Predicting Diverse Functional Connectivity from Structural Connectivity Based on Multi-contexts Discriminator GAN

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Abstract. Revealing structural-functional relationship is an important issue in neuroscience study since it helps to understand brain activities. Structural Connectivity (SC) represents the fibers connection between the brain regions, which is relatively static. Functional Connectivity (FC) represents the active signal correlations between the brain regions, which is relatively dynamic and diverse. Many works predict FC from SC and achieve unique FC prediction. However, FC is diverse since it represents brain activities. In this work, we propose the MCGAN, a **m**ulti-**c**ontexts discriminator based **g**enerative **a**dversarial **n**etwork for predicting diverse FC from SC. The proposed multi-contexts discriminator provides three kinds of supervisions to strengthen the generator, i.e. edge-level, node-level and graph-level. Since FC represents the connection of the brain regions, it can be regarded as edge-based graph. We adopt edge-based graph convolution method to model the context encoding. Moreover, to introduce the diversity of generated FC, we utilize monte-carlo mean samples to bring in more FC data for training. We validate our MCGAN on Human Connextome Project (HCP) dataset and Alzheimer's Disease Neuroimaging Initiative (ADNI) dataset. The results show that our method can generate diverse and meaningful FC from SC, revealing the one-to-many relationship between the individual SC and the multiple FC. The significance of this work is that once we have anatomical structure of brain represented by SC, we can predict diverse developments of brain activities represented by FC, which helps to reveal individual brain's static-dynamic structural-functional mode.

Keywords: Structural Connectivity · Functional Connectivity · Diverse Generation · GAN

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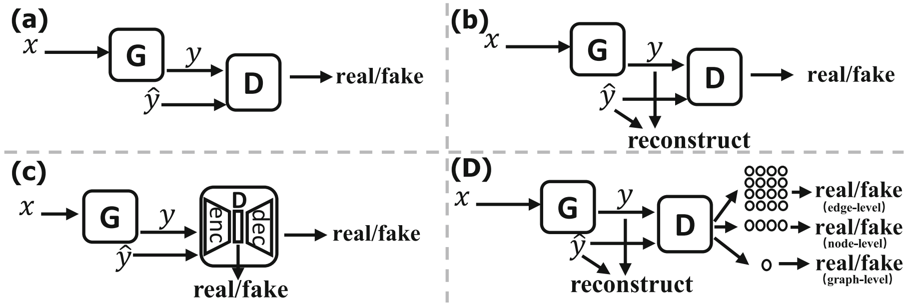

Fig. 1. Illustration of GAN [3] (a), GAN with reconstruct supervision in generator [9] (b), GAN with more supervisions in discriminator [14] (c), and our MCGAN (d).

1 Introduction

Recently, the study of exploring structural-functional relationship raises lots of attentions in neuroscience which helps to reveal individual behaviors of human brain [1]. Typically, Structural Connectivity (SC) [16] represents the fibers connection between the brain regions while Functional Connectivity (FC) [4] represents the Blood-Oxygen-Level-Dependent (BOLD) signal correlations between the brain regions. In comparing, SC is relatively static since it demonstrates the anatomical structure of brain, and FC is relatively dynamic and diverse since it demonstrates the development of the brain activities [2]. To explore the relationship and mapping between them, some works predict SC from FC [18,19] while some works map the structural to functional [21] and both of these works achieve unique prediction. It is accountable for predicting SC from FC since SC is relatively static. However, since the FC is relatively dynamic, the predicting FC from SC is quite challenging and it should be diverse predictions rather than deterministic prediction. In general, it is necessary and challenging to explore the one-to-many relationship between the one subjects's SC and the FC by predicting diverse FC from SC [2]. The significance of this work is that once we have anatomical structure of brain represented by SC, we can predict diverse developments of brain activities represented by FC, which helps to reveal individual brain's static-dynamic structural-functional mode.

In this work, we propose the diverse generations with the idea of conditional GAN [12], i.e. the input of the generator is random noise to realize diverse generations and is in condition of SC to generate FC. To improve the quality of generation, some works introduce the reconstruct supervision in generator while some works provide more supervisions in discriminator. In this work, we propose MCGAN, a multi-contexts discriminator based generative adversarial network to take both advantages. The comparison is shown in Fig. 1. Specifically, the multi-contexts discriminator provides three kinds of supervisions, i.e. edge-level, node-level and graph-level, to strengthen the generator. We adopt edge-based graph convolution method [11] to model the FC encoding. In addition, we utilize monte-carlo mean samples to enlarge the FC data for supervision. We validate our MCGAN on the HCP dataset [15] and ADNI dataset [10] and the results show that our method can generate diverse and meaningful FC. To the best of our knowledge, our method is the first to explore one-to-many SC-FC relationship.

2 Method

2.1 Model Overview

The framework of our proposed MCGAN is shown in Fig. 2 and detailed below.

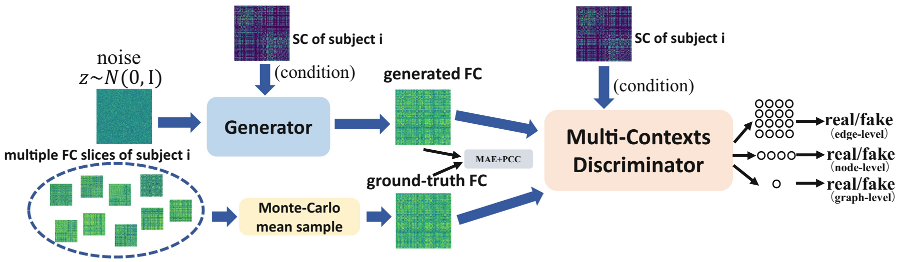

Fig. 2. Illustration of our proposed MCGAN.

The objective of this work is to predict diverse functional connectivity (FC) with the instruction of structural connectivity (SC). The proposed MCGAN is based on the generative adversarial network (GAN) framework [3], which consists of two parts. (a) Generator. For FC generation of subject i, the input of the generator is random noise which introduces the diverse generations and is in condition of SC of subject i. We utilize monte-carlo mean FC samples of subject i for supervision. (b) Multi-contexts Discriminator. The discriminator distinguishes the generated FC and real one. We introduce multi contexts supervision to discriminator, i.e. edge-level, node-level and graph-level, to strengthen the generator. We adopt edge-based graph convolution method [11] to model the FC encoding. In the prediction stage, for a specific subject, the generator predicts diverse FC with corresponding numbers of random noise input and in condition of the same SC of subject.

2.2 MCGAN

The adversarial objective of generating FC from SC with GAN model is defined as:

$$
\begin{aligned}
L_{adv} &= L^G + L^D, \\
L^G &= -E_{x,y}[logD(G(x,z))], \\
L^D &= -E_{x,y}[logD(x,y)] - E_{x,z}[log(1 - D(G(x,z)))].
\end{aligned}
\tag{1}
$$

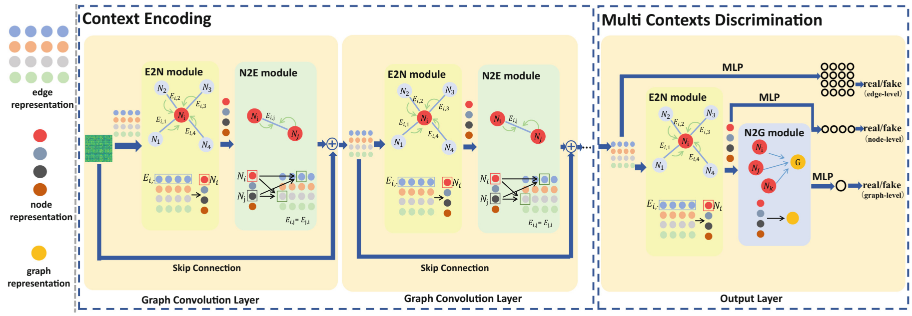

Fig. 3. Illustration of the proposed multi-contexts discriminator which consists of the context encoding and multi contexts discrimination.

where $z \in R^{n \times n}$ denotes the noise sample from $\mathcal{N}(0, I)$ to introduce the diversity of the generated FC. $x \in R^{n \times n}$ denotes the SC is the condition which instructs the generation of FC [12] and $y \in R^{n \times n}$ denotes the real FC.

Multi-contexts Discriminator

The original discriminator learns the global representation of synthetic or real data to distinguish them. However, it is insufficient to provide powerful feedback to encourage the generator to predict realistic data. Many works improve the discriminator and show that the stronger the discriminator is, the better the generator is [13,14]. Motivated by this insight, we propose a multi-contexts discriminator, which provides edge-level, node-level and graph-level supervisions to implicitly and explicitly strengthen the generator. The multi-contexts discriminator shown in Fig. 3 consists of two parts, context encoding and multi contexts discrimination.

Context Encoding. The context encoding is for feature extraction. For brain network, regions are represented as nodes and the links between regions are represented as edges. Since FC is defined as the correlation between the active brain regions, it represents the edge feature. However, most of the graph convolution networks (GCN) model the node feature extraction. To address the FC encoding, we adopt the edge-based graph convolution method for feature extraction [11]. There are three basic modules, i.e. E2N module (edge to node), N2E module (node to edge), N2G module (node to graph).

E2N module. Given a FC $E \in R^{n \times n}$, where $E_{i,j}$ denotes the edge between region i and region j, it aggregates the linking edges of region i into a node representation:

$$N_i = \sum_{k=1}^{n} E_{i,k} w_k, \quad i = 1, 2, ..., n \tag{2}$$

where w_i is trainable weight and N_i is the feature of $i^t h$ node.

N2E module. It propagates the feature of node i and node j to their linking edge:

$$E_{i,j} = N_i + N_j = \sum_{k=1}^{n}(E_{i,k} + E_{j,k})w_k, \tag{3}$$

The network stacks the graph convolution layers for FC encoding. A graph convolution layer is comprised of a E2N module and a N2E module for FC feature learning and reserve the structure of FC. Meanwhile, the skip connection [5] is applied in graph convolution layer.

N2G module. It integrates all the nodes feature into a graph representation:

$$G = \sum_{i=1}^{n} N_i w_i. \tag{4}$$

The output layer of the network is comprised of a E2N module and a N2G module to encode the FC representation into the node representation and the graph representation in series.

Multi Contexts Discrimination. The original discriminator $D(\cdot)$ classifies the input data to be real or fake. In contrast, our proposed multi-contexts discriminator provides three kind of supervisions, i.e. edge-level, node-level and graph-level, to implicitly and explicitly strengthen the generator. Mathematically, our discriminator loss is comprised of three parts:

$$\begin{aligned}
&L^D = L^D_{edge} + L^D_{node} + L^D_{graph}, \\
&L^D_{edge} = -E_{x,y}[\sum_{i,j} logD_{edge}(x,y)_{i,j}] - E_{x,z}[\sum_{i,j} log(1 - D_{edge}(x, G(x,z))_{i,j})], \\
&L^D_{node} = -E_{x,y}[\sum_{n} logD_{node}(x,y)_n] - E_{x,z}[\sum_{n} log(1 - D_{node}(x, G(x,z))_n)], \\
&L^D_{graph} = -E_{x,y}[logD_{graph}(x,y)] - E_{x,z}[log(1 - D_{graph}(x, G(x,z)))].
\end{aligned} \tag{5}$$

In the output layer, we first use three MLP to transform the three kinds of context representation. Then the $D_{edge}(\cdot)$, $D_{node}(\cdot)$, $D_{graph}(\cdot)$ respectively classify the transformed edge representation, node representation and graph representation to be real or fake.

Correspondingly, the objective of the generator is:

$$\begin{aligned}
L^G = -E_{x,z}[\quad &\sum_{i,j} logD_{edge}(x, G(x,z))_{i,j} + \\
\sum_{n} logD_{node}(x, G(x,z))_n + \quad &logD_{graph}(x, G(x,z)) \quad].
\end{aligned} \tag{6}$$

The multi contexts supervision improves the discriminator, which implicitly strengthens the generator in adversarial training process. Meanwhile, it feedbacks the fine-grained information to the generator by backpropagation, which explicitly strengthens the generator and encourages it to predict realistic FC.

Monte-Carlo Mean Samples of FC
FC represents the development of brain activities so that it is relatively dynamic. While SC represents the fibers connection to indicate the anatomical structure of brain [2], which is relatively static. Since the limited of FC data and the supervision of the generated FC should not be limited in finite subspace, we augment the FC data via monte-carlo mean:

$$y = \frac{1}{m} \sum y_i. \tag{7}$$

where y_i denotes multiple real FC of each subject and m can be fixed or dynamic during training, which denotes the monte-carlo sampling, $m = 1, 2, ...M$, M is the maximum samples for each subject of dataset. The linear combination of FC enlarges the data space for supervision, making the generator predict diverse FC.

Reconstruction Loss of Generator
We adopt reconstruction loss in generator to make it predict realistic FC which includes the mean absolute error (MAE) and Pearson's correlation coefficient (PCC) between the generated FC and the training FC sample.

$$L_{rec} = E_{x,z,y}[|y - G(x, z)|] + E_{x,z,y} PCC(y, G(x, z)). \tag{8}$$

Full Objective
In summary, the objective function of the MCGAN is defined as:

$$L = L_{adv} + L_{rec}. \tag{9}$$

where L_{adv} optimizes the adversarial training of the generator and discriminator, L_{rec} optimizes the generator for realistic prediction.

3 Experiments

3.1 Setup

Datasets. We evaluate our MCGAN on the Human Connectome Project (HCP) dataset [15] and Alzheimer's Disease Neuroimaging Initiative (ADNI) dataset [10]. We apply the standard preprocessing procedures [20] for both datasets. We use diffusion magnetic resonance imaging (diffusion MRI) as the SC and resting state functional magnetic resonance imaging (rs-fMRI) as FC. We divide the BOLD signal into 20 slices for HCP and 10 slices for ADNI for each subject and obtain FC by calculating Pearson's correlation coefficient (PCC) between the segmented signal series. Both of the SC and FC are normalized.

Evaluation Metrics. (a) Quality. Instinctively, for each subject, the generated FC should be similar to one of the real FC. Therefore, for each generated FC of a subject, we calculate the minimum mean absolute error and the maximum Pearson's correlation coefficient to evaluate the quality of generation with the

Table 1. Performance comparison of the quality and diversity.

HCP/ADNI	Prediction	MAE ↓	PCC ↑	FID ↓
GAN [3]	Diverse	1.09/1.12	0.02/0.04	116.5/130.2
PixelGAN [9]	Diverse	0.28/0.30	0.52/0.49	63.5/70.2
UNet-GAN [14]	Diverse	0.89/0.96	0.09/0.05	40.5/49.2
MGCN-GAN [18]	Deterministic	0.12/0.12	0.80/0.76	76.6/79.2
MCGAN	Diverse	0.24/0.26	0.56/0.51	18.8/22.3

most similar real FC. (b) Diversity. We use Frechet Inception distance (FID) [6] to evaluate the diversity of the FC generation. FID compares the distribution of the generated and real data, to simultaneously evaluate the quality and diversity. The lower FID score indicates the better quality and diversity.

Implementation Details. Both of the generator and discriminator are in condition of SC and we set the almost equivalent parameters for them to ensure the efficient adversarial training. We respectively set the learning rate of 0.0001 and 0.0004 for generator and discriminator. At prediction stage, we generate corresponding number of FC samples with dataset for each subject (i.e. 20 for HCP and 10 for ADNI).

3.2 Results

Main Results. We compare our MCGAN with the original GAN [3], PixelGAN which is with reconstruct supervision in generator [9], UNet-GAN which is with more supervisions in discriminator [14]. In addition, many works perform the deterministic prediction on structural or functional prediction [8,17,18]. We compare our MCGAN with MGCN-GAN which is a deterministic prediction to map FC to SC [18]. The results are shown in Table 1. PixelGAN achieves good reconstruction but not well in diversity, which is demonstrated in original paper. UNet-GAN achieves ordinary diversity but fails to reconstruct meaningful FC. MGCN-GAN achieves the best reconstruction since it is a deterministic prediction method but lacks of diversity. In comparing, our MCGAN achieves quality-diversity trade-off.

Ablation Study. We conduct ablation study to investigate the contribution of different components and the results are shown in Table 2. The multi contexts discrimination improves the quality and diversity, indicating that it strengthens the generator for better prediction. The reconstruction provides the supervision to better quality and the monte-carlo mean samples provide the better diversity.

Visualization. We generate multiple FC for each subject and we visualize two FC of each subject. The visualization of the generated and real FC is shown in Fig. 4. Each column denotes the generated FC and the corresponding most similar real FC. It shows that our method achieves diverse predictions rather than only one deterministic prediction.

Table 2. Comparison of ablation study.

HCP/ADNI	MAE ↓	PCC ↑	FID ↓
MCGAN	0.24/0.26	0.56/0.51	18.8/22.3
w/o multi contexts discrimination	0.30/0.33	0.49/0.47	29.8/33.5
w/o mae&pcc	0.84/0.93	0.12/0.10	39.7/45.3
w/o monte-carlo samples	0.19/0.26	0.58/0.52	31.5/31.9

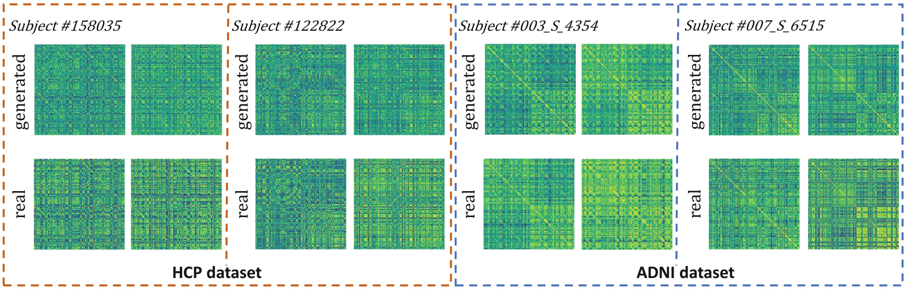

Fig. 4. Visualization of the generated and the real FC. Each column denotes the generated FC (first row) and the corresponding most similar real FC (second row) of multi-slices label of subject. It shows that our method can generate the diverse and realistic FC.

4 Discussion

Despite this work predicts diverse FC to explore one-to-many SC-FC relationship, the generated FC is not quite diverse enough to some extent. In our implementation, we attempt to use the diffusion model [7] to generate FC and it achieves better effect in diversity than this work. By visualization, we find that it generates diverse FC. However, since the diffusion model is trained with the only objective of noise prediction for its particularity and without the reconstruction task, it does not perform well in the evaluation metrics of MAE and PCC, indicating that it can not generate meaningful FC similar to this work. In general, the prediction of FC from SC should be diverse since the SC is relatively static and the FC is relatively dynamic and diverse. To the best of our knowledge, our method is the first to explore one-to-many SC-FC relationship and this task is challenging and significant. We lead to the future work for further exploration and there are many questions to be resolved. Moreover, to reveal individual brain's static-dynamic structural-functional mode, predicting original functional signals is more flexible than predicting FC since it directly explores the development of the brain activities.

5 Conclusion

In this work, for diverse generations, we propose a multi-contexts discriminator based GAN named MCGAN, which provides three kind of supervisions to strengthen the generator, including edge-level, node-level and graph-level. We adopt edge-based graph convolution method for FC encoding and we utilize monte-carlo mean samples to enlarge the FC data for supervision. The experiments show that our method can generate diverse and meaningful FC from SC. We are the first to explore the one-to-many relationship between one subject's individual SC and multiple FC, which helps to reveal individual brain's static-dynamic structural-functional mode. We lead to the future work for further exploration and there are many questions to be resolved.

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References

1. Amiez, C., Petrides, M.: Neuroimaging evidence of the anatomo-functional organization of the human cingulate motor areas. Cereb. Cortex **24**(3), 563–578 (2014)
2. De Benedictis, A., et al.: Anatomo-functional study of the temporo-parieto-occipital region: dissection, tractographic and brain mapping evidence from a neurosurgical perspective. J. Anat. **225**(2), 132–151 (2014)
3. Goodfellow, I., et al.: Generative adversarial networks. Commun. ACM **63**(11), 139–144 (2020)
4. Gratton, C., et al.: Functional brain networks are dominated by stable group and individual factors, not cognitive or daily variation. Neuron **98**(2), 439–452 (2018)
5. He, K., Zhang, X., Ren, S., Sun, J.: Deep residual learning for image recognition. In: Proceedings of the IEEE Conference on Computer Vision and Pattern Recognition, pp. 770–778 (2016)
6. Heusel, M., Ramsauer, H., Unterthiner, T., Nessler, B., Hochreiter, S.: GANs trained by a two time-scale update rule converge to a local Nash equilibrium. In: NeurIPS, vol. 30 (2017)
7. Ho, J., Jain, A., Abbeel, P.: Denoising diffusion probabilistic models. In: NeurIPS, vol. 33, pp. 6840–6851 (2020)
8. Hu, D., et al.: Reference-relation guided autoencoder with deep CCA restriction for awake-to-sleep brain functional connectome prediction. In: de Bruijne, M., et al. (eds.) MICCAI 2021. LNCS, vol. 12903, pp. 231–240. Springer, Cham (2021). https://doi.org/10.1007/978-3-030-87199-4_22
9. Isola, P., Zhu, J.Y., Zhou, T., Efros, A.A.: Image-to-image translation with conditional adversarial networks. In: CVPR, pp. 1125–1134 (2017)
10. Jack, C.R., Jr., et al.: The Alzheimer's disease neuroimaging initiative (ADNI): MRI methods. J. Magn. Reson. Imaging: Official J. Int. Soc. Magn. Reson. Med. **27**(4), 685–691 (2008)
11. Li, Y., et al.: Brain connectivity based graph convolutional networks and its application to infant age prediction. IEEE Trans. Med. Imaging **41**(10), 2764–2776 (2022)

12. Mirza, M., Osindero, S.: Conditional generative adversarial nets. arXiv preprint arXiv:1411.1784 (2014)
13. Odena, A., Olah, C., Shlens, J.: Conditional image synthesis with auxiliary classifier GANs. In: ICML, pp. 2642–2651. PMLR (2017)
14. Schonfeld, E., Schiele, B., Khoreva, A.: A U-Net based discriminator for generative adversarial networks. In: CVPR, pp. 8207–8216 (2020)
15. Van Essen, D.C., et al.: The human connectome project: a data acquisition perspective. Neuroimage **62**(4), 2222–2231 (2012)
16. Yeh, F.C., et al.: Quantifying differences and similarities in whole-brain white matter architecture using local connectome fingerprints. PLoS Comput. Biol. **12**(11), e1005203 (2016)
17. Yu, X., et al.: Longitudinal infant functional connectivity prediction via conditional intensive triplet network. In: Wang, L., Dou, Q., Fletcher, P.T., Speidel, S., Li, S. (eds.) MICCAI 2022. LNCS, vol. 13438, pp. 255–264. Springer, Cham (2022). https://doi.org/10.1007/978-3-031-16452-1_25
18. Zhang, L., Wang, L., Zhu, D.: Recovering brain structural connectivity from functional connectivity via multi-GCN based generative adversarial network. In: Martel, A.L., et al. (eds.) MICCAI 2020. LNCS, vol. 12267, pp. 53–61. Springer, Cham (2020). https://doi.org/10.1007/978-3-030-59728-3_6
19. Zhang, L., Wang, L., Zhu, D., Initiative, A.D.N., et al.: Predicting brain structural network using functional connectivity. Med. Image Anal. **79**, 102463 (2022)
20. Zhu, D., et al.: Connectome-scale assessments of structural and functional connectivity in MCI. Hum. Brain Mapp. **35**(7), 2911–2923 (2014)
21. Zhu, Z., Huang, T., Zhen, Z., Wang, B., Wu, X., Li, S.: From sMRI to task-fMRI: a unified geometric deep learning framework for cross-modal brain anatomo-functional mapping. Med. Image Anal. **83**, 102681 (2023)