DUAL EXTREMAL CROSS-FREQUENCY INTERACTIONS IN BRAIN CONNECTIVITY

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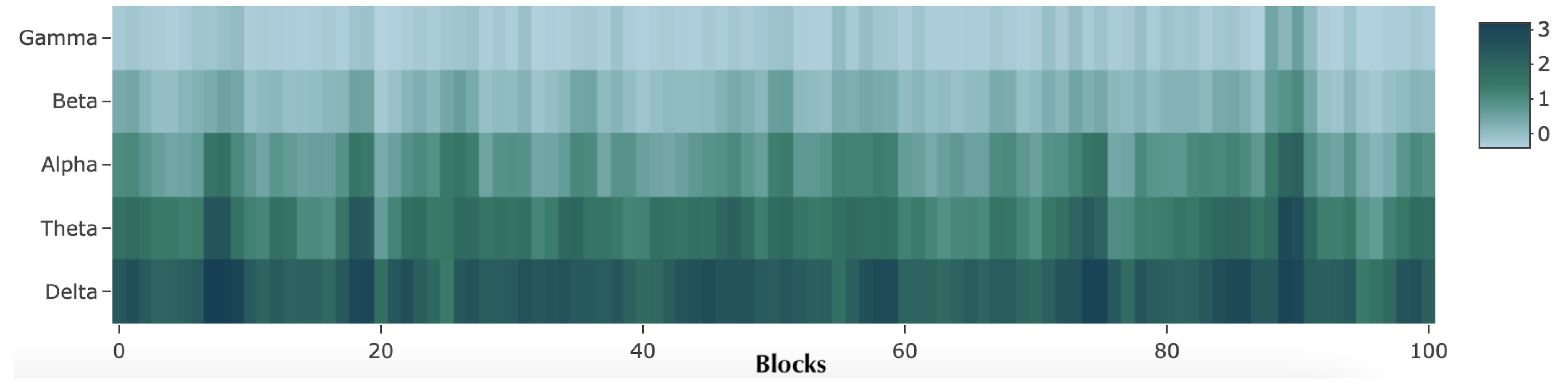
Background

- Increase in the power of **high frequencies** has been found in brain signals during the onset of an epileptic seizure.
- **Hypothesis:** By analyzing the tail of the brain energy distribution during high-frequency oscillations, we can reveal key channels that could **trigger bursts of electrical activity** in brain signals.
- Key channels that induce seizures may only reveal themselves during the **burst-phase**.
- **Contributions**: (a) metric for the comparison of tail associations of bursts for ictal and non-ictal neonates; and (b) reveal key channels in brain connectivity of patients at risk of epilepsy.

Time-Frequency Analysis for Non-stationary Series



Time-Varying Periodogram:

- X(t) is a locally stationary time series
- At time block b of length M, compute the local periodogram:

$$I(b,\omega_k) = \frac{1}{M}\left|\sum_{t\in b} X(t)\exp(-i2\pi\omega_k t)\right|^2$$

where $\omega_k = k/(\mathrm{SR} \times \mathrm{seconds})$

- Compute the periodograms at the frequency bands delta (0 - 4 Hertz (Hz)), theta (4 - 8 Hz), alpha (8 - 12 Hz), beta (12 - 30 Hz), and gamma (30 - 50 Hz). The periodogram at band Ω is equation $I(b,\Omega) = 1/||\Omega|| \sum_{\omega_k\in\Omega} I(b,\omega_k)$.

Spectral Clustering can be used for quicker detection of burst and suppression phase in EEG [2]. Consider the similarity measure of blocks contained in matrix S such that $S_{b,b'}$ is the similarity between two blocks b and b', given as: $S_{b,b'} = \exp\left(-\frac{||(\Sigma(h{=}0,b),\Sigma(h{=}0,b'))||_F^2}{2\gamma}\right)$,

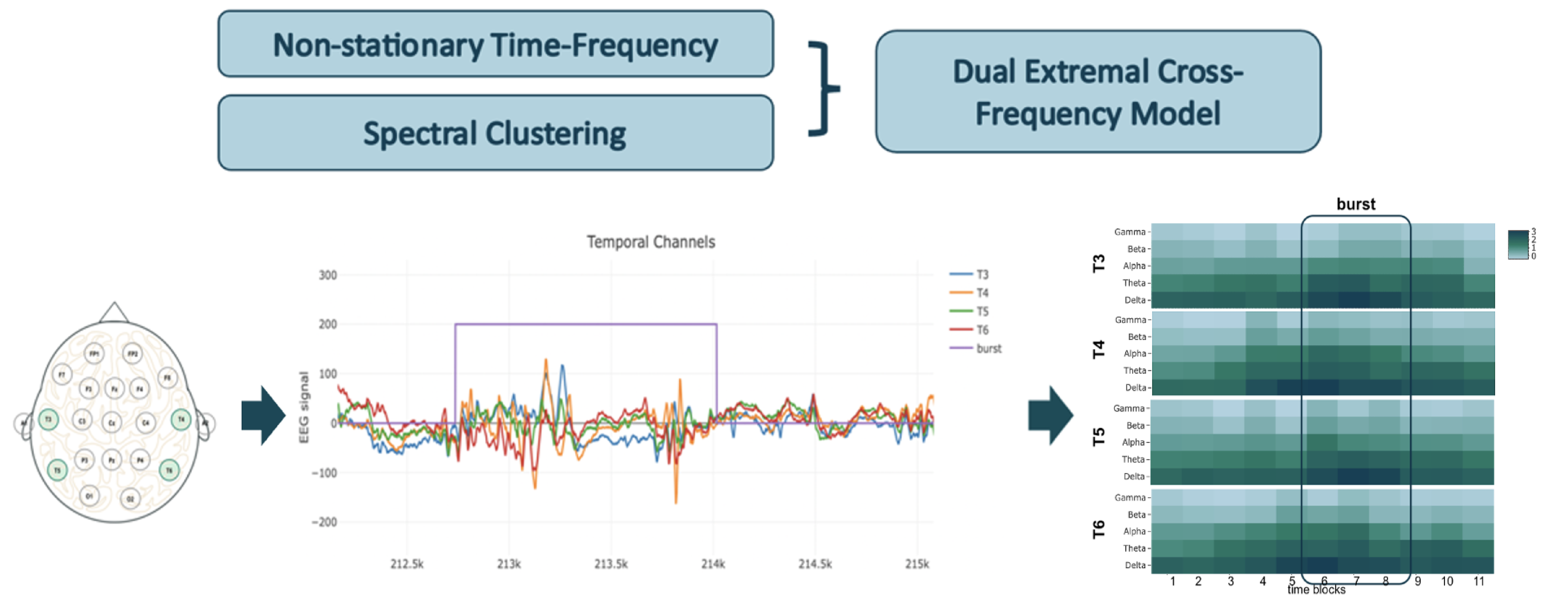
- Let $\mathrm{L} = \mathrm{D} - \mathrm{S}$, where $\mathrm{D} = diag\{d_1, d_2, ..., d_{B=1000}\}$ and d_i is the degree of a vertex $v_b = \sum_{i=b}^{B} S_{b,b'}$. The clustering is done by performing k-means on eigenvectors of $Lu = \lambda Du$.

Framework

Consider four channels at the temporal lobe namely T3, . . . , T6 indexed by $p = 1, \ldots, 4$. **DEC Model** is defined for $\boldsymbol{I}_d(b,\omega) := (I_{1,d}(b,\omega), \ldots, I_{4,d}(b,\omega))'$. Denote by $\boldsymbol{I}_{-p,d}(b,\omega)$ the vector $\boldsymbol{I}_d(b,\omega)$ with its p^{th} component removed; $d = 1$ and $d = 2$ correspond to burst and non-burst phases. Then, for all $u_{p,d} > v_{p,d}$ for some high threshold $v_{p,d} > 0$, the [1] model asserts that

$$\left(\boldsymbol{I}_{-p,d}(b,\omega) \,\middle|\, I_{p,d}(b,\omega) = u_{p,d}\right) = \boldsymbol{\phi}_{-p,d} I_{p,d}(b,\omega) + I_{p,d}(b,\omega)^{\boldsymbol{\psi}_{-p,d}} \boldsymbol{Z}_{-p,d}(b,\omega), \quad (1)$$

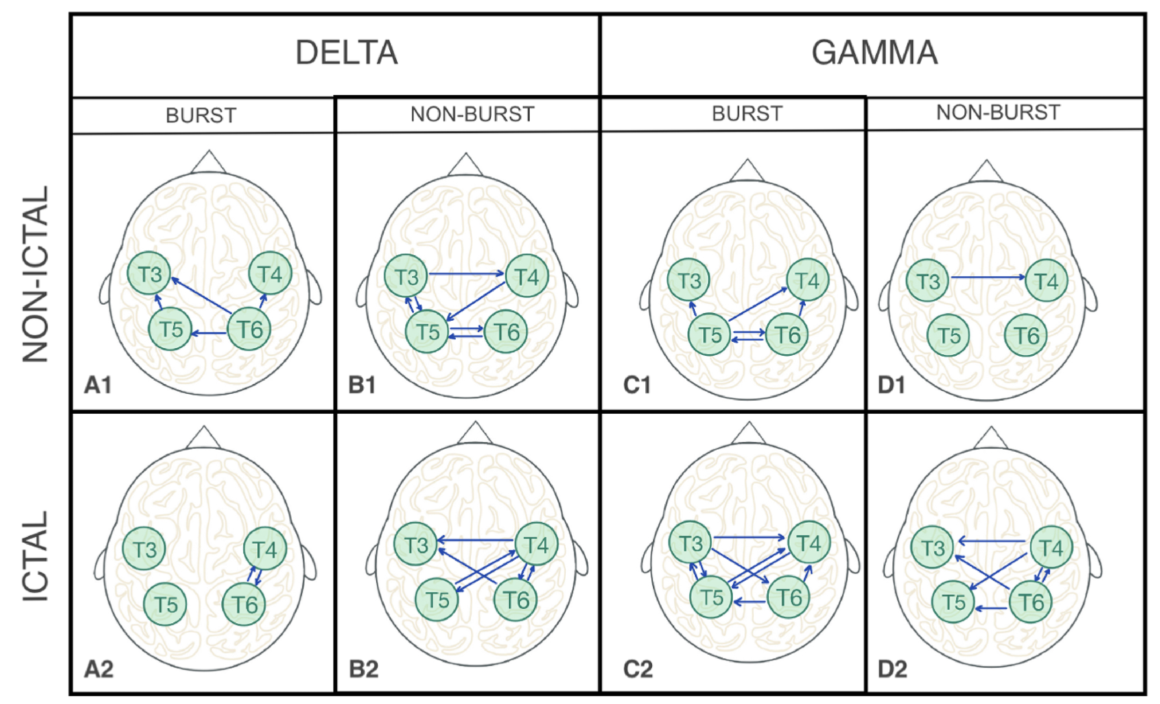
with parameter vectors $\boldsymbol{\phi}_{-p,d} \in [-1,1]^3$ and $\boldsymbol{\psi}_{-p,d} \in (-\infty,1)^3$ dependent on channel p and phase-type $d \in \{1,2\}$. $\boldsymbol{Z}_{-p,d}(b,\omega) \sim \mathrm{MVN}(\boldsymbol{\mu}_{-p,d}, \Sigma_{-p,d})$ for mean vector and covariance matrix $\boldsymbol{\mu}_{-p,d}$ and $\Sigma_{-p,d}$, respectively.

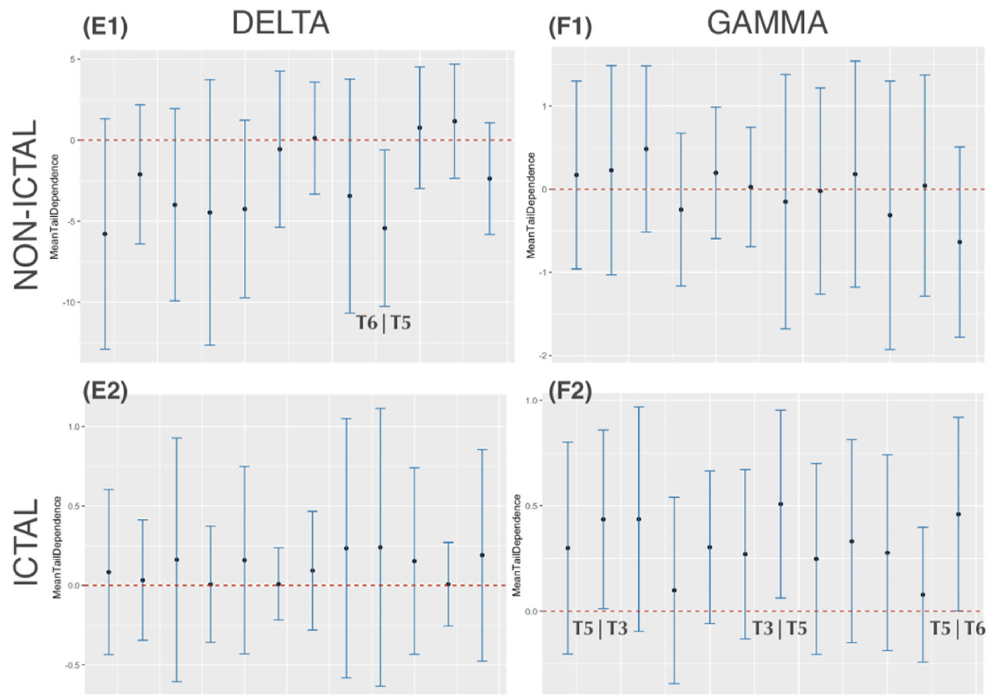


- **Conditional expectation** combines information from both $\boldsymbol{\phi}_{-p,d}$ and $\boldsymbol{\psi}_{-p,d}$: $m_{p,q;d}(\omega) = \hat{E}[I_{q,d}(b,\omega)|I_{p,d}(b,\omega) = u_{p,d}] = \hat{\phi}_{-p,q;d} u_{p,d} + u_{p,d}^{\hat{\psi}_{-p,q;d}} \hat{\mu}_{-p,q;dj}, p \neq q$, [3]
- **Bootstrap**: We used a non-parametric bootstrap to estimate parameter uncertainty of the DEC model. For each clusters, we resampled the blocks then re-fitted the DEC model to each resamples to obtain bootstrap estimates for $\phi_{\mathrm{p,q;d}}$ and conditional mean difference (i.e., $m_{diff} = m_{p,q;1} - m_{p,q;2}$) for all pairwise combination of channels.

Subject Level Results and Future Work

Subject Level Analysis:





Future Work:

- **Multi-subject DEC**; utilize Extreme Vector Autoregressive Model with subject-specific effects: $\left(\boldsymbol{I}_{-i}^{(s)}(b,\omega) \,\middle|\, I_i^{(s)}(b,\omega) = u_i^{(s)}\right) = \boldsymbol{F}^{(s)}(b,\omega) + \boldsymbol{D}^{(s)}(b,\omega)$; for all $u_i^{(s)} > v_i^{(s)}$.
- $\boldsymbol{F}^{(s)}(b,\omega)$ is the subject-specific fixed-effects, while $\boldsymbol{D}^{(s)}(b,\omega)$ has the subject-specific tail connectivity matrices of four clusters. We will use **D** to represent the **DEC model**.
- The simplest case of $D^{(s)}(b+h,\omega) = D_\omega^{(s)}(b+h)$ is for lag 1 fixing $\boldsymbol{\Psi} = 0$ which is given by:

$$\boldsymbol{D}_\omega^{(s)}(b) = [\boldsymbol{\Phi}_{1,1}^{(s)} E_{1,b}^{(s)} + \boldsymbol{\Phi}_{2,1}^{(s)} E_{2,b}^{(s)}]\boldsymbol{D}_\omega^{(s)}(b-1) + \boldsymbol{e}^{(s)}(b)$$

where $E_{c,b}^{(s)} = E_c^{(s)}(b,\omega)$ is 1 when the block is in extreme set of cluster c and 0 otherwise. The term $\boldsymbol{e}^{(s)}(b)$ is a zero-mean white noise multivariate process.

References

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[2] Narula, G., Haeberlin, M., Balsiger, J., Strässle, C., Imbach, L.L., and Keller, E.: *Detection of EEG burst-suppression in neurocritical care patients using an unsupervised machine learning algorithm* Clinical Neurophysiology 132, no.10 (2021): 2485–2492.

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