NATIONAL Center *for* RESEARCH resources

biomedical computation, visualization, imaging & informatics resources

Biomedical Computation, Visualization, Imaging, & Informatics Resources of the National Center for Research Resources—Participating Centers

Center for Bioelectric Field Modeling, Simulation, and Visualization
University of Utah, Chris Johnson

High-Performance Computing for Biomedical Research
Pittsburgh Supercomputing Center, Ralph Roskies

Laboratory of Neuro Imaging Resource
University of California Los Angeles, Arthur Toga

Multiscale Modeling Tools for Structural Biology
The Scripps Research Institute, Charles Brooks III

Biomedical Informatics Research Network
University of California San Diego, Mark Ellisman

National Center for Microscopy and Imaging Research
University of California San Diego, Mark Ellisman

National Biomedical Computation Resource
University of California San Diego, Peter Arzberger

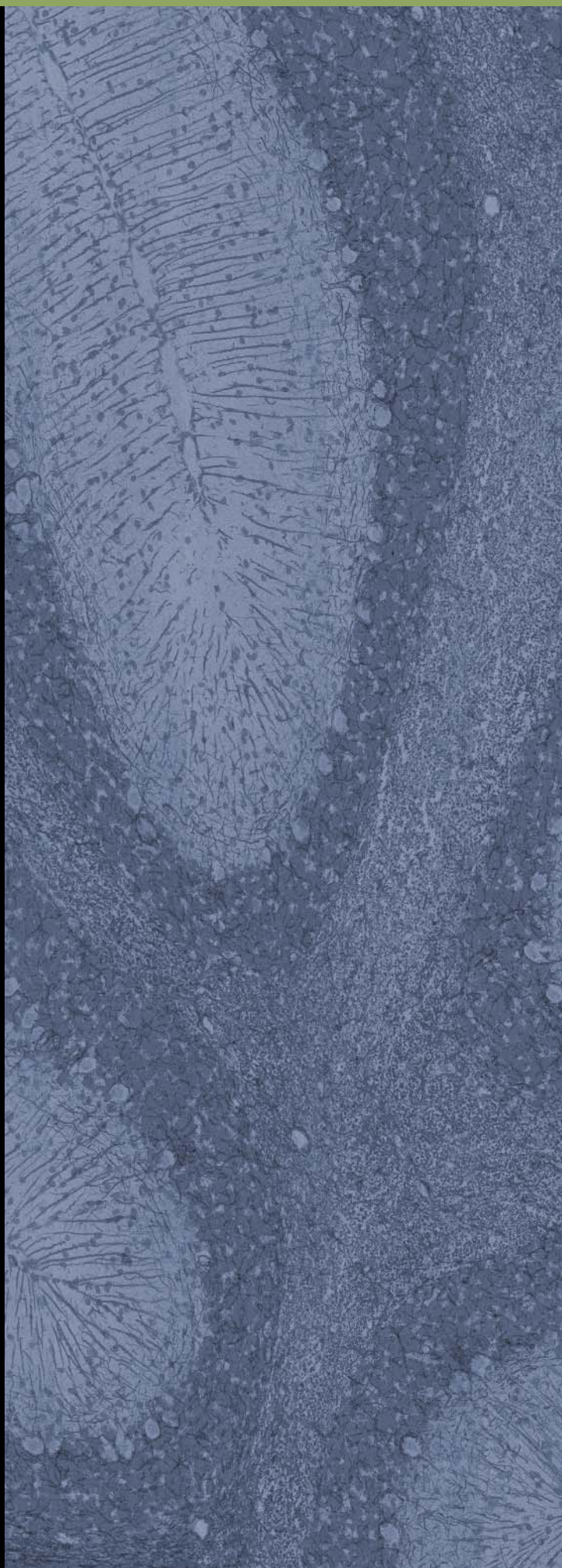
National Center for Macromolecular Imaging
Baylor College of Medicine, Wah Chiu

National Resource for Cell Analysis and Modeling
University of Connecticut Health Center, Leslie Loew

Resource for Biocomputing, Visualization and Informatics
University of California San Francisco, Tom Ferrin

Resource for Macromolecular Modeling and Bioinformatics
University of Illinois, Klaus Schulten

National Center for Research Resources



NCRR MISSION

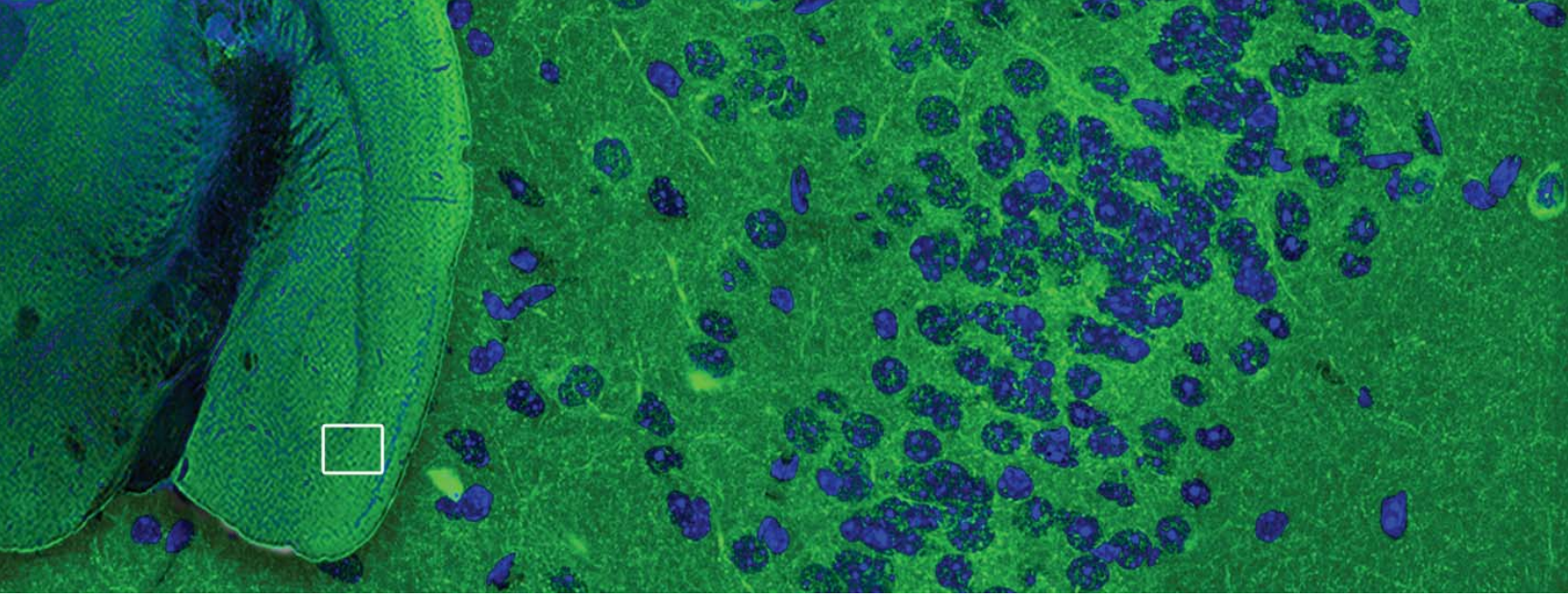
The National Center for Research Resources (NCRR) serves as a "catalyst for discovery" by creating and providing critical research technologies and shared resources. This infrastructure underpins biomedical research and enables advances that improve the health of our Nation's citizens.

Biomedical research investigators supported by the Institutes and Centers of the National Institutes of Health require a broad array of technologies, tools and materials critical to their research efforts. From the models required for research on diseases and disabilities, to the biomedical technology and instrumentation necessary to elucidate cellular and molecular structure, to the clinical settings in which to conduct studies to discern the cause of disease and in which novel clinical trials of new therapies can be developed, biomedical researchers must have access to the necessary resources in order to continue to make progress against human disease and disability.

The NCRR has a unique responsibility at the National Institutes of Health: to develop critical research technologies and to provide cost-effective, multidisciplinary resources to biomedical investigators across the spectrum of research activities supported by the NIH. This has four major facets:

1. Create resources and develop technologies that are cost-effective, accessible and responsive to the research needs of the biomedical research community. To meet these needs the NCRR must be in the vanguard of evolving trends in basic and clinical research so that resources will be available to facilitate that research.
2. Provide shared clinical, primate and biotechnology resources for use by investigators supported by all the NIH Institutes and Centers. These resources, primarily centers, serve more than 10,000 researchers, supported through well over $1 billion of categorical research resource Institute funds, thus leveraging those funds for more cost-effective and efficient research.
3. Develop quick, flexible approaches to new and emerging biomedical research needs and opportunities. These innovations often involve high-risk research, but the payoffs may be substantial.
4. Strengthen the nation's biomedical research infrastructure through programs to develop and enhance the capacity of minority institutions and centers of emerging excellence to participate in biomedical research, to increase the exposure of K-12 students and their teachers to the life sciences, to improve the condition of research animal facilities, and to construct or renovate facilities for biomedical and behavioral research.

The NCRR plays a key role in addressing pressing trans-NIH research issues such as: access to state-of-the-art instrumentation and biomedical technologies; containment of the escalating costs of highly sophisticated clinical research; development of appropriate, specialized research models both animal and non-animal; and remedying the shortage of independent clinical investigators and the underrepresentation of minority investigators. Present and future program directions emphasize "smart," network-connected technologies, computer-aided drug design, development and testing of gene and molecular therapies, bioengineering approaches to decrease health care costs, and enhanced training and career development for patient-oriented research.



BIOMEDICAL INFORMATICS RESEARCH NETWORK

BIRN Cyberinfrastructure Supports Test Bed Collaborative Projects

Through the Biomedical Informatics Research Network (BIRN) initiative, the NIH National Center for Research Resources (NCRR), the NSF National Partnership for Advanced Computational Infrastructure (NPACI), and the NSF Middleware Initiative (NMI) are pioneering the use of Grid infrastructure for medical research and patient care.

Established in 2001, BIRN developed and continues to evolve the hardware, software, and protocols necessary to share and mine data for basic and clinical research. Central to the project is a scalable cyberinfrastructure consisting of advanced networks, federated distributed data collections, computational resource, and software technologies that are integrated to meet the evolving needs of collaborative test bed investigators. By pooling domain expertise, specialized research facilities, instrumentation, applications, and regional information, these investigators are tackling disease studies of greater scope and complexity than are independently possible.

The BIRN cyberinfrastructure is developed by the BIRN Coordinating Center and driven by the requirements of three research groups: the Function, Morphometry, and Mouse test beds. The Function BIRN comprises 11 universities studying regional human brain dysfunctions related to schizophrenia. The Morphometry BIRN, consisting of nine research institutions, investigates whether structural differences in the human brain distinguish diagnostic categories in unipolar depression, mild Alzheimer's disease, and mild cognitive impairment. The Mouse BIRN is composed of four institutions studying animal models of disease at different anatomical scales to test hypotheses associated with human neurological disorders including schizophrenia, attention-deficit hyperactivity disorder, multiple sclerosis, and Parkinson's disease.

As additional biomedical research and clinical care test beds evolve, the BIRN will continue to expand the boundaries of information technology infrastructure, enriching the Global Grid movement by providing application pull from these new domains.

Principal Investigators
BIRN Coordinating Center
Mark H. Ellisman, Ph.D., UCSD
858-534-2251 (phone); 858-534-7497 (fax)
mark@ncmir.ucsd.edu (email)

Function BIRN: Steven Potkin, M.D., UC Irvine
949-824-8040 (phone); 949-824-7873 (fax)
sgpotkin@uci.edu (email)

Morphometry BIRN: Bruce Rosen, M.D., Ph.D., Harvard
617-726-5122 (phone); 617-726-7422 (fax)
bruce@nmr.mgh.harvard.edu (email)

Mouse BIRN: G. Allan Johnson, Ph.D., Duke
919-684-7754 (phone); 919-684-7158 (fax)
gaj@orion.mc.duke.edu (email)

Image: Mouse BIRN researchers are using multi-scale imaging methods to characterize a mouse model of Parkinsonism. Shown here are an MRI volume (Duke CIVM) with an overlying high-resolution, large scale image from a transgenic animal that overexpresses alpha-synuclein. Alpha-synuclein is a protein that is the main constituent of Lewy bodies—a hallmark of Parkinsonian pathology. The montaged image is composed of thousands of individual images tiled together. One such image is identified on the large scale image (white inset square) and shown at full magnification. In this magnified image, alpha-synuclein has been immunolabeled (green) and is shown with stained cell bodies (blue).

SCI INSTITUTE *NIH Center for Bioelectric Field Modeling, Simulation & Visualization*

The overall goal of the NCRR Center for Bioelectric Field Modeling, Simulation, & Visualization is to develop and disseminate new methods, algorithms, and programs for use in the study of experimental, clinical, and computational bioelectric field problems.

Scientific Focus

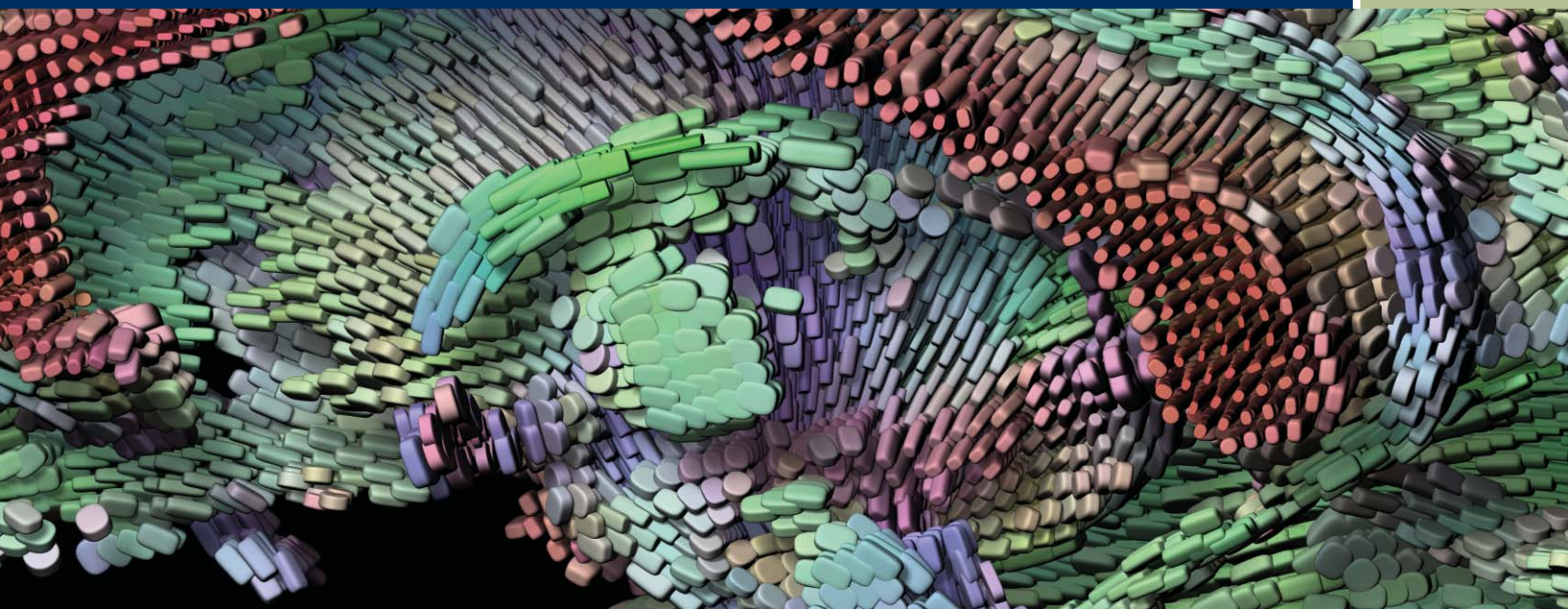
1. Develop and implement techniques and software for the efficient manipulation and processing of bioelectric field data: geometric model generation and manipulation, bioelectric field simulation, and scalar and vector field visualization.
2. To use the resulting techniques & software in supporting research projects within the Center & in combination with its collaborators in computational, clinical & basic electrocardiology and electroencephalography.
3. Develop an integrated, extensible, problem solving environment that features a computational steering framework for interactive modeling, simulating, and visualizing of bioelectric field problems.
4. Incorporate the techniques and software modules developed within the Center into the problem solving environment. Disseminate state-of-the-art software for geometric modeling, simulation and visualization in basic & clinical bioelectric field research. Specific software tools include:
   a. *Modeling tools: semi-automatic segmentation, surface generation, automatic mesh generation, parametric representations of surfaces and volumes, and a set of CAD-type tools for viewing and editing models.*
   b. *Finite element, finite difference, and boundary element, techniques for the numerical solution of bioelectric field problems.*
   c. *Regularization techniques to constrain effects of the ill-posed nature of the ECG, EEG & MEG inverse problems. Techniques will include singular value decomposition, Tikhonov, Twomey, admissible solution approaches, frequency domain & maximum entropy methods.*
   d. *Adaptive refinement techniques for forward and inverse approximation methods.*
   e. *Visualization tools: interactive scalar field display, isocontour and isosurface extraction, volume and surface rendering, vector field visualization, methods for the characterization, representation, and presentation of error and uncertainty due to modeling, simulation, and visualization methods & line integral convolution.*
5. Provide an on-line database consisting of a test suite of geometric models and simulation data to bioelectric field researchers for use in testing and comparing new methods and results.
6. Conduct workshops on the use of the software tools and instruct & aid researchers in incorporating their own programs into the BioPSE software system.
7. Make available to other bioelectric field researchers, via the world wide web, the software infrastructure developed within the Center.

Principal Investigator: Chris R. Johnson, Ph.D.
801-581-7705 (phone); 801-585-6513 (fax)
crj@cs.utah.edu (email)

Contact Greg M. Jones, Ph.D.
801-587-9825 (phone); 801-585-6513 (fax)
gjones@sci.utah.edu (email)

Image: Mid-sagittal cut through a diffusion tensor data of a human brain. Individual tensor samples exceeding an anisotropy threshold are visualized by superquadric tensor glyphs. The glyph coloring is a combination of red, green, and blue according to the axis alignment of the principal diffusivity direction. Red glyphs in image center corrospond to the corpus callosum.

w w w . s c i . u t a h . e d u



www.psc.edu/biomed

PITTSBURGH SUPERCOMPUTING CENTER

BIOMEDICAL SUPERCOMPUTING INITIATIVE

High-performance Computing for Biomedical Research

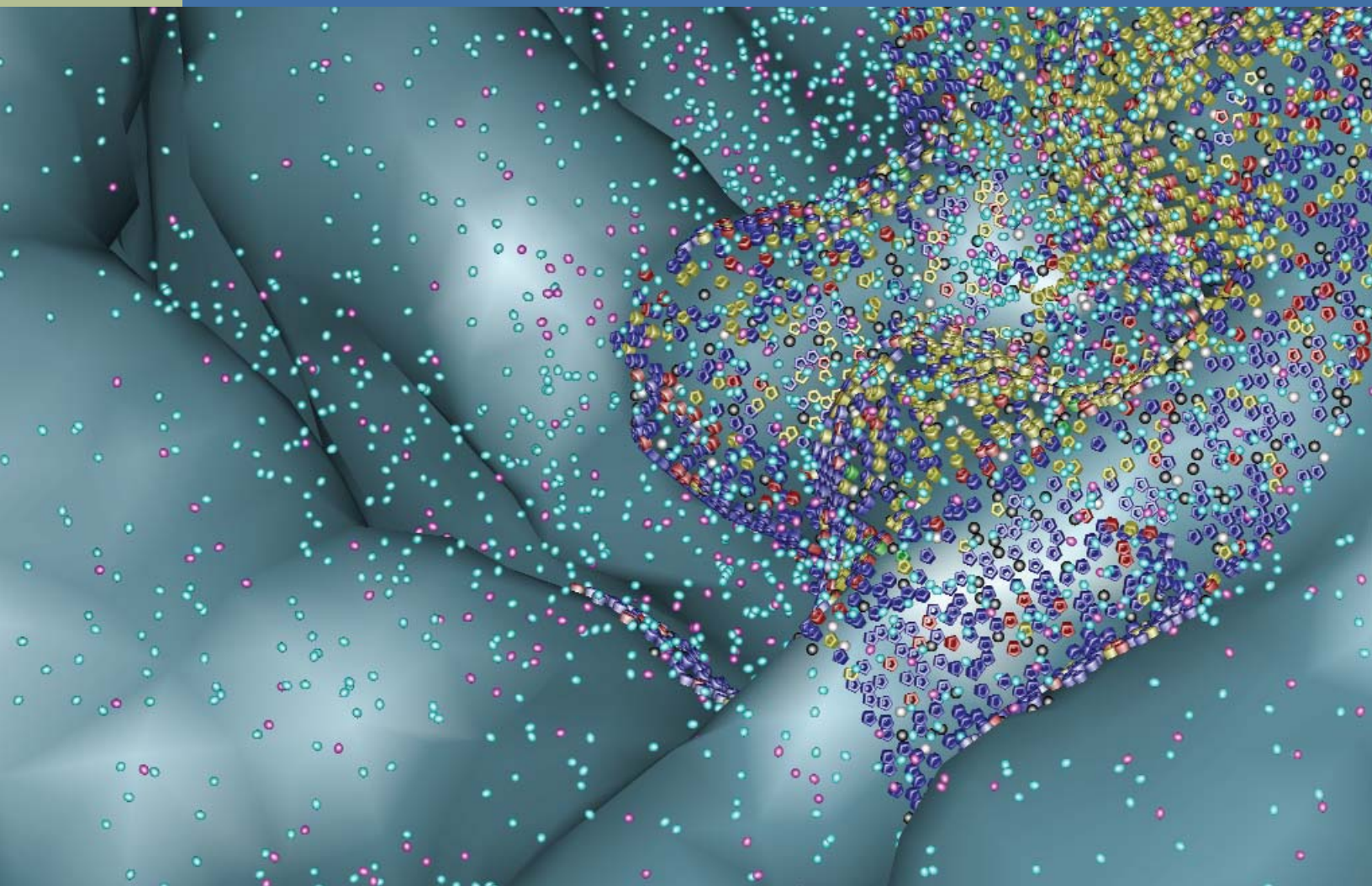
The resource develops new methods, optimize existing approaches, and undertake research projects in biomedical areas that require high-performance computing, broadly construed to include large-scale data management, high-speed networking, and visualization as well as high speed computing. The resource also identifies new biomedical application areas that could benefit from high-performance computing, and speed the introduction of high-performance computing techniques into these areas.

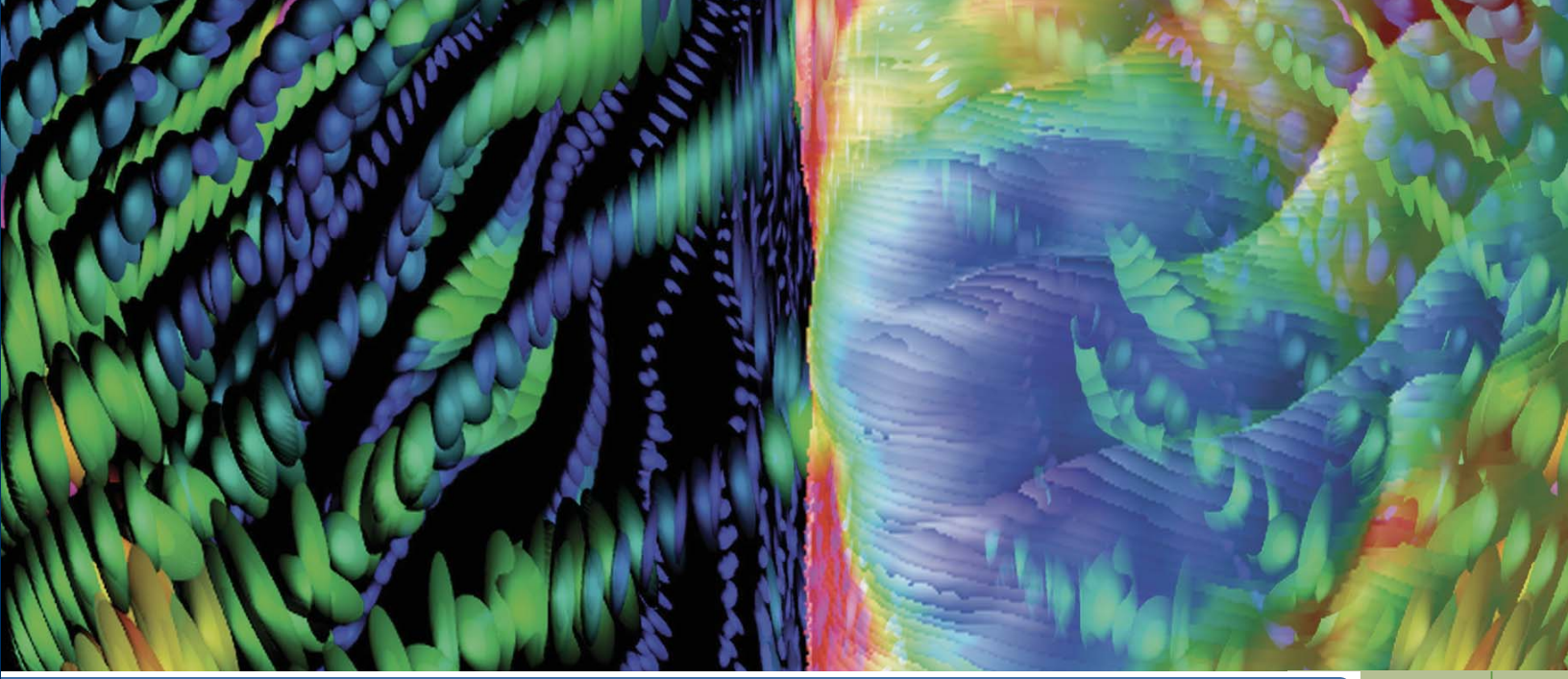
Current efforts are in structural biology, bioinformatics, cellular microphysiology, neural modeling, and exploring large to very large volumetric image datasets. Specific projects include development and application of algorithms for sequence-sequence, sequence-structure, and multiple sequence alignment; classification and analysis of gene and protein superfamilies; understanding divalent metal ion binding sites in proteins and nucleic acids; incorporation of polarization effects in simulations of biopolymers; realistic three-dimensinal cell modeling including simulation of neural transmission (Mcell); simulation of neural networks on parallel platforms (NEOSIM); analysis of multi-electrode recordings of brain activity; and arbitrary plane display of volumetric image datasets that can vary over time or specimen. There is a strong emphasis on sevice and training.

Principal Investigator Ralph Z. Roskies, Ph.D
412-268-4960 (phone); 412-268-5832 (fax)
roskies@psc.edu (email)

Contact David W. Deerfield II, Ph.D.
412-268-4960 (phone); 412-268-8200 (fax)
deerfiel@psc.edu or biomed@psc.edu (email)

Caption: Results from the MCell (www.mcell.psc.edu) simulation of a mouse neck reconstructed synapse. The extracellular face of the muscle membrane is blue, and the nerve terminal has been removed for clarity. The color-coded structures represent individual synaptic molecules (neurotransmitter, receptor and enzyme proteins) in different chemical states during the simulation. For clarity, only a fraction of the molecules are shown.





THE LONI PIPELINE PROCESSING ENVIRONMENT

Laboratory of Neuro Imaging Research at the UCLA School of Medicine

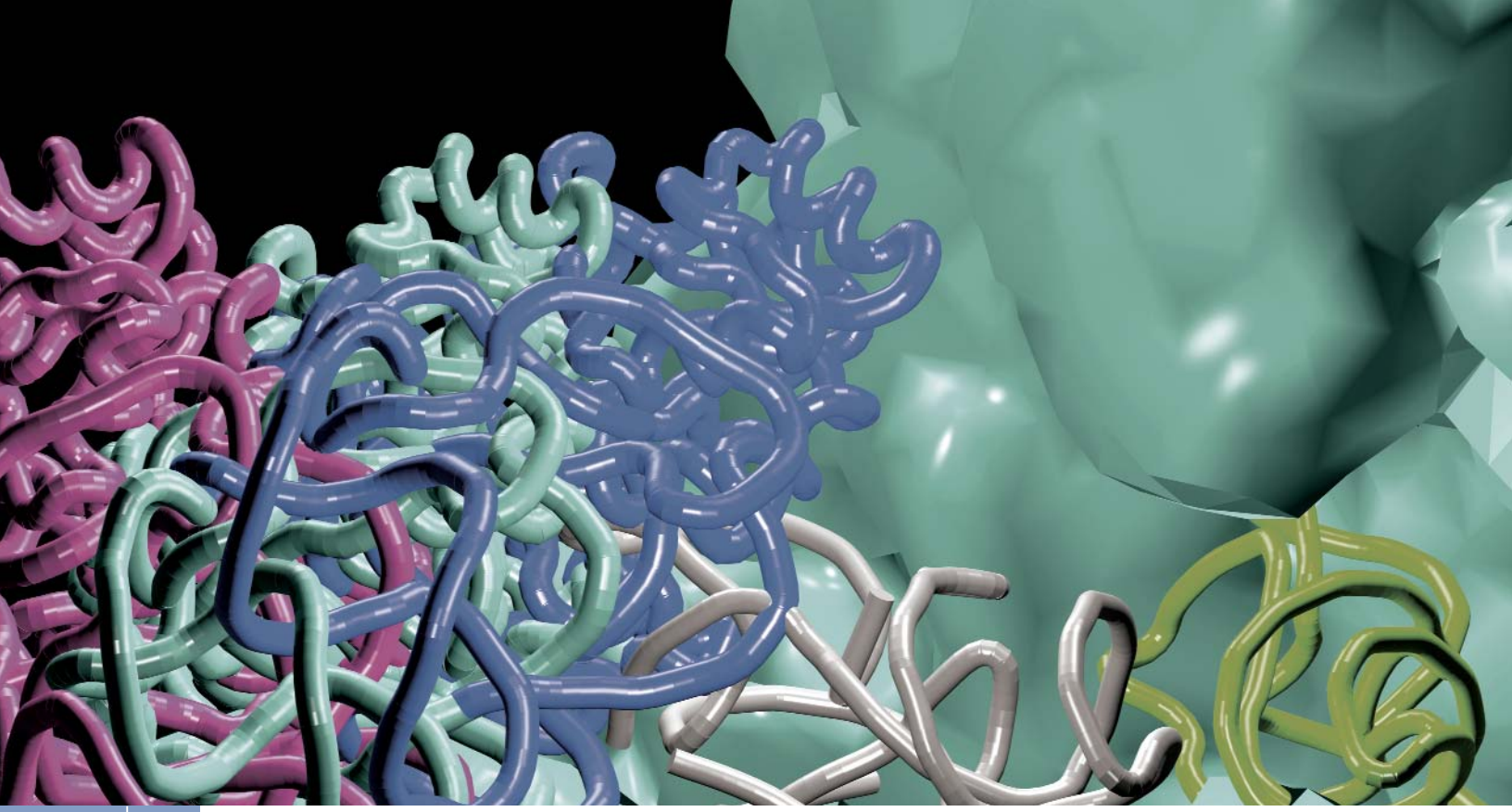
The primary goal of our Resource is the continued development and refinement of a multidimensional modeling environment. To this end we have developed an environment that allows users access to a wide array of computational resources, a state-of-the-art visualization facility, the LONI Image Database, the LONI software archive, and the LONI research protocols. This vast collection of resources provides both national and international networks of collaborators with a diverse array of tools to create, analyze, visualize, and interact with models of the brain.

The LONI Pipeline Processing Environment, created in Laboratory of Neuro Imaging at UCLA, was developed to address the increasingly complex analysis and growing computational processing needs of the brain mapping community. Data analysis in neuroimaging has become an arduous process entrenched in advanced mathematical, statistical, and computational concepts. There are large amounts of raw data that need to be organized, classified, modeled, analyzed, and contrasted. Intermediate datasets are being formed that need to be stored and handled properly. Many of the processing programs have vastly different input and output requirements, employ different file formats, and often run on specific computer architectures. Additionally, there are often many ways to accomplish a given step in the analysis, each of which has its benefits for particular situations. The LONI Pipeline Processing Environment was developed to address these needs by providing a simple, platform-independent, visual programming interface that allows the linking together of many independently developed analysis programs into a processing pipeline. On execution of a pipeline the environment keeps track of temporary intermediate files and datasets for the user, automatically parallelizes data-independent sections of the analysis using a dataflow model, and provides the ability to save a complex analysis for later use on new datasets or for distribution to the rest of the brain mapping community. The pipeline environment also provides application and CPU cycle serving abilities from Pipeline Servers-providing an interface to programs, complete analyses, computer architectures, and even supercomputing facilities that the average scientist may not have access to.

Principal Investigator/Contact Arthur W. Toga, Ph.D.
310-206-2101 (phone); 310-206-5518 (fax)
toga@loni.ucla.edu (email)

Co-Investigators
Richard Leahy, Ph.D.
David Shattuck, Ph.D.
Paul M. Thompson, Ph.D.
Roger P. Woods, M.D.

Image: Analysis pipeline in the LONI Pipeline Processing Environment: Tensor based analysis of the structure of the human brain providing data about how regions of the brain vary across the given subject population. Volumetric whole-head MRI scans from the subjects are processed though multiple steps to extract the brains from the scans, compute a 6th order polynomial transformation aligning the subjects to a provided atlas space, and derive the statistics representing the anatomic variability for the population.



MULTISCALE MODELING TOOLS FOR STRUCTURAL BIOLOGY

The Scripps Research Institute

Problems in structural biology increasingly require researchers to move between models of low-resolution and detailed atomic models to fully explore and exploit experimental information. This resource focuses on development of new and integrated approaches to multiscale modeling, with an emphasis on modeling large-scale assemblies of nucleic acids and proteins with nucleic acids; developing methods that combine lattice-based dynamic Monte Carlo and all atom molecular dynamics; studying physical processes involved in and developing models for the interactions associated with virus assembly; and establishing new tools for the combined treatment of crystallographic and low-resolution structural models from cryo-electron microscopy. These research threads are tied together through the development and distribution of computer codes to make such multiscale simulations and modeling readily accessible to the scientific community at large.

This group's research focus includes: Modeling very large conformational changes occurring in proteins, nucleic acids, and their assemblies; developing methods and models to explore virus swelling and associated large-scale capsid dynamics during viral maturation; exploring of meso-scale distortions of molecular assemblies using low-resolution data from electron microscopy, in the absence of any atomic level structural information; providing links between low-resolution images of functional states of the ribosome during translocation and the near-atomic structural distortions that comprise these motions; characterization of protein-protein interfaces in assembled virus capsids from an energetic and structural standpoint, providing a basis for understanding large-scale molecular assembly. Ongoing development of methods for, and applications to, protein folding, loop, and homology modeling, including participation in CASP6, to perfect physics-based approaches to structural genomics. Develop and test software to extend the range of atom-based modeling methods to larger systems.

Principal Investigator and Contact
Charles L. Brooks III, Ph.D.
858-784-8035 (phone); 858-784-8688 (fax)
brooks@scripps.edu (email)

Co-Investigators David A. Case, John E. Johnson, Vijay S. Reddy, Steve Harvey, Jeff Skolnick

Image: Exploring the dynamics of protein synthesis on the ribosome using multiscale elastic network normal mode analysis reveals key functional motions associated with translocation.

mmtsb.scripps.edu

The Scripps Research Institute

NATIONAL BIOMEDICAL COMPUTATION RESOURCE

Advancing Biomedical Research by Developing Tools to Provide Access to Advanced Cyberinfrastructure

NBCR's mission is to conduct, catalyze, and enable biomedical research by harnessing forefront computational & information technologies. To fulfill this mission, NBCR efforts are focused on four key activities:

- Develop and deploy advanced computational tools for modeling and simulation, query and integration of data resources, 3-D image processing, and interactive visualization,
- Integrate computational, data and visualization resources in a transparent advanced grid environment to enable transparent access to distributed data, computational resources, and instruments,
- Implement and support advanced grid/cyber-infrastructure for biomedical researchers,
- Train a cadre of researchers with interdisciplinary knowledge of both biology and the relevant computation technologies.

The key aim of the resource is to provide transparent access to the new & emerging grid infrastructure that will deliver integrated compute, data, physical, experimental, & human resources to biomedical scientists investigating a wide range of medically important problems spanning scales of biological organization from small molecule drug design & comparative genomics to diagnostic brain imaging & cardiovascular disease.

NBCR is part of UCSD's Center for Research on Biological Systems. The technology research and development activities of NBCR involves researchers at UCSD, the San Diego Supercomputer Center, California Institute for Telecommunication and Information Technology, The Scripps Research Institute, & Washington University, Saint Louis. Core research projects include

- Integrative Modeling of Subcellular Processes: Application to Synaptic Activity and Pharmaceutical Discovery,
- Data Integration and Analytic Tools for Molecular Sequences,
- Structurally and Functionally Integrated Modeling of Cell and Organ Biophysics,
- Creating Visualization Environments for Multi-Scale Biomedical Modeling,
- Grid Computing and Analysis for Multi-scale Biomedical Applications.

Through its broader team of researchers, NBCR is able to leverage other national (OptIPuter, *www.optiputer.net*, NSF Middle Initiative project) and international projects (Pacific Rim Application & Grid Middleware Assembly, *www.pragma-grid.net*) for the benefit of the biomedical community.

Principal Investigator Peter W. Arzberger, Ph.D.
858-822-1079 (phone); 858-822-4767 (fax)
parzberg@ucsd.edu (email)

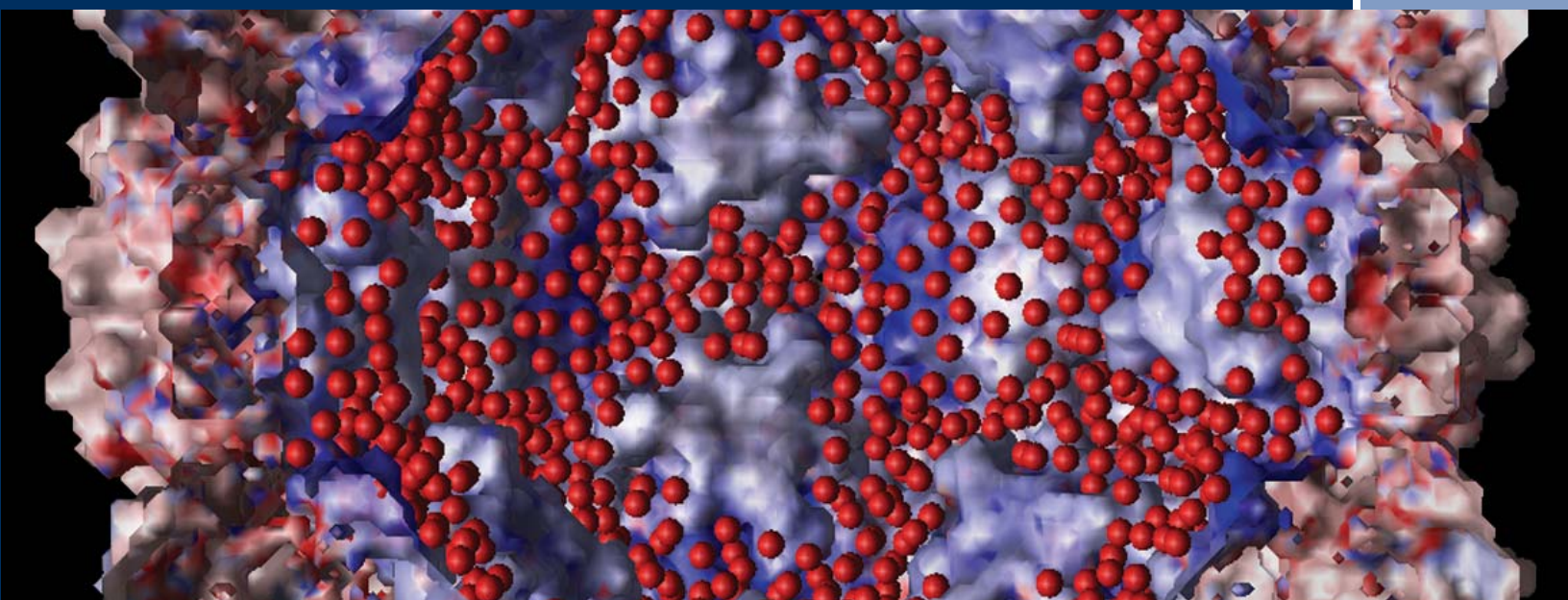
Contact Teri Simas
858.534.5034 (phone); 858.822.5407 (fax)
simast@sdsc.edu (email)

Wilfred Li
858.822.0974 (phone); 858.822.0861 (fax)
wilfred@sdsc.edu (email)

nbcr.net

NBCR

Image: RNA-protein interaction in CCMV (CCMV is cowpea chlorotic mottle virus).



ncmi.bcm.tmc.edu

NATIONAL CENTER FOR MACROMOLECULAR IMAGING

3D electron Microscopy of Macromolecules

Technology and research development efforts are focused on extending the resolution, speed, and flexibility of electron cryomicroscopy for three-dimensional structure determination of biological macromolecular assemblies. The resource tackles structural problems that are too complex or too difficult for X-ray crystallography and NMR spectroscopy. In the center, researchers have demonstrated the feasibility of visualizing secondary structure elements such as alpha helices and beta sheets of protein components in a number of large assemblies. They are developing technology for routine structure determinations at subnanometer resolution, approaching a resolution sufficient for tracing a polypeptide backbone. Generally they focus on macromolecular assemblies ranging from 300 kDa to 30 MDa and can produce structures from very small quantities of purified specimens.

Experimentally, researchers are involved in evaluation of new instruments for single particle imaging, development of automation techniques for high-throughput data collection, and improvements to cryo-preparation techniques. Computationally, they are developing algorithms and improving computational efficiency for the three-dimensional reconstruction of single particles toward atomic resolution. This software is embodied in EMAN and SAVR, which offer complete solutions for low symmetry and icosahedral single particles. In addition, they have produced SAIL, a set of specialized modules for producing professional-quality scientific animations. All three suites and a number of other tools are distributed free of charge.

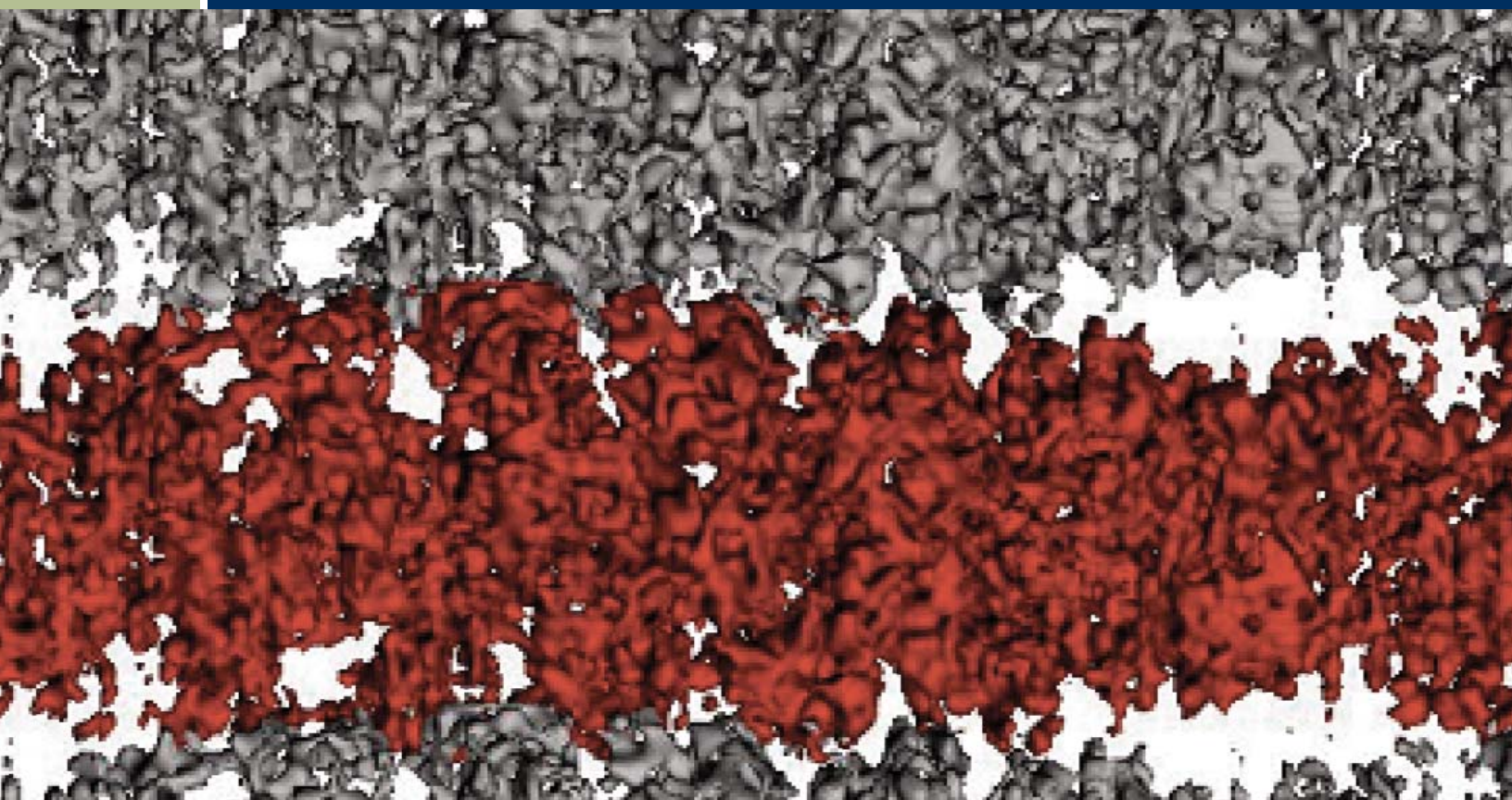
The majority of efforts are focused on collaborative and service projects with a variety of groups around the world. Current biological projects include cytoskeletal filaments and bundles, ion channels, membrane transporters, icosahedral viruses, and large oligomeric proteins. In addition, the resource sponsors workshops and symposia on a regular basis to disseminate its imaging technology to a broader community.

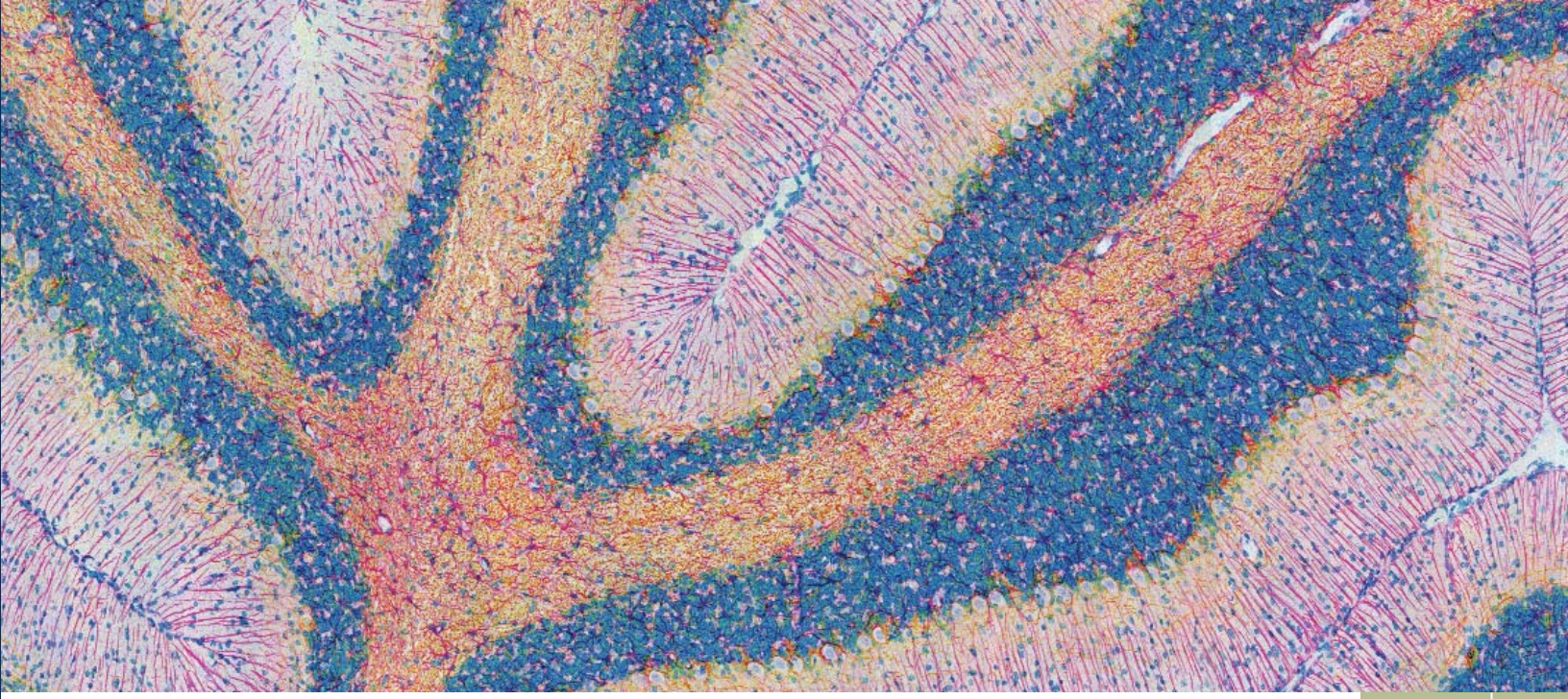
Principal Investigator and Contact Wah Chiu, Ph.D.
713-798-6985 (phone); 713-798-1625 (fax)
wah@bcm.tmc.edu (email)

Co-Investigators
Michael F. Schmid, Ph.D.
mschmid@bcm.tmc.edu (email); 713-798-5734 (phone)

Steven J. Ludtke, Ph.D.
sludtke@bcm.tmc.edu (email); 713-798-9020 (phone)

Image: RNA-protein interaction in CCMV (CCMV is cowpea chlorotic mottle virus)





NATIONAL CENTER FOR MICROSCOPY & IMAGING RESEARCH

An Introduction to the Telescience Tool Suite

The National Center for Microscopy and Imaging Research (NCMIR), supported by the NIH National Center for Research Resources, developed Telescience as a comprehensive, platform-independent, Grid-enabled system that allows researchers to perform end-to-end electron tomography and large field light microscopy. Telescience is performed through the "Telescience Portal," a web interface with a single user name and password that allows biologists to access the suite of tools that manages this process.

Telescience provides the biologist with the power of the computational Grid while masking the complexity of its administration. Users have access to resource scheduling, multi-site remote instrumentation, and parallel tomographic Grid-based reconstruction. Tools for visualization, segmentation, and image processing are also available. An efficient data management system allows archiving of data through heterogeneous distributed file systems and transparent deposition of data products into cellular structure databases, including NCMIR's Cell Centered Database.Utilities for shared whiteboard image annotations and chatting enables communication among multiple sites.

Telescience has been selected as one of the driving applications for the Pacific Rim Applications and Grid Middleware Assemblies (PRAGMA). This association has led to international collaborations with such facilities as Osaka University, Taiwan's National Center for High Performance Computing (NCHC), and the Korea Basic Science Institute (KBSI). Osaka University assists in the development of IPv6-compliant technologies for remote control of high voltage electron microscopes in San Diego and the ultra-high voltage electron microscope in Osaka. Taiwan's NCHC assists in the expansion of Telescience tools for visualization and analysis of massive data. The KBSI is implementing Telescience technologies into their eScience program to facilitate remote use of their 1.25-million-volt ultra-high voltage electron microscope and high throughput electron microscopic tomography.

Advances in Telescience illustrate the benefits of a scalable and persistent infrastructure produced by integrating and sharing resources, technology, and experience of globally distributed partners.

Principal Investigator/Contact Mark H. Ellisman, Ph.D.
858-534-2251 (phone); 858-534-7497 (fax)
mark@ncmir.ucsd.edu (email)

Image: One of the fundamental limitations of light microscopy is that to obtain high spatial resolution, one must use high magnification/high numerical aperture optics, which greatly restrict the field of view in an individual image. This limitation can be overcome by combining high speed 2-photon microscopy with a precision automated montaging stage and computational methods to enable the generation of single "ultra wide-field" high resolution composite images of tissue created from thousands of "image tiles" that are automatically pieced together. The image shown is of a large region of rat cerebellum in which glial cells, neurofilaments, and cell nuclei are stained (shown in pseudo color).

ncmir.ucsd.edu https://telescience.ucsd.edu

NCMIR NATIONAL CENTER for MICROSCOPY and IMAGING RESEARCH
A NIH-NCRR-supported resource center at UCSD

THE VIRTUAL CELL PROJECT *National Resource for Cell Analysis & Modeling*

The National Resource for Cell Analysis and Modeling is housed within, and is the principal venture of, the Center for Cell Analysis and Modeling at the University of Connecticut Health Center. The resource contains state of the art facilities for studying living cells, and has developed a new technology, the Virtual Cell, for analyzing and synthesizing this knowledge.

The Virtual Cell is a general software framework for modeling cell biological processes that is deployed as a freely accessible distributed application to be used over the Internet. Biochemical and electrophysiological data describing individual reactions are associated with experimental microscopic image data that describes their subcellular locations. Individual processes are integrated within a physical and computational infrastructure that will accommodate any molecular mechanism. Current development is focused on expanding the generalized mathematical descriptions of biological mechanisms, enhancing accessibility to non-mathematically savvy biologists, and integrating the interface with a database of experimental data and models, as well as other external databases. A wide range of applications of the Virtual Cell are being developed both as in-house research projects (e.g. calcium dynamics in neuronal cells and RNA trafficking in oligodendrocytes) and external collaborations. Additionally, to date more than 500 independent users worldwide have created and run simulations with the Virtual Cell.

Principal Investigator Leslie M. Loew, Ph.D.
les@volt.uchc.edu (email)

Contact Ann E. Cowan, Ph.D.
860-679-1452 (phone); 860-679-1039 (fax)
acowan@nso2.uchc.edu (email)

Image: The Virtual Cell (screenshots in background) facilitates simulation of cellular processes on real geometries from microscopy data at any scale, such as the depicted 3D reconstructions of an oligodendrocyte or a mitochondrial crista (top right).

www.nrcam.uchc.edu

RESOURCE FOR BIOCOMPUTING VISUALIZATION & INFORMATICS *Multiscale Structural Modeling with UCSF Chimera*

The Resource for Biocomputing, Visualization, and Informatics (RBVI), an NIH/NCRR Biomedical Technology Resource Center, creates innovative computational and visualization-based data analysis methods and algorithms; implements these as professional-quality, easy-to-use software tools; and applies these tools for solving a wide range of genomic and molecular recognition problems within the complex biological sequence -> structure -> function triad. Application areas include gene characterization and interpretation, drug design, understanding variation in drug response due to genetic factors, protein engineering, biomaterials design, and prediction of function from sequence and structure.

One of the software packages developed by the RBVI is UCSF Chimera, a highly extensible, interactive molecular graphics program. Chimera allows developers to quickly incorporate novel algorithms and analysis tools by providing many built-in sophisticated real-time graphics rendering and data management functions, allowing developers to focus on coding features unique to their application. About 30 extensions have been written to date, including ones focused on the display and manipulation of large volumetric data sets and multiscale molecular models as shown here.

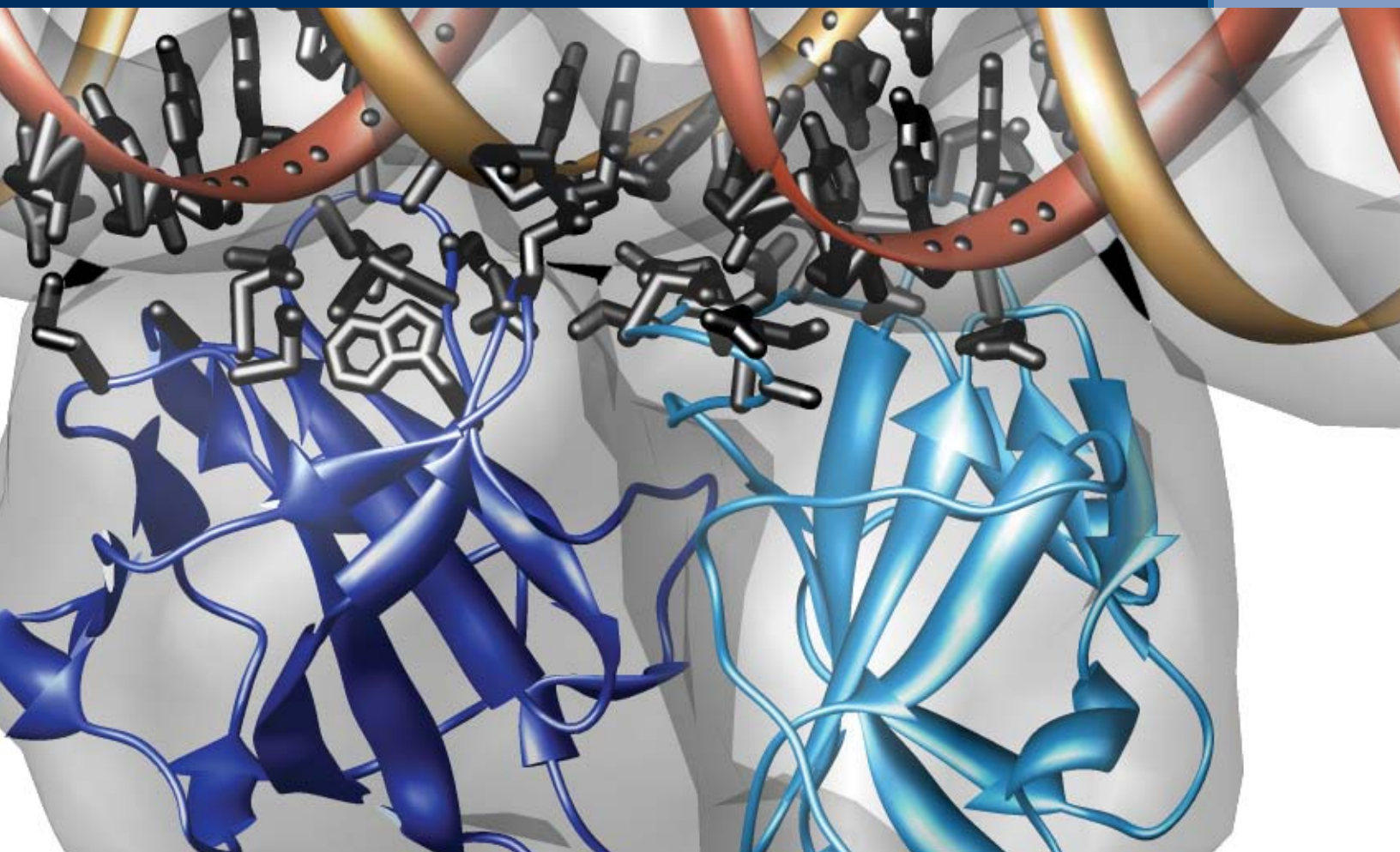
Principal Investigator Thomas E. Ferrin, Ph.D.
415-476-2299 (phone); 415-502-1755 (fax)
tef@cgl.ucsf.edu (email)

Co-Investigators
Patricia C. Babbitt, Ph.D.
415-476-3784 (phone); 415-514-4260 (fax)
babbitt@cgl.ucsf.edu (email)

Conrad C. Huang, Ph.D.
415-476-0415 (phone); 415-502-1755 (fax)
conrad@cgl.ucsf.edu (email)

Image: Surface proteins from bluetongue virus, which infects cattle, sheep & goats and has caused epidemics affecting millions of animals as well as a corresponding large economic burden, are shown bound to viral RNA. This sequesting of RNA is thought to play a key role in preventing an immune response in host cells. The image was created using the MultiScale extension to UCSF Chimera, an extensible molecular graphics system developed by the RBVI.

RBVI



MACROMOLECULAR MODELING & BIOINFORMATICS

Theoretical & Computational Biophysics Group at UIUC

The Resource studies living systems that constitute themselves through self-organized aggregation of their molecular components. Research focuses, in particular, on the formation, structure, and function of biopolymer aggregates forming bioenergetic proteins, complexes of membranes with proteins, or complexes of DNA with chromosomal and regulatory proteins. The investigations explore the physical mechanisms underlying the transformation of light energy into electrical membrane potentials and the synthesis of ATP in photosynthetic systems, as well as the mechanical functions of proteins, e.g. in muscle.

The Resource develops software for large-scale simulations. Software tools include NAMD, recipient of a 2002 Gordon Bell Award, a molecular dynamics simulation program used for classical, atomistic molecular dynamics simulations of large biomolecular aggregates; VMD, a molecular visualization program for displaying, animating, and analyzing both large and small biomolecular systems using 3-D graphics and built-in scripting; BioCoRE, a web-based, tool-oriented collaboratory for biomedical research and training.

The Resource has integrated recently its VMD and NAMD software into a comprehensive research tool which permits interactive molecular dynamics with a haptic (force feedback) interface that allows researchers to manipulate biomolecular model systems in parallel with single molecule experiments, e.g., atomic force microscopy studies.

Ongoing investigations include studies of aquaporin channels, mechanosensitive channels, ATP synthase, a chloride channel, photosynthetic proteins, visual receptors, and proteins with mechanical functions. Development seeks efficient evaluation of force fields and integration schemes for simulation of very large biomolecular systems as well as efficient distributed molecular dynamics programs on workstation clusters and massively parallel machines.

Learn more about the NIH Resource for Macromolecular Modeling and Bioinformatics, visit *www.ks.uiuc.edu.*

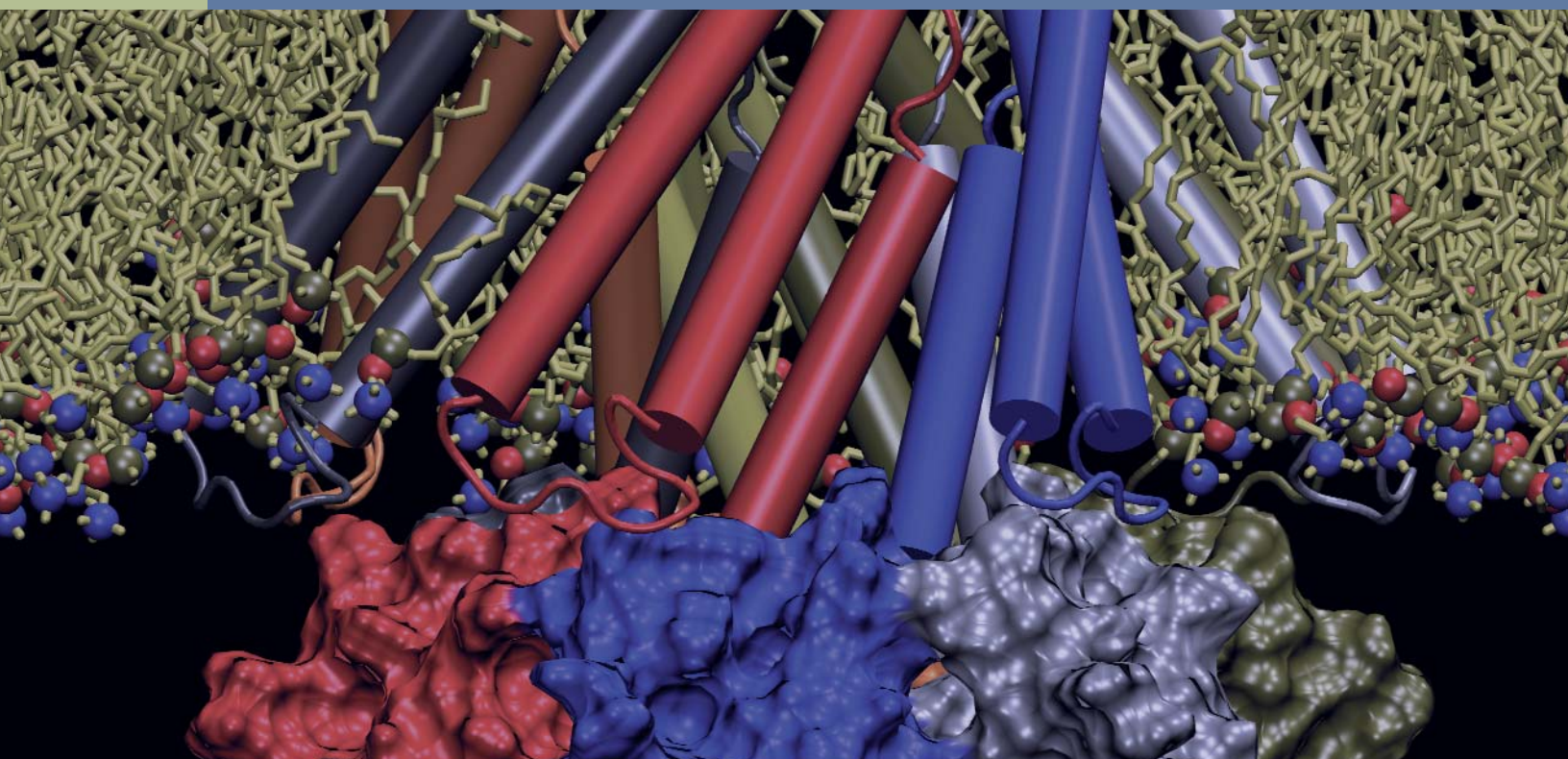
Principal Investigator Klaus J. Schulten, Ph.D.
217-244-1604/2212 (phone)
217-244-6078 (fax)
kschulte@ks.uiuc.edu (email)

Contact Emad Tajkhorshid, Ph.D.
217-244-6914 (phone); 217-244-6078 (fax)
emad@ks.uiuc.edu (email)

w w w . k s . u i u c . e d u

TCBG Theoretical and Computational Biophysics Group

Image: The image shows a simulated model of a membrane embedded mechanosensitive channel (220,000 atoms), representing large scale biological simulations conducted by the Resource.



The Resource represented in the brochure are supported by NCRR/NIH. The NCRR/NIH award P 41 RR08605 to the National Biomedical Computation Resource has supported the publication of this document.

National Center for Research Resources

November 2004