BIOMEDICAL INFORMATICS PROGRAM

Committee: (Chair and Program Director) Russ B. Altman; *(Associate Director)* Lawrence M. Fagan; Douglas L. Brutlag, Parvati Dev, Alan M. Garber, Teri Klein, Mark A. Musen, Gio Wiederhold

Participating Faculty and Staff by Department:

Opportunities for research are not limited to the specific faculty and departments listed.

Anesthesia: David M. Gaba (Professor)
Biochemistry: Douglas L. Brutlag (Professor)
Biostatistics: Richard A. Olshen (Professor)
Business: Alain C. Enthoven (Professor, emeritus)
Computer Science: Edward A. Feigenbaum (Professor), Richard E. Fikes (Professor, Research), Daphne Koller (Assistant Professor), Gio Wiederhold (Professor, Research), Terry Winograd (Professor)
Economics: Alan M. Garber (Professor, by courtesy)
Electrical Engineering: Albert Macovski (Professor, emeritus)
Genetics: David Botstein (Professor), Stanley N. Cohen (Professor), Richard M. Myers (Professor)
Health Research and Policy: Byron W. Brown, Jr. (Professor, emeritus), Alan M. Garber (Professor, by courtesy), Mark A. Hlatky (Professor), Richard A. Olshen (Professor)
Management Science and Engineering: Samuel Holtzman (Consulting Associate Professor), Ronald A. Howard (Professor), Ross D. Shachter (Associate Professor)
Mathematics: Samuel Karlin (Professor, emeritus)
Mechanical Engineering: Scott L. Delp (Associate Professor)
Medicine: Russ B. Altman (Associate Professor), Terrance Blaschke (Professor), Robert W. Carlson (Professor), Parvati Dev (Senior Research Scientist), Lawrence M. Fagan (Senior Research Scientist), Alan M. Garber (Professor), Mary Goldstein (Associate Professor), Michael Higgins (Consulting Associate Professor), Peter D. Karp (Consulting Assistant Professor), Teri Klein (Senior Research Scientist), John Koza (Consulting Professor), Mark A. Musen (Associate Professor), Douglas K. Owens (Associate Professor), Glenn Rennels (Consulting Assistant Professor), Thomas C. Rindfleisch (Senior Research Scientist), Gillian Sanders (Assistant Professor, Research), Michael Walker (Consulting Assistant Professor)
Neurosurgery: John R. Adler (Professor), Ramin Shahidi (Assistant Professor, Research)
Obstetrics and Gynecology: W. LeRoy Heinrichs (Professor, emeritus)
Radiation Oncology: Arthur L. Boyer (Professor), Lei Xing (Assistant Professor, Research)
Radiology: Gary H. Glover (Professor), Sandy A. Napel (Associate Professor), Norbert J. Pelc (Professor), Geoffry Rubin (Associate Professor)
Statistics: Trevor J. Hastie (Professor)
Structural Biology: Michael Levitt (Professor)
Surgery: Thomas Krummel (Professor), Charles Taylor (Assistant Professor, Research)

This interdisciplinary program was created in response to a recognized need for well-trained researchers and academic leaders in the expanding field of medical information sciences (medical informatics), which includes both bioinformatics and clinical informatics.

Stanford University's extensive computing facilities are described in the "Computer Science" section of this bulletin. In addition, the Biomedical Informatics Program has a network of personal computers, workstations, and servers running the Unix, Windows NT, Windows 95, and Macintosh operating systems. These machines are available for course work and research projects by trainees in the program.

GRADUATE PROGRAMS

The Biomedical Informatics Program is interdepartmental and offers instruction and research opportunities leading to M.S. and Ph.D. degrees in Biomedical Informatics, also known as Medical Informatics. All students are required to complete the core curriculum requirements outlined below, and also to elect additional courses to complement both their technical interests and their goals in applying medical informatics methods to clinical informatics, bioinformatics, or imaging informatics. Students who fail to maintain a 3.0 grade point average (GPA) in a category of the core curriculum are expected to pass a comprehensive exam in that area before the graduate degree is granted. In addition, all degree candidates must pass an oral examination that tests the student's ability to integrate the various components of the curriculum and to relate them to the overall field of medical informatics.

The core curriculum is common to all degrees offered by the program but is adapted or augmented depending on the interests and prior experience of the student. Deviations from the core curriculum outlined below must be justified in writing and approved by the student's Biomedical Informatics academic adviser and the chair of the Biomedical Informatics Committee. It should be noted, however, that the program is intended to provide flexibility and to complement other opportunities in applied medical research that exist at Stanford (for example, the Program on Engineering in Biology and Medicine). Although most students are expected to comply with the basic program of study outlined here, special arrangements can be made for those with unusual needs or those simultaneously enrolled in other degree programs within the University. Similarly, students with prior relevant training will have the curriculum adjusted to eliminate requirements that were met as part of their prior training.

CORE CURRICULUM

All students are expected to participate regularly in the Medical Informatics Student Seminar (201) and Colloquia (200), regardless of whether they register for credit in those courses. In addition, all students are expected to fulfill requirements in the following five categories:

1. *Core Biomedical Informatics* (15 units): students are expected to understand current applications of computers in medicine and to develop a broad appreciation for research in the management of biomedical information. Required courses are the two-quarter sequence Biomedical Informatics 210A and 210B (Introduction to Medical Informatics), plus 212 (Project Course), all of which should be taken during the first year in the program. Students must also take an additional 6 units of Biomedical Informatics course work (which may include cross-listed courses from other departments, but not including Biomedical Informatics 200, 201, 299, 302, or 303), selected in consultation with the academic adviser.
2. *Computer Science* (9 units): the student is expected to acquire a knowledge of the use of computers, computer organization, programming, and symbolic systems. It is assumed that students have had prior computing experience at least equivalent to Computer Science (CS) 109 and 150. All students are required to take a minimum of 9 units of courses in the Department of Computer Science. If similar courses have not been taken previously, these units must include CS 121, 161, and a course that requires significant programming and knowledge of machine architectures (for example, Electrical Engineering 182, CS 110, or the CS 193 series). For those who have taken such courses previously, replacement units may be taken from any other course in CS selected by the student and approved by the academic adviser. A course in databases is especially recommended. With the exception of CS 109 and 110, all other courses applied to the degree requirements must be numbered 137 or higher.
3. *Decision Science and Statistics* (9 units): students are required to take at least three courses that span the following four topics: basic probability theory, Bayesian statistics, decision analysis, and experimental-design techniques. Prior courses in statistics at least equivalent to Statistics 60 and calculus equivalent to Mathematics 42 are prerequisites. A prior course in linear algebra equivalent to Mathematics 103

or 113 is recommended. For the probability requirements, students may, for example, take Management Science and Engineering (MS&E) 120, Statistics 116, or MS&E 221. For the statistics requirements, options include, for example, Statistics 200 or 201, or Biomedical Informatics 233. For the third course requirements, options include, for example, decision analysis (MS&E 152 or 252), or cost effectiveness analysis (Biomedical Informatics 432). Specific courses, including possible substitutions, should be chosen in consultation with the student's academic adviser. Also recommended is a course in the psychology of human problem solving (for example, Psychology 256).
4. *Biomedical Domain Knowledge* (9 units): students are expected to acquire an understanding of pertinent life sciences and how to analyze a domain of application interest. Prior courses in biology at least equivalent to Biological Sciences 31 and 32 are prerequisites.
5. *Social and Ethical Issues* (6 units): candidates are expected to be familiar with key issues regarding ethics, public policy, financing, organizational behavior, management, and pertinent legal topics. Students may select at least 6 units from suitable courses that include, for example, Biomedical Informatics 250, 256, and 432; CS 201; Health Research and Policy 390, 391, and 392, or any other advanced course in policy and social issues proposed by the student and approved by the Biomedical Informatics academic adviser.

The core curriculum generally entails a minimum of 46 units of course work, but can require substantially more or less depending upon the courses selected and the previous training of the student. The varying backgrounds of students are well recognized and no one is required to take courses in an area in which he or she has already been adequately trained; under such circumstances, students are permitted to skip courses or substitute more advanced work. Students design appropriate programs for their interests with the assistance and approval of their Biomedical Informatics academic adviser. At least 30 units of formal course work are expected.

MASTER OF SCIENCE

The University requirements for the M.S. degree are described in the "Graduate Degrees" section of this bulletin.

This degree is designed for individuals who wish to undertake in-depth study of biomedical informatics. Normally, a student spends two years in the program and will implement and document a substantial project during the second year. The first year involves acquiring the fundamental concepts and tools through course work and research project involvement. All first- and second-year students are expected to devote 50 percent or more of their time participating in research projects. Research rotations are not required, but can be done with approval of the academic adviser or training program director. Graduates of this program are prepared to contribute creatively to basic or applied projects in biomedical informatics.

PROGRAM REQUIREMENTS

Programs of at least 54 units that meet the following guidelines are normally approved:

1. Completion of the core curriculum.
2. A minimum of 6 additional units of courses in Computer Science numbered 135 or higher, courses in Management Science and Engineering or Statistics numbered 200 or higher, Psychology 256 or 267, or relevant courses in other departments approved by the student's academic adviser.
3. Electives: additional courses to bring the total to 54 or more units.
4. Teaching: all students are expected to act as Teaching Assistants (TAs) for at least one course during their first two years of training. This will generally be Medicine 292 (the medical informatics short course), although another course approved by the program faculty may occasionally be substituted.

DOCTOR OF PHILOSOPHY

The University's basic requirements for the doctorate (residence, dissertation, examination, and so on) are discussed in the "Graduate Degrees" section of this bulletin.

Individuals wishing to prepare themselves for careers as independent researchers in medical informatics, with applications experience in bioinformatics, clinical informatics, or imaging informatics, should apply for admission to the doctoral program. The following are additional requirements imposed by the Biomedical Informatics Interdisciplinary Committee:

1. A student should plan and successfully complete a coherent program of study including the core curriculum, oral examination, and additional requirements for the master's program. In addition, doctoral candidates are expected to take at least two more advanced courses (see categories under item '2' of the master's program requirements). The master's requirements, including the oral examination, should be completed by the end of the second year in the program (six quarters of study, excluding summers). Doctoral students are generally advanced to Ph.D. candidacy after completing the oral examination. A student's academic adviser has primary responsibility for the adequacy of the program, which is regularly reviewed by the Graduate Study Committee of the Biomedical Informatics program.
2. To remain in the Ph.D. program, each student must attain a grade point average (GPA) as outlined in the master's programs above, and must pass a comprehensive exam covering introductory level graduate material in any curriculum category in which he or she fails to attain a GPA of 3.0. The student must fulfill these requirements and apply for admission to candidacy for the Ph.D. by the end of six quarters of study (excluding summers). In addition, reasonable progress in the student's research activities is expected of all doctoral candidates.
3. During the third year of training, generally in the Winter Quarter, each doctoral student is required to give a preproposal seminar that describes evolving research plans and allows program faculty to assure that the student is making good progress toward the definition of a doctoral dissertation topic. By the end of nine quarters (excluding summers), each student must orally present a thesis proposal to a dissertation committee that generally includes at least one member of the Graduate Study Committee of the Biomedical Informatics program. The committee determines whether the student's general knowledge of the field, and the details of the planned thesis, are sufficient to justify proceeding with the dissertation.
4. As part of the training for the Ph.D., each student is required to complete 2 units of teaching assistant service in Biomedical Informatics courses, 1 unit (10 hours per week for one quarter) being required during the first two years as evidence of satisfactory progress toward the degree.
5. The most important requirement for the Ph.D. degree is the dissertation. Prior to the oral dissertation proposal and defense, each student must secure the agreement of a member of the program faculty to act as dissertation adviser. The principal adviser need not be an active member of the Biomedical Informatics program faculty, but all committees should include at least one departmental faculty member.
6. No oral examination is required upon completion of the dissertation. The oral defense of the dissertation proposal satisfies the University oral examination requirement.
7. The student is expected to demonstrate an ability to present scholarly material orally and present his or her research in a lecture at a formal seminar.
8. The student is expected to demonstrate an ability to present scholarly material in concise written form. Each student is required to write a paper suitable for publication, usually discussing his or her doctoral research project. This paper must be approved by the student's academic adviser as suitable for submission to a refereed journal before the doctoral degree is conferred.
9. The dissertation must be accepted by a reading committee composed of the principal dissertation adviser, a member of the program faculty, and a third member chosen from anywhere within the University.

The principal adviser and at least one of the other committee members must be Academic Council members.

COURSES

170Q. Stanford Introductory Seminar: Decision Making in Law and Medicine—Preference to sophomores. Legal and medical decisions are difficult for both the client/patient and the attorney/physician, especially when the stakes (financial or physical well-being) are high. Medical and legal professionals have developed different strategies for framing decisions and implementing this framework: who is the final decision maker, what are the ethical implications of different standards for decision making, and how to use the decision making process to make the health care legal system more comprehensible. The role of financial considerations in the decision making process for the client/patient, lawyer/doctor, financial stakeholders, community, and society. Readings from the decision analytic literature of medicine and psychology, and the client-counseling literature in law. Examples from law and medicine.
3 units, Win (Altman, Merino)

200. Biomedical Informatics Colloquium—Series of colloquia offered by program faculty, students, and occasional guest lecturers. Credit available only to students in a Biomedical Informatics degree program. (May be taken no more than three times for credit.)
1 unit, Aut, Win, Spr

201. Biomedical Informatics Student Seminar—For all students and faculty. Participants report on recent relevant articles from the Biomedical Informatics literature or their research projects. The ongoing experience, with feedback from faculty, is intended to teach presentation skills to Biomedical Informatics trainees. Credit available only to students in an Biomedical Informatics degree program. (May be taken no more than three times for credit.)
1 unit, Aut, Win, Spr

202. Clinical Diagnosis—Open only to students in a Biomedical Informatics degree program. Designed for learning the techniques of interviewing and symptom analysis through the study of a variety of common and well-defined clinical entities, and by role-playing in a problem-solving setting. See instructor.
2 units, not given 2000-01

205. Introduction to Biomedical Environments—Open only to students in a Biomedical Informatics or Health Services Research degree program who are not enrolled in the M.D. program and do not have an M.D. degree. Background introduction to the sites to be visited. Selected faculty introduce a variety of settings at Stanford Medical Center and the Veterans Affairs Medical Center: the medical wards, radiology, molecular biology research laboratories, outpatient clinics, emergency room, operating room, intensive care unit, psychiatry ward, and clinical lab. See instructor.
1 unit (Staff) not given 2000-01

210A. Introduction to Biomedical Informatics: Fundamental Methods—(Same Computer Science 270A.) Issues in the modeling, design, and implementation of computational systems for use in biomedicine. Topics: controlled terminologies in medicine and biological science, ontologies, fundamental algorithms, basic knowledge representation, information dissemination and retrieval. Emphasis is on the principles of modeling data and knowledge in biomedicine and on the translation of resulting models into useful automated systems.
3 units, Aut (Musen, Altman)

210B. Introduction to Biomedical Informatics: Systems and Requirements—(Same as Computer Science 270B.) Continuation of 210A. Survey of the major application areas in medical informatics, including clinical information systems, imaging systems, bioinformatics, public policy, decision support, and signal processing. Emphasis is on the system requirements, relevant data, algorithms, and implementation issues in each area. Prerequisite: 210A.
3 units, Win (Shahar, Dev)

212. Biomedical Informatics Project Course—(Same as Computer Science 272.) For students who have completed 210A, 210B, or 214, and who wish to implement those ideas in a computer program. Students may take 214 concurrently and complete a project that is coordinated between the two courses. Prerequisites: programming experience, 210B.
3 units, Sum (Altman, Koza)

214. Representations and Algorithms for Computational Molecular Biology—(Same as Computer Science 274.) Introduction to the basic computational issues and methods used in bioinformatics, including access and use of biological data sources on the Internet. Topics: basic algorithms for alignment of biological sequences and structures, computing with strings, phylogenetic tree construction, hidden Markov models, computing with networks of genes, basic structural computations on proteins, protein structure prediction, protein threading techniques, homology modeling, molecular dynamics and energy minimization, statistical analysis of 3D biological data, integration of diverse data sources, knowledge representation and controlled terminologies for molecular biology, graphical display of biological data, genetic algorithms and genetic programming applied to biological problems. See instructor for unit options. Prerequisites: programming skills and understanding of matrix algebra.
1-4 units, Spr (Altman, Koza)

216. Lectures on Representations and Algorithms for Molecular Biology—Lecture series for 214. Recommended: familiarity with biology.
1 unit, Spr (Altman, Koza)

226. Genetic Algorithms and Genetic Programming—(Same as Computer Science 426.) The genetic algorithm is a domain-independent algorithm for search, optimization, and machine learning patterned after Darwinian natural selection and naturally occurring genetic operators such as recombination; mutation; gene duplication, deletion, regulation; and embryonic development. Genetic programming is a domain-independent automatic programming technique that extends the genetic algorithm to the breeding of populations of computer programs capable of producing human-competitive results. Topics: introduction to genetic algorithms and genetic programming; the mathematical basis for genetic algorithms; implementation on parallel computers and field-programmable gate arrays; applications to problems of system identification, control, classification, analysis of genome and protein sequences; automatic synthesis of the design of topology, sizing, placement, and routing of analog electrical circuits; automatic synthesis of controllers; and automatic synthesis of other complex network structures.
3 units, Spr (Koza)

228. Influence Diagrams and Probabilistic Networks—(Enroll in Management Science and Engineering 355.)
3 units, Win (Shachter)

230. Seminar on Knowledge Acquisition for Expert Systems—For graduate students. Discussion of experimental approaches to the construction of expert-system knowledge bases. Topics: interviewing techniques, formal and informal approaches to modeling expert knowledge, and automated tools that facilitate knowledge acquisition. Enrollment limited to 20. Prerequisite: one course in artificial intelligence.
2 units, Spr (Musen) alternate years, not given 2001-02

231. Computational Molecular Biology—(Same as Biochemistry 218.) For molecular biologists and computer scientists desiring a practical, hands-on approach to computational molecular biology; recommended for molecular biologists and computer scientists desiring to understand the major issues concerning representation and analysis of biological sequences and structure. Existing methods are critically described with the strengths and limitations of each. Future directions for the development of new methods. Practical assignments utilizing the tools described. Topics: accessing molecular databases, pattern search, classification of sequence and structure, alignment of sequences, rapid similarity searching, phylogenies, automated pattern learning, representing protein structure, modeling protein structure by homology, protein-protein docking and protein-ligand docking. Final project utilizes or analyzes the methods presented. Lecture/lab. Enrollment limited to 40. Prerequisite: introductory molecular biology at the level of Biological Sciences 52 or consent of instructor. Recommended: 210A,B.

3 units, all quarters via Internet (Brutlag)

233. Intermediate Biostatistics: Analysis of Discrete Data—(Enroll in Health Research and Policy 261.)

3 units, Win (Staff)

239. Computer-Based Medical Education—Directed reading and research for graduate-level students in the use of modern web-based hypermedia and simulation techniques in education. Possible topics: replacement of a lecture or a lab session, distance learning, student models, and clinical case simulations.

1-6 units, any quarter (Dev)

250. The U.S. Health Care System and Health Policy—(Enroll in Health Research and Policy 205.)

2 units, Win (Baker)

256. Economics of Health and Medical Care—(Same as Economics 156/256, Health Research and Policy 256.) Institutional, theoretical, and empirical analysis of the problems of health and medical care. Topics: institutions in the health sector; measurement and valuation of health; nonmedical determinants of health; medical technology and technology assessment; demand for medical care and medical insurance; physicians, hospitals, and managed care; international comparisons. Prerequisite: Economics 50 and 102A or equivalent statistics, or consent of instructor. Recommended: Economics 51.

5 units, Win (McClellan)

278. Probabilistic Models in Artificial Intelligence—(Enroll in Computer Science 228.)

3 units, Win (Koller)

299. Directed Reading and Research—For students wishing to receive credit for directed reading or research time.

any quarter

301. Special Topics in Medical Informatics

1-6 units, any quarter (Staff)

302. Introduction to Current Research—Survey of Stanford-based research in medical informatics, with weekly seminars led by faculty and senior researchers. Prerequisite: BMI degree candidacy, or consent of instructor.

1 unit Aut (Staff)

315. Topics in Image Informatics—In-depth study of selected active research topics in image informatics chosen from: scientific and medical visualization, biomedical simulation, interfaces, virtual environments, visual and haptic standards for storage and transmission. Readings from the literature, presentations, and a project. Prerequisites: programming experience in any of C, C++, Java, Matlab, and some prior exposure to graphics or image processing.

3 units, Spr (Dev)

328. Protein and Nucleic Acid Structure, Dynamics, and Engineering—(Enroll in Structural Biology 228.)

3 units, Win (Levitt)

348. Computer Graphics: Image Synthesis Techniques—(Enroll in Computer Science 348B.)

4 units, Spr (Hanrahan)

432. Cost-Benefit Analysis in Health Care—(Same as Business E332, Health Research and Policy 392.) How do you do cost-benefit analysis when the "output" is difficult or impossible to measure? How do the M.B.A. analytic tools apply in health services? Study/discussion of the main literature on the principles of cost-benefit analysis applied to health care. Critical review of actual studies. Emphasis is on the art of practical application.

4 units, Aut (Garber, Sanders)