Multilevel hybrid principal components analysis for region-referenced multilevel functional EEG data

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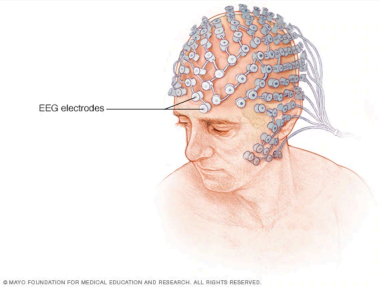
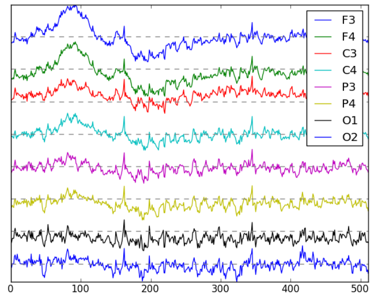
Data collection

- Electroencephalography (EEG): non-invasive and low-cost modality to analyze the brain and its behavior
- Categorized into two groups:
  - Resting state: analyzed on the frequency domain via the power spectral density (PSD)
  - Event-related: analyzed on the time domain via the event-related potential (ERP) created by time-locking the brain response to the onset of the stimulus





Data structure

- Generated data viewed as functional objects collected across the scalp across varying experimental conditions within a single longitudinal visit or across multiple visits
    - Termed region-referenced multilevel functional data

- Common analysis of EEG reduces the data complexity by collapsing one of the dimensions
    - Functional: analyze peak or mean amplitude of the ERP or power within a specific frequency band
    - Regional: averaging functions across all electrodes to create a scalp-wide average

Current methods

- Hybrid PCA: uses the concept of **weak separability** to decompose variation into regional and functional dimensions (Scheffler, 2020)
  - Weak separability: assumes the direction of variation along one of the dimensions stays constant across slices of the other dimension so estimates directions of variation utilizing marginal lower-dimensional covariances
  - Uses both vector and functional PCA
  - Assumes regions are non-exchangeable

- Multilevel FPCA: **functional ANOVA model** that decomposes total variation into between- and within-subjects variation (Di, 2009)
  - Uses FPCA
  - Assumes levels are exchangeable

- These approaches can be extended for exchangeable levels and non-exchangeable regions to decompose multilevel region-referenced functional data

M-HPCA algorithm

- Proposed M-HPCA borrows ideas from HPCA and M-FPCA: decomposes the total variation into between- and within-subjects variation then assumes weak separability on both of these covariance processes
- Results in participant-specific and repetition-specific eigenvectors and eigenfunctions that are highly interpretable as participant-specific and repetition-specific regional and functional directions of variation, respectively
- Enables computationally efficient estimation and inference through the use of a minorization-maximization (MM) algorithm

Model

- $Y_{dij}(r,t)$ denotes the functional observation for subject i, $i = 1, \ldots, n_d$, from group d, $d = 1, \ldots, D$, in region r, $r = 1, \ldots, R$, at time t, $t \in \mathcal{T}$ and is modeled as

$$Y_{dij}(r,t) = \mu(t) + \eta_{dj}(r,t) + Z_{di}(r,t) + W_{dij}(r,t) + \epsilon_{dij}(r,t)$$

  - $\mu(t)$: overall mean function
  - $\eta_{dj}(r,t)$: group-region-repetition-specific shift from the overall mean
  - $Z_{di}(r,t)$: subject-region-specific deviation
  - $W_{dij}(r,t)$: subject-region-repetition deviation
  - $\epsilon_{dij}(r,t)$: independent measurement error

Decomposed model

- Between covariance: $K_{d,B}\{(r,t),(r',t')\} = \text{cov}\{Z_{di}(r,t), Z_{di}(r',t')\}$

- Within covariance: $K_{d,W}\{(r,t),(r',t')\} = \text{cov}\{W_{dij}(r,t), W_{dij}(r',t')\}$

- Covariances marginalized by averaging over the other dimension

- $\phi^{(1)}_{d\ell}(t)$ and $\phi^{(2)}_{dm}(t)$ are the level 1 and level 2 eigenfunctions, and $\text{v}^{(1)}_{dk}(r)$ and $\text{v}^{(2)}_{dp}(r)$ are the level 1 and level 2 eigenvectors

- Utilizing the marginal eigenfunctions and eigenvectors

$$
\begin{aligned}
Y_{dij}(r,t) &= \mu(t) + \eta_{dj}(r,t) + Z_{di}(r,t) + W_{dij}(r,t) + \epsilon_{dij}(r,t) \\
&= \mu(t) + \eta_{dj}(r,t) + \sum_{k=1}^{R}\sum_{\ell=1}^{\infty} \zeta_{di,k\ell}\text{v}^{(1)}_{dk}(r)\phi^{(1)}_{d\ell}(t) \\
&\quad + \sum_{p=1}^{R}\sum_{m=1}^{\infty} \xi_{dij,pm}\text{v}^{(2)}_{dp}(r)\phi^{(2)}_{dm}(t) + \epsilon_{dij}(r,t)
\end{aligned}
$$

Application: Language impairment in autism

- Autism spectrum disorder (ASD): developmental disorder that affects communication and behavior

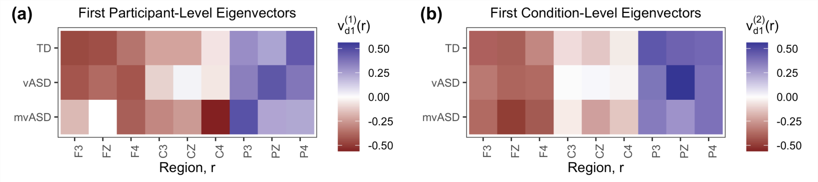
- Goal: study the neural mechanisms underlying language impairment in children with ASD (DiStefano, 2019)

- Study cohort: 31 children aged 5-11 years old were recruited
  - Typically Developing (TD): n = 14
  - Verbal ASD (vASD): n = 10
  - Minimally Verbal (mvASD): n = 7

Audio odd-ball paradigm

- Multilevel: A picture was presented and an audio recording of a spoken word was played that either matched or did not match (match vs. mismatch)
- Regional: 9 electrodes
- Functional: 137 equally spaced time points between -96ms to 992ms
- Three ERP components of interest:
  - P200: attention
  - N400: semantic processing
  - N600-900 or late negative component (LNC): semantic integration

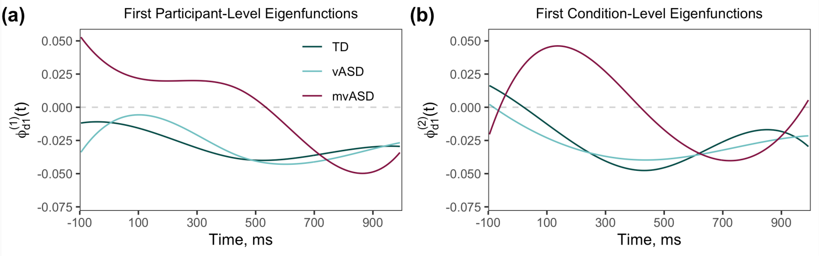
Marginal eigenvectors



- Leading eigenvectors at both levels represent a contrast between electrodes at the front and back of the scalp for all groups

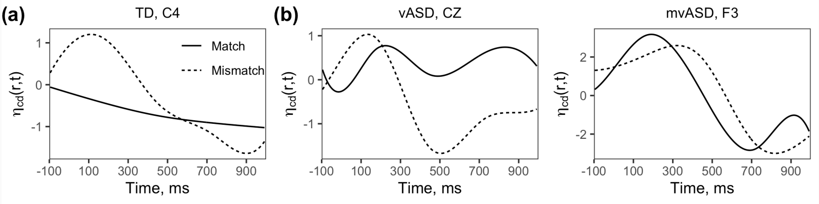
- Related to the dipole effect: observed signals are exact opposites on opposing sides of the scalp

Marginal eigenfunctions



- TD and vASD: leading participant- and condition-level eigenfunctions in the TD and vASD groups signal variability in N400 and LNC components
- mvASD: most of the variation at the participant level is observed in the late LNC component and most of the variation at the condition level is observed in the contrast between P200 and LNC components

Condition differentiation



- TD: only trending condition differentiation was detected at C4 ($p = 0.055$), but estimated condition-specific mean functions from almost all regions visually showed a condition difference
- vASD: condition differentiation strongest at Cz ($p = 0.025$), difference between conditions was mostly driven by the N400 and LNC
- mvASD: detected at F3, partly due to the late LNC ($p = 0.045$)

Thank you!

References

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- Di CZ, Crainiceanu CM, Caffo BS, Punjabi NM. Multilevel Functional Principal Component Analysis. Ann Appl Stat. 2009;3(1):458-488. doi:10.1214/08-AOAS206SUPP
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Covariances

- Total covariance:

$$K_{d,\text{Total}}\{(r,t),(r',t')\} = \text{cov}\{Y_{dij}(r,t), Y_{dij}(r',t')\}$$

- Between-subject covariance:

$$K_{d,B}\{(r,t),(r',t')\} = \text{cov}\{Y_{dij_1}(r,t), Y_{dij_2}(r',t')\} = \text{cov}\{Z_{di}(r,t), Z_{di}(r',t')\}$$

- Within-subject covariance

$$\begin{aligned} K_{d,W}\{(r,t),(r',t')\} &:= K_{d,\text{Total}}\{(r,t),(r',t')\} - K_{d,B}\{(r,t),(r',t')\} \\ &= \text{cov}\{W_{dij}(r,t), W_{dij}(r',t')\} \end{aligned}$$

Marginal covariances

- Functional marginal between and within covariance surfaces

$$\Sigma_{d,\mathcal{T},B}(t,t') = \sum_{r=1}^{R} K_{d,B}\{(r,t),(r,t')\} = \sum_{\ell=1}^{\infty} \tau_{d\ell,\mathcal{T}}^{(1)} \phi_{d\ell}^{(1)}(t)\phi_{d\ell}^{(1)}(t')$$

$$\Sigma_{d,\mathcal{T},W}(t,t') = \sum_{r=1}^{R} K_{d,W}\{(r,t),(r,t')\} = \sum_{m=1}^{\infty} \tau_{dm,\mathcal{T}}^{(2)} \phi_{dm}^{(2)}(t)\phi_{dm}^{(2)}(t'),$$

- Regional marginal between and within covariance matrices

$$(\Sigma_{d,\mathcal{R},B})_{r,r'} = \int_{\mathcal{T}} K_{d,B}\{(r,t),(r',t)\}dt = \sum_{k=1}^{R} \tau_{dk,\mathcal{R}}^{(1)} \mathrm{v}_{dk}^{(1)}(r)\mathrm{v}_{dk}^{(1)}(r')$$

$$(\Sigma_{d,\mathcal{R},W})_{r,r'} = \int_{\mathcal{T}} K_{d,W}\{(r,t),(r',t)\}dt = \sum_{p=1}^{R} \tau_{dp,\mathcal{R}}^{(2)} \mathrm{v}_{dp}^{(2)}(r)\mathrm{v}_{dp}^{(2)}(r'),$$

- $\phi_{d\ell}^{(1)}(t)$ and $\phi_{dm}^{(2)}(t)$ are the level 1 and level 2 eigenfunctions, $\mathrm{v}_{dk}^{(1)}(r)$ and $\mathrm{v}_{dp}^{(2)}(r)$ are the level 1 and level 2 eigenvectors, and $\tau_{d\ell,\mathcal{T}}^{(1)}$, $\tau_{dm,\mathcal{T}}^{(2)}$, $\tau_{dk,\mathcal{R}}^{(1)}$, and $\tau_{dp,\mathcal{R}}^{(2)}$ are the respective eigenvalues

Mean function