Source level Information flow Analysis using Event Related Potential (ERP) data

Presented by

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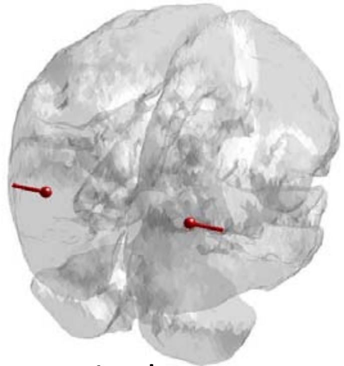
Electroencephalography (EEG)

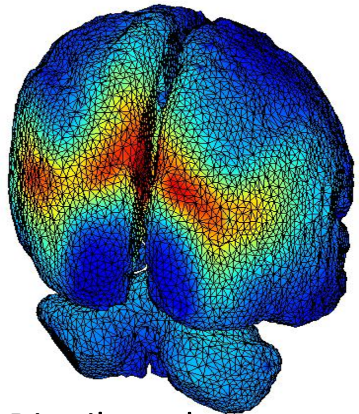
- 1^{st} level analysis

Localization of brain regions participating in a certain cognitive process

(Regions of interest/activations)



Dipole sources



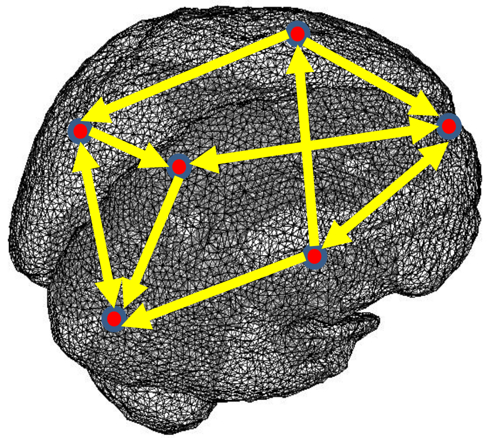
Distributed sources

EEG

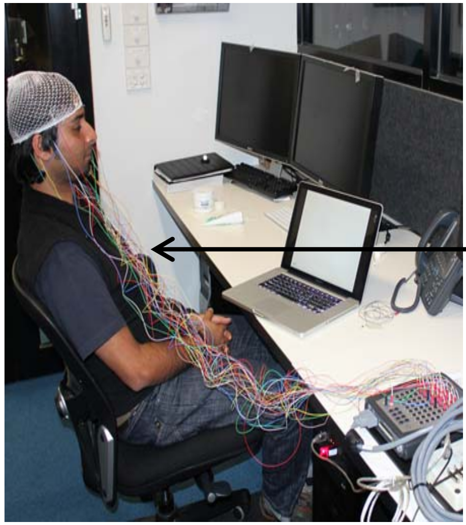
- A mixture signal acquired through scalp mounted electrodes
- Measures brain's electrical activity at the synapses

- 2^{nd} level analysis

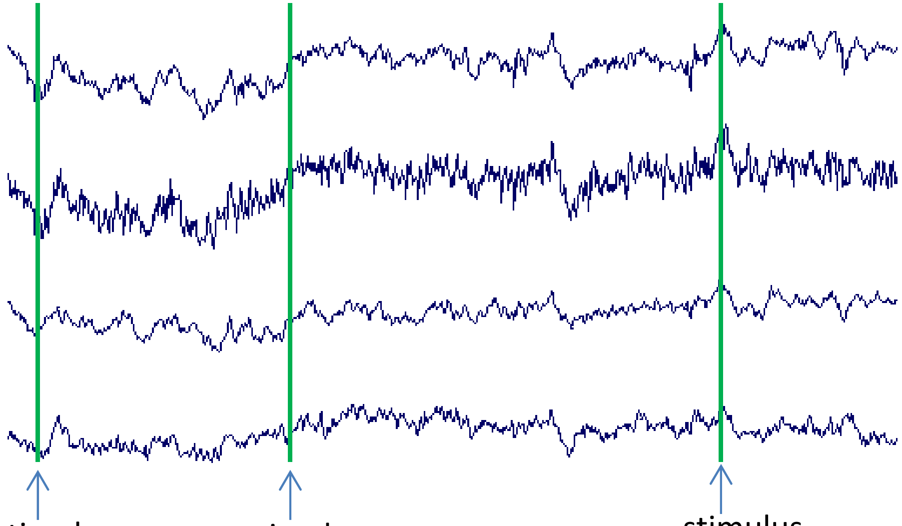
Functional integration of the brain areas (a.k.a effective connectivity or information flow)



Event Related Potential (ERP) Technique



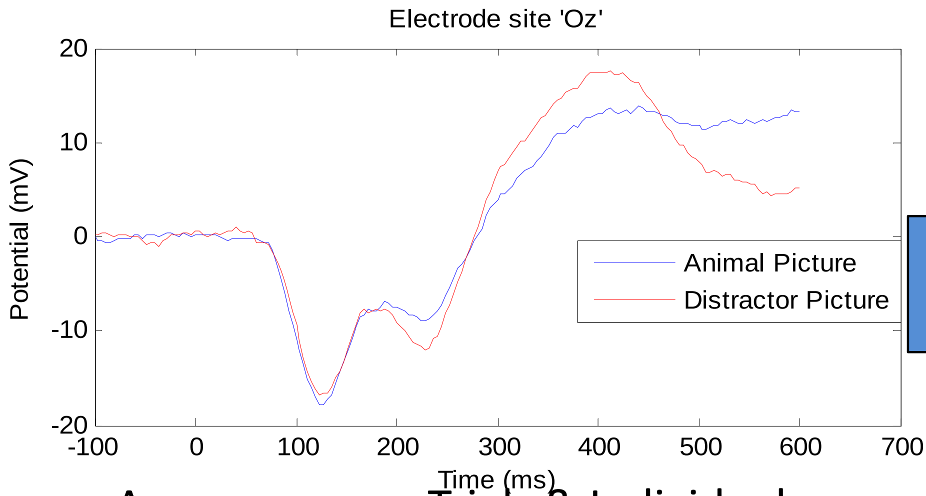
Raw EEG



Visual categorisation task data set for animal/distractor pictures - ***Delorme et al., 2002***

Pre-processing of the raw data

- Re-reference
- High-pass/Low-pass filter data
- Reject continuous data
- Epoch data w.r.t. stimulus
- (eg:-1000ms to 2000ms)
- Reject artifactual epochs



ERP

Average across Trials & Individuals to obtain a "Grand average"

DEAKIN UNIVERSITY AUSTRALIA Worldly

CISR

ERPs

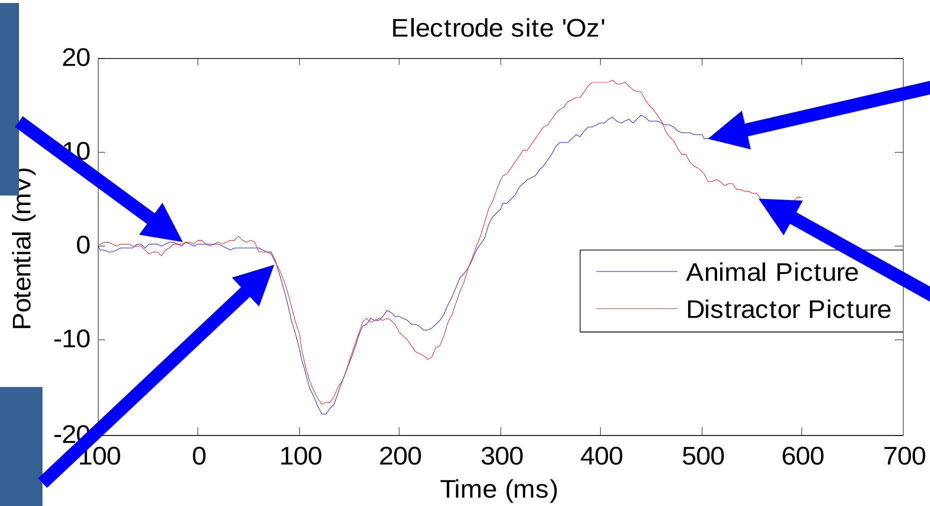
ERPs are the,

Electrical potentials associated with specific sensory, motor perceptual, or cognitive events

From EEG to ERP…

– Time-locked average of EEG from many trials involving same 'event'. This results in increasing the signal/noise ratio.

Stimulus presented
Time locked to this
'event' time = '0'



Condition 1 :
Animal Picture

Condition 2 :
Distractor Picture

During early visual
processing both
waveforms overlap

Visual categorisation task data set for animal/distractor pictures - ***Delorme et al., 2002***

Effective Connectivity

- Functional Connectivity is the correlation between two brain regions. No information on the causal interaction.
- Effective Connectivity is the directional influence one brain region can have on the other.
- Popular analysis tools are;
  1. Dynamic Causal Modeling (DCM)
     - Use physiologically inspired models
  2. Granger causality Modeling (GCM)
     - Data driven method

Dynamic Causal Modeling (DCM)

DCM framework consists of a general model that described the neuronal coupling of brain regions.

- A single brain region is represented by neural mass models
- deterministic state-space model stated in terms of ordinary differential equations.
- Variational Bayesian approach to estimate the parameters of the model

Advantage :both extrinsic and intrinsic anatomic connections, those between and within cortical regions, can be parameterized explicitly.

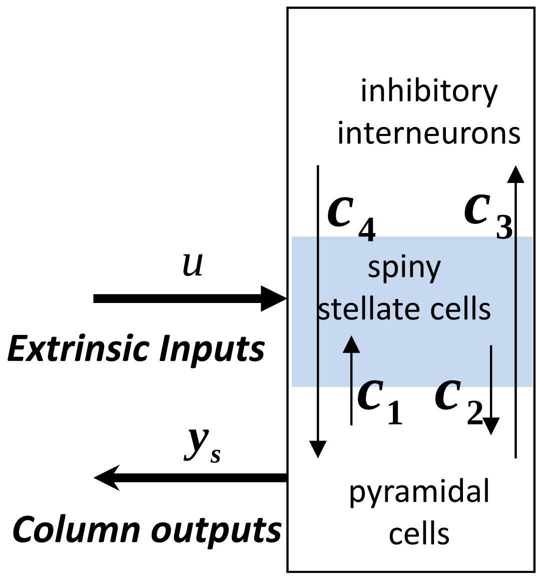
Drawback: *apriori* knowledge on the network structure required

Source model in DCM

Source: cortical mini-column organisation based neural mass models

A column representation of the source is modelled by three neuronal subpopulations,

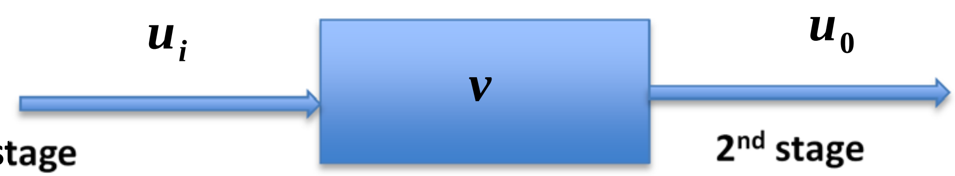
1. Excitatory pyramidal cells : receives inhibitory feedback from the local interneuron and excitatory input from the spiny stellate cells
2. Spiny stellate cells: receives extrinsic inputs and excitatory inputs from pyramidal cells
3. Inhibitory interneuron



c_{1-4} : ***Intrinsic connectivity constants***

Jansen & Rit, Biol. Cybern., 1995

Each of the neuron populations is modeled at two stages.



1st stage

Transforms the average pulse density of presynaptic input u_i into an average postsynaptic membrane potential (v) which can be either excitatory or inhibitory. This is a linear transformation with an impulse response given by,

$$v = h \otimes u_i$$

$$h = \frac{H_{e,i}}{\tau_{e,i}} t e^{\left(-t/\tau_{e,i}\right)}$$

2nd stage

Transforms the average membrane potential of a neural population into an average ring rate through a nonlinear transformation described by a sigmoid function

$$u_0 = S(v) = \frac{2e_0}{1+e^{-rv}} - e_0$$

David et al., 2005

Source model in DCM contd.

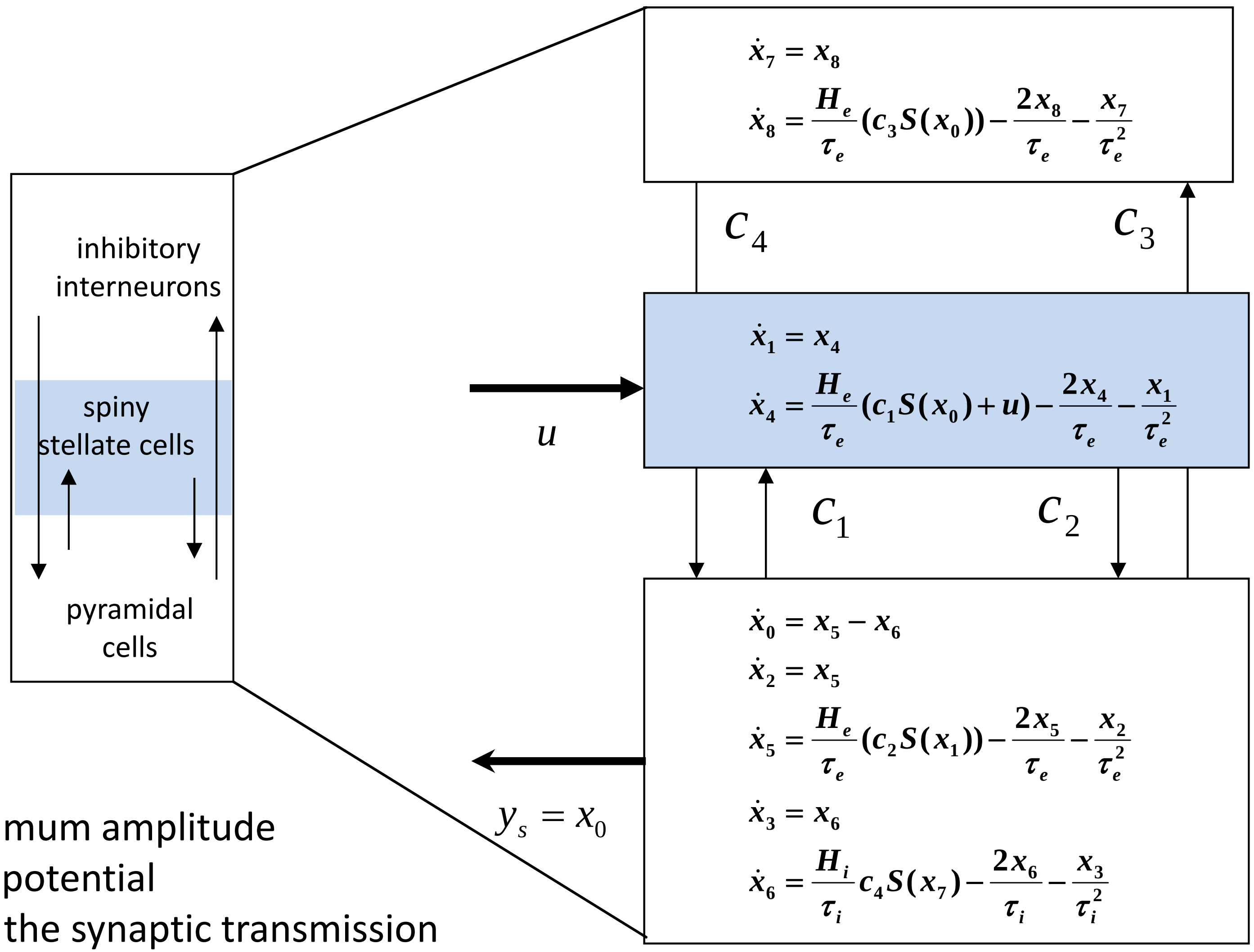
$$v = h \otimes u_i$$

$$h = \frac{H_{e,i}}{\tau_{e,i}} t e^{\left(-t/\tau_{e,i}\right)}$$

State space model

$$\dot{v} = x;$$

$$\dot{x} = \frac{H_{e,i}}{\tau_{e,i}} u_i - \frac{2x}{\tau} - \frac{v}{\tau^2}$$

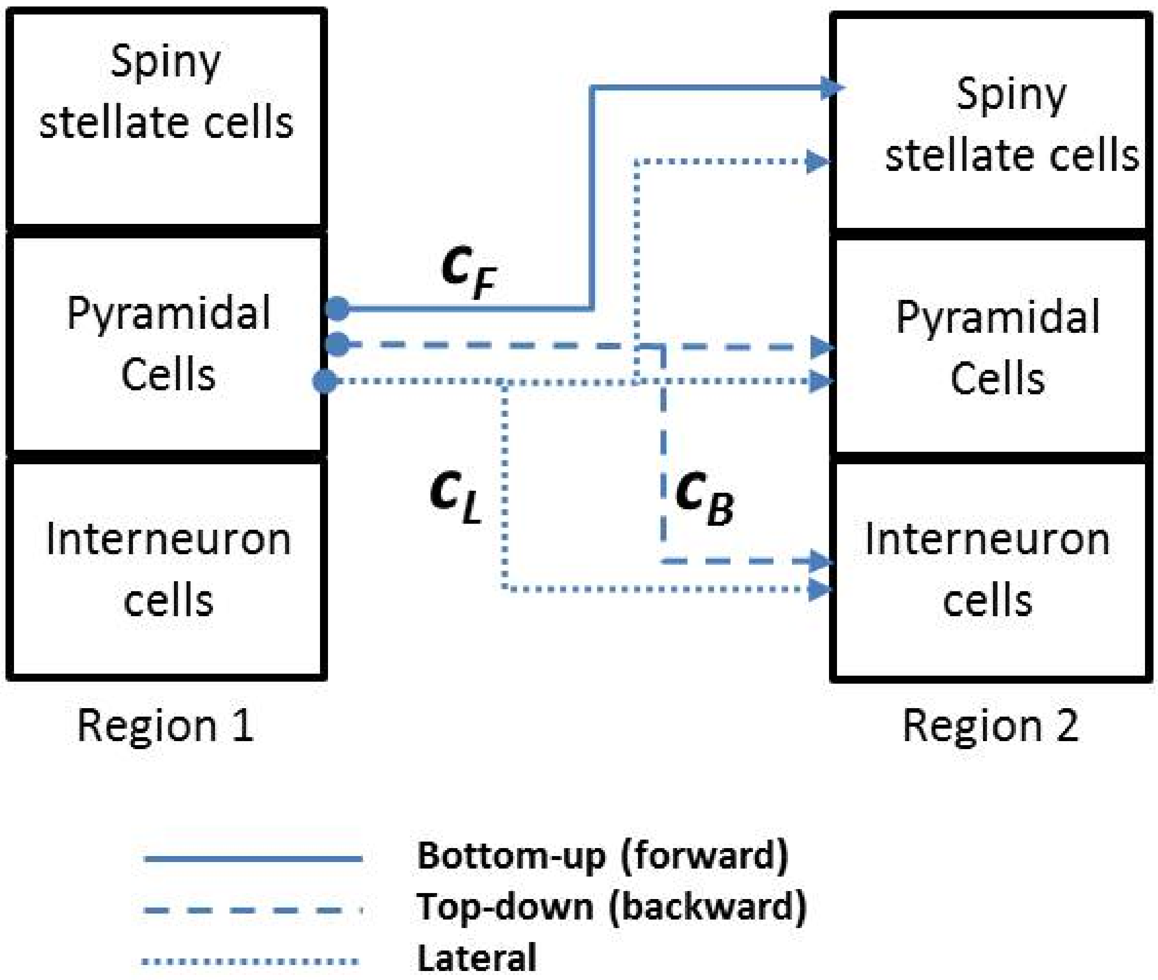


$H_{e,i}$ - determines the maximum amplitude of the post synaptic potential

$\tau_{e,i}$ - Determines delay of the synaptic transmission

e,i - denotes excitatory and inhibitory respectively

Connectivity Rules used in DCM

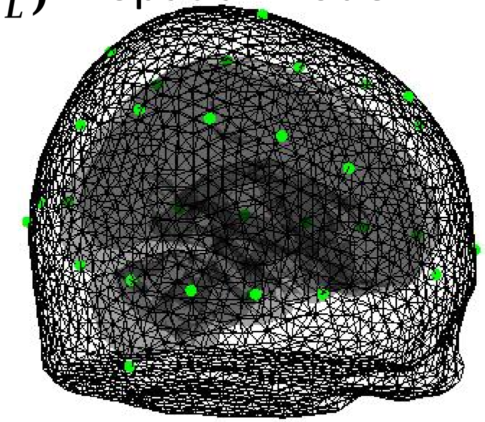


Felleman & Van Essen, Cereb. Cortex, 1991
David et al., NeuroImage, 2003

DCM :Estimation of model parameters

The generative forward model can be represented as;

$L(\theta_L)$ Spatial model



$$\dot{x}(t) = f(x, u, \theta)$$

$$y = L(\theta_L)x_0 = g(x, \theta)$$

Bayesian estimation

$$p(\theta \mid y) \propto p(y \mid \theta)\, p(\theta)$$

Likelihood:
- Source model
- Spatial forward model

$p(y \mid \theta)$ $p(\theta)$

Priors on:
- Extrinsic/intrinsic connectivity parameters
- Parameters of source dynamics $(H_{e,i}, \tau_{e,i})$
- Conduction delays
- Input parameters

The differences in ERPs can be explained by the modulation to connectivity in the DCM

Kiebel et al., 2008

Granger Causality Modeling (GCM)

- Based on the Grangers principle that knowledge of the drivers time series at a time should improve the prediction of the receivers time series at a later time (*Granger, 1969)*
- GC-based effective connectivity analysis is formulated through Multivariate Autoregressive (MVAR) modeling of time-series data. For k time-series the MVAR model can be given as,

$$Y(n) = \sum_{i=1}^{P} A_r(i)Y(n-i) + E(n)$$

Where,

- $n = 1, 2, \ldots, L$ denotes a time point
- P is the model order
- $Y(n) = [y_1(n), \ldots, y_k(n)]^T$ y_j denotes the j^{th} *signal source*
- $A_r(i) = \begin{bmatrix} a_{11}(i) & \cdots & a_{1k}(i) \\ \vdots & \ddots & \vdots \\ a_{k1}(i) & \cdots & a_{kk}(i) \end{bmatrix}$ is the model coefficient matrix at lag i
- $E(n) = [e_1(n), \ldots, e_k(n)]^T$ is a zero mean white noise input with covariance $\sum_E$
- Sationarity and Stability are assumed when using MVAR models.
- Due to EEG data being Non-stationary adaptive estimation of autoregressive parameters is required.

Frequency domain MVAR measures

Frequency Domain Representation of the MVAR model ,

$$Y(f) = A^{-1}(f)E(f)$$

$$Y(f) = H(f)E(f)$$

Where,

$$A(f) = \left[I - \underbrace{\sum_{k=1}^{P} e^{-i2\pi fk} A_r(k)}_{\text{Fourier transform of the MVAR coefficients}} \right]$$

is the inverse transfer matrix.

Based on MVAR model there are many time-domain and frequency domain measures developed for effective connectivity estimation such as,

Partial Directed Coherence (PDC)

$$PDC_{ij}(f) = \frac{A_{ij}(f)}{\sqrt{\sum_{m=1}^{k} |A_{mj}(f)|^2}}$$

Baccala & Sameshima, 2001

Directed Transfer Function(DTF)

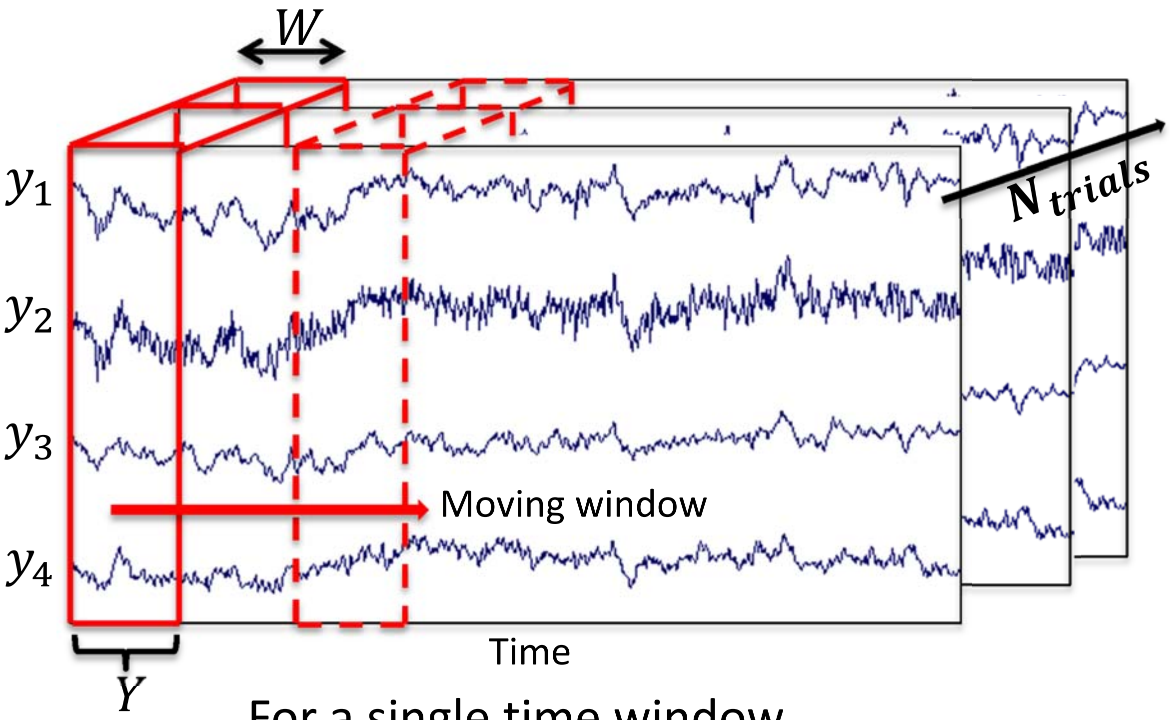
$$DTF_{ij}(f) = \frac{|H_{ij}(f)|}{\sqrt{\sum_{m=1}^{k} |H_{im}(f)|^2}}$$

Kaminski & Blinowska, 1991

Time-varying MVAR estimation

1. Short time window-based (STW) approach

The entire signal is divided into short overlapping time intervals using a Hamming window.



For a single time window,

$$Y(n) = \sum_{i=1}^{P} A_r(i)Y(n-i) + E(n)$$

- For $n = 1, \dots, n_w$ windows the estimation will result in n_w number of, $\{A_r(i)\}_{i=1 \dots P}$ model coefficient matrices.
- Connectivity measures are calculated for each window which naturally results in a time varying connectivity estimation a.k.a. Information flow
- Results are interpreted through time-frequency plots showing the information flow for each channel/source combinations

Time-varying MVAR estimation contd.

2. Adaptive Kalman Filtering

The MVAR model is represented by a state space formulation. MVAR matrix parameters are re-arranged into a state vector of the dynamical system. Subsequently a linear Adaptive Kalman filter is utilised to estimate the parameter vector.

$$a(n) = a(n-1) + V(n)$$

$$Y(n) = C(n)a(n) + E(n)$$

Where,

- $v(n)$ is the state noise, a multivariate Gaussian with zero mean and covariance $\sum_v$.
- $a(n) = \begin{pmatrix} vec[A_r^T\,(1,n)]^T \\ \vdots \\ vec[A_r^T\,(P,n)]^T \end{pmatrix}$ is the concatenation of vectorised $\{A_r(i,n)\}_{i=1}^{P}$
- $C(n) = I_k \otimes \begin{bmatrix} Y^T(n-1) \\ \vdots \\ Y^T(n-P) \end{bmatrix}$ is the concatenated matrix of past measurements, $\otimes$ is the kronecker-product and I_k is the $(k \times k)$ identity matrix.

Extended MVAR (eMVAR) Modeling

- MVAR modeling consider only time-lagged effect in regression
- In the presence of instantaneous communication or zero lag effects between sources the conventional MVAR will not capture them.
- These correlations will be accounted in a non-diagonal covariance matrix of the $\sum_E$ MVAR fitting residuals
- With a correlated noise structure in the MVAR residuals the frequency domain connectivity measures will be inaccurate giving spurious connections.
- So we use an eMVAR,

$$Y(n) = \sum_{i=0}^{P} B_r(i,n)Y(n-i) + W(n)$$

Erlaa et al., 2009
Faes et al., 2010

Where,

- $B_r(i,n)$ is the model coefficient matrix at lag i at time point n.
- $\mathrm{W}(n) = [w(n), \ldots, w_k(n)]^T$ is a zero mean white noise input with covariance $\sum_w$.
- However the estimation is non trivial due to the B_r (0) matrix, with instantaneous connections.

Relationship between MVAR and eMVAR

The eMVAR model can be rearranged as,

$$Y(n) = B_r(0,n)Y(n) + \sum_{i=1}^{P} B_r(i,n)Y(n-i) + W(n)$$

$$Y(n) = [I - B_r(0,n)]^{-1} \sum_{i=1}^{P} B_r(i,n)Y(n-i) + [I - B_r(0,t)]^{-1} W(n)$$

If, $L = [I - B_r(0,n)]^{-1}$ then,

$$A_r(i,n) = LB_r(i,n)$$

$$\Sigma_E = L\,\Sigma_W\, L$$

If $B_r(i,n) = 0$ i.e. no instantaneous connections present in the data $L = I$

eMVAR model can be regarded as a generalised model for Granger Causality-based connectivity analysis

Connectivity measures-based on eMVAR

Frequency domain representation of the eMVAR model,

$$B_r(f) = B_r(0) + \sum_{m=1}^{P} B_r(m) exp(-2\pi i m f)$$

Erlaa et al., 2009
Faes et al., 2010

$$B(f) = [I - B_r(f)]$$

Extended PDC (ePDC),

$$ePDC_{j\to i}(f) = \frac{\frac{1}{\sigma_i} B_{ij}(f)}{\sum_{m=1}^{k} \frac{1}{\sigma_m^2} |B_{mj}(f)|^2}$$

Instantaneous

+

Lagged causality

Instantaneous PDC (iPDC),

$$\bar{B}(f) = \left[I - \sum_{m=1}^{P} B_r(m) exp(-2\pi i m f) \right]$$

$$iPDC_{j\to i}(f) = \frac{\frac{1}{\sigma_i} \bar{B}_{ij}(f)}{\sum_{m=1}^{k} \frac{1}{\sigma_m^2} |\bar{B}_{mj}(f)|^2}$$

Lagged causality only

STW- based eMVAR identification

1. Fit the MVAR model to data and calculate the coefficient matrices A_r and $\sum_E$.
2. Since $\sum_w$ is a diagonal matrix, apply a Cholesky decomposition to $\sum_E$ to obtain L, using $\sum_E = L \sum_w L$.
3. Estimate B_r *(0,t)* and B_r *(i,t)* using,

$$L = [I - B_r(0,t)]^{-1}$$
$$A_r(i,t) = LB_r(i,t)$$

4. Due to the Cholesky decomposition B_r *(0,t)* is a lower diagonal matrix with null diagonal. i.e. Instantaneous connections are constrained from i to j for i<j only

Identiability issues of the eMVAR model can be overcome through a constrained instantaneous transfer path specification via temporal ordering of the multivariate time-series.

Kalman filtering for eMVAR identification

Temporal ordering can be determined using,

- *apriori* knowledge of the measured time-series
- non-gaussianity of the MVAR model residuals (*Hyvärinen et al., 2008)*

The state space formulation for the eMVAR model can be given as,

$$x(n) = x(n-1) + \bar{v}(n)$$

$$Y(n) = G(n)x(n) + W(n)$$

Constrained by, $Dx(n) = d$

Where,

- $\bar{v}(n)$ is the state noise, a multivariate Gaussian with zero mean and covariance $\sum_{\bar{v}}$.
- $x(n) = \begin{pmatrix} vec[B_r^T\ (0,n)]^T \\ \vdots \\ vec[B_r^T\ (P,n)]^T \end{pmatrix}$ is the concatenation of vectorised $\{B_r(i,n)\}_{i=0}^{P}$
- $G(n) = I_k \otimes \begin{bmatrix} Y^T(n) \\ \vdots \\ Y^T(n-P) \end{bmatrix}$ is the concatenated matrix of past measurements, $\otimes$ is the kronecker-product and I_k is the $(k \times k)$ identity matrix.

Constrained Adaptive Kalman Filtering

Hettiarachchi, Imali T., Mohamed, Shady, Nyhof, Luke and Nahavandi, Saeid, "An extended multivariate autoregressive framework for EEG-based information flow analysis of a brain network", In Proceedings of the 35th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC 2013), pp. 3945-3948, 2013.

- Time Update

$$\begin{aligned} \hat{x}(n|n-1) &= \tilde{x}(n-1|n-1) \\ P(n|n-1) &= P(n-1|n-1) + \Sigma_V(n) \\ \tilde{Y}(n) &= Y(n) - C(n)\hat{x}(n|n-1) \end{aligned}$$

apriori state estimate

Estimation error covariance

Measurement residual

- Measurement Update

$$\begin{aligned} \Sigma_E(n) &= \alpha\Sigma_E(n-1) + (1-\alpha)\tilde{Y}\tilde{Y}^T \\ S(n) &= C(n)P(n|n-1)C(n)^T \\ &\quad +\Sigma_E(n) \\ K(n) &= P(n|n-1)C(n)^T S(n)^{-1} \\ \hat{x}(n|n) &= \hat{x}(n|n-1) + K(n)\tilde{Y}(n) \\ \tilde{x}(n|n) &= \hat{x}(n|n) - P(n|n)D^T \\ &\quad (DP(n|n)D^T)^{-1} \\ &\quad .D\hat{x}(n|n) \\ P(n|n) &= [I - K(n)C(n)]P(n|n-1) \\ \Sigma_V(n) &= I(1-\alpha)trace(P(n|n))/P \end{aligned}$$

Residual covariance matrix

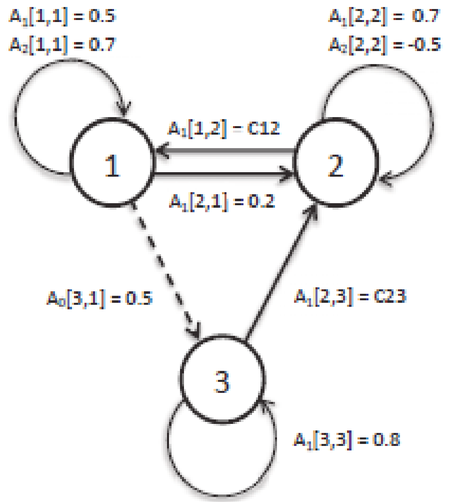
Kalman gain

Unconstrained filter est.

Constrained filter est.

aposteriori est. Error cov.

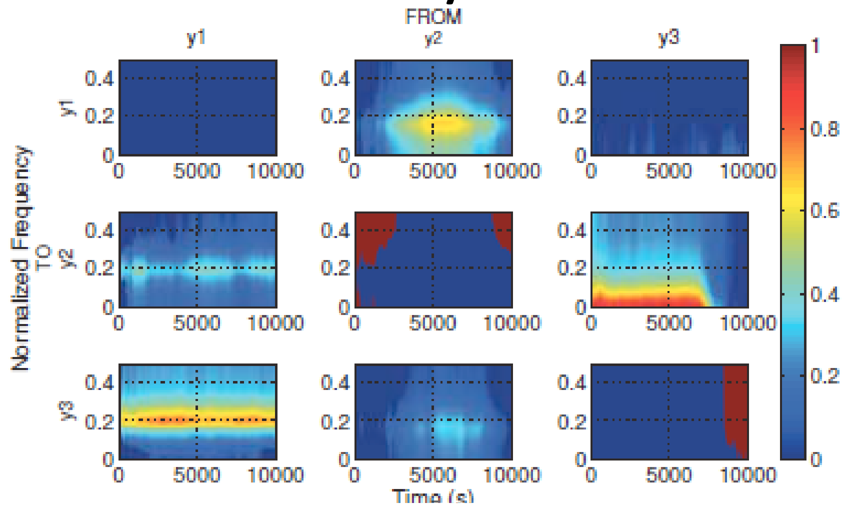
Simulations with zero lag connectivity



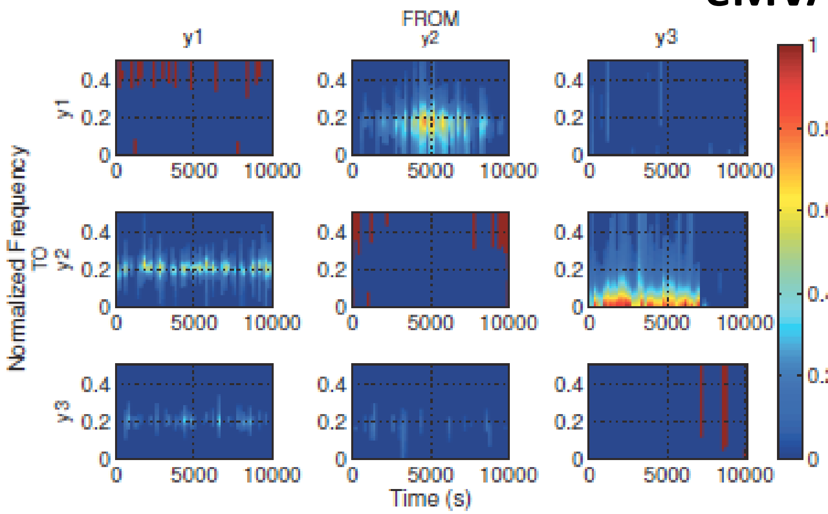
$$c_{12}(n) = \begin{cases} n/L & n \leq L/2 \\ (L-n)/L & n > L/2 \end{cases}$$

$$c_{23}(n) = \begin{cases} 0.4 & n \leq 0.7L \\ 0 & n > 0.7L \end{cases}$$

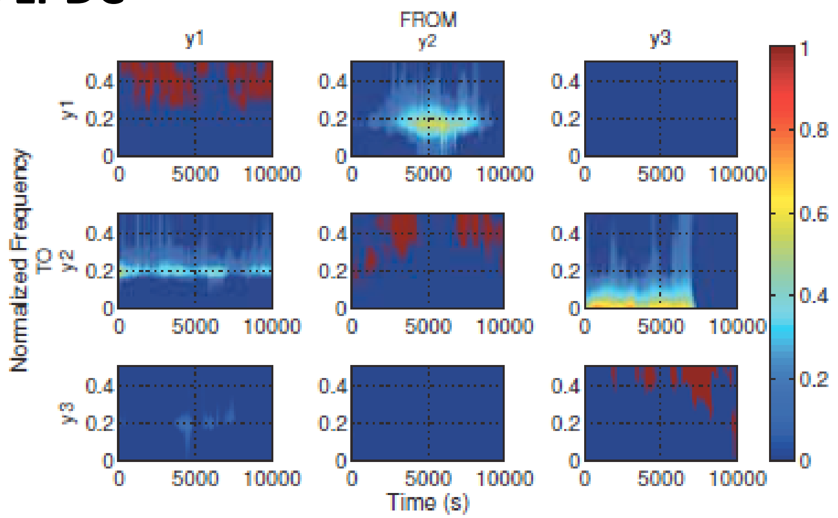
MVAR/PDC



eMVAR/LPDC



Short time windowing

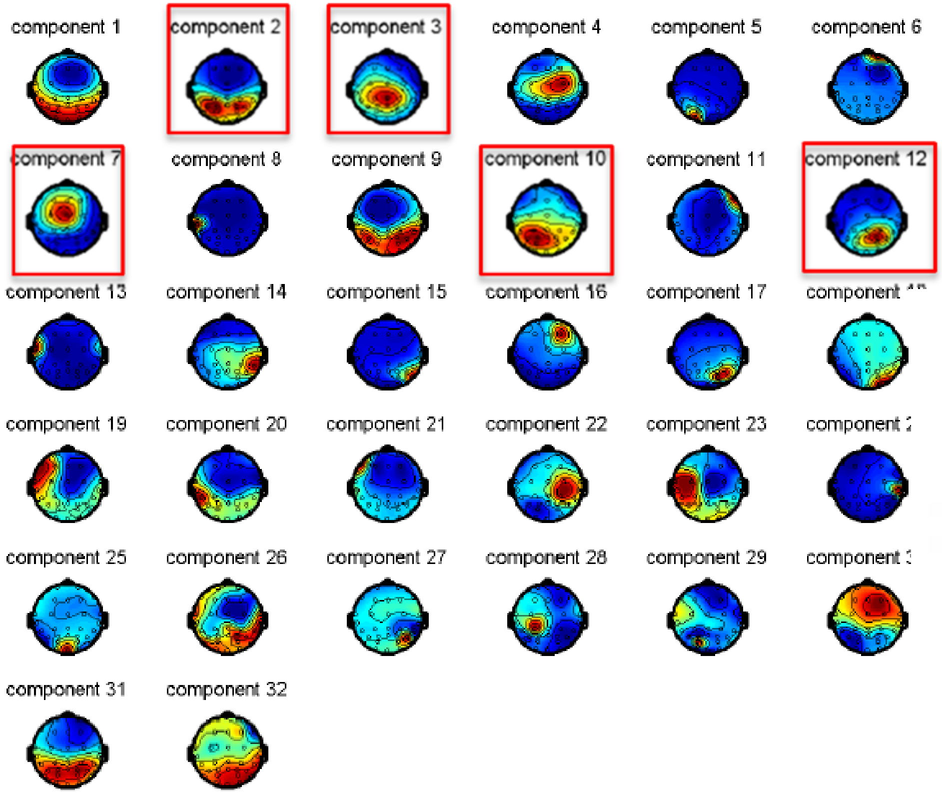


Constrained Adaptive Kalman Filter

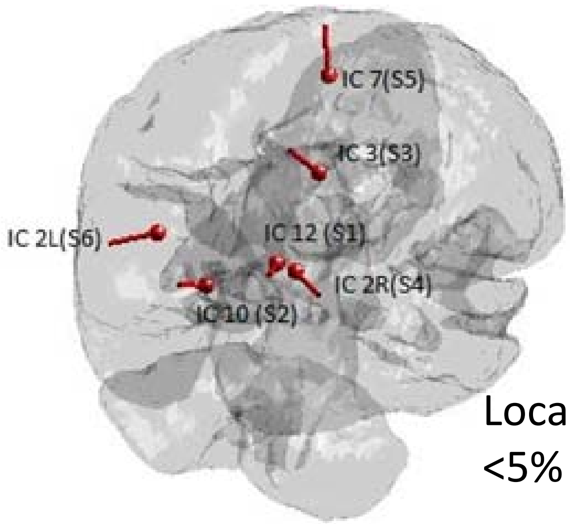
Information flow analysis using real data

For the demonstration purposes a visual categorisation task data set for animal/distractor pictures is used(***Delorme et al., 2002).*** A single subject results for the ‘animal’ stimulus is presented here.

We use a two step approach in the source connectivity analysis.
STEP 1: Source Reconstruction and extraction of source signals
STEP 2: Connectivity analysis using MVAR/eMVAR modeling of the source time-series



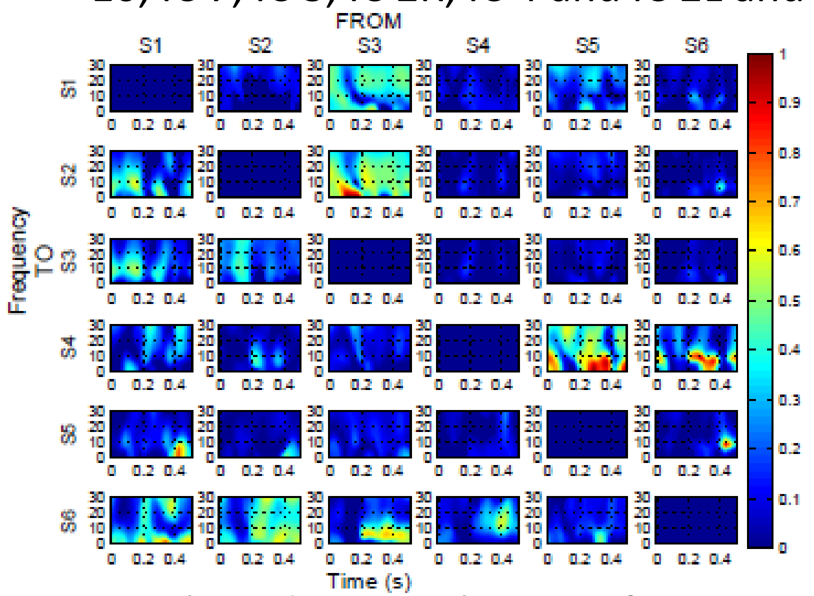
ICA algorithm decomposes the preprocessed multi-trial recordings to determine spatially fixed and temporally independent sources, contributing towards the VEP.



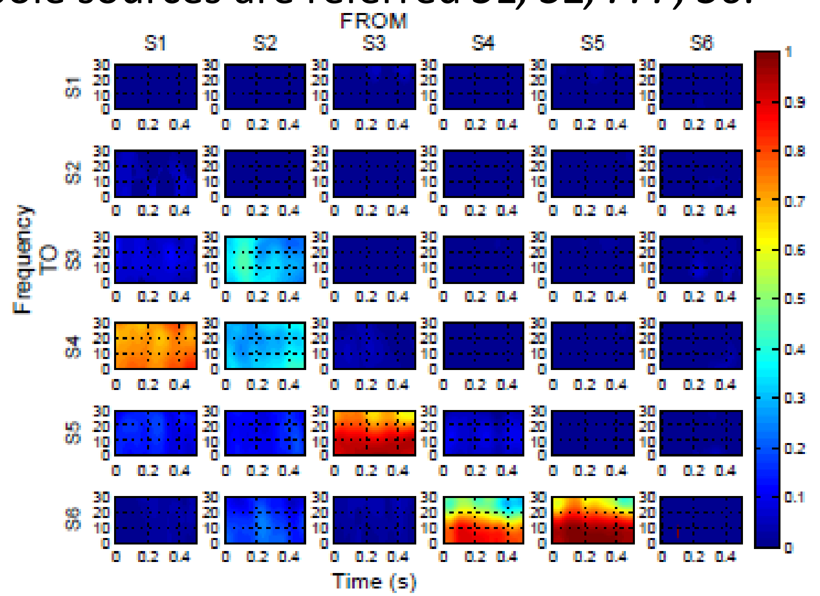
Localised dipole sources with <5% residual variance.

Information flow analysis using real data

- The temporal order in which the component dipoles are activated was determined as IC 12, IC 10, IC 7, IC 3, IC 2R, IC 4 and IC 2L and these dipole sources are referred *S*1, *S*2, . . . , *S*6.



MVAR-based PDC in the time-frequency representation



eMVAR-based LPDC in the time-frequency representation

- Significantly different information flow patterns observed.
- Only a few connectivities seen in PDC appear in LPDC . For instance *S*1 → *S*6 is no longer seen in LPDC, while the connectivity *S*1 → *S*4 is estimated very high in and LPDC, which is reasonable due to IC 2R and IC 12 are located spatially very close to each other .
- Preliminary results presented, which requires further validation

Conclusion

- Dynamic causal modeling and Granger causality modeling are two tools that can be used for the information flow analysis using ERP data.
- DCM contains physiologically meaningful parameters however requires *apriori* knowledge on the underlying connectivity structure for the estimations to be accurate.
- GCM uses a simple MVAR model parameterised only by its model order. Used in many ERP studies during the past years and found wide acceptance.
- We use the eMVAR model as a generalised model for Granger causality-based connectivity analysis.
- We have proposed a novel constrained adaptive Kalman filter framework for the eMVAR identification which performs better than the existing STW-approach.

Question Time

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