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Uncovering low-dimensional structure in high-dimensional electrophysiological recordings of epilepsy

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Introduction

Advances in neural recording technology and signal processing now yield very high-dimensional descriptors of brain activity. However, the essential process of visual inspection in a high-dimensional space can become too challenging. Thus, it is useful to derive low-dimensional representations, especially in applications to neurological disorders. Here we compare t-distributed stochastic neighbor embedding (t-SNE) with principal components analysis (PCA) for building low-dimensional representations of high-dimensional descriptors of multi-electrode-array recordings of epilepsy.

Methods

Recordings

We examined 4 x 4 mm^2 10 x 10 signals recorded by a microelectrode array (MEA) from medial temporal cortex in a patient with focal seizures (Figure 1a-b; Truccolo et al., 2014, Wagner et al., 2015). We analyzed a six-hour-and-twenty-minute block containing three spike-and-wave seizures. Figures 2 and 3 depict activity of the first seizure.

LFP/MUA/Highpassed Signal Envelope

For each electrode (number of reliable electrodes nElectrodes=90), from the MEA signal we extracted LFPs (lowpass filtering Fc=500 Hz, Figure 2a) and high-frequency activity (highpass filtering Fc=500 Hz, Figure 2b).

For each highpass filtered electrode signal, we counted, in 1 ms time windows, the number of negative voltage deflections of the high-frequency activity below minus three times its standard deviation (MUA count, Figure 2c), and we extracted the envelope of the high-frequency activity (Figure 2d).

High-Dimensional Feature Extraction

For each electrode, we computed its LFP power spectrum (multitaper method) in one second time windows, in steps of 0.5 seconds. We averaged this power spectrum into ten frequency bands (nFreq=10; 0-4; 4-8; 8-12; 12-18; 18-25; 25-50; 50-80; 80-150; 150-300; 300-500 Hz; Figure 3a). Thus, for each time window the dimension of the power spectrum feature was nElectrodes x nFreq = 90 x 10 = 900).

For each electrode, we summed the MUA counts (Figure 2c) in each one second time window (Figure 3b). Thus, for each time window the dimension of the MUA count feature was nElectrodes = 90.

For all pairs of electrodes and for each one second time window, we computed the correlation of their MUA counts, building a MUA count correlation matrix (Figure 2e). From this matrix we extracted the leading eigenvector (eigenvector centrality; Figure 3c) and leading eigenvalue (Figure 3d). Thus, for each time window the dimension of the MUA count eigenvector centrality feature was nElectrodes = 90, and the dimension of the MUA count leading eigenvalue feature was 1.

As for the MUA count, for the highpassed signal envelope we computed its correlation matrix (Figure 2f) and from this matrix we extracted the eigenvector centrality (Figure 3e) and leading eigenvalue (Figure 3ef).

Combining the previous features, the dimension of the high-dimensional space was 1,172 elements per sample time.

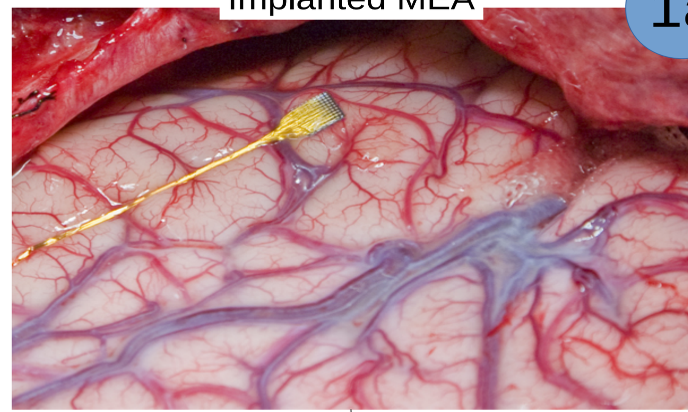
Low-Dimensional Feature Extraction

PCA: we reduced the dimensionality of the high-dimensional space (1,172 dimensions) to a two-dimensional space using PCA (Figure 4a).

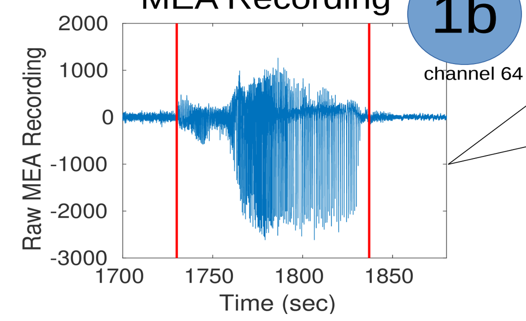
t-SNE: we first reduced the dimensionality of the high-dimensional space (1,172 dimensions) using principal components analysis, keeping 84 principal components accounting for 90% of the variance. We then reduced the dimensionality of this 84-dimensional PCA space to a two-dimensional space using t-SNE (Figure 4b; van der Maaten and Hinton, 2008).

High-Resolution Multi-Electrode_Array Recordings in Humans → **LFP/MUA/ Highpassed_Signal_ Envelope** → **High-Dimensional Feature Extraction (1,172-D space)** → **Low-Dimensional Feature Extraction (2-D space)**

Implanted MEA 1a

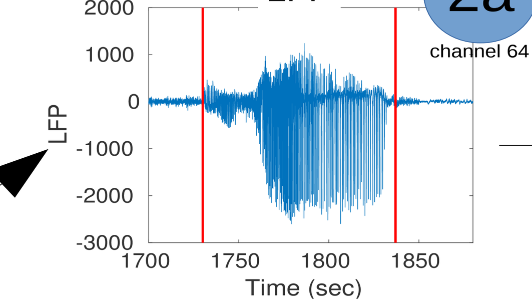


MEA Recording 1b

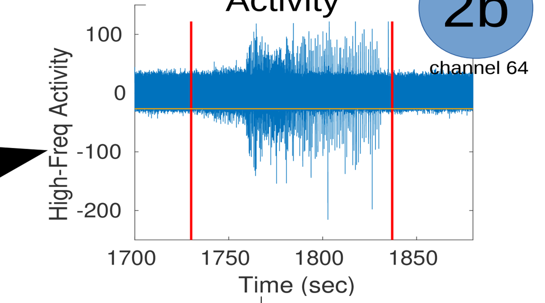


lowpass filtering
highpass filtering

LFP 2a

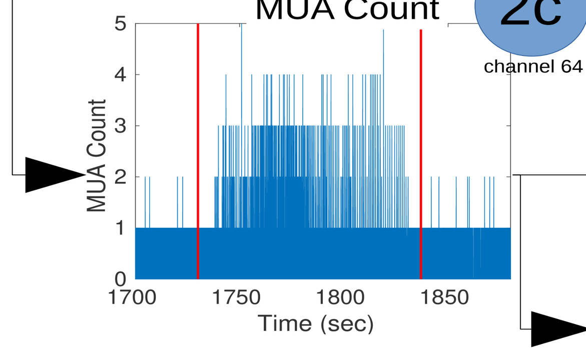


High-Frequency Activity 2b

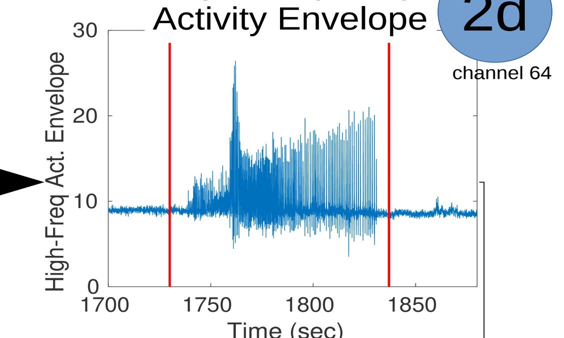


square + lowpass (Fc=10 Hz)
detect deflections (1ms bin)

MUA Count 2c

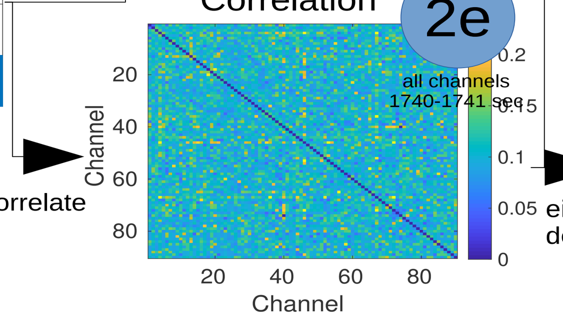


High-Frequency Activity Envelope 2d



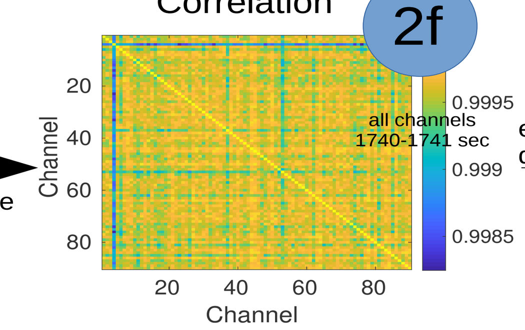
correlate

MUA Count Correlation 2e



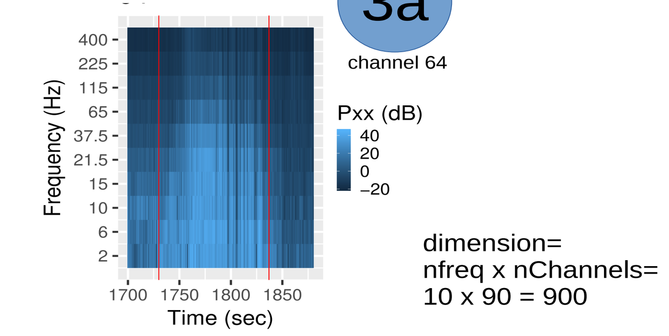
correlate

High-Frequency Activity Envelope Correlation 2f



multi-taper

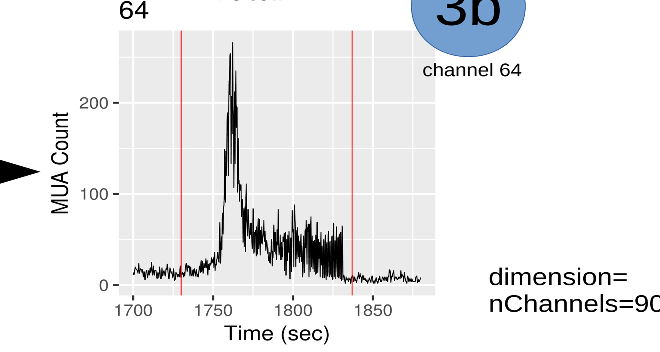
Power Spectrum 3a



dimension= nfreq x nChannels= 10 x 90 = 900

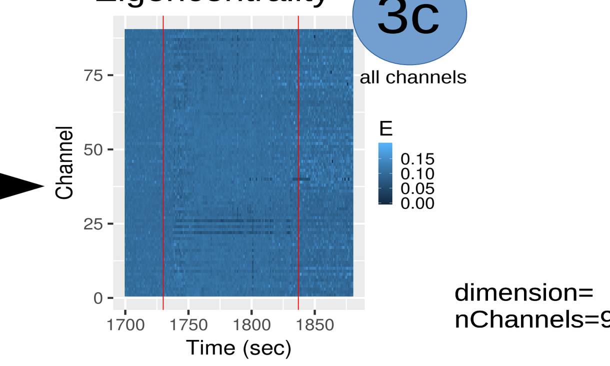
re-bin (1sec bin)

MUA Count Total 3b



dimension= nChannels=90

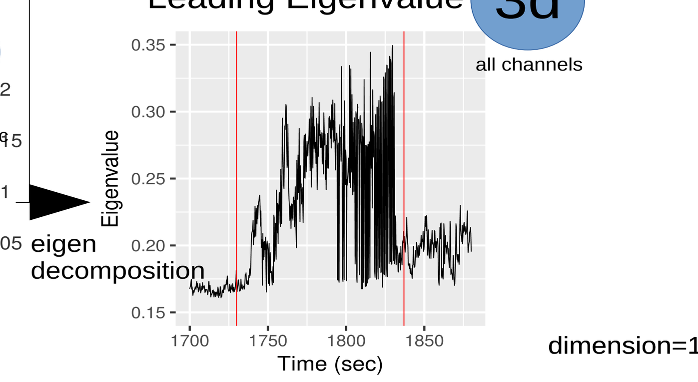
MUA Count Eigencentrality 3c



dimension= nChannels=90

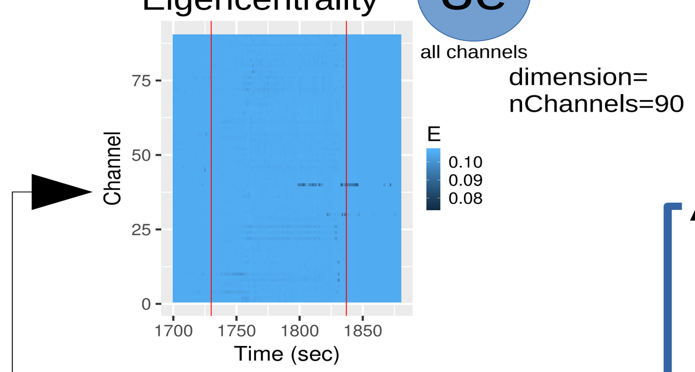
eigen decomposition

MUA Count Leading Eigenvalue 3d



dimension=1

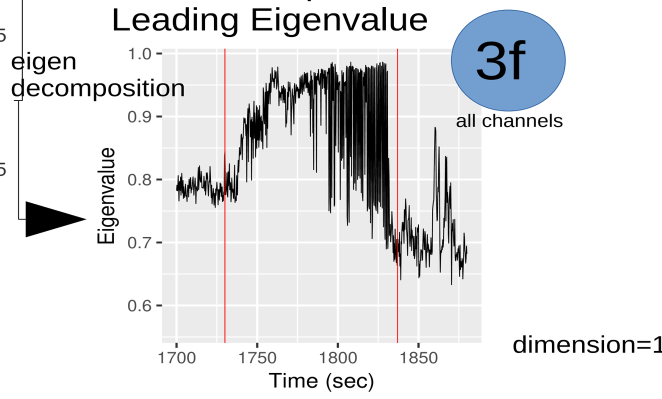
Envelope Eigencentrality 3e



dimension= nChannels=90

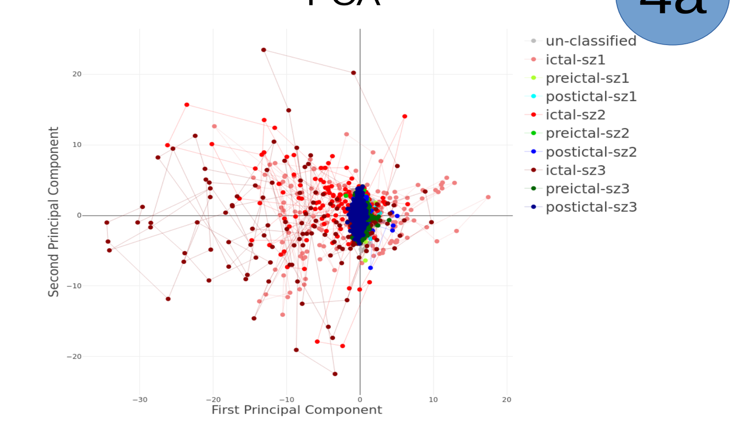
eigen decomposition

Envelope Leading Eigenvalue 3f

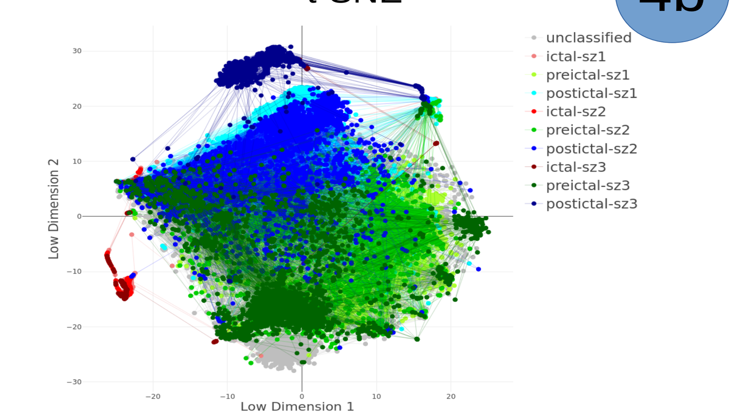


dimension=1

PCA 4a

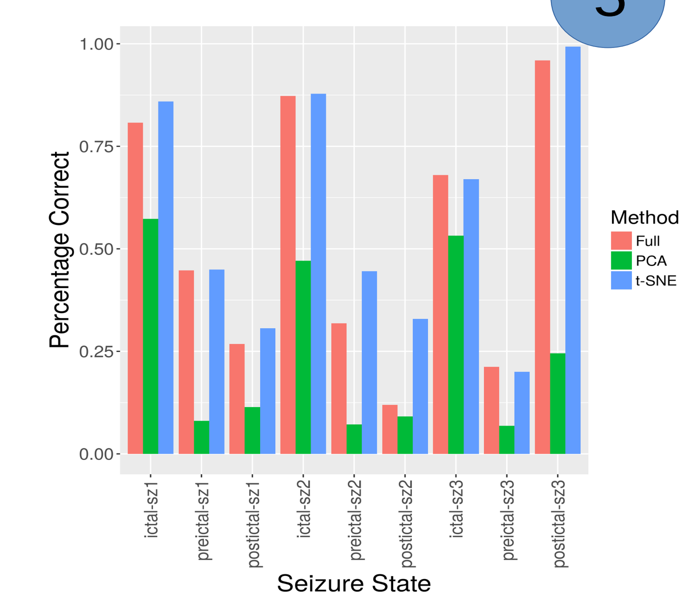


t-SNE 4b



Evaluation

5



Results

Figures 4a and 4b show the 2D-representations obtained by PCA and t-SNE, respectively. Green, red and blue colors correspond to pre-ictal (30 minutes before seizure initiation), ictal (seizure duration), and post-ictal (30 minutes after seizure termination) epilepsy states, respectively. Different shades of color indicate different seizures.

Qualitatively, in the t-SNE low-dimensional representation (Figure 4b) different states appear well separated (green, red and blue clusters are spatially separated), transitions between states are not gradual but abrupt (large separation between green and red clusters and between red and blue clusters) and ictal features are highly stereotypical (i.e., different from non-ictal ones and similar across seizures). In contrast, PCA failed to separate non-ictal features (Figure 4a).

We quantified the quality of the low-dimensional representations by classifying (k-nearest-neighbors) time windows from a given seizure and state (e.g., ictal windows from seizure 1) using labeled data from all the other seizures and states. For all seizures and states the percentage of correct classifications was substantially larger with t-SNE than with PCA. The percentage of correct classifications using t-SNE was comparable to, and sometimes better than, that using the full high-dimensional representation (Figure 5).

Conclusions

t-SNE low-dimensional representations appear useful for visualizing high-dimensional descriptors of epileptic recordings (compare Figures 4a and 4b).

t-SNE yields superior classification of seizures stages (pre-ictal, ictal and post-ictal) than PCA. Also classifications of seizure stages based on t-SNE low-dimensional representations are comparable to, and sometimes better than, classifications based on the full-dimensional descriptors (Figure 5). This suggests, at least for classifying seizure stages, t-SNE preserves the relevant information from the full-dimensional representation and possibly eliminates noise.

Acknowledgments

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