Imaging (fMRI), Diffusion Tensor Imaging (DTI), and Dynamic Contrast-Enhanced MRI (DCE-MRI). In the discussion we want to summarize some of the activities in the area of neuroimaging software in R in general.

On features of R

R is a high-level programming environment which is typically used by its command-line interface (though Graphical User Interfaces (GUI) do also exist). It allows for interactive data analysis as well as easy creation of scripts for bulk data processing. R is the quasi-standard environment for the development of new statistical methods, often overtaking commercial statistical packages. Yet its matrix computational capabilities also compare well with those e.g. in Matlab.

The concept of packages as extensions to the R base system is one of its greatest strengths. R easily integrates compiled code

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written in low-level languages like C/C++, or FORTRAN providing the ground for efficient programming of computationally expensive algorithms combined with an easy-to-use interface at the scripting level.

One of the major difficulties when using R with neuroimaging datasets is R's memory usage. By default R stores data in computer main memory. Data are usually retained in double precision. R has no reference type, and therefore usually generates a copy of the data every time a function is called. This can, in case of inefficient programming, lead to several copies of the data in memory and a situation where demand exceeds the available memory. This can be avoided by calls to low-level languages.

Regardless of largely increased memory in recent years, there are also several projects and packages for R to overcome the limitations for huge datasets and grant access to it as fast and easy as in memory. One of them is the **ff** (Adler et al., 2010) which provides flexible data structures that are stored on disk but behave (almost) as if they were in RAM by transparently mapping only a section (pagesize) in main memory. Another project is the BigMemory project (`http://www.bigmemory.org`) which supports the creation, storage, access, and manipulation of massive matrices. On mid-term these technologies will be included in the packages described in this paper.

R supports modern concepts like object-oriented programming, which is provided as implementation of so-called S4-classes and methods (Chambers, 2008). While not as strict as in low-level languages like C/C++ it allows for class/method definition, data encapsulation, polymorphism, etc.

The analysis of huge datasets with sophisticated methodology comes at the cost of large computational expenses. R provides the possibility to parallelize code natively in R, or within the C/C++ code. It is also possible to include computation on a graphic card (GPU) instead of CPU, which in appropriate cases may benefit by orders of magnitude from the speed of modern GPU's.

Data Input/Output

The industry standard format, for data coming off a clinical imaging device, is DICOM (Digital Imaging and Communications in Medicine). The DICOM "standard" is very broad and very complicated. Roughly speaking each DICOM-compliant file is a collection of fields organized into two four-byte sequences (group,element) that are represented as hexadecimal numbers and form a tag. The (group,element) combination announces what type of information is coming next. There is no fixed number of bytes for a DICOM header.

The packages **oro.dicom** (Whitcher, 2010), **fmri** (Tabelow and Polzehl, 2010c) and **tractor.base** (Clayden, 2010b) provide R functions that read DICOM files and facilitate their conversion to ANALYZE or NIfTI format.

Although the industry standard for medical imaging data is DICOM, another format has come to be heavily used in the image analysis community. The ANALYZE format was originally developed in conjunction with an image processing system (of the same name) at the Mayo Foundation (Biomedical Imaging Resource, 2001). An Analyze (7.5) format image is comprised of two files, the "img" and "hdr" files, that contain the data and information about the acquisition itself. A more recent adaption of this format is known as NIfTI-1 and is a product of the Data Format Working Group (DFWG) from the Neuroimaging Informatics Technology Initiative (NIfTI). The NIfTI-1 data format is almost identical to the ANALYZE format, but offers a few improvements: merging of the header and image information into one file (.nii), re-organization of the 348-byte fixed header into more relevant categories and the possibility of extending the header information.

The packages **AnalyzeFMRI** (Marchini and Lafaye de Micheaux, 2010), **fmri**, **tractor.base**, and **dcemriS4** (Whitcher et al., 2010a) all provide functions that read/write ANALYZE and NIfTI files.

Additionally **fmri** provides capabilities to read and write AFNIs HEAD/BRIK files.

Functional MRI

Functional Magnetic Resonance Imaging (fMRI) has become the most informative tool for in-vivo examination of human brain function on small spatial scales. It is nowadays utilized both in research as well as in clinical applications such as diagnosis and treatment of brain lesions.

Package AnalyzeFMRI

AnalyzeFMRI is a package originally written by J. Marchini (Marchini, 2002) for the processing and analysis of large structural and functional MRI data sets under the ANALYZE format. It has been updated to include new functionality: conversion from ANALYZE to NIfTI, complete NIfTI input/output, functions to obtain spatial coordinates from voxel indices and vice-versa, various geometrical utilities, cross-platform visualization based on Tcl/Tk components, and spatial/temporal ICA (Independent Component Analysis) via a graphical user interface (GUI), see figure 1.

Independent component analysis is a statistical technique that can recover hidden underlying source signals from an observed mixture of these sources. The only hypothesis made to solve this problem (known as the blind source separation problem) is that the sources are statistically mutually independent and not Gaussian. ICA is now used to analyze fMRI data since the late 1990's (McKeown et al., 1998) and has been detailed in many papers (see e.g. Stone, 2002; Thomas et al., 2002). Note that ICA can be defined in two dual approaches: spatial ICA (sICA) and temporal ICA (tICA), the latter being not really used in fMRI studies due to computational difficulties in diagonalizing the huge data correlation matrix in this case. This is why, as far as we know, tICA has never been applied on the whole functional brain data but only on a few slices of the brain, or on a very reduced portion of it (Calhoun et al., 2001; Seifritz et al., 2002; Hu et al., 2005). Yet, supposing that we have temporally independent source signals can be seen as natural in several fMRI studies. The R package **AnalyzeFMRI** uses a

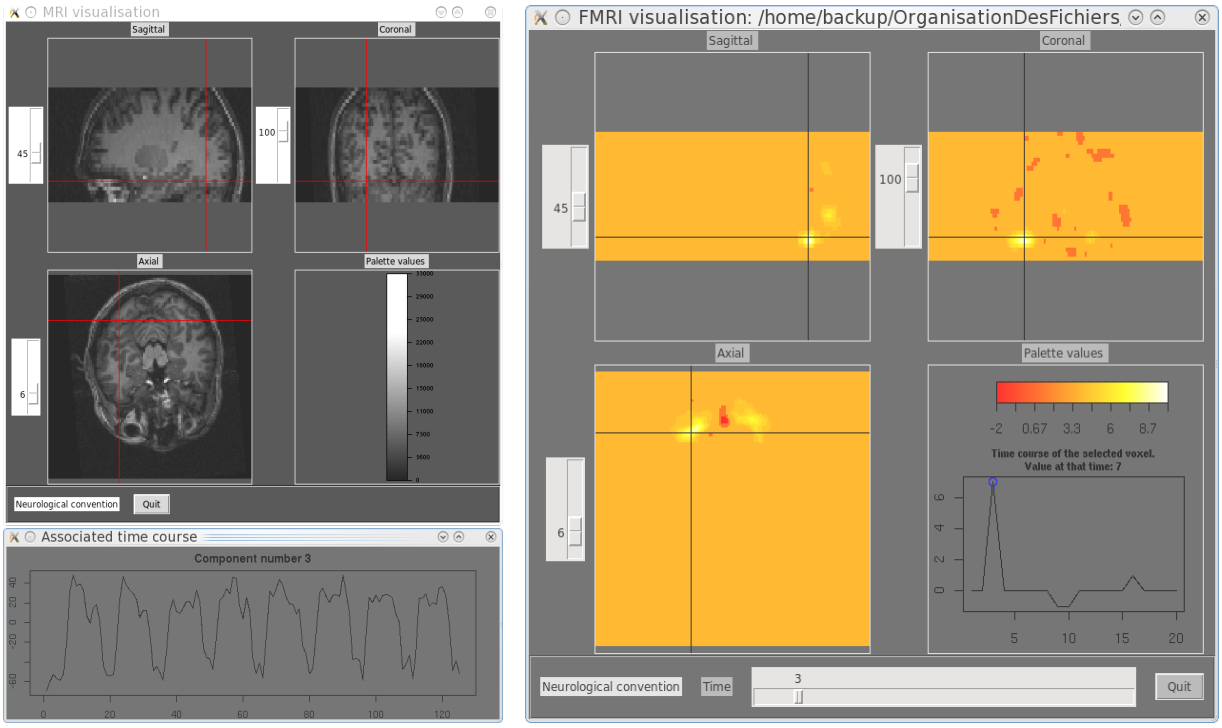

Figure 1: Visualization of temporal ICA results. Bottom left: One of the extracted temporal components. Right: Its associated spatial map of activations. Top left: corresponding anatomical image

nice property of the singular value decomposition that permits one to obtain the non-zero eigenvalues of the aforementioned correlation matrix, and their associated eigenvectors. It then becomes feasible to perform tICA for fMRI data on the whole brain volume. All the theoretical details, as well as a complete analysis of simulated and real data, can be found in (Bordier et al., 2011).

tICA results presented in figure 1 have been obtained very easily using the R function `f.icast.fmri.gui()` (included in the package **AnalyzeFMRI**) which displays a GUI where one has to select the original ANALYZE/NIfTI file, and eventually a mask file. Visualization of the extracted temporal components, as well as their associated spatial maps, is performed by means of the function `f.plot.volume.gui()`. The specific fMRI experiment performed here was a block design visual experiment, and the third temporal component was the one found to be mostly correlated with the signal of the stimulus. Note that our GUI visualization tool also displays the anatomical images, thus enabling via a cross-cliking link with ICA spatial maps, the anatomical localization of the most active voxels. They are located in the occipital part of the cortex.

Package fmri

The R-package **fmri** adopts the common view, (Friston et al., 1995; Worsley et al., 2002), of a linear model for the time series Y_i in each voxel i

$$Y_i = X\beta_i + \varepsilon_i, \tag{1}$$

where X denotes the design matrix and ε_i the error vector (Polzehl and Tabelow, 2007). The package requires motion correction, registration, and normalization to be performed by third-party tools. Note, that within the workflow using the package smoothing is not considered as a pre-processing step. Such a pre-processing is prone to a loss in detailed information that is needed in the structural adaptation approaches employed within the package. The fMRI data should therefore not be smoothed in advance.

The package includes functions for input/output of data in some standard imaging formats (ANALYZE, NIfTI, AFNI, DICOM). Linear modeling of the data according to Eq. (1) includes the description of temporal correlations with an autoregressive AR(1) model. The estimated correlation parameters are bias corrected (Worsley et al., 2002) and can be smoothed (Worsley, 2005). The linear model of the prewhitened data results in a statistical parametric map (SPM) which is a voxelwise array of estimated parameter β and its estimated variance. This information is then used to perform a structural adaptive smoothing method (Tabelow et al., 2006). The result of this algorithm is twofold: it improves the estimates for β by reducing their variance and it simplifies the inherent multiple test problem by introducing a specified smoothness under the null hypothesis. The package then uses Random Field Theory to determine thresholds for the test statistics. The method allows for a significant signal enhancement and reduction of false positive detections without reducing the effective spatial resolution, in contrast to traditional non-adaptive smoothing methods. This has been demonstrated in a series of papers (Voss et al., 2007; Tabelow et al., 2008b), especially for the analysis of high-resolution functional MRI (Tabelow et al., 2009). Note, that the smoothing method (Tabelow et al., 2006)

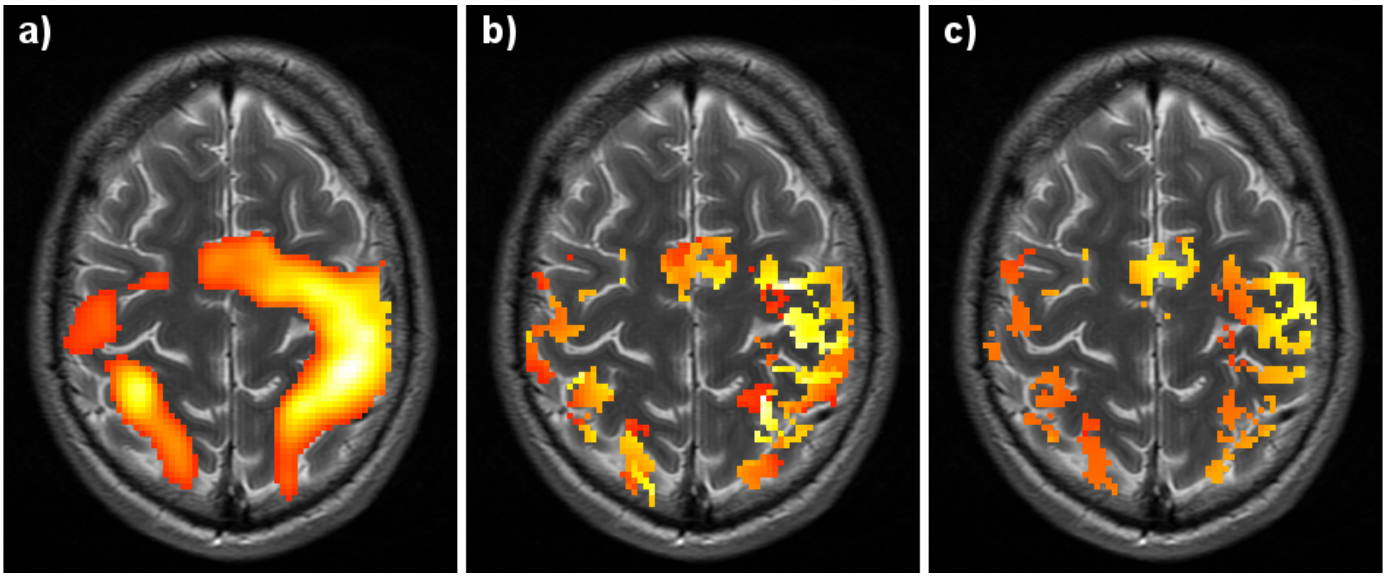

Figure 2: Signal detection using the package **fmri** using different smoothing methods (multiple test corrected $p = 0.05$): a) signal detection using Gaussian smoothing, b) signal detection using structural adaptive smoothing (Tabelow et al., 2006) with signal detection by Random Field Theory, c) results using structural adaptive segmentation. Since the algorithm provides only two segments (activation/no-activation) additional information can be overlayed in color. Here the estimated β is shown. For more details, see Polzehl et al. (2010).

accounts for the intrinsic spatial correlation of the data.

In a recent contribution (Polzehl et al., 2010) the structural adaptive smoothing algorithm has been refined and now integrates both the smoothing and the signal detection step. It is based on a multiscale test performed in the iterative smoothing procedure. The algorithm has been named structural adaptive segmentation since it divides the region of interest into a segment of no activation and a segment where the null hypotheses has been rejected. The algorithm is implemented in the package **fmri**. Figure 2 shows the signal detection results using different smoothing methods. The images were produced using the packages **fmri** and **adimpro** (Tabelow and Polzehl, 2010a).

It is worth noting that the computational time for a complete single-subject fMRI analysis including linear modeling, smoothing signal detection and graphical output is usually in the order of one minute only. Although the structural adaptive smoothing algorithm is in principle computationally expensive through its iterative nature, the fact that it operates on the estimated SPM rather than the single volumes makes it very efficient.

Diffusion Tensor Imaging (DTI)

While functional MRI focuses on the brain grey matter functionality, diffusion weighted imaging (DWI) measures directional water diffusion, which is highly anisotropic in the brain white matter. Among the models for DWI data is the widely used diffusion tensor model, where the directional dependence is described by a local diffusion tensor. The anisotropy can be directly associated with the anatomical structure in the brain; mainly (but not solely) the white matter fiber structure.

Package dti

The R-package **dti** (Tabelow and Polzehl, 2010b) has been written for the analysis of diffusion weighted MR data. Using a Gaussian model of diffusion, the data can be described by a rank-2 diffusion tensor $\mathcal{D}$, which is represented by a symmetric positive definite 3×3 matrix:

$$\mathcal{D} = \begin{pmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{xy} & D_{yy} & D_{yz} \\ D_{xz} & D_{yz} & D_{zz} \end{pmatrix}. \tag{2}$$

Assuming homogeneity within a voxel diffusion weigthed image intensities S_b associated with a gradient direction $\vec{g}$ a b-value b are related to unweighted image intensities S_0 by

$$S_b = S_0 e^{-b\vec{g}^\top \mathcal{D}\vec{g}}. \tag{3}$$

This model is known as diffusion tensor imaging (DTI, Basser et al., 1994a,b).

The package **dti** uses the package **fmri** for reading diffusion weighted data from DICOM or NIfTI files. The package provides estimation of diffusion tensors using non-linear regression (Polzehl and Tabelow, 2009) or a linearization of Eq. (3). Inference on the diffusion tensor is provided by estimating rotationally invariant tensor characteristics like mean diffusivity, fractional anisotropy, main diffusion direction, and others. The package can be used (combined with the R-package **adimpro** and ImageMagick) to create publication ready images of color-coded directional FA maps or 3D tensor visualizations in common image formats like JPEG, PNG, and many others.

One key feature of the package is the implementation of a structural adaptive smoothing method for the analysis of diffusion weighted data in the context of the DTI model. Due to its

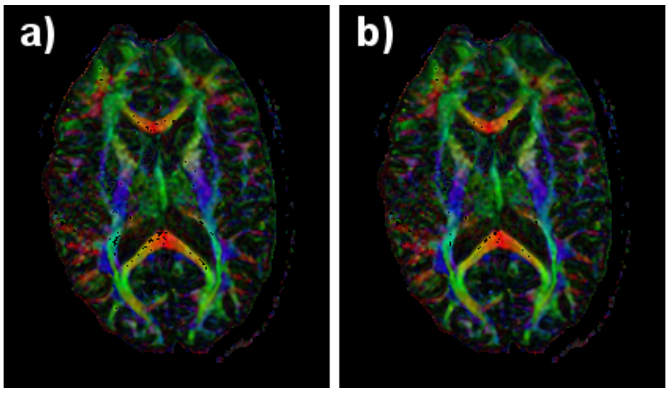

Figure 3: Application of the structural adaptive smoothing algorithm in (Tabelow et al., 2008a) to a brain scan: color coded directional map weighted with FA of an axial slice obtained by voxelwise analysis of the DWI data consisting of 55 diffusion weighted images (a). Directional map resulting from structural adaptive smoothing (b). In all images, black regions inside the brain denote areas in which at least one of the eigenvalues was negative. The color coding is red for RL, green for AP, and blue for IS. For more details, see Tabelow et al. (2008a).

edge preserving properties these smoothing methods are capable of reducing noise without compromising significant structures (e.g., fiber tracts) (Tabelow et al., 2008a). Smoothing is performed directly on the diffusion weighted images using information from the low-dimensional space of diffusion tensors for adaptation of weights. In each iteration step the diffusion tensor is re-estimated from the smoothed diffusion weighted images. The iteration is performed from small to larger scales. In contrast to other smoothing methods based on PDE (Ding et al., 2005) the method exhibits an intrinsic stopping criterion. See figure 3 for color-coded FA images of one slice before and after smoothing.

The package **dti** provides methods for analysis of HARDI data (Tabelow et al., 2010). The reconstruction of the orientation distribution function (ODF) from a spherical harmonics expansion of the diffusion weighted data can be performed as well as the estimation of mixed tensor models and the expansion of the weighted ODF into central angular Gaussian distribution functions. The package also implements a streamline fiber tracking algorithm for tensor and mixed tensor models. 3D visualization using OpenGL is also included.

The package is completely written using the S4 object oriented model. As for the package **fmri** the implementation of structural adaptive smoothing methods is potentially computationally expensive through its iterative nature. A typical DTI analysis including structural adaptive smoothing takes about 30 minutes on common hardware. However, as the amount of data for diffusion weighted imaging is rather large, large memory is advisable. This issue will be solved in future versions of the package by using efficient memory usage using **ff** or **bigmemory**. For a more complete survey on algorithmic and computational details we refer to Polzehl and Tabelow (2009).

The TractoR project

The TractoR (Tractography with R) project provides tools for working with diffusion MRI and fibre tractography, with a strong focus on groupwise analysis. The project is currently built upon four R packages, but also provides an interface for performing common tasks without direct interaction with R. Full source code is available at the project web site, `http://code.google.com/p/tractor`.

The **tractor.base** package provides data structures and functions for reading images from DICOM, ANALYZE or NIfTI storage formats, visualizing and manipulating images—for example, by thresholding or masking—and writing images back to file. The second package, **tractor.utils**, provides various utility functions, primarily for use by the project interface. The **tractor.session** package provides a file hierarchy abstraction, designed to facilitate working with large numbers of data sets; and also provides R interfaces to third-party image analysis software packages, including the FMRIB Software Library (FSL) and Camino (Cook et al., 2006; Smith et al., 2004). Finally, the **tractor.nt** package provides reference implementations of "neighbourhood tractography" methods, which use anatomical prior information and probabilistic models to segment white matter structures in groups, with high robustness and consistency.

Neighbourhood tractography overcomes a number of problems with standard diffusion tractography methods, particularly the difficulty of choosing suitable seed points to initialise tracking, by introducing anatomical prior information in the form of reference tracts (Clayden et al., 2006, 2007; Muñoz Maniega et al., 2008). In this way, high levels of reproducibility and consistency can be achieved for diffusion-based measurements within white matter tracts, without time-consuming and error-prone manual intervention (Clayden et al., 2009b). Finally, the approach of explicitly modelling tract shape variability across individuals offers a natural solution to the common problem of false positive pathways generated by tractography methods (Fig. 4; Clayden et al., 2009a). The statistical pedigree of R makes it an ideal environment in which to develop and apply machine learning techniques for neuroimaging.

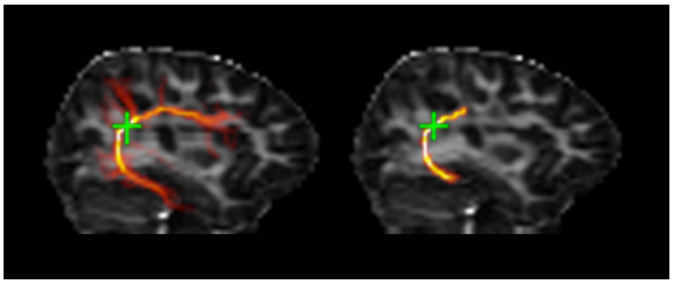

Figure 4: Rejection of false positive streamlines using a predefined reference tract and statistical shape model, as described in Clayden et al. (2009a). After "pruning" (right) the main curve of the arcuate fasciculus appears without any superfluous branching structures.

Dynamic Contrast-Enhanced MRI (DCE-MRI)

The **dcemriS4** package contains a collection of functions to perform quantitative analysis from a dynamic contrast-enhanced MRI (DCE-MRI) acquisition on a voxel-by-voxel ba-

sis. Patients undergoing a DCE-MRI acquisition have several minutes of T1-weighted scans performed, with a typical temporal resolution between 3-15 seconds, where a bolus of gadolinium is injected after a sufficient number of pre-contrast scans have been acquired. Assuming that the biology is explained by a system of linear differential equations, the model of contrast agent concentration over time is given by a sum of exponentials convolved with an arterial input function.

The workflow may be defined by the following steps: motion correction and/or co-registration, T1 estimation, conversion of signal intensity to gadolinium contrast-agent concentration and kinetic parameter estimation. The S4 object classes for common medical image formats, specifically ANALYZE and NIfTI, are provided by the **oro.nifti** package (Whitcher et al., 2010b) along with the ability to extend the NIfTI data format header via extensions. Users are allowed to add extensions to newly-created NIfTI S4 objects using various functions and the **XML** package (Temple Lang, 2010). All operations that are performed on a NIfTI object will generate a so-called *audit trail* that consists of an XML-based log. Each log entry contains information not only about the function applied to the NIfTI object, but also various system-level information; e.g., version of R, user name, date, time, etc. When writing NIfTI-class objects to disk, the XML-based NIfTI extension is converted into plain text and saved appropriately (ecode = 6).

The estimation of voxel-wise T1 relaxation, and subsequent conversion of the signal intensity to contrast agent concentration for the dynamic acquisition, has been implemented using the relationship between signal intensity and flip angle for spoiled gradient echo (SPGR) sequences and fitting the nonlinear curve to all available flip-angle acquisitions (Buckley and Parker, 2005). The estimated T1 values are then used to convert signal intensity into contrast agent concentration $C_t(t)$ for the dynamic acquisition using

$$[\text{Gd}] = \frac{1}{r_1}\left(\frac{1}{T_1} - \frac{1}{T_{10}}\right), \tag{4}$$

where r_1 is the spin-lattice relaxivity constant and T_{10} is the spin-lattice relaxation time in the absence of contrast media (Buckley and Parker, 2005). For computational reasons, we follow the method of Li et al. (2000).

Whereas quantitative PET studies employ arterial cannulation on the subject to characterize the arterial input function (AIF) directly, it has been common to use literature-based AIFs in the DCE-MRI literature. Examples include

$$C_p(t) = D\left(a_1 e^{-m_1 t} + a_2 e^{-m_2 t}\right), \tag{5}$$

where D is the dose of the contrast agent and $\theta = (a_1, m_1, a_2, m_2)$ are parameters taken from the literature (Weinmann et al., 1984; Tofts and Kermode, 1984; Fritz-Hansen et al., 1996). There has been progress in measuring the AIF using the dynamic acquisition and fitting a parametric model to the observed data. The **dcemriS4** package has incorporated these literature-based models and a data-driven model given by

$$C_p(t) = A_B t e^{-\mu_B t} + A_G\left(e^{-\mu_G t} + e^{-\mu_B t}\right) \tag{6}$$

(Orton et al., 2008), which is applied to the observed data using nonlinear regression using the Levenberg-Marquardt algorithm.

A common parametric model for DCE-MRI data is the "extended Kety model" given by

$$C_t(t) = v_p C_p(t) + K^{\text{trans}}\left[C_p(t) \otimes \exp(-k_{\text{ep}} t)\right], \tag{7}$$

where $C_t(t)$ is the concentration of the contrast agent in tissue as a function of time t, v_p is the volume of contrast agent in the plasma, K^{trans} is the transfer rate constant from plasma to EES (extravascular extracellular space) and k_{ep} is the rate parameter for transport from the EES to plasma (Parker and Buckley, 2005). The parametric model (7) may be applied to all voxels in a pre-specified region of interest (ROI), independently, using two distinct procedures: nonlinear regression with the Levenberg-Marquardt algorithm, using the **minpack.lm** package (Elzhov and Mullen, 2009), and Bayesian estimation (Schmid et al., 2006).

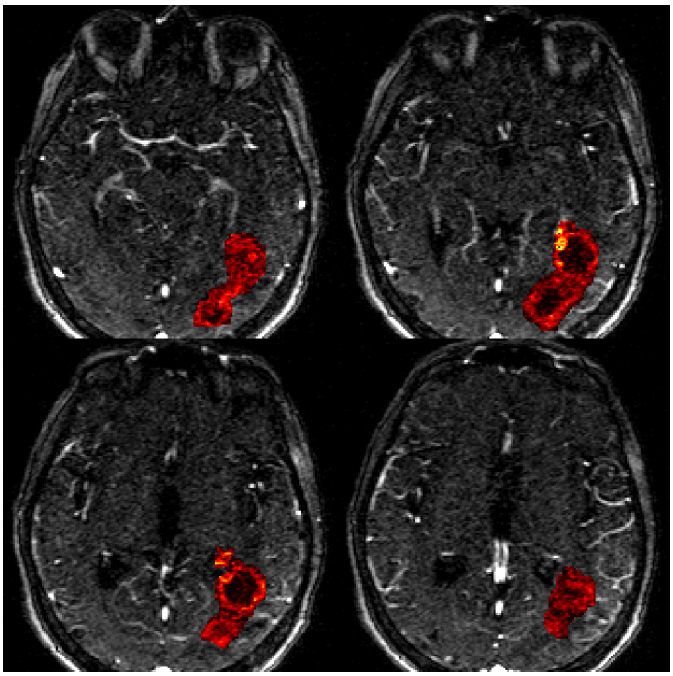

Figure 5: Perfusion characteristic K^{trans}, the transfer rate constant from plasma to extravascular extracellular space, estimated via non-linear regression in a dynamic contrast-enhanced MRI acquisition. Displayed values are in the range $[0, 0.15]\,\text{min}^{-1}$.

An illustration of the parametric model is provided via the National Biomedical Imaging Archive (`http://cabig.nci.nih.gov/tools/NCIA`). Figure 5 displays the estimated K^{trans} values for a region-of-interest (ROI) approximately covering a brain tumor. The uptake of the contrast agent varies drastically across the tissue in the ROI, exhibiting a hypovascular response in the core of the tumor and a potentially hypervascular response in the tumor rim. While statistical images provide an invaluable tool for exploratory data analysis, longitudinal assessment of disease progression or treatement response would have to be evaluated using a suitable scalar summary of the tumor ROI; e.g., using hierarchical models (Schmid et al., 2009).

Discussion

A number of packages specific to medical imaging, and in particular neuroimaging, have been developed within the R-Community. In this paper we concentrate on packages that have reached a level of maturity that guarantees that the described functionality is likely to be stable. New functionality is expected to be added and the underlying code is expected to be improved, especially concerning memory management and speed, over time. The packages described in the present paper cover functional Magnetic Resonance Imaging (fMRI), Diffusion Tensor Imaging (DTI), and Dynamic Contrast-Enhanced MRI (DCE-MRI). However, there is much more activity concerning NeuroImaging in R. Information on this is collected in the Medical Imaging task view at `http://cran.r-project.org/web/views/MedicalImaging.html`. This website provides a brief overview over existing packages and a classification with respect to their main area of application without going into methodological or implementational detail.

In Table 1 we summarize the main features of the packages described in the present papers and give the applicable license.

Finally, we want to draw attention to additional packages and activities which are not covered by this paper.

NeuroImage (within the neuroim project on R-Forge, `http://neuroim.r-forge.r-project.org/`) provides an object-oriented approach for handling multi-dimensional images. The **Rniftilib** (Granert, 2010) package provides read/write capabilities for the NIfTI-1 format. It provides a R-interface to the C reference library provided by the Neuroimaging Informatics Technology Initiative. In contrast to other R-packages supporting the ANALYZE and NIfTI-1 format, this package comes without additional functions for data processing and is restricted to functions for data handling as provided by the C reference library. The aim of the package is to serve as a common basis for the work with multi-dimensional volumetric (neuro)imaging data.

PTAk (Principal Tensor Analysis on k modes) is an R package that uses a multiway method to decompose a tensor (array) of any order (Leibovici, 2010), as a generalisation of a singular value decomposition (SVD) also supporting non-identity metrics and penalisations. A 2-way SVD with these extensions is also available. The package also includes additional multiway methods: PCAn (Tucker-n), PARAFAC/CANDECOMP and FCAk (multiway correspondence analysis).

Activated Region Fitting (ARF) is a program for functional magnetic resonance imaging (fMRI) data analysis. The R-Forge project **arf** uses Gaussian shape spatial models to parameterize active brain regions (Weeda et al., 2009).

As already mentioned R is also capable of making use of parallel computing techniques, CPU as well as GPU based. Compute Unified Device Architecture (CUDA) is a software platform for massively parallel high-performance computing on NVIDIA GPUs. **cudaBayesreg** (Ferreira da Silva, 2010) provides a CUDA implementation of a Bayesian multilevel model for the analysis of brain fMRI data. The CUDA programming model uses a separate thread for fitting a linear regression model at each voxel in parallel. The global statistical model implements a Gibbs Sampler for hierarchical linear models with a normal prior. This model has been proposed by Rossi et al. (2005, Chapter 3) and is referred to as "rhierLinearModel" in the R-package **bayesm**.

Finally we want to mention the package **RNiftyReg** (Clayden, 2010a) which provides an interface to the NiftyReg (`http://sourceforge.net/projects/niftyreg/`) image registration tools.

Conclusions

R provides an excellent environment for all levels of analysis with neuroimaging data, from basic image processing to advanced statistical techniques via the current list of contributed packages in the Medical Imaging task view. These packages can assist user-guided data analysis for fMRI, DCE-MRI, and DWI data as well as automated bulk analysis of imaging data. The user is free to create additional data structures or analysis routines using the programming environment in R—making it easily customized. It is very easy to link R to compiled C/Fortran code for speed improvements. R may be run in either interactive or batch-processing modes in order to scale with the application, and may be combined with other computing environments (e.g., Matlab or NIPY) to allow even greater flexibility.

Acknowledgments

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Package	Data type	Main features	Licence
oro.nifti, **oro.dicom**	general	Reading/writing DICOM and NIfTI files	BSD
AnalyzeFMRI	fMRI	sICA/tICA analysis for fMRI data	GPL ≥ 2
fmri	fMRI	Linear modeling, structural adaptive smoothing, signal detection for single subject fMRI data	GPL ≥ 2
dti	DWI	Diffusion tensor analysis for diffusion weighted MR data, structural adaptive smoothing, Modelling of HARDI data	GPL ≥ 2
tractor	DWI	Diffusion tensor analysis for diffusion weighted MR data, probabilistic tractography, segment specific tracts	GPL
dcemriS4	DCE-MRI	Voxel-wise quantitative analysis of dynamic contrast-enhanced or diffusion-weighted MRI data	BSD

Table 1: Main features and licenses of the packages described in this paper.

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