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Literature Review on Activation Detection and Estimation Efficiency in fMRI Methodology

Advances in neuroimaging have come from the need to improve methods already widely utilized in practice. In methodology and in the analysis of such methodology, there are trade-offs to consider. The current literature review considers a 2001 study by Thomas Liu, who recognized the need to strike a balance between detection power and estimation efficiency as a function of the design of fMRI experiments. The present paper's novelty comes from its proposal of a theoretical model that describes the relationship between estimation efficiency and detection power, a relationship of trade-off in which maximum detection power cannot be attained with a design of maximum estimation efficiency and maximum estimation efficiency does not permit the attainment of maximum detection power. Predictability is introduced as a metric for the perceived randomness of a design since a study design's predictability may elicit a different response (contrary to other responses of interest) within experimental participants. Considering how experimental designs capture their outcome of interest with high fidelity in certain aspects and with lower fidelity in other aspects, Liu recognizes that there is necessity in analyzing how these aspects are related to each other and in understanding how to balance fidelity in all aspects.

Detection of brain activation and estimating HDR are two important tasks in fMRI imaging. Liu recognized that these two tasks needed to be treated separately, as per Buxton: "Which stimulus pattern provides the most sensitive estimate of the local hemodynamic response when the shape is unknown?...Which stimulus pattern provides the most sensitive detection of activation when the shape of the hemodynamic response is unknown?" (Buxton et al, p. S457). Both tasks are plagued by statistical shortcomings, explained by Liu to be the result of a fundamental trade-off between detection power and estimation efficiency. In exploring the theory needed to explain this trade-off and to ultimately propose a mixed design, Liu refers to the work of Scharf and Friedlander on the detection of subspace signals in subspace interference. In adapting Scharf and Friedlander's detection problem to the fMRI design problem, Liu expresses fMRI time series data in terms of a general linear model $\mathbf{y} = \mathbf{Xh} + \mathbf{Sb} + \mathbf{n}$, where $\mathbf{y}$ is an observed time series, $\mathbf{X}$ is a design matrix with columns that span a signal subspace, $\mathbf{h}$ is a parameter vector, $\mathbf{S}$ is a nuisance model function matrix having columns that span an interference subspace, $\mathbf{b}$ is a vector of nuisance parameters, and $\mathbf{n}$ is a vector of additive Gaussian noise; the fMRI time series vector $\mathbf{y}$ projects obliquely onto $\mathbf{X}$ and $\mathbf{S}$. $\mathbf{X}_{\perp} = \mathbf{P}_{\mathbf{S}}^{\perp}\mathbf{X}$ is the design matrix when nuisance effects have removed from each column (Liu, p. 760). Scharf and Friedlander pose the detection problem this way: "The null hypothesis H_0 says that the data consist of noise…only. The alternative hypothesis H_1 says that the data consist of a sum of signal…and noise…", and the test statistic for this test is the F statistic (Scharf and Friedlander, pp. 2146, 2155). Liu tests the same hypotheses (no signal present versus signal present), and in doing so demonstrates that "both detection power and estimation efficiency depend on the distribution of the eigenvalues of $\boldsymbol{X}_{\perp}^{T}\boldsymbol{X}_{\perp}$" (Liu, pp. 762, 764). Considering this space, there is an angle θ between an assumed hemodynamic response $\mathbf{h}_0$ and dominant eigenvector $\mathbf{v}_1$ of $\boldsymbol{X}_{\perp}^{T}\boldsymbol{X}_{\perp}$; another eigenvector $\mathbf{v}_2$ (where the eigenvalue of $\mathbf{v}_1$ is greater than or equal to the eigenvalue of $\mathbf{v}_2$) does not determine θ but is an eigenvector of this space. Detection power is maximized when θ = 0° and minimized when θ = 90° (respectively, $\mathbf{v}_1$ is parallel to $\mathbf{h}_0$ and $\mathbf{v}_1$ is orthogonal to $\mathbf{h}_0$) (Liu, p. 764). Theoretical signal processing methodology thus serves as a primary springboard for Liu to develop his ideas on fMRI design and its relation to activation detection and estimation efficiency.

Confounding is not often discussed in the literature as being ameliorated by unpredictable study design components, which is the premise for Liu's proposal of a metric of predictability. Randomness in study design may address the effects of common confounders such as habituation and anticipation. Rosen notes that "fMRI is sensitive to transient phenomena and can provide at least some degree of quantitative information on the underlying neuronal behavior…it should be possible to interpret transient fMRI signal changes in ways directly analogous to electrophysiologic evoked potentials" (Rosen, p. 775). Rosen considers another experiment with the delay/no-delay paradigm, and within it "The no-delay condition exhibited sensory-motor activation well before similar activation in the delay condition. Within a blocked task paradigm, the two temporally separate events likely would have been blurred together" (Rosen, p. 776). Rosen finds that an event-related fMRI paradigm with "on" and "off" states corresponding to delayed or separated fMRI images assigned "does not take advantage of the transition information in the hemodynamic response and makes limited fixed assumptions about the shape of the hemodynamic response" (Rosen, p. 776). From this, Liu recognizes that a study design should be able to account for spurious activation from habituation or anticipation, and so considers an "average 'predictability'…the probability of a subject correctly guessing the next event in [a] sequence" (Liu, p. 766). This is the primary motivation for Liu's incorporation of predictability into his model and construction of new study designs.

The statistical properties of fMRI methodologies presenting stimuli come from the choice of block or event-related design, but the current Liu paper considers why both designs falter and how a novel mixed design brings these desired properties together. When stimuli are presented in patterns that have interstimulus intervals that are randomized from trial to trial, optimal estimation efficiency and relatively low detection power are achieved. In block designs, individual trials are clustered into “on” activation periods and “off” control periods; this provides high detection power but low estimation efficiency (Liu 759). An idea to have both statistical properties is to mix designs, and one approach reviewed by Liu was Friston’s dynamic stochastic design said to regain some detection power from block designs and some of the reduction of confounding from random designs. Friston sought to address a problem of choosing the interstimulus interval (or stimulus onset asynchrony (SOA)) for event-related fMRI since SOA helps maximize response estimation efficiency (Friston, p. 607). Designs are created from the combination of the probability with which an event will occur at a set of time points and from the set of events to occur at a prespecified times; these are respectively deterministic and stochastic designs, where stationary stochastic designs have constant probabilities and non-stationary stochastic events have probabilities that change over time (Friston, p. 607). Friston found that greater efficiency came from those designs with slow modulation of occurrence probabilities and that the conventional block design is the most efficient design but found (most critically) that a design that is most efficient for one effect may not be so for another (Friston, p. 607). In pursuing generalizability and flexibility in design setup, Liu proposes a design that combines block and event-related design.

Liu proposes a semirandom design and a mixed design which combines block and semirandom designs. The semirandom design lies between having maximum detection power (to determine which brain regions are activated in an experiment) and maximum estimation efficiency (to characterize HDR shape in a given region), with possible designs being evaluated by two cost criteria that Liu introduced, one for relative estimation time and one for relative detection time (Liu, p. 765). Relative estimation time is a function of a design with parameter α (a measure of the spread of eigenvalues), and relative detection time is a function of parameters α and θ (as defined earlier). Although the time required to obtain desired efficiency and desired power is calculated by finding the greater of relative estimation time and detection time for a given α, Liu argues that the best design is the one that takes the minimum, not the maximum, of these relative times, since relative estimation time increases with α and relative detection time decreases with α, there must be a minimum time where the functions for these times intersects (Liu, pp. 765-766). Therein lies the fundamental tradeoff between estimation efficiency and detection power, and these cost criteria lead to selection among mixed and semirandom designs.

Liu’s present work flows organically from the work of his colleagues and academic community. He first recognizes that detection power and estimation efficiency come from two separate questions and should be addressed separately. He then adapts signal processing theory in order to formally define aspects of fMRI design (and its resulting time series data) in terms of activity in signal and interference subspaces and considers event-related fMRI methods (tapping into transition information in HDR data) with the aim of addressing predictability in a strategy to get around the confounding that is inherent to fMRI methods. In recognizing the need to consider the strengths and weaknesses of block and event-related designs, and to combine them, he looks into dynamic stochastic designs and ultimately proposes semirandom and mixed designs, using cost as a criterion in determining which designs best balance detection power and estimation efficiency. Liu has solidly built up to and justified his novel approaches to fMRI design, as well as explained a fundamental trade-off inherent to fMRI methodology, and in the process brought together two potential solutions to two major research questions into one cohesive study.

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