Decoding fMRI Brain Activity At Multiple Levels of Organization

From Areas to Columnar-Level Feature Codes

IPAM Workshop "Multimodal Neuroimaging", Los Angeles, March 07, 2013

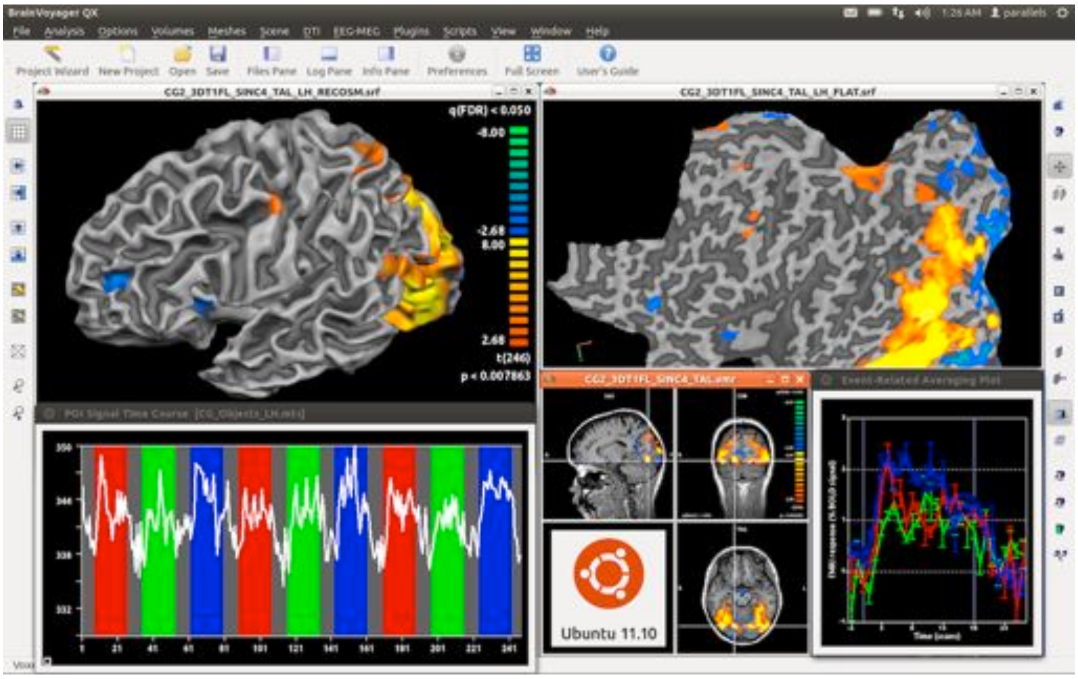
Rainer Goebel

Maastricht Brain Imaging Center (M-BIC), Dept. of Cognitive Neuroscience, Maastricht University & National Institute of Neuroscience (NIN) of the Royal Netherlands Academy of Arts and Sciences, Amsterdam, The Netherlands & CEO Brain Innovation & CSTO Brains Unlimited

Overview

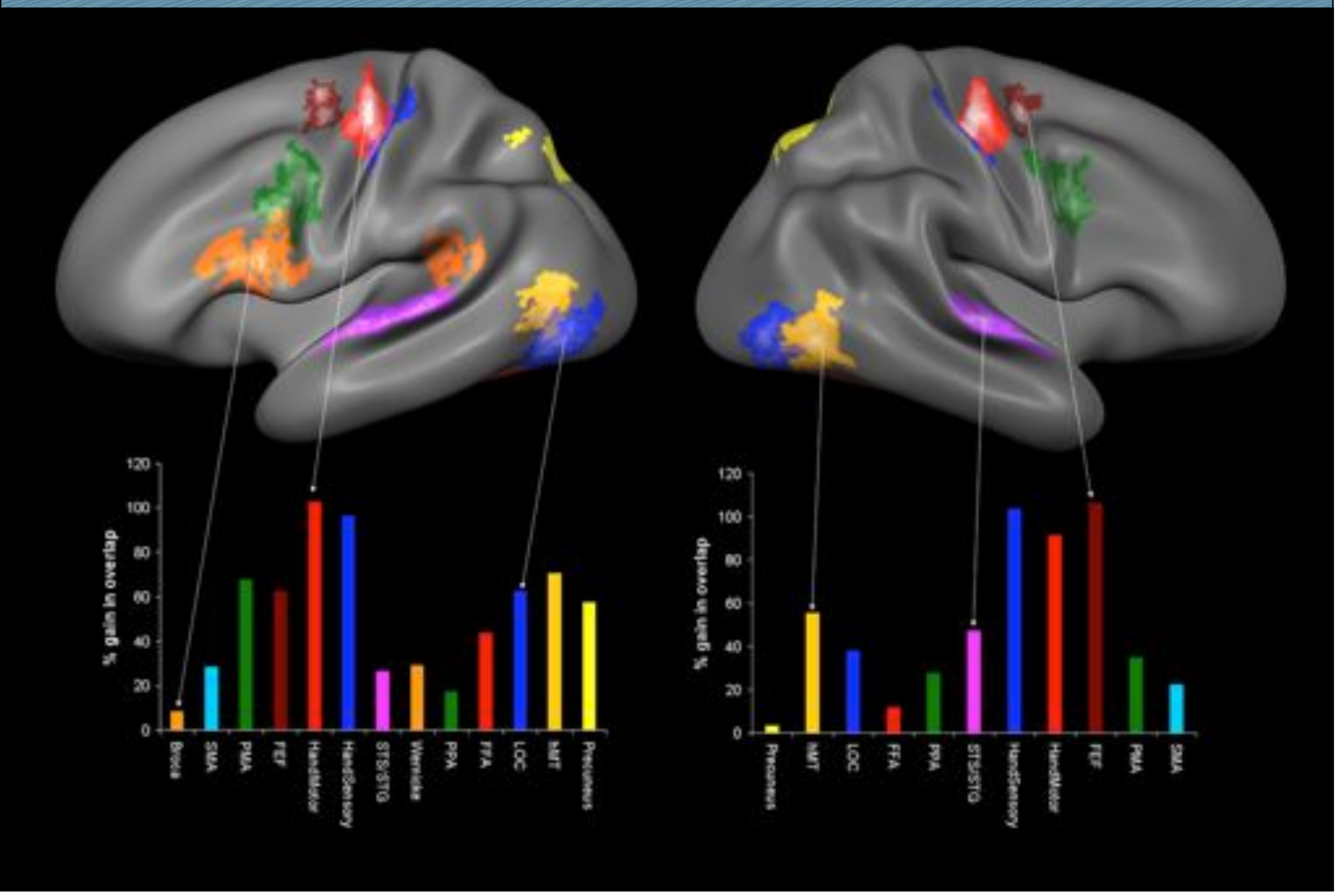
- **20 Years of fMRI - What kind of Insights?**
  - Characterization of *specialized* brain areas and (intrinsic) *networks*
  - Mental chronometry, effective connectivity, causality
- **Translation of Insights into Clinical Applications**
  - Real-time fMRI neurofeedback for Parkinson and Depression
  - Real-time fMRI Brain Reading for Communication BCI
- **Levels of Description in Cognitive Neuroimaging**
  - What is the appropriate level of organization to understand perception and cognition?
- **Cracking the Feature Code At Columnar Level?**
  - Mapping columnar-level features using ultra-high field fMRI
  - Towards new content-rich columnar-level BCIs
  - Towards laminar-level MVPA and effective connectivity
- **Summary and Conclusions**
  - Integration: Multi-modal columnar-level neural network models

Current Resolution of fMRI: Specialized Areas and Networks

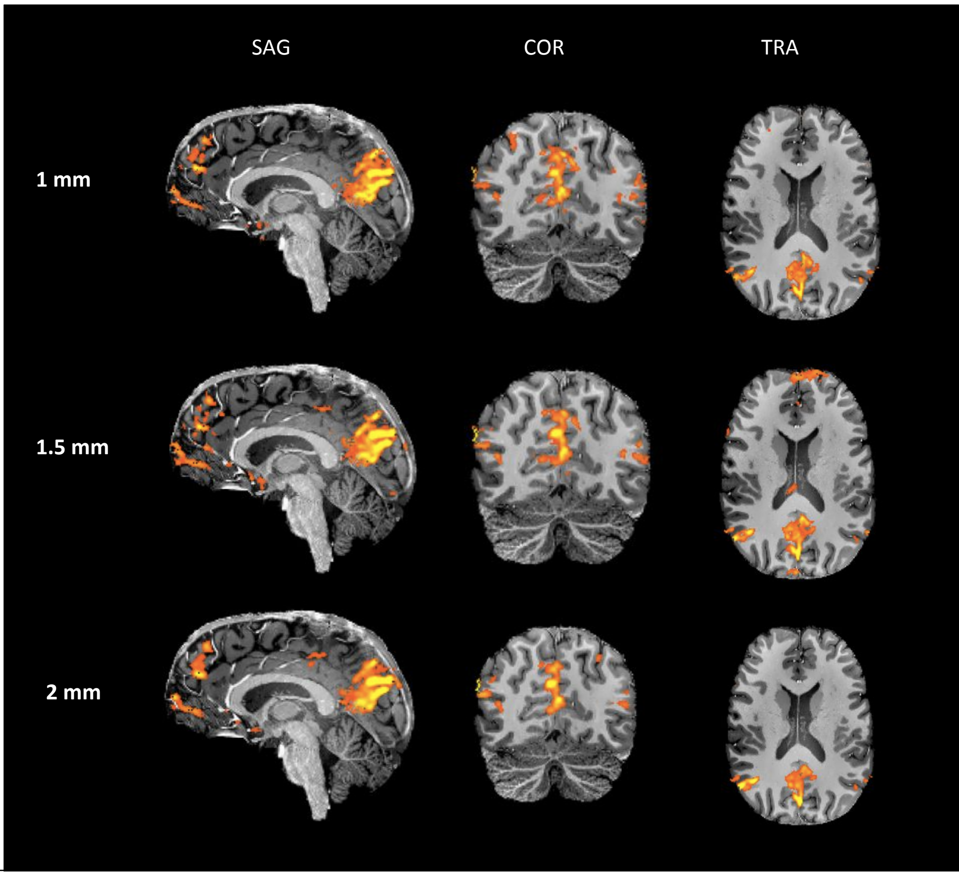


Probabilistic Atlas of Specialized Functional Brain Areas

Frost, M. & Goebel, R. (2012), *NeuroImage*, **59**, 1369 - 1381.



Resting State - Whole Brain Functional Networks @ 7T

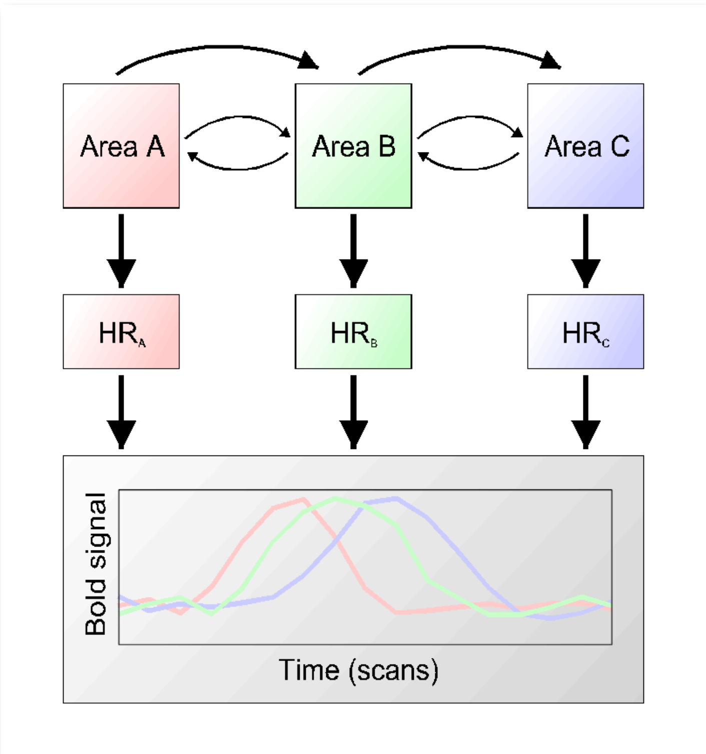


De Martino et al. (2011), *Neuroimage*, **57**, 1031.

5

What is resolved in *time-resolved* fMRI ?

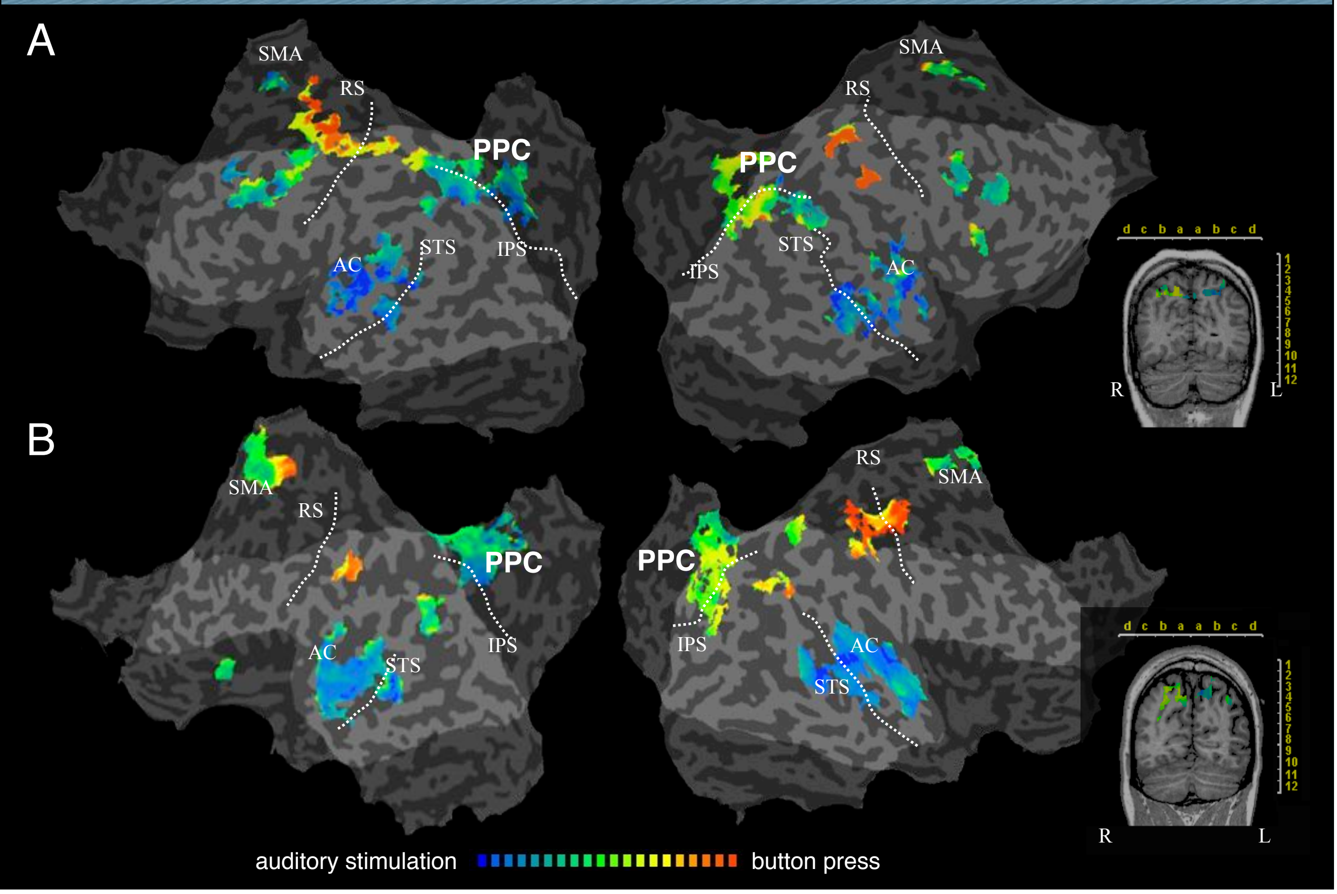
Neuronal *vs* cognitive timing



Formisano & Goebel (2003), *Current Opinion in Neurobiology*, 13, 174-184.

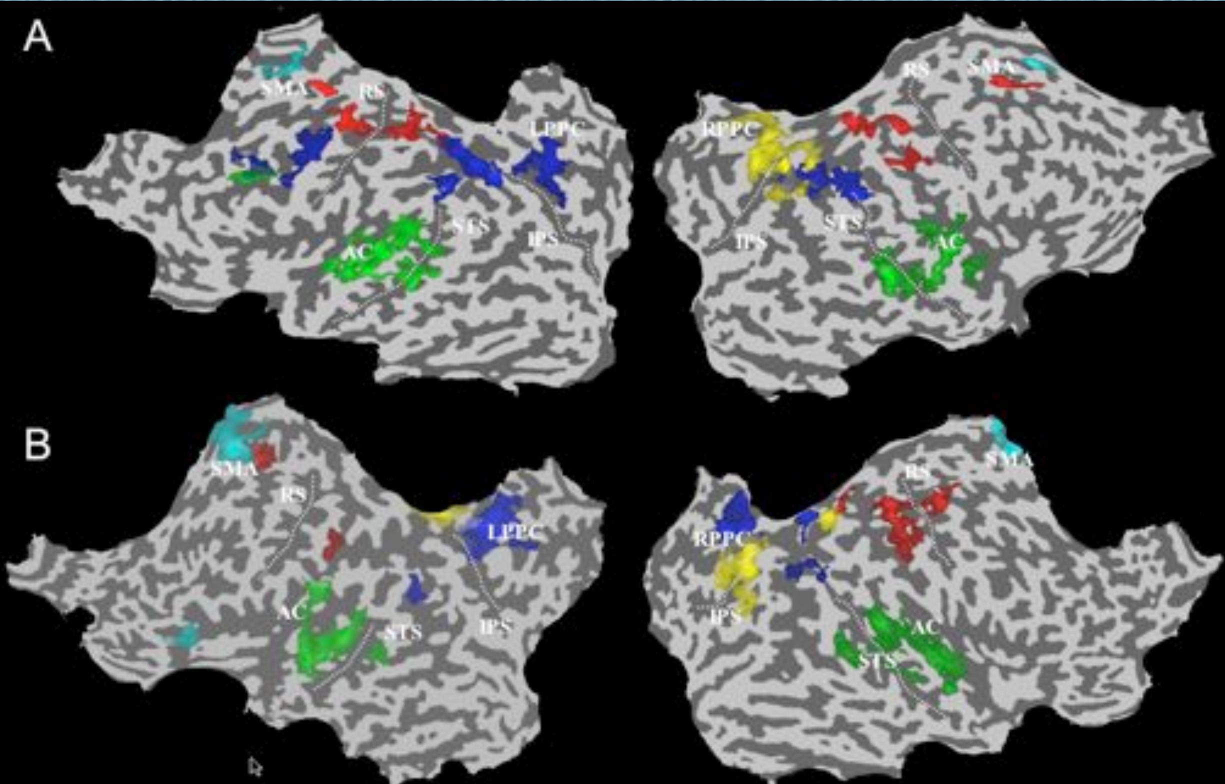
6

The mental clock task - *Single-subject BLM results*



7

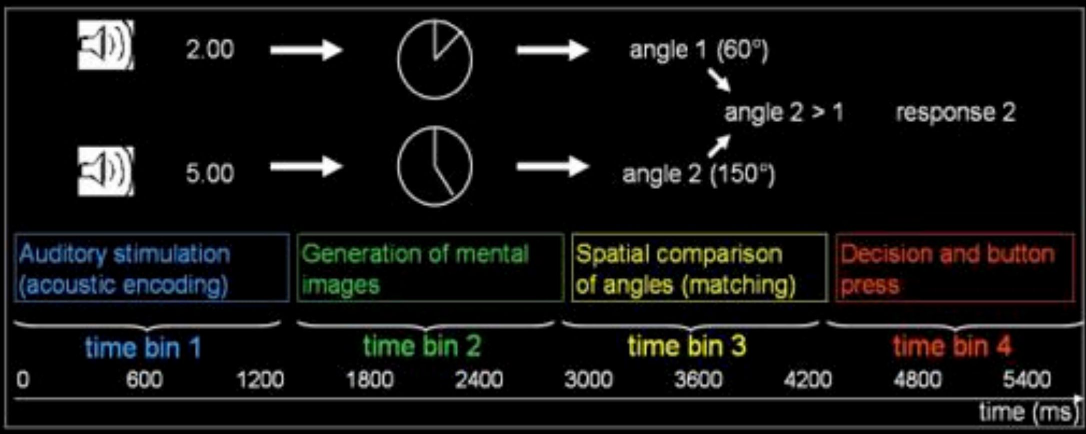
Mental clock task – *Cortex-based ICA analysis*

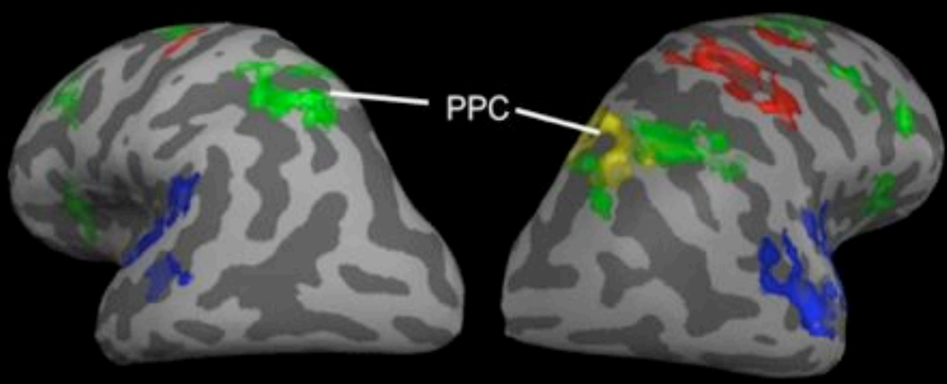


Formisano, Esposito, DiSalle & Goebel (2004), *Magnetic Resonance Imaging*, **22**, 1493-1504.

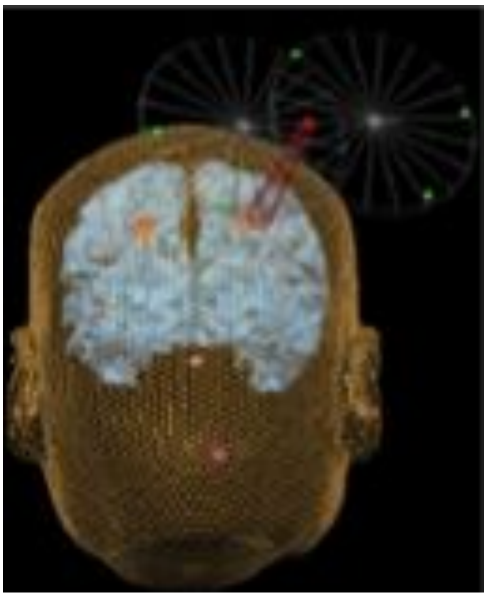
8

Mental clock task – *Cognitive and neurobiological model*





Real-Time TMS Neuronavigation



Sack AT, Kadosh RC, Schuhmann T, Moerel M, Walsh V, Goebel R (2009). Optimizing Functional Accuracy of TMS in Cognitive Studies: A Comparison of Methods. *Journal of Cognitive Neuroscience*, **21**, 207-221.

Mental Clock Task - *Cobmined rTMS and tpTMS*

Hypotheses - inspired by fMRI mental chronometry:

- Can we use single pulse TMS to directly test a temporal involvement of right PPC in late stage (spatial comparison) of mental imagery task?
- Can we demonstrate the hypothesized compensatory mechanism assumed to take place in the right PPC?

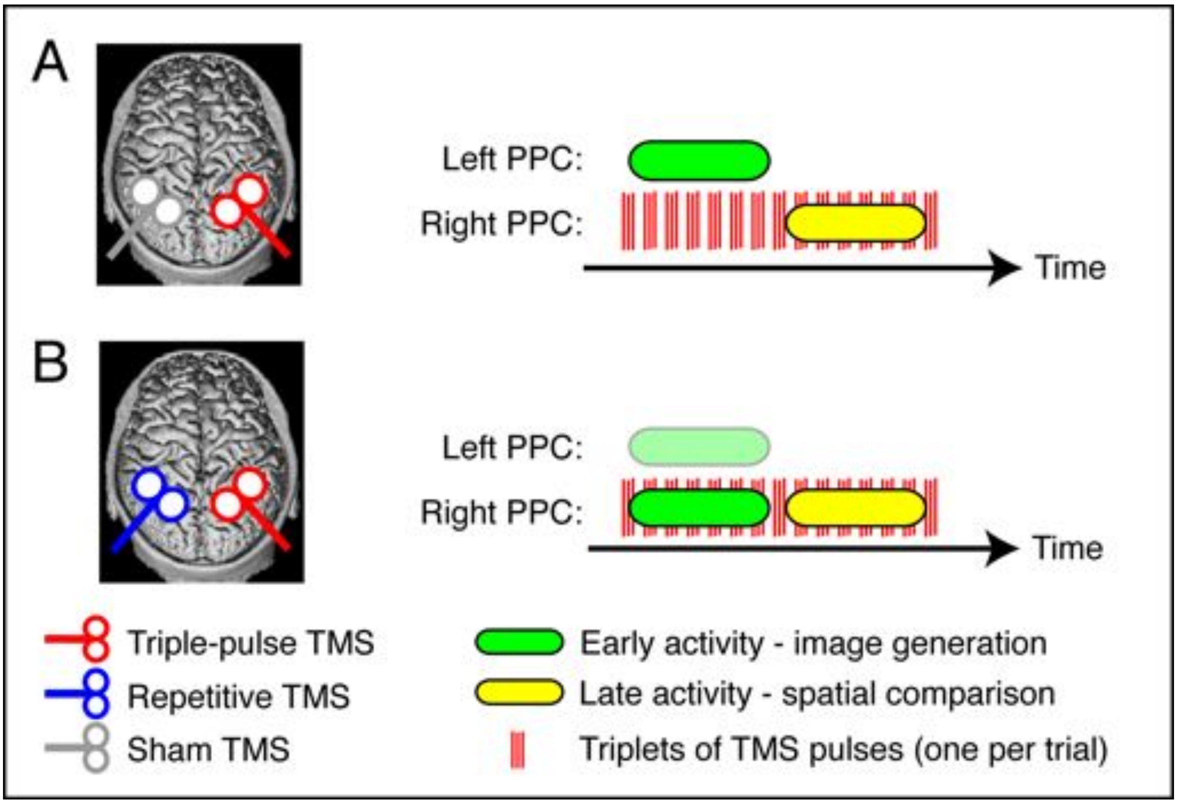
Experiment:

- Use rTMS to “lesion” left PPC (control with sham)
- Use tpTMS over right PPC to test critical time points within a trial

Reference:

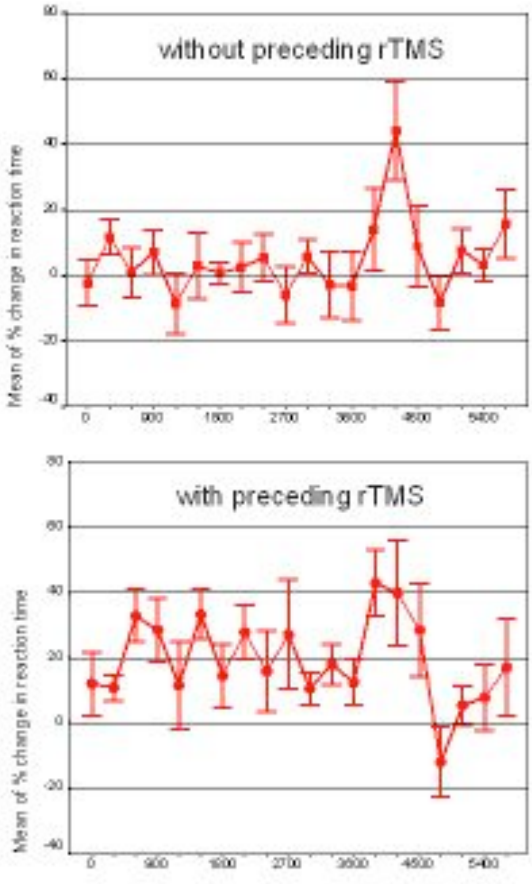
- Sack,A, Camprodon, JA, Pascual-Leone, A & Goebel, R (2005). The dynamics of interhemispheric compensatory processes in mental imagery”, *Science*, **308**, 702-704.

Combined rTMS and tpTMS - *Experimental design*



tpTMS: 20 time windows from 0 to 5700 ms in steps of 300 ms; rTMS: 1 Hz for 600 s

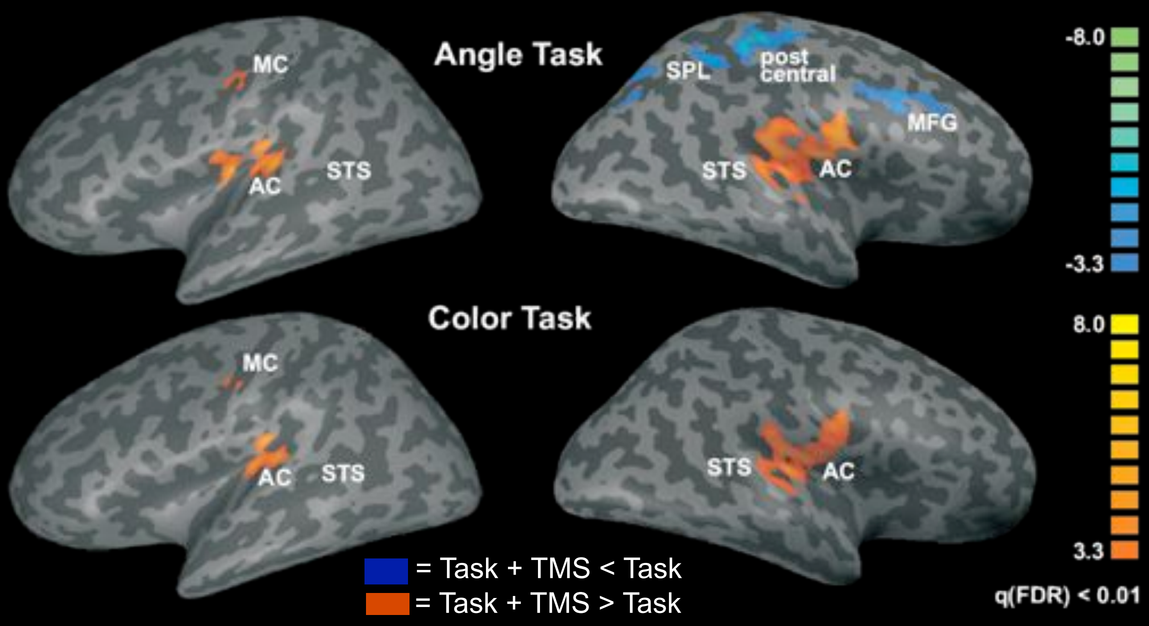
Combined rTMS and tpTMS - *Results*



Behavioral Impairments following right parietal tpTMS

Sack,A, Camprodon, JA, Pascual-Leone, A & Goebel, R (2005). *Science*, **308**, 702-704.

Simultaneous TMS - fMRI – Mapping Results

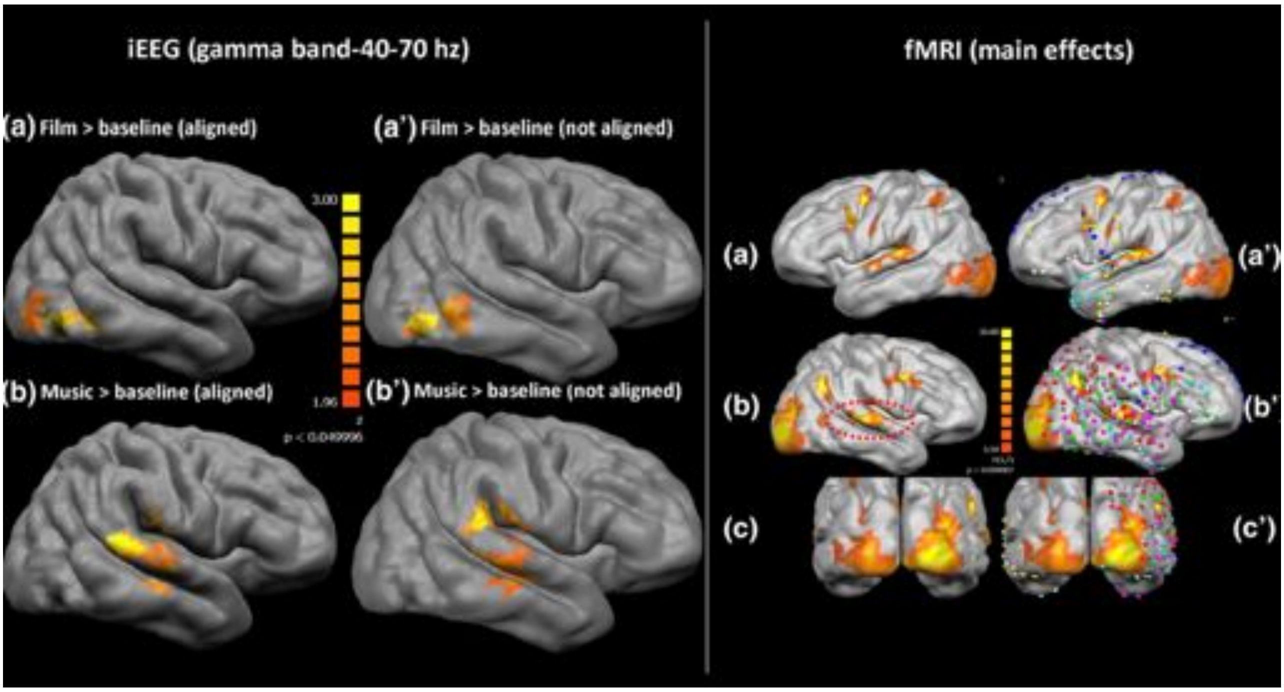


Contrast: **Task with TMS - Task without TMS**:

- Increased BOLD Response During (additional) TMS in the Auditory Cortex
- Reduced BOLD Response During TMS (blue) in the SPL and MFG
- Significant Interaction Between Task (ANGLE vs COLOR) and TMS in the IPS

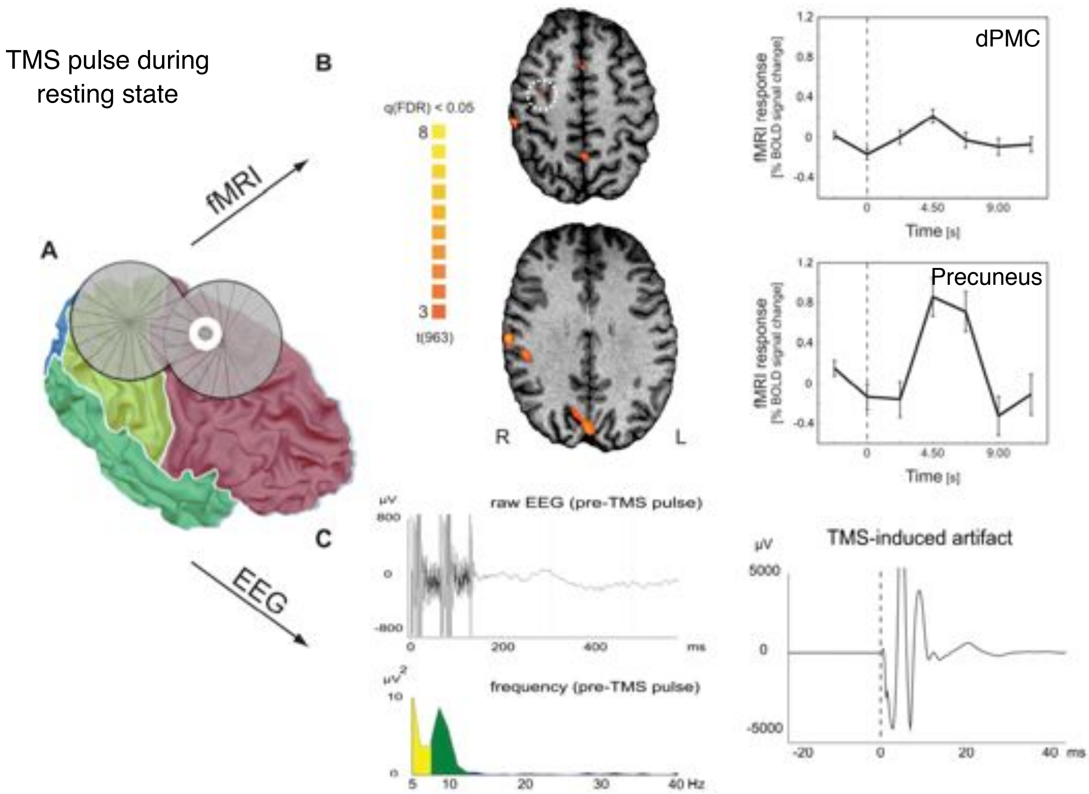
Sack, Kohler, Bestmann, Linden, Dechent, Goebel, Baudewig (2007) *Cerebral Cortex*, **17**, 2841-52.

Combining iEEG and fMRI in Cortex-Aligned Group Space



Esposito, Singer, Podlipsky, Fried, Hendler, Goebel (2013). Cortex-based inter-subject analysis of iEEG and fMRI data sets: Application to sustained task-related BOLD and gamma responses, *Neuroimage*, **66**, 457-468.

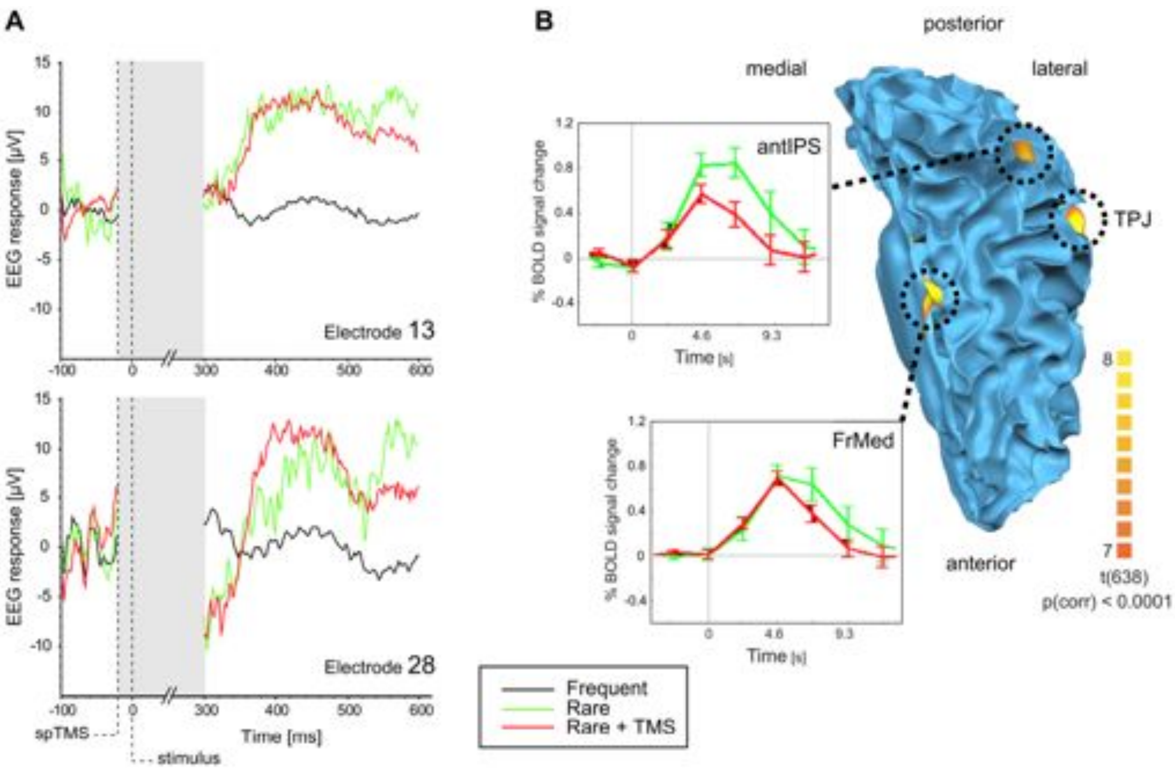
Multi-Modal Challenge: Concurrent TMS - fMRI - EEG



Peters, Reithler, Schuhmann, De Graaf, Uludag, Goebel, Sack (2013). On the feasibility of concurrent human TMS-EEG-fMRI measurements, *Journal of Neurophysiology*, **109**, 1214-1227.

Multi-Modal Challenge: Concurrent TMS - fMRI - EEG

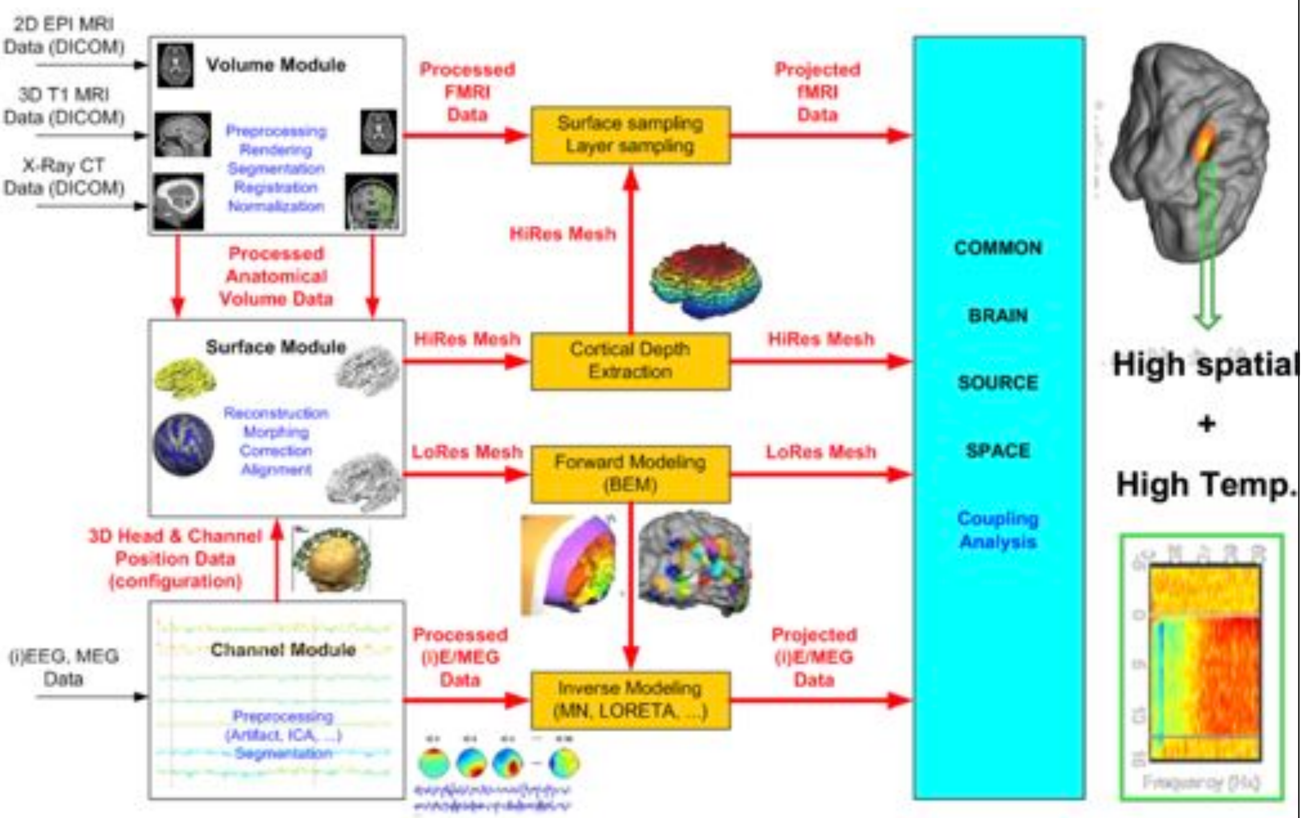
TMS during oddball task



Peters, Reithler, Schuhmann, De Graaf, Uludag, Goebel, Sack (2013). On the feasibility of concurrent human TMS-EEG-fMRI measurements, *Journal of Neurophysiology*, **109**, 1214-1227.

17

Multi-Modal Brain Imaging Framework in BrainVoyager



18

Towards Clinical Real-Time fMRI Applications

Goebel (2012). BrainVoyager: Past, present, future. *Neuroimage*.

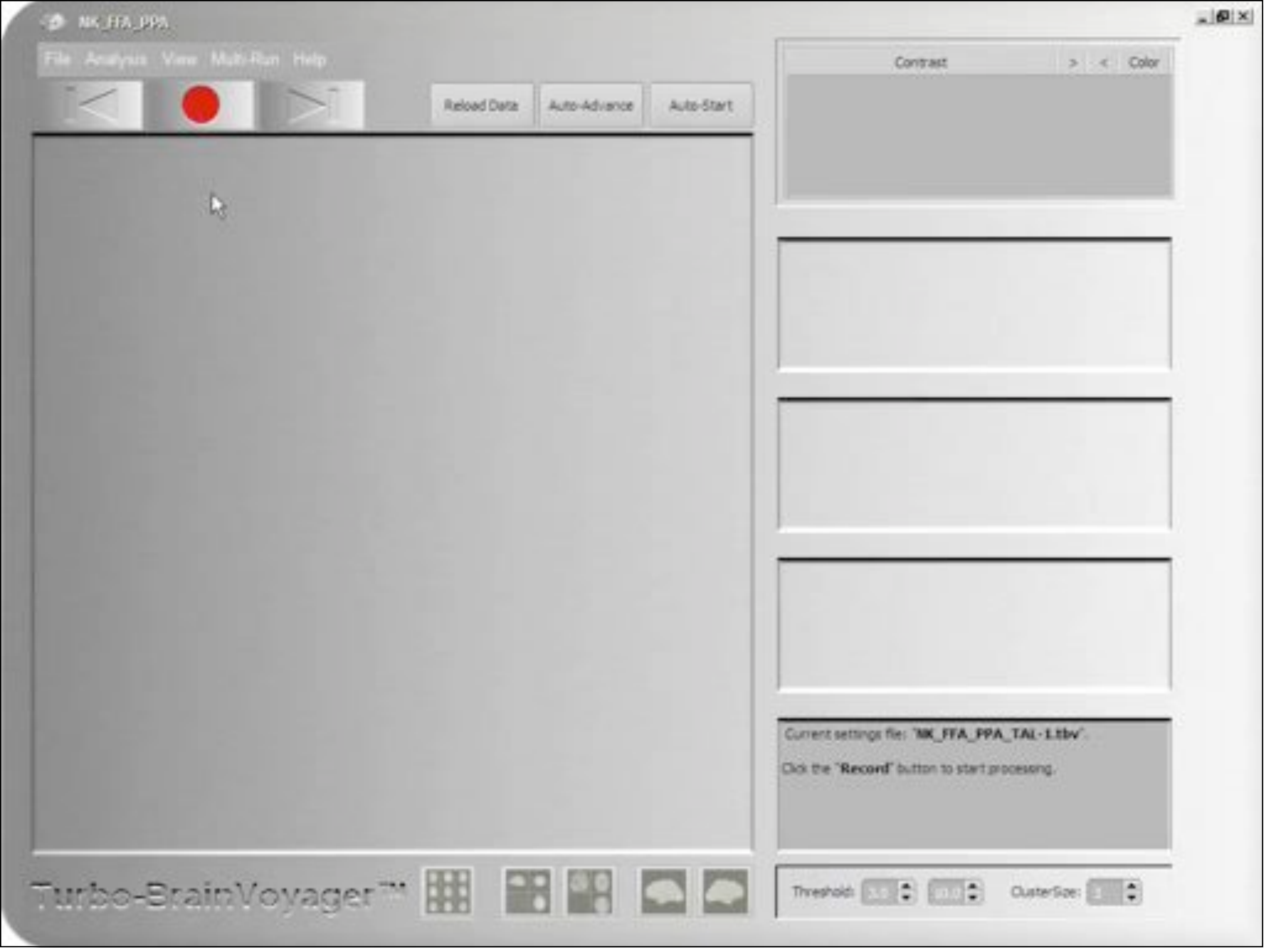
Related background work:

- Multivariate searchlight mapping (Kriegeskorte, Goebel, Bandettini, *PNAS*, 2006)
- Real-time fMRI-based Neurofeedback and BCIs (Goebel et al., *Imaging in Medicine,* 2010)
- Feature-Level Classifiers (Formisano, DeMartino, Bonte, Goebel, *Science*, 2008)

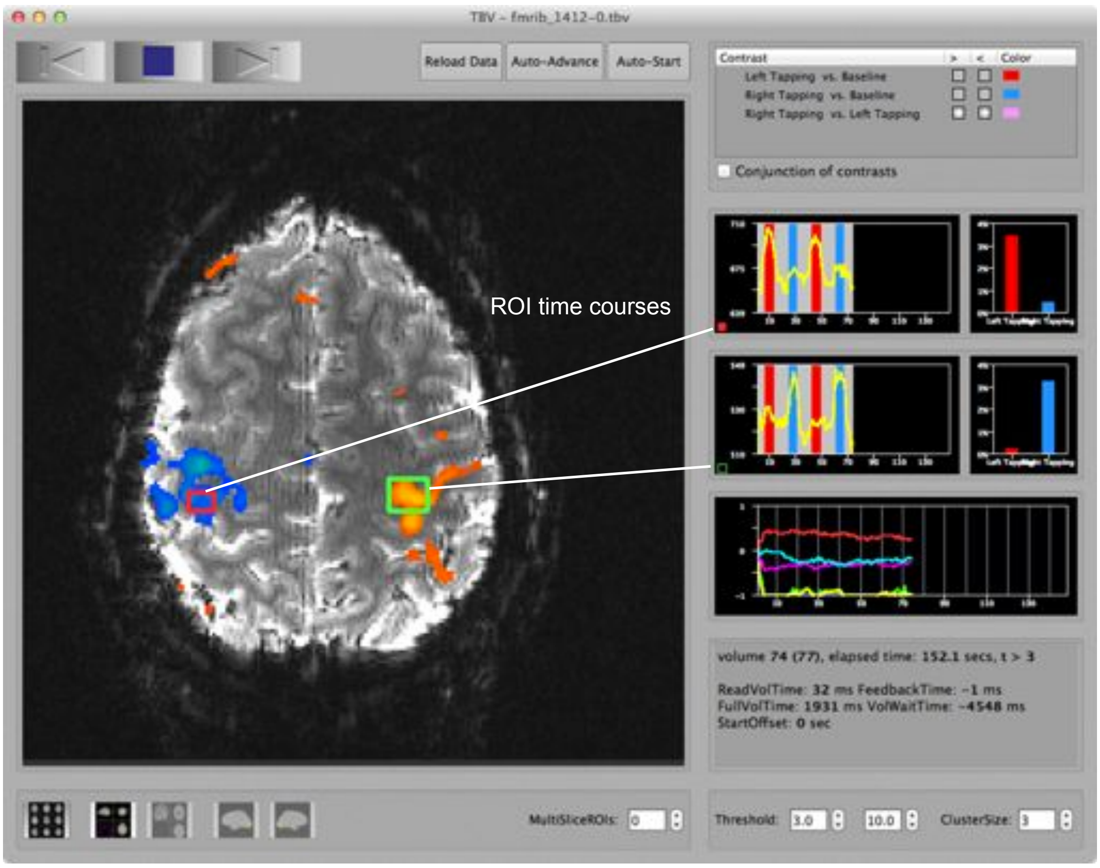
Real-Time fMRI

During functional runs, the following computations are repeatedly performed in real-time fMRI within the time window of ***one time point*** (brain volume):

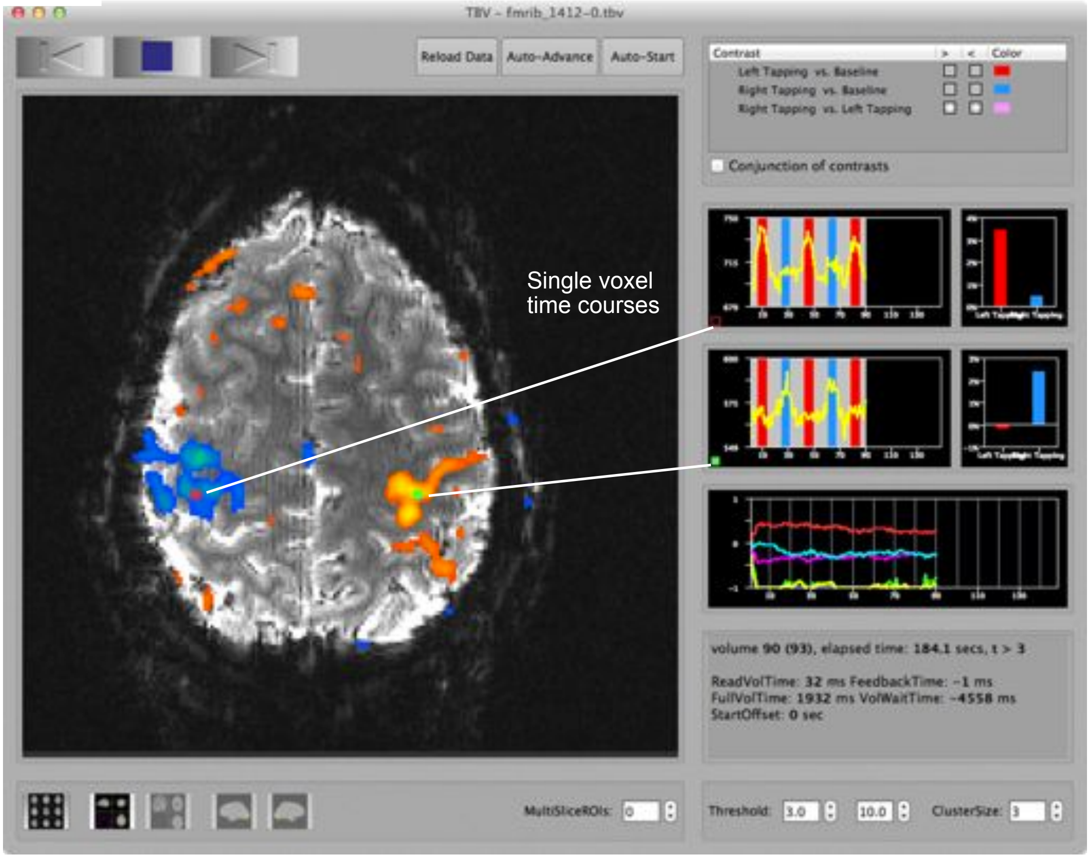
- Reading of EPI slices into working memory
- 3D motion correction (with sinc interpolation if GPGPU available)
- 3D spatial smoothing
- Incremental statistical analysis (RLS GLM)
- Nonlinear drift removal via design matrix
- Incremental event-related averaging
- Real-time ICA (Esposito et al 2003, *Neuroimage*, **20**, 2209)
- Real-time SVM Classifier (LaConte et al., 2007; Sorger et al., 2010)
- Thresholding, clustering and color-coding of resulting statistical maps
- Visualization of the maps on EPI images, intra- or extra-session 3D data and rendered cortical surfaces
- Handles more than million voxels @ 7 Tesla



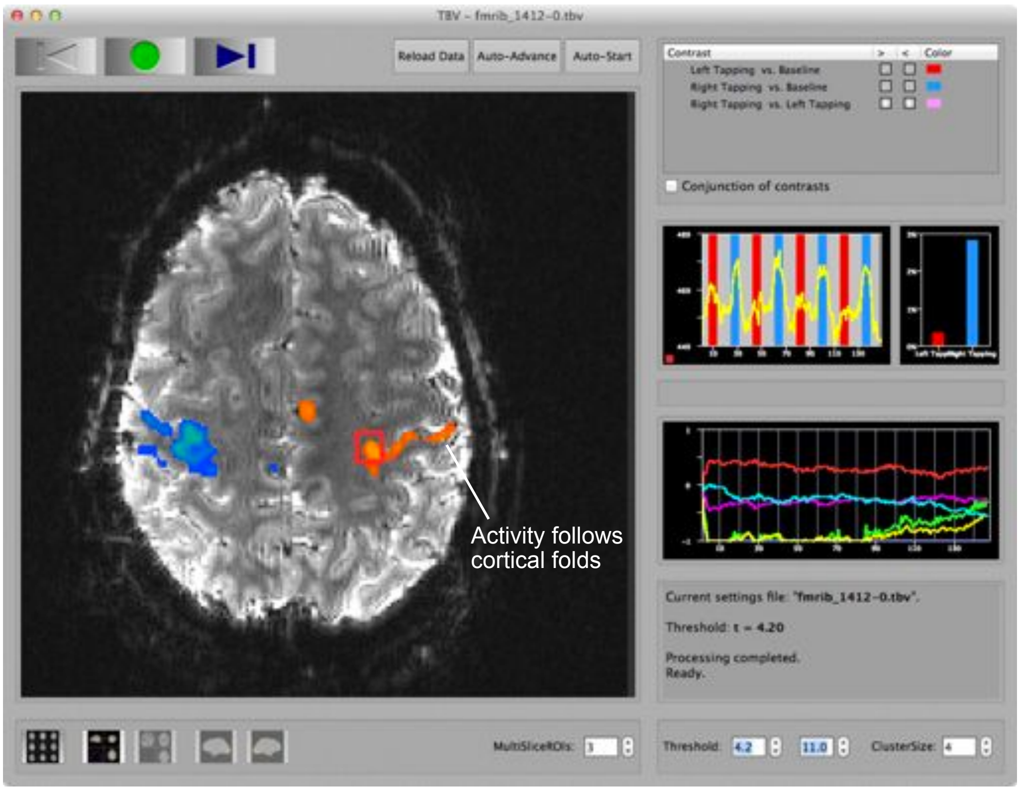
Real-time fMRI Data Analysis @ 7 Tesla



Real-time fMRI Data Analysis @ 7 Tesla



Real-time fMRI Data Analysis @ 7 Tesla



3T: ca. 30 x [64 x 64] = 122,800 voxels per time point

7T: ca. 50 x [192 x 192] = 1.843,200 voxels (multi-band sequence)

Incremental GLM: Recursive Least Squares

The beta values and inverted **X'X** matrix can be updated *incrementally* using only information of the new time point with the following recursive equations:

$$\mathbf{b}_{t+1} = \mathbf{b}_t + (\mathbf{X}_t'\mathbf{X}_t)^{-1}\mathbf{x}_{t+1}\frac{(y_{t+1} - \mathbf{x}_{t+1}\mathbf{b}_t)}{1 + \mathbf{x}_{t+1}'(\mathbf{X}_t'\mathbf{X}_t)^{-1}\mathbf{x}_{t+1}}$$

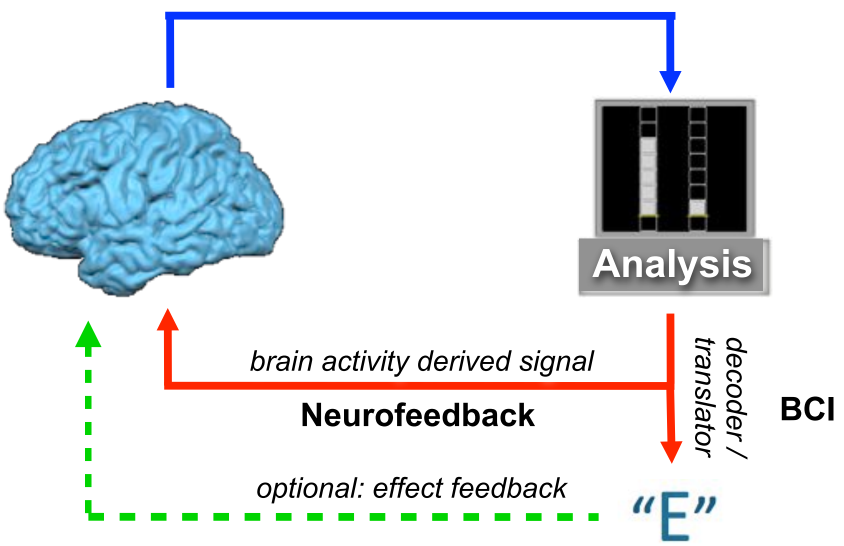
$$(\mathbf{X}_{t+1}'\mathbf{X}_{t+1})^{-1} = (\mathbf{X}_t'\mathbf{X}_t)^{-1} - \frac{(\mathbf{X}_t'\mathbf{X}_t)^{-1}\,\mathbf{x}_{t+1}\mathbf{x}_{t+1}'\,(\mathbf{X}_t'\mathbf{X}_t)^{-1}}{1 + \mathbf{x}_{t+1}'(\mathbf{X}_t'\mathbf{X}_t)^{-1}\mathbf{x}_{t+1}}$$

Note: Since the **X'X**$^{-1}$ term is the same for all voxels, it can be precomputed before solving for **b** for individual voxels.

-> Incremental algorithms provide **constant calculation time** per data point (volume), i.e. they avoid the risk of conventional approaches to lag behind the incoming data; the calculation time of conventional algorithms (e.g. standard GLM) increases with growing data sets.

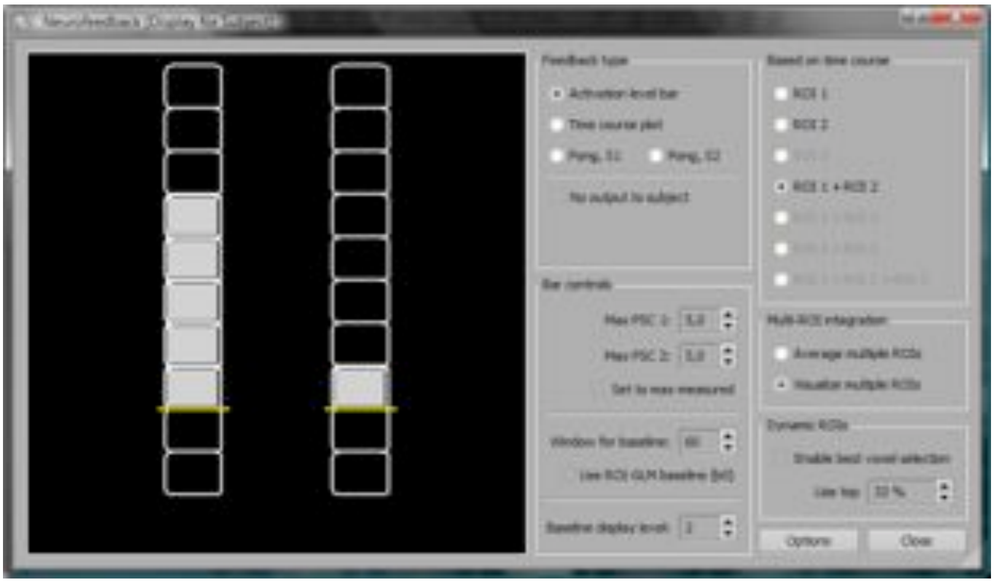
Applications Of Real-Time fMRI Data Analysis

Online "brain reading" for neurofeedback and communication BCI



Collaboration with David Linden (Cardiff), Nikolaus Weiskopf (London)

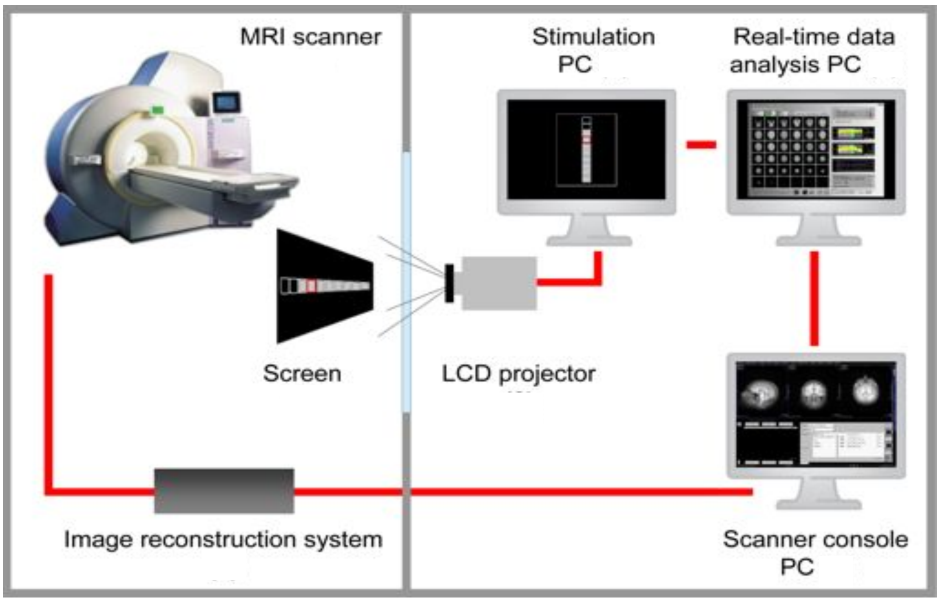
Real-Time fMRI Neurofeedback



- Real-time fMRI enables monitoring changes in the BOLD response ***online***.
- The high spatial resolution of fMRI offers the possibility to investigate the control over ***localized*** brain regions -> ***Feedback is content-specific***.
- Subjects can learn to influence own brain activity from ***one*** or ***multiple*** circumscribed brain regions.

fMRI Neurofeedback as a Therapeutic Tool

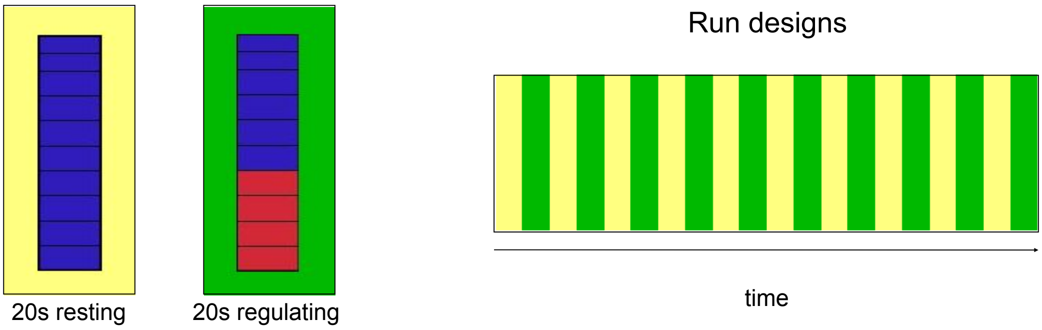
Technical setup and data flow of fMRI-based neurofeedback training study



Neurofeedback therapy for patients with depression

- patients with recurrent depressive episodes after unsuccessful conventional therapy

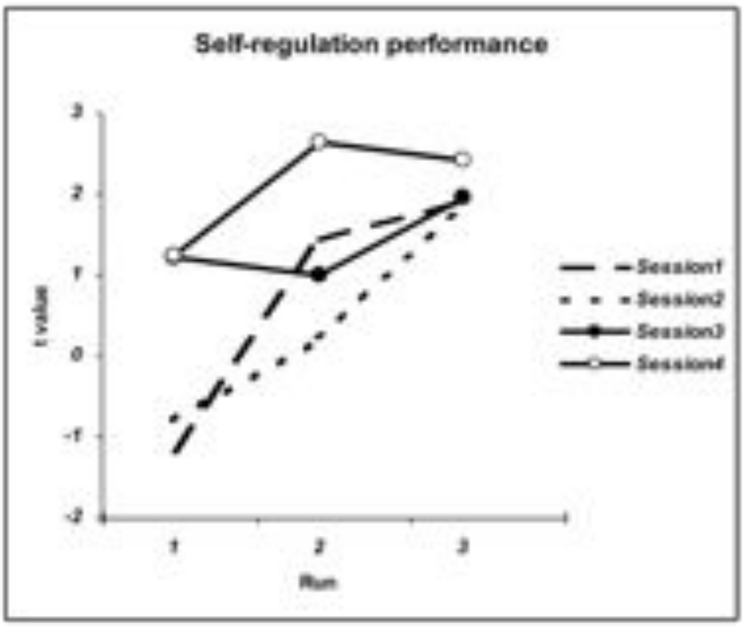
- neurofeedback therapy
  - learning to up-regulate brain activation within the emotion network (amygdala, prefrontal cortex *etc.*)
  - 4 sessions (within 4 weeks)
  - one session = 3 runs (1h)



Linden, D.E.J., Habes, I., Johnston, S.J., Linden, S., Tatineni, R., Subramanian L., Sorger, B., Healy, D., Goebel, R. (2012) Real-time Self-regulation of Emotion Networks in Patients with Depression. *PLOS One*, **7**, e38115.

Neurofeedback therapy for patients with depression

Effect of the neurofeedback training on the reached brain activation level within the emotion network (group results)

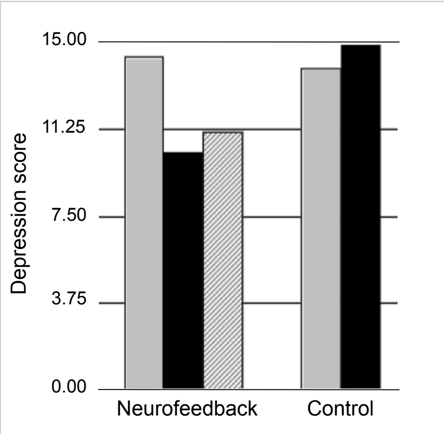


Linden, D.E.J., Habes, I., Johnston, S.J., Linden, S., Tatineni, R., Subramanian L., Sorger, B., Healy, D., Goebel, R. (2012) Real-time Self-regulation of Emotion Networks in Patients with Depression. *PLOS One*, **7**, e38115.

Neurofeedback therapy for patients with depression

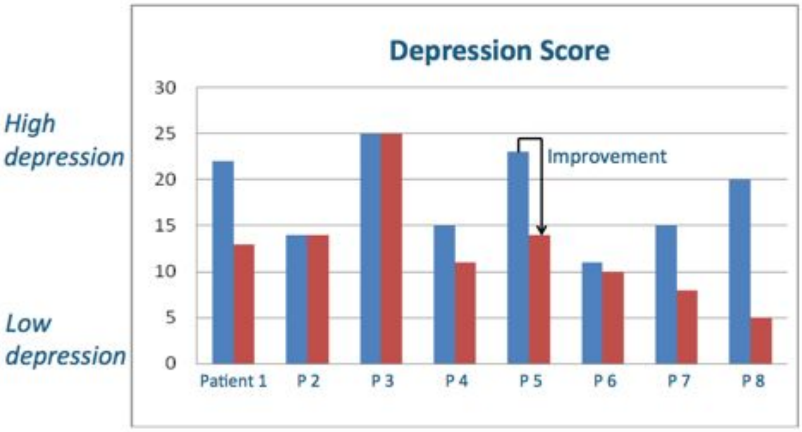
Behavioral effects of neurofeedback training after 4 sessions (HRSD score)

group results



- ☐ pre
- ■ post
- ▨ follow-up

single-subject results

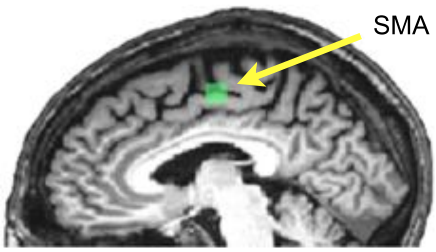


- pre
- post

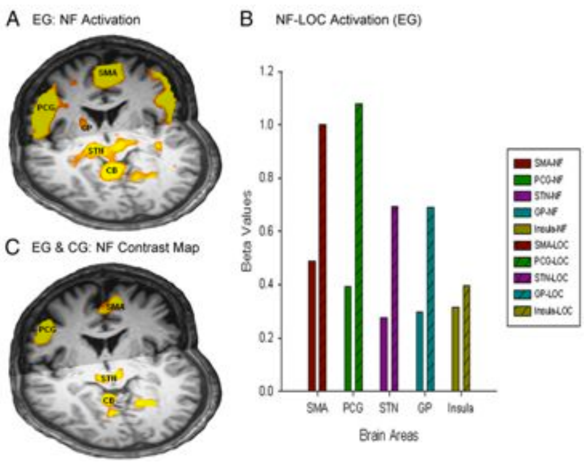
-> First clinical trial study in UK

Linden, D.E.J., Habes, I., Johnston, S.J., Linden, S., Tatineni, R., Subramanian L., Sorger, B., Healy, D., Goebel, R. (2012) Real-time Self-regulation of Emotion Networks in Patients with Depression. *PLOS One*, **7**, e38115.

Neurofeedback therapy for Parkinson patients



SMA - Neurofeedback target region



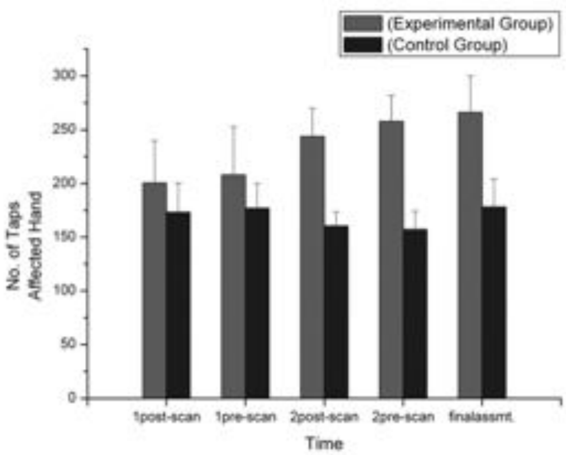


Figure 5. The functional improvement was apparent from the increase in finger-tapping frequency. Mean number of finger taps is shown for all sessions, with error bars showing the SD. Patients in the experimental group were able to increase the number of finger taps from session 1 to session 3 (the final assessment) ($p < 0.05$).

Subramanian, Hindle, Johnston, Roberts, Husain, Goebel, Linden (2011) *The Journal of Neuroscience*, **31**, 16309-16317.

Further application possibilities

- Chronic pain [deCharms *et al.*, 2005]
- Tinnitus [Haller *et al.*, 2009]
- Depression [Linden, Sorger, Goebel *et al.*, 2012)
- Movement disorders in Parkinson's disease [Linden, Goebel *et al.*, JNS, 2011]
- Movement disorders in Stroke patients [Luehrs, Goebel, collab. with Heidi Johansen-Berg, Oxford]
- Attention-Deficit/Hyperactivity Disorder (ADHD) [Zilverstand, collab. with Jan Buitelaar, Nijmegen]
- Schizophrenia - feedback of connectivity measures [basic research: Zilverstand, Goebel et al)
- Autism
- Psychopathy, antisocial behavior (Birbaumer group)
- Anxiety disorders, *e.g.*, spider phobia (Zilverstand, Sorger, Arntz, Goebel)
- Personality disorders
- Nicotine/drug dependence

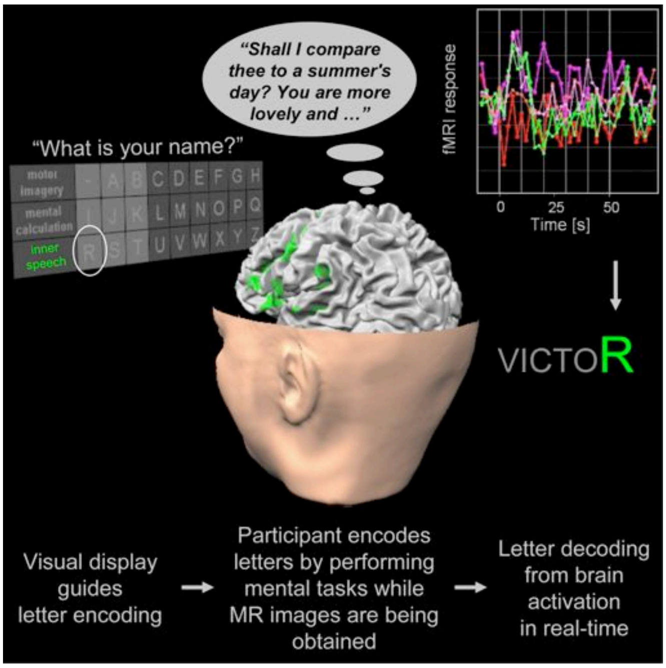
Needed

→ *more neuroscience research to define brain states correlating with the desirable mental states*

→ *extensive clinical trials with appropriate control groups and careful evaluation ('follow-up' studies, cost-benefit analyses)*

Online Decoding of Mental States

A Communication BCI for Patients with Severe Motor Impairments



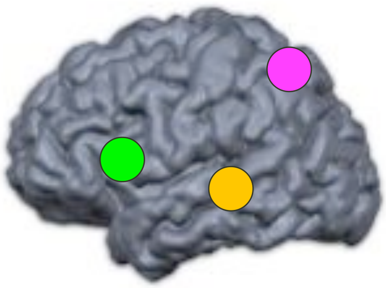
Sorger, B., Reithler, J., Dahmen, B. & Goebel, R. (2012). A Real-time fMRI-based Spelling Device Immediately Enabling Robust Motor-independent Communication. *Current Biology*, **22**, 1333-1338.
Research Highlight in *Nature*, **487**, 8.

A Communication Brain Computer Interface

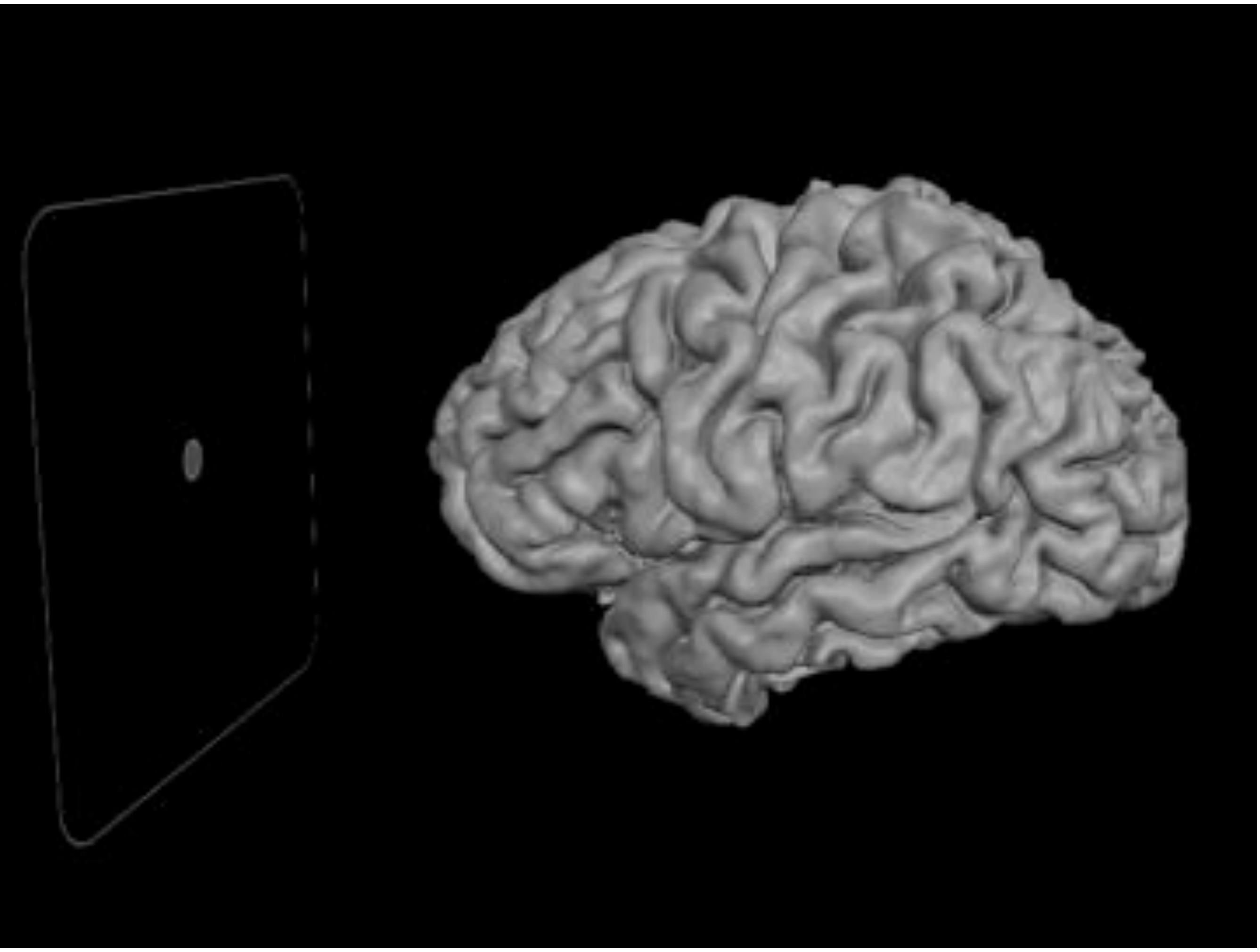
A novel multi-dimensional coding technique

Variation of:

a) 3 (simple) mental paradigms
(e.g. **inner speech**, **mental calculation**, **mental music**)



Sorger, Reithler, Damen & Goebel (2012), *Current Biology*, 22, 1333-1338.



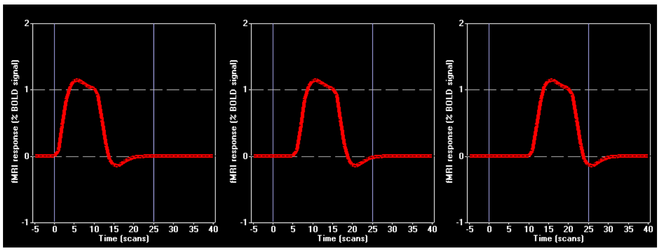
A Communication Brain Computer Interface

A novel multi-dimensional coding technique

Variation of:

a) 3 (simple) mental paradigms
(e.g. **inner speech**, **mental calculation**, **mental music**)

b) performance onset (0s, 10s, 20s)



Sorger, Reithler, Damen & Goebel (2012), *Current Biology*, 22, 1333-1338.

A Communication Brain Computer Interface

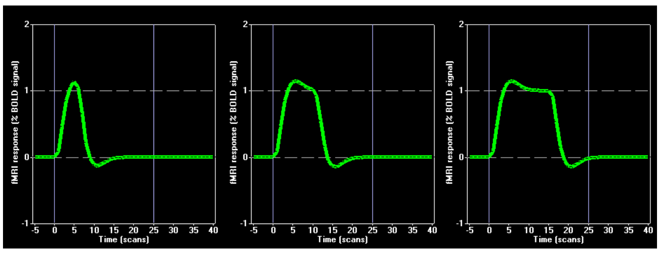
A novel multi-dimensional coding technique

Variation of:

a) 3 (simple) mental paradigms
(e.g. **inner speech**, **mental calculation**, **mental music**)

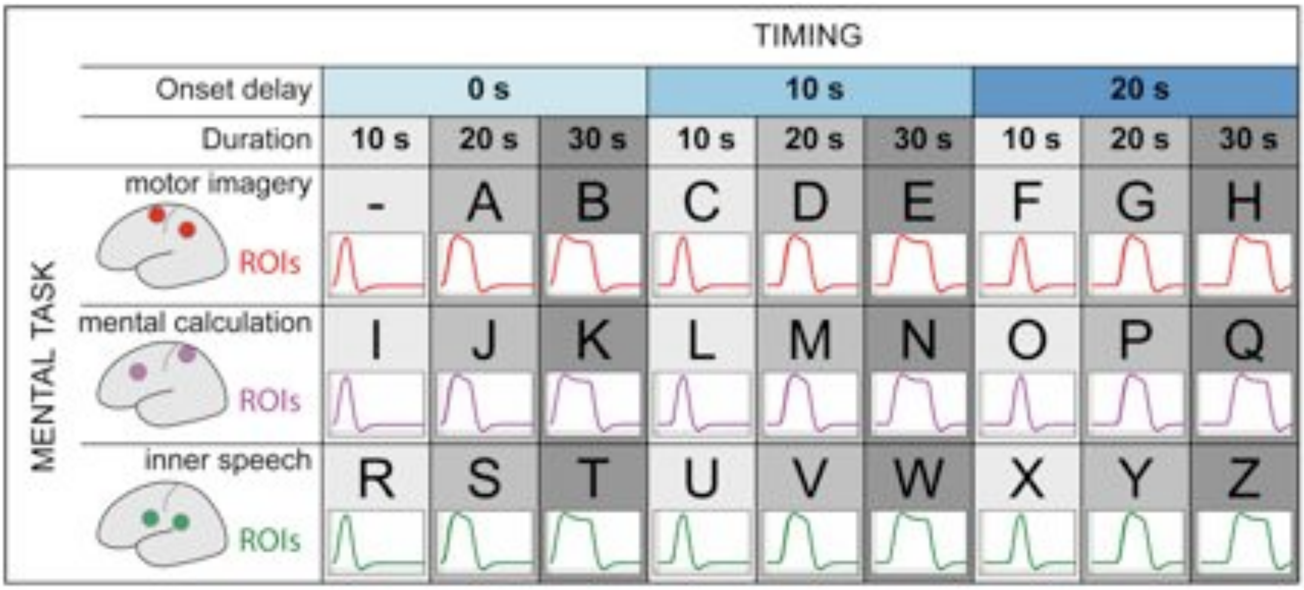
b) performance offset (0s, 10s, 20s)

c) performance duration (10s, 20s, 30s)



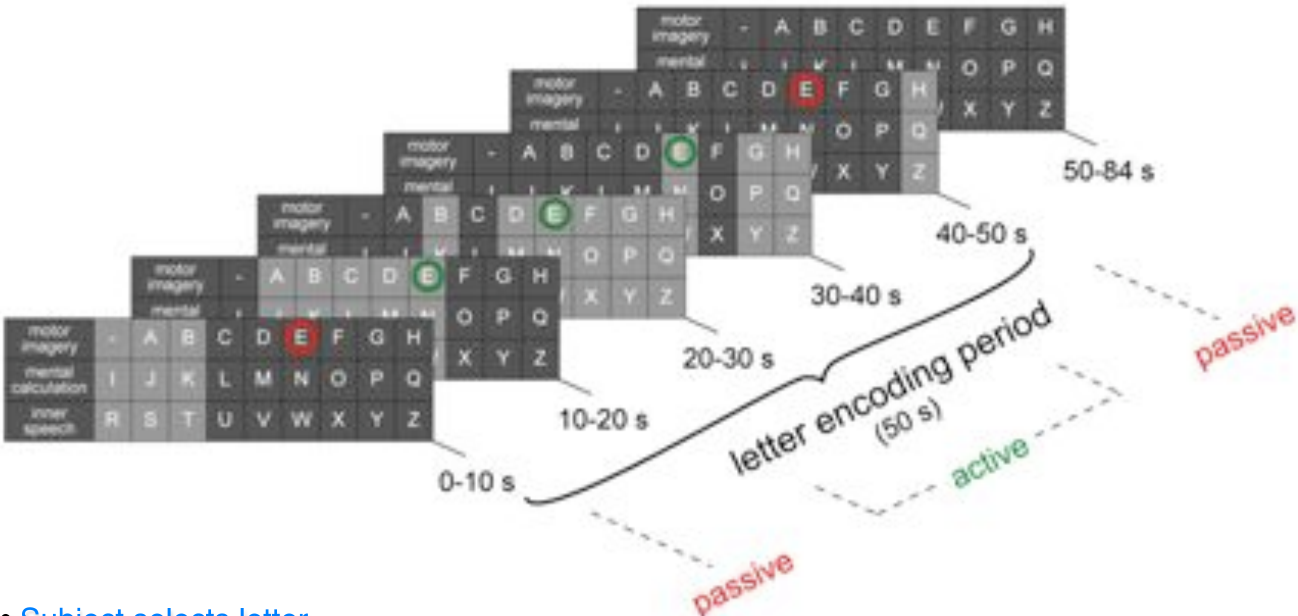
Sorger, Reithler, Damen & Goebel (2012), *Current Biology*, 22, 1333-1338.

A Communication Brain Computer Interface



Sorger, Reithler, Damen & Goebel (2012), *Current Biology*, 22, 1333-1338.

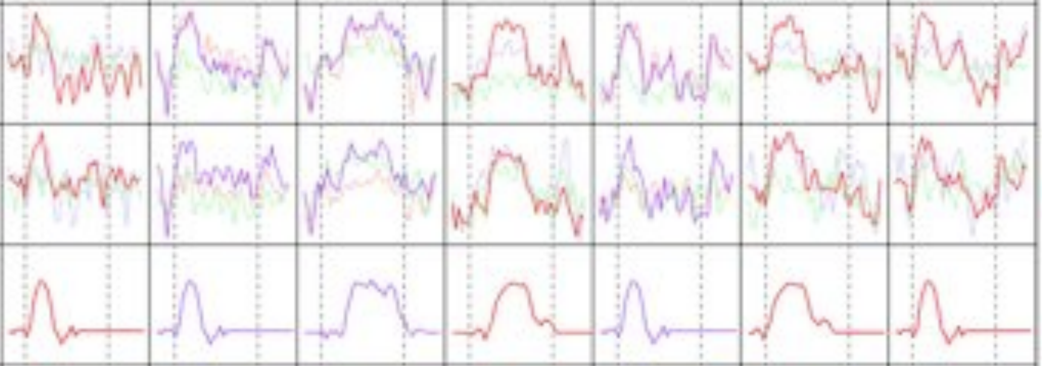
Easy-to-use instructive display



- Subject selects letter
- Row of letter determines task
- Task performed when letter is highlighted
  → BOLD shape

Sorger, Reithler, Damen & Goebel (2012), *Current Biology*, 22, 1333-1338.

A Communication Brain Computer Interface

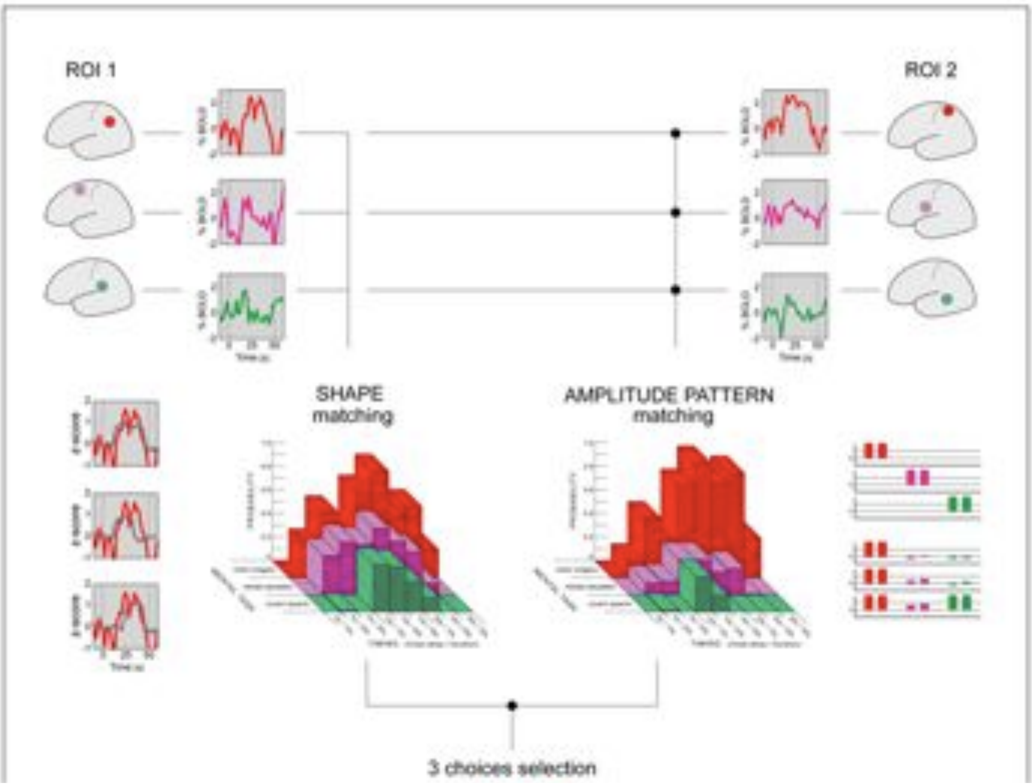


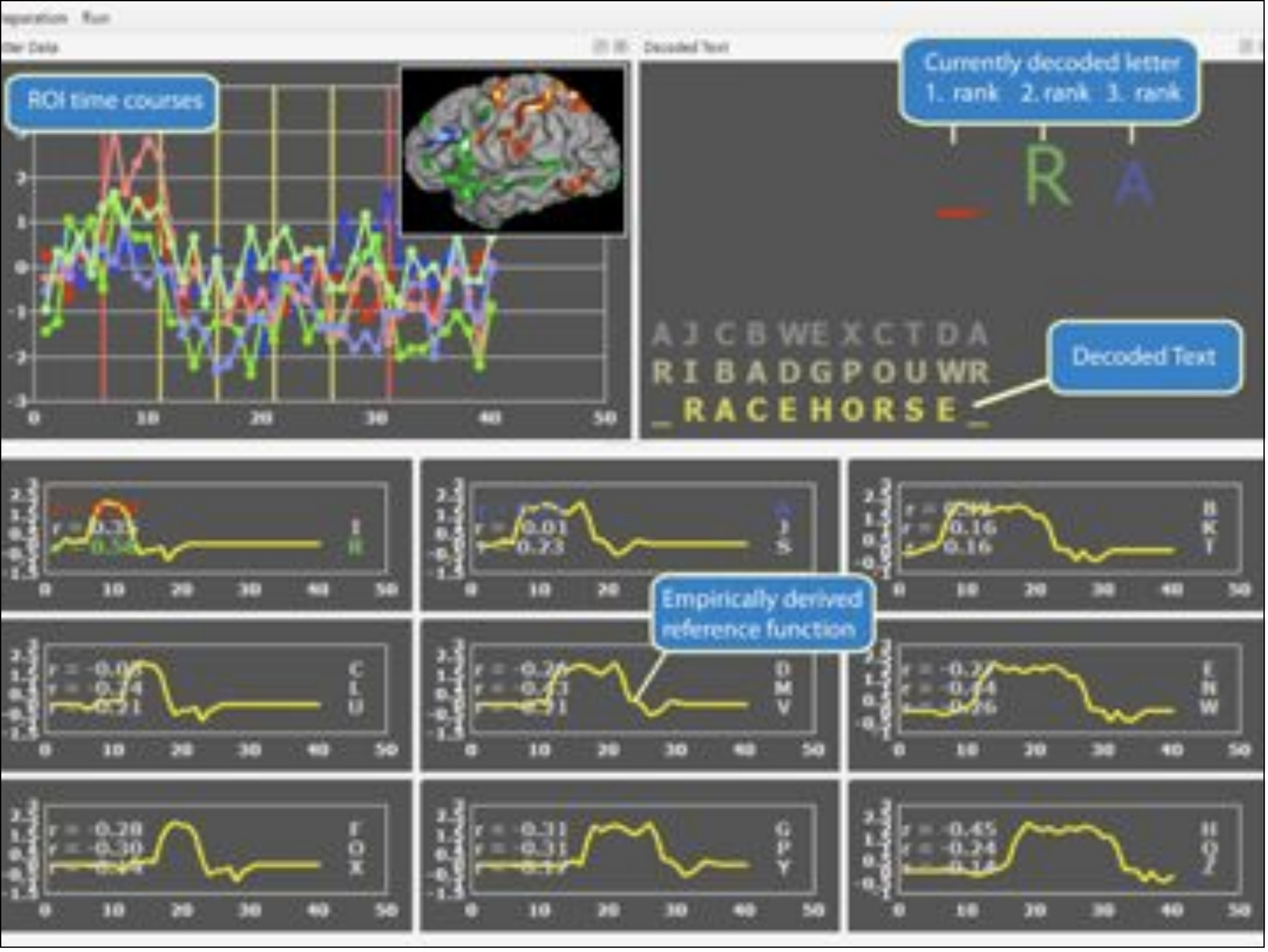
encoded answer	-	I	N	D	I	A	-
BOLD signals ('shape/pattern' ROIs)							
BOLD signals ('pattern only' ROIs)							
indRTC							
automated decoding (1st letter choice)	-	I	N	D	I	A	-

Sorger, Reithler, Damen & Goebel (2012), *Current Biology*, 22, 1333-1338.

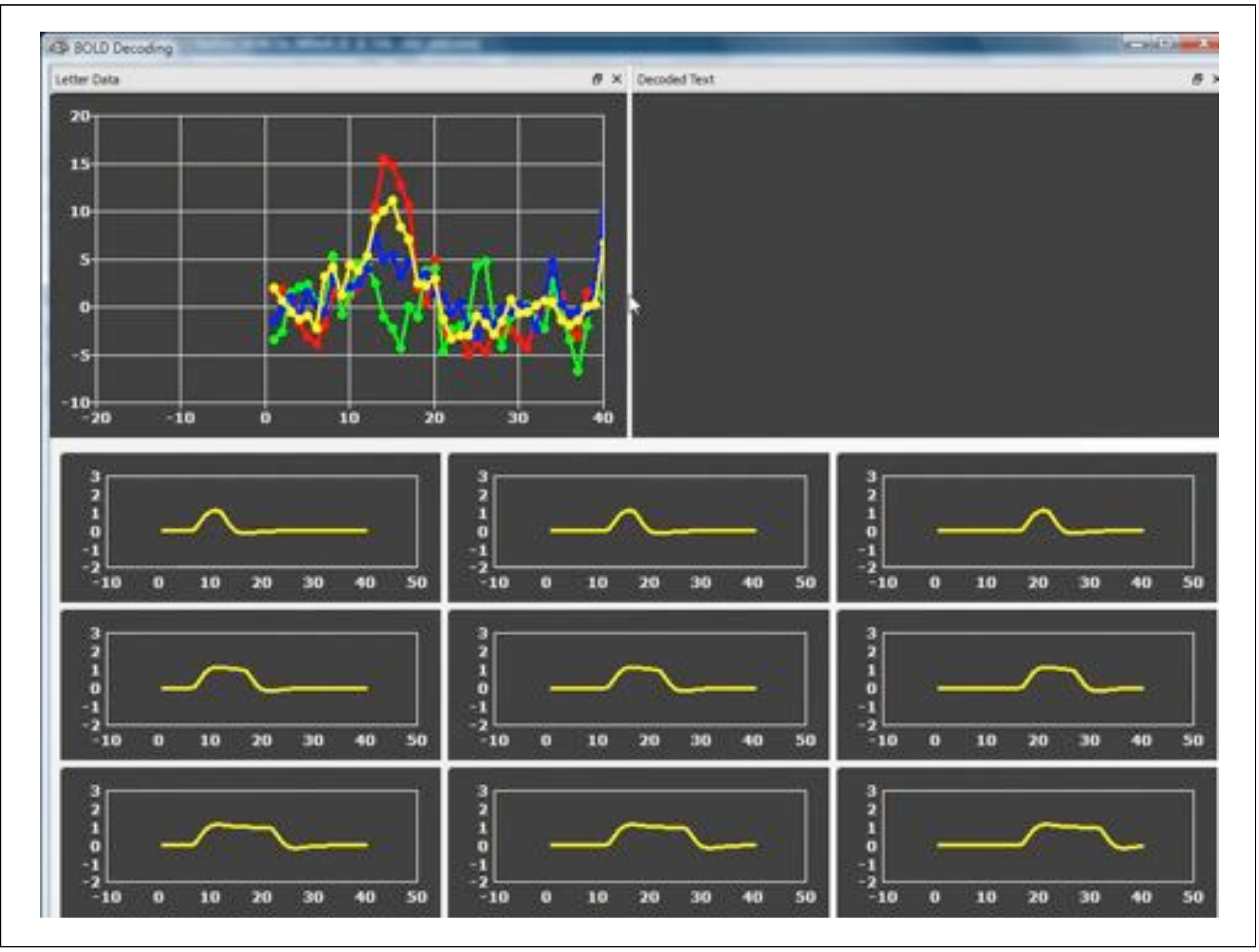
Communication BCI - Automatic Decoder

Sorger et al (2012). *Current Biology*, in press.




ROI time courses
Currently decoded letter
1. rank 2. rank 3. rank
_ R A
A J C B WE X C T D A
R I B A D G P O U WR
_ R A C E H O R S E _
Decoded Text
Empirically derived reference function

43


BOLD Decoding
Letter Data
Decoded Text

44

“BOLD” Conversations

Sorger et al (submitted)

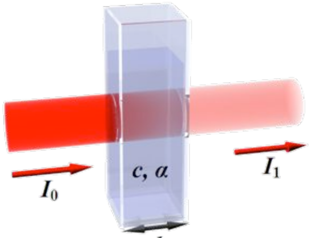
participant	'initial' question		'follow-up' question	
	stated question	decoding output/ human interpreter's decision	stated question	decoding output/ human interpreter's decision
1	"What is your hobby?"	- P H O T O G R A P H Y - O G M X X E I C N O W R R N E P S V H S - Y Z X I I - P H O T O G R A P H Y -	"What did you PHOTOGRAPH last?"	- O Y - H O M E - R M W R Z M O G R A T Z S G V T W A - M Y - H O M E -
2	"Where did you spend your most recent vacation?"	- I N D C N E R C A - A F O F M M O S I - A I R O G O O F J O C B - I N D O N E S I A -	"What did you like most in INDONESIA?"	- T E K P L E S - I R G M X U O J I A S O L Q M G R A - T E M P L E S -
3	"Where did you spend your most recent vacation?"	- I N D I A - S - E B - C A U A M E A B B - I N D I A -	"What do you consider most typical for INDIA?"	- C L O S H I N G - A A J X T G R M E A R O U P R E A V D R - C L O T H I N G -
4	"What is your hobby?"	- O R S C U S R R N G - R C I T O S U S I P E R A B - R S T R U F M F I - D I S C U S S I N G -	"What is your favorite DISCUSSION topic?"	- A W Y T H I N G - A - N Z S O R P E I B K P M Y Z J W H A - A N Y T H I N G -
5	"What are you interested in?"	- X O V I D R A V M U R E S I M X W - N J - M O V I E S	"Which MOVIE did you watch last?"	T O P F U N - V X N N L M I U Y O G J P A T O P G U N -

From fMRI to fNIRS

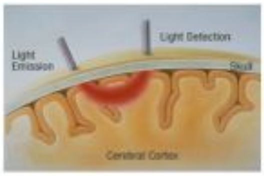
Towards a Mobile Hemodynamic Communication BCI

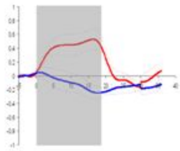
Multi-Channel Functional Near-Infrared Spectroscopy (fNIRS) (Part of DECODER EU Project)

Illustration of near infrared wavelengths traveling through human tissue



Beer-Lambert Law allows to calculate change in concentration





Like fMRI, fNIRS measures changes in oxygenated and deoxygenated blood

- Transfer previously gained knowledge with real-time fMRI to build advanced fNIRS BCI system
- Bootstrap placement of optodes by fMRI scan
- Goal: Affordable Communication BCI at patient bedside (Project in EU "*DECODER*" grant)
- First measurements using same paradigms as in fMRI BCI are very promising

Functional Near-Infrared Spectroscopy (fNIRS)

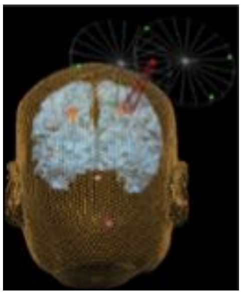
GLM Analysis (Oxy-Hg Concentration)

fNIRS Communication BCI

Comparison with fMRI / Learning from fMRI

- Advantages: Mobile, reduced costs as compared to fMRI
- Disadvantages: Limited brain coverage and low spatial resolution prevent selection of “deep” ROIs.
- Does not provide good signals in all subjects -> Multi-modal approach: Use fMRI to optimally place optodes

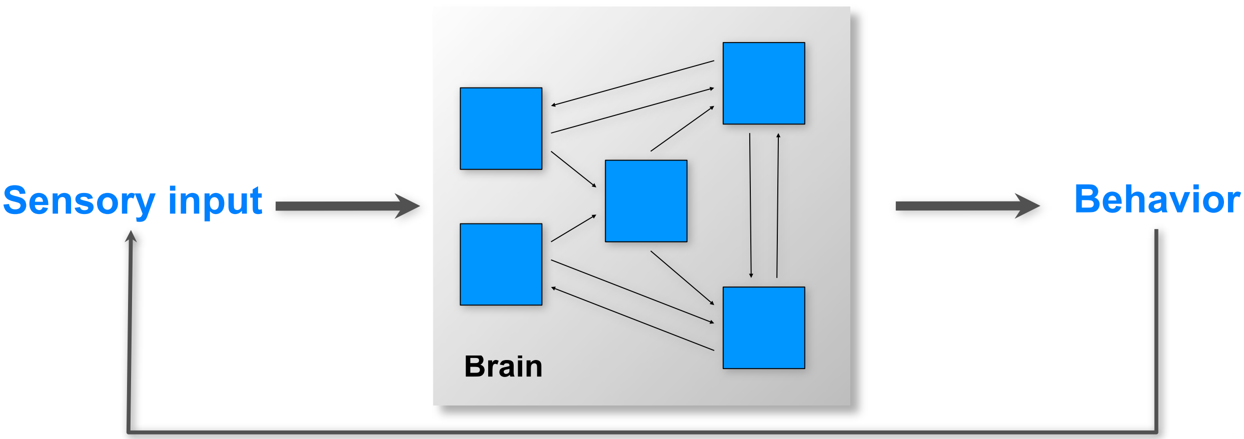
Neuronavigated optode placement



fMRI

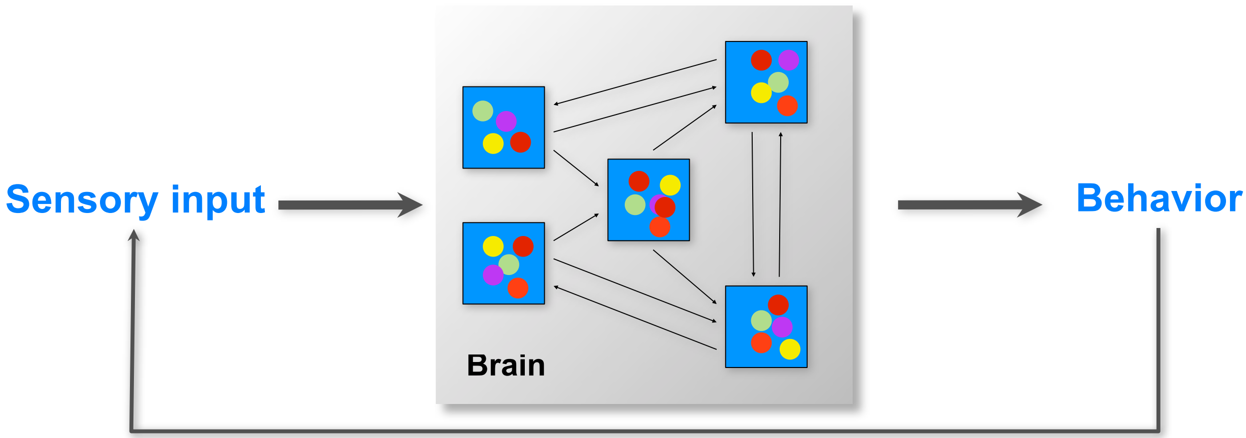
fNIRS

Functional Organization of the Brain
Level I: Specialized Areas and Large-Scale Networks



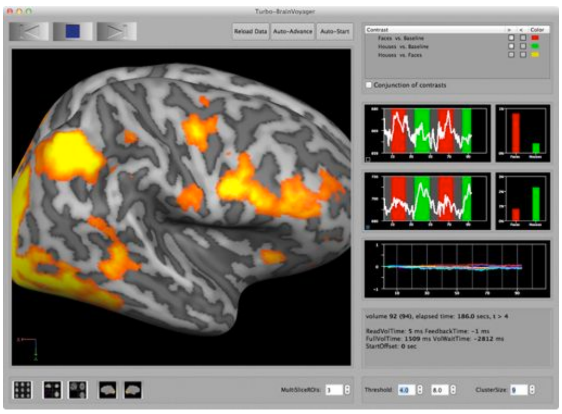
- **What are elementary mental/neural functional components?** Understand representations and processes in “modules of the mind” and how they are embedded in areas and networks of the brain.
- **How do basic components interact and unfold over time?** Understand communication between brain regions, i.e. direction of information flow (anatomical and effective connectivity).

Functional Organization of the Brain
Level II: Features Coded Within Specialized Areas



- **What are elementary mental/neural functional components?** Understand representations and processes in “modules of the mind” and how they are embedded in areas and networks of the brain.
- **How do basic components interact and unfold over time?** Understand communication between brain regions, i.e. direction of information flow (anatomical and effective connectivity).

Current Resolution of fMRI Relates to Functional Organization Level I



Answers important questions such as:

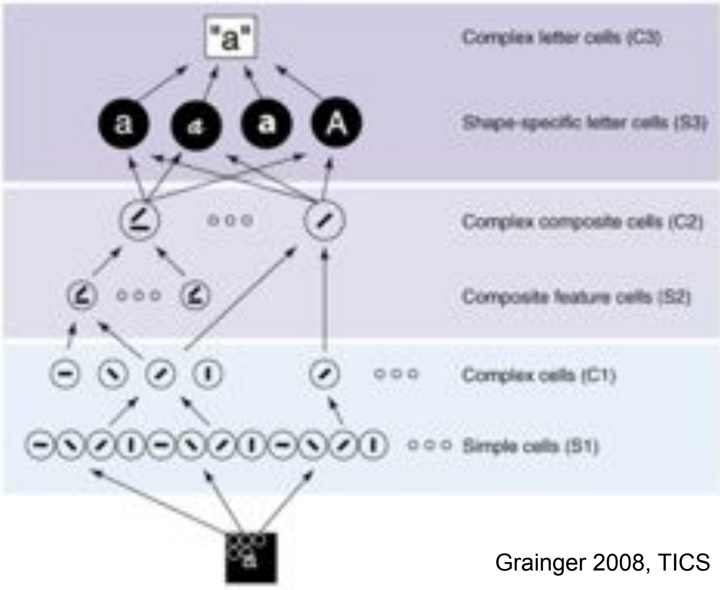
- Which areas contribute to reading?
- Is the fusiform face area (FFA) more active when presenting happy vs neutral faces?
- Can activity fluctuations in resting state networks be used to characterize brain states as biomarkers for diseases?

How Does the Brain Perform Cognitive Functions?

Questions such as:

- How is a specific face identified?
- How is reading possible, e.g. how does the brain recognizes letter “a”?

In principle, we ***can*** provide answers to such questions e.g. with neural network models ***but*** we do not know the features and connections used by the brain!



Grainger 2008, TICS

This leads to the following ***challenging goals for brain research***:

- Reveal what features are coded within specialized brain areas!
- Reveal how features are connected within and across areas!

Example: Feature Decoding with MVPA

“Who” Is Saying “What”? Brain-Based Decoding of Human Voice and Speech

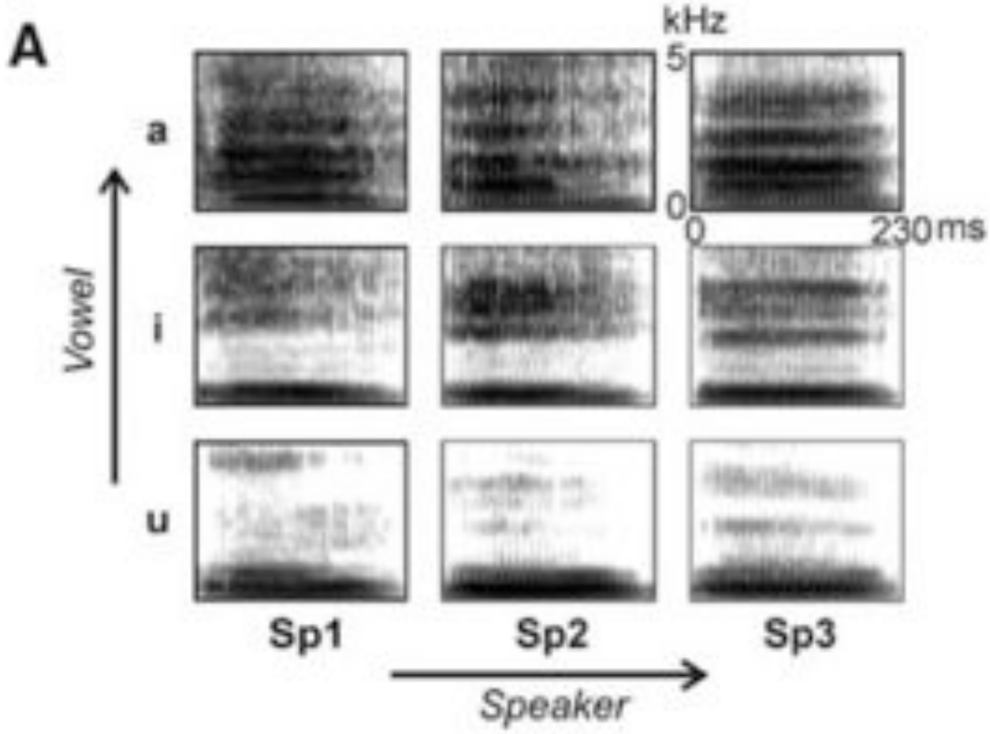
Elia Formisano,* Federico De Martino, Milene Bonte, Rainer Goebel

Can we decipher speech content (“what” is being said) and speaker identity (“who” is saying it) from observations of brain activity of a listener? Here, we combine functional magnetic resonance imaging with a data-mining algorithm and retrieve what and whom a person is listening to from the neural fingerprints that speech and voice signals elicit in the listener’s auditory cortex. These cortical fingerprints are spatially distributed and insensitive to acoustic variations of the input so as to permit the brain-based recognition of learned speech from unknown speakers and of learned voices from previously unheard utterances. Our findings unravel the detailed cortical layout and computational properties of the neural populations at the basis of human speech recognition and speaker identification.

In everyday life, we automatically and effortlessly decode speech into language independently of who speaks. Similarly, we recognize a speaker’s voice independently of what she or he says. Cognitive and connectionist models postulate that this efficiency depends on the ability of our speech perception and speaker identification systems to extract relevant features from the sen-

7 NOVEMBER 2008 VOL 322 SCIENCE www.sciencemag.org

Factorial Design: Two Classifiers

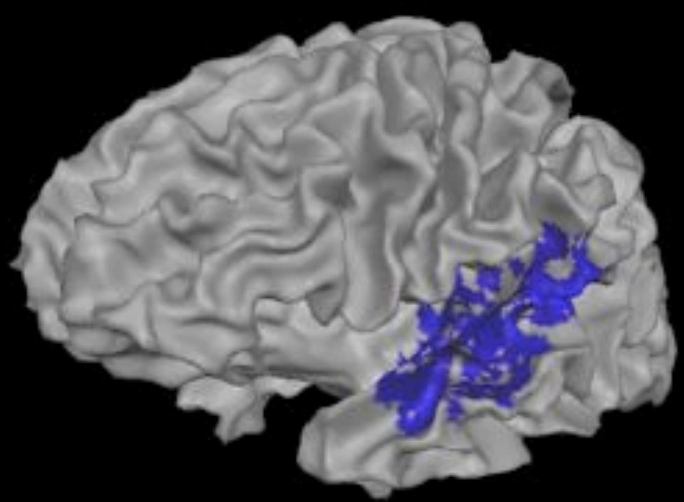


55

Recursive Feature Elimination

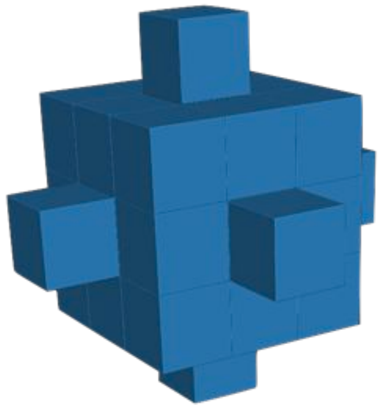
Level 1

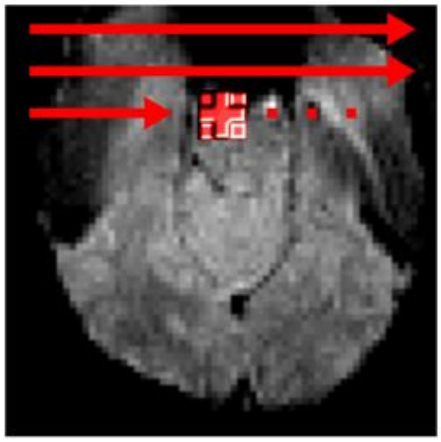
Correctness = 0.65



56

The Searchlight MVPA Approach
Detecting distributed feature content within specialized areas using *locally multivariate mapping*



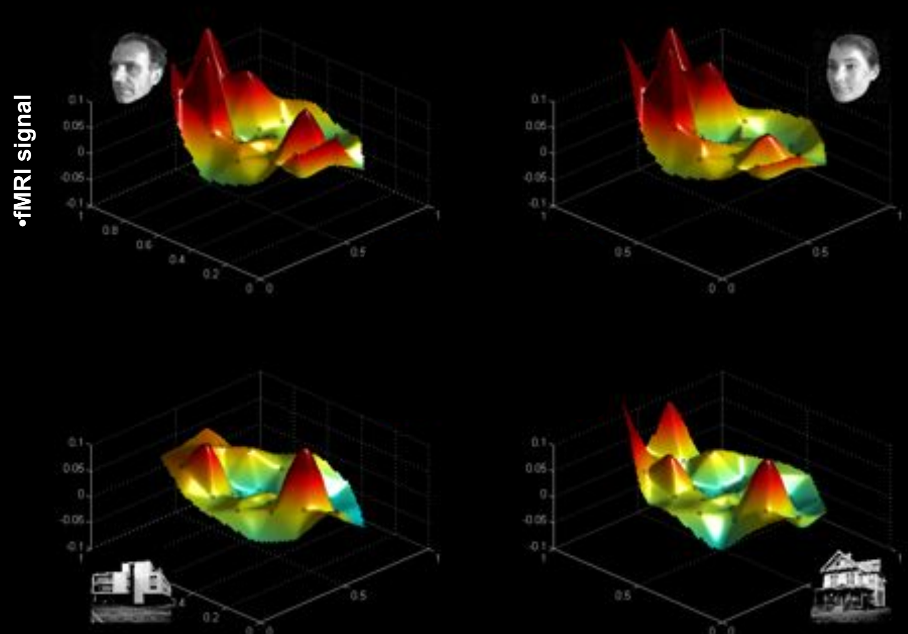


Kriegeskorte, Goebel, Bandettini (2006). Information-based functional brain mapping. *PNAS*, **103**, 3863-3868.

Kriegeskorte, Formisano, Sorger, Goebel (2007). Individual faces elicit distinct response patterns in human anterior temporal cortex. *PNAS*, **104**, 20600-20605.

Fusiform face region (FFA): pattern effects

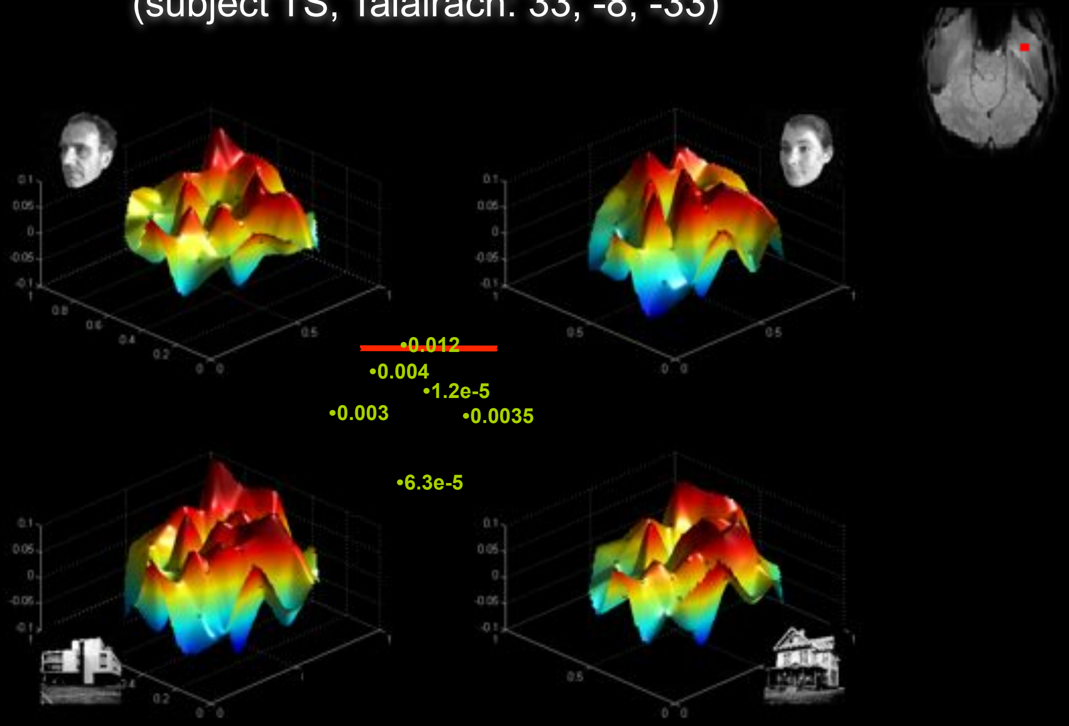
•run B



Subject DP, right hemisphere, 7T slow event-related experiment, MANCOVA test

Anterior inferotemporal face-exemplar region

(subject TS, Talairach: 33, -8, -33)



Prewhitened, fisherAtestB: double-sided test and info estimate

From MVPA to Direct Feature Mapping

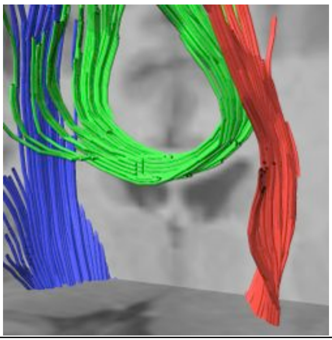
- Multivariate pattern analysis (as well as the adaptation paradigm) provide **indirect** information about coded features within specialized brain areas.
- While one can learn something about spatial distribution of decoded information by inspecting voxel weights (when using linear kernels), classifiers are mainly treated as “**black boxes**”.
- Is it possible to **directly map** the features within specialized brain areas? This would:
  - ★ help link neuroimaging closer to (animal) electrophysiology
  - ★ offer the potential to unravel unknown feature codes in human cortex
  - ★ could provide *compositionality*, i.e. understanding entity representations of *new* stimuli from patterns with known features
  - ★ offer the potential to gain insight in putative differences in feature coding in disorders (e.g. dyslexia)

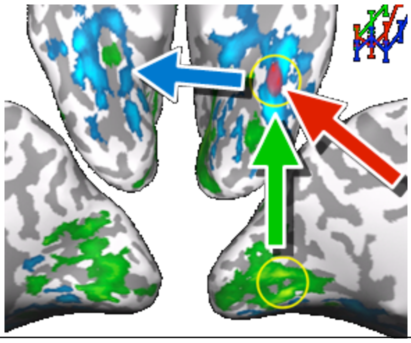
Possibilities of Ultra-High Fields for Cognitive Neuroscience: Only "*more of the same*"?

What many cognitive neuroscientists expect from 7T⁺ (f)MRI (in analogy to the move from 1.5 to 3 Tesla):

- Higher sensitivity to detect specific response profiles of **specialized areas**
- Improved diffusion-weighted imaging data and analysis to visualize connections **between areas** (connectome)
- Improved effective connectivity **between areas**

DTI



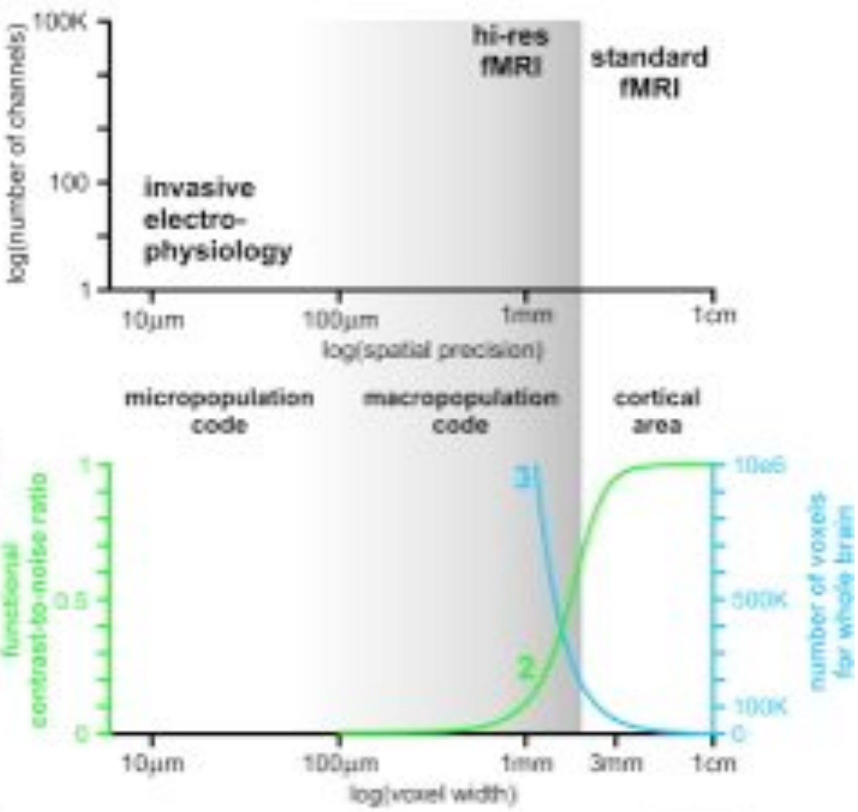


Effective Connectivity

fMRI

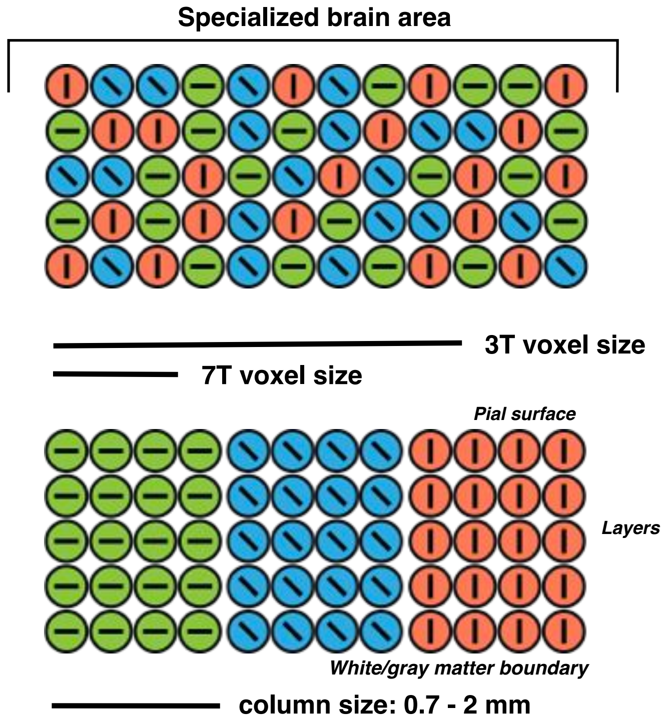
Ultra-high field MRI – New possibilities

Bridging the gap between the micro- and macro view of the brain

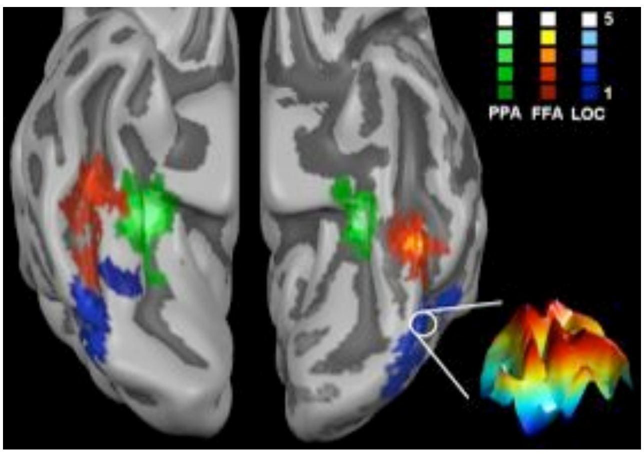


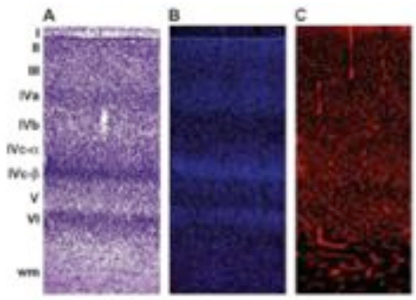
When a Quantitative Improvement of Resolution Turns into a Qualitative Change

- **Individual neurons** code features but they are **too small** to be detected with high-resolution human fMRI.
- If **neurons** would be **distributed randomly**, ultra-high field imaging would provide only quantitative improvement.
- If neurons **cluster into functional units**, we might be able to reveal fine-grained "neuron-like" representations.
- There is indeed substantial evidence that the (whole?) cortex is organized in vertically extending **columns** that contain neurons with rather similar response profiles.



Unraveling Feature Coding:
Towards Columnar-Level fMRI





Weber et al., 2008

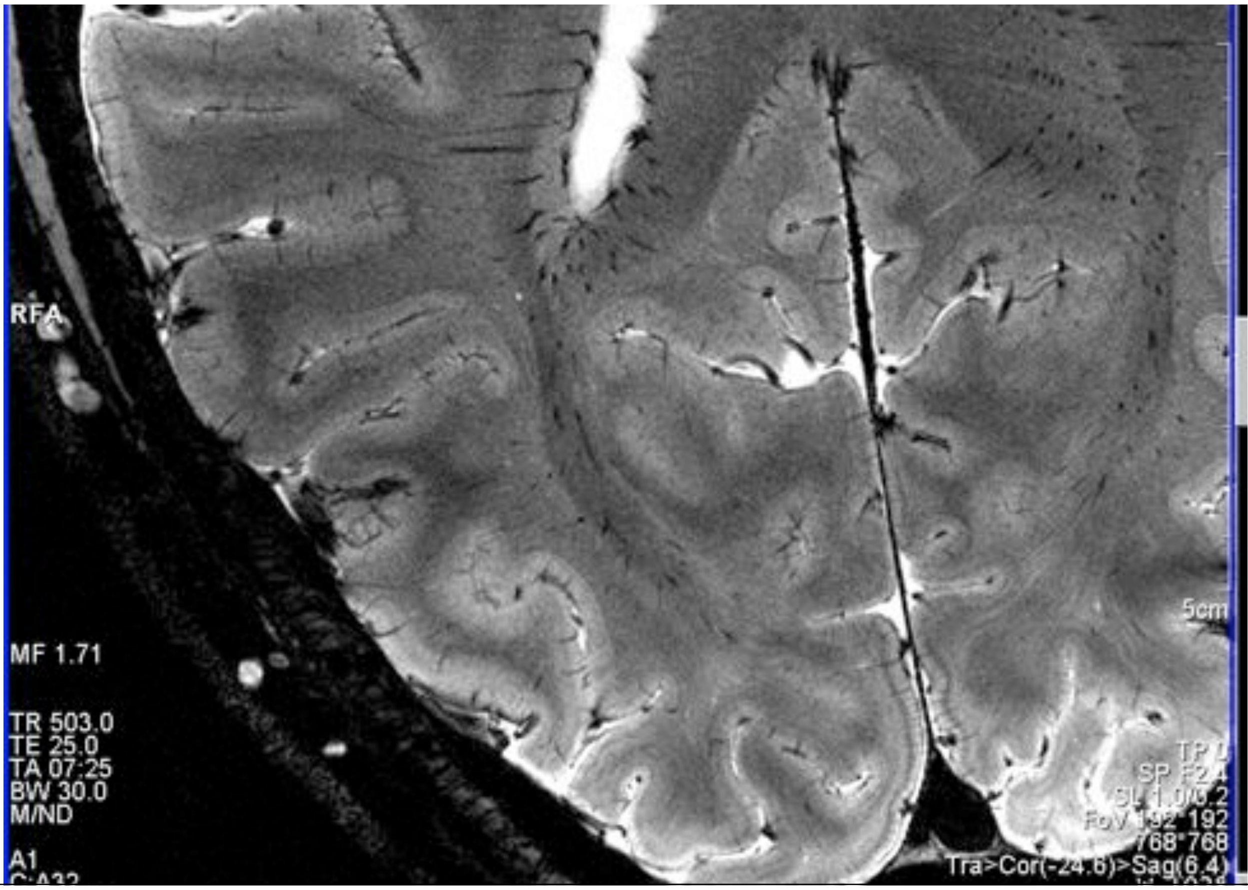
European Research Council (ERC) Advanced Investigators Grant:
"Cracking the columnar-level code in the visual hierarchy: Ultra high-field functional MRI, neuro-cognitive modelling and high-resolution brain-computer interfaces"

May 29 2012: 3T Arrived

July 12 2012: 7T (June 14 2012: 7T Arrived)

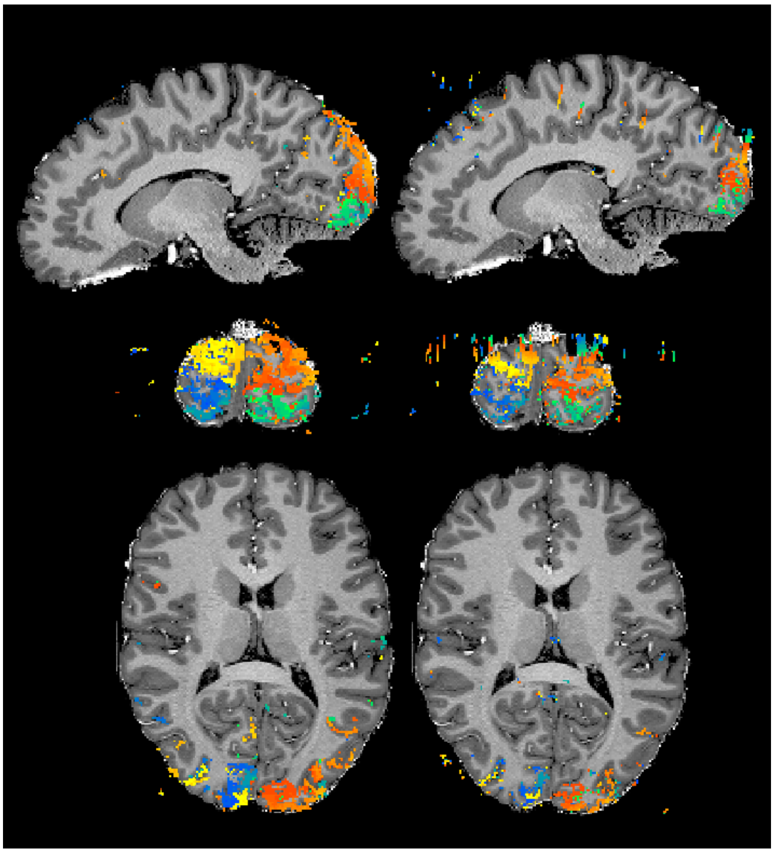
May 2013: 9.4T

First Images from Maastricht 7T



67

First Retinotopic Data at Maastricht 7T Scanner



Polar angle mapping

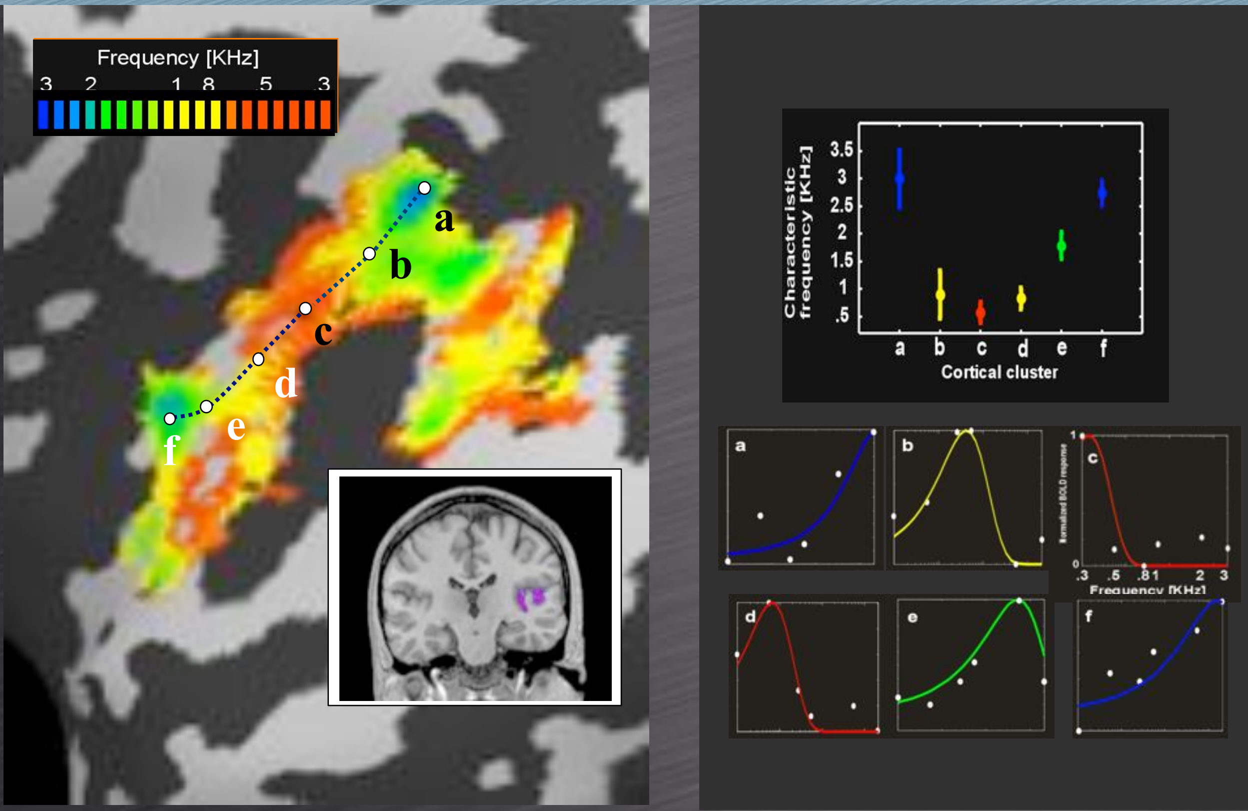
Using parallel imaging and multi-band MR pulse sequence

1.1 mm isotropic GRAPPA 2 MB 2   0.8 mm isotropic GRAPPA 2 MB 3

68

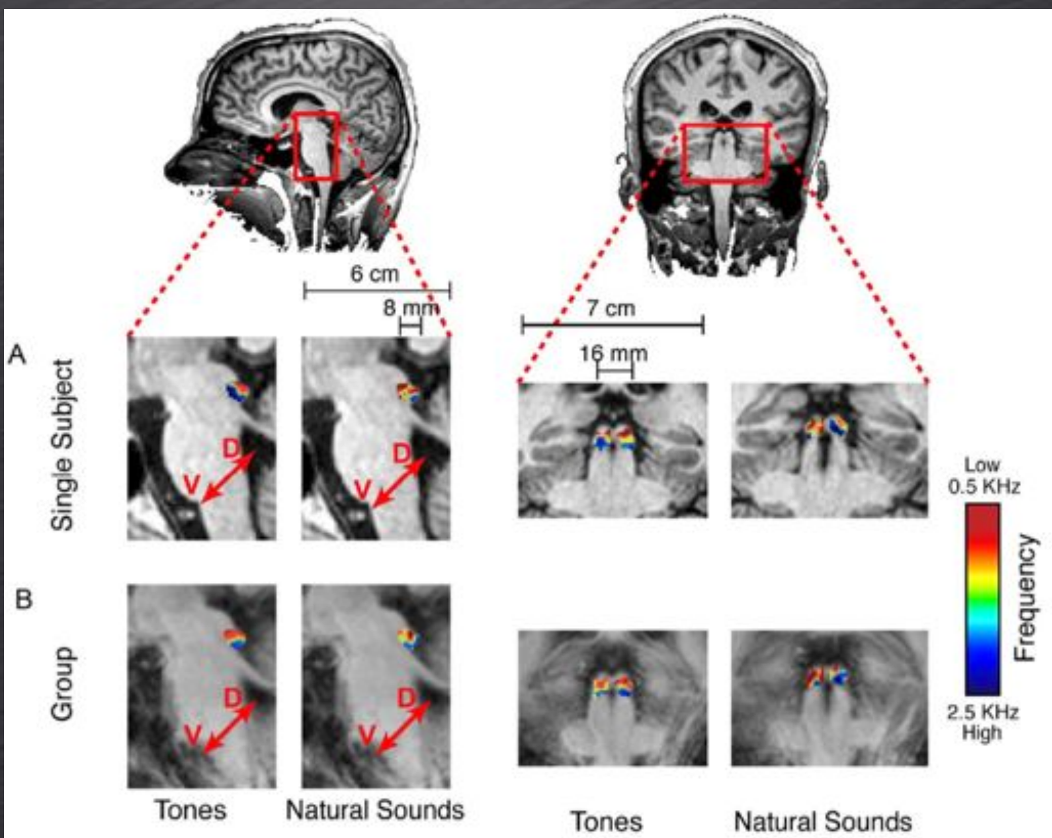
fMRI of the Auditory Cortex at 7 Tesla

Results: Mirror-Symmetric Tonotopic Maps



Formisano, Kim, Di Salle, van de Moortele, Ugurbil, Goebel (2003), *Neuron*, **40**, 859-869.

Tonotopy in the Inferior Colliculus @ 7 T



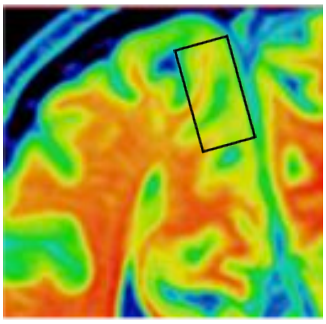
DeMartino, Moerel, van de Moortele, Ugurbil, Goebel, Yacoub, Formisano (2013). Spatial organization of frequency preference and selectivity in the human inferior colliculus. *Nature Communications*, **4**, 1386.

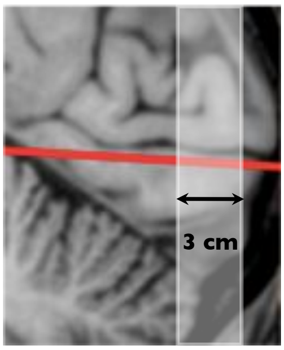
Investigation of Columnar-Level Organization in Humans Using fMRI at Ultra-High Magnetic Fields

High-resolution fMRI provides the unique opportunity to investigate these basic computational units in the human brain.

Columns have been imaged non-invasively in the human primary visual cortex (V1) lying within selected subjects flat calcarine sulci.

Single thick slices with high in plane resolution (0.5 mm) were prescribed to anatomically identified calcarine sulcus due to limitations of inner-volume SE-EPI.

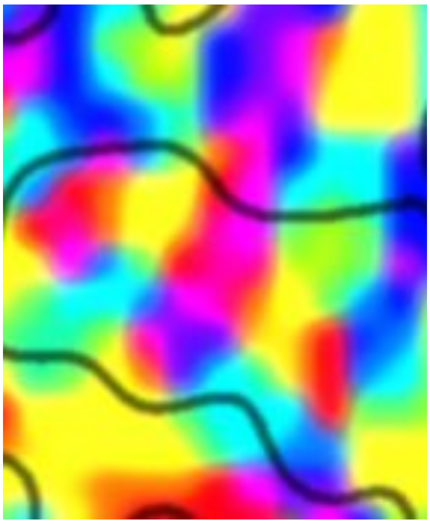




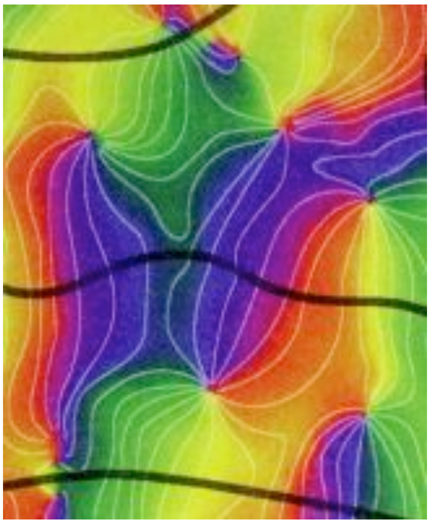
Yacoub, Harel, Ugurbil (2008) *Proc Natl Acad Sci USA,* **105**, 10607-10612.

High-Resolution fMRI Reveals Orientation Columns in V1

Human - fMRI (SE, 7T)



Monkey - Optical Imaging

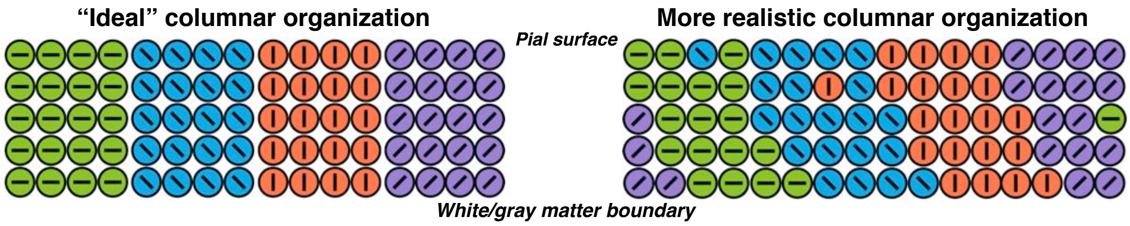


A seminal paper: Yacoub, Harel, Ugurbil (2008) *Proc Natl Acad Sci USA,* **105**, 10607-10612.

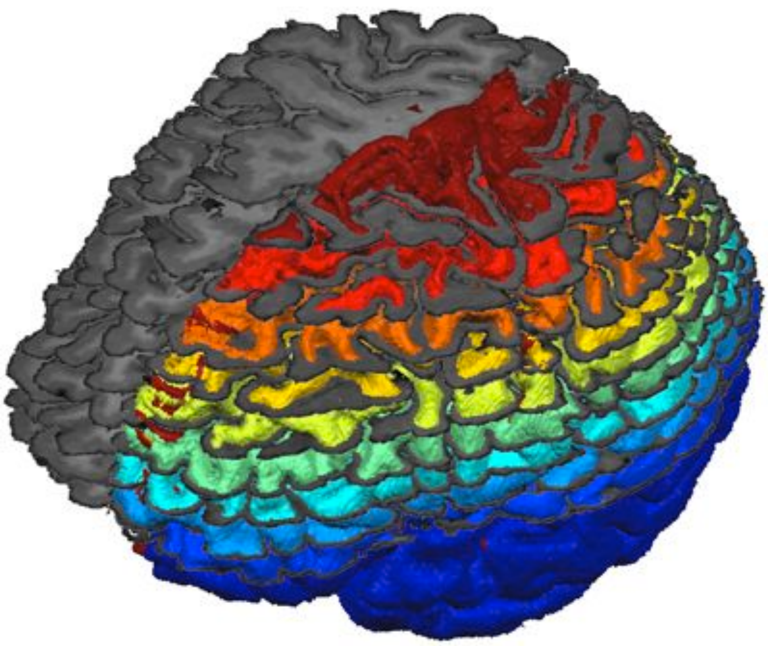
Mapping of the (larger) ocular dominance columns had already been reported earlier (e.g. Cheng et al., 2001; Goodyear and Menon, 2001; Yacoub et al., 2007) but this was the first study revealing detailed maps of the much smaller orientation columns!

Columnar-Level Features At Different Relative Cortical Depth Levels

- The classical model of a cortical column assumes a nearly perfect vertical penetration through the cortex.
- It has been, however, shown that in areas of monkey IT cortex columns do show strong irregularities across different layers (e.g. Keiji Tanaka, 2011)
- To reveal how feature codes eventually change across cortical laminae, it is important to map the topography of features within specialized areas at different relative cortical depth levels.
- We developed two methods to sample topographic information at different cortical depth levels: 1) based on reconstructed cortex meshes (see also Polimeni et al., 2010), and 2) with a novel regular-grid sampling technique.



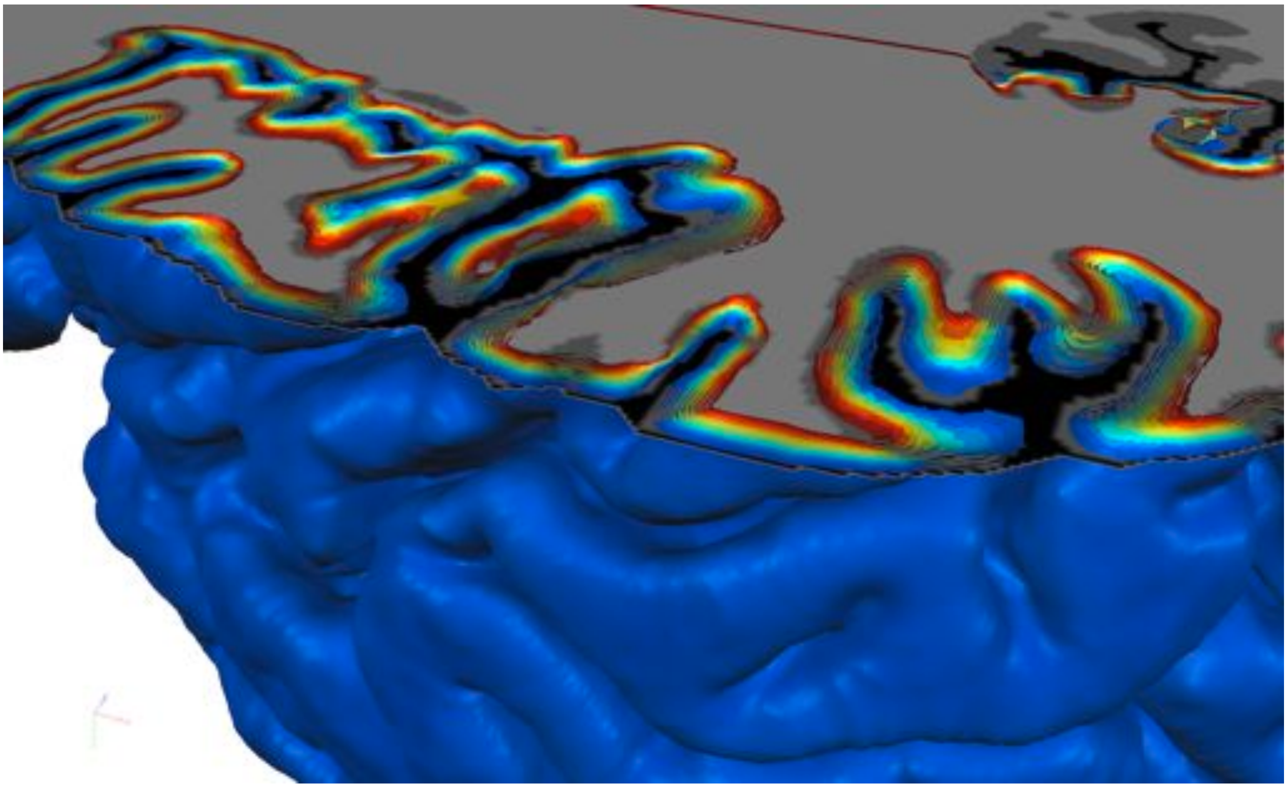
Whole-Cortex Mesh-Based Sampling At Multiple Cortical Depth Levels



- 10 meshes (left hemisphere) at different **relative cortical depth levels**:
  0.05 (dark red)
  0.15 (light red)
  :
  0.85 (light blue)
  0.95 (dark blue).
- Each high-resolution mesh (1.2 million triangles with 0.5 mm edge length) samples high-resolution (whole-brain) map data at specific depth level.

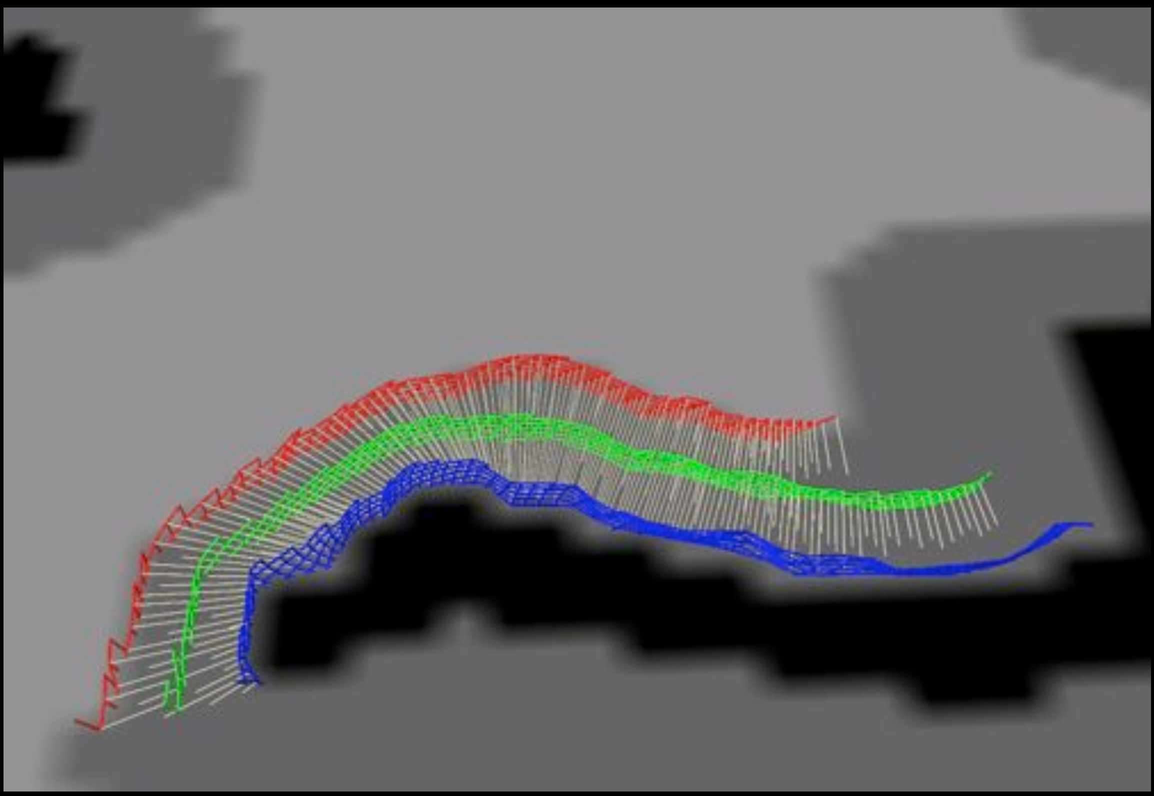
See also Polimeni et al. (2010) for a similar approach

Whole-Cortex Mesh-Based Sampling At Multiple Cortical Depth Levels

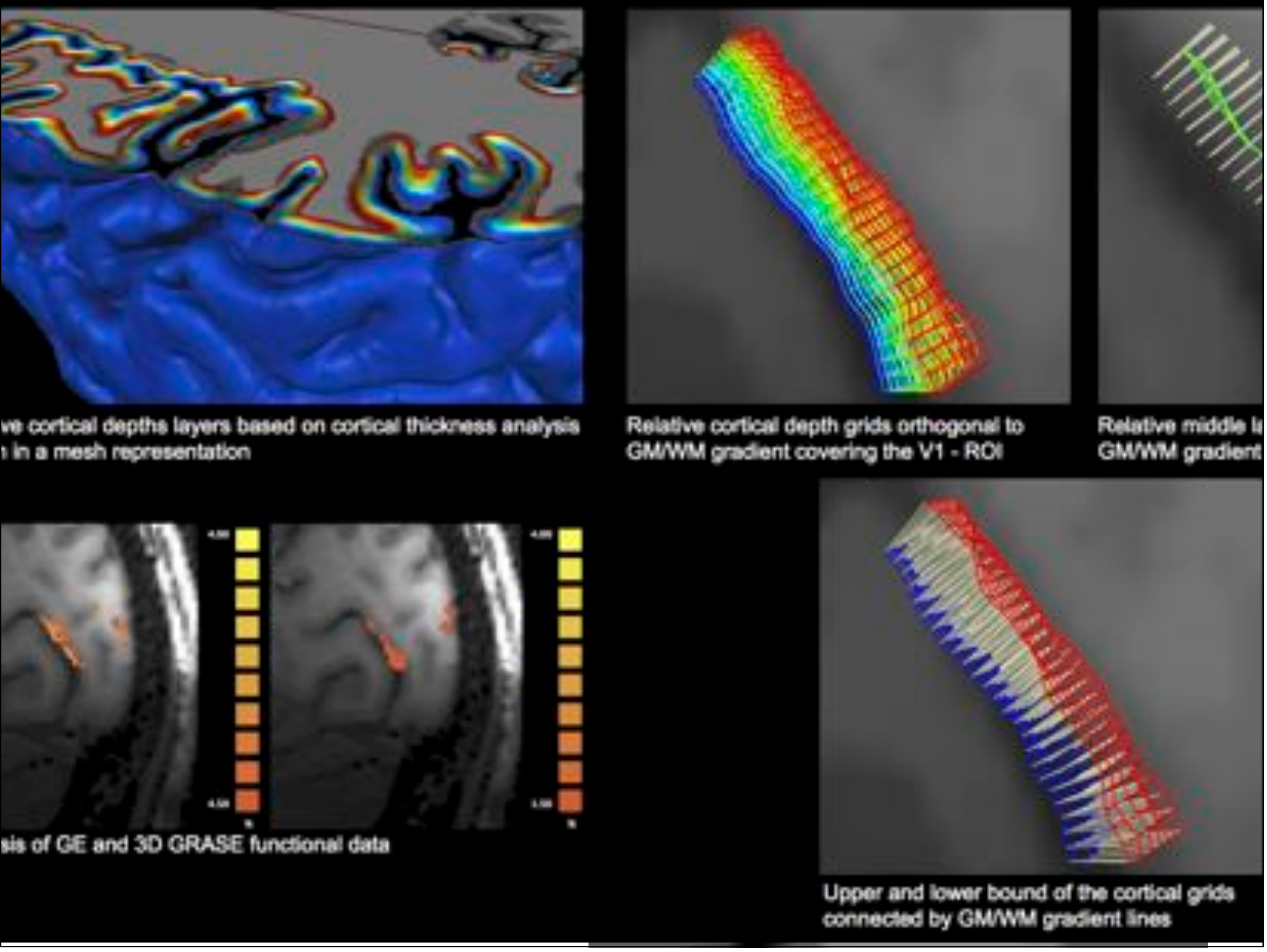


75

High-Resolution 2D Grid Sampling At Multiple Cortical Depth Levels

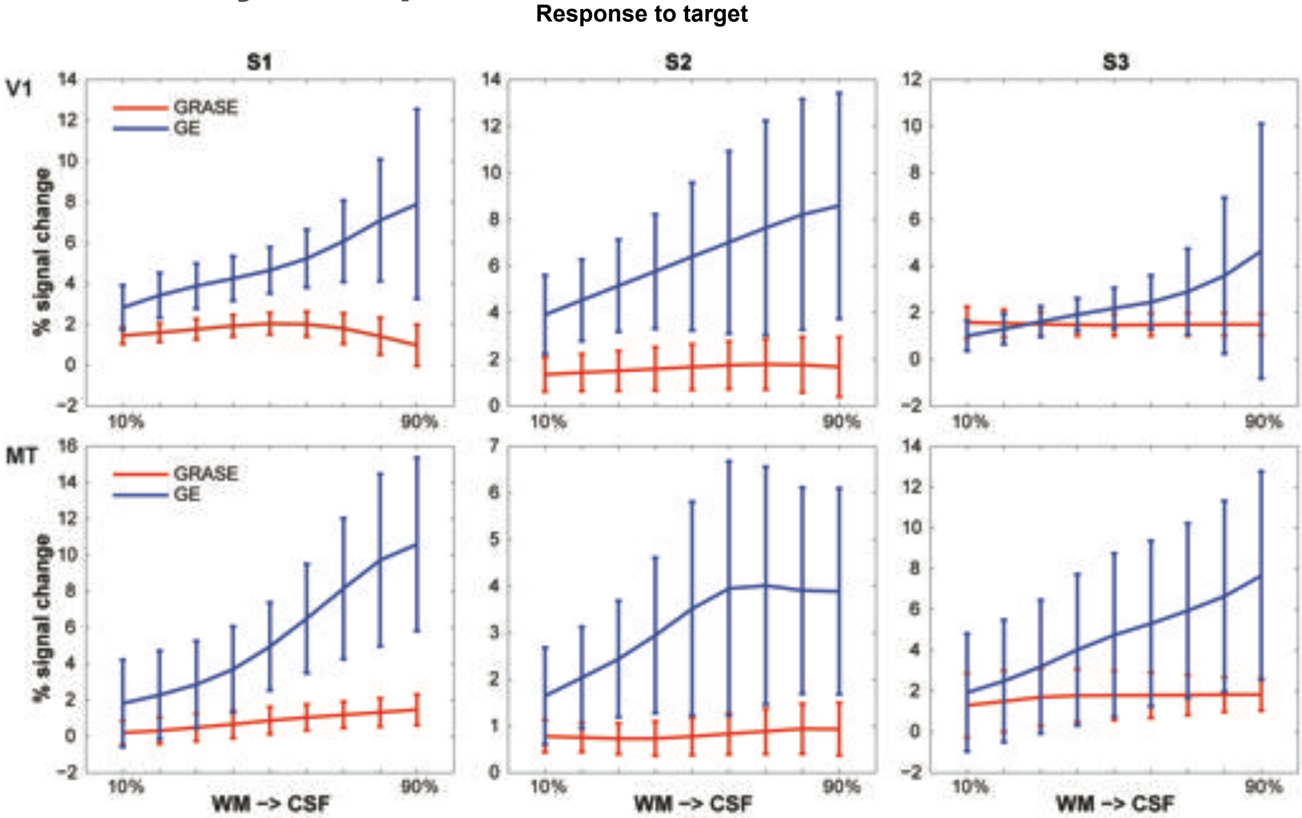


76



77

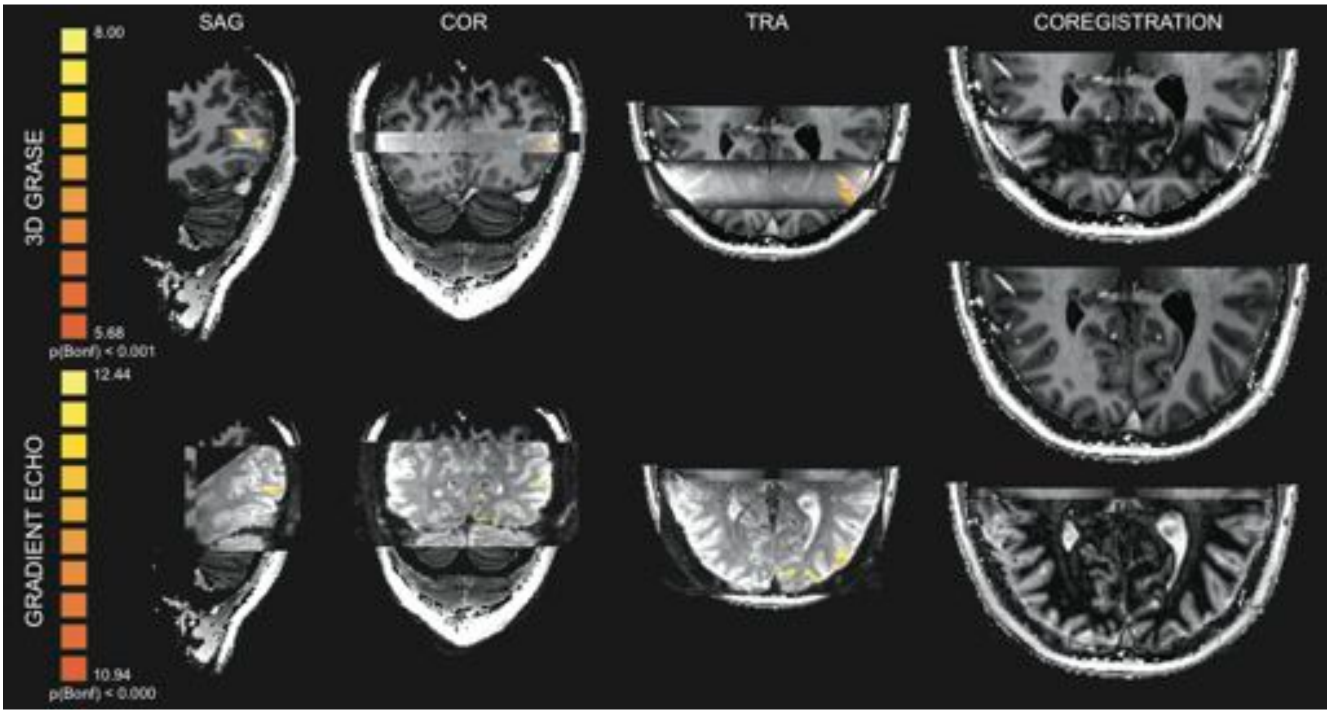
Why using GRASE and not standard GE EPI? Layer responses in different visual areas



De Martino et al., in preparation

78

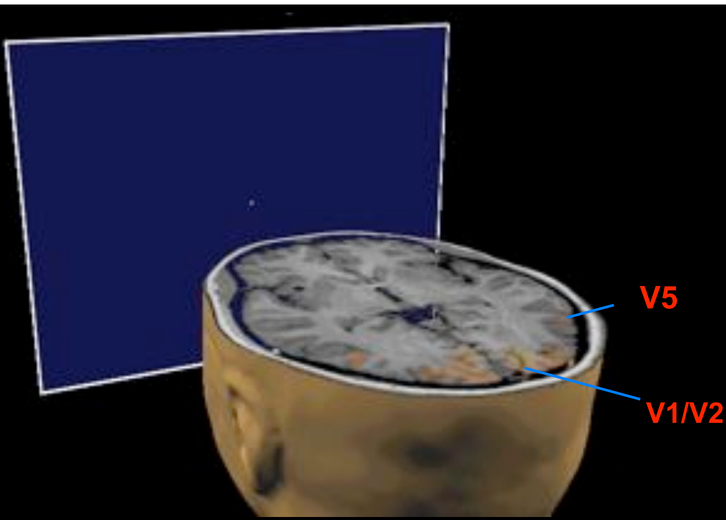
Limitations of GRASE - Brain Coverage

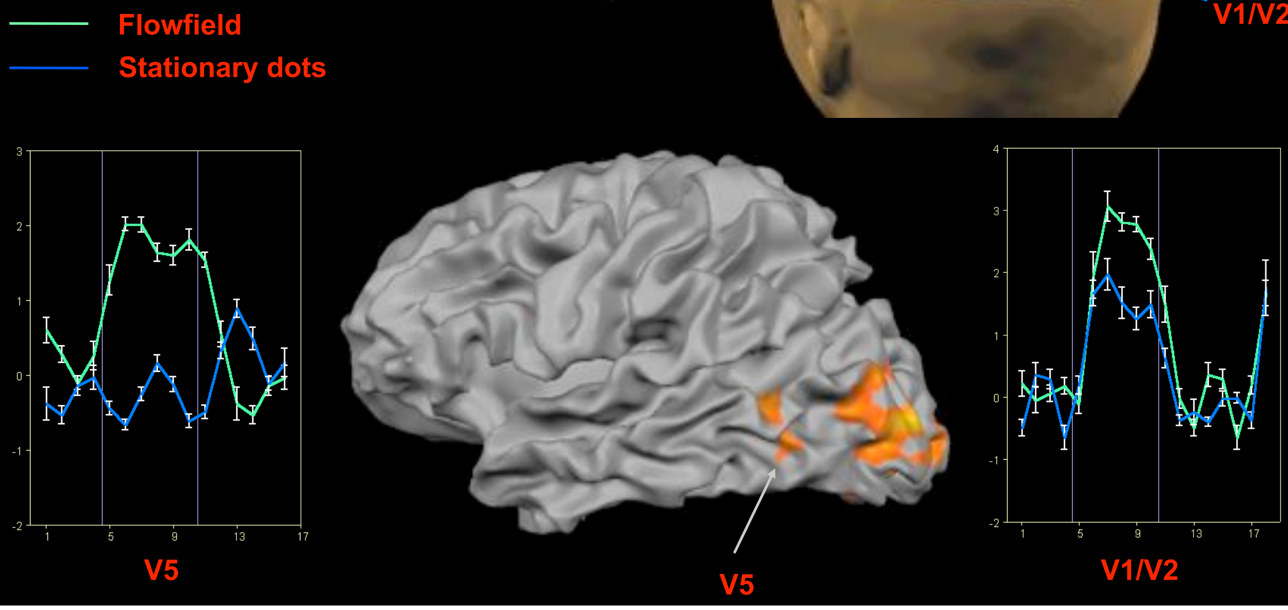


De Martino et al., in preparation

Functional Localizer: Identifying V5/hMT+

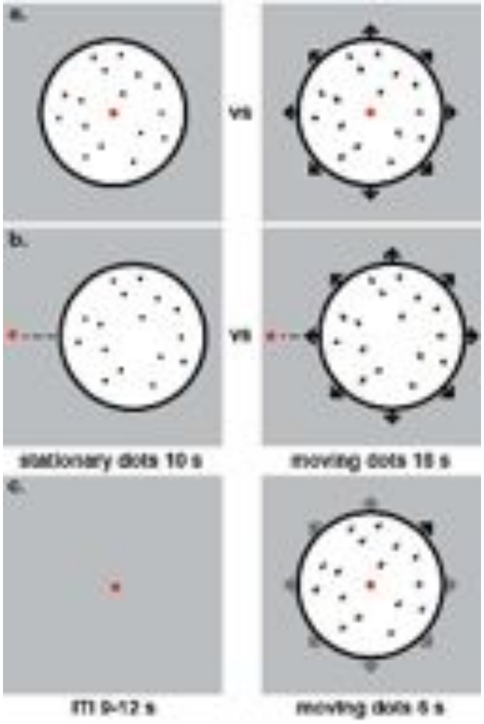
Features within hMT?





Experimental procedures

Stimuli used:



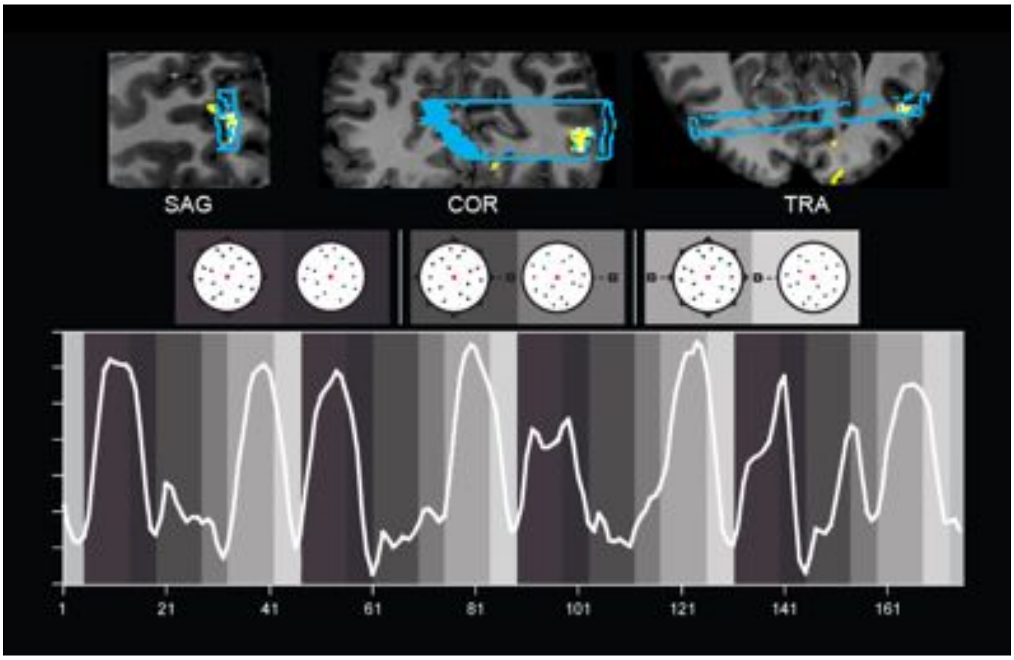
MR-acquisition: 7 Tesla Siemens MRI
Custom RF-coil

GE-EPI:
Voxelsize: 1.45 × 1.45 × 1.5 mm^3
FOV: 128 × 128 × 60 mm^3

3D GRASE (via inner volume selection)
Voxelsize: 0.8 × 0.8 × 0.8 mm^3
FOV: 25.6 × 204.8 × 9.6 mm^3

81

Mapping Motion Direction-Selectivity in Human Area MT

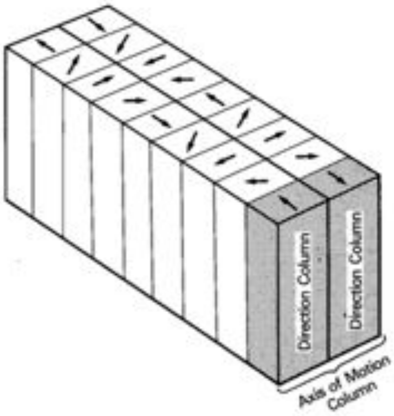


Functional identification of hMT vs hMST based on
ipsilateral response profile: No response to motion in left visual field
(following logic of Huk, Dougherty, Heeger, 2002)

82

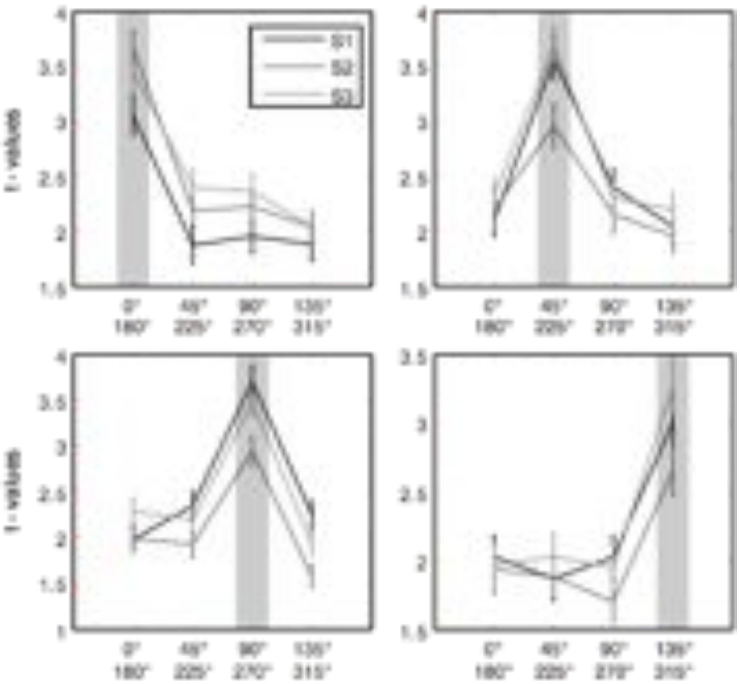
Mapping Columnar Organization of Motion Area hMT+/V5

All 8 presented motion directions were grouped into 4 opposing axis of motion directions to increase the size of the underlying columns.



Model of columnar organization of macaque MT (Albright et al., 1984)

Tuning for Axis-of-Motion in Human Area MT

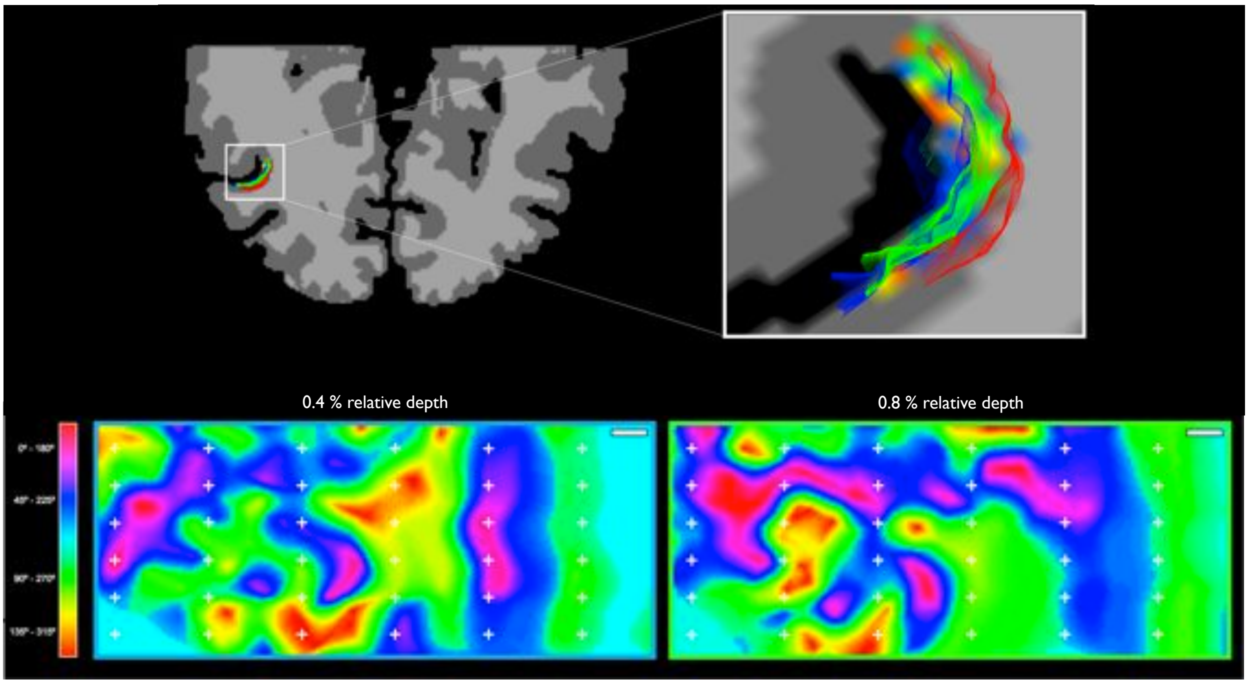


Average voxel tuning curves

Tuning curves computed using cross validation

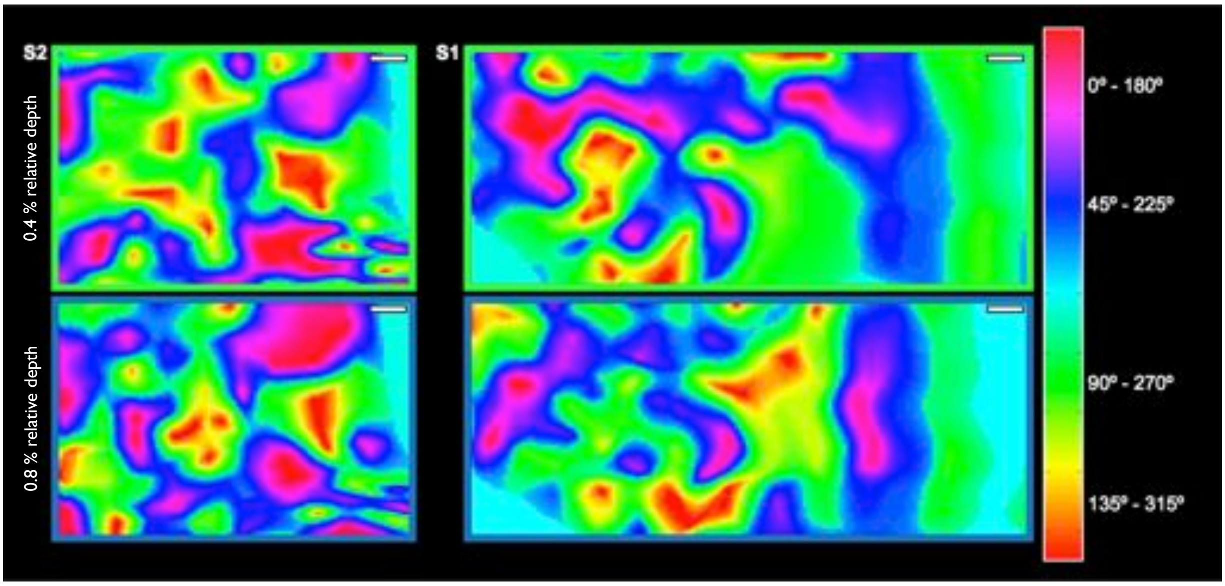
Zimmermann, Goebel, De Martino, Adriani, Van de Moortele, Feinberg, Chaimov, Shmuel, Ugurbil, Yacoub (2012). *PLoS One*, **6**(12), e28716.

Mapping Axis-of-Motion Columns at Different Cortical Depth Levels using High-Resolution Grid Sampling



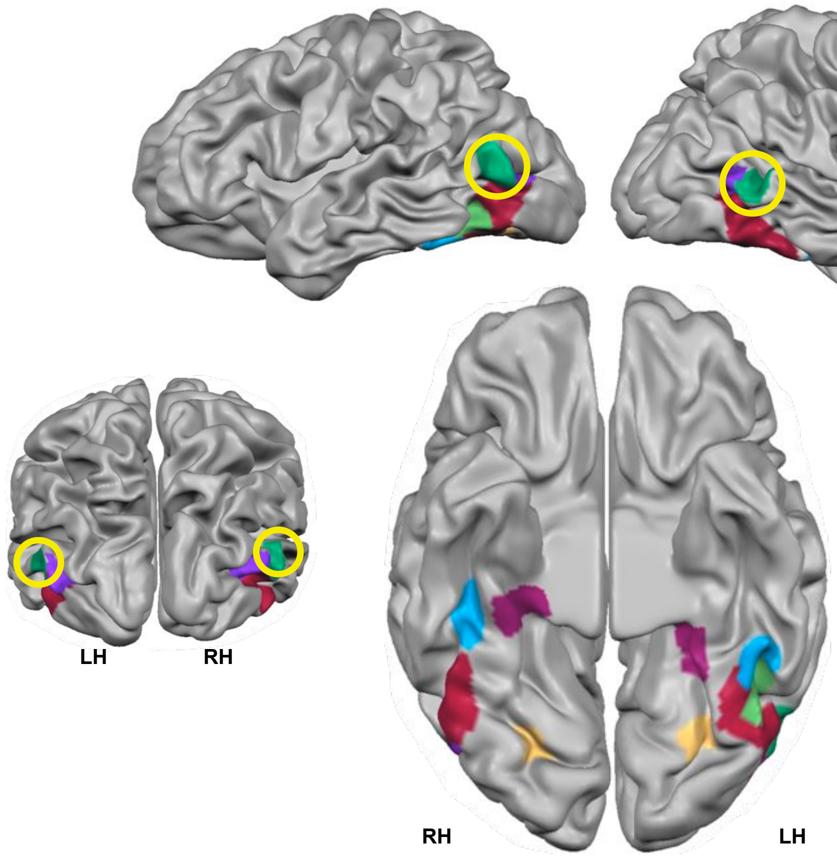
Zimmermann, Goebel, De Martino, Adriani, Van de Moortele, Feinberg, Chaimov, Shmuel, Ugurbil, Yacoub (2012). *PLoS One*, **6**(12), e28716.

Mapping Axis-of-Motion Columns at Different Cortical Depth Levels using High-Resolution Grid Sampling



Zimmermann, Goebel, De Martino, Adriani, Van de Moortele, Feinberg, Chaimov, Shmuel, Ugurbil, Yacoub (2012). *PLoS One*, **6**(12), e28716.

The Considered Mid-Level Visual Areas



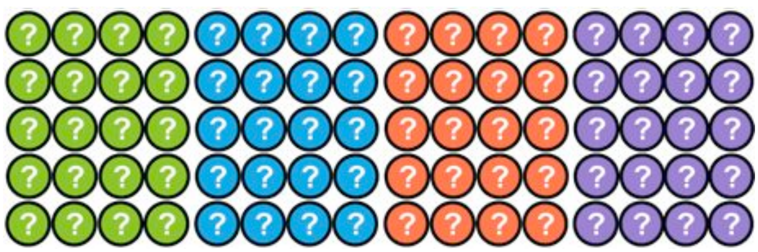
V5/hMT	– Motion
EBA	– Bodies
LOC	– Objects
V4	– Colors
FFA	– Faces
PPA	– Places
VWFA	– Words

Suggested Research Strategy = The Real Challenge:

“Crack” the columnar-level code in as many brain areas as possible

Distributed coding of shapes across columns in monkey IT (e.g. Tanaka, 1996)

Columnar-level features in LOC



Goal: Unraveling columnar-level feature representations in mid-level and higher-level areas of the visual hierarchy, auditory system and multi-modal regions (STS)

In V1/ V5 *features were known*! It is a much more challenging task to map features that are hitherto unknown. Cracking the columnar-level code involves not only high-end technology (7T+, GRASE) but also smart experimentation! Areas that will be analyzed include: LOC, letter area, VWFA, OFA, FFA, and invariance transformation across areas of the ventral stream

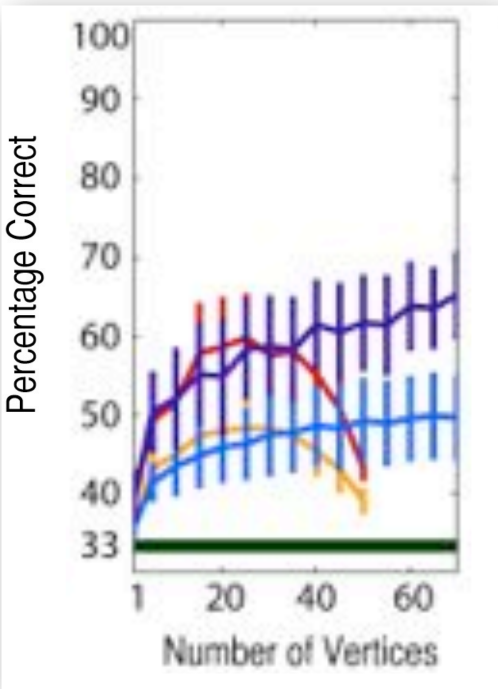
Columnar-Level BCI: Changing Direction of Motion in Stimulus Based on *Imagined Motion Direction*

- Investigation of attention and imagery effects at columnar and laminar level
- 7T+ real-time fMRI: Use distributed columnar-level patterns of activity as the basis for more precise feedback information (within-category information) and to develop columnar-level BCIs (e.g. direct letter imagery)
- First experiment:

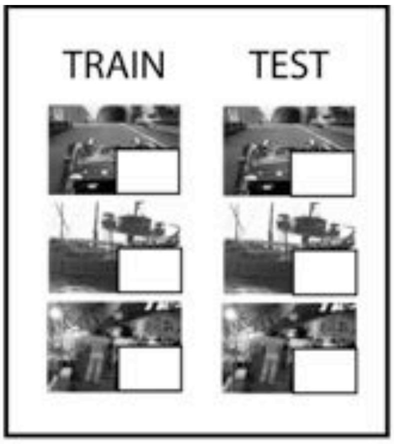
1. Dots appear static on screen
2. Subject imagines specific direction of motion for about 10 seconds
3. Motion direction is decoded in real-time using classifier operating at columnar-level feature representations
4. Decoded stimulus direction is used to show corresponding motion direction to subject

(does not work at 3T using SVM classifier; might work at columnar axis-of-motion resolution)

Context Decoding in V1 - Top-Down Feedback to *Non-Stimulated* Area?

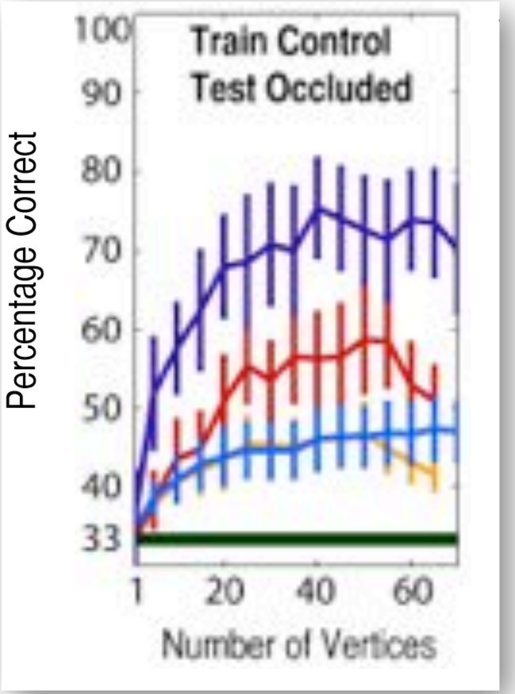


(SEM)
n=6

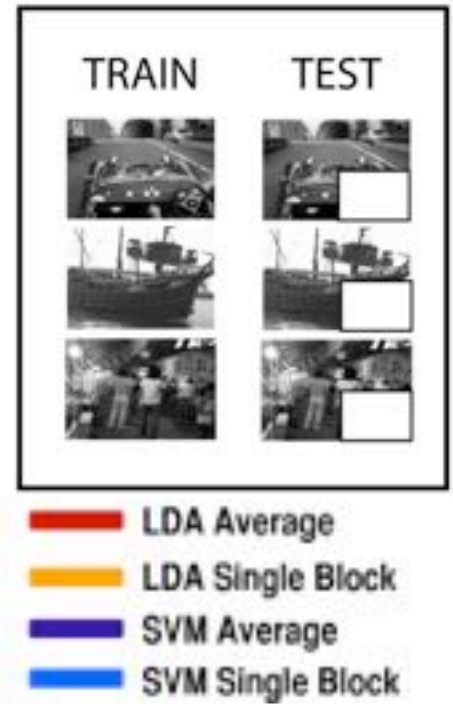


Smith & Muckli (2010)

Context Decoding in V1 - Cross-Condition Generalization



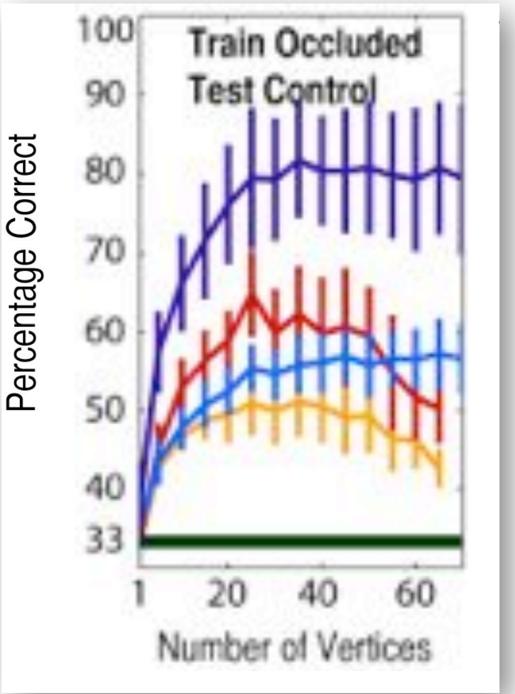
(SEM)
n=6



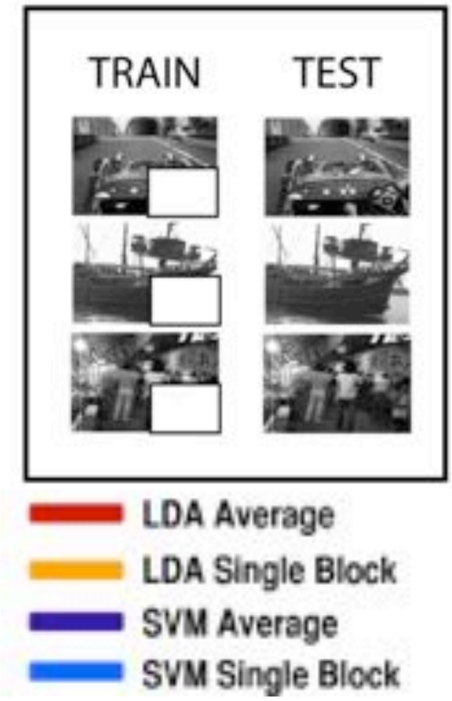
Smith & Muckli (2010)

91

Context Decoding in V1 - Cross-Condition Generalization



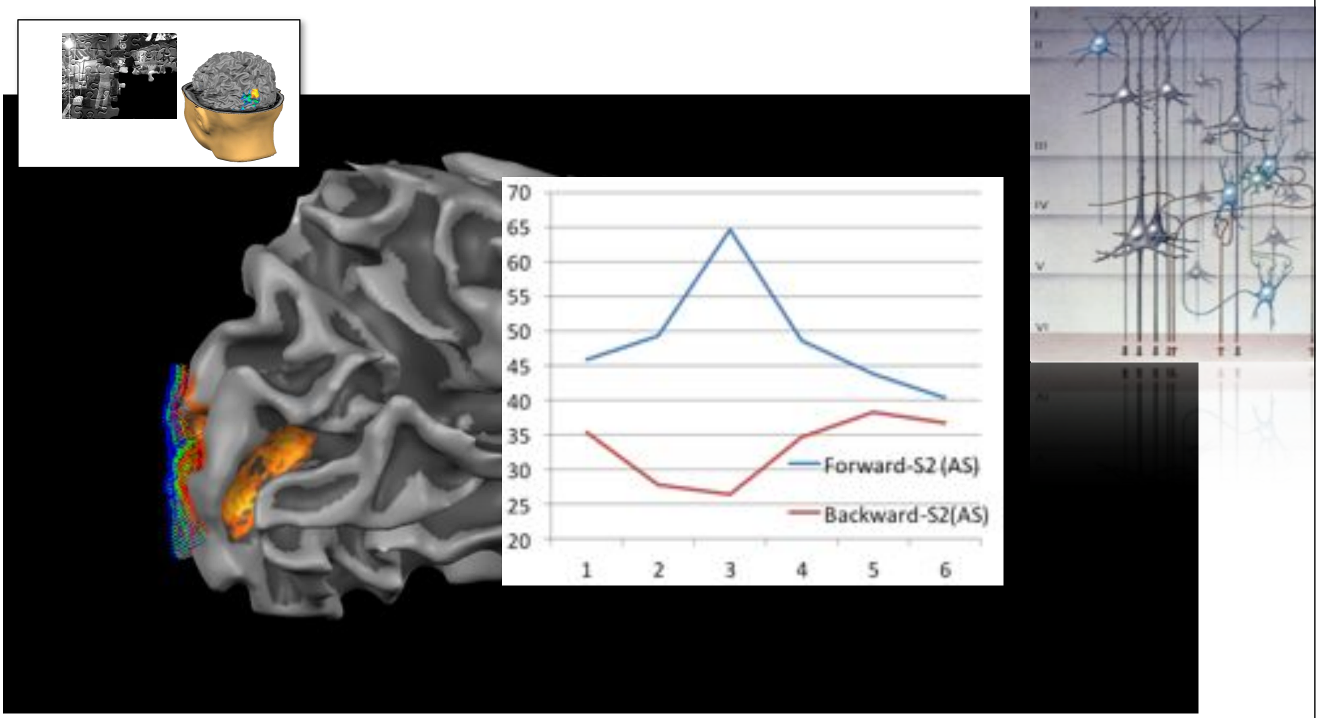
(SEM)
n=6



Smith & Muckli (2010)

92

Layer-Specific MVPC Performance @ 7 T



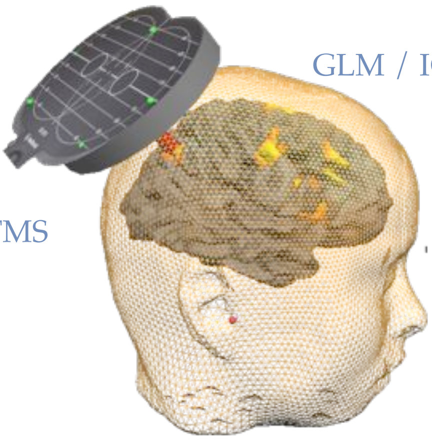
Collaboration with Lars Muckli, Essa Yacoub, Federico De Martino, Jan Zimmermann

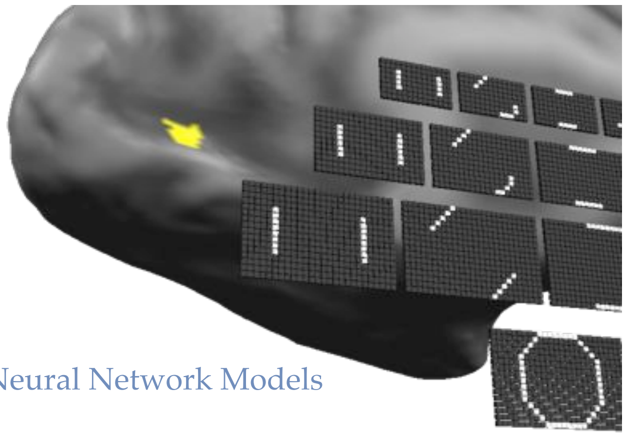
93

Modeling Multi-Modal Neuroimaging Data

GLM / ICA

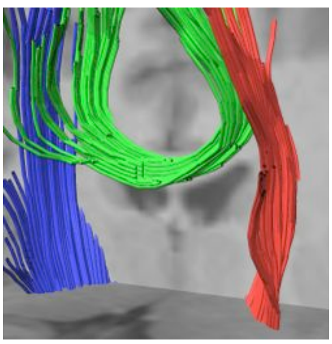
TMS

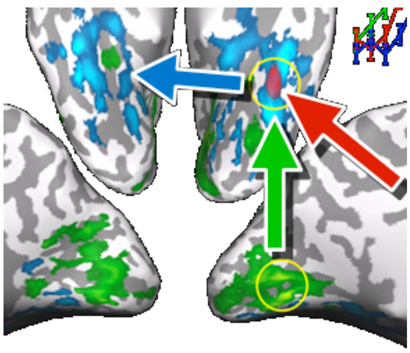


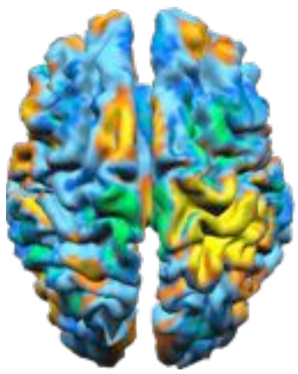


Neural Network Models

DTI







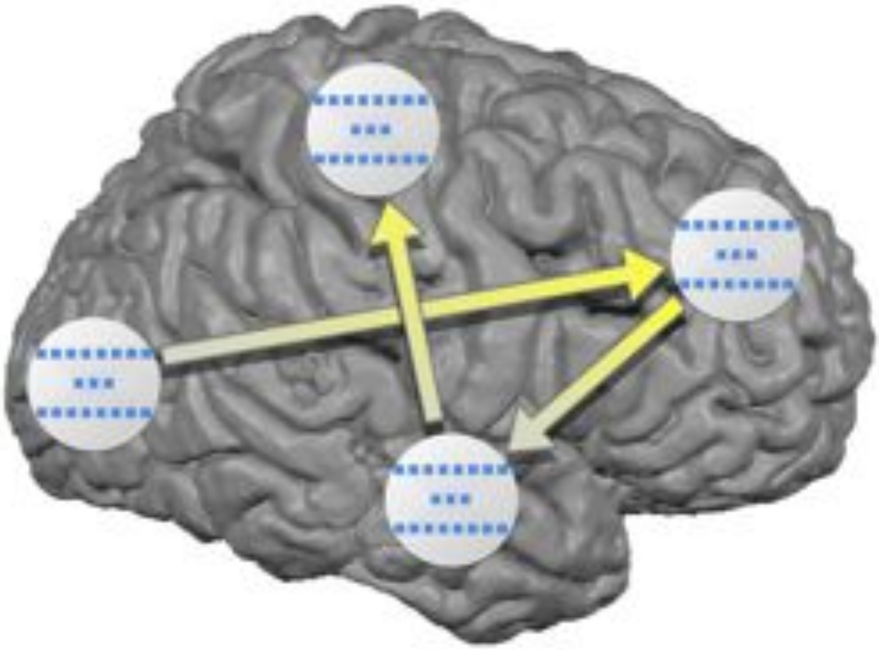
Effective Connectivity: GCM

EEG / MEG

94

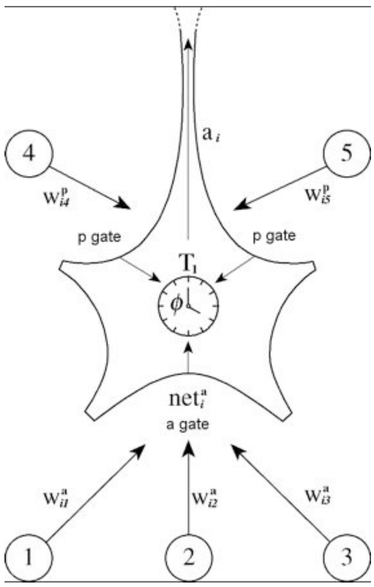
Modeling Multi-Modal Neuroimaging Data At Columnar-Level Feature Representations

Columnar Network Models (CNM)



95

Neuronal Elements



"Burst oscillator" units (Goebel, 1993)
"one unit -> one cortical column"

$$
\begin{aligned}
\tau_E \frac{\mathrm{d}E_i(t)}{\mathrm{d}t} &= -(E_i(t) - E^0) - (g_i(t) - g^0)(E_i(t) - E^k) + \eta_i(t) \\
&\quad - \left[\sum_{j,w_{ij}>0} w_{ij} \cdot o_j(t - \tau_{ij})\right] (E_i(t) - E^{ex}) \\
&\quad - \left[\sum_{j,w_{ij}<0} |w_{ij}| \cdot o_j(t - \tau_{ij})\right] (E_i(t) - E^{in})
\end{aligned}
$$

$$
\tau_\Theta \frac{\mathrm{d}\Theta_i(t)}{\mathrm{d}t} = -(\Theta_i(t) - \Theta^0) + c(E_i(t) - E^0) \quad 0 \le c \le 1
$$

$$
\tau_g \frac{\mathrm{d}g_i(t)}{\mathrm{d}t} = -(g_i(t) - g^0) + \tau_g b o_i(t)
$$

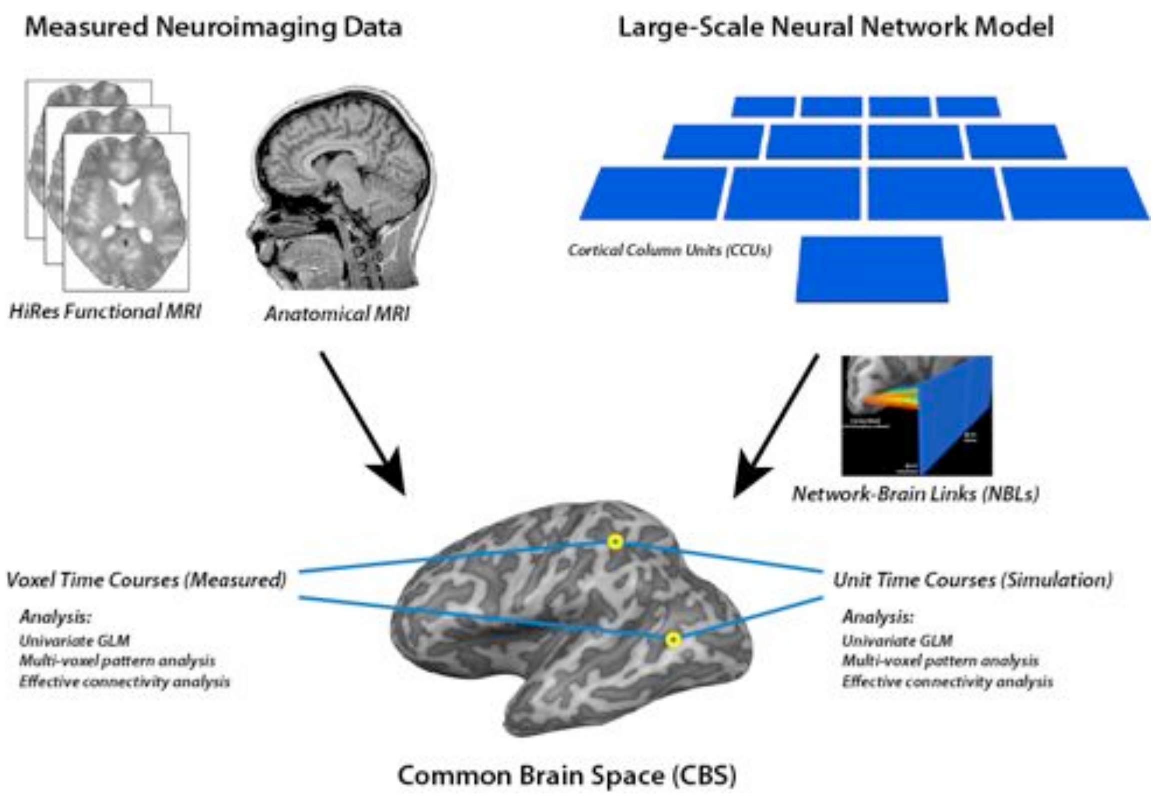
$$
o_i(t) = \begin{cases} \delta(E_i - \Theta_i) & \text{if } E_i > \Theta_i \\ 0 & \text{sonst.} \end{cases}
$$

MacGregor spiking neuron model

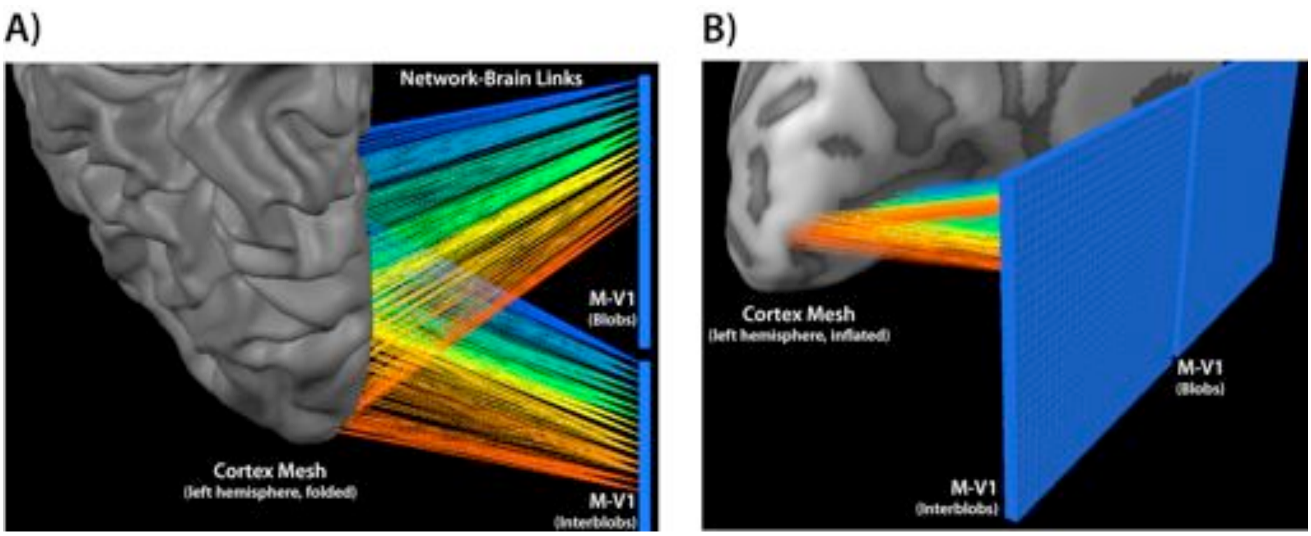
(leaky integrator with dynamic threshold)

96

Common Brain Space for Networks and Imaging Data



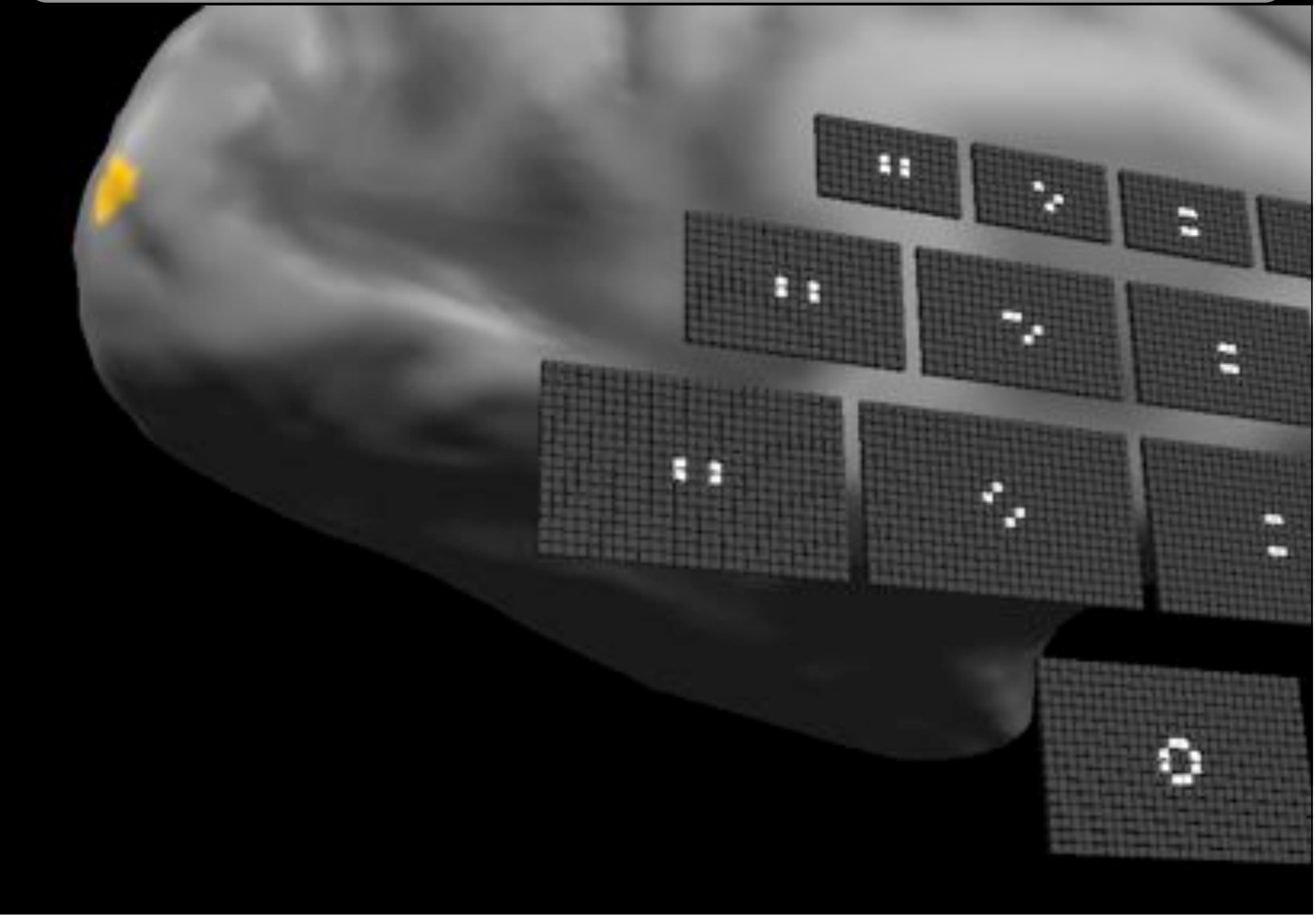
Network-Brain Links (NBLs) - Linking Units to Voxels



Spatial hypotheses are expressed via NBLs at different resolutions:

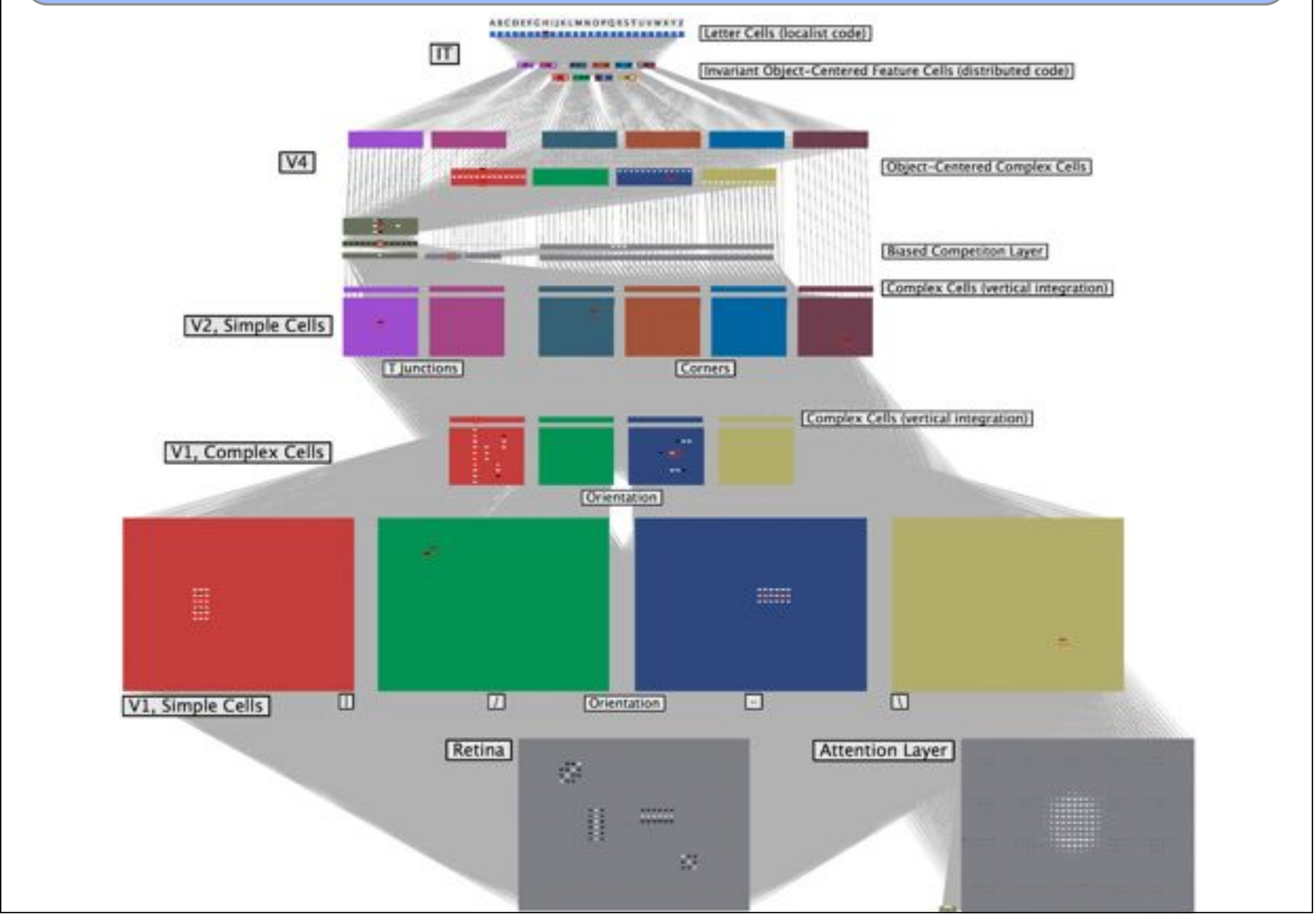
- at level of brain areas (diffuse connections of ~ 1cm spread)
- at level of topological (e.g. retinotopic) mapping (~ 2mm resolution)
- at columnar-level (~ 0.5mm resolution required)

Common Brain Space for Networks and Imaging Data



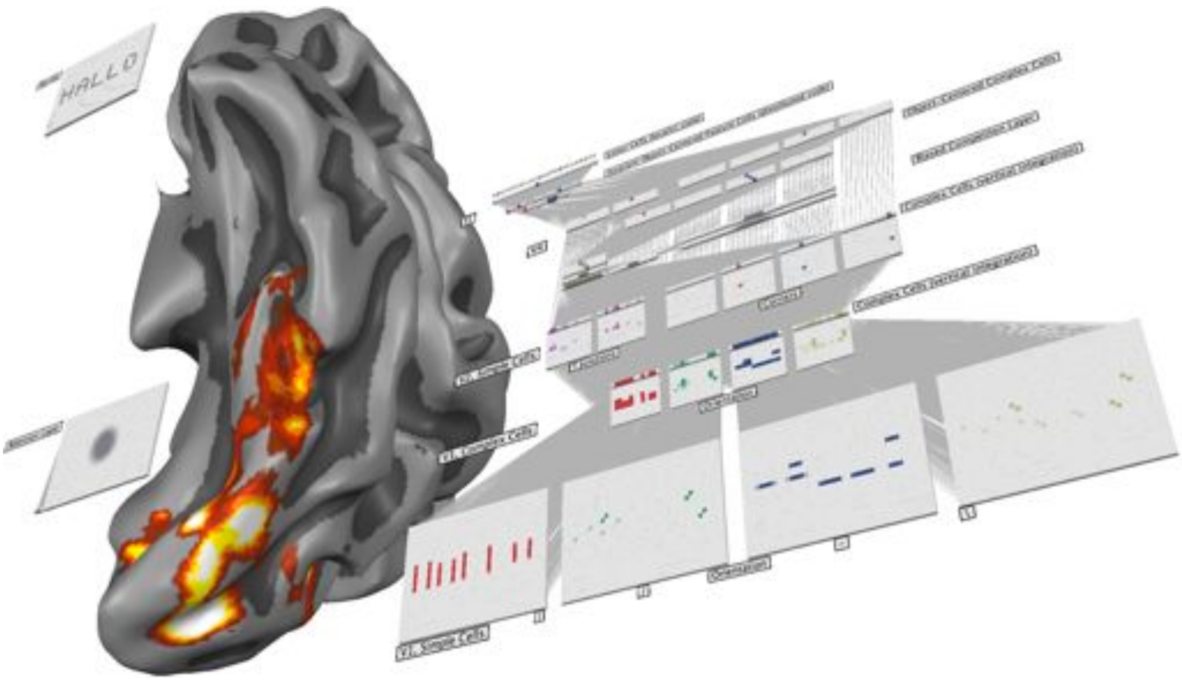
99

Towards Large-Scale Columnar-Level Neural Networks



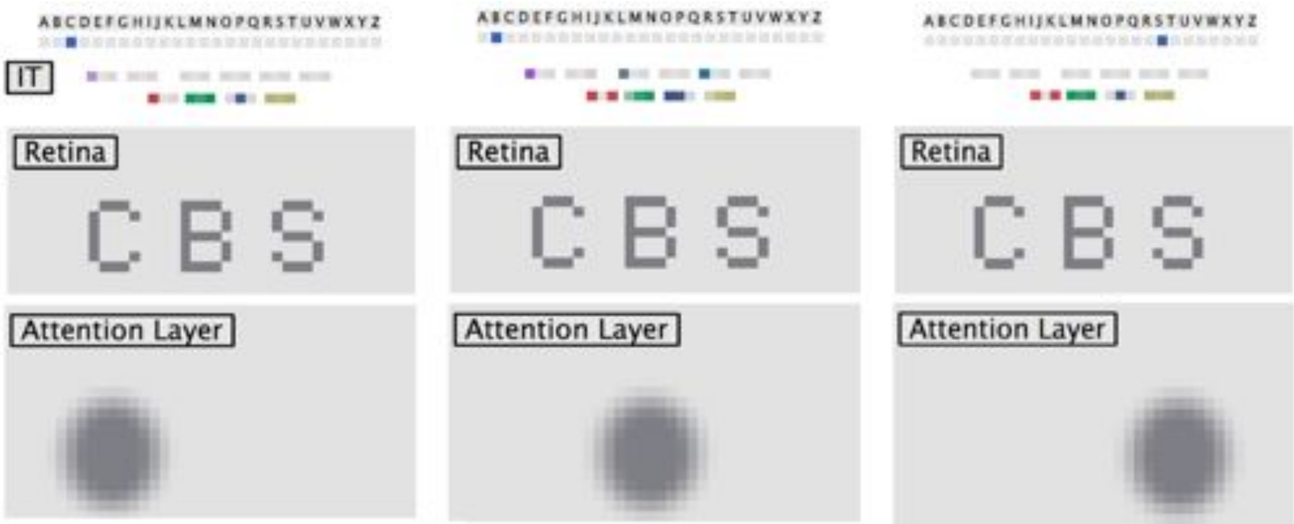
100

Towards Large-Scale Columnar-Level Neural Networks



Letter recognition model and mesh with fMRI activity in common brain space (CBS). The activity shown is from the fMRI scan of a subject reading letter strings.

Towards Large-Scale Columnar-Level Neural Networks



Results of invariant processing in the model when "reading" the constant input string "CBS" letter-by-letter following spatial attention shifts.

Towards Large-Scale Columnar-Level Neural Networks

Upcoming years:
Combined imaging and modeling at level of columnar feature representations and different layers in order to obtain a deeper understanding how cognitive phenomena arise as emergent properties from massively parallel distributed brain processes.

References

Peters, Reithler & Goebel (2012). Modeling invariant object processing based on tight integration of simulated and empirical data in a Common Brain Space. *Frontiers in Computational Neuroscience*, **6**, 12.

van de Ven, V., Jans, B., Goebel, R., De Weerd, P. (2012). Early human visual cortex encodes surface brightness induced by dynamic context. *Journal of Cognitive Neuroscience*, **24**, 367-377.

Peters, Jans, Van de Ven, De Weerd & Goebel (2010). Dynamic brightness induction in V1: Analyzing Simulated and Empirically Acquired fMRI Data in a “Common Brain Space” Framework. *Neuroimage*, **52**, 972-984.

Goebel & De Weerd (2009). Perceptual Filling-in: From Experimental Data to Neural Network Modeling. In: Gazzaniga (Ed). *The Cognitive Neurosciences IV*.

Modeling software “*Neurolator 3D*” will be freely available for download.

Summary and Conclusions

- Specialized functional brain areas and networks are routinely localized and further characterized with functional MRI at 3 Tesla.
- Multi-modal brain imaging and TMS allows to test precise temporal hypotheses about time course of cognitive sub-components within trial.
- Clinical applications of fMRI neurofeedback are emerging (e.g. treatment of pain, Parkinson, depression, anxiety disorders).
- fMRI Communication BCI: Allows transmission of distinct information units, i.e. letters at a single trial level without extensive pre-training.
- Recent experiments show that it is possible to map *known* columnar-level representations in specialized brain areas (V1, hMT) using 7 Tesla fMRI.
- It remains a challenge to crack the functional code for areas where the “alphabet of features” is hitherto unknown. This challenge requires a combination of ultra high-field fMRI, (neuronal network) modeling and adaptive stimulation paradigms.
- If the ultra-high field code cracking approach is successful, it will likely provide groundbreaking contributions to (cognitive) neuroscience.

Acknowledgements

Jan Zimmermann (UM)
Federico de Martino (UM, CMRR)
Essa Yacoub (CMRR)
Kamil Ugurbil (CMRR)
van de Moortele (CMRR)
Gregor Adriany (CMRR)
David Feinberg (Berkeley)
Bettina Sorger (UM)
David Linden (Cardiff, UK)
Nikolaus Weiskopf (FIL, UK)
Elia Formisano (UM)
Martin Frost (UM)
Brigitte Dahmen (UM)
Steven Laureys (Liege)
Audrey Maudoux (Liege)
Joel Reithler (UM)
Judith Peters (UM)
Fabrizio Esposito (UM)
Peter de Weerd (UM)

SIEMENS

European Research Council erc

Université de Liège

DECODER
BCI and Detection of Consciousness

NWO
Netherlands Organisation for Scientific Research

BrainGain