Epidemic outbreak prediction by machine learning and artificial intelligence in medical education

What Is Machine Learning?

- A branch of **artificial intelligence**, concerned with the design and development of algorithms that allow computers to evolve behaviors based on empirical data.

- Arthur Samuel (1959). Machine Learning: Field of study that gives computers the ability to learn without being explicitly programmed.

- Tom Mitchell (1998) Well-posed Learning Problem: A computer program is said to learn from **experience E** with respect to some **task T** and some **performance measure P**, if its performance on T, as measured by P, improves with experience E.

What Is Machine Learning? Example

- "A computer program is said to learn from experience E with respect to some task T and some performance measure P, if its performance on T, as measured by P, improves with experience E."
- Suppose your email program watches which emails you do or do not mark as spam, and based on that learns how to better filter spam.
  - Classifying emails as spam or not spam ---> Task T
  - Watching you label emails as spam or not spam ---> Experience E
  - The number (or fraction) of emails correctly classified as spam/not spam ---> Performance measure P

Slide credit: Andrew Ng

ML Applications

The Learning Setting

- Imagine learning algorithm is trying to decide which loan applicants are bad credit risks.
- Might represent each person by n features. (e.g., income range, debt load, employment history, etc.)
- Take sample S of data, labeled according to whether they were/weren't good risks.
- Goal of algorithm is to use data seen so far produce good prediction rule (a "hypothesis") $h(x)$ for future data.

Slide credit: Avrim Blum

The learning setting example

% down	recent delinq?	other accts	mmp/ inc	high debt?	Good risk?
10	N	Y	0.32	N	Y
10	N	N	0.25	Y	Y
5	Y	N	0.30	N	N
20	N	Y	0.31	N	Y
5	N	N	0.42	N	N
10	Y	N	0.38	Y	N
10	N	N	0.25	Y	Y

- Given this data, some reasonable rules might be:
    - Predict YES iff (!recent delinq) AND (%down > 5).
    - Predict YES iff 100*[mmp/inc] – 1*[%down] < 25.
    - ...

Slide credit: Avrim Blum

Big Questions

(A) How might we automatically generate rules that do well on observed data? ---> Algorithms

(B) What kind of confidence do we have that they will do well in the future? ---> Performance Evaluation

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The machine learning framework

$$\mathbf{y} = \mathbf{f}(\mathbf{x})$$

Output Prediction Function Input

Training: given a training set of labeled examples $\{(\mathbf{x}_1,y_1), \ldots, (\mathbf{x}_n,y_n)\}$, estimate the prediction function f by minimizing the prediction error on the training set

- **Testing:** apply f to a never before seen *test example* $\mathbf{x}$ and output the predicted value $y = f(\mathbf{x})$

ML in a Nutshell

- Every machine learning algorithm has three components:
  - Representation
  - Evaluation
  - Optimization

Representation

- Decision trees
- Sets of rules / Logic programs
- Graphical models (Bayes/Markov nets)
- Neural networks
- Support vector machines
- …

Evaluation

- Accuracy
- Precision and recall
- Squared error
- Likelihood
- Posterior probability
- Cost / Utility
- Margin
- Entropy
- K-L divergence
- …

Optimization

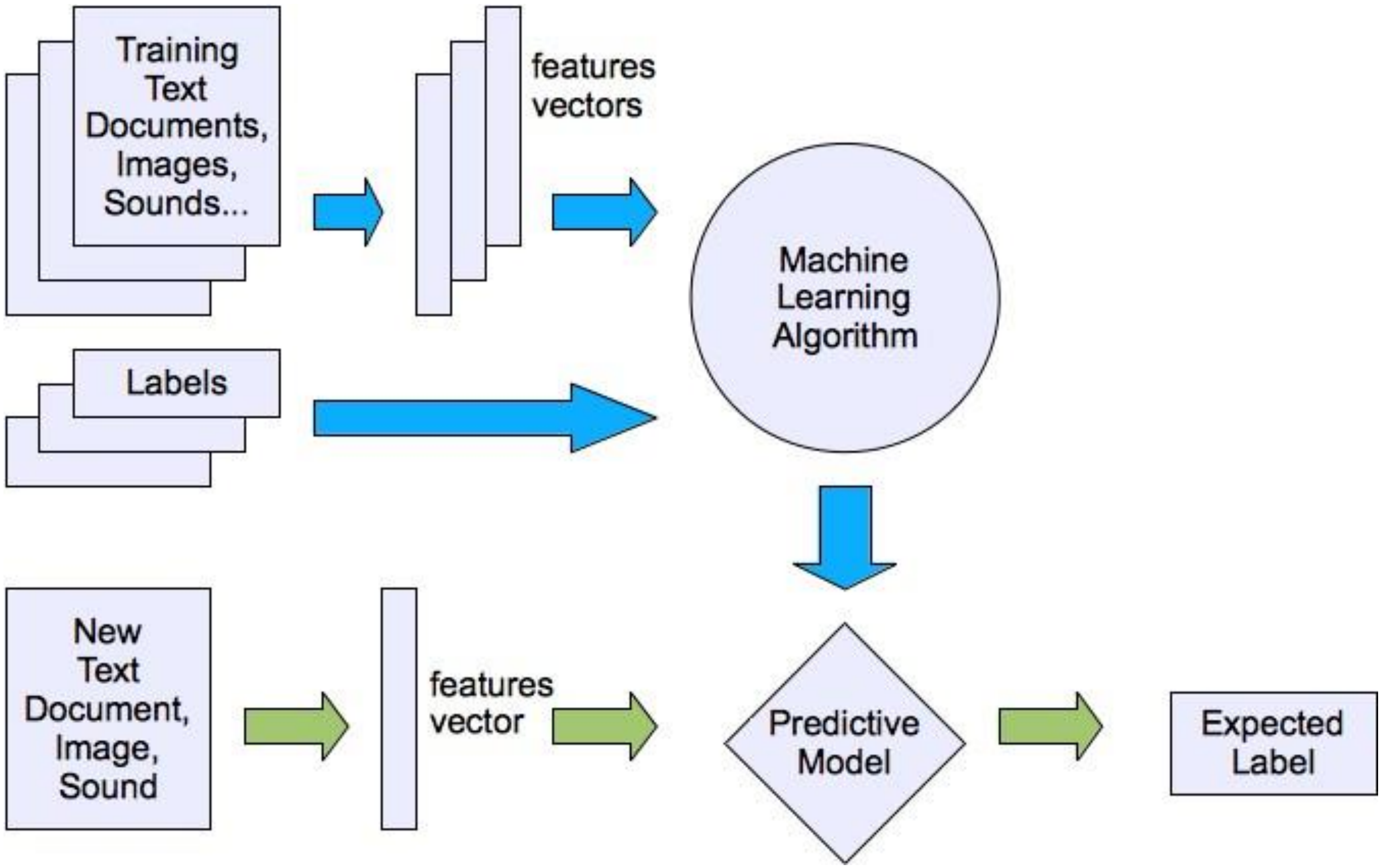
- Combinatorial optimization
  - E.g.: Greedy search
- Convex optimization
  - E.g.: Gradient descent
- Constrained optimization
  - E.g.: Linear programming

Machine Learning Algorithms

- Supervised Learning
  - Training data includes desired outputs
- Unsupervised Learning
  - Training data does not include desired outputs
- Semi-supervised learning
  - Training data includes a few desired outputs

- Others: Reinforcement learning, recommender systems

Supervised Learning

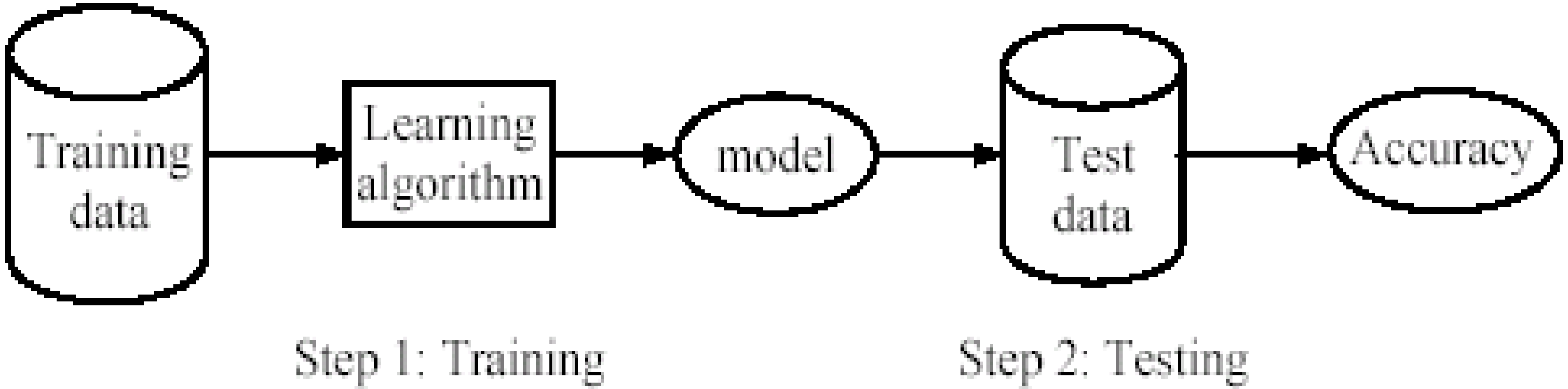


Slide credit: Yi-Fan Chang

Supervised learning process: two steps

- Learning (training): Learn a model using the training data
- Testing: Test the model using unseen test data to assess the model accuracy

$$Accuracy = \frac{\text{Number of correct classifications}}{\text{Total number of test cases}},$$



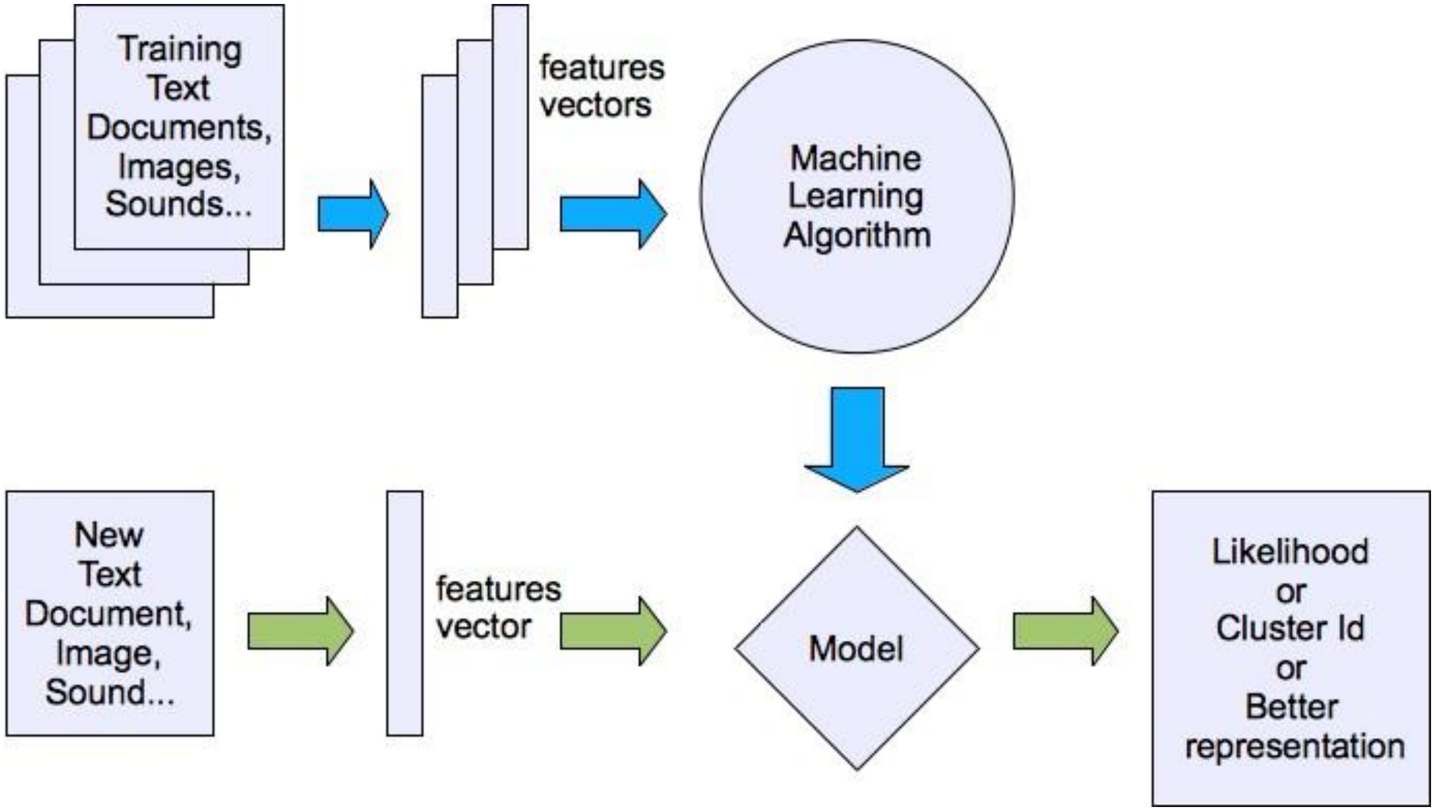
Slide credit: Bing Liu

Unsupervised Learning

- *Learning patterns from unlabeled data*

- Tasks
  - understanding and visualization
  - anomaly detection
  - information retrieval
  - data compression

Unsupervised Learning (Cont.)



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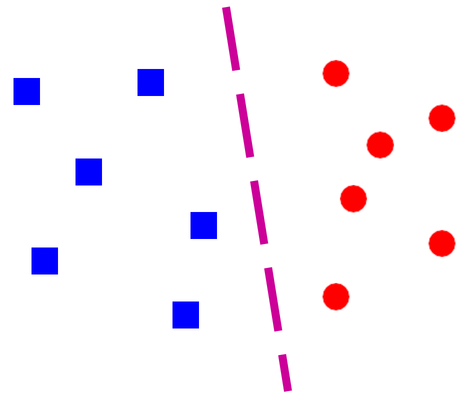
Supervised Learning (Cont.)

- Supervised learning categories and techniques
  - **Linear classifier** (numerical functions)
  - **Parametric** (Probabilistic functions)
    - Naïve Bayes, Gaussian discriminant analysis (GDA), Hidden Markov models (HMM), Probabilistic graphical models
  - **Non-parametric** (Instance-based functions)
    - *K*-nearest neighbors, Kernel regression, Kernel density estimation, Local regression
  - **Non-metric** (Symbolic functions)
    - Classification and regression tree (CART), decision tree
  - **Aggregation**
    - Bagging (bootstrap + aggregation), Adaboost, Random forest

Unsupervised Learning (Cont.)

- Unsupervised learning categories and techniques
  - **Clustering**
    - K-means clustering
    - Spectral clustering
  - **Density Estimation**
    - Gaussian mixture model (GMM)
    - Graphical models
  - **Dimensionality reduction**
    - Principal component analysis (PCA)
    - Factor analysis

Supervised Learning: Linear Classifier

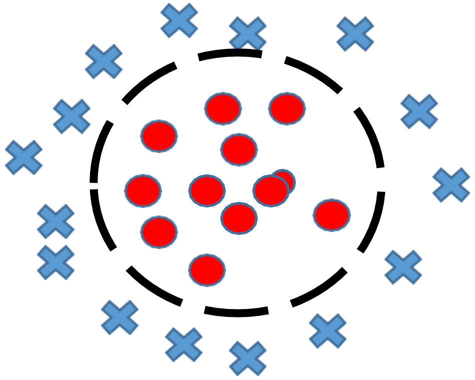


$$g(x_n) = sign(w^T x_n)$$

, where *w* is an *d*-dim vector (learned)

- Find a *linear function* to separate the classes
- Techniques:
  - Perceptron
  - Logistic regression
  - Support vector machine (SVM)
  - Ada-line
  - Multi-layer perceptron (MLP)

Supervised Learning: Non-Linear Classification



$$x_n = [x_{n1}, x_{n2}]$$

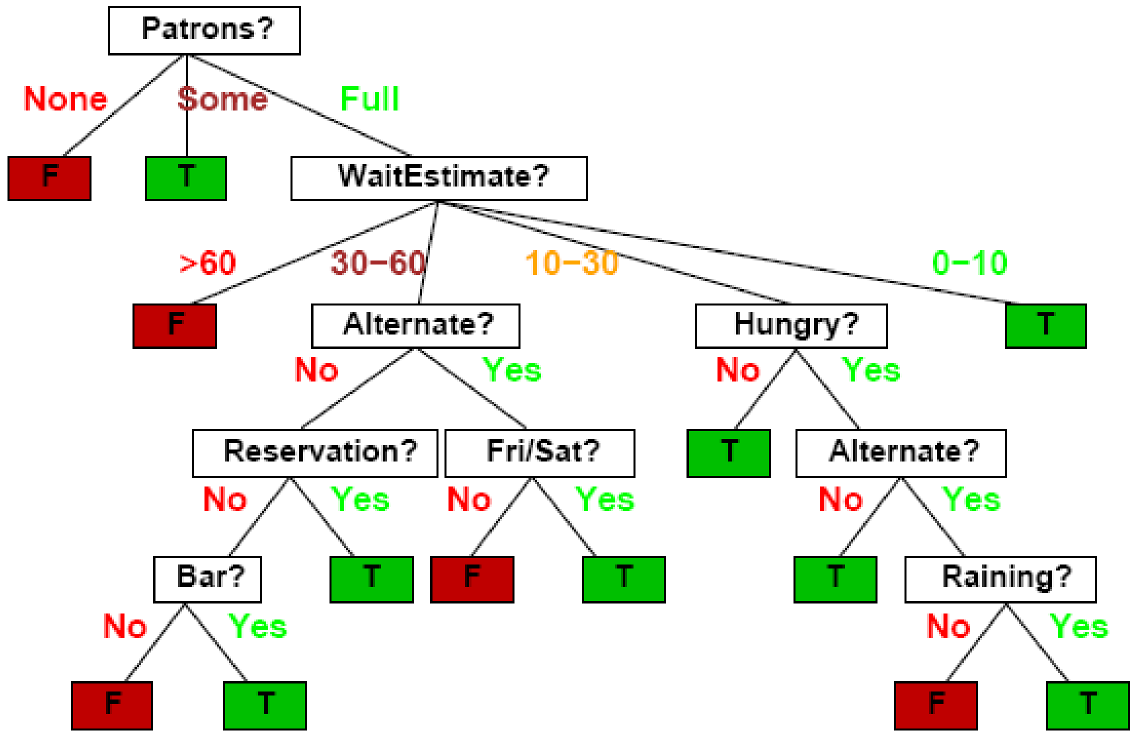
$$x_n = [x_{n1}, x_{n2}, x_{n1} * x_{n2}, {x_{n1}}^2, {x_{n2}}^2]$$

$$g(x_n) = sign(w^T x_n)$$

- Techniques:
  - Support vector machine (SVM)
  - Neural Networks
  - …

Supervised Learning: Decision Trees

Should I wait at this restaurant?



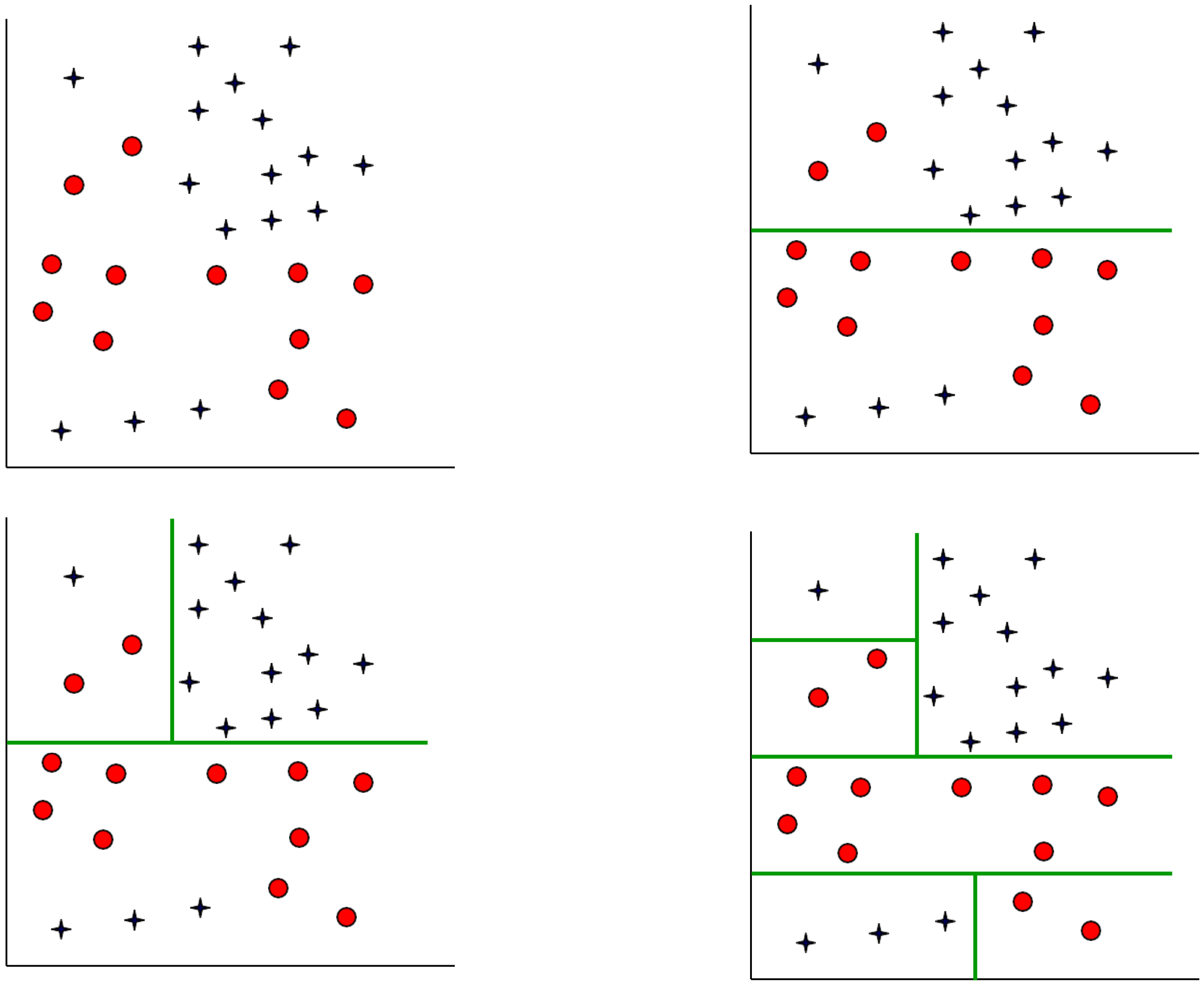
Decision Tree Induction

(Recursively) partition examples according to the *most important* attribute.

Key Concepts

- *entropy*
  - impurity of a set of examples (entropy = 0 if perfectly homogeneous)
  - (#bits needed to encode class of an arbitrary example)
- *information gain*
  - expected reduction in entropy caused by partitioning

Decision Tree Induction: Decision Boundary



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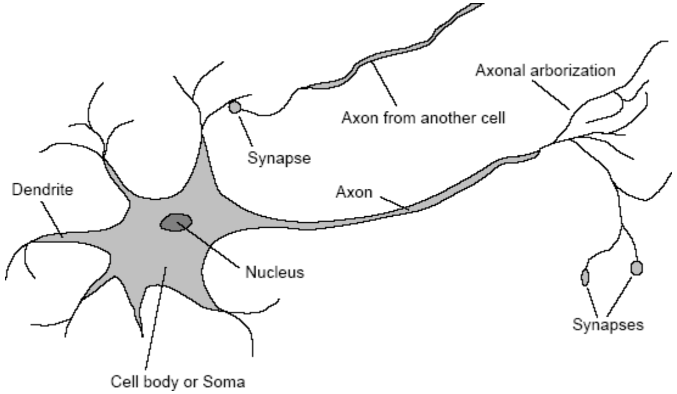
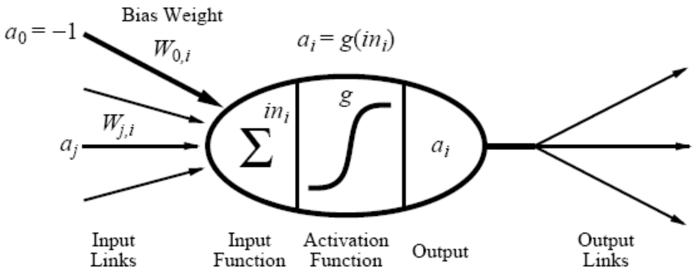
Supervised Learning: Neural Networks

- Motivation: human brain
  - massively parallel (*10^{11} neurons, ~20 types*)
  - small computational units with simple low-bandwidth communication (*10^{14} synapses, 1-10ms cycle time*)

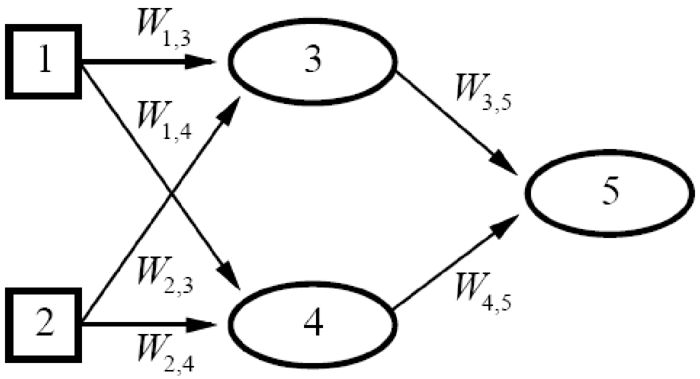


- Realization: neural network
  - *units* (≈ neurons) connected by *directed weighted links*
  - *activation function* from inputs to output

$a_i \leftarrow g(in_i) = g\left(\Sigma_j W_{j,i} a_j\right)$



Neural Networks (*continued*)



$$
\begin{aligned}
a_5 &= g(W_{3,5} \cdot a_3 + W_{4,5} \cdot a_4) \\
&= g(W_{3,5} \cdot g(W_{1,3} \cdot a_1 + W_{2,3} \cdot a_2) + W_{4,5} \cdot g(W_{1,4} \cdot a_1 + W_{2,4} \cdot a_2))
\end{aligned}
$$

- *Neural Network = parameterized family of nonlinear functions types*

Neural Network Learning

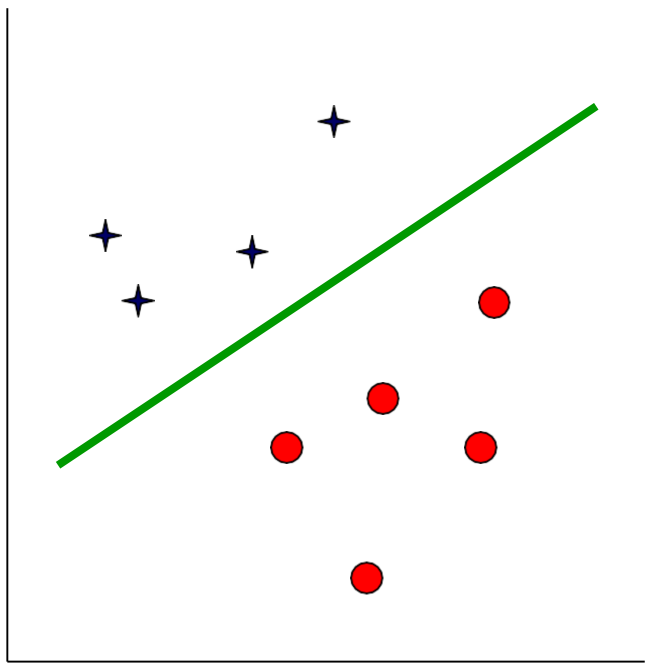
- *Key Idea*: Adjusting the weights changes the function represented by the neural network (*learning = optimization in weight space*).

- Iteratively *adjust weights* to reduce *error* (difference between network output and target output).

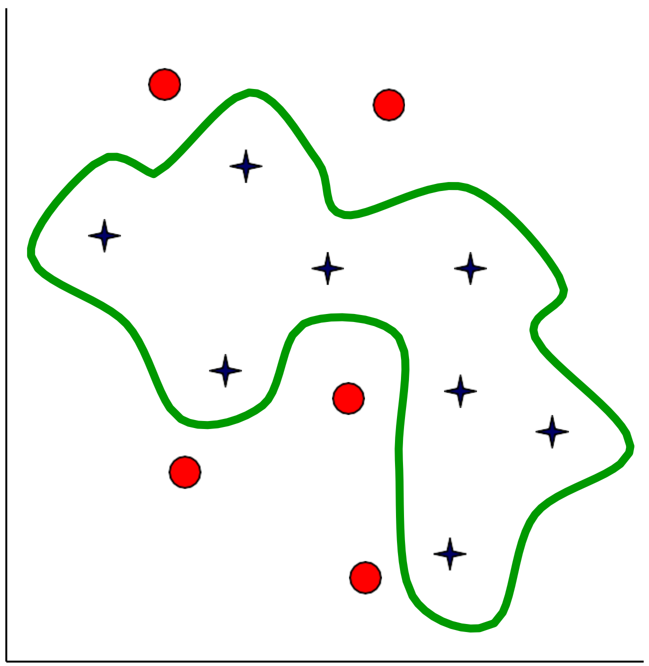
- Weight Update
  - *perceptron training rule*
  - *linear programming*
  - *delta rule*
  - *backpropagation*

Slide credit: SRI International

Neural Network Learning: Decision Boundary



single-layer perceptron

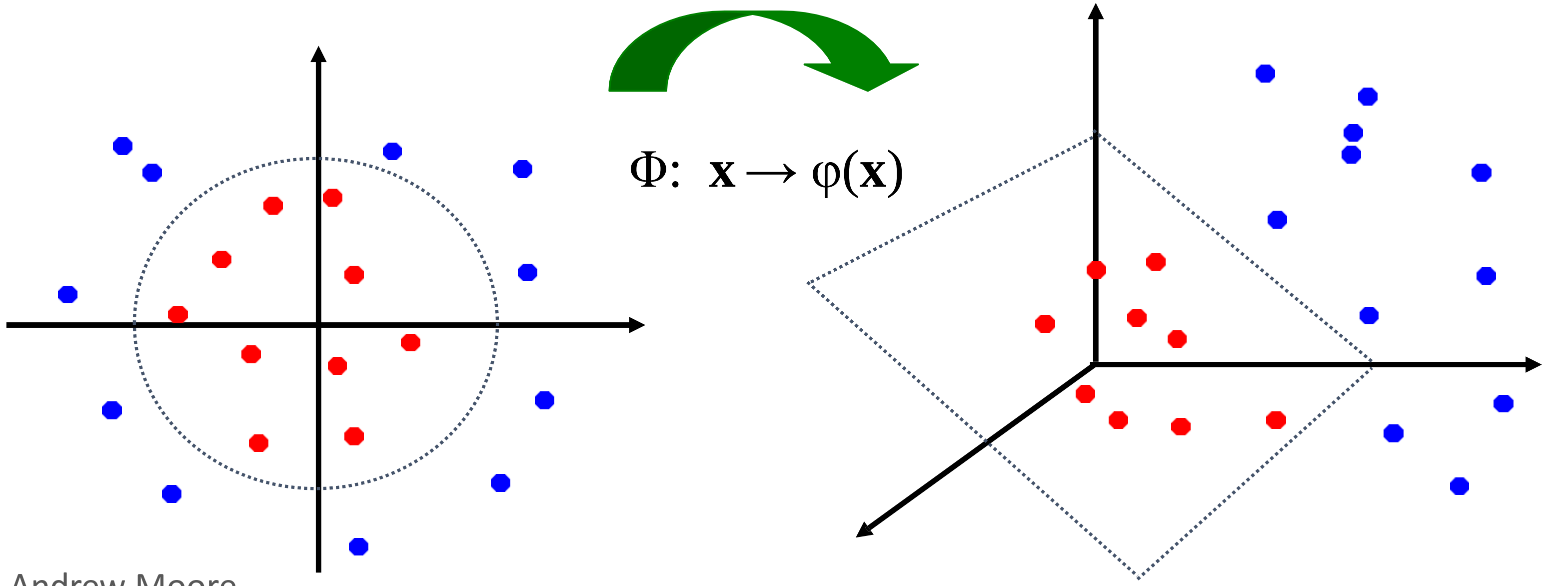


multi-layer network

Slide credit: SRI International

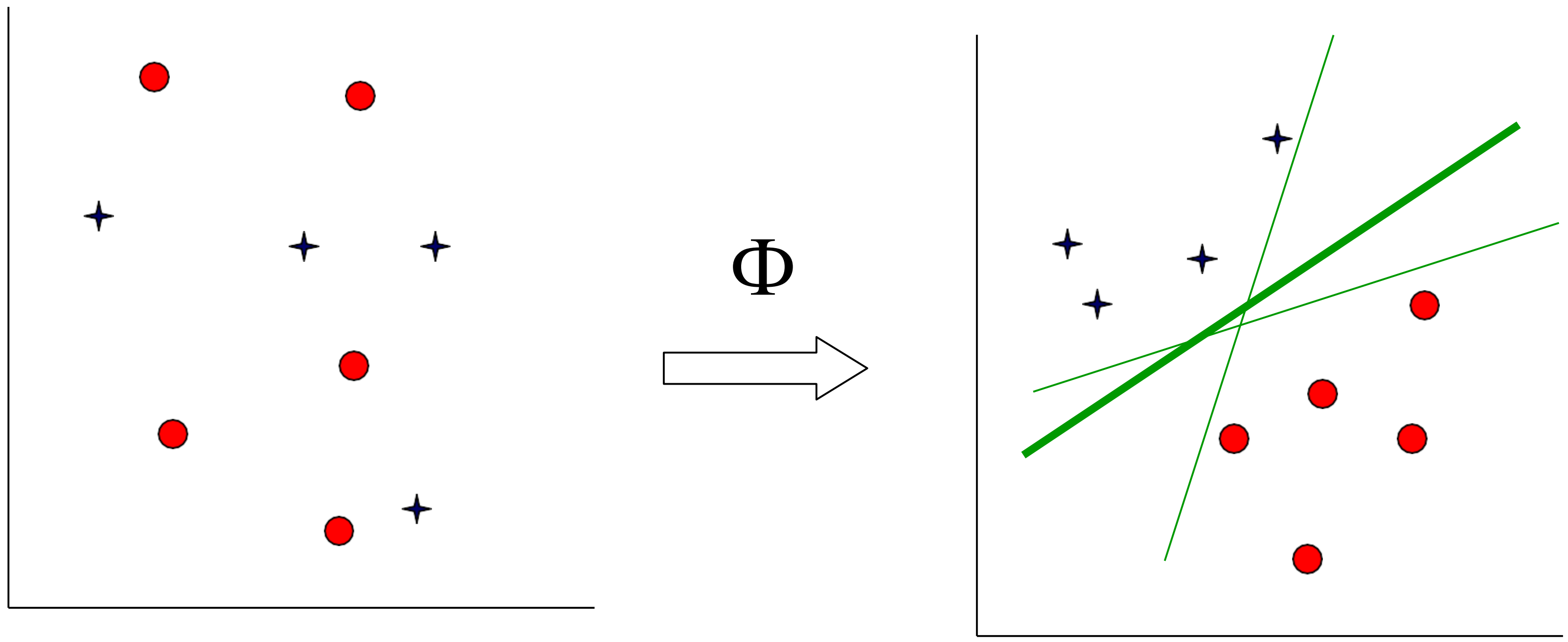
Supervised Learning: Support Vector Machines

- *Kernel Trick*: Map data to *higher-dimensional space* where they will be *linearly separable*.
- Learning a Classifier : optimal linear separator is one that has the *largest margin* between positive examples on one side and negative examples on the other



Slide credit: SRI International & Andrew Moore

Support Vector Machines: Decision Boundary



Supervised Learning: Nearest Neighbor Models

- *Key Idea*: Properties of an input *x* are likely to be *similar* to those of points in the *neighborhood* of *x*.

- *Basic Idea*: Find (*k*) nearest neighbor(s) of *x* and infer target attribute value(s) of *x* based on corresponding attribute value(s).

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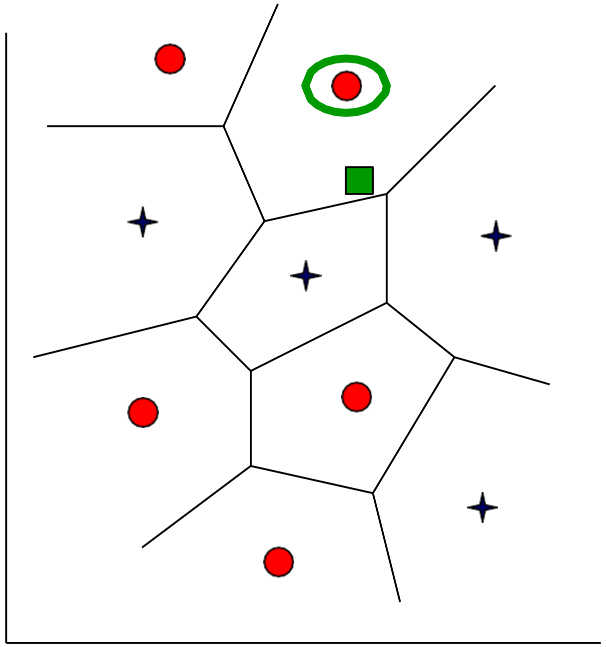
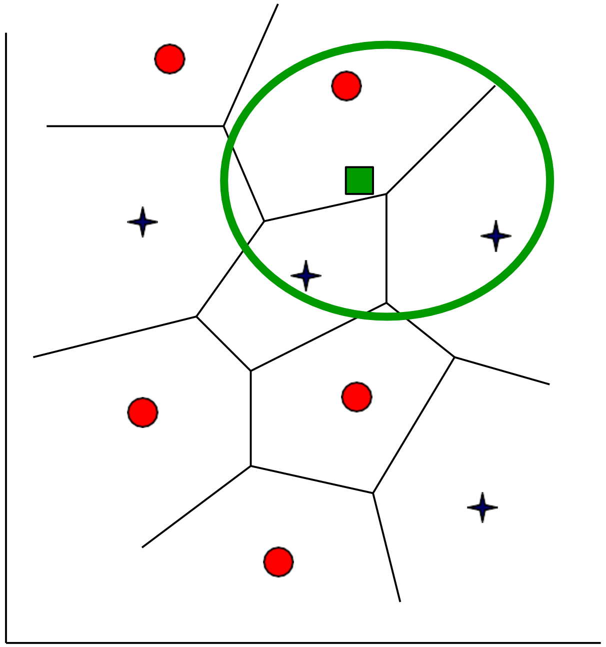
Nearest Neighbor Model: Decision Boundary





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Evaluating classification methods

- Predictive accuracy

$$Accuracy = \frac{\text{Number of correct classifications}}{\text{Total number of test cases}},$$

- Efficiency
  - time to construct the model
  - time to use the model
- Robustness: handling noise and missing values
- Scalability: efficiency in disk-resident databases
- Interpretability:
  - understandable and insight provided by the model
- Compactness of the model

Performance Evaluation

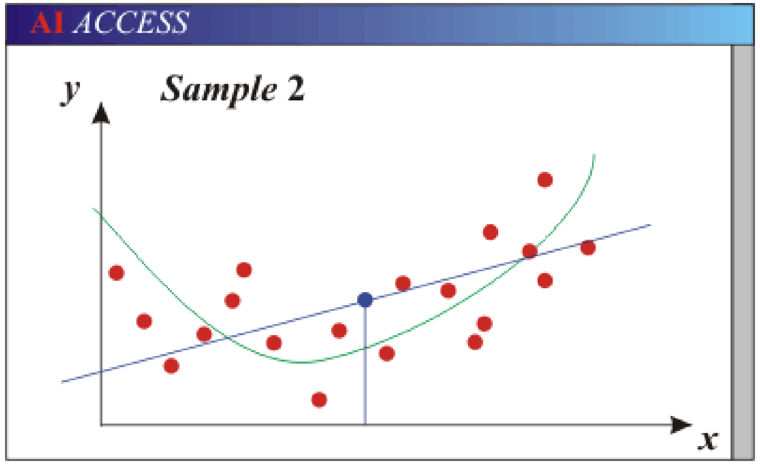
- Randomly split examples into *training set U* and *test set V*.
- Use training set to learn a hypothesis *H*.
- Measure % of *V* correctly classified by *H.*
- Repeat for different random splits and average results.

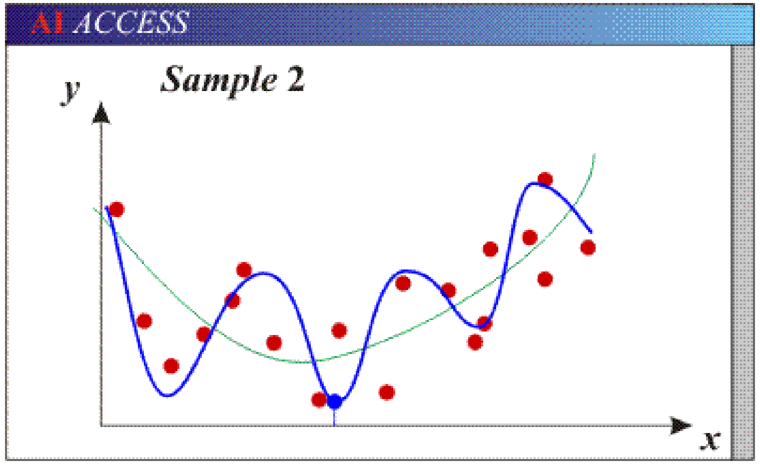
Slide credit: SRI International

Generalization

- Components of generalization error
  - **Bias:** how much the average model over all training sets differ from the true model?
    - Error due to inaccurate assumptions/simplifications made by the model
  - **Variance:** how much models estimated from different training sets differ from each other
- **Underfitting:** model is too “simple” to represent all the relevant class characteristics
  - High bias and low variance
  - High training error and high test error
- **Overfitting:** model is too “complex” and fits irrelevant characteristics (noise) in the data
  - Low bias and high variance
  - Low training error and high test error

Bias-Variance Trade-off





- Models with too few parameters are inaccurate because of a large bias (not enough flexibility).

- Models with too many parameters are inaccurate because of a large variance (too much sensitivity to the sample).

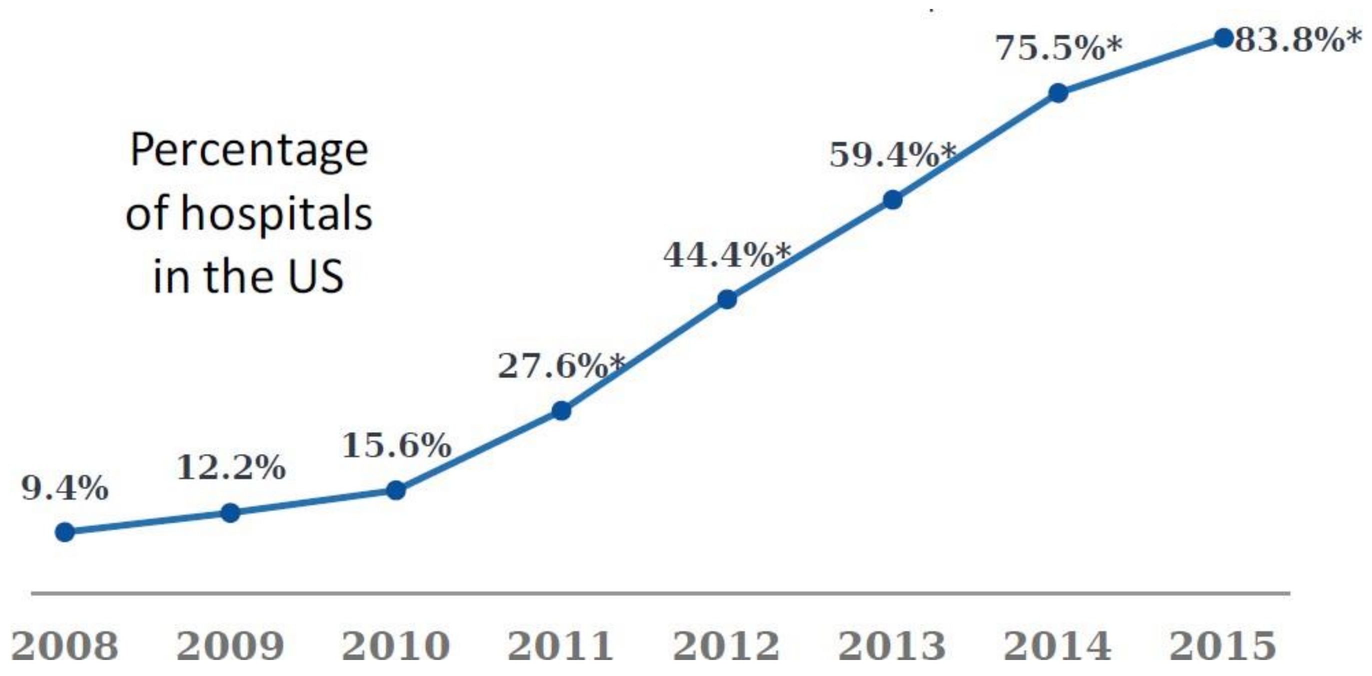
Machine Learning for Healthcare

Applying Machine Learning to Healthcare

- Healthcare sector is being transformed by the ability to record massive amounts of information
- Machine learning provides a way to automatically find patterns and reason about data
- It enables healthcare professionals to move to personalized care known as precision medicine.

Why to use ML?

- Adoption of Electronic Health Records (EHR) has increased 9x since 2008



[Henry et al., ONC Data Brief, May 2016]

Why to use ML?

- Large datasets
  - MIT Laboratory for Computational Physiology de-identified health data from ~40K critical care patients
  - Demographics, vital signs, laboratory tests, medications, notes, …
  - Available data on nearly 230 million unique patients since 1995

Slide credit: David Sontag

Why to use ML?

- Diversity of digital health data

Why to use ML?

- Standardization
  - Diagnosis codes: ICD-9 and ICD-10 (International Classification of Diseases)
  - Laboratory tests: LOINC codes
  - Pharmacy: National Drug Codes (NDCs)
  - Unified Medical Language System (UMLS): millions of medical concepts

[https://blog.curemd.com/the-most-bizarreicd-10-codes-infographic/]

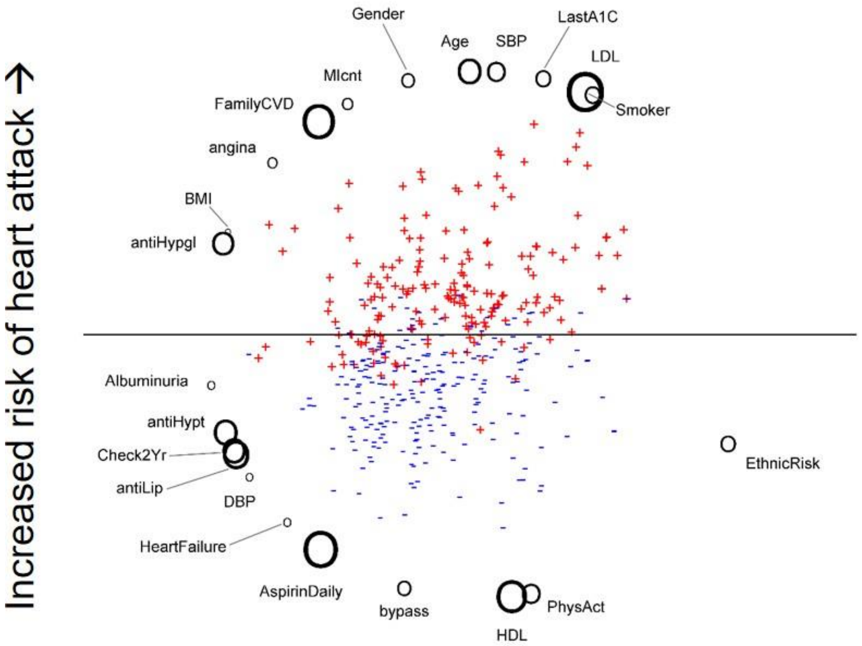
Industry interest in AI & healthcare

What can machine learning do for the healthcare industry?

- Improve accuracy of diagnosis, prognosis, and risk prediction.
- Reduce medi
- Model and s.
- Optimize h nd patient flow.
- Identify pa n medicine.
- Discover ne t practices).
- Automate detection of relevant findings in pathology, radiology, etc.

Improve quality of care and population health outcomes, while reducing healthcare costs.

Example Application: Improve accuracy of diagnosis and risk prediction



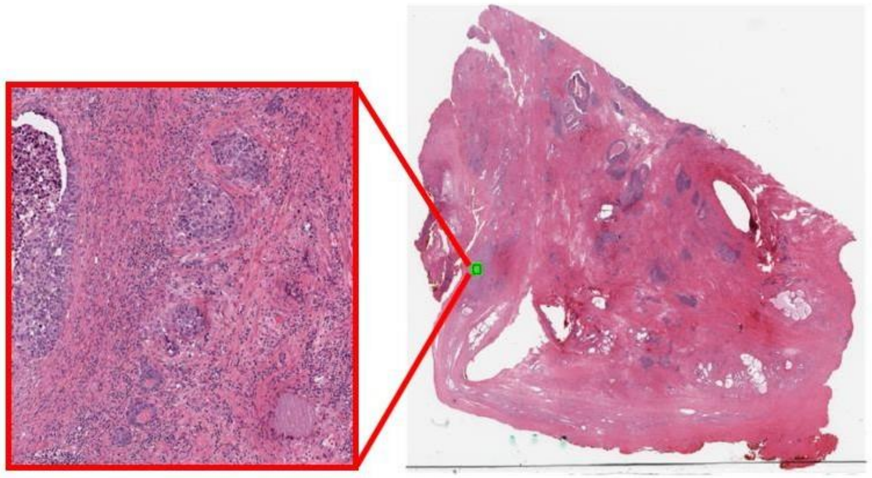
- New methods are developed for chronic disease **risk prediction** and **visualization.**
- These methods give clinicians a comprehensive view of their patient population, risk levels, and risk factors, along with the estimated effects of potential interventions.

Example Application: Optimize hospital processes

- By early and accurate prediction of each patient's **Diagnosis Related Group** (DRG), demand for scarce hospital resources such as beds and operating rooms can be better predicted.

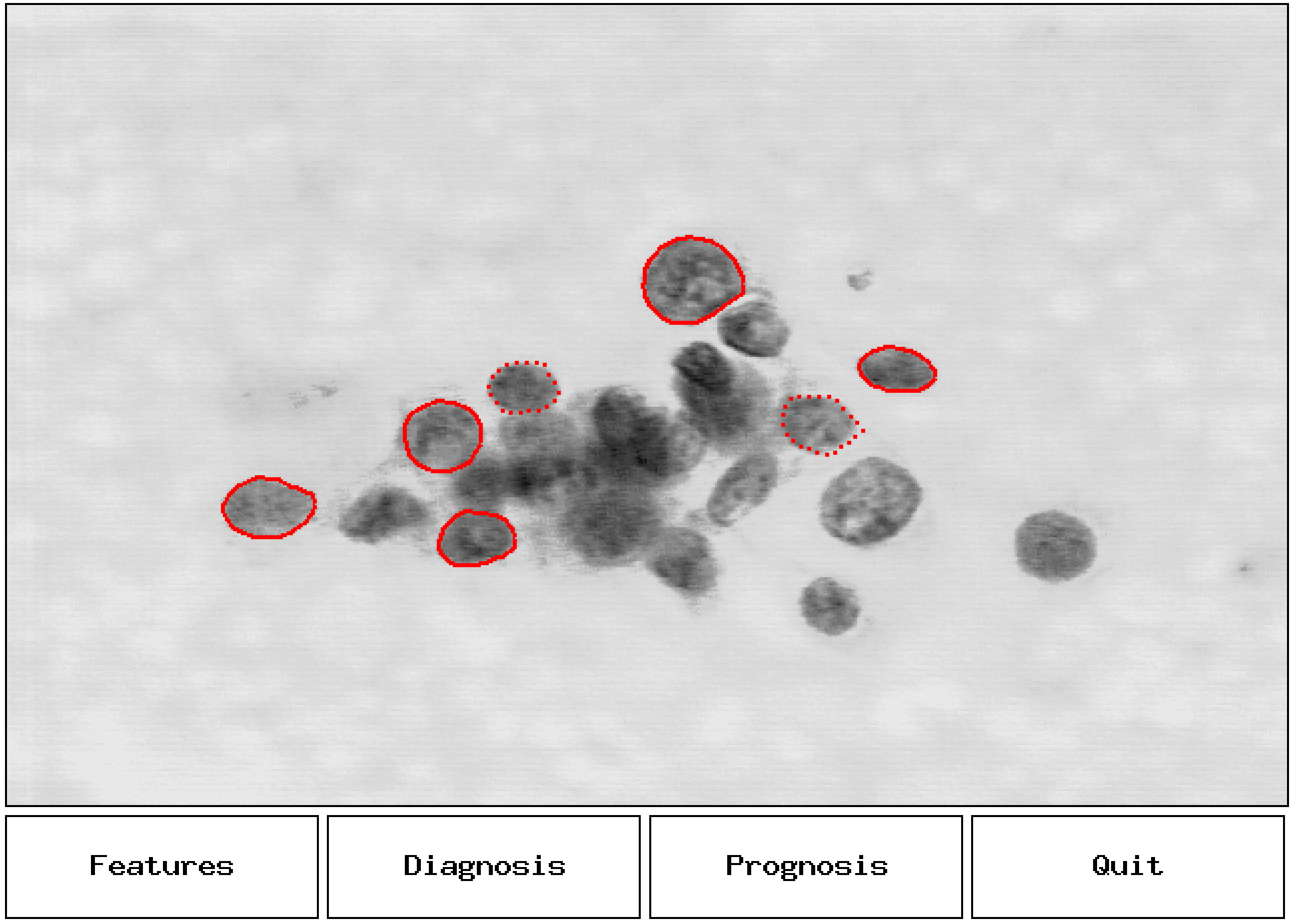
Example Application: Automate detection of relevant findings

- Pattern detection approaches have been successfully applied to detect regions of interest in digital pathology slides, and work surprisingly well to detect cancers.



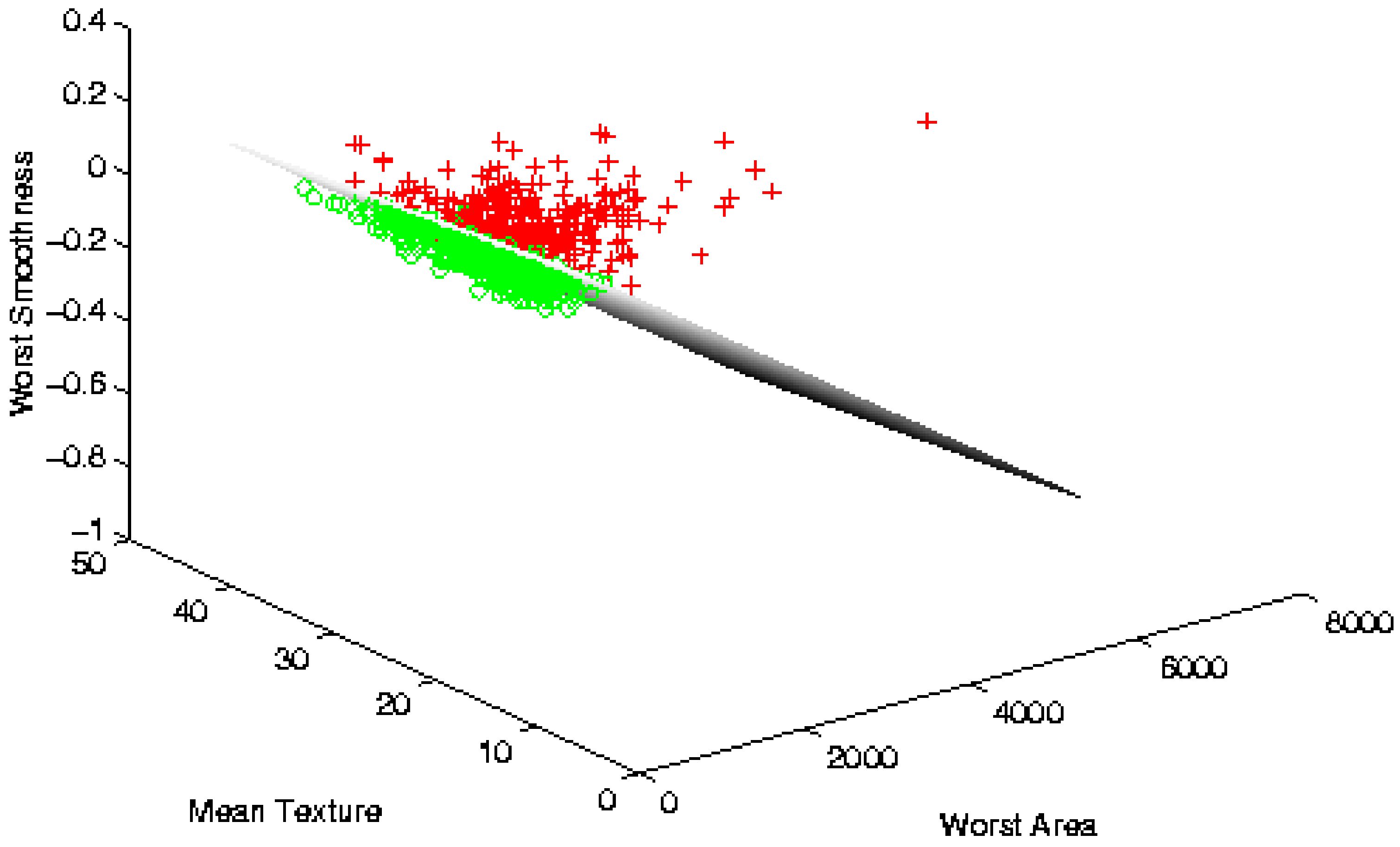
- Automatic detection of anomalies and patterns is especially valuable when the key to diagnosis is a tiny piece of the patient’s health data.

Example Application: Breast Cancer Diagnosis



Research by Mangasarian,Street, Wolberg

Breast Cancer Diagnosis Separation



Research by Mangasarian,Street, Wolberg

Example Application: ICU Admission

- An emergency room in a hospital measures 17 variables (e.g., blood pressure, age, etc) of newly admitted patients.
- A decision is needed: whether to put a new patient in an intensive-care unit.
- Due to the high cost of ICU, those patients who may survive less than a month are given higher priority.
- Problem: to predict high-risk patients and discriminate them from low-risk patients.

What is unique about ML in healthcare?

- Life or death decisions
  - Need robust algorithms
  - Checks and balances built into ML deployment
  - (Also arises in other applications of AI such as autonomous driving)
  - Need fair and accountable algorithms
- Many questions are about unsupervised learning
  - Discovering disease subtypes, or answering question such as “characterize the types of people that are highly likely to be readmitted to the hospital”?
- Many of the questions we want to answer are causal
  - Naïve use of supervised machine learning is insufficient

Slide credit: Bing Liu

What makes healthcare different?

- Often very little labeled data (e.g., for clinical NLP)
  - Motivates semi-supervised learning algorithms
- Sometimes small numbers of samples (e.g., a rare disease)
  - Learn as much as possible from other data (e.g. healthy patients)
  - Model the problem carefully
- Lots of missing data, varying time intervals, censored labels

What makes healthcare different?

- Difficulty of de-identifying data
  - Need for data sharing agreements and sensitivity
- Difficulty of deploying ML
  - Commercial electronic health record software is difficult to modify
  - Data is often in silos; everyone recognizes need for interoperability, but slow progress
  - Careful testing and iteration is needed

Slide credit: Bing Liu