Functional MRI: Basics and Beyond

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Technology MRI	Diff. tens 1.5T,3T, 4T EPI on Clin. Syst. Real Nav. pulses Local Human Head Gradient Coils Quar ASL Spiral EPI Dynar BOLD Multi-shot fMRI	sor Mg ⁺ 7T >8 channels al time fMRI Venography Int. ASL Z-shim Baseline Susceptibility amic IV volume Simultaneous ASL and BOLD Current Imaging?
Methodology Baseline IVIM	Correlation Analysis Motion o Parametric Design Surface Mapp Phase Mapping Linear Regression Event-related Deco	CO ₂ Calibration Correction Latency and Width Mod Multi-Modal Mapping ping ICA Free-behavior Designs Mental Chronometry Multi-variate Mapping convolution Fuzzy Clustering
Interpretation Blood T2 Hemoglobin	BOLD models PET corr B _o dep. IV vs EV Pre-undershoo TE dep Resolution Dep. Post-undershoot SE vs. GE CO ₂ effect NIRS Correlation Fluct Veins Inflow	relation ASL vs. BOLD Dt PSF of BOLD Extended Stim. Linearity Ctuations Balloon Model Excite and Inhibit Excite and Inhibit
Applications	Complex motor Language Ima Motor lear BOLD -V1, M1, A1 Presurgical Volume - Stroke V1, V2mapping ∆ Volume-V1 Plasticity	hagery Memory Emotion rning Children Tumor vasc. Drug effects al Attention Ocular Dominance Mirror neurons Priming/Learning Clinical Populations ry Face recognition
86 82 <u>88</u>	89 90 91 92 93 94 95 9	96 97 98 99 00 01 02 03

FMRI Basics and Beyond

- Information Content
- Sensitivity
- Resolution
- Image quality
- Paradigm Design and Processing

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Contrast in Functional MRI

- Blood Volume (invasive)
 - Contrast agent injection and time series collection of T2* or T2 weighted images.
- BOLD
 - Time series collection of T2* or T2 weighted images.
- Perfusion
 - T1 weighting
 - Arterial spin labeling
- CMRO₂
 - BOLD and Perfusion w/
 - Normalization to global perfusion change with global stress.
- Blood Volume (noninvasive)
 - Time series collection with IV signal removed.

Blood Volume Imaging

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





Photic Stimulation

MRI Image showing activation of the Visual Cortex

From Belliveau, et al. Science Nov 1991

ISC - perfusion



Susceptibility Contrast

Susceptibility-Induced Field Distortion in the Vicinity of a Microvessel \perp to B₀.





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.

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



Local Signal Increase in T2 and T2* - weighted sequences

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.





The vascular response

Factors influencing [Deoxy-Hb] concentration



Courtesy of Arno Villringer

Time course of BOLD signal



Courtesy of Arno Villringer

Blood Perfusion Imaging

EPISTAR





FAIR



TI (ms)FAIREPISTAR200



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: $H_2^{15}O$





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.

Anatomy



BOLD



Perfusion



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.

T1 - weighted

Flow weighted





BOLD weighted

T1 and T2* weighted

Flow and BOLD weighted





P. A. Bandettini, E. C. Wong, Echo planar magnetic resonance imaging of human brain activation, *in* "Echo Planar Imaging: Theory, Technique, and Application" (F. Schmitt, M. Stehling, R. Turner, Eds.), p.493-530, Springer -Verlag, Berlin, 1997

Volume

BOLD

unique informationbaseline information

• multislice trivial

- invasive
- low C / N for func.

• highest C / N

- easy to implement
- multislice trivial
- non invasive
- highest temp. res.

complicated signal no baseline info.

Perfusion

- unique information
- control over ves. size
- baseline information
- non invasive

- multislice non trivial
- lower temp. res.
- low C / N

Hemodynamic Specificity



Mapping of CMRO₂

Activation:	Flow CMRO ₂ Blood Oxygenation	
CO ₂ stress:	Flow CMRO ₂ Blood Oxygenation	

Hemdodynamic Stress Calibration



12% 02

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).

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

BOLD CBF 20 3 (% increase) 15 CBF (% increase) 2 10 BOLD -10 1000 1200 1400 200 400 600 800 1000 1200 1400 0 0 200 400 600 800 Time (seconds) Time (seconds)

Simultaneous Perfusion and BOLD imaging during graded visual activation and hypercapnia

Hoge, et al.

CBF-CMRO₂ coupling



Characterizing Activation-induced CMRO₂ changes using calibration with hypercapnia

Hoge, et al.

Computed CMRO₂ Changes





Subject 1

Subject 2

Quantitative measurements of cerebral metabolic rate of oxygen utilization using MRI: a volunteer study

Hongyu An,¹ Weili Lin,²* Azim Celik³ and Yueh Z. Lee²



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



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/(π d² σ). From Biot-Savart:

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

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

r = 4cm (measurement distance when using MEG) the resulting value is: $B \approx 0.002 \text{ fT}$

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:

$$B_{MRI} = B_{MEG} \left(\frac{r_{MEG}}{r_{MRI}}\right)^2 = B_{MEG} \left(\frac{4 cm}{0.1 cm}\right)^2 = 1600 B_{MEG} \qquad \mathsf{B}_{\mathsf{MRI}} \approx 0.2 \mathrm{nT}$$

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).





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).

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.



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

*: activity#: scanner pump frequency

Petridou et al.




What we observe..

- Magnitude
- Location
- Parametric Dependence
- Latency

What we observe..

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Baseline Signal

Basic Concepts of TE and Field Strength Dependence of BOLD

80

100



Neuroimaging at 1.5 T and 3.0 T: Comparison of Oxygenation-Sensitive Magnetic Resonance Imaging

Gunnar Krüger,* Andreas Kastrup, and Gary H. Glover



Functional Contrast at Optimal TE





1.5

3.0

1.5

3.0

Neuroimaging at 1.5 T and 3.0 T: Comparison of Oxygenation-Sensitive Magnetic Resonance Imaging

Gunnar Krüger,* Andreas Kastrup, and Gary H. Glover



compartment size

2.5 to 3 μ m 3 to 15 μ m 15 to $\infty \mu$ m

Contras







Gradient-Echo EPI



Bolus Injection of Gadolinium: Simultaneous GE and SE

GE TE = 30 ms

SE TE = 110 ms









2.5 to 3 μ m 3 to 15 μ m 15 to $\infty \mu$ m compartment size

Gradient - Echo



Spin - Echo



no diffusion weighting

diffusion weighting





Summary of Diffusion-Weighted fMRI Data



J. L. Boxerman, P. A. Bandettini, K. K. Kwong, J. R. Baker, T. L. Davis, B. R. Rosen, R. M. Weisskoff, The intravascular contribution to fMRI signal change: monte carlo modeling and diffusion weighted studies in vivo. *Magn. Reson. Med.* **34**, **4-10** (1995).



J. L. Boxerman, P. A. Bandettini, K. K. Kwong, J. R. Baker, T. L. Davis, B. R. Rosen, R. M. Weisskoff, The intravascular contribution to fMRI signal change: monte carlo modeling and diffusion weighted studies in vivo. *Magn. Reson. Med.* **34**, **4-10** (1995).

What we observe..

- Magnitude
- Location
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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.

Location



Perfusion



Angiogram Perfusion BOLD



The spatial extent of the BOLD response

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

Neurolmage, 19: 132-144, (2003).



What we observe..

- Magnitude
- Location
- Parametric Dependence
- Latency

Motor Cortex



Auditory 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.

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

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 \rightarrow 1% BOLD

Simultaneous Recording of Evoked Potentials and T^{*}₂-Weighted MR Images During Somatosensory Stimulation of Rat

Gerrit Brinker, Christian Bock, Elmar Busch, Henning Krep, Konstantin-Alexander Hossmann, and Mathias Hoehn-Berlage



FIG. 3. Correlation of the increase of T₂^{*}-weighted imaging signal intensity with the peak-to-peak amplitude of the somatosensory evoked potential (SEP) during forepaw stimulation at increasing frequencies (data are from one individual animal; r = 0.82).

Negative BOLD effect



Percent Signal Change

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



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



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



The Underpinnings of the BOLD Functional Magnetic Resonance Imaging Signal

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In summary, MUA mostly represents the spiking of neurons, with single-unit recordings mainly reporting on the activity of the projection neurons that form the exclusive output of a cortical area. LFPs, on the other hand, represent slow waveforms, including synaptic potentials, afterpotentials of somatodendritic spikes, and voltage-gated membrane oscillations, that reflect the input of a given cortical areas as well as its local intracortical processing, including the activity of excitatory and inhibitory interneurons. Logothetis et al. (2001) "Neurophysiological investigation of the basis of the fMRI signal" Nature, 412, 150-157



Evidence that inhibitory input produces increased blood flow

Jawmal of Physiology (1998), 512.2, pp.555-568

Modification of activity-dependent increases of cerebral blood flow by excitatory synaptic activity and spikes in rat cerebellar cortex

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Figure 1. Schematic three-dimensional drawing of experimental set-up, including neurones of interest and position of laser Doppler probe, stimulating and recording electrodes

The positions of the three eerebellar layers, molecular (Mol, with a thickness of 400 μ m), Purkinje cell (PaL, about 100 μ m) and gramlar (GrL, 400-500 μ m), are indicated. The molecular layer contains gramle cell axons, called parallel fibres, the dendrites of Purkinje cells, stellate cells (S) and basket cells (B). The gramle cell layer contains gramle cells (Gr) and Golgi cells (GC). The superficial parallel fibres were stimulated by a bipolar stimulating electrode, while elimbing fibres (CF) were stimulated by a monopolar electrode lowered into the caudal part of the inferior clive (IO). Field potentials and single unit apike activity were recorded with a glass microelectrode. CBF was recorded by a laser Doppler flowmetry (LDF) probe located 0.3-0.5 mm above the pial surface (Pia).

Divergence of spike rate and blood flow during parallel fiber stimulation



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

NEUROIMAGE **6, 270–278 (1997)** ARTICLE NO. NI**970300**

Characterizing the Relationship between BOLD Contrast and Regional Cerebral Blood Flow Measurements by Varying the Stimulus Presentation Rate

Geraint Rees, A. Howseman, O. Josephs, C. D. Frith, K. J. Friston, R. S. J. Frackowiak, and R. Turner The Wellcome Department of Cognitive Neurology, Institute of Neurology, Queen Square, London WC1N 3BG, United Kingdom



Flow modulation is not necessarily the same as BOLD modulation

Negative BOLD in carotid artery disease



Röther et al. NeuroImage 2002

Courtesy of Arno Villringer

Increase in deoxy-Hb and oxy-Hb during focal seizure



Courtesy of Arno Villringer

Altered neurovascular coupling: Pathology, drugs

Pathologic state / Drug	Reference
Carotid occlusion	Röther et al. 2002
Transient global ischemia	Schmitz et al. 1998
Penumbra of cerebral ischemia	Mies et al. 1993, Wolf et al. 1997
Subarachnoid hemorrhage	Dreier et al. 2000
Trauma	Richards et al. 2001
Epilepsy	Fink et al. 1996, Brühl et al. 1998, von Pannwitz et al. 2002
Alzheimer's disease	Hock et al. 1996, Niwa et al. 2000
Theophylline	Ko et al. 1990, Dirnagl et al. 1994
Scopolamine	Tsukada et al. 1998

Courtesy of Arno Villringer




P. A. Bandettini, K. K. Kwong, T. L. Davis, R. B. H. Tootell, E. C. Wong, P. T. Fox, J. W. Belliveau, R. M. Weisskoff, B. R. Rosen, (1997). "Characterization of cerebral blood oxygenation and flow changes during prolonged brain activation." *Human Brain Mapping* 5, 93-109.



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).





Bandettini, et al., The functional dynamics of blood oxygenation level contrast in the motor cortex, 12'th Proc. Soc. Magn. Reson. Med., New York, p. 1382. (1993).



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.

Results – visual task



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

Results – motor task



Results – motor task

Nonlinearity

Magnitude

Latency







Reproducibility

Visual task











Experiment 1



Experiment 2

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.

BOLD Signal: ePts Change (SD Units) 9.00 BOLD LFP 6.00 6.00 MUA SDF 3.00 3.00 to gnal **BOLD Si** -3.00 20 25 30 35 10 15 40 **Time in Seconds**

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





Different stimulus "ON" periods



Brief stimulus OFF periods produce smaller decreases than expected

What we observe..

- Magnitude
- Location
- Parametric Dependence
- Latency

Time Course Comparison Across Brain Regions 0.75 0.50 0.25 0

TIME (sec)

12

13

Latency

Magnitude











A tangent into venograms (3 Tesla)









MP-RAGE

3D T-O-F MRA 3D Venous PC

MR Venogram









Regions of Interest Used for Hemi-Field Experiment



Right Hemisphere

Left Hemisphere







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

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Communicated by Leslie G. Ungerleider, National Institutes of Health, Bethesda, MD, December 19, 2002 (received for review October 31, 2002)

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







Formisano, E. and R. Goebel, *Tracking cognitive processes with functional MRI mental chronometry.* Current Opinion in Neurobiology, 2003. **13**: p. 174-181.

No calibration

Laminar specificity of functional MRI onset times during somatosensory stimulation in rat

Afonso C. Silva* and Alan P. Koretsky

Laboratory of Functional and Molecular Imaging, National Institute of Neurological Disorders and Stroke, Bethesda, MD 20892

I5182–15187 | PNAS | November 12, 2002 | vol. 99 | no. 231



No calibration

11.7 T

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

FMRI Basics and Beyond

- Information Content
- Sensitivity
- Resolution
- Image quality
- Paradigm Design and Processing

Maximizing Signal

• Higher Bo Field

- Linear or greater increase in S/N
- Tradeoff in susceptibility artifacts

Radio frequency Coils

- Smaller the coil the higher the S/N
- Tradeoff in coverage

• Choice of repetition time (TR)

- Faster is better (more data points to average)
- Tradeoff in coverage (10 slices/sec)
 - min TR = (time/slice) x number of slices in volume
- Diminishing returns because of noise correlation

Voxel volume

- Linear relationship between S/N and voxel volume
- Larger voxels increase partial volume averaging -> reduction of functional signal

Averaging

- Increase in sensitivity by sqrt(N)
- System and subject instabilities increase with longer

Temporal vs. Spatial SNR-3T





Physiologic Fluctuations

Cardiac0.6 to 1.2 HzRespiratory0.1 to 0.2 HzLow Frequency 0.0 to 0.1 Hz

0.25 Hz Breathing at 3T



0.68 Hz Cardiac rate at 3T


Neuroimaging at 1.5 T and 3.0 T: Comparison of Oxygenation-Sensitive Magnetic Resonance Imaging

Gunnar Krüger,* Andreas Kastrup, and Gary H. Glover



Temporal S/N vs. Image S/N



N. Petridou

Temporal vs. Image S/N Optimal Resolution Study



Petridou et al

Human data

Temporal vs. Image S/N Optimal Resolution Study



Phantom data

Petridou et al



Resolution, Speed, Surface Coils, Field Strength, etc..

Doubling Sensitivity with RF coils



Single shot full k-space echo-planar-imaging with an eight-channel phase array coil at 3T. Jerzy Bodurka¹, Peter van Gelderen², Patrick Ledden³, Peter Bandettini¹, Jeff Duyn² ¹Functional MRI Facility NIMH/NIH, ²Advance MRI NINDS/NIH, ³Nova Medical Inc.

Quadrature Head Coil

8 Channel Array

SNR

TSNR



Reducing Physiologic Fluctuations

- Filtering
- Pulse sequence
 - single vs. multishot
 - strategies for multishot

• Gating with correction for variable TR

Temporal Artifacts

- System instabilities
 Motion

 Drift
 - Stimulus correlated
 - Stimulus uncorrelated

Minimizing Temporal Artifacts

Recognize?

- •Edge effects
- Shorter signal change latencies
- •Unusually high signal changes
- •External measuring devices

Correct?

- Image registration algorithms
- Orthogonalize to motion-related
- function (cardiac, respiration, movement)
- •Navigator echo for k-space alignment *(for multishot techniques)*
- •Re-do scan

Bypass?

- Paradigm timing strategies..
- Gating (with T1-correction)

Suppress?

- Flatten image contrast
- Physical restraint
- •Averaging, smoothing

FMRI Basics and Beyond

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Single Shot EPI



EPI Readout Window

 ≈ 20 to 40 ms



Imaging System Components



Echo Planar Imaging at the Medical College of Wisconsin

1991-1992







Imaging System Components



General Electric 3 Tesla Scanner



Multishot Imaging



Window 2

EPI

Multi Shot EPI



Partial k-space imaging



Single - Shot EPI at 3T: Half NEX, 256 x 256, 16 cm FOV



Single shot full k-space echo-planar-imaging with an eight-channel phase array coil at 3T. Jerzy Bodurka¹, Peter van Gelderen², Patrick Ledden³, Peter Bandettini¹, Jeff Duyn² ¹Functional MRI Facility NIMH/NIH, ²Advance MRI NINDS/NIH, ³Nova Medical Inc.

Quadrature Head Coil

8 Channel Array

SNR

TSNR



SENSE: Sensitivity Encoding for Fast MRI



Pruessmann, et al.

SENSE Imaging



Pruessmann, et al.

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." <u>J Neurophysiol</u> 77(5): 2780-7.



Optical Imaging

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

FMRI Basics and Beyond

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3D z-Shim Method for Reduction of Susceptibility Effects in BOLD fMRI

Gary H. Glover*



Optimization of Static Field Homogeneity in Human Brain Using Diamagnetic Passive Shims

James L. Wilson, Mark Jenkinson, and Peter Jezzard*



FIG. 1. Photograph of the mouth shim, comprising four plates of pyrolytic graphite, without the polymorph mold. The shallow end of the shim is placed near the front of the roof of the mouth. The shim is 33 mm in length and 26 mm in width, and each plate is 3 mm thick.

Optimization of Static Field Homogeneity in Human Brain Using Diamagnetic Passive Shims

James L. Wilson, Mark Jenkinson, and Peter Jezzard*



FIG. 3. Example of B_0 inhomogeneity reduction. Nine axial slices, from the bottom of the ITC to the top of the IFC, of manually brain masked B_0 maps of subject C are shown (a) without any passive shims, (b) with the mouth shim, and (c) with the mouth shim and ear shims. B_0 range is -1.2 ppm (white) to +1.2 ppm (black). Decreases in the IFC and ITC inhomogeneities are significant with placement of the mouth and ear shims, respectively, without compromising other brain regions.

Optimization of Static Field Homogeneity in Human Brain Using Diamagnetic Passive Shims

James L. Wilson, Mark Jenkinson, and Peter Jezzard*



FIG. 4. Example of EPI susceptibility artifact reduction. Nine axial slices of subject C, corresponding to those shown in Fig. 3, are shown. A standard T_1 -weighted structural image is provided in row **d** as a reference with an outline of the IFC mask of this subject superimposed. Unwarped gradient-echo EPI images are shown (**a**) without any passive shims, (**b**) with the mouth shim, and (**c**) with the mouth shim and ear shims. A considerable reduction in signal loss artifact in the IFC is evident with placement of the mouth shim. A smaller reduction in the IFCs is apparent with placement of the ear shims.

FMRI Basics and Beyond

- Information Content
- Sensitivity
- Resolution
- Image quality
- Paradigm Design and Processing

Neuronal Activation Input Strategies

- 1. Block Design
- 2. Frequency Encoding
- 3. Phase Encoding
- 4. Event Related
- 5. Orthogonal Block Design
- 6. Free Behavior Design.



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P. A. Bandettini, A. Jesmanowicz, E. C. Wong, J. S. Hyde, Processing strategies for time-course data sets in functional MRI of the human brain. *Magn. Reson. Med.* **30**, **161-173** (1993).





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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.

Event Related Advantages

- Task Randomization
- Post acquisition, Performance-based, data binning
- Natural presentation
- Reduction of habituation effects
- Overt responses
- Reduction of scanner noise effects
- More precise estimation of hemodynamic respons

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^{†‡}









fMRI during tasks that involve brief motion





R. M. Birn, P. A. Bandettini, R. W. Cox, R. Shaker, Event - related fMRI of tasks involving brief motion. *Human Brain Mapping* 7: 106-114 (1999).

Overt Word Production



R. M. Birn, P. A. Bandettini, R. W. Cox, R. Shaker, Event - related fMRI of tasks involving brief motion. *Human Brain Mapping* 7: 106-114 (1999).

Speaking - Blocked Trial



R. M. Birn, P. A. Bandettini, R. W. Cox, R. Shaker, Event - related fMRI of tasks involving brief motion. *Human Brain Mapping* 7: 106-114 (1999).

Speaking - ER-fMRI





Motion-Decoupled fMRI: Functional MRI during of overt word production



"block-trial" paradigm

Motion induced signal changes resemble functional (BOLD) signal changes



"single-trial" paradigm

Motion induced and BOLD signal changes are separated in time

R.M. Birn, et al.

Tongue Movement



Jaw Clenching



Swallowing - Event-Related



Detectability – constant ISI







P. A. Bandettini, R. W. Cox. Functional contrast in constant interstimulus interval event - related fMRI: theory and experiment. *Magn. Reson. Med.* 43: 540-548 (2000).



P. A. Bandettini, R. W. Cox. Functional contrast in constant interstimulus interval event - related fMRI: theory and experiment. *Magn. Reson. Med.* 43: 540-548 (2000).





0 sec2 sec4 sec



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).

Estimation accuracy 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).

Varying "ON" and "OFF" periods

Rapid event-related design with varying ISI

MM_MM_M_M_M_M_M_M_M_M_25% ON

75% ON

Varying "ON" and "OFF" periods



ODC Maps using fMRI



 Identical in size, orientation, and appearance to those obtained by optical imaging¹ and histology^{3,4}.

¹Malonek D, Grinvald A. *Science* 272, 551-4 (1996). ³Horton JC, Hocking DR. *J Neurosci* 16, 7228-39 (1996). ⁴Horton JC, et al. *Arch Ophthalmol* 108, 1025-31 (1990).

Why short is better than long

It is argued that fMRI cannot achieve submillimeter functional resolution because a saturated hyperoxic vascular response to neural activity spreads over many millimeters^{1,2}.

However, optical imaging has demonstrated that the hyperoxic response can yield well-localized maps when using short duration stimuli (<5 sec)¹.

The vascular response to brief neural stimulation

¹Malonek D, Grinvald A. Science 272, 551-4 (1996). ²Kim D-S, Duong T, Kim S-G. Nat Neurosci 3, 164-9 (2000).

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Example of a Set of Orthogonal Contrasts for Multiple Regression

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- 3. Phase Encoding
- 4. Single Event
- 5. Orthogonal Block Design
- 6. Free Behavior Design.

Free Behavior Design

Use a continuous measure as a reference function:

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

Resting Hemodynamic Autocorrelations

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

The Skin Conductance Response (SCR)

Skin Conductance Dynamics

Boucsein, Wolfram (1992). Electrodermal Activity. Plenum Press, NY
Venables, Peter, (1991). Autonomic Activity ANYAS 620:191-207.

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).

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Simultaneous EEG and fMRI of the alpha rhythm

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Received 28 October 2002; accepted 30 October 2002

DOI: 10.1097/01.wnr.0000047685.08940.d0

FMRI Basics and Beyond

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Technology MRI	Diff. tens 1.5T,3T, 4T EPI on Clin. Syst. Real Nav. pulses Local Human Head Gradient Coils Quar ASL Spiral EPI Dynar BOLD Multi-shot fMRI	sor Mg ⁺ 7T >8 channels al time fMRI Venography Int. ASL Z-shim Baseline Susceptibility amic IV volume Simultaneous ASL and BOLD Current Imaging?
Methodology Baseline IVIM	Correlation Analysis Motion o Parametric Design Surface Mapp Phase Mapping Linear Regression Event-related Deco	CO ₂ Calibration Correction Latency and Width Mod Multi-Modal Mapping ping ICA Free-behavior Designs Mental Chronometry Multi-variate Mapping convolution Fuzzy Clustering
Interpretation Blood T2 Hemoglobin	BOLD models PET corr B _o dep. IV vs EV Pre-undershoo TE dep Resolution Dep. Post-undershoot SE vs. GE CO ₂ effect NIRS Correlation Fluct Veins Inflow	relation ASL vs. BOLD Dt PSF of BOLD Extended Stim. Linearity Ctuations Balloon Model Excite and Inhibit Excite and Inhibit
Applications	Complex motor Language Ima Motor lear BOLD -V1, M1, A1 Presurgical Volume - Stroke V1, V2mapping ∆ Volume-V1 Plasticity	hagery Memory Emotion rning Children Tumor vasc. Drug effects al Attention Ocular Dominance Mirror neurons Priming/Learning Clinical Populations ry Face recognition
86 82 <u>88</u>	89 90 91 92 93 94 95 9	96 97 98 99 00 01 02 03

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 llana 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