

INTELLIGENT NETWORK MANAGEMENT AND FUNCTIONAL CEREBELLUM SYNTHESIS

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ABSTRACT

Transdisciplinary modelling of the cerebellum across histology, physiology and network engineering provides preliminary results at three organization levels: I/O links to central nervous system networks, links between the six neuron populations in the cerebellum and computation among the neurons of the populations. Older models probably underestimated the importance and role of climbing fiber input which seems to supply write as well as read signals, not just to Purkinje but also to basket and stellate neurons. The well-known mossy fiber-granule cell-Golgi cell system should also respond to inputs originating from climbing fibers. Cortico-nuclear microcomplexing might be aided by stellate and basket computation and associative processing. Technological and scientific implications of the proposed cerebellum model are discussed.

INTRODUCTION

James Clerk Maxwell was a strong proponent of the "cross-fertilization of Sciences". In his Rede Lecture on "The Telephone", he honored Alexander Bell for not being a specialist who "builds up particular sciences", but for being one "who opens such communications between the different groups of builders as will facilitate a healthy interaction between them" [1]. Maxwell had exploited what he called "that partial similarity between the laws of one science and those of another which makes each of them illustrate the other" as a tool to build a unified theory of electromagnetism using mechanical analogies. Michael Idvorsky Pupin later adapted the very same tool to transform acoustical into electrical machinery [2]. The need to accelerate reciprocal transdisciplinary crossings between neuroscience and computer science was highlighted recently [3]. Some neuroscientists recognize the benefits to be expected from infusion of engineering and other ideas into their field [4] and anticipate a symbiotic relationship between modelling and experimental research [5].

This paper is a preliminary report of research recently undertaken under the auspices of RIACS at NASA's Ames Research Center. The work described here is carried out jointly with Jim Keeler (now at MCC), with Coe Miles-Schlichting of RECOM, and David Rogers of RIACS, both at NASA Ames Research Center. The goal is to develop a mathematical model of a mammalian cerebellum and to construct a functioning hardware implementation of one of its portions. We are attempting to preserve as many of its salient network topology and information processing features as is reasonably possible. In this we hope to follow the design philosophy of RCA's 1960-61 functional optoelectronic model of the frog retina [6] which culminated in the 1963 construction of the largest and most complex functional and parallel processing neural networks in existence at that time [7].

Thus far we critically sifted through books, bibliographies, abstracts and articles of a vast literature and selected those few that we expect to rely upon. As new experimental techniques produce more accurate findings, older theories and models get challenged and sometimes discarded. In order to synthesize the truest-to-life cerebellar functions, we have attempted to reconcile contradictions in reported facts and proposed interpretations. For example, we think that a modified functionality should be assigned to neurons targeted by climbing fiber collaterals since this seems to better fit recent physiological results.

During our attempts to classify the information and rank it, we tried to resist the "all too convenient" temptation to overlook inconvenient facts in order to simplify the model and to follow Einstein's dictum that everything should be made as simple as possible, but not any simpler.

CURRENT FRONTIERS OF NETWORK MANAGEMENT

Churchland and Sejnowski point to two recent reviews by Goldman-Rakic and Mountcastle (see their reference 8) which suggest a "democratic" organization of

processing in webs of strongly interacting networks in the association areas and the prefrontal cortex [5]. They think that this points to a distributed control instead of the more generally assumed single control center. They believe that "coming to grips with systems having distributed control will require both new experimental techniques and new conceptual advances". We agree. However, in our opinion their suggestion to study "models of interacting networks of neurons" needs to be paired and crossfertilized with research on networks of closely and loosely coupled state-of-the-art computers. The latter type research is exemplified by the pioneering work of Amnon Barak and coworkers who have been experimenting with a general-purpose, time-sharing operating system that induces a cluster of loosely connected independent homogeneous computers to act as a single-machine UNIX system [8,9]. We suspect that some of the principles employed by the Barak and other groups may aid in the study of interactivity between different parts of the central nervous system, and that some of the work suggested by Churchland and Sejnowski could in turn provide ideas and insights for future designs of intelligent distributed management within the rapidly growing networks of computing machines.

AN ENGINEERING VIEW OF THE BRAIN

Sir Charles Scott Sherrington, the corecipient of the 1932 Nobel Prize, had observed that the increase of brain complexity during vertebrate evolution correlates both with a greater functional unification of organisms (a closer functional welding of parts) and with greater dominance over their environment (richer and more manifold commerce with the environment). He stressed that connecting originally unconnected structures to act jointly, results in more than a simple sum of the activities of the separate component parts.

It has been pointed out that technological evolution follows principles closely analogous to biological evolution and that wholesale knowledge transfer from biology to technology is possible [10]. Maxwellian exploitation of their mutual similarities can and does provide technologically based inspiration and guidance for theory builders in biosciences. This is especially true for neuroscience and computer technology. The evolution of computer technology has already produced a greater functional unification within large and complex human organizations, as well as greater dominance over their environments.

In this paper we adopt a distributed computer network point of view of the brain. Because computers and their nets are still at a very early stage of their evolution, extreme caution is necessary in setting up the brain/computer analogy. It is well to remember that many brain functions are yet to be duplicated by engineers. Nevertheless, the recent revival of neural network modelling and building offers promise for overcoming conceptual barriers which impede transdisciplinary crossfertilization between technology and biology in general and between neuroscience and computer science in particular.

SYSTEM INTEGRATION OF THE CEREBELLUM

The cerebellum is a major part of the brain. The brain and the spinal cord constitute the central nervous system (CNS). A simplified brain taxonomy breaks up the brain into five parts: the end brain, the interbrain, the midbrain, the afterbrain, and the hindbrain. The end brain and interbrain constitute the forebrain, while the remaining three parts constitute the brain stem. The two major subsystems of the brain are the cerebral hemispheres, which are part of the end brain and the cerebellum which is part of the afterbrain. The other parts of the afterbrain, the pons and cerebellar peduncles, connect the cerebellum to other portions of the CNS. While the physical size of the cerebellum is smaller than that of the cerebral hemispheres, they contain similar numbers of neurons; i.e., between ten billion and one hundred billion.

The cerebellum subdivides into the cerebellar cortex and four pairs of deep cerebellar nuclei (DCN). The neuronal networks of the cerebellar cortex are compactly arranged within a folded three-dimensional matrix whose central layer comprises a regular two-dimensional lattice of flat Purkinje (P) neurons whose bodies define the Purkinje cell layer (PL). The layer above, toward the cortical surface, is the molecular layer (ML) and the layer below, toward the DCN is the granular layer (GL). Many rows of stacked P neurons combine into folia, which further combine into a hierarchically organized structure of sublobules, lobules and lobes. Many columns of P-cells are aggregated into separate zones which are associated with different axonic projections onto different DCN target neurons. This coordinate system allows a high degree of experimental reproducibility and permits the generation of "demographic" maps of sensory and motor projections onto relatively small populations of neurons spell within the cerebellar network [11].

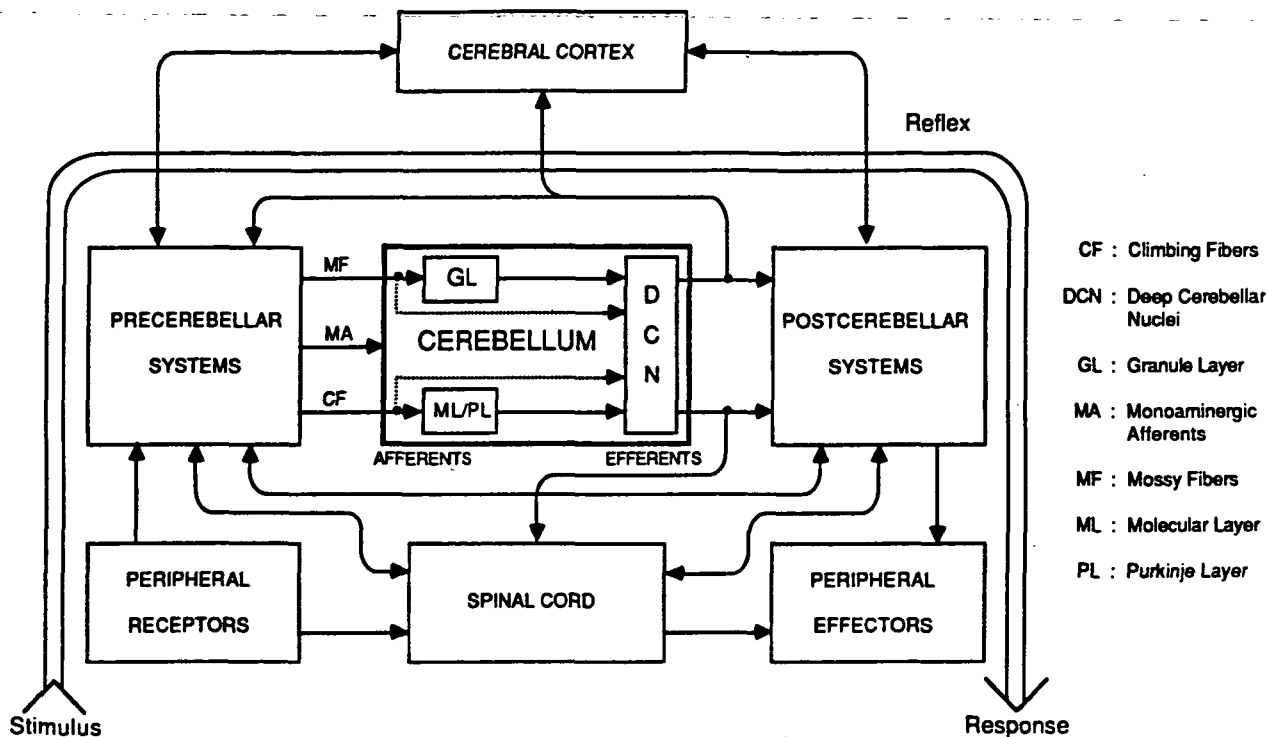


Figure 1. Cerebellar I/O Network

From a network and functional point of view the cerebellum is situated at the midpoint of a great multitude of reflex arcs, which are paths followed by nerve impulses that are responsible for many hundreds of different reflex actions. This we have indicated on Figure 1 which depicts a highly schematized flow diagram of impulse transmission from a sensory receptor source near the point of stimulation via afferent neurons to one or more reflex centers in the spinal cord or brain, and back from these centers through efferent neurons to a motor effector sink near a point of response. Our diagram lumps this great multitude of reflex centers and/or afferent and efferent relay stations into four generalized brain locations: the pre- and post-cerebellar systems, the cerebellum and the cerebral cortex. Neglecting the presence of a great variety of reflex and relay centers in each of these generalized locations, one can still deduce from the network topology of the diagram that there are at least thirty different general paths through this network which connect sensory sources to motor sinks. If we estimate the number of different paths through the large variety of individual reflex centers and relay centers, we arrive at many thousands of reflex arcs, a great fraction of which involve at least one passage through the cerebellum.

This should not be very surprising since the literature contains observations on many kinds of reflexes. A cursory examination revealed over 120. Ito's book lists at least 27 reflexes that involve the cerebellum.

The cerebellum receives three kinds of inputs and produces four kinds of outputs. It receives a high rate of pulses via mossy fibers (MF) which can originate from a very great multitude of precerebellar systems, the spinal cord or the cerebral cortex. It receives a much lower rate of pulses via the climbing fibers (CF) which originate in the inferior olive, a precerebellar system in the hindbrain, that receives inputs from over twenty other centers. These two kinds of inputs have quite different termination topologies. MFs terminate solely in the GL, while CFs terminate in all three layers. The MFs supply constant monitoring of sensory input data [12] while the CFs seem to be dedicated to inputting attention generating sensory data that signals time-uncertain or unanticipated events [13-14]. The third input to the cerebellum are monoaminergic afferent fibers (MA). There are at least two types. The noradrenergic type originates in the locus coeruleus and the serotonergic in the raphe complex. Their function remains obscure. Cerebellar output is produced

in DCNs. In rhesus monkey and cat, the ratio of input GL neurons to output DCN neurons is about a hundred thousand. If we allow for a twenty-five-fold increase in pulse rate from Purkinje to DCN cells, we estimate 4,000 input pulses per cerebellar output pulse. This ratio provides a measure of cerebellar processing power, i.e., its data rate reduction capability.

It should be noted that Figure 1 shows a direct connection of MFs and CFs to the DCNs, bypassing the cerebellar cortex. This supports the fact that absence of the cerebellar cortex does not result in loss of sensation or intelligence. It does result in ataxia, proprioceptive misperception, poor muscular coordination and inability to adapt to changing environmental conditions. Such behavior can be compared to an orchestra that lacks a conductor. The music score is followed but there are difficulties with coordination and synchronization of the players and any to-be-remembered changes in their performance.

CEREBELLUM AS A PROCESSOR OF INFORMATION

In synthesizing a functional model of the cerebellar processing architecture we try to adhere to the principle that reliable and up-to-date experimental biological knowledge should constrain inventive modelling. We desire to preserve relative numbers of various classes of neurons that form the "circuitry" and logic of the processor network. Their connectivities, as represented by their respective fan-outs and fan-ins should also be approximated. This can best be visualized with the aid of Figure 2 which has been constructed using our best estimates of numbers and topologies found in the massive but incomplete literature on the subject. It seems appropriate to remark at this point that this state of affairs has hardly changed since the days when Sherrington observed that exact knowledge regarding CNS anatomy and physiology is extremely inadequate although there exists a vast body of detailed fact. Since the numbers of the various kinds of

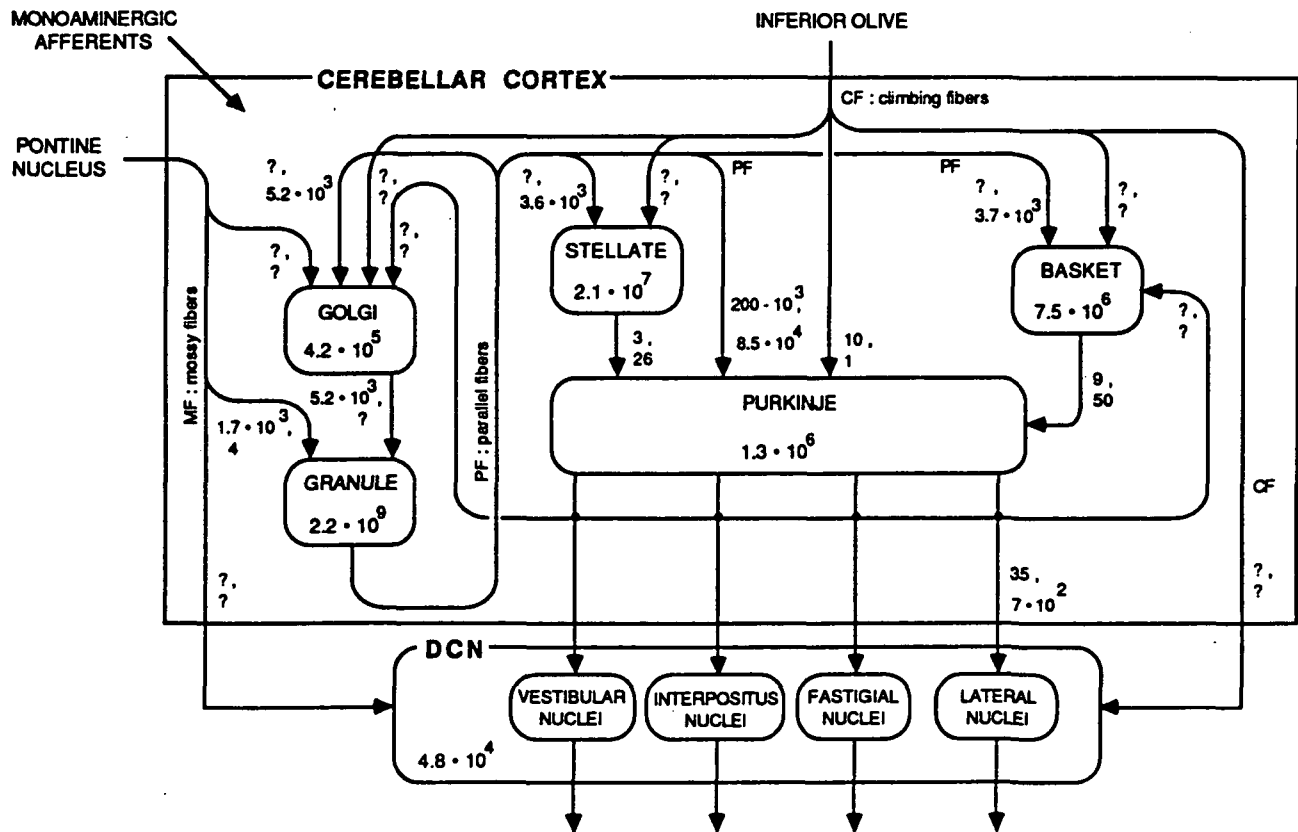


Figure 2. Cerebellar Interconnect Diagram

cerebellar neurons vary from specie to specie, we have standardized upon cat, whose facts are the most numerous and least inadequate.

Listed within their respective boxes are the population counts of the six kinds of neural cells found in the cerebellum. We discuss them in descending order. By far the most numerous are the very small granule cells. There estimated number is 2.2 billion in cat and 50 billion in man. They seem to be the most numerous neuron of the CNS in most species at the upper rungs of the evolutionary ladder. Then follow the two kinds of ML interneurons which in part interpose themselves in the major data processing path connecting the granule "input" cells to the Purkinje "output" cells. There are 20 million stellate cells and 7.5 million basket cells. The function of these interneurons has been thus far largely neglected by investigators of the cerebellum. The fourth kind of cell is the dominant Purkinje cell. It numbers 1.3 million in cat. This large and very regularly arrayed cell is also the most investigated one. Its false color photomicrograph adorns the cover of the special "Frontiers in Neuroscience" November 4, 1988 issue of SCIENCE. The photo belongs to a paper reporting microfluorometric imaging of intracellular calcium concentrations as a function of voltage-dependent electrical activity in cerebellar Purkinje cells [15]. The least numerous neurons of the cerebellar cortex are the Golgi cells. Their population count is less than half-a-million. They are among the most successfully modelled neurons of the cerebellum [16-18]. We agree with past modellers that the evidence is strong that Golgi cells regulate sensory data transmissions from the granule to the Purkinje cells via a negative feedback loop. However, in contradistinction to the presuppositions made in the above models [16-17] we think that Golgi cells receive inputs not only from MFs and granule cells, but that their activity is also subject to control by the second major cerebellar input, the CFs [19]. In comparison to the cell population counts in the cerebellar cortex, the population of DCN cells is truly diminutive. The largest DCN in the cat contains less than ten thousand cells while the sum total in all its DCNs is less than fifty thousand.

A concern of massive parallel processing design is fan-ins and fan-outs between successive processor stages. A major result of our preliminary investigation has been the establishment of histological facts about axonic connections projecting onto the six types of cerebellar

neurons. We show our findings in Figure 2. Where known, the directional interconnect gives two numbers. The upper number signifies the average number of target neurons which are reached by axons of a source neuron, while the lower number signifies the average number of source neurons that contribute inputs to target a neuron. On average, hundreds of Purkinje cells get an input from a granule cell while, about 85 thousand granule cells contact a Purkinje cell. The corresponding numbers for the stellate and basket to Purkinje connections are 3,16 and 9,50. These fan-ins of ML interneurons strongly suggest that they participate in logic processing, a role mostly overlooked by others. We believe that histologists need to fill-in numbers missing in our diagrams before their detailed functions can be clarified. Direct Purkinje cell to Purkinje cell links also need further attention. The large distributory role of CFs, supports Llinas' view that P-cells act in ensembles [12]. Fan-ins onto DCN targets give further credence to this view, especially when combined with an interpretation of the reported negative, as well as positive, changes in simple spike activities of P-cells [14]. The Marr model needs adjustment in light of the CF-Golgi connection and the CF read-out theory. In the absence of data we intend to simulate the above circuits. Our results increase the options for locating the thus far elusive, seat of memory in cerebellar network models.

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