Visual Complexity of the Time-Frequency Image Pinpoints the Epileptogenic Zone: A Deep-Learning Tool to Analyze Interictal Intracranial EEG

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Introduction:
Intracranial EEG (iEEG) is often used to estimate the epileptogenic zone (EZ) in children with drug-resistant epilepsy (DRE) and target it during surgery. Conventionally, iEEG signals are inspected in the time domain by human experts aiming to locate epileptiform activity.
Visual scrutiny of the iEEG time-frequency (TF) images can be an alternative way to review iEEG allowing a detailed inspection in both the time and frequency domain. Though, this can be arduous for the human reader: subtle features of the TF image may be interictal indicators of the EZ that are not perceptible by the human eye.
Here, we use deep-learning (DL) to measure the visual complexity of the interictal TF images with the goal of developing a presurgical tool to analyze interictal iEEG and help surgical planning.
We hypothesize that low visual complexity of the TF images is an interictal biomarker of the EZ as it reflects underlying epileptic activity rather than chaotic background.

Methods:
We analyzed interictal iEEG (**Fig 1A**) from 33 children with DRE who had epilepsy surgery (21 good outcomes; 3,351 contacts).
For each iEEG contact, we generated three wavelet-based TF images (**Fig 1B**; spike: 1-70 Hz; ripples: 70-250 Hz; fast-ripples: 250-500 Hz). To extract the visual complexity of the TF images, we used an unsupervised DL tool (pretrained *VGG16 network*) that deconstructs the input image in 13 layers (or images; **Fig 1C**). From each layer (L1-13), we extracted the *unsupervised activation energy* (UAE), a measure of TF image visual complexity, obtaining 13 features of visual complexity per iEEG contact per frequency.
UAE was compared (*Wilcoxon sign-rank* test) between inside and outside the resection (defined using postop MRIs) separately for good and poor outcomes in order to assess whether TF visual complexity discriminates between epileptogenic and non-epileptogenic tissue.

Results:
In the spike frequency (**Fig 2A**), we found that UAE (i.e. visual complexity) of some TF image layers was lower inside than outside resection both in good and poor outcome patients. This suggests that, in the spike frequencies, the proposed TF analysis would likely locate the same area that was already resected in poor outcomes.
In the ripple frequency (**Fig 2B**), UAE of all image layers (L1-13) were lower inside than outside resection in good but not poor outcome patients, suggesting the potential of these interictal biomarkers to pinpoint areas outside resection in poor outcome cases.
Finally, for fast ripples (**Fig 2C**), no differences were seen in UAE values, suggesting the inability of these TF images to capture underlying epileptogenicity.

Conclusion:
We developed a novel DL tool to extract interictal signatures of underlying epileptogenicity from iEEG contacts through a fully automated analysis of their TF images. The proposed DL tool is able to quantify the visual complexity of the iEEG TF image at different levels (or layers) and frequency bands via the UAE.
We found that low visual complexity of the icEEG TF image in the ripple frequency is a potential new interictal biomarker of the EZ that may help surgical planning and outcome prediction.

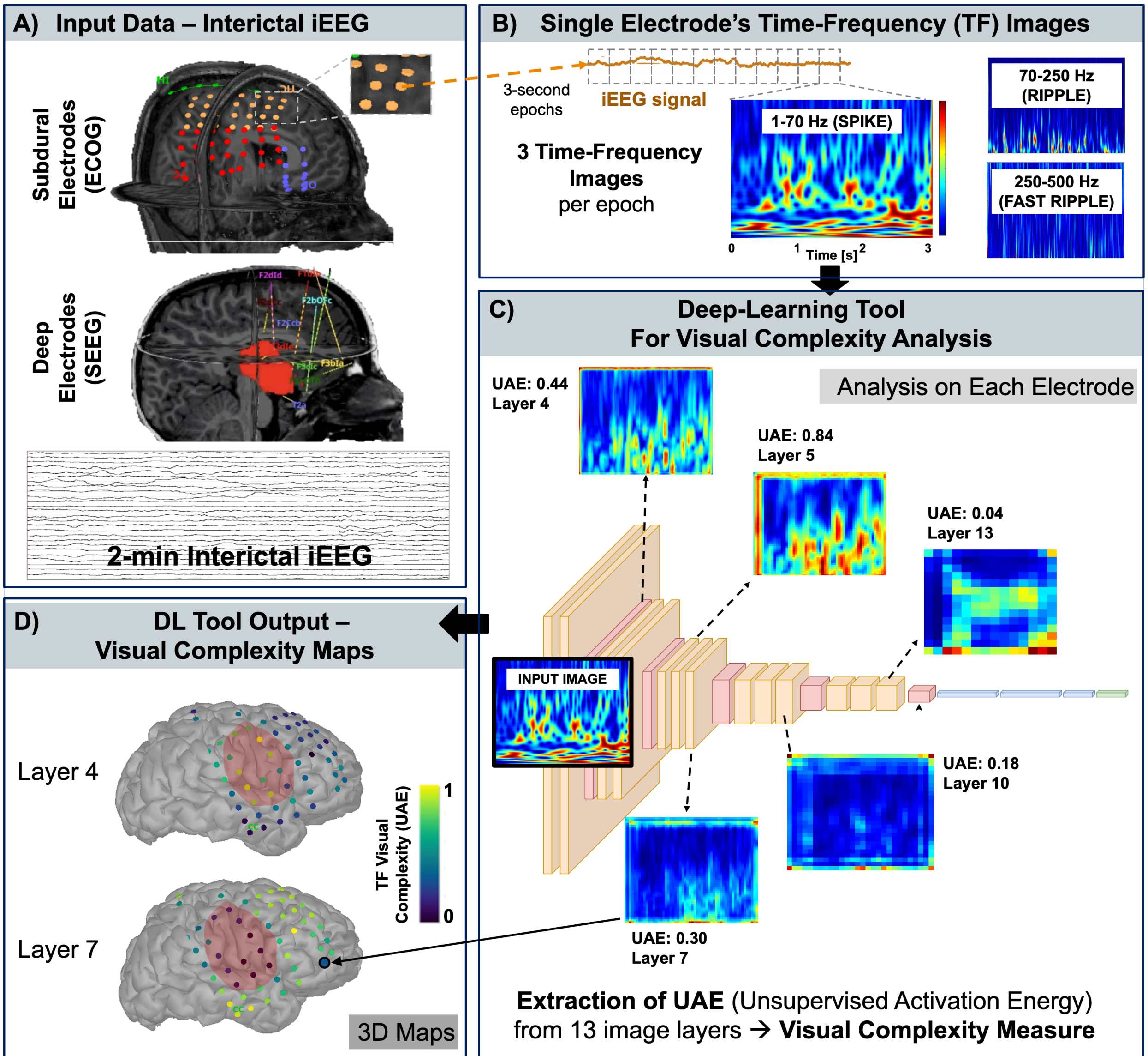

Figure 1. Methodological Pipeline. A) Input intracranial EEG (icEEG) Data. **B)** Time-Frequency (TF) Images extracted from each icEEG contact in three frequency ranges (TF analysis was performed every 3 s). **C)** Design of the Deep Learning (DL) tool that was used to extract values of visual complexity from each TF image. The input image is deconstructed into 13 layers (13 different images). For each layer of the image, we computed the unsupervised activation energy (UAE) that is a measure of the image visual complexity. **D)** Output of the proposed DL tool (two of the 13 layers are shown): 3D maps of the UAE (i.e., TF visual complexity) across the icEEG contacts are generated and values inside versus outside the resection are compared.

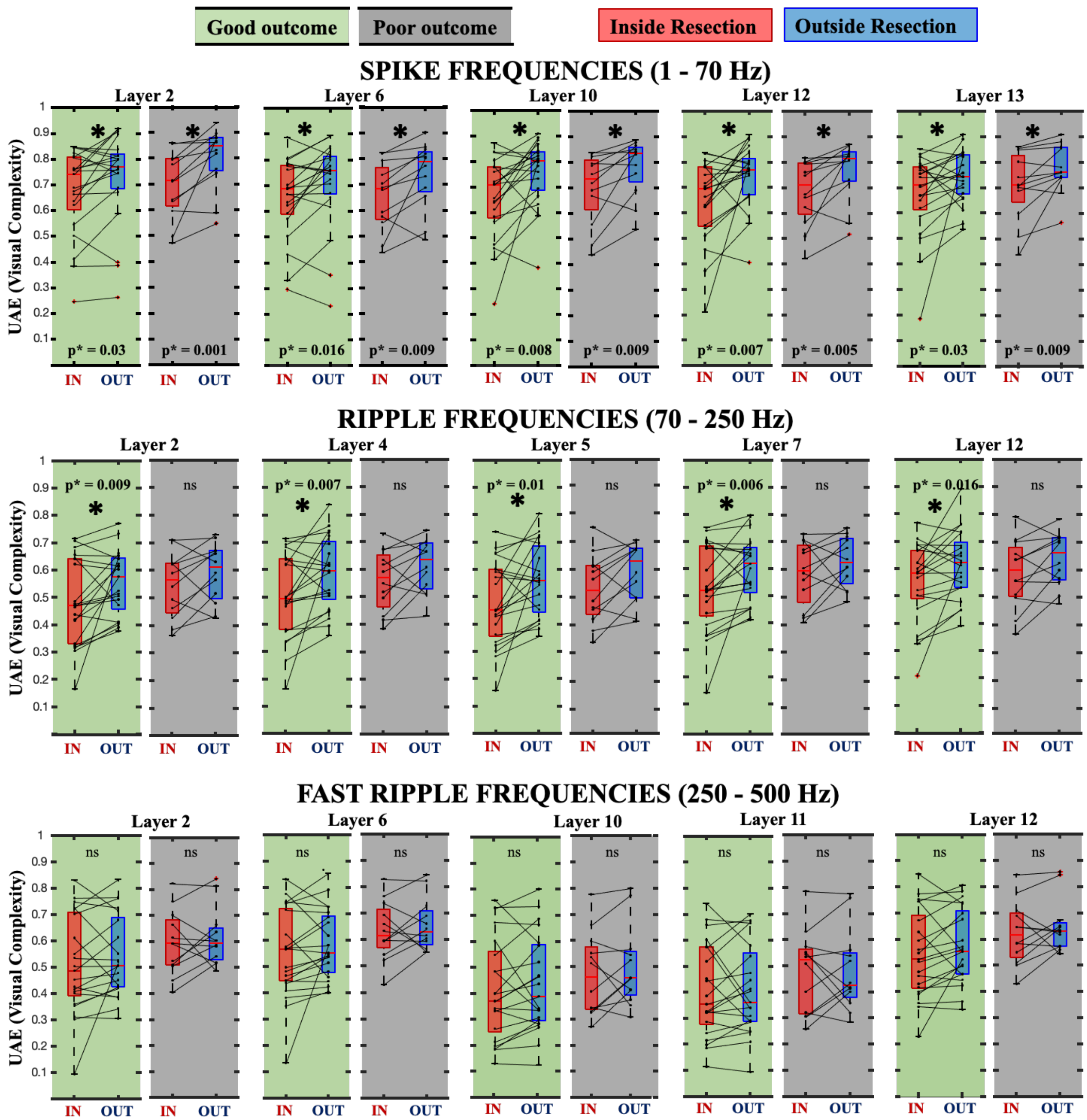

Figure 2. Results from the comparisons between UAE values inside (red) and outside (blue) resection in patients who had a good (green) or a poor (grey) postsurgical outcome and in three frequency bands (spike, ripple, fast ripple). Results are reported for some of the investigated layers of the TF image. P-values <0.05 are considered significant (Wilcoxon sign-rank test)