International Workshop on Neuroinformatics

- from Gene to Brain -

10 am - 5 pm May 13 (Sunday), 2001
at Ohkouchi Hall, RIKEN, Wako-city, Japan

Sponsored by RIKEN BSI in cooperation with
the NRV project under MEXT, Japan

International Workshop on Neuroinformatics
- from Gene to Brain -

It is our pleasure to welcome you at the first workshop on Neuroinformatics in Japan. Thanks to the support from RIKEN BSI and the NRV Project*, it has been made possible to bring together this excellent forum of researchers.

Recalling the origins - in a recent report from the OECD Megascience Forum the new field of neuroinformatics (NI) was defined as "the combination of neuroscience and information sciences to develop and apply advanced tools and approaches essential for a major advancement in understanding the structure and function of the brain". In the context of this and other international activities, the present workshop will discuss a possible future scope for NI related areas in the brain and nervous system functions, especially the visual function.

An emerging trend in modeling and understanding brain processes is that understanding brain at one level can be greatly enhanced by considering the process embedded in its context. Equally important is consideration of complexities of neuronal processes operating in much detailed sub-systems. The aim of this workshop is to bring together scientists with experimental, computational and theoretical approaches. Span across multiple research activities should provide an opportunity for interaction between methodological and phenomenological approaches.

Significant goal is to explore how abstractions at different levels are related, e.g. the pathways from molecular to system levels. Another critical goal is to discuss the disposition of the computational approach to support effective modeling across abstractions and sub-systems. It is our belief, that the very nature of this workshop shall provide a base-ground for fruitful discussions, expression of novel concepts and ideas, and expansion of further collaboration.

Speaking of 'the very nature' of this workshop, allow us mention a few remarks regarding the session organization:

- In the morning session, several friends from US, EU and Asia who are attending the OECD NI-WG meeting will actively participate in the workshop.
- In the afternoon, we start the session by reviewing the different "Japanese Activities in Brain Science" - from gene to brain.
- Then, we focus on NRV (Neuroinformatics Research in Vision) project, with activities consisting mostly of demonstrations of the tentative Visiome Platform.

In the name of organizers, we wish you have a great time. We sincerely hope you'll find the participation in this workshop exciting and useful for our future efforts.

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Program

Neuroinformatics: An enabling approach toward understanding nervous system function and structure through data sharing and modeling

Stephen H. Koslow
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Neuroinformatics combines research in neuroscience and informatics science and computational science to develop and apply advance tools and approaches needed to understand the brain. This includes databases, analytical tools and biological models that emulate the structural and functional systems in all aspects. The Human brain is exceedlingly complex and remains one of the greatest scientific challenges of this century. The Adult Human brain is made up of 100 billion nerve cells, with a million billion connections, 2 million miles of "wires", 1.5 liters in volume, 3.3 pounds in weight and 10 watts of energy. The brain regulates and controls our sensory, motor, and homeostatic systems including the cardiovascular, respiratory, food intake and metabolism, water balance, endocrine, reproductive, circadian and sleep systems. In addition it is responsible for our behaviors including, motivation and reward systems, and our cognitive capabilities including language and communication, emotions, cognition, learning, memory and attention. In many cases it performs all of these functions efficiently and simultaneously. Neuroscientists study the brain from many vantage points ranging from the molecular through the behavioral including all intervening levels. These studies are carried in out health and disease on humans and many species depending on the particular question under study.

In the last two decades the field of Neuroscience research has had a great increase in number of researchers (Fig 1) and in the tools utilized for studying the brain. These new tools allow for: the identification of complex anatomical connections; understanding the biochemistry, molecular and genetic mechanism serving brain structure and functions; capability to measure and visualize human brain function during activity; and the ability to monitor neural activity simultaneously in complicated networks of neurons. The impact of all of this is that to use these newer approaches neuroscientists have become more specialized resulting in a high degree of fractionation of the data into niche research areas, which is frequently published in very specialized journals (Fig 2). There is also occurring an exponential increase in data and information. The creation of complete primary data sets, and appropriate analytical tools on the World Wide Web will facilitate out ability to integrate scientific data and information into new knowledge.

While still incomplete we have learned much about the individual elements of the nervous system and their connectivity and molecular mechanisms and we continue to learn more each day adding to the incremental amount of data. Unfortunately this data is only published in a summary, or representative fashion in Journals and is not available for either reanalysis, mining or for use to understand or model integrative brain function. We have evolved into a field of research where there is now diverging specialization. The field of Neuroinformatics

Figure 1

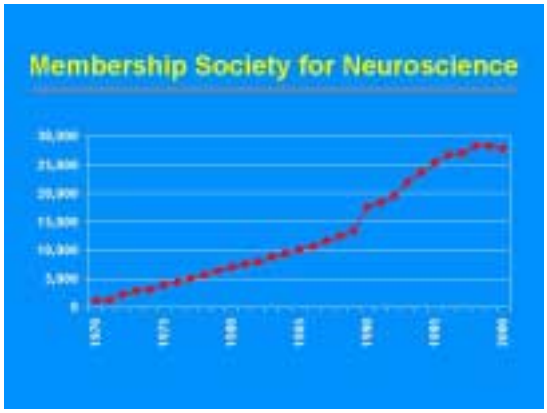

Figure 2

should enable the field to move toward converging integration (Figure 3)

In 1993 the United States Federal Government initiated the Human Brain Project in order to deal with the complexity of neuroscience data and its multiple dimensions, and multiple scales, which are highly interconnected and interdependent and dynamic. The goals of this research program are to create databases and analytical tools that will allow for this convergence through the sharing of primary published data. The databases

are to be distributed and made available on the World Wide Web for others to reanalyze, use in models or to mine to test their own new hypothesis without repeating the same experiments. In this manner it is perceived that we can make research more efficient and also obtain the goal of understanding the brain and all its complexity as an integrated organ.

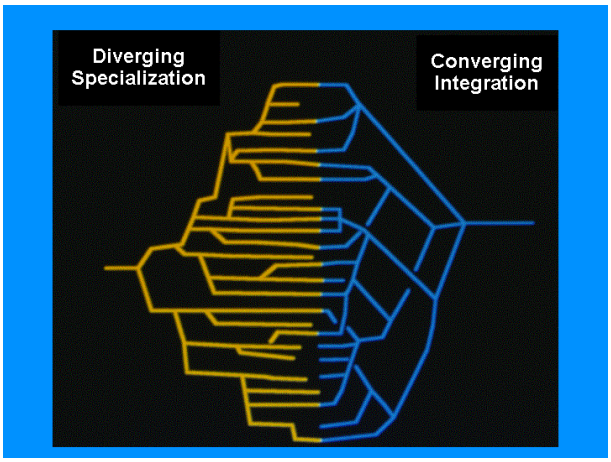

Figure 3

This presentation will review in more detail the complexity of data sets and types that are contributing to this rich and diverse information currently being produced by the Neuroscience community worldwide. In addition examples will be given of current distributed databases, analytical tools and models being developed under the US Human Brain Project. These projects range from the molecular and ultrastructural, through systems neuroscience and extend to behavior and imaging of human brain activity. There are also biologically relevant models being explored to model the activity of ion channels and the growth of neurons.

This enabling approach of Neuroinformatics offers much to the scientific community and it also challenges the current paridigm of research. These issues will be discussed in terms of the sociological, legal, ethical and evaluation and reward systems for scientists. Since Neuroscience research is worldwide a number of initiatives have been undertaken to make this a global activity. Information will be presented on the activities of the Office for Economic Cooperation and Development Global Science Forum Neuroinformatics Working Group as well as the European Community-United States Neuroinformatics Committee.

References

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Realistic modeling of the cerebellum

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Neuroinformatics includes the application of many different computing technologies towards understanding the brain. In this talk I will focus on the computational modeling aspect, describing some of our recent results in studying the operation of the circuitry of cerebellar cortex using the GENESIS and NEOSIM simulation environments. We have used a large-scale network simulation of the granular layer of cerebellar cortex to study the function of Golgi cells. This work is closely intertwined with our experimental work and I will highlight only a few main points. Because of its non-linear response characteristics it is unlikely that the Golgi cell operates as a gain controller as suggested in standard theories of cerebellar function, instead we think it controls timing of granule spikes through a synchronization of Golgi and granule cell populations. The parallel fiber excitation of Golgi cells is very important in this behavior and we have found evidence that natural stimuli evoke coronal beams of activated Golgi cells, as predicted by the network modeling. A morphologically and biophysically accurate compartmental model of Purkinje cells has been used extensively to study the role of its active dendrite in synaptic integration. Here I will focus on recent modeling results in the context of learning of a pattern recognition task using LTD of the parallel fiber synapse as proposed in classic theories of cerebellar learning. We have previously shown that short bursts of parallel fiber activity, as expected to occur during natural stimulation, cause a localized influx of calcium which amplifies the synaptic input in a location-independent manner. This also has a specific effect on the Purkinje cell firing pattern: it evokes a short burst of spikes, followed by a pause. When plasticity was induced we found that the only reliable effect of learning, as measured by a signal-to-noise ratio, was to decrease the length of this pause through a reduction of the pattern-evoked calcium influx. This result predicts that the net result of LTD-based learning will be an increase of Purkinje cell output and consequently a decrease of cerebellar output.

Brain Atlasing in Health and Disease

Arthur W. Toga
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UCLA School of Medicine, USA

This talk will review recent developments in brain mapping and computational anatomy that have greatly expanded our ability to analyze brain structure and function. The enormous diversity of brain maps and imaging methods has spurred the development of population-based digital brain atlases. These atlases store information on how the brain varies across age and gender, across time, in health and disease, and in large human populations. We describe how brain atlases, and the computational tools that align new datasets with them, facilitate comparison of brain data across experiments, laboratories, and from different imaging devices. The major methods are presented for the construction of probabilistic atlases, which store information on anatomic and functional variability in a population. Algorithms are reviewed that create composite brain maps and atlases based on multiple subjects. We have collected large cohorts of normal adults, developing subjects from childhood through adolescence and performed morphological studies of diseases such as Schizophrenia and Alzheimer's by computing structural atlases of these subpopulations. Results from these and related studies will be presented. We show that group patterns of cortical organization, asymmetry, and disease-specific trends can be resolved that may not be apparent in individual brain maps. Finally, we describe the creation of four-dimensional (4D) maps that store information on the dynamics of brain change in development and disease. Digital atlases that correlate these maps show considerable promise in identifying general patterns of structural and functional variation in human populations, and how these features depend on demographic, genetic, cognitive, and clinical parameters.

Measuring and modeling networks of human brain function using PET and MR neuroimaging, EEG, and statistical modeling techniques.

Gary F. Egan*
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Introduction

Neuronal processing in the human brain occurs over centimetre distances, for 100 msec time durations, is highly parallelised, and generally involves networks of interacting regions. This presentation will focus on measuring and modeling brain networks using positron emission tomography (PET) and magnetic resonance (MR) neuroimaging techniques, scalp electrical potential measures (electroencephalography , EEG), and statistical analysis and modeling techniques. Structural and functional MR images are able to volumetrically localise brain function to neuroanatomical structures with good spatial resolution (5 mm), but poor temporal resolution (>0.5 sec), whilst EEG has excellent temporal resolution (10 msec) but poor spatial resolution. Diffusion tensor MR imaging (DTI) can provide anisotropy maps of white matter tracts which may be able to provide neuronal connectivity constraints.

Using statistical probability maps obtained from PET activation single subject studies, weighted solutions of the fundamentally under-constrained EEG or MEG inverse problems of cortical electrical or magnetic activity can be obtained. These solutions can then be used with structured equation modeling techniques to develop dynamic models of joint haemodynamic and electrical neural activity, albeit at the gross neuroanatomical level. Present development work involves incorporation of DTI to further constrain the dynamic models from the inverse solutions. A short review of recent results and new developments in these areas will be presented.

Methods

PET actvation and EEG data have been acquired whilst a normal subject performed a working memory task, involving sequential presentation of a series of words, in two different conditions (fixed and variable target words). The regions differentially activated in the variable target condition compared to the control condition reflect areas specifically involved in the updating of working memory. The 128 channel EEG electrode positions were firstly aligned to each subject's structural MR image, which was segmented to create a head model consisting of four meshes representing the scalp, outer-skull, inner-skull and cortex respectively. The cortical mesh was used as a solution space for the EEG inverse solution, and cortical surface electrical current densities were calculated using a minimum-norm boundary element method. The solution space was weighted before the inverse calculation with the measured locations of the PET activation regions. The EEG inverse solution was calculated at different points in the EEG time series to produce a temporally resolved activation pattern.

Modeling of the dynamic activation pattern using structured equation modeling techniques together these neuroimaging techniques now enables neuroanatomically defined models of brain function and connectivity to be developed and tested.

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Activities on Brain Science Research in Japan

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A strategic target time table developed for the areas of “Understanding the Brain”, “Protecting the Brain” and “Creating the Brain”

		5 years from now	10 years from now	15 years from now	20 years from now
Understanding the Brain Elucidation of brain functions	Examples of advantages of understanding the brain	Understanding basic mechanisms of the brain	Understanding the brain system	Useful information on child rearing and education	Understanding human beings and the development of society
Protecting the Brain Elimination of brain disorders	Examples of brain disorders to be overcome	Encephalitis, drug dependence	Huntington’s disease, psychosomatic diseases, multiple sclerosis (MS)	Prevention of Alzheimer’s disease, Parkinson’s disease, cerebrovascular diseases	Control of the brain’s aging process, schizophrenia, bipolar disorder and other psychiatric disorders
Creating the Brain Development of brain-style computers	Examples of brain-style computers to be developed	Information-processing technologies working in fluctuating, uncertain and fuzzy environments	Active information-processing technologies based on associative memory and flexible recall intuitive thinking	Basis for developing an information-oriented society with intelligence	System which understands and responds to human intentions and emotions

Creating the Brain

development of brain-style computers

	5 years from now	10 years from now	15 years from now	20 years from now
Examples of brain-style computers to be developed	Information-processing technologies working in fluctuating, uncertain and fuzzy environments	Active information-processing technologies based on associative memory and flexible recall intuitive thinking	Basis for developing an information-oriented society with intelligence	System which understands and responds to human intentions and emotions
To establish and elucidate the principles involved in information processing in the brain	• Determination of the calculation principle for cognitive and motion control • Establishment of brain measurement technology and brain data analytical methods	• Determination of the calculation principle for decisions, memory and information integration • **Establishment of neuroinformatics**		
To develop brain-style devices and neural architecuture	• Development of memory neurochips with synapse modification (one million synapse scale) • To develop mutimodal intelligent recognition chips	• Development of a neural architecture for thinking mechanisms (100 million synapsescal) • Development of a memory-based machine with self-acquired algorithms	[Integration] • Development of computer systems equipped with intellectual, emotional and willing abilities • Design of novel creative information systems	• Development of human-friendly network-compatible neurocomputers that are symbiotic with human beings • Development of robot systems that support human intellectual life
To design brain-style systems for information generation and processing	• Development of brain-style dynamic memory systems • Development systems for planning and supervising adaptive control • Development of systems for thinking and decision making based on neural and chaotic dynamics	• Development of a self-organizing memory system with information integration • Development of a system for the integration of intuitive thinking a logical reasoning		

Brain Genomics: Cerebellar Development Transcriptome Project

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Recently, the first draft sequence of human genome, a vertebrate's DNA, has been come out. The human genome would be estimated to be 30,000 and 40,000 genes (as opposed to earlier estimates of 100,000 or so); only about twice the number needed to make a fruit fly, worm or plant, although it is not the final answer. However, the genes in humans are more complex, with more 'alternative splicing' generating a large number of protein products, which has important implications for the complexity of human gene expression. The brain is the complex and expensive organ in our body. A huge proportion of genes are thought to be involved in constructing, wiring up and maintaining it. Current estimates range from 30 to 40% or most. However, no one knows exactly how many genes are expressed and what all these genes do in the development, function, and dysfunction of the brain.

The development of the brain necessitates a variety of neuronal developmental events such as neuronal proliferation, migration, differentiation, dendrogenesis, axogenesis, synaptogenesis, cell death, all of which occur serially and precisely according to an established developmental schedule. Thus the brain is regarded as the product of a series of such developmental events. In terms of the genetic program that control the brain development, specific gene groups should be timely expressed on each developmental scene to conduct it, although many of the molecular mechanisms of brain development remain secret.

To decipher a "blueprint", that is, a molecular design based on genetic information, for the brain development, we focus on the postnatal development of mouse cerebellum. The mouse cerebellum is a good model system, since not only its cellular organization and neural circuit that develop postnatally through the series of developmental events are well studied, but also the mouse genome is expected to have a similar number and organization of genes as those in humans. We are attempting to elucidate the genetic program for the postnatal development of mouse cerebellum by extensively investigating gene groups differentially expressed during the developmental stages.

By using a 'fluorescence differential display' (FDD) technique, we searched genes specifically expressed at the developmental stages of mouse cerebellum ('transcriptome' analysis). From about 12,000 RT-PCRed FDD products analyzed, we detected about 2,000 as development-specific, and classified into three groups: 32%, down-regulated; 18%, transient; 50%, up-regulated. By cloning and sequencing all of these, we succeeded in obtaining 2,430 non-redundant clones. Homology search with DNA databases indicated that there were 675 known genes (27.8%), 327 homologous sequences (13.5%), 507 ESTs (expressed sequence tags) (20.9%, including 150 RIKEN mouse full-length cDNAs, 6.2%), and 921 novel sequences (37.9%). The number of genes differentially expressed peaks at the first and second postnatal weeks ('a wave in the complexity of gene expression'), when the active cellular and morphological events (such as cell proliferation and migration, axogenesis and dendrogenesis, synaptogenesis, foliation) are concentrated.

'DNA array' technology is one of the genome-wide, quantitative parallel measurements of expression levels for thousands of genes at a time in the post-genomic era. By application of oligonucleotide probe arrays (Affymetrix GeneChip), we monitored the expression profiles of genes during brain development. About 81.6% of the genes represented on the DNA chip (about 13,000 mouse genes) were expressed at any stages of mouse cerebella (from E18 to P56). Among these genes, about 8.7% (897 genes) showed apparent differential expression with more than two fold changes between the highest and lowest expression levels: 450 known genes, 71 unknown genes, 376 ESTs. In addition, about 7.8% of genes on the same chips were also differentially expressed during the embryonic brain development (from E12 to E18). Functional clustering of the known genes (such as CGDD, cell growth, differentiation & death; CSC, cell structure & communication; IMTN, intra/intercellular molecular transport & neurotransmission; ST, signal transduction; NNM, nucleotide & nucleic acid metabolism; TTPM, transcription, translation & protein modification; CLAM, carbohydrate, lipid, amino-acid metabolism) indicates that the differential gene expression is indeed finely correlated with the corresponding developmental stages.

At present, we are studying the *in situ* gene expression for identifying expressing cell-types. We are also attempting to systematize the genome-scale information concerning these spatio-temporal expression profiles of genes probably involved in the cerebellar development, and to generate a transcriptome database for the brain development that be made broadly available to the scientific community.

Overview of NRV (Neuroinformatics Research in Vision) Project

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One of the frontiers of the 21st century is the elucidation of the complicated and elaborate functions of the brain, such as sensory perception, recognition, memory, emotion, etc. The specialization and segmentation of advanced research topics make it very difficult to integrate related evidence so as to understand the functions of the brain. The introduction of information science technology in the analysis, processing, transmission, storage, integration, and utilization of information is indispensable.

Neuroinformatics is the new research approach for the 21st century, which fuses the experimental techniques with the mathematical and information science techniques. In particular, mathematical models are used to describe and integrate data and results obtained from a number of research fields. These mathematical models can be regarded as the platform that supports the simulation experiment indispensable for studying and understanding the function and mechanism of the human brain.

In general, Neuroinformatics should construct the support environment that integrates the databases devoted to various research fields with the data analysis techniques. This should promote research relying on mathematical models, and advance the comprehension and knowledge of brain neuronal systems. If the research of each conventional field is a warp, neuroinformatics is the woof which links them.

The NRV project (Japanese Neuroinformatics Research in Vision PI:Shiro Usui) is the first project in Japan started in 1999 under the Science and Technology Agency of Japan, aimed at building the foundation of neuroinformatics research. Because of the wealth of data on the visual system, the NRV project will use vision research to promote experimental, theoretical and technical research in neuroinformatics.

The first goal of the project is to construct mathematical models for each level of vision (single neuron, retinal neural circuit, visual function). The second goal is to build resources for neuroinformatics utilizing information science technologies and the research support environment which integrates them. The third goal is to realize a new vision device based on the brain-type information processing principle.

The NRV Project has the following research groups and their sub-themes (Details can be found at: http://www.neuroinformatics.gr.jp/):

Group1: Modeling a single neuron by mathematical reconstruction

Intracellular information processing mechanism between nerve cells are described by mathematical models. This group carries out the construction of "virtual nerve cell" by integrating knowledge obtained from molecular biology, biophysics, electrophysiology and anatomy, to produce models of single neurons. Such mathematical models can reproduce behavior of realistic neurons on a scale of molecular to simple neural circuit, spatially, and sub-millisecond to year, temporally. They are considered as the smallest functional units of a model family.

Study on the analysis and modeling of single cell signaling
Masahiro Sokabe (Nagoya University)
Creation and analysis of 3D biochemical reaction models for neuronal cells
Kazutoshi Ichikawa (Fuji Xerox Co., Ltd)
Synaptic integration in neuronal cells
Hiroyoshi Miyakawa (Tokyo University of Pharmacy and Life Science)
Research on dynamics of cultured neuronal networks
Akio Kawana (Takushoku University)
Mathematical model of insect brain neural network
Hidetoshi Ikeno (Himeji Institute of Technology)

Group2: Realization of virtual retina based on cell physiology

The retina is an ideal preparation for studying brain structure and function as well as neural signal processing in the brain, partly because it is a very accessible and self-contained part of the brain. Consequently there is a considerable amount of research results on all aspects of retinal visual information processing. A mathematical model of a retinal neural circuit will be constructed from neurophysiological

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experimental data and from the characteristics of single neurons obtained from G1. This retinal neural circuit will form the base for "virtual retina". Multiple circuits will be integrated into a mathematical model of the retinal-neural-circuit information processing mechanism that encompasses everything from the light energy conversion mechanism in a photoreceptor, which is the input, to the encoding mechanism of impulse sequence in a ganglion cell, which is the output cell of a retina.

Physiological studies on ion channels and synaptic mechanisms of retinal neurons
Akimichi Kaneko (Keio University)
Parallel information processing and neural coding in the visual system
Masao Tachibana (University of Tokyo)
A neuroinformatics study on the model of the vertebrate retina
Yoshimi Kamiyama (Aichi Prefectural University)

Group3: Study on the visual function by computational and systems' approach

Two kinds of information flow exist in the visual system: One part of the visual system processes information related to intrinsic object properties or discrimination of objects, such as color and shape. Another part is concerned with the discrimination of motion and position (spatial vision). This group evaluates the information processing mechanisms in both the object discrimination and motion perception, and constructs mathematical models for these visual functions.

A model study for self-organization of functional maps in visual cortex
Masanobu Miyashita (NEC)
Mathematical modeling of information integration for visual perception
Shigeru Tanaka (RIKEN)
A neurocomputational model for color perception
Shigeki Nakauchi (Toyohashi University of Technology)
Brain dynamics of visual perception and cognition
Hidehiko Komatsu (NIPS)
Neural network model for spatial recognition based on motion parallax
Susumu Kawakami (Fujitsu Ltd.)
Cognitive and computational approaches to non-rigid 3D object recognition
Shigeru Akamatsu (ATR)
Derivation of qualia from spatiotemporal activity patterns in neural networks
Yoshihide Tamori (Kanazawa Institute of Technology)
Neural network model for the mechanism of visual pattern recognition
Kunihiko Fukushima (Tokyo University of Electrocommunications)
Binocular information processing mechanism in the visual cortex
Izumi Ohzawa (Osaka University)

Group4: Realization of artificial vision devices and utilization of silicon technology for recording and stimulation

Movement detection is based on the spatio-temporal information processing in vision. It is one of the most basic and important functions of human and other living creatures. This study carries out research on the realization of new devices, circuits, and networks which fuse the visual information processing mechanisms of movement detection with semiconductor devices or circuit functions. It aims at the development of the analog-digital hybrid vision device with the ability that exceeds human's vision (for example, ultra-high speed). In order to record signals form nerve cells, or stimulate nerve cells, we utilize silicon technology and aim at developing multi-channel electrode array, which could be implanted on intact visual neural system.

Analog vision chip for early vision
Hiroo Yonezu (Toyohashi University of Technology)
Hybrid vision chips for intelligent image processing
Yoshihito Amemiya (Hokkaido University)
Fabrication of micro 3D sensor array with ultra-small Si wire electrodes and applications to measurement of retina cell potentials
Makoto Ishida (Toyohashi University of Technology)

Group5: Fundamental neuroinformatics research and development

The total support environment for experimental data analysis, model parameter estimation, simulations, etc. will be developed. The results of this project will be made available on the internet in a database (VISOME Platform) that integrates morphological and physiological knowledge, mathematical models, related studies, and references.

Study on the learning algorithms for neural data analysis
Andrej Cichocki (Riken)
Study on algorithms for analyzing brain and neuronal visual system
Yasunari Yokota (Gifu University)
Development of computer support environment for neuroinformatics
Keisuke Takebe (Nagaoka National College of Technology)
Construction of a neuroinformatics database for neuronal visual system
Isao Yamaguchi (Fuji Xerox Co., Ltd.)
Research and development on building the integrative support environment for modeling and simulation
Yasuo Fujii (DSP Technology CO., Ltd.)

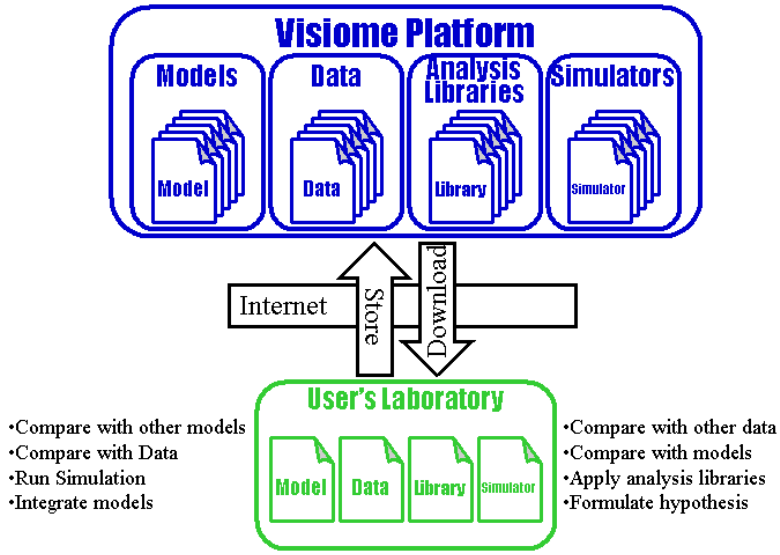
Visiome Platform: A Neuroinformatics Database for Neuronal Visual System

Isao Yamaguchi
Corporate Research Center, Fuji Xerox Co., Ltd.

Understanding the brain function requires integration of many and diverse information from level of molecule to level of neuronal networks. However, the huge amount of information is making it almost impossible for any individual researcher to make an integrated view of the brain. To solve this problem, it is needed to make useful neuroinformatics tools for information storing, maintenance and sharing. In the present study, we constructed a database system for neuronal visual system named “Visiome Platform” as a test bed for useful neuroinformatics tools.

The basic concept of the Visiome Platform is to make a web site integrating mathematical models, experimental data and related information. The Visiome Platform has two major characteristic features. First, it will allow researchers to reuse the models and experimental data in the database. Researchers can see how the models work or compare their own results with other experimental data, improve or integrate models, and formulate their own hypothesis into a model. Second, it will provide novel index system (Visiome Index) of research field of the visual system specially oriented to the model studies. The Visiome Index is based on neuronal and cognitive functions that are important targets of model studies. The Visiome Index will help researchers to understand the visual system from the aspect of visual functions and to construct models formulating their own hypotheses.

The Visiome Platform will provide more than just a database of models and data. Powerful analysis libraries and simulation tools will be also available from the system. The Visiome Platform will realize a virtual environment for global electronic collaborations by making available to researchers useful tools for simulation and data analysis with reusable models and data.



BLIND SIGNAL SEPARATION AND EXTRACTION IN APPLICATION TO BIOMEDICAL SIGNALS, IMAGES AND TIME SERIES ANALYSIS

Andrzej CICHOCKI

Summarry of OECD Talk

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ABSTRACT

In this paper we discuss various approaches and techniques to blind an semi-blind signal processing, especially dynamic independent component analysis (DICA), blind signal separation, blind signal extraction (BSE), single and multichannel blind deconvolution and equalization of source signals using state space models, especially when the measured sensor signals are contaminated by additive noise. Emphasis is given to an information-theoretical unifying approach, adaptive filtering models and development of simple and efficient associated on-line adaptive nonlinear learning algorithms. Extensive computer simulations have confirmed usefulness and good performance of the developed algorithms.

1. INTRODUCTION

Blind and semi blind signal processing, especially independent component analysis (ICA) and blind source separation is emerging field of research with many potential applications in neuroinformatics and brain science. A most general blind signal processing (BSP) problem can be formulated as follows. We observe records of sensors signals $\mathbf{x}(t) = [x_1(t), x_2(t), \ldots, x_n(t)]^T$ from an MIMO (multiple-input multiple-output) nonlinear dynamic system The objective is to find an inverse system, termed a reconstruction system, neural network or an adaptive inverse system, if it exists and is stable, in order to estimate primary input signals $\mathbf{s}(t) = [\mathbf{s}_1(t), s_2(t), \ldots, s_m(t)]^T$. This estimation is performed on the basis of the output signals $\mathbf{y}(k) = [y_1(t), y_2(t), \ldots, y_m(t)]^T$ and sensors signals as well as some *a priori* knowledge of the mixing system. Preferably, it is required that the inverse system should be adaptive, so that it has some tracking capability in non-stationary environments (see Fig.1). Instead of estimating the source signals directly, it is sometimes more convenient to identify an unknown mixing and filtering dynamic system first (e.g., when the inverse system does not exist or number of observation is less than number of source signals) and then estimate source signals implicitly by exploiting some *a priori* information and applying a suitable optimization procedure.

In many cases, source signals are simultaneously linearly filtered and mutually mixed. An aim is to process these observations so that the original source signals are extracted by adaptive system. The problems of separating and estimating the original source waveforms from the sensor array without knowing the transmission channels characteristics can be expressed briefly as a number of related problems: Independent Components Analysis (ICA), Blind Source Separation (BSS), Blind Signal Extraction (BSE) or Multichannel Blind Deconvolution (MBD) [1] - [13]. All these problems can be considered as semi-blind rather than completely blind because some a priori information about the model and sometimes about the sources are necessary to solve the specific problem efficiently.

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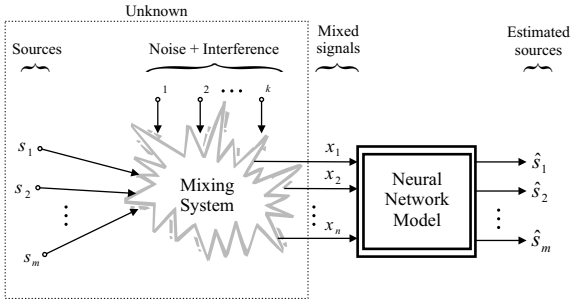


Figure 1: Block diagrams illustrating blind signal processing or blind identification problem

In semi-blind signal processing problems, the mixing and/or filtering processes of the unknown input sources $s_j(t)$ may have different mathematical or physical models, depending on specific applications.

In the simplest case, mixed signals $x_i(t)$ are linear combinations of unknown statistically independent, zero mean source signals $s_j(t)$, and are noise-contaminated. They are written as

$$\mathbf{x}(t) = \mathbf{H}\mathbf{s}(t) + \boldsymbol{\nu}(t), \tag{1}$$

where $\mathbf{H}$ is an unknown full rank mixing matrix.

While several recently developed algorithms have shown promise to solve this practical tasks, they may fail to separate on-line (non-stationary) signal mixtures containing both sub- and super-Gaussian distributed source signals, especially when the number of sources is unknown and changes dynamically over time. The problem of on-line estimation of sources in the case where the number of sources is unknown is relevant in many practical applications like analysis of biomedical signals (EEG/MEG) and the "cocktail party problem" where the number of source signals changes usually over time.

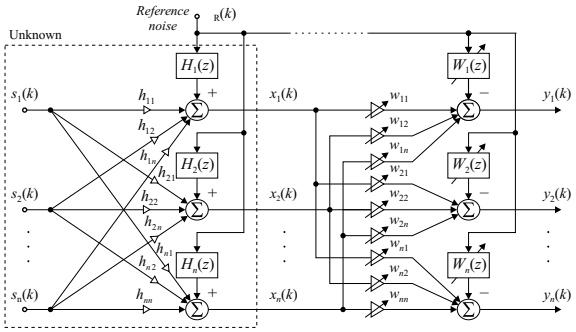


Figure 2: Illustration of noise cancellation and blind separation/ deconvolution problem

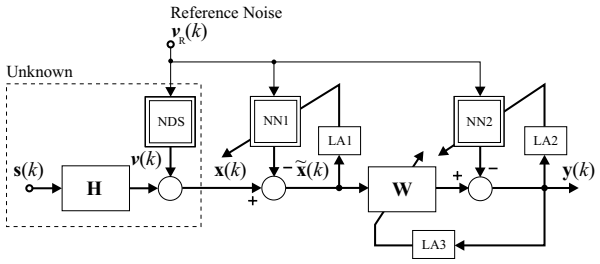


Figure 3: Block diagrams illustrating multistage nonlinear noise cancellation and blind source separation. An additive noise modeled by nonlinear dynamic system (NDS) and adaptive neural networks (NN1 and NN2); LA1 and LA2 mean learning algorithms performing LMS or back-propagation supervising learning rules and LA3 is learning algorithm for BSS

2. ROBUST INDEPENDENT COMPONENT ANALYSIS FOR NOISY DATA

As the estimation of a separating (demixing) matrix $\mathbf{W}$ (with $\mathbf{y} = \mathbf{W}\mathbf{x}$) and a mixing matrix $\widehat{\mathbf{H}}$ in the presence of noise is rather difficult, the majority of past research efforts have been devoted to the noiseless case where $\boldsymbol{\nu}(t) = \mathbf{0}$. One of the objective of this paper is to present several approaches and adaptive learning algorithms that are more robust with respect to noise than standard techniques or that can reduce the noise in the estimated output vector $\mathbf{y}(t) = \mathbf{W}\mathbf{x}(t)$.
In general, the problem of noise cancellation is difficult and even impossible to treat because we have $2n$ unknown source signals (n sources and n noise signals) and only n observation (see Fig. 2). However, in many practical situations, we can measure or model the environmental noise. Such noise is termed referenced noise (denoted by $\boldsymbol{\nu}_R$). The noise $\nu_R(k)$ may influence each sensor in some unknown manner due to environmental effects. Hence, effects such as delays, reverberations, echos, nonlinear distortions etc. may occur. It may be assumed that the reference noise is processed by some unknown dynamic system before reaching the sensors. In a simple case, a convolutive model of noise is assumed where the reference noise is processed by some FIR filters (see Fig. 2). In this case, two learning processes are performed simultaneously. An unsupervised learning procedure performs blind separation and a supervised LMS/RLS learning algorithm performs noise reduction [10].

Linear adaptive noise cancellation systems may not achieve acceptable level of cancellation of noise for some real world problems when interference signals are related the measured reference signals in a complex dynamic and nonlinear way. In such applications, especially in biomedical signal processing the optimum interference and noise cancellation usually requires nonlinear adaptive processing of recorded and measured on-line signals. In such cases we can use instead linear filters neural network models and train them, e.g. by back-propagation algorithms (see Fig 3). Such approach has been successfully applied to the elimination of noise under the assumption that the reference noise is available [10].

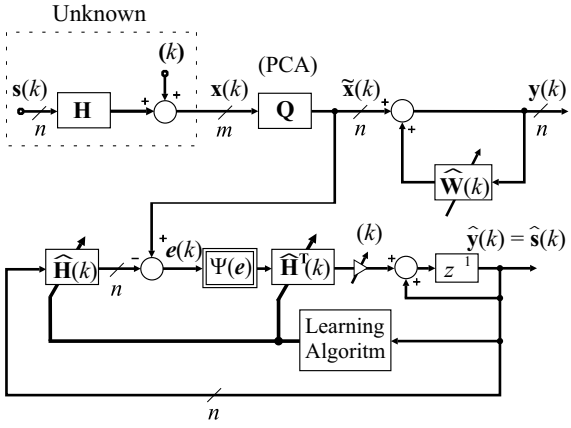


Figure 4: Architecture of Amari-Hopfield kind recurrent neural network for simultaneous noise reduction and the mixing matrix identification: conceptual discrete time model

3. AMARI-HOPFIELD NEURAL NETWORK FOR ICA/BSS

Alternative approach is to use recurrent Amari-Hopfield neural network shown in Fig. 4 and Fig. 5 [4].

Let us consider on-line estimation of the mixing matrix $\mathbf{H}$ rather than estimation of the separating matrix $\mathbf{W}$. It is easy to derive such a learning algorithm taking into account that $\widehat{\mathbf{H}} = \mathbf{W}^{+}$ and, for $m \geq n$, from $\mathbf{W}\widehat{\mathbf{H}} = \mathbf{W}\mathbf{W}^{+} = \mathbf{I}_n$ we have the simple relation [2]

$$\frac{d\mathbf{W}}{dt}\widehat{\mathbf{H}} + \mathbf{W}\frac{d\widehat{\mathbf{H}}}{dt} = \mathbf{0}. \tag{2}$$

Hence, we can obtain the learning algorithm [4, 2]:

$$\frac{d\widehat{\mathbf{H}}(t)}{dt} == -\mu_1(t)\widehat{\mathbf{H}}(t)][\mathbf{\Lambda}(t) - \mathbf{f}[\mathbf{y}(t)]\mathbf{y}^T(t)]. \tag{3}$$

We can replace the output vector $\mathbf{y}(t)$ by an improved estimate

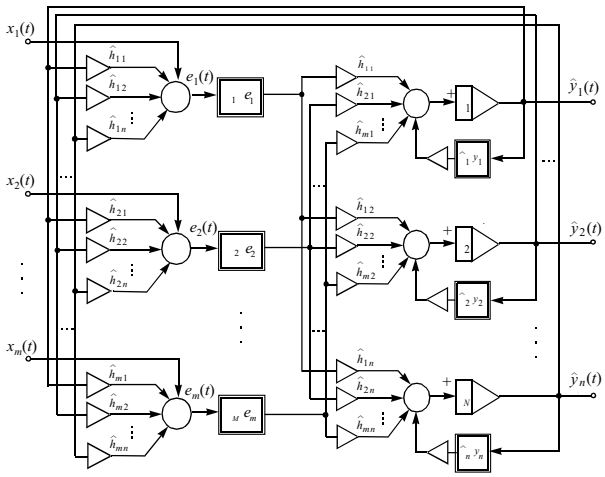


Figure 5: Detailed architecture of continuous -time Amari-Hopfield recurrent neural network with regularization

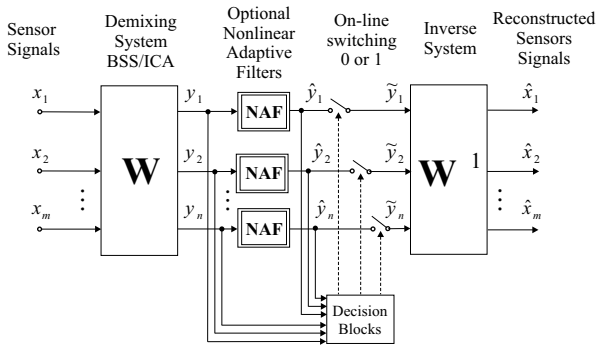


Figure 6: Conceptual models for cleaning multi-sensory (e.g. EEG/MEG) data using nonlinear adaptive filters and hard switches.

$\widehat{\mathbf{y}}(t)$ to derive a learning algorithm as

$$\frac{d\widehat{\mathbf{H}}(t)}{dt} = -\mu_1(t)\widehat{\mathbf{H}}(t)\left[\mathbf{\Lambda}(t) - \mathbf{f}[\widehat{\mathbf{y}}(t)]\widehat{\mathbf{y}}^T(t)\right] \tag{4}$$

and

$$\frac{d\widehat{\mathbf{y}}(t)}{dt} = \mu(t)\widehat{\mathbf{H}}^T(t)\,\mathbf{\Psi}[\mathbf{e}(t)], \tag{5}$$

or in discrete-time,

$$\begin{aligned}\Delta\widehat{\mathbf{H}}(k) &= \widehat{\mathbf{H}}(k+1) - \widehat{\mathbf{H}}(k) \\ &= \eta_1(k)\widehat{\mathbf{H}}(k)\left[\mathbf{\Lambda}(t) - \mathbf{f}[\widehat{\mathbf{y}}(k)]\widehat{\mathbf{y}}^T(k)\right]\end{aligned} \tag{6}$$

and

$$\widehat{\mathbf{y}}(k+1) = \widehat{\mathbf{y}}(k) + \eta(k)\widehat{\mathbf{H}}^T(k)\mathbf{\Psi}[\mathbf{e}(k)], \tag{7}$$

where $\mathbf{e}(k) = \mathbf{x}(k) - \widehat{\mathbf{H}}(k)\widehat{\mathbf{s}}(k)$ and $\mathbf{x}(k) = \widehat{\mathbf{x}}(k) + \boldsymbol{\nu}(k)$ and the optimal choices of nonlinearities $\Psi_i(e_i)$ depend on the noise distributions [4].

4. STANDARD PCA AND ICA/BSS APPROACHES FOR PRELIMINARY NOISE REDUCTION

One important advantage of PCA approach is that it enables not only reduction in the noise level, but also allows us to estimate the number of sources [10]. A problem arising from this approach, however, is how to correctly set or estimate the threshold which divides eigenvalues into the two subsets (signal and noise subspace), especially when the noise is large (i.e., the SNR is low).

Recently, it has been realized that ICA or at least combining of both techniques: PCA and ICA, is more appropriate for noise reduction and moreover such approach reveal underlying structure of signals better than PCA alone. Moreover, using ICA we can achieve better results in the sense that PCA use only second-order statistics, but ICA can estimate a better basis by taking into account higher-order statistics inherent in the data and allow to build nonlinear estimator instead of linear one. ICA algorithms can be also robust, what is very important for noise cancellation applications. ICA allows to separate sources $\mathbf{s}(t)$ based on observations $\mathbf{x}(t)$ using maximum *a posteriori* method that is dispose of *a priory* information problem and allows to realize blind scenario. Using ICA we can find independent components, which are undesirable and can be thought as noisy sources and eliminated.

Independent Component Analysis (ICA) and related methods like Adaptive Factor Analysis (AFA) are promising approaches for elimination of artifacts and noise from EEG/MEG data. However, most of the methods require manual detection and classification of interference components and estimation of cross-correlation between independent components and reference signals corresponding to specific artifacts [7, 9].

One of the challenging and open problems is how to automatically detect and eliminate noise and artifacts and classify independent 'brain sources'. The automatic detection and on-line elimination of artifacts and other interferences is especially important for long recordings, e.g. EEG/MEG recording during sleep.

A conceptual model for elimination of noise and other undesirable components from multi-sensory data is depicted in Figure 6. Firstly, ICA is performed using any robust algorithms (with respect to Gaussian noise) [4] by a linear transformation of sensory data as $\mathbf{y}(t) = \mathbf{W}\mathbf{x}(t)$, where vector $\mathbf{y}(t)$ represents independent components. However, robust ICA methods allow us only to obtain an unbiased estimate of demixing matrix $\mathbf{W}$, but due to memoryless structure they, by definition, can not remove the additive noise. This can be done using optional nonlinear adaptive filtering and nonlinear noise shaping. In the next stage, we classify independent signals $\hat{y}_i(t)$ and remove noise and undesirable components by switching corresponding switches "off" (see Fig. 6. Projection of interesting or useful independent components (e.g. independent activation maps) $\tilde{y}_i(t)$ back onto the sensors (electrodes) can be done by: $\hat{\mathbf{x}}(t) = \mathbf{W}^+\tilde{\mathbf{y}}(t)$, where $\mathbf{W}^+$ is the pseudo inverse of demixing matrix $\mathbf{W}$. In the typical case, when the number of independent components is equal to the number of sensor $\mathbf{W}^+ = \mathbf{W}^{-1}$.

It should noted that the uncorrelated principal components are ordered by decreasing values of their variances, while independent components (ICs) are typically extracted without any order. In this paper we propose to apply first ICA and next ordering the independent components (ICs) according to decreasing absolute value of their normalized kurtosis rather than their variances; since

the normalized kurtosis $\kappa_4(y_i) = \frac{E\{y_i^4\}}{E^2\{y_i^2\}} - 3$ is natural measure of Gaussianity of signals. Using $\kappa_4(y_i)$ we can easily detect and remove white (colored) Gaussian noises form raw sensory data. Optionally, we can use more robust nonlinear measures to detect and classify specific ICs.

One of such measure is the Hurst exponent H and associated fractal dimension $D = 2 - H$ parameter that characterize time series [7]. Hurst in 1965 develop the rescaled range (R/S) analysis for time series $y(k)$, $(k = 0, 1, 2, ...)$. Firstly, the range R defined as a difference between maximum and minimum "accumulated" values:

$$R(T) = \max_{1 \le k \le T} \{Y(k,T)\} - \min_{1 \le k \le T} \{Y(k,T)\}, \tag{8}$$

where

$$Y(k,T) = \sum_{k=1}^{T} \{y(k) - < y(k) >\},$$

and secondly, standard deviation S estimated from the observed value $y(k)$

$$S = \left(\frac{1}{T} \sum_{k=1}^{T} [y(k) - < y(k) >]^2 \right)^{\frac{1}{2}}. \tag{9}$$

Hurst found that the ration R/S is very well described for large number of phenomena by the following nonlinear empirical relation:

$$\frac{R}{S} = (cT)^H, \tag{10}$$

where T is the number of samples, c is some constant (typically $c = \frac{1}{2}$) and H is the Hurst exponent in the range from 0 to 1. With this definition a Hurst exponent of value 0.5 correspond to a time series that is a truly random (e.g. Brown noise or Brownian motion). A Hurst exponent of $0 < H < 0.5$ shows so called anti-persistent behavior, e.g. white uniform distributed noise has $H \cong 0.15$. At limit of $H = 0$ the time series must change direction every sample. On the other hand, a Hurst exponent of $0.5 < H < 1$ describes a temporally persistent or trend reinforcing time series. At limit a straight line with non zero slope will have a Hurst exponent of 1.

It was found by many researchers that a Hurst exponent H has value $0.70 - 0.76$ for many natural, economic and human phenomena. Usually independent components $\hat{y}_i(t)$ can be considered as random or temporally independent processes if $H \le 0.6$. These components can be easily eliminated by open of switches in corresponding channels (see Figure 6). From the other hand, the most interesting or desirable components have a Hurst exponent in the range $H = 0.70 - 0.76$. These components can be projected by pseudo inverse matrix $\mathbf{W}^+$ so corrected sensor signals enable us to localize corresponding "interesting" brain sources with temporal structure. Furthermore, we have found by extensive computer experiments that some artifacts like eye blinking or heart beat artifacts have characteristic value of H, so they could be automatically identified and removed from sensor signals on basis of value of a Hurst exponent.

4.1. Simulation results

In this section we present the exemplary results of a computer simulations. We performed simulations both for artificially generated noisy signals as well as real-world single trial ECG with 8 electrodes and EEG/MEG data with 21/149 sensors.

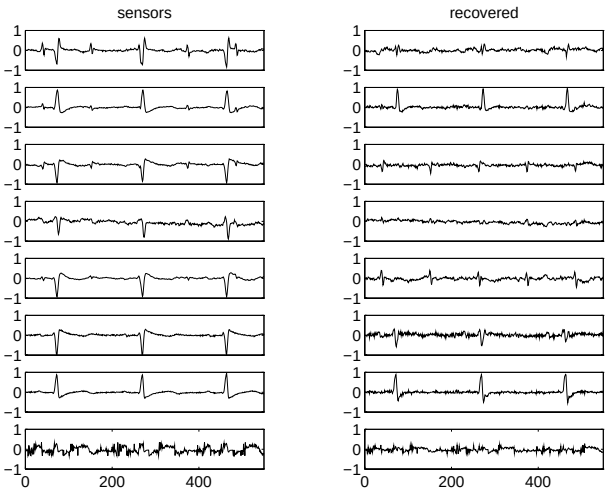


Figure 7: Eight ECG signals separated into: four maternal signals, two fetal signals and two noise signals. The mixed signals were obtained from 8 electrodes located on the abdomen of a pregnant woman. The signals are 2.5 seconds long, sampled at 200 Hz.

4.1.1. Extraction of Fetal ECG source

The ECG data of pregnant women as shown in Figure 7 (a) are the potential recordings during an 8-channel experiment. Only 2.5 seconds of recordings (sampled at 200 Hz) are displayed. In this experiment, the electrodes were placed on the abdomen and the cervix of the mother. Abdominal signals measured near fetus are shown in channel 1 to 5. The weak fetal contributions are contained in x_1 to x_5, although they are not clearly visible. The ECG raw data measured through 8 channels are dominated by mother's ECG (MECG). The natural gradient ICA algorithm [2] was applied to process the ECG raw data, and the result are shown in Figure 7(b) and in more details on Figure 8. The 3rd and 5th independent components (output signals y_3, y_5 correspond to the FECG signal (Fig. 8). The 2nd and 7th independent component contain the MECG. The rest of extracted signals might contain noise contributions. The weak FECG signal was well extracted by the ICA algorithm, whereas the PCA had a difficulty to extract it.

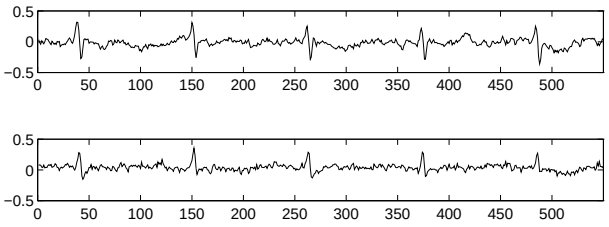


Figure 8: Extracted fetal ECG signals.

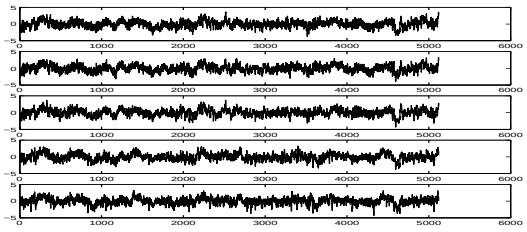
4.1.2. Analysis of EEG/MEG data

Similar experiments were performed for EEG and MEG signals with 21 and 149 sensors respectively. The exemplary observed selected EEG signals are shown in Figure 9 (a). Here we plotted only 5 from 21 sensor signals. After application of ICA/BSS procedure for separation of the sensor 21 EEG signals we have obtained the results shown in the Figure 9 (b) (due to limit of space only first 5 independent components are shown). Analysis of the values H_i and $\|\mathbf{b}_i\|$ for observed sensor signals and separated signals (independent components) have completely different distributions and identification or detection of random signals is only possible after applying ICA. For this case ICs number 3 and 5 should be removed.

Table 1: Hurst exponent H_i and norm of vector $\mathbf{b}_i$ of linear predictor for each signal shown in Fig. 9 (a) and (b)

Signal number i	H_i		$\max \|\mathbf{b}_i(t)\|$	
	$x_i(t)$	$y_i(t)$	$x_i(t)$	$y_i(t)$
1	0.7290	0.7513	0.3657	1.0431
2	0.7117	0.6989	0.3348	0.4245
3	0.6970	0.5418	0.4647	0.0173
4	0.7120	0.7361	0.5257	0.9348
5	0.7232	0.6452	0.5333	0.2197

(a)



(b)

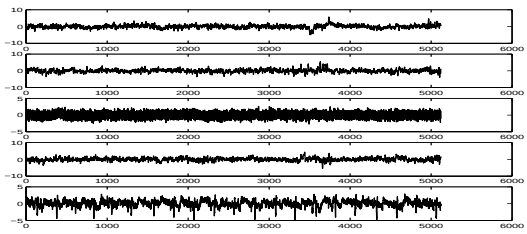


Figure 9: (a) Exemplary observed noisy EEG data (only first 5 channels are shown) and (b) plots of the first 5 ICs for EEG data.

5. GENERALIZED MULTICHANNEL BLIND DECONVOLUTION – STATE SPACE MODELS

The state space demixing and filtering models are flexible and universal linear or nonlinear systems which includes as special cases standard ICA/BSS as well as the standard multichannel deconvolution model with FIR, Gamma filters or more general models: AR, MA, ARMAX models as special cases [5,6, 11,13]. Moreover, such a dynamic demixing model enables us to generate many canonical realizations

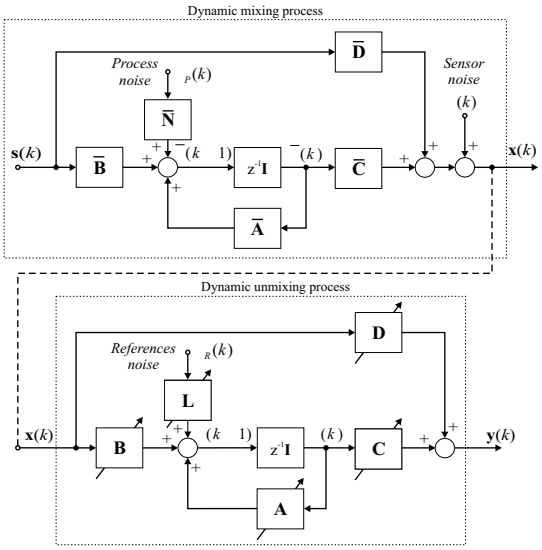


Figure 10: Conceptual block diagram illustrating general linear state space mixing and self-adaptive demixing model for Dynamic ICA (DICA). Objective of learning algorithms is estimation of set matrices $\{\mathbf{A}, \mathbf{B}, \mathbf{C}, \mathbf{D}\}$

In general, any linear stable demixing model can be described by a linear state-space system as (see Fig. 10)

$$\boldsymbol{\xi}(k+1) = \mathbf{A}\boldsymbol{\xi}(k) + \mathbf{B}\mathbf{x}(k) + \mathbf{L}\boldsymbol{\nu}_R(k), \quad (11)$$

$$\mathbf{y}(k) = \mathbf{C}\boldsymbol{\xi}(k) + \mathbf{D}\mathbf{x}(k), \quad (12)$$

where the unknown state-space matrices have dimension: $\mathbf{A} \in \mathbb{R}^{M\times M}$, $\mathbf{B} \in \mathbb{R}^{M\times m}$, $\mathbf{C} \in \mathbb{R}^{m\times M}$, $\mathbf{D} \in \mathbb{R}^{m\times m}$, with $M \geq r$ (i.e. the order of the demixing system should at least the same or larger than the order of the mixing system.

It is easy to see that the linear state space model is an extension of the instantaneous mixture blind source separation model. In the special case when the matrices $\overline{\mathbf{A}}, \overline{\mathbf{B}}, \overline{\mathbf{C}}$ in the mixing model and $\mathbf{A}, \mathbf{B}, \mathbf{C}$ in the demixing model are null matrices, the problem is simplified to the standard ICA problem. In general, the matrices $\boldsymbol{\Theta} = [\mathbf{A}, \mathbf{B}, \mathbf{C}, \mathbf{D}, \mathbf{L}]$ are parameters to be determined in a learning process on the basis of knowledge of the sequence $\mathbf{x}(k)$ and some a priori knowledge about the system. The above linear state-space demixing and filtering model can be relatively easily generalized to a flexible nonlinear model as (see Fig. 11)

$$\boldsymbol{\xi}(k) = \mathbf{f}[\underline{\mathbf{x}}(k), \underline{\boldsymbol{\xi}}(k)], \quad (13)$$

$$\mathbf{y}(k) = \mathbf{C}(k)\boldsymbol{\xi}(k) + \mathbf{D}(k)\mathbf{x}(k), \quad (14)$$

where $\boldsymbol{\xi}(k) = [\xi_1(k) \cdots \xi_M(k)]^T$ is the state vector, $\mathbf{x}(k) = [x_1(k) \cdots x_m(k)]^T$ is an available vector of sensor signals, $\mathbf{f}[\underline{\mathbf{x}}(k), \underline{\boldsymbol{\xi}}(k)]$ is an M-dimensional vector of nonlinear functions (with $\underline{\mathbf{x}}(k) = [\mathbf{x}^T(k) \cdots \mathbf{x}^T(k-L_x)]^T$ and $\underline{\boldsymbol{\xi}}(k) = [\boldsymbol{\xi}^T(k) \cdots \boldsymbol{\xi}^T(k-L_x)]^T$), $\mathbf{y}(k) = [y_1(k) \cdots y_m(k)]^T$ is the vector of output signals, and $\mathbf{C} \in \mathbb{R}^{m\times M}$ and $\mathbf{D} \in \mathbb{R}^{m\times m}$ are output matrices [5].

It should be noted that the equation (13) describes the NARMA model while the output model (14) is linear. Our objective will be

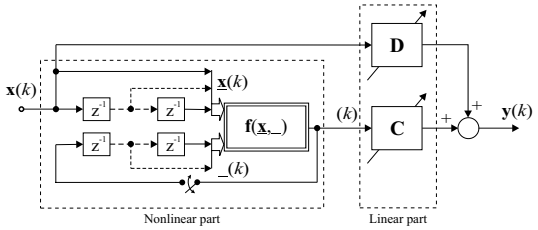


Figure 11: Block diagram of simplified nonlinear demixing NARMA model. For the switch open we have feed-forward MA model and for the switch closed we have recurrent ARMA model

No.	Algorithm		
1.	$\Delta\mathbf{C}$	$=$	$-\eta\mathbf{f}(\mathbf{y})\boldsymbol{\xi}^T$
	$\Delta\mathbf{D}$	$=$	$\eta(\mathbf{I}-\mathbf{f}(\mathbf{y})\mathbf{x}^T\mathbf{D}^T)\mathbf{D}$
2.	$\Delta\mathbf{C}$	$=$	$\eta((\mathbf{I}-\mathbf{f}(\mathbf{y})\mathbf{y}^T)\mathbf{C}-\mathbf{f}(\mathbf{y})\boldsymbol{\xi}^T)$
	$\Delta\mathbf{D}$	$=$	$\eta(\mathbf{I}-\mathbf{f}(\mathbf{y})\mathbf{y}^T)\mathbf{D}$
3.	$\Delta\mathbf{C}$	$=$	$\eta((\boldsymbol{\Lambda}-\mathbf{f}(\mathbf{y})\mathbf{y}^T)\mathbf{C}-\mathbf{f}(\mathbf{y})\boldsymbol{\xi}^T)$
	$\Delta\mathbf{D}$	$=$	$\eta(\boldsymbol{\Lambda}-\mathbf{f}(\mathbf{y})\mathbf{y}^T)\mathbf{D}$
4.	$\Delta\mathbf{C}$	$=$	$\eta((\mathbf{I}-\langle\mathbf{f}(\mathbf{y})\mathbf{y}^T\rangle)\mathbf{C}-\langle\mathbf{f}(\mathbf{y})\boldsymbol{\xi}^T\rangle\boldsymbol{\Lambda})$
	$\Delta\mathbf{D}$	$=$	$\eta(\mathbf{I}-\langle\mathbf{f}(\mathbf{y})\mathbf{y}^T\rangle)\mathbf{D}$
5.	$\Delta\mathbf{C}$	$=$	$\eta(\mathbf{I}-\mathbf{f}(\mathbf{y})\boldsymbol{\xi}^T)\mathbf{C}$
	$\Delta\mathbf{D}$	$=$	$\eta(\mathbf{I}-\mathbf{f}(\mathbf{y})\mathbf{y}^T)\mathbf{D}$
6.	$\Delta[\mathbf{C}\ \mathbf{D}]$	$=$	$-\eta\nabla l\begin{bmatrix}\mathbf{I}+\mathbf{C}^T\mathbf{C} & \mathbf{C}^T\mathbf{D}\\ \mathbf{D}^T\mathbf{C} & \mathbf{D}^T\mathbf{D}\end{bmatrix}$

Table 2: Family of adaptive learning algorithms for linear and nonlinear state space models

to estimate the output matrices $\mathbf{C}$ and $\mathbf{D}$, as well as to identify the NARMA model by using a neural network on the basis of sensor signals $\mathbf{x}(k)$ and source (desired) signals $\mathbf{s}(k)$ which are available only for short time windows [5,6,13].

On basis of Natural Gradient (NG) approach developed by Amari [1, 2] we have derived several efficient adaptive learning algorithms for estimation of output matrices $[\mathbf{C}, \mathbf{D}]$ which are summarized in Table 1 [12, 13, 6, 5].

6. CONCLUSIONS

In this paper we have discussed several promising models and associated learning algorithms for biomedical signal separation, extraction and deconvolution for multisensor recordings. Several promising models are described which are useful for multisensor data corrupted by noise and artifacts. Application of Hurst exponent together with ICA/BSS has been investigated for automatic elimination of noise and undesirable interference. Of course, these methods exploit only small part of possible techniques which can be used together with ICA/BSS for noise and interference cancellation. Especially, higher order and nonlinear correlation methods are very promising. The proposed and investigated methods appear to be simple and efficient for specific applications, especially for enhancement of single trial EEG/MEG data, what has been confirmed by computer simulation experiments.

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Models and Simulators on cellular level

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A brain is a highly complex and dynamical system. To understand a complex and dynamical system, we need to have means to integrate what is known about the system, means to test the ideas, and means to share the understandings. I understand that the aim of neuroinformatics is to provide these means. Because a brain is a network of vast number of neurons, we need to have basic ideas or understandings regarding how NEURONS, the building blocks of the brain, work. But neurons themselves are already highly complex and dynamical with various shapes and various electrical properties. At the cellular level, at the sub-cellular level, and at the molecular level, a huge amount of experimental data has been, and will be accumulated. The traditional ideas of ball-and-stick model neuron is far from real. We now have come to a stage where we should integrate new findings and come up with novel images of neurons. Therefore we need NeuroInformatics at the cellular and at the sub-cellular level. I believe what we should do to materialize neuroinformatics at cellular level is to organize efforts to construct 'VIRTUAL NEURONS'. That way, data will became more easily available, the findings will be integrated, the novel ideas can be tested, and the ideas will be shared.

To illustrate the idea I would like to show some of my recent experimental studies and how I have been trying to make use of compartmental simulation tools to analyze and to make sense of the data. In one example, colleagues of mine and I measured spread of EPSPs along the entire length of hippocampal CA1 pyramidal neurons by using fast voltage-sensitive dye imaging. To estimate passive cable parameters such as Rm (specific membrane resistance) and Ri (specific intracellular resistance), we downloaded a multicompartmental model neuron simulator NEUORN (M. Hines), fed in our experimental data, played with parameters till the model reproduce the behavior of real neurons.

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Biochemical and Biophysical Modeling of Synaptic Plasticity in a Spine Using A-Cell

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Long-term potentiation (LTP) and depression (LTD) are thought to be an elementary process for learning and memory. We constructed a model for LTP and LTD based on biochemical and biophyical processes within a spine using A-Cell, which was developed for the construction of models for neurons. In this presentation, we first introduce A-Cell. Second, a model for LTP and LTD is shown, and finally a prediction of the model and the experimental observation supporting the prediction will be discussed. The model is composed of biochemical reactions including activation of calcineurin (CaN), and Ca^{2+}/calmodulin-dependent protein kinase II (CaMKII). The model expressed on A-Cell is shown in Fig.1. From simulations we found that at low or high stimulation frequencies the concentration of activated CaN ([CaN^*]) was higher or lower than that of activated CaMKII ([$CaMKII^*$]) suggesting the induction of long-term potentiation (LTD) or depression (LTP), respectively. These results were consistent with experimental observations. Interestingly, however, at very high stimulation frequencies [$CaMKII^*$] was lower than [CaN^*] again suggesting the induction of LTD, which was not reported before (Fig.2). Thus the model predicted that at very high stimulation frequencies, the synaptic efficacy is depressed instead of potentiated. This offers an important property of preventing the saturation to a ceiling in the synaptic efficacy.

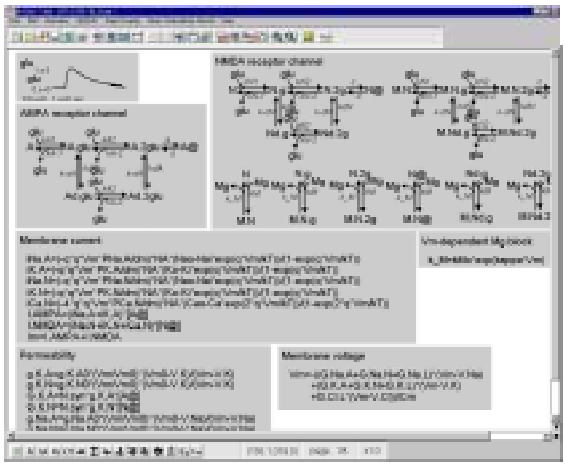

Fig.1 A model for LTP and LTD using A-Cell

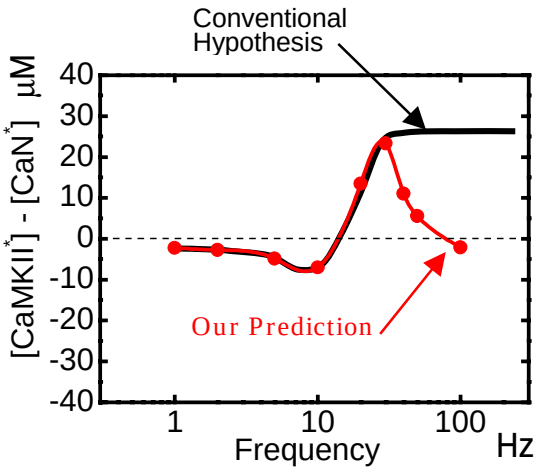

Fig.2 A prediction of the model

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Neuroinformatics Study on the Vertebrate Retina

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The vertebrate retina has been intensively studied over the past decades using physiological, morphological and pharmacological techniques. Since the retina is a unique and interesting neural system from the viewpoints not only of neuroscience but also of engineering, which has been thought to be a window to the brain because of its accessibility and suitability for the investigation. The retina is an ideal model of neural network system and neural information processing system. Since the early 1980s, enzymatic dissociation techniques have been employed for the isolation of a variety of retinal cells, including photoreceptors, horizontal cells and bipolar cells. Using isolated cell preparations, membrane ionic currents of solitary retinal cells have been studied in a quantitative fashion using the voltage-clamp techniques. These data provide information concerning the functional role of the ionic currents in generating and shaping the light response of the retinal neurons. However, the detailed experimental data alone are not enough to understand how the retinal neurons work. A combination of experimental work and mathematical modeling is necessary to clarify the complicated retinal functions. We believe mathematical modeling and simulation analysis with the advanced computer system have a potential to understand the relationships between the microscopic characteristics and its integrative functions of the neural system including the brain.

The purpose of this study is to develop a realistic model of the retina which replicates the detailed neurophysiological structures and retinal functions. This approach allows the exploration of the computational functions performed by retinal neurons including the role and interaction of ionic channles and receptors, and the subcellular events such as transmitter release, binding and uptake.

In the present study, mathematical descriptions of the membrane ionic currents in the retinal neurons, photoreceptors, horizontal cells, bipolar cells and ganglion cells are realized. Electrical properties of each neuron is described by a parallel conductance circuit. The voltage- and time-dependent characteristics of ionic conductance is modeled by Hodgkin-Huxley types of equations. The developed model is capable of accurately reproducing the voltage- and current-clamp responses of retinal neurons. Any electrical response including light response which depends on the dynamic balance of different ionic currents is quantitatively analyzed by the model. Therefore, hypotheses on how the retina processes visual information are understood at the cellular and subcellular level. Neuroinformatics model can be used to summarize what we know and what we need to find out on the retina.

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Computational model for color perception

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The goal of this study is to understand functional role of color vision: coding, representation and interpretation of color information by the visual pathway. To this end, a computational models are developed to explain various phenomena relating to color perception, including color transparency, constancy, categorical color perception and visual attention to color.

Since the NRV project has started, color transparency have been studied as one of the target phenomena of the computational theory. Perception of transparency refers to the phenomenon that an observer sees not only surfaces behind a transparent medium but also the transparent medium itself. Since the light reaching the retina after having passed through the transparent medium does not contain specific information about the characteristics of the transparent layers, the perception of transparency can be thought to originate in the neural information processing in the visual system. The visual system is probably able to decompose the image into an underlying surface and a transparent overlapping medium by calculating inverse-optics of the color mixture. This study proposes a computational theory of color transparency dealing with wavelength-selective objects both for additive and subtractive color mixture. We begin by describing forward optics which link surface reflectance, transmittance and sensory responses to four different colors at an X-junction. Based on these models, we propose algorithms for recovering reflectance of an underlying surface and transmittance of an overlapping medium from a set of sensory responses to colors at an X-junction by inverse-optics calculations. Recovery algorithms are derived from the inverse-optics equations by incorporating them with finite-dimensional models for surface reflectance and transmittance functions in order to reduce the dimensionality of the problem. Also, in order to decompose a given color image into multiple layers, we propose algorithms for determining the depth ordering of surfaces and the type of color mixture, by checking the physical realizability of recovered functions.

The heart of computational theory/models of color perception is shedding light on a problem how color information is represented in the visual pathway. Several types of experiments provide evidence that imply the existence of higher-order color mechanisms which visual cortex is thought to be a more likely substrate for. Psychophysical experiments are now being planed to explore the color representation mediating color detection/discrimination and color segregation, and attentional effect on color perception. Experimental results should provide hints for mathematical description of the color representation in the computational models of color perception.

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Effects of lateral connections on the orientation and direction selectivity in the visual cortex: model study

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We built a neural network model of the lateral geniculate nucleus (LGN) and visual cortex using integrate-and-fire units. In the model LGN we assumed four types of cells: ON- and OFF-center cells with lagged and nonlagged response properties, which were modeled by spatio-temporal separable receptive fields observed by Ohzawa et al using the reverse correlation method. The model LGN cells generate spikes according to the Poisson process in which the mean firing rate is given by the convolution of the receptive fields and visual stimuli. In the model visual cortex, excitatory and inhibitory neurons are represented by integrate-and-fire units that receive not only geniculo-cortical afferent inputs but also lateral inputs from other excitatory and inhibitory cortical cells. The afferent input pattern was determined by the activity-dependent self-organization. Therefore we can see orientation and direction preference in individual cells and orientation and direction joint maps even without the lateral connections. On the other hand, for finite synaptic strength of the lateral connections with the similar extent of lateral connections as used in the simulation of self-organization, it was found that cells' responses to nonpreferred directions of stimulus motion are suppressed and orientation and direction selectivity is enhanced. Iso-orientation and direction domains were also sharply delineated with basic structure of the maps being preserved. Furthermore, low-pass filter-like maps often obtained only from the self-organization of afferent inputs changed to band-pass filter-like maps. This indicates that lateral connections work for map regularization as well as enhancement of response selectivity.

Neuroinformatics of the early visual cortex: model, computation, and data

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Recent advances in electrophysiological measurement techniques allow construction of detailed computational models of the circuitry involved in information processing in the early visual cortex. Predictions from computational models may be tested against the physiological data(1). In particular, receptive field mapping data in the joint spatial and temporal domain (including that of 3-D depth) provide rich information needed to constrain free parameters in computational models(2). Using these data and the corresponding models, I will discuss how Neuroinformatics Research in Vision (NRV) project can help integrate many of the components that comprise modern brain research efforts.

One of the primary goals of the NRV project is to build a system that is more than a repository of reference information that points to published materials and provides links to other sites offering primary sources of information. It should not be a mere portal site with a search capability, although such capabilities should exist as a matter of course.

A key feature that we are incorporating into our system is the ability to perform an on-line modeling computation using server-side computational resources. Utilities of such on-line simulation capabilities go beyond providing a simple limited demo of model computations. Some of the models that will be featured in the NRV project go beyond the capabilities of a typical workstation, let alone consumer level PCs. Therefore, for such models, the server-side computation may be the only way by which the model can be simulated. Even if a potential user is willing to expend necessary resources to prepare computing environments, it is important to determine if a particular model is suitable for a given task. By offering the on-line simulation capability via a server-client configuration, a potential user of the model will be able to examine a given modeling environment without costly investments of time and efforts.

Another use of the client-server configuration is accessing experimental data. A concerted effort is being made to make primary data from experiments available on the NRV platform. One of the problems in creating a database of neurophysiological data is the diversity and variations of data formats. Unlike genetic sequence data, experimental data from neurophysiological experiments are usually very specific to each researcher and software used. Although efforts are being made to standardize data formats across different laboratories, we will nevertheless have to expect wide variations of data formats.

By employing a client-server configuration, a bank of server-side data filters can absorb variations in the primary data formats. In this manner, each user of the data is able to pick the best data format for downloading selected data. A simplified demonstration of such a system will be given.

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