



US-Europe Workshop  
“Reverse Engineering of the Human Brain”  
23-26 May 2010, Grand Hotel Park, Dubrovnik, Croatia

## Workshop Report



## Contents

### Table of Contents

1	Background	3
2	Scientific scope	3
3	Organizing Committee	4
4	Workshop participants	6
5	Plenary lectures	8
6	Breakout sessions	9
6.1	Session 1: Engineering Brain Functions	9
6.1.1	State of the art	9
6.1.2	Open questions	9
6.1.3	Technological challenges	9
6.1.4	Needs	10
6.2	Session 2: Engineering Brain Circuitry	10
6.2.1	State of the art	10
6.2.2	Challenges	10
6.2.3	Needs	11
6.2.4	Potential for synergies between US/Europe	11
6.2.5	Educational needs	11
6.3	Session 3: Understanding Brain Function	11
6.3.1	State of the art	11
6.3.2	General Challenges	12
6.3.3	Measurements' methodologies	12
6.3.4	Investigating complexity	13
6.3.5	Needs	13
6.4	Session 4: Understanding Brain Circuitry	13
6.4.1	State of the art	13
6.4.2	Challenges	13
6.4.3	Needs	14
7	Defining future research directions and outlining a roadmap towards the reverse engineering of the human brain	15
7.1	Case example 1: the Oculomotor System	15
7.2	Case example 2: Social Cognition	16
7.3	Towards a roadmap for understanding and engineering brain functions	17
7.4	Towards a roadmap for the understanding and engineering of brain circuitry	19
8	General Recommendations	21
9	Workshop Resolution	22
10	Workshop Program	23
11	List of abbreviations	26

## 1 Background

This workshop is a follow-up of occasional but successful series of joint ESF-NSF meetings which started in 2002 around the PESC Research Networking Programme CONVIB<sup>1</sup>. The topics have successively moved into the territory of the EuroCORES S3T<sup>2</sup> programme launched in 2007. Most recently, the workshop on "Bio-inspired Engineering of Sensors, Actuators and Systems" held in 2008 in Taormina, has led to the development of the ESF EuroBioSAS EUROCORES programme<sup>3</sup> and, in parallel, to the NSF "BioSensing & BioActuation: Interface of Living and Engineered Systems (BSBA)"<sup>4</sup> emerging frontiers in research and innovation programme.

The topic proposed for the 2010 workshop was "Reverse engineering of the human brain" and due to its interdisciplinary nature, all ESF standing Committees were invited to join. As a result, the workshop was jointly organized through a collaborative effort of four European Science Foundation Standing Committees (European Medical Research Council - EMRC, Life Earth and Environmental Sciences - LESC, Physical and Engineering Sciences – PESC and Standing Committee for the Humanities - SCH), the US National Science Foundation (NSF), and the US Air Force Office of Scientific Research (AFOSR).

## 2 Scientific scope

There is a great interest in understanding of how human brain manipulates data and develops solutions. During the past decade scientists and engineers have conducted extensive research in developing a better understanding of human brain functions such as, transformation of the sensed physical world into representations useful to recognize and to act; sensorial, cognitive and motor data storage and retrieval; and the use of this information for decision-making and social interactions. The main objectives of this workshop are to:

- Create a platform for scientific dissemination, exchange of ideas and discussions among neuroscientists, cognitive scientists, engineers, and computer scientists from the US and Europe in the areas of reverse engineering of the human brain.
- Create opportunities for the enhancement of existing collaborative links and for the creation of new prospects.
- Provide consolidated strategic recommendations for the benefit of funding agencies, industry, research organisations, and academia. This includes foresight for research planning, promotion and dissemination of knowledge, formulation of standards and best practices.

The workshop aim was to identify technological challenges, basic research issues, and to outline a research roadmap for collaboration between the US and Europe in this exciting area.

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<sup>1</sup> <http://www.esf.org/convib>

<sup>2</sup> <http://www.esf.org/s3t>

<sup>3</sup> <http://www.esf.org/eurobiosas>

<sup>4</sup> <http://www.nsf.gov/eng/efri>

The workshop was chaired by Professor Giulio Sandini (University of Genova, Italy) and Professor Rahmat Shoureshi (University of Denver, US).

Workshop attendance was by invitation only and a total of forty scientists (20 from US and 20 from Europe) were invited following suggestions by the four organizing ESF standing committees and the chairs. In addition, ESF science officers and NSF programme officers attended the workshop.



Figure 1. Afternoon meeting of session chairs (left) and coffee break (right)

### 3 Organizing Committee

The workshop organizing committee was composed of:

- **Workshop chairs**

**Professor Rahmat Shoureshi (Chair)** is Dean and Professor at the School of Engineering & Computer Science, Department of Engineering & Computer Science, of the University of Denver in the US. He completed his graduate studies at MIT in 1981 with a Ph.D. in electromechanical systems, and with a minor in Organizational Dynamics and Marketing from the MIT Sloan School of Management. From 1981 through 1983, he was on the faculty of Wayne State University. In 1983, he joined the School of Mechanical Engineering at Purdue University where he was chairman of the Manufacturing and Materials Processing area, chairman of the Systems, Measurement and Control area ('92-94), and founder and director of the Advanced Control of Energy and Power Systems (ACEPS). In August of 1994, he joined the Colorado School of Mines as the G.A. Dobelman Distinguished Chair professor of Engineering, Director of Center for Automation, Robotics and Distributed Systems (CARDI) and Director of CSM-PSERC. In 1998, he became the founding Director of NSF Center for Intelligent Biomedical Devices and Musculoskeletal Systems (IBDMS). In addition to directing these three research centers, he has progressively assumed greater administrative roles which include: Associate Vice President for Technology Transfer (OTT) (reporting directly to the President), chair of the newly developed undergraduate and graduate programs in Bioengineering and Life Sciences (BELS), and chair of the CSM Academy, a think tank charged with long term strategic planning for the school. He also has

across-institutional administrative position as chairperson for the Colorado Alliance for Bioengineering (CAB), which currently includes CSM, University of Colorado Health Sciences Center, CU-Boulder, CU-Denver, Colorado State University, and the University of Denver.

**Professor Giulio Sandini (Chair)** is Director of Research at the Italian Institute of Technology and full professor of bioengineering at the University of Genoa. After his graduation in Electronic Engineering (Bioengineering) at the University of Genova in 1976 he was research fellow and assistant professor at the Scuola Normale Superiore in Pisa until 1984. During this period, working at the Laboratorio di Neurofisiologia of the CNR, he investigated aspects of visual processing at the level of single neurons as well as aspects of visual perception in human adults and children. He has been Visiting Research Associate at the Department of Neurology of the Harvard Medical School in Boston where he developed diagnostic techniques based on brain electrical activity mapping. After his return to Genova in 1984 as associate professor, in 1990 he founded the LIRA-Lab (Laboratory for Integrated Advanced Robotics, [www.liralab.it](http://www.liralab.it)). In 1996 he was Visiting Scientist at the Artificial Intelligence Lab of MIT.

Since July 2006 Giulio Sandini is on absence of leave from University of Genoa as he has been appointed Director of Research at the Italian Institute of Technology where he has established and is currently directing the department of Robotics, Brain and Cognitive Sciences. RBCS department concentrates on a multidisciplinary approach to human centered technologies encompassing machine learning and artificial cognition, exploring the brain mechanisms at the basis of motor behavior, learning, multimodal interaction, and sensorimotor integration.

- **ESF, NSF and AFOSR representatives**

**Dr. Hugh DeLong (AFOSR):** Program Manager with Air Force Research Laboratory's Air Force Office of Scientific Research

**Dr. Graham Harrison (NSF):** Program Officer in the Office of International Science and Engineering (OISE) at the U.S. National Science Foundation.

**Dr. Ana Helman (ESF):** Science Officer in the Physical and Engineering Sciences Unit

**Dr. Les Lee (AFOSR):** Program Manager for Mechanics of Multifunctional Materials & Microsystems at the U.S. Air Force Office of Scientific Research (AFOSR)

**Dr. Eva Hoogland (ESF):** Science Officer for Cognitive Sciences in the Humanities Unit

**Dr. Lars Kristiansen (ESF):** Science Officer for Neurosciences in the Life, Earth and Environmental Sciences Unit

## 4 Workshop participants

FIRSTNAME	SURNAME	AFFILIATION	COUNTRY
Wayne	Aldridge	<i>University of Michigan</i>	United States
Stjepan	Bogdan	<i>University of Zagreb</i>	Croatia
Michael	Baratta	<i>Massachusetts Institute of Technology</i>	United States
Michael S	Beauchamp	<i>University of Texas</i>	United States
Gert	Cauwenberghs	<i>University of California at San Diego</i>	United States
Yoonsuck	Choe	<i>Texas A&amp;M University</i>	United States
Hugh	DeLong	<i>Air Force Office of Scientific Research</i>	United States
Peter	Dominey	<i>Institut des Sciences Cognitives, CNRS, Bron</i>	France
Rodney	Douglas	<i>Institute of Neuroinformatics, Zurich</i>	Switzerland
Dominique	Durand	<i>Case Western Reserve University</i>	United States
Timothy	Ellmore	<i>University of Texas Medical School at Huston</i>	United States
Andrew	Felch	<i>Dartmouth College</i>	United States
Erik	Fransen	<i>Royal Institute of Technology, Stockholm</i>	Sweden
Jennifer	Gresham	<i>Air Force Office of Scientific Research</i>	United states
Lars Kai	Hansen	<i>Technical University of Denmark</i>	DanmarkDanemark
Graham M.	Harrison	<i>National Science Foundation</i>	United States
Ana	Helman	<i>European Science Foundation-PESC</i>	France
Eva	Hoogland	<i>European Science Foundation-SCH</i>	France
Roland	Johansson	<i>Umea University</i>	Sweden
Milos	Judas	<i>Croatian Institute for Brain Research, Zagreb</i>	Croatia
Ranu	Jung	<i>Arizona State University</i>	United States
Cherie	Kagan	<i>University of Pennsylvania</i>	United States
Danica	Kragic	<i>Royal Institute of Technology, Stockholm</i>	Sweden
Lars	Kristiansen	<i>European Science Foundation, LESC</i>	France
Norbert	Kruger	<i>University of Southern Denmark</i>	Denmark
Stephen	LaConte	<i>Baylor University</i>	United States
Les	Lee	<i>Air Force Office of Scientific Research</i>	United States
Giorgio	Metta	<i>Italian Institute of Technology, Genova</i>	Italy
Steven	Ojemann	<i>University of Colorado</i>	United States
Stefano	Panzeri	<i>Italian Institute of Technology, Genova</i>	Italy
Jose	Principe	<i>University of Florida</i>	United States
Thomas	Ragole	<i>University of Colorado</i>	United States
Sylvie	Renaud	<i>Laboratoire de l'Integration du Matériau au Systeme, CNRS, Bordeaux</i>	France
Alexa	Riehle	<i>Institut de Neurosciences Cognitives de la Méditerranée, CNRS, Marseille</i>	France
Helge	Ritter	<i>Faculty of Technology, Bielefeld University</i>	Germany
Tony	Ro	<i>City University of New York</i>	United States
Philip N.	Sabes	<i>University of California San Francisco</i>	United States

## US Europe Workshop « Reverse Engineering of the Human Brain » REPORT

<b>Giulio</b>	<b>Sandini</b>	<i>Italian Institute of Technology, Genova</i>	Italy
<b>Gregor</b>	<b>Schoëner</b>	<i>Institut für Neuroinformatik, University of Bochum</i>	Germany
<b>Rahmat</b>	<b>Shoureshi</b>	<i>University of Denver</i>	United States
<b>Garrett B.</b>	<b>Stanley</b>	<i>Georgia Institute of Technology</i>	United States
<b>Paul</b>	<b>Verschure</b>	<i>Catalan Institute of Advanced Research (ICREA), Universitat Pompeu Fabra</i>	Spain
<b>Sethu</b>	<b>Vijayakumar</b>	<i>University of Edinburgh</i>	United Kingdom
<b>Patrick</b>	<b>Wolf</b>	<i>Duke University</i>	United States

## 5 Plenary lectures

At the opening of the workshop, the two chairs, Prof. Sandini and Prof. Shoureshi, presented the concept and the goals of the workshop, in particular the main topics of understanding/engineering of brain circuitry and brain functions. Participants of the workshop were assigned to the four parallel sessions and would initially work on the four areas by identifying the state of the art and challenges and finally by proposing a roadmap. The structure of the working group remained flexible and the participants rotated between groups.

The representatives of the organisations funding the workshop (ESF, NSF, AFOSR) gave short presentations where they provided an overview of current activities supported in the field and stated their respective expectations in terms of outcome.

Given the nature of this workshop and the framework, the time dedicated to plenary presentations was limited to one half-day and four lectures which provided a general introduction to the topics of the workshop:

- *Neural Coding of Reward in the Ventral Pallidum* by J. Wayne Aldridge
- *The Neuromorphic Brain* by Rodney Douglas
- *Silicon and Biological Adaptive Neural Circuits* by Gert Cauwenberghs
- *Towards a Neurophysiologically Grounded Cognitive Architecture for Cooperative Human Robot Interaction* by Peter Ford Dominey

In the first presentation, Wayne Aldrige illustrated how the combination of anatomy, behaviour and *in vivo* recording of neural activity is used to study the encoding of motivation for “taste” rewards in rats. The shift of neural representations toward motivational value after dopaminergic activation was discussed. Rodney Douglas presented the most recent developments in neuromorphic circuit brain architectures and introduced the discussion about the definition and the meaning of the term “reverse engineering”. Gert Cauwenberghs provided a detailed overview of the state of the art in silicon CMOS technology used as platform for neural computation and illustrated several examples for *in vivo* recording, stimulation and imaging in animals and humans. The presentation given by Peter Ford Dominey concentrated on cognitive systems engineering for co-operative human-robot interactions. The presentations can be found in Annex 1 of this report.

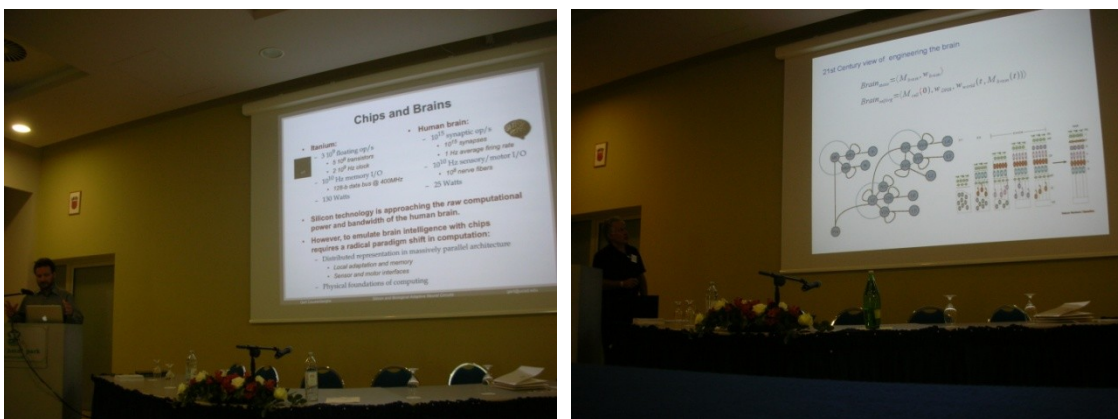


Figure 2. Presentations by G. Cauwenberghs (left) and R. Douglas (right)



## 6 Breakout sessions

The first four parallel sessions developed around the four thematic areas identified prior to the workshop based on the assignments filled in by participants (Annex 2) and aimed at establishing the state of the art and main challenges. Each of the four session was chaired and recorder by one of the participants. The results were presented on the following day.

Session	Chair	Recorder
<b>S1</b> Engineering Brain Functions	Paul Verschure	Michael Baratta
<b>S2</b> Engineering Brain Circuitry	Cherie Kagan	Sylvie Renaud
<b>S3</b> Understanding Brain Functions	Roland Johannson	Garrett Stanley
<b>S4</b> Understanding Brain Circuitry	Dominique Durand	Stefano Panzeri

### 6.1 Session 1: Engineering Brain Functions

#### 6.1.1 State of the art

- Creation of technologies that permit human-machine cognitive interaction
- Application of sensory/motor functions to guide machines for realizing adaptive control
- Developing and testing sensory/motor models in both biological- and machine-based systems
- Interfacing of brain with external devices
- Brain function engineering through understanding of central nervous system activity patterns (e.g., obtained from functional magnetic resonance imaging (fMRI))

#### 6.1.2 Open questions

- Define inputs and outputs of any given abstraction layer within a system
- Investigate the common principles that drive sensory systems and perception including the encoding of information.
- How do we represent interaction patterns among various cognitive capabilities such as motion intelligence, communication, attention, and memory/learning?
- How do brains assemble knowledge through learning and what architectures are suitable for such representations?
- How precisely can we link behaviors and physiology?
- To what extent do the differences in the physical embodiments of robots and biological systems affect reverse engineering?
- Which levels of description do we choose to guide hardware development?

#### 6.1.3 Technological challenges

- Develop/Expand the ability of machines to acquire and use knowledge
- Use connectivity in combination with neurochemistry as a route for determining the function of single components in a system

- Which new kinds of hardware need to be developed to implement reverse engineering of the brain?
- How do we push the advancement of sensing/actuation technologies in order to extract principles of brain function?
- How do we push the development of processing elements mimicking the associative nature of brain functions and memory?
- How do we measure specific components of different abstraction layers simultaneously, in real-time?
- How do we implement motivation, problem solving, and other cognitive components into hardware models and artificial systems?

#### 6.1.4 Needs

- More powerful computational architectures, new design and testing tools for synthesis and analysis of artificial systems
- Novel recording, imaging, and perturbational tools to simultaneously measure and manipulate components of any given system at different abstraction levels

### 6.2 Session 2: Engineering Brain Circuitry

#### 6.2.1 State of the art

- Sensory implants and stimulators (cochlear, retinal, DBS...)
- Basic experiments of artificial systems closing the loop from neural signal recording to neural stimulation
- No FDA-approved clinical device to measure neural signal and Deep Brain Stimulation (DBS) feedback but imminent approval of closed-loop devices to control epileptic seizures is expected
- Optical two photons detection for the study of living tissue with higher resolution
- Microelectronics devices mimicking neural morphology (Neuromorphic devices) are becoming programmable and dynamically reconfigurable
- Systems implementing large-scale simulation of neural networks (billions of synapses) are currently available
- Event-based communication protocol is becoming standard in neuromorphic circuits
- Neuromorphic devices working in real time

#### 6.2.2 Challenges

- Understand and construct brain-like processing networks, architectures and algorithms that support real world, real-time behaviour
- Understand nervous system as a process and find the relevant circuits architecture and computational basis for neuromorphic engineering
- Implement testable and reliable neural-machine interface
- Improve invasive and non-invasive electrodes (mapping, resolution) for bidirectional neural machine interface and solve technical issues for long term chronic recordings
- Fabricate embodied, autonomous systems modelling brain circuits in a “real world” testing environment

- Develop circuitry with for functional rehabilitation and restoration
- Integrate multidisciplinary contribution to improve circuitry function (e.g. computation, materials, microelectronics). Interface modalities/properties/materials
- Integrate different methodologies for simultaneous recording and stimulation (electrical/optical/chemical)
- Improve stimulation resolution (up to millions of neurons)
- Develop robust closed-loop adaptive systems
- Understand brain functionalities (see Session 3)
- Use Electron Microscopy (EM) to reconstruct volumes and connectivity (from micro to macro)
- Develop hybrid sensors to test connectivity (sensors composed of living and artificial matter)
- Develop technologies exploiting 3D processing architectures based on silicon and plastic materials
- Study the principles of morphological development of biological neural structures and implement them using synthetic materials
- Develop brain-implanted data reduction systems for brain machine interface.
- Develop bio mimetic sensors with on-board processing (smart sensors)

#### 6.2.3 Needs

- New mechanics/materials including reliable electrodes
- Solve power and Radio Frequency (RF) link issues in implanted circuitry
- Synthesis/compiling tool for neuromorphic/biomimetics IC design
- Reduce technology cost
- Address regulatory, ethical and political issues

#### 6.2.4 Potential for synergies between US/Europe

- Create international framework with strong funding links and joint calls with interdisciplinary focus
- Create joint spin-off organizations (like: INE Institute of Neuromorphic Engineering)
- Develop common standards (like AER, PyNN<sup>5</sup>)
- Establish collaborations that can help overcome regulatory policies, especially for pre-clinical trials

#### 6.2.5 Educational needs

- Multi-disciplinary education
- Joint PhD programs
- *Focus* workshops and schools.

### 6.3 Session 3: Understanding Brain Function

#### 6.3.1 State of the art

- Rapidly advancing microstructuring techniques

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<sup>5</sup> PyNN is a simulator-independent language for building neuronal network models.

- Possible use of different/complementary measurement modalities
- Expansion of focused behavioral studies for conditioned response
- Emerging human electrophysiology studies
- Fast signal optical imaging, near infrared spectroscopy techniques usable “through the skull” and recording fast activity with 8mm spatial resolution,
- Multiplicity of complementary recording/stimulation techniques: MRI (BOLD signals), EEG (Electroencephalography – electric fields induced by neural activity), MEG (Magnetoencephalography - magnetic fields induced by neural activity), DTI (Diffusion Tensor Imaging - water diffusion for neural tract images - connectivity), multi-photon imaging, VSD (voltage sensitive dye imaging), multi-electrode recording and stimulation
- New techniques for fMRI: parallel arrays, higher magnet strength, multi-voxel pattern analysis
- Behavioral monitoring over long time periods, tracking/high speed videography. Statistics only now being really characterized, collection of massive data, post-hoc analysis
- Transcranial Magnetic Stimulation (TMS) study brain function through non-invasive stimulation
- Optogenetics techniques to refine the analysis of cell-type specific brain functions
- Gene manipulation and therapy - injection of genes therapeutically to change behavior/circuitry.

### 6.3.2 General Challenges

- Exploiting the complementarity of different measurement modalities (local field, fMRI, single/multi unit, cell spiking, oscillations)
- Understand information storage and its retrieval on a network level
- Map and understand communication between different brain areas and their timing
- Identification and mapping of complex nonlinearly connected neural areas from data
- Representation of functions in multiple time scales
- Meaning of neural codes (understanding the information content and flow)
- Study of hedonic mechanisms and the neurophysiology of motivation, urge, etc.
- Study the significance of the variability within same subject, and across brains, anatomy, structure, folding patterns, patterns of activity
- Relationship between development and function, plasticity in general (neurogenesis)

### 6.3.3 Measurements' methodologies

- Measuring/Mapping connectivity at different levels of detail
- Magnetic Resonance spectroscopy measurements of different substances in body tissues through spectral signatures
- Measurements of synaptic activity through mRNA techniques
- Measure laminar sources non-invasively
- Develop fast optical imaging
- Better coordination between animal and human studies
- Improve selectivity of artificial activation of neural circuits to cellular sub-classes (by for example optogenetics)

- Improvement of TMS for connectivity studies and for selective targeting of deeper structures
- Optimize protocols
- Develop transcranial direct current stimulation (TDCS)
- Development of knockout models, and use of twin studies

#### 6.3.4 Investigating complexity

- Study behavioral complexity in a free, natural context (currently limited by measurement techniques, eg. fMRI)
- Selective gating of information flow through top-down selection, in different sensory modalities
- Better understand some “integrative” (eg. cerebellum) or broadly affecting centers (eg. reticular formation)

#### 6.3.5 Needs

- Coordination of experimental questions and recording techniques
- Core equipment or facilities (not common in neuroscience) since equipment is more and more expensive
- Synergy and joint funding – leverage the differences in science management, and levels of expectation (blue sky versus incremental). Funding in Europe supports to some extent “blue sky” research while, in some aspects, in the US research tends to be “incremental”
- US/Europe “pool” to draw from in terms of collaboration
- Address complementary differences between US/Europe would increase likelihood of synergies
- Animal research - attitude/infrastructure differences across US/Europe
- European student pool – quantitatively trained students

### 6.4 Session 4: Understanding Brain Circuitry

#### 6.4.1 State of the art

- Recording of neural activity from multiplicity of individual neurons as well as neural population
- Modeling of neurons or networks
- Histological identification of cells
- Some measures of connectivity with imaging (DTI, functional connectivity) are available
- Measurement of functional activity over large scales with fMRI
- Fine scale imaging of small networks
- Optical detection of specific cell types
- Analysis of small populations or small datasets

#### 6.4.2 Challenges

- Develop technologies to bring together structure and function
- Develop methods for the analysis and interpretation of large scale recordings
- Develop technology to record neural activity *in vivo* during unconstrained behavior

- Develop techniques for imaging at high resolution (space and time) a large number of brain areas
- Identify the smallest set of parameters and elements that are critical for building a causal theory of individual brain functions
- Identify the minimal structures that can be understood as a functional unit
- Understand circuits at different scales and reconstruct the information at each scale
- Infer rules and principles, and reduce the number of variables to build comprehensive and tractable models
- Develop tracers to identify and label paths

#### 6.4.3 Needs

- Recording as many neurons as possible *in vivo* and for long periods of time
- Mathematical and statistical tools to analyze and interpret large scale data
- Record data during controlled behavior
- Establish and strengthen integration among disciplines
- Integration of different scales
- Retina is a good example of success in understanding the circuitry. What may be next? Oculomotor system as good system to start?
- Establish the instruments required to foster and take full advantage of combining the complementary expertise of biologists, mathematicians, statisticians, physicists, engineers, etc.
- Establish and improve communication across disciplines

## 7 Defining future research directions and outlining a roadmap towards the reverse engineering of the human brain

The roadmap should help in bringing neuroscientists and engineers together to communicate more effectively by identifying common problems and by addressing them together. The emphasis should be put on synergies needed to address issues in a constructive way. For this, **common targets** need to be defined that can drive the research, engineering and the collaboration between disciplines.

A shared view is that *“No one knows how best to engineer a brain and no one knows how the brain functions”*. Therefore, the first step in the process of establishing fruitful cooperation across disciplines is to define what specific information (reverse) engineers need from basic research and *vice versa*.

There is also need for a consensus on the **important functions to be studied**, the order and their dependencies. A related issue is to define the smallest components that need to be understood first before larger functions can be addressed. This means that a hierarchical structure / architecture should be built up by progressively adding on complexity to an initially simple system of study. The roadmap should also reflect this scaling up along the complexity of the system and its function(s).

### 7.1 Case example 1: the Oculomotor System

It is proposed to first use a case example of the **Oculomotor System** since it offers several advantages:

- It allows studying sensory-motor integration
- It is relatively well understood, inputs and outputs are well-known, simple and fixed
- One small module can provide abstract general principles for other brain systems
- It has direct impact on vision technologies and laboratories studying machine vision and robotics

Some of the following **questions** need to be addressed in the development of the roadmap:

- Which are the core inputs/outputs to begin constructing an artificial system with?
- What is the hardware needed?
- Which new behavioral experiments are needed?

Addressing these questions would imply the following:

- Development and application of modern techniques to study a system at a network level (past studies rely too heavily on single unit recording experiments)
- New insights should be gathered by recording from multiple sites simultaneously
- Correlations between motor commands and sensory inputs should be addressed systematically and in depth

The proposed **steps/methodologies** to achieve this are:

- Use DTI to map connectivity
- Include memory mechanisms
- Use TMI, fMRI, new complex tools, parietal-prefrontal interactions, recording of oscillatory activity, etc.

The desired result would be a system that is characterized well enough to be able to perform some other interesting behavior like scene analysis.

The timeframe corresponding to the graded complexity in Road Map Goals could be:

Timeline	Objective
3 years	active sensing, binocular oculomotor control including vestibular contribution and eye-head coordination.
5 years	object recognition and generalization (initial), search, ventral stream functions, eye-head-hand coordination
10 years	complex scene analysis, motor memory for eye searching, integration with other sensory systems (such as touch)

Table 1. Oculomotor system case study roadmap

### 7.2 Case example 2: Social Cognition

Social neuroscience is a new discipline and one of its goals is to create machines which have social capabilities in order to deal with agents in the external world. This also includes more generally the human-machine interaction.

The **starting points** to be addressed are:

- What abstraction layers do we begin with?
- Social cognition should be addressed through all into constituents: attention, types of emotions, model of self, theory of mind
- Focus on the development of cognitive capabilities and not only on the adult-form of these capabilities since learning and adaptation are central to social cognition.

The **methodology** includes:

- Building a robot model for experimental, bimanual, sensory-based manipulation to yield insight into how “social cognition” arises in humans

Generic processing features include:

- Adaptation, learning and plasticity
- Dynamic stability of the evolving processes
- Motor control based on force measure and compliance
- feedback on different time scales

A social cognition model can then serve to inform on psychiatric and related developmental disorders.



Timeline	Objective
3 years	passive perception/action, recognition of eye movements, gestures, face recognition, intentions, internal models for unexpected information
5 years	understands personal space, neural basis of imitation, copy actions of others, mirror gestures, goal-directed actions
10 years	robot that uses brain principles and can manipulate psychological world, interacts with physical world, hides intent, detects lying

**Table 2. Social cognition case study roadmap**

### ***7.3 Towards a roadmap for understanding and engineering brain functions***

In the broad context of the “reverse engineering” problems, a more comprehensive and extensive characterization of complex brain function is necessary. In order to achieve this, an expansion of tools for data acquisition, storage, analysis, and model formulation is necessary. It is clear that specific reverse engineering goals will lead to prioritization of particular aspects.

The characterization of brain functions can be divided into “internal” and “external” according to the following definitions:

*Internal* (proprioceptive)– related to understating the functions of brain regions involved in controlling internal parameters and their interaction (eg. oculomotor, social cognition, sensorimotor integration of limb kinematics, etc.)

*External* (exteroceptive)– addressing the functions required to characterize the external, observable environment (eg. tracking eye movement in natural environment, joint/limb kinematics, contact forces). This part also includes social cues and interactions.

The steps to achieve extensive characterization of “internally focused” and “externally focused” brain functions include measurements, formulation of models, iterations with engineering, etc. The **general goals** are to:

- Fully measure and characterize multiple brain regions, and their interactions, involved in complex tasks simultaneously
- Better understand “integrative” (eg. cerebellum) or broadly affecting centers (eg. reticular formation) or relationship to ascending/descending pathways (spinal cord function and plasticity)
- Understand the relationships between different measurement modalities at different spatial and temporal scales (eg. metabolic vs. spiking vs. oscillations, local vs. global, etc.)
- Obtain representations on multiple time/spatial scales and develop models at different scales
- Determine how episodes are linked in details (neurons, synapses) – eg. during oculomotor tasks, or social interactions
- Selectively gate the information flow through top-down selection, in different sensory modalities

- Elucidate hedonic mechanisms, utility networks of the brain and how they affect the entire brain including “lower level” structures ; reward systems with dopamine ; neurophysiology of motivation, urge, identification of internal “state” that drives autonomy.

The **specific “internal” methodological goals** are:

- To use MR spectroscopy to measure different substances in body tissue through spectral signatures. This is a big challenge in the brain since it can only identify a very limited aspect of neural activity currently
- Enhance current and emerging technologies (eg. fMRI, EEG, MEG, electrode recording, fast optical imaging, DTI, multi-photon, VSD, combinations)
- Manipulate and observe specific transmitters and neuron types in real-time ; record and control measurements of synaptic activity through mRNA techniques
- Measure laminar sources non-invasively
- Develop fast optical imaging
- Coordinate animal and human studies
- Some measures of glial cell function, evidence for spiking activity, inhibitory regulation, calcium balance, modulatory control of neural function, may play role in BOLD signal
- Selective artificial activation of neural circuits - activation of cellular sub-classes (optogenetics), chronic implantation
- TMS use for connectivity studies, virtual lesions. TMS needs to improve significantly to be able to selectively target deeper structures
- TDCS - transcranial direct current stimulation
- Development of knockout models Real-time interface, voltage-clamp to dynamic clamp to more abstract high level interactions, recorded “output” used to guide “input” stimulation, in real-time, these models need matching complexity/richness in periphery

The main **specific “external” methodological goal** is to fully measure the body with advanced external instrumentation (eg. contact forces between individual and objects) and extend the measurements to social interaction.

***The combination of external and internal characterization should result in the capability of performing long-term recording during real-world behavior involving handling of massive, complex, multi-modal datasets, their storage, analysis, and formulation of models.***

The issue of **variability** both internal (within same subject, and across brains, anatomy, structure, folding patterns, patterns of activity, etc) and external (variance in motor output like eye movement patterns, limb kinematics, social interaction, etc) should be considered and addressed in all of the above mentioned aspects.

Based on this information, the following timeline is proposed:

Timeline	Objectives
1-3 years	- Develop technology to acquire, store, and synthesize internal/external data (videography, sensor arrays, observation,

	<p>multi-scale, simultaneous recording)</p> <ul style="list-style-type: none"> <li>- Develop and characterize social paradigms, to better understand communication protocols between brains</li> <li>- Complete identification of brain regions associated with specific tasks/behaviors</li> <li>- Identify and implement artificial systems implementing sensorimotor brain functions with learning capabilities</li> </ul>
<b>3-5 years</b>	<ul style="list-style-type: none"> <li>- Formulation of detailed models of interconnected relationships between regions and relationship to external environment</li> <li>- Extension to development</li> <li>- Identify and implement artificial systems implementing basic social interaction behaviour with adaptation capabilities</li> </ul>
<b>5-10 years</b>	<ul style="list-style-type: none"> <li>- Extension to multi-agent characterization of circuits involved in behaviour of two or more interacting individuals</li> <li>- Identifying and implementing artificial, biomimetic systems implementing social behaviour with learning, adaptation and perceptual generalization.</li> </ul>

**Table 3. Understanding and Engineering of Brain Functions timeline**

#### ***7.4 Towards a roadmap for the understanding and engineering of brain circuitry***

The current **state of the art technologies** available for addressing the topic of understanding and engineering of brain connections are:

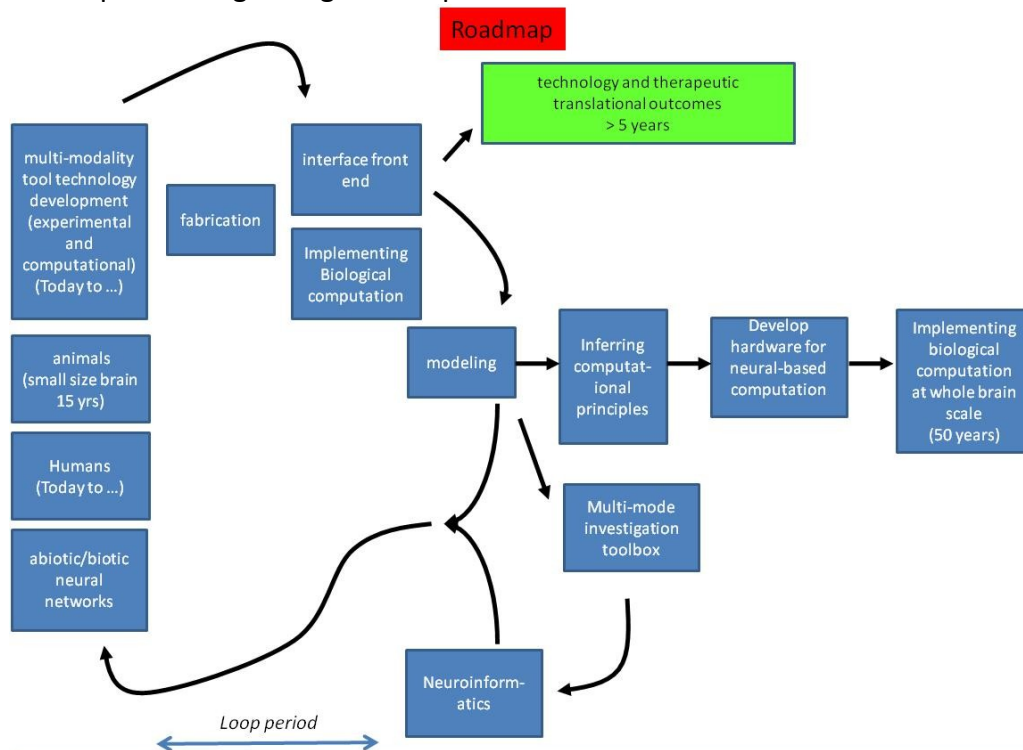
- High resolution histology
- Specific cell type identification
- Low resolution imaging of function
- Low resolution imaging of connections
- Mixed modalities i.e. : EEG-fMRI
- Interfacing with limited number of neurons
- Cell-specific optical stimulation
- Limited understanding of the tissue response
- Reverse engineering of small structures (retina)
- Neuromorphic devices with large sets of cells but limited function

The main **goals** of the roadmap are the following:

- Extract the computational principles in biological systems
- Interface between synthetic materials and neurons; big materials and computational problems, reliable and robust interfaces, biocompatibility, cost; moving beyond silicon (to biological systems)
- Provide accessible, reliable, robust, biocompatible, low cost electrodes
- Multiple time scales for multiple modalities for both experiment and computation in the real environment, real-time
- Tools that can work at various scales and resolutions
- Cooperation between experimentalists, theoreticians, computationalists, engineers (need to train a new generation)

- Combined tool development to acquire and analyze data of structural to functional activity; invasive and non-invasive; and stimulate
- Design and build circuits that can compute *in vitro* to link structure and function to the “Omics” (glycomics, proteomics, genomics)
- Hardware implementation and translation of biological computation
- Engineering new devices for multi-mode investigation: new materials, common platform (hardware and software) to develop a toolbox
- Develop real-time, closed-loop hybrid systems interacting with brains
- Develop an infrastructure for broad-scale production and distribution
- Computation infrastructures (eg. connection to INCF)
- Develop method for real-time measurement of activity (fMRI/EEG) in the behaving brain (IR, head mounted devices, cortical implants for epilepsy patients)
- Combine modalities to provide optimal multiple scale data, i.e. optical genetics and fMRI
- Determine concentrations of neurotransmitters (by for eg. high resolution NMR)
- Map and understand glial cell networks: role in development and self healing
- Solve biological computation at various scales simultaneously

Based on the point above a schematic representation of the steps need to achieve the ultimate goal of implementing biological computation at a scale of the whole brain has been developed.



**Figure 3. Schematic representation of the roadmap and cycles toward the Reverse Engineering of Brain Connections**

## 8 General Recommendations

As a result of the intensive interactions generated during the strategic workshop “Reverse Engineering of the Human Brain”, it is evident that further developments in this complex, multi-faceted and highly multi disciplinary field require joint efforts. In this respect, and in a global context, **strengthening US-Europe collaborations** would be an important step forward and would promise to significantly advance the field.

To this end, it is recommended to set up a **structural framework** to facilitate US-Europe collaboration **on the medium to long-term**. This could for example be implemented by joint funding schemes, bi- or multilateral funding agreements, co-funded institutions, common standards and regulatory practices, etc. This would enable the creation and the support of a truly interdisciplinary community of scientists and teachers addressing this field of research.

In particular, the following recommendations require immediate attention:

- Empower **inter-disciplinary collaborations**. An important example of type of interactions that needs to be strengthened is the collaboration between clinicians and scientists/engineers. As a main underlying motivation for such an effort, is the requirement to address brain functions and circuits from science to technology and engineering (from “knowing” to “doing”).
- Support **inter-disciplinary education**. For example, what is particularly needed are scientists and engineers with a combined computational and biological knowledge. Also biologists with a thorough theoretical background are indispensable – and relatively rare.
- Establish and maintain **joint experiments and facilities**. Coordinate the development of new instruments, equipment, techniques and infrastructures.
- Develop **common standards** and harmonized regulatory practices (most urgently, for pre-clinical trials).

The emphasis in these efforts should be put on synergies needed to address pre-identified challenges. For this, **common targets** need to be defined that will drive the research, engineering and the collaboration between disciplines. Examples of such targets include the:

- Creation of new technologies
- Understanding of higher functions of the human brain where simpler functions or animals are seen as intermediate goals

As to the **methodologies** to investigate brain functions and circuitry, focus should be put on merging complementary techniques to improve our knowledge of brain connection from the spatial as well as temporal perspective.

## 9 Workshop Resolution

The US-Europe **Reverse Engineering of the Human Brain** Workshop, held during May 23-26, 2010, in Dubrovnik, Croatia, brought together leading trans-national researchers, including 22 from the US and 22 from Europe, with a common interest in multi-disciplinary research on the understanding of the human brain functions and structure. Program officers representing the ESF, NSF and AFOSR were present and contributed to the workshop.

Participants in the workshop discussed the current state-of-the-art in both brain functions, and technologies associated with brain-like machines and circuitry, specifically highlighting the current needs, capabilities, grand challenges and collaborative opportunities surrounding **Reverse Engineering of the Human Brain**. The group was charged with developing a vision of the science and engineering research opportunities and revolutionary capabilities including formulation of the broader context and transformative advances gained through this cross-disciplinary US-European collaboration. Strong synergies for collaboration were found among the participants. As a result of our work on this charge, **we the workshop participants unanimously resolve:**

- A compelling new research frontier exists in the basic science and engineering of Reverse Engineering of the Human Brain which will form the basis for revolutionary brain-inspired technologies.
- Tremendous opportunities exist for synergistic ESF-NSF-AFOSR cooperative research on the transformational science and engineering pertaining to **Reverse Engineering of the Human Brain** and engineered systems including strengthening our basic understanding of these systems and societal outcomes derived from related technological advances for the environment, health, security, and energy.
- Scientific research should be performed, and technologies developed, ethically, and for the common good of humankind, and the **promotion of peaceful international cooperation**.
- NSF, AFOSR and ESF should strengthen existing bonds and build new ties facilitating US-Europe interactions, synergies and strengths by supporting these multi-disciplinary research initiatives on a global scale.
- Given that science and technological discoveries have no borders, it is strongly recommended that trans-continental research funding mechanisms and financial resources to support these initiatives be developed and committed.

Major interdisciplinary research grand challenges were identified that will maximize the impact of the cross-disciplinary brain-inspired research initiatives and technologies envisioned by the workshop participants. The realization of these challenges will lead to fundamental new discovery and significant advances in science and engineering.

## 10 Workshop Program

### **Sunday May 23, 2010**

17:00-19:00 Registration

18:00 – 19:00 Preparatory meeting (Organizing Committee, Session Chairs and Recorders only)

19:00 – 19:15 Introduction by workshop chairs: Rahmat Shoureshi & Giulio Sandini

19:15 – 19:45 Welcome by the funding organizations

Graham Harrison (NSF), Les Lee (AFOSR), Hugh DeLong (AFOSR), Ana Helman (ESF), Eva Hoogland (ESF), Lars Kristiansen (ESF).

20:00 – 21:30 Workshop opening cocktail & dinner

### **Monday May 24, 2010**

#### Plenary Lectures

9:00 – 9:45 *Neural Coding of Reward in the Ventral Pallidum* by J. Wayne Aldridge

9:45 – 10:30 *The neuromorphic brain* by Rodney Douglas

10:30 – 11:00 Coffee Break

11:00 – 11:45 *Neural Silicon and Biological Adaptive Neural Circuits* by Gert Cauwenberghs

11:45 – 12:30 *Towards a neurophysiologically grounded cognitive architecture for cooperative human robot interaction* by Peter Ford Dominey

12:30 – 14:00 Lunch Break

14:00 – 16:00 Four Parallel Sessions: Identifying the main challenges in:

**Engineering Brain Functions** (Session 1) Chair: Paul Verschure Recorder: Michael Baratta

**Engineering Brain Circuitry** (Session 2) Chair: Cherie Kagan Recorder: Sylvie Renaud

**Understanding Brain Functions** (Session 3) Chair: Roland Johansson Recorder: Garrett Stanley

**Understanding of Brain Circuitry** (Session 4) Chair: Dominique Durand Recorder: Stefano Panzeri

16:00 – 16:30 Coffee Break

16:30 – 18:00 Continuation of four parallel sessions

18:00 – 18:45 Organizing Committee and Sessions Chairs & Recorders progress meeting

18:00 – 19:30 Break

19:45 – 20:00 Bus transport to Restaurant Nautika

20:00 – 22:00 Workshop Banquet

### **Tuesday May 25, 2010**

9:00 – 10:30 Presentations from each Session (plenary)

Regrouping of participants into breakout groups

US Europe Workshop « Reverse Engineering of the Human Brain » REPORT

10:30 – 11:00 Coffee Break

11:00 – 12:30 Continuation of parallel sessions

12:30 – 14:00 Lunch Break

14:00 – 16:00 Work in two parallel sessions addressing Brain Functions and Brain Circuitry

16:00 – 16:30 Coffee Break

16:30 – 18:00 Continuation of the two parallel sessions

18:00 – 18:45 Organizing Committee, Sessions Chairs & Recorders progress meeting

**Wednesday May 26, 2010**

9:00 – 10:30 Two presentations on Brain functions and Brain Circuitry

10:30 – 11:00 Coffee Break

11:00 – 12:30 General discussion and conclusion

12:30 – 13:00 Concluding remarks by co-chairs of the workshop

13:00 – 14:00 Lunch Break

14:00 – 16:00 Organizing Committee, Sessions Chairs and Recorders meet to draft the workshop report

16:00 Workshop adjourned



**Monday May 24 - Grouping**

<b>S1 : Engineering Brain Functions</b>	<b>S2 Engineering Brain Circuitry</b>	<b>S3 : Understanding Brain Functions</b>	<b>S4 : Understanding Brain Circuitry</b>
L.K. Hansen	R. Douglas	P. Dominey	E. Fransen
N. Kruger	<b>S. Renaud (R)</b>	<b>R. Johansson (C)</b>	H. Kennedy
G. Metta	G. Cauwenberghs	J. Porrill	<b>S. Panzeri (R)</b>
H. Ritter	A. Felch	G. Shoener	A. Riehle
<b>P. Vershure (C)</b>	R. Jung	M. Beauchamps	M. Judas
S. Vijakaumar	<b>C. Kagan (C)</b>	T. Ellmore	W. Aldridge
S. Bogdan	P. Wolf	S. Ojemann	<b>D. Durand (C)</b>
<b>M. Baratta (R)</b>	D. Kragic	T. Ro	P. Sabes
T. Ragole	Y. Choe	<b>G. Stanley (R)</b>	P. Shoureshi

**Tuesday May 25 - Grouping**

<b>S1 : Engineering Brain Functions</b>	<b>S2 : Engineering Brain Circuitry</b>	<b>S3 Understanding Brain Functions</b>	<b>S4 Understanding Brain Circuitry</b>
<b>P. Vershure (C)</b>	<b>C. Kagan (C)</b>	<b>R. Johansson (C)</b>	<b>D. Durand (C)</b>
<b>M. Baratta (R)</b>	<b>S. Renaud (R)</b>	<b>G. Stanley (R)</b>	<b>S. Panzeri (R)</b>
P. Dominey	G. Shoener	G. Metta	S. Ojemann
T. Ellmore	M. Beauchamps	H. Ritter	J. Porrill
G. Cauwenberghs	T. Ro	T. Ragole	S. Vijakaumar
A. Felch	P. Sabes	P. Wolf	S. Bogdan
D. Kragic	N. Kruger	Y. Choe	R. Douglas
M. Judas	P. Shoureshi	A. Riehle	R. Jung
W. Aldridge	H. Kennedy	E. Fransen	L. K. Hansen

(C) Chair

(R) Recorder

## 11 List of abbreviations

AER	Address Event Representation
BOLD	Blood-Oxygen-Level Dependent
CMOS	Complementary Metal Oxide Semiconductor
DBS	Deep Brain Stimulation
DTI	Diffusion Tensor Imaging
EEG	Electroencephalography
EM	Electron Microscopy
FDA	Food and Drug Administration
fMRI	Functional Magnetic Resonance Imaging
IC	Integrated Circuit
INCF	International Neuroinformatics Coordinating Facility
IR	Infrared
MEG	Magnetoencephalography
MR	Magnetic Resonance
MRI	Magnetic Resonance Imaging
NMR	Nuclear Magnetic Resonance
RF	Radio Frequency
Si	Silicon
TDCS	Transcranial Direct Current Stimulation
TBI	Traumatic Brain Injury
TMS	Transcranial Magnetic Stimulation
VSD	Voltage Sensitive Dye