



Center for

*Computational
Biology (CCB)*

Arthur W. Toga

<http://www.ccb.ucla.edu/>

Computational Brain Atlas

■ Computational Atlas

Interactive environment

Integrating:

Phenotype

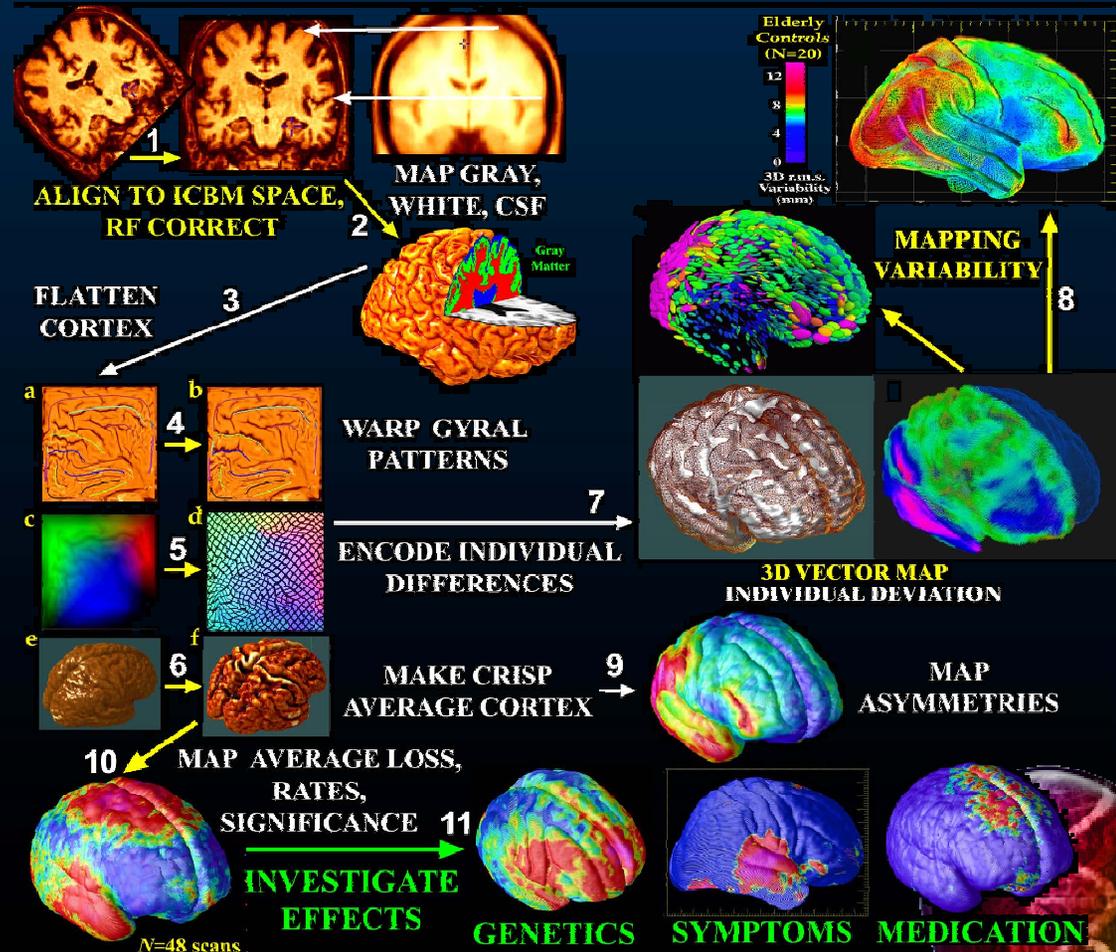
(anatomies, maps, alignments,

Demographics)

Genotype,

Shape descriptors &

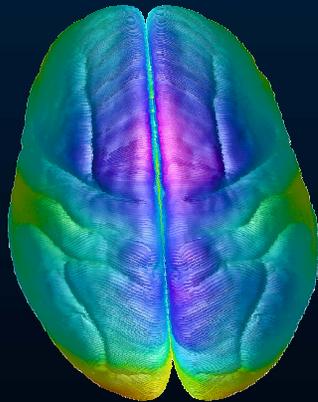
Scientific findings



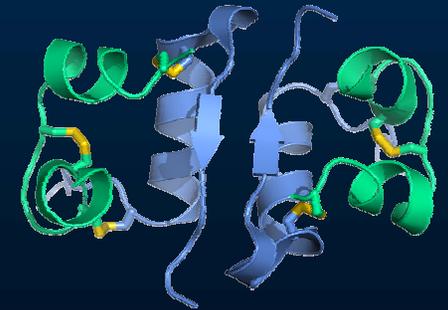
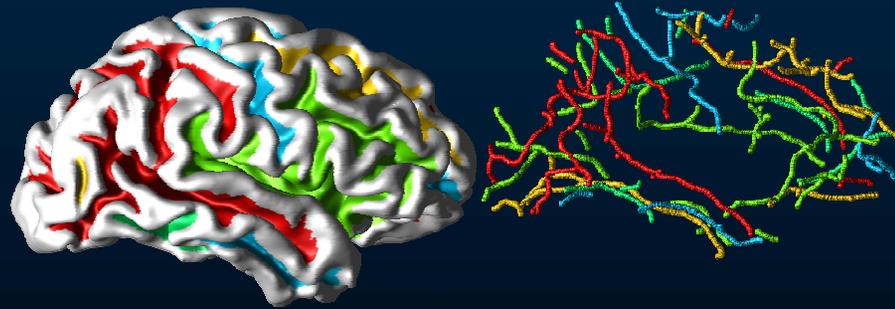
Modeling of Biological Shape

- A unified mathematical framework for modeling & analysis of biological shape, form and size

Canonical Representation of the Cortex

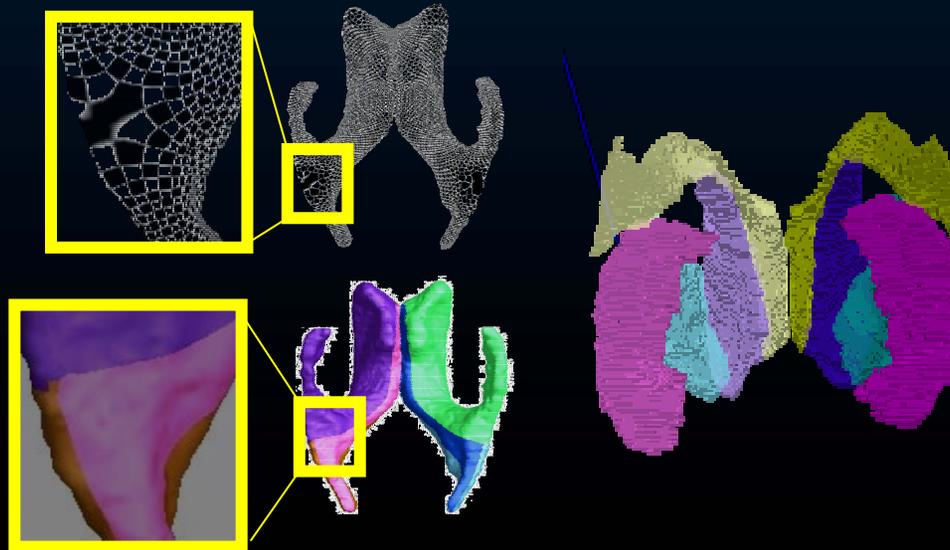


Global and Local Shape Descriptors



Shape of Insulin:
primarily α -helical

Conformal surface representation using intrinsic geometric features



Characteristics of Shapes:
Statistics Features
Geometry
Appearance
Topology
etc.



Software Tools

- CCB Software

<http://www.loni.ucla.edu/CCB/Software>

- CCB CVS

http://www.loni.ucla.edu/CCB/Resources/CCB_CVS.jsp

- NCBC Software Ontologies Working Group

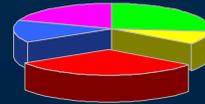
http://www.loni.ucla.edu/twiki/bin/view/CCB/CCB_NCBC_Resources

Peter Lyster, Karen Skinner, Ivo Dinov, Daniel Rubin, Bill Lorensen, Shawn Murphy, Mike Sherman, David States, Aris Floratos.

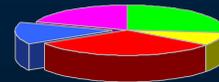


CCB Publications (2005-2006)

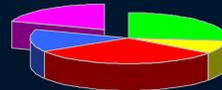
■ Scientific Journals: 38



■ Articles *in press*: 12



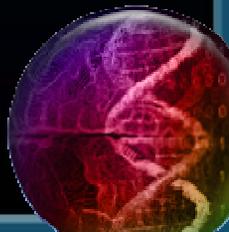
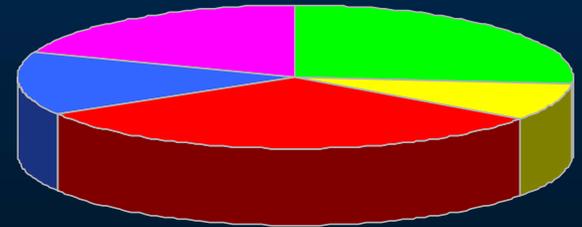
■ Submitted Articles: 45



■ Conference Proceedings: 20

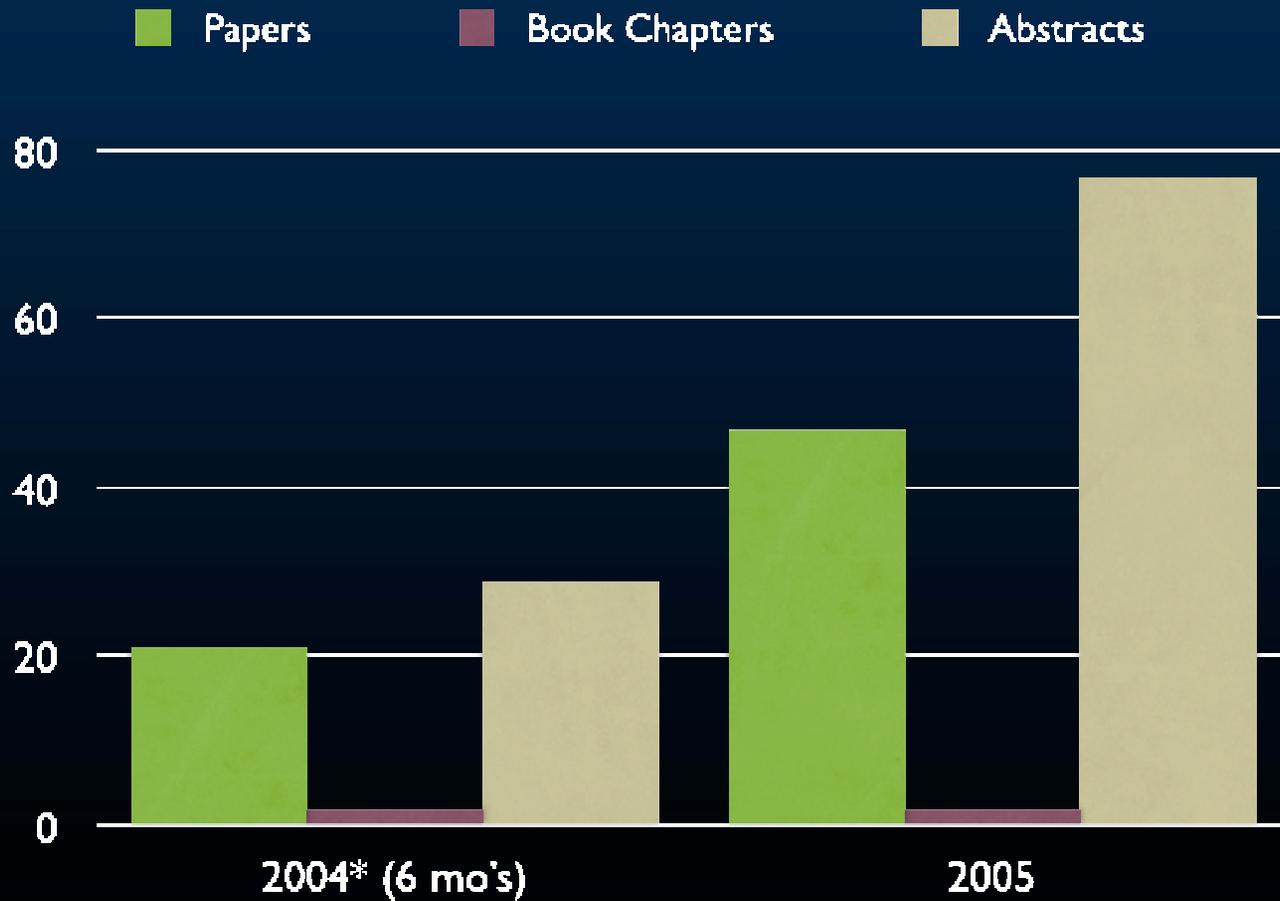


■ Abstracts: 28

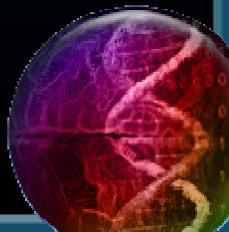
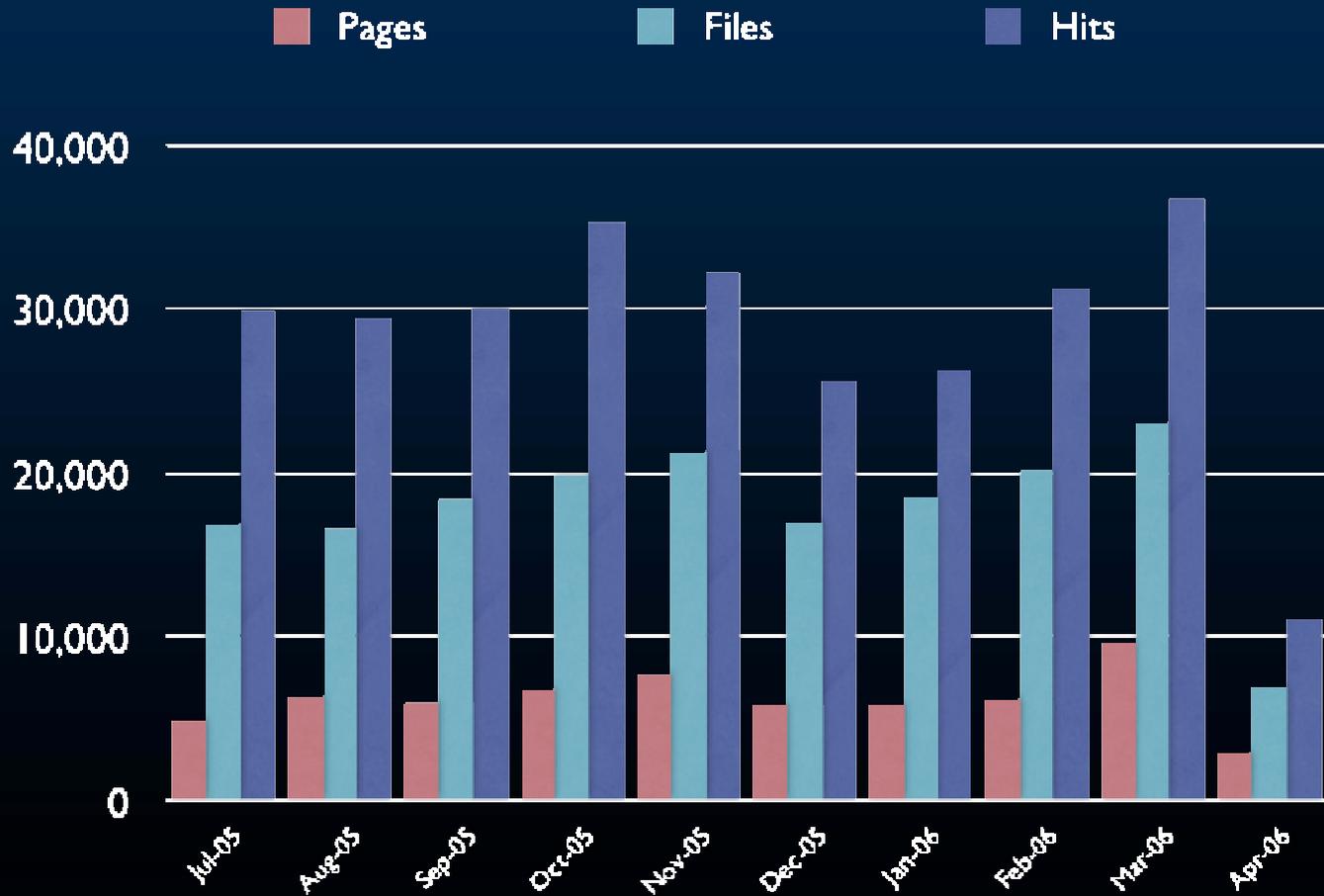


Research Publications

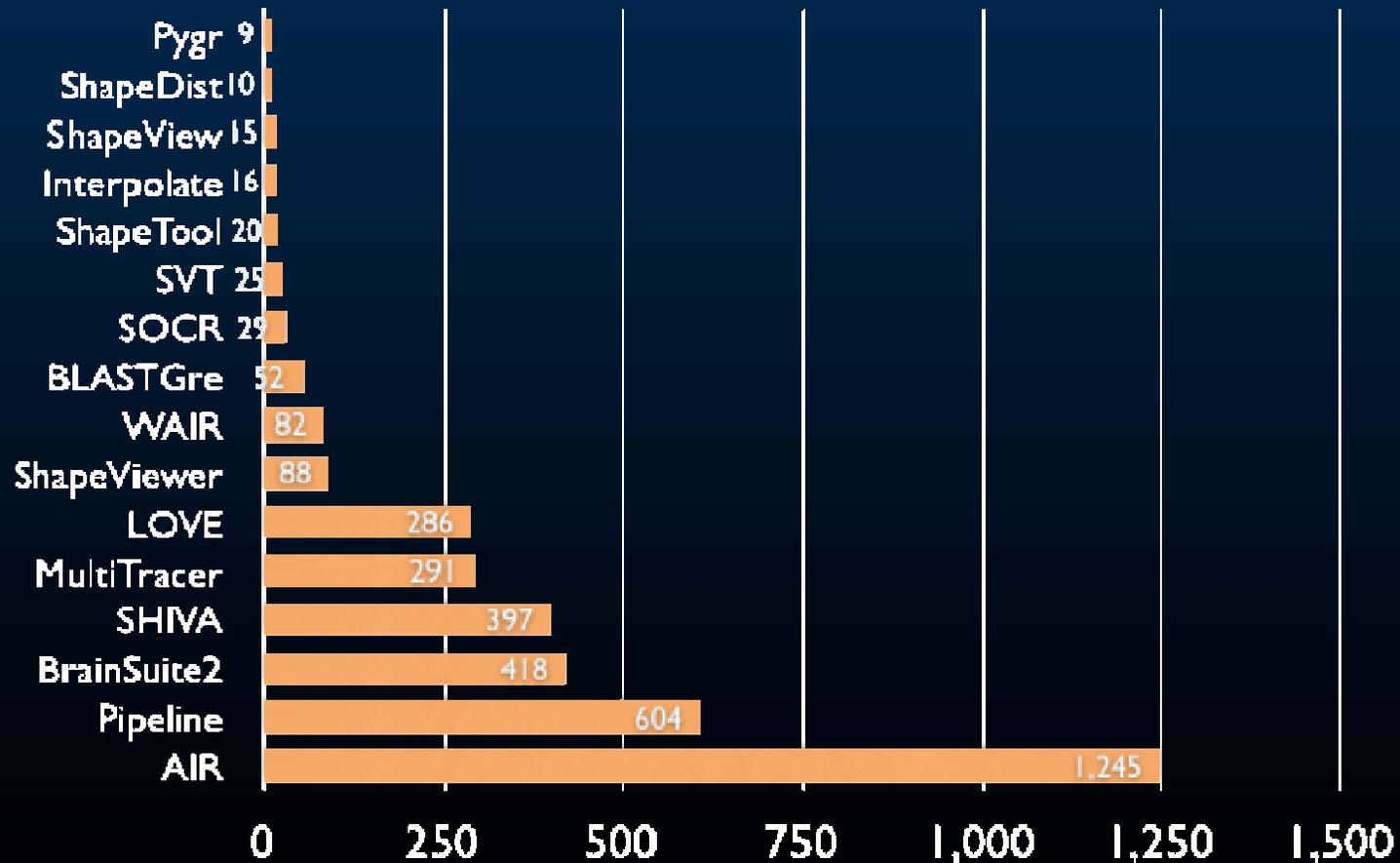
(July 2004-December 2005)



Web Stats



CCB Downloads March 2005 - March 2006



CCB Computational Science

■ 2005-2006 Developments

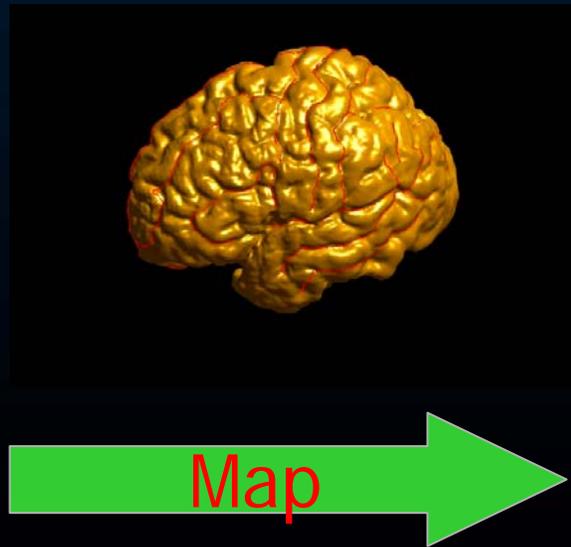
- Developed a new 3D **integrated segmentation and registration algorithm**.
- Developed a new math **definition of biological shape**
- Developed a learning-based method for **automatic detection of the cortical sulci** from MRI volumes.
- Developed a new **volumetric parsing method** based on statistical learning.



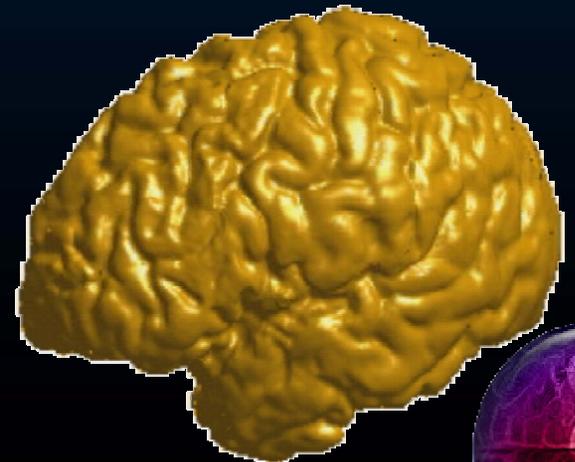
CCB Computational Science

- Direct Surface Mapping
 - Cortex (using manual or semi-automated sulcal boundaries)
 - Subcortical (hippo - automated intrinsic boundaries)
- Automatic mapping of one cortex onto another

Individual Subject Cortex

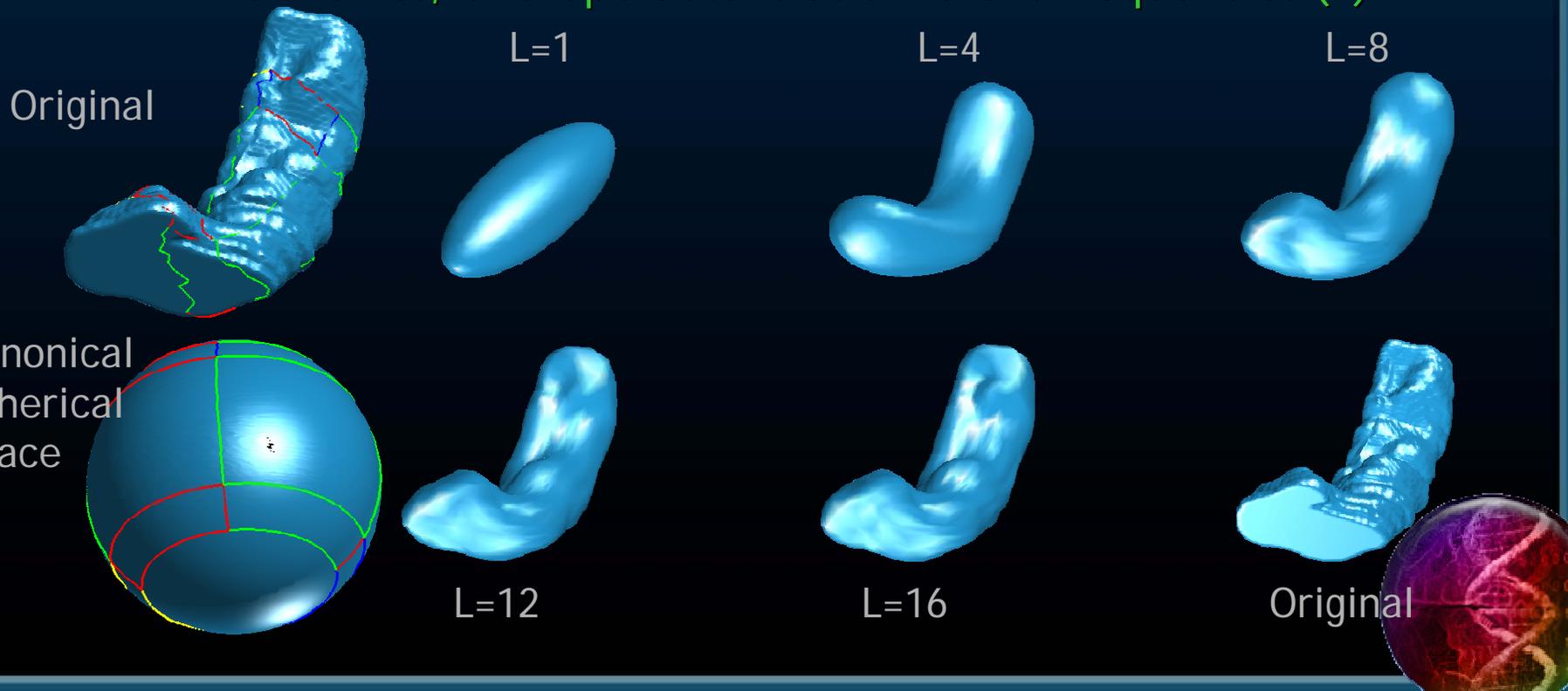


Atlas Template Cortex



CCB Shape Modeling

- Multi-resolution representation of biological shape
 - Wavelet-based Representation
 - Fourier Spherical Harmonics
 - Reconstructing Hippocampus from Different spherical harmonics, or shape details at different frequencies (L)



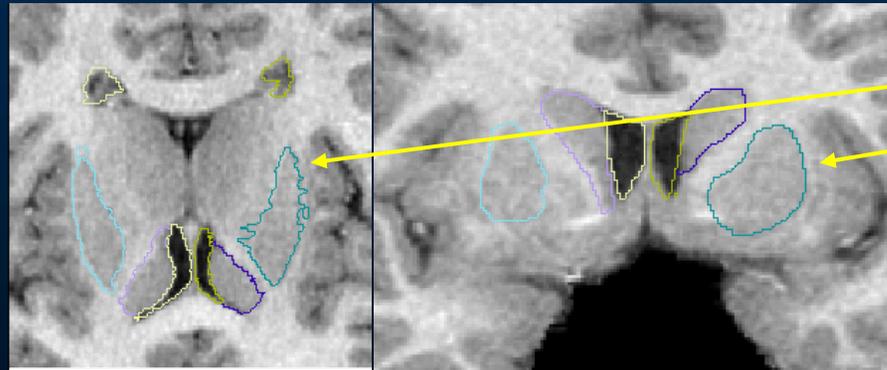
CCB Computational Tools

- Developed several new tools for modeling and analysis of biological shape, form and size
- Designed new data processing protocols utilizing Grid Infrastructure and Pipeline Environment
- We showed experimentally that many of the sequences of cancer-associated genes found in public databases represent tumor-specific forms that are not found in normal tissue.

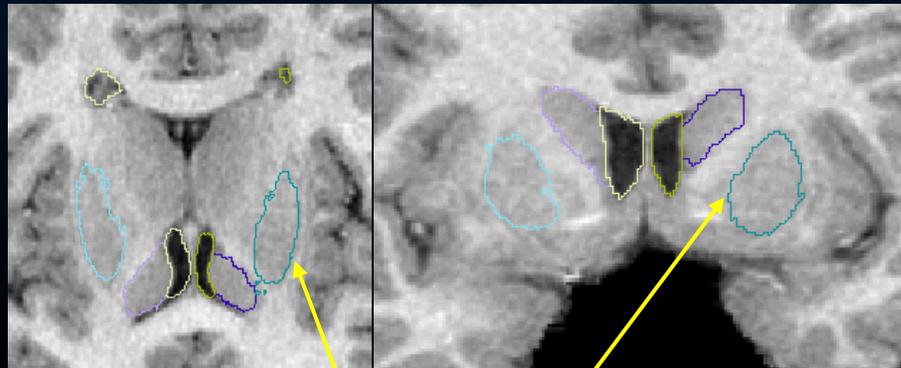


CCB Computational Tools

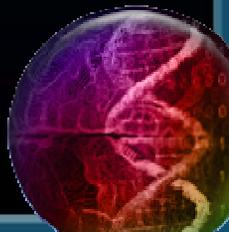
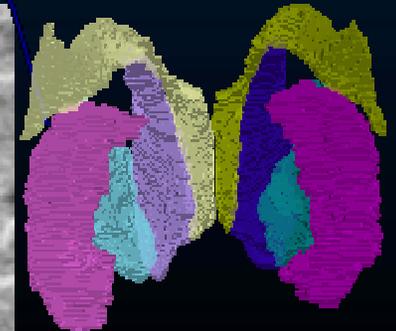
Statistical learning approach for automated volume parsing



Manual subcortical delineations (in coronal plane)



Automatic delineations (in 3D)



CCB DBPs

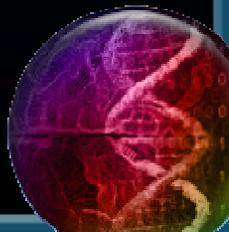
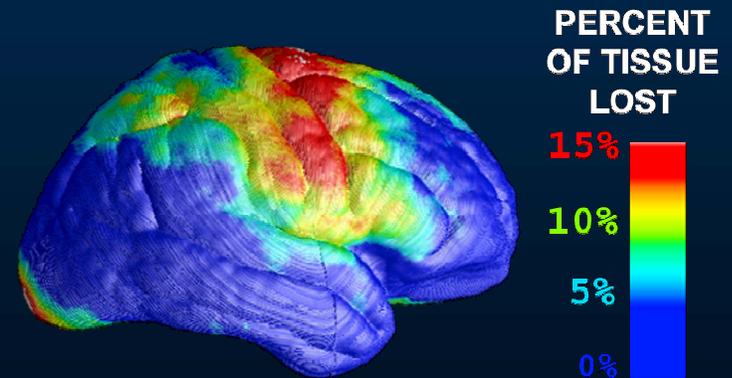
■ 2005-2006

- **HIV-induced Dementia:** Applying brain mapping algorithms we developed to detect brain changes in dementia, we reported the first maps of how HIV/AIDS damages the brain

- **Schizophrenia:** Map of Schizo heritability of cortical gray matter using ACE in healthy Twins.

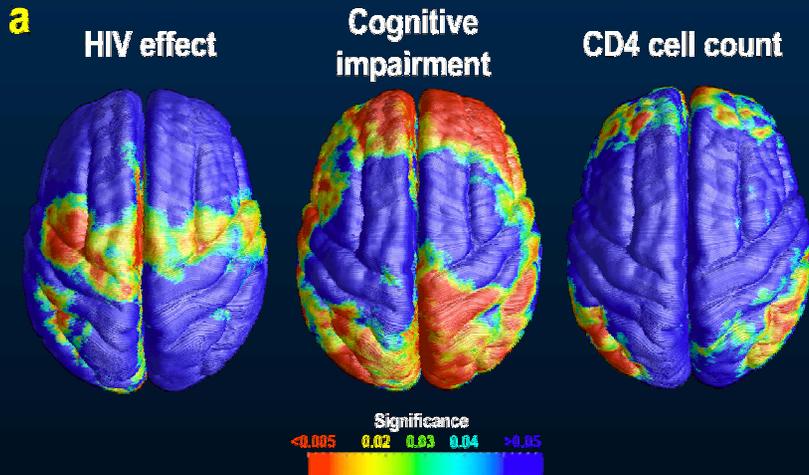
Cannon *et al.* 2006, *NeurInformatics*

Brain Tissue Loss in AIDS

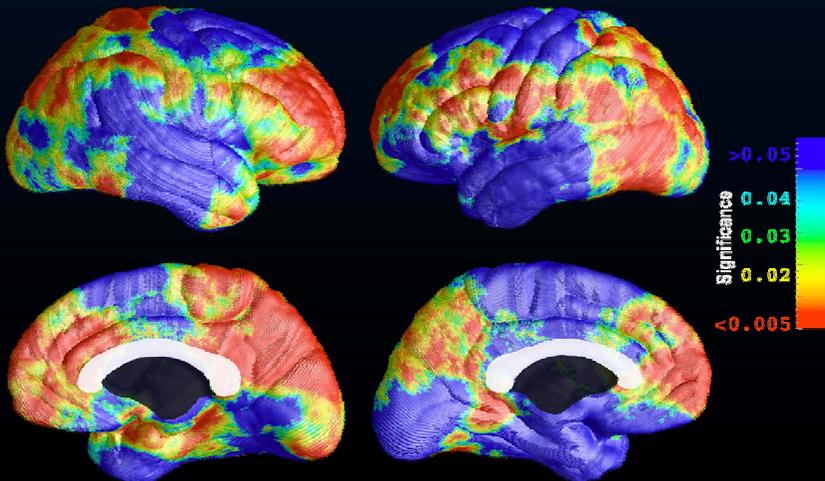


CCB DBPs

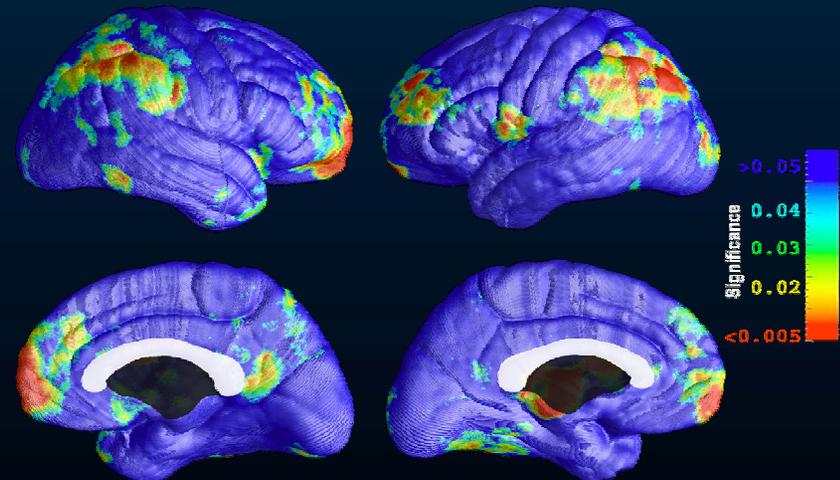
■ AIDS Inflicts Specific Pattern of Brain Damage



b Brain deficits that link with cognitive impairment



c Brain deficits that link with immune system deterioration

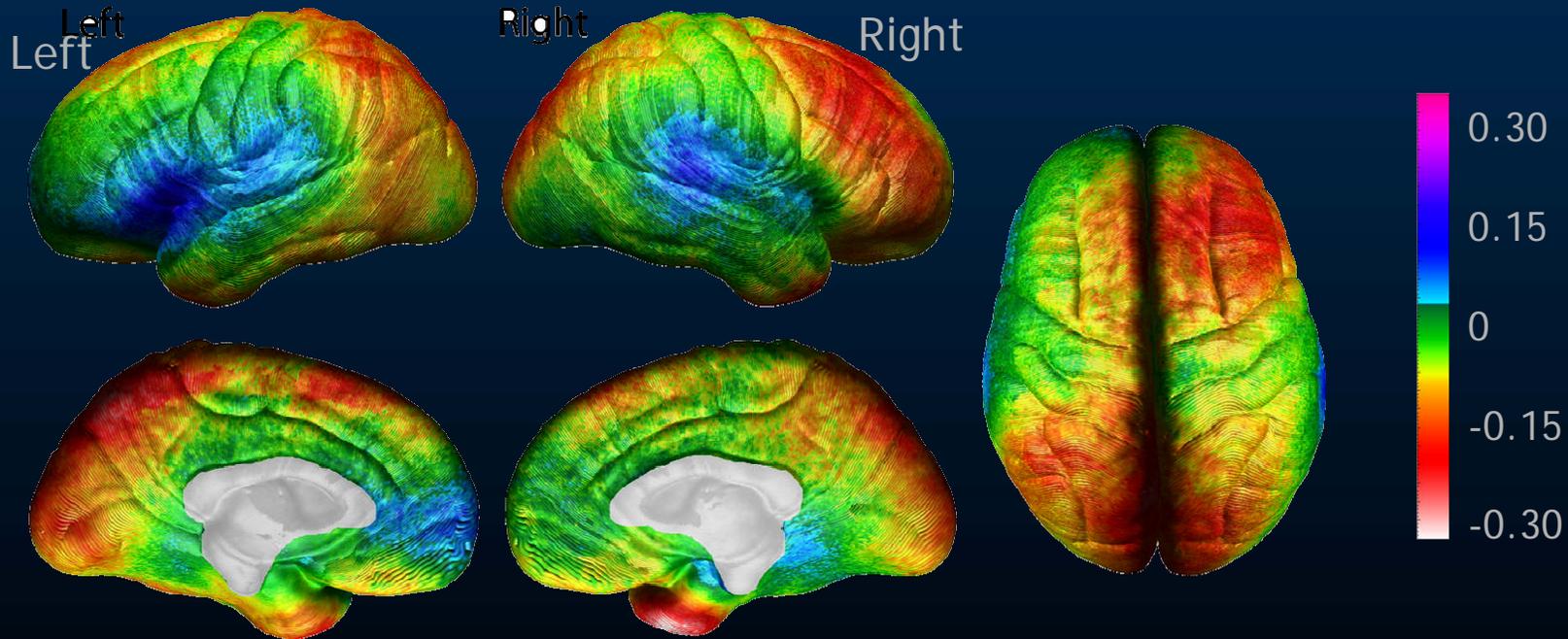


Thompson *et al.* 2005, PNAS.



CCB DBPs

■ Mapping brain maturation



Annualized rate of change in cortical thickness, shown in millimeters according to the color bar on the right (maximum gray-matter loss is shown in shades of red and maximum gray-matter gain is shown in shades of blue). 45 children were studied twice (two-year scan interval) between 5 and 11 years of age.



CCB Infrastructure

- **SUN Grid Engine**: The 600+ CPU, 8-rack SUN Microsystems compute cluster is fully operational and integrated with the Pipeline
- Services - **Bugtracking** and **Ticketing System**: **Mantis** is a versatile, web-based bugtracking system written in PHP
- **Central User Registration Service (CURS)**: CCB relies on CURS for web and app-specific access
- **CVS**: hardened version of CVS



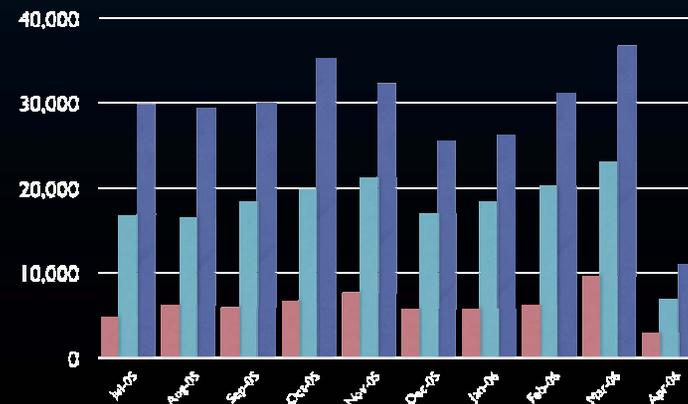
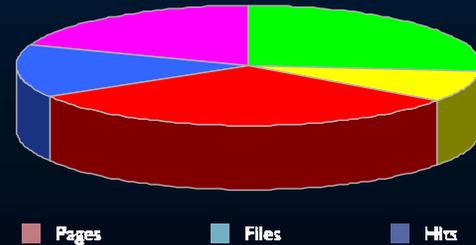
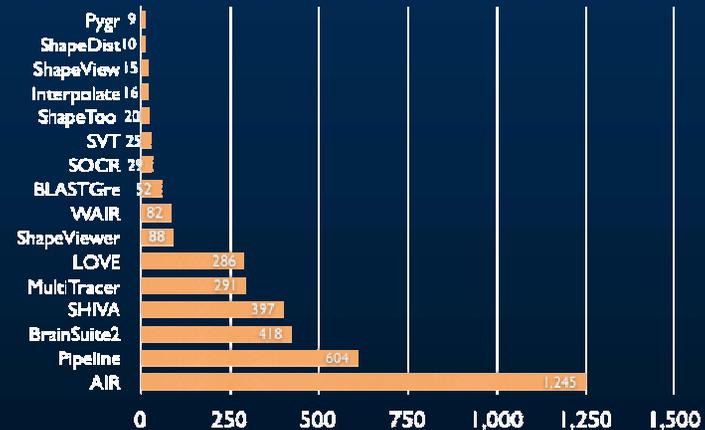
CCB Education & Training

- 2005-2006 Summary
 - 11 graduate and undergrad **courses**
 - 8 weekly **SIG** and seminar series
 - Dozens of **graduate students, postdocs and trainees**
 - 40+ **Presentations** at National and International Meetings
 - Organized 2 International **Workshops**
 - A dozen of **CCB Presents** colloquia
 - <http://www.loni.ucla.edu/CCB/Training>



CCB Dissemination

- Training of novice users
- Training of expert users
- Web resources
- Scientific publications



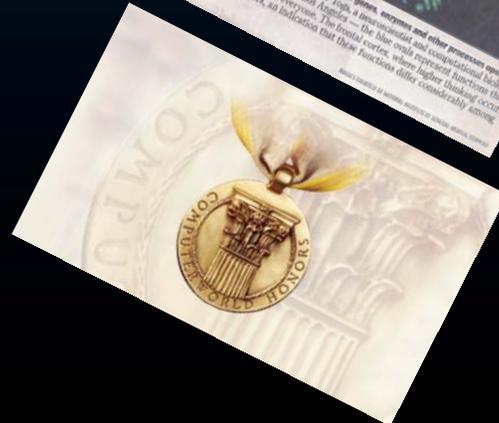
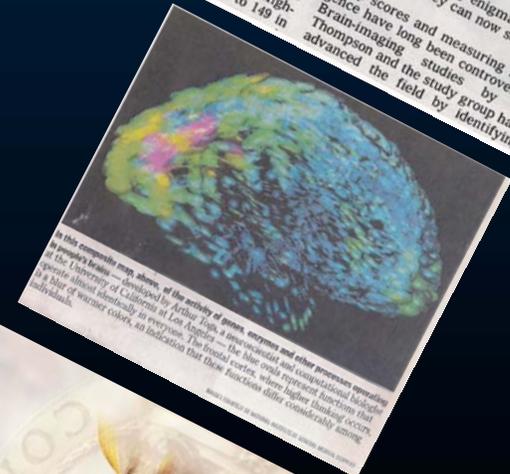
CCB Administration

- Focused the CCB research activities into modeling, analysis and interpretation of biological shape,
- Bi-weekly CCB Principals Meetings
- CCB Calendar
- CCB Collaborations
 - Computational Science
 - Driving Biology
- NCBC-wide activities (e.g., "Tool Yellow-Pages/Ontology")
- CCB/SOs/PO Quarterly VTC/TCons
- Weekly Administrative Reports



Media Coverage

- New York Times (March 30, 2006). Scans Show **Different Growth for Intelligent Brains**
- Washington Post Article (05/01/06). From **Research Labs, Glowing Colors and Images**
- BBC News: Scans show how **HIV attacks brain** (Oct. 11, 2005)
- NPR News: (October 11, 2005). UCLA Study Shows **AIDS Drugs May Not Protect Brain**
- 2006 ComputerWorld Honors Award Laureate



CCB (NCBC?) Challenges

- **Scientific** developments
- New DBP and Collaborative projects
- Handling **large number of active collaborations**
- **Training and Education** (how to maximize effects of training courses, workshops, visits, internships)
- **Software Cycle**: Design, Engineering, Prototype, Testing, Validation & Dissemination
- User **Support**, Software maintenance & Documentation
- Hardware **Infrastructure**
- **NCBC Program** interactions



CCB, NCBC and Interactions

- NAMIC, <http://www.na-mic.org>
 - SLIPIE (Slicer-LONI Pipeline Integration Environment)
 - Java ← JNI mediation → C/C++ tools
 - Level-set segmentation techniques
- I2B2, <http://www.i2b2.org>
 - HIVE cells
 - Pipeline modules
- National Center for Neurogenetics (e.g., Huntington's), DB & biosequence analysis
Physics-based Simulation of Biological Structures
Stanford University
- SimBios, <http://simbios.stanford.edu>
 - Structure Modeling Tools → Pipeline Modules
 - CCB Compute/Viz Libs → SimTK
 - Simulating Temporal Brain Changes
 - Simulating Kinetics using Random Distribution Sampling
- NCBO, <http://bioontology.org>
 - DBPs, Anatomy and Imaging ontologies
- NCIBI, <http://www.ncibi.org>
 - Databasing
- C2B2, <http://magnet.c2b2.columbia.edu>
 - Molecular data integration

National Center for Multi-Scale
Study of Cellular Networks,
Columbia University

National Center for
Integrative Biomedical Informatics,
University of Illinois

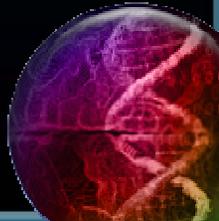
→ Neuroscience Pipelines

→ HIVE Objects

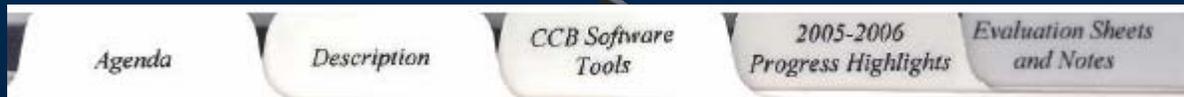
National Center for
Imaging Computing,
Informatics for Integrating Biology and the Bedside,
Johns Hopkins University

National Center for Neurogenetics
Physics-based Simulation of Biological Structures
Stanford University

Center for Computational Biology
University of California at Los Angeles



CCB Dissemination Event - Wed 07/19/06



Hosted by CCB
LSO: [John Haller](#) &
PO: [Greg Farber](#)

Lister Hill 38A
9:00AM - 12:00 PM
Wed. 07/19/06



CCB Dissemination Event - Agenda

- Roger Woods - Shape Representation and ShapeViewer (9:00 - 9:45 AM)
- David Shattuck - SHIVA and other CCB Computational Tools (9:45-10:30 AM)
- Chris Lee - Mapping Evolutionary Pathways of HIV-1 Drug Resistance (10:30-11:05)
- Break (11:05-11:15)
- Duygu Tosun - Automated Shape feature extraction and modeling (11:15-11:35)
- Zhuowen Tu - Volumetric Object Parcellization using Generative & Discriminative Models (11:35-11:55)

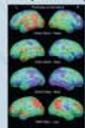
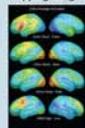


Modeling, Analysis & Viz of Shape

Driving Biological Projects

Project 1

Mapping Language Development Longitudinally



We have successfully studied 21 normally developing children between the ages of 3 and 17 years of age. Of these children, 10% had advanced structural imaging data. This is a fully quantitative high resolution structural imaging project in which we have obtained standard but not collected the data where as many as 50% have been imaged for our analyses. Of these 21 children, 17 have completed the Orthographic processing and Letter Rime tasks, and 20 successfully completed the Rhyme task. We have conducted analysis of the fMRI data for all of these tasks using FSL, in each of which we have carefully controlled for behavioral performance in the scanner. We also evaluated children's brain activation during a working memory task and 17 of the children completed that task. We have completed functional/structural MRI correlation analyses for the Orthographic processing task; the results of which are shown below.

Brain activation maps for the Orthographic processing task. The top row shows the unsmoothed data, and the bottom row shows the smoothed data. The left column shows the data for the Letter Rime task, and the right column shows the data for the Rhyme task. The top row shows the data for the Letter Rime task, and the bottom row shows the data for the Rhyme task. The left column shows the data for the Letter Rime task, and the right column shows the data for the Rhyme task.

Brain activation maps for the Rhyme task. The top row shows the unsmoothed data, and the bottom row shows the smoothed data. The left column shows the data for the Letter Rime task, and the right column shows the data for the Rhyme task. The top row shows the data for the Letter Rime task, and the bottom row shows the data for the Rhyme task. The left column shows the data for the Letter Rime task, and the right column shows the data for the Rhyme task.

Project 2

Clinical Progression of MS and EAE

We use cutting edge imaging tools developed in the CCB to determine the imaging and pathologic correlates in a mouse model of multiple sclerosis (MS), experimental autoimmune encephalomyelitis (EAE). In order to obtain an understanding of the pathologic events that underlie brain imaging changes in the human disease (MS).



Microscopic images showing brain tissue pathology. The top row shows the unsmoothed data, and the bottom row shows the smoothed data. The left column shows the data for the Letter Rime task, and the right column shows the data for the Rhyme task. The top row shows the data for the Letter Rime task, and the bottom row shows the data for the Rhyme task. The left column shows the data for the Letter Rime task, and the right column shows the data for the Rhyme task.

Computational Science

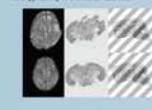
Conformal Mapping

This year, we have developed new conformal mappings that are useful for modeling imaging and analyzing biological structures represented compactly as 2D surfaces.



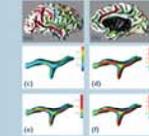
Non-linear Volumetric Registration & Segmentation

In 2005-2006, one of our core interests was the development and evaluation of a morphological combined registration and segmentation tool in the form of a pipeline that we called the 'Flow'.



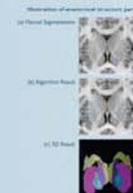
Automated Sulcal Fundi Extraction

This example illustrates the Sulcal region (A) & (B); shape index measure (C) contouring of a region; and (D) speed function on the contouring the gradient and tracked back to the original 3D volume.



Volumetric Brain Parsing

We proposed a unified framework to efficiently and effectively segment subcortical structures into multiple modalities. It has three key components: (1) A 3D shape index measure; (2) A region growing algorithm; and (3) A speed function on the contouring the gradient and tracked back to the original 3D volume.



Modeling, Analysis and Visualization of Biological Shape, Form and Size

CCCB

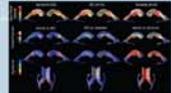


Center for Computational Biology

Project 3

Mapping Brain Changes in Alzheimer's Disease

We developed a powerful new algorithm (Chang et al., 2006; Lee et al., 2006) that automatically tracks and visualizes brain changes in longitudinally acquired images. I.e., the same person scanned repeatedly at three diverse progressions. This algorithm detects subtle changes in brain structure, a robust and highly automated. It will allow high throughput in clinical trials of drugs to slow neurodegenerative disease. It is in progress or planned in ADNI Cognitive impairment, AD, and APOE4, but only in 10% of ADNI subjects. Building on 18 year work, this brain change mapping algorithm pinpoints the regions and rates of greater brain changes in subjects with dementia. It provides statistics on rates of degeneration change for each brain region, based on the volume collected longitudinally.



Project 4

Genetic Influences on Brain Structure in Schizophrenia

We develop new computational tools to investigate the interaction of sequencing and genetics and applications of these tools to the structure and expression of schizophrenia. In the past year we have published our results on a novel based genetic association and large analysis of the ERCC1 gene in relation to cortical gray matter density in schizophrenia and applied these methods for novel brain imaging and association analysis (Cannon et al., 2009, 2006).



Computing Software Tools

Analysis

Image Analysis

Diffusion Tensor Imaging Tractography via Non-Stationary Radial Flow modeling & Quantification of white matter hyperintensities.

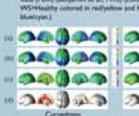


Neuroanatomical Validation

Diffusion Tensor Imaging Tractography via Non-Stationary Radial Flow modeling & Quantification of white matter hyperintensities.

Shape Analysis

Correlations and Shape Index measures mean (μ) of individuals with Williams Syndrome and (N) of healthy individuals. (S) Group mean difference (MS - Healthy). (R) Regions with significant mean difference (P < 0.05, corrected for multiple comparisons using False Discovery Rate (FDR) (Benjamini et al., 1995) (color coding for significance maps: WD/Healthy colored in red/blue and Healthy/MS colored in blue/red).



Direct Cortical Mapping

Direct Cortical Mapping (DCM) is a novel method for mapping brain structures directly from MRI data. It is based on the principle of direct cortical mapping (DCM) and is used to map brain structures directly from MRI data.

Biosequence Analysis

Biosequence Analysis (BSA) is a novel method for analyzing biological sequences. It is based on the principle of biosequence analysis (BSA) and is used to analyze biological sequences.

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Interaction

Pipeline Processing Environment

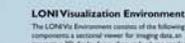


- Pipeline Features:
 - User interface
 - Server/Client communication via TCP
 - ADI encrypted communications
 - Ontology enabled data processing using OBI
 - Runtime processing of Resources
 - Automatic cache management
 - Grid engine integration
 - File sharing
 - GUI engine and data resource abstraction
 - Comprehensive logging
- Process domain capturing
- Integrated console
- User-friendly GUI
- Centralized monitoring
- Multi-connection topology
- Multiple node operations
- Runtime for processing
- Batch shell script output
- Distributed node type update framework
- Documentation on Wiki, Design, and Journals

Visualization

SHIVA

The Functional Neurological Image Viewing Architecture (SHIVA) is a Java-based image viewing environment. SHIVA provides a framework for image processing and visualization. It is used to visualize brain scan images.



LONI Visualization Environment

The LONI Visualization Environment consists of the following components: a relational server for imaging data, an interactive 3D display for surface and volume rendering of MRI data, a brain structure viewer, and an external database query system. The synchronization of all components is done in a comprehensive BrainGraph functionality which directly maps between position, structure name, database and functional connectivity information.

LONI Visualization Environment (LONI-VIZ) is a Java-based image viewing environment. It is used to visualize brain scan images.

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Computational Infrastructure

Computational Cluster

Clusters

SUN Grid Engine and the Pipeline Environment

Storage Area Network

Distributed Visual Computing Environment

There is a clear need for computing environments that promote interoperability so that data analysis tools and products can be imported from other sources and used as building blocks for new studies. The CCB Pipeline is one solution to this problem that includes a graphical interface to facilitate simple and intuitive modifications of the selection and order of processing modules. New protocols may be added to the Pipeline environment easily and quickly. The modular architecture of the environment improves performance and provides a means to disseminate new algorithms and computing power. The design of the Pipeline, and the ease of use throughout, enables it to run on any platform in a fully parallel processing environment (e.g., CCB Grid Engine or PCC). Investigators who do not have adequate computational resources to perform the newest and most sophisticated types of analyses can get access to such resources. This allows for the rapid development and deployment of new methods and technologies.

Web Information Sharing Environment

Central User Registration Service (CURS)

Data Immersive Visualization Environment (DIVE)

Education and Training

CCB Presents seminar series

http://www.loni.ucla.edu/CCB/Training/CCB_Presents.shtml

Courses

<http://www.loni.ucla.edu/CCB/Training/Courses>

Training

<http://www.loni.ucla.edu/CCB/Training>

Workshops

http://www.loni.ucla.edu/CCB/Training/CCB_Workshops.shtml

Collaborations

CCB DBP Projects

<http://www.loni.ucla.edu/twiki/bin/view/CCB/CCBDBPs>
These projects provide new exciting and challenging biomedical problems and applications that will serve as driving forces for the development of novel computational models and computational tools within the CCB.

CCB Collaborations

<http://www.loni.ucla.edu/CCB/About/Collaborators>
There are two major types of CCB collaborative endeavors: Projects and Pilot-Projects. Typically, Projects are considered independent R01 NIH-funded initiatives. And Pilot-Projects may be partially supported by current CCB infrastructure and resources.

Researchers at the Center for Computational Biology (CCB) develop, implement and test computational biology techniques for modeling and representation of biological shape. These new methods are applicable across spatial, scales and biological systems.

Dissemination

Web Materials and Tools

Training of four major types of users: Novice and expert users, web resources and scientific publications.

Publications

<http://www.loni.ucla.edu/CCB/Research/Publications>
In 2005-2006, CCB researchers produced over 38 scientific journal publications, 42 review articles, 47 novel submitted articles, 36 conference proceedings and a number of conference datasets.



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