

Advanced Biomedical Computing Center

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Overview

The Advanced Biomedical Computing Center (ABCC) supports scientific research at Frederick National Laboratory for Cancer Research, NCI at Frederick, NCI-Bethesda, NIH, and other federal agencies through the Economy Act. ABCC provides bioinformatics, mathematical simulation and modeling, image analysis and visualization, nanoinformatics, and proteomic analysis expertise to these communities. In addition, ABCC provides core infrastructure and data integration support for scientific projects through database maintenance and development, software maintenance, and scientific web application development. ABCC support is provided through a variety of mechanisms, ranging from provisioning of bioinformatics applications and databases to help with experimental design, data and results interpretation through consultation, collaboration and training, technology development and enhancement, outreach to local academic communities and national resources provided at other national labs, and serving as an interface with commercial and nonprofit organizations.

Expertise

Data Mining and Systems Biology

- Disease and species agnostic data mining and integration
- Large scale Clinical and Genomic integration
- Multi-omics data integration
- Analysis on longitudinal data

Simulation and Modeling

- Advanced Data Analysis
- Protein and DNA Modeling
- Electronic Structure of Proteins and Nanoparticles
- High-Level Calculations of Drug Reactions

Scientific Web Development

- Project tracking and Content Management Systems
- Database design, implementation and management
- User Interface (UI) Design and Graphic Development
- Scientific Applications Design for web and mobile

Nanobiology

- Structure Characterization
- Quantitative Structure Activity Relationships (QSAR)
- Toxicity

Imaging and Visualization

- 3D Biomedical Visualization
- Quantitative Image Analysis
- Information Visualization
- Image Archive

CCR-Bioinformatics

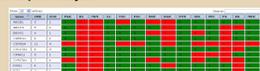
- Experimental Design
- NGS and Microarray Data QC and analysis
- Data Integration and Visualization
- NGS Data Management

CCR-Sequencing

- Sequencing Strategy Consultation
- Support second and third generation sequencing platforms
- Illumina, IonTorrent as well as PacBio support
- DNA, RNA and Epigenetic sequencing support and data analysis

Data Mining

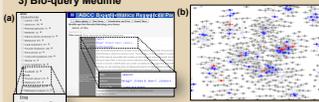
1) Variant Impact Analysis



2) Protein Features: Query and Visualize



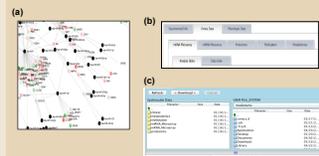
3) Bio-query Medline



- 1) Tabular report summarizing the impact of all variants in a VCF file
- 2) Image displaying variants and features on SPTAG
- 3a) Results for querying Medline using BiO-query and then filtering on drugs and pathways; (b) interactive co-author network of all authors who published on BRAF, with the red nodes highlighting authors from the user's search and all blue nodes showing their co-authors
- 4a) bioDBnet integration of hundreds of biological identifiers across species; (4b) Google analytics map showing the current usage of bioDBnet across the world

Systems Biology

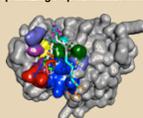
Screen Shots from SysBioCube, a Systems Biology Portal developed and supported for the U.S. Army Center for Environmental Health Research (USACEHR)



- a) Network view displaying the differentially expressed mRNA from mRNA microarrays and the expression levels of the corresponding mRNA targets from mRNA microarray data
- b) A tabbed page automatically created through corflig, files and database queries to explore all the available data sets in several studies
- c) Role-based secure downloads for sharing project data across collaborators
- d) Gene expression patterns observed using a custom algorithm on time-series data
- e) Interactive pathway spikes generated for in-depth analysis on gene patterns seen in (5c)

Simulation and Modeling

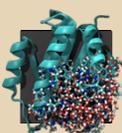
Optimizing Peptide Inhibitors of CRAF



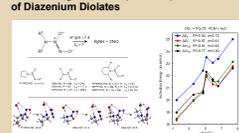
In collaboration with Dr. Deborah Morrison (CCR), the SAAMM Group examined putative peptide inhibitors of BRAF and CRAF dimerization. Starting with the interacting residues in the dimer interface, amino acid substitutions were performed to maximize the binding energy.

All-Atom Modeling of Active Sites

New quantum mechanical techniques can be used to model the electronic properties of proteins. Electronic modeling can now be performed on systems with over 18,000 atoms. The extended active site of RAS is shown to the left, and covalently bound inhibitors can now be examined.

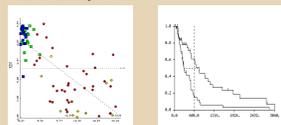


Determining Chemical (NO/HNO) Release Rates of Diazenium Diolates



In collaboration with Dr. L. Keefer, accurate quantum chemical calculations of transition state energies were found to correlate well with experimentally observed NO release rates.

Numerical Analysis of Data



- Biomarker detection
- Survival analysis
- Machine learning
- Hypothesis testing
- Pattern detection
- Algorithm and software development

Nanobiology

Nanoparticle Reconstruction from EM Data

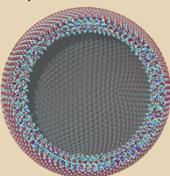
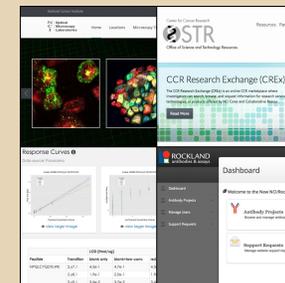


Image of self-assembled biologically active nano particle performed by ABCC for Dr. Nadya Tarasova (NCI, CCR). The final model included 1.6 million atoms. The EM data was collected using a low voltage electron microscope in collaboration with Bowe State University. The particle is 23 nanometers in size.

Scientific Web Development



Clinical Proteomic Technologies for Cancer Initiative (CPTC) Antibody Portal

URL: www.fredbiotech.cancer.gov

Protein Capture Reagents Program Data Portal

URL: www.ccrbiotech.cancer.gov

Clinical Proteomic Tumor Analysis Consortium Assay Portal

URL: www.usabcc.cancer.gov

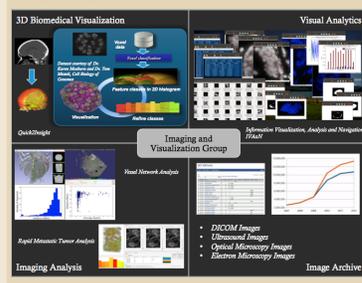
The Office of Science and Technology Resources (OSTR) Technology Resource Catalog

URL: www.usabcc.cancer.gov

Publications from Select Projects

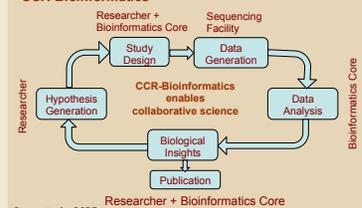
- Jianxin Shi, et al. Rare missense variants in POT1 predispose to familial cutaneous malignant melanoma. *Nature Genetics*. 2014 May;46(5):482-486.
- Debarjan Biswas, Joseph A. Hrabie, Joseph E. Saavedra, Zhao Cao, Larry K. Keefer, Joseph Ivancic, Ryan J. Holland. Aminolysis of an N-diazenuclidolated amide as an approach to diazeniumdiolated ammonia. *J. Org. Chem.* 2014 May;16(78):104512-6.
- Ji Y. Abrams N, Zhu W, Salinas E, Yu Z, Palmer DC, Jallwala P, Franco Z, Roychoudhuri R, Stahlberg E, Gattinoni L, Restifo NP. Identification of the Genomic Insertion Site of Pmel-1 TCR α and β Transgenes by Next-Generation Sequencing. *PLoS One*. 2014 May;14(5):e96650.
- Ming Yi, Yongmei Zhao, Li Jia, Electron Kebebew, Robert Stephens. Performance comparison of SNP detection tools with illumina exome sequencing data: an assessment using both family pedigree information and sample-matched SNP array data. *Nucleic Acids Res.* 2014 May; 42(12):e101.
- S. Ravichandran, N. Singh, D. Donnelly, M. Migliore, P. Johnson, C. Fitzhick, B.T. Luke, B. Martin, S. Maudsley, S.D. Fugmann, R. Moaddel. Pharmacophore model of the quercetin binding site of the SIRT6 protein. *Journal of Molecular Graphics and Modelling*. 2014 Apr;49:38-46.
- Vuong H1, Stephens RM, Volkovskiy N. AViK: an interactive web-server for annotation, visualization and impact analysis of genomic variations. *Bioinformatics*. 2014 Apr;30(7):1013-4.
- Rauli E. Cacho et al. Soft nanomaterials characterization using low voltage-high contrast electron microscopy and advanced image reconstruction techniques. *SPIE Photonics West - BIOS: Biomedical Optics*, Volume 8964, January 31-February 7, 2014.
- Muthuman UB, Khoo M, Respetits S, Venkatesaram G, Che A, Luke BT, Girard FP, Stephens RM. Knowledge and theme discovery across very large biological data sets using distributed queries: a prototype combining unstructured and structured data. *PLoS One*. 2013 Dec; 2:8(12):e80503.
- Yanling Lu, Lisle, C., Collins, J. Quick2Insight: A user-friendly framework for interactive rendering of biological image volumes. *Biological Data Visualization (BioVis)*, 2011 IEEE Symposium on, pp. 1.8, 23-24, Oct. 2011.
- Jhuraney A, Velkova A, Johnson RC, Kessling B, Carvalho RS, Whitley P, Spurdle AB, Vreesevik MPG, Caputo S, Milot GA, Vega A, Coquelle N, Galil A, Eccles D, Blak MJ, Pa T, van der Luit RB, Perna MS, Neuhansen SL, Donenberg T, Machakova E, Thomas S, Vallée M, Tavtigian SV, Glover JNM, Carvalho MA, Brody LC, Sharan SK, Monteiro AN, on behalf of the ENGIMA Consortium. BRCA1/2/3-CIRCOS: A visualization resource for functional analysis of missense variants. *Journal of Medical Genetics*. (In Press).

Image Analysis and Visualization



See poster for ABCC – Imaging and Visualization Group

CCR-Bioinformatics



See poster for CCRB

CCR-Sequencing



See poster for CCR Sequencing Facility

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