脑磁图系统与实践

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➢ 脑磁图系统硬件概述

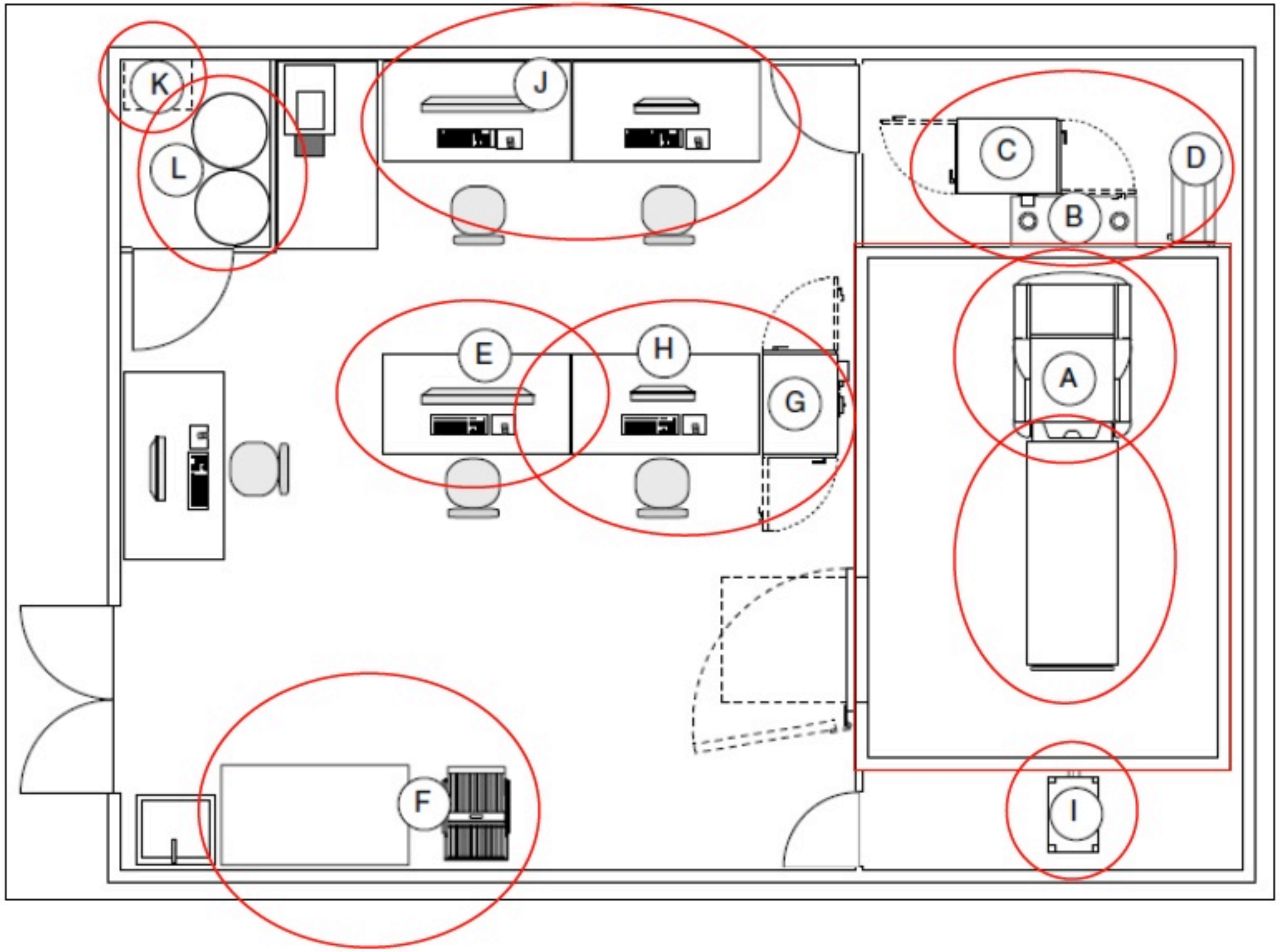
- 硬件组成及连接
- 脑磁图传感器分布
- 液氦循环系统
- 刺激反馈设备

➢ 脑磁图数据实践

- General Workflow
- 实验设计
- 数据采集实操
- 数据分析workflow
- 溯源方法
- 常用数据分析软件包

Main components

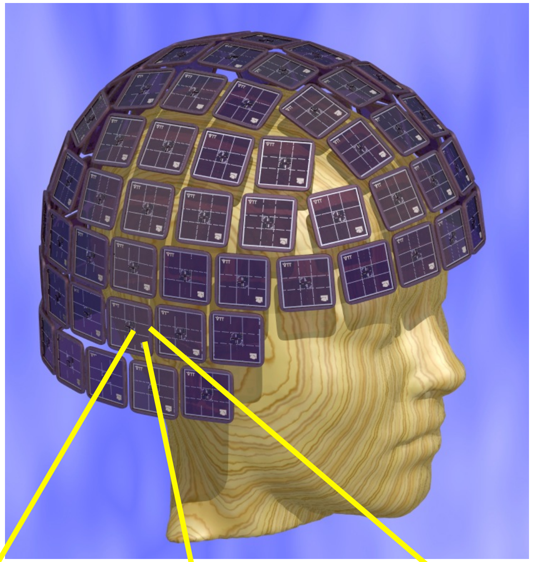
(A) Gantry with probe insert
(B) Feedthrough filter unit
(C) Electronics cabinet
(D) Lifting unit
(E) Data acquisition ws
(F) 3D digitizer
(G) Stimulus cabinet
(H) Stimulus control computer
(I) Projector
(J) Data analysis ws
(K) Isolation transformers
(L) Helium storage



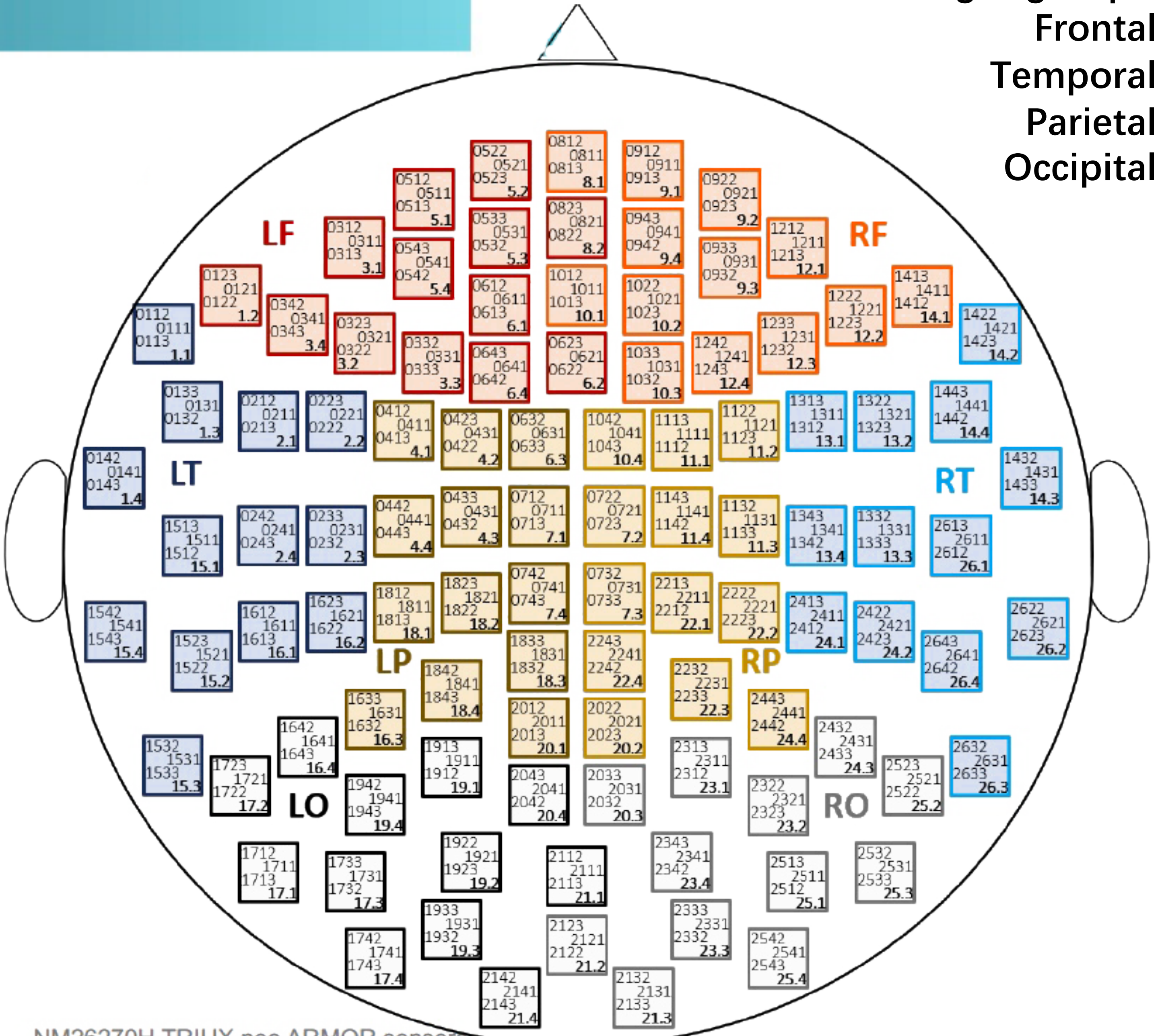
ARMOR^{TM}传感器阵列

Left and right groups:
Frontal
Temporal
Parietal
Occipital

306-channel
SQUID sensor array

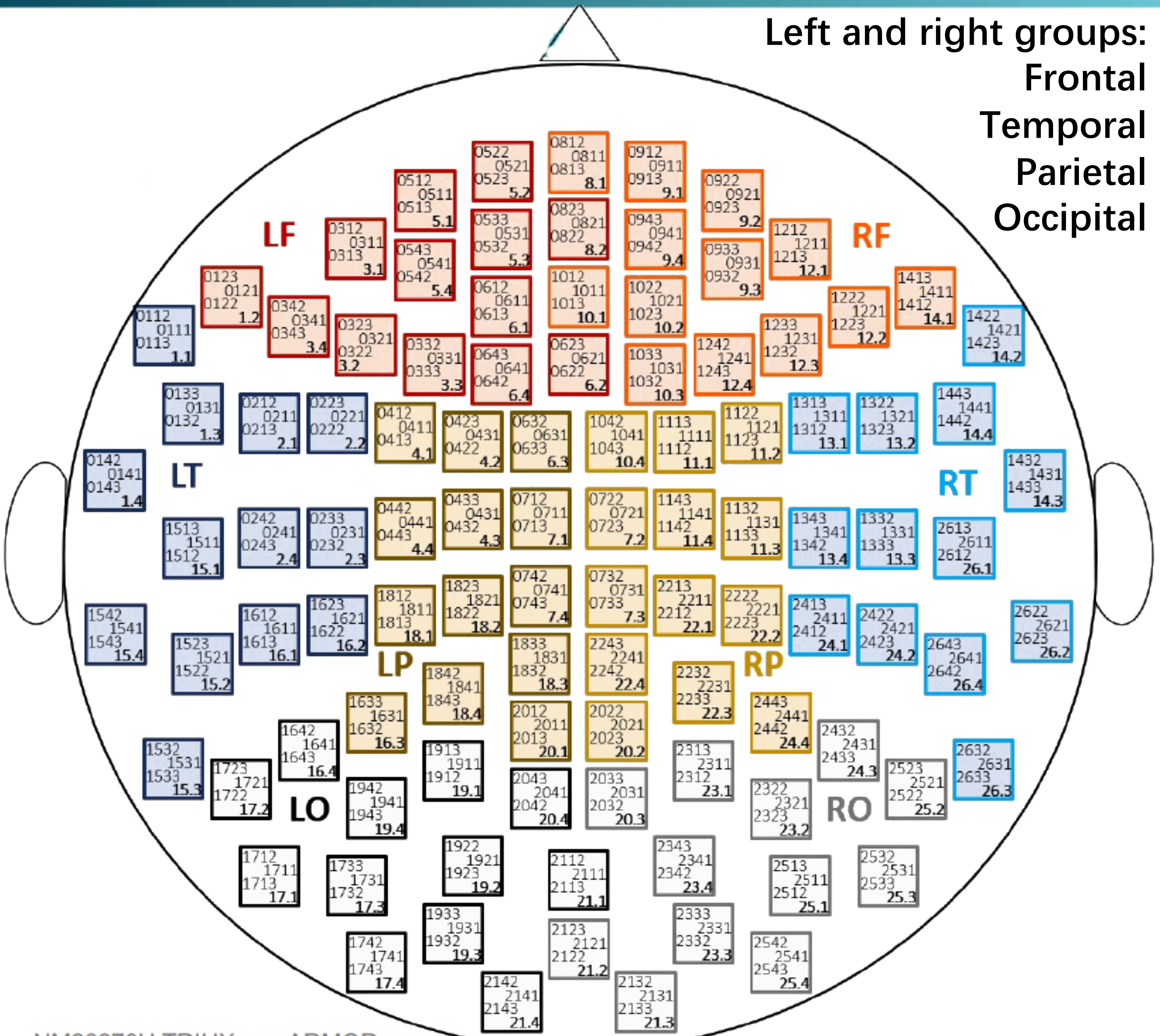


Planar gradiometer   Magnetometer



NM26270H TRIUX neo ARMOR sensors

ARMOR™传感器阵列



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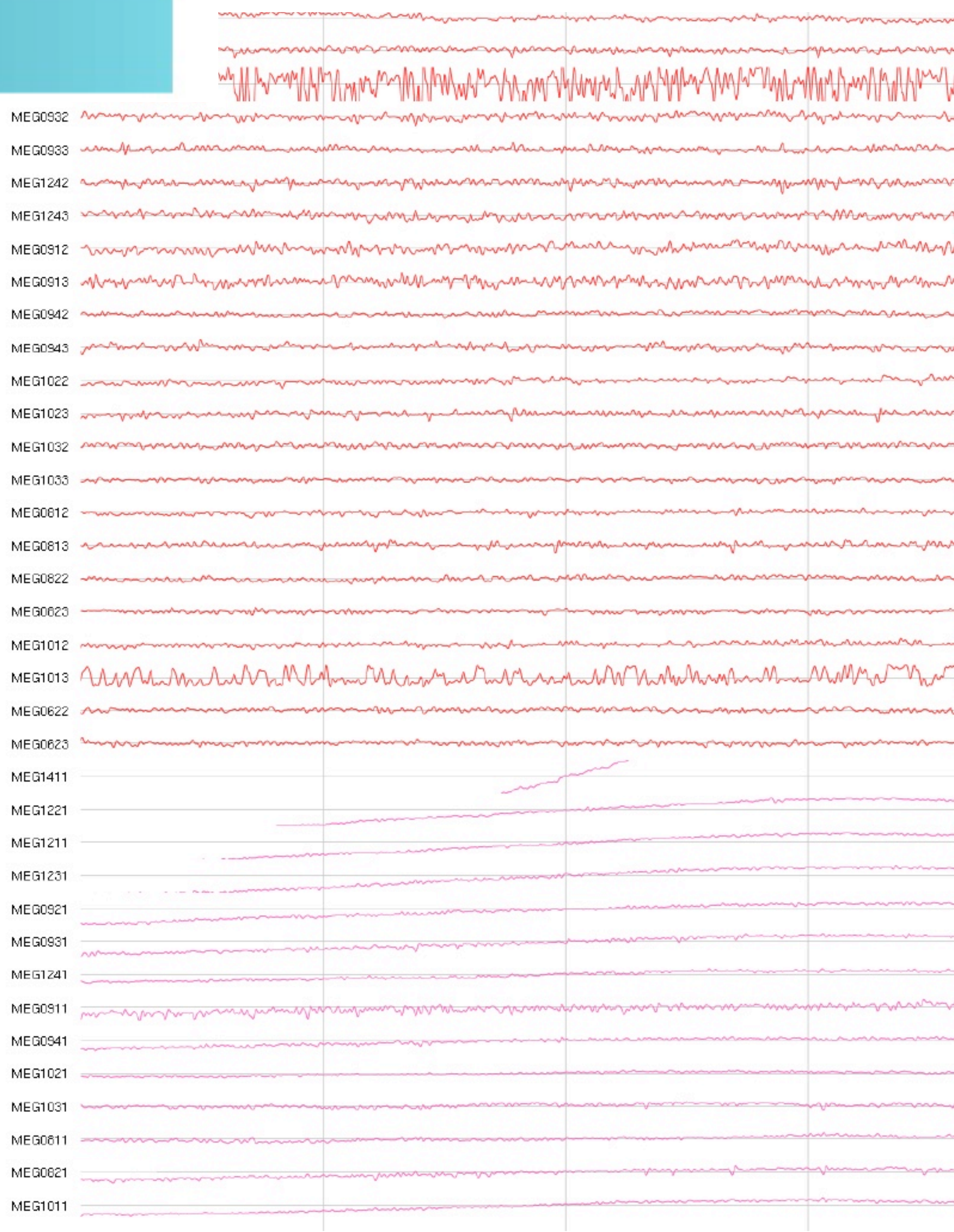
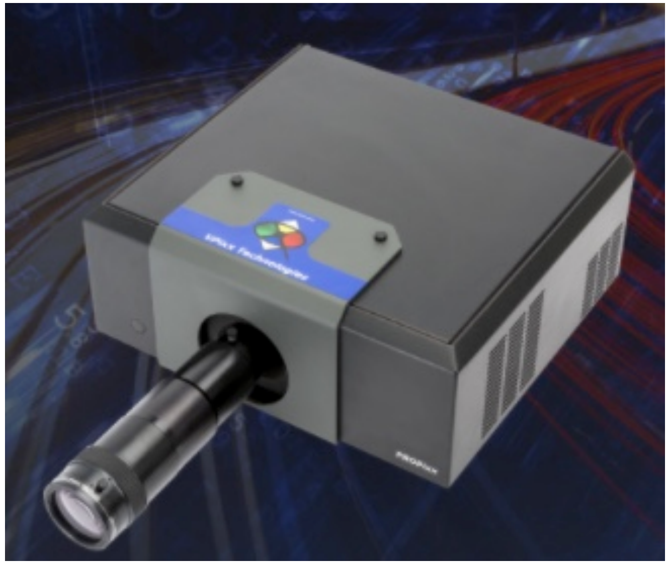


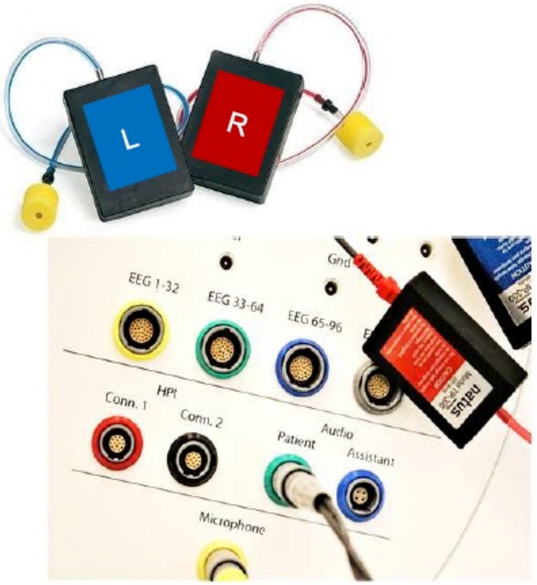
MEG 刺激及反馈设备

- ➢ 视觉刺激系统



- PROPixx MEG/MRI
- 投影 + 镜子 + 背投屏
- 120Hz(500Hz RGB; 1440Hz greyscale)

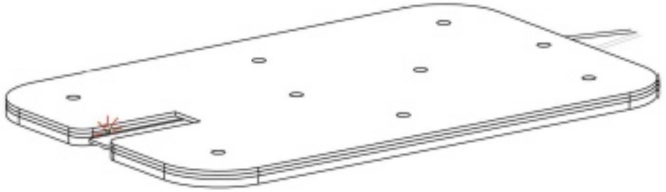
- ➢ 听觉刺激系统



- 管式耳机
- 电转声式系统

- ➢ NAtA脑磁兼容反馈系统

- ➢ 光纤运动反馈板



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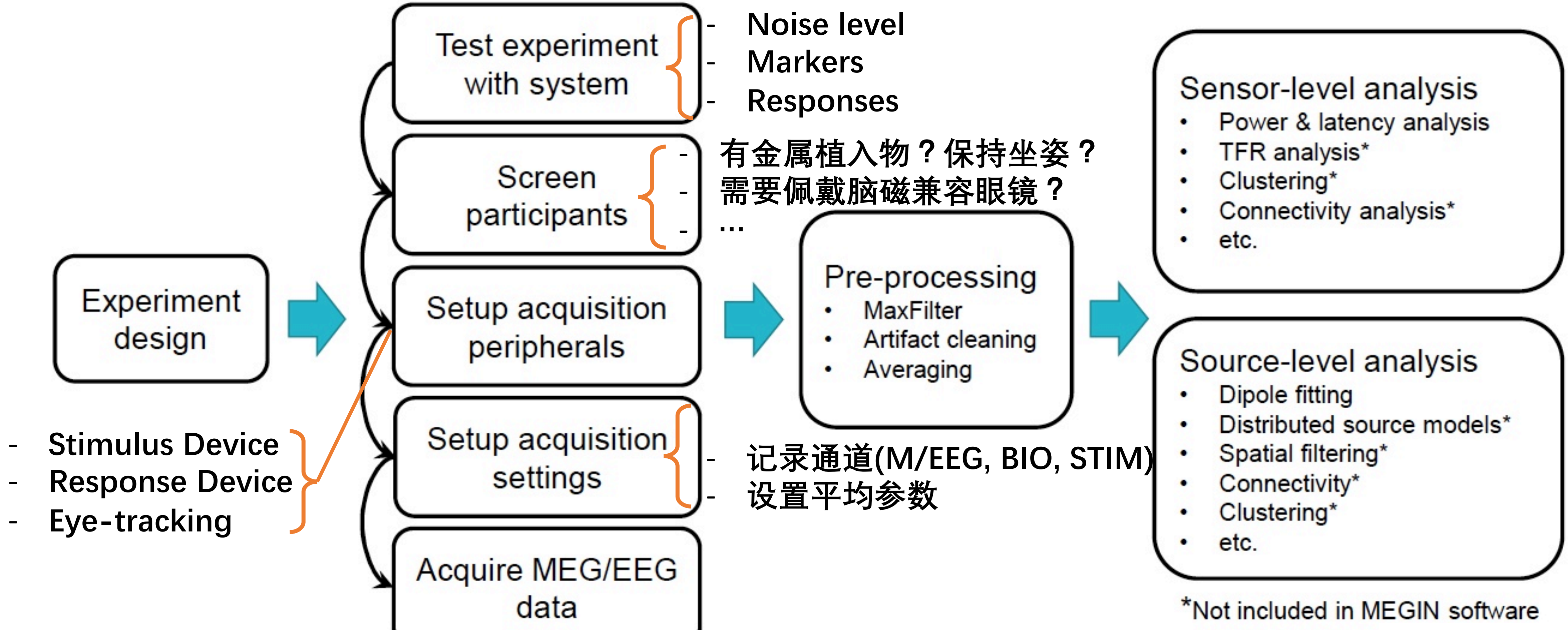
General workflow



MEG experiment

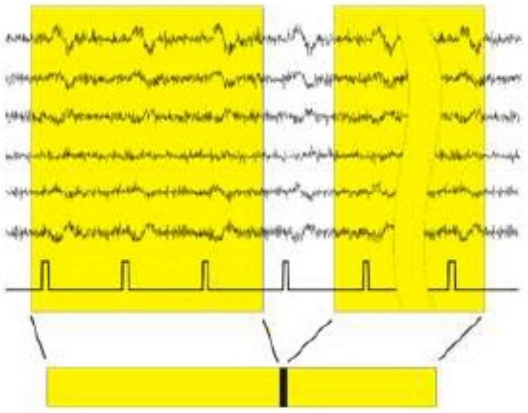
Spontaneous vs evoked response study

Stimuli (if any)
- auditory
- visual
- somatosensory
- olfactory
- ...

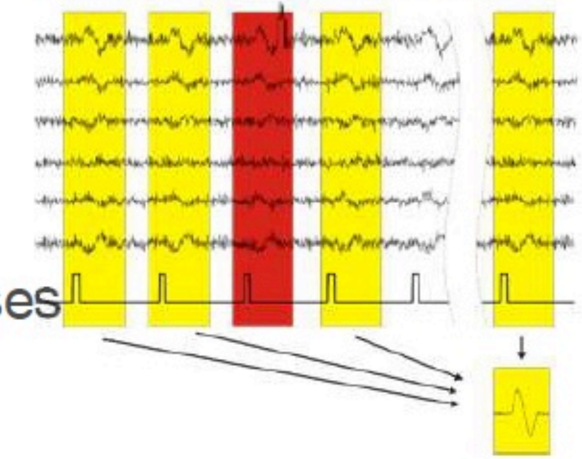
Task
- attend/ignore
- detect + react
- detect + count
- imagine
- observe/imitate
- ...

Behavioural responses
- limb/finger movement
- speech
- ...

Spontaneous data



Evoked responses



Experiment design

Consider the design carefully

- Analysis methods
  - Sensor level or source level analysis?
  - Only MEG, or are EEG and other physiological data required?
    - **ECG?**
    - **EMG?**
  - Artifact reduction techniques, i.e. use EOG/ECG and ICA to remove physiological artifacts
  - Do you need noise covariance for the data analysis?
    - **Empty room recording**
    - **Pre-stim/Resting state recording**
  - If event related stimulus, increase the contrast between baseline and data, i.e. time or freq domain averaging
    - **Increase SNR**
  - What are the considerations for participants? Age, gender, healthy/diseased, #of participants, etc.
  - Stimulus delay?
    - **Auditory**
    - **Visual： 9 ms**

Experiment design

Consider the design carefully

- Special populations
  - Depending on age there should be a care taker inside MSR
  - Stimulus access to care taker
  - Use cHPI and later movement compensation*
  - Pediatric MEG chair can be used to reduce movement
  - Children friendly stimulus / movies
  - Prior mocking of MEG could be helpful

*Not available in the US, works in progess

Experimental parameters

- Experimental conditions
  - Number of trials
  - Inter-trial or inter-stimulus interval (ITI or ISI)
  - Length of recordings
  - Total duration of experiment
  - Behavioral responses
- Quality of stimulation

Experimental parameters

- Number of trials
  - Single subject analysis often desirable
  - Stimulus-locked, evoked ~60-100 trials
  - Steady state 40-50 trials - data integrated over extended time intervals
- Stimulus duration
  - Evoked responses - 100-200ms
  - Increased risk of saccades during long trials
  - Longer duration may evoke response at stim onset and offset

Experimental parameters

- Inter-stimulus interval
  - Allow for neural response to return to baseline
  - Evoked responses, > 200ms
  - Modulation of rhythmic activity, 500-1000ms
  - Elicit or avoid expectation with jitter
- Length of recordings
  - 8-10 minutes
  - Shorter for difficult populations or boring tasks
- Total duration of experiment
  - < 75 minutes
  - Too long and data quality and performance degrades

Experimental parameters

- Behavioral responses
  - Keep subject alert, i.e. a distractor task
  - Voluntary movement causes ‘artifacts’ - 肌电
  - Keep responses away from period of interest, i.e. delayed responses
  - Avoid eye movements, e.g. during a feedback screen
  - Alternate hands for yes/no conditions - 实验条件打乱；试次顺序平衡
  - Responses collected in all conditions equally
  - Collect EMG, eye positions, speech onset, etc. to define artifacts

脑磁图实验需要注意的问题：

- 脑磁图技术和研究问题是否相匹配；

  Accurate localization – fMRI; MEG – earliest sensory response, timing, dynamic neural mechanism;

- 预先估计激活的脑区；

  e.g. not too deep, not to close to each other, not totally radial …

- 预实验（技术、被试）；

  检验实验setup、伪迹(on-line, off-line)、主试体验、EEG test (一个硬币的两个面)

- 设置on-line平均参数以检查数据质量；

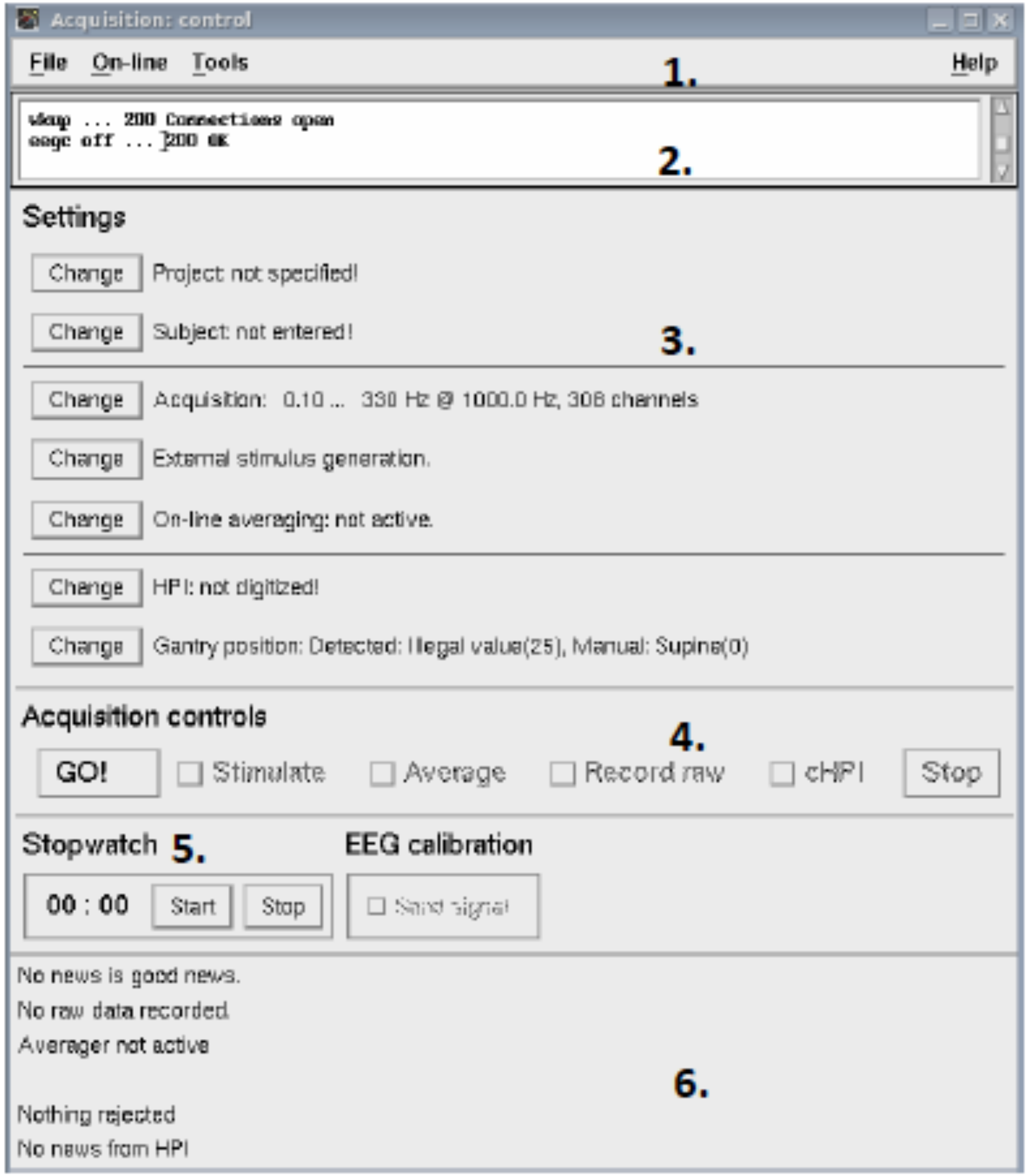
Magnetoencephalography: From Signals to Dynamic Cortical Networks, 2019

数据采集实操

- 准备屏蔽间和机器位置；
- 检查噪音水平；
- 打开记录软件;

  Acquisition: control

- 键入Project & Subject Name；
- 设置采集参数；



数据采集实操

- 准备屏蔽间和机器位置；
- 检查噪音水平；
- 打开记录软件;

  Acquisition: control
- 键入Project & Subject Nam
- 设置采集参数；
- 设置平均参数；
- 准备被试 (HPI, BIO)；
- 头部数字化；
- 将被试带入屏蔽间；
- 开始数据采集；

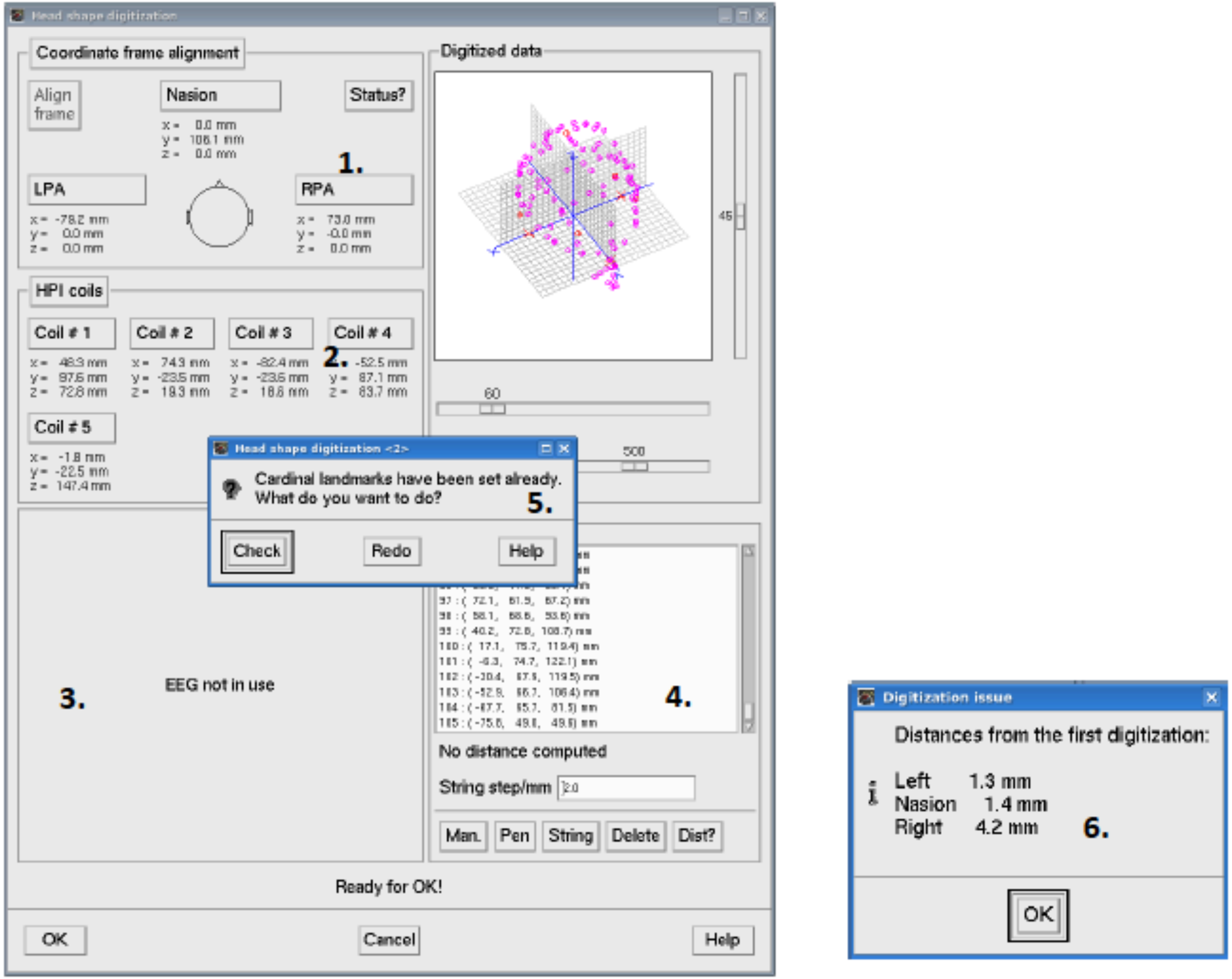
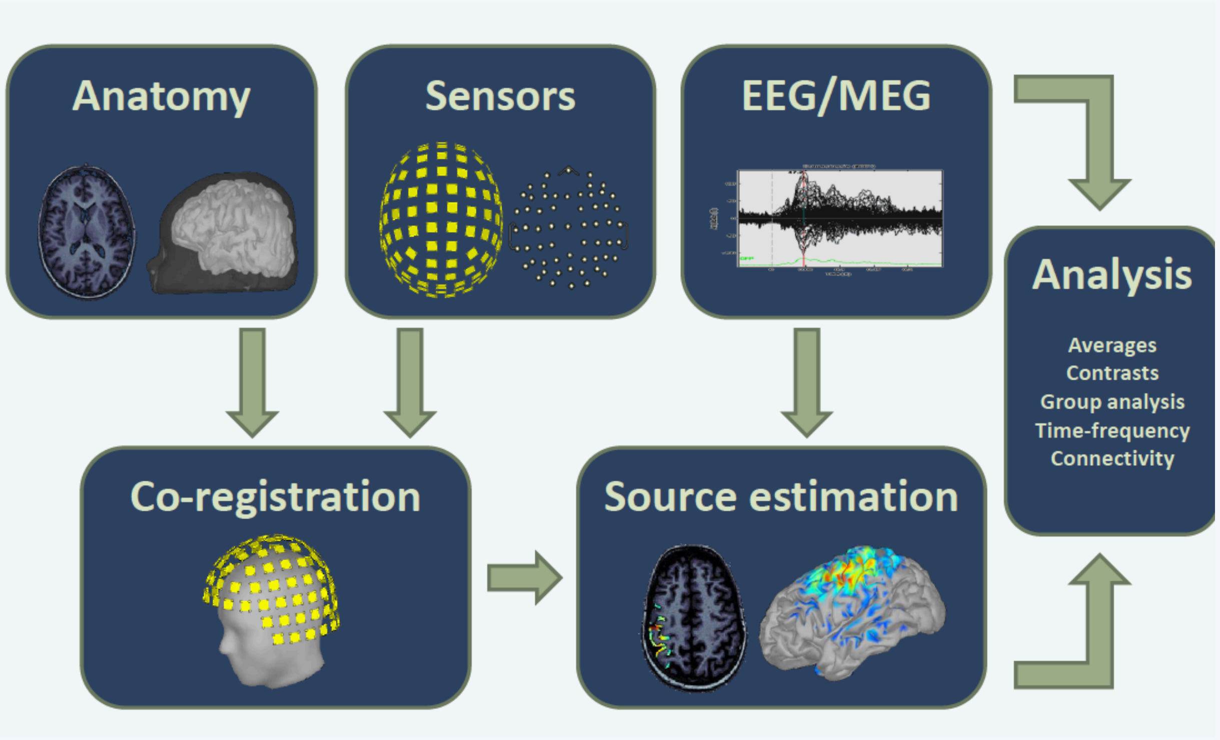


Figure 7: Head digitization. 1. Cardinal landmarks, 2. HPI coils, 3. EEG, 4. Additional points, 5. Check landmarks (quality control), 6. Distances should be < 5mm.

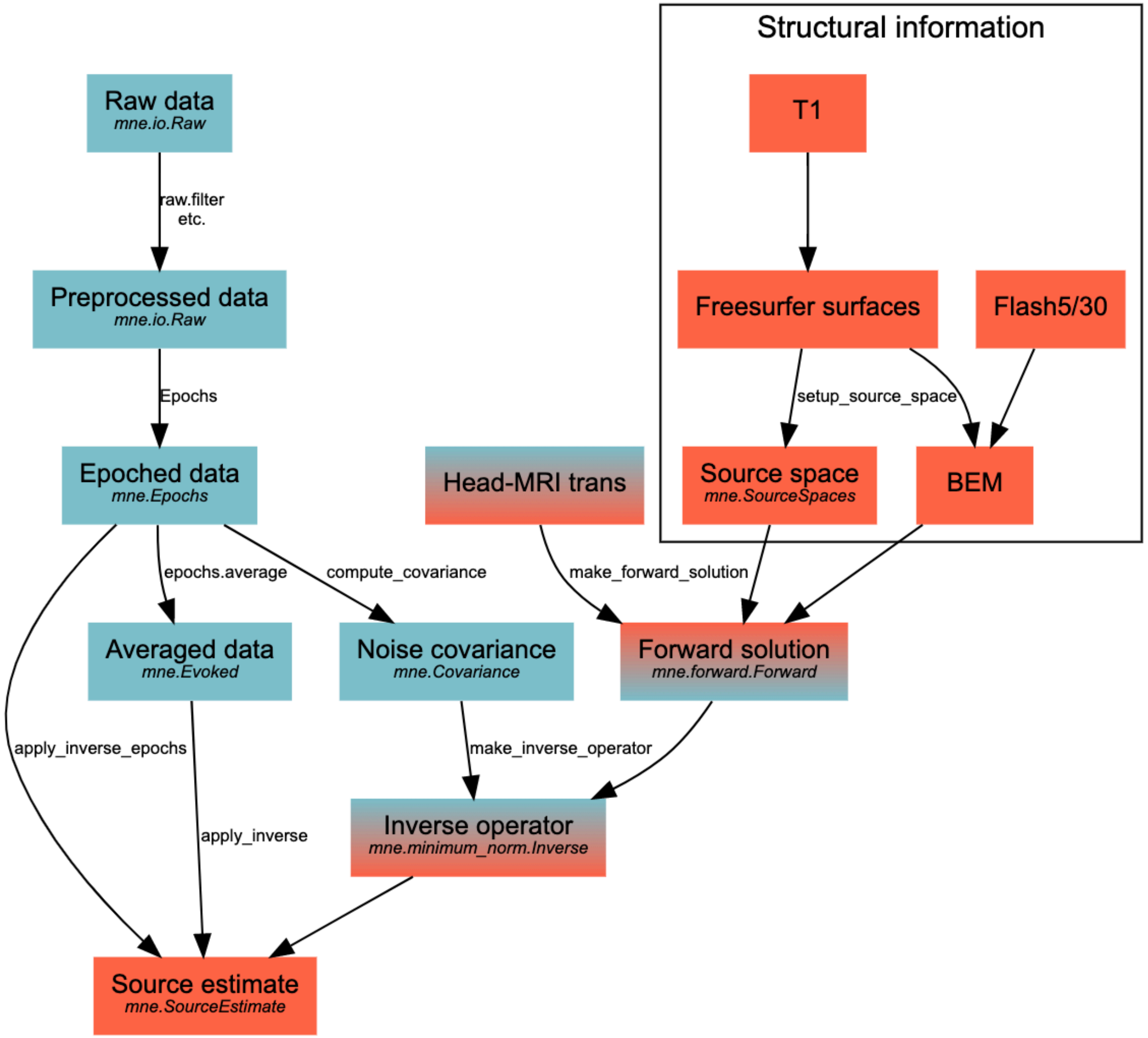
MEG 数据格式

- FIFF: Functional Image File Format;
- 数据结构类似DICOM；
- FIFF files中可包含
  - 连续或平均的MEG/EEG数据；
  - 原始或分割后的影像数据（MR、CT）；
  - 采集参数：采样率、滤波设置、传感器类型、Head-to-MEG坐标转换；
  - 补偿环境磁场噪音的SSP（Signal-space projection）向量；
  - 单个文件最大容量2GB，1000 Hz ~ 26 mins，5000 Hz ~ 5 mins；

Data Analysis Workflow

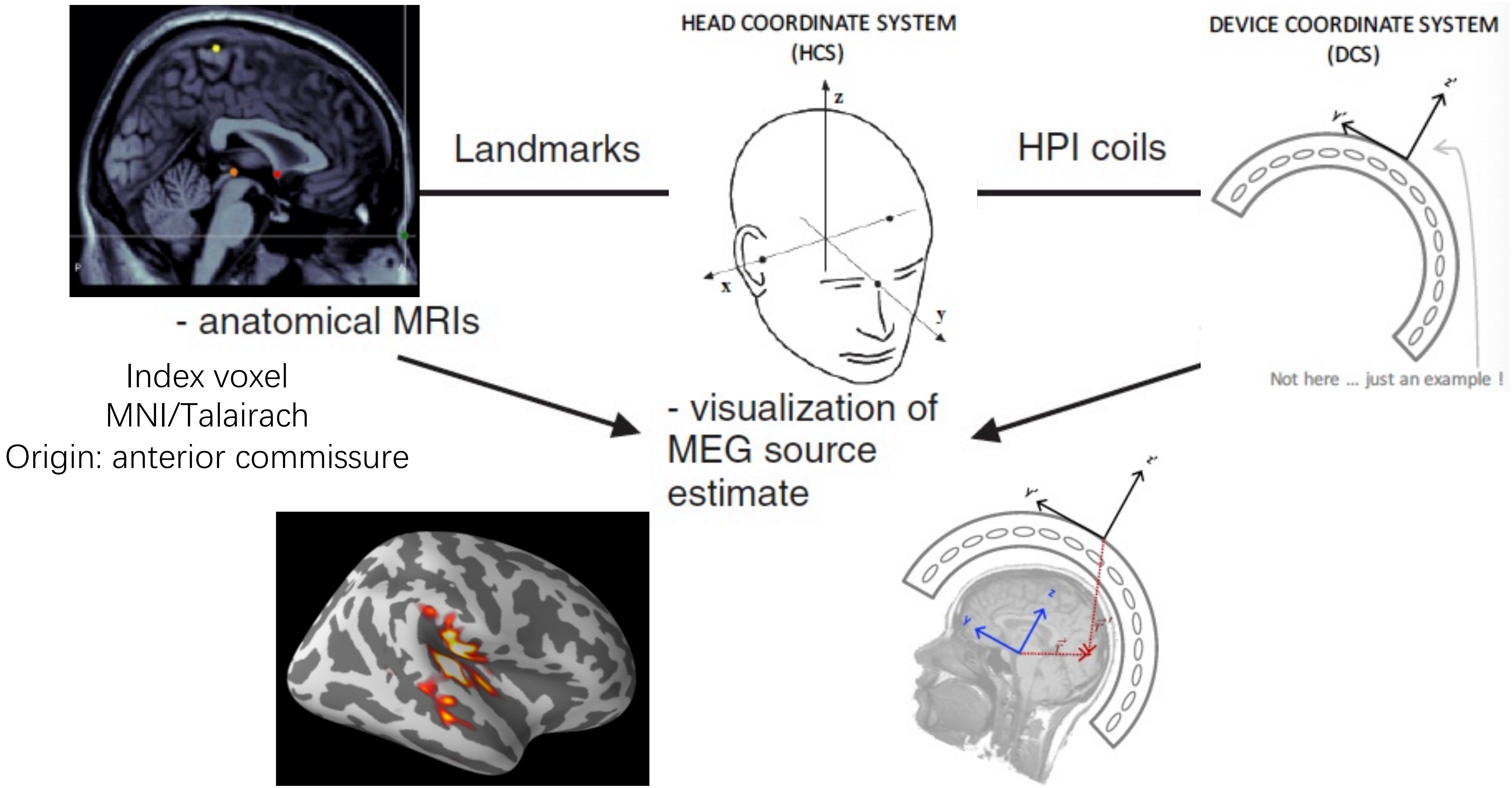


Workflow of the Brainstorm software



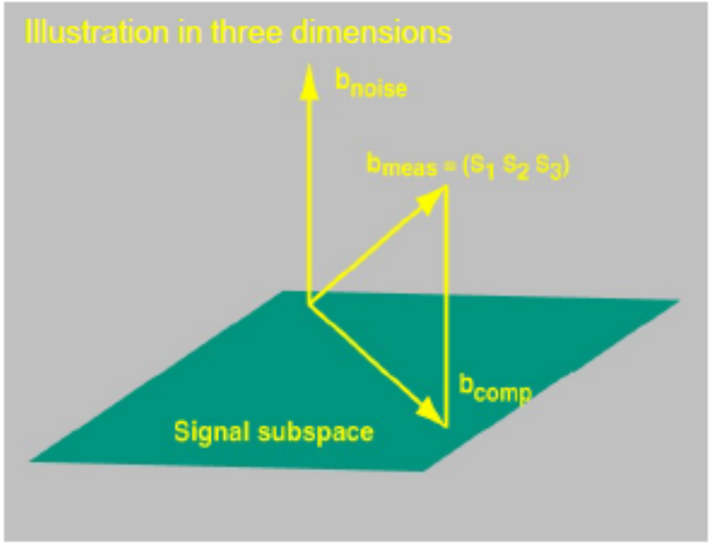
Workflow of the MNE software

MEG数据分析中的坐标系一览



MEG 去噪方法

- Signal Space Projection (SSP)

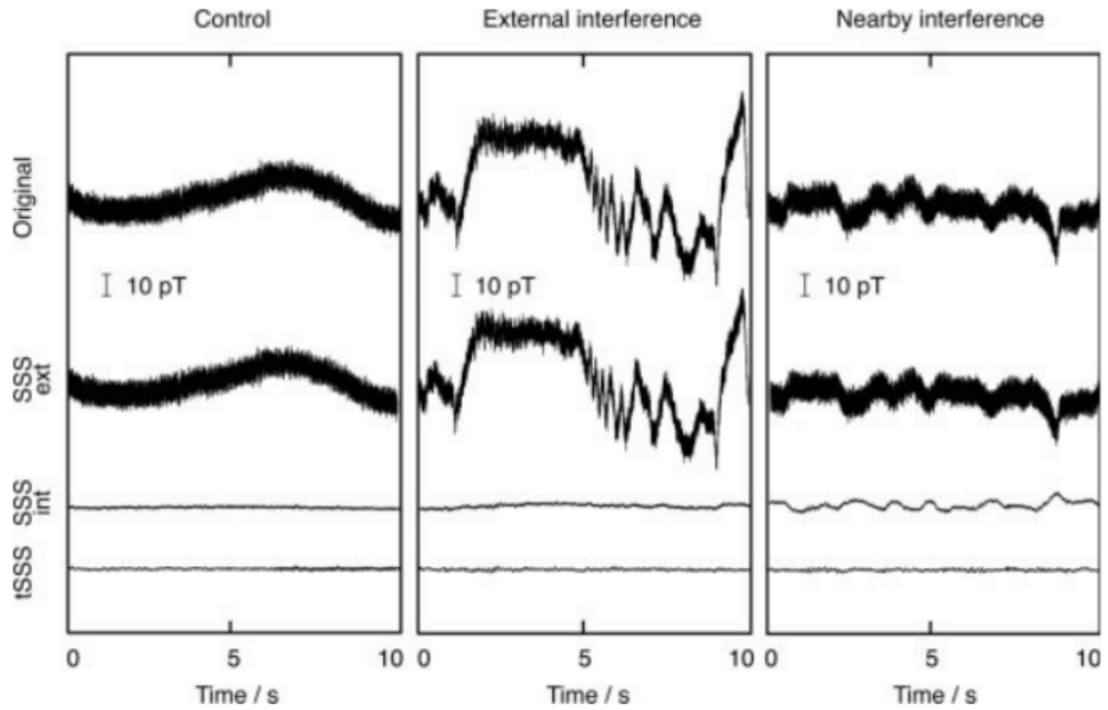


- 306通道的数据理解为306维的信号空间；
- 利用PCA方法分解信号矩阵（奇异值最大的向量）
- 磁力计：3 个向量　梯度计：5个向量；
- 以不同机位和状态采集空房间的数据；

- Signal Space Separation (SSS)

- $b = b_{in} + b_{out} + n$，
- 磁场标量势展开为包含内外磁场信息的谐波函数的叠加，随后分离重建出b_{in}；
- Temporal SSS – 去除在时间尺度上有相似特征的噪音
- 头动补偿 + tSSS　　close-to-sensor artifacts

Performance of SSS & tSSS

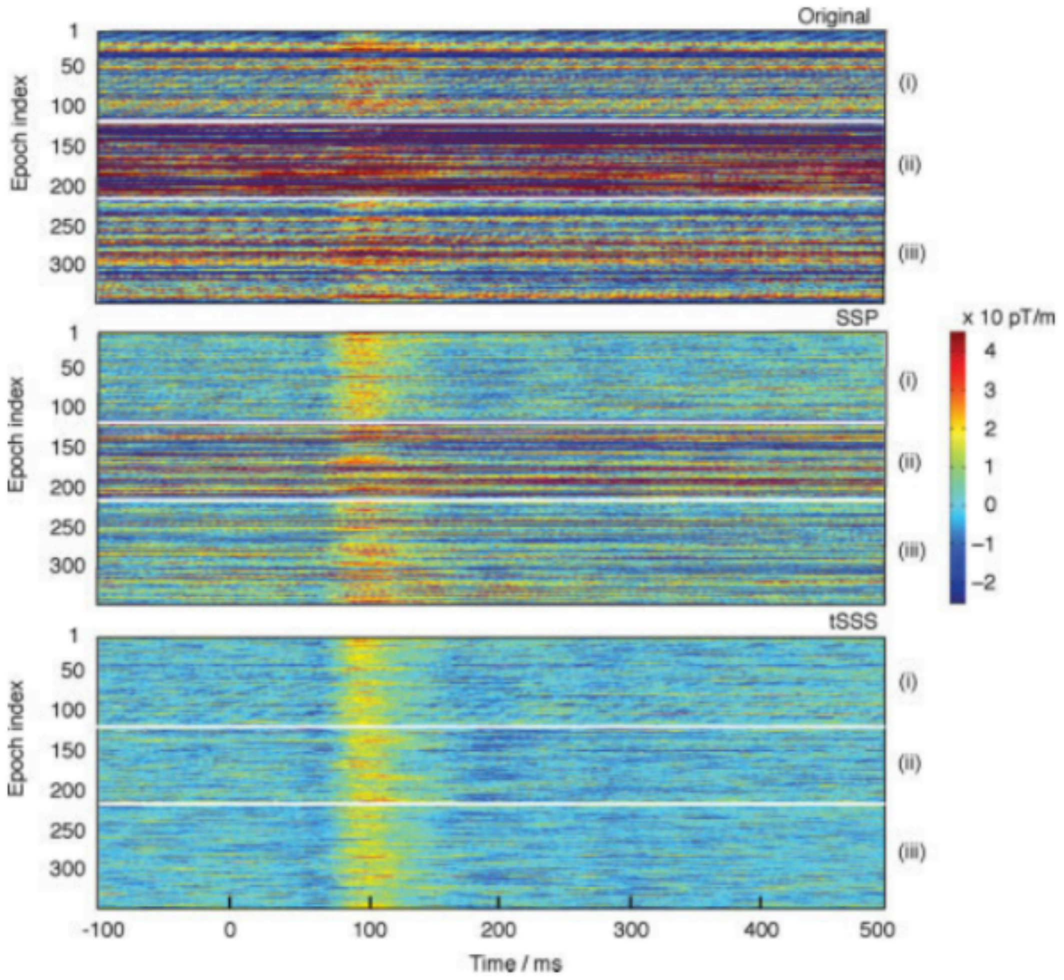


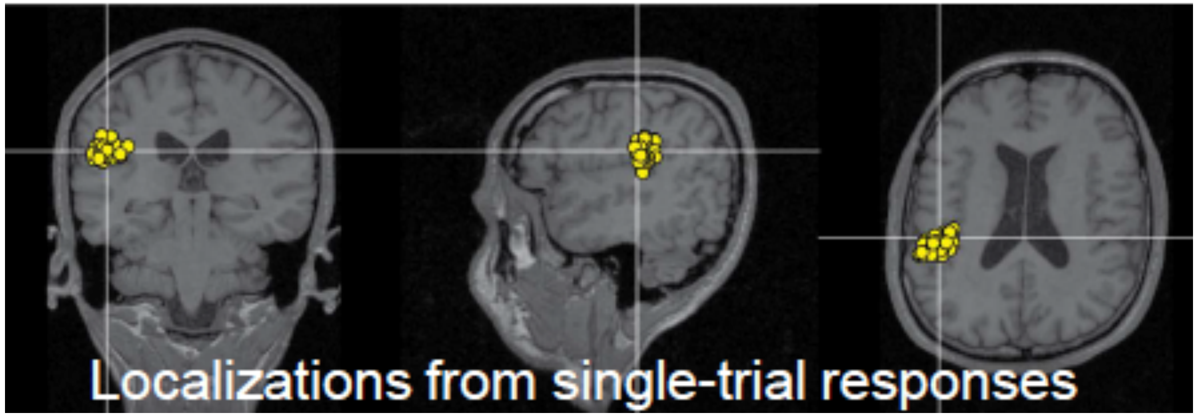
控制条件
无干扰

在屏蔽室
外侧旋转
三块磁铁

在被试嘴唇
固定一根磁
化的金属线

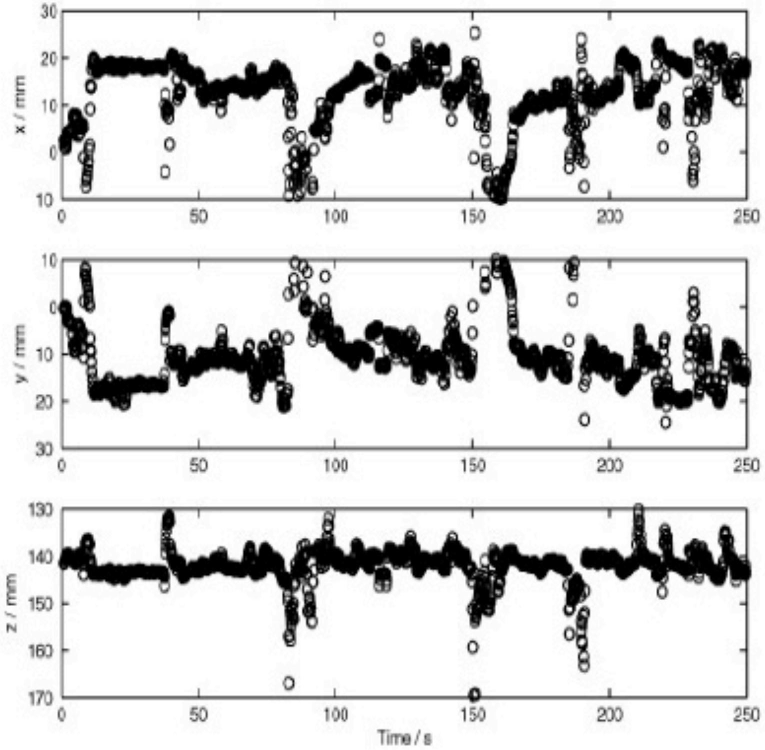
Taulu and Hari, *Hum Brain Mapp*, 2009





SSS-based head movement compensation*

Research example: Movement of a six months old subject



- 头部定位线圈（HPI）

HPI coil digitization order:

1. Blue 293 Hz
2. White 307 Hz
3. Red 314 Hz
4. Black 321 Hz
5. Yellow 328 Hz

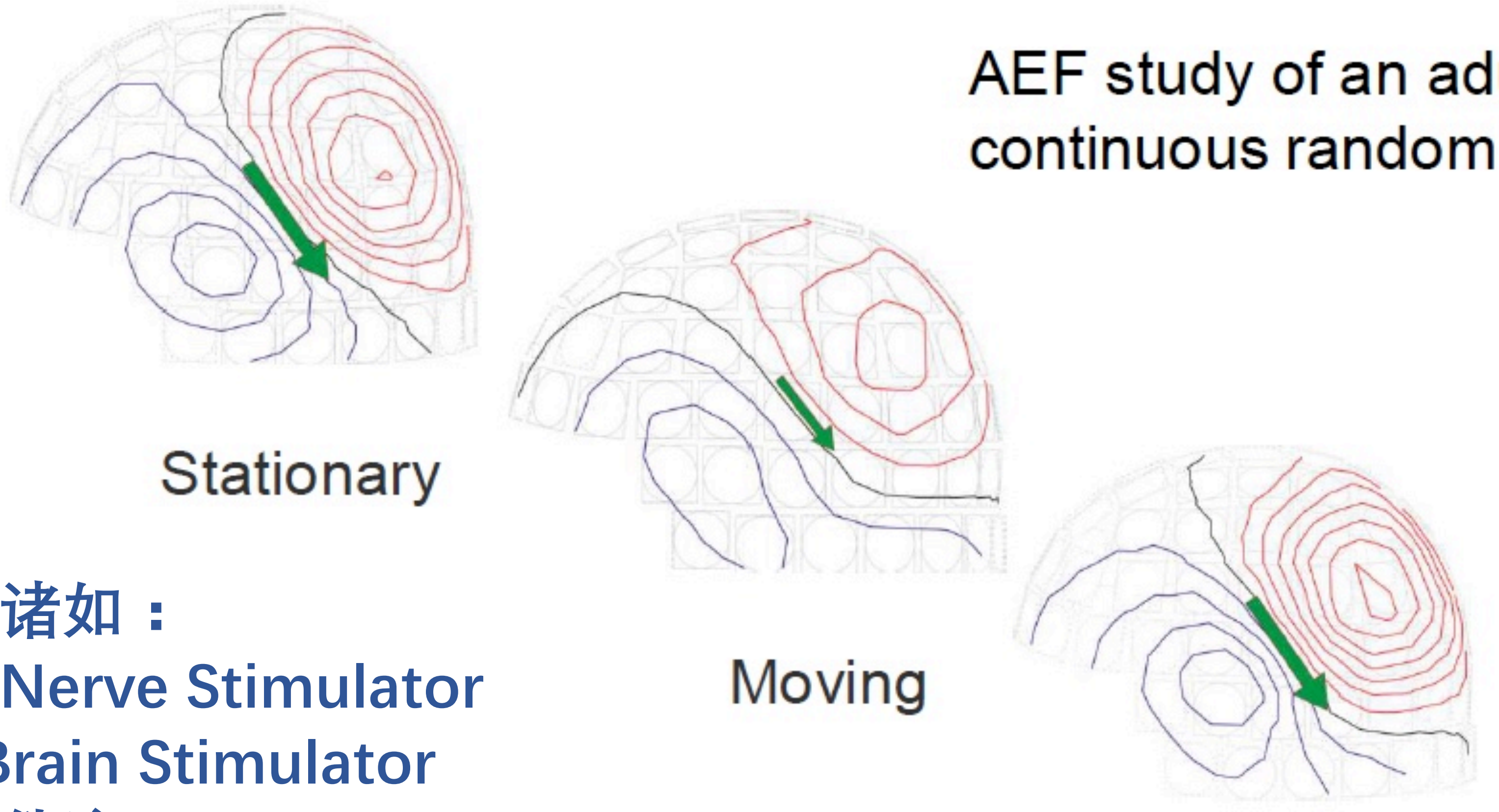
- Continous HPI ✓
- 小于3cm的头动

*Not available in the US, works in progess

Uutela, Taulu, Hämäläinen, NeuroImage, 14(6), 1424-31, 2001

Research example of SSS movement compensation*

AEF study of an adult subject, continuous random head movement

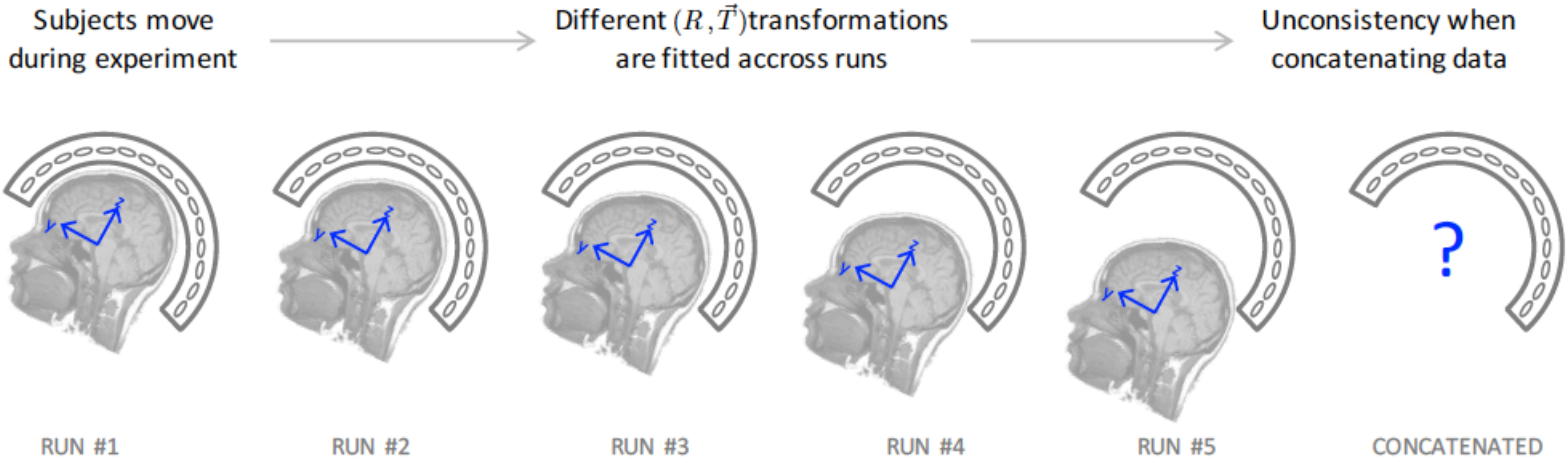


也能去除诸如：
- Vagus Nerve Stimulator
- Deep Brain Stimulator

等造成的伪迹

*Not available in the US, works in progess

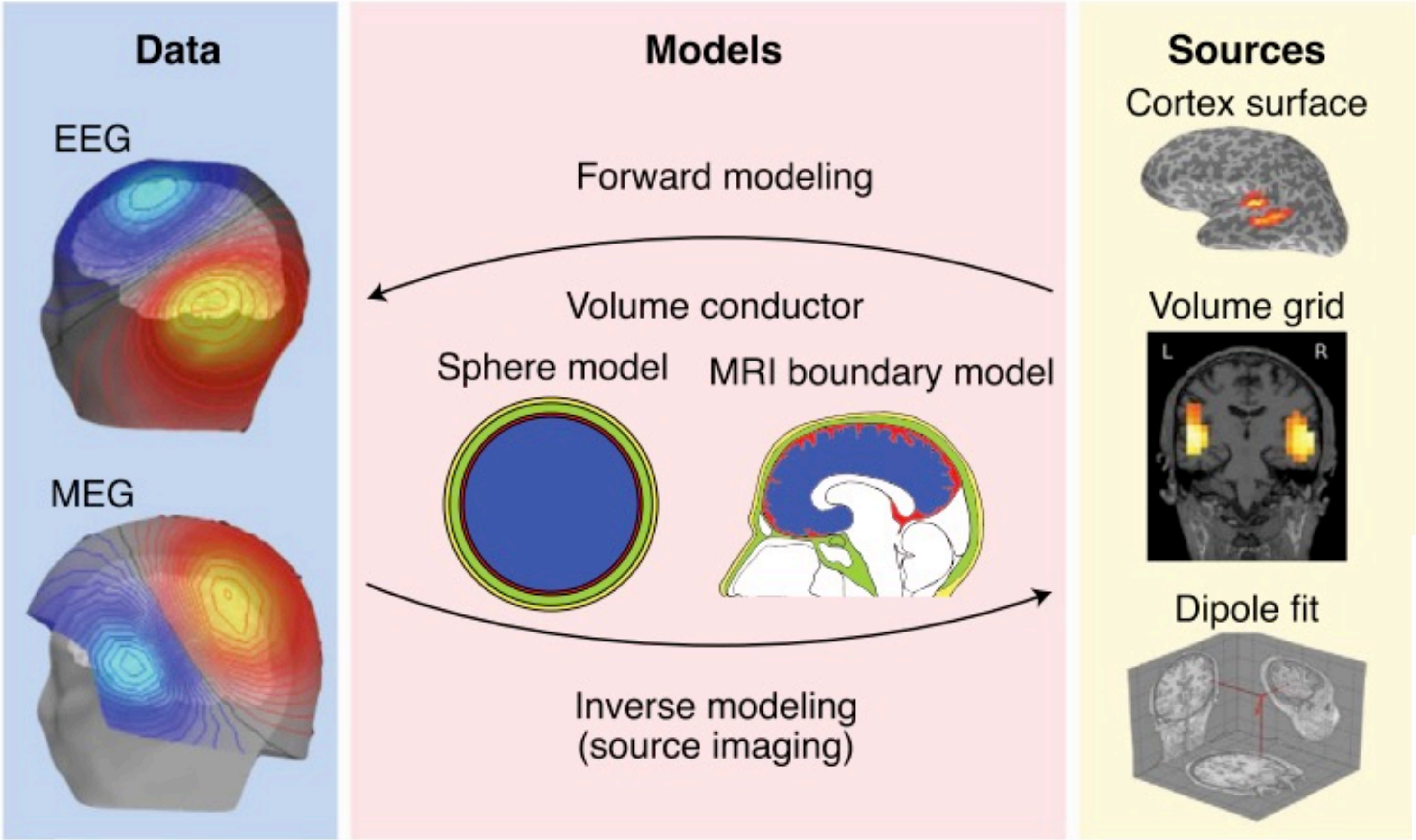
MEG头动校正-without cHPI



- ➢ 实验前和实验中
- - 优化实验设计；
- - 在保证舒适性下使被试头顶尽可能贴近头盔；
- - 实验间隙进入屏蔽室调整座椅高度；

- ➢ 数据分析
- - 源空间分析时分别对每个run进行配准；
- - 传感器空间分析时将所有run配准至最优坐标系，fiff_mean_trans + Maxfilter 实现；

脑磁图的溯源问题



$$\mathbf{b}(t) = \mathbf{G}\mathbf{q}(t) + \mathbf{n}(t)$$

传感器空间
磁场信号

引导场矩阵

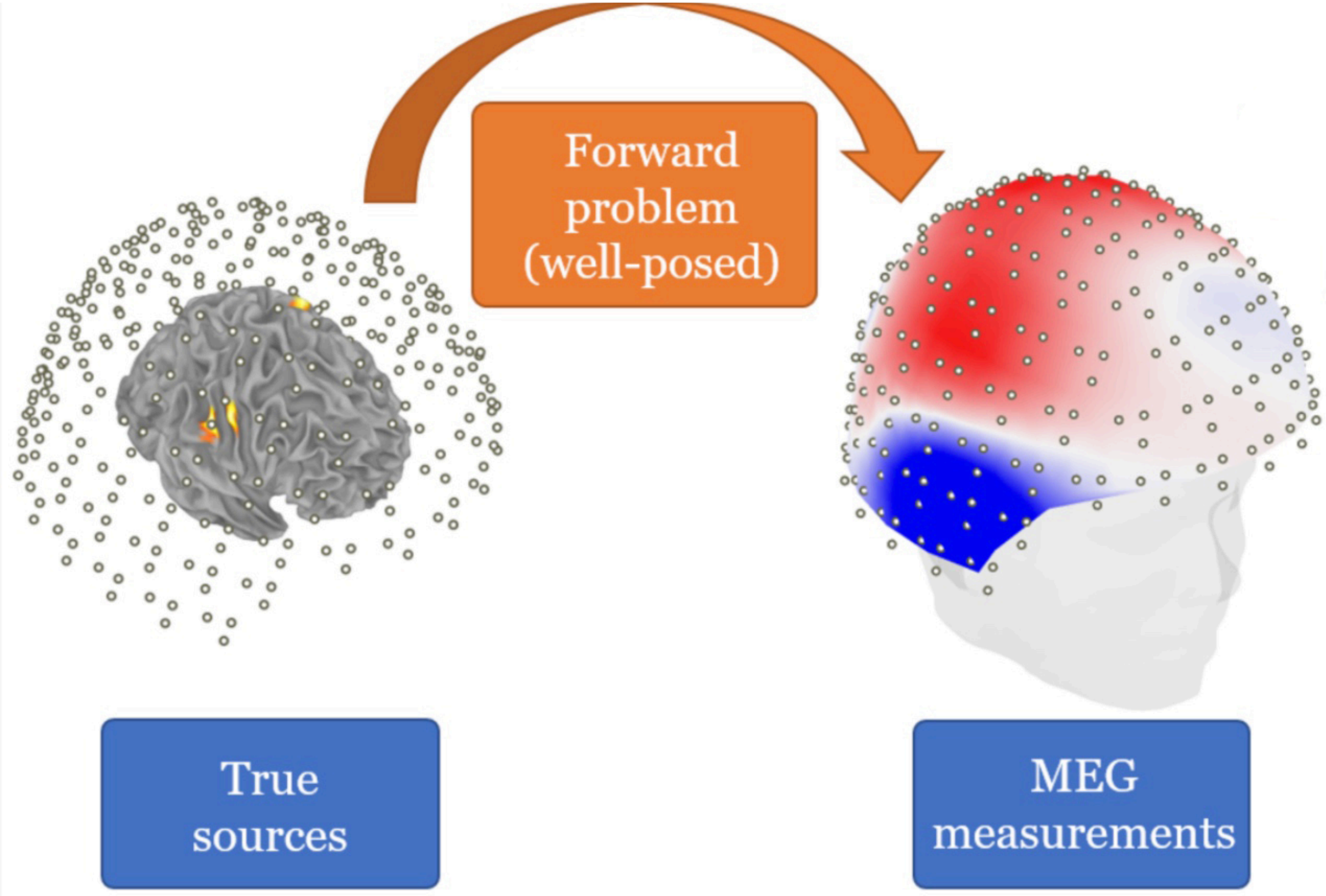
源空间
等效电流偶极子强度

噪音

$$\begin{bmatrix} \mathbf{b}_1 \\ \cdots \\ \mathbf{b}_M \end{bmatrix} = \begin{bmatrix} \mathbf{G}_1(r_1, l_1) & \cdots & \mathbf{G}_1(r_1, l_P) \\ \cdots & \cdots & \cdots \\ \mathbf{G}_M(r_M, l_1) & \cdots & \mathbf{G}_M(r_M, l_P) \end{bmatrix} \begin{bmatrix} q_1 \\ \cdots \\ q_P \end{bmatrix}$$

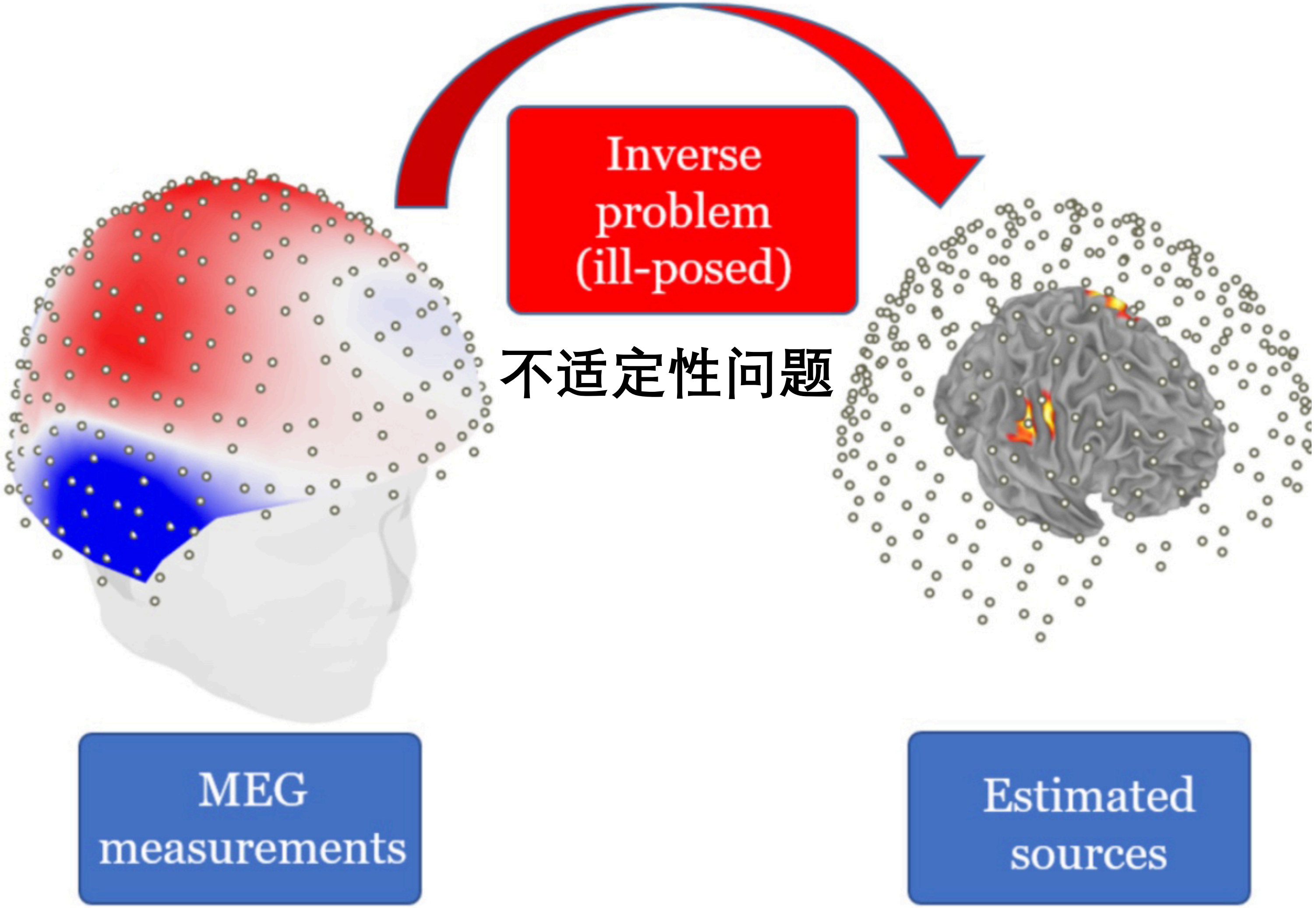
306×1 $\quad$ 306×15000 $\quad$ 15000×1

Forward Problem



- 正问题：适定性问题；
- 对于给定的神经元电流分布和头部电导率分布，通过Maxwell求解传感器空间的磁场分布；
- 球对称模型：假设大脑由具有不同电导率的球壳组成；
- BEM/FEM：边界元/有限元模型
BEM：颅内空间、头骨、头皮；
FEM：四面体-传导的各向异性；

Inverse Problem

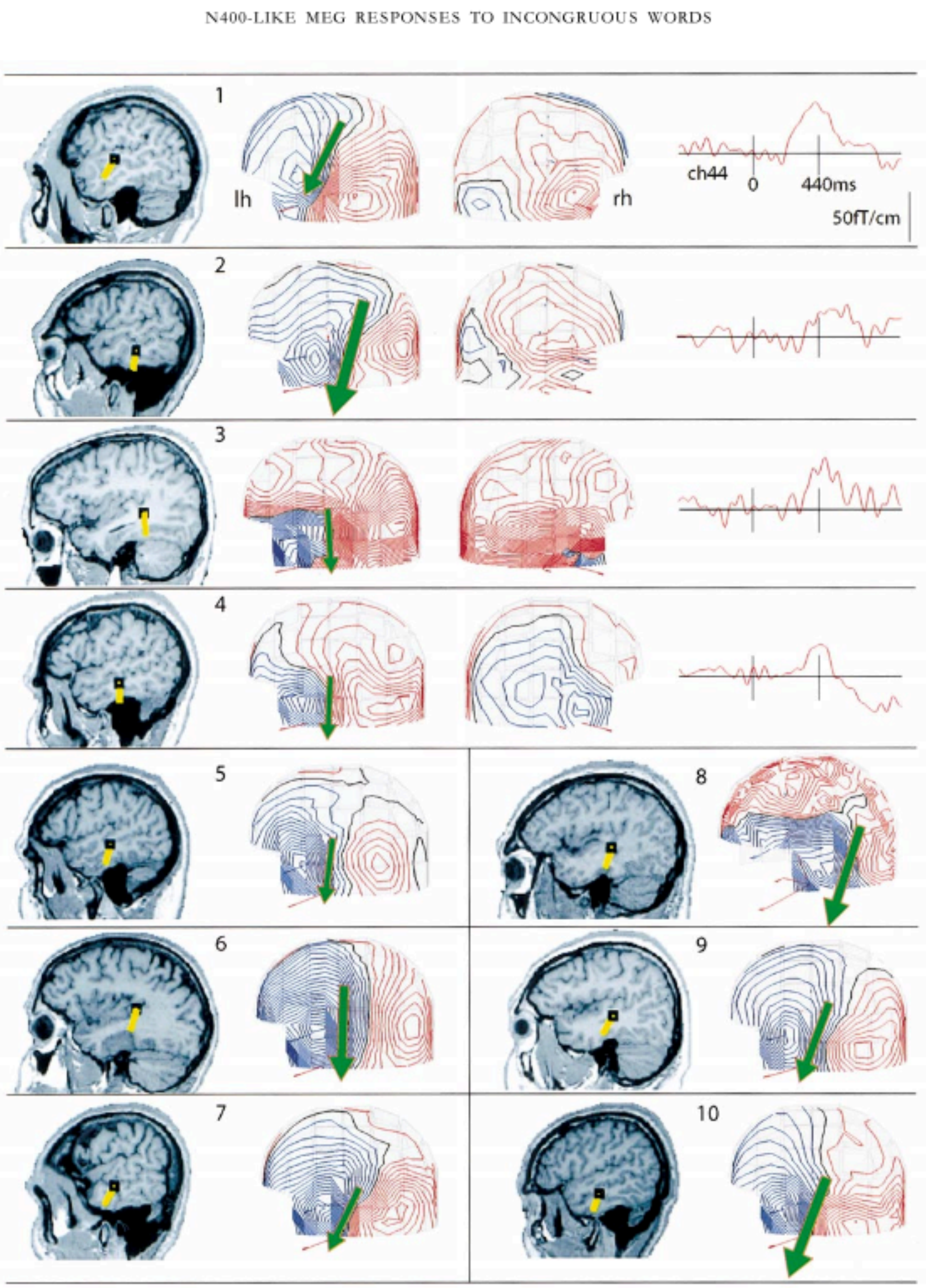


- 参数源模型；
Parametric source model
- 分布源估计；
Distributed current estimates
- 扫描方法；
Scanning approach

参数源模型 Parametric source model

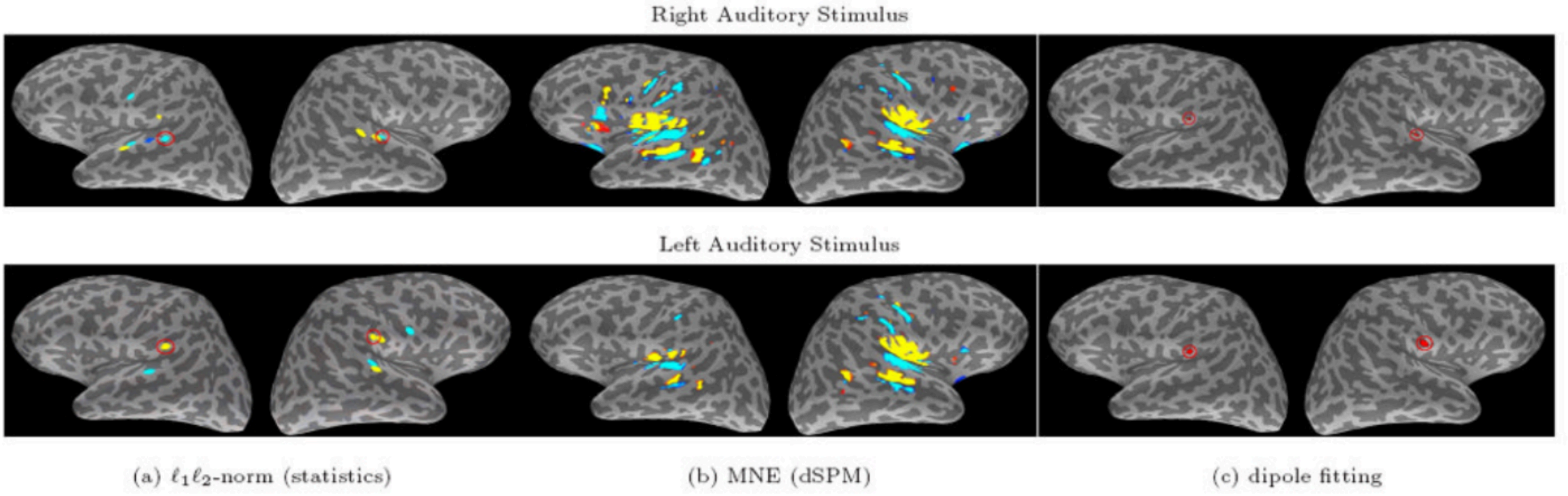
- Equivalent Current Dipoles 等效电流偶极子模型
- **假设**：MEG探测下的皮层源活动具有稀疏性、集中性、预先设定偶极子数量 (有限，2 ~ 5);
- Over-determined：方程数目远多于未知数
- 认知：Primary and secondary sensory responses;
- 临床：癫痫棘波定位；

Halgren et al., *NeuroImage*, 2002



分布源估计 Distributed current estimates

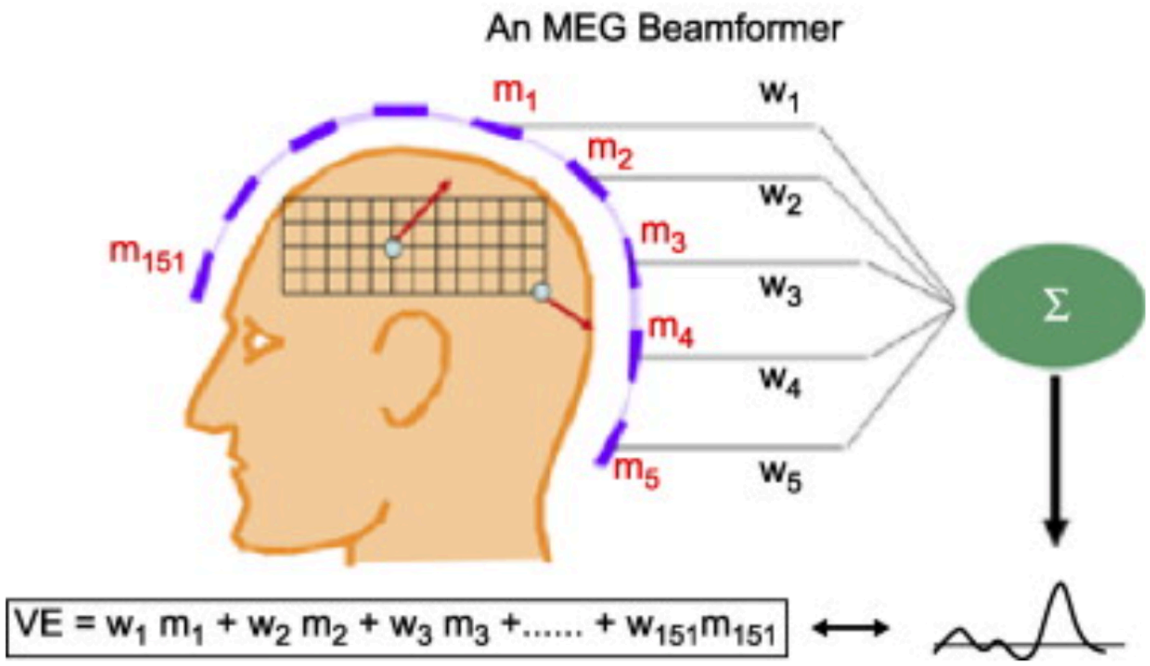
- **假设**：大脑中存在分布的源，源的分布被施加限制，以能拟合传感器空间结果；
- Minimum-Norm Estimate (L_2-norm): 满足分布源的总能量最小，结果呈现弥散性;
- Minimum Current Estimates (L_1-norm): 满足最小一次模最小，呈现稀疏性；



Ou et al., *NeuroImage*, 2009

扫描方法 Scanning approach

- Beamformer：波束成型（空间滤波器）
- 假设：No two distant cortical areas ~cm generate coherent local field potentials over long time scales. ~10^2ms
- 有效利用在induced response的溯源中；
- 缺点：如果大脑中多个脑区存在高度相关的神经活动，受限于假设，该方法只能溯出单个源。



Hillebrand and Barnes, *Inter. Rev. Neuro.*, 2005

MEG 数据处理软件

- 商用软件

- BESA
- CURRY

- 免费软件

- Brainstorm
- Fieldtrip
- MNE
- SPM
- Freesurfer

Free packages

Brainstorm (http://neuroimage.usc.edu/brainstorm/)

- Collaborative, open-source application dedicated to the analysis of brain recordings: MEG, EEG, fNIRS, ECoG, depth electrodes and animal invasive neurophysiology
- Runs on Matlab, provides standalone with matlab runtime
- Provides user friendly graphical user interface (GUI), and a scripting interface
- User forum and online tutorials
- Features
  - Powerful and versatile visualization
  - MRI visualization and coregistration
  - Databasing
  - Graphical batching tools
  - Head modelling and source modelling
    - Minimum norm imaging
    - LCMV beamformer
    - Dipole modeling
  - Time-frequency decomposition
  - Functional connectivity
  - Machine learning

Free packages

FieldTrip (www.fieldtriptoolbox.org)

- Developed at the Donders Institute for Brain, Cognition and Behaviour, Radboud University (Nijmegen, the Netherlands)
- MEG/EEG signal processing platform, including
  - Time-frequency analysis
  - Dipole modelling
  - Distributed (L2) modelling
  - Beamformers, including DICS
  - Non-parametric statistical testing
- Usage via the Matlab command line
  - Requires some Matlab knowledge, allows scripting
- Links to other support packages, such as "FastICA"
- Open-source code and website maintained in https://github.com/fieldtrip
- Tutorials and training courses

- Minimum norm imaging
- LCMV beamformer
- Dipole modeling

Free packages

- **Friendly with FIFF (read & save)**

MNE-suite (https://mne.tools/)

- Community-driven software package for processing EEG and MEG data providing versatile tools and workflows for:
  - Preprocessing and denoising
  - Source estimation
  - Time–frequency analysis
  - Statistical testing
  - Estimation of functional connectivity
  - Applying machine learning algorithms
  - Visualization of sensor- and source-space data
- MNE includes a large set of Python routines supplemented by tools compiled from C code for the LINUX and Mac OSX operating systems, as well as a MATLAB toolbox
- Open-source code maintained in https://github.com/mne-tools/mne-python
- Tutorials and training courses

Free packages

SPM12 (http://www.fil.ion.ucl.ac.uk/spm/software/spm12/)

- SPM12 is developed by the Wellcome Centre for Human NeuroImaging, UCL Queen Square Institute of Neurology (London, UK)
- Further development by EEG/MEG community
- Features:
  - Runs on Matlab, supports both GUI, script and batch scripts
  - Automated MRI/MEG coregistration, segmentation and modeling
  - Processing of raw/epoched MEG/EEG data
  - Time-frequency analysis
  - Source modelling using DAiSS extension - **Data Analysis in Source Space**
  - Advanced statistics
  - Uses internally some functions of FieldTrip toolbox
  - Easy interface with other SPM extensions
  - Code maintained at https://github.com/spm/spm12

Free packages

FreeSurfer (http://freesurfer.net)

- Developed by the Martinos Centre (Harvard University)
- Runs on Linux, requires hardware-accelerated 3D graphics (OpenGL)
- Reads MRI slices in DICOM and other common formats
- Features:
  - Automatic segmentation of the cranium and grey matter sheet
  - Inflation and flattening of the cortex
  - Morphing maps (based on the sulcal-gyral structure) to transform locations from subject to another or to a standard/average brain
  - Talairach transformation
  - Template-based parcellation of the cortex; volumetric measures
- Used by MNE-suite for segmentation of the cortex/gray matter and visualization of functional MEG/EEG analysis results

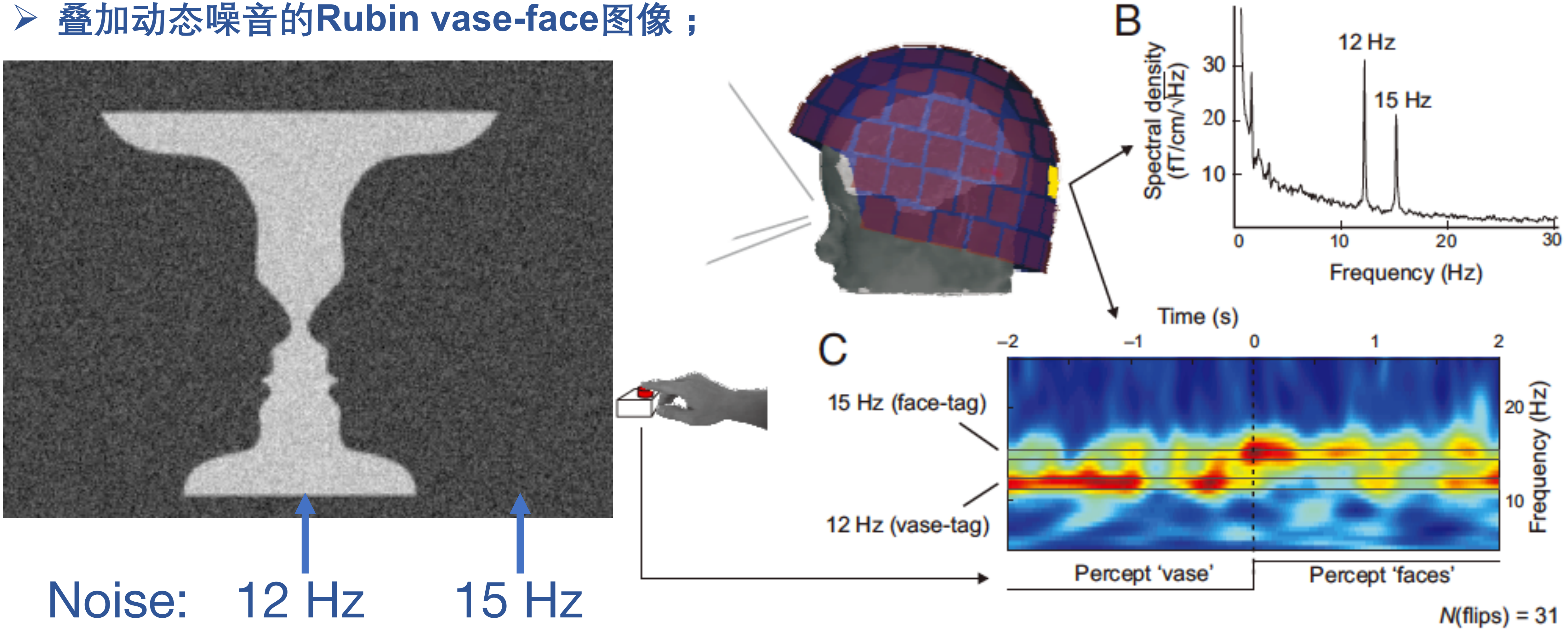
Need any assistance with MEG?

- Questions and problems related to MEGIN products: email to support@megin.fi
- General MEG questions: https://www.biomagcentral.org
  MEG community
- Americal Clinical MEG Society: www.acmegs.org
  - Clinical MEG guidelines
  - Case examples
  - Webinars
- The forums of main free packages

Early visual brain areas reflect the percept of an ambiguous scene

Lauri Parkkonen[a,1], Jesper Andersson[a,b], Matti Hämäläinen[c,d], and Riitta Hari[a,e,1]

- 叠加动态噪音的Rubin vase-face图像；



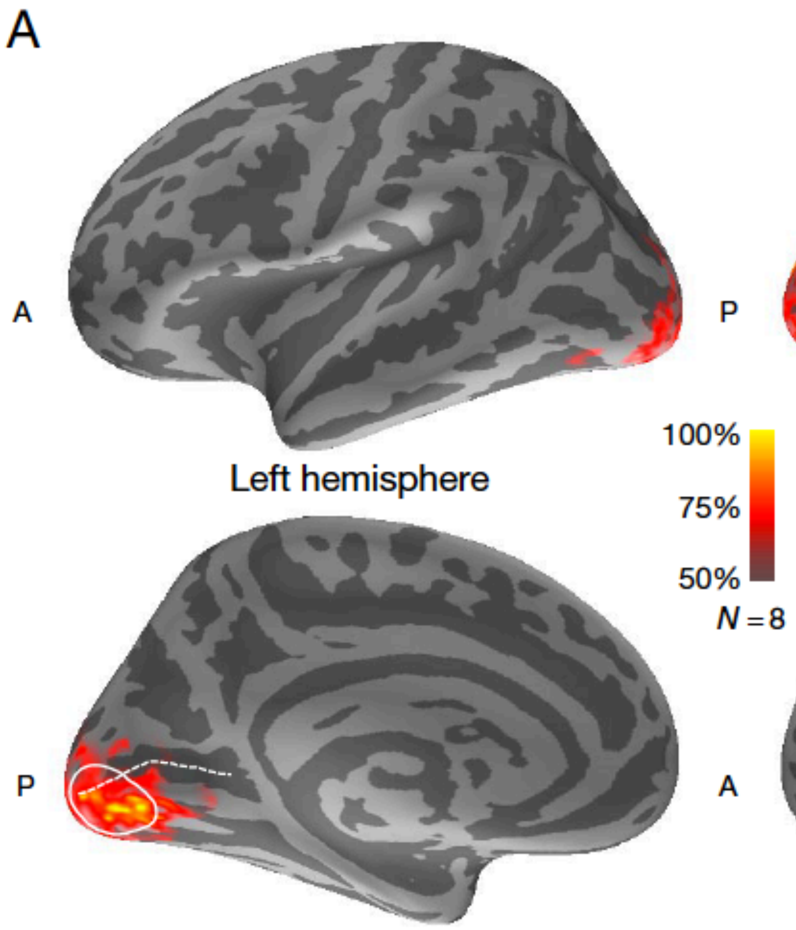
Noise: 12 Hz 15 Hz

PNAS 2008

Early visual brain areas reflect the percept of an ambiguous scene

Lauri Parkkonen[a,1], Jesper Andersson[a,b], Matti Hämäläinen[c,d], and Riitta Hari[a,e,1]

➢ 两种频率标记下源空间结果



- 将数据切分成1s的epoch;

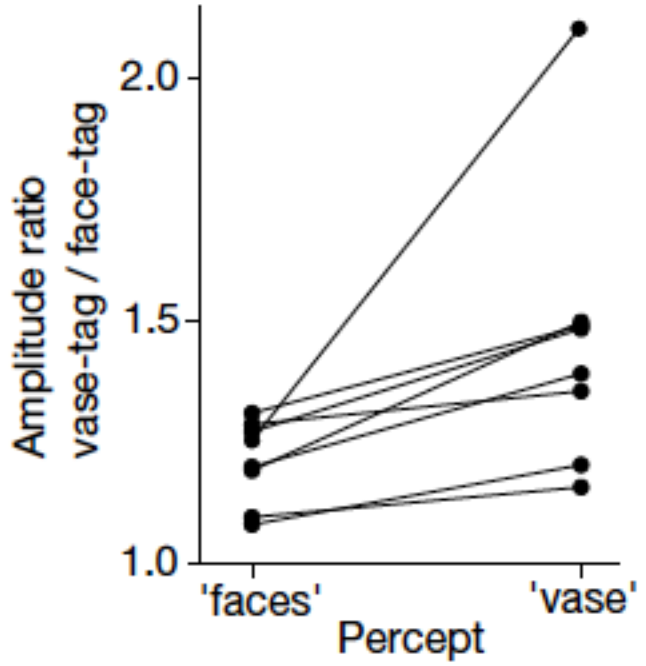
+

- GLM；

+

- MEG溯源 (MNE)；

➢ ROI analysis



PNAS 2019

Neural dynamics of semantic composition

Bingjiang Lyu[a], Hun S. Choi[a], William D. Marslen-Wilson[a], Alex Clarke[a], Billi Randall[a], and Lorraine K. Tyler[a,1]

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- 大脑在进行语义组合加工时的动态神经机制；
- 材料：简单口语句子
  动词+直接宾语 (eat the apple);
- E/MEG溯源 + MVPA + 计算语义模型
- SPM12: Empirical Bayesian MEG and EEG data fusion scheme