Magnetic Resonance Imaging of Human Brain Function: Methods, Issues, and Opportunities

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Unit on Functional Imaging Methods

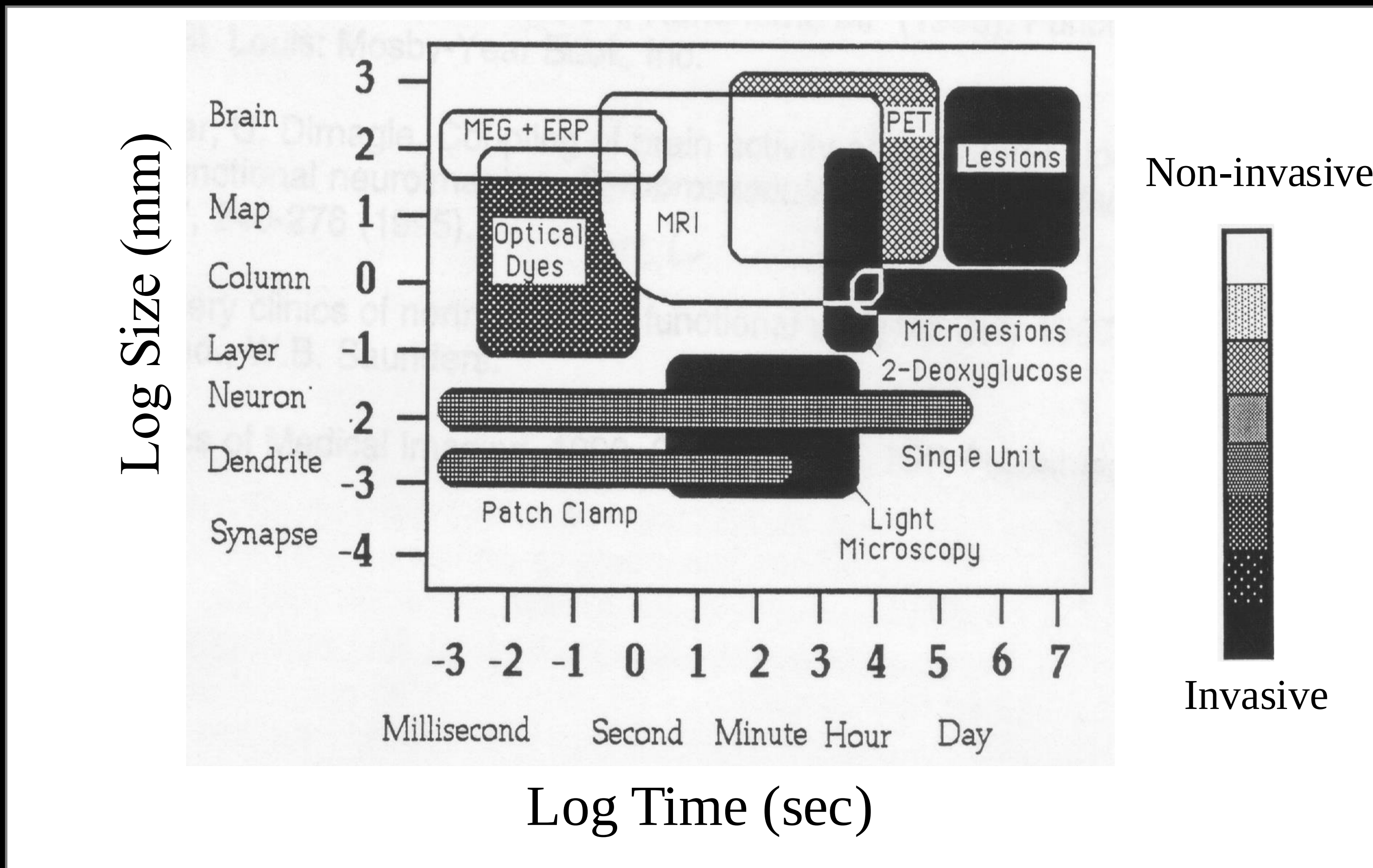
&

Functional MRI Facility

Laboratory of Brain and Cognition

National Institute of Mental Health

Functional Neuroimaging Techniques

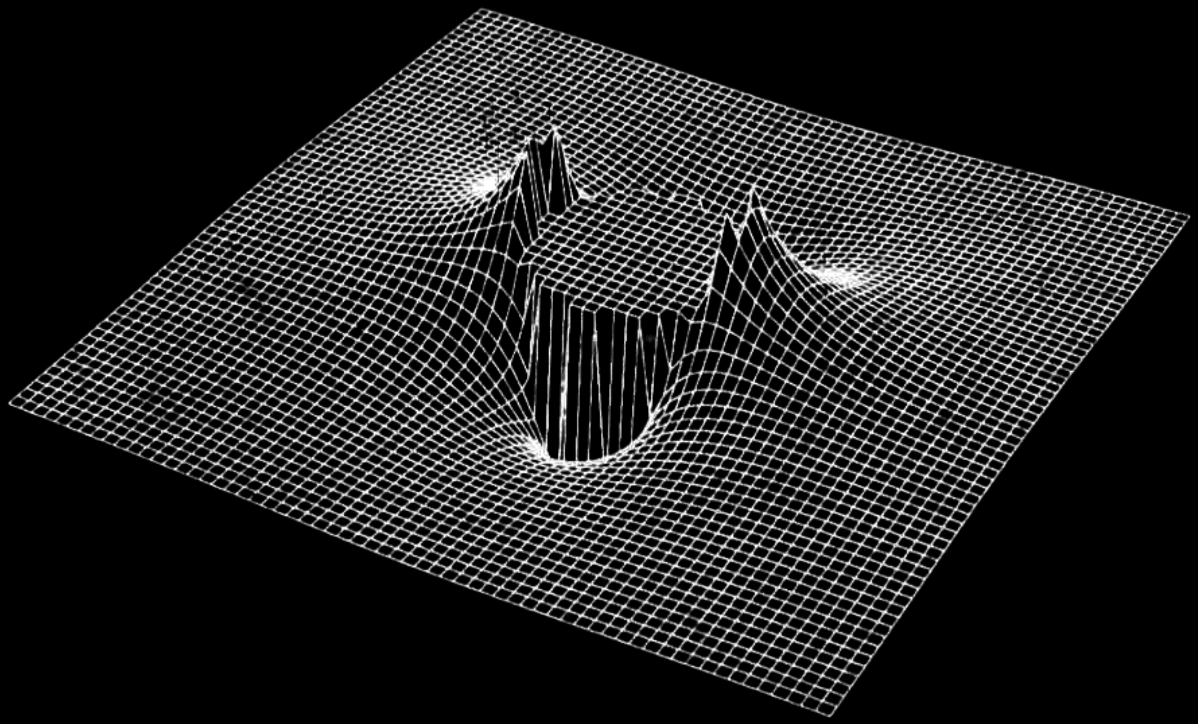


Types of Functional MRI Contrast

- Blood Volume
- BOLD
- Perfusion
- $CMRO_2$

Bulk Susceptibility Contrast

Susceptibility-Induced Field Distortion in the Vicinity of a Microvessel ⊥ to B_O.



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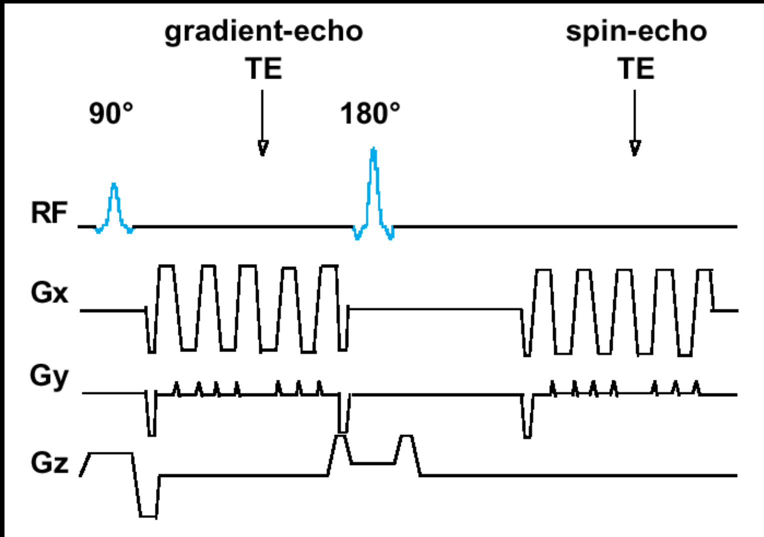
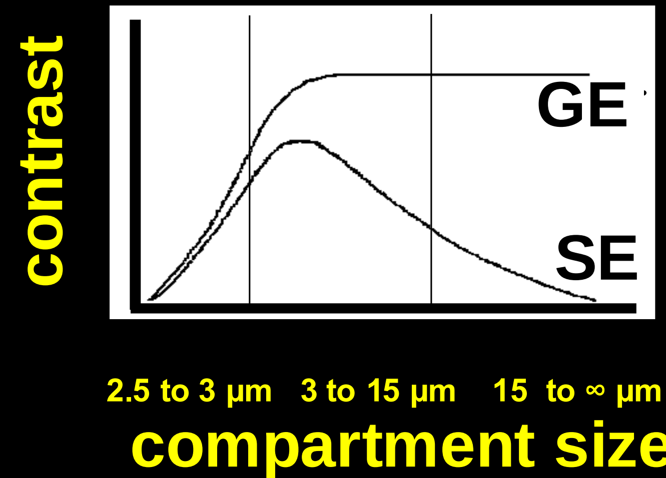
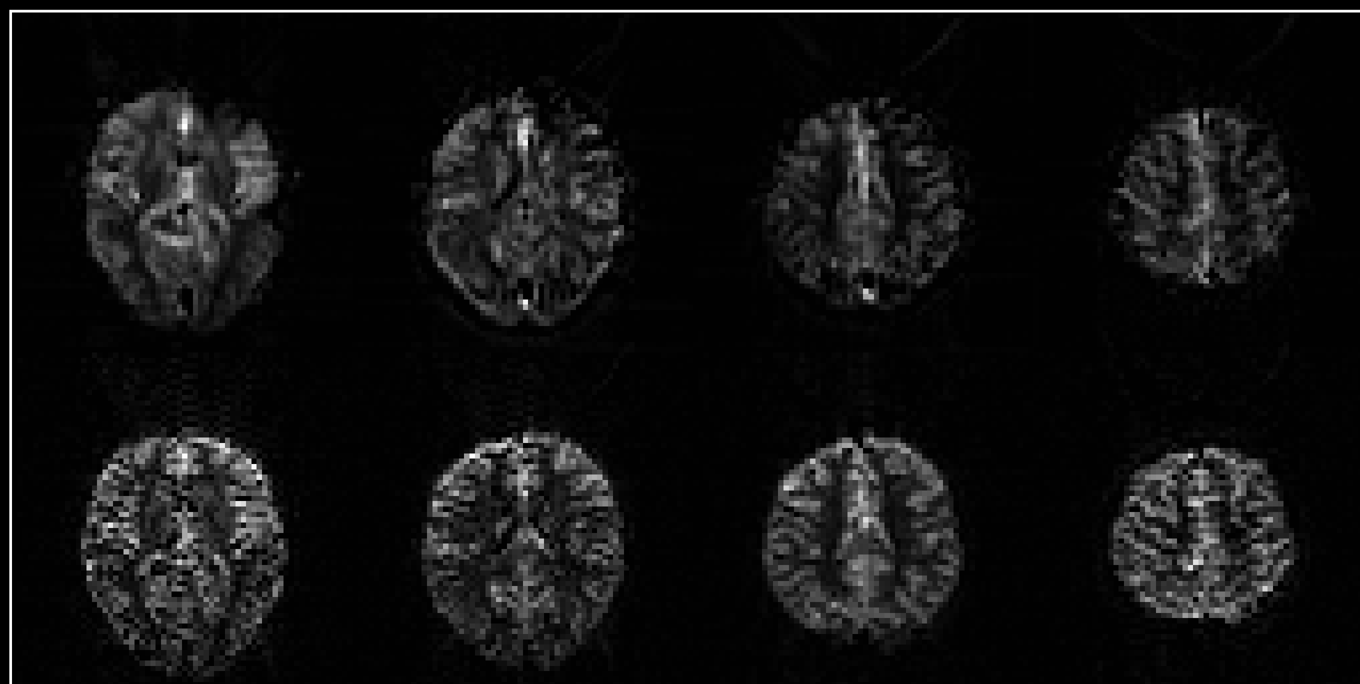




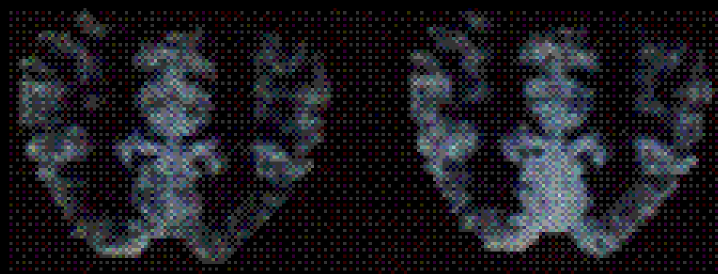
GE
TE = 30 ms

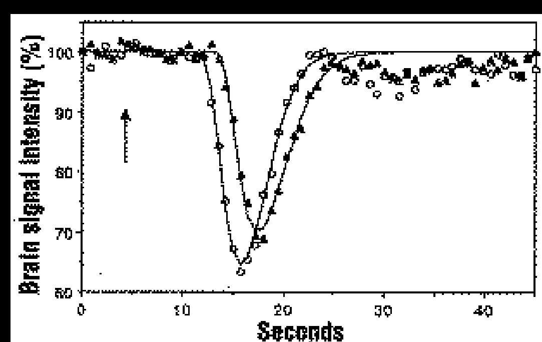
SE
TE = 110 ms

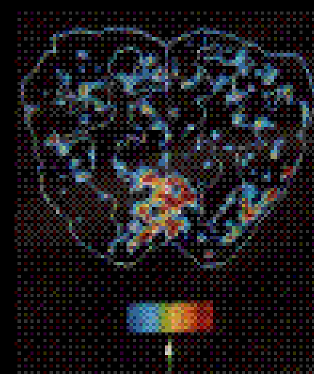


Activation-Induced Blood Volume Change

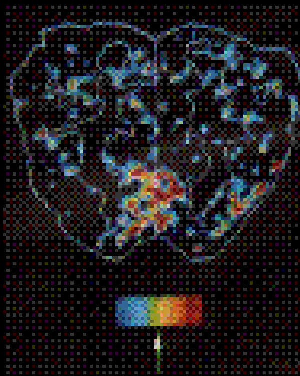
Resting Active

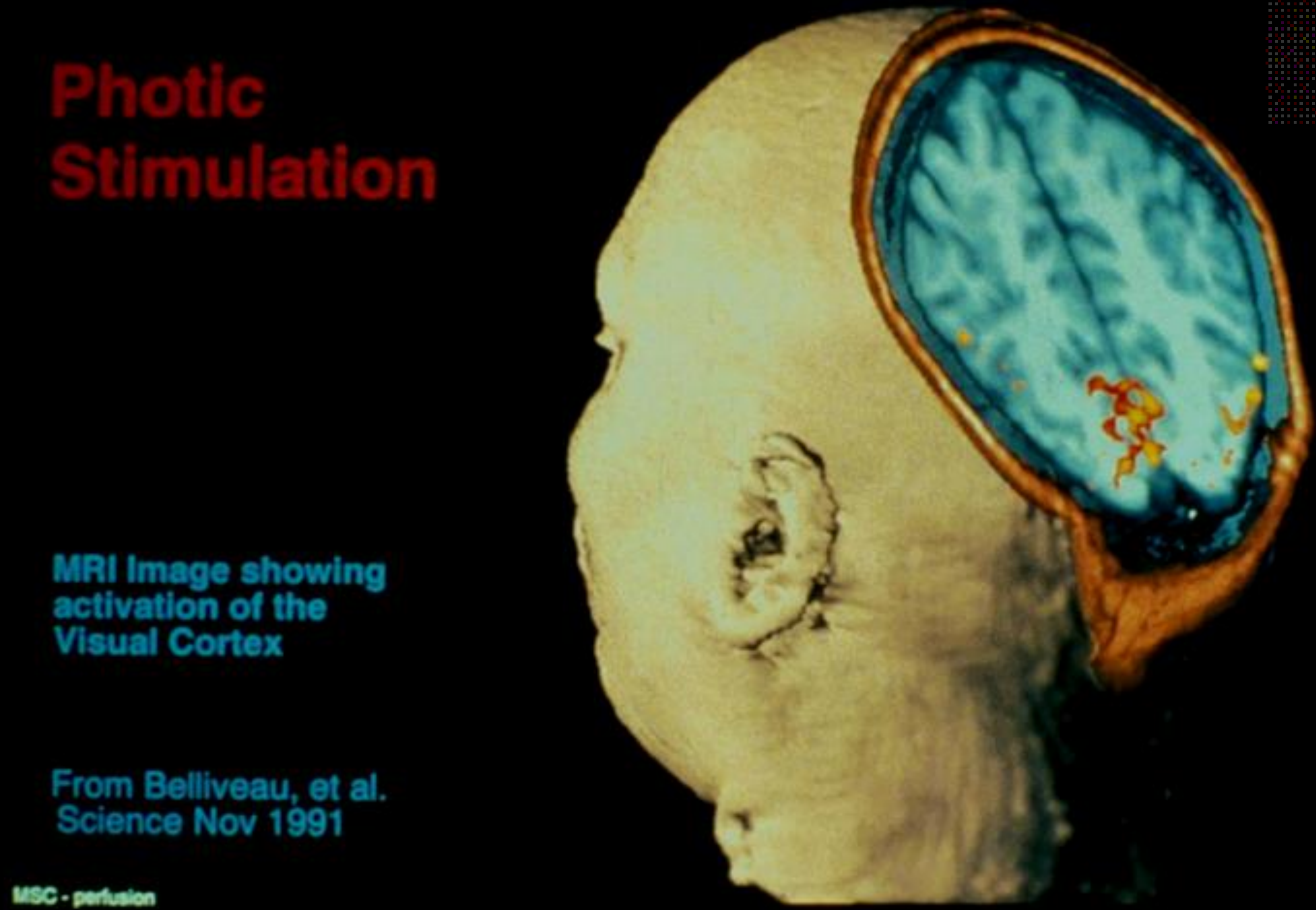






Blood Volume





Types of Functional MRI Contrast

- Blood Volume
- BOLD
- Perfusion
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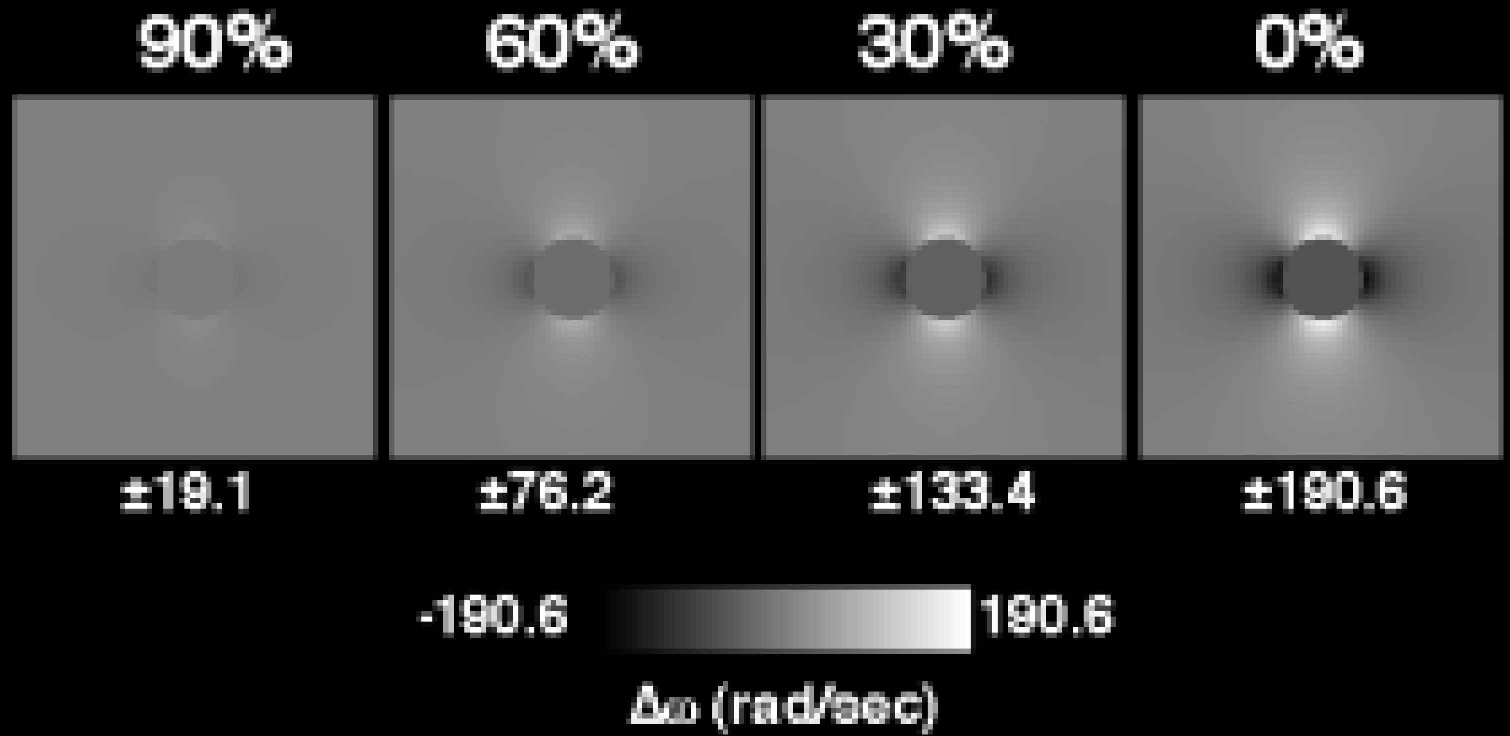
L. Pauling, C. D. Coryell, (1936) "The magnetic properties and structure of hemoglobin, oxyhemoglobin, and carbonmonoxyhemoglobin." Proc.Natl. Acad. Sci. USA 22, 210-216.

Thulborn, K. R., J. C. Waterton, et al. (1982)."Oxygenation dependence of the transverse relaxation time of water protons in whole blood at high field." Biochim. Biophys. Acta. 714: 265-270.

S. Ogawa, T. M. Lee, A. R. Kay, D. W. Tank, (1990) "Brain magnetic resonance imaging with contrast dependent on blood oxygenation." Proc. Natl. Acad. Sci. USA 87, 9868-9872.

R. Turner, D. LeBihan, C. T. W. Moonen, D. Despres, J. Frank, (1991). Echo-planar time course MRI of cat brain oxygenation changes. Magn. Reson. Med. 27, 159-166.

Δ O_2 saturation



BOLD Contrast in the Detection of Neuronal Activity

Cerebral Tissue Activation

↓

Local Vasodilation

↓

Increase in Cerebral Blood Flow and Volume → **Oxygen Delivery Exceeds Metabolic Need**

↓

Increase in Capillary and Venous Blood Oxygenation

↓

Decrease in Deoxy-hemoglobin

Deoxy-hemoglobin: paramagnetic
Oxy-hemoglobin: diamagnetic

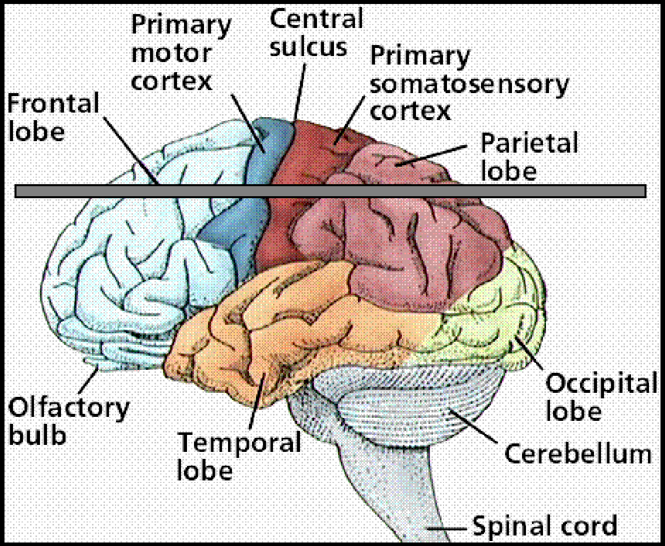
↓

Decrease in susceptibility-related intravoxel dephasing → **Increase in T2 and T2***

↓

Local Signal Increase in T2 and T2* - weighted sequences

Alternating Left and Right Finger Tapping



~ 1992

K. K. Kwong, et al, (1992) "Dynamic magnetic resonance imaging of human brain activity during primary sensory stimulation." Proc. Natl. Acad. Sci. USA. 89, 5675-5679.

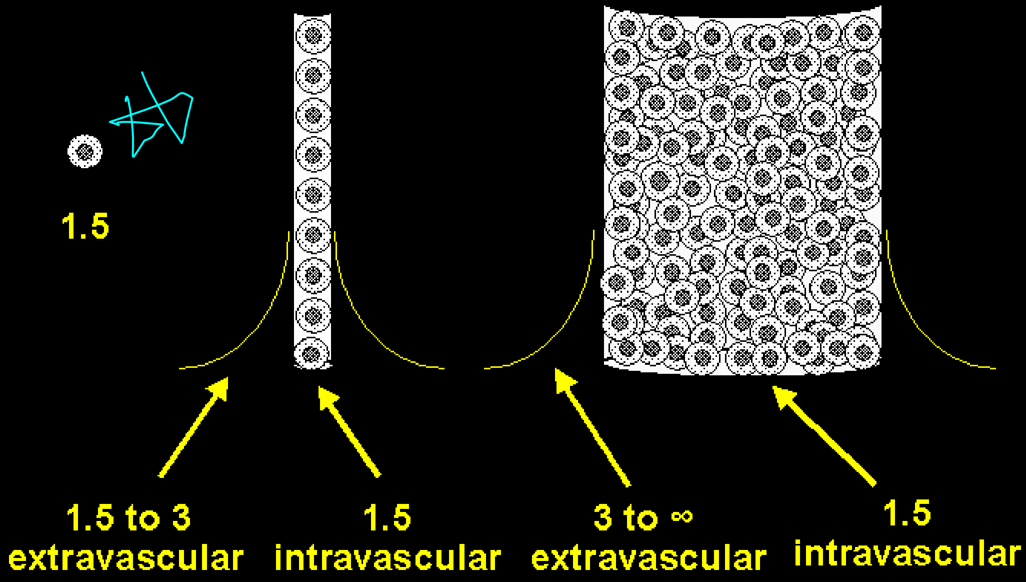
S. Ogawa, et al., (1992) "Intrinsic signal changes accompanying sensory stimulation: functional brain mapping with magnetic resonance imaging. Proc. Natl. Acad. Sci. USA." 89, 5951-5955.

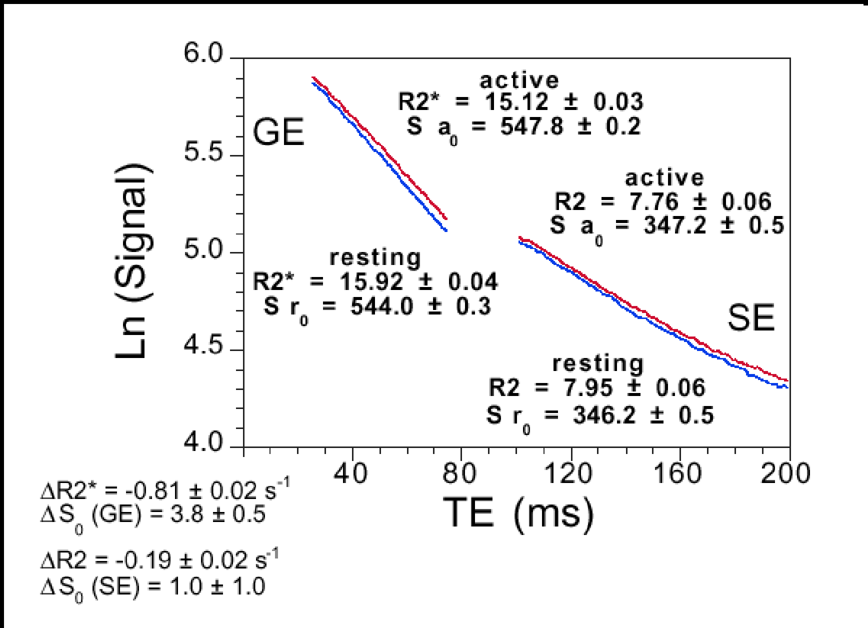
P. A. Bandettini, et al., (1992) "Time course EPI of human brain function during task activation." Magn. Reson. Med 25, 390-397.

Blamire, A. M., et al. (1992). "Dynamic mapping of the human visual cortex by high-speed magnetic resonance imaging." Proc. Natl. Acad. Sci. USA 89: 11069-11073.

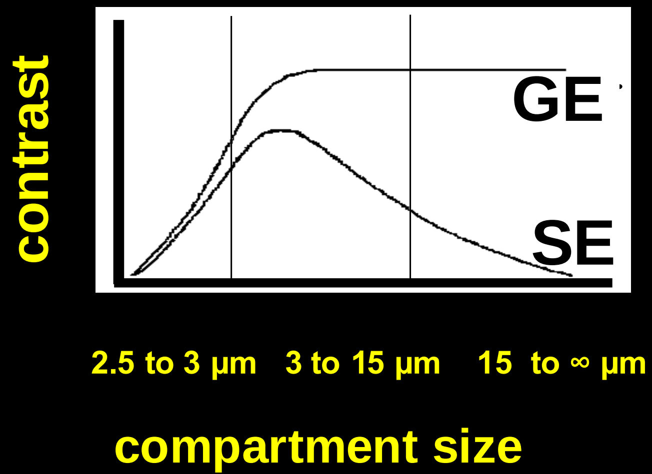
Correlation analysis, Fourier analysis, t-test, f-test…

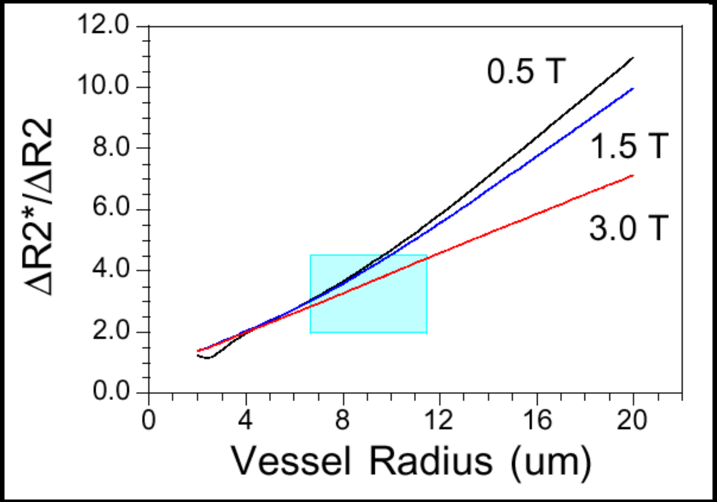
$\Delta R2^* / \Delta R2$

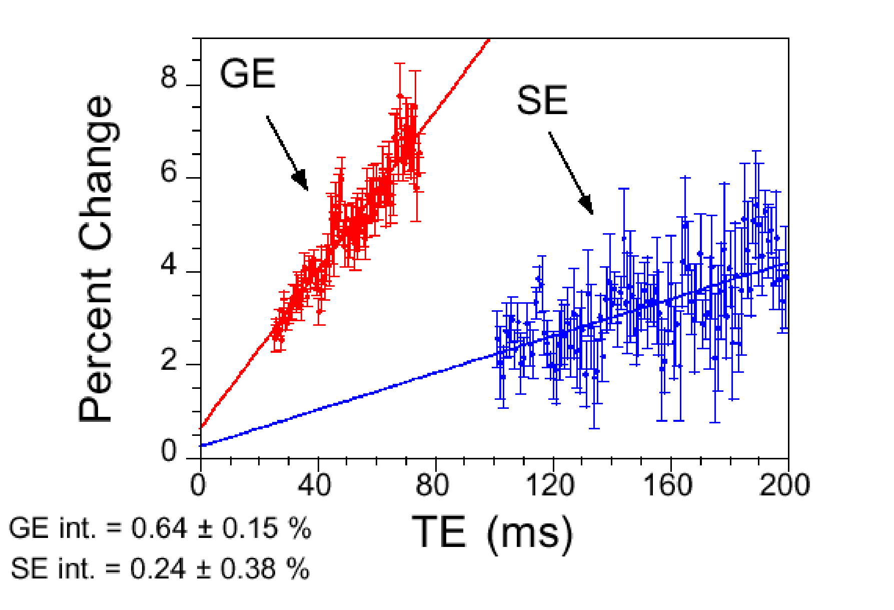


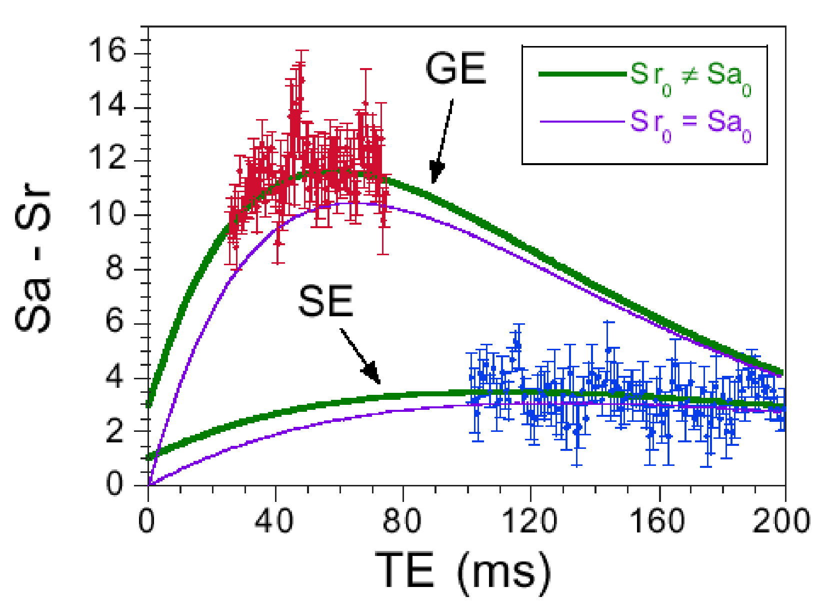


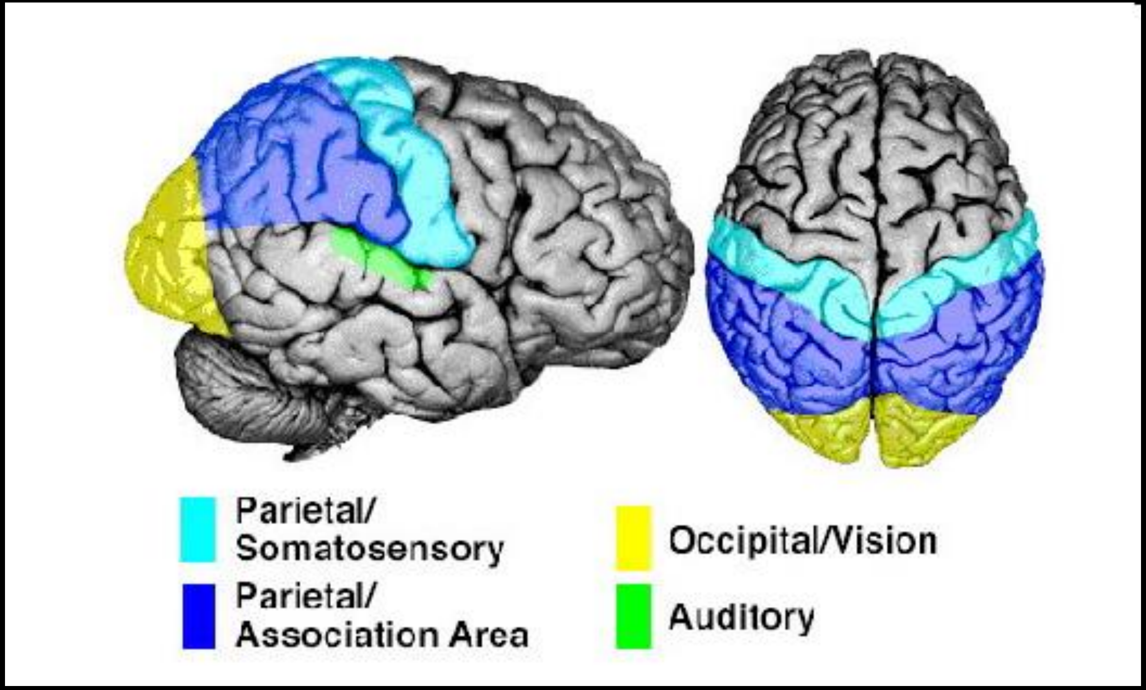
average $\Delta R2^* / \Delta R2 \approx 3$ to 4

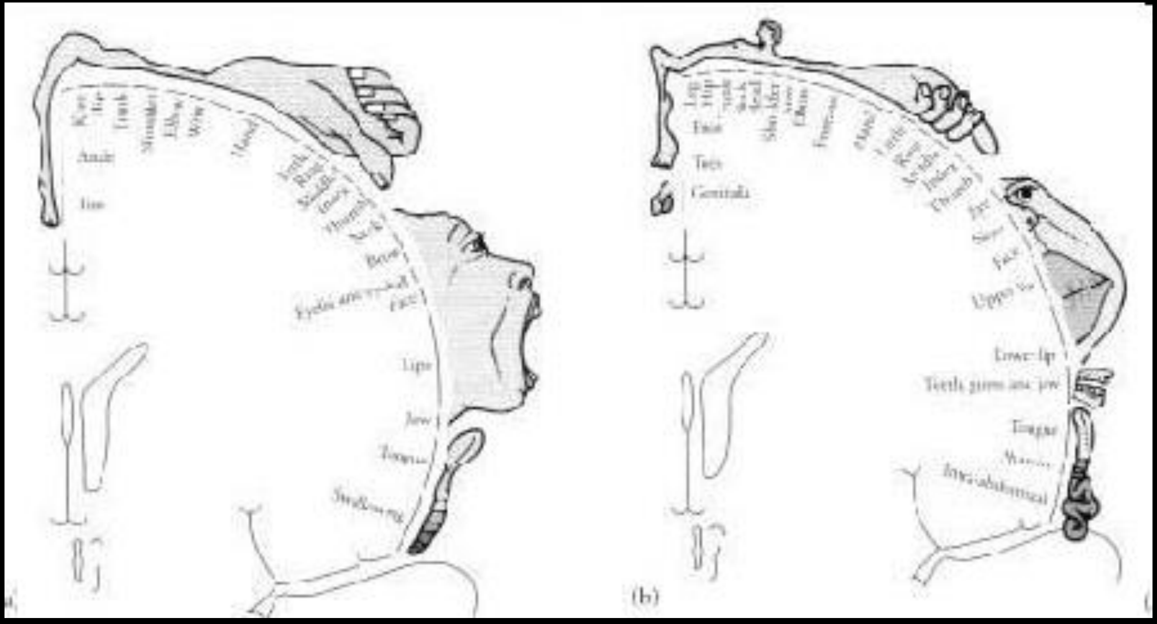





GE
SE
Percent Change
TE (ms)
0
2
4
6
8
0
40
80
120
160
200
GE int. = 0.64 ± 0.15 %
SE int. = 0.24 ± 0.38 %

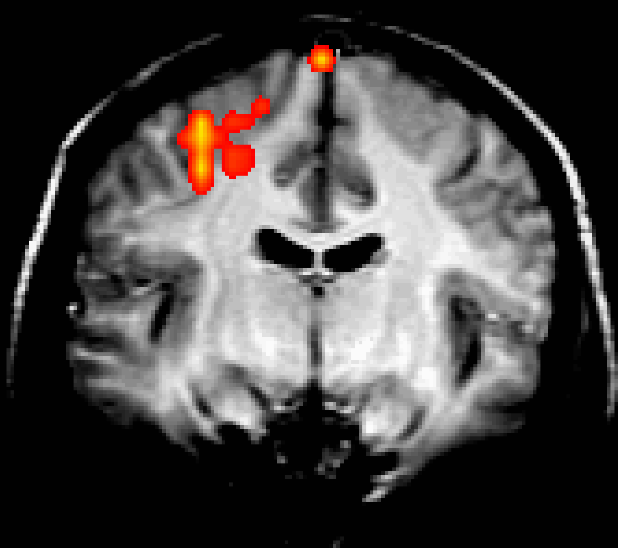

GE
SE
$Sr_0 \neq Sa_0$
$Sr_0 = Sa_0$
Sa - Sr
TE (ms)
0
2
4
6
8
10
12
14
16
0
40
80
120
160
200


Parietal/
Somatosensory
Parietal/
Association Area
Occipital/Vision
Auditory

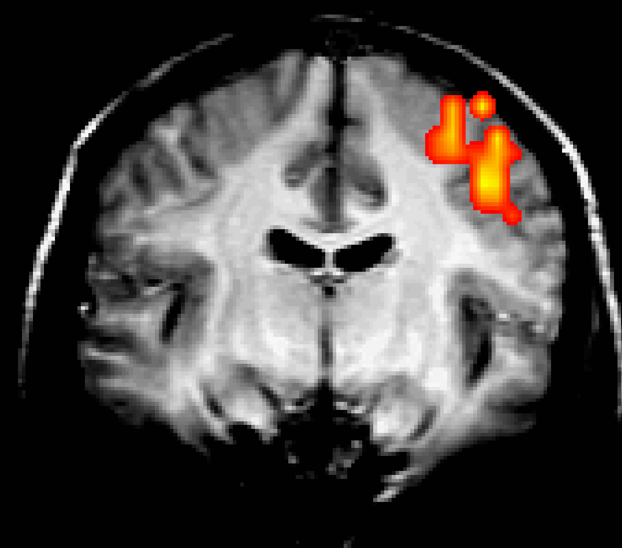

Lips
Jaw
Brow
Neck
Face
Foot
Toes
Genitalia
Lower lip
Tongue
Intra-abdominal
(b)

Finger Movement

Left

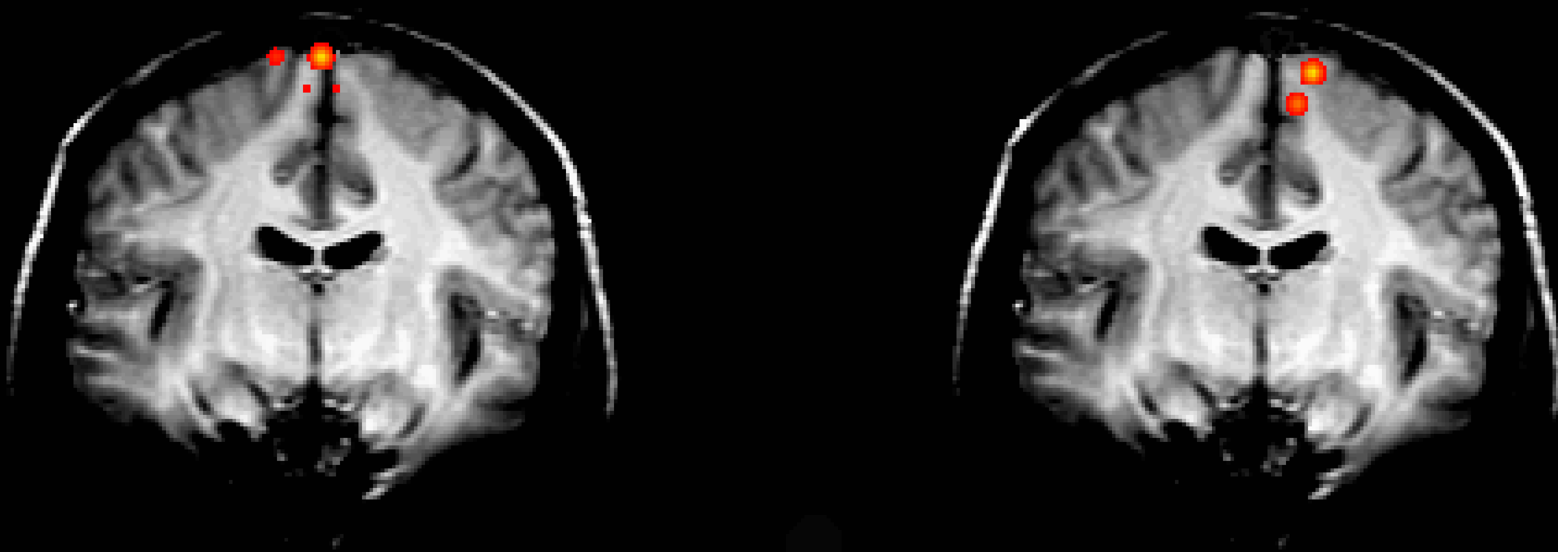


Right

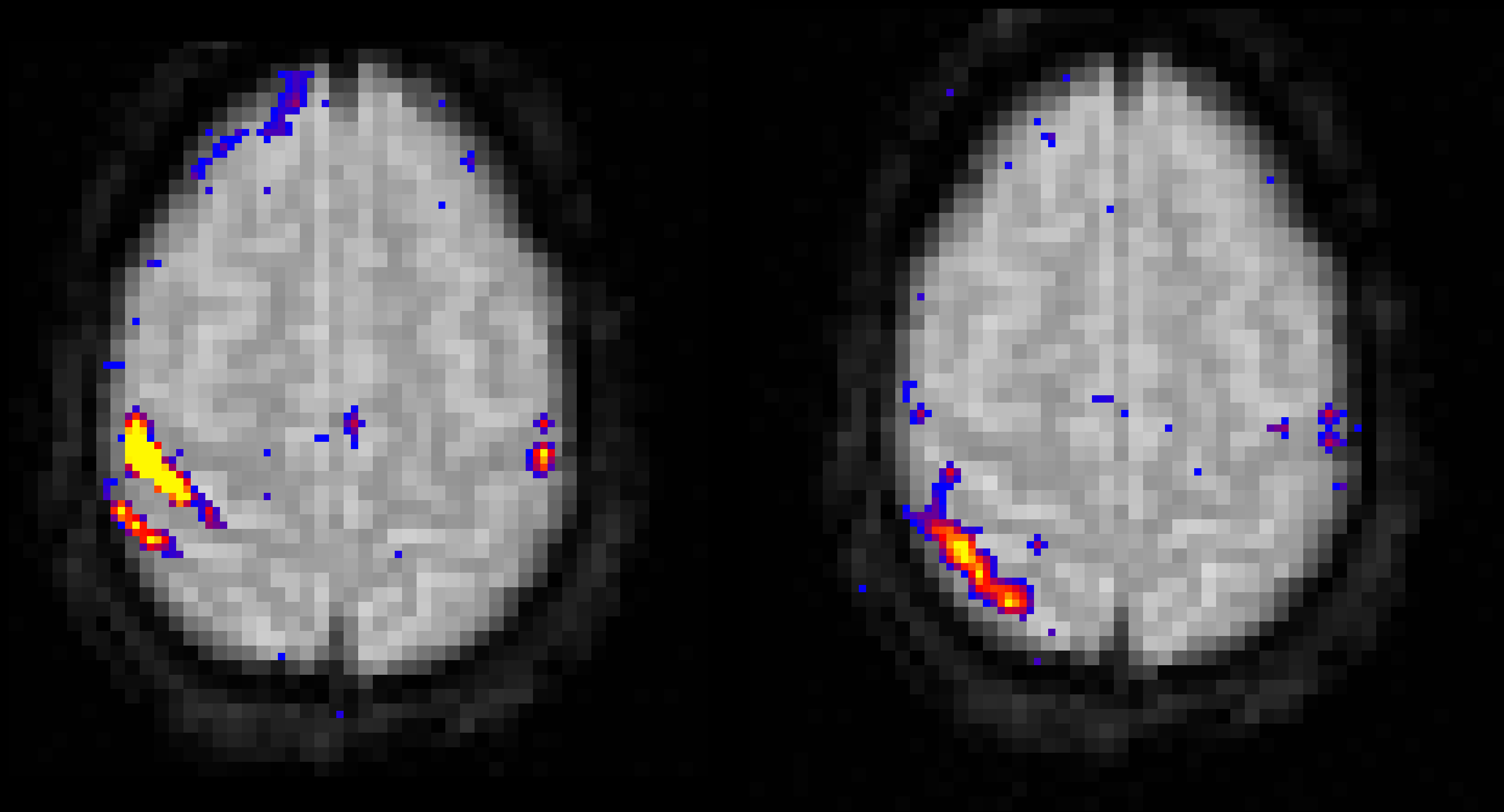


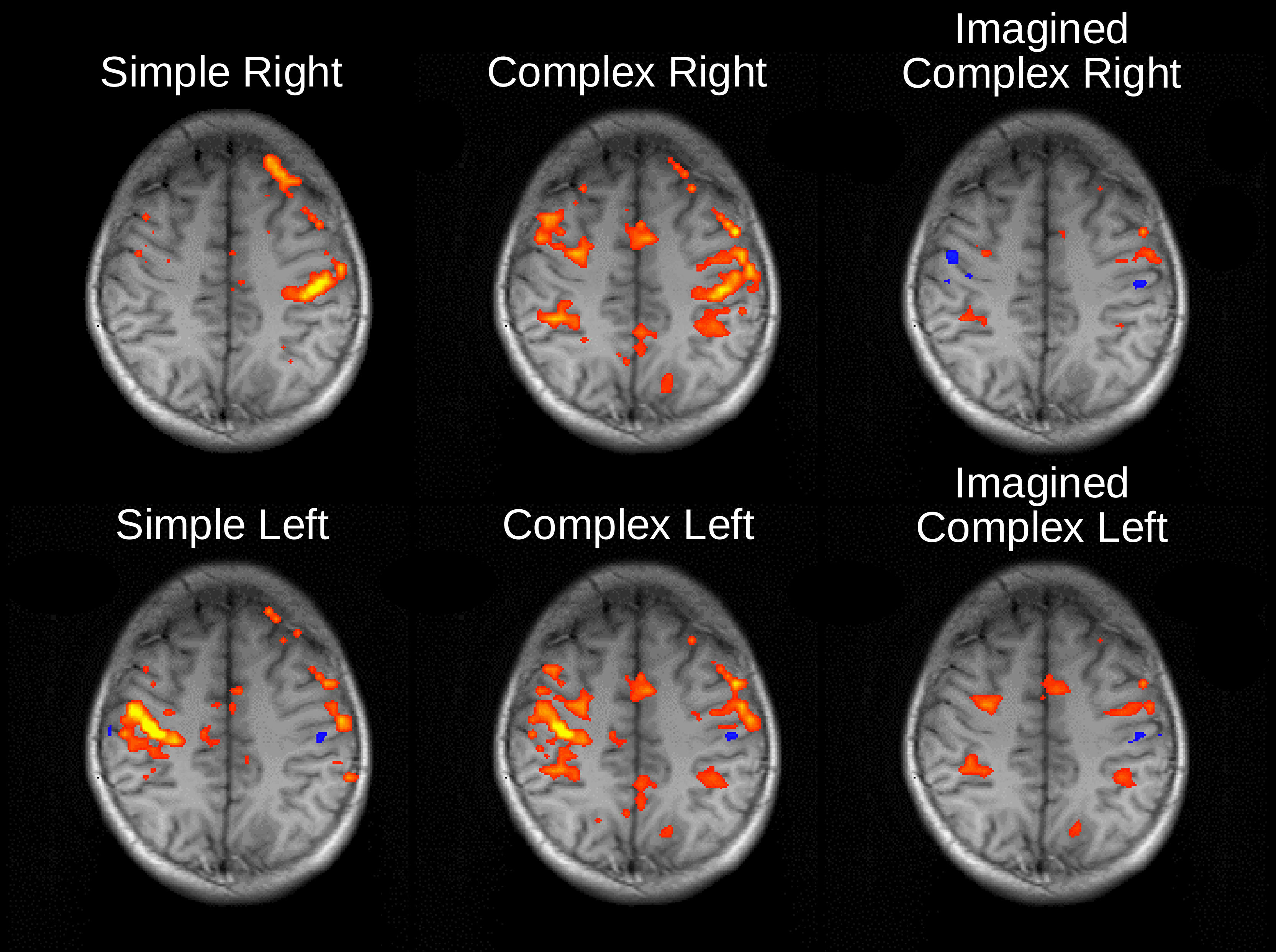
Toe Movement

Left Right

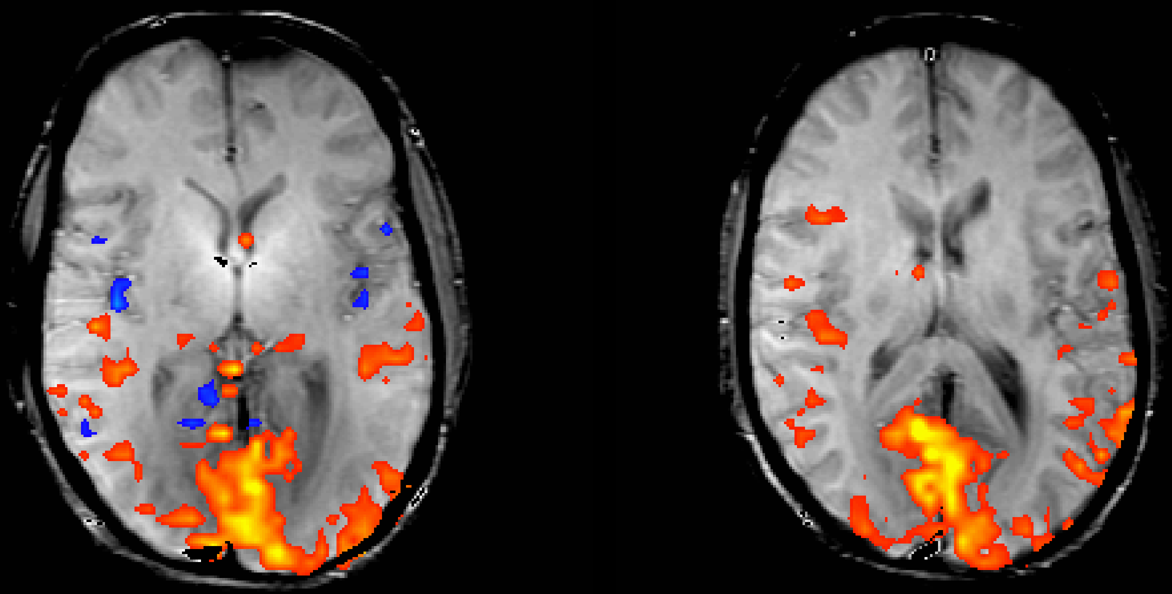


Finger Movement **Tactile Stimulation**

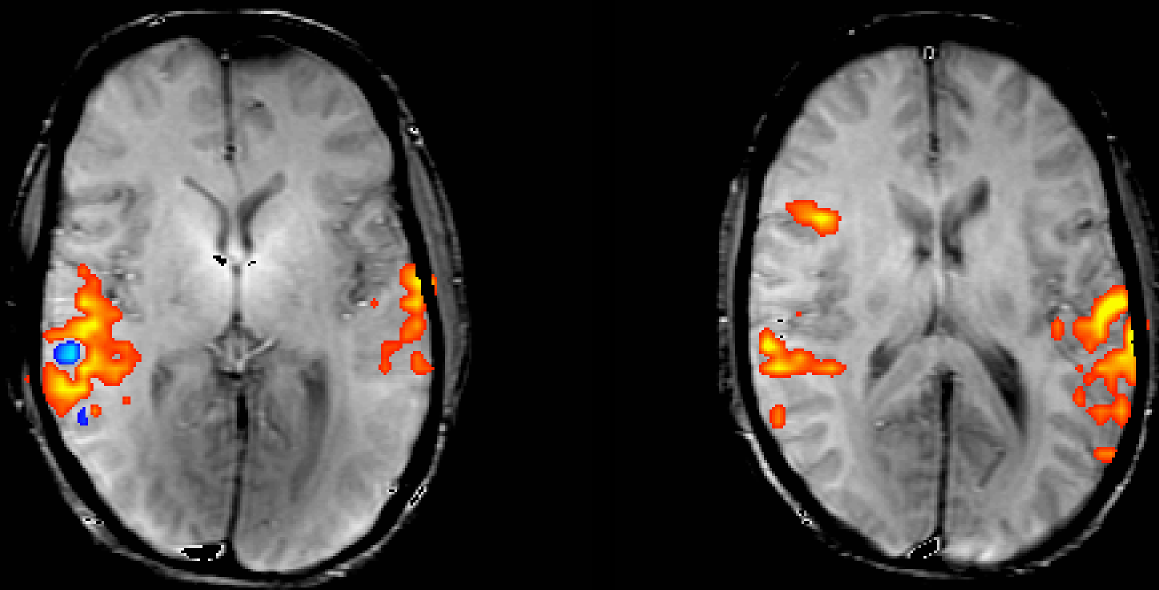



Simple Right
Complex Right
Imagined
Complex Right
Simple Left
Complex Left
Imagined
Complex Left

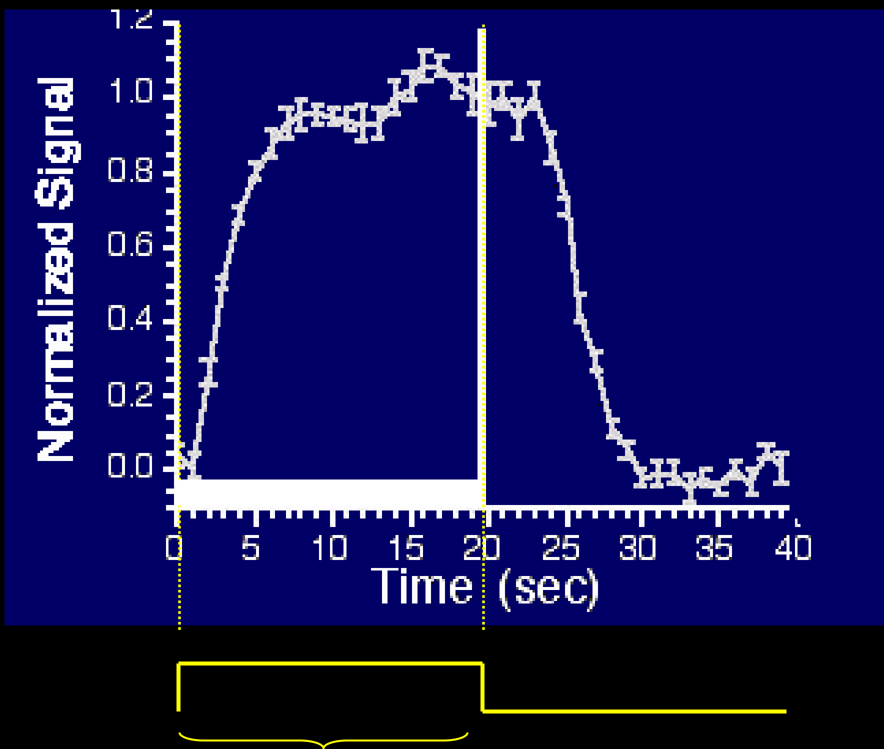
Reading



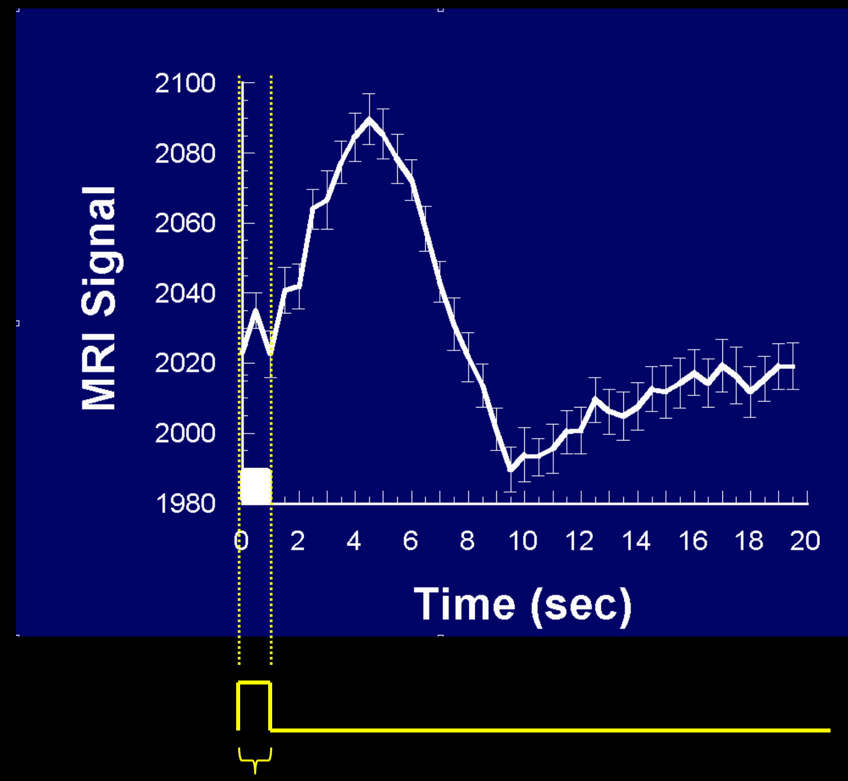
Listening to Spoken Words



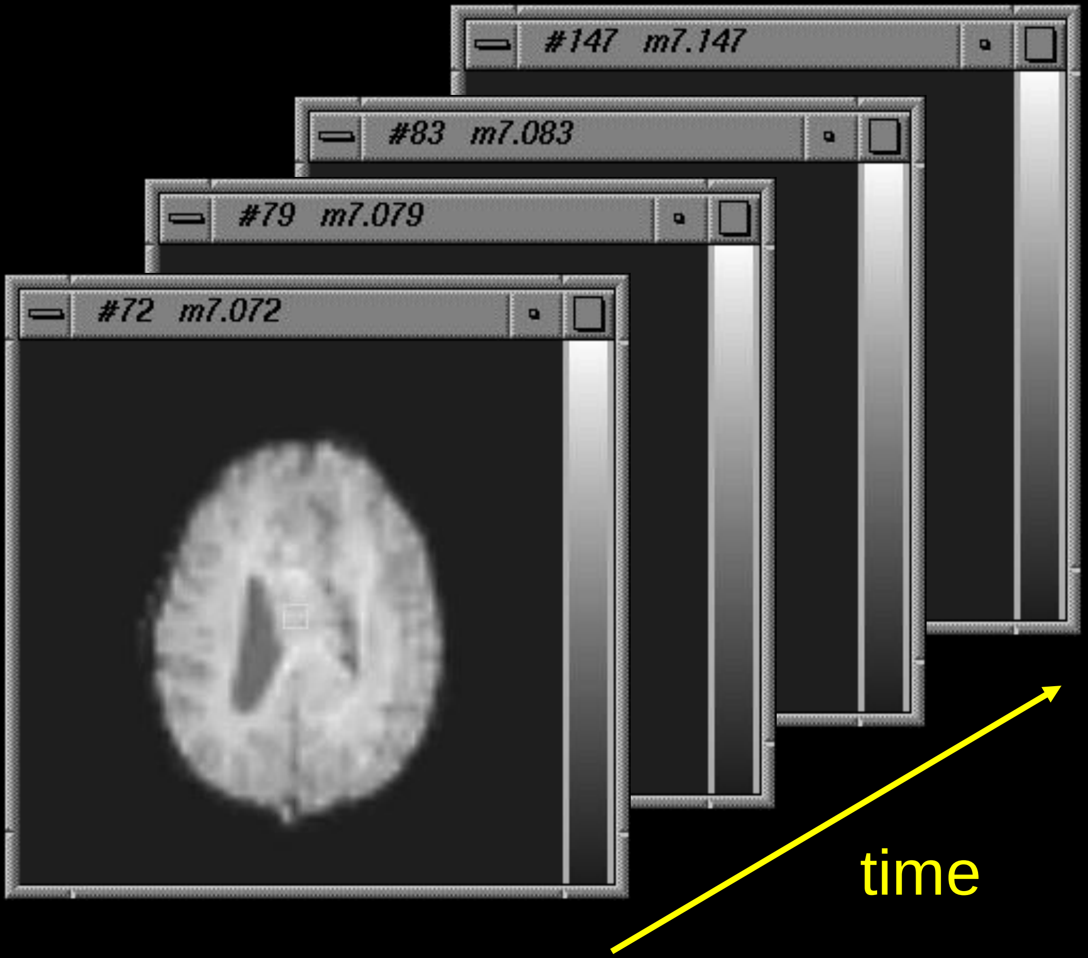
BOLD dynamics



activation



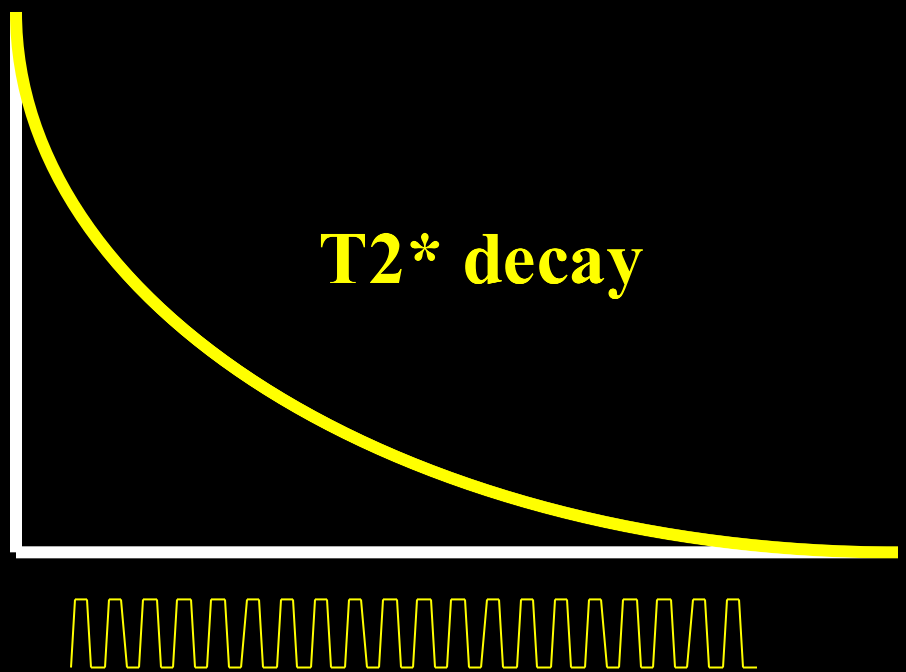
activation



Anatomic

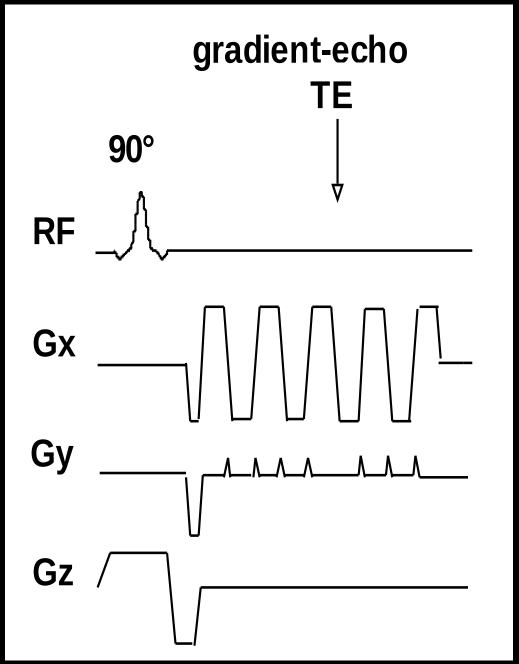
Functional

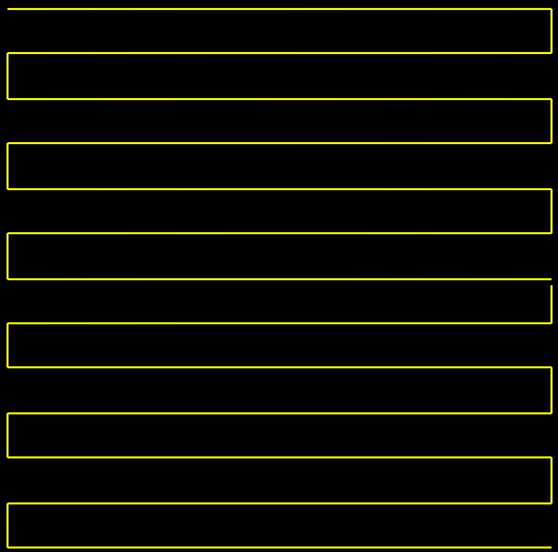
Single Shot Echo Planar Imaging (EPI)



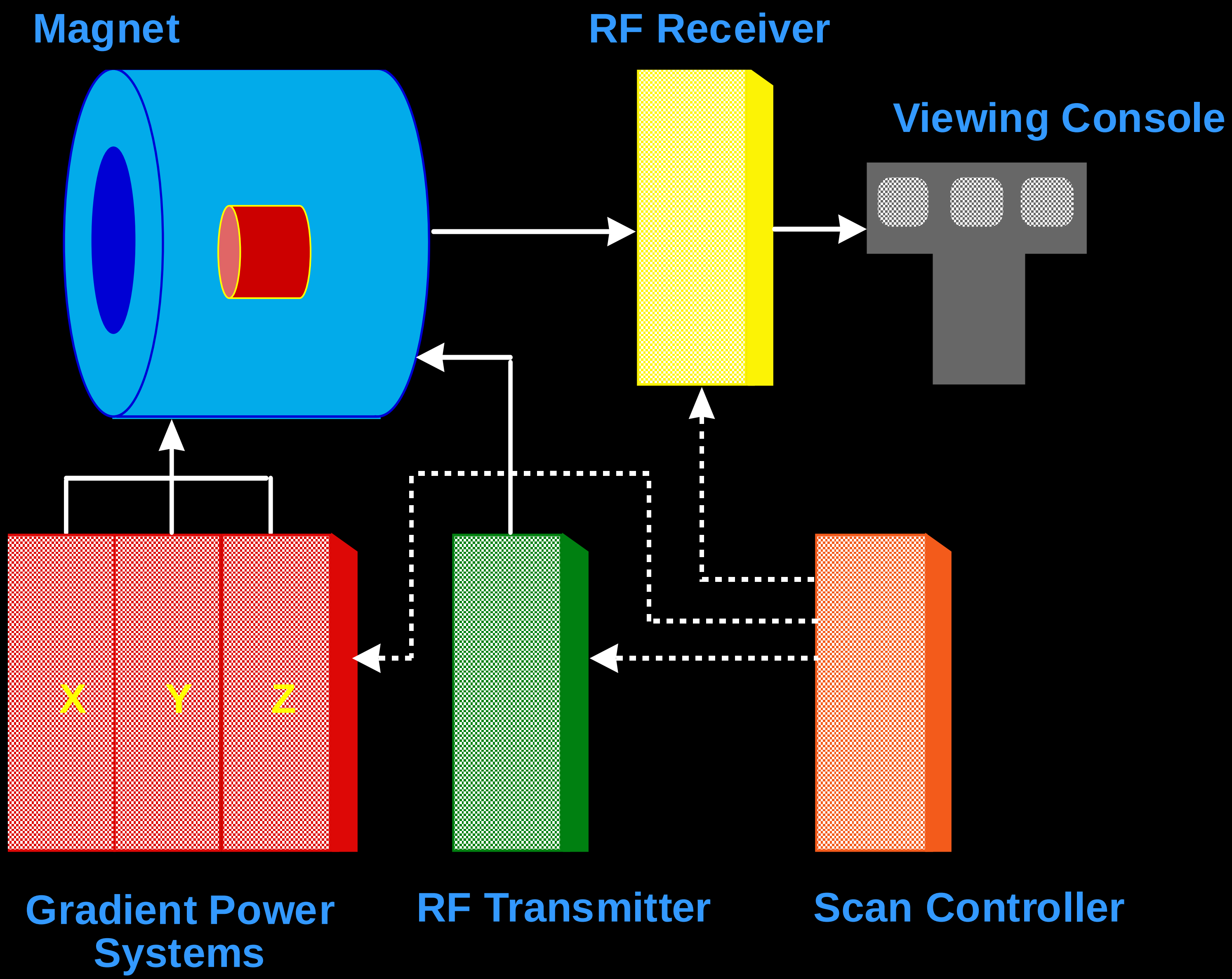
EPI Readout Window

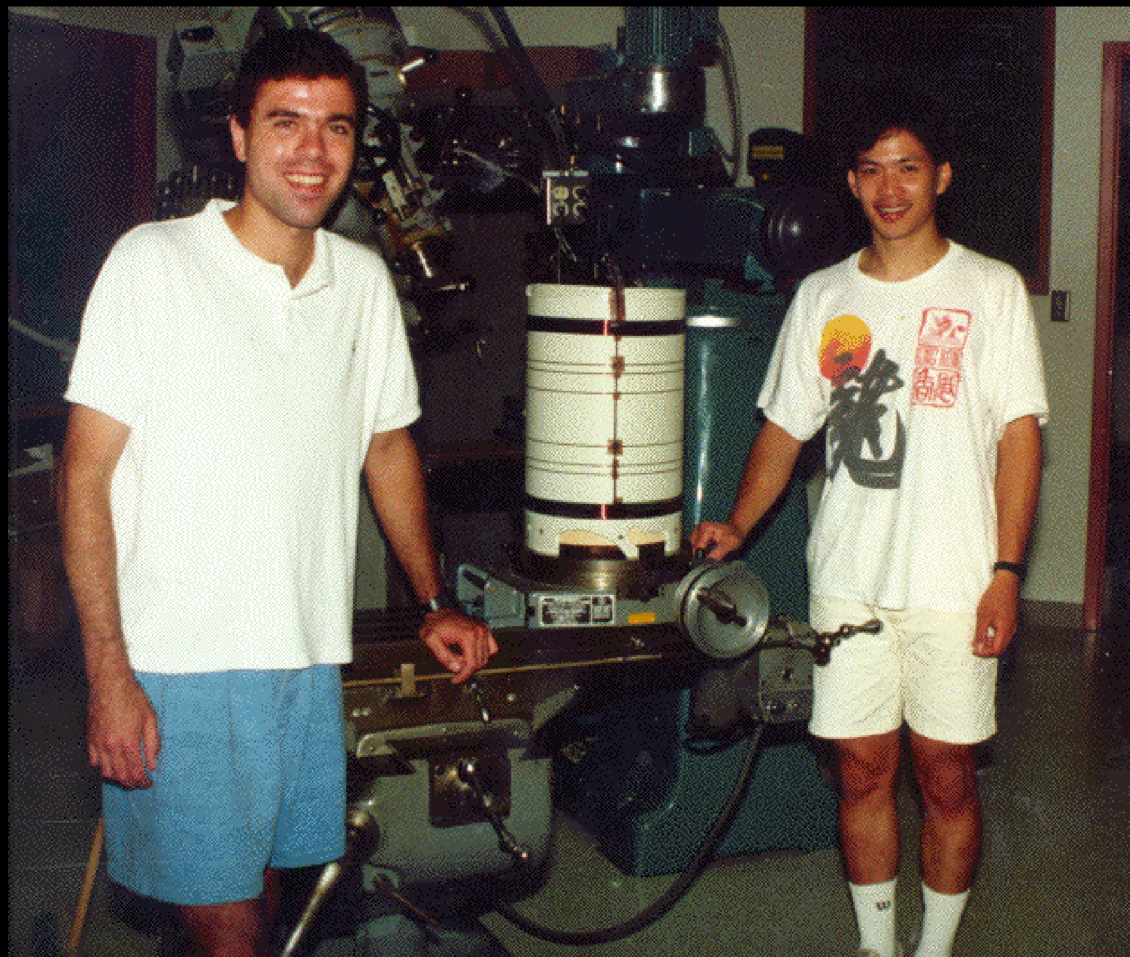
≈ 20 to 40 ms





Imaging System Components

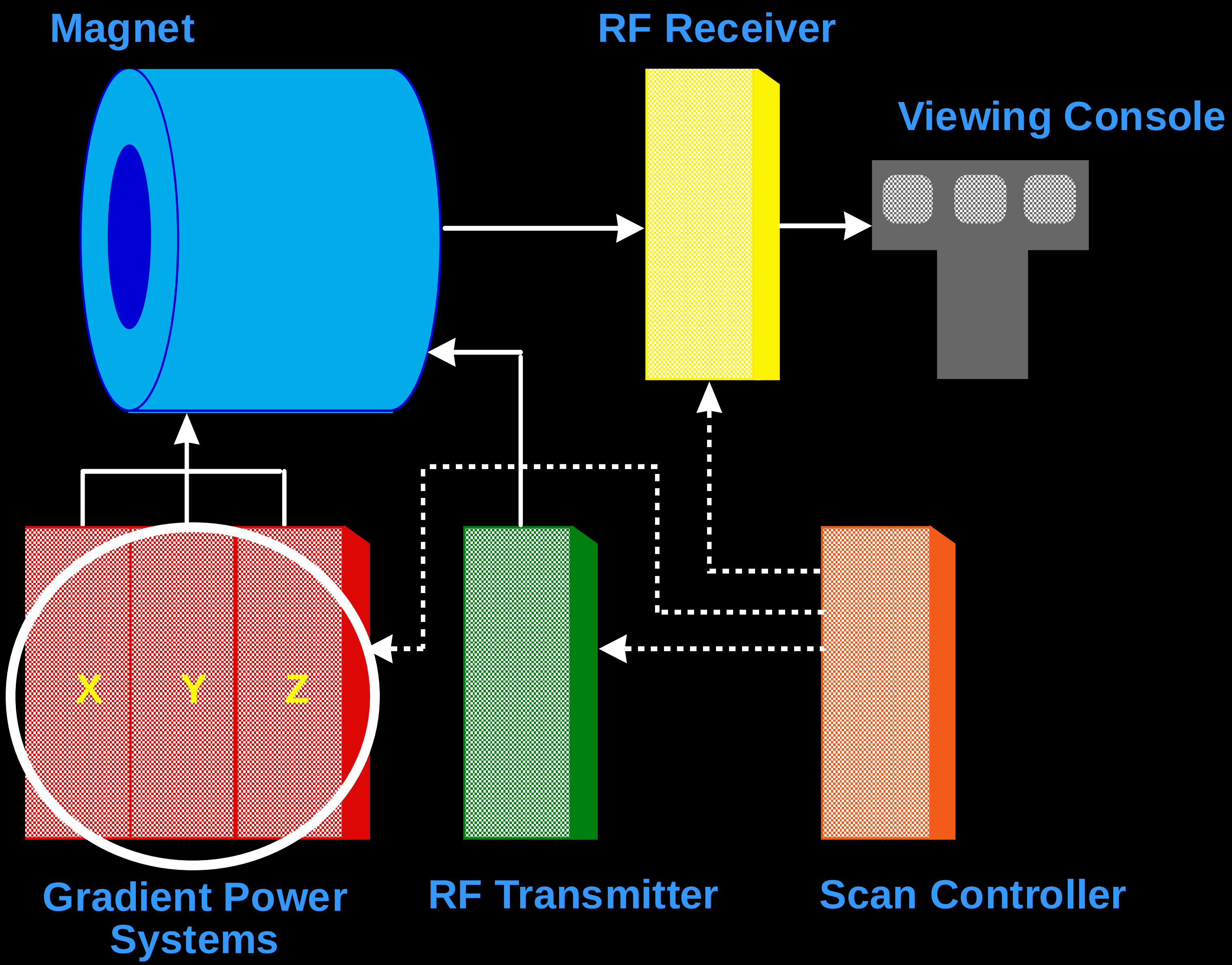




1991-1992

1992-1999

Imaging System Components



General Electric 3 Tesla Scanner

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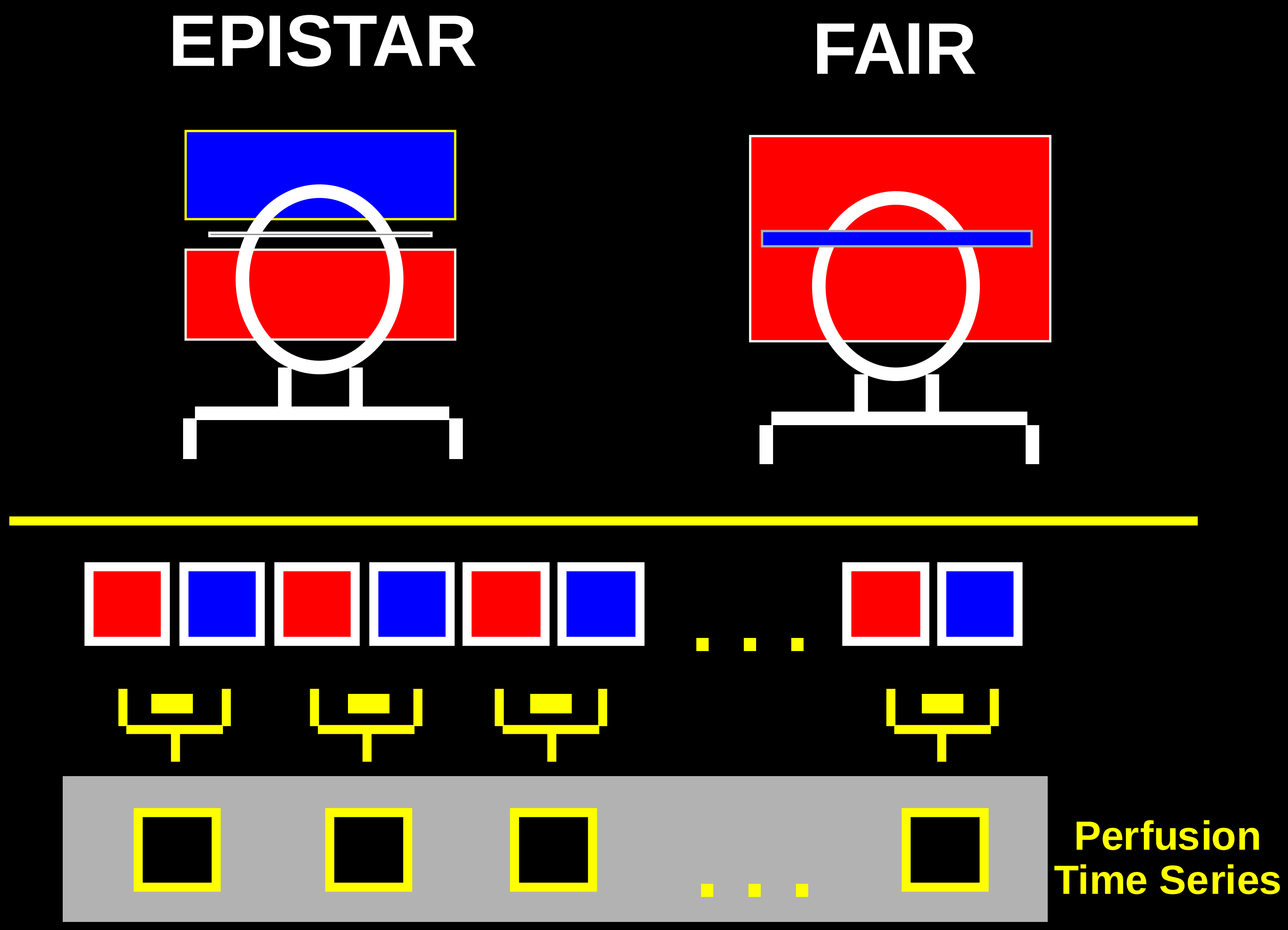
Blood Perfusion



TI (ms) FAIR EPISTAR

200

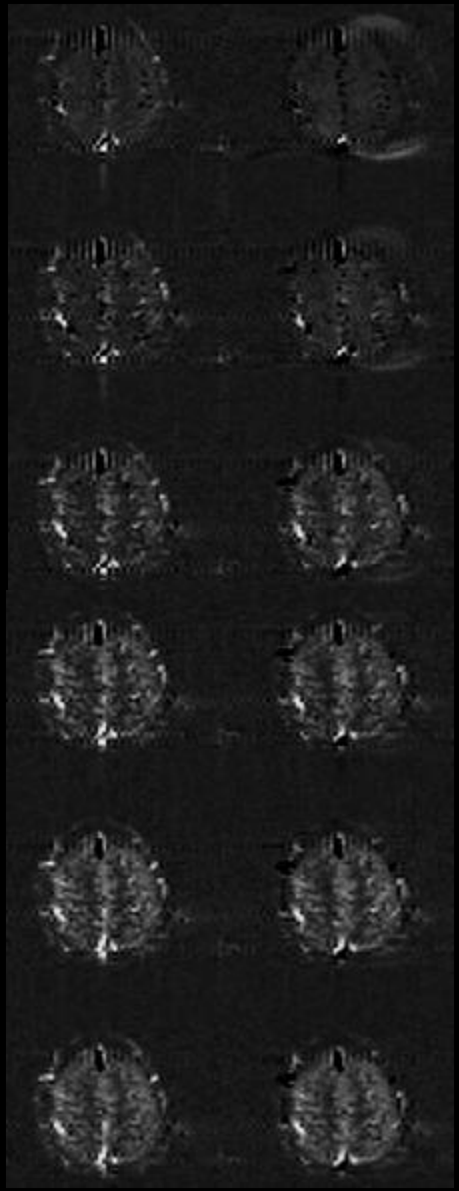
400

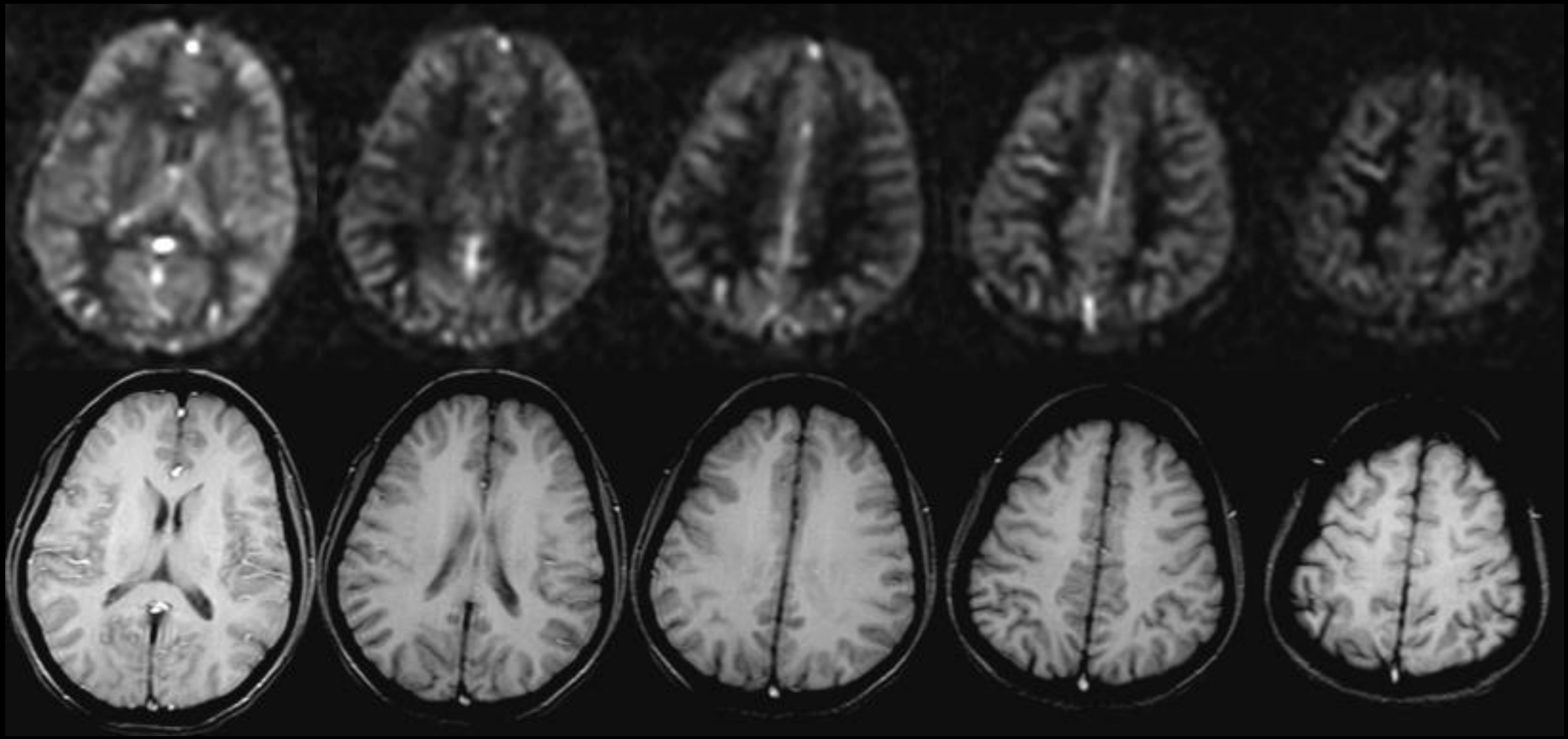
600

800

1000

1200





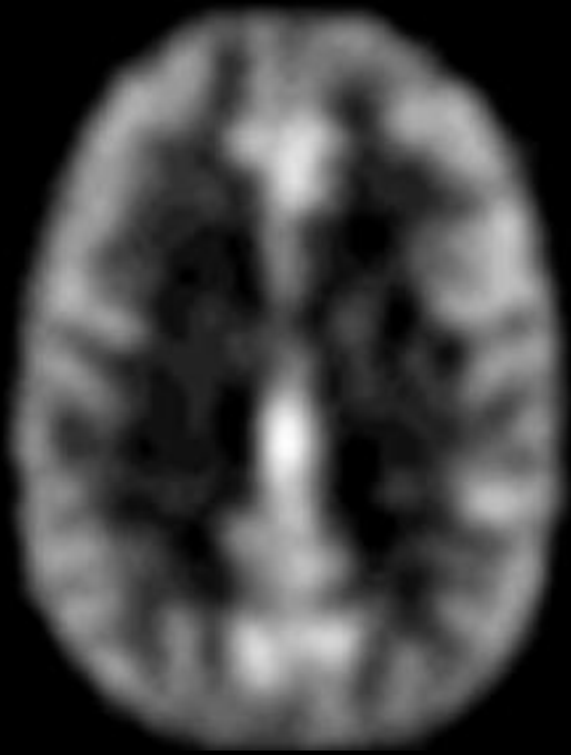
Williams, D. S., Detre, J. A., Leigh, J. S. & Koretsky, A. S. (1992) "Magnetic resonance imaging of perfusion using spin-inversion of arterial water." Proc. Natl. Acad. Sci. USA 89, 212-216.

Edelman, R., Siewert, B. & Darby, D. (1994) "Qualitative mapping of cerebral blood flow and functional localization with echo planar MR imaging ans signal targeting with alternating radiofrequency (EPISTAR)." Radiology **192**, 1-8.

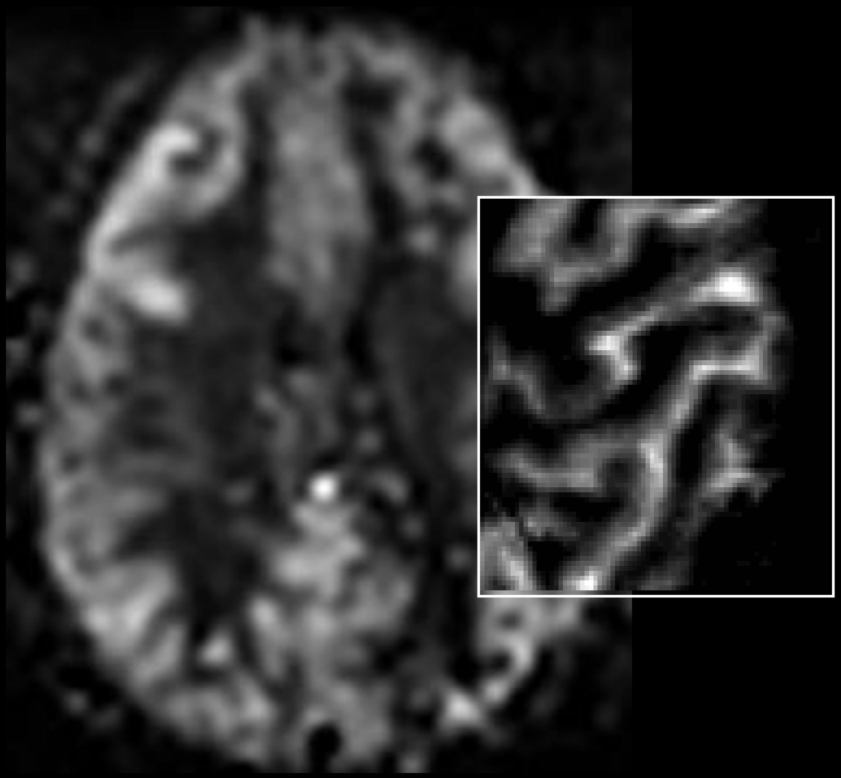
Kim, S.-G. (1995) "Quantification of relative cerebral blood flow change by flow-sensitive alternating inversion recovery (FAIR) technique: application to functional mapping." Magn. Reson. Med. **34**, 293-301.

Kwong, K. K. et al. (1995) "MR perfusion studies with T1-weighted echo planar imaging."Magn. Reson. Med. **34**, 878-887.

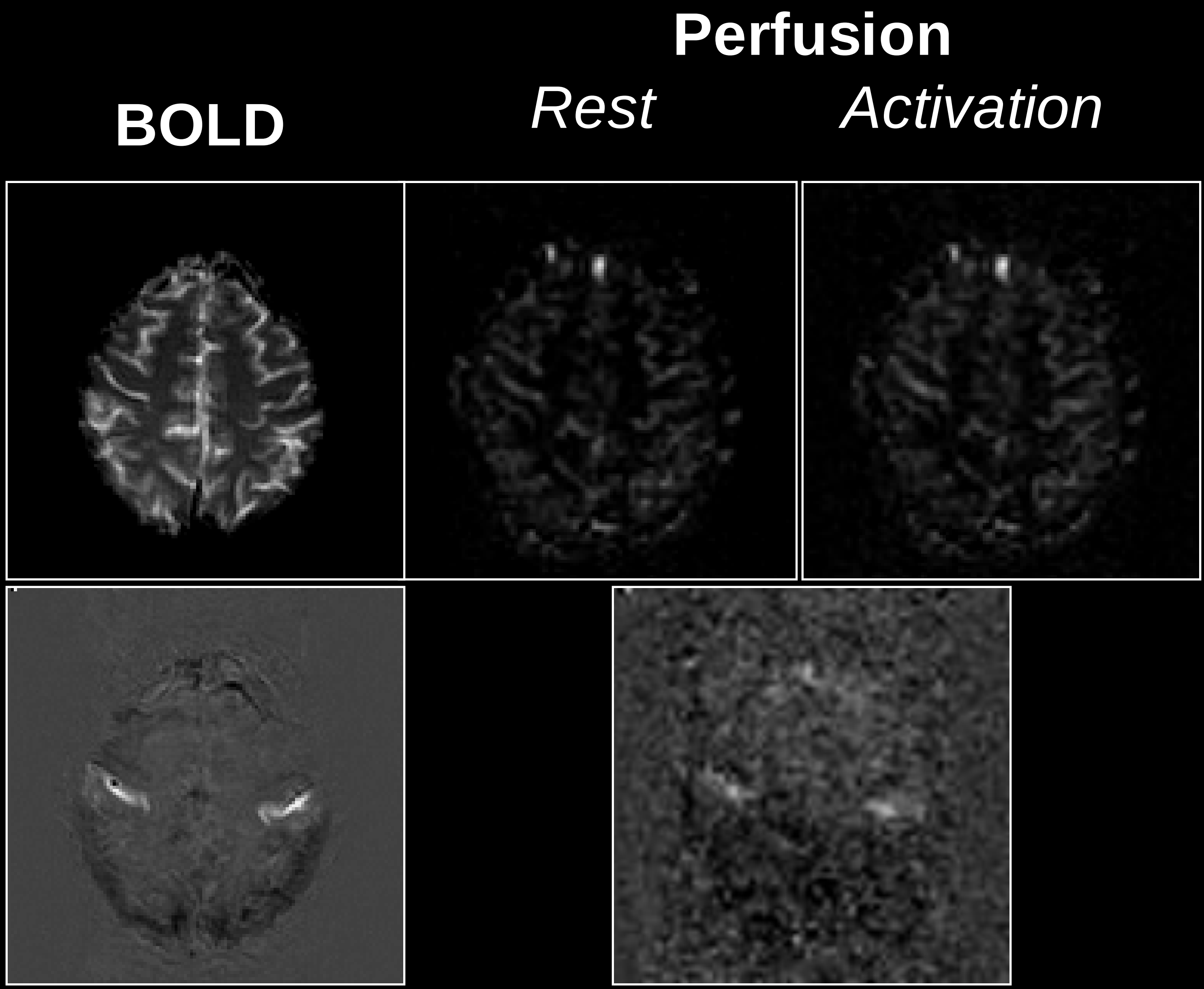
Comparison with Positron Emission Tomography



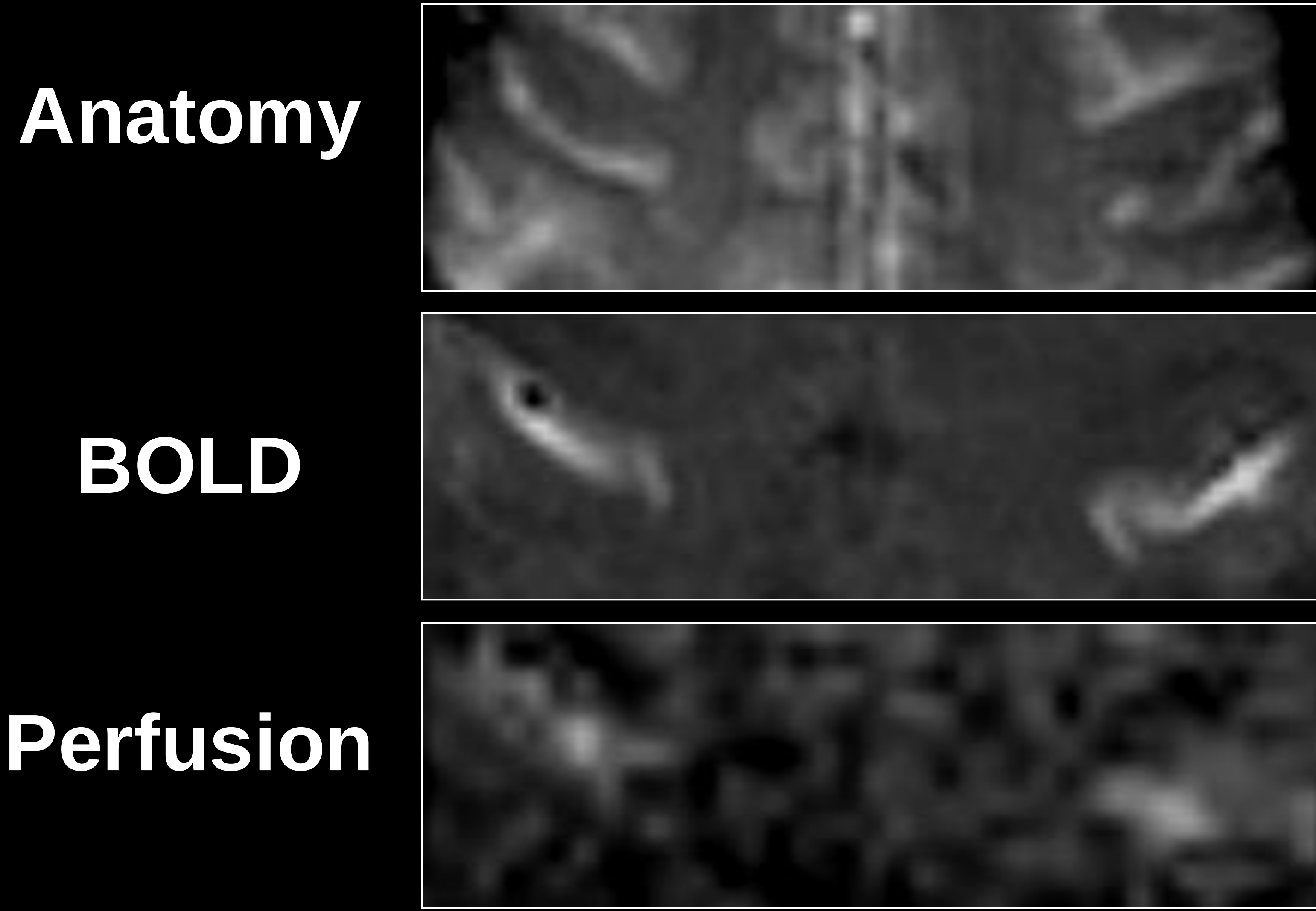
PET: $H_2{}^{15}O$



MRI: ASL



P. A. Bandettini, E. C. Wong, Magnetic resonance imaging of human brain function: principles, practicalities, and possibilities, *in* "Neurosurgery Clinics of North America: Functional Imaging" (M. Haglund, Ed.), p.345-371, W. B. Saunders Co., 1997.



P. A. Bandettini, E. C. Wong, Magnetic resonance imaging of human brain function: principles, practicalities, and possibilities, *in* "Neurosurgery Clinics of North America: Functional Imaging" (M. Haglund, Ed.), p.345-371, W. B. Saunders Co., 1997.

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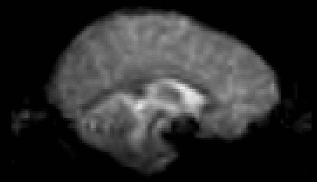
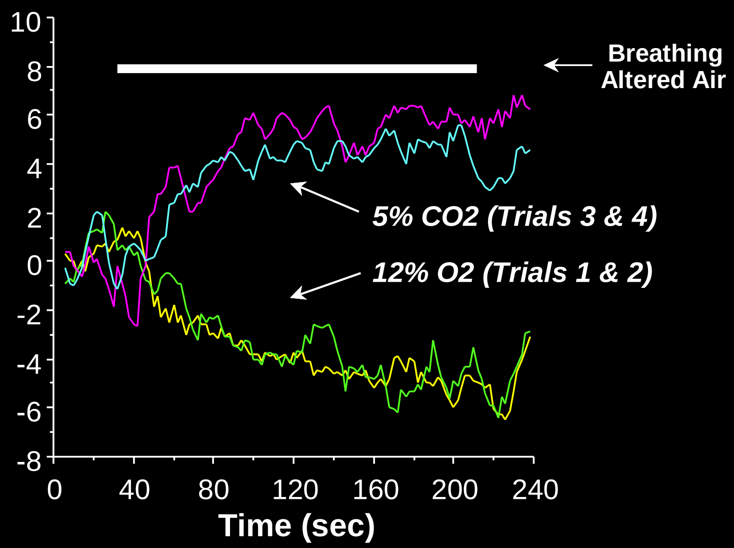
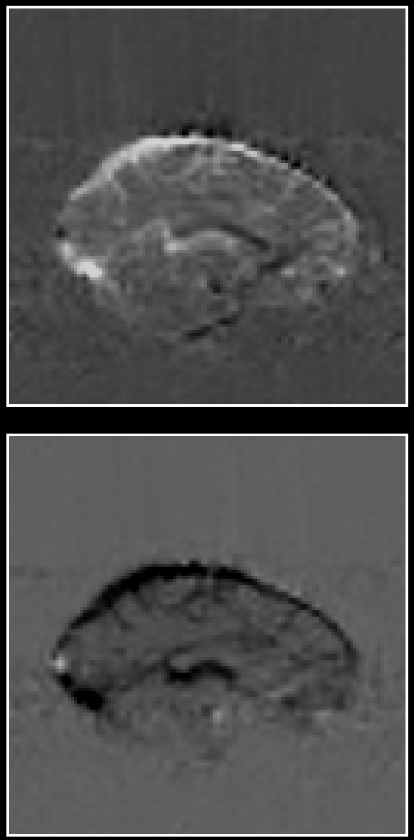
Hemodynamic Stress Calibration





5% CO_2



12% O_2

P. A. Bandettini, E. C. Wong, A hypercapnia - based normalization method for improved spatial localization of human brain activation with fMRI. *NMR in Biomedicine* 10, 197-203 (1997).

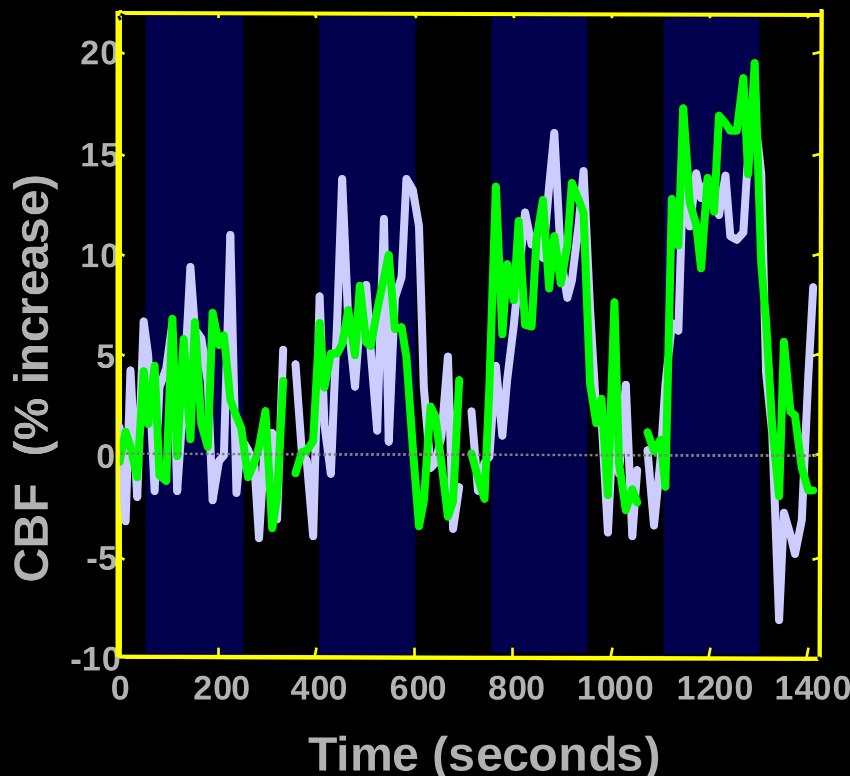
Proc. Natl. Acad. Sci. USA
Vol. 96, pp. 9403–9408, August 1999
Neurobiology

Linear coupling between cerebral blood flow and oxygen consumption in activated human cortex

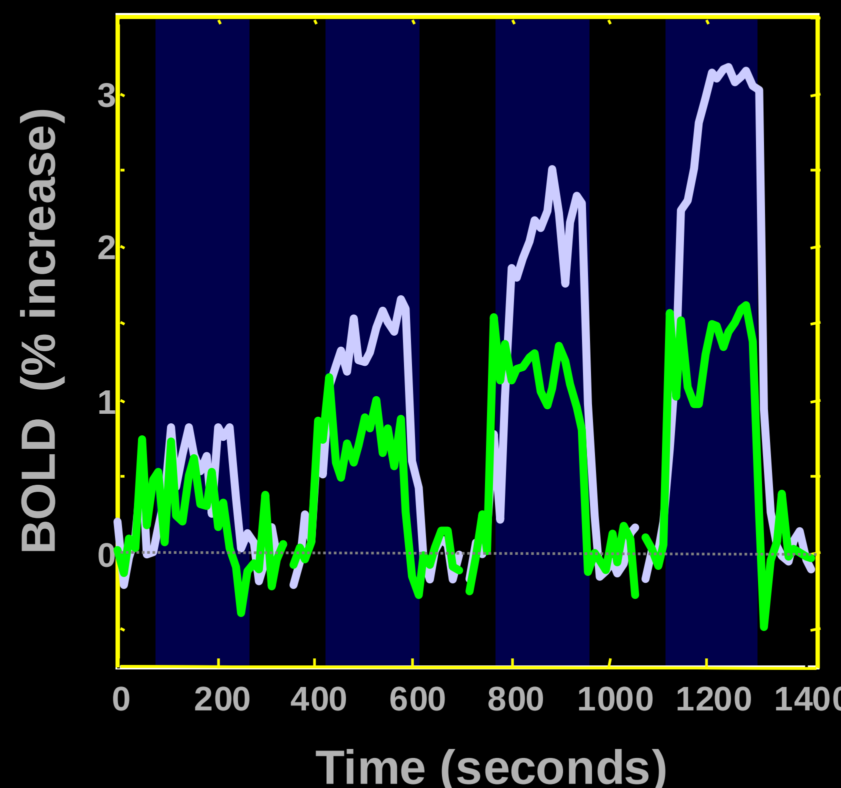
RICHARD D. HOGE*†, JEFF ATKINSON*, BRAD GILL*, GÉRARD R. CRELIER*, SEAN MARRETT‡, AND G. BRUCE PIKE*

*Room WB325, McConnell Brain Imaging Centre, Montreal Neurological Institute, Quebec, Canada H3A 2B4; and ‡Nuclear Magnetic Resonance Center, Massachusetts General Hospital, Building 149, 13th Street, Charlestown, MA 02129

CBF



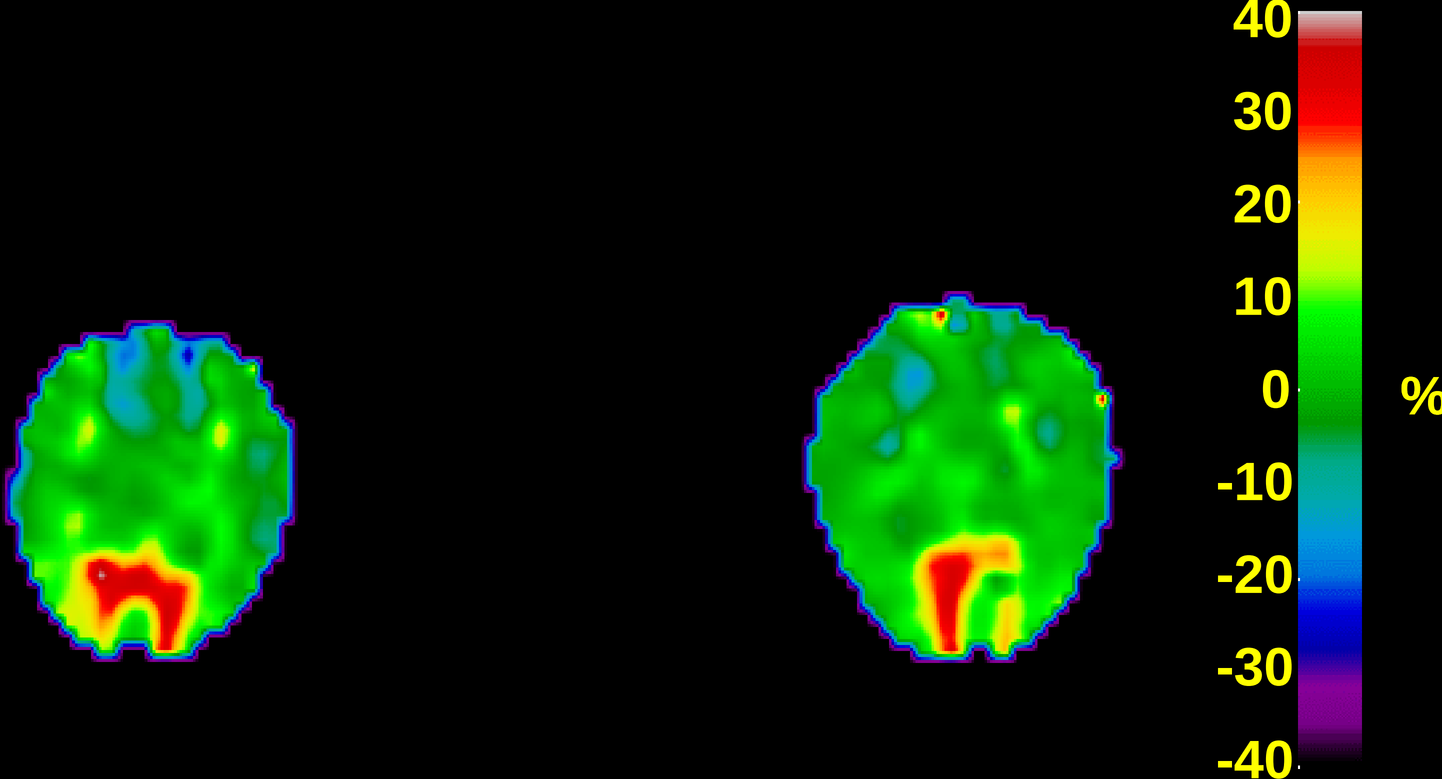
BOLD



Simultaneous Perfusion and BOLD imaging during graded visual activation and hypercapnia

N=12

Computed $CMRO_2$ Changes



Subject 1 **Subject 2**

R. Hoge et al.

Direct Neuronal Current Imaging?

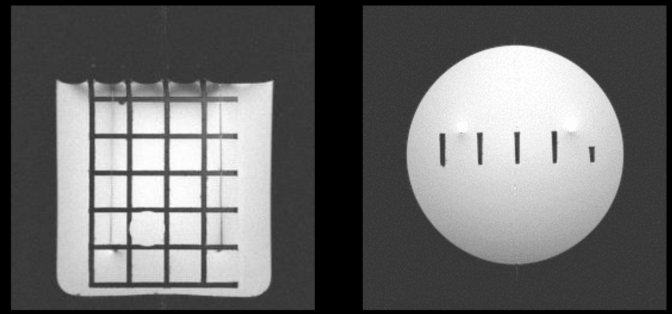
Toward Direct Mapping of Neuronal Activity: MRI Detection of Ultraweak, Transient Magnetic Field Changes

Jerzy Bodurka[1*] and Peter A. Bandettini[1,2]

- **Preliminary models suggest that magnetic field changes on the order of 0.1 to 1 nT are induced (at the voxel scale) in the brain.**

- **These changes induce about a 0.01 Hz frequency shift or 0.09 deg (@ TE = 30 ms) phase shift.**

- **Question: Is this detectable?**



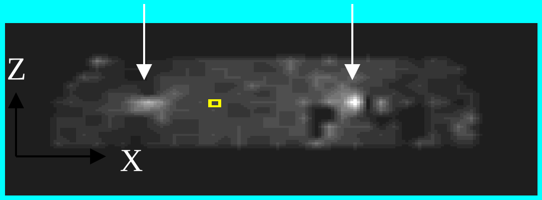
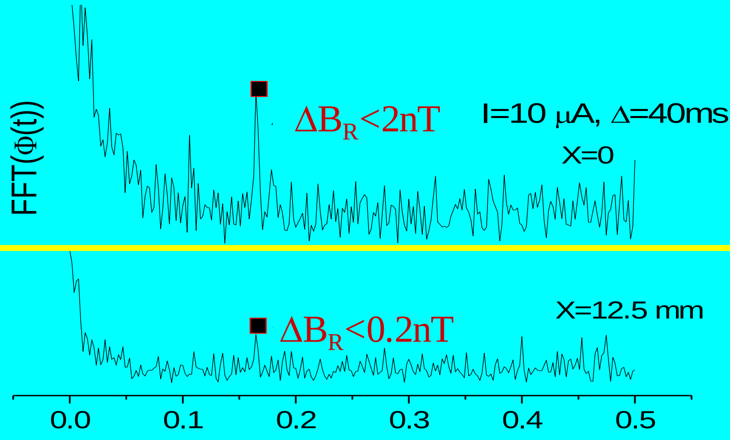
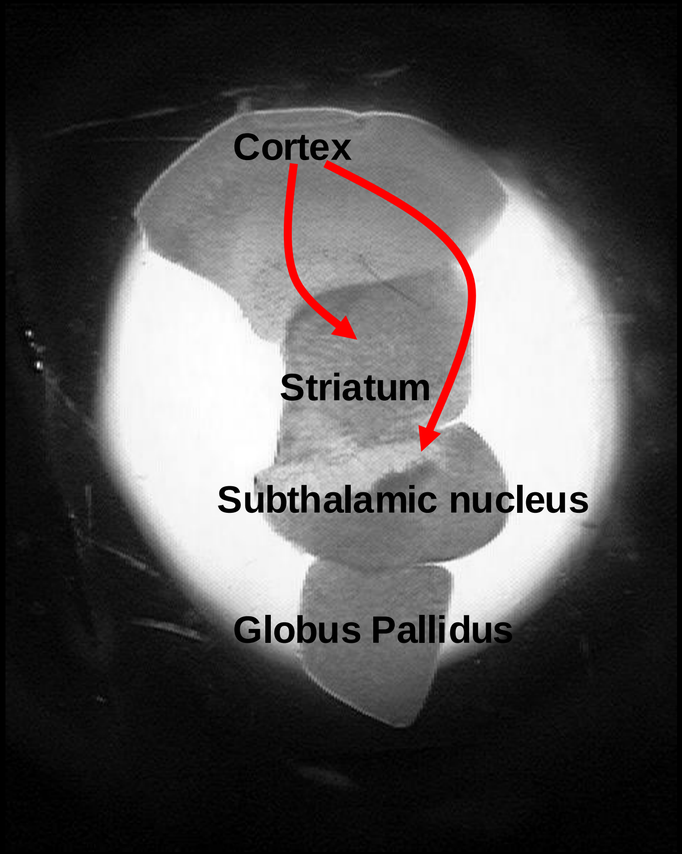

Z
X

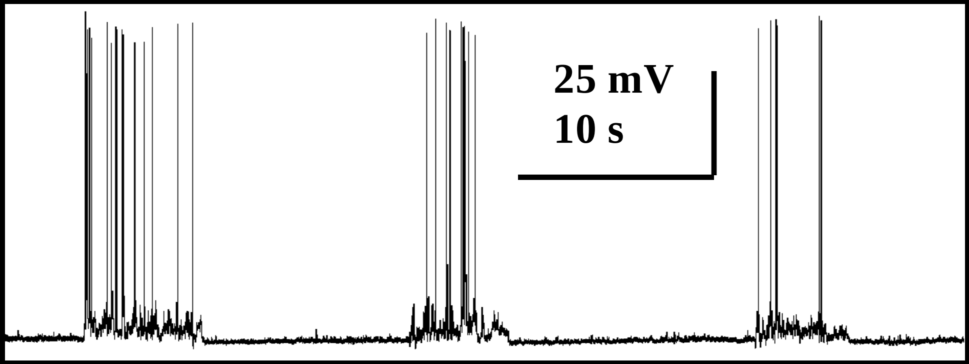
Figure 1


FFT(Φ(t))
ΔB_R<2nT
I=10 μA, Δ=40ms
X=0
ΔB_R<0.2nT
X=12.5 mm
0.0
0.1
0.2
0.3
0.4
0.5

In Vitro Results

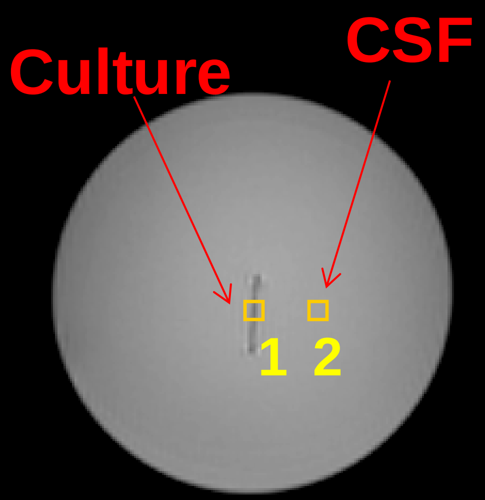
Newborn rat brains have been found to exhibit spontaneous and synchronous firing at specific frequencies



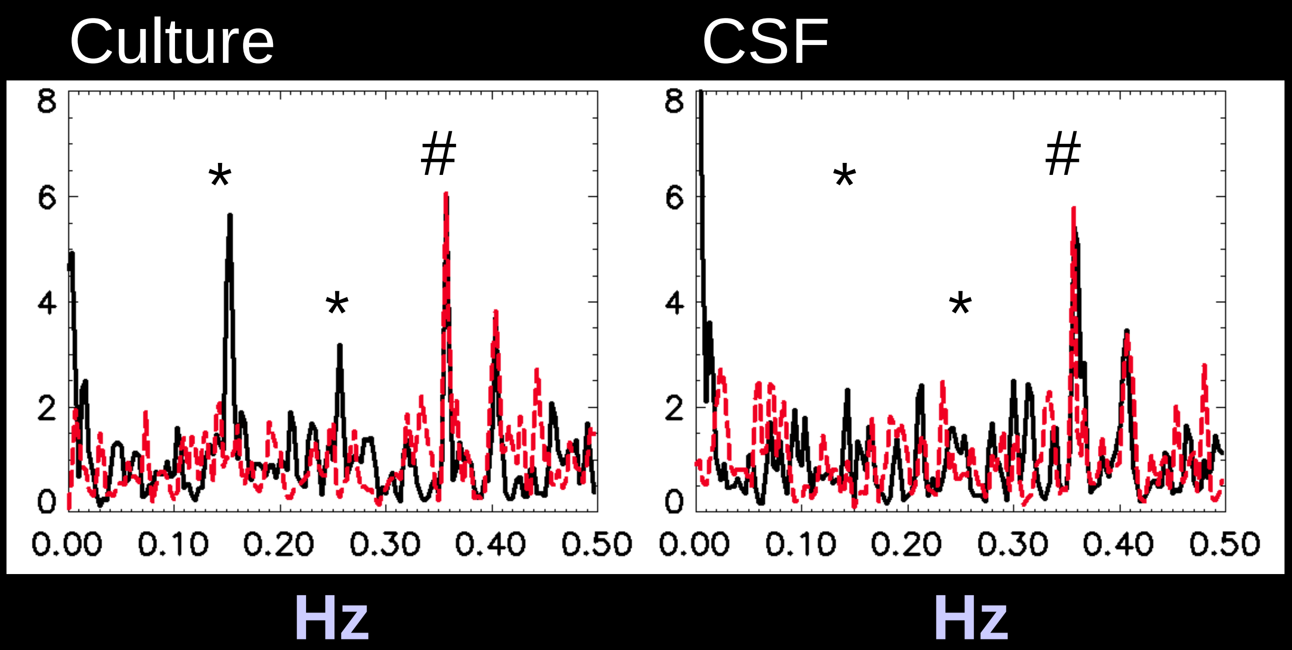


Plenz, D. and S.T. Kital. Nature, 1999. **400**: p. 677-682.

Results



FSE image



Active state: 10 min, Inactive state: 10 min after TTX admin.

*: **activity**

#: **scanner pump frequency**

Petridou et al.

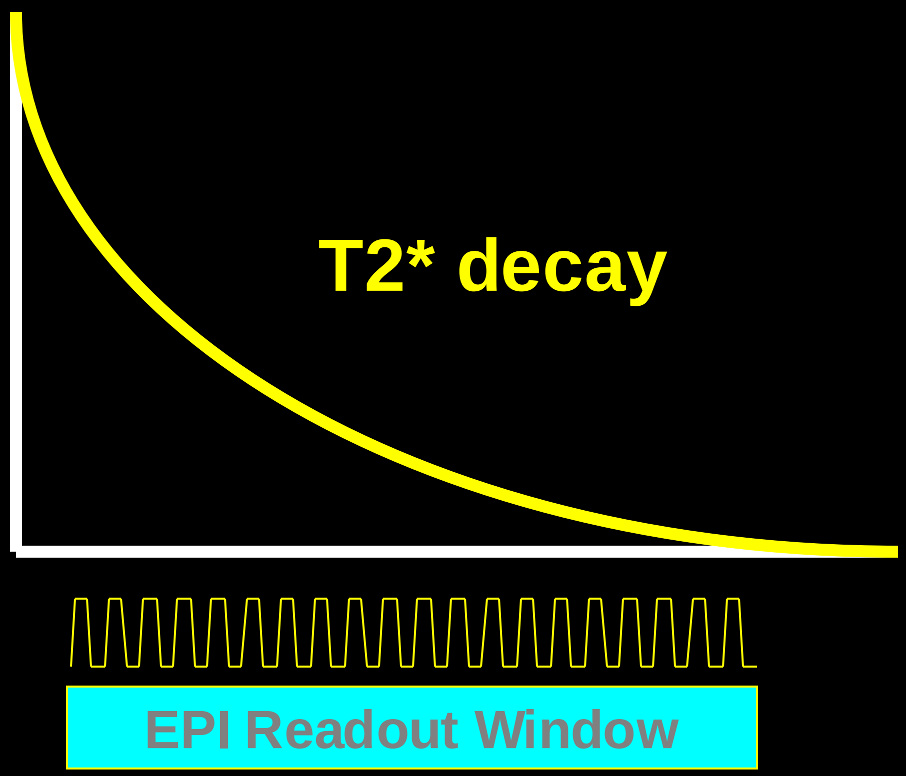
Latest Developments…

1. Temporal Resolution
2. Spatial Resolution
3. Sensitivity and Noise
4. Information Content
5. Implementation

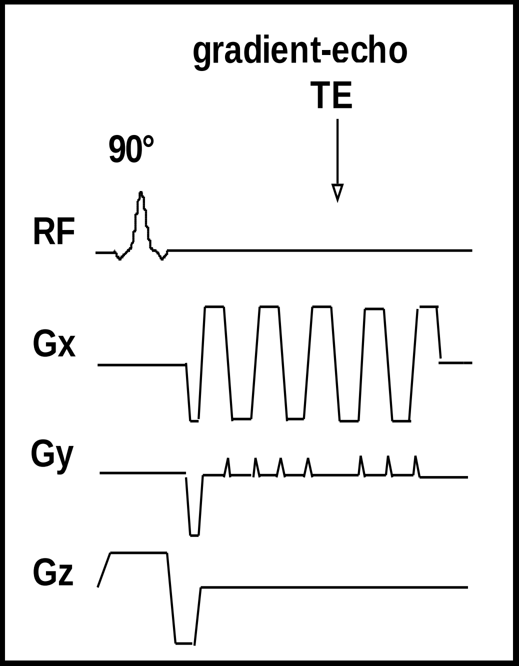
Latest Developments…

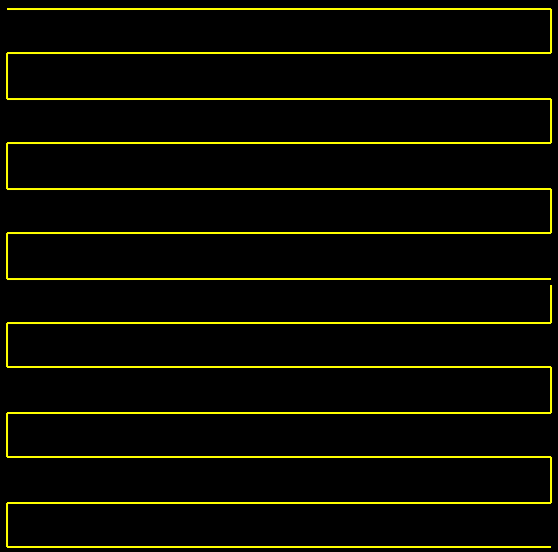
1. Temporal Resolution
2. Spatial Resolution
3. Sensitivity and Noise
4. Information Content
5. Implementation

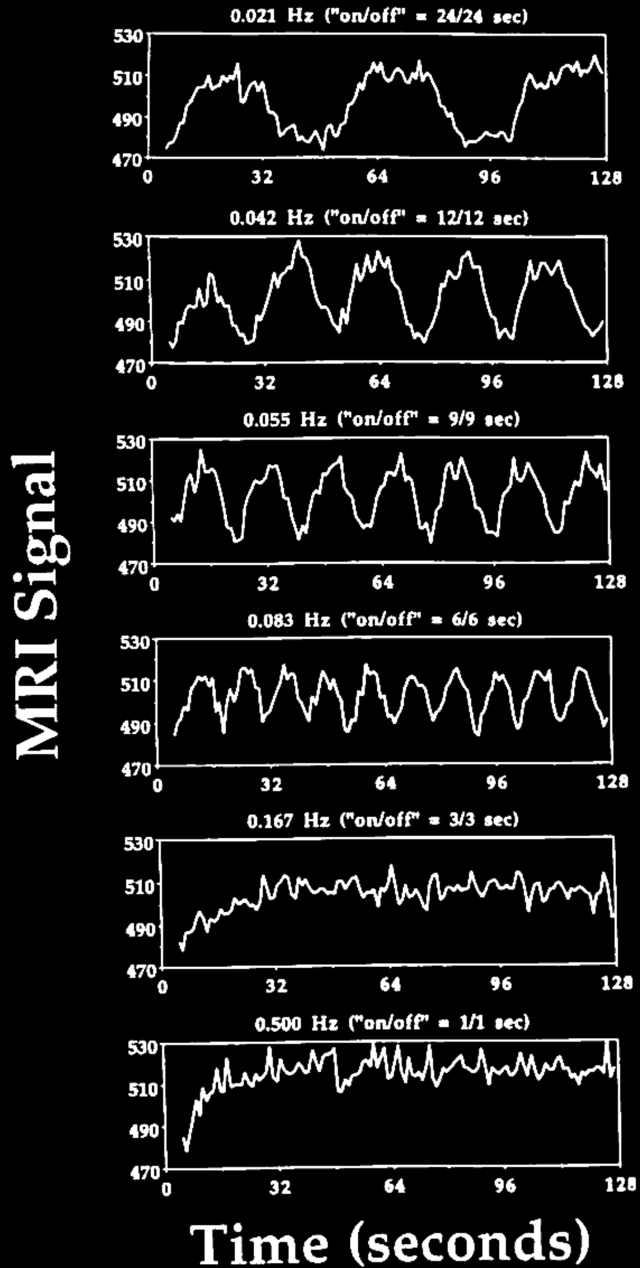
Single Shot EPI

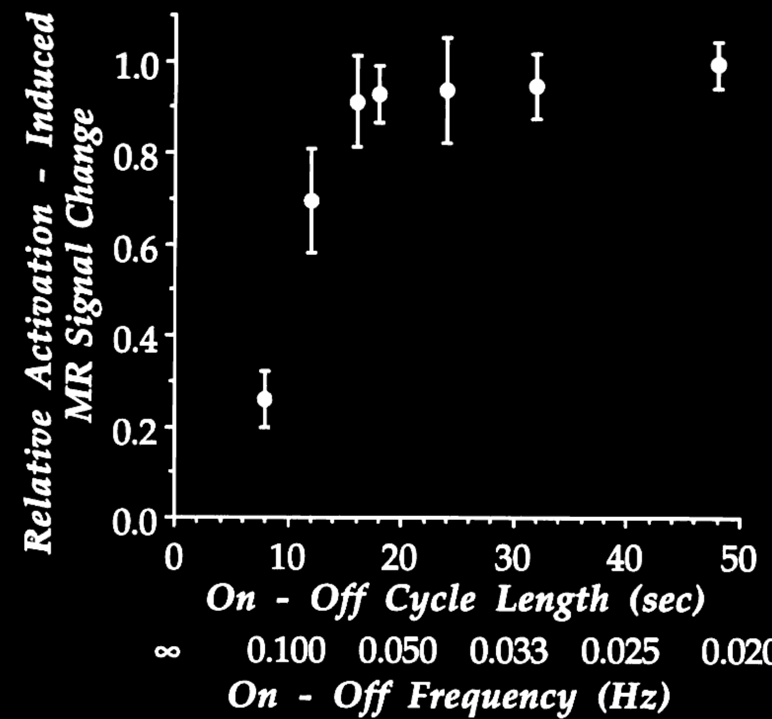


≈ 20 to 40 ms

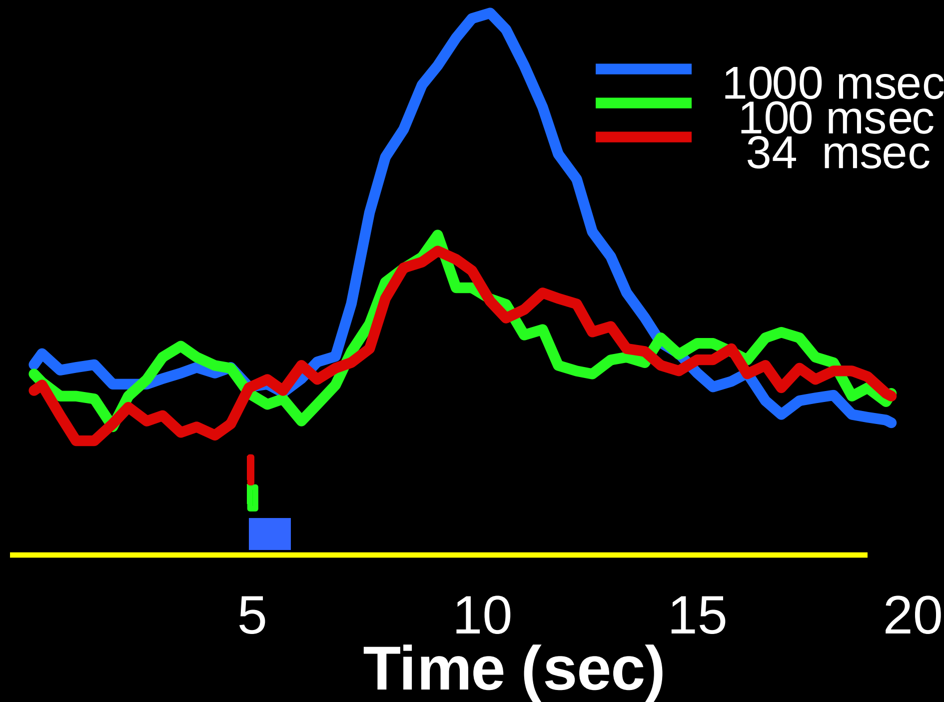




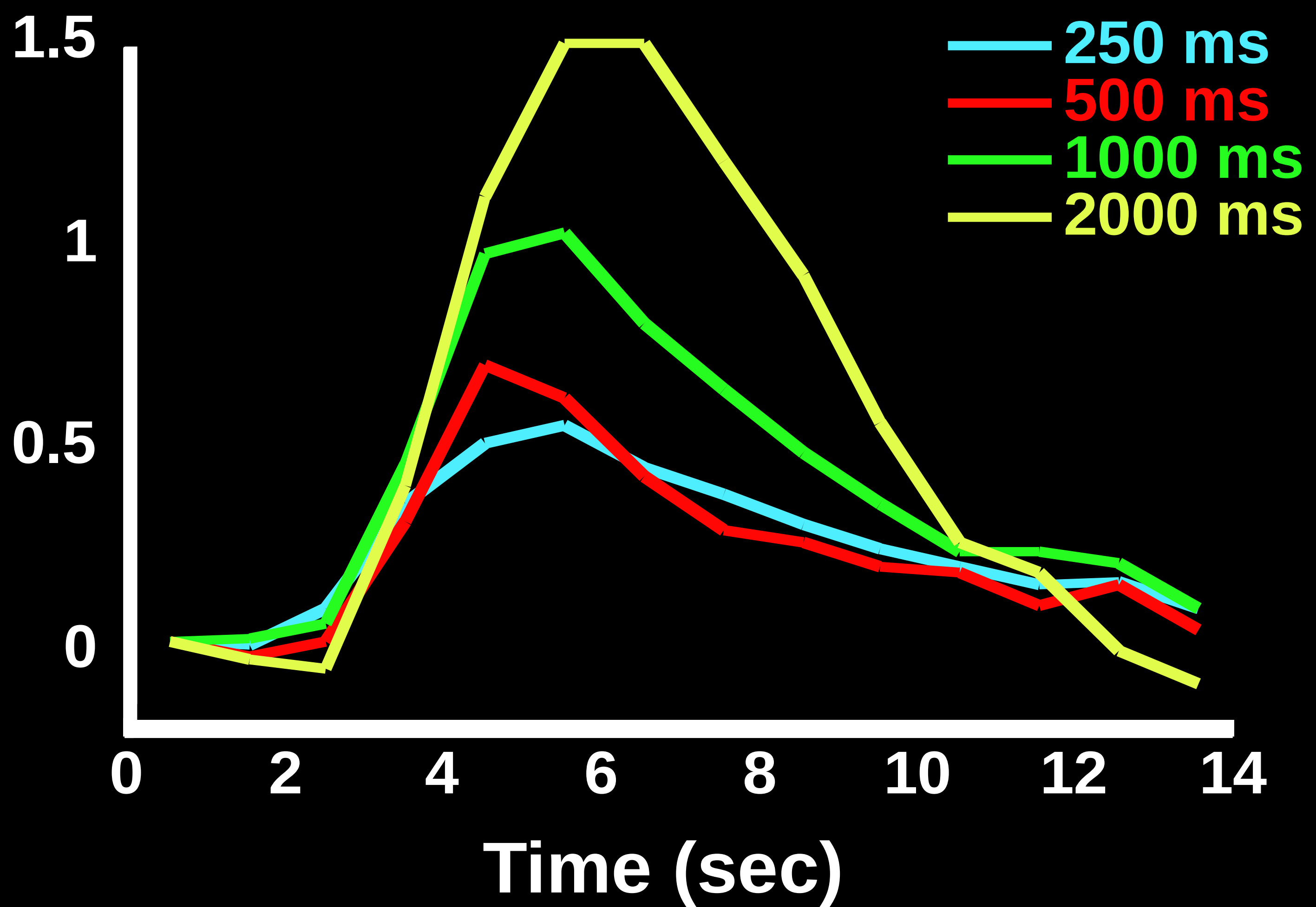




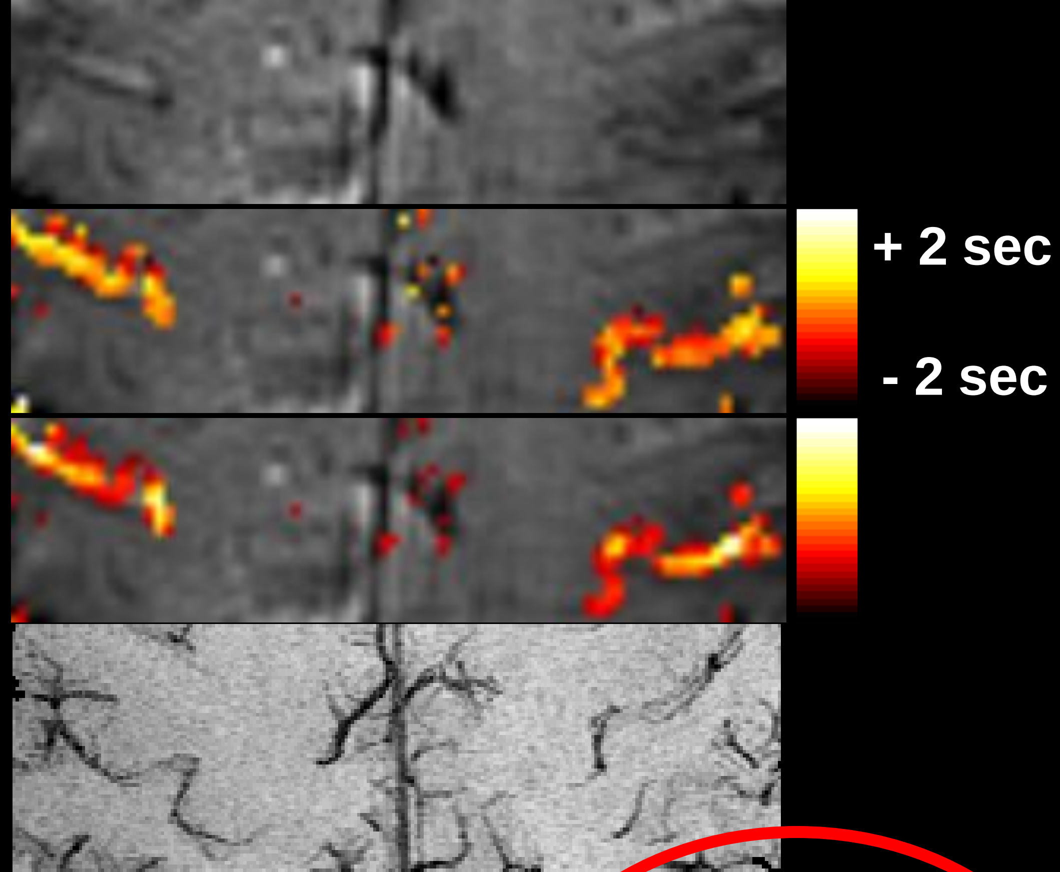
P. A. Bandettini, Functional MRI temporal resolution *in* "Functional MRI" (C. Moonen, and P. Bandettini., Eds.), p. 205-220, Springer - Verlag,. 1999.

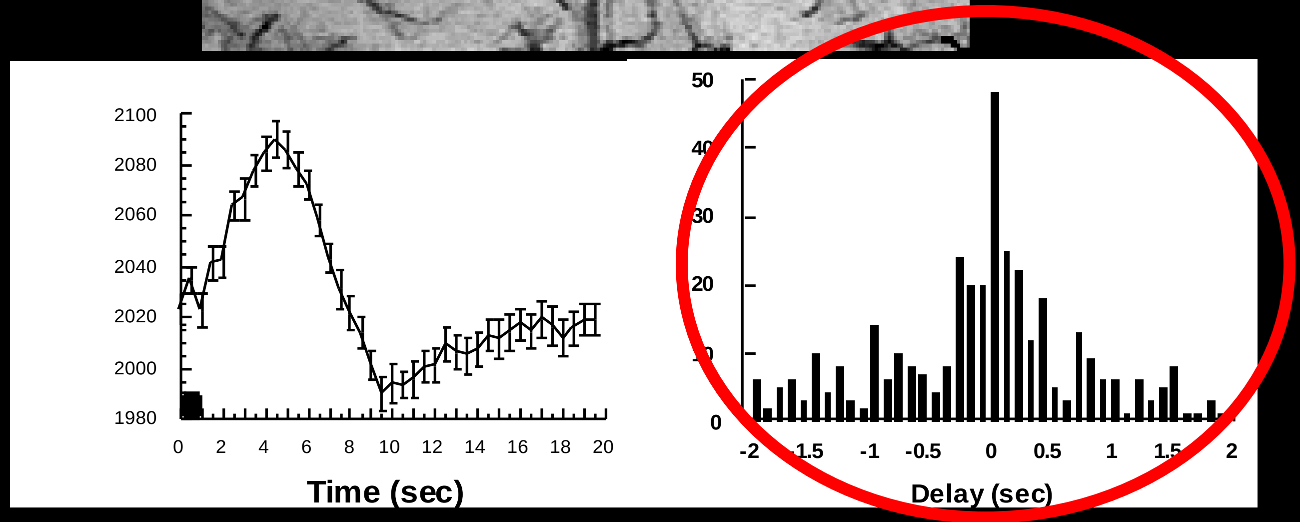


R. L. Savoy, et al., Pushing the temporal resolution of fMRI: studies of very brief visual stimuli, onset variability and asynchrony, and stimulus-correlated changes in noise [oral], 3'rd Proc. Soc. Magn. Reson., Nice, p. 450. (1995).


250 ms
500 ms
1000 ms
2000 ms
1.5
1
0.5
0
0
2
4
6
8
10
12
14
Time (sec)

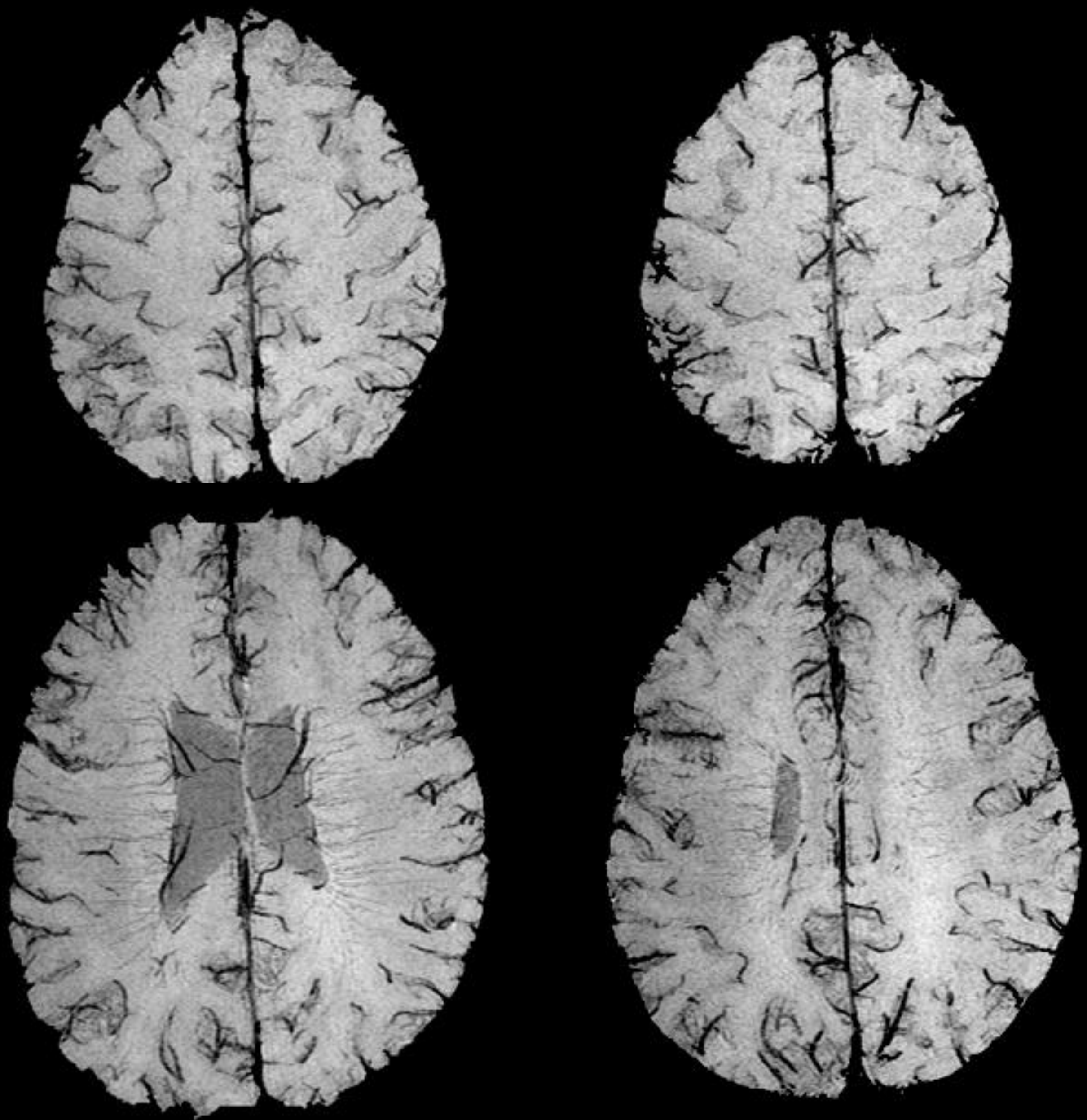
The major obstacle in BOLD contrast temporal resolution:

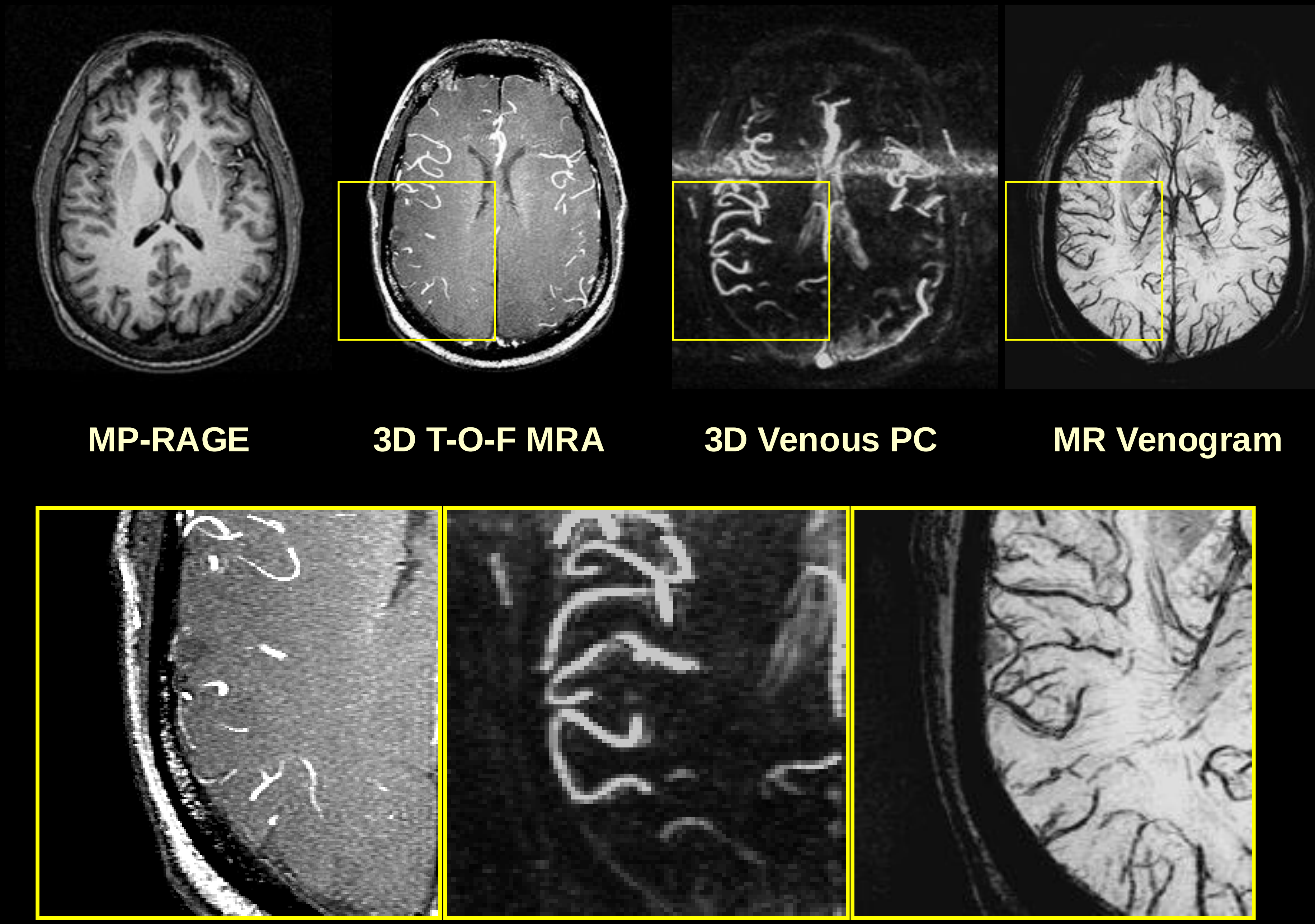




P. A. Bandettini, The temporal resolution of Functional MRI *in* "Functional MRI" (C. Moonen, and P. Bandettini., Eds.), p. 205-220, Springer - Verlag,. 1999.

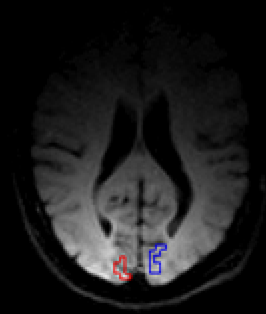
A tangent into venograms
(3 Tesla)



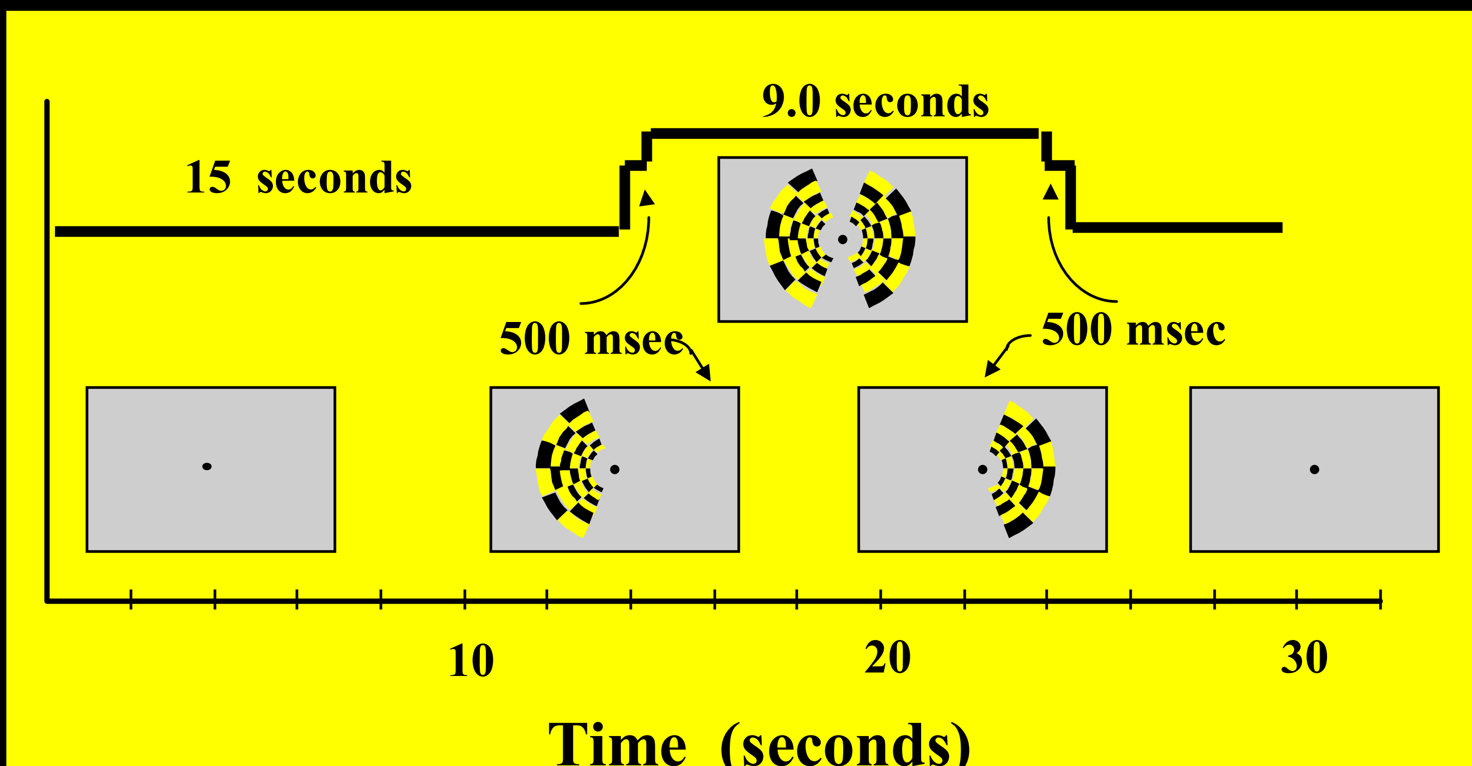

MP-RAGE
3D T-O-F MRA
3D Venous PC
MR Venogram

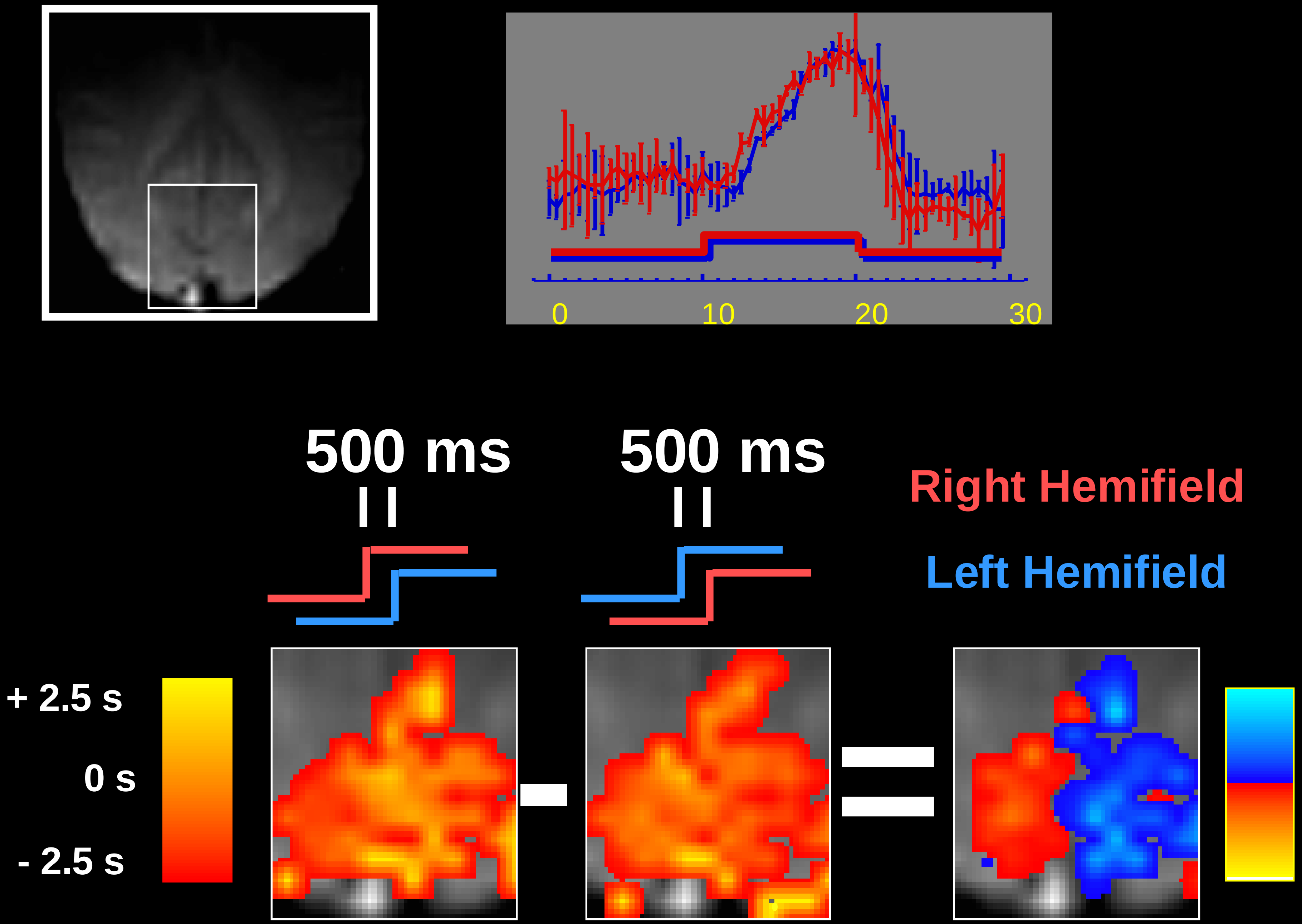
Hemi-Field Experiment

Right Hemisphere



Left Hemisphere

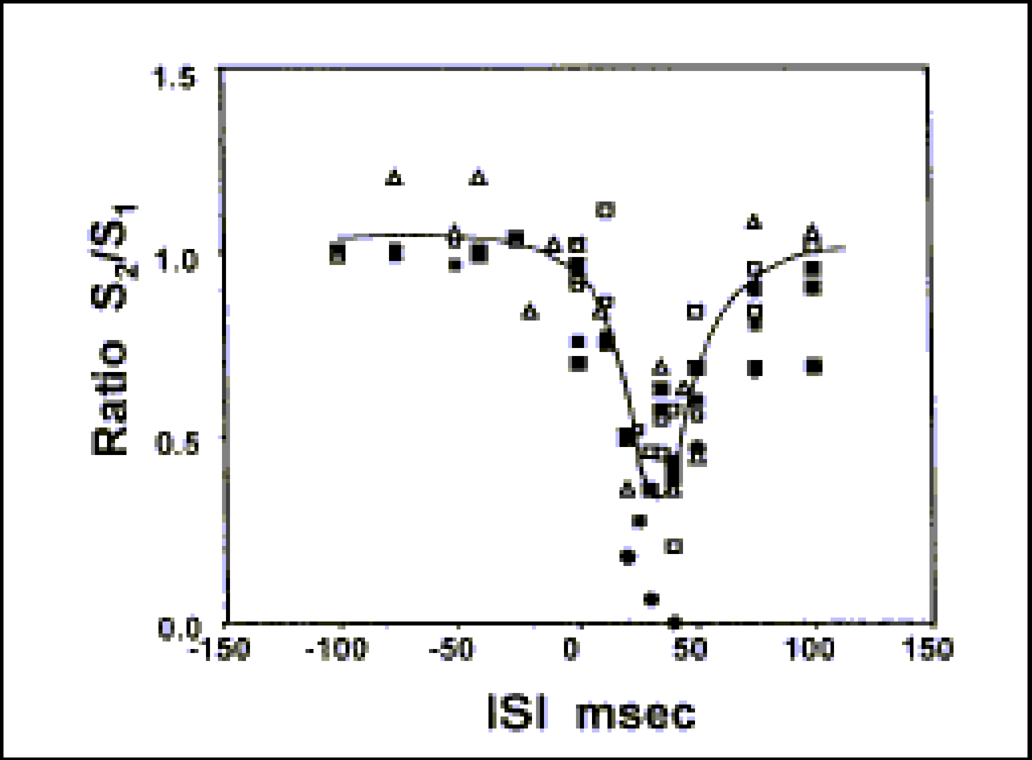



0
10
20
30
500 ms
||
500 ms
||
Right Hemifield
Left Hemifield
+ 2.5 s
0 s
- 2.5 s
-
=

An approach to probe some neural systems interaction by functional MRI at neural time scale down to milliseconds

Seiji Ogawa[†‡], Tso-Ming Lee[†], Ray Stepnoski[†], Wei Chen[§], Xiao-Hong Zhu[§], and Kamil Ugurbil[§]

[†]Bell Laboratories, Lucent Technologies, Murray Hill, NJ 07974; and [§]Center for Magnetic Resonance Research, University of Minnesota Medical School, Minneapolis, MN 55455

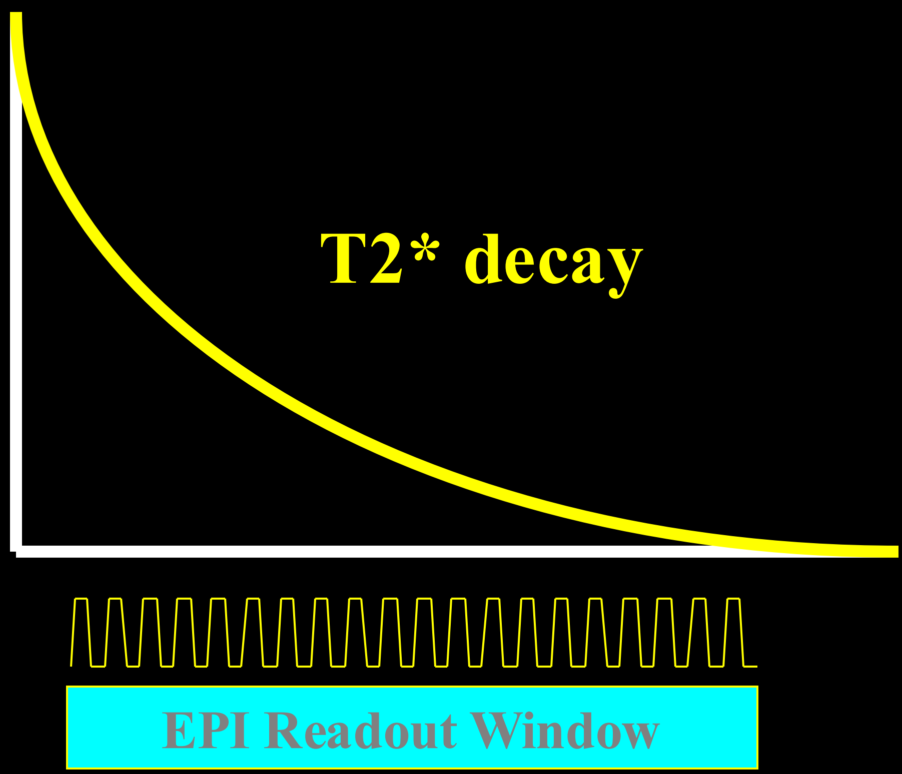


11026–11031 PNAS **September 26, 2000** vol. 97 no. 20

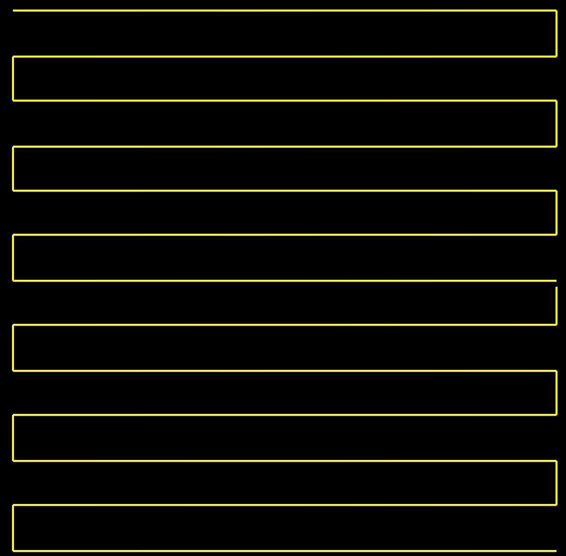
Latest Developments…

1. Temporal Resolution
2. Spatial Resolution
3. Sensitivity and Noise
4. Information Content
5. Implementation

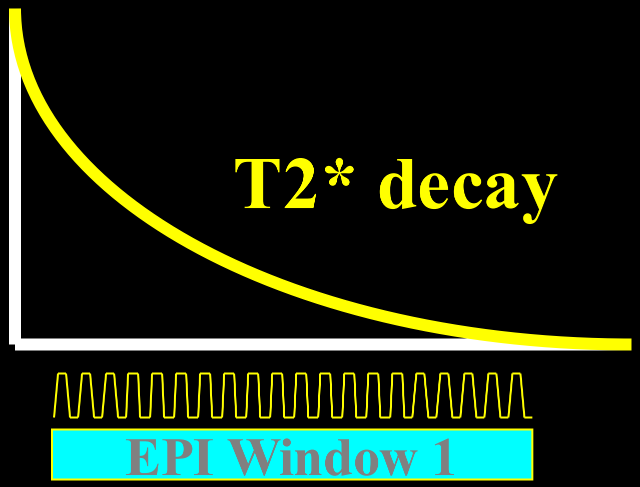
Single Shot Imaging

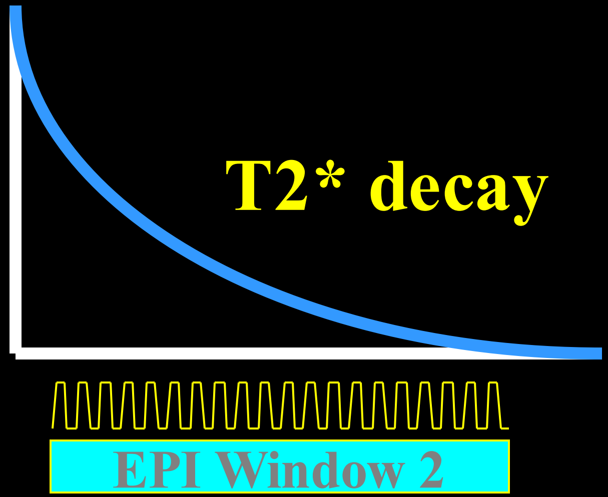


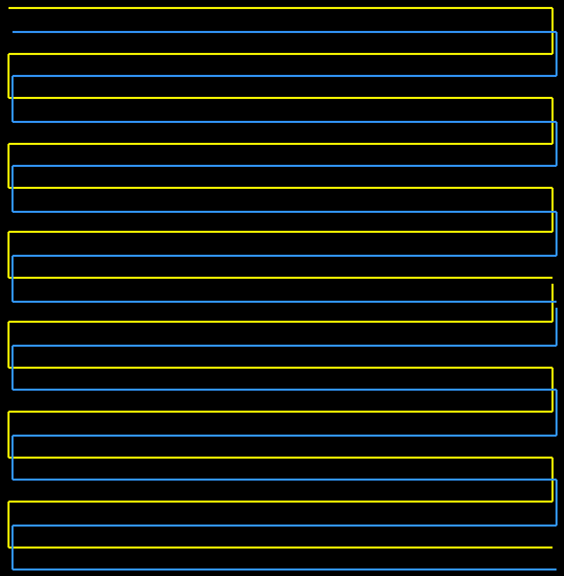
≈ 20 to 40 ms



Multishot Imaging

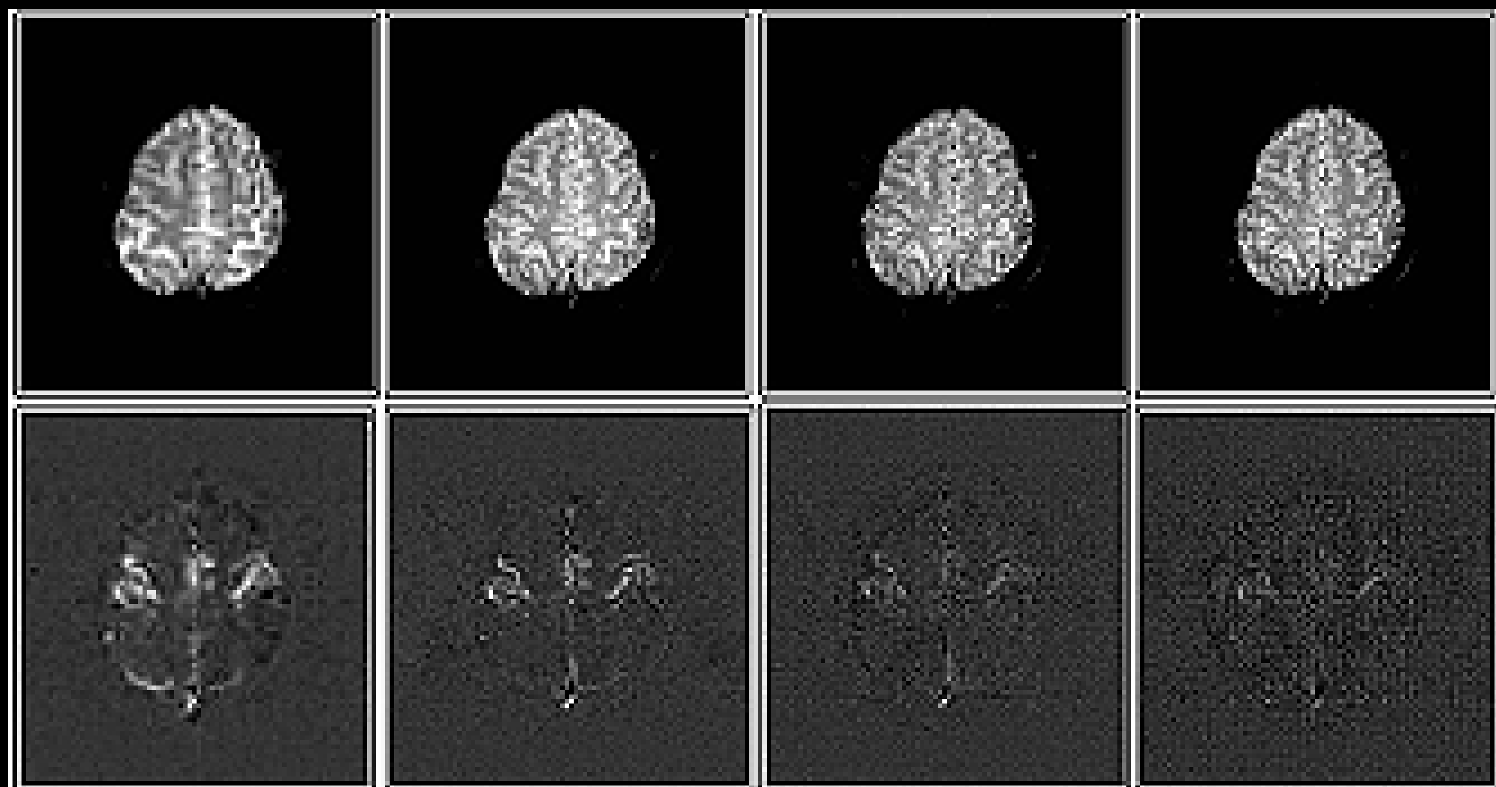




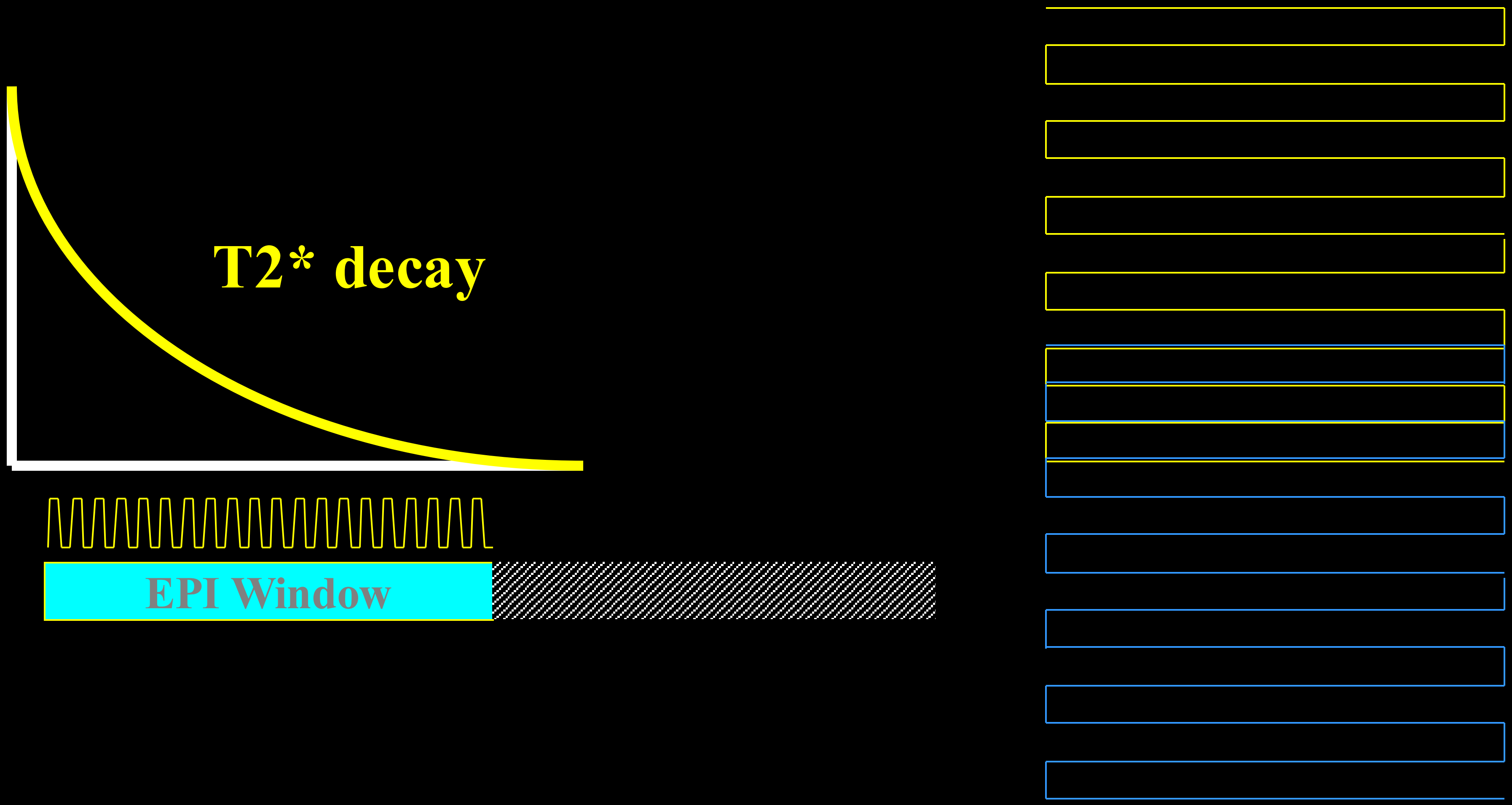


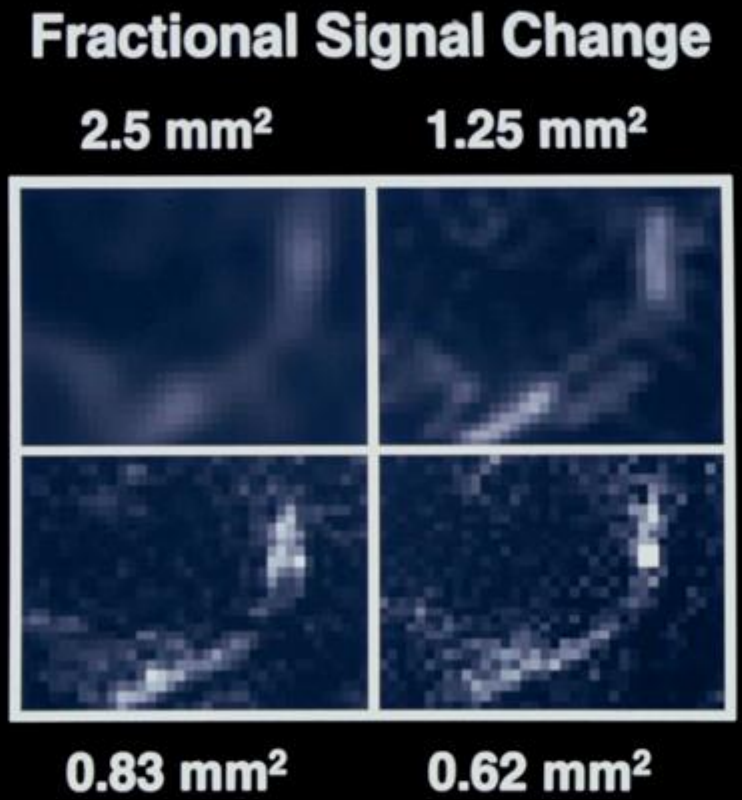
Multi Shot EPI

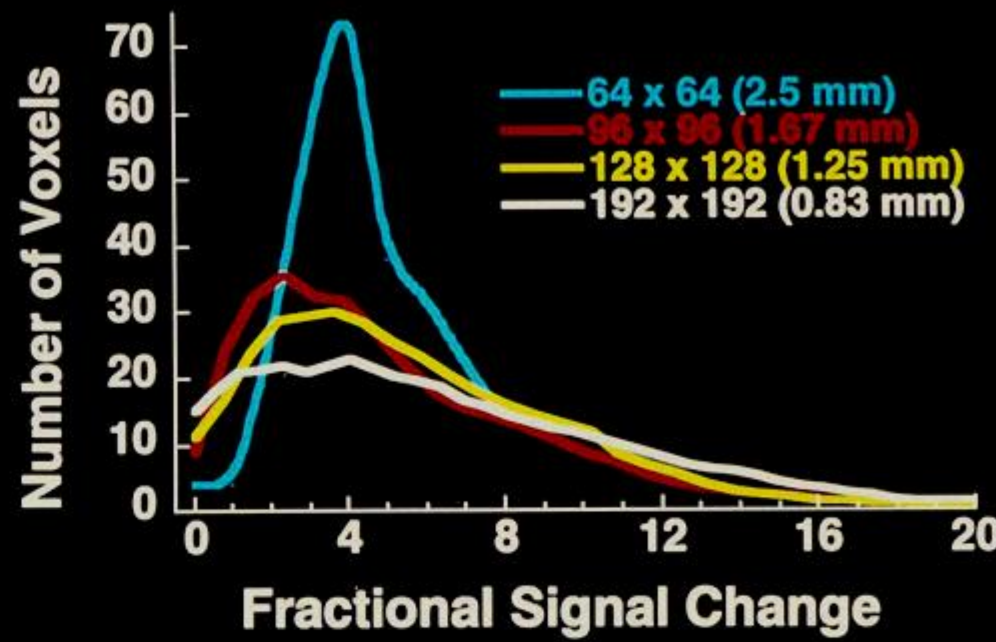
Excitations 1 2 4 8
Matrix Size 64 x 64 128 x 128 256 x 128 256 x 256



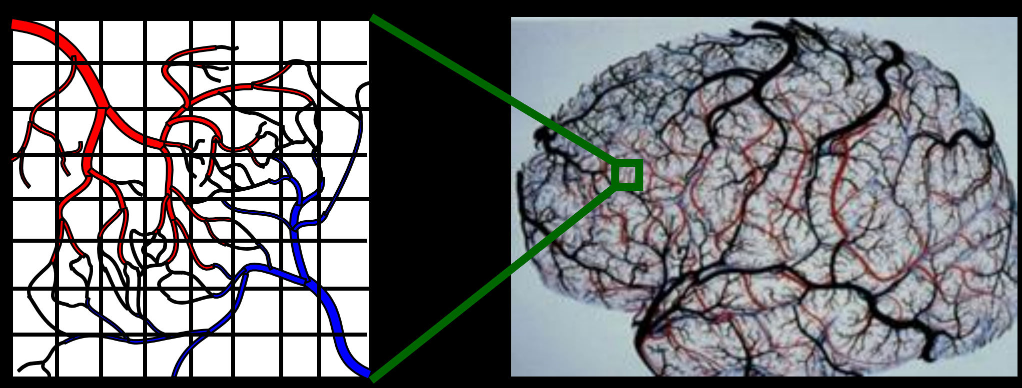
Partial k-space imaging



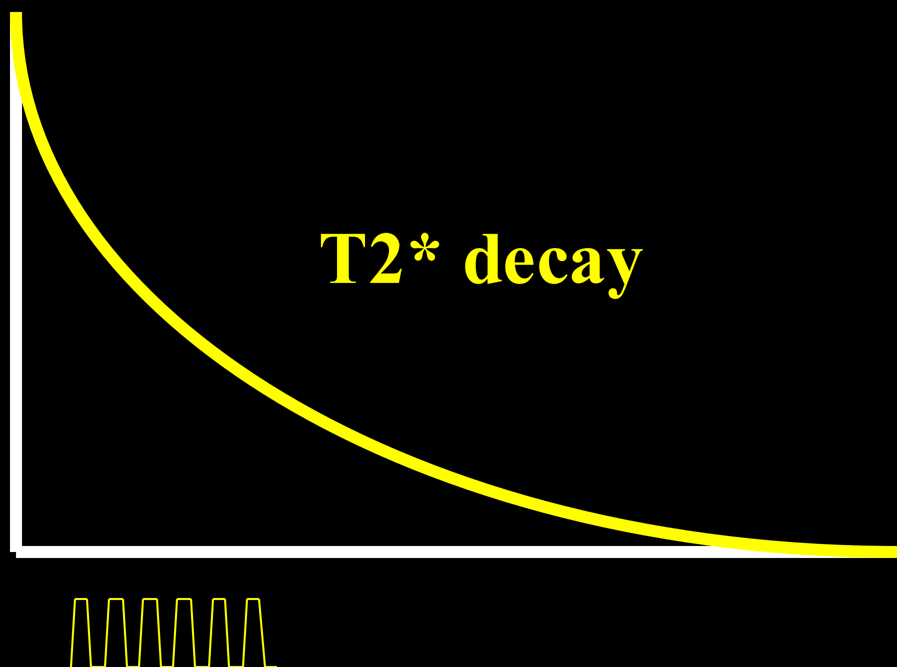




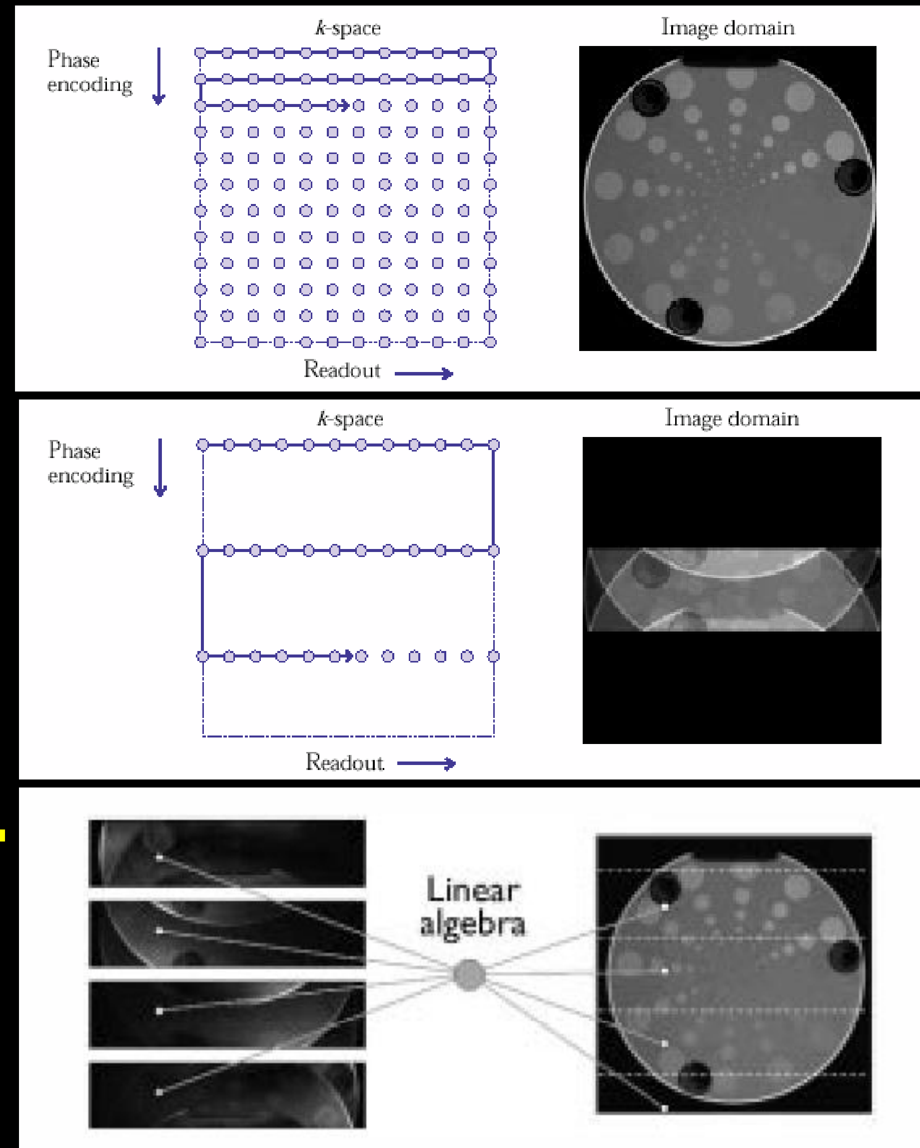
Jesmanowicz, P. A. Bandettini, J. S. Hyde, (1998) "Single shot half k-space high resolution EPI for fMRI at 3T." *Magn. Reson. Med.* 40, 754-762.



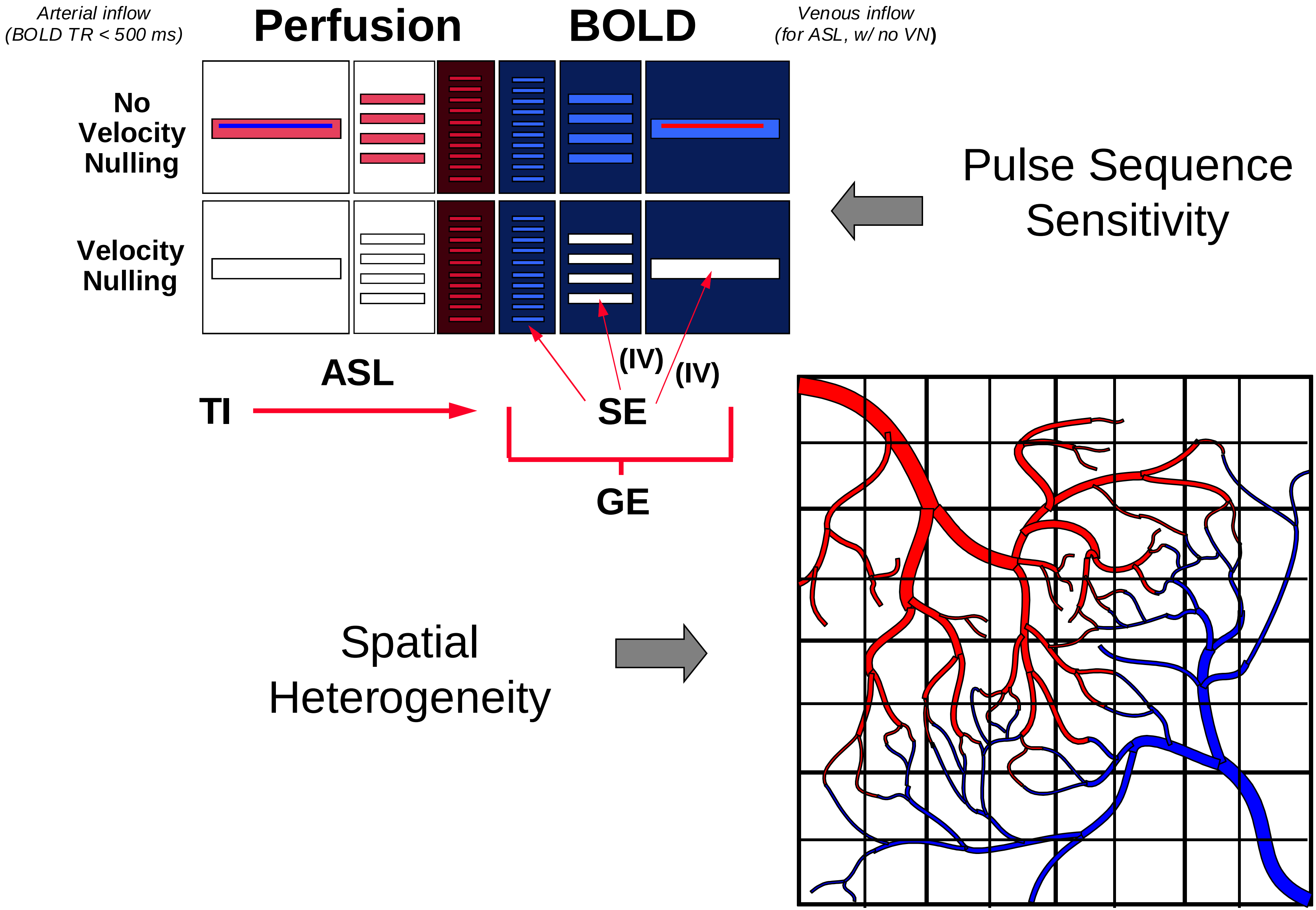
SENSE Imaging



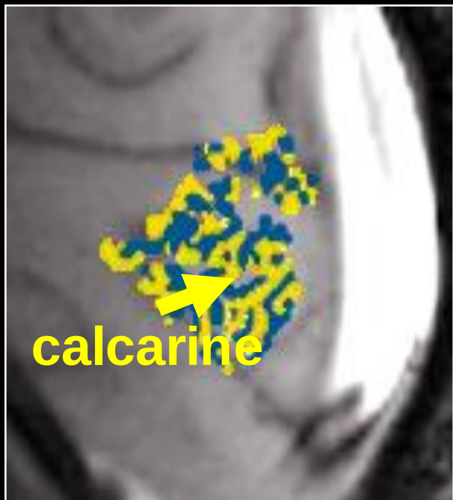
as low as 5 ms

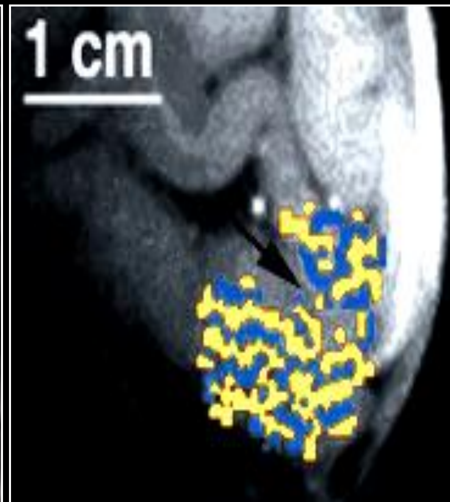


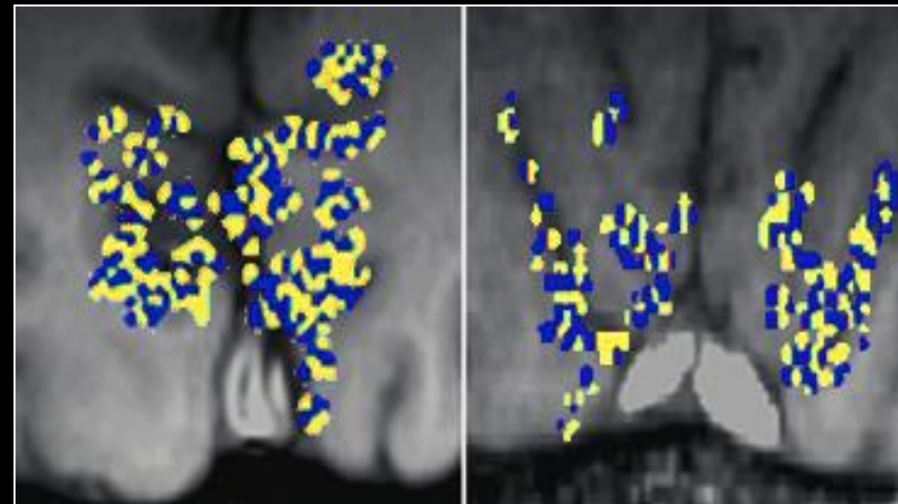
Pruessmann, et al.


Arterial inflow
(BOLD TR < 500 ms)
Perfusion
BOLD
Venous inflow
(for ASL, w/ no VN)
No Velocity Nulling
Velocity Nulling
Pulse Sequence Sensitivity
ASL
TI
(IV)
(IV)
SE
GE
Spatial Heterogeneity

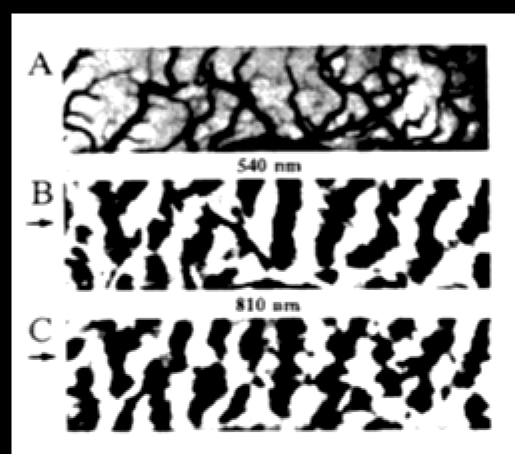
Ocular Dominance Column Mapping using fMRI







Menon, R. S., S. Ogawa, et al. (1997). “Ocular dominance in human V1 demonstrated by functional magnetic resonance imaging.” J Neurophysiol 77(5): 2780-7.



Optical Imaging

R. D. Frostig et. al, PNAS 87: 6082-6086, (1990).

Latest Developments…

1. Temporal Resolution
2. Spatial Resolution
3. Sensitivity and Noise
4. Information Content
5. Implementation

The spatial extent of the BOLD response

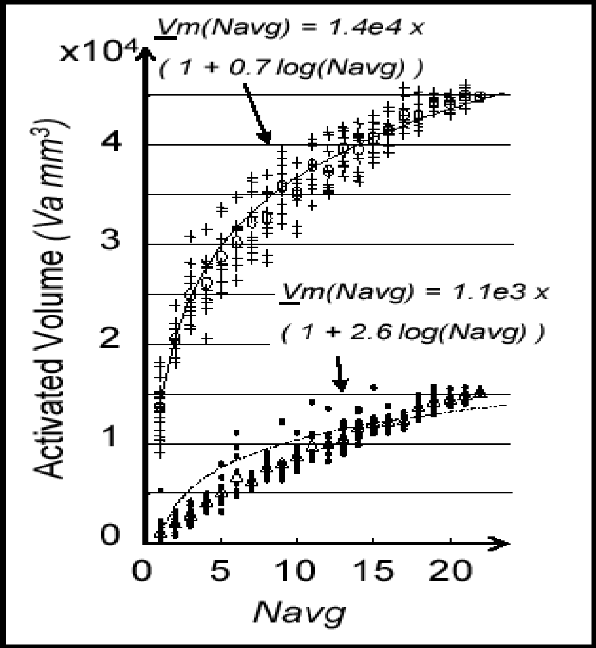
Ziad S. Saad,[a,b,*] Kristina M. Ropella,[b] Edgar A. DeYoe,[c] and Peter A. Bandettini[a]

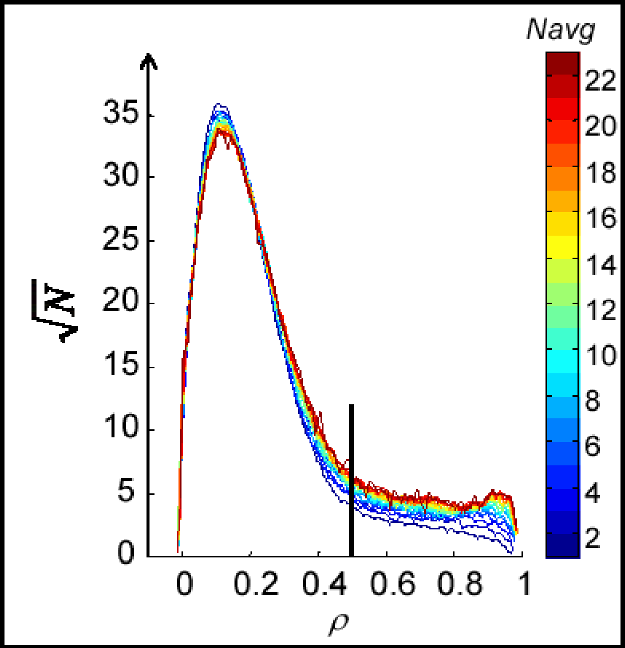
[a] Laboratory of Brain and Cognition, National Institute of Mental Health, NIH, Bethesda, MD 20892-1148, USA
[b] Department of Biomedical Engineering Marquette University, Milwaukee, WI 53233, USA
[c] Department of Cell Biology, Neurobiology and Anatomy, Medical College of Wisconsin, Milwaukee, WI 53226, USA

Received 16 August 2002; revised 29 October 2002; accepted 21 November 2002

NeuroImage

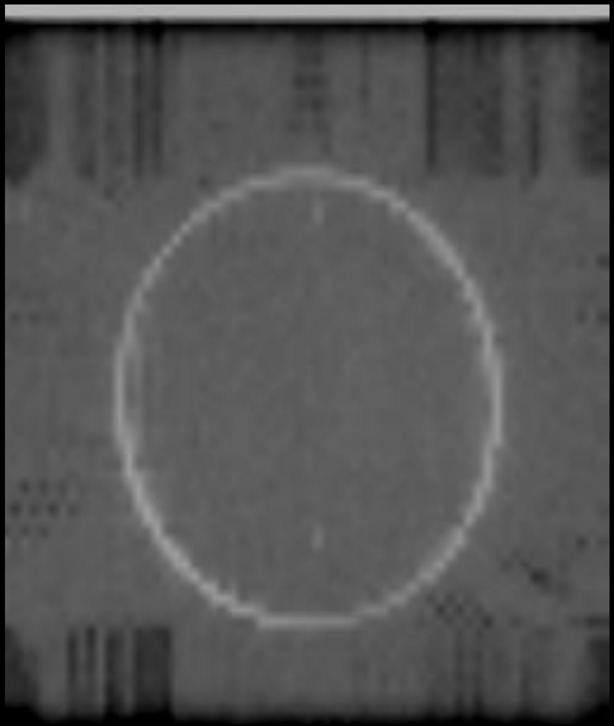
Question: What is the "true" spatial extent of BOLD contrast?
Paradigm: Repeated averaging of simple visual task





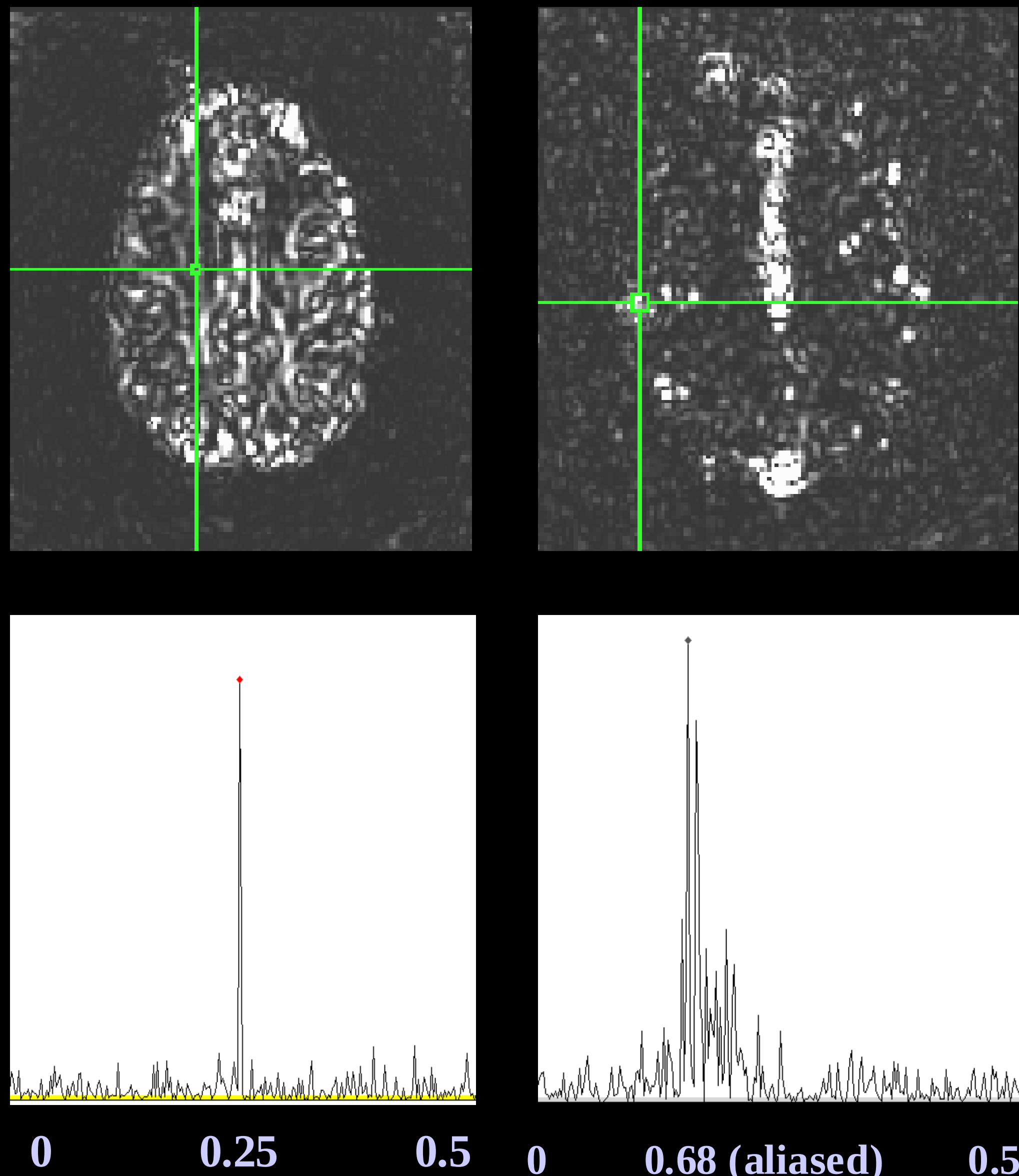
Temporal Standard Deviation

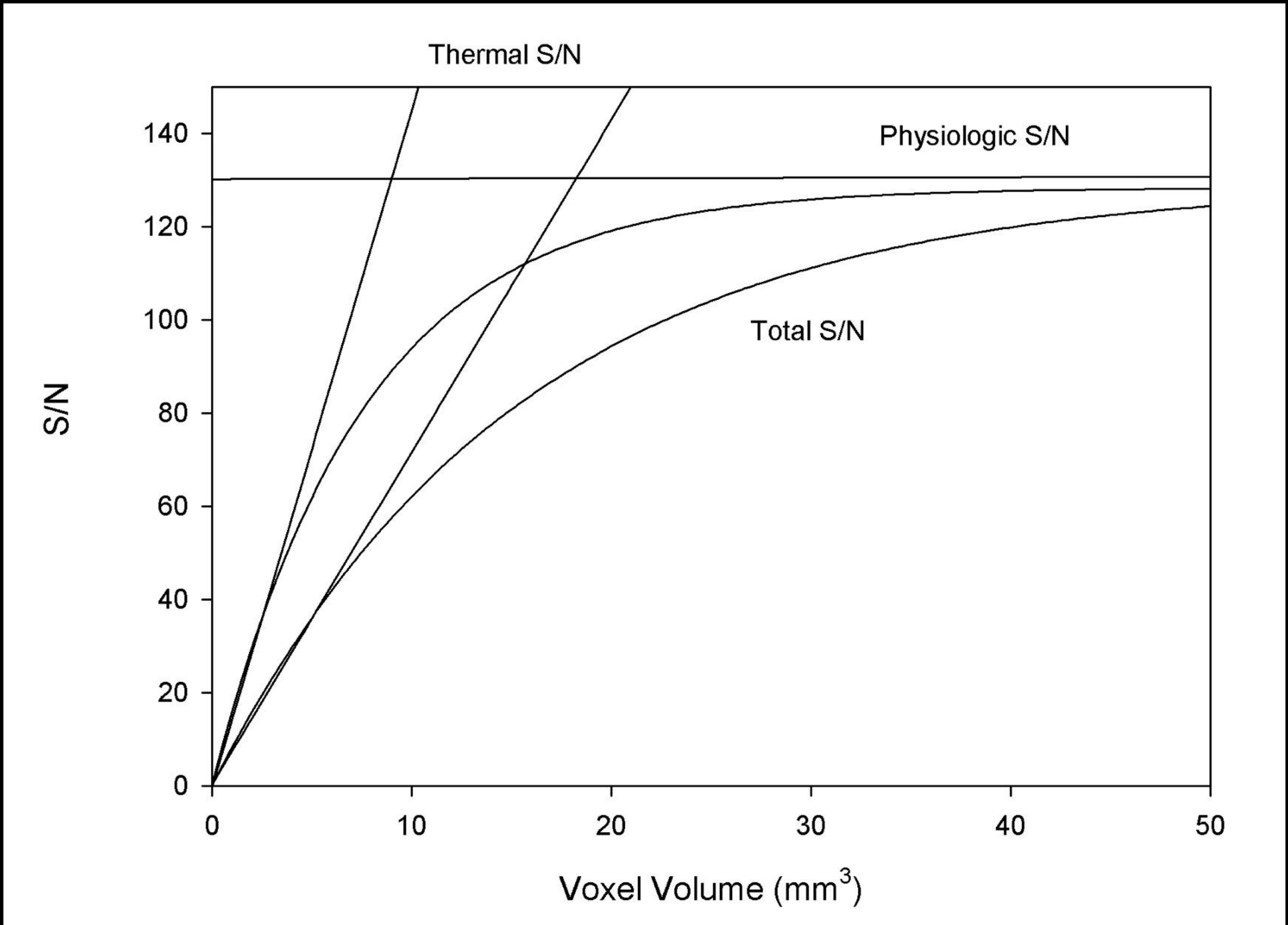
Human Brain



Bottle of Water

Respiratory | Cardiac

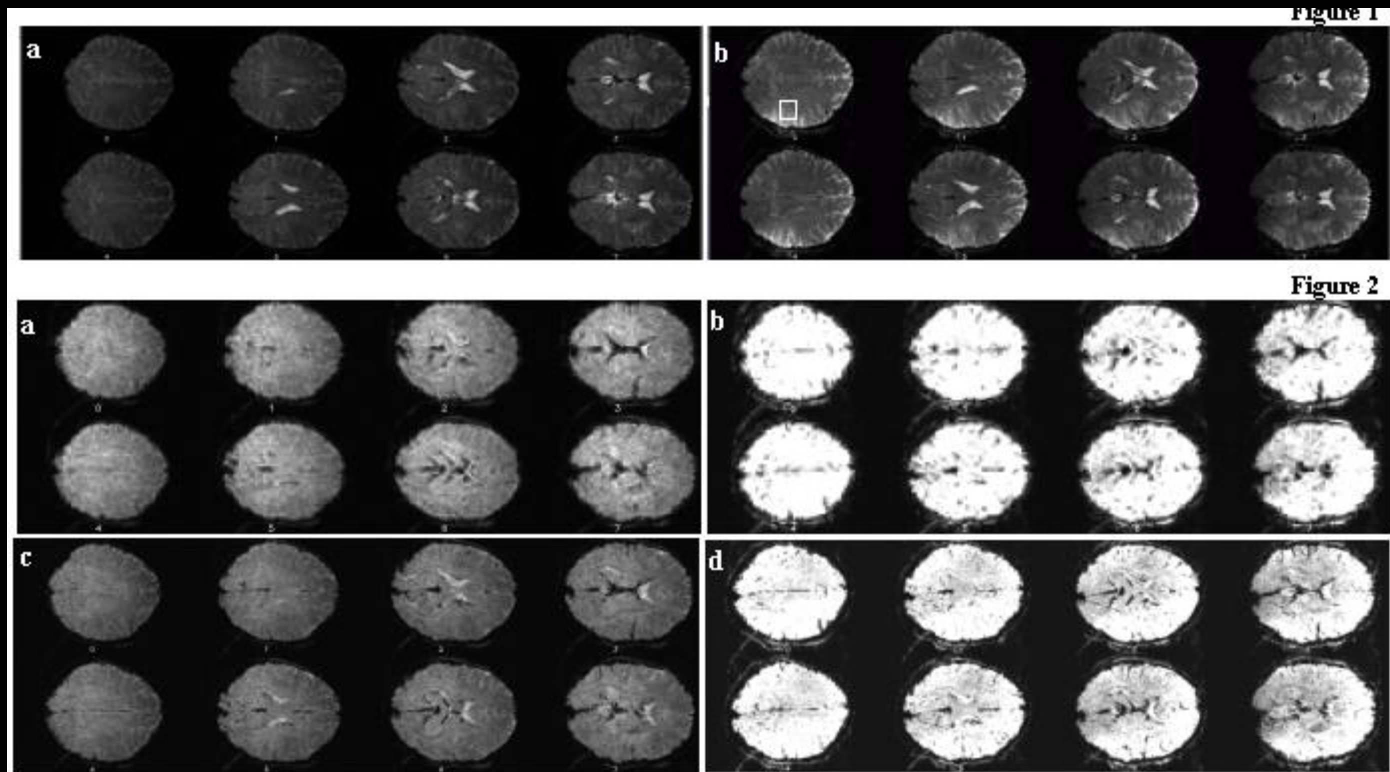



Thermal S/N
Physiologic S/N
Total S/N
S/N
Voxel Volume (mm^3)
0
20
40
60
80
100
120
140
0
10
20
30
40
50

Single shot full k-space echo-planar-imaging with an eight-channel phase array coil at 3T.

Jerzy Bodurka[1], Peter van Gelderen[2], Patrick Ledden[3], Peter Bandettini[1], Jeff Duyn[2]
[1]Functional MRI Facility NIMH/NIH, [2]Advance MRI NINDS/NIH, [3]Nova Medical Inc.

Quadrature Head Coil — 8 Channel Array



128 x 96 — SNR

64 x 48 — TSNR

128 x 96 — TSNR

Latest Developments…

1. Temporal Resolution
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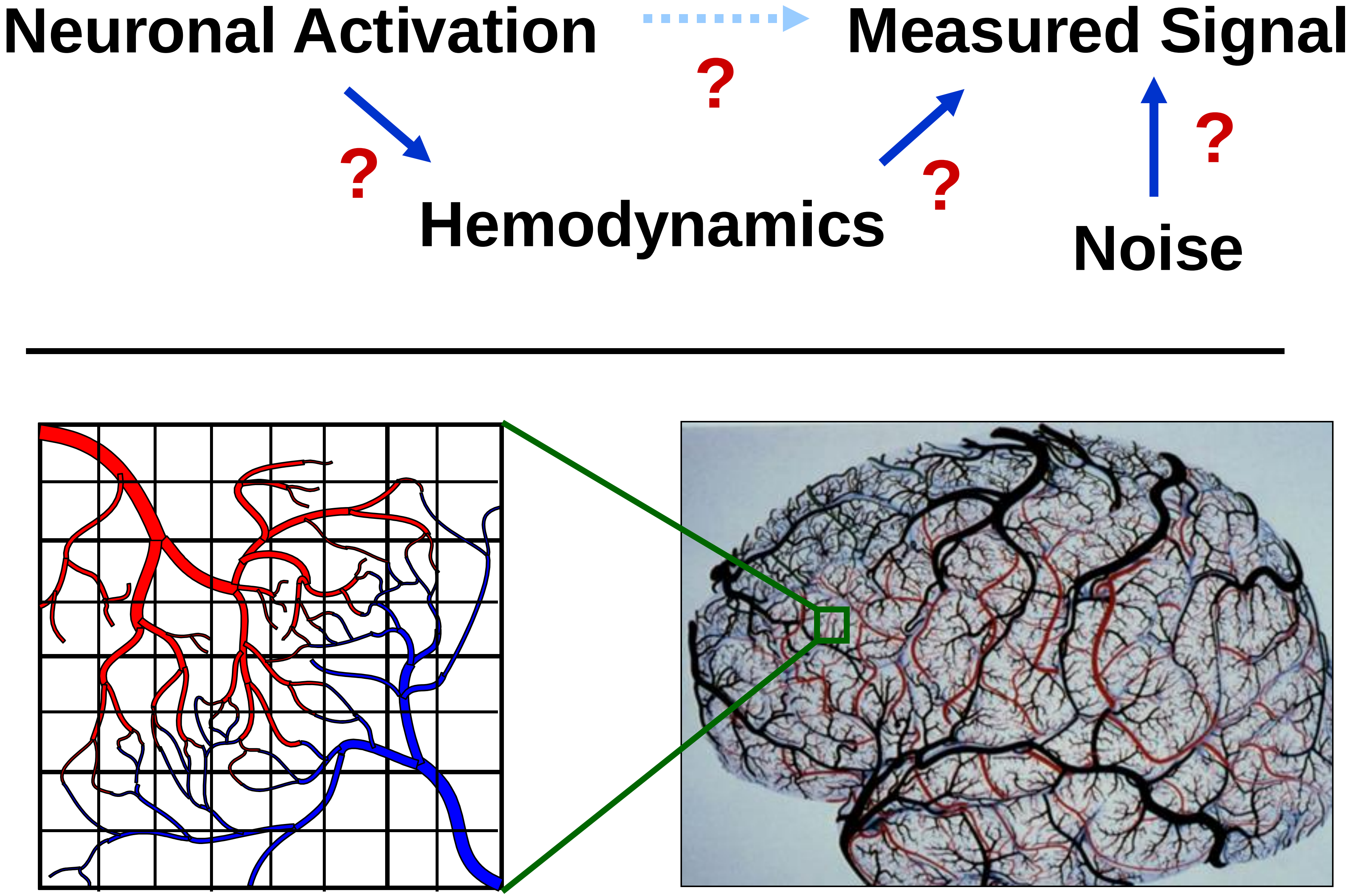
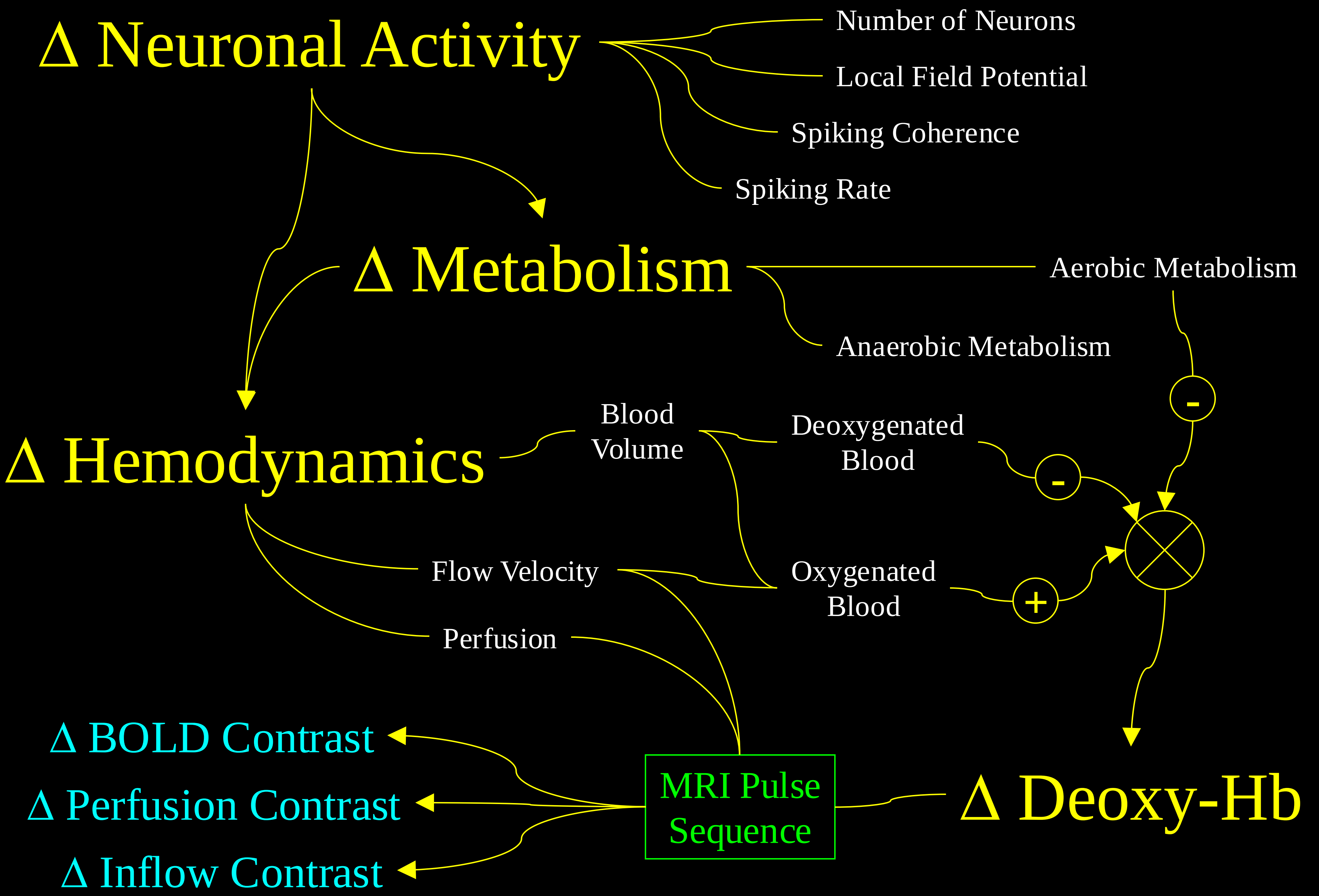
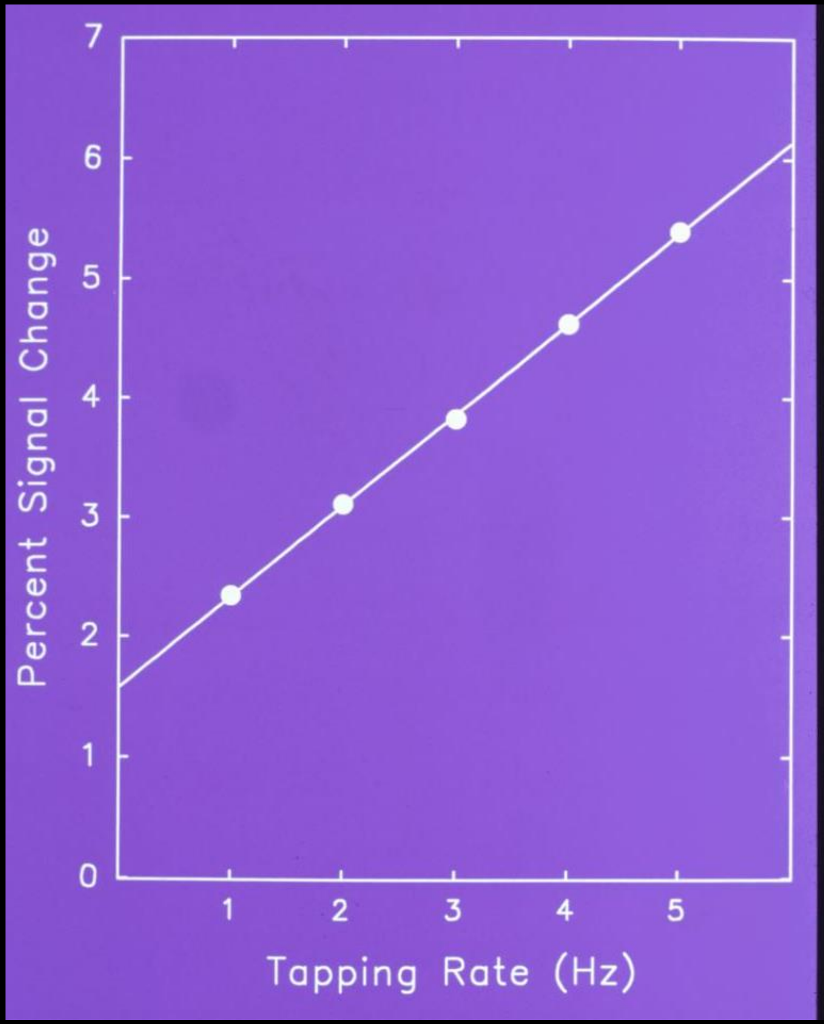
5. Implementation


Neuronal Activation
Measured Signal
?
?
?
?
Hemodynamics
Noise

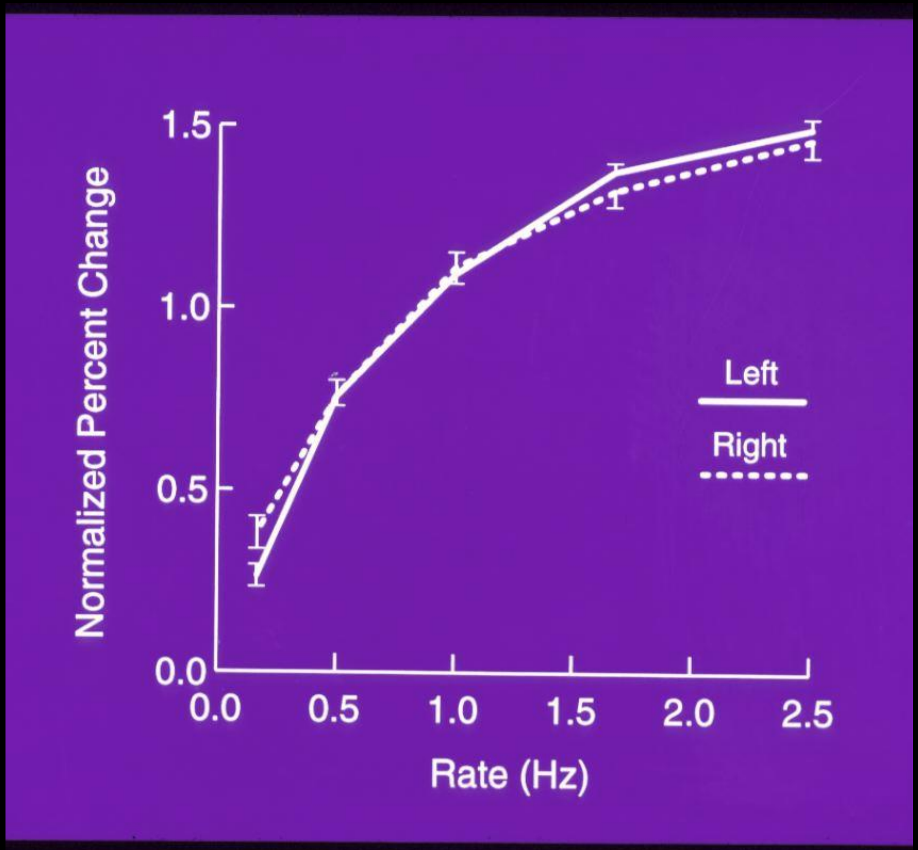

Δ Neuronal Activity
Number of Neurons
Local Field Potential
Spiking Coherence
Spiking Rate
Δ Metabolism
Aerobic Metabolism
Anaerobic Metabolism
Δ Hemodynamics
Blood Volume
Deoxygenated Blood
Oxygenated Blood
-
-
+
Flow Velocity
Perfusion
Δ BOLD Contrast
Δ Perfusion Contrast
Δ Inflow Contrast
MRI Pulse Sequence
Δ Deoxy-Hb

Motor Cortex

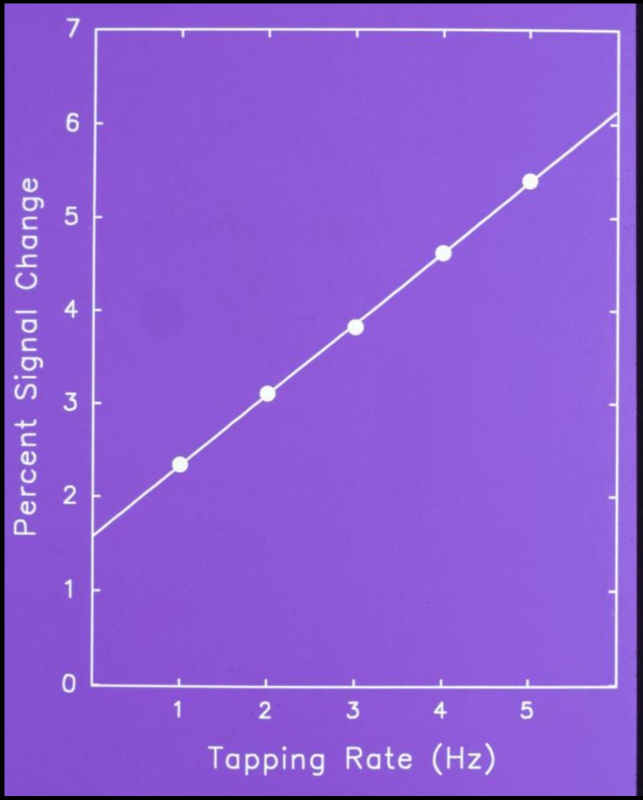


S. M. Rao et al, (1996) "Relationship between finger movement rate and functional magnetic resonance signal change in human primary motor cortex." *J. Cereb. Blood Flow and Met.* 16, 1250-1254.

Auditory Cortex

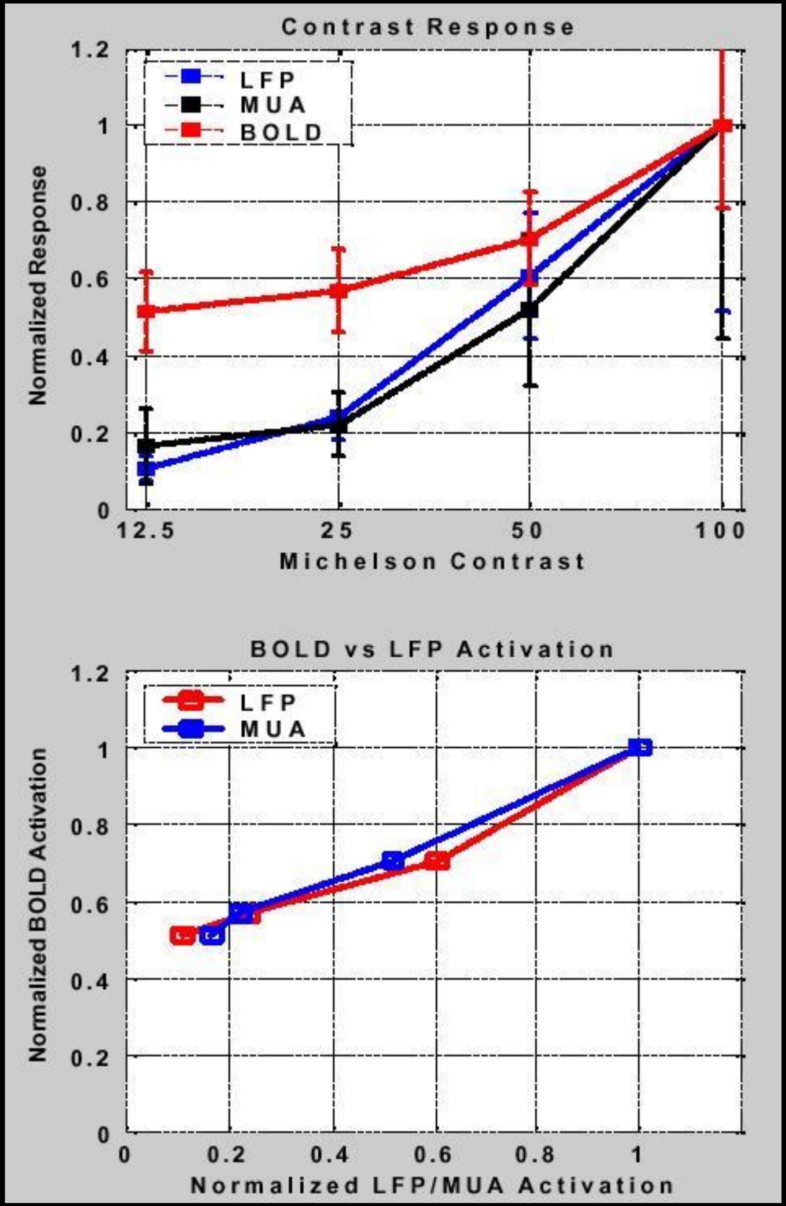


J. R. Binder, et al, (1994). "Effects of stimulus rate on signal response during functional magnetic resonance imaging of auditory cortex." *Cogn. Brain Res.* 2, 31-38



S. M. Rao et al, (1996) "Relationship between finger movement rate and functional magnetic resonance signal change in human primary motor cortex." ***J. Cereb. Blood Flow and Met.*** **16, 1250-1254.**

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



Spatial Heterogeneity of the Nonlinear Dynamics in the FMRI BOLD Response

Rasmus M. Birn, Ziad S. Saad, and Peter A. Bandettini

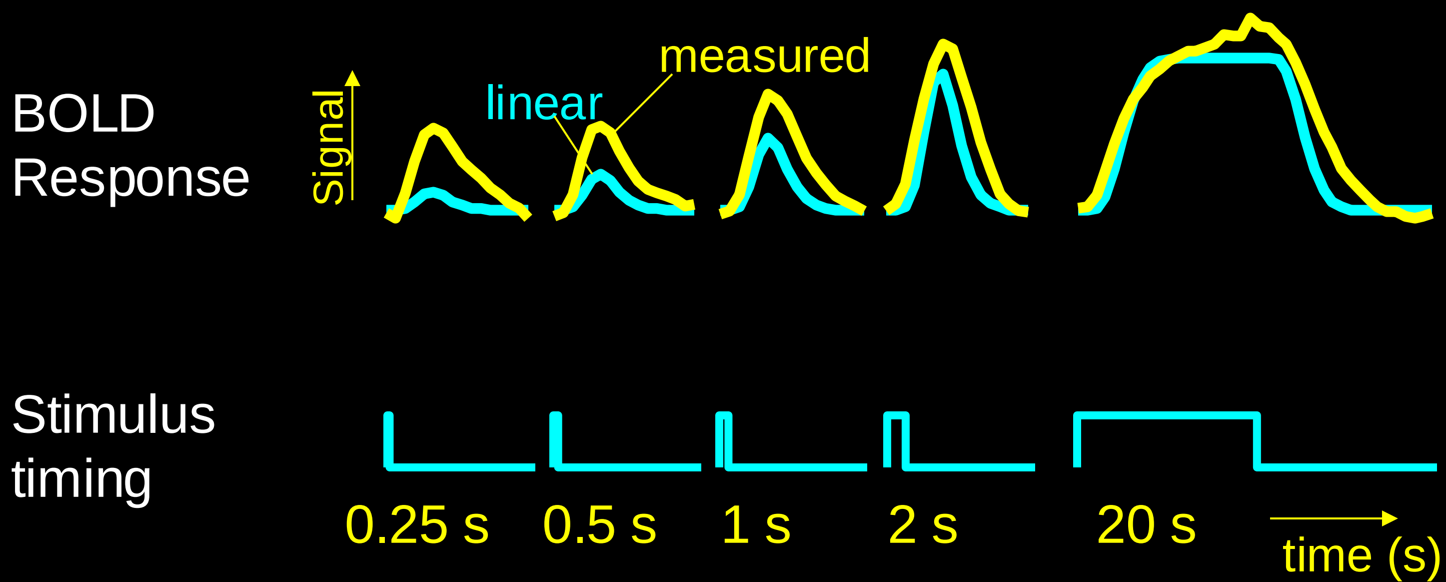
Laboratory of Brain and Cognition, National Institute of Mental Health, NIH Bethesda, Maryland

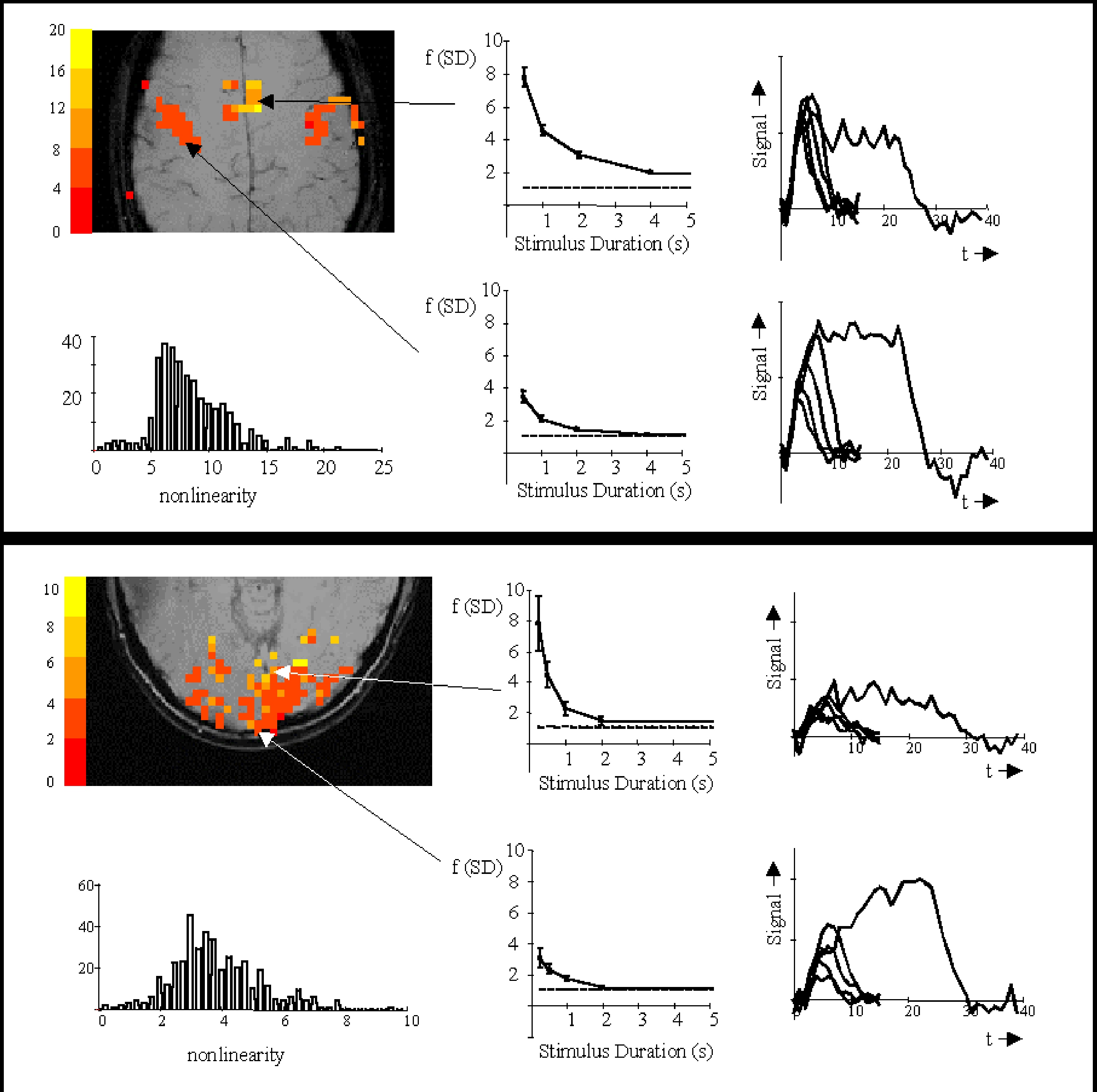
Received October 18, 2000

NeuroImage

Question: Do BOLD nonlinearities exhibit spatial heterogeneity?

Paradigm: Stimulus duration modulation from 50 ms to 20 sec.

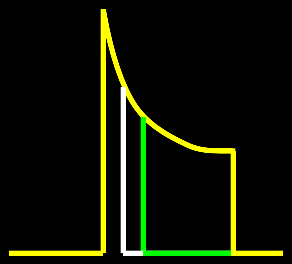




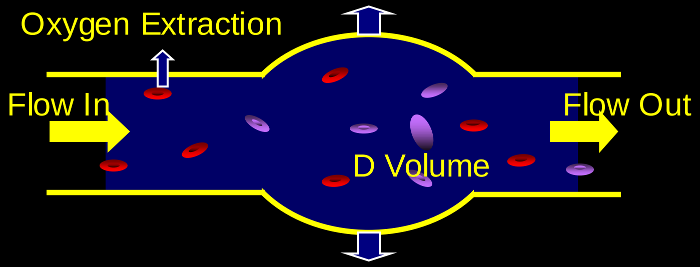
f (SD)
Stimulus Duration (s)
Signal
t
nonlinearity
f (SD)
Stimulus Duration (s)
Signal
t
nonlinearity

Sources of this Nonlinearity

- Neuronal

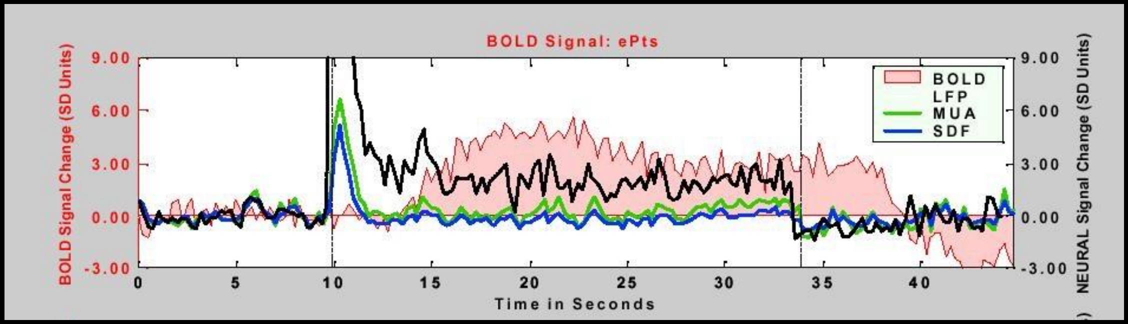


- Hemodynamic
  - Oxygen extraction
  - Blood volume dynamics

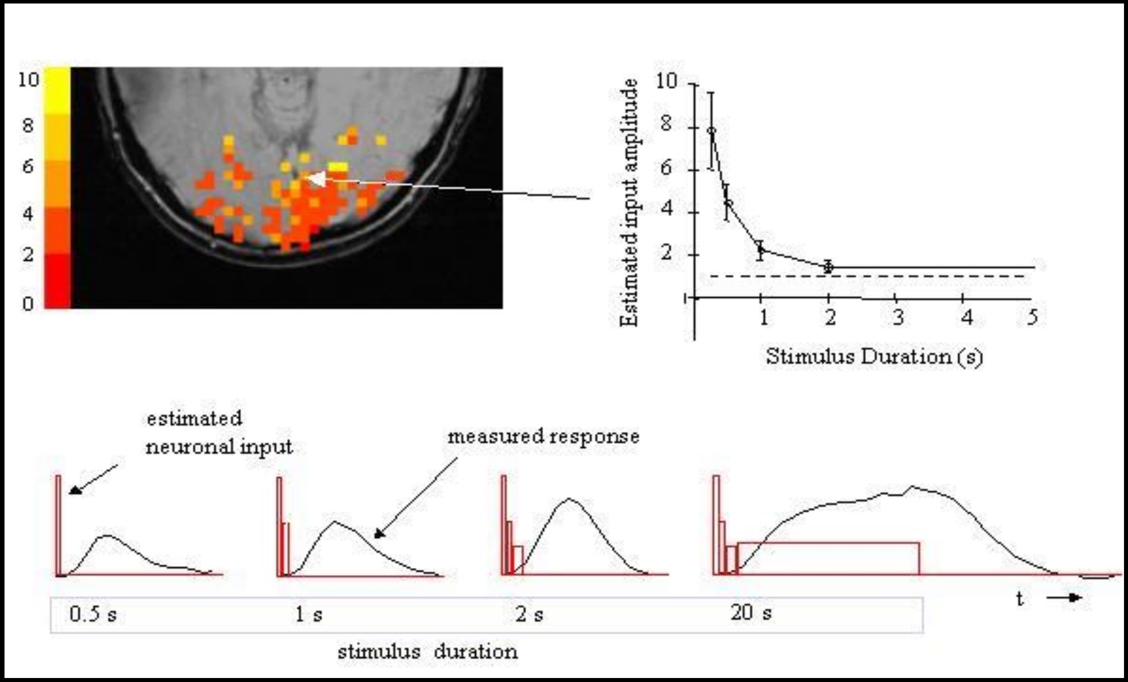


BOLD Correlation with Neuronal Activity

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



P. A. Bandettini and L. G. Ungerleider, (2001) "From neuron to BOLD: new connections." Nature Neuroscience, 4: 864-866.

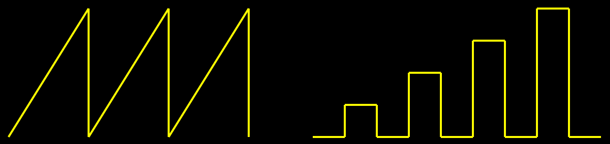


Latest Developments…

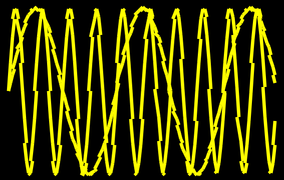
1. Temporal Resolution
2. Spatial Resolution
3. Sensitivity and Noise
4. Information Content
5. Implementation

Neuronal Activation Input Strategies

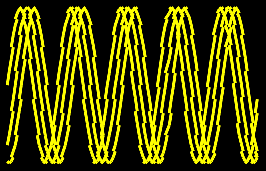
1. Block Design
2. Parametric Design



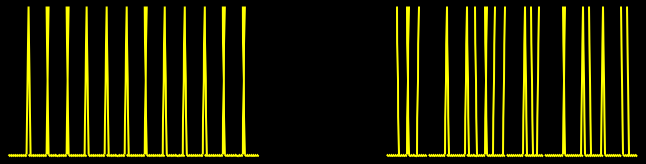
3. Frequency Encoding



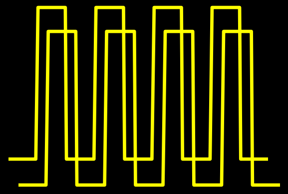
4. Phase Encoding



5. Event Related



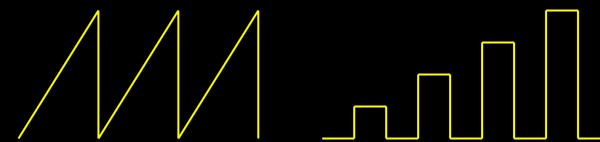
6. Orthogonal Design



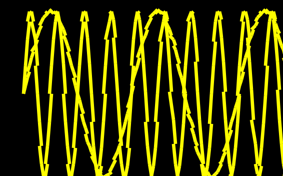
7. Free Behavior Design

Neuronal Activation Input Strategies

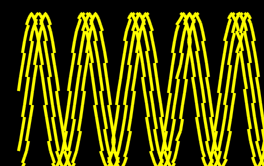
1. Block Design
2. Parametric Design



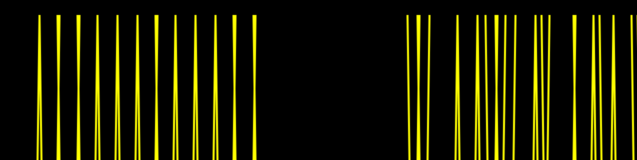
3. Frequency Encoding



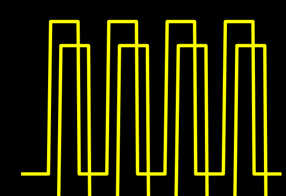
4. **Phase Encoding**



5. Event Related



6. Orthogonal Design

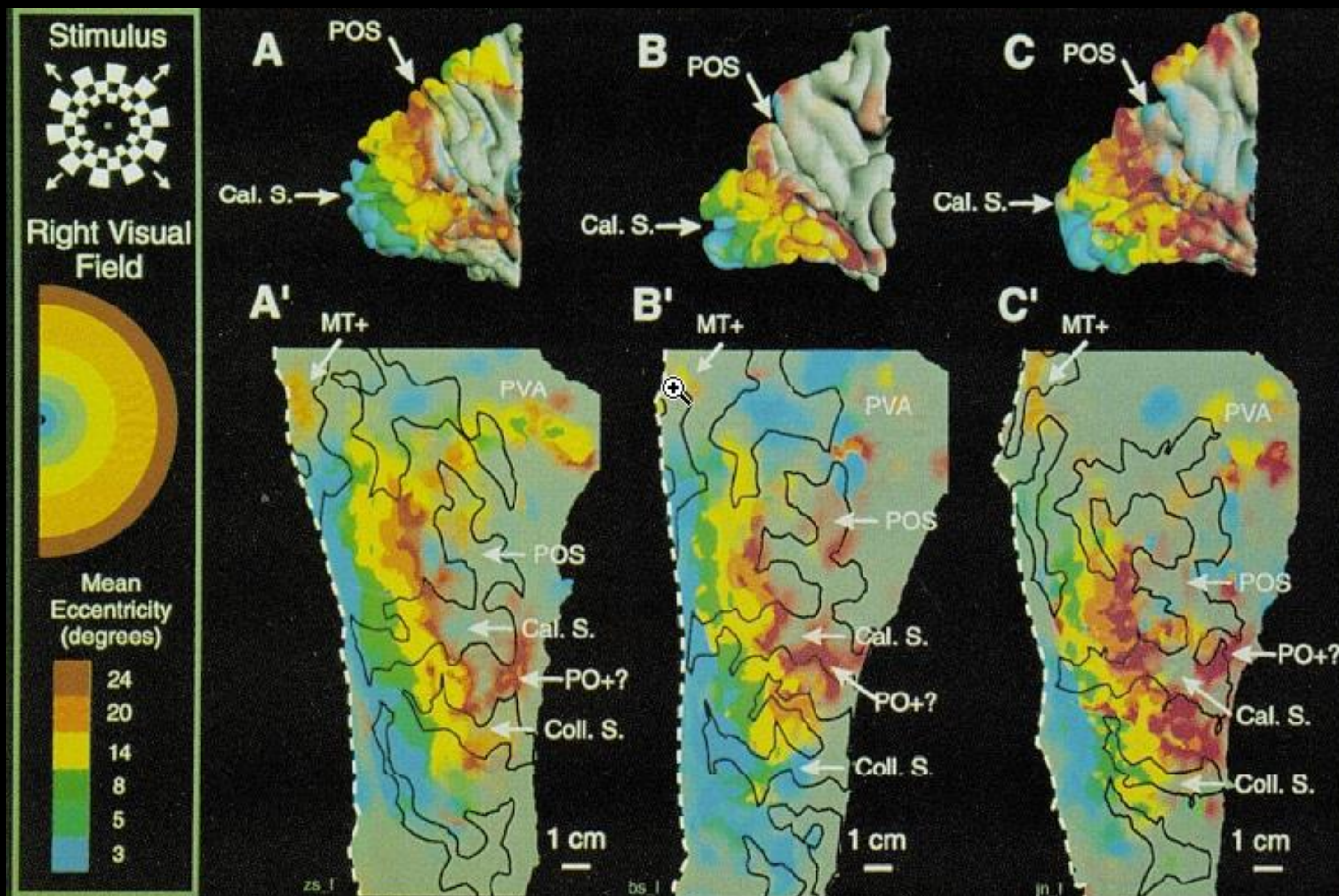


7. Free Behavior Design

Proc. Natl. Acad. Sci. USA
Vol. 93, pp. 2382–2386, March 1996
Neurobiology

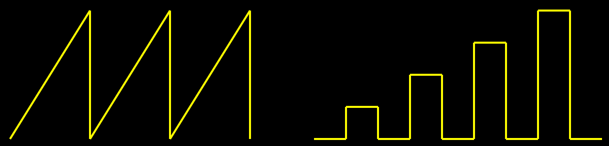
Mapping striate and extrastriate visual areas in human cerebral cortex

Edgar A. DeYoe*, George J. Carman†, Peter Bandettini‡, Seth Glickman*, Jon Wieser*, Robert Cox§, David Miller¶, and Jay Neitz*

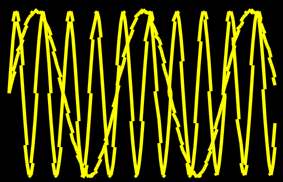


Neuronal Activation Input Strategies

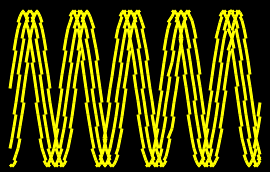
1. Block Design
2. Parametric Design



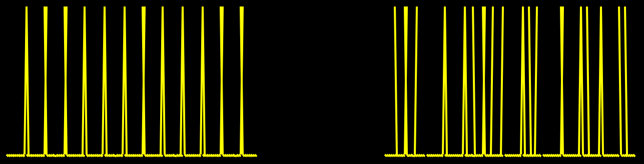
3. Frequency Encoding



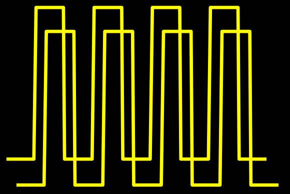
4. Phase Encoding



5. Event Related



6. Orthogonal Design



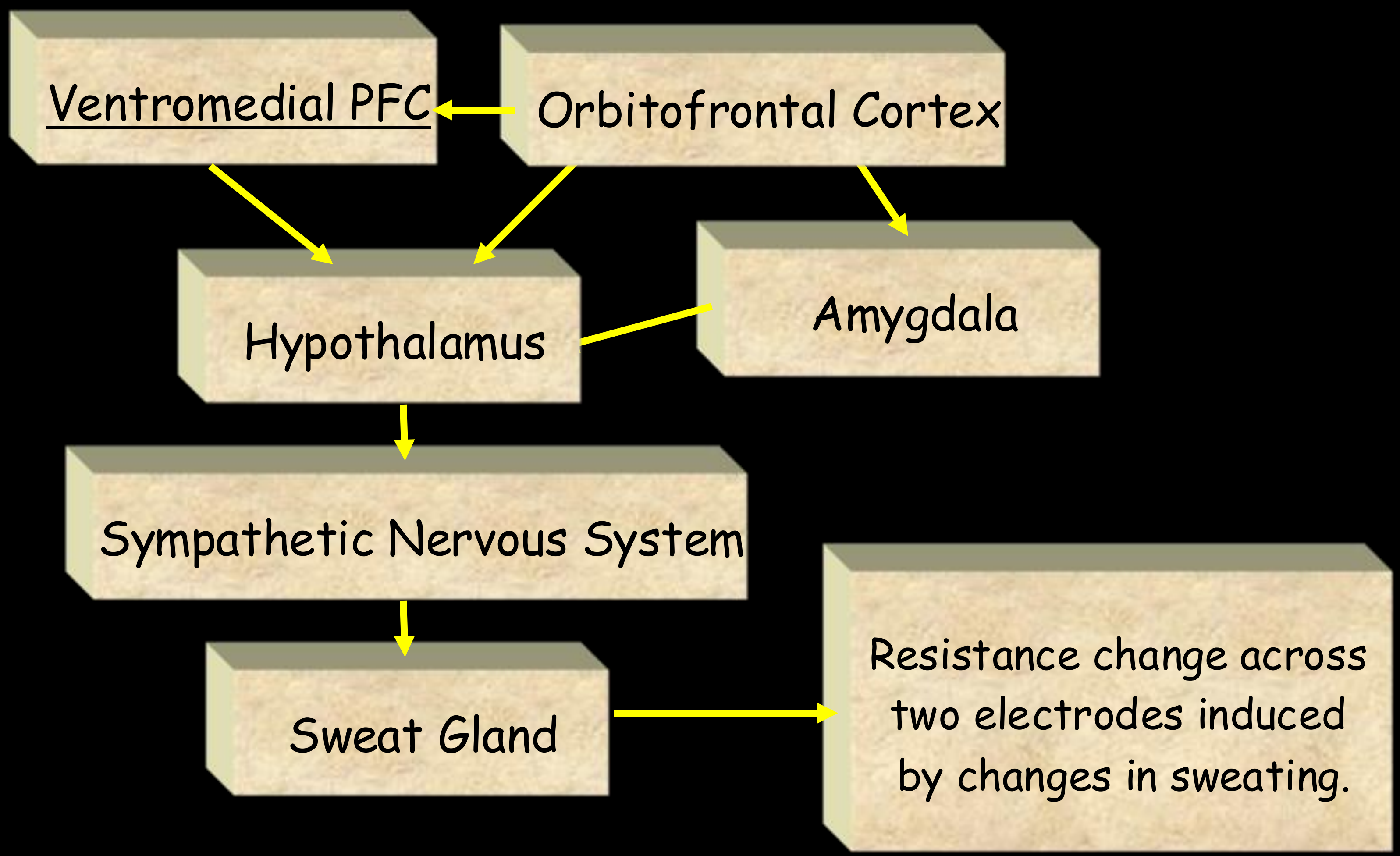
7. Free Behavior Design

Free Behavior Design

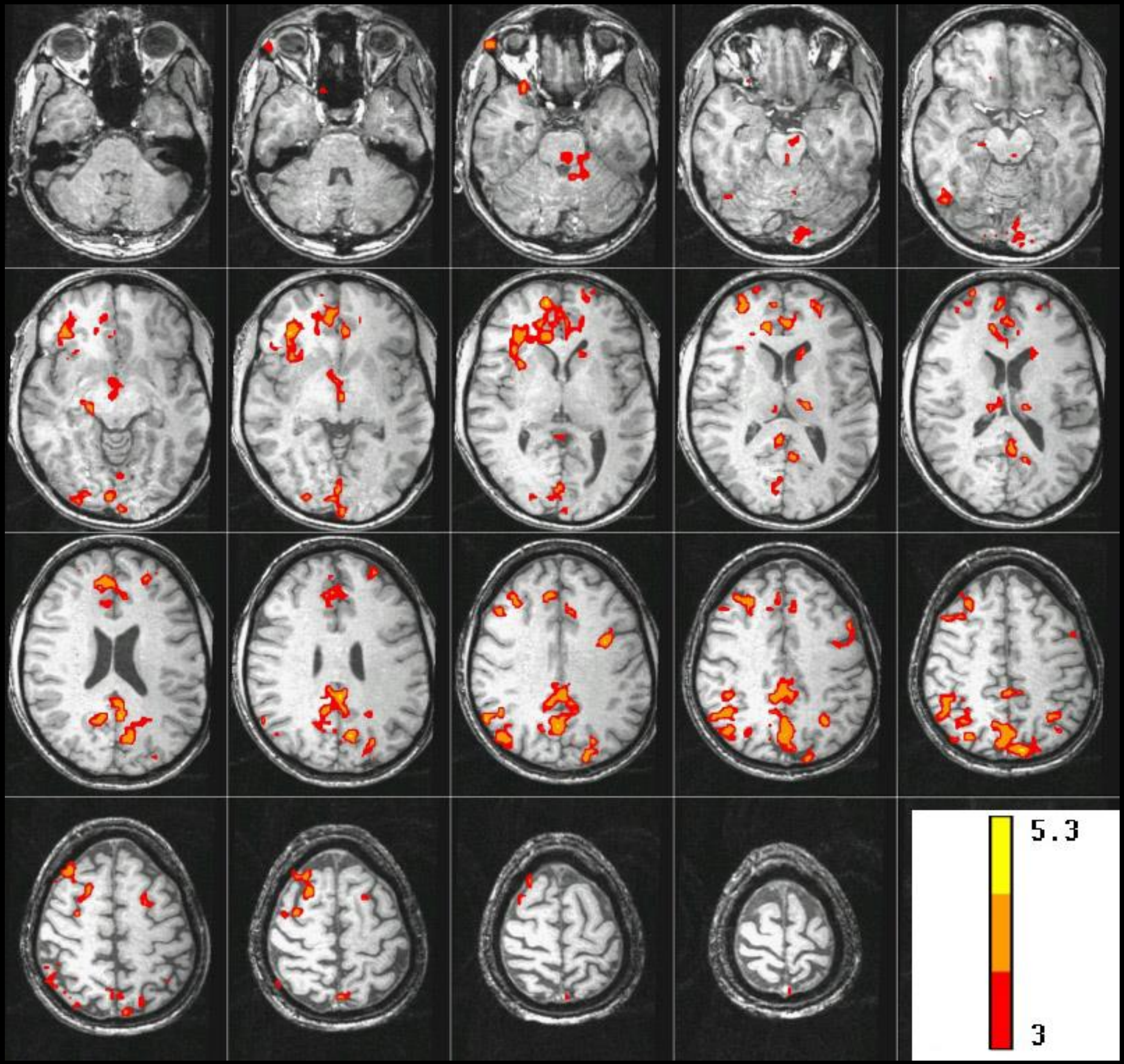
Use a continuous measure as a reference function:

- **Task performance**
- **Skin Conductance**
- **Heart, respiration rate..**
- **Eye position**
- **EEG**

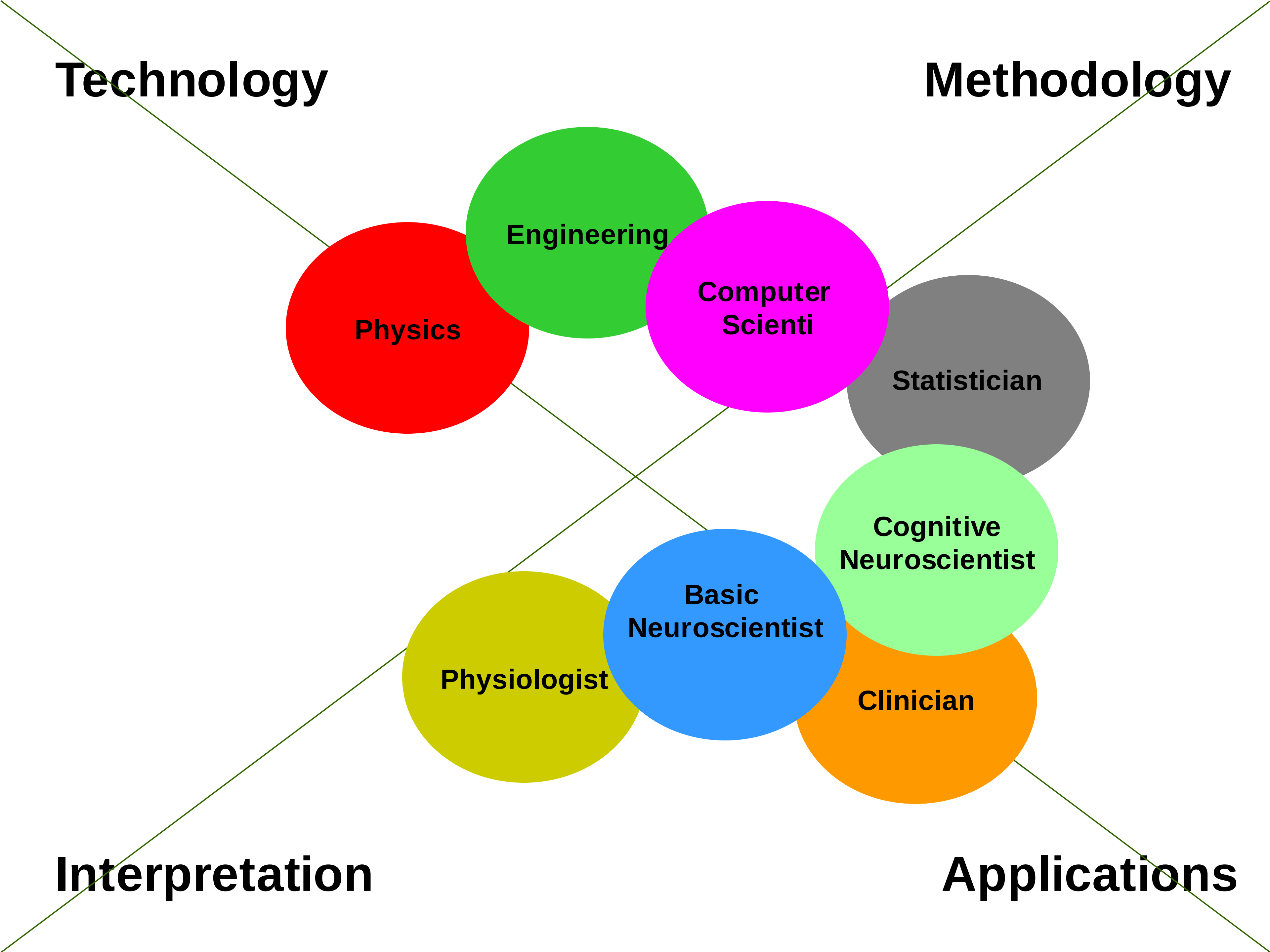
The Skin Conductance Response (SCR)



Brain activity correlated with SCR during "Rest"



J. C. Patterson II, L. G. Ungerleider, and P. A Bandettini, Task - independent functional brain activity correlation with skin conductance changes: an fMRI study. *NeuroImage* ***17****: 1787-1806, (2002).*


Technology
Methodology
Engineering
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Computer
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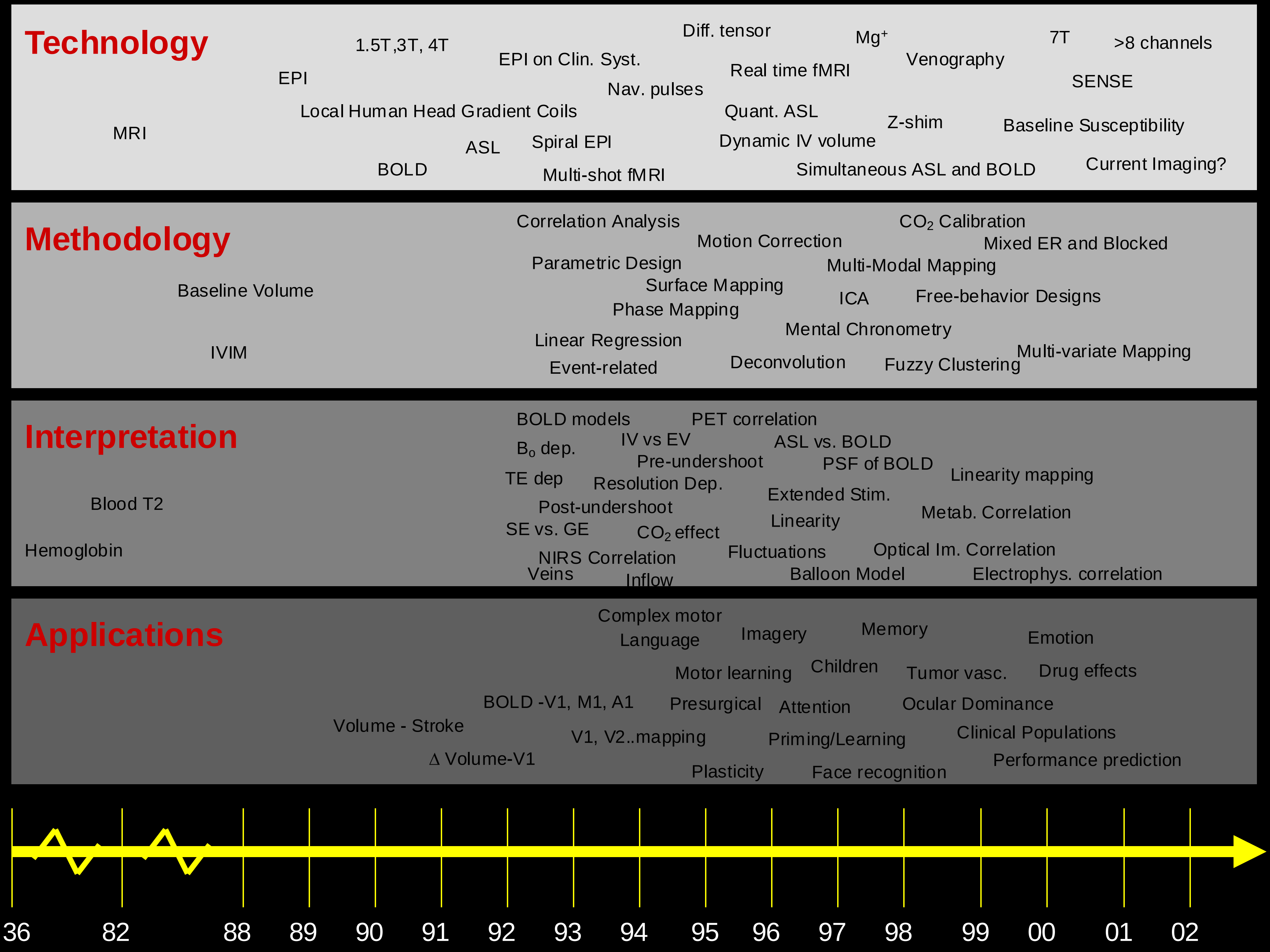
Neuroscientist
Basic
Neuroscientist
Physiologist
Clinician
Interpretation
Applications



Technology
MRI
EPI
1.5T,3T, 4T
Local Human Head Gradient Coils
BOLD
ASL
EPI on Clin. Syst.
Spiral EPI
Multi-shot fMRI
Diff. tensor
Nav. pulses
Real time fMRI
Quant. ASL
Dynamic IV volume
Mg^+
Venography
Z-shim
Simultaneous ASL and BOLD
7T
>8 channels
SENSE
Baseline Susceptibility
Current Imaging?
Methodology
Baseline Volume
IVIM
Correlation Analysis
Parametric Design
Linear Regression
Event-related
Motion Correction
Surface Mapping
Phase Mapping
Deconvolution
Multi-Modal Mapping
ICA
Mental Chronometry
CO_2 Calibration
Mixed ER and Blocked
Free-behavior Designs
Fuzzy Clustering
Multi-variate Mapping
Interpretation
Blood T2
Hemoglobin
BOLD models
B_0 dep.
TE dep
SE vs. GE
Post-undershoot
NIRS Correlation
Veins
IV vs EV
Pre-undershoot
Resolution Dep.
CO_2 effect
Inflow
PET correlation
ASL vs. BOLD
PSF of BOLD
Extended Stim.
Linearity
Fluctuations
Balloon Model
Linearity mapping
Metab. Correlation
Optical Im. Correlation
Electrophys. correlation
Applications
Volume - Stroke
∆ Volume-V1
BOLD -V1, M1, A1
V1, V2..mapping
Complex motor
Language
Motor learning
Presurgical
Plasticity
Imagery
Children
Attention
Priming/Learning
Face recognition
Memory
Tumor vasc.
Ocular Dominance
Emotion
Drug effects
Clinical Populations
Performance prediction
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