Dynamic Brain Connectivity Mapping

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Neural connectivity based on EEG recording

- In EEG recording, each electrode records current from many sources, all electrodes are correlated with each other.
- The estimation of brain connectivity allows describing the functional links established between different cortical areas during the execution of a particular experimental task and is an important step to the understanding of the brain functional organization.
Neural connectivity based on EEG recording

Subject performing a mental task (e.g. motor imagery, language processing)
Neural connectivity based on EEG recording

Neural connectivity based on EEG recording

L. Astolfi and F. Babiloni, “Methods for monitoring effects of drugs and other chemicals in the CNS by using high resolution EEG”, Frontiers in Science,
Methodology of Brain Connectivity
Brain connectivity is viewed as central for the understanding of the organized behavior of cortical regions.

Aim at describing these interactions as connectivity patterns which hold the direction and strength of the information flow between cortical areas.

W.J. Freeman et al. / BioSystems 59 (2001)
• Defined as the temporal correlation between spatially remote neurophysiologic events.

• The connection methods typically involve the estimation of some covariance properties between the different time series measured from the different spatial sites, during motor and cognitive tasks based on EEG and ECoG.

W.J. Freeman et al. / BioSystems 59 (2001)
Coherence

• Due to the evidence that important information in the brain signals are coded in frequency rather than in time domain, spectral coherence between the activity of pairs of channels is focused to detect frequency-specific interactions in EEG or ECoG signals.

• The coherence between multi-channel series \([x_1(t) \ldots x_N(t)]\) is a real-valued function that is defined as:

\[
\eta_{kl}(f) = \frac{S_{kl}(f)}{\sqrt{S_{kk}(f)S_{ll}(f)}}
\]

where \(S_{kl}(f)\) is an element of spectral matrix \(S(f)\), and spectral matrix is defined by multivariate model:
Coherence

- A multivariate model is defined as:
  \[ X(t) = -\sum_{\tau=1}^{p} A_\tau X(t - \tau) + E(t) \]
  where \( X(t) = [x_1(t) \ldots x_N(t)] \), \( N \) represents channels number, and \( p \) is the model order.

- When we use Fourier transform to both side:
  \[ X(f) = H(f)E(f) \]
  where \( H(f) \) is the transfer function:
  \[ H(f) = \left( \sum_{\tau=0}^{p} A_\tau e^{-i2\pi f \Delta t} \right)^{-1} \]

- By these, we obtain spectral matrix
  \[ S(f) = H(f) \sum H^*(f) \]
  where \( \sum \) is the noise covariance matrix.
Coherence Analysis of Human Depth EEG During Seizure Activity

*John Klopp et.al., 1996, Complexity International*
Coherence of Spiking and LFP across time during memory-saccade task

Bijan Pesaran et al., 2002, Nature Neuroscience
Partial Coherence

- In order to distinguish between direct and cascade flows, partial coherence was proposed. It could be defined in terms of MVAR coefficients transformed to the frequency domain.

- The formal definition of the normalized Partial Directed Coherence (PDC) is the following:

\[
\chi^2_{lk}(f) = \frac{M^2_{lk}(f)}{M_{ll}(f)M_{kk}(f)}
\]

where \(M_{ll}(f)\) is an element of the inverse of spectral matrix \(S(f)\). Partial coherence describes direct relationships between signals.
Directed connection

- However, coherence analysis has not a directional nature, actually, it just examines whether a link exists between time series, by describing instances when they are in synchronous activity, and it does not provide the direction of the information flow.
- Multivariate spectral techniques called Directed Transfer Function (DTF) or Partial Directed Coherence (PDC) were proposed to determine the directional influences between any given pair of channels in a multivariate data set. Both DTF and PDC can be demonstrated to rely on the key concept of Granger causality between time series (Granger, C., 1969).
Granger Causality

- Granger theory mathematically defines what a “causal” relation between two signals is. According to this theory, an observed time series $x(n)$ is said to cause another series $y(n)$ if the knowledge of $x(n)$’s past significantly improves prediction of $y(n)$; this relation between time series is not necessarily reciprocal, i.e., $x(n)$ may cause $y(n)$ without $y(n)$ causing $x(n)$. This lack of reciprocity allows the evaluation of the direction of information flow between structures.
Granger Causality

- The Granger causality at frequency $f$ is obtained as the fraction of the total power at that frequency at one electrode that can be explained by the causal influence from the other electrode. The value ranges from 0 to 1, where 0 represents no causal influence and 1 denotes total causal influence from the other electrode.
Granger Causality

- We get Granger causality spectral analysis by:

\[
I_{k \rightarrow l}(f) = \frac{(Z_{kk} - Z_{lk}^2 / Z_{ll})|H_{lk}(f)|^2}{|S_{ll}(f)|}
\]

and

\[
I_{l \rightarrow k}(f) = \frac{(Z_{ll} - Z_{kl}^2 / Z_{kk})|H_{kl}(f)|^2}{|S_{kk}(f)|}
\]

where \(Z_{kk}, Z_{kl}, Z_{ll}\) and \(Z_{lk}\) are elements of the covariance matrix \(Z\) of the noise vector of the bivariate model, and \(|S_{ll}(f)|\) and \(|S_{kk}(f)|\) are the power spectra of time series obtained above.
Beta oscillations in sensorimotor cortical network: Directional influences revealed by Granger causality

Brovelli A et al. 2004, PNAS
Directed Transfer Function

- Kaminski and Blinowska (1991) proposed a multivariate spectral measure, called the Directed Transfer Function (DTF), which can be used to determine the directional influences between any given pair of channels in a multivariate dataset. DTF is an estimator that simultaneously characterizes the direction and spectral properties of the interaction between brain signals and requires only one multivariate autoregressive (MVAR) model to be estimated simultaneously from all the time series.
Directed Transfer Function

- The Directed Transfer Function, representing the causal influence between $l$th channel and $k$th channel at the frequency $f$, is defined in terms of elements of the transfer matrix $H(f)$:

$$\theta_{lk}^2(f) = |H_{lk}(f)|^2$$

- And normalized DTF to compare the results obtained from cortical waveforms with different power spectra, by dividing each estimated DTF by the squared sums of all elements of the relevant row:

$$\gamma_{lk}^2(f) = \frac{|H_{lk}(f)|^2}{\sum_{m=1}^{N} |H_{lm}(f)|^2}$$
Application of the Directed Transfer Function Method to Mesial and Lateral Onset Temporal Lobe Seizures.

A: Mesial onset of the seizure near the depth array. B: 27 seconds after A, where rhythmic 7.5Hz activity visible from all electrodes.

DTF of B(left). Horizontal is scale of frequency 0-25Hz, vertical is scale of DTF 0-0.5.

Piotr J. Franaszczuk et al., 1998, Brain Topography
Piotr J. Franaszczuk et al., 1998, Brain Topography

Application of the Directed Transfer Function Method to Mesial and Lateral Onset Temporal Lobe Seizures.  

Integrated DTF of 7-8Hz
Assessing cortical functional connectivity directed transfer function.

Piotr J. Franaszczuk et al., 1998, Brain Topography

Top: a selection of the ERPs gathered from the standard electrode.
Bottom: The current density waveforms, represented for some selected ROIs on the realistic cortex.
The onset of the electromyographic (EMG) signal for the start of the movement of the right finger is at the 0ms.

The percentage differences of the computed DTF values between the PRE and POST periods.

\[ \text{DIFF} = \left( \frac{\text{PRE} - \text{POST}}{\text{PRE}} \right) \times 100 \]
Modification of DTF

- Full frequency Directed Transfer Function (ffDTF), in which a new normalization procedure for DTF was used. The ffDTF is defined as:

\[ \gamma_{lk}^2(f) = \frac{|H_{lk}(f)|^2}{\sum_{f} \sum_{m=1}^{N} |H_{lm}(f)|^2} \]

- The summation (or integration) over the whole frequency band assures that the denominator of the expression does not change with frequency. Spectral properties of ffDTF depend only on the outflow from that channel.
Modification of DTF

- Multiplying ffDTF by partial coherence we emphasize only direct connections. The new function is given by:

\[
\delta_{lk}(f) = \chi_{lk}(f)\gamma_{lk}(f)
\]

- We called the function obtained this way a direct Directed Transfer Function (dDTF). It combines information from partial coherence function with information about direction of influence in one measure.
**Dynamics of Event-Related Causality in Brain Electrical Activity based on ECoG by Short time dDTF**

Anna Korzeniewska et al., 2008, Human Brain Mapping

Positions of electrodes for ECoG recording. White discs indicate electrodes implanted for clinical purposes. Numbered discs indicate recording sites analyzed for this study.

Time-frequency plots of splined/smoothed Short time dDTF for between two channels (E3 and E9 in left), showing the entire analyzed frequency range. Horizontal axis is time with vertical lines demarcating stimulus onset (s), stimulus offset (o), and response onset (r).
SdDTF of twelve-channel MVAR for ECoG signals recorded during auditory word repetition.

Anna Korzeniewska et al., 2008, Human Brain Mapping
Integrals of ERC for frequency range 82 – 100 Hz calculated for three stages of auditory word repetition task

Statistically significant event-related changes in SdDTF, referred as Event Related Causality

Anna Korzeniewska et al., 2008, Human Brain Mapping
Phase directionality index

- Phase directionality index is a nonlinear approach that is firstly developed by Rosenblum and Pikovsky to describe characteristics of coupling between two oscillatory systems from their time series.
- It is based on the basic idea that weak coupling affects the phase of the system first rather than the amplitude.
Phase directionality index

- Instantaneous phase \( \phi_i(t_n) \) of time series are obtained by Hilbert transform:

\[
y_i(t) = H(x_i(t)) = pv \cdot \frac{1}{\pi} \int_{-\infty}^{\infty} \frac{x_i(t')}{t-t'} \, dt'
\]

where \( pv \) indicates that the Cauchy principal value is taken in the integral, and \( y_i(t) \) represents the imaginary part of the complex analytic signal \( z_i(t) = x_i(t) + jy_i(t) = A_i(t)e^{j\phi_i(t)} \).

- Coupling model between two time series is constructed as differenti \[
\begin{align*}
\dot{\phi}_1(t) &= \omega_1 + G_1(\phi_1(t), \phi_2(t)) + \xi_1(t) \\
\dot{\phi}_2(t) &= \omega_2 + G_2(\phi_1(t), \phi_2(t)) + \xi_2(t)
\end{align*}
\]

where \( w_i \) govern the natural frequencies of signals, and \( G_i \).
Phase directionality index

- For digital signals, difference equations defined model is more conveniently to be considered:

\[ \Delta_1(t_n) = F_1[\phi_1(t_n), \phi_2(t_n)] + \eta_1 \]
\[ \Delta_2(t_n) = F_2[\phi_1(t_n), \phi_2(t_n)] + \eta_2 \]

where \( \Delta_1(t_n) \) is the increments of phase series \( \phi_1(t) \). \( F_1 \) and \( F_2 \) could be estimated by trigonometric polynomials:

\[ F_1 = \sum_{m,n}[a_{1,m,n}\cos(m\phi_1 + n\phi_2) + b_{1,m,n}\sin(m\phi_1 + n\phi_2)] \]
\[ F_2 = \sum_{m,n}[a_{2,m,n}\cos(m\phi_1 + n\phi_2) + b_{2,m,n}\sin(m\phi_1 + n\phi_2)] \]

- Phase influence (\( c_{1,2}^2 \)) and coupling directionality (\( d \)) are:

\[ c_{1,2}^2 = \frac{1}{2\pi^2} \int_0^{2\pi} \int_0^{2\pi} \left( \frac{\partial F_{1,2}}{\partial \phi_{2,1}} \right)^2 \, d\phi_{1,2} \, d\phi_{2,1} \]

\[ d = \frac{c_2 - c_1}{c_2 + c_1} \]

directionality:

1 \( \rightarrow \) 2 when \( d > 0 \)
2 \( \rightarrow \) 1 when \( d < 0 \)
The estimation of coupling direction for pairwise short time series is defined as:

$$\hat{\delta} \equiv \hat{\gamma}_2 - \hat{\gamma}_1$$

where $\hat{\gamma}_2$ and $\hat{\gamma}_1$ are the short time correction of $c_{1,2}^2$:

$$\hat{\gamma}_1 = \hat{\epsilon}_1^2 - \sum_{m,n} n^2 \left( \hat{\sigma}_{\hat{a}_{1,m,n}}^2 + \hat{\sigma}_{\hat{b}_{1,m,n}}^2 \right)$$

The confidence interval for estimation of $c_{1}^2$ is defined as

$$\left[ \hat{\gamma}_1 - \alpha \hat{\sigma}_{\hat{\gamma}_1}, \hat{\gamma}_1 + \beta \hat{\sigma}_{\hat{\gamma}_1} \right]$$

where $\hat{\sigma}_{\hat{\gamma}_1}$ is semiempirical obtained (not detailed):

$$\hat{\sigma}_{\hat{\gamma}_1}^2 = \begin{cases} \sum_{m,n} n^4 \left( \hat{\sigma}_{\hat{a}_{1,m,n}}^2 + \hat{\sigma}_{\hat{b}_{1,m,n}}^2 \right), & \hat{\gamma}_1 \geq 5 \left( \sum_{m,n} n^4 \left( \hat{\sigma}_{\hat{a}_{1,m,n}}^2 + \hat{\sigma}_{\hat{b}_{1,m,n}}^2 \right) \right) \\ \frac{1}{2} \sum_{m,n} n^4 \left( \hat{\sigma}_{\hat{a}_{1,m,n}}^2 + \hat{\sigma}_{\hat{b}_{1,m,n}}^2 \right), & otherwise. \end{cases}$$
Simulation study of phase based directional Connectivity from Human ECoG

Simulation data are constructed from one channel of real ECoG recording with cascaded time delay and Gaussian noise.

Left: Phase dependence function between signal A and signal B.
Upper right: Simulation result of coupling directionality and its short time correction.
Computation of phase based dynamic directional connectivity mapping of human ECoG during hand open-close experiment:

(a) ECoG recording (Channel 40 and channel 53) of after 0.15~300Hz bandpass filter and common average reference (CAR). (b) Short time correction of phase influence. (c) Short time correction of directionality during hand movement.

Normalized short time coupling direction index in 64-electrodes ECoG grid during hand movement, with window size 1000 ms.

Short time coupling directionality between motor cortex and sensory cortex in patient during hand movement, with frequency band 70~100Hz, windows 1250 ms & overlapping 1000 ms.
Time-varying Dynamic Bayesian Network

- In TVDBN, the conditional probability of observing a given value at time $t$ given a value at previous time $P(X^t | X^{t-1})$, a first order Markov model in which the state of $X$ at time $t$ depends only on its previous state.

- In the model, the distribution of temporal transitions can be described as a linear model: $X^t = A^t X^{t-1} + \mathcal{E}$, $A_{ij}^t$ is the connectivity weight from the $i$th to the $j$th channel from time $t-1$ to time $t$.

The $A^t$ term can be estimated at time $t$ with:
Time-varying Dynamic Bayesian Network

- The $A^t$ term can be estimated at time $t$ with:

$$\hat{A}^t_i = \arg\min_{A^t_i \in R^{1 \times N}} \frac{1}{T} \sum_{t^* = 1}^T w^t(t^*)(x_i^{t^*} - A^t_i X^{t^*}) + \lambda \|A^t_i\|$$

where The parameter $\lambda$ defines a regularization term that shrinks the sparseness of the connection matrix $A$. And the weight of an observation at time $t^*$ is given by:

$$w^t(t^*) = \frac{K_h(t^* - t)}{\sum_{t^* = 1}^T K_h(t^* - t)}$$

in which $K_h(\cdot) = e^{(-t^2/h)}$, a Gaussian kernel function.

- The network can be solved as a weighted regression problem by least squares.
Time-varying Dynamic Bayesian Network

- Implementation TVDBN on ECoG data.

ECoG grids in human brain

Select electrode subsets by their correlation with hand movements: Activation Index
Time-varying Dynamic Bayesian Network

(a) Hand joint angle. (b) Connections between ECoG electrodes by TVDBN during hand movements. (3) Average connections between electrodes and their variances across movement trials.
Time-varying Dynamic Bayesian Network

Up: Connections between electrodes.
Down: Hand joint angle.
## Conclusions

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<th>SNR</th>
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<th>Time resolution</th>
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<td>High</td>
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<td>Medium</td>
<td>High</td>
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Beyond Current BCI means

1. Highly Dynamic Directionality Mapping

2. Two Ways Indexed (Parameterized) Communication

3. Robust and Global Optimization
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