

1 Literature review

Some of the important citations regarding Connectivity models for functional studies are compiled here.

The first work we are going to discuss is the one made by Škoch *et al.* (2022). Understanding the complex computational system of the human brain hinges on neuroimaging techniques revealing its structure and function. In this context, Škoch *et al.* (2022) undertakes a pivotal role, harnessing diffusion-weighted imaging and probabilistic diffusion tractography to chart the organization of white matter. Partitioning tractography findings unveils a structural connectivity matrix that illuminates intricate relationships between distinct brain regions. However, the intricacies of processing raw data, compounded by the need for expert oversight, often pose challenges, particularly for novice researchers. Addressing this concern, readily accessible brain structural connectivity matrices are presented, democratizing research opportunities across the scientific community. Modern neuroscience harnesses magnetic resonance imaging (MRI) to examine information integration across various brain regions. Notably, Functional connectivity, driven by analysis of statistical dependencies using activity time series, and structural connectivity, focusing on the physical links, mainly white matter tracts between gray matter regions, constitute fundamental dimensions of brain examination. The structural connectivity matrix, a guiding blueprint for information flow, impacts activity dynamics and interacts with the functional connectivity matrix. Extensively explored, this interplay extends to disease dynamics and deeper structural characteristics.

Amid the push for open sharing of neuroimaging data, Škoch *et al.* (2022) introduces a dataset encompassing raw diffusion and structural data from 88 healthy subjects, coupled with derived structural connectivity matrices detailing connections among 90 cortical regions, meeting the demand for accessible preprocessed connectivity matrices.

The functional organization of the human medial frontal cortex (MFC) has attracted significant research attention, with a focus on its diverse psychological processes through the lens of fMRI studies. Previous research by de la Vega *et al.* (2016) has associated the MFC with a range of functions, including motor control, cognitive regulation, affective processing, and social cognition. Despite these insights, there remains a limited comprehensive mapping of distinct psychological functions onto specific subregions of the MFC.

To bridge this gap, de la Vega *et al.* (2016) employ a meta-analytic, data-driven approach using a vast compilation of nearly 10,000 fMRI studies. This comprehensive analysis identifies distinct MFC regions and discerns their preferential activation patterns in response to various psychological states. This innovative methodology reveals three main functional zones along the rostrocaudal axis, each comprising smaller subregions. For instance, the posterior zone is associated predominantly with motor function, the middle zone with cognitive control, pain, and affect, and the anterior zone with reward, social processing, and episodic memory. de la Vega *et al.* (2016) further demonstrate how within each of these zones, subtle variations in psychological functions are evident among the finer-grained subregions.

This study contributes a fresh perspective to the understanding of the MFC's functional organization, building upon earlier research that focused on structural and functional connectivity. Task-based fMRI findings illuminate the specific associations between MFC activation and distinct psychological manipulations. Notably, the supplementary motor area (SMA) and pre-SMA are linked to movement planning, while the midcingulate cortex (MCC) is implicated in cognitive control, fear, and pain processing. The anterior medial prefrontal cortex (mPFC) and rostral anterior cingulate cortex (rACC) are highlighted for their roles in affective processes and internally focused functions. By seamlessly integrating meta-analysis with multivariate classification, de la Vega *et al.* (2016) offer a comprehensive and unbiased functional map of the human MFC, laying the foundation for future empirical studies to rigorously test these proposed functional associations.

With a more generalized approach, and by using the keywords "Functional Connectivity", "Effective connectivity", "Models", another important set of papers was found.

Penny *et al.* (2004) review two different approaches to modelling effective connectivity from fMRI data, structural equation models (SEMs) and dynamic causal models (DCMs). The structural equation modeling (SEM) is the most used method to estimate effective connectivity in neuroscience, and its typical application is on data related to brain hemodynamic behavior tested by functional magnetic resonance imaging (fMRI), whereas the directed transfer function (DTF) method is a frequency-domain approach based on both a multivariate autoregressive (MVAR) modeling of time series and on the concept of Granger causality. Astolfi *et al.* (2004) present advanced methods for the estimation of cortical connectivity by applying SEM and DTF on the cortical signals estimated from high-resolution electroencephalography (EEG) recordings, since these signals exhibit a higher spatial resolution than conventional cerebral electromagnetic measures. Stevens

et al. (2006) estimate functional connectivity of a real landscape by modelling dispersal for the endangered natterjack toad (*Bufo calamita*) using cost distance. Functional magnetic resonance imaging (fMRI) and dynamic causal modeling (DCM) were used to study multiregional effective connectivity in early-stage PPA ($n = 8$) and control ($n = 8$) subjects performing semantic word matching and visual letter matching tasks Sonty *et al.* (2007). Rajapakse & Zhou (2007) propose to use dynamic Bayesian networks (DBN) to learn the structure of effective brain connectivity from functional MRI data in an exploratory manner. To the knowledge Stephan *et al.* (2009) provide the first formal evidence that probabilistic knowledge of anatomical connectivity can improve models of functional integration. Antoine *et al.* (2009) propose a functional connectivity indicator by adapting the 'volume to breakthrough' concept: the degree of surface connection as a function of the surface storage filling. Friston *et al.* (2014) introduce a dynamic causal model (DCM) for resting state fMRI time series based upon observed functional connectivity—as measured by the cross spectra among different brain regions. Thomas *et al.* (2014) analyze functional connectivity in multiple brain resting state networks (RSNs) in a cross-sectional cohort of participants with ADAD ($n = 79$) and LOAD ($n = 444$), using resting-state functional connectivity magnetic resonance imaging at multiple international academic sites. Park *et al.* (2018) use a discrete cosine transform basis set or eigenvariates (i.e., expression of principal components) to model fluctuations in effective connectivity over windows.

Literatur

- Antoine, Michael, Javaux, Mathieu, & Biielders, Charles. 2009. What indicators can capture runoff-relevant connectivity properties of the micro-topography at the plot scale? *Advances in Water Resources*, **32**(8), 1297–1310.
- Astolfi, L, Cincotti, F, Mattia, D, Salinari, S, Babiloni, Claudio, Basilisco, A, Rossini, PM, Ding, L, Ni, Y, He, B, *et al.* 2004. Babiloni F. Estimation of the effective and functional human cortical connectivity with structural equation modeling and directed transfer function applied to high-resolution EEG. *Magnetic Resonance Imaging*, **22**, 1457–1470.
- de la Vega, Alejandro, Chang, Luke J, Banich, Marie T, Wager, Tor D, & Yarkoni, Tal. 2016. Large-scale meta-analysis of human medial frontal cortex reveals tripartite functional organization. *Journal of Neuroscience*, **36**(24), 6553–6562.
- Friston, Karl J, Kahan, Joshua, Biswal, Bharat, & Razi, Adeel. 2014. A DCM for resting state fMRI. *Neuroimage*, **94**, 396–407.
- Park, Hae-Jeong, Friston, Karl J, Pae, Chongwon, Park, Bumhee, & Razi, Adeel. 2018. Dynamic effective connectivity in resting state fMRI. *NeuroImage*, **180**, 594–608.
- Penny, Will D, Stephan, Klaas E, Mechelli, Andrea, & Friston, Karl J. 2004. Modelling functional integration: a comparison of structural equation and dynamic causal models. *Neuroimage*, **23**, S264–S274.
- Rajapakse, Jagath C, & Zhou, Juan. 2007. Learning effective brain connectivity with dynamic Bayesian networks. *Neuroimage*, **37**(3), 749–760.
- Škoch, Antonín, Reháč Bučková, Barbora, Mareš, Jan, Tintěra, Jaroslav, Sanda, Pavel, Jajcay, Lucia, Horáček, Jiří, Španiel, Filip, & Hlinka, Jaroslav. 2022. Human brain structural connectivity matrices—ready for modelling. *Scientific Data*, **9**(1), 486.
- Sonty, Sreepadma P, Mesulam, M-Marsel, Weintraub, Sandra, Johnson, Nancy A, Parrish, Todd B, & Gitelman, Darren R. 2007. Altered effective connectivity within the language network in primary progressive aphasia. *Journal of Neuroscience*, **27**(6), 1334–1345.
- Stephan, Klaas Enno, Tittgemeyer, Marc, Knösche, Thomas R, Moran, Rosalyn J, & Friston, Karl J. 2009. Tractography-based priors for dynamic causal models. *Neuroimage*, **47**(4), 1628–1638.
- Stevens, Virginie M, Verkenne, Catherine, Vandewoestijne, Sofie, Wesselingh, Renate A, & Baguette, Michel. 2006. Gene flow and functional connectivity in the natterjack toad. *Molecular ecology*, **15**(9), 2333–2344.
- Thomas, Jewell B, Brier, Matthew R, Bateman, Randall J, Snyder, Abraham Z, Benzinger, Tammie L, Xiong, Chengjie, Raichle, Marcus, Holtzman, David M, Sperling, Reisa A, Mayeux, Richard, *et al.* 2014. Functional connectivity in autosomal dominant and late-onset Alzheimer disease. *JAMA neurology*, **71**(9), 1111–1122.