SPECTRAL GRAPH MODEL OF BRAIN OSCILLATIONS:

A) Fitting to empirical fMRI and MEG
B) Dynamics and stability of model
C) Applications in neurological disease

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Declaration of Financial Interests or Relationships

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I have no financial interests or relationships to disclose with regard to the subject matter of this presentation.
MULTIMODAL INTEGRATION VIA NETWORKS

THE STRUCTURE-FUNCTION QUESTION

- **FC** = Statistical corr of signals from 2 regions
- Anatomic = structural connectivity (SC)
- The exact relationship between FC and anatomic connectivity is an unresolved, major question
- SC $\Rightarrow$ FC, but NOT vice versa
- Can math models predict FC, given SC?

Key ideas in this lecture:
1) Connectivity graph is an excellent medium for cross-modality integration
2) Need math/graph models rather than statistical associations
3) Simple, linear network models can capture SC-FC better than non-linear generative models
Mapping Human Whole-Brain Structural Networks with Diffusion MRI
Patric Hagmann, Maciej Kurant, Xavier Gigandet, Patrick Thiran, Van J. Wedeen, Reto Meuli, Jean-Philippe Thiran, PLoS ONE 2(7)
A LINEAR NETWORK DIFFUSION MODEL OF ACTIVITY SPREAD

• Between any two regions R1 and R2, the signal is $x_1(t)$ and $x_2(t)$

\[
\frac{dx_1(t)}{dt} = \beta \left( \frac{1}{V_1} c_{1,2} \frac{1}{\delta_2} V_2 x_2(t) - x_1(t) \right)
\]

• On whole brain

\[
\frac{dx(t)}{dt} = -\beta \mathcal{L} x(t),
\]

\[
\mathcal{L} = I - \Delta^{-1/2} C \Delta^{-1/2},
\]

\[
x(t) = \exp(-\beta \mathcal{L} t) x_0,
\]

\[
C_f(t_{crit}) = \exp(-\beta \mathcal{L} t_{crit}).
\]

SPECTRAL” GRAPH THEORY OF SC-FC

• SC and FC are related by graph spectra (eigens)

Abdelnour, Voss, Raj. NeuroImage 2014
Network Eigenmodes of the Structural Connectome

A Graph Signal Processing Perspective on Functional Brain Imaging

By Weiyu Huang, Thomas A. W. Bolton, Student Member IEEE John D. Medaglia, Danielle S. Bassett, Alejandro Ribeiro, and Dimitri Van De Ville, Senior Member IEEE

Human brain networks function in connectome-specific harmonic waves

Selen Atasoy, Isaac Donnelly & Joel Pearson

Nature Communications 7, Article number: 10340 (2016) | Download Citation

Functional brain connectivity is predictable from anatomic network's Laplacian eigen-structure

Farras Abdelnour, Michael Dayan, Orrin Devinsky, Thomas Thesen, Ashish Raj
Structural Eigenmodes and Resting State fMRI Networks


Abdelnour et al, Neuroimage (2018)


Atasoy et al., Neuroscientist
GRAPH EIGENMODES CAN SPARSELY REPRESENT FC

Atasoy, 2016

SPECTRAL GRAPH THEORIES OF FMRI AND FC


• Farras Abdelnour, Michael Dayan, Orrin Devinsky, Thomas Thesen, and Ashish Raj. Functional brain connectivity is predictable from anatomic network’s Laplacian eigen-structure. NeuroImage, 172:728–739, 2018

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INTRODUCING A “COMPLEX” LAPLACIAN

• Novel concept in brain graph theory

\[ \frac{dx_1(t)}{dt} = \beta \left( \frac{1}{V_1} c_{1,2} \frac{1}{\delta_2} V_2 x_2(t) - x_1(t) \right) \]

\[ t \rightarrow t - \tau_{1,2} \]

• Delays become phases in Fourier space: \( \mathcal{F}(x(t - \tau_{1,2})) = X(\omega)e^{-i \tau_{1,2}\omega} \)

• Hence define a complex connectivity matrix \( C^*(\omega) = \{c_{jk}e^{-i \tau_{jk}\omega}\} \)

 where delays come from global speed constant: \( \tau_{jk} = \frac{d_{jk}}{v} \)

 and the complex Laplacian

\[ \mathcal{L}(\omega|v, \alpha) = I - \alpha C^*(\omega|v) \]

• Define a "wavenumber" \( k = \omega/v \), then we define \( \mathcal{L}(k, \alpha) \)

Xie, Cai, Damasceno, Nagarajan, Raj. Emergence of canonical functional networks from the structural connectome, NeuroImage, 2021
WHAT DO THESE EIGENMODES LOOK LIKE?

• A few e-modes are sufficient to predict any FCN
• Complex e-modes are better than real ones; and both are better than random conns
• Complex e-modes respond to specific FCNs

X Xie, C Cai, P Damasceno, S Nagarajan, A Raj, Emergence of canonical functional networks from the structural connectome, NeuroImage, 2021
STRUCTURE-FUNCTION MAPPING

• Highlighting the eigen-mapping technique:
  • Reasonable performance with very simply approach
  • Exploits the relationship between the eigenvalues and eigenvectors of the FC and SC (esp latter’s Laplacian)
  • FC eigenvectors == Laplacian eigenvectors
  • FC eigenvalues = func(Lap eigenvalues)

• Example results

Ghosh, Raj, Nagarajan. submitted
SUGGESTED READING


• Cassiano Becker, Sérgio Pequito, George Pappas, Michael Miller, Scott Grafton, Danielle Bassett, Victor Preciado. Spectral mapping of brain functional connectivity from diffusion imaging. Nature Scientific Reports, 8(1411), 2018


• Xie, Cai, Damasceno, Nagarajan, Raj. Emergence of canonical functional networks from the structural connectome, NeuroImage, 2021
IMPROVING SC-FC CORRESPONDENCE USING GRAPH SPECTRA

- Further improvements can come from better mapping between FC and SC e-values
- E.g. replace exponential decay with Gamma function
- Adding latent and hard-to-measure inter-hemispheric connections between homologous regions greatly improves performance


- Future extensions could explore other data-driven mappings
Can models fit spectral features (0 – 0.25 Hz) of fMRI?

Need new analysis methods!

**Presenting a simple rate model for fMRI**

- **Signal equation**
  \[
  \frac{dx_i(t)}{dt} = -\frac{1}{\tau} f(t) * (x_i(t) - \alpha \sum_{l \neq m} c_{i,m} x_m) + p_i(t)
  \]

- **Laplacian Matrix**
  \[
  \mathcal{L}(\alpha) = I - \alpha C
  \]

- **Graph equation**
  \[
  \frac{dx(t)}{dt} = -\frac{1}{\tau} f(t) * \mathcal{L}(\alpha)x(t) + p(t).
  \]
  \[
  X(\omega) = \sum_{k=1}^{N} \frac{u_k u_k^\dagger}{j\omega + \tau^{-1} \lambda_k(\alpha) F(\omega)^2} P(\omega)
  \]

Frequency-response of fMRI can be explicitly written as sum over eigenmodes of Lap!

Eigenmodes predict spatial patterns

Each pattern has a spectral response that is a function of e-values
• SGM predicts both FC matrix and regional power spectra of fMRI
• Fitted model parameters may be interpreted as “computational biomarkers” of brain state or disease?
• Perhaps the first model that predicts and exploits higher-frequencies of fMRI?

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IS THIS SAME AS SPECTRAL DCM?

Spectral DCM also seeks frequency-dependent generative model of fMRI

• DCM Signal equation

\[
\frac{dx(t)}{dt} = Ax(t) + Bu(t) + v(t)
\]

• In Fourier domain, written as transfer function involving the cross-spectral density of \( x \) and \( v \):

\[
PSD_x(\omega) = TF(\omega) \cdot PSD_v(\omega)
\]

• Usually, \( v \) is assumed an autocorrelative signal

• Both SGM and spectral DCM use spectral features of signal

• BUT: this is where similarities end
  • Spectral DCM: estimate \( A = \{a_{ij}\} \)
  • SGM: use a known matrix \( \mathcal{L} \), fit for global parameters that determine shape of spectral response
  • Hence SGM seeks a structure-function model, DCM seeks effective connectivity
MEG AND EEG: A SPECTRAL GRAPH MODEL OF HIGHER BRAIN OSCILLATIONS

Spectral graph theory of brain oscillations

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Local neural assemblies $g_{ee}, g_{ii}, g_{ei}$, $\tau_e, \tau_i$

White noise

Macroscopic long-range connections $\tau_e, \alpha, \tau_G, \nu$

Str connectivity matrix

Frequency spectra -- Magnetoencephalography

Spectral graph theory model (SGM)
MODELING HIGHER FREQUENCIES – EEG/MEG

- Need to introduce conduction speed, cortical processing delays
- The model is no longer network diffusion, strictly
- Closed form solution of steady state frequency behaviour

\[
\frac{dx_{e/i}(t)}{dt} = - \frac{1}{\tau_{e/i}} f_{e/i}(t) * x_{e/i}(t) + \frac{1}{\tau_{e/i}} f_{e/i}(t) * \sum_{j,k} c_{jk} x_{e/i}(t - \tau_{jk}) + p_{e/i}(t)
\]

\[
C^*(\omega|\nu) = \{c_{jk} \exp(-i \tau_{jk} \omega)\}
\]

\[
\mathcal{L}(\omega|\nu, \alpha) = 1 - \alpha C^*(\omega|\nu)
\]

\[
X(\omega) = \sum_{i} \frac{u_i(\omega)u_i^H(\omega)}{j\omega + \frac{1}{\tau_{G}} \lambda_i(\omega)F_e(\omega)} H_{local}(\omega)P(\omega)
\]

Verma et al. SGM Revisited, Neuroimage 2022

- SGM correctly fits empirical MEG power spectra
- Does better than NMM
- Sensitive to model parameters (need to be optimized)
- Simultaneously predicts spatial patterns!

Verma et al., 2022, *Neuroimage*

**Band-specific spatial distribution**
<table>
<thead>
<tr>
<th><strong>Neural Mass Model</strong></th>
<th><strong>Spectral Graph Model</strong></th>
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<tbody>
<tr>
<td>• Node-level local NMMs coupled via connectome</td>
<td></td>
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<tr>
<td>• Solved by differential equations</td>
<td></td>
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<tr>
<td>• Can simulate neural activity on the whole brain network</td>
<td></td>
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<td>• Proven in M/EEG and fMRI</td>
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</tbody>
</table>

| • Large # of coupled non-linear 2\textsuperscript{nd} order Diff Eqns |
| • Numerical integration used to simulate over long model times |
| • Activity and FC patterns indirectly observed from simulations |
| • Parameter inference is very tough |
| • Requires step-wise, manual or heuristic optimization |

| • Linear vector-valued 1st order Diff Eqn |
| • Has closed-form solution in Fourier domain! |
| • Activity and FC directly given by solution |
| • Going to linear does not cause loss of performance! |
| • Frequently better than coupled NMMs |
| • Parameter inference is simple and fast, no hand-selection needed |
SGM: STABILITY AND DYNAMICS

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Local neural assemblies - $g_{ee}$, $g_{ii}$, $g_{ei}$, $\tau_e$, $\tau_i$

White noise

Macroscopic long-range connections - $\tau_e$, $\alpha$, $\tau_G$, $\nu$

Structural connectivity matrix (Diffusion MRI)

Frequency spectra -- Magnetoencephalography
In a linear system, stability is a function strictly of model parameters, not of input noise.

Recall in nonlinear coupled NMMs, meta-/multi-stability is governed by noise.

Verma et al., 2022, Network Neuroscience
Stability of local SGM

Verma et al., 2022, Network Neuroscience
Local neural assemblies - $g_{ee}$, $g_{ii}$, $g_{ei}$, $\tau_e$, $\tau_i$

Macroscopic long-range connections - $\tau_e$, $\alpha$, $\tau_G$, $\nu$

White noise

Structural connectivity matrix (Diffusion MRI)

Frequency spectra -- Magnetoencephalography

Spectral graph theory model (SGM)
Stability of macroscopic SGM

Stability regimes

Simulations in different regimes

Peak frequency of macro signal

Verma et al., 2022, Network Neuroscience
Stability and dynamics of a spectral graph model of brain oscillations

Poster No: 1732
Submission Type: Abstract Submission
Authors: Parul Verma, Srikantan Nagarajan, Ashish Raj

Verma et al., 2022, Network Neuroscience

RAJ LABORATORY, CHINA BASIN, UCSF
SGM: APPLICATIONS IN NEUROLOGICAL DISEASE (ALZHEIMER'S)

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Wish to infer model parameters that give rise to given MEG, EEG and fMRI
SGM gives a small set of only 6 biophysically interpretable global model parameters
Local model inferred by fitting regional frequency spectra
Global parameters by fitting regional spectra AND spatial distributions of different frequency bands
Application: inferred parameters can serve as biomarkers of disease
  • e.g. Schizophrenia, autism, epilepsy, Alzheimer,…

Extension: time-varying (dynamic) models to capture brain states
**LOCAL NEURAL ASSEMBLIES – APPLICATION TO AD**

- AD shows a strong down-shift in alpha band power and frequency
  - Strong up-shift in delta-theta power
- First we explore local-only models
- i.e. local (mesoscopic) parameters as biomarkers

Ranasinghe et al., 2022, eLife, in print
MACROSCOPIC SGM – APPLICATION TO AD

- Fitting macroscopic SGM only (keep all local parameters uniform)
- SGM needs only 6 biophysical global parameters

Example: global fitting to MEG in Alzheimer's disease

Verma et al., 2022, submitted
We are hiring!

Please contact for inquiries and job opportunities
- Ashish.raj@ucsf.edu
- https://radiology.ucsf.edu/research/labs/brain-networks-lab
- Lots of code on GitHub: https://github.com/Raj-Lab-UCSF