nCREANN: Nonlinear Brain Connectivity and Diverse Applications

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Abstract

Understanding directed brain connectivity is crucial in neuroscience, yet traditional linear connectivity methods may oversimplify neural interactions. We introduce nCREANN, nonlinear causal relationship estimation by artificial neural networks, which models the neural dynamics by a nonlinear multivariate autoregressive (nMVAR) process and estimates directed connectivity. This method leverages the Taylor expansion of nonlinear input-output mapping of the neural network to dissociate linear and nonlinear connectivity patterns. We summarize considerations and diverse applications of nCREANN in neuroscience studies. Results highlight distinct linear and nonlinear connectivity patterns in Autism Spectrum Disorder (ASD) and Attention-Deficit/Hyperactivity Disorder (ADHD) subjects, a superior classification accuracy of ADHDs (up to 99%), and deeper insights into neural mechanisms underlying adaptive behavior, event segmentation, metacontrol processes, and dynamic working memory gating. nCREANN provides a powerful tool for uncovering nuanced brain dynamics and enhancing understanding of neural disorders.

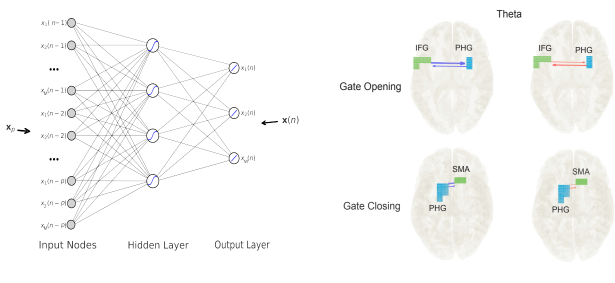
Keywords: Directed functional connectivity; nonlinear analysis; EEG; ASD; ADHD; cognitive control

Introduction

Understanding the intricate communication between different brain regions is fundamental to unraveling the neural underpinnings of cognition and behavior. Conventional linear methods may oversimplify the complex and inherently nonlinear dynamics of brain activity. To address this limitation, a novel method called nCREANN (Talebi et al., 2019) has been developed which leverages the capabilities of artificial neural networks (ANNs) to estimate both linear and nonlinear components of directed connectivity, offering a more comprehensive insight into brain functioning in both healthy and disordered states. This paper will explore the methodology of the nCREANN method and highlight its diverse applications in various neuroscientific domains, demonstrating its potential as a powerful tool for investigating brain dynamics.

Method

The nCREANN method is based on an nMVAR model, which posits that the current activity of a brain region is predicted by the past activity of itself and other interconnected regions. This temporal causality is captured using a single-hidden-layer feed-forward network. The past samples of the multivariate time series (e.g., cortical source signals from different brain regions) serve as the input to the network, and the network is trained to predict the subsequent samples as its output (Figure 1(a)). The model parameters are optimized using a training dataset, and model performance is evaluated to ensure robustness and generalizability.



(a) (b)

Figure 1 (a) Network structure in nCREANN; (b) Linear (blue/left) and nonlinear (red/right) connectivity patterns between regions (Elmers et al., 2024)

The key innovation of nCREANN lies in its ability to distinguish between linear and nonlinear components of effective connectivity. This is achieved by separating the linear and nonlinear parts of the network's input-output mapping. Mathematically, the nMVAR model can be represented as:

$$\mathbf{x}(n) = \boldsymbol{f}(\mathbf{x}_p) + \boldsymbol{\sigma}(n) \quad (1)$$

where $\mathbf{x}(n)$ is the vector of current samples of M brain regions, $\mathbf{x}_p$ is the vector of *p* previous samples of these regions, $\boldsymbol{f}(.)$ is a nonlinear function representing the interactions, and $\boldsymbol{\sigma}(n)$ is the model residual. Relying on the Taylor expansion of the hidden neurons' activation function, nCREANN method decomposes this function into its linear ($\boldsymbol{f}^{Lin}$) and nonlinear ($\boldsymbol{f}^{NonLin}$) components:

$$\boldsymbol{f} = \boldsymbol{f}^{Lin} + \boldsymbol{f}^{NonLin} \quad (2)$$

Linear Connectivity ($LC_{i \to j}$) is then determined using $\boldsymbol{f}^{Lin}$ to quantify the linear influence of region *i* on region *j*, while Nonlinear Connectivity ($NC_{i \to j}$) is derived from $\boldsymbol{f}^{NonLin}$, reflecting the nonlinear causal influence. This dissociation provides a more nuanced understanding of the information flow within the brain compared to methods that solely focus on linear relationships.

A significant consideration when analyzing EEG data for connectivity is the volume conduction effect, which can lead to spurious connectivity results. Therefore, nCREANN is often applied to current sources reconstructed from EEG recordings using inverse methods (Veen et al., 1997). To assess connectivity patterns across different frequency bands (e.g., theta, alpha, beta), a common approach is that EEG data undergo time-frequency decomposition to identify frequency-specific neural oscillatory patterns before computing the connectivity values.

Applications of nCREANN

The nCREANN method has demonstrated its utility in investigating brain connectivity patterns across various neurological and cognitive domains.

ASD: nCREANN revealed reduced linear and enhanced nonlinear connectivity patterns in resting-state EEG of ASD compared to typically developing (TD) children, highlighting potential biomarkers for ASD neural dynamics (Talebi et al., 2019).

ADHD: In visual attention tasks, nCREANN identified distinct directed connectivity profiles in children with ADHD, fusion of linear and nonlinear measures achieved classification accuracy of 99% between ADHD and TD children (Talebi & Motie Nasrabadi, 2022).

Inhibitory Control and Adaptive Behavior: The role of neuronal cytoskeletal integrity in inhibitory control has been investigated using nCREANN (Elmers et al., 2025). The results revealed that cytoarchitectonic integrity modulates nonlinear directional connectivity within a theta band activity-related neural network during response inhibition. Furthermore, nCREANN analysis during cognitive conflict and adaptive behavioral tasks indicated stronger top-down control processes necessary for adaptive behaviors and conflict resolution (Talebi et al., 2024).

Event Segmentation: Investigations of event segmentation showed altered connectivity networks in adolescents with ADHD highlighted discrepancies in event perception, elucidating potential neural mechanisms underlying ADHD symptomatology (Prochnow et al., 2024)

Metacontrol and Action Selection: nCREANN has been used to explore how metacontrol states (persistence vs. flexibility) modulate both linear and nonlinear information flow between cortical modules. This provides insights into the dynamic interplay of brain regions involved in adapting cognitive control strategies to environmental demands (Wang et al., 2024).

Working Memory Gating: nCREANN has also been to explore the network supporting threshold-dependent management of dynamic working memory gating. The study can shed light on how information is effectively routed and protected within working memory networks based on specific gating mechanisms (Elmers et al., 2024).

Conclusion

The nCREANN method represents a significant advancement in the analysis of directed connectivity by providing a framework to quantify and differentiate between linear and nonlinear causal interactions within the brain. Its application in diverse neuroscientific fields demonstrates its versatility and potential. By moving beyond the limitations of purely linear models, nCREANN offers a richer and more accurate depiction of the complex dynamics underlying brain function, paving the way for new insights into the neural mechanisms of behavior and the pathophysiology of neurological and psychiatric conditions. Future research employing nCREANN on larger and more diverse datasets, and in conjunction with other neuroimaging modalities, promises to further enhance our understanding of the intricate and often nonlinear communication within the human brain.

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