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NeuCube: A spiking neural network architecture for mapping, learning and understanding of spatio-temporal brain data

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ABSTRACT

The brain functions as a spatio-temporal information processing machine. Spatio- and spectro-temporal brain data (STBD) are the most commonly collected data for measuring brain response to external stimuli. An enormous amount of such data has been already collected, including brain structural and functional data under different conditions, molecular and genetic data, in an attempt to make a progress in medicine, health, cognitive science, engineering, education, neuro-economics, Brain–Computer Interfaces (BCI), and games. Yet, there is no *unifying computational framework* to deal with all these types of data in order to better understand this data and the processes that generated it. Standard machine learning techniques only partially succeeded and they were not designed in the first instance to deal with such complex data. Therefore, there is a need for a new paradigm to deal with STBD. This paper reviews some methods of spiking neural networks (SNN) and argues that SNN are suitable for the creation of a unifying computational framework for learning and understanding of various STBD, such as EEG, fMRI, genetic, DTI, MEG, and NIRS, in their integration and interaction. One of the reasons is that SNN use the *same computational principle* that generates STBD, namely spiking information processing. This paper introduces a new SNN architecture, called NeuCube, for the creation of concrete models to map, learn and understand STBD. A NeuCube model is based on a 3D evolving SNN that is an approximate map of structural and functional areas of interest of the brain related to the modeling STBD. Gene information is included optionally in the form of gene regulatory networks (GRN) if this is relevant to the problem and the data. A NeuCube model learns from STBD and creates connections between clusters of neurons that manifest chains (trajectories) of neuronal activity. Once learning is applied, a NeuCube model can reproduce these trajectories, even if only part of the input STBD or the stimuli data is presented, thus acting as an associative memory. The NeuCube framework can be used not only to discover functional pathways from data, but also as a predictive system of brain activities, to predict and possibly, prevent certain events. Analysis of the internal structure of a model after training can reveal important spatio-temporal relationships 'hidden' in the data. NeuCube will allow the integration in one model of various brain data, information and knowledge, related to a single subject (personalized modeling) or to a population of subjects. The use of NeuCube for classification of STBD is illustrated in a case study problem of EEG data. NeuCube models result in a better accuracy of STBD classification than standard machine learning techniques. They are robust to noise (so typical in brain data) and facilitate a better interpretation of the results and understanding of the STBD and the brain conditions under which data was collected. Future directions for the use of SNN for STBD are discussed.

1. Spatio/spectro-temporal information processes in the brain

1.1. Spatio-temporal information processes in the brain

The brain is a complex integrated spatio-temporal information processing machine. An animal or a human brain has a range of structural and functional areas that are spatially distributed in a constrained 3D space. When the brain processes information, either triggered by external stimuli, or by inner processes, such as visual, auditory, somatosensory, olfactory, control, emotional, environmental, social, or all of these stimuli together, complex spatio-temporal pathways are activated and patterns are formed across the whole brain. For example, '…the language task involves transfer of stimulus information from the inner ear through the auditory nucleus in the thalamus to the primary auditory cortex (Brodmann's area 41), then to the higher-order auditory cortex (area 42), before it is relayed to the angular gyrus (area 39)…' (Benuskova & Kasabov, 2007). Many other studies of spatio-temporal pathways in the brain have been conducted, e.g. birdsong learning (Hahnloser, Wang, Nager, & Naie, 2008).

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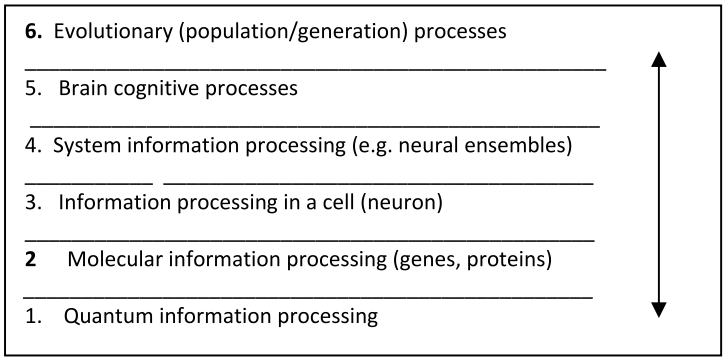


Fig. 1. Different 'levels' of information processing in the brain.
Source: From Kasabov (2007).

In principle, different 'levels' of spatio-temporal information processing can be observed in the brain, e.g. Fig. 1 (Kasabov, 2007), all 'levels' acting in a concert. STBD related to each of these 'levels' can be collected, but how do we integrate this information in a machine learning model?

1.2. Spatio-temporal brain data and brain atlases

Different types of STBD have been collected at the different 'levels' from Fig. 1. At the highest, cognitive level, the most common types are EEG, MEG, fMRI, DTI, NIRS. Electroencephalography (EEG) is the recording of electrical signals from the brain by attaching surface electrodes to the subject's scalp (Craig & Nguyen, 2007; Lotte, Congedo, Lécuyer, Lamarche, & Arnaldi, 2007). These electrodes record brain waves which are electrical signals naturally produced by the brain. EEGs allow researchers to track electrical potentials across the surface of the brain and observe changes taking place over a few milliseconds. EEG data is spatio/spectro-temporal in the high frequency spectrum.

Functional MRI (fMRI) combines visualization of the brain anatomy with the dynamic image of brain activity into one comprehensive scan (e.g. Broderson et al., 2011, 2012; De Charms, 2008 and Mitchel et al., 2004). This non-invasive technique measures the ratio of oxygenated to deoxygenated hemoglobin which have different magnetic properties. Active brain areas have higher levels of oxygenated hemoglobin than less active areas. An fMRI scan can produce images of brain activity at the time scale of seconds with precise spatial resolution of about 1–2 mm. Thus, fMRI provides both a 3D anatomical and functional view of the brain in the lower frequency spectrum.

Other methods for whole brain data recording include MEG, DTI (Diffusion Tensor Imaging), single unit electrode data and others (Toga, Thompson, Mori, Amunts, & Zilles, 2006). Magnetoencephalography (MEG) measures millisecond-long changes in magnetic fields created by the brain's electrical currents. MEG machines use a non-invasive, whole-head, 248-channel, *superconducting-quantum-interference-device* (SQUID) to measure small magnetic signals reflecting changes in the electrical signals in the human brain. New methods for brain data collection are being developed and this area of research is likely to be further developed in the future.

Several structural brain atlases have been created to support the study of the brain and to better structure brain data. Probably the first attempt was made by Korbinian Brodmann, who created a cytoarchitectonic map of the human brain, published in 1909. The map presents 43 distinctive areas of the cerebral cortex. Each Brodmann area (BA) is characterized by a distinct type of cells, but it also represents distinct structural area, distinct functional area (e.g. BA17 is the visual cortex), distinct molecular area (e.g. number of neurotransmitter channels) (Zilles & Amunts, 2010). EEG and fMRI data are often mapped into BA for a better interpretation of results (Eickhoff et al., 2005).

An important contribution to the overall brain study and particularly to brain data analysis is the creation of a common coordinate system that can be used for a standardized study of brain data from different subjects and collected by different methods. Talairach and Tournoux (1988) created a co-planar 3D stereotaxic atlas of the human brain (Fig. 2(a)). A software was also made available, called The Talairach Daemon (www.talairach.org) to calculate the Talairach coordinates (x, y, z) of any given point in a brain image along with the corresponding BAs (Fig. 2(b)) (Lancaster et al., 2000).

While the Talairach Atlas was derived from the analysis of a single brain, much further development in stereotaxic mapping was achieved with the introduction of the Montreal Neurological Institute (MNI) coordinates, based on averaged MRI data across individuals, e.g. MNI152, MNI305 (Evans et al., 1993). Mapping of standard brain stereotaxic coordinates was further developed by the International Consortium for Brain Mapping (ICBM) with the release of several brain map templates, such as: ICBM452; ICBM Chinese56; ICBM AD (Alzheimer Disease); MS (multiple sclerosis) and others (Toga et al., 2006). Brain activity measurements, such as EEG and fMRI of any subject can be represented in standard MNI coordinates. MNI coordinates can be translated into Talairach coordinates and Brodmann Areas, and vice versa. The brain gene atlas, discussed further below, contains gene expression data collected from brain areas with identified MNI coordinates. MNI is a common standard now supported by many software systems, e.g. SPM (Ashburner, 2009).

At the lowest 'level' of information processing in the brain (Fig. 1) is the molecular information processing. Spatio-temporal activity in the brain depends on the internal brain structure, on the external stimuli and also very much on the dynamics at gene–protein level. This complex interaction is addressed through computational neurogenetic modeling (Benuskova & Kasabov, 2007). The first issue is how to obtain gene data related to brain structures and functions. The Brain Atlas (www.brain-map.org) of the Allen Institute for Brain Science (www.alleninstitute.org) has shown that at least 82% of the human genes are expressed in the brain. For almost 1000 anatomical brain areas of two healthy subjects, 100M data points were collected that indicate gene expressions of several thousand genes and underlie the biochemistry of the sites (Hawrylycz et al., 2012). This is in addition to the previously developed Mouse Brain Atlas.

The enormousness of brain data available and the complexity of the research questions that need answering through integrated models for brain data analysis are grand challenges for the areas of machine learning and information science in general as already pointed in some recent publications (Gerstner, Sprekeler, & Deco, 2012; Koch & Reid, 2012; Poline & Poldrack, 2012; Van Essen et al., 2012).

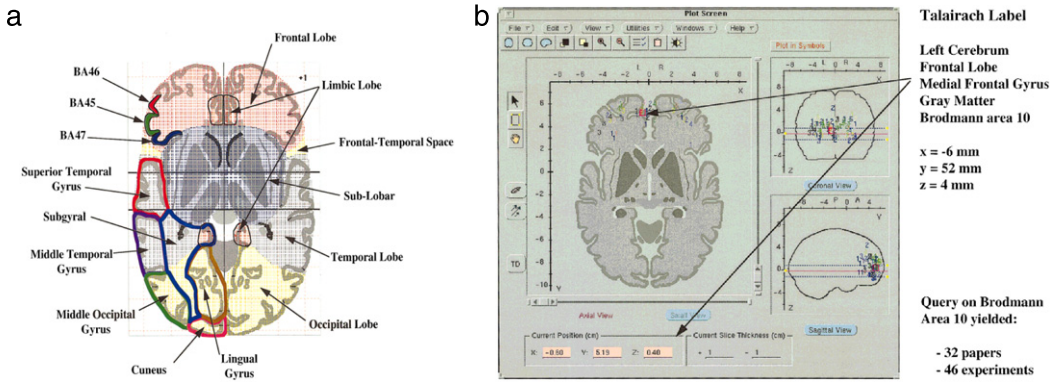


Fig. 2. (a) Talairach stereotaxic brain atlas; (b) the Talairach Daemon software.
Source: From Lancaster et al. (2000).

1.3. The challenge: Is it possible to develop a unifying computational approach for modeling and understanding of STBD?

While the correct brain data analysis is of utmost importance for many areas of science and engineering, there are no efficient machine learning methods that can deal with complex and heterogeneous STBD and integrate different sources of data, information and knowledge. The researchers who deal with brain data still use traditional statistical and AI methods. While methods such as Support Vector Machines (SVM), Multilayer Perceptron neural networks (MLP), Bayesian methods and many more, have been successfully used so far mainly on static brain data, they are not efficient in capturing complex spatio-temporal relationships from STBD neither they can accommodate prior knowledge about the brain in the models. An appropriate modeling paradigm specific to STBD would enable researchers to find efficient solutions to important problems such as:

- Accurate EEG data analysis for medical applications, e.g. epileptic seizure prediction (Fiasché, Schliebs, & Nobili, 2012; Ghosh-Dastidar & Adeli, 2007) stroke occurrence prediction (Barker-Collo, Feigin, Parag, Lawes, & Senior, 2010); Alzheimer's Disease (AD) (Morabito, Labate, La Foresta, Morabito, & Palamara, 2012);
- Accurate EEG data analysis (possibly non-invasive) for brain–computer interfaces (BCI) (Nicolelis, 2012);
- Accurate fMRI data analysis for cognitive function detection (e.g.: Broderson et al., 2012 and Mitchel et al., 2004);
- Good interpretability of the brain data models;
- Integrating different types of brain data, e.g. EEG, MEG, fMRI, DTI, etc. and prior knowledge about the brain into one model for a better accuracy and better interpretation of results. This could be possible only if there is common computational framework across different types of data, so that using one type of data will leave a 'memory', 'trace' in the model before the other type is used;
- Integrating brain activity data with gene data (Gerstner et al., 2012) for neurogenetic modeling and applications for prognosis and prevention of brain diseases.

Some of the above problems have already been addressed although only partially by a variety of models and frameworks. One of them is the graph theoretical analysis method (Bullmore & Sporns, 2009), which offers a tool to capture brain structural connectivity and functional connectivity from data, but it has limited abilities for learning from STBD. Another one, the Generative Embedding Model (Broderson et al., 2012) transforms voxel space of fMRI data into a generative space before applying SVM for classification. While this model works for some classification problems, it processes fMRI data only as spatial, rather than as spatio-temporal, and does not offer interpretability in terms of revealing functional pathways.

Accurate models of the brain have been developed (e.g. Izhikevich & Edelman, 2008; Markram, 2006; Toga et al., 2006). However, they cannot be used for machine learning and pattern recognition of STBD as their goal is to model the brain structurally and functionally and not learn and mine brain data. The human brain has evolved throughout more than 5M years of human evolution with the more recent 10,000 years of human civilization. The accurate brain modeling may require modeling the principles of evolution in nature rather than just the brain as its product. Modeling the brain is a challenging task for many years to come (e.g. the EU Human Brain Project), but modeling and understanding brain data, that is available *now*, is a task that the neural network community needs to address *now*.

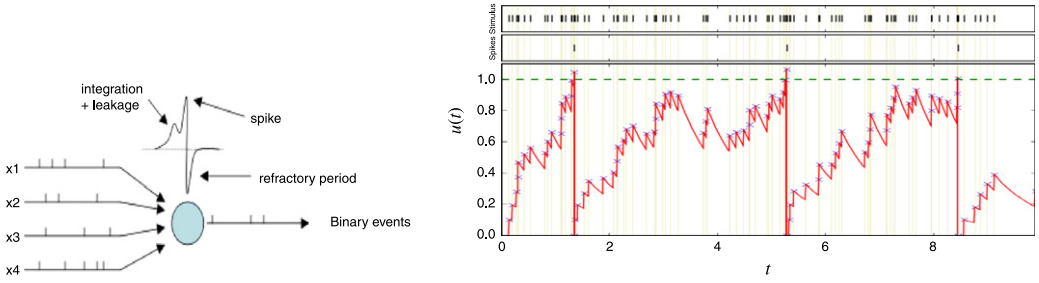
In this paper we offer a computational architecture for the creation of efficient computational models from STBD that utilize the following principles:

(1) The model can accommodate and integrate various STBD.
(2) The model has a spatial structure that approximately maps the spatially located areas of the brain where STBD is collected;
(3) The same information paradigm—spiking information processing, that ultimately generates STBD at a low level of brain information processing, is used in the model to represent and to process this STBD.
(4) Brain-like learning rules are used in the model to learn STBD, mapped into designated spatial areas of the model;
(5) A model is evolving in terms of new STBD patterns being learned, recognized and added incrementally, which is also a principle of brain cognitive development;
(6) A model retains a spatio-temporal associative memory that can be mined and interpreted for new knowledge discovery; this memory may be represented as a spatio-temporal finite automaton.

2. Why should we use SNN for learning, pattern recognition and understanding of STBD?

2.1. SNN as brain-inspired NN

The human brain has the amazing capacity to learn and recall patterns that occur at different time scales, ranging from milliseconds, to – years and possibly to – millions of years (e.g. genetic information, accumulated through evolution). Thus the brain can be considered the ultimate inspiration for the development of new machine learning techniques for STBD. Indeed, brain-inspired SNN have in principle the potential to process STBD by using trains of spikes (binary temporal events) transmitted among spatially located synapses and neurons (Hodgkin & Huxley, 1952; Hopfield, 1982). Both spatial and temporal information can be encoded in SNN as locations of synapses and neurons and time of their spiking activity respectively.



(a) The structure of a LIFM. (b) Functionality of a LIFM.

Fig. 3. A Leaky Integrate and Fire model (LIFM) of a spiking neuron: (a) schematic representation; (b) functioning, showing an input train of spikes (top row), the emitted output spikes (second row) and the membrane potential.

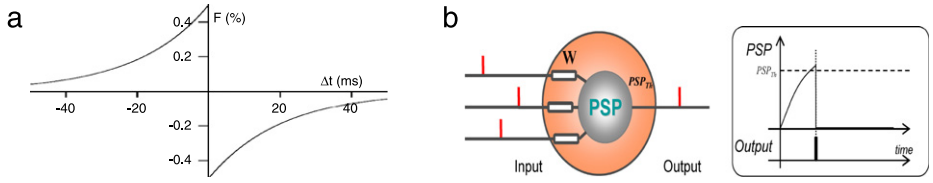


Fig. 4. (a) Synaptic change in a STDP learning neuron (Song et al., 2000); (b) rank-order learning neuron.

Models of spiking neurons as well as computational SNN models, along with their respective applications, have been already developed and explored (Bohte, 2004; Bohte, Kok, & La Poutre, 2005; Brette et al., 2007 Gerstner, 1995, 2001; Hodgkin & Huxley, 1952; Hopfield, 1982; Izhikevich, 2006; Maass, Natschlaeger, & Markram, 2002; Thorpe & Gautrais, 1998. The evolving connectionist systems paradigm and the evolving spiking neural networks (eSNN) in particular (Kasabov, 2007) further extend the traditional neuro and hybrid systems (Kasabov, 1996). eSNN can learn data incrementally by one-pass propagation of the data via creating and merging spiking neurons. In Wysoski, Benuskova, and Kasabov (2010) a simple eSNN is designed to capture features and to aggregate them into audio and visual perceptions for the purpose of person authentication using vector-based image and speech data. Information processing methods based on SNN, such as: methods for transformation of continuous input signals into spike trains; computational models of spiking neurons; methods for connecting and learning in SNN; and many more support the main argument here that SNN are a suitable paradigm for STBD. A brief explanation of some SNN methods is given below.

2.2. Models of spiking neurons and methods of learning in SNN

Several spiking neuronal models have been proposed so far (e.g. Gerstner, 2001; Hodgkin & Huxley, 1952; Izhikevich, 2006; Maass et al., 2002). Fig. 3(a) and (b) illustrate the structure and the functionality of the popular Leaky-Integrate and Fire Model (LIFM). The neuronal post-synaptic potential (PSP), also called membrane potential $u(t)$, increases with every input spike at a time t, multiplied by the synaptic efficacy (strength), until it reaches a threshold θ. After that, an output spike is emitted and the membrane potential is reset to an initial state. The membrane potential can have certain leakage between spikes, which is defined by a temporal parameter τ.

Different learning rules for SNN have been introduced. The STDP learning rule (Spike Timing Dependent Plasticity) (Song, Miller, & Abbott, 2000) utilizes Hebbian plasticity (Hebb, 1949) in the form of long-term potentiation (LTP) and depression (LTD) (Fig. 4(a)). Efficacy of synapses is strengthened or weakened based on the timing of post-synaptic action potential in relation to the pre-synaptic spike. If the difference in the spike time between the pre-synaptic and post-synaptic neurons is negative (pre-synaptic neuron spikes first) then the connection weight between the two neurons increases, otherwise it decreases. Connected neurons, trained with STDP learning rule, learn consecutive temporal associations from data. New connections can be generated based on activity of consecutively spiking neurons. Pre-synaptic activity that precedes post-synaptic firing can induce long-term potentiation (LTP), reversing this temporal order causes long-term depression (LTD).

STDP and other fundamental learning methods have been recently used to develop new types of eSNN models for spatio-temporal pattern recognition (http://ncs.ethz.ch/projects/evospike) (Kasabov, 2012a, 2012b) such as: SPAN (Mohemmed, Schliebs, Matsuda, & Kasabov, 2012, 2013); deSNN (Kasabov, Dhoble, Nuntalid, & Indiveri, 2013); reservoir eSNN (Schliebs, Hamed, & Kasabov, 2011; Schliebs, Kasabov, & Defoin-Platel, 2010; Schliebs, Mohemmed, & Kasabov, 2011; Schliebs, Nuntalid, & Kasabov, 2010). Applications include moving object recognition (Dhoble, Nuntalid, Indiveri, & Kasabov, 2012; Schliebs, Kasabov et al., 2010; Schliebs, Nuntalid et al., 2010), sign language recognition (Schliebs, Hamed et al., 2011); EEG pattern recognition (Nuntalid, Dhoble, & Kasabov, 2011).

The dynamic eSNN (deSNN) (Kasabov et al., 2013) combines rank-order and temporal (e.g. STDP) learning rules. The initial values of synaptic weights are set according to the rank-order learning assuming the first incoming spikes are more important than the rest. The weights are further modified to accommodate following spikes activated by the same stimulus, with the use of a temporal learning rule—STDP.

The rank-order learning rule (Thorpe & Gautrais, 1998) uses important information from the input spike trains, namely the rank of the first incoming spikes on the neuronal synapses (Fig. 4(b)). It establishes a priority of inputs (synapses) based on the order of the spike arrival on these synapses for a particular pattern. This is a phenomenon observed in biological systems as well as an important information processing concept for some engineering problems, such as computer vision and control (Berry, Warland, & Meister, 1997; Rokem et al., 2005 and Theunissen & Miller, 1995). The rank-order learning has several advantages when used in SNN, mainly: fast, one-pass learning (as it uses the extra information of the order of the incoming spikes) and asynchronous data entry (synaptic inputs are accumulated into the neuronal membrane potential in an asynchronous way). The post-synaptic potential of a neuron i at a time t is calculated as:

$$PSP(i,t) = \sum mod^{order(j)} w_{j,i} \quad (1)$$

where: mod is a modulation factor, that has a value between 0 and 1; j is the index for the incoming spike at synapse j, i and $w_{j,i}$ is

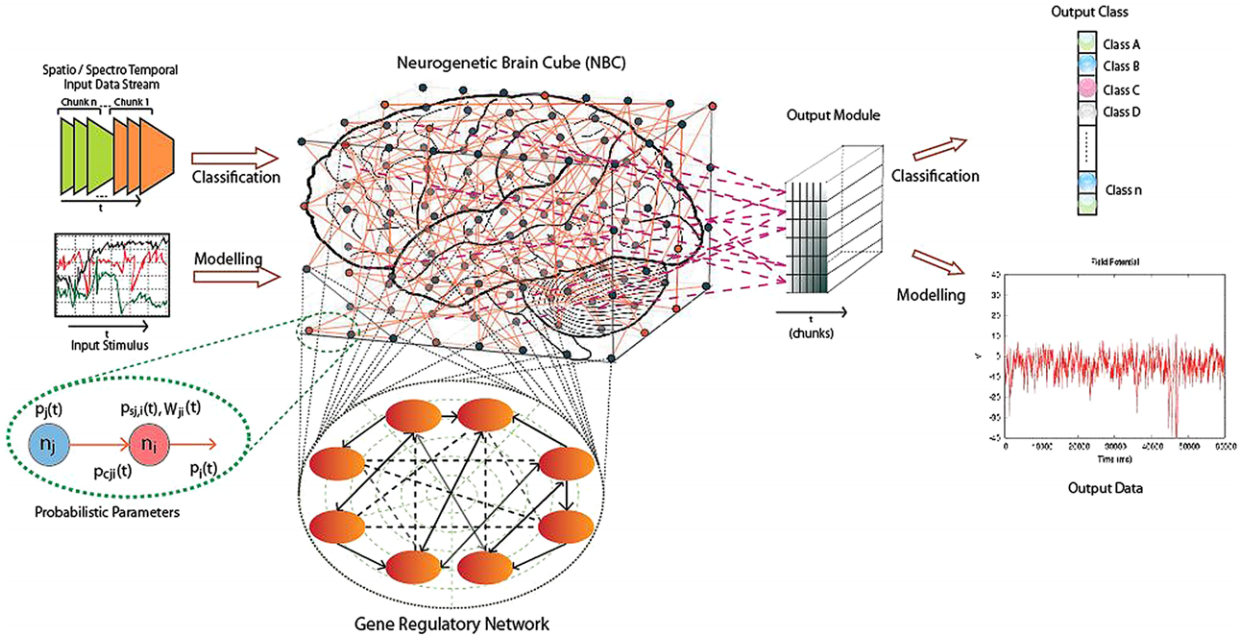


Fig. 5. A diagram of the general NeuCube architecture, consisting of: input data encoding module; 3D SNNr module; output function module (e.g. for classification or prediction); gene regulatory networks (GRN) module (optional).
Source: From Kasabov (2012a).

the corresponding synaptic weight; $order(j)$ represents the order (the rank) of the spike at the synapse j, i among all spikes arriving from all m synapses to the neuron i. The $order(j)$ has a value 0 for the first spike and increases according to the input spike order. An output spike is generated by neuron i if the $PSP(i, t)$ becomes higher than a threshold $PSP_{Th}(i)$. During the training process, for each training input pattern there is a new output neuron created and its connection weights are calculated based on the order of the incoming spikes:

$$\Delta w_{j,i}(t) = mod^{order(j,i(t))}. \quad (2)$$

SPAN is an algorithm for both classification and spike pattern association (Mohemmed et al., 2012, 2013). The connection weights of a neuron are updated after the presentation of the whole spatio-temporal spiking pattern, rather than spike by spike as it is in the deSNN model. Delta rule is used for the purpose (Widrow & Lehr, 1990). SPAN learns to generate an output spike at a certain time, or a pattern of temporally distributed spikes over time, when a certain spatio-temporal pattern of input spikes is recognized (Mohemmed et al., 2012, 2013). SPAN is a suitable algorithm for *control applications*, so that when a certain spatio-temporal pattern is recognized, a series of motor control signals are emitted at different times on one or several outputs. In principle, SPAN is a further development of an existing class of algorithms, including: ReSuMe (Ponulak & Kasinski, 2010); Chronotron (Florian, 2010); Tempotron (Gutig & Sompolinsky, 2006).

Despite the available now SNN methods and neuromorphic platforms (Furber, 2012; Furber & Temple, 2007; Indiveri, Chicca, & Douglas, 2009; Indiveri et al., 2011; Indiveri, Stefanini, & Chicca, 2010) there are no specific machine learning methods yet developed for STBD based on SNN. Next in the paper we discuss and illustrate a new SNN based framework for STBD, called NeuCube, which implements the six information principles from Section 1.3.

3. NeuCube—a SNN architecture for STBD

3.1. The NeuCube architecture

Some general principles of the NeuCube architecture were presented in Kasabov (2012a). The NeuCube architecture is depicted in Fig. 5. It consists of the following functional modules:

- Input data encoding module;
- 3D SNN reservoir module (SNNr);
- Output function (classification) module;
- Gene regulatory network (GRN) module (Optional).

The process of creating a NeuCube model for a given STBD takes the following steps:

a. Encode the STBD into spike sequences: continuous value input information is encoded into trains of spikes;
b. Construct and train in an unsupervised mode a recurrent 3D SNN reservoir, SNNr, to learn the spike sequences that represent individual input patterns;
c. Construct and train in a supervised mode an evolving SNN classifier to learn to classify different dynamic patterns of the SNNr activities that represent different input patterns from SSTD that belong to different classes;
d. Optimize the model through several iterations of steps (a)–(c) above for different parameter values until maximum accuracy is achieved.
e. Recall the model on new data.

The above modules from (a) to (e) are described further in this section.

3.2. Input data encoding module

Continuous value input data can be transformed into spikes so that the current value of each input variable (e.g. pixel, EEG channel, fMRI voxel) is entered into a population of neurons that emit spikes based on how much the input value belongs to their receptive fields. This method is called population rank coding (Bohte, 2004)—the higher the membership degree, the earlier a spike is generated (Fig. 6(a)).

Another method is the Address Event Representation (AER) method as demonstrated in the Silicon Retina (Delbruck, 2007; Lichtsteiner & Delbruck, 2005). This is based on thresholding the difference between two consecutive values of the same input variable over time (Fig. 6(b)). This is suitable when the input data is

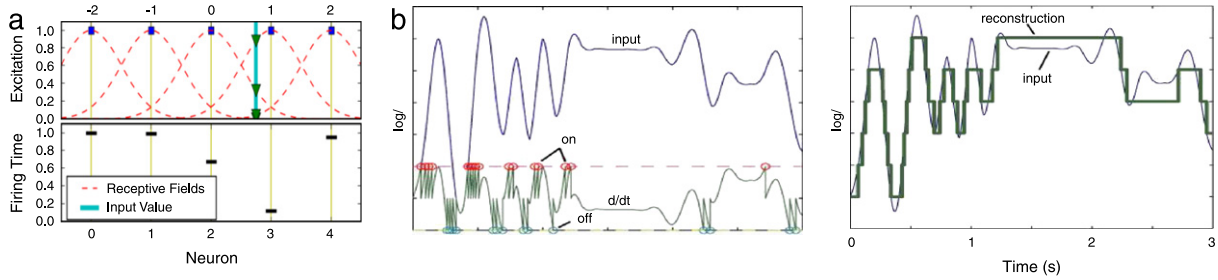


Fig. 6. (a) Population rank order coding of input information; (b) Address Event Representations (AER) of continuous value time series input data into spike trains and recovery of the signals from the spike train (Delbruck, 2007).

a stream and only the changes in consecutive values can be processed.

In some specific applications, a method called Ben's Spike Algorithm (BSA) has been used for EEG data transformation into spike trains (Nuntalid et al., 2011).

The transformed input data into spike series is entered (mapped) into spatially located neurons from the SNNr. The mapping will depend on the problem in hand. Here we enter brain data sequences to spatially located neurons in the SNNr that represent spatially brain areas where data is collected. Spike trains are continuously fed into the SNNr in their temporal order.

3.3. The SNNr module

The SNNr is structured to spatially map brain areas for which STBD or/and gene data is available. A neuronal SNNr structure can include known structural or functional connections between different areas of the brain represented in the data. Setting up a proper initial structural connectivity in a model, is important in order to learn properly spatio-temporal data, to capture functional connectivity and to interpret the model (Honey, Kötter, Breakspear, & Sporns, 2007). More specific structural connectivity data can be obtained using for example Diffusion Tensor Imaging (DTI) method.

Functional connectivity of the brain manifests the small-world organization across different time scales (e.g. seconds, milliseconds) (Bullmore & Sporns, 2009). Neurons in a structural or functional area of the brain are more densely interconnected and the closer these areas are, the higher the connectivity between them (Braitenberg & Schüz, 1998). Both structural connectivity, measured through MRI (Chen, He, Rosa-Neto, Germann, & Evans, 2008) and functional connectivity, measured through EEG and MEG (Stam, 2004) of the brain show small-world organization. This is the main reason for suggesting a type of small-world connectivity for a NeuCube initial structure, where clusters of neurons correspond to structural and functional areas related to the STBD (Bullmore & Sporns, 2009). If DTI data is available, this data can be used to preset some connections of the SNNr before the model is trained on the STBD.

The initial structure of the SNNr is defined based on the available brain data and the problem, but this structure can be evolving through the creation of new neurons and new connections based on the STBD using the ECOS principles (Kasabov, 2007). If new data do not sufficiently activate existing neurons, new neurons are created and allocated to match the data along with their new connections.

In a current implementation, the SNNr has a 3D structure connecting leaky-integrate and fire model (LIFM) spiking neurons with recurrent connections. The input STBD is propagated through the SNNr and a method of *unsupervised learning* is applied, such as STDP. The neuronal connections are adapted and the SNNr learns to generate specific trajectories of spiking activities when a particular input pattern is entered. On Fig. 5 a special class of LIFM is shown—the probabilistic neuronal model that has probability parameters attached to the connections, the synapses and the output of the spiking neuron (see Section 5). The SNNr accumulates temporal information of all input spike trains and transforms it into dynamic states that can be classified over time. The recurrent reservoir generates unique accumulated neuron spike time responses for different classes of input spike trains. As an illustration, Fig. 7(a)–(c) show the spiking activity (a) and connectivity of a SNNr before training (b) and after training—(c) on illustrative SSTD, where the SNNr has 1471 neurons and the coordinates of these neurons correspond directly to the Talairach template coordinates with a resolution of 1 cm^3. It can be seen that as a result of training new connections have been created that represent *spatio-temporal interaction* between input variables captured in the SNNr from the data. The connectivity can be dynamically visualized for every new pattern submitted. Fig. 7(d) and (e) show visualizations of a SNNr of 2.4M neurons that correspond to Talairach coordinates with a resolution of 1 mm^3.

3.4. Evolving output classification module

After the SNNR is trained on the STBD in an unsupervised model, the same input data is propagated again through the SNNr, pattern by pattern, the state of the SNNr is measured for each pattern and an output classifier is trained to recognize this state in a predefined output class for this input pattern. For fast learning, we use evolving SNN classifiers (eSNN). All neurons from the SNNr are connected to each of the evolved LIFM neurons of the eSNN classifier.

One of the originality of the proposed NeuCube architecture is that it utilizes the ability of the eSNN to learn to recognize complex spatio-temporal patterns generated in the SNNr before the whole input data pattern is entered. Different types of eSNN can be used as presented in Section 2, e.g.: eSNN (Kasabov, 2007), (Schliebs & Kasabov, 2013); Dynamic eSNN (deSNN) (Kasabov et al., 2013), SPAN (Mohemmed et al., 2012). The recall procedure can be performed using different recall algorithms applying different methods:

(a) A spike sequence that represents the response of the trained SNNr to new input data is propagated to all trained output neurons and the first one that spikes (its PSP is greater that its threshold) defines the output. The assumption is that the neuron that best matches the input pattern will spike earlier, based on the PSP threshold (membrane potential). This method is called eSNNm (deSNNm).

(b) The second method implies a creation of a new output neuron in the eSNN for each new input pattern from the SNNr, in the same way as the output neurons were created during the learning phase in the eSNN, and then—comparing the connection weight vector of the new one to the already existing neurons using Euclidean distance. The closest output neuron in terms of synaptic connection weights is the 'winner'. This method uses the principle of transductive reasoning and nearest neighbor classification in the connection weight space. It compares spatially distributed synaptic weight vectors of a new neuron that captures a new input pattern and existing ones. This method is called eSNNs (deSNNs).

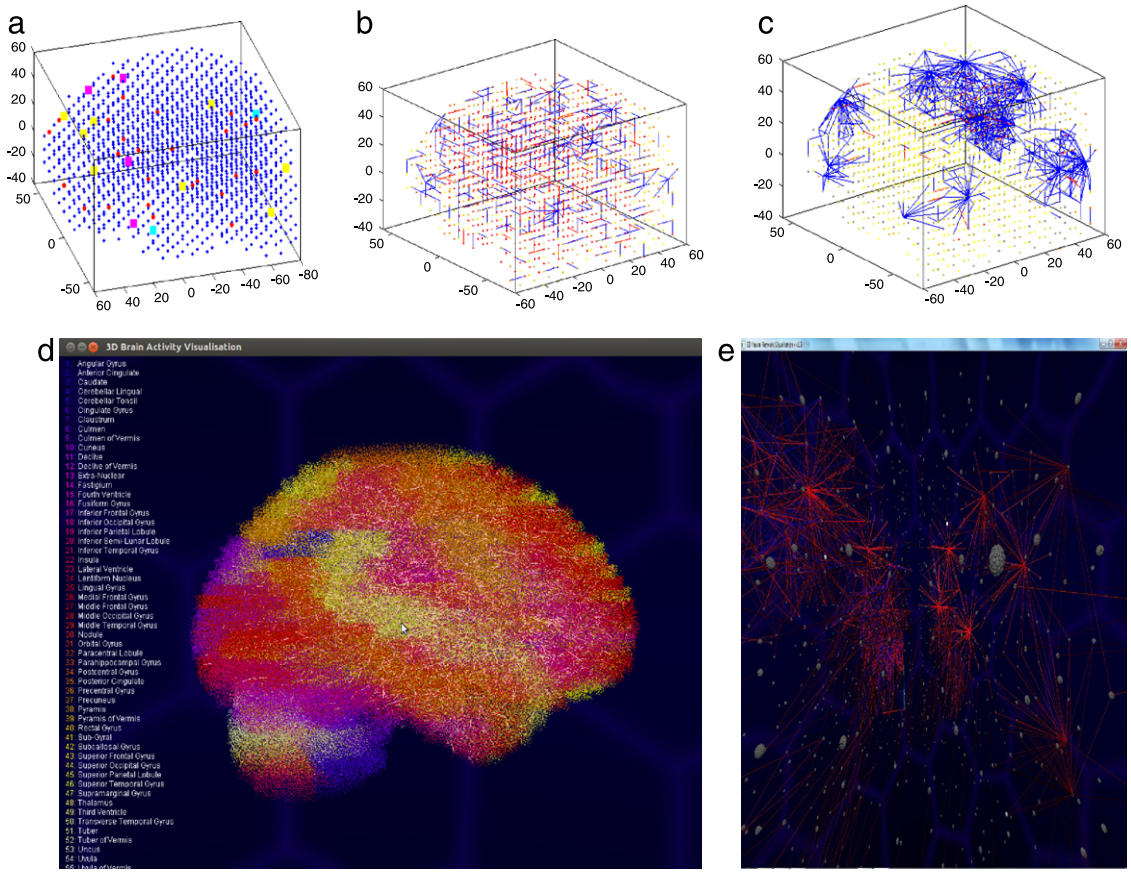


Fig. 7. Illustrative visualization of connectivity and spiking activity of a SNNr: (a) spiking activity—active neurons are represented in red color and large size; (b) connectivity before training – small world connections – positive connections are represented in blue and negative—in red; (c) connectivity after training; (d) connectivity of a NeuCube with 2.4M neurons; (e) zoomed visualization of connectivity of a small internal section from the NeuCube.

The main advantage of the eSNN, when compared with other supervised or unsupervised learning and classification SNN models, is that it is computationally inexpensive and boosts the importance of the order in which input spikes arrive, thus making the eSNN suitable for on-line learning and early prediction of temporal events.

4. EEG STBD classification in NeuCube

4.1. Mapping EEG data into the SNNr of the NeuCube

EEG channels are spatially distributed on the scalp. An example of the positioning of 64 EEG channels on a human head is shown in Fig. 8(a) while their representation in a 3D space is shown in Fig. 8(b). The spatially defined positions of the channels can be mapped into a SNNr using different approaches.

One of them is using the Talairach template (Fig. 2(a) and (b)). The neurons in the SNNr are located following the same (x, y, z) coordinates of the Talairach template and the EEG channels are mapped according to the standard mapping given in the Appendix (Koessler, Maillard, & Benhadid, 2009). The spiking sequences that represent EEG channels, after transformation of continuous value signals into spike trains, are entered into the correspondingly located neurons before a training procedure (e.g. STDP) is applied.

4.2. A case study of EEG STBD recognition in a NeuCube model

To illustrate the principles of building a NeuCube model for STBD modeling and classification, here we have used EEG data collected using a standard 14-channel EEG recording device (Emotiv, 2013). The data was collected following two scenarios which were labeled as either the "relax" or the "memory" scenario. The EEG data was recorded from a single healthy subject over a period of 40 s for each of the two scenarios. The length of a session was chosen in accordance with the duration of the memory task. The experiment labeled "relax" was recorded with closed eyes, in order to avoid disturbing artifacts from blinking and the subject was asked to avoid thinking or planning thoughts as much as possible. For the "memory" experiment the Stenberg's Memory Scanning Test (SMT) was adopted (von der Elst, van Boxtel, van Breukelen, & Jolles, 2007). The experiment was performed using the Presentation software (Buteneers, Schrauwen, Verstraeten, & Stroobandt, 2008). The SMT method has been used in a wide range of scientific areas as it is an easy and practical model for evaluating information processing in working memory. Both scenarios were each repeated five times, resulting in $2 \times 5 = 10$ sessions with a total of 400 s of recorded data. The data was segmented in 8 s samples, totaling to 50 samples, representing 2 classes.

A NeuCube model was trained and tested with the parameters shown in the screenshot of Fig. 9. An AER input data encoding method was used. The SNNr comprised 1471 LIFM neurons, located according to the Talairach template and the Koessler et al. (2009) mapping as shown in the Appendix. The classification accuracy obtained was 85% (100% for class 1 and 70% for class 2), but further parameter optimization, that could lead to an improved accuracy, can be done as discussed in Section 5.2. When same EEG data, averaged across time, was used with traditional machine learning methods, the classification accuracy in 3 fold cross validation was much less: MLRegression (72%); SVM (74%; polynomial kernel of 1st degree); MLP (78%; 10 hidden nodes, 500 training iterations).

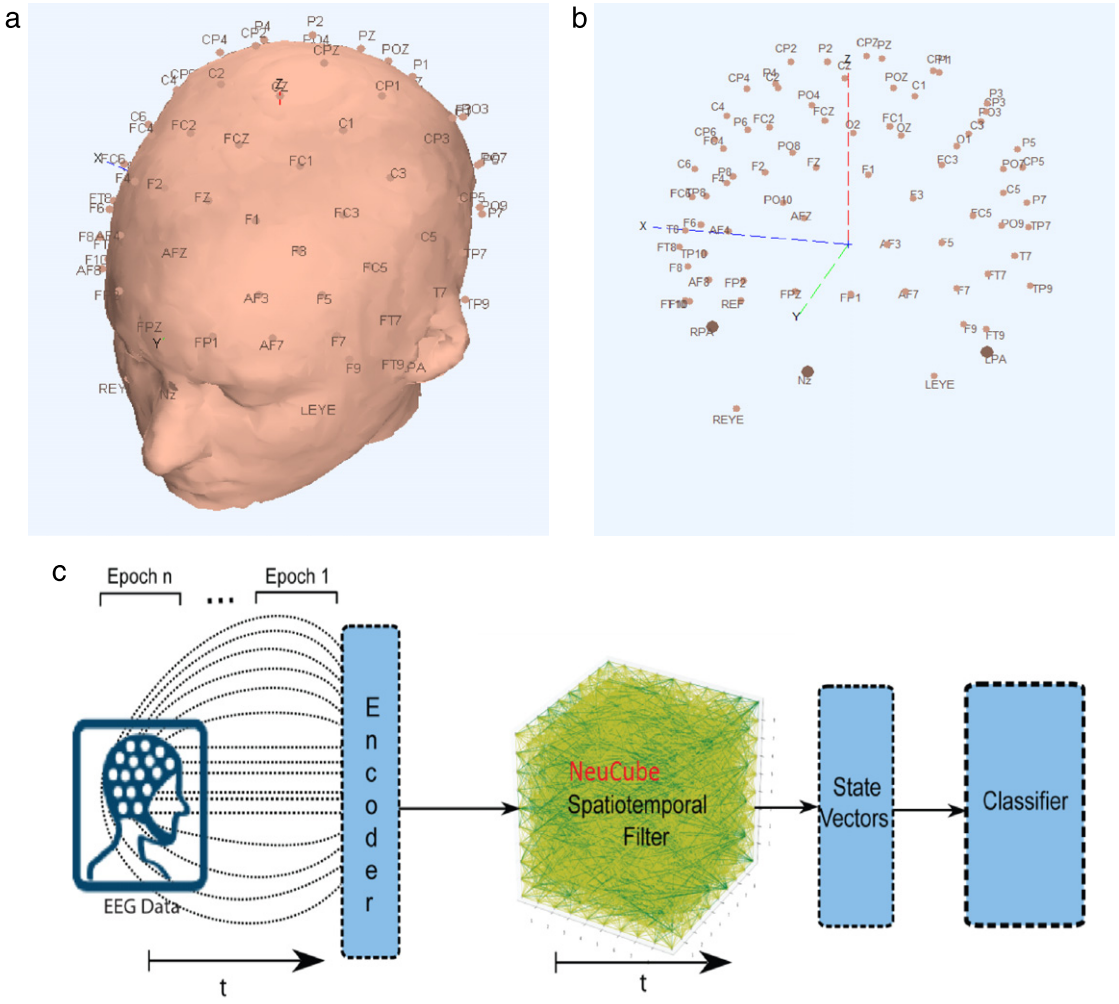


Fig. 8. (a) Spatial distribution of EEG channels; (b) 3D spatial representation of EEG channels (from the EEG Lab); (c) experimental setting for the EEG NeuCube model for BCI.

In addition to the higher classification accuracy, the NeuCube model is interpretable that helps to understand the data and the brain processes that generated it (as illustrated in Fig. 7(a)–(c)).

4.3. Practical applications of NeuCube models for EEG STBD modeling and pattern recognition

EEG pattern recognition with NeuCube can be directed to practical medical and brain–computer interfaces (BCI) applications, such as: epilepsy on-set prediction (Fiasché et al., 2012; Ghosh-Dastidar & Adeli, 2007; Mammone, Labate, Lay-Ekuakille, & Morabito, 2012); stroke occurrence risk analysis (Baker-Colo et al., 2005); AD (Morabito et al., 2012). NeuCube cannot only learn meaningful functional pathways from data, but it can be used as a predictor for future brain states, utilizing it as associative memory. EEG data can be combined with fMRI data to study spatio-temporal functional and structural connectivity pathways in the brain at different frequency scales, high—EEG, and low—fMRI.

BCI is a fast growing area (Isa, Fetz, & Muller, 2009). A NeuCube architecture can be evolved and dynamically visualized to represent and memorize the learning process of a subject when trying to communicate with a device or with another subject via computer in order to improve this communication. Another area of potential applications of the NeuCube trained on EEG STBD is robotics (Bellas, Duro, Faiña, & Souto, 2010; Lotte et al., 2007). A challenging task would be to create computer models that are trained by thoughts to control a process of building physical or software constructs using ready elements. If it is possible for a NeuCube to learn brain signals from a subject who is constructing a physical or software object, it may be possible to simulate this process and possibly prevent faults in the construction.

5. Discussions and further development

There are different aspects and potential applications of the NeuCube architecture, some of them discussed in this section.

5.1. Learning and recognition of fMRI STBD

Previous fMRI machine learning methods have been restricted to mainly deal with single ROI data classification and have used traditional statistical and AI methods that are not appropriate for learning important spatio-temporal functional pathways. This is, to put it mildly, a very inefficient use of the rich of information fMRI STBD. There is no memory, no ‘trace’ left after this type of learning has taken place, to help understand complex brain processes from data. fMRI data is a dynamic data that consists of a large number of voxels, measured over time, to represent a subject’s brain activity (e.g. Hanke et al., 2009; Haxby et al., 2011).

In order to normalize fMRI data across a population of subjects before using the NeuCube architecture, a standard 3D coordinate system can be used (e.g. MNI, Talairach) to represent uniformly

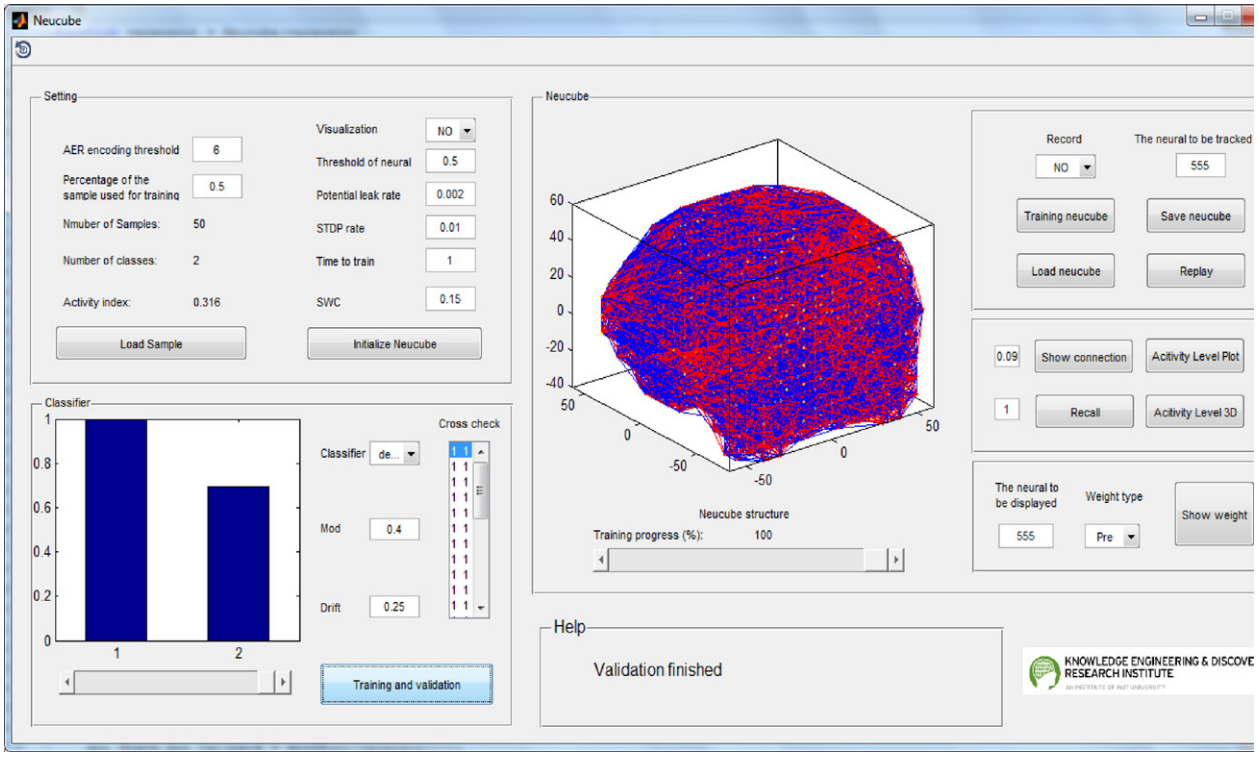


Fig. 9. A snapshot of a software implementation of the NeuCube architecture for classification of 2-class EEG data. The parameter values are shown in the parameter boxes. The connectivity of the SNNr after training can be analyzed through specialized visualization functions. The classification accuracy of 50/50 cross validation is 100% for class 1 and 70% for class 2. The used classification model is deSNNs with parameters *Mod* = 0.4 and *Drift* = 0.25. Only one learning pass is used for both the SNNr training (unsupervised, STDP) and the deSNNs training (supervised).

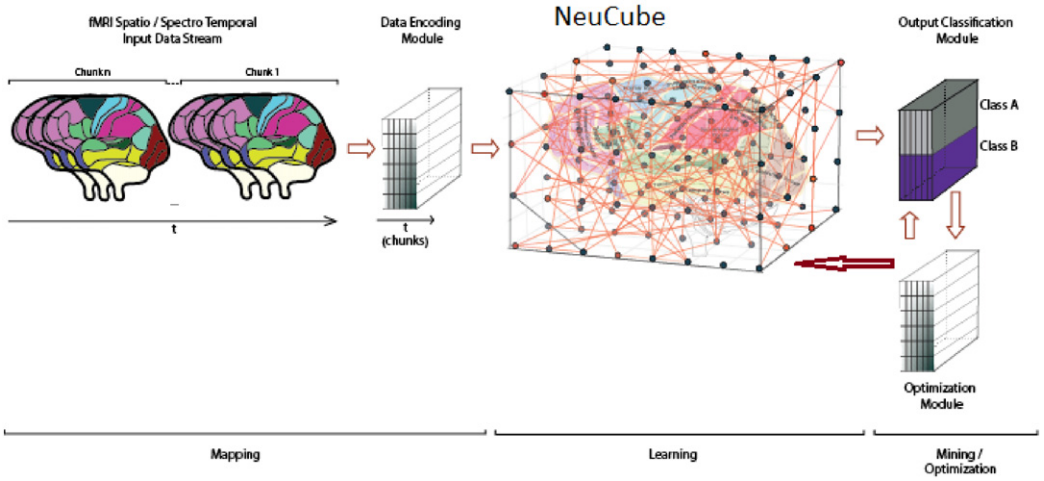


Fig. 10. A schematic representation of using NeuCube for mapping, learning and mining of fMRI data.

same structural and functional areas of the brain across subjects. Standard coordinates are mapped first into spatially defined neurons (clusters of neurons) of a 3D SNNr structure. Then fMRI voxel data is mapped into the corresponding neurons in the SNNr and learning is applied so that the whole sequence of fMRI data is learned as one spatio-temporal pattern. Fig. 10 shows graphically the idea of mapping, learning and mining fMRI data with the use of the NeuCube framework.

There are many applications of mapping, learning and mining of fMRI data across domain areas, e.g.: medical and health areas; neuroinformatics, neuroeconomics, cognitive science (for a review, see De Charms, 2008). Honey and Sporns (2008) demonstrated how graphical models of fMRI can be used to understand dynamic consequences of lesions in strokes and traumatic brain injuries. Experiments can be conducted with the same data using the NeuCube approach, which could result in a better accuracy and the discovery of new spatio-temporal pathways.

5.2. NeuCube model optimization

A major problem with NeuCube models is optimization of the numerous parameters. For each NeuCube model, to select an optimal subset of features (input variables), SNNr parameter values and classifier parameter values (for the deSNN classifier—they are *Mod*, *Sim*, *C*, *Drift*), different values for all these parameters can be tested in their combination. One approach is to use evolutionary computation methods. Several efficient evolutionary computation methods have been developed recently that can be applied for

this purpose, such as: Particle Swarm Optimization (PSO) methods for SNN (Mohemmed et al., 2013); quantum inspired genetic algorithm (Defoin-Platel, Schliebs, & Kasabov, 2009; Schliebs, Defoin-Platel, Worner, & Kasabov, 2009); quantum inspired PSO (Nuzly, Kasabov, & Shamsuddin, 2010). The quantum inspired evolutionary methods can deal with a very large dimensional space. They belong to the class of probability density estimation algorithms and each quantum-bit chromosome represents the whole space, every point of it—to certain probability (Defoin-Platel et al., 2009).

Another approach is to use genes from the GRN for representing different parameters of the SNNr. It is practical to use the same parameter values (same GRN) for all neurons in a functional area of the SNNr. That will result in a significant reduction of the number of parameters to be optimized. This can be interpreted as 'average' parameter value for all neurons in one area. When defining parameters of the NeuCube, prior knowledge about the association of spiking parameters with relevant genes/proteins (neurotransmitter, neuro-receptor, ion channel, neuro-modulator) can be also used (Kasabov, Dhoble, Nuntalid, & Mohemmed, 2011; Kasabov, Schliebs, & Kojima, 2011) as discussed further in this section. The second approach does not exclude using evolutionary computation to optimize the GRN as it is the case in the CNGM simulator (Kasabov, 2007; Wysoski et al., 2010).

5.3. What spatio-temporal patterns can be learned in a NeuCube model?

As pointed before, a NeuCube model can be created to learn spatio-temporal patterns in both unsupervised and supervised ways:

- In an unsupervised learning, the STBD is entered into relevant areas of the SNNr over time. Unsupervised learning is performed to modify the initially set connection weights. The SNNr will learn to activate same groups of spiking neurons when similar input stimuli are presented, also known as a *polychronization* effect (Izhikevich, 2006).
- In a supervised learning, first the SNNr is trained in an unsupervised mode, and then its spiking activity is used to train a classifier.

A NeuCube model can learn spatio-temporal patterns in its three forms of 'memory', similar to the brain memory:

- Short-term memory, represented as changes of the PSP and temporary changes of synaptic efficacy;
- Long-term memory, represented as a stable establishment of synaptic efficacy—LTP and LTD, in the SNNr and the output eSNN classifier;
- Genetic memory, represented as a GRN.

As spatio-temporal patterns from data are learned in the recurrent SNNr as pathways of connections, when only a small initial part of input data is entered, the SNNr will 'synfire' and 'chainfire' *learned connection pathways* to reproduce *learned functional pathways* (Abeles, 1991; Humble, Denham, & Wennekers, 2012; Izhikevich, 2006, 2010). The NeuCube can be used as an *associative memory* and as a predictive system for brain states based on some initial brain signals.

There are some challenging questions that need to be further explored, for example: What is the capacity of a NeuCube in terms of robust learning of both spatial and temporal characteristics from STBD? How much noise can be tolerated? How do we model and understand transitions between spatio-temporal states triggered by external stimuli? Can we make the SNN learn and model mental states represented as brain data and their transitions? How do we model for example the transition between a SNNr state that represents a brain state of 'mild depression' to a state that represents 'happiness'; from a state of 'stroke' to a state of 'full cognitive recovery', from a state of 'clinical depression' to a state of 'suicidal mode'; from a state of 'anger' to a state of 'attack'?

Another fundamental question is to represent a NeuCube model as a spatio-temporal finite automata (FA) model. Modeling FA with SNN has been a long time interest for the SNN community (Natschlager & Maass, 2002), but only SNN FA with small number of states have been demonstrated so far as 'toy' examples and there has not been even an attempt made to model a large number of spatio-temporal states in a SNN FA. Some recent studies defined a state of an SNN as a dynamic chaotic attractor (Neftci, Chicca, Indiveri, & Douglas, 2012). Even though this concept was successfully implemented in a neuromorphic hardware and experimented on a small number of states, it is still difficult to explain biological perception and mental states with dynamic chaotic attractors. It is also difficult to formally describe and to realize such SNN FA for a larger number of states. This leads to the need for a new paradigm that would allow for the modeling of spatio-temporal behavior of a large number of neuronal ensembles.

In Humble et al. (2012) and Szatmary and Izhikevich (2010) polychronous neuronal groups are studied. Since the number of such groups of synchronously activated neurons is very large, this may bring along a new development of the FA theory, where a state of a system is not a static entity, but a *spatio-temporal* one. In the case of NeuCube we can talk about FA for Spatio-Temporal States (FASTS). A spatio-temporal state $S_i(T)$ is a sequence $(S_i(t1), S_i(t2), \ldots, S_i(tk))$ of consecutive spiking patterns of polychronous groups of neurons in the SNNr within a time interval $T = (t1, t2, \ldots, tk)$ that represents a classified output O_i (e.g. a mental state of 'happiness'). The state transition is triggered by external input signals (stimuli) which can be spatio-temporal, e.g.: music; environmental changes, such as atmospheric pressure, over a period of time, etc. A formal description of FASTS can be given as:

$$\text{FASTS} = \{X, P, S, O, f, g\} \tag{3}$$

where: X is a set of input signals that can be spatio-temporal; P is a set of system parameters; S is a set of spatio-temporal states; f is a probabilistic state transfer function; g is a probabilistic output function that produces an output O_i if the FASTS is in a state S_i. A further investigation on the functionality of the FASTS models is needed before any conclusion about their applicability is made.

5.4. Neurogenetic modeling

In order to integrate different types of STBD, including stochastic data and molecular information, a new model of a spiking neuron can be used in the NeuCube architecture (presented so far with the use of only LIFM). Here we will describe a probabilistic neurogenetic model (PNGM). It combines the probabilistic model (Kasabov, 2010) (Fig. 11(a) and (b)) and the neurogenetic model (Benuskova & Kasabov, 2007; Kasabov, Benuskova, & Wysoski, 2005) (Table 1) of a neuron as explained below. As a partial case, when no probability parameters and no genetic data are used, the model is reduced to the LIFM (Fig. 2(a), (b)).

In the PNGM four types of synapses for *fast excitation, fast inhibition, slow excitation, and slow inhibition* are used. The contribution of each one to the PSP of a neuron is defined by the level of expression of different genes/proteins along with the presented external stimuli. The model utilizes known information about how proteins and genes affect spiking activities of a neuron. Table 1 shows what proteins affect each of the four types of synapses. This information is used to calculate the contribution of each of the *four* different synapses j connected to a neuron i to its post-synaptic potential $PSP_i(t)$:

$$\varepsilon_{ij}^{synapse}(s) = A^{synapse}\left(\exp\left(-\frac{s}{\tau_{decay}^{synapse}}\right) - \exp\left(-\frac{s}{\tau_{rise}^{synapse}}\right)\right) \tag{4}$$

where: $\tau_{decay/rise}^{synapse}$ are time constants representing the rise and fall of an individual synaptic PSP; A is the PSP's amplitude; $\varepsilon_{ij}^{synapse}$

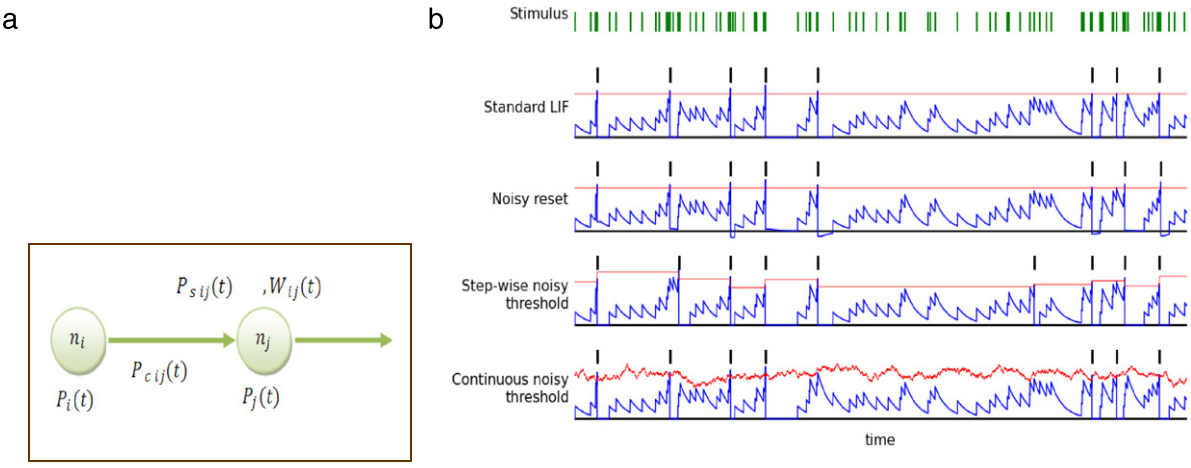


Fig. 11. (a) A probabilistic model of a neuron (from Kasabov, 2010); (b) different types of stochastic thresholds in a probabilistic neuronal model (Nuntalid et al., 2011).

Table 1
Neuronal action potential parameters and related proteins and ion channels in the computational neuro-genetic model of a spiking neuron: AMPAR—(amino-methylisoxazole-propionic acid) AMPA receptor; NMDR—(N-methyl-D-aspartate acid) NMDA receptor; $GABA_AR$—(gamma-aminobutyric acid) $GABA_A$ receptor, $GABA_BR$–$GABA_B$ receptor; SCN—sodium voltage-gated channel, KCN—kalium (potassium) voltage-gated channel; CLC—chloride channel.
Source: From Benuskova and Kasabov (2007).

Different types of action potential of a spiking neuron	Related neurotransmitters and ion channels
Fast excitation PSP	AMPAR
Slow excitation PSP	NMDAR
Fast inhibition PSP	$GABA_AR$
Slow inhibition PSP	$GABA_BR$
Modulation of PSP	mGluR
Firing threshold	Ion channels SCN, KCN, CLC

represents the type of activity of the synapse between neuron j and neuron i that can be measured and modeled separately for a fast excitation, fast inhibition, slow excitation, and slow inhibition (it is affected by different genes/proteins). External inputs can also be added to model background noise, background oscillations or environmental information. Genes that relate to the parameters of the neurons are also related to the activity of other genes, thus forming a GRN.

The PNGM is a probabilistic model (Kasabov, 2010)— Fig. 11(a), (b). In addition to the connection weights $w_{j,i}(t)$ parameters, three probabilistic parameters are defined:

- A probability $p_{cj,i}(t)$ that a spike emitted by neuron n_j will reach neuron n_i at a time moment t through the connection between n_j and n_i. If $p_{cj,i}(t) = 0$, no connection and no spike propagation exist between neurons n_j and n_i. If $p_{cj,i}(t) = 1$ the probability for propagation of spikes is 100%.
- A probability $p_{sj,i}(t)$ for the synapse $s_{j,i}$ to contribute to the $PSP_i(t)$ after it has received a spike from neuron n_j.
- A probability $p_i(t)$ for the neuron n_i to emit an output spike at time t once the total $PSP_i(t)$ has reached a value above the PSP threshold (a noisy threshold).

The total $PSP_i(t)$ of the spiking neuron n_i is now calculated using the following formula:

$$PSP_i(t) = \sum_{p=t_0,\ldots,t} \left(\sum_{j=1,\ldots,m} e_j f_1(p_{cj,i}(t-p)) \times f_2(p_{sj,i}(t-p)) w_{j,i}(t) + \eta(t-t_0) \right) \quad (5)$$

where: e_j is 1, if a spike has been emitted from neuron n_j, and 0 otherwise; $f_1(p_{cj,i}(t))$ is 1 with a probability $p_{cj,i}(t)$, and 0 otherwise; $f_2(p_{sj,i}(t))$ is 1 with a probability $p_{sj,i}(t)$, and 0 otherwise; t_0 is the time of the last spike emitted by n_i; $\eta(t-t_0)$ is an additional term representing decay in the PSP_i. As a special case, when all or some of the probability parameters are fixed to "1", the above probabilistic model will be simplified and will resemble the LIFM.

It has been demonstrated that a SNN that utilizes probabilistic neuronal model can learn better spatio-temporal patterns than traditional SNN with simple LIFM, especially in a nosy environment (Schliebs, Hamed et al., 2011; Schliebs, Mohemmed et al., 2011). The effect of each of the above three probabilistic parameters on the ability of a SNN to process noisy and stochastic information was studied in Schliebs, Kasabov et al. (2010) and Schliebs, Nuntalid et al. (2010).

Prior bioinformatics and neuroinformatics knowledge can be used when designing neurogenetic NeuCube models. For example, post-synaptic AMPA-type glutamate receptors (AMPARs) mediate most fast excitatory synaptic transmissions and are crucial for many aspects of brain functioning, including learning, memory and cognition (Henley, Barker, & Glebov, 2011). Kang et al. (2011) performed weighted gene co-expression network analysis to define modules of co-expressed genes and identified 29 such modules, associated with distinct spatio-temporal expression patterns and biological processes in the brain. The genes in each module form a gene regulatory network (GRN). Spiking activity of a neuron may act as a feedback and affect the expression of genes. As pointed out in Zhdanov (2011) on a time scale of minutes and hours the function of neurons may cause changes in the expression of hundreds of genes transcribed into mRNAs and also in microRNAs. This information helps to link together short-term, long-term and genetic memories of the NeuCube.

The anatomically comprehensive atlas of the adult human brain *trascriptome* (www.brain-map.org) is a rich repository of brain-gene data that will definitely trigger new directions for research and computational modeling of neurogenetic data (Hawrylycz et al., 2012). Gene expression patterns clearly distinguish structural and functional areas of the brain. Specific genes define specific functions in different areas of the brain. Specific genes relate to specific types of neurons and types of connections. For example, the gene expression level of genes related to dopamine-signaling (e.g. DRD5-DRD1, COMPT, MAOB, DDC, TH, etc.) is higher in areas of a normal subject brain that consist of neurons with larger number of dopamine regulated ion channels. These areas relate to dopamine-driven cognition, emotion and addiction. Such areas are: hippocampus, striatum, hypothalamus, amygdala, pons. If

these areas are activated normally it means that there is a sufficient dopamine signaling. In a diseased brain a non-activated area may suggest lack of dopamine.

Zilles and Amunts (2010) demonstrated that changes in the neurotransmitter receptor densities for important neurotransmitters coincide with Brodmann cytoarchitectonic borders. These neurotransmitter receptors are: $\alpha 1$, noradrenergic $\alpha 1$ receptor; $\alpha 2A$ noradrenergic $\alpha 2A$ receptor; AMPAR, α-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid receptor; GABAB, GABA (γ-aminobutyric acid)-ergic GABAB receptor; M2, cholinergic muscarinic M2 receptor; M3 cholinergic muscarinic M3 receptor; NMDAR, N-methyl-d-aspartate receptor.

The probabilistic parameters of the model have also their biological analogues and are controlled by specific genes (Kasabov, Dhoble et al., 2011; Kasabov, Schliebs et al., 2011). For example, the probability of a synapse to contribute to the post-synaptic potential after it has received a spike from a pre-synaptic neuron may be affected by different proteins, e.g.: proteins that affect the transmitter release mechanism from the pre-synaptic terminal such as the SNARE proteins (Syntaxin, Synaptobrevin II, SNAP-25), SM proteins (Munc18-1), the sensor Synaptotagmin, and Complexin, and also the proteins such as PSD-95 and Transmembrane AMPA receptor regulatory proteins (TARPs) in the post-synaptic site. The probability for a neuron to emit an output spike at the time when the PSP has reached a value above the threshold may be affected by different proteins, e.g.: density of the sodium channels in the membrane of the triggering zone. The time decay parameter in a LIFM may be affected by different genes and proteins depending on the type of the neuron. Such proteins are: transporters in the pre-synaptic membrane, the glial cells and the enzymes, which uptake and break down the neurotransmitters in the synaptic cleft (BAX, BAD, DP5); metabotropic GABAB Receptors; KCNK family proteins that are responsible for the leak conductance of the resting membrane potential.

Since the NeuCube structure maps brain structural areas through standard stereotaxic coordinates (e.g. MNI, Talairach, etc.) gene data can be added to the NeuCube architecture and this can be used for integrated brain-gene data machine learning. Gene expression data can be mapped to neurons and areas from a NeuCube as a fifth dimension, in addition to the 3 spatial and one temporal dimensions, so that a vector of gene expression can be allocated for every neuronal group. Some of these genes would be directly involved in the function of the PNGM of the neurons. Neurons can share same expression vectors in a cluster. This is possible because spatial locations of neurons in the SNNr correspond to stereotaxic coordinates of the brain (Hawrylycz et al., 2012). Furthermore, there are known chemical relationships between genes, or between groups of genes related to same brain function, forming gene regulatory networks (GRN) (Schliebs, 2005). Therefore, the fifth dimension in a SNNr can be represented as a GRN.

The relationship between genes and spiking neuronal activities can be explored through varying gene expression levels and performing simulations, especially when both gene and brain data are available for some special cognitive or abnormal brain states. Data related to expression of genes in different areas of the brain under different conditions are available from the Brain Atlas of the Allen Brain Institute and this makes it possible to build neurogenetic NeuCube models. Since the available brain and gene information is overwhelming in size and variety, it may be useful to organize it in Ontology (e.g.: Brain Ontology; Brain-Gene Ontology BGO (Kasabov, 2014).

5.5. Modeling cognition and emotion

Building artificial cognitive systems (e.g. robots, AI agents) that are able to communicate with humans in a human-like way has been a goal for computer scientists for decades now. Cognition is closely related with emotions. Basic emotions are happiness, sadness, anger, fear, disgust, surprise, but other human emotions play role in cognition as well (pride, shame, regret, etc.). Some primitive emotional robots or simulation systems have already been developed (e.g. see Meng, Jin, Yin, & Conforth, 2010). The area of affective computing, where some elements of emotions are modeled in a computer system, is growing (Picard, 1997).

The proposed NeuCube framework would make it possible to model cognition–emotion brain states that could further enable the creation of human-like cognitive systems. That would require understanding relevant brain processes at different levels of information processing. For example, it is known that human emotions depend on the expression and the dynamic interaction of neuromodulators (serotonin, dopamine, noradrenalin and acetylcholine) and some other relevant genes and proteins (e.g., 5-HTTLRP, DRD4, DAT), that are functionally linked to the spiking activity of the neurons in certain areas of the brain. They have wide ranging effects on brain functions. For example, Noradrenaline is important to arousal and attention mechanisms. Acetylcholine has a key role in encoding memory function. Dopamine is related to aspects of learning and reward seeking behavior and may signal probable appetitive outcome, whereas serotonin may affect behavior with probable aversive outcome. Modifying gene and protein expression levels of genes used in a particular NeuCube model would affect the learning and pattern recognition properties of that model. For example, the modification could cause connections and functional pathways to become stronger or weaker, which could be observed and further interpreted in terms of cognitive and emotional states. Some of these ideas have already been used by Mark Sagar in his model of 'Baby X' demonstrated at 'TEDxAuckland 2013' (also on YouTube).

5.6. Neurogenetic modeling of brain diseases

Based on prior information and available data, different NeuCube models can be created for the study of various brain states, conditions and diseases (Benuskova & Kasabov, 2007; Genes and Diseases) such as: epilepsy (Fiasché et al., 2012; Ghosh-Dastidar & Adeli, 2007; Mammone et al., 2012); schizophrenia; mental retardation; brain aging; Parkinson disease; clinical depression; stroke; AD (Kasabov, 2014; Kasabov, Dhoble et al., 2011; Kasabov, Schliebs et al., 2011; Morabito et al., 2012; Schliebs, 2005).

Once learned in a NeuCube model, the already known two-way links between spiking activity of the brain and gene transcription and translation, can be potentially used to evaluate gene mutations and the effects of drugs based only on recorded and learned STBD.

For example, one of the most studied brain disease is Alzheimer's Disease (AD). Gene expression data at a molecular level from both healthy and AD patients have been published in the Brain Atlas (www.brain-map.org). Interactions between genes in AD subjects have been studied and published (e.g. Schliebs, 2005). Atlases of structural and functional pathways data of both healthy and AD subjects have also been made available (Toga et al., 2006).

A possible scenario of studying AD through neurogenetic modeling in a NeuCube model will involve for example the GRIN2B gene. Data is available in the Allen Brain Atlas. It has been found that subjects affected by AD have a deficit of NMDAR subunit, with GRIN2B level decreased in the hippocampus. A GRN of NMDAR will be constructed as the synthesis of this receptor is possible only due to the simultaneous expression of different genes, which are responsible for the subunits that form the macromolecule. Such genes are: GRIN1-1a, GRIN2A, GRIN2B, GRIN2D and GRIN3A. A GRN of AMPAR genes can also be developed and the two GRNs connected in a NeuCube SNNr.

A similar approach can be applied for modeling data for Parkinson's disease, multiple sclerosis, stroke and other brain diseases for which both molecular and STBD is available.

5.7. NeuCube as a generic tool for modeling temporal or spatio-temporal data across domain areas

This paper proposes a SNN architecture called NeuCube and how it can be used for modeling STBD. But the use of NeuCube is not restricted to STBD. Potentially, it can be used for modeling any temporal or spatio-temporal multivariable data. The efficiency of this modeling will depend not only on the parameters of the NeuCube, but also on the way the spike trains that result from the input data encoding are mapped into the SNNr and on its size. NeuCube can be potentially used for modeling environmental and climate data, process data and many more, for example: predicting establishment of harmful species based on climate data (see Schliebs, Kasabov et al., 2010; Schliebs, Nuntalid et al., 2010); individual prediction of stroke occurrence based on both personal and climate data (Barker-Collo et al., 2010); predicting risk of earthquakes based on spatio-temporal data from sites where that has already happened; discovering new patterns from radio-astronomy data, collected from many radio-telescopes (e.g. the SKA project—https://www.skatelescope.org/).

6. Conclusions

We have argued that the use of SNN and more specifically—the proposed NeuCube unifying computational architecture, allow for the integrative modeling of various STBD, including: structural and functional data, gene data, prior knowledge. This can open new opportunities for a better understanding of STBD. It can also lead to a better accuracy achieved for classification and pattern recognition tasks. A NeuCube model can be used as associative memory to predict brain events.

Many interesting questions can be addressed in the future, including: encoding and mapping of both stimuli and STBD data into one NeuCube model; encoding and mapping of both genetic data and STBD into one NeuCube model; evaluating the information capacity of a NeuCube architecture and in particular—its capacity as associative memory; dynamic multidimensional visualization of a NeuCube activity including gene expression data; using NeuCube for finding causal links between high frequency data (EEG/MEG), low frequency data (fMRI) and gene data.

Potential practical applications would include: personalized BCI (Lotte et al., 2007); neuro-rehabilitation robots (Wang, Hou, Zou, Tan, & Cheng, 2008); neuro-prosthetics (Nicolelis, 2012); control and navigation of wheelchair (Craig et al., 2007); cognitive and emotional systems; affective computing; games; neuro-economics; personalized prognostic systems (Kasabov et al., 2013). The study of *creativity* could be enhanced with the use of this modeling paradigm (Kasabov, 2014).

The implementation of a NeuCube model, based on the probabilistic neurogenetic model of a neuron with four types of synapses and probabilistic parameters, in a neuromorphic chip (Indiveri et al., 2009, 2011, 2010) and in a SpiNNaker high performing SNN system of thousands and millions of neurons will boost the application of the NeuCube architecture across domain areas. That would allow for example to build neuromorphic systems that can learn continuously from data, obtained from fast spike-based sensors (e.g. silicon retina; silicon cochlea; touch and smell sensors, etc.) and the creation of fast, accurate and energy efficient systems for large streams of data.

Future directions include the development of systems for modeling and pattern recognition of spatio-temporal data across many areas of application as discussed in Section 5.7.

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Appendix. From Koessler et al. (2009)

Anatomical locations of international 10–10 EEG cortical projections into Talairach coordinates. Same coordinates are used in a SNNr of a NeuCube model.

EEG Talairach coordinates Gyri Brodmann Area.

Chan. *x* avg (mm) *y* avg (mm) *z* avg (mm)

FP1 −21.2 ± 4.7 66.9 ± 3.8 12.1 ± 6.6 L FL Superior frontal G 10
FPz 1.4 ± 2.9 65.1 ± 5.6 11.3 ± 6.8 M FL Bilat. medial 10
FP2 24.3 ± 3.2 66.3 ± 3.5 12.5 ± 6.1 R FL Superior frontal G 10
AF7 −41.7 ± 4.5 52.8 ± 5.4 11.3 ± 6.8 L FL Middle frontal G 10
AF3 −32.7 ± 4.9 48.4 ± 6.7 32.8 ± 6.4 L FL Superior frontal G 9
AFz 1.8 ± 3.8 54.8 ± 7.3 37.9 ± 8.6 M FL Bilat. medial 9
AF4 35.1 ± 3.9 50.1 ± 5.3 31.1 ± 7.5 L FL Superior frontal G 9
AF8 43.9 ± 3.3 52.7 ± 5.0 9.3 ± 6.5 R FL Middle frontal G 10
F7 −52.1 ± 3.0 28.6 ± 6.4 3.8 ± 5.6 L FL Inferior frontal G 45
F5 −51.4 ± 3.8 26.7 ± 7.2 24.7 ± 9.4 L FL Middle frontal G 46
F3 −39.7 ± 5.0 25.3 ± 7.5 44.7 ± 7.9 L FL Middle frontal G 8
F1 −22.1 ± 6.1 26.8 ± 7.2 54.9 ± 6.7 L FL Superior frontal G 6
Fz 0.0 ± 6.4 26.8 ± 7.9 60.6 ± 6.5 M FL Bilat. medial 6
F2 23.6 ± 5.0 28.2 ± 7.4 55.6 ± 6.2 R FL Superior frontal G 6
F4 41.9 ± 4.8 27.5 ± 7.3 43.9 ± 7.6 R FL Middle frontal G 8
F6 52.9 ± 3.6 28.7 ± 7.2 25.2 ± 7.4 R FL Middle frontal G 46
F8 53.2 ± 2.8 28.4 ± 6.3 3.1 ± 6.9 R FL Inferior frontal G 45
FT9 −53.8 ± 3.3 −2.1 ± 6.0 −29.1 ± 6.3 L TL Inferior temporal G 20
FT7 −59.2 ± 3.1 3.4 ± 5.6 −2.1 ± 7.5 L TL Superior temporal G 22
FC5 −59.1 ± 3.7 3.0 ± 6.1 26.1 ± 5.8 L FL Precentral G 6
FC3 −45.5 ± 5.5 2.4 ± 8.3 51.3 ± 6.2 L FL Middle frontal G 6
FC1 −24.7 ± 5.7 0.3 ± 8.5 66.4 ± 4.6 L FL Superior frontal G 6
FCz 1.0 ± 5.1 1.0 ± 8.4 72.8 ± 6.6 M FL Superior frontal G 6
FC2 26.1 ± 4.9 3.2 ± 9.0 66.0 ± 5.6 R FL Superior frontal G 6
FC4 47.5 ± 4.4 4.6 ± 7.6 49.7 ± 6.7 R FL Middle frontal G 6
FC6 60.5 ± 2.8 4.9 ± 7.3 25.5 ± 7.8 R FL Precentral G 6
FT8 60.2 ± 2.5 4.7 ± 5.1 −2.8 ± 6.3 L TL Superior temporal G 22
FT10 55.0 ± 3.2 −3.6 ± 5.6 −31.0 ± 7.9 R TL Inferior temporal G 20
T7 −65.8 ± 3.3 −17.8 ± 6.8 −2.9 ± 6.1 L TL Middle temporal G 21
C5 −63.6 ± 3.3 −18.9 ± 7.8 25.8 ± 5.8 L PL Postcentral G 123
C3 −49.1 ± 5.5 −20.7 ± 9.1 53.2 ± 6.1 L PL Postcentral G 123
C1 −25.1 ± 5.6 −22.5 ± 9.2 70.1 ± 5.3 L FL Precentral G 4
Cz 0.8 ± 4.9 −21.9 ± 9.4 77.4 ± 6.7 M FL Precentral G 4
C2 26.7 ± 5.3 −20.9 ± 9.1 69.5 ± 5.2 R FL Precentral G 4

C4 50.3 ± 4.6 −18.8 ± 8.3 53.0 ± 6.4 R PL Postcentral G 123
C6 65.2 ± 2.6 −18.0 ± 7.1 26.4 ± 6.4 R PL Postcentral G 123
T8 67.4 ± 2.3 −18.5 ± 6.9 −3.4 ± 7.0 R TL Middle temporal G 21
TP7 −63.6 ± 4.5 −44.7 ± 7.2 −4.0 ± 6.6 L TL Middle temporal G 21
CP5 −61.8 ± 4.7 −46.2 ± 8.0 22.5 ± 7.6 L PL Supramarginal G 40
CP3 −46.9 ± 5.8 −47.7 ± 9.3 49.7 ± 7.7 L PL Inferior parietal G 40
CP1 −24.0 ± 6.4 −49.1 ± 9.9 66.1 ± 8.0 L PL Postcentral G 7
CPz 0.7 ± 4.9 −47.9 ± 9.3 72.6 ± 7.7 M PL Postcentral G 7
CP2 25.8 ± 6.2 −47.1 ± 9.2 66.0 ± 7.5 R PL Postcentral G 7
CP4 49.5 ± 5.9 −45.5 ± 7.9 50.7 ± 7.1 R PL Inferior parietal G 40
CP6 62.9 ± 3.7 −44.6 ± 6.8 24.4 ± 8.4 R PL Supramarginal G 40
TP8 64.6 ± 3.3 −45.4 ± 6.6 −3.7 ± 7.3 R TL Middle temporal G 21
P9 −50.8 ± 4.7 −51.3 ± 8.6 −37.7 ± 8.3 L TL Tonsile NP
P7 −55.9 ± 4.5 −64.8 ± 5.3 0.0 ± 9.3 L TL Inferior temporal G 37
P5 −52.7 ± 5.0 −67.1 ± 6.8 19.9 ± 10.4 L TL Middle temporal G 39
P3 −41.4 ± 5.7 −67.8 ± 8.4 42.4 ± 9.5 L PL Precuneus 19
P1 −21.6 ± 5.8 −71.3 ± 9.3 52.6 ± 10.1 L PL Precuneus 7
Pz 0.7 ± 6.3 −69.3 ± 8.4 56.9 ± 9.9 M PL Superior parietal L 7
P2 24.4 ± 6.3 −69.9 ± 8.5 53.5 ± 9.4 R PL Precuneus 7
P4 44.2 ± 6.5 −65.8 ± 8.1 42.7 ± 8.5 R PL Inferior parietal L 7
P6 54.4 ± 4.3 −65.3 ± 6.0 20.2 ± 9.4 R TL Middle temporal G 39
P8 56.4 ± 3.7 −64.4 ± 5.6 0.1 ± 8.5 R TL Inferior temporal G 19
P10 51.0 ± 3.5 −53.9 ± 8.7 −36.5 ± 10.0 L OL Tonsile NP
PO7 −44.0 ± 4.7 −81.7 ± 4.9 1.6 ± 10.6 R OL Middle occipital G 18
PO3 −33.3 ± 6.3 −84.3 ± 5.7 26.5 ± 11.4 R OL Superior occipital G 19
POz 0.0 ± 6.5 −87.9 ± 6.9 33.5 ± 11.9 M OL Cuneus 19
PO4 35.2 ± 6.5 −82.6 ± 6.4 26.1 ± 9.7 R OL Superior occipital G 19
PO8 43.3 ± 4.0 −82.0 ± 5.5 0.7 ± 10.7 R OL Middle occipital G 18
O1 −25.8 ± 6.3 −93.3 ± 4.6 7.7 ± 12.3 L OL Middle occipital G 18
Oz 0.3 ± 5.9 −97.1 ± 5.2 8.7 ± 11.6 M OL Cuneus 18
O2 25.0 ± 5.7 −95.2 ± 5.8 6.2 ± 11.4 R OL Middle occipital G 18

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