COMMISSION FOR HIGHER EDUCATION
Friday, September 11, 2009

DISCUSSION ITEM B: **Overview of Indiana Innovation Alliance Plan Presented by Indiana University and Purdue University**

Staff Recommendation For discussion only.

Background

As a part of their 2009-11 biennial budget requests**,** Indiana University and Purdue University submitted a joint funding proposal to develop the Indiana Innovation Alliance (IIA). The IIA is intended to "unite the state's largest research universities with business, economic development organizations, healthcare enterprises, and state government to expand Indiana's share of national investment in bioscience research and development" (from budget request). The IIA will focus on three key areas: (1) enhancing core research capabilities; (2) expanding IU's medical education network; and (3) expanding the Purdue University Technical Assistance Program.

The Commission recommended funding for the IIA in the 2009-11 higher education budget recommendations. The General Assembly appropriated funding for the IIA in the following amounts:

Each of FY 2010 and FY 2011:	
Core Research	$5,000,000
Technical Assistance	$2,000,000
Medical Educ. Centers Expansion	$3,000,000

Indiana University and Purdue University have agreed to come present to the Commission their plans for these specific expenditures and for the Indiana Innovation Alliance.

Supporting Document Indiana Innovation Alliance Cores Proposal, Plan for the Expansion of the Indiana University School of Medicine Education Campuses – September 2009, Purdue University – Technical Assistance and Advanced Education, Appendix 1, Biomedical Device and Biotechnology Core, *attached*.

INDIANA INNOVATION ALLIANCE CORES PROPOSAL

September 2009

I. Introduction

Research core laboratories are service facilities that house cutting edge scientific equipment needed by a wide range of scientific disciplines but which are too expensive to be purchased, maintained, and upgraded by a single academic unit or small business. To function effectively as service facilities, core laboratories must be staffed by excellent technicians and PhD research scientists who can provide technical and consultative expertise to scientists and businesses that wish to utilize the resource.

Indiana University and Purdue University propose to utilize the $10M appropriated for core research to launch two statewide Indiana Innovation Alliance research Cores: 1) The Biomedical Device and Bionanotechnology Core and 2) The Indiana Biomedical Imaging Research and Development Core (I-BIRD). Both universities will fully participate in and contribute resources and expertise to each core. Purdue will serve as the lead institution for operation of the Biomedical Device and Bionanotechnology Core, while Indiana University will serve as the lead institution for I-BIRD.

These two cores are built upon existing areas of strength in the two institutions that also represent opportunities and needs of the private sector. These research cores collectively represent cutting edge technology and expertise that is not readily available in many companies or even in colleges/universities but may be essential for competitive product development. It is important to note that the two cores are complementary. Indeed, new imaging technologies are currently being developed through nanotechnology applications. The appropriated funds will be used to coordinate activities within the respective cores across institutions, enhance existing capabilities, add new capabilities to stay abreast of the latest technology, and enable the two universities to offer these resources to other academic institutions and private companies across Indiana and beyond at a reasonable cost. Considered together, these two cores will enhance our ability to design, prototype, and evaluate novel life sciences diagnostics, therapeutic devices, and instruments and will enable a variety of structural biology, neuroimaging, and advanced clinical research studies.

II. Vision

The ultimate goal of the two Cores is to establish an internationally renowned capability for basic research, translational research and prototyping in the life sciences. Unique will be the collaboration and coordination across multiple institutions and a friendly interface between academia and the private sector.

III. Biomedical Device and Bionanotechnology Core

A. Overview

Faculty across several Purdue and Indiana University Colleges and Schools currently conduct research in the area of biomedical devices and materials and will benefit from the Biomedical Device and Bionanotechnology Core resources. Many of these projects involve industrial collaborators as well as faculty. Schools that will be involved include Veterinary Medicine, Pharmacy, Engineering (including Purdue bio-engineering at both West Lafayette and Indianapolis), Science and Agriculture at Purdue and the School of Medicine, the School of Science at IUPUI, and College of Arts and Sciences at Indiana University. While the two universities already collectively provide enviable world-class research resources, the existing facilities lack key infrastructure and support that is necessary to seamlessly tie together discovery-based research, innovation, device prototyping and translation in the biomedical arena. The proposed Core will fill in gaps and create new capabilities that leverage and synergistically link existing resources across the two universities. Creation of a continuity of activities will benefit economic development in Indiana through mobilization of an unparalleled resource for world class science and engineering, product development and testing, and workforce training.

Industrial partners will directly benefit from these core facilities through improved materials and device characterization capabilities as well as improved prototype development. Among the Indiana industrial partners that will benefit are those that are already engaged with university faculty, including Cook (Bloomington and West Lafayette), Biomet, Depuy and Zimmer (Warsaw), Hill-Rom (Batesville), Aptuit (West Lafayette) and Ft. Wayne Metals (Ft. Wayne). Numerous startup companies in Indianapolis, West Lafayette, Warsaw, and in the Purdue and IU Research parks, including Nanovis [presently a tenant in the Birck Nanotechnology Center's (BNC) Nanotech Incubator], Intelliphage, and BioVitesse will also benefit from the Core capabilities. Additional corporate partnerships will be facilitated through programs such as the Midwest-based Nanobusiness Alliance and the Center for Agricultural and Pharmaceutical Nanotechnology (CAPN), a nascent industry/university cooperative research center between Purdue and the University of Illinois at Urbana-Champaign that has recently been awarded an NSF planning grant. CAPN has already attracted interest from 20 potential member companies, many of which employ Indiana residents.

B. Resources

The Core will house equipment for characterization of biomedical materials and devices in addition to facilities to develop prototypes. Facility upgrades and equipment will complement the analytical, nanotechnology, machining, veterinary and biological testing facilities already existing at Purdue, IUSM, and IUB. In addition, the Core will complement the preclinical development team that is a principal component of the NIH-supported *Indiana Clinical and Translational Sciences Institute (CTSI)*. Thus, full capabilities from basic research through prototype development and testing within a live organism will be a reality through collaborations between the proposed Biomedical Devices and Bionanotechnology Core, the existing expertise in machining and prototype development, and the preclinical development team.

The following is the proposed budget for the Core:

Category	Year 1	Year 2	Project Total
Equipment	$642,000	$1,242,000	$1,884,000
Facility Upgrades	900,000	300,000	1,200,000
Operations and Research Core Support	600,000	600,000	1,200,000
Personnel	358,000	358,000	716,000
Totals	$2,500,000	$2,500,000	$5,000,000

IV. Indiana Biomedical Imaging Research and Development Core (I-BIRD)

A. Overview

Modern life science research depends heavily on "seeing" molecules and macromolecular objects including peering inside humans. Powerful imaging strategies coupled with dramatic improvements in computational tools have developed over the last 10 – 15 years and provided researchers and clinicians with an unprecedented ability to see into biological systems. Imaging needs can be a particular challenge for industry and especially start-up companies as the infrastructure cost is so high as to not allow a single company to implement its needs. Thus, developing a Core in this area that is attentive to industry's needs will not only facilitate Indiana's private sector but also has great potential to attract users from afar thereby bringing new business to Indiana. Purdue and Indiana Universities have invested heavily in these essential technologies and will work in a coordinated fashion

so that these resources can be used efficiently minimizing unnecessary duplication and making them accessible to the Indiana life sciences community, both academic and private.

We will create the **Indiana Biomedical Imaging Research and Development Core (I-BIRD)** that will promote the application of advanced imaging methods in academic and commercial R&D research. The Imaging Core will allow industrial partners access not only to the technology but to the all-important technical expertise as well. Several examples already exist for collaboration between Indiana companies and imaging capabilities at both Purdue and IU including DowAgrosciences, Amgen and Millipore and early-stage Indiana companies such as AEON Imaging, Kylin Therapeutics, Prosolia, Aquascience, IkoTech, BioVitesse, InPhoton, Fast Diagnostics and PDS Biotechnology.

In order to maintain a national/international leadership position, both people and laboratory resources need to be continually enhanced. Key resource needs include:

1. Salary funding for faculty time to assist academic and industry scientists with new project study design, implementation, and data analysis.
2. Salary funding for a non-faculty scientific support team with dedicated time to support core service functions and industry contract service and clinical trial needs, including but not limited to, imaging project management, implementation of core services, quality control and maintenance of core instruments, image processing and data analysis, and final report generation.
3. Funding to establish the IT, image processing, and data analysis infrastructure needed to facilitate remote participation and analysis of data collected within this program.
4. Funding to enhance imaging probe development capabilities. This potentially would include new automated chemistry synthesis modules for the generation of radioactive and non-radioactive imaging probes and highly trained support staff to provide imaging probes suitable for human administration on a daily basis.
5. Upgrading of high tech imaging systems on a regular life cycle basis as well as implementing new, innovative imaging modalities.

In addition, by developing specific training programs, I-BIRD offers the opportunity to enable a new generation of Indiana workers to be able to take advantage of future job opportunities in Imaging Science.

B. Resources

Current extensive capabilities in biological imaging already exist at IU and Purdue. Although there is currently cooperation across campuses and institutions, collaboration is ad hoc and a function of individual investigators and small groups finding one another and deciding how to work together. I-BIRD will bring a formal approach to efficient utilization of resources and will facilitate academic and industrial partnerships developing through the recently funded *Indiana CTSI*. In so doing, it will minimize duplication of technology, determine in a collaborative fashion where technology investments should be made, determine where people infrastructure should be enhanced, and offer a service mentality to public and private users alike. The proposed budget allocations for the Core are highlighted below.

Category	Year 1	Year 2	Project Total
Equipment	$1,300,000	$1,300,000	$2,600,000
Facility Upgrades	300,000	300,000	600,000
Operations and Research Core Support	500,000	500,000	1,000,000
Personnel	400,000	400,000	800,000
Totals	$2,500,000	$2,500,000	$5,000,000

V. Metrics

Key metrics will include:

- Number of users overall and new users from both academia and industry
- IP generation
- New company formation
- Prototypes developed and translated to industry
- Number of learners participating in Core activities
- Trainees who enter the work force in Indiana
- New revenues to the State such as grants supporting academic research, small business innovation awards, or fees for services rendered

VI. Management Plan

Success of the Alliance and its Cores depends on effective management oversight and sound decision-making to ensure optimal use of funding and other IIA resources. Thus, the IIA initiative proposes that the Alliance establish a management committee composed of two representatives each from Purdue and IU, two representatives of industry (e.g., trade organization and life sciences company), and a representative of state government. This seven member Alliance management committee would oversee the annual budget for Core support and regularly monitor Core operating and equipment procurement expenditures. In addition, the lead institution for each Core will identify a Managing Director to coordinate the day to day operations of the Core and a scientific committee to review and recommend areas for funding. The support institution for each Core will identify a staff liaison to work closely with the Managing Director to ensure that the two universities are coordinated in their efforts. The entire program will be managed in conjunction with the Indiana Clinical and Translational Sciences Institute, an organization that is already established as a partnership among IIA components. This organizational approach will not only result in effective management of this IIA program but will also enhance the ability to renew the CTSI award in a few years as it will serve as a powerful example of both institutional collaboration and of State support for the CTSI.

Plan for the Expansion of the Indiana University School of Medicine Education Campuses – September, 2009

Overview

The Indiana University School of Medicine (IUSM), the sole medical education institution serving Indiana, proposes a plan to expand its medical student enrollment by 30 percent, from 280 per class to 364. The expansion plan started with students matriculating in August 2007 and will continue for eight years to completion in 2015. At that time, the IU School of Medicine M.D. student enrollment would reach its maximum of 1,456 medical students.

Why Expand the Class Size?

A physician workforce study, conducted and released in 2006 by the Indiana University School of Medicine in collaboration with the State of Indiana, found a shortage of physicians in many parts of Indiana, and predicted an even greater disparity between available physicians and patients served, by 2020. According to studies conducted by the Association of American Medical Colleges, the American Medical Association, and the Committee for Graduate Medical Education, the reasons for the shortage of physicians across the country, including Indiana, are multiple. They include a predicted increase in demand for medical care by the population, in large part driven by the substantial increase in the elderly; earlier retirement of the current physician work force; a decrease in hours worked by practicing physicians (especially women physicians); and an increasing number of people approaching or older than age 65 (the "baby boomers"). The forecasts predict a scarcity of physicians, particularly in primary care, in non-urban communities and in historically underserved communities.

The IUSM Expansion Plan

The IU School of Medicine has provided its medical educational program statewide since implementation in the 1960s. Currently there are nine campuses throughout Indiana delivering this medical education program (see figure 1).

Currently, medical students complete their first two years assigned in a distributed manner among the nine Centers of Medical Education. For the third and fourth years of medical school, students are currently assigned to the Indianapolis campus for their clinical experiences in the eleven required clinical clerkships. Similarly, clinical electives are completed in-and-around the Indianapolis campus, although there is no geographic requirement to do so. Indiana ranks second in the United States in retaining its medical school graduates to practice in Indiana (Arkansas ranks ahead). Reasons for this retention are multiple, including: greater

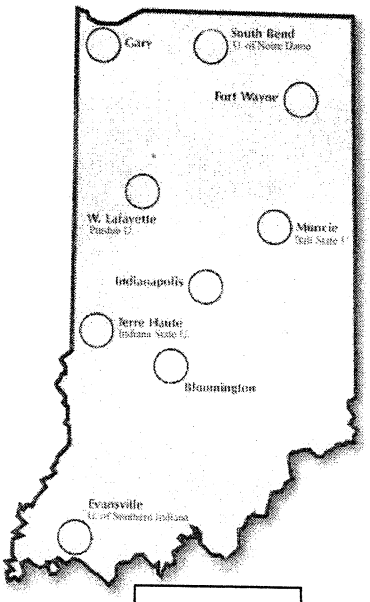

Figure 1

than 40% retention rate of medical school graduates into post graduate residency training programs throughout Indiana; a favorable clinical malpractice climate; family in Indiana; and personal and professional relationships made during medical school. Data now confirm a positive retention rate of medical graduates returning to the areas of our Regional Medical Campuses, if the graduate completed the first two years of medical school at that center, as well as increased likelihood of entering primary care practice.

It is our belief that the 2007-2015 medical school expansion plan will be fundamentally important to solving the physician shortage problems in the state of Indiana. It should be implemented fully, so that by the year 2020, when the physician demand model predicts the shortage to occur, Indiana will already be producing enough physicians, from its medical school and residency training programs, to care for its people. It is also important to acknowledge that the physician workforce needs of Indiana go beyond simple headcounts. The School of Medicine also recognizes that it must aggressively address the need for more primary care physicians, in addition to those who enter practice in smaller or rural communities. Our centers of medical education provide an ideal system to simultaneously address all the dimensions of physician staffing needs.

Because of Indiana's unique distributed medical educational system, we are prepared to prevent the physician shortage in Indiana by an expansion that is economical, educational, logical, and ultimately beneficial for the citizens of the State of Indiana. The following stepwise plan will necessitate a willing partner in our State Government, since new base funding support for the Centers of Medical Education will be required to both implement and maintain the program.

1. Expansion plans for the Centers in years one and two

The first step in the IUSM expansion calls for all expanded matriculants to be assigned to the current regional medical campuses in Terre Haute, South Bend, Evansville, Lafayette, Muncie, Bloomington, Gary, and Fort Wayne. Each center will absorb at least 8 new students; some will increase by more (see the attachment).

Because most of the IUSM campuses have recently constructed new facilities, there will be ample room for the expanded number of medical students (the Lafayette facility is the exception). Each campus will require some minor renovations and new equipment such as anatomy dissecting tables, IT equipment, etc. Since these are marginal one-time costs, expansion in the first two years will require minimal fiscal, educational, or programmatic changes beyond what we are doing now. Although current faculty numbers are adequate to provide the necessary instruction in the competency-based curriculum, increased staff support at the regional campuses will be necessary to provide academic, career, and personal counseling. In addition, educational administrative support for the Dean's Offices of Medical Student Affairs and Medical Education and Curricular Affairs will be necessary (1 FTE per Office).

2. New Clerkships and Hospital Partners at the Regional Medical Centers

The expansion will require IUSM to provide an increased number of third- and fourth-year clinical experiences outside of Indianapolis. Clinical rotations will occur in the major hospitals and clinics in the cities of our regional Centers of Medical Education. It is expected that many medical students who complete their first two years at one of the regional campuses will still move to Indianapolis as their "home base" for years three and four. Some regional medical students may chose to remain for clinical clerkships at that regional campus because of family, financial, and other individual reasons and would be permitted to do so. These students may complete many of their required clinical clerkships, up to eleven, at the regional hospitals. Students at Indianapolis would complete three or four of their required clerkships outside the metropolitan Indianapolis area in major hospitals where our campuses are located. At steady state, we expect there to be at least eighty-four (84) students annually in clinical rotations statewide, not at Indianapolis.

Discussions have begun with hospital administrators and physicians in two regions where a regional medical school campus does not currently exist. These new potential "clinical" campuses would include Reid Hospital in Richmond, IN; and Floyd Memorial and Clark Memorial Hospitals in New Albany IN and Clarksville, IN, respectively. These are areas of physician shortages yet each carries a population base and excellent hospital facilities that would be ideally suited for clinical education of medical students. In addition, it would provide students with experiences among community physician practices for comparable careers after residency training.

3. Faculty and Staffing Model

The Center Director, in the role of the chief academic officer at the regional medical school campus, will oversee the third- and fourth-year clinical clerkships. Each clinical center will need a Clinical Coordinator to coordinate these clerkships. The responsibilities of this coordinator will include: assisting with the educational programming; acting as a liaison among campuses; assisting the clerkship directors in recruitment and retention of community-based volunteer faculty; acting as an administrative liaison among the students, faculty, and administration of the regional campuses and the hospitals; and ensuring all faculty achieve volunteer or adjunct appointments in the Indiana University School of Medicine.

All clinical clerkships at the regional centers will each require an assistant clerkship director for each specialty rotation. The assistant clerkship director will be responsible for delivering the educational objectives of the clerkship; assuring adequate patients for teaching; recruiting necessary community-based volunteer faculty from the medical staff; mentoring the medical students; and providing individual, career, or academic counseling as needed. Assistant clerkship directors will be responsible for reviewing all evaluations of medical student performance, test results, competency evaluations, and other evaluative materials, prior to subsequent forwarding to clerkship and competency directors in IUSM Indianapolis, where final grades for the clerkships and rotations are determined.

Community-based practicing physicians will be recruited as volunteer faculty for the clinical rotations. These individuals will earn volunteer or adjunct faculty appointments; gain access to the Ruth Lilly Library resources; and participate in the IUPUI academic e-mail systems.

Due to the overall increased number of students in our IUSM expansion plans, the Offices of Medical Education and Curricular Affairs, Medical Student Affairs, and the Simulation Center will need additional personnel and funding.

4. Housing for students in clerkships at the eight centers

Medical students who rotate for 4-6 week clerkships at campuses away from their home base will require housing provided by the IU School of Medicine or the host campus or hospital.

5. Specific New Programs at the Regional Centers

IUSM intends to enhance the curriculum of its regional education campuses with emphasis upon the health and medical needs of their community's population, whether urban, rural, or underserved. For example, the School has already implemented a Rural Health education program at the Terre Haute Center to ensure that Indiana's rural communities are served with adequate numbers of primary care physicians. In addition, our Northwest Center's curriculum will emphasize urban medicine and health disparities among economically challenged urban population. A team of experts from IUSM-Northwest and the Dean's Office of Medical Education and Curricular Affairs are together developing a new curricular theme for the regional campus.

Costs and Budget Overview

The statewide infrastructure of IUSM provides an attractive economical model to expand the enrollment of medical students to provide the state of Indiana with its requisite physicians to care for its citizens. The proposed budget would serve as an increase in base support to the medical school, so IUSM can accomplish the expansion goals as described.

The budget presented below outlines the costs of the plan annually until it reaches full implementation in 2016. The budgeted dollars are driven by: number of clerkships and the enrollments in those clerkships by center and location. Understandably, in this revised model, some projections could potentially change, depending upon: success in recruiting volunteer preceptors; participation of regional and critical access hospitals; and student enrollments in the various clerkships and electives. IUSM's experience delivering medical education statewide provides cost-effective regional platforms for this expansion plan.

INDIANA UNIVERSITY SCHOOL OF MEDICINE
MEDICAL STUDENT ENROLLMENT EXPANSION
REVISED IMPLEMENTATION PLAN: BUDGET VERSION 25AUGUST2009

		Single Campus Cost	Fiscal Year: 2010 All Centers	2011 All Centers	2012 All Centers	2013 All Centers	2014 All Centers	2015 All Centers
	EXPENDITURE BUDGETS							
1	**Existing RMC Operating Budgets**	*(FY 2010)*	$ 13,702,690	$ 14,048,677	$ 14,470,138	$ 14,904,242	$ 15,351,369	$ 15,811,910
	Expansion Budget Requirements							
	1st and 2nd Year Expansion Costs:							
2	Total Increased Absentia Fees		$ 37,528	$ 41,806	$ 46,497	$ 50,891	$ 100,046	$ 189,169
3	Total Increased Facilities Operating Costs		$ 1,082,954	$ 1,126,272	$ 1,171,323	$ 1,218,176	$ 1,266,903	$ 1,925,906
	Subtotal - 1st and 2nd Year Expansion Costs		**$ 1,120,482**	**$ 1,168,078**	**$ 1,217,820**	**$ 1,269,068**	**$ 1,366,949**	**$ 2,115,075**
	3rd and 4th Year Expansion Costs:							
4	Clinical Coordinator (salary plus fringe)	$ 100,000	$ 400,000	$ 832,000	$ 973,440	$ 1,012,378	$ 1,169,859	$ 1,216,653
5	Clerkship Costs	$ 25,000	$ 775,000	$ 1,144,000	$ 1,324,960	$ 1,574,810	$ 1,959,513	$ 2,037,894
6	Payment to Clinical Instructors (Community MDs) *(IUSM Clin. Teaching Cost @ mkt rates / 280 students * 84 new students / 82 clerkships)*	$ 123,659	$ 3,624,319	$ 5,349,963	$ 6,954,952	$ 8,942,803	$ 11,625,645	$ 13,797,588
7	Regional clinical competency evaluations and simulations		$ 16,800	$ 17,472	$ 22,714	$ 42,520	$ 44,221	$ 51,099
8	Facilities Costs for New/Expanded Facilities *(5000 s.f. * $23.00/s.f. annually, incl. utilities)*	$ 115,000	$ 460,000	$ 837,200	$ 870,688	$ 1,164,234	$ 1,345,337	$ 1,399,151
9	Administrative Costs at the RMCs *(Incl. one clerical posn, one I/T posn, one development posn, phones, computers, etc.)*	$ 121,623	$ 469,272	$ 976,086	$ 1,142,020	$ 1,187,701	$ 1,372,455	$ 1,427,353
10	IUSM Central Admin. Costs (Includes All 4 yrs)	$ 184,626	$ 1,720,067	$ 1,788,870	$ 1,860,425	$ 1,934,842	$ 2,012,236	$ 2,092,725
11	Housing for 8 students/campus based on renting 4 apartments for a year that would accommodate the students ($80k/campus)	$ 80,000	$ 320,000	$ 332,800	$ 692,224	$ 809,902	$ 842,298	$ 973,322
12	Faculty Development	$ 15,000	$ 60,000	$ 140,400	$ 146,016	$ 151,857	$ 175,479	$ 182,498
13	Testing Materials (1st and 2nd yr students)	$ 5,920	$ 29,600	$ 1,471	$ 2,520	$ 3,837	$ 5,353	$ 8,908
14	Testing Materials (3rd and 4th yr students)	$ 3,300	$ 13,200	$ 13,728	$ 32,124	$ 37,121	$ 34,745	$ 40,150
	3rd and 4th Year Expansion - Total Cost	**$ 784,948**	**$ 7,888,259**	**$ 11,433,990**	**$ 14,022,082**	**$ 16,862,004**	**$ 20,587,139**	**$ 23,227,341**
	TOTAL - Base (Ongoing) Expansion Budget Requirements		**$ 9,008,741**	**$ 12,602,068**	**$ 15,239,902**	**$ 18,131,072**	**$ 21,954,088**	**$ 25,342,416**
	TOTAL - RMC EXISTING AND EXPANSION EXPENDITURE BUDGET REQUIREMENTS		**$ 22,711,431**	**$ 26,650,745**	**$ 29,710,040**	**$ 33,035,314**	**$ 37,305,457**	**$ 41,154,326**
	LESS:							
	Existing Regional Medical Campus + Medical Sciences Program Budgets		$ 13,702,690	$ 14,048,677	$ 14,470,138	$ 14,904,242	$ 15,351,369	$ 15,811,910
15	Total Tuition Revenue from Expansion (70% R; 30% N-R)		$ 2,272,270	$ 2,991,294	$ 3,525,739	$ 4,170,050	$ 5,159,358	$ 6,221,139
16	Cost Share - Host Campuses: Total Increased Absentia Fees		$ 37,528	$ 41,806	$ 46,497	$ 50,891	$ 100,046	$ 189,169
17	Cost Share - Community MDs: Payments to Clinical Instructors		$ 3,624,319	$ 5,349,963	$ 6,954,952	$ 8,942,803	$ 11,625,645	$ 13,797,588
18	Cost Share - Hospital Partners: Facilities Costs for New/Expanded Facilities		$ 460,000	$ 837,200	$ 870,688	$ 1,164,234	$ 1,345,337	$ 1,399,151
	Less Total Existing Funding Sources, New Tuition Revenue, and Cost Shares		**$ 20,096,807**	**$ 23,268,940**	**$ 25,868,013**	**$ 29,232,221**	**$ 33,581,755**	**$ 37,418,958**
	TOTAL - REGIONAL MEDICAL CAMPUS FUNDING REQUEST		**$ 2,614,624**	**$ 3,381,805**	**$ 3,842,027**	**$ 3,803,093**	**$ 3,723,702**	**$ 3,735,368**

Footnotes/Assumptions:

1 State line item budget, inflated at 3.0% per year beginning FY 2012.
2 Represents only absentia fees charged for expansion (additional) students at RMCs where host institution assesses this fee. Inflated at 4.0% per year.
3 Represents only cost of new Ft. Wayne facility and new South Bend facility for which there was no plant expansion funding provided by the State.
4 Assumes one clinical clerkship coordinator per RMC starting at $71,124 plus fringe benefit costs. Inflated at 4.0% per year. Each RMC's clerkship coordinator assumed hired one year prior to students being enrolled in its clerkships.
5 Some RMCs assumed to have 11 clerkships, other RMCs assumed to have less. 11 clerkships per RMC at $25,000 per clerkship = $275,000 per RMC. Inflated at 4.0% per year.
6 Applies FY 2006 IUSM 3D Cost of Education Analysis by dividing $33,800,000 total clinical teaching cost by 280 students to arrive at a cost per clinical student (3rd or 4th year) of $120,714, or an average cost per RMC of $1,013,832, and
7 To reimburse students for cost of traveling to other RMCs to take clerkships. Assumes 15% of expansion students traveling to other RMCs in any given year for this purpose. Assumes $1,000 annual cost per traveling student. Inflated at 4.0% per year.
8 These facilities costs represent space required for 3rd and 4th year students to assemble for group didactic teaching and other required functions. Inflated at 4.0% per year.
9 Additional administrative costs result from a 30% increase in students.
10 Additional administrative costs result from a 30% increase in students.
11 To cover the cost of temporary housing for students who are traveling to RMCs other than their assigned/home RMC for the purpose of taking clerkships. Inflated at 4.0% per year.
12 To cover the increased cost to central organizations, such as MECA and he Office of Faculty Affairs and Professional Development of providing faculty development and training opportunities to RMC faculty, including volunteer faculty. Inflated at 4.0% per
13 To cover costs of additional NBME exams at $40 per exam plus a $100 score charge per respective discipline for only additional 1st and 2nd medical students.
14 To cover costs NBME exams at $40 per exam plus a $100 score charge per respective clerkship for only additional 3rd and 4th medical students.
15 Projection of tuition paid by expansion (additional) students, assuming 70% are residents and 30% non-residents. Begins with actual FY09 tuition and inflates by 4.0% per year.
16 Additional Host Campus charges associated with medical student expansion.
17 Assumes host institutions, hospitals, and community physicians will contribute these costs to IUSM and not charge for them. If this does not occur, IUSM will need to request that support from the State. The worst case scenario if there is no "cost-sharing".
18 Minor renovations to existing RMC facilities needed in order to accommodate increased class size (expansion students). This is a one-time cost.

INDIANA UNIVERSITY SCHOOL OF MEDICINE
MEDICAL STUDENT ENROLLMENT EXPANSION
REVISED IMPLEMENTATION PLAN: BUDGET VERSION 25AUGUST2009

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1ST AND 2ND YEAR Medical Student Headcount Expansion Plan By Regional Medical Campus

Biennium:		2007-09		2009-11		2011-13		2013-15			
Fiscal Year:		2008	2009	2010	2011	2012	2013	2014	2015		
Matriculation Year:		2007	2008	2009	2010	2011	2012	2013	2014		
Graduation Year:		2011	2012	2013	2014	2015	2016	2017	2018	New Students	Expansion Total
Regional Medical Campus	Current Students										
IUSM-Terre Haute otco ISU	16	8								8	24
IUSM-Muncie otco BSU	16	6	2							8	24
IUSM-Ft. Wayne otco IPFW	16			5	3	6	2			16	32
IUSM-South Bend otco UND	16		6	2			6			14	30
IUSM-Evansville otco USI	16							4	4	8	24
IUSM-Lafayette otco PU	16							4	4	8	24
IUSM-Northwest otco IUNW	18		6	2				2	4	14	32
IUSM Medical Sciences Program - Bloomington	28			5	3					8	36
IUSM-Indianapolis	138									-	138
Total	280	14	14	14	6	6	8	10	12	84	364
Total School		$ 294	$ 308	322	328	334	342	352	364		

3RD AND 4TH YEAR Clerkship Expansion Plan By Regional Medical Campus

Biennium:		2007-09		2009-11		2011-13		2013-15		
Fiscal Year:		2008	2009	2010	2011	2012	2013	2014	2015	
Matriculation Year:		2007	2008	2009	2010	2011	2012	2013	2014	
Graduation Year:		2011	2012	2013	2014	2015	2016	2017	2018	
Regional Medical Campus										Projected Clerkship Capacity by Site
IUSM-Terre Haute otco ISU				6	5					11
IUSM-Muncie otco BSU							2	4		6
IUSM-Ft. Wayne otco IPFW				6	5					11
IUSM-South Bend otco UND			8	3						11
IUSM-Evansville otco USI						3	3	5		11
IUSM-Lafayette otco PU						2	2	2		6
IUSM-Northwest otco IUNW			1	7	3					11
IUSM Medical Sciences Program - Bloomington									8	8
IUSM-Richmond						3	3	3	2	11
IUSM-New Albany						3	3	3	2	11
IUSM-Indianapolis										
Total New Clerkships		0	9	22	13	11	13	17	12	97

Indiana Innovation Alliance
Purdue University--Technical Assistance and Advanced Education
$2,000,000 2009-10 $2,000,000 2010-11

Purdue proposes to use Indiana Innovation Alliance funds to support three specific programs: pharmacy residency in communities across Indiana, post graduate specialized education in biomedical engineering, and technical assistance to rural hospitals. These elements are described below.

I. Postgraduate Pharmacy Residency

We propose to establish 20 postgraduate pharmacy residents in at least 15 training sites across Indiana. This will enable us to reduce the 'brain-drain' of pharmacy graduates seeking advanced training and improve healthcare outcomes. As the complexity and cost of pharmaceuticals continues to increase, the need for pharmacists with advanced training becomes increasingly important in assuring optimal healthcare outcomes.

The training cycle for postgraduate pharmacy residents is July 1 to June 30. December is the key recruitment month and the first group of residents would begin July 1, 2010. Purdue will immediately hire a faculty coordinator and support staff, negotiate agreements with residency sites, recruit candidates, and develop a reporting and evaluation structure.

Tentative sites at which we plan to place residents are indicated below. We have had preliminary discussions at several of these sites, each of which has expressed high interest in partnering with Purdue in postgraduate residency training. Final site selection will depend on successfully completing collaboration agreements with the residency institutions. Some sites may have two residents, and more sites may be identified. In the event a collaborative agreement cannot be reached with a particular institution, we will place multiple residents at other locations or add new sites.

Proposed Pharmacy Residency Sites	Location	Setting
Clarian/Arnett	Lafayette	Health System
Fagen Pharmacy	Valparaiso	Community
Freedom Pharmacy	Indianapolis	Long Term Care
Good Samaritan	Vincennes	Health System
Lutheran Health	Fort Wayne	Health System
Medco	Zionsville	Mail-Order
Memorial Health	South Bend	Health System
Porter	Valparaiso	Health System
St. Anthony Memorial	Michigan City	Health System
St. Mary's	Evansville	Health System
Supervalu	Northwest IN	Community
Union Hospital	Terre Haute	Health System
Williams Brothers	Washington	Community
Wishard Health Services	Indianapolis	Health System

II. Post-Graduate Specialization in Biomedical Engineering

For more than 30 years, Purdue biomedical engineers have been making technical breakthroughs that improve the lives people around the world. Implantable defibrillators, natural tissue repair devices, implantable drug delivery systems, and novel artificial joints are just a few of the

technologies designed and developed by the Weldon School of Biomedical Engineering. Rapidly evolving technologies in biomedical engineering has created a need for an advanced education and professional development masters program targeted specifically toward working engineers and scientists.

Target Audience. Purdue will offer a masters-level training program aimed at working engineers and scientists, with a focus on enhancing technical and scientific skills and knowledge that will advance their careers in the broad fields of biomedical engineering, bioengineering, and biotechnology. A wide range of professionals are expected to take advantage of this non-thesis degree training. Useful background for this degree will include experience or undergraduate coursework in basic biology, mechanics, electronics, and statistics/probability.

A unique feature of this program will be its emphasis on practical regulatory affairs at both the initial approval and compliance stages. Students will gain valuable in-depth knowledge of regulatory requirements as well as guided practice with effective regulatory document submissions. This advanced education in quality and regulatory compliance will prepare students for rapid integration into regulatory affairs teams in critical areas of the medical products industry.

We anticipate that the majority of the students enrolling in this program will be working in, or associated with Purdue partner companies. Purdue currently has over 30 partner companies throughout Indiana (e.g., in Bloomington, Warsaw, Fort Wayne, Batesville, Indianapolis) and an even larger regional pool, from which to draw students.

Faculty. Faculty for this masters program will come primarily from the Weldon School of Biomedical Engineering, with additional expertise available through the various schools of engineering that participate in Engineering's distance education programs. Additional content and specialized training will come from experts selected from our partner companies.

Degree Objectives. Professionals completing this Purdue Biomedical Engineering specialization program will possess:

- New technical and scientific knowledge in biomedical engineering
- Skills in translating ideas into medical products
- Demonstrated ability to prepare regulatory documentation
- Heightened awareness of emerging technologies and novel biomedical engineering applications

This degree will require 30 credit hours of coursework. Of these, 18 credits must be in engineering. Following admission, each student will have responsibility to develop a plan of study requiring approval of their academic advisory committee.

Delivery Format. Courses will be available primarily through streaming video over the internet and downloadable MPEG-4 files. Enrolled students will be able to interact with course materials at any time and place during the semester. Students also can interact with faculty and staff through electronic communication avenues. This format provides a nearly unlimited capacity for student participation with a dedicated focus on the working engineer/scientist.

Future Business Model. Our goal is to grow enrollment to where this specialized training program becomes self-sustainable in terms of faculty and staff support. In the steady state, some

additional support will likely be required for infrastructure staff support, technology upgrades, as well as ongoing marketing and promotion. At some point after the initial roll-out period we anticipate the enrollment will be 20 to 30 participants per course. Not all of these will be pursuing the full M.S.E. / M.S. degree training. Some may be only seeking to upgrade specific skills areas or technical deficits. By offering an average of five courses per year, at our projected steady state enrollment, we project that the registration revenues will generate a revenue stream sufficient to sustain the instructional costs of the program. Approximately $100,000 additional revenue will be needed to pay for equipment upgrades and maintenance, continued course development, marketing and promotion.

III. Technical Assistance to Rural Healthcare Providers

Applying science and engineering principles to healthcare delivery reduces costs. These strategies contain costs by implementing best practices and developing more efficient healthcare systems, without compromising care. Purdue's Healthcare Technical Assistance Program (HTAP) has developed training and management tools that are quite effective in reducing costs in hospitals and other healthcare organization. The cost of this program is typically about $25,000 and is typically recovered within 6 to 12 months. Rural hospitals have been slow to implement this program.

Program Delivery: Healthcare TAP is prepared to start immediately to:

- Deliver its Lean Healthcare curriculum to approximately 40 rural and critical access hospitals over the next two years. The primary objectives will be to: a) improve clinical quality, productivity, and safety, b) contain operating expenses, and c) help keep rural hospitals open.
- Deliver the curriculum to approximately 800 employees. Each participant will receive the HTAP Lean Healthcare certificate. CEU's are available.
- Assist participating employee with projects that address enhanced productivity and regulatory compliance, including new Medicare and Medicaid regulations

Expected Training Outcomes: Recent examples of training outcomes with several hospitals include the following:

- Operating Room savings of $1 million in supply costs within 6 months
- Overtime savings of $100,000
- Increased productivity by 12%
- Decreased patient wait time by 30%
- Decreased overtime pay by 30% within six months
- Decreased "admit to bed" time by 50% (before completion of the training).

HTAP will target 40 hospitals in rural communities at an anticipated average cost of $25,000 each, for a total of $1 million over two years ($500,000 each year).

Proposed Budget

Program	2009-10	2010-11
Postgraduate Pharmacy Residency		
Faculty and staff salaries & benefits	$200,000	$200,000
Resident salaries & benefits (20@ $65,000)	NA	1,300,000
Post-Graduate Specialization in Biomedical Engineering		
Curriculum Development	200,000	150,000
Infrastructure Development	200,000	50,000
Instructional Support	150,000	250,000
Administrative Support	100,000	100,000
Engagement and Marketing	50,000	50,000
Totals	700,000	600,000
III. Technical Assistance to Rural Healthcare Providers		
HTAP assistance costs (20 per year @$25,000)	500,000	500,000
Totals	$1,400,000	$2,600,000
Two year total	$4,000,000	

Appendix 1: Biomedical Device and Bionanotechnology Core

Commercialization and Industrial Interactions

Private Sector Collaborators: Cook (Bloomington and West Lafayette), Biomet (Warsaw), Depuy (Warsaw), Zimmer (Warsaw), Hill-Rom (Batesville), Aptuit (West Lafayette), Ft. Wayne Metals (Ft. Wayne), Nanovis (West Lafayette), Intelliphage (West Lafayette), BioVitesse (West Lafayette).

Start-up Companies: The following new companies in the life sciences sector have been assisted or enabled by Discovery Park or the Weldon School for Biomedical Engineering at Purdue University.

BioVitesse, Akina (drug delivery), Andara Life Sciences (spinal cord repair), Moerae Matrix (molecular therapeutics), Cook Biotech (tissue engineering), Nano Vis (orthopedics), SonarMed(critical Care), Glytrix (wound healing).

Examples of Recent Invention Disclosures at Purdue in the Life Sciences: The following is a selection of Purdue invention disclosures relating to biomedical devices or bionanotechnology submitted during the first six months of 2009:

- Use of an MK2 Inhibitor to Enhance Nerve Regeneration
- Development and application of purified collagen technology
- Collagen-Binding Peptidoglycans for Wound Healing
- Biomimetic biodegradable scaffolds for the enhancement of nerve & tissue regeneration
- A Diagnostic Tool for Detection of Otitis Media
- A Device that is Used for the Immediate Onset of Hypoglycemic Events
- An Alarm System for Injecting an Anti-Hypoglycemic Solution
- A Device that Injects an Anti-Hypoglycemic Solution
- Living Cell Biosensor Using Electrochemical Detection of Pyocyanin
- Variable Volume Mixing and Automatic Fluid Management for Programmable Microfluidics
- AFM-Coupled Microscale Radiofrequency Probe for Magnetic Resonance Imaging Spectroscopy
- Directed Attraction and Wiring of Neurons to Implanted Electrodes by DSCAM-Silica Sol-Gel Coatings
- Miniature Stent-based Implantable Wireless Monitoring Devices
- A nanofluidic channel with embedded transverse nanoelectrodes
- Effective Repair of Traumatically Injured Spinal Cord by Block Copolymer Micelles: A Pilot Study
- Ultra-Soft Atomic Force Microscope (USAFM) for Biological Applications

Purdue Nanotechnology Resources in Discovery Park and the Weldon School of Biomedical Engineering

Weldon School of Biomedical Engineering at Purdue University

The Weldon School of Biomedical Engineering at Purdue University is built on a tradition of applied research with significant industrial and clinical ties. The School is rapidly expanding its educational programs, research capacity, and extramural partnerships to meet a broader set of healthcare and life science needs. This expansion over the past decade includes hiring 20 new faculty members, tripling the size of its graduate programs, and constructing a $25M state-of-the-art facility. Through this strategic growth, the Weldon School is positioning itself at the academic forefront of engineering applied to medicine. A culture of innovation and entrepreneurship in biomedical engineering at Purdue has been fostered for over 30 years, beginning with the formation of the Hillenbrand Biomedical Engineering Center by Leslie Geddes in 1974. This culture is maintained today as evidenced by collaborative development projects between AMIPurdue and four different BME faculty members, the continuous stream of disclosures and the numbers of startup companies formed around Weldon School disclosures. Located across the street from Purdue's Discovery Park, The Weldon School is situated ideally to impact the Biomedical Device and Bionanotechnology Core.

Discovery Park at Purdue University

The Birck Nanotechnology Center is one of nine core centers in Purdue's $400M 40-acre Discovery Park. Discovery Park provides an intellectual environment and facilities for multidisciplinary approaches to interdisciplinary challenges and opportunities spanning the domains of energy, the environment, healthcare, economic development, information access and homeland security. *Discovery* is intimately coupled with *delivery* in Discovery Park. Whether it be commercialization, community outreach, public policy, education or clinical translation, researchers in Discovery Park have their sights set on impact, and the resources and expertise needed to expedite the process to impact are integrated into the fabric of Discovery Park.

The Birck Nanotechnology Center in Discovery Park

Overview. The Birck Nanotechnology Center (BNC) is an interdisciplinary research unit that provides infrastructure for 160 affiliated faculty members and their research groups from 36 academic units at Purdue. The new 187,000 sq ft. facility includes a 25,000 sq. ft. ISO Class 3-4-5 (Class 1-10-100) nanofabrication cleanroom – the Scifres Nanofabrication Laboratory – that includes a 2,500 sq. ft. ISO Class 6 (Class 1000) pharmaceutical-grade biomolecular cleanroom. In addition to the cleanroom, the facility provides 22,000 sq. ft. of specialized laboratories and offices for 45 resident faculty members, 30 post-docs, 30 staff, and approximately 200 graduate students. A flexible Nanotechnology Incubator lab may be leased by companies through the Purdue Research Foundation.

All of the equipment in the BNC is shared, and is accessible to qualified and trained users from Purdue and from academic, industrial, and government laboratories outside Purdue. Most of the major equipment is available through recharge centers that support maintenance, supplies and the time of dedicated staff scientists. Support for the facility, equipment, and processes is provided by a staff of 24 scientists, engineers, and support personnel with over 425 years of experience in academia and industry. Five of these staff members are Ph.D.-level scientists.

The Scifres Nanofabrication Laboratory

Cleanroom. The nanofabrication cleanroom consists of 25,000 sq. ft. of bay-chase cleanroom, with 45% of the bays operating at ISO 3 (Class 1), 40% operating at ISO 4 (Class 10), and the remaining 15% operating at ISO 5 (Class 100). The three-level structure consists of a full subfab, the cleanroom level, and an air-handling level above the cleanroom. A perforated raised floor ensures unidirectional airflow and bulkhead-mounted equipment separates operational functions from maintenance functions. A combination of careful control of the airflow path, multiple stages of filtration, careful choice of materials, and non-ionic-steam humidification ensure the control of both particulate and molecular contamination. A very tight waffle slab provides NIST "A" vibration rating, approximating quiet, slab-on-grade construction.

Lithography. Lithographic capability spans the nano and micro scale, with the capability of integrating nanoscale structures within micro-scale devices. A Vistec VectorBeam VB-6 UHR-UWF electron-beam lithography system provides the capability of 6 nanometer lines in resist across a 1.3 mm field. A Raith e-beam nanolithography system is scheduled to arrive in December 2007, and will provide 20 nanometer resolution. An interference lithography system provides 100 nanometer resolution for less-critical operations.

Optical lithography is used in many operations in BNC, and is supported by a maskmaking operation and single- and double-sided mask alignment. 10x and 5x Criss-Cross Pattern Generator/Step-and-Repeat maskmaking systems, coupled with specialized image-reversal systems, provide a variety of photomasks to support research efforts.

Etching. Wet- and dry-etch capabilities allow the etching at high aspect ratios in a variety of materials. Two STS DRIE systems, a xenon difluoride etcher, an Oxford PlasmaTech system, and a Panasonic chlorine/fluorine system anchor the etching capabilities.

Deposition. Metal deposition is a strength in the BNC. Six evaporators and three sputterers allow the deposition of more than 20 different materials. Additionally, plasma-enhanced deposition systems and an LPCVD system provide further capabilities. Of special interest are two atomic-layer-deposition (ALD) systems designed especially for high-integrity high-k dielectric films.

Furnaces. A three-tube bank of process furnaces include clean (i.e., gate) oxidation, LTO, and LPCVD capabilities. This is supplemented by a separate two-tube pyrogenic oxidation system and several smaller high-temperature tubes and lower-temperature annealing tubes. Low temperature annealing and activation can be performed on two rapid-thermal-processing systems.

Ultra-Pure Water. The ultra-pure water (UPW) system at BNC supplies all laboratories and the cleanroom with incredibly pure water. Termed nano-grade water, this water is below the measurement limits of 15 parts per trillion of boron, the ion most loosely bound to the mixed beds and therefore the most likely ionic impurity in the water. This water also contains less than 225 parts per trillion of total oxidizable carbon (TOC) and less than 1 part per billion of dissolved oxygen.

Biocleanroom. Integrated into the Scifres Nanofabrication Laboratory is a pharmaceutical-grade cleanroom to allow sterile processing. This cleanroom is entered through a separate gowning room and has a completely separate air-handling system, but has a pass-through to the nanofabrication cleanroom to allow materials to be transferred into this facility without breaking cleanliness. Designed for sanitization, it trades a perforated floor for coved sheet-vinyl flooring and boasts a special pharmaceutical wall and ceiling system. Outside the entrance to the biocleanroom is an enclosed overhead walkway to Bindley Bioscience Center.

Specialized Laboratory Facilities

Overview. In addition to the cleanroom, the BNC includes a suite of specialized laboratories that provide outstanding capabilities to researchers. All BNC laboratories are designed for low acoustic noise, less than 1 milligauss EMI, and +/- 1 degree C temperature stability. Additionally, the first-floor laboratories achieve NIST A vibration rating. From this base, certain laboratories have been modified to provide even more stringent limits to accommodate specialized needs. For example, the TEM laboratory has tighter temperature controls, has specialized airflow patterns, and has special acoustic materials on the walls and floors.

Hall Nanometrology Laboratory and Scanning Tunneling Microscopy. For highly sensitive functions, the Kevin G. Hall Nanometrology Laboratory provides enhanced control of temperature, vibration, acoustic noise, and EMI. Temperature is controlled to +/- 0.01 degree C, EMI is controlled to less than 0.1 milligauss, acoustic noise is within NC-35 criteria, and vibration is controlled to NIST A-1 criteria. An Omicron UHV Scanning Tunneling Microscope located in the laboratory allows the study and manipulation of materials on the atomic scale.

Scanning Laser-Doppler Vibrometry. A specialized laboratory that meets NIST A-1 vibration criteria houses the Scanning Laser-Doppler Vibrometer. The Polytec MSA-400 Micro System Analyzer uses a variety of methods to characterize motion in micro- and nanostructures.

Scanning Probe Microscopy. Seven atomic force microscopes provide topographical data on surfaces as well as allowing the manipulation of materials at the nano scale.

Electron Microscopy. Four electron microscopes provide the ability to image nanoscale devices and materials, as well as to study reaction mechanisms at the atomic scale. An FEI Titan 80-300 keV Field Emission Environmental Transmission Electron Microscope – Scanning Transmission Electron Microscope provides resolutions to 0.7 by 1.0 Angstrom units. The system contains an in-situ reaction chamber, and is equipped with a high-performance camera and data server.

Supplementing the capabilities of the Titan are an FEI Field-Emission Scanning Electron Microscope, an FEI "Novalab" Focused Ion Beam – Scanning Electron Microscope system, and a dual-function JEOL Scanning Electron Microscope with electron-beam direct-write capability.

Surface Analysis. The surface analysis laboratory contains a Kratos Imaging x-Ray Photoemission Spectrometer (XPS) with an in-situ reaction cell and an Omicron surface analysis cluster tool. The XPS has a 15 micrometer spot size, and provides atomic-level analysis of materials. The cluster tool contains multiple devices to characterize the surfaces of materials, including a high-resolution electron-energy-loss spectrometer (EELS), a scanning electron microscope (SEM), a scanning auger spectrometer, a hemispherical electron spectrometer for XPS, AES, UPS, ISS, and a focused ion beam (FIB) system – all connected under ultra-high vacuum.

x-Ray Diffraction. The x-ray diffraction laboratory contains a high-resolution PANalytical "x"Pert Pro x-ray diffraction system.

Epitaxy. Several BNC laboratories contain equipment for specialized, highly precise epitaxial growth. A Varian Gen II Molecular Beam Epitaxy system for III-V epitaxy, an Epigress VP-508 hot-wall CVD reactor for SiC, and an Aixtron AIX 200/4 metal-organic chemical vapor deposition (MOCVD) system for GaN, allow the growth of a variety of homoepitaxial and heteroepitaxial materials .

Deposition. An ASTeX plasma-enhanced chemical vapor deposition system allows film growth of specialized materials.

Biosafety Level 2 Laboratories. The BNC has two biosafety level 2 laboratories, one containing two tissue-culture rooms that operate at biosafety level 2+. These specialized laboratories allow for the safe handling of biological materials used in the development of devices and delivery methods.

Biosafety Level 1 and Nanochemistry Laboratories. The BNC also provides four laboratories for less hazardous nano-bio and nanochemistry research. These laboratories, classified at BSL-1 or below, are used for both mechanical and wet-chemical research activities.

Electrical Characterization Laboratories. A significant amount of BNC laboratory space is allocated to electrical characterization. From a soon-to-be-operational 8 Tesla, liquid-helium-cooled Hall Effect measurement system to multiple shielded probe stations with hot and cold testing capabilities, these laboratories provide the equipment and facilities necessary to evaluate new materials, structures, and devices.

Laser Laboratories. Specialized laboratories for optical materials development, optically enhanced deposition, and optical characterization methods have been implemented in the BNC. Using lasers of various power levels – up to Class 4 – BNC researchers are able to develop materials, processes, and devices for energy conversion and other applications. These laboratories also support research strengths in nanoelectronics and nanophotonics.

Nanoincubator Laboratory. The BNC provides flexible laboratory space that can be leased by companies through the Purdue Research Foundation. This space is designed to provide a secure, specialized laboratory for companies wishing to use the infrastructure of the BNC while maintaining private laboratory space for specialized or proprietary work.

Indiana University Nanotechnology Resources

IUB NANOSCIENCE CENTER

Research in Self-Assembly at Indiana University

The strength of Purdue University is in device development. An emerging strength at IU, which is complementary to Purdue's strength, is in self-assembly. IU has several well-established groups investigating assembly processes in natural and synthetic systems. How molecules assemble to form complex functional systems, from viruses, to cells, to humans is poorly understood. We are developing a physical, chemical, and biological understanding of these processes. With this knowledge we should be able to mimic these capabilities in artificial systems and develop applications in drug delivery, biomedical engineering, electronics, optics, and related fields. This research effort is multidisciplinary and brings together research groups from Chemistry, Physics, and Biochemistry.

Self-assembly often spans a wide range of length scales and time scales. The wide range of scales involved makes it difficult to study, and there is a lack of suitable tools. To fill this void, groups at IU are developing new analytical methods and theoretical tools to investigate self assembly. Knowledge of assembly processes is expected to lead a number of applications, including therapeutic opportunities (antiviral vaccine development). In addition, these studies will lead to potential opportunities in drug delivery, for example using virus capsids as delivery vectors to carry a drug to its target, such as a cancer cell. Another application of this research is in the development of novel materials: For example, metamaterials with unique optical dielectric properties can be made by self-assembly. Other groups at IU are investigating self assembly on surfaces. These studies can lead to surfaces with tailored properties with potential practical applications, e.g. planes that do not require de-icing. It should also be possible to design surfaces of which certain properties change in response to the environment. Other groups seek to exploit self-assembly of specially designed molecules to achieve tailored molecular architectures or functions such as the conversion of chemical energy into motion. All these studies require a well-developed infrastructure that includes theoretical groups and state of the art characterization tools.

IUB - Nanoscale Characterization Facility

The Nanoscale Characterization Facility (NCF) is housed on the ground floor in Simon Hall, our multidisciplinary sciences building, and has 2000 ft^2 of laboratory space and 1300 ft^2 of clean room space. The NCF will provide faculty, staff, postdoctoral fellows, and graduate and undergraduate students with state-of-the-art instrumentation for generating and characterizing materials having features with nanometer dimensions. We expect the NCF to grow over the next three to five years as a university resource, and the instrumentation within the facility will be available to all research groups at IU.

NCF Equipment (Simon Hall):

JEOL JEM-3200FS Cryogenic Transmission Electron Microscope. The JEOL JEM 3200FS transmission electron microscope (TEM) is an intermediate voltage (300 kV) electron microscope. This electron microscope uses a thermal field emission gun (FEG) as its electron source, providing an extremely bright and coherent beam of electrons for use in imaging and analysis. The 3200FS installed in Simon Hall is equipped with an in-column energy filter and a Gatan UltraScan 4000 CCD camera. In addition to the TEM capabilities of the 3200FS, the instrument is also equipped with scan coils and detectors that allow it to function as a scanning transmission electron microscope (STEM).

FEI Quanta 600F Scanning Electron Microscope. The Quanta 600F scanning electron microscope (SEM) is a versatile, high-performance instrument with three modes (high vacuum, low vacuum, and environmental) to accommodate the widest range of samples of any SEM system. The SEM system is equipped with an energy dispersive spectrometer and electron backscatter detector. In addition, the field emission gun (FEG) system contain a S/TEM detector for bright-field and dark-field sample imaging. The motorized stage has 150mm of travel in the X and Y directions and 60 mm of travel in the Z direction.

JC Nabity Lithography Systems Nanometer Pattern Generation System. The nanometer pattern generation system (NPGS) provides a user-friendly environment for the delineation of complex structures using a commercial electron microscope, e.g., FEI Quanta 600F. The SEM combined with NPGS is a powerful lithography tool for basic research and R&D applications and can be used for the fabrication of a wide variety of devices. Pattern sizes may range from the nanometer scale up to the maximum field of view of the microscope, which can be as

large as 10 mm. There are three basic steps to the pattern generation process: pattern design, parameter run file creation, and pattern writing with alignment for multilevel lithography.

Asylum Research MFP3D Atomic Force Microscope. The MFP-3D integrates optical microscopy and atomic force microscopy (AFM). Sample features are located using brightfield, phase contrast, or fluorescence, then probed at the nanometer scale with an AFM scan. AFM is combined with such powerful optical microscopy techniques as confocal microscopy, including the capability to synchronize with confocal measurements. The superluminescent diode and additional optics minimize interference with fluorescent signals. Advanced software capabilities allow the researcher to display results intuitively in 3D, then use powerful analysis and scripting tools to extract and graph quantitative information.

Asylum Research Cypher Atomic Force Microscope. Cypher is the first completely new small sample atomic force microscope (AFM)/ surface probe microscope (SPM) in over a decade and is the world's highest resolution AFM. The Cypher AFM achieves closed loop atomic resolution using sensors in all three axes, combining the accuracy and control of closed loop with atomic resolution for the most accurate images and measurements possible today. In addition to its superior capabilities for imaging and measurement, Cypher uses point-and-click automated laser and photodetector alignment. Additional unique capabilities include interchangeable light source modules that allow laser spot sizes down to 3 □m for broad application and scan mode flexibility, and support for high-speed AC imaging (>10x faster) with cantilevers smaller than 10 □m. The system also includes an integrated enclosure which provides acoustic and vibration isolation, as well as excellent thermal control for image and measurement stability.

TA Instruments Q5000 Thermal Gravimetric Analysis Instrument. The automated Q5000 is used for complex thermogravimetric analysis (TGA) applications, low-level detection of impurities, kinetic studies, off-gas analysis, and high heating rate operation. Its design integrates a thermobalance engineered for maximum baseline flatness and high sensitivity, with the power and flexibility of an infrared furnace, and a proven horizontal purge gas system. User convenience features include the 25-position autosampler, the integral electromagnet, and software for scheduling automatic calibration, verification and diagnostic tests.

Malvern Instruments Nano-ZS Zetasizer. The Zetasizer Nano-ZS can measure (1) particle size of particles and molecules from 0.6 nm to 6 micrometers using non-invasive back-scatter (NIBS) technology and dynamic light scattering, (2) zeta potential in aqueous and non-aqueous dispersions using M3-PALS technology, and (3) molecular weight with an absolute measurement using static light scattering and the sensitivity from an avalanche-photodiode detector and fiber detection optics. The Nano-ZS can measure all three parameters with no performance compromises and allows measurements of samples with little or no dilution. The unique disposable zeta potential cell ensures no cross contamination of samples.

Bruker VERTEX 70v Fourier Transform Infrared Spectrometer. The VERTEX 70v is equipped with optical components to cover the spectral range from 10 cm^{-1} in the far IR/THz, through the mid and near IR up to the visible/UV spectral range at 28,000cm^{-1}. With its pre-aligned optical components and permanently aligned interferometer, range change is easy and maintenance free. With the evacuable optics bench of the 70v spectrometer, sensitivity in the mid-, near and far IR/THz regions are obtained without masking very weak spectral features caused by water vapor or CO_2 absorptions. Outstanding results, e.g. in the area of nano-science research down to sub-monolayers, can be obtained.

Linde Auto 306 Thin Film Deposition System. The Auto 306 FL400 Thin Film Deposition System is set up for sequential evaporation of up to four materials without breaking vacuum. The pumping system incorporates a 540-liter/sec turbo molecular pump backed by an XDS10 dry running primary pump. A rotary work holder is fitted to the chamber top plate. Film thickness is monitored using a Sigma SQM160 quartz crystal film thickness deposition monitor with digital display of deposition rate and deposition thickness. There is the capability to control up to 2 source shutters automatically and close the electromagnetic source shutter when pre-programmed termination thickness values are achieved. Substrate heating is via 500W Quartz lamp heater assembly with lamp.

Reactive Ion Etching Instruments. The reactive ion etching (RIE) instruments are designed to supply research and failure analysis laboratories with state-of-the-art plasma etch capability using single wafers, dies or parts with fluorine, chlorine, and oxygen-based chemistries. The systems have a compact, modular design built on a space-saving platform. Because metal and compound semiconductor etch processes use corrosive chemistries and are

often sensitive to atmospheric moisture, consistent results as well as safety are achieved by isolating the reaction chamber from the atmosphere.

Veeco Dektak 6M Surface Profiler. The Dektak 6M benchtop stylus profiler incorporates reliability with a low inertia sensor head to provide step height, surface roughness, and waviness measurements for samples up to 150 millimeters. The profiler can accurately measure step heights on any surface, with a programmable stylus force down to 1 milligram and a Z-height capability up to 1 millimeter. In addition, the instrument delivers high horizontal resolution, with up to 30,000 data points per scan. The easy-to-use software interface allows automatic comparisons of analytical results from multiple scans, and calculations of the mean, standard deviation, and maximum/minimum.

OAI 205S and Suss MicroTec MA4Mask Aligner/Exposure Systems. The OAI 205S and Suss MicroTec MA4 mask alignment and UV exposure systems are bench top tools that requires minimal clean room space. Utilizing an air bearing / vacuum chuck leveling system, the substrate is leveled quickly and gently, for parallel photomask alignment and uniform contact across the wafer during contact exposure. The systems are capable of one micron resolution and alignment precision. The alignment module features mask insert sets and quick-change wafer chucks that enable the use of a variety of substrates and masks without requiring tools for reconfiguration. Both systems provide collimated UV light in near UV using 500W lamps.

Focused Ion Beam Instrument. The focused ion beam (FIB) instrument is used particularly in the semiconductor and materials science fields for site-specific analysis, deposition, and ablation of materials. The FIB instrument uses a focused beam of ions, e.g., Ga ions, and is incorporated in a system with both electron and ion beam columns, allowing the same feature to be investigated using either or both beams. Source ions are then accelerated to an energy of 5-50 keV (kiloelectronvolts), and focused onto the sample by electrostatic lenses. When the high-energy gallium ions strike the sample, they will sputter atoms from the surface. Because of the sputtering capability, the FIB is used as a micro-machining tool, to modify or machine materials at the micro- and nanoscale. The common smallest beam size is 2.5-6 nm.

X-ray Diffraction in Extreme Environments. This system utilizes a Rigaku RU-200 Rotating Anode source with both copper and silver anodes. The diffractometer employs a scintillation counter to cover scattering angles ranging from 1-120 degrees. SPECS software is used for data acquisition and Full Prof is available for Rietveld refinements. An Air Products closed cycle refrigerator can be used to carry out measurements between 10 K and 300 K. A Lakeshore Cryotronics temperature bridge provides temperature control with a stability of +/- 0.05 K. Gas handling systems for either integrated adsorption isotherms (0-1 bar) with non reactive gases or high pressure studies (0-100 bar) are available.

Small Angle X-ray Scattering. The S-MAX3000 pinhole SAXS camera is coupled to a Rigaku RU-200 high brilliance rotating anode x-ray generator. A focusing optic provides high fluxes for small sample measurement. A 3-meter, fully evacuated camera length provides both high intensity and high resolution. Coupled with a fully integrated 2-dimensional multi-wire proportional counter, the system is capable of making highly sensitive measurements from both isotropic and anisotropic materials. An automated sample changer is available for measurements of multiple samples. Available sample environments include a water bath and a closed cycle refrigerator.

Small Angle Neutron Scattering. The NBL1-SANS instrument at the Low Energy Neutron Source utilizes a pin-hole collimation and covers a Q-range of 0.005 – 0.5 $Å^{-1}$ with an expected neutron flux of ~$2*10^4$ $n/cm^2/sec$ at the final configuration of the proton accelerator. Sample inhomogeneities on a length scale of 20 -1000Å can be probed. The Sample Area consists of a 71 cm diameter sample rotation table, on which a variety of sample environment equipment can be mounted, such as refrigerator, sample changer, cryostat, sample heater, humidity/temperature chamber, pressure cell, etc., depending on the particular scientific application of the SANS experiment. The Secondary Flight Path consists of an evacuated stainless steel tank (Si entrance window), the 2D detector (manufactured by ORDELA), and a beam stop assembly.

Quantum Design Vibrating Sample Magnetometer. The Quantum Design VSM is a fully automated system for the measurement of sample magnetization of samples in the temperature range of 2K-300K. The system employs a SQUID based magnetometer that is sensitive to magnetization changes as small as 10^{-6} emu. Measurements can be carried out in ambient fields up to 10T. A zero field option is also available. Proprietary Quantum Design software is available for data collection and analysis.

MRI applications: Cryogen-free physical properties measurement system

Other Related Facilities at Indiana University

Molecular Structure Center. The Molecular Structure Center has a full complement of single crystal and powder diffraction equipment used to characterize crystalline materials using the techniques of X-ray crystallography. Researchers in the laboratory can determine the three-dimensional structure of nearly any material that can be crystallized.

Physical Biochemistry Instrumentation Facility. The Physical Biochemistry Instrumentation Facility was established to facilitate research in the structures, stabilities, and interaction of biomolecules and to provide a centralized resource for training and education in modern physical biochemistry. Located in the new, state-of-the-art Simon Hall, it houses state-of-the-art biophysical instrumentation that is available for use by faculty and students.

Mass Spectrometry Facility. The Mass Spectrometry Facility provides top-quality mass spectrometry support to the faculty research groups in the Chemistry Department and at IU. The facility specializes in walk-up mass spectrometry and accurate mass spectrometry of unique samples.

Nuclear Magnetic Resonance Facility. The Nuclear Magnetic Resonance Facility provides high-resolution NMR for a variety of solution-state experiments. The facility supports research in organic, inorganic, biochemical, and materials synthesis. Also, the facility's new 800 MHz spectrometer is a state-of-the-art instrument for structural analysis of biomolecules and biomolecular interactions.

Low Energy Neutron Source (LENS). The Low Energy Neutron Source (LENS) is a novel, university-based pulsed neutron source at the Indiana University Cyclotron Facility. The source utilizes a low energy reaction in Be coupled with a high-current, variable-pulse-width proton accelerator to produce either short or long neutron pulses. A highly optimized moderator produces cold and very cold neutrons for use by a suite of neutron scattering instruments and development facilities.

LENS is a regional university facility for research, innovation, education and outreach with a national impact. The emphasis on cold and very cold neutrons makes it suitable for materials research, particularly in the area of nanoscale structures which are a research focus of many universities in the region. The flexible scheduling and technical resources available at IUCF make it ideal for developing innovative new neutron scattering techniques and instrumentation that will provide national benefits. At the same time, LENS's location in a university environment supports educational development at a local, regional and national level.

Appendix 2: I-BIRD

Current private sector collaborators:

Abbott; Actelion; AEON Imaging; Alcon Labs; Amgen; Antech; Aptuit (SSCI); Ariad Pharmaceuticals; AstraZeneca; Baxter; Beckman; Biogen; BioVitesse; Boehringer-Ingelheim Pharmaceuticals; Boston Micromachines; Bristol-Myers Squibb; Burroughs Wellcome; Celgene; CIVCO; Cook, Inc.; Covance; Cytoviva; DowAgrosciences; Dupont; Eisai; Elan; Eli Lilly & Co.; EntreMed, Inc; Essilor; Genentech; General Electric; Genzyme; GlaxoSmithKline; Green Tech America; IkoTech; Intelliphage; ISIS; Kylin Therapeutics; Kyphon; Medigus; Medivation, Inc; Medtronic; Merck; Millipore; NonoVis; Novartis; Octapharm; PDS Biotechnology; Pfizer; PHILIPS; Physical Sciences, Inc; Pixel Optics; Proacta; Prosolia; Protherics; PTC Therapeutics, Inc; Quadraspec; Quark Pharmaceutical; Repligen; Sanofi-Aventis Pharmaceuticals; Scherring Plough; Semafore; Seyet; Siemens; Sonexa; Teva; Tibotec; TrueFUSE; Wright Medical Technologies

Current new company formation and IP activity:

New companies:

PETNET Indiana LLC was created as a joint venture between PETNET Radiopharmaceuticals (Siemens Medical Systems) and a for profit subsidiary of Indiana University Radiology Associates to provide Positron Emission Tomography Radiopharmaceuticals throughout Indiana and the Midwest region of the United States. PETNET Indiana LLC currently has annual revenues of approximately $1.6M and delivers approximately 8500 radiopharmaceutical doses per year in support of clinical PET imaging procedures . Assuming a typical $2000 technical fee and $225 professional fee reimbursement per clinical PET procedure, PETNET Indiana provides crucial infrastructure support for nearly $19M of annual clinical revenue to hospitals and imaging centers primarily in Indiana with backup support for neighboring states.

INphoton: Light microscopic service oriented company with Phase I and now Phase II NIH STTR funding and 21st Century funding. A very exciting part of this company MO is to work with University faculty to develop R21 and Phase I STTR grants in organs other than the kidney. At present we are working on solid tumor, bone marrow, and liver phase I STTRs.

FAST Diagnostics: Device company based on the ICBM:IURTC patent listed above. Company has received Phase I and II STTR grants, 21st Century and BioCrossroads funding. The company is working in conjunction with Rose Hulman University.

Quarryman Optics was a company that was funded through two phase 1 and a phase 2 funding cycle. The company developed wavefront technology for evaluating the optical properties of the eye, and while it has recently closed its doors, the principles remain well funded from Industrial contacts and efforts that were developed by the company.

AEON Imaging: Aeon Imaging, LLC, is a start-up company incorporated in Indiana for the purpose of creating new knowledge and health delivery in the field of imaging and image display. This company has Phase I and Indiana Economic Development funding. The technology is based on patents allowed in the US, Canada, and Australia, and under examination elsewhere (Elsner AE. Device for Digital Retinal Imaging. US Pat. No. 7,331,669). A second family of patents has been submitted, and a third is in preparation.

Advanced Bioimaging Systems; formed in 2009 to commercialize an innovative label free bacterial imaging and classification technology. The company sponsors proof-of-concept research in the Bindley Bioscience Center and has a proposal pending with the 21 Fund for additional seed investment.

Coferon: intellectual property co-developed at Cornell University Medical College and Purdue led to the foundation of this therapeutics development company that has developed extensive angel investment and is

currently seeking $10M in venture capital funding. The technology will enable rapid development of high affinity chemistries for various disease targets as well as modification of existing chemicals

Intelliphage: a food safety startup with license option for Purdue technology to detect microbial contamination with an engineered and automatically reporting bacterial virus. Company is cooperating with Center for Food Safety Engineering and is developing SBIR and 21 Fund proposals for seed funding.

***Aquascience*:** Focused on products to improve health and efficiency in aquaculture, the company is preparing SBIR funding proposals for USDA. Research and development activity with Purdue's Bindley Bioscience Center is anticipated.

Additional Intellectual Property Disclosures:

Imaging Resolution Recovery Techniques: Patent being submitted

3D Phantom Printing for Performance Evaluation and Standardization of Imaging System in Clinical Trials: Provisional patent application submitted

Fluorescence Technologies, Method and Apparatus for Kidney Function and Analysis

Phantoms for testing and calibration of diagnostic medical imaging systems; provisional patent application

Fluorescence Technologies, Method and Apparatus for Kidney Function and Analysis

Cytospec Software for Analysis of Spectral Data; provisional patent application

Web-based Software Application to Remotely Control an Accessible Microscope System; provisional patent application

Detection of Arthritic Lesions Using Folate-Linked Conjugates; provisional patent application

Image Processing Apparatus and Image Processing Method; provisional patent application

Multiplexed Pathogen Detection; provisional patent application

Virtual Simultaneous Pinhole Scanning Spectroscopic Imaging Using Low-Coherence Enhanced Backscattering; provisional patent submitted.

Development of Lissajous Trajectory Confocal Microscopy; provisional patent submitted.

Compound Raman Microscope; provisional patent submitted.

High Anisotropy-Induced Diffuse Light Suppression for Large-area Microvascular Imaging; provisional patent application

AFM-coupled Microscale Radiofrequency Probe for Magnetic Resonance Imaging Spectroscopy; provisional patent application; provisional patent application.

Ultrasoft Atomic Force Microscope (USAFM) for Biological Applications; provisional patent application.

Multimodal Nonlinear Optical Microscope – integration of coherent anti-Stokes Raman Scattering (CARS), two-photon fluorescence (TPF), second and third harmonic generation imaging modalities; provisional patent submitted.

Detail of current capabilities:

IU Bloomington:

Light Microscopy Imaging Center

BD Pathway 855 High-Content Bioimager
The BD Pathway 855 is a versatile system for automated, high-content confocal imaging of live or fixed samples. It is designed for specimen formats ranging from single slides to multi-well (24-384) plates using confocal fluorescence, widefield fluorescence, and brightfield modes. Equipped for drug and small molecule screens of live cells, this device has an environmental specimen chamber, automated liquid dispensing, an associated robotic plate-loading crane, and CO2 plate holding incubator. Both laser and image-based autofocus coupled with a moving objective lens design combine for minimal specimen agitation. This machine has a proven track record for a broad range of high-content applications. The 855 includes powerful imaging software to perform a broad range of fluorescence-based kinetic and endpoint biological assays.

BD Pathway 435 High-Content Bioimager
This system is similar to the BD Pathways 855, but is specialized for imaging fixed specimens. The device is designed for specimen formats ranging from single slides to multi-well (24-384) plates using confocal fluorescence, widefield fluorescence, and brightfield modes. It can automatically image multiple sites per slide or well and every well of a multiwall plate. It includes the same powerful imaging software to perform a broad range of fluorescence-based endpoint biological assays.

Leica SP5 Laser Scanning Confocal Microscope
This system has 5 sensitive detectors enabling the simultaneous imaging of up to 4 different spectrally resolved fluorescence wavelengths plus a brightfield image. It presently has 3 lasers providing 7 excitation wavelengths (458,476,488,496,514,561 and 633nm) and a prism spectrometer to control emission wavelengths to make this a very versatile system compatible with most combinations of fluorophores. The system is based on a Leica DMI 6000 CS inverted microscope platform and is automated for time-lapse, FRAP, and 3-D image reconstruction.

Spinning Disk Confocal Microscope
The spinning disk imaging system is optimized for live-cell imaging and features a sensitive Cascade-II EM-CCD camera in conjunction with the Yokogawa CSU-10 spinning disk confocal head. The reduced photobleaching and photo-toxicity of this system allows imaging of sensitive specimens over longer time periods. The imaging system is based on a Nikon TE2000U iInverted microscope with a large complement of objective lenses, laser-based illumination for common fluorophores, and a Mosaic FRAP/Photoactivation module from Photonics Instruments Inc. The entire system is driven by MetaMorph imaging software from Molecular Devices.

Nikon C1 Laser Scanning Confocal Microscope
This imaging system is built on the Nikon Eclipse Ti inverted microscope and includes a motorized X-Y stage and the Nikon automated Perfect Focus system. This system is built to maintain focus throughout long-term live imaging experiments. It has three lasers that provide four excitation wavelengths (440, 488, 514 and 543nm) for common live cell probes.

Deltavision Deconvolution Microscope
The Applied Precision DeltaVision Restoration Microscopy System is optimized for deconvolution microscopy. Deconvolution is a software technique that mathematically de-blurs images before reconstructing a 3-dimensional image. This system features a precision motorized stage for control of X, Y, and Z plane movements. Multiple sites on a slide can be marked and revisited. Images are collected on a Photometrics CH350-CCD camera, and the entire device is controlled by the SoftWorx software package.

Veritas Laser Capture Microdissection System
The Veritas LCMD is a fully automated microscope system designed to dissect out microscopic areas of tissue from fixed specimens for later evaluation by molecular biology techniques. This device allows researchers to visualize a specimen and dissect out only the regions of the specimen desired for analysis. Typical applications include examining differential gene expression in local tissue domains from developing or disease affected specimens. The specific device uses both IR-based and laser-cutting based methods for isolating areas of tissue for analysis.

Nikon E800 Widefield Fluorescence Microscope
The Nikon E800 is a general-purpose high-end upright research microscope with a motorized Z-axis stage. It is equipped for brightfield, DIC and epifluorescence imaging. The microscope has 4X to 100X objectives and a Hamamatsu Orca ERII CCD camera driven my MetaMorph software.

Zeiss Axioplan Widefield Fluorescence Microscope
The Axioplan is a general purpose research microscope. It is equipped for brightfield, phase-contrast, and epifluorescence imaging. Images are captured using a Princeton Instruments RTE/CCD camera controlled by the basic Zeiss imaging software

Image Storage and Processing
The LMIC at IU-B houses a 14TByte server (HP) being developed for high-speed secure data transfer and storage. The facility also houses a workstation class PC running the IMARIS imaging package (Bitplane) com-linked to MATLAB for use of in house processing routines.

Ultrastructure Groups in Life Sciences

JEOL JEM-1010 Transmission Electron Microscope (IMBI)
This standard electron microscope has a useful magnification range of 50-500,000x with an accelerating voltage of 40kV-100kV. The microscope is equipped with a tilting goniometer stage for small area electron diffraction.

JEOL JSM-5800LV Scanning Electron Microscope (IMBI)
This SEM has both high and low vacuum modes for analysis of standard metal shadowed specimens and for viewing of higher water content specimens. The SEM has a useful magnification range between 18-300,000x. The specimen chamber is a full 8in in diameter for containment of larger specimens.

JEOL JEM 3200FS Cryo-Transmission Electron Microscope
This intermediate voltage (300kV) transmission electron microscope uses a field emission electron gun providing both standard TEM and FE-SEM capabilities. The device includes an in-column energy filter and EDS detector for spatial mapping of elements within specimens. The cryogenic stage and tilting specimen holders were acquired for cryo-tomography of thick specimens allowing reconstruction of protein and viral structures. The main image detector is a Gatan 4kx4k Ultrascan 4000 CCD camera for capturing extremely high-resolution images with 16-bit data resolution over a wide linear signal range.

Imaging Research Facility (IRF):

Siemens 3 Tesla TIM Trio MRI scanner with state-of-the-art magnetic gradient system (maximum magnitude of 200 T/m, and slew rate of 45 T/m/s). The high performance gradient system generates less scanning noise and image artifacts. Besides the standard RF headcoils (CP headcoil and 12 channel headcoil), the scanner is equipped with a 32-channel head coil, allowing for imaging with much higher signal-to-noise ratio, spatial resolution and the option to speed up data acquisition. The 3T MRI scanner has the capability to perform studies on structure, function and chemistry in living tissues in human and animal subjects. It is used primarily for brain imaging, but is a total body imaging system.

Applied Science Laboratories Long Range Optic MRI-safe eye tracking system which is used to track eye movements in the MRI scanner.

Kappametrics MRI-safe 21 channel EEG system, consisting of sensor caps, EEG amplifiers and PC based computer for data acquisition and analysis. This equipment makes simultaneous acquisition of fMRI/EEG signal available.

In-house constructed Mock MRI scanner which simulates real MRI scanner for acclimation of subjects prior to studies. The mock scanner matches the real MRI scanner in all aspects except that there is no magnetic field. It creates an ideal environment for the subjects to become familiar with MRI scanner and activation tasks prior to the real scanning session.

EGI high-density (256 channel) EEG system (non-MRI compatible), which includes sensor cap arrays, data acquisition and analysis (MAC based) computing systems, and an 11 camera photogrammetry system for localization of recording sensors in 3D space.

SmartEye infrared dual eye tracking system (PC based) designed to interface to EGI EEG system. Allows measurement of eye position and pupil dilation.

Magstim Rapid transcranial magnetic stimulator with Brainsight MRI-guided infrared frameless stereotaxic control system, and 2 Figure-of-8 stimulation coils designed to perform non-invasive brain stimulation studies.

Computerized stimulus delivery and response collection systems which allow visual, auditory and tactile stimulation to be performed within the MRI/Mock scanner and in the EEG/TMS laboratory (including fiberoptic MRI-compatible response boxes).

PC and MAC data analysis workstations (total of 8) for processing fMRI, EEG and TMS data and integrating data across these methods.

Optometric Imaging

The Adaptive Optics Optical Coherence Tomography Scanner has been developed as part of a multi-center Bioengineering partnership between Indiana University, Lawrence Livermore National Lab, University of California Davis, Duke University, as well as the National Science Foundation's Center for Adaptive Optics. The Indiana University AOOCT scanner is capable of scanning at a resolution of 3x3x3 microns for volumetric imaging in the living human eye. This system is also capable of polarization sensitive imaging.

The Adaptive Optics Flood Illuminated Camera is a high resolution, non-coherence camera for studying the function of the normal human retina. This system is capable of multi-wavelength retinal imaging and provides stable measurements for time resolved processes of cell renewal and change.

The Adaptive Optics Scanning Confocal Imaging system has been developed as an NIH funded Bioengineering partnership which includes not only Indiana University, but the University of Rochester, University of California Berkeley, University of Montana, and Physical Sciences, Inc. The system is capable of generating 3 micron resolution images of the human retina over a 4 mm region of the human retina at a rate of 20 million pixels per second, providing high resolution structural and functional estimates of the human retina. This system is being used to further develop automated montaging systems and as a platform for new developments in high speed retinal imaging.

The Compact Adaptive Optics Scanning Laser Ophthalmoscope is a real-time imaging technology using high stroke MEMS mirror technology under development by Boston Micromachines, Inc. This new system, designed for deployment to multiple clinics, is the result of a Phase II development collaboration between Boston Micromachines and Indiana University.

High Speed Tear film imaging system has been developed to study the rapid changes in the tear-film of the eye. This system can be used to understand how different strategies for correcting the focus of the eye (such as contact lenses and surgery) impact the comfort and vision of observers.

The COAS High resolution Optical Aberrometer is used to study the detailed optical properties of the eye, and how they are affected by refractive interventions. This cutting edge, high resolution system is a collaboration between Indiana University and AMO Wavefront Sciences.

The Retinal Function mapping system (Veris) is available for electrical mapping of the retinal response. This system is used to map out functional changes to the retina in glaucoma and retina degenerations at both short and long time scales.

The Laser Scanning Digital Camera is a device designed to bring low cost confocal imaging for the underserved population. This imaging system can obtain moderate resolution confocal images of the entire posterior pole of the eye without requiring eye drops and is being used both for investigations of diabetic retinopathy and as a platform technology for new methods in fluorescence imaging and microscopy, as well as for retinal imaging.

The Ophthalmic Imaging suite is a set of imaging technologies that are available with the Borish Center for Ophthalmic Imaging for use via contracts and partnerships. This includes Topcon 2000 Imaging system, a Heidelberg Spectralis coherent imaging system, IOL master optical biometry, systems for corneal topography measurements, and a COAS clinical aberrometer.

The Multi-wavelength Scanning Confocal Imaging system is a confocal microscope optimized for retinal imaging at wavelengths ranging from the 480 nm to 1000 nm. It is highly configurable and can be used to measure photopigments, as well as to make fluorescein an ICG studies of the human retina in vivo.

The Scientific Computing Core is an new, NIH supported, core module for aiding individuals in extracting information from multi-dimensional datasets. The core will be designing algorithms for information extraction and disseminating the information through code sharing.

IU School of Medicine:

Small Animal Imaging Systems

EVS-R9 microCT. The EVS-R9 microCT scanner (Enhanced Vision Systems Corp, London, Ontario N6G 4X8) operates at 50 kVp and 1 mA maximum tube current. It is capable of 50 micron or 100 micron voxel resolution with 2x2 or 4x4 binning in the detector panel. The radiation dose associated with various imaging parameters (exposure time and angular samplings) is measured to obtain a guideline on imaging protocol designing. For each radiation dose level, image noise is also measured by the standard deviation of CT number in the water region. The noise to dose relationship is established for various detectorbinning modes.

IndyPET II. The IndyPET-II scanner has been developed at Indiana University by Dr. Hutchins as a high resolution, high sensitivity research PET scanner for use in small animal imaging studies. The system consists of four, approximately planar detector banks mounted on a rotating gantry. The detectors cover a transaxial FOV of 23cm and an axial FOV of 15 cm. This configuration reduces parallax distortions and produces a relatively uniform resolution throughout the FOV. The two pairs of opposing detectors banks are offset to give increased sampling density and increased spatial resolution. The average (radial and transverse) FWHM resolution is 2.5mm at the center of the FOV and increases to less than 3.5mm at the edge of the FOV. The NEMA-2001 sensitivity is 9030 cps/MBq at the center of the scanner and 4250 cps/MBq at a radius of 10cm. The NEMA-1994 sensitivity is 23.0 cps/MBq/ml.

IndyPET III. The IndyPET III scanner was developed at Indiana University by Dr. Hutchins The system was designed to achieve 1 uL volumetric spatial resolution suitable for whole body mouse imaging. The scanner uses 8 planar detector banks consisting of 48/spl times/108 array of 20 mm long LSO crystals with an array pitch of 0.87 mm coupled to two Hamamatsu H8500 large area, 64-anode photomultiplier tubes. The detector modules are mounted on a rotatable gantry offset from the center of rotation to allow increased sampling density. Transaxial resolution is 1.1 mm FWHM with an axial resolution of 1.5 mm FWHM. Sensitivity has been measured to be 4.0% of all decays. The scanner design allows for the

addition of 14 additional detector banks for improved resolution and sensitivity.

Varian 9.4T MRI Horizontal Bore. The Varian 9.4 T / 31 cm actively shielded horizontal bore MR system is suitable for in vivo imaging and sprectroscopy investigations of small animals ranging from mice to rabbits. The system is equipped with two sets of actively shielded gradient sets: 1) a 21 cm inner diameter gradient set capable of generating 20 G/cm, and 2) a 12 cm inner diameter gradient set capable of generating 40 G/cm. The state-of-the-art Varian Unity Inova console on the system is capable of performing multinuclear investigations and has waveform generators on all RF and gradient channels, which allow arbitrary pulse shaping and easy implementation of sophisticated imaging and spectroscopy pulse sequences. A number of single-tuned quadrature and dual-tuned linear imaging coils, slotted tube resonators and surface coils are available for multinuclear MR studies. MR methods, which are used for a variety of applications, include echo-planar imaging, diffusion weighted imaging, back-plane reconstruction, single voxel localized spectroscopy, chemical-shift imaging, gradient-enhanced spectral editing, multiple-quantum techniques and other specialty pulse sequences.

Berthold LB981 NightOwl . The NightOWL system consists of a Peltier cooled CCD camera (578 x 385 pixels) housed within a 102x60x40 cm light tight enclosure for imaging luciferase and GFP expression in small animals. The system is interfaced to a Pentium 200 MHz for data acquisition and analysis.

Interventional Radiology Research Laboratory. This laboratory is focused on research in atherosclerosis, restenosis, and directed drug delivery for the treatment of the cancer and vascular disease. The laboratory includes an animal operating room for microsurgeries as well as intraabdominal and intrathoracic surgeries, two Toshiba X-ray machines with fluoroscopic and DSA imaging capabilities, and associated ancillary equipment for subject monitoring and support.

Human Imaging Systems

Siemens MAGNETOM Trio 3T Unlimited MRI. The Trio 3T MRI, located in the R2 building, is a 3 tesla whole body imaging system operating with Syngo software. The system is equipped with a 200 T/m/s gradient system and 8 RF-channels. The flexible RF system has the capability of performing multinuclear and spectroscopy studies.

GE Signa Advantage 1.5T MRI. A dedicated research MRI system is located in the high technology imaging center of University Hospital. This system is a 1.5 tesla General Electric Signa Advantage system operating under software version 9.0. The system currently has the capability to perform hydrogen magnetic resonance spectroscopy and functional brain imaging studies using Echospeed. Two additional 1.5T General Electric MRI systems (1 each in University and Riley hospitals) have echo-planar imaging capabilities and are available on a limited basis for research studies.

Siemens ECAT HR+ PET. The Siemens ECAT HR+ PET scanner is located in the R2 building. The whole body imaging system has an axial field-of-view of 15 cm, is equipped with BGO detector technology and has retractable septa for 3-D volumetric imaging. Both conventional filtered backprojection and OSEM reconstruction algorithms are available and used routinely.

Siemens Biograph PET/CT. The Biograph PET/CT scanner is located in the Clinical building located in the IUPUI campus and is scheduled to be relocated to the R2 building. This system is a whole-body static imaging system equipped with BGO detector technology and capable of 3-D volumetric imaging. The axial field-of-view is 15 cm. Both conventional filtered backprojection and OSEM reconstruction algorithms are available and used routinely.

Alternative Animal Imaging Systems

Optosonics Thermoacoustic Tomography System. This new imaging modality, conceived and developed at Optosonics, Inc (Indianapolis, IN) in collaboration with the Indiana-CEBI, produces images of tissue RF absorption contrast by detecting sonic waves produced by thermal expansion of tissue. A small animal system has been constructed using a tunable laser enabling optical absorption spectroscopy and imaging. The current system has a spatial resolution of 200 microns and can image using optical wavelengths in 532-1064nm wavelength range using an Optotek, Inc laser.

Radionuclide Production Systems

RDS-Eclipse Cyclotron: Housed within the BRTC building is a Siemens RDS-Eclipse cyclotron. This system consists of an 11 MeV proton cyclotron, target systems for the production of 11C, 18F,13N and 15O used in the synthesis of PET tracers.

IIBIS Imaging Services Core

The IIBIS provides a range of services that include education of investigators on the capabilities and application of imaging technologies, consultation to assist with imaging study design, production of PET tracers, performance of imaging studies, resources for image processing and data analysis, and quality control for all chemistry and imaging systems housed within the R2 and BRTC facilities. A brief description of the core services follows:

PET Tracer Production: PET Carbon-11, Nitrogen-13, Oxygen-15 and Fluorine-18 tracers are produced for PET imaging studies. Numerous tracers are in various stages of development for support of cancer, cardiovascular and neuroscience research.

PET Research & Routine Production Radiotracers

1. Heart acetylcholinesterase imaging agents (dog and rat heart imaging):Cardiac acetylcholinesterase imaging agents [11C]edrophonium, [11C]pyridostigmine
2. Choline kinase imaging agent (tumor mice): [11C]Choline
3. MMP (Matrix metalloproteinase) imaging agents (tumor mice): [C-11]Me-CGS 27023A and its analogs, [C-11]Me-halo-CGS 27023A analogs, [C-11]Biphenylsulfonamide analogs
4. Alkylguanine-DNA alkyltransferase (AGT) imaging agents (tumor mice): Radiolabeled O6-benzylguanine analogs
5. Herpes simplex virus thymidine kinase (HSV-TK) reporter probes (tumor mice): [18F]FHBG and other fluorine-18 labeled penciclovir and ganciclovir analogs
6. Brain dopamine and serotonin transporters ligands (human, pig and rat brain imaging): [11C]β-CFT, [11C]β-CIT, [11C]β-CNT for the study of Parkinson's Disease.
7. Muscarinic Receptor Ligands (dog heart imaging): [C-11]Methyl-QNB, [C-11]Methyl-TRB
8. Peripheral Benzodiazepine Receptor Ligand (tumor mice and rat): [11C]DAA1106
9. D2/D3 receptor ligand (human and rat brain imaging): [11C]Raclopride
10. β-Amyloid Plaques Ligand for Alzheimer's Disease (human brain imaging): [11C]PIB
11. Vesicular monoamine transporter ligand (rat brain imaging): [11C]DTBZ
12. Sympathetic Nervous System (human and dog heart imaging) : [11C]HED
13. High-affinity choline uptake (HACU) ligands (rats and mice, tumor and heart imaging): [11C]HC-15 and [11C]HC-3
14. SKCa channels ligand (rat heart imaging): [11C]NML
15. Vagal Nervous System (dog heart imaging): [11C]Neostigmine
16. Luciferase reporter probes (tumor mice): [C-11]D-luciferin methyl ester and [C-11]D-luciferin methyl ether
17. Blood Flow (human and dog): [O-15]Water, [N-13] Ammonia
18. Glucose Metabolism (human and animal): [F-18]FDG
19. Blood Volume (tumor mice): [C-11]CO

20. Free Fatty Oxidation Rates (human and animal): [C-11]Acetate

Performance of Imaging Studies: The imaging center provides experienced and trained technologists for the acquisition and basic image processing required for all studies. Investigators, or their staff, work closely with the imaging center technologists in the performance of specific studies. The imaging center staff administer anesthesia to the animals, administer PET tracers or contrast agents, and operate the imaging systems. The only exception to this model is for bioluminescence/biofluorescence imaging where investigators can operate the system without support once trained. The imaging center staff is also responsible for all necessary image reconstruction or processing needed for the study. An emphasis for all imaging studies is placed on the collection of data that permits quantitative or semi-quantitative analysis of results.

Image Processing and Data Analysis: The imaging center maintains numerous servers and software packages for the analysis of imaging data. A large base of in-house developed imaging processing software (based upon IDL and/or MATLAB) is maintained by the faculty and staff in the imaging center. This software enables the generation of multimodality fusion images, navigation throughout image volumes in standard and non-standard image planes, definition of region-of-interests, application of semiquantitative data analysis methods (SUVs), application of quantitative data analysis methods (compartmental models), and 3-D visualization tools (projections, maximum intensity projections) for subjective evaluation of image data. Tools for the registration of multimodality images have been developed and validated in our laboratory and are utilized routinely so that fused data sets can be easily generated. Access to all software and servers is made available to interested cancer center investigators using X-window emulators and VPN clients. A limited number of image processing workstations are also available in the imaging processing laboratory housed in the imaging center.

Confocal Microscope Systems

An **Olympus FV1000-MPE Confocal/Multiphoton Microscope** equipped with an Argon laser (458, 488, 515 nm excitation lines), and three diode lasers (405, 559, and 635 nm excitation lines) for confocal microscopy and a Spectra Physics MaiTai Deep See laser (tunable from 710 to 990 nm) with dispersion compensation for multiphoton microscopy. The confocal system is configured for three channels of fluorescence detection plus one channel for transmitted light detection. Channels one and two are spectral detectors with user-specified min and max wavelengths for the emission bandpass. The system is also equipped with two external detectors for multiphoton imaging, with dichroic mirrors available for collection of either blue and green or green and red emission. The system is mounted on an Olympus IX81 inverted microscope stand.
A **Bio-Rad MRC1024 Confocal/Multiphoton Microscope** is equipped with a Krypton-Argon (488, 568, 647 nm excitations) laser for confocal microscopy and a tunable Titanium-Sapphire laser (using a 5W Millennia diode solid state pump laser) for multiphoton microscopy. The system is equipped with 3 detectors in both the epi-illumination and transillumination paths, as well as three channel external detectors for 2-photon imaging. The system supports confocal imaging of green, red and far-red emitting fluorophores and multi-photon imaging of blue, green and red emitting fluorophores. The system can also be used to collect bright field and Nomarski images. The system is mounted on a Nikon TE-200 inverted microscope.
A Zeiss **LSM-510 Meta Confocal/Multiphoton Microscope** equipped with an Argon laser (458, 488, 514nm excitation) and two Helium-Neon Lasers (543 NM and 633 NM excitation) for confocal microscopy, and a tunable Titanium-Sapphire laser (using a 10W Millennia diode solid state pump laser) for multiphoton microscopy. The epifluorescence can be captured via two conventional PMT detectors or via the new Meta system. The Meta system is an array of 32 detectors, which permits collection of the total emission spectrum from a fluorescent sample. This system allows users to configure the system to collect specific emission ranges or, when combined with the linear unmixing software, to deconvolve sample emissions to allow sensitive discrimination of a large number of spectrally overlapping flourophore Multiphoton microscopy images can be collected either via these detectors or two external detectors. This system supports confocal imaging of green, red and far-red emitting fluorophores by

confocal microscopy, and multi-photon imaging of blue, green and red emitting fluorophores. The system is mounted on a Zeiss upright microscope.
A Zeiss **UV LSM-510 Confocal Microscope** equipped with a UV Argon Laser (351 NM, 364 NM excitation), a visible Argon laser (458, 488nm excitation) and two Helium-Neon Lasers (543 NM and 633 NM excitation). The microscope is equipped with four epifluorescence detectors and one transillumination detector. This system supports confocal imaging of blue, green, red and far-red emitting fluorophores and can also be used to collect bright-field or Nomarski images. The system is mounted on a Zeiss Axiovert 100 inverted microscope.
A **Spinning Disk Confocal Microscope** equipped with 3 lasers providing excitations at 442 NM, 488nm, 514 NM, 568 NM and 647 NM This system utilizes a unique spinning disk that simultaneously scans hundreds of spots over a sample, simultaneously collecting images with an Ixon air cooled EMCCD camera (Andor). This design allows the system to collect images at over 30 frames per second with very low levels of illumination. The reduced photobleaching and phototoxicity of this system makes it especially suited to live cell imaging. This system is configured to rapidly collect images of cells expressing CFP and YFP, or labeled with green, red and far-red emitting fluorophores. It can also collect bright-field and phase contrast images. The system mounted on a Nikon TE-2000U inverted microscope.

Widefield Microscope Systems

A **Nikon Eclipse TE200 Inverted Microscope** equipped with a **Hamamatsu 1394 Orca-ER Cooled CCD Camera** and Micro-Manager software. The highly sensitive Hamamatsu Orca-ER camera is ideal for detection of fluorescence in live samples and in samples that have low signal levels. This high performance widefield microscope system is also equipped with Differential Interference Contrast optics (DIC). The inverted microscope stand accomodates slides or culture dishes. Best results are obtained using thin samples, such as well spread single cells. The system is equipped to collect images of blue, green, red and far-red emitting fluorophores.
A **Nikon Diaphot 200 Inverted Microscope** equipped with a **Diagnostic Instruments SPOT color camera**. The limited sensitivity of this system makes it inappropriate for epifluorescence of anything but very bright probes, but the system is optimized for high-resolution Nomarski, DIC and phase contrast imaging. An Eppendorf micromanipulator and microinjector is available to mount on the stage of the microscope making it particularly useful for imaging living cells over time.
A **Nikon Microphot SA Upright Microscope** equipped with a sensitive **Diagnostic Instruments SPOT RT Slider color camera** capable of capturing moderately low-light level images of blue, green and red emitting fluorophores. This system is very simple to use, and in addition to providing excellent epifluorescence images, is capable of collecting color, bright field and phase contrast images.

Auxiliary Equipment available for use with scopes:

(3) Warner DH-35 dish warmers, a PMDI Open Perfusion Micro-incubator, a Warner RC-50 Transepithelial imaging chamber, and(2) Warner OW objective warmers.

Computer Systems

In addition to the scope systems, the facility has a 5.4 terabyte IBM Fileserver and two public workstations. Web and remote file services are available via a failover linux cluster. Interactive 3D (voxel-based) image processing is performed using PCs equipped with 3.2 GHz Xeon processors, FireGL and Radeon-based video boards, and 6 to 8GB of memory. Various other image-oriented programs are also run on the PCs, including Media Cybernetics' AutoDeblur for deconvolution, Universal Imaging's Metamorph for image analysis/processing, NIH's ImageJ, Amira, Adobe Illustrator and Photoshop for image editing, and Premiere for making movies.

Publication-quality images and graphics can be generated on a Kodak 8670 PS dye sublimation photo printer, Xerox Phaser 7300 color laser printer, and an Epson Photo 2200. Most PCs are equipped with CD burners and some offer DVD-R/RW recorders. Core microscopy systems and workstations are connected by gigabit ethernet.

Purdue University

Electron Microscopy

FEI Titan 80-300kV Field Emission Environmental Scanning/Transmission Electron Microscrope - enables EM level imaging under variable vacuum conditions. Environmental chambers provide for in situ materials processing with a resolution of 1Å and various imaging modalities with a high performance camera and data handling system.

FEI Titan Krios TEM (FEG) – A state of the art transmission electron microscope capable of atomic resolution. This instrument is the most advanced electron microscope currently available. It has accessories to permit examination of frozen hydrated samples, a Gatan Tridiem energy filter to improve electron tomograms and an automatic loading device, eliminating the need for a technician to be present during each sample change. With optimized performance throughout the 80 to 300kV range and a Gatan 4K CCD camera, this instrument is highly versatile and designed for high throughput studies and can be remotely operated. (Expected installation date, November, 2009)

FEI Cryo-Electron Microscope CM300 (FEG) - A dedicated 300kV instrument with a Schottky field emission source permitting ultra-high brightness, low energy spread and high coherence, this instrument is capable of achieving high resolution images on the thickest of EM specimens. The high accelerating voltage combined with high-tilt Gatan cryo-holders and the 4K Tietz CCD Camera and software allow for automated collection of tomograms. A secondary 1K high-speed Tietz CCD gives real time imaging/feedback to the operator.

FEI Cryo-Electron Microscope CM200F (FEG) - A system similar to the CM300 except operating at 200kV and equipped with Gatan 4K CCD camera and imaging software.

All instruments are computer interfaced and under service contract to limit down time. The Biological Electron Microscopy Facility, where these instruments are located, is also furnished with all the ancillary equipment required to prepare samples for cryo-electron microscopy or cryo-electron tomography. This includes several high resolution scanners, an FEI Vitrobot, two carbon evaporators and two Gatan dry pumping stations. An older FEI EM420 TEM (120 kV) is also available for screening of samples and training purposes.

Light Microscopic Systems

Bio-Rad Radiance 2100 multiphoton microscope purchased in 2003. This instrument has a 10 Watt Mai-Tai femtosecond laser as well as 488, 532 and 633nm lasers. There are 3 internal detectors and 2 external high-speed detectors that also have the Becker and Hickl lifetime module. The inverted Nikon microscope is also equipped with an environmental chamber for small cell culture systems and is shielded to reduce light contamination of data.
An **Olympus total internal fluorescence microscope (TIRFM)** system built upon an IX71 inverted microscope equipped for TIRFM, wide-field fluorescence, phase-constrast and DIC. Laser illumination from three separate lasers (488 nm Argon laser, green He-Ne laser (543 nm) and red He-Ne laser (633 nm) is ported into the microscope through the Olympus TIRFM module. Image capture is via a 512 X 512 Hamamatsu EM back-thinned CCD camera controlled with Scanalytics IP Labs software.
The integrated **Picoquant Microtime 200 system** provides for single molecule tracking by fluorescence correlation spectroscopy (FCS) and also includes high-end capabilities for fluorescence lifetime imaging microscopy (FLIM) and Förster resonance energy transfer (FRET). FCS measures the thermodynamic fluctuations of diffusing molecules in a confocal detection geometry (600-800nm) and facilitates the monitoring of molecular noise (brightness) over a large dynamic range (GHz to Hz) covering photophysics, conformational transitions, diffusion rates, single molecule binding kinetics, transport properties of labeled biomolecules, and on/off rates. Detection volume used is thus very small (~1 femtoliter) and the concentration range spans ~100nM

to 10pM, thus enabling diffusion and interaction studies of single molecules (5-10nm) at picoMolar concentration.
Bruker Senterra Raman confocal microscope systems with 6-wavelength capability. This range of capability enables optimal signal-to-noise ratios and expands the range of samples that may be assessed with this technology, which provides both images and spectra from biological samples.
iCys laser scanning cytometer from Compucyte is a high speed, microtiter plate-compatible and high resolution light microscopy system can provide critical linkage between phenotype and genotype. This laser scanning cytometer provides subsecond confocal automated imaging from light and dark field microscopy.
Veeco Bioscope II wet surface compatible Atomic Force Microscope (AFM) with environmental control stage. The system integrates AFM with an Olympus inverted BX17 optical systems and software that associates AFM and microscopic information. The system accommodates standard and customized AFM tips for structural and functional analyses.
AutoPix Laser Capture Microdissection (Arcturus) To specifically isolate cells from tissues most pertinent to a disease category or experimental question. The instrument combines automated upright microscope architecture, three-dimensional optical control of the dissecting laser beam and the dissected area, non-contact tissue sampling and motorized post-dissection handling.
Cyntellect Laser Enabled Analysis and Processing (LEAP) instrument platform enables both specific cell ablation and very high efficiency transformation. A Q-switched, diode-pumped, solid-state, Nd:YAG laser is coupled with a novel fluorescence imaging system. The average power output of this laser at 532nm is about 50mW. It pulses at a 1kHz frequency with a pulse width of 0.75ns, and peak power output of above 50kW at 532nm. The instrument was designed with an achromatic F-theta lens that, when combined with high-speed galvanometer mirrors, allows for large surface area imaging with an intensified CCD cameras. Custom software is used to direct the laser beam pulses at targets that can be user-selected or auto-selected by the custom software. The pulsed laser can be used to either eliminate cells for sorting or to laser-opto-inject genes and other molecules into live single cells with cell viabilities greater than 95 percent.
Spinning Disk (Yokogawa) **Confocal Microscope** attached to a Nikon T200 stand. Excitation is provided by a Coherent Innova 70c mixed gas laser with an acoustic-optical tuned filter. It is capable of providing lines at 488, 514, 568 and 647 nm. This platform must be upgraded for high speed and time-lapse molecular imaging.

Custom systems

Mulitmodal Nonlinear Optical Microscope has been developed that provides integration of coherent anti-Stokes Raman Scattering (CARS), two-photon fluorescence (TPF), second harmonic generation, and third harmonic generation imaging modalities on a single optical platform. This system enables ready integration of labeled and label-free microscopic imaging and the outstanding resolution of non-linear imaging.

BARDOT is a novel system designed to image and automatically classify pathogenic bacteria. The simple diode laser based system uses light scattering and a powerful software package to detect and identify bacterial colonies on a standard Petri dish culture support.

Mulitvariate Hyper-Spectral Imaging Instrument employs a high resolution spatial light modulator to detect full spectral responses with a high sensitivity single channel photomultiplier tube. This NSF-funded system enables either direct imaging of cells and cellular components or reconstruction of complete high resolution spectral images to provide chemical information (a 'chemical' microscope).