Bio-Medical Computing
(6.872/HST.950)

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http://stellar.mit.edu/S/course/6/fa10/6.872/

Tue, Thu 9:30–11:00am, 32–144

Medical Informatics

- Intersection of medicine and computing
- Plus theory and experience specific to this combination
- =Medical Computing, ~Health Informatics

- Science
- Applied science
- Engineering

Types of Bio-Medical Informatics

- Cellular level: Bioinformatics, Systems Biology
- Patient level: Clinical Informatics, Health I., Medical I., …
- Population level: Public Health I.
- Imaging Informatics

Bio-Medical Informatics

- Phenotype = Genotype + Environment
- In humans, we rely on “natural experiments”
- Measurements
  - Genotype: sequencing, gene chips, proteomics, etc.
  - Environment: longitudinal surveys, etc.
  - Phenotype: clinical records, assembled to longitudinal data
Outline (today)

• What is biomedical informatics?
• BMI is defined by goals and methods of health care
• The genomic revolution
• The science of health care
  – Genotype, phenotype, environment
  – From associations to mechanisms
• What is health?
• Practice of health care
• Challenges

Outline (semester)

• Clinical and Genomic Data
• Methods of modeling
• Combining clinical and genetic data
• “Translational medicine”
• Engineering the health care system
• Decision support to improve health care
• Personalized medicine
• Public health
• The developing world
• Your projects

The Medical Cycle

Care Processes

• Data: instrumentation, monitoring, telemetry
• Information: interpretation, filtering, sampling, smoothing, clustering
• Diagnosis: inference, model-based reasoning, classification
• Prognosis: prediction, natural course, experience
• Therapy: planning, predicting effects, anticipating
Meta-level processes

- Acquisition and application of knowledge
- Education
- Quality control and process improvement
- Cost containment
- Reference (library)

The “Learning Health Care System”

Dogma

- Phenotype = Genotype + Environment
  - Traits: Gene sequence
  - Diseases: SNP’s
  - Behaviors: Expression data
  - …
  - Diet, smoking, drugs, …
  - Insults and injuries
  - Exposures
  - …

- What is the functional form?
- How do we investigate these relationships?
- Can we take advantage of the exponential growth of genomic data?
Growth in Gene Expression Omnibus Measurements

Fall 2004: ~30,000 submissions, ~5B measurements

Today (9/2010): ~472,929 samples

Where are the Phenotype and Environment-related Data?

Phenotype = Genotype + Environment

- Traits
- Diseases
- Behaviors
- Gene sequence
- SNP’s
- Expression data
- Diet, smoking, drugs, ...
- Insults and injuries
- Exposures

• Perform Controlled Experiments?
  - Unethical using human subjects!!!
  - OK on rats.

Experimental Subjects

High-throughput phenotyping at Medical College of Wisconsin
Where are the Phenotype and Environment-related Data?

- Environment
  - (Hardest to get)
  - Questionnaires,
    - e.g., Nurses' Health Study, Framingham Heart Study
  - Monitoring
    - e.g., LDS hospital infectious disease monitors

- Phenotype
  - “Natural Experiments”
  - : Clinical Data

The fantasy: Informatics for Integrating Biology & Bedside

Plausibility
Butte & Kohane, Nature Biotech 2006

- Phenome-Genome Network
  - Gene Expression Omnibus
    - expression data
    - annotations: tissue, disease, exp. conditions, …
  - Interpret annotations to UMLS
  - Differential expression vs. condition
  - Interesting relations:
    - 11 genes & aging
    - DDX24 and leukemia
    - 2 genes & injury

Clinico-Genomic Research

- Identify a highly specific clinical population, and controls
- Gene-wide association studies (GWAS)
- Hope that notable differences appear between those with/those without disease
- Disease models:
  - Mendelian
  - Single-nucleotide polymorphisms
  - Private variation
  - ?
What is Asthma?

Asthma Epidemiology/Significance

- 17.3 million cases in U.S.
- 80% increase in prevalence 1980-94
- Most common reason for hospitalization in children
- Most common reason for days lost from school
- 20 million in health care costs/year
- A tractable problem

Specific Aims of Asthma Proj.

- Develop and implement methods of detecting sub-phenotypes of asthma and COPD
- Apply the methods developed in Specific Aim 1 to the experimental design of genetics and pharmacogenetics research at Partners

Time scale in medicine

- Cure—usually acute illness
- Manage—long-term, chronic illness
- Prevent
- Predict (especially based on genetics)
WHO Constitution defines "health"

"a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity"

- Physical
- Mental
- Social
—very hard to measure

Distribution of Ages

• Life table deaths by year (Japan, 1989)

Life table death rates by age

Life table cohort survival
Measures of Health

• Longevity at birth (CIA World Fact Book, 2001)

<table>
<thead>
<tr>
<th>Country</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rwanda</td>
<td>38.35</td>
<td>39.65</td>
</tr>
<tr>
<td>Kenya</td>
<td>46.57</td>
<td>48.44</td>
</tr>
<tr>
<td>South</td>
<td>47.64</td>
<td>48.56</td>
</tr>
<tr>
<td>Cambodia</td>
<td>54.62</td>
<td>59.12</td>
</tr>
<tr>
<td>Brazil</td>
<td>58.96</td>
<td>67.73</td>
</tr>
<tr>
<td>Russia</td>
<td>62.12</td>
<td>72.83</td>
</tr>
<tr>
<td>Albania</td>
<td>69.01</td>
<td>74.87</td>
</tr>
<tr>
<td>USA</td>
<td>74.37</td>
<td>80.05</td>
</tr>
<tr>
<td>Japan</td>
<td>77.62</td>
<td>84.15</td>
</tr>
</tbody>
</table>

Causes of death
(industrialized countries, 1989)

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Circulatory system</td>
<td>48%</td>
</tr>
<tr>
<td>Malignant neoplasms</td>
<td>19%</td>
</tr>
<tr>
<td>Accidents</td>
<td>7%</td>
</tr>
<tr>
<td>Others</td>
<td>26%</td>
</tr>
</tbody>
</table>

Quality of life

• Value of a total life depends on
  – Length (assume now is $N$)
  – Quality ($q$) over time
  – Discounts ($g$) for future or past (depends very much on what the value is to be used for)

$$ V_N = \int_{t=0}^{T} q(t)g(t - N)dt $$

Modeling life quality
Mortality, Disability, Morbidity

Top 10 Chronic Conditions
Persons aged ≥ 65

<table>
<thead>
<tr>
<th>Condition</th>
<th>Both</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arthritis</td>
<td>49.6</td>
<td>40.7</td>
<td>55.7</td>
</tr>
<tr>
<td>Hypertension</td>
<td>39.0</td>
<td>33.0</td>
<td>43.2</td>
</tr>
<tr>
<td>Hearing impairment</td>
<td>30.0</td>
<td>35.2</td>
<td>26.3</td>
</tr>
<tr>
<td>Heart disease</td>
<td>25.7</td>
<td>26.9</td>
<td>24.9</td>
</tr>
<tr>
<td>Orthostatic impairment</td>
<td>16.8</td>
<td>15.7</td>
<td>17.8</td>
</tr>
<tr>
<td>Cataracts</td>
<td>15.5</td>
<td>11.3</td>
<td>18.4</td>
</tr>
<tr>
<td>Chronic sinusitis</td>
<td>15.2</td>
<td>13.7</td>
<td>16.2</td>
</tr>
<tr>
<td>Visual impairment</td>
<td>10.1</td>
<td>12.0</td>
<td>8.8</td>
</tr>
<tr>
<td>Genitourinary</td>
<td>9.9</td>
<td>11.3</td>
<td>8.9</td>
</tr>
<tr>
<td>Diabetes</td>
<td>8.9</td>
<td>7.8</td>
<td>9.7</td>
</tr>
</tbody>
</table>


Next 10 Chronic Conditions
Persons aged ≥ 65

<table>
<thead>
<tr>
<th>Condition</th>
<th>Both</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Varicose veins</td>
<td>7.7</td>
<td>3.4</td>
<td>10.8</td>
</tr>
<tr>
<td>Hernia</td>
<td>7.6</td>
<td>9.1</td>
<td>6.5</td>
</tr>
<tr>
<td>Hemorrhoids</td>
<td>7.6</td>
<td>7.1</td>
<td>8.0</td>
</tr>
<tr>
<td>Psoriasis, dermatitis, dry skin</td>
<td>7.4</td>
<td>6.3</td>
<td>8.3</td>
</tr>
<tr>
<td>Hardening of arteries</td>
<td>7.4</td>
<td>7.3</td>
<td>7.4</td>
</tr>
<tr>
<td>Tinnitus</td>
<td>7.3</td>
<td>7.6</td>
<td>7.1</td>
</tr>
<tr>
<td>Corns, calluses &amp; bunions</td>
<td>7.3</td>
<td>4.2</td>
<td>12.7</td>
</tr>
<tr>
<td>Constipation</td>
<td>6.5</td>
<td>4.4</td>
<td>8.0</td>
</tr>
<tr>
<td>Hay fever</td>
<td>6.4</td>
<td>6.4</td>
<td>6.5</td>
</tr>
<tr>
<td>Cerebrovascular</td>
<td>5.7</td>
<td>5.6</td>
<td>5.8</td>
</tr>
</tbody>
</table>


Societal quality of life

- Aggregation of individual qualities
- + Equity (distributions)
- Is more better? (Population control.)
- Is less better?
- How much to spend?
Who makes decisions?

“In those days there was no bureaucratic regimentation, there were few forms to fill out, malpractice premiums were affordable, and the overhead costs of running a practice were reasonable. Our bills were simple, spelled out so anybody could understand them without the use of codes. Patients usually paid their own bills, promptly too, for which an ordinary receipt was given. Hospital charges were set by the day, not by the aspirin. Medical care was affordable to the average person with rates set by the laws of the marketplace, and care was made available to all who requested it regardless of ability to pay. Doctors were well respected; rarely were we denigrated by a hostile press for political reasons. Yes, in the days before government intervention into the practice of medicine, doctor’s fees were low, but the rewards were rich; those were truly the ‘golden years’ for medicine.”

Edward Annis, past President of AMA

Code Blue, 1993

Aggregation

• Trend: social aggregation leads to decisions at a larger scale
  – Multi-specialty providers
  – Government guarantees and mandates
  – Risk sharing
  – Oregon-wide spending “optimization”;
  – British NHS

Changing Context of Health Care

• Fee-for-service
• HCFA (Health Care Financing Agency) pays for Medicare
• Capitation
  – HMO’s (Health Maintenance Organizations) take overall responsibility to care for patient for fixed fee
  – Pushing risk down to the physician or group

Determining Factors:
Exponentially growing expense of health care

- More healthcare than steel in GM cars
- Increased demand
  - Much more possible
  - Better tests, therapies
  - High human motivation
- No pushback
- Waste
  - Unnecessary procedures
    - ½ of health expenses in last year of life
  - Marginally useful procedures
    - Defensive medicine
  - Bad Medicine

Managed Care

“Decisions that were once the exclusive province of the doctor and patient now may be examined in advance by an external reviewer—someone accountable to an employer, insurer, health maintenance organization (HMO), or other entity responsible for all or most of the cost of care. Depending upon the circumstances, this outside party may be involved in discussions about where care will occur, how treatment will be provided, and even whether some treatments are appropriate at all.”

Controlling Costs and Changing Patient Care IOM, 1989

How is care managed?

- Active case management:
  - Preadmission review
  - Continued-stay review
  - Second surgical opinion
- Selective case management—high-cost cohorts
- Institutional
  - Capitation
  - Institutional arrangements (referrals, hospitals, pharmacies, …)
  - Control “leakage”

Managed Care Scorecard

- “U.M. has helped to reduce inpatient hospital use and to limit inpatient costs…”
- “The impact of U.M. on net benefit costs is less clear. Savings on inpatient care have been partially offset by increased spending for outpatient care and program administration.”
- “U.M. … does not appear to have altered the long-term rate of increase in health care costs.”
  IOM, 1989
What is Insurance?

- Purpose is to reduce variance of (cost) experience over a population
- What population
  - U.S. (275M people), vs.
  - Ten employees of a small company, vs.
  - One individual
- Insurance for small populations is just deferred cost payment
- Power through aggregation. You can’t argue with MGH about the cost of your appendectomy, but Blue Cross can about the cost of 1,000.

Insurance without Risk

- Insurer aggregates many “lives”
- Competition for capitated coverage by HMO’s and their ilk
- HMO (e.g., Harvard Pilgrim) further passes risk down:
  - Capitated contract for primary care (e.g., Harvard Vanguard)
  - Capitated contract for cardiology, …
- Risk borne by lowest-level contractor; some group practices lose their shirts (WGBH Frontline, 2000)

U.S. Alternatives

- Return to fee-for-service; individual health savings accounts; individual responsibility
- Single-payer nationally-aggregated insurance, with managed care
- 1993 Clinton health plan: “managed competition”
- 2010 Obama health insurance plan: “universal” insurance, little cost control
- … or nothing planned, but development dictated by market forces, laws, discoveries.

Obama Proposals

- Universal coverage: everyone must get insurance
  - Employer
  - Insurance collaborative
  - Government (?) — rejected
- Insurance companies cannot deny insurance, cancel coverage, impose reimbursement limits based on illness, past or present
- Government assistance to poor people, small companies
- Health Information Technology (HIT) to smooth info flow
- Cost savings from avoiding billing disputes, ceasing to reimburse only procedures, evidence-based medicine.
Quality Improvement

- IOM Study: 96,000 US deaths/year from medical error (perhaps half preventable?)
- Information intervention at the point of decision making can improve decisions
- DPOE: Direct Physician Order Entry allows such intervention
- Leapfrog Group: Large employers ($$$) require DPOE from providers
- Patient Involvement: Indivo Health, Google Health, Microsoft Healthvault

Outline

- MI defined by goals and methods of health care
- Medical data: essential
  - History of medical record keeping
  - Organization of medical records
  - Computerized medical records
    - Why
    - Key issues
    - Failures and successes
  - Current approaches
- Expertise (methods)

Implications of Health Care Organization for Informatics

- Money determines much
  - Medicine spends 1-2% on IT, vs. 6-7% for business overall, vs. 10-12% for banking
  - “Bottom line” rules, therefore emphasis on
    - Billing
    - Cost control
    - Quality control, especially if demonstrable cost savings
    - Retention and satisfaction (maybe)
  - Management by accountants

Challenges

- Computerized Medical Records (EMR/ CPR/…)
- Usability of systems in the workflow of health care
- Large-scale “Engineering Systems” problem
- Genomic Medicine