Comments and Controversies

Reply to Friston and David
After comments on: The identification of interacting networks in the brain using fMRI: Model selection, causality and deconvolution

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We thank the commentators (Friston, this issue; David, this issue) for their thoughtful discussion and careful detailing of their arguments and views on issues of connectivity analysis and causality. We limit ourselves here to specific replies to comments and refer to other contributions in this section for both further detail and overview.

On realistic biophysical observation models

“Only biophysical modelling, such as the one proposed in DCM or other generative frameworks, that tries to correct for experimental biases will ensure to stick to the core of biological processes that are the true events of interest.” (David, this issue)

Generative frameworks with complex realistic accounts of how measured signals are generated certainly hold promise for connectivity models of neuroimaging data, as David argues above. However, the parameters in a complex nonlinear model with hidden variables cannot always be uniquely estimated from observed data, that is, the model is not necessarily identifiable.

Any hemodynamic model with sufficient degrees of freedom will do; in the sense that the neuronal parameters are largely unaffected by changing the form of the hemodynamic model. […] In brief, the only thing that matters is the generalized convolution kernel of the optimized hemodynamic mapping, not the form or parameterization of its underlying differential equations.” (Friston, this issue)

This is an important point that touches on identifiability and an accurate qualification for the use of realistic biophysical observation models. Identifiability of a nonlinear model is dependent on i) the conditional dependencies between the parameters, i.e., the degree of redundancy in the parameterization of the differential equations and ii) the sensitivity of the model output to changes in the parameters, which is itself a function of the complexity of the input, i.e., the experimental design (Deneux and Faugeras, 2006). In this context, the sufficient degrees of freedom in a hemodynamic model in order for neuronal parameters to remain unaffected can also be interpreted as the maximum identifiable complexity (and inevitably: veridicality) that still allows the parameters of the model to be uniquely estimated in practice. An important challenge lies in the usage of different imaging modalities (possibly simultaneously) to increase the complexity and realism of connectivity models that can be identified and compared (Valdes-Sosa et al., 2009).

On model comparison and selection

“Conditional estimates of effective connectivity from a full graph (network) are often very consistent with estimates based on subgraphs. This speaks to a common misconception about DCM; namely, that one will get misleading answers if key regions are omitted. This is not the case. Effective connectivity is the ‘effective’ influence one region exerts over another and can be mediated polysynaptically through other (omitted) regions.” (Friston, this issue)

Both here and in the discussion of realistic biophysical observation models, the key seems to be to specify precisely ‘how wrong models have to be, not to be useful.’ Rigorous investigations, perhaps using simulations, of exactly how connectivity estimates behave when small subgraphs of the generating system are used are currently lacking. The inability of log-evidence based model comparison to perform structural model selection (as opposed to dynamical model selection as nicely separated by Friston), at least in fMRI, makes it hard to quantify general statements that ‘sub-graphs are good enough.’
“Proper model comparison (based on the evidence as opposed to just the accuracy or fit) prevents over-fitting for free; because the log-evidence includes a complexity term.” (Friston, this issue)

First, we need to reiterate that model comparison operates only to select the ‘best’ model within the chosen model set, as discussed in some detail in our contribution and both comments. Second, some qualification is warranted on the degree to which over-fitting can be prevented ‘for free.’ The choice for a different complexity penalty (which can be a function of the number of parameters, their priors, posteriors, and conditional dependencies) can lead to a different choice of ‘best’ model. The way in which different approximations to the log evidence (e.g., AIC, BIC, or free energy) express preference for one model over another by balancing fit to the available data with a complexity penalty is well discussed in the literature (see also Daunizeau et al., this issue), but the inherent approximation to the actual capacity to generalize is important to keep in mind. An interesting recent idea in this regard is to assess the capacity of connectivity models to predict the cognitive state or experimental condition for unseen data (rather than predicting the data itself), based on the network dynamics that distinguished those states in a training dataset (Smith et al., submitted for publication). This instantiation of ‘training-set/test-set’ logic, which characterizes many pattern classification approaches to fMRI data analysis, has the additional advantage that it can also perform structural model selection for fMRI.

On dynamical signal models

“There is no necessary mapping between the parameters of a VAR model (the autoregression coefficients \( A \in \mathbb{R}^{m \times m} \)) and the coupling parameters (effective connectivity \( \tilde{A} \in \mathbb{R}^{m \times n} \)) that mediate the influence of one state over another. In other words, the effective connectivity associated with the VAR coefficients does not necessarily exist.” (Friston, this issue)

This conclusion should be qualified, particularly when effective connectivity is defined saying that:

“Effective connectivity is the ‘effective’ influence one region exerts over another and can be mediated polysynaptically through other (omitted) regions.” (Friston, this issue)

First, it should be noted that the discussion here centers more fundamentally on continuous vs. discrete signal models than on a fundamental divide between DCM and VAR, unless one insists DCM to be continuous-time and VAR models to be discrete-time (which need not be the case: continuous LSM models are well studied). As Friston nicely sets out, the relation between the system matrix \( A \) of a continuous signal model and the system matrix \( \tilde{A} \) of the corresponding model for discretely sampled data is given by the matrix exponential:

\[
A = \exp(\Delta t \tilde{A}) = \sum_{i=0}^{\infty} \frac{\Delta t^i \tilde{A}^i}{i!}
\]

The power series expansion of the matrix exponential shows it to be a weighted sum of successive powers \( \tilde{A}^i \) of the continuous time system matrix. Thus, the discrete system matrix \( A \) will contain contributions from direct (in \( A \)) and indirect (in \( i \) steps in \( A^i \)) causal links between the modeled areas. The contribution of the more indirect links is progressively down-weighted with the number of causal steps from one area to another and is smaller when the sampling interval \( \Delta t \) is smaller. These qualifications make clear that multivariate (more than bivariate) discrete signal models have some undesirable properties for coarsely sampled signals (i.e., a large \( \Delta t \) with respect to the system dynamics), such as fMRI data. Critically, entirely ruling out indirect influences is not actually achieved merely by employing a multivariate model. Furthermore, estimated connectivity (particularly the relative contribution of indirect links) is dependent on the employed sampling interval. However, the discrete system matrix still represents effective influences, possibly mediated through other regions, which can be highly useful in investigations that draw careful qualified conclusions.

References

