# From worms to humans: common principles of large-scale organization in the nervous system

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Despite the significant differences in the number of neurons and structures observed in the brains across the animal kingdom, the nervous systems of all animals suffer of similar limitations to aquire reliable information from the environment and serve the same functional purpouses. These limitations and goals are the main driving forces shaping the large-scale architecture of the neuronal connectivity. We review knowledge gained in the recent years by means of complex network analysis on the organization of both anatomical and functional connectivity of few species. They share a few fundamental architectural features: (i) neural systems posses short but abundant alternative processing paths, (ii) neurons and cortical regions form clusters of densely interconnected elements, and (iii) neural systems contain few network hubs. This architecture supports the idea that brain function is to be understood as emerging from the collective working of its constituents without a single coordinating center. The modular organization is a consequence of the specialization of different parts, and the highly interconnected hubs help in the integration and/or coordination of multisensory information.

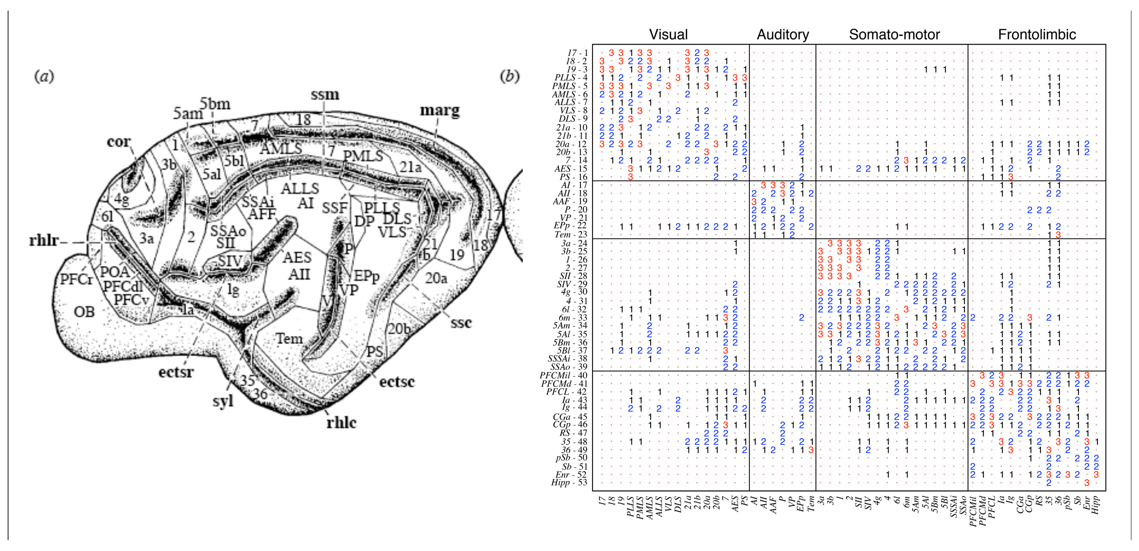
## MOTIVATION

The neurons in a nervous system form a vast and complex network of communication, whose architecture has been shaped during evolution as a trade to overcome **limitations** (poor computational capacity of neurons, energy consumption, etc.) and to serve its f**unctional necessities** (collect and process sensory information).

Comprehensive data of anatomical connectivity is scarce and difficult to obtain. A complete map ef every neuron and their axonal projections in a brain is out of technological reach. **Tract-tracing** experiments permit to identify long-range fibers by following the dispersion of chemical dyes. For humans, non-invasive **neuroimaging and electro-physiological** techniques are a window to connectivity.

## CAT CORTICAL CONNECTIVITY

The cat cortico-cortical connectivity data of cats was first published by [Scannell, 1993] as a collation of tract-tracing experimental reports. Graph analysis of this corticocortical network has revealed striking topological properties:




**Figure–1: CORTICAL NETWORK OF CATS**

The network consists of a parcellation of the cortex (**a**) into 53 cortical areas which are connected by 826 long-range fibers. (**b**) Adjacency matrix of the network.

**1) Modular organization:** Clustering analysis of the network reveals four **network modules** (groups of densely interconnected areas) which contain areas involved in either visual, auditory or somatosensory functions, and a fourth module composed of frontolimibic areas [Hilgetag, 2000].

**2) Short processing paths.** Average pathlength is of only L ~ 1.83. Areas influence each other either by direct projections or are separated by only two processing steps.

**3) Multiple routes of information.** Statistical analysis of the corticocortical communication paths reveals several alternative paths between pairs of cortical areas [Zamora-López, 2009].

**4) Cortical hubs.** Few cortical areas are largely connected to other areas. Two major implications of the presence of these hubs are the following:

- Communication paths between different modules are ***not random but centralised***, they go through the cortical hubs [Zamora-López, 2009].
- Cortical hubs are densely interconnected, forming a ***rich-club*** structure [Zamora-López, 2010].

The network is organised into a ***modular architecture with centralised hierarchy***, whose top level is formed by the cortical hubs. This architecture represents the physical substrate that permits the brain to simultaneously process information of different modalities (***parallel processing***) and to ***integrate*** that information toward the generation of a coherent, global representation of the reality.

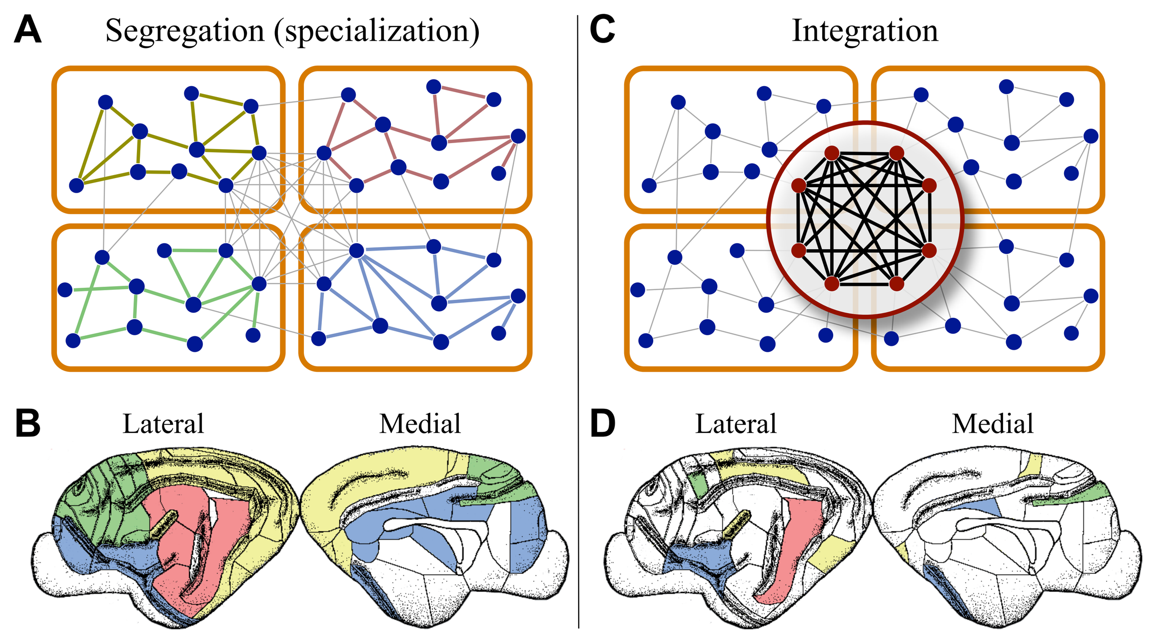



**Fig-2: DISTRIBUTED "*CENTER OF CONTROL*"**

Cortical hubs form a functional module on top of the modular architecture of the cat cortical network, giving rise to a modular structure with centralized hierarchy. Contrary to typical rules of cortical organization, the module formed by the cortical hubs is distributed all along the cortex.

Beyond integration, **cross-modal connections** can be associated to modulation of the neuronal activity in other modalities [Driver, 2000]. A detailed analysis of the multisensory connectivity in the cat reveals: **1)** most cortical areas have afferent and efferent projections to areas of other sensory modality and **2)** we can classify cortical areas into three categories: **unimodal**, **multimodal** and **supramodal** [Zamora-López, 2011].

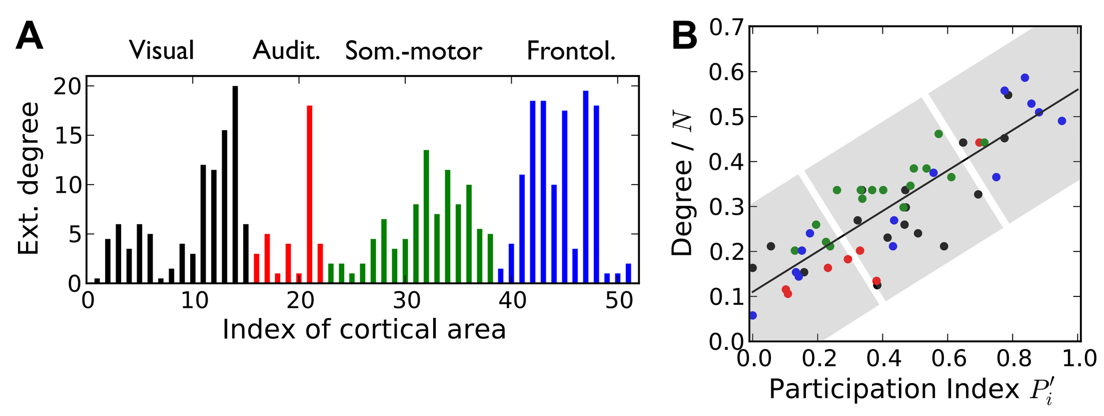



**Figure-3: MULTISENSORY CONNECTIVITY**

(**A**) Number of cross-modal connections of each cortical area in the cat. (**B**) Mapping of the multisensory importance of cortical areas. The ascending trend is a particular characteristic of the modular organization with centralised heirarchy of the network.

## *CAENORHABDITIS ELEGANS*

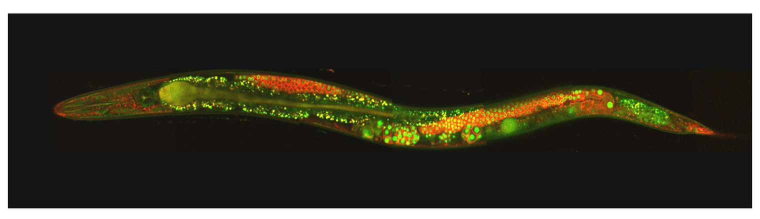


**Figure-4: CAENORHABDITIS ELEGANS**

The nervous system of the nematode *C. elegans* has been fully mapped by reconstruction of electron micrographs of sectioned specimens [Durbin, 1987; Varshney, 2011] . It contains 302 neurons and approximately 6400 chemical synapses and 900 gap junctions.

Clustering analysis of the network shows that its neurons are arranged into a **modular hierarchical architecture** [Pan, 2010]. The modules contain neural circuits which play a vital role in performing different functions: chemosensation, thermotaxis, mechanosensation, feeding, etc. [Arenas, 2008].

The network is characterised by **short processing paths** (*L* ~ 4.0). **Hub neurons** have been found [Varshney et al., 2011] which are central in information processing. In particular, command interneurons (responsible for worm locomotion) have high degree centrality.

## HUMAN BRAIN

Data of human brain connectivity is obtained by non-invasive methods which lack the accuracy of methods for animal models. **Tractography,** based on neuroimaging have revealed human large connectivity networks (white matter). Functional imaging and electroencephalography permit to reconstruct **functional networks** as correlated dynamical inferences between brain regions or sensors.

Although they differ in terms of experimental methodology and cortical parcellation, most studies reveal highly clustered networks, with most pathways existing between areas that are spatially close and functionally related. These **modules** are interlinked by **hub regions**, ensuring that overall path lengths across the network are short [Bullmore, 2009; Meunier, 2010].

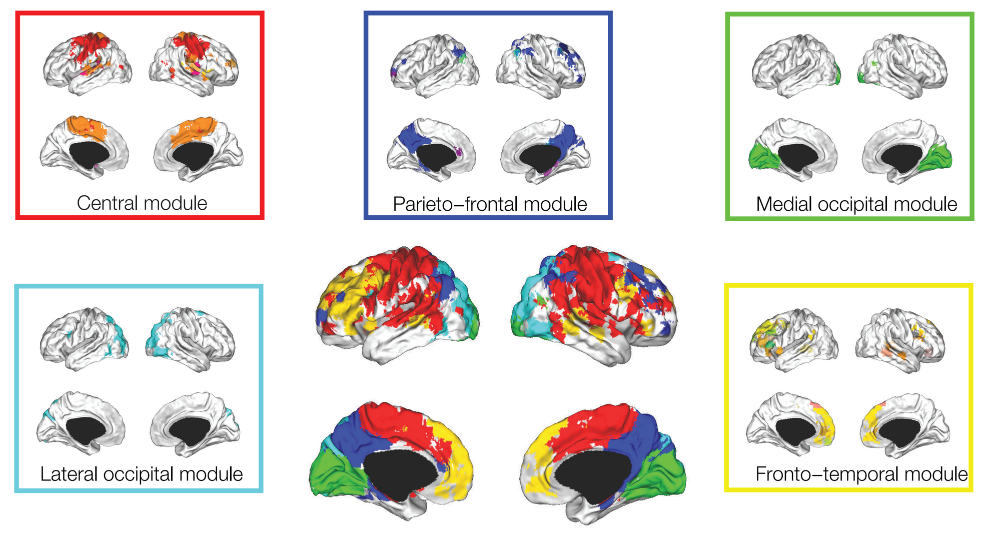



**Figure-5: HIERARCHICAL MODULARITY**

Clustering analysis of functional brain networks reveal hierarchical modularity, i.e, modules which can be decomposed in further submodules.

## DISCUSSION

All neural connectivity studies report the following: **1)** ***short and abundant processing paths***, **2)** ***hierarchical / modular organization***, and **3)** the presence of ***highly connected hubs***. These common principles of organisation arise because the nervous system of all animals serve the same functional purpouses and suffer from similar limitations to collect and processe sensory information. Combined together, these characteristics imply that the neural networks are **highly interactive systems**.

**SPECIALIZATION LEADS TO MODULARITY**

Sensory neurons collect only one type of sensory information. Therefore, the paths of sensory processing of different modal information remain segregated of each other giving rise to groups of neurons specialised in the processing one modal information (parallel processing).

**HUBS LEAD TO INTEGRATION**

But, a collection of specialized functional modules alone cannot give rise to a coherent perception of the reality. For that, information of different modalities needs to be combined. Cortical and neural hubs play a crucial role by centralizing the paths of information between modalities.

## REFERENCES

Arenas, Fernández et al.. *Lect. Notes Comput. Sci.* **515**, 9 (2008).
Bullmore & Sporns *Nat. Rev. Neurosci.* **10**, 1 (2009).
Driver & Spence, *Curr. Biol.* **57**, 11 (2000).
Durbin. *Ph.D Thesis, Kings College*, Oxford (1987).
Hilgetag et al. *Phil. Trans. R. Soc. London,* **355**, 71 (2000).
Meunier, Lambiotte & Bullmore, *Front. Neurosci.* **4**, 200 (2010).
Pan, Chatterjee & Sinha, *PLoS ONE* **5**, e940 (2010).
Scannell & Young, *Curr. Biol* **3**, 191-200 (1993).
Varshney, Chen et al. *PLoS Comput. Biol.* **7**, e1001066 (2011).
Zamora-López, Zhou & Kurths, *Chaos* **19**, 015117 (2009).
Zamora-López, Zhou & Kurths, *Front. Neuroinf.* **4**, 1 (2010)
Zamora-López, Zhou & Kurths. *Front. Neurosci.* **5**, 83 (2011).

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