Using fMRI to Model Nonlinear Interactions Between Brain Regions

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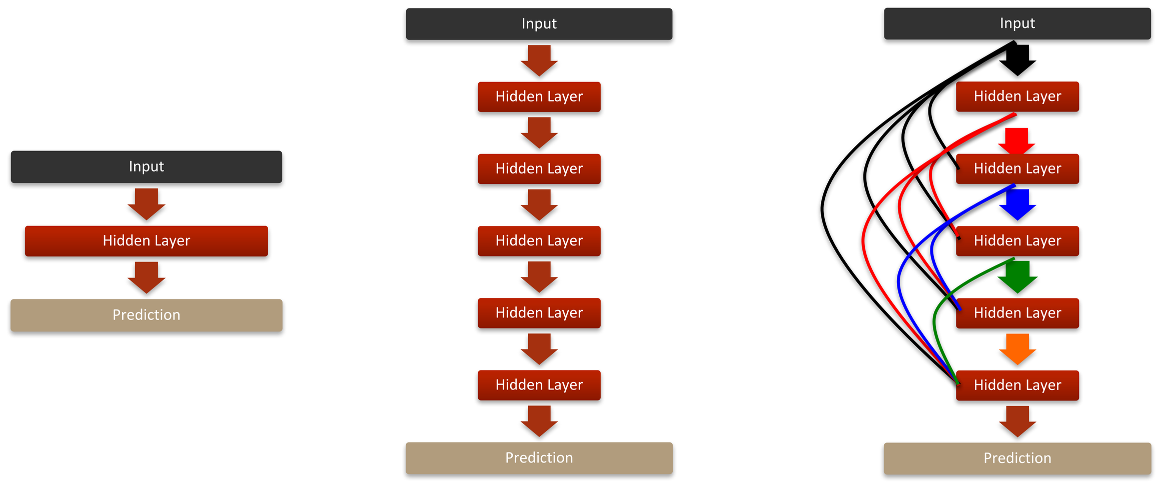
Abstract

Whenever we perform a cognitive task, multiple brain regions are engaged, and information is transformed from brain region to brain region. A new method (MVPD, Anzellotti et al. 2017, Li et al. 2019, Fang et al. in preparation) goes beyond standard functional connectivity, capturing the interactions between multivariate patterns of response in different brain regions. In addition to being multivariate, interactions between brain regions are likely nonlinear. However, it remains unknown whether nonlinear models of the interactions between brain regions can be effectively estimated from fMRI data. We used artificial neural networks to model the interactions between brain regions during the viewing of complex visual stimuli (the film *Forrest Gump*), comparing out-of-sample predictions of linear and nonlinear versions of three different neural network architectures. The relative effectiveness of linear and nonlinear models depended on the network's architecture, the brain regions analyzed, and the denoising method .

Materials and Methods

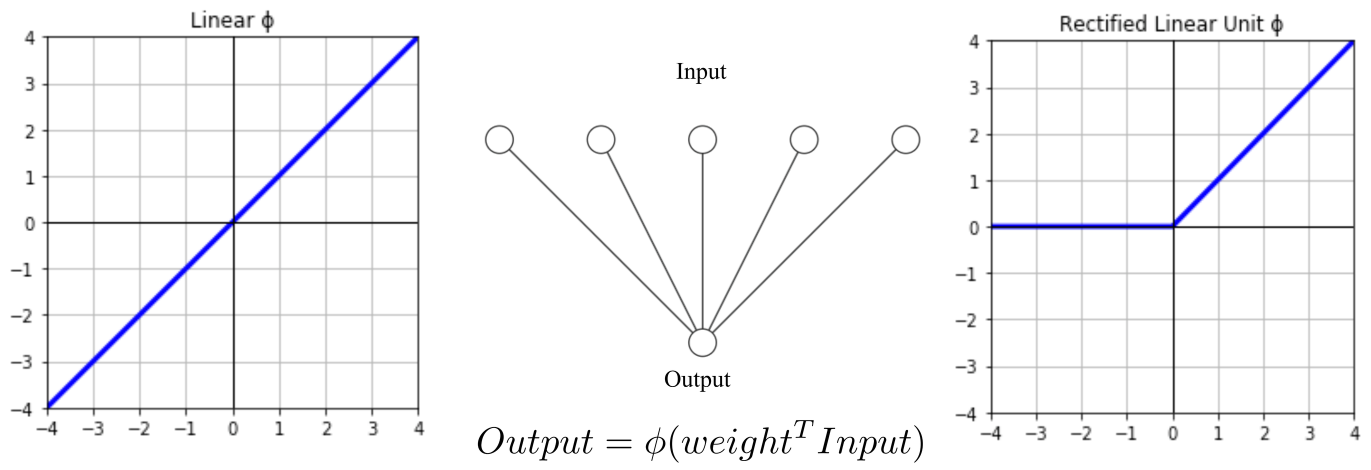
- *studyForrest* dataset (14 subjects; 6 female; ages 21-39).
- Subjects watched *Forrest Gump* in the scanner over 8 sessions.
- Preprocessing of the data was performed using fMRIPrep.
- Data were denoised in 8 separate ways using CompCorr: "full denoised" (using 5 principal components (PCs) extracted from a combination of white matter (WM) and cerebrospinal fluid (CSF)), "WM denoised" (using 5 PCs extracted from the WM), "CSF denoised" (using 5 PCs extracted from the CSF), and once each using successive PCs from the combined WM and CSF data. Nondenoised data were processed as a control.
- For each subject, the FFA, OFA, and face-STS were identified with an independent localizer.
- Using these regions as input, we trained linear and nonlinear versions of 3 neural network architectures' (1 layer, 5 layer, and 5 layer dense). We then tested their ability to predict the responses in other brain regions (in independent data), and how it is affected by the denoising method.
- Networks were trained in pytorch using stochastic gradient descent on a mean squared error loss function (learning rate = .001, momentum = .9)

Architectures



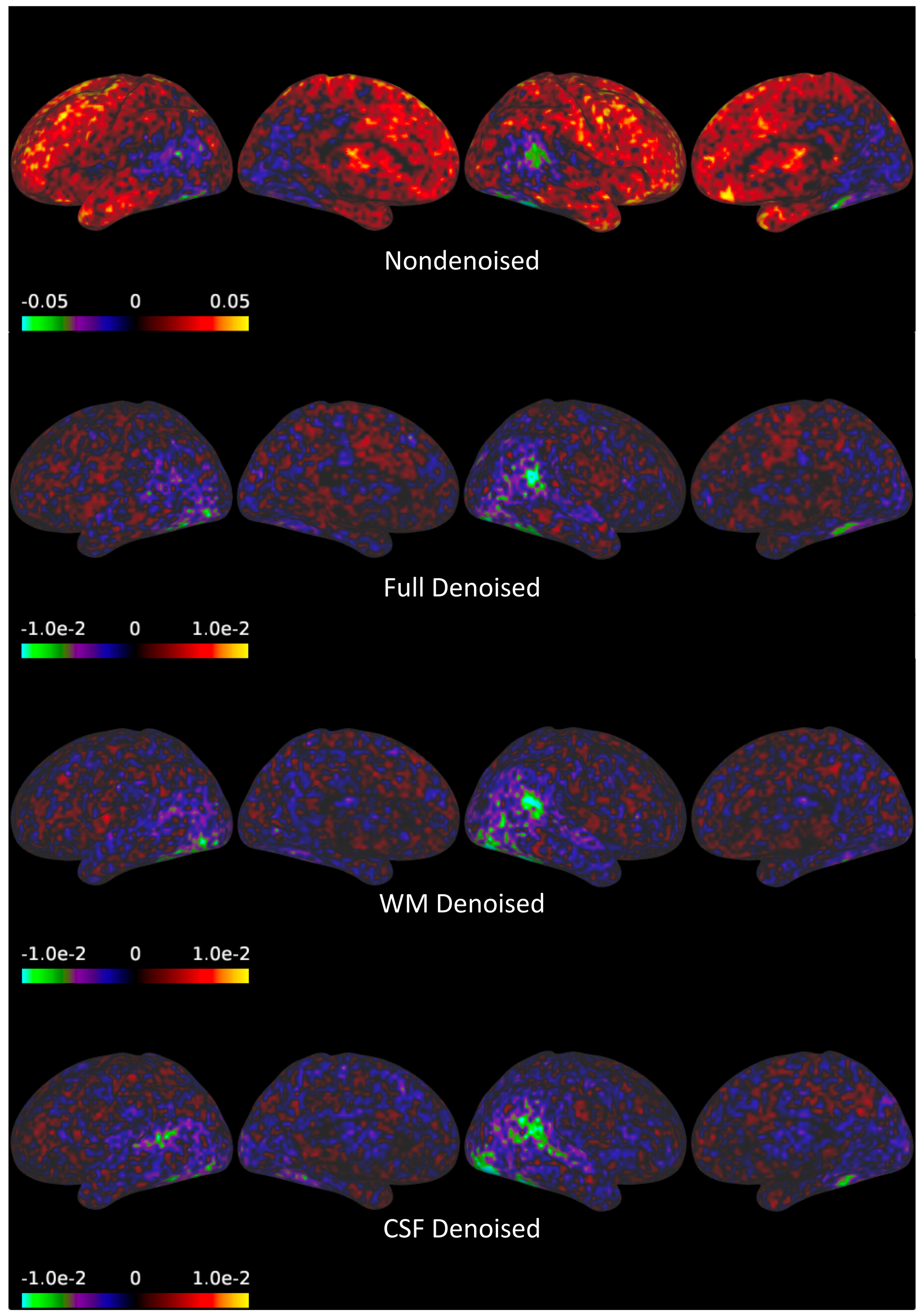
1 Layer 5 Layer 5 Layer Dense

Linear and Nonlinear Activation Functions



$Output = \phi(weight^T Input)$

1 Layer Network Results

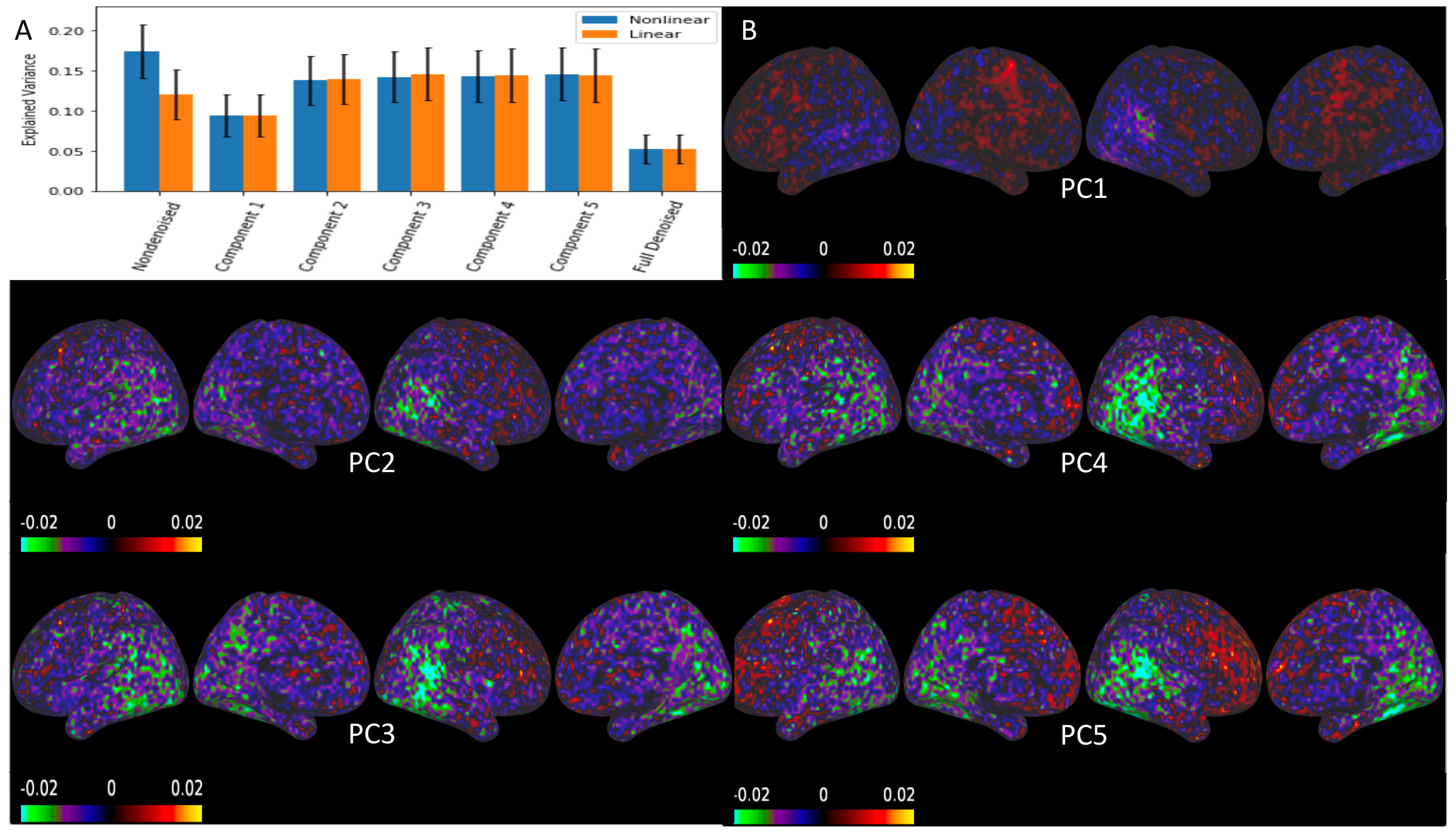


By subtracting the explained variance of the 1 layer linear network architecture from the explained variance of the 1 layer nonlinear network, we created heat maps in which voxels that are better explained by the nonlinear network appear as warm colors, while voxels that are better explained by the linear network appear as cool colors.

Nondenoised, Full Denoised: In the nondenoised data, the nonlinear network out performs the linear network in anterior regions of the brain. However, this effect is largely removed in the denoised data, even if the denoising method is *linear*. We then tested whether either CSF or WM contributed more to these nonlinear interactions.

WM Denoised, CSF Denoised: Removing WM and CSF each parallel the findings from the full denoised analysis. Extracting PCs from each noise source reduces the nonlinear interactions in the front of the brain. Contrasting the findings in the nondenoised data, in both the WM and CSF denoised data, linear networks perform on par with, or better than nonlinear networks in frontal regions. It is worth noting that the magnitude of the difference between the explained variance of the nonlinear and linear networks in all three denoised datasets is 5 times less than the scope of the differences in the nondenoised data. This suggests that denoising with either WM or CSF alone seems to be sufficient for removing nonlinear interactions between brain regions and thus, neither source of noise has a larger contribution to these nonlinear interactions.

A: 1000 voxels which showed the largest contrast in explained variance (nonlinear > linear) were selected from the network predictions of the nondenoised data. In each separately denoised dataset the average explained variance of these 1000 voxels was plotted for the nonlinear and linear networks. Each pair of bars represents how the denoising process affects the linear and nonlinear interactions in the brain. Here, we see that removing each PC reduces the nonlinear interactions from the nondenoised baseline. However, removing PCs 2-4 improves the linear network's prediction, diminishing the difference between the explained variance of the linear and nonlinear networks. Error bars represent standard error of the mean across subjects.

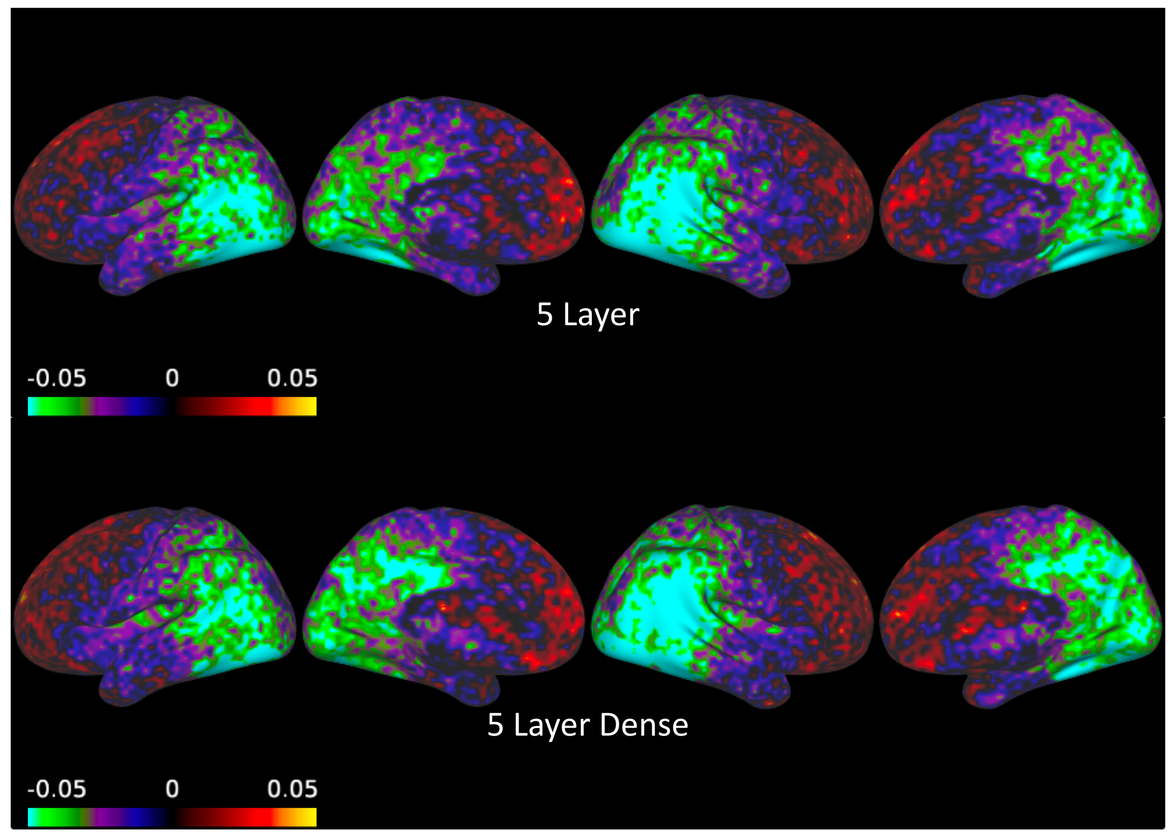


B: Difference in explained variance of the 1 layer nonlinear network and the 1 layer linear network for data denoised with PCs 1 through 5. All individual components greatly reduce the difference between the variance explained by nonlinear and linear networks. However, fine-grained differences exist in the pattern of nonlinear vs. linear performances that provide insight into how the individual components contribute to the reduction of these nonlinear interactions. Importantly, in the data denoised with PCs 2, 3, and 4, we see a global reduction in nonlinear interactions. However, in the data denoised using components 1 and 5, the nonlinear interactions, specifically in the front of the brain, are preserved.

5 Layer Networks

Using 1 layer networks, we found that a nonlinear net out performed its linear counterpart in the frontal regions of the brain in nondenoised data. To test whether this finding was a functin of the network architecture, we also analyzed the nondenoised data using more complex network structures (a 5 layer and a 5 layer dense net). We found that nonlinear interactions in the frontal brain regions are consistent across network structures. In bother 5 layer architectures, we found a simmilar pattern to the 1 layer network results, in which variance explained was larger for nonlinear networks in anterior regions of the brain and linear networks in the posterior regions.

Below: Difference in explained variance (nonlinear – linear) for a 5 layer network and a 5 layer dense network.



Conclusion

- CompCorr removes nonlinear interactions between brain regions.
- Using either WM or CSF to predict noise is sufficient to remove nonlinear interactions.
- Each PC extracted from the combined WM and CSF differentially affect the connectivity between brain regions. In this case, using PCs 1 and 5 preserved the spatial distribution of nonlinear vs. linear interactions across the brain.
- Patterns of frontal nonlinear interactions before denoising were consistent across network architectures. Future work can determine whether CompCorr also removes this relationship.

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