Connectivity measures in electrophysiology

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April 4, 2017

Measuring brain activity

ECoG

invasive

fMRI

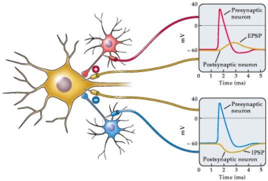
bad temporal resolution ($\approx$ 1s)

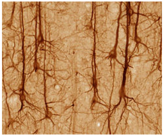
MEG

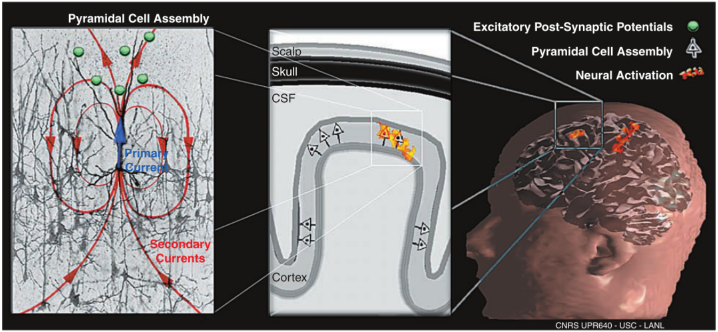
EEG

EEG and MEG allow to measure electromagnetic brain activity directly, noninvasively and with good temporal resolution

Source of electorphysiological activity in MEG/EEG

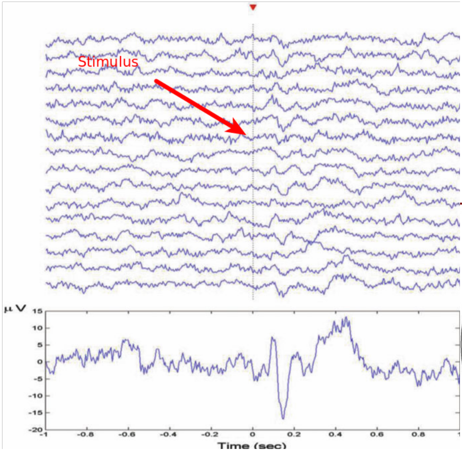


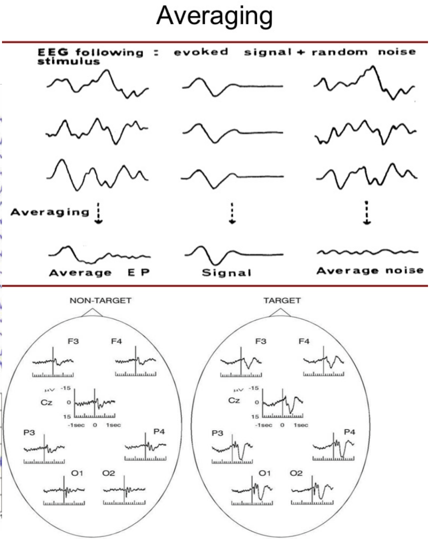




[Baillet et al., *Electromagnetic brain mapping*, 2001]

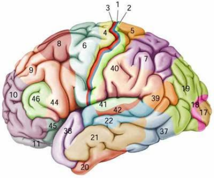
Subject is presented with stimulus repetitively while we measure his brain activity

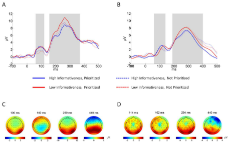




Studying brain activity...

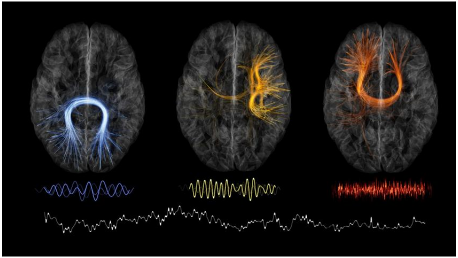
From evoked responses





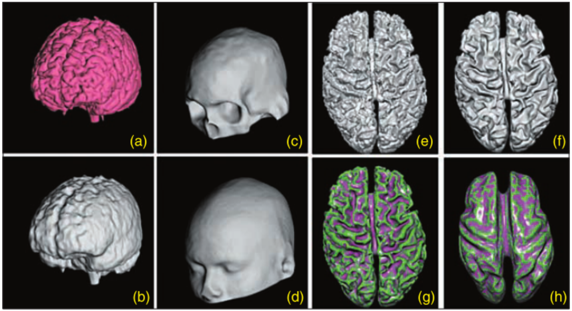
... to connectivity analysis

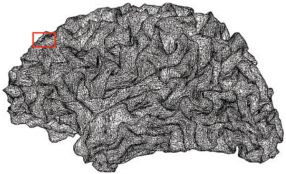
Functional / Effective

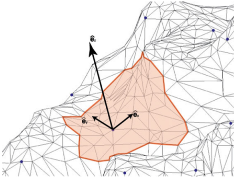


Anatomical

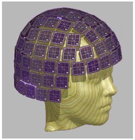
Forward modeling



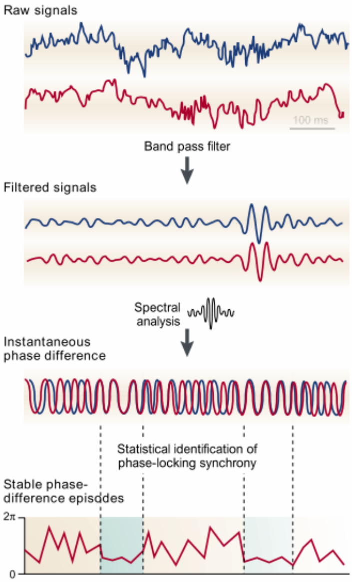




Forward operator: G



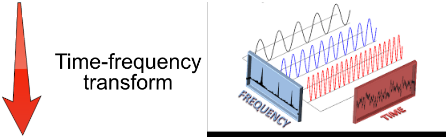
Studying phase synchrony



$$C_{xy}(\tau) = \int_u \hat{x}(u)\hat{y}(u-\tau)du \qquad (1)$$

where $\hat{x}$ is the zero-mean, normalized transform of x (EQN 2):

$$\hat{x}(u) = \frac{(x(u) - \langle x\rangle_{time})}{\sqrt{\int_{time}(x(u) - \langle x\rangle_{time})^2 dv}} \qquad (2)$$

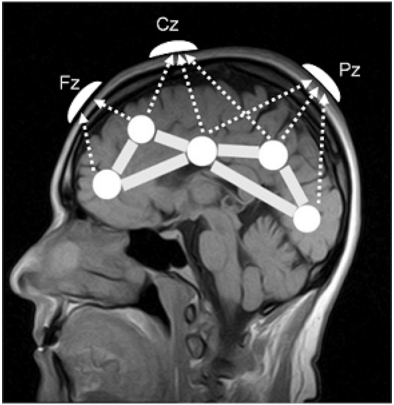


$$\tilde{x}(f,t) = a(t)\exp(i(ft + \phi_x(t))) \qquad (3)$$

$$\Phi_{xy}(t) = |n\phi_x(t) - m\phi_y(t)| \qquad (4)$$

Signal leakage problem

Simultaneous recording of the same brain activity on different electrodes leads to false positive detections of connectivity



Generative model

$$\begin{pmatrix} m_1 \\ m_2 \end{pmatrix}(t) = \begin{pmatrix} g_1^1 & g_2^1 \\ g_1^2 & g_2^1 \end{pmatrix} \begin{pmatrix} s_1 \\ s_2 \end{pmatrix}(t) =$$
$$= \begin{pmatrix} g_1^1 \\ g_1^2 \end{pmatrix} s_1(t) + \begin{pmatrix} g_2^1 \\ g_2^2 \end{pmatrix} s_2(t) = \vec{g}_1 s_1(t) + \vec{g_2} s_2(t) \quad (1)$$

$m_{1,2}(t)$ - MEG/EEG measurements
$\{g_i^j\}$ - matrix of a forward model
$s_{1,2}(t)$ - unknown timeseries on cortex

Time-frequency transformation

Apply time-frequency transform to (1)...

$$\begin{pmatrix} M_1 \\ M_2 \end{pmatrix} (f,t) = \vec{g}_1 S_1(f,t) + \vec{g_2} S_2(f,t) \qquad (2)$$

... and write cross-spectrum:

$$\mathbf{C}^{MM}(t,f) \stackrel{def}{=} \mathbf{E}\{\mathbf{M}(t,f)\mathbf{M}^H(t,f)\} \qquad (3)$$

N.B.

M_1, M_2, S_1, S_2 after time-frequency transformation are complex

Let's substitute (2) into (3)

$$\mathbf{C}^{MM}(t,f) = \mathbf{E}\left\{ \begin{pmatrix} M_1\bar{M}_1 & M_1\bar{M}_2 \\ M_2\bar{M}_1 & M_2\bar{M}_2 \end{pmatrix} (f,t) \right\} =$$

$$\mathbf{E}\left\{ \left(\vec{g}_1 S_1(f,t) + \vec{g_2} S_2(f,t)\right) \cdot \left(\vec{g}_1^T \bar{S}_1(f,t) + \vec{g_2}^T \bar{S}_2(f,t)\right) \right\} \quad (4)$$

Let's substitute (2) into (3)

$$\mathbf{C}^{MM}(t,f) = \mathbf{E}\left\{ \begin{pmatrix} M_1\bar{M}_1 & M_1\bar{M}_2 \\ M_2\bar{M}_1 & M_2\bar{M}_2 \end{pmatrix} (f,t) \right\} =$$

$$\mathbf{E}\left\{ \Big(\vec{g}_1 S_1(f,t) + \vec{g}_2 S_2(f,t) \Big) \cdot \Big(\vec{g}_1^T \bar{S}_1(f,t) + \vec{g}_2{}^T \bar{S}_2(f,t) \Big) \right\} \quad (4)$$

N.B.

$\vec{g}_i$ are real $\implies \vec{g}_i{}^H = \vec{g}_i{}^T$

Let's substitute (2) into (3)

$$\mathbf{C}^{MM}(t,f) = \mathbf{E}\left\{\begin{pmatrix} M_1\bar{M}_1 & M_1\bar{M}_2 \\ M_2\bar{M}_1 & M_2\bar{M}_2 \end{pmatrix}(f,t)\right\} =$$

$$\mathbf{E}\left\{\Big(\vec{g_1}S_1(f,t) + \vec{g_2}S_2(f,t)\Big)\cdot\Big(\vec{g_1}^T\bar{S}_1(f,t) + \vec{g_2}^T\bar{S}_2(f,t)\Big)\right\}$$
$$= \vec{g_1}\vec{g_1}^T\mathbf{E}\{S_1(f,t)\bar{S}_1(f,t)\} + \vec{g_1}\vec{g_2}^T\mathbf{E}\{S_1(f,t)\bar{S}_2(f,t)\} +$$
$$+ \vec{g_2}\vec{g_1}^T\mathbf{E}\{S_2(f,t)\bar{S}_1(f,t)\} + \vec{g_2}\vec{g_2}^T\mathbf{E}\{S_2(f,t)\bar{S}_2(f,t)\} \quad (4)$$

Let's substitute (2) into (3)

$$\begin{aligned}
&\mathbf{C}^{MM}(t,f) = \\
&\quad = \vec{g_1}\vec{g_1}^T\mathbf{E}\{S_1(f,t)\bar{S_1}(f,t)\} + \vec{g_1}\vec{g_2}^T\mathbf{E}\{S_1(f,t)\bar{S_2}(f,t)\} + \\
&\quad + \vec{g_2}\vec{g_1}^T\mathbf{E}\{S_2(f,t)\bar{S_1}(f,t)\} + \vec{g_2}\vec{g_2}^T\mathbf{E}\{S_2(f,t)\bar{S_2}(f,t)\}
\end{aligned} \tag{4}$$

Finally, we've got

$$\begin{pmatrix} c_{11}^{MM} & c_{12}^{MM} \\ c_{21}^{MM} & c_{22}^{MM} \end{pmatrix} = \\ = \vec{g_1}\vec{g_1}^T c_{11}^{SS} + \vec{g_1}\vec{g_2}^T c_{12}^{SS} + \vec{g_2}\vec{g_1}^T c_{21}^{SS} + \vec{g_2}\vec{g_2}^T c_{22}^{SS} \quad (5)$$

Or in matrix form:

$$\begin{pmatrix} c_{11}^{MM} & c_{12}^{MM} \\ c_{21}^{MM} & c_{22}^{MM} \end{pmatrix} =$$

$$= \begin{pmatrix} g_1^1 g_1^1 & g_1^1 g_1^2 \\ g_1^2 g_1^1 & g_1^2 g_1^2 \end{pmatrix} c_{11}^{SS} + \begin{pmatrix} g_1^1 g_2^1 & g_1^1 g_2^2 \\ g_1^2 g_2^1 & g_1^2 g_2^2 \end{pmatrix} c_{12}^{SS} +$$

$$+ \begin{pmatrix} g_2^1 g_1^1 & g_2^1 g_1^2 \\ g_2^2 g_1^1 & g_2^2 g_1^2 \end{pmatrix} c_{21}^{SS} + \begin{pmatrix} g_2^1 g_2^1 & g_2^1 g_2^2 \\ g_2^2 g_2^1 & g_2^2 g_2^2 \end{pmatrix} c_{22}^{SS} \quad (5)$$

Or in matrix form:

$$
\begin{pmatrix} c_{11}^{MM} & c_{12}^{MM} \\ c_{21}^{MM} & c_{22}^{MM} \end{pmatrix} =
$$

$$
= \begin{pmatrix} g_1^1 g_1^1 & g_1^1 g_1^2 \\ g_1^2 g_1^1 & g_1^2 g_1^2 \end{pmatrix} c_{11}^{SS} + \begin{pmatrix} g_1^1 g_2^1 & g_1^1 g_2^2 \\ g_1^2 g_2^1 & g_1^2 g_2^2 \end{pmatrix} c_{12}^{SS} +
$$

$$
+ \begin{pmatrix} g_2^1 g_1^1 & g_2^1 g_1^2 \\ g_2^2 g_1^1 & g_2^2 g_1^2 \end{pmatrix} c_{21}^{SS} + \begin{pmatrix} g_2^1 g_2^1 & g_2^1 g_2^2 \\ g_2^2 g_2^1 & g_2^2 g_2^2 \end{pmatrix} c_{22}^{SS} \tag{5}
$$

Signal leakage

Drop the real part of this equation away [Nolte et al., 2004] to deal with true connectivity only

Or in matrix form:

$$\begin{pmatrix} c_{11}^{MM} & c_{12}^{MM} \\ c_{21}^{MM} & c_{22}^{MM} \end{pmatrix} =$$
$$= \begin{pmatrix} g_1^1 g_1^1 & g_1^1 g_1^2 \\ g_1^2 g_1^1 & g_1^2 g_1^2 \end{pmatrix} c_{11}^{SS} + \begin{pmatrix} g_1^1 g_2^1 & g_1^1 g_2^2 \\ g_1^2 g_2^1 & g_1^2 g_2^2 \end{pmatrix} c_{12}^{SS} +$$
$$+ \begin{pmatrix} g_2^1 g_1^1 & g_2^1 g_1^2 \\ g_2^2 g_1^1 & g_2^2 g_1^2 \end{pmatrix} c_{21}^{SS} + \begin{pmatrix} g_2^1 g_2^1 & g_2^1 g_2^2 \\ g_2^2 g_2^1 & g_2^2 g_2^2 \end{pmatrix} c_{22}^{SS} \quad (5)$$

Signal leakage

Drop the real part of this equation away [Nolte et al., 2004] to deal with true connectivity only

DICS algorithm [Gross et al., 2001]

We want to estimate coherence of two cortical sources:

$$\mathbf{M}_{i,j}(f) = \frac{|\mathbf{C}_{i,j}(f)|^2}{\mathbf{C}_{i,i}(f)\mathbf{C}_{j,j}(f)} . \qquad \textbf{[1]}$$

Beamformer: construct a spatial filter which passes activity from source r with unit gain while suppressing activity coming from other sources

$$\min[\mathscr{E}\{\|\mathbf{AD}\|^2\} + \alpha\|\mathbf{A}\|^2] \quad \text{subject to } \mathbf{AL}(\mathbf{r}) = \mathbf{I} , \qquad \textbf{[2]}$$

Where D - time-frequency-transformed data
$L(r)$ - forward problem solution for two orthogonal tangential dipoles at r
A - inverse operator (we want to find it)
Solve minimization problem:

$$\mathbf{A}(\mathbf{r},f) = (\mathbf{L}^T(\mathbf{r})\mathbf{C}_r(f)^{-1}\mathbf{L}(\mathbf{r}))^{-1}\mathbf{L}^T(\mathbf{r})\mathbf{C}_r(f)^{-1} , \qquad \textbf{[3]}$$

with $\mathbf{C}_r(f) = \mathbf{C}(f) + \alpha\mathbf{I}$, where $\mathbf{C}(f)$ is the cross spectral density matrix at frequency f or averaged across a frequency band centered at f, and superscript T indicates the matrix transpose.

$$\mathbf{C}_s(\mathbf{r}_1,\mathbf{r}_2,f) = \mathbf{A}(\mathbf{r}_1,f)\mathbf{C}(f)\mathbf{A}^{*T}(\mathbf{r}_2,f) . \qquad \textbf{[4]}$$

$$\mathbf{P}(\mathbf{r},f) = \mathbf{C}_s(\mathbf{r},\mathbf{r},f) . \qquad \textbf{[5]}$$

$$c_s(\mathbf{r}_1,\mathbf{r}_2,f) = \lambda_1\{\mathbf{C}_s(\mathbf{r}_1,\mathbf{r}_2,f)\} , \qquad \textbf{[7]}$$

where $\lambda_1\{\}$ indicates the larger singular value of the expression in braces.

Analogously, the power in the dominant direction is

$$p(\mathbf{r},f) = \lambda_1(\mathbf{P}(\mathbf{r},f)) , \qquad \textbf{[8]}$$

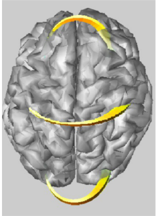
and we obtain the coherence from Eqs. **7** and **8** as

$$M(\mathbf{r}_1,\mathbf{r}_2,f) = \frac{|c_s(\mathbf{r}_1,\mathbf{r}_2,f)|^2}{p(\mathbf{r}_1,f)p(\mathbf{r}_2,f)} . \qquad \textbf{[9]}$$

Apply the imaginary coherence idea to DICS:

$$C_s(r_1, r_2, f) = Im(A(r_1, f)C(f)A^{*T}(r_2, f))[4^*]$$

To evaluate algorithm performance we simulate MEG recordings with three networks active across trial



1. We add artificial brain noise
2. ... and sensor noise
3. Networks are active with different time profiles
4. Signal to noise ratio and phase lag are varied during the experiment