Masterplan Neuroinformatics

Neuroinformatics Steering Group

Prof. Stan Gielen (RUN)
Dr. Arjen van Ooyen (VUA)
Dr. Jaap van Pelt (chairman) (NIN)
Prof. Arno Siebes (RUU)
Prof. Harry Uylings (Neurofederation)
Prof. Wytse Wadman (UVA)
Dr. Gerrit van Ark (advisor) (ZonMw)

22 May 2006

1. Executive Summary

Brain function is still 'terra incognita' in the life sciences

The brain is the most complex system known to mankind. Unraveling how it functions, has been a challenge of all times. Not only because it touches on our own mere existence but also because of its enormous societal impact. As with many other forms of modern science, brain research is strongly technology driven. The last decade has convinced everyone, that the next leap forward will have to be built on intelligent handling of the enormous data generation power of modern techniques (for example, brain imaging) and on the conceptional level by integrating computational science into the existing theoretical approaches. As in the past, Nobel prizes are awaiting for those who will succeed in uncovering the roads that lead through terra incognita of brain function. At the societal level, the costs of problems related to brain dysfunction are so high that solving only a few of them could bring society a most substantial rise in welfare.

Brain function is still a scientific mountain which is drilled from all sides, but none of the shafts have really reached each other giving way to an explanation of brain function from molecules, via neuronal networks, interacting networks to behavioral and cognitive functions.

The main reason is that the brain is a complex information processing machine of yet unchallenged proportions. Not only its mere size, the human cerebral cortex has 10^{14} -10^{15} scalable connections (synapses) between neuronal cells, but also its hierarchical organization and parallel operation, make it far superior to modern computers in almost all aspects. It is anticipated that discovering the basic principles that determine perception, attention, self organization and adaptation of the brain will ultimately also revolutionarize informatics and the way we program our computers. On the other hand, it has been completely agreed on that if we want to have even the slightest chance of understanding the brain, we will be heavily depended on computational support of modern modeling and informatics. Any hypothesis formulated for such a complex system as the brain needs to be evaluated with computational rigor.

The ICT revolution has also given us the computer power to do high-resolution brain imaging that brings the day closer on which neurobiological and cognitive scientists can shake hands. Brain imaging has revolutionarized medicine and is now the platform on which neurobiologists and cognitive scientists interpret their experiments and can look for the first time in the functioning living brain. Modeling circuits and functions based on vast amounts of data is yet another emerging common platform on which neurobiology and cognition meet informatics. These examples illustrate how joint efforts between ICT and Neuroscience, i.e., Neuroinformatics, help us understanding the most fascinating and most important system in the world.

The world wide Neuroinformatics effort

It is often overestimated what is possible within two years but underestimated what is possible in a decade. Realizing - on the arguments mentioned above - that the latter may be the case in furthering our understanding of brain function the OECD has taken the lead in a world wide initiative on neuroinformatics. In 2005 the OECD Global Science Forum (GSF) on Neuroinformatics initiative was formalized with the establishment of the International Neuroinformatics Coordination Facility in Stockholm. Ten countries - including the USA, Japan, France, Germany and Sweden - have already joined the initiative. The Netherlands need to join this community now, if we want to consolidate our international scientific position and stay a member of this world wide neuroscience information exchange initiative.

The master plan on Neuroinformatics in the Netherlands

To join the OECD-GSF initiative on Neuroinformatics, the Netherlands

1. Has created an active Dutch Neuroinformatics Community, which has been successfully accomplished during the last three years with the support of the four NWO-departments for medical science, life sciences, exact science and behavioral sciences (see: www.neuroinformatics.nl),

2. Has to join the OECD-GSF initiative formally preferable through its leading Science Research Council NWO,

3. The Dutch Neuroinformatics Community has to acquire the funds to establish the Netherlands Neuroinformatics Node in the global network, and

4. The Dutch Neuroinformatics Community has to develop a Dutch Programme on Neuroinformatics and to acquire the funds to execute this programme.

This master plan asks NWO to join the OECD-GSF initiative on Neuroinformatics now. The basis is the successful creation of a Dutch Neuroinformatics Community in the recent years. The other pillars are the implementation plans laid out by the neuroinformatics community to establish the Netherlands Node on Neuroinformatics, to establish Netherlands Expert Centres on Neuroinformatics and to develop a Netherlands Neuroinformatics Education Programme.

The finances for these implementation plans have to be acquired by the Dutch Neuroinformatics Community from different sources including innovation funds like FES, SmartMix and the NWO-NRI initiative and, of course, from the universities and industries interested in establishing joint Expert Centres and Education Programmes on Neuroinformatics.

2. Mission

Our mission is to provide a general framework of computational tools and modeling approaches in order to advance our understanding of the working of the brain. To do this, we want to develop in the Netherlands the new interdisciplinary field of neuroinformatics, which combines data basing / sharing, data analysis, and computational modeling. Current research in neuroscience is hampered by a lack of data integration and conceptual insight. Neuroinformatics aims at taking away these barriers by enabling research at higher levels of complexity, dynamics and integration and paving the way towards a better understanding of the brain in health and disease.

Why neuroinformatics?
How does the brain work? How do tremendously complex processes such as perception, decision-making, learning, memory, and even (self) consciousness and human behavior arise from interactions among many billions of "mindless" neurons? How do genes affect neurodevelopment and neuronal architecture and how do neurotransmitters and drugs, via their effect on neurons and their interconnections, influence neuronal activity and ultimately cognition and behavior? How do impairments in the wiring of the brain cause serious brain diseases? Despite decades of intensive neurobiological research at the levels from molecule to cognition, these questions remain largely unanswered. The brain is one of our most important organs, yet at the same time the least understood. Without exaggeration, we can state that understanding the brain is one of the greatest challenges of 21st science. The brain is one of the most complex systems that exist, with enormous information processing powers. The abilities of the brain dwarf any man-made system with regard to, for example, pattern recognition, cognition, and reasoning. Even the brains of so-called simple organisms, such as ants and bees, surpass our most advanced computer systems in many tasks.

It is not because of a lack of data that we still do not have a fundamental understanding of how the brain operates. Over the past decades, floods of data have been and are still being produced in ever increasing amounts. We know more, for example, about the hundreds of different ion channels and receptors and about the many different neuron types that exist in the brain than we did ever before. We know, down to finest details, how neurons generate electrical activity and how a large variety of molecules modulates this activity. We know a great deal about the detailed anatomy of the brain and the myriads of interconnections between the different brain areas. With the newest experimental techniques, we are able to monitor complex spatiotemporal patterns of neuronal activity by measuring from many neurons simultaneously. Yet, this gathering of data, with each group of researchers concentrating on one particular level of biological organization, may not be sufficient for yielding major new concepts and breakthroughs about how the brain carries outs and coordinates its many tasks. Just collecting more and more data, with the expectation that the important principles would in due course become clear, is a strategy that will probably fail.

The new interdisciplinary field of neuroinformatics provides in our view a way by which we can seriously attempt to tackle one of the remaining scientific mysteries, the functioning of the brain. In order to forward our conceptual understanding of the brain and the nervous system in general, we need not only gather data, but also and especially integrate the different types of data - ranging from molecules to cells to neuronal networks and extending all the way up to cognition and behavior - and use computational and mathematical modeling to bridge these different levels of investigation. To do this, neuroinformatics combines neuroscience-related life sciences with information sciences and related disciplines such as computer science, mathematics, statistics, and physics. Both from a practical (e.g., data bases and data mining, mathematical and computational modeling) and a conceptual point of view (e.g., machine learning) there are many points of contact, and the synergies between these domains should be developed and exploited. To achieve its mission, neuroinformatics stands on three pillars:

- *Databasing / datasharing*. Neuroscience is a global and strongly growing scientific activity, which produces ever increasing amounts of heterogeneous data. Progress in neuroscience is partly hampered by the lack of methods to manage, integrate, and share this flood of data. Neuroinformatics therefore aims at developing and applying data bases and data-mining tools to improve the accessibility, sharing, and integration of neuroscientific data.
- *Data analysis and visualization*. New experimental techniques, such as microarrays, multi-electrode and photodiode arrays, and brain imaging, produce large amounts of complex spatiotemporal data that require sophisticated ways of analysis. Neuroinformatics will develop and apply mathematical and statistical methods to analyse and visualize the huge quantity and great complexity of neuroscientific data.
- *Computational and mathematical modeling*. To make significant progress in our efforts to understand the brain, better concepts, ideas and hypotheses should be generated about the functioning of the nervous system. Qualitative and quantitative modeling is an essential step to make progress. Modeling provides precise and exact ways of expression, which allow us to go beyond the insights that intuitive or common sense reasoning alone can yield. Models give structure and meaning to empirical data. Models especially enable us to study how phenomena at higher levels of biological organization (e.g., cognitive processes such as learning and memory) arise from processes at lower levels of organization (e.g., changes in the strength of synaptic connections between neurons) - that is, models act as bridges between levels of understanding. Neuroinformatics therefore aims at constructing and applying computational and mathematical modeling across all levels, from gene to synapse to cognition. The insights and predictions obtained by modeling in turn guide and feed the experiments with scientific hypotheses that are more focussed, quantitative and of higher complexity than what is seen nowadays.

In our view, neuroinformatics is an indispensible discipline for helping us understanding the most fascinating and most important system ("we are our brains") in the world. It is our conviction that in the end we will be able to make significant progress in explaining brain function from molecule to mind. We hope to make important steps in understanding how learning and memory emerge from the interactions among millions of neurons, how genes affect human cognition and behavior and how medicines alter brain function. We anticipate that neuroinformatics could also contribute to finding new strategies for treating brain diseases. Equally important, a better insight in the enormous information processing capacity of the brain will provide inspiration to build better artificial learning systems (machine learning, robotics).

3. Objectives

The goal of the National Program on Neuroinformatics is at least two-fold. First, it will provide the vehicle that will allow the Netherlands to join as a clearly visible, innovative high-tech partner the International Initiative on Neuroinformatics (details in Chapter 5). Secondly, it will allow the existing neuroinformatics field to bundle its forces. The Netherlands has a large potential of excellent research groups working on neuroinformatics but they are distributed according to the classical divisions of disciplines and subfields, including medicine, neuroscience, life science, biology, information sciences, computer science, mathematics, statistics, chemistry and physics; often spread out over general universities, technical universities and specialized institutes.

The National Program on Neuroinformatics will organize the field in (virtual) centers that combine sufficient mass and interdisciplinary expertise to run several relatively large programs that will push specific well defined topics (focus) in neuroinformatics forward. Such groups shall be large enough to represent the Netherlands in the International Arena; and given the high-tech component in almost any aspect of neuroinformatics, they shall also form an interesting partner for (Dutch) innovative industries that deal with neuroinformatics.

Last but not least, the new field of neuroinformatics can only flourish in the long run if it attracts and trains the best of the young scientists to create a next generation of experts well equipped to the task. It is explicitly not the aim of the neuroinformatics field to create a new subdiscipline in the ever more colorful landscape, but we realize that working in an interdisciplinary field that ranges from neurobiology to computer science, requires scientists that are trained in discussing common problems with colleagues with a different background. Scientists who know how to exploit synergies between fields and who have learnt how to incorporate their own expertise in a complex field like neuroinformatics. They can however still have received their basic training in one of the fields mentioned above.

A National Program on Neuroinformatics must provide the context for the formulation of a national research program, for national coordination by forming a National Node, developing an education and training program, providing a plan for acquiring enabling resources, providing a plan for sustainability, and for providing mechanisms for quality control.

3.1 Benefits

A National Program on Neuroinformatics is expected to have significant beneficial spin-offs for many areas in science and society.

For the neurosciences - The neuroscientists will be able to (i) organize their experimental data in structured data bases that are interoperable within a worldwide network, (ii) share data in collaborative projects, (iii) apply tools for data analysis and visualization and for in depth data exploration, (iv) analyze working hypotheses by means of quantitative computational models at a much higher level of complexity, (v) validate working hypotheses and predictions against experimental data. In other words, neuroinformatics advocates a quantitative, data oriented approach in neuroscience.

For the informatics and computer sciences - The computer scientists are challenged to integrate neuroscience data, knowledge, and models into a network of interoperable information systems. They are also challenged to translate new insights of how the brain processes information into new computing algorithms and technology (bio-inspired computing).

For the physical sciences - Researchers in the physical sciences are trained in developing quantitative models of natural systems and mechanisms. Such expertise is needed for the development of quantitative models in neuroscience. In particular, physically trained researchers are challenged to derive general 'laws' in the organization of living systems, built-in during a long-lasting evolutionary process, in addition to the physical constraints. Neuroscience could be a goldmine for physically trained people.

For the medical sciences - The accessibility of neuroscience data and information will in particular be beneficial for the medical field. Medical practice goes with a daily production of huge amounts of data which, after proper processing and storage in accessible data bases, can be of great value for further use, for reason of comparison in clinical practice, or for further scientific exploration. The availability of analytical and visualization tools and computational models directly enhances practical functionality.

For the industry - Industry is expected to be interested for several reasons. The availability of data and tools is one aspect but the standardization that is aimed at by the international Neuroinformatics program will in particular be appealing for companies producing data generating equipment (such as imaging equipment). The global neuroinformatics facility may become a particular market for new products enhancing its functionality.

For the public and public institutions – Neuroinformatics facilities for databasing and datasharing open ways to feedback on the public and governmental institutions in the case of public funded research.

For the international position of research in the Netherlands - The international program on neuroinformatics already stimulated and triggered new research programs in several countries, and by this has proven to impact on the advancement of science. With a clear presence in neuroscience and computer sciences it is also for the Netherlands of crucial importance to maintain at the forefront of these developments and to adhere to the international program. Not in the least to implement the quantitative data oriented approach advocated by the neuroinformatics program in the national scientific practice.

For the young scientists - Neuroscience is an extremely challenging field of research, working towards understanding the brain, the most complex organ in our body. Neuroscience integrates a great diversity of scientific disciplines and attracts students and scientists with many different backgrounds. It is expected that the goals of a neuroinformatics program will attract many young people to invest their energy and creativity in this field of research.

For the disabled - New developments in brain-machine interfacing hold promises for the development of neuroprostheses and brain controlled actions that may improve the quality of life of the disabled.

4. Implementation

4.1 Organization

It is imperative for the international position of the Dutch Neuroinformatics Initiative that the Netherlands join the International Organization and thus establish the National Node according to the rules set by this Organization. The Node will be relatively small and will also execute several of the organizational tasks that need to be coordinated nationally. The Node will present a stable and easily recognized entry point into the Dutch Neuroinformatics Program; which may compensate some of the drawbacks of the highly dynamic virtual Institute organization proposed for the rest of the field.

The size of the Netherlands and the state of modern technology, which is an inherent part of this initiative (such as GRID computing, and WEB based data-bases), permits a first stage of organization into research clusters that operate as virtual (distributed) expertise centers composed much more on a content-based definition than on a geographical or institutional organization. Such an organization is also in line with the actual situation where expensive scanning / imaging facilities, large computing facilities and specialized research facilities are already shared and often operated on a remote basis.

For the field to get organized, a limited number of common themes will guarantee the best focus and critical mass. One road to evolve to such themes is by means of self-organization into a few Dutch neuroinformatics clusters. Most likely such clusters will be highly multi-disciplinary, but the collaborations must first and for all be functionally important and provide added value. It is not imperative that each virtual center incorporates all known disciplines. The optimal outcome is a limited number of broad, yet distinct and well balanced centers that cover the complete field described in the National Program on Neuroinformatics with only overlap where such is functional. Another road, that is proposed here, is to start with a number of common themes that, given the national scientific landscape, fully exploit the expertises in the Netherlands. A proposal for such common themes (i) Web-based Datasharing Infrastructure, (ii) Computational Platforms for Data Analysis, and (iii) Computational Modeling in order to organize the typical neuroinformatics expertises and (iv) Brain Imaging and (v) Brain-Machine Interfacing as typical integrative themes.

The following aspects should be covered by the full Program Initiative on Neuroinformatics:

- *Databasing / datasharing* - Research in the area of data basing and data sharing is essential for integrating recent developments in informatics and computer sciences into the daily practice of the neurosciences, which will be promoted by developing interoperable database systems with intuitive user interfaces. Exchange of unique data, often generated in one context at high cost, can be extremely useful and cost effective to other scientist under the condition that data formats up to a high level are exchangeable, experimental conditions are well retrievable, and IP, ethical and other legal aspects related to privacy are solved. Other important issues are quality control and content lifetime, the need for ontologies, and maintenance and sustainability, computing and storage resources, operations. Neuroinformatics should take the lead in this arena and guarantee that solutions will evolve that meet international standards. *The objective is to develop web-based facilities for data basing and sharing, and integration of neuroscientific data*.
- *Analytical Tool Development* - Tools need to be developed for data handling, data analysis, data visualization and data exploration. The enormous diversity in data types and data

formats, the multitude of different experimental devices from which they originate and the even larger diversity of fields of scientific research in which they are being collected, requires continuous choices on generality and specificity in analytical tool development. In addition, the environment in which data is being produced is continuously changing, requiring an ongoing evolution of analytical tools. Generally, much more information is contained in experimental data than is extracted from in daily practice. Powerful tools for data exploration will contribute essentially to the impact of experimental investigations. *The objective is to work on the availability of these analytical tools and on the compatibility of these tools with all relevant data formats.*

- *Theoretical and Computational Modeling* - There is a strong need for good conceptual models / theories, but also for tools that allow testing of such models with (existing) data. Modeling approaches may range from highly abstract views to very complex implementations of neurobiological systems. Especially in those areas that rely heavily on large amount of specialized data or of large system complexity, neuroinformatics should be the key player in this field. *The objective is the stimulation of the application of computational modeling approaches and the integration into experimental practices.*
- *Man machine interfacing, robotics and neural control systems*. The technological advances in interfacing artificial devices with the nervous system set increasing challenges at the level of signal and information processing, and the control of complex motor functions. Understanding brain activity and brain plasticity is a prerequisite for successful applications and here can neuroinformatics play an important role in addition to the development of powerful tools for data analysis, and information extraction and coding. *The objective is to apply neuroinformatics tools and approaches to the further development of man-machine interfacing.*
- *Brain Imaging.* - Although many research and clinical institutions have facilities for brain imaging, there are no well-developed facilities for data sharing. Such exchange and sharing of data, however, is highly beneficial for the field. *The objective is to built the facilities for data basing and data sharing in the field of brain imaging*.

All the centers should collaborate on educational aspects. Given the size of the scientific community and the multidisciplinary approach needed, we propose a National Neuroinformatics Educational Program, preferably together with comparable groups in Flanders, Belgium. Two tracts are foreseen, one aimed at (PhD / Master) students from informatics(-like) science that need education in Neuroscience and another one for students in Neuroscience that need education in Informatics and computational and mathematical modeling.

4.2 Workplan

The workplan includes the following actions

- The organization of (virtual) expert centers around the above mentioned neuroinformatics themes (i) Web-based Datasharing Infrastructure, (ii) Computational Platforms for Data Analysis, (iii) Computational Modeling, (iv) Brain Imaging, and (v) Brain-Machine Interfacing. These expert centers will each give focus to their research programs and bundling of their expertises, but need to operate in close mutual collaboration and tuning of their research projects.
- Developing a neuroinformatics education and training program. This program integrates the typical disciplines of neuroinformatics (neuroscience, informatics, cognitive and exact sciences) and educates students in a common language. Many research groups support

educational programs that already contain relevant components for neuroinformatics. A national educational facility can therefore be created by coordination of existing facilities and development of new programs. It is further crucial to work on the promotion of career opportunities for young scientists.

- Organization of national activities into a National Node and linkage to INCF. This implies coordination of research, of community activities, of the web-based data sharing infrastructure, of educational program. With coordination into a National Node, the Netherlands will be prepared to become linked to the international INCF program.
- Building a plan for acquiring enabling resources. Plans need to be developed by the neuroinformatics community for utilizing funding opportunities such as the larger public programs as FES, SmartMix, and the NWO-NRI program Brain & Cognition, the 'smaller' regular funding programs of NWO (departments), support from universities and research institutes, as well as the European Commission. Industrial interest for neuroinformatics will create a source for private funding. It is anticipated that these institutions are in particular interested in supporting (joint) expert centers for neuroinformatics research and education / training.
- Providing a plan for sustainability and mechanisms for quality control. Databases, analytical tools and computational models need continuous update with scientific progress. Plans need to be developed to assure that these facilities maintain the user/researcher at the leading edge of science.

4.3 Integrated approach

The success of this program critically depends on integrative multidisciplinary collaboration, and thematic coherence between and within the different centers. These centers integrate national expertises and can be organized as a central or a distributed facility. Each center need to develop a focussed research program supporting the overarching objectives of neuroinformatics.

Expert Center for Web-based Datasharing Infrastructure
This center will work on the development and implementation of tools for data basing, data sharing, data mining, developing guidelines, standards for data, metadata and quality control, ontologies, dissemination of knowledge, outreach to other communities. The center can build on the current national initiatives for eScience and BioGrid.

Expert Center for Computational Platform for Data Analysis
This center will work on the development of tools for data analysis, visualization and data exploration for the neurosciences. These tools need to be developed for the neuroscientific practise and be compatible with used data structures.

Expert Center for Computational Modeling
This center will promote the development and use of computational modeling tools in integration with experimental approaches. The aim is to advance our understanding of how the brain works by enabling research at higher levels of complexity, dynamics and integration.

Thematic Center of Brain Imaging
This center will work on the development and implementation of neuroinformatics tools for brain imaging including data basing, data sharing and image analysis. The ongoing technological developments in the quality of the images need ongoing development of computational tools to analyze and visualize the data, as well to explore and interpret the information contained in the data.

Thematic Center for Brain Machine Interfacing, Robotics and Neural Control Systems
This center will work on the neuroinformatics of brain machine interfacing (BMI). The technological advances in interfacing artificial devices with the nervous system set increasing challenges at the level of signal and information processing, and the control of complex motor functions.

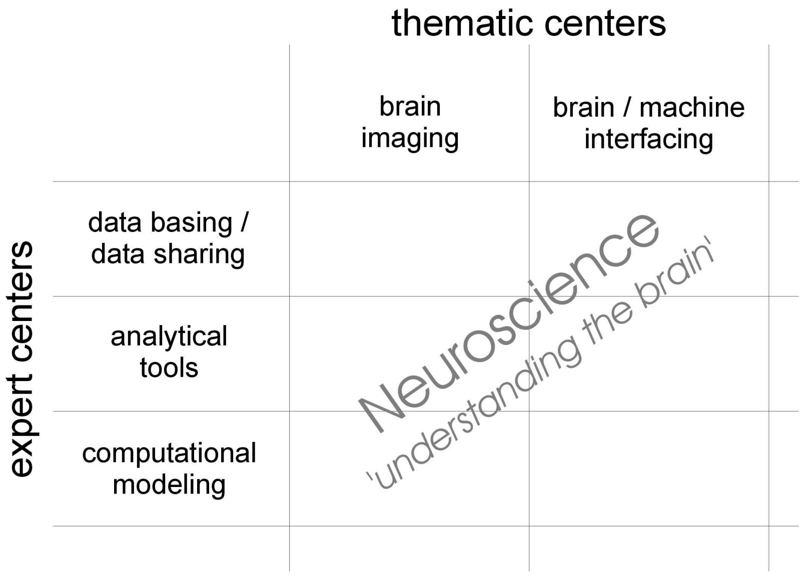

Figure 1. Illustration of how expert centers and thematic centers form an integrated field of research providing a neuroinformatics platform for the Neurosciences to help furthering our understanding of the brain.

4.4 National Node

The international neuroinformatics program, coordinated by INCF, relies on the existence of National Nodes that constitute the national organization of its participants. A National Node coordinates the neuroinformatics activities within a country and is represented in INCF (see Chapter 5). Its tasks include the coordination and facilitation of local neuroinformatics research activities, the promotion of sharing neuroinformatics data, the development of the description of standards of meta data of the contents and quality of databases, analytical tools and computational models, advising on IPR, and the coordination of management of data base administrators.

4.5 Education and Training Program

Education and training of students and researchers in the multidisciplinary field of neuroinformatics is important for developing common language, skills and knowledge and, of course, it is crucial for the future of the field. It is the task of the neuroinformatics centers and other relevant educational institutions to organize, in collaboration, a neuroinformatics education and training program. Given the size of the scientific community and the multidisciplinary approach needed, we propose a National Neuroinformatics Educational Program, preferably together with comparable groups in Flanders, Belgium. Two tracts are foreseen, one aimed at (PhD / Master) students from informatics(-like) science that need education in Neuroscience and another one for students in Neuroscience that need education in Informatics and computational and mathematical modeling. A national educational program may build on existing courses and training schemes, but may also need new curricula to be developed. It is proposed that a national education committee is being formed in order to develop such a coordinated program. This includes the formulation of educational goals, evaluation of existing facilities, development of new courses, etc. It is important to anticipate on similar programs in other countries in order to broaden education and training facilities for the students. It is also crucial to work on the promotion of career opportunities for young scientists.

4.6 Coordination

The program needs coordination at the level of the neuroinformatics centers and at the national level. Coordination at the neuroinformatics center level is needed for optimally running these (virtual) multidisciplinary centers. National coordination is needed to organize the neuroinformatics activities in the Netherlands into a national node (NN), for the coordination of the NN tasks in the INCF program (Chapter 5), for the organization of regular meetings, for running the website, for the representation in the INCF board, for communication with other platforms such as BioGrid, for the organization of fundraising, for implementing mechanisms for quality control, and for organizing a plan for sustainability. For this coordination an executive committee could be formed composed of the expert center coordinators and a national coordinator. The NI program should further be supported by a Neuroinformatics Program Committee, with representatives from NWO, Users Groups, the National Initiative Brain & Cognition, etc. Progress monitoring, quality evaluation and call preparation are among the tasks that further need to be allocated to these committees

4.7 Business Plan

For bootstrapping a National Program on Neuroinformatics the first step is to adhere to the international program via INCF membership (120k$ / year), and the appointment of a national node coordinator (1 fte). The following steps concern fund raising to get started the neuroinformatics centers.

Neuroinformatics Centers will be defined and evaluated on the basis of a consistent and coherent research program, covering the issues mentioned above. The Centers are based on guaranteed input from existing sources and they will compete for additional resources made available on a temporal basis.

Scale and critical mass. Typically, neuroinformatics centers work on integrated and collaborative projects for a period of at least 5 years, with the joint participation of about 6 - 10 scientists. The total program must be implemented with sufficient critical mass for the different themes to integrate national expertise. The implementation in terms of five centers brings the program up to the level of about 15 - 25 MEuro for a period of 5 years (based on 0.1 MEuro / manyear).

4.8 Evaluation

The success of a national neuroinformatics program can be formulated in terms of facilities that have been developed and built up, research progress, the incorporation of neuroinformatics tools and approaches in neuroscience practice towards quantitative data and model-based approaches, attitudes to better manage and share data and knowledge, and education and training programs. Funding organizations will further provide existing instruments for evaluation and quality control.

5. Position Neuroinformatics in International Organizations

5.1 International Neuroinformatics Coordinating Facility - INCF

The growth of the field of Neuroinformatics is illustrated by the start of many neuroinformatics research programs, and new neuroinformatics journals. Much of these developments have been fuelled by the OECD Global Science Forum initiative to support an international program in Neuroinformatics, that officially has started in 2005. This international program aims at building an international neuroinformatics facility for managing and sharing neuroscience data and knowledge, and for developing tools for data analysis and computational modeling. The program is supported by an International Neuroinformatics Coordinating Facility (INCF) responsible for the required international coordination and standardization. Ten member countries have presently signed as a member of INCF, and committed themselves to the INCF objectives. The INCF secretariat is hosted in Stockholm, Sweden. The international program is based on the coordination of national neuroinformatics activities through National Nodes and international coordination through INCF. The operation of INCF is laid down in the INCF Business Plan. All the documents prepared by the OECD Global Science Forum Working Group Neuroinformatics, defining the international program are accessible through http://www.neuroinformatics.nl. For the development of neuroinformatics in the Netherlands it is crucial that also this country signs up. Present activities of the INCF board concern the staffing of the secretariat, which is now started with the selection of the executive director. Once this is realized the INCF will become into full operation.

In summary, the INCF Business Plan specifies the operations of the central facility, the Secretariat, and the distributed facility, the National Nodes, to coordinate and harmonize national and regional neuroinformatics efforts. It is to promote international collaboration for standards, guidelines, ontology and software tools designed to facilitate interoperability and use on multiple platforms. In addition, the Secretariat is responsible for maintenance and currency of these core infrastructure elements. The INCF workplan includes the development of (i) databases, (ii) infrastructure (e.g., portals, communication channels, database federations, grid middleware), (iii) tools (e.g., simulation environments for computational neuroscience, computational devices, data analysis, data mining, data warehousing, middleware), and (iv) the construction and dissemination of models of the nervous system and simulation of neural processes. Other activities include the development of guidelines, standards, ontologies, dissemination of knowledge, outreach to other communities. INCF further encourages the development of interdisciplinary training programs, and facilitate joint funding agreements to carry out specific projects or meet specific goals. In particular INCF aims at implementing the Program in Neuroinformatics (PIN) as a mechanism of support of development of neuroinformatics.

National Nodes implement the national coordination. National Nodes are expected to participate in the implementation of the INCF work programs, (i) to coordinate and facilitate local neuroinformatics research activities, (ii) promote the sharing of neuroinformatics data under a common set of standards, consistent with the INCF, (iii) promote the development of neuroinformatics in support of the INCF, (iv) develop a description of an accepted standard of meta data of the contents and quality of databases, analytical tools and computational models, (v) advise on the policy of Intellectual Property Rights and protection of experimental subjects, and (vi) coordinate the management by data base administrators.

5.2 Neuroinformatics in the European Community

The international program INCF has also received strong interest for support from the European Commission (EC) as being expressed during a special EC Workshop *Future of Neuroinformatics in Europe*}, Brussels, June 9, 2005. Several support instruments were proposed in the form of Special Support Actions, and Coordination Actions (requiring involvement of legal entities such as universities and research institutes), the ERA-NET Scheme (requiring national bodies responsible for financing research activities), and Articles 169 & 171 High Level Integration (requiring involvement and commitment of member states). A proposal for a European Initiative in Neuroinformatics (EIN) to establish an organisation and communication infrastructure was discussed.

The Commission recently issued a call for a Special Support Action on neuroinformatics coordinating activities. A proposal, focusing on support for INCF organized workshops and other activities, has been submitted by the INCF chairman Dr. Grillner and the UK Medical Research Council. The total budget of this proposal is around 600.000 Euro and the 5 work packages cover support for - workshops (5) of specialists, covering the primary areas of neuroinformatics (databases, tools, modeling), to be held at the secretariat and counseled by the Executive Director – establishing an inventory of PhD programmes, other training programmes and research activities within neuroinformatics on a global scale - strategic planning at different time scales, defining a road map - developing best practice schemes for training - exploring the possibility of establishing an open access journal for neuroinformatics.

The European Commission has recently decided to support a Special Support Action on the organization of a workshop: Databasing the brain. This will result in an international meeting to be held in Oslo, June 25-27, 2006.

5.3 International context

Member countries of INCF as well as other countries will start or have already running national programs in neuroinformatics, such as Czech Republic, Finland, France, Germany, Italy, Japan, Norway, Sweden, Switzerland, USA, UK, Belgium, Australia, Canada, China, India. The neurosciences in these countries (accomodating by far the major world-wide activities in neuroscience) will benefit directly from these neuroinformatics programs. Examples of national programs are listed in the Appendix B.

5.4 Journals

A Neuroinformatics Committee has been established by The Society for Neuroscience. This committee will provide recommendations for the role of journals in supporting or interacting with databases, developing data sharing and database interoperability recommendations, and in developing terminology / ontology standards.

5.5 Related international developments

The neuroinformatics program fits in a general scientific development in which life sciences research adopts integrative and systems approaches. Based on the availability of large amounts of highly granular information at the different levels of biological organization, present-day computing power and modeling approaches now make it possible to study living systems from an integrative approach. Therefore, Systems Biology and Integrative Neuroscience are strongly growing fields of research. The promises are clear, i.e. getter deeper understanding of the complex organization of living systems. Many centers and research institutes abroad have started programs in systems biology and integrative neuroscience.

6. National Resources

6.1 Neuroinformatics Research

In anticipation to the international developments a *Steering Committee Neuroinformatics in the Netherlands* was formed in 2004 in order to work on the conditions for a neuroinformatics program in the Netherlands. The steering committee has worked on (i) an inventory of national resources enabling such a program, and (ii) the creation of a national community in neuroinformatics, through (iii) the organization of workshops, the promotion and awareness of neuroinformatics, and the creation of a website (www.neuroinformatics.nl) for dissemination of information. The steering committee also invested in gaining support from scientific, governmental and industrial organizations. Three documents were produced for the *Objectives* of a national program, for a number of *Statements* by which participants express their commitments to the program, and for a *Roadmap* with the main steps to arrive at a national program (available via www.neuroinformatics.nl).

Many research groups have since then expressed their interest in a national neuroinformatics program. This list (see Appendix) makes clear that a national neuroinformatics program can build on a large community of scientists from a full range of expertises needed for a successful neuroinformatics program. The groups represent basic, clinical and computational neuroscience, biophysics, mathematics, informatics and computer sciences, cognitive and psychological sciences, and biomedical engineering. Almost all general universities and all technical universities are represented, as well as several research institutes. The scientific programs of these research groups include common themes as (i) physiological processes and information processing in the brain, (ii) structural organization of the brain, (iii) computational platforms for the analysis of images and physiological data, (iv) computational platforms for modeling brain structure and function, (v) non-invasive brain imaging, (vi) data basing and data mining, grid technology, (vii) bioinformatics, and (viii) neural control and man-machine interfacing. The inventory also made clear that the participating research groups provide possibilities for a full range of education and training programs on neuroinformatics topics. Thus, the neuroinformatics community has the expertise, the quality, the research and educational facilities and, above all, the enthusiasm, for making the Netherlands well prepared to execute a national neuroinformatics program at the highest international competitive standards.

Within a neuroinformatics program the field must organize its research and education into coherent collaborative projects. The organization into a few overarching neuroinformatics themes will guarantee focus and critical mass per theme. A number of themes that seems best representing the expertises in the neuroinformatics community are (i) Web-based Datasharing Infrastructure (ii) Computational Platform for Data Analysis, (iii) Computational Modeling, (iv) Brain Imaging, and (v) Brain-Machine Interfacing,.

The interest and enthusiasm of the field has already resulted in several recent initiatives to start local neuroinformatics research and training programs. For instance, a neuroinformatics program is now running at the Center for Neurogenomics and Cognitive Research (CNCR) at the Vrije Universiteit in Amsterdam, and at the Radboud University in Nijmegen. With the eBioscience initiative also the University of Amsterdam is preparing such a program.

6.2 Industry

Industry shows increasing interest in the life sciences. For instance, companies active in brainscan and braininterface equipment show great interest in the neuroinformatics objectives, research and in the multidisciplinary education and training of young neuroinformatics researchers. A national neuroinformatics program will therefore provide unique opportunities for joint projects. Examples of such complementing interests are when industry is mainly involved in the production of equipment for acquiring data from brain structure and function, and neuroinformatics research concentrates on data analysis / exploration and data management. Or industry is involved in equipment for brain stimulation and needs the knowledge and the computational models from neuroinformatics for optimizing stimulation schemes.

6.3 Funding

The importance of neuroinformatics, as initially strongly advocated by the OECD Global Science Forum, has also be acknowledged by the Ministry of Education, Culture and Science and several NWO departments with, in particular, ZonMw supporting materially to the preparatory activities of the Neuroinformatics Steering Committee.

The finances for the implementation of the program itself have to be acquired by the Dutch Neuroinformatics Community. Opportunities for funding are the larger public programs as FES, SmartMix, and the NWO-NRI initiative Brain & Cognition, the 'smaller' regular funding programs of NWO (departments), and the support from universities and research institutes. Industrial interest for neuroinformatics will create a source for private funding. It is anticipated that these institutions are in particular interested in supporting (joint) expert centers for neuroinformatics research and education / training.

Funding may also come from the European Commission who has expressed its interest in neuronformatics. This will, in particular, be relevant with international collaborative proposals prepared within the international neuroinformatics program of INCF and, thus, requires that the Netherlands is member of INCF.

7. Cross links with other platforms

7.1 Biogrid

A proposal for the organization of a national infrastructure for e-science on the basis of grid technology (BIG GRID) has recently been selected for awarding by NWO. The e-Science infrastructure to be built is intended to provide Grid based facilities for databasing / archiving, data communication and computing power for data analysis. Because these facilities implement basic resources for a neuroinformatics program, the NI steering committee has strongly supported this Big Grid proposal. Big Grid facilities are especially beneficial when resource demands are high, such as in the case of image data bases requiring large amounts of storage capacity, and in the case of large scale brain modeling, requiring substantial compute power. Facilities for secure communication with on the fly encryption via dedicated optical links may be highly relevant for ethical and IPR-sensitive applications. The optimal architecture concerning centralized / distributed facilities needs further to be investigated.

7.2 Neurofederation

In December 2005 the Dutch Neurofederation formulated her vision on next decade brain research in the *Strategienota 2005-2015*. There is a great societal need for brain research because of brain diseases, aging, educational challenges, understanding human behavior, and for the development of man-machine interfaces. New challenges are identified at gene-environment interaction, brain & cognition, plasticity and (de)regeneration. Integrative neurosciences and neuroinformatics are seen as key approaches for the realization of these challenges.

7.3 Systems Biology

In line with international developments Systems Biology is also an emerging field in the Netherlands, not in the least by the activating work of the Dutch Platform for System Biology. With the promotion of computational modeling approaches to integrate data and knowledge over different levels of biological organization, there is great resonance with neuroinformatics, focussing on the nervous system.

7.4 e-BioScience

At the UVA efforts are ongoing to start a local e-BioScience initiative as a *multidisciplinary approach to answer biological questions by organizing flexible computer networked collaborations and distributed data sources, and by utilizing new developments in computer science, physics, mathematics and information and communication technology*. Organized as a virtual institute, collaborative research activities concern (i) datahandling, preprocessing & fusion, (ii) data integration & knowledge representation, (iii) process modeling & dynamic simulation, and (iv) complex systems research. These are just the ingredients of neuroinformatics when applied to the neurosciences.

7.5 National Initiative Brain & Cognition

A National Initiative Brain & Cognition is presently in preparation. This initiative aims at bundling and integrating national research of the brain and cognition into a coherent program for fundamental and applied research. Such an integrated program is timely because of the advancements in science and technology now enabling the bridging of cognitive and brain science. With this initiative a platform is formed for applied research towards learning and memory, communication, brain disorders, and integrative cognition and neuroscience. The initiative will put a strong requirement on the integration of data and knowledge and the availability of tools for data analysis and exploration and for computational modelling. Neuroinformatics will therefore play a crucial role in the realization of this initiative.

Appendix A - Participating Research Groups

Listed in alphabetical order on organisation

CWI - Department of Information Systems - Prof. Martin Kersten

CWI - Center for Mathematics and Computer Science - Prof. Jan Verwer

Institute for Adaptive and Neural Computation (Edinburgh, U.K.) - Dr. Mark van Rossum

LUMC - Afdeling Radiologie en Neurologie - Prof. Mark van Buchem

NIN - Netherlands Institute for Neuroscience - KNAW – Research Group Neurons & Networks - Dr. Jaap van Pelt

NIN - Netherlands Institute for Neuroscience - KNAW – Research Group Prefrontal Cortex \& Cognition - Prof. Harry B.M. Uylings

NIN - Netherlands Institute for Neurosciences - KNAW – Retinal Signal Processing Group - Dr. Maarten Kamermans

NIN – Netherlands Institute for Neuroscience – KNAW – Vision and Cognition Group – Prof. Pieter Roelfsema

RUG - Department of Mathematics and Computer Graphics - Prof. Jos B.T.M. Roerdink

RUG - Institute of Mathematics and Computing Science – Research group Intelligent Systems - Prof.dr.sc.techn. N. Petkov, Dr. M. Biehl, Dr M. Wilkinson

RUN - Department of Biophysics - Prof. C.C.A.M. Gielen

RUN - F.C. Donders Center - Prof. Peter Hagoort

RUN - F.C. Donders Centre for Cognitive Neuroimaging - Dr. Ole Jensen

TU Delft - Neuromuscular Control Group (NMC) - Prof. Frans C.T. van der Helm, Dr. DirkJan Veeger, Dr. Ir. Alfred C. Schouten, Dr. Ir. Erwin de Vlugt, Ir. David A. Abbink, Drs. Wendy W. de Graaf, Ir. Jasper Schuurmans.

TUE - Department of Biomedical Engineering – Technische Universiteit Eindhoven - Dr. Peter A.J. Hilbers, Dr. ir. H.M.M. ten Eikelder, N. Kuijpers

TUE - Department of Biomedical Engineering - Group Biomedical Image Analysis - Prof. Bart M. ter Haar Romeny

University of Maastricht - Department of Psychology – Neuroimaging and Cognitive Neuroscience - Prof. Rainer Goebel

UMCU / RMI - Functional Neuroimaging Unit - Prof. N.F. Ramsey

UMCU / RMI - Structural Neuroimaging Section - Dr. Hilleke Hulshoff Pol, Dr. Hugo Schnack

UT - Department of Biomedical Signals and Systems – Group Neurotechnology - Prof. Wim L.C. Rutten

UU - Functional Neurobiology, Helmholtz Institute, Faculty Biology, Utrecht University. Prof. A.V. (Bert) van den Berg, Dr. Martin J.M. Lankheet, Dr. Richard J.A. van Weezel.

UU - Large Distributed Databases Research Group - Prof. Arno Siebes

UVA - SILS Center for Neuroscience - Prof. Wytse J. Wadman

UVA - Department of Psychology - Prof. J. van der Pligt UVA - Psychonomics - Prof. J. Raaijmakers, Prof. V. Lamme, Prof. A. Kok UVA - Developmental Psychology - Prof. M. van der Molen, Prof. H. van der Maas, Prof. K.R. Ridderinkhof UVA - Psychological Methods - Prof. P. Molenaar

UVA - Department of Social Science Informatics - Dr. Machiel Jansen

VUA - Center for Neurogenomics and Cognitive Research (CNCR), Department of Experimental Neurophysiology - Prof Arjen B. Brussaard, Dr. Arjen van Ooyen, Dr. Niels Cornelisse, Dr. Ronald van Elburg, Dr. Klaus Linkenkaer-Hansen, Dr. Ildiko Vajda

VUA - MEG Centrum VUMC - Dr. Jan C. de Munck

VUA - Centre for Integrative Bioinformatics - Prof. Jaap Heringa

Appendix B - National Programs in Other Countries

Germany (member INCF) - In 2005 the German Network for Computational Neuroscience has started. The network has four Bernstein Centers for Computational Neuroscience located in Berlin (http://www.bccn-berlin.de/), Freiburg (http://www.cndf.uni-freiburg.de/), Goettingen (http://www.bccn-goettingen.de/) and Munich (http://www.bccn-munich.de/start.shtml). The network runs with support from the Federal Ministry for Education and Research.

UK (working on membership INCF) - The UK has organized its neuroinformatics activities in a UK Neuroinformatics Network (http://www.neuroinformatics.org.uk/) aiming at *establishing a forum for the UK neuroinformatics community, and to define and action a set of activities that will identify issues critical to the field. The forum will provide a channel for discussion, a means for developing neuroinformatics, and a voice to represent the community in discussions with other scientific areas, commercial organisations, funding/governmental and international agencies*.

USA (member INCF) - The Human Brain Program (HBP), being launched in 1993) was the first to support Neuroinformatics as a new science and has, since then, significantly contributed to its growth and success (http://www.nimh.nih.gov/neuroinformatics/index.cfm).

Japan (member INCF) - The Riken Brain Science Institute is active in developing Neuroinformatics activities in Japan (http://www.brain.riken.go.jp/bsi-news/bsinews24/indexe.html). Supported by the Ministry of Education, Culture, Sports, Science and Technology, a program *Neuroinformatics of the visual system* has started towards a standardization of neuroinformatics databases. (http://platform.visiome.org/index.html).

Sweden (member INCF) - The secretariat of the INCF is located in Stockholm at the Karolinska Institute.

Italy (member INCF) and **India** have started a collaborative Neuroinformatics Program supported by a ministerial collaborative agreement (MoU on the establishment of a research hub on Neuroinformatics between the Consiglio Nazionale delle Ricerche - ITB Institute of Biomedical Technology, Milano and the National Brain Research Centre, Gurgaon).

Australia (working on membership INCF)

Canada (working on membership INCF)

China (negociating membership INCF)

India (negociating membership INCF)

Belgium (working on membership INCF)

Czech Republic (member INCF)

Finland (member INCF)

France (member INCF)

Norway (member INCF)

Switzerland (member INCF)