Granger causality analysis of steady-state EEG during propofol-induced anaesthesia

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What are the neural correlates of conscious level?

Theory suggests directed information flow between brain regions plays a key role in modulating conscious level:

- Edelman’s dynamic core hypothesis (1994)
- Tononi’s integrated information theory (2004, 2008)
- Seth’s causal density (2005, 2008)

However, measuring information flow is technically challenging even given relevant data.
**Contexts**

- With **real data** most studies compute simpler quantities, e.g. gamma power, synchrony.

- However these measures are not consistently reliable markers.

- When behavioural markers absent, still difficult to assess C. e.g. coma, anaesthesia.

- **Granger causality** is emerging as a promising, pragmatic measure of information flow.
  - Causal density inspired by this.
  - Granger techniques may help test Tononi’s $\Phi$.

In this talk:

• New thorough and rigorous Granger causality method for steady-state EEG.

• Application to data from propofol-induced anaesthesia.
Granger (G-)causality

Causality based on prediction:

How well does past of $Y$ help predict future of $X$?

(Over and above past of $X$ itself and past of the rest of the system.)

Prediction by linear regression.

Uses many past states as predictors.
**G-causality**

Full regression (X and Y):

\[ X_t = \sum_{i=1}^{p} a_i X_{t-i} + \sum_{i=1}^{p} b_i Y_{t-i} + \varepsilon_t \]

Restricted regression (just X):

\[ X_t = \sum_{i=1}^{p} c_i X_{t-i} + \varepsilon'_t \]

G-causality log-ratio of prediction errors (residuals):

\[ GC_{Y\rightarrow X} = \log \frac{\text{var}(\varepsilon')}{\text{var}(\varepsilon)} \]

**Useful note:** (i) Formula ensures invariance under overall increase in power.

(ii) In sample, \( GC > 0 \) always, and hence biased.

(iii) If have 3\(^{rd}\) variable, \( Z \), then include past of \( Z \) in both regressions.
**Frequency domain G-causality**

\[ GC_{Y \rightarrow X}(f) \]

Based on Fourier transform of full regression.

Roughly the proportion of power of X at frequency \( f \) that derives from interaction with Y.

Time domain GC is mean of \( GC(f) \) over all frequencies.
Application to EEG / Propofol

- Source localised hd-EEG recorded during waking and loss-of consciousness (LOC).
- Anterior cingulate (ACC) and posterior cingulate (PCC) cortices showed increased gamma activity.
- Several minutes of clean data from 7 subjects.

[Murphy et al 2011]
Methods

- Multiple source localized voxels from each region, kept mean time-series from each ROI.
- Filter out 50 Hz line noise.

40s sample from ACC during LOC

- Pick a **time-scale** for analysis: **Downsample** to 250 Hz.
- Choose segment length of 2s. This represents a trade off:
  - For **long segments** have problem of **non-stationarity**.
  - For **short segments** have **poor parameter estimates**.
Methods

For each segment:

- Look at model order recommended by Akaike Information Criterion (AIC).
- Took model order of 20 (80ms), which was 95\textsuperscript{th} percentile of AIC.
- Calculated GC in both directions at frequencies from 1-40Hz. Note we’re safe from line noise filtering artefacts at these frequencies. [Barnett & Seth submitted]

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[Matlab toolbox: Anil Seth]
Methods

Had at least 70 segments per condition per subject.

Problem: GC measurements are biased.

- To estimate bias, compute mean GC between 1000 randomized pairs of segments.

- Subtract off estimated bias from raw GC values.

(Do this process separately for each frequency band and direction and condition and subject.)
Results

- Increase in bidirectional G-causality during LOC.
- Increases most pronounced in beta/gamma bands.
- Increase more consistent across subjects than previously reported changes in gamma synchrony.

Plots of means

[Barrett, Seth et al, in preparation]
Results: Tables of significant changes

- Granger changes more consistent but harder to detect than synchrony changes.

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+: increase during LOC

+/−: significant at false discovery rate <0.01; (+/−) sig at FDR <0.05; [+/−] sig at p<0.05.

Under Wilcoxon rank sum test of distribution across segments after removing bias.

[Barrett, Seth et al, in preparation]
Conclusion 1: G-causality and Conscious Level

- Theory suggests mean G-causality (causal density) should decrease during LOC.
- However, this is applicable when considering several regions (not just 2), so increase here is not evidence against information integration theories of consciousness.
- Increase observed here could be from common thalamic input to both regions.
- We aim to extend our analysis to more regions, although sensitivity of method will decrease with number of regions (conditional G-causality, more parameters to fit).
Conclusion 2 - Summary

- **New method** for rigorously applying G-causality analysis to steady-state EEG data that
  - Systematically removes bias.
  - Deals with non-stationarity.

- **Significant** changes in G-causality are harder to detect than changes synchrony.

- **Inter-subject consistency of results** illustrate utility of G-causality in exposing functional neural interactions underlying different conscious levels.
Acknowledgments

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Collaborators:

**Analysis:** Sussex – Anil Seth, Lionel Barnett

**Data Collection:** Coma Science Group, Liège - Mélanie Boly, Steven Laureys, Pierre Boveroux, Quentin Noirhomme, Marie-Aurélie Bruno

**Data Processing:** Wisconsin – Mike Murphy, Giulio Tononi