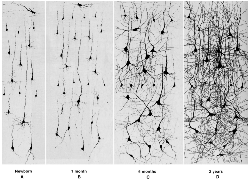
Problem 4: Bounds in the variability of brain coordinated activity in health and disease

August 20, 2010


Newborn
A
1 month
B
6 months
C
2 years
D

Techniques

- Statistical Analysis of Channel Time Series
  - Singular-Value Decomposition
  - Diagnostic of markers via cross-correlation
  - Complex Coherence
- Mathematical Modeling
  - Spatio-Temporal Model features

Singular Value Decomposition

- The singular values along the diagonal in D are ordered.

$$\lambda_1 \geq \lambda_2 \geq \cdots \geq \lambda_p$$

- If the singular values are of the same order then the columns of X are likely to be uncorrelated.
- If a few singular values dominate then most of the variation among the columns of X can be explained by the first few principal components.

Are time series $x_i(t), x_j(t)$ correlated?

Define *cross-variance and cross-correlation*

$$\sigma_{ij}(\tau) := \frac{1}{N-1}\sum_{t=1}^{N}(x_i(t-\tau)-\mu_i)(x_j(t)-\mu_j) \tag{1}$$

$$r_{ij}(\tau) := \frac{\sigma_{ij}(\tau)}{\sqrt{\sigma_{ii}(0)\sigma_{jj}(0)}} \tag{2}$$

- Compute correlation coefficients $r_{ij}(0)$, check for statistical significance.

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$$P_{ij}(\omega) := \sum_{n=-\infty}^{\infty} \sigma_{ij}(n)\exp(\imath\omega n) = \mathcal{F}(x_i)(\omega)\overline{\mathcal{F}(x_j)}(\omega)$$

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- Mean-squared coherance

$$R_{ij}(\omega) := \frac{P_{ij}(\omega)}{\sqrt{P_{ii}(\omega)P_{jj}(\omega)}}$$

Statistical Analysis: Diagnostic via cross-correlation

- Cross-correlation: correlation of series x_t and y_{t-l}
- Measure of synchrony between series (time-domain)
- Computed mean, min, max cross-correlation in a sample of known healthy (n=6) & unhealthy patients (n=7)
- This allowed us to compare the variability in category

Reuslts of Cross-Correlation Analysis

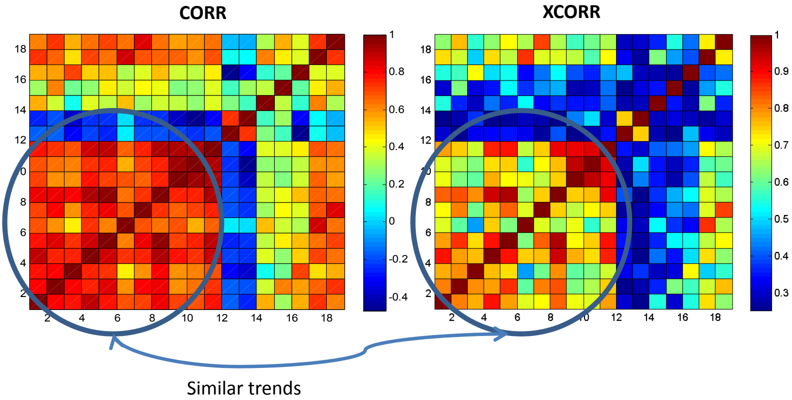
- Mean Channel Correlation:
    - Normal: 0.14
    - Traumatic Brain Injury: 0.17
- Fairly similar, which does not confirm our intuition. (TBI specific?)
- Variable over subsets

Correlations and Cross-Correlations

- Correlations calculated between all pairs of channels via Matlab's CORR function.
- Cross-correlations calculated between all pairs of channels via Matlab's XCORR function.
- Results were not identical but showed similar trends.
- Matlab's pcolor is a good way to quickly visualize results.

Correlations and Cross-Correlations

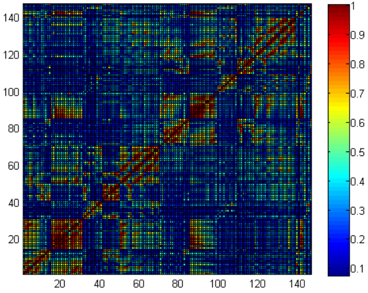
Hyperventilation Data – 19 channel EEG:
Corr and Xcorr show similarities in trends.



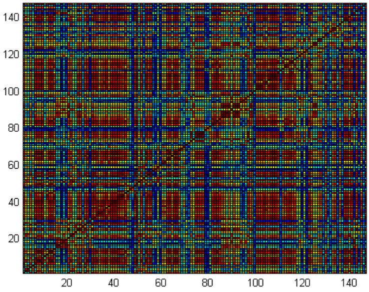
Cross-Correlations

Cross correlation is affected by window size and choice.

MEG data – normal subject : 147 channel cross-correlations via matlab



5 minute window



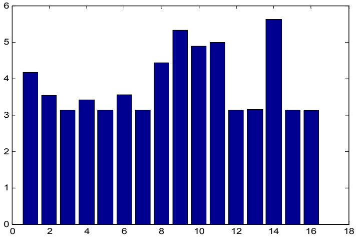
First 1.25 minutes of same data

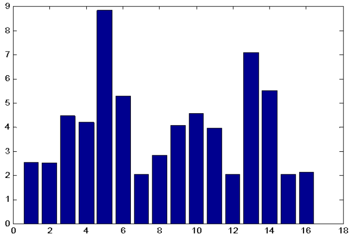
Spectral Analysis

- Distributions of energies over channels not equal
- Energy distributions over channels can change, even for same condition (e.g. sleep)

Sleep EEG data – sampled at 250Hz, 16 channels.

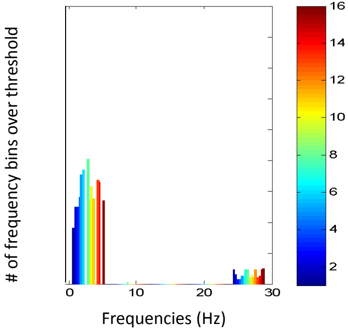
Energy per channel (sum of squared FFT amplitudes over all frequencies)





Spectral Analysis

- FFTs show definite spikes at certain frequencies
- For sleep data, frequency content below 5Hz and at $\approx$ 29 Hz.
- Did not investigate for enough conditions or signals but observations are that the spikes in frequencies at each channel should be investigated.



16 Channel sleep data

Comparing channels

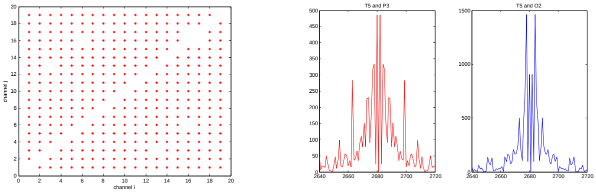


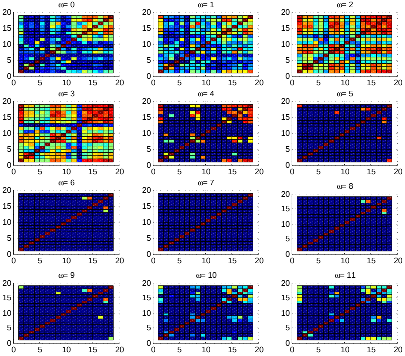
Figure: L: Statistically significant correlation. R: Cross spectral density, (T5+P3) and (T5+O2).

Windowing time series and then comparing

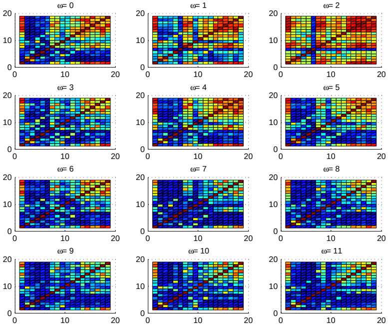
Select sub-intervals in time, and compute measures of correlation per window. Compare over all windows.

Measuring correlation: data segmented in time

Hyperventilation data

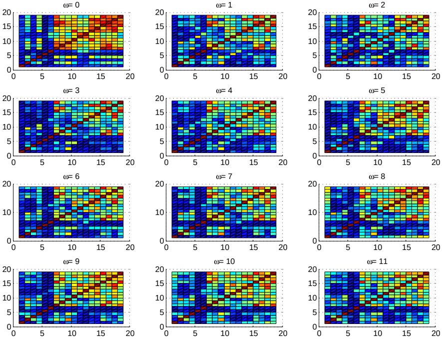


Hyperventilation data: 30 s



Hyperventilation data: end of experiment

Select sub-intervals in time, and compute measures of correlation per window. Compare over all windows.



Spatio-temporal mean field theory of cortical activity

Liley, Cadusch et al [2001] propose a PDE model for electrocortical activity.

- "Spatially averaged neuron": averages neurons over small regions;
- Model mean soma membrane potentials for excitory and inhibitory neurons, h_e, h_i;
- h_e is directly measurable using EEG;
- Synaptic activity between e, i neurons part of model;
- Includes short and long range cortical connectivity;
- Model includes wave equation for cortical connectivity, allowing for pattern formation;

"Patch" of cortex

van Veen, D.Liley et al [2006] simplified full PDE model for electrocortical activity to 1 local patch:

- h_e, h_i = excitory and inhibitory potentials;
- $I_{k,l}$ where $k, l = i, e$ denote feedback/feedforward synaptic activity, modeled as critically damped oscillators
- 4 second-order ODE for synaptic activities, 2 first-order ODE for potentials.

Prototypical equations:

$$\tau_e \frac{d}{dt} h_e = \underbrace{h_{er} - h_e}_{\text{deviation from resting potential}} - C_1 h_e I_{ee} - C_2 h_e I_{ie} \tag{3}$$

$$\frac{d^2}{dt^2} I_{ee} + C_3 \frac{d}{dt} I_{ee} + C_4 I_{ee} = C_5 [N_{ee} \underbrace{S_e(h_e)}_{\text{mean firing rate}} + p_{ee}] \tag{4}$$

Here p_{ee} is excitatory input from distant cortical neurons. van Veen et al perform bifurcation analysis to predict chaos, with p_{ee}

Rudimentary model for workshop

- Take two "spatially averaged neurons" at a distance d, with strength of connection ϵ;
- Connect them by setting excitatory input for neuron 1 $p_{ee} = \epsilon I_{ee}/d$ from neuron 2 and vice-versa
- Assess behaviour of h_e for both neurons as ϵ varies.

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Prototypical equations (similar for $h_i, I_{ie}, I_{ei}, I_{ii}$)

$$\tau_e \frac{d}{dt} h_e = \underbrace{h_{er} - h_e}_{\textit{deviation from resting potential}} \quad -(1 - C_1)h_e I_{ee} - (1 \tag{5}$$

$$\frac{d^2}{dt^2} I_{ee} + C_3 \frac{d}{dt} I_{ee} + C_4 I_{ee} = C_5 [N_{ee} \quad \underbrace{S_e(h_e)}_{\textit{mean firing rate}} \quad + {\color{red}p_{ee}}] \tag{6}$$

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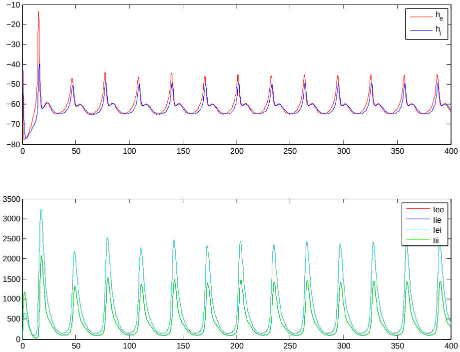
Rudimentary model for workshop

- Take two "spatially averaged neurons" at a distance d, with strength of connection ϵ;
- Connect them by setting excitatory input for neuron 1 $p_{ee} = \epsilon \mathit{interactionterm}/d$ from neuron 2 and vice-versa
- Assess behaviour of h_e for both neurons as nature of coupling or ϵ varies.

Single space-averaged neuron

membrane potentials in mV, synaptic activities in bottom



Coupling of neurons

Types of coupling tried:

- Both neurons are identical, and experience the same interaction terms;
- The neurons are not identical, and experience a different immediate neighbourhood;
- The effect of the neurons on each other is felt through a distributed delay.

Identical coupled neurons

$$long - range\ forcing\ term\ p_{ee,1} \longrightarrow \epsilon_e I_{ee,2}$$
$$long - range\ forcing\ term\ p_{ee,1} \longrightarrow \epsilon_i I_{ee,2}$$

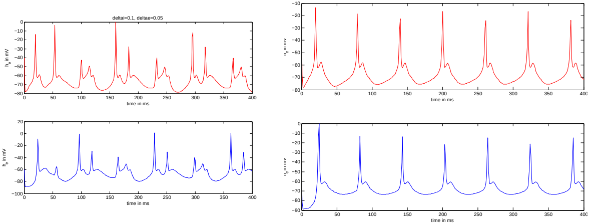


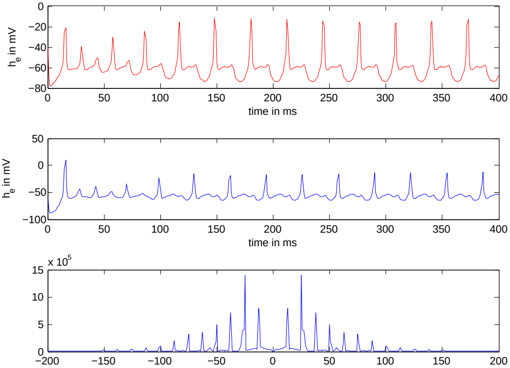
Figure: L: different inhibitory ϵ_e and excitory interaction ϵ_i; R: weaker interaction (magnitudes)

Distinct coupled neurons

Neighbourhood influence on neurons is different:

$$p_{ee,1} \longrightarrow p_{ee,1} + \epsilon_1 I_{ee,2}$$

etc. Top: excitory membrane potentials. Bottom: cross-spectral density of the time series.

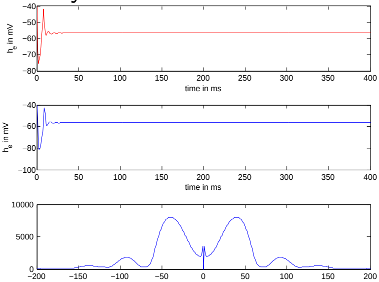


Coupling via delay

$$\frac{d^2}{dt^2} I_{ee} + C_3 \frac{d}{dt} I_{ee} + C_4 I_{ee} = C_5 [N_{ee} \underbrace{S_e(h_e)}_{\text{mean firing rate}} + p_{ee}]$$

$$+ C_6 \underbrace{S_e(h_{e,2}(t-\tau))}_{\text{mean firing rate of ,neuron2 delayed}}$$

B: cross-spectral density of the time series.



Future work

- Determine physiologically reasonable parameter values for 2-"neuron" coupling model with delay
- Simulate mean-field PDE model (developed for normal functioning), and add single disorder such as autism.
- Compare various statistical measures of EEG cross-channel correlation for robustness, sensitivity and specificity for diagnostic purposes.
- Feature selection to identify important channels and reduce dimensionality.
- Analysis by specific condition.