Clustering biological systems using generative embedding

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1 Summary

- Complex biological systems can be studied using dynamic models that are based on differential equations describing how system elements interact in time. In two recent studies, we introduced a novel approach to utilizing such models in neurobiology using the idea of generative embedding.
- In the first study, we used a generative model of local field potentials (LFP) in mice to decode the trial-wise identity of a sensory stimulus from activity in somatosensory cortex [1].
- In the second study, we used a model of functional magnetic resonance imaging (fMRI) data to diagnose aphasia in human stroke patients, based on activity in non-lesioned brain regions during speech processing [2].
- In this work, we address the open question of whether generative embedding could also serve to discover new structure in data.

2 Experimental design

The first dataset was based on electrophysiological recordings in mice, where on each trial either of two whiskers was being stimulated. We designed a DCM that describes how neural activity within interconnected populations of neurons evolves over time in response to sensory perturbation. We then inverted this model separately for each trial and submitted the resulting trial-specific parameter estimates for model-based clustering.

The second dataset was based on fMRI data acquired from mildly aphasic patients and healthy controls (n = 37) in the context of a speech-processing task [4]. Using a DCM of the activity in non-lesioned thalamo-temporal regions during speech processing, we asked what structure would emerge when representing the data in a model-based feature space constructed from subject-specific coupling strengths.

3 Model-based clustering

We introduce generative embedding for model-based clustering using a combination of dynamic causal models (DCM) and k-means clustering.

4 Predictive validity

We assessed the predictive validity of the obtained clustering solutions by evaluating how well the inferred structure matched known structure in the data. Specifically, we plotted the balanced purity, a measure of agreement between identified clusters and known class structure, as a function of the number of clusters.

5 Mechanistic interpretation

Model-based clustering solutions can be interpreted in terms of the parameters of the underlying generative model. Here, we illustrate interpretability using the 4-cluster solution on dataset 1, in which patients and healthy controls were separated with a purity of 84%.

6 Conclusions

- In contrast to conventional approaches, model-based clustering may provide more accurate results by exploiting discriminative information encoded in hidden physiological quantities such as synaptic connection strengths.
- Critically, using a generative model for clustering enables a mechanistic interpretation of the discovered structures.
- Model-based approaches may become particularly relevant for generating novel mechanistic hypotheses for clinical applications. In the domain of spectrum disorders, for example, one could decompose groups of patients with similar symptoms into pathophysiologically distinct subgroups.

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