New Frontiers in Functional Imaging

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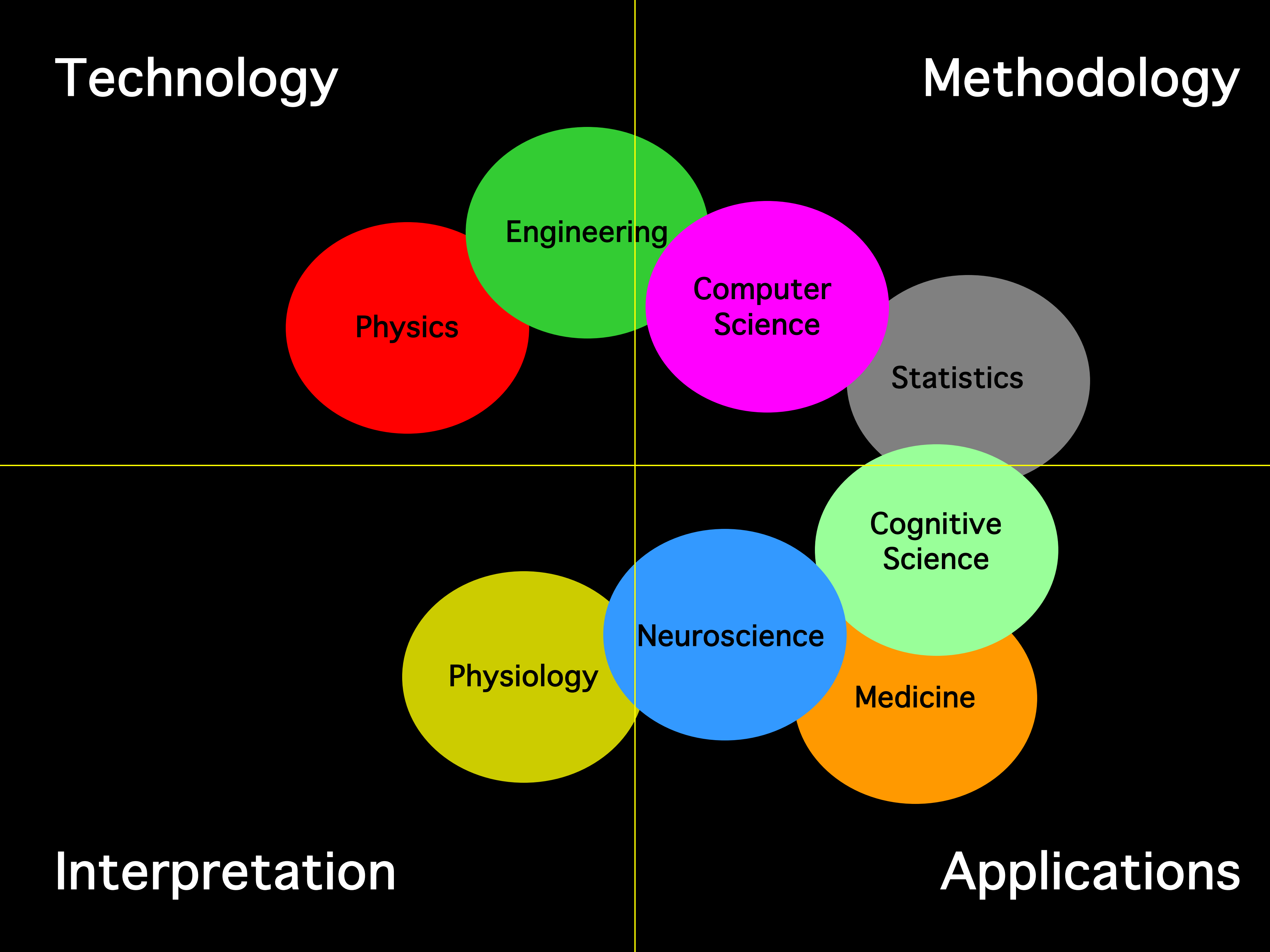
Unit on Functional Imaging Methods
Laboratory of Brain and Cognition
&
Functional MRI Core Facility

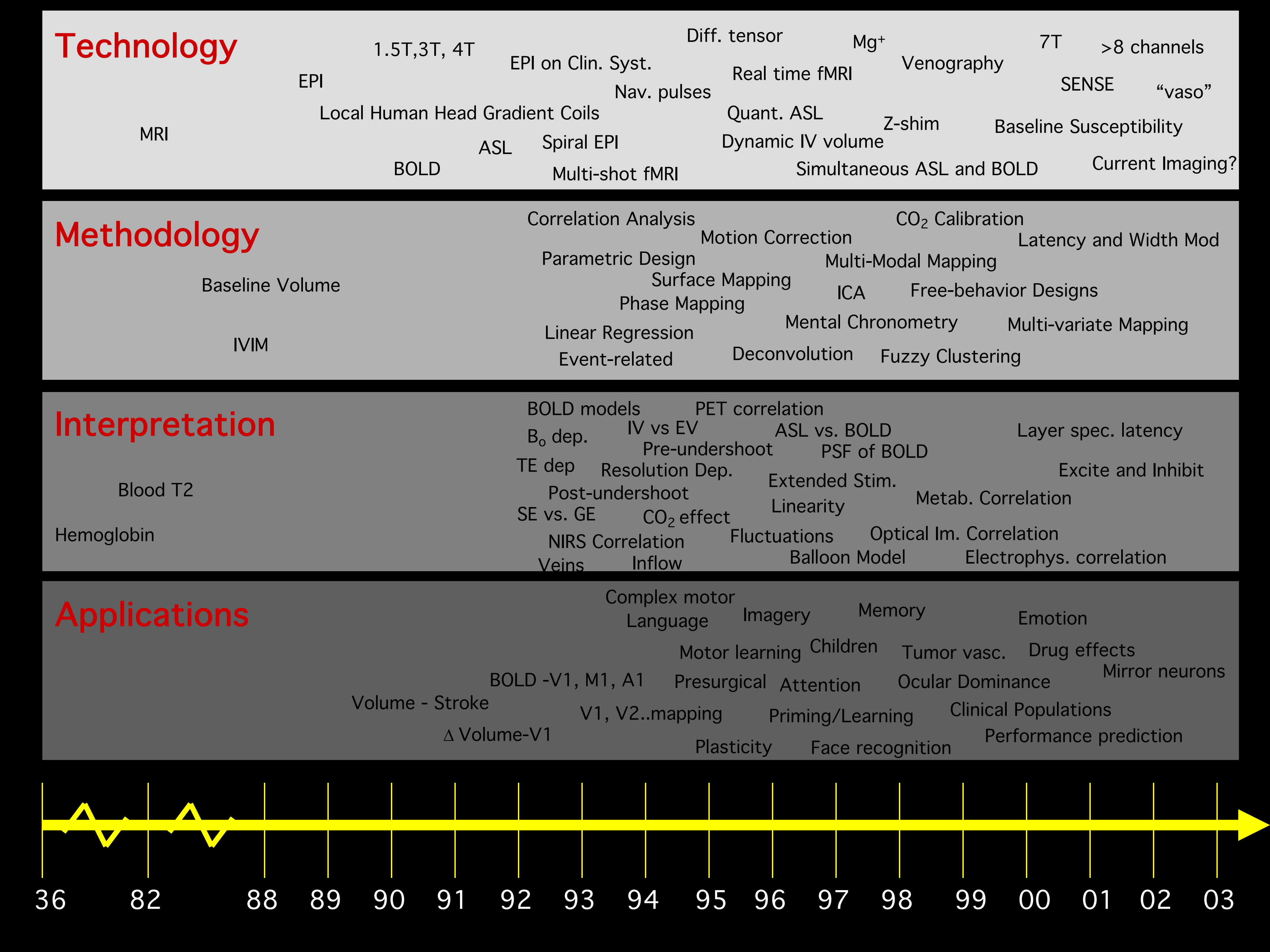
National Institute of Mental Health


Technology
Methodology
Engineering
Physics
Computer Science
Statistics
Cognitive Science
Neuroscience
Physiology
Medicine
Interpretation
Applications

Focus of most of this talk is fMRI

...but the key to neuroimaging advances is in the integration of multiple techniques

-electrical, hemodynamic, metabolic changes with activation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- Functional contrast
- Signal interpretation
- Hardware and pulse sequences
- Paradigm design and processing

- Overview
- Current Limits
- Future Prospects

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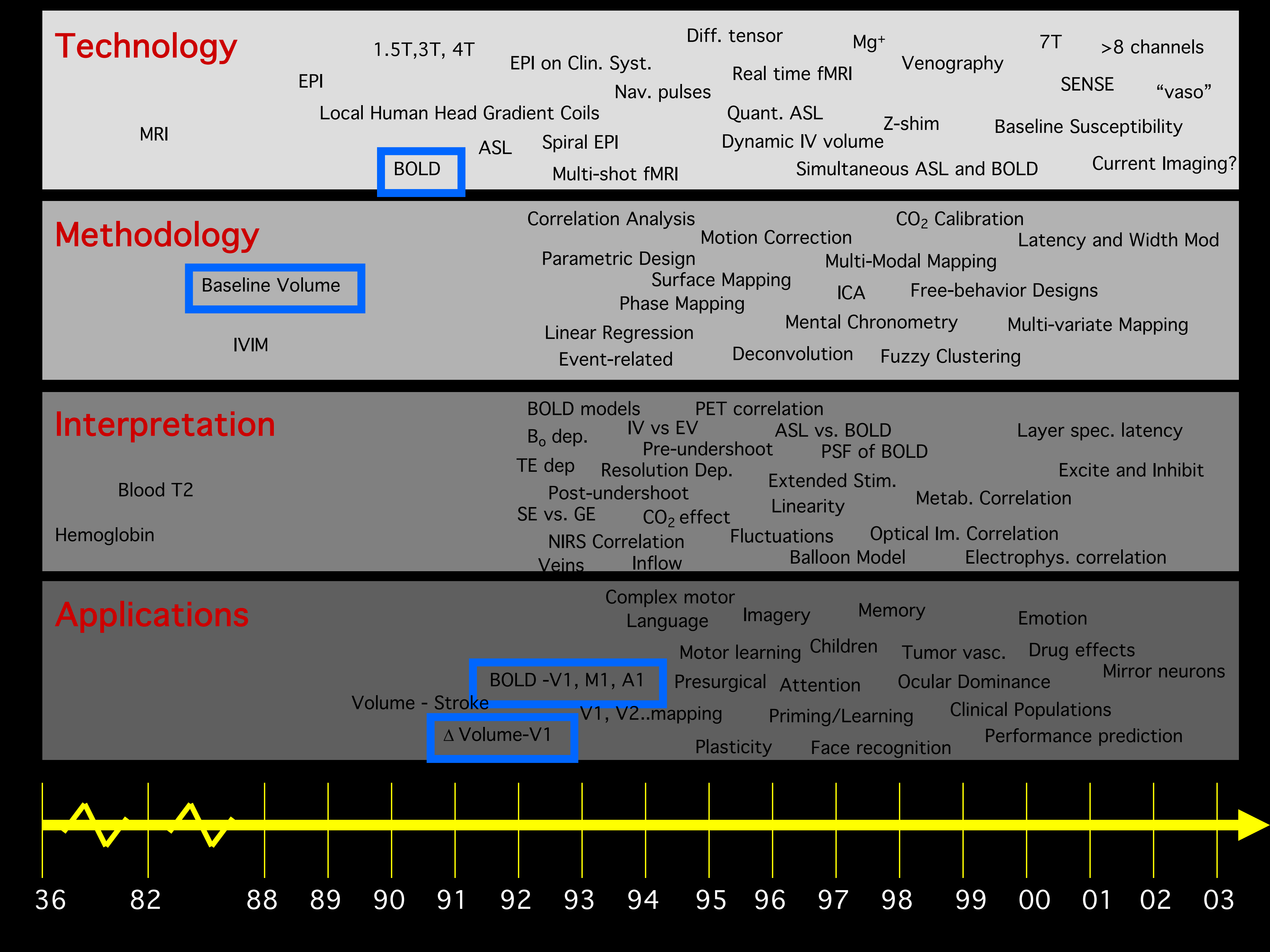

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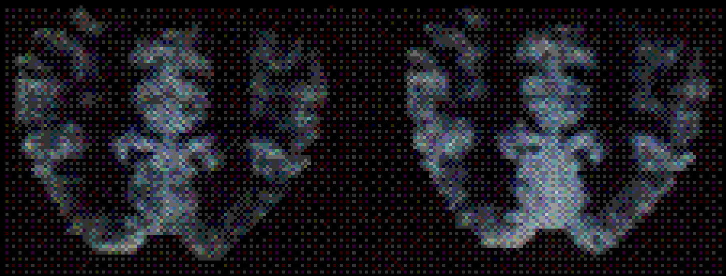
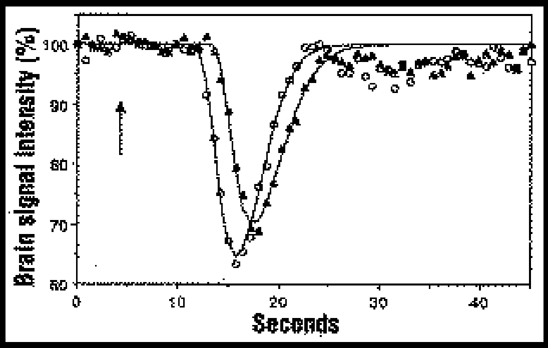
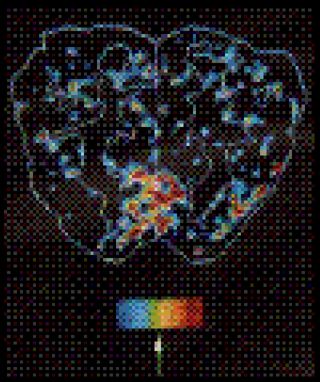
Blood Volume Imaging

Susceptibility Contrast agent bolus injection and time series collection of T2* or T2 - weighted images

Resting Active







Photic Stimulation

MRI Image showing activation of the Visual Cortex

From Belliveau, et al. Science Nov 1991

MSC - perfusion

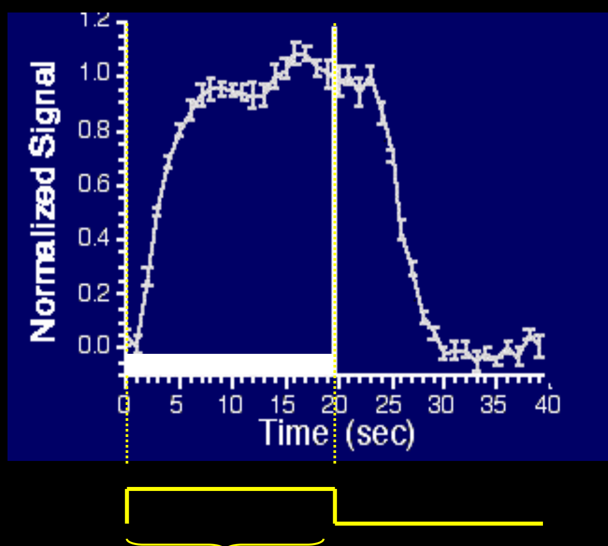
Blood Oxygenation Imaging

•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.



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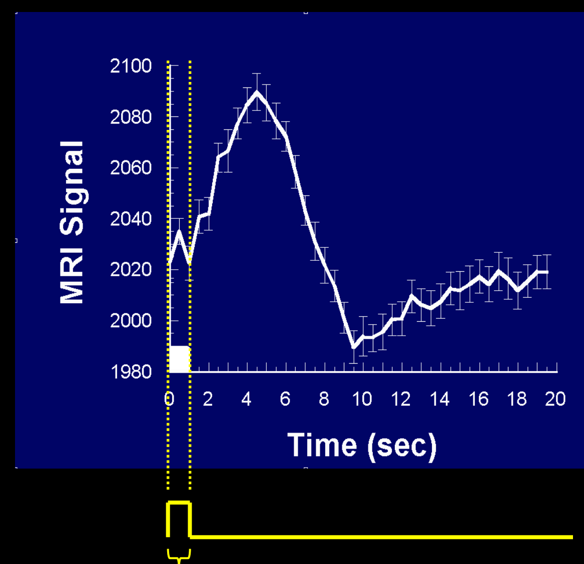

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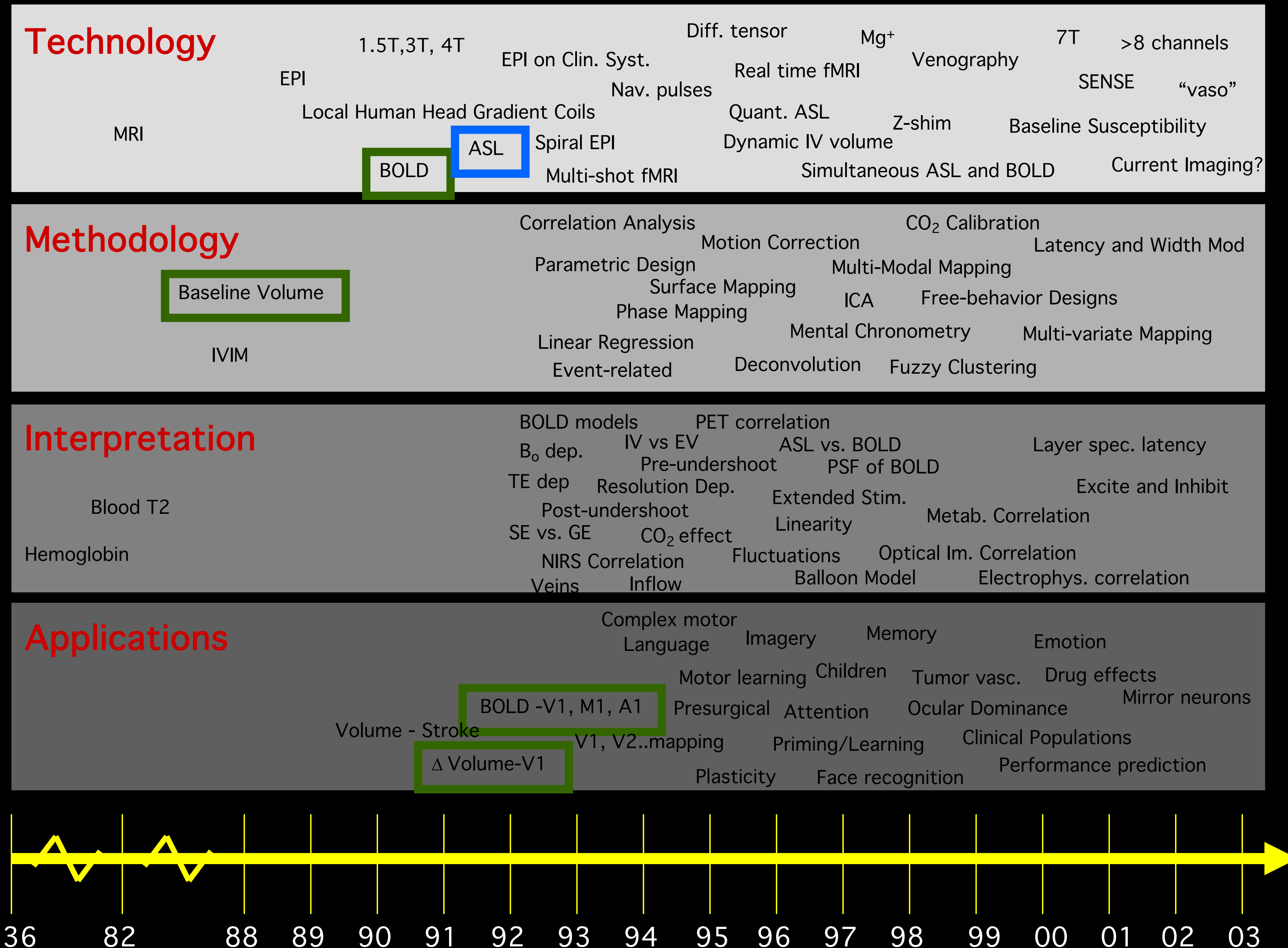

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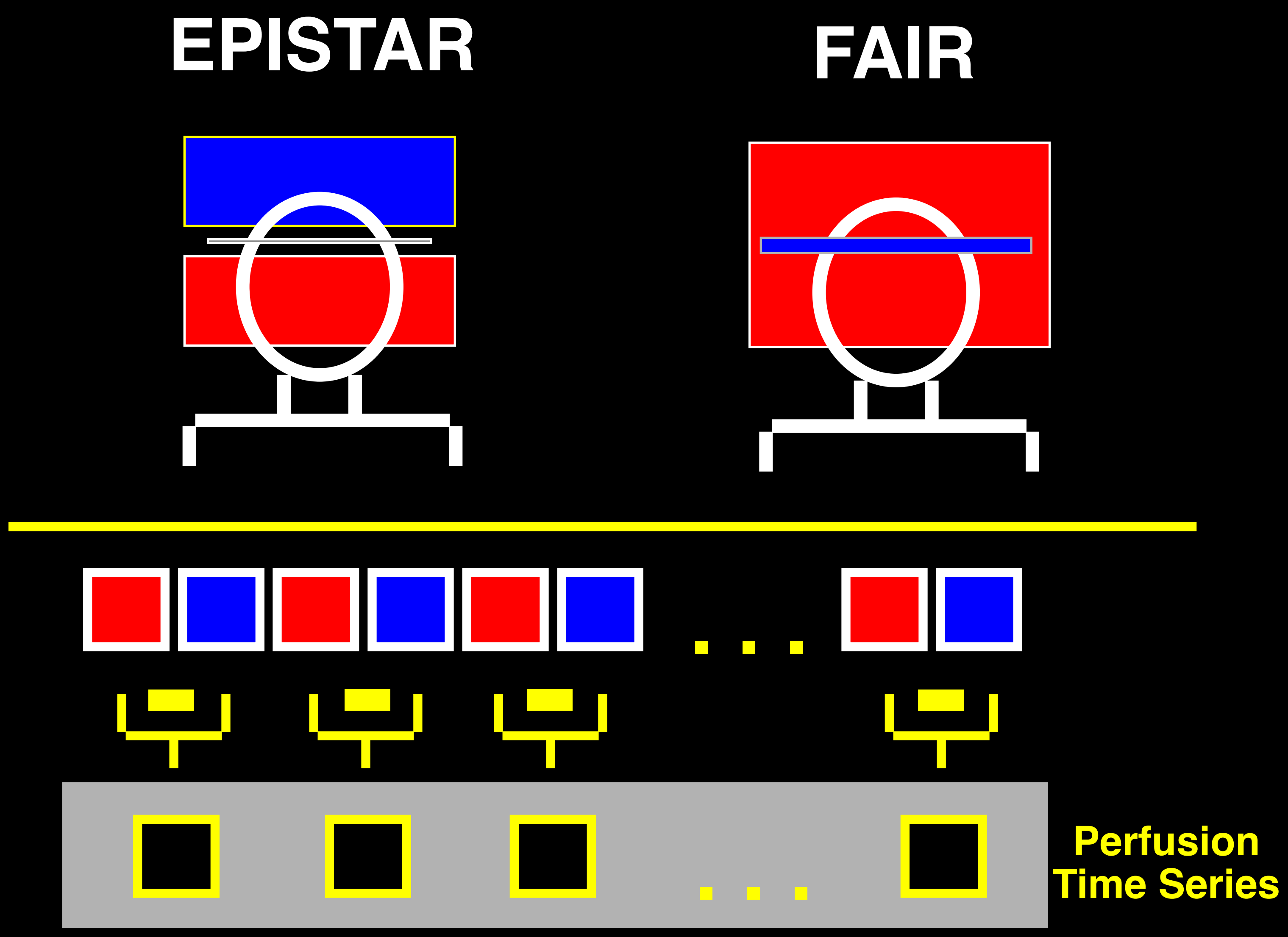
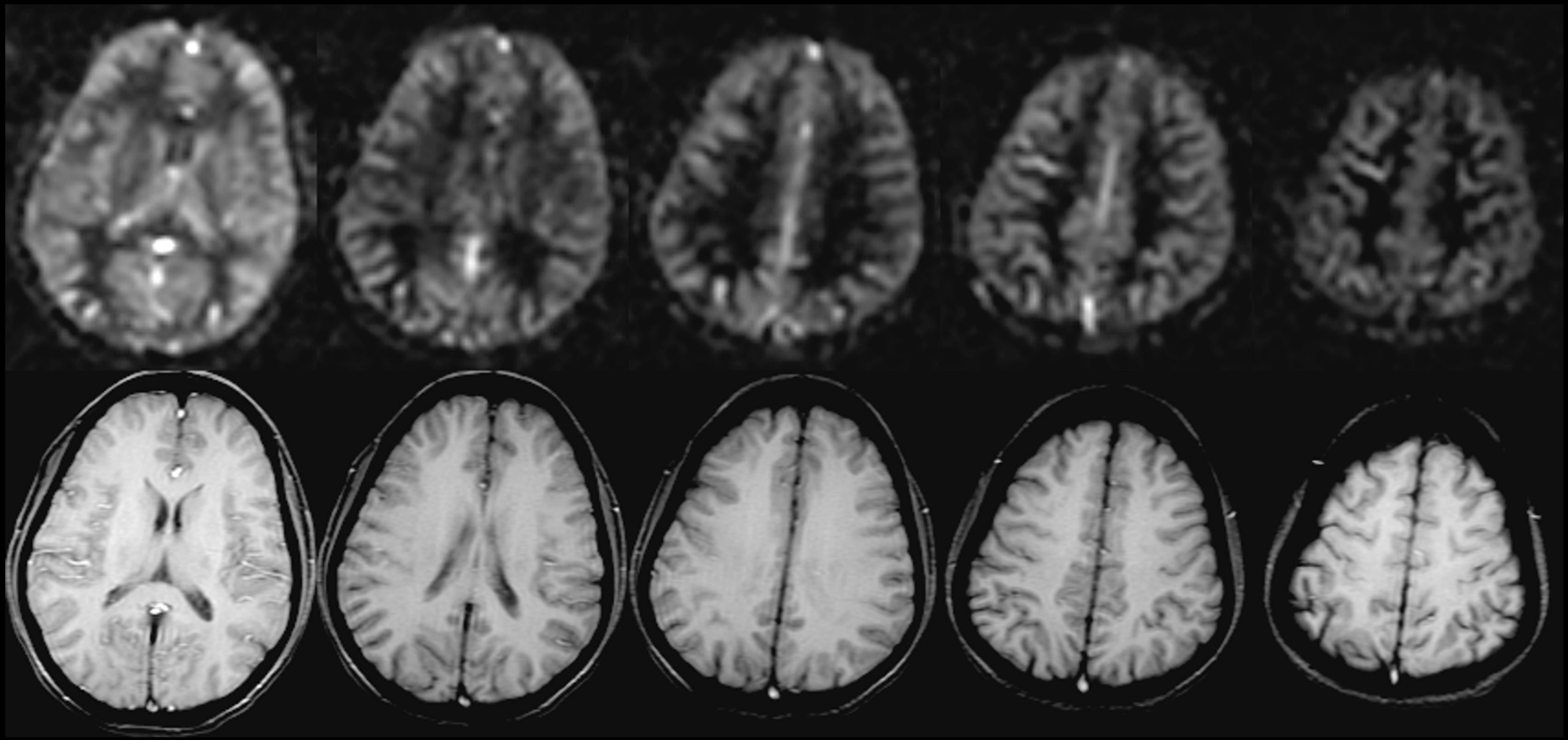
Blood Perfusion Imaging



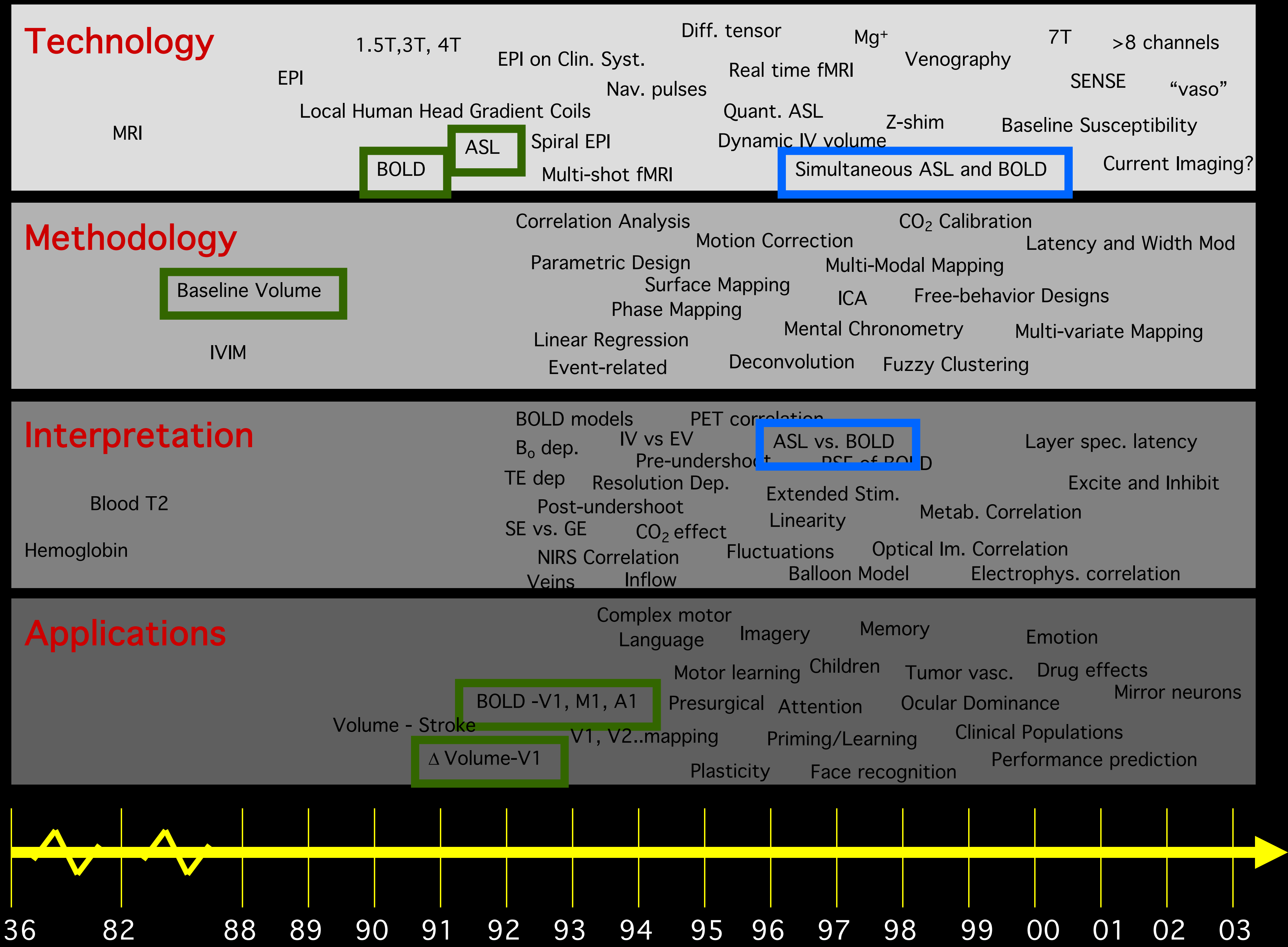


Williams, D. S., Detre, J. A., Leigh, J. S. & Koretsky, A. S. (1992) “Magnetic resonance imaging of perfusion using spin-inversion of arterial water.” Proc. Natl. Acad. Sci. USA 89, 212-216.

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.



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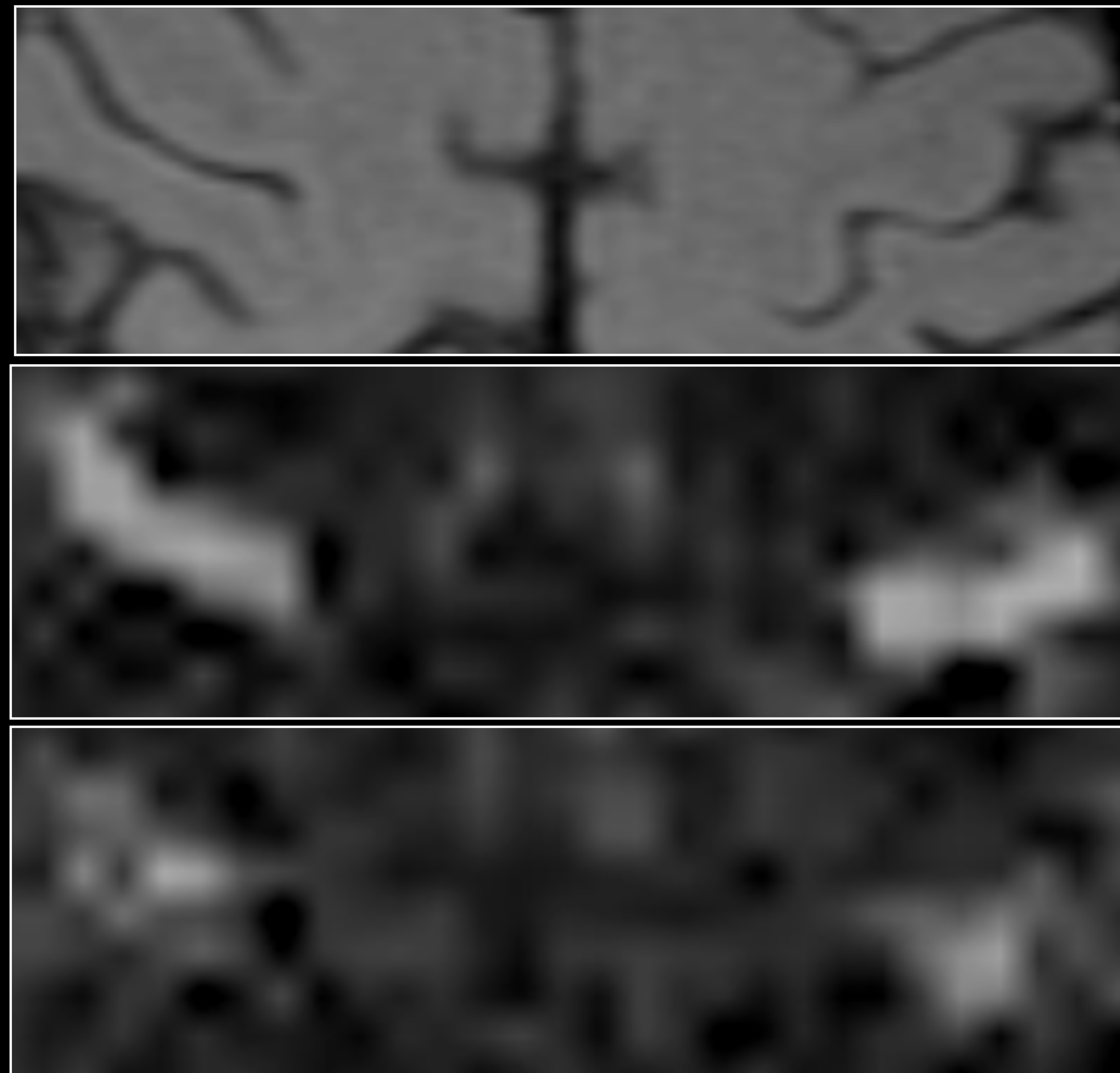
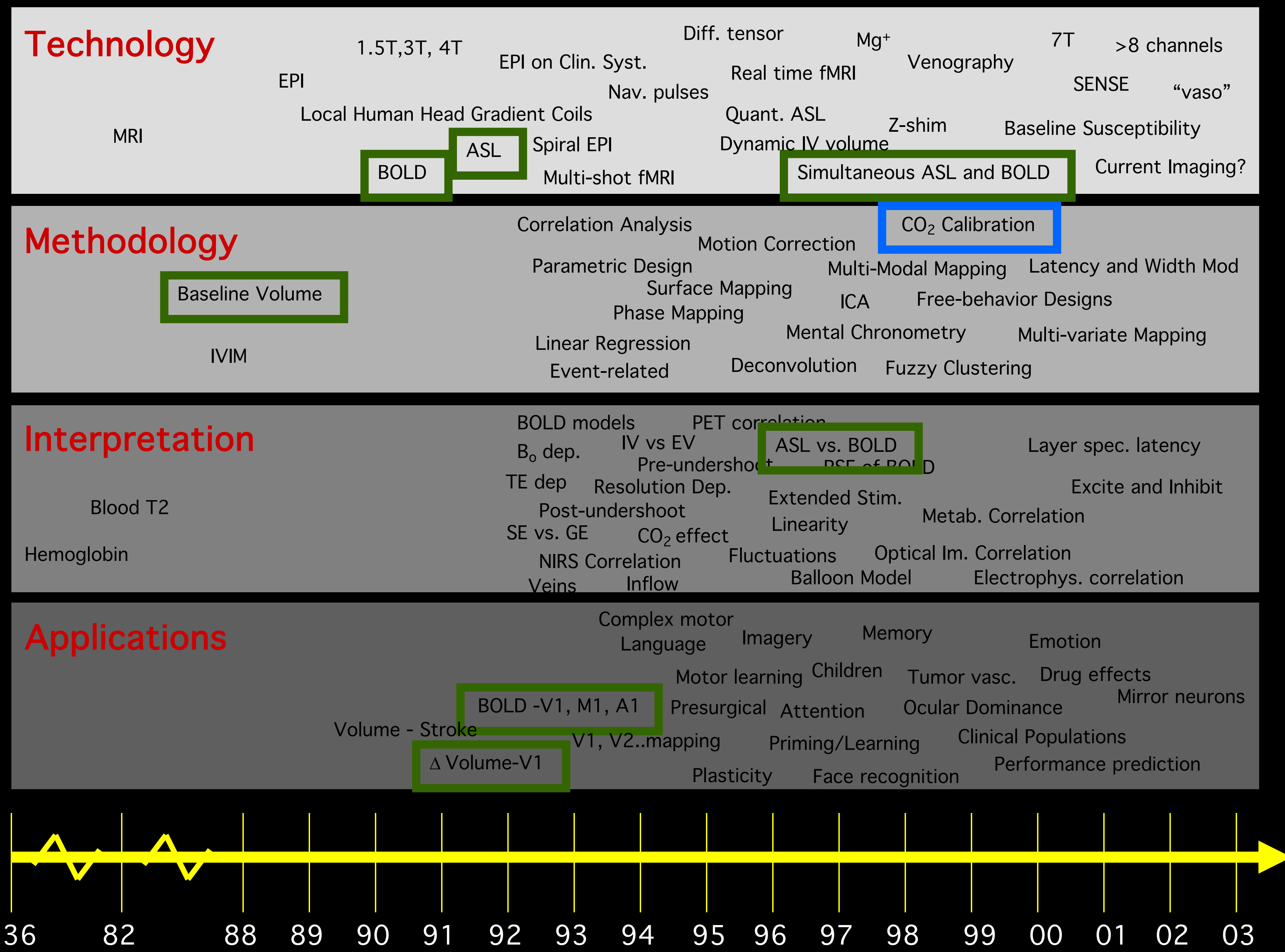
Simultaneous BOLD and Perfusion



BOLD

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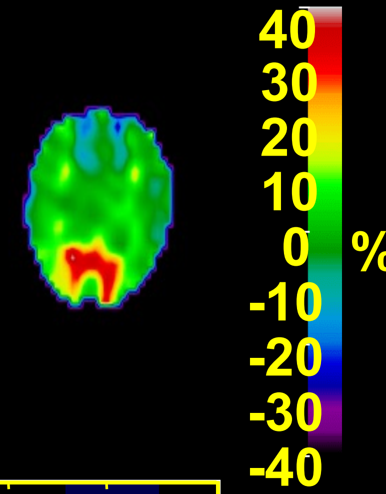
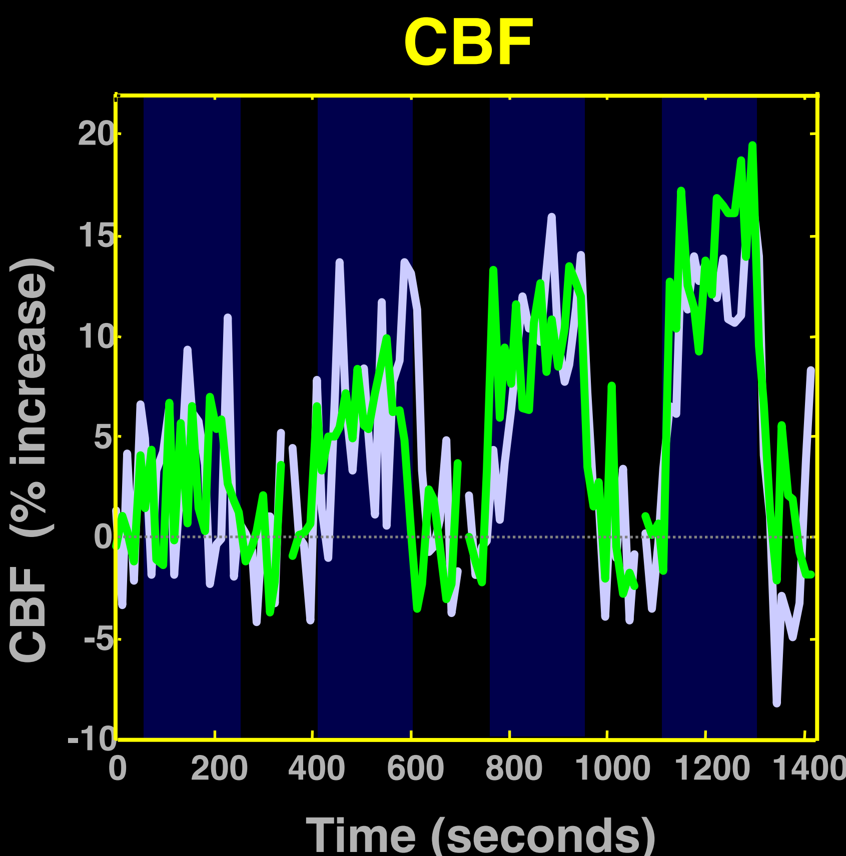
Proc. Natl. Acad. Sci. USA
Vol. 96, pp. 9403–9408, August 1999
Neurobiology

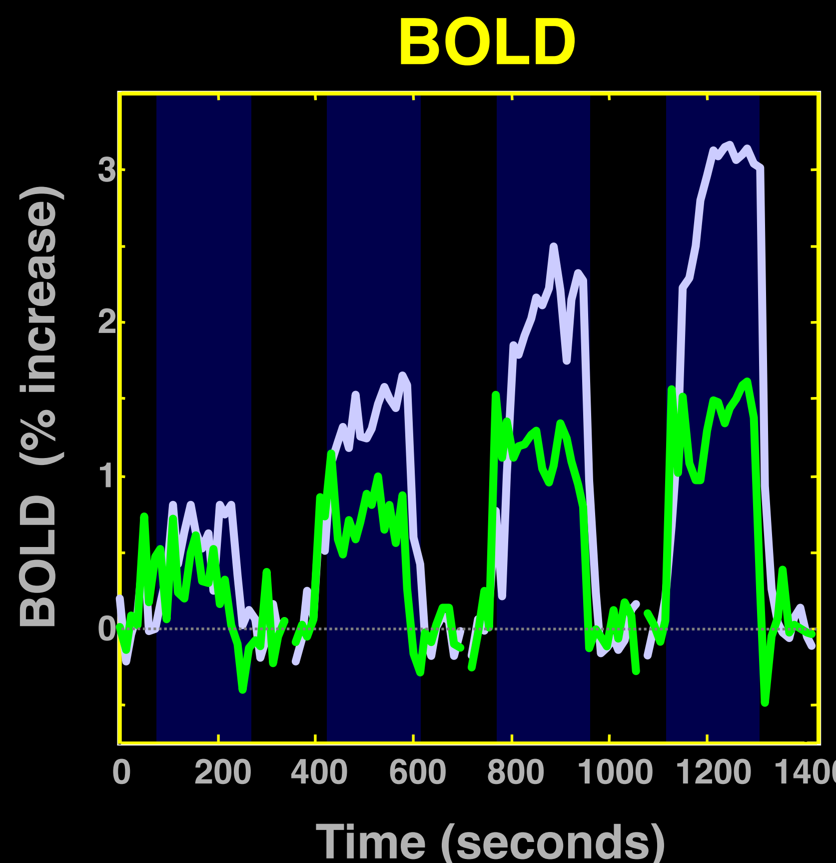
Linear coupling between cerebral blood flow and oxygen consumption in activated human cortex

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

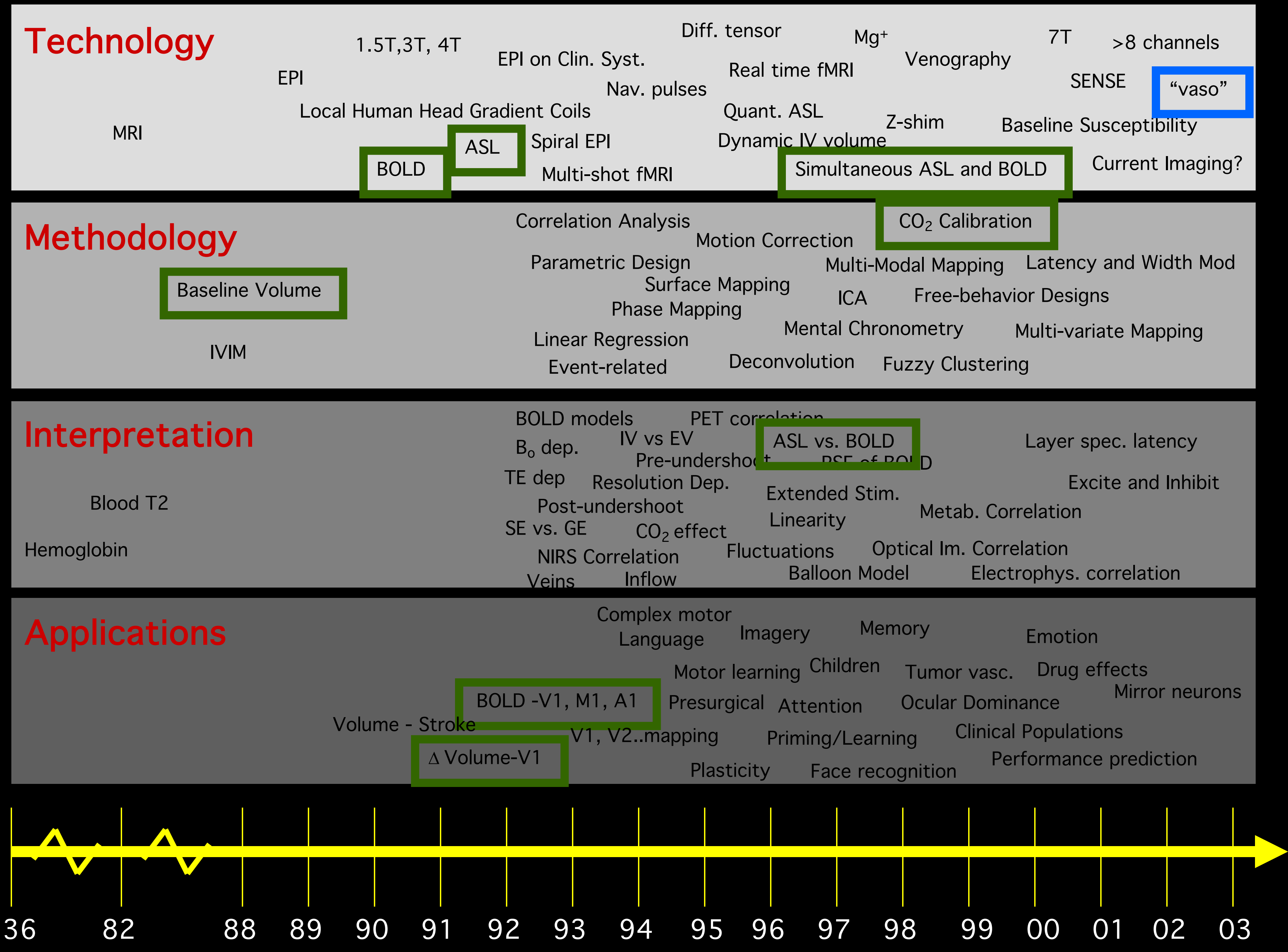
*Room WB325, McConnell Brain Imaging Centre, Montreal Neurological Institute, Quebec, Canada H3A 2B4; and ‡Nuclear Magnetic Resonance Center, Massachusetts General Hospital, Building 149, 13th Street, Charlestown, MA 02129







Simultaneous Perfusion and BOLD imaging during graded visual activation and hypercapnia



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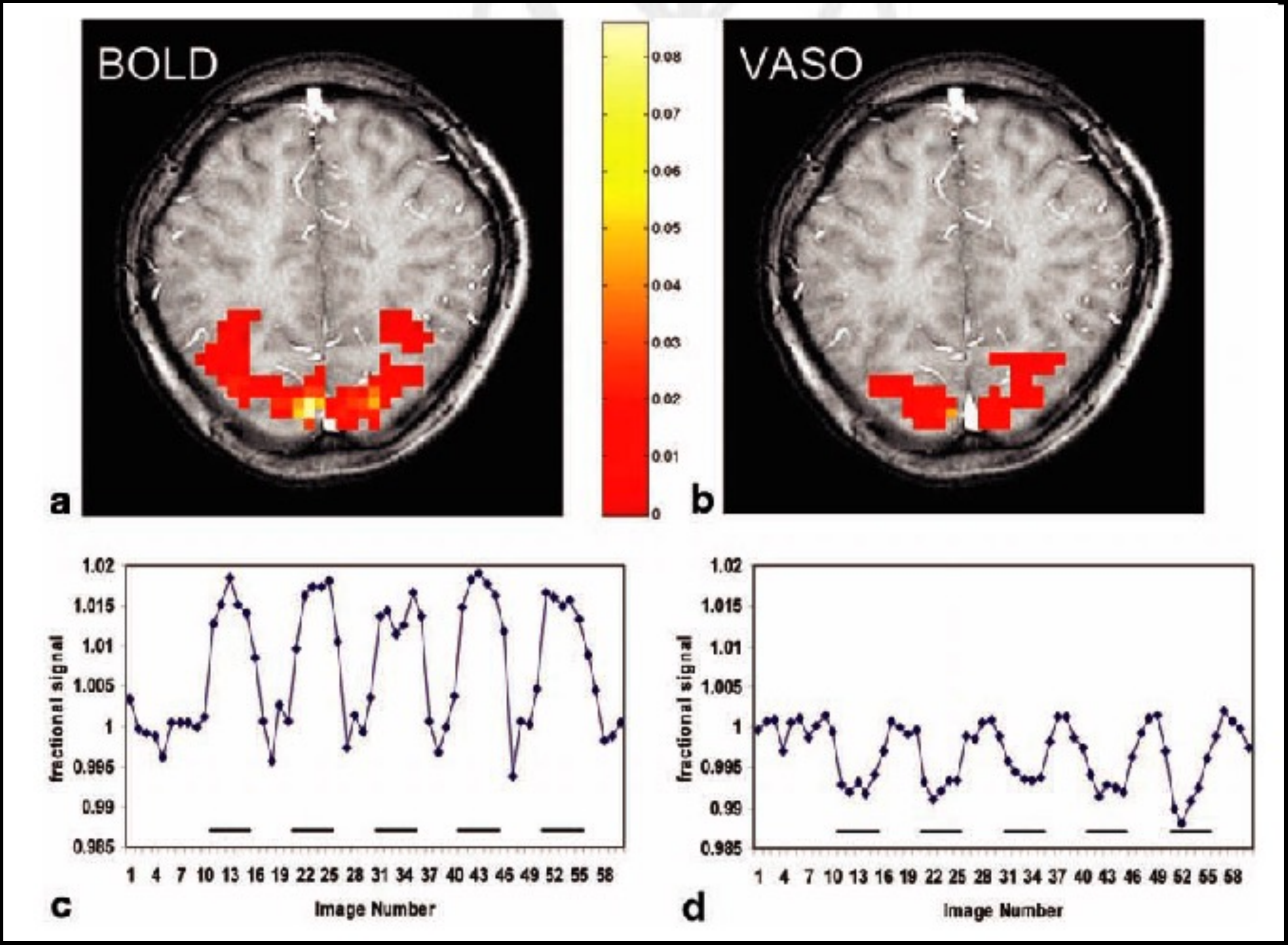
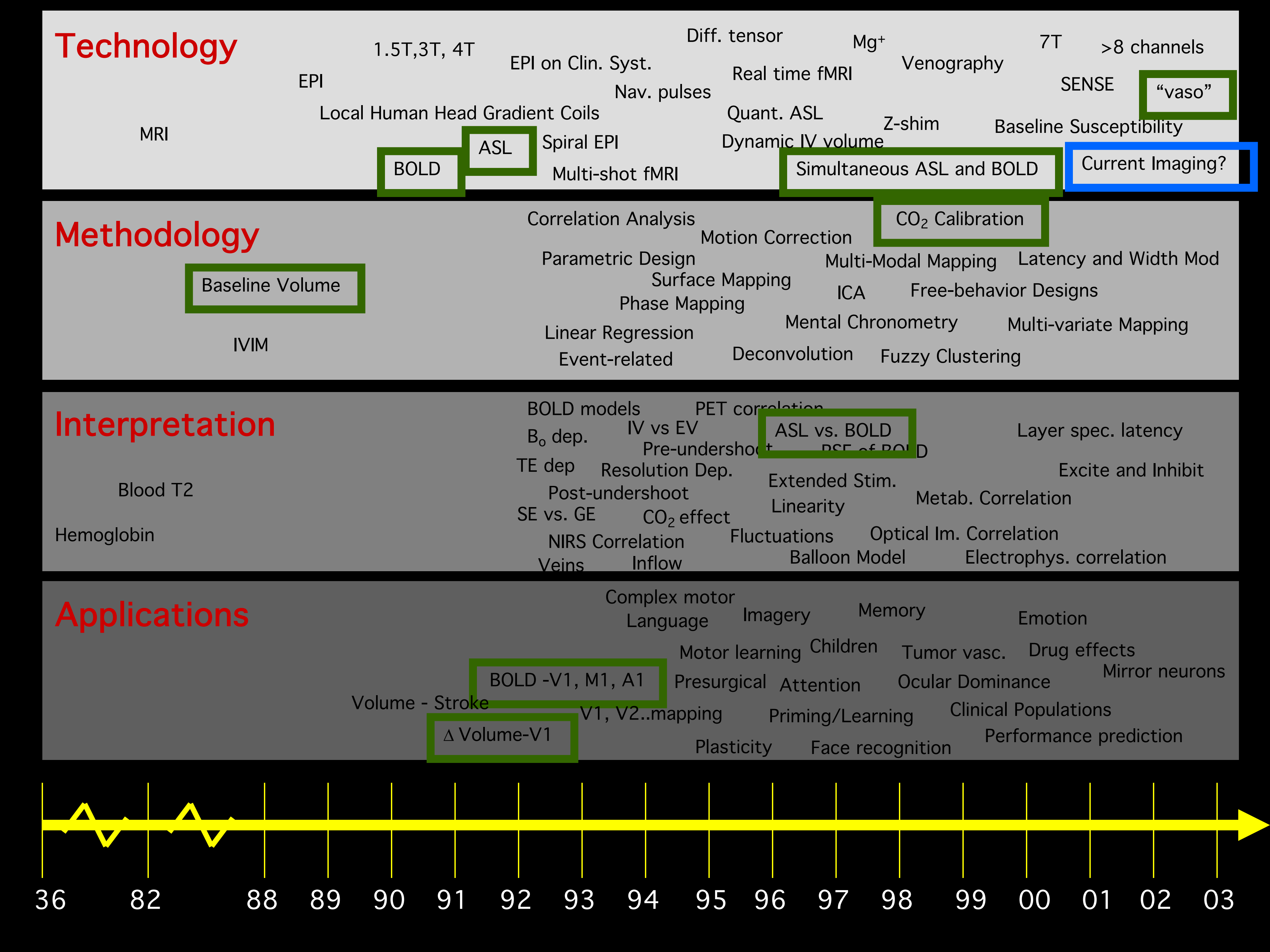
Functional Magnetic Resonance Imaging Based on Changes in Vascular Space Occupancy

Hanzhang Lu,[1–3] Xavier Golay,[1,3] James J. Pekar,[1,3] and Peter C.M. van Zijl[1,3*]

MAGNET RESON MED 50 (2): 263-274 AUG 2003

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Neuronal Current Imaging

- Neuronal activity is directly associated with ionic currents.
- These bio-currents induce **spatially distributed and transient** magnetic flux density changes and magnetic field gradients.
- In the context of MRI, these currents therefore alter **the magnetic phase** of surrounding water protons.

Derivation of B field generated in an MRI voxel by a current dipole

Single dendritic tree having a diameter d, and length L behaves like a conductor with conductivity σ. Resistance is R=V/I, where $R=4L/(\pi d^2 \sigma)$. From Biot-Savart:

$$\mathbf{B} = \frac{\mu_0}{4\pi}\frac{Q}{r^2} = \frac{\mu_0}{16}\frac{d^2 \sigma V}{r^2}$$

by substituting d = 4μm, $\sigma \approx 0.25\ \Omega^{-1}\ m^{-1}$, V = 10mV and

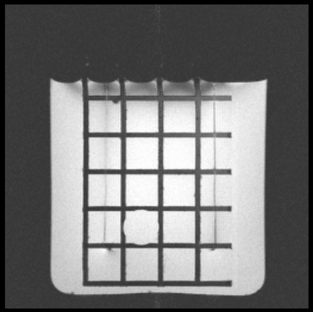
r = 4cm (measurement distance when using MEG) the resulting value is: **B≈0.002 fT**

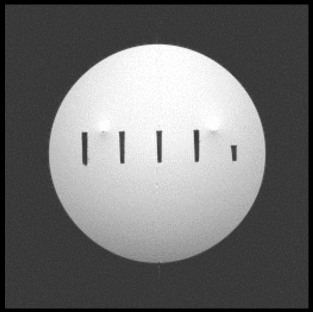
Because **B_{MEG}=100fT** (or more) is measured by MEG on the scalp, a large number of neurons, (0.002 fT x 50,000 = 100 fT), must coherently act to generate such field. These bundles of neurons produce, within a typical voxel, 1 mm x 1 mm x 1 mm, a field of order:

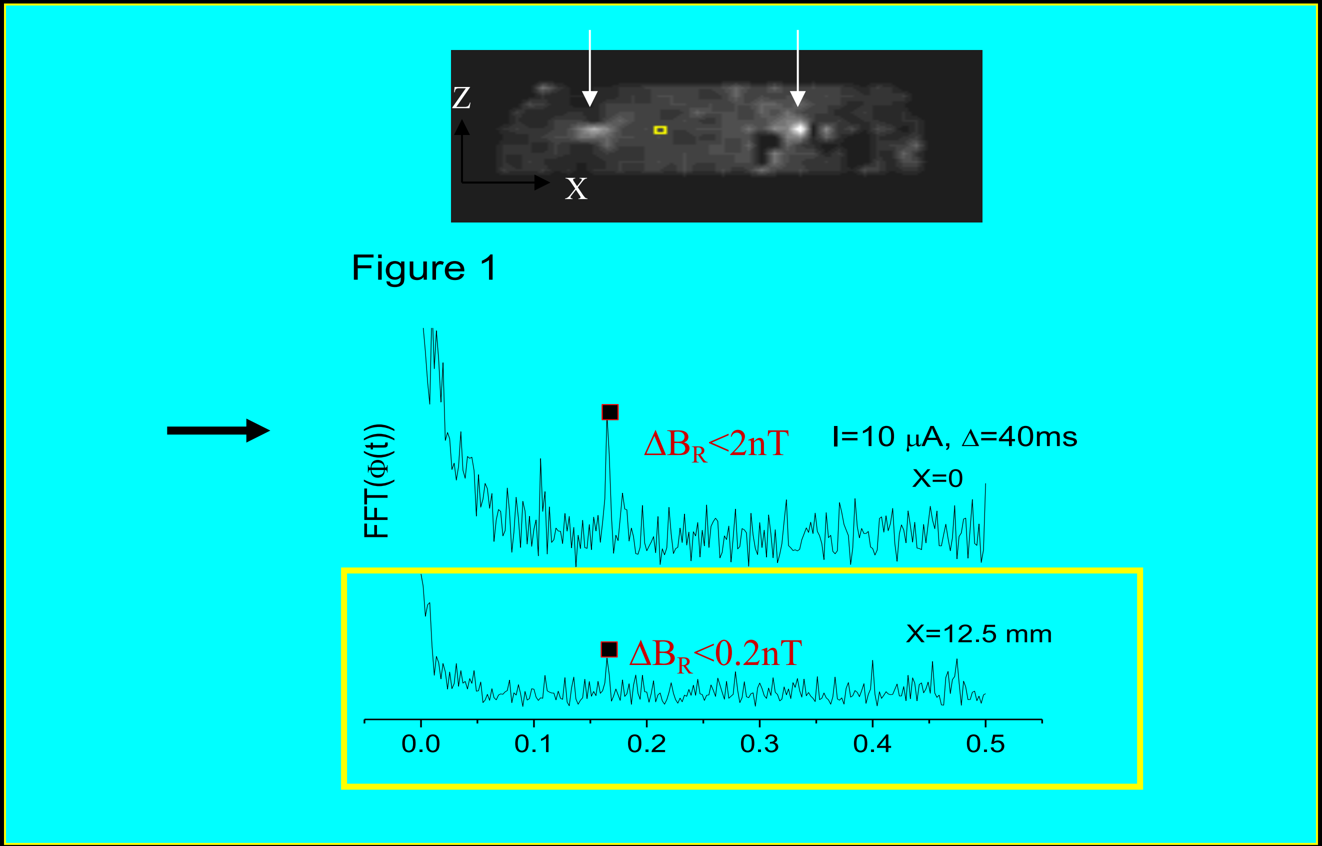
$$B_{MRI} = B_{MEG}\left(\frac{r_{MEG}}{r_{MRI}}\right)^2 = B_{MEG}\left(\frac{4\,cm}{0.1\,cm}\right)^2 = 1600\,B_{MEG}$$

B_{MRI} ≈0.2nT

J. Bodurka, P. A. Bandettini. Toward direct mapping of neuronal activity: MRI detection of ultra weak transient magnetic field changes, Magn. Reson. Med. 47: 1052-1058, (2002).







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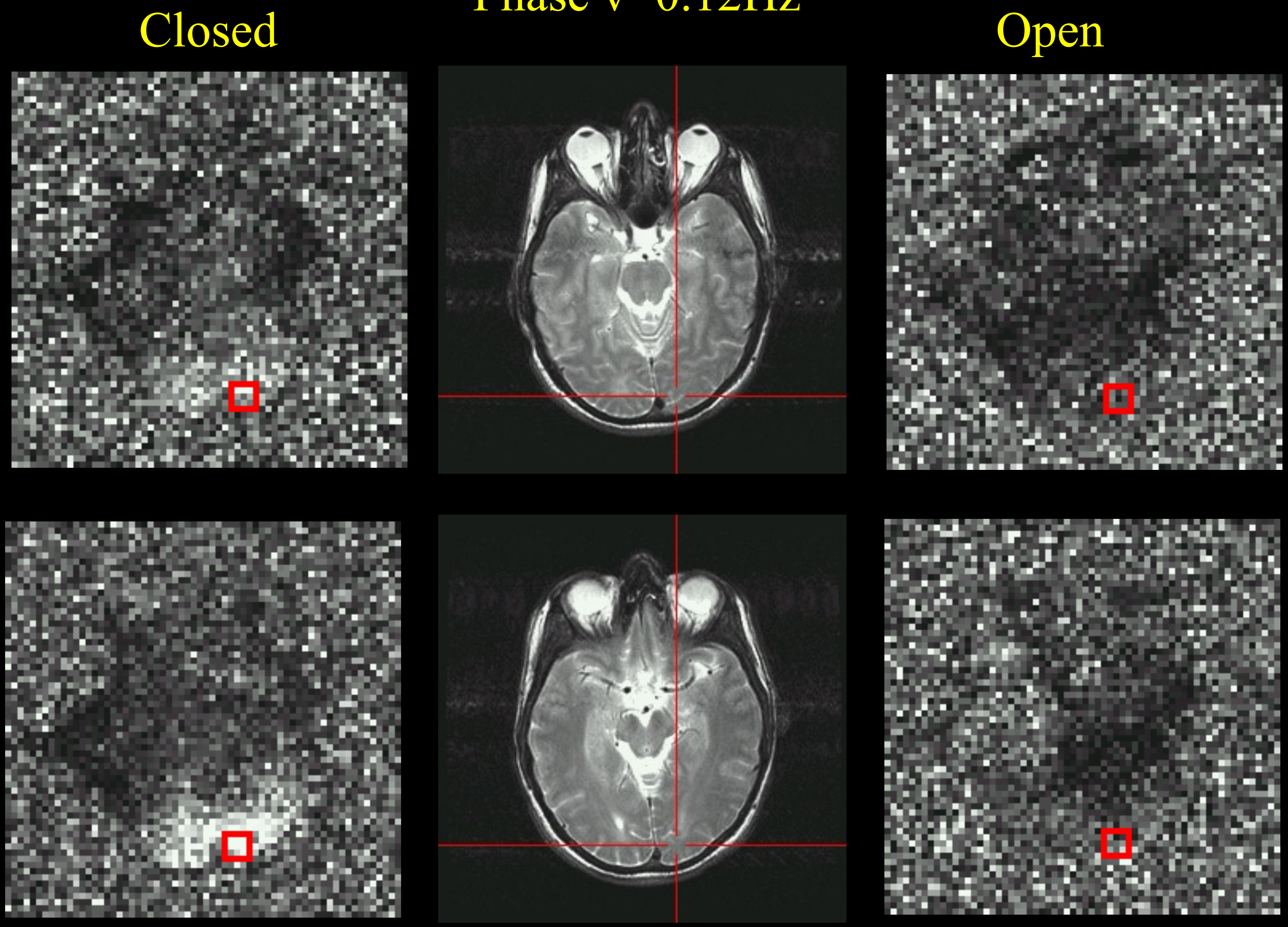
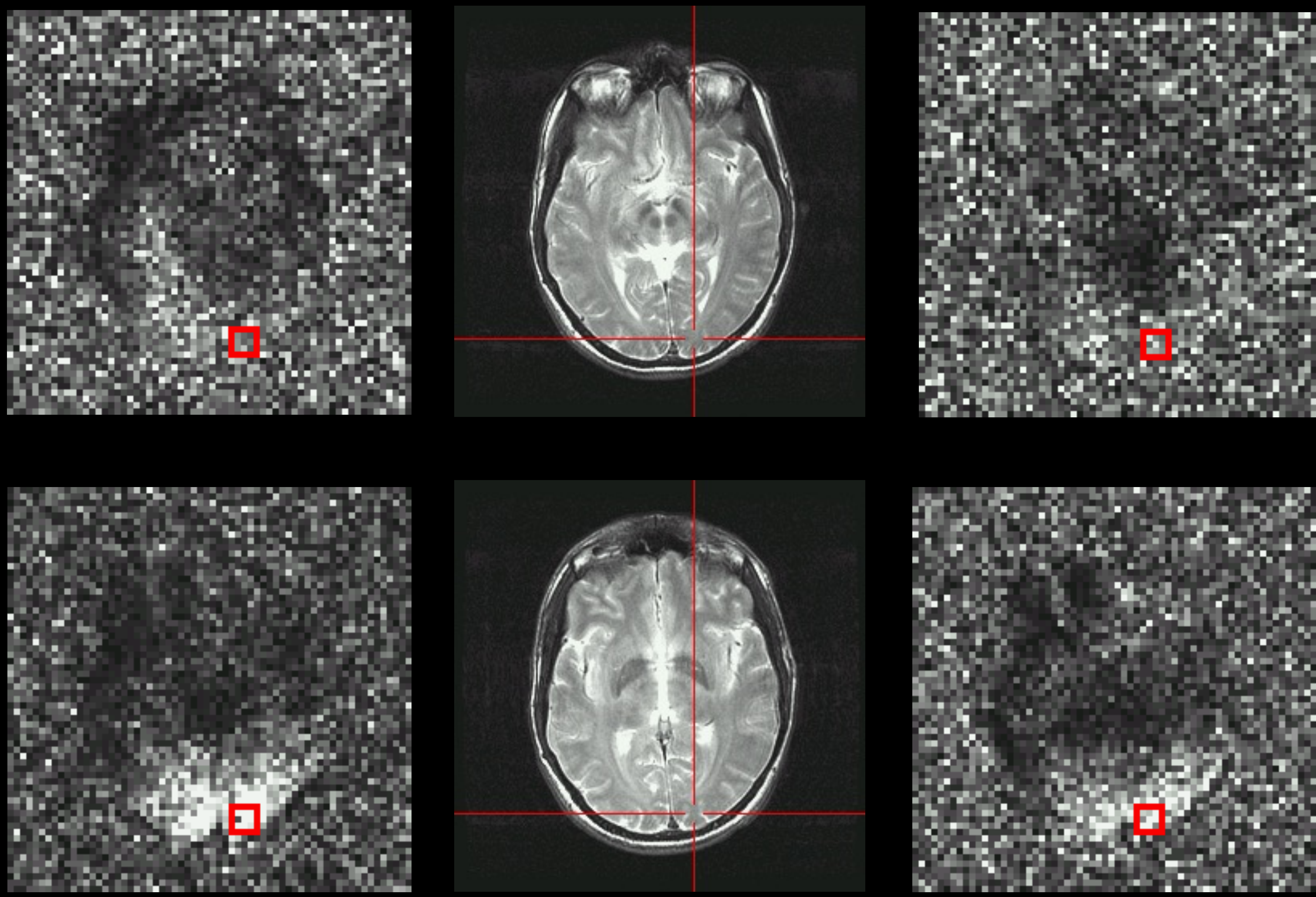
Phase v=0.12Hz

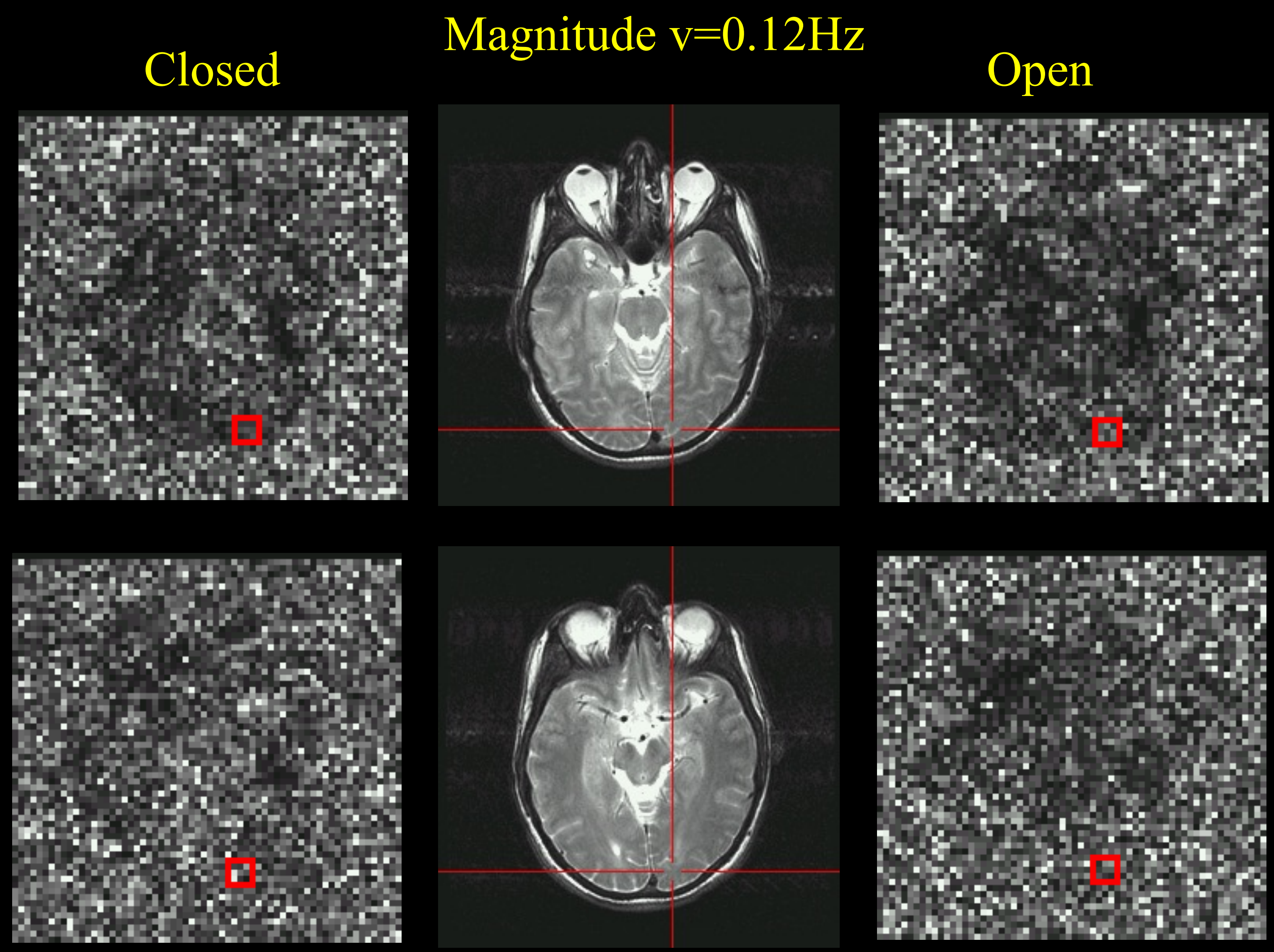


Phase v=0.12Hz

Closed

Open

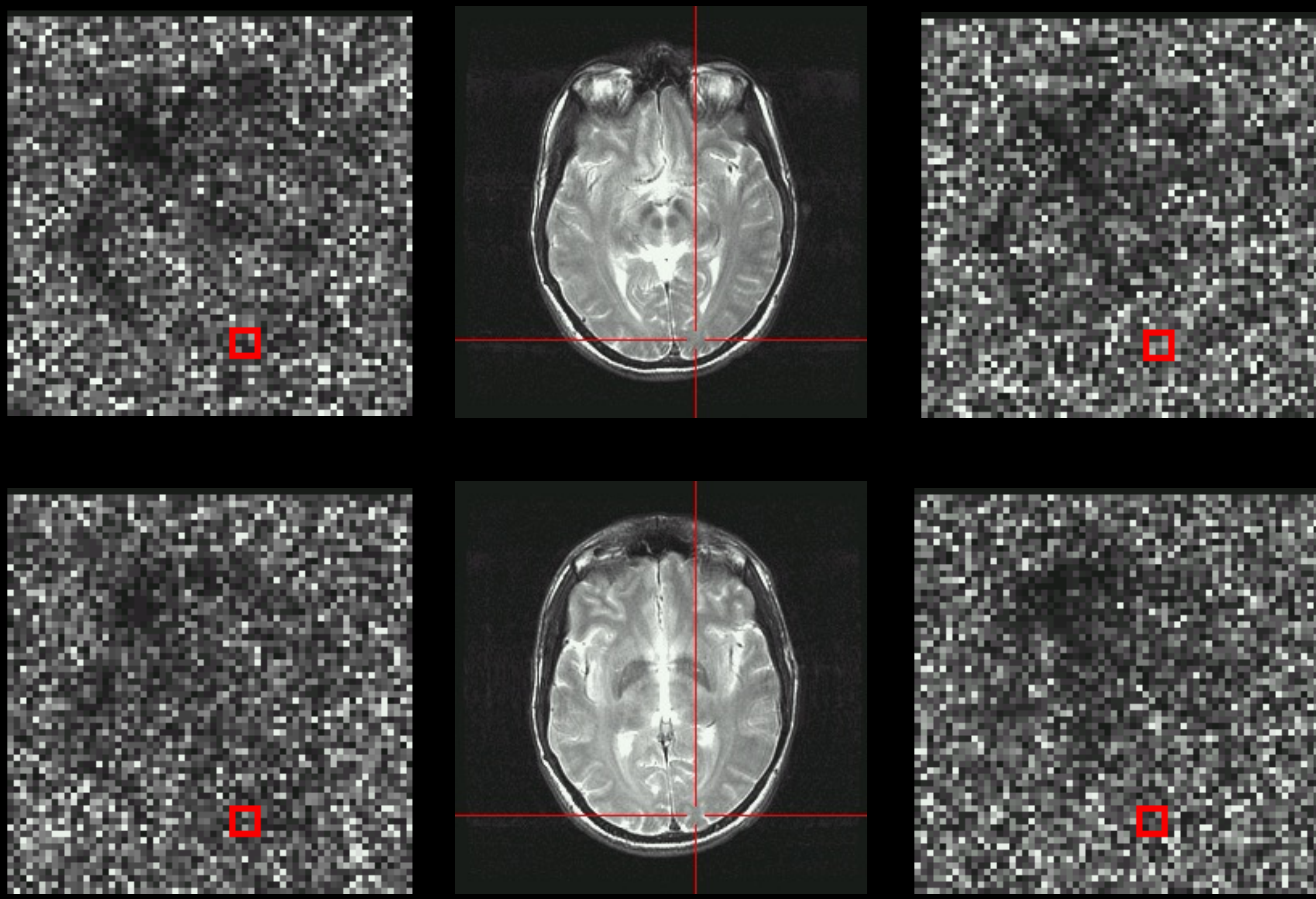



Magnitude v=0.12Hz
Closed
Open

Magnitude v=0.12 Hz

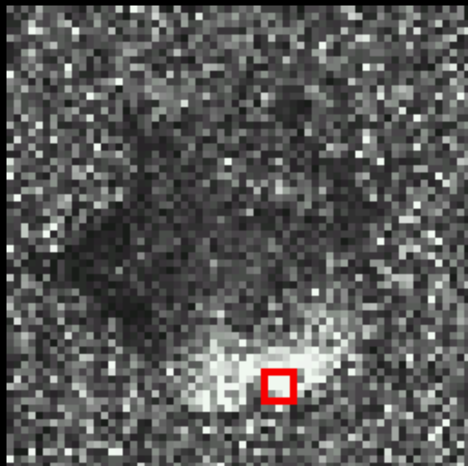
Closed

Open

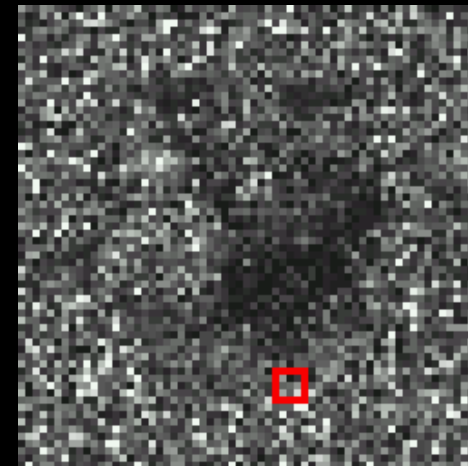


Phase v=0.12Hz

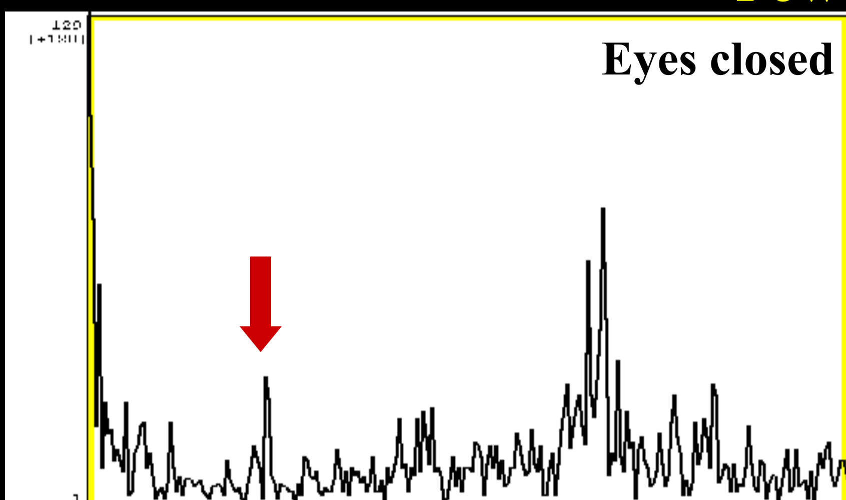
Closed



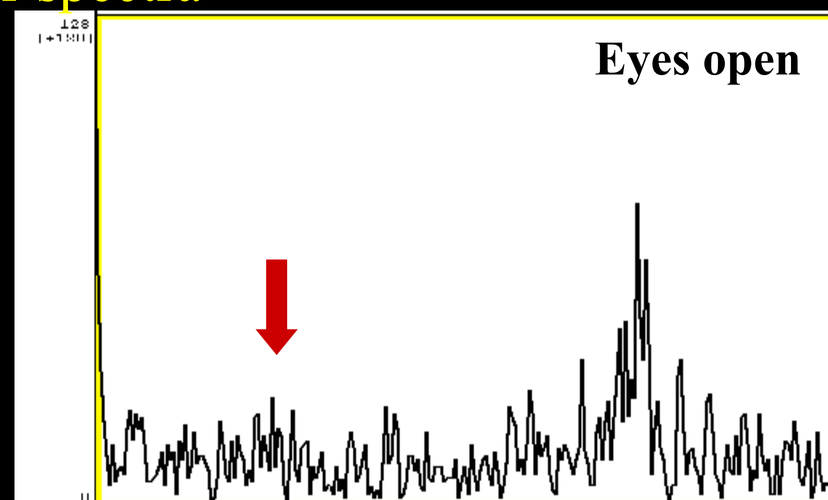
Open



Power spectra



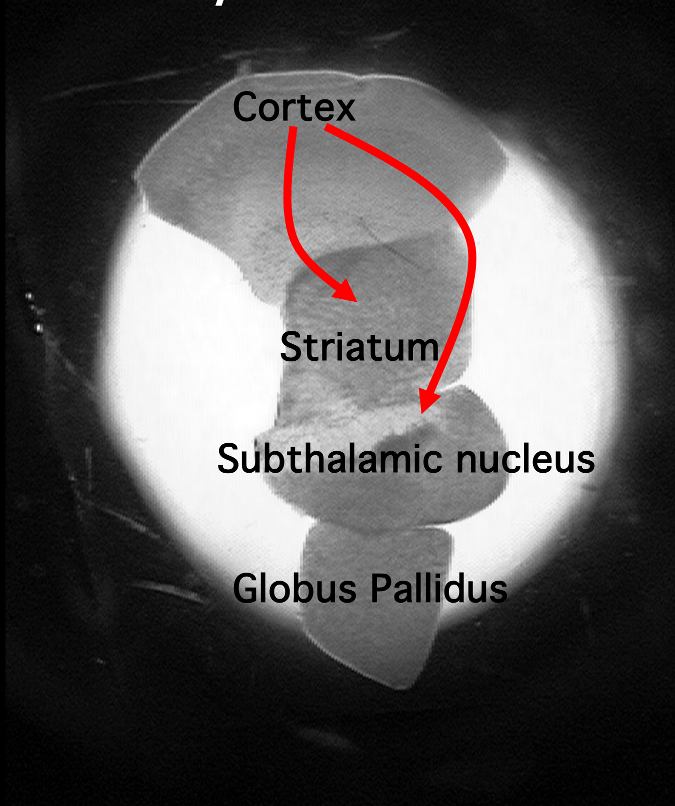
0.5 Hz

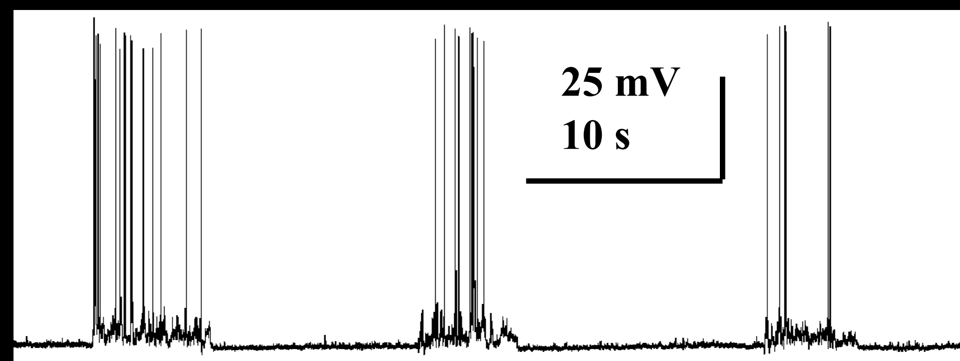


0.5 Hz

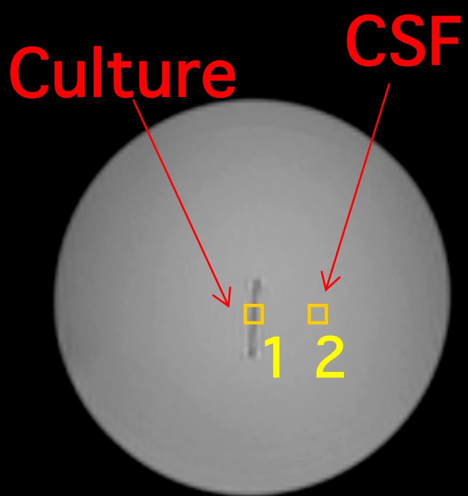
In Vitro Results

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

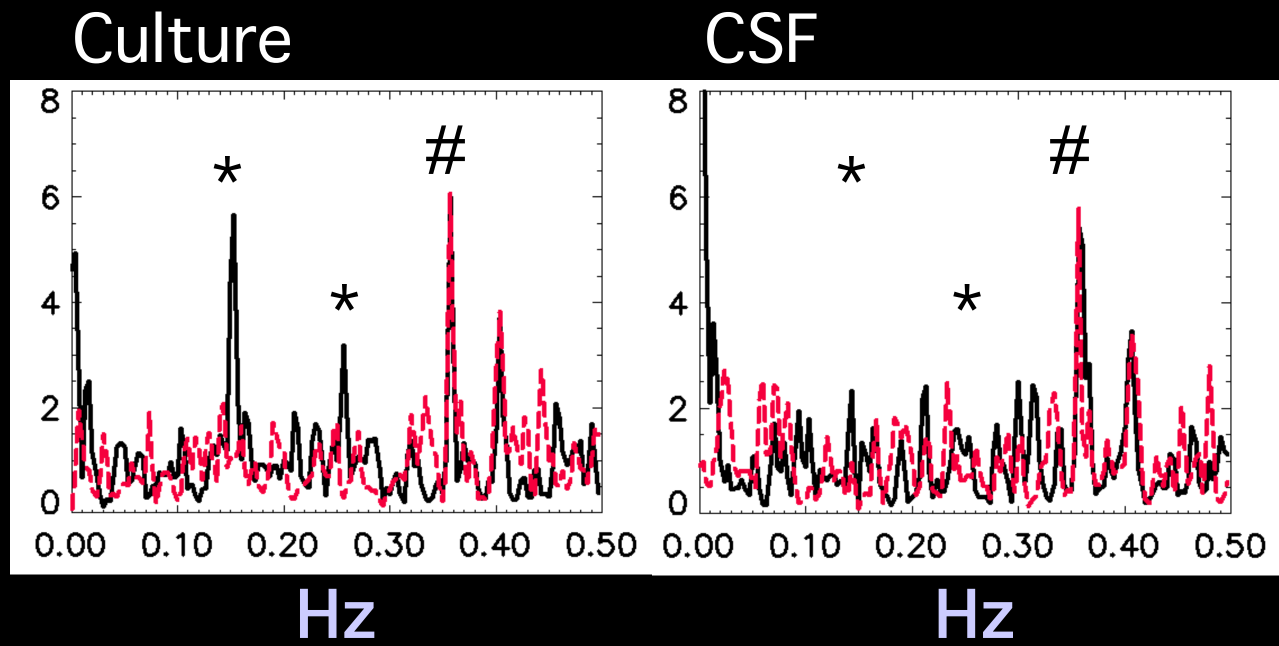




Plenz, D. and S.T. Kital. Nature, 1999. **400**: p. 677-682.



FSE image



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

*: activity

#: scanner pump frequency

Petridou et al.

- Functional contrast
- Signal interpretation
- Hardware and pulse sequences
- Paradigm design and processing

- Overview
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- Future Prospects

Neuronal Activation

?

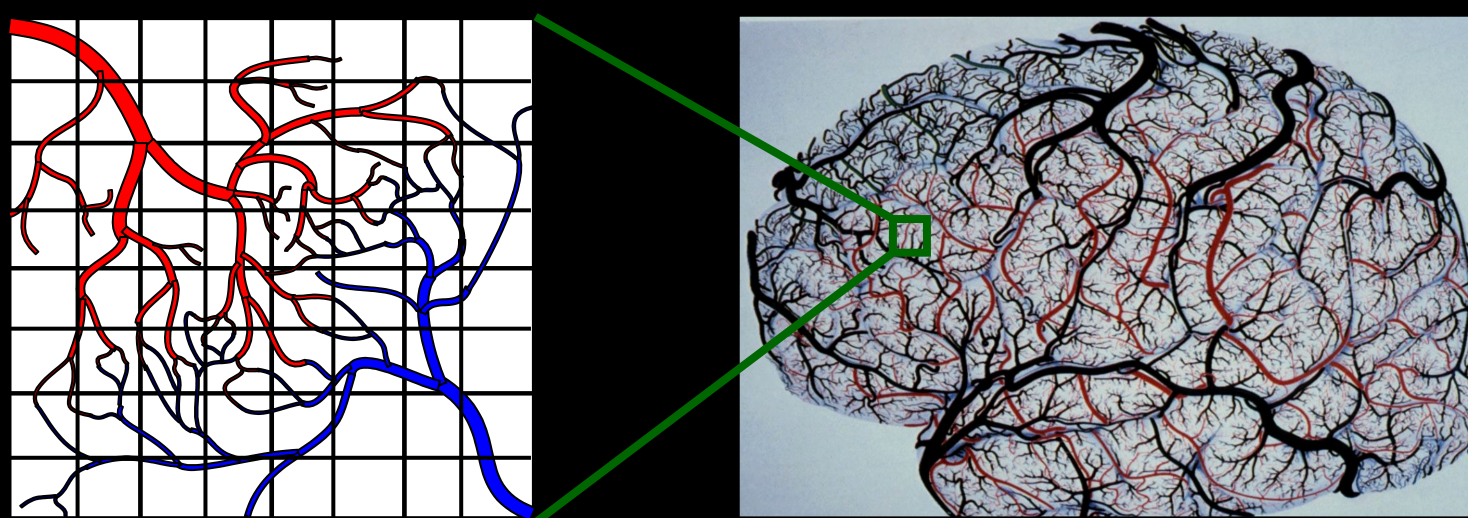
Hemodynamics

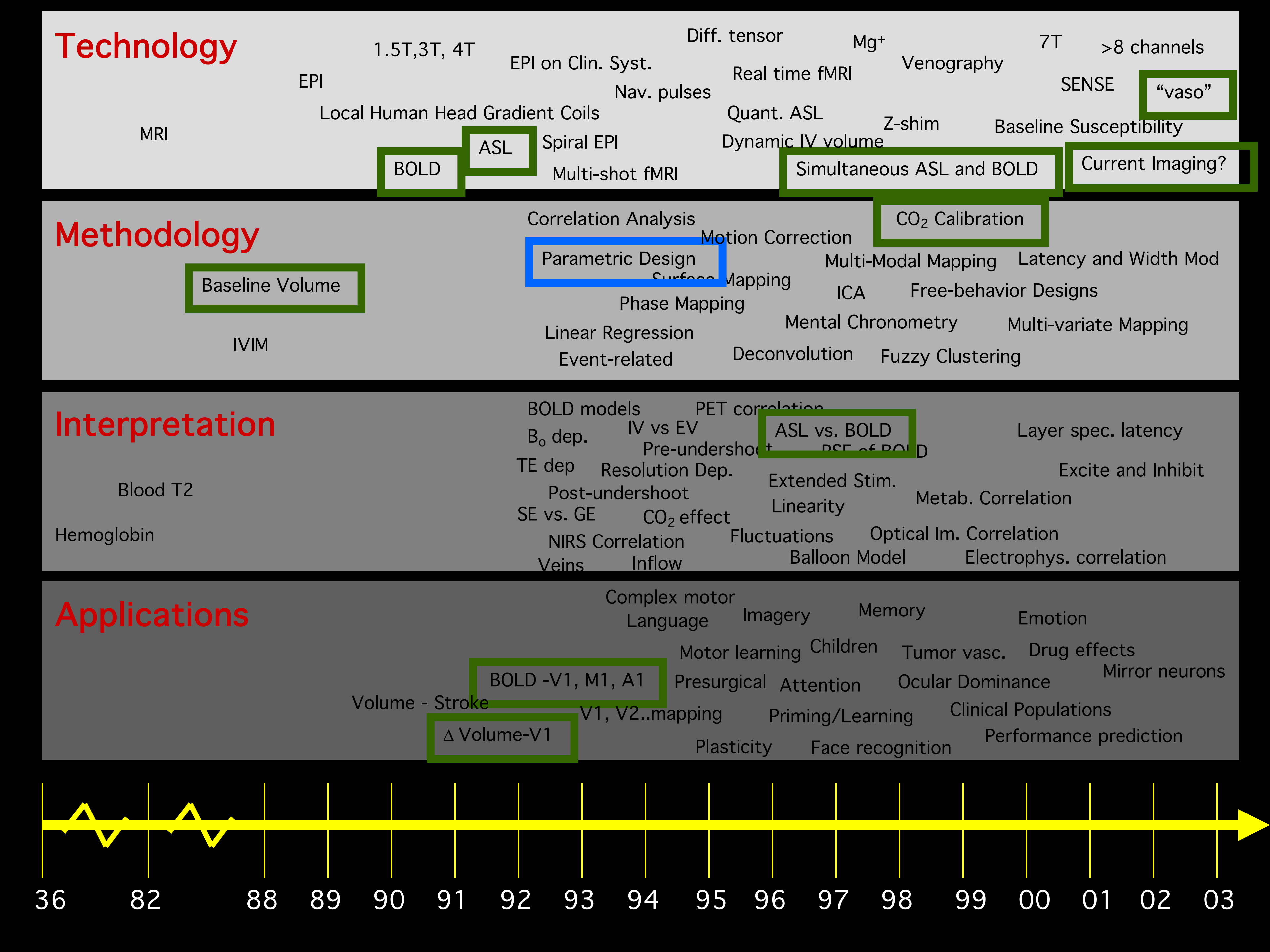
?

Measured Signal

?

Noise





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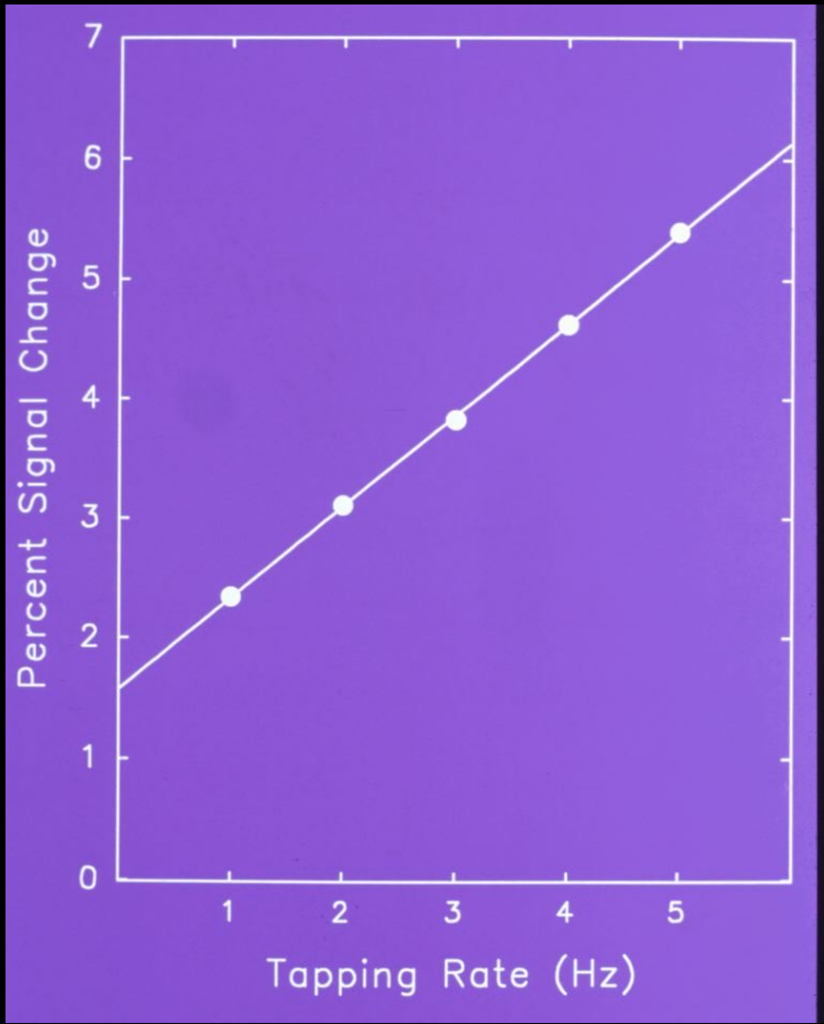
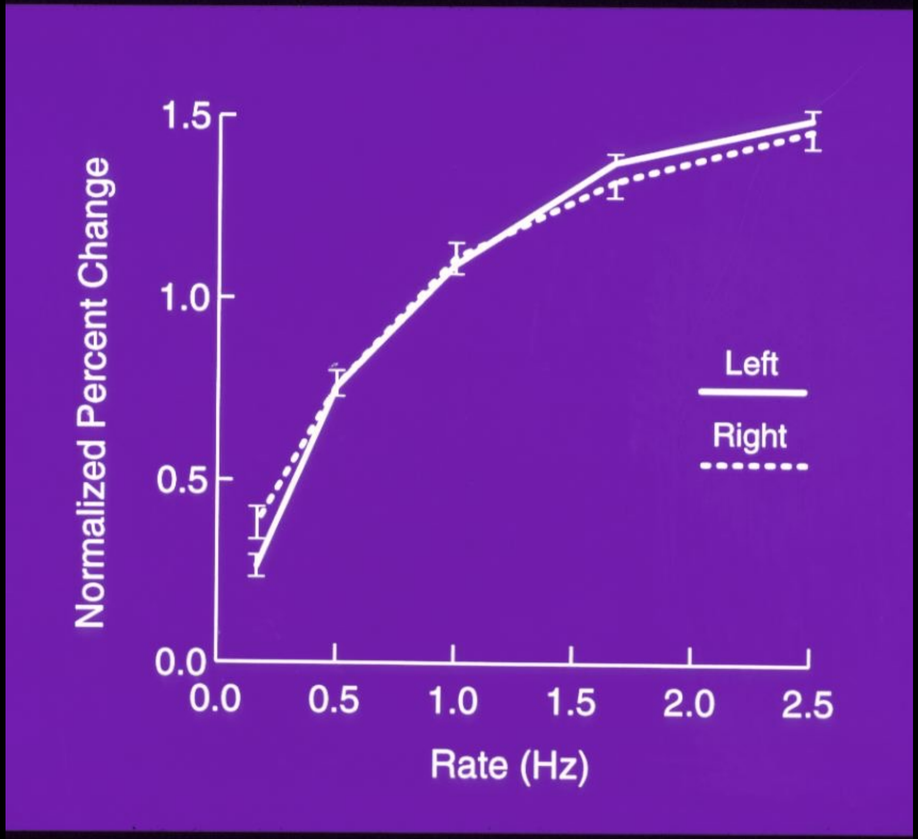
Motor Cortex

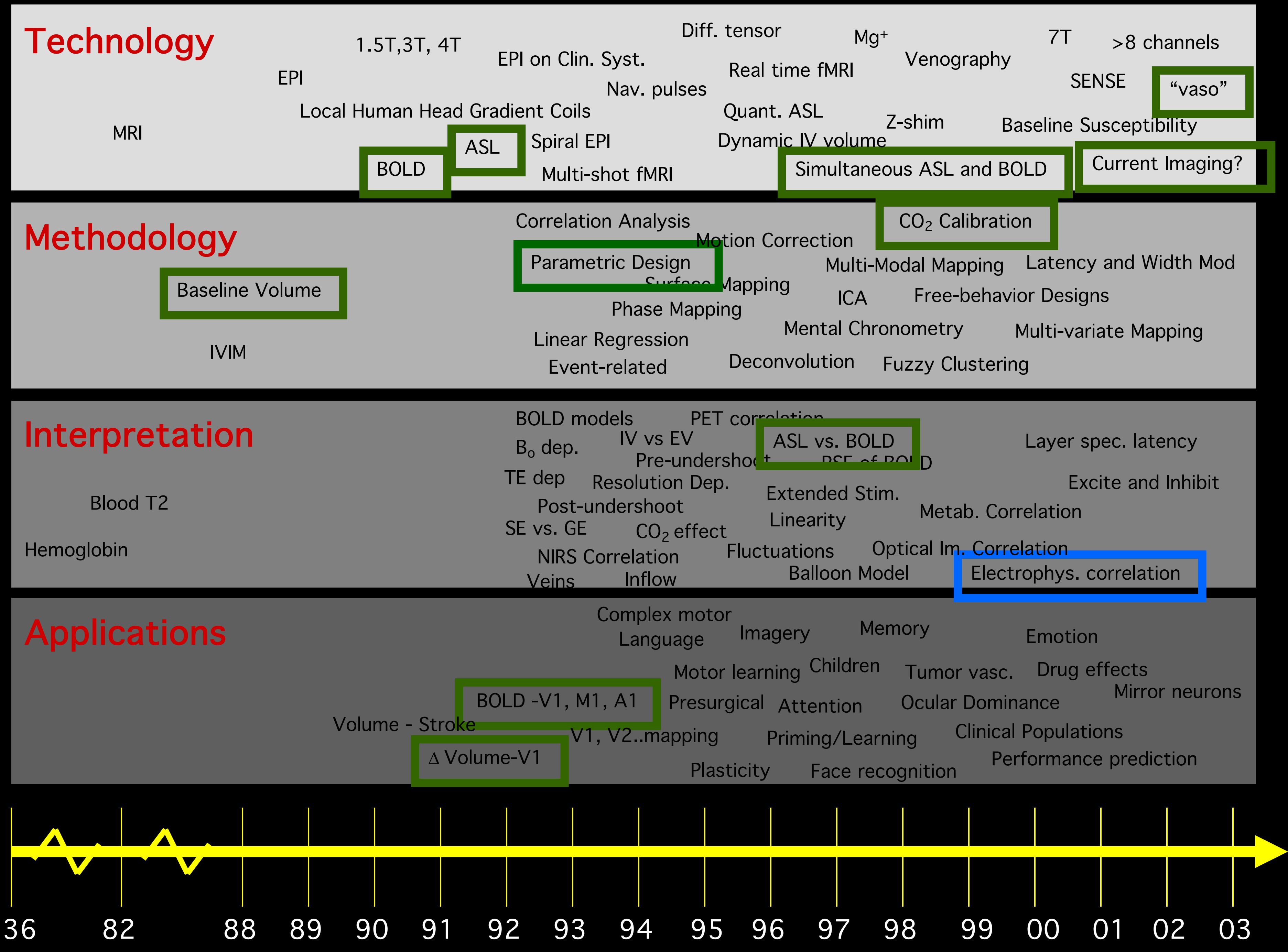


S. M. Rao et al, (1996) "Relationship between finger movement rate and functional magnetic resonance signal change in human primary motor cortex." *J. Cereb. Blood Flow and Met.* 16, 1250-1254.

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



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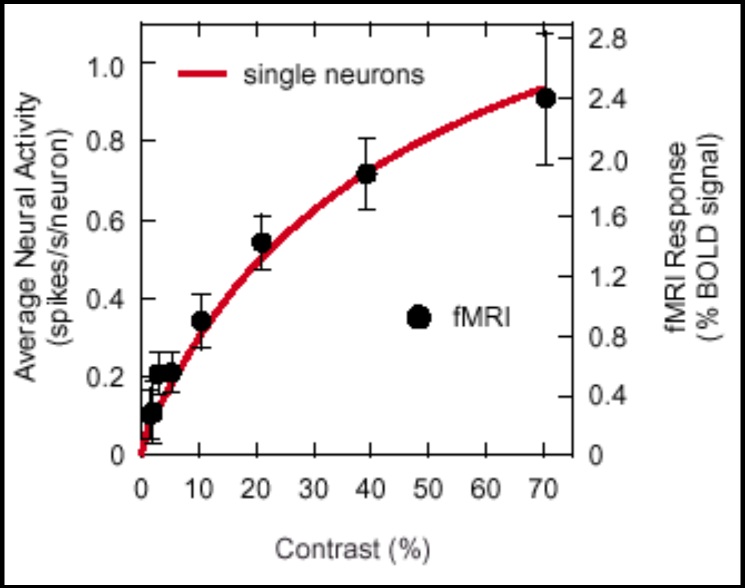
fMRI responses in human V1 are proportional to average firing rates in monkey V1



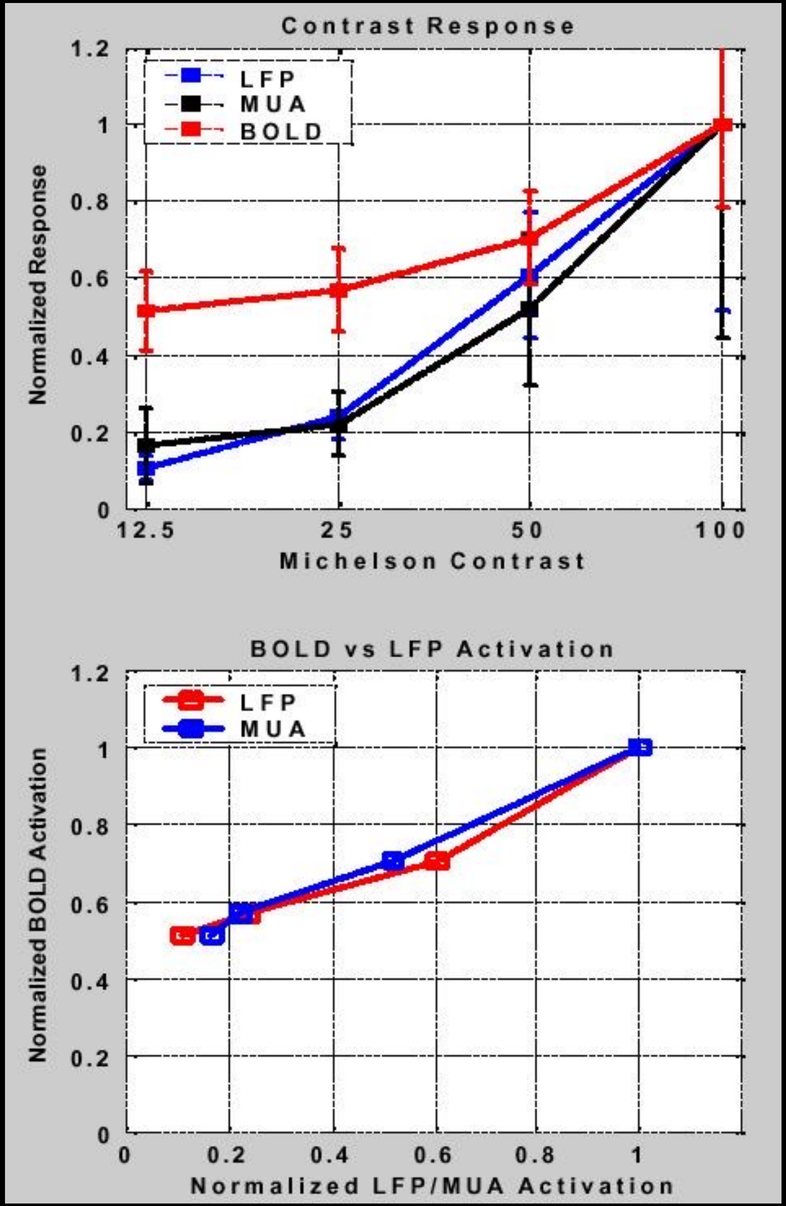
Heeger, D. J., Huk, A. C., Geisler, W. S., and Albrecht, D. G. 2000.Spikes versus BOLD: What does neuroimaging tell us about neuronal activity? *Nat. Neurosci.* **3:** 631–633.

0.4 spikes/sec -> 1% BOLD

Rees, G., Friston, K., and Koch, C. 2000. A direct quantitative relationship between the functional properties of human and macaque V5. *Nat. Neurosci.* **3:** 716–723.

9 spikes/sec -> 1% BOLD

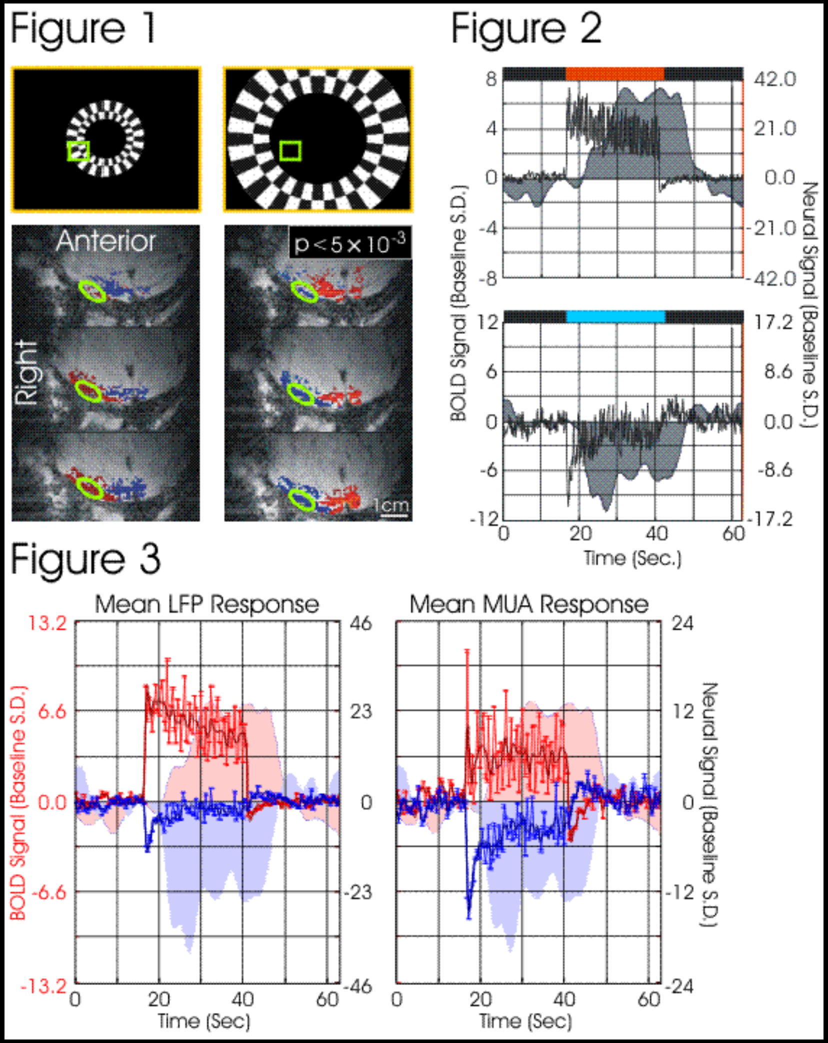
Logothetis et al. (2001) "Neurophysiological investigation of the basis of the fMRI signal" Nature, 412, 150-157

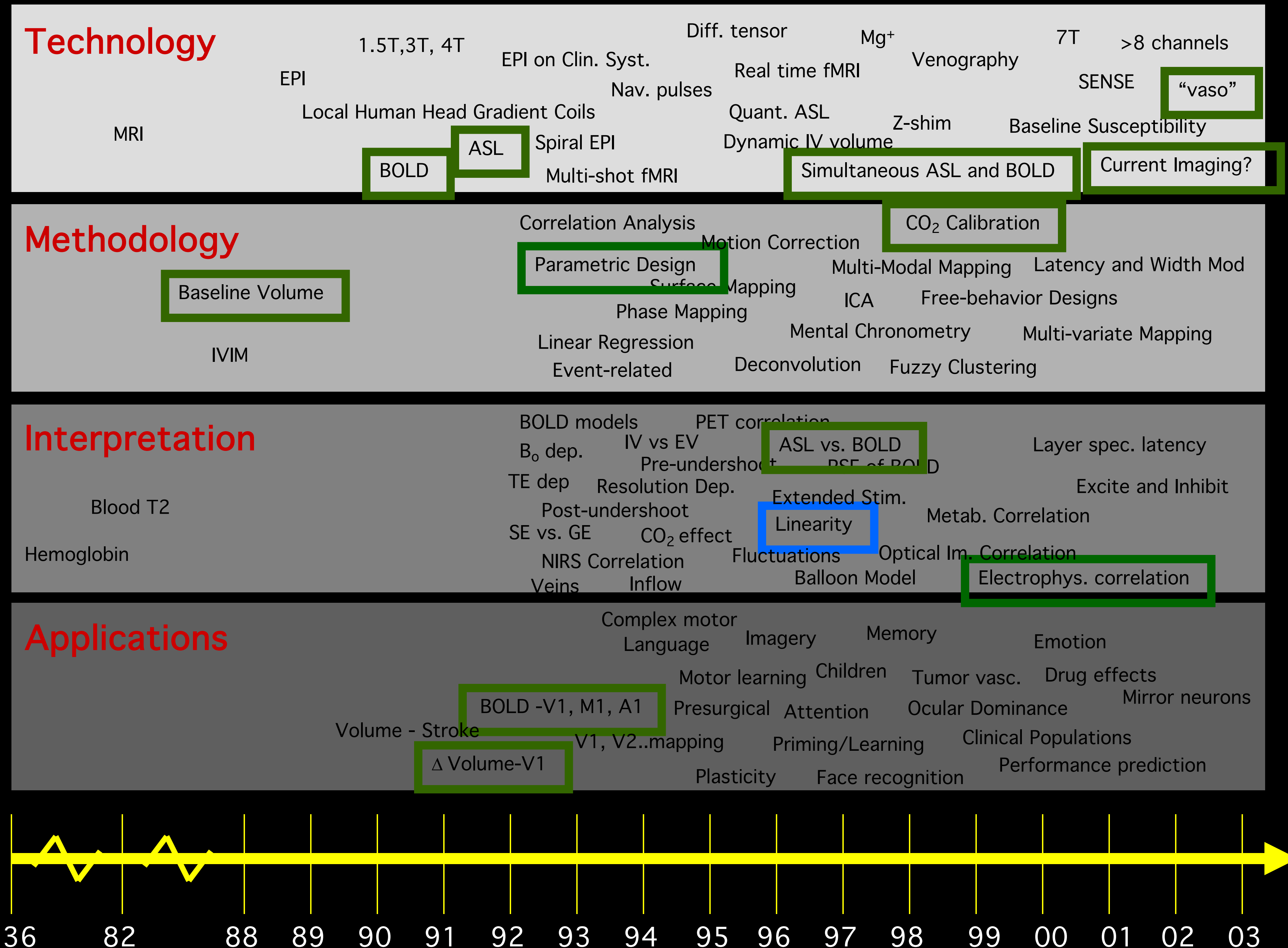


HBM 2003
Poster number: 308

The Negative BOLD Response in Monkey V1 Is Associated with Decreases in Neuronal Activity

Amir Shmuel*†, Mark Augath, Axel Oeltermann, Jon Pauls, Yusuke Murayama, Nikos K. Logothetis

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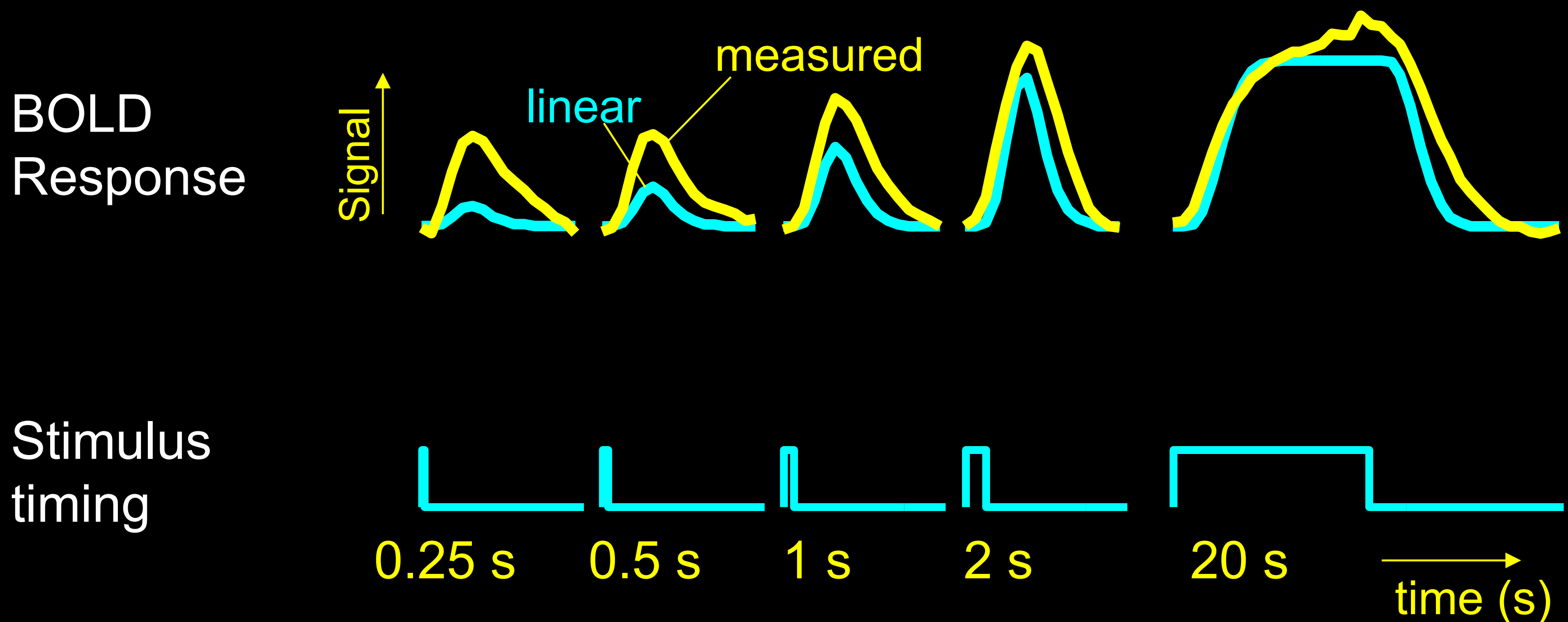
Dynamic Nonlinearity Assessment

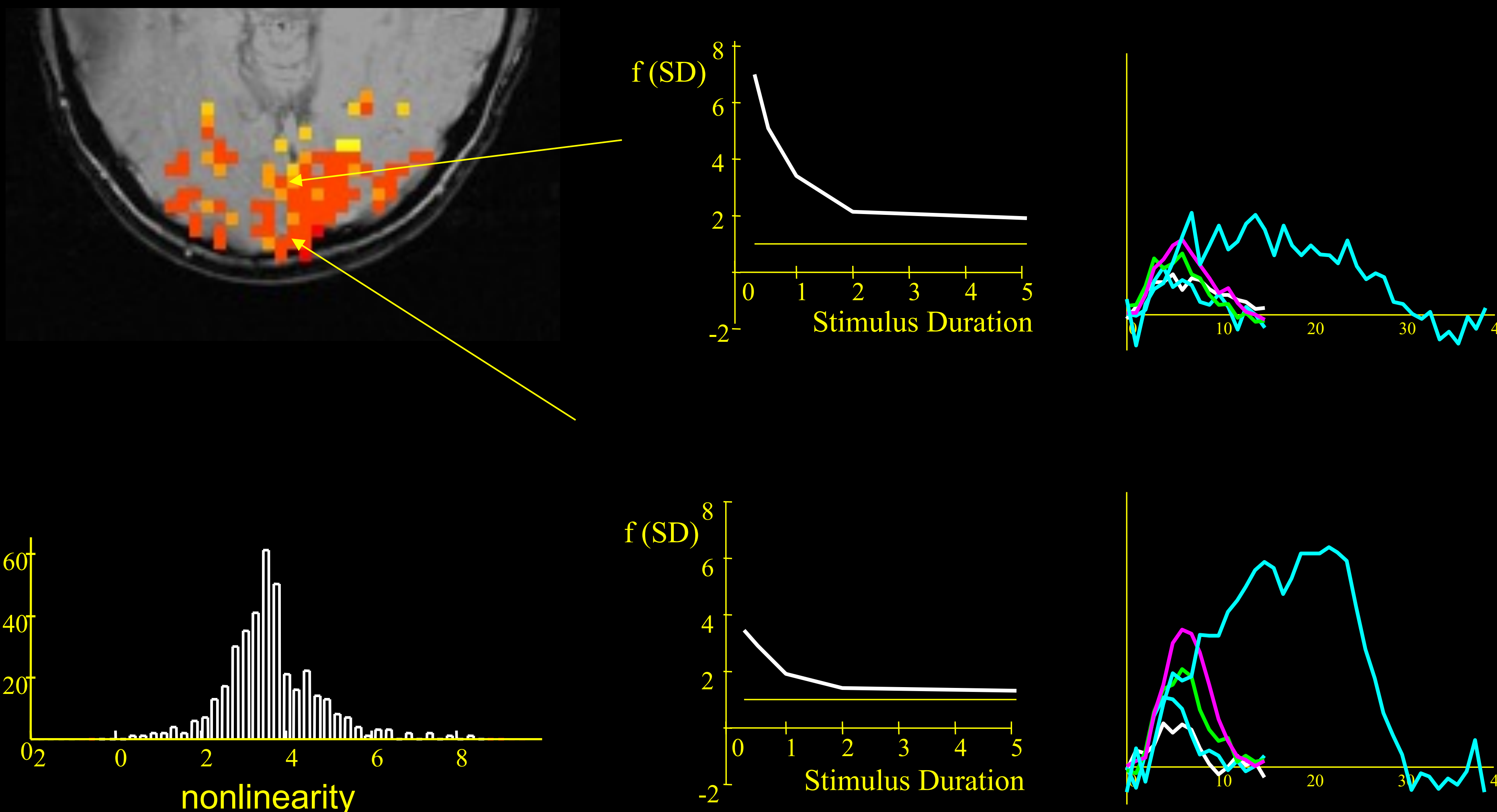
Different stimulus "ON" periods



Brief stimuli produce larger responses than expected

R. M. Birn, Z. Saad, P. A. Bandettini, (2001) "Spatial heterogeneity of the nonlinear dynamics in the fMRI BOLD response." ***NeuroImage*****, 14: 817-826.**

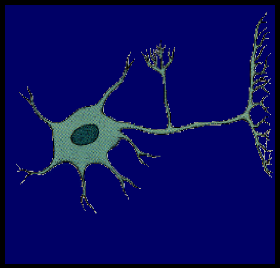
Spatial Heterogeneity of BOLD Nonlinearity

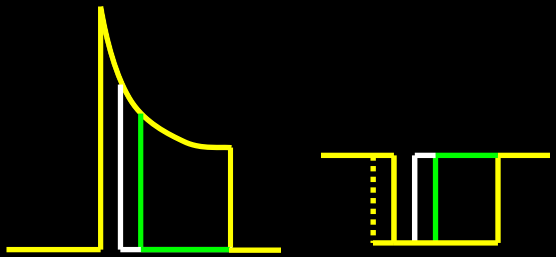


R. M. Birn, Z. Saad, P. A. Bandettini, (2001) "Spatial heterogeneity of the nonlinear dynamics in the fMRI BOLD response." ***NeuroImage*****, 14: 817-826.**

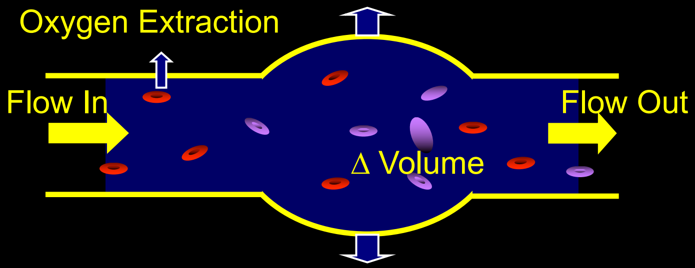
Sources of this Nonlinearity

- Neuronal



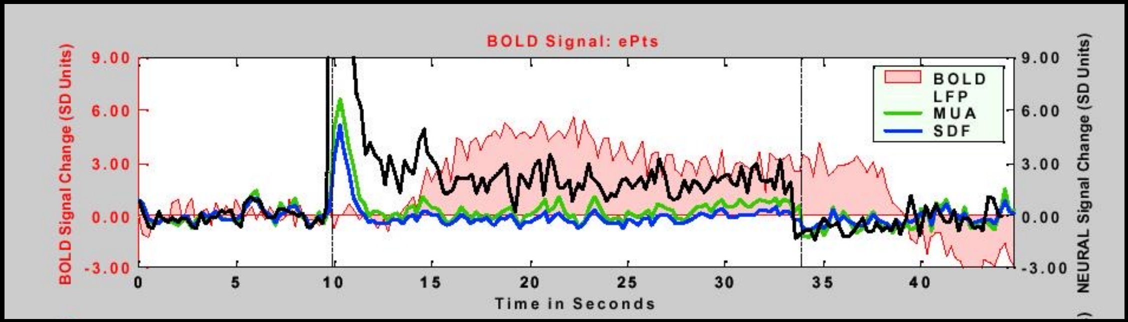


- Hemodynamic
  - Oxygen extraction
  - Blood volume dynamics

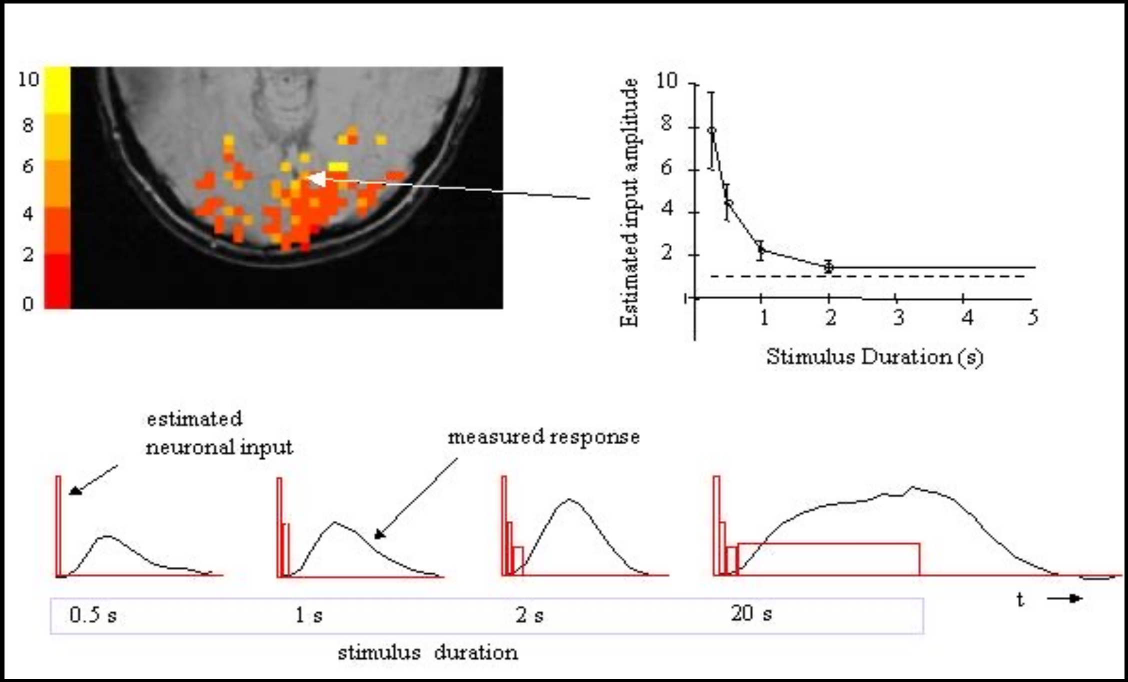


BOLD Correlation with Neuronal Activity

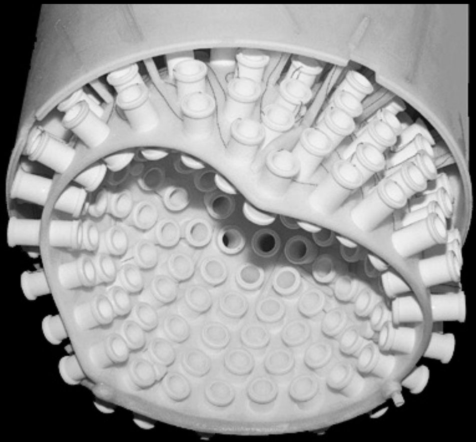
Logothetis et al. (2001) "Neurophysiological investigation of the basis of the fMRI signal" Nature, 412, 150-157.



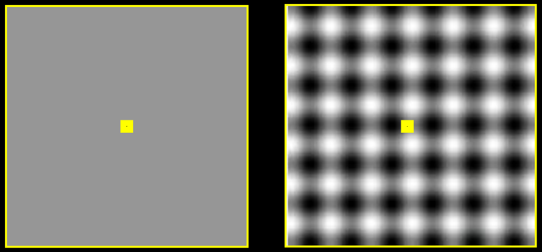
P. A. Bandettini and L. G. Ungerleider, (2001) "From neuron to BOLD: new connections." Nature Neuroscience, 4: 864-866.



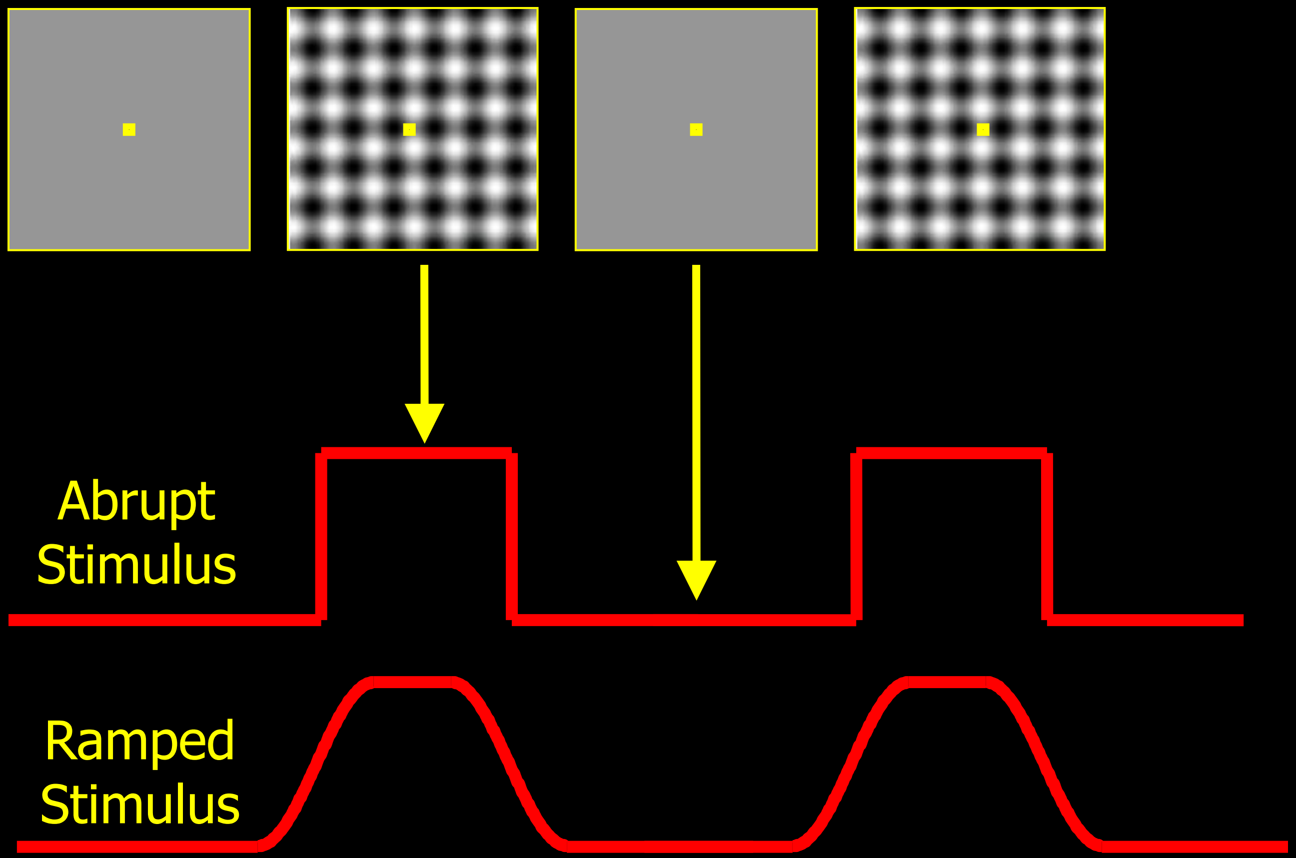
MEG and Ramped Stimulus



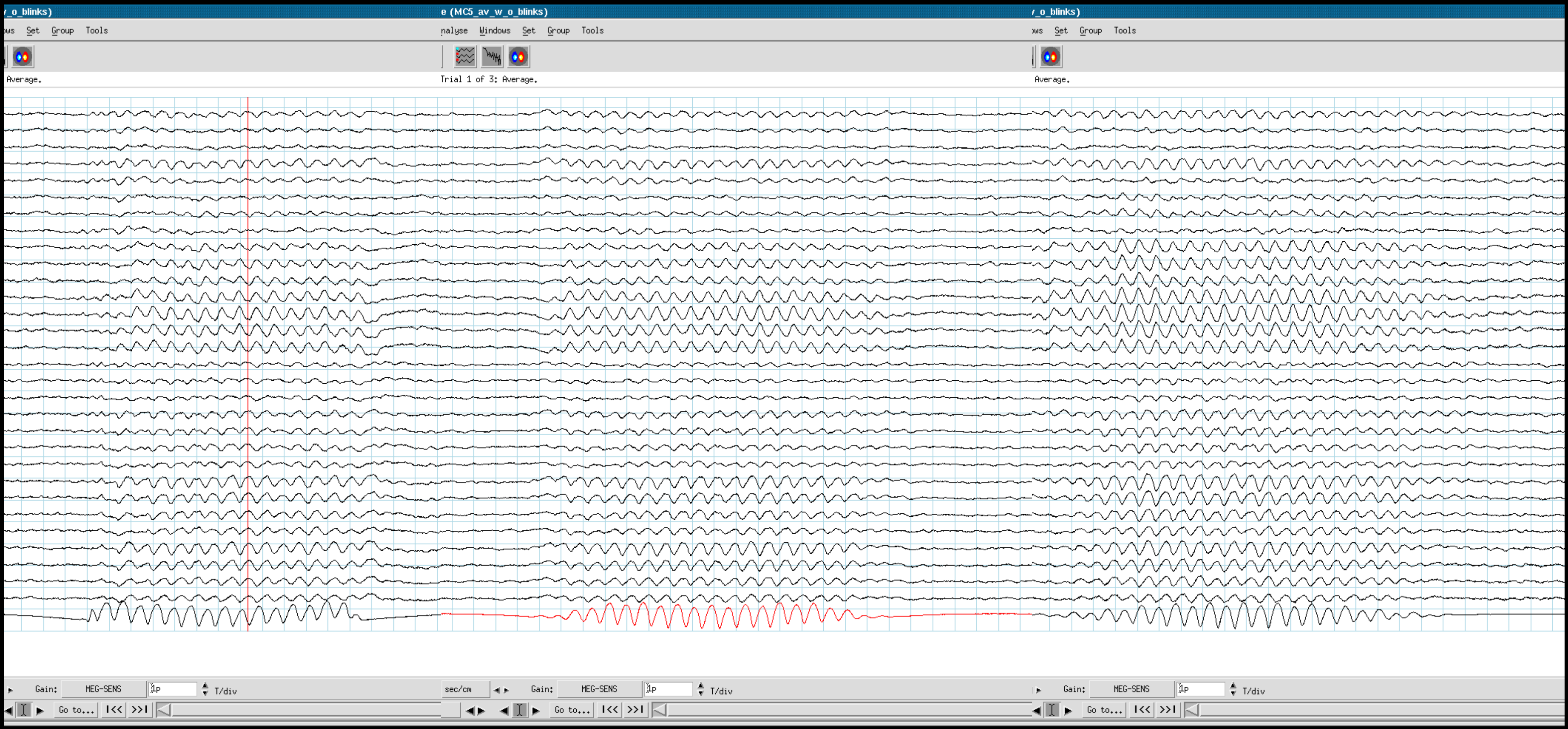
- 6 subjects
- SD: 1 or 2 seconds
- Ramp: 0, 0.5, 1 second
- 8 Hz Counterphase-modulated checkerboards
- Fixation without task
  - No blinking point
- 45 repeats
- 3 sec ISI
- 275 channels
- 600 Hz



MEG – Ramped stimuli



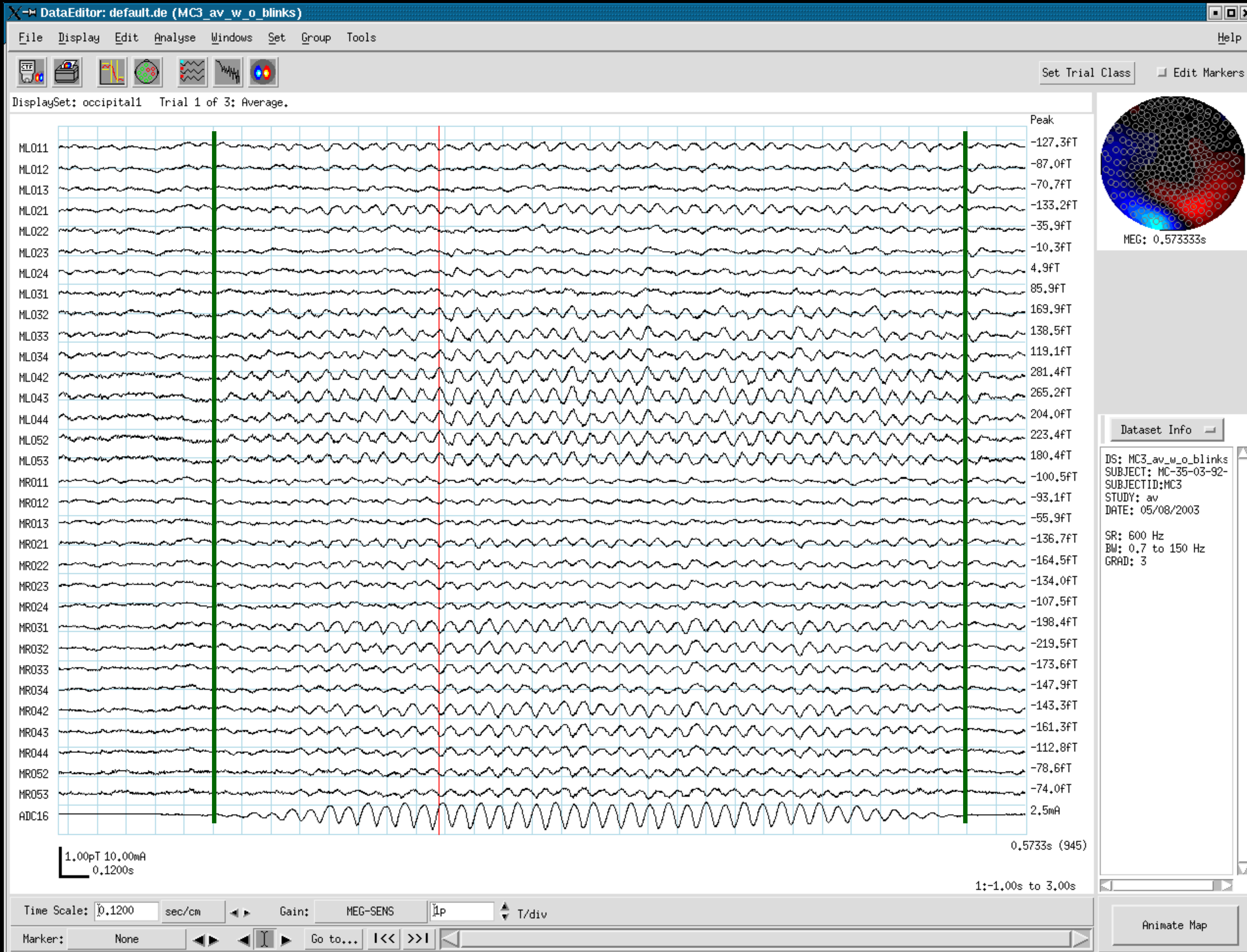
Composite – 1 second Stimulus Duration



No Ramp

0.5 second Ramp

1 second Ramp


DataEditor: default.de (MC3_av_w_o_blinks)
File Display Edit Analyse Windows Set Group Tools Help
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ML021 -133.2fT
ML022 -35.9fT
ML023 -10.3fT
ML024 4.9fT
ML031 85.9fT
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ML042 281.4fT
ML043 265.2fT
ML044 204.0fT
ML052 223.4fT
ML053 180.4fT
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MR012 -93.1fT
MR013 -55.9fT
MR021 -136.7fT
MR022 -164.5fT
MR023 -134.0fT
MR024 -107.5fT
MR031 -198.4fT
MR032 -219.5fT
MR033 -173.6fT
MR034 -147.9fT
MR042 -143.3fT
MR043 -161.3fT
MR044 -112.8fT
MR052 -78.6fT
MR053 -74.0fT
ADC16 2.5mA
1.00pT 10.00mA
0.1200s
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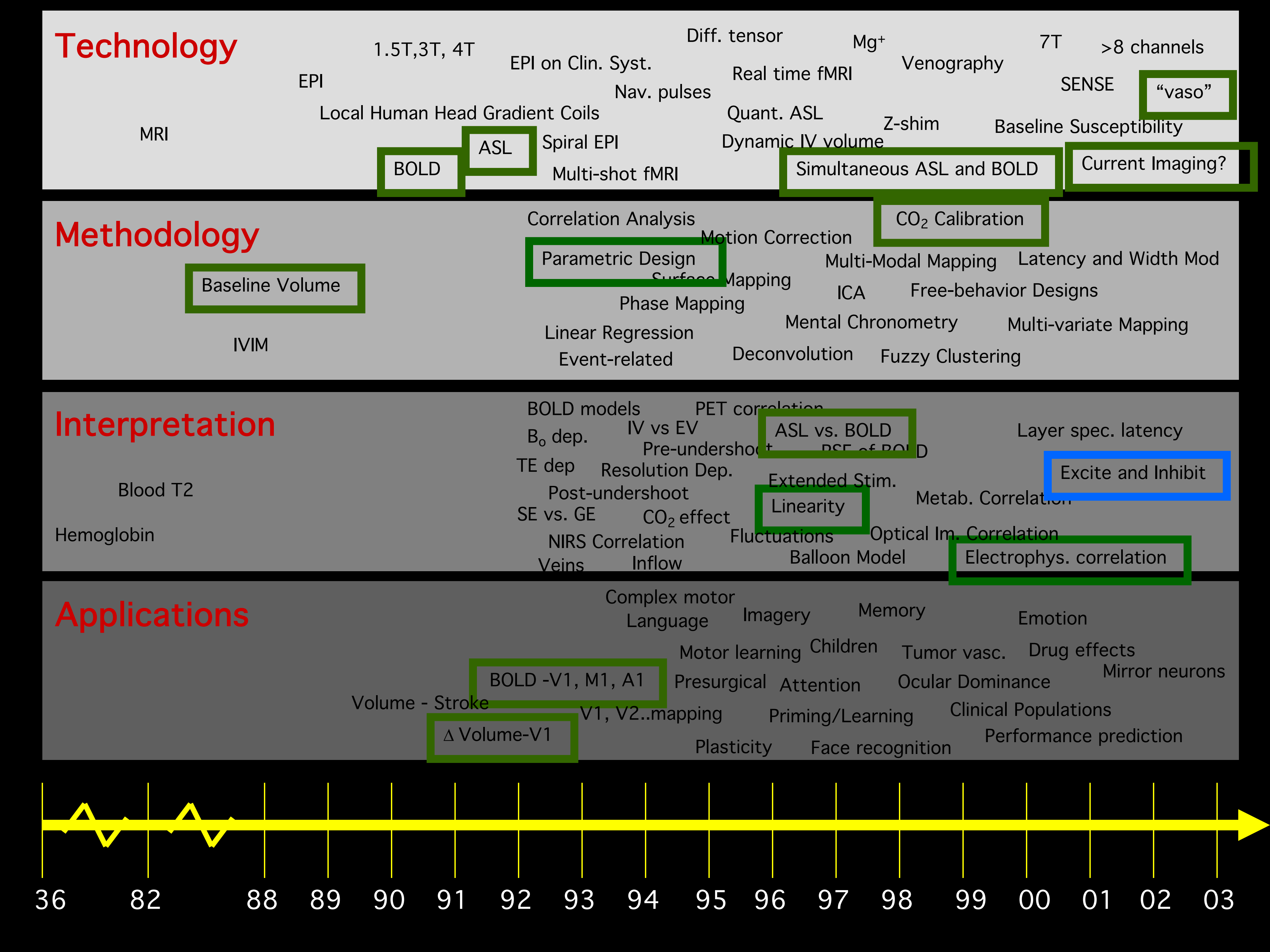
1:-1.00s to 3.00s
MEG: 0.573333s
Dataset Info
DS: MC3_av_w_o_blinks
SUBJECT: MC-35-03-92-
SUBJECTID:MC3
STUDY: av
DATE: 05/08/2003
SR: 600 Hz
BW: 0.7 to 150 Hz
GRAD: 3
Time Scale: 0.1200 sec/cm
Gain: MEG-SENS 1p T/div
Marker: None
Go to...
Animate Map



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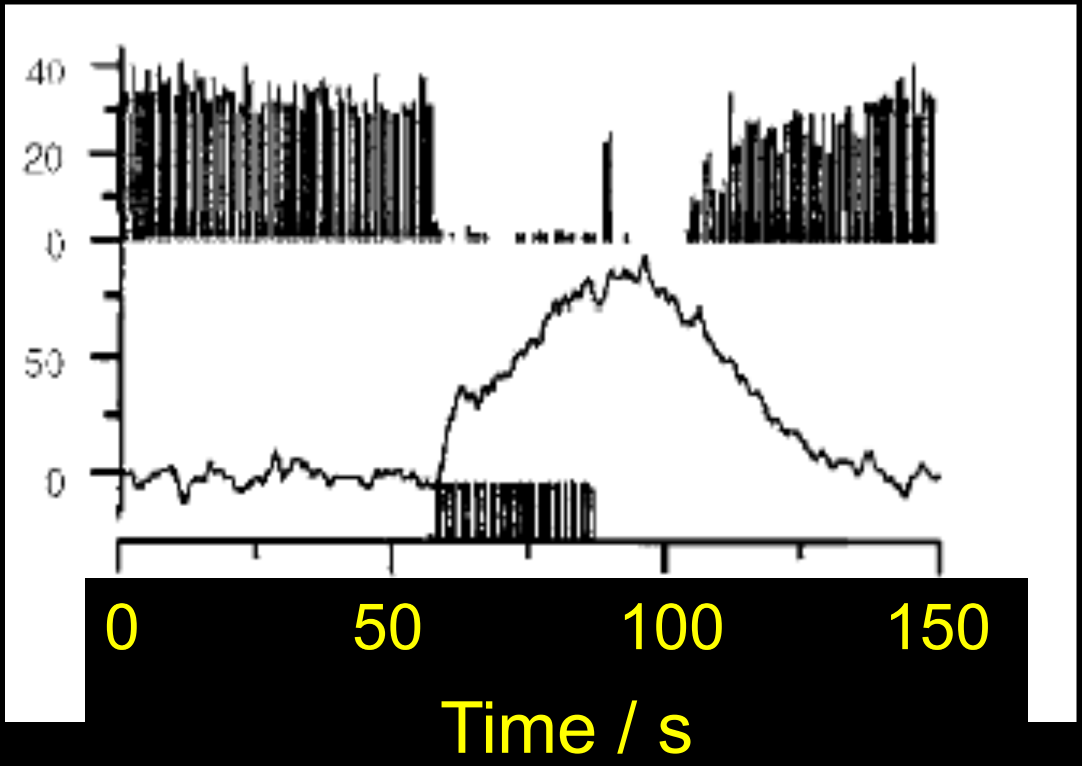
Divergence of spike rate and blood flow during parallel fiber stimulation



Mathiesen, Caesar, Akgören, Lauritzen (1998), J Physiol 512.2:555-566

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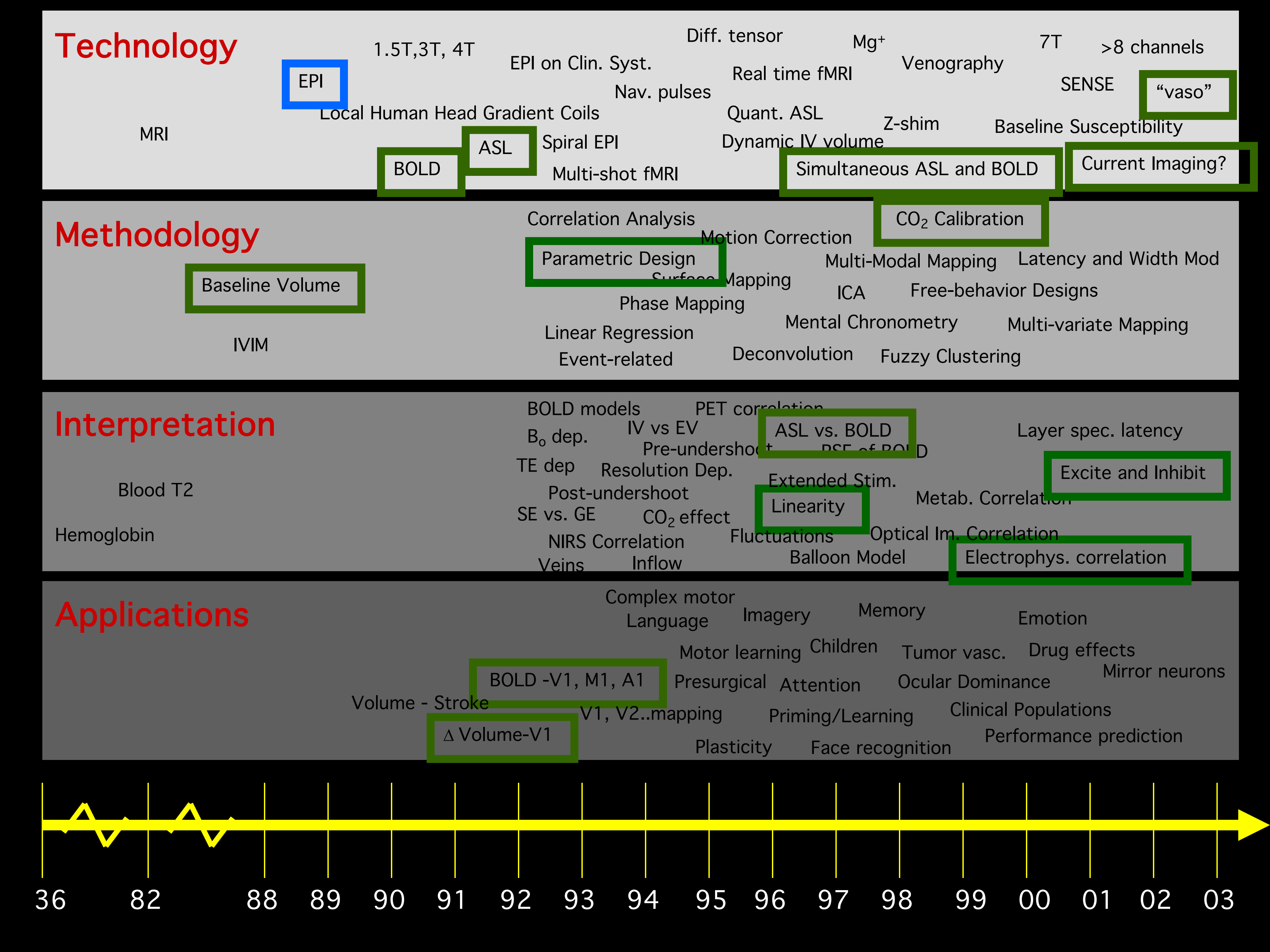

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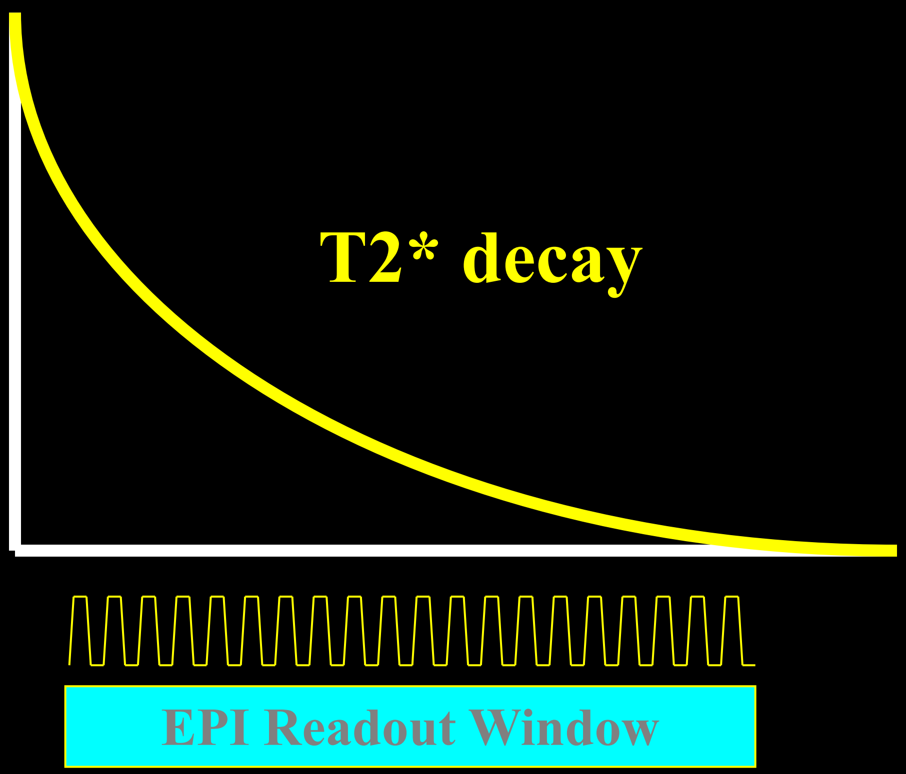
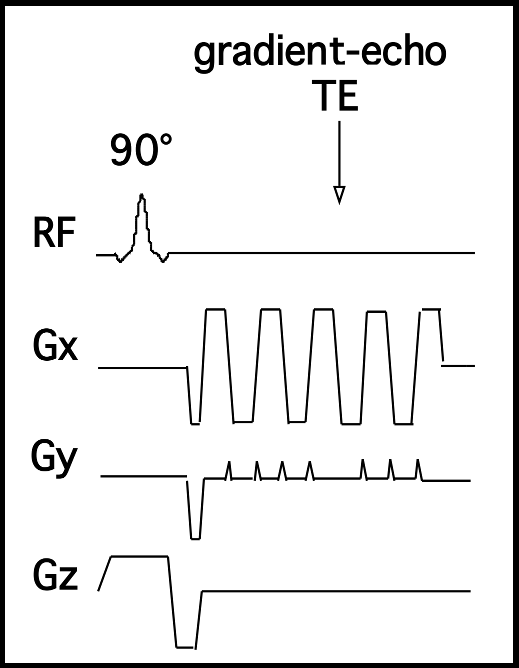
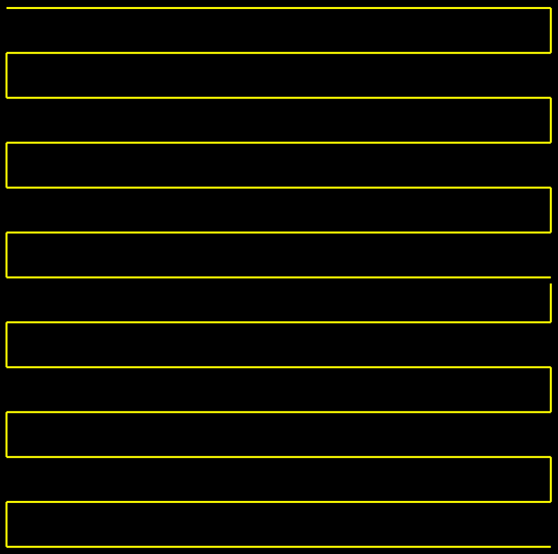
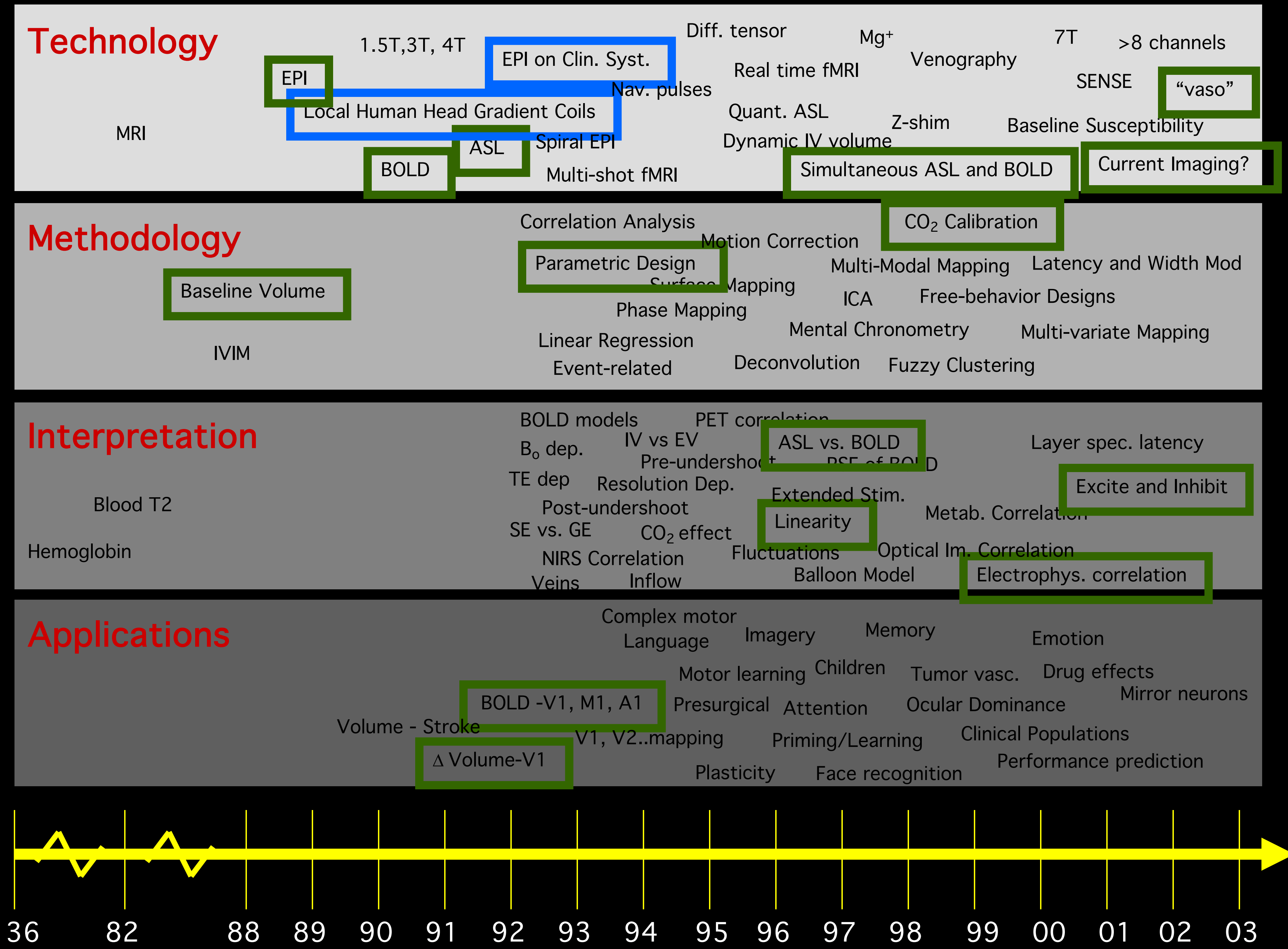
Single Shot EPI



≈ 20 to 40 ms







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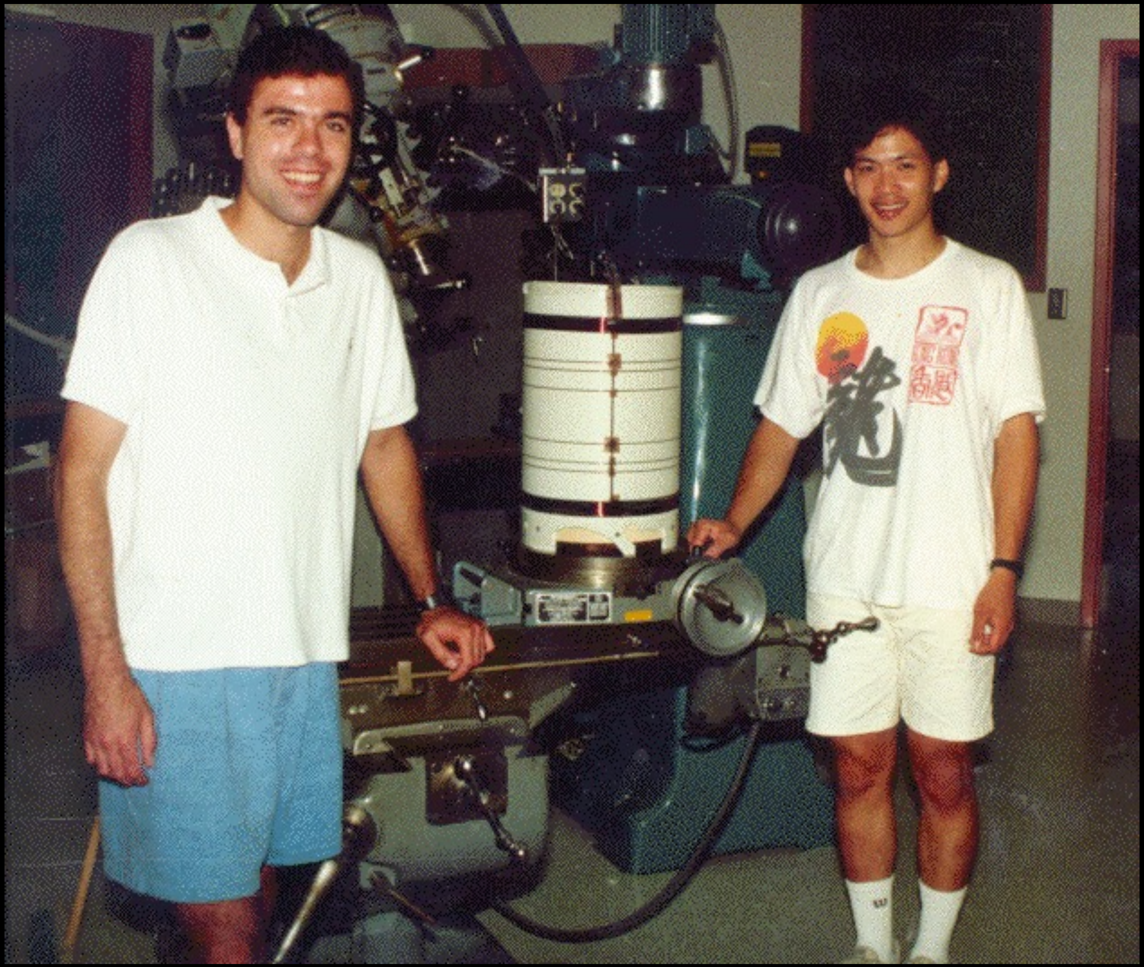
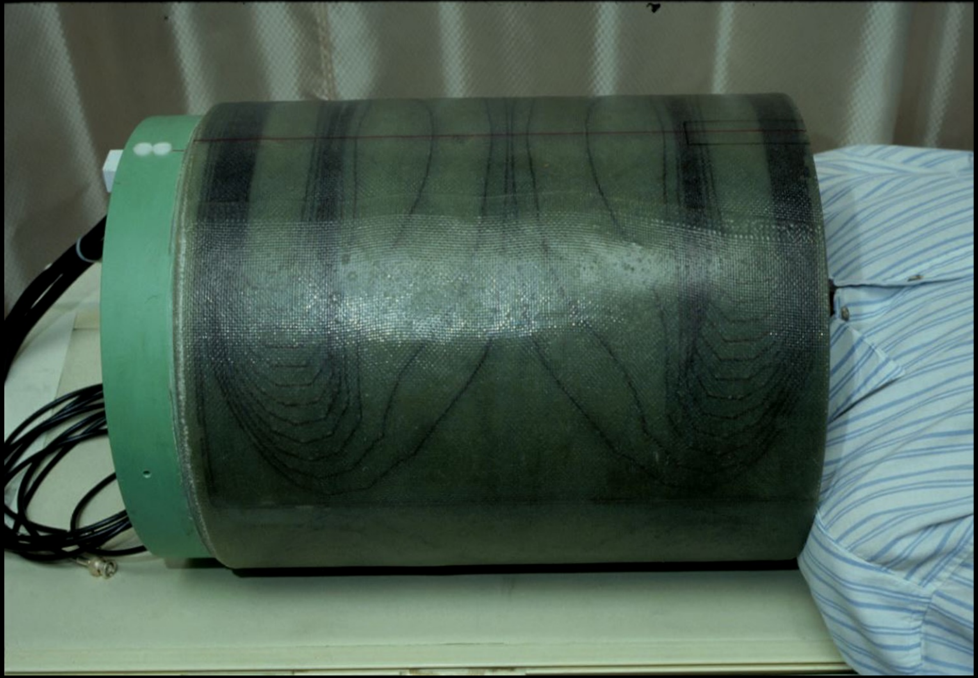
Local gradients solved the problem



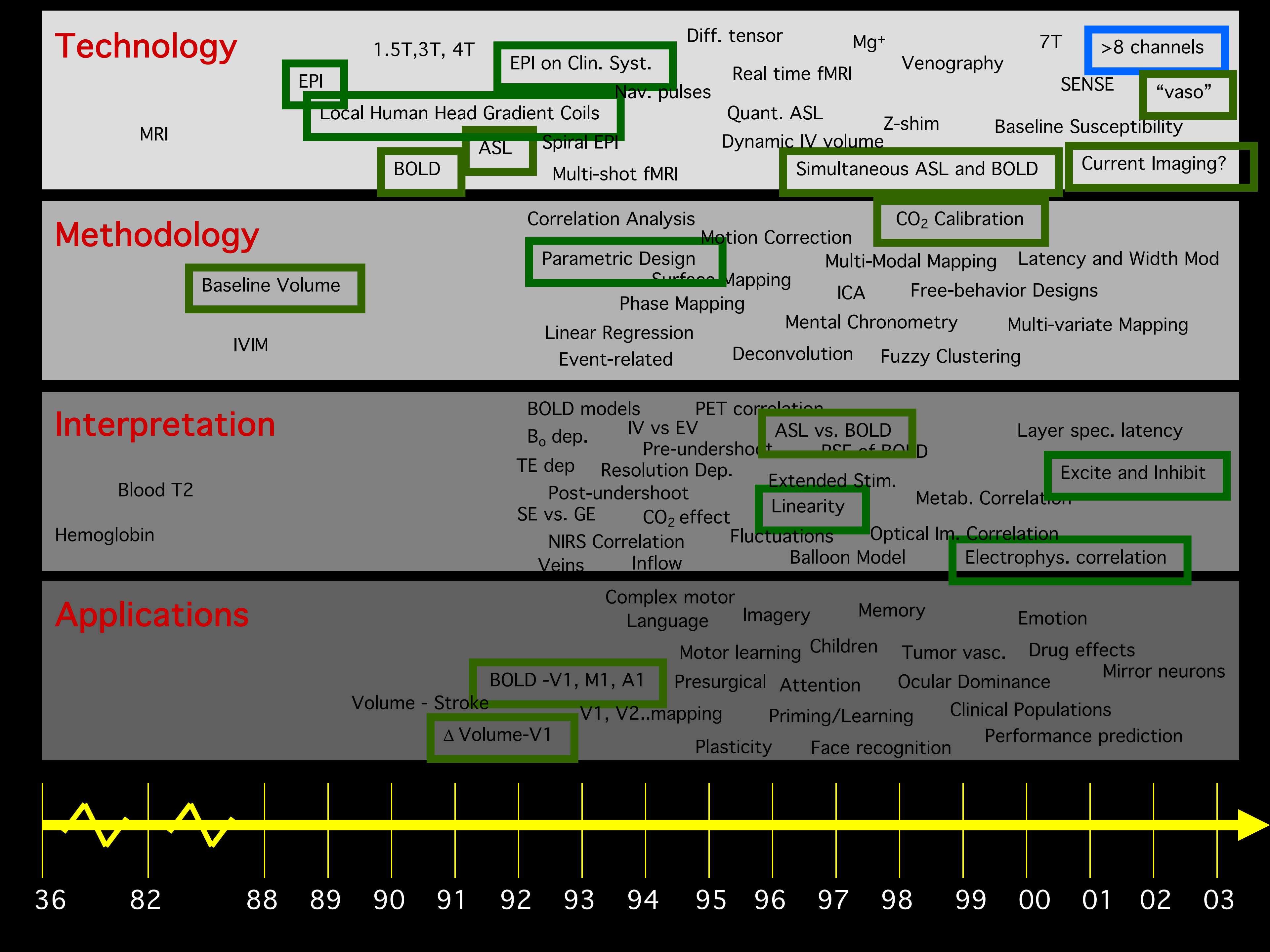
August, 1991

1991-1992

1992-1999



General Electric 3 Tesla Scanner



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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.

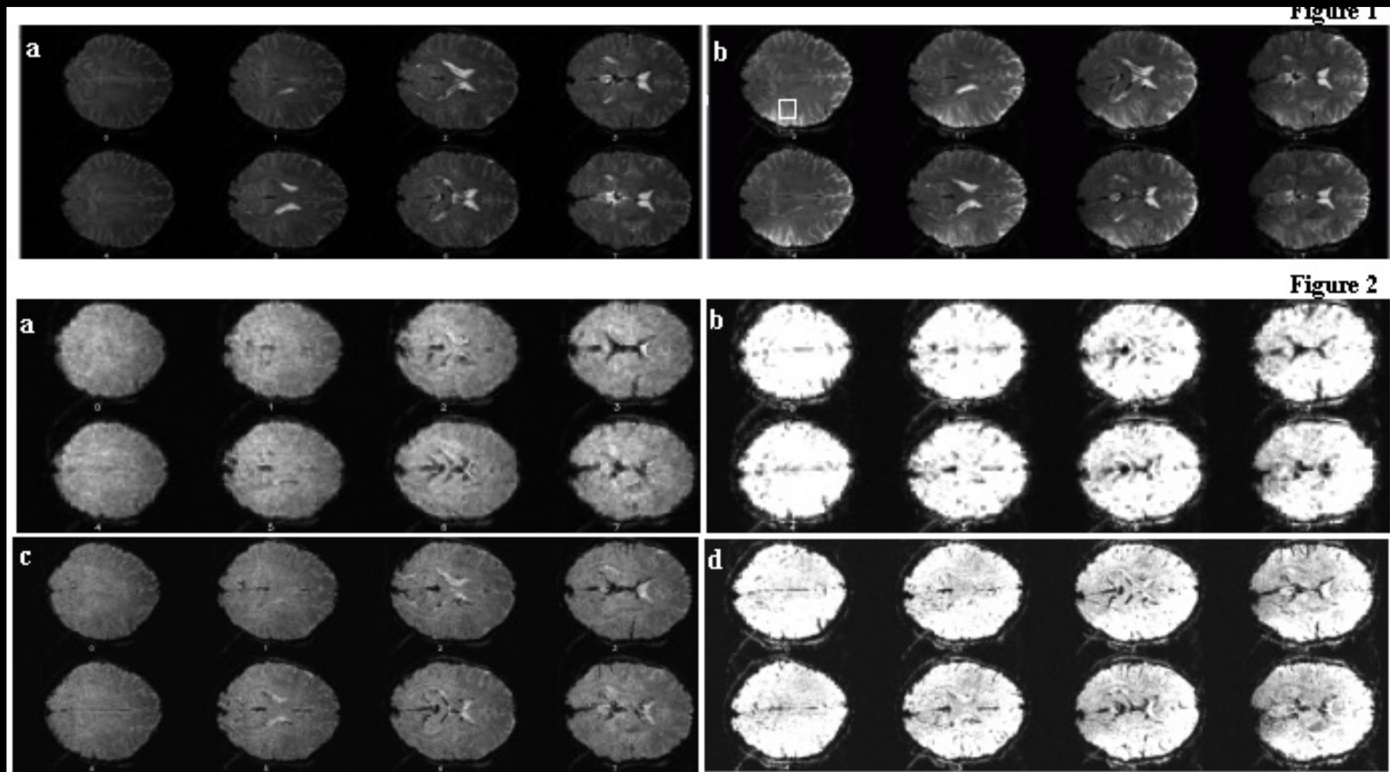
Quadrature Head Coil

8 Channel Array

128 x 96

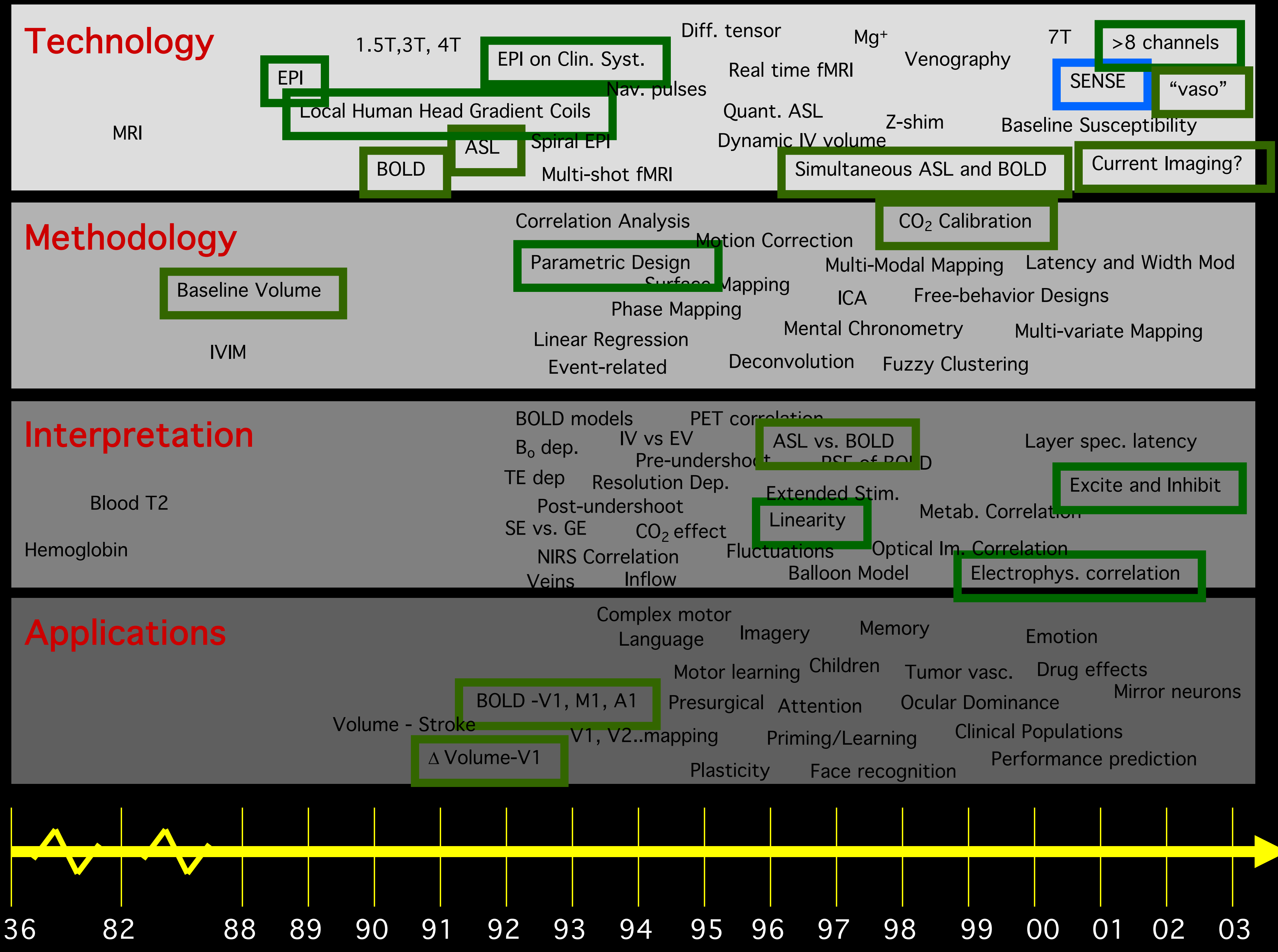
64 x 48

128 x 96



SNR

TSNR



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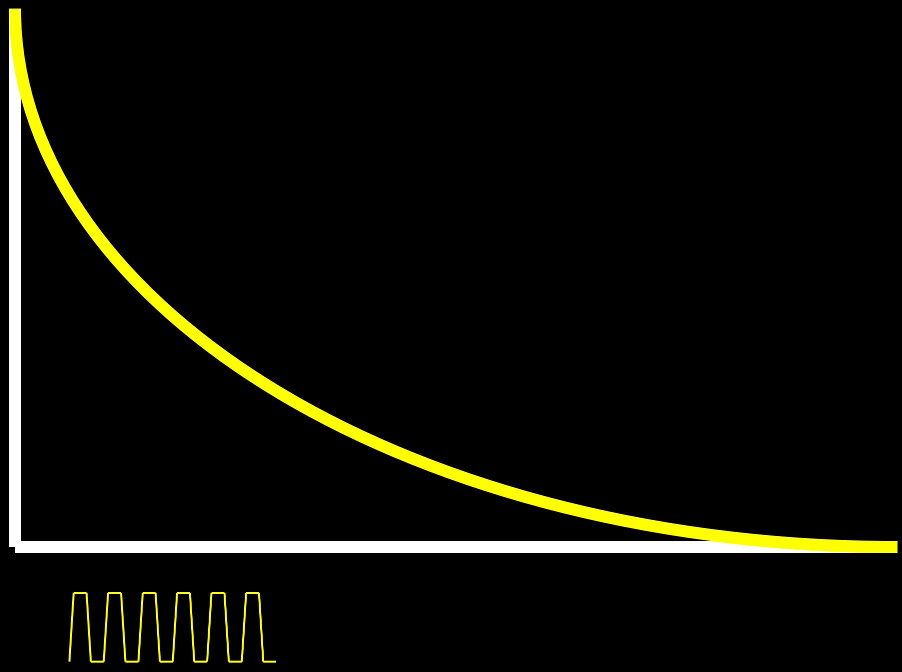
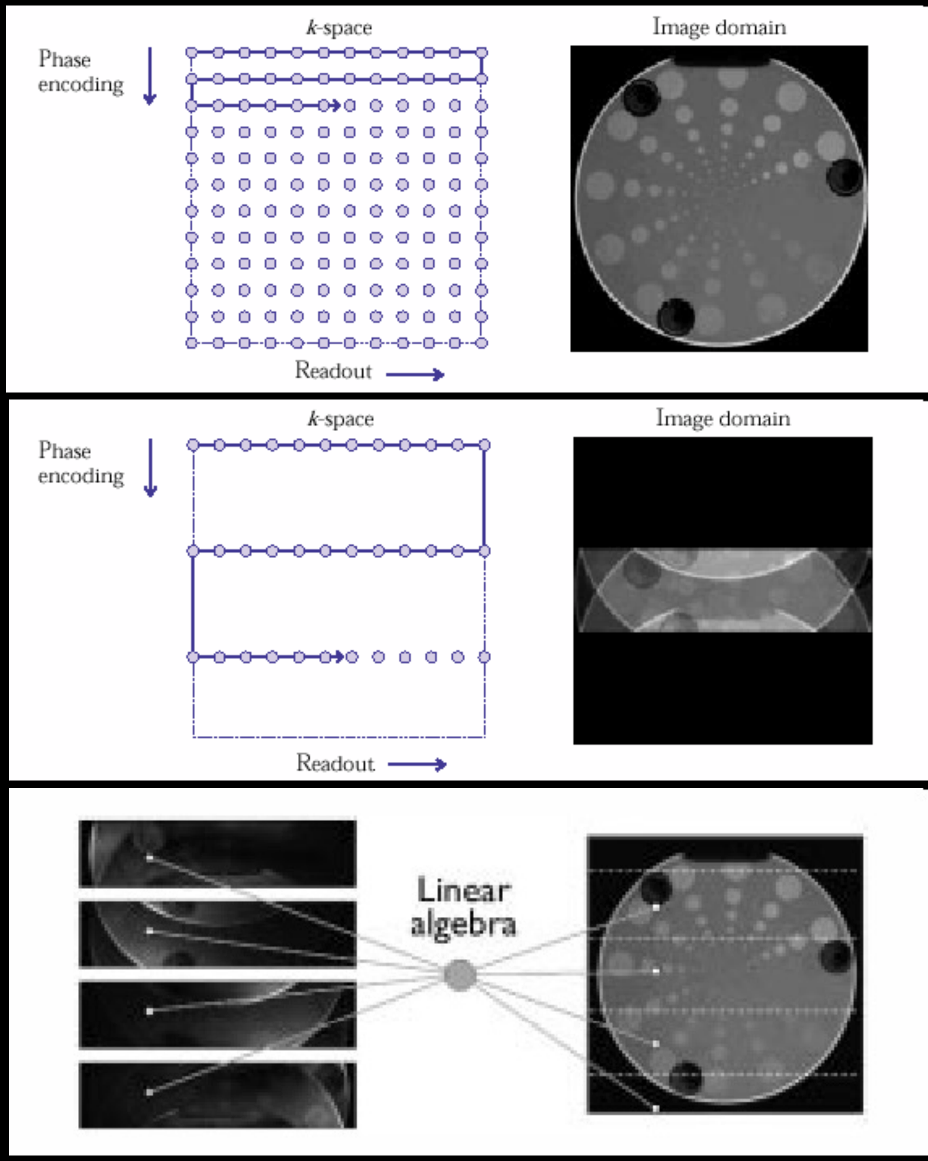
SENSE Imaging





≈ 5 to 30 ms

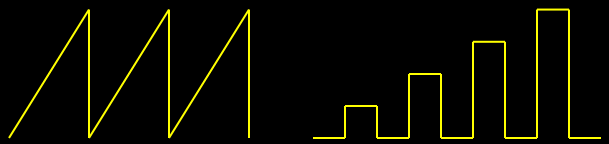
Pruessmann, et al.

- Functional contrast
- Signal interpretation
- Hardware and pulse sequences
- Paradigm design and processing

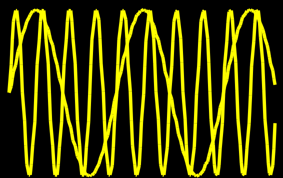
- Overview
- Current Limits
- Future Prospects

Neuronal Activation Input Strategies

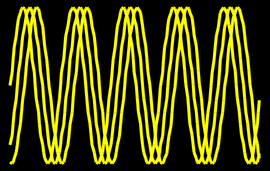
1. Block Design
2. Parametric Design



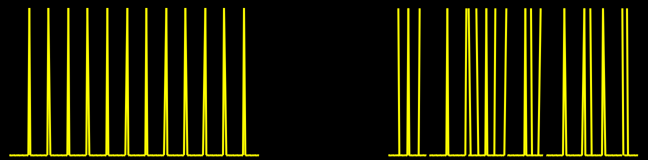
3. Frequency Encoding



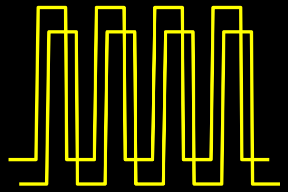
4. Phase Encoding



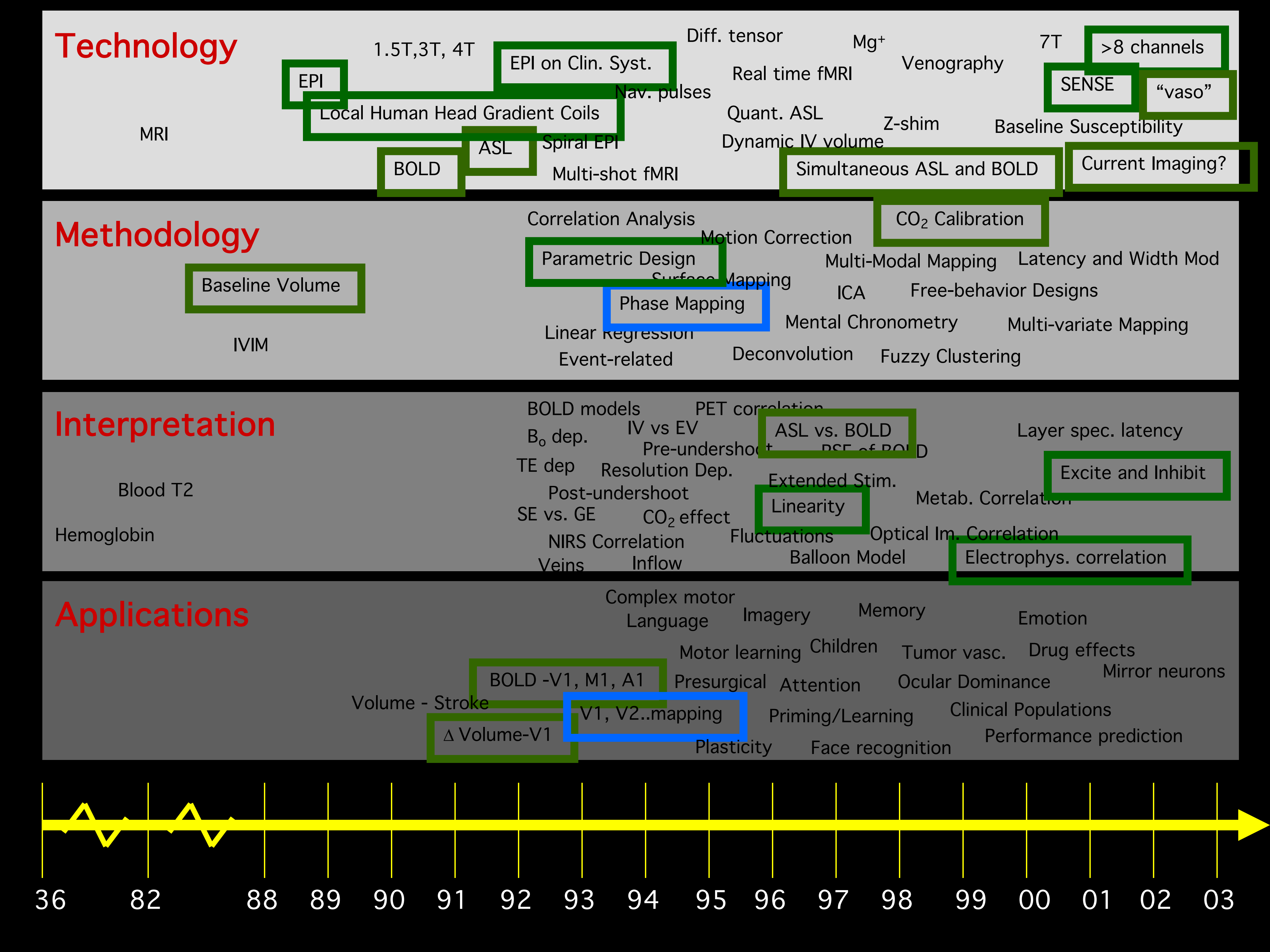
5. Event Related



6. Orthogonal Design



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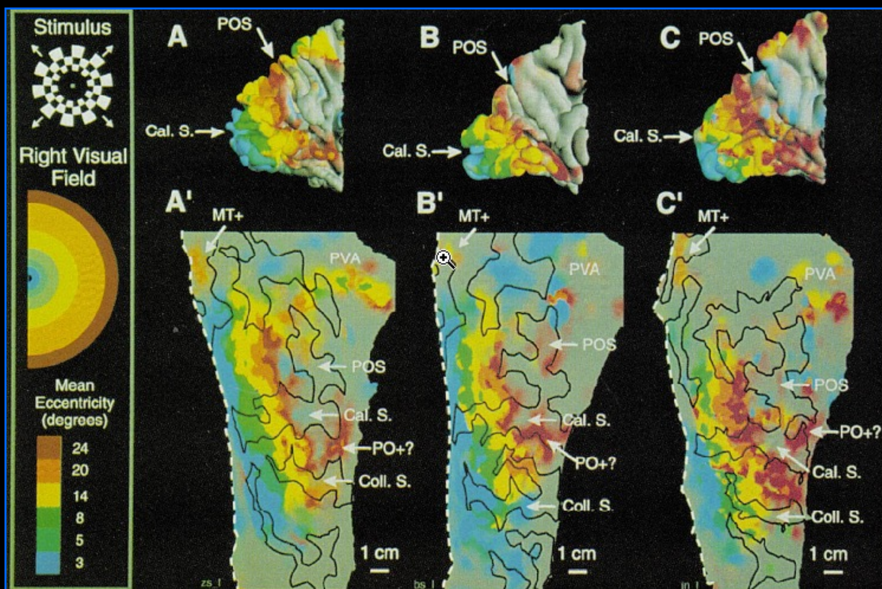
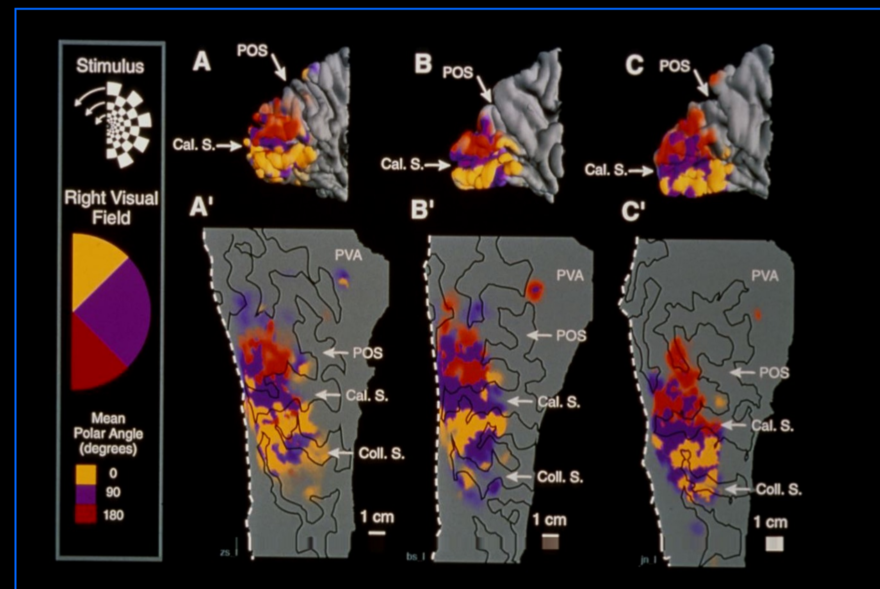
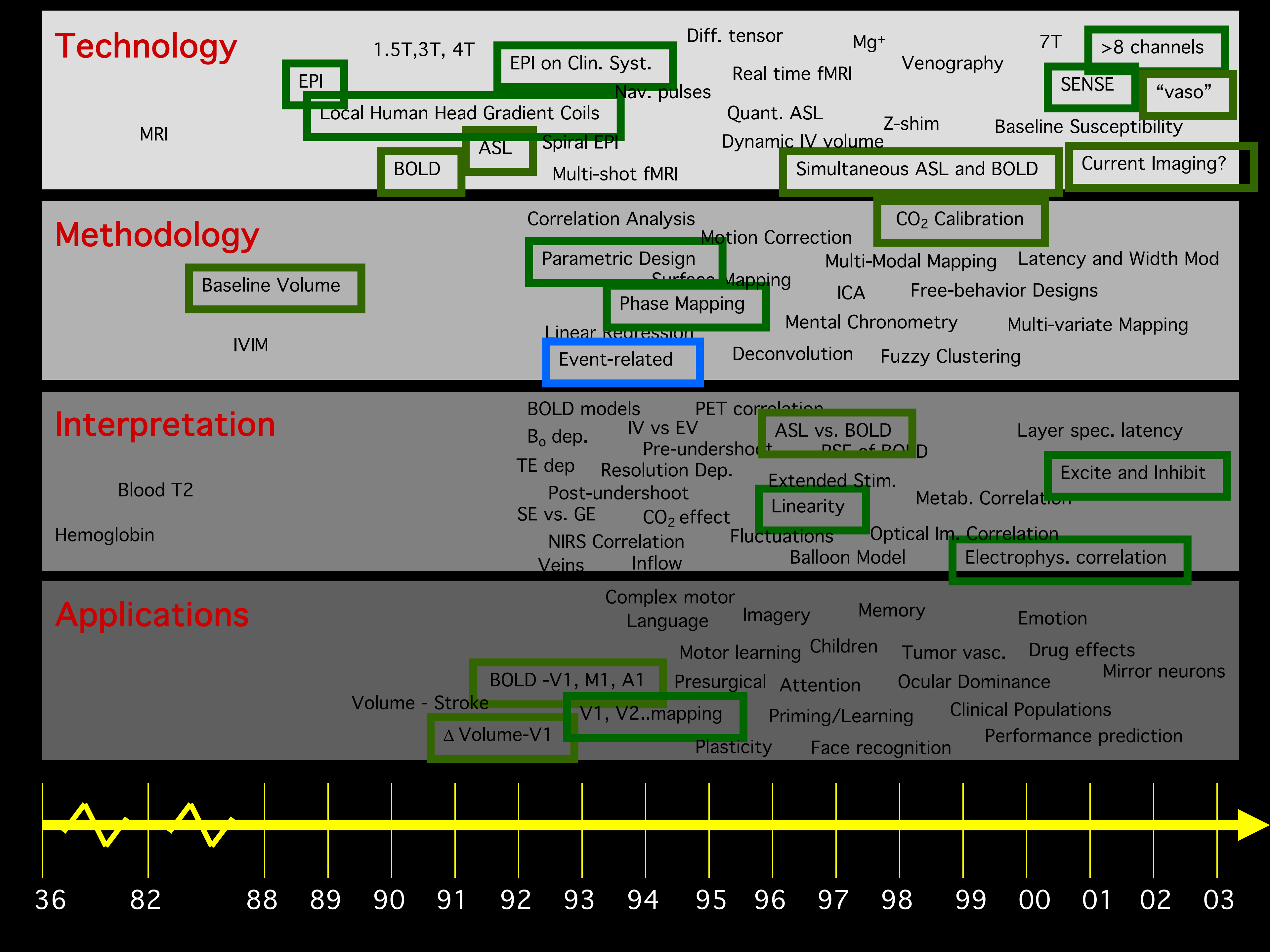
Proc. Natl. Acad. Sci. USA
Vol. 93, pp. 2382–2386, March 1996
Neurobiology

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*



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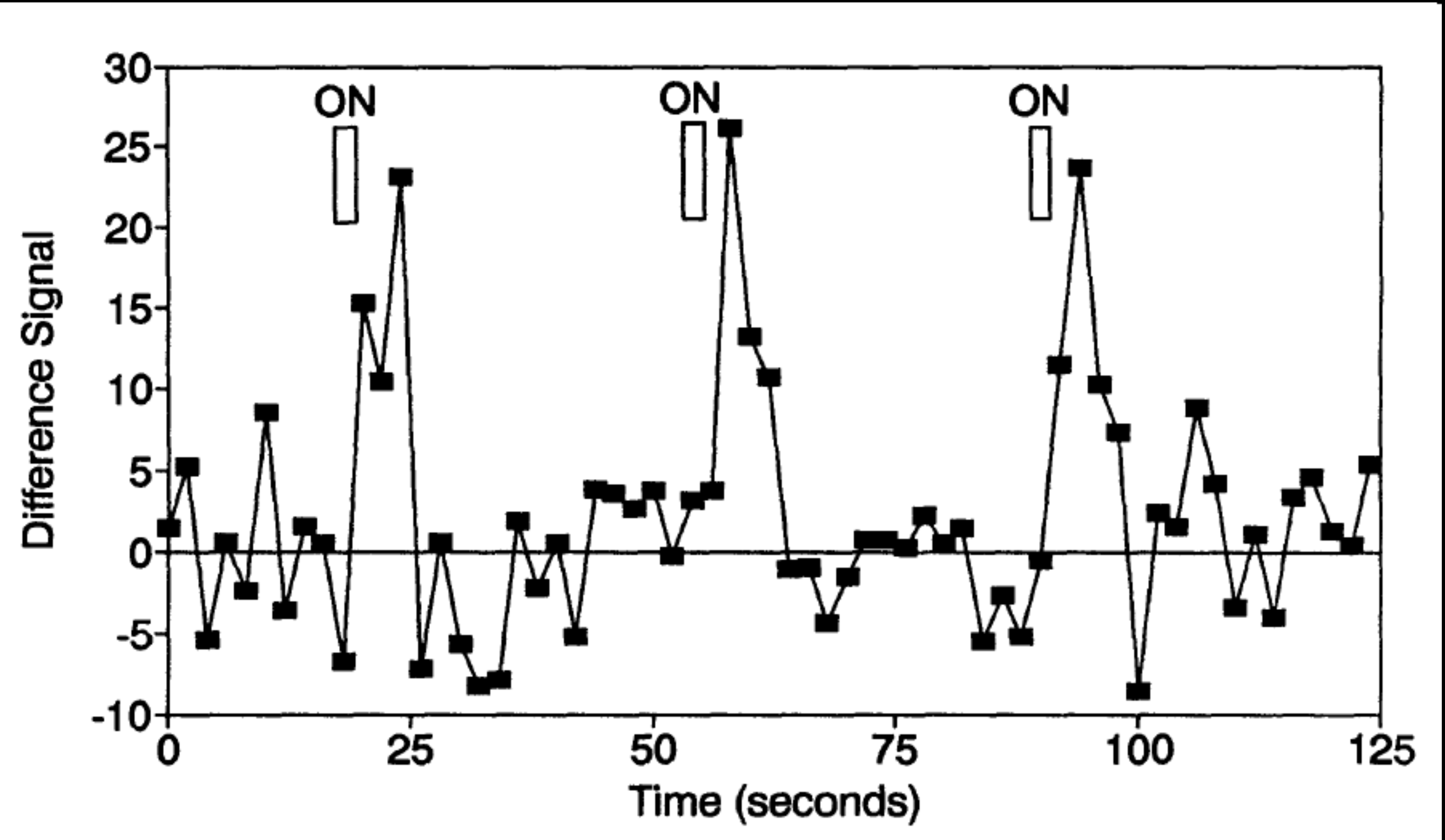
First Event-related fMRI Results



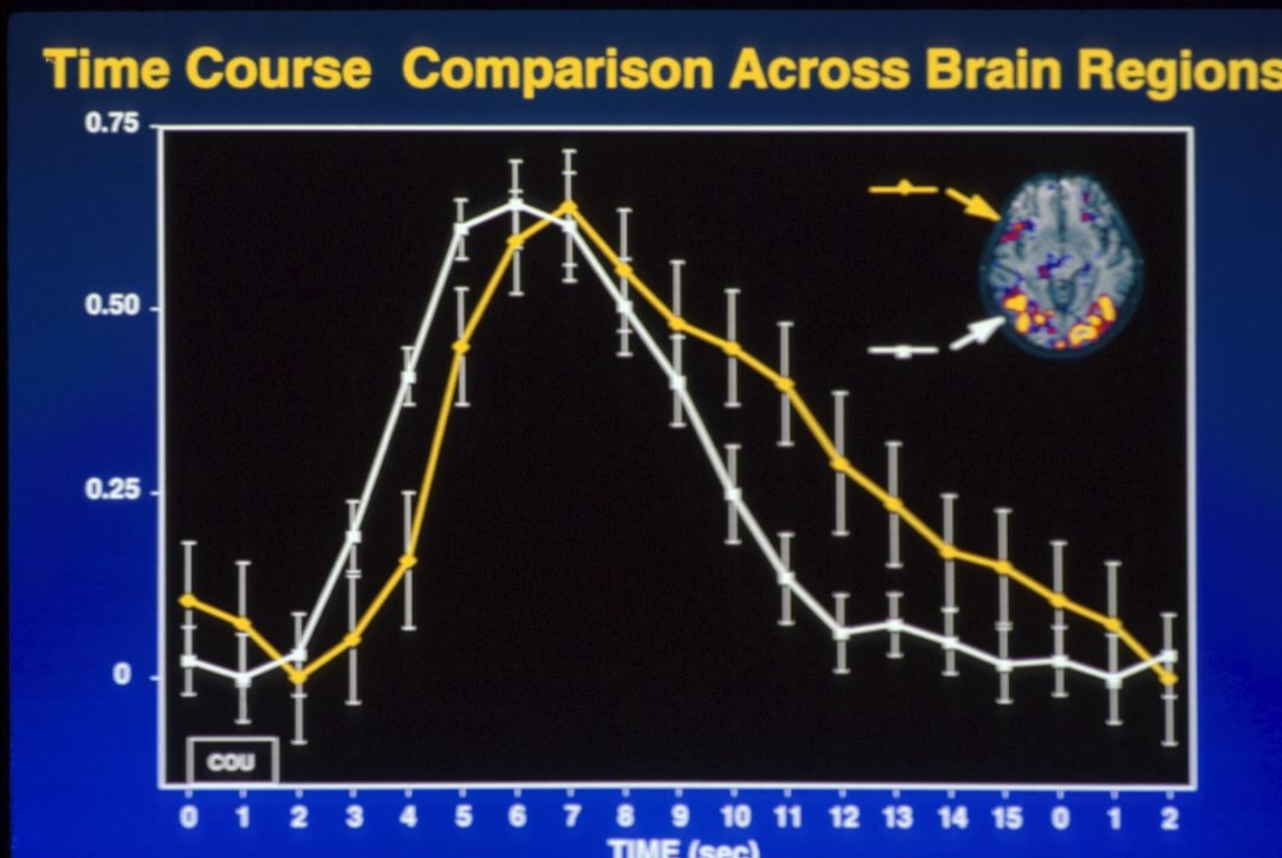
Blamire, A. M., et al. (1992). "Dynamic mapping of the human visual cortex by high-speed magnetic resonance imaging." Proc. Natl. Acad. Sci. USA 89: 11069-11073.

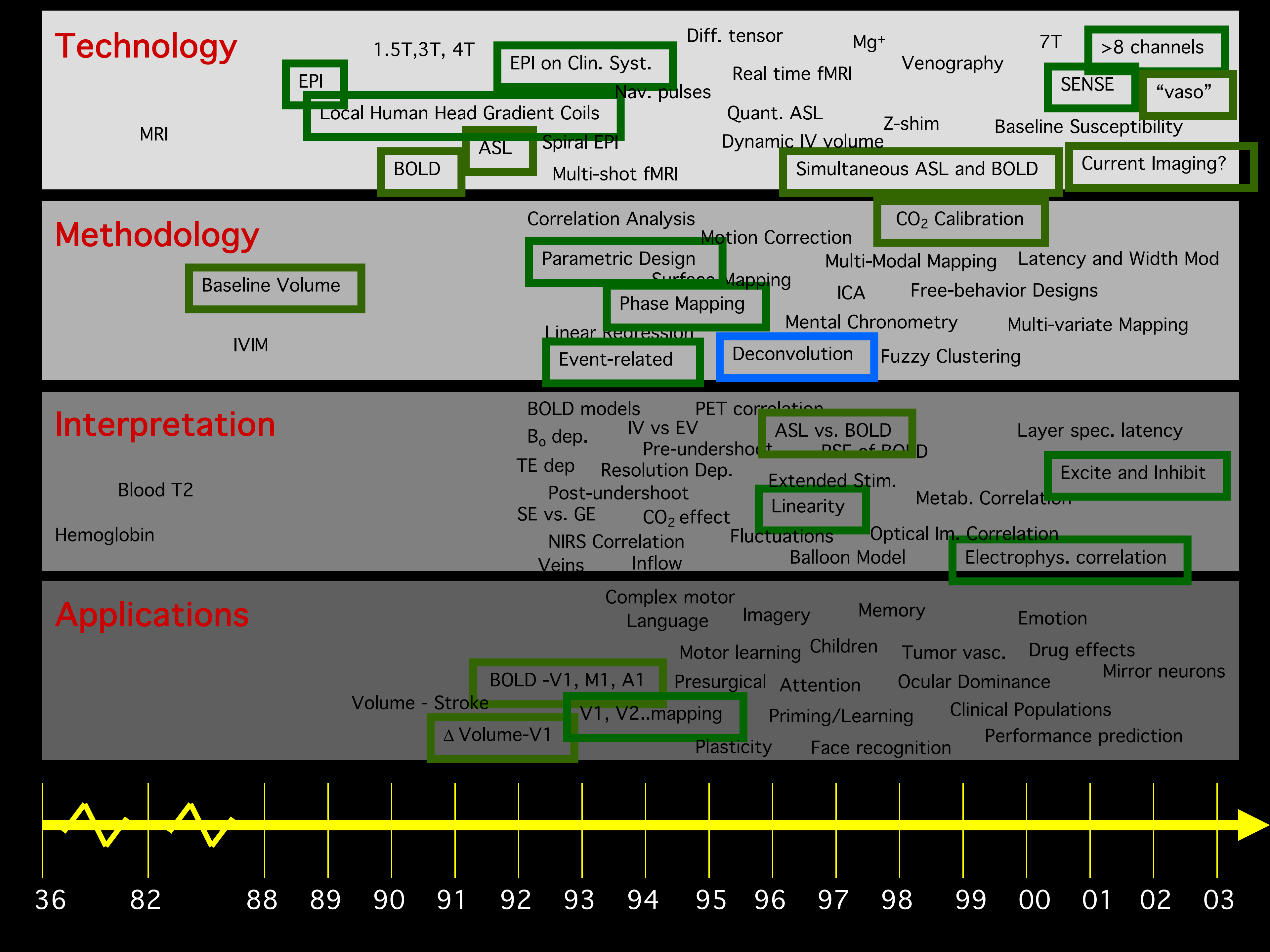
Proc. Natl. Acad. Sci. USA
Vol. 93, pp. 14878–14883, December 1996
Neurobiology

Detection of cortical activation during averaged single trials of a cognitive task using functional magnetic resonance imaging

(neuroimaging/single trial/language/prefrontal)

RANDY L. BUCKNER[†‡§¶], PETER A. BANDETTINI[†‡], KATHLEEN M. O'CRAVEN[†‖], ROBERT L. SAVOY[†‖], STEVEN E. PETERSEN[**††], MARCUS E. RAICHLE[§**††], AND BRUCE R. ROSEN[†‡]





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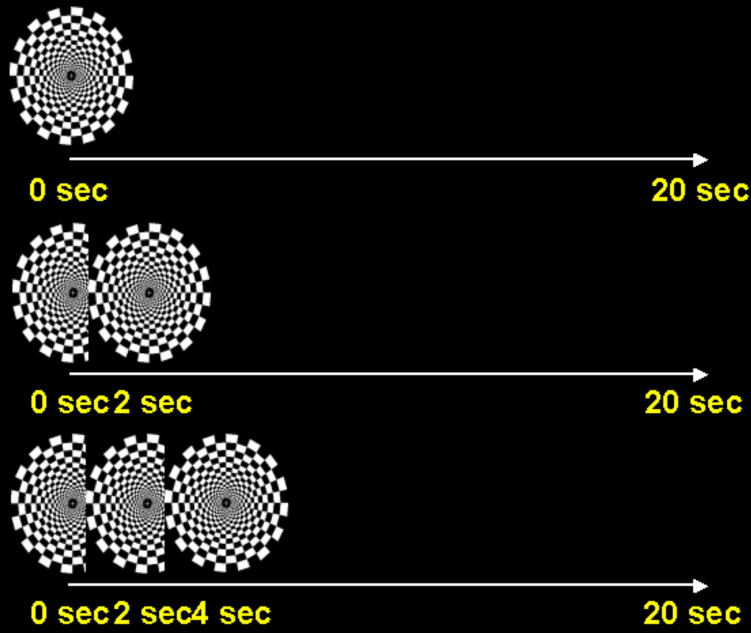
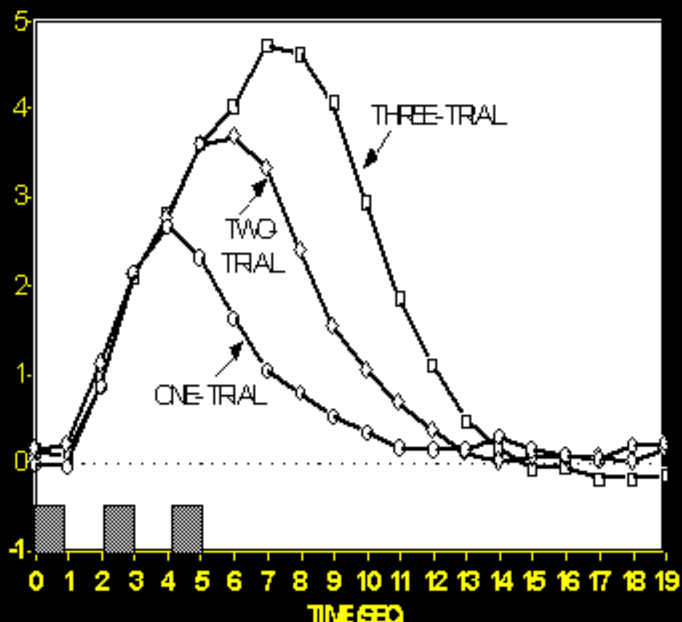



• Human Brain Mapping 5:329–340(1997) •

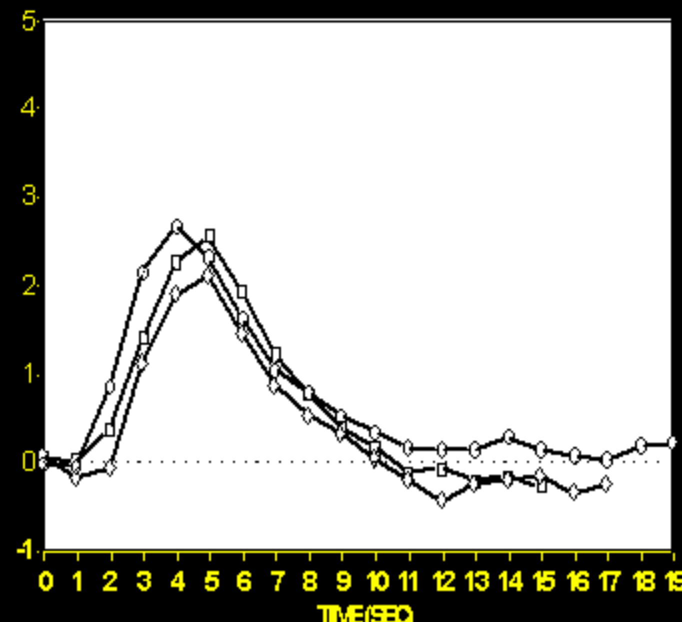
Selective Averaging of Rapidly Presented Individual Trials Using fMRI

Anders M. Dale* and Randy L. Buckner

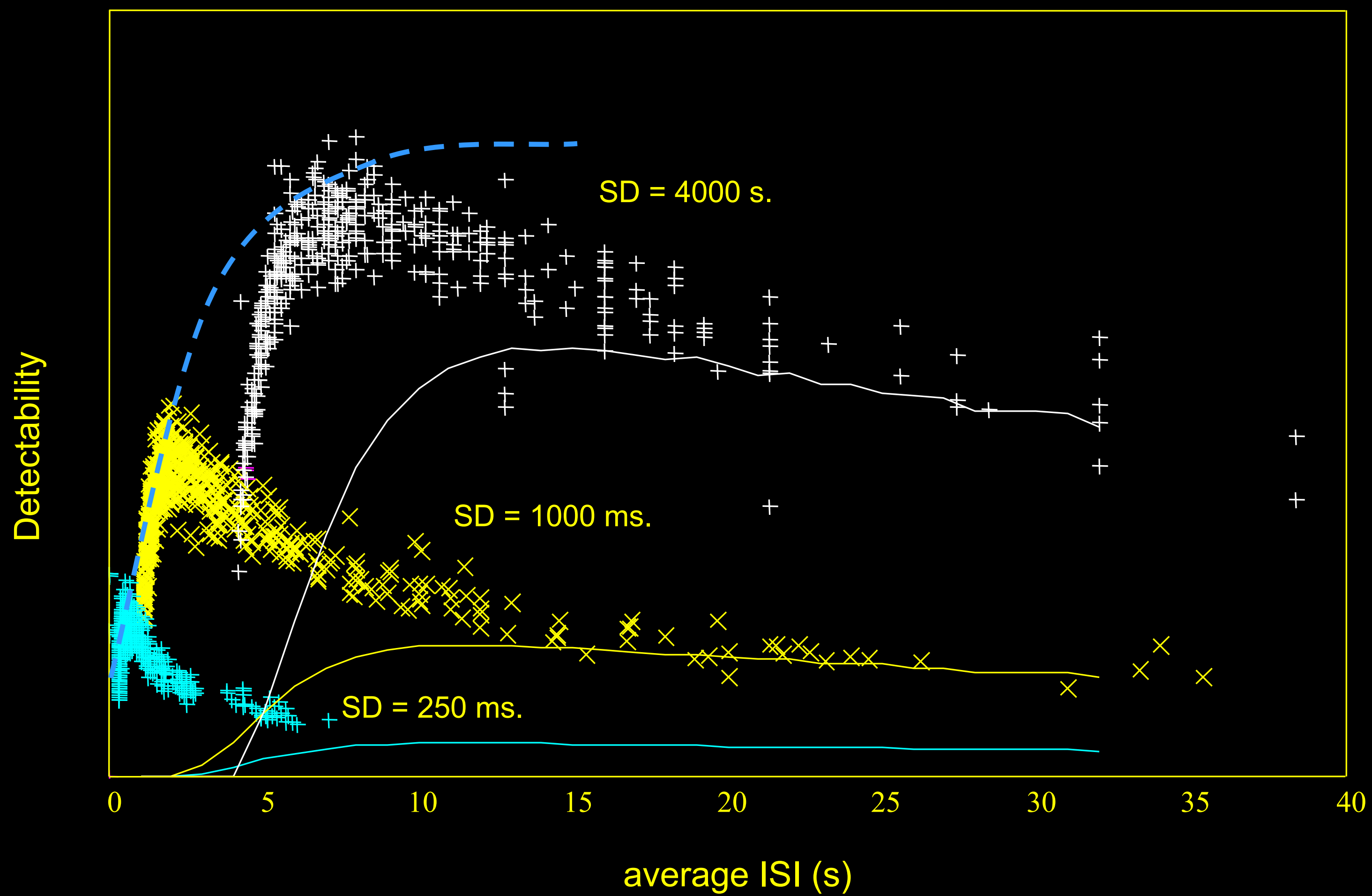
RAW DATA



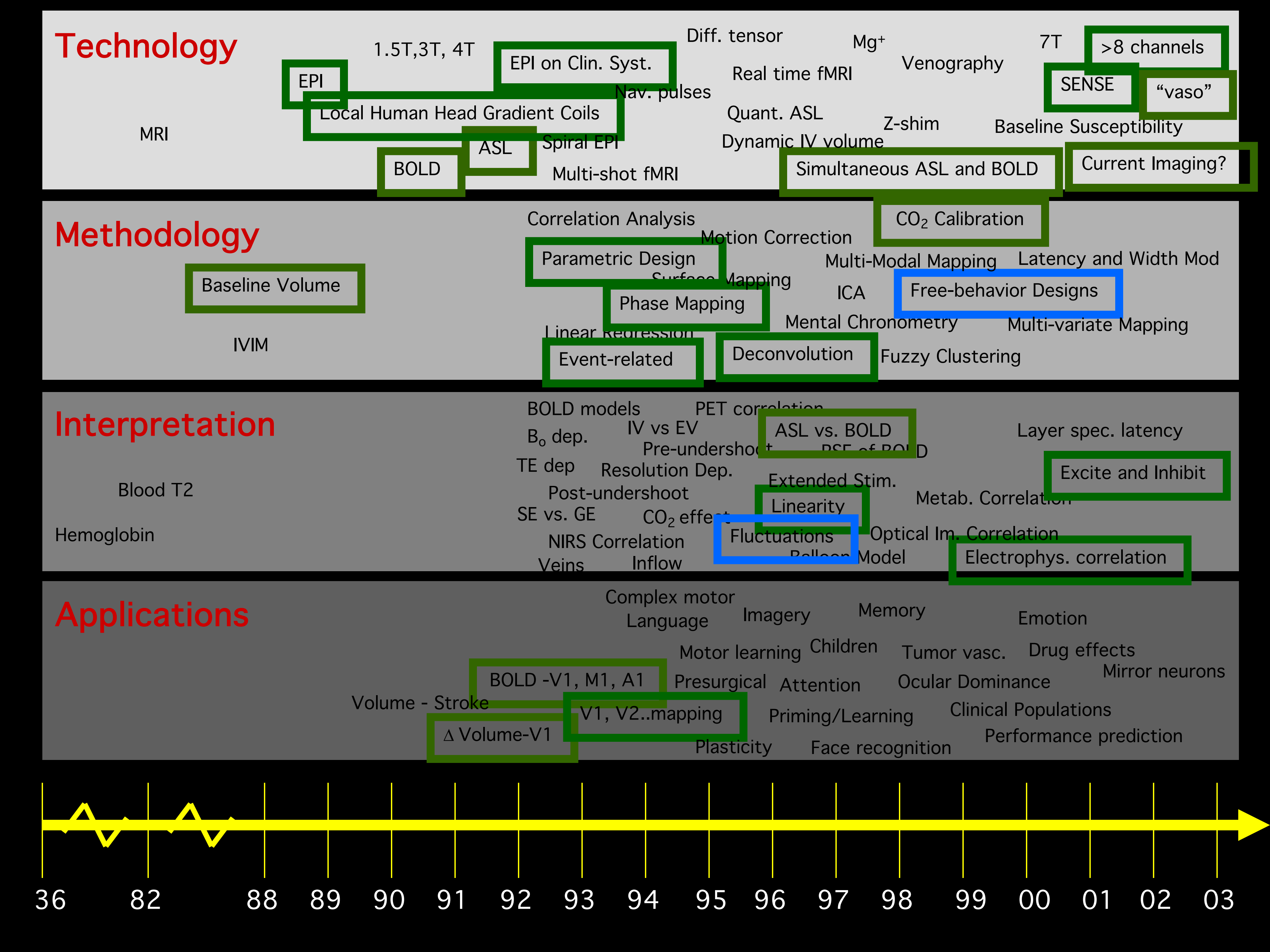
ESTIMATED RESPONSES



Detectability vs. Average ISI



R. M. Birn, R. W. Cox, P. A. Bandettini, Detection versus estimation in Event-Related fMRI: choosing the optimal stimulus timing. *NeuroImage* 15: 262-264, (2002).



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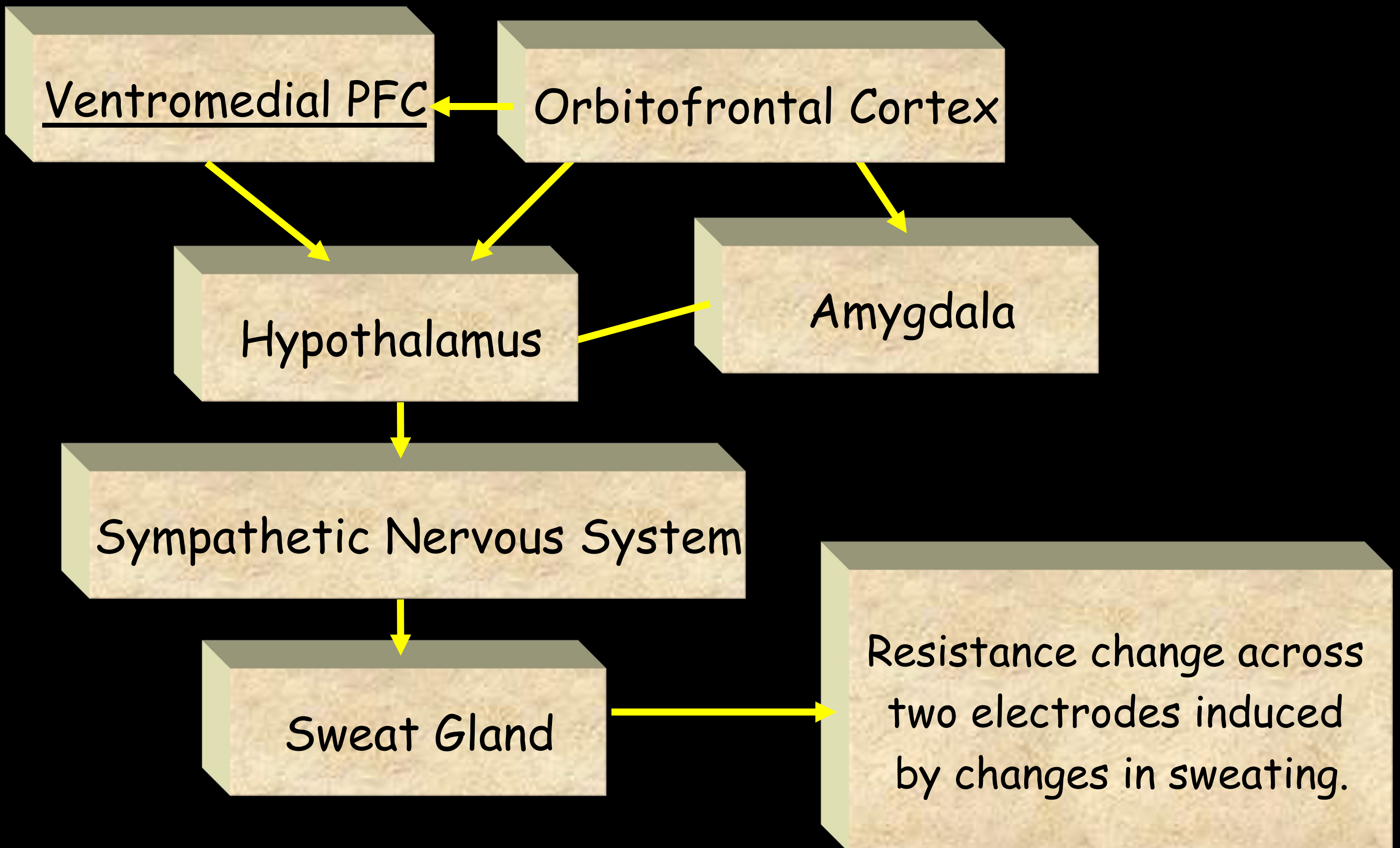
Free Behavior Design

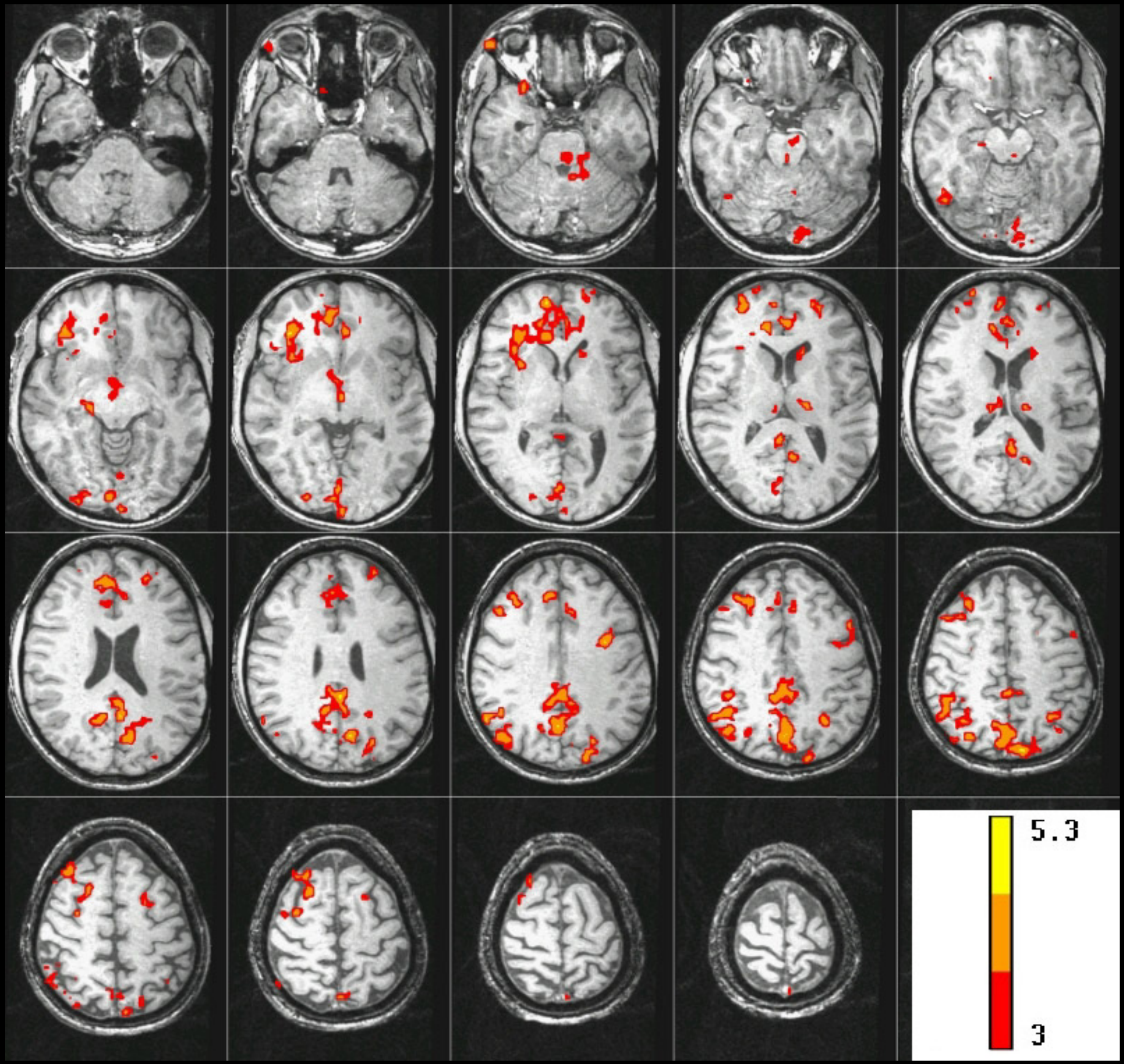
Use a continuous measure as a reference function:

- 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).*

Simultaneous EEG and fMRI of the alpha rhythm

Robin I. Goldman,[2,CA] John M. Stern,[1] Jerome Engel Jr[1] and Mark S. Cohen

Ahmanson-Lovelace Brain Mapping Center, UCLA, 660 Charles Young Drive South, Los Angeles, CA 90095; [1]Department of Neurology, UCLA School of Medicine, Los Angeles, CA; [2]Hatch Center for MR Research, Columbia University, HSD, 710 W. 168th St., NIB-1, Mailbox 48, NY, NY 10032, USA

[CA,2]Corresponding Author and Address: rg2146@columbia.edu

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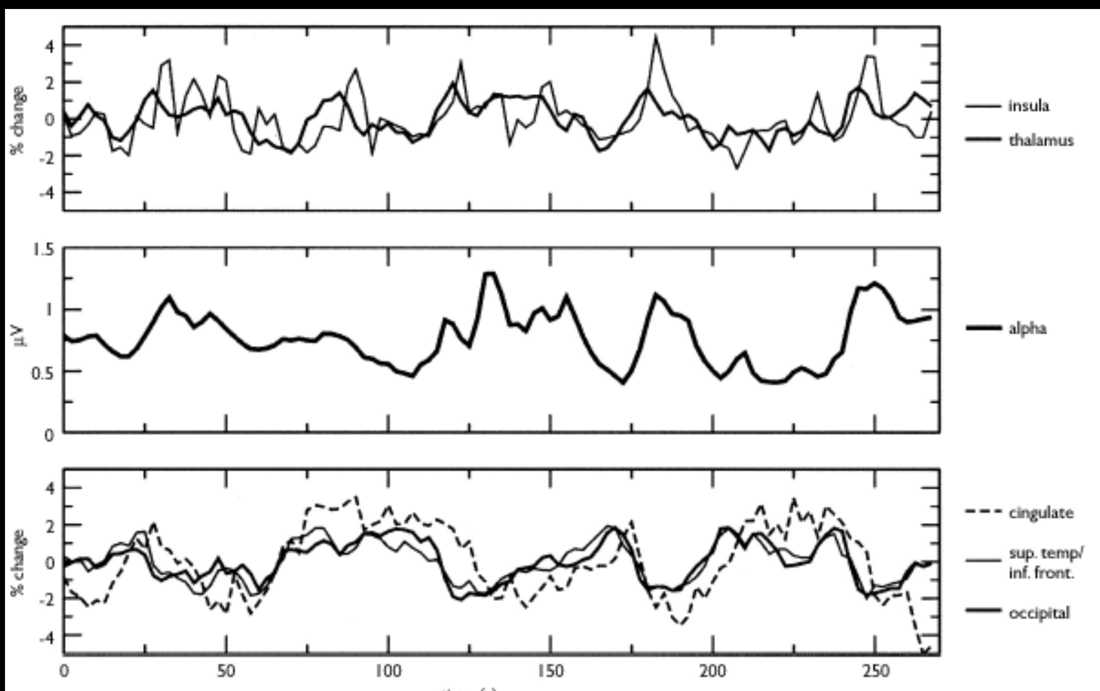
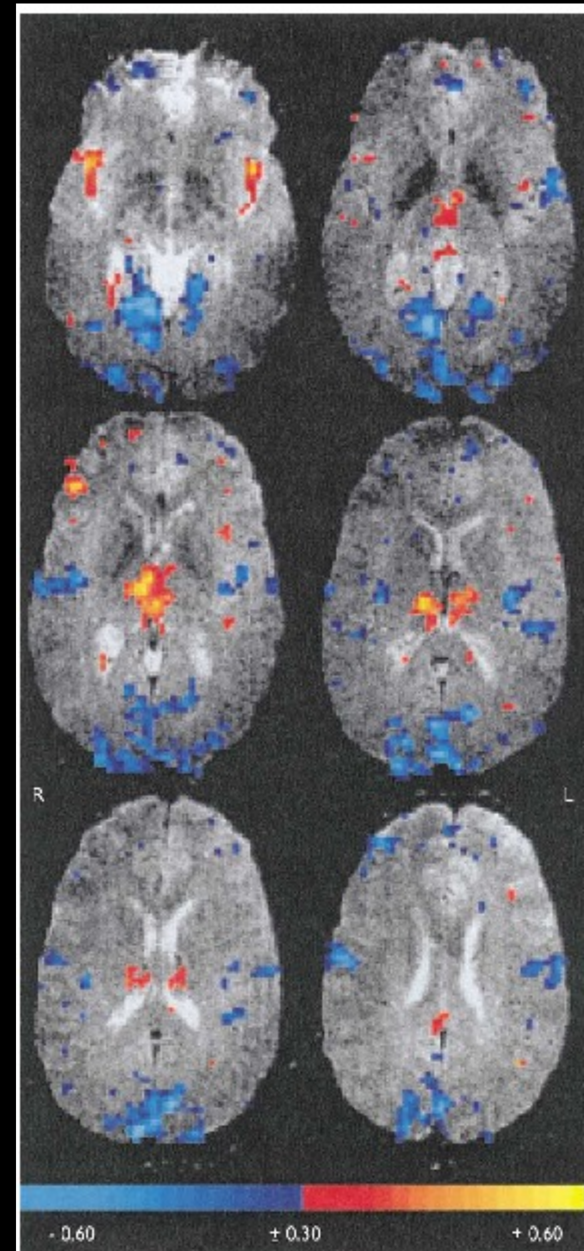
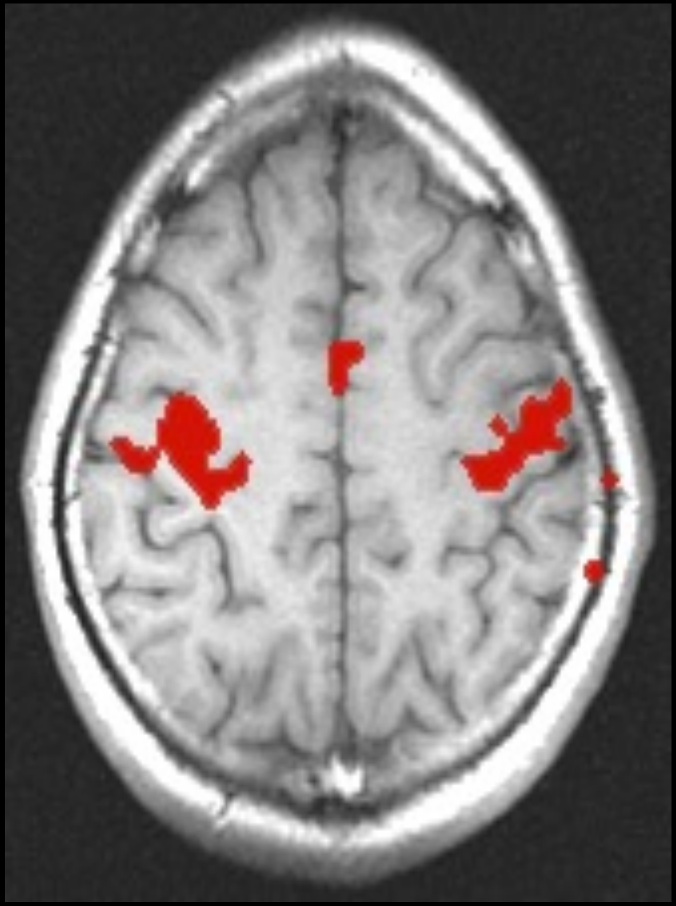
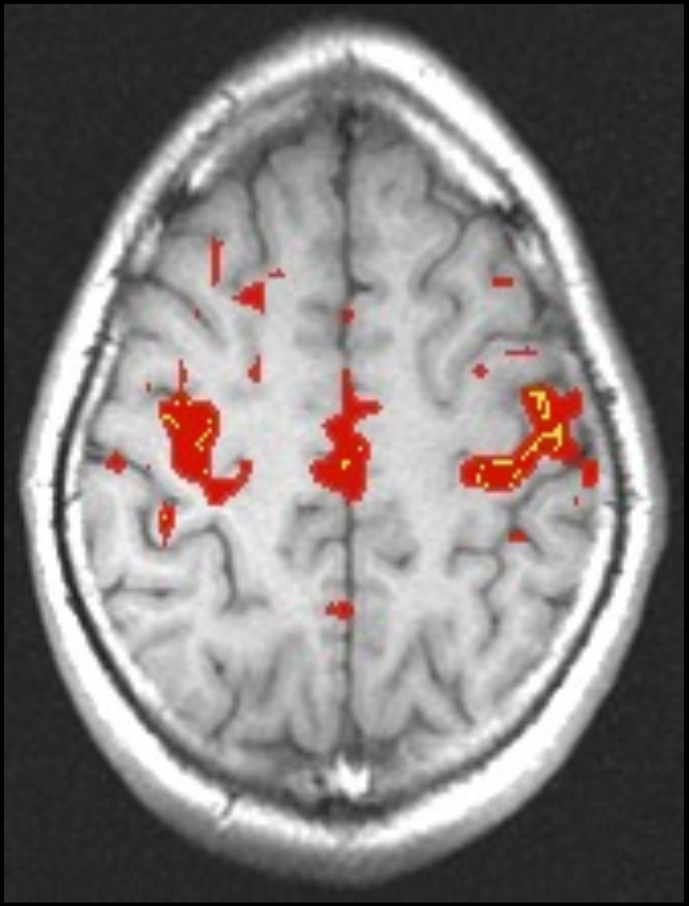


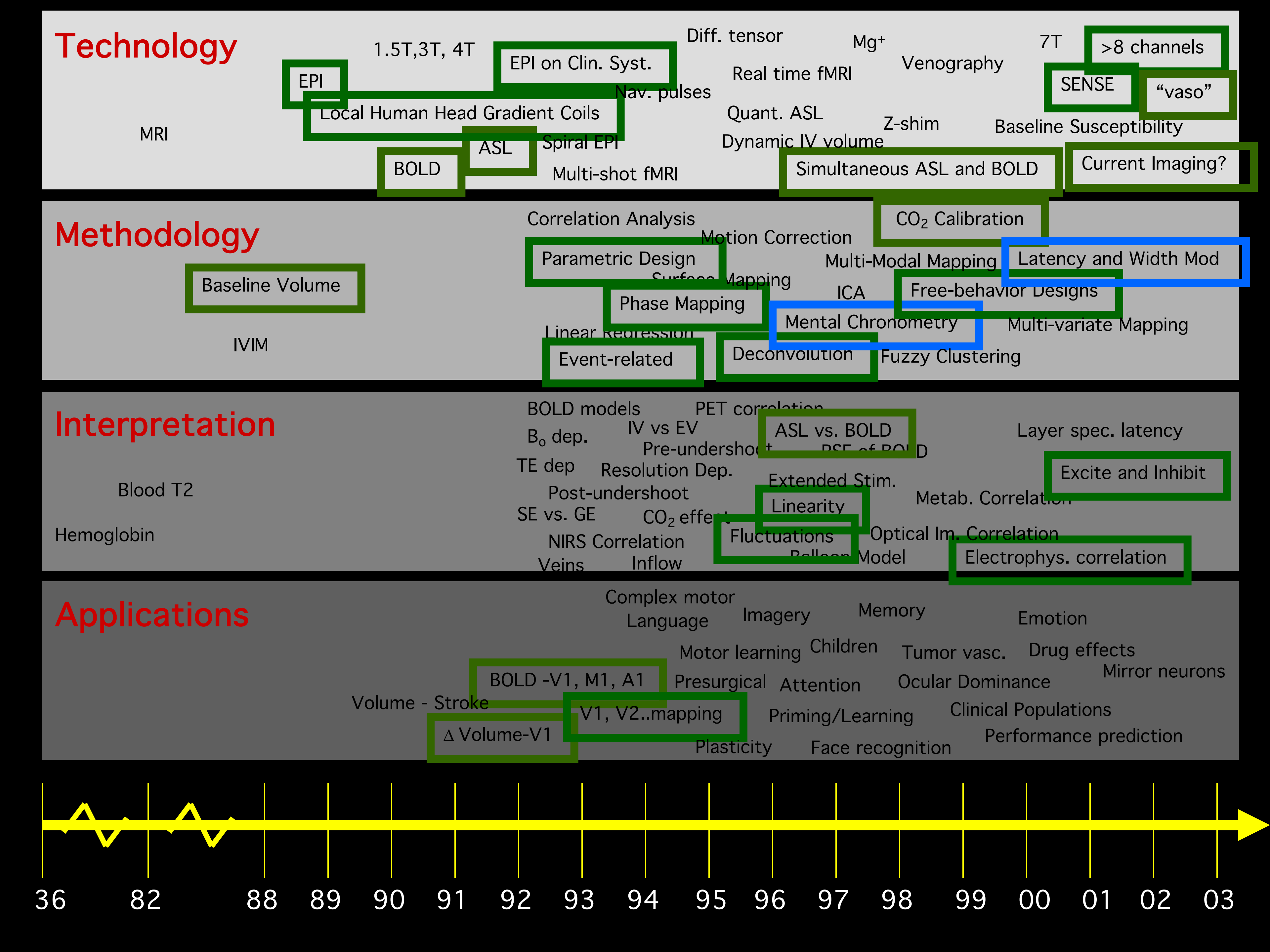


Resting State Fluctuations





B. Biswal *et al*., MRM, 34:537 (1995)



Technology
MRI
EPI
1.5T,3T, 4T
EPI on Clin. Syst.
Local Human Head Gradient Coils
Nav. pulses
BOLD
ASL
Spiral EPI
Multi-shot fMRI
Diff. tensor
Real time fMRI
Quant. ASL
Dynamic IV volume
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Venography
Z-shim
Simultaneous ASL and BOLD
7T
>8 channels
SENSE
“vaso”
Baseline Susceptibility
Current Imaging?
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Baseline Volume
IVIM
Correlation Analysis
Parametric Design
Motion Correction
Surface Mapping
Phase Mapping
Linear Regression
Event-related
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CO_2 Calibration
Multi-Modal Mapping
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Latency and Width Mod
Free-behavior Designs
Mental Chronometry
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B_o dep.
IV vs EV
TE dep
Resolution Dep.
Pre-undershoot
Post-undershoot
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△ Volume-V1
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Emotion
Drug effects
Mirror neurons
Performance prediction
36
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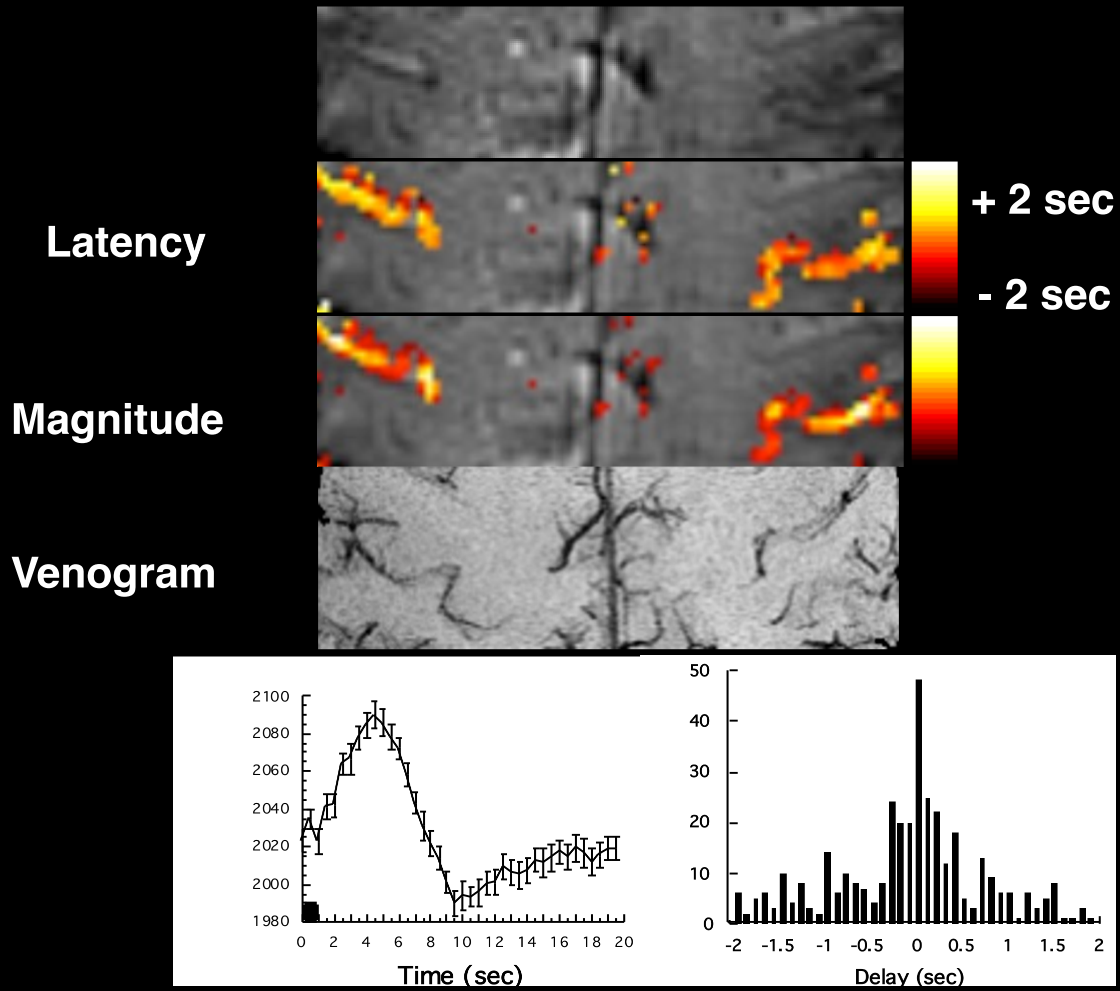
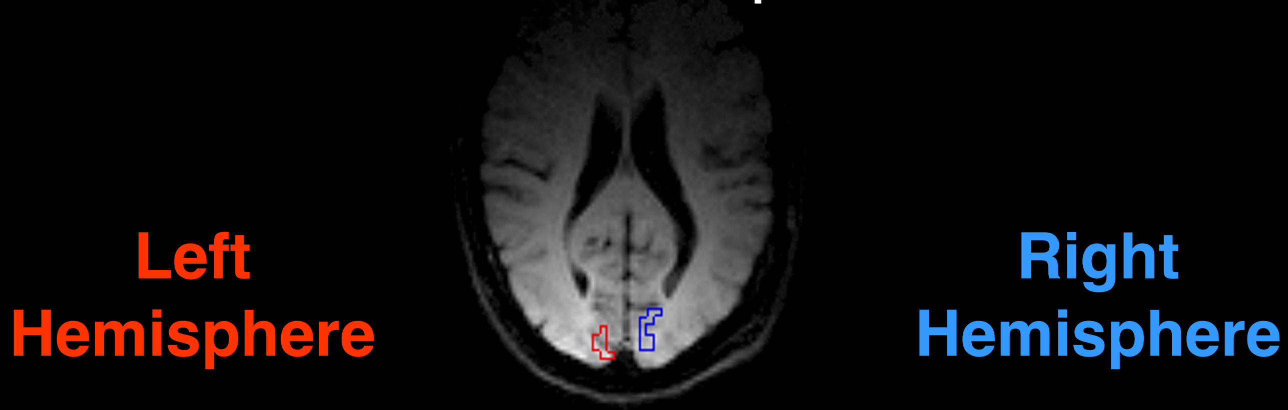
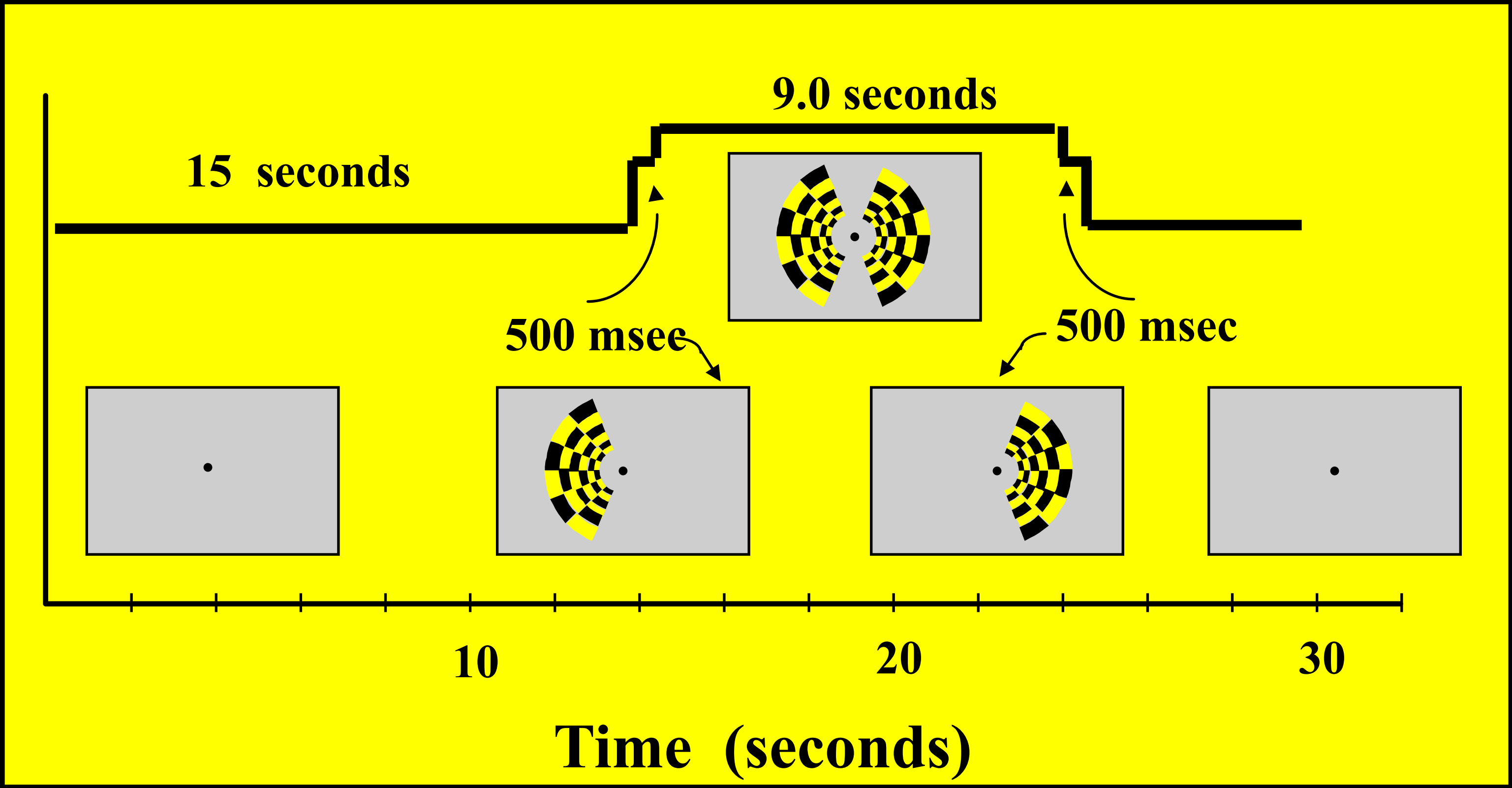
Latency and Width

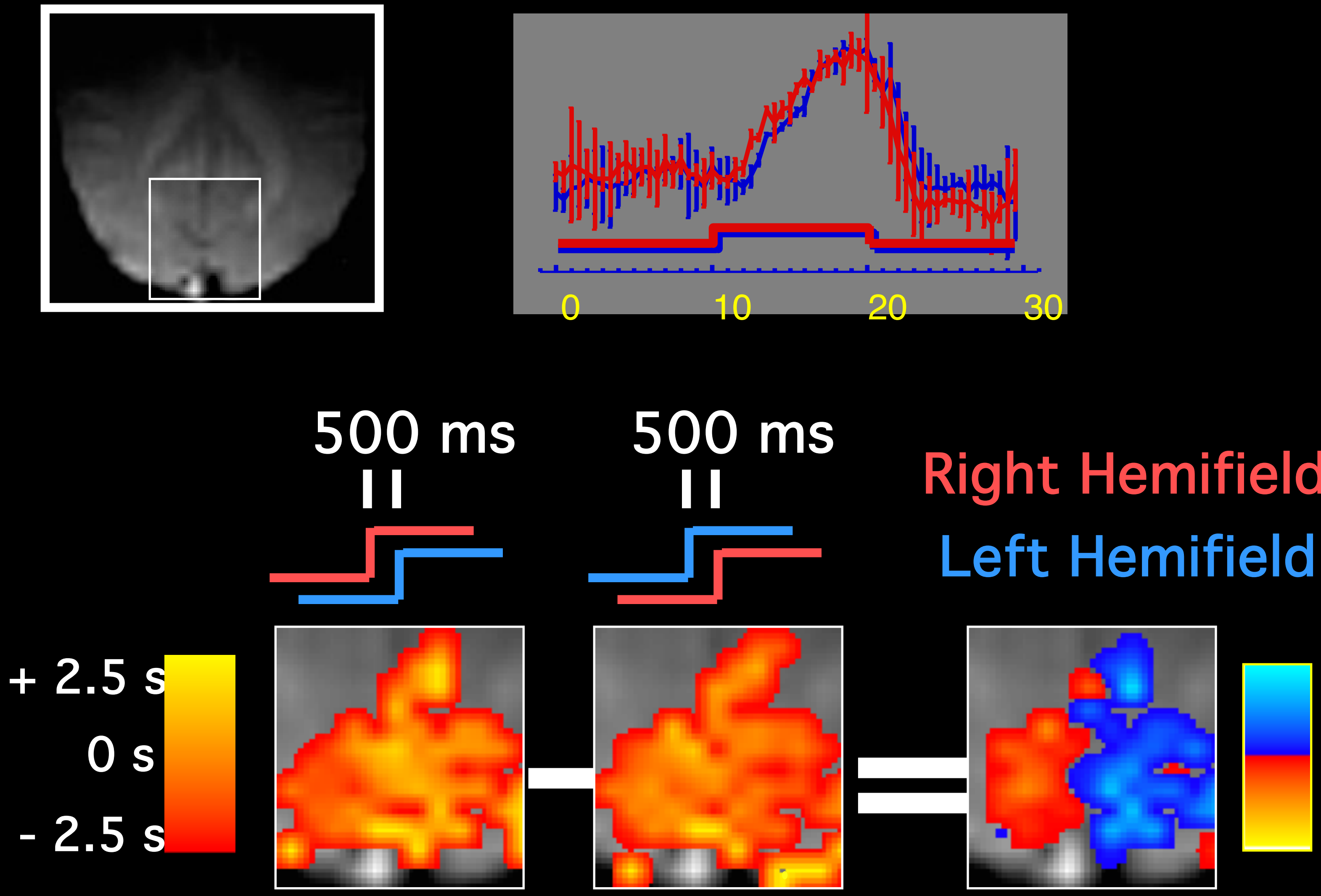


Hemi-Field Experiment





Timing Modulation (calibration)



Understanding neural system dynamics through task modulation and measurement of functional MRI amplitude, latency, and width

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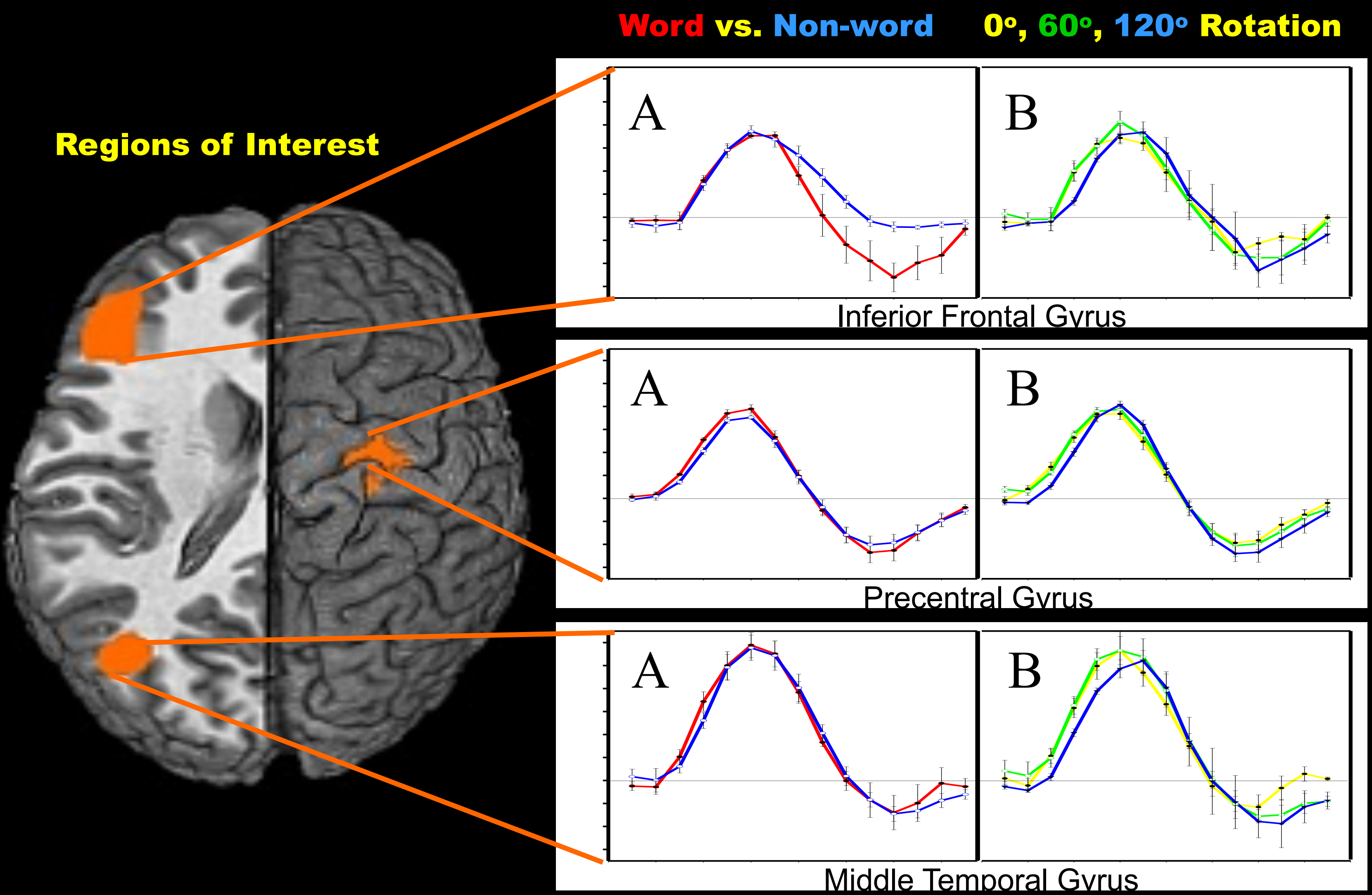
Proc. Nat'l. Acad. Sci. USA **100**, 1415-1419 (2003).

Lexical Delay

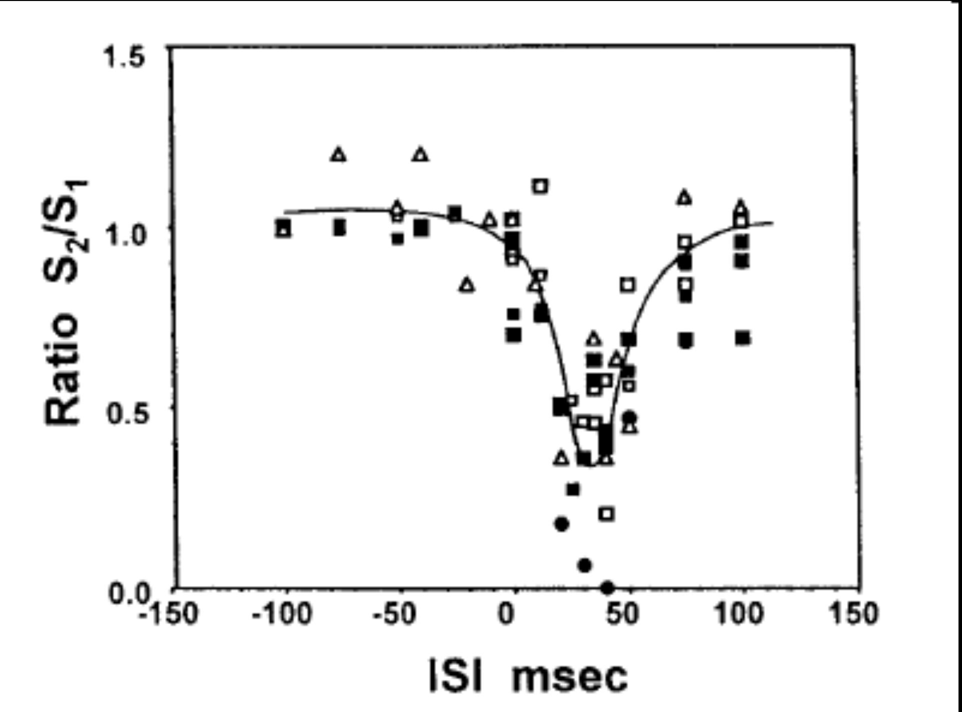
Rotational Delay	Words	Non-Words	Mean Reaction Time
0^0	smudge	dierts	823 ms
60^0	frolic	cuhlos	891 ms
120^0	slouch	gedmus	1446 ms
Mean Reaction Time	986 ms	1219 ms	



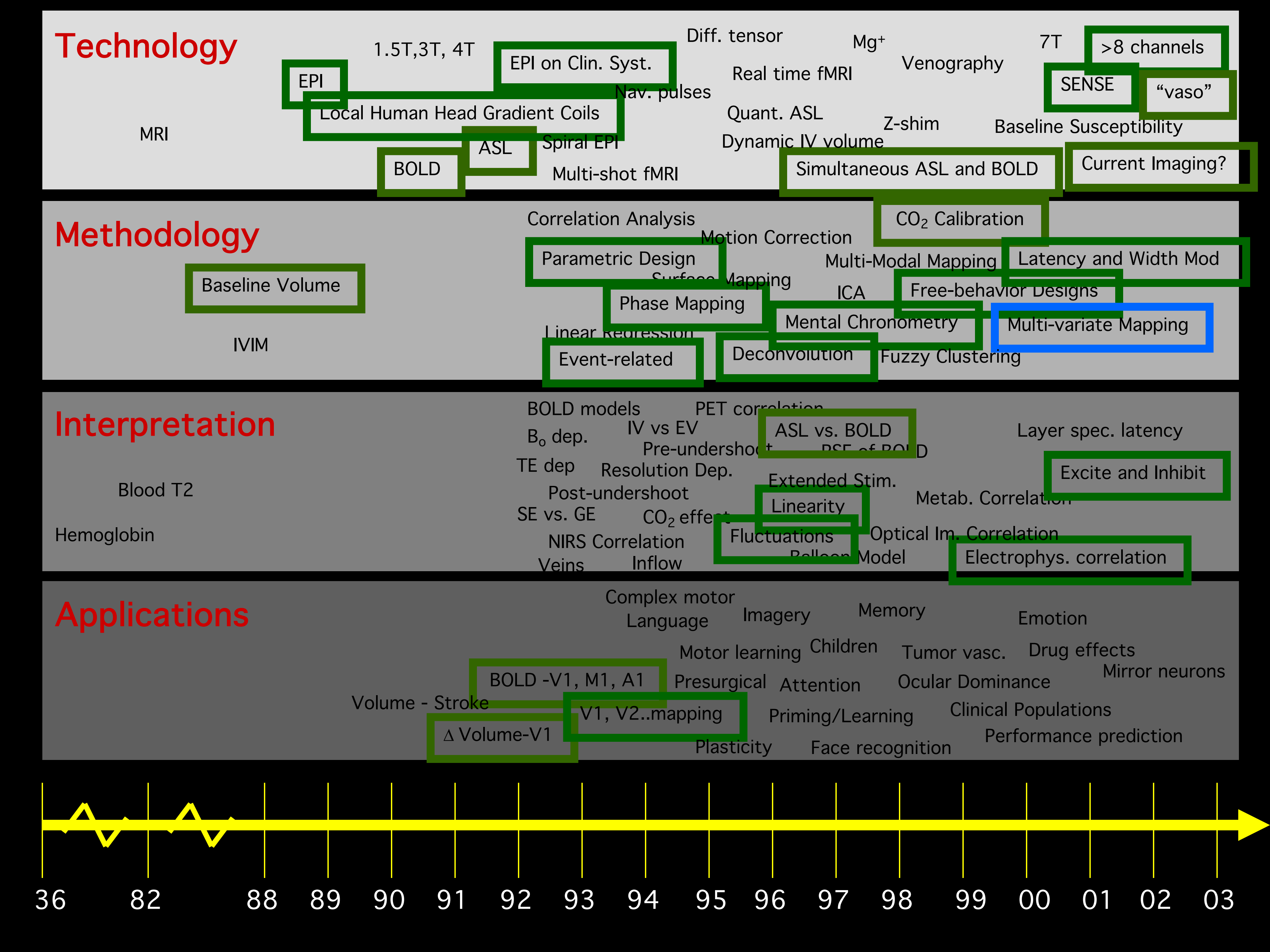
Word vs. Non-word
0º, 60º, 120º Rotation
Regions of Interest
A
B
Inferior Frontal Gyrus
A
B
Precentral Gyrus
A
B
Middle Temporal Gyrus

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[§]



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



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Functional magnetic resonance imaging (fMRI) "brain reading": detecting and classifying distributed patterns of fMRI activity in human visual cortex

David D. Cox[a,b,*] and Robert L. Savoy[a,b,c]

[a] Rowland Institute for Science, Cambridge, MA 02142, USA
[b] Athinoula A. Martinos Center for Structural and Functional Biomedical Imaging, Charlestown, MA 02129, USA
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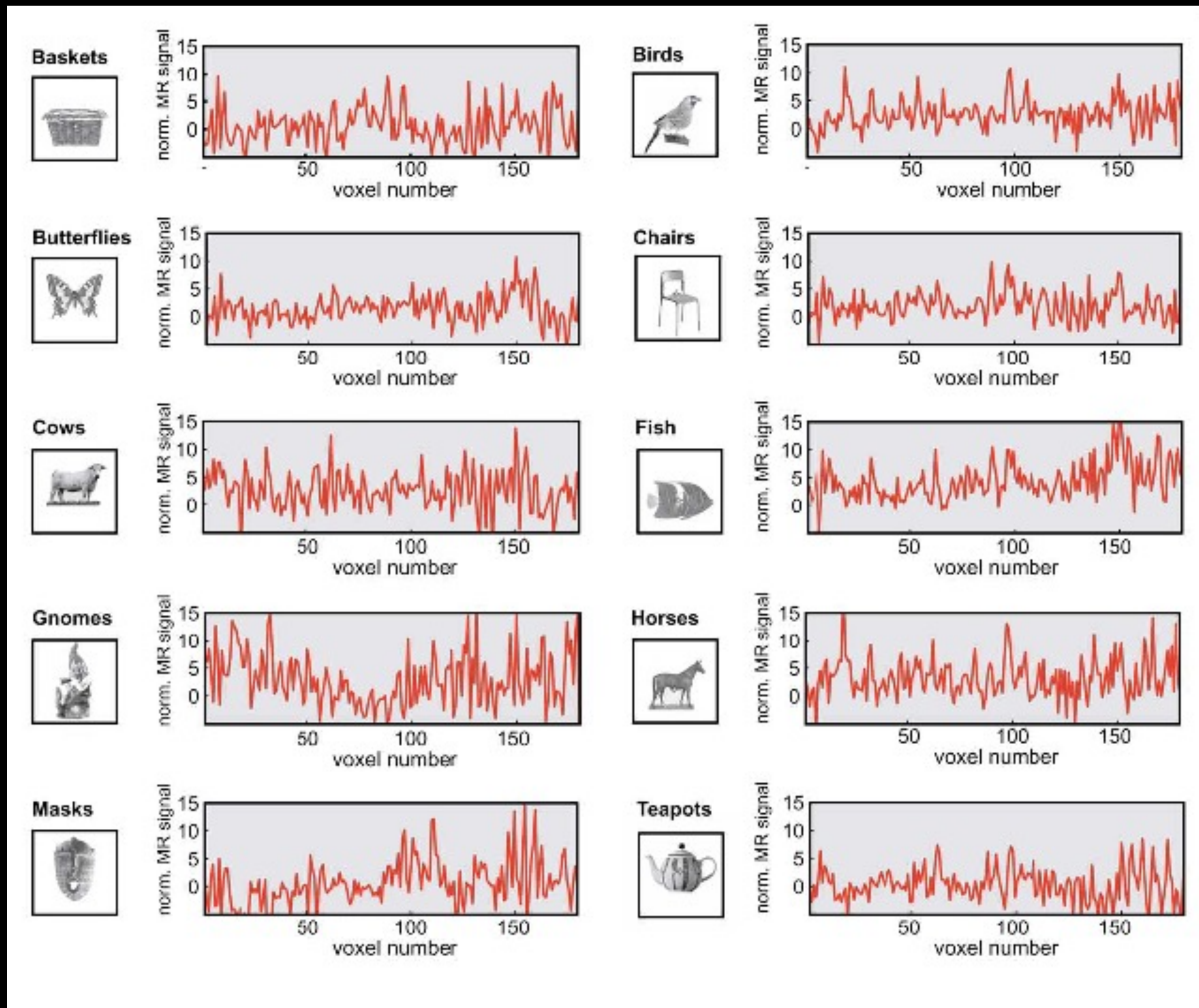

The Future

Sensitivity
Resolution
Calibration
Integration
Correlation

FIM Unit & FMRI Core Facility

Director:
Peter Bandettini

Staff Scientists:
Sean Marrett
Jerzy Bodurka
Frank Ye
Wen-Ming Luh

Computer Specialist:
Adam Thomas

Post Docs:
Rasmus Birn
Hauke Heekeren
David Knight
Anthony Boemio
Patrick Bellgowan
Ziad Saad

Graduate Student:
Natalia Petridou

Post-Back. IRTA Students:
Hanh Ngyun
Ilana Levy
Elisa Kapler
August Tuan
Dan Kelley

Visiting Fellows:
Sergio Casciaro
Marta Maieron
Guosheng Ding

Clinical Fellow:
James Patterson

Psychologist:
Julie Frost

Summer Students:
Allison Sanders
Julia Choi
Thomas Gallo
Jenna Gelfand
Hannah Chang
Courtney Kemps
Douglass Ruff
Carla Wettig
Kang-Xing Jin

Program Assistant:
Kay Kuhns

Scanning Technologists:
Karen Bove-Bettis
Paula Rowser
Alda Ottley