



Andreas Holzinger
VO 709.049 Medical Informatics
18.11.2015 11:15-12:45

## Lecture 06 Multimedia Data Mining and Knowledge Discovery

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http://hci-kdd.org/biomedical-informatics-big-data



#### Schedule of the course



- 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 6<sup>th</sup> Lecture**



- Artificial neural networks
- Bayesian network
- Curse of dimensionality
- Deep Learning
- Data Mining
- Knowledge Discovery in medical data
- Medical text mining
- Model based clinical decision making
- Supervised learning
- Support Vector Machines (SVM)
- Unsupervised learning

#### Advance Organizer (1/2)



- Artificial neural network (ANN) = a computational adaptive model (inspired by biological neural networks), consisting of interconnected groups of artificial neurons; processes information using a connectionist approach.
- Association rule learning = a set of techniques for discovering interesting relationships, i.e., "association rules," among variables in large databases used for data mining;
- Classification = a set of techniques to identify the categories in which new data points belong, based on a training set containing data points that have already been categorized; these techniques are often described as supervised learning because of the existence of a training set; they stand in contrast to cluster analysis, a type of unsupervised learning; used e.g. for data mining;
- Cluster analysis = statistical method for classifying objects that splits a diverse group into smaller groups of similar objects, whose characteristics of similarity are not known in advance; a type of unsupervised learning because training data are not used in contrast to classification; used for data mining.
- **Data mining** = a set of techniques to extract patterns from large data by combining methods from statistics and machine learning with database management (e.g. association rule learning, cluster analysis, classification, regression, etc.);
- Knowledge Discovery (KD) = process of identifying valid, novel, useful and understandable patterns out of large volumes of data

#### Advance Organizer (2/2)



- Deep Learning = class of machine learning algorithms using layers of non-linear processing units for feature extraction (remember: features are key for learning and understanding) - learning representations from data;
- Knowledge Extraction = is the creation of knowledge from structured (relational databases, XML) and unstructured (text, documents, images) sources;
- Multimedia = several data of different modalities are processed at the same time, i.e. encompassing audio data (sound, speech), image data (b/w and colour images), video data (time-aligned sequences of images), electronic ink (sequences of time aligned 2D and 3D coordinates of a stylus, pen, data gloves etc.)
- Principal Component Analysis (PCA) = statistical technique for finding patterns in high-dimensional data;
- **Supervised learning** = inferring a function from supervised training data on the basis of training data which consist of a set of training examples, the input objects (typically vectors) and a desired output value (also called the supervisory signal).
- Supervised learning algorithm = analyzes the training data and produces an inferred function, called a classifier (if the output is discrete) or a regression function (if the output is continuous); the algorithm generalizes from the training data to unseen situations.
- Support vector machine (SVM) = concept for a set of related supervised learning methods to analyze data and recognize patterns, used for classification and regression analysis.
- Unsupervised learning = establishes clusters in data, where the class labels of training data is unknown.



- ANN artificial neural network
- ANN = Artificial Neural Network
- ANOVA = Analysis of Variance
- AUC area under the curve
- CDT = Clinical Decision Tree
- DM = Data Mining
- KDD = Knowledge Discovery from Data(bases)
- MDM = Multimedia Data Mining
- MELD model for end-stage liver disease
- MM = Multimedia
- NLP = Natural Language Processing
- ROC receiver-operating characteristic
- SVM = Support Vector Machine

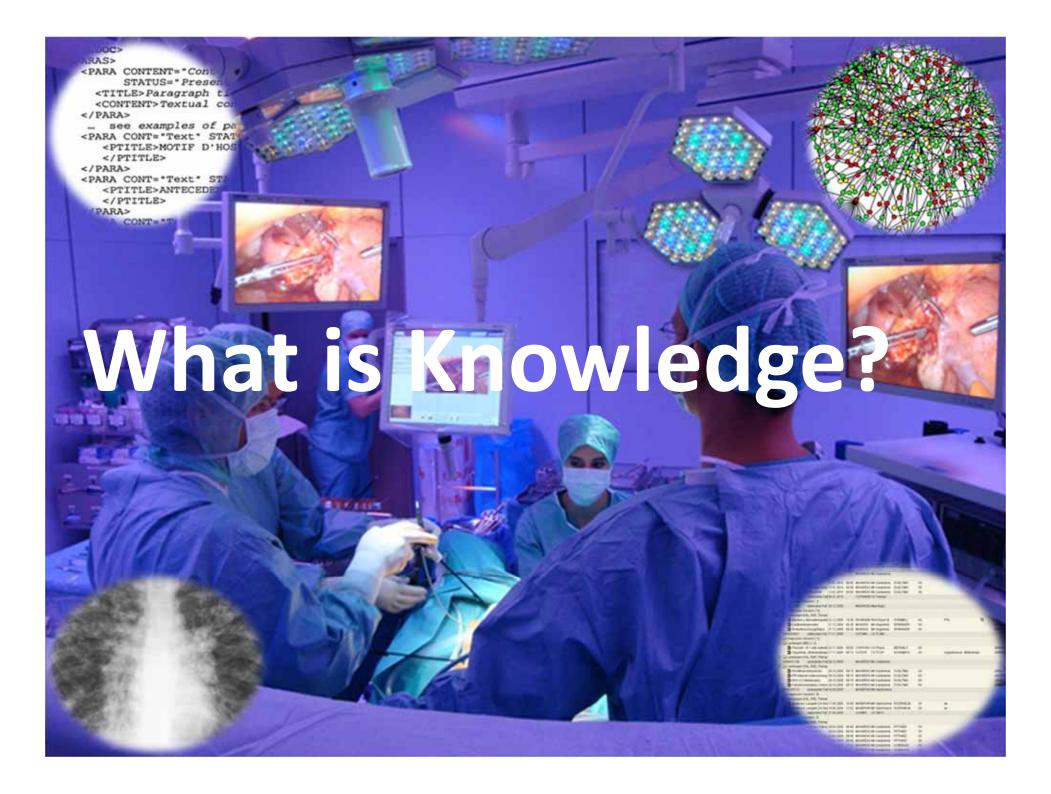


- ... are aware of the importance of gaining knowledge from (big) data;
- ... know the <u>differences</u> between Data Mining and Knowledge Discovery;
- ... understand the basic process of knowledge discovery from data(bases) (KDD-chain);
- ... have an overview on some <u>data mining</u> algorithms used in biomedical informatics;
- ... have seen some examples of data mining applied in the biomedical domain;

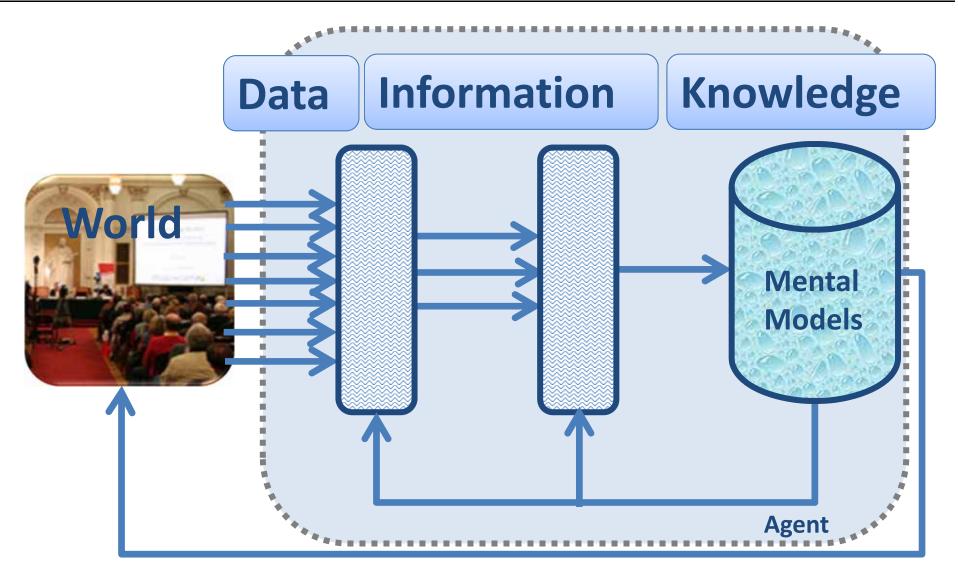
#### Slide 6-1: Key Challenges



- 1) Cross-disciplinary cooperation with domain experts
- 2) Data-driven challenges including
  - a) Massive data sets;
  - b) Heterogeneous Data;
  - c) Streaming Data (e.g. from sensor nets, Multimedia, etc.);
  - d) Graph Data (e.g. Protein Network data, etc.);
  - e) Data restrictions (accessibility, privacy, safety, security, legal restrictions, fair use, etc.);
- 3) Context Data Mining in a particular context
- 4) Interpretability
- 5) Computational Resources
- 6) Benchmarking against Gold-Standards
- 8) Embedded data mining



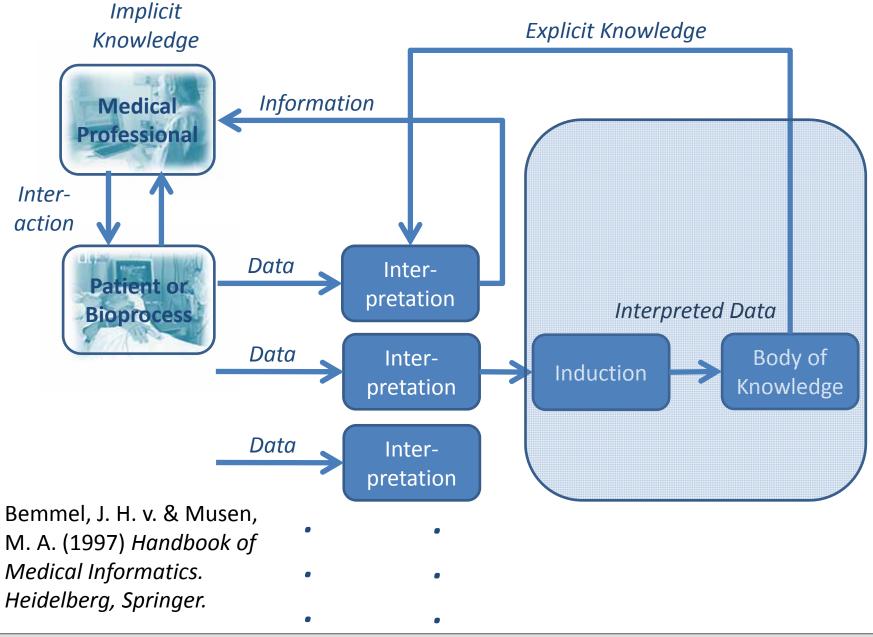




**Knowledge** := a set of expectations

#### Slide 6-2: Implicit vs. Explicit Knowledge





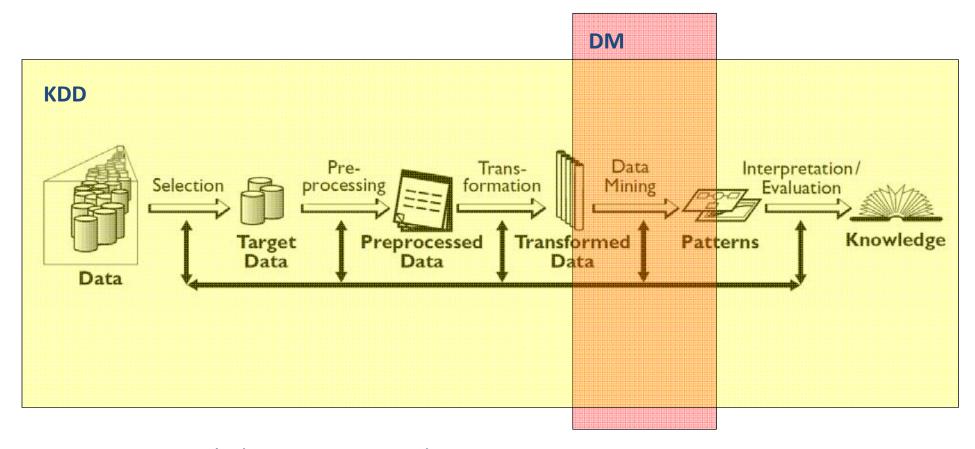


## What is the difference between **Knowledge Discovery** and Data Mining?

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#### Slide 6-3: The classic differentiation between DM and KDD





- KDD = Knowledge Discovery and Data Mining
- DM = Data Mining

Fayyad, U., Piatetsky-Shapiro, G. & Smyth, P. (1996) The KDD process for extracting useful knowledge from volumes of data. *Communications of the ACM, 39, 11, 27-34.* 







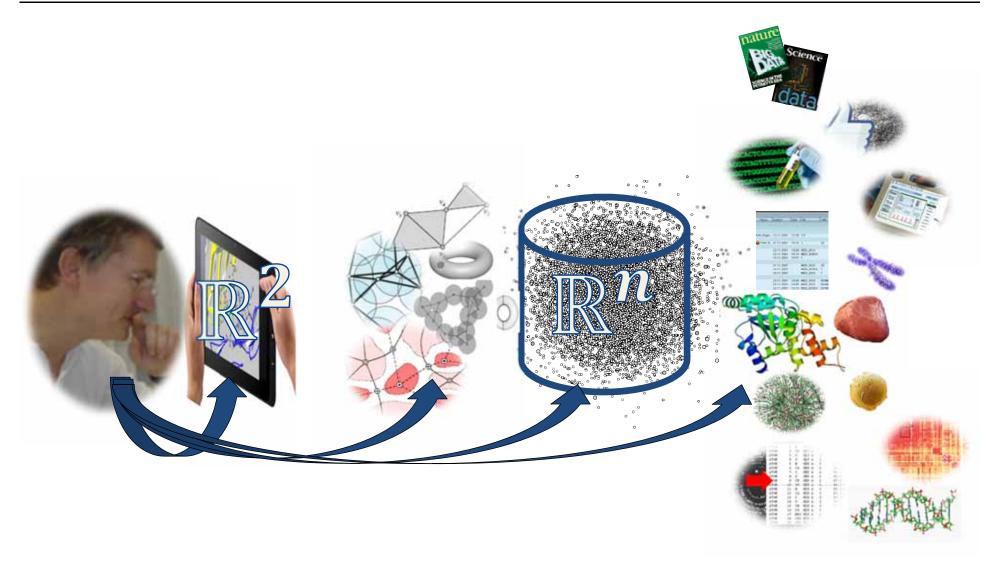
#### Work areas & Research Topics of the Holzinger Group

#### Data Interactive Knowledge Discovery Mining Mining Data Data Prepro-Data Visualization Algorithms Mapping cessing **Fusion** HCI **GDM** Graph-based Data Mining **EDM** Entropy-based Data Mining TDM Topological Data Mining

Privacy, Data Protection, Safety and Security

#### Slide 6-4 Interactive Knowledge Discovery and Data Mining





#### Slide 6-5 The Knowledge Discovery Process Chain





**HCI**, Interactive

**Decision Support** 



Visualization, Analytics,

**Topological Data Mining - Pattern Discovery** 

Sampling, Cleansing, Preprocessing, Mapping

**Data Integration Data Fusion** Pre-selection

Privacy, Data Protection, Data Security, Data Safety



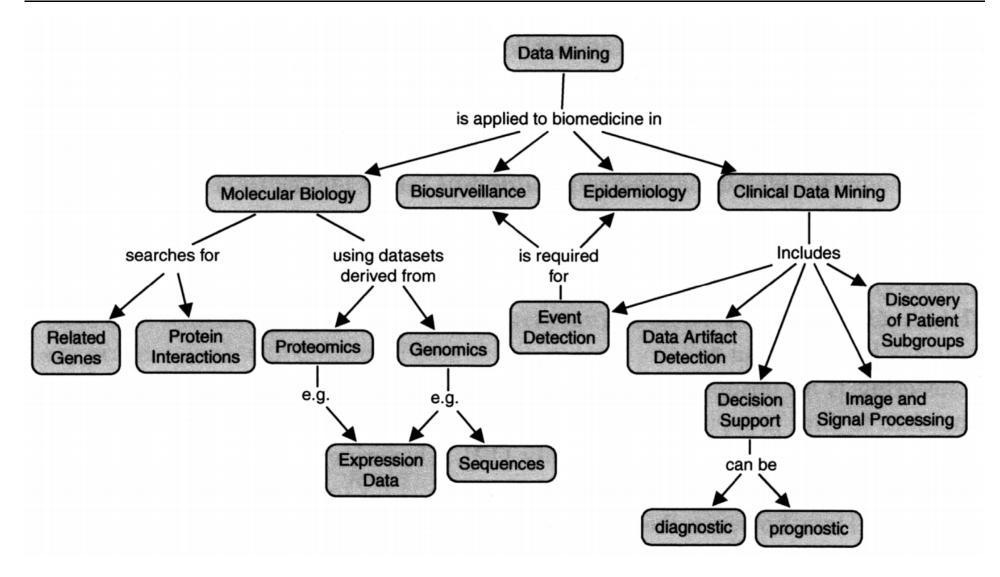


- Data mining is the set of methods and techniques for exploring and analyzing (big) data sets;
- in an automatic or semi-automatic way, in order to find certain unknown or hidden rules, associations or tendencies;
- relevant essentials of the useful information while reducing the quantity of data;
- descriptive (or exploratory) techniques are designed to bring out information that is present but buried in a mass of data;
- predictive (or explanatory) techniques are designed to extrapolate new information based on the present information;

Tufféry, S. (2011) Overview of Data Mining. Data Mining and Statistics for Decision Making (Wiley Series in Computational Statistics). New York, John Wiley & Sons, Ltd, 1-24.

#### Slide 6-7 Data Mining in Biomedical Engineering





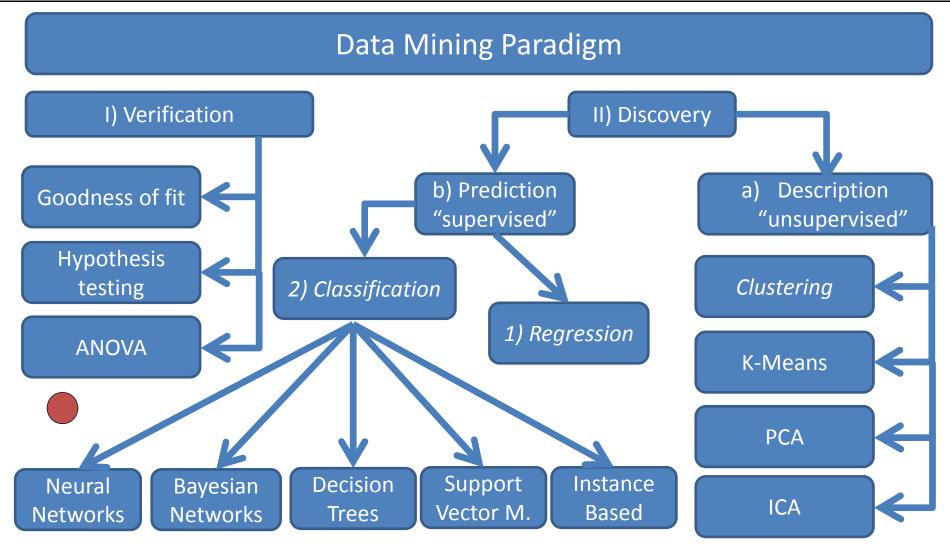
Suh, S. C., Gurupur, V. P. & Tanik, M. M. (2011) *Biomedical Engineering: Health Care Systems, Technology and Techniques. New York, Springer.* 



- Clustering: assigning a set of objects into groups
- Classification: predicting an item class, identifying to which set of categories a new observation belongs
- Associations: finding for example that A & B & C occur frequently together
- Visualization: to facilitate human cognition
- Deviation Detection: finding changes
- Anomaly Detection: finding anomalies
- Estimation: predicting a continuous value
- Link Analysis: finding relationships
- Forecasting: predicting a trend

#### **Slide 6-9 Taxonomy of Data Mining Methods**





Maimon, O. & Rokach, L. (Eds.) (2010) Data Mining and Knowledge Discovery Handbook. Second Edition, New York, Dordrecht, Heidelberg, London, Springer.



### Data Mining, Knowledge Discovery, Machine Learning

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- Machine learning is NOT a well defined field: it refers to a broad range of various algorithms within a feature space; hence:
- Features are key to machine learning and knowledge discovery!
- Tom Mitchell: A scientific field is best defined by the central questions it studies.
- ML seeks to answer the question "How can we build computer systems that automatically improve with experience, and what are the fundamental laws that govern all learning processes?"

#### Machine Learning is the most growing technical field ...



 Progress in ML is driven by the ongoing explosion in the availability of online data and at the same time lowcost computation.

Jordan, M. I. & Mitchell, T. M. 2015. Machine learning: Trends, perspectives, and prospects. Science, 349, (6245), 255-260.





# What is a best practice example of Machine Learning

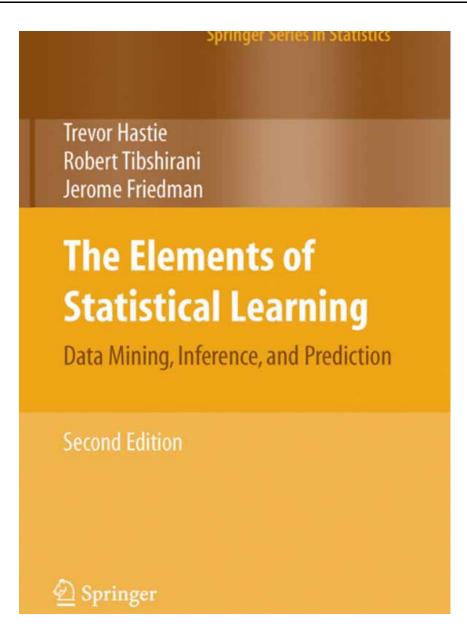
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#### **Machine Learning and Statistics are closely related**



- Machine Learning is the development of algorithms which can learn from data
- Machine Learning has a pre-history in statistical learning, which is the application of statistical models and the assessment of uncertainty





#### Unsupervised learning (e.g. clustering)

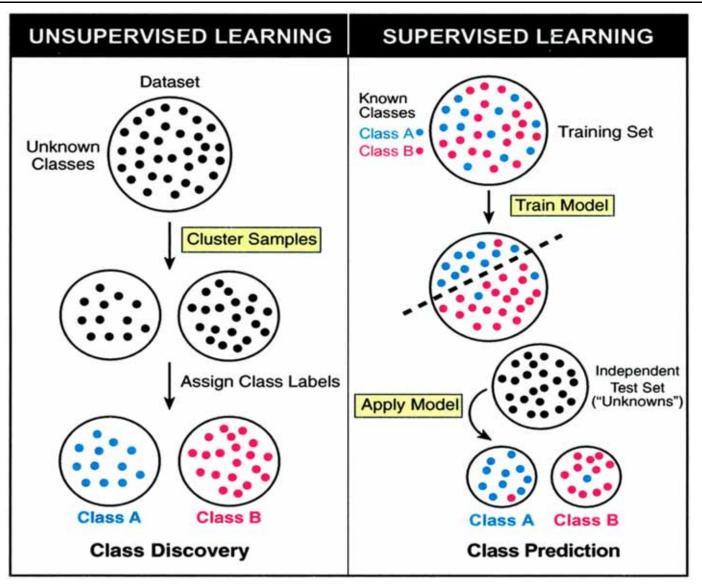
- The class labels of training data is unknown
- Given a set of measurements, observations, etc. with the aim of establishing the existence of clusters in the data;

#### Supervised learning (e.g. classification)

- Supervision = the training data (observations, measurements, etc.) are accompanied by labels indicating the class of the observations;
- New data is classified based on the training set

#### Slide 6-11 Example Unsupervised vs. supervised learning

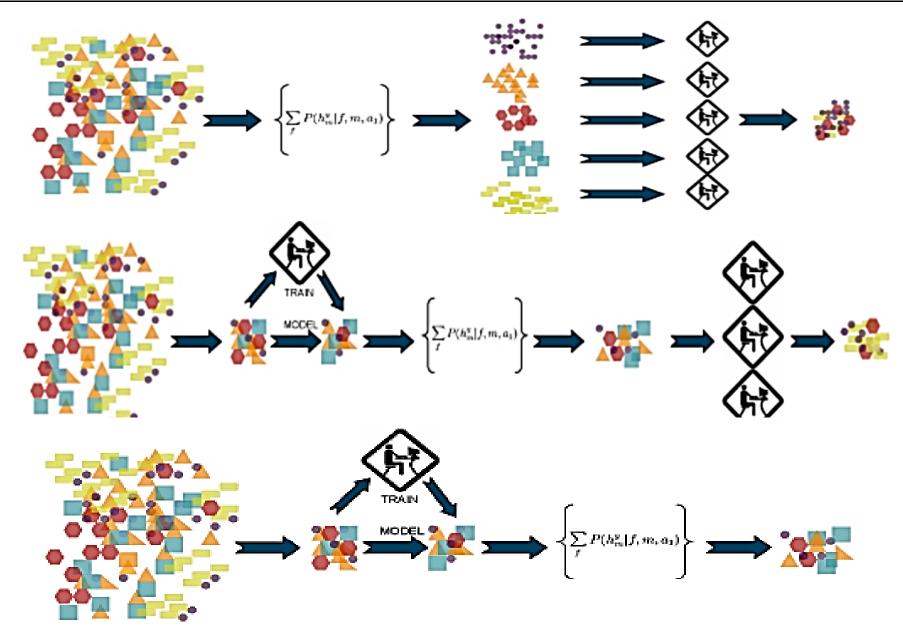




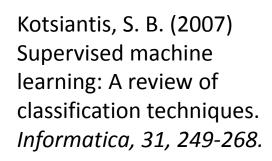
Ramaswamy, S. & Golub, T. R. (2002) DNA Microarrays in Clinical Oncology. *Journal of Clinical Oncology, 20, 7, 1932-1941.* 

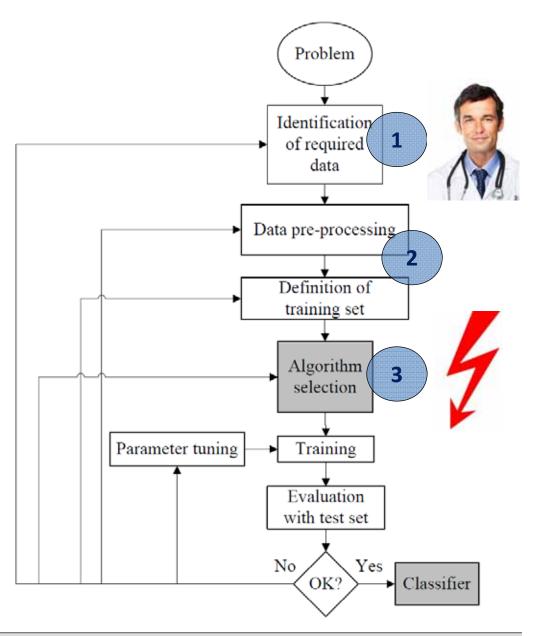
#### Slide 6-12 Unsupervised > Supervised > Semi-Supervised











#### Slide 6-14 Example for supervised learning: ANN

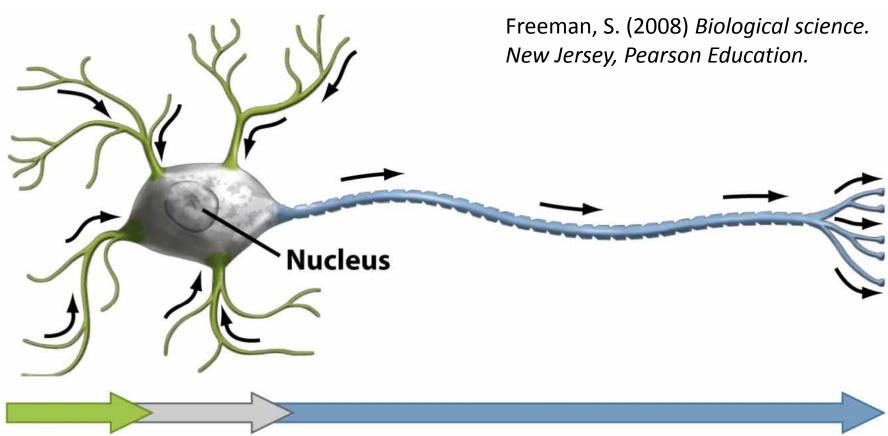




Mikula, S., Trotts, I., Stone, J. M. & Jones, E. G. (2007) Internet-enabled high-resolution brain mapping and virtual microscopy. *NeuroImage*, *35*, *1*, *9-15*. *http://brainmaps.org* 

#### Slide 6-15: Neuron - Information flow through





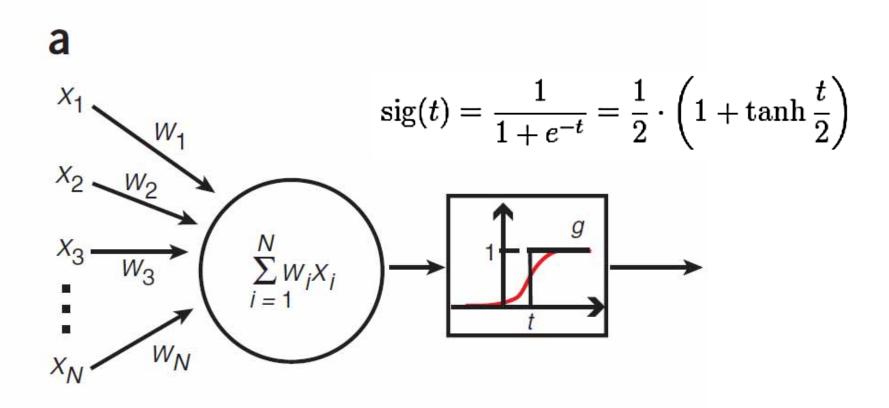
**Collect** electrical signals

**Dendrites Cell body** Integrates incoming signals and generates outgoing signal to axon

Axon

Passes electrical signals to dendrites of another cell or to an effector cell

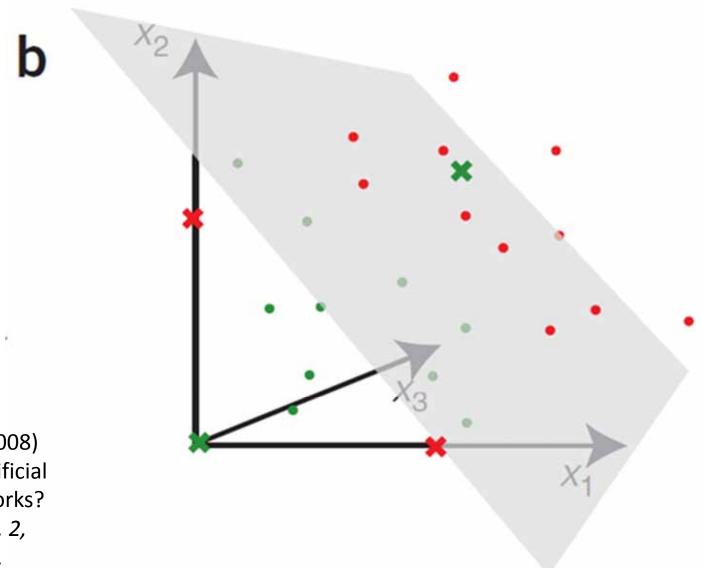




$$\sum_{i=1}^{N} W_i X_i = W_1 X_1 + W_2 X_2 + \dots + W_N X_N$$

Krogh, A. (2008) What are artificial neural networks? Nature, 26, 2, 195-197.

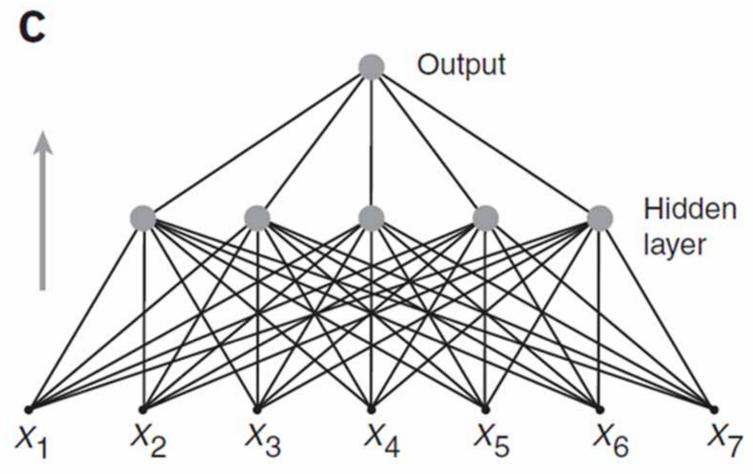




Krogh, A. (2008) What are artificial neural networks? Nature, 26, 2, 195-197.

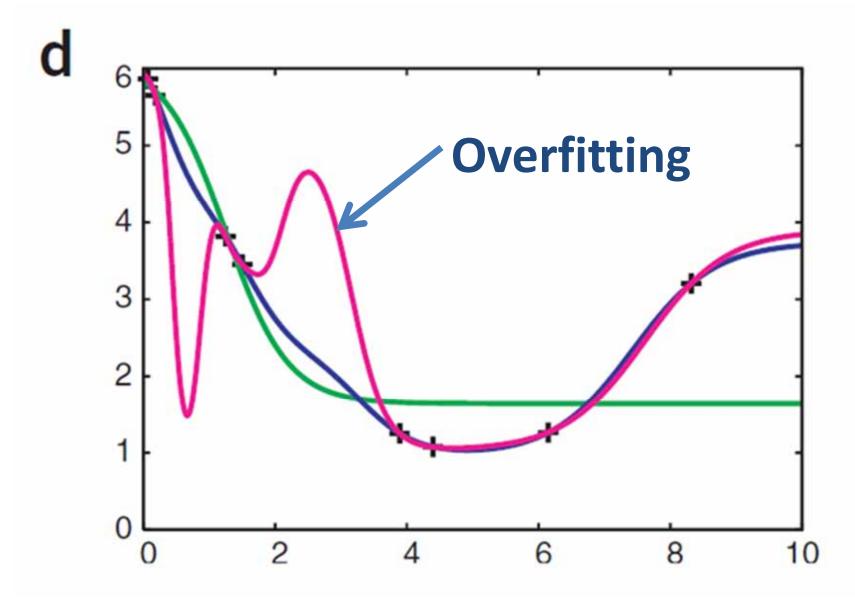


### **Feed Forward Network**



Krogh, A. (2008) What are artificial neural networks? *Nature, 26, 2, 195-197.* 



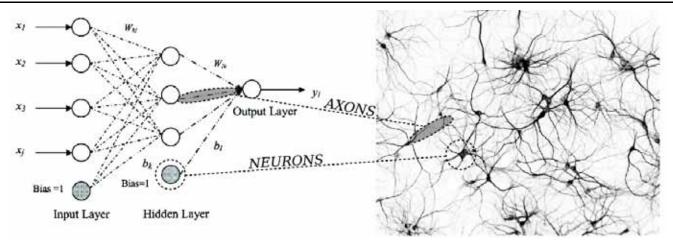


Krogh, A. (2008) What are artificial neural networks? Nature, 26, 2, 195-197.

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### Slide 6-20: Neural Networks in Biomedical Engineering





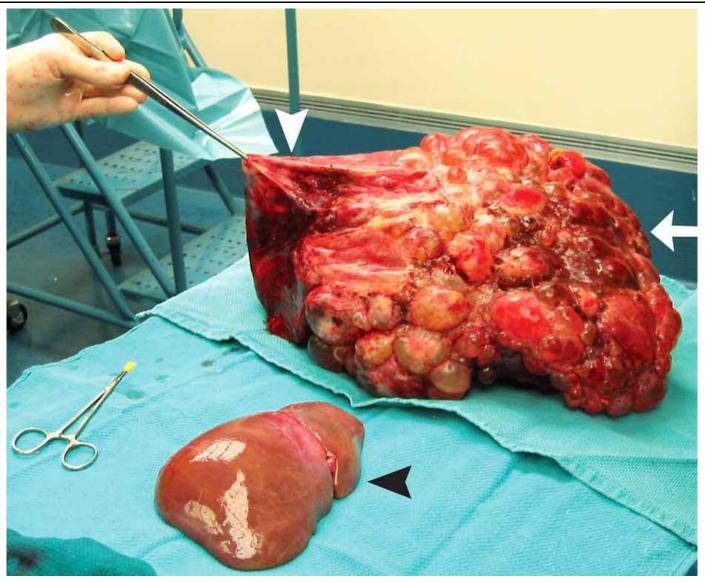
- Many applications, many other networks, for example:
- Hopfield networks,
- Boltzmann machines,
- Kohonen nets,
- Unsupervised networks, ...



# Biomedical Examples

### Slide 6-21: Risky Medical Example: Liver transplantation





Wall, W. J. (2007) Liver Transplantation for Polycystic Liver Disease. *New England Journal of Medicine*, 356, 15, 1560-1560.

### Slide 6-22: Model for End-Stage Liver Disease (MELD)



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MELD	≤9	10-19	20-29	30-39	≥40
Hospitalized	4% (6/148)	27% (28/103)	76% (16/21)	83% (5/6)	100% (4/4)
Ambulatory noncholestatic	2% (5/213)	5.6% (14/248)	50% (15/30)		E STATE OF THE STA
Ambulatory PBC	1% (3/308)	13% (2/16)	0% (0/2)	<del></del> 6	_
Historical	8% (55/711)	26% (90/344)	56% (47/84)	66% (23/35)	100% (5/5)

TABLE 2. Validity of MELD in Predicting Mortality

N = 2,278

	Hospitalized N = 282	Ambulatory Noncholestatic N = 491	Ambulatory PBC N = 326	Historical N = 1179
1-Week mortality	0.95 (0.88-1.00)	0.80 (0.67-0.94)	2 <del></del>	0.84 (0.78-0.89)
3-Month mortality	0.87 (0.82-0.92)	0.80 (0.69-0.90)	0.87 (0.71-1.00)	0.78 (0.74-0.81)
1-Year mortality	0.85 (0.80-0.90)*	0.78 (0.70-0.85)	0.87 (0.80-0.93)	0.73 (0.69-0.76)†

NOTE. Values reported are the concordance statistic (95% CI).

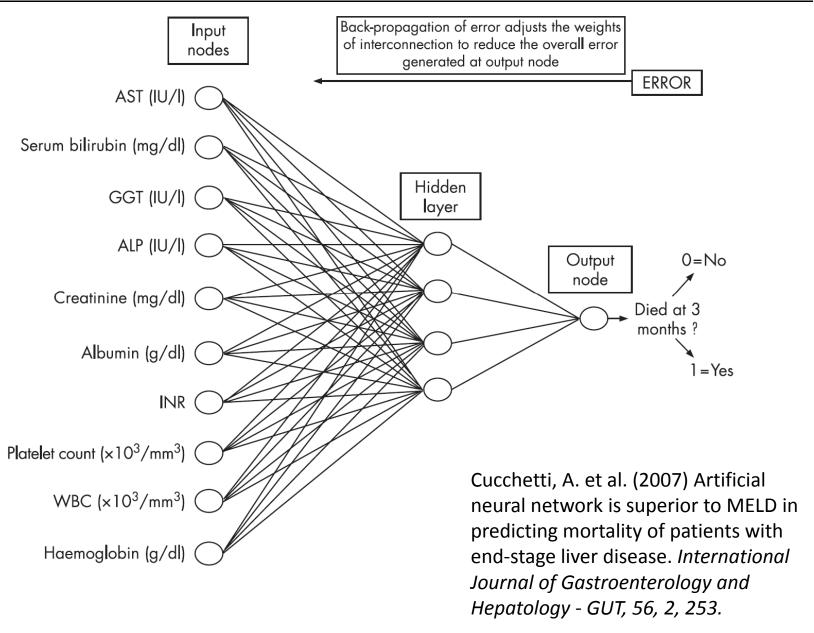
Consists of serum bilirubin and creatinine levels, International Normalized Ratio (INR) for prothrombin time, and etiology of liver disease. Kamath, P. S., Wiesner, R. H., Malinchoc, M., Kremers, W., Therneau, T. M., Kosberg, C. L., D'Amico, G., Dickson, E. R. & Kim, W. (2001) A model to predict survival in patients with end-stage liver disease (MELD). *Hepatology*, 33, 2, 464-470.

<sup>\*</sup> N = 257; 25 patients lost to follow-up.

<sup>†</sup> N = 1,108; 71 patients lost to follow-up.

### Slide 6-23: ANN application Example: Liver transplantation

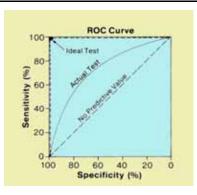




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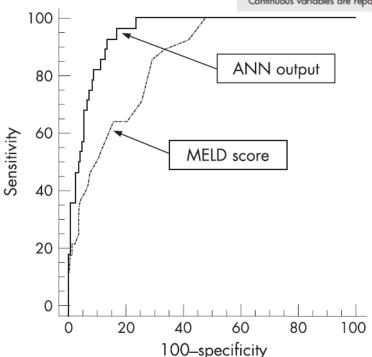
### Slide 6-24: Diagnostic accuracy of the ANN





	Internal cohort (Bologna)			External cohort (Lond	External cohort (London)		
Variable	Survivors (n = 213)	Dead (n = 38)	p Value	Survivors (n = 120)	Dead (n = 17)	p Value	
AST (IU/I)	93.7 (68.6)	116.6 (105.8)	0.207	84.2 (65.6)	116.1 (101.9)	0.253	
Total bilirubin (mg/dl)	3.4 (2.9)	11.7 (9.6)	0.001	4.1 (5.4)	9.0 (8.5)	0.015	
GGT (IU/I)	77.3 (63.9)	43.1 (25.4)	0.001	186.7 (43.3)	81.0 (79.5)	0.007	
ALP (IU/I)	357.1 (219.0)	302.9 (110.1)	0.137	281.1 (152.5)	224.7 (204.9)	0.469	
Creatinine (mg/dl)	0.92 (0.21)	1.02 (0.29)	0.011	1.28 (1.23)	1.79 (1.64)	0.044	
Albumin (g/dl)	3.1 (0.4)	2.9 (0.4)	0.016	3.1 (0.6)	2.5 (0.8)	0.001	
INR	1.57 (0.31)	2.11 (0.54)	0.001	1.21 (0.37)	1.68 (0.83)	0.017	
Platelet count (×10 <sup>3</sup> /mm <sup>3</sup> )	74.7 (53.8)	64.6 (37.8)	0.267	149.1 (135.3)	112.7 (103.5)	0.294	
WBC (×10 <sup>3</sup> /mm <sup>3</sup> )	4.3 (1.6)	5.5 (2.2)	0.002	6.1 (5.1)	7.5 (6.3)	0.236	
Haemoglobin (g/dl)	12.1 (5.7)	10.2 (1.3)	0.038	11.1 (1.9)	10.6 (2.4)	0.229	

ALP, alkaline phosphatase; AST, aspartate aminotransferase; GGT,  $\gamma$ -glutamyl-transpeptidase; INR, international normalised ratio; WBC, white cell. Continuous variables are reported as mean (SD).



**Table 3** Receiver-operating characteristic analysis of the artificial neural network in comparison with the model of the end-stage liver disease performance

	ANN		MELD score		
	AUC	95% CI	AUC	95% CI	p Value*
Training/cross validation Internal validation External cohort	0.98 0.95 0.96	0.94 to 0.99 0.86 to 0.99 0.91 to 0.98	0.86 0.85 0.86	0.80 to 0.91 0.74 to 0.96 0.79 to 0.91	0.002 0.032 0.044

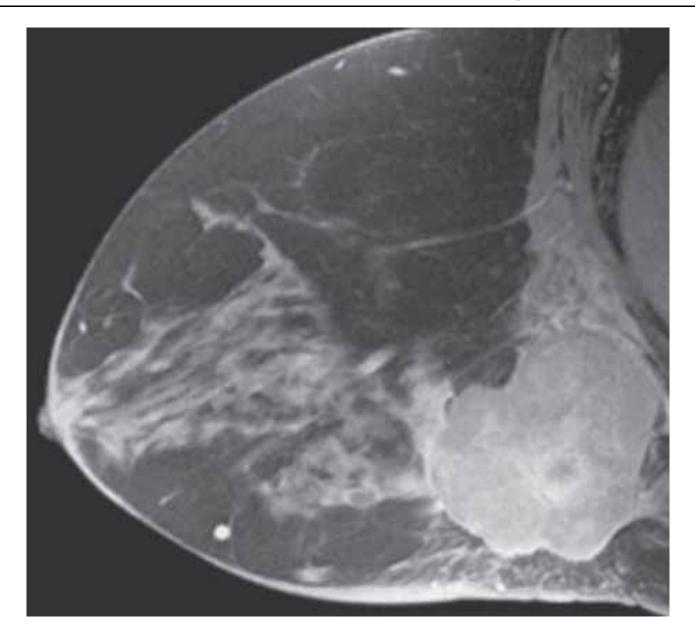
ANN, artificial neural networks; AUC, area under the curve; MELD, model for end-stage liver disease.

\*p values of each ANN subgroup compared with the MELD score of the same subgroup (Hanley-McNeil method).

Cucchetti, A. et al. (2007) Artificial neural network is superior to MELD in predicting mortality of patients with end-stage liver disease. *International Journal of Gastroenterology and Hepatology - GUT, 56, 2, 253.* 

### Slide 6-25: Another Clinical Case Example



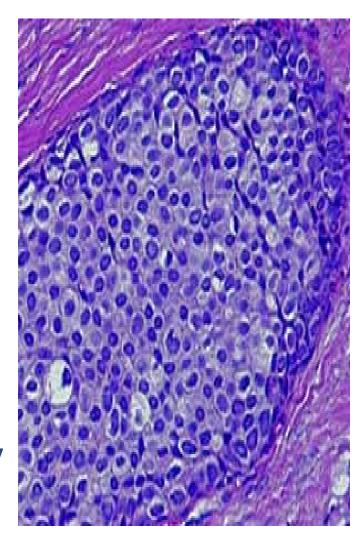


Overmoyer, B. A., Lee, J. M. & Lerwill, M. F. (2011) Case 17-2011 A 49-Year-Old Woman with a Mass in the Breast and Overlying Skin Changes. New England Journal of Medicine, 364, 23, 2246-2254.

### Slide 6-26: Important in Clinical practice -> prognosis!



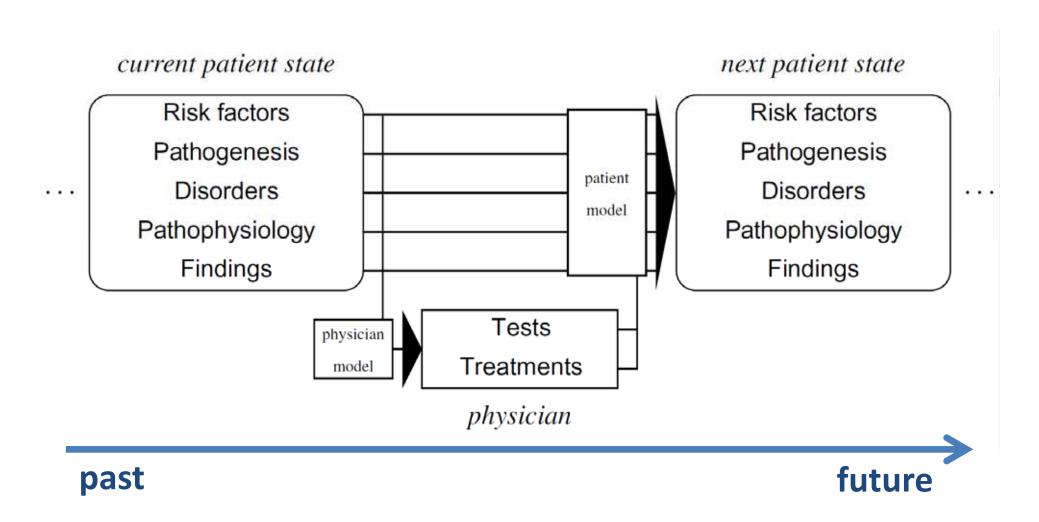
- = the prediction of the future course of a disease conditional on the patient's history and a projected treatment strategy
- Danger: probable Information!
- Therefore valid prognostic models can be of great benefit for clinical decision making and of great value to the patient, e.g., for notification and quality of-life decisions



Knaus, W. A., Wagner, D. P. & Lynn, J. (1991) Short-term mortality predictions for critically ill hospitalized adults: science and ethics. *Science*, *254*, *5030*, *389*.

### Slide 6-27 Model-based Clinical Decision Making Strategy





van Gerven, M. A. J., Taal, B. G. & Lucas, P. J. F. (2008) Dynamic Bayesian networks as prognostic models for clinical patient management. *Journal of Biomedical Informatics*, 41, 4, 515-529.



## Note: Probable Information p (x)!



- is a probabilistic model, consisting of two parts:
- 1) a dependency structure and
- 2) local probability models.

$$p(x_1, ..., x_n) = \prod_{i=1}^n p(x_i | Pa(x_i))$$

Where  $Pa(x_i)$  are the parents of  $x_i$ 

BN inherently model the <u>uncertainty in the data.</u> They are a successful marriage between probability theory and graph theory; allow to model a multidimensional probability distribution in a sparse way by searching independency relations in the data. Furthermore this model allows different strategies to integrate two data sources.

Pearl, J. (1988) Probabilistic reasoning in intelligent systems: networks of plausible inference. San Francisco, Morgan Kaufmann.

### Slide 6-29: Example: Breast cancer - Probability Table



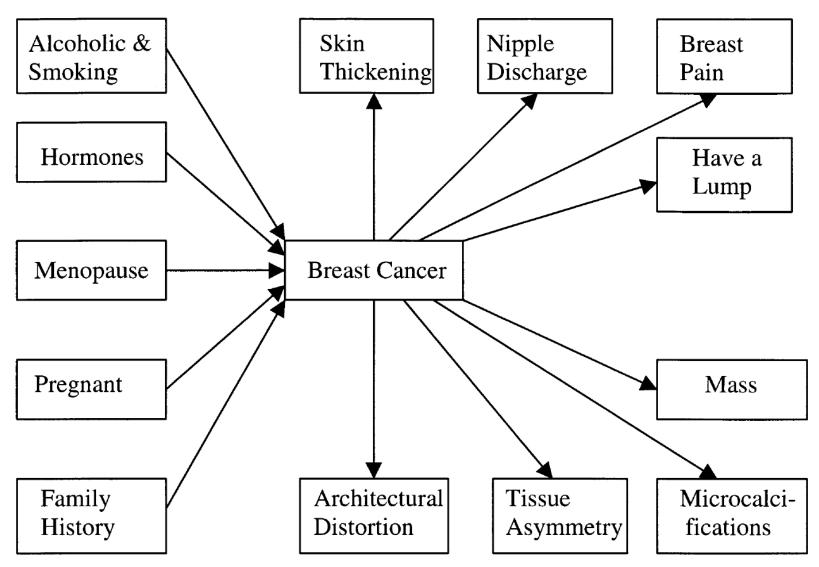
Category	Node description	State description
Diagnosis	Breast cancer	Present, absent.
Clinical history	Habit of drinking alcoholic beverages and smoking	Yes, no.
•	Taking female hormones	Yes, no.
	Have gone through menopause	Yes, no.
	Have ever been pregnant	Yes, no.
	Family member has breast cancer	Yes, no.
Physical find- ings	Nipple discharge	Yes, no.
	Skin thickening	Yes, no.
	Breast pain	Yes, no.
	Have a lump(s)	Yes, no.
Mammo- graphic findings	Architectural distortion	Present, absent.
C	Mass	Score from one to three, score from four to five, absent
	Microcalcification cluster	Score from one to three, score from four to five, absent
	Asymmetry	Present, absent.

Wang, X. H., et al. (1999) Computer-assisted diagnosis of breast cancer using a data-driven Bayesian belief network. *International Journal of Medical Informatics*, 54, 2, 115-126.

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### Slide 6-30 Breast cancer – big picture – state of 1999



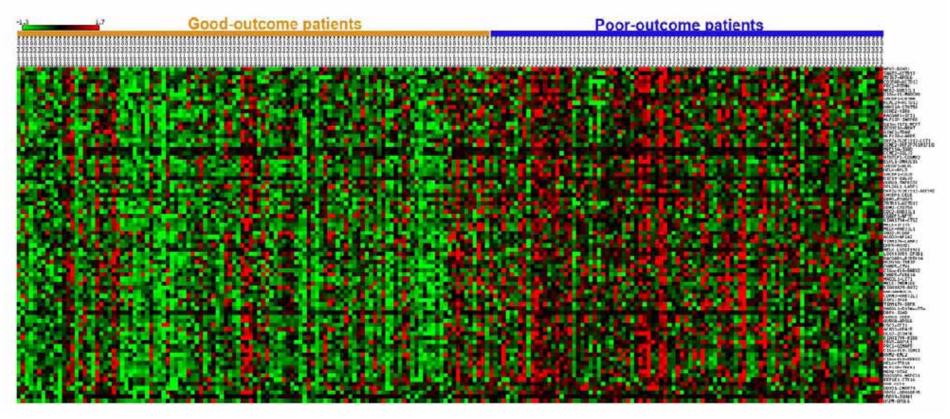


Wang, X. H., et al. (1999) Computer-assisted diagnosis of breast cancer using a data-driven Bayesian belief network. *International Journal of Medical Informatics*, *54*, *2*, *115-126*.

### Slide 6-31: 10 years later: Integration of microarray data



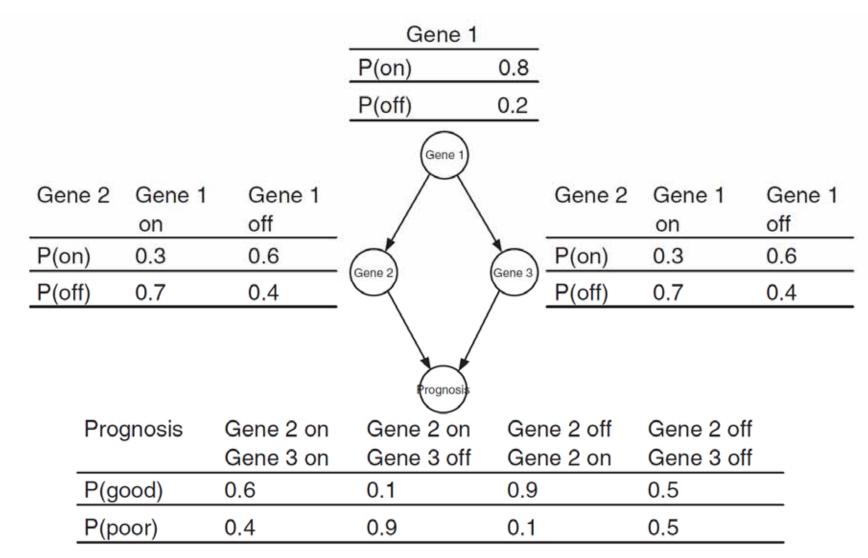
- Integrating microarray data from multiple studies to increase sample size;
- = approach to the development of more robust prognostic tests



Xu, L., Tan, A., Winslow, R. & Geman, D. (2008) Merging microarray data from separate breast cancer studies provides a robust prognostic test. *BMC Bioinformatics*, 9, 1, 125-139.

### Slide 6-32 Example: BN with four binary variables





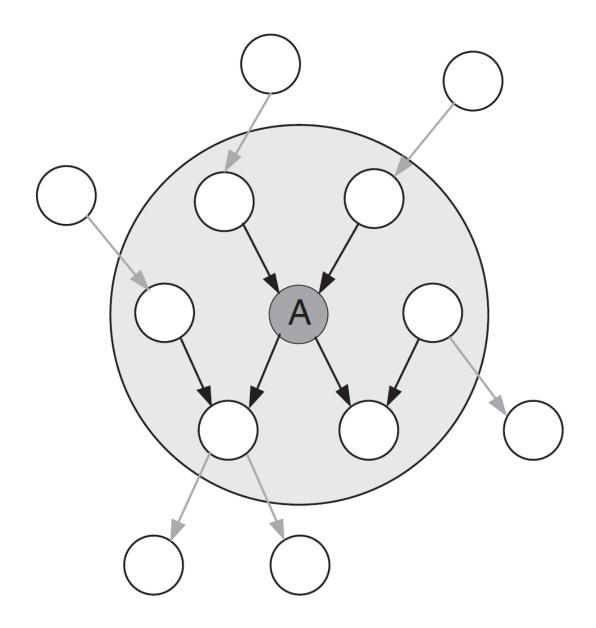
Gevaert, O., Smet, F. D., Timmerman, D., Moreau, Y. & Moor, B. D. (2006) Predicting the prognosis of breast cancer by integrating clinical and microarray data with Bayesian networks. *Bioinformatics*, 22, 14, 184-190.

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### **Slide 6-33 Concept Markov-Blanket**



Gevaert, O., Smet, F. D., Timmerman, D., Moreau, Y. & Moor, B. D. (2006) Predicting the prognosis of breast cancer by integrating clinical and microarray data with Bayesian networks. *Bioinformatics*, 22, 14, 184-190.



### Slide 6-34: Dependency Structure -> first step (1/2)



- First the structure is learned using a <u>search strategy</u>.
- Since the number of possible structures <u>increases</u> super exponentially with the number of variables,
- the well-known greedy search algorithm K2 can be used in combination with the <u>Bayesian Dirichlet (BD) scoring metric</u>:

$$p(S|D) \propto p(S) \prod_{i=1}^{n} \prod_{j=1}^{q_i} \left[ \frac{\Gamma(N'_{ij})}{\Gamma(N'_{ij} + N_{ij})} \prod_{k=1}^{r_i} \frac{\Gamma(N'_{ijk} + N_{ijk})}{\Gamma(N'_{ijk})} \right]$$

 $N_{ijk}$  ... number of cases in the data set D having variable i in state k associated with the j-th instantiation of its parents in current structure S.

n is the total number of variables.

### Slide 6-35: Dependency Structure – first step (2/2)



- Next,  $N_{ij}$  is calculated by summing over all states of a variable:
- $N_{ij} = \sum_{k=1}^{r_i} N_{ijk} \cdot N'_{ijk}$  and  $N'_{ij}$  have similar meanings but refer to prior knowledge for the parameters.
- When no knowledge is available they are estimated using  $N_{ijk} = N/(r_i q_i)$
- with N the equivalent sample size,
- $r_i$  the number of states of variable i and
- $q_i$  the number of instantiations of the parents of variable i.
- $\Gamma(.)$  corresponds to the gamma distribution.
- Finally p(S) is the prior probability of the structure.
- p(S) is calculated by:
- $p(S) = \prod_{i=1}^{n} \prod_{l=1}^{p_i} p(l_i \to x_i) \prod_{m_i=1}^{o_i} p(m_i x_i)$
- with  $p_i$  the number of parents of variable  $x_i$  and  $o_i$  all the variables that are not a parent of  $x_i$ .
- Next,  $p(a \rightarrow b)$  is the probability that there is an edge from a to b while p(ab) is the inverse, i.e. the probability that there is no edge from a to b

### Slide 6-36: Parameter learning -> second step



- Estimating the parameters of the local probability models corresponding with the dependency structure.
- CPTs are used to model these local probability models.
- For each variable and instantiation of its parents there exists a CPT that consists of a set of parameters.
- Each set of parameters was given a uniform Dirichlet prior:

$$p(\theta_{ij}|S) = Dir(\theta_{ij}|N'_{ij1}, \dots, N'_{ijk}, \dots, N'_{ijr_i})$$

Note: With  $\theta_{ij}$  a parameter set where i refers to the variable and j to the j-th instantiation of the parents in the current structure.  $\theta_{ij}$  contains a probability for every value of the variable  $x_i$  given the current instantiation of the parents. Dir corresponds to the Dirichlet distribution with  $(N'_{ij1}, \dots, N'_{ijr_i})$  as parameters of this Dirichlet distribution. Parameter learning then consists of updating these Dirichlet priors with data. This is straightforward because the multinomial distribution that is used to model the data, and the Dirichlet distribution that models the prior, are conjugate distributions. This results in a Dirichlet posterior over the parameter set:

$$p(\theta_{ij}|D,S) = Dir(\theta_{ij}|N'_{ij1} + N_{ij1}, ..., N'_{ijk} + N_{ijk}, ..., N'_{ijr_i} + N_{ijr_i})$$

with  $N_{ijk}$  defined as before.



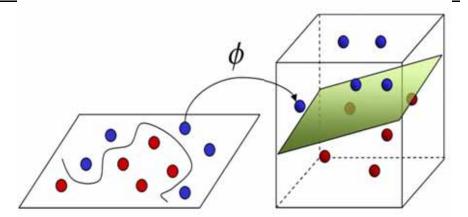
### Are there alternatives to such network approaches?

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### Slide 6-37: Support Vector Machine SVM – (Vapnik, 1992)

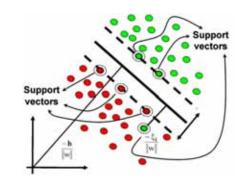


 Uses a <u>nonlinear mapping</u> to transform the original data (input space) <u>into a higher</u> <u>dimension</u> (feature space)



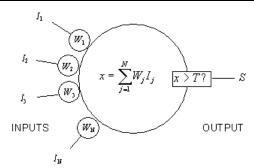
- = classification method for both <u>linear and nonlinear</u> data;
- Within the new dimension, it searches for the linear optimal separating hyperplane (i.e., "decision boundary");
- By nonlinear mapping to a sufficiently high dimension, data from two classes can always be separated with a hyperplane;
- The SVM finds this hyperplane by using support vectors (these are the "essential" training tuples) and margins (defined by the support vectors);





### SVM

- Deterministic algorithm
- Nice generalization properties
- Hard to learn learned in batch mode using quadratic programming techniques
- Using kernels can learn very complex functions

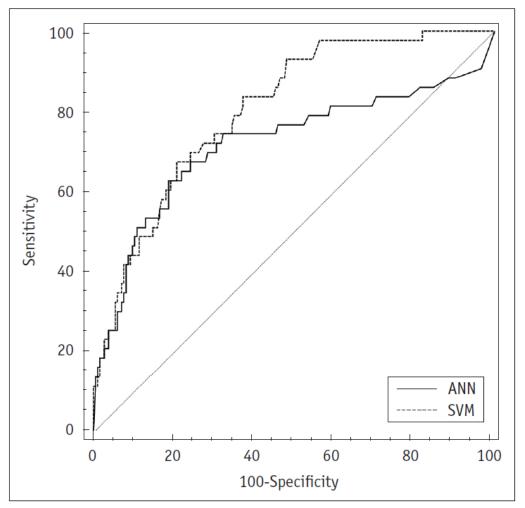


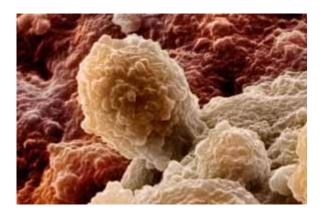
### ANN

- Nondeterministic algorithm
- Generalizes well but doesn't have strong mathematical foundation
- Can easily be learned in incremental fashion
- To learn complex functions—use multilayer perceptron (nontrivial)

### Slide 6-39 Clinical use: SVM are more accurate than ANN







Kim, S. Y., Moon, S. K., Jung, D. C., Hwang, S. I., Sung, C. K., Cho, J. Y., Kim, S. H., Lee, J. & Lee, H. J. (2011) Pre-Operative Prediction of Advanced Prostatic Cancer Using Clinical Decision Support Systems: Accuracy Comparison between Support Vector Machine and Artificial Neural Network. *Korean J Radiol*, 12, 5, 588-594.

### Slide 6-40 The 10 top data mining algorithms

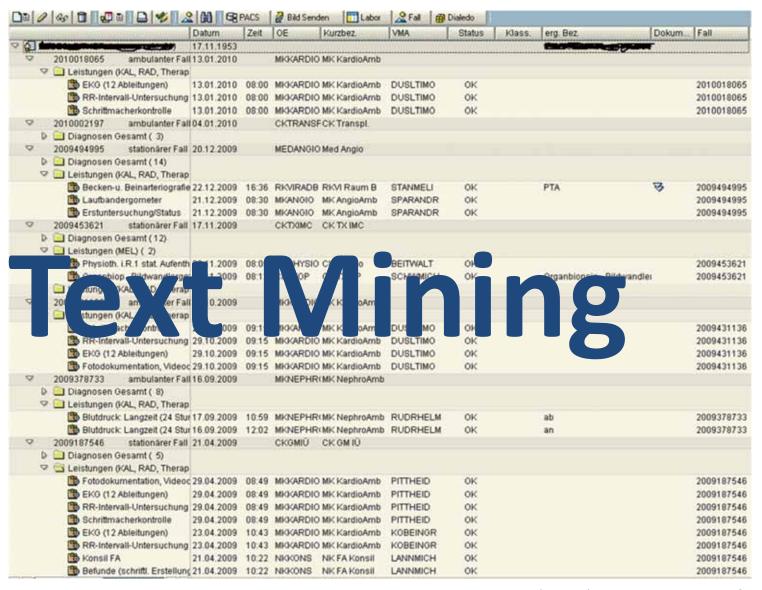


- C4.5 = for generation of decision trees used for classification, (statistical classifier, Quinlan (1993));
- k-means = a simple iterative method for partition of a given dataset into a user-specified number of clusters, k (Lloyd (1957));
- Apriori = for finding frequent item sets using candidate generation (Agrawal & Srikant (1994));
- **EM** = Expectation—Maximization algorithm for finding maximum likelihood estimates of parameters in models (Dempster et al. (1977));
- PageRank = a search ranking algorithm using hyperlinks on the Web (Brin & Page (1998));
- Adaptive Boost = one of the most important ensemble methods (Freund & Shapire (1995));
- k-Nearest Neighbor = a method for classifying objects based on closest training examples in the feature space (Fix & Hodges (1951));
- Naive Bayes = can be trained very efficiently in a supervised learning setting (Domingos & Pazzani (1997));
- CART = Classification And Regression Trees as predictive model mapping observations about items to conclusions about the goal (Breiman et al 1984);
- **SVM** = support vector machines offer one of the most robust and accurate methods among all well-known algorithms (Vapnik (1995));

Wu et al. (2008) Top 10 algorithms in data mining. Knowledge & Information Systems, 14, 1, 1-37.

### Still a big problem ... Text





Kreuzthaler, M., Bloice, M. D., Faulstich, L., Simonic, K. M. & Holzinger, A. (2011) A Comparison of Different Retrieval Strategies Working on Medical Free Texts. *Journal of Universal Computer Science*, 17, 7, 1109-1133.

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- Latent Semantic Analysis (LSA)
- Probabilistic latent semantic analysis (PLSA)
- Latent Dirichlet allocation (LDA)
- Hierarchical Latent Dirichlet Allocation (hLDA)
- Semantic Vector Space Model (SVSM)
- Latent semantic mapping (LSM)
- Principal component analysis (PCA)

Holzinger, A., Schantl, J., Schroettner, M., Seifert, C. & Verspoor, K. 2014. Biomedical Text Mining: State-of-the-Art, Open Problems and Future Challenges. In: Lecture Notes in Computer Science LNCS 8401. Berlin Heidelberg: Springer pp. 271-300.



### Future Outlook

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- ... is a grand challenge in future computing
- ... most of information in the hospital is unstructured and based on natural language
- ... masses of information is not easily processable by humans
- ... legacy approaches have all failed; "searching" not the right approach- Search is a way to gather information – but not to answer questions
- A new approach is needed, leveraging content analytics and natural language processing [1]

[1] Holzinger, A., Stocker, C., Ofner, B., Prohaska, G., Brabenetz, A. & Hofmann-Wellenhof, R. 2013. Combining HCI, Natural Language Processing, and Knowledge Discovery - Potential of IBM Content Analytics as an assistive technology in the biomedical domain. *Springer Lecture Notes in Computer Science LNCS 7947*. Heidelberg, Berlin, New York: Springer, 13-24.

### Slide 6-45: Watson – a Workload Optimized System



- 90 x IBM Power 750 servers
- 2880 POWER7 cores
- POWER7 3.55 GHz chip
- 500 GB per sec on-chip bandwidth
- 10 Gb Ethernet network
- 15 Terabytes of memory
- 20 Terabytes of disk, clustered
- Can operate at 80 Teraflops
- Runs IBM DeepQA software
- Scales out with and searches vast amounts of unstructured information with UIMA & Hadoop open source components
- Linux provides a scalable, open platform, optimized to exploit POWER7 performance
- 10 racks include servers, networking, shared disk system, cluster controllers





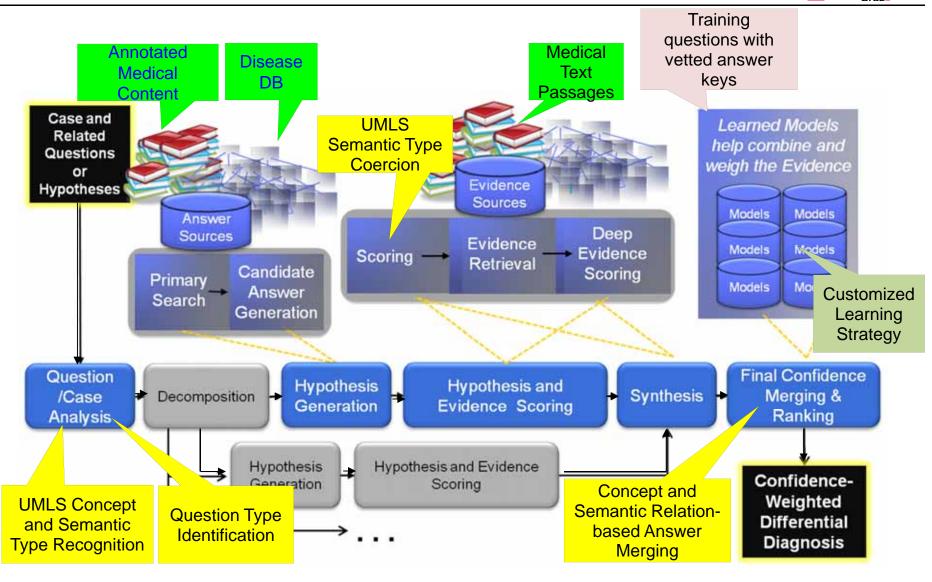




Ferrucci, D., Brown, E., Chu-Carroll, J., Fan, J., Gondek, D., Kalyanpur, A. A., Lally, A., Murdock, J. W., Nyberg, E. & Prager, J. 2010. Building Watson: An overview of the DeepQA project. *AI magazine*, 31, (3), 59-79.

### Slide 6-46: Example: IBM Watson for Healthcare





Ferrucci, D., Levas, A., Bagchi, S., Gondek, D. & Mueller, E. T. 2013. Watson: Beyond Jeopardy! *Artificial Intelligence*, 199–200, (0), 93-105.

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### Slide 6-47 IBM Watson at work













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SEARCH >

Location: Academic Organisations » Knowledge for All Foundation Limited » Alan Turing Centenary Conference Manchester, 2012

### Beyond Jeopardy! The Future of Watson

author: David Ferrucci, IBM Thomas J. Watson Research Center published: July 10, 2012, recorded: June 2012, views: 279

Top » Computer Science » Artificial Intelligence Top » Computers



Alan Turing Centenary Conference Manchester, 2012







"Natural language understanding remains a tremendously difficult challenge, and while Watson demonstrated a powerful approach, we have only scratched the surface," says David Ferrucci.







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### Future Outlook: Image data mining open research issues



Task	Approach/Application	Issue
Preprocessing	Pixel, region and grid level	Global vs. local level features
Feature	Color histograms [135], color	Sensitive to the parameters e.g.,
extraction and	moments [134], color sets [130],	number of bins, bin boundaries,
transformation	shape descriptors, texture	selection of feature vectors
	descriptors, edges	(Fourier etc.)
Image classification	GMM [30], SVM [141], Bayesian	Large training data needed for
	classifier [140] to classify image	GMM, SVM kernel functions, etc.
Image clustering	K-means in preprocessing stage	Unknown number of clusters
	to identify patterns [63]	
Image association	A-priori based association	Scalability issue in terms of
	between structures and functions	number of candidate patterns
	of human brain [91]	generated

Bhatt, C. & Kankanhalli, M. (2011) Multimedia data mining: state of the art and challenges. *Multimedia Tools and Applications*, *51*, *1*, *35-76*.

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## **Future Outlook: Video data mining open research issues**



Task	Approach/Application	Issue
Preprocessing	Shot level, frame level, scene level, clip level	Depends on video structure and application type
Feature extraction and transformation	Image features at frame level as well as motion descriptors, camera metadata like motion [161], date, place, time etc.  Motion calculation is computationally expensive	
Video classification	Human body motion recognition [18], goal detection [161], gestures etc.	Not enough training data to learn events of interest, domain knowledge dependence
Video clustering	Clustering of shots [152, 153], segments [100] for video, for indexing etc.	Scalability for large video clusters is an issue
Video association	A-priori based association finding sequence of events in movies [127]	Finding semantic event boundaries and temporal distance thresholds

Bhatt, C. & Kankanhalli, M. (2011) Multimedia data mining: state of the art and challenges. *Multimedia Tools and Applications*, *51*, *1*, *35-76*.

## **Future Outlook: Audio data mining open research issues**



Task	Approach/Application	Issue
Preprocessing	Phoneme level, word level, window of fixed sizes	Domain dependence e.g., phoneme level if foreign terms, segmenting out silence, noise etc.
Feature extraction and transformation	Pause rate, zero crossing rate, Mel frequency cepstral coefficients [19], bandwidth, spectral centroid, frequency spectrum	Sensitive to the parameters e.g., number of bins, frequency resolution, smoothing factors etc.
Audio classification	HMM [24], GMM [67], SVM [46], Bayesian classifier to do segmentation and classification of speech, music etc.	Model based approaches have problem to work well in real time as more number of iterations and lot of data are needed for training.
Audio clustering	Clustering speaker gender/speech segment of same speaker [92]	Large clusters are sometimes biased

Bhatt, C. & Kankanhalli, M. (2011) Multimedia data mining: state of the art and challenges. *Multimedia Tools and Applications*, *51*, *1*, *35-76*.

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# **Future Outlook: Text data mining open research issues**



Task	Approach/Application	Issue
Preprocessing	Part of speech tagging, stemming, stop word removal, text chunking etc.	Resolving ambiguity is main problem, single word different meaning in different context
Feature extraction and transformation	Identification of important keywords using TF, IDF [117] etc.	Different sizes and contexts of the documents
Text classification	K-nearest neighbor classification, decision tress, naïve bayes classifier [34]	Final decisions depends on relatively few terms
Text clustering	Bi section k means clustering, co clustering [34]	Finding good distance measures

Bhatt & Kankanhalli (2011)



Task	Approach/Application	Issue
Preprocessing	Treat multiple streams separately [99] or consider multiple streams as one [161]	Multimodal data stream synchronization
Feature transformation	Metadata fusion [146]	External knowledge fusion
Multimodal classification	Pre filtering: heuristic rule based [16], SVM classifier based [14], sub space based [129]; fusion: late [99], early [161] and meta [81, 82]	Class imbalance, multimodal classifier fusion
Multimodal clustering	Mixed media graph [103], clustering [7, 42, 148], EEML [47]	Cross modal correlation discovery
Multimodal association	Generalized sequence pattern mining [90, 126]	Automatic identification of temporal structures

Bhatt, C. & Kankanhalli, M. (2011) Multimedia data mining: state of the art and challenges. Multimedia Tools and Applications, 51, 1, 35-76.

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## **Sample Questions (1)**



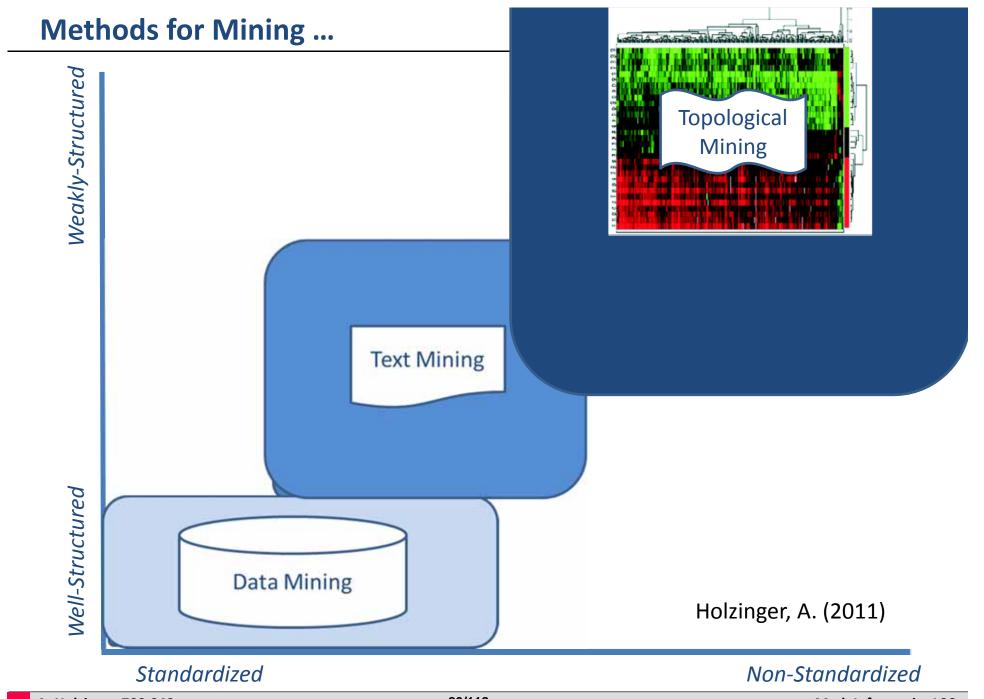
- What is the main goal in knowledge discovery?
- Describe the classical process of KDD!
- How do we define a data object?
- What are the most important data mining tasks?
- What is the difference between supervised and unsupervised learning?
- What is the difference between classification and numeric prediction?
- Why is cluster analysis in medicine important?
- How is data mining defined?
- Describe the taxonomy of data mining paradigms!
- What is a neural network and a neuron?
- What is a artificial neural network?
- How does an ANN work?



- Provide an example on the use of ANN for medical decision making!
- What can you infer from a Receiver Operating Characteristic (ROC)?
- How can you rate the diagnostic accuracy of an ANN?
- What is model based clinical decision making?
- What is very important in clinical patient management?
- What is a Bayesian Network (BN Definition)?
- Why do we need a Markov-Blanket?
- What is the principal function of a Support Vector Machine?
- How would you describe the differences between ANN and SVM?
- Why is text mining in the medical domain practice so difficult?
- Just name some important semantic methods for NLP!
- What is the typical system architecture of a NLP System?



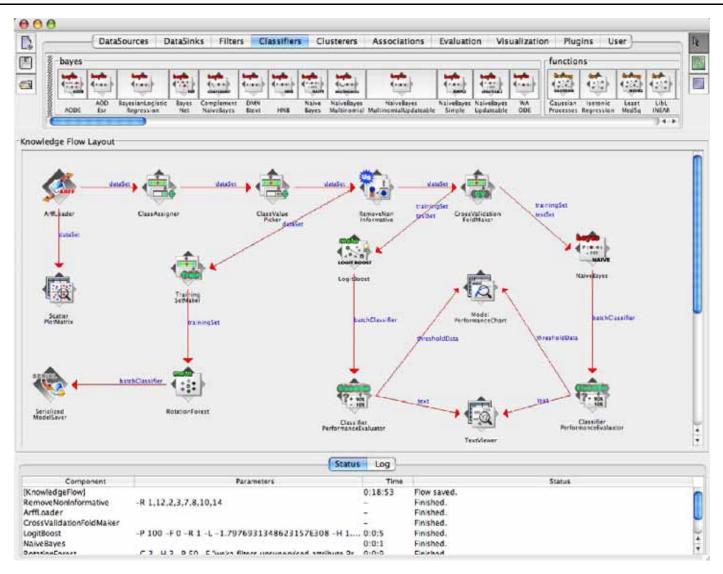
- http://www.cs.waikato.ac.nz/~ml/weka/
- http://www.youtube.com/watch?v=eDYOH9q2QdA &feature=list\_related&playnext=1&list=SPA45CD9B ACEC8B923 (intro to neural networks)
- http://lcn.epfl.ch/tutorial/english/index.html (Neural networks simulation)
- http://leenissen.dk/fann/wp/ (Fast Artificial Neural Network Library)
- http://www.neurosolutions.com/ (End-user friendly Neural Network Development Environment)
- http://www.support-vector-machines.org
- http://www.kernel-machines.org



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## **Appendix: WEKA Tool – The knowledge flow interface**





Hall, M., Frank, E., Holmes, G., Pfahringer, B., Reutemann, P. & Witten, I. H. (2009) The WEKA data mining software: an update. *ACM SIGKDD Explorations Newsletter*, 11, 1, 10-18.

## Appendix: Criteria for selecting a data mining system



- Scalability
  - Row (or database size) scalability
  - Column (or dimension) scalability
  - Curse of dimensionality: it is much more challenging to make a system column scalable that row scalable
- Availability of Visualization tools
  - Visualization categories: data visualization, mining result visualization, mining process visualization, and visual data mining
- Data mining query language and graphical user interface
- Easy-to-use and high-quality graphical user interfaces are essential for end-user guided, highly interactive data mining systems

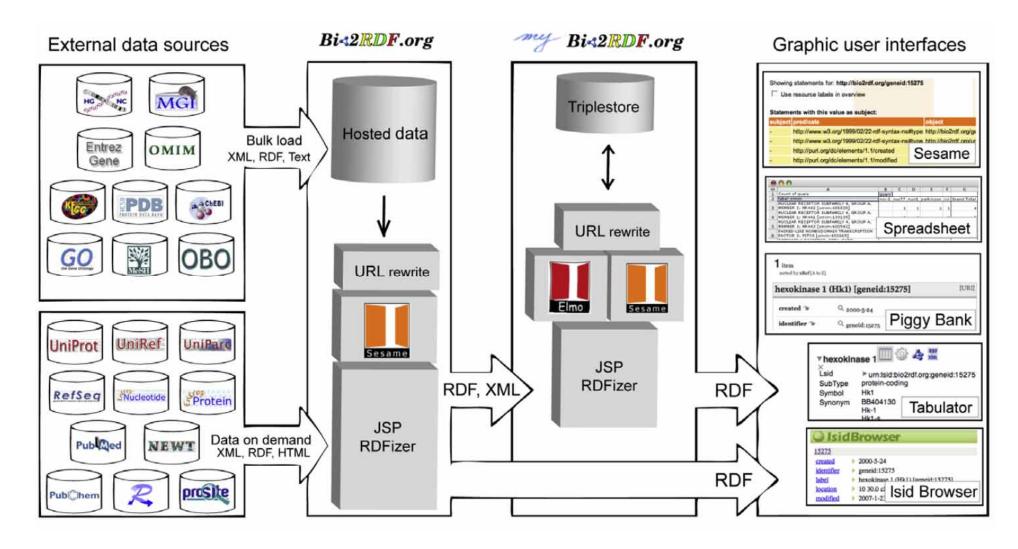
## **Appendix: Examples of professional data mining systems**



- Mirosoft SQLServer 2005 (Integrated DB and OLAP with mining Support OLEDB for DM standard)
- SAS Enterprise Miner (A variety of statistical analysis tools, Data warehouse tools and multiple data mining algorithms)
- IBM Intelligent Miner (A wide range of data mining algorithms; Scalable mining algorithms; Toolkits: neural network algorithms, statistical methods, data preparation, and data visualization tools; Tight integration with IBM's DB2 relational database
- SGI MineSet (advanced statistics and visualization tools)
- Clementine (SPSS integrated data mining development environment – multiple data mining algorithms)

### **Appendix: Example Bio2RDF Architecture**



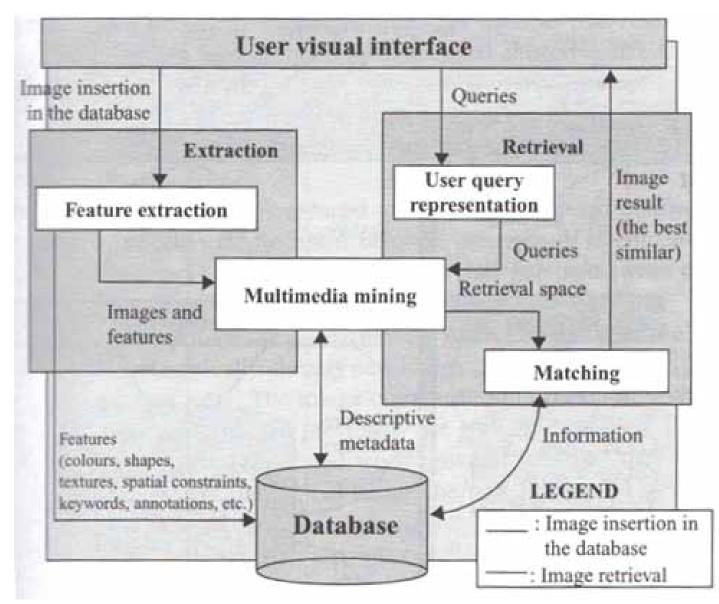


Belleau, F. et al. (2008) Bio2RDF: Towards a mashup to build bioinformatics knowledge systems. *Journal of Biomedical Informatics*, 41, **5**, **706-716**.

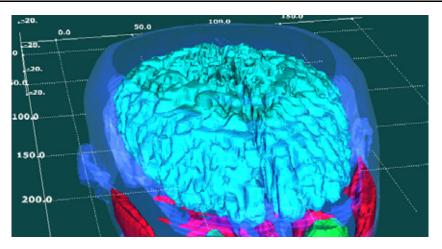
### **Appendix: Sample Architecture for a visual retrieval system**



Bouet, M. & Aufaure, M.-A. (2007) New **Image Retrieval** Principle: Image Mining and Visual Ontology. In: Petrushin, V. A. & Khan, L. (Eds.) Multimedia Data Mining and Knowledge Discovery. London, Springer.







- Data sets are made up of data objects.
- Each data object represents an entity.
- Data objects are described by attributes.
- We want to mine samples (aka examples, instances, data points, objects, tuples) out of databases
- Database rows → data objects;
   columns → attributes

#### **Schedule**

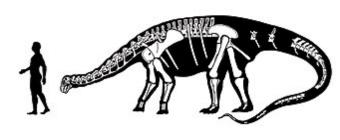


- 1. Intro: Computer Science meets Life Sciences, challenges, future directions
- 2. Back to the future: Fundamentals of Data, Information and Knowledge
- 3. Structured Data: Coding, Classification (ICD, SNOMED, MeSH, UMLS)
- 4. Biomedical Databases: Acquisition, Storage, Information Retrieval and Use
- 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



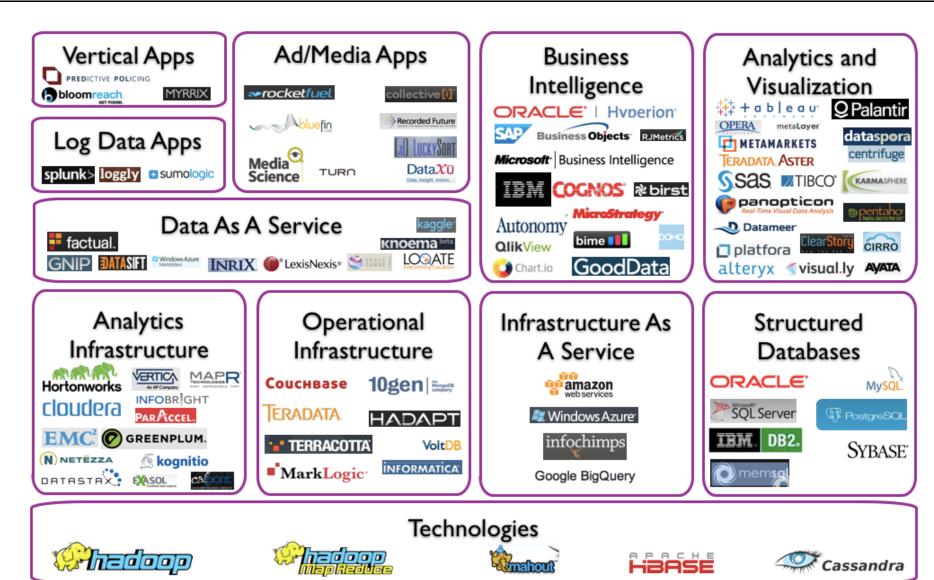
- Masses of data –
- Graph-based data may contain information about design principles and/or the evolutionary history of complex systems
- As in Paleontology: Discovery from past data





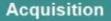






Feinleib (2012), http://www.forbes.com/sites/davefeinleib/2012/06/19/the-big-data-landscape/







#### Marshalling



#### **Analysis**



#### Action

**Data Acquisition** 









Including Complex Event Processing (CEP) tools

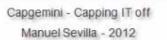
















**Data Governance** 





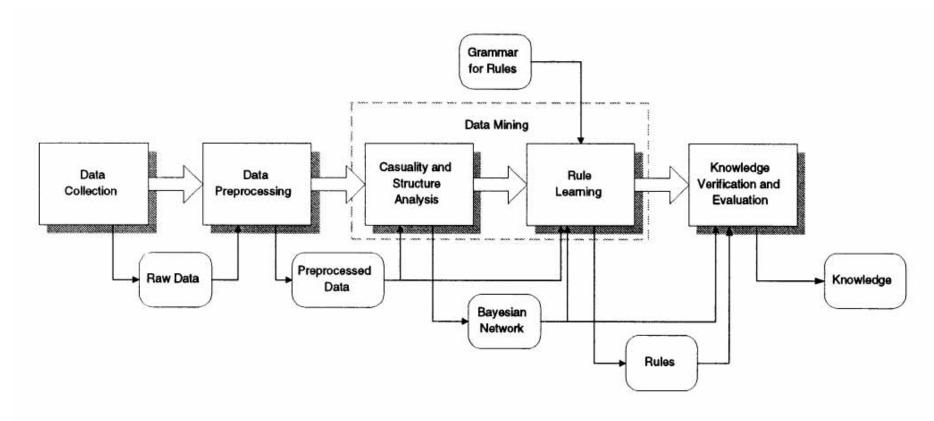


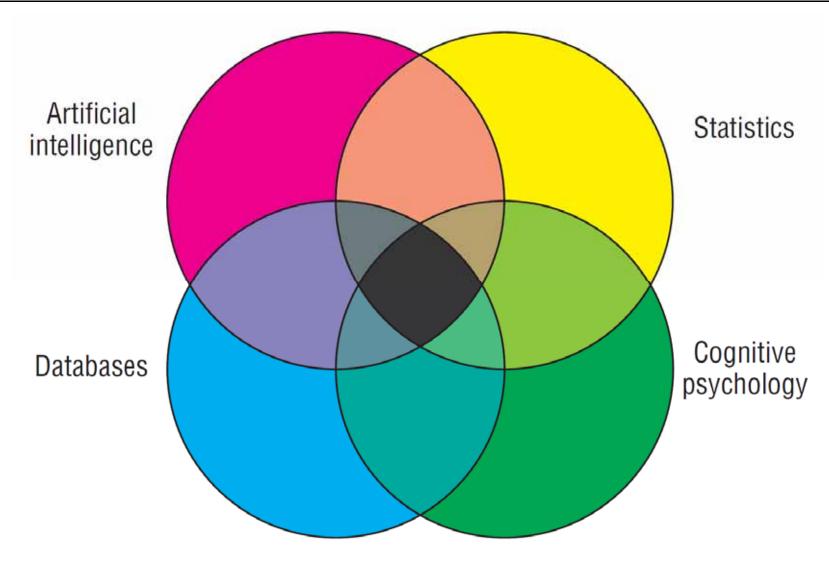
Fig. 1. The knowledge discovery process.

Shun Ngan, P., Leung Wong, M., Lam, W., Leung, K. S. & Cheng, J. C. Y. 1999. Medical data mining using evolutionary computation. *Artificial Intelligence in Medicine*, 16, (1), 73-96.

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# The fields of KDD (Interaction is missing!)





Pazzani, M. J. (2000) Knowledge discovery from data? *Intelligent Systems and their Applications, IEEE, 15, 2, 10-12.* 





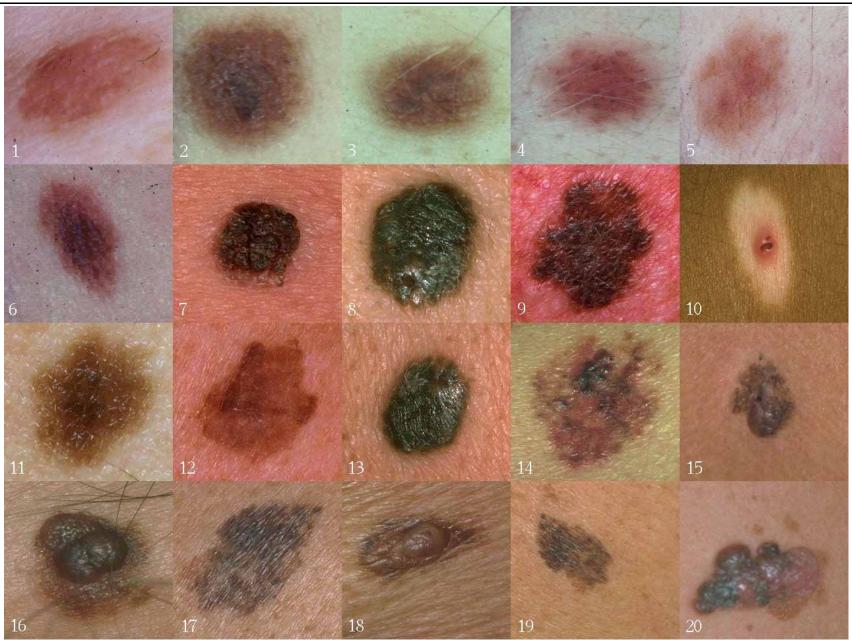


- Medical Decision: is a tumor malign or benign?
- Classification = predicts categorical class labels (discrete or nominal)
  - classifies data (constructs a model) based on the training set and the values (class labels) in a classifying attribute and uses it in <u>classifying new data</u>
- Numeric Prediction = models continuous-valued functions, i.e., predicts unknown or missing values

Image Source: John Nguyen (2010)

# Slide 6-13 Which one is malign – which one is benign?

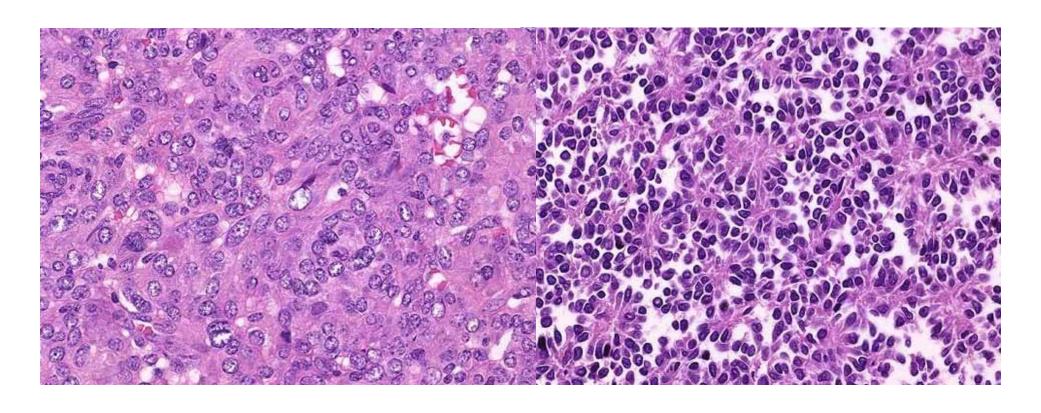




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# Slide 6-14 Example: Benign vs. Malign – molecular level

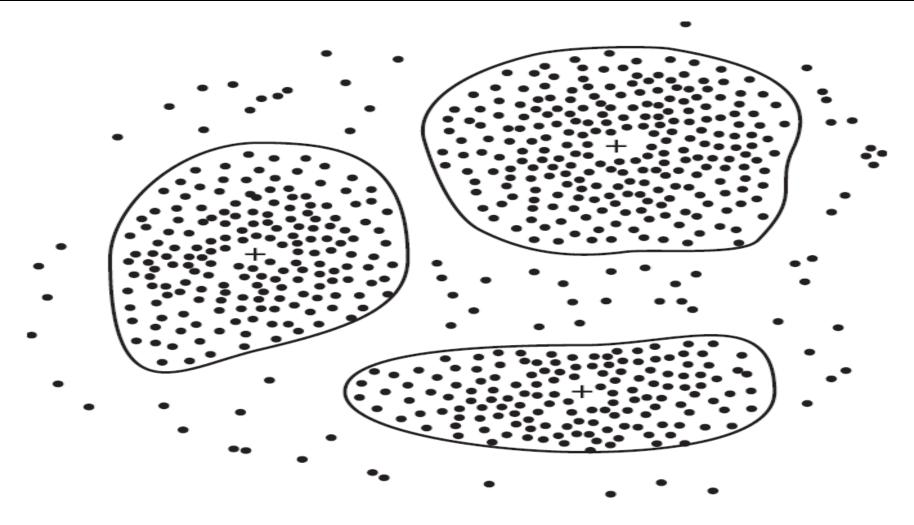




webpathology.com

Am J Surg Pathol 2002 March; 26(3):320-7

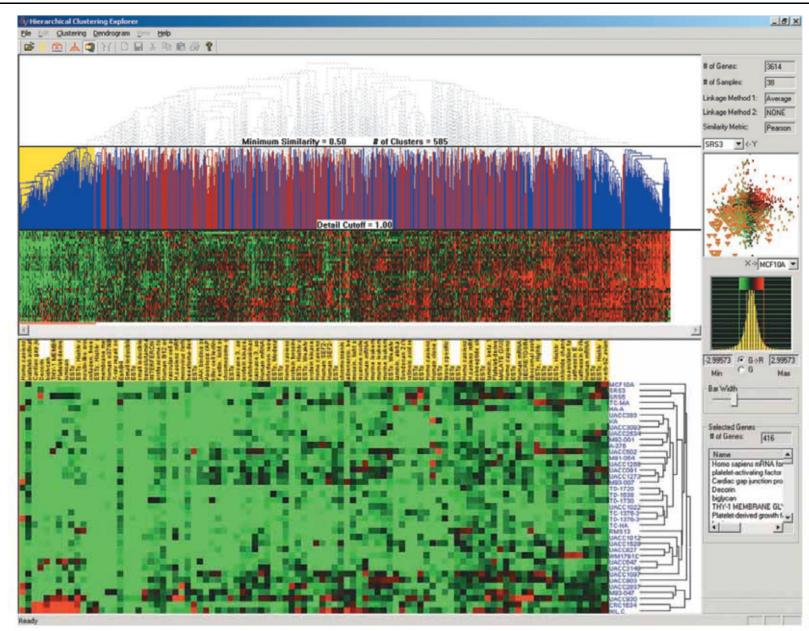




Han, J., Kamber, M. & Pei, J. (2011) Data Mining: Concepts and Techniques (Third Edition). The Morgan Kaufmann Series in Data Management Systems. San Francisco, Morgan Kaufmann Publishers.

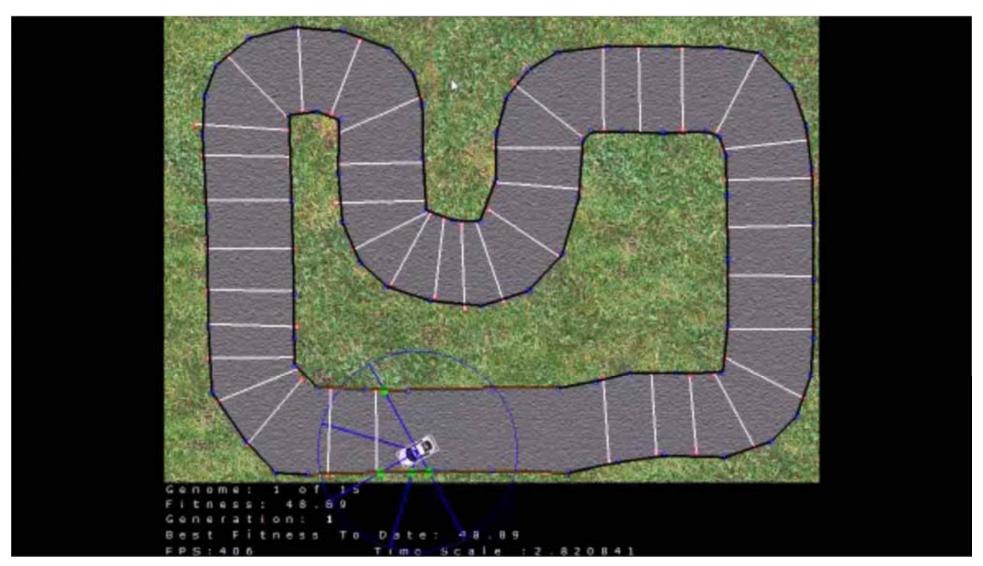
# Slide 6-16 H. Clustering Explorer: melanoma gene expression TU





Seo, J. & Shneiderman, B. (2002) Interactively exploring hierarchical clustering results in gene identification. Computer, 35, 7, 80-86.

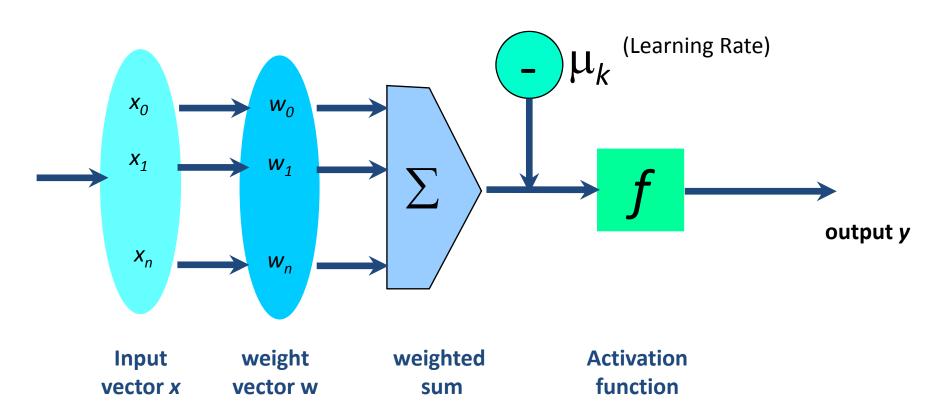




http://www.youtube.com/watch?v=0Str0Rdkxxo



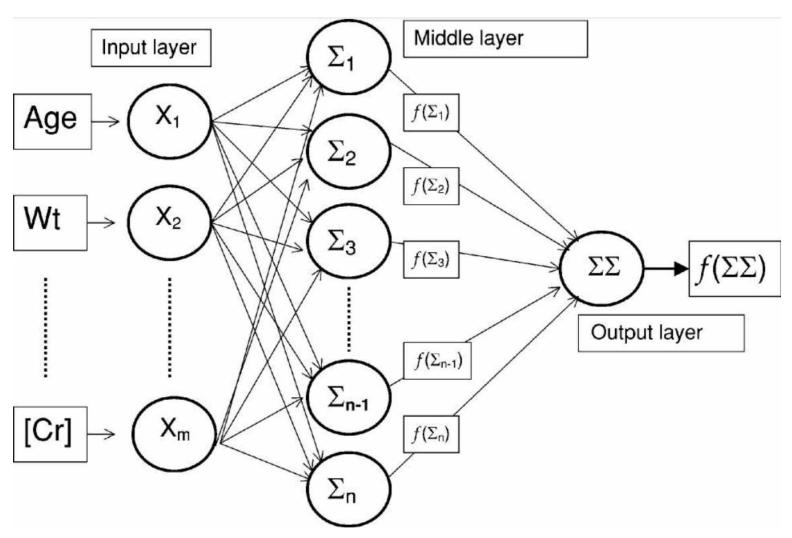
 The n-dimensional input vector x is mapped into variable y by means of the scalar product and a nonlinear function mapping



Han, J., Kamber, M. & Pei, J. (2011) Data Mining: Concepts and Techniques (Third Edition). The Morgan Kaufmann Series in Data Management Systems. San Francisco, Morgan Kaufmann Publishers.

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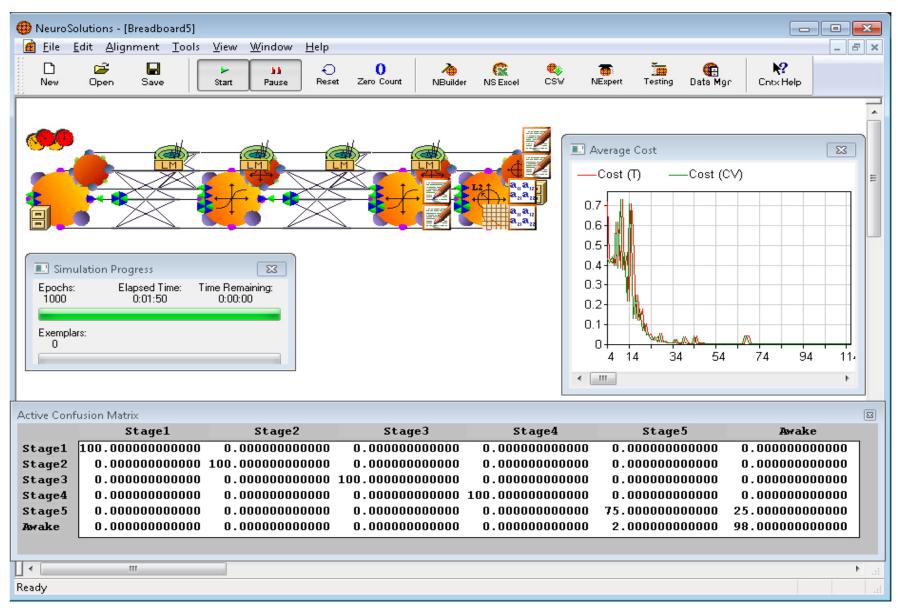




Tangri, N., Ansell, D. & Naimark, D. (2008) Predicting technique survival in peritoneal dialysis patients: comparing artificial neural networks and logistic regression. *Nephrology Dialysis Transplantation*, 23, 9, 2972.

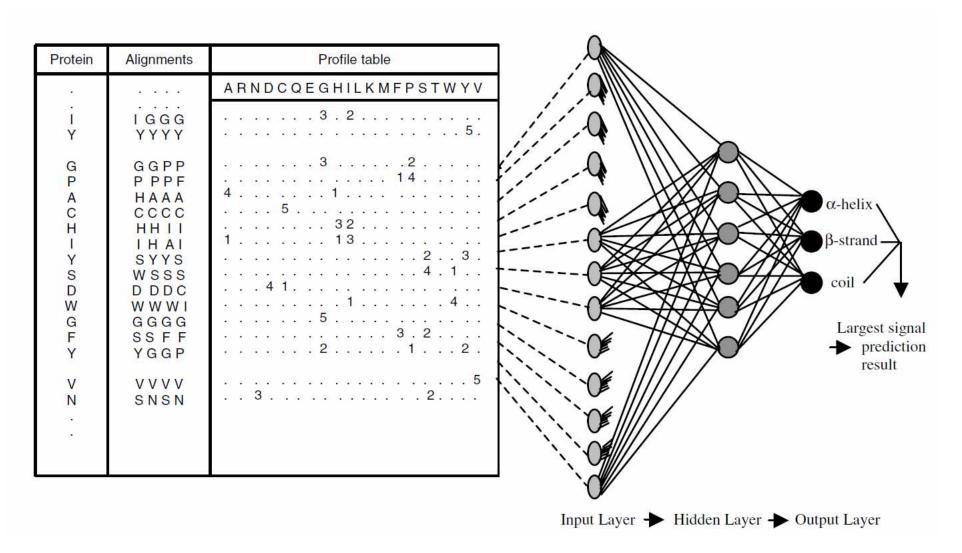
### The Tool of the Liver Transplantation Example





http://www.neurosolutions.com

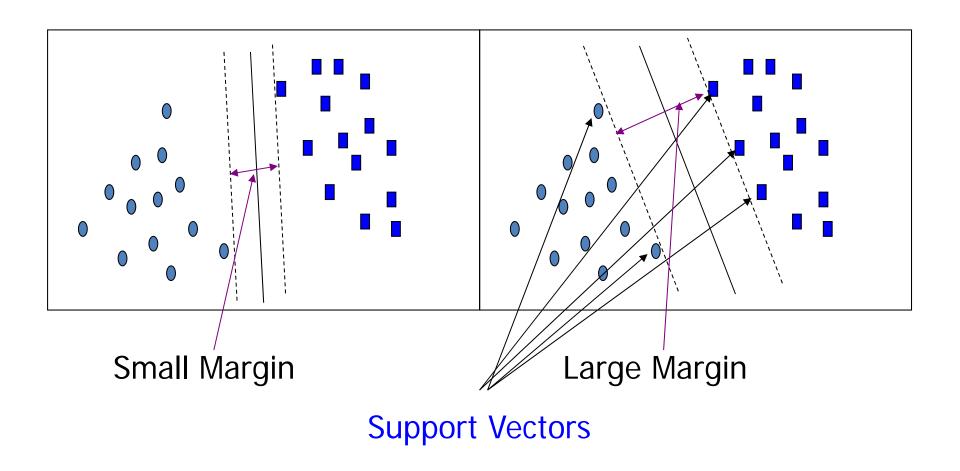




Hu, X. & Pan, Y. 2007. Knowledge discovery in bioinformatics: techniques, methods, and applications, Hoboken (NJ), Wiley.

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Han, J., Kamber, M. & Pei, J. (2011) Data Mining: Concepts and Techniques (Third Edition). The Morgan Kaufmann Series in Data Management Systems. San Francisco, Morgan Kaufmann Publishers.

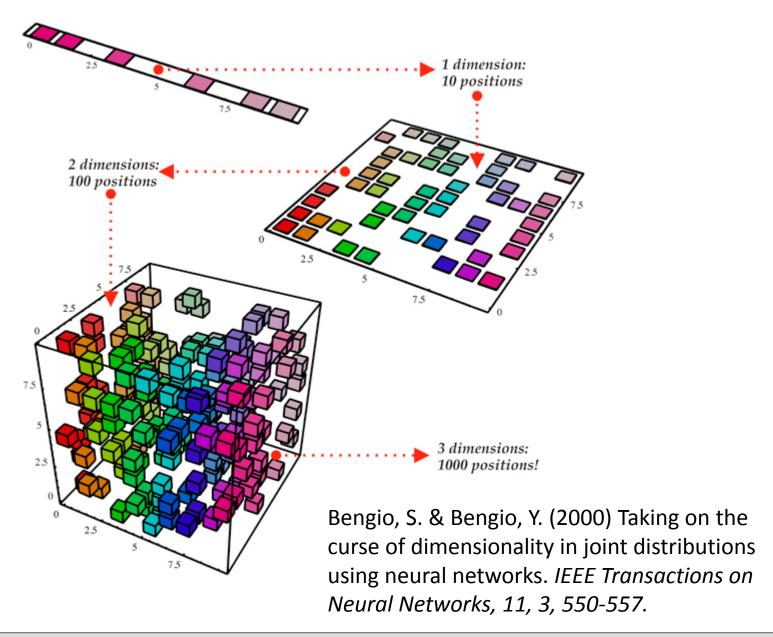


Video removed due to file size

SVM with a polynominal Kernel – Visualization by Udi Aharoni

## **Remember: The Curse of Dimensionality**





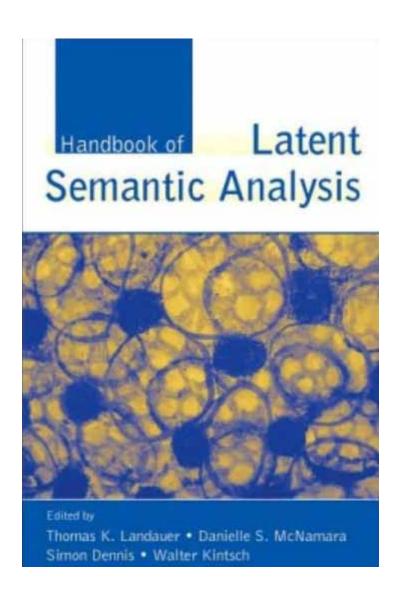
#### SVM advantages in high dimensional data



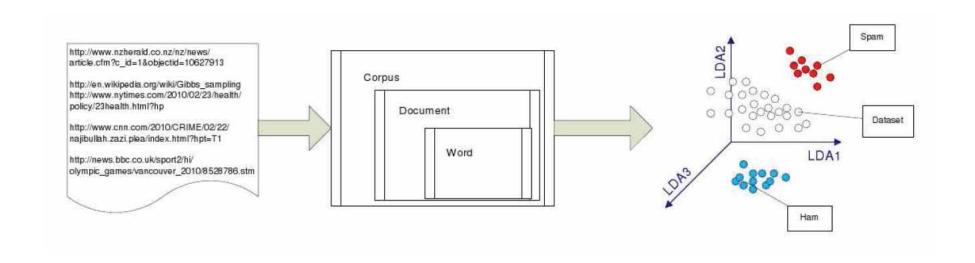
- The complexity of trained classifier is characterized by the # of support vectors – not the dimensionality of the data
- The support vectors are the essential or critical training examples —they lie closest to the decision boundary
- If all other training examples are removed and the training is repeated, the same separating hyperplane would be found
- The number of support vectors found can be used to compute an (upper) bound on the expected error rate of the SVM classifier, which is independent of the data dimensionality
- Thus, an SVM with a small number of support vectors can have good generalization, even when the dimensionality of the data is high

Han, J., Kamber, M. & Pei, J. (2011) Data Mining: Concepts and Techniques (Third Edition). The Morgan Kaufmann Series in Data Management Systems. San Francisco, Morgan Kaufmann Publishers.



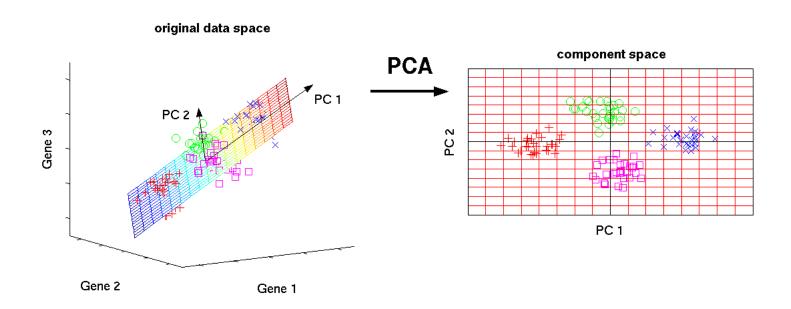






http://www.csmining.org/index.php/latent-dirichlet-allocation.html

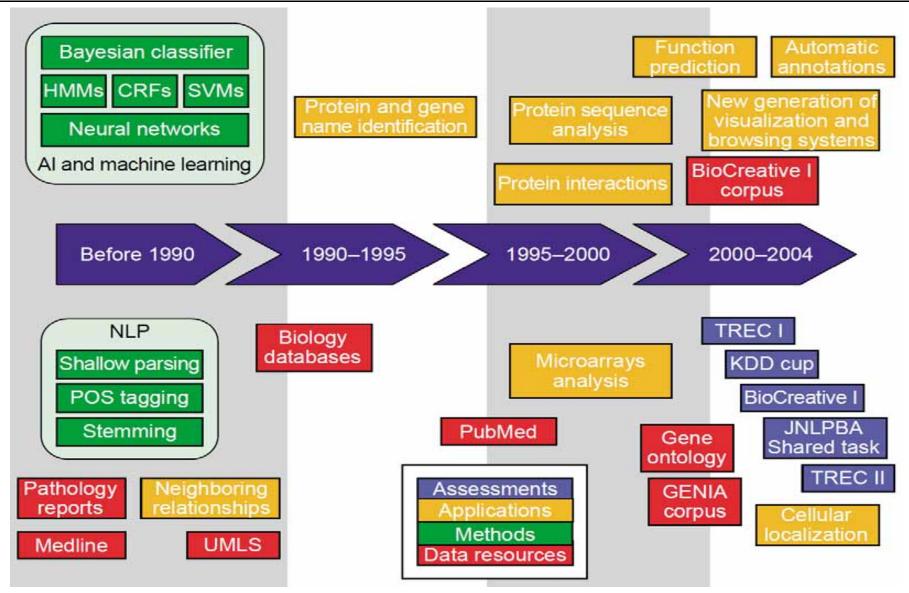




http://www.nlpca.org/pca\_principal\_compone nt\_analysis.html

## History of using NLP in biomedicine and molecular biology

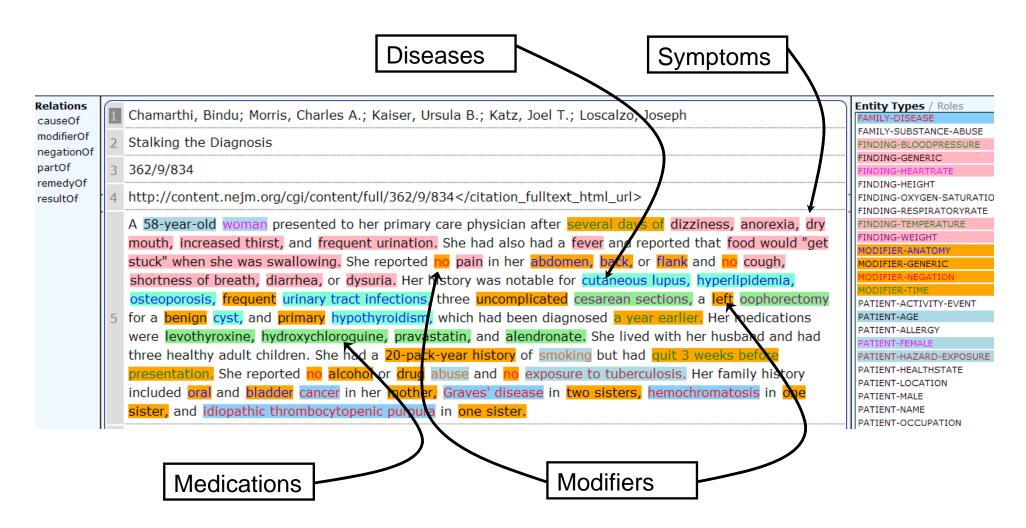




Krallinger, M., Erhardt, R. A. A. & Valencia, A. (2005) Text-mining approaches in molecular biology and biomedicine. *Drug Discovery Today, 10, 6, 439-445.* 

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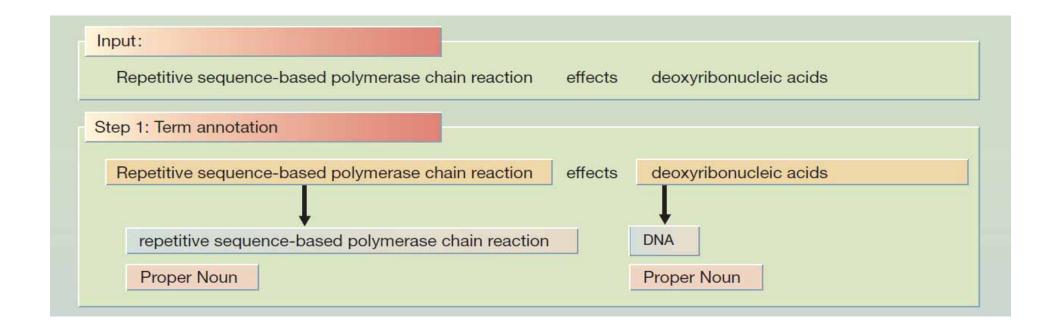




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## **Example: Medical Text Mining process (1)**



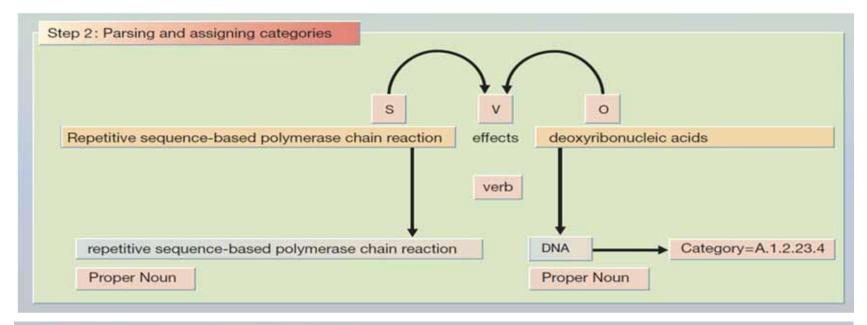


Uramoto, N., Matsuzawa, H., Nagano, T., Murakami, A., Takeuchi, H. & Takeda, K. (2004) A text-mining system for knowledge discovery from biomedical documents. *IBM SYSTEMS JOURNAL, 43, 3, 516-533.* 

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# **Example: Medical Text Mining process (2)**



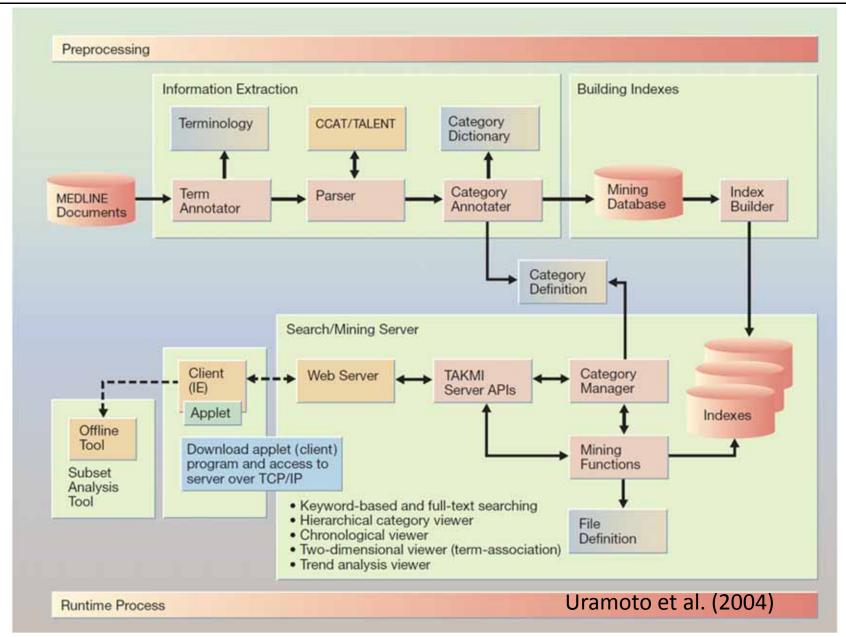


Proper Noun	repetitive sequence-based polymerase chain reaction
A.1.2.23.4	DNA
verb	effect
SV	repetitive sequence-based polymerase chain reaction effect
SV0	repetitive sequence-based polymerase chain reaction effect DNA

Uramoto, N. et al. (2004)

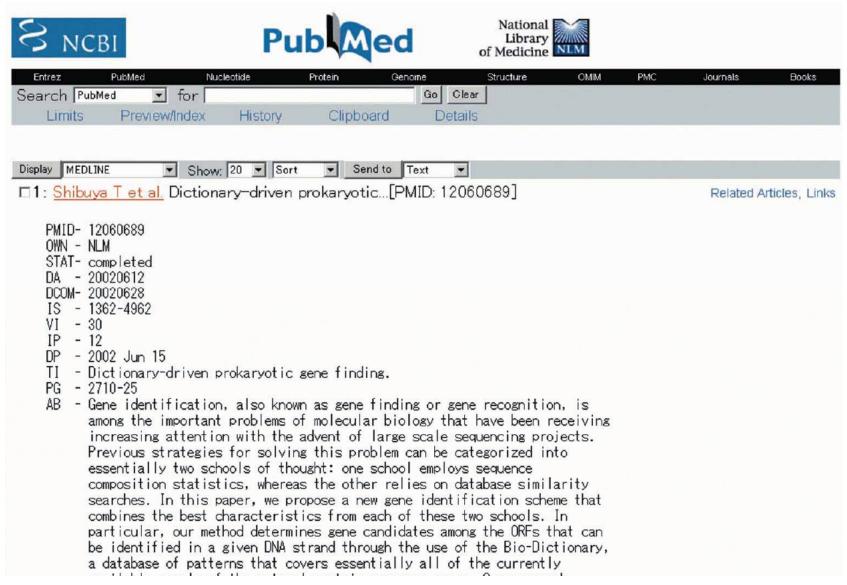
## **Example: Medical Text Mining architecture (3)**





## **Example: Medical Text Mining results (4)**

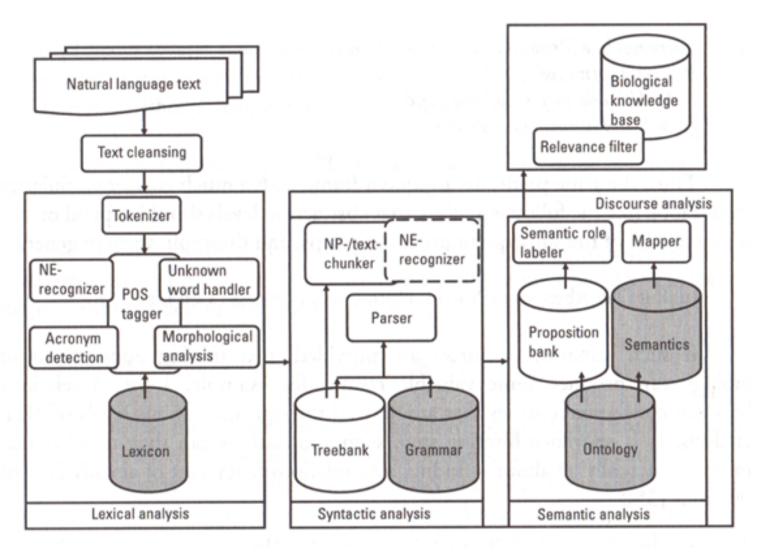




Uramoto et al. (2004)

## NLP system architecture for text mining in biology



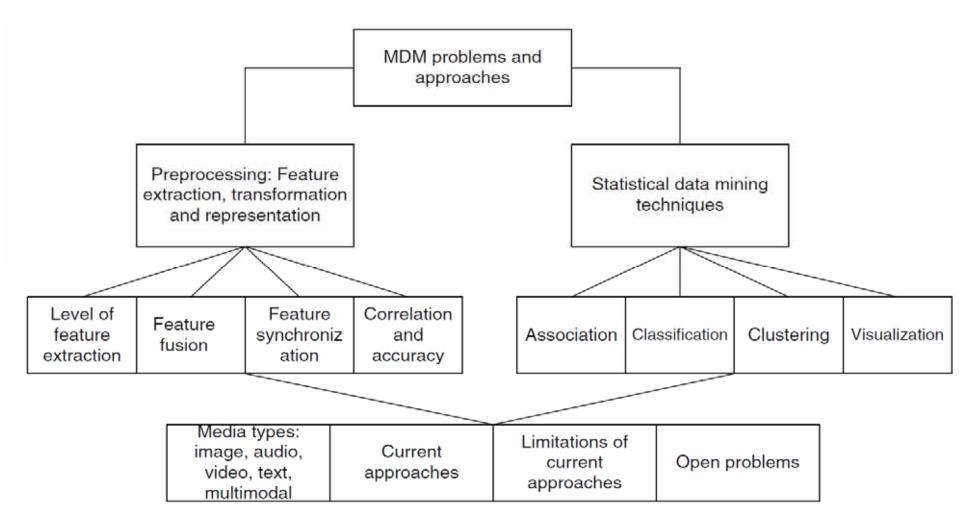


Hahn, U. & Wermter, J. (2006) Levels of Natural Language Processing for Text Mining. In: Ananiadou & McNaught (Eds.) *Text Mining for Biology and Biomedicine. Boston, Artech, 13-41.* 

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## **Summary: Multimedia Data Mining Overview**





Bhatt, C. & Kankanhalli, M. (2011) Multimedia data mining: state of the art and challenges. *Multimedia Tools and Applications*, *51*, *1*, *35-76*.

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## **Slide 6-5 The Knowledge Discovery Process Chain**





**HCI**, Interactive

**Decision Support** 



Visualization, Analytics,

**Topological Data Mining - Pattern Discovery** 

Sampling, Cleansing, Preprocessing, Mapping

**Data Integration Data Fusion** Pre-selection

Privacy, Data Protection, Data Security, Data Safety