### Reconstruction of functional brain networks from MEG sensor data

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- Background on MEG
- Inverse modeling of MEG signals
- Assessing brain connectivity with MEG
- Bias reduction

## Magnetoencephalography (MEG)





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## Generation of MEG signals

MEG signals are generated by synchronized currents ( $>\approx 1 \text{cm}^2$ ) in the apical dendrites of cortical pyramidal neurons.



The relation between the cortical current density and the generated magnetic fields is described by Maxwell's equations (Biot-Savard).

The mapping from the cortical current density to the generated magnetic fields is obtained by numerically solving Maxwell's equations for a volume-conductor model of the head  $\rightarrow$  leadfield matrix  $L \in \mathbb{R}^{n \times p}$  (n < p).

**MEG forward model** (time-frequency domain): Y(f) = LX(f) + E(f) $X(f) \in \mathbb{C}^{p \times k}$  cortical current density ("brain activity")  $Y(f) \in \mathbb{C}^{n \times k}$  sensor data  $E(f) \in \mathbb{C}^{n \times k}$  sensor noise

Two popular linear reconstruction methods:

**Ridge regression:**  $X^* = \underset{X \in \mathbb{C}^{p \times k}}{\operatorname{argmin}} ||Y - LX||_F^2 + \lambda ||AX||_F^2$  **Adaptive filter:**  $X_j^* = w_j^{\dagger} Y$  with  $w_j = \underset{w \in \mathbb{C}^n}{\operatorname{argmin}} w^{\dagger} \Sigma_Y w$  subject to  $w^{\dagger} L_j = 1$   $\Sigma_Y = YY^{\dagger}$  sensor covariance matrix  $w^{\dagger} \Sigma_Y w = \mathbb{V}(X_j^*)$  output power  $w^{\dagger} L_j = w^{\dagger}(Le_j) = 1$  unit-gain constraint

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# Example: Spontaneous alpha ( $\sim 10 \text{ Hz}$ ) oscillations<sup>1</sup>



<sup>1</sup>Hindriks et al. 2017

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### Functional brain connectivity

Refers to any statistical relationship between signals x and y recorded from different cortical locations.

One of the many measures is **coherence:**  $\rho = \frac{\langle xy^* \rangle}{\sqrt{\langle |x|^2 \rangle \langle |y|^2 \rangle}} = \frac{\langle a_x a_y e^{i(\phi_x - \phi_y)} \rangle}{\sqrt{\langle |a_x|^2 \rangle \langle |a_y|^2 \rangle}}.$ 

Spontaneous hemodynamic activity<sup>2</sup> is organized into distributed correlated patterns (resting-state networks).



Do resting-state networks have an electrophysiological origin? This question can (potentially) be answered with MEG.

 $<sup>^{2}\</sup>mathrm{As}$  measured with functional MRI.

Reconstructed signals  $X^*$  are low-dimensional projections of the true signals X:

$$\begin{split} Y &= LX \to X^* = L^{\sharp}Y = L^{\sharp}LX = RX\\ L^{\sharp} \in \mathbb{R}^{p \times n} \text{ inverse operator}\\ R &= L^{\sharp}L \in \mathbb{R}^{p \times p} \text{ resolution operator with rank } \leq n < p. \end{split}$$

 $\rightarrow$  spurious interactions:  $\Sigma^* = R\Sigma R^T$ , in particular:  $\Sigma = I \rightarrow \Sigma^* = RR^T$ .

However: R is real-valued, hence if  $\Sigma$  is real-valued, then so is  $\Sigma^*$ . This can be exploited by only considering  $\text{Im}(\Sigma^*)$ .

Most currently used connectivity measures are variations on this.

One of these is the **imaginary phase-locking factor**  $\left\langle \frac{\operatorname{Im}(xy^*)}{|x||y|} \right\rangle = \left\langle \sin\left(\phi_x - \phi_y\right) \right\rangle$ .

## Detecting resting-state networks with MEG

Using one of these measures (orthogonalized amplitude correlation) resting-state networks were observed using  $MEG^3$ .



<sup>3</sup>Hipp et al. 2012.

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Main drawback of existing measures is that instantaneous interactions ( $\Sigma$  real-valued) cannot be detected.

To mitigate this, exploit the relation  $Vec(\Sigma^*) = (R \otimes R)Vec(\Sigma)$ .<sup>4</sup> Write  $\Sigma = \Sigma^+ + \Sigma^-$ .

 $Vec(\Sigma^*) = (R \otimes R)Vec(\Sigma^+) + (R \otimes R)Vec(\operatorname{Re}(\Sigma^-)) + (R \otimes R)Vec(\operatorname{Im}(\Sigma^-))i.$ 

The three vectors are contained in:

 $S_0 = \operatorname{span}\{r_i \otimes r_i\}$  (leakage subspace)

 $S_1 = \operatorname{span}\{r_i \otimes r_j + r_j \otimes r_i\}$  (instantaneous interaction subspace)

 $S_2 = \operatorname{span}\{r_i \otimes r_j - r_j \otimes r_i\} \text{ (lagged interaction subspace)}$ 

Approach: Construct a series of operators  $\pi_j$  on  $\mathbb{C}^{p^2}$  that project  $Vec(\Sigma^*)$  onto the orthogonal complement of the first j left singular vectors of  $[r_i \otimes r_i]$ .

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<sup>&</sup>lt;sup>4</sup>Ossadtchi et al. (2018) and Hindriks (2020).

Intra-cortical potentials generated by a current source (Poisson's equation):

$$V = \frac{1}{\sqrt{h^2 + (x-y)^2}}.$$

Two oscillatory monopoles with covariance matrix  $\Sigma = \begin{bmatrix} 1 & \gamma e^{i\phi} \\ e^{-i\phi} & 1 \end{bmatrix}$ 



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#### Effect of bias reduction



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