OPINION

The Blue Brain Project

Henry Markram

Abstract | IBM's Blue Gene supercomputer allows a quantum leap in the level of detail at which the brain can be modelled. I argue that the time is right to begin assimilating the wealth of data that has been accumulated over the past century and start building biologically accurate models of the brain from first principles to aid our understanding of brain function and dysfunction.

Alan Turing (1912–1954) started off by wanting to "build the brain" and ended up with a computer. In the 60 years that have followed, computation speed has gone from 1 floating point operation per second (FLOPS) to over 250 trillion — by far the largest man-made growth rate of any kind in the ~10,000 years of human civilization. This is a mere blink of an eye, a single generation, in the 5 million years of human evolution and billions of years of organic life. What will the future hold — in the next 10 years, 100 years, 1,000 years? These immense calculation speeds have revolutionized science, technology and medicine in numerous and profound ways. In particular, it is becoming increasingly possible to simulate some of nature's most intimate processes with exquisite accuracy, from atomic reactions to the folding of a single protein, gene networks, molecular interactions, the opening of an ion channel on the surface of a cell, and the detailed activity of a single neuron. As calculation speeds approach and go beyond the petaFLOPS range, it is becoming feasible to make the next series of quantum leaps to simulating networks of neurons, brain regions and, eventually, the whole brain. Turing may, after all, have provided the means by which to build the brain.

On 1 July 2005, the Brain Mind Institute (BMI, at the Ecole Polytechnique Fédérale de Lausanne) and IBM (International Business Machines) launched the Blue Brain Project[1]. Using the enormous computing power of IBM's prototype Blue Gene/L supercomputer[2] (FIG. 1), the aims of this ambitious initiative are to simulate the brains of mammals with a high level of biological accuracy and, ultimately, to study the steps involved in the emergence of biological intelligence.

Concepts of intelligence

IBM built the computer Deep Blue[3] to compete against and eventually beat Garry Kasparov at chess, shaking the foundations of our concepts of intelligence. Deep Blue combined conventional methods from computer science, but was able to win by brute force, considering 200 million moves per second using if–then-like routines (BOX 1). Nevertheless, this defeat of a human master by a computer on such a complex cognitive task posed the question of whether the relevant world of an organism could simply be described by enough if–then conditions. It could perhaps be argued that artificial intelligence, robotics and even the most advanced computational neuroscience approaches that have been used to model brain function are merely if–then-like conditions in various forms. Adaptation and learning algorithms have massively enhanced the power of these systems, but it could also be claimed that these approaches merely enable the system to automatically acquire more if–then rules. Regardless of the complexity of such an operation, the quality of the operation is much the same during any stage of the computation, and this form of intelligence could therefore be considered as 'linear intelligence'.

From a biological perspective, there are quantum leaps in the 'quality' of intelligence between different levels of an organism. Atoms are differentially combined to produce a spectrum of molecules, which are qualitatively very different from atoms in terms of their properties and the information they contain. After all, molecules cannot be understood by the study of atoms alone. DNA molecules can be strung together in numerous sequences to produce different genes, which collectively produce hundreds of thousands of proteins that are qualitatively different from their building blocks. Different combinations of proteins produce qualitatively different types of cell that can be combined in various ways in the brain to produce distinct brain regions that contain and process qualitatively different types of information. The brain seems to make the next quantum leap in the quality of intelligence, beyond the physical structures to form dynamic electrical 'molecules'. The ultimate question, therefore, is whether the interaction between neurons drives a series of qualitative leaps in the manner in which information is embodied to represent an organism and its world. As computers approach petaFLOPS speeds, it might now be possible to retrace these elementary steps in the emergence of biological intelligence using a detailed, biologically accurate model of the brain.

Detailed models

In 1952, Hodgkin and Huxley published the highly successful model of ionic currents that allowed simulation of the action potential[4]. These simulations revealed the emergent behaviour of ion channels, and showed how only two types of ion channel can give rise to the action potential — the currency of the brain. These insights fuelled experiments and simulations for decades, and now explain how different combinations of ion channels underlie electrical diversity in the nervous system. Wilfred Rall realized that the complexity of the dendritic and axonal arborizations of neurons would profoundly affect neuronal processing, and developed cable theory for neurons[5] despite fierce resistance from the entire community, which argued against the need to consider such complexity. Rall's framework explains the 'passive' spatiotemporal integration in neurons and is key to

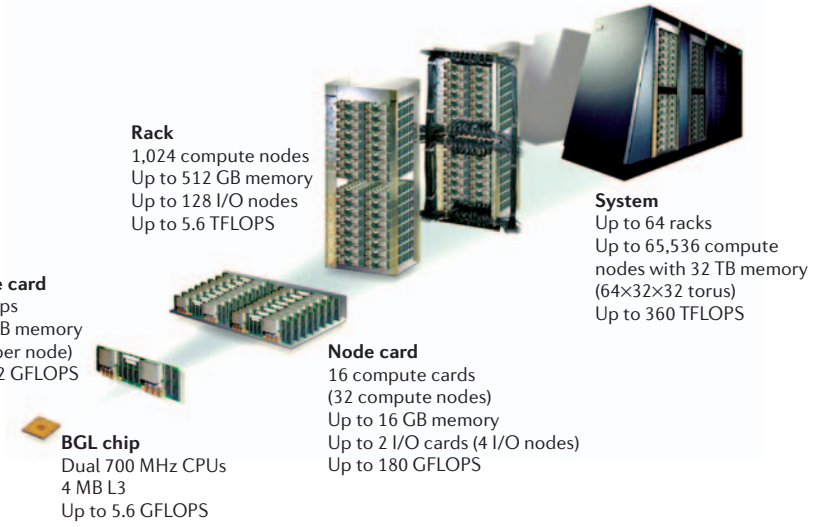

Figure 1 | **The Blue Gene/L supercomputer architecture.** Blue Gene/L is built using system-on-a-chip technology in which all functions of a node (except for main memory) are integrated onto a single application-specific integrated circuit (ASIC). This ASIC includes 2 PowerPC 440 cores running at 700 MHz. Associated with each core is a 64-bit 'double' floating point unit (FPU) that can operate in single instruction, multiple data (SIMD) mode. Each (single) FPU can execute up to 2 'multiply-adds' per cycle, which means that the peak performance of the chip is 8 floating point operations per cycle (4 under normal conditions, with no use of SIMD mode). This leads to a peak performance of 5.6 billion floating point operations per second (gigaFLOPS or GFLOPS) per chip or node, or 2.8 GFLOPS in non-SIMD mode. The two CPUs (central processing units) can be used in 'co-processor' mode (resulting in one CPU and 512 MB RAM (random access memory) for computation, the other CPU being used for processing the I/O (input/output) of the main CPU) or in 'virtual node' mode (in which both CPUs with 256 MB each are used for computation). So, the aggregate performance of a processor card in virtual node mode is: 2 x node = 2 x 2.8 GFLOPS = 5.6 GFLOPS, and its peak performance (optimal use of double FPU) is: 2 x 5.6 GFLOPS = 11.2 GFLOPS. A rack (1,024 nodes = 2,048 CPUs) therefore has 2.8 teraFLOPS or TFLOPS, and a peak of 5.6 TFLOPS. The Blue Brain Project's Blue Gene is a 4-rack system that has 4,096 nodes, equal to 8,192 CPUs, with a peak performance of 22.4 TFLOPS. A 64-rack machine should provide 180 TFLOPS, or 360 TFLOPS at peak performance. BGL, Blue Gene/L; torus, torus-like connectivity between processors. Modified with permission from IBM (International Business Machines) © (2005) IBM Corporation.

understanding 'active' integration due to nonlinear conductances in dendrites[6–10]. This has been fundamental to understanding synaptic transmission, integration and plasticity, the significance of ion channel densities and distributions in dendrites, and active electrical generation and electrochemical compartmentalization in spines and dendrites.

Neurons themselves are anatomically and electrically highly diverse, and the next step was to place the neurons in their natural environment — with other neurons. A natural progression is then to simulate neurons embedded in microcircuits, microcircuits in the local circuits of brain regions, and circuits within regions and the whole brain. This progression began by incorporating Hodgkin–Huxley-type active properties in Rall-type neuronal models to simulate realistic microcircuits carrying out realistic neural operations, such as feedback and lateral inhibition[11–13].

In the cortex, a pioneering series of simulations of oscillatory behaviour of hippocampal circuits was initiated by Roger Traub and colleagues, beginning with 100 neurons[14] and progressing to 1,000 pyramidal cells, each with 19 branches (compartments), and 200 inhibitory interneurons[15]. Since then, increasing computational capacity has spawned various multi-neuron, multi-compartment cortical, thalamocortical and cerebellar models from many laboratories[16–32]. The current state-of-the-art is a model of a thalamocortical column comprising 3,650 multi-compartment neurons (~100 compartments) representing diverse types, including superficial and deep pyramidal neurons, spiny stellates, fast-spiking interneurons, low-threshold spiking interneurons, thalamocortical relay neurons and reticular nucleus neurons[32]. Traub's model has given insight into the neural properties that underlie diverse cortical circuit operations such as gamma oscillations, spindles and epileptogenic bursts.

These studies provide sound proof of principle that multi-compartment, multi-neuron circuit simulations are possible, and give valuable insight into cortical network properties. The size of the current models seemed a remote prospect in the early days of modelling. They provide a strong foundation for taking the next quantum step, to further increase the size of the modelled network to an unprecedented level.

At this point, some may ask, why not use this computing power to simulate cortical circuits with artificial neural networks, in which the entire neuron is represented by one summing node (point neuron), connectivity is simplified to reciprocal interactions between all nodes, and functional properties are simplified as 'integrate and fire' types of activity. Such simulations provide a powerful exploratory tool, but the lack of biological realism severely limits their biological interpretation. The main problem is that there are always many ways to engineer a function, and which model is correct is always open debate. A new approach is now possible that involves a quantum leap in the level of biological accuracy of brain models.

Box 1 | **Intelligence of Deep Blue**

In May 1997, the second chess match between IBM's Deep Blue and chess grandmaster Garry Kasparov resulted in victory for Deep Blue, leading to a flurry of questions about the nature of intelligence. After all, Deep Blue only combined a number of relatively conventional methods from computer science: it maintained an encyclopaedic collection of opening games, contained a complete analysis of endgame positions and was programmed to rapidly search a large number of state spaces (state space being the set of all possible legal moves) using if–then-like routines to evaluate parts of the state space (W. Pulleyblank and M. Campbell, personal communication). Is this intelligence? Deep Blue beat Kasparov in a clock-limited tournament because, in the permitted time, the computer managed a huge data collection and searched enough layers of possible chess moves to compete with a human expert who was using a quite different approach. It was a combination of raw calculation speed and careful software engineering that gave Deep Blue the edge: whereas Kasparov could consider two or three positions per second, Deep Blue could handle 200 million. In the case of Blue Brain, processors act like neurons and connections between processors act as axons, allowing a fundamentally different form of intelligence to emerge.

The quantum leap

Neurons receive inputs from thousands of other neurons, which are intricately mapped onto different branches of highly complex dendritic trees and require tens of thousands of compartments to accurately represent them. There is therefore a minimal size of a microcircuit and a minimal complexity of a neuron's morphology that can fully sustain a neuron. A massive increase in computational power is required to make this quantum leap — an increase that is provided by IBM's Blue Gene supercomputer[2] (FIG. 1). By exploiting the computing power of Blue Gene, the Blue Brain Project[1] aims to build accurate models of the mammalian brain from first principles.

The first phase of the project is to build a cellular-level (as opposed to a genetic- or molecular-level) model of a 2-week-old rat somatosensory neocortex corresponding to the dimensions of a neocortical column (NCC) as defined by the dendritic arborizations of the layer 5 pyramidal neurons. The quest to understand the detailed microstructure of the NCC started more than 100 years ago with the pioneering work of Santiago Ramón y Cajal (1854–1934). This work, which was continued by a series of prominent anatomists, has provided a wealth of data, but the combination of anatomical and physiological properties of neurons was missing. Alexandra Thomson performed the first paired recordings in the neocortex, allowing simultaneous characterization of the morphology and physiology of individual neurons as well as the synaptic connections between many neurons[33]. The combination of infrared differential interference microscopy in brain slices[34,35] and the use of multi-neuron patch-clamping[36] allowed the systematic quantification of the molecular, morphological and electrical properties of the different neurons and their synaptic pathways in a manner that would allow an accurate reconstruction of the column.

Over the past 10 years, our laboratory has prepared for this reconstruction by developing the multi-neuron patch-clamp approach, recording from thousands of neocortical neurons and their synaptic connections, and developing quantitative approaches to allow a complete numerical breakdown of the elementary building blocks of the NCC (FIG. 2). The recordings have mainly been in the 14–16-day-old rat somatosensory cortex, which is a highly accessible region on which many researchers have converged following a series of pioneering studies driven by Bert Sakmann. Much of the raw data is located in our databases, but a major initiative is underway to make all these data freely available in a publicly accessible database. The so-called 'blue print' of the circuit, although not entirely complete, has reached a sufficient level of refinement to begin the reconstruction at the cellular level.

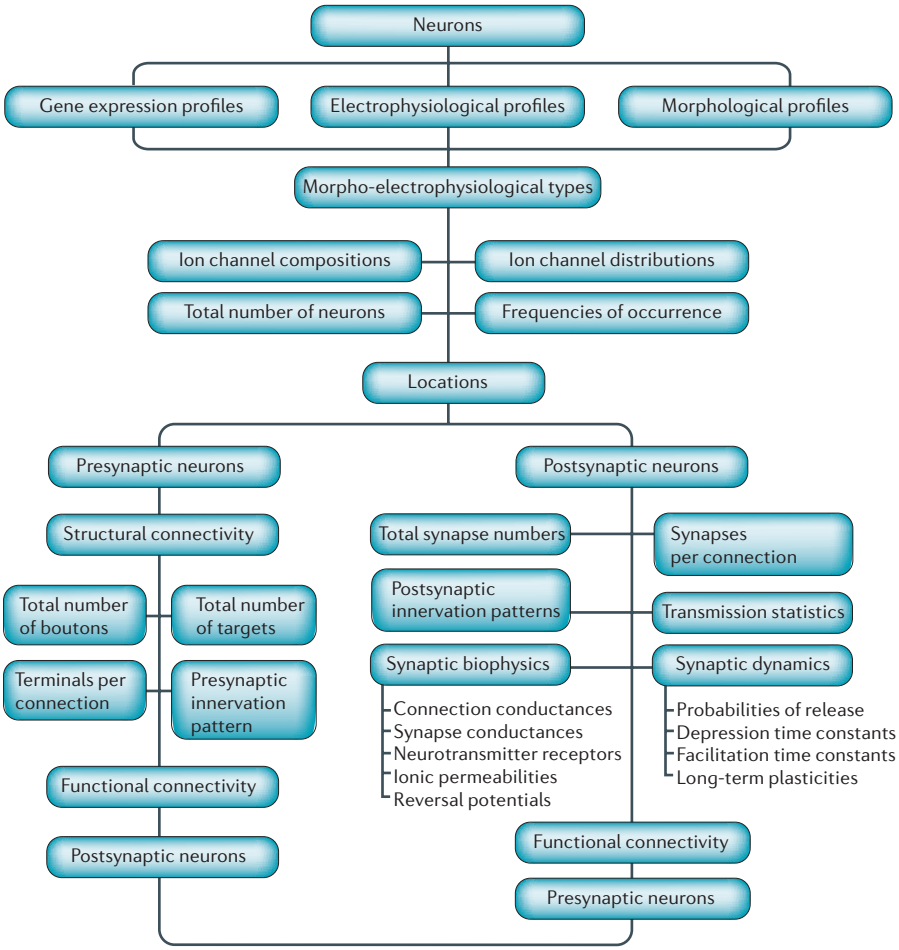

Figure 2 | **Elementary building blocks of neural microcircuits.** The scheme shows the minimal essential building blocks required to reconstruct a neural microcircuit. Microcircuits are composed of neurons and synaptic connections. To model neurons, the three-dimensional morphology, ion channel composition, and distributions and electrical properties of the different types of neuron are required, as well as the total numbers of neurons in the microcircuit and the relative proportions of the different types of neuron. To model synaptic connections, the physiological and pharmacological properties of the different types of synapse that connect any two types of neuron are required, in addition to statistics on which part of the axonal arborization is used (presynaptic innervation pattern) to contact which regions of the target neuron (postsynaptic innervation pattern), how many synapses are involved in forming connections, and the connectivity statistics between any two types of neuron. For a detailed description of some of these building blocks and examples of these for the neocortical microcircuit, see REF. 16.

Highly quantitative data are available for rats of this age, mainly because visualization of the tissue is optimal from a technical point of view. This age also provides an ideal template because it can serve as a starting point from which to study maturation and ageing of the NCC. As NCCs show a high degree of stereotypy, the region from which the template is built is not crucial, but a sensory region is preferred because these areas contain a prominent layer 4 with cells specialized to receive input to the neocortex from the thalamus; this will also be required for later calibration with *in vivo* experiments. The NCC should not be overly specialized, because this could make generalization to other neocortical regions difficult, but areas such as the barrel cortex do offer the advantage of highly controlled *in vivo* data for comparison.

The cat visual cortex is probably functionally and anatomically the most thoroughly characterized brain region. A considerable amount is also known about the microcircuit[37], but the key building blocks

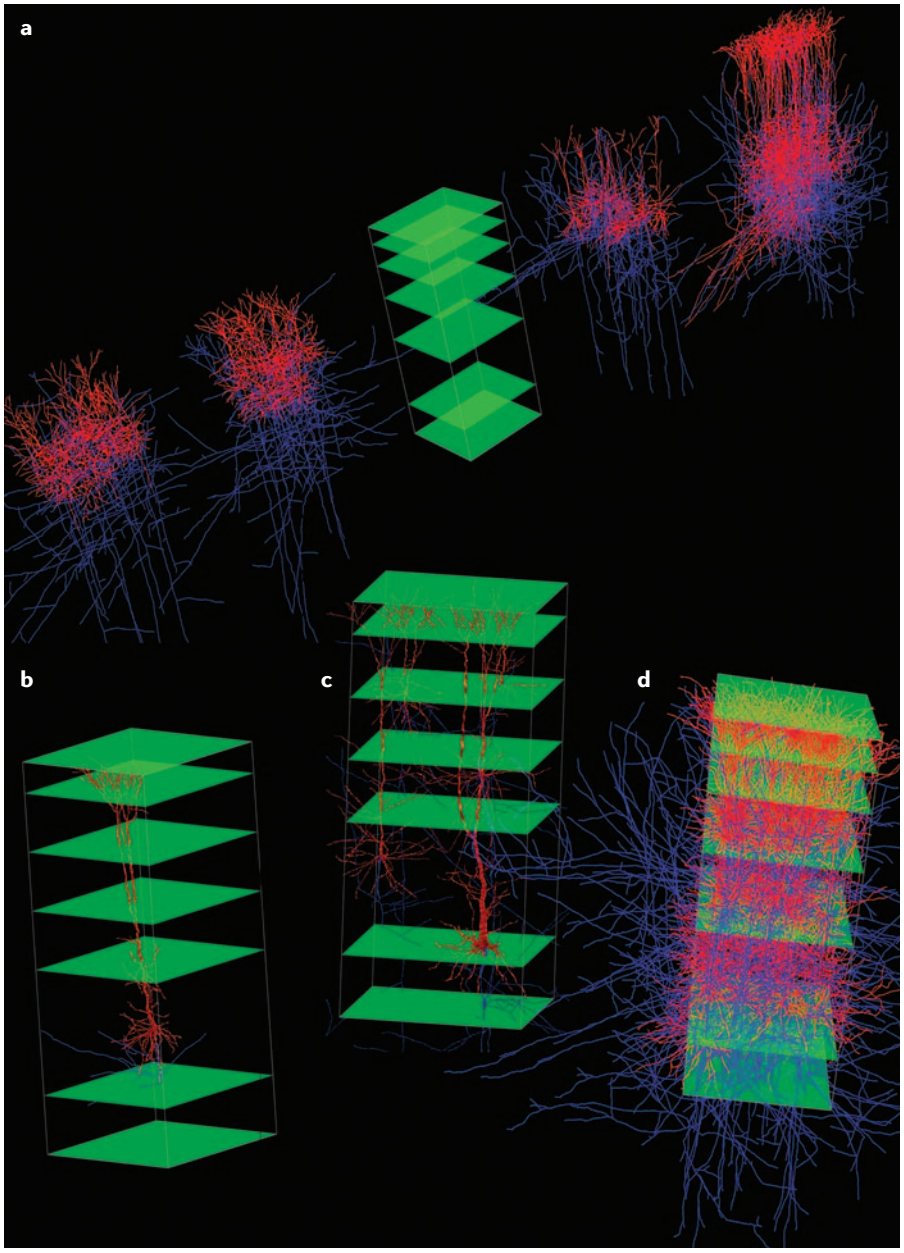

Figure 3 | **Reconstructing the neocortical column.** The images show the neocortical column (NCC) microcircuit in various stages of reconstruction. Only a small fraction of reconstructed, three-dimensional neurons is shown. Red indicates the dendritic and blue the axonal arborizations. The columnar structure (green) illustrates the layer definition of the NCC. **a** | The microcircuits (from left to right) for layers 2, 3, 4 and 5. **b** | A single thick tufted layer 5 pyramidal neuron located within the column. **c** | One pyramidal neuron in layer 2, a small pyramidal neuron in layer 5 and the large thick tufted pyramidal neuron in layer 5. **d** | An image of the NCC, with neurons located in layers 2 to 5.

that are missing are the anatomical and physiological properties of the synaptic connections and the ion channels that support the different types of electrical behaviour. Obtaining such quantitative data requires an immense number of brain-slice experiments, and the cat and primate are therefore not the ideal species for reverse engineering the NCC. The visual cortex is perhaps too poorly developed in the 14-day-old rat, and so the somatosensory or auditory regions are preferred. The mouse might have been the best species to begin with, because it offers a spectrum of molecular approaches with which to explore the circuit, but mouse neurons are small, which prevents the detailed dendritic recordings that are important for modelling the nonlinear properties of the complex dendritic trees of pyramidal cells (75–80% of the neurons).

The Blue Column

So, the young sensory column, which is evolutionarily one of the simplest and is also highly accessible, is an ideal starting point from which the column can be 'matured' to study development, 'transformed' to study regional specialization and 'evolved' to study evolution of the neocortex. These variations are possible because of the considerable degree of stereotypy of these circuits[38]. The template — the Blue Column — will be composed of ~10,000 neocortical neurons within the dimensions of a neocortical column (~0.5 mm in diameter and ~1.5 mm in height) (FIG. 3). The Blue Column will include the different types of neuron in layer 1, multiple subtypes of pyramidal neuron in layers 2–6, spiny stellate neurons in layer 4, and more than 30 anatomical–electrical types of interneuron with variations in each of layers 2–6. In the rat somatosensory cortex, there are ~2,000 neurons in each of layers 2–6 (~1,500 in layer 5), ~25% of which are interneurons, although the proportions of different types of interneuron differ between layers (see REF. 36). The neurons are connected according to the fraction of neurons targeted and precisely mapped together using axonal and dendritic maps derived experimentally (which show the location and distribution of the presynaptic boutons on axons of the presynaptic neuron and synapses on the postsynaptic neuron). Synaptic connections are modelled from the physiological recordings, which provide synaptic biophysics (conductances and kinetics) and dynamics (probability of release, depression and facilitation time constants). Synaptic plasticity rules are implemented locally and globally to allow adaptation of the NCC. These constraints provide the initial conditions for the NCC, and iterations between simulations and experiments are expected to provide further constraints on the model.

Building the Blue Column

Building the Blue Column requires a series of data manipulations (FIG. 4). The first step is to parse each three-dimensional morphology and correct errors due to the *in vitro* preparation and reconstruction. The repaired neurons are placed in a database from which statistics for the different anatomical classes of neurons are obtained. These statistics are used to clone an indefinite number of neurons in each class to capture the full morphological diversity. The next step is to take each neuron and insert ion channel models in order to produce the array of electrical types. The field has

reached a sufficient stage of convergence to generate efforts to classify neurons, such as the Petilla Convention — a conference held in October 2005 on anatomical and electrical types of neocortical interneuron, established by the community.

Single-cell gene expression studies of neocortical interneurons now provide detailed predictions of the specific combinations of >20 ion channel genes that underlie electrical diversity[39]. A database of biologically accurate Hodgkin–Huxley ion channel models is being produced. The simulator NEURON[40] is used with automated fitting algorithms running on Blue Gene to insert ion channels and adjust their parameters to capture the specific electrical properties of the different electrical types found in each anatomical class. The statistical variations within each electrical class are also used to generate subtle variations in discharge behaviour in each neuron. So, each neuron is morphologically and electrically unique. Rather than taking ~10,000 days to fit each neuron's electrical behaviour with a unique profile, density and distribution of ion channels, applications are being prepared to use Blue Gene to carry out such a fit in a day. These functionalized neurons are stored in a database.

The three-dimensional neurons are then imported into BlueBuilder, a circuit builder that loads neurons into their layers according to a 'recipe' of neuron numbers and proportions. A collision detection algorithm is run to determine the structural positioning of all axo-dendritic touches, and neurons are jittered and spun until the structural touches match experimentally derived statistics. The execution of this algorithm is computationally much more intense than the actual simulation of the NCC, and also requires Blue Gene. Probabilities of connectivity between different types of neuron are used to determine which neurons are connected, and all axo-dendritic touches are converted into synaptic connections. The manner in which the axons map onto the dendrites between specific anatomical classes and the distribution of synapses received by a class of neurons are used to verify and fine-tune the biological accuracy of the synaptic mapping between neurons. It is therefore possible to place 10–50 million synapses in accurate three-dimensional space, distributed on the detailed three-dimensional morphology of each neuron.

The synapses are functionalized according to the synaptic parameters for different classes of synaptic connection within statistical variations of each class, dynamic synaptic models are used to simulate transmission[41], and synaptic learning algorithms are introduced to allow plasticity. The distance from the cell body to each synapse is used to compute the axonal delay, and the circuit configuration is exported. The configuration file is read by a NEURON subroutine that calls up each neuron and effectively inserts the location and functional properties of every synapse on the axon, soma and dendrites. One neuron is then mapped onto each processor and the axonal delays are used to manage communication between neurons and processors. Effectively, processors are converted into neurons, and MPI (message-passing interface)-based communication cables are converted into axons interconnecting the neurons — so the entire Blue Gene is essentially converted into a neocortical microcircuit.

We developed two software programs for simulating such large-scale networks with morphologically complex neurons. A new MPI version of NEURON[40] has been adapted by Michael Hines to run on Blue Gene. The second simulator uses the MPI messaging component of the large-scale NeoCortical Simulator (NCS), which was developed by Philip Goodman[42], to manage the communication between NEURON-simulated neurons distributed on different processors. The latter simulator will allow embedding of a detailed NCC model into a simplified large-scale

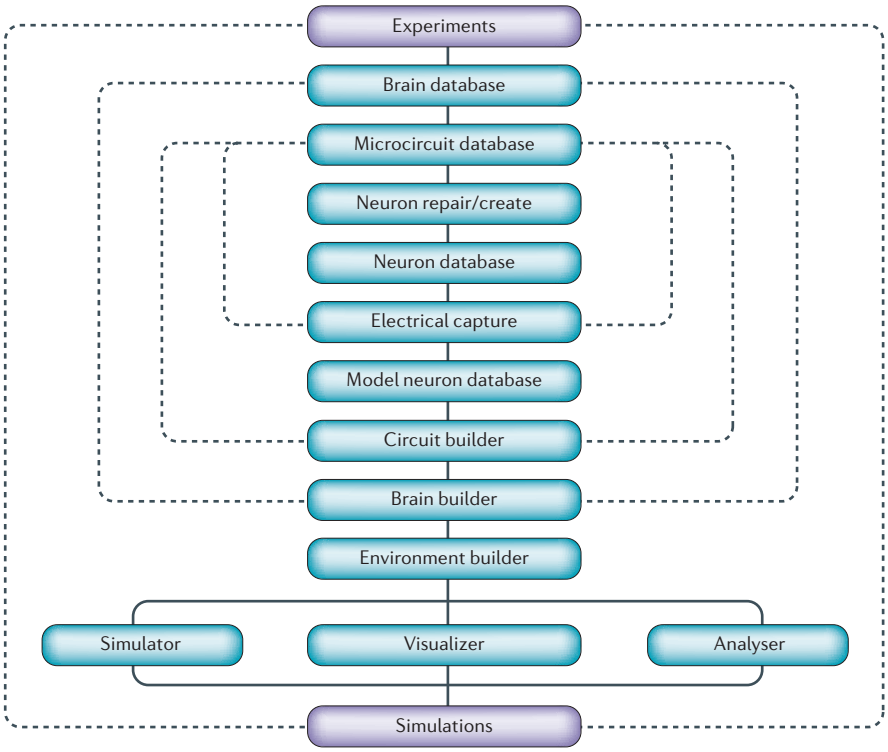

Figure 4 | **The data manipulation cascade.** Software applications and data manipulation required to model the brain with biological accuracy. Experimental results that provide the elementary building blocks of the microcircuit are stored in a database. Before three-dimensional neurons are modelled electrically, the morphology is parsed for errors, and for repair of arborizations damaged during slice preparation. The morphological statistics for a class of neurons are used to clone multiple copies of neurons to generate the full morphological diversity and the thousands of neurons required in the simulation. A spectrum of ion channels is inserted, and conductances and distributions are altered to fit the neuron's electrical properties according to known statistical distributions, to capture the range of electrical classes and the uniqueness of each neuron's behaviour (model fitting/electrical capture). A circuit builder is used to place neurons within a three-dimensional column, to perform axo-dendritic 'collisions' and, using structural and functional statistics of synaptic connectivity, to convert a fraction of axo-dendritic touches into synapses. The circuit configuration is read by NEURON, which calls up each modelled neuron and inserts the several thousand synapses onto appropriate cellular locations. The circuit can be inserted into a brain region using the brain builder. An environment builder is used to set up the stimulus and recording conditions. Neurons are mapped onto processors, with integer numbers of neurons per processor. The output is visualized, analysed and/or fed into real-time algorithms for feedback stimulation.

Box 2 | **What can we learn from Blue Brain?**

Detailed, biologically accurate brain simulations offer the opportunity to answer some fundamental questions about the brain that cannot be addressed with any current experimental or theoretical approaches. These include:

Completing a puzzle. Experiments can obtain and view only small parts of the structure and function of the puzzle at any one time. Assembling the pieces of the neocortical column according to the blue print could reveal the overall picture.

Defining functions of the basic elements. Despite a century of experimental and theoretical research, we are unable to provide a comprehensive definition of the computational function of different ion channels, receptors, neurons or synaptic pathways in the brain. A detailed model will allow fine control of any of these elements and allow a systematic investigation of their contribution to the emergent behaviour.

Understanding complexity. At present, detailed, accurate brain simulations are the only approach that could allow us to explain why the brain needs to use many different ion channels, neurons and synapses, a spectrum of receptors, and complex dendritic and axonal arborizations, rather than the simplified, uniform types found in many models.

Exploring the role of dendrites. This is the only current approach to explore the dendritic object theory, which proposes that three-dimensional voltage objects are generated continuously across dendritic segments regardless of the origin of the neurons, and that spikes are used to maintain such dendritic objects[45].

Revealing functional diversity. Most models engineer a specific function, whereas a spectrum of functions might be possible with a biologically based design.

Understanding memory storage and retrieval. This approach offers the possibility of determining the manner in which representations of information are imprinted in the circuit for storage and retrieval, and could reveal the part that different types of neuron play in these crucial functions.

Tracking the emergence of intelligence. This approach offers the possibility to re-trace the steps taken by a network of neurons in the emergence of electrical states used to embody representations of the organism and its world.

Identifying points of vulnerability. Although the neocortex confers immense computational power to mammals, defects are common, with catastrophic cognitive effects. At present, a detailed model is the only approach that could produce a list of the most vulnerable circuit parameters, revealing likely candidates for dysfunction and targets for treatment.

Simulating disease and developing treatments. Such simulations could be used to test hypotheses for the pathogenesis of neurological and psychiatric diseases, and to develop and test new treatment strategies.

Providing a circuit design platform. Detailed models could reveal powerful circuit designs that could be implemented into silicone chips for use as intelligence devices in industry.

model of the whole brain. Both of these softwares have already been tested, produce identical results and can simulate tens of thousands of morphologically and electrically complex neurons (as many as 10,000 compartments per neuron with more than a dozen Hodgkin–Huxley ion channels per compartment). Up to 10 neurons can be mapped onto each processor to allow simulations of the NCC with as many as 100,000 neurons. Optimization of these algorithms could allow simulations to run at close to real time.

The circuit configuration is also read by a graphic application, which renders the entire circuit in various levels of textured graphic formats. Real-time stereo visualization applications are programmed to run on the terabyte SMP (shared memory processor) Extreme series from SGI (Silicon Graphics, Inc.)[43]. The output from Blue Gene (any parameter of the model) can be fed directly into the SGI system to perform in silico imaging of the activity of the inner workings of the NCC. Eventually, the simulation of the NCC will also include the vasculature, as well as the glial network, to allow capture of neuron–glia interactions. Simulations of extracellular currents and field potentials, and the emergent electroencephalogram (EEG) activity will also be modelled.

Whole-brain simulations

The main limitations for digital computers in the simulation of biological processes are the extreme temporal and spatial resolution demanded by some biological processes, and the limitations of the algorithms that are used to model biological processes. If each atomic collision is simulated, the most powerful supercomputers still take days to simulate a microsecond of protein folding, so it is, of course, not possible to simulate complex biological systems at the atomic scale. However, models at higher levels, such as the molecular or cellular levels, can capture lower-level processes and allow complex large-scale simulations of biological processes.

The Blue Brain Project's Blue Gene can simulate a NCC of up to 100,000 highly complex neurons at the cellular level (about five times the number of neurons in *Aplysia californica*), or as many as 100 million simple neurons (about the same number of neurons found in a mouse brain). However, simulating neurons embedded in microcircuits, microcircuits embedded in brain regions, and brain regions embedded in the whole brain as part of the process of understanding the emergence of complex behaviours of animals is an inevitable progression in understanding brain function and dysfunction, and the question is whether whole-brain simulations are at all possible.

Computational power needs to increase about 1-million-fold before we will be able to simulate the human brain, with 100 billion neurons, at the same level of detail as the Blue Column. Algorithmic and simulation efficiency (which ensure that all possible FLOPS are exploited) could reduce this requirement by two to three orders of magnitude. Simulating the NCC could also act as a test-bed to refine algorithms required to simulate brain function, which can be used to produce field programmable gate array (FPGA)-based chips. FPGAs could increase computational speeds by as much as two orders of magnitude. The FPGAs could, in turn, provide the testing ground for the production of specialized NEURON solver application-specific integrated circuits (ASICs) that could further increase computational speed by another one to two orders of magnitude. It could therefore be possible, in principle, to simulate the human brain even with current technology.

The computer industry is facing what is known as a discontinuity, with increasing processor speed leading to unacceptably high power consumption and heat production. This is pushing a qualitatively new transition in the types of processor to be used in future computers. These advances in computing should begin to make genetic- and molecular-level simulations possible.

A global initiative

The production of the template NCC will provide the framework as well as the applications for researchers to build detailed circuits of different regions of the brain. The second phase of the Blue Brain Project will open up these applications to the community to allow a global and spontaneous effort to build software models of the brain. To facilitate this process, the Blue Brain Project is preparing a brain-like framework from three-dimensional atlases with 'slots' for the different microcircuits. Researchers worldwide will be able to build and simulate different microcircuits and regions, as well as insert and connect these microcircuits into a Blue Brain. It will also be possible to insert these models at various levels of detail — from point neuron level to molecular-level models, depending on the degree of knowledge available for a microcircuit. As computing power increases, it will become possible to run and view simulations of the brain or of parts of the brain on Blue Gene via media streaming-enabled web interfaces. Model frameworks for different mammalian species and at different stages of development will also be established to facilitate the global reconstruction effort. Models will be linked with the rapidly growing databases initiated by the Human Brain Project to allow a novel access point, a gateway and a dynamic virtual brain library — one that can also execute and view simulations at different levels.

Future perspectives

Molecules cannot be understood by studying atoms alone, cells cannot be understood by studying proteins alone and, similarly, understanding the emergent properties of the brain requires the assembly of its components. The synthesis era in neuroscience started with the launch of the Human Brain Project[44] and is an inevitable phase triggered by a critical amount of fundamental data. The data set does not need to be complete before such a phase can begin. Indeed, it is essential to guide reductionist research into the deeper facets of brain structure and function. As a complement to experimental research, it offers rapid assessment of the probable effect of a new finding on pre-existing knowledge, which can no longer be managed completely by any one researcher. Detailed models will probably become the final form of databases that are used to organize all knowledge of the brain and allow hypothesis testing, rapid diagnoses of brain malfunction, as well as development of treatments for neurological disorders. In short, we can hope to learn a great deal about brain function and dysfunction from accurate models of the brain (BOX 2).

The time taken to build detailed models of the brain depends on the level of detail that is captured. With current data and technology, a highly accurate Blue Column is possible within the next 2 years. Indeed, the first version of the Blue Column, which has 10,000 neurons, has already been built and simulated; it is the refinement of the detailed properties and calibration of the circuit that takes time. A point neuron model of the neocortex is already feasible, and a detailed cellular-level model is feasible within 5 years. A model of the entire brain at the cellular level will probably take the next decade. A molecular-level model of a NCC is probably feasible within 5 years, and linking biochemical pathways to models of the genome will probably have been achieved within 10 years.

There is no fundamental obstacle to modelling the brain and it is therefore likely that we will have detailed models of mammalian brains, including that of man, in the near future. Even if overestimated by a decade or two, this is still just a 'blink of an eye' in relation to the evolution of human civilization.

As with Deep Blue, Blue Brain will allow us to challenge the foundations of our understanding of intelligence and generate new theories of consciousness.

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FURTHER INFORMATION
Blue Gene: http://www.research.ibm.com/bluegene
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