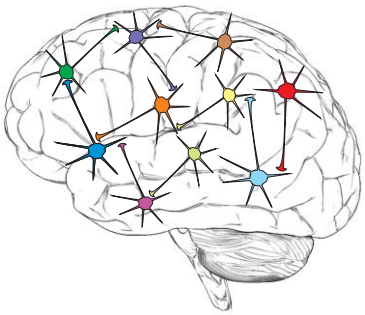
NeuroNET Research Center

5-year Strategic Plan

July, 2015



1. Introduction:

The NeuroNET Research Center (hereafter referred to as "the Center") was formed in July, 2014. At the University of Tennessee Knoxville, criteria for a unit to be termed a research center include factors pertaining to how it enhances the research potential of the university, and what additional benefits it will bring to the University and surrounding community. The name NeuroNET (Neuroscience Network of East Tennessee) was chosen to represent the rapidly growing Neuroscience research and teaching presence across the University of Tennessee, Knoxville (UTK), the UT Medical Center of Knoxville (UTMCK) and the Oak Ridge National Laboratory (ORNL). At the time of this writing, the Center comprises more than 100 members. The members participate in collaborative research spanning 5 broad areas of Neuroscience.

The Center includes a unique set of resources, research capabilities, and clinical expertise that are strengthened through interactions with other interdisciplinary organizations at UTK and UTMCK, such as the National Institute for Mathematical and Biological synthesis (NIMBioS), the Institute for Biomedical Engineering (iBME), and the Brain and Spine Institute. These interactions have already led to external funding to NeuroNET from the Kavli Foundation, and our collaborative efforts have helped launch the Pat Summitt Alzheimer's Clinic at the UT Medical Center.

Funding from the UT Office of Research and Engagement (ORE) has allowed NeuroNET to bring in external speakers, hold annual research retreats, and provide seed funding for new interdisciplinary neuroscience research projects. These initiatives have broadened NeuroNET membership, enhanced networking across multiple departments, colleges, and institutions, fostered at least 13 new collaborative research projects, and led to at least 5 new research proposals for external funding.

The NeuroNET Research Center also serves as the organizing center for coordinating and maximizing the success of 1) a new undergraduate interdisciplinary major in Neuroscience, 2) a local Society for Neuroscience Chapter, and 3) a student-led organization, Advancement of Neuroscience at UT. Together with these groups, NeuroNET is working to enhance Neuroscience research, education, and outreach within our individual institutions and the surrounding community.

This 5-year strategic plan has been created with several key purposes in mind.

- First, and foremost it will serve as a roadmap for our activities moving forward, clarifying for faculty and our departmental, college, and university stakeholders where we want to be 5 years from now.
- Second, it will help neuroscience faculty prioritize our efforts. Given all that we want to accomplish with finite financial and personnel resources, we need clear priorities for managing those resources.
- Third, the strategic plan sets strict accountability of the NeuroNET leadership to its members and to the University for accomplishing our goals. By delineating specific actions and metrics related to each goal, our success will be easily assessed.

2. Mission Statement:

The Mission of the NeuroNET Research Center is to:

- Provide a well-defined intellectual and physical environment that facilitates neuroscience-related research and educational activities.
- Stimulate and cultivate collaborative efforts among participating neuroscience researchers and clinicians that will generate extramural grant applications and substantial funding.
- Enhance training opportunities for undergraduate and graduate students as well as postdoctoral research associates.

3. Vision Statement:

The NeuroNET Research Center seeks to unite and expand Neuroscience research and education in and around the University of Tennessee Knoxville, the UT Knoxville Medical Center, and the Oak Ridge National Laboratory. The Center functions as a catalyst for innovative Neuroscience research that will attract world-class scientists, clinicians, and students.

4. NeuroNET Goals (details in subsequent section):

- Increase research publications through enhancing communication and research collaborations
- Facilitate competition for extramural funding
- Increase Neuroscience education

5. NeuroNET Organization:

NeuroNET members represent a broad range of research interests. A full list of NeuroNET members and their affiliations is provided in **Appendix A**. The research areas/expertise of NeuroNET members can be viewed as clusters with the following overlapping areas:

- Cellular and Molecular Neuroscience
- Cognitive and Behavioral Neuroscience
- Systems Neuroscience
- Neural Engineering and Computational Neuroscience
- Clinical Neuroscience/Nervous System Disorders

Due to the interdisciplinary nature of neuroscience, most members are affiliated with more than one of these research areas. Within this broad panorama of basic and clinical science there are several foci where NeuroNET members coalesce in their research interests. These areas of convergence represent potential topics for initial extramural funding proposals.

6. Areas of Potential Synergy:

- Aging/Dementia/Neuropathology/Traumatic Brain Injury
- Stress/Addiction/PTSD
- Sleep and Circadian Homeostatic Processes
- Auditory/Speech Processing
- Neural Sensing, Imaging, Integration, and Interfacing
- Neural/Cognitive Development

7. Assets:

The NeuroNET Research Center, which was officially created less than one year ago, has foundational strengths that are actively promoting its progress:

a) Knowledge/Expertise: NeuroNET encompasses a range of scientific knowledge that spans the entire range of neuroscience, from 'bench to bedside'. This wealth of expertise is generating new lines of research and clinical projects. Specific examples include research to enhance data acquisition from EEG recordings; identifying biomarkers of stress resiliency in specific brain areas; investigating biomarkers associated with traumatic brain injury; assessing miRNA-linked susceptibility to Herpes Simplex Encephalitis; developing technology to assist in stroke rehabilitation; and investigating how play behavior alters stress vulnerability and neuronal plasticity.

b) Equipment: NeuroNET members have access to a range of scientific and clinical instrumentation and support staff distributed across its 3 main organizations (see **Appendix B** for list).
c) Students: NeuroNET researchers have an abundance of students eager to participate in research projects. There are a large number of undergraduates (>100) already in the interdisciplinary Neuroscience major, and there is a small but growing number of graduate students distributed across the different departments.
d) Administration: NeuroNET has received consistent support from UTK and UTMCK. Leadership is currently in transition right now at ORNL, but we hope to continue a strong working relationship with ORNL administration. This support, including funding, administrative expertise, and organizational guidance, has provided the critical infrastructure that has helped initiate formation of NeuroNET.
e) Positive attitude: NeuroNET members, students, and the associated administrative units all possess a positive mindset that is critical for sustaining collegiality and increasing collaborations. In support of this, NeuroNET hosts regular networking events, an annual retreat, and a Spring symposium that all encourage continued collegiality and research productivity.

8. Challenges:

Although the NeuroNET Research Center has substantial assets available, there are also challenges to reaching our vision of a Nationally Recognized Neuroscience Center. Many of these challenges reflect changing national priorities, as noted in data from the Federation of American Societies for Experimental Biology (FASEB) documenting challenges facing U.S. biomedical research: http://www.faseb.org/pdfviewer.aspx?loadthis=http%3A%2F%2Fwww.faseb.org%2FPortals%2F2%2FPDFs%2Fopa%2F2014%2F11.6.14%2520NIH%2520Funding%2520Cuts%25202-pager.pdf.

However, there are also challenges specific to NeuroNET:

a) Resources: In addition to the scientific equipment we currently have, additional instrumentation will substantially enhance our research capacity. As an example, imaging systems such as functional magnetic resonance imaging (fMRI), Positron Emission Tomography Imaging for Small Animals (microPET), and Diffusion Tensor Imaging (DTI) would be extremely beneficial. We are coordinating efforts with UT, UTMCK and ORNL to expand imaging instrumentation and analysis capabilities.
b) Communication: Improved communication between NeuroNET members as well as to a broader audience is critical to reaching our goals. NeuroNET is in the process of developing a website, investigating better options for secure file-

sharing, and expanding the frequency and diversity of networking events in and around campus.

c) Collaboration Barriers: There are procedural and logistical barriers, as well as fundamental differences in priorities and missions, between UTK, UTMCK, and ORNL that hinder research collaborations and networking. Examples of needed improvements include facilitated procedures allowing students to participate in research projects; researchers having access to scientific resources and equipment; cross-institutional time-sharing arrangements to facilitate collaborative research; and clarifying/simplifying regulatory procedures to allow grant proposal submissions that span multiple research units. Continued discussions at both administrative and researcher levels are needed to reconcile the distinct goals of each institution in order to expand collaborative cross-institutional research. NeuroNET is actively working with the UT ORE, UTMCK and ORNL administrations to identify and eliminate specific problems impeding research collaborations.
d) Infrastructure: The ability of the NeuroNET Research Center to attract new researchers, a critical component of our success moving forward, faces severe limitations with respect to salary lines and laboratory/equipment space.
e) Education: The undergraduate Neuroscience major is growing at a rapid rate. Moving forward, the Center needs a Graduate Neuroscience Program that will attract a large number of high-quality doctoral students.
f) Center Directorship: Given the expanding time needed to oversee the growth in NeuroNET members and the diversity of Center activities, leadership of the NeuroNET Research Center should be incentivized financially and with a decreased teaching load.

9. Management plan:

To achieve our goals, as assessed through the identified metrics (**Appendix C**) within the desired timeframe (**Appendix D**), NeuroNET needs to implement a broad "plan of action", including the following:

a) The Executive Committee will hold regular monthly meetings (with additional meetings called when needed) to monitor NeuroNET activities related to the three goals, as well as new opportunities and developments as they arise.
b) The Executive Committee, in coordination with the University, will generate a specific plan for supporting the position of NeuroNET Center Director via salary and/or teaching time compensation. In addition, there needs to be funding for a part-time business manager/executive assistant position to help with the day-to-day Center operations and grants/budget management.

c) The Executive Committee will identify specific individuals to act as “coordinators” for individual actions outlined under the 3 goals (see **Appendix D**). These coordinators will be responsible for organizing the specific activity and/or overseeing a committee assigned to carry out the action. Coordinators will also be responsible for assessing progress on the action every 6 months, and submitting a written report to the Executive Committee outlining the progress made, whether it matches the timeline, and what corrective steps/adjustments have been made in implementing the action.
d) The Executive Committee will evaluate the 6-month assessment reports and suggest additional changes as needed.
e) Once a year the Executive Committee will generate a progress report based on the semi-annual assessments that re-evaluates the goals of the strategic plan in light of the progress made, and suggest changes to maximize our forward progression. The progress report will be submitted to the NeuroNET members, the associated college Deans, and the Vice-Chancellor for Research and Engagement.
f) At the end of 5 years, the Executive Committee will conduct an in-depth evaluation of the 5-year strategic plan and generate a new strategic plan. The evaluation will include input from NeuroNET members, associated college Deans, administration officials from each institution, and industry partners. The finalized plan will be submitted to the Dean and the Vice-Chancellor for Research and Engagement. Portions of the strategic plan will be made public through the NeuroNET website.

Goal 1: Increase research publications through enhancing communication and research collaborations

(metrics **in Appendix C**; timeline in **Appendix D**)

Actions:

1. Create a website that includes a list of members with contact information, areas of ongoing research, equipment, funding opportunities, and upcoming events. Other information can be added as needed/desired.
   a) Gather information (members/affiliations, research interests, equipment, list of events, updates on funding opportunities. Design and implement website.
   b) Assess and update website as needed.
   c) Identify and provide support for individual to maintain the website.

2. Initiate imaging systems user group meetings.
   a) Create group, start meeting; recruit additional members periodically.
   b) Work towards major research instrumentation grant proposal if sufficient interest.

3. Have frequent formal and informal networking events.
   a) Publicize faculty pub meetings.
   b) Have at least 1 NeuroNET sponsored gathering each semester.

4. Support web-based networking mechanism for members to share data/ideas to foster more collaborative research.
   a) Determine if alternatives to Sharepoint exist.
   b) Improve or replace Sharepoint website so it is more useable/accessible.

5. Sponsor yearly 2-day Neuroscience symposium that includes community outreach.
   a) Organize, get external speakers; Coordinate with venues such as Baker Center. Bring in groups such as the Neuroscience student organization, undergraduate majors, and the Society for Neuroscience chapter to help.

6. Have regular Neuroscience seminars, co-sponsored with departments when possible.
   a) Continue to solicit names of external speakers from members.
   b) Continue to coordinate with relevant departments to bring in more speakers.

7. Finalize and implement by-laws.
   a) Finalize edits; hold membership vote.

8. Continue funding seed grants to support new, high-quality collaborative research efforts with identified extramural funding opportunities, and that have clear accountability requirements.
   a) Re-apply for ORE funding for 3rd year of support.
   b) Improve seed grant application/evaluation procedures so funds are awarded earlier in each fiscal year.
   c) Generate additional funds to support seed funding for future years.

9. Provide support for faculty writing/submitting grants and publications.
   a) Create list of reviewers to read/evaluate manuscripts prior to submission.

Goal 2: Facilitate competition for extramural funding

(metrics **in Appendix C**; timeline in **Appendix D**)

Actions:

1. Form External Advisory Council
   a) Solicit names of potential members.
   b) Send invitations/form council.
   c) Hold yearly meetings with advisory council.

2. Apply for Center-led equipment grant(s) (e.g., NSF 15-04; NIH PAR 14-073)
   a) Determine what equipment is needed to support existing/new research initiatives.
   b) Coordinate with the Office of Research and Engagement (ORE), Colleges, University, UTMCK, ORNL, and industry partners.
   c) Prepare and submit proposals.

3. Apply for Center-led University/Industry collaboration grant(s) (e.g., NSF 13-594)
   a) Hold discussions with NeuroNET members, industry partners, institutional representatives to assess critical needs, benefits for all parties.
   b) Prepare and submit proposals.

4. Identify and pursue extramural funding opportunities for research groups as well as for the Center.
   a) Identify and communicate funding opportunities for individual research groups from Federal Institutions and private foundations.
   b) Pursue funding for center-based funding from federal institutions.
   c) Pursue support from private individuals/foundations.

5. Submit Center-led Research Network grant (e.g., NSF Research Coordination Networks program; NSF 13-250).
   a) Investigate potential funding opportunities and pull together critical people to write proposal.

6. Obtain Approval for joint faculty positions.
   a) Get University permission for joint appointments.
   b) Approve joint appointments as needed.

7. Provide support for faculty writing/submitting grants.
   a) Coordinate with ORE to sponsor at least 1 grant writing workshop per semester.
   b) Create list of reviewers to read/evaluate manuscripts prior to submission.

8. Foster cooperative arrangements with Industry partners, such as Siemens, Eli Lily, and Neuroscience Associates.
    a) Meet with industry representatives to discuss mutually beneficial arrangements that foster research, training, education, and improved instrumentation for all groups.
    b) Generate agreements.

Goal 3: Increase Neuroscience education

(metrics **in Appendix C**; timeline in **Appendix D**)

Actions:

1. Continue improving undergraduate major.
   a) Adjust curriculum and course availability based on student feedback and course enrollment numbers.
   b) Identify more research opportunities.
   c) Add research track/scholarships.
   d) Start portfolio requirement.
   e) Partner with industry, etc. to create internships.
   f) Improve communication about summer internships, graduate programs, workshops, etc.
   g) Coordinate with departments to increase the number of Neuroscience faculty.

2. Start regular brown-bag meetings primarily involving presentations by students and postdoctoral/research fellows. Can also have specific research/technique themes.
   a) Initiate on trial basis.
   b) Continue based on level of interest.

3. Create graduate major in Neuroscience.
   a) Create plan of action re: faculty, courses, administrative steps, etc.
   b) Coordinate across departments/colleges; get administrative approval.

4. Expand Neuroscience Outreach
   a) Increase number of public-oriented seminars/workshops/panels, in coordination with the Society for Neuroscience chapter and student organization. Coordinate activities with external groups such as Alzheimer's Tennessee, Pat Summitt Foundation, Cole Neuroscience Center, and other local groups.

Appendix A: NeuroNET Members

I. Institutional Units represented by NeuroNET Members:

Within UT Knoxville, members are distributed across the following colleges and departments:

1. College of Arts and Sciences
    - Dept. of Biochemistry and Cellular and Molecular Biology
    - Dept. of Chemistry
    - Dept. of Mathematics
    - Dept. Modern Foreign Languages and Literatures
    - Dept. of Psychology
2. College of Communication and Information
    - School of Advertising and Public Relations
3. College of Education, Health and Human Sciences
    - Dept. of Child and Family Studies
    - Dept. of Kinesiology, Recreation, and Sports Studies
4. College of Engineering
    - Dept. of Electrical Engineering and Computer Science
    - Dept. of Chemical and Biomolecular Engineering
    - Dept. of Materials Science and Engineering
    - Dept. of Mechanical, Aerospace, and Biomedical Engineering
5. College of Nursing
6. College of Social Work

Within the UT Institute of Agriculture, members are distributed across the following colleges and departments:

- Dept. of Animal Science
- College of Veterinary Medicine

Within the UT Medical Center of Knoxville, members are distributed across the following departments and units:

- Brain and Spine Institute
- Cole Neuroscience Center
- UT Graduate School of Medicine
- Dept. of Anesthesiology
- Dept. of Family Practice
- Dept. of Radiology
- Dept. of Medicine
- Dept. of Neurology

- Dept. of Neurosurgery
- Dept. of Surgery

Within the UT Health Sciences Center, members are in the:

- Dept. of Audiology and Speech Pathology

Within ORNL, members are distributed across the following divisions:

- Biosciences
- Computational Sciences and Engineering
- Computer Science and Mathematics
- Electrical and Electronics Systems Research

Within the Knoxville community, we have members affiliated with:

- The Boy Scouts of America
- Neuroscience Associates, Inc.
- Siemens, Inc.

II. Members listed by Units:

UT Knoxville

1. College of Arts and Sciences

a) Dept. Biochemistry and Cellular and Molecular Biology

Hall, Jim jhall1@utk.edu
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Park, Jae H jhpark@utk.edu
Prosser, Rebecca A rprosser@utk.edu

b) Dept. Chemistry

Campagna, Shawn Robert campagna@utk.edu
Kabalka, George W kabalka@utk.edu

c) Dept. Mathematics

Schwartz, Fernando fernando@math.utk.edu

d) Dept. Modern Foreign Languages and Literatures

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e) Dept. Psychology

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Hay, Jessica Sari jhay@tennessee.edu

2. College of Communication and Information

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3. College of Education, Health and Human Sciences

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b) Dept. of Kinesiology, Recreation, and Sports Studies
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4. College of Engineering

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6. College of Social Work
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UT Institute of Agriculture

1. Dept. of Animal Science
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UT Medical Center of Knoxville

1. **Brain and Spine Institute**
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   Naugle, Nate nnaugle@mc.utmck.edu
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2. **Cole Neuroscience Center**
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8. **Dept. of Neurosurgery**
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9. **Dept. Neurology**
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10. **Dept. Surgery**
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UT Health Science Center

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Oak Ridge National Lab

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Knoxville Community

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2. **NeuroScience Associates, Inc**
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3. **Siemens, Inc**
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Appendix B: Shared Instrumentation/Facilities

UTK Facilities

1. Advanced Microscopy and Imaging Center

Contact: John Dunlap
101 Science and Engineering Research Facility
University of Tennessee
Knoxville, Tennessee 37996-0830
Phone: (865) 974-6197
Email: jrdunlap@utk.edu

Optical Microscopy

- Nikon Eclipse E600
- Leica SP2
- Nikon Ti

Transmission Electron Microscopy

- Zeiss Libra 200MC

Scanning Electron Microscopy and Focused Ion Beam

- LEO 1525
- Zeiss Auriga

Atomic Force Microscopy

- Asylum Research MFP 3D

Sample Preparation Equipment

- Dimpling grinder
- Fischione plasma cleaner
- Gatan Cryoplunge Cp3
- Gatan precision ion polisher
- Ladd critical point dryer
- Leica EMFC7 ultramicrotome
- Leica (Reichert) OMU3 ultramicrotome
- Multi-prep polishing system
- Slow speed diamond saw
- SPI sputter coater

2. Molecular Biology Resource Facility (in the College of Arts and Sciences)

Contact: Joseph A. May, Manager
Molecular Biology Resource Facility
A211 Walters Life Sciences Bldg.
University of Tennessee
Knoxville , TN 37996-0830
Phone: (865) 974-6231
Email: bioseq@utk.edu

Services Available:

- Sanger Sequencing and Gene Scan Fragment Analysis
- Next Gen Library Prep and Other Services
- Affymetrix GeneChip Processing
- Millipore Guava Easy Cyte 6HT-2L Flow Cytometer
- Diagenode Bioruptor Sonication System UDC 300
- Sage Science Pippin Prep
- DNA Quantification

Instrument	Application	Type of use
Analytical Services		
Atomic Spectroscopy	Detect Elements	Service
Laser Diffraction	Particle size measurement	Service
Bioinformatics		
Worksatation	SeqMan NGen & CLC	Assemble & analyze Sequences
Cellomics		
Accuri Flow Cytometer	Flow Cytometry	Analyze samples
Cellometer Vision	Measure cell conc & Viability	Brightfiels & Fluorescence
Genomics		
CEQ8000	AFLP & RFLp	Equipment usage
Experion	Quantify DNA, RNA & Proteins	Equipment usage
MyCycler	PCR	Equipment

		usage
Nanodrop	Quantify DNA, RNA & Proteins	Equipment usage
QIAxel	Capillary electophoresis	Equipment usage
Qubit	Quantify DNA, RNA & Proteins	Equipment usage
Transcriptomics		
ABI7900HT Fast	Real Time PCR	Equipment usage
Maui Hyb	Microarray Hyb station	Equipment usage
GenePix 4000	Microarray slide scanner	Equipment usage
Proteomics		
Luminex	Immunoassay system	Equipment usage
2D Gel Electrophoresis		
IEF	Isoelectric Focusing	Equipment usage
Protean Plus Dodeca	Gel Electrophoresis	Equipment usage
Typhoon gel imager	Visualize Fluorescent gels	Equipment usage
Ettan Spot picker	Pick protein from gels	Equipment usage
BioTek Plate Reader	Absorb,Fluor,Luminsc	Equipment usage
Metabolics		
HPLC	PDA, RI detector, Fraction collection	Equipment usage
Imaging		
Phosphoimager	32P,33P,35S,14C,3H and 125I	Equipment usage
Supporting Resources		
Biomek 2000	Liquid handling robot	Equipment

		usage
Dishwasher	Sterilization	Clean glassware
CO2 Tank	Dry Ice	Gas usage
Liq. Nitrogen Tank		Gas usage

Computers for Next Generation sequence analysis:

Dell Studio XPS 9000	Dell 7600
24 GB RAM	**250 GB RAM**
3 TB disk space	4 TB disk space
CLC Genomics	NGen/DNaStar

Software available:

- CLC BIO
- CLC BIO - Tutorials
- SeqMan NGen
- Lasergene software consists of an integrated suite of 7 modules.
  The modules are:
- SeqBuilder - visualization, sequence editing, Primer design and virtual cloning
- SeqMan Pro - sequence assembly, Next-Gen sequence analysis and SNP discovery
- MegAlign - sequence alignment
- PrimerSelect - oligo primer design
- Protean - protein structure analysis & prediction
- GeneQuest - gene finding
- EditSeq - utility for importing unusual file types

Next Generation sequencing platforms:

- Ion Torrent
- 454
- Solexa
- Illumina
- ABI SOLID
- Helicos
- Sanger method

Additional Software available:

- Sequencher
- Image Quant

- Milliplex Analyst
- Primer Express
- DeCyder
- LCsolution
- Quantity One

3. Biological and Small Molecule Mass Spectrometry Core (BSMMSC): Chemistry Dept.

Contact: Dr. Shawn Campagna, Core Director
Department of Chemistry
University of Tennessee
618 Buehler Hall
Knoxville, TN 37996
Phone: 865-974-7337
Email: campagna@utk.edu

The Biological and Small Molecule Mass Spectrometry Core (BSMMSC) is housed in the department of chemistry at the University of Tennessee, Knoxville. It's located at Buehler Hall 613

Instrumentation:

- TSQ Quantum Discovery Max Triple Quadrupole Mass Spectometer
- Exactive Quadrupole-Orbitrap Mass Spectrometer

Analyses and Rates:

Type	Manufacturer/Model	Proposed FY 2015 Billing Rate
HPLC—Triple Quadrupole MS*	Thermo/TSQ Quantum Discovery Max	Assisted: $18.00/hour Internal $26.75/hour External Academic Unassisted: $5.00/hour Internal $7.50/hour External Academic
HPLC—QTOF MS*	Applied Biosystems/ QStar Elite	Assisted: $18.00/hour Internal $26.75/hour External Academic Unassisted:

		$5.00/hour Internal $7.50/hour External Academic Without HPLC: $10.50/hour Internal $15.75/h External Academic
UPLC—Orbitrap MS*	Thermo Scientific/ Exactive Plus	Assisted: $18.00/hour Internal $26.75/hour External Academic Unassisted: $5.00/hour Internal $7.50/hour External Academic
UPLC—Orbitrap MS*	Thermo Scientific/ Exactive Plus	Assisted: $18.00/hour Internal $26.75/hour External Academic Unassisted: $5.00/hour Internal $7.50/hour External Academic
UPLC—Orbitrap MS*	Thermo Scientific/ Exactive Plus	Assisted: $18.00/hour Internal $26.75/hour External Academic Unassisted:

		$5.00/hour Internal $7.50/hour External Academic
MALDI-TOF	Applied Biosystems/ Voyager-DE PRO	$10.50/hour Internal $15.75/h External Academic
UPLC—Quadrupole-Orbitrap MS	Thermo Scientific/ Q-Exactive	Assisted: $18.00/hour Internal $26.75/hour External Academic Unassisted: $5.00/hour Internal $7.50/hour External Academic

4. Bioanalytical Resource Facility (housed within the BCMB Dept)

Contact: Dr. Ed Wright, Facility Manager
Email: edwright@utk.edu

Instrumentation:

- **Analytical Ultracentrifuge (AUC)** A Beckman XL-I is utilized in the department to study proteins, peptides and nucleic acids. This technique is used to determine sedimentation coefficient, molar mass, purity and oligomeric state of a sample, as well as the stoichiometry and affinity of interactions.
- **Circular Dichroism (CD)** An Aviv 202 CD spectrophotometer is used by researchers in the department to determine whether a protein is folded, characterize the global secondary structure of a protein and monitor folding and unfolding as a function of temperature, pH or denaturant concentration.
- **Differential Scanning Calorimeter (DSC)** A VP-DSC is available to measure protein stability and energetics of unfolding and folding.
- **Electron Paramagnetic Resonance (EPR)** Bruker EMX (X-band) Spectrometer is used to identify paramagnetic metals in a sample, quantify metal binding to a protein, study conformational changes and protein dynamics and monitor changes in the redox state of a system.
- **Fluorescence Spectroscopy** A Perkin Elmer LS 55 to monitor protein folding, conformational changes, dynamics and binding interactions.
- **High Performance Liquid Chromatography (HPLC)** An Agilent 1200 system is used in the department for separation of proteins, peptides and small molecules. This instrument is often used to prepare samples for mass spectrometry.
- **Isothermal Titration Calorimeters (ITC)** Two VP-ITC instruments are used to measure affinity and thermodynamic parameters of interactions. Experiments evaluating protein-protein, protein-small molecule, protein-nucleic acid and protein-metal complexes are currently being performed in the department.
- **Mass Spectrometry** A Bruker MALDI-TOF Mass Spectrometer is used in the department for accurate mass measurements of proteins and peptides
- **Surface Plasmon Resonance Spectrometer (SPR)** A Biacore 3000 is used in the department to study biomolecular interactions. This technique not only measures binding affinity, but also quantifies the kinetics of the interaction. Binding events involving proteins, nucleic acids, carbohydrates and other small molecules are amenable to SPR analysis.
- **Rigaku R-axis IV diffractometer** used for structure determination by X-ray crystallography.
- **Art Robbins Instruments Phoenix liquid handling system** for automated screening of crystallization conditions.

5. NMR Facilities (Dept. of Chemistry)

Contact: Carlos A. Steren, Ph.D., Facilities Manager
321 Buehler Hall
Dept. of Chemistry
University of Tennessee
Knoxville, TN 37996-1600
Phone: (865) 974-3386
Email: steren@ion.chem.utk.edu

Instrumentation:

- Varian VNMRS 600 MHz
- Varian VNMRS 500 MHz
- Varian Inova 400 MHz
- Bruker Avance 400 MHz
- Varian Mercury 300 MHz
- Bruker AC 250 MHz

6. UT CCI-ORNL User-Experience Laboratory (College of Communication and Information)

Contact: Rachel Volentine, lab coordinator
Rm 230 Communication Bldg.
1345 Circle Park Drive
Knoxville, TN 39776
Email: rvolenti@utk.edu

The College of Communication and Information User-Experience Lab is the brainchild of a collaboration between the College and Oak Ridge National Laboratory (ORNL). The user-experience lab provides an environment conducive to studying how users interact with a system and conducive to gaining insight into the system's usability. For example, the lab can be used to conduct behavioral science-related studies measuring task performance and emotional reactions. The lab supports interdisciplinary research by UTK faculty members, graduate students, and ORNL researchers. Several Ph.D. students staff the user-experience lab while using the lab to support their own research agendas.

Physical Layout of the Lab:

The lab is partitioned into three areas: (1) two participant rooms, which house the MORAE Recorder, (2) an observation room, which houses the MORAE Observer/Manager, and (3) a waiting lounge.

Participant Rooms

Experiments are conducted using the Recorders in the two participant rooms. Both rooms have the same hardware configurations, including a Microsoft Windows-based personal computer with dual monitors, web camera with a built-in microphone, a laser printer, and speakers. The web camera is used to capture the participants' facial expressions. The built-in microphone is designed to record participants' verbalizations as part of the thinking aloud protocol found in many studies. Also note the computers in the participant rooms are connected to the campus network.

Observation Room

The observation room is located between the two participant rooms. The observation room is equipped with two-way mirrors attached to the participant rooms to facilitate observations during experiments. The observation room is also equipped with a shared laser printer; speakers; and two Microsoft Windows-based computers, each of which

can be connected to the participant rooms and to the Internet. In addition, the computers in the observation room have dual-monitor settings, speakers, and a shared laser printer.

7. Health Information Technology & Simulation Laboratory

Health Information Technology and Simulation Laboratory (HITS) is an organized research unit (ORU) at The University of Tennessee, Knoxville. It is built on collaborative research partnership between the College of Nursing and the College of Engineering and led by co-directors of Drs. Tami Wyatt and Xueping Li. The mission of the Health Information Technology and Simulation (HITS) ORU is to advance the science of health information technology and ways HITS enhance consumer health and professional health education.

HITS has more than 7,600 square feet of simulated healthcare space in which to provide a replica of the patient care environment where health care providers learn to apply cognitive, technical and psychomotor skills using an interdisciplinary approach.

The vision for the center is to instruct and facilitate learning that measures the learner's performance and competency in the health care environment and develops health care providers who continue to evaluate and apply principals learned in simulation to direct patient care.

For more information, see http://ilab.engr.utk.edu/hits/

Contact: Dr. Tami Wyatt
Email: twyatt@utk.edu

8. Equipment (Listed with IBME)

Contact: Institute of Biomedical Engineering (iBME)
311 Perkins Hall
1506 Middle Drive
Knoxville, TN 37996
Phone: (865) 974-7673
Fax: (865) 974-6394
info@ibme.utk.edu
http://ibme.utk.edu/about-us/equipment/

- Accuri C6 Flow Cytometer
- Aqueous GPC System
- Biograph 6
- Brice-Phoenix Differential Refractometer-Model BP-2000-V
- Femtojet Microinjector and Micromanipulator
- Inveon SPECT/PET/CT
- Jupiter Vapor Pressure Osmometer
- Knauer Membrane Osmometer
- Leica SP2 LSCM
- LEO 1525
- LV EM5 Low Voltage Electron Microscope (SEM & TEM)
- MFP-3D Atomic Force Microscope
- MicroCAT II + SPECT Hybrid Scanner
- Multimode Scanning Probe Microscope (SPM)
- Nikon Eclipse E600
- Nikon Ti
- PDExpert Multi-Angle Light Scattering
- Polymer Labs GPC120
- Polymer Labs GPC220
- PowerTome X Ultramicrotome
- TA Instruments Q-1000 DSC
- TA Instruments Q-50 TGA
- TA Instruments Q-800 DMA
- Tosoh EcoSEC GPC System
- Uprint 3D Printer
- ViscoSystems AVS 370 Dilute Solution Viscometer
- Waters GPC System
- Wyatt Technology Multi-Angle Light Scattering and Refractometer
- Zeiss Auriga
- Zeiss Libra 200 MC

9. Biology Service Facility

Contact: David E. Pratt.
Technical Director
125 Austin Peay Bldg.
University of Tennessee
Knoxville , TN 37996-0910
Phone: (865) 974-4219
Fax: (865) 974-0639
Email: depratt@utk.edu

Computer Services: The first point of contact within the Division of Biology for all computing issues.

Supported Operating Systems:

- MS Windows
- MAC OS
- Linux
- Unix

The service includes, but is not restricted to the following:

- System Administration & Server Support
- Specification of computer hardware.
- Installing software.
- Reloading Operating Systems.
- Removing spyware and viruses.
- Troubleshooting network problems.
- Instrumentation computing issues.

Electronic Services: Maintenance of Laboratory Instrumentation

The service includes, but is not restricted to, the following list of instruments.

1. UV/VIS, IR, Fluorescence, AA spectrophotometry
2. Radiation counting
3. Ultra-centrifugation
4. Low-speed preparative centrifugation
5. Clinical centrifugation
6. Particle counting
7. Chromatography
8. General laboratory measurement instrumentation, e.g., pH, physiograph, recorder, etc.

9. Environmental maintenance instrumentation, e.g., growth chambers, incubators, waterbaths, shakers, etc.
10. Refrigeration, low temperature incubators, freezers and ultralow freezers.
11. General mechanical laboratory equipment, e.g., vortex, stir, hot plate, etc.
12. Autoclaves
13. Microscopes (technicians factory trained)
14. Balances (technicians factory trained)
15. Audio/visual (excluding office equipment)

Machine Services: Maintenance and Development of Laboratory Instrumentation

This service includes the following types of hardware:

1. Vacuum Pumps
2. Compressors
3. Autoclaves (mechanical systems)
4. Environmental maintenance instrumentation, e.g., growth chambers, incubators, waterbaths, shakers, etc. (mechanical systems)

Hardware Design and Development

BSF uses the following materials:

1. Most ferrous metals
2. 204 or lighter grade stainless steel
3. Most non-ferrous metals
4. Most rigid plastics materials

Wood working Services

General carpentry and cabinet services include the following:

1. General repair
2. Minor laboratory renovation
3. Laboratory furniture construction

ORNL Facilities

A. User Facilities:

- **CFTF** Carbon Fiber Technology Facility

Oak Ridge National Laboratory is home to the Department of Energy's (DOE) Carbon Fiber Technology Facility (CFTF)—a 42,000 sq. ft. innovative technology facility. The CFTF offers a highly flexible, highly instrumented carbon fiber line for demonstrating advanced technology scalability and producing market-development volumes of prototypical carbon fibers, and serves as the last step before commercial production scale.

The facility, with its 390-ft. long processing line, is capable of custom unit operation configuration and has a capacity of up to 25 tons per year, allowing industry to validate conversion of their carbon fiber precursors at semi-production scale.

- **CNMS** Center for Nanophase Materials Sciences

The Center for Nanophase Materials Sciences (CNMS) at Oak Ridge National Laboratory (ORNL) integrates nanoscale science with neutron science; synthesis science; and theory, modeling, and simulation. Operating as a national user facility, the CNMS supports a multidisciplinary environment for research to understand nanoscale materials and phenomena.

- **CSMB** Center for Structural Molecular Biology

The Center for Structural Molecular Biology at ORNL is dedicated to developing instrumentation and methods for determining the 3-dimensional structures of proteins, nucleic acids (DNA/RNA) and their higher order complexes. The tools of the CSMB will help understand how these macromolecular systems are formed and how they interact with other systems in living cells. The focus of the CSMB is to bridge the information gap between cellular function and the molecular mechanisms that drive it. The suite of tools being developed by the CSMB includes:

- Bio-SANS, a Small-Angle Neutron Scattering (SANS) facility for biological samples, has been completed at the ORNL High-Flux Isotope Reactor (HFIR). The CSMB is also closely aligned with researchers at the Spallation Neutron Source (SNS).
- Isotope Labeling Laboratories for cloning, gene expression, purification and characterization of labeled biological macromolecules are planned; our Bio-Deuteration Lab is currently operational and accepting proposals.

- Computational Techniques have been developed for the study of macromolecular complexes by SANS. Combined with selective Deuterium-labeling, it is now possible to develop detailed structural models that will enable the understanding of function.

Another computation technique developed for the study of calculates solution small-angle X-ray and neutron scattering intensity profiles by ORNL-SAS. This makes it possible to develop from a wide variety of structures, including atomicresolution models of proteins and protein complexes, low-resolution models defined in any manner, or combinations of both.

Neutron diffraction, spectroscopy and scattering are excellent tools for studying biological systems because neutrons interact differently with hydrogen and its isotope deuterium. As a result, it is possible to:

- pinpoint individual hydrogen positions in proteins
- probe the structure and dynamics of proteins, nucleic acids and membranes
- characterize higher order complexes

These studies use neutrons to address questions that have not - or cannot - be answered by other techniques.

SANS can be used to study biological systems under near physiological conditions, providing insight into interactions within complexes and conformational changes in response to stimuli. Through the use of specific deuterium labeling SANS makes it possible to highlight and map components within larger complexes (e.g. viruses, ribosome). The SANS instruments at ORNL's High Flux Isotope Reactor and Spallation Neutron Source will open new opportunities for studying conformational changes and molecular processes on biologically relevant timescales.

- **HFIR** High Flux Isotope Reactor

Scientific investigation with neutrons gives researchers unprecedented capabilities for understanding the structure and properties of materials important in biology, chemistry, physics, and engineering. ORNL provides two of the most powerful neutron science facilities in the world—the High Flux Isotope Reactor and the Spallation Neutron Source. The HFIR produces one of the brightest steady-state neutron streams on Earth, and the SNS produces the world’s most intense pulsed neutron beams. Through materials research, scientists are discovering remarkable ways to address our energy

needs, such as superconducting power cables that eliminate power-transmission losses and prevent outages, liquid transportation fuels produced from biomass, and magnetic refrigerators that use half the energy of conventional appliances.

To bring such technologies into common use, researchers need to be able to view materials from the atom-to-atom scale to a full systems view. Developing these advanced materials requires manipulating the properties of alloys at the atomic level, and neutron scattering is a key tool in this quest.

Neutrons show where atoms are and what they are doing at scales smaller than the best electron microscopes. They let researchers see in real time how the atomic lineup in a material shifts with changes in temperature, pressure, and magnetic or electronic fields. They trace the electron motions that give materials properties such as magnetism or the ability to conduct electricity—all essential information in the quest for energy savings.

Satisfying the world's growing hunger for energy requires finding ways to use power more frugally and developing methods for sustainably producing additional energy. Neutron scattering aids the creation of new materials engineered for both purposes.

- **MDF** Manufacturing Demonstration Facility

As the nation's premier research laboratory, ORNL is one of the world's most capable resources for transforming the next generation of scientific discovery into solutions for rebuilding and revitalizing America's manufacturing industries. Manufacturing industries engage ORNL's expertise in materials synthesis, characterization, and process technology to reduce technical risk and validate investment for innovations targeting products of the future.

DOE's Manufacturing Demonstration Facility, established at ORNL, helps industry adopt new manufacturing technologies to reduce life-cycle energy and greenhouse gas emissions, lower production cost, and create new products and opportunities for high paying jobs.

- **OLCF** Oak Ridge Leadership Computing Facility

Computational science plays a very important role in many things that we see in our daily life. There's the design of aircraft, for instance, or the fundamental elements of industrial design. The virtual environment provides a much quicker way for us to improve our understanding of older problems and break ground in our understanding of new phenomena with ramifications for how we live our lives. Machines like Titan and activities like the Titan project will be the vehicles that allow us to explore these

fundamental things in computational science. They will provide a framework for better product design, new and innovative technologies, and new materials. And they will enable new insights into how very complex, nonlinear systems work; that, again, has implications for a lot of the technologies that we take for granted.

OLCF is a user facility that recognizes that its products are scientific discovery and technical innovation, and we will achieve this vision working with strong partners. These partnerships will be developed through our calls for proposals and our outreach efforts to the scientific, technology, and industrial communities. To broaden the scope of leadership computing, we need to engage through our networks, through our relationships, and encourage users from new communities that can take good advantage of these resources to move us forward in scientific discovery, industrial competitiveness, and sustainability. Partnerships and alliances are a big part of what is important about our research. In terms of challenges, clearly we're at a cusp in technology moving to hybrid architectures. This implies a lot of hard work by a lot of people. But it also is a game changer.

- **SNS** Spallation Neutron Source

SNS is an accelerator-based neutron source in Oak Ridge, Tennessee, USA. This one-of-a-kind facility provides the most intense pulsed neutron beams in the world for scientific research and industrial development.

The 80-acre SNS site is located on Chestnut Ridge and is part of Oak Ridge National Laboratory.

Although most people don't know it, neutron scattering research has a lot to do with our everyday lives. For example, things like medicine, food, electronics, and cars and airplanes have all been improved by neutron scattering research.

Neutron research also helps scientists improve materials used in a multitude of different products, such as high-temperature superconductors, powerful lightweight magnets, aluminum bridge decks, and stronger, lighter plastic products.

To support SNS's unprecedented capability, a world-class suite of instruments is being developed that makes optimal use of SNS and that is suited to the needs of users across a broad range of disciplines. Instruments are available to researchers with varying degrees of experience, from new graduate students and first-time neutron users to experienced users with an interest in instrument design.

B. Microscopy:

1. Advanced Scanning Electron Microscopy (SEM) and Spectroscopy

- **Zeiss Merlin VP SEM**
  This SEM features variable-pressure capability to optimize studies of nonconductive samples or samples with low vapor pressures. Equipped with BF-STEM detector, surface profile backscatter imaging, and EDS spectroscopy.
  More info …

2. Advanced Transmission Electron Microscopy (TEM), Scanning Transmission Electron Microscopy (STEM), Electron Energy Loss Spectroscopy (EELS), and Energy Dispersive Spectroscopy (EDS)

- **Soft Matter TEM (Zeiss Libra 120 TEM**)
  This TEM features variable voltage (60 to 120 kV) and offers enhanced capabilities for studies of soft nanomaterials while maintaining precision needed for work in catalysts and other "hard" nanomaterials. The instrument is equipped with in-line EELS, providing real-time energy filtered imaging, high angular resolution nano-diffraction, and has cryogenic specimen-loading capabilities.
  More info ...
- **Hitachi HF3300 high-resolution TEM-STEM**
  Instrument combines high-resolution TEM structure imaging (<1.2Å) with high-resolution STEM (HAADF and BF) detectors and a secondary electron (SE) detector for SEM imaging. Primary operation is conducted at 300 kV. Microscope features a Gatan Quantum EELS/GIF and a Bruker silicon drift detector (SDD) for EDS spectrum imaging. Specialized in-situ holders are available for heating (up to 1200°C Protochips Aduro), cryo-transfer (Gatan CT3500), Hitachi 360° rotation micropillar tomography, nanoindenter (Hysitron), and liquid flow cell (Hummingbird).
  More info ...
- **Nion UltraSTEM 100 (U100) dedicated aberration-corrected STEM** Instrument features a 3rd-generation C3/C5 aberration corrector, 0.5 nA current in atomic-size probe, ~1.0-1.1Å HAADF-STEM imaging resolution at 60 kV and 100 kV operating voltages. The Nion U100 features a Gatan Enfina EELS and a cold FEG for energy resolutions <350 meV at 100kV. This instrument has an unparalleled combination of atomic-resolution imaging and spectroscopy at mid- and low-voltages, and is especially valuable for the characterization of 2-dimensional materials (graphene, BN, transition metal dichalcogenides, etc.), catalysts, and other beam-sensitive materials.
  More info ...

- **FEI Titan S aberration-corrected TEM-STEM**
  Probe-corrected microscope features a Gatan Quantum EELS and Gatan Imaging Filter (GIF), with dual-EELS and fast spectrum imaging capabilities, an 'extreme Schottky' high-brightness field emission gun (X-FEG), and variable operating voltages (60, 120, and 300 kV). Instrument is equipped with high-angle annular dark field (HAADF), annual dark field (ADF), and bright field (BF) STEM detectors for sub-Å imaging. Specialized in-situ holders are available for experiments requiring heating (up to 1200°C – Protochips Aduro), biasing (Protochips PE), Nanofactory AFM/STM, liquid cell electrochemistry (Protochips Poseidon 500), electron tomography (both high-tilt and 360° rotation), and LN2-cooling.
  More info ...

3. Instruments for Atom Probe Tomography (APT)

- **Cameca Instruments Local Electrode Atom Probe (LEAP) 4000X HR**
  Advanced LEAP features a 1 MHz laser and 250 kHz high-voltage pulse generator, reflectron energy compensating lens, and a crossed delay line, single atom, position-sensitive detector. Instrument is used for the atomic level 3-dimensional compositional characterization of a wide range of materials, including metallic conductors, semi-conductors, oxides, and nanostructured materials.
  More info ...
- **FEI Nova 200 dual beam focused ion beam (FIB)-SEM**
  The FIB is dedicated to precision preparation and annular milling of needles required for APT, and is equipped with an annual STEM detector for site-specific FIB-milling, a Kleindiek nano-manipulator, and EDS.
  More info ...

4. Helium-ion Microscopy

- **Zeiss Orion NanoFab**
  The Zeiss Orion Nanofab helium-ion microscope (HIM) features three primary capabilities: imaging, detailed ion-milling/patterning using He-ions, and high-rate milling using heavier Neon ions. It is located in the CNMS cleanroom to facilitate clean transfer of samples.

  This instrument has the ability to image, in the manner of an SEM, at unprecedented resolution and with high surface sensitivity; and the ability to pattern through direct ion-milling and exposure of lithographic resists, down to feature sizes of about 5 nm. The instrument is complementary to a Focused Ion

Beam (FIB), but capable of feature sizes 10-20 times smaller. Scientifically, the instrument allows users to explore entirely new types of devices and engineered nanostructures that cannot be fabricated with other techniques.
More info ...

5. X-ray Diffraction

- **2-circle X-ray diffraction**
  - X-ray powder diffraction with temperature-controlled sample environment. 77K to 1200K at 1 Bar, 273K to 1200K up to 10 Bar. Reactive gasses such as H2, CO for varying chemical composition in sample environment.
- **• 4-circle X-ray diffraction**
  4-circle plus translation stage, high temperature, in-plane thin film diffraction. Also texture, reflectivity, microdiffraction, reciprocal space mapping.
- **• Small-angle X-ray scattering, SAXS**
  Anton Paar SAXSess instrument for small-angle scattering to obtain nanoscale structural information. Also equipped for grazing-incidence measurements on nanomaterial films.

6. Neutron Scattering

- Center for Nanophase Materials Sciences (CNMS) users are encouraged to take advantage of the world-class neutron scattering facilities that are available at ORNL's High-Flux Isotope Reactor (HFIR) and the Spallation Neutron Source (SNS). Beamlines of particular relevance to CNMS Scientific Themes include the small-angle scattering and diffractometry instruments on the HFIR cold source, HFIR thermal neutron diffraction and spectroscopy capabilities, and instruments at the SNS including the backscattering spectrometer and the liquids and magnetism reflectometers. Please visit the ORNL Neutron Sciences website for more information about these neutron scattering facilities.

  CNMS users who would like to incorporate neutron scattering as a supporting component in their user proposals may request neutron beamtime by checking the appropriate box on the CNMS proposal form and attaching the 2-page Neutron Scattering appendix to provide details of their beamtime request. However, if the primary thrust of the proposal is to obtain access to neutron scattering, prospective users must submit the proposal directly to the neutron scattering user program.

C. Biosciences microscopy:

- **Live Cell Zeiss LSM 710 High Resolution Confocal Microscopy**
  A Carl Zeiss 710 confocal microscope with an environmentally controlled stage is available for live cell multi-channel imaging of biological samples.
- **Zeiss Elyra Super-resolution Confocal Microscope**
  Structured Illumination Microscopy (SR-SIM) and Photo-activated Localization Microscopy (PAL-M) offer sub-diffraction limited resolution imaging of biological and material samples.
- **Confocal Fluorescence Microscopy**
  A Leica TCS SP2 MP scanning laser confocal laser system for multiphoton excitation and Red (HeNe, 633 nm/10mW), Green (HeNe, 543/1.2mW) and Blue (Ar 458/5mW; 476nm/5 mW; 488nm/20mW; 514nm/20mW) laser systems and a 6-channel Acousto Optical Tunable Filter for laser line selection and attenuation. The optical system is uv compatible. The inverted stage system is equipped with transmitted light detection for recording bright field images and a 50W mercury arc lamp for epifluorescent illumination. Heated sample holders and perfusion systems are in hand.
- **Epifluorescent Microscopy**
  The Zeiss Axioskop 2 FS plus fluorescence microscope is equipped with epifluorescent (top) illumination, Nomarski phase contrast optics (bottom) and either top or bottom illumination using 12W halogens lamps. A 12 bit Retiga color CCD camera is mounted on the microsope for image collection. A Burleigh PCS-5000 Series Patch Clamp Micromanipulator and ceramic objectives for electrophysiology measurements.
- **Combined SPM / Fluorescence Imaging System**
  A Molecular Imaging PicoPlus scanning probe microscope system is available. This system contains small (10 µm) and large (100 µm) closed-loop multipurpose scanners with low-coherence lasers and a Picoscan 3000 controller. The closed loop motion control allows for reproducible positioning and lithography on the nanometer scale. Liquid cells, flow cells and temperature control equipment are included. The system contains magnetic and acoustical cantilever oscillation modes and the PicoTrec system that allows for simultaneous topography and chemical recognition. A video imaging system allows for sample viewing from above and through the scan head. Alternatively, the system is mountable onto a Zeiss Axiovert 135 epifluorescent microscope.

UTK Medical Center Facilities

Contact: Dr. Jon Wall, Professor of Medicine
Director, Amyloid and Preclinical Molecular Imaging Laboratory
University of Tennessee Graduate School of Medicine
1924 Alcoa Highway
Knoxville, TN 37920
Tel: (865) 305 5447
Imaging Lab: (865) 305 8497
Fax: (865) 305 6865
JWall@mc.utmck.edu

Alan Stuckey
(astuckey@utmck.edu)

http://gsm.utmck.edu/research/preclinical

http://gsm.utmck.edu/research/ACTP

Preclinical and Diagnostic Molecular Imaging Program at the University of Tennessee Graduate School of Medicine, Knoxville

In September 2005 the Preclinical and Diagnostic Molecular Imaging Laboratory (PDMIL), was constructed in the UT Medical Center immediately below a suite of radiochemistry laboratories, the cyclotron and a, high-resolution, low-count research mCT PET scanner with a 52 cm axial field of view (Siemens Medical Solutions, Knoxville).

The imaging facility boasts 4 imaging suites the first housing a microCAT II +SPECT hybrid scanner (Siemens Preclinical Solutions, Knoxville), the second, a P4 microPET (Siemens Preclinical Solutions) and lastly, a trimodality Inveon SPETC/PET/CT system (Siemens Preclinical Solutions) in suite 3. All suites are equipped with oxygen and vacuum lines and a full anesthesia (vaporizer) station (Summit Medical, Seattle, WA) with heated mouse chambers and pads for live animal imaging. A BioVet™ system (Summit Medical) for monitoring respiration rate, ECG, body temperature provides a signal for cardiac PET gating or respiratory CT gated imaging. The PDMIL has a dedicated image analysis office (computer lab) with 2 seats of Amira 3.1 or higher (TGS, San Diego, CA), a real-time CT reconstruction station, and 2 seats of Inveon research Workplace software (Siemens Preclinical Solutions). Data is stored securely on a 7 TB server with RAID configuration that is backed up to tape at a centralized location.

The animal preparation and analysis laboratory contains a gamma counter for biodistribution studies and areas for tissues collection and storage. An Animal Care and Use Committee (ACUC)-approved satellite holding facility, with 3 rooms and preparation area is also located in the PIL. This permits the housing of up to 3 different species indefinitely to allow time for longitudinal studies and using tracers with extended clearance rates.

The microCAT II +SPECT (currently needs repair) is a fully shielded high-resolution hybrid x-ray (CT) and single photon emission computed tomography (SPECT) *in vivo* imaging system. The x-ray source is a 40 W, tungsten anode, 35-80 kVp source mounted on a rotating gantry capable of step-and-shoot acquisition over the full 360° around the subject positioned on the animal bed. The x-ray detector is a 2048 $\times$ 3096 pixel CCD coupled to a high-resolution phosphor screen via a fiber optic taper. It boasts a 61 $\times$ 91 mm field of view and a resolution of 27 μm. The digitized images are 12 bit depth and the detector dynamic range when using 2 $\times$ 2 or 4 $\times$ 4 binning (standard in our mode of operation) is 72 dB. The CT data are reconstructed using the cone-beam Feldkamp algorithm, although iterative reconstruction methods are being developed and evaluated in our program. Real time reconstruction is performed using the Cobra software package (Exxim Computing Corporation, Pleasanton, CA) running on a dual-processor Dell workstation with 8 GB of memory. A standard 512 $\times$ 512 $\times$ 768 (4 $\times$ 4 binned image) volumetric reconstruction onto 77 μm^3 voxels usually completes within 2 minutes after the final projection of a 360-projection acquisition (1° azimuths). Offline reconstruction can alternatively be conducted using an in-house developed parallel implementation of the Feldkamp algorithm. This code is capable of providing volumetric images of the same dimensions as above in less than 5 mins using a small group of PCs.

The SPECT detectors are mounted on stepper motor driven stages so that they can be readily retracted form the CT field of view. Detectors are available optimized for either high or low energy photon emitting nuclides and are housed within a 10 mm-thick casing of 6% antimonial lead. For low energy nuclides (< 170 KeV; such as ^{125}I, ^{123}I, and ^{99m}Tc) we employ two large-area detectors mounted facing each other on the rotating gantry and at 90° to the x-ray source and detector. The detector heads are 150 $\times$ 150 mm^2 and composed of 5 mm-thick sodium iodide (NaI) crystals with a 1.5 $\times$ 1.5 mm or 1.25 $\times$ 1.45 mm crystal spacing. For high energy photon imaging (up to 300 KeV, e.g. ^{111}In) similarly sized detectors (150 $\times$ 150 mm^2) are available with 10 mm long NaI crystals and a crystal spacing of 2.2 $\times$ 2.2 mm.

For both sets of detectors parallel, pinhole and multi-pinhole collimator configurations are available. Composed of 12 mm-thick 6% antimonial lead, the collimators can be fitted with pinholes made of 15 mm-thick tungsten containing either a 0.5, 1.0, 2.0, or 3.0 mm diameter aperture. For our standard mouse scans using ~ 100 μCi of tracer we use the 2.0 mm pinhole collimators on both detectors, which provides a modest degree of magnification and statistically good count rates (even when each detector is reconstructed independently). The SPECT data from each detector may be reconstructed either independently or following summation as a single ("multiple-detector") file. Reconstruction is performed post-acquisition using a dedicated ordered subset expectation maximization (EM) algorithm. A 52 × 52 × 68 image typically computes in approximately 2 minutes. Further upsampling of the image to smaller voxel sizes is normally performed post-reconstruction using the Lanczos filtering kernel in Amira.

The Inveon trimodality SPECT/PET/CT

Inveon SPECT/PET/CT: The Inveon high resolution SPECT detectors deliver sub-millimeter resolution with the largest pixelated detector heads in the industry. The SPECT module detects gamma rays from 30 keV to 300 keV, providing sensitivity to the most widely used research and clinical single photon isotopes. The detector head has a large active area (150 mm x 150 mm) that permits greater pinhole magnification, improving sensitivity while maintaining a large field of view (FOV) while maintaining small detector crystals (2 mm x 2 mm x 10 mm) to provide high intrinsic detector resolution. The Inveon collimators are numerous and include 0.5, 1.0, 2.0, and 3.0 mm single pinhole collimators, a LEAP (low-energy all-purpose) parallel hole collimator for planar imaging and a pair of mouse brain or mouse whole-body multi-pinhole collimators.
Multi-pinhole image reconstruction and calibration software permits the production of high resolution images in a fraction of the time required with traditional collimators.

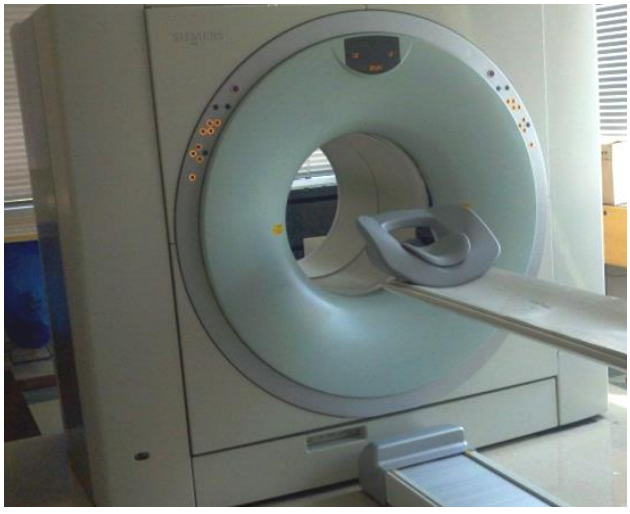
The Inveon PET system is a third generation PET imaging system that incorporates several key technical features and advancements that deliver exceptional image quality and quantitative accuracy. The detector design in Inveon includes an innovative high efficiency light guide that delivers more photons to the photomultiplier tube, thereby improving energy and timing resolution. The detector also features a large 20 x 20

crystal array that increases the scanners axial field of view (FOV) and improves system sensitivity. With minimal gap between crystal elements and a 92% packing fraction, the net result is a PET system with exceptional spatial resolution and sensitivity.

The new Inveon data processing architecture improves PET count rate performance, energy resolution, and timing resolution. Count rate performance is improved through a store and forward coincidence processing technique that virtually eliminates the electronic deadtime associated with traditional multiplexing architectures. Improved energy resolution using high speed analog-to-digital converters and improved timing resolution through the use of 312 ps time bins, results in a PET system with exceedingly high singles and coincidence data rates, as well as, excellent random and scattered event rejection. Attenuation Correction is achieved using a rapidly-acquired low resolution CT dataset.

The Inveon CT has an 80 W, tungsten anode, 35-80 kVp standard source (less than a 50 micron focal spot) that provides a high X-ray flux for high speed scanning and a large cone angle for high magnification studies. The maximum achievable resolution with this X-ray source and the standard detector is 40 microns. Typical scan times are less than 5 minutes. The 125 mm Detector: The detector has 3072 x 2048 pixels and may be configured for a FOV as large as 8.4 cm x 5.5 cm. With a 12 bit deep readout of the raw data, this detector has a dynamic range of 69 dB (1 x 1 binning) to 72 dB (2 x 2 and 4 x 4 binning), providing excellent signal-to-noise ratio.

Data is reconstructed in real time on a dedicated high speed platform during a scan. The real time reconstruction engine allows reconstruction to start as the projection data is being acquired.



The large animal and clinical research Biograph 6 PET/CT.

In addition to the small animal imaging systems described above, for larger animals we have recently added a clinical research PET/CT to the floor above the PDMIL. **The Biograph 6** (Siemens Medical Solutions USA, Inc.) is a dedicated research PET/CT for use in large animal and human studies. This is an LSO-based PET system with a 6-slice CT. The system boasts a 21.6 cm axial PET FOV with TrueV™ technology and a 190 cm patient scan range. This extended FOV also provides an increased sensivity and

count rate performance. This system is equipped with HD•PET™ enabling point spread function-based reconstruction that provides improved resolution and a uniform FOV.

The CT system has an isotropic resolution of 0.33 mm with z-Sharp™ technology. Data from the CT unit are automatically registered to the acquired PET data. The CT data is used for attenuation and scatter correction enabling quantitative PET imaging with anatomical CT imaging.

Radiolabeling Area: We have a dedicated radiolabeling area for the preparation of radio-iodinated tracers for human use. The room contains a positive pressure sealed inner room that has a dedicated sterile-filtered air flow. This inner area has a chemical cabinet in which we perform the radiolabeling. This room also houses (outside the sterile area) a spectrophotometer for assessing the concentration of radiolabeled biological molecules, a certified well counter (Capintec), 37° incubator for performing sterility testing, a small refrigerator, and bench space. GLP-grade peptide p31 will be radiolabeled in this area for use in Shar pei dogs.

Summary of Major Equipment Preclinical and Diagnostic Molecular Imaging Program at the University of Tennessee Graduate School Of Medicine, Knoxville

A **microPET P4** as well as **MicroCAT II + SPECT**, **mCT** clinical PET/CT, and **Inveon trimodailty SPECT/PET/CT**, all described in detail above.

1480 Wallac Wizard 3 Automatic Gamma counter (Perkin Elmer) – A single detector universal counter with a 75 mm solid lead shield. It counts vials or tubes of any shape up to 20 mL in volume and up to 28 mm in diameter. There are up to 20 simultaneous counting regions and its energy range is up to 2000 keV.

Capintec CRC 15 PET digitally controlled dose calibrator.

Anesthesia apparatus for delivering isoflurane:oxygen anesthesia for small animal imaging.

BioVet apparatus for monitoring for small animal respiration rate, ECG, temperature and provided an output trigger for gated PET and CT image acquisition.