Collaborative Research in Computational Neuroscience (CRCNS)

2005 Principal Investigators' Meeting

Report of PI Breakout Discussions

National Science Foundation
Directorate for Computer and Information Science and Engineering
Directorate for Biological Sciences
Directorate for Social, Behavioral, and Economic Sciences
Directorate for Engineering
Directorate for Mathematical and Physical Sciences

National Institutes of Health
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National Institute of Mental Health
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National Institute on Deafness and Other Communication Disorders
National Institute on Alcohol Abuse and Alcoholism
National Institute on Aging
National Eye Institute
National Institute of Biomedical Imaging and Bioengineering
National Institute of Dental and Craniofacial Research

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Introduction and Summary

Collaborative Research in Computational Neuroscience (CRCNS; http://www.nsf.gov/crcns) is an interagency program supporting interdisciplinary science and engineering research on brain function. The program stresses innovation and collaboration, supporting interdisciplinary teams that are tackling the complex problems of the nervous system by bringing together biological, computational, engineering, mathematical, statistical, and cognitive perspectives.

As of this writing, the program supports 71 projects through the combined efforts of five participating Directorates of the National Science Foundation (NSF), nine Institutes of the National Institutes of Health (NIH), and the National Geospatial-Intelligence Agency. These projects address problems from the level of molecules and cells to systems, behavior, cognition and diseases, exploiting techniques including (but not limited to) computational modeling of phenomena ranging from the biophysical to the cognitive, numerical simulations of dynamical systems, and data mining, machine learning, and statistical approaches to large-scale databases, imaging, and genomics.

The program's first Principal Investigators' Meeting, held in April 2005, was attended by researchers from 45 of the 49 projects that were funded at the time; program officers from NSF, NIH, and other funding agencies; and international observers from Germany, Finland, and the United Kingdom. Research reports were organized into eight topical themes representing the breadth of this emerging field. An evening discussion session was led by Nancy Kopell, Dan Margoliash, Tomaso Poggio, and Rob de Ruyter. Breakout discussions covered seven topics that were identified by participating investigators and program directors as having greatest interest to the research community and relevance to the advancement of the field.

The full proceedings of the meeting are available at http://www.nsf.gov/cise/iis/crcns2005.

This report collates the summaries of the breakout discussions and their implications for the research and funding communities. The original capsule descriptions of the breakout discussion sessions follow below.

Education, Training, and Career Development. How can CRCNS maximize the educational and training potential of collaborative research projects? What educational and training needs are most critical for the field? What should CRCNS do to encourage and support early career investigators?

Collaborative Research. How has CRCNS worked for you? What have you achieved through collaboration that would have been difficult or impossible through other mechanisms of support? What have you needed, logistically, to make your collaborations productive? What future needs and opportunities do you anticipate?

International Collaboration. What types of international collaborations are most important for the field? What specific opportunities would be of greatest benefit to your projects?

Data and Algorithm Sharing. What are the best ways for computational neuroscientists to share data and algorithms? If sharing is required, how should such a requirement be implemented?

Brainstorming for FY07 and Beyond. In an era of increased competition for finite research funds, how should computational neuroscience be presented in order to ensure continued development of this inherently multidisciplinary field?

Role of Computation in Functional Imaging. What is the current state of the art in imaging of biological processes, and what kinds of work are needed to facilitate development of new ways of visualizing and analyzing biological processes?

Role of Computation in Multi-Neuron Analysis. With technology now developed to the point of making simultaneous recordings of hundreds, if not thousands, of individual nerve cells, how must the field be developed in terms of new computational, mathematical, and statistical tools to allow analysis and interpretation of such enormous data sets?

Several common themes emerged across multiple breakout sessions along three main items of discussion: **Research**, **Training**, and **Continuity**.

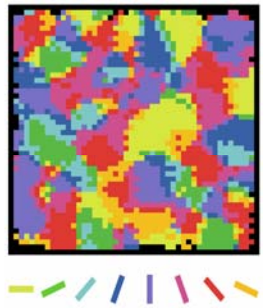
Regarding the theme of **research** content, two aspects were raised repeatedly. The first concerned the *development and improvement of analytic, visualization and modeling tools.* Examples of the neuroscience subfields and/or technique that embody this theme include the integrating of experimental results across data modalities (e.g., anatomy, physiology, and imaging); visualization tools, both for numerical and imaging data; and modeling tools for networks from small- to large-scale. The second element of intense discussion regarded the *sharing of data, algorithms, tools and models.* In particular, it was noted that the community is at an early stage of data and model sharing. Alternative models of sharing were discussed (e.g., informal vs. formal; central vs. distributed repositories; mandatory vs. recommended). The consensus was, on the one hand, to encourage greater, clearly documented contributions (both to existing and to-be-developed data repositories); and on the other hand, to support the continuous development of tools for data sharing, including the establishment of a one-stop-shopping for theorists to obtain large and varied data sets, along with existing analytic tools, for incorporating into their models.

With respect to **training** (including education, career development and, by extension, community building), several commonalities were singled out. Multidisciplinary programs should begin early in the students' careers, and provide research opportunities, especially for undergraduates. "Re-training" programs (such as mentored career awards) of scientists not originally in biomedical field will enhance computational neuroscience. Early career support is needed for investigators whose work would fall between the cracks of the highly segmented academic community (e.g., doing biological work in a Physics Department). Traditional departmental structures and longstanding interdisciplinary barriers appear to devalue crosscutting work. Yet the CRCNS PIs and computational neuroscience community should seek departments and institutional “buy in” support on cross-disciplinary training and career development in computational neuroscience. Opportunities for interactions (e.g., meetings, workshops, courses) should be fostered to help investigators from different disciplines develop common language, respect and trust that can lead to successful collaborations. One way to do this is by combining scholarly efforts (e.g., co-affiliating satellite symposia at conferences) and leveraging experience across communities (e.g., establishing working groups). The CRCNS web site is a potentially useful avenue to disseminate information related to research, training, and resources (e.g., course material and success stories), and for sharing data, algorithm, documentation, and tools.

Finally, the theme of **continuity** elicited discussion in many breakout sessions. There was widespread agreement that the CRCNS program positively initiated a rich compendium of exciting projects. Overall consensus was expressed for the necessity to allow investigators to pursue what they were set up to achieve, even if it takes longer than the initial “seed support” period. In particular, adequate capability needs to be established at NIH to ensure appropriate review for competing continuations. Starting new multidisciplinary projects, e.g., through the CRCNS program, provides the “jump start” for establishing new research fields, which will eventually become mainstream science. The CRCNS program lacks the resources to provide continuous, renewable support to the large number of projects for which it has provided initial funds. It is therefore essential for the established research funding organizations be able to incorporate these projects into their programmatic portfolios. In addition, the need to leverage resources across agencies, institutions and even countries was stressed to provide broadly based support for a wide range of research projects while minimizing the cost to each participating unit. Multiple sources of funding reflect the needs (and biases) of different agencies. These areas of emphasis can be exploited by the computational neuroscience community to support widely varying research topics.

This report, the 2005 PI meeting, and in fact the success of the whole CRCNS program, were made possible by the enthusiastic work and vision of several people. We heartfully acknowledge all breakout session chairs for leading the discussions, writing the summaries, and providing feedback on this report, and the agency leadership for promoting work that goes across individual shops and stovepipes. As Editor of this report, I personally thank Drs. Dennis Glanzman, Yuan Liu, and Ken Whang, for their continuous and substantive help, encouragement, and wisdom.

Giorgio A. Ascoli, PhD
(ascoli@gmu.edu)



Education, Training and Career Development

Chaired and Summarized by Mark Nelson, University of Illinois

The cross-disciplinary nature of computational neuroscience imposes challenges for ensuring effective training and productive career trajectories for members of the computational neuroscience community. This breakout session considered training-related issues at multiple career stages, from the undergraduate level through early career investigators. The session participants came from diverse backgrounds representing many of the disciplinary backgrounds within the computational neuroscience community, including mathematics, physics, biology, engineering and computer science. The group discussed strategies for addressing education and training needs, both in the context of programmatic approaches that could be facilitated by the funding agencies, as well as practices that could be implemented at home institutions or adopted by the community of currently funded CRCNS investigators. Following is a brief synopsis of the main discussion topics and the group's recommendations.

What are the most pressing educational and training issues for the field?

At the undergraduate level, it is important to make students aware that the field exists and to provide appropriate courses and/or research opportunities that get them interested in computational neuroscience. This is particularly an issue for undergraduates in non-biological fields (e.g., math, physics, engineering) who may never be exposed to computational neuroscience as a possible research area. Success will likely require getting departments to "buy in" to the benefit of exposing undergraduates to cross-disciplinary options. The graduate level is ideal for establishing and delivering effective cross-disciplinary training. Funding mechanisms such as the NSF Integrative Graduate Education and Research Traineeship (IGERT) Program and the NIH Roadmap Initiative in Interdisciplinary Research Training are important at this stage. Successful training programs should have stable, long-term support mechanisms that continue after the initial seed phase. Beyond the graduate level, one of the biggest concerns is the potential "productivity hit" associated with the extra time needed to achieve cross-disciplinary expertise. Postdocs and early career investigators are concerned that their CV may not look as strong compared to peers that follow traditional disciplinary trajectories. Even when cross-disciplinary efforts are productive and successful, the contributions may be discounted due to disciplinary biases..."is this really math, physics, etc.?"

Illustration: Development of orientation maps in a silicon cortex chip. Kwabena Boahen, University of Pennsylvania.

How can CRCNS and related programs maximize educational and training impact?

The availability of external funding for interdisciplinary research and training programs can help promote the necessary institutional and cultural changes to ensure long-term success. Funding mechanisms that are explicitly cross-disciplinary such CRCNS, IGERT and certain Roadmap initiatives provide an incentive to institutions to help establish and develop serious cross-disciplinary training programs and research groups. CRCNS and related programs could provide modest supplements for course development and for sharing of course materials (with new money from educational sources). CRCNS can play an important role in community building. Community activities need to have representation from all levels of career development and facilitate mentoring relationships across levels and across fields (vertical and horizontal). Finally CRCNS investigators can play a key role in spreading enthusiasm for the field.

What can programs do to encourage and support early career investigators?

CRCNS and similar programs should continue to give a funding priority to independent, early career investigators for research awards. There is also a need for mechanisms that support cross-training and retraining of individuals at all career stages. Although mechanisms for early career individuals do exist (e.g., NSF Faculty Early Career Development Program; NIH Mentored Research Scientist Development Award), it is often difficult for young investigators to discover these and other appropriate sources of support for further cross-training. CRCNS can help spread knowledge about the availability of new and existing support mechanisms across multiple funding agencies. The CRCNS web page could be used to disseminate this kind of information to the community.

How can CRCNS PIs work together to improve education and training?

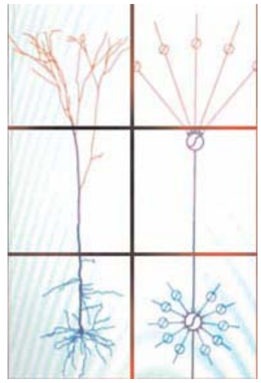
Student exchanges between CRCNS-funded labs could be an effective mechanism for cross-disciplinary training within the community. These exchanges could be supported by modest supplements to existing grants. The PI meeting serves as a good venue for finding out what other groups are doing and where students could productively cross train. Having a CRCNS meeting that includes student and postdoc poster presentations would be an effective mechanism for community building. This larger meeting could be held in addition to, or alternate with, the annual PI meeting. Another potential area for cooperation is in sharing information about training-related success stories at home institutions. Information on successful courses, graduate training programs, and strategies for promoting departmental and institutional support could be collected and posted on the CRCNS web site.

Conclusions

In summary, the group came up with the following general recommendations:

- Find ways to get students informed and excited about computational neuroscience at an early stage; efforts at the undergraduate level are often very successful.

- Try to target funds directly to students/postdocs via training grants and individual fellowships, especially ones that allow a lot of freedom.
- Find mechanisms to ensure long-term stability of successful training programs.
- For community building, consider holding a CRCNS meeting that includes students and postdocs; this could be in addition to, or alternating with, the annual PI meeting.
- Use the CRCNS web site as a portal for sharing training-related information and resources.



Collaborative Research

Chaired and Summarized by Otto Friesen, University of Virginia,
and Bill Ditto, University of Florida

Biosciences, medicine and engineering are merging in ways that were unimaginable just a few years ago. Collaborative labs need to flexibly pursue research directions in a multidisciplinary environment: where the physical and disciplinary infrastructure and distance is minimized to reduce communications problems and to encourage true collaborations. The engine that makes novel discoveries happen these days in the biosciences, biomedical and bioengineering fields are “true” collaborations that involve disciplinary, interdisciplinary and multidisciplinary researchers. Philosophically, we embraced the “laboratory without walls” concept that allows (and encourages) researchers, students and staff to commingle both casually and as part of particular research directions. Interestingly, many of the investigators in these sessions had a background in physics.

What steps led up to your CRCNS application?

Meetings that brought together experimentalists and computational scientists were considered critical for many of the successful applications. One person indicated that the collaboration was an outgrowth of a seminar series. Another person talked about a course that was taught 50/50 by physical scientists and biologists. It was felt that meetings held on a regular basis (monthly, biweekly, weekly) as well as cross-training would be important for continuation of these types of collaborations. One investigator indicated that it was exciting to do experiments based on theory.

How has CRCNS worked for you?

Frequent contact between researchers, by meeting, telephone, or email was considered an essential feature of these collaborations.

Illustration: Two views of a hippocampal pyramidal neuron. Nelson Spruston, Northwestern University.

What have you achieved through collaboration that would have been difficult or impossible through other mechanisms of support?

It was widely agreed that the CRCNS program has begun to accomplish its stated objectives of bringing together neuroscientists and quantitative scientists to apply their combined expertise to research questions of common interest. Research is now ongoing that would not have occurred without this program. It is very difficult to obtain other funding for the research funded through this initiative. One investigator indicated that when similar work was proposed to NIH, a reviewer commented that the computational/theoretical specific aims were tangential to the project. One investigator stated that being able to bring graduate students from other departments in to be involved in neuroscience research was a real plus and would not have been possible without this initiative. A proposal such as the one awarded in CRCNS would be considered risky in engineering. So it seems that mainstream communities in both biomedical and engineering would consider the work too much on the fringe. Therefore, having this particular initiative requiring the collaboration of a modeler and an experimentalist is unique, and much needed to expand both communities to "think outside of the box."

What have you needed, logistically, to make your collaborations productive?

One participant indicated that he had not been able to organize an interdisciplinary course because the faculty couldn't get release time for that. Another person pointed out that it was hard to get a department to focus on cross-disciplinary issues. This was thought to be a particular problem in medical schools.

What future needs and opportunities do you anticipate?

There is a concern of funding sources for continuing these collaborative research efforts. Collaborative, computational research requires broadly based reviewers. This approach may not be widely accepted in the next few years; hence grant applications that are explicitly collaborative may not be rated highly by mainstream review panels. It may be essential for the continuing success of collaborative research for the CRCNS program to fund renewals of current grants. Additional noted needs included: appropriate expertise for this field in review panels; fostering of interdisciplinary training; availability of seed money to create seminars and on-campus meetings to bring groups together; and development of training programs and grants.

It was pointed out that it is critically important for future NIH funding that renewal applications submitted to NIH (for those projects that were funded by NIH) for the investigators to emphasize the relationship of the work to biomedical research (NIH's mission). Likewise, it will be critical for NIH study sections to appoint members who have the expertise that is necessary to review computational applications. Four scientific review administrators from NIH were involved in the CRCNS reviews, so hopefully, they will be sensitive to the computational neuroscience community in terms of finding appropriate reviewers. A final question: How can women and underrepresented minorities be attracted to this research area?

Conclusions

It was noted that real barriers to collaborative research exist and include:

- Collaborations of narrow, disciplinary teams should be avoided. Collaborations of broad, multidisciplinary teams (with evidence of “true” collaborations) should be encouraged.
- Study sections that are composed of narrow, disciplinary reviewers should be avoided. Study sections that are composed of reviewers with individually demonstrated breadth and depth should be encouraged.
- The merging of multiple disciplines and teams should be integrated into all facets of research and education with an eye towards focusing the categorization of research by the class of problems/research (by the multidisciplinary teams) to be pursued rather than the individual disciplines and techniques.
- Emphasize more multimodal approaches to research and training.

Overall consensus was that the encouragement of multidisciplinary collaborative research, true collaborations, is critical moving forward to better the human condition and human knowledge. This non disciplinary approach, all too often espoused but rarely executed is where the CRCNS has shown real progress and should be expanded and encouraged.

International Collaboration

Chaired and Summarized by Geoffrey Goodhill, University of Queensland

The focus of this session was on issues regarding collaboration between US-based researchers are those in other countries. There was general agreement that while such collaborations are extremely important for the health of computational neuroscience as a research field, a number of real or perceived barriers currently exist to pursuing such collaborations.

Why do we need international collaborations?

Although the term “interdisciplinary” is now used quite frequently across many areas of science, Computational Neuroscience is more profoundly interdisciplinary than most areas. This is primarily because it brings together people trained in the physical, computational, and mathematical sciences with those trained in the biological sciences. In the US at least, these two streams of training tend to diverge very early in a student’s career, and by the time they are doing research they often find it almost impossible to understand the intellectual framework underlying the other stream. This immediately severely reduces the pool of potential collaborators for those wishing to reach across the gulf. Added to this, projects in computational neuroscience tend to be quite specialized. Building good models requires a good understanding of the data, and this is usually only obtained by a strong focus on specific questions. Therefore, the small pool of potential collaborators is reduced still further to those who have just the right combination of training and expertise. Finally, the usual set of personal compatibility issues comes into play, leaving a very small pool indeed. Thus, it is crucial to extend the net as widely as possible, including to other countries, to find the right combinations of people.

Moreover, styles of scientific training vary between different countries. In particular, certain participants felt that some countries, for instance in Europe, teach biological science in a more “theoretically oriented” way. Thus, although the gulf mentioned above still exists, it may not be as wide in some countries as it is in the US. Therefore, overseas may be a particularly suitable place to find appropriate collaborators for computational neuroscience projects.

What programs currently exist for international collaboration?

NSF supports workshops and planning visits for international collaboration, international research experiences for students, supplements to existing projects for international work, and larger-scale partnerships for international research and education. NSF's Office of International Science and Engineering (OISE; http://www.nsf.gov/oise/) serves as the focal point for international science and engineering activities at NSF.

Most NIH programs targeted for international scientists and/or collaborations are offered through the Fogarty International Center (http://www.fic.nih.gov/), but other specific opportunities exist, such as the US-Japan Brain Research Cooperation Program (http://grants.nih.gov/grants/guide/notice-files/NOT-NS-04-014.html).

The participants in this session were largely unaware of these programs. While the funding agencies representatives obviously encouraged these researchers to examine their published materials more closely, many researchers felt that these opportunities could/should be better advertised.

Perceived barriers to including an international component

There seemed to be quite a lot of confusion regarding what international components were permissible on particular grant mechanisms, such as NIH R01s. For instance, some researchers had the impression that nothing was allowed, while others had heard that although not forbidden, an international component meant the whole grant had to jump over a higher bar to get funded. Such concerns obviously dampened people's enthusiasm for international collaborations. The participants felt the funding agencies should make clearer and more definitive statements in this regard. The NIH position on grant applications from outside the United States is described in the *All About Grants* web site (http://www.niaid.nih.gov/ncn/grants/), especially the sections on foreign grants (http://www.niaid.nih.gov/ncn/grants/basics/basics_b6.htm and http://www.ninds.nih.gov/funding/grants_eligibility.htm).

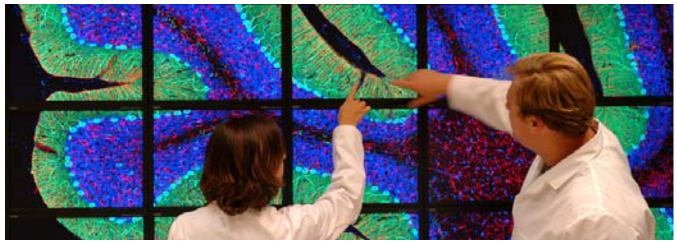
What international programs would we like to see?

Some currently existing programs were discussed whereby a cross-border grant is simultaneously reviewed in both countries. However, there was the perception of "double jeopardy" in these cases, whereby one was doubling one's chance of receiving negative comments and, thus, the grant not getting funded. We suggest instead bilateral funding schemes, whereby governments of both countries contribute funds in a coordinated was and there is one coordinated review process. The Human Frontiers Science Program was cited as an example of how this can work.

Furthermore, many researchers would like to see more funding for short-term visits to/from abroad, not just as an adjunct to an existing collaboration but also as a way of promoting new collaborations. They would also like to see more internationally oriented training opportunities, e.g., summer schools.

Conclusions

- Computational Neuroscience is deeply interdisciplinary, more so than most areas. The intellectual distance between a mathematician and a biologist is usually greater than between, e.g., a chemist and an anatomist.
- Each specific project is quite specialized, and people with the right combination of training/expertise for that project are rare. That small set of potential collaborators is then narrowed still further by the usual issues of compatibility on a personal level. So you need to cast a very broad net geographically to get the right people.
- Styles of scientific training in some other countries are different from in the US, and may be more relevant for computational neuroscience. For instance, at least one member of the group felt that neuroscience training in Europe has a more “theoretical” perspective than in the US.
- Many researchers are not aware of the NSF/NIH opportunities that currently exist for funding projects with an international component. This needs to be remedied somehow.
- Many researchers felt including a foreign component in a grant application, especially a salary component, put the whole grant at risk, thereby dampening their enthusiasm for proposing such collaborations. How real this concern is should be clarified.
- Many researchers would like to see bilateral funding schemes, whereby governments of both countries put in money and there is one coordinated review process.
- Many researchers would like to see more funding for short-term visits to/from abroad, not just as an adjunct to an existing collaboration but also as a way of promoting new collaborations. They would also like to see more internationally oriented training opportunities, e.g., summer schools.



Data and Algorithm Sharing

Chaired and Summarized by Maryann Martone, University of California, San Diego

The initial discussion focused on best ways for the computational neuroscience community to share models and data (rather than algorithms and tools). The CRCNS informatics community is nascent. This represents a challenge in that there are no obvious clusters of CRCNS investigators ready to engage in IT-intensive software and data sharing methods. It also represents an opportunity in that the community is potentially flexible to new ideas. Regular meetings of the CRCNS community may be able to forge new collaborations and use new methods for software and data sharing. Multiple issues were tackled during the breakout discussion. In particular: What are the best ways for computational neuroscientists to share data and algorithms? Is there a critical mass of investigators under CRCNS to develop common software repositories? Should a broader community be engaged? What are successful examples of data/tool sharing? What was the overhead required for the consumer/provider? If sharing is required, what will be the standard, how will it be implemented, and how will one know if it is being met? What informatics/infrastructure-related research is required to meet the needs of the computational neuroscience community? What could we build using off-the-shelf technology and appropriate coordination and what would require research investment to meet the needs of the community 5 to 10 years from now? What are the main cyberinfrastructure, grid, and middleware issues?

Central repositories vs. personal venues

Participants acknowledged that centralized repositories have had significant impact in the genomic community but questioned whether they were appropriate for this community. Some were familiar with some of the databases that have been created for modeling data, e.g., the Machine Learning database at UC Irvine and ModelDB at Yale, yet a perception was voiced that these efforts have not had the impact in this community that the genomic databases have had on the biomolecular community. Nevertheless, the Machine Learning database at UC Irvine was mentioned as a successful resource and has been very useful for providing benchmark data. It was estimated that 40 to 50% of the machine learning community used this resource, although only 1% contributed to it. There was some support for establishing groups to consider standards for model annotation and exchange. It was noted, however, that

Photo: A high-resolution "bio wall" at the National Center for Microscopy and Imaging Research. Maryann Martone, University of California, San Diego.

this effort was not likely to occur without some outside push and would probably prove difficult.

An alternative to the use of centralized repositories is for more informal sharing through e-mail and other forms of personal contact. The concern was voiced that models and resulting simulation data cannot be properly understood without sufficient context, which needs to be given in person. Without this personal contact, a model might be misused. Perhaps researchers should set up their own web sites for sharing of their models—this represents a typical and appropriate approach for nascent communities. It was suggested that the community develop a set of tags that could indicate the existence of a resource willing to share through Google. On the other hand, it was noted that using this mechanism does little to further the development of standards for sharing models/code and lacks persistence. Consideration of centralized vs. distributed models of sharing need not be exclusive; there are probably cases where both would work.

Implementation of data sharing

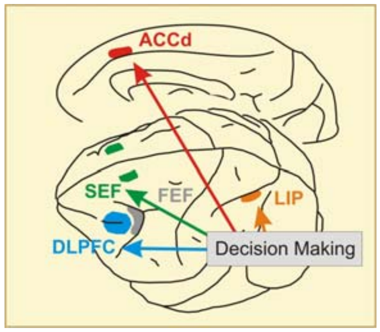
The next major topic of discussion concerned how a data sharing requirement could be implemented, if it were required. The two major venues for this requirement were funding agencies vs. journals. Journals have a vested interest in promoting data sharing because it can potentially give the model more impact. Access to models was also viewed as important for reproducibility of results. Such a requirement would have to specify what exactly should be shared: Simulation data? Models? The issue of what is useful to the community has not yet been determined and because simulations have the ability to generate voluminous amounts of data, the requirement to share everything might place an undue burden on the researcher. Better tools for management and annotation of models are certainly needed to reduce the burden on researchers. At this point, it was felt that a recommendation for appropriate data sharing was more appropriate than an across-the-board requirement.

Cyberinfrastructure for data sharing

Towards the end of the discussion, we had a brief presentation by Dr. Sangte Kim, head of NSF's Division of Shared Cyberinfrastructure. He pointed out that heterogeneity and maturity for data sharing and infrastructure already exists in some fields (e.g., the Protein Data Bank), but other fields are more nascent—CRCNS is likely somewhere in between. The new emphasis in cyberinfrastructure is on data, rather than computation and networking, as in the past. In his experience, every scientific community feels that their needs are different and cannot be served by existing resources. He stressed the need to move beyond "not invented here" attitudes, because government agencies cannot fund every community separately. Scientific communities need to leverage experience across disciplines. There was some brief discussion about "middleware" and what it might constitute in the computational neuroscience community, but there wasn't time to explore the level of knowledge about grids and what they might mean to the computational community.

Conclusions

Following the formal discussion period, the chairs got together to summarize the discussion and their overall impressions regarding the stage of the community in considering data sharing issues. The impression was that the computational neuroscience community represented by CRCNS was at a fairly early stage in considering data sharing mechanisms, although some groups, e.g., machine learning, have started using repositories and recognizing their value. Some members were content with informal sharing; others felt the need for standards and venues for model sharing, particularly to provide benchmark data sets. Little discussion occurred specifically on the issue of sharing of algorithms and code, and it was perhaps surprising that no call was made for a central repository or a managed federation of repositories. If a requirement is going to be made for data/tool sharing, then one of the first issues that needs to be tackled is what needs to be shared and what tools can be used to reduce the administrative overhead of making one's data available. Several members felt that this breakout session was a useful starting point to open discussion, although there was no simple or clear path for moving forward.



Brainstorming for FY07 and Beyond

Chaired and Summarized by Giorgio Ascoli, George Mason University

The goal of this session was to provide government agencies with ideas to optimally present computational neuroscience in their effort to grow the field and ensure funding at an adequate level. The session was attended by over 30 CRCNS participants, and a broad consensus emerged that the CRCNS program is filling a very essential and unique niche, and should be emphatically supported, maintained, and continued. Detailed discussion developed over several lines.

How can we facilitate the development of a synergistic community? What are our success stories (within CRCNS and beyond)?

The widespread sentiment was that successful research often implies interactions among different specializations and across the experimental/computational divide. Yet the type of neuroscience in which a project goes back and forth between "wet" bench and computer simulation is not as common as in other fields of science. It was proposed that computational neuroscience will achieve real success only when it finally "disappears" by becoming a part of the fabric of all of neuroscience, i.e., when the inclusion of quantitative models into research becomes standard. There was general agreement that exchange of trainees (students and postdocs) is particularly essential. This is the hands-on education that will create the next generation of thinkers (and referees).

As for the importance of research in this area, it is clear that any clinical treatments or novel engineering devices that emerge from computational neuroscience should be prominently featured. It is also important, however, to argue for the importance of basic research. Computational neuroscience is an unfamiliar field, often confused with artificial intelligence. It is important to convince funding agencies and the public of the fundamental importance of not overly targeting efforts before the basic science has developed. There is an inevitable time lag between fundamental basic science and development and applications, which cannot be shortened without losing many of the most creative, exciting and productive discoveries.

One of the reasons for the resounding success of bioinformatics is the clarity of the content: the code is known, and when you clone something, it's there. In comparison, neuroscience

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Illustration: Key areas of the macaque brain involved in decision-making. Daeyeol Lee, University of Rochester.

may appear mushy, and we do not yet agree as to what to model, and how to model it. Yet this situation can be turned into a strength. In neuroscience (unlike molecular biology) computational models are used to quantify hypotheses, and ultimately to define the field. Here computational neuroscientists are a step ahead other biological fields, as a summary diagram is viewed as a starting rather than ending point.

What will the next generation of computational neuroscientists look like? What are the growth areas, and how can we encourage new and non-traditional computational models? How about important frontiers in theoretical neuroscience and neuroinformatics beyond the central activity of modeling neural systems (e.g., data mining, information theory, etc.)?

One of the impressive features of CRCNS that was noted is the actual variety of topics and approaches. Although physiology appears to be predominant in CRCNS (and in computational neuroscience in general), developmental and molecular approaches are growing more rapidly than physiology in the broad neurobiology community. Rather than seeing this as a threat to computational neuroscience, we have an opportunity to integrate computational genomics into neuroscience models. Similarly, and more generally, a higher degree of synergy and cross-fertilization with computational cognitive modeling (including artificial intelligence), and behavioral sciences, on one hand, and molecular biology, on the other, would be desirable. Same for the integration between numerical simulations ("classical models"), theoretical approaches, and data mining, all the way to machine learning. Finally, computational neuroscience with its increasing emphasis on the network level can naturally interact with several theoretical and applied fields of "network sciences" (e.g., the grid, social networks, etc.).

In a period of budget uncertainty and tight competition for resources, computational neuroscience risks getting caught in the middle, viewed as an essentially biomedical endeavor by programs supporting engineers, and considered too theoretical by the biomedical community (thus funded by neither). Is it possible to expand the funding horizon by involving other government agencies, even companies? How did the PIs interact with other funding sources to extend the appeal of computational neuroscience? How were the PIs' research interests connected with the agency funding priorities, and vice versa?

Several PIs reported on their experience with the Office of Naval Research and the Department of Energy. These agencies were seen as extremely supportive, but with a strong emphasis on the eventual need to "build something". In addition, when they stop funding, they typically do so fairly precipitously. The Defense Advanced Research Projects Agency continues to have very unconventional (and often high-risk/high-payoff) programs in neuroscience. Traditional funding agencies, such as NIH, are still quite interested in subjects that resonate with computational neuroscience. A recent council report of NIMH indicated a change in priorities, favoring basic research to integrate across levels of analysis, interdisciplinary research and training, and emphasizing computational models. The Conte centers were brought as examples reflecting the desire by NIMH officials to push toward computation and interdisciplinarity.

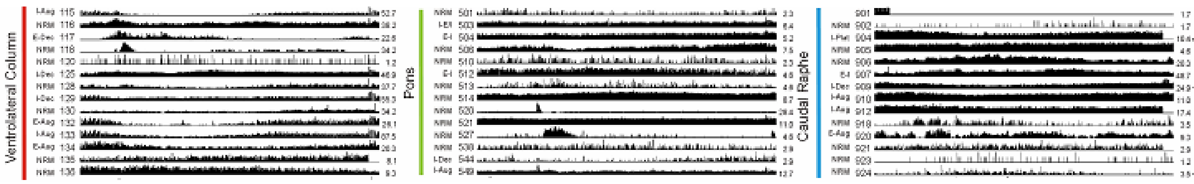
Yet several PIs felt that (unlike NSF) NIH was not particularly open to computer-based research strategies, with informatics grants getting a deflation of grades. There are exceptions, however, such as the dynamical systems community, which according to some PIs has been more generously funded by NIH than by NSF. Others disagreed however, and felt that, while NSF grants are generally smaller than NIH grants, NSF has been a steady supporter of the dynamical systems community for a much longer period of time (and for a larger number of investigators) than NIH. The need was raised for robust statistics to track these types of issues. Several NIH program were also mentioned that encourage computational proposals, such as the Biomedical Information Science and Technology Initiative (BISTI), the Neuroimaging Informatics Technology Initiative (NIfTI), etc. In recent times NIH has been seeing more computational applications and computationally oriented reviewers, but necessarily has a problem with applications so theoretical that they lack a clear biomedical application. Again, CRCNS was highlighted for the broad range of research it is supporting. Such breadth is the result, at least in part, of the "broad spectrum" concept of computational neuroscience in the announcement, as well as of the openness of the panels and style of review.

Needs and recommendations. What would PIs like to see as opportunities for computational neuroscience? What works well and what doesn't in the CRCNS mechanisms? How about the format of the CRCNS meeting, from the PI's perspective?

The issue of grant review was discussed at length. Certainly one of the advantages of CRCNS is to have a special review panel that is entirely dedicated to computational and collaborative proposals. The same proposals might not fare as well in traditional study sections. This is not an NSF or NIH problem, it is an issue of educating our own colleagues. It would be tragic to stop CRCNS now, as the field has not had the time to develop: what it takes is a change in culture, and this cannot be done in 4 to 5 years. At the same time, it would be beneficial to create piloting mechanisms to "insert" successful CRCNS PIs into standard NIH/NSF panels, perhaps at the time of renewal (a seamless follow-on to the program), to help bootstrapping computational research into traditional study sections.

The need for considerable funding was raised specifically for successful collaborative research (which typically takes more than one-student collaborations). For example, there are funding programs that look for innovation in data sharing (considered a very important problem by researchers and agencies alike) and data management. In many cases, it is the nuts and bolts of data sharing that are relevant to computational neuroscience, not particularly novel technical solutions. It is still hard to propose often expensive infrastructures that are not necessarily innovative for the informatics experts. It was also felt that computational neuroscience specifically needs long-term, reliable funding more than substantial one-time funding.

CRCNS was viewed as serving as a nucleus for computational neuroscience, and in this sense it might be useful to involve other organizations, events, and courses into future CRCNS PI meetings (e.g., NIPS, Woods Hole, etc.). The need was also stressed to educate the computational neuroscience community. Rather than a large number of models all developed independently (and often independent of experimental evidence too), we should strive to seriously build on each other’s work. Appropriate workshops could be organized to build the core of a more scholarly scientific community.



Role of Computation in Multi-Neuron Analysis

Chaired and Summarized by Michael Black, Brown University

A variety of multi-electrode devices have made it possible to record populations of neurons ranging from 10's of cells to upwards of 500 cells. This breakout session addressed the issues and opportunities that arise as a result of this fairly recent technological shift. The participants represented a wide variety of opinions and included modelers and experimentalists with experience recording in slices, invertebrates and vertebrates including chronic recoding in awake behaving animals. While the definition of "multi-neuron" varied among the participants from 2 to 1000 or more cells, the consensus was that it was common now to record from 150 cells simultaneously and that in a few years this will increase by an order of magnitude. Our breakout session focused on the issues of multi-electrode extra-cellular recordings. We did not cover issues in multi-neuron intracellular recording or emerging recording techniques such as fluorescent dye imaging. The group identified five primary areas in which multi-neuron recordings differ from single-neuron recordings and require special attention.

Spike Sorting

Manual sorting of 1000 cells is impractical, laborious and error prone. Experiments with awake behaving animals are delayed while spike sorting is performed. In human clinical settings spike sorting must happen every day and involves the assistance of a trained technician. Accepted, reliable, automated methods are needed. For comparison of results, common methods are required. At the same time, the accuracy of manual sorting is variable and suspect. Studies of human spike sorting performance have suggested that there is wide variability in the spike trains sorted by humans. Experimenter bias is a concern that would be reduced by standardized automated methods. Moreover, there are no accepted measures of reliability/confidence. Errors induced by human sorters are not well understood and confidence measures are not provided for manually sorted data. Automated methods should be evaluated on a variety of data and their error rates and failure modes quantified. Results based on sorted data should include the method of sorting and the confidence in the derived results. It is important to note that just because humans do not report reliability of sorting does not mean that there are no errors in the sorted spike trains. In summary, there is a need for a widely available and accepted methods for automated sorting (with confidence measures).

Illustration: Multi-array recordings from the respiratory brainstem. Bruce Lindsey, University of South Florida.

Statistical Analysis

Most statistical methods assume independent and identically distributed data. In behaving animals this assumption is almost certainly violated. Statistical analysis methods do exist for dealing with large populations and point process data (e.g., tests for excess synchrony). An emphasis should be placed on formulating clear null hypotheses that can be tested. Most techniques are based on firing rates. There are no accepted statistical models for multivariate point processes. The analysis of data from large populations often relies on probabilistic models of firing rate or point-process data. This is true for both information theoretic analyses and methods for population decoding. Such data are characterized by being non-Gaussian and highly correlated and consequently are poorly represented by currently available parametric models. At the same time researchers are increasing the complexity of stimuli and behaviors resulting in even more complex probabilistic relationships to neural activity. The large amounts of data from multi-neuron recordings make the task of fitting complex probabilistic models computationally challenging. In conclusion, existing statistical methods need to be more widely disseminated to the community. There is a need for more sophisticated statistical tests and appropriate hypotheses and new probabilistic modeling tools for high dimensional population data. Support from programs like CRCNS is critical for engaging statisticians and computer scientists in the mathematical and computational challenges.

Modeling Neural Architecture and Dynamics

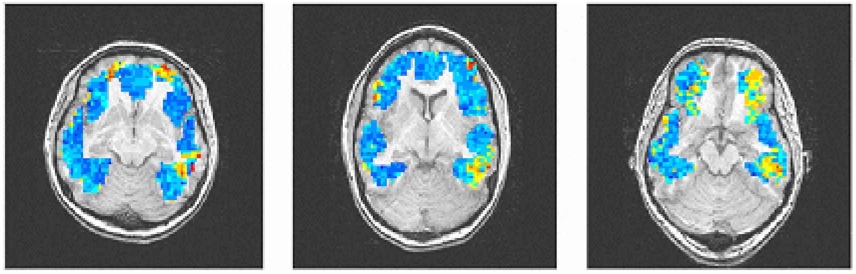
How are the cells related when 100 electrodes are inserted? Multi-neuron recordings provide large amounts of data but typically do not provide information about the spatial connectivity of the cells. Correlation resulting from un-modeled connectivity may result in colored noise which may violate modeling assumptions. Such recordings pose problems and opportunities for modelers. Representing the micro-architecture and the network dynamics to model large populations is a challenge. Local field potentials should be recorded and rhythmic and synchronous activity may provide clues to the dynamics. Thus, tools are needed for modeling dynamics in networks of 100's of cells. While models of the neural architecture and dynamics are needed, so too are methods for fitting these models to large amounts of data. Given the complexity of realistic models, the computational challenges of fitting and simulation are great. On the other hand, multi-neuron recordings rarely include information about what types of cells are being recorded. Incorrectly categorizing different neuron types may invalidate statistical analyses. Not knowing the types of cells exacerbates the problems of modeling network dynamics. This points to the need for better models to relate spikes and local field potentials to the architecture and dynamics; there is a large gap between the current theory and the ability to record large populations.

Visualization

Exploratory visualization facilitates understanding and helps experimenters generate hypotheses. Historically neuroscientists use various visualization methods to the behavior of individual cells and the relationship between their activity and simple stimuli. Beyond tens of cells and with complex stimuli or behavior such methods break down. Exploratory data analysis is unlikely to be supplanted by fully automated statistical tools and consequently methods for visualizing population activity, correlations, and network dynamics will be necessary. Visualization is likely to remain important as a first step in understanding what are the relevant variables (these are often not know *a priori*) and for hypothesis generation. At the same time, standard single cell or small population methods (PSTHs, cross-correlation, etc) break down when looking at 100's of cells. During the discussions one of the experimentalists talked about the problem of visualizing the correlations in a population of 100 cells. Using traditional cross-correlation methods they manually viewed 10,000 cross-correlation plots. Of course, such a method is impractical and doesn't scale to higher-order correlations. The take-home message here is that new visualization tools are needed and the CRCNS community should engage the scientific visualization community in multi-neuron analysis problems.

What role does CRCNS play?

One key aspect is to encourage sharing of data and software. The discussion of data sharing in this community is always complex (see summary of related breakout session). Many of the issues above, however, involve data or software sharing between researchers or communities. The discussion raised common concerns about such efforts including the large time commitment this requires on part of PIs. The social barriers are strong and can be summarized as "it took months to gather and I want to mine it before others do." Sharing requires annotation of data and this implies some agreed-upon standards. One of the benefits of sharing data with colleagues from mathematical and computational disciplines is that it helps expose them to how "ugly" real data are. In summary, a high priority for sharing of data and software is in the area of automated spike sorting. To address this we propose a CRCNS-sponsored workshop on spike sorting that would provide challenge data sets on which participants would test their algorithms (or human sorting) and compare results. This would serve the purpose of "a community lab meeting" to understand what works and what does not. CRCNS could help by providing resources to maintain and manage a repository of data. This would relieve the PIs who contribute data of some of the burden of dealing with queries.



Role of Computation in Functional Imaging

Chaired and Summarized by Tom Mitchell, Carnegie Mellon University

Our subgroup took a broad view of functional imaging, including imaging methods such as functional MRI, diffusion tensor imaging and diffusion tensor tractography, MEG, PET, evoked response potentials, and guided multi-resolution imaging of living nerve cells. The group discussed a variety of needs and opportunities to develop computer algorithms and new software to support functional brain imaging. The following three primary themes emerged from this discussion.

There is a significant need within the computational neuroscience community for new computer tools for analysis, visualization, and modeling for many of these imaging methods, along with a need for improvements to imaging resolution and sensitivity.

Improvements to imaging resolution/sensitivity/directability will be increasingly coupled to improvements in computational methods. For example, to achieve guided, real-time imaging of living nerve cells at multiple resolutions (e.g., as discussed by Peter Saggau at this meeting), it will be essential to provide real-time computation to allow researchers to navigate the image. Furthermore, informed navigation will require more than mere visualization in real time; it will also require real-time analysis and modeling to support intelligent decisions regarding where to focus next.

There are two distinct computational needs here. First, there is a need for research to develop new, more powerful and more targeted computer *algorithms* for modeling, analysis, visualization of the growing types of functional imaging data. Second, a need for robust, well-documented *software implementations* of these algorithms, that can be easily disseminated and used by computational neuroscience researchers. It is important to realize these are distinct, and that funding for either one alone will fail to fill the need.

Illustration: fMRI voxels color-coded by their predictiveness of semantic categories. Tom Mitchell, Carnegie Mellon University.

We need to develop community-wide toolkits for specific imaging modalities, and for integrating data collected from multiple imaging modalities.

Within the fMRI research community, software packages such as AFNI and SPM are in widespread use. While these packages do not fulfill every need of fMRI researchers, they do cover a large fraction of what is needed, and they provide an example of the great utility of shared software. For example, these packages enable researchers everywhere to benefit from the insights of the developers regarding how best to handle image noise of various types, and how best to extract the essential signal from the data. Similar tools are needed for newer imaging modalities such as DTI and MEG.

A major opportunity/need is for algorithms and software to integrate data from *multiple* imaging methods (e.g., fMRI, MEG, and ERP). Multi-modal analysis is likely to become more common over the next few years, and the lack of algorithms to merge these data could easily become a bottleneck to its widespread use.

There is a strong opportunity to leverage research on statistical machine learning to support cognitive neuroscience. Statistical machine learning is a rapidly developing research field dealing with computational/statistical approaches to data analysis and automatic hypothesis formation and refinement.

Many problems in functional neuroimaging involve observing brain activation that is the combined result of multiple overlapping sources occurring simultaneously (e.g., multiple cognitive processes and noise sources contributing to the single observed functional image). Statistical learning algorithms such as Independent Components Analysis (ICA) provide a means of automatically inferring the most probable set of independent sources reflected in the combined data. As a second example, many functional imaging data sets are time series data that are the combined result of multiple hidden processes that change/appear/disappear over time. Statistical learning algorithms such as Dynamic Bayesian Networks provide a principled probabilistic approach to estimating the most probable sequence of hidden processes that could have generated these data. Both of these examples highlight active research areas in statistical machine learning that are of broad relevance to computational neuroscience.

We recommend a more aggressive approach to enlist the statistical machine learning community in computational neuroscience problems. Current efforts in the form of joint meetings (e.g., the recent Statistical Analysis of Neuronal Data (SAND) meetings, and similar meetings at Woods Hole) have brought together statisticians and researchers in some types of neuronal data. Additional meetings of this type should be held to cover a broad variety of functional imaging methods, and to enlist researchers whose emphasis is on new algorithm development (e.g., by holding a workshop at the annual International Conference on Machine Learning, or NIPS meetings).

Participants

Giorgio Ascoli, George Mason University
German Barrionuevo, University of Pittsburgh
Randall Beer, Case Western Reserve University
Richard Bertram, Florida State University
John Bishop, Center for Scientific Review, National Institutes of Health
Michael Black, Brown University
Kwabena Boahen, University of Pennsylvania
Christiane Buchholz, Federal Ministry for Education and Research, Germany
Neil Buckholtz, National Institute on Aging
Paul Carney, University of Florida
Sean Carver, University of Maryland
Stacey Chambers, National Institute of Neurological Disorders and Stroke
Jiang-Fan Chen, Boston University School of Medicine
Zhiyi Chi, University of Chicago
Hillel Chiel, Case Western Reserve University
David Chopp, Northwestern University
Chris Clark, University of Pennsylvania
Costa Colbert, University of Houston
Jeffery Colombe, The MITRE Corporation
Barry Davis, National Institute on Deafness and Other Communication Disorders
Joel Davis, Office of Naval Research
Rob de Ruyter, Indiana University
Thomas DeMarse, University of Florida
Semahat Demir, National Science Foundation
William Ditto, University of Florida
Marcel Egli, Swiss Federal Institute of Technology
Gregory Farber, National Center for Research Resources, National Institutes of Health
Judith Finkelstein, National Institute on Aging
W. Otto Friesen, University of Virginia
Jia-Hong Gao, University of Texas Health Science Center at San Antonio
Stuart Geman, Brown University
Bijoy Ghosh, Washington University
Cole Gilbert, National Science Foundation
Dennis Glanzman, National Institute of Mental Health
Geoffrey Goodhill, University of Queensland
Lawrence Grover, Marshall University School of Medicine
John Guckenheimer, Cornell University
Mary Harrington, Smith College
Kenneth Harris, Rutgers University
Michael Hasselmo, Boston University
Christopher V. Hollot, University of Massachusetts

Group photo, April 22, 2005

William Holmes, Ohio University
Kyosoo Hong, New York University School of Medicine
Timothy Horiuchi, University of Maryland
Tetsuya Iwasaki, University of Virginia
David Jaffe, University of Texas at San Antonio
John Jeka, University of Maryland
Marcel Just, Carnegie Mellon University
Ioannis Kakadiaris, University of Houston
William Kath, Northwestern University
Tim Kiemel, University of Maryland
Sangtae Kim, National Science Foundation
Randal Koene, Boston University
Nancy Kopell, Boston University
Jeffrey Kretsch, National Geospatial-Intelligence Agency
P.S. Krishnaprasad, University of Maryland
Daeyeol Lee, University of Rochester
Anthony Leung, Massachusetts Institute of Technology
Abel Lin, University of California, San Diego
David Lin, Cornell University
Bruce Lindsey, University of South Florida
Yuan Liu, National Institute of Neurological Disorders and Stroke
Peter Lyster, National Institute of General Medical Sciences
Marcelo Magnasco, Rockefeller University
Zachary Mainen, Cold Spring Harbor Laboratory
Daniel Margoliash, University of Chicago
Maryann Martone, University of California, San Diego
Thomas McKenna, Office of Naval Research
Mayank Mehta, Brown University
Tom Mitchell, Carnegie Mellon University
Kendall Morris, University of South Florida Medical Center
Cynthia Moss, University of Maryland
Declan Mulkeen, Medical Research Council, United Kingdom
Mark Nelson, University of Illinois
Ernst Niebur, Johns Hopkins University
Makoto Nishiyama, New York University School of Medicine
Michael Oberdorfer, National Eye Institute
Thomas Palmeri, Vanderbilt University
Joseph Pancrazio, National Institute of Neurological Disorders and Stroke
Michael Pazzani, National Science Foundation
Steven Peltier, University of California, San Diego
Grace Peng, National Institute of Biomedical Imaging and Bioengineering
Christopher Platt, National Institute on Deafness and Other Communication Disorders
Tomaso Poggio, Massachusetts Institute of Technology
Robi Polikar, Rowan University
Jose Principe, University of Florida
Mikhail Rabinovich, University of California, San Diego
Sohi Rastegar, National Science Foundation
A. David Redish, University of Minnesota
Kay Robbins, University of Texas at San Antonio
Ilya Rybak, Drexel University
Peter Saggau, Baylor College of Medicine
Stephanie Schaerer, German Aerospace Center
Paul Schnur, National Institute on Drug Abuse
Allen Selverston, University of California, San Diego
David Shurtleff, National Institute on Drug Abuse
Hava Siegelmann, University of Massachusetts
Karen Skinner, National Institute on Drug Abuse

Roger Sorensen, National Institute on Alcohol Abuse and Alcoholism
Nelson Spruston, Northwestern University
Dalin Tang, Worcester Polytechnic Institute
David Tank, Princeton University
Frederic Theunissen, University of California, Berkeley
Mika Tirronen, Academy of Finland
Philip Ulinski, University Of Chicago
Jeffrey Urbach, Georgetown University
Susan Volman, National Institute on Drug Abuse
Rudiger von der Heydt, Johns Hopkins University
Xiao-Jing Wang, Brandeis University
Paul Werbos, National Science Foundation
Kenneth Whang, National Science Foundation
Gene Yeo, Salk Institute