

# **5th Nordic Neuroinformatics Workshop**

**27.10.2007**

**Life Science Center, Espoo, Finland**

# **ABSTRACTS**



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# **ORAL PRESENTATIONS**



# The Role of a Generic Information Model in Data Management

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Biological research is changing as evolving experimental methods and technologies bring more data from new data domains. This change offers unique possibilities to transform predominantly measurement centric research towards a more system centric research paradigm where multiple data domains are used together in the knowledge-building process. This allows a continuous refinement of the results through new observations. However, more strict data management also becomes necessary. First, the analysis of multidimensional data is possible only if metadata is available to provide context. Then, as new data is gathered, both versioning and data provenance become critical issues as well. Here, we focus only on the unified information model for biological data, a fundamental element of our data management and analysis infrastructure. The information model enables integration and modeling of evolving biological information and could be extended to include the field of neuroinformatics.

**Background :** Technological development has stimulated the emergence of explorative high throughput imaging and 'omic' science disciplines, which are large-scale efforts to document more or less dynamic events and to catalog biological component structures. Together with hypothesis-driven experimentation and clinical analyses, they can provide a sufficient base for the advancement of system centric research and its application to the understanding and treatment of complex neurological diseases. System centric research uses multiple data domains simultaneously and it has a specific need for highly dimensional data on dynamic processes. Since both data and methodologies change over time, data management issues are pivotal. We identify the unified information model as a key to efficient data management.

**Methods :** The Medicel unified information model is based on general systems theory and has a broad biological knowledge representation power. The information model (1) distinguishes different component structures through objective identification (2) represents the relations and connections between the components (3) binds quantitative measurement data to qualitative components and connection data. This unified information model can describe different layers of abstraction, from very general statements about populations or individuals through intermediate levels of tissues or cell interactions to highly detailed statements about molecular structures. The information model is also used to tag measurement data with captured and recorded metadata to provide context. Contextual information is essential for integrative analysis and plays a key role in the management of collaborative projects.

**Results :** The Medicel information model provides formalism to the description of biological systems, covering measurement data as well as contextual metadata. Using this model, we have integrated various proprietary data with about 20 large public databases covering components, systems or states. The generic aspect of the information model supports long term integration and precise description (modeling) of primary and derived data from public data sources alongside with patient and other data from the research organization and its collaborators. The comprehensive nature of the information model simplifies the development of analysis methodologies and software applications for the management of biological information and its processing into new knowledge and translation into diagnostics, treatment or prevention of disease.

## **GAMIXTURE+MRFSEG: A flexible tool for voxel classification**

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GAMIXTURE+ MRFSEG is a collection of open-source software tools written in C that implement a flexible and extendable voxel classification framework for brain imaging applications. The framework is based on a novel genetic algorithm based finite mixture model (GAMIXTURE) [1] and a standard 3-D Markov random field (MRF) based on the iterative conditional modes (ICM) algorithm (MRFSEG) [2]. The purpose is to 1) estimate the tissue class parameters by GAMIXTURE, and 2) classify voxels in a 3-D image by MRFSEG using these parameters. Ready made shell scripts implementing this pipeline are available.

The GAMIXTURE algorithm allows for fast and robust solution of the finite mixture model parameters, and is designed to handle explicit models of the partial volume effect (see [3]). The algorithm allows for constraining mixing parameters of the finite mixture models, which is likely to be useful when the mixture model matches only approximately to the true (unknown) distribution of image intensities. Each tissue class can either present a pure tissue type (e.g. white matter), or partial volume tissue type (e.g. mixtures of gray and white matter). From the end user's point of view, a key novelty is the use of a configuration file to control the number and the type of tissue classes, MRF parameters, and constraints for the finite mixture model. This allows for easy testing of different model alternatives for a tissue classification task. For example, the number of tissue classes, the MRF parameters, the constraints on the mixture model and how the partial volume effect is handled can be tuned without re-compiling. These programs as well as source-code are distributed without charge. They can be obtained from <http://www.loni.ucla.edu/Software> and <http://www.cs.tut.fi/~jupeto/software>.

[1] J. Tohka et al IEEE-TMI, 26(5):696 - 711, 2007.

[2] J. Besag, J R Stat Soc Ser B 48(3) 259 - 302, 1986.

[3] J. Tohka et al NeuroImage 23:84 - 97, 2004.

# Extracellular potentials from single-neuron and population activity

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Single-unit extracellular recordings have for decades given an experimental window into physiological properties of single neurons. The high-frequency part of local field potentials has provided a reliable means of recording action potentials, but the low-frequency part has proved difficult to interpret. The technology for large-scale electrical recordings using various types of multi-electrodes is rapidly improving, and there is a need for new methods for extraction of relevant information from electrical potential recordings<sup>1</sup>. In the talk results from several projects aimed at this are presented.

The extracellular potentials are in general due to complicated sums of contributions from transmembrane currents, and such potentials are calculated by a combination of (1) compartmental modelling providing the transmembrane currents following neural activity and (2) electrostatic forward modelling. In the first study<sup>2</sup> the influence of neural morphology and passive electrical parameters on the width and amplitude of extracellular spikes (action potentials) from individual neurons is investigated by combined analytical and numerical investigations of idealized and anatomically reconstructed pyramidal and stellate neuron models. The main results are:

1. All models yield a low-pass filtering effect, that is, a spike-width increase with increasing distance from soma.
2. A neuron's extracellular spike amplitude is seen to be approximately proportional to the *sum of the dendritic cross-sectional areas* of all dendritic branches connected to the soma. Thus, neurons with many, thick dendrites connected to soma will produce large amplitude spikes, and therefore have the largest radius of visibility.
3. The spike shape and amplitude are found to depend on the membrane capacitance and axial resistivity, but not on the membrane resistivity.
4. The spike-amplitude decay with distance  $r$  is found to depend on dendritic morphology, and is decaying as  $1/r^n$  with  $1 < n < 2$  close to soma and  $n > 2$  far away.

The second model study<sup>3</sup> investigates the validity of methods used to interpret linear (laminar) multielectrode recordings such as the *current-source density* (CSD) method and the *laminar population analysis* method. In computer experiments extracellular potentials from a synaptically activated population of about 1000 pyramidal neurons are calculated. The somas of the pyramidal neurons are located in a 0.4 mm high and wide columnar cylinder, mimicking a stimulus-evoked layer-5 population in a neocortical column. The main findings are:

1. *Current-source density* (CSD) analysis of the low-frequency part ( $< 500\text{Hz}$ ) of the calculated potentials (*local field potentials*, LFP) based on the *inverse CSD method*<sup>5</sup> is, in contrast to the *standard CSD method*<sup>6</sup>, seen to give excellent estimates of the true underlying CSD.
2. The high-frequency part ( $> 750\text{Hz}$ ) of the potentials (*multi-unit activity*, MUA) is found to scale approximately as the population firing rate to the power  $3/4$  and to give excellent estimates of the underlying population firing rate for trial-averaged data.
3. With 1000 neurons receiving synaptic inputs, LFP signals with similar amplitudes as in experimentally observed whisker-flick responses in rat somatosensory (barrel) cortex<sup>4</sup> are found. However, to obtain realistically sized MUA signals only about 40 of the 1000 neurons in the population must be assumed to fire an action potential during each stimulus presentation.
4. The MUA signal is found to decay much sharper with distance outside the columnar populations than the LFP.

<sup>1</sup>G Buzsaki, *Nature Neurosci* **7**, 446-51 (2004). <sup>2</sup>KH Pettersen and GT Einevoll, *Biophys J*, in press.

<sup>3</sup>KH Pettersen, E Hagen and GT Einevoll, *J Comp Neurosci*, in press. <sup>4</sup>GT Einevoll, KH Pettersen, A. Devor, I Ulbert, E Halgren, AM Dale, *J Neurophysiol* **97**, 2174-90 (2007). <sup>5</sup>KH Pettersen, A Devor, I Ulbert, AM Dale, GT Einevoll, *J Neurosci Meth* **154**, 116-33 (2006). <sup>6</sup>C Nicholson, JA Freeman, *J Neurophysiol* **38**, 356-68 (1975).

# Could single-cell measurements be predicted using MRI and mathematical modeling?

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Single-cell recordings in primate visual cortex have provided a detailed description of the area over which visual cortical neurons process information. As a result, models of visual neuron function are currently able to predict the activity of visual neurons as a function of stimulation area rather well [1]. Even biophysically mechanistic models are also emerging [2]. A typical observed pattern is summation up to a certain stimulus size (the grating summation field, GSF) and suppression from areas beyond the grating summation field.

Summation and suppression have been thoroughly assessed in human subjects. The centre-surround paradigm usually employed does not allow the quantitative analysis and modeling of the GSF and suppressive surround size. In this study, we used a stimulation that is often used in single-cell studies, drifting sine-wave gratings with no predetermined centre or surround. We measured fMRI-signal change as a function of grating size in 10 subjects.

The measured functions were qualitatively similar to those obtained from single-cell recordings. However, the sizes of the GSFs and the suppressive surrounds were consistently larger than those observed in primate neurons. To study the differences between single-cell method and fMRI, we made three modifications to one of the prevailing single-cell models [1].

- 1) Single cell was replaced with a 2.5 mm<sup>3</sup> voxel encompassing a number of neurons with receptive fields at different distances from the stimulus centre.
- 2) The 1-D summation reported in many single cell models was replaced by a more realistic 2-D summation in which case the number of evenly distributed receptive fields at a given eccentricity increases with eccentricity.
- 3) Subpopulations of neurons behaving in a non-typical way, which are conventionally excluded from single-cell analyses, were included.

These modifications bring the model to a much better agreement with our data, suggesting that models based on primate neurophysiology can be used to predict population responses as measured in fMRI and conversely that the fMRI can be used to predict single-cell responses.

[1] J.R. Cavanaugh et al., *Journal of Neurophysiology*. **88** 2530-2546 (2002)

[2] L. Schwabe et al., *Journal of Neuroscience*. **26** 9117-9129 (2002)

## Spike statistics for a high-conductance cortical network model

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My talk is based on earlier work by John Hertz in which he measured neuronal cross-correlations in a model network of a single cortical column [1]. With tonic input, the cross-correlations are extremely small, but the rapidly time-varying input induces much larger cross-correlation values, of about the same size as those found experimentally.

To examine the cross-correlations and higher-order statistics in greater detail, we have, in the work I will report here, binned the spike records into 10-ms bins and tried to find the distribution of the firing patterns across the neuronal population, ignoring temporal correlations. Following the idea of Schneidman et al [2], we try to model this distribution by an Ising model:  $P[S] = Z^{-1} \exp(\sum J_{ij} S_{ij} + h_i S_i)$ . We use both Boltzmann machine learning and inversion of Thouless-Anderson-Palmer equations to estimate the parameters  $J_{ij}$  and  $h_i$  [3]. We have performed these fits for groups of neurons of sizes between 10 and 160. The mean  $J_{ij}$  varies inversely with the size  $N$  of the group, while the standard deviation falls off much more slowly, approximately like  $N^{-1/6}$ . The  $J$ 's and  $h$ 's we find in these fitting procedures for the data with rapidly time-varying input appear to be qualitatively similar to those found by Schneidman et al for data from retinal networks. As in their work, it does not appear to be necessary to include higher order couplings in the model. However, the models obtained never appear to be in a spin glass phase for any of the sizes studied, in contrast to the finding of Tkačik et al [4] for the retinal data, who reported spin glass behaviour at  $N=120$ . Extrapolation from our results predicts spin glass behaviour only for  $N>5000$ , which is larger than the networks originally simulated. We also find that the distributions of  $J$ 's obtained when the original simulated network is driven tonically are quite similar to those with rapidly time-varying input, despite the big difference in the average cross-correlations in the two cases.

[1] J. Hertz, *paper in preparation* (2007)

[2] E. Schneidman *et al.*, *Nature* **440** 1007-1012 (2006)

[3] T. Tanaka *et al.*, *Physical Review E* **58** 2302-2310 (1998)

[4] G. Tkačik *et al.*, *arXiv:q-bio.NC/0611072 v1* (2006)

## Role of gap junctions in the striatum – effects on spiking activity and synchronization

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Recent experimental studies have found gap junctions between striatal fast spiking interneurons (FSN) [1]. Gap junctions in the striatum may cause synchronized spiking, as has been suggested for neocortical FSNs. To explore the quantitative effects of gap junctions on network activity and spike synchronization, we built a network model of FSNs where each FSN connects to 30 - 40% of its neighbours, as found experimentally [1,2]. Each FSN in the network is activated by simulated corticostriatal synaptic inputs [3], or by current injections.

Simulation experiments show that the proportion of synchronous spikes in coupled FSNs increases with gap junction conductance. However, the synchronization effects are moderate for experimentally estimated gap junction conductances [4]. Instead, the presence of gap junctions change the total number of spikes generated in the network. When the network FSNs are activated by current injections or synchronous synaptic inputs, the total number of spikes exceeds the number observed in networks without gap junctions. In contrast, in response to independent synaptic inputs FSNs coupled with gap junctions have a reduced number of spikes compared to FSN networks lacking gap junctions. These findings suggest a functional striatal organization in which FSN populations, coupled with gap junctions, function as collective input detectors which are especially sensitive to synchronized synaptic inputs received by the neighbouring cells in the network.

- [1] T Koos and J.M. Tepper, *Nat. Neurosci.* **2** 467-72 (1999)
- [2] J.M. Tepper *et al.*, *Trends in Neurosci.* **27** 662-669 (2004)
- [3] J Hellgren Kotaleski *et al.*, *J. Neurophysiol.* **95** 331-41 (2006)
- [4] M Galarreta and S. Hestrin, *PNAS* **99** 12438–12443 (2002)

# Stochastic modelling of neuronal excitability: modelling, simulation and parameter estimation

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Stochasticity plays a crucial role in shaping the dynamic behaviour of a neuron. Therefore, it must be taken into account when modelling, for example, the electroresponsiveness of a neuron. In this work, we present a way of incorporating stochasticity to the well-known Hodgkin-Huxley (HH) neuron model and a methodology for fitting the resulting stochastic differential equation model to irregular current-clamp data which contains subthreshold oscillations, spontaneous action potentials and clusters of action potentials, among other stochastic features. This kind of fitting and the use of irregular data have not been possible with the existing deterministic models and deterministic parameter estimation techniques.

We use a Bayesian estimation technique which relies on transforming the probability distributions of the estimation problem into distributions which are easy to sample. This transformation allows us to use Sequential Monte Carlo (SMC) approach when drawing samples from the desired posterior distributions. Based on these samples, a Maximum Likelihood (ML) estimation technique is utilised for producing ML estimates for the selected model parameters; these include maximal conductances of ionic currents and the intensity of random fluctuations in the current-clamp data.

We show that we are able to obtain accurate ML estimates for the selected model parameters based on the learning data. This data has been created with the stochastic HH model using different intensities of random fluctuations, and has been corrupted with different levels of measurement noise. The approximation of the likelihood function allows us also to study the sensitivity of the model parameters and the effects of the changes in their values to the model behaviour. The sharper the peak is in the likelihood, around the correct parameter value, the more sensitive is the model behaviour with respect to value of that parameter.

In conclusion, the presented method offers an attractive way to perform parameter estimation in situations where it has not been possible with the deterministic models and methods. Our approach also provides a comprehensive set of analytical tools to analyse model behaviour and the estimation problem, since the theory of stochastic calculus has been widely studied in the field of mathematics. However, our estimation method is, in its present form, rather computationally heavy. In the future, other methods of approximating the likelihood and speeding up the computations will be considered. In spite of the heavy computing, SMC methods offer a set of methods which are very flexible, relatively easy to implement, parallelisable, and applicable in very general settings.

# Cerebellar model tested in control of a load-carrying robot

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The cerebellum is an evolutionarily old structure that participates in the coordination of motor actions in a predictive manner. It has been suggested that motor learning in the cerebellum involves the development of new input-output associations depending on the context of the task [1].

In order to complete meaningful motor actions, we also need information about our current state provided by our visual, auditory, and somatosensory systems. Each of these modalities has dedicated cortical areas that process mainly information of a single modality. Multisensory regions include posterior auditory association cortex, superior temporal polysensory area, and ventral intraparietal sulcus [2], and subcortical structures such as superior colliculus [3].

We are using a neural model of the cerebellum to stabilize a simulated robot consisting of wheels and an upright body, analogous to an inverted pendulum. The cerebellum receives inputs from its motor (wheels) and sensory systems (position and tilt). It learns to associate and predict its own modified state with its motor actions using a hierarchical reflex as a teaching signal.

The complexity of the stabilization problem increases when the system needs to account for delays in the afferent inputs or changes in context, e.g. changes in the robot's dynamics when carrying a non-stationary load. The cerebellum is able to overcome the delays, but cortical, possibly multisensory, processing is needed to deduce the context. We aim at finding a representation of the context that the cerebellum can utilize in its stabilization task.

[1] D. Manzoni, *Cerebellum* **6** 24-37 (2007)

[2] C.E. Schroeder and J.J. Fox, *Cogn Brain Res.* **14** 187-198 (2002)

[3] J.C. Alvarado *et al.*, *J Neurophysiol.* **97** 3193-3205 (2007)

**POSTER  
PRESENTATIONS**



## Stochastic simulation of the function of IP<sub>3</sub> receptor using neuroinformatic tool

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Stochastic Engine for Pathway Simulation (STEPS) is a tool that extends the Gillespie stochastic simulation algorithm (SSA) with diffusion of molecules in realistic 3D geometries. In this work the effect of stochasticity was studied using this neuroinformatic tool. Transient rises in cytosolic calcium (Ca<sup>2+</sup>) concentration play a crucial role in formation of memory and learning. Particularly, Ca<sup>2+</sup> release from endoplasmic reticulum is important in induction of long-term depression (LTD) of synaptic activity, an electrophysiological phenomenon crucially related to learning of motor functions in cerebellum. Ca<sup>2+</sup> release is mediated by inositol-1,4,5-trisphosphate (IP<sub>3</sub>) receptors (IP<sub>3</sub>Rs) which are highly expressed in dendritic spines of cerebellar Purkinje cell. The small volume of the spine, as well as the small number of molecules involved, increase stochasticity (randomness) in the biochemical processes. In this study, the importance of stochasticity in simulation of the function of IP<sub>3</sub>R was examined. Even though several mathematical models have been presented for IP<sub>3</sub>R activation, most models have been deterministic until recent years. STEPS was used to produce the stochastic simulation results. We used the GENESIS/Kinetikit simulation environment as a reference to produce the deterministic simulation results. Based on an extensive literature review, two different IP<sub>3</sub>R models [1,2] were selected and implemented into STEPS and GENESIS/Kinetikit. In steady-state conditions, no difference was seen between deterministic and stochastic simulations and both models reproduced well the classical bell-shaped curve of open probability. In dynamic simulations, the time evolution of cytosolic Ca<sup>2+</sup> concentration was studied. We found that there was a significant difference between deterministic and stochastic simulation results when using small initial concentration of Ca<sup>2+</sup> or IP<sub>3</sub>. This effect was seen with both models. Therefore, deterministic simulations of IP<sub>3</sub>R activation may not produce realistic results under all conditions. The present work sets a foundation for developing structurally and functionally more relevant models for IP<sub>3</sub>R to reproduce correct time series behavior, and, ultimately, to model the processes related to LTD induction and information storage in brain.

[1] D. Fraiman and S.P. Dawson, *Cell Calcium* **35** 403-413 (2004)

[2] T. Doi *et al.*, *J. Neurosci.* **25** 950-961 (2005)

## **Three-dimensional atlas system for mouse and rat brain imaging data**

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Tomographic neuroimaging techniques allow visualization of functionally and structurally specific signals in the mouse and rat brain. The interpretation of the image data relies on accurate determination of anatomical location, which is frequently obstructed by lack of structural information in the data sets. Positron emission tomography (PET) generally yields images with low spatial resolution and little structural contrast, and many experimental magnetic resonance imaging (MRI) paradigms give specific signal enhancements but often limited anatomical information. Side-by-side comparison of image data with conventional atlas diagram is hampered by the 2-D format of the atlases, and by the lack of an analytical environment for accumulation of data and integrative analyses. We here present a method for reconstructing 3-D atlases from digital 2-D atlas diagrams, and exemplify 3-D atlas-based analysis of PET and MRI data. The reconstruction procedure is based on two seminal mouse and brain atlases, but is applicable to any stereotaxic atlas. Currently, 30 mouse brain structures and 60 rat brain structures have been reconstructed. To exploit the 3-D atlas models, we have developed a multi-platform atlas tool (available via The Rodent Workbench, <http://rbwb.org>) which allows combined visualization of experimental image data within the 3-D atlas space together with 3-D viewing and user-defined slicing of selected atlas structures. The tool presented facilitates assignment of location and comparative analysis of signal location in tomographic images with low structural contrast.

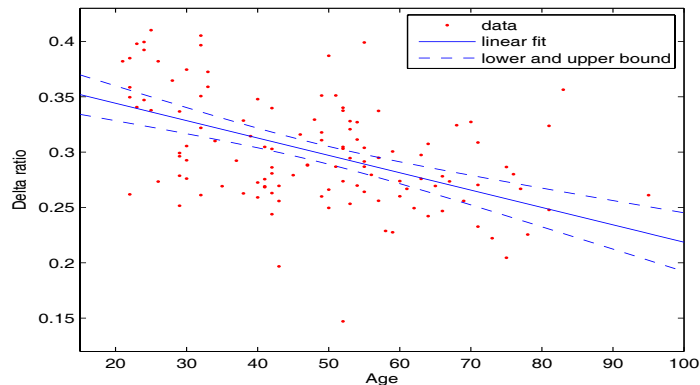
# Data mining of the SIESTA polygraphic sleep recording database

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The SIESTA polygraphic sleep recording database [1] was collected for the purposes of developing automatic sleep analysis further. It consists of overnight recordings of 16 polygraphic signals of over 200 subjects of various age groups recorded in several different sleep laboratories. The subjects were both normal and abnormal with documented diagnoses. On the day following the recording the subjects attended psychological and vigilance tests to which the polygraphic data can be correlated.

In this study the potential of the use of the database is shown through the analysis of the EEG delta band activity throughout the night as a function of the age. The spectral power of the EEG leads was calculated in the 0.5 – 3.5 Hz band in 120 subjects.



**Figure 1: Delta ratio as function of the age. Delta ratio is the ratio between delta band activity and total activity between 0 and 40 Hz. The value of the delta ratio is approximately  $0.375-1.569e-03 \cdot \text{age}$ .**

This result in Figure 1 shows an example of what neurological data can be extracted from this database. Although quality control was applied in the collection of the SIESTA data set, certain somewhat disturbing factors were impossible to eliminate from the data set. The sampling frequencies of the signals were not the same in all recording laboratories which means that the signal analysis methods have to be adapted to a few different sampling frequencies. The amplitude calibrations of the EEG signals were not available for the recordings of all participating laboratories and therefore care should be taken in making conclusions about absolute amplitude values using the data set. With these and some other limitations in mind, it is, however, possible to discover many new facts from sleep EEG and sleep polygraphy in general by using the SIESTA data set.

[1] Klösch, G., Kemp, B., Penzel, T., Schlög, A., Rappelsberger, P., Trenker, E., Gruber, G., Zeithofer, J., Saletu, B., Herrmann, W. M., Himanen, S. L., Kunz, D., Barbanoj, M. J., Röschke, J. Värri, A. & Dorffner, G. 2001. The SIESTA Project Polygraphic and Clinical Database. IEEE Engineering in Medicine and biology 20 3, pp. 51-57

## Role of different K<sup>+</sup> conductances in coding of visual information in cockroach photoreceptors

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Neuronal information is coded by action potentials (AP) and by graded potentials. Whereas most insects code visual information in their photoreceptors exclusively in graded potential, some seem to combine AP and graded signal coding. In the photoreceptor soma of the cockroach *Periplaneta americana*, concerted activation of light gated channels and voltage dependent K<sup>+</sup> channels forms the graded signal, which is proposed to be changed into an AP code in the photoreceptor axon [1].

The graded potential following a light stimulus is shaped by the voltage-dependent and -independent properties of the photoreceptor membrane. In flies the distribution of K<sup>+</sup> channels has been shown to be correlated with the lifestyle of the species [2]. Non-inactivating K<sup>+</sup> channels in photoreceptors of fast-flying animals enable coding of rapid changes in voltage responses, whereas slow-flying animals express inactivating K<sup>+</sup> channels which make the photoreceptor slower but save energy at the same time.

Overall, the function of the cockroach visual system seems different from other studied insects. One reason for this can be postulated to be an extreme adaptation to low light levels, i.e. small number of photons. This makes the photoreceptor responses inherently very noisy under normal operating conditions. When cockroach photoreceptors code information in both graded signals in the soma and AP signals in the long axon (vs. pure graded in most insects), is the role of different K<sup>+</sup> channels the same as it is in other studied species? To seek the answer to this question, we studied voltage- and light-dependent and passive properties of *Periplaneta* photoreceptors using patch clamp and intracellular recordings. Two distinctively different types of K<sup>+</sup> channels were found: a fast-activating K<sup>+</sup> conductance that inactivates, and a slow non-inactivating K<sup>+</sup> conductance.

The data obtained from electrophysiology was implemented in a mathematical model of the photoreceptor, which will be used to test the role of the two K<sup>+</sup> conductances with simulated light responses. Using the model and electrophysiology, we hope to obtain more knowledge about how visual information can be coded in low light environment.

[1] K. Heimonen *et al.*, *J Neuroscience* **26(52)** 13454-13462 (2006)

[2] S.B. Laughlin & M. Weckström, *J Comp Physiol A* **172** 593-609 (1993)

# Estimation of two-layer statistical model of natural images using score matching leads to complex cell properties

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We present a two-layer model of natural images that produces outputs similar to Complex Cells. Unsupervised learning using the novel method *Score Matching (SM)* is used to estimate the model. In contrast to our previous work, both layers are freely learned from the data. The second layer has a very sparse connectivity as predicted by the Hubel and Wiesel Model of primary visual cortex, and describes local dependencies between first layer features.

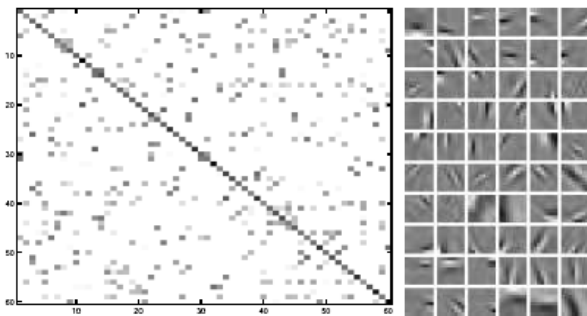
Score Matching is a locally consistent estimation method for non-normalized statistical models. By making use of the Score Function (the gradient of the log-probability), an estimation without knowledge of the partition function is possible. This is in contrast to Monte Carlo methods such as Contrastive Divergence, which rely on slow random sampling, or methods based on approximations.

We apply the method to a model of the form

$$\log p(\mathbf{x}|\mathbf{W}, \mathbf{V}) = \sum_i \sqrt{\mathbf{v}_i (\mathbf{W}\mathbf{x})^2} - \log Z$$

where  $x$  is a data vector,  $\mathbf{V}$  and  $\mathbf{W}$  are weight matrices and  $Z$  is the intractable partition function. The nonlinearities are applied element-wise. We can compute an objective function in terms of derivatives of the score function, which is then optimized by stochastic gradient descent.

When applied to natural image patches, the first layer converges to Gabor-type features. The second layer, however exhibits a very sparse connectivity, where each row has significant activity only for a few similar first layer features. These features that are pooled by the second layer have similar size, position and orientation, but differ in spacial frequencies. This local pooling is in contrast to similar two-layer models, in which the second layer describes more global structure. Similar results are obtained for a range of overcomplete model specifications and data dimensionalities.



*Left: The matrix  $\mathbf{V}$  with white representing zero and darker colors representing stronger activation. The sparse connectivity is evident. In the non-overcomplete case the number of units in the second layer is the same as in the first layer, so several output units share a similar receptive field.*

*Right: The features given by rows of  $\mathbf{W}$ . The features  $\mathbf{W}$  have been sorted according to subspaces as identified by  $\mathbf{V}$ .*

# Towards understanding the relationship between local luminance and contrast in natural images

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Previous research has suggested that visual systems process luminance and contrast separately (eg. [1,2,3]). This separate processing has been attributed to weak statistical dependencies between these two quantities in natural images [1,2].

We studied local luminance and contrast in natural images using established measures, and found that when these two quantities are examined as spatial channels, spatial across-channel dependencies are revealed [4]. These dependencies were not apparent in previous pointwise analyses. We present a few simple experiments demonstrating the dependency of luminance and contrast, and show that the luminance channel can be used to approximate the contrast channel. We also show that relying on higher-order statistics, Independent Component Analysis learns paired spatial features for luminance and contrast. These features are shown to share orientation and localization, with the filters corresponding to the features dependent in their outputs. Finally, we demonstrate that the found dependencies also exist in artificial images generated from a dead leaves model, implying that simple image phenomena may suffice to account for the dependencies.

Our results suggest that the separate processing of local luminance and contrast can not be attributed to their independence in natural images.

[1] V. Mante *et al.* Independence of luminance and contrast in natural scenes and in the early visual system. *Nature Neuroscience*, **8**(12): 1690—1697 (2005)

[2] R. A. Frazor and W. S. Geisler. Local luminance and contrast in natural images. *Vision Research*, **46**(10):1585—1598 (2006)

[3] R. Allard and J. Faubert. Double dissociation between first- and second-order processing. *Vision Research*, **47**(9):1129—1141 (2007)

[4] J. T. Lindgren *et al.*, Spatial dependencies between local luminance and contrast in natural images. *Submitted*.

## Cerebellar control for coordination

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The cerebellum is known to be responsible for fine-tuning and coordinating complex movements in mammals[1].

The learning algorithm implemented by the cerebellum is simple but powerful: if a reflex is triggered in response to an event, the system will associate the action of the reflex with the states that preceded the event. The next time a similar state is observed, the system will anticipate the reflex by performing the reflex action beforehand.

There have been two main branches of cerebellum research. On the one hand, more and more accurate biological models have been developed (e.g., [2]). On the other hand, simple functional models that exhibit the main features of the cerebellar algorithm have been developed to control physical systems (e.g., [3, 4, 5]). With suitably chosen reflexes and learning coefficients, a controller using the cerebellar algorithm learns to, for instance, keep a dynamically balanced wheeled robot upright[6].

We look at the case of an articulated, compliant multi-jointed robotic arm with delay. This is a very difficult system to control, because the dynamics of the different degrees of freedom are connected mechanically: moving one joint causes a force to be exerted on the other joints, which can easily lead to unstable and chaotic states. The cerebellar controller is able to learn to control this system by compensating for the position and motion of other joints proactively.

- [1] M. Ito. (2002), *Annals of the New York Academy of Sciences* **978**:273-288
- [2] D. Bullock, J.C. Fiala, and S. Grossberg (1994), *Neural Networks* **7**(6-7):1101-1114
- [3] M. Kawato, K. Furukawa, and R. Suzuki (1987), *Biol.Cybernetics* **57**:169-185
- [4] R. Smith (1998), Ph.D. thesis “Intelligent Motion Control with an Artificial Cerebellum”, Univ. of Auckland, New Zealand
- [5] A.G. Barto, A.H. Fagg, N. Sitkoff, and J.C. Houk (1999), *Neural Computation* **11**(3):565-594
- [6] H. Valpola (2006), In Proceedings of the Ninth Scandinavian Conference on Artificial Intelligence, Espoo, Finland, 2006, 135-142

# Stochastic modeling of neuronal signal transduction

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Mathematical modeling and simulation of neuronal signal transduction is receiving considerable attention due to the increasing availability of experimental knowledge and computing power. In addition to deterministic methods, several stochastic methods have been introduced to model chemical reactions. The use of stochastic methods is important because small numbers of chemical species are involved in intracellular environment and chemical reactions can occur stochastically. The problem with stochastic simulation is often the greater computation time compared to deterministic simulation especially when large-scale systems are simulated. On the other hand, computationally fast stochastic methods are often complicated to implement.

The main objective of this study is to find computationally fast and reliable stochastic methods that are implementable in modeling the time-series behavior of neuronal signal transduction. In this work, several deterministic and stochastic methods are studied: the law of mass action, the Michaelis-Menten equation, the chemical master equation, the Gillespie stochastic simulation algorithm, the chemical Langevin equation, and the chemical Fokker-Planck equation (see e.g. [1]). Several neuronal signal transduction networks are used as test cases in method development and comparative analyses. In addition to developing new methods, several simulation tools intended for describing the time-series behavior of biochemical systems are evaluated to gain further understanding of the suitability of the available methods (see e.g. [2]). As the main result of this work, five different kinds of Itô stochastic differential equation models [3], [4] are developed, implemented, tested, and benchmarked with the previously developed deterministic and stochastic methods. The best ones of the Itô stochastic differential equation models are found to produce reliable time-series data, to be computationally several orders faster than the Gillespie stochastic simulation algorithm, and to overcome the problem of obtaining negative values in contrast to the chemical Langevin equation [4], [5].

In summary, this work will have an impact on how the development of stochastic methods, and subsequently the development of simulation tools, will evolve in the field of neuroinformatics in future.

- [1] D. T. Gillespie, *Annu. Rev. Phys. Chem.* **58** 35-55 (2007)
- [2] E. Mäkiraatikka *et al.*, *Proc. 2nd Conf. on Found. of Systems Biol. in Eng. (FOSBE 2007)* 171-176 (2007)
- [3] T. Manninen *et al.*, *Neurocomputing* **69** 1066-1069 (2006)
- [4] T. Manninen *et al.*, *Comput. Biol. Chem.* **30** 280-291 (2007)
- [5] T. Manninen *et al.*, *Proc. IASTED Int. Conf. Comput. and Systems Biol. (CASB 2006)* **540** 89-94 (2006)

## Non-AMPA and non-NMDA bursts in cultured cortical networks

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Cortical neurons cultured on microelectrode arrays provide a simplified, yet feasible, platform to explore general information processing properties and plastic interactions in the nervous system [1,2]. After four weeks *in vitro*, cultured neurons have formed a mature network, where 90% of the electrical activity resides in series of spikes termed bursts. The bursts are relevant for plasticity and information transfer within neuronal networks, but the mechanisms behind bursting are not fully known [2]. In order to model, control, and understand bursting and its impact on information processing in neuronal networks, it is essential to decompose activity of the network. Here we apply increasing concentrations of glutamatergic AMPA and NMDA ion channel antagonists (NBQX and APV, respectively) to mature cultured cortical networks grown on microelectrode arrays to identify excitatory components necessary for producing and shaping bursts.

We analyzed antagonist induced changes in spiking, single channel bursts, and bursts occurring synchronously across the network. AMPA -channel blockage resulted in a binomial distribution of the number of spikes in a burst and tuned the precision of intervals between the bursts. The network-wide burst intervals were also binomial with two distinct regimes of 2 and >20 seconds. When NMDA -channels were blocked, the bursts shortened dose-dependently. The inter-burst intervals and the network-wide burst intervals were wider distributed in time and the network-wide burst counts reduced 3-fold. Blocking both channels abolished bursting as well as most of the spiking activity. We conclude that both channel types affect bursting and that the blockade of neither of the channels alone is able to prevent bursting. Furthermore, our results suggest that NMDA -channel activation facilitates the formation of discontinuous clusters of network-wide bursts, whereas AMPA -channel activation plays a role in recurrent, short bursting, but cannot maintain the activation levels required for the synchronized network-wide bursts.

[1] G. Shahaf and S. Marom, *J. Neurosci.* **21** 8782-8 (2001)

[2] D. A. Wagenaar *et al.*, *BMC Neurosci.* **7** art. no. 11 (2006)

## Evaluation of Stochastic Simulation Tools for Neuronal Signaling

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Several stochastic simulation tools have been developed for studying cellular, e.g. neuronal, signaling systems. These systems consist of reactions involving minute quantities of molecules. Therefore, the dynamic time-series behavior of these signaling systems needs to be studied by stochastic means. We evaluate and compare simulation tools which utilize Gillespie stochastic simulation algorithm. The current state of development in this area is then studied by simulation of a test case.

First, existing simulation tools (altogether more than 110) are examined superficially. Then, freely downloadable stochastic simulation tools, which support Systems Biology Markup Language (SBML), are chosen for closer evaluation. Hence, simulation tools are selected due to three criteria. The tool: 1. Uses Gillespie stochastic simulation algorithm. 2. Is freely downloadable. 3. Supports SBML. Tools can be downloaded from <http://sbml.org/>.

As a test case for both qualitative and quantitative analysis of simulation tools we use gene expression/protein function hybrid model. The model describes the expression of the gene coding luciferase and the function of this enzyme. The model is derived from the models introduced by Kierzek *et al.* [1] and Yu. Brovko *et al.* [2]. We first implement the model to Mediceal Integrator, which is a modular software platform for biological and biomedical research and development. We also export the model to SBML format using Mediceal Integrator. By importing the SBML model to several simulation tools we analyze the properties of the tools. Also the outcome of the time-series simulation is statistically analyzed using the Kolmogorov-Smirnov test.

The results show that only three of the vast amounts of tools are capable of importing and simulating the selected test case in SBML format. In addition, the usage of the tools varies in user-friendliness and applicability. The outcome of the simulations does not differ statistically significantly between the simulation tools. Therefore, the user can freely select the tool according to the properties one wishes the simulation tool to have.

Considerable effort is presently invested in developing a better simulation tool. This can be seen e.g. from the number of available simulation tools. However, as our study shows, the interoperability between the tools is still poor. Even though SBML is one step toward efficient interoperability between the tools, a model can hardly be reused in a different tool. The future versions of XML for Computational Neuroscience (NeuroML) will interface with SBML. This will make it possible to incorporate the different types of cell signaling models already available in SBML format in the future versions of neuroinformatics tools.

- [1] A.M. Kierzek *et al.*, *J. Biol. Chem.* **276** 8165-8172 (2001)
- [2] L.Yu. Brovko *et al.*, *Biochem. (Moscow)* **59** 195-201 (1994)

# A model of cerebellar automation of voluntary basal-ganglia control

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Cerebellar learning can be roughly categorized as supervised learning, while reinforcement learning is used as a model of basal-ganglia function [1]. Basal-ganglia learn voluntary actions by trial and error [2], whereas cerebellum is among other things specialized in automation and fine tuning of motor control [3].

Cerebellum is often modeled as a feedback error learner, where the output signal of a non-adaptive feedback controller is used as a teaching signal for the adaptive feed-forward controller [4]. Biologically this teaching signal can be thought of as a *reflex*.

In this scheme, learning new tasks would require a new handcrafted reflex signal every time. Moreover, designing workable reflex signal becomes increasingly tedious with the growing task complexity. This can be circumvented by using a reinforcement learner to learn a coarse version of the required feedback controller from one-dimensional reward signal [5].

Here we use a basal-ganglia-style actor-critic algorithm [6], instead of a hardwired reflex, in concert with the cerebellar predictor. Addition of the cerebellar model can speed up the learning in a typically slow reinforcement based algorithm.

Actor-critic algorithms and cerebellar models have traditionally been studied separately (but see [5]). In a combined model, the role of cerebellum overlaps with the actor part of the reinforcement learning algorithm. Our goal is to learn, how the division of labor between the modules could be optimized.

[1] K. Doya (1999), *Neural Networks*. **12**(7-8):961-974.

[2] A. Graybiel (1995), *Curr. Opin. Neurobiol.* **5**(6):733-41.

[3] M. Ito. (2002), *Annals of the New York Academy of Sciences* **978**:273-288.

[4] M. Kawato (1997), *Biol. Cybern.* **57**(3):169-85.

[5] H. Kambara et al. (2004), *Proc. of the 26<sup>th</sup> Conference of the IEEE EMBS*: 486-489.

[6] R. Sutton & A. Barto (1998), *Reinforcement Learning: An Introduction*.

## Independent component analysis of neuromagnetic data reveals extrinsic and intrinsic cortical networks during natural stimulation

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Activation changes in the brain can be either extrinsic (stimulus-related) or intrinsic. To differentiate such oscillatory brain networks, we studied [1] the modulation of MEG signals in 4 subjects during an 8-min continuous sequence of visual, auditory and tactile stimuli in blocks of 6–33 s, presented in a random order. Cortical currents were first estimated by means of a cortically-constrained minimum norm method [2], following which their envelopes (in frequency bands of 1–4, 4–7, 7–13, 17–23 and 27–43 Hz) were subjected to spatial independent component analysis (ICA). ICA was performed both at the individual and group levels. Each obtained independent component (IC) represents a patch or network of cortical voxels co-varying in time [3]. To identify stimulus-related ICs from their time courses, we postulated an oscillatory response function (ORF), analogous to the canonical haemodynamic response function in fMRI data analysis. The ORF was obtained by a non-linear transformation of the stimulus sequence, and it consisted of amplitude suppression and rebound following stimulus onset and offset, respectively, each with a predefined time lag. For the frequency bands centered at 10 and 20 Hz, the temporal behavior of several ICs, including those enclosing MI, SI, V1/V2 and higher visual areas, were well predicted by the ORFs of the corresponding stimulus type. Several other ICs lacked any consistent stimulus-related modulation; these networks comprised regions in the temporal lobes, prefrontal cortex and posterior cingulate/medial parietal lobes of both hemispheres. Thus, ICA of the oscillatory brain signals, together with the *a priori* information embedded in the ORFs, effectively resolved extrinsic brain networks during a complex stimulation sequence. This approach also offers a handle to probe potentially intrinsic brain networks while the subject is not explicitly at rest.

[1] Ramkumar, Parkkonen, He, Raichle, Hämäläinen & Hari, *Society for Neuroscience, Abstracts* 2007.

[2] Dale *et al.*, *Neuron* **26** 55–67 (2000)

[3] Malinen *et al.*, *NeuroImage* 25 131–139 (2007)

# Independent Component Analysis of Multielectrode Field Potential Measurements from the Brain

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Observing independent functional neural populations (FUPOs) and the frequency contents of independent hippocampal signals, based on calculating independent component analysis (ICA) [1] on subsets of electrophysiological multielectrode field potential measurements (MFPMs) in a running window, is proposed. The method is demonstrated with an example with three concurrent measurements from the hippocampus of an anesthetized rat. Our method is described in detail in [2,3], and can be applied in analysis of any recordings of neural networks in which contributions from a number of neural populations are simultaneously recorded via a number of measurement points, as well in vivo as in vitro.

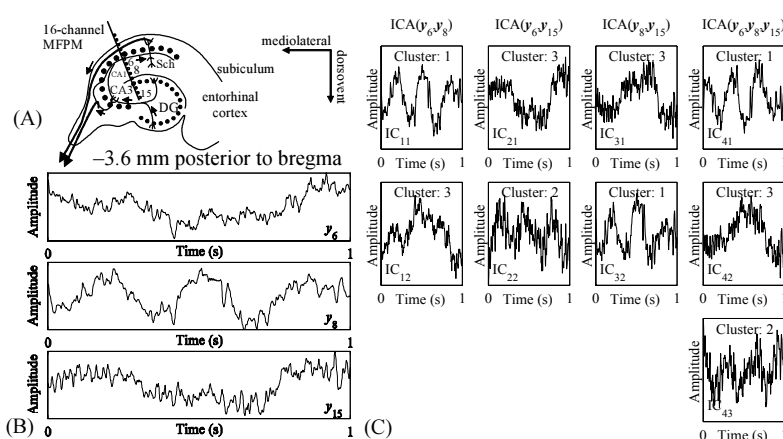


Fig. 1. (A) Schematic illustration of the rat hippocampus and the recording electrode with Channel 6 in Cornu Ammonis layer 1 (CA1) pyramidal cell layer, Channel 8 amongst Schaffer collaterals (Sch), and Channel 15 in dentate gyrus (DG). Open circles on the electrode shaft illustrate the channels used in ICA. (B) One second of MFPMs measured simultaneously via Channels 6, 8, and 15, denoted by  $y_6$ ,  $y_8$ ,  $y_{15}$ , respectively. (C) ICs from ICAs on all the subsets of the signals seen in (B). ICs from different ICAs are shown in columns. Also shown are the IC clustering results. The amplitude range is equal for all the subplots in (C).

The measurement locations are illustrated in Fig. 1A, with three measured signals shown in Fig. 1B. Independent components (ICs) from ICAs on all the subsets of the measurements in Fig. 1B are shown in Fig. 1C. The results illustrate that it is possible to find ICs from such multielectrode measurement data. Clustering the ICs from different ICA calculations, yields sets of similar signals, thus possibly making it possible to reason, which ICs are carried by which measured signals, thus at least partially overcoming the inherent ambiguity of ICA of unknown IC order. Here, one possible conclusion is that Cluster 1 ICs represent a Sch FUPO, Cluster 2 ICs CA1/DG FUPO, and Cluster 3 ICs a global FUPO. Thereafter, FUPO frequency content time evolution can be observed as in [2,3].

- [1] A. Hyvärinen, J. Karhunen, E. Oja, *Independent Component Analysis* (Wiley, NY, 2001).  
[2] J. M. A. Tanskanen, J. E. Mikkonen, M. Penttonen, *J. Neurosci. Meth.* **145**, 213–232 (2005). <http://dx.doi.org/10.1016/j.jneumeth.2005.01.004>  
[3] J. M. A. Tanskanen, J. E. Mikkonen, J. A. K. Hyttinen, M. Penttonen, in *Proc. 28th Annual Int. Conf. IEEE Engineering in Medicine and Biology Society* (New York, Aug.–Sept. 2006), pp. 727–730.

## Developing human SH-SY5Y neuroblastoma cell cultures for microelectrode array recordings and neural network modeling

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Various commercial microelectrode array systems (MEAs) have recently been developed for studies on excitable tissues and networks of cultured cells. Considering the newness of MEAs, their interdisciplinary integration into neuroinformatics creates an astonishing combination of two technologies that is one of a kind. In this survey, we have tested the suitability of different surface coatings, such as poly-L-lysine (PLL), poly-D-lysine (PDL), poly-ethyleneimine (PEI) together with laminin, and laminin alone for microelectrode array plates (Standard MEA, Multi Channel Systems®, Reutlingen, Germany, see [1]) to follow the growth and attachment of cultured human SH-SY5Y neuroblastoma cells. The cells have also been cultured on glass slides without any coating. Preliminary results show that the coating agents PLL and PDL with laminin are good alternatives to be used for attaching SH-SY5Y cells on MEA plates. However, in contrast to earlier publications, the SH-SY5Y cells were also able to attach to the MEA plates without any coating treatments.

Additionally, differentiation of the all-trans-retinoic acid (RA) treated SH-SY5Y cells has been followed both on the various treated MEAs and the glass slides. The success of the differentiation was verified with AM1-43 fluorescence staining, which detects vesicle exocytosis and endocytosis. The RA-differentiated cells were further depolarized with high potassium solution to study in detail the presence of synaptic vesicles in these cells [2]. The number of fluorescent dots in differentiated cells representing active pre-synaptic vesicles was compared to the number of dots in the non-differentiated cells on coated MEAs and non-coated glass slides. The differentiated and depolarized cells expressed more AM1-43 positive dots than the non-differentiated cells, on both MEAs and glass slides. The data obtained from MEA recordings on differentiated neural cell cultures can be used for modeling the connectivity of neural networks, the induction and maintenance of synaptic activities, and ultimately the learning process associated with biological neural networks.

[1] Microelectrode Array (MEA) User Manual, [http://www.mcs-download.com/download\\_data/manuals/MEA\\_Manual.pdf](http://www.mcs-download.com/download_data/manuals/MEA_Manual.pdf) **3/21** (2007)

[2] J.-R. Sarkanen *et al.*, *J. Neurochem.* **102** 1941-1952 (2007)

# Towards a digital atlas system for tracing axonal connectivity in the entire rat brain

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Knowledge about the presence, strength and topographical distribution of axonal connections in the brain is of fundamental importance for the understanding of normal function and pathological dysfunction of brain systems. Despite an overwhelming number of research reports, the architecture of axonal connections in the brain is far from fully elucidated, and detailed information about the spatial distribution or topographical organization of axonal terminal fields is not readily available from legacy data. A major problem in this respect relates to the narrow focus of most investigations, and the limited amount of data that can be extracted from published text, tables, or illustrations. Recently, there has been an increasing awareness of the need for accumulating comprehensive, spatially normalized neuroscience data in web-accessible atlas systems, and several online three-dimensional atlas systems are being developed for the rodent [1]. Inspired by these developments, we have undertaken the task of initiating a new line of development and research, with the ultimate goal of providing a platform for visualization and analyses of axonal connections throughout the entire brain from histological section data. We here present the first milestone of this project, a digital image repository that provides an extensive overview of anterograde and retrograde labeled axonal connections across the whole rat brain. In our example case, biotinylated dextran amine (BDA) was injected into a single whisker representation in the primary somatosensory cortex. Following sectioning and tissue processing to visualize BDA, coronal sections sampled at 100  $\mu$ m spacing were counterstained with Neutral Red to simultaneously display cytoarchitectonic boundaries. High-resolution mosaic images of the sections were assigned bregma-related stereotaxic coordinates and assembled in an image repository connected to a custom made viewer tool for interactive zooming and panning of the images. Our preliminary results demonstrate a wealth of anterograde and retrograde axonal connections, resembling the full pattern of previously described cortical and subcortical projections of the barrel cortex [2]. The present study serves as a precursor for a comprehensive histological database resource of global brain connections from which important questions pertaining to connectivity may be answered. Ultimately, the digital atlas system will allow a wide range of question to be posed, by in-depth use of individual data sets as well as combinations of different data sets, for discovery based research.

[1] Lein et al., *Nature* **445** 168-176 (2007)

[2] Welker et al., *Exp Brain Res.* **73** 411-435 (1988)

# Computational model of co-operating covert attention and learning

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This work combines neocortex-like attention and learning in one neural network. Learning tries to form useful representations for the complex entities in the world while attention selects the most relevant ones at each time instant. An essential feature of the model is that attention guides learning.

Desimone and Duncan [1] have proposed a biased-competition model for attention in the cortex. According to this model, global attention emerges from local decisions in all parts of the cortex. The decisions are biased with contextual information, such as top-down expectations. Neurophysiological evidence for the biased-competition model has been presented [2] and computational implementations showing that attention emerges in these kind of networks exist [3]. However, learning is not integrated into the behaviour of these models.

Experience of the animal is known to shape the representations in all levels of cortical hierarchies [4]. Learning occurs mostly from attended targets [5]. Thus, the representational capacity of the network is allocated for relevant objects and features.

Our model combines learning of invariant representations and the biased-competition model. At each time instant, each local part of the network tries to select information that is the most important for being represented. This selection helps in learning, too. If attention succeeds in focusing on coherent targets, learning associations and features becomes feasible, as different objects are separated by attention.

Simulation results show that the system is able to develop coherent selective attention. Neural populations are able to represent a single object even though the inputs contain multiple objects. At the same time, the network learns a hierarchy of invariances corresponding to the statistics of the input data.

- [1] R. Desimone and J. Duncan, (1995). *Ann. Rev. Neurosci.*, **18** 193-222 (1995)
- [2] J. H. Reynolds et al., *J. Neurosci.*, **19** 1736-1753 (1999)
- [3] G. Deco and R. T. Rolls, *Vision Research*, **44** 621-642 (2004)
- [4] C. Gilbert, C. et al., *Neuron*, **31** 681-697 (2001)
- [5] M. Ahissar and S. Hochstein, *Proc. Natl. Acad. Sci.*, **90** 5718-5722 (1993)

## **Functional Elements and Networks in MRI**

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Independent component analysis (ICA) is commonly used in fMRI studies to identify, in a blind manner, spatially independent functional elements of brain activity. With complex stimuli, or complex brain functions, individual elements may not be directly relatable to the stimulus goals. We propose a two-step approach for the analysis of functional magnetic resonance images, in the the context of natural stimuli. In the first step, elements of functional brain activity emerge, based on spatial independence assumptions. The second step exploits temporal covariation between the elements and given features of the natural stimuli to identify functional networks. The networks can have complex activation patterns related to common task goals.

# **Automatic human brain hemisphere segmentation in MRI including brain compartmental decomposition**

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Performance of the mid-sagittal plane for human brain hemisphere segmentation in MRI is restricted by the fact that human brain is never perfectly symmetric and the interhemispheric boundary is actually a curved surface. An obvious idea to solve this problem is to register a brain template into a specific brain image nonlinearly, and then produce a curved hemisphere segmentation surface for the target brain image using the transformation computed from the nonlinear registration. But the validity of this idea was poorly documented. A novel automatic method segmenting human brain hemispheres in 3D MRI, denoted as SB-PVestimation method, was developed by us in [1]. This was based on the shape bottlenecks algorithm [2] and a partial volume estimation approach [3]. It can produce much higher segmentation accuracy than the mid-sagittal plane based method, and is robust and insensitive to certain artifacts. However its segmentation performance for the brainstem is always problematic, and it can not separate the cerebral hemispheres from the cerebellum+brainstem. In this work, firstly we evaluated the validity of the nonlinear registration for brain hemisphere segmentation in MRI. Nonlinear registration provided by Statistical Parametric Mapping package (SPM) [4] was applied to 10 simulated T1-weighted MR images. The segmentation accuracy was compared with the mid-sagittal plane method and the SB-PVestimation method. The inferior segmentation performance demonstrated that the nonlinear registration was not valid for brain hemisphere segmentation in MRI. In the major part of this work, we improved the SB-PVestimation method by combining a novel brain compartmental decomposition method with it, which decomposed the brain mask into cerebrum, cerebellum and brainstem. This improved method was applied to segment cerebral hemispheres for clinical T1-weighted MR images of 18 schizophrenic subjects and 21 healthy controls. The volume size ratios between cerebral hemispheres, left and right parts of cerebral grey matter, and left and right parts of cerebral white matter were computed. The cerebral volume asymmetry was analyzed for schizophrenic subjects and healthy controls with the computed volume size ratios. Although no significantly meaningful findings were obtained for the cerebral volume asymmetry of schizophrenics, the high-quality segmentation performance of the improved SB-PVestimation method for every testing image proved its applicability and reliability in human brain asymmetry study based on MRI.

- [1] L. Zhao, J. Tohka, U. Ruotsalainen. SCIA07, LNCS, 4522: 581-590, 2007.
- [2] J. Tohka, A. Zijdenbos, A.C. Evans. NeuroImage 23(1):84-97, 2004.
- [3] J.-F. Mangin, J. Regis, V. Frouin. IEEE Work. MMBIA. 319-328, 1996.
- [4] K.J. Friston. Human brain function, Frackowiak et al. (Eds.), 2nd Edition, 2003.

