International Journal of Pharmaceutical Science and Research
ISSN: 2455-4685, Impact Factor: RJIF 5.28
www.pharmacyresearchjournal.com
Volume 1; Issue 4; May 2016; Page No. 09-14

Blue brain: Novel tool of drug discovery for brain disorders

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Abstract
Blue brain is the name of the world's first virtual brain. That means a machine can function as human brain. Today scientists are in research to create an artificial brain that can think, response, take decision, and keep anything in memory. Today, there are only very few brain disorders whose causes are fully understood and very few drugs whose mechanism of action is known or that offer more than symptomatic relief. The Blue brain project will offer new opportunities for clinicians and for researchers. Groups working in the project have already collected and analyzed very large volumes of imaging data from hospitals, and have used informatics based analysis to achieve highly effective early diagnosis of brain disease. The Blue brain project will develop this work, which we expect to yield clinically useful results in the relatively short term. In a medium-term perspective, the Blue brain project simulation platform will make it possible to explore hypotheses of causation for brain diseases, and begin simulating the effects of drug candidates. Simulation-based prototypes will enormously facilitate the development of neuroprosthetic devices. These new possibilities will shorten design cycles, lower costs and improve prospects for the development of effective treatments. To allow effective drug simulation, the project will make an important effort to explore and simulate molecular level mechanisms.

Keywords: Blue brain project, Simulation, Brain diseases, Drug Discovery etc

Introduction

The human brain is a massively complex information processing system with a hierarchy of different yet tightly integrated levels of organization: from genes, proteins, synapses and cells to microcircuits, brain regions, and the whole brain. Today, we know a lot about the individual levels. What we do not have is a causal understanding of the way events at the lowest level in the hierarchy cascade through the different levels to produce human cognition and behavior. If we could understand the brain we could prevent or cure brain diseases such as autism, depression and Alzheimer's; we could also produce new computing technologies that share the brain's ability to operate reliably on very little power, and its ability to learn. Medical research has identified over five hundred brain diseases, ranging from migraine and addiction to depression and Alzheimer's.

Today, these diseases are usually diagnosed in terms of symptoms and syndromes, an approach that makes it very difficult to produce correct diagnoses, or even to select patients for clinical trials. To prevent and cure brain disease [1-5].

The man is called intelligent because of the brain. But we loss the knowledge of a brain when the body is destroyed after the death. "BLUE BRAIN"-The name of the world's first virtual brain. That means a machine that can function as human brain. Within 30 years, we will be able to scan ourselves into the computers. So, even after the death of a person we will not lose the knowledge, intelligence, personalities, feelings and memories of that man that can be used for the development of the human society. Scientists think that blue brain could also help to cure the Parkinson's disease [6-8]. The brain circuitry is in a complex state of flux, the brain rewiring itself every moment of its existence. If the scientists can crack open the secret of how and why the brain does it, the knowledge could lead to new breed of brain does it, the supercomputers.

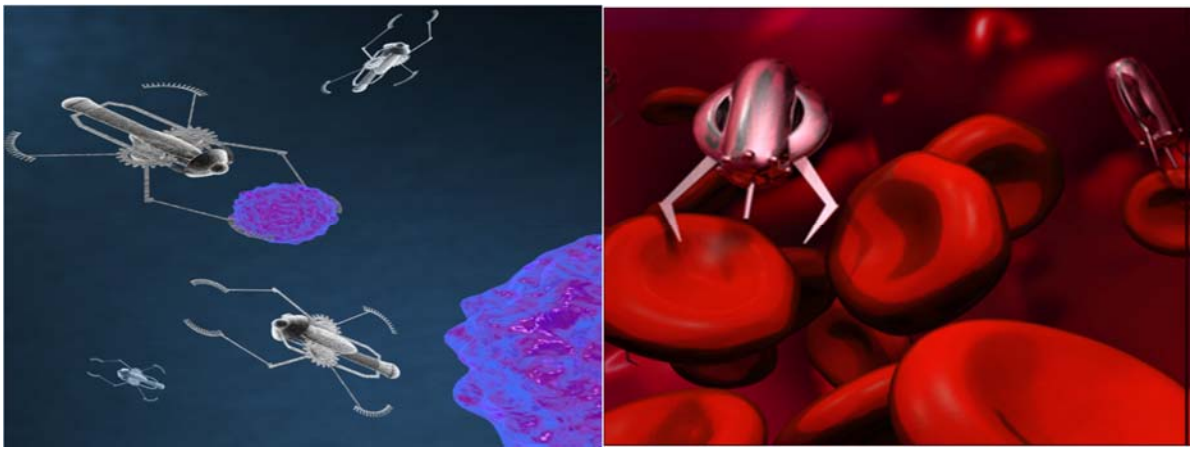
The Brain

The brain is populated with billions of *neurons*, each connected to thousands of its neighbors by dendrites and axons, a kind of biological "wiring". The brain processes information by sending electrical signals from neuron to neuron along these wires. In the cortex, neurons are organized into basic functional units, cylindrical volumes 0.5 mm wide by 2 mm high, each containing about 10,000 neurons that are connected in an intricate but consistent way. These units operate much like microcircuits in a computer [9-10]. The *cerebral cortex*, the convoluted "grey matter" that makes up 80% of the human brain, is responsible for our ability to remember, think, reflect, empathize, communicate, adapt to new situations and plan for the future.

Virtual brain

Virtual brain is an artificial brain, which does not actually the natural brain, but can act as the brain. It can think like brain, take decisions based on the past experience, and response as the natural brain can. It is possible by using a super computer, with a huge amount of storage capacity, processing power and an interface between the human brain and this artificial one. Through this interface the data stored in the natural brain can be uploaded into the computer.

The uploading is possible by the use of small robots known as the nanobots. These robots are small enough to travel throughout our circulatory system Traveling into the spine and brain, they will be able to monitor the activity and structure of our central nervous system They will be able to provide an interface with computer while we still reside in our biological form [11-14].



Nanobots Traveling into Human System

Blue Brain

The IBM is now developing a virtual brain known as the BLUE BRAIN. It would be the world's first virtual brain. The designers say that "Blue Brain" was willful and unpredictable from day one. When it was first fed electrical impulses, strange patterns began to appear with lightning-like flashes produced by 'cells' that the scientists recognized from living human and animal processes. Neurons started interacting with one another until they were firing in rhythm. At the end of 2006, the Blue Brain project had created a model of the basic functional unit of the brain, the neocortical column. At the push of a button, the model could reconstruct biologically accurate neurons based on detailed experimental data, and automatically connect them in a biological manner, a task that involves positioning around 30 million synapses in precise 3D locations [15-17].

A very good example of utilization of blue brain is the case "short term memory". Another situation is that when a person gets older, then he starts forgetting or takes a bit more time to recognize to a person. For the above reason we need a blue brain. It is simple chip that can be installed into the human brain for which the short term memory and volatile memory at the old age can be avoided. There are some advantage and limitation of blue brain which are given below-

Advantages	Limitations
• We can remember things without any effort. • Decision can be made without the presence of a person. • Even after the death of a man his intelligence can be used. • The activity of different animals can be understood. • It would allow the deaf to hear via direct nerve stimulation, and also be helpful for curing many psychological diseases.	• We become dependent upon the computer systems. • Others may use technical knowledge against us. • Computer viruses will pose an increasingly critical threat. • The real threat, however, is the fear that people will have of new technologies. That fear may culminate in a large resistance.

Ural Brain Vs Simulated Brain

Simulated Brain

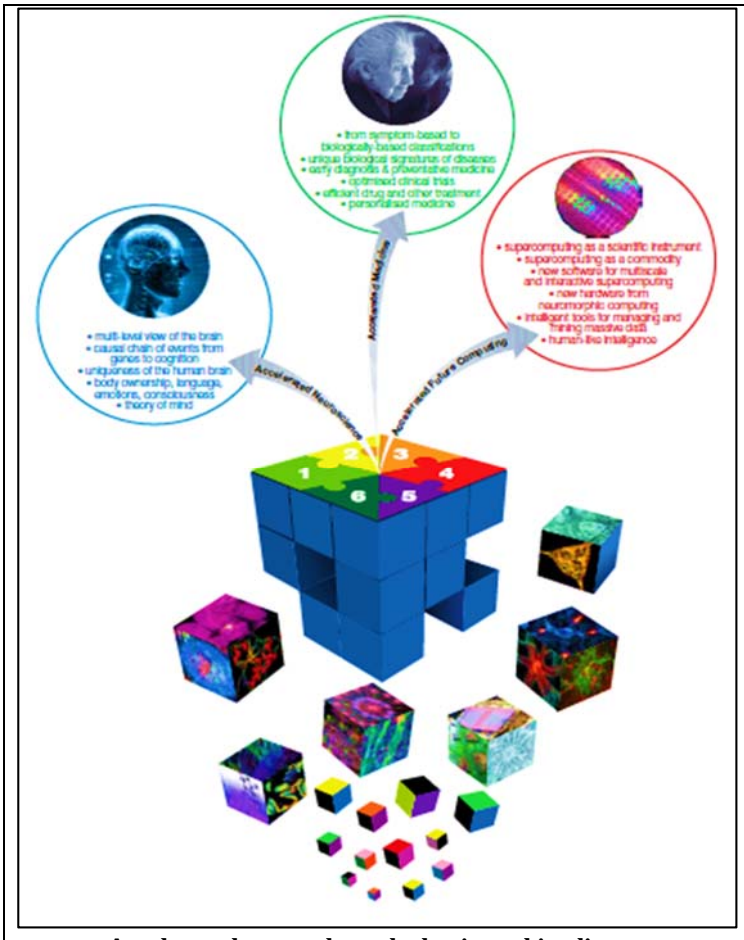
Currently, the time required to simulate the circuit is about two orders of magnitude larger than the actual biological time simulated. The Blue Brain team is working to streamline the computation so that the circuit can function in real time - meaning that 1 second of activity can be modeled in one second.

Artificial Consciousness

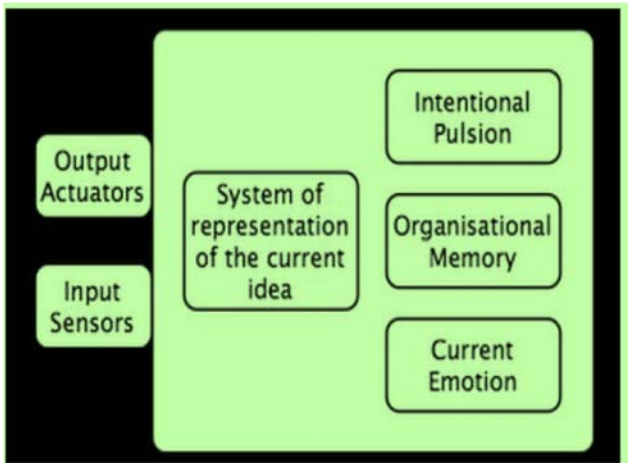
Subsystem building in a strictly constructivist way the current artificial idea here and now: that is the construction of the Current idea like the well-controlled activity of some large agent organization. A subsystem generating emotions as the alteration of the activity of the subsystem expressing the current idea, that is some specific field altering the focus of this generation, according to the specificity of the emotion. An input–output subsystem linking the system producing artificial consciousness facts with the body of a robot or any software data flow [17-18].

Natural Brain	Simulated Brain
INPUT - sensory cells & neurons	INPUT - artificial neurons & sensory cells
INTERPRETATION - accomplished by the means of certain states of many neurons	INTERPRETATION - by means of a set of register
OUTPUT - sensory cells & neurons	OUTPUT - artificial neurons & sensory cell
MEMORY - permanent state neuron	MEMORY - registers can be stored permanently
PROCESSING - past experience stored and the current input	PROCESSING - stored states and the received input & by performing some arithmetic and logical calculations.

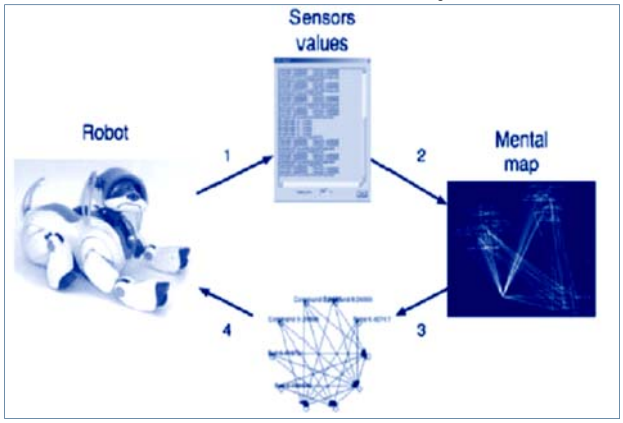
Natural Brain Vs Simulated Brain



Accelerated research on the brain and its disease



General architecture of the system



Pathway of Data Transfer and monitoring

Artificial Emotions

The principle of generation of an emotion is therefore the next One. The input sensors, via agents of interface, make to speed up structuring agents that make speed up the corresponding morphology agents. The incentive organization generates a specific form in the morphology that is to reach: the incentive morphology. The current morphology describing the aspectual activity has to transform itself into the incentive morphology. For that, the aspectual agents have to make some specific activity. The analysis agents control them in that way. The

characters of the incentive and of the current morphologies are the determinants for the emotion. If the current morphology has a complicated shape, far away from the incentive morphology, the system expresses a state of tension that it is going to try to systematically reduce [19-21].

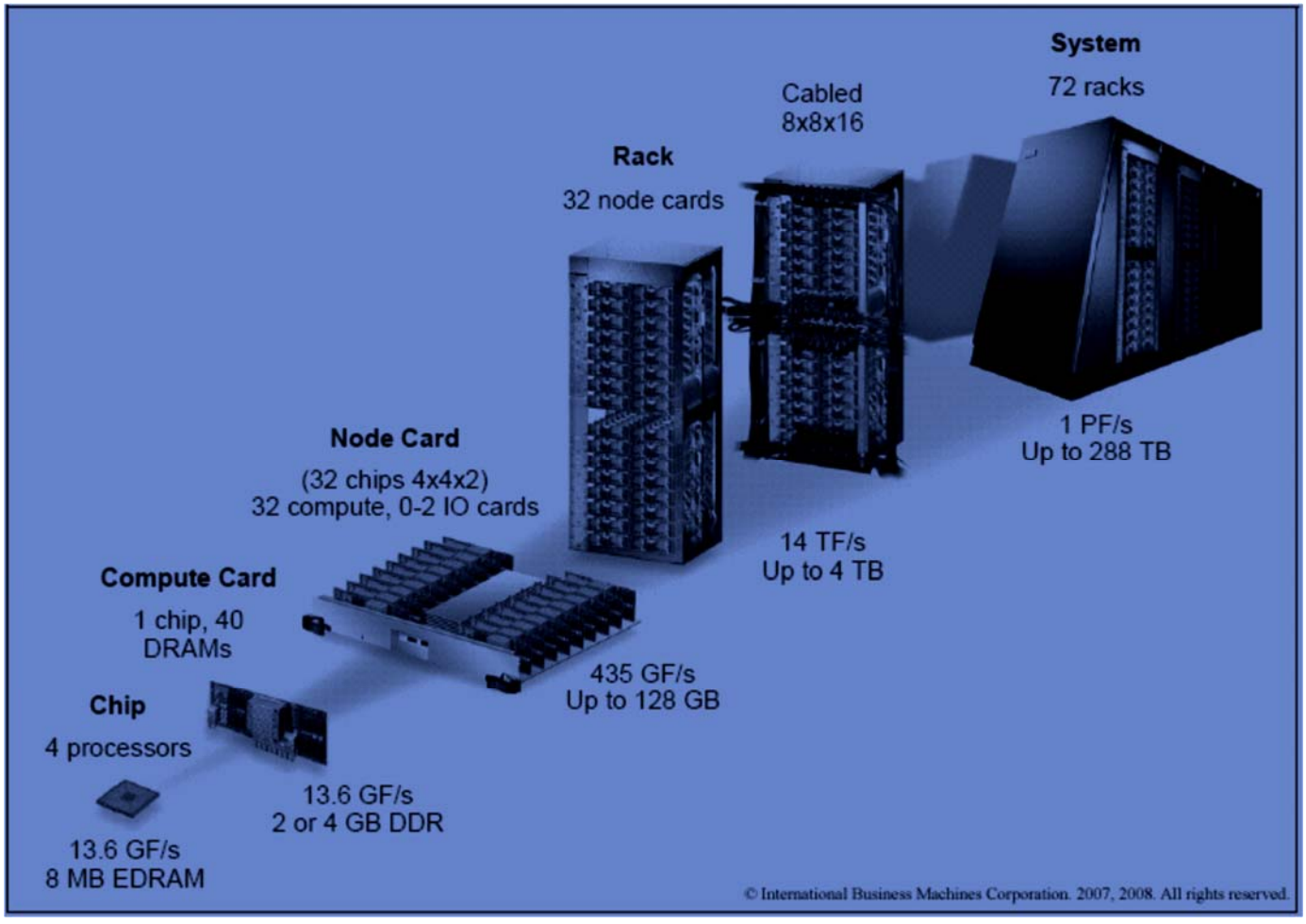
Modeling Neurons

A neuron's electrical properties are determined to a large extent by a variety of ion channels distributed in varying densities throughout the cell's membrane. To model the neocortical column, it is essential to understand the composition, density and distribution of the numerous cortical cell types. Each class of cells is present in specific layers of the column. Each neuron is connected to thousands of it sneighbors at points where their dendrites or axons touch, known as synapses [22].

Blue Brain Project

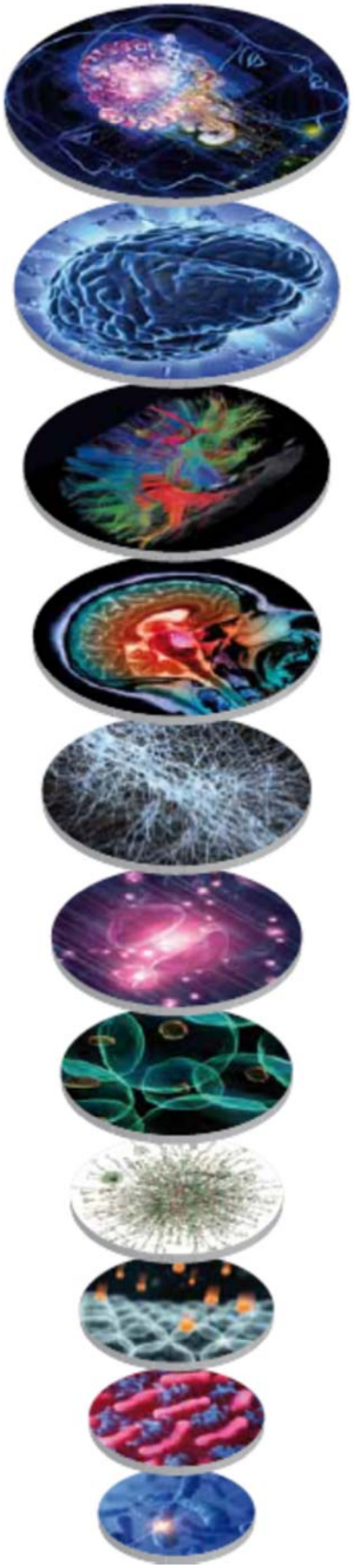
Information from the molecular and genetic level will be added to the algorithms that generate the individual neurons and their connections, and thus this level of detail will be reflected in the circuit's construction. The simulations can be used to explore what happens when this molecular or genetic information is altered situations such as a genetic variation in particular neurotransmitters, or what happens when the molecular environment is altered via drugs. The Blue brain project will therefore also produce a virtual library to explore in 3D the micro architecture of the neocortex and access all key research relating to its structure and function.

Understanding the functions of different elements and pathways of the NCC will provide a concrete foundation to explore the cellular and synaptic bases of a wide spectrum of neurological and psychiatric diseases. The impact of receptor, ion channel, cellular and synaptic deficits could be tested in simulations and the optimal experimental tests can be determined. A molecular level model of the NCC will provide the substrate for interfacing gene expression with the network structure and function. The NCC lies at the interface between the genes and complex cognitive functions. Establishing this link will allow predictions of the cognitive consequences of genetic disorders and allow reverse engineering of cognitive deficits to determine the genetic and molecular causes. This level of simulation will become a reality with the most advanced phase of Blue Gene development [23-26].



The blue Gene/Super computer architecture

Skeleton of multi-level data as a catalyst for future community research



Multi-level data required for multiscale brain models

Cognition. Structured cognitive tests, combined with fMRI and MEG, constrain brain circuit models for visual perception-action, decision and reward, memory encoding and retrieval, space, time, number and language. Changes in circuits during development and aging and differences between adults constrain network models of cognition at different ages and provide benchmark data to validate detailed cellular brain models.

Whole brain. Multi-modal sensory physiology and anatomy map how different brain regions come together to shape perception-action and our sense of body ownership, awareness and consciousness, and can help validate human brain models. Whole brain synchrotron scans reveal the vasculature supporting cognition, and provide constraints for models of blood flow and brain metabolism.

Connectivity. Whole brain fibre tract tracing and DTI yield paths and fibre densities for connectivity within and between brain regions and provide global fibre projection parameters constraining connectivity in brain models. Whole brain ultramicroscopy yields constraints for single neuron projections and provides high-resolution validation of DTI tracts. EM provides high-resolution images of the synapses formed on individual neurons, principles of fibre selection, and structural features of synapses.

Brain regions. Structural and functional MRI yield dimensions of brain regions which can be used to build models. Region-specific cellular architecture and densities constrain the cellular composition of model regions. Receptor, ion channel, signalling and other protein distributions further constrain neurochemical organisation within and across brain regions. Correlations between protein distributions, cognitive circuits and genomic variability point to neural mechanisms of cognition, provide global constraints for detailed brain models and generate data for model validation.

Microcircuits. The cellular and molecular composition of microcircuits supports their role in cognition. Single-cell gene expression yields sets of genes that form different types of neurons and glia and determine their morphological and electrical properties. Global brain maps of gene and protein distributions constrain the cellular composition of microcircuit models. Cell geometry and synaptic selection rules constrain local synaptic connectivity in microcircuit models. Electrophysiology, multi-electrode recordings, voltage sensitive dye mapping and optogenetic studies provide data to validate microcircuit models.

Cells. 3D reconstruction of the anatomy of single cells yields the structural geometry needed to establish the morphological properties of different cell types. Correlations between gene expression and the geometric properties of cells constrain the artificial synthesis of cellular morphologies from gene expression patterns, as well as models of morphological plasticity. Single-cell gene expression, combined with general rules for the production and distribution of proteins and for protein interactions, constrain molecularly detailed models of neurons and glia.

Synapses. Physiological, biophysical and imaging studies of synaptic transmission, plasticity and neuromodulation constrain synaptic models. Pair-wise single cell gene expression constrains the repertoire of synaptic proteins at the synapses between pairs of neurons of known type, making it possible to model synapse diversity. The dynamics of single cell gene expression constrain long-term molecular changes in synapses in response to environmental stimuli. Comparing synaptic proteins across species constrains species-specific synaptic models.

Metabolome. The intricate biochemical network linking neurons, synapses and glia constrains molecular brain models, in which activity, plasticity, neuromodulation, homeostasis and nutrition depend on metabolic processes. Coupling neurotransmitter receptors and their signalling pathways to the biochemical pathways that supply energy to cells and synapses, constrains activity-driven changes in blood flow, and the resulting fMRI signals.

Proteome. The number and different types of proteins cells produce, the different parts of the cell where they are located, and their respective life cycles all constrain how many and which proteins can come together in a single cell. The set of proteins, other biochemicals, and ions that each protein binds to and reacts with forms the protein's interactome. Results on protein-protein interactions from biochemical studies, molecular dynamic simulations, and predictive informatics constrain reaction-diffusion models of cells.

Transcriptome. Combined with data on the genes expressed in single cells, 3D maps of gene expression constrain the total number of neurons in the brain and the types of genetically identifiable cells the brain can produce. Single cell gene expression changes in response to stimulation, determining how cells can change with experience. Single cell gene expression, combined with predictions of which proteins the cell can produce and basic principles of proteomics, constrains detailed molecular-level cell models.

Genome. The state of the chromosome reflects when genes are active or inactive and constrains gene network models. It is likely that the genome constrains the number of genetic cell types in the brain, the size of brain regions, connectivity between brain regions, and total brain size. It may also predict cognitive functions, behavioural traits, epigenetic vulnerability, and brain disorders.

Applications of Blue Brain

Cracking the Neural Code, to develop a new breed of supercomputer, Understanding Neocortical Information Processing, A Novel Tool for Drug Discovery for Brain Disorders, A Global Facility, A Foundation for Whole Brain Simulations, A Foundation for Molecular Modelling of Brain Function. We will be able to transfer ourselves into computers at some point. It will bring both benefits and harm to human society. Eventually aim of applying terrific computer power to the simulation of an entire brain.

Conclusions

These technologies can enormously accelerate brain research. They can also open the road to treatments that prevent and cure brain disease and to new computing technologies with the potential to revolutionize industry, the economy and society. Medical informatics can mine enormous volumes of clinical data allowing us to understand the basic causes of brain diseases, a pre-condition for early diagnosis, prevention and cure. Very soon this technology will be highly accepted whole over the world.

References

1. The Brain Scales Project. Brain Scales- Brain-inspired multi-scale computation in neuromorphic hybrid systems. 2011, Available from: http://brainscales.kip.uni-heidelberg. de/.
2. The ECHORD Project. ECHORD – European Clearing House for Open Robotics Development. 2011, Available from: http://www. echord.info/wikis/website/home.
3. The Spinnaker Project. Spinnaker -A Universal Spiking Neural Network Architecture. 2011, Available from: http://apt.cs.man. ac.uk/projects/Spinnaker/.
4. Marques AC, Ponting CP. Catalogues of mammalian long noncoding RNAs: modest conservation and incompleteness. Genome Biol, 2009; 10(11):R124.
5. Lein ES. Genome-wide atlas of gene expression in the adult mouse brain. Nature, 2007; 445(7124):168-76.
6. Bayes A. Characterization of the proteome, diseases and evolution of the human postsynaptic density. Nature Neuroscience, 2011; 14(1):19-21.
7. Belgard TG. A transcriptomic atlas of mouse neocortical layers. Neuron, 2011; 71(4): 605-16.
8. Boyden ES. A history of optogenetics: the development of tools for controlling brain circuits with light. F1000 Biol Rep, 2011; 3:11.
9. Bussey TJ. New translational assays for preclinical modelling of cognition in schizophrenia: the touchscreen testing method for mice and rats. Neuropharmacology, 2012; 62(3):1191-203.
10. Legenstein RD, Pecevski, Maass W. A learning theory for rewardmodulated spike-timing-dependent plasticity with application to biofeedback. PLoS computational biology, 2008; 4(10):e1000180.
11. Maass W, Natschläger T, Markam H. Real-time computing without stable states: A new framework for neural computation based on perturbations. Neural Computation 2002; 14(11):2531-2560.
12. Fremaux N, Sprekeler H, Gerstner W. Functional requirements for reward-modulated spike-timing dependent plasticity. J Neurosci. 2010; 30(40):13326-37.
13. Wierstra D. Recurrent policy gradients. Logic Journal of the Igpl, 2010; 18(5):620-634.
14. Buesing L. Neural dynamics as sampling: a model for stochastic computation in recurrent networks of spiking neurons. PLoS Comput Biol, 2011; 7(11):e1002211.
15. Pechura CM, JB. Martin, Mapping the brain and its functions. Integrating enabling technologies into neuroscience research Washington D.C.: National Academiy Press, 1991.
16. Amari S. Neuroinformatics: the integration of shared databases and tools towards integrative neuroscience. J Integr Neurosci. 2002; 1(2):117-28.
17. Gupta A. Federated access to heterogeneous information resources in the Neuroscience Information Framework (NIF). Neuroinformatics, 2008; 6(3):205-17.
18. Bechara HD, Damasio A. Emotion, decision making and the orbito frontal cortex. Cerebral Crotex, 2000, 10.
19. Brooks Brooks R. Intelligence without reason, in Proc. of the 1991 International Joint Conference on Artificial Intelligence, 1991, 569-591,
20. Campagne Campagne JC, Cardon A. Using Morphology to Analyse and Steer Large Multi-Agents Systems at Runtime, Selmas'04 IEEE, Edinburg, Scotland, 2004; 04:24-25.
21. Campagne JC, Cardon A, Collomb E, Nishida T. Massive Multi-Agent System Control, FAABS III 2004, IEEE Workshop on Formal Approaches on Agents-based Systems, NASA Goddard Space Center, Greenbelt MA, USA, 2004,
22. Cardon-Lesage Cardon A, Lesage F. toward Adaptive Information Systems: considering concern and intentionality, KAW'98, Banff, Canada, 1998, 17-23.
23. Dautenhahn Dautenhahn K. Biologically inspired robotic experiments on interaction and dynamic agent-environment coupling, in Proc. Workshop SOAVE'97, Ilmenau, 1997, 14-24.
24. Dretske F. Explaining Behavior, MIT Press, 1988.
25. Freud Freud S. The Complete Psychological Works of S. Freud, J Strachey, he Hogarth Press, London, 1966.
26. Lesage Lesage F, Cardon A, Tranouez P. A multiagent based prediction of the evolution of knowledge with multiple points of view, KAW' 1999, 99.