# New Tools for Analysis of MRI Datasets

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AFNI [1] is open source (C/Unix) software for the analysis and visualization of 3D and 3D+time image datasets, originally for functional MRI, but with many modules applicable to other MRI modalities. AFNI can be downloaded in source or binary formats from http://afni.nimh.nih.gov. We briefly present significant capabilities that have been added to AFNI over the past year.

## Speedy Serial Correlation Correction and Slice-wise Regression in FMRI Time Series Analysis

The principal effect of temporal correlation in the FMRI time series noise on the GLM results is bias in the estimation of the noise variance, when ordinary least squares or maximum likelihood is used to estimate the signal model response amplitudes. Bias in the variance estimate leads to bias in the statistics ($t$ and $F$) used to form individual subject activation maps. Allowing for serial correlation, using generalized least squares, is simple—provided that the temporal correlation structure is known or estimated accurately. This estimation is a nonlinear problem, and to carry it out for each voxel time series using the standard REML (REstricted Maximum Likelihood) method is very computationally intensive. Most FMRI software analysis tools make some simplifying assumptions to minimize the computational requirements. The new 3dREMLfit program is based on our careful and efficient implementation of the REML method to estimate an ARMA(1,1) model separately for each voxel time series, avoiding such simplifications. Since 30,000+ time series need to be processed, many of the time consuming steps in the REML estimation can be pre-computed. The resulting speedup is significant, and the program only takes about 3 times as long to run as the corresponding ordinary least squares regression analysis, and can properly deal with censored time points and non-contiguous catenation of data from multiple echo-planar imaging runs. In addition, 3dREMLfit can deal with slice-wise regressors, and scripts are included to generate RETROICOR-based physiological time series for noise cancellation. 3dREMLfit can also produce per-event/per-block amplitude estimates, rather than average activation amplitudes for each stimulus class; the collection of these per-trial amplitudes can be used as input to connectivity analyses or to group analysis via LME.

## Improving $T_1$-to-$T_2$* (Structural-to-EPI) Registration for Brain Images

We discovered that conventional image matching functions, such as Mutual Information and Correlation Ratio, fail 10-15% of the time when applied to alignment of structural and EPI volumes. In many cases, the brain outlines appear to match, but internal structures such as the ventricles do not overlap properly. We developed a new image matching function specifically for the purpose of registering such 3D datasets. This function is a nonlinear average of the Pearson correlation coefficient between the two images, each correlation being calculated locally over a set of about 1000 non-overlapping regions covering the brain volume, before combination. This new alignment method works very robustly [3], yielding clear matches between internal structures visible in both volumes.

## Generalizing ANOVA: Linear Mixed Effects Analysis

LME can be thought of as a generalization of ANOVA, based on linear regression and using the REML method to estimate variance/covariance parameters, which allows for missing data, unequal sample sizes, heteroscedasticity, correlated measurements, and a mixture of fixed and random effects. The new 3dLME program incorporates options for all of these capabilities. This tool is now the focus of our FMRI group analysis software development efforts.

## Realtime Feedback of FMRI Activation to the Subject in the Scanner

AFNI has had realtime FMRI analysis capabilities since 1996, and realtime 3D registration since 1998. The software has recently been extended to allow realtime feedback of activation amplitudes to the subject in the scanner, a technique that is actively being researched as a biofeedback tool for management of chronic pain, anxiety, and other maladies.

## Mn-Contrast MRI for Tracing Anatomical Connections

Manganese, taken up by calcium channels in the brain, is also an MRI $T_1$-enhancing contrast agent. AFNI now includes a set of software tools to produce whole brain day-by-day maps that trace significant Mn-related signal enhancements [2].These maps provide *in vivo* anatomical connectivity in rodent and primate brains.

## Nonlinear DCEMRI Model: Studies of Glioblastoma Multiforme

Dynamic Contrast Enhanced MRI uses the wash-in curve of a $T_1$-enhancer (e.g., Gd-DTPA) to estimate the kinetic parameters resulting from blood-brain barrier damage in tumors. AFNI includes a kinetic model that can simulate the MRI signal time series, given the kinetic parameters. The nonlinear least squares regression program (3dNLfim) in AFNI can be used to fit this model on a voxel-wise basis, and is parallelized to take advantage of shared-memory multi-CPU systems. These components of AFNI are currently being used in clinical studies of GBM at the NIH.

## Multivariate Granger Causality Network Modeling

A vector autoregressive implementation of multivariate GC network modeling that handles discontinuities of multi-run FMRI time series, covariates, produces path coefficients for multiple lags, and preserves correlational directionality for group analysis.

## References

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