Beyond Pairwise Linearity: Nonlinear and Higher-Order Connectivity in Brain Activity

Understanding brain activity requires capturing both statistical dependencies (functional connectivity) and directed influences (effective connectivity). We discuss several recent advances beyond standard network characterization methods, focusing on two key directions: the subtle but important presence of nonlinear dependencies in fine-scale brain signals, and the need for genuinely multivariate, higher-order causality concepts that capture synergistic interactions beyond traditional pairwise frameworks.

First, we show that while large-scale human neuroimaging data (e.g., fMRI, EEG) are largely dominated by linear interactions, more detailed modalities (iEEG, spikes) exhibit robust non-Gaussian, nonlinear dependencies. Using mutual information (MI) and surrogate-based testing, we quantify the extent and spatial distribution of these effects and separate genuine nonlinearity from spurious contributions (e.g., nonstationarities, preprocessing artifacts).

Second, we extend the information-theoretic framework of causal inference to define higher-order effective connectivity. Standard measures such as transfer entropy do not distinguish between additive and truly synergistic causal structures. We propose a refined approach that captures hyperedges in causal graphs, assigning causal status to sets of variables only when their joint contribution is irreducible. This is illustrated on simulated and biophysically realistic neuronal models, including dendritic XOR computations, demonstrating exclusive joint causality not detectable by pairwise methods.

We shall discuss these contributions in the context of existing approaches and practical challenges in describing brain dynamics. Together, they illustrate possible paths along a shift from linear pairwise connectivity analysis to richer representations incorporating nonlinear structure and higher-order causality.