杂谈功能磁共振成像（fMRI）和心理学研究

Renmin University of China
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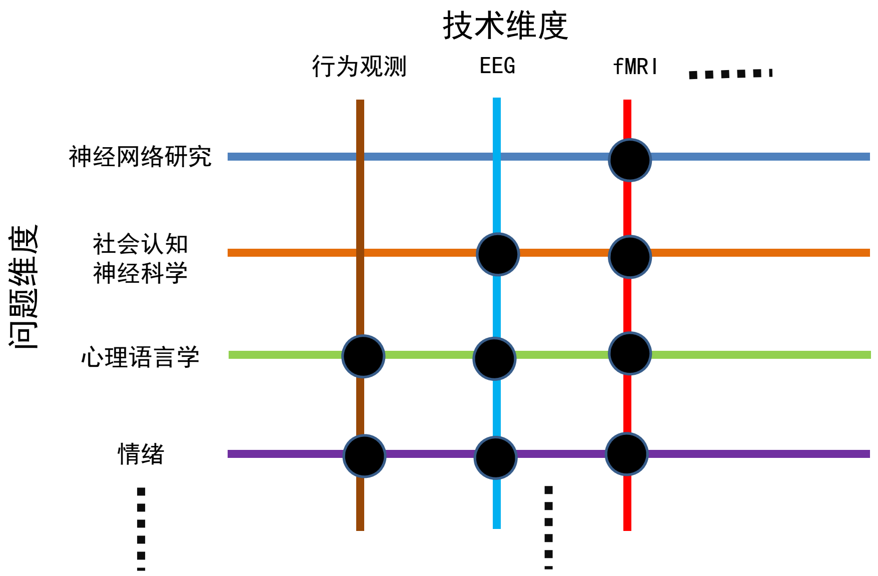
About me

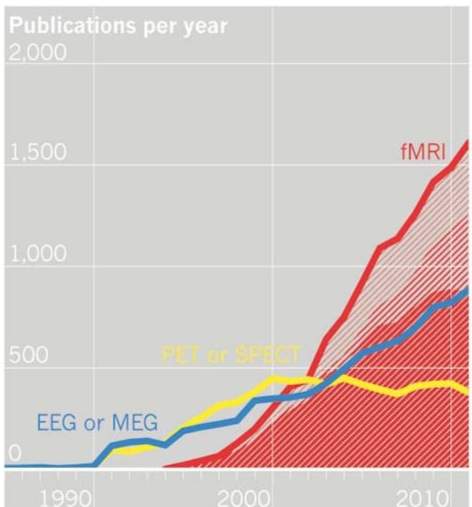
- 2008, Graduated from Nation lab of Cognitive Neuroscience and Learning, Beijing Normal University, China
- 2008-2013, Worked in Biomedical Engineering Department，University of Florida，USA
- 2013-now, Associate Professor, Psychology Department, Renmin University of China.

与本课程其他讲座的关系



了解fMRI的意义

Brain imaging: fMRI 2.0
Functional magnetic resonance imaging is growing from showy adolescence into a workhorse of brain imaging.
•**Kerri Smith**
04 April 2012



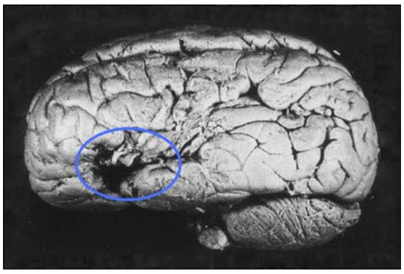
fMRI publications by subject:

内容

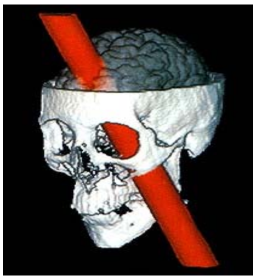
- 历史和背景
- MRI/fMRI基本原理
- fMRI的神经解释
- fMRI的基本分析方法
- 基于fMRI的心理学实验设计的演变
- 前沿问题
- 基于fMRI的大脑功能网络分析拓展
- fMRI的未来

历史和背景

心智的生物学基础：脑损伤研究

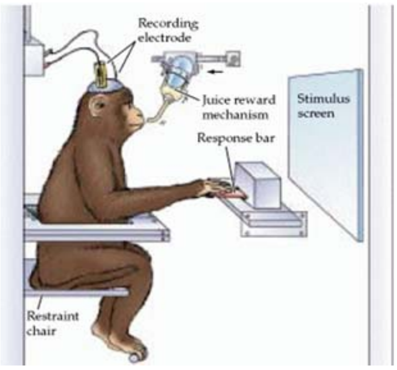


the first area of the brain to be
associated with a specific function

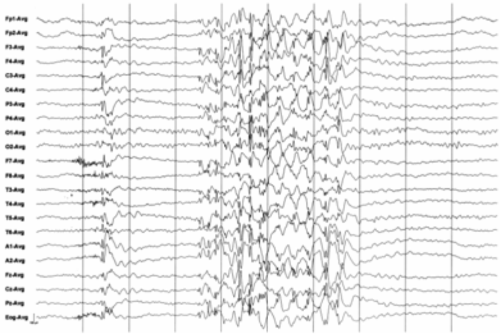


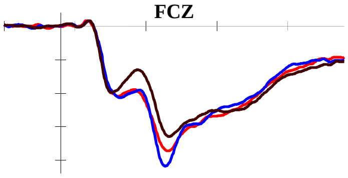
Case of Pineas Gage. In 1848

动物和侵入性研究

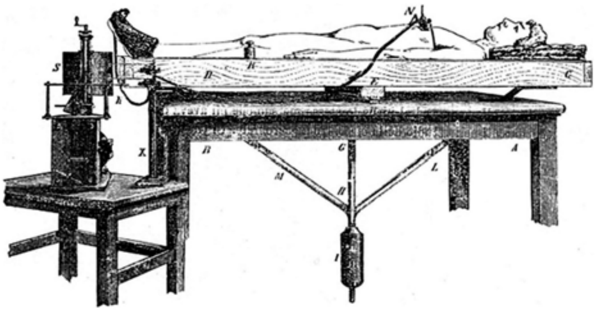


用非损伤的方法研究心智的脑基础：EEG





用非损伤的方法研究心智的脑基础：脑血流研究



Around 1884

Angelo Mosso

功能磁共振成像fMRI

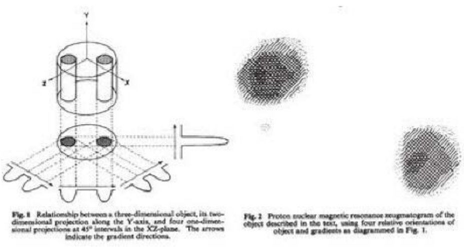
- 功能磁共振成像： Functional Magnetic Resonance Imaging.

MRI的历史

- **1882 Nikola Tesla** discovered the Rotating Magnetic Field in Budapest, Hungary. This was a fundamental discovery in physics.
- **1937** Columbia University Professor **Isidor I. Rabi** working in the Pupin Physic Laboratory in New York City, observed the quantum phenomenon dubbed nuclear magnetic resonance (NMR). He recognized that the atomic nuclei show their presence by absorbing or emitting radio waves when exposed to a sufficiently strong magnetic field.
- **1946** Felix Bloch and Edward Purcell discover magnetic resonance phenomenon.
- **1950s** Herman Carr creates a one-dimensional MR image.

- **1956** The "Tesla Unit" was proclaimed in the Rathaus of Munich, Germany by the International Electro-technical Commission-Committee of Action. All MRI machines are calibrated in "Tesla Units". The strength of a magnetic field is measured in Tesla or Gauss Units. The stronger the magnetic field, the stronger the amount of radio signals which can be elicited from the body's atoms and therefore the higher the quality of MRI images.
- **1971** Raymond Damadian, a physician and experimenter working at Brooklyn's Downstate Medical Center discovered that hydrogen signal in cancerous tissue is different from that of healthy tissue because tumors contain more water. More water means more hydrogen atoms. When the NMR machine was switched off, the bath of radio waves from cancerous tissue will linger longer then those from the healthy tissue.
- **1972** Raymond Damadian applies for a patent, which describes the concept of NMR being used for above purpose. He illustrates major parts of MRI machine in his patent application.

- **1974 Paul Lauterbur**, a chemist and an NMR pioneer at the State University of New York, Stony Brook, produced the first NMR image. It was of a test tube.



- **1975** Richard Ernst proposes using phase and frequency encoding and Fourier transform for acquisition of MR images.

- **1977** Raymond Damadian produces MR image of the whole body. **Peter Mansfield** improves mathematics behind MRI and develops **echo-planar technique**, which allows images to be produces in seconds and later becomes the basis for fast MR imaging.
- On July 3, 1977, nearly five hours after the start of the first MRI test, the first human scan was made as the first MRI prototype. The image above is of **Dr. Damadian** with the history-making prototype of his MRI scanner.

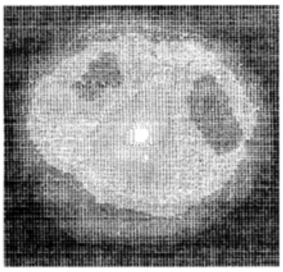
- 1983 Ljunggren and Tweig introduce k-space.
- 1986 Le Bihan publishes an article in Radiology, which describes diffusion weighted imaging (DWI).
- 1987 Real time MR imaging of the heart is developed.
- 1991 Filler and colleagues describe imaging of axonal transport of supermagnetic metal oxide particles, a technique, which later becomes important in imaging of neural tracts.
- 1993 Functional MR imaging of the brain is introduced.
- 1994 The first intraoperative MR unit developed by GE and Harvard is installed in the Brigham and Women's Hospital in Boston.
- 1990s In addition to research centers and large hospitals, small remote hospitals and imaging centers begin to utilize MRI predominantly for neuroimaging and musculoskeletal imaging.
- **2000s Cardiac MRI, Body MRI, fetal imaging, functional MR imaging are further developed and become routine in many imaging centers. Research centers make significant strides forward in imaging cartilage on high field scanners. The number of free standing MRI centers, most of which utilize low or moderate field MR scanners significantly increases.**

MRI科学家的成就

- Paul Lauterbur and Peter Mansfield won Nobel Price in 2003

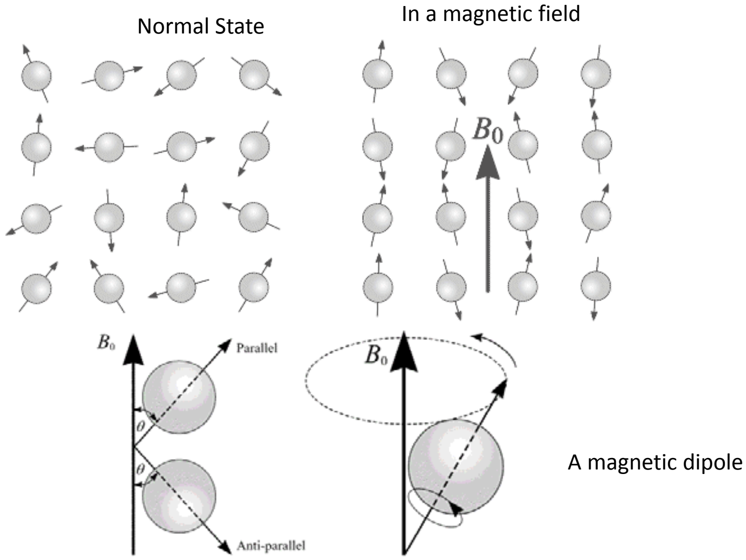
Cross-section of a mouse →
(shadows are lungs)

← Oil in peanuts

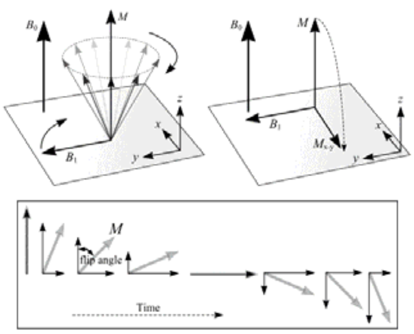


MRI/fMRI基本原理

Magnetization and precessing：分子（磁极）在静磁场B0中会绕静磁场方向进动

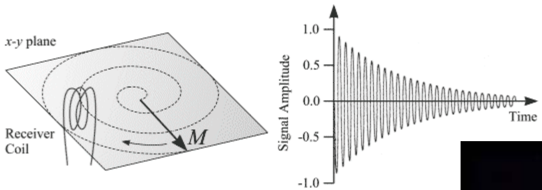


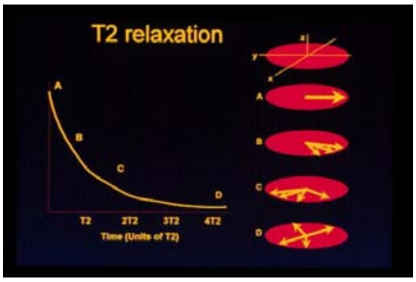
Resonance with RF：外加磁场B1（和B0垂直）变化频率（RF）如果和磁极进动频率相同，则发生共振，磁极吸收RF能量，自身能量升高



(a) After a 90 degrees RF pulse, M lies in the x-y plane and rotates about the z-axis. The component of M in the x-y plane decays over time. An alternating current, shown in Figure (b), is induced in the receiver coil.

Relaxation：当B1被消除，磁极重新恢复到平衡状态，这个过程能量以电磁波的形式释放，最后共振消失



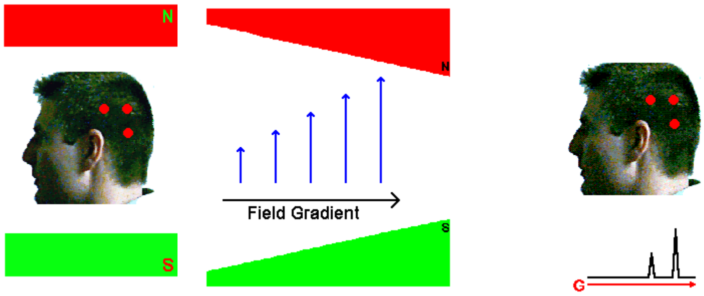


(a) After a 90 degrees RF pulse, M lies in the x-y plane and rotates about the z-axis. The component of M in the x-y plane decays over time. An alternating current, shown in Figure (b), is induced in the receiver coil.

空间编码的思路

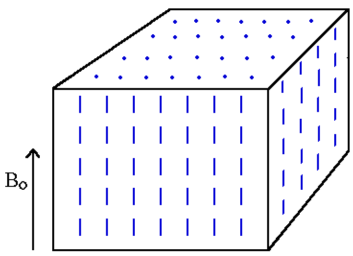
- 身体不同的组织有不同的磁化特性。
- 在弛豫过程中，如果能够让不同位置发出的信号不同，则可以通过解读信号的空间来源。从而对组织进行成像。
- 问题是，如何让不同位置发出不同的信号呢（如何对空间位置进行编码）

Frequency Encoding：让不同空间位置净磁场强度不同，从而让磁极以不同的频率震动



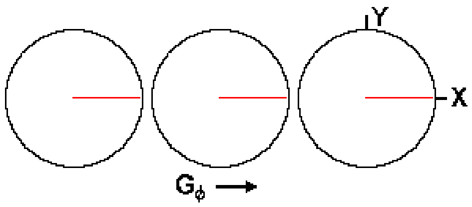
三维编码的第一步：Slice Selection (in ideal scenario)

When a Gradient B applied, an RF input with certain frequency will only rotate the spines (e.g. 90 degrees) in a narrow space with certain B strength, and their signals will be picked up, which means a certain slice with very small thickness is selected.

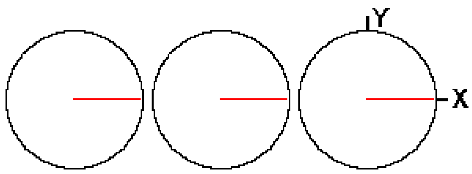


三维编码的第二步：Phase encoding gradient

A gradient is applied along X, the three vectors will precess at different frequencies given by the resonance equation, and their phase is different.

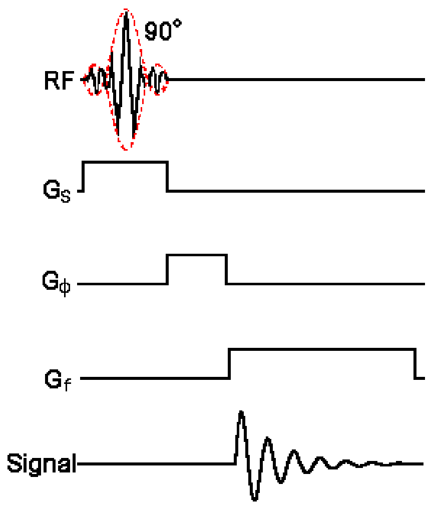


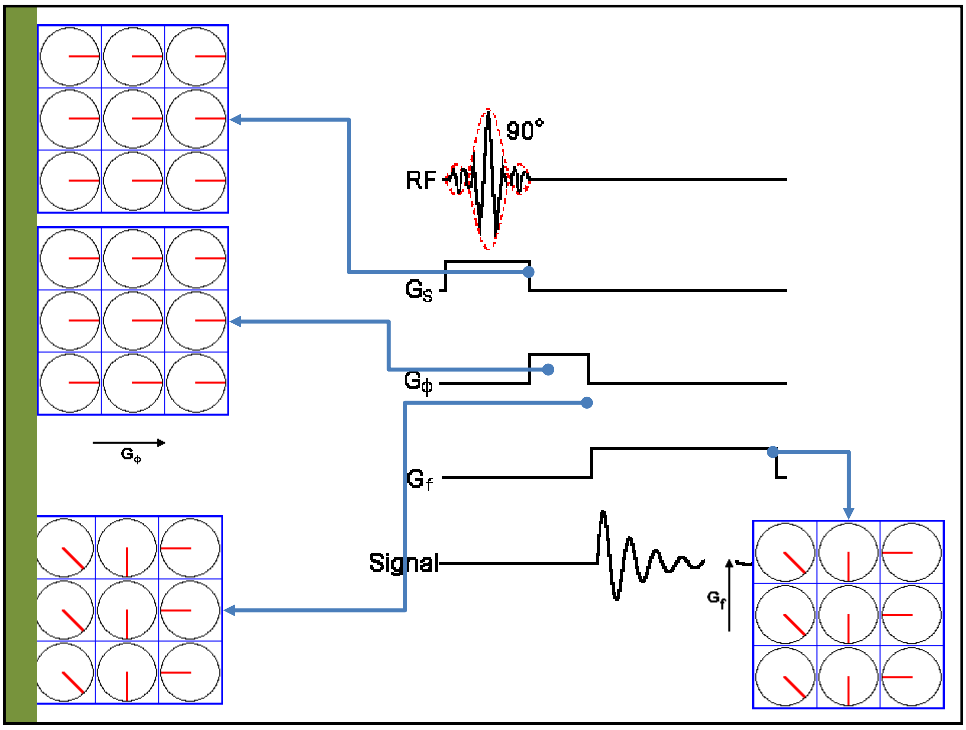
If the gradient is off, the magnetic field is identical everywhere, the spin vectors precess at the same frequency, but with different phase, which is determined when the gradient is off



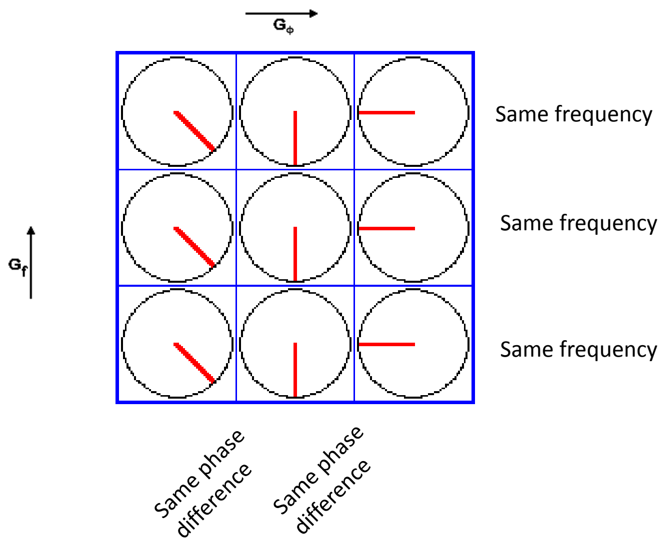
三维编码的第三步：Frequency encoding

Gradient			
Slice Plane	Slice	Phase	Frequency
XY	Z	X or Y	Y or X
XZ	Y	X or Z	Z or X
YZ	X	Y or Z	Z or Y

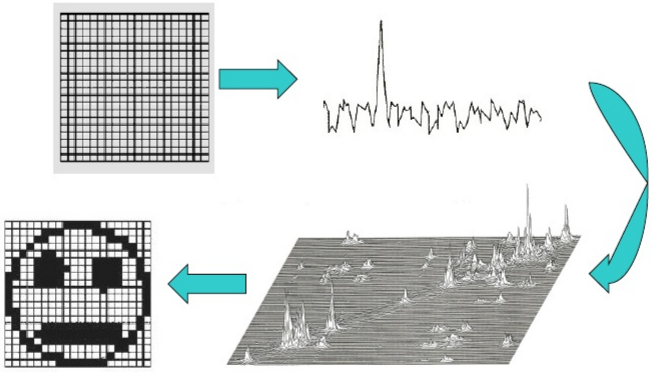



90°
RF
G_S
G_ϕ
G_f
Signal
G_ϕ
G_f

某一片上的二维编码


G_ϕ
G_f
Same frequency
Same frequency
Same frequency
Same phase difference
Same phase difference

图像的重构



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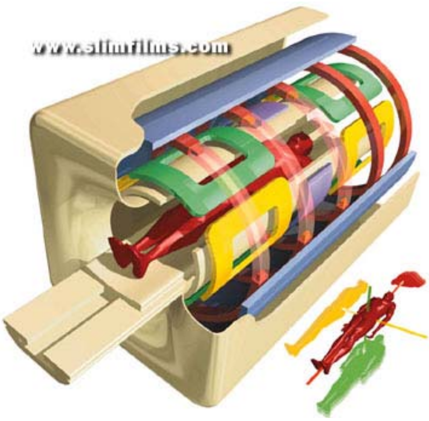
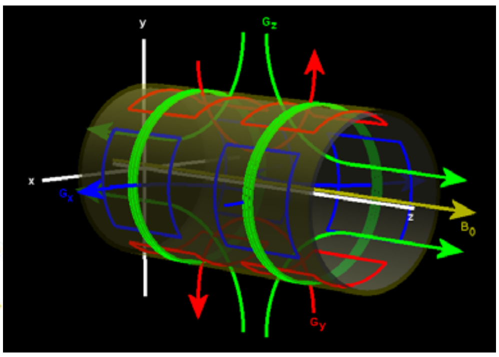
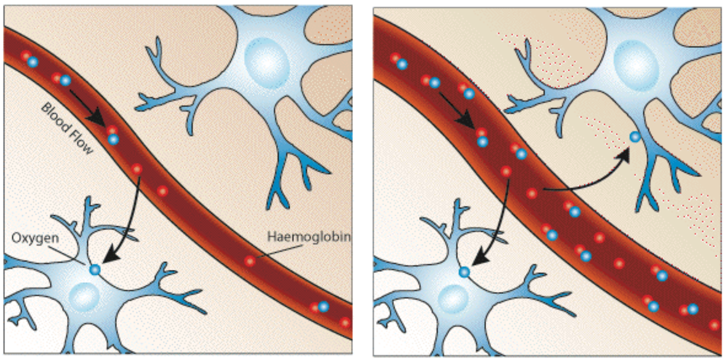
MRI的硬件构架



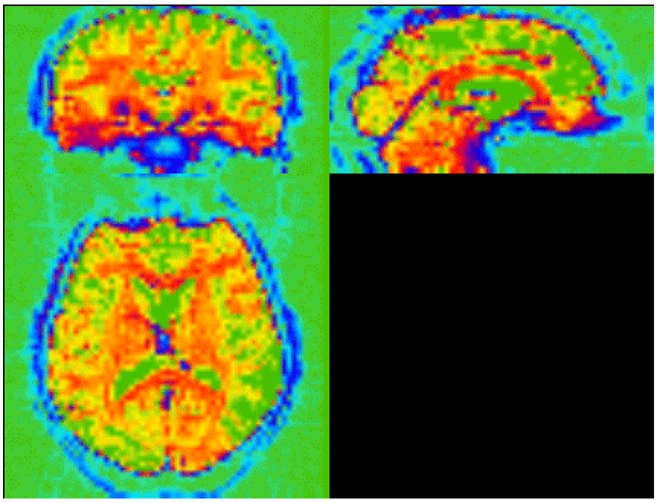


Blood oxygen level dependence change (BOLD)

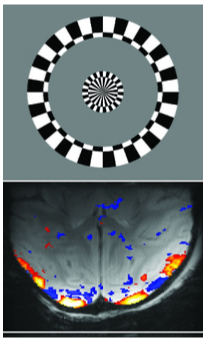


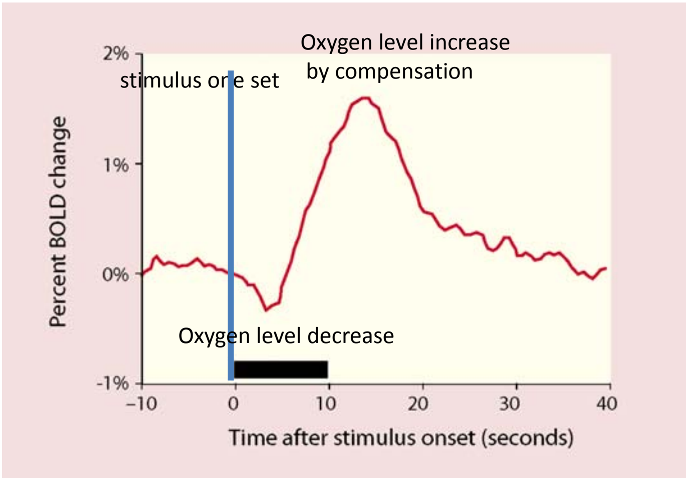
Resting　　Activated

fMRI时间序列

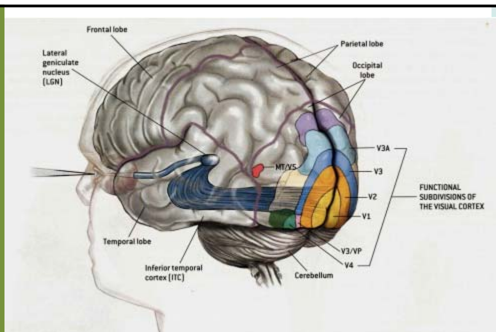


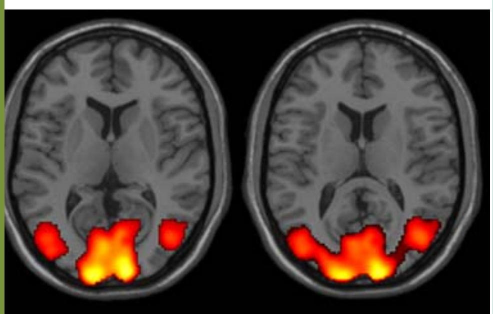
Blood oxygen level dependence change (BOLD)

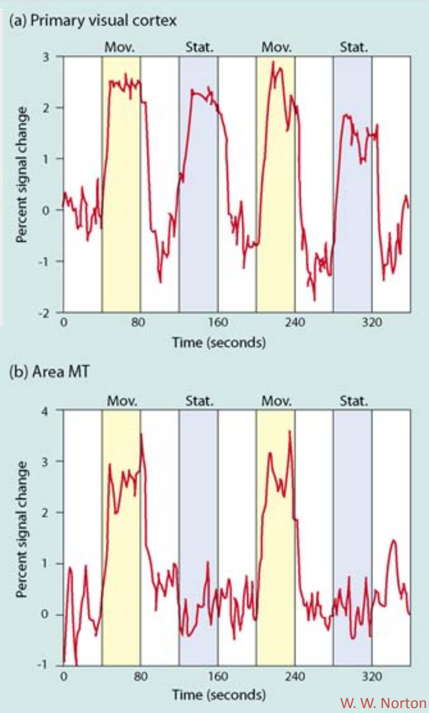




ong, T.Q., Kim D.S., Ugurbil, K., and Kim, S.G. (2000). Spatiotemporal dynamics of the BOLD fMRI signals: Toward mapping submillimeter cortical columns using the early negative response. *Magn. Reson. Med.* 44:231-242.





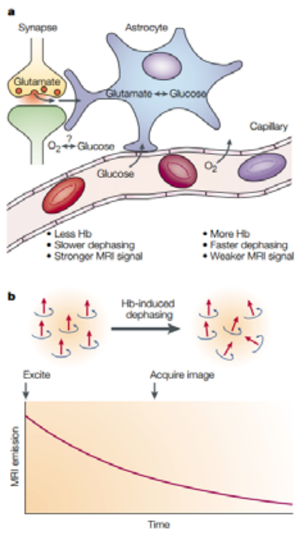


W. W. Norton

fMRI信号的神经解释

问题：fMRI信号是什么东西？？

- 神经信号的变化是迅速的
- BOLD（fRMI）信号的变化是缓慢的
- 两者如何统一？
- fMRI信号是否只是和血流有关？
- 是否只具有生理学意义？



David J. Heeger and David Ress, 2001, Nature

fMRI的神经解释：Boynton的线性模型

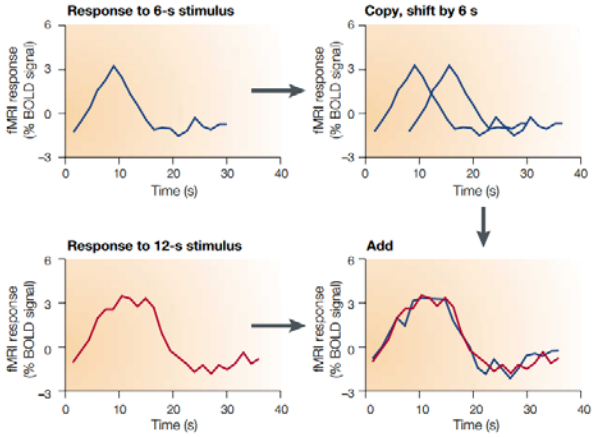
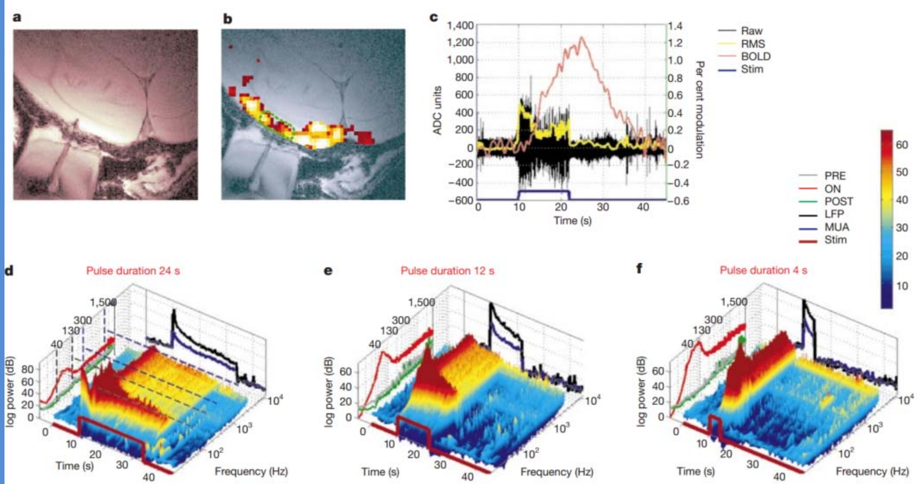


Figure 2 | **Temporal summation of fMRI responses.** Left: measured functional magnetic resonance imaging (fMRI) responses from the visual cortex for 6- and 12-s stimulus presentations. Right: the procedure for measuring temporal summation, by comparing the responses to the two different stimulus durations. BOLD, blood oxygen level dependent. Modified with permission from REF. 13 © 1996 Society for Neuroscience.

Boynton, G. M., Engel, S. A., Glover, G. H. & Heeger, D. J. Linear systems analysis of functional magnetic resonance imaging in human V1. J. Neurosci. 16, 4207–4221 (1996).

fMRI的神经解释：Logothetis的研究

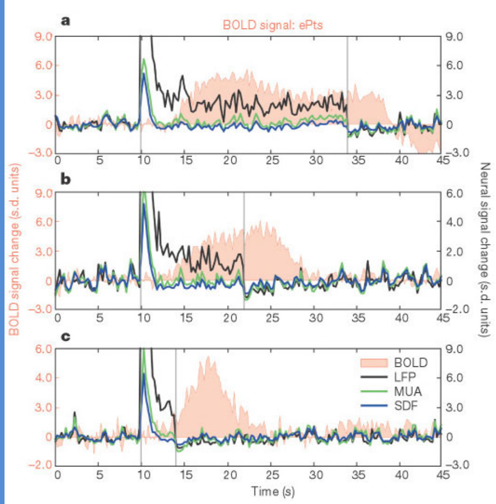


Logothetis, N. K., Pauls, J., Augath, M., Trinath, T. & Oeltermann, A. Neurophysiological investigation of the basis of the fMRI signal. Nature 412, 150–157 (2001)

LFP and MUA的一般知识

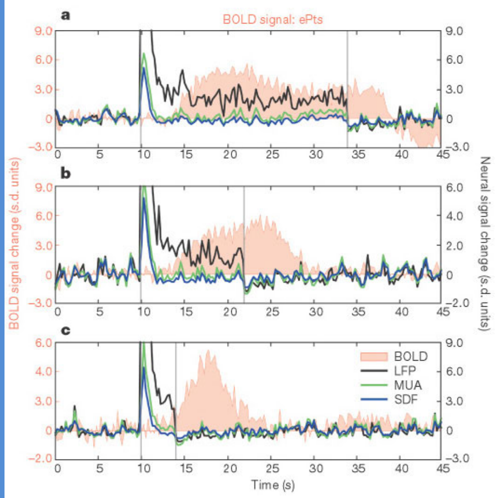
- An electrode small enough allows indirect observation and recording of action potentials from a single cell, and is termed **single-unit recording**. Depending on the preparation and precise placement, an extracellular configuration may pick up the activity of several nearby cells simultaneously, and this is termed **multi-unit recording （for MUA）**.
- As electrode size increases, the resolving power decreases. Larger electrodes are sensitive only to the net activity of many cells, termed **local field potentials (LFP)**.

BOLD增强在时间上和LFP、MUA的增强是有关的



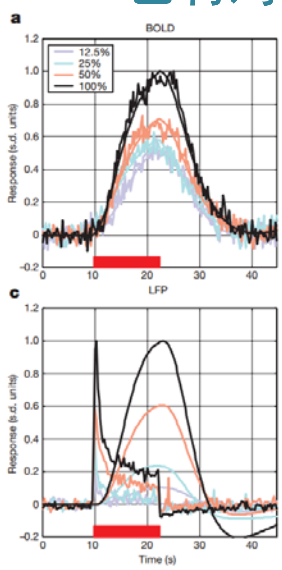
- 25% of MUA show a transient response returning to baseline after 2-4s.
- Conversely, LFP was always elevated for the duration of the stimulus.
- Suggests that BOLD may reflect more the neural activity related to the input and local processing in any given area, rather than the spiking activity commonly thought of as the output of an area.

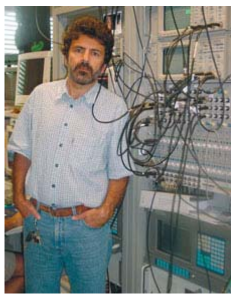
BOLD和LFP关系最为密切，LFP反映了局部脑区的信号输入



LFP reflects the neural input to the local area rather than output.
↓
BOLD activation of a region is related to neural input to that region

BOLD增强的幅度和LFP增强的幅度也有对应关系





fMRI的神经解释

- **BOLD unequivocally reflects an increase in neural activity.**
- Increase in Increase in LFPs during stimulation is significantly stronger than that of during stimulation than that of MUA.
- 25% of MUAs show transient activity and return to baseline, while LFP are sustained throughout the stimulus duration. **LFP response gives a better estimate of BOLD response than the MUA (modeling data).**
- **SNR of neural signal was at least 10X higher than BOLD SNR, suggesting the fMRI analyses probably underestimate actual neural activity.**
- **There is a linear relationship between the neural activity and BOLD response.**
- **BOLD seems to reflect incoming input and local processing in an area rather than spiking activity.**
- Consequentially, fMRI may reveal activation in areas where there is no single--unit activity.

fMRI的基本分析方法

时间序列分析，从神经电信号到fMRI信号

- 电信号的基本分析方法
- 基于广义线性模型的fMRI信号激活分析
- 功能连接分析方法
- 有效连接分析方法

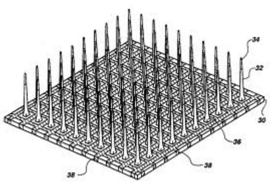
电信号的基本分析方法

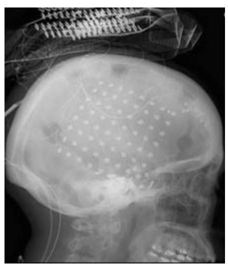
信号的种类

- Single Unit Recoding
- Multi Unit Recoding
- ECoG
- EEG/MEG
- ERP

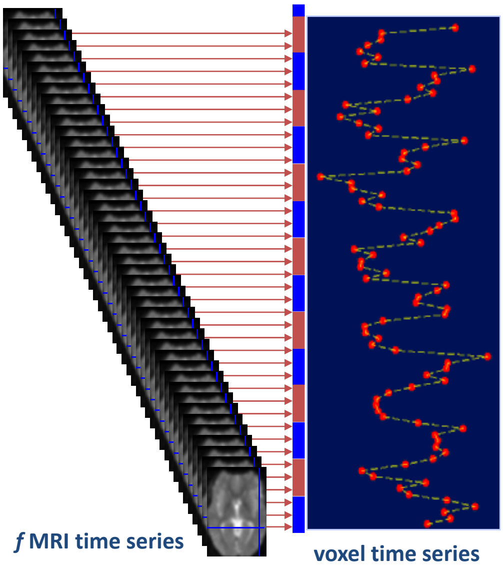
信号分析方法

- ERP分析
- 源定位
- 谱分析-时频分析
- 相位分析
- 相关分析、相干分析
- Granger因果模型

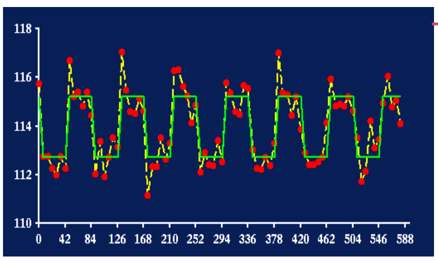


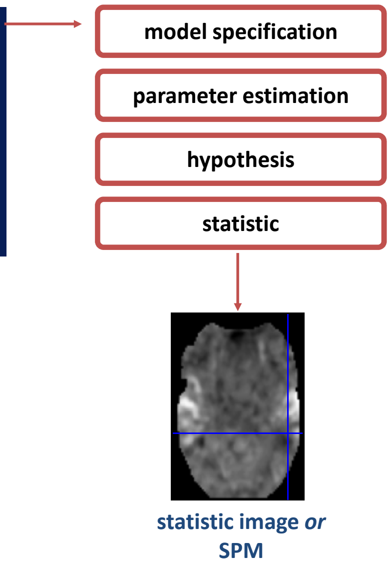


BOLD活动的fMRI记录

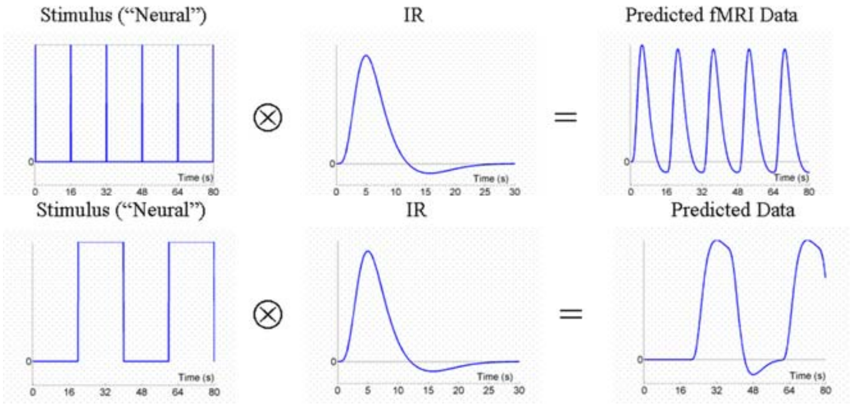


激活分析的本质是检测fMRI信号和心理学实验设计之间的关系

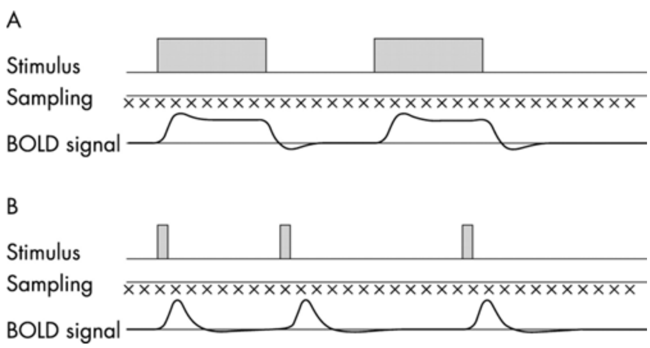


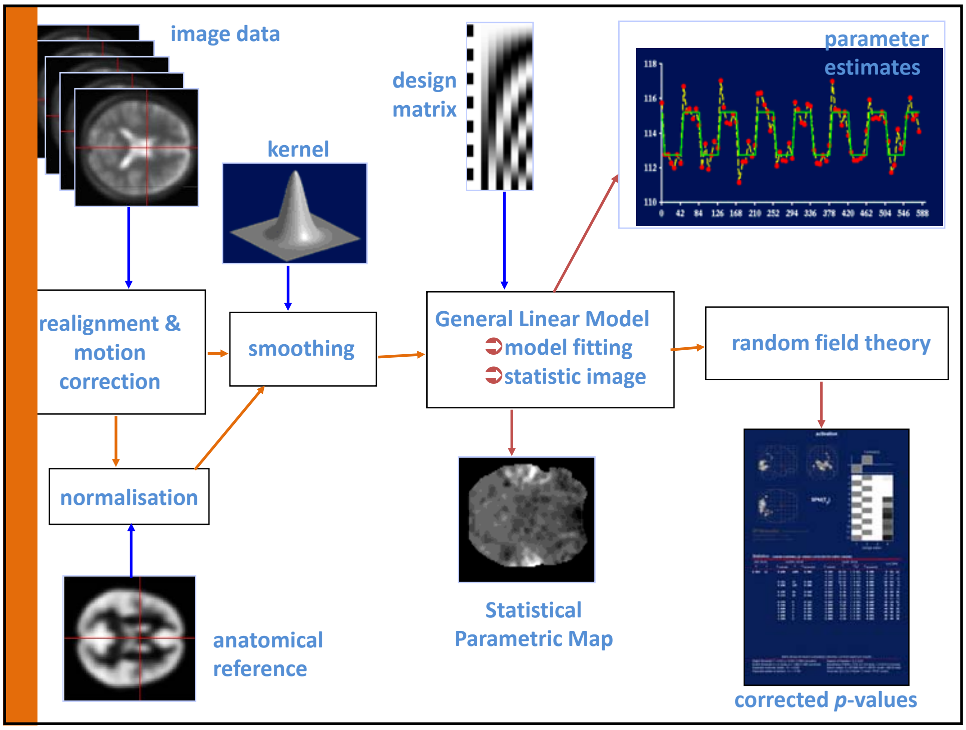


BOLD信号可以看成是心理/神经事件和HRF血液动力学模型的卷积

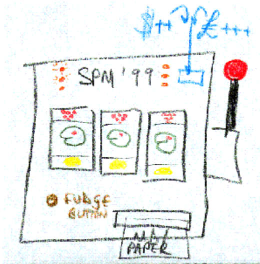


BOLD 信号的理论模型





使用基于广义线性模型的SPM软件实现激活分析（Friston的贡献）



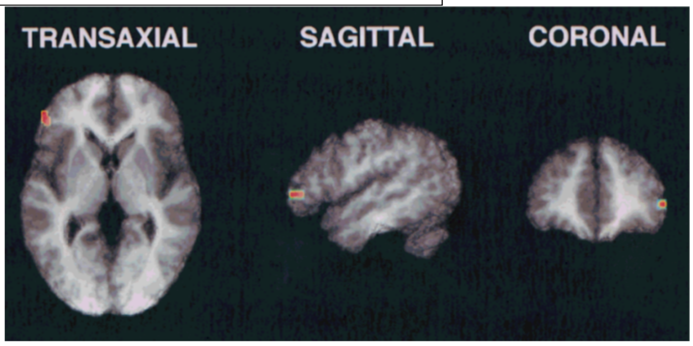
Karl Friston

fMRI与心理/认知研究的紧密结合

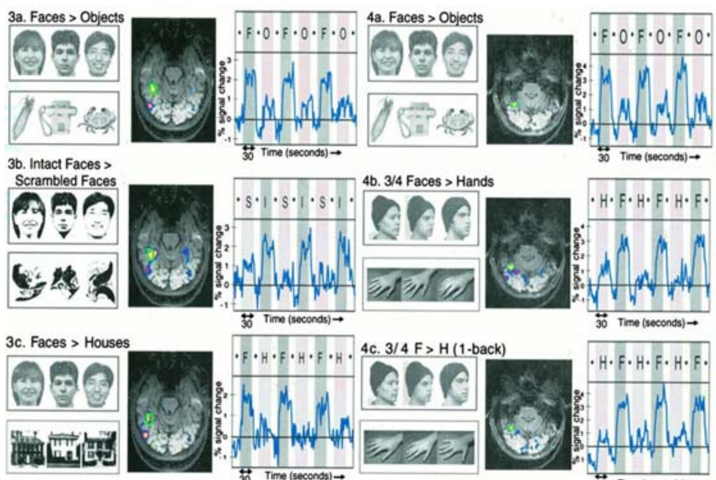
• Human Brain Mapping 9:65–71(2000) •

Activation of Broca's Area by Syntactic Processing Under Conditions of Concurrent Articulation

David Caplan,[1*] Nathaniel Alpert,[2] Gloria Waters,[3] and Anthony Olivieri[1]



fMRI与心理/认知研究的紧密结合



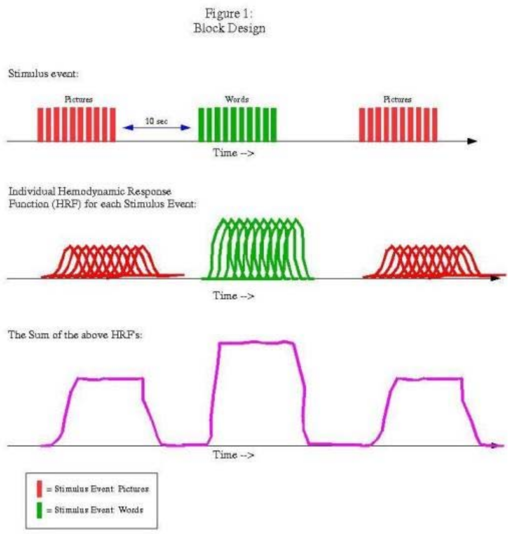
Kanwisher, N., McDermott, J., & Chun, M. M. (1997). The fusiform face area: a module in human extrastriate cortex specialized for face perception. The Journal of Neuroscience, 17(11), 4302-4311.

基于fMRI的心理学实验设计的演变

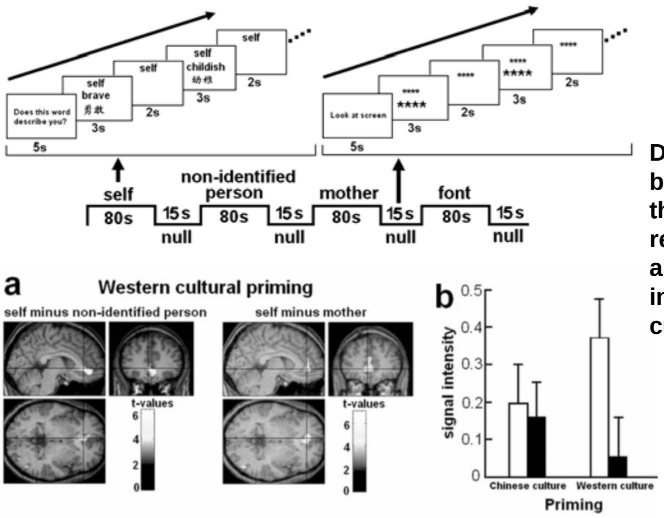
基于fMRI的心理学实验设计技术

- BLOCK design
- ER design
- Fast ER design
- 混合 design
- Natural vision design

BLOCK design



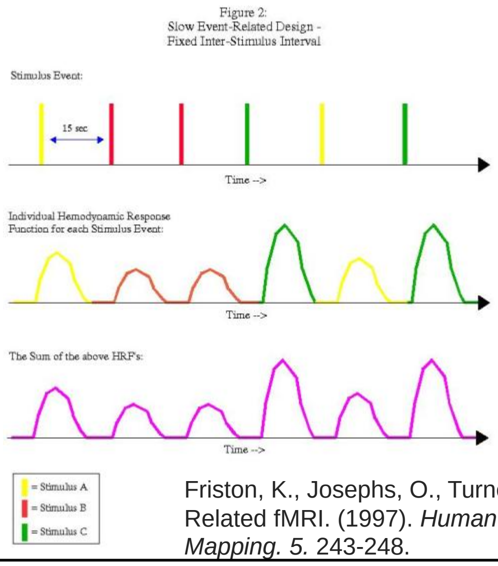
双文化脑研究中的block design



Dynamic bicultural brains: fMRI study of their flexible neural representation of self and significant others in response to culture primes

Sik Hung Ng, Shihui Han et al. 2010

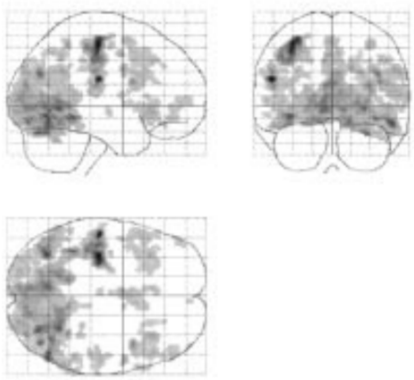
Slow ER design



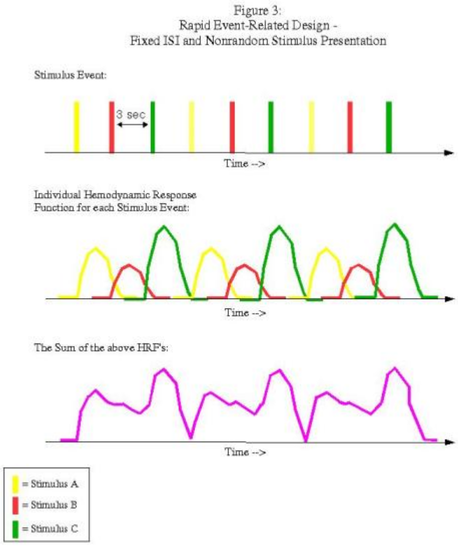
Friston, K., Josephs, O., Turner, R. Event-Related fMRI. (1997). *Human Brain Mapping. 5.* 243-248.

Words recognition study using ER fMRI

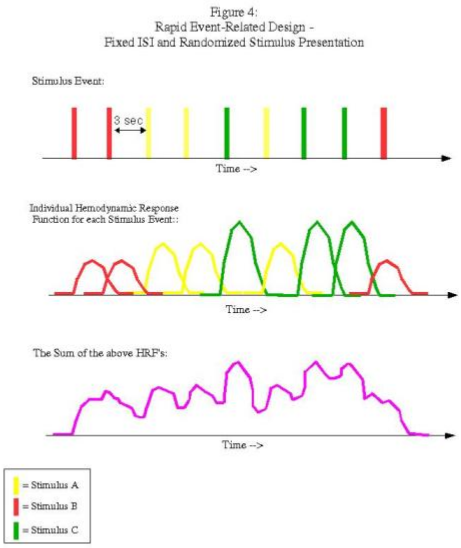
- Experiment:Words were presented every 16 s in a pseudorandom order. The subject was asked to discriminate novel from studied words by a keypress using the middle or index finger of the right hand.



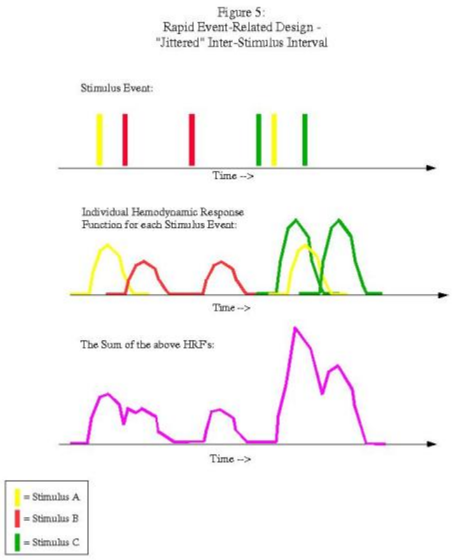
How about using Rapid ER?



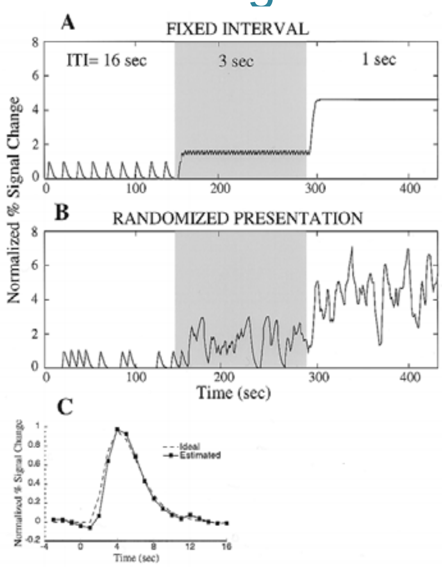
Rapid ER design with fixed ISI (inters stimulus interval)



Rapid ER design with jittered ISI



Why randomize the ISI in rapid ER design?



快速ER设计在视觉研究中的应用

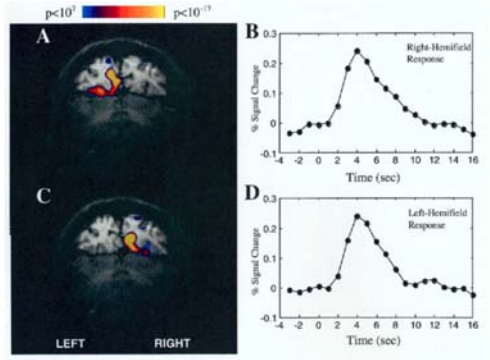
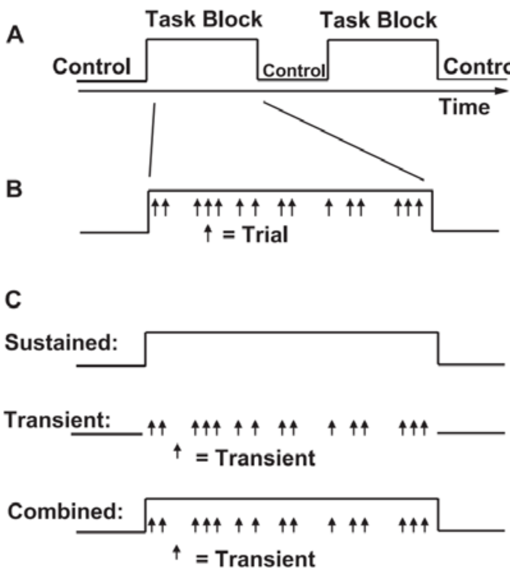


FIG. 2. Statistical parametric maps of event-related visual cortex activation and estimated hemodynamic responses for rapidly presented trials of left and right hemifield stimuli. (**A,C**) Statistical activation maps overlaid on echo-planar anatomic images. The images come from a slice through the occipital lobe, perpendicular to the calcarine sulcus. (A) Activation due to 250 ms right hemifield trials. (C) Activation due to 250 ms, left hemifield trials. (**B,D**) Averaged hemodynamic response functions computed over the statistically significant regions shown in (A) and (C). For both plots, 3 s of prestimulus baseline are plotted; the flatness of the estimated responses during the prestimulus period illustrates the effectiveness of the overlap removal. It should be noted that the original timecourses from which these responses were estimated resembled the third epoch in Fig. 1B.

Buckner, M., Burock, M., Dale, A., Rosen, B., Woldorff, M. Randomized event-related experimental designs allow for extremely rapid presentation rates using functional MRI. (1998) *NeuroReport. 19.* 3735-3739.

Mixed block/event related design

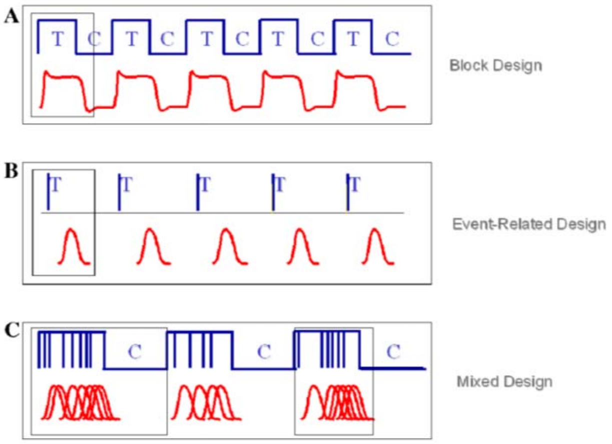



NeuroImage

Comparison of sustained and transient activity in children and adults using a mixed blocked/event-related fMRI design

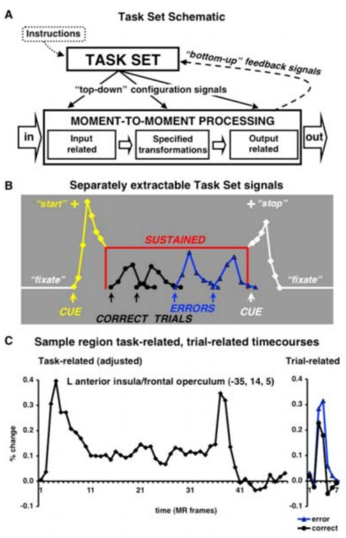
Kristin K. Wenger,[a] Kristina M. Visscher,[a] Francis M. Miezin,[a,b] Steven E. Petersen,[a,b,c,d] and Bradley L. Schlaggar[a,b,c,e,*]

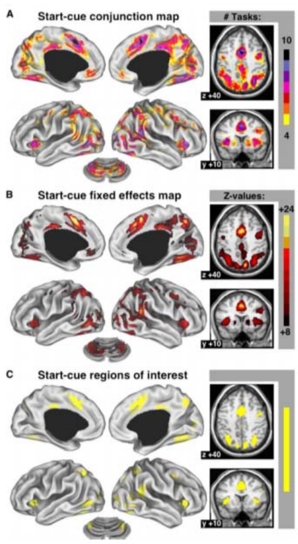
Mixed design



Amaro Jr., Gareth J. Barker, Study design in fMRI: Basic principles,Edson 2006 Brain and Cognition

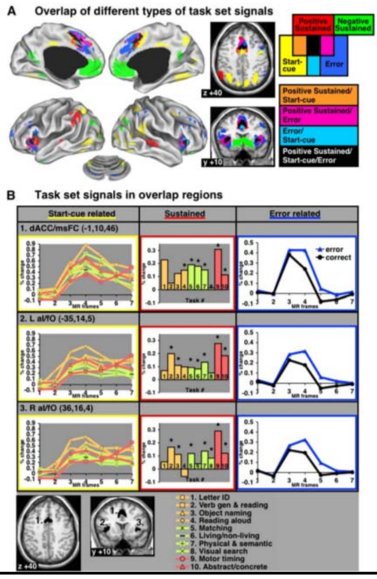
The discovery of task evoked components





Dosenbach et al., 2006

Core system for task control

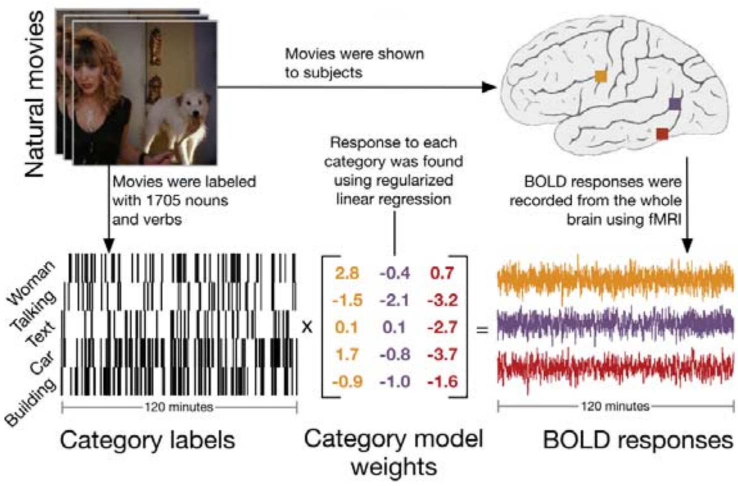


Dosenbach et al., 2006

Natural vision design

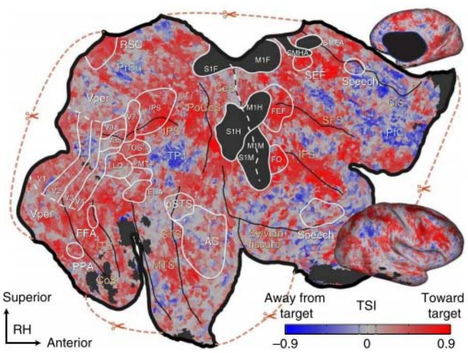
Cell PRESS

Neuron
Article

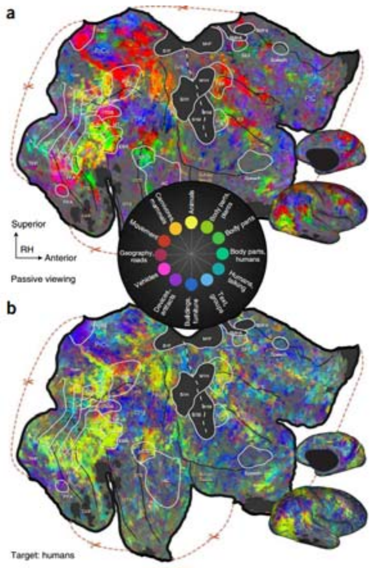


Alexander G. Huth, Shinji Nishimoto, An T. Vu, and Jack L. Gallant, （2012）A Continuous Semantic Space Describes the Representation of Thousands of Object and Action Categories across the Human Brain. Neuron

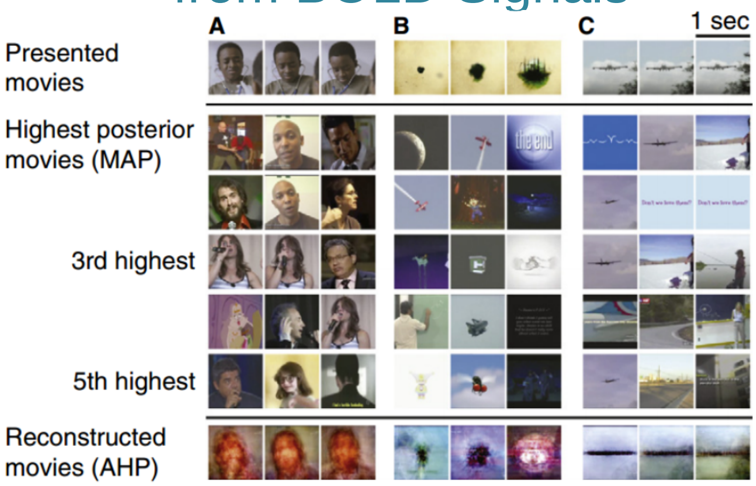
Decoding the brain based on fMRI



Tolga Çukur, Shinji Nishimoto, Alexander G Huth & Jack L Gallant (2013) Attention during natural vision warps semantic representation across the human brain, nature neuroscience



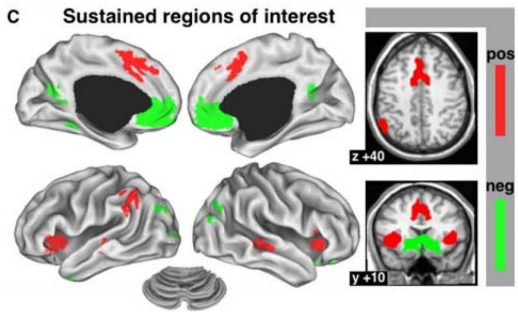
Reconstructions of Natural Movies from BOLD Signals



Shinji Nishimoto and Jack L. Gallant et al. (2011) Reconstructing Visual Experiences from Brain Activity Evoked by Natural Movies, Current Biology.

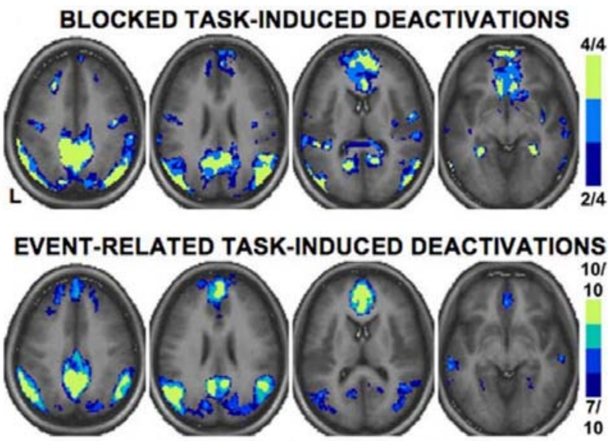
几个前沿问题

前沿问题1：神秘的负激活



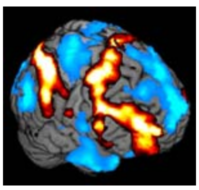
Dosenbach et al., 2006

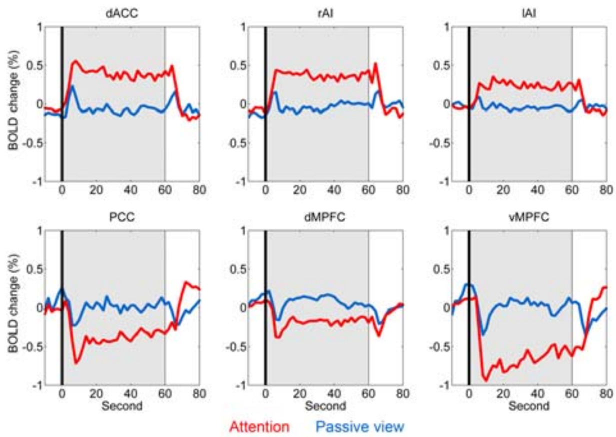
前沿问题1：神秘的负激活



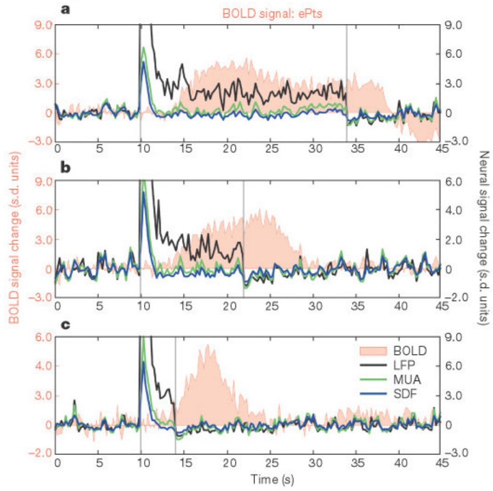
Shannon et al., 2006

Positive BOLD and negative BOLD往往同时存在





过去的研究只探讨BOLD正激活的神经解释



Logothetis et al., (2001) **Neurophysiological investigation of the basis of the fMRI signal**. Nature 412, 150-157.

- Local field potential (LPF) is strongly related to BOLD activation.
- LFP reflects the neural input to the local area rather than output.
- BOLD activation of a region is related to neural input to that region

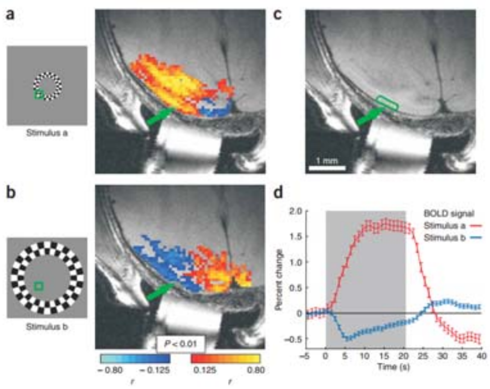
Neural basis of Negative BOLD?

- Blood stealing (?)
  - The negative BOLD signal reflects a decrease in CBF, which is likely induced by a reallocation of blood flow from the less demanding areas to the most CBF demanding regions. (Harel, et al., 2002)

Neural basis of BOLD deactivation?

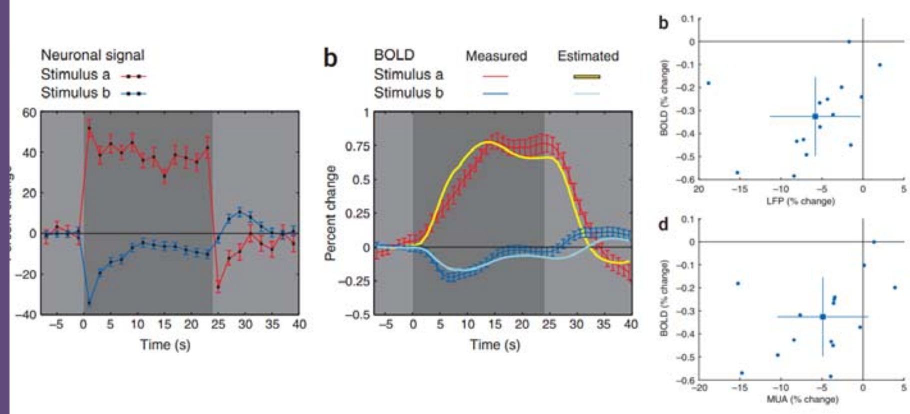
- Blood stealing (?)
- Negative BOLD responses s are related to reduced activity (?)
  - Selective to task, stimulus, and (or) response.
  - Spatial patterns show cognitive significance (Such as DMN, contralateral deactivation of motor cortex, **stimulus induced deactivation in visual cortex**)

来自视皮层的证据

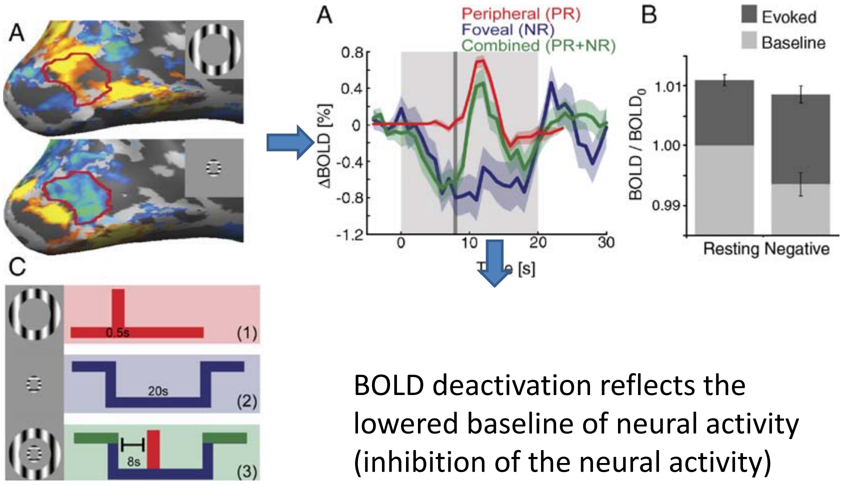


Amir Shmuel, Mark Augath, Axel Oeltermann & Nikos K Logothetis.(2006) Negative functional MRI response correlates with decreases in neuronal activity in monkey visual area V1, Nature

负激活可能和减少的神经活动有关



负激活可能表现了降低的神经活动基线（神经活动的抑制？）



BOLD deactivation reflects the lowered baseline of neural activity (inhibition of the neural activity)

Pasley BN, Inglis BA, Freeman RD (2007) Analysis of oxygen metabolism implies a neural origin for the negative BOLD response in human visual cortex.Neuroimage. 36(2):269-276.

更多的证据？？

- LFP & BOLD
- Deactivation & baseline change
- BOLD Anticorrelation
- Laminar differences of BOLD activation/deactivation

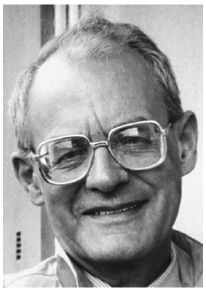
前沿问题2：自发活动和功能连接分析

- 基于fMRI的：
  - 相关分析
  - 相干分析
  - ICA分析
  - 全依赖分析

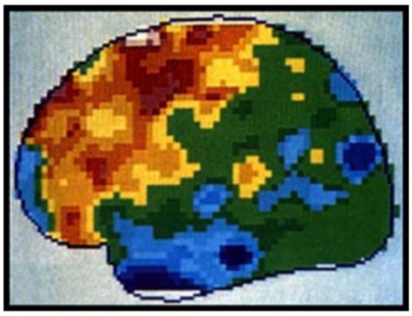
为什么大脑即使在休息的状态下依然消耗大量的能量（Dark energy of the brain，2% of the mass consumes 20% of the energy）

- David Ingva的发现

An early PET image of regional cerebral blood flow (rCBF)

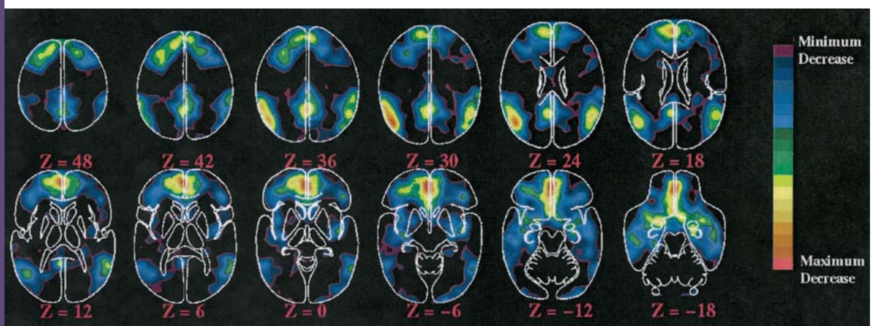


Swedish brain physiologist

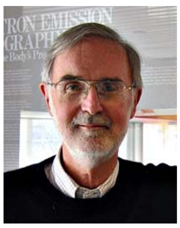


Ingvar 1979

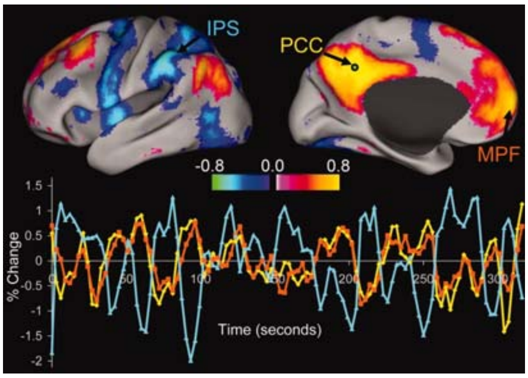
默认网络（Default Mode Network）的发现和定义



Raichle, M. E., MacLeod, A. M., Snyder, A. Z., Powers, W. J., Gusnard, D. A., et al. (2001). A default mode of brain function. Proc. Natl. Acad. Sci. U.S.A., 98, 676–82

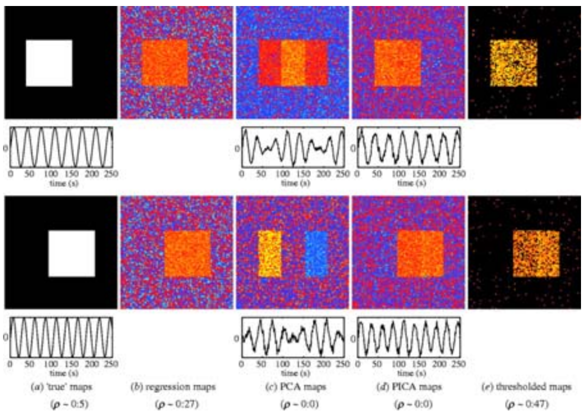


大脑的自发BOLD活动与它们之间的关系



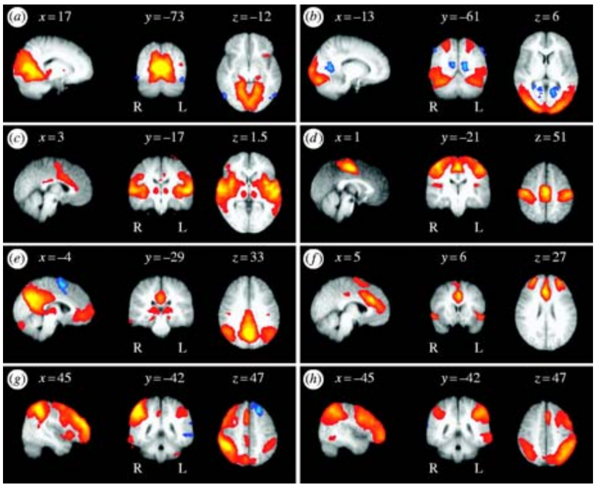
Fox et al., (2005) The human brain is intrinsically organized into dynamic, anticorrelated functional networks.PNAS

ICA和各种静息态功能网络的发现



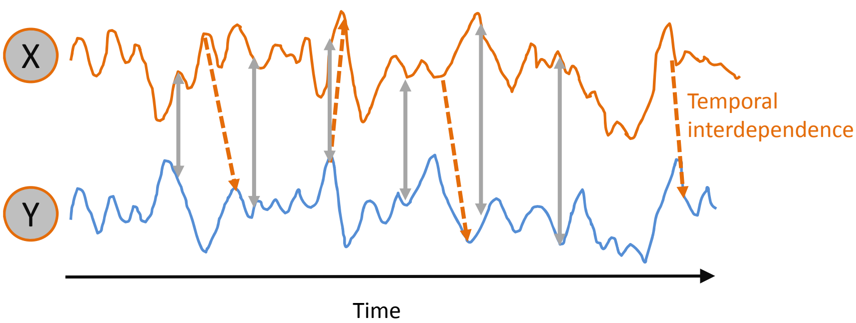
C.F. Beckmann, M. DeLuca, J.T. Devlin and S.M. Smith. Investigations into resting-state connectivity using independent component analysis Philos Trans R Soc Lond, B, Biol Sci, vol. 360 (1457):1001-13, 2005.

ICA和各种静息态功能网络的发现



功能连接分析的局限性

问题：相关分析和ICA只能检测零延迟的依赖关系。不能提供方向性信息。

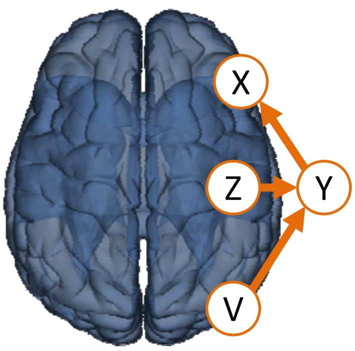


前沿问题3：有效连接分析方法

- 结构方程
- 动态因果模型 DCM
- 贝叶斯网络
- Granger 分析方法，争议与发现

Granger 分析方法，争议与发现

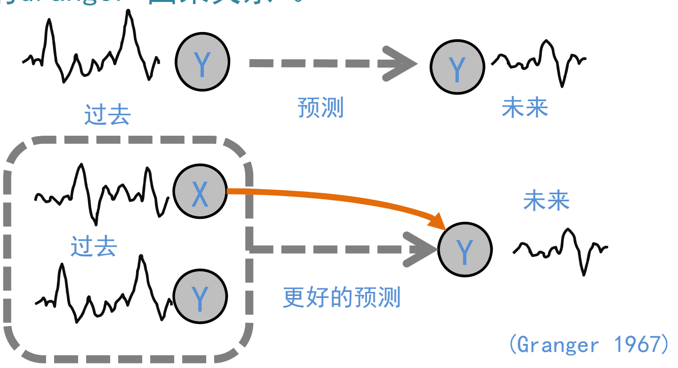
研究背景：在无损伤和无介入的条件下研究一个脑区如何对另一个脑区产生影响？



- 基于fMRI的有效连接分析
  - 模型驱动：SEM （ McIntosh and Gonzalez-Lima, 1994），DCM（ Friston et al., 2003）等
  - **数据驱动：Granger因果模型** (Ding et al., 2006)

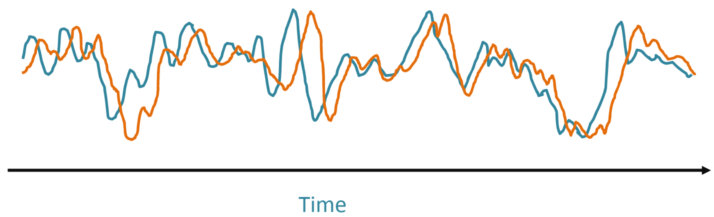
Granger 的基本原理

方法：用Granger因果模型（GC）直接测量脑区间的信息交互。原理——如果使用X和Y的历史信息比只使用Y的历史信息能更好的预测Y的未来，则称存在X→Y的Granger 因果关系 。



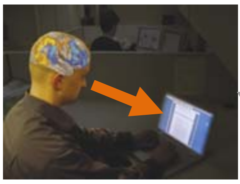
不同区域之间脑信号的Granger因果关系

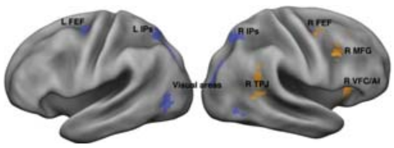
- 存在X→Y的Granger 因果关系
- 存在从X到Y的信息传递
- X的活动影响了Y的活动



注意控制网络之间的交互机制研究

背景：背侧和腹侧额顶叶注意网络（DAN和VAN）分担不同注意控制功能(Corbetta et al. 2008)，它们之间交互机制尚不清楚





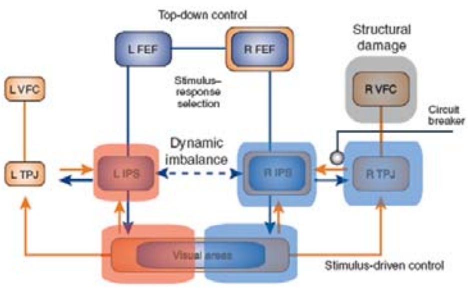
内源性的Top-down 注意控制

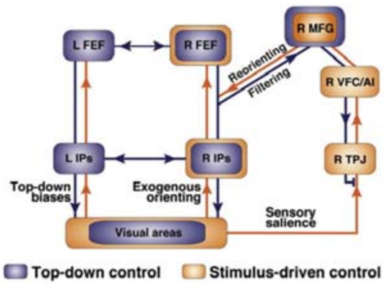
背侧注意网络
Dorsal attention network
DAN

腹侧注意网络
Ventral attention network
VAN

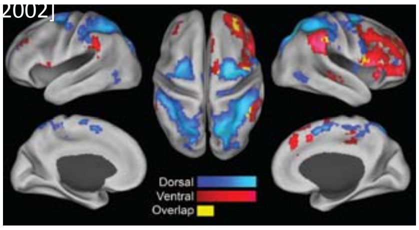
外源性的Bottom-up 干扰

理论模型



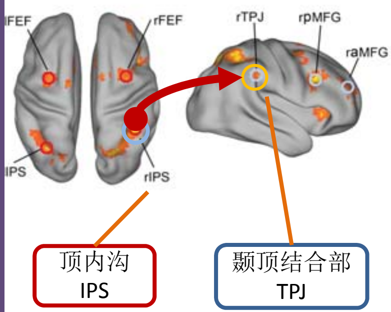


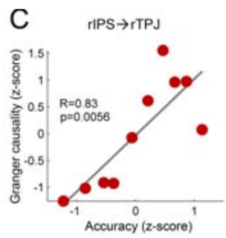
2002]



交互机制

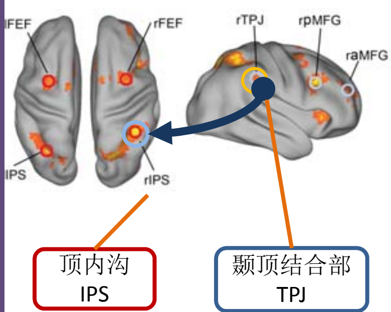
主要结果：（1）从DAN脑区到VAN脑区的GC强度和行为表现正相关，体现了增强的top-down注意控制。

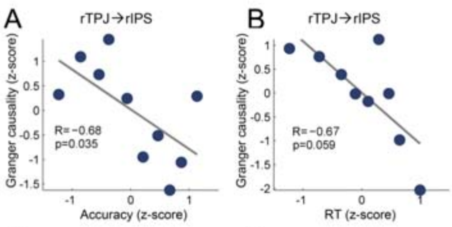




交互机制

主要结果：（2）从VAN脑区到DAN脑区的GC强度和行为表现负相关，体现了bottom-up的干扰对注意控制的削弱（验证了注意控制环路打断器假设 Corbetta et al., 2008）





研究默认网络与任务控制网络的交互机制

目的指向的认知控制

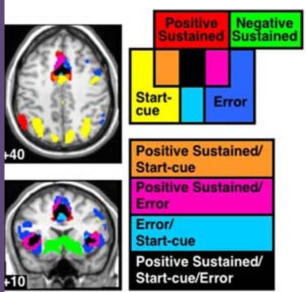
从事艰巨的任务…
注意控制…
监视行为…
解决矛盾冲突…
调节心理状态…

内部心理活动

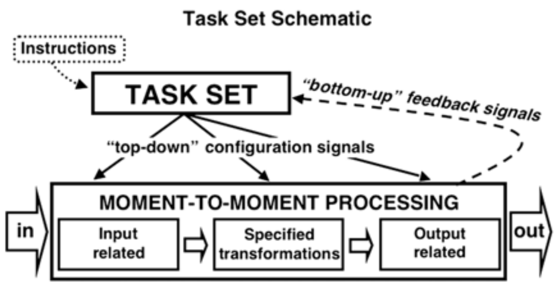
自由思想…
自我意识…
思维游走…
情绪…

理论模型和已有发现

背景：任务控制理论（或认知控制）认为任务控制网络（TCN）对额-顶叶感知觉网络进行控制，以完成需要注意的复杂认知任务。



黑色重叠区域为任务控制网络 TCN



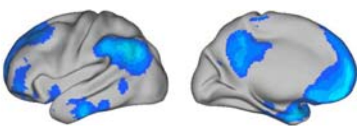
(Dosenbach et al., 2006)

理论模型和已有发现

问题：经典任务控制理论仅讨论了TCN和任务激活网络之间的交互关系，但未讨论TCN和和任务失活的默认网络（DMN）之间的交互机制。

（1）目的指向控制和内部默认心理活动之间的相互影响？

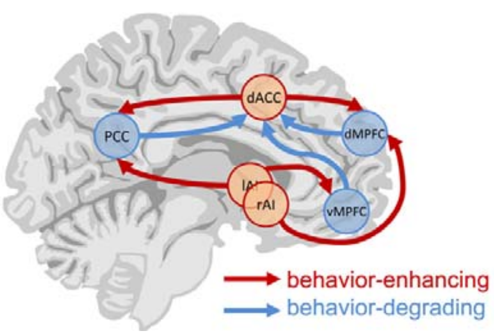
（2）认知控制受损为什么常常和默认网络活动异常密切相关 （如发育障碍、老年痴呆、酗酒、脑外伤等）

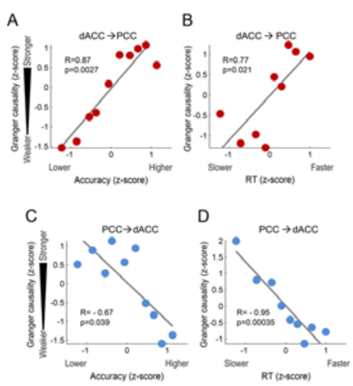


默认网络：自由思想、情绪、自我意识、思维游走
（DMN： PCC， MPFC）
(Buckner et al.， 2008)

交互机制

结果：(1)从TCN脑区到DMN脑区的GC强度和行为表现正相关. (2)从DMN脑区到TCN脑区的GC强度和行为表现负相关.



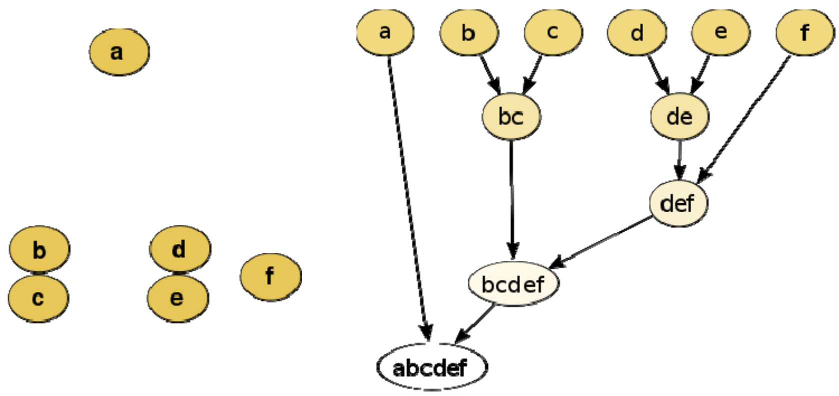


基于fMRI的大脑功能网络分析拓展

大脑功能网络分析方法学的拓展

- 聚类分析 （Clustering）
- 图论分析 （Graph theory ）

聚类分析基本原理



首先计算两个向量之间的距离

Names	Formula
Euclidean distance	$\|a-b\|_2 = \sqrt{\sum_i (a_i - b_i)^2}$
Squared Euclidean distance	$\|a-b\|_2^2 = \sum_i (a_i - b_i)^2$
Manhattan distance	$\|a-b\|_1 = \sum_i \|a_i - b_i\|$
maximum distance	$\|a-b\|_\infty = \max_i \|a_i - b_i\|$
Mahalanobis distance	$\sqrt{(a-b)^\top S^{-1}(a-b)}$ where S is the Covariance matrix

然后根据距离和特定的准则将向量聚合

- The maximum distance between elements of each cluster (also called complete-linkage clustering):

$$\max\{\, d(x,y) : x \in \mathcal{A},\, y \in \mathcal{B}\,\}.$$

- The minimum distance between elements of each cluster (also called **single-linkage** clustering):

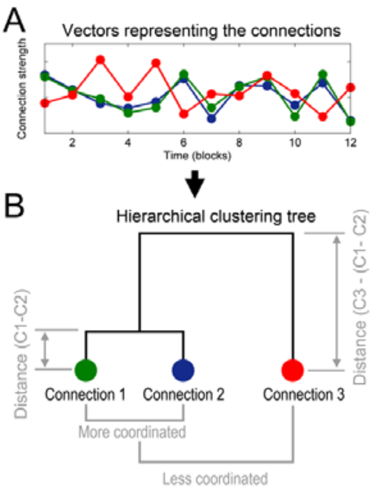
$$\min\{\, d(x,y) : x \in \mathcal{A},\, y \in \mathcal{B}\,\}.$$

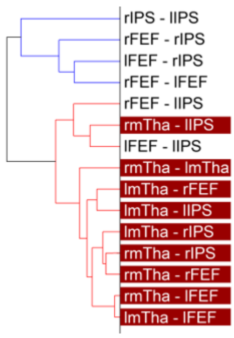
- The mean distance between elements of each cluster (also called **average linkage clustering**）；

$$\frac{1}{|\mathcal{A}| \cdot |\mathcal{B}|} \sum_{x \in \mathcal{A}} \sum_{y \in \mathcal{B}} d(x,y).$$

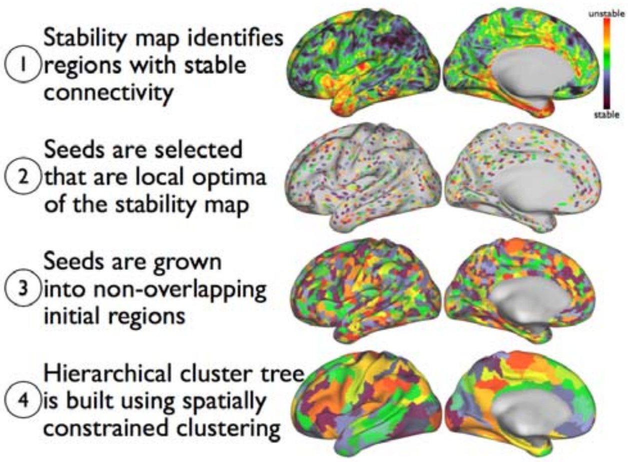
- The sum of all intra-cluster variance.
- The increase in variance for the cluster being merged (**The minimum variance criterion**, or **Ward's method**)

Clustering the brain activities



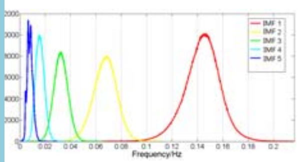


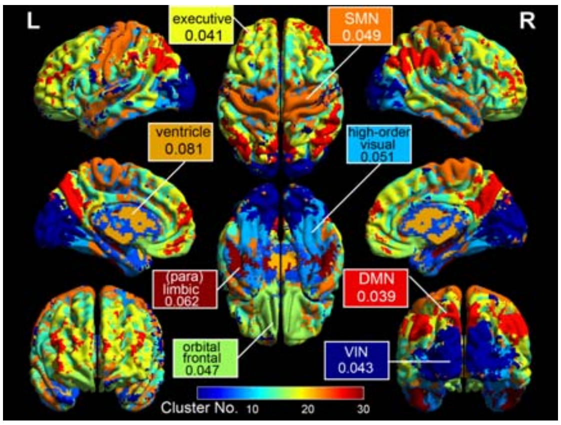
Hierarchical parcellation of the brain



Thomas Blumensath et al., (2013) Spatially constrained hierarchical parcellation of the brain with resting-state FMRI. NeuroImage

Clustering analysis based on frequency characteristic of the fMRI signal





Song et al., (2014) Frequency Specificity of Regional Homogeneity in the Resting-State Human Brain

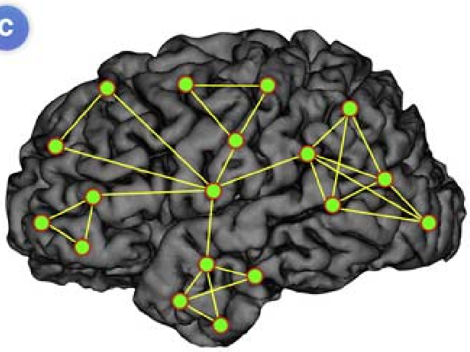
用图论分析研究大脑功能网络的组织方式

- Both functional and structural data show that the human brain forms integrative complex network(s), linking all brain regions and sub-networks together into one complex system.

- Graph theory provides a theoretical framework in which the topology of complex networks can be examined, and can reveal important information about both the local and global organization of functional brain networks.

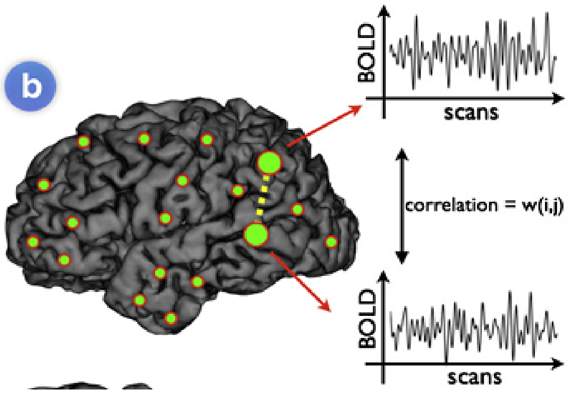
Graph Theory

- Using graph theory：
- **G=(V,E)**
- G：graph
  V： the collection of nodes reflecting the brain regions；
  E： the functional connections between these brain regions.



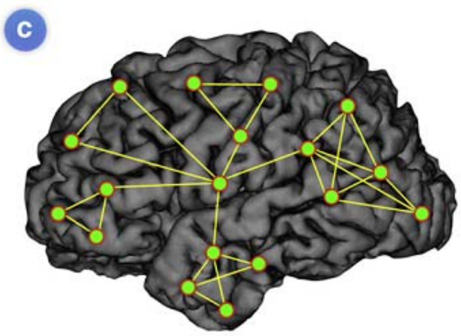
Nodes：cortical regions

Graph Theory



The existence of a connection between two points can be defined as whether their level of functional connectivity exceeds a certain predefined threshold.

Graph Theory



1.Computing the level of functional connectivity between all possible node-pairs；

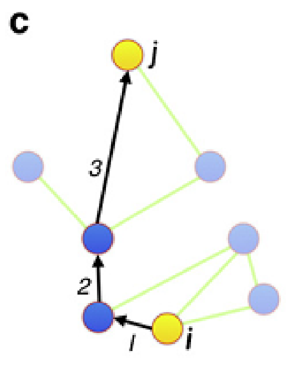
2.Determining the existence of a functional connection by using a predefined cut-off threshold or by using a weighted approach；

3.Using graph theory organize a graph representing the functional brain network.

Properties of complex networks

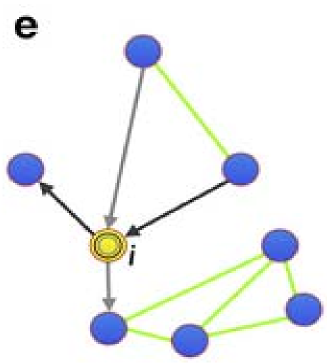
- Clustering-coefficient (聚合系数)
- Characteristic path length (特征路径长度)
- Node degree (节点度)
- Centrality (中心性)
- Modularity (模块性)

characteristic path length (特征路径长度)



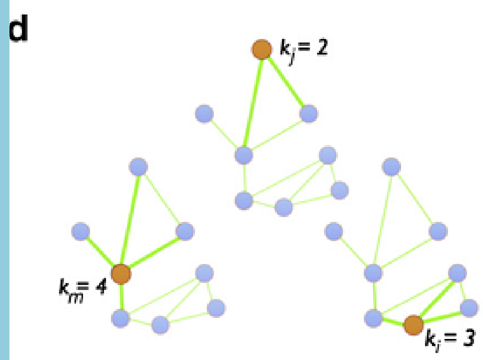
- The characteristic path length of node i provides information about how close node i is connected to all other nodes in the network
- Distance d (I , j) between node i and all other nodes j in the network. Distance d(I , j) can be defined as the number of connections that have to be crossed to travel from node i to node j in the graph.
- Characteristic path length L provides important information about the level of global communication efficiency of a network.

Node degree (节点度)



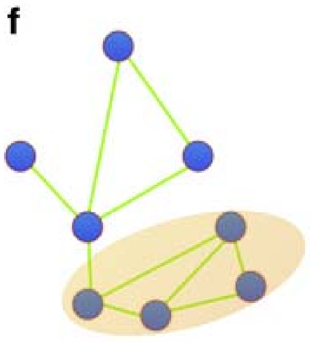
- The degree of node i is defined as its total number of connections.

Centrality (中心性)



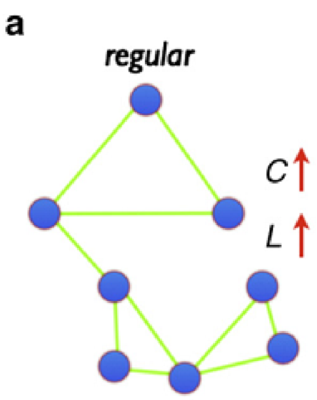
- The level of centrality of a node i indicates how many of the shortest paths between the nodes of the network pass through node i.
- A high centrality indicates that this node is important in interconnecting the nodes of the network, marking a potential hub role of this node in the overall network.

Modularity (模块性)



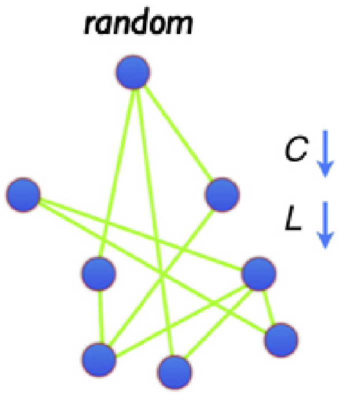
- The modularity of a graph describes the possible formation of communities in the network, indicating how strong groups of nodes form relative isolated sub-networks within the full network.

Regular network



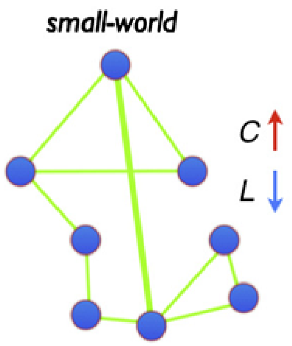
- A regular network has a rather local character,
- high clustering-coefficient (C)
- high path length (L)
- taking a large number of steps to travel from a specific node to a node on the other end of the graph.

Random network



- All connections randomly across the network.
- Low C
- Low L

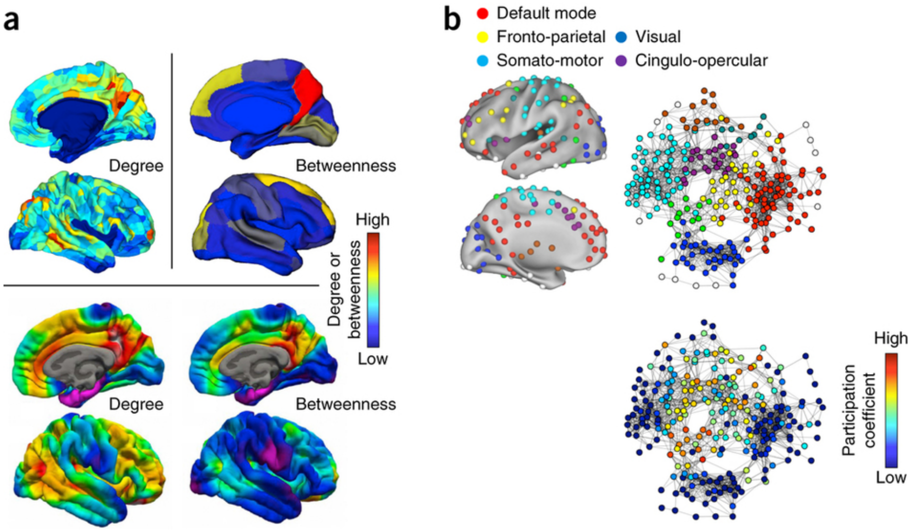
Small word network



- A **small-world network** is a type of mathematical graph in which most nodes are not neighbors of one another, but most nodes can be reached from every other by a small number of hops or steps.

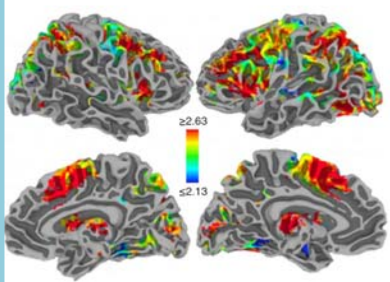
- High C
- Relatively short length

大脑的功能网络是小世界网络么？



结构连接网络

功能连接网络

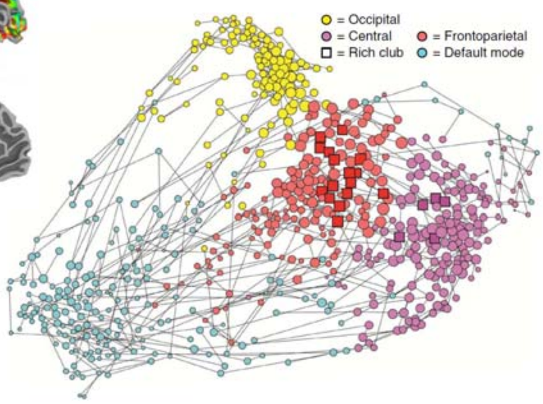


REVIEW

nature neuroscience

Contributions and challenges for network models in cognitive neuroscience

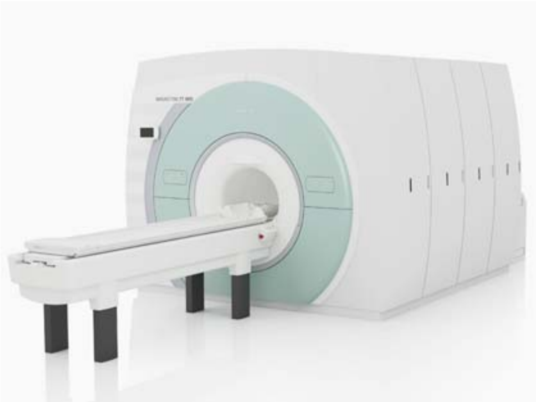
Olaf Sporns



- Graph analysis of resting-state time-series have suggested an efficient organization of functional communication in the brain network, indicating that the human brain is not just a random network, but one with an organization optimized towards a high level of local and global efficiency.

fMRI的未来

超高场MRI的出现



MAGNETOM 7T is a powerful solution for visualizing anatomical detail and functional information as never before – supporting neurosciences and clinical research with ultra-deep insights.

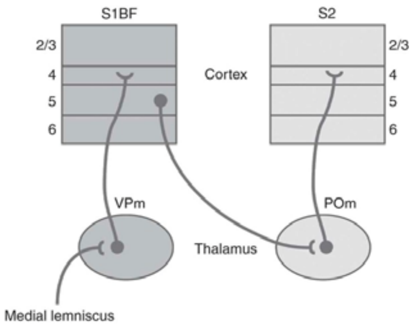
超高场fMRI的意义

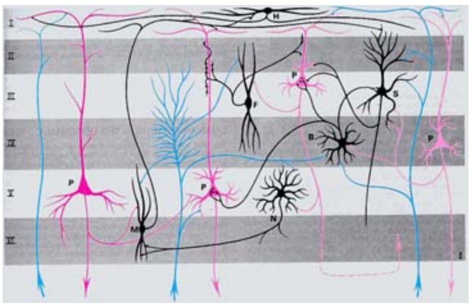
- B0的增大可以提高fMRI的空间分辨率和时间分辨率。
- 超高场fMRI将给基于fMRI时间序列的数据分析带来新的机遇和挑战。
- 人们将对认知系统的信号处理理论倾向和联接主义理论倾向具备更深刻的理解。

High-Resolution fMRI Reveals Laminar Differences in Neurovascular Coupling between Positive and Negative BOLD Responses

Jozien Goense,
Hellmut Merkle,
Nikos K. Logothetis.
Neuron 2012

Background

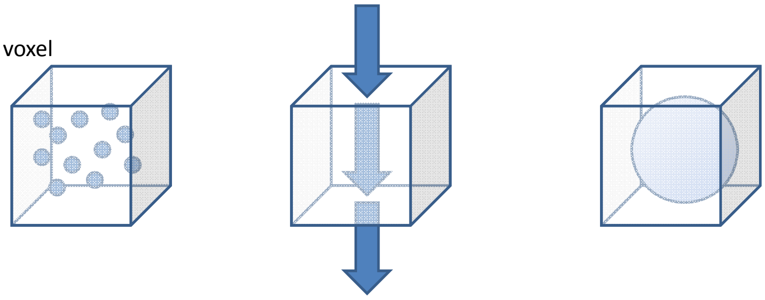




This work aimed to investigate the laminar difference of neurovascular coupling (BOLD, CBF, CBV) using high spatial resolution fMRI.

Method

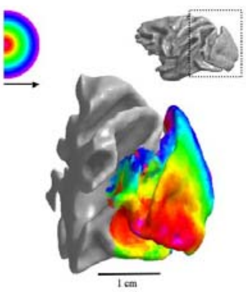
A voxel



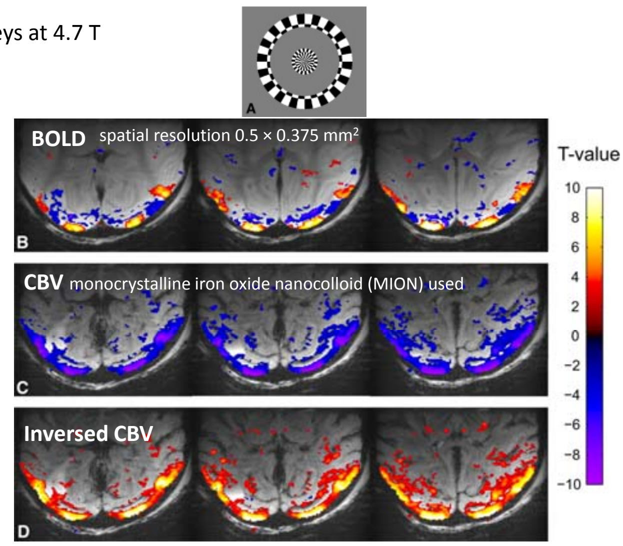
Blood Oxygen Level Dependence	Cerebral Blood Flow	Cerebral Blood Volume
BOLD	**CBF**	**CBV**
Energy consumption in the voxel	How fast the blood is refreshed in the voxel	The mass of the blood in the voxel
fMRI	fMRI, PET.	fMRI, PET.
	Agent injection needed.	Agent injection needed.

Experiment and results

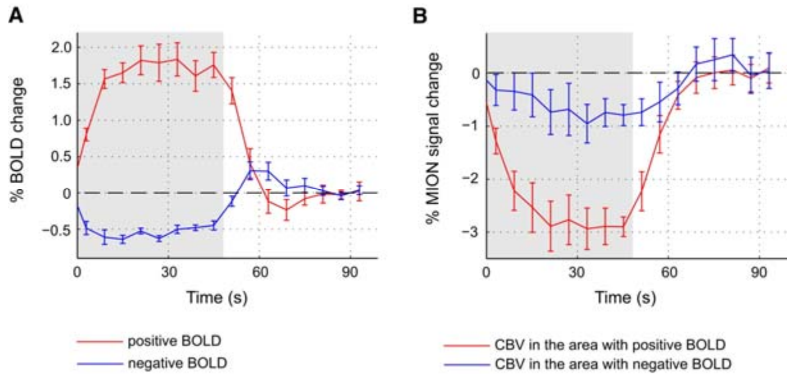
Eight anesthetized monkeys at 4.7 T

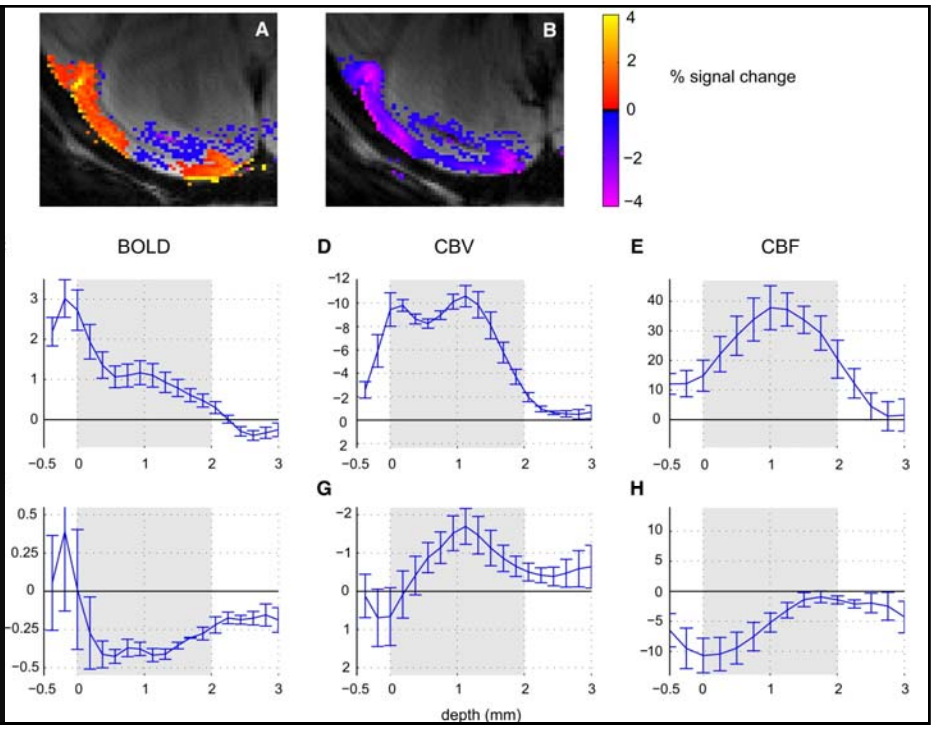


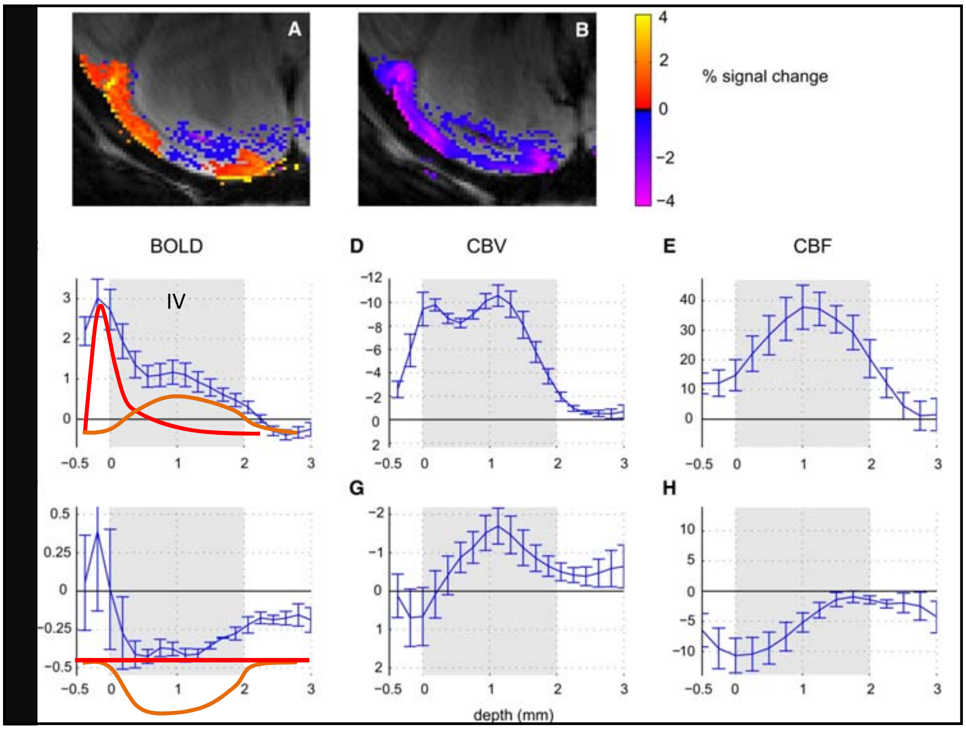
Retinotopic mapping

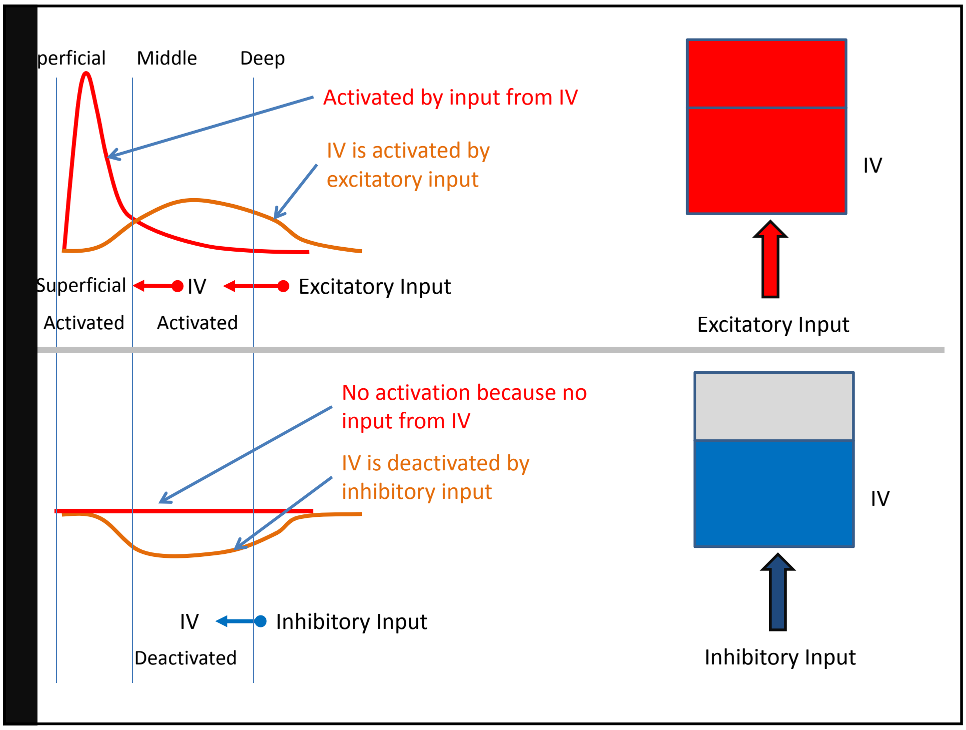


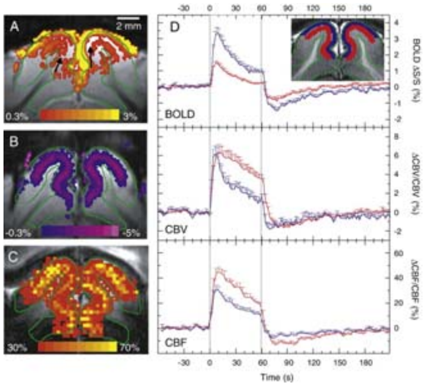
Overall activation/deactivaiton

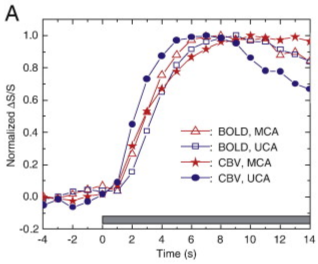





A
B
% signal change
BOLD
IV
D
CBV
E
CBF
G
H
depth (mm)


perficial
Middle
Deep
Activated by input from IV
IV is activated by
excitatory input
Superficial
IV
Excitatory Input
Activated
Activated
IV
Excitatory Input
No activation because no
input from IV
IV is deactivated by
inhibitory input
IV
Inhibitory Input
Deactivated
IV
Inhibitory Input



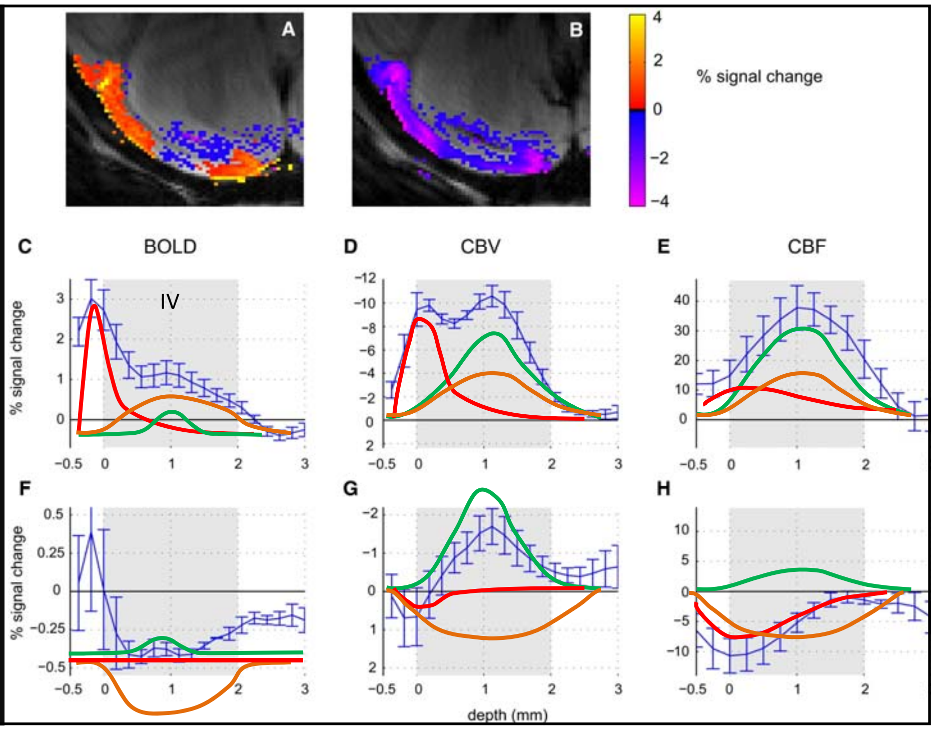


Jin and Kima 2008

Cortical layer-dependent dynamic blood oxygenation, cerebral blood flow and cerebral blood volume responses during visual stimulation

MCA: middle cortical area

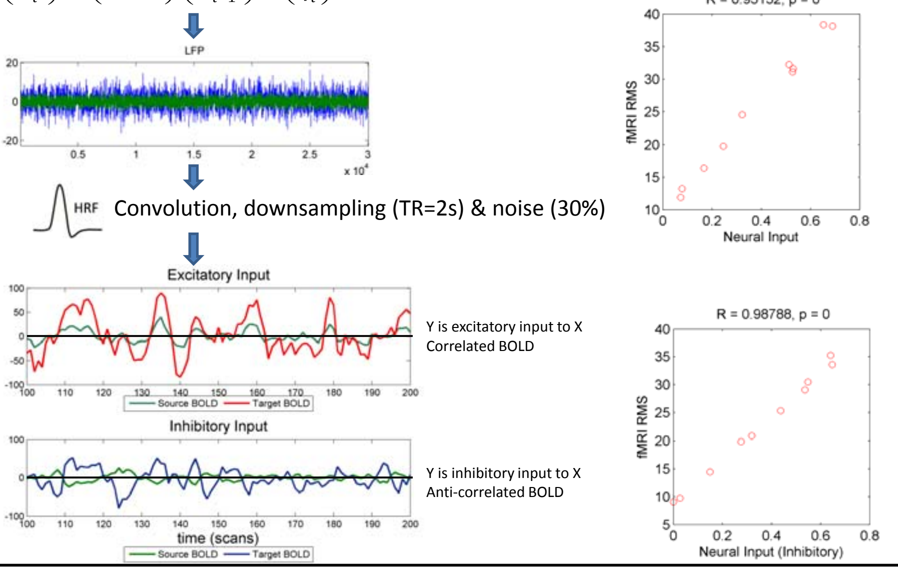
UCA: upper cortical area

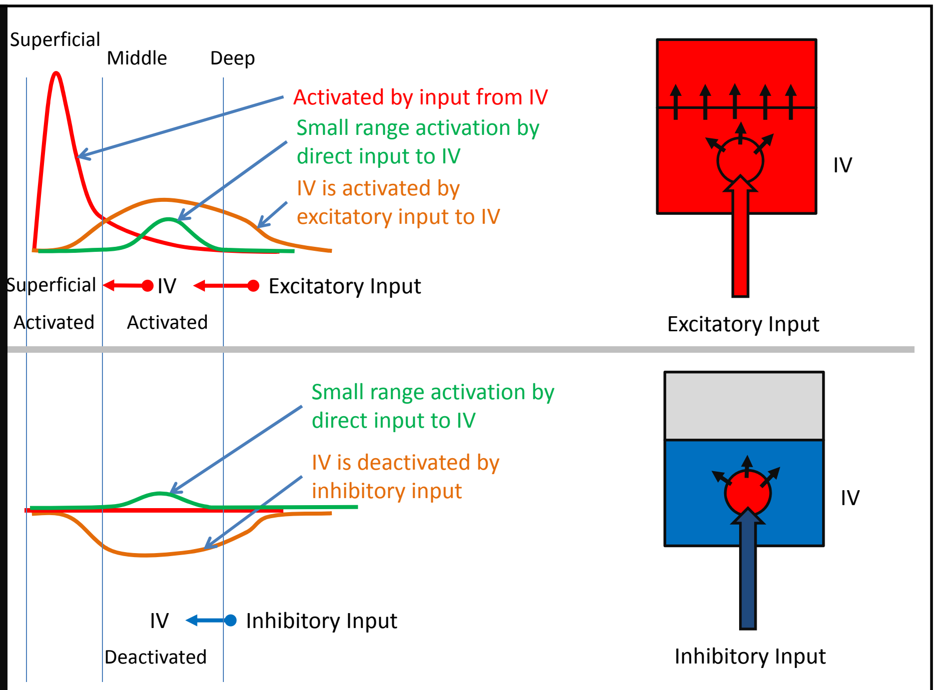


Neural signal of X may have negative impact to neural signal and BOLD of Y

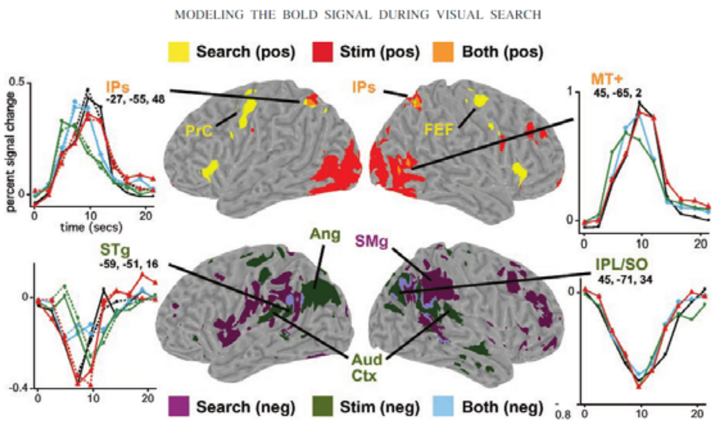
$$\begin{pmatrix} X_t \\ Y_t \end{pmatrix} = \begin{pmatrix} a & b \\ 0 & d \end{pmatrix} \begin{pmatrix} X_{t-1} \\ Y_{t-1} \end{pmatrix} + \begin{pmatrix} \varepsilon_t \\ \eta_t \end{pmatrix}$$

b>0; Y is an excitatory input to X
b<0; Y is an inhibitory input to X

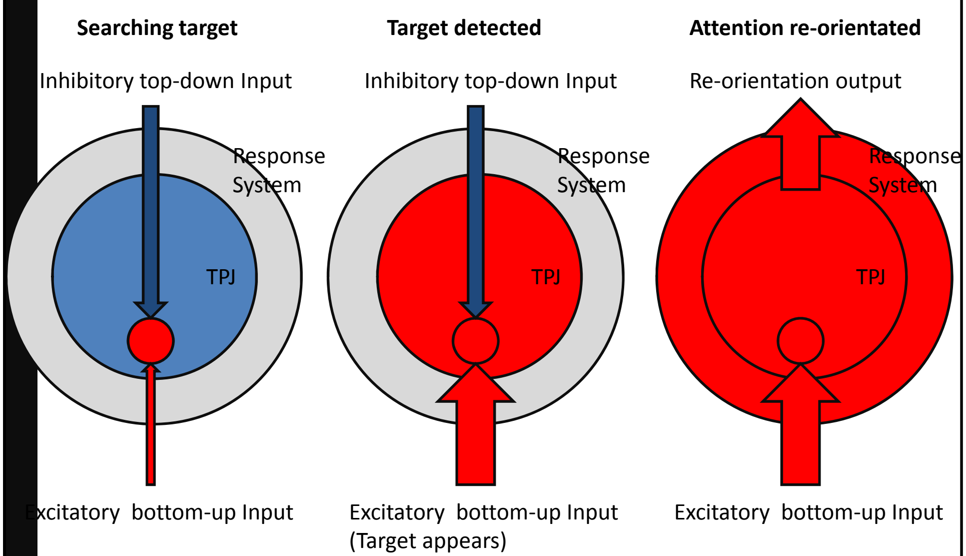


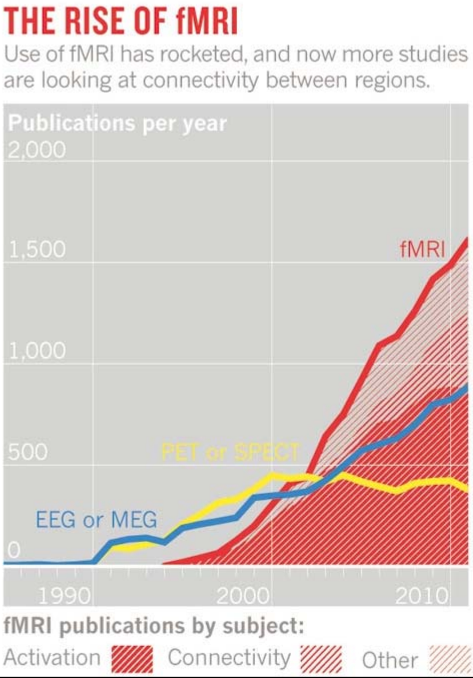


超高场空间分辨率带来的好处



Shulman GL, Astafiev SV, McAvoy MP, Davossa G, Corbetta M (2007) **Right TPJ deactivation during visual search: Functional significance and support for a filter hypothesis.**




THE RISE OF fMRI
Use of fMRI has rocketed, and now more studies are looking at connectivity between regions.
Publications per year
2,000
1,500
1,000
500
0
fMRI
PET or SPECT
EEG or MEG
1990
2000
2010
fMRI publications by subject:
Activation
Connectivity
Other


谢谢！