



BraInstaRT



ФЕДЕРАЛЬНЫЙ ЦЕНТР
МОЗГА
И НЕЙРОТЕХНОЛОГИЙ

LIFE
Life Improvement by Future Technologies Center



Кортикальные волны и решение обратной задачи ЭЭГ и МЭГ для локализации нефакторизуемых в пространстве и времени нейрональных источников

Алексей Осадчий, Ph.D., д.ф.-м.н.

Нелинейные волны, Нижний Новгород, 2024



Neurointerfaces

- Non-invasive**
 - Rehabilitation
 - Fan
- Invasive**
 - Motor decoding
 - Speech decoding
 - Eloquent cortex mapping
 - Bidirectional interfaces
- Electromyographic**

Neurofeedback

- Technology**
 - Instantaneous neurofeedback
 - NFBLab - software for flexible experiments
- Fundamentals**
 - Nature of changes in EEG
 - Alpha training and its behavioral correlates
- Applications**
 - SMR training in epilepsy management
 - Brain-state contingent stimulation

Neurovisualization

- Real-time cortical mapping**
 - Cognigraph software
 - Application for post-stroke rehabilitation
- Magnetoencephalography**
 - Novel sensors
 - Inverse modelling
 - Cortical waves prior
 - Synchronous sources (Anti-PSIICOS)
 - Functional networks
 - PSIICOS
 - DTI regularized PSIICOS
 - Tools for epilepsy diagnostics



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ЦЕНТР
БИОЭЛЕКТРИЧЕСКИХ
ИНТЕРФЕЙСОВ

Технология
мгновенной
нейрообратной
связи
iNeurofeedback

Новые методы
решения обратной
задачи МЭГ

Многоканальная
магнитоэнцефалография
на основе
магнитометров с
оптической
накачкой

Математические
методы
локализации
кортикальных волн
по неинвазивным
МЭГ и ЭЭГ данным

Цифровой двойник
fMRI на основе
ЭЭГ

Исследование
нейрофизиологии
медитации

Электромиографические
интерфейсы для
бионических
протезов с большим
числом степеней
свободы

Неинвазивная
локализация
эпилептогенных зон
по МЭГ и ЭЭГ
данным пациентов
с эпилепсией

Центр биоэлектрических интерфейсов

Новости Сотрудники Зеркальная лаборатория Оборудование и методы Учебная деятельность Публикации Партнеры Вакансии Как на

Для сотрудников

Основной целью Центра является разработка информационной технологии двунаправленных коммуникаций с использованием кортикографического интерфейса в сочетании с современными методами обработки многомерных данных и соматосенсорной обратной связью посредством электростимуляции или сенсорного замещения.

Проект выполняется совместно с клиническим медицинским центром Московского Государственного медико-стоматологического университета им. А.И. Евдокимова и Российским НИИ нейрохирургии им. А.Л. Поленова, которые являются клиническими базами этого междисциплинарного проекта.

[Подробнее о Центре биоэлектрических интерфейсов](#)

Новости -



Опубликована статья в журнале NeuroImage!

5

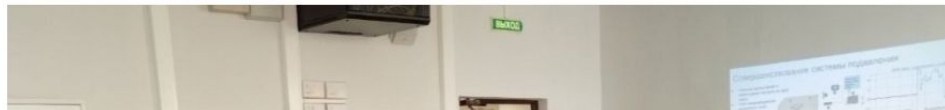
ОКТ
2024

Статья: «Representational dissimilarity component analysis (ReDisCA)».
Авторы: Алексей Осадчий, Илья Семенков, Анна Журавлёва, Владимир Козунов, Олег Сериков, Екатерина Волошина.

[репортаж о событии](#)

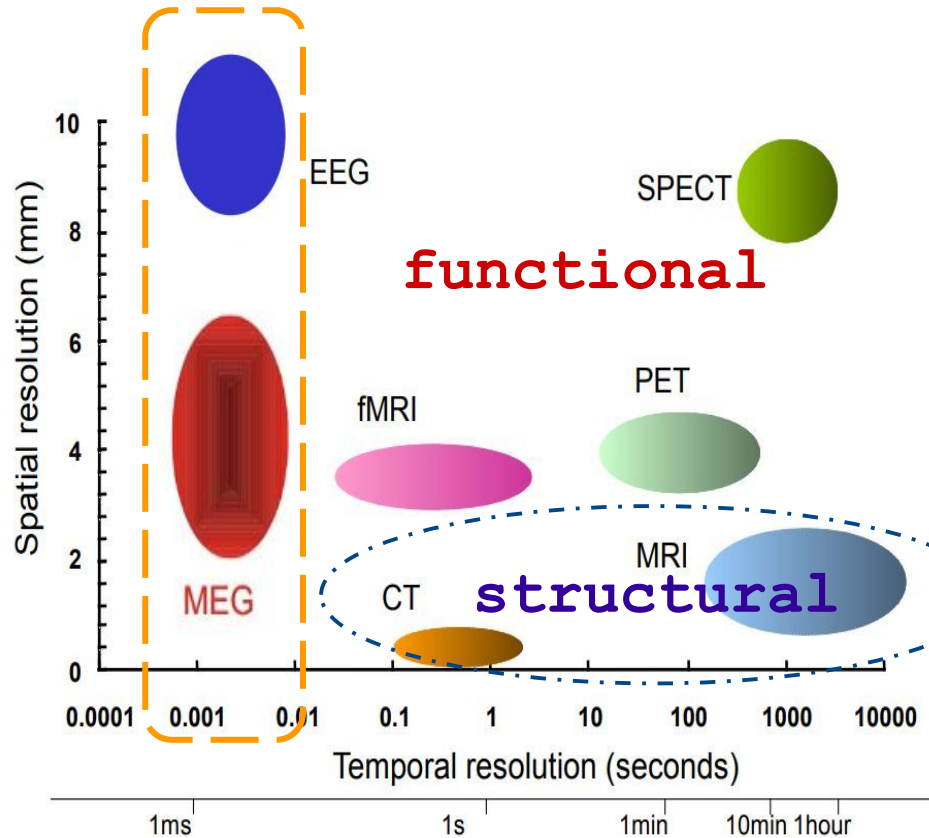


30

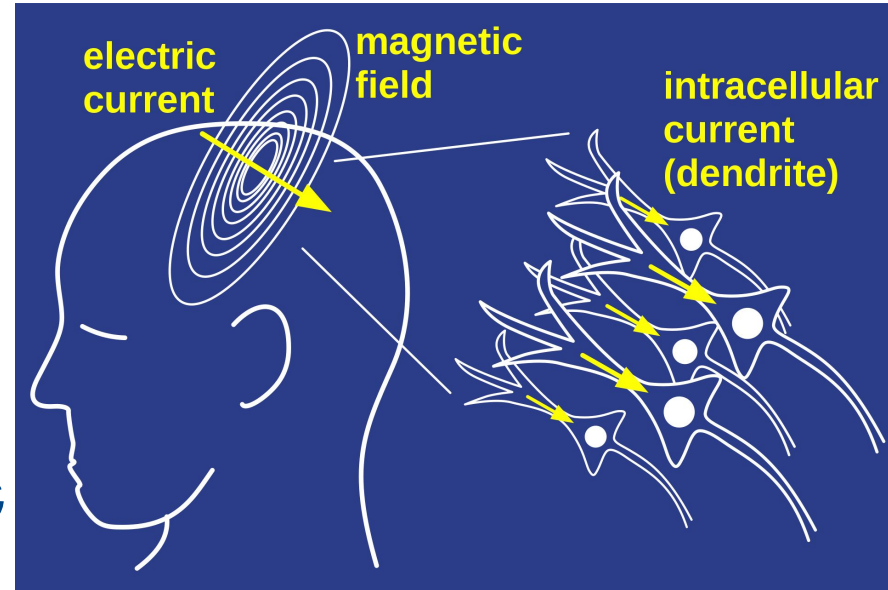


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MEG's typical intro



MEG's signal origin

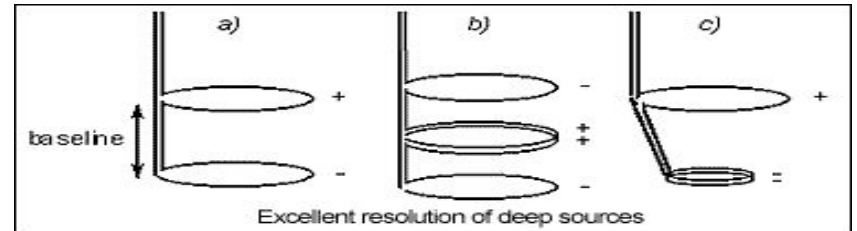
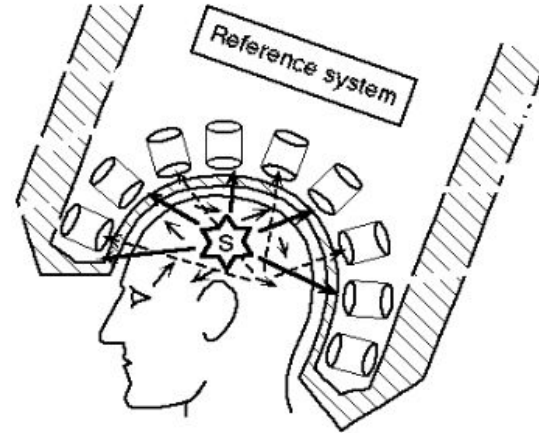


Modern SQUID-based MEG machine

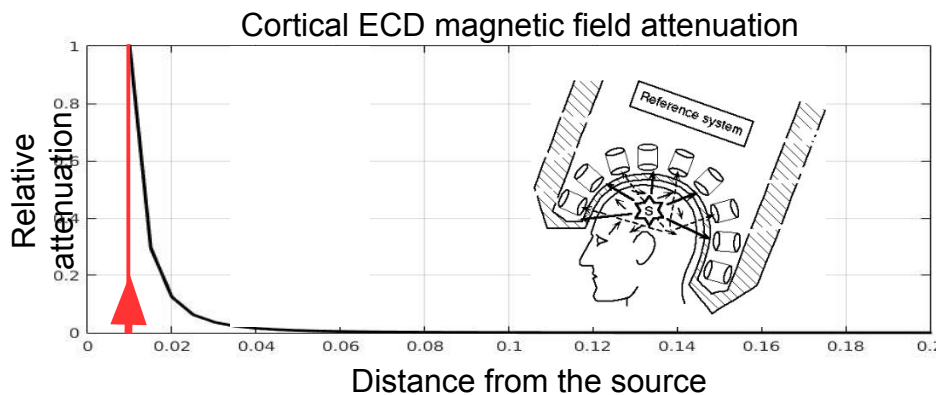
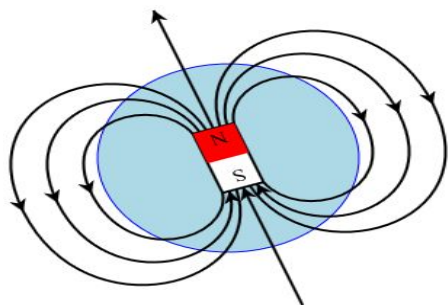
Neuromag Elekta: 102 sites
2 planar gradiometers, 1 magnetometer



CTF: up to 275 sites
1 radial gradiometer

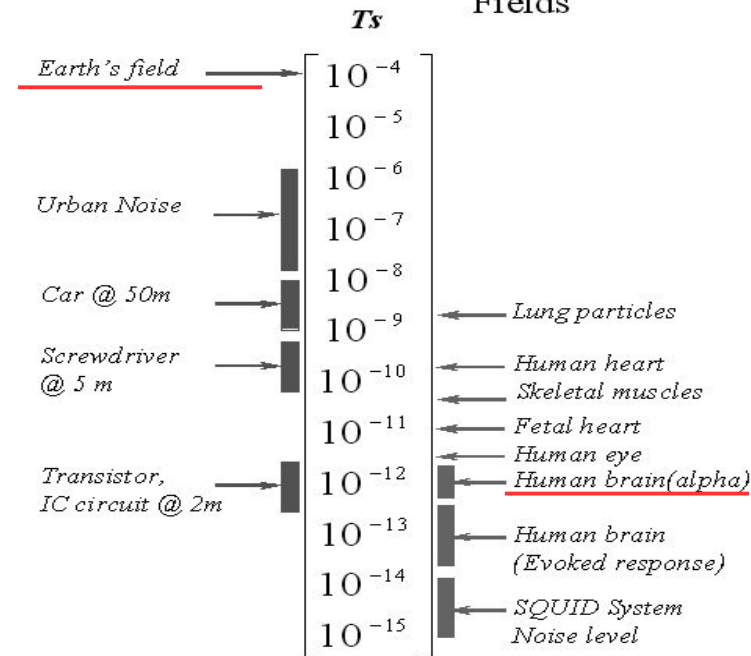


The magnetic field of brain sources is 8 orders of magnitude weaker than that of the Earth!



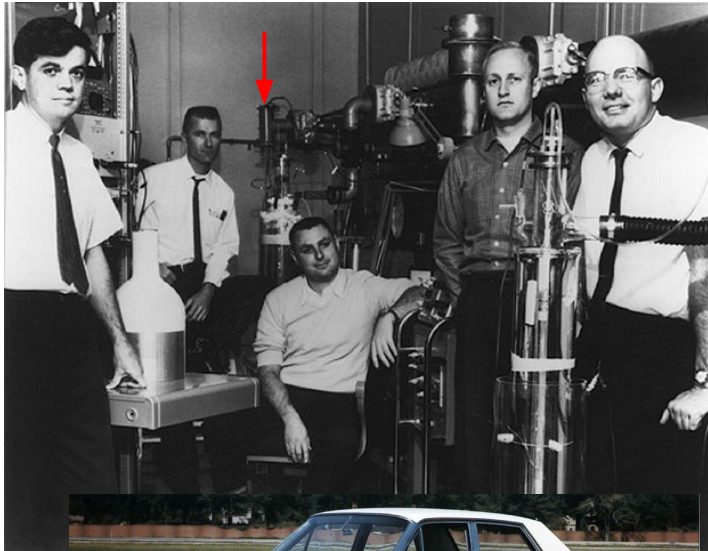
External Fields

Bio-magnetic Fields

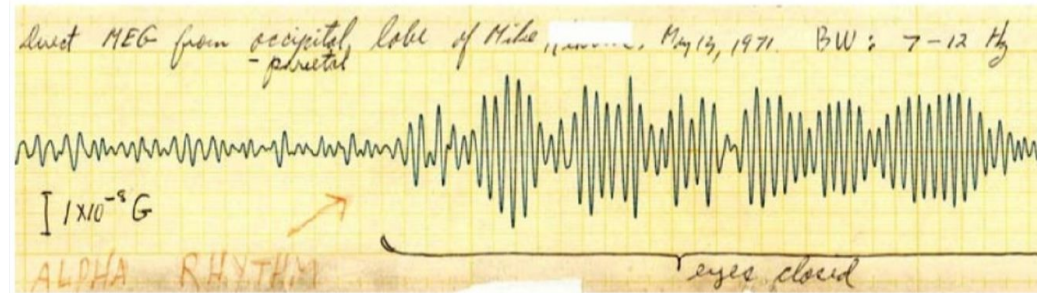
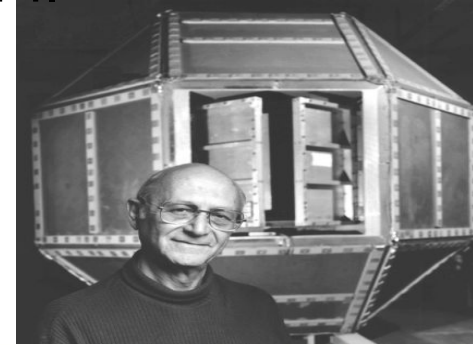


First MEG recordings with SQUIDS

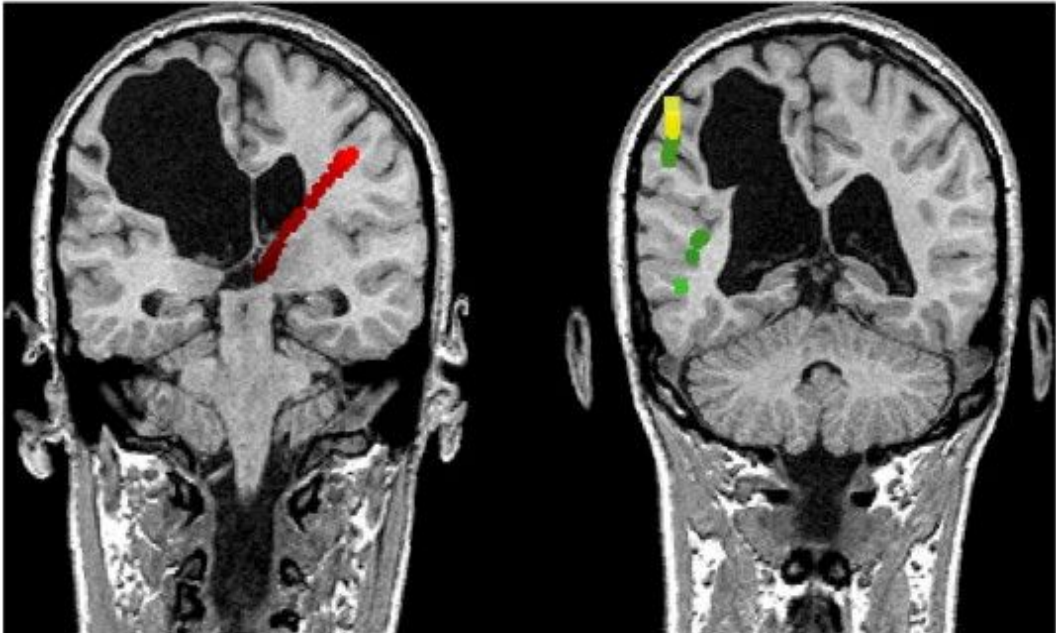
SQUID, Jim Zimmerman
1965



David Cohen, Edgar Edelsack
1971



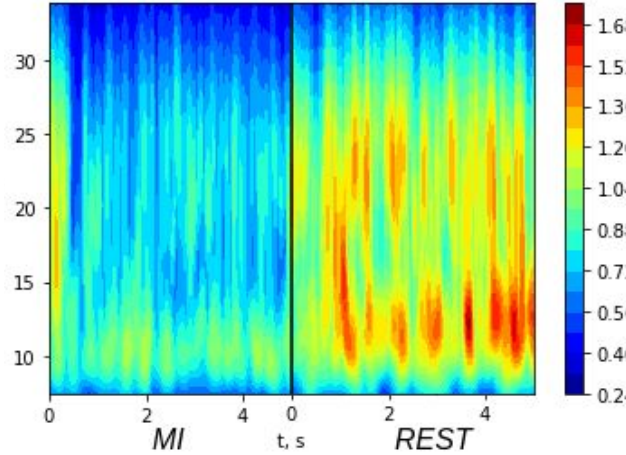
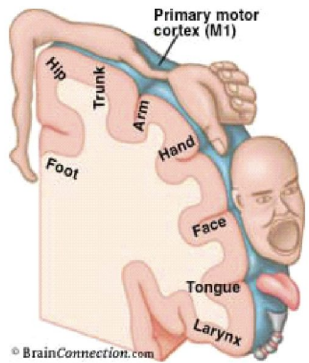
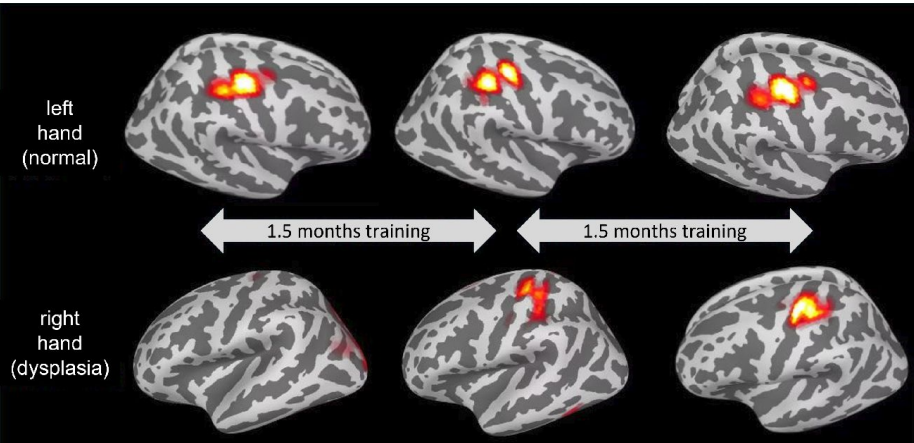
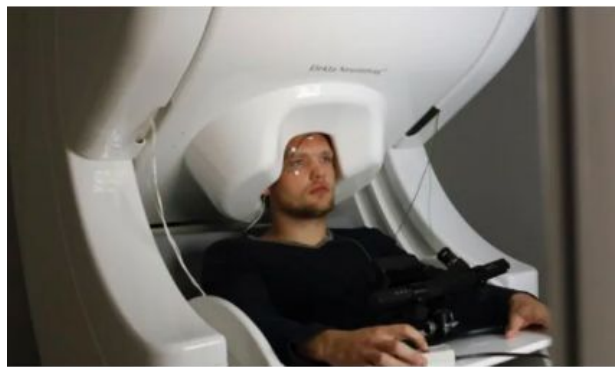
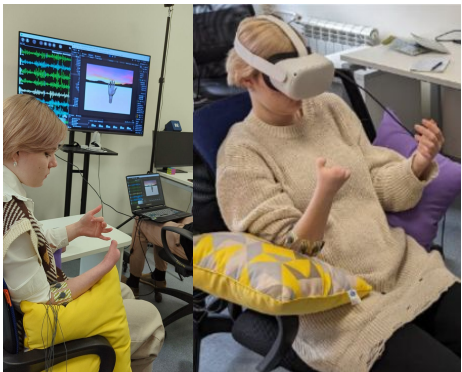
Tracking thalamo-cortical propagation via axonal tracts with MEG



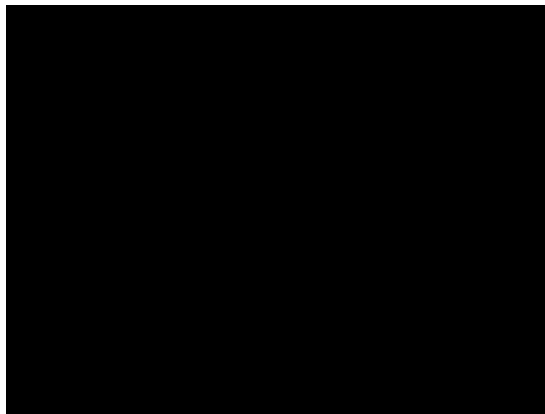
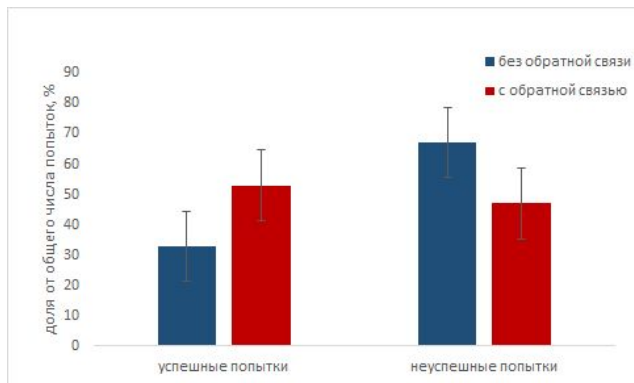
Congenital hypoplasia patient trained in EMG + VR, screened with MEG



Train
(3 months)



Bidirectional ECoG based BCI (2019)



Electro-tactile stimulation



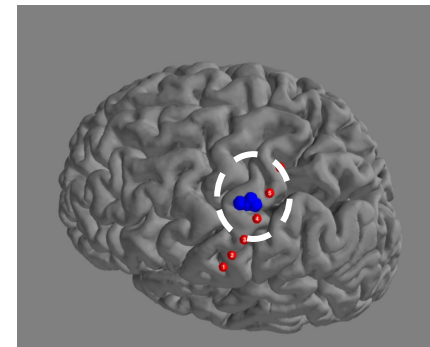
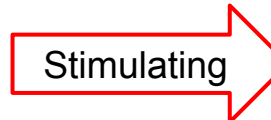
Source localization



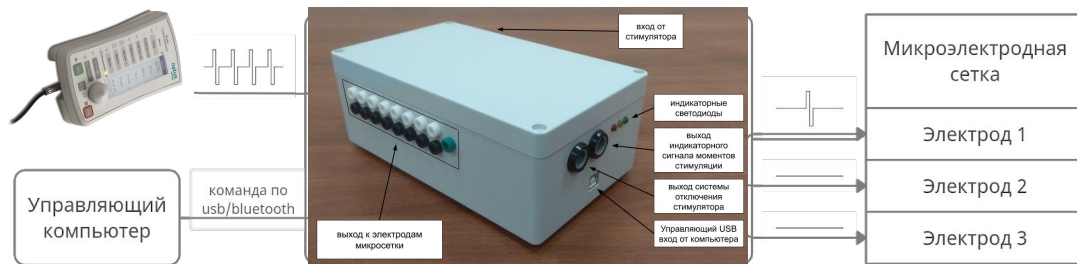
Decoding



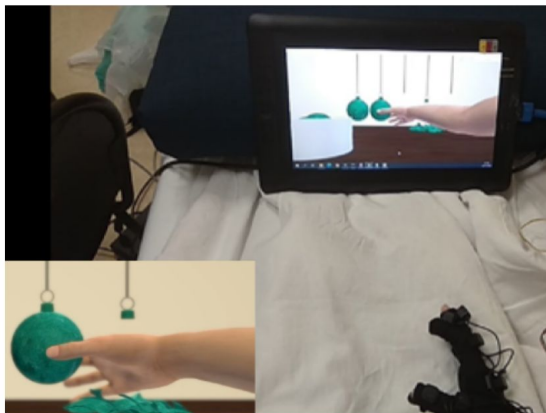
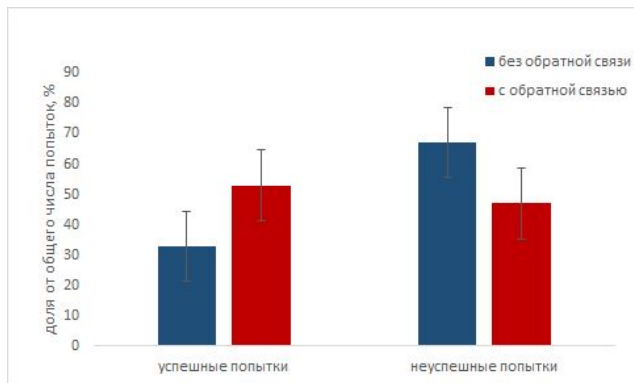
Stimulating



Устройство для распределенной стимуляции



Bidirection ECoG based BCI (2019)



Electro-tactile stimulation



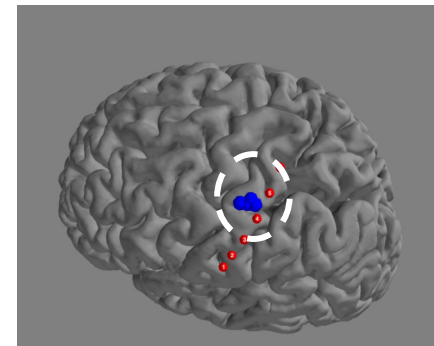
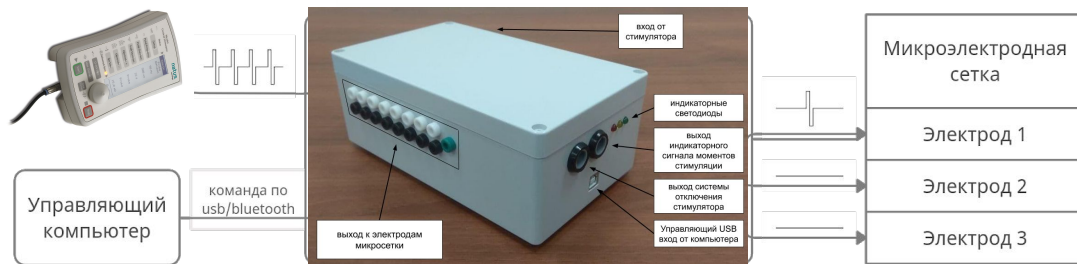
Source localization



Decoding

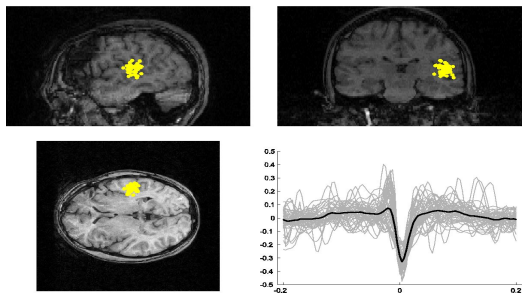
Stimulating

Устройство для распределенной стимуляции

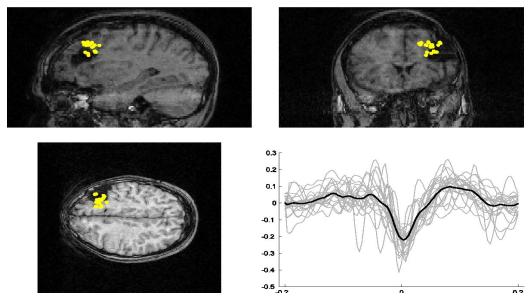


MEG for non-invasive seizure onset zone localization

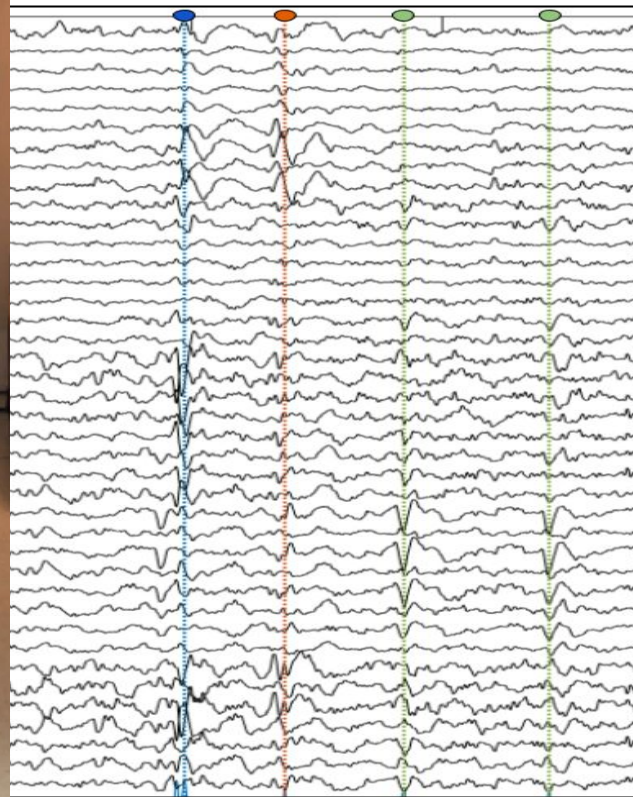
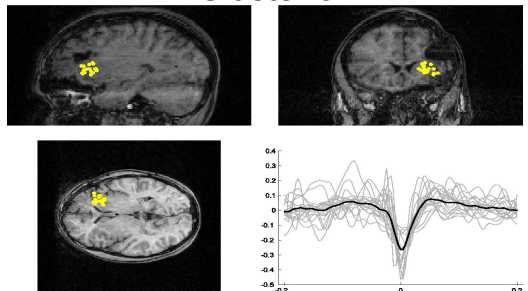
Cluster 1



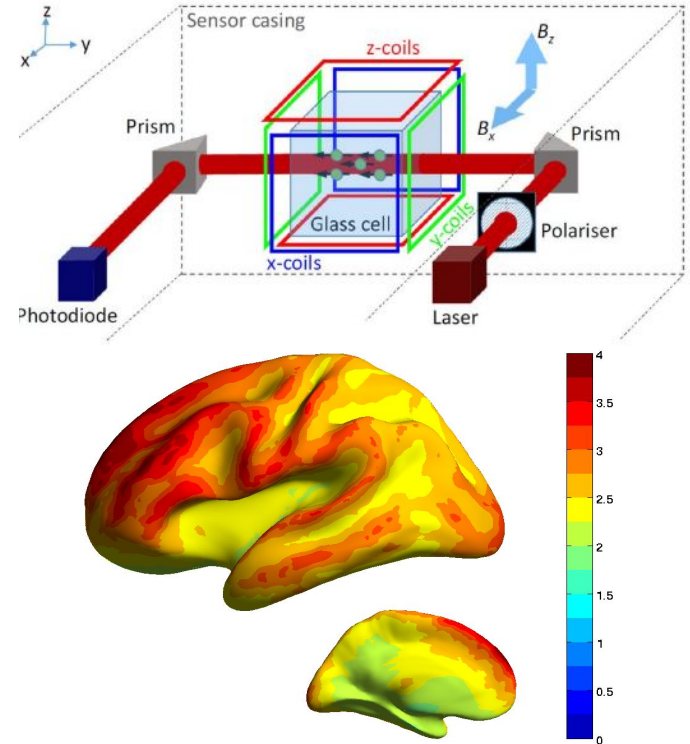
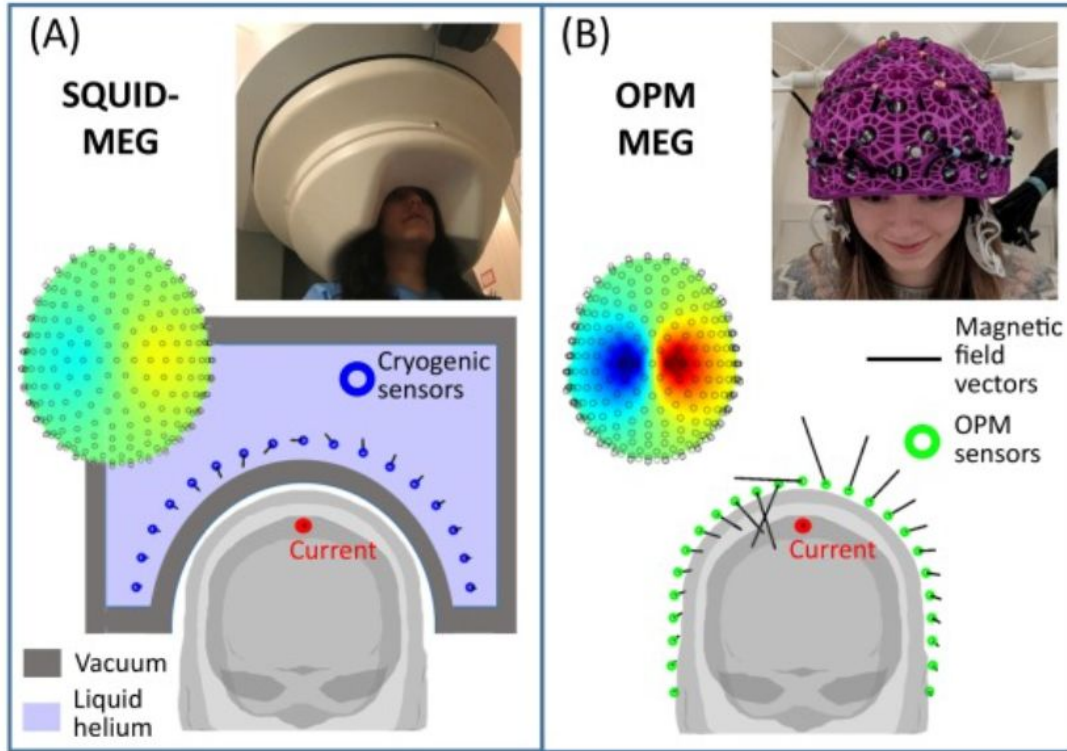
Cluster 2



Cluster 3

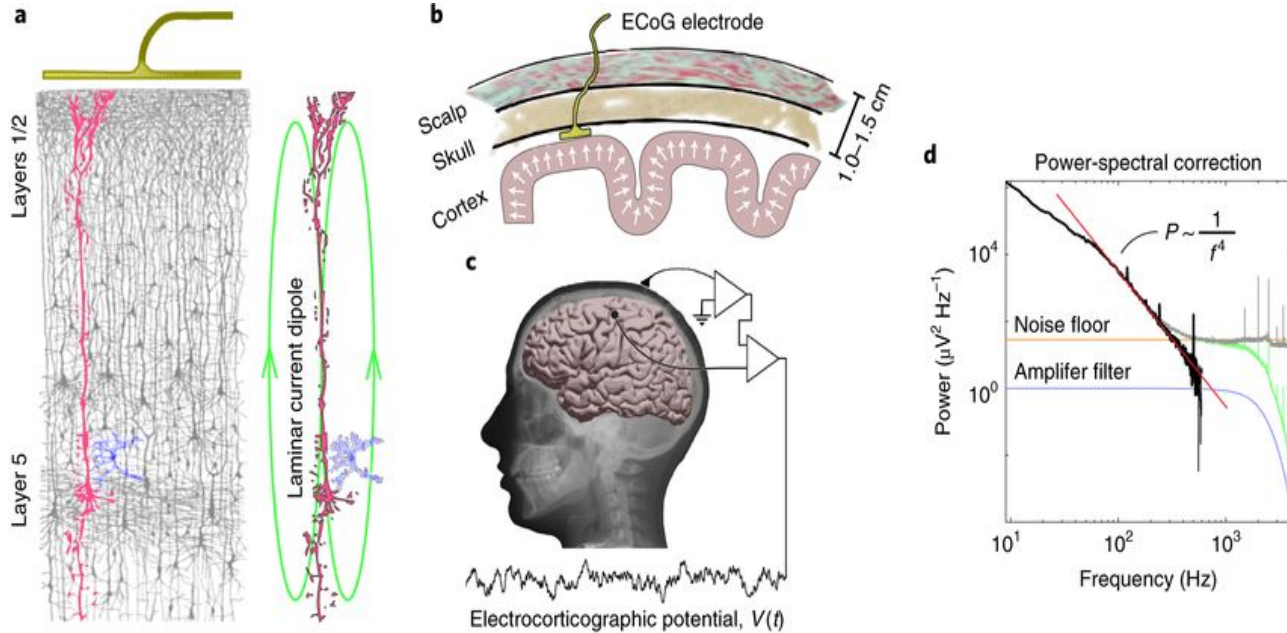


From SQUIDs to wearable OPM MEG sensors

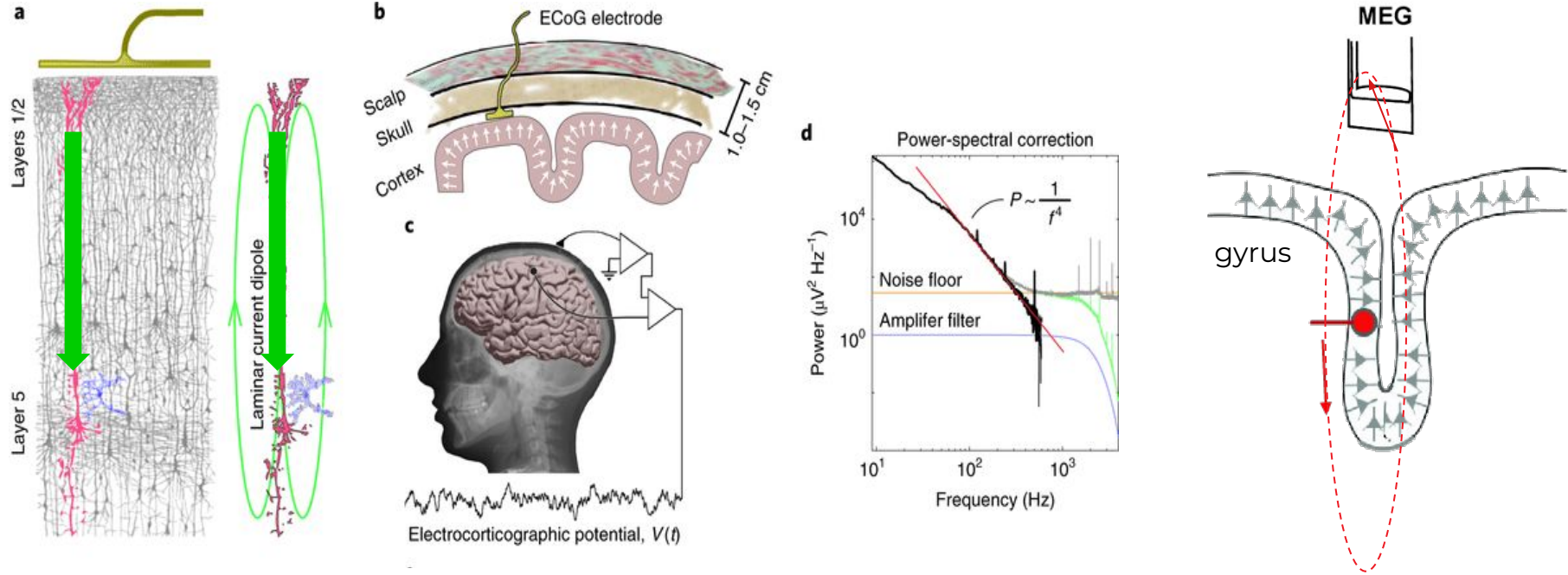


Brookes, Matthew J., et al. "Magnetoencephalography with optically pumped magnetometers (OPM-MEG): The next generation of functional neuroimaging." *Trends in Neurosciences* (2022); Iivanainen, J., Stenroos, M., & Parkkonen, L. (2017). Measuring MEG closer to the brain: Performance of on-scalp sensor arrays. *NeuroImage*, 147, 542-553.

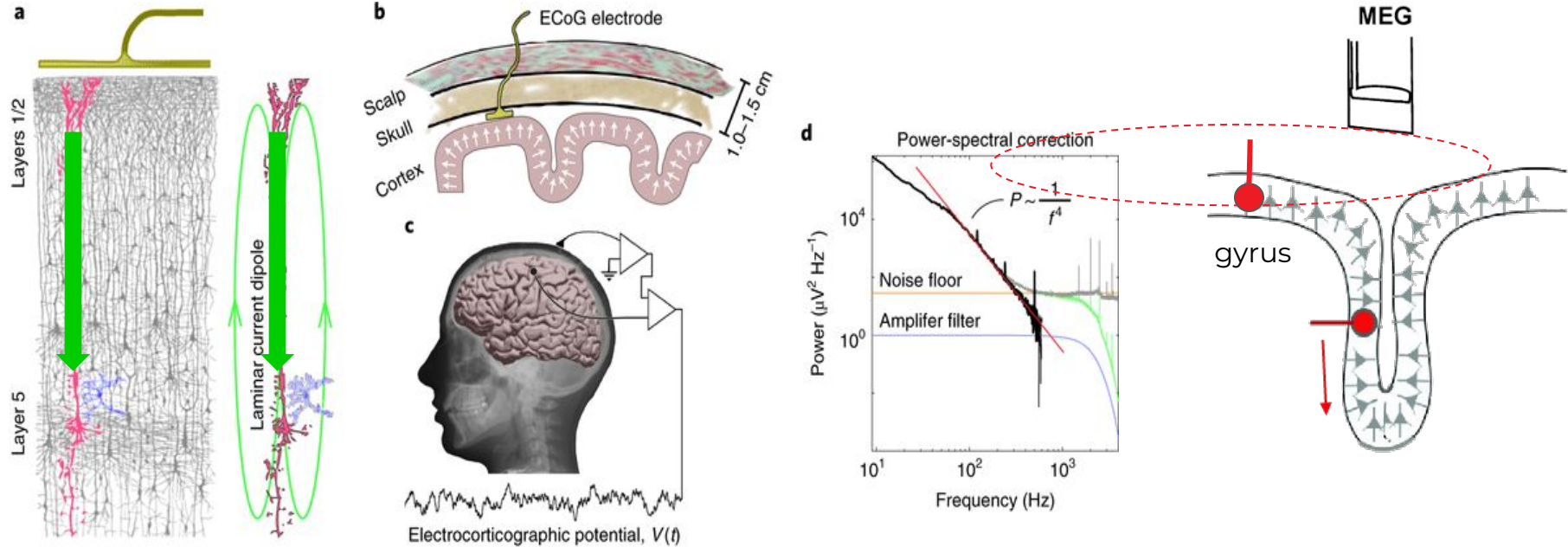
Electrophysiological signal origin



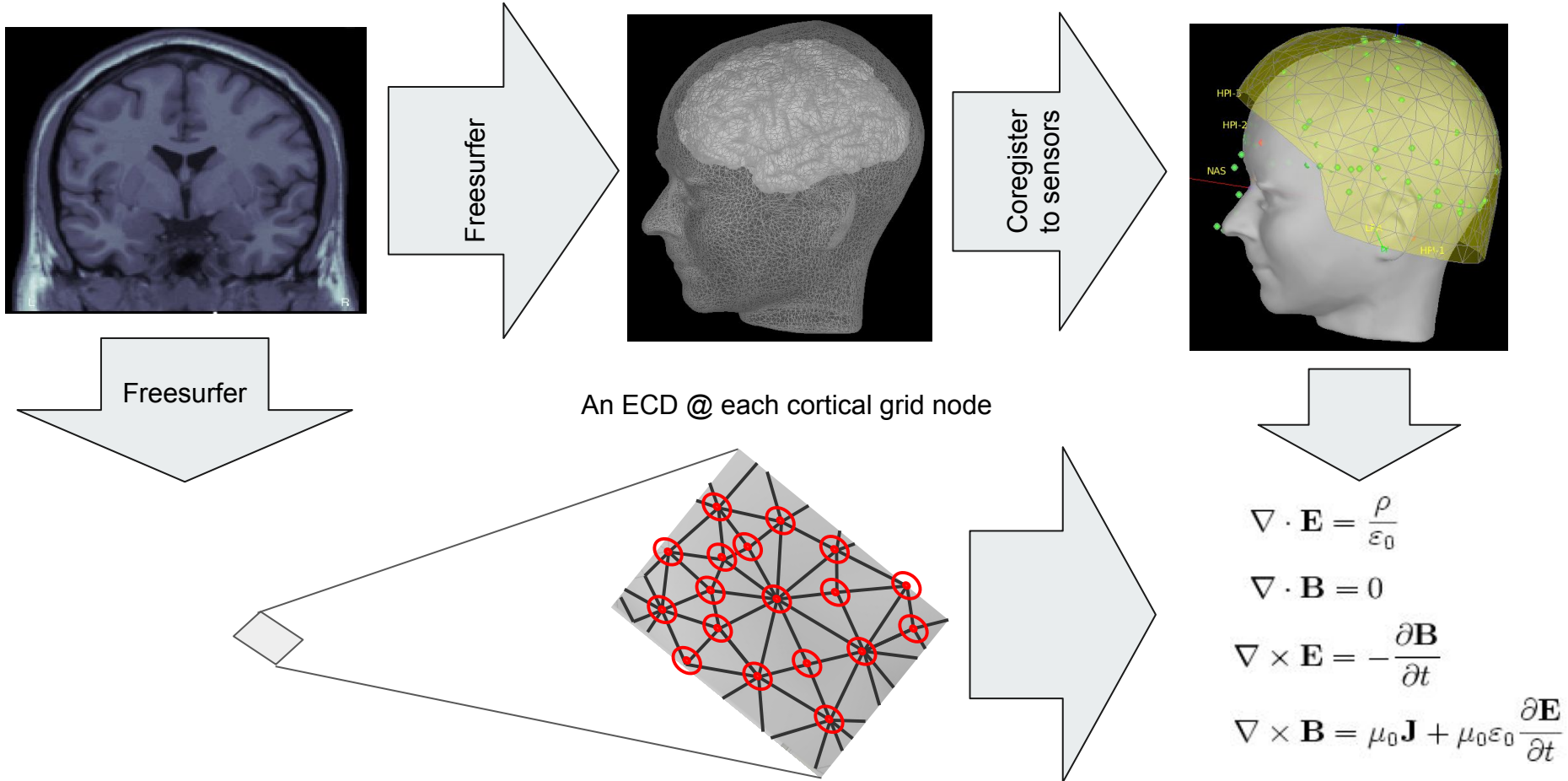
Equivalent current dipole



Equivalent current dipole

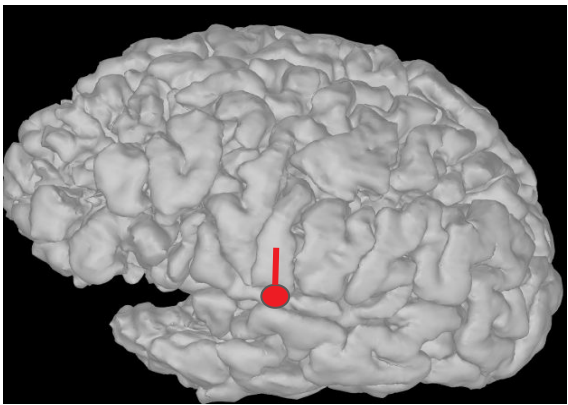


Structural model of the neuronal “source space”

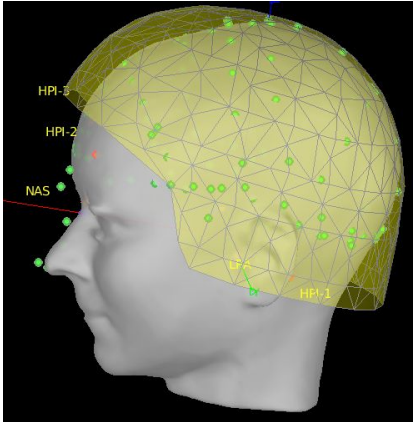


The notion of topography

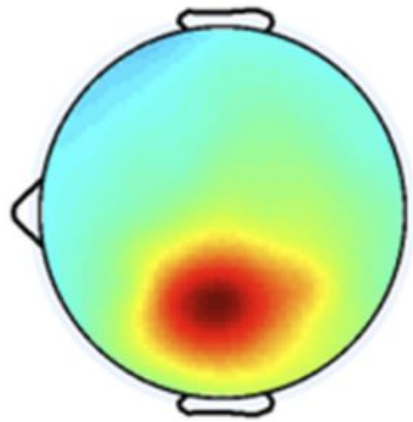
Equivalent current dipole
(our source)



Located inside the head
surrounded by sensors



Produces this field
(and the corresponding
measurements on the sensors)



Forward model (matrix)

Sensor measurements

Forward model matrix

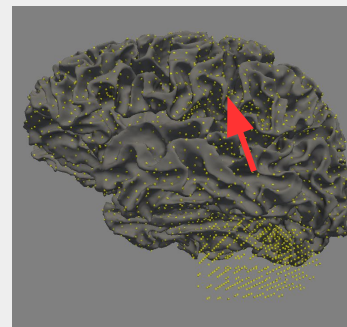
Source activity



=

$$\begin{bmatrix} \mathbf{g}_{11} & \dots & \dots & \mathbf{g}_{1N} \\ \vdots & \ddots & & \vdots \\ \mathbf{g}_{M1} & \dots & \dots & \mathbf{g}_{MN} \end{bmatrix}$$

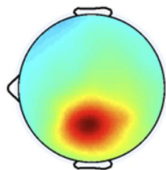
x



$$\mathbf{g}_i = \text{EM}(\mathbf{r}, \boldsymbol{\theta})$$

@

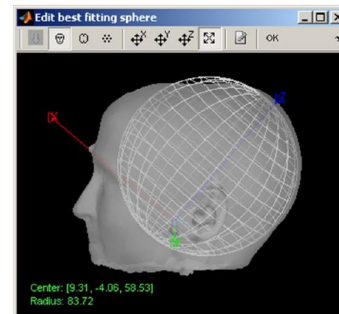
$$\mathbf{r} = \mathbf{r}_i, \boldsymbol{\theta} = \boldsymbol{\theta}_i$$



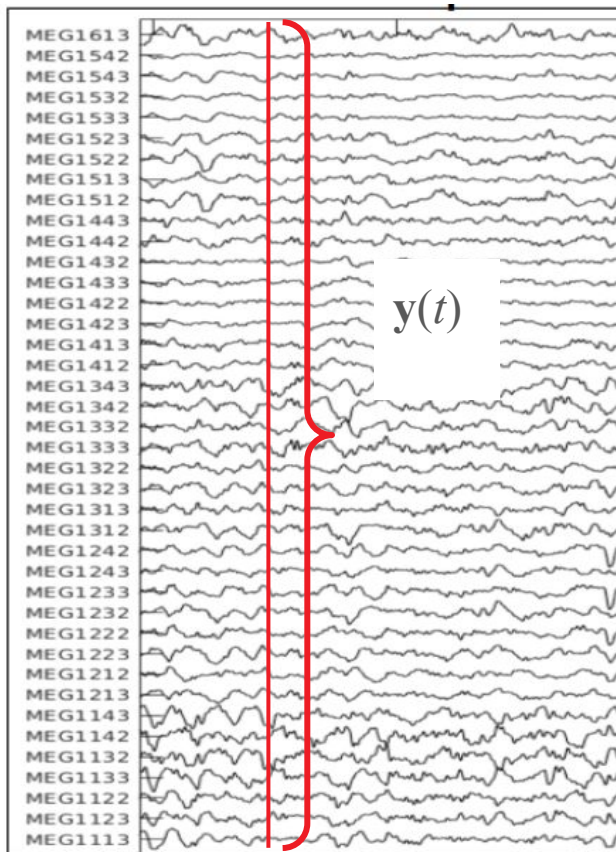
$$\begin{aligned} \nabla \cdot \mathbf{E} &= \frac{\rho}{\epsilon_0} \\ \nabla \cdot \mathbf{B} &= 0 \\ \nabla \times \mathbf{E} &= -\frac{\partial \mathbf{B}}{\partial t} \\ \nabla \times \mathbf{B} &= \mu_0 \mathbf{J} + \mu_0 \epsilon_0 \frac{\partial \mathbf{E}}{\partial t} \end{aligned}$$



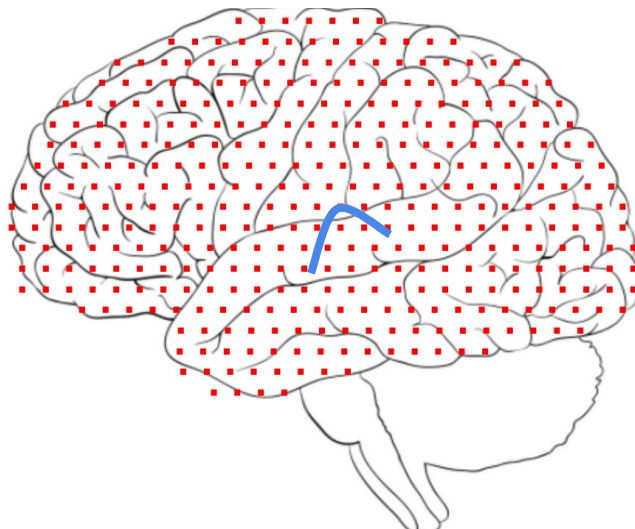
Volume conductor model



Observation equation & inverse problem



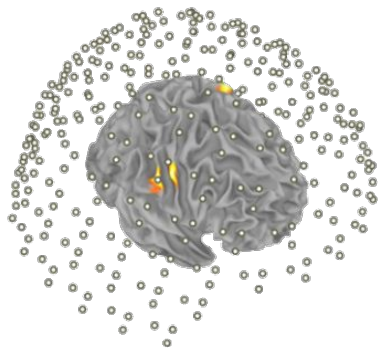
$$\mathbf{y}(t) = \sum_{i=1}^N \mathbf{g}_i s_i(t) + \mathbf{v}(t)$$



Поиск источников активности головного мозга

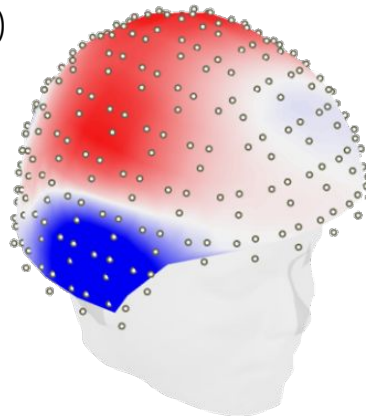
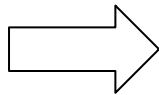
$$\mathbf{y}(t) = \sum_{i=1}^N \mathbf{g}_i s_i(t) + \mathbf{v}(t)$$

$$10 = s_1 + s_2$$



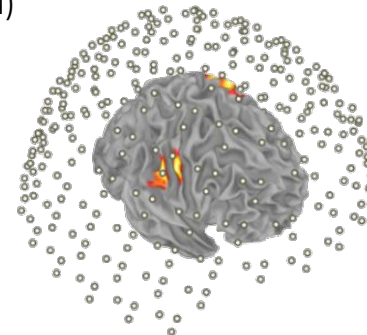
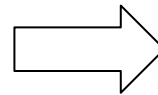
Истинные
источники

Прямая задача
(корректно
поставленная)



ЭЭГ/МЭГ
измерения

Обратная задача
(некорректно
поставленная)



Предполагаемые
источники

Поиск источников активности головного мозга

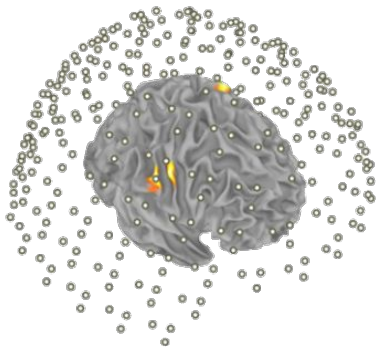
$$\mathbf{y}(t) = \sum_{i=1}^N \mathbf{g}_i s_i(t) + \mathbf{v}(t)$$

$$10 = s_1 + s_2$$

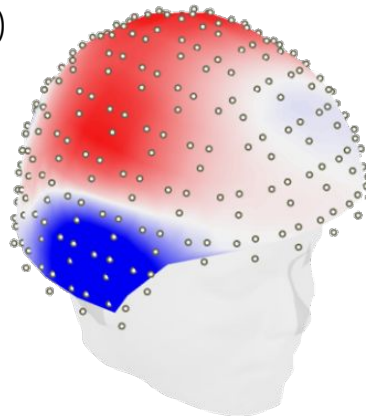
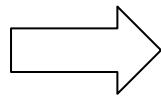
$$s_1 \approx s_2$$

Прямая задача
(корректно поставленная)

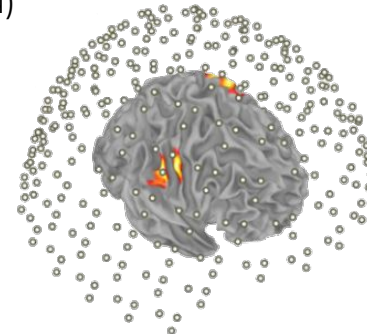
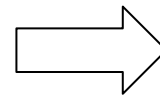
Обратная задача
(некорректно поставленная)



Истинные источники



ЭЭГ/МЭГ измерения

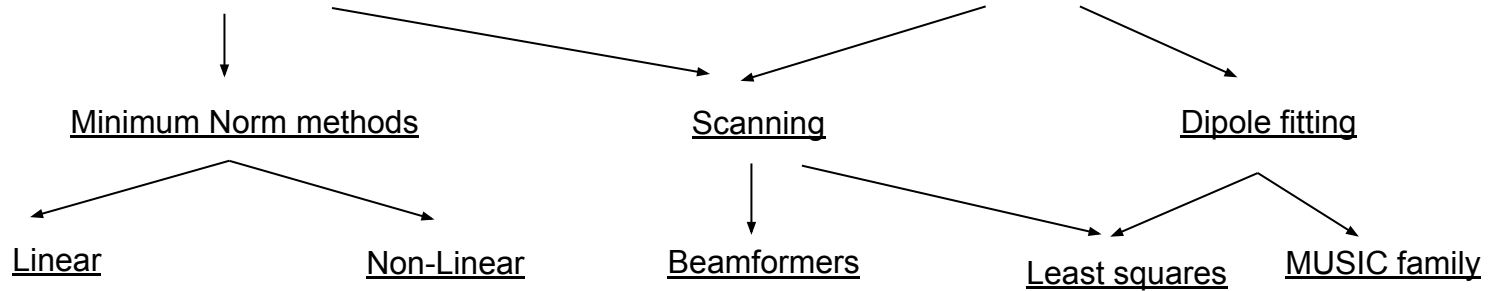


Предполагаемые источники

EEG\MEG inverse modelling methods

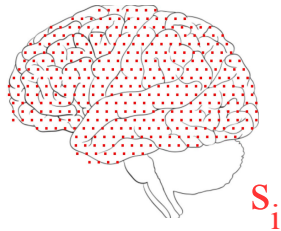
Imaging methods (distributed source model)

Parametric methods (focal source model)



- Tikhonov reg-ed Inverse (MNE)

- LORETA



S_i

$i = 1, \dots, N, N \sim 10^4$

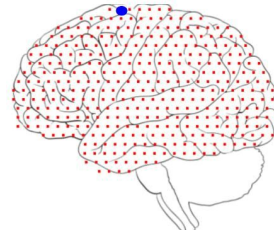
- L_p norm techniques, e.g. MCE($L1$)

-Markov random fields (MRF) based

-Variational Bayesian techniques

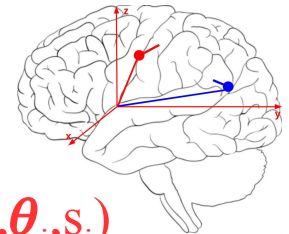
-GALA

sLoreta, SAM, WROP, Neural Activity Index **ReciPSIICOS**



- Moving dipole
- Multistart

- RAP-MUSIC,
- R-MUSIC
- TRAP-MUSIC



$(\mathbf{r}_i, \boldsymbol{\theta}_i, S_i)$

$i = 1, \dots, N, N < 10$

EEG\MEG inverse modelling methods

Imaging methods (distributed source model)

Parametric methods (focal source model)

Minimum Norm methods

Scanning

Dipole fitting

Linear

Non-Linear

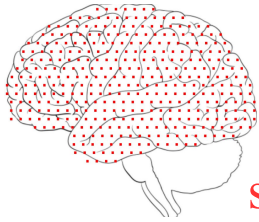
Beamformers

Least squares

MUSIC family

- Tikhonov reg-ed
Inverse (MNE)

- LORETA



S_i

$i = 1, \dots, N, N \sim 10^4$

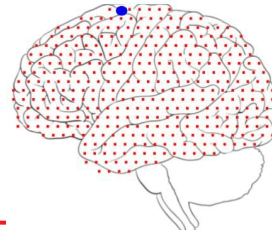
- L_p norm techniques,
e.g. MCE($L1$)

-Markov random fields
(MRF) based

-Variational Bayesian
techniques

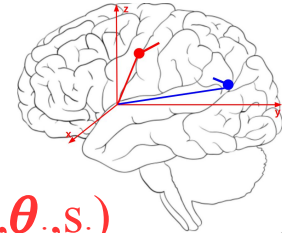
-GALA

sLoreta,
SAM,
WROP,
Neural Activity
Index
ReciPSIICOS



- Moving dipole
- Multistart

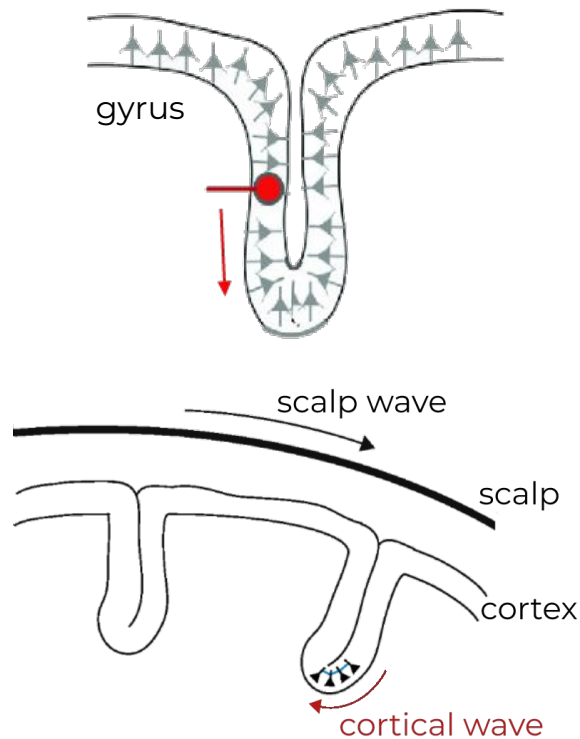
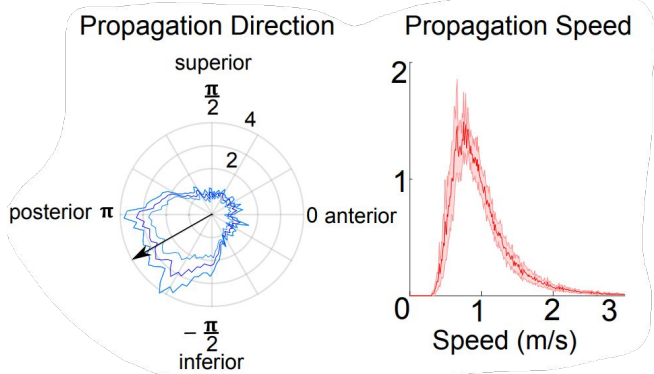
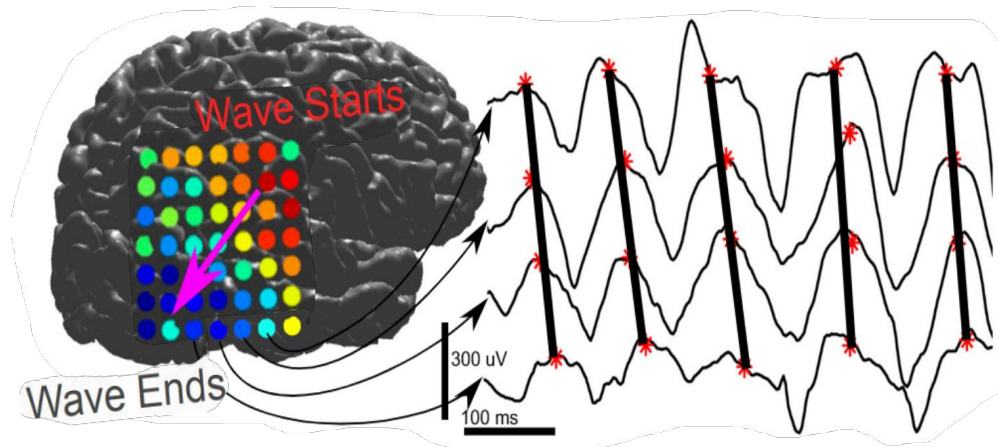
- RAP-MUSIC,
- R-MUSIC
- TRAP-MUSIC



$(\mathbf{r}_i, \boldsymbol{\theta}_i, S_i)$

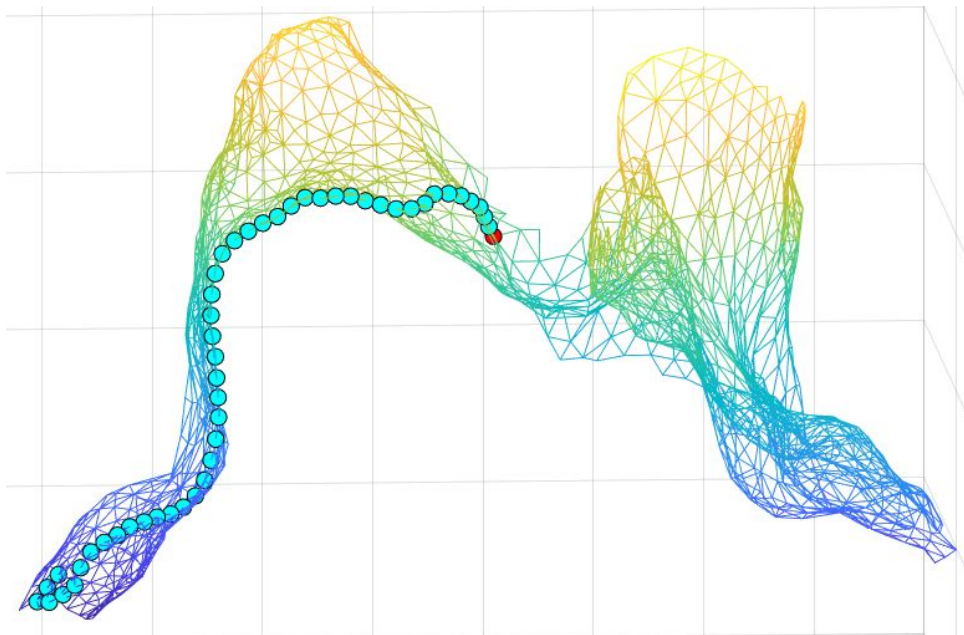
$i = 1, \dots, N, N < 10$

Sources are not static. Cortical traveling waves.

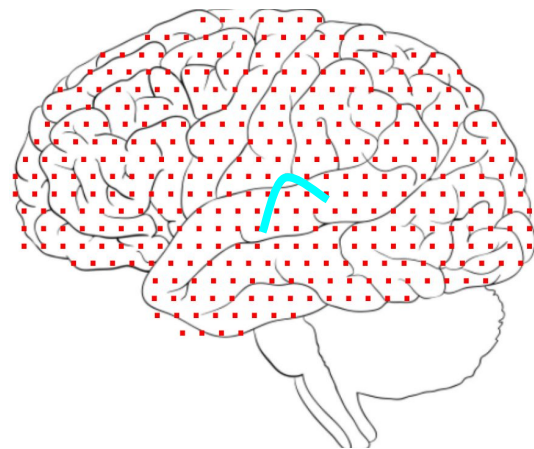


Halgren et al. (2019). The generation and propagation of the human alpha rhythm

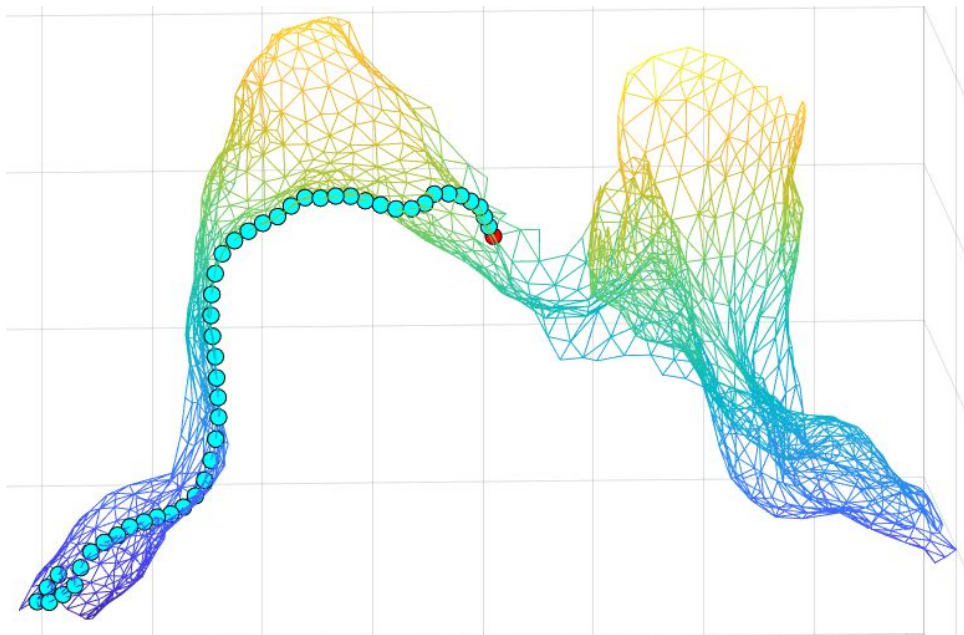
Observation equation



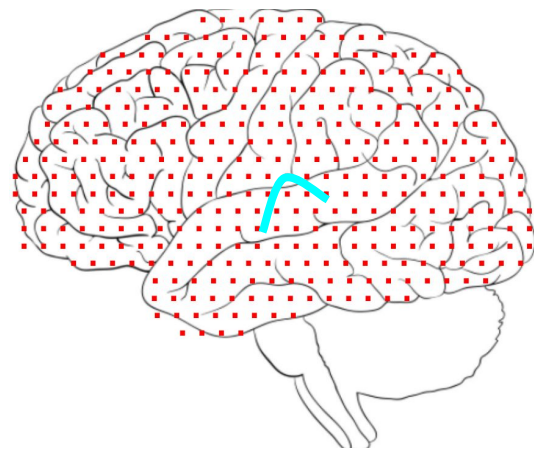
$$\mathbf{y}(t) = \sum_{i=1}^N \mathbf{g}_i s_i(t) + \mathbf{v}(t)$$



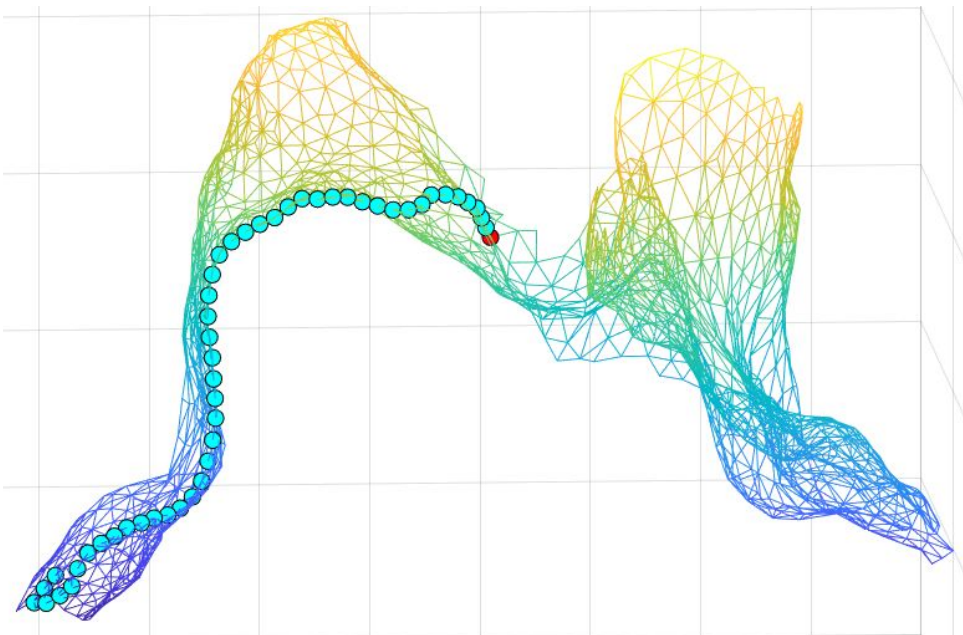
Observation equation



$$\mathbf{y}(t) = \mathbf{g}(t)s(t) + \mathbf{v}(t)$$



Observation equation

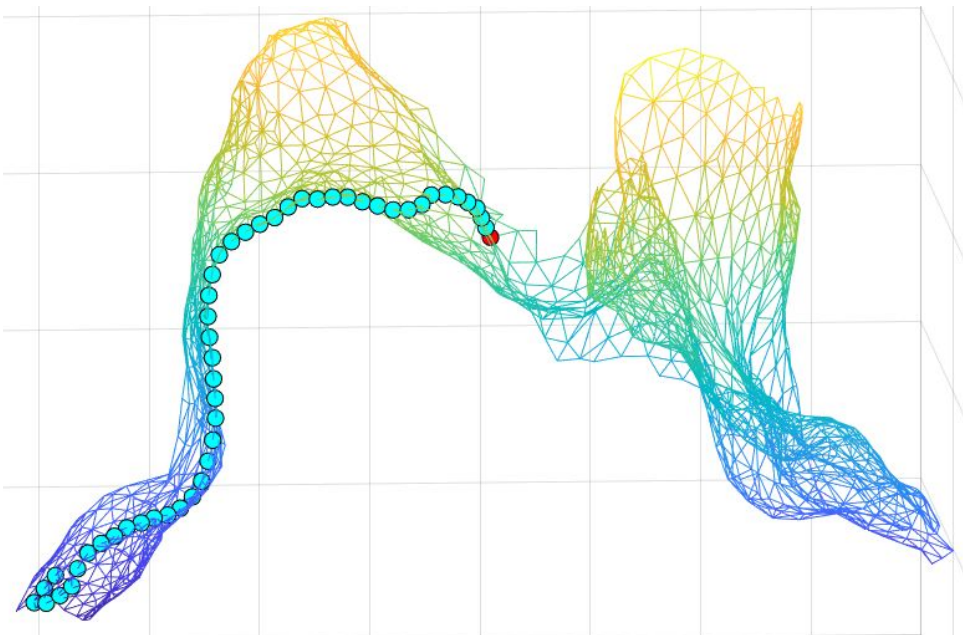


Specify (low dimensional) spatial
dynamics properties

$$\mathbf{y}(t) = \mathbf{g}(t)s(t) + \mathbf{v}(t)$$

Specify temporal
dynamics properties

Observation equation



Specify multiple (low dimensional)
spatial dynamics properties

$$\mathbf{y}(t) = \sum_{i=1}^N \mathbf{g}_i(t) s_i(t) + \mathbf{v}(t)$$

Specify temporal
dynamics properties

Modeling $g(t)$

$$y(t) = g(t)s(t) + v(t)$$

$$y(t) = s_1(t) \underbrace{\sum_{i=1}^k a_i(t) \mathbf{u}_i^{**}}_{g(t)} + v(t)$$

$$\mathbf{a}(t) = \begin{pmatrix} a_1(t) \\ a_2(t) \\ a_3(t) \end{pmatrix}$$

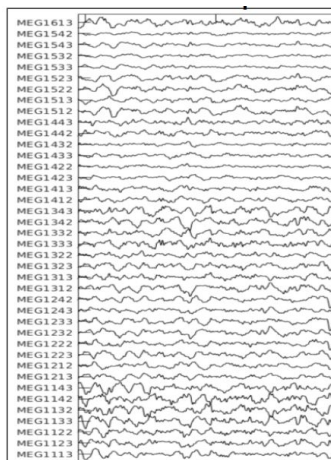
– spatial propagation
(wondering) coeffs.

$$\mathbf{a}(t) = \mathbf{A}\mathbf{a}(t-1) + \mathbf{b}(t)$$

* Динамически (медленно) меняющаяся топография источника, $g(t)$

** Пространственные базисные вектора – левые сингулярные вектора сегмента данных

Сегмент данных



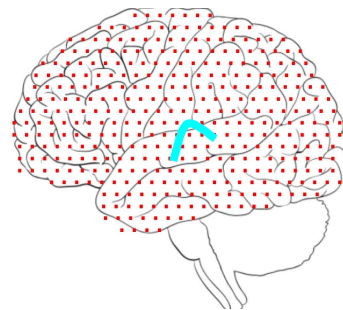
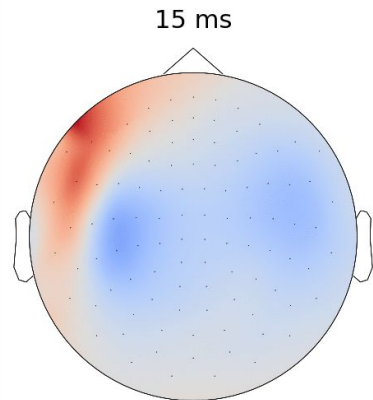
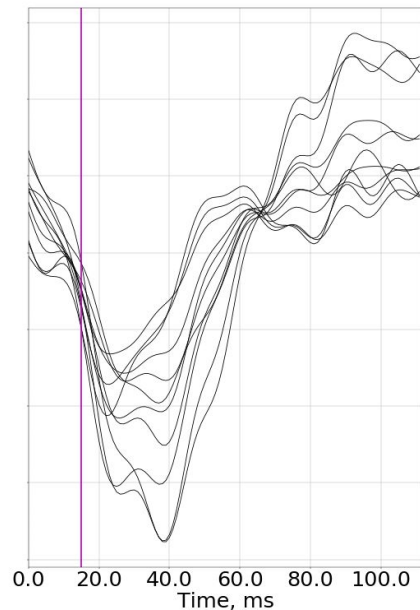
$\mathbf{g}(t)$ - spatial wandering process, subspace confined walk

$$\mathbf{a}(t) = \mathbf{A}\mathbf{a}(t-1) + \mathbf{b}(t)$$

$$\mathbf{a}(t) = \begin{pmatrix} a_1(t) \\ a_2(t) \\ a_3(t) \end{pmatrix} \text{ - slowly evolving linear combination coefficients}$$

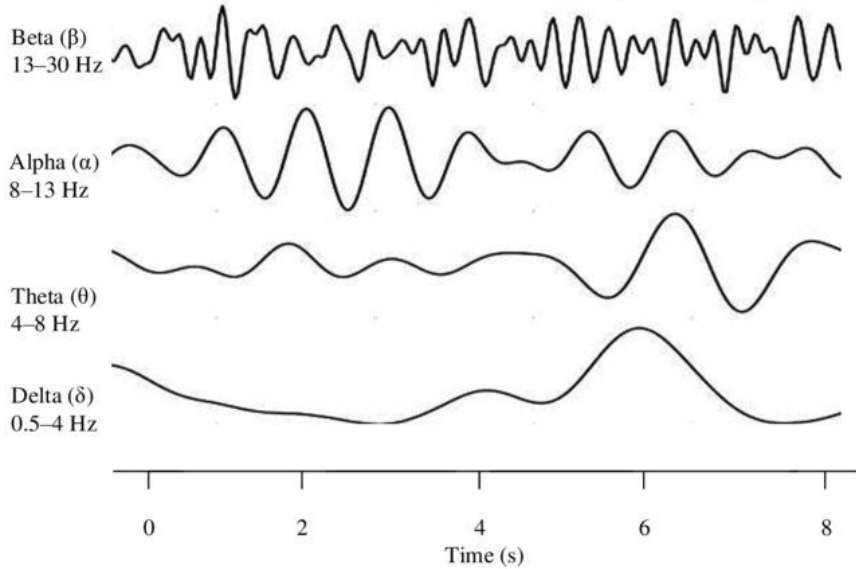
$$\mathbf{y}(t) = s(t) \underbrace{\sum_{i=1}^3 a_i(t) \mathbf{u}_i}_{\mathbf{g}(t)} + \mathbf{v}(t)$$

$\mathbf{u}_i, i = 1, \dots, R$ - span the subspace

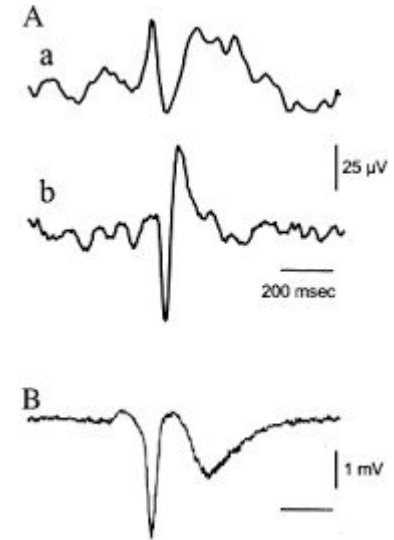


Two different temporal dynamical patterns

Brain rhythms

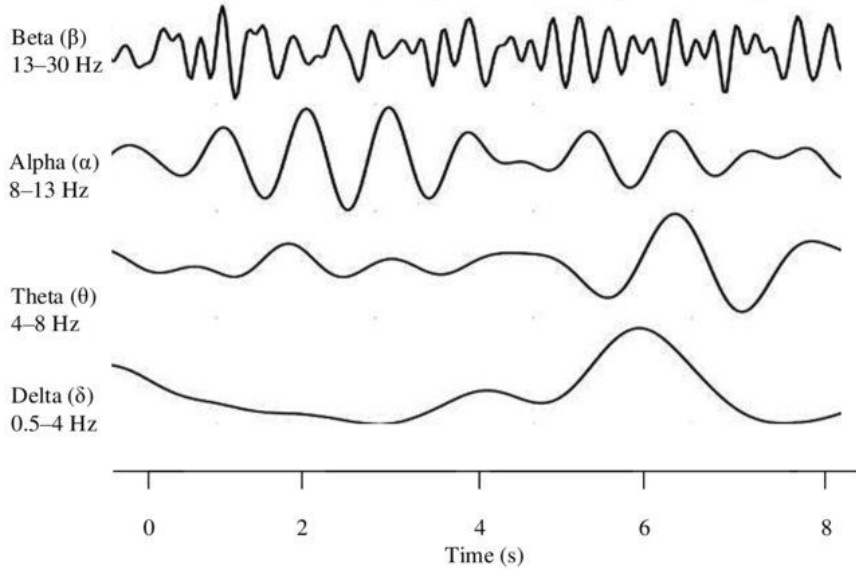


Interictal spikes (epilepsy)

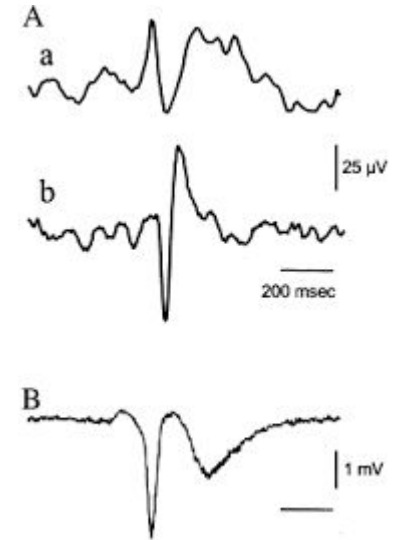


Two different temporal dynamics patterns

Brain rhythms

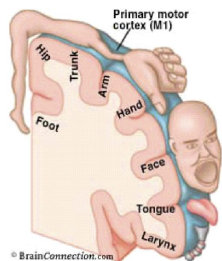
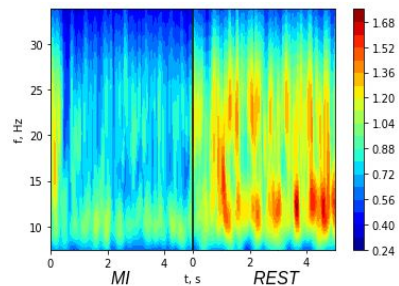


Interictal spikes (epilepsy)

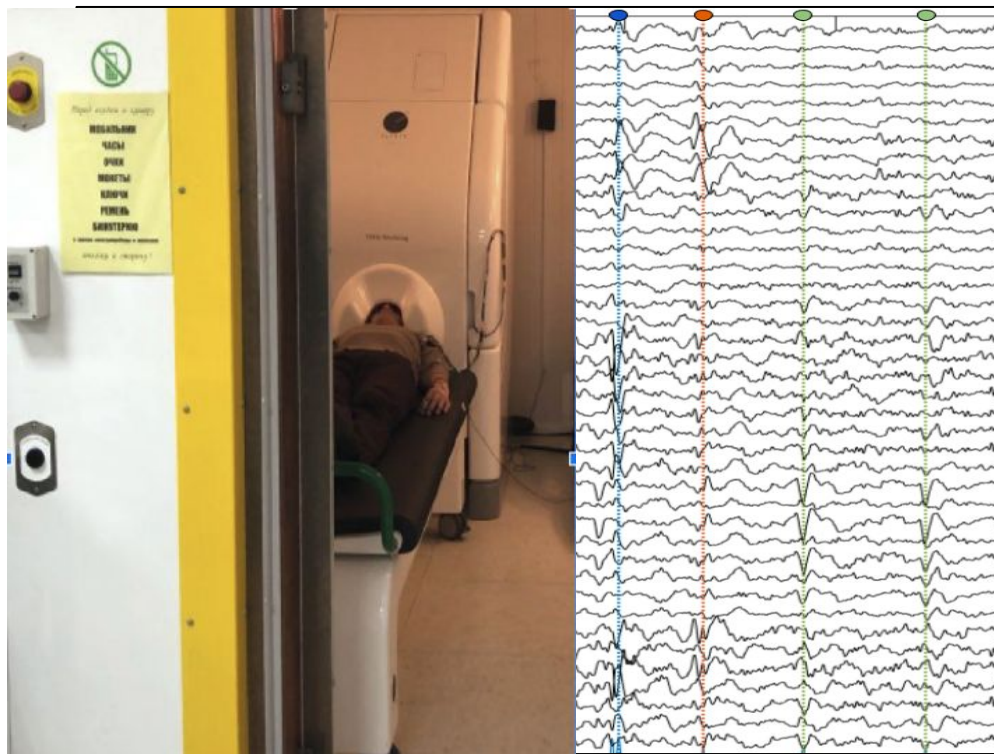


Two different temporal dynamical patterns

Brain rhythms



Interictal spikes (epilepsy)



Observation model

$$\mathbf{y}(t) = \mathbf{g}(t)s(t) + \mathbf{v}(t)$$

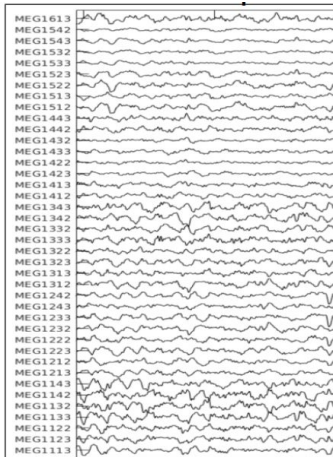
$$\mathbf{y}(t) = s_1(t) \sum_{i=1}^k a_i(t) \mathbf{u}_i^{**} + \mathbf{v}(t)$$

* Динамически (медленно) меняющаяся топография источника, $g(t)$

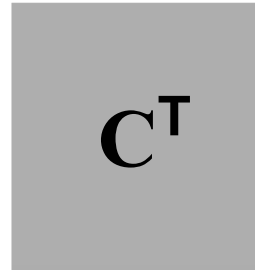
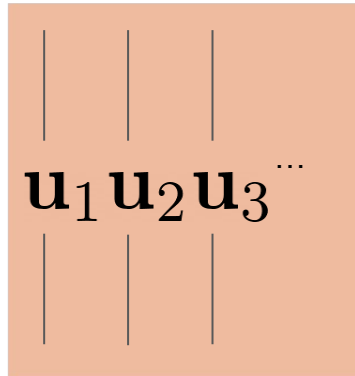
** Пространственные базисные вектора – левые сингулярные вектора сегмента данных

$$\mathbf{a}(t) = \begin{pmatrix} a_1(t) \\ a_2(t) \\ a_3(t) \end{pmatrix} \quad \text{– spatial propagation (wondering)}$$

$\mathbf{s}(t)$ – electrical activity evolution



=



$s(t)$, electrical activity model - brain rhythm as a frequency modulated process

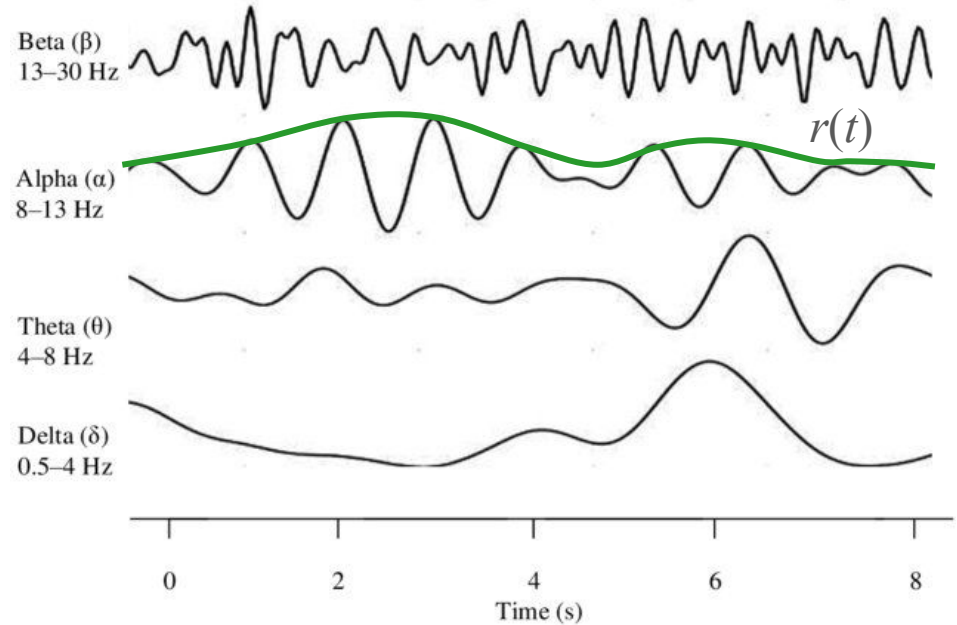
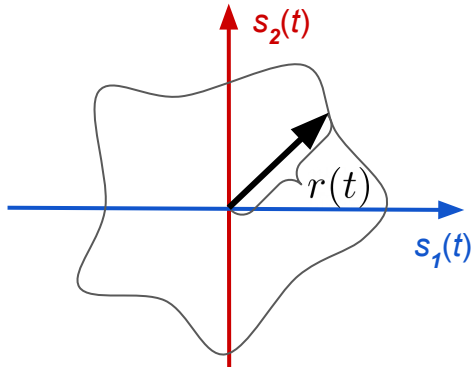
$$s(t) = \mathbf{F}s(t-1) + \mathbf{w}(t) \quad - \text{electrical activity evolution}$$

Ритм мозга — это частотно-модулированный процесс:

$$\mathbf{F} = c_{\mathbf{F}} \cdot \begin{pmatrix} \cos(2\pi f \Delta t) & -\sin(2\pi f \Delta t) \\ \sin(2\pi f \Delta t) & \cos(2\pi f \Delta t) \end{pmatrix}$$

Аналитический сигнал

$$z(t) = s_1(t) + js_2(t) = r(t)e^{j2\pi ft}$$



Our model summary

Observation₃ model

$$\mathbf{y}(t) = s(t) \sum_{i=1}^3 a_i(t) \mathbf{u}_i + \mathbf{v}(t)$$

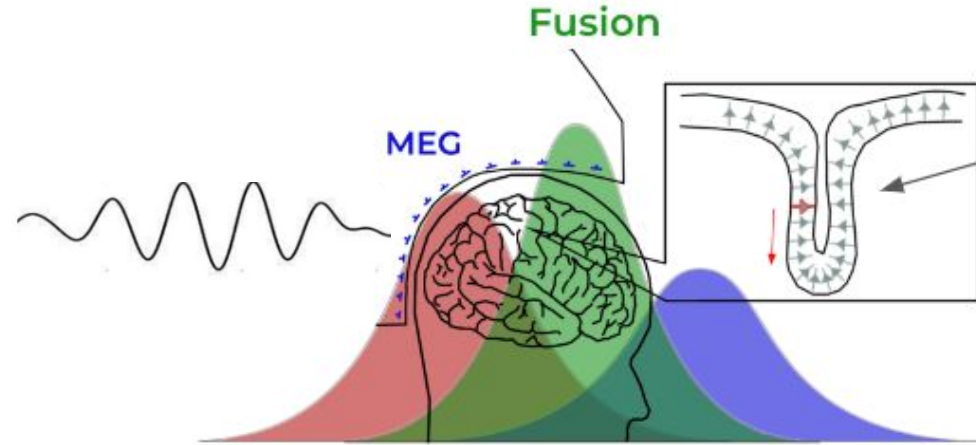
State evolution (process) models

$$\mathbf{s}(t) = \mathbf{F}\mathbf{s}(t-1) + \mathbf{w}(t)$$

– electrical activity evolution (fast)

$$\mathbf{a}(t) = \mathbf{A}\mathbf{a}(t-1) + \mathbf{b}(t)$$

– spatial dynamics (slow propagation)



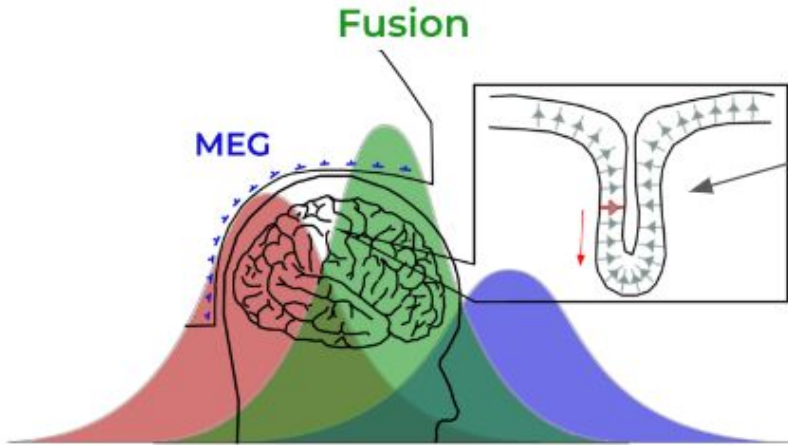
$$\begin{aligned} \mathbf{x}_{k+1} &= F(\mathbf{x}_k, \mathbf{v}_k) \\ \mathbf{y}_k &= H(\mathbf{x}_k, \mathbf{n}_k) \end{aligned}$$

Unscented Kalman Filter

$$\mathbf{x}_{k+1} = F(\mathbf{x}_k, \mathbf{v}_k)$$

$$\mathbf{y}_k = H(\mathbf{x}_k, \mathbf{n}_k)$$

~~$$\mathbf{x}_{k+1} \approx \mathbf{A}\mathbf{x}_k + \mathbf{B}\mathbf{v}_k, \mathbf{y}_k \approx \mathbf{C}\mathbf{x}_k + \mathbf{D}\mathbf{n}_k$$~~



Use sigma points and see how they propagate through non-linearity at each step

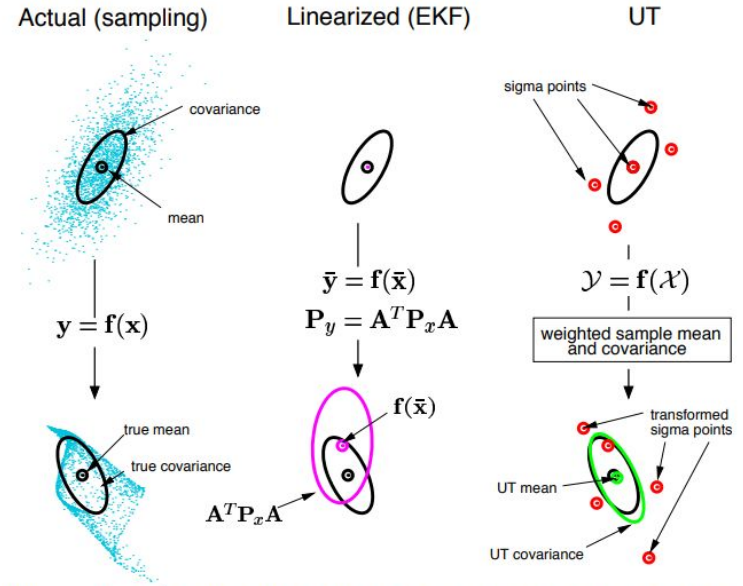
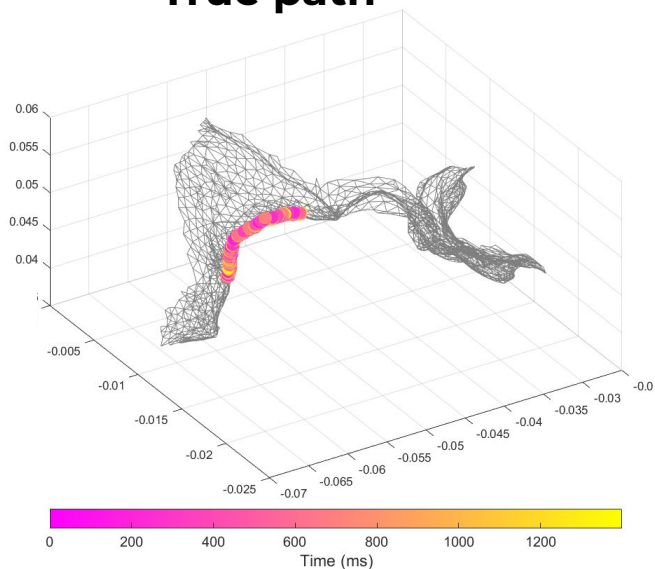


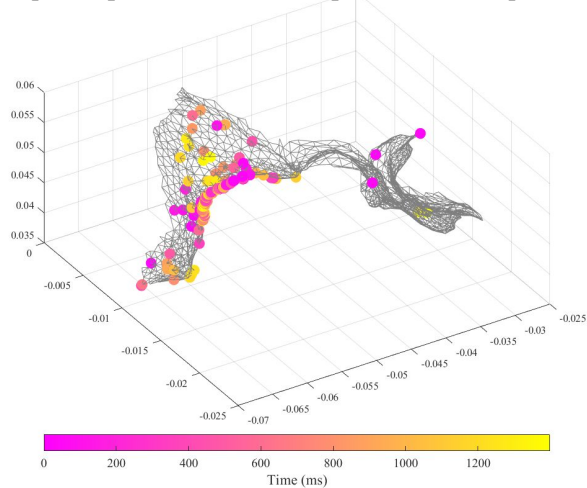
Figure 1: Example of the UT for mean and covariance propagation. a) actual, b) first-order linearization (EKF), c) UT.

Results: wave path reconstruction

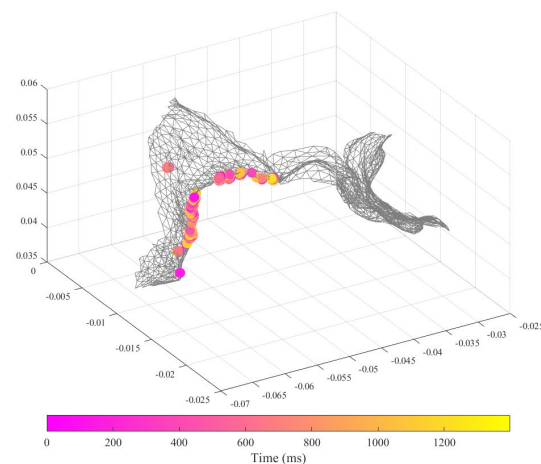
True path



Reconstructed path (sequential dipole fits)

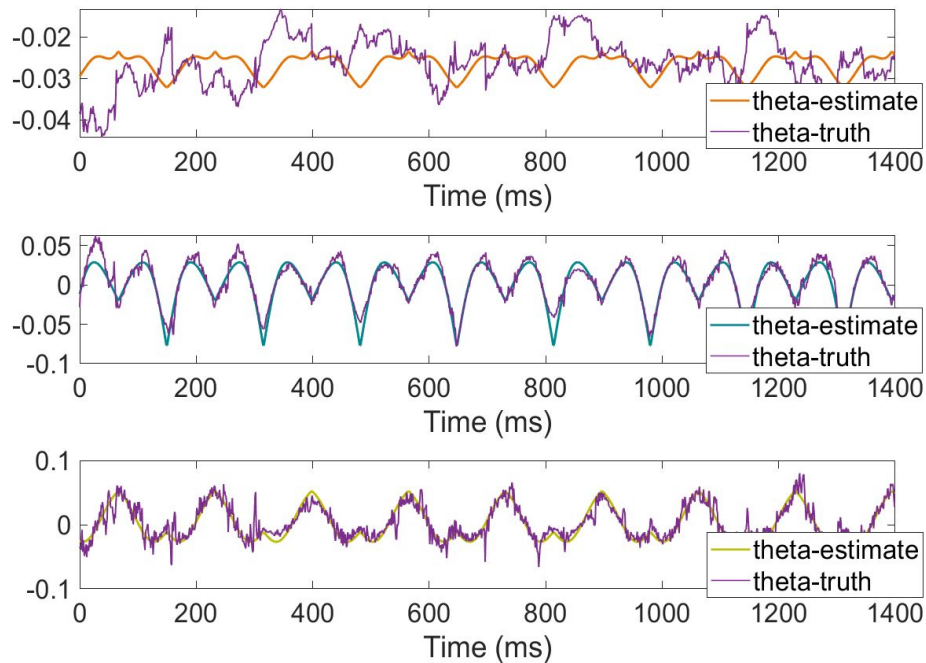


Reconstructed path (UKF)

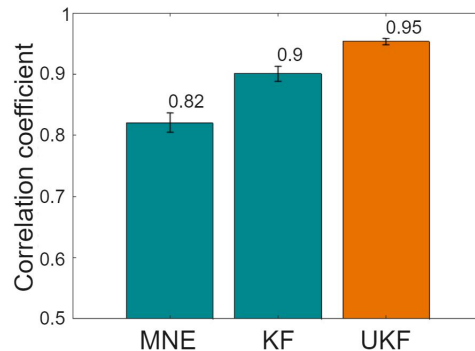
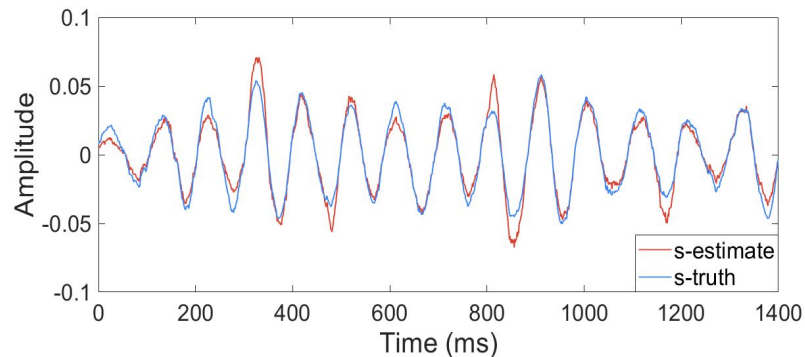


Точность восстановления пространственной и временной динамики

Оценка пространственных коэффициентов $\hat{\theta}_i(t)$



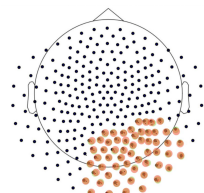
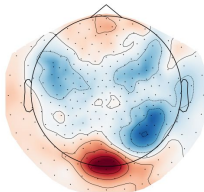
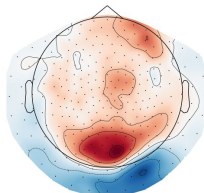
Оценка электрической компоненты $\hat{s}_1(t)$



* Коэффициент корреляции между временным рядом истинного сигнала и его оценкой

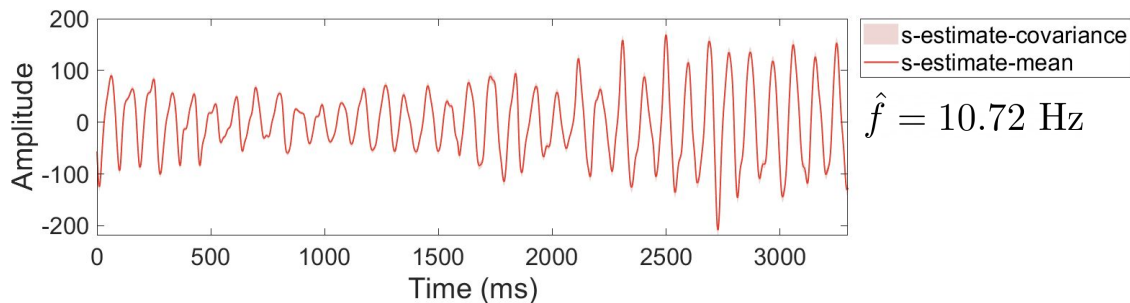
Результаты анализа МЭГ данных

CTF MEG System
состояние покоя
(глаза закрыты)

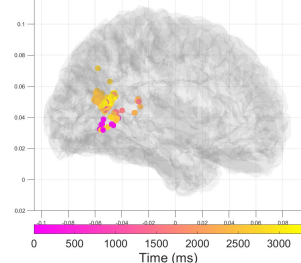
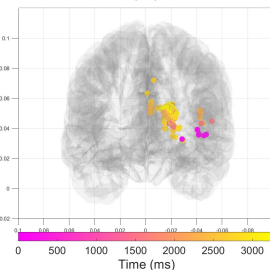
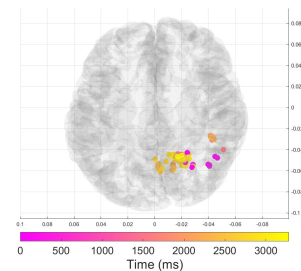
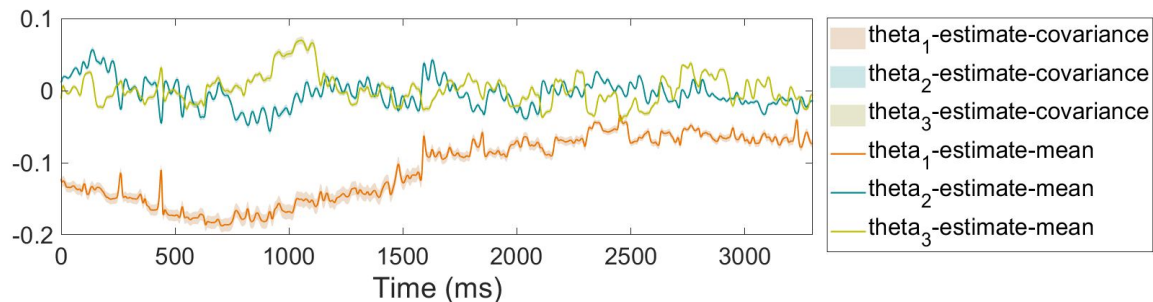


ROI: 59 канала

Оценка электрической компоненты $\hat{s}_1(t)$

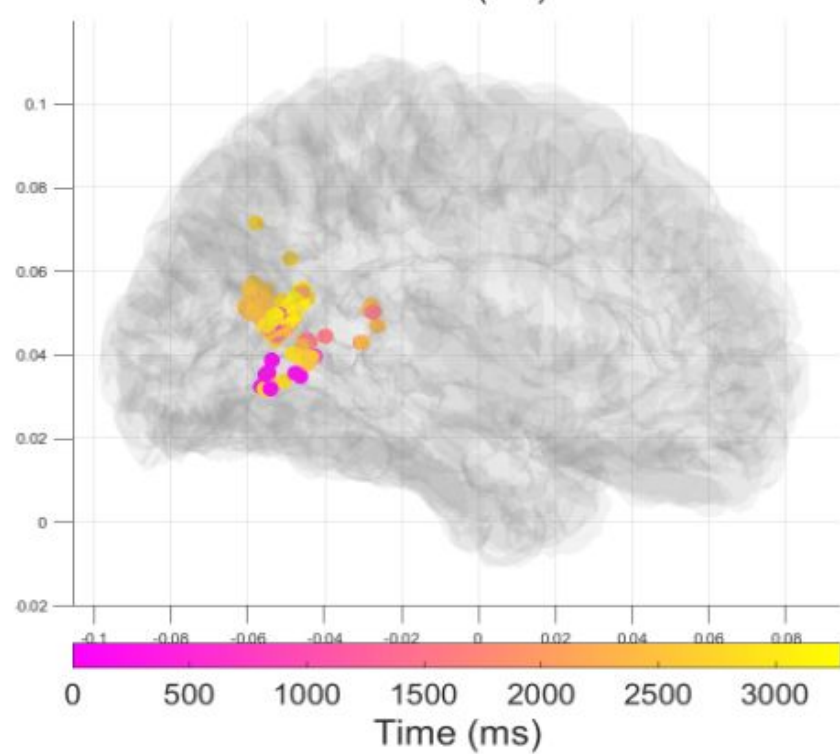
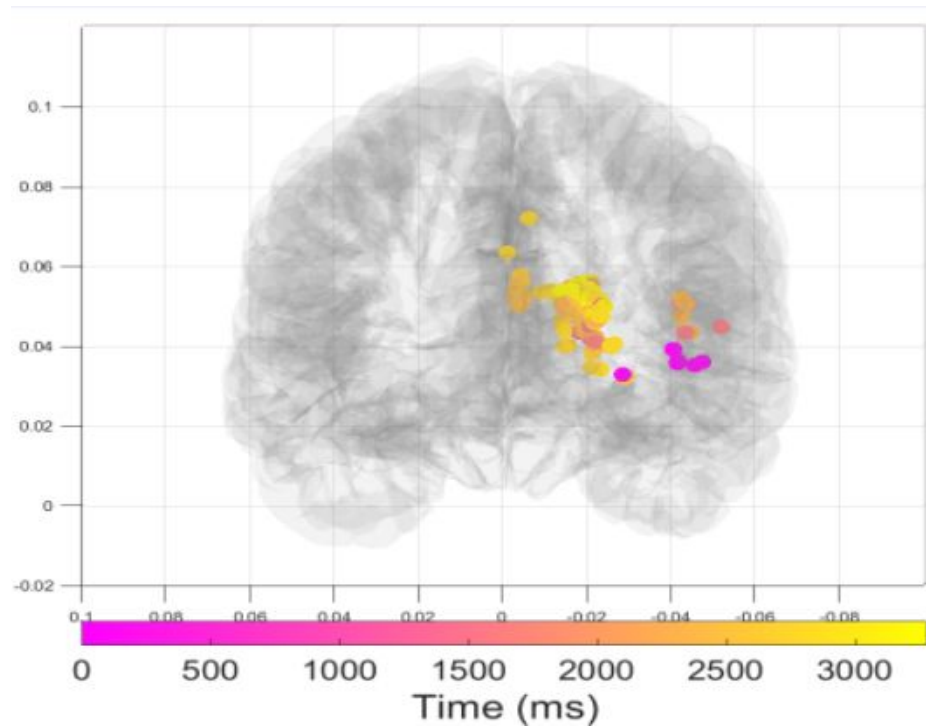


Оценка пространственных динамических коэффициентов $\hat{\theta}_i(t)$



Результаты анализа МЭГ данных

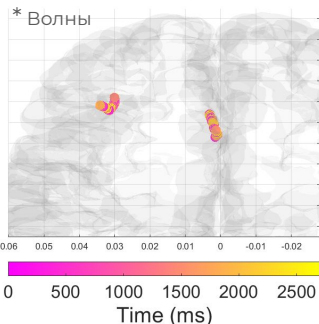
Оценка электрической компоненты



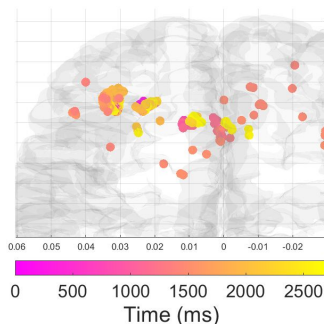
Traveling wave or a pair of dipoles ?

Расширенная модель для двух источников (волна vs статика)

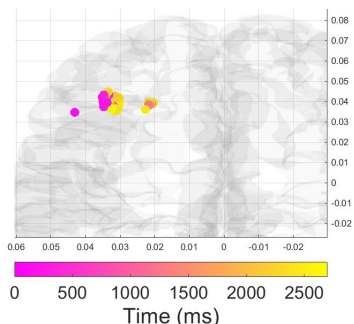
Смоделированные пути



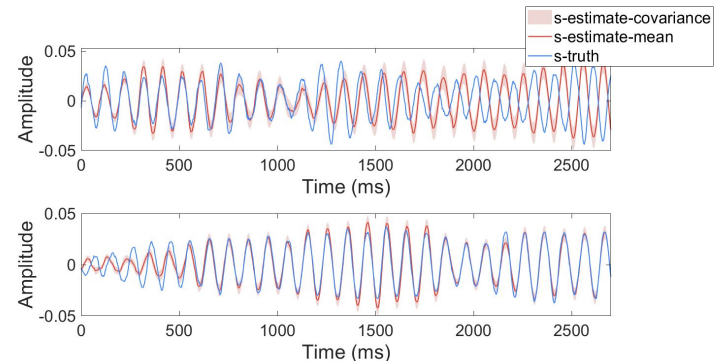
Восстановление 1-го пути



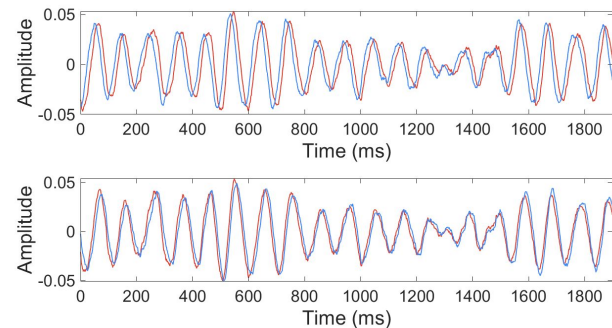
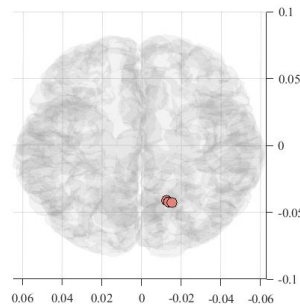
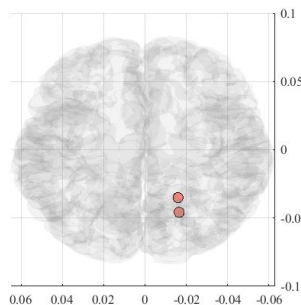
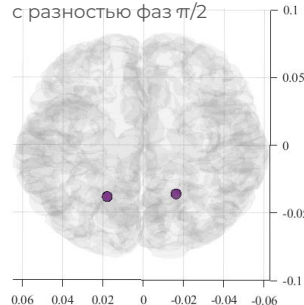
Восстановление 2-го пути



Оценка электрической компоненты

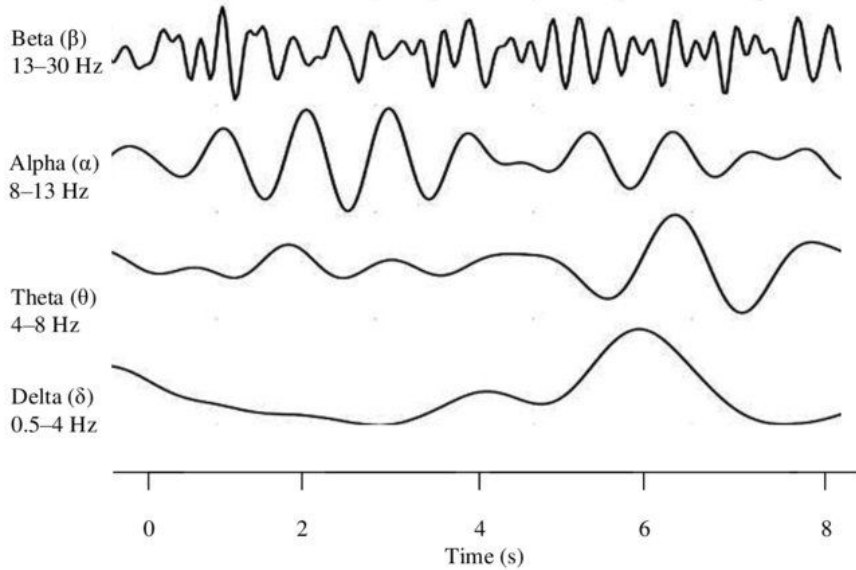


* Статические источники
с разностью фаз $\pi/2$

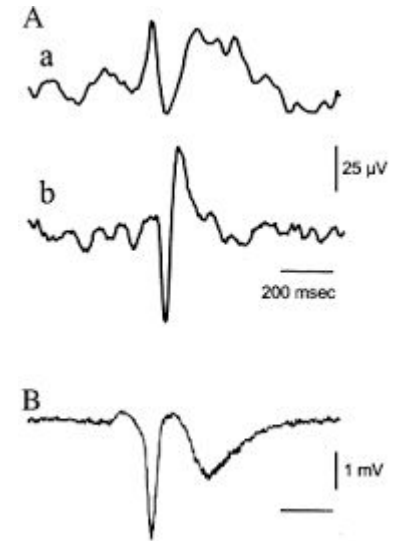


Two different temporal dynamics patterns

Brain rhythms



Interictal spikes (epilepsy)



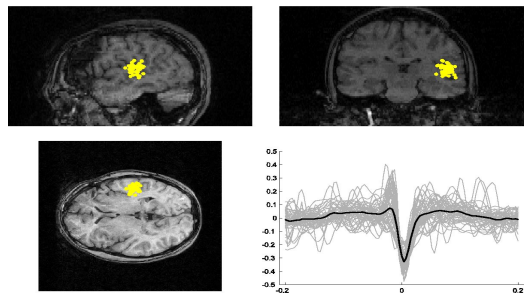
Epilepsy and interictal activity

- 30% of epileptic patients suffer from intractable epilepsy
- Identification of **the initiation zone of epileptogenesis** is the main goal of presurgical diagnostics
- Analysis of **large scale** propagation dynamics of interictal and ictal activity holds promise in identifying the primary epileptogenic foci (Ossadtchi et al. 2005)
- **Local interictal spike dynamics** is overlooked, yet modern MEG instrumentation allows for its noninvasive exploration using appropriate computational techniques
- Parameters of local dynamics may appear useful for a more detailed classification of epilepsy and guide surgeons to a more sparing resection

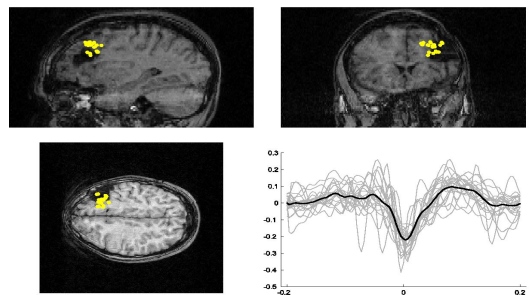


Non-invasive seizure onset zone localization

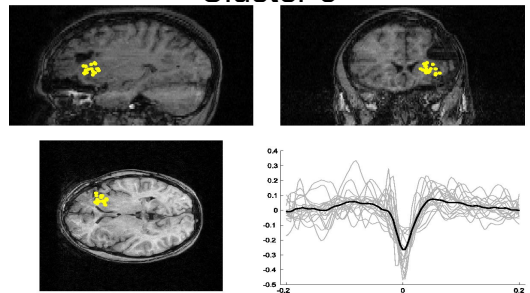
Cluster 1



Cluster 2



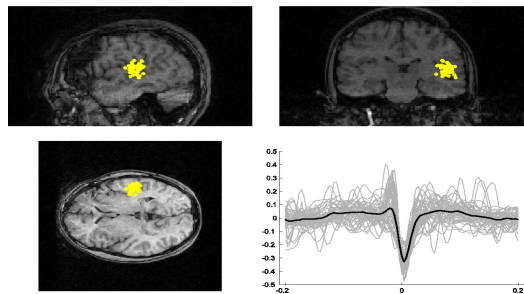
Cluster 3



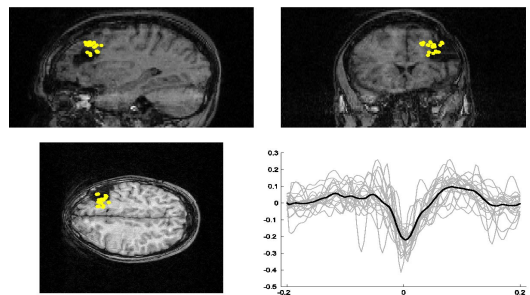
Ossadtchi et al., 2004, 2005, 2011
Kuznetsova et al., 2022, Kleeva et al., 2023

Non-invasive seizure onset zone localization

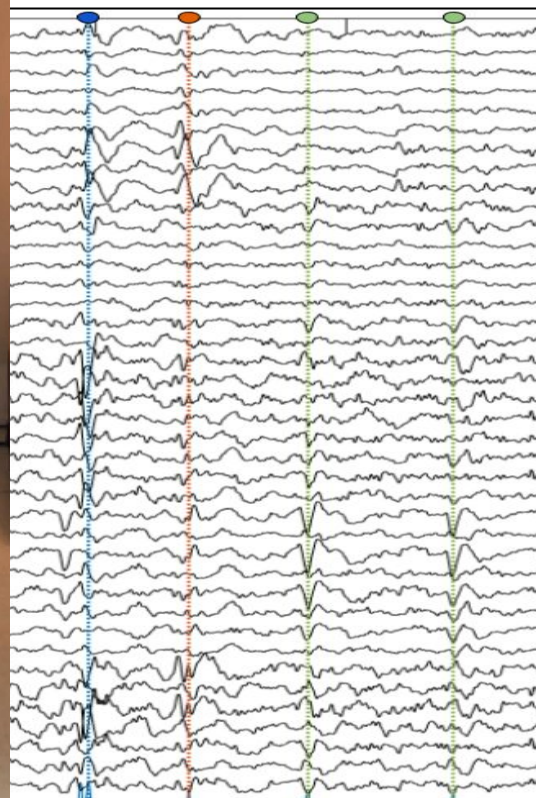
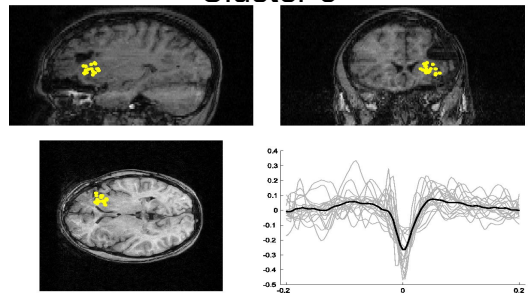
Cluster 1



Cluster 2

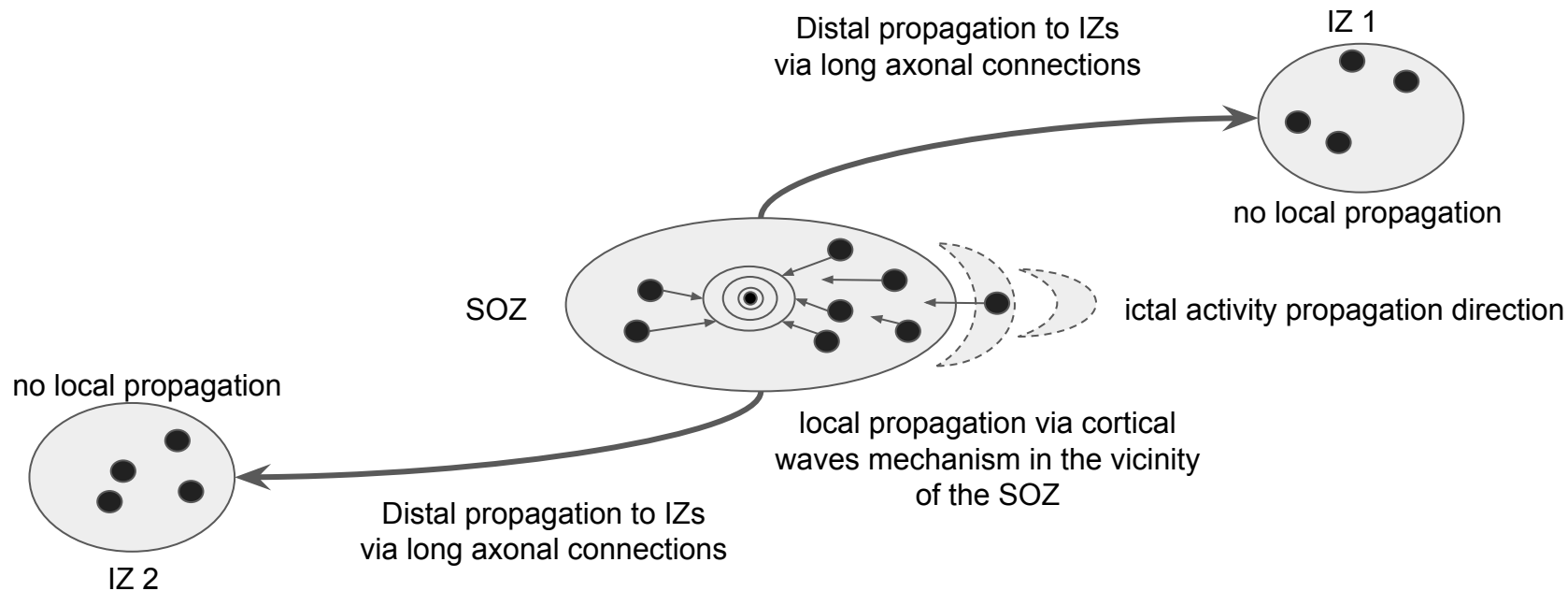


Cluster 3



Ossadtchi et al., 2004, 2005, 2011
Kuznetsova et al., 2022, Kleeva et al., 2023

Traveling waves - predictors of the EZ



+ оба вида распространения мы можем видеть неинвазивно при помощи МЭГ и, возможно, ЭЭГ

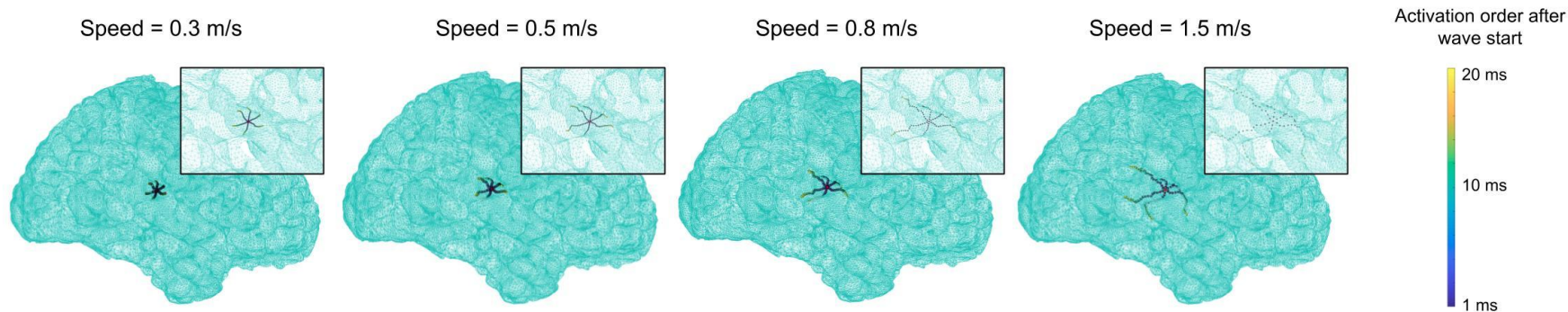
Multidirectional wave propagation model

$$\mathbf{X} = \alpha_0 + \alpha_1 \mathbf{W}_1 + \alpha_2 \mathbf{W}_2 + \dots + \alpha_N \mathbf{W}_N + \epsilon$$

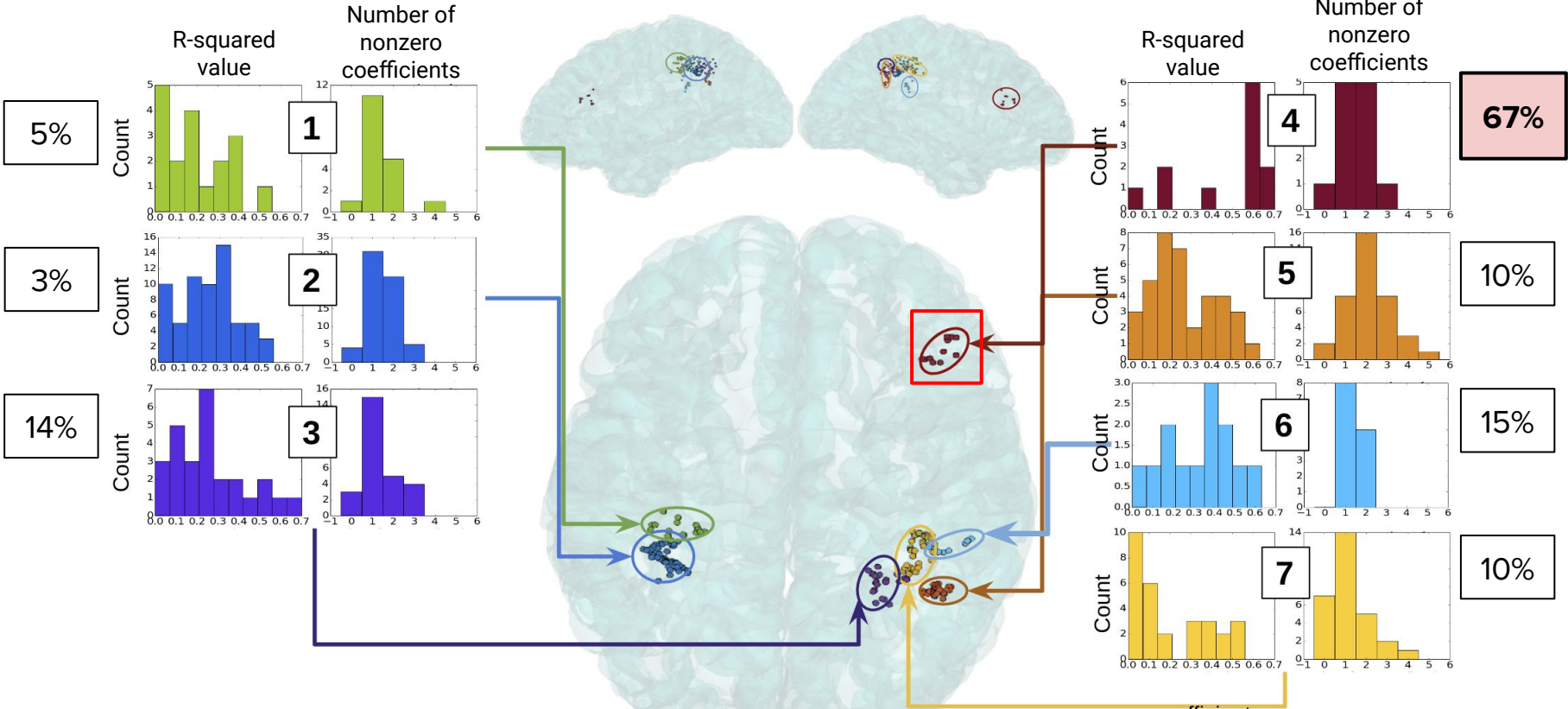
\mathbf{X} – MEG data with interictal spike (40 ms duration)

$\mathbf{W}_1 \dots \mathbf{W}_N$ – generated basis waves (20 ms duration) for chosen speed

N – number of propagation directions from chosen cortical location



Results example:



Статистика по n = 9 пациентам

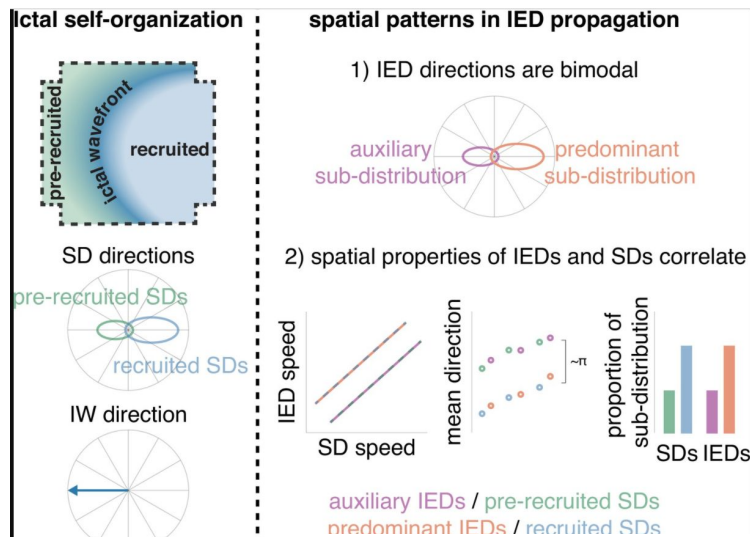
	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8	Patient 9
1	3 %	70 %	0 %	0 %	31 %	36 %	61 %	24 %	0 %
2	5 %	57 %	69 %	38 %	36 %	42 %	31 %	25 %	0 %
3	14 %	34 %	7 %	4 %			36 %	33 %	0 %
4	67 %	4 %		11 %			48 %	30 %	0 %
5	10 %	11 %		14 %			32 %	12 %	0 %
6	15 %	25 %		7 %			58 %	38 %	
7	10 %	0 %		33 %			27 %	20 %	
8		11 %		8 %			8 %	17 %	
9		0 %							
10		30 %							

Table 2: The percentage of spikes well-explained with a traveling wave model in each cluster in nine patients. We consider an interictal spike as well-explained, if R^2 is greater or equal to 0.6.

	Area of Resection	Surgical Outcome	High R^2 value percentage in corresponding cluster	Best cluster coincide with area of resection
Patient 1	Right frontal	I	67%	Yes
Patient 2	Left temporal	I	70%	Yes
Patient 3	Occipital	I	69%	Yes
Patient 4	Right temporal	I	38%	Yes
Patient 5	Left temporal	I	36%	Yes (focal epilepsy)
Patient 6	Right temporal	I	42%	Yes
Patient 7	Right temporal	I	61%	Yes (focal epilepsy)
Patient 8	Left medial temporal	I	20%	No
Patient 9	Left temporal	I	No good clusters	-

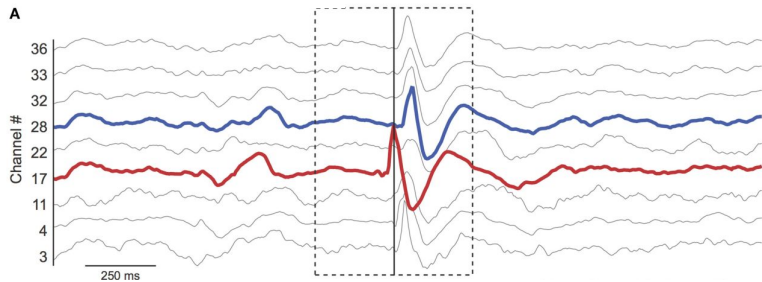
Table 3: Information about epileptogenic zone localization, area of resection and surgical outcome.

Analysis of propagation dynamics reveals diagnostic patterns non-invasively

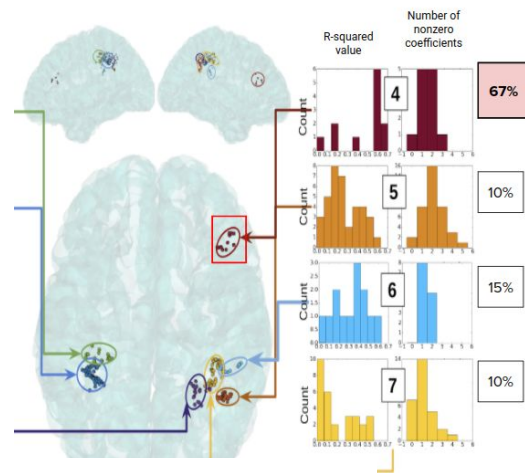


Smith et al., 2022

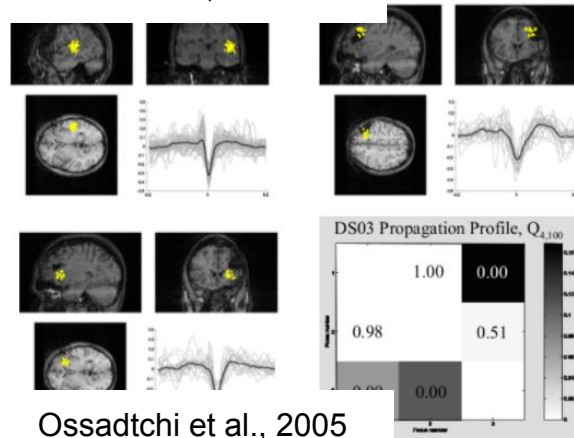
+ Stead et al. 2010, Vanleer et al. 2016



Tomlinson et al., 2016



Kuznetsova et al., 2021-22



Ossadtchi et al., 2005

Conclusions

- MEG is a fantastic time-resolved brain imaging modality. New sensor types mounted on scalp allow for even more detailed functional neuroimaging than it has been possible with cryogenic sensors located relatively far from the head.
- Inverse problem remains ill-posed. Physiological priors derived from the phenomenological properties of nominal activity of the nervous tissue need to be employed to constrain an MEG inverse solver. Cortical traveling wave is one of such a priori models.
- Modeling dynamical properties of spatial and electrical components of activity allows for improved tracking of dynamic cortical sources.
- Looking for traveling waves in the interictal MEG data of patients with epilepsy allows for pinpointing (out of several EZ candidates) the seizure onset zone, something that has been so far possible only invasively.



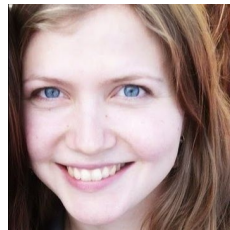
Аня Кубяк



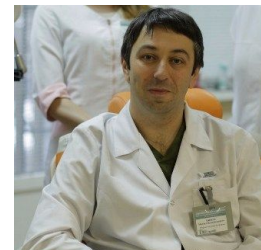
Никита Федосов



Дария Клеева



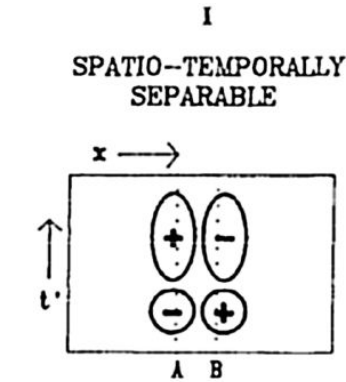
Александра Кузнецова



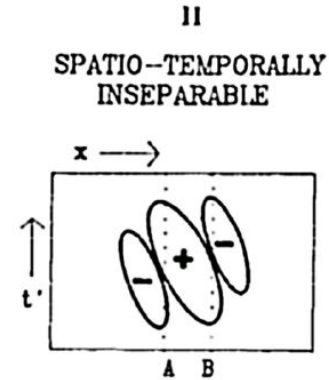
Михаил Синкин

Спасибо!!

Spatial-temporal non-separable activation



$$F(x, t) = S(t) \cdot G(x)$$



$$F(x, t) = S(t) \cdot G(x, t)$$

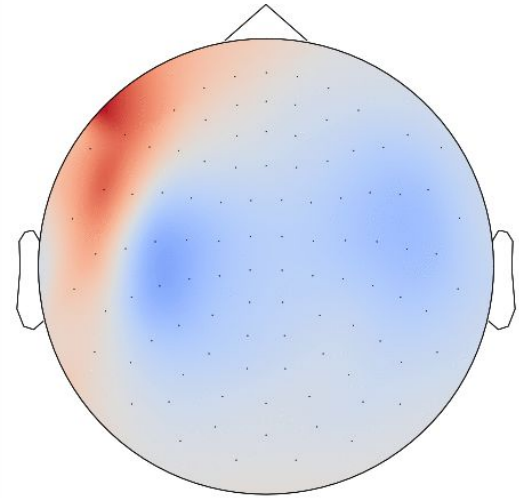
$F(x, t)$ – spatiotemporal activation of the cortex
 $S(t)$ – time course of the activation
 $G(x)$ or $G(x, t)$ – topography of the activation

Observation equation



$$\mathbf{y}(t) = \sum_{i=1}^N \mathbf{g}_i s_i(t) + \mathbf{v}(t)$$

15 ms



$$\mathbf{y}(t) = \mathbf{g}(t)s(t) + \mathbf{v}(t)$$