MULTIDISCIPLINARY GRADUATE CURRICULUM ON INTEGRATIVE BIOINTERFACIAL ENGINEERING

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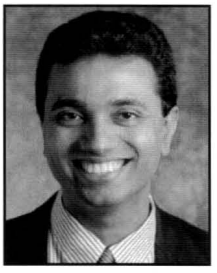
Biointerfaces arise at contacts between biologically derived systems—living and nonliving—and synthetic systems, typically comprised of synthetically designed materials. Many new technologies in cell-based diagnostics and therapies, tissue engineering, biomolecular therapies, and biosensors are critically dependent on advances in biointeractive surfaces.[1, 12, 22] Rapid advances have taken place in identifying new biological molecules and in the initial design of diverse materials capable of biomimicry and scale-specific bio-recognition.[42] Consequently, the field of biomaterials is poised for a major impact on our society. In contrast to the traditional development of the materials and biology fields, which largely occurred independently, the next generation of bio-inspired and bio-interactive materials will be systematically developed through the integration of these disciplines, with strong links to traditional molecular/cellular biology, structural biochemistry, and nano/microsystems materials sciences and engineering.[2, 11, 37] To realize these opportunities, a structured framework is needed for cooperative graduate learning and research scholarship that cuts across engineering, physical, and life sciences while focusing on mainstream "biointerfacial" problems and opportunities. Based on the educational core of a new National Science Foundation-supported IGERT initiative at Rutgers, we propose a new Integrative



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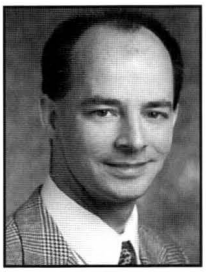

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Biointerfacial Engineering (IBE) curriculum that involves a three-pronged focus on molecular/cellular engineering; micro/nanoscale biomaterials; and tools to quantitatively probe biointerfaces (see Figure 1). While such a curriculum can be best rooted within a bioengineering core (designated bio-x-engineering), the integrative curriculum is designed to effectively resonate among a diverse range of nonengineers. In the following section we review the core curriculum and the best instructional practices of the IBE curriculum.

TECHNOLOGICAL CONTEXT FOR CURRICULUM: RESEARCH PROGRAMS ON BIOINTERFACES

The curriculum on biointerfaces can be designed to articulate with the specific areas of research expertise of each graduate institution. The research thrusts are an important prerequisite, as they provide the technological context and research infrastructure for the courses. Three major thrusts were identified at Rutgers: (1) living cell biointerfaces, *i.e.*, engineered cellular/intracellular systems that elucidate/affect biointerfacial phenomena; (2) biologically interactive nanoscale and microscale interfaces; and (3) systems or devices built from designed biointerfaces.

Thrust 1 involves studies at the interfaces that occur between living cells and biomaterials, between living cells and supported biomolecules (ligands), and intracellular interfaces between cytoskeletal proteins and signaling targets within living cells. Such interfaces are fundamental to any cell-based diagnostic, therapeutic, or model systems used to study stem-cell development, pathology, and bio-inspired devices. The interpretation and modeling of cellular dynamics on more complex ligand substrates is also an area that often falls outside the expertise of cell biologists, but is central to the integrated curriculum proposed here. A recent report in the *Annals of Biomedical Engineering* describes a curriculum concentrating on cellular engineering[20] that embraces many of these principles.

Thrust 2 involves investigation of inorganic and polymeric substrates from micron-sized cell interfaces to nano-sized peptide/protein interfaces. Such interfaces are widely emerging in biophotonics, bioMEMs, single-cell studies, and therapeutic approaches to tissue regeneration and drug delivery. For example, interfaces created by micropatterning proteins on synthetic polymeric substrates can be fabricated using microlithographic or microcontact printing technologies, then analyzed using microscopic, spectroscopic, and cellular approaches. The capabilities of microfabrication—the physicochemical characterization—and biological studies fall outside the expertise of any single discipline and, therefore, constitute a major area in the integrated training approach we envision.

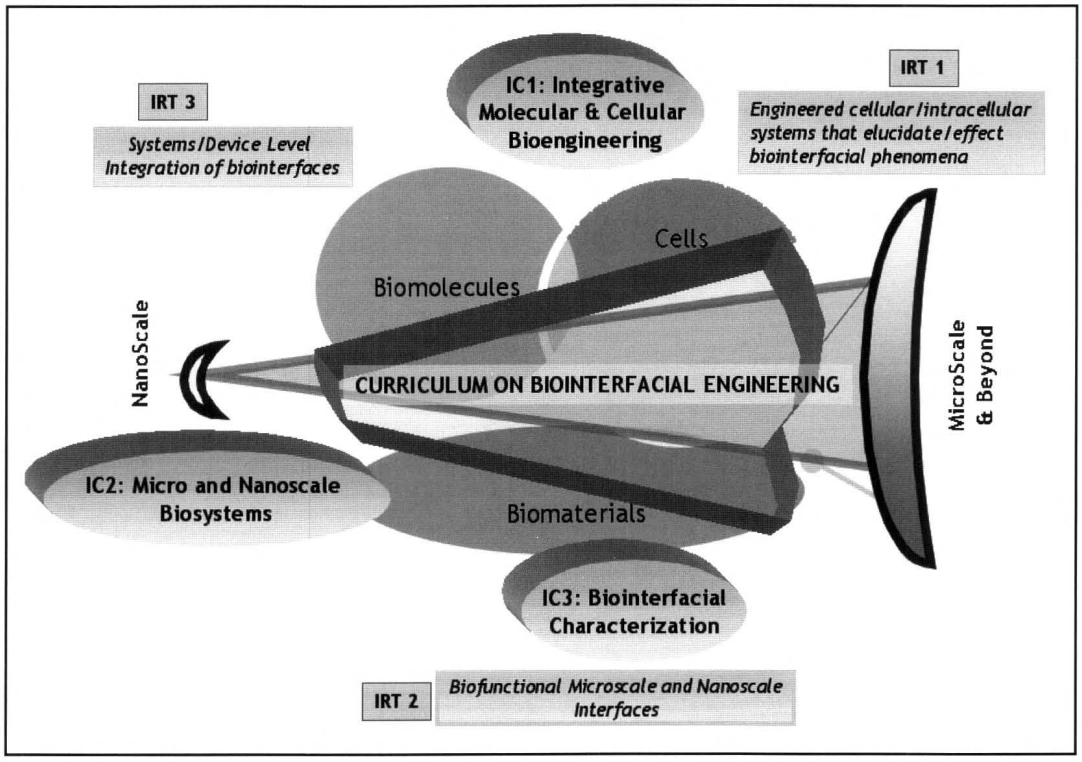

Figure 1. *A triad of graduate courses has been designed to capture the synthetic and analytical approaches related to biointerfacial problems involving living engineered cells on: substrates; micro- and nanoscale biofunctional materials; and biosystems and processes for cell signaling, biosensing, and actuation. The schematic backdrop illustrates the landscape of the curriculum in terms of (a) the biointerfacial confluence of cells, biomolecules, and materials; and (b) interdisciplinary research thrusts denoted as IRT's. Emerging opportunities allow engineers and life scientists to address biointerfacial problems at the nano- through microscales.*

Thrust 3 involves studies of systems or processes involving

biomaterial substrates designed to elicit systematic responses from living cells or biomolecular moieties (*e.g.*, oligonucleotides, peptides/proteins), called bio-responsive interfaces; substrates designed to detect and sense biomolecules and cells, called biosensors; and substrates engineered to be physiologic, three-dimensional,[19] and/or actuated through the mediation of biologic mechanisms or motors. Such interfaces are fundamental to the development of therapeutic implantable biomaterials, implantable biosensors, and biomicro-electromechanical systems (BioMEMS).

COURSE LEVEL AND PREREQUISITES

The biointerfacial engineering curriculum is aimed at second-year or higher graduate students in chemical and biomolecular engineering, biomedical engineering, allied engineering disciplines (mechanical and materials engineering), and physical and life sciences. At Rutgers, nearly 60 graduate students (50% chemical and bio-engineers; 10% mechanical and materials engineers; 25% molecular bioscientists; and 10% physical scientists) participated in these courses in academic year 2005-6. Because students enter the curriculum from diverse backgrounds, prerequisites are expressed topically rather than by specific course numbers, and consultation with course instructors and/or IGERT administration is encouraged. Prerequisites include undergraduate life sciences courses (general biology, cell biology/biochemistry/molecular biology) as well as structured undergraduate courses in the physical and quantitative sciences, such as physical chemistry and advanced calculus. The curriculum builds laterally on graduate core engineering courses such as transport phenomena, analytical methods in chemical and bioengineering, and thermodynamics and kinetics. The curriculum does not typically add any further to the courseload beyond the expected graduate electives for a Ph.D. degree. For example, the Rutgers Chemical and Biochemical Engineering graduate program requires 15 elective credits (beyond 15 core credits), for which any or all of the three integrative courses (IC) described below may be used. Further, engineering graduate programs that have recently instituted a life science course requirement can easily adopt any IC courses. Similarly, biomedical engineering graduate programs, such as those at Rutgers, require three bioengineering electives (9 credits), which can be readily met through the IC courses.

CURRICULUM COMPOSITION

The proposed curriculum involves a triad of courses, denoted as IC1, IC2, and IC3 (see Table 1). We utilize an integrative philosophy to develop curricular themes. For example, we designed courses that integrate biointerfaces across the range of organization of biological components of the interfaces (*e.g.*, genes, proteins, cells: see IC1), or size

TABLE 1
Course Syllabus for Integrative Biointerfaces Curriculum

Course and underlying integrative philosophy	Syllabi of course modules
IC1: **Molecular and Cellular Bioengineering** (integrated across scales of bio-organization)	*Module 1*: Genes—sequence and function technologies and databases; gene expression profiling; genetic engineering *Module 2*: Proteins—structure and function; molecular recognition; protein adsorption; nanopatterning of proteins; proteomic technologies *Module 3*: Biochemical Networks—gene expression data mining; metabolic flux analysis; signal transduction and gene network modeling *Module 4*: Cells—growth and differentiation; cell-material responses; expression-phenotype relationships; actuated cell responses; stem cells
IC2: **Microscale and Nanoscale Biointerfaces** (integrated across scales)	*Module 1:* Microlithography and microfabrication *Module 2:* Nanoscale processing and fabrication *Module 3:* Soft tissue—nanostructures, microstructures, macrostructures *Module 4:* Hard tissue—nanostructures, microstructures, and functional components *Module 5:* Nanostructures and microstructures of biosensors, bioseparations, implantable devices, bioMEMs
IC3: **Biointerfacial Characterization** (integrated across biointerfacial phases: chemical, physical, biological)	*Module 1*: Chemical surface characterization; electron spectroscopy *Module 2:* Physical surface characterization—topography, surface energetics, microscopy, spectroscopies (surface Raman; single molecule; FTIR); nanoparticle sizing and morphology *Module 3:* Biological Surface Characterization—proteins at interfaces and protein arrays; cell dynamics at interfaces (adhesion; migration; endocytosis; growth/differentiation); biofunctionalized substrates; gene micro-arrays *Module 4:* Integrative design, applications, and case

scales (*e.g.*, nano-micro-macroscales: see IC2), or the two phases that constitute a typical biointerface (*e.g.*, the gene element, plus the siliconwafer, that form a class of gene-chips: see IC3). In the future, other integrative philosophies can be envisioned as well (*e.g.*, integration across time scales for dynamic interfaces).

INTEGRATIVE TREATMENT OF THE CURRICULUM

A variety of fundamental tools and phenomena are introduced in each of the three courses within the context of significant technological problems. In order to provide a cohesive framework in the overall curriculum, many key problems are dissected within all three courses. Naturally, each course treats the problem differently, as illustrated in Table 2. For example, the problem of tissue-specific targeting of drug nanoparticles is discussed in IC1 at the level of receptor-ligand binding, and in the theory and analysis of binding affinity; IC2 treats the nanofabrication of particles and biofunctionalization; while IC3 treats the experimental tools for nanoparticle characterization. These tools include the use of dynamic laser scattering and zeta potential measurements to characterize nanoparticle charge and sizing, and quartz-crystal microbalance and surface plasmon resonance techniques to evaluate ligand-receptor affinity. Other cross-cutting topics are summarized in Table 2.

BEST PRACTICES

In developing the new curriculum, an overarching goal has been integration of the graduate students' research and learning experiences, *i.e.*, to help usher the frontiers of biointerfacial science and engineering into the classroom. The instructors have identified several instructional approaches that have proven to be particularly effective in merging active learning with emerging scientific advances and technological applications. These approaches include the selected inclusion of faculty experts as guest lecturers, extensive incorporation of readings from current research literature, and demonstrations of techniques and instrumentation at laboratories around campus. Additionally, mid-course corrections in response to student feedback have occurred.

Use of the Current Biointerfacial Research Literature

For all three courses, each major topic was contextualized through extensive use of recent, leading publications in the field. The manuscripts were assigned prior to respective lectures, and significant portions of class were allotted to critical review and discussion. In IC3, following each lecture students were assigned homework based on the key publication. The homework involved writing a short essay highlighting key principles, insights obtained, and shortcomings of biointerfacial characterization techniques treated in each reading.

TABLE 2
Breakdown of Topics Treated Across the Triad of Integrative Courses

CROSS-CUTTING PROBLEMS	SPECIFIC TOPICS AND REFERENCES		
	IC1	IC2	IC3
High-Content Living Cell Assays	Signal transduction; cell cycle and proliferation; differentiation; metabolic engineering[6, 30, 40]	Cell microreactors[32]	Cell adhesion and motility characterization[4, 10, 44, 45, 47]
DNA and Protein Microarrays	Applications of microarrays; interpretation of data[3, 23]	Photolithography; surface attachment and functionalization[25, 34]	Chemical, physical, and functional characterization[36, 48]
Discovery and Applications of Novel Biological Transformations	Protein molecular recognition and function[5]	Micro/nano-scale organic substrates[8, 31]	Single molecule and FRET imaging[21, 38] function[5]
Targeted Biofunctionalized and Drug Carriers	Ligand-receptor binding and intracellular trafficking[29]	Fabrication of micro- and nanoscale inorganic and organic substrates[7, 4, 15, 17, 22]	Size; charge; biofunctional characterization; fluorescence spectroscopy[18, 28, 33, 35]
Regenerative Biomaterials Scaffolds	Protein adsorption and biocompatability[46]	Fabrication of nano- and microporous scaffolds and fibers[16, 24]	Molecular modeling; conformation; topography and microstructure characterization[27, 41, 43]
Multicellular Tissue Assembly and Engineering	Cell-cell and cell-matrix communication[9, 26, 39]	Cell-matrix assembly and patterning[13]	Cellular phenotypic and signaling within tissue assemblies[19]

Retrospectively, students have reported this exercise was critical to understanding the key elements of each technique within an application area. As described below, student feedback to the use of scientific literature has been consistently enthusiastic.

Tracking Student Learning and Integrative Outcomes

Careful attention has been given to choosing student assessment vehicles that both support the research-centric and integrative goals of the new curriculum and address the divergence in student backgrounds and preparation (*i.e.,* the enrollment across engineering, physical sciences, and life sciences graduate programs). All three courses used a threefold combination of short (homework) assignments, mid-term and/or final exams, and class projects—thereby providing students with different ways to demonstrate mastery of the material. Class projects, in particular, have proven to be a valuable mechanism for promoting integration of classroom learning and student research, and promoting cross-disciplinary interactions.

In all three courses, students were assigned one or more integrative project reports to prepare over the course of the semester. Students presented their findings orally to the entire class and also submitted their slides and/or a paper to the instructor. Students were challenged to select topics that related to their own thesis research, and to consult the course instructors should they need help in doing so. Several strategies were adopted to encourage cross-disciplinary dialog and learning during the course projects. For example, the IC1 course projects allowed pairs of students to work on such reports, with the teams composed of students from different graduate disciplines. In IC2, Rutgers graduate students from remote fields were asked to review and comment on student projects. The instructor for IC3 encouraged each student to select another student from an orthogonal field to be a consultant on his or her project.

Student Early Assessment and Curriculum Refinement

Given the diverse backgrounds of students, a first-day survey administered by the instructors has proven invaluable in assessing the knowledge base of each student population, and appropriately customizing the focus of the modules within each course. For instance, in IC1, which has now been offered twice, the student body was further along in research and more familiar with tissue engineering and other bioengineering topics. The second year's class was, on average, still formulating research projects and had a preponderance of students with bioinformatics backgrounds. Mid-course surveys also proved helpful in refining the course delivery. For example, students asked for additional background information, such as further definitions of specific terms and references to foundational papers. These modifications were readily implemented as postings on the course Web sites.

Curriculum Assessment

Given the interdisciplinary nature and lack of precedent for such a curriculum, continuing assessment is necessary to assure that it meets its goals and the needs of constituents. The ultimate goal of the curriculum is to provide students with knowledge that will increase the quality and productivity of their research. While the current curriculum form has been at Rutgers since 2003, a more comprehensive quantitative assessment of this outcome will have to wait for curricular knowledge to be translated to research output. Comments on course assessments suggest that students feel more knowledgeable and empowered in the areas of this interdisciplinary curriculum.

The curriculum serves as an effective platform for evaluating the success of students from diverse backgrounds. To gather additional data on possible differences in student performance, based on disciplinary background and/or IGERT participation, all students in IC3 were asked to evaluate each other's oral course project presentations using a structured questionnaire designed by the instructor. Evaluation criteria included not only presentation quality (clarity, organization, etc.), but also the appropriateness of the characterization methods chosen and the degree to which the chosen research problem was significantly biointerfacial. As rated by their peers, IGERT Fellows and non-IGERT students fared comparably, on average, indicating that the student learning outcomes were not systematically biased by their training program affiliation. Likewise, engineers, biologists, and chemists all fared similarly, with some students from each discipline giving stronger presentations than others from the same discipline.

An excellent source of data about student feedback on courses is the "Student Instructional Ratings Survey" (SIRS) program that is administered by the Rutgers Center for Advancement of Teaching. All courses at Rutgers are evaluated using a standard 10-question survey with a one- to five-point rating scale. The survey is reproduced, along with actual ratings for the first offering of the three IC courses, as Table 3 (next page). Additionally, three open-ended questions were posed to acquire qualitative feedback (not shown for brevity). To put the curriculum feedback in context, we calculated an average "bio-x-eng" response by using the SIRS data for "mean of responses from all courses this level" from the biomedical engineering and chemical and biochemical engineering graduate programs at Rutgers for the two academic semesters the IC courses were offered.

Generalizable Positive Comments

Students complimented the teaching quality of all three courses, which is consistent with the high numerical scores for each of the three lead instructors in Questions 1–5. Students noted the care given to the choice of topics (both breadth and relevance) and to the organization and delivery of the course material. Many comments addressed the ways in which all three courses incorporated current research literature into the course curriculum. Students appreciated the time devoted to discussion of the papers, and how these discussions, together with written assignments, helped students develop "alternative way(s) to look at data and critically review papers." Finally, students appreciated the attempts to tie course content and assignments to the biointerfacial aspects of their graduate dissertation research. The projects/presentations assigned in all three courses were useful in terms of "covering topics of interest instead of recycling research or spending too much time out of research." As expressed by another student, instructor and peer feedback from classroom presentations of final projects "will be important in directing and focusing the research in a biointerfacial twist."

Student Constructive Criticisms

Students in IC1, which did not use guest lecturers, expressed interest in having a few guest lecturers. Conversely, students in IC2 and IC3 felt that courses might be improved by fewer guest lecturers and/or better quality control. In IC2, students were primarily concerned that they sometimes could not deduce the relevance of a certain lecture, *i.e.*, its relationship to the overall curriculum. Other constructive criticism and suggestions of the students focused on not decreasing—and perhaps increasing—the frequency of short assignments and other ongoing student assessments. In IC2, there was concern about the difficulty of knowing what to study and having too much weight attributed to a final exam. In IC1, there was input that optional short exercises, calculations, and readings could be provided to address respective gaps in students' backgrounds. Finally, some students suggested the creation of a textbook for IC3, and a more modular organization of topics as in IC1.

TABLE 3
Rutgers Student Instructional Rating Survey (SIRS)

Questions	N=15	N=13	N=16	
	IC1	IC2	IC3	bio-x-eng
1. The instructor was prepared for class and presented the material in an organized manner	4.75	4.67	4.75	4.32
2. The instructor responded effectively to student comments and questions	4.63	4.60	4.67	4.30
3. The instructor generated interest in the course material	4.44	4.73	4.67	4.09
4. The instructor had a positive attitude toward assisting all students in understanding course material	4.63	4.53	4.58	4.40
5. The instructor assigned grades fairly	4.38	4.20	4.38	4.22
6. The instructional methods encouraged student learning	4.31	4.00	4.50	3.98
7. I learned a great deal in this course	4.50	4.27	4.58	3.97
8. I had a strong prior interest in the subject matter and wanted to take this course	4.56	4.53	4.42	3.73
9. I rate the teaching effectiveness of the instructor as	4.44	4.33	4.77	4.10
10. I rate the overall quality of the course as	4.25	4.13	4.77	4.08

CURRICULUM EVOLUTION AND INSTITUTIONALIZATION

The Rutgers curriculum on biointerfacial engineering was first structured around the core graduate training pathway of the IGERT program (<www.igert.rutgers.edu>). We expect the curriculum to evolve in response to the emerging areas of biomaterials and biointerfaces. The dynamic participation of a large number of research-active institutional faculty with access to state-of-the-art research infrastructure and tools will be integral to ensuring the timely evolution of the curriculum. The biointerfacial engineering area also resonates particularly well with the field of biomaterials science and engineering. Given the close ties of our IGERT to the New Jersey Center for Biomaterials (<www.nj.biomaterials.org>), we expect to offer the IC courses along with core biomaterials-related courses as part of a comprehensive certificate program at Rutgers on biointerfaces and biomaterials. The certificate program, to be established fall 2006, indicates successful institutionalization of the curriculum and will help sustain an identity for the curriculum.

CONCLUSIONS

A new graduate curriculum on integrative biointerfacial engineering was developed. This curriculum treats the

synthesis, analysis, and design of biological interfaces in terms of the constituent components (biologics, materials, systems), and with an eye to emerging technological applications such as tissue engineering, biotechnology, nanobiomaterials, and biomedicine. Each course within the curriculum is designed based on a fundamental integrating philosophy. The node for the curriculum lies within bio-x-engineering, while the breadth of the curriculum enables life scientists, physical scientists, and other bio-engineers to participate fully within the curriculum. Various instructional strategies were adopted to more fully integrate the multiple disciplines represented in the field. Based on student perception during early student assessment, the curriculum is equivalently amenable to students from a wide range of disciplines, effectively structured and rigorous, dynamic in embodying state-of-the-art research advances, and fills a major void in the graduate education of engineers and scientists. Graduate curriculum on integrative biosciences and bioengineering would resonate well in other American and international universities, particularly those with significant research strengths in molecular biosciences, advanced materials, and engineering sciences.

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