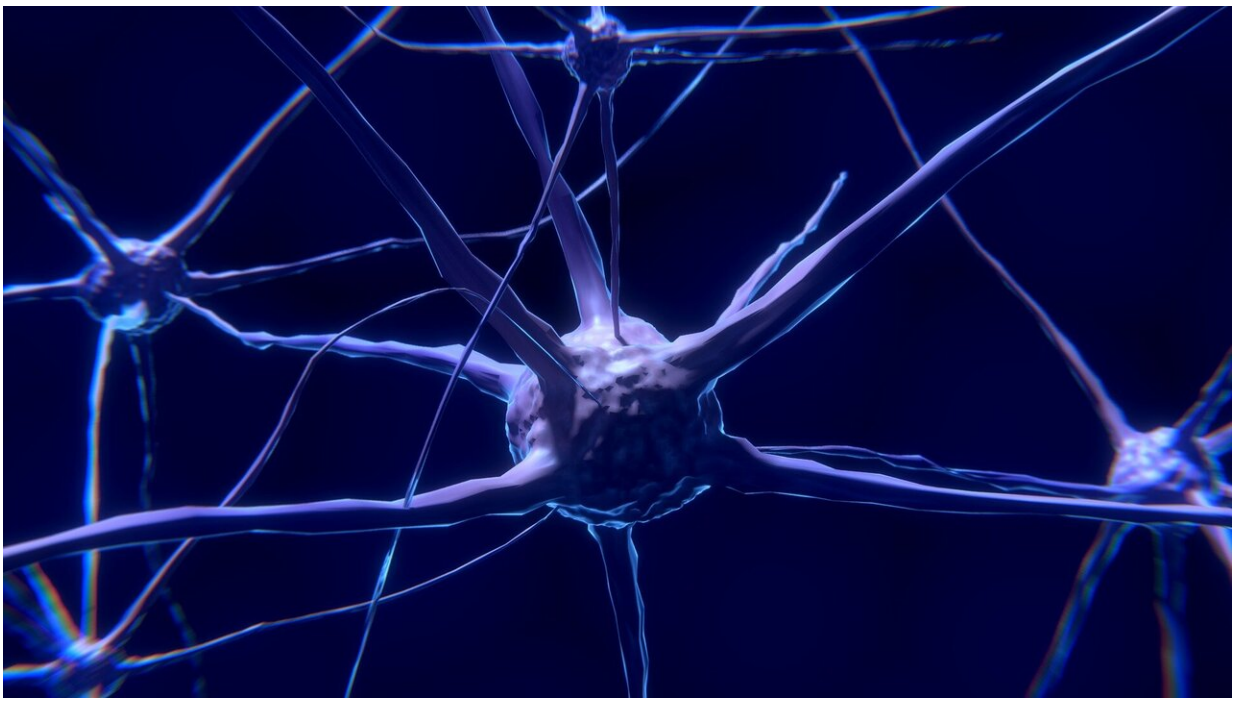
SYNGO Consortium releases public data resource for universal reference in synapse research

June 3 2019



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Synapses, the junctions that serve as specialized contacts between nerve cells, are the brain's fundamental information processing units. A loss of coordinated activity at the synapse lies at the root of many brain disorders (collectively called "synaptopathies"). However, to date,

researchers have lacked any centralized, systematic repositories of information dedicated to synapse biology.

The SYNGO Consortium, a collaboration bringing together 15 laboratories worldwide and the Gene Ontology (GO) Consortium, has released SYNGO 1.0, the first version of a knowledge base (http://www.SYNGOportal.org) that aims to represent the neuroscience community's current scientific knowledge about the genetic architecture of the synapse. Using structured frameworks called ontologies, SYNGO 1.0 provides nearly 3,000 descriptions of more than 1,100 unique synaptic genes, compiling published experimental information about their protein products' localization and/or function and making this curated information available in both human- and machine-readable formats. SYNGO is fully integrated in the GO knowledge base (http://geneontology.org), the world's largest source of information on the functions of genes.

In an accompanying paper in the journal *Neuron*, consortium members use SYNGO 1.0 to show that synaptic genes have changed little over the course of evolution (that is, are evolutionarily well-conserved), and are functionally much more sensitive to (that is, less tolerant of) mutations than other genes expressed in the brain. In addition, the authors also show that variations in many synaptic genes are significantly associated with such traits as intelligence, educational attainment, ADHD, autism, and bipolar disorder. Synaptic genes are also much more likely than other brain-expressed genes to bear mutations associated with neuropsychiatric disorders.

The SYNGO Consortium was established in 2015 by Steven Hyman and Guoping Feng of the Stanley Center for Psychiatric Research at the Broad Institute of MIT and Harvard in Cambridge (MA), and is coordinated by Guus Smit and Matthijs Verhage of the Center for Neurogenomics and Cognitive Research (CNCR) at VU University,

Amsterdam, The Netherlands; and, for the GO Consortium, Paul Thomas at the University of Southern California.

A public knowledge portal

The transmission of signals from one nerve cell to another is orchestrated by a large collection of proteins located on the surfaces of the neurons on either side of a synapse, together encoded by probably a few thousand genes. Decades of research have provided "parts lists" for different types of synapses, as well as many hints as to how these proteins work together to drive synaptic functions. The SYNGO Consortium came together to synthesize this available knowledge and begin to provide an over-arching framework or model for describing it.

As a public knowledge base for synaptic research, SYNGO provides:

1. A standardized framework of definitions (an ontology) for describing the functions, locations, and relationships of proteins and genes in the context of the synapse.
2. Expert-curated, literature-based annotations linking synaptic genes and proteins to specific terms.
3. Online analysis and visualization tools for evaluating the locations and functions of individual synaptic genes or to perform 'enrichment' studies.

The SYNGO knowledge base portal allows researchers to:

1. Search for synaptic proteins, find related proteins, evaluate the evidence for their synaptic localization and/or function, and use links to other information on synaptic proteins/genes.
2. Analyze gene/protein sets from user-provided -omics data and discover a) how such data is structured, b) which proteins are synaptic, c) whether synaptic proteins are over-represented in

such data, d) where proteins localize in the synapse, and e) what they may do. SYNGO web tools helps users to explore their data, and visualize the analysis results. SYNGO uses a machine-searchable format, and is fully integrated in the widely-used GO framework.

3. Contribute new annotations for synaptic genes and proteins.

"SYNGO is a unique resource," said Verhage, a member of the CNCR board of directors and head of the departments of functional genomics at Vrije Universiteit's Faculty of Life Sciences and the VU University Medical Center. "It is collectively supported by the international synapse research community, as the first all-inclusive ontology of the synapse. It represents all synaptic localizations and all aspects of synaptic function in a single ontology in an unbiased manner."

"The consortium built SYNGO exclusively based on evidence from published experiments that can be evaluated by users," added Smit, head of molecular and cellular neurobiology and chairman of the board at CNCR. "And its intuitive web tools provide users advanced analysis and visualization opportunities."

The SYNGO Consortium

SYNGO was initiated in 2015 with a meeting of international experts on the synapse at the Stanley Center that explored the possibilities of forming a consortium to generate a world-wide acceptable format for synapse ontology and annotation. Spearheaded by the CNCR, the GO Consortium, and the Stanley Center, SYNGO builds on prior initiatives generated in European synapse research consortia (i.e., EU-Synapse, EuroSpin, SynSys).

SYNGO's first activity was to partner with key opinion leaders in the neuroscience field to build a consensus ontology, annotation, and

curation framework. The SYNGO database relies on the active participation of and knowledge contributions from the synapse biology community. SYNGO can only expand by the help of many, and to that end, the consortium has developed a web-based, transparent, open structure tool—available at SYNGOportal.org—for synaptic annotation with minimal a priori decisions, whereby anyone in the community can add to or modify information in the knowledge base.

"The biology of synapses is critical to understanding the functional connectivity of the brain, which in turn underlies the functioning of the brain in health and disease," said Steven Hyman, director of the Stanley Center and a core institute member of the Broad. "By advancing the empirical foundations and creating effective processes for comprehensively capturing what we know about the synapse, SYNGO will help us identify patterns that might be otherwise invisible and accelerate the progress of neuroscience in understanding and addressing neuropsychiatric and neurodevelopmental disorders."

More information: *Neuron* (2019). DOI: 10.1016/j.neuron.2019.05.002

Provided by Broad Institute of MIT and Harvard