Andreas Holzinger

Lecture 8 – Version WS 2012/13
Biomedical Decision Making: Reasoning and Decision Support

VO 444.152 Medical Informatics

a.holzinger@tugraz.at
Schedule Winter term 2011/12

- 1. Intro: Computer Science meets Life Sciences, challenges, future directions
- 3. Structured Data: Coding, Classification (ICD, SNOMED, MeSH, UMLS)
- 4. Biomedical Databases: Acquisition, Storage, Information Retrieval and Use
- 5. Semi structured and weakly structured data (structural homologies)
- 6. Multimedia Data Mining and Knowledge Discovery
- 8. Biomedical Decision Making: Reasoning and Decision Support
- 9. Intelligent Information Visualization and Visual Analytics
- 10. Biomedical Information Systems and Medical Knowledge Management
- 11. Biomedical Data: Privacy, Safety and Security
Learning Goals: At the end of this 8th lecture you ...

- can apply your knowledge gained in lecture 7 to some example systems of decision support;
- have an overview about the core principles and architecture of decision support systems;
- are familiar with the certainty factors as e.g. used in MYCIN;
- are aware of some design principles of DSS;
- have seen similarities between DSS and KDD on the example of computational methods in cancer detection;
- have seen basics of CBR systems;
Keywords of the 8th Lecture

- Artificial intelligence
- Case based reasoning
- Computational methods in cancer detection
- Cybernetic approaches for diagnostics
- Decision support models
- Decision support system (DSS)
- Fuzzy sets
- MYCIN
- Radiotherapy planning
Case-based reasoning (CBR) = process of solving new problems based on the solutions of similar past problems;

Certainty factor model (CF) = a method for managing uncertainty in rule-based systems;

CLARION = Connectionist Learning with Adaptive Rule Induction ON-line (CLARION) is a cognitive architecture that incorporates the distinction between implicit and explicit processes and focuses on capturing the interaction between these two types of processes. By focusing on this distinction, CLARION has been used to simulate several tasks in cognitive psychology and social psychology. CLARION has also been used to implement intelligent systems in artificial intelligence applications.

Clinical decision support (CDS) = process for enhancing health-related decisions and actions with pertinent, organized clinical knowledge and patient information to improve health delivery;

Clinical Decision Support System (CDSS) = expert system that provides support to certain reasoning tasks, in the context of a clinical decision;

Collective Intelligence = shared group (symbolic) intelligence, emerging from cooperation/competition of many individuals, e.g. for consensus decision making;

Crowdsourcing = a combination of "crowd" and "outsourcing" coined by Jeff Howe (2006), and describes a distributed problem-solving model; example for crowdsourcing is a public software beta-test;
**Advance Organizer (2)**

- **Decision Making** = central cognitive process in every medical activity, resulting in the selection of a final choice of action out of several alternatives;
- **Decision Support System (DSS)** = is an IS including knowledge based systems to interactively support decision-making activities, i.e. making data useful;
- **DXplain** = a DSS from the Harvard Medical School, to assist making a diagnosis (clinical consultation), and also as an instructional instrument (education); provides a description of diseases, etiology, pathology, prognosis and up to 10 references for each disease;
- **Expert-System** = emulates the decision making processes of a human expert to solve complex problems;
- **GAMUTS in Radiology** = Computer-Supported list of common/uncommon differential diagnoses;
- **ILIAD** = medical expert system, developed by the University of Utah, used as a teaching and testing tool for medical students in problem solving. Fields include Pediatrics, Internal Medicine, Oncology, Infectious Diseases, Gynecology, Pulmonology etc.
- **MYCIN** = one of the early medical expert systems (Shortliffe (1970), Stanford) to identify bacteria causing severe infections, such as bacteremia and meningitis, and to recommend antibiotics, with the dosage adjusted for patient's body weight;
- **Reasoning** = cognitive (thought) processes involved in making medical decisions (clinical reasoning, medical problem solving, diagnostic reasoning;
Can Computers help doctors to make better decisions?
Computers to help human doctors to make better decisions

"If you want a second opinion, I'll ask my computer."

http://biomedicalcomputationreview.org/content/clinical-decision-support-providing-quality-healthcare-help-computer
Two types of decisions (Diagnosis vs. Therapy)

- Type 1: Decisions related to the diagnosis, i.e. computers are used to assist in diagnosing a disease on the basis of the individual patient data. Questions include:
  - What is the probability that this patient has a myocardial infarction on the basis of given data (patient history, ECG)?
  - What is the probability that this patient has acute appendices, given the signs and symptoms concerning abdominal pain?

- Type 2: Decisions related to therapy, i.e. computers are used to select the best therapy on the basis of clinical evidence, e.g.:
  - What is the best therapy for patients of age x and risks y, if an obstruction of more than z % is seen in the left coronary artery?
  - What amount of insulin should be prescribed for a patient during the next 5 days, given the blood sugar levels and the amount of insulin taken during the recent weeks?

### Taxonomy of Decision Support Models

<table>
<thead>
<tr>
<th>Decision Model</th>
<th>Quantitative (statistical)</th>
<th>Qualitative (heuristic)</th>
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</thead>
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<tr>
<td>Supervised</td>
<td>Bayesian</td>
<td>Truth tables</td>
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<td>Neural network</td>
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<td>Critiquing systems</td>
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Where are the roots in Decision Support?
E. Feigenbaum, J. Lederberg, B. Buchanan, E. Shortliffe


Early Knowledge Based System Architecture

Static Knowledge versus dynamic knowledge

**Static Knowledge**
- Production Rules
  - Judgmental Knowledge about domain

**Dynamic Knowledge**
- Facts about the problem entered by user
- Deductions made by system

**User**
- Consultative advice
- Explanations

**Rule Interpreter**

Shortliffe & Buchanan (1984)
The information available to humans is often imperfect.
This is especially in the medical domain the case.
An (human) expert can cope with deficiencies.
Classical logic permits only exact reasoning:
IF A is true THEN A is non-false and
IF B is false THEN B is non-true
Most real-world problems do not provide this exact information, mostly it is inexact, incomplete, uncertain and/or un-measurable!
MYCIN – rule based expert system - certainty factors

- MYCIN is a rule-based Expert System, which is used for therapy planning for patients with bacterial infections
- Goal oriented strategy (Rückwärtsverkettung)
- To every rule and every entry a certainty factor (CF) is assigned, which is between 0 and 1
- Two measures are derived:
  - MB: measure of belief
  - MD: measure of disbelief
- Certainty factor – CF of an element is calculated by:
  \[ CF[h] = MB[h] - MD[h] \]
- CF is positive, if more evidence is given for a hypothesis, otherwise CF is negative
  - \( CF[h] = +1 \) -> h is 100% true
  - \( CF[h] = -1 \) -> h is 100% false
\[ h_1 = \text{The identity of ORGANISM-1 is streptococcus} \]
\[ h_2 = \text{PATIENT-1 is febrile} \]
\[ h_3 = \text{The name of PATIENT-1 is John Jones} \]

\[ \text{CF}[h_1, E] = .8 \quad : \quad \text{There is strongly suggestive evidence (.8) that the identity of ORGANISM-1 is streptococcus} \]

\[ \text{CF}[h_2, E] = -.3 \quad : \quad \text{There is weakly suggestive evidence (.3) that PATIENT-1 is not febrile} \]

\[ \text{CF}[h_3, E] = +1 \quad : \quad \text{It is definite (1) that the name of PATIENT-1 is John Jones} \]

MYCIN was not really a success in the clinical practice
What challenges are in the development of DSS?
Let us look into the practice today ...
Some remarks on design and development of DSS

- Human–Computer cooperation is essential to the decision support process.
- Consequently, Human–Computer Interaction (HCI) is a fundamental aspect for building intelligent, interactive DSS,
- because the design of such systems heavily relies on a user-centered approach.
- It is necessary to combine and integrate methods from Software Engineering (SE) and HCI.
- Traditional methods and models are limited because the system is highly interactive and
- usually these methods do not integrate the end-user explicitly and systematically.
How to combine SE and HCI for effective development of DSS?
Unified Process (UP) from SE and the U-model from HCI.

Remember the similarities between DSS and KDD

Ayed et al. (2010)
The Design Phases

Ayed et al. (2010)
What is the simplest possibility of decision support?
Clinical guidelines are **systematically** developed documents to assist doctors and patient decisions about appropriate care;

- In order to build DS, based on a guideline, it is **formalized** (transformed from natural language to a logical algorithm), and
- **implemented** (using the algorithm to program a DSS);

To increase the quality of care, they must be linked to a **process of care**, for example:

- “80% of diabetic patients should have an HbA1c below 7.0” could be linked to processes such as:
  - “All diabetic patients should have an annual HbA1c test” and
  - “Patients with values over 7.0 should be rechecked within 2 months.”

**Condition-action rules** specify one or a few conditions which are linked to a specific action, in contrast to narrative guidelines which describe a series of branching or iterative decisions unfolding over time.

- Narrative guidelines and clinical rules are two ends of a continuum of clinical care standards.
Are there other possibilities for DS?
Example: Exon Arrays

Exon array structure. Probe design of exon arrays. (1) Exon—intron structure of a gene. Gray boxes represent introns, rest represent exons. Introns are not drawn to scale. (2) Probe design of exon arrays. Four probes target each putative exon. (3) Probe design of 3' expression arrays. Probe target the 3' end of mRNA sequence.

Computational methods in leukemia cancer detection (2/6)

Corchado et al. (2009)
Computational methods in leukemia cancer detection (3/6)

A = acute, C = chronic, 
L = lymphocytic, M = myeloid

- **ALL** = cancer of the blood AND bone marrow caused by an abnormal proliferation of lymphocytes.
- **AML** = cancer in the bone marrow characterized by the proliferation of myeloblasts, red blood cells or abnormal platelets.
- **CLL** = cancer characterized by a proliferation of lymphocytes in the bone marrow.
- **CML** = caused by a proliferation of white blood cells in the bone marrow.
- **MDS** (Myelodysplastic Syndromes) = a group of diseases of the blood and bone marrow in which the bone marrow does not produce a sufficient amount of healthy cells.
- **NOL** (Normal) = No leukemias

Corchado et al. (2009)
Classification CLL—ALL. Representation of the probes of the decision tree which classify the CLL and ALL to 1555158_at, 1553279_at and 1552334_at

Corchado et al. (2009)
The model of Corchado et al. (2009) combines:

1) methods to reduce the dimensionality of the original data set;
2) pre-processing and data filtering techniques;
3) a clustering method to classify patients; and
4) modern extraction of knowledge techniques.

The system reflects how human experts work in a lab, but

1) reduces the time for making predictions;
2) reduces the rate of human error; and
3) is able to work with exon array data of high dimensionality
What is Case-based reasoning?
Thinking – Reasoning – Deciding – Acting
Case Based Reasoning (CBR) Basic principle

The task-method decomposition of CBR

Aamodt & Plaza (1994)
Case Based Reasoning Example: Radiotherapy Planning (1/6)

Source: http://www.teachingmedicalphysics.org.uk
Case Based Reasoning Example: Radiotherapy Planning 2/6

Case Based Reasoning Example: Radiotherapy Planning (3/6)

Examination of patient → CT scan/ MRI scan → Outline planning target volume

Review of the dose plan ← Dose in I and II phase ← Dose volume histogram

Measures:
1) Clinical Stage = a labelling system
2) Gleason Score = grade of prostate cancer = integer between 1 to 10; and
3) Prostate Specific Antigen (PSA) value between 1 to 40
4) Dose Volume Histogram (DVH) = pot. risk to the rectum (66, 50, 25, 10 %)

Gleason score evaluates the grade of prostate cancer. Values: integer within the range

Dose plan suggested by Dempster-Shafer rule (62Gy+10Gy)

Dose received by 10% of rectum is 56.02 Gy (maximum dose limit =55 Gy)

Proposed dose plan
  Yes
  Feasible dose plan
  No
  Modification

Modification of dose plan:
New dose plan: 62Gy +8 Gy
Dose received by 10% of rectum is: 54.26 Gy (feasible dose plan)
Thank you!
Sample Questions

- What is human intelligence?
- What different decision models can be applied in medical informatics?
- How can we deal with uncertainty in the real world?
- What is the principle of a rule based expert system?
- Sketch the basic architecture of a DSS!
- Which basic design principles of a DSS must be considered?
- How does the U-model work?
- Which similarities exist between DSS and KDD?
- What are clinical guidelines?
- What is interesting in the computational method model of cancer detection of Corchado et al. (2009)?
- What is the basic principle of Case Based Reasoning?
Some Useful Links

- [http://www-formal.stanford.edu/jmc/whatisai/whatisai.html](http://www-formal.stanford.edu/jmc/whatisai/whatisai.html)
- [http://aaai.org/AlTopics](http://aaai.org/AlTopics)
- [http://www.stottlerhenke.com/ai_general/history.htm](http://www.stottlerhenke.com/ai_general/history.htm)
- [http://rfs.acr.org/gamuts](http://rfs.acr.org/gamuts) (Gamuts in radiology - DSS for radiological imaging)
- [http://www.isradiology.org/gamuts/Gamuts.htm](http://www.isradiology.org/gamuts/Gamuts.htm) (Web-based Gamuts in Radiology)
Reasoning Foundations of Medical Diagnosis

Symbolic logic, probability, and value theory aid our understanding of how physicians reason.

Robert S. Ledley and Lee B. Lusted

The purpose of this article is to analyze the complicated reasoning processes inherent in medical diagnosis. The importance of this problem has received recent emphasis by the increasing interest in the use of electronic computers as an aid to medical diagnostic processes fitted into a definite disease category, or that it may be one of several possible diseases, or else that its exact nature cannot be determined.” This, obviously, is a greatly simplified explanation of the process of diagnosis, for the physician might also comment that after seeing a
difficulty are the ones who do remember and consider the most possibilities.”

Computers are especially suited to help the physician collect and process clinical information and remind him of diagnoses which he may have overlooked. In many cases computers may be as simple as a set of hand-sorted cards, whereas in other cases the use of a large-scale digital electronic computer may be indicated. There are other ways in which computers may serve the physician, and some of these are suggested in this paper. For example, medical students might find the computer an important aid in learning the methods of differential diagnosis. But to use the computer thus we must understand how the physician makes a medical diagnosis. This, then, brings us to the subject of our investigation: the reasoning foundations of medical diagnosis and treatment.

Medical diagnosis involves processes that can be systematically analyzed, as well as those characterized as “intangible.” For instance, the reasoning foundations of medical diagnostic procedures
Appendix: CDS Tools and EHR for quality measures

Appendix: Discovery of new expressions & co-occurrences

The problem pace of all possible sequences

Important expressions already known

[“3”, n * “0”, “2”] n ∈ {1..3}

Search for new key sequences

Generalization of similar sequences into new expressions

Cases with diagnosed patients and their RSA series

Case 1348

Derivation of co-occurrence relations between expressions and diagnosis

Known and new expressions with their consequent probability

Expression n4
[“4”, n+1, “2”] n ∈ {0..2}
Diagnosis c1: 70%
Diagnosis c2: 27%

Funk & Xiong (2006)
Appendix: Evaluation of a Sequence

Given a sequence $s$ there may be a set of probable consequent classes \( \{C_1, C_2, \ldots, C_k\} \)

The strength of the co-occurrence between sequence $s$ and class $C_i$ ($i = 1, \ldots, k$) can be measured by the probability, $p(C_i \mid s)$, of $C_i$ conditioned upon $s$

\[
P D(s) = \max_{i=1 \ldots k} P(C_i \mid s)
\]

\[
P(C_i \mid s) = \frac{P(s \mid C_i)P(C_i)}{P(s)}
\]

\[
P(s) = P(s \mid C_i)P(C_i) + P(s \mid \bar{C}_i)P(\bar{C}_i)
\]

\[
P(C_i \mid s) = \frac{P(s \mid C_i)P(C_i)}{P(s \mid C_i)P(C_i) + P(s \mid \bar{C}_i)P(\bar{C}_i)}
\]

\[
P(C_i \mid s) \approx \frac{N(C_i, s)}{N(s)}
\]

Funk & Xiong (2006)
Appendix: Example - Gamuts in Radiology


GAMUT G.25
EROSIVE GASTRITIS*

COMMON
1. Acute gastritis (eg, alcohol abuse)
2. Crohn's disease
3. Drugs (eg, aspirin; NSAID; steroids)
4. Helicobacter pylori infection
5. Idiopathic
6. [Normal areae gastricae]
7. Peptic ulcer; hyperacidity

UNCOMMON
1. Corrosive gastritis
2. Cryptosporidium antiris
3. [Lymphoma]
4. Opportunistic infection (eg, candidiasis (moniliasis); herpes simplex; cytomegalovirus)
5. Postoperative gastritis
6. Radiation therapy
7. Zollinger-Ellison S.; multiple endocrine neoplasia (MEN) S.

* Superficial erosions or aphthoid ulcerations seen especially with double contrast technique.

[ ] This condition does not actually cause the gamutted imaging finding, but can produce imaging changes that simulate it.

http://rfs.acr.org/gamuts/data/G-25.htm
Appendix: Example for Interactive Group Decision Support

Appendix: Crowdsourcing - Example Disaster Management


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**Gamut F-137**

**PHRENIC NERVE PARALYSIS OR DYSFUNCTION**

**COMMON**
1. Iatrogenic (eg, surgical injury; chest tube; therapeutic avulsion or injection; subclavian vein puncture)
2. Infection (eg, tuberculosis; fungus disease; abscess)
3. Neoplastic invasion or compression (esp. carcinoma of lung)

**UNCOMMON**
1. Aneurysm, aortic or other
2. Birth trauma (Erb’s palsy)
3. Herpes zoster
4. Neuritis, peripheral (eg, diabetic neuropathy)
5. Neurologic disease, (eg, hemiplegia; encephalitis; polio; Guillain-Barré S.)
6. Pneumonia
7. Trauma

**Reference**
Example: Pleo robot - Intelligent behaviour?
Clinical Decision Tree (CDT) is still state-of-the-art

Example (Part B): Leukemia

This 79 y/o female with chronic myeloid leukemia presented with rapidly enlarging spleen. The splenectomy specimen showed a dark red surface devoid of white pulp. Majority of the large tumor cells seen here were positive for CD34. This is a case of chronic myeloid leukemia in **blast transformation (Richter’s Syndrome)** Source: webpathology.com