New physiological framework for dynamic causal modeling of fMRI data

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Objectives

Dynamic causal modeling (DCM) [2] is widely used approach for assessing effective connectivity (EC) from fMRI data. DCM uses a forward model of biophysical processes, linking neuronal activity to the observed hemodynamic response. For a decade, DCM has been used for the analysis of fMRI data albeit with simplifications on the physiological level.

We propose and test a new physiologically motivated forward model for DCM, which extends the standard DCM (S-DCM) [2] and the two-state DCM (2S-DCM) [3].

At the neuronal level, we model local (regional) activity as exhibiting excitatory and inhibitory (E-I) balance [3].

- We introduce a new model of neurovascular coupling (NVC) to link the output of the neuronal model with blood flow.
- We test blood volume as potentially uncoupled from blood flow, as in the original balloon model [5].
- We test the new physiologically motivated DCM model (P-DCM) on anterior spin labeled (ASL) fMRI data measuring both the BOLD signal and blood flow, and compare its performance using Bayesian model selection (BMS) [7].

DCM generative model properties

S-DCM

- Only excitatory neuronal dynamics.
- Does not model dynamics as observed using electrophysiological recordings.
- NVC.
- Based on feedforward-backward mechanism - physiologically unlikely!
- Generates undershoot in blood flow and BOLD signal - not correct!

Hemodynamic model (HDM):

- Does not include balloon effect; i.e. slow recovery of blood volume to produce BOLD post stimulus undershoot.
- Very rigid - does not allow model variability of responses commonly observed in fMRI.

2S-DCM

Modelled both excitatory and inhibitory neuronal populations.
- But produces very limited range of neuronal dynamics - not useful.
- NVC and HDM.
- Same limitations as S-DCM.

P-DCM

- Properties models E-I balance.
- Can model all neuronal dynamics commonly observed using electrophysiological recordings (in LFPs and MUA responses).
- Can model post-stimulus deactivation.
- Based on strictly feedforward mechanism - physiologically plausible!

DCM connectivity properties

S-DCM

- Can model both positive and negative responses within the same network.
- Limited in modeling hemodynamic transients (i.e. undershoots and overshoots).

2S-DCM

- Unable to model transformation from positive to negative (neuronal) BOLD response.

P-DCM

- Overcomes limitations of S-DCM and 2S-DCM.
- Includes both positive and negative neuronal and vascular responses.
- Enables transformation from positive to negative (neuronal) BOLD response.


New fMRI physiological model

Neuronal and vascular contribution to BOLD

Overcomes limitations of S-DCM and 2S-DCM.

sients (i.e. undershoots and overshoots).

Can model both positive and negative responses within the same network.

Can model all neuronal dynamics comprehensively.

Can model post-stimulus deactivation.

Based on strictly feedforward mechanism - physiologically plausible!

Examples of BOLD responses fitted by DCMs

We have introduced a new physiologically realistic DCM and applied it to ASL-fMRI data that models E-I neuronal balance, proper neurovascular coupling, and the actual blood effect. New P-DCM is clearly more accurate compared to S-DCM and 2S-DCM as indicated by a better fit to test metrics, including precisely modeling of neuronal and vascular origins of the hemodynamic response undershoot. Therefore, we suggest that P-DCM will play an important role in assessing effective connectivity from fMRI data.

References

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ASL-fMRI data acquisition and analysis

ASL-fMRI data (N=6) were acquired on 3T Siemens Prisma scanner (Scanneus, Maastricht, NL) using a POCORE-Q1TIPS sequence with the following parameters: TR/TE=2000/17 ms, flip angle=80°, voxel size=3x3x3 mm3, T1/T2=1000/1600 ms, 10 oblique slices. Six subjects performed a block-design visual-motor task in 4 runs, each 40s long. Data were realigned, smoothed (4 mm FWHM) and analyzed using modified SPM12 functions. From GLM results (p<0.05, FWE, 5 ROIs (r=10 mm) were selected (V1 and M1 from left and right hemispheres and SMA) and average (detrended) ASL time courses were used for DCM. S-DCM, 2S-DCM and P-DCM were used for fitting ASL data (1) and they were compared using Bayesian model selection (BMS).

Bayesian model selection

- Using BMS, P-DCM was selected as the most likely model compared to S-DCM and 2S-DCM, scoring the highest relative model log-evidence (note that only results of main models are shown in Fig. 3).
- Inconsistency is most likely across all six subjects.
- All new model components, i.e. neuronal model, NVC and balloon effect were found statistically better than older versions (results not shown).
- Compared to S-DCM, 2S-DCM exhibits about 27% less between subject variability in estimated connectivity parameters (see Fig. 4).

- We can see strong differences in estimated connectivity patterns between S-DCM, 25-DCM and P-DCM. One might wonder why P-DCM is not explaining BOLD post-stimulus undershoot (see left M1).
- Incompleteness connectivity patterns provided by S-DCM and 2S-DCM result from large fitting errors to the data (see below).
- Unlike S-DCM and 2S-DCM, P-DCM is consistent with physiological observations, provides good model fits, and is statistically superior to S-DCM and 2S-DCM.

We have introduced a new physiologically realistic DCM and applied it to ASL-fMRI data that models E-I neuronal balance, proper neurovascular coupling, and the actual blood effect. New P-DCM is clearly more accurate compared to S-DCM and 2S-DCM as indicated by a better fit to test metrics, including precisely modeling of neuronal and vascular origins of the hemodynamic response undershoot. Therefore, we suggest that P-DCM will play an important role in assessing effective connectivity from fMRI data.

Conclusions

Fig. 1. Comparison of sustained stimulus generated by S-DCM, 2S-DCM, and P-DCM, showing the highest relative model log-evidence (note that only results of main models are shown in Fig. 3).

These results are consistent across all six subjects.

Overall, it can produce very rich dynamics of neuronal, blood, and oxygen response. For a decade, DCM has been used for the analysis of fMRI data albeit with simplifications on the physiological level.

Fig. 2. Comparison of fitted BOLD responses according to effective connectivity (EC) from fMRI data.

Fig. 3. Comparison of fitted BOLD responses according to DCM generative model properties.

Fig. 4. Relative log-evidence of main models (S-DCM, 2S-DCM, P-DCM) for fitting ASL data (1).

Fig. 5. Comparison of BOLD responses and blood flow responses.

Fig. 6. Comparison of fitted BOLD responses according to effective connectivity (EC) from fMRI data.