A discussion on network modelling for fMRI data

David Sinclair

September 26, 2014

Structure

The order of today's presentation is as follows

1. Description of fMRI data
2. Modes of Connectivity
3. Utilization of diffusion MRI results

Acquiring the data

The MRI machine measures magnetic changes in ferromagnetic metals

- Iron, for example, is a ferromagnetic metal, which is contained in blood cells
- Oxygen binds to the iron, and when it leaves it changes the magnetic properties
- This allows us measure blood flow to any region of the brain, known as the *Blood Oxygenation Level Dependent* signal (BOLD)
- We are looking at resting state fMRI experiments

This is useful because of the assumption that blood being sent to a region of the brain implies that area of the brain has been activated

Acquiring the data

A inverse fourier transform is used to give an image of the brain from the magnetic wave readings

- Brain is scanned approximately every 2-5 seconds, to obtain a 3D image with approximately 100,000 pixels referred to henceforth as *voxels*
- A single trial will have about 250 scans
- At each voxel we have a measure for the BOLD response

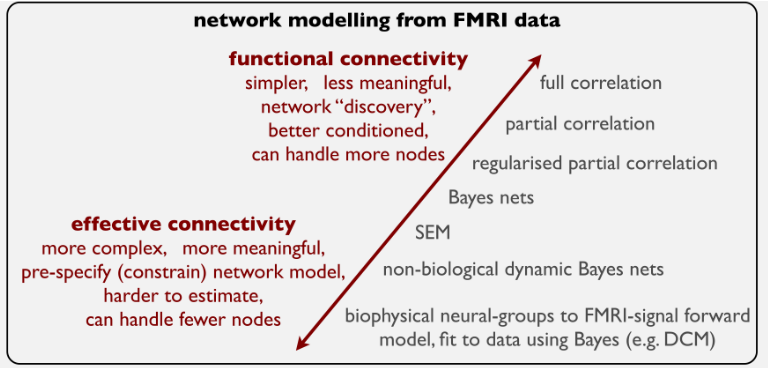
The data

For $i = 1, \ldots, N$ voxels,
$j = 1, \ldots, M$ subjects,
$t = 1, \ldots, T$ timepoints

Our data is $x_{ij}(t)$ the BOLD response at time t of voxel i in person j.

Refer to Matlab

Modes of Connectivity



Smith, S., (2012) The future of fMRI connectivity. NeuroImage (62) 1257-1266

Partial Correlation

Partial correlation is done in a seemingly naive way, although has been shown to perform very well even when compared to more complex models (Smith 2011).
We will describe partial correlation as in Marrelec 2006.

- Recall that we have $i = 1, \ldots, N$ as our voxels
- Say we have $\mathcal{R} = \{R_1, \ldots, R_D\}$ as our predetermined regions of interest, such that $i \in R_k$ implies the voxel represented by i is in the k^{th} region

Partial Correlation

For subject j and region k, recall $x_{ij}(t)$ as the BOLD signal for the i^{th} voxel as defined earlier. Define the signal for that region to be

$$x_k^j(t) = \sum_{i \in R_k} \frac{x_{ij}(t)}{|R_k|}$$

that is to say, the spatial average.
Normalize these for each region and subject to have mean 0 and variance 1.

Partial Correlation

Then assume, for all subjects j and regions k that

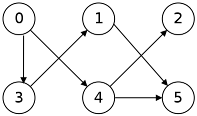
$$(x_1^j(t), \ldots, x_D^j(t)) \sim \mathcal{N}_D(0, \Sigma)$$

Then partial correlations can be obtained from the zeros in the inverse of the estimated Σ matrix.

(As I've probably said by now) You can use the graphical lasso on this in order to regularize.

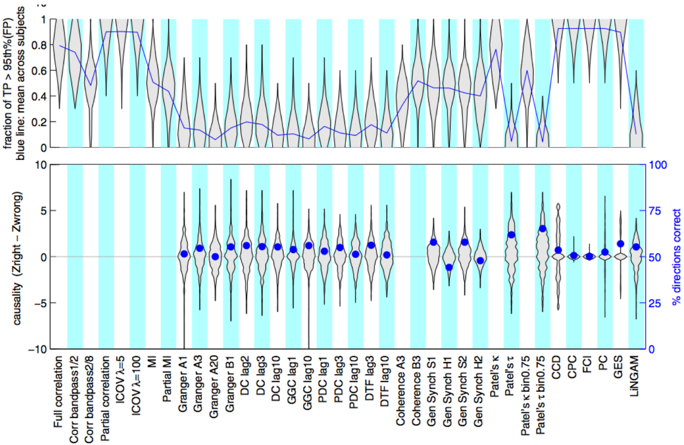
Bayes Net

Bayes network methods are another term for Directed Acyclic Graphs (DAG)



- The Bayes Net methods used in [4] for the most part are extensions of the PC method [8]
- Assumes that the true casual model forms a DAG
- Basically starts with an undirected graph and adds direction and removes edges based on independence and conditional independence tests

Smith Paper Results



Smith., S. M. et al (2011). Network modelling methods for fMRI. *NeuroImage* **54** 875-891

Structure

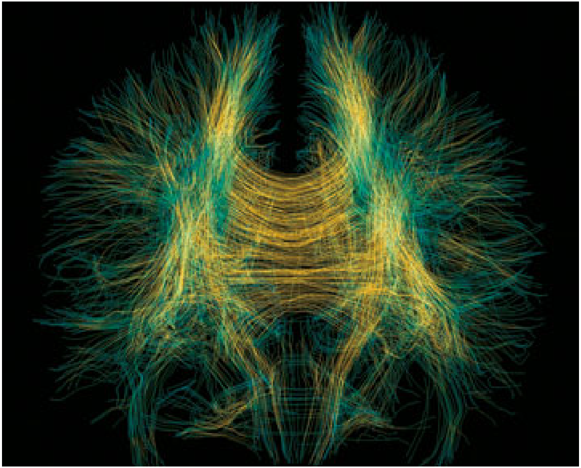
1. ~~Description of fMRI data~~
2. ~~Modes of Connectivity~~
3. Utilization of diffusion MRI results

diffusionMRI

Now we look at network structure determined anatomically

- The diffusion MRI allows you to detect water in the brain
- Myelin is 40% water and can be thought of the wiring system for neurons
- We can use this wiring system to define a network within the brain to do our analyses

diffusionMRI



Nature Neurology February 2012 vol 8 no 2 cover

Network Diffusion Model

For predetermined regions $\{R_1, \ldots, R_D\}$, let $x_i(t)$ be the spatial average of activation over region i.

- Let $C = (c_{ij})$, where c_{ij} is proportional to the number of myelin tracts going from i to j
- Let $\delta_i = \sum_{j=1}^{D} c_{ij}$ be the *degree of* R_i
- Let V_i be the number of voxels in R_i
- Assume the activation $x_i(t)$ is proportional to the number of firing neurons per voxel, and the number of neurons per voxel is fixed across the brain

Network Diffusion Model

Assume for now $D = 1$.

- The simpliest behavior of a damped dynamic system is

$$\frac{\partial x_1(t)}{\partial t} = -\beta x_1(t)$$

- this corresponds to exponential decay in the signal

Network Diffusion Model

Now assume there are 2 regions, i.e. $D = 2$

- By assumption $V_2 x_2$ is proportional to the number of neurons firing in R_2
- The number of neurons firing in R_2 that affect R_1 is proportional to

$$c_{12} \frac{1}{\delta_2} V_2 x_2$$

- and then we normalize for the size of V_1 to say the larger V_1 is the less affect another region can have on it

$$\frac{1}{V_1} c_{12} \frac{1}{\delta_2} V_2 x_2$$

Network Diffusion Model

Including the decay from R_1, combined with the decay from R_2 on the previous slide, we now have

$$\frac{\partial x_1(t)}{\partial t} = \beta \left(\frac{1}{V_1} c_{1,2} \frac{1}{\delta_2} V_2 x_2(t) - x_1(t) \right)$$

Now assuming D, the number of regions, is arbitary, we can extend the equation above to obtain

$$\frac{\partial x_i(t)}{\partial t} = \beta \left(\frac{1}{V_i} \sum_j c_{i,j} \frac{1}{\delta_j} V_j x_j(t) - x_i(t) \right) \tag{1}$$

Network Diffusion Model

A simplifying assumption is to assume that $V_i \propto \sqrt{\delta_i}$, i.e. the number of tracts leading into R_i is proportional to the squared size of R_i. If $a^2\delta_i^2 = V_i$ then in (1) this simplifies to

$$\frac{\partial x_i(t)}{\partial t} = \beta \left(\frac{1}{\delta_i^2} \sum_j c_{i,j}\delta_j x_j(t) - x_i(t) \right)$$

which gives us the following matrix equation

$$\frac{d\mathbf{x}(t)}{dt} = -\beta\mathcal{L}\mathbf{x}(t) \qquad (2)$$

Where $\mathcal{L} = I - \Delta^{-1/2} C \Delta^{-1/2}$ and Δ is the diagonal matrix of degrees

Network Diffusion Model

This differential equation can then be solved as

$$\mathbf{x}(t) = \exp(-\beta \mathcal{L} t)\mathbf{x}_0$$

Thus

$$C_f(t) = \exp(-\beta \mathcal{L} t)$$

can be thought of the connectivity matrix. Since if $(C_f(t))_{ij} = 0$ then the activation of the i^{th} region has no affect on j^{th} region after time t.

In the modelling t is used as a parameter, along with β. The goal is to find t_{crit} and β such that this model is closest to the data

diffusionMRI

Table 1
Models' comparison.

Subject	SC	lFC	nlFC	Network diffusion FC	Fisher's *p*-value
1	0.24	0.31	0.36	0.41	0.0036
2	0.27	0.35	0.41	0.45	0.0490
3	0.23	0.31	0.31	0.37	0.0010
4	0.23	0.35	0.34	0.41	0.0001
5	0.27	0.36	0.38	0.42	0.0250
6	0.24	0.33	0.34	0.38	0.0180
7	0.24	0.33	0.37	0.42	0.0041
8	0.24	0.32	0.38	0.43	0.0041

Correlation coefficients for all subjects. SC, lFC as proposed in (Galán, 2008), nlFC: non-linear estimate (Honey et al., 2009), and the proposed network diffusion FC. Last column lists Fisher's *p*-value for all subjects.

Abdelnour, F., Voss. H.U., Raj, A., (2014) Network diffusion accruately models the relationship between structural and functional brain connectivity networks. *NeuroImage* **90** 335-347

References

(1) Linquist, M. A. (2008). The Statistical Analysis of fMRI Data. *Stat. Sci* **23** 439-464

(2) Friston. K. J. (2011). Functional and Effective Connectivity: A Review *Brain Connect.* **1**

(3) Marralec, G. et. al. (2006). Partial Correlation for functional brain interactivity investigation in functional MRI. *Neuro Image* **32** 228-237

(4) Smith., S. M. et al (2011). Network modelling methods for fMRI. *NeuroImage* **54** 875-891

(5) Friendman, J., Hastie, T., Tibshirani, R., (2008) Sparse inverse covariance estimation with the graphical lasso. *Biostatistics* **9**,3 432-441

(6) Abdelnour, F., Voss. H.U., Raj, A., (2014) Network diffusion accruately models the relationship between structural and functional brain connectivity networks. *NeuroImage* **90** 335-347

References

(7) Smith, S.M., (2012) The Future of fMRI connectivity. *NeuroImage* **62** 1257-1266

(8) Meek, C., 1995. Causal inference and causal explanation with background knowledge. Proceedings of the 11th Annual Conference on Uncertainty in Artificial Intelligence, pp. 403-410