M.S. Thesis Defense

Analysis of fNIRS Signals

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Preview

- Cognitive Neuroscience
- Computer-based Experimental Procedures
- PET, fMRI
- **F**unctional **N**ear **I**nfra**R**ed **S**pectroscopy
- Objective of the Present Work

Outline

- **Introduction**
- Statistical Characterization of fNIRS Data
- Time-Frequency Characterization
- Functional Activity Estimation
- Conclusion

Introduction

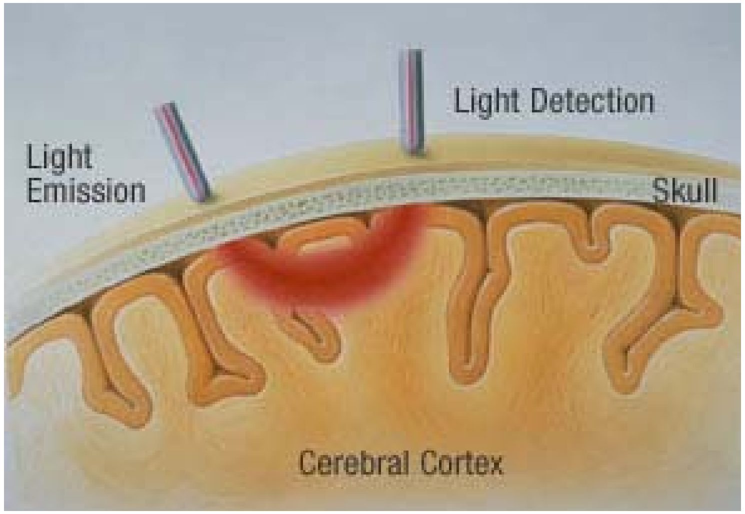
- Functional Neuroimaging
  - PET, fMRI
    - Non-invasive
    - Measure correlates of neuronal activity
    - High spatial, but low temporal resolution
    - Expensive
    - Uncomfortable for patients or volunteers

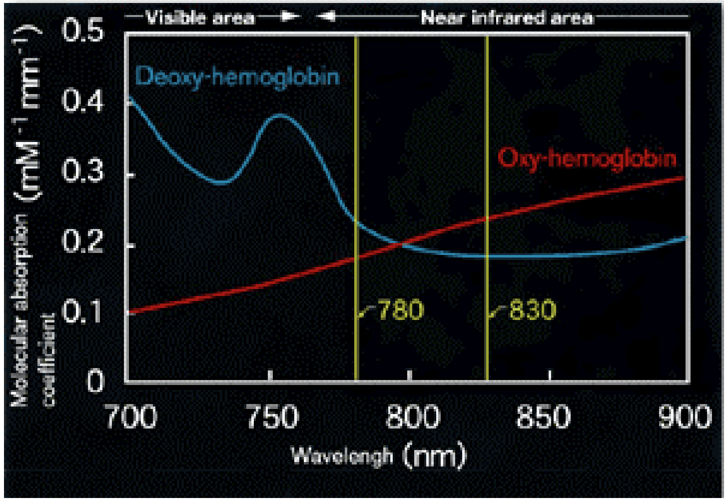
Introduction

- Functional Neuroimaging
  - fNIRS
    - Non-invasive
    - Measure correlates of neuronal activity
    - Low spatial, but potentially high temporal resolution
    - Inexpensive
    - Less distressing for patients or volunteers

Introduction

- The fNIRS Principle
  - NIR light (650-950 nm) can pass through the skull and reach the cerebral cortex up to a depth of 3 cm
  - NIR light absorption spectra of *HbR* and *HbO_2* are distinct
  - Using the modified Beer-Lambert law, it's possible to quantifiy the changes in the concentrations of these hemoglobin agents





Introduction

- Motivation behind fNIRS Study
  - Both fMRI and fNIRS measure a correlate of oxygen availability in a particular brain region
  - *HbR* ↓, then BOLD signal of fMRI ↑

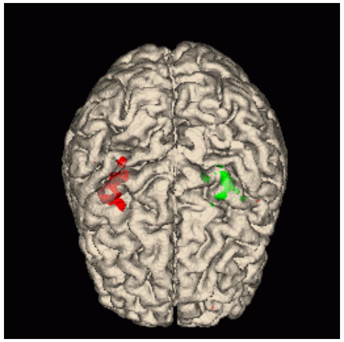
    [Boynton et al., 1996]
  - Simultaneous BOLD and fNIRS recordings do exhibit strong correlations

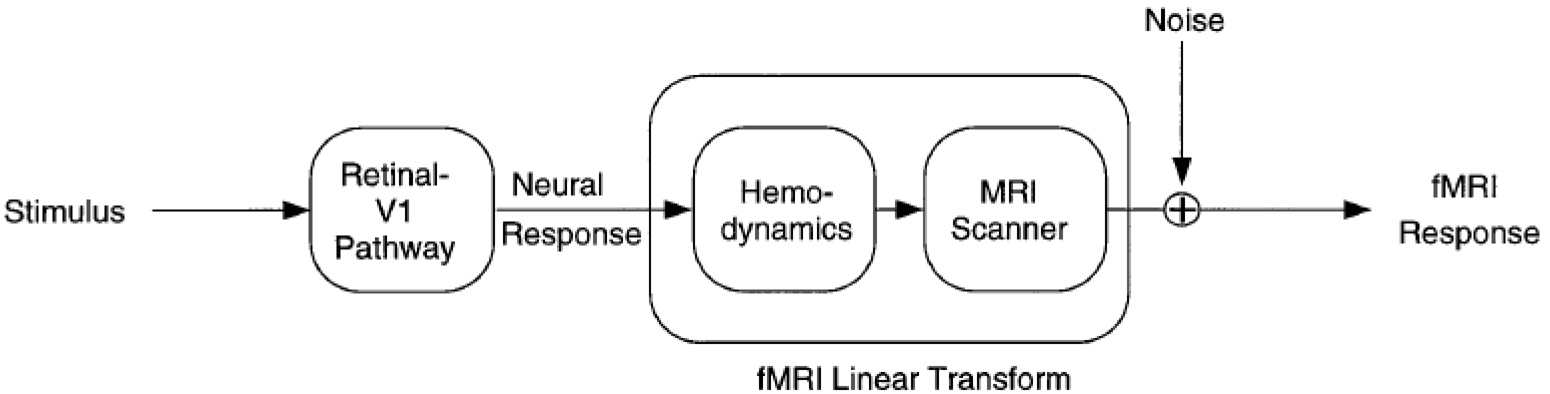
    [Strangman et al., 2002]

BOLD: **B**lood **O**xygen **L**evel **D**ependent

Introduction

- Motivation behind fNIRS Study
  - Two problems of fMRI
    - Activity Detection → functional activity maps
    - **B**rain **H**emodynamic **R**esponse (BHR) Function Estimation





[Boynton et al., 1996]

Introduction

- Motivation behind fNIRS Study
  - From the perspective of fNIRS
    - Activity detection is not an issue unless more spatial resolution is provided
    - BHR function may be estimated more accurately thanks to high temporal resolution
    - fNIRS can be more efficiently used in characterizing the baseline physiology
      - *HbO_2*, *HbR*, *blood volume*, *oxygenation*

Outline

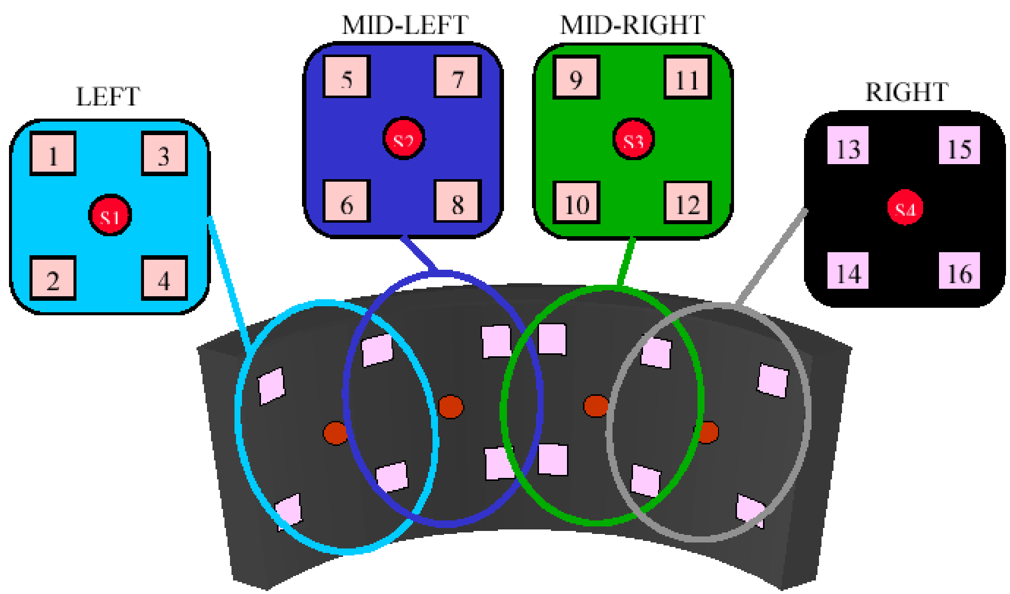
- ✓ Introduction
- **Statistical Characterization of fNIRS Data**
- Time-Frequency Characterization
- Functional Activity Estimation
- Conclusion

Statistical Characterization

- **How are data acquired?**
- Does the signal result from a *stationary* process?
- Is the signal process *Gaussian*?

Statistical Characterization

- The fNIRS Device
  - Light sources and photodetectors
  - Measurements at 730 nm, 805 nm, 850 nm
  - Modified Beer-Lambert Law

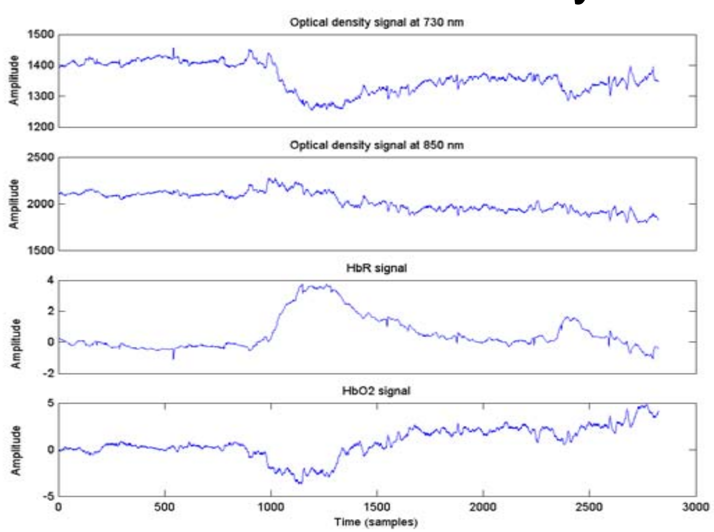


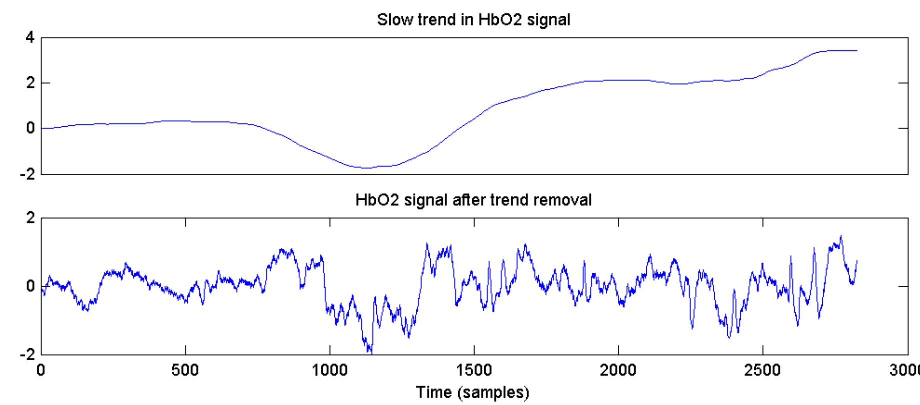
Statistical Characterization

- Target Categorization task
  - Context stimuli OOOOO
    - Avoids habituation effects
    - Comes every 1.5 secs
  - Target stimuli XXXXX
    - Expected to trigger functional activity → BHR
    - 8 sessions, 8 trials per session → 64 instances per experiment
    - In a given session, random onsets every 18-29 secs
    - The target arrival pattern is the same for every session
  - Both types last 0.5 sec → impulsive stimulus
- Sampling rate F_s=1.7 Hz
- An experiment lasts ~25 minutes
- 16×3 optical density signals per experiment, 5 subjects

Statistical Characterization

- Preprocessing of fNIRS Data
  - Elimination of corrupted data
  - Applying MBLL to the raw measurements at 730 nm and 850 nm
    - *HbR*
    - ✓ *HbO_2*
    - 72 *Hb*-component signals remain
  - Trend removal by moving average filtering





Statistical Characterization

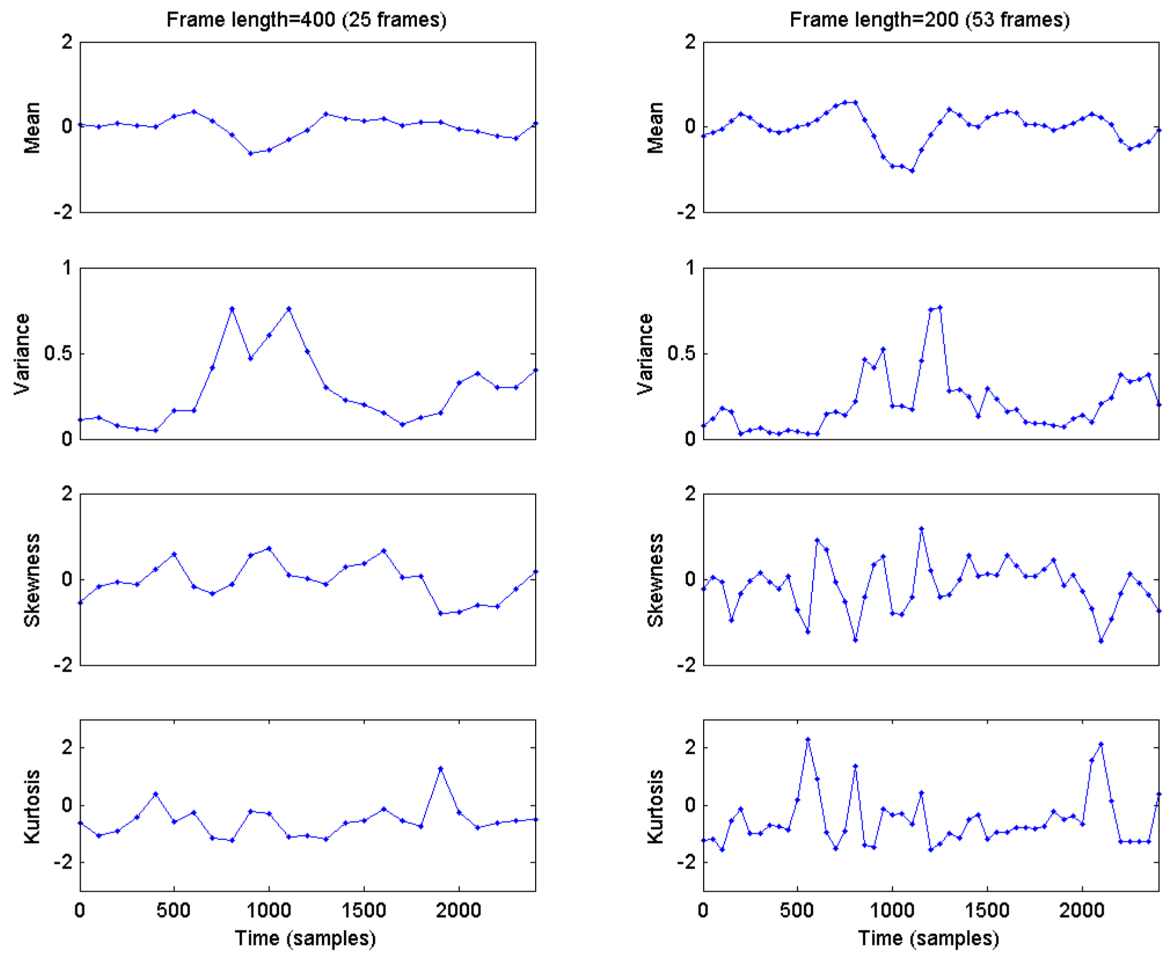
- ✓ How are data acquired?
- **Does the signal result from a *stationary* process?**
- Is the signal process *Gaussian*?

Statistical Characterization

- Stationarity of fNIRS-HbO_2 Signals
  - Strict-sense vs. Wide-sense
  - Graphical investigation
    - Profiles of short-time estimates of statistics up to 4^{th} order
      - *Mean*
      - *Variance*
      - *Skewness*
      - *Kurtosis*
  - Run tests

Statistical Characterization

- Graphical Investigation of Stationarity



Statistical Characterization

- Run tests at significance level $\alpha = 0.01$
  - 50 frames of length $2N$ per signal
    - 3600 cases to test

Frame length $2N$	Number of times the stationarity hypothesis is retained	Test statistic R		The range of R for the stationarity hypothesis to be retained
		Mean	Std. Dev.	
400	1	39	28	177-224
200	19	22	16	84-117
100	82	14	9	39-62
50	326	9	6	17-34
30	793	7	4	9-22

  - *HbO_2* signals, definitely, are non-stationary unless short observation window is chosen

Statistical Characterization

- ✓ How are data acquired?
- ✓ Does the signal result from a *stationary* process?
  - ➔ The signals are globally non-stationary
  - ➔ Short-time processing is plausible (30-50 samples)
- **Is the signal process *Gaussian*?**

Statistical Characterization

- Graphical Investigation of Gaussianity (normality)
  - Normal probability plot

- Hypothesis Testing

$$H_0 : \text{Gaussianity Hypothesis}$$

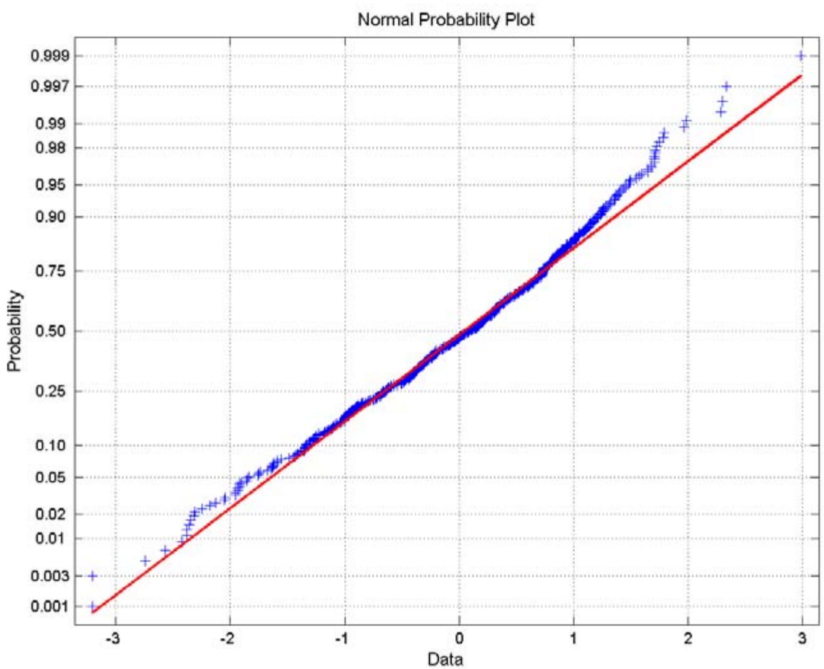
  - Kolmogorov-Smirnov (*K-S*) Test
  - Jarque-Bera (*J-B*) Test

  → require i.i.d. data

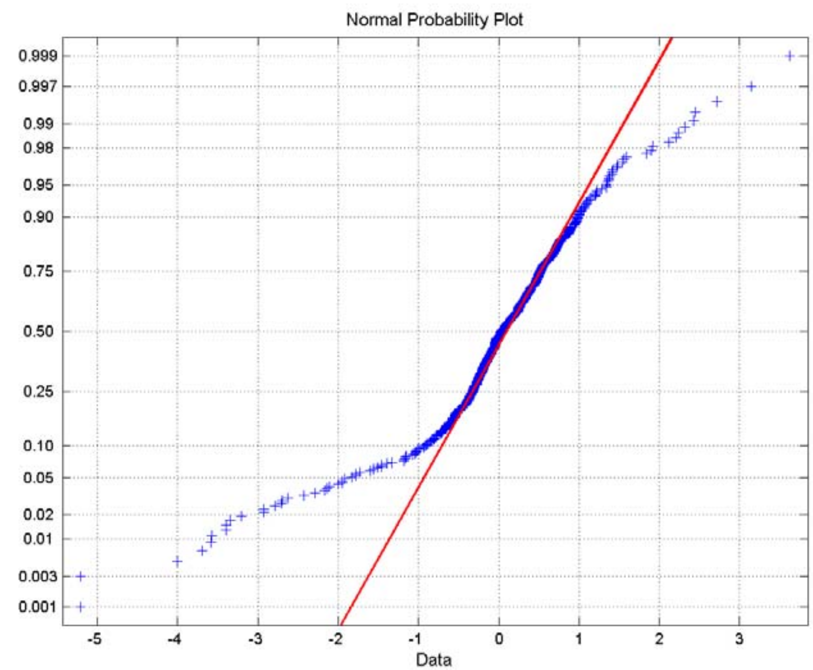
  - Hinich's test → designed for time-series data

Statistical Characterization

- Graphical Investigation of Normality



A collection of randomly selected HbO_2 samples



Another collection of randomly selected HbO_2 samples

Statistical Characterization

- *K-S* Test Results

	Signal Set					
	Γ^1	Γ^2	Γ^3	Γ^4	Γ^5	Γ
Number of records	150	120	130	160	160	720
Number of times H_0 retained	72	99	81	84	33	398
Result of the combined tests (based on P_{ks})	Reject H_0 at significance 10^{-11}	Reject H_0 at significance 0.02	Reject H_0 at significance 10^{-10}	Reject H_0 at significance 10^{-25}	Reject H_0 at significance 10^{-79}	Reject H_0 at significance 10^{-67}

Statistical Characterization

- *J-B* Test Results

	Signal Set					
	Γ^1	Γ^2	Γ^3	Γ^4	Γ^5	Γ
Number of records	150	120	130	160	160	720
Number of times H_0 retained	44	43	20	24	4	143
Result of the combined tests (based on P_{jb})	Reject H_0 at significance 10^{-36}	Reject H_0 at significance 10^{-25}	Reject H_0 at significance 10^{-60}	Reject H_0 at significance 10^{-91}	Reject H_0 at significance 10^{-225}	Reject H_0 at significance 10^{-286}

  – *J-B* test has a more pronounced tendency to reject Gaussianity

Statistical Characterization

- Hinich Test Results

	Signal Set					
	Γ^1	Γ^2	Γ^3	Γ^4	Γ^5	Γ
Number of records	750	600	650	800	800	3600
Number of times H_0 retained	236	238	297	468	359	1583
Result of the combined tests (based on P_{hin})	Reject H_0 at significance 10^{-165}	Reject H_0 at significance 10^{-83}	Reject H_0 at significance 10^{-103}	Reject H_0 at significance 10^{-43}	Reject H_0 at significance 10^{-88}	Reject H_0 at significance 0

Statistical Characterization

- ✓ How are data acquired?
- ✓ Does the signal result from a *stationary* process?
  - ➔ The fNIRS-HbO_2 signals are globally non-stationary
  - ➔ Short-time processing is plausible (30-50 samples)
- ✓ Is the signal process Gaussian?
  - ➔ The fNIRS-HbO_2 process is non-Gaussian

Outline

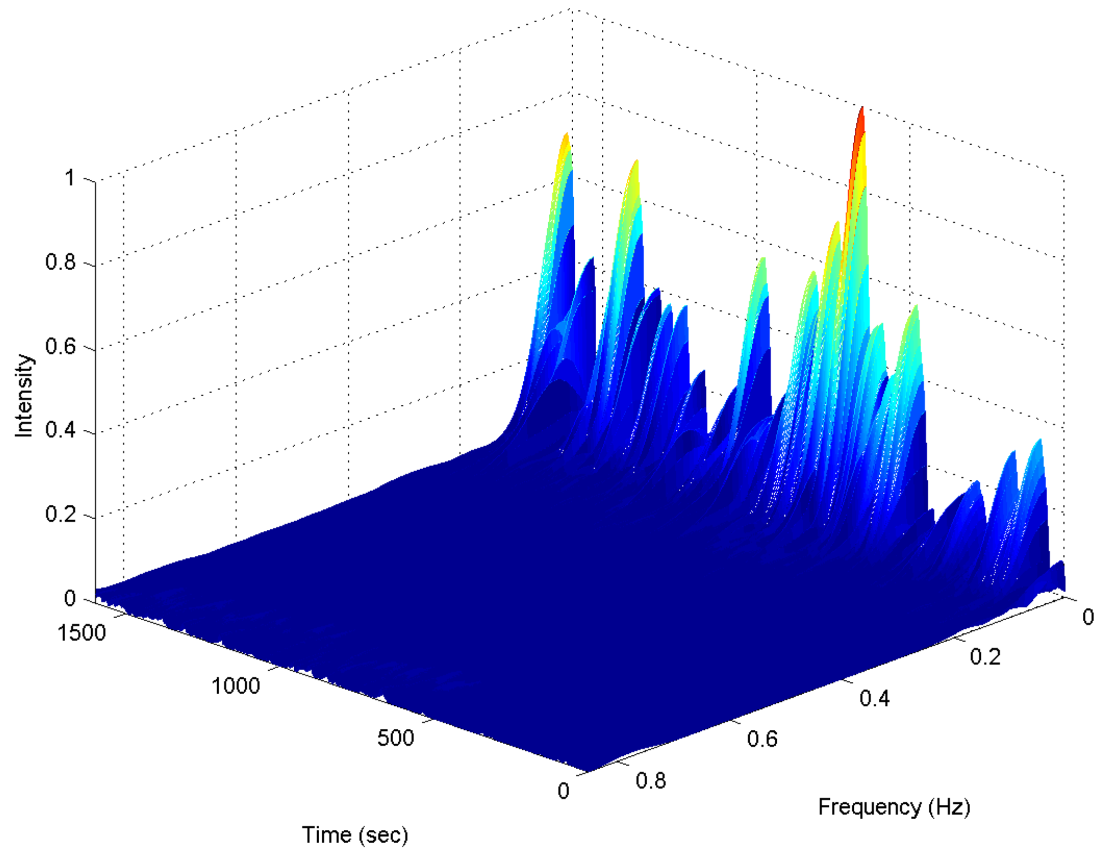
- ✓ Introduction
- ✓ Statistical Characterization of fNIRS Data
- **Time-Frequency Characterization**
- Functional Activity Estimation
- Conclusion

Time-Frequency Characterization

- **The Typical fNIRS-*HbO_2* Spectrum**
- Selection of Relevant Frequency Bands
- Does fNIRS measure cognitive activity?

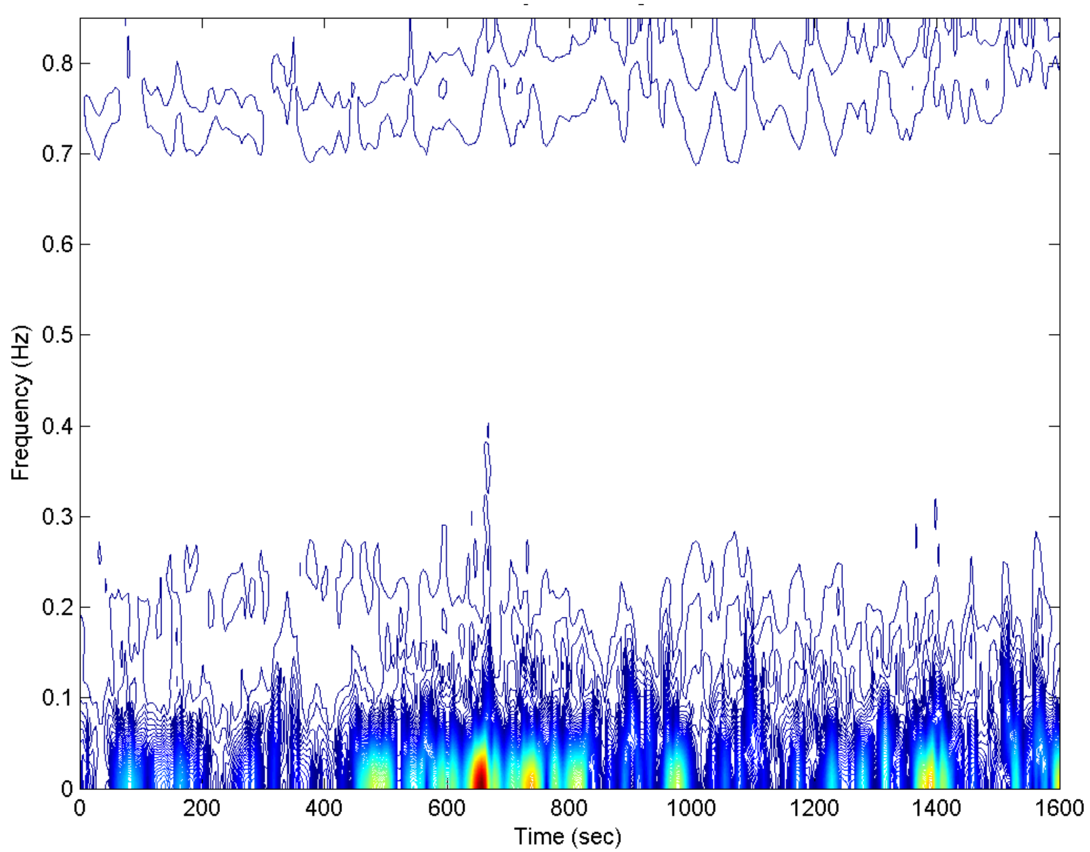
Time-Frequency Characterization

- The Typical fNIRS-HbO_2 Spectrum
  - 3D Normalized Intensity Graph



Time-Frequency Characterization

- The Typical fNIRS-HbO_2 Spectrum
  - Intensity Level Diagram



Time-Frequency Characterization

- ✓ The Typical fNIRS-HbO_2 Spectrum
  - ➔ The spectrum is essentially low-pass (<100 mHz)
  - ➔ In the range of 700-850 mHz, there is a slight increase in the time-frequency plane
- **Selection of Relevant Frequency Bands**
- Does fNIRS measure cognitive activity?

Time-Frequency Characterization

- Selection of Relevant Frequency Bands
  - Parsing the signal spectrum into dissimilar subbands
  - Relative power profile per band

$$R_n(t) = \frac{I_n(t)}{I(t)}$$

$I_n(t)$: Time-series of the power at the n^{th} subband

$I(t)$: Time-series of the total power

Time-Frequency Characterization

- Selection of Relevant Frequency Bands
  - Dissimilarity is measured by

$$d(\mathbf{R}_p,\mathbf{R}_q)=1-\frac{\langle \mathbf{R}_p,\mathbf{R}_q\rangle}{\|\mathbf{R}_p\|.\|\mathbf{R}_q\|}$$

  - We evaluate $R_n(t)$ in

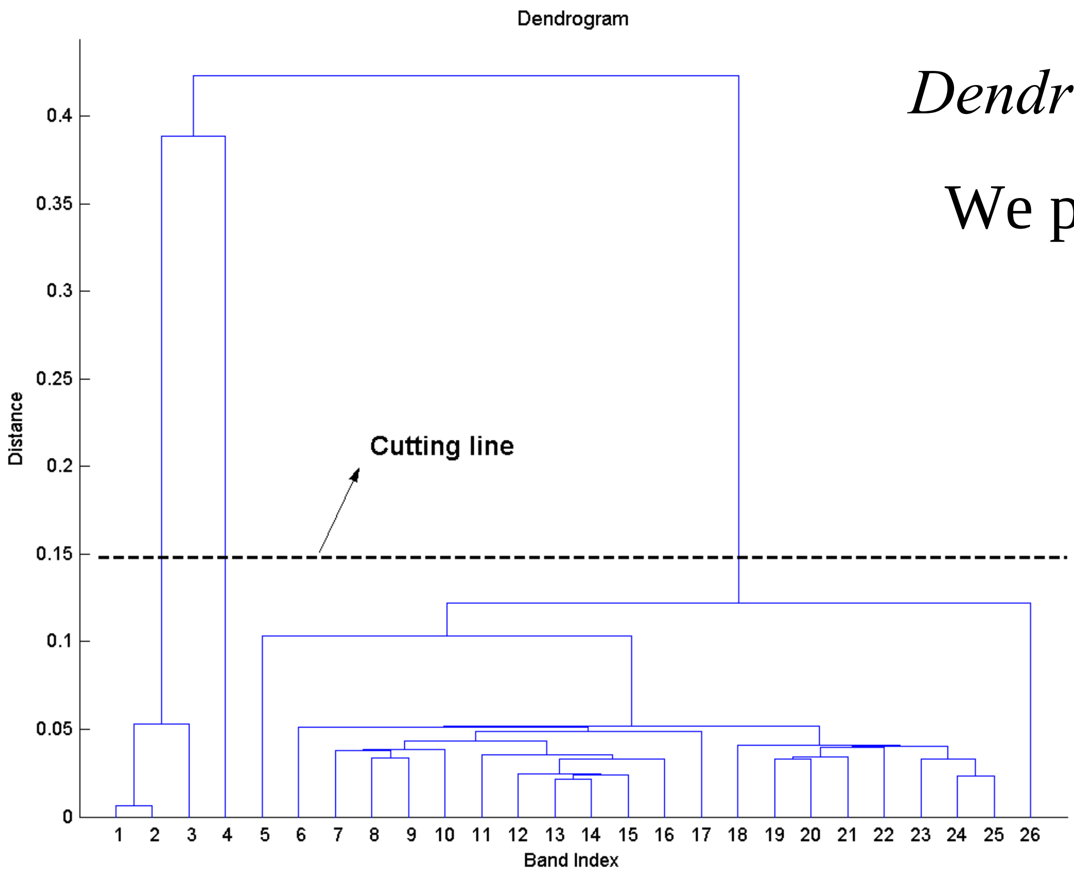
$$\underbrace{0-10\ \mathrm{mHz}, 10-20\ \mathrm{mHz}, \cdots, 240-250\ \mathrm{mHz}}_{\textbf{25 narrow bands of width 10 mHz}},\ \underbrace{250\text{-}850\ \mathrm{mHz}}_{\textbf{One large band}}$$

Time-Frequency Characterization

- Selection of Relevant Frequency Bands
  - Agglomerative clustering: For a given signal
    1. Assign each $R_n(t)$ to its own cluster
    2. Compute all pairwise distances between each cluster
    3. Merge the two clusters until only one cluster remains, i.e., return to ii.
       - Single linkage criterion
  - The end product is a dendrogram

Time-Frequency Characterization

- Selection of Relevant Frequency Bands



Dendrogram:

We prune it! $C = 3$

Time-Frequency Characterization

- Selection of Relevant Frequency Bands
  - We have 72 signals → 72 different partitionings
  - Each partitioning consists of 3 subbands → 72×3 candidates
    We count the number of occurences for each subband
  - We identify possible partitionings where
    - The bands are non-overlapping
    - The bands collectively cover the whole spectrum

Spectrum partitioning	Votes	Percentage
0-30 mHz, 30-40 mHz, 40-250 mHz, 250-850 mHz	142	65.7 %
0-40 mHz, 40-250 mHz, 250-850 mHz	114	52.8 %
0-30 mHz, 30-250 mHz, 250-850 mHz	86	39.8 %
0-40 mHz, 40-850 mHz	63	29.2 %
0-50 mHz, 50-250 mHz, 250-850 mHz	48	22.2 %

Time-Frequency Characterization

- The Canonical Bands of fNIRS Signals

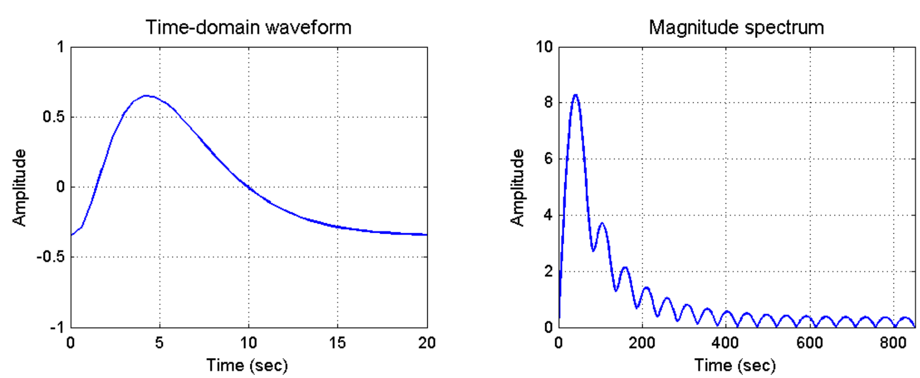
Bands (mHz)	0 -30 *A*	30-40 *B*	40-250 *C*	250-850 >> *D*
Votes	35	28	35	44

Baseline

Cognitive activity

Cognitive activity
Respiratory signal
Vasomotion

Random fluctuations
Cardiac pulses



Time-Frequency Characterization

- ✓ The Typical fNIRS-HbO_2 Spectrum
  - ➔ The spectrum is essentially low-pass (<100 mHz)
  - ➔ In the range of 700-850 mHz, there is a slight increase in the time-frequency plane
- ✓ Selection of Relevant Frequency Bands
  - ➔ *A*-Band: 0-30 mHz, *B*-Band: 30-40 mHz, *C*-Band: 40-250 mHz, *D*-Band: 250-850 mHz
- **Does fNIRS measure cognitive activity?**

Time-Frequency Characterization

- Evidence of cognitive activity
  - Cognitive stimuli are quasi-periodic
    - Inter-Target Interval (ITI): uniform in (30,50) samples
  - We expect to find evidences of such periodicity in the HbO_2 signals by LSPE
  - Bands *B* and *C* are more likely to reflect this information
    - We prefilter the signals in the *BC*-Band, i.e., 30-250 mHz
    - Prefiltering helps also to mitigate non-stationarity

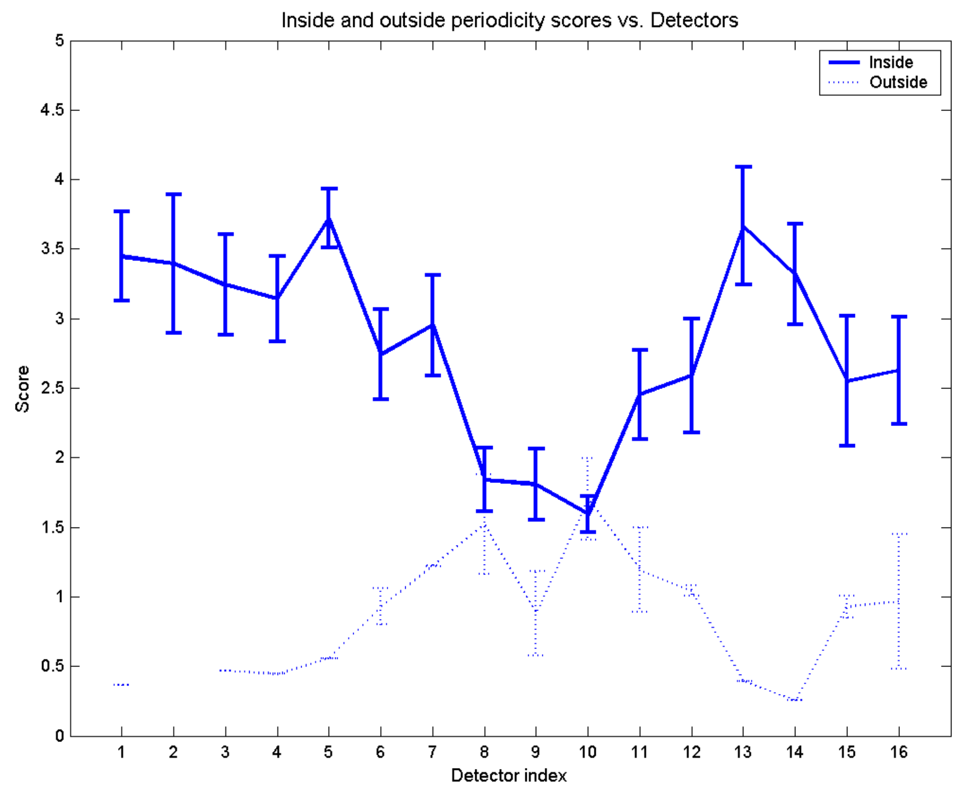
LSPE: **L**east-**S**quares **P**eriodicity **E**stimation

Time-Frequency Characterization

- Evidence of cognitive activity
  - Treatment of real data
    - session-by-session
      - Another way to mitigate non-stationarity
    - in the (20, 60) samples range
    - Local maxima selection, (-3, 3) samples range
    - A small threshold at 0.1
    - For each session, we let the algorithm return the period with largest confidence
      - 8 candidate periods per signal

Time-Frequency Characterization

- S_{in} and S_{out} profiles for Subject 4



Time-Frequency Characterization

- Evidence of cognitive activity

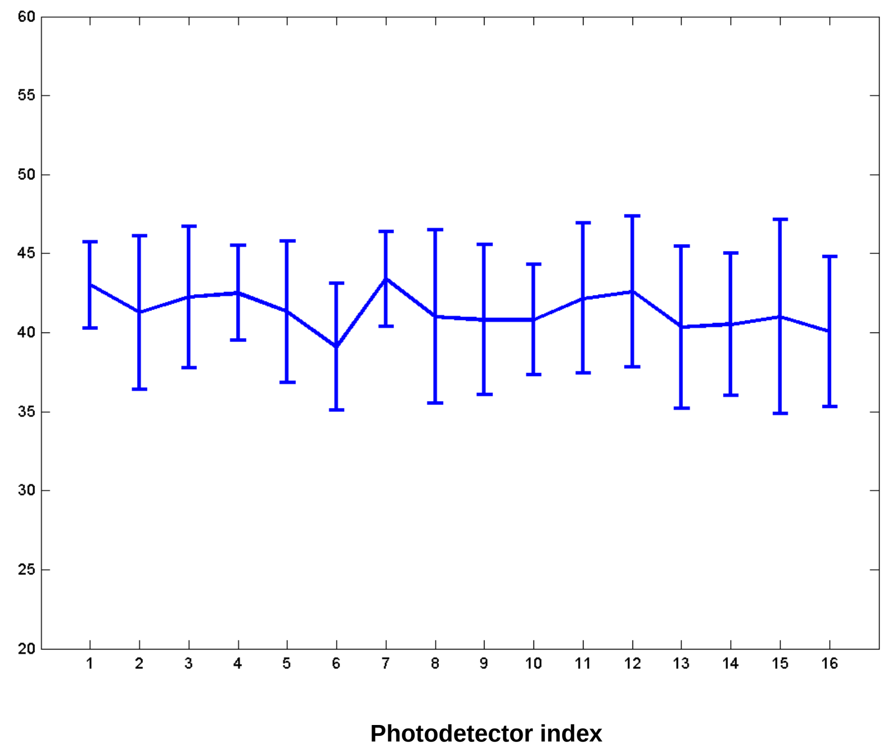
Responsive subjects/photodetectors

Subject		Photodetector quadruples			
Index	Alias	left (1-4)	mid-left (5-8)	mid-right (9-12)	right (13-16)
1	AA005	3 and 4	5 to 8 (all)	10, 11 and 12	16
2	GY002	-not any-	8	9,11 and 12	13 to 16 (all)
3	KI003	4	5 to 8 (all)	9 to 12 (all)	15 and 16
4	KP001	1 to 4 (all)	5 to 8 (all)	9, 11 and 12	13 to 16 (all)
5	MJ007	1 to 4 (all)	5 and 7	9, 11 and 12	13 to 16 (all)

Time-Frequency Characterization

- Evidence of cognitive activity
  - Inside periodicities averaged over all subjects for a given photodetector

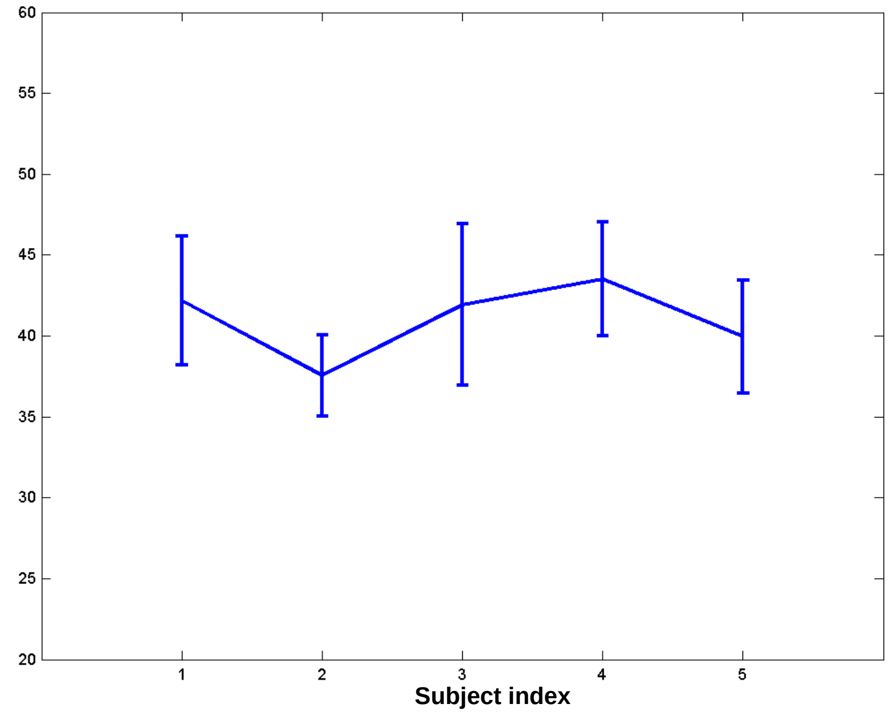
$$\overline{P}_{subjects}(k)$$



Time-Frequency Characterization

- Evidence of cognitive activity
  - Inside periodicities averaged over all photodetectors for a given subject

$$\overline{P}_{\text{detectors}}(j)$$



Time-Frequency Characterization

- ✓ The Typical fNIRS-HbO_2 Spectrum
  - ➔ The spectrum is essentially low-pass (<100 mHz)
  - ➔ In the range of 700-850 mHz, there is a slight increase in the time-frequency plane
- ✓ Selection of Relevant Frequency Bands
  - ➔ *A*-Band: 0-30 mHz, *B*-Band: 30-40 mHz, *C*-Band: 40-250 mHz, *D*-Band: 250-850 mHz
- ✓ Does fNIRS measure cognitive activity?
  - ➔ For some subjects/detectors, we encountered to the evidence of protocol-induced periodicity

Outline

- ✓ Introduction
- ✓ Statistical Characterization of fNIRS Data
- ✓ Time-Frequency Characterization
- **Functional Activity Estimation**
- Conclusion

Functional Activity Estimation

- The problem
  - We try to estimate cognitive-activity related waveforms (CArW)
  - CArW are the counterparts of BHR
  - We use fNIRS vectors that consist of m signal samples just after the target onsets

Functional Activity Estimation

- We consider two approaches
  - Independent Component Analysis (ICA)
  - Clustering of cubic B-spline coefficients
- We consider different types of datasets

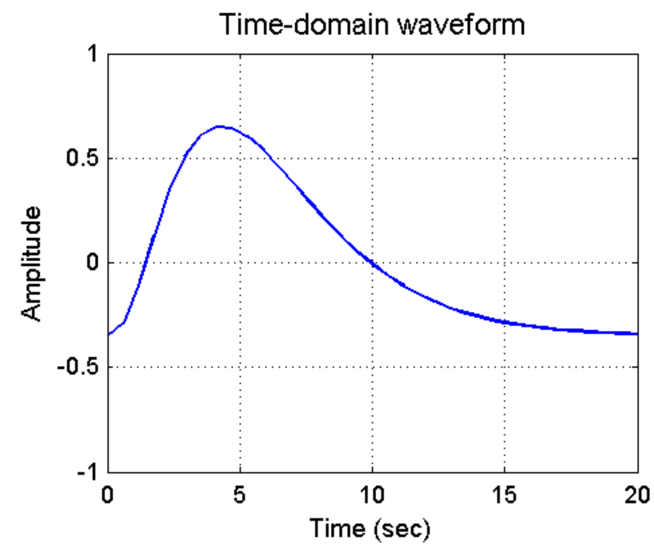
Subject	Photodetector quadruples				
Index	left (1-4)	mid-left (5-8)	mid-right (9-12)	right (13-16)	all (1-16)
1	(H1): X^1_{left}	(H1): $X^1_{mid-left}$	(H1): $X^1_{mid-right}$	(H1): X^1_{right}	(H2): X^1
3	(H1): X^3_{left}	(H1): $X^3_{mid-left}$	(H1): $X^3_{mid-right}$	(H1): X^3_{right}	(H2): X^3
4	(H1): X^4_{left}	(H1): $X^4_{mid-left}$	(H1): $X^4_{mid-right}$	(H1): X^4_{right}	(H2): X^4
1,3 and 4	(H3): X_{left}	(H3): $X_{mid-left}$	(H3): $X_{mid-right}$	(H3): X_{right}	

- We rank the estimated vectors based on their similarity to the Gamma waveform model

Functional Activity Estimation

- Ranking the estimated vectors
  - The Gamma Function Model

$$h(t) = \begin{cases} A(t-T)^2 e^{-(t-T)/\tau} & \text{for } t \geq T \\ 0 & \text{for } t < T \end{cases}$$



$$A : \text{Gain}$$
$$T : \text{Delay} \ (\sim 2\text{-}3 \ \text{secs})$$
$$\tau : \text{Time-constant in the } (1, 4) \text{ range}$$

$$\min_{A,T,\tau} \arg \sum_{l=1}^{m} \left[z_l - h_l(A, T, \tau) \right]^2$$

Functional Activity Estimation

- ICA Approach

Data vector
*m*x1 *vector*

Weights
*n*x1 *vector*

$$\mathbf{x} = \begin{bmatrix} \underbrace{\mathbf{a}_1}_{\text{CArW}} & \underbrace{\mathbf{a}_2}_{\text{Baseline}} & \cdots & \underbrace{\cdots \quad \mathbf{a}_n}_{\text{Other neurophysiological components}} \end{bmatrix} \begin{bmatrix} s_1 \\ s_2 \\ \vdots \\ \vdots \\ s_n \end{bmatrix} = \mathbf{As}$$

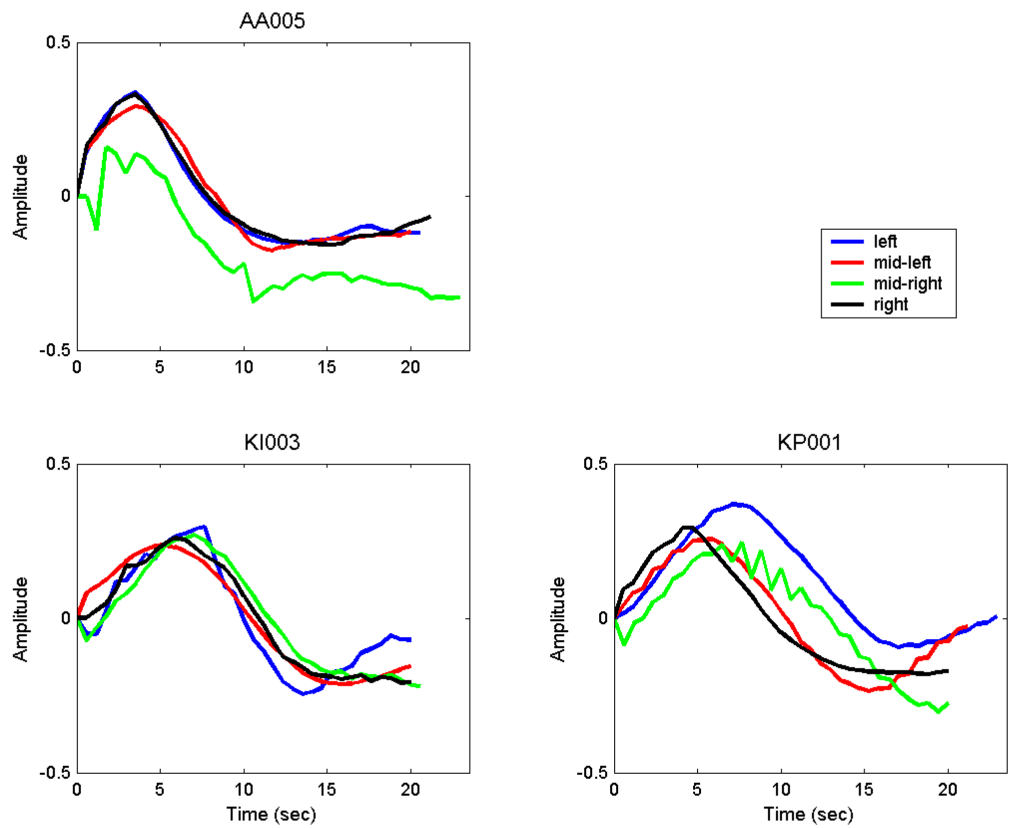
Functional Activity Estimation

- ICA Settings

Parameter	Value (or range)
Dimensionality of input vectors m	40
Reduced dimension n	4
Number of basis vectors n	4
Range for delay T	(0,3) seconds or (0,5) samples
Range for time constant τ	(1,4)

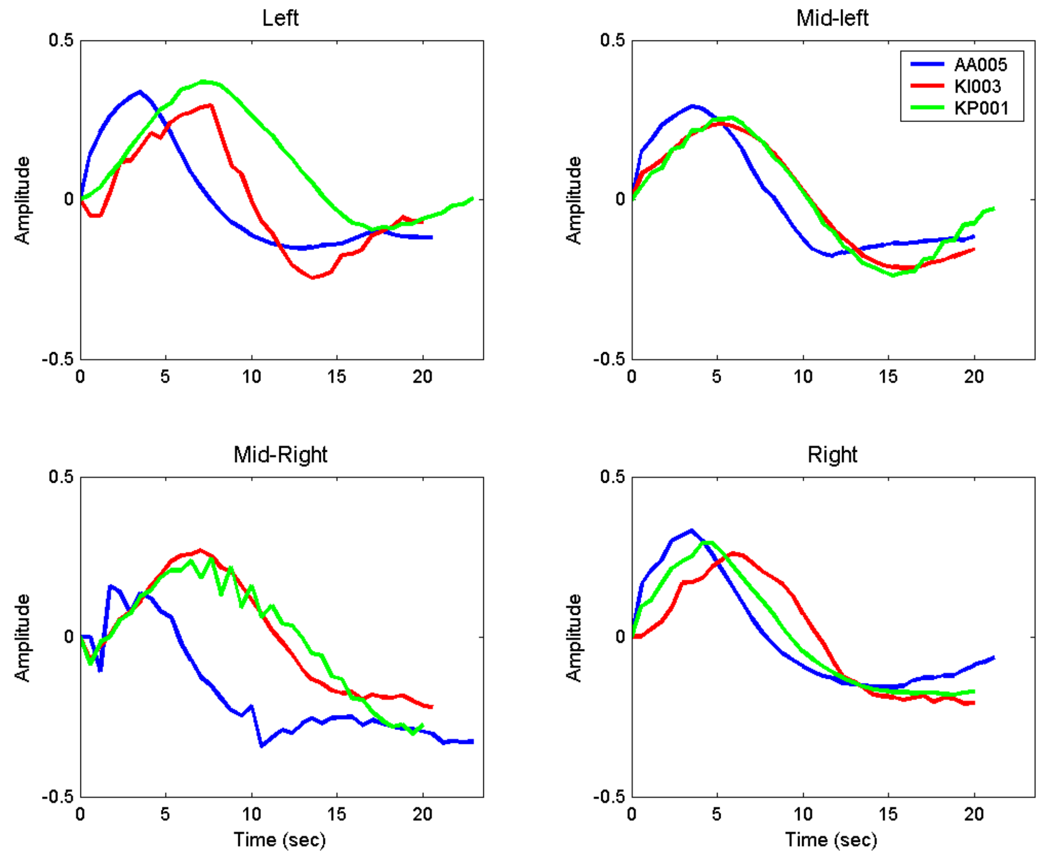
Functional Activity Estimation

- ICA Results: (H1)-type datasets subject-by-subject



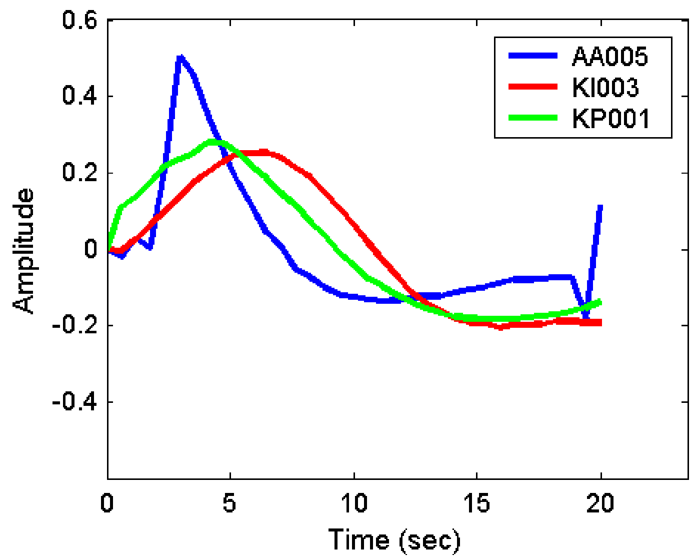
Functional Activity Estimation

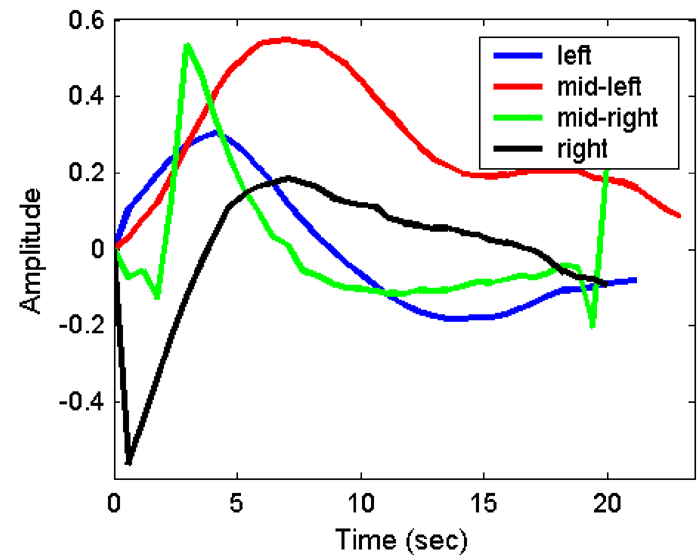
- ICA Results: (H1)-type datasets quadruple-by- quadruple



Functional Activity Estimation

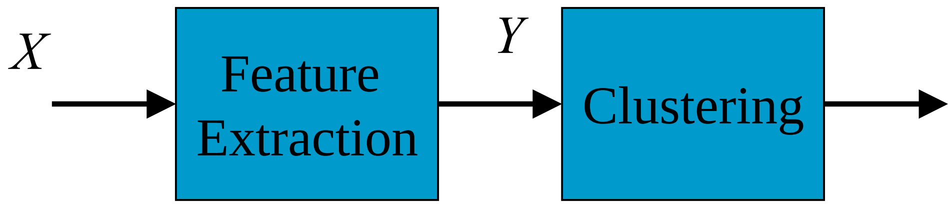
- ICA Results: (H2)-type and (H3)-type datasets





Functional Activity Estimation

- Clustering Approach



$$Q = \{ Q_c, \mathbf{q}_c \mid c = 1, \ldots, C \}$$

Q_c : c^{th} Cluster

$\mathbf{q}_c$: centroid of Q_c

- Features → B-spline coefficients [Unser et al., 1993]
  - emphasize functional nature of data
- Agglomerative clustering
  - Distance metric $d[\mathbf{y}(i), \mathbf{y}(j)] = 1 - \dfrac{\langle \mathbf{y}(i), \mathbf{y}(j) \rangle}{\|\mathbf{y}(i)\| . \|\mathbf{y}(j)\|}$
  - Average-linkage criterion

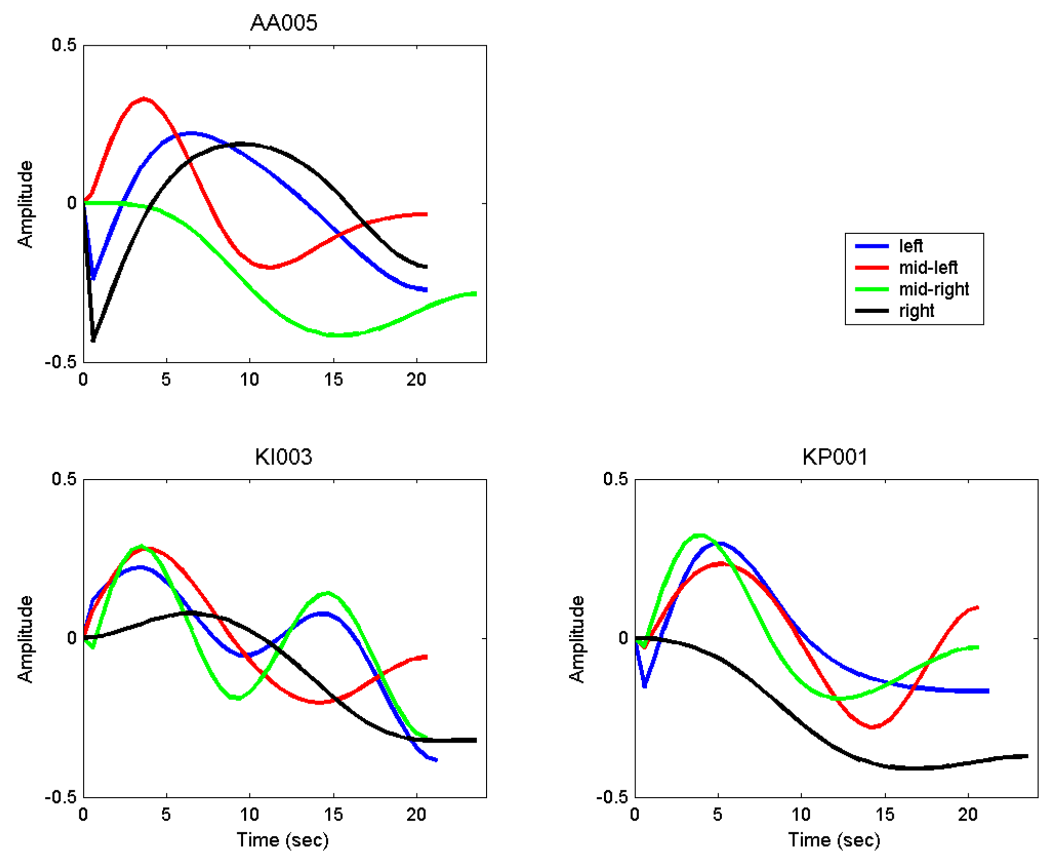
Functional Activity Estimation

- Clustering Settings

Parameter	Value (or range)
Dimensionality of input vectors m	41
Reduced dimension n	5
Number of clusters C	5
Distance metric	One-minus-the-normalized correlation coefficient
Closeness criterion	Average linkage
Range for delay T	(0,3) seconds or (0,5) samples
Range for time constant τ	(1,4)

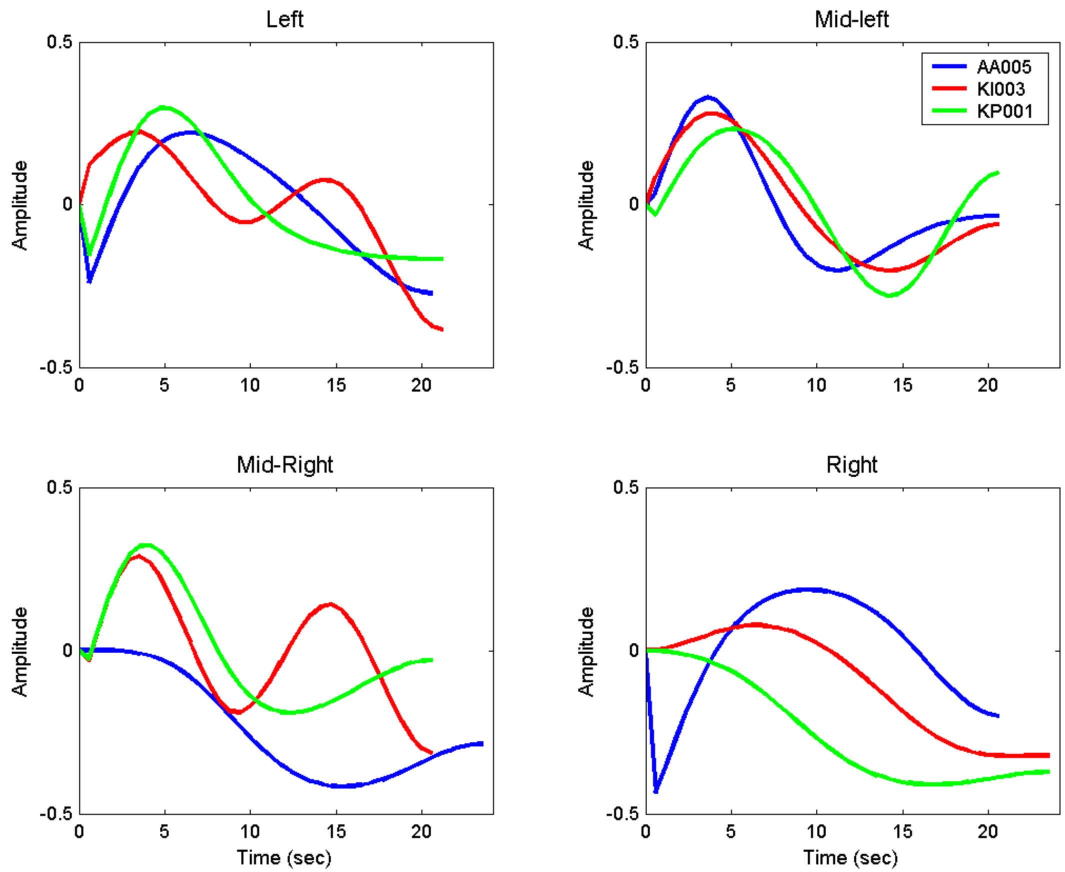
Functional Activity Estimation

- Clustering Results: (H1)-type datasets subject-by-subject



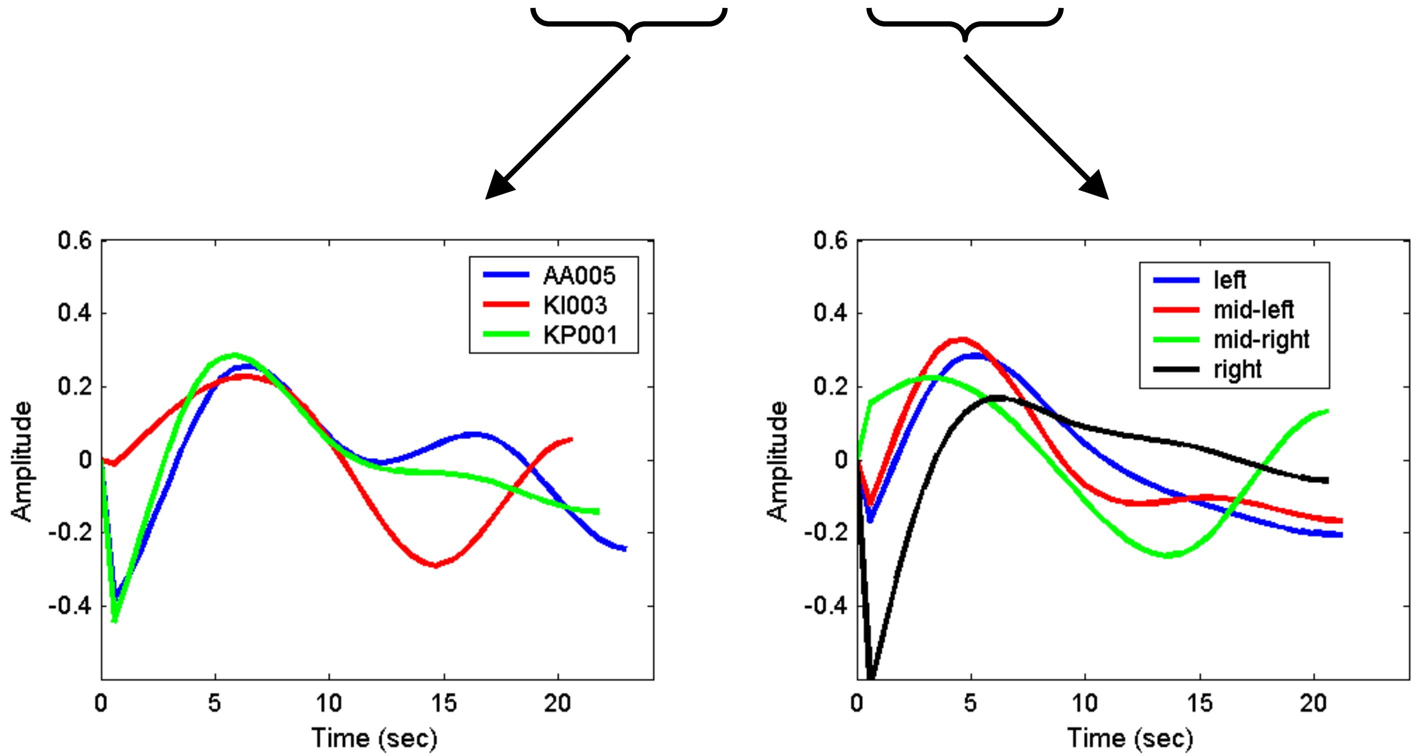
Functional Activity Estimation

- Clustering Results: (H1)-type datasets quadruple-by-quadruple



Functional Activity Estimation

- Clustering Results: (H2)-type and (H3)-type datasets



Functional Activity Estimation

- In summary;
  - Both approach yield CArWs that are similar to BHR modeled as the Gamma function
  - ICA is more consistent in the results it produces
  - Both inter-subject and inter-detector variations exist

Outline

- ✓ Introduction
- ✓ Statistical Characterization of fNIRS Data
- ✓ Time-Frequency Characterization
- ✓ Functional Activity Estimation
- **Conclusion**

Conclusion

- fNIRS as a Random Process
- Relevant Spectral Bands
- CArW Extraction
- Future Prospects
- Remarks on Experimental Protocols and Measurements

Conclusion

- fNIRS as a Random Process
  - Stationarity
    - Long-term non-stationarity is most probably due to the baseline
    - Short-time processing is plausible
      - 30 to 50 samples
      - ITI in the cognitive protocol was random in (30, 50) samples

Conclusion

- fNIRS as a Random Process
  - Gaussianity
    - The fNIRS process is non-Gaussian
      - The linear minimum mean-squared error (MSE) estimators will not be globally optimal, in extracting CArW.
      - The use of ICA is plausible in CArW extraction.
    - The underlying distribution is symmetric with heavy tails.

Conclusion

- Relevant Spectral Bands
  - The short-time spectrum is not very helpful in localizing temporal events
  - The Canonical Bands
    - *A*-Band: (0-30 mHz) baseline, independent of task-related activity
    - *B*-Band: (30-40 mHz) fundamental frequency of cognitive activity (the centered Gamma waveform)
    - *C*-Band: (40-250 mHz) protocol-induced periodicity information, respiratory signal, vasomotion
    - *D*-Band: (250-mHz) respiratory signal, random fluctuations, aliased part of the heartbeat signal

Conclusion

- CArW Extraction
  - Inter-subject and inter-quadruple-of-detectors variations exist.
  - In terms of the conformance to Gamma function model, waveforms estimated by ICA are more plausible to be cognitive-activity related than those estimated by clustering.
  - ICA decomposition yields not only the CArW, but also others that can potentially be used to model the baseline interference.
  - The BHR can be more flexibly parametrized as compared to Gamma model which relegates all the characteristics to a single parameter. Instead, B-spline coefficients represent the global waveform while preserving locality property.

Conclusion

- Future Prospects
  - Process Characterization
    - Distribution of fNIRS Data
      - Density estimation
    - Alternative time-frequency features [Blanco et al., 1995]
      - Mean weight frequency profile
      - Main peak frequency profile
      - Monofrequency deviation profile
    - Alternative subband partitioning scheme [Blanco et al., 1998]
      - Wavelet Packet Analysis

Conclusion

- Future Prospects
  - Alternative CArW Extraction Methods
    - ICA of B-spline coefficients
      - ICA → independence assumption seem to be reasonable
      - B-splines → summarize the data very efficiently
    - Fuzzy clustering of B-spline coefficients
      - Crisp clustering may lead to misinterpretation of data
    - Self-Organizing Map
      - Would allow a natural visualization of CArW variations

Conclusion

- Future Prospects
  - Alternative CArW Extraction Methods
    - Bayesian Modeling [Ciuciu et al., 2002]

$$\mathbf{y}_k = \mathbf{h} + \mathbf{C}\mathbf{d}_k + \mathbf{v}_k$$

$\mathbf{y}_k = \left[y_{t_k}, y_{t_k+1}, \cdots, y_{t_k+m-1}\right]^T$: Observed sequence after k^{th} target

$\mathbf{h} = \left[h_0, h_1, \cdots, h_{m-1}\right]^T$: Unknown time-invariant BHR waveform

$\mathbf{C} = \begin{bmatrix} \mathbf{c}_1, \cdots, \mathbf{c}_Q \end{bmatrix}$: A set of orthonormal basis functions

$\mathbf{d}_k = \left[d_{1,k}, d_{2,k}, \cdots, d_{Q,k}\right]^T$: Vector of unknown weights

$\mathbf{v}_k = \left[v_{t_k}, v_{t_k+1}, \cdots, v_{t_k+m-1}\right]^T$: Noise, unwanted random physiological fluctuations

Conclusion

- Future Prospects
  - Alternative CArW Extraction Methods
    - Dynamic Bayesian Modeling

$$\mathbf{h}_{k+1} = \boldsymbol{\Gamma}(k+1,k)\mathbf{h}_k + \mathbf{w}_k$$
$$\mathbf{y}_k = \mathbf{h}_k + \mathbf{C}\mathbf{d}_k + \mathbf{v}_k$$

$$\Gamma(k+1,k) : \text{State - transition matrix}$$
$$\mathbf{w}_k : \text{Process noise}$$

Conclusion

- Future Prospects
  - Alternative CArW Extraction Methods
    - Non-linear neurovascular Coupling Models

$$\mathbf{y}_k = f(\mathbf{X})\mathbf{h} + \mathbf{C}\mathbf{d}_k + \mathbf{v}_k$$

$$\mathbf{X}: \text{Binary stimulus onsets matrix}$$

$$f(\cdot): \text{Non-linear function to model neural pathways}$$

Conclusion

- Remarks on Experimental Protocols and Measurements
  - Simultaneous fNIRS and fMRI recordings
    - Combine advantages of both approaches
  - Stimulus Design for fNIRS [Liu et al., 2001]
    - Block Designs
      - Good detection power, minimum estimation efficiency
    - Randomized Designs
      - Poor detection power, maximum estimation efficiency

    ⇨ Randomized designs are more suitable for fNIRS

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