Bio-Medical Computing
(6.872/HST.950)

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http://stellar.mit.edu/S/course/6/fa08/6.872J/
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

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

observe

patient

plan

data

information

decide

therapy

diagnosis

initial presentation
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)

Enterprise-level Clinical Process Automation...

The “Learning Health Care System”

Dogma

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>Genotype + Environment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Traits</td>
<td>Gene sequence, Diet, smoking, drugs, ...</td>
</tr>
<tr>
<td>Diseases</td>
<td>SNP’s, Insults and injuries</td>
</tr>
<tr>
<td>Behaviors</td>
<td>Expression data, Exposures</td>
</tr>
</tbody>
</table>

- 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

Figure 1: INS databases statistics. Complete technical sample measurements collected by INS are shown. Technical sample measurements were generated weekly, as indicated by the dates on the x-axis. Measurements were completed on July 28, 2006.
Where are the Phenotype and Environment-related Data?

<table>
<thead>
<tr>
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</tbody>
</table>

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

Experimental Subjects

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

- 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 leukaemias
    - 2 genes & injury

Butte & Kohane, Nature Biotech 2006
# 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

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<tr>
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</table>

# 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 Africa</td>
<td>47.64</td>
<td>48.56</td>
</tr>
<tr>
<td>Cambodia</td>
<td>54.62</td>
<td>59.12</td>
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<tr>
<td>Brazil</td>
<td>56.96</td>
<td>67.73</td>
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<tr>
<td>Russia</td>
<td>62.12</td>
<td>72.83</td>
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<tr>
<td>Albania</td>
<td>69.01</td>
<td>74.87</td>
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<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)

<table>
<thead>
<tr>
<th>Cause</th>
<th>Percentage</th>
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<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 $T$)
  - Quality ($q$) over time
  - Discounts ($g$) for future or past (depends very much on what the value is to be used for)

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

Modeling life quality

Top 10 Chronic Conditions
Persons aged $\geq 65$

<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>

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:

$£€¥R

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
  - 1/5 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

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

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