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Connectomics: a need for comparative studies

Introduction

The brain, like any biological entity, is a product of natural evolution. This statement applies equally to the brain of humans as it does to that of flies or red-eyed tree frogs. An evolutionary or comparative perspective on brain function can be informative on at least two levels: the *mechanistic*, by identifying inherited features (e. g., molecular and biophysical components) and the *algorithmic*, by pointing to similar forms of solutions to common problems (e. g., circuit graphs, cellular and circuit operations). Of particular interest are cases where common algorithms are not inherited from a common ancestor but rather result from evolutionary convergence (i. e., independent histories and paths towards solutions, in response to similar physical constraints) [11]. Those instances, clear evidence for which is still admittedly rare, are extremely useful because they point to the essence of neural circuit operations, separating computational and algorithmic solutions from the nitty-gritty details of a specific implementation. A comparative approach to understanding brains as information processing systems thus meets David Marr's classical distinction between levels of understanding-computation, algorithm, implementation [6].

What to compare?

An evolutionary approach to brain function requires comparisons. One great practical difficulty in this exercise lies in defining the objects of these comparisons. Should they be gene or protein sequences [8], spatio-temporal gene expression patterns, cell morphologies, architectonics, connectivity graphs, cir-cuit motifs, gross structural features, biophysical and synaptic characteristics, emergent properties (e. g., travelling waves, consciousness), or functional consequences (e. g., scaling, recognition, selection, transformation), to take only a few examples? In other words, what are the relevant dimensions? At a time when modern technology takes us from an artisanal to an industrial era of neuroscientific investigation, should we acquire all data that can be obtained, on the premise that any data are useful? If so, how do we harmonize data acquisition, archiving, and cataloguing? Can we agree on a taxonomy, even for operations and computations, the nature of which we do not even necessarily know or fully understand yet? Or do we make some practical operational choices? If so, which ones? These questions are very important if we wish, for example, to cluster and compare datasets. The answers depend much on how we conceive of "understanding the brain". Understanding implies reducing the description, i. e., throwing away. But what can we throw away? How do we know *a priori*? A comparative approach is thus useful also in that it forces us to identify, or at least be explicit about, the features that matter to reach a functional understanding.

Examples of comparative analysis

This laboratory has worked extensively with insect nervous systems in the past and some of this work has led to the description of computational phenomena, such as cellular multiplication for looming detection in vision [2, 3] that have an algorithmic equivalent in thala-mic neurons of birds [13]. The common ancestor of insects and chordates lived between 530 and 580 million years ago and was, to the best of our present knowledge, a type of worm, with neither visual thalamus nor optic lobes. This is as close as one can get to evidence for convergent evolution of computation. Similarly, our work on olfaction led to the discovery of a spike-timing-dependent plasticity rule in locusts [1], with a shape and temporal dependence remarkably similar to those established earlier in vertebrate nervous systems [5]. While Hebbian STDP in vertebrate brains occurs at glutamatergic synapses, the locust synapses at which STDP is found may instead be cholinergic (though what the excitatory neurotransmitter actually is at this synapse remains frustratingly unclear in any insect so far examined). Other recent work in insects [12] reveal the existence of neurons not unlike rodent hippocampal head-direction cells [14], and of prey-capture behavior implying the existence of predictive internal models of prey movement [10], not unlike those observed in humans [9]. These parallels further illustrate the interesting dichotomy between computation and implementation. It is not that one aspect is more or less interesting than the other: details of implementation will obviously matter if your goal is therapeutics development for human medicine. But these examples illustrate the value of diversity in model systems and approaches for modern neuroscience, precisely because they enable us to separate implementation detail from function and computation. If our ultimate goal is to derive a theory of the brain, our best hope is to identify computational principles, and our goal should be to avoid unnecessary intricacies with accidental

roots in evolutionary history. I would argue that such diversity will be just as important in the area of connectomics, that is, in the search for structural motifs and for their possible computational functions. The diversity of mammalian early visual system cortical architecture, for example, suggests that some macroscopic structural attributes identified in original experimental studies (e. g., maps of orientation in cat or macaque primary visual cortex) may not be a general rule [7].

Conclusion

In closing, it is appropriate to remind the reader that the need for operational open-mindedness is not specific to biological and evolutionary questions. Yakov Frenkel, the famous 20th century Russian scientist, advocated model diversity in his own domain, condensed matter physics, in these terms:

A good theoretical model of a complex system should be like a good caricature: it should emphasize those features which are most important and should downplay the inessential details. Now the only snag with this advice is that one does not really know which are the inessential details until one has understood the phenomena under study. Consequently, one should investigate a wide range of models and not stake one's life (or one's theoretical insight) on one particular model only [4].

I'd argue that, to help our thinking about circuits and the computational logic of their micro-architecture, we should exploit the diversity generated by evolution to identify the deep underlying rules that govern their operations.

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Gilles Laurent: a French citizen, was born in 1960 in Casablanca, Morocco. After a PhD in Neuroethology from the University Paul Sabatier of Toulouse (France) and a Doctorate in Veterinary Medicine in 1985, he worked as a postdoc and a Locke Research Fellow of the Royal Society at the University of Cambridge/UK. In 1990, he joined the faculty of the Biology Division at the California Institute of Technology (Pasadena, CA, USA), where he became Lawrence A. Hanson Professor of Biology in the field of "Computation and Neural Systems" in 2002. His interests are in experimental and computational neuroscience, with an emphasis on coding and circuit computation in the olfactory and visual systems. In 2008, Gilles Laurent was appointed Director of the Department of Neural Systems and Coding at the Max Planck Institute for Brain Research in Frankfurt am Main (Germany).

Compliance with ethical guidelines

Conflict of interest. G. Laurent state that he has no competing interest.

This article does not contain any studies with human participants or animals performed by any of the authors.

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Connectomics: a need for comparative studies

Abstract
Connectomics, the study of circuit architecture, has the potential to reveal the connectivity of any brain or brain area with single-synapse resolution. This is extremely exciting but at the same time quite daunting. The exciting part is obvious. The daunting part is less so, and relates to the challenge of extracting principles from overwhelming masses of high-resolution data. You might say that it is a nice problem to have, and I will agree. What I will argue here is that, if our goal is to derive from such data a general and theoretical understanding of the brain, we must now more than ever take advantage of comparative approaches.

Keywords
Comparative neuroscience · Brain evolution · Neural circuit

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