UCSF Department of Radiology and Biomedical Imaging

Machine Learning Algorithms for Electromagnetic Brain Imaging: Application in Alzheimer's disease

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Department of Radiology & Biomedical Imaging

UCSF Bakar Computational Health Sciences Institute

1

Outline

1. Novel reconstruction algorithms for Electromagnetic Brain Imaging
2. Resting-state brain oscillations in Alzheimer's disease (AD)
3. Neurophysiological trajectories in AD progression using event-based modeling (EBM)
4. Spectral Graph Modeling (SGM) of neural oscillations in AD

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2

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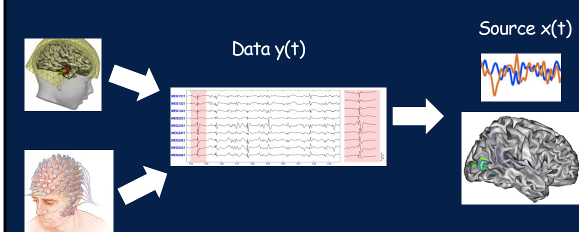
Electromagnetic Brain imaging - Reconstruction of neural oscillations from non-invasive recordings (MEG & EEG) of brain's electrophysiological activity



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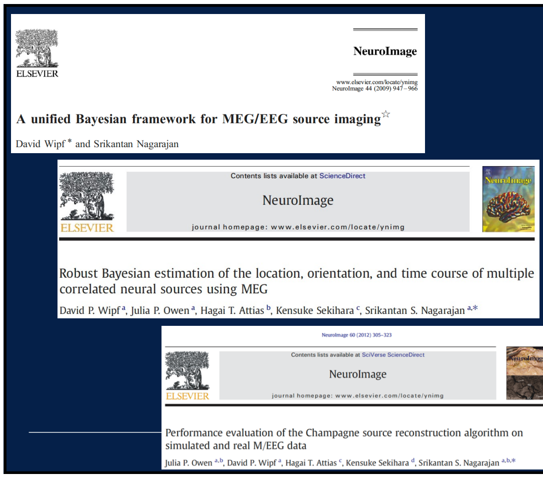
4

Bayesian Reconstruction of Brain Networks

- Past work
  - Formulation of the source reconstruction problem as sparse regression problem
    - Robust sparse signal estimation
    - Independent Noise estimates available

5


ELSEVIER

NeuroImage

www.elsevier.com/locate/ynimg
NeuroImage 44 (2009) 947–966

A unified Bayesian framework for MEG/EEG source imaging

David Wipf * and Srikantan Nagarajan

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg

Robust Bayesian estimation of the location, orientation, and time course of multiple correlated neural sources using MEG

David P. Wipf [a], Julia P. Owen [a], Hagai T. Attias [b], Kensuke Sekihara [c], Srikantan S. Nagarajan [a,*]

NeuroImage 60 (2012) 305–323

Contents lists available at SciVerse ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg

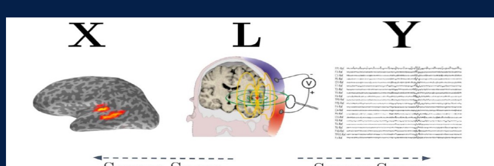
Performance evaluation of the Champagne source reconstruction algorithm on simulated and real M/EEG data

Julia P. Owen [a,b], David P. Wipf [a], Hagai T. Attias [c], Kensuke Sekihara [d], Srikantan S. Nagarajan [a,b,*]

6

Electromagnetic Brain Imaging as Sparse Linear Regression

$\mathbf{Y} = \mathbf{LX} + \mathbf{E}$	Linear regression problem
$\mathbf{Y} \in \mathbb{R}^{M \times T}$	M:#Sensors, T:#Samples,
$\mathbf{X} \in \mathbb{R}^{N \times T}$	N:#Sources, ($M \ll N$)
$\mathbf{L} \in \mathbb{R}^{M \times N}$	Lead Field Matrix (Known)



7

Type I vs Type II Estimation

Ill-posed inverse problem: ($M = 32 \sim 256$ vs $N = 10^3 \sim 10^4$)

1. Type-I MAP methods: ℓ_1, ℓ_2, $\ell_{1,2}$-norms, sparsity in transformed domains (Gabor).

$$\mathbf{X}^* = \underset{\mathbf{X}}{\operatorname{argmin}} \underbrace{\|\mathbf{Y} - \mathbf{LX}\|_F^2}_{\text{Likelihood}:p(\mathbf{Y}|\mathbf{X})} + \lambda \underbrace{\mathcal{R}(\mathbf{X})}_{\text{Prior}:p(\mathbf{X})}$$

2. Type-II ML approaches: different sparse Bayesian learning (SBL) variants.

$$\text{Type-II Loss}: \mathcal{L}^{\text{II}}(\mathbf{\Gamma}, \mathbf{\Lambda}) = \log|\mathbf{\Lambda} + \mathbf{L\Gamma L}^\top| + \frac{1}{T}\sum_{t=1}^{T} \mathbf{y}(t)^\top \left(\mathbf{\Lambda} + \mathbf{L\Gamma L}^\top\right)^{-1} \mathbf{y}(t).$$

8

Bayesian Reconstruction of Brain Networks

- Recent work
  - Formulation of the source reconstruction problem as sparse regression problem
    - Sparse signal estimation
    - Simultaneous Noise estimation
  - Novel and robust Bayesian algorithms for joint estimation of signal and noise

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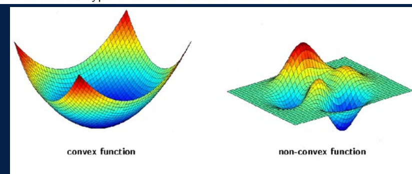
9

Champagne Algorithm – Joint Signal and Noise Learning

$$\text{Type}-\text{II Loss}: \mathcal{L}^{\text{II}}(\boldsymbol{\Gamma},\boldsymbol{\Lambda}) = \log|\boldsymbol{\Lambda}+\mathbf{L}\boldsymbol{\Gamma}\mathbf{L}^{\top}| + \frac{1}{T}\sum_{t=1}^{T}\mathbf{y}(t)^{\top}\left(\boldsymbol{\Lambda}+\mathbf{L}\boldsymbol{\Gamma}\mathbf{L}^{\top}\right)^{-1}\mathbf{y}(t)\,.$$

1. Non-convex Type-II ML loss function: Non-trivial to solve.



Our contributions: The Champagne Algorithm - Joint Estimation of regression parameters and noise distributions with diagonal and full structure covariance with Type II loss.

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10

Leveraging Majorization-Minimization Framework for Joint Signal and Noise Learning

NeuroImage 225 (2021) 117411

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/neuroimage

ELSEVIER

Robust estimation of noise for electromagnetic brain imaging with the champagne algorithm

Chang Cai[a,b,*,**], Ali Hashemi[c,d,e], Mithun Diwakar[b], Stefan Haufe[c,f], Kensuke Sekihara[g,h], Srikantan S. Nagarajan[b,**]

NeuroImage 239 (2021) 118309

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/neuroimage

ELSEVIER

Unification of sparse Bayesian learning algorithms for electromagnetic brain imaging with the majorization minimization framework

Ali Hashemi[a,b,c,d], Chang Cai[e,f], Gitta Kutyniok[g,h], Klaus-Robert Müller[b,i,j,k,*], Srikantan S. Nagarajan[e,*], Stefan Haufe[a,c,l,m,*]

11

Majorization-Minimization Framework

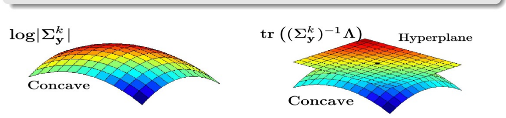
Theorem

Optimizing $\mathcal{L}^{\text{II}}(\boldsymbol{\Gamma},\boldsymbol{\Lambda})$ with respect to $\boldsymbol{\Lambda}$ is equivalent to optimizing the following majorzing function:

$$\mathcal{L}^{\text{conv}}_{\text{noise}}(\boldsymbol{\Gamma}^k,\boldsymbol{\Lambda}) = \text{tr}((\mathbf{C}^k_{\text{N}})^{-1}\boldsymbol{\Lambda}) + \text{tr}(\mathbf{M}^k_{\text{N}}\boldsymbol{\Lambda}^{-1})\,,$$

where $\mathbf{C}^k_{\text{N}}$ and $\mathbf{M}^k_{\text{N}}$ are defined as:

$$\mathbf{C}^k_{\text{N}} := \left(\boldsymbol{\Sigma}^k_{\mathbf{y}}\right)\,,\quad \mathbf{M}^k_{\text{N}} := \frac{1}{T}\sum_{t=1}^{T}(\mathbf{y}(t)-\mathbf{L}\bar{\mathbf{x}}^k(t))(\mathbf{y}(t)-\mathbf{L}\bar{\mathbf{x}}^k(t))^{\top}\,.$$



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12

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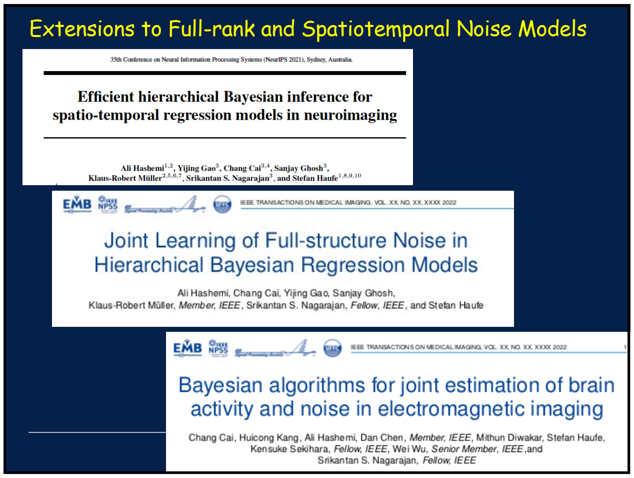
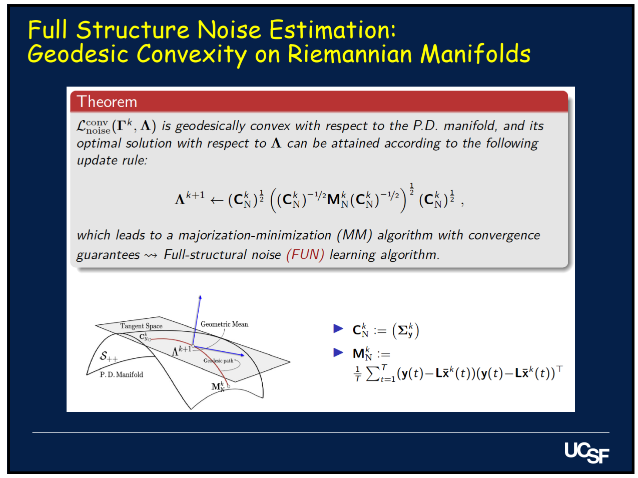

Extensions to Full-rank and Spatiotemporal Noise Models
35th Conference on Neural Information Processing Systems (NeurIPS 2021), Sydney, Australia.
Efficient hierarchical Bayesian inference for spatio-temporal regression models in neuroimaging
Ali Hashemi1,2, Yijing Gao3, Chang Cai3,4, Sanjay Ghosh3, Klaus-Robert Müller2,5,6,7, Srikantan S. Nagarajan3, and Stefan Haufe1,8,9,10
IEEE TRANSACTIONS ON MEDICAL IMAGING, VOL. XX, NO. XX, XXXX 2022
Joint Learning of Full-structure Noise in Hierarchical Bayesian Regression Models
Ali Hashemi, Chang Cai, Yijing Gao, Sanjay Ghosh, Klaus-Robert Müller, Member, IEEE, Srikantan S. Nagarajan, Fellow, IEEE, and Stefan Haufe
IEEE TRANSACTIONS ON MEDICAL IMAGING, VOL. XX, NO. XX, XXXX 2022
Bayesian algorithms for joint estimation of brain activity and noise in electromagnetic imaging
Chang Cai, Huicong Kang, Ali Hashemi, Dan Chen, Member, IEEE, Mithun Diwakar, Stefan Haufe, Kensuke Sekihara, Fellow, IEEE, Wei Wu, Senior Member, IEEE, and Srikantan S. Nagarajan, Fellow, IEEE

13


Full Structure Noise Estimation:
Geodesic Convexity on Riemannian Manifolds
Theorem
$\mathcal{L}^{\text{conv}}_{\text{noise}}(\mathbf{\Gamma}^k, \mathbf{\Lambda})$ is geodesically convex with respect to the P.D. manifold, and its optimal solution with respect to $\mathbf{\Lambda}$ can be attained according to the following update rule:
$\mathbf{\Lambda}^{k+1} \leftarrow (\mathbf{C}^k_{\mathrm{N}})^{\frac{1}{2}} \left((\mathbf{C}^k_{\mathrm{N}})^{-1/2}\mathbf{M}^k_{\mathrm{N}}(\mathbf{C}^k_{\mathrm{N}})^{-1/2}\right)^{\frac{1}{2}} (\mathbf{C}^k_{\mathrm{N}})^{\frac{1}{2}}$,
which leads to a majorization-minimization (MM) algorithm with convergence guarantees $\rightsquigarrow$ Full-structural noise (FUN) learning algorithm.
Tangent Space
Geometric Mean
$\mathcal{S}_{++}$
P. D. Manifold
Geodesic path
$\mathbf{C}^k_{\mathrm{N}} := (\mathbf{\Sigma}^k_{\mathbf{y}})$
$\mathbf{M}^k_{\mathrm{N}} := \frac{1}{T}\sum_{t=1}^{T}(\mathbf{y}(t)-\mathbf{L}\bar{\mathbf{x}}^k(t))(\mathbf{y}(t)-\mathbf{L}\bar{\mathbf{x}}^k(t))^\top$
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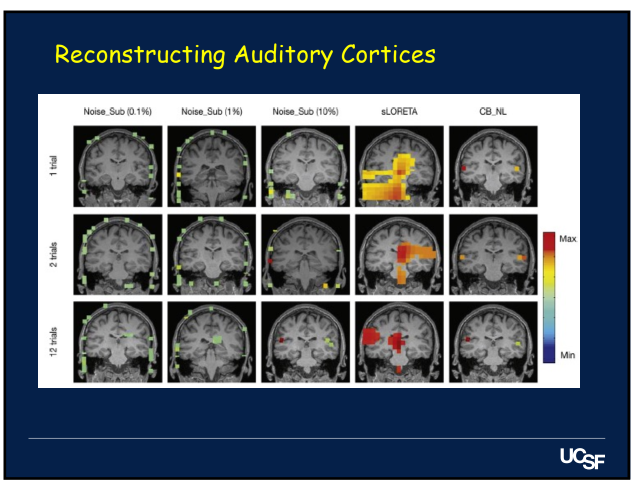
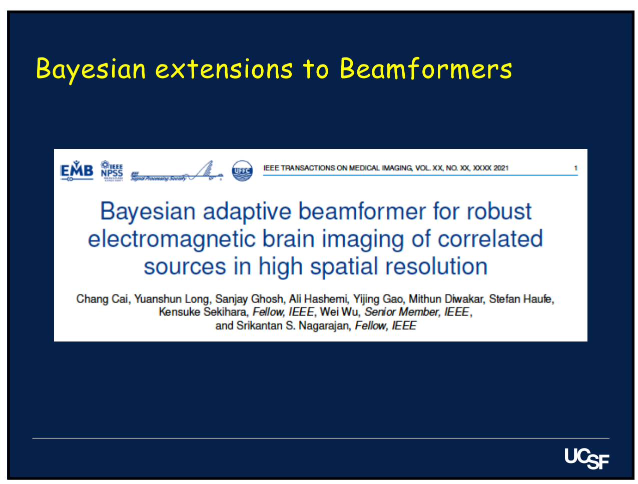
14


Reconstructing Auditory Cortices
Noise_Sub (0.1%)
Noise_Sub (1%)
Noise_Sub (10%)
sLORETA
CB_NL
1 trial
2 trials
12 trials
Max
Min
UCSF

15


Bayesian extensions to Beamformers
IEEE TRANSACTIONS ON MEDICAL IMAGING, VOL. XX, NO. XX, XXXX 2021
Bayesian adaptive beamformer for robust electromagnetic brain imaging of correlated sources in high spatial resolution
Chang Cai, Yuanshun Long, Sanjay Ghosh, Ali Hashemi, Yijing Gao, Mithun Diwakar, Stefan Haufe, Kensuke Sekihara, Fellow, IEEE, Wei Wu, Senior Member, IEEE, and Srikantan S. Nagarajan, Fellow, IEEE
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16

Sparse Bayesian Learning Regularization

Model Covariance $\boldsymbol{\Sigma_Y} = \boldsymbol{L}\alpha\boldsymbol{L}^\top + \boldsymbol{\Lambda}$

SBL Beamformer $\hat{\boldsymbol{w}}_n^{SBL-BF} = \boldsymbol{\Sigma_Y}^{-1}\boldsymbol{l}_n(\boldsymbol{l}_n^\top\boldsymbol{\Sigma_Y}^{-1}\boldsymbol{l}_n)^{-1}$

- Alternative to Statistically Regularized Beamformers
- Robust to Source Correlations

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17

Time-frequency Extensions

NeuroImage 258 (2022) 119369

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/neuroimage

ELSEVIER

Empirical Bayesian localization of event-related time-frequency neural activity dynamics

Chang Cai[a,b,*], Leighton Hinkley[b], Yijing Gao[b], Ali Hashemi[c,d,e], Stefan Haufe[c,f], Kensuke Sekihara[g,h], Srikantan S. Nagarajan[b,**]

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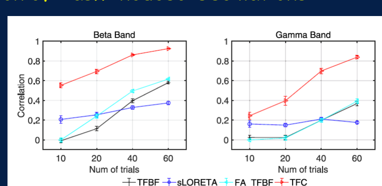
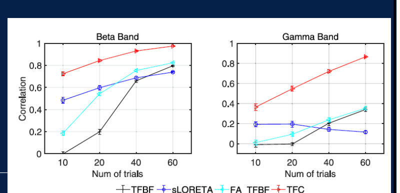
18

Robust reconstruction of Task-induced Oscillations

Finger movement



Picture Naming



19

Reconstruction Algorithms - Summary

- Robust reconstruction of spontaneous and task-induced frequency specific brain oscillations can be achieved with sparse Bayesian learning algorithms that include joint signal and noise estimation

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20

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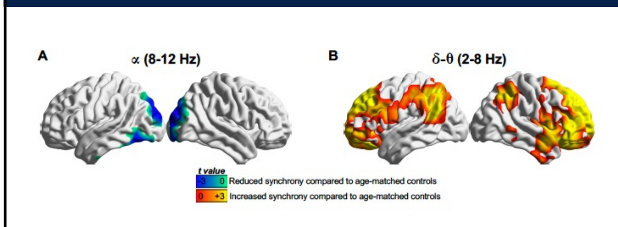
21

Frequency specific abnormal long-range neural synchrony in Alzheimer's disease



Information similar to that obtained from two radionucleotide PET imaging

SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE

ALZHEIMER'S DISEASE

Neurophysiological signatures in Alzheimer's disease are distinctly associated with TAU, amyloid-β accumulation, and cognitive decline

Kamalini G. Ranasinghe[1]*, Jungho Cha[1], Leonardo Iaccarino[1], Leighton B. Hinkley[2], Alexander J. Beagle[1], Julie Pham[1], William J. Jagust[3], Bruce L. Miller[1], Katherine P. Rankin[1], Gil D. Rabinovici[1,2], Keith A. Vossel[1,4]†, Srikantan S. Nagarajan[2]†

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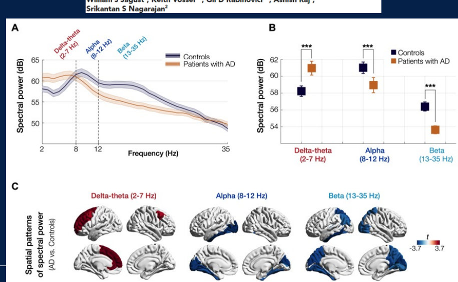
22

Abnormal local-neural synchrony in AD

Altered excitatory and inhibitory neuronal subpopulation parameters are distinctly associated with tau and amyloid in Alzheimer's disease

Kamalini G Ranasinghe[1]*, Parul Verma[2], Chang Cai[2], Xihe Xie[2], Kiwamu Kudo[2,3], Xiao Gao[2], Hannah Lerner[1], Danielle Mizuiri[2], Amelia Strom[1], Leonardo Iaccarino[1], Renaud La Joie[1], Bruce L Miller[1], Maria Luisa Gorno-Tempini[1], Katherine P Rankin[1], William J Jagust[4], Keith Vossel[1,5], Gil D Rabinovici[1,2], Ashish Raj[2], Srikantan S Nagarajan[2]



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23

Exploring temporal dynamics of resting-state in AD

NeuroImage 254 (2022) 119131

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/neuroimage

ELSEVIER

Time-varying dynamic network model for dynamic resting state functional connectivity in fMRI and MEG imaging

Fei Jiang[a,1,*], Huaqing Jin[b,1], Yijing Gao[c], Xihe Xie[c], Jennifer Cummings[c], Ashish Raj[c,2], Srikantan Nagarajan[c,2]

NeuroImage 281 (2023) 120358

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg

ELSEVIER

Dynamic functional connectivity MEG features of Alzheimer's disease

Huaqing Jin[a], Kamalini G. Ranasinghe[a,c], Pooja Prabhu[a], Corby Dale[a], Yijing Gao[a], Kiwamu Kudo[e], Keith Vossel[d], Ashish Raj[a], Srikantan S. Nagarajan[a], Fei Jiang[b,*]

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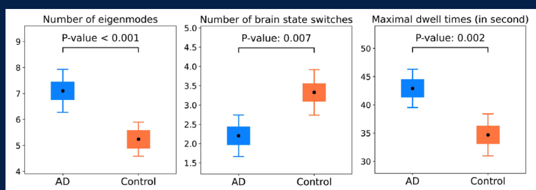
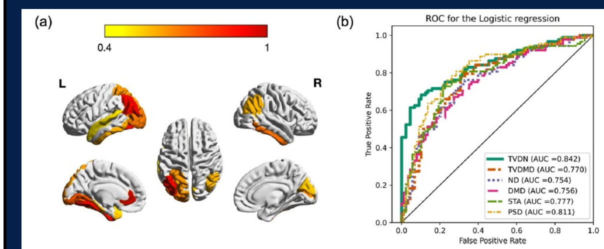
24

Dynamic features are abnormal in AD



25

Time-varying network dynamics predict AD



26

Summary

- Both local and long-range neural synchrony is disrupted in dementia
- Time-varying network dynamic abnormalities are important features of AD

27

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28

Neurophysiological trajectories in Alzheimer's disease progression

Kiwamu Kudo[1,2†*], Kamalini G. Ranasinghe[3†], Hirofumi Morise[1,2], Faatimah Syed[3], Kensuke Sekihara[4], Katherine P. Rankin[3], Bruce L. Miller[3], Joel H. Kramer[3], Gil D. Rabinovici[3,5], Keith Vossel[3,6], Heidi E. Kirsch[1], Srikantan S. Nagarajan[1]

Elife, under public review

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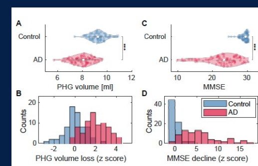
29

Atrophy-Cognition Event-based Modeling (EBM)



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30

Event Based Modeling

$$P(Z|S)=\prod_{j=1}^{J}\sum_{k=1}^{N+1} p(t_j=k|S)\,p(Z_j|S,t_j=k),$$

$$p(Z_j|S,t_j=k)\propto\prod_{i=1}^{I}\exp\left(-\frac{(z_{ij}-\mu_i(k))^2}{2}\right).$$

$$p(t_j=k|Z_j,\bar{S})=\frac{p(Z_j|\bar{S},t_j=k)}{\sum_{k'}p(Z_j|\bar{S},t_j=k')}.$$

$$\bar{x}_i(k)=\frac{\sum_{j=1}^{J}p_j(k)\cdot x_{ij}}{\sum_{j=1}^{J}p_j(k)}$$

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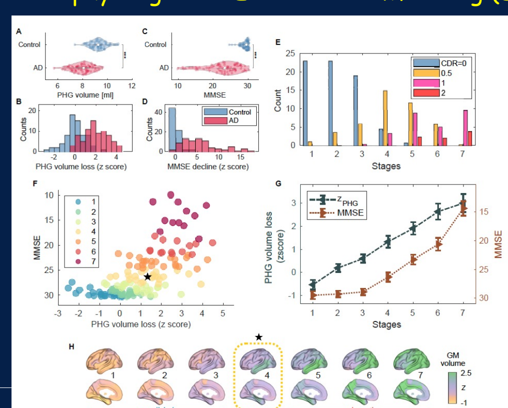
31

Atrophy-Cognition Event-based Modeling (EBM)



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32

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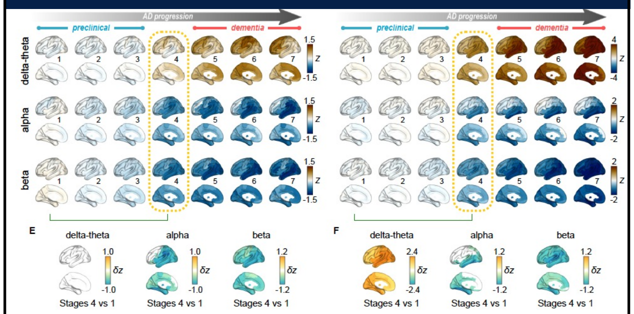
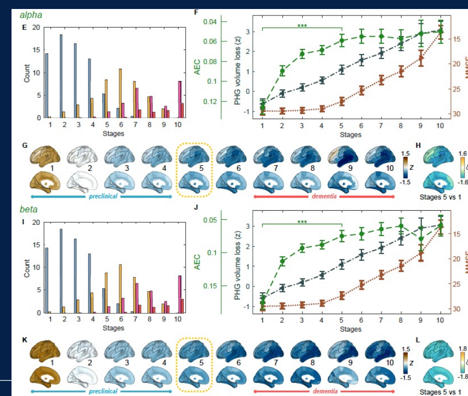
Electrophysiological Trajectories



33

Long-range Synchrony-Atrophy-Cognition EBM



34

Summary

- Long-range neural synchrony in the alpha and beta bands represent the earliest manifestation of Alzheimer's disease progression

36

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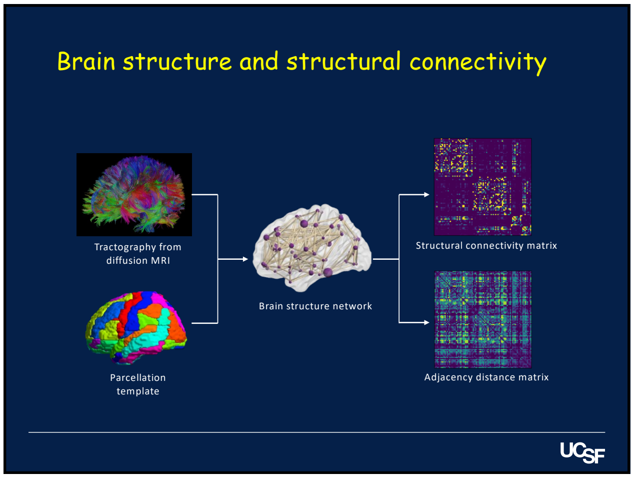
37


Brain structure and structural connectivity
Tractography from diffusion MRI
Parcellation template
Brain structure network
Structural connectivity matrix
Adjacency distance matrix
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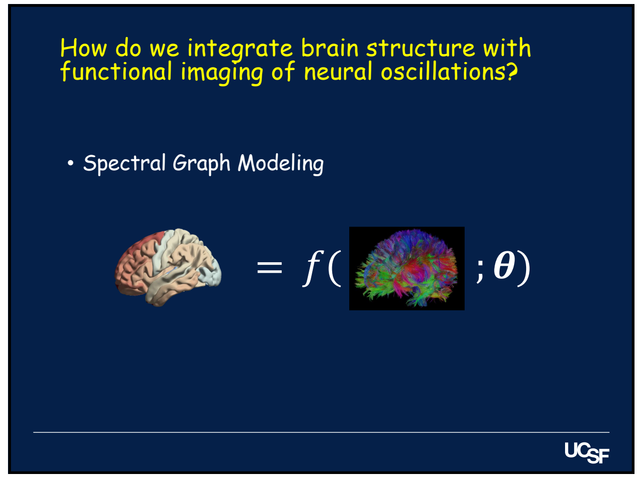
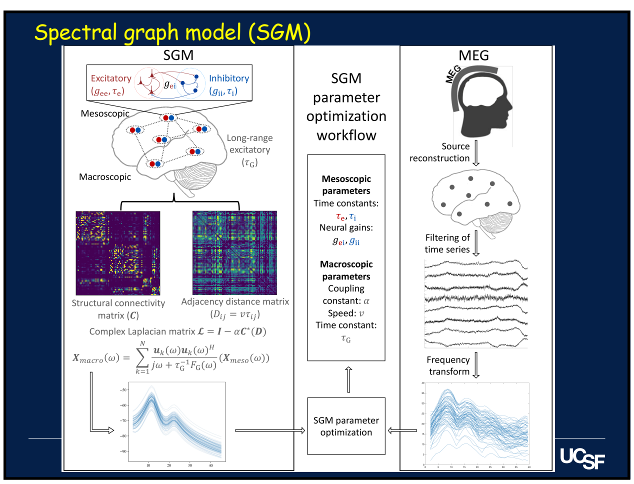
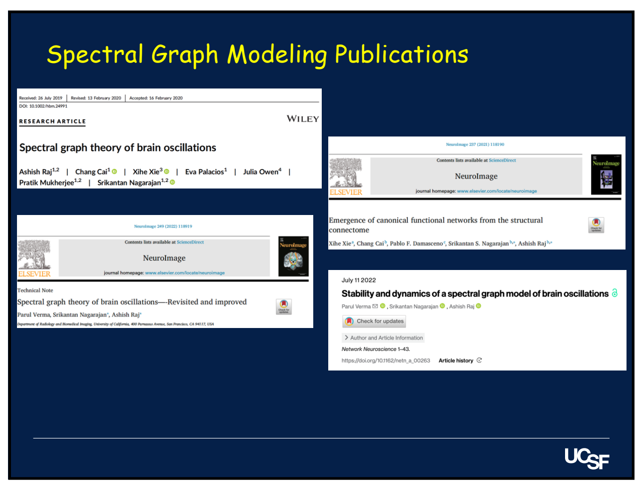
38


How do we integrate brain structure with functional imaging of neural oscillations?
• Spectral Graph Modeling
$= f(\quad ; \boldsymbol{\theta})$
UCSF

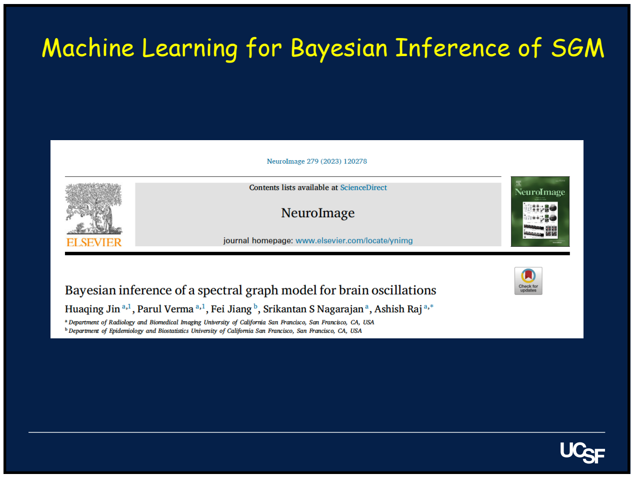
39


Spectral graph model (SGM)
SGM
Excitatory (g_{ee}, τ_e)
g_{ei}
Inhibitory (g_{ii}, τ_i)
Mesoscopic
Long-range excitatory (τ_G)
Macroscopic
Structural connectivity matrix $(\boldsymbol{C})$
Adjacency distance matrix $(D_{ij} = v\tau_{ij})$
Complex Laplacian matrix $\mathcal{L} = \boldsymbol{I} - \alpha \boldsymbol{C}^*(\boldsymbol{D})$
$X_{macro}(\omega) = \sum_{k=1}^{N} \frac{\boldsymbol{u}_k(\omega)\boldsymbol{u}_k(\omega)^H}{j\omega + \tau_G^{-1}F_G(\omega)}(X_{meso}(\omega))$
SGM parameter optimization workflow
Mesoscopic parameters
Time constants: τ_e, τ_i
Neural gains: g_{ei}, g_{ii}
Macroscopic parameters
Coupling constant: α
Speed: v
Time constant: τ_G
SGM parameter optimization
MEG
Source reconstruction
Filtering of time series
Frequency transform
UCSF

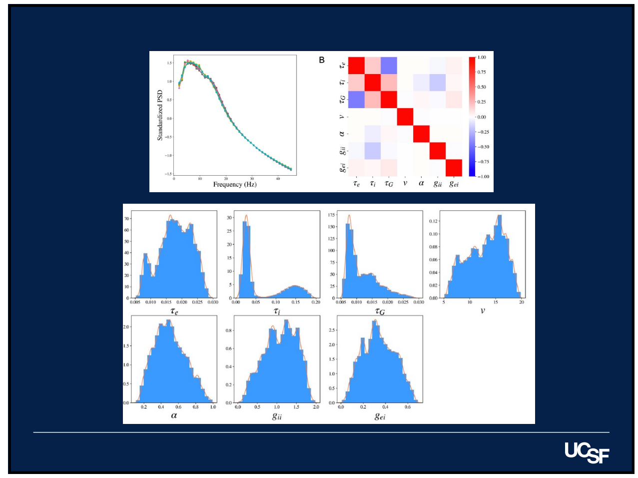
40


Spectral Graph Modeling Publications
RESEARCH ARTICLE
WILEY
Spectral graph theory of brain oscillations
Ashish Raj | Chang Cai | Xihe Xie | Eva Palacios | Julia Owen | Pratik Mukherjee | Srikantan Nagarajan
NeuroImage
Technical Note
Spectral graph theory of brain oscillations—Revisited and improved
Parul Verma, Srikantan Nagarajan, Ashish Raj
NeuroImage
Emergence of canonical functional networks from the structural connectome
Xihe Xie, Chang Cai, Pablo F. Damasceno, Srikantan S. Nagarajan, Ashish Raj
July 11 2022
Stability and dynamics of a spectral graph model of brain oscillations
Parul Verma, Srikantan Nagarajan, Ashish Raj
Check for updates
Author and Article Information
Network Neuroscience 1-43.
Article history
UCSF

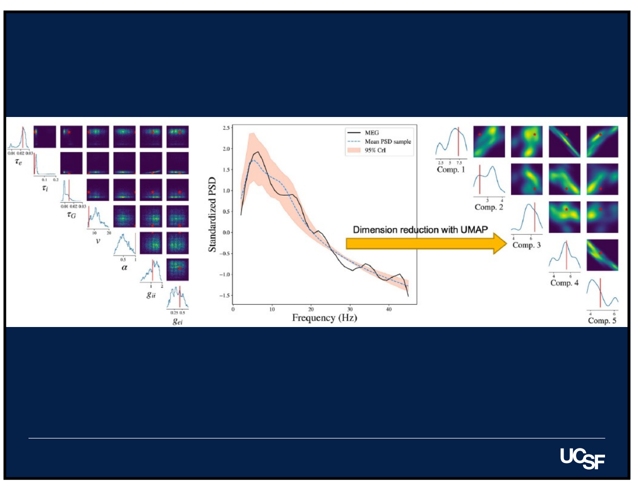
41


Machine Learning for Bayesian Inference of SGM
NeuroImage 279 (2023) 120278
Contents lists available at ScienceDirect
NeuroImage
journal homepage: www.elsevier.com/locate/ynimg
ELSEVIER
Bayesian inference of a spectral graph model for brain oscillations
Huaqing Jin a,1, Parul Verma a,1, Fei Jiang b, Srikantan S Nagarajan a, Ashish Raj a,*
a Department of Radiology and Biomedical Imaging University of California San Francisco, San Francisco, CA, USA
b Department of Epidemiology and Biostatistics University of California San Francisco, San Francisco, CA, USA
UCSF

42


Standardized PSD
Frequency (Hz)
B
UCSF

44


Standardized PSD
Frequency (Hz)
MEG
Mean PSD sample
95% CrI
Dimension reduction with UMAP
Comp. 1
Comp. 2
Comp. 3
Comp. 4
Comp. 5
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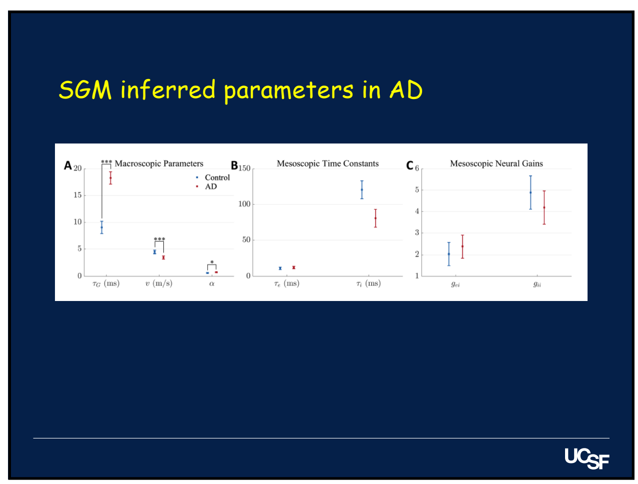
45


SGM inferred parameters in AD
A
Macroscopic Parameters
Control
AD
B
Mesoscopic Time Constants
C
Mesoscopic Neural Gains
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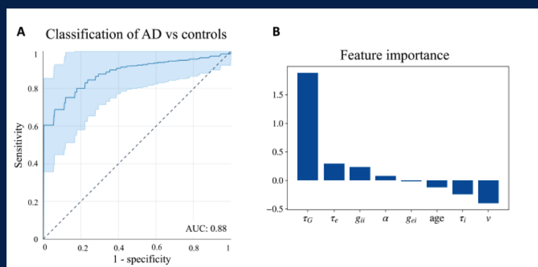
46

Discriminability of AD from SGM parameters



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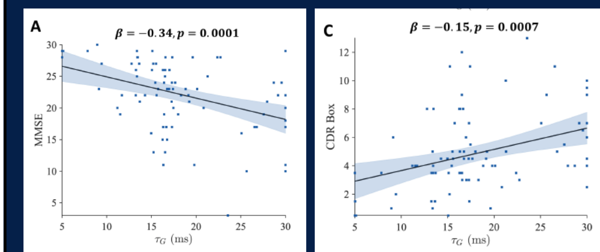
Association of SGM parameters with cognitive decline



Increase in τ_G is associated with more cognitive decline

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48

Summary

1. Robustness of novel Bayesian algorithms for Electromagnetic Brain Imaging (EBI)
2. Evidence for abnormal neural synchrony and network dynamics in AD
3. Neural synchrony is an early manifestation in AD
4. Spectral Graph Modeling (SGM) as a unifying framework for understanding electromagnetic brain imaging data

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Credits - Collaborators

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50

Credits – Incredible team of past and current members of the UCSF-BIL!

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51

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Questions or Comments?

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52