NeuroImage xxx (2013) xxx–xxx

Contents lists available at SciVerse ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg

Review

The history of CoCoMac

Klaas Enno Stephan *

Translational Neuromodeling Unit (TNU), Institute of Biomedical Engineering, University of Zurich & Swiss Federal Institute of Technology (ETH Zurich), Switzerland
Laboratory for Social and Neural Systems Research (SNS), University of Zurich, Switzerland
Wellcome Trust Centre for Neuroimaging, University College London, UK

ARTICLE INFO

Article history:
Accepted 7 March 2013
Available online xxxx

Keywords:
Connectivity
Network
Circuit
Database
Tract tracing
Computational neuroscience
Neuroinformatics
Objective relational transformation
ORT

ABSTRACT

CoCoMac, the "Collation of Connectivity Data for the Macaque" is a relational database system which presently constitutes the largest electronic repository of published neuroanatomical connectivity data. Developed since 1996, CoCoMac comprises approximately 40,000 experimental findings on anatomical connections in the macaque brain, as derived from neuroanatomical tract tracing studies. In this historical review, I describe the origin and the history of CoCoMac from a personal perspective, illustrate the principles of its structure and outline the impact it has had on systems neuroscience, in particular as a prelude to the "Human Connectome" research programme.

© 2013 Elsevier Inc. All rights reserved.

Contents

Introduction: The origin of CoCoMac

The history of CoCoMac dates back to 1996 when I started as doctoral student of Rolf Kötter and Karl Zilles in the C. & O. Vogt Institute for Brain Research at the Heinrich-Heine-University of Düsseldorf. Rolf and I had met two years earlier, in autumn 1994, in the human anatomy dissection course of the university's medical curriculum. Rolf was a young lecturer in anatomy at the time and had recently returned from Dunedin, New Zealand, where he had trained in computational neuroscience, a field that was still rather new and not widely recognised in the early 1990s. In the dissection course, he supervised eight medical students who, over the course of six months, jointly dissected a whole corpse. During this slow and at times almost meditative process, we had ample opportunity to talk and soon discovered similarities in thinking and perspectives. In particular, both of us had a background in computer science and shared the strong belief that many aspects of brain function could only be understood properly on the basis of mathematically formal and biophysically plausible system models. One difference was that Rolf had a very general, almost philosophical, interest in understanding how the brain works. In contrast, my motivation was more strongly driven by clinical questions. In particular, I was under the (slightly delusional) belief that the anatomical and physiological properties of

* Translational Neuromodeling Unit (TNU), Institute of Biomedical Engineering, University of Zurich & Swiss Federal Institute of Technology (ETH Zurich), Wilfriedstr. 6, 8032 Zurich, Switzerland.
E-mail address: stephan@biomed.ee.ethz.ch.

1053-8119/$ – see front matter © 2013 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.neuroimage.2013.03.016

ARTICLE IN PRESS

single neurons and neuronal populations were sufficiently well known that all that remained to do in order to understand complex brain functions and their alterations in disease was to model a sufficiently large number of neuronal units and study the behaviour that would emerge from their interactions. My dream was that such a model would eventually comprise the whole brain and enable a quantitative and formal characterisation of the mechanisms underlying complex brain diseases which had so far escaped our understanding.

Following the dissection course, Rolf and I started working together informally (on historical and conceptual aspects of the "limbic system"; (Kötter and Stephan, 1997)), until I started officially as doctoral student under his and Karl Zilles' supervision in April 1996. (In the German system, it is quite common to complete a dissertation in parallel to one's medical studies or during an intermediate break). The initial goal of my dissertation was to construct a large-scale model of the spread of activity during photosensitive epilepsy. This particular type of epilepsy arises in predisposed individuals after prolonged exposure to flickering light stimuli (typically around 10 Hz). It had been studied in great detail in a baboon model, with the interesting finding that the earliest epileptiform activity appeared in motor cortex, preceding epileptic responses in other parts of the brain (Menini and Silva-Barrat, 1998; Silva-Barrat et al., 1988). One possible explanation rested on the connectivity of the system, assuming a confluence of cortical and subcortical visual inputs in motor cortex with catastrophic resonance effects that would eventually lead to local runaway excitation and its subsequent spread, via long-distance connections, to the rest of the brain. To demonstrate the plausibility of this putative mechanism, I wanted to construct a large-scale model of interacting neuronal populations whose local dynamics was governed by established biophysical equations (e.g., the Hodgkin–Huxley formalism) and which interacted according to the anatomical long-distance connections between the different regions involved. In other words, the hope was that the large number of published neuroanatomical tract tracing studies in the monkey would enable me to build a realistic whole-brain network into which I simply had to plug in conventional biophysical models of neuronal populations. I thus turned my attention to the neuroanatomical connectivity databases for the macaque monkey which were available at the time.

The first database of this kind had become available in 1991. This was the pioneering work by Felleman and Van Essen (1991) who had collected data from numerous tract tracing studies in the visual system of the macaque. Their approach was straightforward and pragmatic: they listed their interpretations of the findings from the tract tracing literature in an Excel spreadsheet, providing a condensed summary of data distributed across hundreds of published studies. Although methodologically based on a simple approach, this initial database enabled statistical analyses of the macaque brain's connectivity layout, such as the hierarchical arrangement of areas in the visual system, which had previously not been possible and which had tremendous impact on neuroscience (as demonstrated by thousands of citations). This work was extended by the group of Malcolm Young at Newcastle who applied additional analyses to the Felleman & Van Essen database (Hilgetag et al., 1996; Young, 1992) and added macaque connectivity data from outside the visual system (Young, 1993). Furthermore, they established connectivity data repositories in other species, such as the rat (Burns and Young, 2000) and the cat (Scannell et al., 1995, 1999).

However, all of these early neuroanatomical connectivity databases suffered from a severe methodological limitation in how the original experimental findings were represented. The problem was that neuroanatomical tract tracing studies do not usually describe their data (i.e., the location of injections and labelled cell bodies and/or terminals) in spatial coordinates but refer to the absence or presence of injections or label within the areas defined by a particular parcellation scheme ("brain map"). Unfortunately, a large number of different parcellation schemes have been proposed over the last few decades, based on different microstructural (e.g., cytoarchitectonic, myeloarchitectonic, chemoarchitectonic) or functional criteria (e.g., neuronal response properties). Since each author chooses his/her favourite (combination of) parcellation scheme(s), a truly Babylonic confusion has arisen in the neuroanatomical literature over the last decades: often the same acronym is used to refer to areas that differ in the definition of the boundaries, e.g. they only partially overlap; more frequently still, different acronyms are used to refer to identically defined areas. Given this problem and the lack of systematic and global attempts in "translating" these different maps, the early connectivity databases by Felleman & van Essen and by the Newcastle group sensibly adopted a pragmatic approach: they chose one particular "reference map" to which they manually translated all original findings from the published literature. This resulted in a compact summary that could be compiled and searched reasonably quickly. However, the disadvantage was that these databases only contained the final results of an opaque transformation that rested on the subjective criteria and judgement of the database creators. This made it impossible to uncover the original data from the database entries and prohibited remapping the original findings into a different parcellation scheme, which was necessary, for example, when the "reference" map was suboptimal for the particular application of the user. Also, the various inconsistencies and contradictions across studies that are prevalent throughout the literature were no longer visible in these databases, making it difficult to judge how one should integrate new data that had arisen since the original publications.

These limitations suggested the creation of an entirely new type of connectivity database: a database that would store the published findings from each paper, described in terms of the parcellation scheme originally used by the authors, and which was equipped with analysis tools that would enable the user to transform the original data into any particular parcellation scheme while leaving the original data completely untouched. From a computer science perspective, this strict division into data representation and data interpretation seemed a natural, and indeed a mandatory, step. I suggested this to Rolf who was initially very sceptical. While I, in my youthful optimism, was convinced that this would be an exercise of at most a few months of hard work, Rolf feared that this methodological challenge would be much harder than I imagined and would distract me from my original goal of building a large-scale system model of photosensitive epilepsy. Of course, he was absolutely right. It took me almost three years to fully develop the theoretical foundations and implement the database structure and algorithms of what came to be known as CoCoMac.

Principles and implementation of CoCoMac

In designing the new database, we started with five general principles; for details, see Stephan et al. (2001). First, objectivity: each entry should be represented in its original nomenclature, with a precise reference to its publication and a citation of the original description. Second, reproducibility: transforming data from one parcellation scheme to another should be based on mathematical algorithms. Third, transparency: not only should the mapping process be fully documented and accessible, but also all inconsistencies and contradictions in the original data should be preserved in the raw data representation. Fourth, flexibility: the user should have the choice of converting the raw data into any chosen target map. And finally, we demanded simplicity: the new database should be able to deal with the existing data in the literature, despite their various shortcomings such as the lack of spatial coordinates.

The algorithmic framework developed on the basis of these five principles was called objective relational transformation (ORT; (Stephan and Kotter, 1999; Stephan et al., 2000b)). ORT consisted of three main components. First, it introduced three classifications: (i) the *Extension Codes* (EC) which described the spatial extent of experimental findings (i.e., the spread of injection or label within an area); (ii) the *Relation Codes* (RC) which comprised all possible logical relations that areas from two different brain maps could have; and

Please cite this article as: Stephan, K.E., The history of CoCoMac, NeuroImage (2013), http://dx.doi.org/10.1016/j.neuroimage.2013.03.016

Download English Version:

https://daneshyari.com/en/article/6028672

Download Persian Version:

https://daneshyari.com/article/6028672

Daneshyari.com