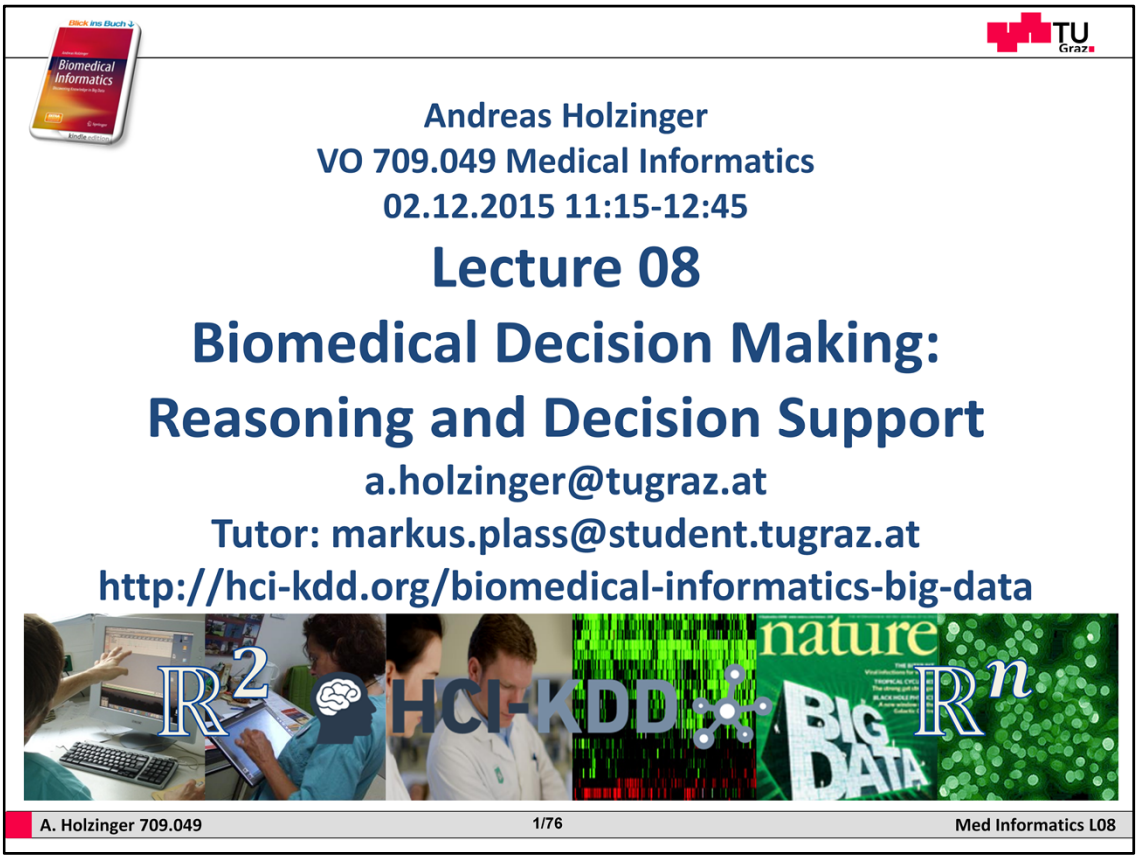

Status as of 01.12.2015 14:00

Dear Students, welcome to the 8th lecture of our course. Please remember from the last lecture:
Knowledge, Decision, Uncertainty, Bayesian Statistics, Probabilistic Modelling
Remember that Bayes law shows the relation between a conditional probability and its reverse form, i.e. the probability of a hypothesis given some observed pieces of evidence and the probability of that evidence given the hypothesis.

Please always be aware of the definition of biomedical informatics (Medizinische Informatik):
Biomedical Informatics is the inter-disciplinary field that studies and pursues the effective use of biomedical data, information, and knowledge for scientific inquiry, problem solving, and decision making, motivated by efforts to improve human health (and well-being).

Schedule

- 1. Intro: Computer Science meets Life Sciences, challenges, future directions
- 2. Back to the future: Fundamentals of Data, Information and Knowledge
- 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
- 7. Knowledge and Decision: Cognitive Science & Human-Computer Interaction
- **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
- 12. Methodology for Info Systems: System Design, Usability & Evaluation

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

Advance Organizer (1)

- **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;

Note: Heuristics are strategies that ignore information to make decisions faster
Small worlds is a situation in which all relevant alternatives, their consequences, and probabilities are known, and where the future is certain, so that the optimal solution to a problem can be determined
Large world is a situation in which some relevant information is unknown or must be
estimated from samples, and the future is uncertain, violating the conditions for rational decision theory;

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;

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;

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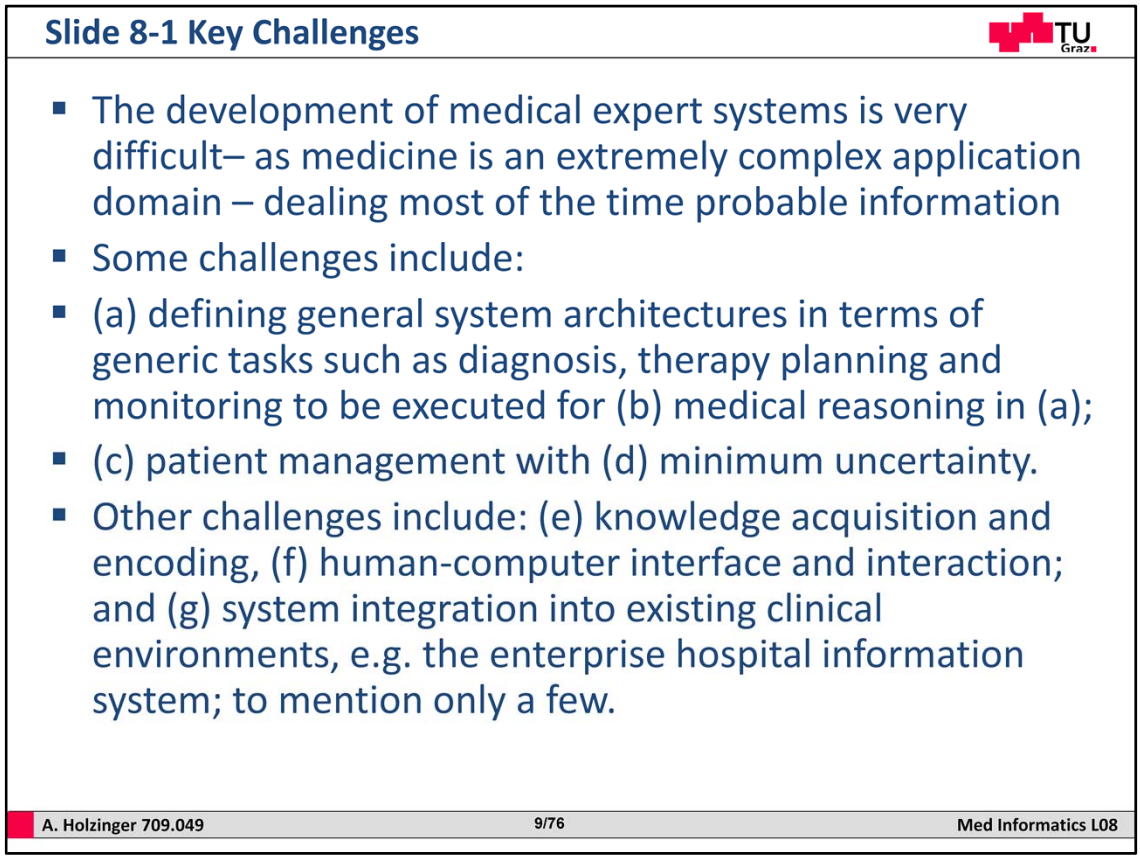
Case based reasoning

Reasoning = Reason, is the capacity for consciously making sense of things, for establishing and verifying facts, and changing or justifying practices, institutions, and beliefs based on new or existing information.

In the previous lecture we have got an overview about some fundamentals of decision making from the human factors perspective; now we will have a closer look on technological solutions. We follow the definition of Shortliffe (2011) and define a medical DSS as any computer program designed to support health professionals in their daily decision making processes.



Health care Information Networks (HINs) help professionals and patients access the right information at the right time and invite a new design and integration of decision support systems within these collaborative workflow processes. The need to share information and knowledge is increasing (e.g., shared records, professional guidelines, prescriptions, care protocols, public health information, health care networks etc.) The well-established 'Evidence-Based Medicine' (EBM) and 'Patient-centered medicine' paradigms representing different visions of medicine are suggesting behaviors, so different that they are also raising dilemmas. Attempts made to standardize care are potentially ignoring the heterogeneity of the patients (Fieschi et al., 2003).

Challenges in the development of DSS

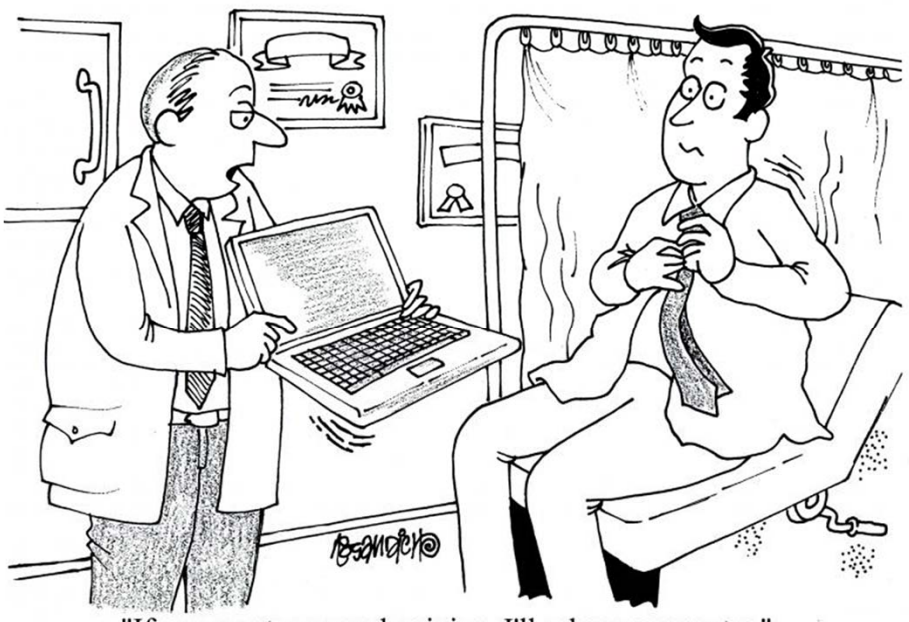
The development of medical expert systems is very difficult– as medicine is an extremely complex application domain – dealing most of the time with weakly structured data and probable information (Holzinger, 2012).

Some challenges include (Majumder & Bhattacharya, 2000):

(a) defining general system architectures in terms of generic tasks such as diagnosis, therapy planning and monitoring to be executed for (b) medical reasoning in (a); (c) patient management with (d) minimum uncertainty. Other challenges include: (e) knowledge acquisition and encoding, (f) human-computer interface and interaction; and (g) system integration into existing clinical environments, e.g. the enterprise hospital information system; to mention only a few.

In the previous lecture we have got an overview about some fundamentals of decision making from the human factors perspective; now we will have a closer look on technological solutions. We follow the definition of Shortliffe (2011) and define a medical DSS as any computer program designed to support health professionals in their daily decision making processes (Shortliffe, 2011).

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

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In a classic cartoon, a physician offers a second opinion from his computer. The patient looks horrified: How absurd to think that a computer could have better judgment than a human doctor! But computer tools can already provide valuable information to help human doctors make better decisions. And there is good reason to wish such tools were broadly available.

About half of the time, doctors fall short of providing quality medical care as defined by national guidelines, according to a 2003 paper in the New England Journal of Medicine. In addition, patients leave their doctors' visits with an average of 1.6 unanswered questions. "That's too many," says Blackford Middleton, MD, assistant professor of medicine at the Harvard Medical School and corporate director of clinical and informatics research and development at Partners Healthcare System in Boston. And because medical professionals have incomplete knowledge or incomplete information about a patient, "we order too many tests, patients are called back, and sometimes bad things happen," Middleton says. "It's embarrassing. That's why I get up every day and run to work."

Slide 8-2 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?

Bemmel, J. H. V. & Musen, M. A. 1997. *Handbook of Medical Informatics, Heidelberg, Springer.*

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In the previous lecture we have got an overview about some fundamentals of decision making from the human factors perspective; now we will have a closer look on technological solutions. We follow the definition of Shortliffe (2011) and define a medical DSS as any computer program designed to support health professionals in their daily decision making processes. Dealing with data in the health care process is often accompanied by making decisions. According to (Bemmel & Musen, 1997) we may determine two types of decision:

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:

a. What is the probability that this patient has a myocardial infarction on the basis of given data (patient history, ECG)?

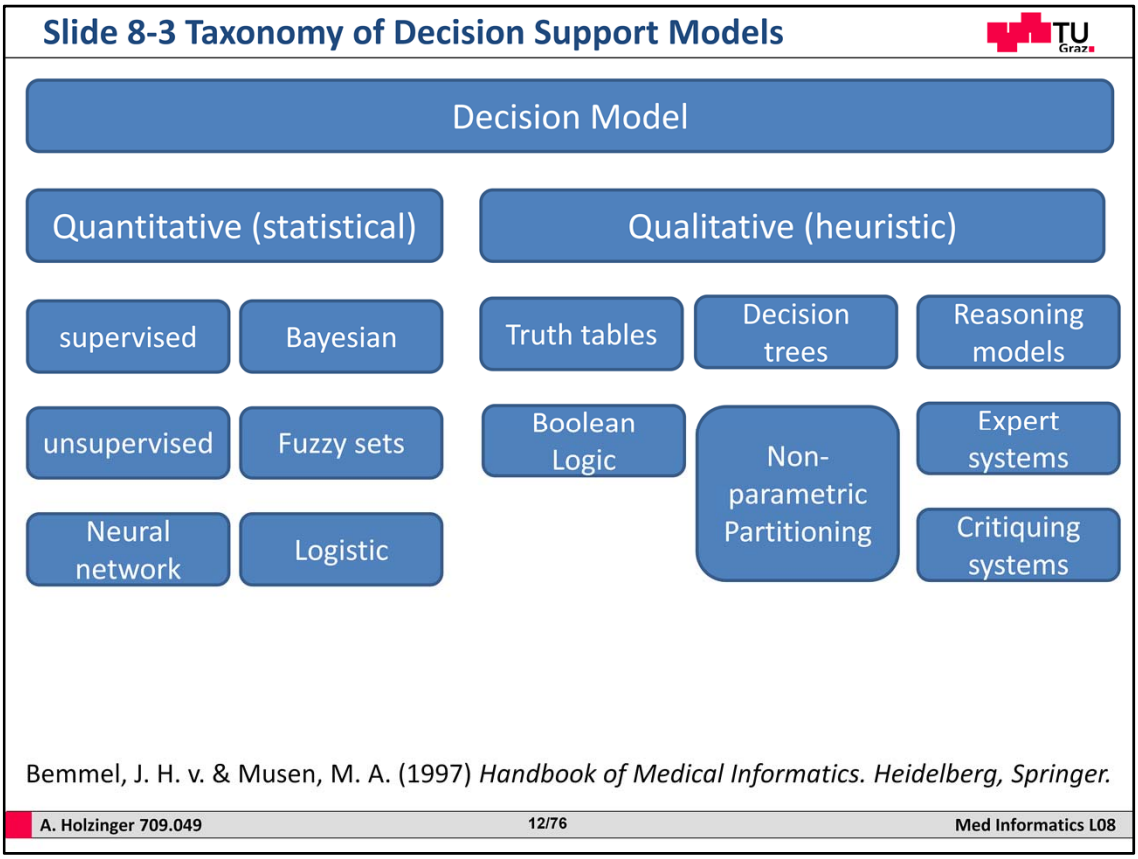
b. What is the probability that this patient has acute appendices, given the signs and symptoms concerning abdominal pain?

Type 2: Decisions related to therapy, i.e. computers are used to select the best therapy on the basis of clinical evidence, e.g.:

c. 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?

d. 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?

For both types we need medical knowledge. On the basis of the available knowledge we can develop decision models on the basis of the available patient data.

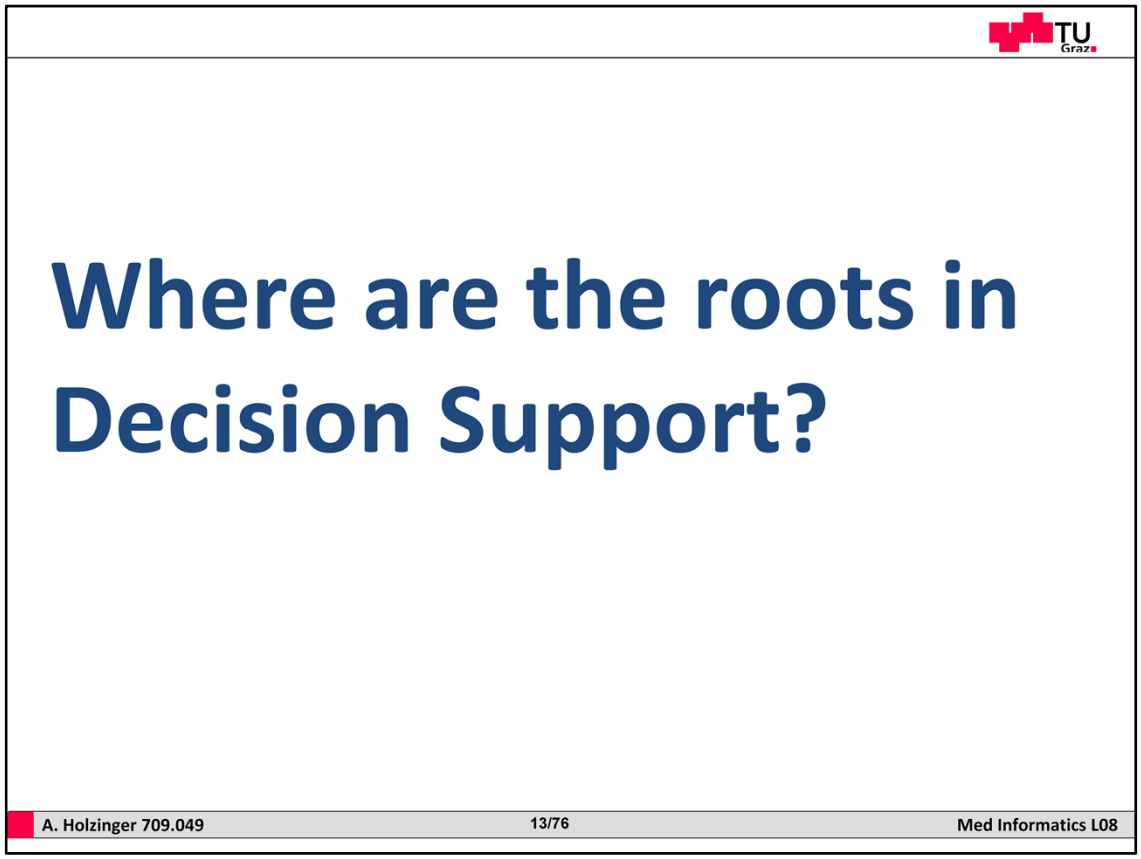


p.239 Fig 15.5 DS models in health care can be grouped into different categories

In Figure 8-1 we see that decision models can be grouped into two main categories:

1) Quantitative: based on formal statistical methods to test the probability of the occurrence of an event, e.g. to test that the probability for "healthy" is higher than that for a certain disease as we have seen in differential diagnostics.

2) Qualitative: relying on symbolic methods, rather than following a strictly formal mathematical basis. Such models are inspired by insights on human reasoning, thus often called heuristics, and perform deductions on symbolic models using logical operations to conclude a diagnosis based on a case model. According to VAN BEMMEL we should avoid the word heuristics and use the term symbolic, because such methods may be composed of elementary two-class, single-feature decision units from the first category. In this slide we see that decision models can be grouped into two main categories:
1) Quantitative: based on formal statistical methods to test the probability of the occurrence of an event, e.g. to test that the probability for "healthy" is higher than that for a certain disease as we have seen in differential diagnostics.
2) Qualitative: relying on symbolic methods, rather than following a strictly formal mathematical basis. Such models are inspired by insights on human reasoning, thus often called heuristics, and perform deductions on symbolic models using logical operations to conclude a diagnosis based on a case model. According to Van Bemmel we should avoid the word heuristics and use the term symbolic, because such methods may be composed of elementary two-class, single-feature decision units from the first category, e.g. E = "x>L"
.



In the early 1950ies decision trees and truth tables were used, followed by systems based on statistical methods, finally followed by expert systems. The history of DSS is very closely related to artificial intelligence (AI), the roots can be traced back to attempts to automate chess play.

Slide 8-4 History of DSS is a history of artificial intelligence

Stanford Heuristic Programming Project
Memo HPP-78-1

Computer Science Department
Report No. STAN-CS-78-649

February 1978

E. Feigenbaum, J. Lederberg, B. Buchanan, E. Shortliffe

Rheingold, H. (1985) *Tools for thought: the history and future of mind-expanding technology. New York, Simon & Schuster.*

DENDRAL AND META-DENDRAL:
THEIR APPLICATIONS DIMENSION

by

Bruce G. Buchanan and Edward A. Feigenbaum

COMPUTER SCIENCE DEPARTMENT
School of Humanities and Sciences
STANFORD UNIVERSITY

Buchanan, B. G. & Feigenbaum, E. A. (1978) DENDRAL and META-DENDRAL: their applications domain. *Artificial Intelligence, 11, 1978, 5-24.*

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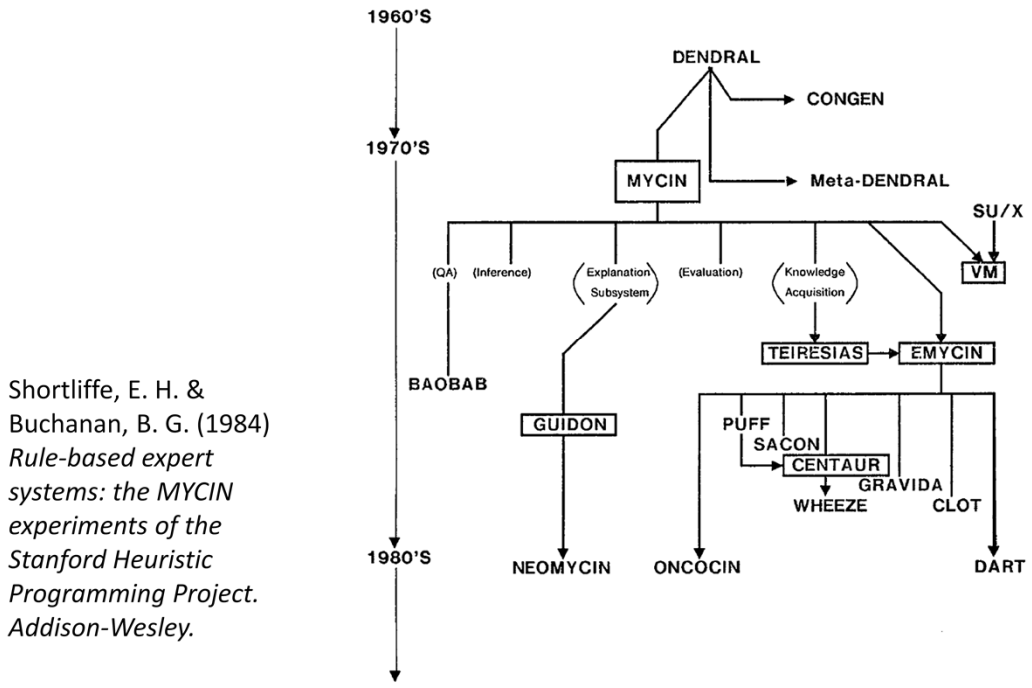
http://www.youtube.com/watch?v=IKahVCzKR8Y

In the early 1950ies decision trees and truth tables were used, followed by systems based on statistical methods, finally followed by expert systems. The history of DSS is very closely related to artificial intelligence (AI), the roots can be traced back to attempts to automate chess play. A famous sample was a fake: the Mechanical Turk (See slide, below, left). Built in 1770 by Wolfgang von Kempelen (1734–1804), the device appeared to be able to play against a human, as well as perform the knight's tour, which require moving a knight to visit every square of a chessboard only once. The “real” start of AI research was in 1955, when John McCarthy coined the term AI and defined it as the science and engineering of making intelligent machines. Edward Feigenbaum was one of first to construct an artificial expert and while looking for an appropriate field of expertise, he met Joshua Lederberg, the Nobel laureate biochemist, who suggested that organic chemists need assistance in determining the molecular structure of chemical compounds (Rheingold, 1985).

Slide 8-5 Evolution of Decision Support Systems



Shortliffe, E. H. & Buchanan, B. G. (1984) *Rule-based expert systems: the MYCIN experiments of the Stanford Heuristic Programming Project. Addison-Wesley.*

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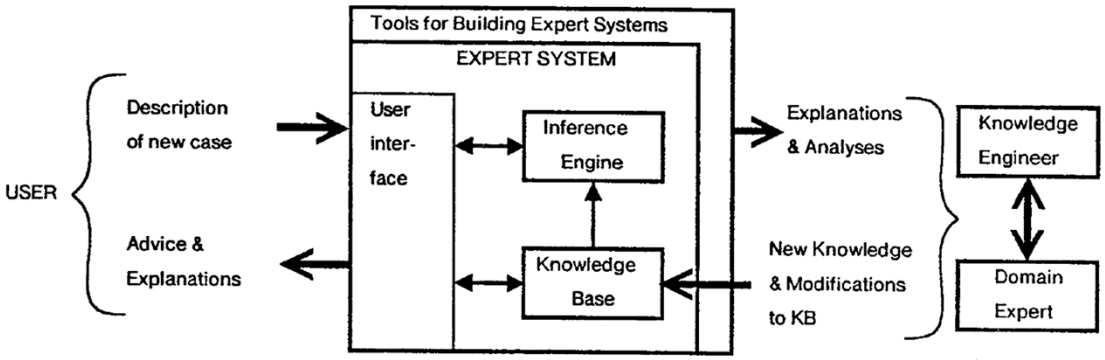
In 1965 Feigenbaum, Lederberg & Buchanan began work on DENDRAL (see top root in the slide), a procedure for non-redundantly enumerating topologically distinct arrangements of any given set of atoms, consistent with the rules of chemical valence (Lindsay et al., 1993). Conventional systems had failed to support organic chemists in forecasting molecular structures. Human chemists know that the possible structure of any chemical compound depends on a number of rules about how different atoms can be bound to one another; and many facts about different atoms in known compounds. By discovering a previously unknown compound, they can gather evidence about the compound by analyzing it with a mass spectroscope, which provides a lot of data, but no clues to what it all means. Look at the slide (Shortliffe & Buchanan, 1984): DENDRAL was followed by MYCIN; and actually MYCIN was the inspiration for many other systems.

Slide 8-6 Early Knowledge Based System Architecture



Shortliffe, T. & Davis, R. (1975) Some considerations for the implementation of knowledge-based expert systems *ACM SIGART Bulletin, 55, 9-12.*

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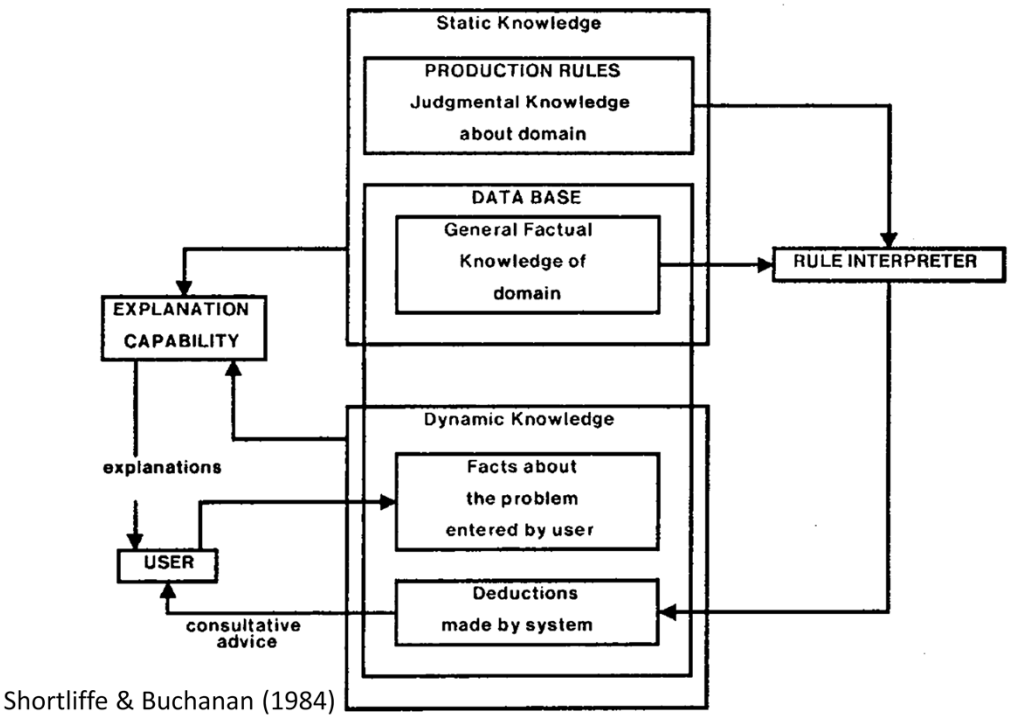
DENDRAL was well known to computational chemists who have incorporated many parts of it in their own software. Although it does no longer exist today, it had a major impact on a newly developed field:
Knowledge engineering (KE), which is both science and engineering of Knowledge-based systems (KBS) and applies methods from artificial intelligence, data mining, expert systems, decision support systems and mathematical logic, as well as cognitive science. A great amount of work is spent in observing human experts and the design of models of their expertise.
One of the first spinoffs from DENDRAL was Meta-DENDRAL, an expert system for people whose expertise lies in building expert systems. By separating the inference engine from the body of factual knowledge, Buchanan was able to produce a tool for expert-systems builders. In this slide we see the first architecture of the basic principle of any expert systems, consisting of a knowledge base, an inference engine and a dedicated user-interface to support the human-computer interaction process (Shortliffe & Davis, 1975).

Slide 8-7 Static Knowledge versus dynamic knowledge



Shortliffe & Buchanan (1984)

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MYCIN was programmed in Lisp and used judgmental rules with associated elements of uncertainty. It was designed to identify bacteria causing severe infections (bacteraemia, meningitis), and to recommend antibiotics, with the dosage adjusted for the patient's body weight. Edward Shortliffe, both a physician and computer scientist was confronted with problems associated with diagnosing a certain class of brain infections that was an appropriate area for expert system research and an area of particularly importance, because the first 24 hours are most critical for the patients. In the slide we see the idea of the separation of static knowledge (the rules and facts) and dynamic knowledge (the entries made by the human user and deductions made by the sytem). This is the principle of rule-based systems (Shortliffe & Buchanan, 1984).

Slide 8-8 Dealing with uncertainty in the real world

- The information available to humans is often imperfect – imprecise - uncertain.
- This is especially in the medical domain the case.
- An **human agent** 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!**

We are already well aware about the notion of probable information. The problem is that 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 – however, most of our real-world problems do not provide this exact information, mostly is inexact, incomplete, uncertain, noisy, and/or un-measurable. This is a big problem in the biomedical area.

1967, Star Trek, I Mudd

Harcourt Fenton Mudd: Now listen, Spock, you may be a wonderful science officer but, believe me, you couldn't sell fake patents to your mother!

Spock: I fail to understand why I should care to induce my mother to purchase falsified patents.

Slide 8-9 MYCIN – rule based 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 und 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

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Shortliffe was aware of the problems involved with classic logic and introduced the certainty factor (CF) which is a number between - 1 and + 1 that reflects the degree of belief in a hypothesis:
Positive CF's indicate evidence that the hypothesis is valid. If CF = 1, the hypothesis is known to be correct (and contrary for CF = –1). If CF = 0, there is either no evidence regarding the hypothesis or the supporting evidence is equally balanced, suggesting that the hypothesis is not true. MYCIN's hypotheses are statements regarding values of clinical parameters for the various nodes in the context tree.
Let us look on an original example in the next slide.

Slide 8-10 Original Example from MYCIN

h_1 = The identity of ORGANISM-1 is streptococcus
h_2 = PATIENT-1 is febrile
h_3 = The name of PATIENT-1 is John Jones

$CF[h_1,E] = .8$	:	There is strongly suggestive evidence (.8) that the identity of ORGANISM-1 is streptococcus
$CF[h_2,E] = -.3$	:	There is weakly suggestive evidence (.3) that PATIENT-1 is not febrile
$CF[h_3,E] = +1$	:	It is definite (1) that the name of PATIENT-1 is John Jones

Shortliffe, E. H. & Buchanan, B. G. (1984) *Rule-based expert systems: the MYCIN experiments of the Stanford Heuristic Programming Project. Addison-Wesley.*

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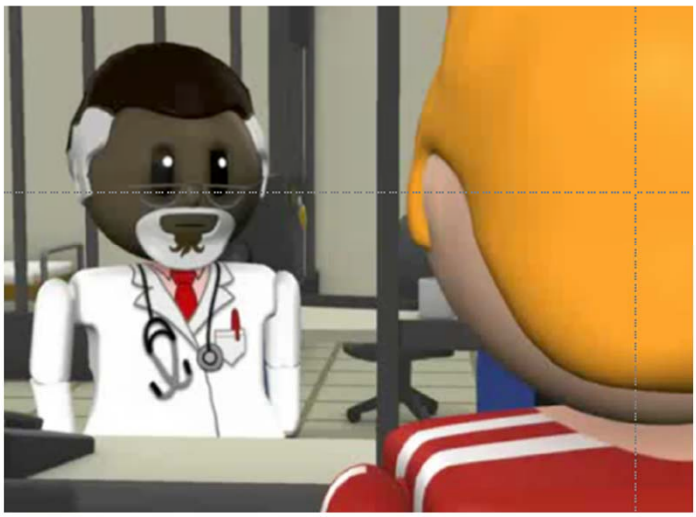
This MYCIN Example makes the of the Certainty Factor CF clear (Shortliffe & Buchanan, 1984).

Slide 8-11 MYCIN was *no* success in the clinical practice

https://www.youtube.com/watch?v=IVGWM0CKNWA ("real nurse triage")



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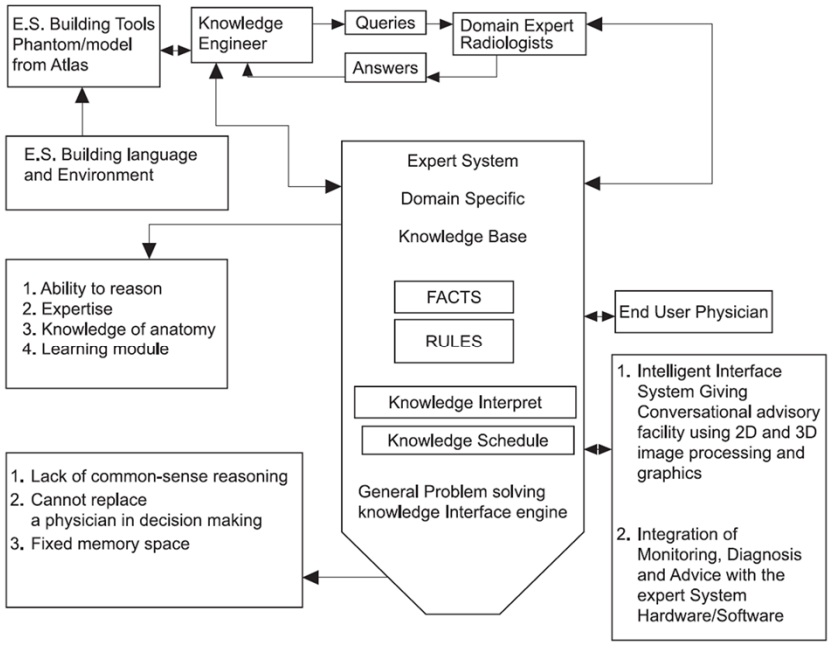
MYCIN was not a success in the clinical practice, however, it was pioneer work for practically each following system, for example ONCOCIN evolved from this work and assisted physicians in managing complex drug regimens for treating cancer patients. It has been built on the results of the MYCIN experiments while gaining experience with regular clinical use of an advice system for use by physicians. The work has also been influenced by data regarding features that may be mandatory if decision support tools are to be accepted by clinicians. Clinical oncology was selected due to the fact that this medical domain meets many of the criteria that has been identified for building an effective consultation tool using AI techniques (Shortliffe, 1986). Up to date, the main architecture of a DSS is the same as developed in the 1970ies.

What challenges are in the development of DSS?

Slide 8-12 Basic Design Principles of a DSS



Majumder, D. D. & Bhattacharya, M. (2000) Cybernetic approach to medical technology: application to cancer screening and other diagnostics. Kybernetes, 29, 7/8, 871-895.

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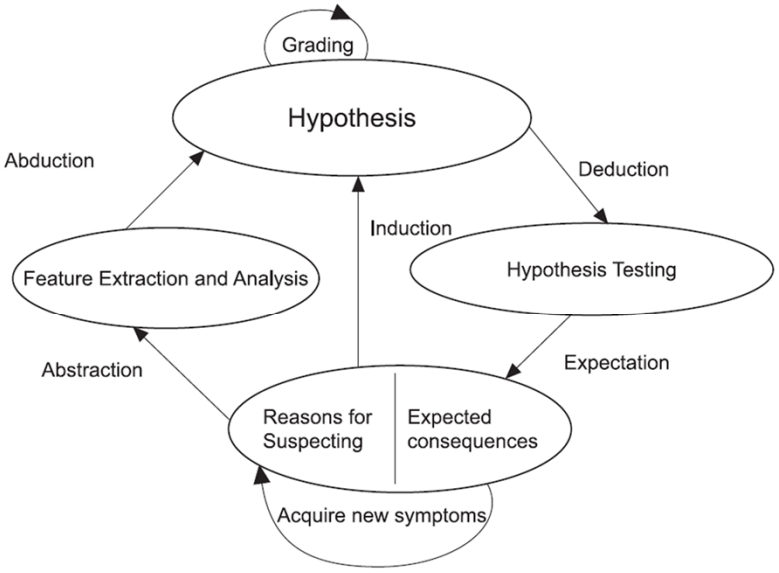
As we have already heard at the very beginning, the development of medical expert systems is very difficult– as medicine is a complex application domain – dealing most of the time with weakly structured data (Holzinger, 2012). Problems include (Majumder & Bhattacharya, 2000):
(a) defining general system architectures in terms of generic tasks such as diagnosis, therapy planning and monitoring to be executed for (b) medical reasoning in (a); (c) patient management with (d) minimum uncertainty. Other challenges include: (e) knowledge acquisition and encoding, (f) human-computer interface and interaction; and (g) system integration into existing clinical environments, e.g. the enterprise hospital information system.

Slide 8-13 Cybernetic approach to medical diagnostics



Majumder, D. D. & Bhattacharya, M. (2000) Cybernetic approach to medical technology: application to cancer screening and other diagnostics. Kybernetes, 29, 7/8, 871-895.

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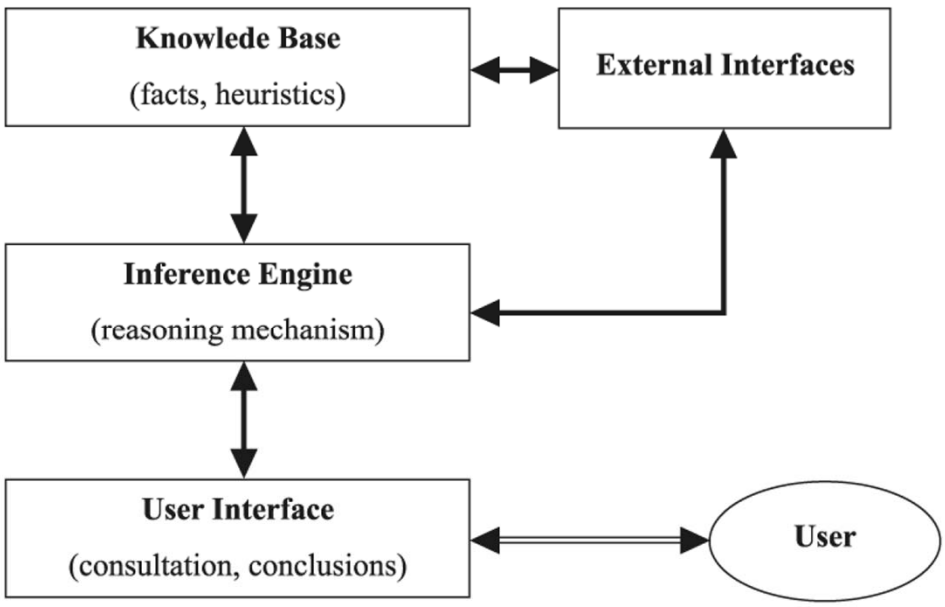
This slide shows the typical workflow of a medical reasoning system: Abduction, deduction and induction represent the basic elements of the inference model of medical reasoning. Clinical patient data is used to generate plausible hypotheses, and these are used as start conditions to forecast expected consequences for matching with the state of the patient in order to confirm or reject these hypotheses (Majumder & Bhattacharya, 2000).

Slide 8-14 State-of-the-art architecture of DSS



Metaxiotis, K. & Psarras, J. (2003) Expert systems in business: applications and future directions for the operations researcher. *Industrial Management & Data Systems, 103, 5, 361-368.*

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Present-day DSS consist of 3 main components:
1) Knowledge base, the heart of the system and contains the expert facts, heuristics, judgements, predictions, algorithms, etc., and the relationships – derived from human experts;
2) Inference engine, examines the status of the knowledge base, and determines the order the inferences are made; it also includes the capability of reasoning in the presence of uncertainty (compare with MYCIN);
3) User interface, enables effective human-computer interaction – additionally there are external interfaces providing access to other databases and data sources (Metaxiotis & Psarras, 2003).

Slide 8-15 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.

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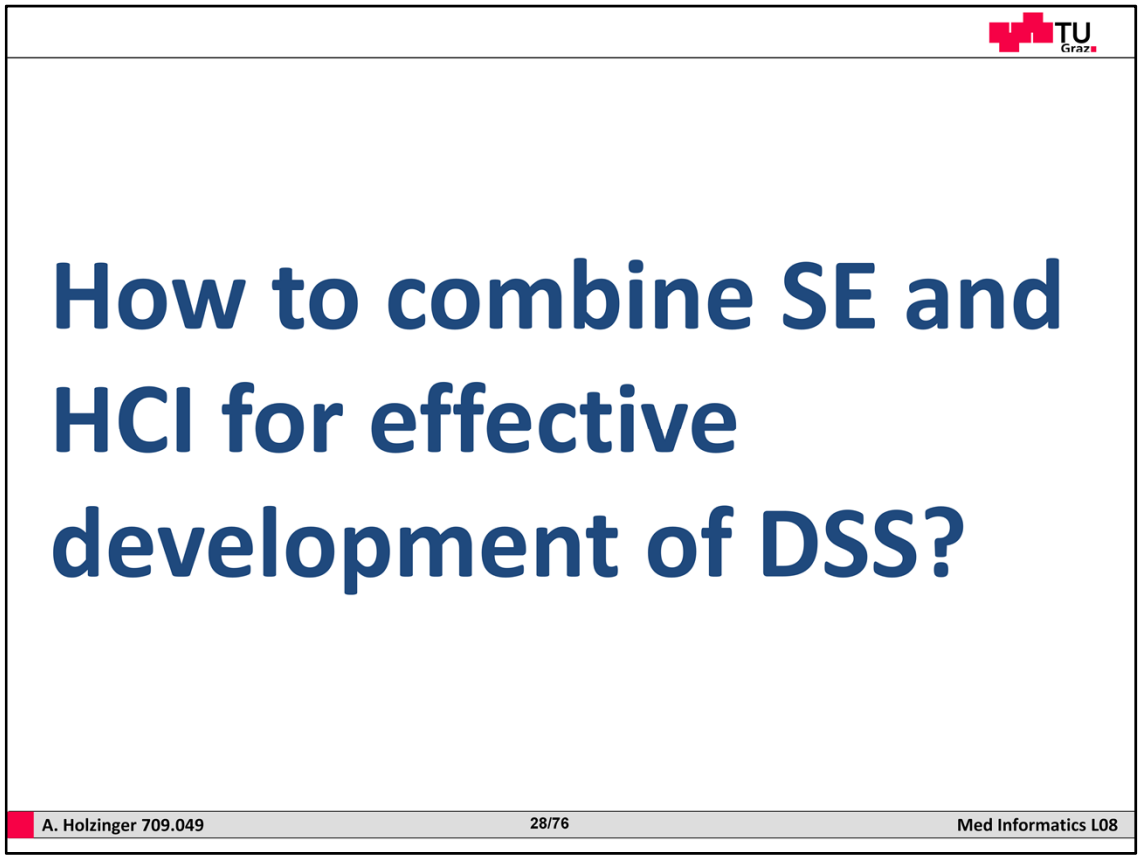
DSS deal with problems based on available knowledge. Some of this knowledge can be extracted using a decision support tool (data mining) which is in fact part of a KDD process (lecture 6). Data mining tools are usually difficult to exploit because most of the end users are neither experts in computing nor in statistics. It is difficult to develop a KDD system that fits exactly to the end user needs. Those difficulties can only be tackled by including end users into DSS development It is necessary to combine methods from Software Engineering (SE) and HCI. Abed, Bernard & Angué (1991) proposed an approach to combine (1) the Unified Process (UP) from SE and (2) the U model from HCI.
The U model (see next slide) considers those steps which do not exist in traditional SE models.



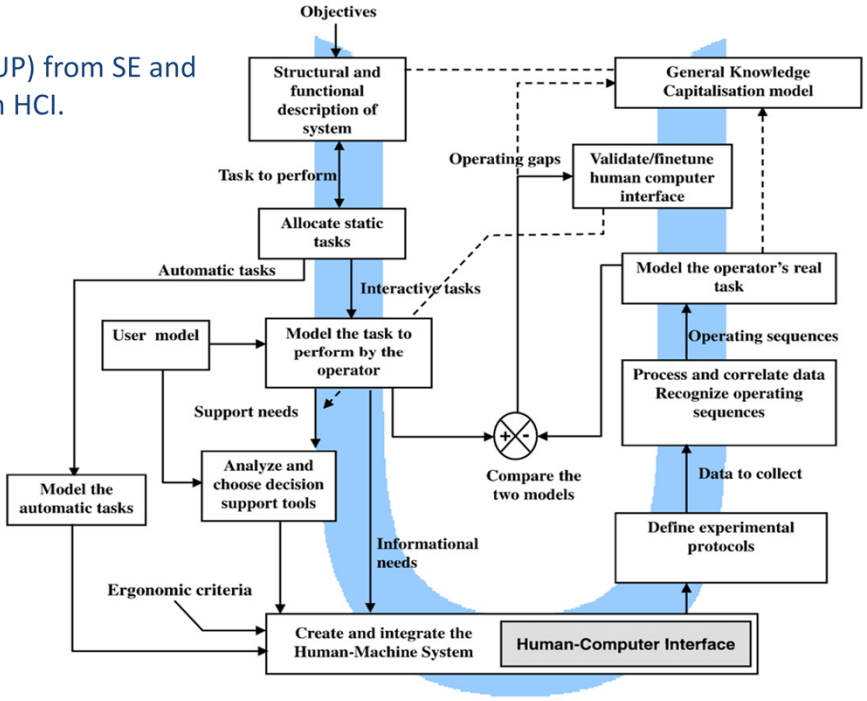
DSS deal with problems based on available knowledge. Some of this knowledge can be extracted using a decision support tool (data mining) which is in fact part of a KDD process (lecture 6). Data mining tools are usually difficult to exploit because most of the end users are neither experts in computing nor in statistics. It is difficult to develop a KDD system that fits exactly to the end user needs.

For the effective use in It is necessary to combine methods from Software Engineering (SE) and HCI.

Slide 8-16 Example: Development following the U model 1/2

Unified Process (UP) from SE and the U-model from HCI.

Abed, M., Bernard, J. & Angué, J. (1991). *Task analysis and modelization by using SADT and Petri Networks. Tenth European Annual Conference on Human Decision Making and Manual Control, Liege, 11-13.*



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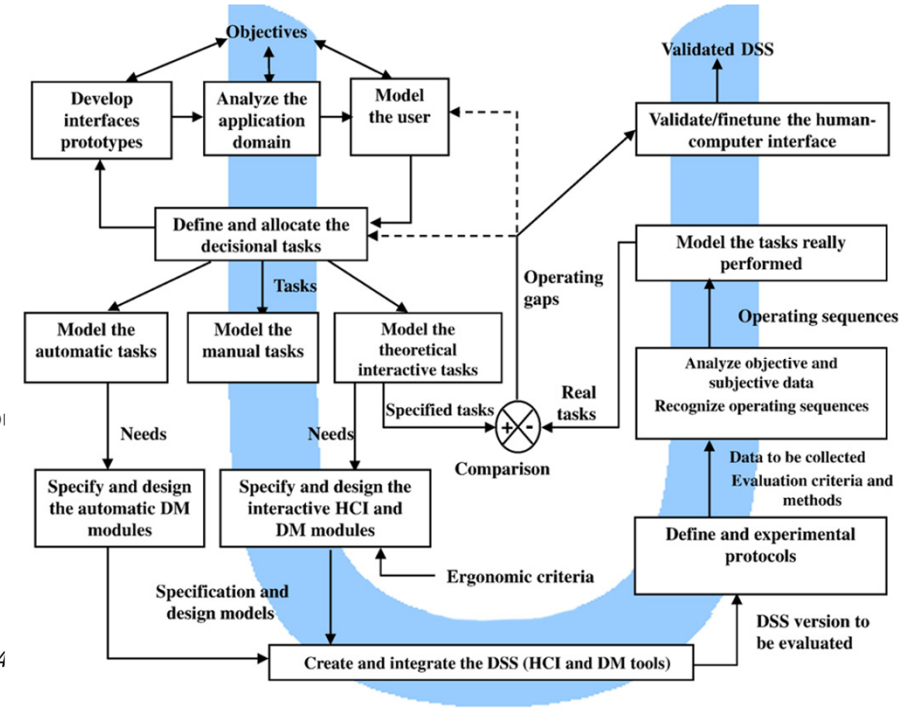
For the effective use in It is necessary to combine methods from Software Engineering (SE) and HCI.
In this U-model we determine two phases:
(1) a descending phase for specification and human–computer systems design and development; and
(2) an ascending phase for the evaluation of the system.
The validation consists of comparing the model of the theoretical tasks specified in the descending phase with the model of the real tasks highlighted in the ascending phase, according to the original principles suggested by (Abed, Bernard & Angué, 1991). The result of the comparison either validates the system or highlights its deficiencies.

Slide 8-17 Improved U model 2/2



Ayed, B. M., Ltifi, H., Kolski, C. & Alimi, A. (2010) A user-centered approach for the design & implementatio of KDD-based DSS: A case study in the healthcare domain. *Decision Support Systems, 50, 64 78.*

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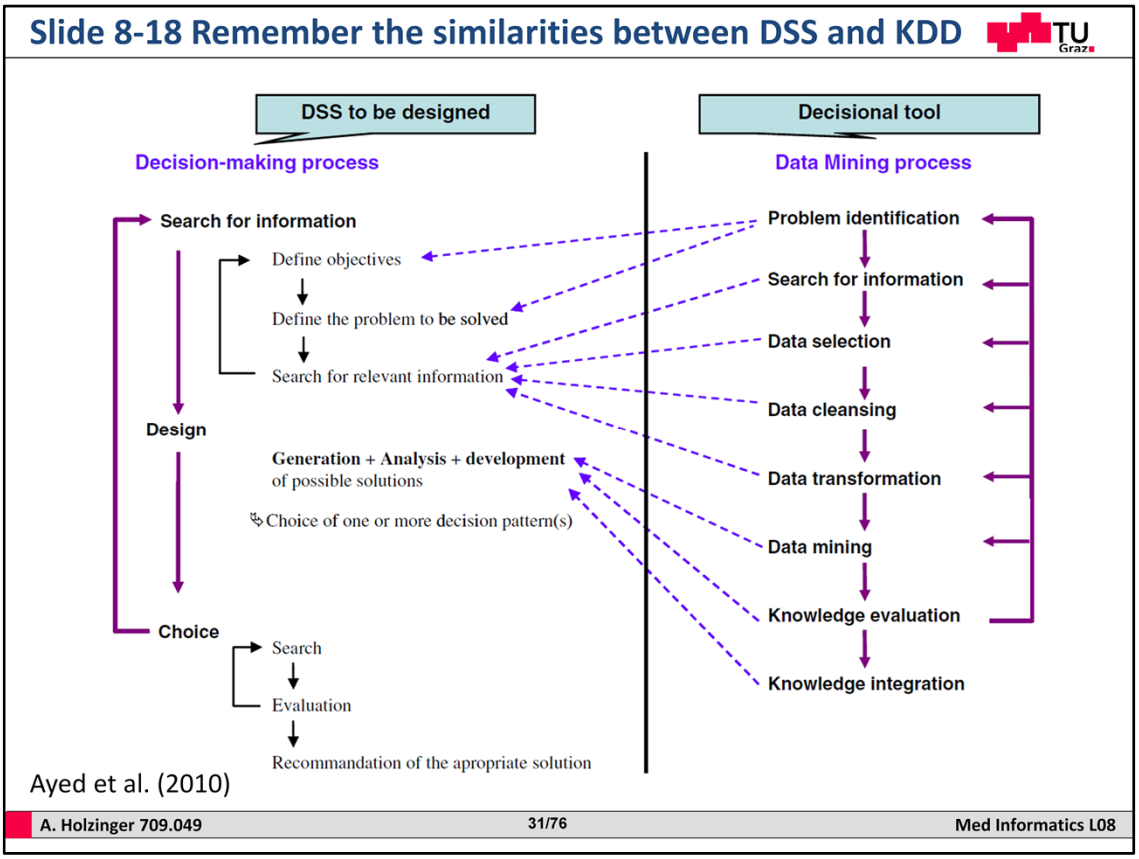
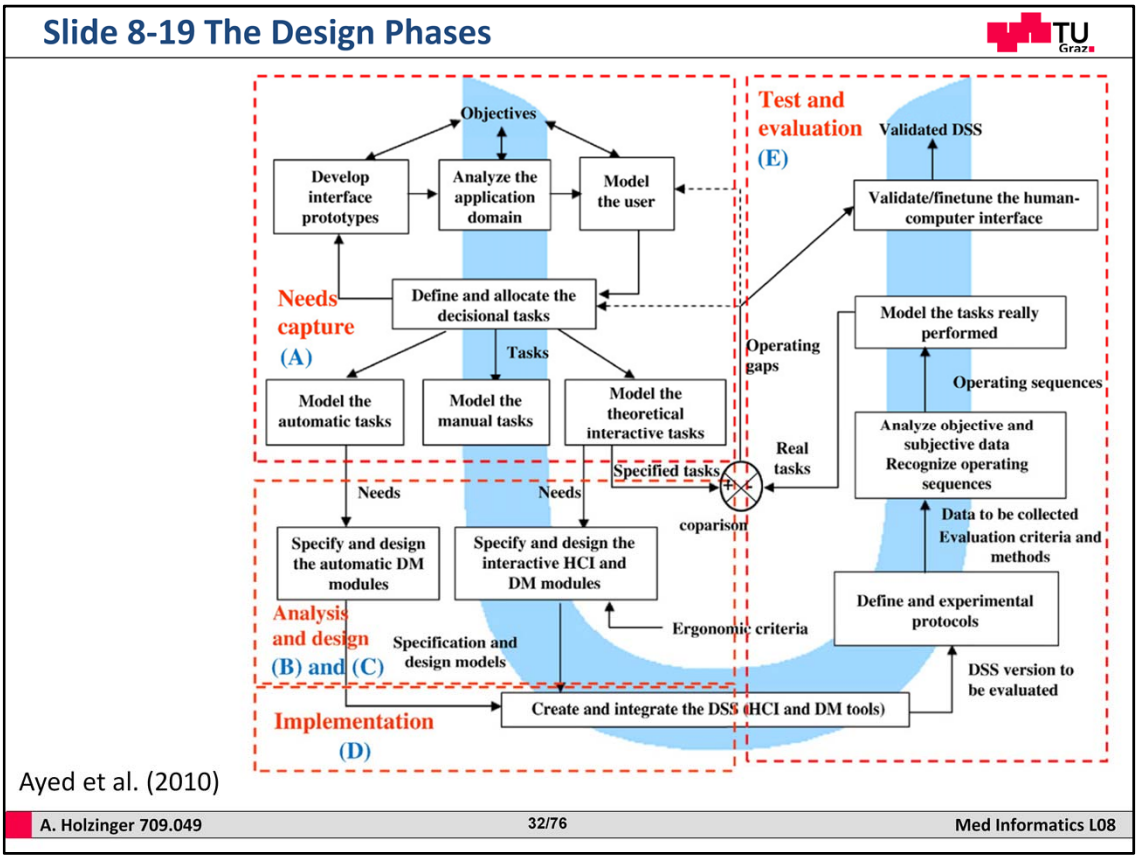
The final model resulting from the assessment allows a generalization of the end users specific behaviour under particular work conditions and context – what traditional often ignore. Ayed et al. (2010) proposed a modified version of the U-model, specifically adapted to DSS and knowledge discovery (KDD):
(1) the analysis of the domain, including the definition of the system objectives, which allows the first functional and structural description of the system to be developed; and
(2) the development of the first interface prototypes (models) for the DSS in question, which, by giving future users an idea of the possible solutions, allows them to be implicated as early as possible in the project life cycle.

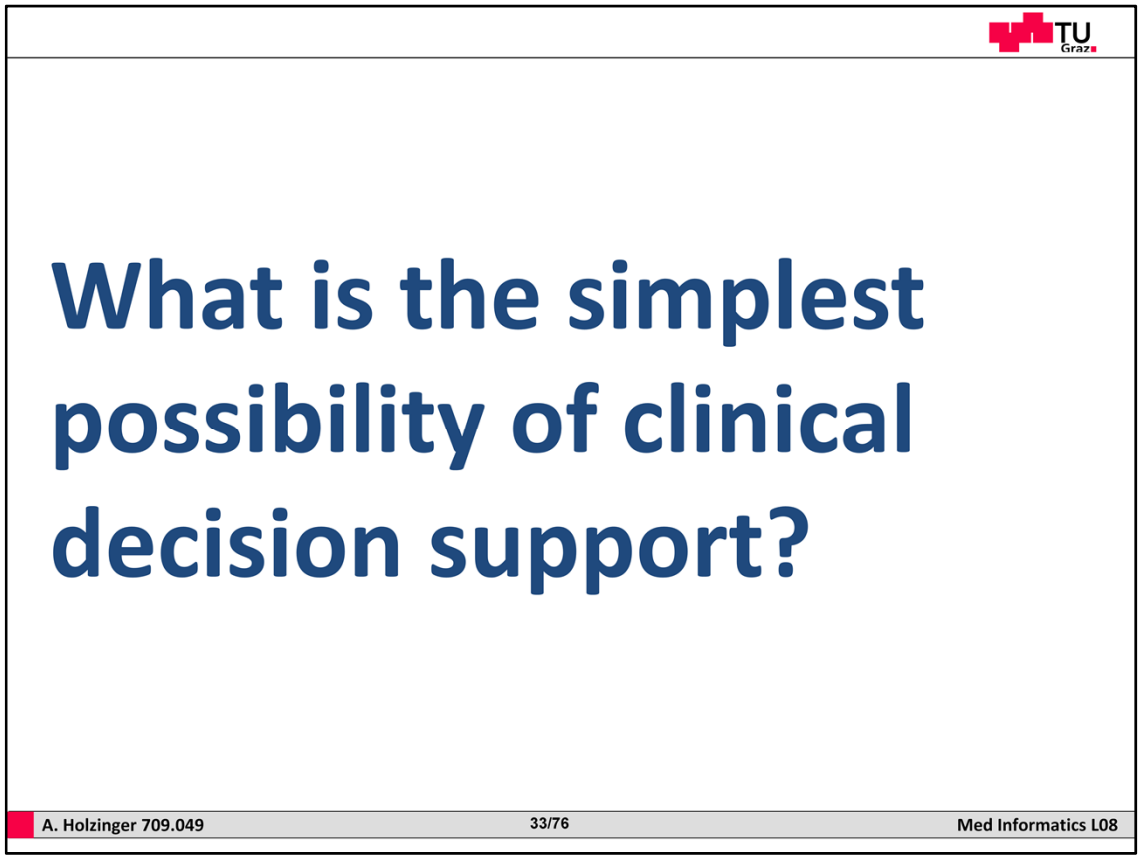


If you look at this slide and compare the DSS process with the KDD (data mining) process, then you will recognize the similarity between decision making processes and data mining processes.



Ayed et al. (2010)

In this slide we can see the various phases (A to E) of the U-Model approach, which is based on the principle of iterative and incremental development, which allows each task accomplished to be evaluated as soon as the first iterations of the development process have been completed:
A = requirements analysis (needs capture)
B = Analysis and Specification
C = Design and Prototyping
D = Implementation
E = Test and Evaluation
Be aware of the user-centred design process, which will be discussed in →Lecture 12!



We have now seen some sophisticated systems.
But on a day to day basis – in every clinical enterprise hospital information system there is the possibility of implementation decision support easily.

Slide 8-20 Clinical Guidelines as DSS & Quality Measure

- 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.

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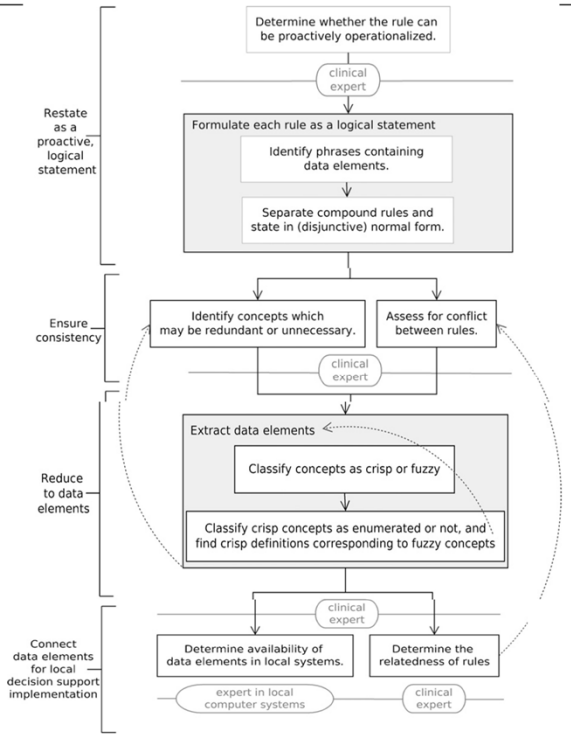
Guidelines have to be formalized (transformed from natural language to a logical algorithm) and implemented (using the algorithm to program decision support software which is used in practice). Work on formalization has focused on narrative guidelines, which describe a process of care with branching decisions unfolding over time (Medlock et al., 2011). Systematic guidelines have potential to improve the quality of patient care.

Quality. The demand for increased quality assurance has led to increased interest in performance indicators and other quality metrics. In order for the quality of care to improve as a result of these measures, they must be linked to a process of care. For example, a rule such as "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." These measure quality and performance at the population level, but in order to improve the quality of care, action is required at the patient level. 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.

Clinical rules represent elementary, isolated care recommendations, while narrative guidelines describe a coherent, unified care process.

Slide 8-21 Clinical Guidelines



Medlock, S., Opondo, D., Eslami, S., Askari, M., Wierenga, P., de Rooij, S. E. & Abu-Hanna, A. (2011) LERM (Logical Elements Rule Method): A method for assessing and formalizing clinical rules for decision support. *International Journal of Medical Informatics, 80, 4, 286-295.*

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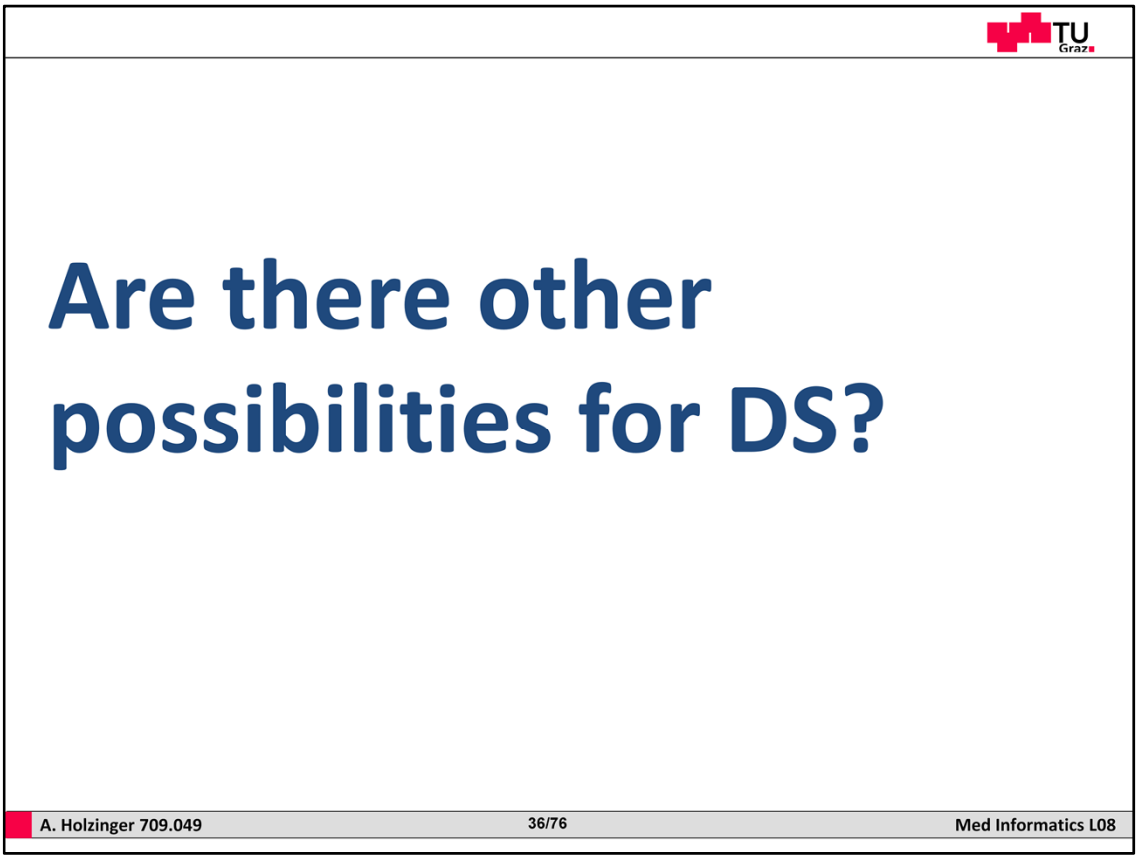
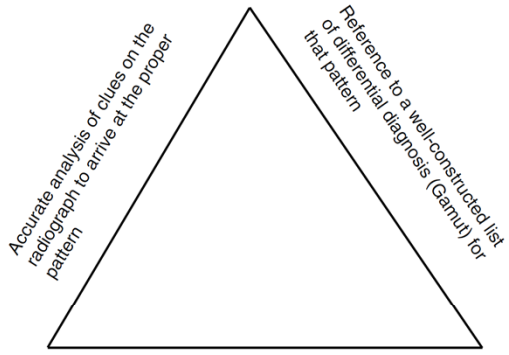
Most work in developing computer-interpretable guidelines has focused on the difficult problem of formalizing the time-oriented structure of guidelines. Medlock et al. (2011) propose the Logical Elements Rule Method (LERM), although presented linearly in the text, in practice some steps may be done in parallel, as shown in this slide. Some steps, such as extracting data elements or checking for conflicts between rules, may need to be repeated with the results of later steps as input.



Yes, there are other possibilities of decision support, let us look into the bioinformatics domain.
An interesting part is in visualization relevant information – we will partiuclarly focus on visualization and visual analytics in the next lecture number 9. Here only some taster from the biology domain.

Slide 8-21b Gamuts: Triangulation to find diagnoses



Correlation of radiographic findings and Gamut with patients' clinical and lab findings to arrive at the most likely diagnosis

Reeder, M. M. & Felson, B. 2003. *Reeder and Felson's gamuts in radiology: comprehensive lists of roentgen differential diagnosis, New York, Springer Verlag.*

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

Reference

1. Prasad S, Athreya BH: Transient paralysis of the phrenic nerve associated with head injury. JAMA 1976;236:2532–2533

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The word gamut is defined as the whole range of anything. It indicates a complete list of causes of a particular roentgen finding or pattern.
Most radiologists use the "Gamut approach" without calling it that. You see an epiphyseal lesion of bone and immediately search your memory bank for causes. You recall perhaps six causes, then eliminate two because of rarity or incompatible roentgen pattern. Then with the clinical information at your elbow in the form of an x-ray requisition or a clinician, you weed out two more that don't fit the clinical setting, leaving you with perhaps one or two likely diagnoses.

Slide -21c Example - Gamuts in Radiology

REEDER AND FELSON'S
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* antritis
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.

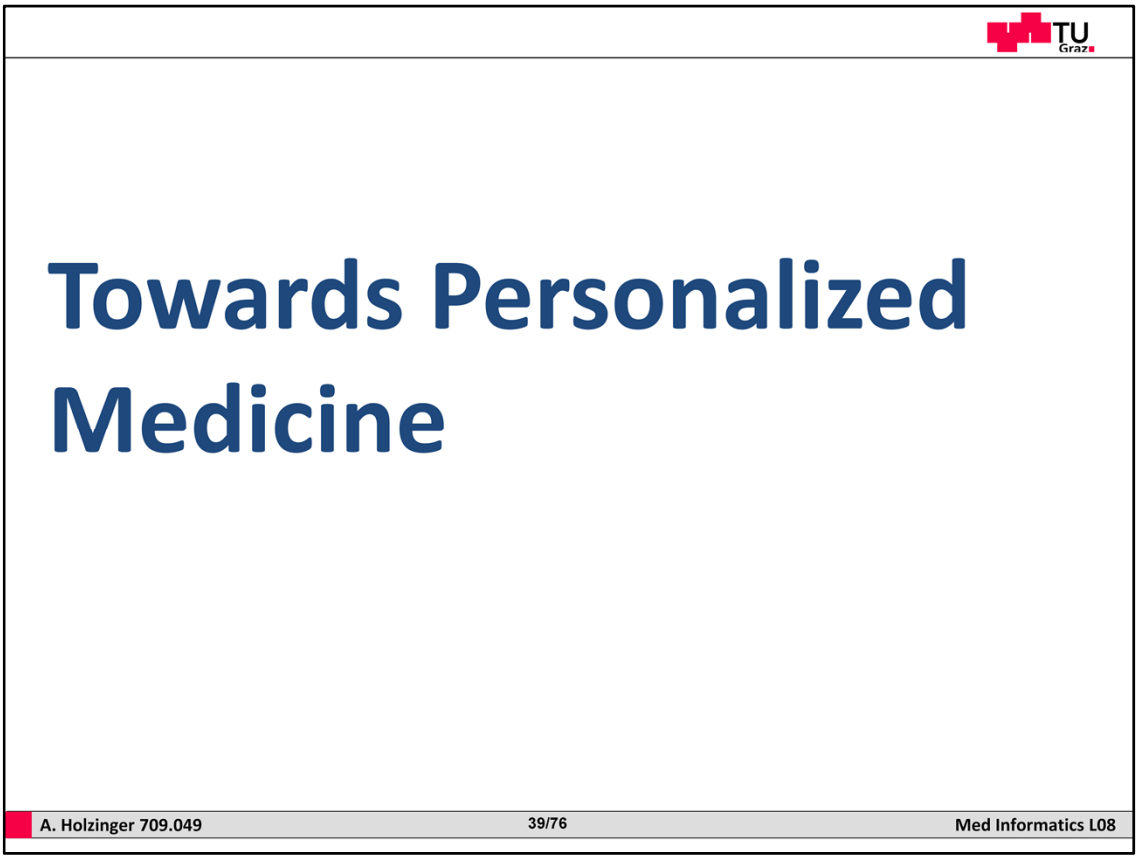
* Superficial erosions or aphthoid ulcerations seen especially with double contrast technique.

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

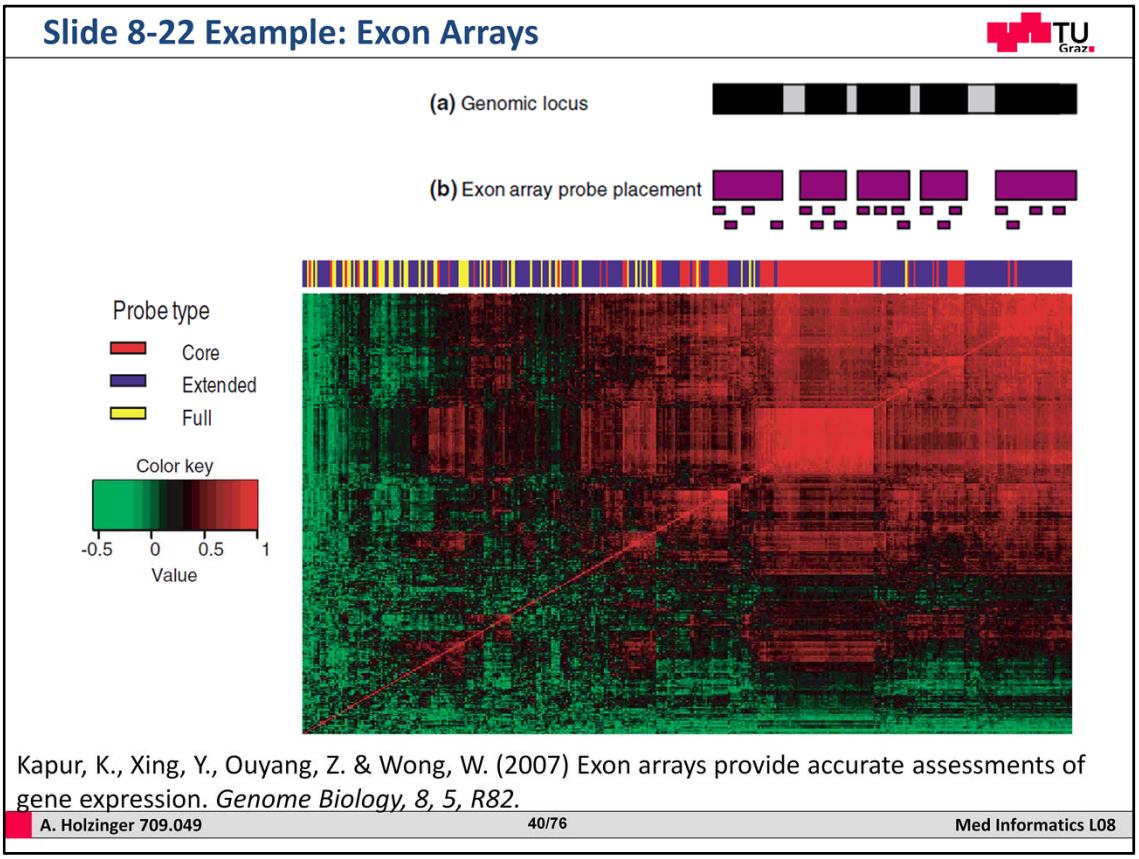
Reeder, M. M. & Felson, B. (2003) *Reeder and Felson's gamuts in radiology: comprehensive lists of roentgen differential diagnosis. New York, Springer Verlag.*

http://rfs.acr.org/gamuts/data/G-25.htm

A. Holzinger 709.049 38/76 Med Informatics L08

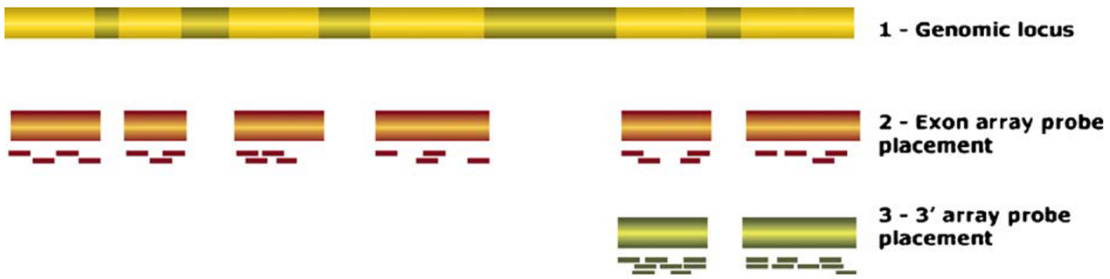


Yes, there are other possibilities of decision support, let us look into the bioinformatics domain.
An interesting part is in visualization relevant information – we will partiuclarly focus on visualization and visual analytics in the next lecture number 9. Here only some taster from the biology domain.



Progress in genomics has increased the data available for conducting expression analysis, used in transcriptomics. This can be very helpful for decision support. It deals with the study of mRNA and the extraction of information contained in the genes. This is reflected in the exon arrays requiring techniques to extract information. This slide shows the correlation of two probe intensities – among 11 tissues (breast, cerebellum, heart, kidney, liver, muscle, pancreas, prostate, spleen, testes, and thyroid): The black boxes represent exons; grey boxes represent introns; (b) Probe design of Exon arrays. 4 probes target each putative exon; below: The top color bar indicates the probe annotation type, core probes (red), extended probes (blue), full probes (yellow). The signal intensities of core probes tend to have high correlation (top right corner of the heatmap) (Kapur et al., 2007). Corchado et al. (2009) provided a tool based on a mixture of experts model which allows the analysis of the information contained in the exon arrays, from which automatic classifications for decision support in diagnoses of leukaemia patients can be made. The proposed model integrates several cooperative algorithms characterized for their efficiency for data processing, filtering, classification and knowledge extraction. This is a mixture of experts tool that integrates different cognitive and statistical approaches to deal with the analysis of exon arrays.

Slide 8-23 Computational leukemia cancer detection 1/6



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 30expression arrays. Probe target the 30end of mRNA sequence.

Corchado, J. M., De Paz, J. F., Rodriguez, S. & Bajo, J. (2009) Model of experts for decision support in the diagnosis of leukemia patients. *Artificial Intelligence in Medicine, 46, 3, 179-200.*

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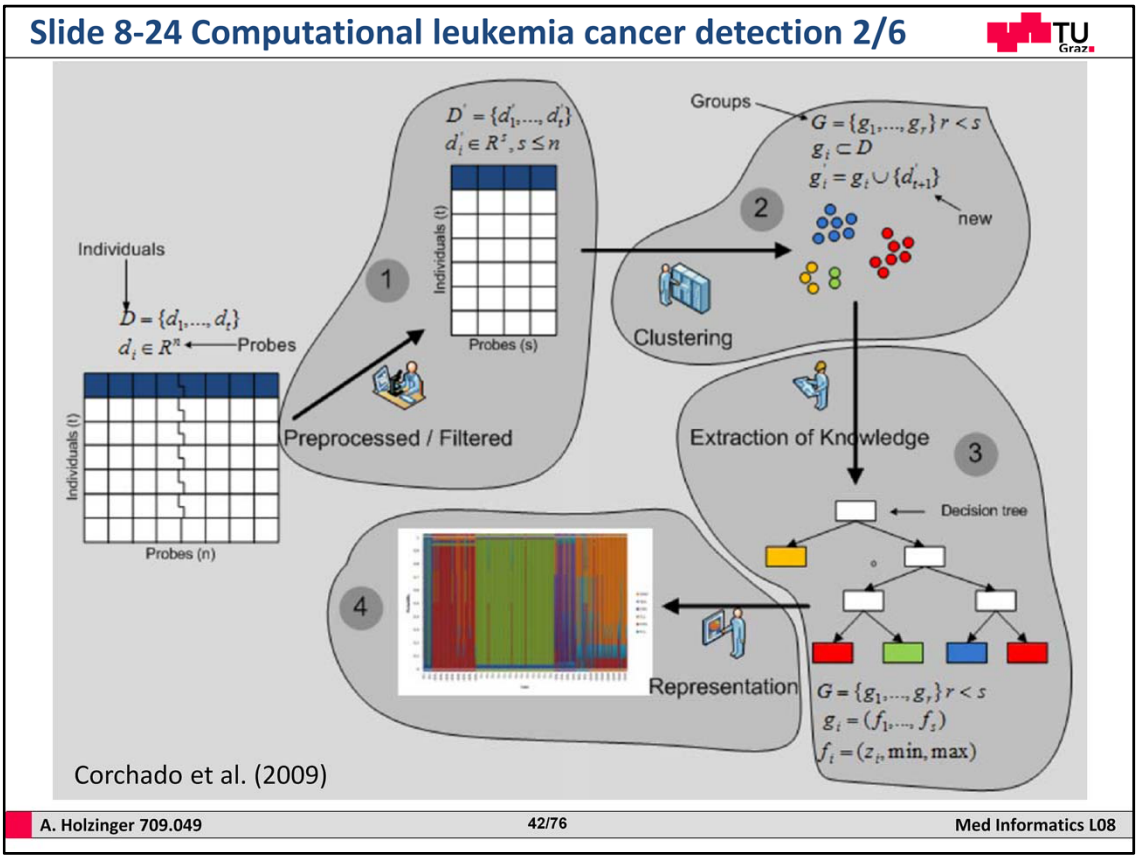
Exon arrays as seen in Slide 8-22 are chips which allow for a large number of data to be analyzed and classified for each patient (6 Million features per array). The high dimensionality of data makes it impossible to use standard techniques for expression array analysis (which contain approximately 50,000 probes).
High dimensionality of data from each exon array implies problems in handling and processing, thus making it necessary to improve each of the steps of expression array analysis in order to obtain an efficient method of classification. An expression analysis basically consists of three steps:
1. normalization and filtering;
2. clustering and classification; and
3. extraction of knowledge.
These steps can be automated and included within an expert system. Since the problem at hand deals with high dimensional arrays, it is important to have a very good pre-processing technique that can facilitate automatic decision-making with regards to selecting the most vitally important variables for the classification process. In light of these decisions, it will be possible to reduce the set of original data. After the organization of groups, patients can be classified and assigned into the group with which they share the most similarities. Finally, an extraction of knowledge system facilitates the interpretation of the results obtained after the pre-processing and classification steps, thus making it possible to learn from the information acquired from the results. The process of extracting knowledge shapes the knowledge obtained into a set of rules that can be used for improving new classifications.
In this slide we see such an exon array structure: (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 (Corchado, De Paz, Rodriguez & Bajo, 2009).



Hybrid System including three experts in sequential order – integrating completely different techniques (which experts may select appropriately) and considered as optimal for solving the problem of classifying leukaemia patients.

The model by Corchado et al (2009) incorporates the mixture of three experts in sequential form, having the advantage of integrating different techniques, considered to be optimal for using in the stages of the expression analysis for the problem of classifying leukaemia patients. Techniques that offer good results in each phase are combined and the model considers the characteristics of each expert in order to achieve an appropriate integration. The structure of the modules can be seen in Figure 8-15, the steps include:
1) pre-processing and filtering;
2) clustering;
3) extraction of knowledge and
4) information representation.
The different modules work independently, to facilitate the modification of any of the proposed experts, or to incorporate new techniques (including new experts). This affects the expert of a single module, while the others remain unchanged. This allows a generalization and making it possible to select the expert best suited to apply in each particular problem.
The initial problem description is composed of all the individuals D={d_1,...d_t } together with the n probes. The first expert pre-processes and filters the probes, reducing the set of probes to s elements but maintaining the t individuals. The second expert executes the clustering, creates r groups and assigns the new individual (t + 1) to one of these groups. The third expert explains how the individual elements have been classified into groups by means of a knowledge extraction technique, and by obtaining a graphical representation

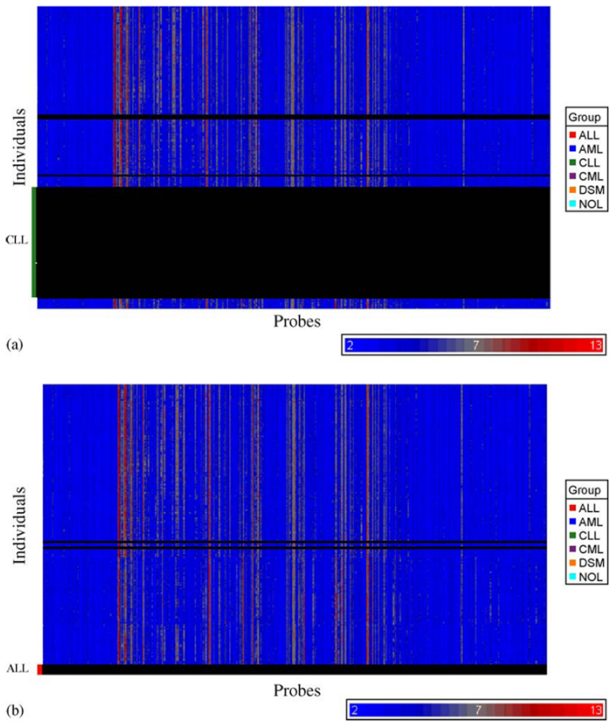
(a tree). The final module represents the probability of assigning individuals to each of the groups depending on the probes selected, taking into account the knowledge extracted (Corchado, De Paz, Rodriguez & Bajo, 2009).

Slide 8-25 Computational 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)



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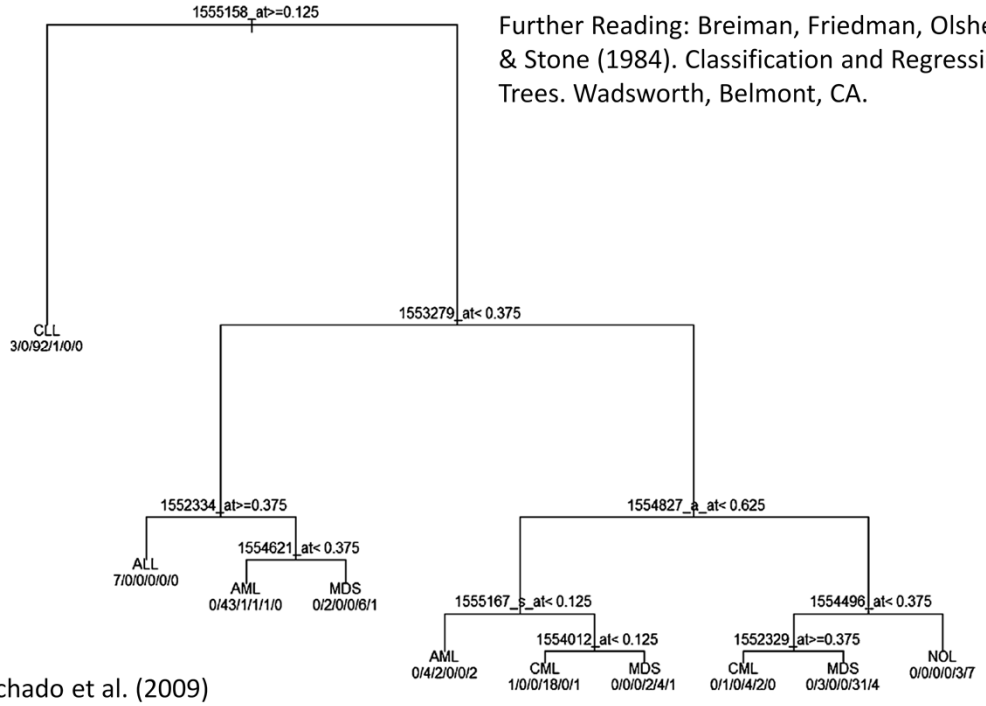
This slide shows the classification performed for patients from groups CLL and ALL. The X axis represents the probes used in the classification and the Y axis represents the individuals. Above we can see, represented in black, most of the people of the CLL group are together, coinciding with the previous classification given by the experts. Only a small portion of the individuals departed from the initial classification. Below we see the classification obtained for the ALL patients. It can be seen that, although the ranking is not bad, the proportion of individuals misclassified is higher. Groups that have fewer individuals have a high classification error.
Classification obtained for (a) ALL patients and (b) CLL patients. Each of the values obtained correspond to the fluorescence intensity for an individual. At the bottom of the image it is shown the fluorescence scale of values, the lowest level is 2 (blue) while the highest is 12 (red) (For interpretation of this images in color please refer to the original article (Corchado, De Paz, Rodriguez & Bajo, 2009)).

8-26 Computational leukemia cancer detection 4/6



Further Reading: Breiman, Friedman, Olshen, & Stone (1984). Classification and Regression Trees. Wadsworth, Belmont, CA.

Corchado et al. (2009)

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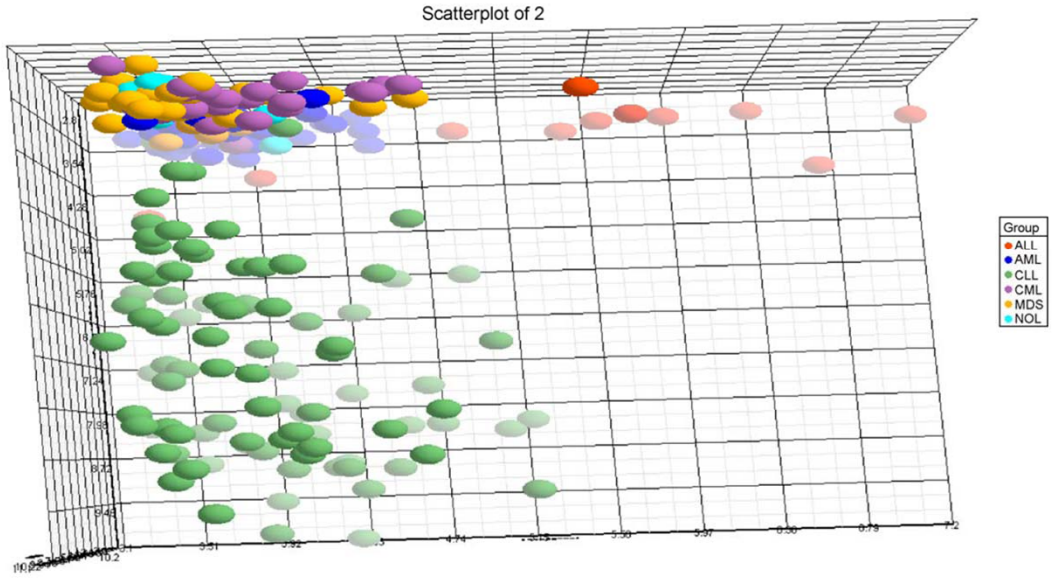
Following the decision tree shown in this slide, the patients were assigned to the expected groups. Only one of the patients was assigned to a different group by both methods. The healthy patients were eliminated in order to proceed with the classification.
The values of the leaf nodes represent the predicted group and the number of elements assigned to each of the groups following the order (ALL, AML, CLL, CML, NOL, MDS). The rest of the nodes represent the probe and the fuzzy value to compare the individual to classify. If the condition is true, then the branch on the left is selected, otherwise, the branch on the right is selected. The tree helps to obtain an explanation of the reason why an individual has been assigned to a group.

8-27 Computational leukemia cancer detection 5/6

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)

A. Holzinger 709.049 45/76 Med Informatics L08

The work of (Corchado, De Paz, Rodriguez & Bajo, 2009) demonstrates a model of experts that uses exon arrays to perform an automatic diagnosis of cancer patients. The system incorporates experts at each phase of the microarray analysis, a process that is capable of extracting knowledge from diagnoses that have already been performed, and that has been used to increase the efficiency of new diagnoses. The model combines

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

Slide 8-28 Computational leukemia cancer detection 6/6

- 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) 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) **works with high-dimensional data** from exon arrays

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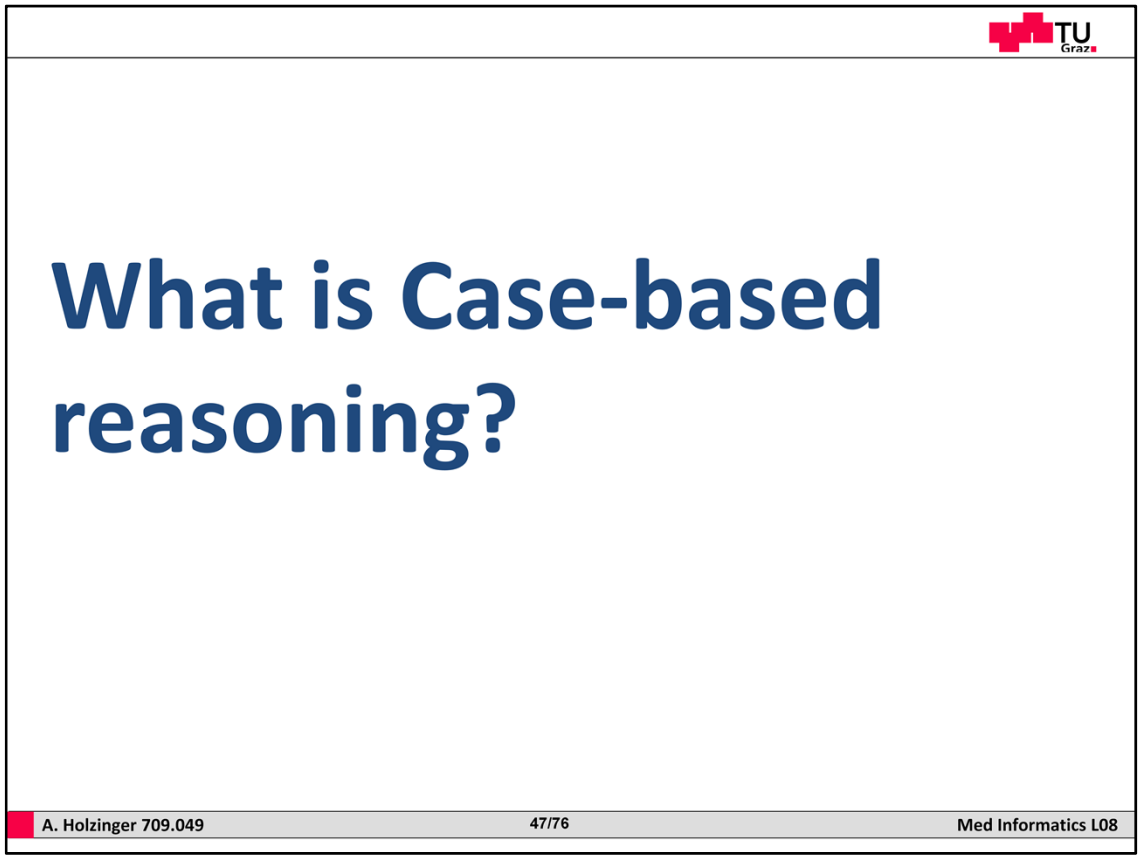
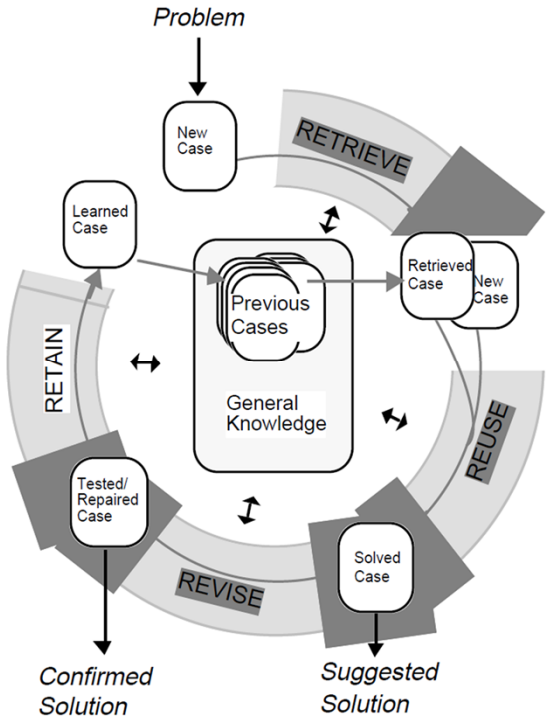
What could we learn by the model from Corchado?
The system of (Corchado, De Paz, Rodriguez & Bajo, 2009) works in a way that is similar to how human specialist teams work in a lab, is also capable of working with big data and making decisions automatically and reduces the time needed for making predictions. The main advantage of this model is the ability to work with exon array data 0; very few tools are capable of working with this type of data because of the high dimensionality. The proposed model resolves this problem by using a technique that detects the importance of the genes for the classification of the diseases by analyzing the available data. For the time being, three experts have been designed, one for each phase of the model.



Case-based reasoning is a problem solving paradigm, different from other AI approaches. Instead of relying solely on general knowledge of a problem domain, or making associations along generalized relationships between problem descriptors and conclusions, CBR is able to utilize the specific knowledge of previously experienced, concrete problem situations (cases).

Note: Always remember that Thinking-Reasoning-Decision-Action is intrinsically tied together. A good primer for clinical thinking is (Alfaro-LeFevre, 2013).

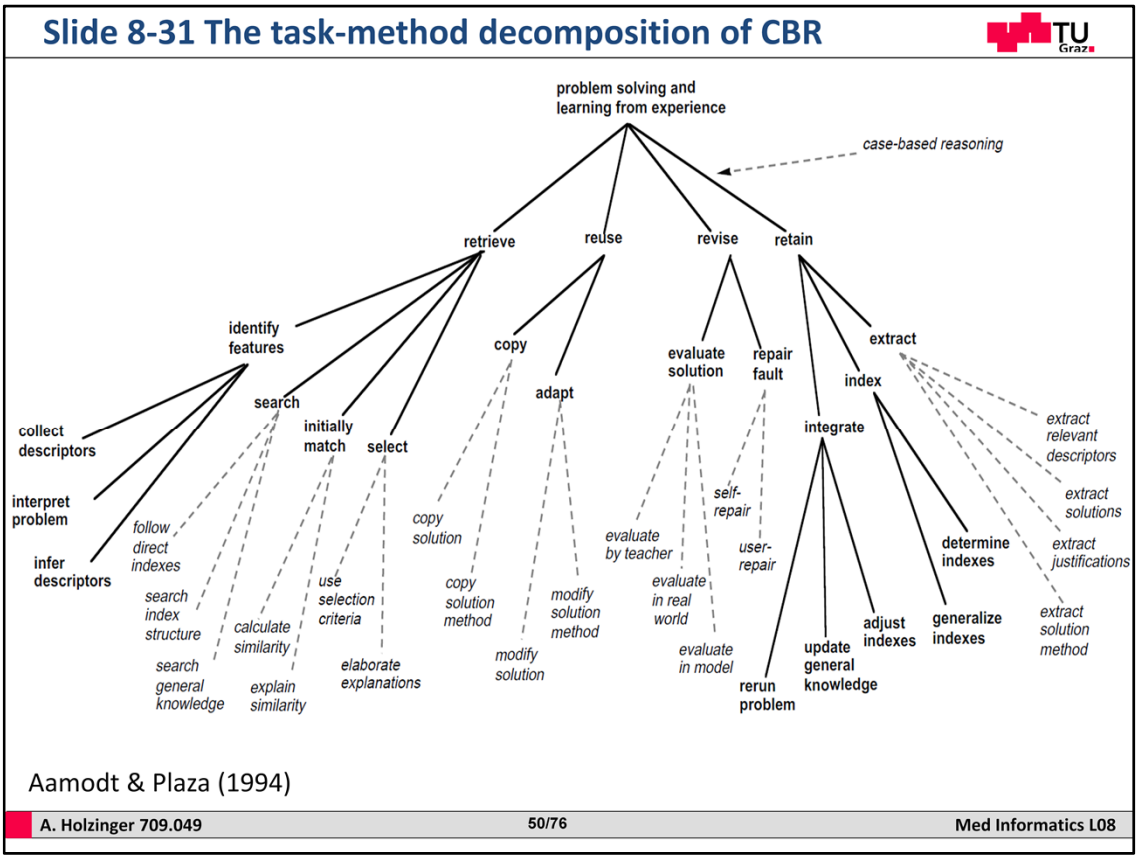
Slide 8-30 Case Based Reasoning (CBR) Basic principle



Aamodt, A. & Plaza, E. (1994) Case-based reasoning: Foundational issues, methodological variations, and system approaches. *AI Communications, 7, 1, 39-59.*

A. Holzinger 709.049 49/76 Med Informatics L08

Case-based reasoning is a problem solving paradigm, different from other AI approaches. Instead of relying solely on general knowledge of a problem domain, or making associations along generalized relationships between problem descriptors and conclusions, CBR is able to utilize the specific knowledge of previously experienced, concrete problem situations (cases). A new problem is solved by finding a similar past case, and reusing it in the new problem situation. A second important difference is that CBR also is an approach to incremental, sustained learning, since a new experience is retained each time a problem has been solved, making it immediately available for future problems. The description of a problem defines a new case. This new case is used to RETRIEVE a case from the collection of previous cases. The retrieved case is combined with the new case - through REUSE - into a solved case, i.e. a proposed solution to the initial problem. Through the REVISE process this solution is tested for success, e.g. by being applied to the real world environment or evaluated by a teacher, and repaired if failed. During RETAIN, useful experience is retained for future reuse, and the case base is updated by a new learned case, or by modification of some existing cases (Aamodt & Plaza, 1994).



In this slide we see the task-method structure: Tasks have node names in bold letters, while methods are written in italics. The links between task nodes (plain lines) are task decompositions, i.e. part-of relations, where the direction of the relationship is downwards. The top-level task is problem solving and learning from experience and the method to accomplish the task is case-based reasoning (indicated in a special way by a stippled arrow). This splits the top-level task into the four major CBR tasks corresponding to the four processes: retrieve, reuse, revise, and retain. All four tasks are necessary in order to perform the top-level task. The relation between tasks and methods (stippled lines) identify alternative methods applicable for solving a task. A method specifies the algorithm that identifies and controls the execution of subtasks, and accesses and utilizes the knowledge and information needed to do this (Aamodt & Plaza, 1994).

Slide 8-32 CBR Example: Radiotherapy Planning 1/6

Source: http://www.teachingmedicalphysics.org.uk

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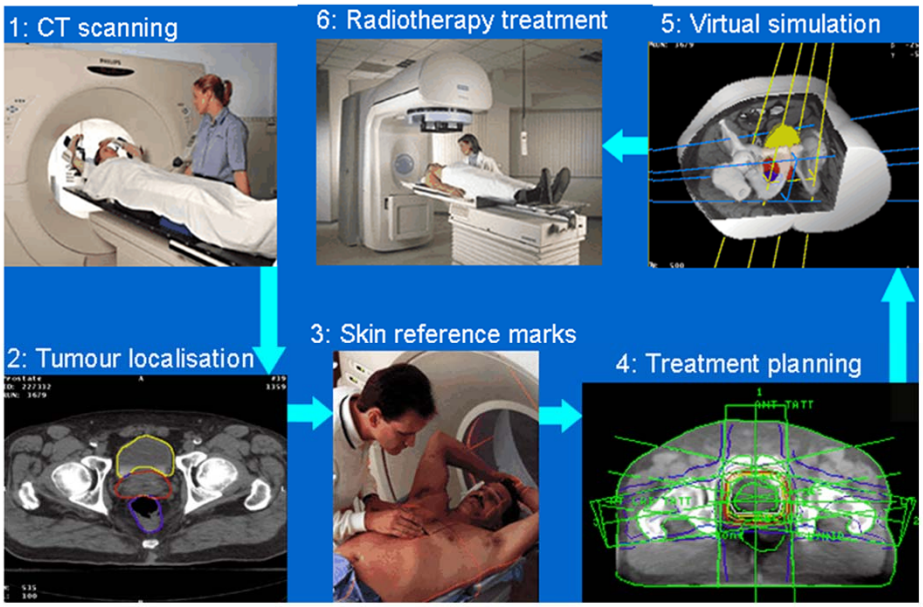
Example: Radiotherapy planning for cancer treatment is a computationally complex problem. An example from (Petrovic, Mishra & Sundar, 2011) shall demonstrate it: Prostate cancer is generally treated in two phases. In phase I, both the prostate and the surrounding area, where the cancer has spread to, will be irradiated, while, in phase II only the prostate will be irradiated. The total dose prescribed by the oncologist is usually in the range of 70–76 Gy, while the dose ranges in phases I and II of the treatment are 46–64 Gy and 16–24 Gy, respectively. The dose is delivered in fractions, each fraction being usually 2 Gy.

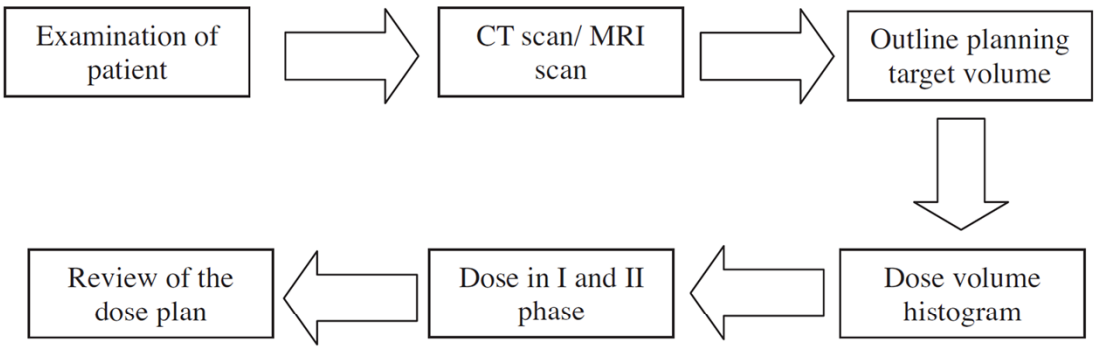
Slide 8-33 CBR Example: Radiotherapy Planning 2/6



Source: Imaging Performance Assessment of CT Scanners Group, http://www.impactscan.org

In this slide we see the workflow of radiotherapy: 1. CT scanning, 2. Tumor localization, 3. Skin reference marks, 4. Treatment planning, 5. Virtual simulation, 6. Radiotherapy treatment;

Slide 8-34 CBR Example: Radiotherapy Planning 3/6



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 %)

Petrovic, S., Mishra, N. & Sundar, S. (2011) A novel case based reasoning approach to radiotherapy planning. *Expert Systems With Applications, 38, 9, 10759-10769.*

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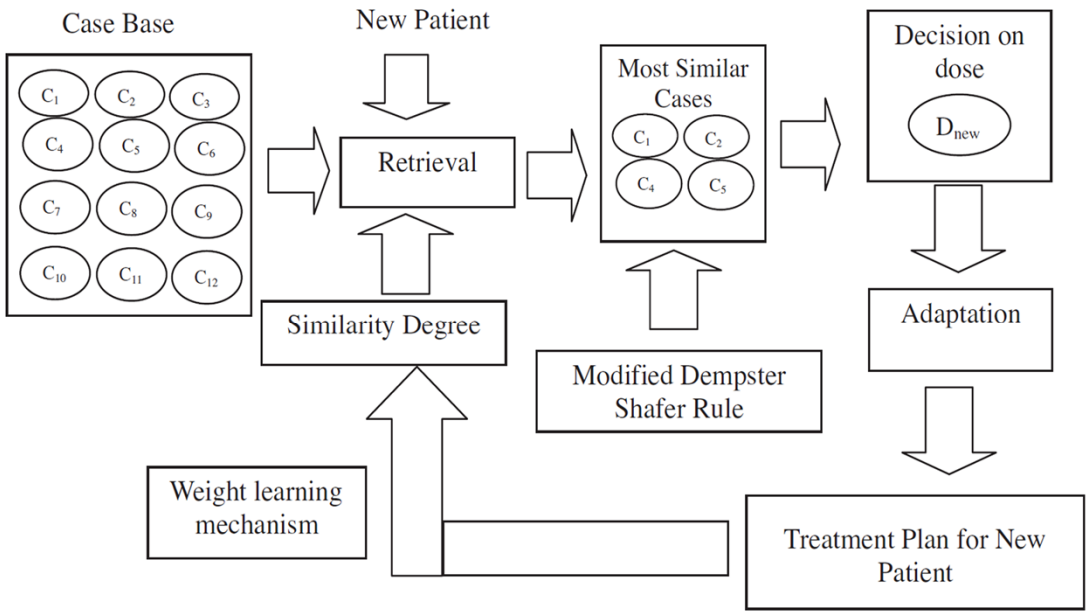
The patient is first examined and then CT scans or MRI are carried out. Thereafter, the generated scans are passed onto the planning department. In the planning department, first, the tumour volume and the organs at risk are outlined by the medical physicist so that the region that contains the tumour can be distinguished from other parts that are likely to contain microscopic (tiny) tumour cells. Afterwards, the medical physicist in consultation with the oncologist defines the planning parameters including the number of beams to be used in the radiation, the angle between beams, the number of wedges , the wedge angles and generates a Distribution Volume Histogram (DVH) diagram for both phases I and II of the treatment. DVH presents the simulated radiation distribution within a volume of interest which would result from a proposed radiation treatment plan. The next task is to decide the dose in phases I and II of the treatment so that the tumour cells can be killed without impairing the remaining body, particularly the organs lying close to the tumour cells, i.e. rectum and bladder. The organs lying close by should preferably not be impaired at all by the treatment. However, the oncologist usually looks for a compromise of distributing the inevitable dose among the organs. Rectum is a more sensitive organ compared to the bladder and is the primary concern of oncologists while deciding the dose plan. There is a maximum dose limit for different volume percentages of the rectum, and it has to be respected by oncologists when prescribing a dose plan. In certain cases, this condition may be sacrificed to some extent so that an adequate dose can be imparted to the cancer cells. Oncologists generally use three groups of parameters to generate a good plan for each patient. The first group of parameters is related to the stage of cancer. It includes Clinical Stage (a labelling system), Gleason Score evaluates the grade of prostate cancer and is a integer between 1 to 10), and Prostate Specific Antigen (PSA) value between 1 to 40. The second group of parameters is related to the potential risk to the rectum (degree of radiation received by different volume percentages of the rectum. It includes the DVH of the rectum for Phases I and II at 66%, 50%, 25%, and 10% of the rectum volume. Example: the DVH states that 66% of the rectum will receive 50% of radiation. It means that if the dose prescribed by the oncologist in the phase I of the treatment is 60 Gy, then the amount of radiation received by 66% of the rectum is 30 Gy. The final PSA value is a parameter related to the success rate of the patient after the treatment.

Slide 8-35 CBR System Architecture 4/6



Petrovic, S., Mishra, N. & Sundar, S. (2011) A novel case based reasoning approach to radiotherapy planning. *Expert Systems With Applications, 38, 9, 10759-10769.*

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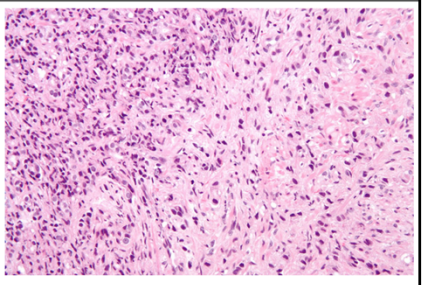
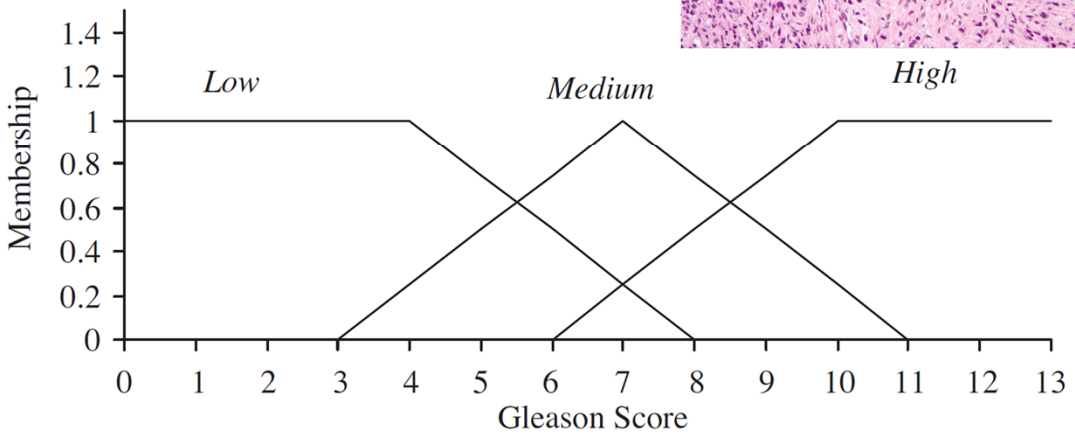
In the system developed by (Petrovic, Mishra & Sundar, 2011), the cases which are similar to the new case are retrieved using a fuzzy similarity measure. A modified Dempster–Shafer theory is applied to fuse the information from the retrieved cases and generate a solution as shown in this slide.
1) The clinical stage of the cancer is of ordinal type and can be divided in seven different categories T1a, T1b, T1c, T2a, T2b, T3a, T3b,
2) the value of the Gleason Score is an integer number from [1, 10] interval,
3) PSA is a real numbers from [1, 40]; and
4) DVH is a real number between [0,1].
In order to use features of different data type, measurement units and scale together in the similarity measure we need to normalise them. However, it would not be easy to define a preferably linear mapping in the [0, 1] interval. Instead, we define fuzzy sets low, medium and high for each feature. They are normalised fuzzy sets whose membership functions take value from [0, 1] interval. In addition, fuzzy sets enable expression of preference of the oncologist. An example of membership functions of fuzzy sets low, medium and high Gleason score is given in Figure Slide 8-36.

Slide 8-36 Membership funct. of fuzzy sets Gleason score 5/6

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





Petrovic, S., Mishra, N. & Sundar, S. (2011) A novel case based reasoning approach to radiotherapy planning. *Expert Systems With Applications, 38, 9, 10759-10769.*

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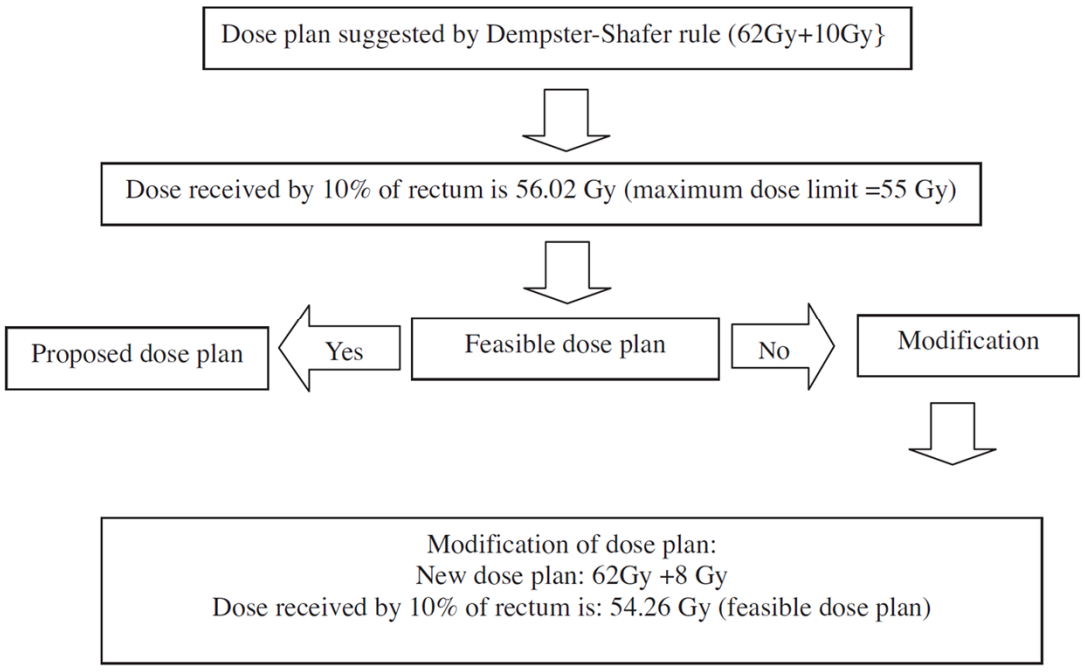
G-Score for the prognosis of men with prostate cancer using samples from a prostate biopsy. Together with other parameters, it is incorporated into a strategy of prostate cancer staging which predicts prognosis and helps guide therapy. A Gleason score is given to prostate cancer based upon its microscopic appearance, Cancers with a higher Gleason score are more aggressive and have a worse prognosis (in the image above GS=5 at the left and 4 at the right).
The parameters of these membership functions are set in collaboration with the oncologist. Each attribute l (Gleason score (l = 1), PSA (l = 2)) of case cp is represented by a triplet (vpl1, vpl2, vpl3), where vplm, m = 1, 2, 3 are membership degrees of attribute l in the corresponding fuzzy sets low (m = 1), medium (m = 2) and high (m = 3).

Slide 8-37 Case Based Reasoning 6/6

Petrovic et al. (2011)



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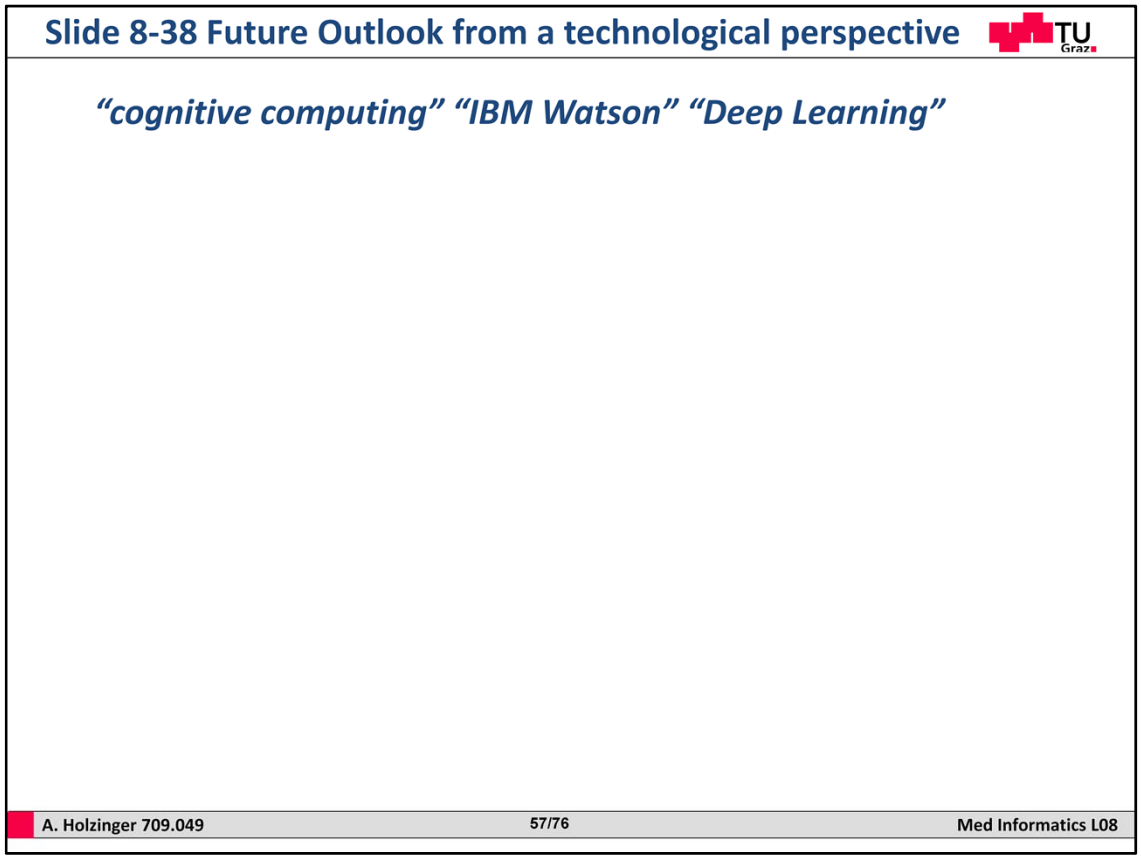
This final slide demonstrates the adaptation mechanism. In this example, the final outcome of the Dempster–Shafer theory is a dose plan having 62 Gy and 10 Gy of radiation in phases I and II of treatment, respectively. This is not a feasible dose plan because the dose received by 10% of the rectum is 56.2 Gy which is larger than the prescribed maximum dose limit (55 Gy). Hence, in order to generate a feasible dose plan, the repair mechanism is performed. The dose corresponding to the phase II of the treatment is decreased by 2 Gy, which leads to the new dose plan 62 Gy and 8 Gy, which is a feasible dose plan.

The Dempster–Shafer theory (DST) is a mathematical theory of evidence and allows the combination of evidence from different sources resulting in a degree of belief (represented by a belief function) that takes into account all the available evidence.

Zadeh, L. A. 1986. A simple view of the Dempster-Shafer theory of evidence and its implication for the rule of combination. AI magazine, 7, (2), 85.



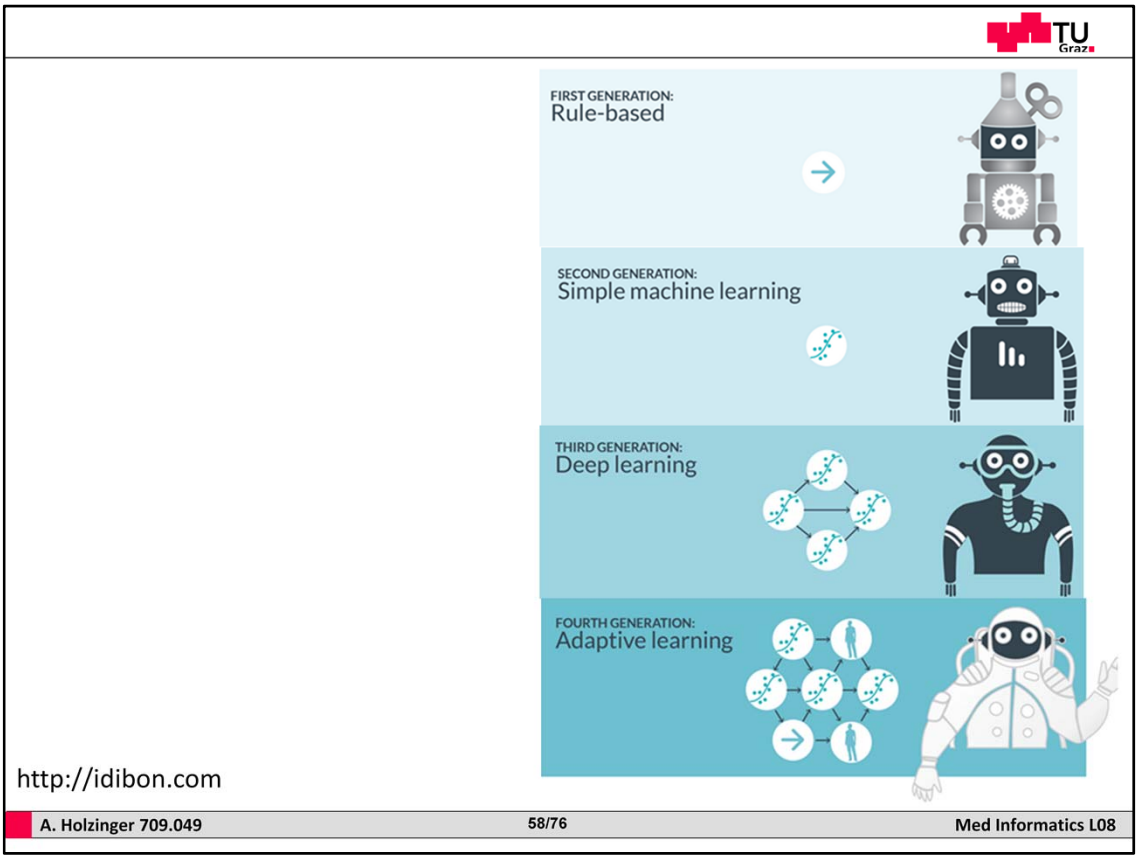
http://www-03.ibm.com/press/us/en/presskit/27297.wss

After proving its prowess on "Jeopardy" two years ago, the Watson "cognitive" computing system is embarking on two new projects designed to help doctors make more accurate decisions and tap into data from electronic medical records (EMRs).

Known as "WatsonPaths" and "Watson EMR Assistant," the two projects announced Tuesday are a collaboration between Big Blue and Case Western Reserve University's Cleveland Clinic Lerner College of Medicine.

http://news.cnet.com/8301-11386_3-57607545-76/ibm-on-watson-our-son-the-doctors-helper/

http://www.research.ibm.com/cognitive-computing/watson/watsonpaths.shtml#fbid=jBn1NNDhmN2



http://idibon.com/wp-content/uploads/2015/09/robots.png

1st generation: Rules

The first generation of machine intelligence meant that people manually created rules. For example, in text analytics someone might create a rule that the word "Ford" followed by "Focus" meant that "Ford" referred to a car, and they would create a separate rule that "Ford" preceded by "Harrison" meant that "Ford" referred to a person.

The rule-based approach is very time consuming and not very accurate. Even after an analyst has exhausted all the words and phrases they can think of, there are always other contexts and new innovations that aren't captured. For one of our clients, their experts analysts were only able to capture 11% of the documents they wanted to analyze using rules: this clearly is too limited.
2nd generation: Simple machine learning

The dominant form of machine intelligence today is simple machine learning. Simple machine learning uses statistical methods to make decisions about data processing. For example, a sentence might have the word "Ford" labeled as a car, and the machine learning algorithm will learn by itself that the following word "Focus" is evidence that "Ford" is a car in this context.

Simple machine learning can be fast, provided that you already have labeled

examples for ‘supervised learning’. It also tends to be more accurate, because statistics are usually better than human intuition in deciding which features (like words and phrases) matter. The major drawback for supervised machine learning is that you need the labeled examples: if you have too few labels or the labels aren’t representative of the entire data set, then the accuracy is low or limited to a specific domain.
3rd generation: Deep learning

There has been a recent rise in the use of machine learning that learns more sophisticated relationships between features, known as deep learning. For example, if you had the sentence “We Will Let Harrison Ford Focus on Star Wars”, there is conflicting evidence between “Harrison” and “Focus” about whether “Ford” is a person or a car.

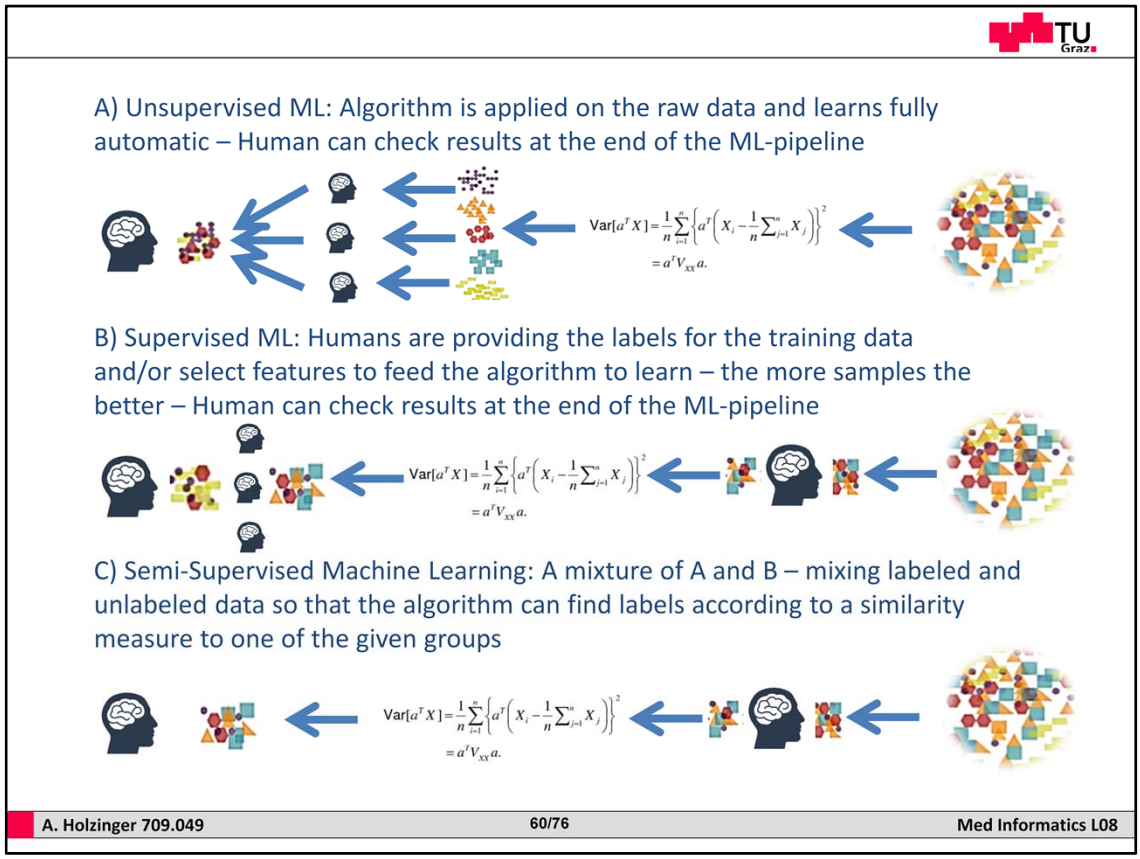
Deep learning can automatically learn how to use combinations of features when making a decision. For simple machine learning, a human has to tell the algorithm which combination of features to consider. Deep learning often cuts down on the amount of human time needed and typically gets up to 5% more accurate results than simple machine learning for text analytics–although only when applied to data from the same sources as it learned from.
4th generation: Adaptive learning

Adaptive learning brings human analysts into the process at every step. This is in contrast to rule-based, simple machine learning and deep learning approaches, where the humans only create rules and label data at the start of the process. For example, if you had the sentence “We Will Help Tom Ford Escape from New York”, and your system hadn’t seen any examples of “Tom Ford” or “Ford Escape”, you will need human input to build the knowledge.

Adaptive learning systems require the least human effort because they only require human input when it matters most and continually expand their knowledge when new information is encountered. As we show here, they are also the most accurate. They combine the three other types of machine intelligence, adding new types of ‘unsupervised machine learning’ and methods for optimizing the input from multiple, possibly disagreeing, humans.

Slide 8-39 Future Outlook

- Sometimes we do not have “big data”, where aML-algorithms benefit.
- Sometimes we have
  - Small data
  - Rare Events
  - NP-hard problems (e.g. k-Anonymization, Protein-Folding, Graph Coloring, Subspace Clustering, …
- Then we still need the “human-in-the-loop”



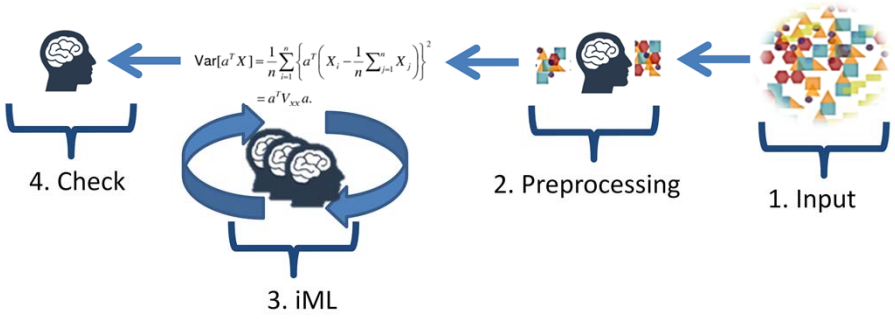
-) Unsupervised: All clear..

-) Supervised machine learning: The training- and test-data split can actually be done fully automatic. I guess what you mean is that humans are providing the LABELS for the training / test data and / or SELECT FEATURES (the latter is also true for unsupervised learning as long as you are not trying to do unsupervised subspace clustering e.g.)

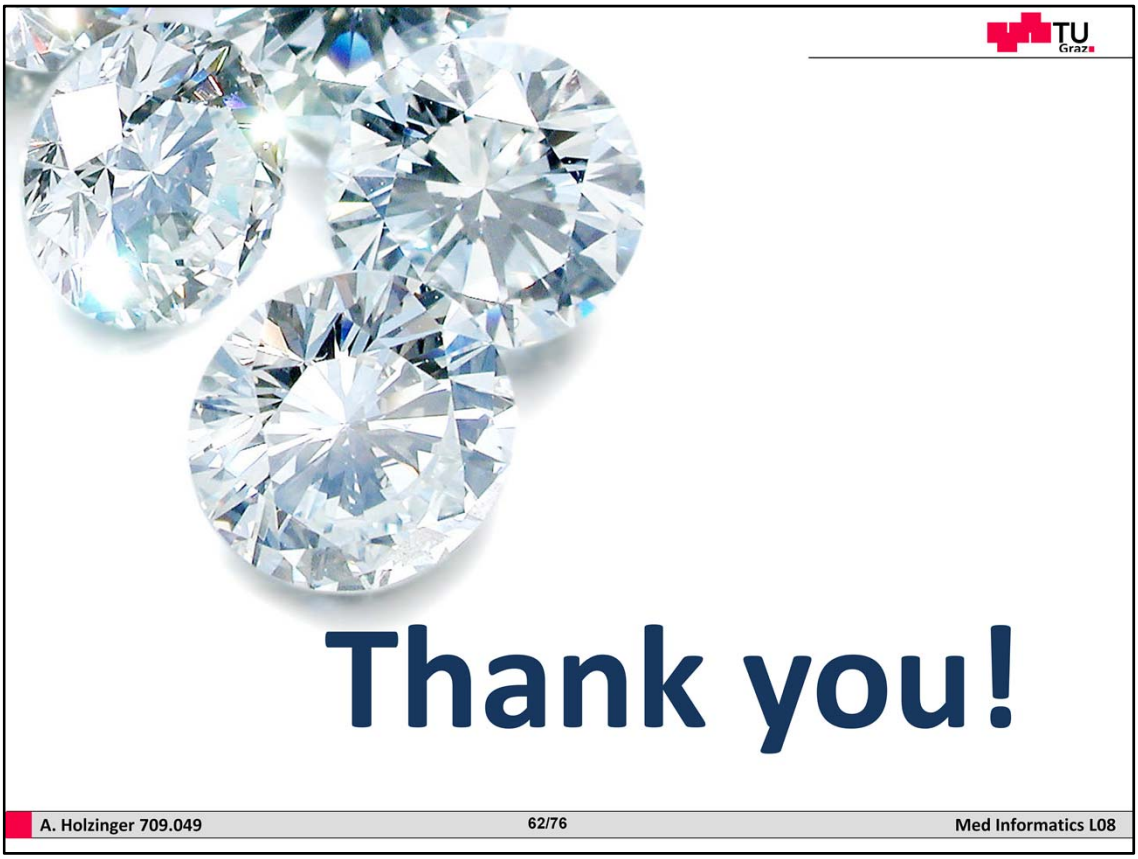
-) Semi-supervised: Isn't this just a method for mixing labeled and unlabeled data so that the algorithm tries to find labels according to a similarity measure to one of the given groups?

-) iML: I think the REALLY important point with iML is that humans are not (only) involved in preprocessing, by selecting data or features, but actually DURING the learning phase which is not the case in the 3 methods described above. See the ppt, slide 2 ;)

D) Interactive Machine Learning: Human is seen as an agent involved in the actual learning phase, step-by-step influencing measures like distance or cost functions …



-) iML: I think the REALLY important point with iML is that humans are not (only) involved in preprocessing, by selecting data or features, but actually DURING the learning phase which is not the case in the 3 methods described above. See the ppt, slide 2 ;)



My DEDICATION is to make data valuable … 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://gaia.fdi.ucm.es/projects/jcolibri
- http://www-formal.stanford.edu/jmc/whatisai/whatisai.html
- http://aaai.org/AITopics
- http://www.stottlerhenke.com/ai_general/history.htm
- http://rfs.acr.org/gamuts (Gamuts in radiology - DSS for radiological imaging)
- http://www.scribd.com/doc/16093558/Gamuts-in-radiology (Reeder & Felsons Original Book on Gamuts)
- http://www.isradiology.org/gamuts/Gamuts.htm (Web-based Gamuts in Radiology)

http://psychology.wikia.com/wiki/Information_retrieval

3 July 1959, Volume 130, Number 3366 SCIENCE

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

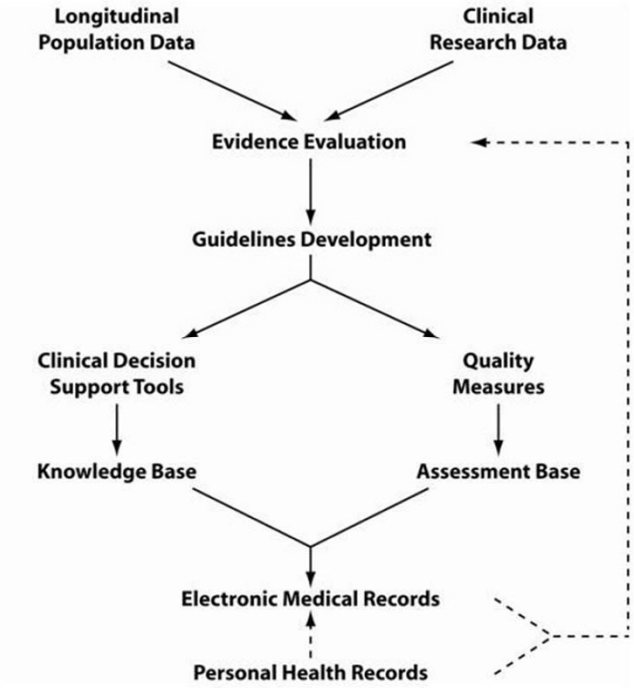
fitted into a definite disease category, or that it may be one of several possible diseases, or else that its exact nature cannot be determined." This, obviously, is a greatly simplified explanation of the process of diagnosis, for the physician might also comment that after seeing a

ance 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



Downing, G., Boyle, S., Brinner, K. & Osheroff, J. (2009) Information management to enable personalized medicine: stakeholder roles in building clinical decision support. *BMC Medical Informatics and Decision Making, 9, 1, 1-11.*

A. Holzinger 709.049 66/76 Med Informatics L08

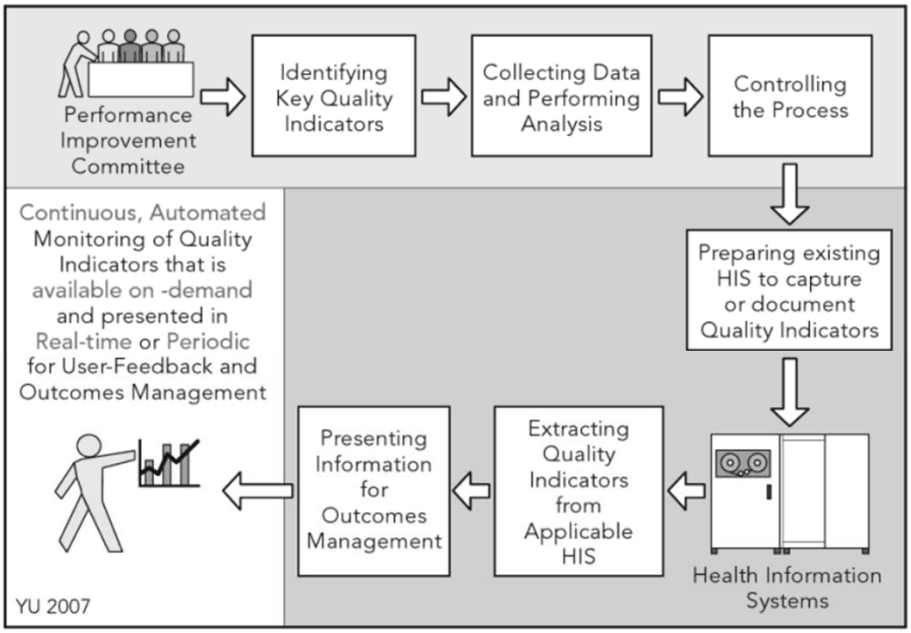
The role of CDS tools and electronic and personal health records in the development of clinical practice guidelines and quality measures. (Solid lines indicate currently available information flow patterns, dotted line represents potential pathways for future data flow).

Stakeholders' Roles in Supporting Individualized Approaches to Health Care

The pathway to use CDS in support of personalized medicine requires many integrated components to be developed in parallel with the emerging EHR foundation in health care. Developing a health care system that optimizes personalized prevention and treatment requires engagement from many diverse stakeholders. Organizing the work that needs to be done by stakeholder organizations is a helpful framework to consider the actors and actions needed for the complete picture of personalized medicine CDS systems to emerge. These include the consumer/patient, molecular diagnostic (laboratory test or device) developer, providers, payor, CDS developers, and oversight and regulatory bodies, among many others.

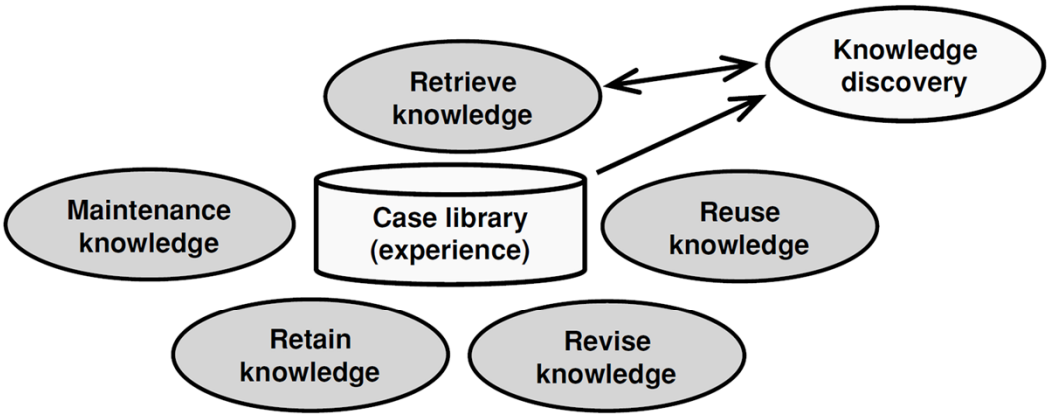
An overview of the continuum of information flow from evidence development through clinical application using EHR technology is shown in Figure 1. Personalized medical practices will increasingly be based on scientific evidence gained from population-based longitudinal studies and clinical research studies such as randomized clinical trials. These inputs provide the evidence that certain medical technologies are recommended or shown to have benefit under various clinical conditions. This becomes the basis for algorithms or treatment recommendations that are integrated into practice guidelines for many medical conditions to be used in patient care encounters in two major applications. First, key program inputs are created for CDS tools and integrated into electronic knowledge base that is used to support the rules used in making rec

Appendix: Quality Improvement and Health Records



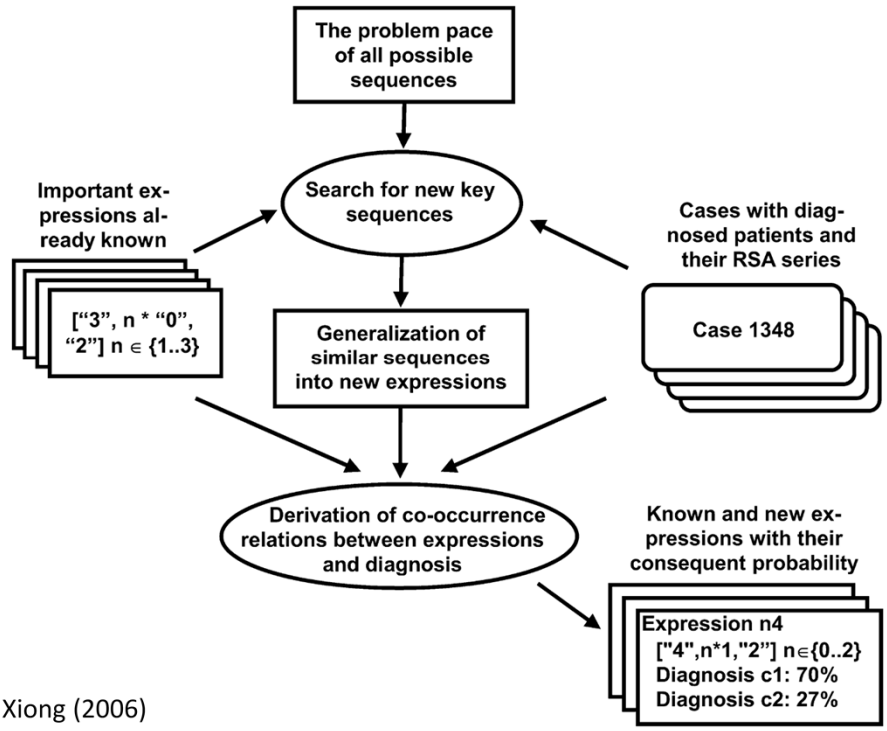
Yu, F.B., Allison, J.J., Houston T.K. (2008) Quality Improvement & the Electronic Health Record: Concepts and Methods. In: Carter, J. H. (2008) *Electronic health records: a guide for clinicians & administrators. ACP Press.*

Appendix: Example for a Knowledge discovery module



Funk, P. & Xiong, N. (2006) Case-based reasoning and knowledge discovery in medical applications with time series. *Computational Intelligence, 22, 3-4, 238-253.*

Appendix: Discovery of new expressions & co-occurrences



Funk & Xiong (2006)

Appendix: Evaluation of a Sequence

Given a sequence *s* there may be a set of probable consequent classes *{C1, C2, . . . ,Ck}*

The strength of the co-occurrence between sequence *s* and class *Ci* (*i* = 1, . . . , *k*) can be measured by the probability, *p*(*Ci* | *s*), of *Ci* conditioned upon *s*

$$PD(s) = \max_{i=1\cdots k} P(C_i \mid s) \qquad P(C_i \mid s) = \frac{P(s \mid C_i)P(C_i)}{P(s)}$$

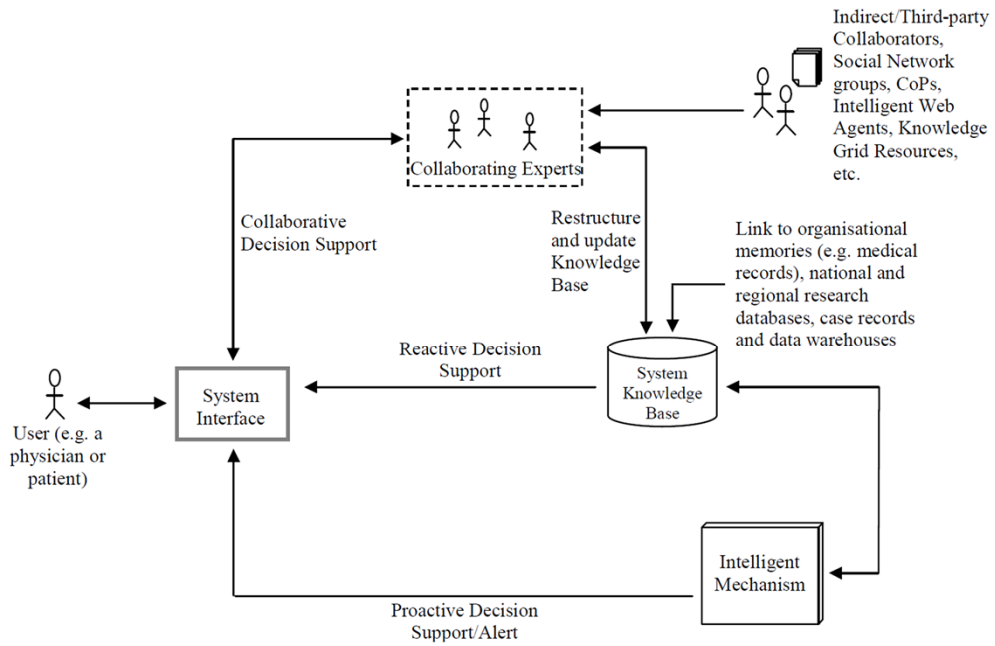
$$P(s) = P(s \mid C_i)P(C_i) + P(s \mid \bar{C}_i)P(\bar{C}_i)$$

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

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

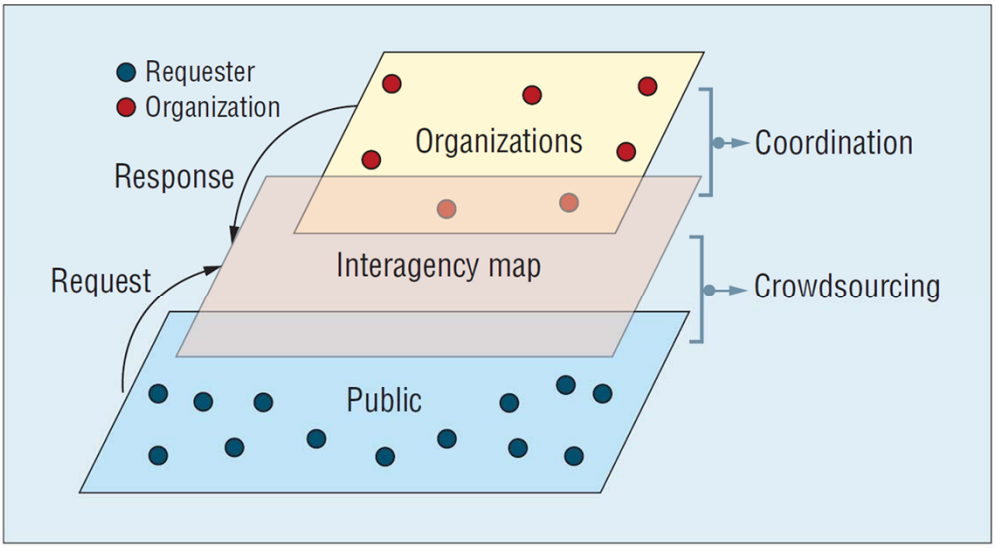
Funk & Xiong (2006)

Appendix: Example for Interactive Group Decision Support



Anya, O., Tawfik, H. & Nagar, A. (2011) Cross-boundary knowledge-based decision support in e-health. *International Conference on Innovations in Information Technology (IIT). 150-155.*

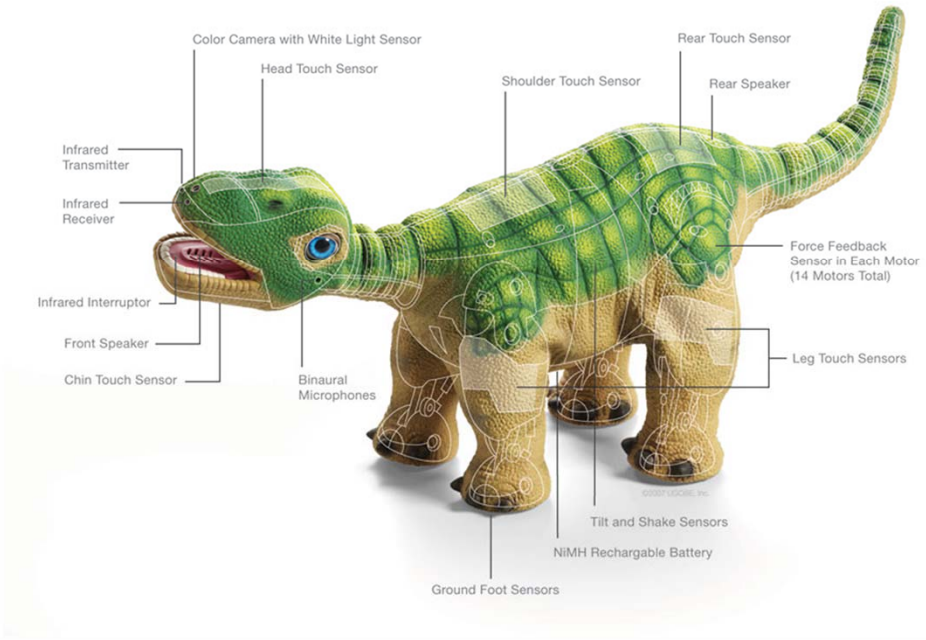
Appendix: Crowdsourcing - Example Disaster Management



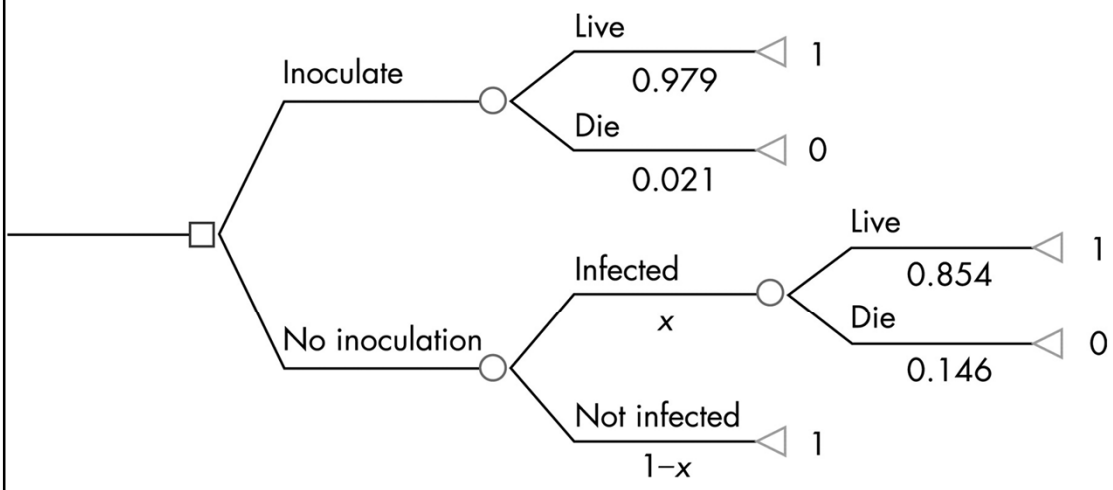
Gao, H., Barbier, G. & Goolsby, R. (2011) Harnessing the Crowdsourcing Power of Social Media for Disaster Relief. *Intelligent Systems, IEEE, 26, 3, 10-14.*

http://www.youtube.com/watch?v=IKahVCzKR8Y

Example: Pleo robot - Intelligent behaviour?

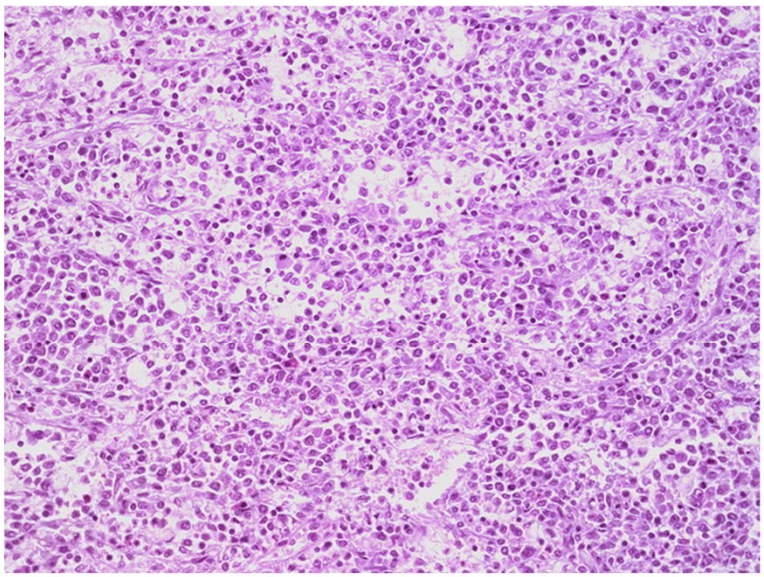


Clinical Decision Tree (CDT) is still state-of-the-art



Ferrando, A., Pagano, E., Scaglione, L., Petrinco, M., Gregori, D. & Ciccone, G. (2009) A decision-tree model to estimate the impact on cost-effectiveness of a venous thromboembolism prophylaxis guideline. *Quality and Safety in Health Care, 18, 4, 309-313.*

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