Introduction to Functional Neuroimaging and Analysis

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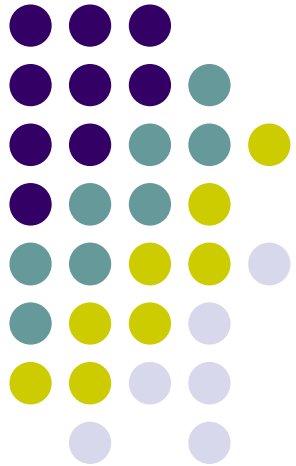
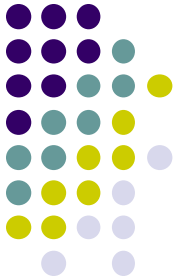




Introduction to Brain and Mind Sciences

Introduction to Functional Neuroimaging

Neuroimaging Data Analysis Methods

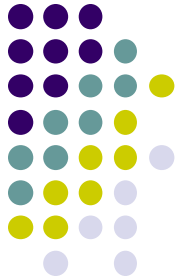
Yogic Neuroscience: Some Glimpses

Conclusions

Why Study the Mind?

- A discipline as old as the humanity
  - Foundation of the ancient Indian thought
  - What is real and what is unreal?
  - Death is the only certainty
  - Who am I?

Why Study the Mind?



- How does matter give rise to mind?
- Happiness – the basis of every human activity
- Psychiatric disorders – robust double digit growth
- Crime, violence, wars, recession
- If only we knew how to manage the mind !!

Studies of Brain

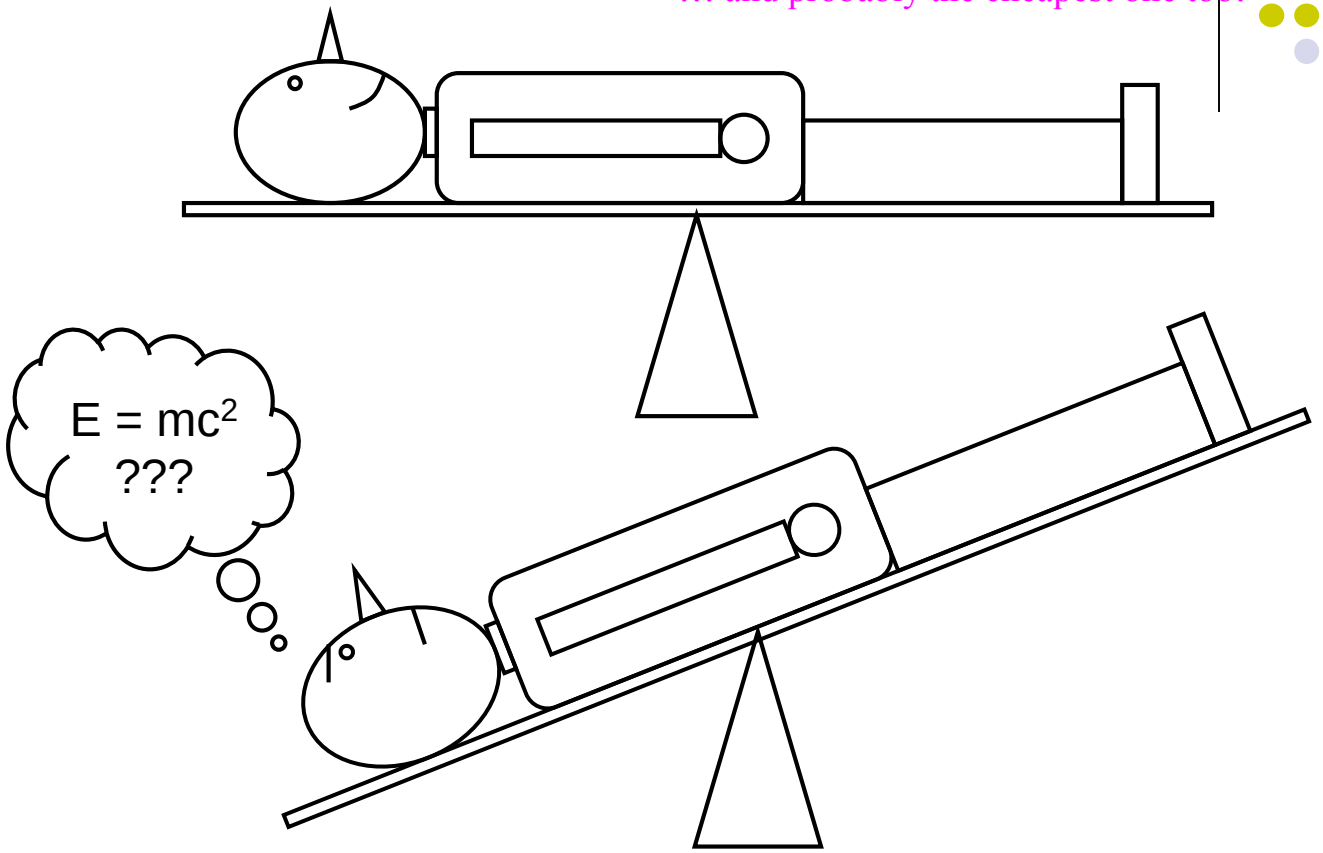
- Earlier studies were based on studying people with brain lesions or some other abnormality

- Now more and more studies use advanced imaging techniques

The First "Brain Imaging Experiment"

… and probably the cheapest one too!

Angelo Mosso
Italian physiologist
(1846-1910)



"[In Mosso's experiments] the subject to be observed lay on a delicately balanced table which could tip downward either at the head or at the foot if the weight of either end were increased. The moment emotional or intellectual activity began in the subject, down went the balance at the head-end, in consequence of the redistribution of blood in his system."

-- William James, *Principles of Psychology* (1890)

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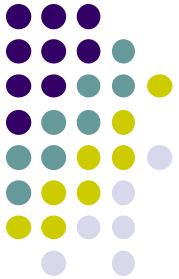
Ramachandran's TED Talk



- Phantom Limbs

The Homunculus Man

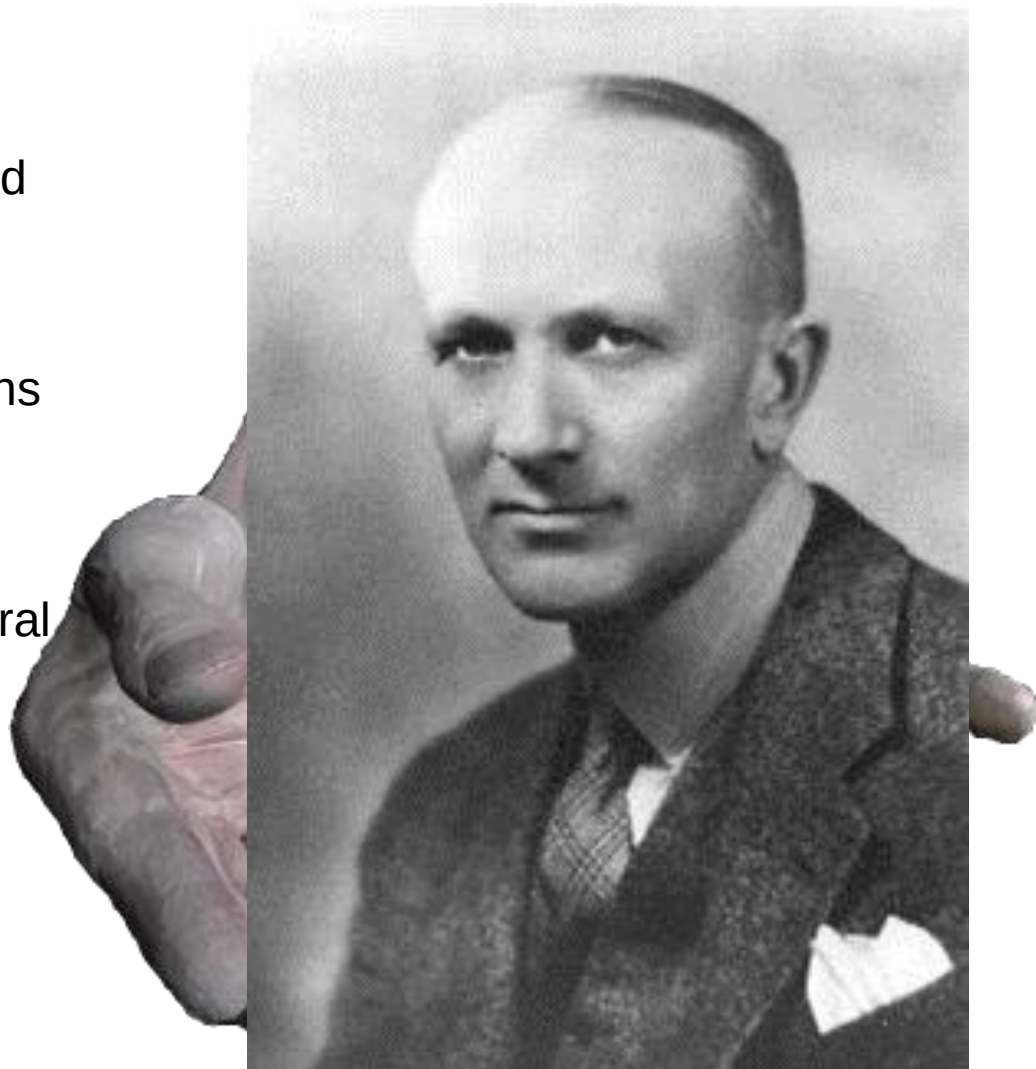
Wilder Graves Penfield
(January 26, 1891 – April 5, 1976)
A pioneering neurosurgeon once dubbed "the greatest living Canadian“.

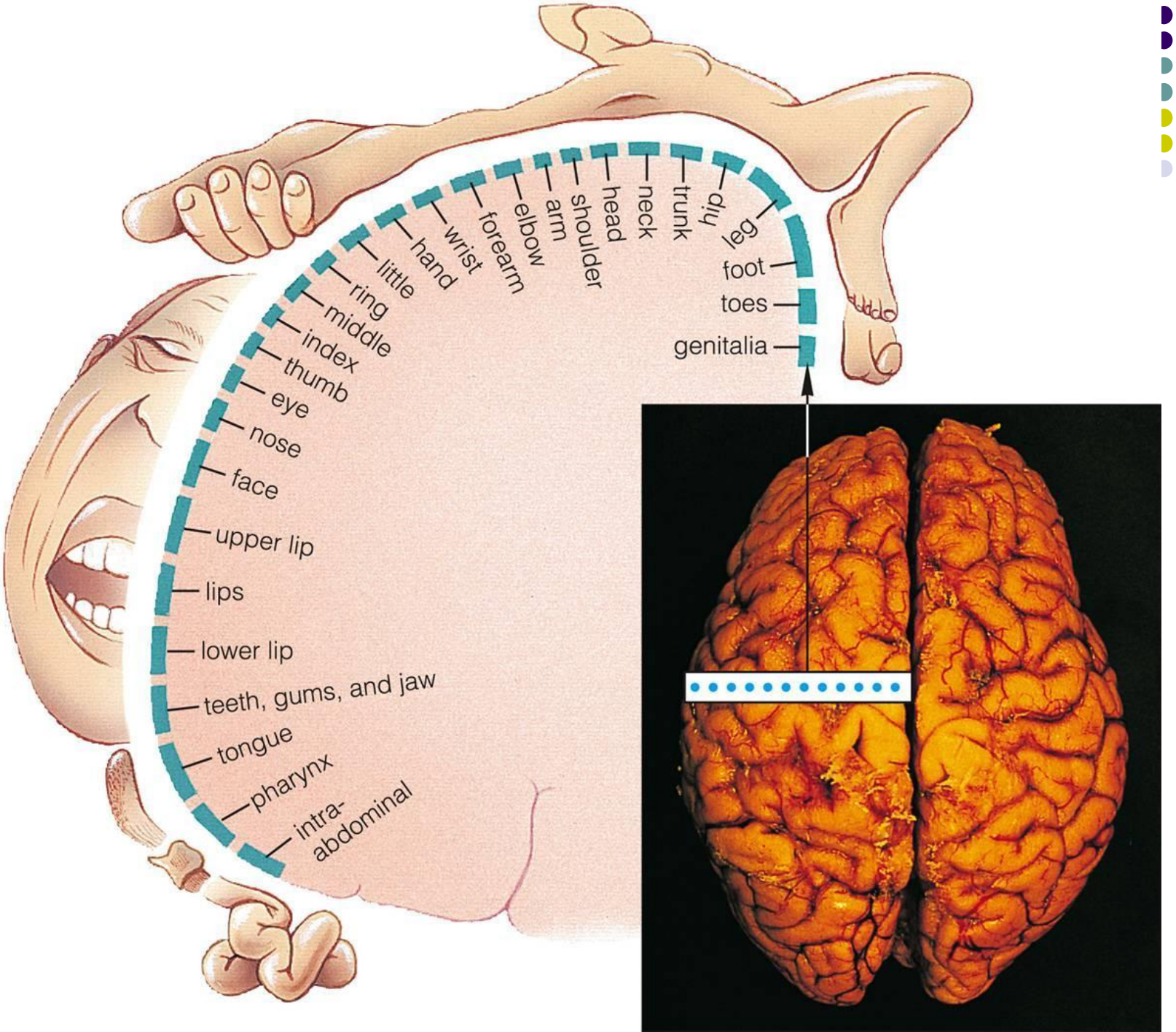
Treating Epilepsy by destroying neurons

Neural stimulation

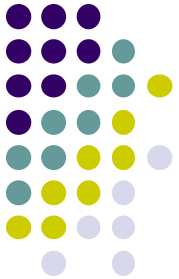
Hallucinations while stimulating temporal cortex

Déjà vu
(The Interpretive Cortex)

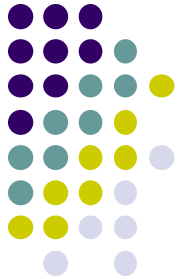



little
ring
middle
index
thumb
eye
nose
face
upper lip
lips
lower lip
teeth, gums, and jaw
tongue
pharynx
intra-abdominal
hand
wrist
forearm
elbow
arm
shoulder
head
neck
trunk
hip
leg
foot
toes
genitalia

Nancy Kanwisher's Ted Talk



- On Functional MRI (or fMRI)



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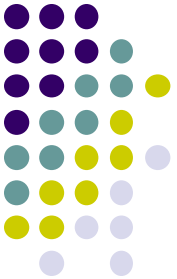
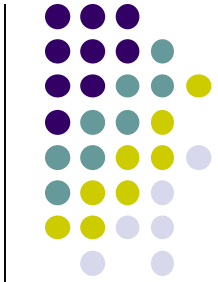
Brain Imaging



- Brain imaging can be separated into two major categories:
  - Structural brain imaging
  - Functional brain imaging
- There exist a number of different modalities for performing each category.

Slide adapted from: A course on Statistical Analysis of fMRI Data by Martin Lindquist, at www.coursera.org

Structural Brain Imaging



- Structural brain imaging deals with the study of brain structure and the diagnosis of disease and injury.
- Modalities include:
  - computed axial tomography (CAT),
  - magnetic resonance imaging (MRI), and
  - positron emission tomography (PET).

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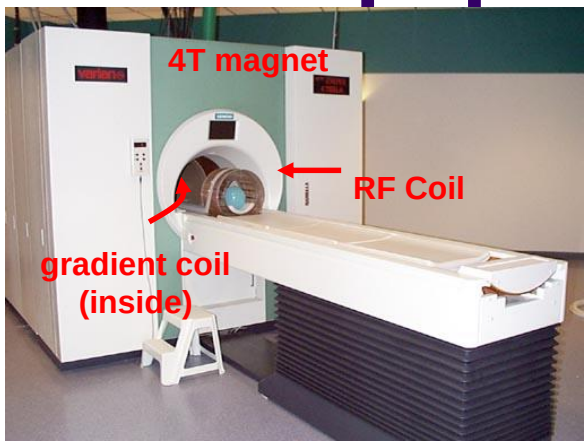
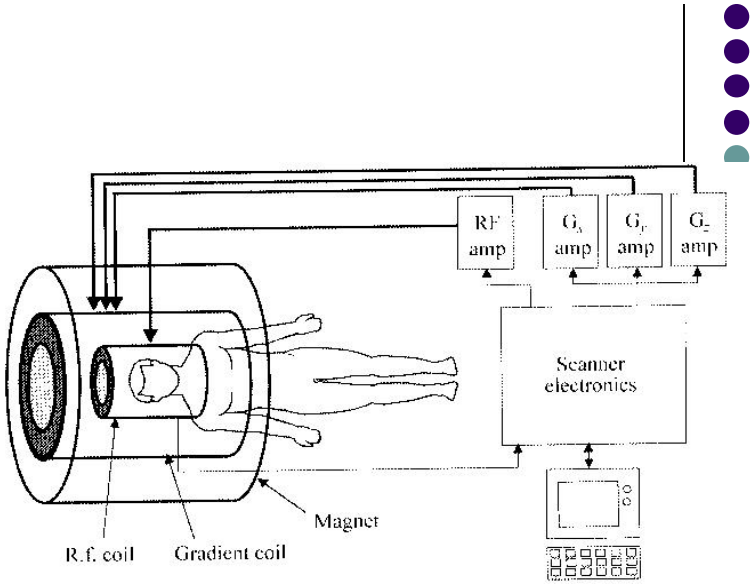
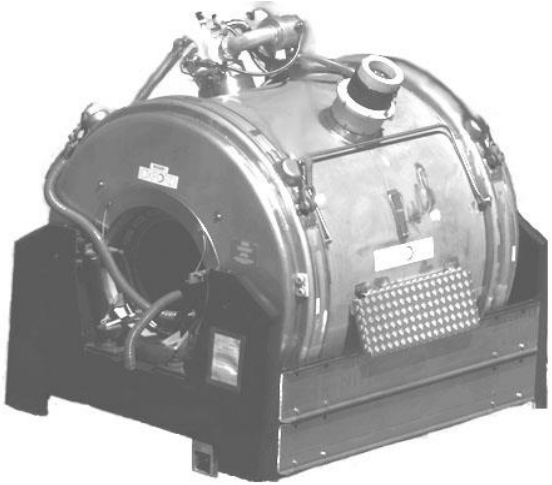
MRI Equipment



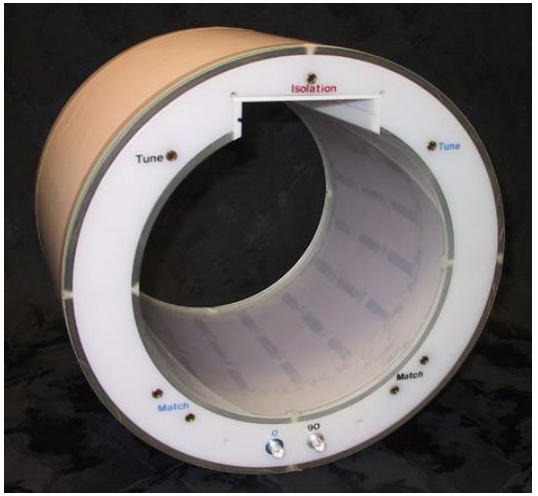


Magnet



Gradient Coil

RF Coil



Source for Photos: Joe Gati

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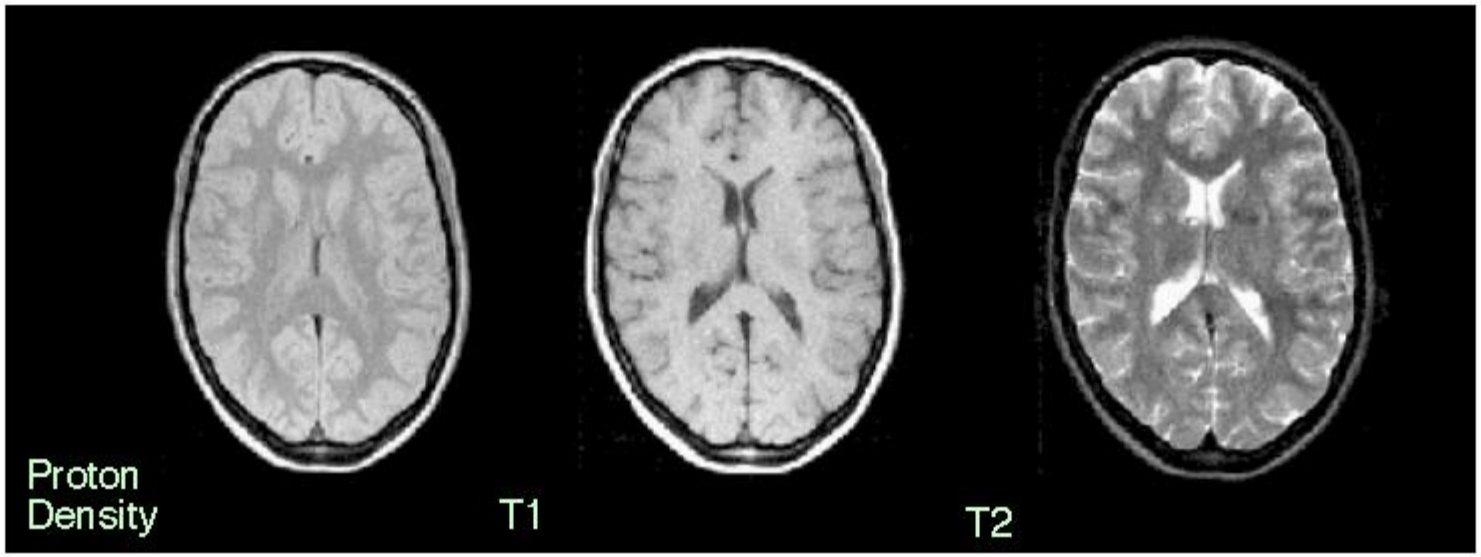
MRI



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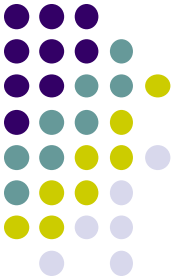
Functional Brain Imaging



- Functional brain imaging can be used to study both cognitive and affective processes.
- Modalities include:
  - positron emission tomography (PET),
  - functional magnetic resonance imaging (fMRI),
  - electroencephalography (EEG), and
  - magnetoencephalography (MEG).

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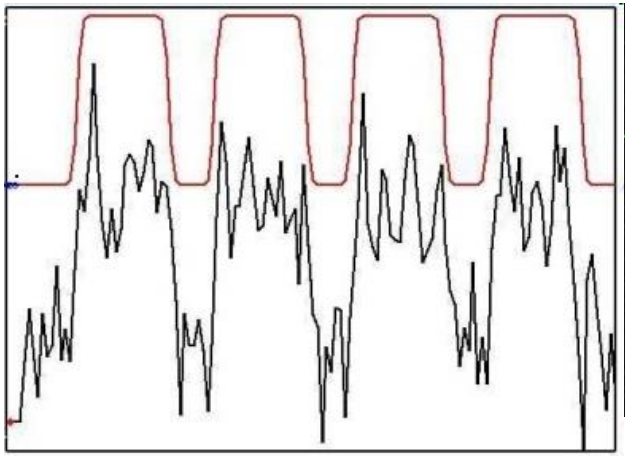
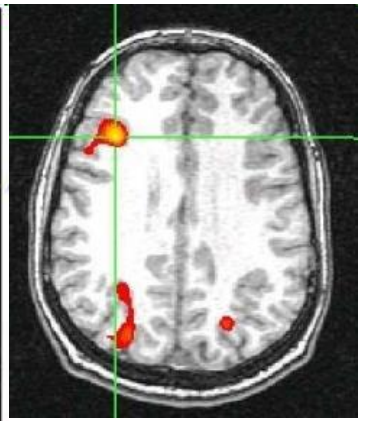
Functional MRI

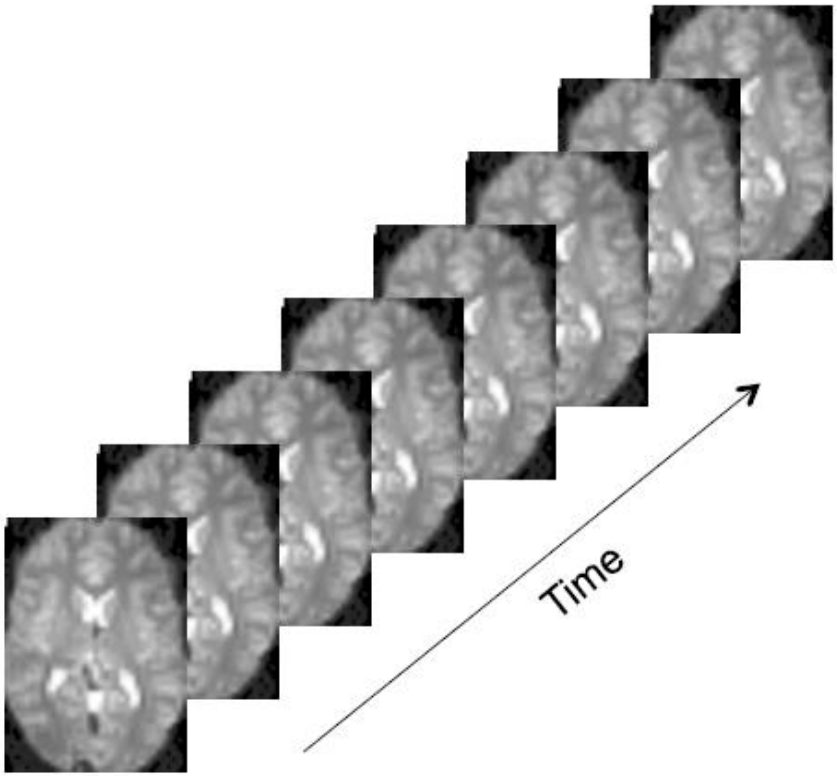
- A 3D movie of brain
- Indirect measure of brain activation
- BOLD response (blood oxygenation level dependent)
- Based on magnetic field inhomogeneities created by blood flow





Figures, courtesy Applied Neuro MRI Lab, University of Wisconsin Madison

fMRI



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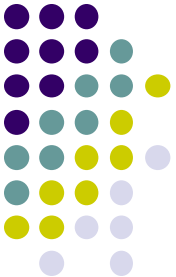
Functional MRI



- Functional magnetic resonance imaging (fMRI) is a non-invasive technique for studying brain activity.
- During the course of an fMRI experiment, a series of brain images are acquired while the subject performs a set of tasks.
- Changes in the measured signal between individual images are used to make inferences regarding task-related activations in the brain.

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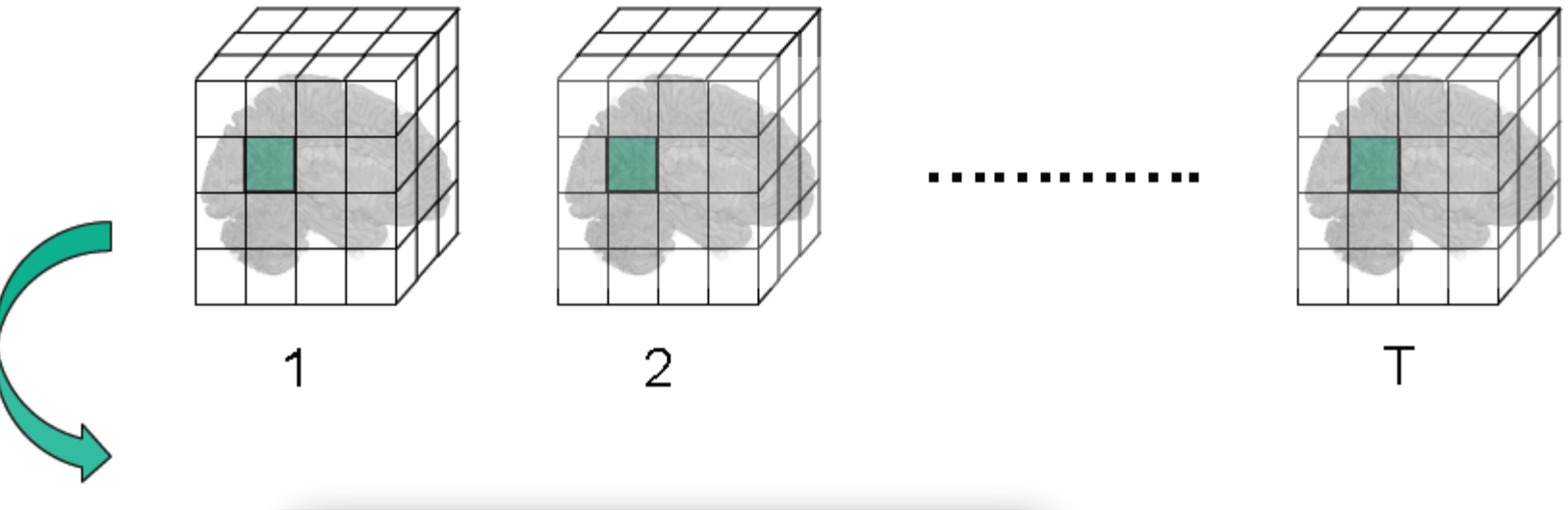
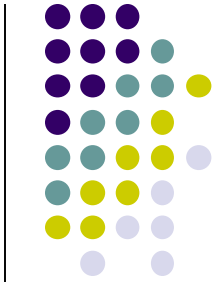
fMRI Data

- Tracking the intensity over time gives us a time series.



BOLD fMRI



- The most common approach towards fMRI uses the Blood Oxygenation Level Dependent (BOLD) contrast.
- BOLD fMRI measures the ratio of oxygenated to deoxygenated hemoglobin in the blood.
- It is important to note that BOLD fMRI doesn't measure neuronal activity directly, instead it measures the metabolic demands (oxygen consumption) of active neurons.

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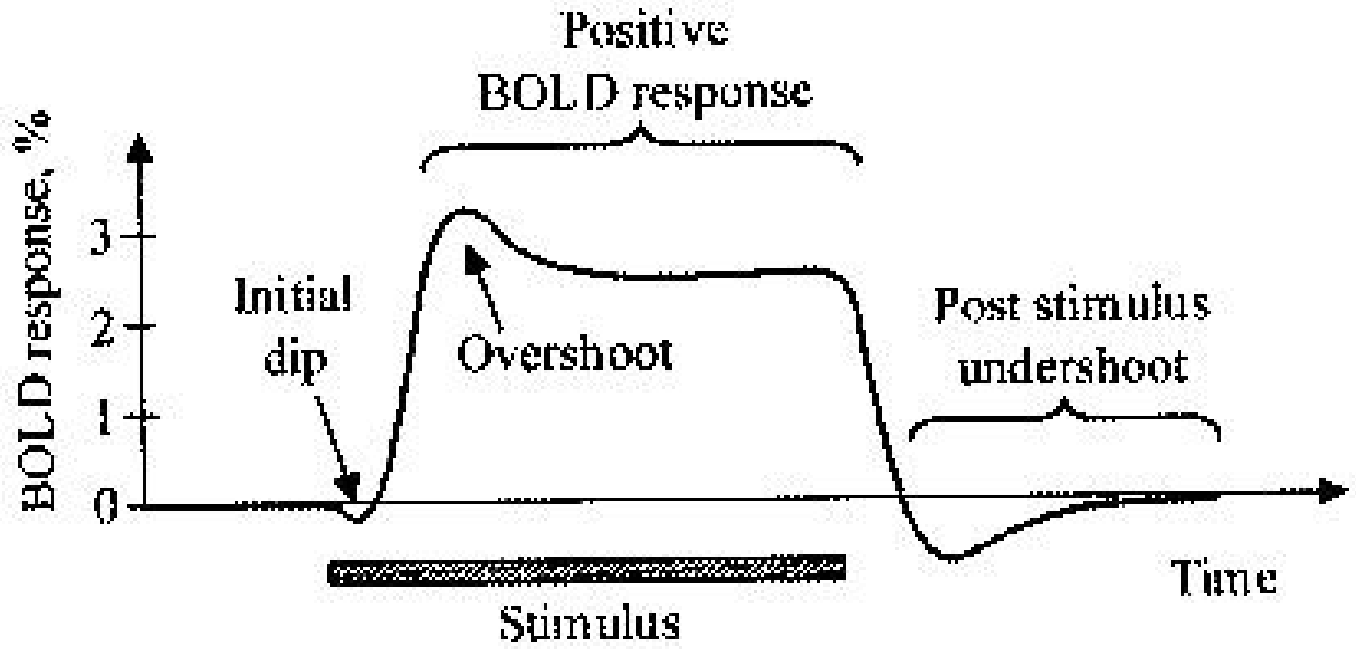
BOLD Time Course



- Significant variability observed
  - Across subjects
  - Across brain regions
  - Across experiments
  - Across trials

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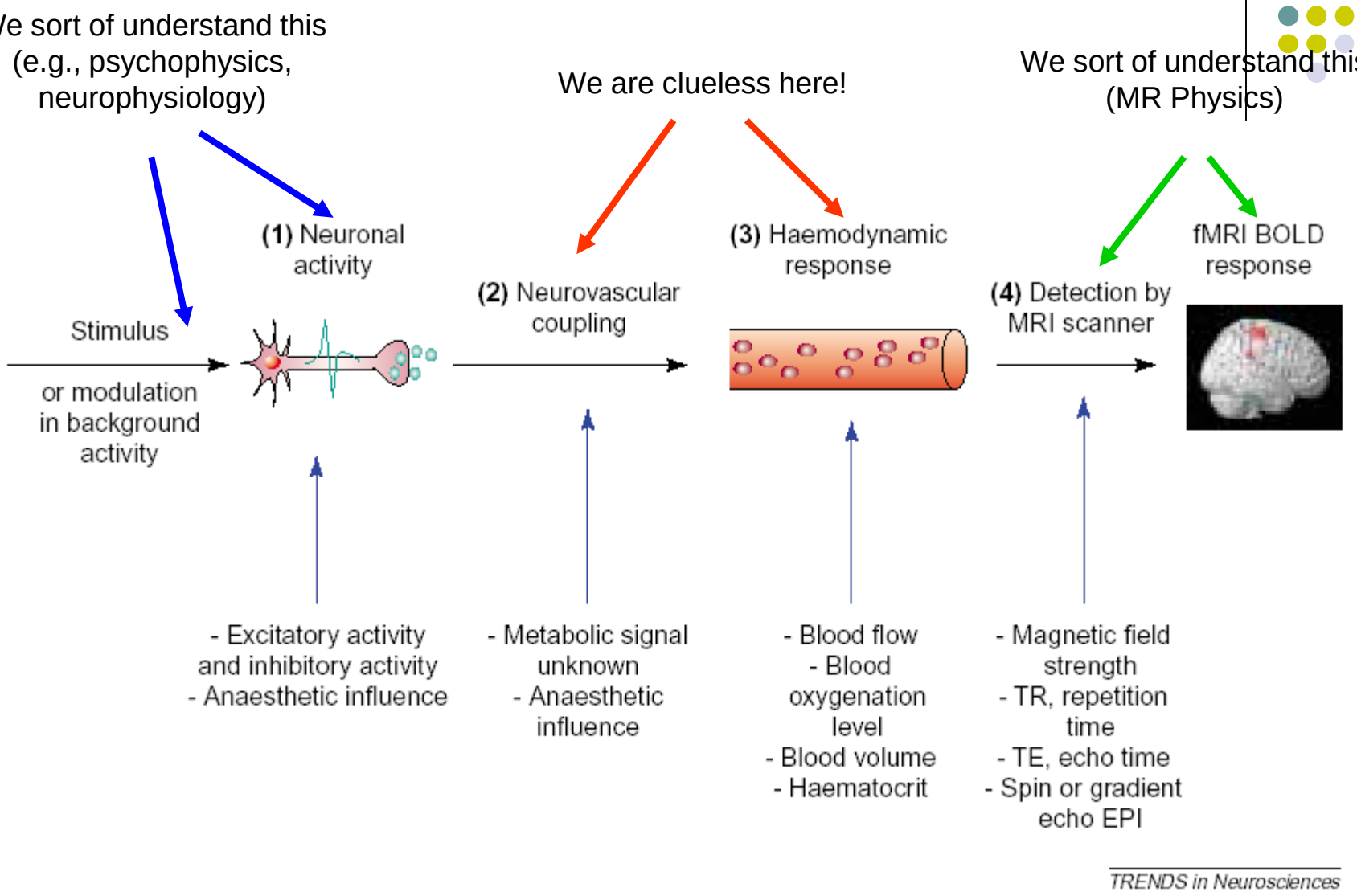
Stimulus to BOLD: Summary



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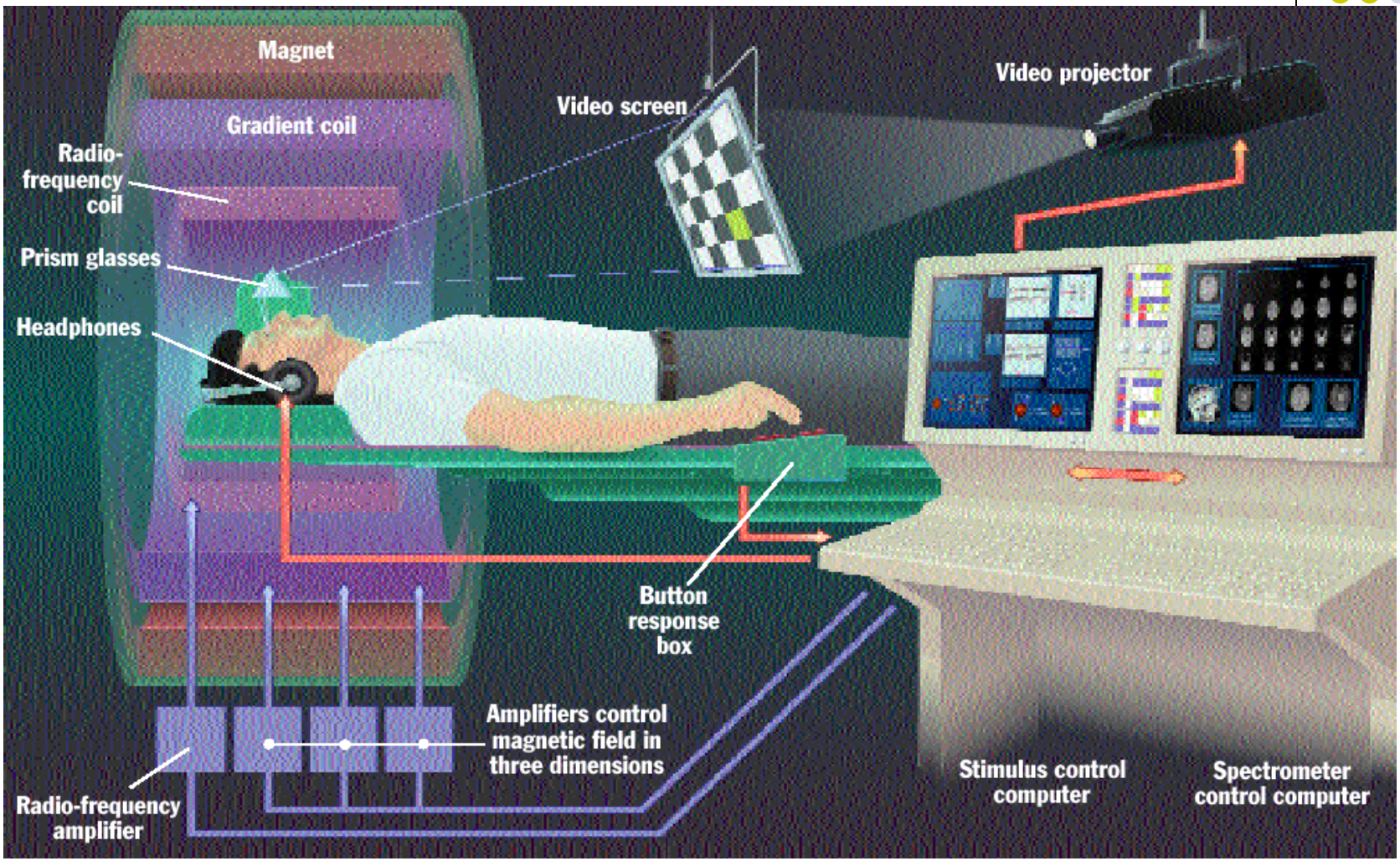
Typical fMRI Setup



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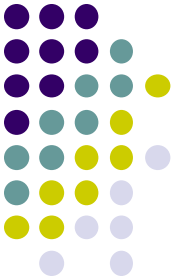
fMRI Data



- fMRI data analysis is a massive data problem.
- Each brain volume consists of ~100,000 voxel measurements.
- Each experiment consists of hundreds of brain volumes.
- Each experiment may be repeated for multiple subjects
  - (e.g.,10–40) to facilitate population inference.
- The total amount of data that needs to be analyzed is staggering.

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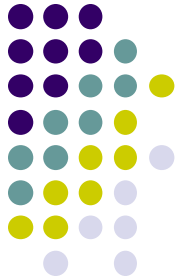

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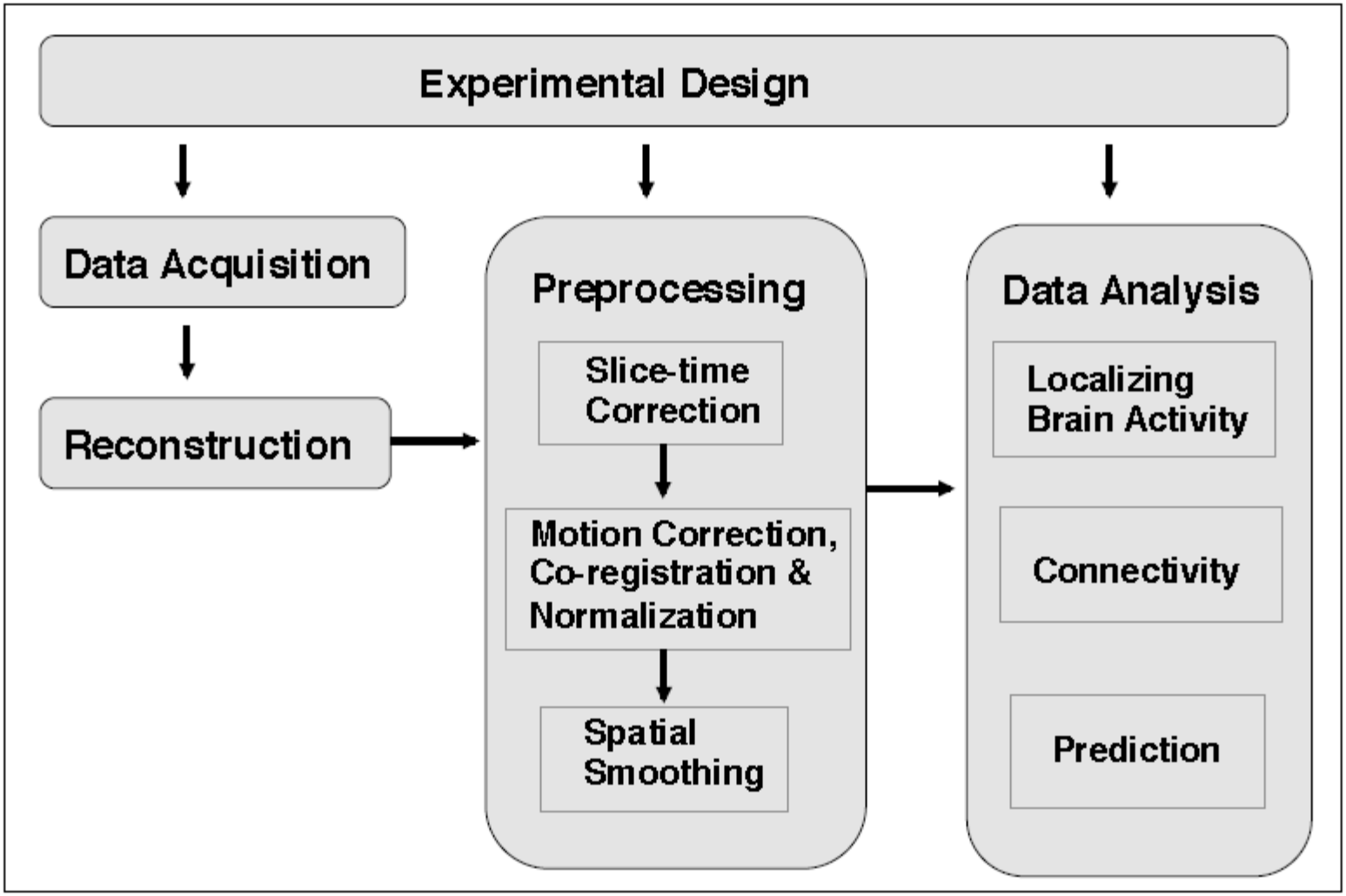
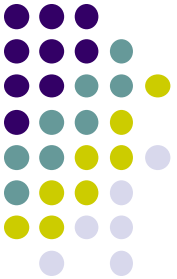
Data Processing Pipeline



Neuroimaging Data Analysis Methods



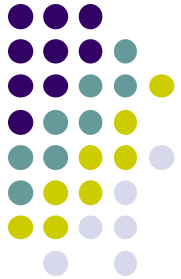
General Linear Model

Functional Connectivity Analysis

Prediction Using fMRI

Decoding Brain Dynamics Using fMRI

Experimental Design



- The goals of experimental design are to:
  - Induce subjects to perform or experience the psychological states you are interested in studying.
  - Effectively detect brain signals related to those psychological states.
- Not always so easy in practice.
- Both psychological and statistical considerations need to be taken into consideration.

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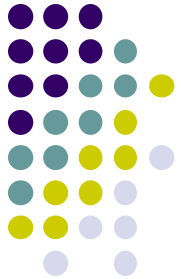
Experimental Design



- Properties of the BOLD signal conspire to make experimental design difficult.
  - The signal is both weak and noisy.
  - It is not an absolute measure of neuronal activity.
  - Need to use contrasts and repetitions to be able to detect effects of interest.
- Compare the task of interest with some control task where subjects are either at rest or performing a simple baseline task.
  - Repeat the tasks as often as possible.

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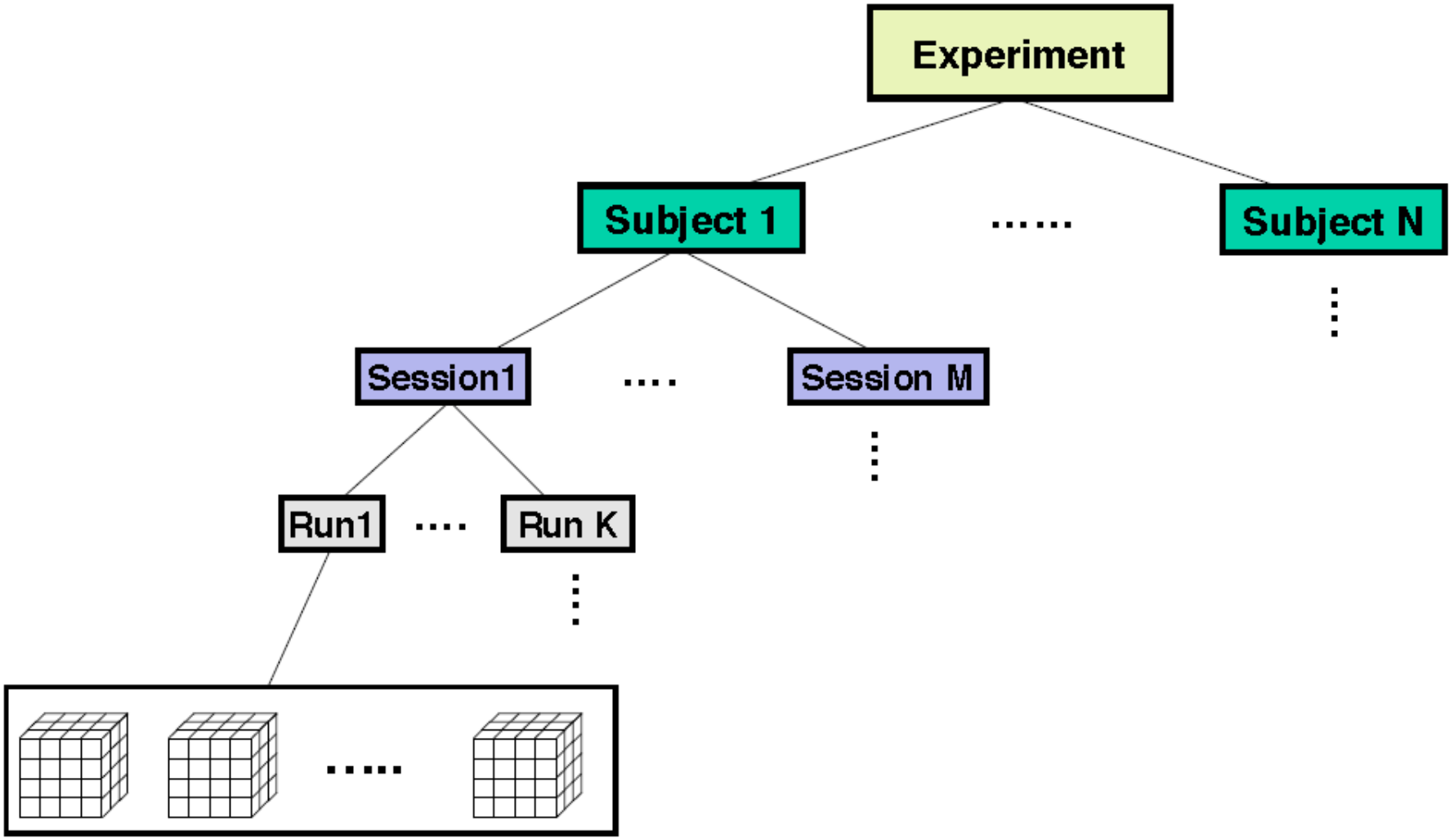
Hierarchical Structure



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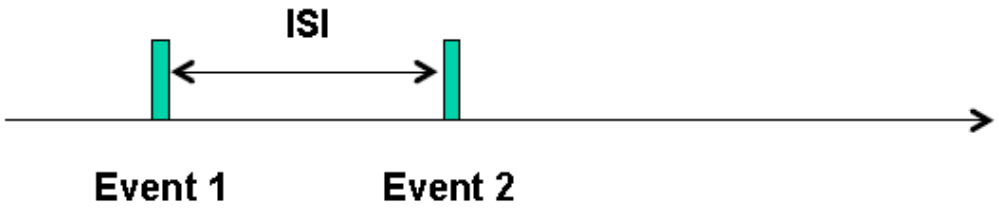
Definitions

- An event is a single experimental manipulation.
- The inter-stimulus interval (ISI) is the time between two successive stimuli.



- A block is a time interval that contains events from a single condition.

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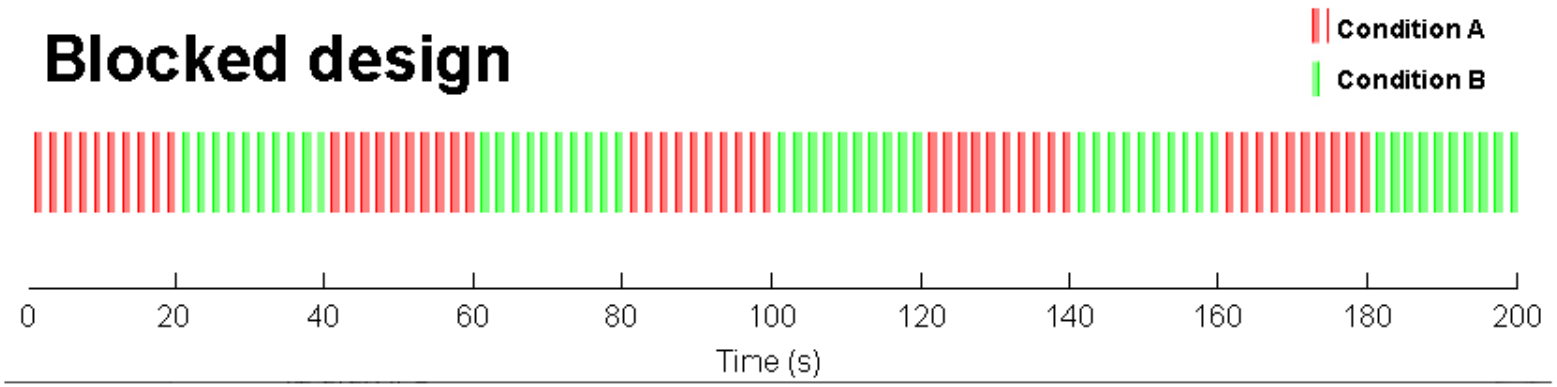
Experimental Design

- Blocked design: Similar events are grouped



- High statistical power to detect activation and robust to uncertainties in the shape of HRF.

- Can't directly estimate features of the HRF.

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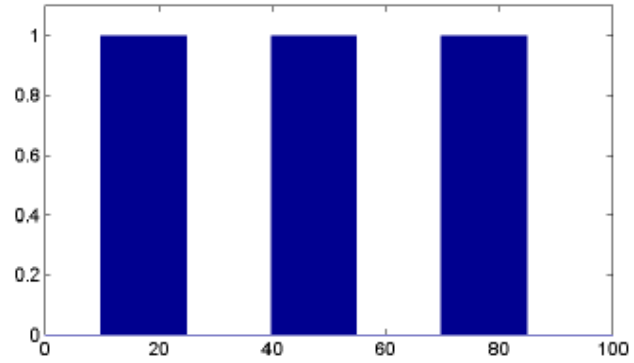
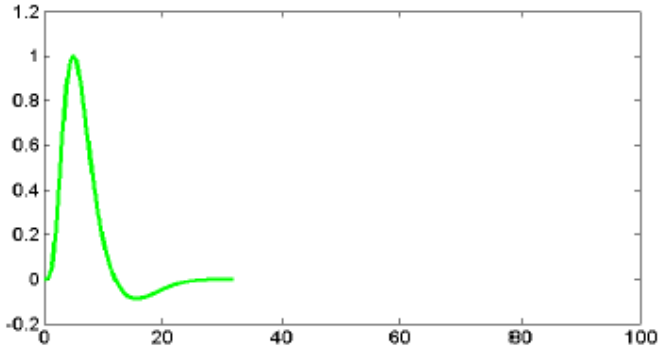
Block Design

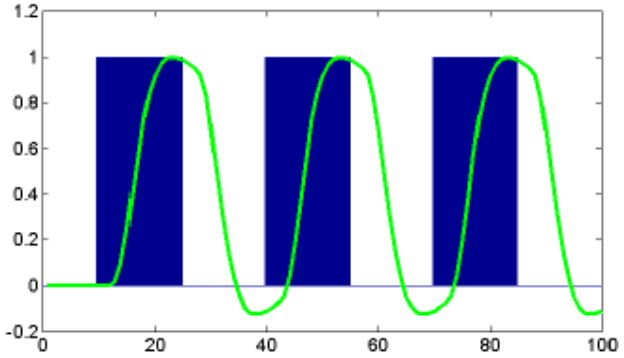
Experimental Stimulus Function



Hemodynamic Response Function



Predicted Response



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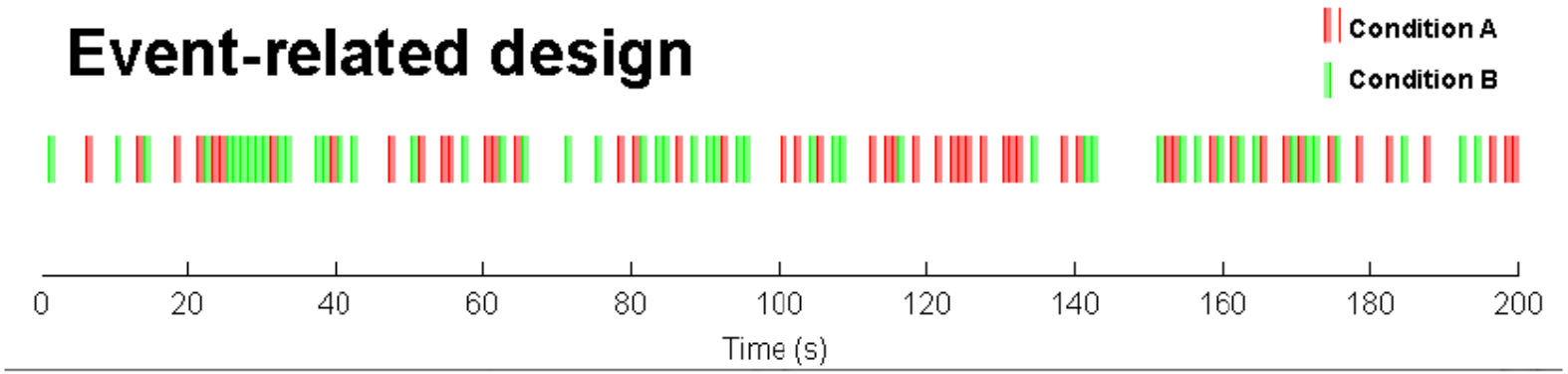
Experimental Design

- Event-related design: Events are mixed



- Allows for the estimation of features of the HRF.

- Decreased power to detect activation.

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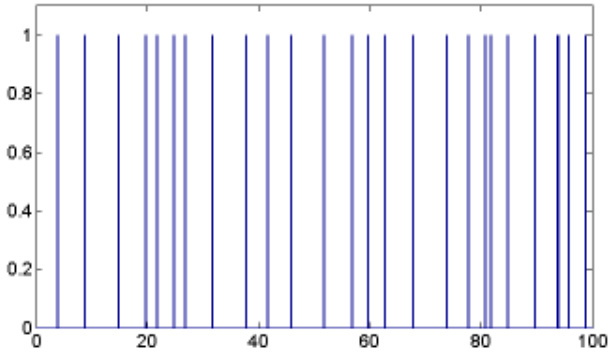
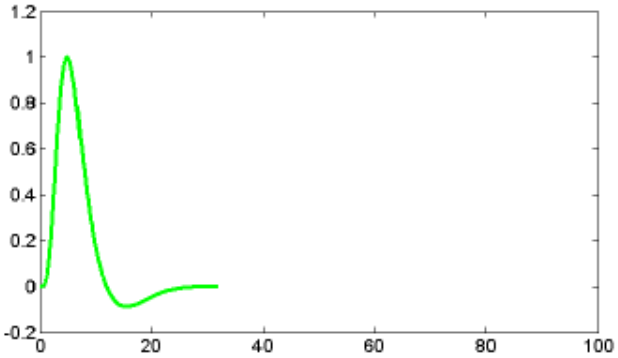
Event-Related

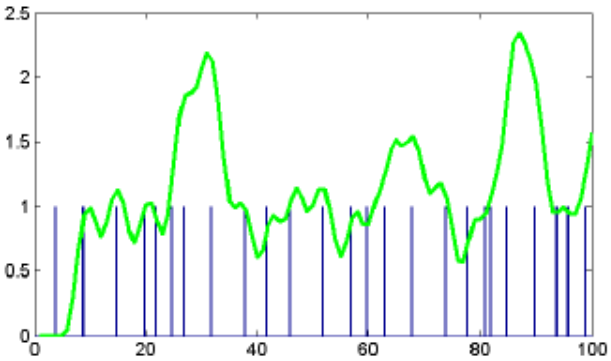
Experimental Stimulus Function



Hemodynamic Response Function



Predicted Response



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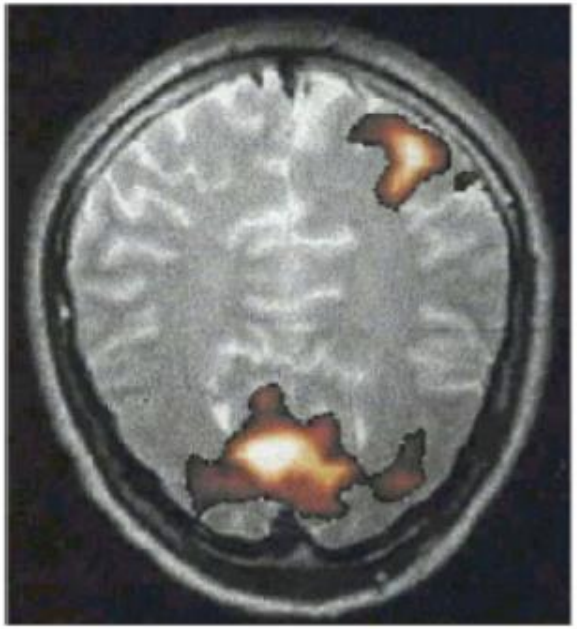
Human Brain Mapping

- The most common use of fMRI to date has been to localize areas of the brain that activate in response to a certain task.

- These types of human brain mapping studies are necessary for the development of biomarkers and increasing our understanding of brain function.



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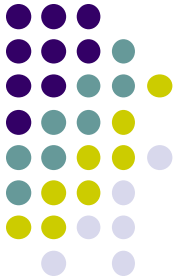
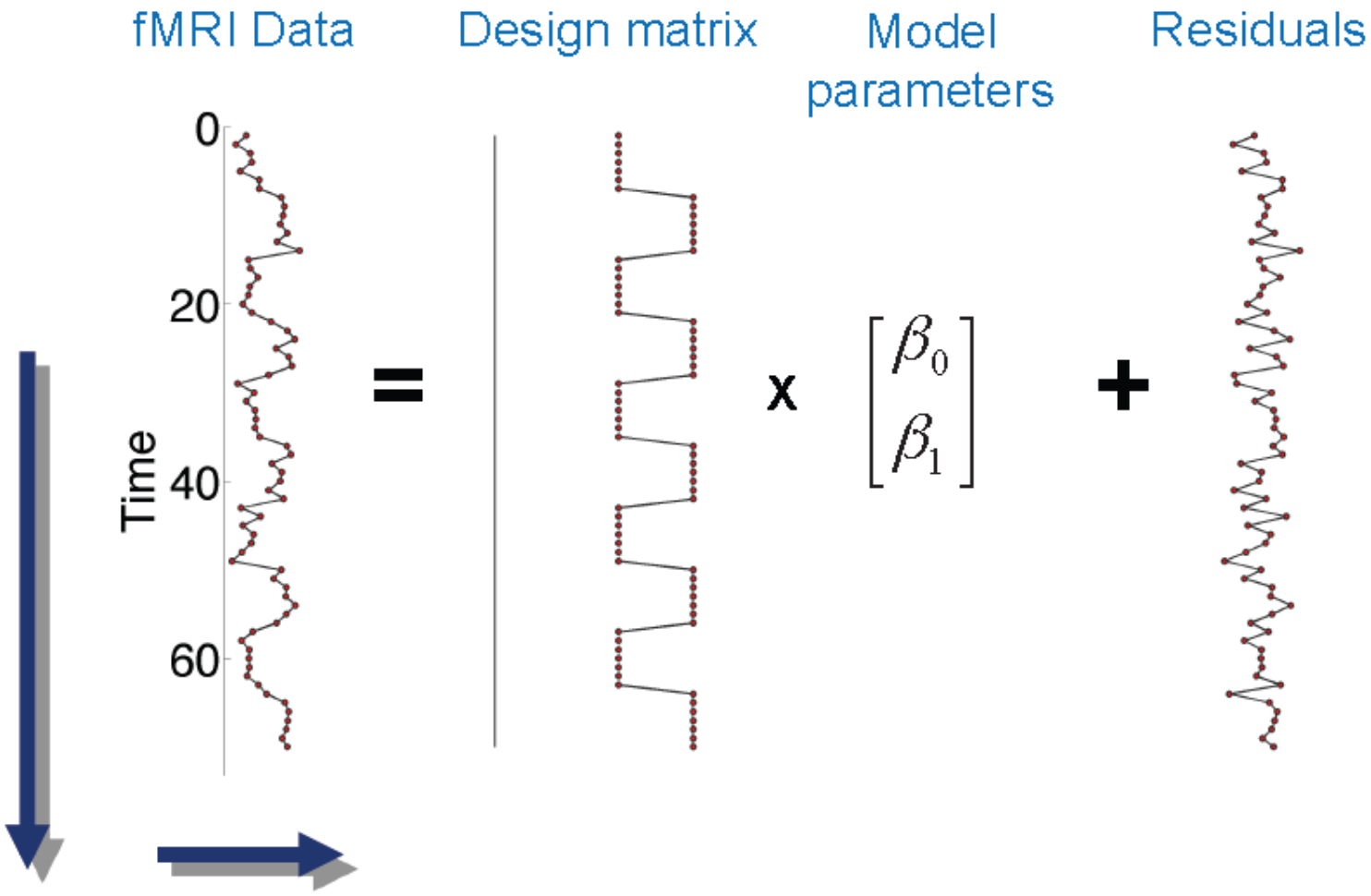
General Linear Model



- The general linear model (GLM) approach treats the data as a linear combination of model functions (predictors) plus noise (error).
- The model functions are assumed to have known shapes, but their amplitudes are unknown and need to be estimated.
- The GLM framework encompasses many of the commonly used techniques in fMRI data analysis (and data analysis more generally).

Slide adapted from: A course on Statistical Analysis of fMRI Data by Martin Lindquist, at www.coursera.org



Slide adapted from: A course on Statistical Analysis of fMRI Data by Martin Lindquist, at www.coursera.org

GLM

A standard GLM can be written:

$$\mathbf{Y} = \mathbf{X}\boldsymbol{\beta} + \boldsymbol{\varepsilon} \qquad \boldsymbol{\varepsilon} \sim N(\mathbf{0}, \mathbf{V})$$

where

$$\begin{bmatrix} Y_1 \\ Y_2 \\ \vdots \\ Y_n \end{bmatrix} = \begin{bmatrix} 1 & X_{11} & \cdots & X_{1p} \\ 1 & X_{21} & \cdots & X_{2p} \\ \vdots & \vdots & & \vdots \\ 1 & X_{np} & \cdots & X_{np} \end{bmatrix} \times \begin{bmatrix} \beta_0 \\ \beta_1 \\ \vdots \\ \beta_p \end{bmatrix} + \begin{bmatrix} \varepsilon_1 \\ \varepsilon_2 \\ \vdots \\ \varepsilon_n \end{bmatrix}$$

fMRI Data

Design matrix

Regression coefficients

Noise

V is the covariance matrix whose format depends on the noise model.

The quality of the model depends on our choice of X and V.

Slide adapted from: A course on Statistical Analysis of fMRI Data by Martin Lindquist, at www.coursera.org

Estimation

- If ε is i.i.d., then Ordinary Least Square (OLS) estimate is optimal

model → estimate

$$\mathbf{Y} = \mathbf{X}\boldsymbol{\beta} + \boldsymbol{\varepsilon} \longrightarrow \hat{\boldsymbol{\beta}} = (\mathbf{X}'\mathbf{X})^{-1}\mathbf{X}'\mathbf{Y}$$

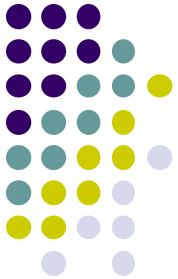
- If $\mathrm{Var}(\varepsilon) = \mathbf{V}\sigma^2 \neq \mathbf{I}\sigma^2$, then Generalized Least Squares (GLS) estimate is optimal

model → estimate

$$\mathbf{Y} = \mathbf{X}\boldsymbol{\beta} + \boldsymbol{\varepsilon} \longrightarrow \hat{\boldsymbol{\beta}} = (\mathbf{X}'\mathbf{V}^{-1}\mathbf{X})^{-1}\mathbf{X}'\mathbf{V}^{-1}\mathbf{Y}$$

Slide adapted from: A course on Statistical Analysis of fMRI Data by Martin Lindquist, at www.coursera.org

Massive Univariate Approach

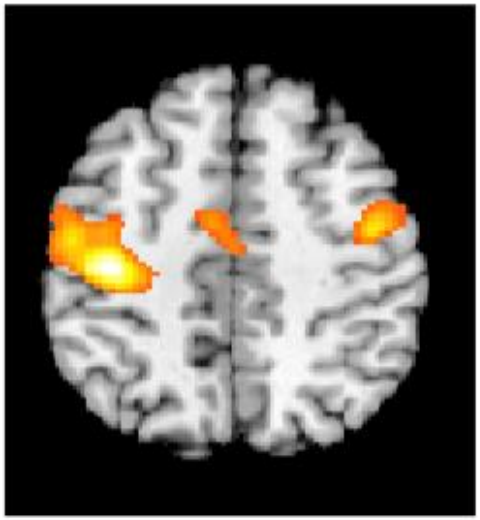


- Typically analysis is performed by constructing a separate model at each voxel
  - The ‘massive univariate approach’.
  - Assumes an improbable independence between voxel pairs……
- Typically dependencies between voxels are dealt with later using random field theory, which makes assumptions about the spatial dependencies between voxels.

Slide adapted from: A course on Statistical Analysis of fMRI Data by Martin Lindquist, at www.coursera.org

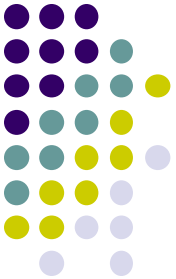
Localizing Activation

3. Choose an appropriate threshold for determining statistical significance.



Statistical parametric map: Each significant voxel is color-coded according to the size of its p-value.

Neuroimaging Data Analysis Methods



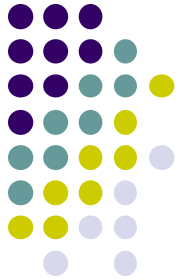
General Linear Model

Functional Connectivity Analysis

Prediction Using fMRI

Decoding Brain Dynamics Using fMRI

Brain Connectivity



- Human brain mapping has primarily been used to construct maps indicating regions of the brain that are activated by certain tasks.
- Recently, there has been an increased interest in augmenting this type of analysis with connectivity studies.
- These studies seek to describe how brain regions interact and how these interactions depend on experimental conditions and behavioral measures.

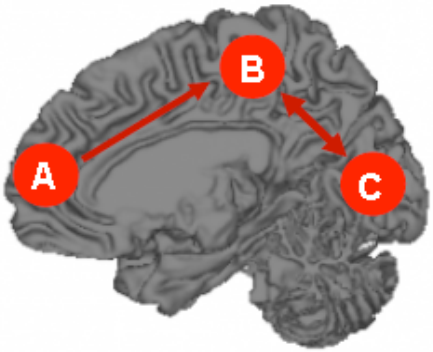
Slide adapted from: A course on Statistical Analysis of fMRI Data by Martin Lindquist, at www.coursera.org

Brain Networks

- It has become common practice to talk about brain networks, i.e. sets of interconnected brain regions with information transfer among regions.

- To construct a network:
  - Define a set of nodes (e.g., ROIs)
  - Estimate the set of connections, or edges, between the nodes.

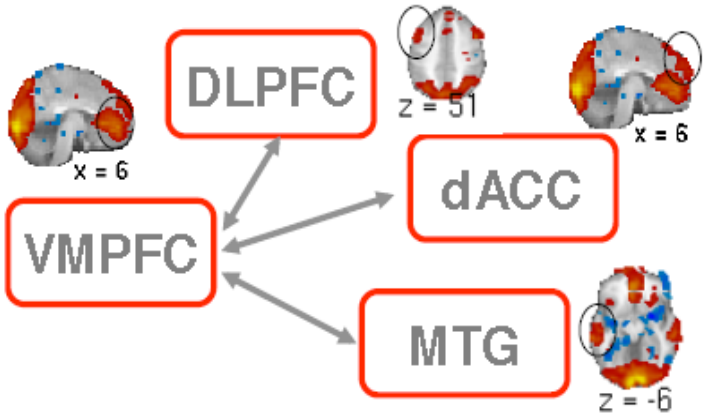
	A	B	C
A	0	1	0
B	0	0	1
C	0	1	0



Slide adapted from: A course on Statistical Analysis of fMRI Data by Martin Lindquist, at www.coursera.org

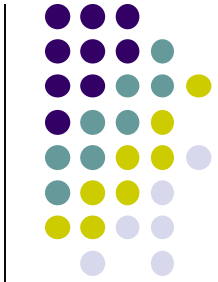
Brain Connectivity

- Functional Connectivity
  - Undirected association between two or more fMRI time series and/or performance and physiological variables.
  - Makes statements about the structure of relationships among brain regions.
  - Usually makes no assumptions about the underlying biology.



Slide adapted from: A course on Statistical Analysis of fMRI Data by Martin Lindquist, at www.coursera.org

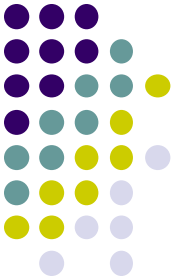
Functional Connectivity



- Methods include:
  - Seed analysis
  - Inverse covariance methods
  - Undirected and directed network analysis
  - Multivariate decomposition methods
    - Principle Components Analysis
    - Independent Components Analysis
    - Partial Least Squares

Slide adapted from: A course on Statistical Analysis of fMRI Data by Martin Lindquist, at www.coursera.org

Neuroimaging Data Analysis Methods



General Linear Model

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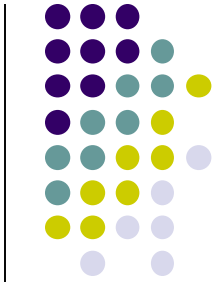
Prediction Using fMRI

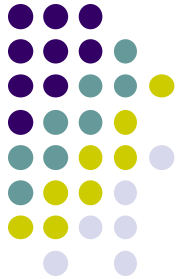
Decoding Brain Dynamics Using fMRI

Classification and Prediction



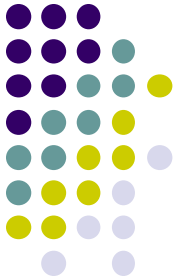
- There is a growing interest in using fMRI data for classification of mental disorders and predicting the early onset of disease.
- In addition, there is interest in developing methods for predicting stimuli directly from functional data.
- This opens the possibility of inferring information about subjective human experience directly from brain activation patterns.

Machine Learning



- Predicting brain states is challenging and requires the application of novel statistical and machine learning techniques.
- Various techniques have successfully been applied to fMRI data in which a classifier is trained to discriminate between different brain states and then used to predict the brain states in a new set of fMRI data.

MVPA

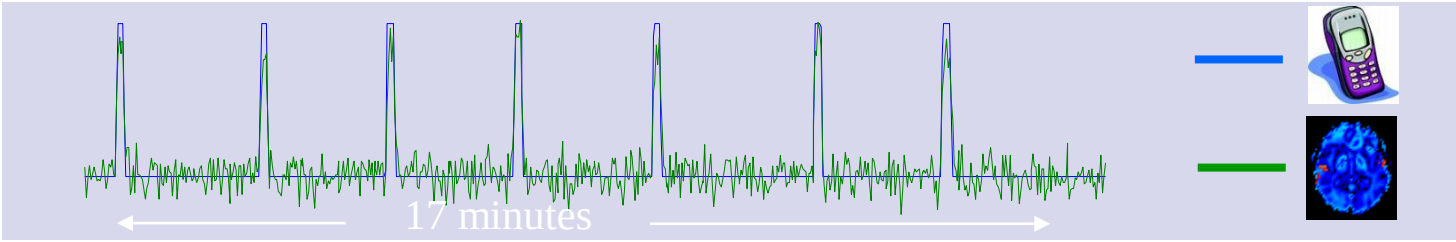


- The application of machine learning methods to fMRI data is often referred to as multi-voxel pattern analysis (MVPA)
- Instead of focusing on single voxels, MVPA uses pattern-classification algorithms applied to multiple voxels to decode the patterns of activity.

PBAIC 2007

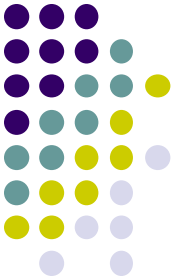
Worldwide open competition

- Learn mapping fMRI↔features in 2 runs
- Predict 24 features for 3rd run based on fMRI
- 3 subjects
- Subjective features:
  - Annoyance
  - Arousal
  - Anxiety
- Objective features:
  - Dog
  - Faces
  - Instructions
  - Correct hits
- 50+ final submissions




24

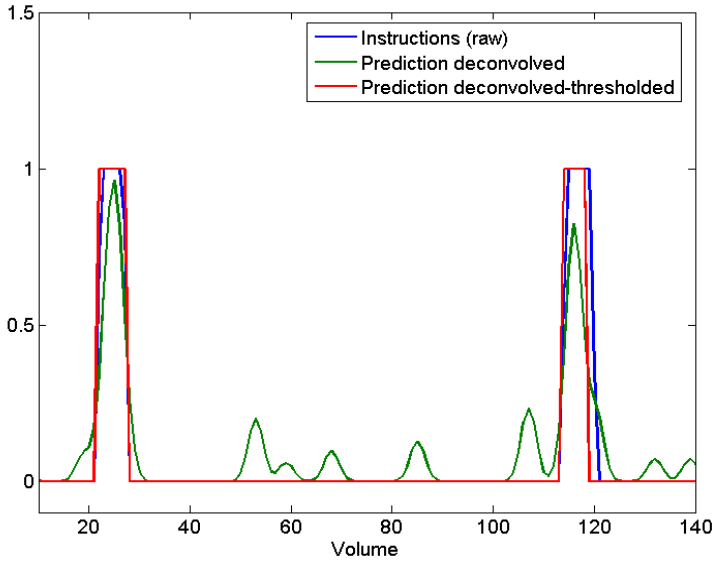
Elastic Net

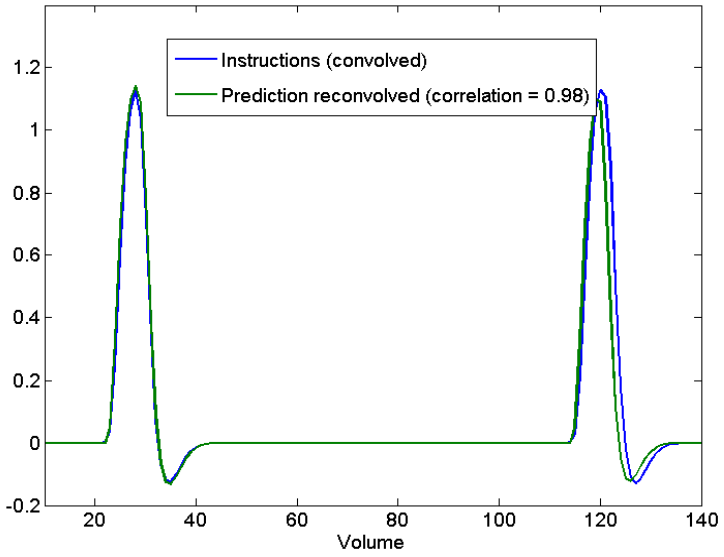


- Accurate prediction when vars >> data points
  - 30K+ variables, at most 1K points
- Interpretability
- Constraint regressors

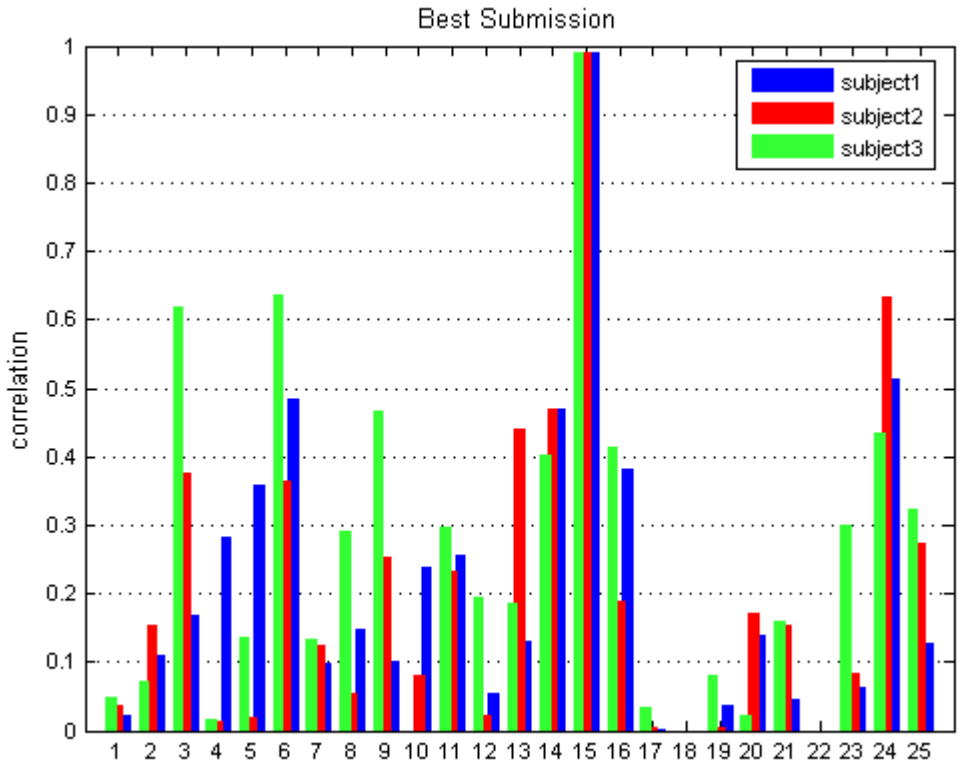
$$L_{\lambda_1,\lambda_2}(\beta) = ||\boldsymbol{y}-\mathbf{X}\beta||_2^2 + \lambda_1||\beta||_1 + \lambda_2||\beta||_2^2$$

Post-processing





Predictions



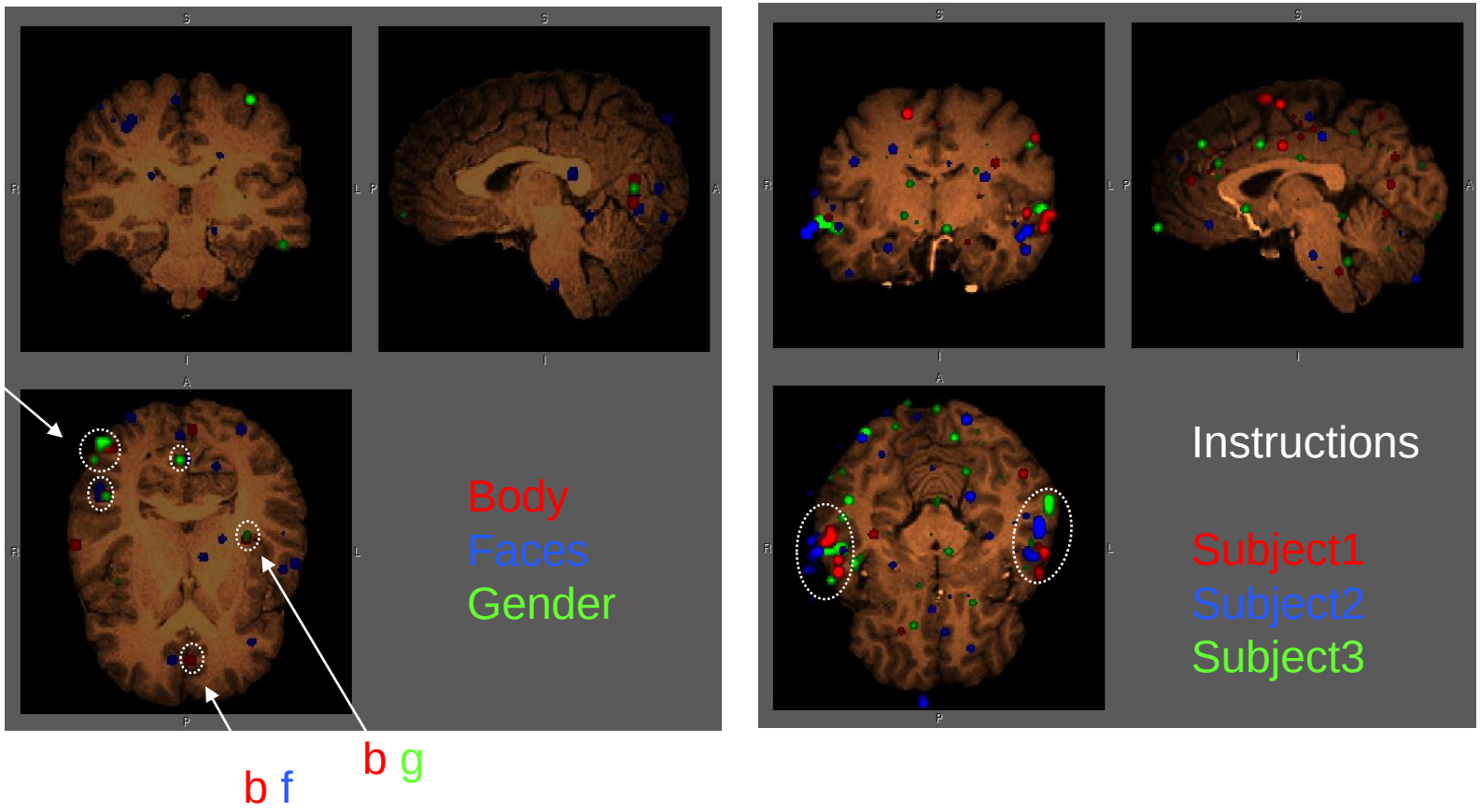
1. AnnoyedAngry
2. Arousal
3. Body
4. DogVisible
5. Dog
6. Faces
7. FearfulAnxious
8. FruitsVegetables
9. Gender
10. Happy
11. HitsFruits
12. HitsPeople
13. HitsWeapons
14. Hits
15. Instructions
16. InteriorExterior
17. ReadSign
18. Sad (X)
19. SearchFruit
20. SearchPeople
21. SearchWeapons
22. VRFixation
23. Valence
24. Velocity
25. WeaponsTools

Ranked 12th, and the "coolest"

Many approaches were used – especially those that won last year…

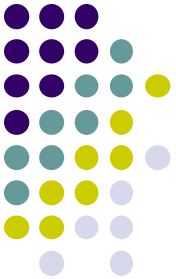
- Most popular:
  - Relevance Vector Machines! (3 of top 6) and support vector machines…
  - Ridge Regression
  - Neural networks
- Cool techniques that could become interesting…
  - Elastic net regularization
  - Fuzzy ARTMap
  - Functional Data Analysis

What did we learn?



Prediction and interpretation of distributed neural activity with sparse models. Melissa K Carroll, Guillermo A Cecchi, Irina Rish, Rahul Garg, A Ravishankar Rao, **Neuroimage**, January 2009.

Neuroimaging Data Analysis Methods



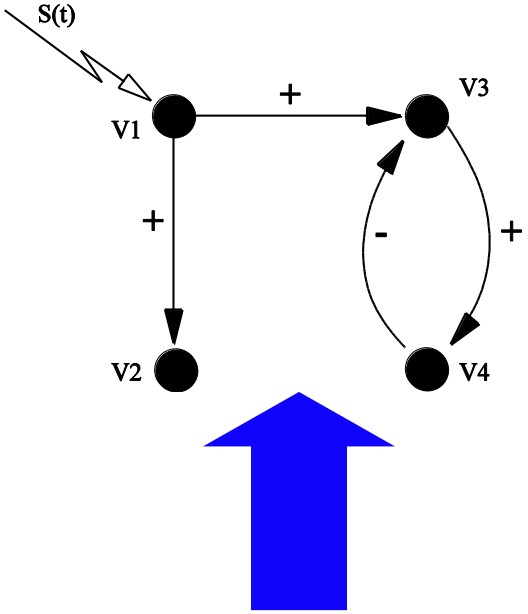
General Linear Model

Functional Connectivity Analysis

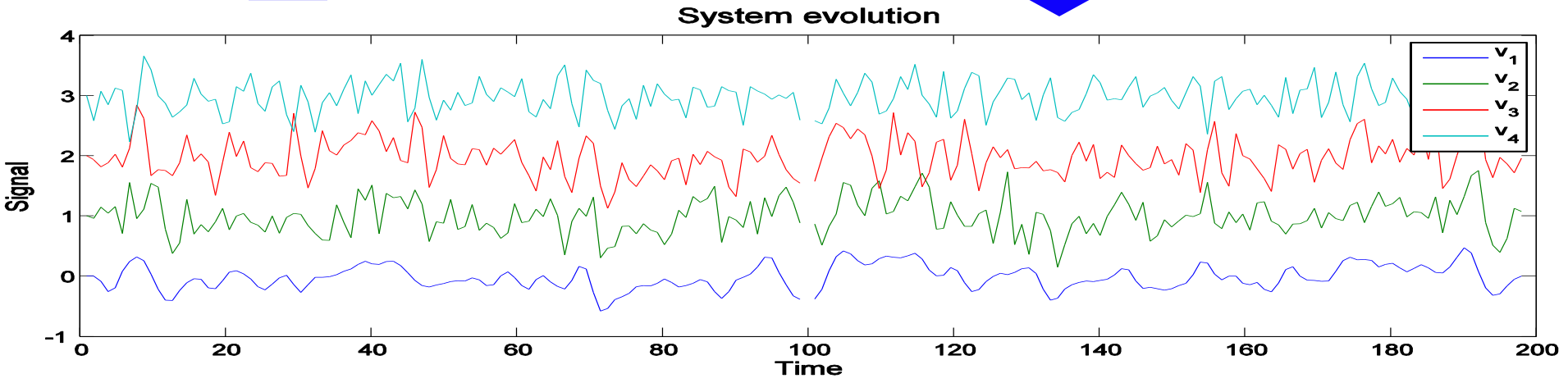
Prediction Using fMRI

Decoding Brain Dynamics Using fMRI

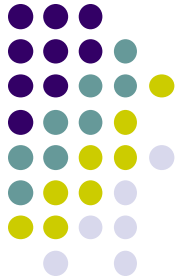
Autoregressive Modeling of Spatiotemporal Brain Dynamics



$$
\begin{aligned}
v_1(t) &= s(t) * h(t) \\
v_2(t) &= v_t(t-1) + 0.5\ \eta_2(t) \\
v_3(t) &= v_1(t-1) - 0.5\ v_4(t-1) + 0.5\ \eta_3(t) \\
v_4(t) &= 0.5\ v_3(t-1) + 0.5\ \eta_4(t)
\end{aligned}
$$

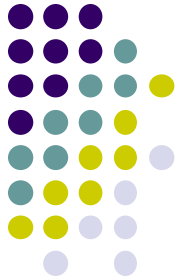


Sparse Regression



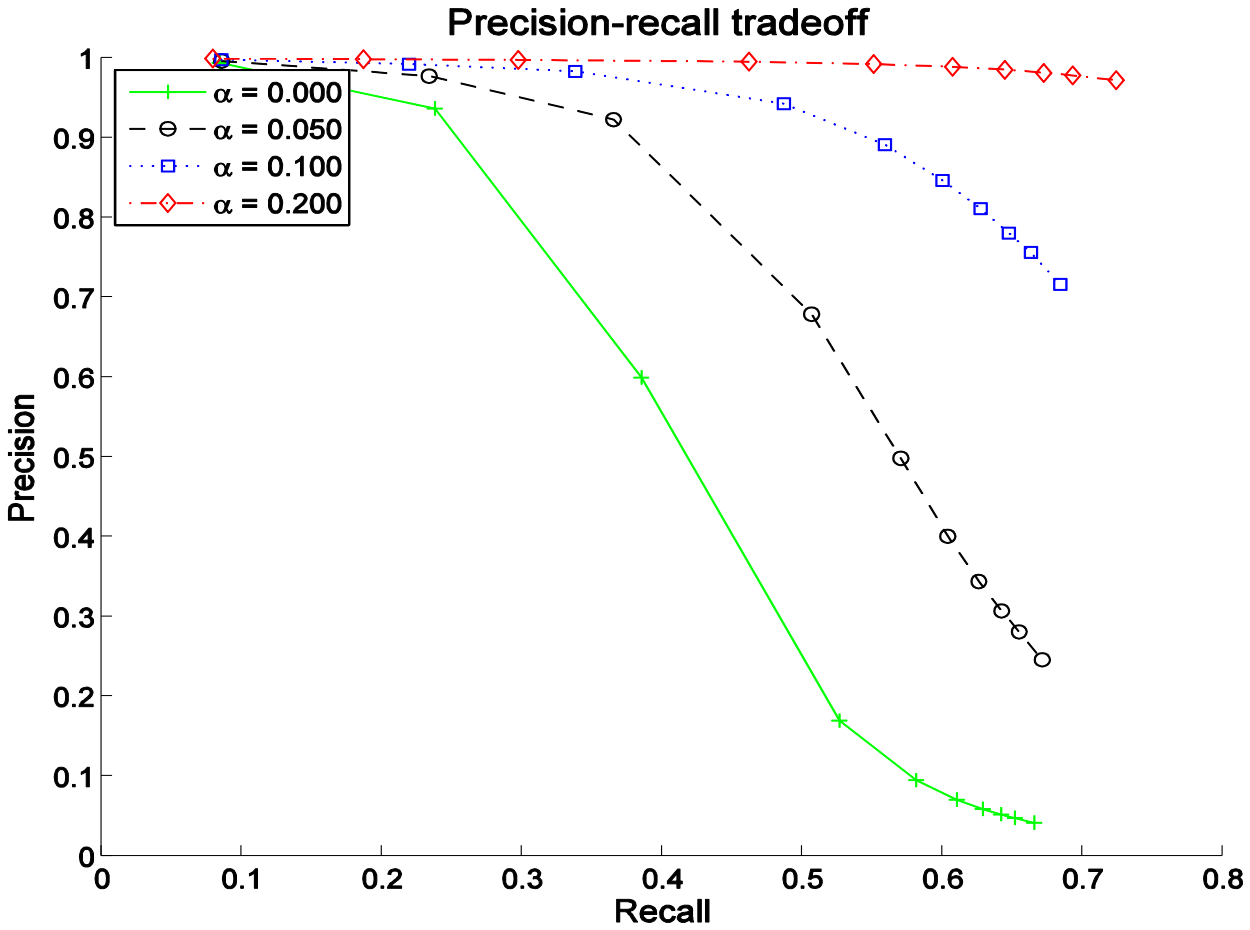
- Solves the system of equations of the form
  - $Ax = b$
  - such that number of non-zero coefficients of x is small.
- Possible to obtain good solutions even if
  - dimensionality (x) >> rank(A)
- Lasso regression
- Use a "L1 regularization penalty" to the least square loss i.e., solves
  - Minimize $||Ax - b||_2$
  - Subject to: $|| x ||_1 < t$

Applications of Sparse Regression



- Model selection in machine learning
  - Given a set of observations Φ (predictors)
  - A response variable y
  - Find the smallest set of observations x (features) that explain the response variable
- Image de-convolution and de-noising
  - $y = x * h + \gamma$
  - y: measured signal
  - h known transfer function
  - γ unknown noise
  - Objective is to find the “best” x
- Sparse PCA
- Compressed sensing and sub-Nyquist sampling
  - A sparse (or compressible) signal x
  - Measured using $y = \Phi x + e$
  - Given y, Φ, the goal is to reconstruct x

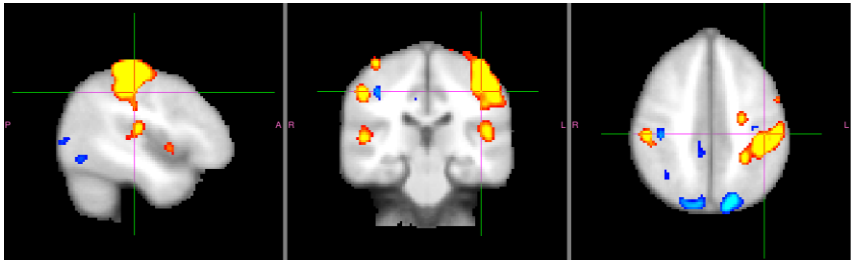
Simulation Results: Precision/Recall Tradeoff



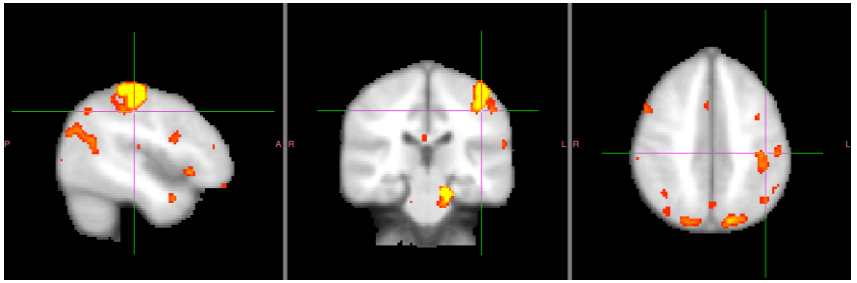
Inferring brain dynamics using Granger causality on fMRI data. Guillermo A. Cecchi, Rahul Garg, A. Ravishankar Rao: **ISBI 2008**: 604-607

Comparisons of Maps

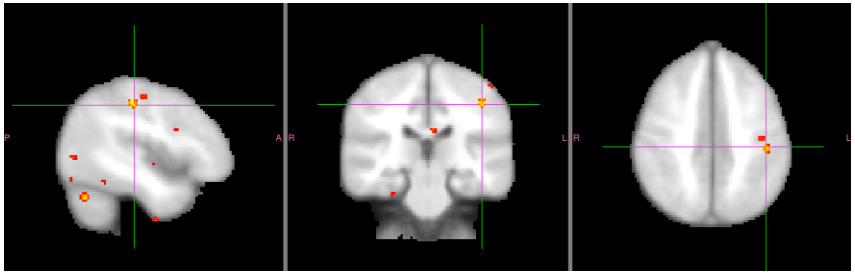
GLM



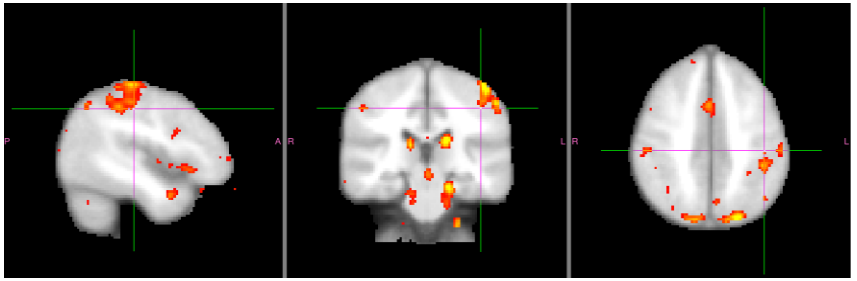
Link density



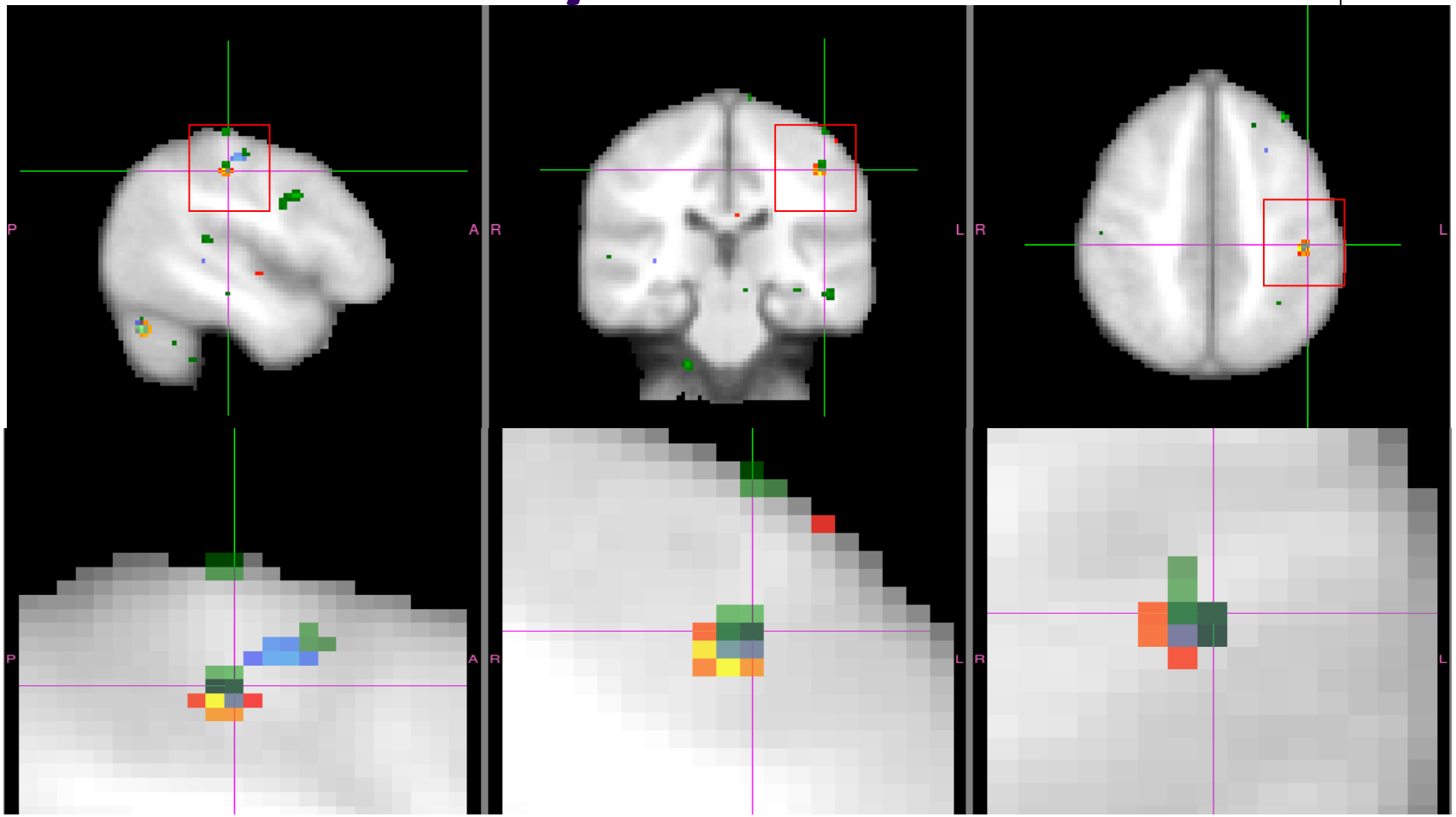
Prediction power



Predictability

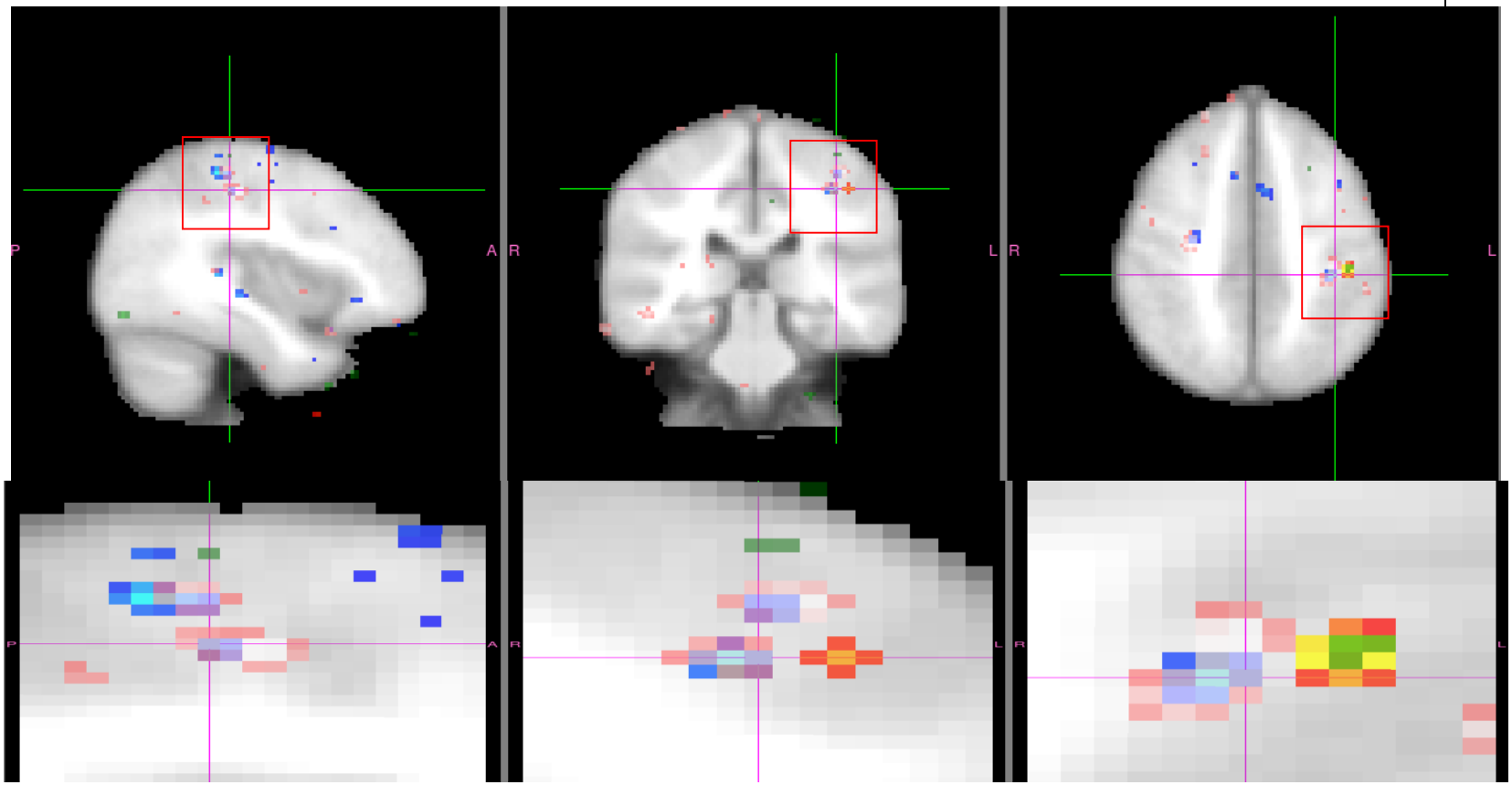


Prediction power maps: Accuracy and consistency



One subject three sessions (red-yellow, blue, green)

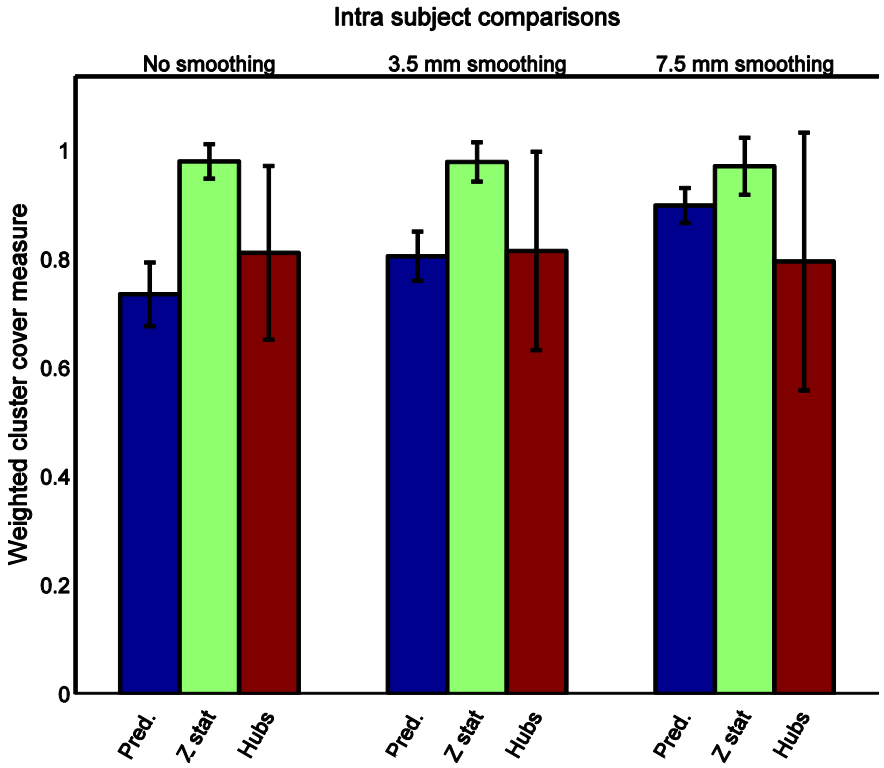
Prediction power maps: Accuracy and consistency

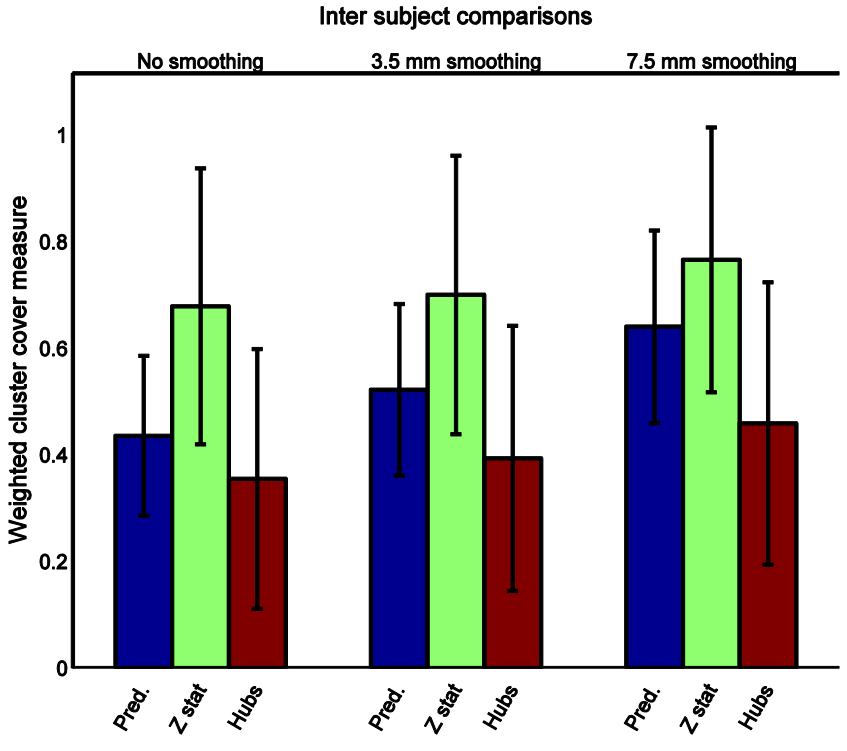


Two subjects two sessions (red-yellow/green, blue/pink)

Characteristics of voxel prediction power in full-brain Granger causality analysis of fMRI data, Rahul Garg, Guillermo Cecchi and Ravi Rao, **SPIE Medical Imaging 2011**

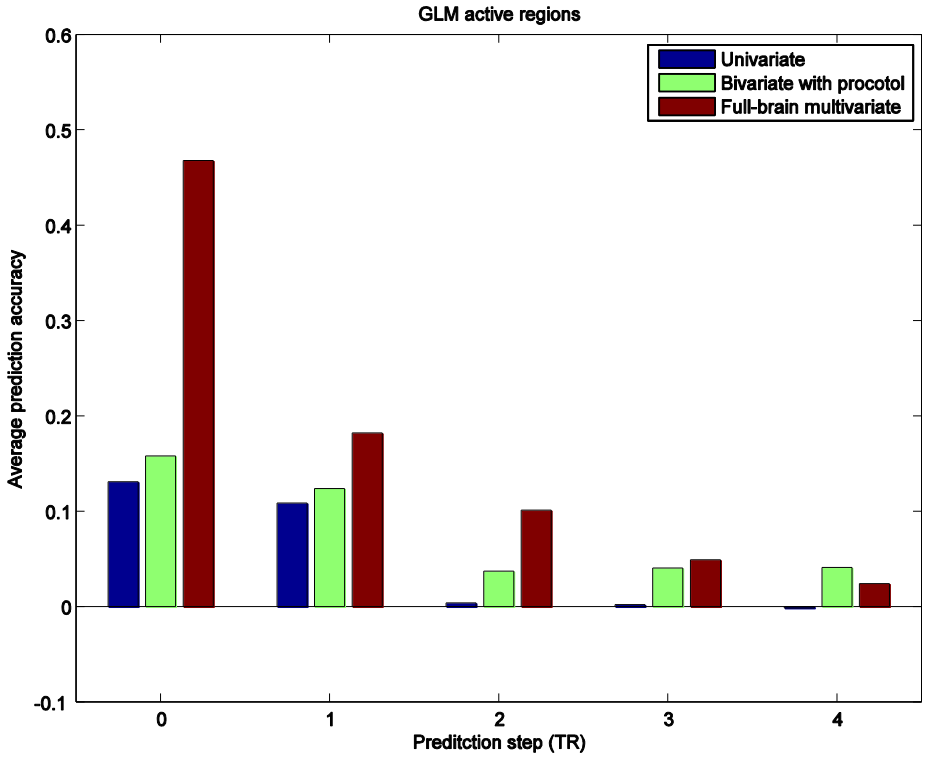
Consistency of Prediction Power Maps



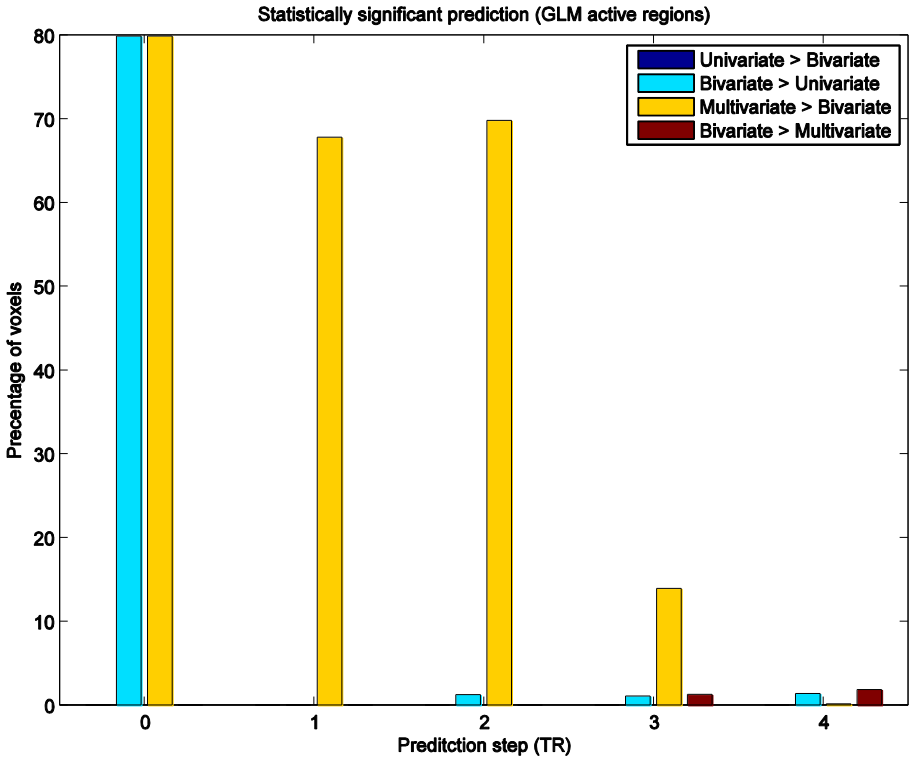


A Cluster Overlap Measure for Comparison of Activations in fMRI Studies, Rahul Garg, Ravi Rao, Guillermo Cecchi, **MICCAI** 2009.

Quality of Prediction: GLM Active Regions



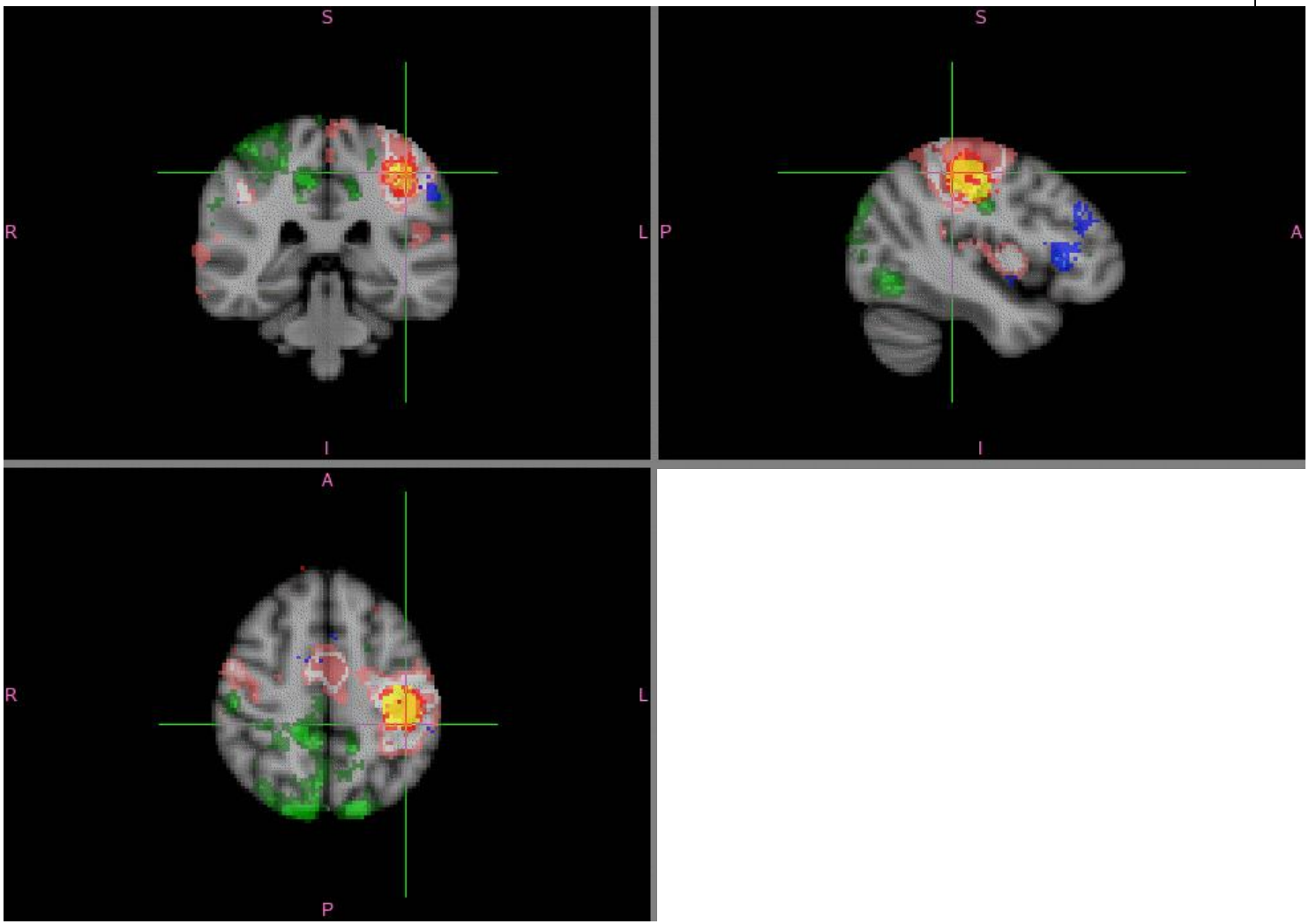
Prediction accuracy



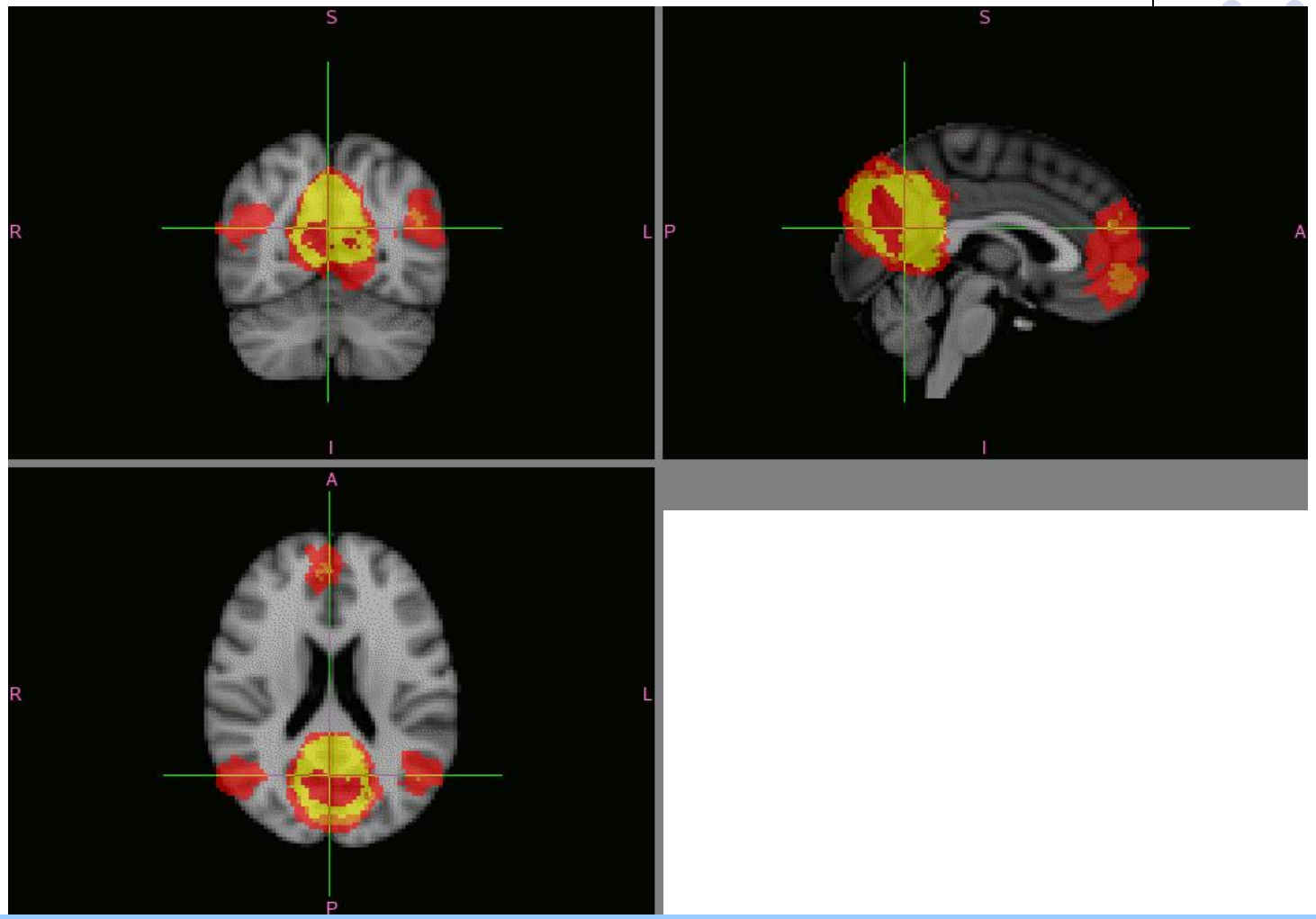
Percent of voxels with better prediction

Brain as a self-predictor: Sparse full-brain auto-regressive modeling in fMRI, Rahul Garg, Guillermo Cecchi, A. Ravishankar Rao, **ISBI** 2011.

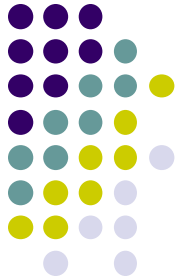
Impulse Response Function: Parietal Stream



Impulse Response Function: Cingulate Stream



Full-brain autoregressive modeling (FARM) using fMRI, Rahul Garg, Guillermo Cecchi and A. Ravishankar Rao, **Neuroimage** 2011.



Introduction to Brain and Mind Sciences

Introduction to Functional Neuroimaging

Neuroimaging Data Analysis Methods

Yogic Neuroscience: Some Glimpses

Conclusions

Unifying the Best of East and West

The 2006 TIME 100

Here's our list of the 100 men and women whose power, talent or moral example is transforming our world

Like 42 Tweet 3 +1 2 Share

SCIENTISTS & THINKERS

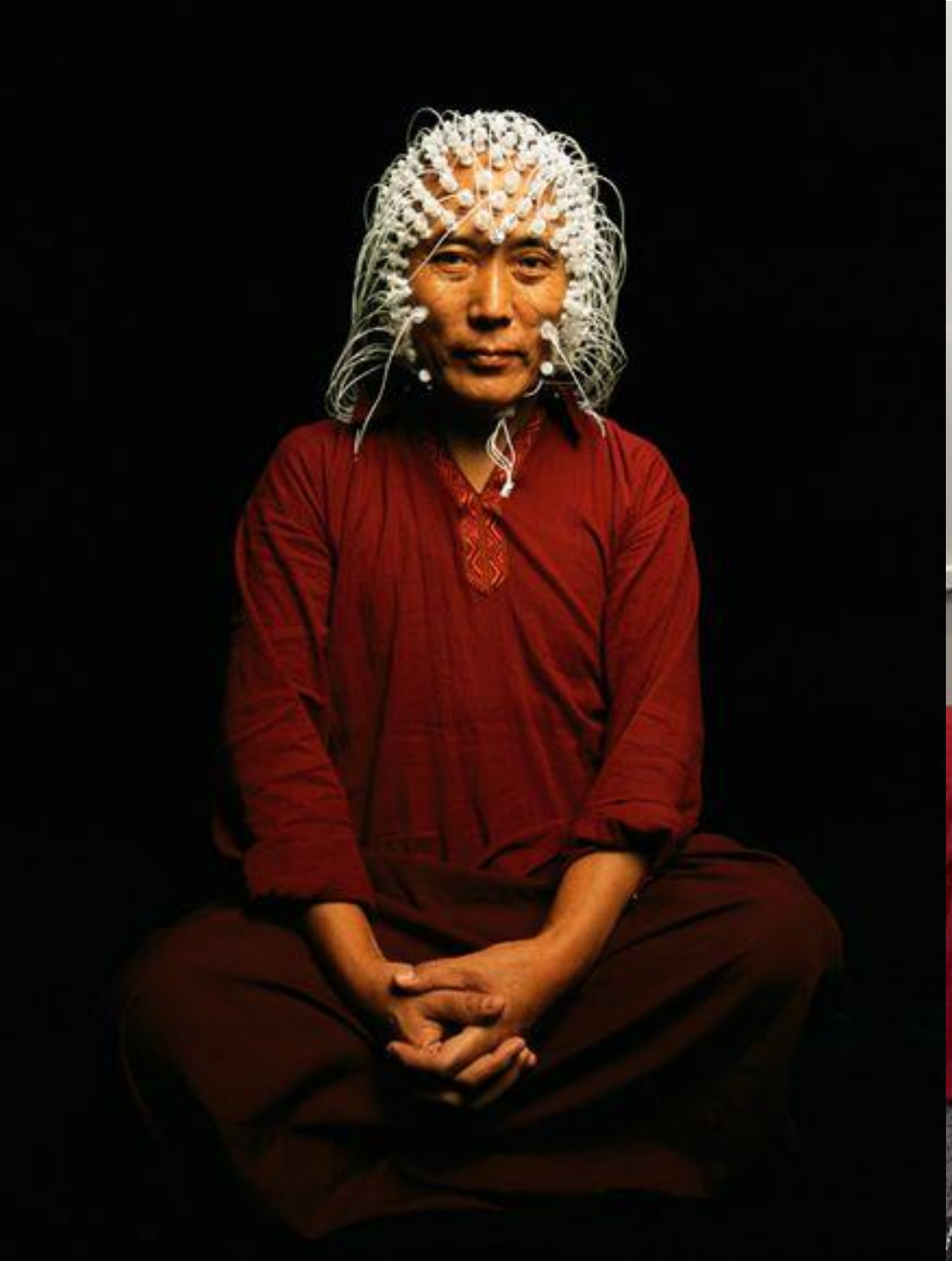
Richard Davidson

88 *of* 102

VIEW ALL

By Andrew Weil, M.D. | Monday, May 08, 2006

Although they both work with the same organ—the brain — the Western tradition represented by neuroscience and the Eastern tradition represented by meditation seemed to have little to do with each other — until Richard Davidson started collaborating with the Dalai Lama. Davidson is a researcher at the University of Wisconsin and a pioneer in the exciting frontier of mind-body medicine. At the university's W.M. Keck Laboratory for Functional Brain Imaging and Behavior, he is correlating mental and emotional states with observable patterns of brain activity.




GETTY IMAGES

The Happiest Man on the Planet

This Professor Says Learning To Be Happy Is 'No Different Than Learning The Violin'

The Huffington Post | By Paige Lavender

Posted: 23/01/2015 19:24 IST | Updated: 24/01/2015 01:29 IST

Free the Mind

Free the Mind is a documentary by Phie Ambo of Danish Documentary, which tracks the impact of Sudarshan Kriya Yoga (SKY), a yoga-based breathing intervention, on their brains and on their lives. SKY is offered to veterans through Project Welcome Home Troops.

Sudarshan Kriya Yoga to US War Veterans

SKY Research in India

ELSEVIER

Journal of Affective Disorders

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Preliminary communication

Antidepressant efficacy of Sudarshan Kriya Yoga (SKY) in melancholia: a randomized comparison with electroconvulsive therapy (ECT) and imipramine

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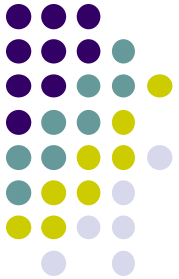


Introduction to Brain and Mind Sciences

Introduction to Functional Neuroimaging

Neuroimaging Data Analysis Methods

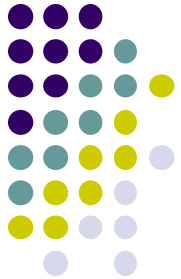
Yogic Neuroscience: Some Glimpses

Conclusions

Conclusions

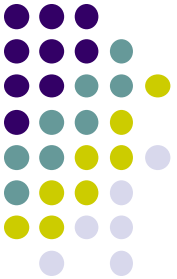
- Brain and Mind Sciences – An exciting area for research
- Combines interdisciplinary knowledge
  - Statistics, Machine learning, Neuroscience, Imaging
- A unique opportunity to combine ancient Indian knowledge with modern scientific tools
- Research already under progress at many places
- Coming soon at IIT-Delhi also

Research in Computer Science at IIT-Delhi



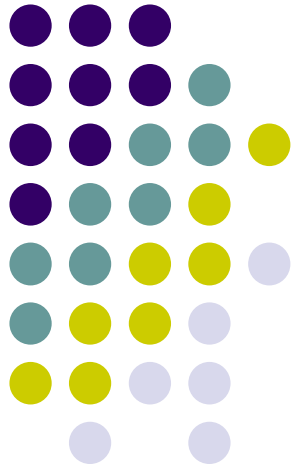
- IIT-Delhi CSE offers many research opportunities
- Globally highly ranked department
- Very strong machine learning presence
- Ongoing work on fMRI data analysis techniques based on machine learning
- Ongoing work on Yoga Nidra – an ancient meditation technique
- Work planned on addiction, SKY etc.
- Yogic Neuroscience in coming years
- Strive to maintain very high scientific standards

How can you participate?



- IITD Department of Computer Science (CSE)
  - Very open and adaptable
- Offers CSE summer research internship
- School of Information Technology – for interdisciplinary work
- National resource centre for value education in engineering (NRCVEE)
- MS-Research option (v.s. M. Tech.)
- Very attractive and flexible PhD programs

Thank you



Who am I?

Srimad Bhagwat Geeta:

अव्यक्तादीनि भूतानि व्यक्तमध्यानि भारत।
अव्यक्तनिधनान्येव तत्र का परिदेवना।।2.28।।

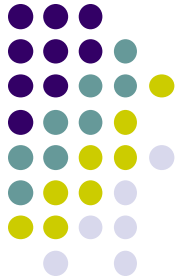
O descendant of harata, all beings remain unmanifest in the beginning;; they become manifest in the middle. After death they certainly become unmanifest. What lamentation can there be with regard to them?

Who am I?

आश्चर्यवत्पश्यति कश्चिदेन
माश्चर्यवद्वदति तथैव चान्यः।
आश्चर्यवच्चैनमन्यः श्रृणोति
श्रुत्वाप्येनं वेद न चैव कश्चित्।।2.29।।

Someone visualizes It as a wonder; and similarly indeed, someone else talks of It as a wonder; and someone else hears of It as a wonder. And some one else, indeed, does not realize It even after hearing about It.

Future Research Plans



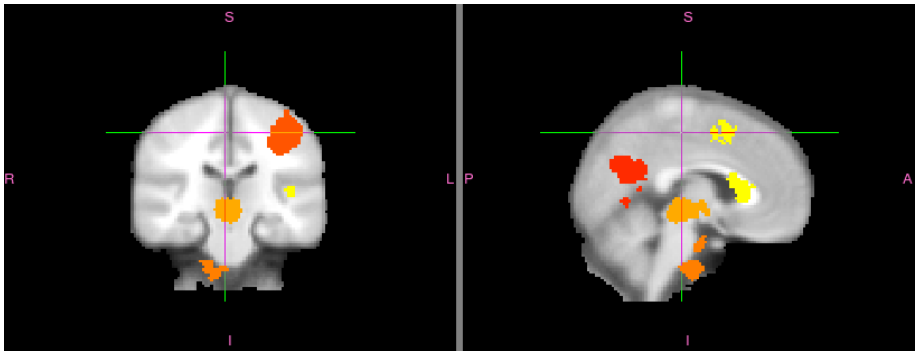
- Research in Neuroscience and Neuroinformatics
  - High performance computing
  - Machine Learning
- How Yoga impacts the mind, body and behavior
  - fMRI analysis of Yoga Nidra
  - Studying the link between breath and emotions
- IT for Society
  - IT in education (MOOC), other applications

Conclusions

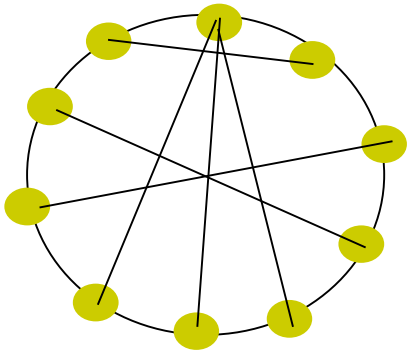
- Functional MRI – a powerful and non-invasive imaging method to learn about brain function
- fMRI generates massive amounts of data
- Analysis is an interdisciplinary field involving radiologists, statisticians and computer scientists
- By GLM analysis, we are barely scratching the tip of the iceberg
- A number of new discoveries are being made using advanced data analysis methods
- Collaborative endeavor is a must for success

What information is present in fMRI signal?

Activations



Functional brain networks



Prediction

Spatiotemporal dynamics