Genomics and Engineering

By Ravi Shankar, Professor, FAU

This report was extracted from a proposal to FAU to establish an undergraduate program in Bioengineering in 1999. FAU has since then developed a Masters Level Certificate program in Bioengineering that is housed in the Electrical Engineering Department.

1. GENOMICS DEFINED

According to Dr. Poste, President, R&D, SmithKline Beecham [Post94], "Genomics, the study of genes and their functional regulation in health and disease, now occupies center stage in biomedical research. Fueled by both public and industrial funding, exploration of the human genome is proceeding faster than could be imagined even a few years ago, with profound implications for the future practice of medicine...". This comment made in 1994 is all the more true today. A genome is the collection of genes that define the characteristics of a human, an animal, or a plant. Study of this holds enormous implications for the future, from customized medicine, production ("Biomanufacturing") of large quantities of many essential drugs (for e.g., Insulin to help Diabetics), to environmentally strong bio-engineered plants and super-gene off-springs . Dupont recently decided to shed its Conoco Oil Unit that yielded half its revenue in 1997, to raise $25 Billion that would be invested in the genomics business [Warr98]. Monsanto, meanwhile, went on a buying spree and spent $4.2 Billion to acquire two biotechnology concerns with Genomic drugs under development [Kilm98]. DuPont and Monsanto both are aggressively pushing research and development on Agricultural Biotech [Sher98, PRNE98]. Novartis Pharma of Basel, Switzerland, committed $250 million to create its own research institute dedicated to tracking down the functions of the many genes being discovered [Penn98].

Perkins-Elmer recently teamed up with Dr. Venter, one of America's most high profile biologists, and head of the non-profit Institute for Genomic Research (TIGR), to decode the entire human genome in three years, way ahead of the federally funded Human genome Project, by using their proprietary rapid parallel sequencing systems [Jaro98, Rich98]. The race is on, to decode the human genome sequence of 100,000 (functional) genes and a sequence of 3 billion or so chemical code letters in the genome. This is expected to cost $300 million, far below the mammoth Human genome project with a budget of $3 billion and hundreds of scientists around the world. The Human genome project would put the results in the public domain, while Perkins-Elmer expects to license out the results. There are many private and public databases, available around the world today, that catalog the gene sequences of various species and disease states.

These databases can be very large. For e.g., E Coli, the bacteria that has been extensively studied, and used as a "factory" to produce Insulin and Human Growth Hormone, has 4100 genes and a database of 4.7 million base pairs [GoWh95, AnGa97]. The corresponding database size for plants and humans would be 50 Mbp and 1

Gbp [Babr98]. This explosion of information has resulted in a new field called "Bioinformatics" that brings the database management techniques of computational sciences to bear upon the biological databases. Unlike the usual informational databases, there is much unknown and new tools, both software and hardware, are being developed [BaBr98, Fodo97, HeSc97, KoMe98]. But the payoff is enormous [Wyke97, Rifk98]. Example application domains are: Medical Applications: Diagnostics (Gene-based screening for cancer, heart diseases, diabetes, etc.), Medical Informatics, and Gene Therapy; Security and Identification (Gene-based "finger printing"); Pharmacogenomics: Customized Drugs (Drugs customized to individuals or subgroups with similar genetic traits) and Drug production ("Biotechnology"); Agriculture (Plants that are resistant to insects and chemical pollutants; Plants to synthesize non-plant products such as Plastics); Food Safety Testing; Disease Control, and so on.

The early lead in genomics will be insurmountable. Any university or region that builds up an infrastructure to address this now will reap enormous benefits in the next twenty years. While the silicon and information technology drove the economy over the past twenty years, the new economic engine for the next 50 years will be the genomics field. The Biotechnology and Pharmacy industries sent clear signals on this during 1998. Bioinformatics will provide the tools to access, interpret, manage and manipulate this genetic information in ways yet to be imagined. Mr. Bill Gates of Microsoft Company donated $100 M to the University of Washington, Seattle, WA, to establish the Department of Molecular Biotechnology [UWA98]. New industries will develop that will take advantage of the breakthroughs in the genomics arena. As an example, Motorola has established an alliance with Abbot Labs to explore biotechnology. Our Biosystems track will facilitate training in this new evolving field.

A recent policy forum on genomics described the impact of genomics on the world's economy thus [Enri98]: Genomics now allows us to study, design, and build biologically important molecules. The flow of genomics information is so massive that it threatens to overwhelm existing R&D budgets, labs, and knowledge bases. The US Patent and Trade Office received 500,000 patent requests for nucleic acid sequences in 1996, up from 4,000 in 1991. Genomics has substantial government support, massive corporate investment, powerful enabling technologies, and short-term cash-generating potential. Genomics is not the biotech of the 1980s, which promised much and delivered little. Biotech companies tended to act alone, trying to integrate from the research bench through the drug counter. They remained relatively small, and their technology did not drive massive divestitures and mergers among the world's largest corporations. The objective of a life science company is no longer to generate breakthroughs in a single area such as medicine, chemicals, or food, but to become a dominant player in all of these. As the article details, there are risks associated with this new Genomics or Life Sciences industry. However, risks not withstanding, this field represents the most dynamic and euphoric field. Maturation of this field could not have come any sooner, without the availability of high speed communication (information) and computer (electronics) technologies that exist today. Further rapid progress in these fields as well as software, medicine, agriculture, and so on, will drive, and in turn be driven by, the genomics field.

Thus the genomics field has a major pivotal role to play in the 21st century.

2. ROLE OF ENGINEERING IN GENOMICS

Molecular biologists study individual genes, in isolation. This has yielded enormous useful information. However, a whole species is much more than an incidental collection of individual genes. These genes interact and control the day to day modulations in the functioning of various living species. Genomics was the first step in extending the study of genes, functional and otherwise, to a whole species. Considering that the human genome has 1 Million genes (of which 100,000 are considered to be functional), and that each gene comprises of, on average, 1500 base pairs, the complexity of the genomics is self-evident. Genomics can provide useful information on a living system's functional regulation in health and disease. Given that the human and other genomes would be mapped more fully over the next few years, we can be said to be in a Post-Genomic era, where our concern is more about how to utilize such enormous quantity of information in an intelligent and meaningful manner to further our health, well-being and life-span.

Our undergraduate program in engineering will provide the framework to understand and facilitate engineering applications to genomics. Our program will be unique: It will provide special tracks in all the three areas of engineering applications to genomics: Bioinformatics, the application of computer science and engineering concepts to data management and mining in genomics; Biosystems, the evolution of new Genomic-inspired sensors and instruments to diagnose, monitor, treat and prolong the lives of humans and other species; and Biomanufacturing, the manufacturing and efficient production of Genetically engineered drugs and plants. Succinctly, Biosystems pertains to design and modeling, while Bioinformatics refers to analysis and synthesis, and Biomanufacturing addresses manufacturing, all as pertinent to the genomics area. More details on the specific fields follow.

Bioinformatics: Soon, there may be a database of about 1 Million genes (or 15 billion base pairs) for each human being. There are both normal and abnormal variations in each human being and genomic studies could be undertaken to determine the subset of functional genes (this Post-Genomic study is called "Relevant Genomics") whose variations correlate well with, and have predictive ability for, a specific set of "macro" (i.e., physiological and pathological) effects, such as in Heart Diseases, Cancer, Diabetes, and so on. Bioinformatics will utilize concepts from Computer Science and Mathematics (Database Management, Data Mining, Statistics, Artificial Intelligence, Machine Learning, Software Engineering, Visualization, etc.,) and Engineering (Massively Parallel Architectures, Neural Networks, Gene Chips, Parallel Computation Algorithms, Data Compression Algorithms, etc.,) to not only speed up the "Wet Lab" procedures in Biology, but also to interpret and present the vast amounts of data in a succinct and useful manner. Bioinformatics will, in addition, provide data banks and data mining techniques for various species of living organisms, which may have many diverse applications (see above).

Biosystems: A new discipline, called Integrative Physiology [BoNo93], has evolved that combines the concepts of molecular biology with the system level fields such as Physiology, Pathology, Neurophysiology, Psychology, etc., to evolve a more powerful paradigm than either is capable of. The traditional Biomedical Engineering discipline has applied engineering concepts to the practice of Medicine at the system level. This new track of Biosystems would include the genomics issues and information synergistically with the traditional Biomedical Engineering principles. The Electrical and Computer engineering concepts of System Analysis, Modeling and Characterization; Data Acquisition, Processing and Reduction; Structured Design, Optimization and Automation; and Communication and Control Theory, that couple the Genomic and Physiological information, will form the basis for this track. Anticipated results are: Powerful and reliable diagnostic and surgical techniques (for e.g., refined methods for MRI Imaging, CAT Scan, Angioplasty, etc.,) and Gene sequencing systems (for e.g., Parallel Sequencing, Gene Chips, Portable PCR for DNA amplification, etc.,). Genetic researchers have devised tests to detect more than 550 genetic disorders from adrenoleuokdystrophy to Zellweger syndrome, and more are on way [McVi98]. The tests today cost much: $150 to $1,500, and take up to two weeks. Also, these tests are blood tests to determine one's genetic susceptibility only, not the status of an existing condition and/or efficacy of gene therapy. Thus, there is much to be accomplished and there is much potential. This field will involve significant interaction with the Medical Sciences, Hospitals, and Biomedical Engineering programs in the region. Genetics research is well established at the University of Miami and the University of Florida, as well as some of the local hospitals, such as The Good Samaritan Medical Center in West Palm Beach [McVi98]. This track can provide engineering support for such programs and improve them significantly. Interaction with Agricultural and Marine Sciences is possible in the long run.

Biomanufacturing may be considered to include the genetic manipulation and production of new breeds of superior plants and medicinal drugs. Genomics database of E-Coli, for e.g., has been used in "mass-production" of Insulin and HGH, hitherto done in a laborious manner with a low yield from human blood. Industrial Engineering, Robotics and Instrumentation will all be needed for the field of Biomanufacturing to produce needed therapeutic drugs and pest-resistant plants. From a different perspective, Tissue Engineering has progressed rapidly so that (artificial) synthesis of various body parts (such as Skin, Bone formations - Fingers, Rip Cage; Internal Organs - Liver, Pancreas, Heart; and Neural Tissues - as Spinal Chord) has either been accomplished or under active R&D [ArCa98]. A collaboration between a Medical Doctor and an Engineer in Boston is a typical example of the future: They helped a boy of 12 years, born with no rib cage, develop a healthy rib cage so that his internal organs could be protected. They used a 3-dimension CAD (Computer-Aided-Design) mechanical engineering package to build a Rib Cage with biodegradable polymers. Bone tissue culture, nurtured in the lab, was transplanted to the rib cage surgically implanted in the boy. After one year, the boy has a normal rib cage that will grow with him. This track will apply concepts in Industrial / Manufacturing Engineering, and Mechanical Engineering to the genomics area.

3. CROSS-DISCIPLINARY COLLABORATION BETWEEN ENGINEERING AND SCIENCE

A typical high-tech system is an epitome and a superlative result of application of engineering, science and management principles, with considerable progress made in engineering as a consequence of significant progress in physics and chemistry. As an example, the two major recent innovations at IBM and Motorola have been with regard to a new technology called SOI (Silicon-on-Insulator) for further scaling of transistors, and the use of Copper instead of Aluminum in the electronic chips to carry current, both benefiting from fundamental research in Sciences. Conversely, Bioengineering would use the concepts of engineering to significantly move forward the field of genomics, hopefully for the benefit of the mankind and the world ecology. This will be similar to the impact of Biomedical Engineering over the practice of Medicine, over the past 20 years. The last twenty years also saw the maturation and explosive use of computers and information technology - the next twenty years are expected to see equally explosive growth in the genomics arena, thanks to the availability of the high-tech engineering technologies to facilitate the same. Without the Internet, high-speed communication links and fast computers, the rapid progress in genomics would not have been possible: As of March 1998, the human gene map contained 30,011 gene tags (Tags are approximate locations of the genes on the Chromosomes), approximately half-way to the full mapping. The latest addition to the genomics tools is the evolution of Gene Chips which will radically change and extend the genomics research and applications, so much so that it is one of the 6 advanced technology programs targeted by NIST (Department of Commerce) for significant funding [ATP98]. These tools have facilitated genomics research till now and will be equally useful for development of applications. However, much progress will come from a collaborative effort such as ours which will integrate knowledge in the two areas, Viz., Engineering and Biology, to take major leaps forward.

4. JOB AND INDUSTRY PERSPECTIVES: AT NATIONAL AND REGIONAL LEVELS

There is a major demand for well-trained bioengineers to address the needs of genomics and Biotechnology industry today and the expected rapid growth of the industry will only exacerbate the need for more bioengineers [DrRy97, Timp96, and Timp97]. The Industries with high wage jobs will naturally impact the local economy in a strongly positive way. Today, South Florida is home to many Software, Biomedical and High Tech companies [FlTr98]. The genomics fields, viz., Bioinformatics, Biosystems and Biomanufacturing, represent "clean" industries, quite similar to, and synergistic with, these "traditional" fields. A strong academic program in bioengineering will lead to a local pool of well-trained graduates and expert faculty members, which in turn will facilitate the migration and establishment of many more Genomic and Biotechnology firms in this area, leading to an economic boom to this area. Our Bioengineering program at the undergraduate level is one of the first around the country. Clearly, we have the infrastructure and expertise to facilitate the same. Early lead in this area will help boost the reputation of FAU and hopefully, will lead to retention of more bright students and engineering graduates from S. Florida region.

Leading company executives have estimated that there will be need for 50,000 such professionals over the next eight years. Assuming that such programs will evolve in other universities, this will require a graduation rate of 120 per year per state. So, a reasonable number for our graduating class is 25 per year, with a significant up potential. Most of the early entrants to this field have been Pharmaceutical, Chemical and Biotech companies, which for historical reasons, were established in the North East (New Jersey, Pennsylvania and Massachusetts) and San Francisco region of California. Florida has a well-established health technology industry (see below) and we expect that this infrastructure will help the genomics field flourish in S. Florida region. The genomics field elsewhere has benefited from the close proximity of software and high-tech electronics firms in those regions. We have a good infrastructure in these fields also, as detailed below.

According to Florida Trends [FlTr98], Florida ranks third in the nation as the location of choice for businesses in the health technology industry. Florida ranks second only to California in both employment and number of firms in the health and allied service industry. International demand for Florida's health technology manufactured products continues to grow. The industry exported products amounting to $1.6 billion in 1993, $1.7 billion in 1994 and $2.2 billion in 1995. The domestic market will continue to be the top growth market for the industry in the US and Florida. Two thousand health technology industry firms operate in Florida and employ more than 250,000 workers. Note: The health technology industry includes manufacturers of medical devices and pharmaceutical drugs, as well as providers of health care services. According to Joint Venture South Florida, a private non-profit company dedicated to enhancing the local economy, there are 6,000 software and information technology companies in Florida, a definite plus as the Genomics field takes hold in S. Florida. Florida's high-tech industry is nationally ranked 7th, as per the American Electronic Association [AEA98], with the communication manufacturing and services industries ranked 3rd nationally. There were 33 high-tech employees for every 1000 workers in the state of Florida, earning an average salary of $42,000 as against $26,000 for others. We expect the bioengineers to earn salaries similar to the high-tech workers. Thus, our program will enhance the base of high-wage earners in S. Florida.

In summary, Florida has well-established and growing health technology, software and other high-tech industries which can serve as the anchor for the Genomics industry to evolve.

5. ENROLLMENT AND JOB TRENDS IN ENGINEERING

Demand for engineers in the U.S is expected to increase 33% by 2006 [Barn98]. However, the number of students going into the field has plummeted 15% nationwide in the past decade. Among the top 10 engineer-producing states in the nation, only Florida has increased its output, by 5%, while the other 9 states registered drops ranging from 7.5% to 37%. Florida universities increased production, from 2,344 in 1987 to 2,457 in 1997. Unfortunately, only four of 10 engineering graduates were working here in Florida five years after receiving a bachelor's degree. The reason seems to be lack of high-tech growth industry in the State [Barn98]. Groups such as Joint Venture South Florida are attempting to reverse that. The Genomics industry would help enhance the job base in Florida by leveraging the infrastructure that already exists, viz., the health, medical, software and other high-tech industries, as described above. In addition, since many of the ensuing companies can be small businesses, as with the software and information technology industry, there is a higher chance of achieving the same.

We now turn our attention to Bioengineering specifically: A study was undertaken at the University of Cincinnati, Cincinnati, OH, in 1996, to determine the enrollment trends in Biomedical Engineering over the five year period 1991-1996 [GrFr97]. Biomedical Engineering (BME) is the closest field to our proposed Bioengineering field, and hence it is appropriate to study these trends. In 1996, the undergraduate BME enrollment represented only 1.6% of current full time undergraduate engineering enrollment of 317,772 students nationwide. This computes to a total of 5,000 students nationwide. Full time undergraduate engineering enrollment declined 6.4% over this 5 year period, while the BME undergraduate engineering enrollment increased by a whopping 37.4%. Women enroll in BME at nearly twice the rate that they do in engineering overall, 37% v 19%. Minorities enroll in BME at a higher rate than they do in engineering overall, 30% v 26%. We can extrapolate this study to bioengineering to deduce the following: While the overall engineering enrollment is decreasing, Bioengineering has the potential for reversing the trends, while attracting more women and minorities to the program. Coupled with the fact that there is a tremendous need for such graduates, our Bioengineering program can be expected to see an explosive growth. A steady state of 25 graduating seniors per year is very reasonable. Information summarized in the previous section indicates potential for a significantly higher enrollment and graduation rate.

6. REFERENCES

Accreditation:

ABET98 Engineering Criteria 2000, Published by the Engineering Accreditation Commission, The Accreditation Board for Engineering and Technology (ABET)

Academic Trends:

CLEM98 Bioengineering at Clemson University. See http://www.eng.clemson.edu/bio

CRAN98 Institute of BioScience and Technology, Cranfield University, UK. See http://www.cranfield.ac.uk/ibst/

GrFr97 Grood, E.S., and Frayne, S., "Bioengineering Undergraduate and Graduate Enrollments." A study at the University of Cincinnati. See http://BME.www.ecn.purdue.edu/BME/jobs/bme-enr.html

PENN98 University of Pennsylvania, Master of Biotechnology program in the School of Engineering and Applied Science. See http://www.upenn.edu

RICE98 Graduate Program in Bioengineering at Rice University, See http://www.ruf.rice.edu/~bioeng

STAN98 Medical Informatics Training at Stanford University School of Medicine. Send email to ehs@smi.stanford.edu

SYRA98 Bioengineering at Syracuse University. See http://128.230.6.180/M.S.Program/MSBENHome.html

UWA98 Molecular Biotechnology: An Overview, Publication of the Graduate Program at the University of Washington, Seattle, WA. Originally Funded with $100 M donation by Mr. Bill Gates, Microsoft. See http://chroma.mbt.washington.edu/ hood_www/

Funds:

ATP97 ATP Focused Program Competition 98-08, "Tools for DNA Diagnostics," Advanced Technology Program, NIST, Dept. of Commerce, December '97

Agne98 Agnew, B., "NIH Plans Bioengineering Initiative," Science, Vol. 280, June 5, 1998, Pages: 1516-1518

Brow98 Borwnler, S., "Dollars for DNA," U.S. News and World Report, May 25, 1998, Pages: 48, 50

Cwik98 Cwiklik, R., "Ivory Tower Inc.: When Research and Lobbying Mesh," The Wall Street Journal, July 1998, Page: B

NHGRI98 National Human Genome Research Institute's Curriculum Development Grants, PAR-98-063, May 1998

NSF98 Several possibilities at NSF. An immediately relevant one: Course, Curriculum, and Laboratory Improvement (CCLI), Deadline: November 1998

Wils96 Wilson, J., "Finding new wonder drugs," Popular Mechanics, Vol. 173, October 1996, Pages: 28-29

Genomics and Engineering:

AnGa97 Anderson, P., and Ganetzky, B., An Electronic Companion to Genetics Workbook, Cogito Learning Media, Inc., New York, NY, 1997

BaBr98 Baldi, P., and Brunak, S., BioInformatics, The Machine Learning Approach, MIT Press, Cambridge, MA, 1998

BoNo93 Boyd, C.A.R., and Noble, D., The Logic of Life, The Challenge of Integrative Physiology, Oxford University Press, Oxford, 1993

Fodo97 Fodor, S., "Massively Parallel Genomics (DNA Sequencing Technology," Science, Vol. 277, July 18, 1997, Pages: 393-394

GoWh95 Gonick, L., and Wheelis, M., The Cartoon Guide to Genetics, Updated Edition, Harper Perennial, Harper Collins Publishers, New York, NY, 1995

Gold98 Goldgaber, A., "Test Kits Speeding Up Pace of Genetic Research," Investor's Business Daily, June 1998

HeSc97 Heller, R.A., Schena, M., et al., "Discovery and Analysis of Inflammatory Disease-Related Genes Using cDNA Microarrays," Proc. Natl. Acad. Sci, Vol. 94, March 1997, Pages: 2150-2155

KoMe98 Kopp, M., de Mello, A.J., and Manz, A., "Chemical Amplification: Continuous Flow PCR on a Chip, Science," Vol. 280, May 15, 1998, Pages: 1046-1048

Rifk98 Rifkin, J., The Biotech Century: Harnessing the Gene and Remaking the World, Penguin Putnam Inc., New York, NY, 1998

Wade97 Wade, N., "Where Computers and Biology Meet: Making a DNA Chip," The New York Times, April 8, 1997. Page B10.See www.affymetrix.com

Wyke97 Wyke, A., 21st Century Miracle Medicine: Robo Surgery, Wonder Cures, and the Quest for Immortality, Plenum Trade, New York, NY, 1997

Industry Trends:

Cohe97 Cohen, J., "The genomics gamble: drug companies, biotechs, and Wall Street Investors are putting their money down on efforts to unlock the secrets of human DNA," Vol. 275, February 7, 1997, Pages: 767-768

FlTr98 Advertising Section, “Miracles in Healthcare: The Next Evolution,” Florida Trends, Pages HC-1 to HC-11, Florida Trends, June 1998

Jaro98 Jaroff, L., “Venter’s Bold Venture,” Time Magazine, June 29, 1998, page: 51

Kilm98 Kilman, S., “Monsanto Buys Two Companies for $4.2 Billion,” Wall Street Journal, May 12, 1998, Page: A2

Lang98 Langreth, R., “Revolution in Genetics Creates New Weapons In the War on Cancer,” The Wall Street Journal, June 1998, Page A2

PR98 PR Newswire Associates, “Monsanto Initiates First Large-Scale, Genome- Wide Application of Incyte’s DNA Microarrays for Functional Genomics,” May 18, 1998

Penn98 Pennisi, E., “Pharma giant creates genomics institute,” Science, Vol. 280, No. 5361, Page 193, April 10, 1998

Rich98 Richards, B., “Perkin-Elmer to Join Venture to Decode Genes,” The Wall Street Journal, May 11, 1998, Page A2

Sher98 Sherrid, P., “Please pass the bioengineered butter,” U.S. News and World Report, March 2, 1998, Pages: 58-60

Warr98 Warren, S., “DuPont Plans to Shed Conoco Oil Unit,” Wall Street Journal, May 12, 1998, Page: A2

Jobs:

Barn98 Barnett, C., “Brain Drain,” Florida Trend, August 1998, Pages: 42-45

DrRy97 Drews and Rysen, “ The role of innovation in drug development” Nature Biotechnology, Vol. 15, No. 13, December 1997, Pages: 1318-1319

Timp96 Timpane, J., “Six hot careers: biotechnology, pharmaceuticals and beyond,” Science, Vol. 273, Sep 27, 1996, Page: 1897-1904

Timp97 Timpane, J., “Open minds, open horizons: careers in biotechnology and pharmaceuticals,” Science, Vol. 276, April 18, 1997, Pages: 443-446

Seminal:

Land96 “The new genomics: global views of biology,” Science, Vol. 274, October 25, 1996, Pages: 536-539. Dr. Landler is with the Whitehead Institute for

Biomedical Research and the Department of Biology, MIT, Cambridge, MA

Post98 Poste, G., “The Study of Genes and Their Functional Regulation.” Speech by Dr. Poste, President, R&D, SmithKline Beecham Pharmaceuticals, delivered at the Jackson Laboratory, Annual Meeting, August 20, 1994