SPATIO-TEMPORAL SIGNAL PROCESSIING FOR MULTISUBJECT FUNCTIONAL MRI STUDIES

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ABSTRACT

We consider signal estimation for functional MRI studies on multiple subjects. There are two major issues; alignment or registration of images across subjects; and using the multi-subject information to capture covariance information: we discuss only the latter. Capturing this covariance information properly can lead to great improvements in statistical efficiency beyond what simple averaging can offer as well as compact description of group features.

1. INTRODUCTION

The last few years have seen a steady development of methods for spatio-temporal system identification associated with functional magnetic resonance imaging (fmri) experiments. Earlier work of [5], [16] involved linear estimation, [8] discussed a principal components approach (unrelated to what we do in this paper below), while [10] introduced the use of wavelets. More recently [7],[12],[14], [6],[13] have used more complex impulse response models as well as spatial regularisation. Model comparison has been most recently adressed in [15],[13].

While these earlier developments have been focused on analysis of data from individual subjects, the majority of neuroimaging experiments are aimed at uncovering brain mechanisms that are common to groups of subjects as well as comparing the brain function between groups of subjects. There are two main issues in the analysis of these multi-subject or longitudinal data. The first issue involves the alignment or registration of data from different subjects onto a common coordinate system. The other issue is concerned with efficient pooling of information across subjects in order to model the spatio-temporal covariance structure of noise and response. We discuss only the latter problem here. We mention briefly that current registration techniques involving spatial warping and folding methods (e.g., [3]) have gone far beyond simple landmark matching based on the Talairach atlas.

Multisubject studies are quite standard in other areas of bioscience and rely on the methods of longitudinal data analysis [4]. Such data typically involve very short time series measured on a proportionately larger number of subjects. In neuroimaging experiments, the opposite is true: With imaging modialities such as fMRI, EEG, and MEG, the number of observations per subject T is much greater than the number of subjects n. In such cases, traditional longitudinal time series methods do not apply since a full-rank TxT covariance matrix cannot be formed. Recently, a new kind of longitudinal data analysis called functional data analysis [9] has been developing to deal with this singular longitudinal data analysis situation.

Early work used time series methods [11], [1], [2], but more recently modern smoothing methods have been applied. A number of these newer techniques are described in the book [9] although no spatio-temporal problems of the kind considered here are discussed. Nevertheless, the ideas are relevant.

2. NONSTATIONARY SPATIO-TEMPORAL SPECTRAL ANALYSIS

We concentrate here on covariance analysis. The potential to achieve precision far beyond what simple averaging can offer is great. There are a number of approaches but the simplest is to approximate the spatio-temporal field by a basis expansion such as Fourier or wavelet. Then a Karhunen-Loeve decomposition is estimated. Neither temporal nor spatial stationarity is assumed.

Let t, τ denote time and P, Q denote pixel positions. Spatiotemporal fields will be indexed by arguments such as t, P or τ, Q. We also introduce basis systems

$$\chi_{t,P}^{(r)}, r = 1, \cdots, L_\chi, \psi_{t,P}^{(u)}, u = 1, \cdots, L_\psi$$

The basis systems need not be orthogonal systems (e.g. B-splines) but for ease of expose' we assume here that they are.The image sequence on individual i is denoted $x_{t,P}^i$. If

$K(t, P; \tau, Q)$ is the covariance kernel of the signal i.e.

$$K(t, P; \tau, Q) = cov(x^i_{t,P}, x^{i,T}_{t,P})$$

then the idea is to estimate the first few terms in the expansion

$$K(t, P; \tau, Q) = \Sigma \lambda_u \phi^{(u)}_{t,P} \phi^{(u)}_{\tau,Q}$$

where $\phi^{(u)}_{t,P}$ are eigenfunctions and $\lambda^{(u)}$ are eigenvalues obeying

$$\int K(t, P; \tau, Q) \phi^{(u)}_{\tau,Q} d\tau dQ = \lambda^{(u)} \phi^{(u)}_{t,P}$$

Using a basis expansion for the field

$$x^i_{t,P} = \Sigma^{L_\phi}_{r=1} \psi^{(r)}_{t,P} d^i_{(r)} = \psi^T_{t,P} d^i$$

and the eigenfunctions

$$\phi^{(u)}_{t,P} = \Sigma^{L_\psi}_{r=1} \psi^{(r)}_{t,P} f^r_{(u)} = \psi^T_{t,P} f_u \qquad (2.1)$$

We approximate the eigenequation as follows. The rank deficient covarance kernel estimator

$$K_n(t, P; \tau, Q) = \frac{1}{n} \Sigma^n_1 x^i_{t,P} x^{i,T}_{\tau,Q}$$

becomes

$$\begin{aligned} K_n &= \psi^T_{t,P} S_d \psi_{\tau,Q} \\ S_d &= \frac{1}{n} \Sigma^n_1 d_i d^T_i \end{aligned}$$

And so the eigenequation becomes

$$\int \psi^T_{t,P} S_d \psi_{\tau,Q} \psi^T_{\tau,Q} f_u d\tau dQ = \lambda^{(u)} \psi^T_{t,P} f_u$$

leading to the matrix system

$$S_d f_u = \lambda^{(u)} f_u$$

and the orthogonality requirements

$$\int \psi^{(u)}_{t,P} \psi^{(v)}_{t,P} dt dP = \delta_{uv}$$

becomes $f^T_u f_v = \delta_{u,v}$. So now we simply carry out a principal components analysis of the reduced data d^i. The eigenvectors are reconstructed from (2.1). In practice d^i needs to be mean corrected. If there is a mean response this will need to be similarly approximated by basis expansion methods. A considerable amount of development is required to show how this can be done, so here we concentrate on the convariance modelling. We deal with a stimulus free experiment consisting of repeat runs on a single individual and we concentrate on determining the noise structure.

3. IMAGING DATA

The data were collected using a GE Signa 1.5 T MRI scanner modified for Echo Planar Imaging (EPI) by Advanced NMR Systems (Wilmington, MA). The data were collected on a single subject with a repetition time of 1 second, with a total of 1024 time points. In order to create a set of registered longitudinal data sets, the original data record was partitioned into 12 temporally-contiguous blocks of 64 seconds length, where each block was separated from the next by 15 seconds to avoid spurious temporal correlations between the data sets. The spatio-temporal analysis was then applied to a 4-by-4 pixel region of interest (ROI) using a Fourier basis set. Based on empirical studies of the noise, the Fourier basis was truncated for temporal frequencies above the 4th harmonic.

4. RESULTS AND DISCUSSION

The eigenvalues Fig.1 of the estimated covariance kernel revealed that most of the covariance structure could be expressed using the first two eigenfunctions. This suggests that the functional data analysis method can yield significant data reduction when applied in this context. Fig.2 and Fig.3 show the spatio-temporal eigenfunctions corresponding to the first and second eigenvalues in Fig.1, respectively. These eigenfunctions are displayed as arrays of time-series, where the position of the time series within the array indicates its position within the 4-by-4 ROI. In Fig.4 we show the mean time series, the histogram for the entire 1024-length record, and the temporal covariance kernel, estimated from the first two eigenfunctions, for a typical pixel. The temporal covariance kernel for this pixel, as well as the others, lacks a Toeplitz structure, suggesting that the noise may by non-stationary.

5. CONCLUSIONS

We have developed a method for doing spatio-temporal longitudinal data analysis for functional MRI data employing functional data analysis methodology. Because of the unique constraints of multi-subject fMRI data, where the number of subjects is far fewer than the number of data points observed, traditional longitudinal data analysis methods are inappropriate. We used this algorithm to study longitudinal fMRI noise data, demonstrating that the covariance structure of the noise can be summarized with just a few eigenfunctions, and that the temporal covariance structure may be non-stationary. These results suggest that the functional data analysis framework could be an effective method for pooling information across subjects in fMRI experiments. Furthermore this method provides a framework for doing full spatio-temporal fMRI analysis without requiring assump-

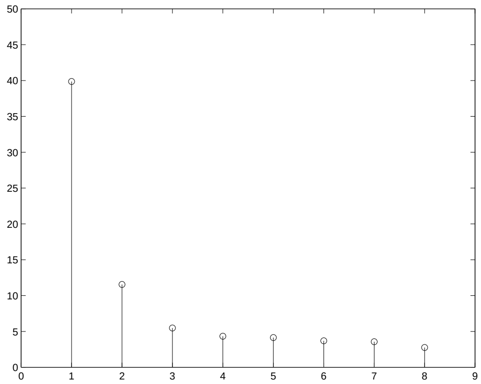

Fig. 1. Eigenvalues for Karhunen-Loeve Decomposition

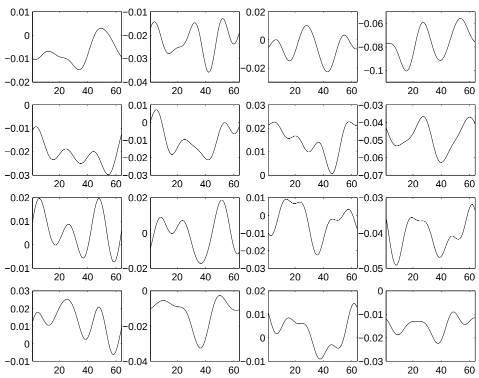

Fig. 2. Spatio-Temporal Eigenfunction corresponding to largest Eigenvalue

tions of stationarity as current methods do. In future work we will extend this methodology to describe the spatio-temporal response to longitudinal experiments with cognitive or sensory stimulation tasks.

6. REFERENCES

[1] D.R. Brillinger. The analysis of time series collected in an experimental design. In *Multivariate analysis III*, pages 241–256. Academic Press, 1973.

[2] D.R. Brillinger. Analysis of variance and problems under time series models. In *Handbook of Statistics vol.I*, pages 237–278. North-Holland, 1980.

[3] A. Daley. *Atmospheric data analysis*. Oxford University Press, Oxford, 1993.

[4] P. Diggle, K.Y. Liang, and S.L.Zeger. *Analysis of Longitudinal data*. Clarendon Press, Oxford, 1994.

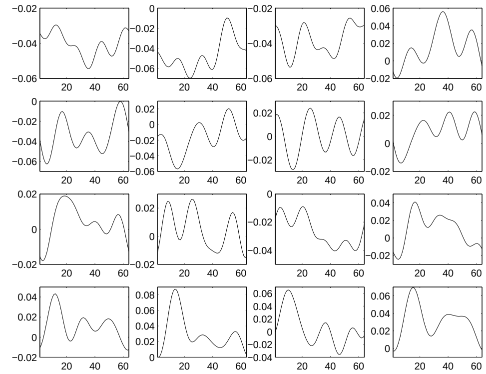

Fig. 3. Spatio-Temporal Eigenfunction corresponding to second-largest Eigenvalue

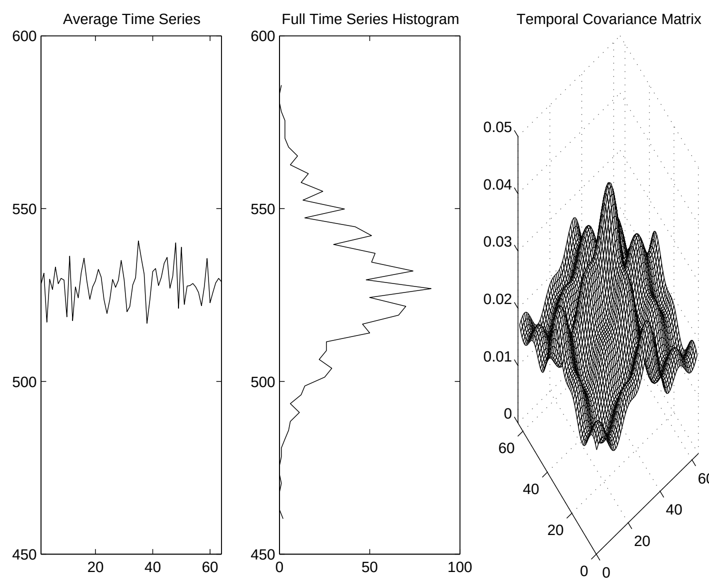

Fig. 4. Mean, Histogram for full Data Record; Estimated Covariance Kernel

[5] K.J. Friston, A. Holmes, J. Poline, P. Grasby, S¿ Williams, R. Frackowiak, and R. Turner. Analysis of fMRI time-series revisited. *Neuroimage*, 2:45–53, 1995.

[6] C.R. Genovese. Statistical inference in functional Magnetic Resonance Imaging. *Dept. Statistics, Carnegie Mellon University*, Tech Rep, 1999.

[7] N. Lange and S.L. Zeger. Non-linear fourier timeseries analysis for human brain mapping by functional MRI. *Appl.Stat*, 46:1–29, 1997.

[8] P.P. Mitra, S. Ogawa, X. Hu, and K. Ugurbil. The nature of spatiotemporal changes in cerebral haemodynamics as manifested in functional MRI. Technical report, Bell Labs, 1996.

[9] J.O. Ramsay and B.W. Silverman. *Functional data analysis*. Springer-Verlag, New York, 1997.

[10] E.E. Ruttiman, M. Unser, R.R. Dawlings, D. Roi, N.F. Ramsey, V.S. Mattay, D.W. Hommer, J.A. Frank, and D.R. Weinberger. Statistical analysis of functional MRI data in the wavelet domain. *IEEE Trans Med Imaging*, 17:142–152, 1998.

[11] R.H. Shumway. Applied regression and analysis of variance for stationary time series. *Jl. Amer. Stat. Assoc*, 65:1527–1546, 1970.

[12] V. Solo, E. Brown, and R. Weisskoff. A signal processing approach to functional MRI. In *Proc. IEEE ICIP97*, volume II, pages 121–124, 1997.

[13] V. Solo, P.Purdon, E. Brown, and R. Weisskof. A signal estimation approach to functional MRI. *IEEE Trans. Med. Imag.*, to appear, 2001.

[14] V. Solo, P.Purdon, E. Brown, and R. Weisskoff. Regularisation functional MRI models. In *Proc. IEEE ICIP98*, 1998.

[15] V. Solo, P.Purdon, E. Brown, and R. Weisskoff. Model comparison for functional MRI. In *Proc. IEEE ICIP99*, 1999.

[16] K.J. Worsley and K.J. Friston. Analysis of fMRI time-series revisited - again. *Neuroimage*, 2:173–181, 1995.