Dynamic Causal Modeling (DCM): Theory & Application

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Oakland UNIVERSITY

SPIE Conference (2012)

We have received an Honorable Mention Poster Award

480 posters
Winning poster rate: 5/480 is 1%

SPIE Conference (2012)

Biomedical Applications in Molecular, Structural, and Functional Imaging Conference 8317

Honorable Mention Poster Award

Comparison between subjects with long- and short-allele carriers in the BOLD signal within amygdala during emotional tasks (8317-61)

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Presented by:

Robert C. Molthen, Zablocki VA Medical Ctr. (USA), and
John B. Weaver, Dartmouth Hitchcock Medical Ctr. (USA)

Medical Imaging 2012
Monday, 6 February 2012

SPIE

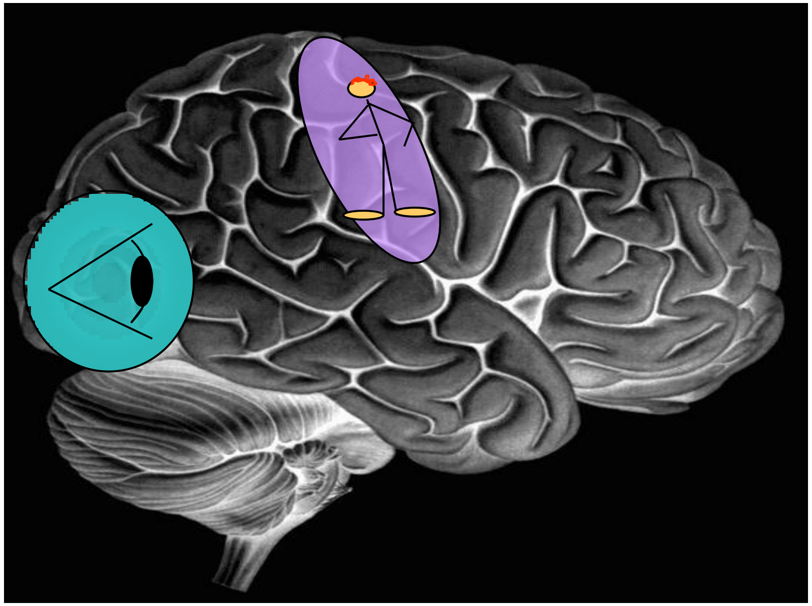
SPIE Medical Imaging

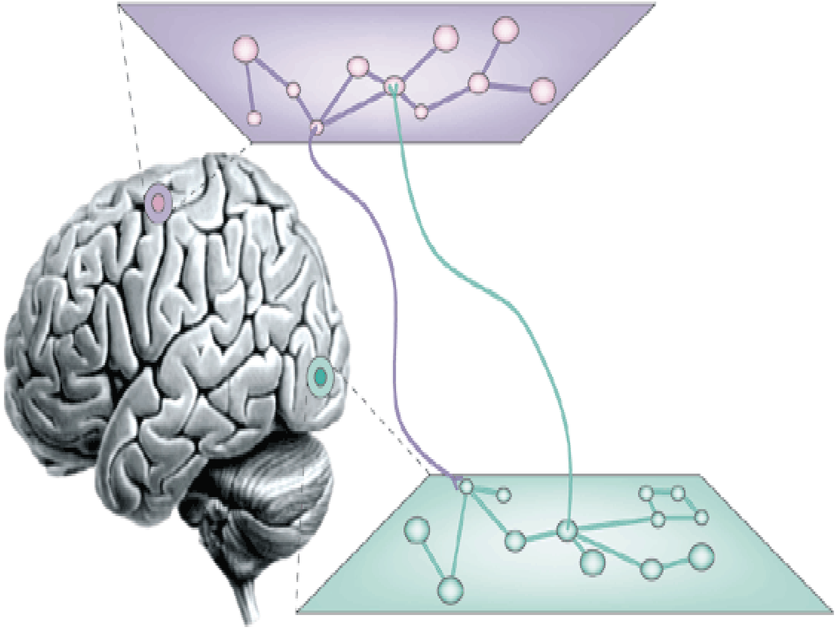
Outline

1

- Functional Integration

Functional connectivity vs. Effective connectivity





1. Analysis of regionally specific effect.
2. Correlation between activity in spatially remote region.
3. Independent of how the. dependencies are caused.

1. Interactions among brain regions.
2. One brain area is influenced by another.
3. Requires a generative model of measured brain responses.

Outline

Objective

1. Determination of facial expression of emotional task is associated with changes in brain connectivity and thus allowed comparison between *s* - allele and *ℓ/ℓ* - allele.
2. To see whether these effects were modulated by emotional stimuli.
3. To show that genotype affects patterns of neuronal activation within limbic circuitry.

Why individuals with 5-HTTLPR short-allele are more prone to anxiety?

Outline

- Introduction
- Objective
- Related Work
  1. Hemodynamic Model
  2. Functional MRI
- Approach
- Dynamic system
- Experiment
- Conclusion

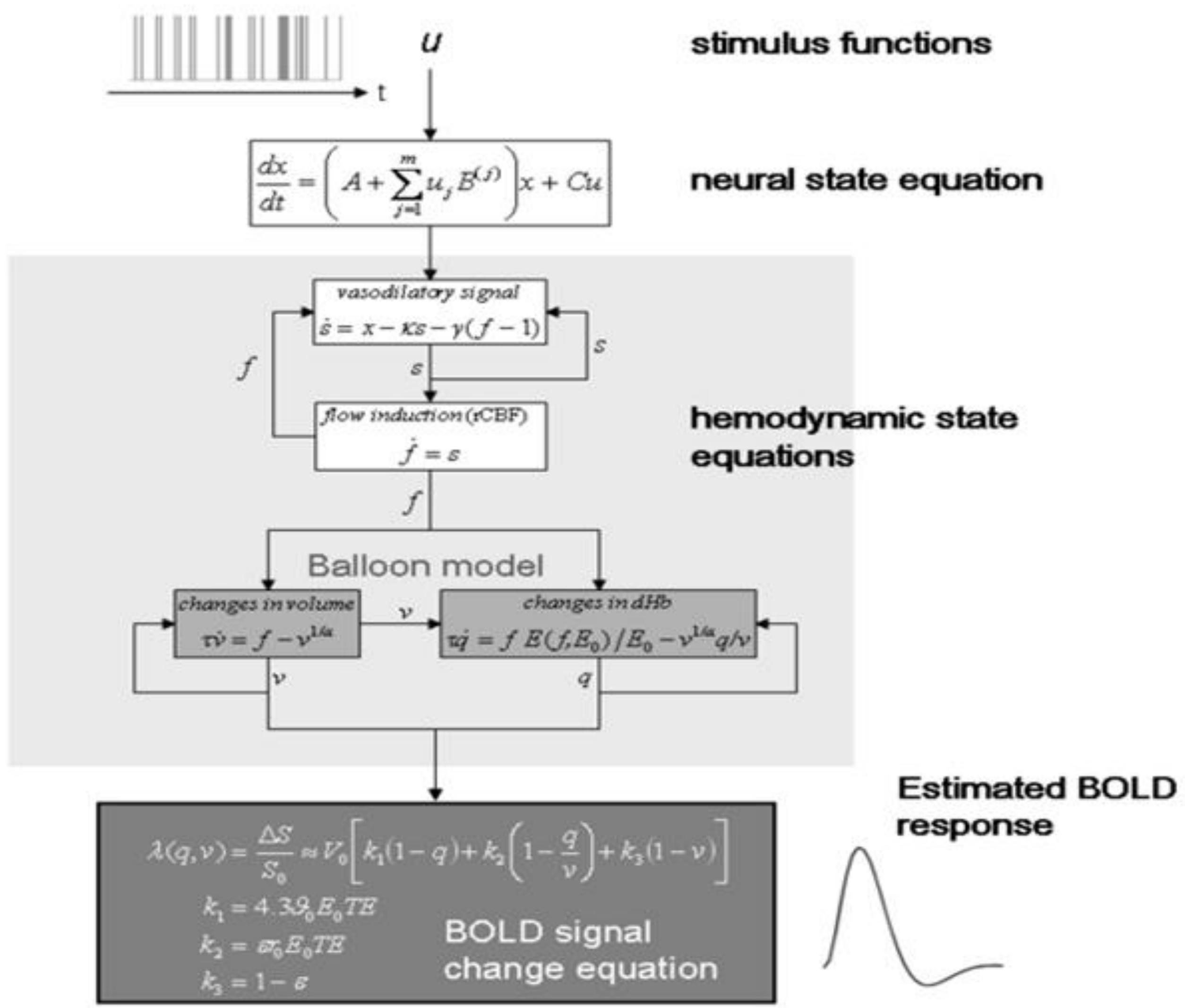
Related work → Hemodynamic Model

u

Activity $x(t)$

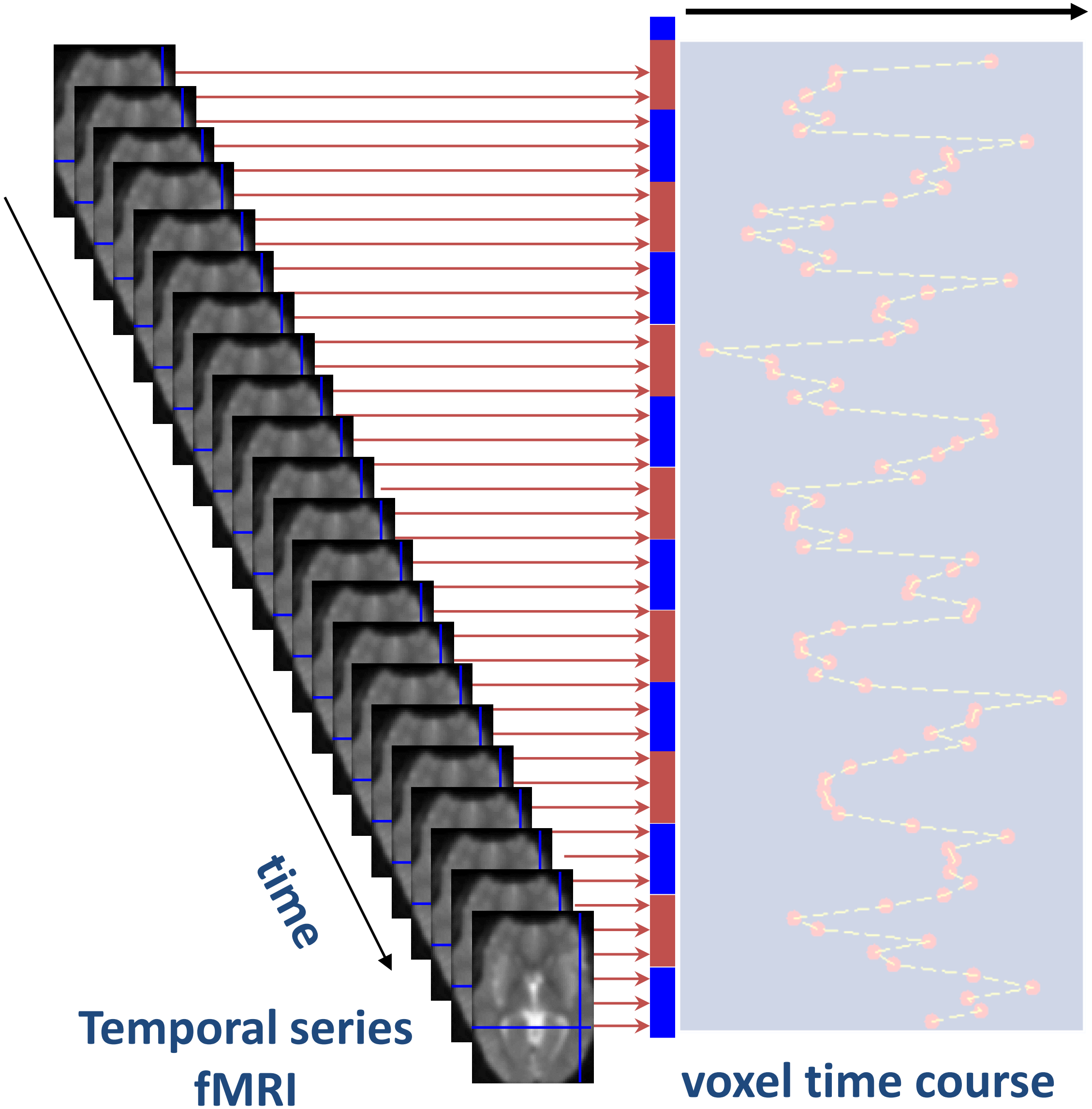
$\lambda(v, q)$

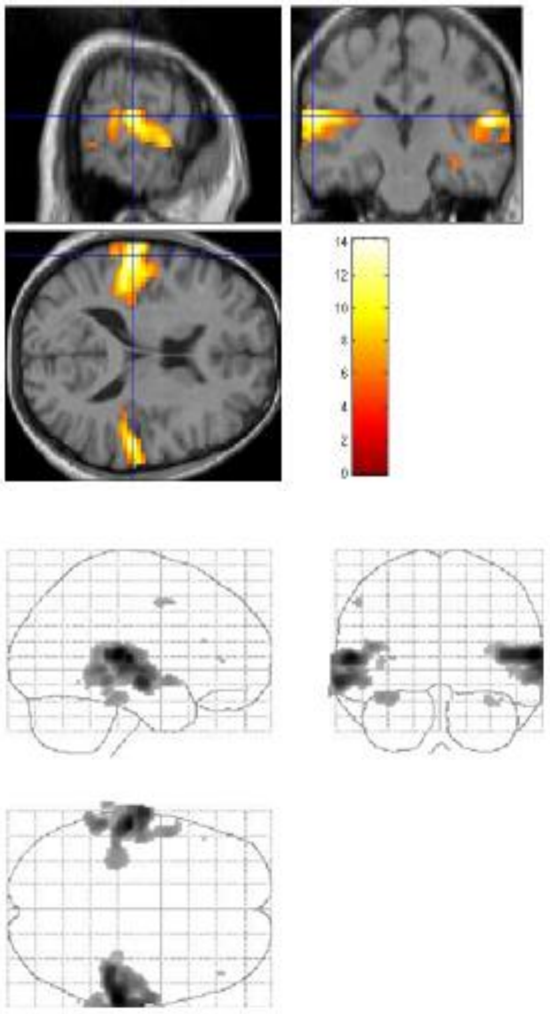
BOLD signal
$y(t) = \lambda(v, q)$



http://www.fil.ion.ucl.ac.uk/spm/doc/papers/Stephan_NeuroImage_38_387_2007.pdf

Related work → fMRI





Outline

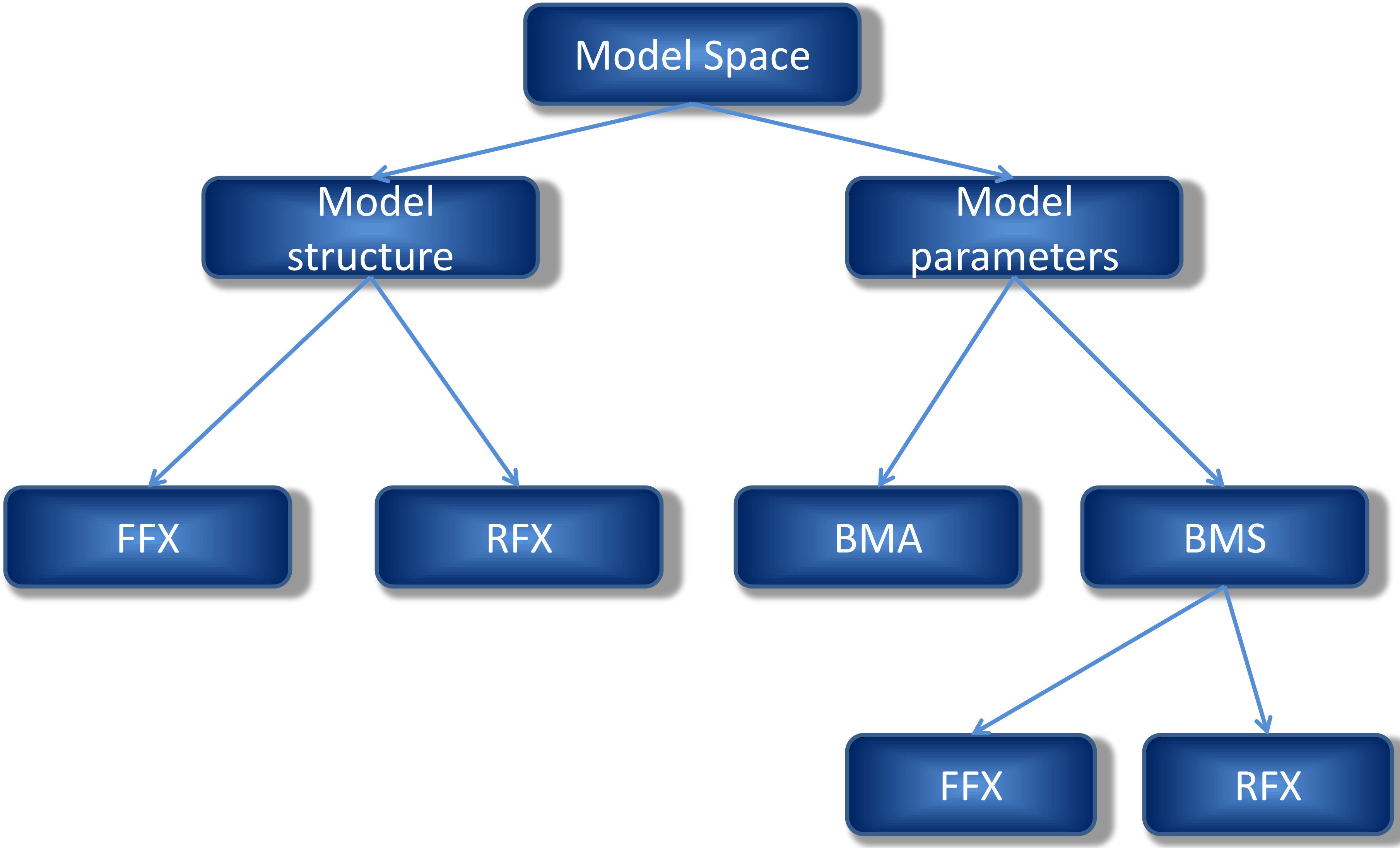
- Introduction
- Objective
- Related Work
- Approach
  1. Dynamic Causal Modeling DCM
  2. Conceptual overview
  3. Bilinear state equations
  4. Neurodynamics
  5. Reciprocal connections
  6. Hemodynamic responses
  7. DCM drawback
  7. The DCM cycle
- Dynamic system
- Experiment
- Conclusion

Approach → Dynamic Causal Modeling (DCM)

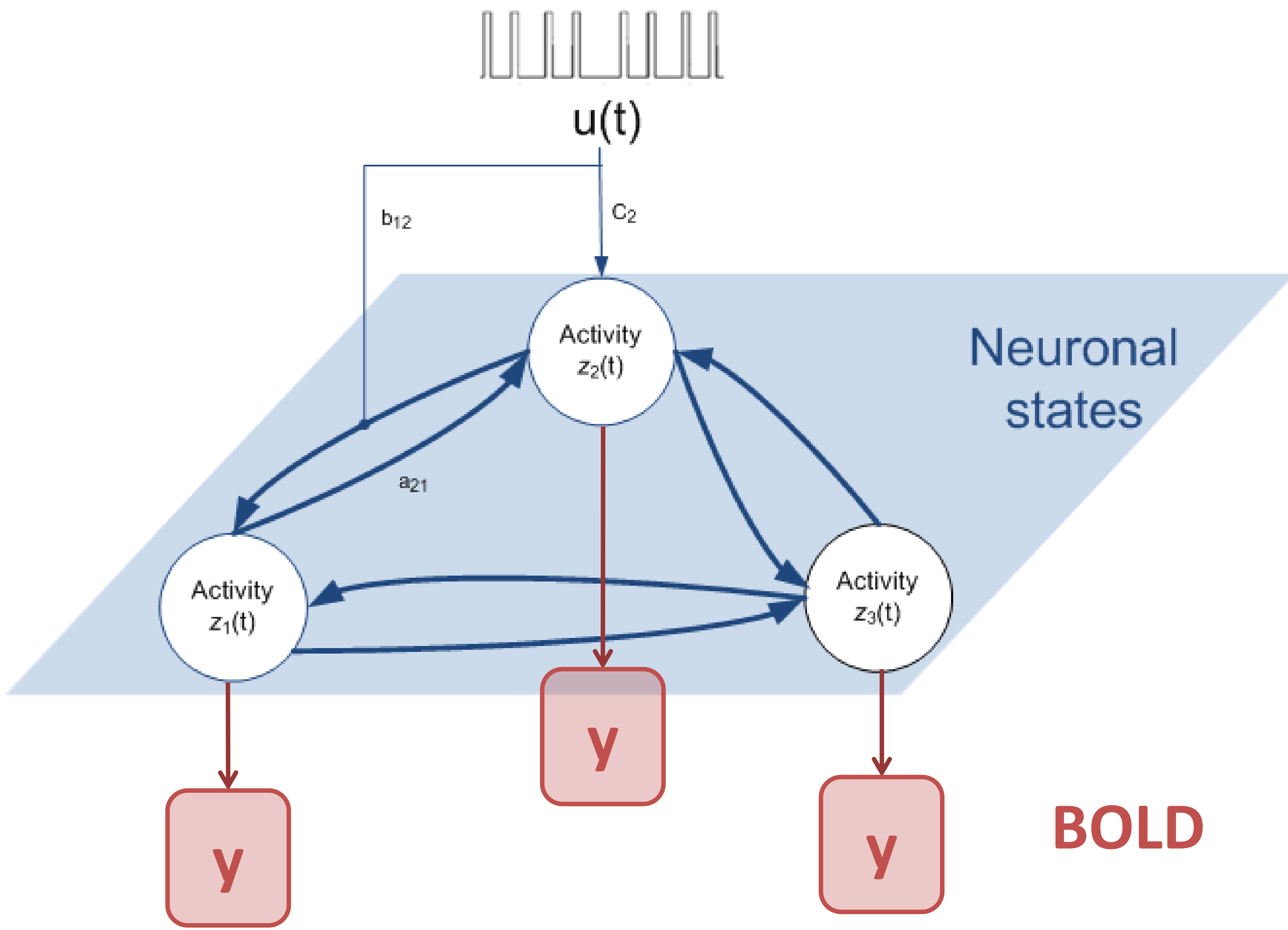
- Dynamic Causal Modelling is a framework for fitting differential equation models of neuronal activity to brain imaging data using Bayesian inference (W. Penny *et al*, 2010).

- The general idea is to estimate the parameters of a reasonably realistic neuronal model.

Approach → Model Space



Approach → Conceptual overview



Approach → Bilinear state equations

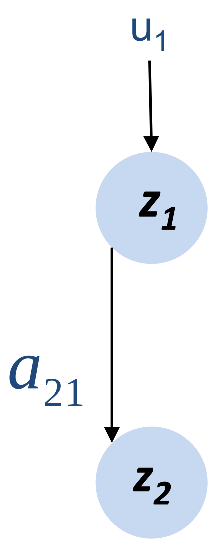
state changes → connectivity → modulation of connectivity → state vector → direct inputs → external inputs

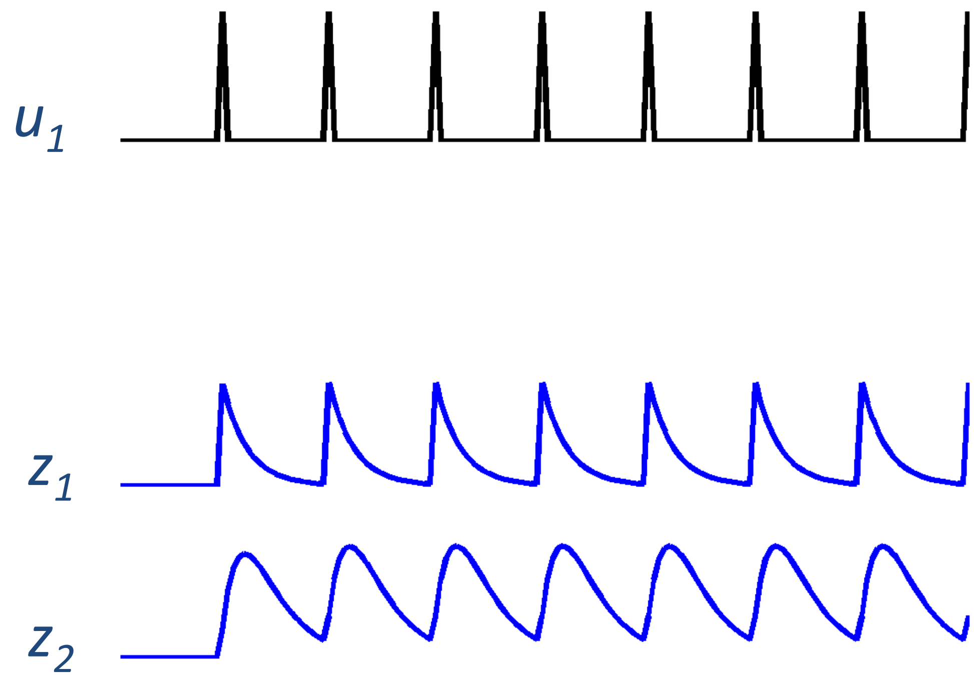
$$\begin{bmatrix} \dot{z}_1 \\ \vdots \\ \dot{z}_n \end{bmatrix} = \left\{ \begin{bmatrix} a_{11} & \cdots & a_{1n} \\ \vdots & \ddots & \vdots \\ a_{n1} & \cdots & a_{nn} \end{bmatrix} + \sum_{j=1}^{m} u_j \begin{bmatrix} b_{11}^{j} & \cdots & b_{1n}^{j} \\ \vdots & \ddots & \vdots \\ b_{n1}^{j} & \cdots & b_{nn}^{j} \end{bmatrix} \right\} \begin{bmatrix} z_1 \\ \vdots \\ z_n \end{bmatrix} + \begin{bmatrix} c_{11} & \cdots & c_{1m} \\ \vdots & \ddots & \vdots \\ c_{n1} & \cdots & c_{nm} \end{bmatrix} \begin{bmatrix} u_1 \\ \vdots \\ u_m \end{bmatrix}$$

n regions — *m* inputs — *m* inputs

$$\dot{z} = (A + \sum_{j=1}^{m} u_j B^{j}) z + Cu$$

Approach → Neurodynamics : 2 nodes + u_1

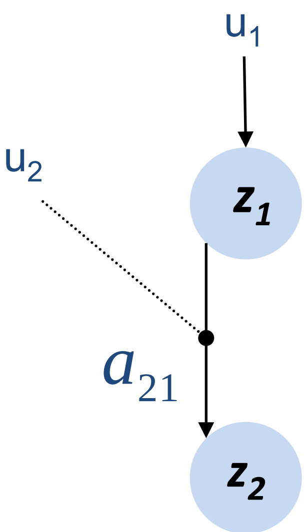


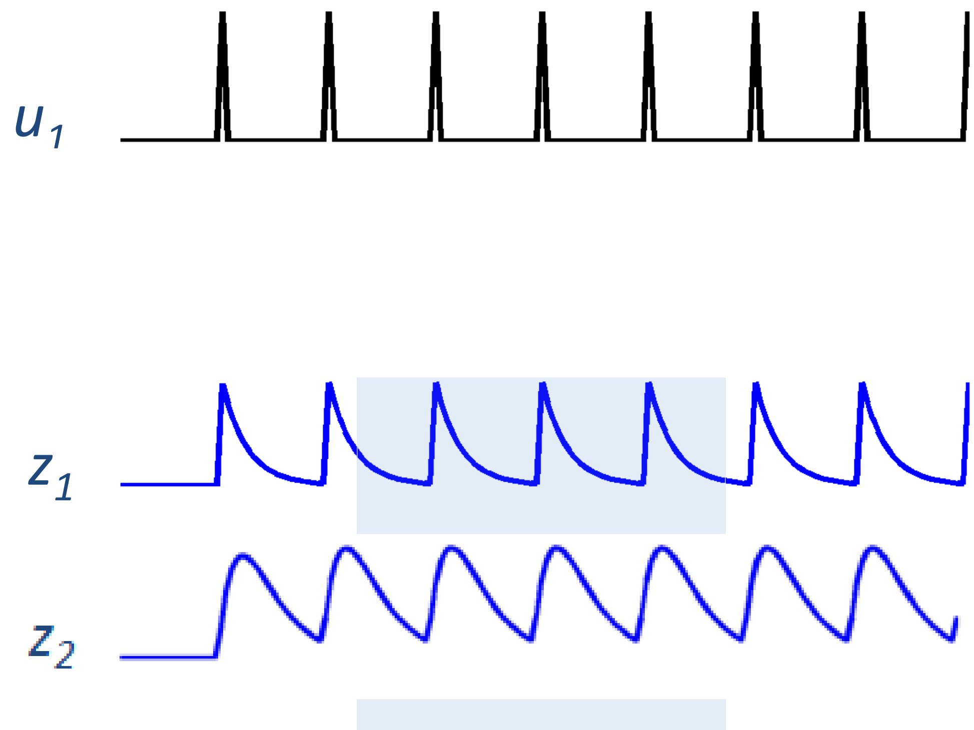


$$\begin{bmatrix}\dot{z}_1\\ \dot{z}_2\end{bmatrix} = s\begin{bmatrix}-1 & 0\\ a_{21} & -1\end{bmatrix}\begin{bmatrix}z_1\\ z_2\end{bmatrix} + \begin{bmatrix}c\\ 0\end{bmatrix}u_1 \qquad a_{21} > 0$$

activity in z_2 is coupled to z_1 via coefficient a_{21}

Approach → Neurodynamics : 2 nodes + u_1 + u_2

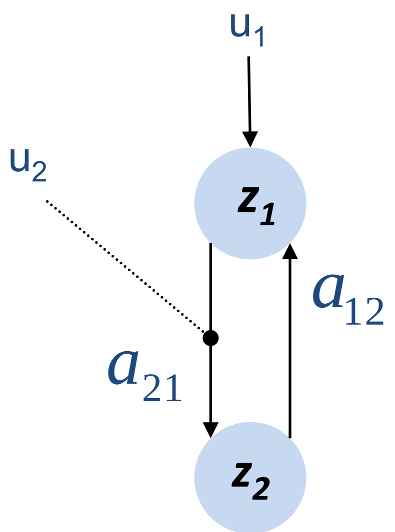


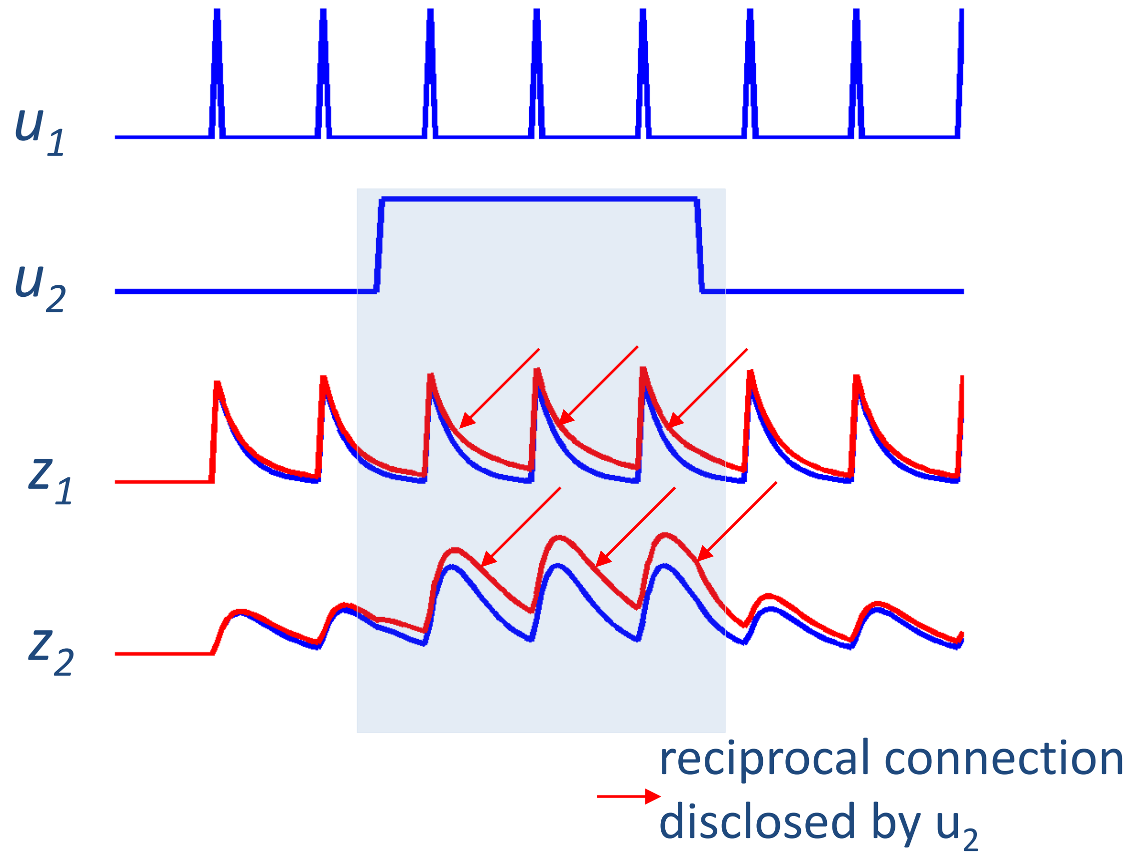


$$\begin{bmatrix} \dot{z}_1 \\ \dot{z}_2 \end{bmatrix} = s \begin{bmatrix} -1 & 0 \\ a_{21} & -1 \end{bmatrix} \begin{bmatrix} z_1 \\ z_2 \end{bmatrix} + u_2 \begin{bmatrix} 0 & 0 \\ b_{21}^2 & 0 \end{bmatrix} \begin{bmatrix} z_1 \\ z_2 \end{bmatrix} + \begin{bmatrix} c \\ 0 \end{bmatrix} u_1$$

modulatory input u_2 activity through the coupling a_{21}

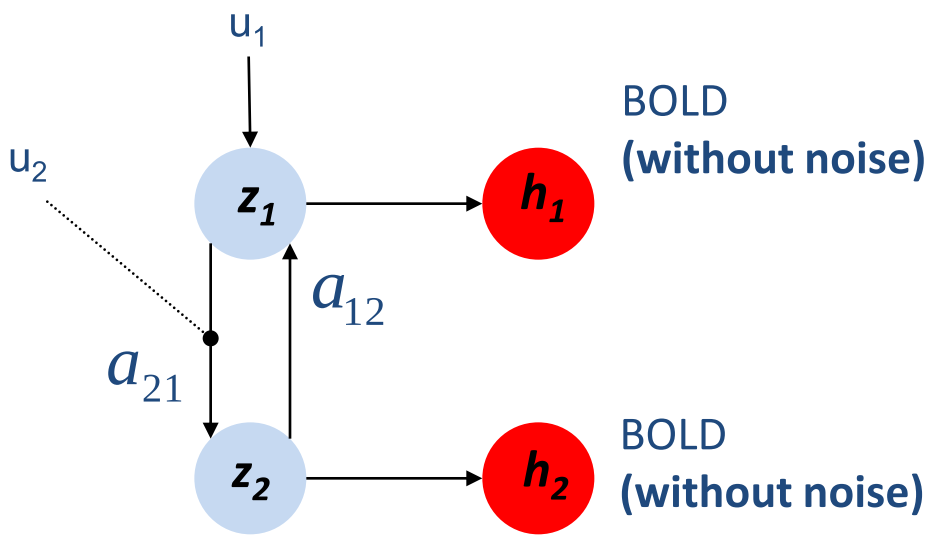
Approach → Reciprocal connections

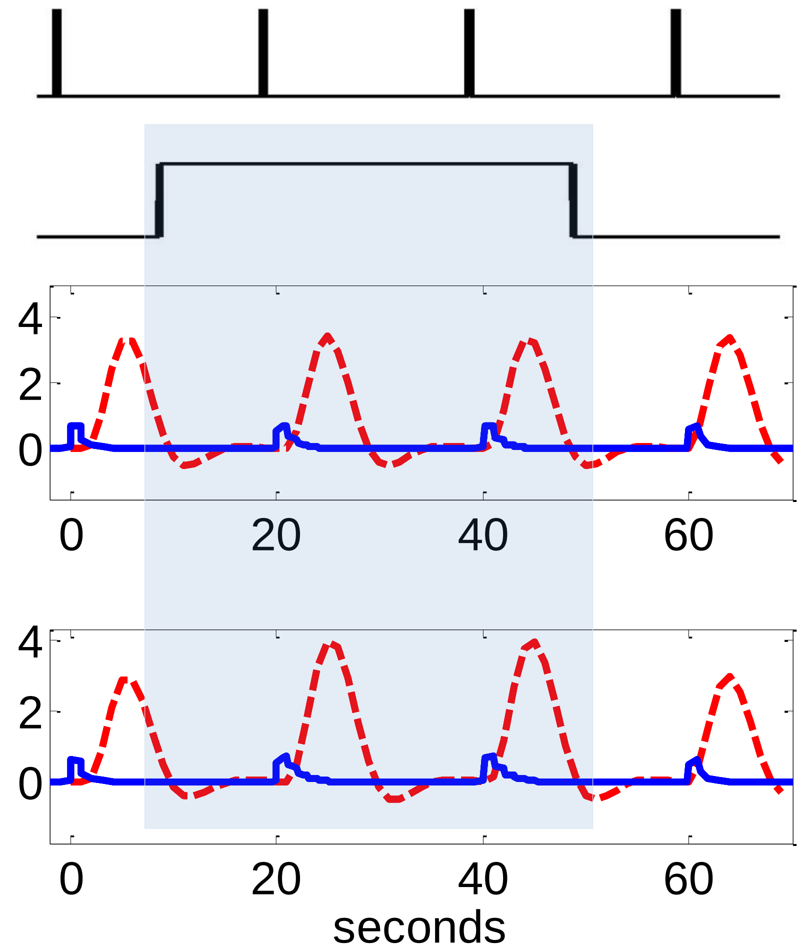




$$\begin{bmatrix}\dot{z}_1\\ \dot{z}_2\end{bmatrix} = s\begin{bmatrix}-1 & a_{12}\\ a_{21} & -1\end{bmatrix}\begin{bmatrix}z_1\\ z_2\end{bmatrix} + u_2\begin{bmatrix}0 & 0\\ b_{21}^2 & 0\end{bmatrix}\begin{bmatrix}z_1\\ z_2\end{bmatrix} + \begin{bmatrix}c\\ 0\end{bmatrix}u_1 \qquad a_{12}, a_{21}, b_{21}^2 > 0$$

Approach → Hemodynamic responses





h(u,ϑ) represents the BOLD response (balloon model) to input

Blue: neuronal activity
Red: bold responses

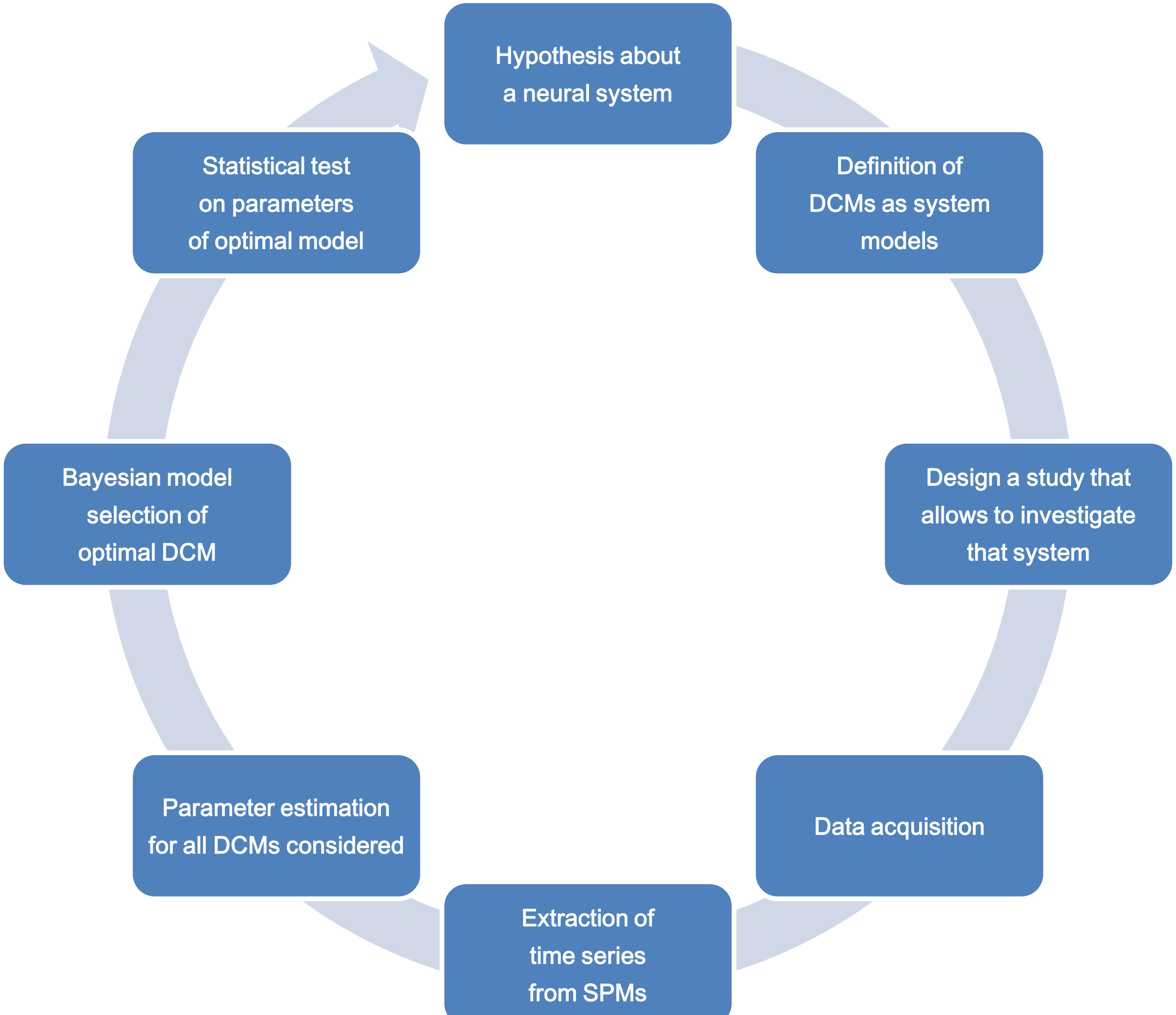
Approach → DCM drawback

1- Needs certain special knowledge.

2- Time consuming.

3- Complicated.

Approach → The DCM cycle



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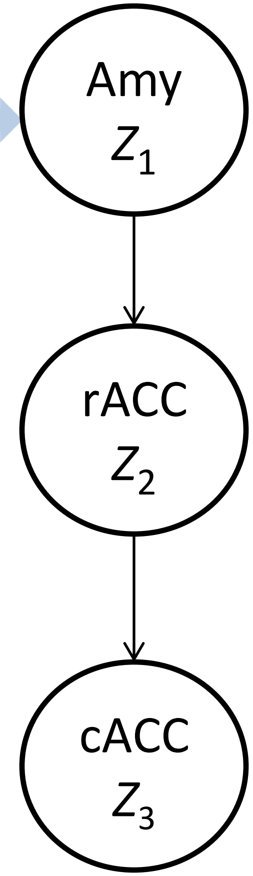
- Dynamic system
  1. Linear model
  2. Bilinear model
  3. Nonlinear model
- Experiment
- Conclusion

Dynamic system→ Linear model

Linear model

Match Shape



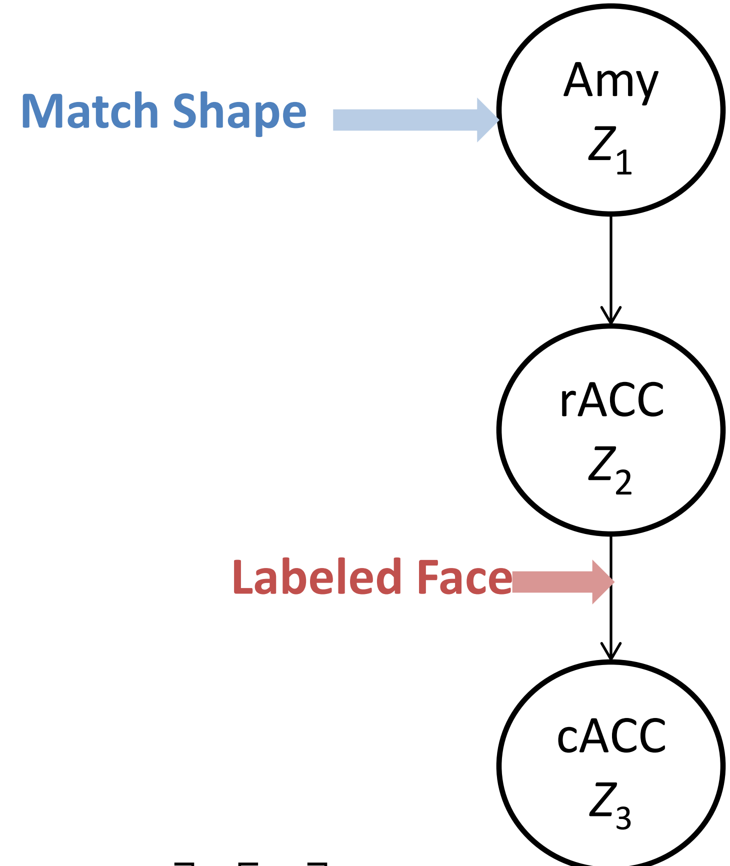
$$\frac{dz}{dt} = Az + Cu$$

$$\begin{bmatrix} \dot{z}_1 \\ \dot{z}_2 \\ \dot{z}_3 \end{bmatrix} = \begin{bmatrix} 0 & 0 & 0 \\ 1 & 0 & 0 \\ 0 & 1 & 0 \end{bmatrix} * \begin{bmatrix} z_1 \\ z_2 \\ z_3 \end{bmatrix} + \begin{bmatrix} 1 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix} * \begin{bmatrix} u_1 \\ u_2 \\ u_3 \end{bmatrix}$$

Dynamic system→ Bilinear model

Linear model

Bilinear model

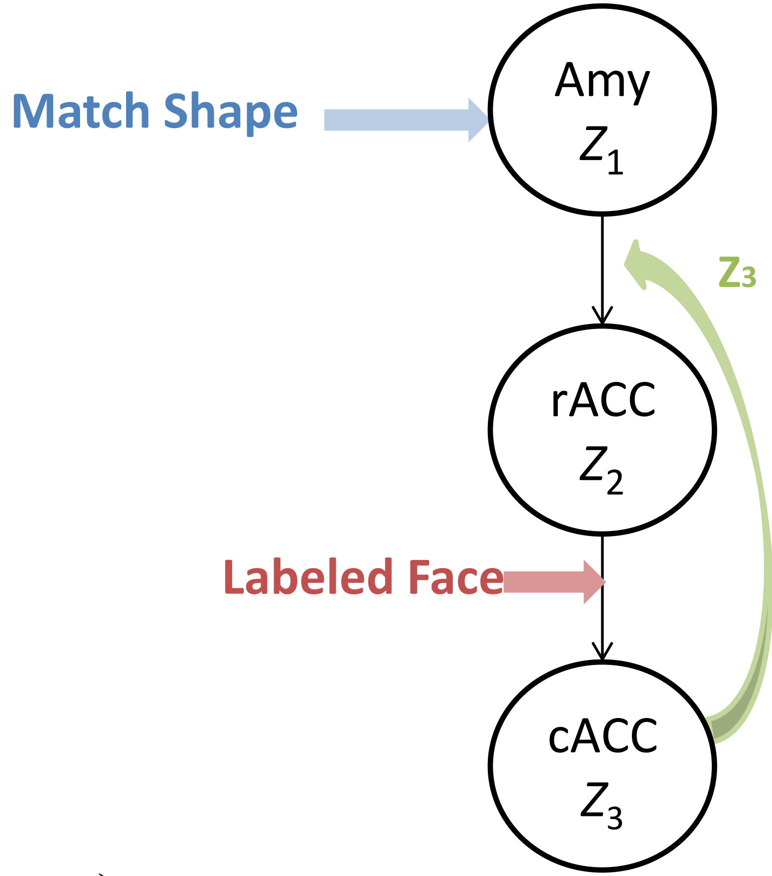


$$\frac{dz}{dt} = \left(A + \sum_{i=1}^{m} u_i B^{(i)} \right) z + Cu$$

$$\begin{bmatrix} \dot{z}_1 \\ \dot{z}_2 \\ \dot{z}_3 \end{bmatrix} = \left(\begin{bmatrix} 0 & 0 & 0 \\ 1 & 0 & 0 \\ 0 & 1 & 0 \end{bmatrix} + u_3 * \begin{bmatrix} 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 1 & 0 \end{bmatrix} \right) \begin{bmatrix} z_1 \\ z_2 \\ z_3 \end{bmatrix} + \begin{bmatrix} 1 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix} * \begin{bmatrix} u_1 \\ u_2 \\ u_3 \end{bmatrix}$$

Dynamic system→ Nonlinear model

- Linear model
- Bilinear model
- Nonlinear model



$$\frac{dz}{dt} = \left(A + \sum_{i=1}^{m} u_i B^{(i)} + \sum_{j=1}^{n} z_j D^{(j)} \right) z + Cu$$

$$\begin{bmatrix} \dot{z}_1 \\ \dot{z}_2 \\ \dot{z}_3 \end{bmatrix} = \left(\begin{bmatrix} 0 & 0 & 0 \\ 1 & 0 & 0 \\ 0 & 1 & 0 \end{bmatrix} + u_3 * \begin{bmatrix} 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 1 & 0 \end{bmatrix} + z_3 * \begin{bmatrix} 0 & 0 & 0 \\ 1 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix} \right) \begin{bmatrix} z_1 \\ z_2 \\ z_3 \end{bmatrix} + \begin{bmatrix} 1 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix} * \begin{bmatrix} u_1 \\ u_2 \\ u_3 \end{bmatrix}$$

Outline

- Introduction
- Objective
- Related Work
- Approach
- Dynamic system
- Experiment
  1. Subjects
  2. Region of interest
  3. Identify the models
  4. Inputs
  5. Paradigms
  6. Results
- Conclusion

Experiment → Subjects

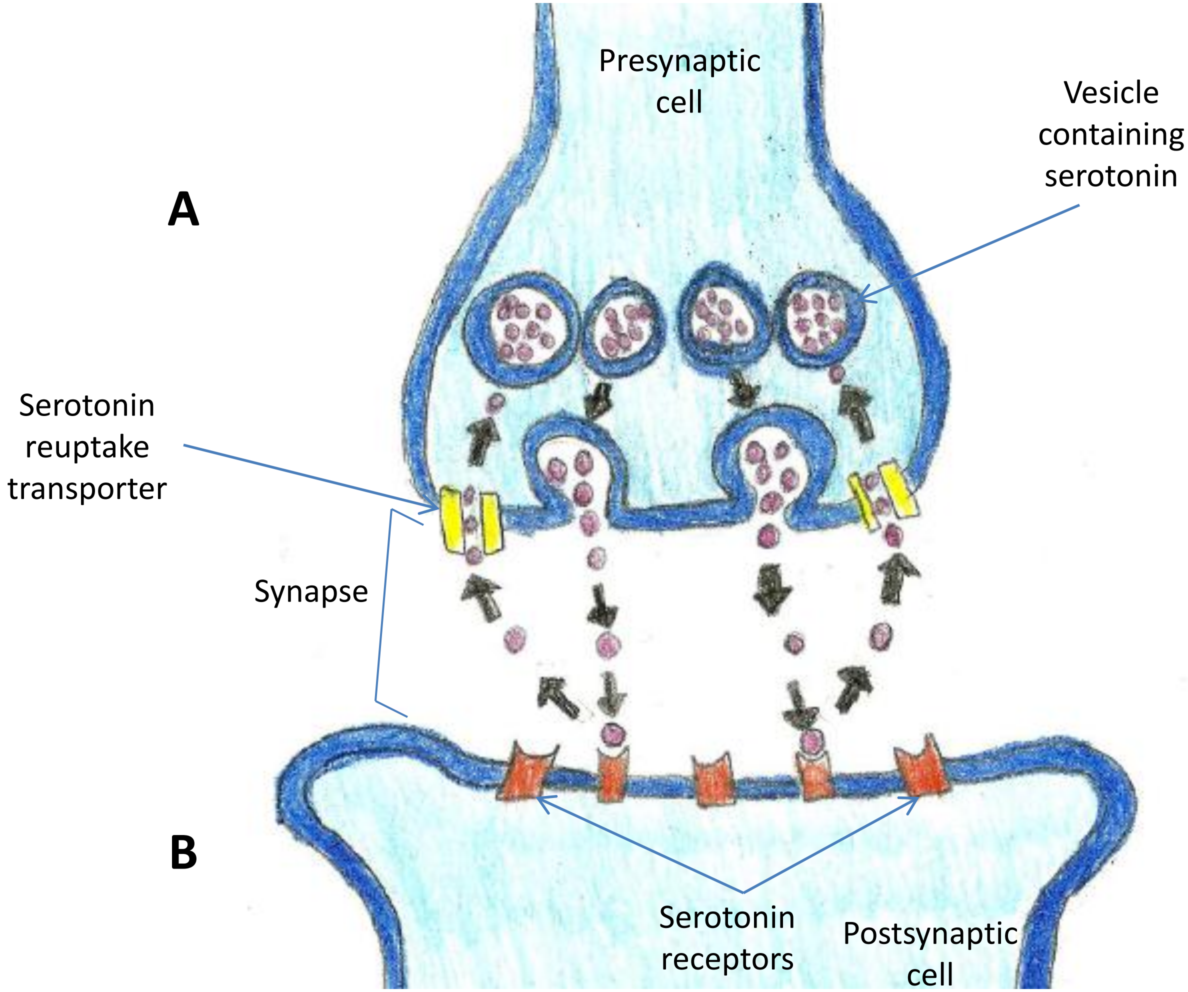
- 37 Caucasian subjects, 15 for long-allele and 22 for short-allele carriers.
- Subjects were selected from a large population after testing to make sure there was no history of neurological illness, any drug or alcohol abuse.

Experiment → Subjects

1- Short promoter region, *s*-allele

2- Long promoter region, *ℓ/ℓ*-allele

Experiment → Subjects



Experiment → Region of interest

1. Left amygdala (L).
2. Right amygdala (R).
3. Rostral Subgenual Posterior Portion of the Anterior Cingular Cortex (r).
4. Caudal Supragenual Portion of the Anterior Cingular Cortex (c).

Experiment → Region of interest

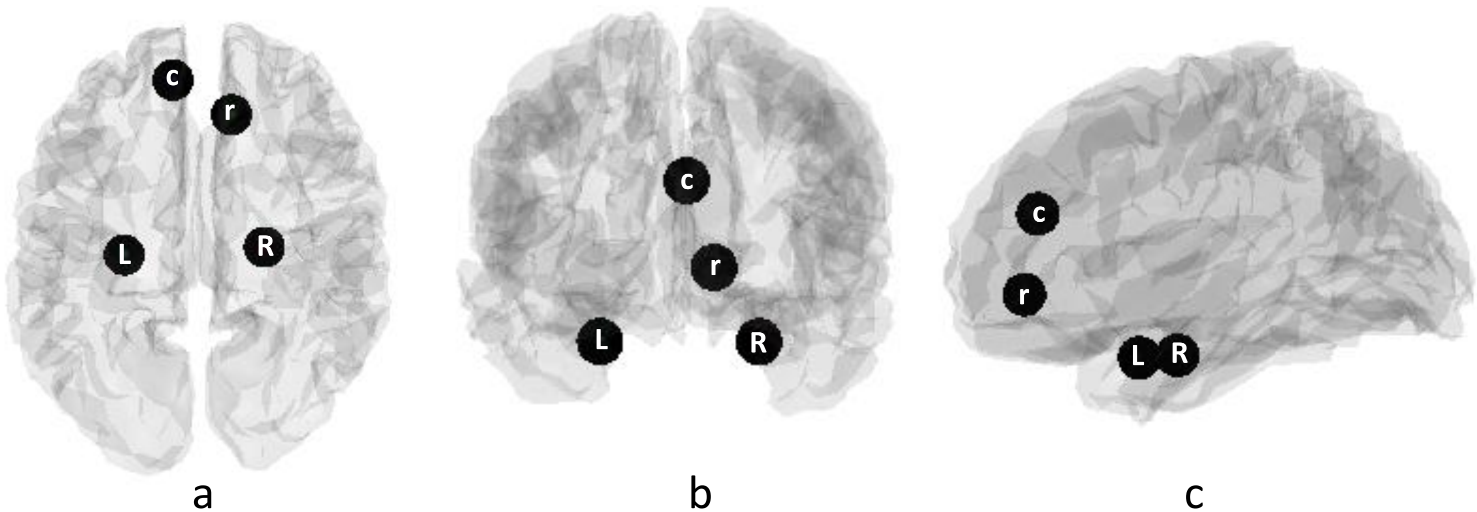
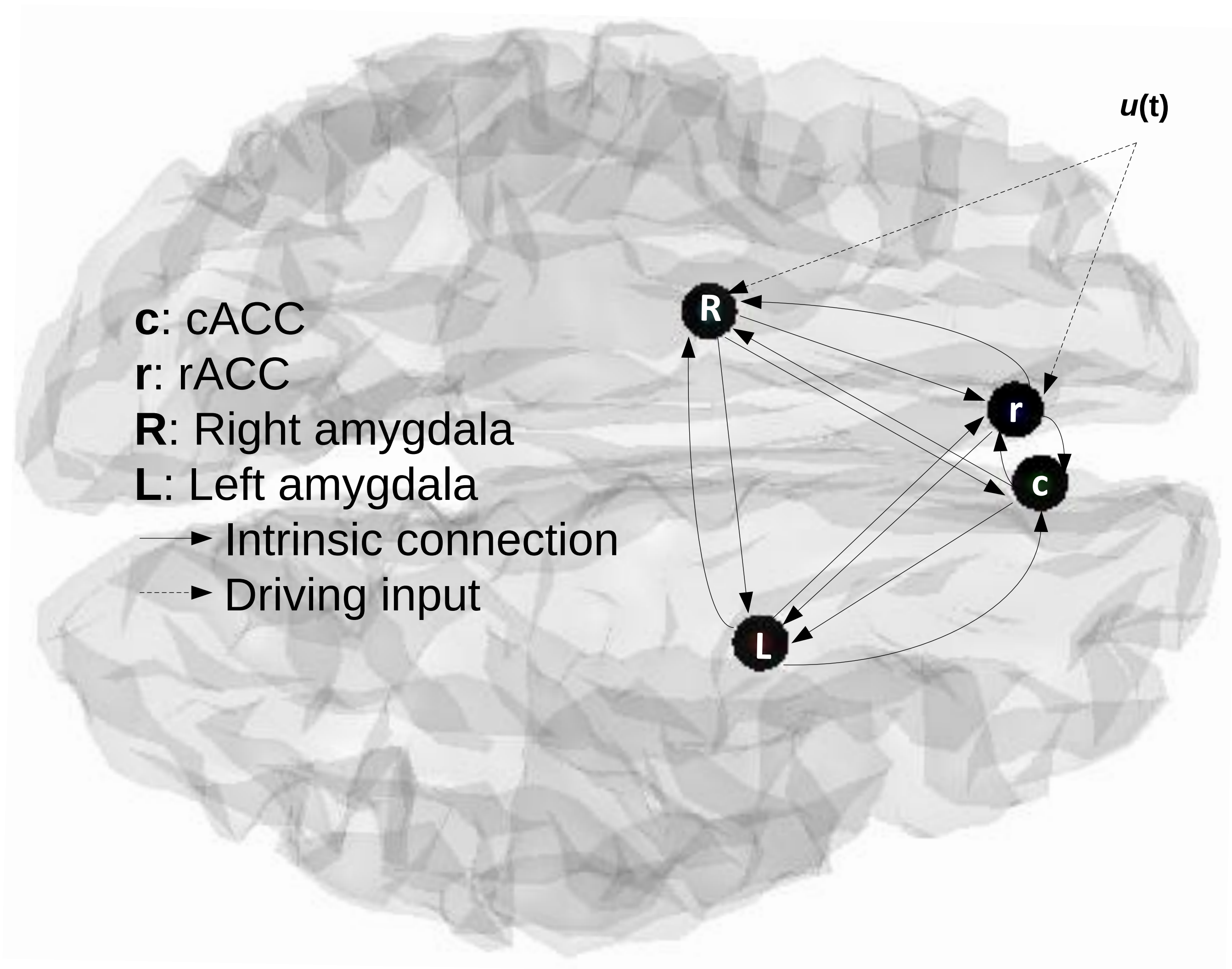


Fig. 3. Brain region locations. a) axial, b) coronal, and c) sagittal

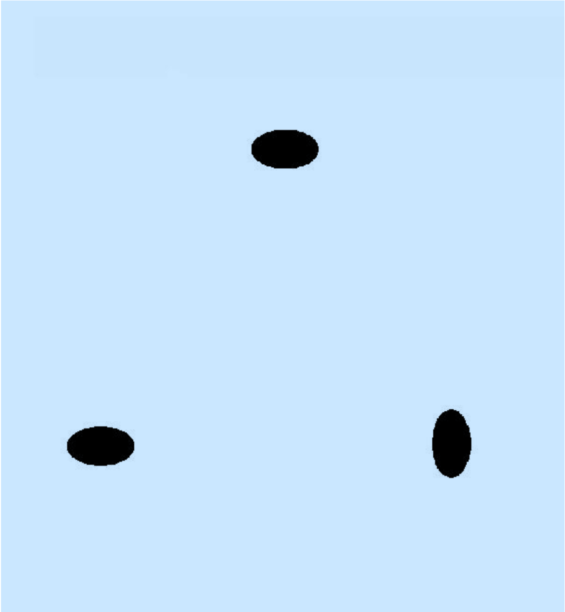
Table 1, Voxel statistics

Brain region	Number of Voxel	Location (mm)		
		X	*Y*	*Z*
Left amygdala (L)	11	-26	-4	-25
Right amygdala (R)	13	22	0	-25
cACC (c)	14	-4	38	21
rACC (r)	11	4	41	-5

Experiment → Identify the models



Experiment → Inputs



Match Shape

Match Face

Labeled Face

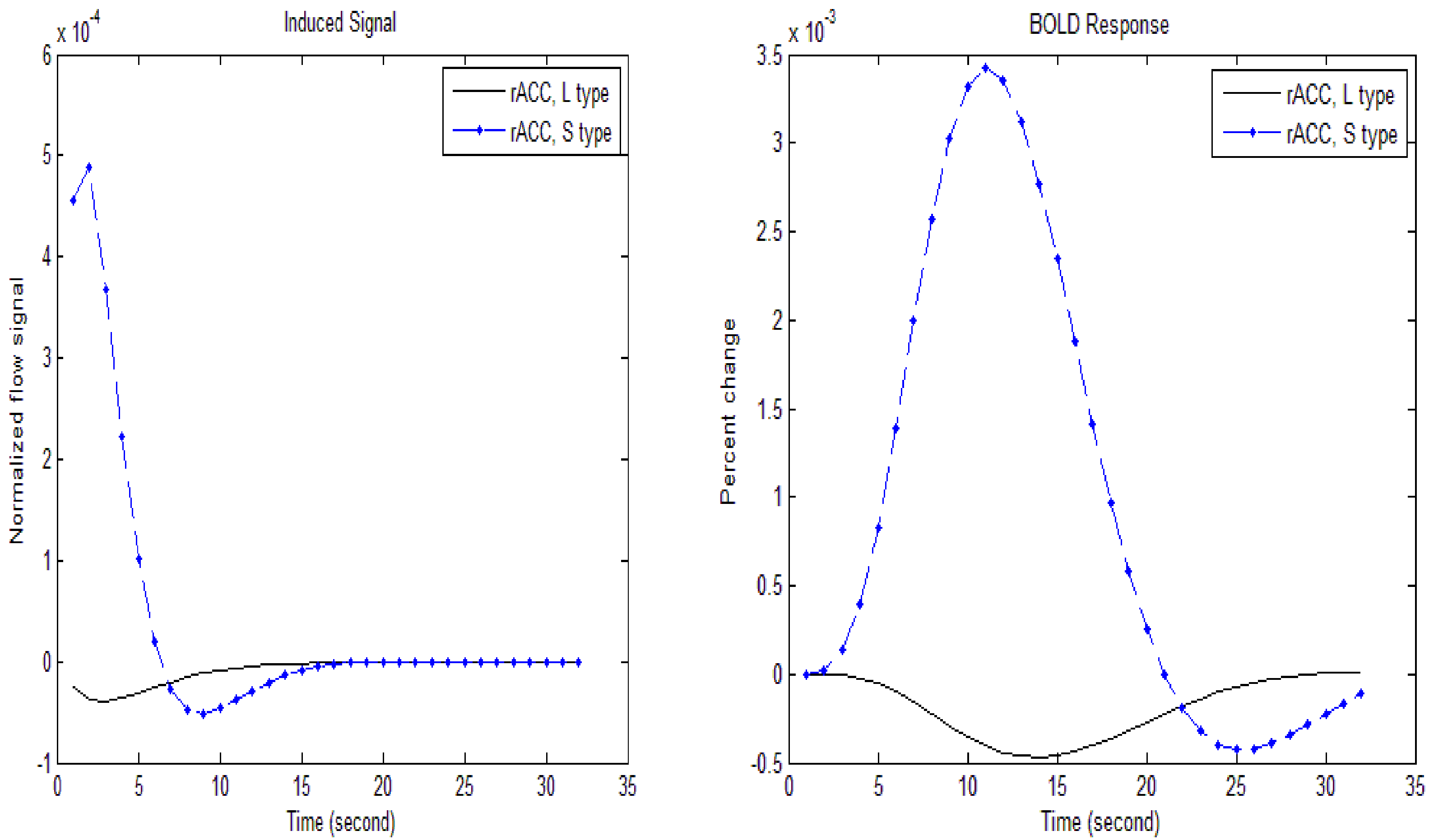
Oakland University

Experiment → Paradigms

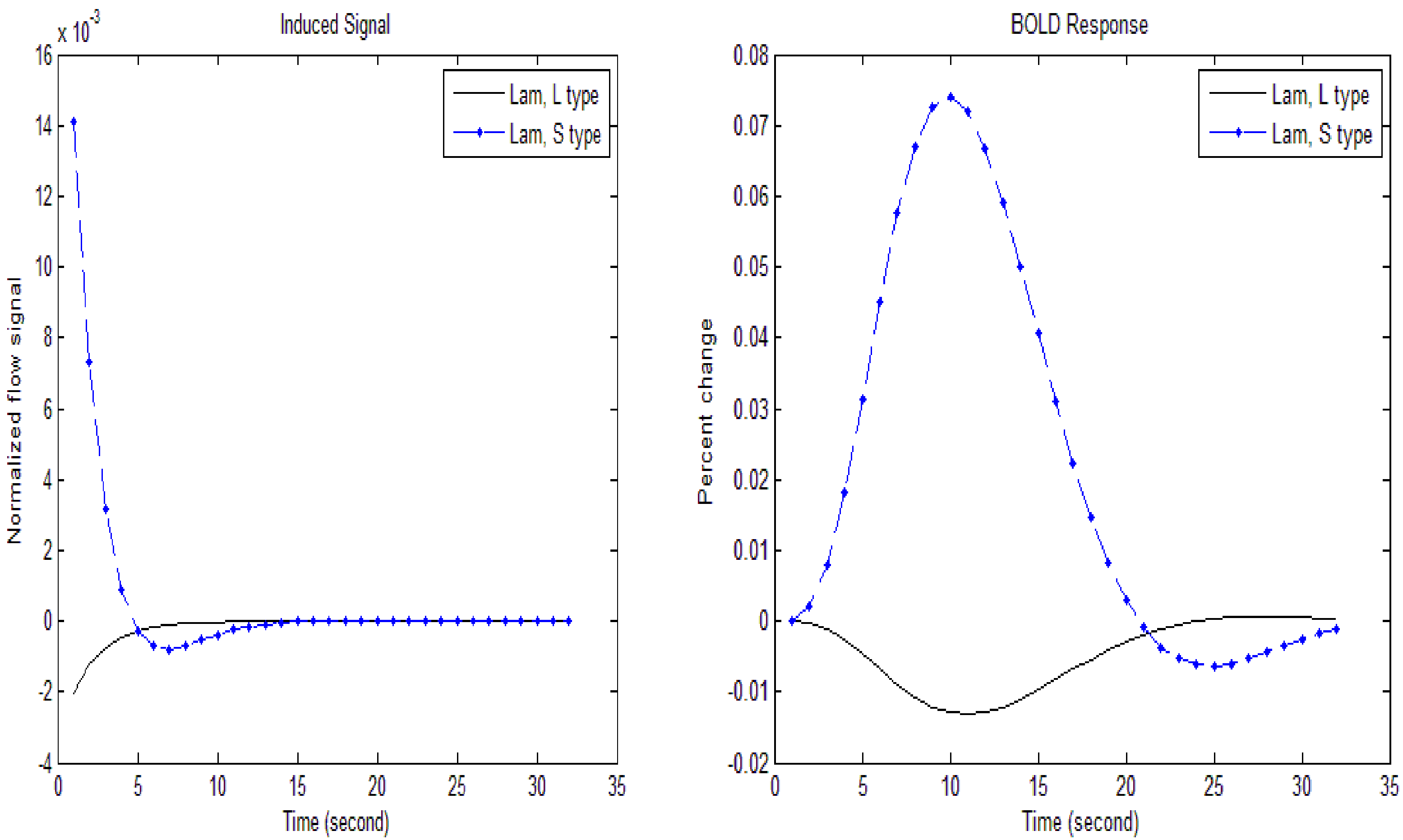
LM	ML	MM
MS	MS	MS
LF	MF	MF
MS	MS	MS
LF	MF	MF
MS	MS	MS
MF	LF	MF
MS	MS	MS
MF	LF	MF
MS	MS	MS

Experiment → Paradigms

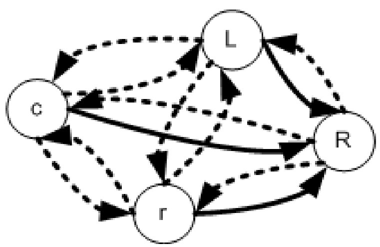
Experiment → Results (Input is *MF*)



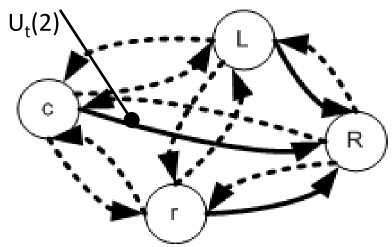
Experiment → Results (Input is *MF*)



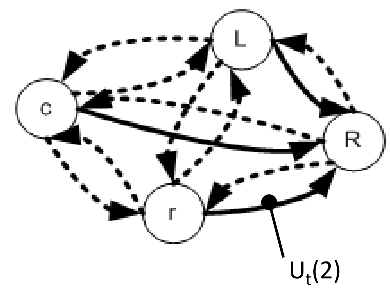
Experiment → Results (Modulatory input)



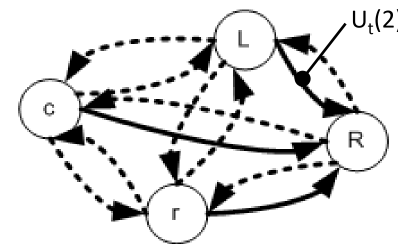
Model 1



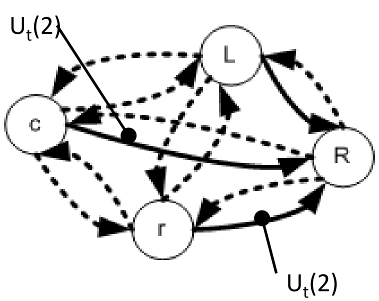
Model 2



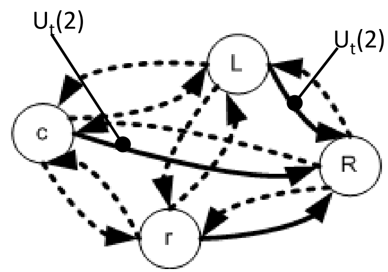
Model 3



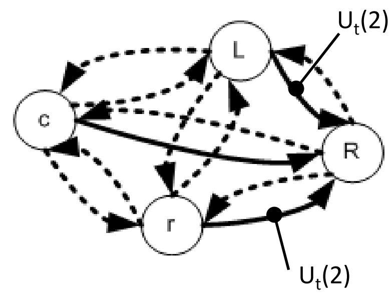
Model 4



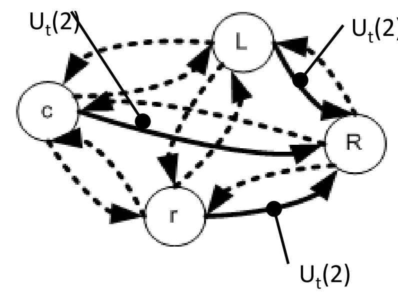
Model 5



Model 6

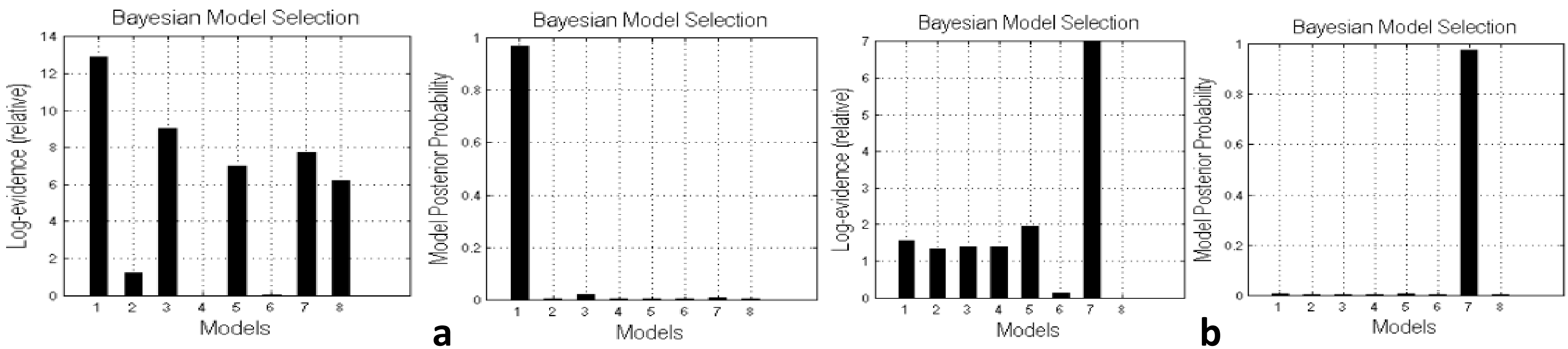


Model 7

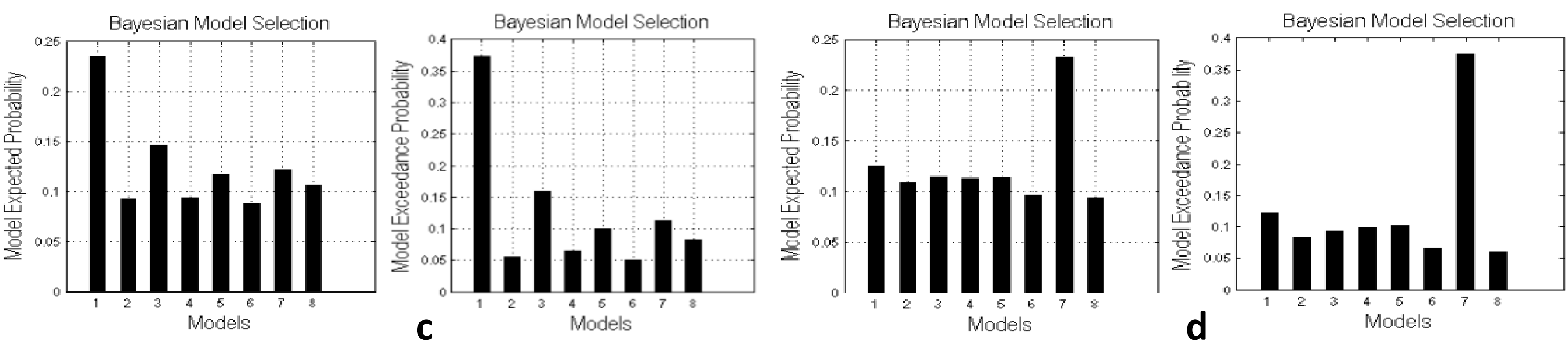


Model 8

Experiment → Results (Winning model)

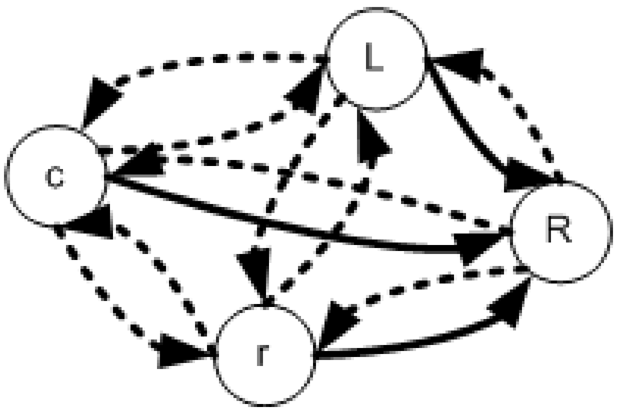


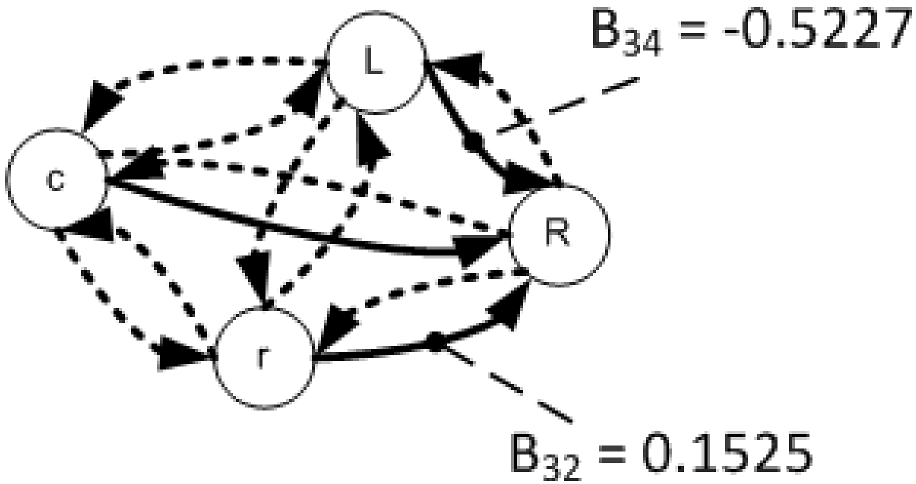
Fixed-effect model inference. Log-evidence and posterior probability for 8 models. a) long-allele individuals. b) short-allele individuals.



Random-effect model inference. Expected probability and exceedance probability for 8 models. c) long-allele individuals. d) short-allele individuals.

Experiment → Results (Winning model)





Model 1

Model 7

Experiment → Results (Winning model)

Endogenous parameters	Minimum		Maximum		Mean		SD		*KS** test	*t* test
	Long	Short	Long	Short	Long	Short	Long	Short	*p*-value~	*p*-value†,^
c → r	-0.0692	-0.0832	0.2845	0.1041	0.0252	0.0215	0.0926	0.0518	0.2463	0.3161
c → R	-0.1607	-0.1097	0.7273	0.5554	0.0911	0.1092	0.2240	0.1844	0.1249	0.4946
c → L	-0.0454	-0.3084	0.2348	0.3315	0.0427	0.0208	0.0759	0.1411	0.3404	0.3333
r → c	-0.3102	-0.5189	0.2091	0.6849	-0.0018	0.1002	0.1406	0.2806	0.1822	0.8039
r → R	-0.1236	-0.1769	0.1808	0.2532	0.0379	0.0529	0.0874	0.0919	0.8862	0.7480
r → L	-0.2824	-0.4271	0.6339	0.7046	0.0940	-0.0398	0.2527	0.2822	0.4380	0.5057
R → c	-0.3252	-0.4355	0.4170	0.4539	0.0694	-0.0049	0.2331	0.2768	0.5687	0.7275
R → r	-0.0783	-0.1333	0.3976	0.3180	0.0705	0.0669	0.1232	0.1093	0.9642	0.6401
R → L	-0.2470	0.0602	0.5200	0.6639	0.1887	0.3912	0.1839	0.1727	0.0145	0.0921
L → c	-0.0939	-0.4101	0.3608	0.6276	0.0917	0.0081	0.1492	0.2269	0.4381	0.5879
L → r	-0.0628	-0.0315	0.6950	0.3115	0.1031	0.0614	0.1975	0.0875	0.7083	0.2622
L → R	-0.0386	-0.4888	0.5586	0.2455	0.0988	-0.0430	0.1749	0.1946	0.0416	0.0194

* *K*olmogorov-*S*mirnov test
~ The null hypothesis is that the long- and short-allele are from the same continuous distribution
† The null hypothesis is that the long- and short-allele are independent random samples from normal distributions with equal means and unknown variances.
^ Averaged over 2000 permutations

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Conclusion

- We have observed a positive BOLD response in the rACC and left amygdala during processing of negative emotion in individuals who carry short-allele carriers. Whereas long-allele individuals produce a negative BOLD signal in the very same regions.
- Model 1 is the best model for long-allele and model 7 is the best model for short-allele.
- Due to the fact that short-allele is associated with less serotonin transporter, reuptake 5-HT from the synapse would be less, presumably resulting in more serotonin signaling. In other words, they respond as they were hyposerotonergic .

Selected Publications

- Stephan, K. E., Harrison, L. M., Kiebel, S. J. and David, O.,
  Analyzing effective connectivity with functional magnetic resonance imaging
  John Wiley & Sons, Cogn Sci, 1(3), 446–459 (2010)
- Kobiella, A., Reimold, M., Ulshofer, D. E., Ikonomidou, V. N., Vollmert, C., Vollstadt-Klein, C., Rietschel, M., Reischl, G., Heinz, A. and Smolka, M.,
  How the serotonin transporter 5-HTTLPR polymorphism influences amygdala function: the roles of in vivo serotonin transporter expression and amygdala structure
  Neuropharmacology, 59(6), 518-526 (2010)
- Beevers, C. G., Gibb, B. E., McGeary, J. E. and Miller, I. W.,
  Serotonin Transporter Genetic Variation and Biased Attention for Emotional Word Stimuli Among Psychiatric Inpatients
  NeuroImage 116(1), 208–212(2007).
- Stephan, K. E., Weiskopf, N., Drysdale, P. M., Robinson, P. A. and Friston, K. J.,
  Comparing hemodynamic models with DCM
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Thank You!

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