**Connectal Coding: Discovering the Structures Linking Cognitive Phenotypes to Individual Histories**

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Introduction

* Neural coding: models of brain activity which links patterns of brain activity to past, ongoing, and future events
* Connectal coding: models of brain connectivity. Links patterns of brain connectivity to past, ongoing and future events

Modeling Brains as Networks

* Mathematical model of the brain as a network could be “Turing-complete” (can solve any computational problem 🡪 A.I.
* Connectome: an abstract mathematical model of brain structure, denoted G, and is a set of two kinds of objects, vertices and edges.
* For connectomes, graphs typically have edge weights as well as node attributes such as semantic label
* Adjacency matrix can be used to describe connectome, but it mathematically is not a regular matrix, meaning the rows and columns cannot be manipulated.

Example Estimated Connectomes (figures 1A-D very helpful/interesting)

* C. elegans. (Only animal with completed connectome) contains two types of edges for two kinds of neural activities
* Drosophila. Edges are weighted based on counting the number of synapses between a pair of neurons, and directed
* Mouse. Connectivity estimated generated by dMRI 🡪 undirected with weights corresponding to the number of tracts estimated between regions
* Human. This multi-connectome estimate is derived from averaging the entire dataset of 3,067 diffusion and 1,760 functional MRI connectomes

The Purpose of Brain Codes

* Connectal codes correspond to the brain’s storage of information
* Activity and connectal codes are random with random probability so they can be analyzed statistically but not precisely predicted
* Likely that the genome encodes a number of statistical principles governing the probability of connections between nodes (we know this b/c there are significantly more neurons and connections that genes)
* Genome also encodes rules for learning new conditions due to plasticity, which are the principles of connectal coding

The Role of Connectomes in Connectal Coding

* Connectotype: the collection of nodes and edges (and potentially their attributes) associated with a given phenotype
  + Individual histories: ancestral, developmental, and experiential histories
  + Cognitive phenotypes: set of observable characteristics of an individual related to cognition
* Connectomes primary value is to generate hypotheses about connectotypes and give insight into the relationship between brain structure and individual histories/cognitive phenotypes

Models of Connectomes

* Three categories of mathematical and statistical approach to analyze connectomes are “bag of edges”, “bag of features”, and statistical modeling of networks.
* Only statistical modeling of networks is sufficient for connectal coding because it can be used on populations of networks with complex attributes

Statistical Models for Connectal Coding

* Estimate the statistical relationships among connectomes and genomes, developmental histories, cognitive phenotypes, and current environment

Taken from article: Let X and Y be random variables; their marginal distributions, P[X] and P[Y], characterize the probability of any particular x or y, and their joint distribution P[X,Y] characterizes the probability of observing x and y. The conditional distribution P[Y|X] characterizes the probability that Y takes a particular value, given that X is some value. In connectal coding, we have the following four random variables:

● B = cognitive phenotypes of an individual, including and as measured by behaviors,

● C = connectome of an individual, spanning spatial and temporal scales,

● D = developmental history of an individual, including past experiences

● E = the current environment acting on individuals, and

● G = genome of an individual, including epigenetic factors.

Connectal Coding Theories

* Hypothesis testing can be used to identify if there is a difference between connectomes, but not where they are
* Signal subgraph searches determine which features are most informative about a covariate. This method takes advantage of the graph structure

Application

* Models from Drosophila investigation and analysis provides a foundation to formulate statistical tests to answer connectal coding problems
* The framework can provide statistical support to scientific claims regarding brain illnesses (schizophrenic and healthy brain comparison example)

Discussion (further application)

* Study cognitive disorders, such as schizophrenia. Ability to develop clinically useful prognostic, diagnostic, and treatment protocols will depend on connectal coding.
* Studying memory in healthy brains
* To learn which connectotypes are required for a brain simulation to exhibit specific cognitive phenotypes
* Machine intelligence advances in waves as more is discovered about how the brain works