Annual Report
(2017-2018)
Networks are all around us, and this connectivity drives human biology. At the individual level, interactions between capable people make successful institutions like Boston University thrive. At the cellular level, physical protein–protein interactions are likewise just as instrumental to virtually all biological processes. They are central to human health, development and disease. Yet while advances in genomics are now providing valuable information about gene function, a major challenge is to understand how genetically encoded proteins work together inside cells and how these interactions are perturbed in disease.

This is the overarching goal of researchers affiliated with BU’s new Center for Network Systems Biology, which opened in October 2017. We aim to devise and implement innovative methods to characterize the protein interaction networks in the various cells and tissues of the human body. Our work addresses fundamental biomedical questions that have major ramifications for understanding and treating important human disorders, such as cancer, heart disease, neurological syndromes and diabetes. How are protein interactions organized inside healthy cells and organs? What are the features and principles that guide the formation and regulation of these networks? How is this organization disrupted in human disease?

The vision of the CNSB is to be the ‘Google Maps™’ for molecular networks, that are hidden to the eye yet which underlie most human biological systems in different clinical contexts. Through our rapidly growing repertoire of innovative technologies, collaborative efforts and basic discoveries, our Center is generating important new data resources, valuable clinical findings and potential diagnostic and therapeutic tools that are relevant to the broader biomedical research community at BU and beyond.

To achieve this, the trainees, staff and faculty affiliated with the CNSB are implementing an ambitious research program aimed at leveraging our unique expertise in precision biochemistry, molecular biology, and Network Systems Biology, with the aim of systematically characterizing and quantifying molecular interaction networks in biological specimens with broad mechanistic significance. We aim to foster cross-disciplinary research, with the goal of international leadership in molecular Network Systems Biology. To this end, we are setting up world-class infrastructure that will enable the systematic characterization of connectivity diagrams of unprecedented biomedical significance, scope and resolution. Since disruption of protein interactions ultimately drives pathology, our work will identify causal, clinically actionable disease relationships and potentially transformative new markers and targets for theranostic development.

In my capacity as the founding director of the CNSB, I have enormous enthusiasm and expectations that we will achieve these goals. In our first year, we have made substantive progress towards high-impact papers and grant applications that will allow us to disseminate valuable tools and resources to the local, national and international biomedical research communities. Our Center is a highly dynamic environment that aims to bridge initiatives across the Charles River and Boston’s South End. I see tremendous opportunities for new collaborations in the highly collegial environment at BU. As pioneers of ‘interactome’ science, projects developed in association with the CNSB have access to state-of-the-art mass spectrometers and other high-throughput technologies that allow researchers to map cellular networks on an unprecedented global scale. The CNSB is also fostering entrepreneurial, forward-looking trainees working on important biomedical problems who will be future leaders in the field in a few short years.

On behalf of our rapidly expanding team, I would like to thank the administration and diversity of researchers we have had the opportunity to engage with at both BU campuses for their warm welcome and support since we opened our Center less than a year ago. Their enthusiasm, assurance and good will is fuel for our own passion and is sure to empower another successful year ahead.

Sincerely,

LETTER FROM THE DIRECTOR
Network Systems Biology is the study of the physical and functional interactions of biomolecules that mediate the diverse complex biological systems that are crucial to health and disease. It is also an emerging strength of Boston University. Elucidating the biological networks that drive human health, development and pathology is fundamental to a deeper mechanistic understanding of cellular processes and disease.

The mission of the Center for Network Systems Biology is to support, enhance and disseminate transformative collaborative research in Network Systems Biology at the Medical and Charles River campuses of BU to drive biological research in the coming decades.

**WE HAVE THE FOLLOWING OVERARCHING GOALS:**

**I. ESTABLISH BU AS A WORLD LEADER IN MAPPING MOLECULAR NETWORKS**

Molecular interactions are crucial to virtually all cellular processes central to human health and disease. Elucidating how such networks form and function normally during development, or become altered in pathological contexts, is fundamental to understanding the mechanistic basis of biological systems and their causal links to clinical disorders. The primary objective of the Center is to investigate how systems of interacting biomolecules drive the cellular functions and pathways essential to human health and disease. This research will enhance the profile and reputation of BU in the domain of Network Systems Biology, establishing an internationally recognized academic center for research excellence that will attract, train and nurture talented investigators at the forefront of the field.

**II. FOSTER COLLABORATIVE INTERDISCIPLINARY RESEARCH AT BU**

Researchers with the CNSB will devise and support ambitious new multi-disciplinary research initiatives across both the Medical and Charles River campuses. Our Center will be a focal point for a growing cadre of basic and translational researchers, clinicians, computational biologists (including bioinformaticians, statisticians, mathematicians), chemists, bioengineers and other scientists tackling important biomedical problems. The Center will continue to build and nurture a highly collaborative and successful entrepreneurial research community at BU.

**III. PROVIDE ACCESS TO INNOVATIVE TECHNOLOGIES UNIVERSITY WIDE AS A NEW RESEARCH PARADIGM**

The Center will pioneer innovative experimental technologies for the systematic large-scale study of molecular interaction networks critical to human health and disease. The CNSB will provide affiliated researchers with timely access to state-of-the-art infrastructure and expertise. These technologies include precision mass spectrometry and new methods for quantitative single cell molecular profiling. The Center continues to build a rigorous computational framework that leverages statistical inference, artificial intelligence and integrative ‘big data’ analytics to combine and mine different types of data to solve complex biomedical problems at the forefront of the field.
OUTSTANDING NEW MEMBERS RECRUITED TO THE CNSB OVER THE PAST YEAR.

DR. PIERRE HAVUGIMANA
Senior Research Scientist (PhD, University of Toronto (Canada), Molecular Genetics) who is studying native human protein assemblies via precision mass spectrometry.

DR. WEIWEI LIN
Post-Doctoral Fellow; PhD – Peking University (China), Pharmaceutical Analysis; who is studying neuroproteomic and metabolomic networks.

DR. FEI BIAN
Visiting Scientist (Professor, Biotechnology Research Center, Shandong Academy of Agricultural Sciences (China)); who is establishing a microbial proteomics platform.

BEN BLUM
Graduate Student (PhD candidate, Program in Biological Sciences, Boston University) who is developing innovative strategies for integrative multi-omics-based molecular profiling of breast cancer cell processes.

2017 HIGHLIGHTS:

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Our new instruments are sufficiently sensitive to analyze only a single plate of cells. Our depth of coverage has improved markedly since we recently acquired an ultrafast scanning Q Exactive HFX hybrid mass spectrometer last fall, which can identify and quantify up to 8,000+ proteins per run. CNSB scientists have found that they can isolate, identify and quantify hundreds of endogenous protein complexes from human cells and tissue using gentle extraction buffers. This allows us to potentially map protein networks even in limiting clinical samples, allowing exciting new collaborations with clinical scientists at BU and beyond.

The CNSB core laboratories have been very active with the installation, training and operation of state-of-the-art precision mass spectrometers and other high-tech instrumentation at the CNSB.

Construction on the Conte core lab facilities, started in late spring, was completed in August 2017. The resulting gleaming new wet lab facilities enable cross-disciplinary research that will place the CNSB at the forefront of the emerging field of Network Systems Biology.

The infrastructure has been in heavy use these past nine months – informal CNSB motto: “Go Big, or Go Bigger!”
THE CNSB IS AN EMERGING HUB FOR INTER-DISCIPLINARY RESEARCH AND TRAINING

CNSB researchers are engaged in active collaborations with other leading groups in the Boston area, including labs at Harvard Medical School, MIT and beyond.

The CNSB has forged extensive links to research faculty and associated educational initiatives at both the Charles River and Medical Campuses, including the Graduate Program in Bioinformatics, a premier cross-campus mentoring venue at BU.

CNSB TRAINEES PARTICIPATE IN INTERACTIVE MULTI-DISCIPLINARY RESEARCH

Mentorship and teamwork form a cornerstone of the CNSB research program. By establishing an open, well-rounded relationship with each trainee to guide self-motivated scientific inquiry and scholarship, our goal is to cultivate research integrity, rigorous inquiry and scientific excellence. Our trainees address important biomedical questions with the goal of long-term impact, not short-term results. In addition to honing trainees’ experimental skills, conceptual knowledge and bioinformatics capabilities, the CNSB demands trainees exercise creativity and critical judgement.

Scientific communication, including presentations, workshops, high impact publications and social media, are central to the broader community outreach of the CNSB.

CNSB trainees draft and review manuscripts, and present and defend their work in formal center meetings. We tailor our management approach to individual trainees’ backgrounds, strengths and shortcomings, aiming for balance through regular coaching, critical feedback and encouragement to ensure they grow intellectually while striving for research excellence. By engaging trainees in highly collaborative projects, while providing stable financial support and exposure to a cutting-edge research platform, trainees at the CNSB will emerge both as well-rounded scientist ‘citizens’ and as knowledgeable experts in molecular biology, ‘omics and network biology. Our overarching guiding principles are that trainees be considerate colleagues, that they pursue their work with passion and document their findings rigorously, and that they publish thoughtful, high impact papers in premier peer reviewed journals. Every member of the CNSB are encouraged to attend and present their work at relevant research conferences and workshops.
The Center for Network Systems Biology is a University-wide interdisciplinary research center reporting to the University Provost through the Vice President and Associate Provost for Research at Boston University. The CNSB is virtual, and so does not consist of any predefined space. Membership will include outstanding current systems biology and molecular biology facility who are housed in a range of locations on both the Charles River Campus and the BU School of Medicine. Professor Emili, the Founding Director, has a substantive newly renovated lab space at the Silvio Conte (K) research building, located on the Medical Campus, where he has established a state-of-the-art mass spectrometry and computational facilities.

Professor Andrew Emili, recruited to BU through the Provost’s Senior Hiring Initiative with joint appointments in the Department of Biochemistry at the Medical Campus and the Department of Biology on the Charles River Campus, was appointed by the Provost as the CNSB’s Founding Director for a renewable five-year term, effective July 1, 2017. Professor Emili is a pioneer and leader in the field of systems biology, and his research group has reported groundbreaking studies documenting the molecular interaction maps of human cells and other model systems. Dr Emili’s laboratory will serve as a hub in the Center by providing access to research instrumentation and experimental expertise needed for collaborative projects involving other CNSB research faculty using experimental techniques in Network Systems Biology. The Conte building also has ample first floor space for hosting social gatherings, seminars, conferences, and workshops organized by the Center. The Director is responsible for the overall activities of CNSB, including personnel, financial resources, and the use of the Center’s facilities, as well as the establishment of collaborative research, education and training programs and their implementation.

The Director intends to recruit a dedicated Senior Project Manager, who will be a seasoned and accomplished scientist with a notable track record in Network Systems Biology, who will assist in the establishment and management of intra-/extra-mural research collaborations, in all scientific outreach activities, and in budgetary compliance. The Director is also supported by an Administrative Coordinator, as well as by the administrative structure of the Departments of Biochemistry and Biology, who will help oversee the Center’s vital operations (e.g., grants administration, meetings, financial). The CNSB research activities are also supported by three Core components:

- The Administrative Core, led by the Director, manages, coordinates, and supervises all scientific, outreach and budgetary activities. A key objective of the Administrative Core is to support wide user uptake of network biology concepts and methods by implementing ongoing outreach and skills training programs. Drawing together an outstanding team of experts in molecular networks, proteomics, functional genomics, mass spectrometry, computational biology, and systems biology, the Administrative Core will nurture scientific expertise, foster new collaborative enterprises, and provide guidance for future growth initiatives at BU.
- The Administrative Core is responsible for training, workshops and all other outreach activities. These include sponsoring regular visiting seminars and a yearly retreat with prominent outside guest speakers in the area of Network Systems Biology, as well as hosting informative project websites, social media and virtual tutorials, and hosting ‘hands on’ physical training sessions and workshops to disseminate skills needed for network data generation and analysis, and to share key findings with both the BU and broader scientific communities.
- The Technology Core deploys cutting-edge high-throughput technologies (e.g. quantitative proteomics, imaging, metabolomics, etc.) for systems-level analysis of samples generated by the Center’s projects, starting primarily in the mass spectrometry facility but also via other emerging technology platforms, such as super resolution imaging.

The Data, Bioinformatics and Modeling Core performs sophisticated computational analyses related to the Center’s projects. These include integrative molecular-level investigations of protein networks, signaling pathways and disease/genomic associations. The Core provides real-time data access for collaborating team members, facilitating data exchange. Once a project is completed and published, the compiled data and models will be made available to the broader scientific community via public databases as well as by dedicated web portals supported and managed by the Core.

The following luminary research scientists serve on the CNSB’s SAB:

- **Richard Smith, PhD**
  - Former Director of Proteomics, Pacific Northwest National Laboratory
  - Field of Study: Proteomics and precision mass spectrometry.

- **Catherine Costello, PhD**
  - William Fairfield Warren Distinguished Professor, Director School of Medicine Biological Mass Spectrometry Center, BU
  - Field of Study: Glycobiology and precision mass spectrometry.

- **Michael MacCoss, PhD**
  - Professor Genome Sciences, University of Washington
  - Field of Study: Quantitative mass spectrometry and MS informatics.

- **Nevan Krogan, PhD**
  - Director Quantitative Biology Institute, University of Toronto
  - Field of Study: Experimental Network Biology.

- **Gerard Cagney, PhD**
  - Principal Investigator, Conway Institute, University College Dublin
  - Field of Study: Computational Network Biology.

- **Gary Bader, PhD**
  - Professor of Molecular Genetics, University of Toronto
  - Field of Study: Computational Network Biology.
AFFILIATED FACULTY – CNSB CORE MEMBERS:

Members have priority access to facility resources, and enhanced project coordination.

Joseph Zala, PhD
Professor of Biochemistry
Field of Study:
Glycoproteomics of the cell surface and extracellular matrix.

Sandor Vajda, PhD
Professor of Bioengineering
Field of Study:
Structural bioinformatics.

Benjamin Wolozin, MD/PhD
Professor of Pharmacology and Neurology
Field of Study:
Molecular and cell biology of neurodegeneration.

John Porco, PhD
Professor of Chemistry
Field of Study:
Chemical synthesis of bioactive compounds.

Daniel Segre, PhD
Professor of Bioengineering
Field of Study:
Structural bioinformatics.

Stefano Monti, PhD
Associate Professor of Medicine and Biostatistics
Field of Study:
Computational Biomedicine.

Christine Cheng, PhD
Assistant Professor of Biology
Field of Study:
Systems biology of transcriptional regulatory networks.

ACADEMIC MEMBERSHIP

Full-time Boston University faculty members are eligible for membership upon invitation by the Director, or after direct request, with decisions about membership made by the Academic Advisory Committee. While retaining all primary responsibilities in their home departments, they will engage in research activities relevant to the goals of the Center for Network Systems Biology. New faculty members will be evaluated on an ad hoc basis by the Academic Advisory Committee, while renewal of existing faculty memberships in the Center will occur during an annual review process. Prior to voting, the AAC will look for evidence of relevant academic and research activity in Systems Biology based on:

A) SIGNIFICANT ACADEMIC AND RESEARCH ACTIVITY IN NETWORK AND/OR SYSTEMS BIOLOGY;
B) A HISTORY OF PARTICIPATION IN CNSB RESEARCH ACTIVITIES INCLUDING COLLABORATION, SERVICE, ATTENDANCE AT MEETINGS AND EVENTS, AND CONTRIBUTION TO THE CENTER’S RESOURCES AND/OR PLATFORMS;
C) COLLABORATION WITH, AND ACKNOWLEDGEMENT OF, CNSB MEMBERS, IN THE SUBMISSION OF PAPERS AND GRANTS; AND
D) DEMONSTRATED COMMITMENT TO ACADEMIC EXCELLENCE AND THE EDUCATIONAL GOALS OF THE CNNSB, INCLUDING SUPPORT AND MENTORING OF AFFILIATED FACULTY MEMBERS, POST-DOCTORAL FELLOWS AND STUDENTS.

Faculty that are invited to become members in the Center for Network Systems Biology will be drawn from a range of institutional units on the Charles River Campus and the BU School of Medicine. These include but are not limited to the Departments of Biochemistry, Biology, Chemistry, Medicine and Biomedical Engineering.
Center Strategic Plan

CNSB aims to be a world leader in interdisciplinary biomedical research. The Center’s open-concept, highly collaborative environment supports ambitious, clinically relevant projects with many avenues for translation. Our research program benefits enormously from the Center’s unique blend of molecular and computational biologists, as well as a diverse landscape of affiliated scientists, who provide complementary skills and perspectives. Our work is supported by a capable administrative staff, who provide professional services (grant management, secretarial support, and procurement) in an efficient manner.

Mapping Macromolecular Networks Essential to Human Health and Development:

Human health and development depend on dynamic networks of physical and functional interactions between the protein products of genes. However, the identity and composition of the molecular ‘machines’ that support cellular processes critical to human development and health are still largely unknown. Despite immense progress in genomics, it remains unclear which proteins associate together to support the formation and function of different cell types and tissues or how these networks go awry in clinical disorders like cancer, neurodegeneration and cardiovascular disease. Because improper connectivity leading to aberrant protein function is now recognized as a root cause of pathology, we expect that our interaction maps will drive the development of more effective diagnostics and treatments.

As pioneers in network biology, researchers at the CNSB have already reported thousands of protein interactions for model systems, like yeast, fly and worm. This includes the largest maps to date of protein macromolecules conserved across animals (Nature 2015) and microbes (Nature Biotechnology 2017). Now, we aim to break new ground by documenting the unique diversity of the protein interaction networks of different human cells and tissues – which has never been done before. Our multipronged collaborative initiatives will define key determinants that are perturbed in important pathologies like cancer, neurodegeneration and metabolic disorders. Because aberrant protein function underlies disease, understanding and manipulating protein interaction networks is a key requirement for precision medicine. With our expert basic and clinical collaborators, and emerging industry partners, scientists affiliated with the CNSB aim to translate the mechanistic knowledge we obtain from our network discoveries into transformative new diagnostic tools and therapeutic leads. To achieve this goal, we will employ multidisciplinary strategies based on complementary experimental methods, including high resolution biochemistry, quantitative mass spectrometry, and genetic engineering.

For example, the CNSB is developing technology to probe: (i) Subcellular compartments in normal and diseased cells and tissues to define the biological systems that determine cell function, differentiation and clinical outcomes; (ii) Cancer-associated signaling protein modules that are important clinical drug targets; (iii) Pathogens that cause clinically important human infections. Our research program aims to address fundamental biomedical problems: What are the features and principles of human protein networks, and how are they perturbed in disease? Why do some patients with the same disease have a complicated course and others a milder phenotype? How can we exploit this knowledge to improve human health?

Leadership, Collaboration, and Mentoring:

Biomedical research is at a crossroads. Breakthrough advances in technology promise to revolutionize medicine, biology and pharmacology, but daunting obstacles cloud the horizon, including an increasingly competitive funding environment and a slowing in drug development pipelines. Accordingly, there is a burgeoning demand for greater translational impact from research investments. Despite the groundswell of ‘omic’ and ‘big data’ science, the imperative remains on the need to analyze biological specimens comprehensively, with rigor and quantitative accuracy. In this context, the CNSB is poised for rapid growth and impact. Our priority this coming year is to establish analytical excellence, and productive new partnerships that aim to break new ground while addressing important research questions.

In the longer term, our objective is to build a transformative enterprise synonymous with research breakthroughs, high impact and community engagement in the years to come. To this end, we will continue to devote considerable effort towards the recruitment and training of junior researchers, from undergraduates to graduate students and post-doctoral fellows, from across the US and the rest of the world. Our goals in this respect are to:
1. Create a multidisciplinary environment that exposes trainees to new research concepts and methods;
2. Extend our leadership in interaction network biology by generating ‘connectivity’ diagrams that are broadly useful to biomedical research groups at BU as well as scientists at other institutions worldwide;
3. Invest energy to ensure the highest possible scholastic achievements that support the long-term development of junior talent in the field of Network Systems Biology.

New Research Projects & Technology Development for 2018-2019

Over the coming year, CNSB aims to be recognized as a world leader in network biology. Scientists at the Center have already pioneered systematic protein ‘interactome’ mapping as a powerful research paradigm. Existing team members were the first to report near comprehensive protein interaction maps for yeast (Nature 2006, 2012), E. coli (Nature Genet 2008), and diverse metazoans such as mouse, fly and worm (Nature 2015). Strikingly, many of the protein complexes we are discovering have proven to be informative about specific human diseases. For example, mutations in the replicative cohesin complex linked to Cornelia de Lange syndrome (CdLS), a rare but severe developmental disorder; implicated a novel interactor we found as a new CdLS locus (not confirmed by others). We have also identified histone modifying, transcriptional, and membrane-associated protein complexes that control cell identity. Yet many more protein interactions relevant to normal biological and disease processes remain to be discovered. Our central premise is that the human protein ‘interactome’ is highly specialized at the cell type and tissue level, and impacted by the alternate programs of expression, alternative splicing and post-translational regulation than is generally appreciated. Exploring network states, dynamics and heterogeneity is critical to the development of basic biological understanding, and the creation of more effective theranostics for precision medicine.

First, our interactome maps for human tissues: The overarching goal of our research program is to map the links connecting human protein complexes, biological systems and disease processes. Building on our groundbreaking work with simpler models, we aim for a great leap forward by investigating human protein interaction networks in different pathological contexts. To achieve this, we will leverage our unique protein
interaction mapping technologies, our world-class infrastructure, and our vast network of expert collaborators to generate human ‘maps’ of unprecedented scope, quality and resolution that we can subsequently develop into valuable community resources, useful clinical tools, and high-impact publications.

Since protein interactions are dynamic, another emerging focus is to devise workflows that can capture transient assemblies, while also defining the structural basis of binary protein interaction interfaces. We are also developing orthogonal separation techniques to enrich specific organelles, like the synaptosomes, to probe macromolecules unique to particular subcellular compartments.

Our focus this coming year is to map the protein networks active in subcellular compartments.

TRANSLATION TO THE CLINIC: Advances in our protein mapping capabilities offer great potential for breakthrough biomedical discoveries. By measuring protein networks in healthy and pathologic cells and tissues from validated animal models, patient explants and phenotyped cell cultures, researchers at the CNSB will be able to identify macromolecular assemblies critical for function that are perturbed during disease onset and progression. Of special interest are enzymes and receptors that are potential pharmaceutical targets. Biochemical, cell biology and genetic studies have identified interactors for just a subset of “druggable” proteins, but the native ligands, binding partners and functions of most are still unknown. This gap limits the amount of clinically actionable information that is available to develop more effective new treatments for chronic diseases.

For example, patients with hypertension, diabetes or neurodegenerative disorders often present with irreversible end-stage cardiac disease. Previous studies of cardiomyopathic hearts by researchers working with the CNSB have identified markers of early-stage heart failure, a major healthcare epidemic. One candidate, IGFBP7, is an excellent prognostic as well. In patients with asymptomatic hypertrophy, elevated blood IGFBP7 predicts cardiac dysfunction much earlier and with higher sensitivity and specificity than existing clinical assays. Remarkably, IGFBP7 predicts hypertensive patient outcomes (randomized to placebo), establishing broad clinical utility. Yet while trials of our other markers, now licensed to Roche Diagnostics, are ongoing, we still do not know how these proteins work together or how they interact with other cardiac proteins in normal or failing hearts, which is essential to understand biological function and causal disease relationships.

Drug development - Many therapeutics are already under development in the Boston area, but most will fail. Knowing how drug leads interact with proteins in cells or tissues is essential to evaluate their mode-of-action and potential toxicity, but surprisingly this information is often lacking. Likewise, while the adsorption of serum proteins is known to affect nanoparticle transport, half-life and tissue uptake, it is currently impossible to reliably predict these associations, and few formulations have been approved for patient care. We propose to address these gaps systematically by probing the interactions of therapeutic leads from our many partners with the goal of improving their pre-clinical efficacy. Researchers at the CNSB have devised powerful mass spectrometry assays to measure the selective binding of bioactive molecules (synthetic compounds or natural products) to individual proteins and protein complexes in cells and tissues. By examining ligand-protein interactions in an unbiased manner, without requiring compound immobilization or labeling, we aim to deconvolute the mode-of-action and ‘off targets’ of chemical probes, drug leads, and even endogenous metabolites. By comparing the binding profiles of bioactive compounds versus inactive analogues, the CNSB platform allows determination of the fundamental structure-function relationships that elicit a biological response. Ramping up our platform this coming year, we plan to characterize the mode-of-action and structure-activity relationships of bioactive compounds of special interest to BU scientists, including novel compounds to treat cancer and other important clinical applications.

Related to this initiative, the CNSB also aims to produce maps of protein-small molecule interaction networks in normal and disease states, the first for primary cell samples, enabling deeper modeling, functional analyses and knowledge translation of human metabolism. Subsequent translation into predictive diagnostics, and potentially new therapeutics or preventative treatments, will benefit greatly from our top-notch biology collaborators, and our proximity to the local pharmaceutical industry. This work is highly innovative. Our technology is the only one currently capable of direct, near-comprehensive mapping of native protein-metabolite assemblies in cells. By documenting differences in the molecular association networks of healthy and diseased specimens, our program will reveal how proteins and bioactive compounds interact normally and how their reversion impacts clinical outcomes. Some of the protein complexes we discover could serve as clinically useful markers and therapeutic targets.
The CNSB is primarily focused on the development, application and dissemination of innovative tools, methods and datasets that create lasting resources for BU, our collaborators, and the broader biomedical research communities. To support widest possible engagement, we are implementing ongoing outreach and skills training programs. By drawing together an outstanding team of experts in network biology, systems biology, molecular biology, chemical biology, metabolomics, proteomics, functional genomics and computational biology/modelling, the CNSB aims to deliver an unprecedented platform for exploring molecular networks and their links to human health and disease.

Center Activities - Outreach, Educational Programs, and Events

The CNSB’s research program is dynamic – we continually engage new experts to address new program needs and opportunities. For example, to pinpoint the maladaptive impact of changes in protein interaction networks we observe in response to physiological stress, we will work closely with biologists on both campuses, to access state-of-the-art functional assays, cell and animal models, and clinical specimens to establish pathophysiological relevance. A key deliverable is generating high-confidence interaction data. We employ several strategies to monitor quality. These include clearly defined metrics to ensure we meet our scientific objectives. We also use an electronic dashboard throughout the lifecycle of each project. Our translation efforts will benefit from ties to healthcare partners to maximize opportunities for long-term impact.

The CNSB sponsors and supports diverse activities aimed at addressing its primary research mandate, and bringing broader national and international attention to BU’s leadership efforts in the Network System Biology domain, which include: (i) documenting macromolecular interactions critical to human health; (ii) exploring how perturbations to molecular interaction networks are associated with developmental, mutant or environmental phenotypes and human pathologies; (iii) define the fundamental biophysical organization of macromolecular networks and their relationships to biological processes, pathways, organelles, cells, tissues, organs and intact organisms.

By working closely with renowned biologists and clinical scientists at BU, and industry partners, the CNSB aims to generate human protein ‘connectivity’ diagrams of unprecedented quality, scope and utility. By charting new directions at the forefront of translational proteomics, we aim to push the boundaries in network biology. By translating our findings into high-impact papers, community resources and clinical tools, we aim to maximize return on investment. By fostering skilled trainees, we aim to enable productive careers and wider knowledge dissemination in academia, industry and medicine.

Invited Speakers / Visitors

Patrick Paddison
Fred Hutchinson cancer Research Center
March 26, 2018 (BUIMC)
Title: “Functional genomic studies in patient-derived tumor stem like cells: putting precision oncology to the test”

Haiyuan Yu
Cornell University
April 12, 1018 (CRC)
Title: “Precision medicine through proteome-scale 3D interactome models and network perturbation studies”

Dr. John LaCava
Rockefeller University
May 14, 2018
Title: “Exploring the interactome of a human genetic parasite: affinity proteomics versus LINE-1 retrotransposons”

Dr. Oscar Yanes
Spanish Biomedical Research Centre in Diabetes and Associated metabolic Disorders
Title: “From spectrometric data to metabolic networks: An integrated quantitative view of cell metabolism”

Dr. Peter Uetz
Dept. Biology, Virginia Commonwealth University
Dr. Alberto Paccanaro
Department of Computer Science, University of London

Dr. Gary Bader
Donnelly center for Cellular and Biomolecular Research, University of Toronto

Dr. David Wishart
Depts. Biological Sciences and Computing Science, University of Alberta

Dr. Michael MacCoss
Dept. of Genome Sciences, University of Washington

Other Relevant Guests, Past and Pending:

Cheryl Haynes
GlaxoSmithKline

Megan Evans
Rothamsted Research

John LaCava
Rockefeller University

OTHER RELEVANT GUESTS, PAST AND PENDING:

HIGHLIGHTS OF FY17 CNSB EVENTS – 2017-2018 (AUG)

Social Media

Web: http://cnsb.bu.edu/
Twitter: @BUCNSB
Facebook: www.facebook.com/BUCNSB
We propose to initiate the National Center for Biomolecular Interaction Mass Spectrometry (CBIM) to respond to critical unmet needs in biomedicine to characterize protein-protein and protein-small molecule interactions that are central to human disease mechanisms. Existing methods demonstrate the feasibility of protein interaction analysis but lack the speed, flexibility and sensitivity necessary for unbiased reconstruction of physical interaction networks for proteins in disease processes. Further, most proteins are post-translationally modified, polymorphic and alternatively spliced, multiplying the number of functional forms of each protein in a network. While existing proteomics methods can identify protein variants and PTMs, they lack the quantitative power required to follow changes in modified protein isoforms, and their association partners, in dynamic network contexts. Our approach will be to develop the analytical and bioinformatics technologies required to define the state(s) of biological networks and then measure mechanistic changes that occur during chemical, genetic or environmental perturbation. These technology development efforts respond to the needs of a set of driving biomedical projects that comprise cancers, metabolic, genetic, neuropathological, and viral diseases. We assert that the mechanisms that determine pathological susceptibility and progression in each of these important classes of disease consist of alterations in protein interaction network dynamics that cannot be comprehensively quantified using existing technologies. We therefore propose technical research and development projects to enable quantification of protein interactions and network dynamics that include the responses of cells and tissues to bioactive small molecules, such as drugs and metabolites, and alternatively spliced, mutated and post-translationally modified protein forms that drive changes in physiology and pathophysiology. We will develop: improved sample preparation, separation and detection methods that allow for more efficient, sensitive and reproducible quantification of both global and local protein interaction networks; innovative technologies to measure the interactions of small molecule ligands with specific components in protein networks; data acquisition methods tailored to precise characterization of the dynamics of alternatively spliced/mutated/PTM-modified protein networks and bioinformatics tools for integrating, analyzing and communicating these results.

We will: demonstrate the power of our new technologies on a set of driving biomedical and collaborative projects; disseminate our tools and data widely; train a new generation of scientists in the appropriate uses of our technologies and computational tools; host hands-on national workshops and in silico scientific training events. We expect this new initiative will showcase the power of a rigorous scientific approach to protein network biology in a manner that builds on and complements recent advances in genomics, such as single cell RNA-seq studies, stem cell biology, and CRISPR/CAS-based genetic screens.
Andrew Emili, PhD
Director
Professor, Departments of Biochemistry & Biology

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