
Region-network sparsity priors for high-dimensional inference in fMRI data

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Abstract

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1 Introduction

Many quantitative scientific domains underwent a recent passage from the classical regime (i.e., "long data") to the high-dimensional regime (i.e., "wide data") [21]. Also in the brain imaging domain, many contemporary methods for acquiring brain signals yield more variables per observation than total observations available in a data sample. This scenario challenges many statistical estimators from classical statistics. For instance, linear regression models without additional assumptions yield an infinity of possible coefficients and, thus, no solution. *Sparsity* assumptions have consequently been introduced and made many ill-posed estimation problems tractable [7, 17]. Domain-specific structure can be imposed on the statistical estimation, thus preassuming that variables have unequal importance and follow existing knowledge [2]. Sparsified supervised and unsupervised learning algorithms have proven to yield statistical relationships that can be readily estimated, reproduced, and interpreted [16]. Yet, what neurobiological structure suggests itself to successfully tackle the *curse of dimensionality* in functional neuroimaging research?

Concepts on human brain organization have long been torn between the two extremes *functional specialization* and *functional integration*. Functional specialization emphasizes that microscopically distinguishable brain regions probably solve distinct classes of computational processes [22]. Functional integration, in turn, emphasizes that brain function is probably enabled by complex connections between these distinct brain regions [28]. These notions were predominantly derived from invasive examination of *structure* (i.e., histological preparation), *connectivity*, (i.e., axonal tracing), and *functional properties* (i.e., single cell recordings) in same animals. Regarding functional segregation into specialized regions, early histological investigations into the microscopic heterogeneity of the human cerebral cortex have resulted in several detailed anatomical maps [5, 32]. Regarding axonal connections, each such cortical area has been observed to possess a unique set of incoming and outgoing connections [24, 34, 26]. Both local cyto- and chemoarchitectonic infrastructure and its unique global connectivity profile together realize computational processes (i.e., function). While cortical modules versus connections between those reflect functional specialization versus functional integration [15, 23], both architectural principles are conceptually inextricable when explaining the emergence of mental operations [31].

Functional specialization has been explored and interpreted based on many different research methods. Single cell recordings and microscopic examination revealed, for instance, the specialization in the visual cortex into V1, V2, V3, V3A, and V4 [18, 36]. Tissue lesion of the mid-fusiform gyrus of the visual system were frequently reported to impair recognition of others' identity from

faces [19]. The localization of sensory, motor, and emotional cognitive functions to cortical areas in the living brain has later been enabled by non-invasive brain imaging with functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) [14]. Further, radioactive mapping of neurotransmitter receptor distributions rendered accessible yet another local characteristic of neuronal populations [37]. In the computational era, automatic clustering methods are increasingly employed to regionally differentiate the cerebral cortex, which can partly be more fine-grained than classical cytoarchitectonic borders [4, 12]. Today, high-throughput computing enables ultrahigh-resolution 3D models of brain anatomy at macroscopical to near-cellular scale [1]. As a crucial common point, all these methodological approaches yield neuroscientific findings that are naturally interpreted according to non-overlapping, discrete region compartments as the basic architectonic framework of brain organization.

It is more recent that the main interpretational focus has shifted from circumscribed regions to network stratifications in systems neuroscience [35, 30]. The higher the processing hierarchy level, the more a cortical area is known to connect to different large-scale networks [33]. Invasive axonal tracing studies in monkeys were complemented by in-vivo diffusion MRI tractography in humans as a now frequently employed method to outline fiber bundles between brain regions [20]. Besides analyses of electrophysiological oscillations [9] and graph-theoretical properties [8], studies of functional connectivity [6] and independent component analysis (ICA) [3] became the workhorses of network discovery in functional neuroimaging. These revealed the important implication of canonical brain networks across cognitive domains, including the so-called “default-mode network” [25], “salience network” [27], and “dorsal attention network” [11]. Characteristic changes in the configuration of these large-scale networks were repeatedly observed to be induced by the onset of given cognitive tasks [13]. Such task-induced mechanisms orchestrating supraordinate networks might be subserved by the right anterior insula [29] and temporo-parietal junction [10]. Ultimately, interpretation of findings from all these methods naturally embraces cross-regional integration by overlapping network compartments as the basic architectonic framework of brain organization, in stark contrast to methods examining regional specialization.

Building on these interpretational traditions, the present study proposes to incorporate known architectonic aspects from both anatomical segregation and integration into unified classification and regression algorithms by means of structured sparsity assumptions. The “true” relative importance of local region compartments and global network compartments is typically unknown but probably varying in degree across diverse neuroscientific questions. Recent advances in multivariate statistical learning techniques enable such adaptive estimators with neurobiologically plausible region and network priors. Using a large reference dataset, we demonstrated that domain-informed supervised models gracefully handle the curse of dimensionality, yield many more human-interpretable results, and generalize better to new samples than domain-naïve models.

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