Biomedical Informatics Training at the University of Wisconsin-Madison

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Summary

Objectives: The purpose of this paper is to describe biomedical informatics training at the University of Wisconsin-Madison (UW-Madison).

Methods: We reviewed biomedical informatics training, research, and faculty/trainee participation at UW-Madison.

Results: There are three primary approaches to training: 1) The Computation & Informatics in Biology & Medicine Training Program, 2) formal biomedical informatics offered by various campus departments, and 3) individualized programs. Training at UW-Madison embodies the features of effective biomedical informatics training recommended by the American College of Medical Informatics that were delineated as: 1) curricula that integrate experiences among computational sciences and application domains, 2) individualized and interdisciplinary cross-training among a diverse cadre of trainees to develop key competencies that he or she does not initially possess, 3) participation in research and development activities, and 4) exposure to a range of basic informational and computational sciences.

Conclusions: The three biomedical informatics training approaches immerse students in multidisciplinary training and education that is supported by faculty trainers who participate in collaborative research across departments. Training is provided across a range of disciplines and available at different training stages. Biomedical informatics training at UW-Madison illustrates how a large research University, with multiple departments across biological, computational, and health fields, can provide effective and productive biomedical informatics training via multiple bioinformatics training approaches.

Keywords
Academic training, training programs, informatics, biomedical informatics


Introduction

A plethora of approaches support biomedical informatics training at the University of Wisconsin-Madison, all of which share a strong focus on interdisciplinary coursework and research. There are three primary approaches to training: 1) The Computation & Informatics in Biology & Medicine Training Program, 2) formal biomedical informatics offered by various campus departments, and 3) individualized programs. Training is supported by institutional and individual pre-doctoral, postdoctoral, and career fellowships. Biomedical informatics training at UW-Madison embodies features that were outlined in a report from a study of the future of informatics training conducted by the American College of Medical Informatics [1]. This study committee defined biomedical informatics as an interdisciplinary field that combines basic informational and computational sciences with application domains that include health care, biological research, and education. They concluded that effective training in informatics consists of: 1) curricula that integrate experiences among computational sciences and application domains, 2) individualized and interdisciplinary cross-training among a diverse cadre of trainees to develop key competencies that he or she does not initially possess, 3) participation in research and development activities, and 4) exposure to a range of basic informational and computational sciences.

Computation & Informatics in Biology & Medicine Training Program

The Computation & Informatics in Biology & Medicine (CIBM) Training Program is a bioinformatics training program for pre-doctoral and post-doctoral trainees, funded by the National Library of Medicine (NLM) since 2002. CIBM’s mission is to provide modern training for a new generation of researchers wishing to solve biomedical problems requiring strengths in both computational and biological science.
Faculty & Trainees

The 41 CIBM faculty span 15 different departments and five colleges at the University of Wisconsin-Madison, and include several at the Marshfield Clinic Research Foundation, as well. The research foci of CIBM faculty are available on the CIBM Program website at www.cibm.wisc.edu. The management team includes George Phillips (Professor of Biochemistry and of Computer Sciences) as the Program Director, David Page (Associate Professor of Biostatistics & Medical Informatics and of Computer Sciences) and Jude Shavlik (Professor of Computer Sciences and of Biostatistics & Medical Informatics) as Co-directors, and a Management Committee that consists of Frederick Blattner (Oliver Smithies Professor of Genetics), Patricia Flatley Brennan (Moehlman Bascom Professor of Nursing, Industrial & Systems Engineering, and of Biostatistics & Medical Informatics), Mark Craven (Associate Professor of Biostatistics & Medical Informatics and of Computer Sciences), David DeMets (Professor and Chair of Biostatistics & Medical Informatics and Professor of Statistics), and Justin Starren (Director of the Biomedical Informatics Research Center, Marshfield Clinic Research Foundation).

The departmental homes of CIBM trainers who have served as primary mentors for CIBM trainees and CIBM trainees are summarized in Table 1. The percentages of trainees and faculty trainers differ because many faculty have joint appointments, and the Biostatistics & Medical Informatics Department does not directly accept graduate students. Joint appointments among faculty facilitate integrated training. Pre and postdoctoral trainees select a primary and a secondary mentor that reflect their primary and cross-training foci respectively. Several students have constructed a special multidisciplinary bioinformatics PhD degree. Additional CIBM faculty trainers are in the Departments of Electrical and Computer Engineering, Oncology, and Statistics. Many are members of the Genome Center of Wisconsin, which administers the CIBM Training Program. Two CIBM faculty are affiliated with the Marshfield Clinic. The Marshfield Clinic is located in 41 centers throughout northern, central and western Wisconsin. Its research division, the Marshfield Clinic Research Foundation, conducts research on healthcare and public health. Areas of focus include clinical research, rural and agricultural health and safety, human genetics, epidemiology and biomedical informatics.

CIBM Curriculum

The CIBM program is not a degree granting program but designed to foster interdisciplinary training. CIBM trainees become well versed in a common language of concepts from computer science, statistics, and biology. Students can use the required CIBM classes to satisfy their PhD minor requirement in their respective home departments. The CIBM Program’s curriculum for pre-doctoral trainees (see Table 2) has three components:

- **Interdisciplinary bioinformatics core courses**: All pre-doctoral students are required to take an introductory class in bioinformatics, an essential skill in an increasingly “data driven” world, as well as Introduction to Bioinformatics. The third course in this group can be chosen from a set of advanced biomedical informatics courses.

- **Molecular-biology training triad**: Students choose three classes from a set of genetics, genomics, and biochemistry courses that best match their research goals to provide education in the basics of molecular biology.

- **Basics of computer science**: All students are expected to take Introduction to Data Structures. The other classes address different aspects of computation that play key research roles in bioinformatics and scientific computation in general.

All CIBM trainees participate in a
### Table 2: CIBM Curriculum

<table>
<thead>
<tr>
<th>Course Code</th>
<th>Course Title</th>
<th>Description/Topics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stat 571</td>
<td>Statistical Methods for Bioinformatics I</td>
<td>Descriptive statistics, distributions, one- and two-sample normal inference, power, one-way ANOVA, simple linear regression, categorical data, etc.</td>
</tr>
<tr>
<td>BMI 576</td>
<td>Intro. to Bioinformatics</td>
<td>Algorithms for computational problems in molecular biology: genome sequencing and mapping, sequence alignment, modelling classes and features, expression data analysis, etc.</td>
</tr>
<tr>
<td>BMI 776</td>
<td>Adv. Bioinformatics</td>
<td>Advanced course covering computational problems in molecular biology and a core set of widely used algorithms.</td>
</tr>
<tr>
<td>Bioch 711</td>
<td>Sequence Analysis</td>
<td>Topics include genetic change; sequencing methods; comparison and alignment algorithms; motif and structure recognition; database searching.</td>
</tr>
<tr>
<td>ISyE 617</td>
<td>Health Information Systems</td>
<td>Covers core concepts of health information systems. Major applications include clinical information systems, language and standards, decision support, image technology and digital libraries.</td>
</tr>
</tbody>
</table>

#### Biomedical Informatics Training at the University of Wisconsin-Madison

Biomedical research problems related to bioinformatics and computational biology. Weekly seminar series; cross-disciplinary exposure to current research in computer science, biostatistics, engineering, biological sciences and biomedical research problems related to bioinformatics and computational biology.
weekly seminar during fall and spring semesters that brings trainees, trainers, and other interested faculty and students together for cross-disciplinary exposure to current research in computer science, bioinformatics, engineering, biological sciences and biomedical research problems related to bioinformatics and computational biology. Presentations are designed to communicate across disciplines and are provided by CIBM trainees, UW-Madison faculty, and faculty from other institutions. The seminar is open to students, faculty, and others interested in bioinformatics. Another excellent training opportunity is the annual CIBM Program fall retreat, which features poster sessions where trainees as well as others in biomedical informatics share their research. Presentations include featured speakers by national and campus informatics scholars. Each year, one of the featured speakers is a UW bioinformatics alum.

### Table 3: Examples of Interdisciplinary Research with CIBM Faculty and Trainees

<table>
<thead>
<tr>
<th>Topic</th>
<th>1Trainers, 2Trainees, &amp; 3Others</th>
<th>Focus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole-Genome Multiple Alignment</td>
<td>1Parnia, 2Darling</td>
<td>Computing whole-genome multiple alignments in the presence of large-scale evolutionary events. Developed algorithm for multiple-genome alignment called Mauve (<a href="http://gel.biochem.wisc.edu/mauve/">http://gel.biochem.wisc.edu/mauve/</a>).</td>
</tr>
<tr>
<td>Inducing Models of Regulatory Networks</td>
<td>1Blattner, Craven, Page, 2Bockhorst, Durfee, McFarlin, Noto, Ong</td>
<td>Developing novel machine-learning algorithms for uncovering gene-regulatory networks. Current and future research directions include a) integrating regulatory-network with metabolic-network models, b) developing methods that are able to exploit all relevant sources of data, including the scientific literature, and c) applying the methods to aid in the understanding of disease-related data sets.</td>
</tr>
<tr>
<td>Structural Bioinformatics</td>
<td>1Phillips, Shavlik, 2Dimaio, Soni</td>
<td>Developing new algorithms for automatically interpreting electron density maps based on pictorial structures and matching. Future directions include employing fully connected Bayesian networks, using machine learning to recognize individual amino acids in electron density maps, scaling up to larger proteins, and handling poorer quality electron density maps.</td>
</tr>
<tr>
<td>Simulations of Biomolecular Information Processing</td>
<td>1Yin, 2Haselaris, Suthers, 3Gourse (Bacteriology), 4Rawlings (Chemical &amp; Biological Engineering)</td>
<td>Write and solve mass-action kinetic models with a focus on simulating the intracellular/viral responses to nutrient shifts. They have pioneered genome-to-organism dynamic models for diverse viruses. Fundamental advances include identifying protein synthesis as the limiting resource for virus growth, quantifying how interactions among genes contribute to virus fitness and robustness, and identifying conditions under which wild-type genome designs are optimal.</td>
</tr>
<tr>
<td>Statistical-Relational Learning Methods Applied to Mammmography</td>
<td>1Burnside, Page, Shavlik, 2Davis</td>
<td>Develop novel statistical relational learning (SRL) algorithms and apply them to the task of creating an expert system for mammography. They have shown that SRL algorithms can benefit from the ability to define new data views that can enhance the accuracy of predicting important fields in the original database.</td>
</tr>
<tr>
<td>Informatics for Clinical and Operational Support</td>
<td>1Brennan, 2Haight, Hsieh, Severtson, Zayas-Gabin, 3Kash, Rayon, Robinson (Industrial and Systems Engineering)</td>
<td>Research in the Brennan lab is aimed at supporting informed decisions at multiple levels within the healthcare system. The HeartCare II project developed, deployed and is evaluating the impact of technology enhanced nursing practice in home care settings. A recently established, Robert Wood Johnson-supported national coordinating center for personal health records brings academic and industry partners together to solve the challenge of creating a seamless link across all health information related to a given person. Mathematical modeling projects include employing Markov models for optimal treatment sequencing decisions, quality engineering and forecasting models to improve access to care for people who need treatment for substance abuse, stochastic simulation and real options models to the challenge of pricing health information exchange alliances.</td>
</tr>
</tbody>
</table>

1 CIBM Faculty Trainers, 2 CIBM Trainees, 3 Other Faculty

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Research Training

The driving forces for the research training opportunities arise from health and life sciences phenomenon. In many cases these questions demand new approaches and technologies. The weaving of cultures from computer sciences, biological sciences, and health sciences are illustrated in short descriptions of a sampling of the many wide-ranging multidisciplinary projects on campus (see Table 3). These
examples illustrate the CIBM culture of research that generates productive interdisciplinary research training.

A key focus of research at UW-Madison is the development of novel bioinformatics algorithms to analyze molecular data, genome sequences, proteins (levels, interactions, structures), and regulatory pathways. These advances are only possible when computer scientists understand enough about the problems to design usable tools and when bioscientists understand what is possible using computational and information technologies. The CIBM Program has established a culture of research that supports the development of these state-of-the-art bioinformatics algorithms. Trainees and faculty have published papers in the leading bioinformatics venues on such critical topics as multiple genome alignment [2], identification of regulatory structures in a genome [3], and analysis of high-throughput biological data [4] including expression data from microarrays [5], single-nucleotide polymorphism data [6], and structural bioinformatics [7 - 13].

As bioinformatics algorithms contribute more to our understanding of biology at a molecular level, there is a need for these algorithms to have a more direct impact on medical diagnostic and treatment processes. The CIBM Program recently added a unique translational medicine component through a collaboration with the Marshfield Clinic expanding its focus to span from molecular data to disease prediction and prevention. An example project in the translational medicine component focuses on the design and deployment of machine learning algorithms to predict responses to a particular treatment from combined single-nucleotide polymorphism (SNP) data and clinical history data. This “Molecules to Bedside” component (see Figure 1) complements CIBM’s tradition of bioinformatics research and expands it - giving trainees the opportunity to apply their bioinformatics algorithms directly to clinical data. The Marshfield Clinic has an electronic medical record that dates back to the 1960s and a new personalized medicine program that already has collected DNA for nearly 20,000 of its patients for genotyping [14]. The clinic is the sole health care provider for many people in central Wisconsin including these 20,000. The Marshfield Clinic’s database is a rare resource of detailed clinical and growing genetic data on patients [15].

Informatics Training within UW-Madison Departments

In addition to the CIBM Program, UW-Madison students have multiple options for pursuing biomedical informatics training. Options include a degree minor, certificate programs, research training programs in various informatics areas, and courses that provide an informatics component within graduate programs. Many of the faculty that provide biomedical informatics training within these departments are CIBM faculty thus providing an integration between these training programs. Formal courses that provide the foundation for academic training in biomedical informatics are housed in various departments. We next provide an overview of the biomedical informatics components within these departments.

Department of Biostatistics and Medical Informatics. The Department of Biostatistics and Medical Informatics, within the School of Medicine and Public Health, serves as a resource for clinical, population and basic sciences investigators. A major goal of the Department faculty and staff is to collaborate in the design, conduct, and analyses of laboratory, clinical, and epidemiologic studies in a variety of biomedical disciplines and departments. Faculty conduct research in statistical methodology and computational methods and participate in three graduate and postdoctoral training programs – one of these is a program in medical informatics. Medical informatics training is offered via 1) a degree minor from this department that can be satisfied by courses in the CIBM Program’s curriculum, 2) MS and PhD programs in Computer Sciences, 3) a Graduate Certificate program for students cur-
rently enrolled in medical science or biological science graduate programs, and 4) a Capstone Certificate program for post-doctoral fellows and employees of local companies working in molecular biology.

Biomedical informatics research, offered in three main areas, illustrates how computation is integrated with medical applications in this department. Professors Craven, Kendzierski, Newton, Page, and Shavlik offer research projects in genetics/genomics. Projects include characterization of the genetic factors involved in susceptibility and resistance to cancer growth, mapping gene locations, analyzing genomic sequence data, analysis of mutagenesis experiments, analyzing gene-expression array data, optical mapping of genomes, predicting genomic regulatory elements, algorithms for analysis of mass spectrometry data, and novel gene-expression measurement technology. Collaborators include the UW Comprehensive Cancer Center, McArdle Laboratory for Cancer Research, Computer Sciences, Pharmacy, Genetics, and Biochemistry. Professors Craven, Page, Shavlik, Burnside and DeMets offer research projects in clinical informatics and bioinformatics. Collaborative projects include computational diagnosis of breast cancer including the determination of which mammogram abnormalities require biopsy, automated methods for extracting information from the biomedical literature, automated interpretation of images from x-ray crystallography, and automated pharmacophore discovery to help guide drug design. Collaborators include the UW Comprehensive Cancer Center, McArdle Laboratory for Cancer Research, Computer Sciences, Pharmacy, Genetics, Biochemistry, and the General Clinical Research Center.

Professors Chung and Dyer are developing algorithms for analyzing MRI images of the brain, where the algorithms perform segmentation, coregistration, and description. Collaborations exist with the Keck Lab (brain imaging), the Department of Ophthalmology and Visual Sciences, the Fundus Photograph Reading Center, Medical Physics, Mechanical Engineering, Waisman Center (speech kinematics), and the Department of Radiology (diagnostic and functional MRI).

**Department of Computer Sciences.** The Department of Computer Sciences is consistently ranked as one of the top ten computer science departments in the country. Most of UW’s formal biomedical informatics courses are offered through this department. In particular, the department has internationally recognized research programs in Artificial Intelligence (primarily Computer Vision and Machine Learning), Computational Biology, Computer Architecture and VLSI (Very Large Scale Integration), Computer Graphics, Computer Networks, Computer Security, Database Systems, Numerical Analysis, Operating Systems, Optimization, Performance Analysis, Programming Languages and Compilers, and Theoretical Computer Science— all of which have relevance to biomedical informatics applications.

A recent project, relevant to both biomedical and public health science, is a collaboration between Professors DeWitt and Shavlik (Computer Science), Hanrahan (Chief Epidemiologist, State of Wisconsin), and Trentham-Dietz (Population Health Sciences) to simultaneously develop algorithms for anonymizing data along with machine-learning algorithms capable of extracting useful information from anonymized data. Maximizing the tradeoff between these two conflicting goals will allow significant scientific knowledge to be extracted from biomedical datasets while guarding patient privacy.

**Health Systems.** Clinical informatics training occurs in a unique environmental spanning the Department of Industrial and Systems Engineering and the School of Nursing. Professor Brennan teaches graduate level health informatics classes in the Department of Industrial and Systems Engineering and the School of Nursing. Training within these departments is primarily in the area of clinical informatics within the health care system. Curricula consist of established courses (for example, Health Systems Design) and special courses. For example, she recently partnered with faculty from three other universities that have a nursing informatics program to offer a cross campus course in Nursing Informatics. This endeavor was under the umbrella of the Committee on Institutional Cooperation (CIC) among ten leading Mid-west universities known as the Big Ten. Her multidisciplinary research, summarized in Table 2, is aimed toward developing informatics solutions that support informed decisions across the health care spectrum—from personal health to RHIO (Regional Health Information Organization) networks. The Brennan Health Systems Lab, comprised of trainees in Industrial and Systems Engineering and Nursing, offers a unique mix of perspectives that bring engineering knowledge to patient care, and the human care dimension to engineering approaches that makes a distinctive contribution to the biomedical informatics literature [16–17]. A hallmark of training with the Brennan lab is that each trainee develops and executes his or her own research. In some cases it directly interfaces with funded lab research, in other cases it has conceptual relevance but is in a different area.

Dr. Brennan also provides informatics training that falls outside of a traditional curriculum. For example, trainees in the
nursing program participate in a video
conference-mediated bi-monthly CIC
Nursing Informatics Journal Club with
participants from Nursing Informatics
Training programs at four of the Big
Ten universities: Indiana University,
University of Iowa, Michigan State
University, and University of Minne-
sota. Participants take turns selecting
the topic, literature, and leading the dis-
cussion. She is also providing training
to UW-Madison and UW-System Clin-
cal Nurse Instructors for incorporating
informatics and genomics content into
nursing curriculum. These non-tradi-
tional training initiatives provide a
mechanism for building collegial rela-
tionships and scholarship among nurs-
ing informatics researchers, and for
translating clinical genomics into nurs-
ing practice via a train-the-trainer ap-
proach.

Health systems informatics research is
supported by several center programs
that allow trainees to participate in
informatics research with various
health care applications. The Center for
Productivity and Quality Improve-
ment, housed in the Department of
Industrial and Systems Engineering,
applies human factors solutions to
health information systems implementa-
tion. Current projects evaluate the
effect of computerized-provider order
entry systems on clinical outcomes and
examine the impact of bar code tech-
nologies on safe medication admin-
istration. This group also benchmarks
technology acceptance patterns among
health care workers and patients. The
Trace Research and Development Cen-
ter develops and deploys adaptive tech-
nologies to insure that people with all
levels of abilities are able to effectively
use electronic health care resources.
The Center for Health Systems Re-
search and Analysis houses a national
repository for quality assessment in
long term care.

Informatics Training via
Individual Fellowships,
Traineeships and Mentorships

Biomedical informatics training at UW-
Madison is also supported via indi-
vidual training fellowships. Two infor-
natics fellows funded by the NLM are
from the Brennan lab. In one exemplary
program, a doctoral candidate at the
School of Nursing constructed a sec-
dondary emphasis in nursing informatics
through intra and extra-mural training.
She has a minor in Computer Sciences
and took five courses in this depart-
ment that support her interest in devel-
op ing computable representations that
accurately characterize concepts rel-
vant to nursing practice. Informatics
expertise that is represented on her dis-
sertation committee include Dr.
Brennan and faculty members from the
UW-Madison School of Library and
Information Studies as well as Stanford
Medical Informatics. She participated
in genomics training offered by the
Jackson Laboratory in Bar Harbor and
works with Dr. Brennan and Clinical
Faculty at UW-Madison to incorporate
informatics and genomics into the un-
dergraduate nursing curriculum. An
NLM-funded postdoctoral fellow works
with Brennan’s HeartCare II research
team. She is applying Brennan’s model
of technology enhanced nursing prac-
tice toward developing informatics re-
sources to support a model of integrated
care for adolescents in the area of men-
tal health. A NLM-funded career fel-
low in the Department of Biochem-
istry, and former CIBM postdoctoral
fellow, is conducting research that will
accelerate understanding proteins and
their structures through the develop-
ment of tools aimed to significantly
speed up understanding of protein struc-
tures by building a probabilistic frame-
work that integrates informatics and
physical models. These examples show
how biomedical informatics training can
occur outside of a structured informatics
program and can meet training needs
over the course of one’s career.

Conclusions

Biomedical informatics training at UW-
Madison is provided across a range of
disciplines and is available at different
training stages. The CIBM program il-
ustrates how a cross-training program
can support highly productive biomed-
ical informatics research training out-
side of a degree granting biomedical
informatics department. This program
fosters a creative synergy that advances
biomedical informatics across multiple
fronts and prepares trainees to partici-
pate in an evolving and multidisci-
plinary field. Biomedical informatics
training offered within established de-
partments adheres to a similar model
of immersing students in multidisci-
plinary training and education that is
supported by faculty trainers that are
conducting collaborative research across
departments. The health systems infor-
matics training complements the bio-
science focus of the other programs and
fosters the application of biomedical
informatics to health care. Individual
fellowships support the development of
biomedical informatics expertise
through individualized training pro-
grams. UW-Madison, with multiple
departments across biological, compu-
tational and health fields, provides a
rich biomedical informatics training
environment that has been harnessed to
create productive biomedical training
programs.

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References


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