

A world survey of artificial brain projects, Part I: Large-scale brain simulations

Hugo de Garis^{a,*}, Chen Shuo^a, Ben Goertzel^{a,b}, Lian Ruiting^a

^a Fujian Key Lab of Brain-Like Intelligent Systems, Cognitive Science Department, School of Information Science and Technology, Xiamen University, Xiamen, Fujian Province, China

^b Novamente LLC, 1405 Bernerd Place, Rockville, MD 20851, USA

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ABSTRACT

Driven by rapid ongoing advances in computer hardware, neuroscience and computer science, Artificial Brain research and development are blossoming. This article constitutes the first half of a two-part world survey of artificial brain projects: this part dealing with large-scale brain simulations, and the second part with biologically inspired cognitive architectures (BICAs). The large-scale brain simulations we consider in depth here include those by Markram, Modha, Boahen, Horwitz, Edelman, Izhikevich, and Just. As well as reviewing the particulars of these simulation projects, we position them in a broader perspective, comparing at the different underlying definitions of the concept of “simulation,” noting that in many ways the projects are modeling neurosystems at different levels as well as using different methodologies.

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1. Introduction

People have been dreaming of building brain-like intelligent machines for centuries. The first Artificial Intelligence conference took place in 1956, so AI is over half a century old. Where then are the intelligent machines? Why has the task proved so much more difficult than the founders of AI anticipated?

A full answer to this question will be clear only in retrospect, once advanced AI has been achieved and a more thorough theoretical understanding of intelligence has been obtained. There are many deep issues involved; for instance, while we know the notion of general intelligence extends far beyond the scope of human-like general intelligence [1], it is not yet clear how non-human an intelligent system can be and still operate effectively in the human-friendly regions of the natural world, displaying human-like commonsense knowledge. But if one restricts attention to AI approaches that are more or less inspired by the human brain, the question “why is there no truly advanced AI yet” has a fairly obvious answer, which comes in two parts, inadequate hardware and inadequate neuroscience knowledge:

- (a) Until very recently, humanity did not have the technical means to build brain-like computers. (From here on, unless the context makes it obvious otherwise, we will use ‘brain’ as a synonym for ‘human brain’ and ‘brain-like’ as a synonym for ‘like a human brain’.) When the first author programmed his first computer in the 1960s as an undergraduate, the computer he used had a central memory capacity of 8K. Compare this number with the

estimated bit processing rate of the human brain, and one understands why there were no intelligent machines built in the 20th century. The human brain has about 100 billion neurons, with each neuron connecting to roughly 10,000 others, with each synapse firing at maximum of about 10 bits per second; hence the total bit processing rate is of the order of 10^{16} bits per second. This number dwarfs the bit processing rates of the computers of the 20th century. Hence one necessary condition for building brain-like intelligent machines, i.e. having a sufficient information (bit) processing rate, was not met.

- (b) Another necessary condition for building brain-like intelligent machines is knowing which connectivity patterns and dynamical parameters to supply to artificial neuronal circuits to get them to behave in brain-like ways. Since the human brain is perhaps the most complex system in the humanly known universe (a quadrillion synapses), it is not surprising that little headway has been made in creating a deep understanding of how our own brains work.

Both of these conditions for brain building are much more closely met now than 5 or 10 years ago, let alone 50 years ago. Arguably, the time for building powerful artificial brains has come—or at least is only a few years or decades away.¹

On the one hand, Moore’s Law is now (i.e. around the year 2010) allowing our supercomputers to reach petaflop information-processing rates, thus arguably approaching human equivalence. On the other hand, humanity is now increasing rapidly its knowledge of the detailed micro-circuitry of the mammalian

* Corresponding author.

E-mail addresses: profhugodegaris@yahoo.com (H. de Garis), ben@goertzel.org, bengoertzel@gmail.com (B. Goertzel).

¹ Ray Kurzweil has posed this argument more rigorously than anyone else; see [1b]. For some scholarly debate about his arguments, both pro and con, see [1c,1d].

brain, synapse by synapse, so that it is now possible to simulate significant parts and aspects of a mammalian brain in detail using state of the art supercomputers. It is now possible for neuroscientists to input signals from the external world into their electronic neurocircuits and observe how their simulated brains function.

1.1. Large-scale brain simulations versus BICAs

Different researchers have different opinions regarding how closely one needs to simulate brain circuits in order to achieve brain-like behavior; and this ties in with different ideas concerning how much processing power is really needed to create brain-like behavior. If close adherence to brain-like structures and dynamics is not needed, then processing requirements may become a lot smaller because architectures and algorithms may then be adopted that are more amenable to current computing hardware than is more intractable neural wetware. Divergent intuitions on this issue have led research on advanced, loosely brain-like AI to bifurcate into two fairly distinct categories of research: “large-scale brain simulations,” surveyed in the present paper, and “biologically inspired cognitive architectures” (BICAs), surveyed in the sequel paper. Both approaches are valuable and both differ from typical work in artificial intelligence. They represent two significantly different approaches to leveraging what is known about the brain to create intelligent digital systems.

As we shall see, at the present state of technology, both of these approaches have their strengths and weaknesses. Large-scale brain simulations inform us with the dynamics of brain regions. They allow us to probe the complexity that underlies structures such as cortical columns, and the emergent nonlinear coherence that arises when large numbers of neurons are appropriately coupled. However, detailed brain simulations do not yet yield intelligent behaviors—in part because we do not yet know the intermediate-scale structure of the brain, so as to be able to encode it into our simulations.

On the other hand, biologically inspired cognitive architectures can carry out useful functions in vaguely brain-like ways, however as yet none of them displays the same flexibility and creativity as the brain. It may be that in order to do so, they must be extended to include some of the dynamical complexity and nonlinear coherence seen in computational brain simulations. In short, our hypothesis is that to create artificial brains truly worthy of the name, one needs either brain simulations with large-scale cognitive architectures (similar to current BICA architectures), or biologically inspired cognitive architectures that emulate or incorporate the lower-level dynamical complexity of large-scale brain simulations. Or, one may seek hybrid architectures in which aspects of large-scale brain simulations are combined with aspects of BICAs.

In this first of this two paper survey we will review seven leading examples of large-scale brain simulation, namely

- (i) Markram’s “Blue Brain Project” (EPFL, Lausanne, Switzerland)
- (ii) Modha’s “Cognitive Computation Project”, (DARPA and IBM Almaden Research Center, California, USA)
- (iii) Boahen’s “Neurogrid Project” (Stanford University, California, USA)
- (iv) Horwitz’s “Large-Scale Brain Modeling” (National Institute of Health, Bethesda, Maryland, USA)
- (v) Edelman’s “Brain-Based Devices” (Neurosciences Institute, San Diego, California, USA)
- (vi) Izhikevich’s and Edelman’s “Large-Scale Model of Thalamo-cortical Systems” (Neurosciences Institute, San Diego, California, USA)

- (vii) Just’s “CAPS Cognitive Neuroarchitectures” (Carnegie Mellon University, Pittsburgh, Pennsylvania, USA).

The first four are spiking neural net simulations, of which the Izhikevich & Edelman work is in some ways the most dramatic, being the first “human scale” simulation of a detailed cortical system. Edelman’s prior work, (v) in the above list, is a bit less low-level, involving neuronal firing rate units that do not attempt equally detailed neuron-level simulation. The latter two projects in the list are more cognitive in nature, but are included here rather than in the sequel paper because of their focus on modeling particular brain regions rather than mainly on achieving overall intelligent functionality in a brain-inspired way. Of course there is much other quality work that we could have covered; but rather than encompassing every relevant piece of research in a very brief and shallow way, we have opted to review a selected handful of projects at a moderate level of detail. The projects were selected based on multiple criteria including quality as well as variety, so the omission of a project from this review should not be taken as a negative assessment of its research value.

1.2. What is a simulation, really?

One of the interesting issues that arise when surveying approaches to large-scale brain simulation is the broad scope of interpretations of the notion of ‘simulation’ itself. Different researchers are approaching the task of large-scale brain simulation with very different objectives in mind. In order of decreasing fidelity, one may think about Table 1.

All of the above are validly called ‘large-scale brain simulations’, yet they constitute very different forms of research. Simulations in the first and second category are adequate to serve as components of BICAs or other AI systems. Simulations in the other categories are useful for guiding neuroscience or hardware development, but are not directly useful for AI. On the other hand, simulations in the fifth category are not directly useful for either neuroscience or AI, but serve as “proofs of principle” intended to lead on to other, more directly useful work.

2. Markram’s “Blue Brain Project”

Perhaps the best known artificial brain project on the planet is Henry Markram’s “Blue Brain Project”, which uses an IBM “Blue

Table 1
Models of decreasing neurobiological fidelity.

- | |
|--|
| 1. Creating models that can actually be connected to parts of the human brain or body, and can serve the same role as the brain systems they simulate. (e.g. Boahen’s artificial cochlea and retina) |
| 2. Creating a precise functional simulation of a brain subsystem, i.e. one that simulates the subsystem’s internal dynamics and its mapping of inputs to outputs with adequate fidelity to explain exactly what the brain subsystem does to control the organism |
| 3. Creating models that quantitatively simulate the generic behavior and internal dynamics of a certain subsystem of the brain, but without precisely functionally simulating that subsystem. (e.g. Markram’s cortical models, Edelman’s brain-based devices, or Izhikevich’s simulations) |
| 4. Creating models that qualitatively simulate brain subsystems or whole brains at a high level, without simulating the particular details of dynamics or I/O, but with a goal of exploring some of the overall properties of the system. (e.g. Just’s CAPS work, and Horwitz’s cognitive simulations) |
| 5. Creating models that demonstrate the capacity of hardware to simulate large neural models based on particular classes of equations, but without any claims about the match of the models in question to empirical neuroscience data. (e.g. Boahen’s Neurogen work, or Modha’s “cat brain” simulation) |

Gene” supercomputer to simulate (at ion-channel level of detail) the neural signaling of a cortical column of the rat brain. The long-term goal of the project is to “be able to simulate the full cortex of the human brain”; and Markram has stated that he believes this goal may be achievable by 2018, thanks to Moore’s Law and allied developments; he has stated, “We will do it by 2018. We need a lot of money, but I am getting it. There are few scientists in the world with the resources that I have at my disposal” [12b]. Due to his links with IBM, he decided to call his project, the “Blue Brain” Project (based on the fact that IBM’s nickname is “Big Blue”).

2.1. Background on cortical architecture

The focus of the Blue Brain simulation project, the human cerebral cortex, takes up about 80% of the volume of the brain, and is mostly responsible for a person’s ability to “remember, think, reflect, empathize, communicate, adapt to new situations, and plan for the future.” This cortex made its first appearance with the mammals. Most interestingly, it is remarkably repetitive, i.e. its structure is fundamentally simple and is found across all of the mammalian species.

The neurons of the cortex are grouped into functional units, in the form of cylinders of dimensions 0.5 mm diameter, and about 2 mm in length. Each cylinder (or cortical column) consists of about 10,000 neurons, which are connected in an elaborate but consistent manner. Markram thinks that “these units operate somewhat like microcircuits in a computer.”

This microcircuit (usually referred to as the ‘neocortical column (NCC)’, see Figs. 1 and 2) is copied several millions of times over the human cortex. Markram states that the only effective difference between the cortex of a human and a mouse is that humans have so many more neocortical columns.

The initial stage of the Blue Brain Project was to simulate accurately this basic microcircuit to the level of detail of individual neurons. This circuit could then be used as a tool in cortical simulations. (For an in-depth view of the project, read Henry Markram’s “Perspectives” article in the February 2006 issue of Nature Reviews Neuroscience [13].)

Neurons in a cortical column are not identical. Their exact shape and structure determine to a large extent their electrical properties and their connectivity with other neurons. In more detail, the electrical properties of a neuron are determined largely by the varying densities and varieties of ion-channels that are distributed over the cell’s membrane.

Neuroscientists have been using the juvenile rat for many years to collect data on the shapes and electrical behaviors of neurons. Such data was used by Markram as the basis for the

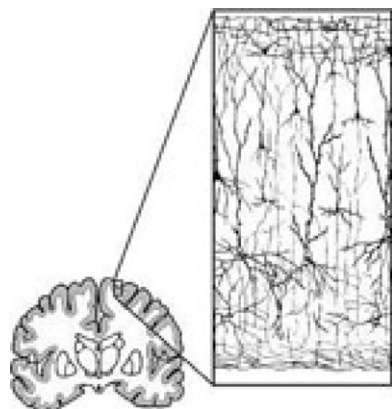


Fig. 1. A neocortical column (NCC) of the mammalian cortex.

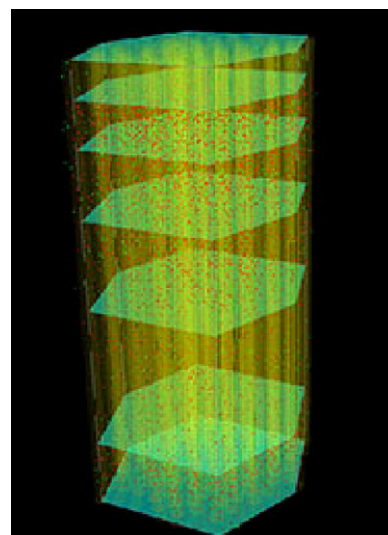


Fig. 2. Markram’s model of the neocortical column.

construction of his cortical-column model that he ran on his IBM “Blue Gene” supercomputer to simulate the 10,000 neurons that make up a true neocortical column.

2.2. Origins of the Blue Brain Project

The roots of the Blue Brain work began in 1993, when Markram was the first to “alter the precise millisecond relative timing of single pre- and post-synaptic action potentials, to reveal a highly precise learning mechanism operating between the neurons—now reproduced in many brain regions and known as spike-timing-dependent synaptic plasticity (STDP)” [15b]. There had been some correlation-sensitive observations made earlier, but Markram’s work was the first study to modify single pre- and post-synaptic spiking times to see what effects this would have on synaptic changes.

After this work, Markram returned to the Weizmann Institute in Israel, where he began his detailed dissection of the neocortical column. He noted that synaptic learning involves changes in the dynamics of synapses (called ‘redistribution of synaptic efficacy’) which was more involved than simply changing the strengths of synapses. He also discovered a host of new principles relating to the structure of neocortical microcircuits, their function and their emergent dynamics. Using these emergent dynamics of the neocortical microcircuit he created a new theory of “liquid computing” (i.e. a form of high entropy computing).

Beginning in 2002, he continued this work at EPFL as a full professor and founder/director of the Brain Mind Institute (BMI) and Director of the Center for Neuroscience and Technology. This phase of the work focused on understanding the basic “blueprint of the neocortical column”, by creating new tools to perform multi-neuron patch clamp recordings, along with multi-site electrical recording, chemical imaging and gene expression analysis.

The Blue Brain project uses the results of these experimental techniques to feed data to large-scale brain simulations, in this way constituting the “first comprehensive attempt to reverse-engineer the mammalian brain, in order to understand brain function and dysfunction through detailed simulations.” Specifically, the project focused on simulating a single neocortical column, based mainly on data gathered from 15,000 experiments

from Markram's and other labs regarding the rat's somatosensory cortex.

The Blue Brain project has focused not only on building a model of the neocortical column, but on developing a "generic facility that could allow rapid modeling, simulation and experimentation of any brain region, if the data can be measured and provided according to specifications". The facility has been used "to build the first model of the neocortical column, consisting of 10,000 3D digitizations of real neurons that are populated with model ion-channels constrained by the genetic makeup of over 200 different types of neurons." Markram uses a parallel supercomputer to build the model and to perform the experiments so that "the behavior of the tissue can be predicted through simulations."

So far, while Markram's simulations display dynamics with strong high- and low-level similarities to real cortical columns, detailed functional simulation has not yet been validated. In other words, it's not yet clear whether Markram's simulated columns can perform the same practical functions as the real columns they model. The envisioned next steps involve expansion of the project in multiple directions, some of which are related to surmounting this limitation.

Firstly, Markram is pushing to extend his facility so that it can model at the subcortical scale, by integrating greater biological details at lower levels with his current neocortical column model. Second, there is an effort to perform simulations at larger scale, moving toward whole-brain simulation. Finally, an initiative is envisioned aimed at using computer science methods to discover more computationally efficient circuits with functions closely identical to those of cortical-column circuits, and then use these 'optimized columns' to carry out practical functions, perhaps embedding them in GPU supercomputers, FPGAs or custom chips in order to achieve pragmatic performance levels without super-computing hardware.

2.3. Modeling connections and columns

For Markram to be able to model the neocortical column with reasonable accuracy, it was essential for him and his research team to understand the properties of the various types of cortical cells. He noted that neurons from each class of cell are present in certain layers of the column, and pieced together various sorts of evidence to make inferences regarding the way different cells are composed to architect a cortical column.

Since a cortical column has about 10,000 neurons, this means it has trillions of possible synaptic connections. Markram used his Blue Gene supercomputer to perform the huge number of calculations to determine the locations of these synapses, by "jiggling individual neurons in 3D space to find the optimal connection scenario."

Using these calculations, Markram was able to create, at the cellular level, a model of the basic microcircuit of a cortical column of a juvenile rat.

This model of the neocortical column (see Fig. 3) was ready by the end of 2006. The following year, in 2007, the Blue Brain Project announced the completion of Phase I of the project, having achieved the following three milestones:

1. The creation of a modeling technique that can be used to construct automatically, and on-demand, microcircuits that are based on biological data.
2. The creation of a new process that simulates and calibrates as well as analyzes systematically, the biological accuracy and consistency of each modification of their neocortical column model.
3. The creation of the first cellular level model of a neocortical column that is constructed entirely from biological data that

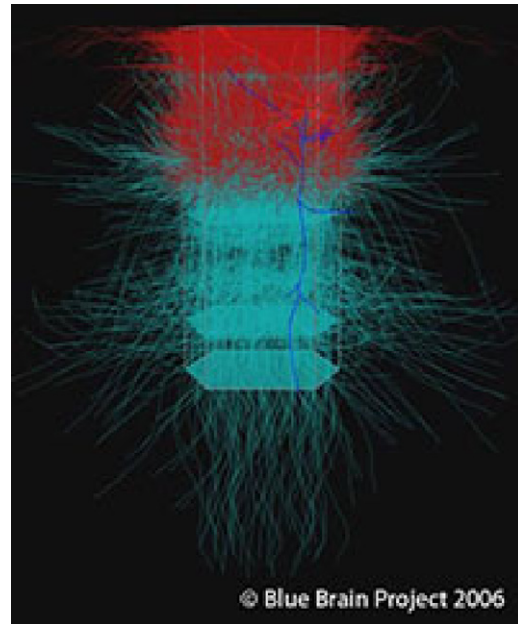


Fig. 3. A cortical column simulation with axons and dendrites.

now provides an essential tool to stimulate research into the simulation of neural micro-circuitry.

2.4. Simulating the microcircuit

After completing their cortical microcircuit, Markram's team could then start on the more glamorous work of actually firing up their circuit. They used all 8K processors of their Blue Gene supercomputer in parallel to solve the many mathematical calculations involved in simulating the electrical reaction of each neuron when a stimulus was applied to it.

In their simulation, as an electrical pulse traveled from one neuron to the next, the results of one neuron's simulation were passed to the next processor in the Blue Gene supercomputer (using MPI inter processor communication). Unfortunately, as of early 2010, the time needed to simulate the microcircuit was still about two orders of magnitude larger than the real biological time taken for the same process. So Markram and his team are now busy trying to reduce the time lag to enable a real-time simulation, so that, in his words, "one second of (real biological) activity (in the neocortical circuit) can be modeled in one second."

Another point worthy of note regarding Blue Brain is that some innovation in the software as well as hardware platform was required. There are no optimized software programs that can carry out very large scale (10,000 s) of simulations of morphologically complex neurons (whereas there are many for simple/point neurons). The software finally utilized for the Blue Brain simulations consisted of a hybrid between two powerful software approaches: (a) large-scale neural network simulations, called Neocortical Simulator (NCS), optimized for the Blue Gene/L supercomputer (developed by Phil Goodmann at Reno University) and (b) a well established program called NEURON (developed by Michael Hines at Yale).

2.5. Cajal Blue Brain

Of the several extensions of the extant Blue Brain work, perhaps the most exciting is the "Cajal Blue Brain" project initiated in May of 2009. It was funded by the Spanish Ministry

of Science and Innovation so that researchers from the Consejo Superior de Investigaciones Científicas (CSIC) and the Technical University of Madrid (UPM) could collaborate with the Blue Brain Project team at the EPFL. The Cajal Blue Brain project combines experts in the fields of “neuron-anatomy and electron microscopy from the CSIC, and experts in informatics and visualization from the UPM”, the aim being to “obtain detailed knowledge of the anatomical ultra-structure of the neocortex”, by using state of the art electron microscopy and by developing new bioinformatics tools to cope with the massive quantity of data needed generated in the Blue Brain Project.

Compared with the original Blue Brain work, this may be viewed as advancement from the cellular toward the molecular level of modeling. An accurate cellular level model of the neocortical column will provide the first major stepping stone towards a gradual increase in the complexity level towards the goal of being able to simulate at the molecular level of detail, i.e. being able to simulate the biochemical pathways of the neurons and supporting cells.

Once a molecular level model of the neocortical column is ready, it can be used as the foundation to connect gene expression with the structure and function of the neuronal network. The cortical-column model lies midway between genetics/proteomics and cognition. Once this foundation is built, it will permit the prediction of the “cognitive consequences of genetic disorders and allow reverse engineering of cognitive deficits to determine the genetic and molecular causes.” The Cajal project is only a step in this direction; but ultimately, Markram envisions this level of simulation as the final phase of his grand scheme for the Blue Brain Project. For further references relevant to Markram’s work, see [2–5,7–11,14].

3. Modha’s “Cognitive Computing (Synaptronics)” Project

In 2008, America’s DARPA launched the “SyNAPSE” (Systems of Neuromorphic Adaptive Plastic Scalable Electronics) Project, which aimed at funding universities and companies to design and build brain-like systems. One of these three grants was given to IBM—but not to the Blue Brain group; rather to a team led by Dharmendra Modha [21–23], a computer scientist and engineer who manages IBM’s “Cognitive Computing Group.” Modha now directs a team comprising IBM researchers and professors from 5 American universities (Stanford, Cornell, Columbia, UC Merced, Wisconsin Madison), from 6 different academic departments, in a project Modha described as “Cognitive Computing via ‘Synaptronics’ and Supercomputing,” with an explicit goal of “understanding and building a brain.”

Modha speaks with enthusiasm of the “Maturation of Neuroscience”, as reflected, e.g. in

- the construction of a “brain atlas” mapping cortical function to highly local cortical regions
- the mapping of white-matter inter-cortical pathways
- the realization that the cortical micro-circuitry of mammalian brains is statistical, meeting certain constraints, and largely similar across cortical areas, and across species.

Similarly to Markram, he speaks of the possibility that there is a “universal canonical microcircuit” that can be reversed engineered.

The university part of his team includes experts in the fields of analog VLSI, asynchronous VLSI, circuit designers, nano-materials, psychologists, neuroscientists, theoretical computer scientists. The IBM part of his team includes experts in the fields of material scientists, nano-circuit design, supercomputing, simulation, virtual environments, neuroscience, computational neuroscience, etc.

The broad goal of Modha’s Cognitive Computing Group is to “build a brain” as cheaply and as quickly as possible—or more explicitly, to engineer “mind-like intelligent business machines at IBM” by “reverse engineering the structure, function, dynamics and behavior of the human brain, and then delivering it in a small compact form factor consuming very low power that rivals the power consumption of the human brain.” This is a cross-disciplinary endeavor involving multiple aspects, which are envisioned as falling into three major categories:

1. *Neuroscience*: To understand the universal constraints that neuroscience has taught us, i.e. learn from neuroscience “what the structural and dynamical constraints are that mammalian brains must obey.” Mammalian cortices of many species are very similar in design.
2. *Supercomputing*: To take the data from neuroscience and incorporate it into mammalian-scale cortical simulations. For example in 2007, Modha’s team performed rat scale cortical simulations, with 55 million neurons, and half a trillion synapses, on a 32,000 processor IBM Blue Gene supercomputer in near real time.
3. *Nanotechnology*: To shrink electronic components to ever smaller sizes, so that “we can begin to see how to rival the density and power consumption of the basic building blocks of the brain”, i.e. the neurons and synapses. “These nano-circuits, just like the brain, will be analog, asynchronous, fault tolerant, reconfigurable, and avoid the traditional computer von Neumann bottleneck, namely the bus connection between a processor and its separated central memory. Nature has found a way to distribute evenly over the cortex, both processing and memory. So this component seeks low power, compact implementations.”

The software and hardware systems created via this methodology “will need to behave intelligently in new environments, in a context-dependent fashion.” Modha hopes his artificial brain will be able to “cope with the input from a massive number of sensors distributed all over a smart planet”, and foresees business playing a large role alongside academia in pioneering such developments.

For the first stage of the project, DARPA has specified the “creation of a nano-scale low-powered material that (a) captures the essential function of the synapse while being scalable to extremely small sizes (100 nm) as well as (b) consuming very low power (1 pJ). Hence, in 1 cm², there would be 10 billion of these artificial synapses (performing distributed computation).”

This hardware must then be programmed with appropriate software. Modha states that “no one knows what the algorithm of the brain is”, but Modha’s team believes that the algorithm, when finally discovered, will take the general form of a “universal microcircuit.” Modha’s team is undertaking simulations and theoretical analyses to try to uncover the “cortical microcircuit building blocks” that could be replicated, to “perform a wide area of functions in action, perception, sensation, cognition, and interaction.”

For the Synapse project in particular, the main aim of Modha’s group is to make a mouse level chip (i.e. of the size and order of complexity of the mouse brain), and in 7 years to have a network of chips at cat level. Although the project is well staffed and well funded, the viability of achieving this ambitious goal on the specified time-frame is unclear. In many ways the project is still at a foundational stage, still addressing basic questions like: “Can we make a nano-scale synapse? Can we make core micro-scale circuits? How would they scale?”

The most recent dramatic achievement of Modha's team is a simulation (at a certain level of accuracy) of the cortex of a cat, with 10^9 neurons, and 10^{13} synapses. This work was widely reported in the media, and has provoked some heated discussion among scientists on what a 'brain simulation' really means.

To carry out this work, Modha's team created a massively parallel cortical simulator, called C2 that "incorporates a number of innovations in computation, memory, and communication." Their C2 simulator ran on an IBM Blue Gene/P supercomputer with 147,456 CPUs and 144 TB of main memory [21–23]. His group "performed two cortical simulations – at unprecedented scale – that effectively saturated the entire memory capacity and refreshed it at least every simulated second." The first simulation consisted of 1.6 billion neurons and 8.87 trillion synapses with experimentally measured gray matter thalamo-cortical connectivity. The second simulation had 900 million neurons and 9 trillion synapses with probabilistic connectivity.

These simulations used phenomenological spiking neurons, synapses capable of learning, axons which incorporated delays, and phenomenological and dynamic synaptic channels. In terms of sheer number of formal neurons, they surpassed in scale the cortex of the cat, achieving a high rank in the scale of cortical simulations. Modha likes to show the table given here as Fig. 4, comparing the SyNAPSE objectives with the number of neurons and synapses in cortices of mammals classically used as models in neuroscience [21–23].

3.1. Simulating the cortex of a cat

Trying to simulate at the scale of a mammalian brain poses major challenges, even with today's supercomputers. The number of processor cycles performed in parallel is vast, so stresses the limits of communication. It is critical that all available memory is filled, and that it is refreshed at least every second of simulation time. All these requirements have demanded highly innovative simulation software design by Modha's team.

Earlier, Modha used "a Blue Gene/L (BG/L) [20] supercomputer, at IBM T.J. Watson Research Center, with 32,768 CPUs and 8 TB of main memory," to construct a cortical simulator "C2" which was able to "perform near real-time simulations at scales of a mouse [21,22] and rat cortices." This was a major milestone in the field of neuroscience simulation.

After their initial rat brain simulations, Modha and his team enriched their simulations "with neurobiological data from physiology and anatomy", and enhanced their C2 simulator with "algorithmic optimizations and usability features." Leveraging these innovations, their next main contribution (using the Lawrence Livermore National Labs' state-of-the-art Dawn Blue Gene/P (BG/P) [24] supercomputer with 147,456 CPUs and 144 TB of total memory) was "to achieve cortical simulations at an unprecedented and historic scale, exceeding even that of the cat cerebral cortex." These simulations used "single-compartment phenomenological spiking neurons [25], learning synapses with spike-timing-dependent plasticity [26], and axonal delays." Some of their specific results are summarized below:

- They "simulated a biologically inspired model with 1.617×10^9 neurons and 0.887×10^{13} synapses, roughly 643 times slower

than real-time per Hertz of an average neuronal firing rate." Their model used "biologically measured gray matter thalamo-cortical connectivity from the cat visual cortex [27], dynamic synaptic channels, and a simulation time step of 0.1 ms."

They also "simulated a model with 0.9×10^9 neurons and 0.9×10^{13} synapses, using probabilistic connectivity and a simulation time step of 1 ms, only 83 times slower than real-time per Hertz of the average neuronal firing rate."

- They "demonstrated that the simulator had nearly perfect weak scaling", which means that "doubling the memory resource would translate into a corresponding doubling of the model size that could be simulated."
- They also "demonstrated that from a strong scaling perspective, at constant model size, that using more CPUs would reduce the simulation time, thus closing the gap to real-time simulations."

3.2. The Markram/Modha controversy

The impressiveness of Modha's group's cat brain simulations from a computing hardware perspective is inarguable, but their neuroscience significance has been disputed by none other than Henry Markram. An IEEE Spectrum magazine article [28] was devoted to a heated controversy generated by Markram who posted an open letter about Modha's work that used some rather strong language and claimed, in essence, that Modha's neural simulations were not "biologically realistic" because the level of sophistication of Modha's simulation of his artificial neurons was "trivial" in comparison to what was needed for a genuine simulation of the brain of a cat. Markram's letter created heavy controversy. Some specialists agreed with him, others thought that Markram's criticism was excessive, and still others claimed that Markram's reverse engineering was also trivial.

Is Markram's criticism valid? It seems to us that what we have here is a lack of common understanding regarding the meaning of a "brain simulation." Neither Markram nor Modha are creating systems validated as detailed functional equivalents of human brain sub-systems. So the question is: in what sense must one's model match human brain data, in order to be considered a brain simulation rather than a brain-inspired dynamic or cognitive model? The term "simulation" is not well-defined in the literature, so it behooves researchers, when presenting a brain simulation, to specify explicitly and in detail the precise sense in which the systems they have constructed are intended to be simulative.

Markram's simulated cortical columns have been shown to closely resemble real cortical columns in terms of their statistical structures and input-output properties. This is different from showing the simulated columns can do exactly the same thing as the real columns, but it was arguably the outer limit of what could be achieved at that time; a number of innovations in experimental technology were needed to gather the detailed electrophysiological data needed to validate Markram's models even to this extent. The Cajal Blue Brain project is attempting to take the next step and create similar simulations providing agreement with even lower-level data.

Modha's simulated cat cortex does not provide agreement with data on the level of Markram's simulations, so that according

	Mouse	Rat	SyNAPSE	Cat	Human
Neurons* 10^8	0.160	0.550	1.0	7.63	200
Synapses* 10^{12}	0.128	0.442	1.0	6.10	200

Fig. 4. The number of neurons/synapses in various animals.

to Markram's definition of simulation, Modha's work does not constitute a valid 'simulation.' While Markram's simulated columns closely emulate the overall behavior of real columns, there is no comparable demonstration that Modha's cat brain closely emulates the overall behavior of a cat brain. Rather, what Modha's simulation does is to emulate the high-level structure of the cat brain, and the low-level neuronal dynamics of the cat brain, but without emulating the inter-neural connection statistics of the cat brain (let alone the individual connections). What Markram points out is that, from the perspective of cognitive simulation, this could be seen as missing the point, since according to the most commonly accepted theories of brain function, the inter-neural connections are where the organism's intelligence lies. On the other hand, once the connection statistics of the cat brain are better known, there is no reason one cannot plug them into Modha's simulation framework and obtain a cat brain simulation that is accurate in Markram's sense. And one could also view Markram's simulations as missing the point: a skeptic could argue that Markram's cortical columns are merely "systems with the general structure and statistical properties of cortical columns," but have not been shown to possess the specific fine-grained structural and dynamical properties associated with intelligence.

Conceivably Markram's simulations, though better empirically grounded than Modha's, might be analogous to a "Microsoft Word simulator" that displays the same structural properties as the Microsoft Word code, and the same statistical input–output properties—but does not actually perform word processing functionality. Pursuing the questionable metaphor further, Modha's work would then be (very loosely!) analogous to a simulator that tries to cover all the software running on a computer at once (not just Word), but displays the same structural properties as the software only on the very low and high level, without worrying about the intermediate level or the input–output functionality.

Both Markram's cortical simulation and Modha's cat brain simulation are pushing in the same ultimate direction – detailed structural, dynamical and functional simulation of neural circuits – and we believe both have value. But we would like to stress the ambiguity of the concept of 'simulation' as used in the literature as well as the popular media, and the need for research reports on brain simulation to contain clear specification of the nature of "simulateness" intended.

One of the core issues underlying this controversy is that Markram and Modha have rather different agendas. Markram is trying to simulate cortical columns with biologically realistic accuracy, but his simulation times are orders of magnitude slower than real cortical function. Modha however, used 147,456 processors and 144 terabytes of memory to simulate the signaling of 1.6 billion neurons and 10 trillion synapses, which are numbers comparable to those in a cat's brain, and managed to achieve near real-time simulation speeds, that admittedly were a lot less biologically accurate by Markram's standards. As stated at the beginning of this review article, two preconditions are needed to create genuine artificial brains with near human level abilities, namely sufficient bit rate capacities (i.e. Modha's priority) and sufficient knowledge of neural micro-circuitry (Markram's priority). For further references relevant to Modha's work, see [16–19,29–46]

4. Boahen's "Neurogrid Project"

We next review the work of Stanford researcher Kwabena Boahen, whose principal research goal is to "understand how cognition arises from neuronal properties [47]." Boahen uses his electronic engineering training to design integrated circuits that

"emulate the way neurons compute, thus linking the (supposedly) disparate fields of electronics and computer science on the one hand with neurobiology and medicine on the other."

So far his "neuromorphic engineering" research group has designed and built both

- a silicon retina, that could be used to give the blind some degree of sight
- a self-organizing chip, that emulated the way a developing brain wires itself up.

This work has attracted wide attention, culminating in a cover story article in the May 2005 issue of Scientific American [57].

On the theoretical side, Boahen's group has managed to demonstrate a number of interesting relationships between neuronal properties and brain rhythms, but still has a long way to go to achieve its stated long-term goal of "explaining how neuronal properties are linked to cognition." Another project aim is to create affordable supercomputers for neural and cognitive modeling using the "Neurogrid" framework, a brain-like hardware infrastructure qualitatively different from the von Neumann architecture.

4.1. Programmable Neural Silicon

The first person to design a neuromorphic chip was Carver Mead in the late 1980s at Caltech with his famous silicon retina. Mead used Moore's Law (i.e. the doubling of computer performance every 18 months), in 1990, to predict correctly that the computers of 2010 would be using (only) 10^7 times more energy per instruction than used by the brain for each synaptic activation.

Boahen was Mead's student, and says Mead's aim was to "close this efficiency-gap by building microelectronic circuits based on the brain." Hence it appears fair to claim, that Boahen was strongly influenced by Mead's basic vision.

Mead managed to mimic successfully the flow of ions across a neuron's membrane, using the analogous phenomenon of the flow of electrons through the channel of a transistor. Boahen thinks that this should not have been surprising, because the same type of physical force was applicable in both cases.

The next advance on Mead's work, undertaken by Boahen, was to make such Mead-like chips programmable, by creating an adaptable analog ion-channel as well as reconfigurable artificial synapses.

4.2. Hardware emulation of ion-channels

Boahen reasoned that the alternative to designing a separate electronic circuit to emulate each type of ion-selective protein pore that covers the membranes of neurons (the way Mead did with his silicon retina, for example), would be to design an adaptable analog chip that is capable of emulating a range of behaviors that these pores express.

Some of these simulated pores (i.e. transistors) opened when the cross membrane voltage was high. Others opened when the voltage was low, as well as intermediate cases.

Those pores that opened always followed a sigmoid like curve, and the time they took to open always followed a bell like curve. Surprisingly and very usefully, only 8 transistors were enough to mimic this behavior closely. Boahen thought that this was due to the fact that common physical forces were responsible for both ion transfer in pores and electron transfer in transistors. With only 8 transistors per simulated pore, it became possible for Boahen to model millions of pores (ion-channels) in a pore population, all on a single chip! Once the chip was fabricated, its sigmoid and bell curves could be fine tuned by programming

(i.e. by using “computer-controlled bias voltages.” to mimic closely any kind of ion-channel that was wanted.

4.3. Addressable synapses

Boahen used a different approach from Mead, when it came to connecting neurons into neural circuits. Instead of hardwiring the connections as Mead did with his silicon retina, Boahen’s team “softwired” them (i.e. put them under programmable control, by giving each neuron a programmable address). This address pointed to a position in RAM memory that in turn held the address of the synapse of the post-synaptic neuron. If a neuron connected to several other neurons, then multiple such addresses were used. Using the address of this post-synaptic neuron which was fed back into the chip, a post-synaptic potential could be initiated in the post-synaptic neuron.

This technique, developed by Boahen’s group, is very efficient. This is because a single post-synaptic circuit processes all the synapses that a neuron receives. These synapses are effectively virtual synapses. Boahen claims that the electronic speed of the encoding, translating, and decoding of an address allows several million spikes per second to be routed, which in turn allows 1000 silicon neurons to make a million synaptic connections.

To reconnect a softwire (i.e. a programmed synaptic connection between two neurons) all that is needed is to overwrite the LUT (look up table) in the RAM. Thus any synaptic connection that is desired becomes possible.

4.4. The challenge of simulating a million neurons

It is very difficult to simulate a whole brain using contemporary technology, because today’s computers usually execute a single instruction at a time (or in the case of multi-core processors, a few instructions at a time), whereas a brain functions massively parallel, with billions of neurons firing simultaneously, in a distributed fashion using a highly interconnected neural network. Offsetting the lack of massive parallelism of the computer is its incredible speed, but it wastes a lot of time and energy moving data from/to memory to/from a central processing unit (CPU). This ‘von Neumann bottleneck’ makes full brain simulations at the cortex scale impossible using today’s computers. Boahen’s team is overcoming this bottleneck by building an affordable supercomputer, called Neurogrid.

4.5. Neurogrid

Boahen feels that he is pioneering a paradigm shift away from the traditional von Neumann architecture of fetch–execute–store style computation, towards a more brain-like architecture that is massively parallel, and interconnected. His new machine, called Neurogrid, uses as its fundamental building blocks, not logic gates as in a Boolean logic based conventional computer, but silicon neurons, whose behaviors and connections can be programmed. This neuromorphic approach, that various researchers have been investigating for the past few decades, is capable of generating far greater levels of efficiency, that (to quote Boahen and his rivalry with Markram) “make Blue-Gene performance affordable on a Dell-cluster budget.” In the first author’s opinion, this is the main reason why Boahen’s approach is of such significance, and makes him one of the planet’s top artificial brain builders.

In Boahen’s view, there is a major alternative to GPUs (Graphical Processing Units) and FPGAs (Field Programmable Gate Arrays) as tools to build artificial brains, namely his Neurogrid architecture. He believes that his approach has sufficient computational speed to be able to test hypotheses

concerning the functionality of the cortex, and importantly, that it does not cost a fortune.

One of the features of Neurogrid is its ability to model interactions between different cortical areas (e.g. in the visual cortex there are more than three dozen), which are connected by projections that are lateral, feedforward and feedbackward. About half of all these connections (often called ‘projections’) are of the feedbackward type. Thus nearly every cortical area feeds back signals to the areas that send feedforward signals to it. Unfortunately today, the detailed functions of these feedback signals remain largely unknown. Boahen feels that one hypothesis for their function might be that they merge the various representations of the areas into a single “coherent percept.”

He thinks that another possible function might be that they act to focus attention, by concentrating on the most ‘informative area’ and ignoring the other areas.

4.6. The Neurogrid board

The \$60K supercomputer GRAPE-6, that has revolutionized physics was an inspiration to Boahen. He modeled his Neurogrid so that it might do to neuroscience what the GRAPE-6 did to physics, namely provide a machine at an affordable price that could be used to simulate whole brains.

The Neurogrid uses analog (rather than digital) computing to emulate the activity of ion-channels, and uses digital communication techniques to “softwire structured connectivity patterns.” Due to the differing nature of these two kinds of computing, they impose different kinds of constraints on their use. For example, analog simulation limits the number of different ion-channel populations that can be simulated, whereas digital simulation, which simply takes more time to run larger simulations. Communicating digitally, puts limits on the number of synaptic connections that can be activated each second, whereas communicating in analog allows one simply to sum additional (voltage) input signals on the same wire.

Neurogrid, of necessity, needs to operate within these constraints, and does so successfully, by having the capability to simulate many cortical areas in real time as well as being able to make the following appropriate choices.

4.7. Hybrid analog-digital circuits

The Neurogrid is capable of simulating a million neurons (using two sub-cellular compartments per neuron, a choice motivated from studies of the cortex, i.e. the nonlinear interactions between projections that terminate in certain layers of the cortex have been simulated using a pyramidal-cell model with only two compartments). By varying the electrical coupling between the compartments, Boahen was able to copy how various pyramidal cell-types fire.

By using the smallest number of compartments whose behaviors were sufficiently similar to real pyramidal neurons, Boahen was able to reduce significantly the number of different ion-channel populations that require simulation.

4.8. Neurogrid vs. Blue Gene

Boahen claims that Neurogrid will rival Markram’s performance level obtained using an IBM Blue Gene supercomputer, i.e. that it will be able to simulate a million neurons in real time, and use a million times less energy (i.e. a single watt instead of Blue Gene’s megawatt).

By using local analog communication, Neurogrid can simulate 6 billion synaptic connections. This was another choice made

from studies of the cortex, e.g. axons in the cortex synapse a lot in a local area, then extend for a while with no synapsing, then synapse a lot again. From this, Boahen concludes that neighboring neurons receive their inputs mostly from the same axons, which is to be expected due to the existence of functional mapping between cortical areas.

In his Neurogrid, he has wires that run locally between neighboring silicon neurons that emulate these ‘patches’, generating post-synaptic potentials with a radius that can be programmed. For Boahen, by using a patch radius equal to 6, he can increase by a factor of 100, the number of synaptic connections (i.e. from 60 million to 6 billion), without the need for further digital communication.

4.9. The Neurocore chip

The Neurocore chip has 61 graded (real valued) and 18 binary parameters, in all of its silicon neurons. Hence the Neurocore chip is capable of modeling a large variety of spike and interaction patterns. These parameter values are set by using a GUI (graphical user interface). Thus a user can simulate a wide variety of neural phenomena, such as (a) modeling cortical layers (or cell-types); (b) adapting silicon neurons to emulate the repertoire of their population’s ion-channels; (c) routing its softwires, so they match their synaptic connection patterns.

The GUI can also be used to visualize simulation results, from the single cell up to a whole cortical layer, and anywhere in between. All of the above can be done, with just a few clicks of the mouse. As Boahen states, “it is no longer a dream to simulate a million cortical neurons in real-time!”

4.10. Growing circuits

It is a well known fact in neurobiology, that there is not enough DNA (with its $\sim 10^9$ bits of information) to specify the position of every synapse in the cortex. To do this would require about a hundred million times more bits of information, in order to list the quadrillion (10^{15}) synaptic connections between the brain’s one hundred billion (10^{11}) neurons.

If one compares the size of this problem with the comparable problem faced by what computer architects have to worry about when faced with the challenge of using a trillion (10^{12}) transistors lying on a silicon wafer then the latter is minor in comparison.

To address this issue, Boahen has ambitions not only to simulate neurocircuitry accurately, but to *grow* that circuitry in what he calls an *epigenetic developmental* manner, hoping to establish a new area in neuro-engineering. By studying phenomena in the epigenetic development of real neurons, he hopes to create a new technology that does much the same in electronics. For example, in neurobiology, he cites the phenomenon that “axon-terminals from randomly activated patches of retinal cells, excite tectal cells to release neurotrophin, a chemical that diffuses to nearby locations.” Axons from neighboring retinal cells can then move up this neurotrophin gradient, to arrive at the neighboring tectal cells.

Boahen’s group simulated this process on a neuromorphic chip, where it is electrons that emulate the neurotrophin and it is softwires that emulate the axon-migration.

As mentioned in the previous paragraph, the genome does not contain enough information to specify the total connectivity of the cortex, so according to Boahen, the synapses “customize themselves through internal and external interaction, a learning process known as epigenesis.”

He states that “models of epigenesis have demonstrated that the brain’s feature maps can be built simply by wiring together

neurons that fire together” (i.e. a form of the well known Hebb’s rule). Boahen gives several concrete examples of this general form of epigenesis, e.g. “(a) light- and dark-sensitive inputs from the retina wire together to produce orientation-tuned cells; (b) left- and right-eye inputs produce depth-tuned cells; and (c) lagged and nonlagged inputs produce (motion) direction-tuned cells.”

Boahen dreams that by the emulation of neural epigenesis, engineers will be able to build more complex systems in the near future.

Since obviously the metal wires in a chip cannot grow, Boahen’s group has developed what they call their softwires (i.e. virtual connections) that do not require a point-to-point wiring approach. Instead Boahen has his softwires directed to their targets by silicon *growth-cones*, which are models of the “motile structures that tow growing axons along chemical trails.”

Boahen’s group is thus well launched to take advantage of Moore’s Law to *grow* their circuits in huge numbers, rather than fabricate them. Perhaps they may choose an evolutionary engineering technique to wire up their virtual connections. This epigenetic approach is a most promising area of neuro-engineering. For further references relevant to Boahen’s work, see [48–56,58–79].

5. Edelman’s “Brain-Based Devices”

Gerald M. Edelman, an American biologist and current Chairman of the Neurobiology Department at Scripps Research Institute, won the Nobel Prize in 1972 in Physiology or Medicine, for work on the immune system, involving the discovery of the structure of antibody molecules. His later work has concentrated on neuroscience and the philosophy of mind, particularly on the nature of consciousness. He has proposed that common evolutionary learning principles underlie the evolution of species, the operation of the immune system, and the intelligent dynamics of the human brain.

For nearly two decades, Edelman and his colleagues have been working on a series of theoretical models which Edelman labels *Brain-Based Devices (BBDs)* [115], which he defines to be “realistic brain models that control robotic devices performing behavioral tasks.”

The driving philosophy behind these models is the belief that the brain does not operate on its own. Instead it is intimately connected to its body, which in turn interacts closely with its environment.

Edelman and his colleagues use BBDs to test hypotheses using models that have to cope with all the noisy inputs and complexity of the real world.

Using their techniques they are able to record signals coming from their model’s entire brain, which today is still not possible with living animals.

Some of the major insights to come out of this work at the Institute, have been the realization of the importance of self-generated movement, while learning percepts, as well as how important is the role of reward systems when their models adapt and learn.

Edelman’s team has emphasized that the unique anatomy of a particular brain region, e.g. the hippocampus, is very important to explain its function.

Edelman and his colleagues began creating a series of neural automata, that he labeled the *Darwin* series. This work began in 1981, initially as purely software simulations. Since 1992 however, these BBDs have taken robotic form (i.e. with real physical bodies) that interact with an environment.

We begin with a little bit of the history of their BBD development and the robots they controlled.

In the year 2000, Edelman’s team developed a BBD called *NOMAD* (an acronym for Neurally Organized Mobile Adaptive

Device) which contained many sensors, for example, (a) a panning tilting color camera used for vision, (b) artificial whiskers used for sensing textures, (c) a compass and the so-called wheel-encoders used to provide knowledge of the direction of the head and self-movement, (d) infra-red transceivers, and (e) a laser rangefinder to sense proximity to objects.

The NOMAD robot moved autonomously in its environment, and in real time, controlled by a simulated nervous system, that ran on a Beowulf PC cluster with up to 64 CPUs. Edelman insisted that these nervous system simulations have realistic neuroanatomy, i.e. that they contain roughly 100,000 artificial neurons, and several million synaptic connections between them.

Four years later, in 2004, the Edelman team began work on their so-called *Segway Platform*, i.e. a BBD built on to a commercial Segway (i.e. the two-wheeled self-balancing scooter), which allowed it to operate outside the highly controlled environment of the normal robot laboratory.

Edelman's team is not the only neuromorphic robotics group [115], in the world. Others include [118–125]. Similar to these other groups, Edelman's group employs BBDs (brain-based devices) to control robots. These BBDs are often sophisticated simulations of nervous systems, a subcategory of neurorobotics, based on characteristics of vertebrate neuroanatomy and neurophysiology that focus on the organism's interaction with its environment.

Edelman requires that the BBDs his team designs be constrained closely by the following design principles:

1. The BBD is situated in a physical environment.
2. The BBD is to perform some behavioral task.
3. This behavior is to be controlled by a nervous system simulation that matches closely the architecture and dynamics of biological brains.
4. The behavior of the BBD, and the behavior of the simulated nervous system that controls it must both allow comparison with empirical data.

Edelman's group found that as a consequence of the above constraints, their BBD simulations necessitated the following:

- (a) networks of artificial neurons on a large scale that match vertebrate brain architecture and dynamics
- (b) the need for powerful computers to be able to run the network in real time
- (c) to embody the network, specialized physical devices had to be engineered.

Edelman claims that his BBD approach is powerful because it enabled the observation and recording of the states of all components of these nervous system simulations simultaneously and at all levels, when a task is being performed in the real world.

5.1. Darwin X and XI

More recently Edelman's group built two BBD models, labeled Darwin X and Darwin XI (using Roman numerals; see Figs. 5, 6, and 8). They were constructed largely to test observations concerning memory formation, namely that

- (a) information from many different sensor types converges on the mammalian brain's medial temporal lobe
- (b) the medial temporal lobe is active in the formation of spatial, multi-modal, and episodic memories

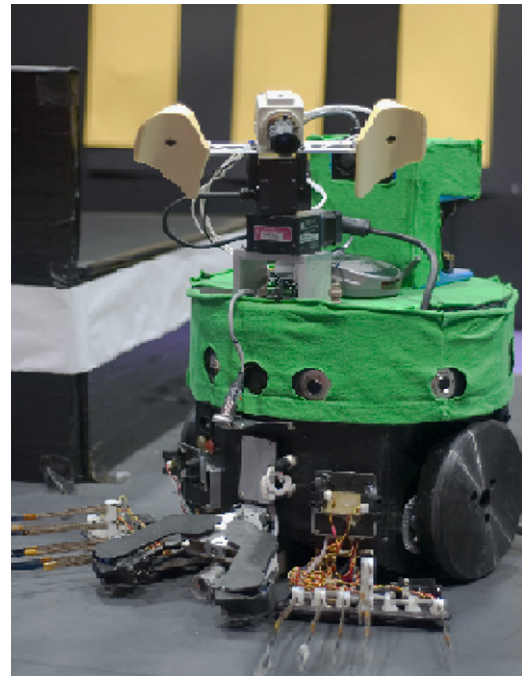


Fig. 6. Darwin XI running a maze, using its rat like simulated hippocampus.

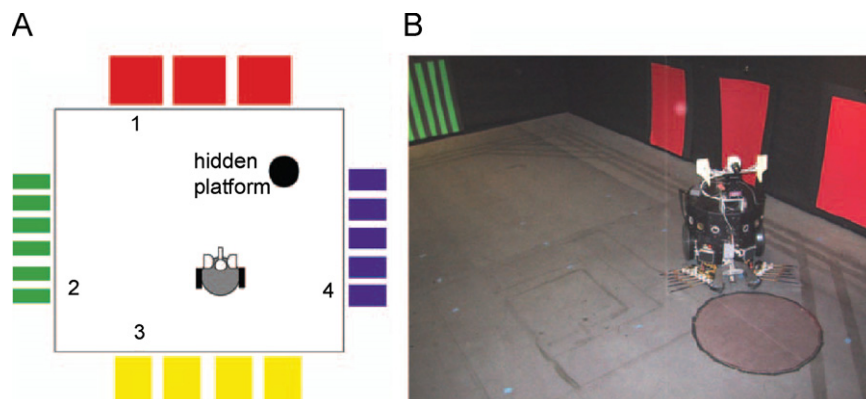


Fig. 5. The enclosure for Darwin X's hidden platform task. Its arena is 16' × 14' with black walls and flooring. Strips of colored paper, of differing widths, were hung on each of the walls.

(c) after information reaches the medial temporal lobe in the mammalian brain, it then travels through various nested loops before passing on to other areas in the cortex.

Edelman and his colleagues formed the hypothesis that these loops that contain highly processed information and over several time scales are very important for the formation of episodic memory.

To test the above hypothesis, Edelman's group then used their BBDs, Darwin X and Darwin XI, to simulate closely some studies in rodent navigation. Their models used many neurons (e.g. about 100K neuronal units, and 1.2M synapses) to simulate the medial temporal lobe and the cortical regions surrounding it. Edelman insisted that these models be neuro-anatomically and neuro-physiologically realistic, which thus allowed him to pose questions concerning how the medial temporal lobe's unique structure plays a role in memory formation.

The overwhelming advantage of this BBD approach in Edelman's view is that using an artificial organism (a BBD) gave his group the ability to observe simultaneously the activity of every neuron in the nervous system simulation, a capability that is not possible at the present time with animals performing in real time.

The *Darwin X* BBD was designed to be a dry land based version of Morris's famous water-maze (i.e. a rat is thrown into a water tank with a slightly submerged invisible island platform that it has to swim around to find so that it can stop swimming and rest. The next time it is thrown into the tank, it tends to swim straight to the submerged platform). The Morris water-maze is a fairly standard experiment in spatial memory in rodents.

In this land version of the Morris test, the Darwin X moved around in an arena with walls containing the so-called *visual landmarks*. The Darwin X equivalent of the Morris platform in this new context was a particular location in the arena, where the robot received an unconditional reward stimulus that the robot sensed only by touch.

After about 20 trials, Darwin X was able to move directly to this reward location, starting from any position in the arena. It was able to do this because the CA1 region of its simulated hippocampus developed a *place field activity* similar to those found in rodents. Note that this ability was not preprogrammed into the simulation.

Interestingly, when Edelman's team analyzed the simulated circuits after their simulation, they found that the so-called *tri-synaptic pathway* was used more to generate place field activity during the earlier learning trials, but was used less once the BBD gained more experience at performing the task (for details, see [117]).

The team also noticed that the tri-synaptic pathway produced different kinds of place activity than the so-called perforant path.

We now discuss the Darwin X experiment in a little more detail. To test the formation of spatial memory in the Darwin X BBD, a dry land variation of the Morris water-maze was undertaken. The Darwin X robot's task was to locate a hidden platform in its arena. The Darwin X had only visual landmarks, and self-movement data to enable it to guide itself to the hidden platform, from anywhere in the arena, which was a 16' × 14' area, surrounded by walls with hanging strips of paper of differing widths and colors (see Fig. 5). The hidden platform equivalent of Morris, was a circular area on the floor of the arena consisting of reflective black construction paper, 24 in in diameter, placed in the center of one quadrant (see Fig. 5). This hidden platform was invisible to Darwin X, and was only detectable by using its IR sensors placed at the front of the robot, and at close range. Fig. 5(A) shows the layout for Darwin X's hidden platform. The hidden platform, 24" in diameter and made of reflective black construction paper was positioned at the center of one of the arena's quadrants.

The Darwin X BBD could detect when it was positioned above the platform by using an IR sensor. Each trial began in one of four starting positions (see numbers 1–4 in Fig. 5(A)). Fig. 5(B) is a photo of the Darwin X robot in its environment [116]. The behavior of the Darwin X BBD is controlled by a nervous system simulation that was based on the anatomy and physiology of the nervous system of mammals. Of course, this simulation (with today's computing power) possesses far fewer neurons, and its architecture is much simpler. This simulated nervous system (see Fig. 7) consisted of several cortical areas, which were labeled using the same analogous labels of the neocortical, hippocampal, and subcortical regions of a biological brain.

Each simulated cortical area contained artificial neural units (artificial neurons) that could be either excitatory or inhibitory. Each of these artificial neurons represented a local population of biological neurons. The average firing rate of an artificial neuron corresponded to the average firing rate of a group of roughly 100 real neurons, and over a time period of approx. 200 ms.

Edelman's next BBD was labeled *Darwin XI* (i.e. the eleventh in a long series of software and hardware neural simulations, over several decades). Its goal was to test the integration of many kinds of sensory information into a single kind of memory.

Darwin XI was a modified Darwin X, i.e. added to the latter were two new sensory input devices, namely (a) artificial whiskers for the sensing of texture and (b) a laser rangefinder used to measure the distance to obstacles.

Darwin XI's goal was to run a so-called "plus maze" (i.e. a maze in the shape of a "+" sign). Such mazes are routinely used on

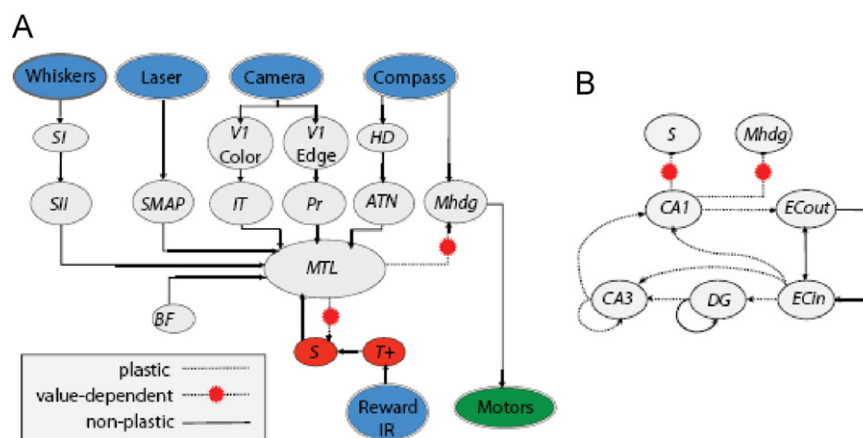


Fig. 7. Circuit of Darwin XI's neural simulation, showing the internal neural modules and their interconnections as well as their connections to external sensors and actuators.

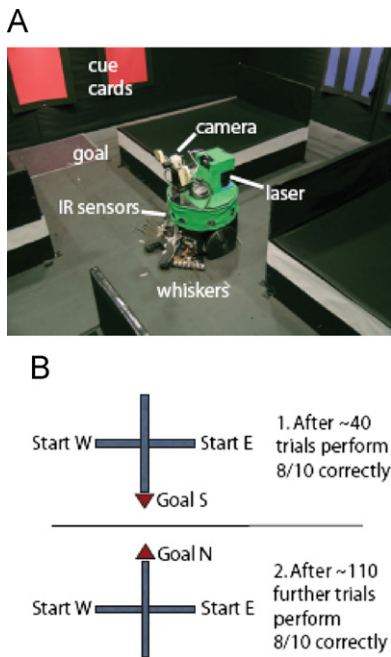


Fig. 8. Darwin XI's enclosure and experimental protocol, during an experiment designed to test the robot's ability to learn how to respond with appropriate actions to visual cues shown on cards.

rodents to investigate their hippocampal activity when they run such journey dependent, i.e. contextual mazes.

By the so-called “journey-dependent activity” of the hippocampus, is meant that hippocampal cells will fire with place fields, only when the rodent takes a particular route to reach that place, but not if the animal has reached that place using a different route.

The task of Darwin XI was to traverse a “plus maze” (i.e. a maze in the form of a ‘+’ sign), see Fig. 8(A). It began in one of the start arms, moved to the intersection, and there chose one of two goal arms (see Fig. 8(A)). At the end of one of the goal arms was a reflective piece of construction paper that Darwin XI was unable to detect visually at a distance, but could detect when nearby using a downward-facing infra-red sensor.

This IR sensor stimulated a “neural reward response” (T+ in Fig. 7(A)), which then stimulated a “value system response” (S, in Fig. 7(A)).

Fig. 7(A) shows the schematic (circuit) of the organization of the simulation. Fig. 7(B) shows details of the MTL (where projections from the cortical sensory areas converge on the entorhinal cortex input layer [117]).

The Darwin XI BBD possessed the following pieces of hardware, (a) a camera for vision processing, (b) artificial whiskers for detecting types of texture, (c) a compass to determine the orientation of its head, and (d) a laser range finder to estimate its position.

The purpose of its whiskers was to follow the wall of a maze. It used its IR sensors to detect the absence of walls when it reached the intersection of the plus maze.

The landmarks of the maze were ambiguous, so the determination of its location required integration from multi-sensory inputs (i.e. from at least two). The maze was built to take full advantage of Darwin XI's multiple sensory input streams, by (a) having different colored strips of paper hanging on the walls surrounding the maze and (b) having different textures in the arms of the maze.

Edelman's team used Darwin XI in 4 experiments, each with the same neural architecture but starting with different distributions of synaptic weights and microscopic connectivities. Each experiment had the robot start in alternative starting arms (i.e. east, then, west, then east, etc.). Training continued until an 80% correct response rate (i.e. finding the reward in the goal arm) was achieved. At the beginning of the training, the reward was placed in the south goal arm. The four Darwin XI experiments took 40, 50, 50, and 30 trials, respectively, to reach the 80% criterion.

The reward arm was later switched to the north, to unlearn the training. It then took much longer to undo the previous learning, for example, the four experiments then took 120, 140, 110, and 70 trials, respectively, to attain the 80% success rate (see Fig. 8(B)).

Fig. 8(A) shows the Darwin XI robot at the position of choice in its plus-maze environment.

As mentioned earlier, the Darwin XI BBD began trials alternately in the east or west start arms, then used its artificial whiskers to move along the maze arm until it reached the position of choice. As the robot moved along the maze wall, its whiskers detected patterns of pegs, its camera detected colored paper strips on the walls, its compass provided head orientation, and its laser range finder supplied distance data to objects.

Fig. 8(B) shows the experimental protocol, i.e. at the beginning of the training, Darwin XI was rewarded when it chose the south goal arm (B1). Having learned that task adequately, the reward was swapped to the north goal arm (B2).

The above experiments showed that Darwin XI, with its simulated hippocampus, exhibited journey-dependent place activity that was similar to what is seen in rodents. This context-dependent hippocampal activity emerged from the realistic neuroanatomy contained in their model, as well as from the experience-dependent plasticity of their artificial synapses.

The above mentioned hippocampal journey-dependent place activity was discovered to be generated by information flow that went through the tri-synaptic pathway more often than in the case of journey-independent (non-contextual) place activity. For further references relevant to Edelman's work, see [113,114,126].

6. Izhikevich's and Edelman's “Large-scale model of mammalian thalamo-cortical systems”

Eugene M. Izhikevich is Chairman and CEO of the ‘Brain Corporation’ in San Diego, California, USA. He was previously a Senior Fellow of Theoretical Neurobiology at the Neurosciences Institute, in San Diego, where he proposed in the year 2007, a computational model based on his many years of research on the mammalian brain. One can claim that Izhikevich is more ambitious than Markram in terms of scale. For example, his *human brain simulation* was on a scale similar to that of the full human brain itself. By simulating the spiking and plasticity features of the neural cortex, he managed to reproduce certain special features of the brain, such as initial states sensitivity, brain wave propagation, etc.

In 2007, Izhikevich and Edelman proposed a detailed and large-scale model of the thalamo-cortical system that was based on experimental data from several mammalian species [92]. This model covered three levels of anatomical detail, namely:

- (i) It was based on the “global” (i.e. white matter) thalamo-cortical anatomy of a human brain, obtained by using DTI (diffusion tensor imaging) techniques.
- (ii) The model contains many thalamic nuclei as well as 6-layered micro-circuitry of the cortex, that are based on biological labels, using three-dimensional models of neurons found in the visual cortex of the cat.

(iii) The model uses 22 different kinds of basic neurons whose laminar distributions of their dendritic trees branch appropriately.

The Izhikevich and Edelman model simulates a million spiking neurons consisting of multiple compartments. The responses of these model neurons were finely tuned so as to copy closely the responses that were recorded from rat (in vitro) neurons.

The number of synapses in the model is nearly half a billion, with the following list of properties that modeled closely those of real synapses, e.g. (a) their receptor kinetics, (b) short-term plasticity, and (c) long-term dendritic spike-timing-dependent synaptic plasticity (dendritic STDP).

Interestingly, when the model was activated, it exhibited behavioral characteristics very similar to normal brain activity that were not previously built in, but simply emerged spontaneously, due to interactions between anatomical and dynamic processes.

For example, they observed the following list of behaviors: (a) spontaneous activity, (b) sensitivity to changes in individual neurons, (c) waves and rhythms emerged, and (d) functional connectivity on different scales emerged.

Much progress has been made in the past ten years regarding neuroscience's understanding of brain dynamics and of those neuronal mechanisms which form the foundations of such dynamics. Connecting such mechanisms to behavior (e.g. perception) is made easier by the using large-scale computer simulations that model closely the anatomy of the cerebral cortex.

These large-scale simulations have various strengths and weaknesses. For example, on the positive side, they have emphasized the micro-circuitry and local dynamics, but on the negative side, they have not modeled the following: (a) multiple cortical regions, (b) corticocortical connections, and (c) synaptic plasticity.

To overcome these weaknesses, Izhikevich and Edelman set out to create a large-scale model of the mammalian thalamo-cortical system that included the components listed above [92].

As mentioned briefly above, the spatiotemporal dynamics of their simulation model displayed characteristics that were very similar to normal brain activity, that were not preprogrammed into the model. Instead these features simply emerged spontaneously.

What was interesting was the way the model created self-generated activity, even when no external inputs were arriving.

Izhikevich and Edelman observed that their model behaved in a way that was *hypersensitive* to the presence of *individual spikes*. For example, they noticed that if they added or removed just one spike from one neuron, then the state of the entire cortex would be completely changed half a second later! This is really quite extraordinary.

They noticed other interesting phenomena as well, e.g. that there were parts of the modeled brain that displayed collective waves and oscillations of local-field potentials, in the alpha, beta and delta ranges, that were very similar to those recorded in humans.

They simulated fMRI (functional (nuclear) magnetic resonance imaging) signals, and noticed that they showed slow anti-phase oscillations in the fronto-parietal region of the cortex, which is a phenomenon also seen in humans.

Their model's basic characteristics i.e. its shape and its connectivity, were determined by *DTI* (Diffusion Tensor Imaging) data, taken from the human brain (see Fig. 9). Three species were used (human, cat, and rat) to obtain experimental data that was included to help construct further details of the model.

Fig. 9 shows the global thalamo-cortical geometry and the white-matter anatomy of the human brain. This data was found by using diffusion tensor imaging (DTI) techniques on a normal human brain.

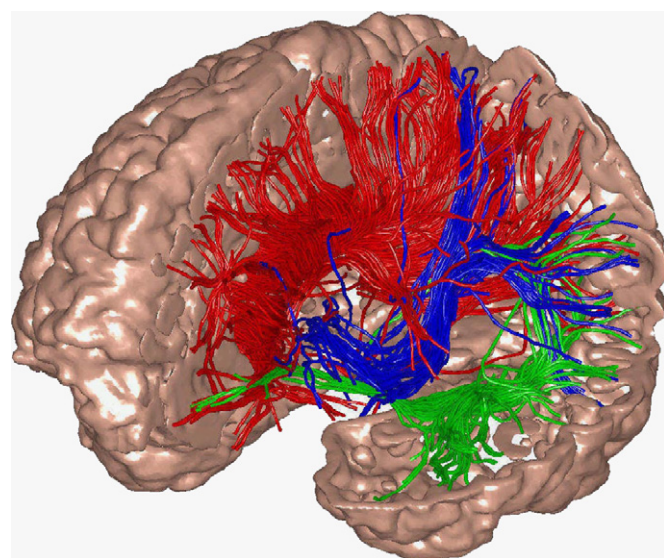


Fig. 9. Izhikevich & Edelman's mammalian thalamo-cortical model.

In the figure, the left frontal, parietal, and part of the temporal cortex have been cut away to display a small number of white-matter fibers, that have been color coded depending on their target region.

Fig. 10 shows a simplified version of the Izhikevich and Edelman's simulated gray matter micro-circuitry.

It was based on detailed modeling of studies of area 17 (i.e. the visual cortex) of the cat, undertaken by Binzegger et al. [96], whose labeling conventions Izhikevich & Edelman used. They detected that there were 8 types of excitatory neurons, namely—p2/3, ss4(L4), ss4(L2/3), p4, p5(L2/3), p5(L5/6), p6(L4), p6(L5/6), which depended on both the neuron's morphology (e.g. was it pyramidal, spiny stellate, basket, non-basket), and on the somatic and the target layers.

In the appendix of their paper [92] they supplied (a) more detailed explanations, (b) an inter-cortical connectivity matrix, and (c) a summary of the sizes of laminar spreads of the axons.

6.1. Microscopic anatomy

They made the further comment that every area of their model cortex had in essence, the same micro-circuitry as shown in Fig. 10.

Izhikevich & Edelman (I&E) modeled each neuron with the following characteristics—each had (a) a somatic part, (b) several dendritic parts, and (c) at least one apical compartment per cortical layer (provided that the neuron's dendritic tree reached into to that cortical layer).

They specified the number of parts for each neuron dynamically, during the start up procedure, allowing each part to have 40 or fewer synapses.

6.2. Neuronal dynamics

I&E state that normally, when an excitatory presynaptic neuron fires, it generates a local EPSP in the post-synaptic dendritic compartment, with an amplitude of about 10 mV, and that these dendritic EPSPs typically generate a submillivolt EPSP at the somatic part. This is due to the electrotonic attenuation of the synaptic current.

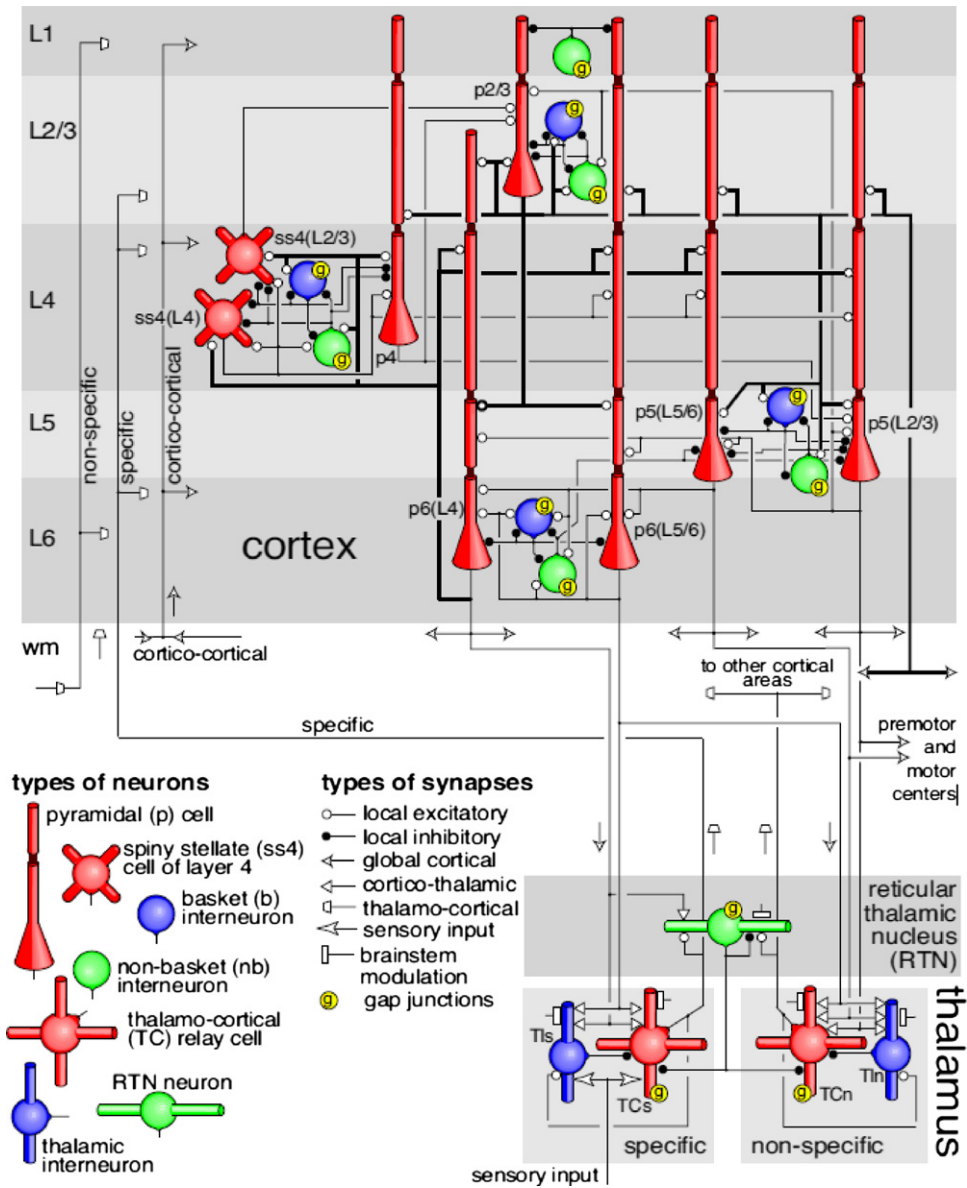


Fig. 10. Simplified micro-circuitry of the cortical laminar structure and thalamic nuclei in Izhikevich and Edelman's thalamo-cortical model.

When 3 or 4 synapses fire simultaneously, (with maximal conductance) in the same compartment (part), this can generate a spike, i.e. a local dendritic action potential, which then travels to the soma where it can generate a spike or a burst of spikes. If similar spikes arrive at different compartments, they would be less likely to generate a response in the somatic part.

The reverse process is also possible, i.e. somatic spikes can propagate back to the dendritic tree and generate dendritic spikes there.

The phenomenological model that was used to simulate the dynamics of the spiking of each neuron and each dendritic compartment was drawn from Izhikevich's previous work, and is summarized below in dimensional format.

$$Cv' = k(v - v_r)(v - v_t) - u + I$$

$$u' = a\{b(v - v_r) - u\}$$

where the various constants and variables are defined as: C is the membrane capacitance, v is the membrane potential (in mV), v_r is the resting potential, v_t is the instantaneous threshold potential, u

is the recovery variable (i.e. the difference of all inward and outward voltage-gated currents), I is the dendritic and synaptic current (in pA), and a and b are parameters.

According to this model, a spike is fired (i.e. an action potential) when the potential attains the peak of the spike, i.e. $v = v_{peak}$. Once that happens, all variables are reset, i.e. $v' \geq c$ and $u \geq u + d$ (where c and d are further parameters). In this model, v_{peak} typically takes a value of about 50 mV.

Note, that this is not the threshold value of the neuron. In this model the firing threshold is not a parameter, but is a dynamic property that depends on the neuron's state. This Izhikevich neuronal model can be contrasted with the classical models of the conductance-based type made famous by Hodgkin–Huxley [99]. In the Izhikevich model, instead of simulating all the ionic currents, the model was designed to simulate firing responses. For example, one can compare the recordings of in vitro measurements and those of the simulations in Fig. 11A. In this model it is possible to scale down (i.e. to depress the membrane potential) or to scale up (i.e. to facilitate) the synaptic conductance (i.e. its

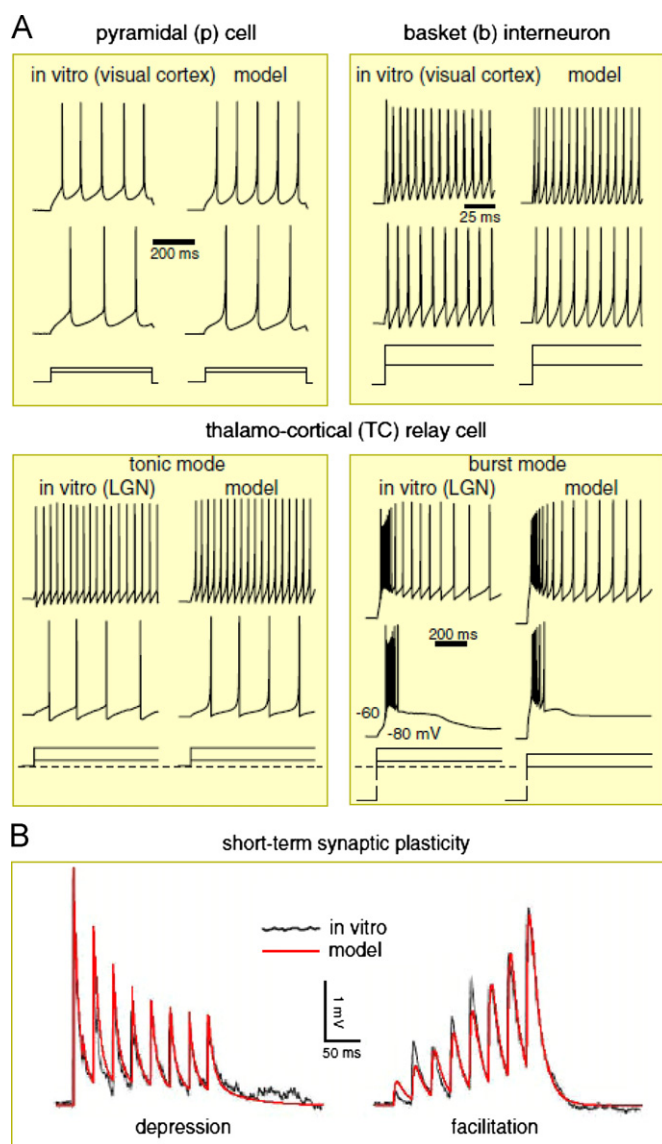


Fig. 11. Firing patterns of Izhikevich's model vs. in vitro.

strength) on a small time scale (e.g. hundreds of milliseconds) by a scalar factor x [100]. This scaling factor (whose value can be chosen for each synapse) promotes computational efficiency.

The model uses the following (one dimensional) equation:

$$x' = (1-x)/c$$

The value x reverts to its equilibrium value with its time constant, but is reset by the arrival of each spike of the pre-synaptic cell to the new value px . By manipulating the parameter value, it is possible to create short-term synaptic depression or synaptic facilitation, as shown in Fig. 11(B). Different synaptic types have different parameter values.

Fig. 11 has two parts. Part A compares four representative in vitro firing patterns (the left columns) with the corresponding simulated firing patterns (the right columns) using the phenomenological model [93–94]. Part B compares the model vs. in vitro cases on short-term synaptic plasticity.

I&E used the phenomenon of STDP (spike-timing-dependent plasticity) to model the long-term conductance changes (i.e. in the synaptic weights) of each synapse. They potentiated or depressed each neuron depending on the firing order of the

presynaptic neuron and on the corresponding (dendritic) compartment that is connected to the post-synaptic neuron.

I&E's simulation program was written in C language, using MPI (parallel programming) software on a Beowulf (PC) cluster with 60 3 GHz processors, each containing 1.5 GB of RAM. Their simulations used a million neurons, tens of millions of neuronal compartments, and nearly half a billion synapses. It took them about 10 min to initialize their model, and then about 1 min to compute 1 s of simulated data (using time steps of a sub-millisecond). Thus their simulation speeds are a bit under two orders of magnitude below real time.

It is this kind of hardware capacity and neuroscience knowledge that augurs so well for the creation of near future, full scale, (human) artificial brains.

Common sense says that if no initial spikes are input at the start of a simulation run (i.e. no synaptic inputs), there will be no new spikes generated, hence the network will remain silent, i.e. it will not fire. I&E were therefore compelled to kick-start their network, by introducing a few seeder (i.e. random) spikes at time $t=0$.

Interestingly, they noticed that independently of the number of seeder spikes or the initial strengths of the synaptic connections, or the size of the network (where their testing used up to 10 million neurons), the network firing still died out during the first second. This phenomenon is shown in Fig. 12.

One way that I&E used to overcome this problem (i.e. a non spiking network), was to generate what they called spontaneous synaptic release, or miniature post-synaptic potentials, mPSPs, or just minis, for short. I&E claim that such minis are observed both in biology and in the lab, and are thought to provide neurons with sufficient tonic level of random input stimulus needed to overcome a silent state.

During the first half hour of model time (i.e. the first 1800 s in the inset of Fig. 12) I&E simulated one spontaneous synaptic release per synapse per second (using a Poissonian probability distribution) then allowed synaptic plasticity to adapt the subsequent connectivity. If, during this time, the minis were switched off, then activity would decrease, but, the longer they were switched on, the longer the activity lasted afterwards.

From their previous studies, I&E knew that STDP is favorable to synaptic connectivity, generating polychronous firing, i.e. firing that is time locked, but not synchronous, and that this firing can spread throughout the network. Hence they had the idea to not turn off the minis for the first 1800 ms. This had the effect that the network did not go silent. See Fig. 12.

Thanks to STDP, I&E found that it finely tuned the synaptic connectivity to generate sufficient inter-neuronal action potentials to sustain global firing. They also noted, for this to happen, that a certain minimum threshold number of neurons was needed, i.e. about 10,000. They then ran their model for the next half hour with the minis switched off (i.e. in a noiseless regime) and then used the final state at the end of this transient period as the initial state for most of the later simulations.

The main graph in Fig. 12 shows that the neural activity (i.e. the average firing rate in the network) dies out after the first few seconds of simulation. This occurs independently of the number of seeder spikes introduced at the start of the simulation. The inset shows that the model simulated was input with noise (i.e. spontaneous synaptic release, or minis) for the first 1800 ms. After the noise source was turned off, the firing continued.

A real brain has resource to many sensory inputs and to neuronal noise, which contrasts with the I&E model. Nevertheless, the latter managed to generate self-sustained firing in a noiseless environment.

I&E wondered whether this autonomous firing was merely chaotic, and hence not very useful, so they undertook a test to see

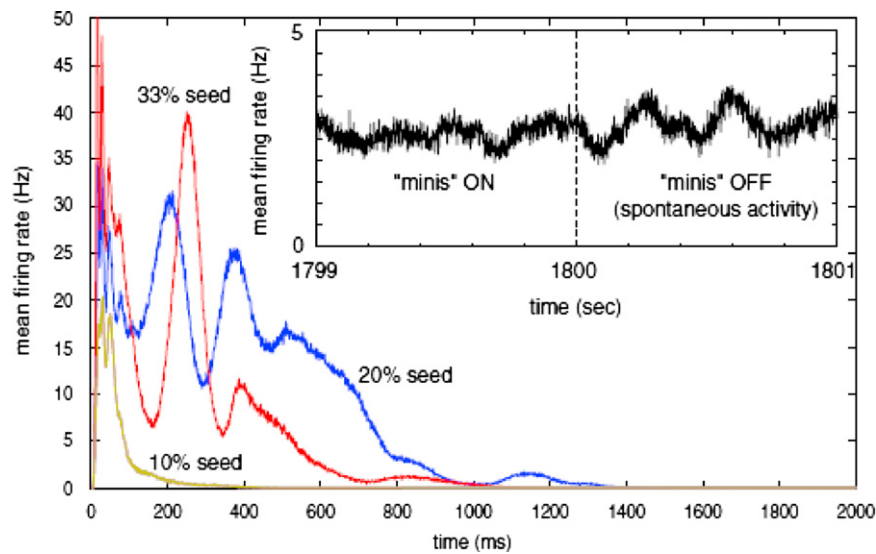


Fig. 12. Spontaneous neuronal activity in the Izhikevich & Edelman model.

whether they could detect the characteristic trait of chaos, namely the sensitivity of the system to a small perturbation of the initial conditions, i.e. the so-called butterfly effect. So they input a single extra spike to see if it could make any difference, i.e. could the state of the whole model's firing pattern be changed by the firing of a single (extra) neuron?

The results of their extra single extra spike experiment are shown in Fig. 13. It shows two traces of total electrical firing (i.e. the sum of local-field potentials at every cortical location). Both traces started from identical initial conditions except for a single extra spike (which I&E introduced manually) in one pyramidal neuron in layer 2/3 of the frontal cortex.

Fig. 13 shows that after only a few hundred milliseconds, the two traces diverged, resulting in very different global firing patterns. The lower part of Fig. 13 shows the difference in the two spike rastergrams. It can be seen that the single extra spike launched an avalanche of extra spikes (blue dots) or missed spikes (red dots). These differences then spread over the entire network and changed the firing pattern of every single neuron.

I&E then undertook a similar experiment by removing a single spike from the initial conditions and found a very similar effect. They also noticed that it did not seem to matter much where in the network, or which type of neuron had a spike added or removed from its firing pattern, the effect was the same.

More precisely they noted that on average, it took about 400 ms for the perturbed activity trace to diverge from the unperturbed trace by a standard deviation. They also noticed that if they increased the size of their network, this divergence became stronger (i.e. faster), although they did not examine this size dependence in detail.

They undertook a further related experiment, by adding a single somatic EPSP. They found that either (a) it took longer for the perturbed signal to spread through the network or (b) frequently, an extra EPSP had no effect on the perturbed neuron or on the network.

I&E noted that the firing patterns of individual pyramidal and non-basket interneurons of the model looked rather Poissonian during self-sustained spontaneous firing, at about two or three spikes per second.

Fig. 13 shows two simulations, with each starting from the same initial condition, except for a single extra spike in one of them.

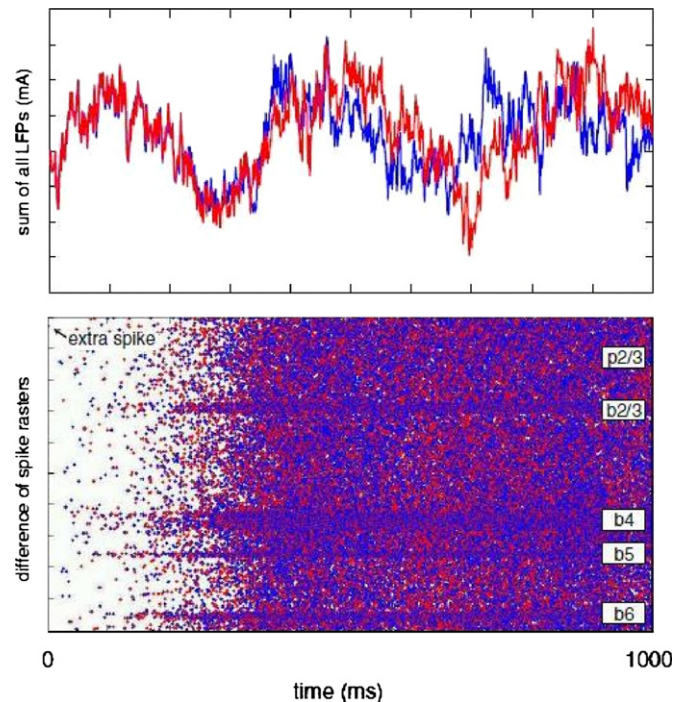


Fig. 13. Sensitivity of the model to the addition of a single extra spike.

They observed that the firing patterns had different phases at different locations in the model. When I&E averaged these firing patterns over a centimeter-size area, they canceled each other, and were barely visible in the power-spectrum of the global electrical activity.

They felt that these simulated findings were consistent with well known experimental observations that gamma rhythms are weaker in EEG and MEG recordings than in LFPs and intracranial EEGs [110].

I&E noticed a significant low-frequency firing that occurred in the entire network. See Fig. 14. This activity was not preprogrammed into any of the neuron types in their model. The main

frequencies of this activity were in the delta (1–3 Hz) and alpha (~10 Hz) ranges. The delta range activity occurs typically during the sleep state of mammals, and the alpha range activity occurs typically during the cortical idling of humans [111].

In Fig. 14 the red (black) dots are spikes of excitatory (inhibitory) neurons.

It is well known amongst neuroscientists that simple spiking network models are capable of self-organizing to generate collective delta-, alpha-, and gamma-frequency rhythms, e.g. [97,109,112]. What was remarkable about the I&E model was that the power spectra of different cortical locations had different dominant rhythms, e.g. the regions that corresponded to the motor and somato-sensory areas had a strong beta rhythm (~20 Hz).

This occurred despite the fact that the micro-circuitry of the cortex is the same in all locations of the model. I&E concluded from this interesting phenomenon, that these differences of rhythms in different areas of the model must be derived mostly from differences in the white-matter connectivity between and among cortical areas.

I&E observed a further notable feature of their model, as is shown in Fig. 15, namely that the oscillatory activity was not uniform. It was comprised of multiple propagating waves of excitation that waxed and waned spontaneously, and in different cortical locations. These waves were spread over about a centimeter and propagated at a speed of ~0.1 m/s.

Studies of human subjects, suggested to I&E that they, (expressed in their own words) “could analyze the resting state correlations of the simulated signals corresponding to fMRI (BOLD signals) on the slow time scales of minutes.”

Using an approach by Fox, they stored signal values at each voxel of the cortical surface, passing them through a low-pass

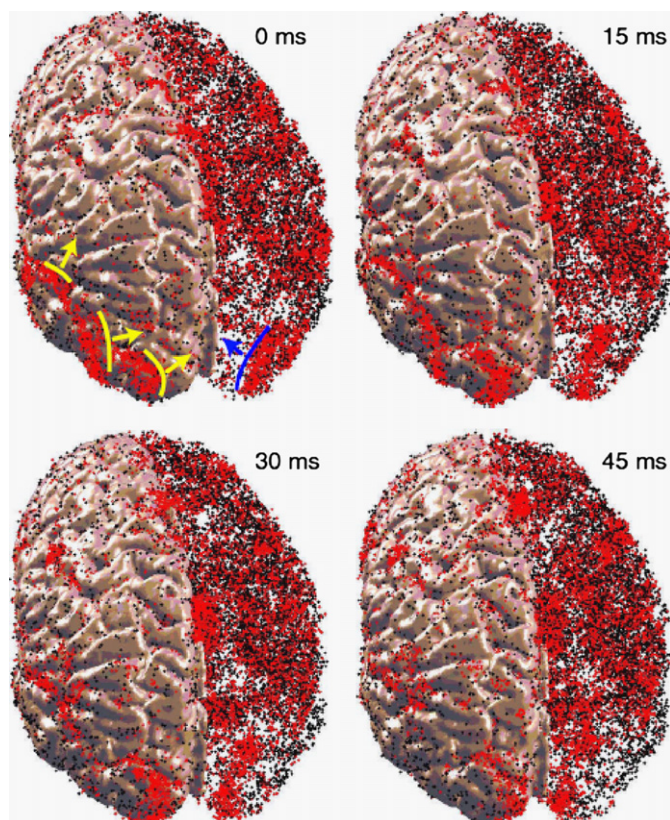


Fig. 14. Propagating waves in the Izhikevich & Edelman model.

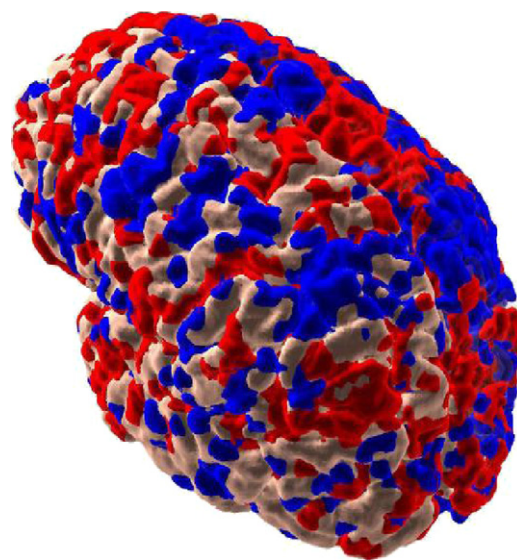


Fig. 15. Intrinsic correlations of fMRI signals between the seeder cortical region in a location corresponding to the posterior cingulate.

filter (between 0.1 and 0.01 Hz), and then correlated the results with a seeder region that corresponded to the posterior cingulate.

Fig. 15 shows those regions that were positively and negatively correlated with this seeder region, as shown in red and blue, respectively. I&E’s results were similar to those of experimental human brain studies, as well as several theoretical studies. They showed that the mammalian brain’s resting state on this scale consists of many anti-correlated functional clusters. For further references relevant to Izhikevich’s work, see [95,98,101–108].

7. Horwitz’s “Brain Imaging and Modeling Project”

We turn next to two large-scale brain simulations that differ from the previous ones in that they lack neuron-level processing elements. These two simulations are more cognitive in nature, yet because they are aimed largely at yielding understanding of specific regions of the brain, rather than mainly at achieving intelligent functionality in a brain-inspired way, we include them in this paper rather than the sequel on Biologically Inspired Cognitive Architectures.

The work of Dr. Barry Horwitz’s group (at the National Institutes of Health (NIH) in Bethesda, Maryland, USA [80a]) focuses on, in Horwitz’s own words, “the dynamic assemblage of neural subnetworks performing cognitive tasks, especially those associated with audition and language, and with an emphasis on the alteration of these networks during brain disorders.” He employs brain imaging using fMRI, PET, or MEG, to provide data for guidance of his simulation work. His research program is more computational neuroscience focused and less engineering focused than even Markram’s work, let alone that of Modha’s or Boahen’s but it does have a scope and ambition pushing toward large-scale brain simulation, rather than typical computational neuroscience.

One of Horwitz’s main interests at the present time is examining the dynamic causal behavior of large-scale neural models, e.g. [90,83]. He uses the term *Dynamic Causal Modeling (DCM)*, which he describes as being a way to estimate and to make inferences concerning how coupling occurs between small numbers of brain areas, as well as how experimental manipulations can influence that coupling.

The conceptual idea underlying DCM is the interoperation of the two principles of functional specialization and functional integration. Functional specialization means that anatomically different and separate cortical and subcortical areas of the brain specialize in performing various tasks, such as perception, cognition and motor control. As a result of extensive functional specialization, a single cortical area is usually unable to perform a complex task on its own—it is too specialized, so it becomes necessary for various specialized areas to interact, to cooperate, in performing some task, even one as simple as a perceptual or motor function task.

Horwitz describes functional integration as the connection patterns that are established between different cortical areas that are unique for a given function.

Traditionally, more emphasis was placed on investigating functional specialization, due to the power of such techniques as functional neuroimaging. Horwitz is critical of this rather narrow focus on the specialized side, by stating that “analyses of neural activity based solely on this (functional specialization) principle provide a limited account of the neuronal substrate of the process under investigation.”

He has therefore, not surprisingly, developed his own methods, to investigate the changes that occur when functionally specific areas integrate.

As mentioned above, DCM is a way to measure and form hypotheses concerning the couplings between a small number of brain areas. It is also concerned with the effects of experimental interventions on those couplings that have been developed especially with the use of functional neuroimaging data in mind. DCM does not however, make realistic models concerning the true functioning of the brain.

Horwitz’s use of DCM is to consider the brain as a deterministic and time-dependent input–output system, where his inputs are traditional stimulus functions that describe experimental interventions.

He interprets the various state variables of his model of the brain as describing the neural activity of various brain regions, and that biophysical states allow one to use the neurodynamics in a brain region to predict the blood flow in that region.

The outputs may be, for example, measured regional blood oxygenation-dependent (BOLD) signals. For example, in a simulation of region-specific BOLD (i.e. blood oxygenation-dependent) time-series [84], Horwitz used DCM to make deductions concerning connectivity by using data derived from a model which used a visual delayed match-to-sample task [91].

Horwitz considers the neurodynamics of any region of the brain (within a DCM context) as deterministic. Hence, in his view, any changes in neuronal activity that occur in a region can only be due to “(a) direct inputs to that area (if specified), (b) intrinsic activity in the area (via self-connections) and (c) activity in other connected regions.”

It is up to the user, (i.e. the DCM modeler) to make such choices as (a) the regions to be investigated, (b) which connections are present, and (c) where the experimental interventions are to be applied, whether as direct inputs to a region or by changing the strengths of connections between regions.

There are points of contention concerning DCM. The major point is the problem, as Horwitz claims, as to how to specify the structure of the latent (interregional) connectivity, because a detailed knowledge as to how the human brain is anatomically connected is largely nonexistent.

A second point is how to specify those connections influenced by variables under experimental control, which reflects the hypotheses being tested.

In practice, Horwitz feels that the above points reduce to empirical questions when he is working with experimental data. He claims that

he can use Bayesian model comparison techniques to distinguish between competing simple neural models of his simulated data.

Horwitz has tried to validate the use of DCM by using synthetic fMRI time-series data that is simulated by a neuromorphic computational model. (See [84] for a review of techniques that combine computational neural modeling with functional neuroimaging.)

Horwitz and his team used such a model to simulate cortical region-dependent BOLD (i.e. blood oxygenation-dependent) time-series. See [85] for details. Horwitz claims that using large-scale neural models allows a partial validation of techniques such as DCM, due to the fact that sufficient basic knowledge of anatomical structure and neuronal physiology exists, which in turn allows these large-scale neural models to examine the neural substrates that serve as the basis to interpret these DCMs. Doing a similar validation against brain data is not currently feasible, because the connectivity structure and mechanisms that generate phenomena such as attention, are simply unknown at the present time.

7.1. Just’s “4CAPS cognitive neuroarchitecture”

Similar to Horwitz’s work, Just’s 4CAPS brain simulations are also largely cognitive in focus—but because of the strong emphasis paid to precise modeling of the cognitive functions of specific brain regions, we include it here rather than in the sequel paper.

Marcel Adam Just is the D.O. Hebb Professor of Cognitive Neuroscience at Carnegie Mellon University, Pittsburgh, Pennsylvania, USA, and Director of the Center for Cognitive Brain Imaging [127]. His main research focuses on using fMRI to determine what he calls are the “underlying cortical components of the cognitive system”, and how they collaborate to perform many kinds of tasks. He works with his close colleague Sashank Varma on the investigation of cognition during tasks such as sentence comprehension, mental rotation, imagery, object recognition, problem-solving, and decision-making—in normal college students or adolescents, as well as special groups such as autists and dyslexic children.

7.2. 4CAPS cognitive neuroarchitecture, Marcel Adam Just and Sashank Varma

Just’s “4CAPS” (i.e. cortical capacity-constrained concurrent activation-based production system) cognitive architecture aims to provide an explanation of both behavioral and neuroimaging data [128]. It is a hybrid architecture combining both symbolic and connectionist (neural net) approaches, functioning in a resource-constrained environment.

The first CAPS architecture was conceived in 1982 [129] and was based on a hybrid symbolic and activation-based processing approach that was popular in the early 1980s, including computational features such as variable-binding and constituent-structured representations, alongside more standard neural net structures and dynamics. Its effectiveness in explaining high-level cognition was shown by its application to modeling various cognitive skills, such as language comprehension [131,129], mental rotation [131], and problem solving [132].

The CAPS architecture of 1982 was followed by the 3CAPS architecture in 1992 [133], which placed further constraints on the resources available for the maintenance and the processing of representations.

Adding constraints to their basic CAPS architecture, allowed Just’s team to model individual differences on a number of tasks, such as sentence comprehension in young adults of different working memory capacities [133]; sentence comprehension in intact “normals” and aphasics [135]; discourse comprehension in young adults [136]; problem solving in normal adults different in

fluid intelligence [137]; problem solving in intact normals and patients with frontal lobe lesions [138]; and human–computer interaction [139]. The successes of these models persuaded just that information processing in humans uses hybrid computational methods within a capacity-constrained environment.

7.3. Operating principles of 4CAPS

After the success of the above models, based on the 3CAPS architecture, Just and his collaborators introduced a new variant, entitled 4CAPS [128], which was a more elaborate version of 3CAPS, 4CAPS is the latest version in a series that includes CAPS [129], and 3CAPS [133]. This series of neuroarchitectures has served as the basis for models that have been applied in many areas of behavioral activity, e.g. mental rotation [131]; analogical problem solving [132]; discourse comprehension [136,129]; human–computer interaction [139,140]; Tower of Hanoi problem solving in normal subjects [137]; on patients with frontal lobe lesions [138]; sentence comprehension in normal readers [133]; and in aphasic readers [135].

7.4. CAPS is based on the following six fundamental operating principles, whose importance merits direct quoting

- *Principle 0*: “Thinking is the product of the concurrent activity of multiple brain areas that collaborate in a large-scale cortical network.”
- *Principle 1*: “Each cortical area can perform multiple cognitive functions, and conversely, many cognitive functions can be performed by more than one area.”
- *Principle 2*: “Each cortical area has a limited capacity of computational resources, constraining its activity.”
- *Principle 3*: “The topology of a large-scale cortical network changes dynamically during cognition, adapting itself to the resource limitations of different cortical areas and to the functional demands of the task at hand.”
- *Principle 4*: “The communications infrastructure that supports collaborative processing is also subject to resource constraints, construed here as bandwidth limitations.”
- *Principle 5*: “The activation of a cortical area as measured by imaging techniques such as fMRI and PET varies as a function of its cognitive workload.”

These principles are now discussed one by one, with a focus on their general importance for artificial brain research as well as their relevance to the CAPS series of architectures.

- *Principle 0*: “Thinking is the product of the concurrent activity of multiple brain areas that collaborate in a large-scale cortical network.”

It has been well confirmed, with 1000s of neuroimaging studies, that multiple areas of the brain are activated when performing any task.

Just thinks that one of the remaining challenges in neuroscience is to provide an answer to the intriguing question, as he puts it—“Why a particular set of cortical areas comes to be activated in a given task?”

Just feels that a further challenge is to understand more than just how multiple areas activate each other, i.e. to understand how they work together actively.

As an example of this, consider the work by the following investigators [141,142] who showed that the functional connectivity between two areas (defined to be the correlation

or covariance between the time series of the activation of activated voxels in each), is usually interpreted as indexing the degree of coordination between them.

This degree of functional connectivity between two activated brain areas can be influenced by several different variables, e.g.

- an increase in working memory load [143]
- an increase in task complexity (e.g. from processing words to processing sentences; [144])
- a decrease in communication band width due to neurological conditions such as autism [145].

Just notes, that as with any correlation, functional connectivity (as measured by the above voxel correlation) does not imply causation, so this leaves open the question as to whether the control between the areas is symmetric, asymmetric, or coordinated by a third area?

The bottom line however for Just is that complex cognitive ability is due to networks, that span several cortical areas, working together in close collaboration.

The zeroth operating principle is that a cognitive system that appears to function as a unit (i.e. is unitary) at the psychological level, is in fact, comprised of multiple cortical information-processing centers. The so-called centers in the 4CAPS architecture were designed so that they corresponded roughly to those cortical epicenters that compose large-scale distributed cortical networks, a proposal made by [146].

- *Principle 1*: “Each cortical area can perform multiple cognitive functions, and conversely, many cognitive functions can be performed by more than one area.”

The first part of this operating principle states that a cortical area can perform multiple tasks. There is plenty of proof of this in the neuropsychological literature; e.g. is it known [147] that Broca’s area serves a key role in both syntax processing and language articulation. Many further examples of this principle have come from reviews of modern studies of functional neuroimaging that show repeatedly that a given cortical area is activated in a number of different types of tasks [148–150]. Just feels that the assignment of multi functionality to a cortical area remains valid, even at spatial scales smaller than typical imaging studies have afforded.

BOLD (blood oxygenation-dependent signals) fMRI typically allows a spatial resolution of about 30–50 mm³ per voxel (i.e. a volume element). These voxels usually depend on many task variables. For example, in the case of sentence comprehension, a large proportion of the activating voxels in Wernicke’s area (i.e. the left posterior of the superior temporal gyrus [STG]) responds to both lexical and syntactic manipulations.

The principle of “multiple specializations” is also consistent with those influential studies that showed that single neurons are active in more than one function.

Another supporting argument for Just’s Principle 1 is the fact that sensory events and motor actions are coded by their patterns of neural activity, similar to waves of activation, showing that individual neurons participate in multiple codings.

The second part of the two-part Principle 1, is more novel to neuroscience, namely that some functions are implemented by more than a single area. Just proposes that there is functional redundancy across cortical areas, i.e. some functions are performed by more than a single brain area, although he does admit that there are variations in the nature of these implementations. This redundancy is made clear when local damage in one cortical area causes recruitment of another area to perform the same function, e.g. when areas normally used in language processing (e.g. Broca’s area) are damaged in a stroke, this can lead to the activation of the homologous right-hemisphere areas [151].

This kind of redundancy may serve as the basis for certain types of cortical plasticity.

Redundancy of function is not restricted to damaged brains, it also occurs in healthy brains, especially when a demanding task demands more computational resources than those possessed by the usual brain areas that are used to execute it. A good example is when a normal young adult attempts to process a sentence that has greater syntactic complexity than usual, in which case, the right homologue of Broca's area shows increased activity [152]. These kinds of discoveries suggest that there is an overlap of language functionality between Broca's area and its right homologue, although Broca's area is predominant (i.e. the more efficient one) for some tasks (e.g. such as syntactic analysis), whereas its right homologue is predominant for other tasks, e.g. prosodic processing.

Just notes that each center can perform multiple cognitive functions and tends to have similar information-processing styles, e.g. the center that corresponds to the intra parietal sulcus (IPS) may specialize in functions that are of spatial and transformational type. Examples of such functions would be rotation, translation, and scaling, and more generally, for performing geometric computations.

Just states however, that despite the possibility that a center may be capable of performing several cognitive functions, it is nevertheless usually specialized for the multiple functions that it does perform.

- **Principle 2:** "Each cortical area has a limited capacity of computational resources, constraining its activity."

Just claims that this operating principle is also rather new. For Just, the act of thinking is actually biological work, i.e. there is an upper limit on the availability of (neuronal) resources. These limits on the resource capacities of brain systems cause performance not only to slow down and degrade when challenged with demanding tasks, but they also have a fundamental effect on the shaping of cortical and cognitive information processing.

Just makes an analogy with the way the "shape of a riverbed constrains the water flow of a river." In both cases, The existence of resource constraints forces the system to reconfigure itself dynamically to adapt to the limitations it faces. In this respect, the constraints on cortical resources not only stifle thinking, but force the adaptivity of human cognition. This is a major theme in Just's work and thinking. Callicott performed an important imaging study on capacity constraints by attempting to overload the limits of the cognitive system [160]. He used a particular mental task (called N-back) to observe the effect on the slope of the activation in several cortical areas, as the number of items to be encoded, retained, and recalled was increased.

It is well known in neuroscience that the prefrontal areas are used (amongst other things) for performing working memory tasks, such as the above. Callicott found that the activation levels grew monotonically, from areas N50 to N51 to N52 (see Fig. 16). There was also a decrease from area N52 to N53 when the majority of subjects gave up when they could no longer perform the task accurately. This phenomenon, i.e. an increase in activation in response to an increase in cognitive workload, is a familiar one in neuroscience, and usually results in an acceptably accurate performance level.

Fig. 16 shows the results of 7 human subjects performing the "N-back" task, and their capacity constraints in the left dorso-lateral prefrontal cortex. These activation levels increased with workload, up to a limit [160].

Just takes the view that "computation is fueled by activation." In Just's CAPS model, the declarative elements must have above-threshold activation levels to match the condition parts of the productions (where a production is an If-Then rule or Conditions-Action rule).

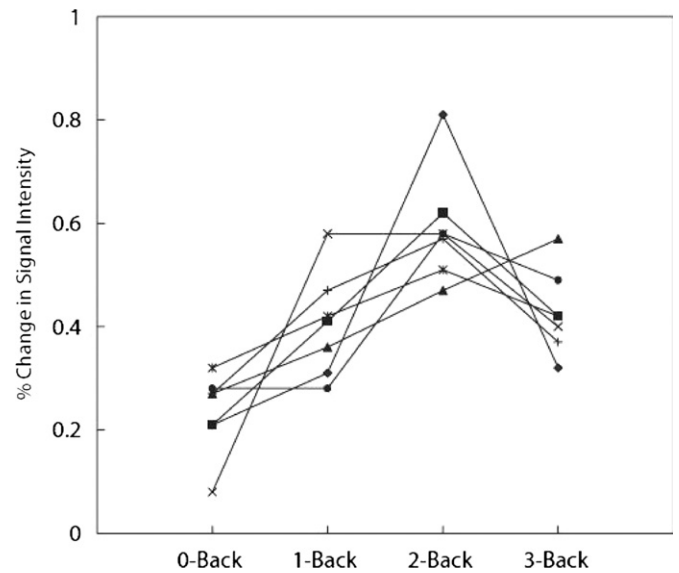


Fig. 16. Capacity constraints in a single area (left dorso-lateral prefrontal cortex).

His model gives each center a limited supply of activation, which is analogous to the biological reality that all biological systems have limits on their available resources. Expressed mathematically, let the resource capacity of the i th center be C_i , then the following constraint on resource consumption is enforced at all times: $C_i > \sum_{j=1, j \neq i}^N (A_{ij} * S_{ij})$, where A_{ij} represents the amount of cognitive function j performed by center i , and S_{ij} represents the specialization of center i for cognitive function j .

- **Principle 3:** "The topology of a large-scale cortical network changes dynamically during cognition, adapting itself to the resource limitations of different cortical areas and to the functional demands of the task at hand."

This third operating principle is central to Just's work. He is convinced that the structure of a large-scale cortical network and its pattern of inter-area connectivity are not fixed but vary dynamically during the performance of tasks.

Just is going against the grain in the sense that the consensus in neuroscience is that each cognitive task is performed by a fixed set of brain areas, i.e. a fixed neural substrate. However, in Just's view, the neural substrate underlying a cognitive task is a moving target that not only changes from one stimulus item to another, but can change (from moment to moment) even within a stimulus item.

Just thinks that it is the constant changing of the availability of resources within brain areas and the changing functional demands of a task that cause the configuration and reconfiguration of a large-scale network.

What Just calls the topology of a network (i.e. the constitution and connectivity of a network) can change as the functional demands of a task increase in quantitative terms. This means that other areas become activated and are recruited into the network.

As an example of this, consider increasing the structural complexity of a sentence when speaking to a subject in a task involving sentence comprehension. The subject's level of activation in his right-hemisphere homologue of Wernicke's area will rise from a very low to a significant level [137]. See Fig. 17.

Just gives the following interpretation to this example of a dynamic reconfiguration of a network.

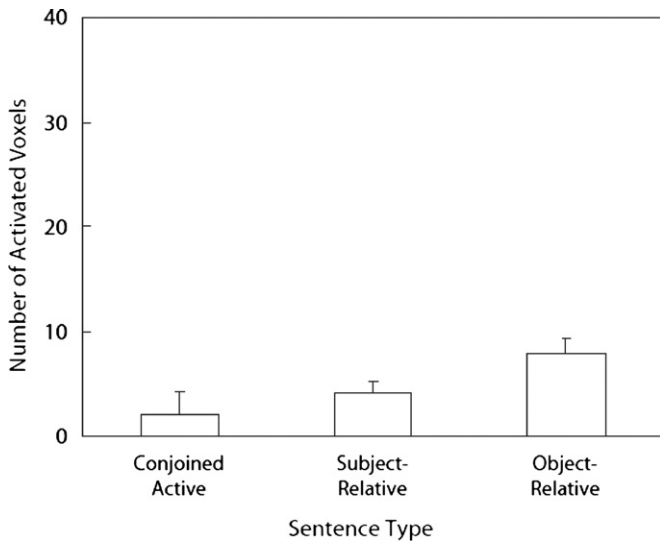


Fig. 17. Progressive activation of the right homologue of Wernicke's area.

When the total (neuronal) resources of a cortical area that is specialized for performing particular tasks (e.g. Wernicke's area) are being used, then further areas that are less specialized for the same tasks (e.g. its right homologue) are recruited into the network to assist in coping with the extra workload.

He thinks also, that when the demands for performing a particular task change qualitatively, then the topology of a network can change appropriately, as for example, when a task becomes increasingly difficult, to the point it requires the initiation of strategic thinking. This happens for example, when understanding a sentence requires problem solving as well as normal language processing.

Under such circumstances, the task will activate dynamically and recruit the left dorso-lateral prefrontal cortex (DLPFC), which is an area involved with the executive function and working memory into the language network [153].

Just further claims that the dynamic addition of extra cortical areas into a large-scale network occurs incrementally and continuously, and is not an all-or-none affair. As an example of this, [153] showed the above mentioned left DLPFC activation occurred either earlier or later in the difficult sentence understanding task, depending on which part of the sentence the heaviest reasoning was needed.

In light of the above, Just claims that this dynamic reconfiguration of the cortex generates a "just-in-time and as-needed" neural support system, for the changing demands of task execution. As stated earlier, Just thinks that the topology of a large-scale network is not static, but changes dynamically as a task is performed.

From an individual center's point of view, there are two factors which determine the extent to which it participates in the network, namely (a) the level of match between the cognitive tasks to be executed, and the level of specialization of the centers for those tasks, i.e. is the center well suited (specialized) for the tasks to be performed, and (b) the availability of resources, i.e. does the center concerned have enough extra resources to fuel the execution of the pending tasks, that it is specialized for.

Just's 4CAPS architecture contains an algorithm for weighing these factors, and assigning pending cognitive tasks to appropriate centers, depending on both their task specialization and resource

availability. This assignment ensures that the large-scale network executes as much of each task as is possible, while at the same time obeying all the constraints on resources. Just affirms that the extent to which a particular center participates in the network depends indirectly on this assignment.

Fig. 17 shows the progressive activation of the right homologue of Wernicke's area, i.e. the right superior temporal gyrus, as a function of the complexity of the sentence [152].

- Principle 4: "The communications infrastructure that supports collaborative processing is also subject to resource constraints, construed here as bandwidth limitations".

Just thinks that his fourth operating principle is perhaps the newest of his 6 proposals. He states that there are not only constraints imposed on the activation of individual areas, but also imposed on the joint functioning of multiple activated cortical areas. He claims that these resource constraints are system wide, and are particularly noticeable, when a subject performs two complex cognitive tasks at the same time.

He feels this might be due to the idea that activation is "less than the sum" due to extra overhead (coordination) costs.

Just noticed that when two demanding tasks were performed simultaneously, e.g. understanding a spoken sentence and performing 3D mental rotation, the general activation level was in fact much less than the sum of the two activations when each was performed alone [154]. See Fig. 18.

Just claims that this observation is consistent with his proposal that some constraints on cortical resources apply to sets of cortical areas.

Such constraints add to those that apply within cortical areas. Just describes these constraints on inter-area resources, as limitations on bandwidth of the communications infrastructure that supports collaborative processing in large-scale networks that execute specific tasks.

One of Just's contributions to neuroscience is the realization that not only are there limits imposed on the consumption of resources in individual centers, there are also limits imposed on the joint activity of groups of centers, as mentioned above. To emphasize the difference between these two types, he coined the terms "intracenter constraints" and "intercenter constraints."

As suggested by these labels, an intracenter constraint applies within a single center. An intercenter constraint makes the availability of resources in one center dependent upon the resource consumption levels in other centers.

Just then developed a formal unified description of these intracenter and intercenter resource constraints, but admits

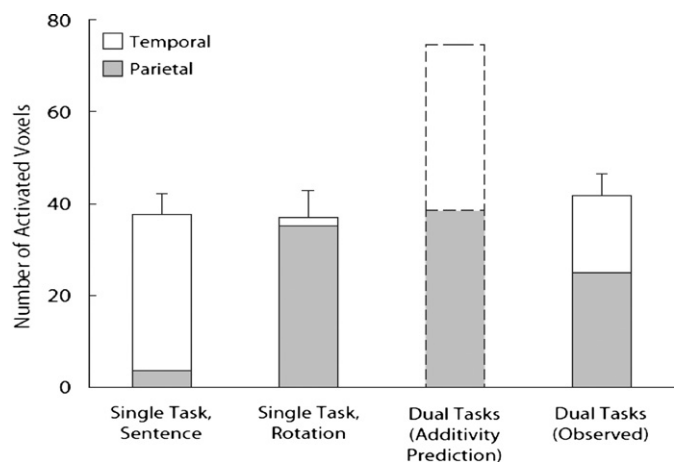


Fig. 18. Activation in two areas during simultaneous language and spatial tasks.

that there is a real possibility that the underlying biological mechanisms may be very different.

He then provided as an example of an intercenter constraint using his bandwidth limitation interpretation as applied to the communications infrastructure over which centers/areas collaborate.

Fig. 18 shows the activation levels in two areas during simultaneous language and spatial tasks, based on the predicted dual-task activation using the assumption that one adds the two individual activations, as well as the observed dual-task activation [154].

- *Principle 5*: “The activation of a cortical area (as measured by imaging techniques such as fMRI and PET) varies as a function of its cognitive workload.”

Just’s final operational principle, his Principle 5, deals with an assumption about measurement that allowed his theoretical ideas to connect with neuroimaging data. He claims that cognition is actually *biological work* and that this idea is essential to the interpretation of fMRI data.

He was not the first to make such a claim, as he admits himself. He cites [161] who coined the term “brain work imaging,” instead of the more usual term functional neuroimaging.

Just feels he has made the work concept (i.e. the property that is measured) more precise. For example, he claims that cortical areas collaborate in order to perform neural computation, and it is this computational collaboration that consumes biological resources. He asserts that the capacity use of a cortical area is the proportion of that area’s resources that are consumed at a given moment, relative to its total supply.

He makes the interesting if not fascinating interpretational claim that the capacity use of a cortical area is indexed by its level of activation as measured by fMRI or PET imaging. Given the highly dynamic nature of fMRI or PET imaging, it follows from Just’s claim that the capacity use of a cortical area is an instantaneous and dynamic property.

More precisely, Just’s method for measuring his capacity use is to measure the average activation level over a long time period that spans several trials, as for example, in studies employing block designs. Another method he uses is to take several measurements during a single trial, as for example with event-related fMRI studies.

Just feels that despite the fact that it is currently unclear how precise physiological mechanisms couple neural computations with the fMRI BOLD response, most such descriptions rest ultimately on some kind of bioenergetic principle that relates to resource consumption and regeneration, e.g. [155].

Just’s mention of a particular biological process is deliberately at a more macro level, because for him, the capacity use of a cortical area can be envisaged as the sum of many resource-bounded neurobiological mechanisms.

7.5. The 4CAPS architecture

Having spent some time presenting Just’s 6 operational principles of cortical processing, we turn now in more detail to his application of these principles to his current neuro-architectural model, that he labels 4CAPS (Cortical Capacity-Constrained Concurrent Activation-based Production System). As an example of a cognitive architecture, Just feels that his 4CAPS is a unified theory of cognition, in the sense specified by Newell in his famous book [156]. Unified theories are computational formalisms that make the ambitious claim of being able to account for all forms of cognition.

The 4CAPS model concentrates on some of the more complex forms of cognition, e.g. language understanding, problem solving, spatial reasoning, and dual-tasking.

Just asserts that since cognitive architectures are computational formalisms, they embody the basic information-processing abilities of the mind. To be able to do this, these cognitive architectures must perform the following roles: (a) they define the representational formats that are available, (b) they specify the operations that transform these representations, (c) they create the control structures used to organize how these operations are applied to the representations over time.

4CAPS goes further than the above definition of a unified theory of cognition. Just claims that his model creates a plausible neural implementation as well. As will be shown in more detail in the paragraphs that follow, this model is significantly different from its competitors, in that it makes no effort to reduce cognitive information-processing mechanisms directly to neural information-processing mechanisms. Instead 4CAPS is based on trying to simulate the patterns of resource utilization in neural systems.

The heart of the 4CAPS model is a set of centers that correspond to cortical areas that are activated to execute a given task. Each 4CAPS center is a hybrid symbolic/connectionist system with a fixed supply of resource capacity. A center is said to be symbolic in the sense that it is a production system, i.e. a set of production rules (i.e. if-the rules). In 4CAPS, declarative knowledge is represented by declarative memory elements. Each memory element contains a number of attributes (i.e. features), and each attribute has a symbolic or numeric value.

Procedural knowledge on the other hand is implemented in the form of production rules (i.e. condition-action rules, or if-then rules), similar to those used in a variety of traditional AI systems [158].

The 4CAPS models also have properties that can be described as connectionist (i.e. neural net based), e.g. they use such features as activation-based representations, graded processing, and parallel control.

Just states that there are parallels between 4CAPS and local connectionist networks. For example, Just has modeled his declarative elements as (neuron) units, his productions as weighted links, and his activations propagate in parallel.

Each declarative element has a corresponding level of activation, in the form of a continuous variable. Just uses the term activation in this context to mean the current availability of a representation, as in [159].

Just uses the word “activation” to refer to activation levels inside 4CAPS, and also to brain activation, as measured by fMRI or PET. To connect these meanings, he specifies that in 4CAPS activation of a declarative element is a vector, not a scalar. Each center has its corresponding vector component, where the value represents the current activation contribution of that center to that element.

Actually, the term “activation” level of a declarative element means the sum of its component values, in other words, those activations that are contributed by the centers that are collaboratively processing it.

Just models the productions in 4CAPS with some connectionist properties. The declarative elements, need to satisfy two conditions, namely (a) they must meet the symbolic constraints of the condition sides of the production rules, and (b) their activation levels must surpass the specified threshold values.

The main action that a production rule executes is also graded. It directs activation from one declarative element to another, via some continuous weight. Productions are also graded in time, in the sense that they do not finish their processing in an instant, but rather they direct activation repeatedly over a time interval.

4CAPS has another connectionist property, i.e. a control scheme that functions in parallel, i.e. at each unit of time (called a cycle), all those productions whose conditions are met, are fired in parallel. This holds both within an individual center as well as across all centers.

Just claims that each 4CAPS center combines the advantages of a production system, i.e. symbolic variable-binding and the processing of structured representations on the one hand, together with the graded, activation-based, and parallel operation of a connectionist network. For further references relevant to Horwitz's work, see [81,82,86–89]. For further references relevant to Just's work, see [130,134,157].

8. Conclusion

Having survived our review of a number of the leading approaches to large-scale brain simulation, the reader may now have a fuller appreciation for the point we raised in the Introduction: that different researchers mean different things by *brain simulation*, and have different goals with their large-scale brain simulations. The reader may wish to review Table 1 above, having now read the reviews of the simulations mentioned therein.

The diversity of approaches in the field seems likely to continue, for multiple reasons: because different simulations with different levels of accuracy serve different research goals, because our knowledge about different subsystems of the brain exists on different levels of accuracy, and because given the contemporary realities of the research funding scene, different aspects of the brain command differential amounts of financial resources (and hence computer power). What we are likely to see as the field progresses is a gradual move toward the more accurate forms of simulation depicted in Table 1. We will see more detailed functional simulations of chosen brain subsystems, e.g. simulated cortical columns that actually explain the precise I/O behavior of cortical columns. We will see more accurate quantitative simulations of the whole brains of organisms, e.g. a simulation of the mouse brain that matches biological data in a much more fine-grained sense than Modha's current simulations. We will see neural implants following Boahen's and other methodologies, allowing simulations to actually carry out neural functions in real brains, for individuals with brain dysfunctions and maybe for others as well. We will see brain simulations capturing various high-level dynamical properties, e.g. those probed by the Izhikevich/Edelman and 4CAPS architectures, and many others. Eventually we will very likely see a detailed simulation of a whole human brain, at the level needed to simulate and explain human intelligent behavior—but during the period before this is achieved, we will see a host of simulations at different levels of accuracy and serving different purposes. Keeping all these simulations straight, and understanding their different objectives as well as their different achievements, will require much ongoing vigilance!

We conclude with a brief reminder of some of the many valuable roles that large-scale brain simulations are projected to serve as science progresses. So far, large-scale brain simulations have proved useful mainly in terms of refining the equations used for modeling neurons and synapses, and helping substantiate conceptual models of brain structure and function by connecting these models with detailed electrophysiological data in working simulations. But if the large-scale brain simulation research program is successful, the biggest benefits are ahead. The following list is adapted from a list of potential benefits of Blue Brain [6,12,13,15] but actually applies more generally:

1. Gathering and testing 100 years of neuroscience data
2. Cracking the neural code (via which the brain represents object and events)
3. Understanding neocortical information processing
4. A novel tool for drug discovery for brain disorders
5. A foundation for whole-brain simulations
6. A foundation for human-like artificial general intelligence.

The final point on this list brings us back to the main theme of the Introduction: large-scale brain simulation is not the only plausible way to approach the problem of building human-like artificial general intelligence, but it's certainly a sensible candidate approach. So far, the goals of brain simulation projects have mainly to do with emulating the general properties of brain subsystems, rather than creating integrated systems (or even subsystems) that carry out intelligent functions analogously to the human brain. But once more progress has been made this may shift, and the line between whole-brain simulations and artificial intelligence systems may blur. Whether this will be the first approach to lead to success at human-like AGI remains unclear, but it is certainly a plausible and promising approach, and Markram and other simulation researchers have their long-term sights set specifically in this direction.

The achievements of these benefits is still speculative, and a great amount of work remains to be done, in brain simulation but also in other areas such as refinement of the underlying neural modeling equations, the gathering of neurophysiological data, and the provision of adequately scalable (and economical) computing hardware. However we see little doubt that large-scale brain simulation has a great amount to contribute in the above areas and others.

The sequel paper turns to biologically inspired cognitive architectures, an alternate way of leveraging the contemporary explosions in computing hardware, neuroscience data and computer science knowledge. BICAs possess some of the potential benefits of whole-brain simulations but not others. They are oriented more directly toward AI, though also with the potential of yielding some insight into neocortical information processing (to the extent that such processing occurs at levels of organization well above the neuron). We expect that large-scale brain simulations and BICAs will provide complementary, though in some measure overlapping, benefits as both fields mature in the coming decades.

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- (b) Zooming out, highlighting a single neuron <<http://ditwww.epfl.ch/cgi-perl/EPFLTV/home.pl/-page=video&lang=2&connected=0&id=333&plugin=9&plugin=1&plugin=2&plugin=3&checkplugin=1>>;
- (c) Close-up of a single neuron <<http://ditwww.epfl.ch/cgi-perl/EPFLTV/home.pl/-page=video&lang=2&id=332&connected=0&plugin=9&plugin=1&plugin=2&plugin=3&checkplugin=1>>.
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Hugo de Garis (born 1947, Sydney, Australia) is a researcher in the sub-field of artificial intelligence (AI) known as evolvable hardware. He became known in the 1990s for his research on the use of genetic algorithms to evolve neural networks using three-dimensional cellular automata inside field programmable gate arrays. He claimed that this approach would enable the creation of what he terms "artificial brains" which would quickly surpass human levels of intelligence. He has also recently been noted for his exploration of the concept of technological singularity, and its potential social and political implications.

de Garis originally studied theoretical physics, but he abandoned this field in favour of artificial intelligence. In 1992 he received his Ph.D. from Université Libre de Bruxelles, Belgium. He worked as a researcher at Advanced Telecommunications Research Institute International (ATR), Japan from 1994 to 2000, a researcher at Starlab, Brussels from 2000 to 2001, and associate professor of computer science at Utah State University from 2001 to 2006. He has recently retired from Xiamen University, where he taught theoretical physics and computer science, and ran the Artificial Brain Lab.



Mr. Shuo Chen was born in Hubei, China. He got his M.S. degree in software engineering from Wuhan University, China in 2007. Presently he is a Ph.D. candidate at the Department of Cognitive Science of Xiamen University. His general interests are in the areas of computational vision and artificial neural networks.



Dr. Ben Goertzel is CEO of AI software company Novamente LLC and bioinformatics company Biomind LLC; Chief Technology Officer of biopharma firm Genescent Corp.; leader of the open-source OpenCog AI software project; Chairman of Humanity+; Advisor to the Singularity University and Singularity Institute; Research Professor in the Fujian Key Lab for Brain-Like Intelligent Systems at Xiamen University, China; and general Chair of the Artificial General Intelligence conference series. His research work encompasses artificial general intelligence, natural language processing, cognitive science, data mining, machine learning, computational finance, bioinformatics, virtual worlds and gaming and other areas. He has published a dozen scientific books, nearly 90 technical papers, and numerous journalistic articles. Before entering the software industry he served as a university faculty in several departments of mathematics, computer science and cognitive science, in the US, Australia and New Zealand. He has three children and too many pets, and in his spare time enjoys creating avant-garde fiction and music, and the outdoors.



Ruiling Lian is a Ph.D. student in the Fujian Key Lab for Brain-Like Intelligent Systems at Xiamen University, China. Her general research interests are Natural Language Processing and Artificial Intelligence.