Machine Learning

Wolfgang Huber
Bernd Fischer
EMBL

What you will learn in this lecture

Multivariate classification: least squares, support vector

Model complexity - ‘overfitting’

Cross-validation

Kernel trick

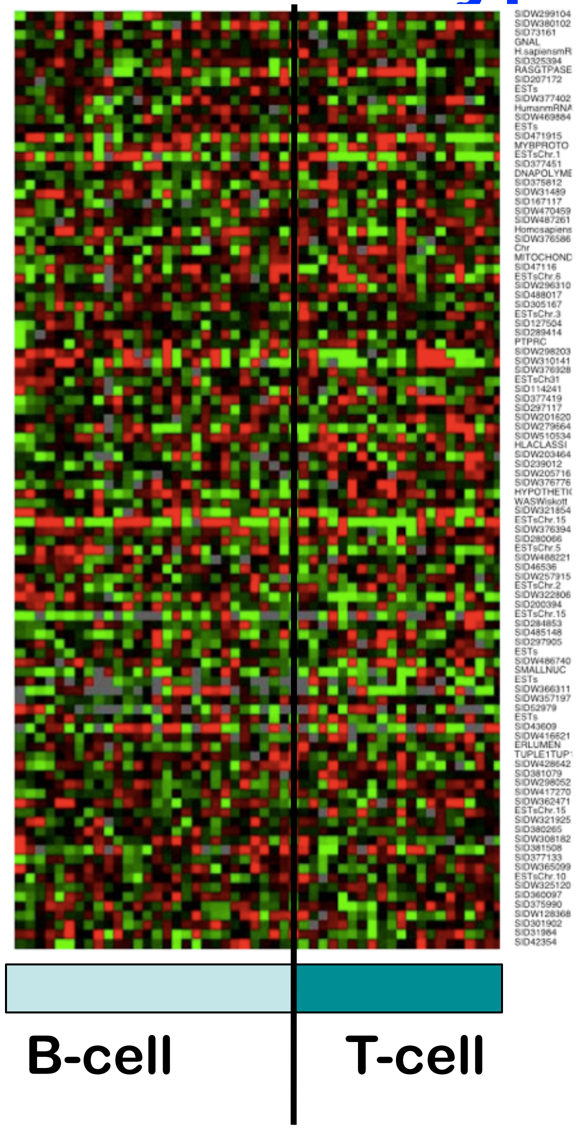
Regularisation, Lasso & Co.

Example: Cancer Subtype Prediction

Differential Expression Analysis:

Which genes are differentially expressed between cancer subtypes?

Output:
p-values or q-values per gene or gene set.



Classification:

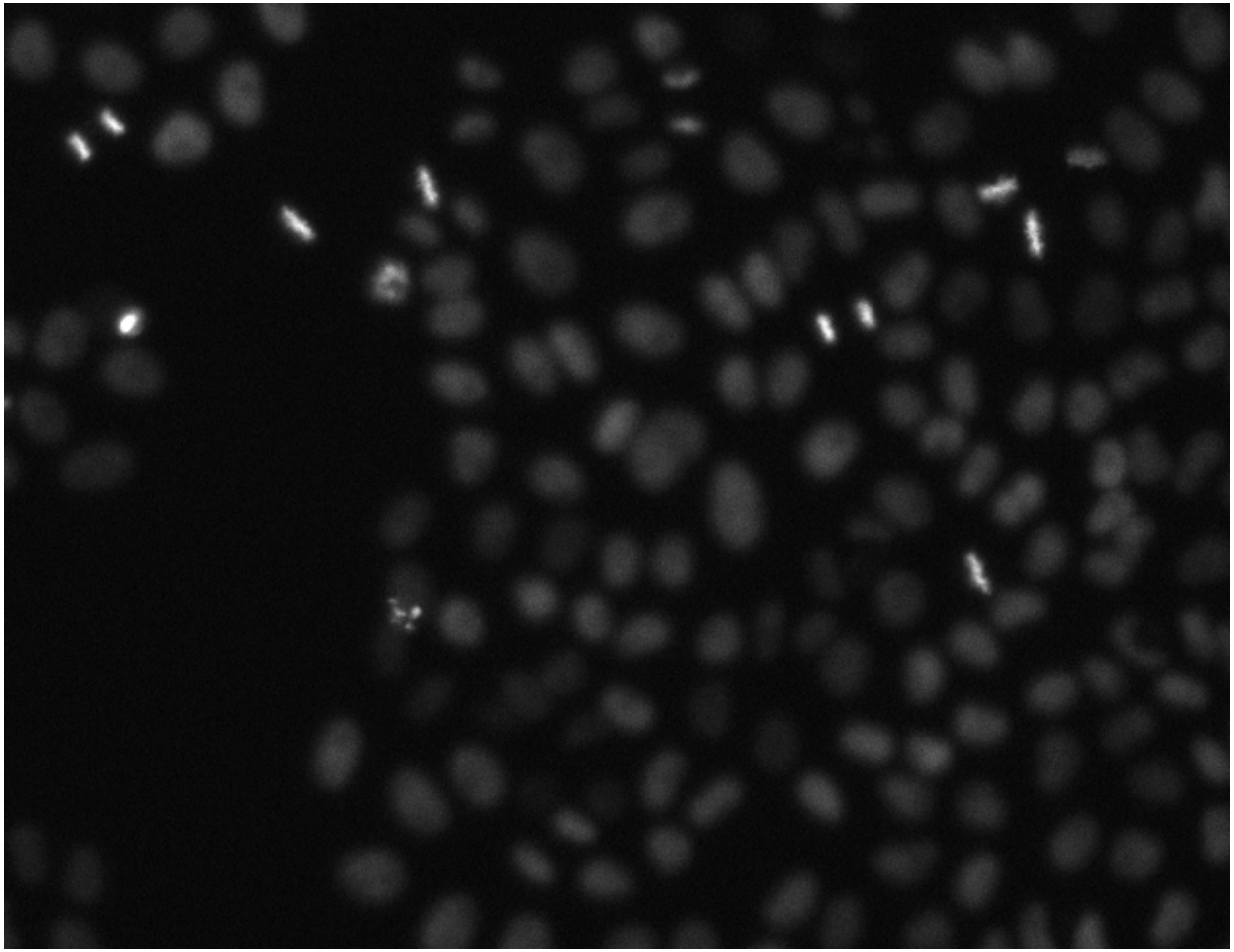
Which cancer subtype does a patient have, given his/her expression profile?

Output:
The cancer subtype of a new patient.

acute lymphoblastic leukemia (ALL)

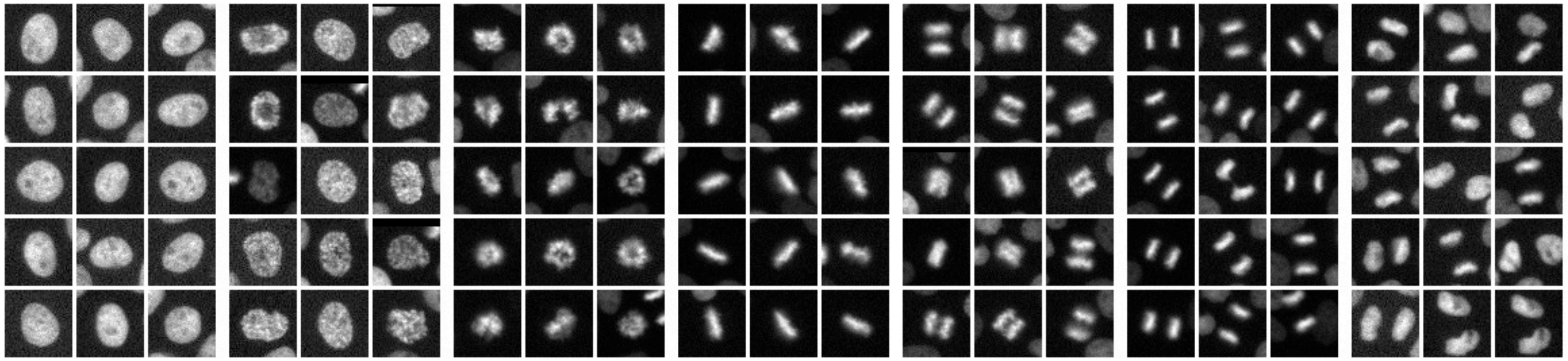
Morphological Phenotyping I

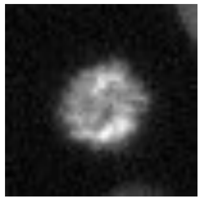
- Image screen with a millions of images



Morphological Phenotyping II

- Provide Human Annotation to a small set of cells:

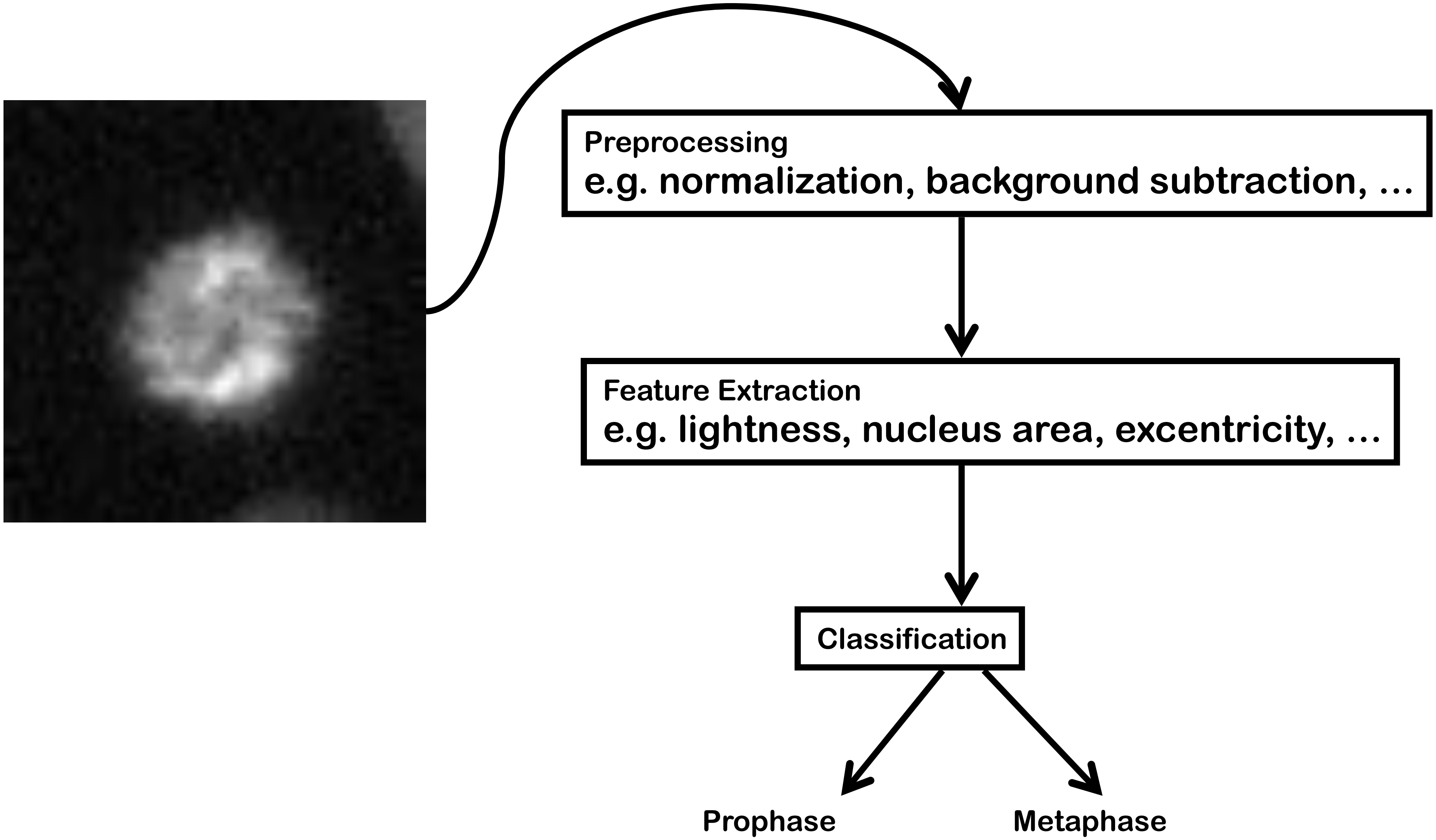




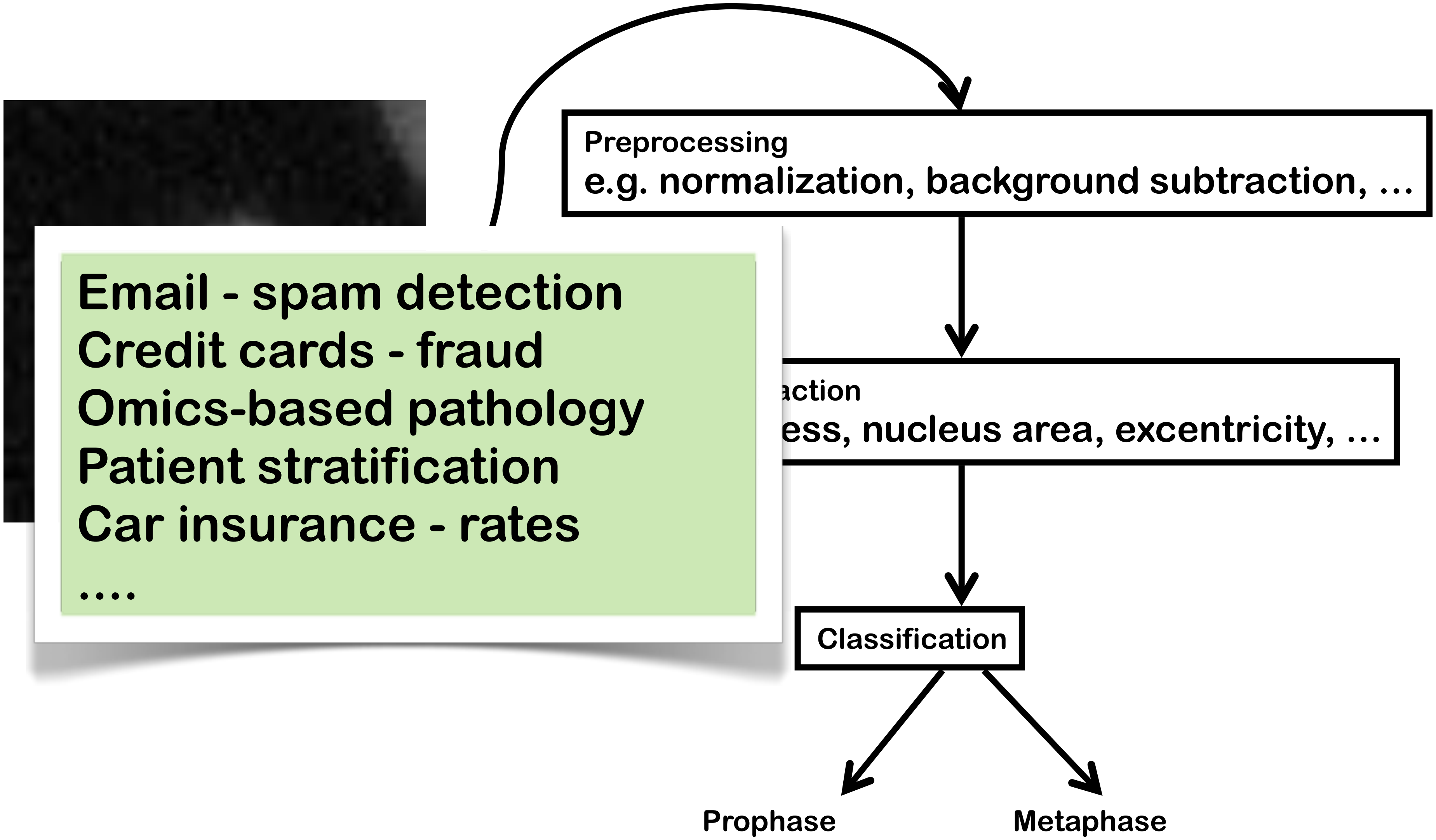
Which mitotic phase?

(Annotate automatically!)

Automatic Classification Workflow


Preprocessing
e.g. normalization, background subtraction, ...
Feature Extraction
e.g. lightness, nucleus area, excentricity, ...
Classification
Prophase
Metaphase

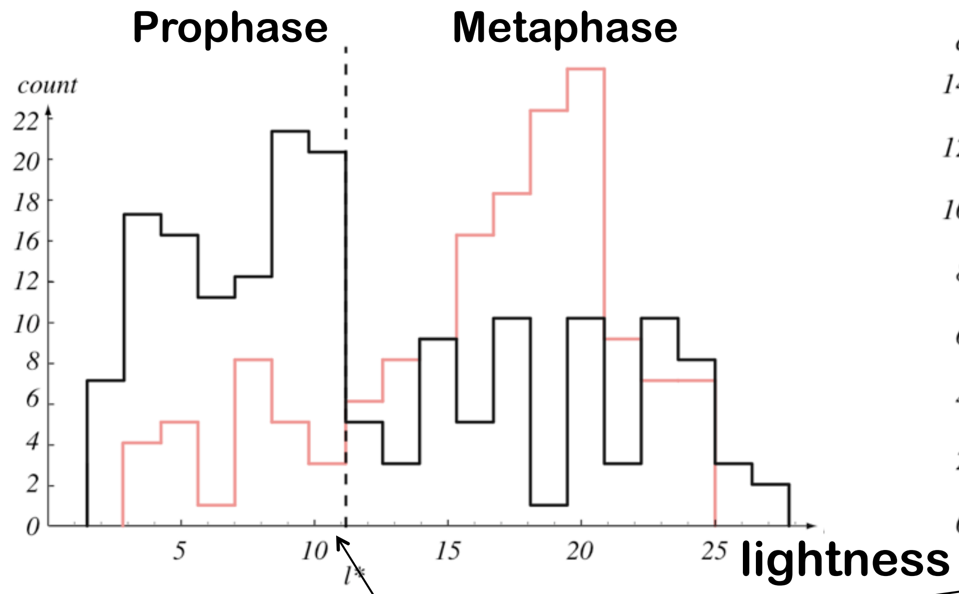
Automatic Classification Workflow


Preprocessing
e.g. normalization, background subtraction, ...
action
ess, nucleus area, excentricity, ...
Classification
Prophase
Metaphase

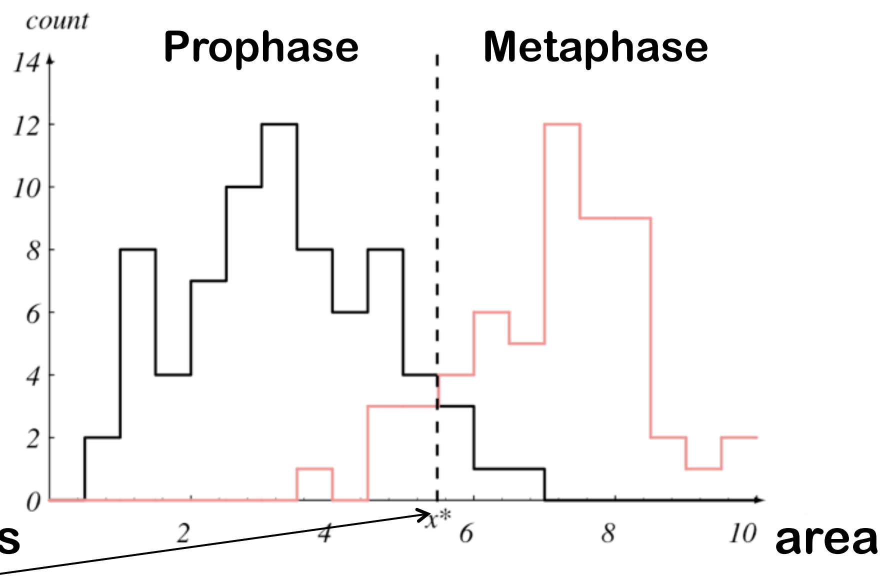
Email - spam detection
Credit cards - fraud
Omics-based pathology
Patient stratification
Car insurance - rates
....

Prophase/ Metaphase Classification

Predict mitotic state based on lightness



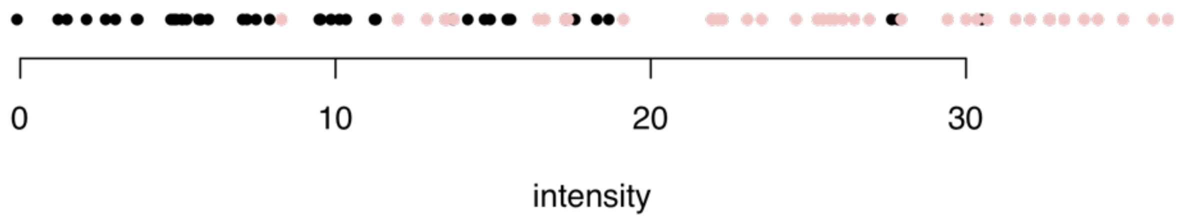
Predict mitotic state based on nucleus area



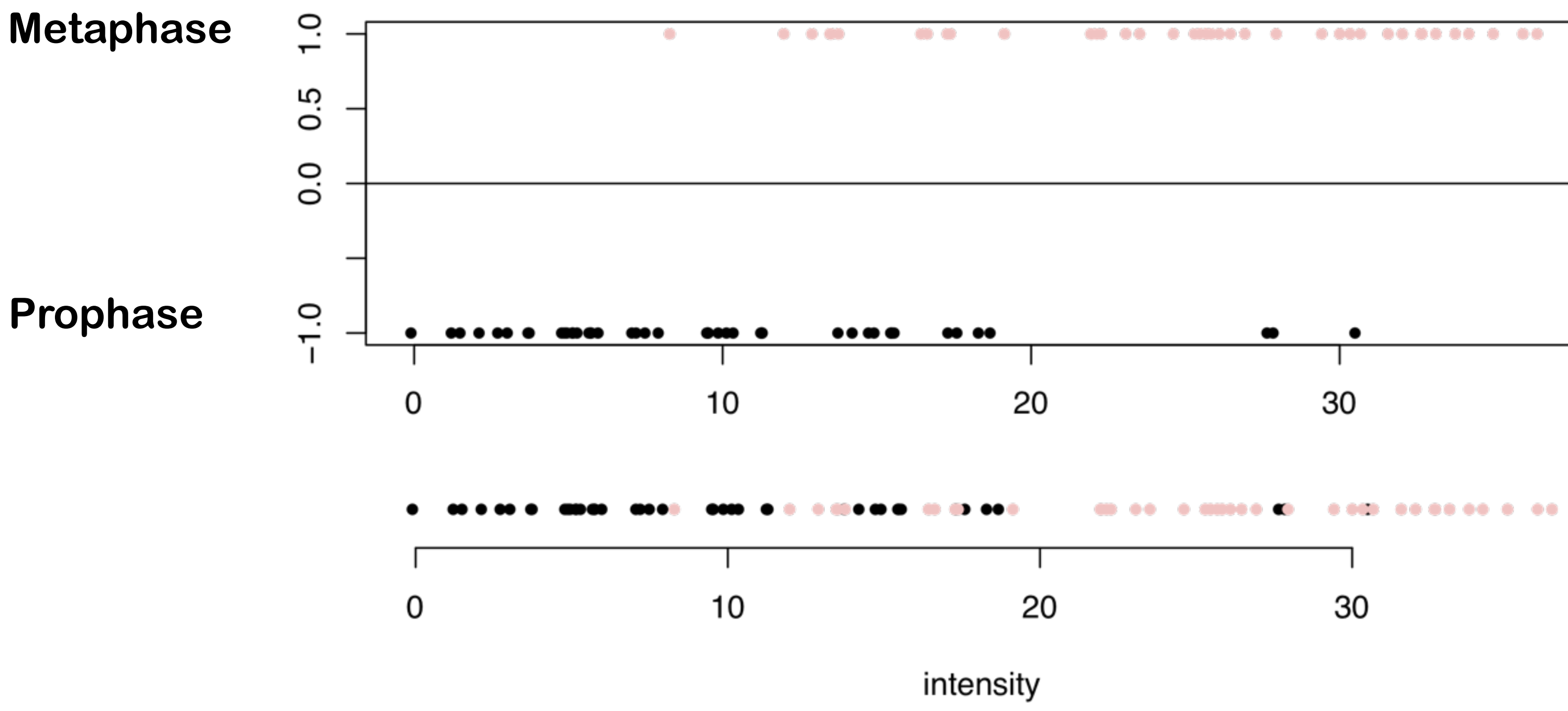
Decision boundary with lowest prediction error

None of the two features individually has a good predictive power

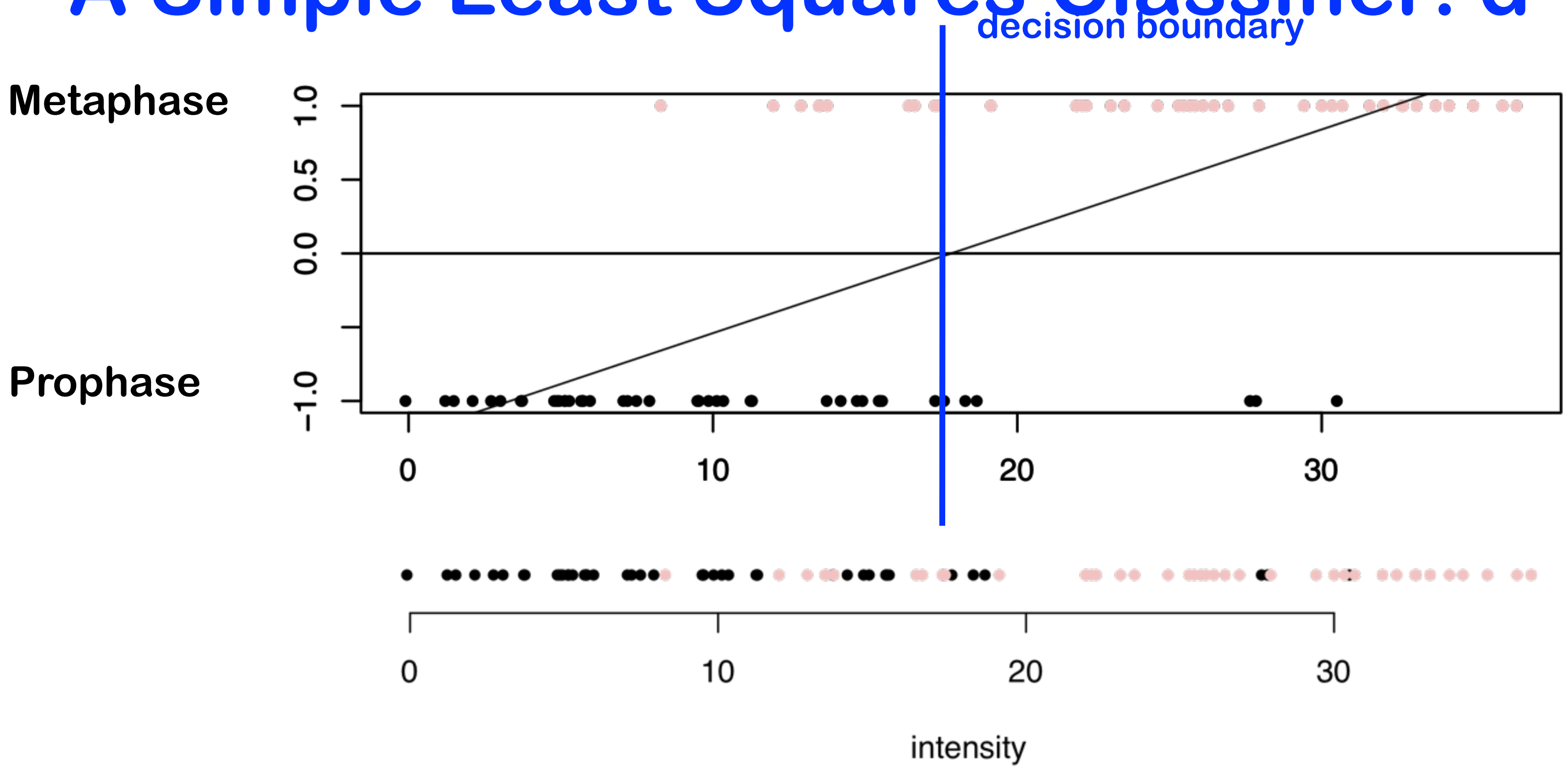
A Simple Least Squares Classifier: d=1



A Simple Least Squares Classifier: d=1

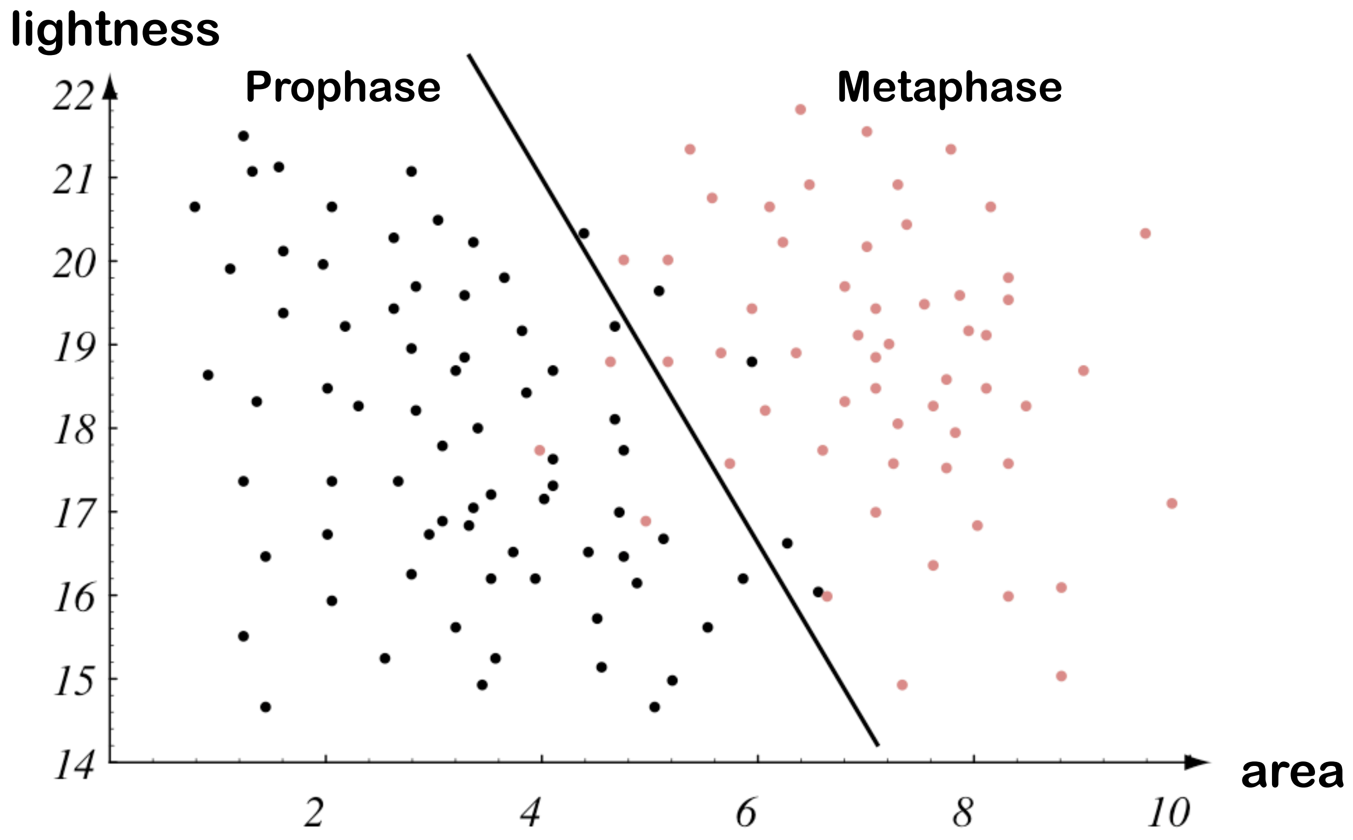


A Simple Least Squares Classifier: d=1



```
y[i]=-1 for pro phase
y[i]=+1 for meta
X[i,]=c(area[i],intensity[i])
model <- lm(y ~ X)
ynew <- predict(model,newdata=Xnew)
ifelse(ynew < 0,-1,1)
```

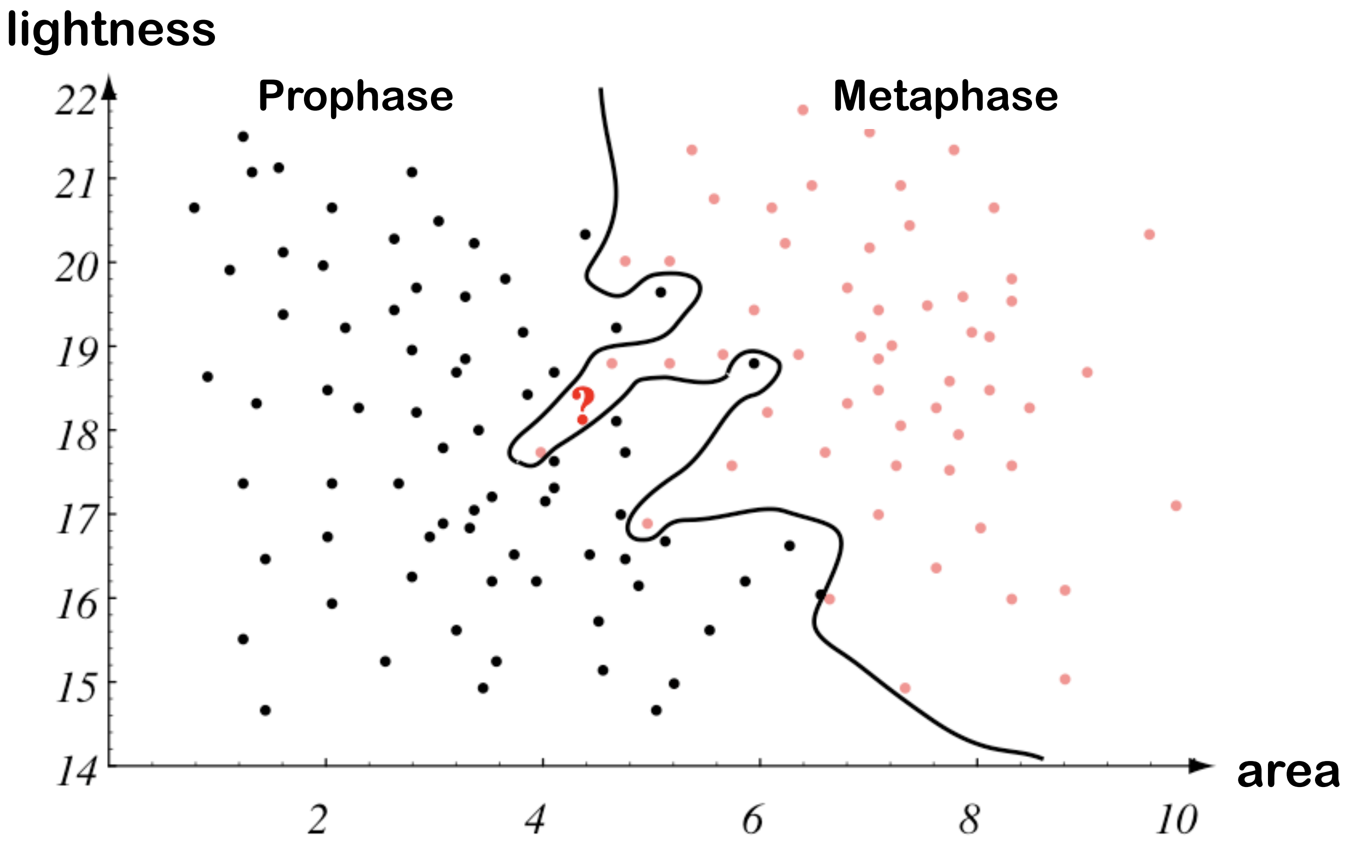
A Simple Least Squares Classifier: d=2



Fit a least squares linear regression model to the data.
Black line shows decision boundary

```
y[i]=+1 for prophase
y[i]=-1 for metaphase
X[i,]=(area[i],lightness[i])
model <- lm.fit(X,y)
ynew <- predict(model,Xnew)
          $fitted.values
ifelse(ynew < 0,-1,1)
```

k-Nearest-Neighbor Classifier



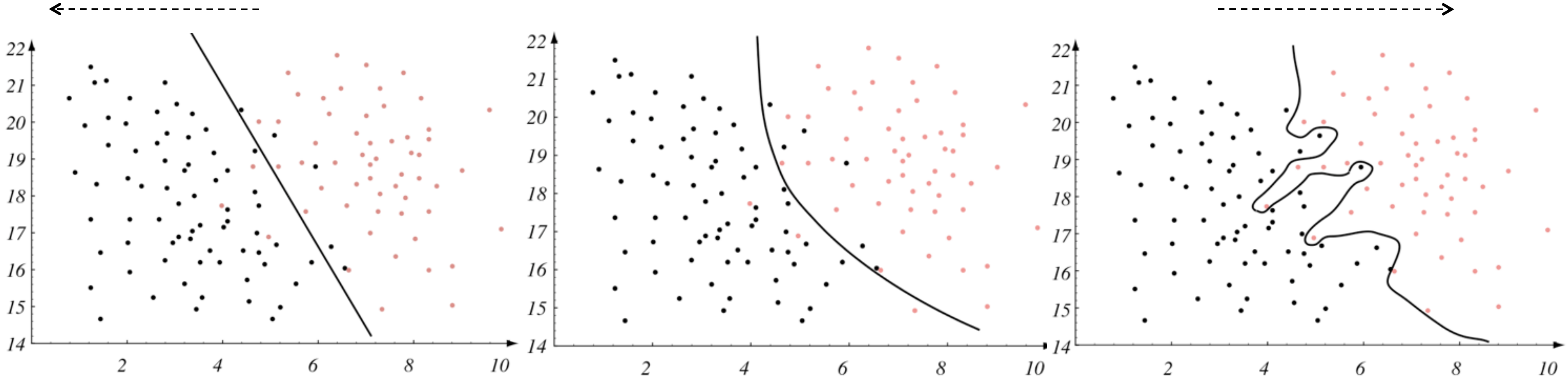
Assign each new cell to the class of its nearest neighbor.
Black line shows decision boundary

```
y[i]=+1 for pro phase
y[i]=-1 for meta phase
X[i,]=(area[i],lightness[i])
library(class)
d = knn(X,Xnew,y,k=1)
```

Which Decision Boundary?

High bias
Low variance

Low bias
High variance

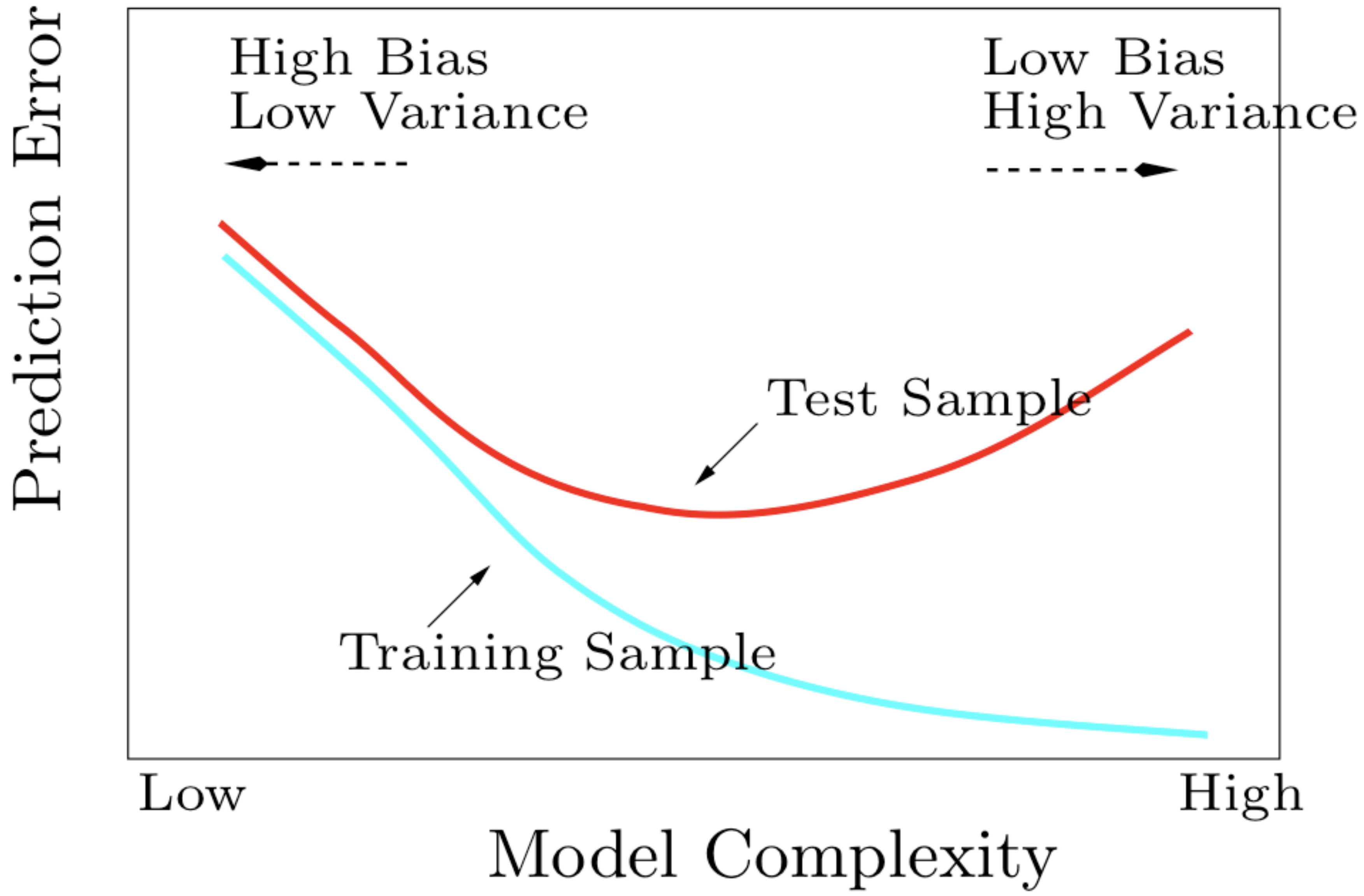


low model complexity
(needs 2 parameters to describe the decision boundary)

high model complexity
(needs hundreds of parameter to describe the decision boundary)

Which decision boundary has the lowest prediction error?

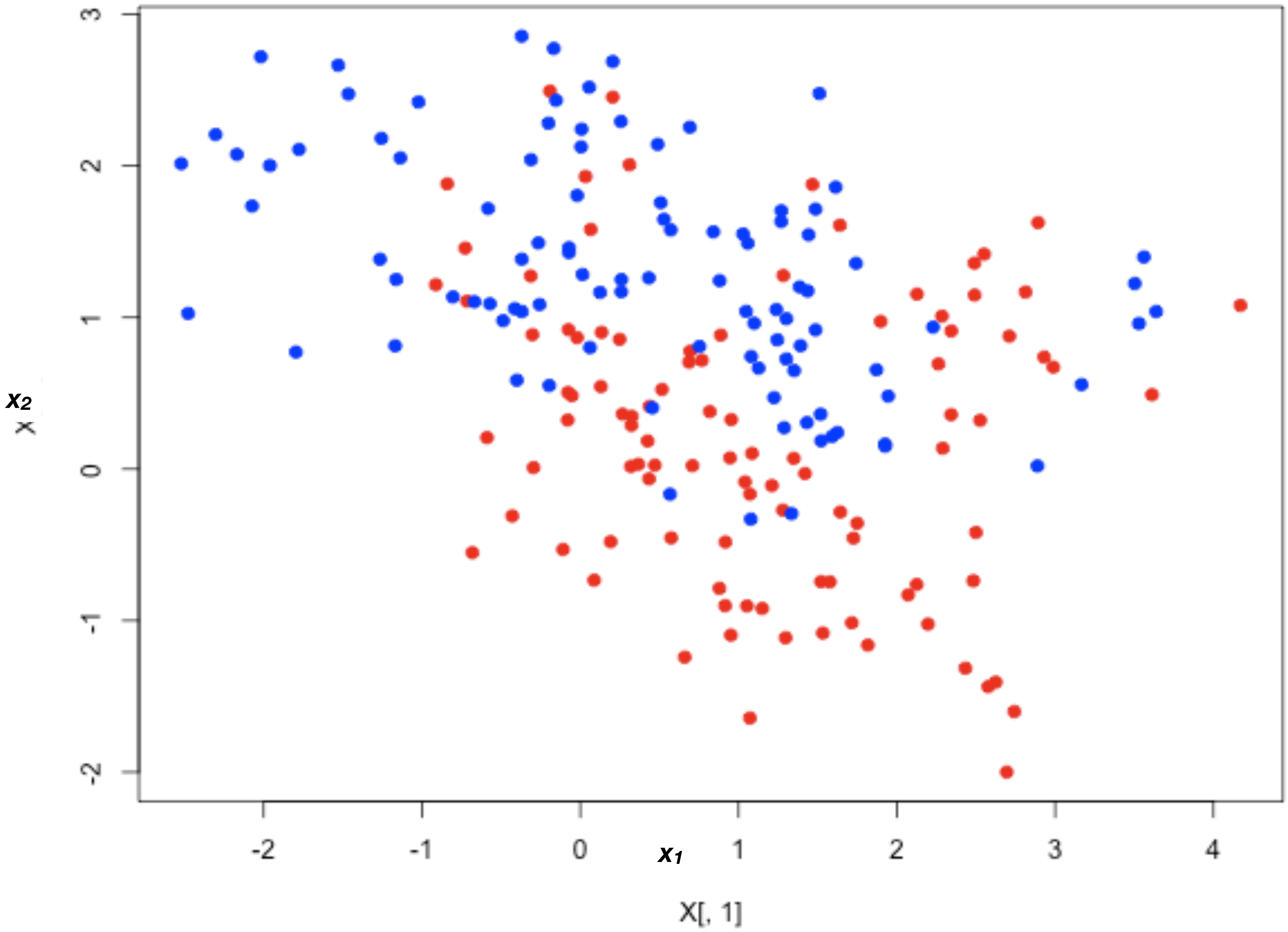
Bias-Variance-Dilemma



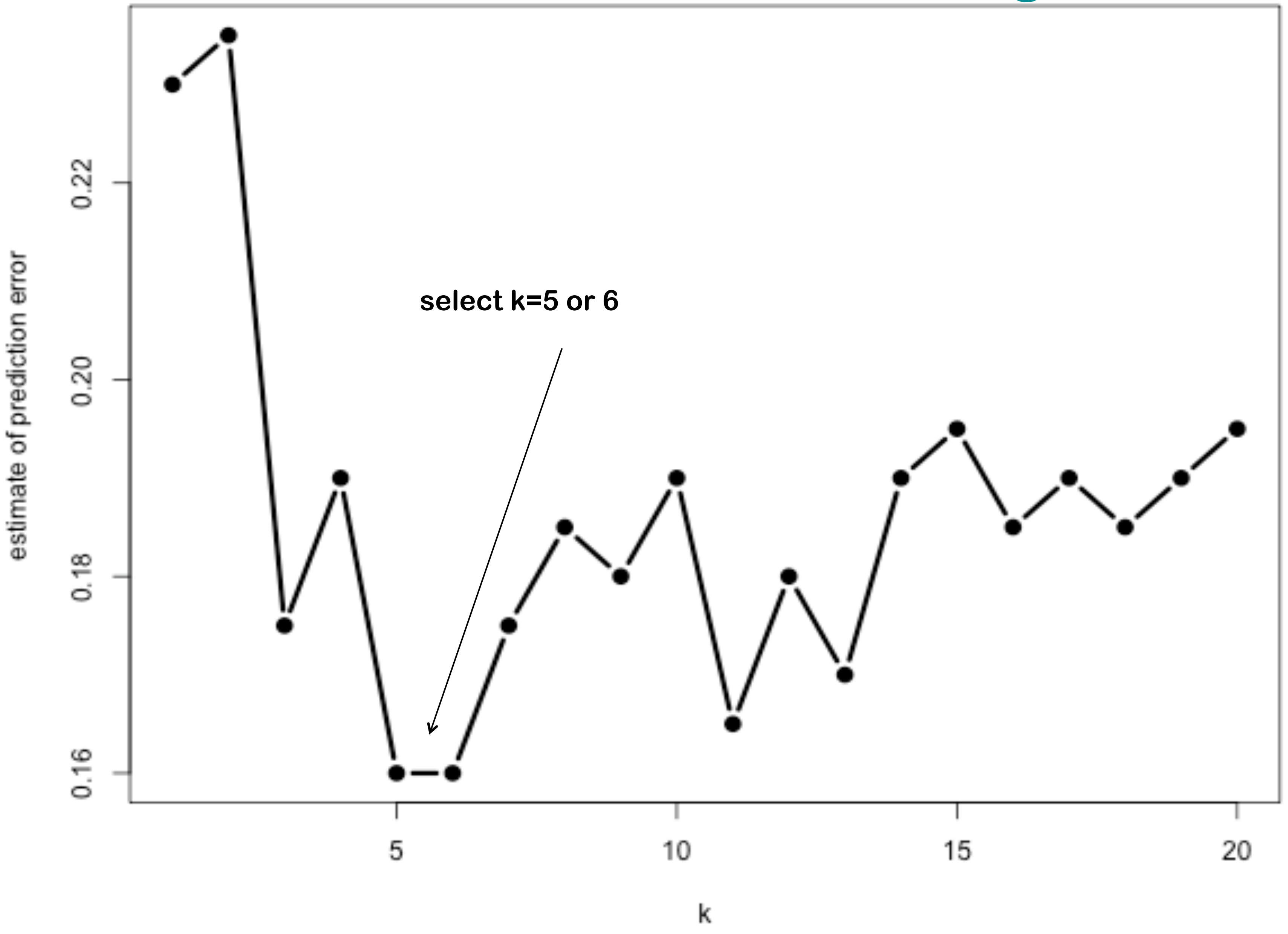
Cross-Validation

- cross validation is an easy & useful method to estimate the prediction error.
- The data consist of *n* samples with *d* features and a known class label
- Method (*m*-fold cross-validation):
  - Split the data into *m* approximately equally sized subsets
  - Train the classifier on (*m*-1) subsets
  - Test the classifier on the remaining subset. Estimate the prediction error by comparing the predicted class label with the true class labels.
  - Repeat the last two steps *m* times (use each subset once as test set)

Example: Two classes, two variables, 200 objects

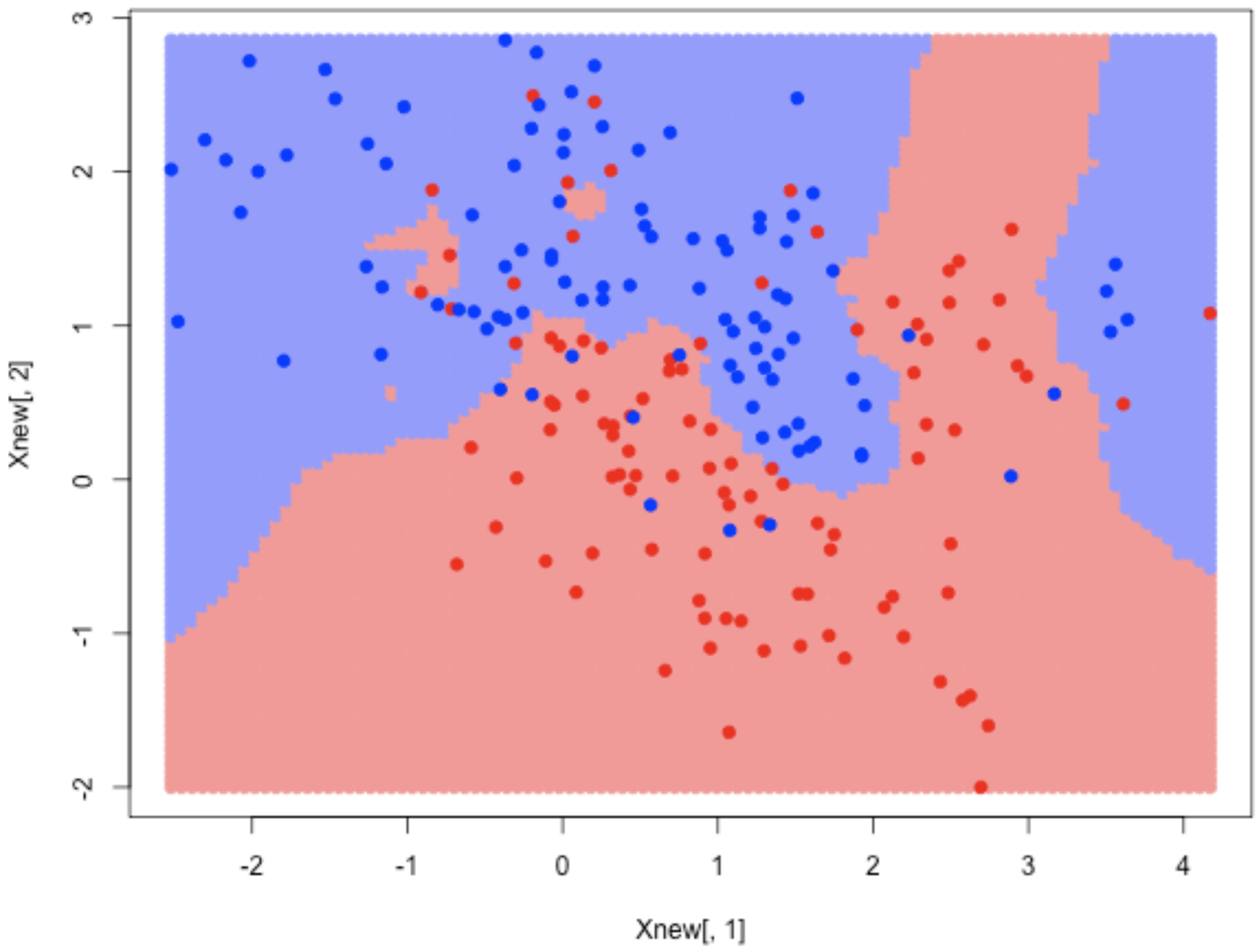


cross-Validation for k-nearest neighbours



Demo: Cross-Validation for k-nearest neighbours

Classification result (k=5)



The k-nearest neighbour classifier works well with low-dimensional data - but what if the data are high dimensional?

Least Squares Classifier

- X: n x d matrix with d-dimensional features for n samples
- y: vector of length n.
  - y[i] = 0 for first class, and 1 for second class
- Fit a linear model by minimizing the squared error:

$$\hat{\beta} = \arg\min_{\beta} \left\| X\beta - y \right\|_2^2$$

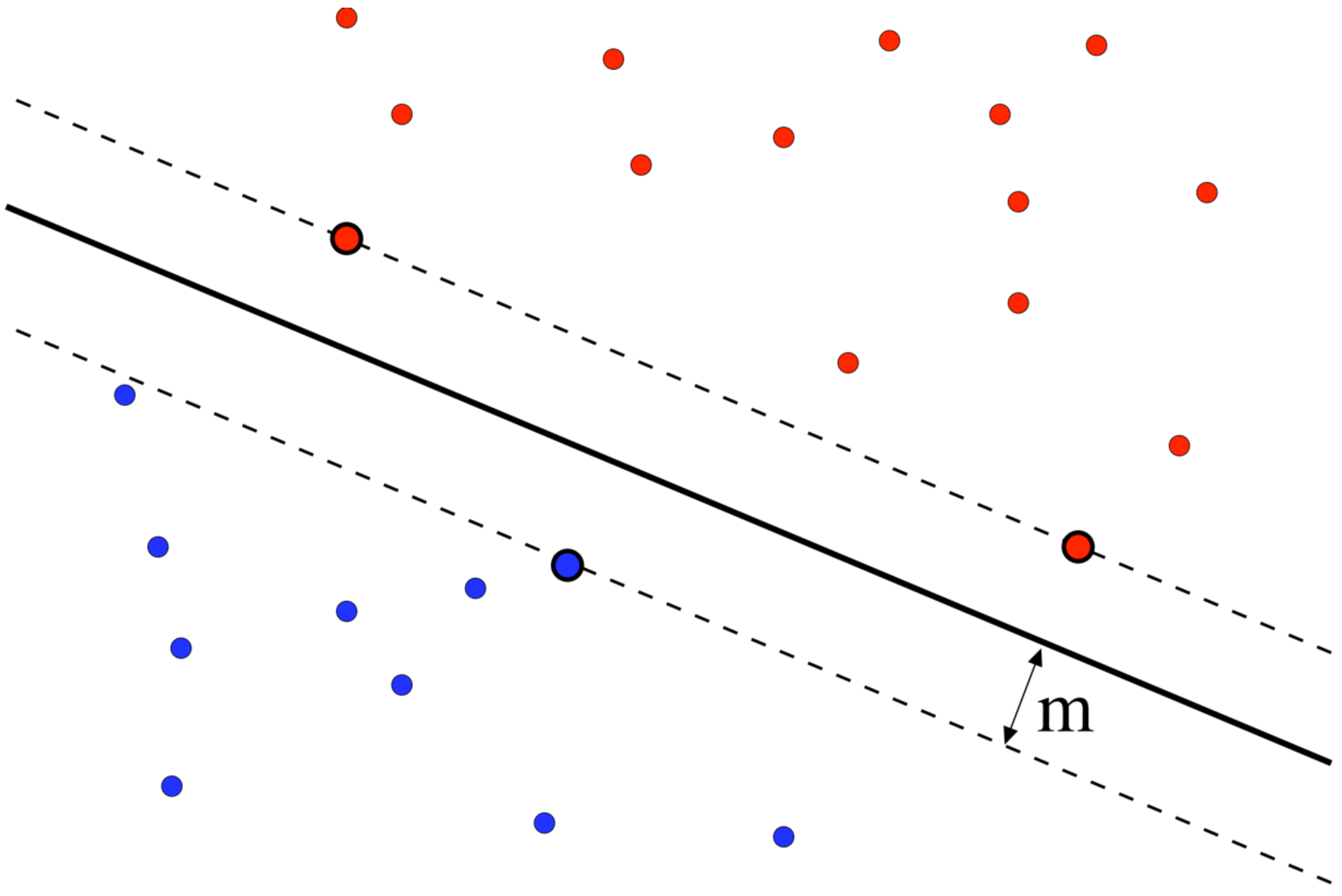
```
> model <- lm.fit(X,y)

> ynew <- predict(model,Xnew)$fitted.values

> ifelse(ynew < 0,-1,1)
```

- Extension to k classes (k > 2):
- Y is a n x k indicator matrix.
  - Each row contains exactly one “1” at column j if the sample belongs to class j. All other entries are zero.

In practice: lda (R-package MASS)

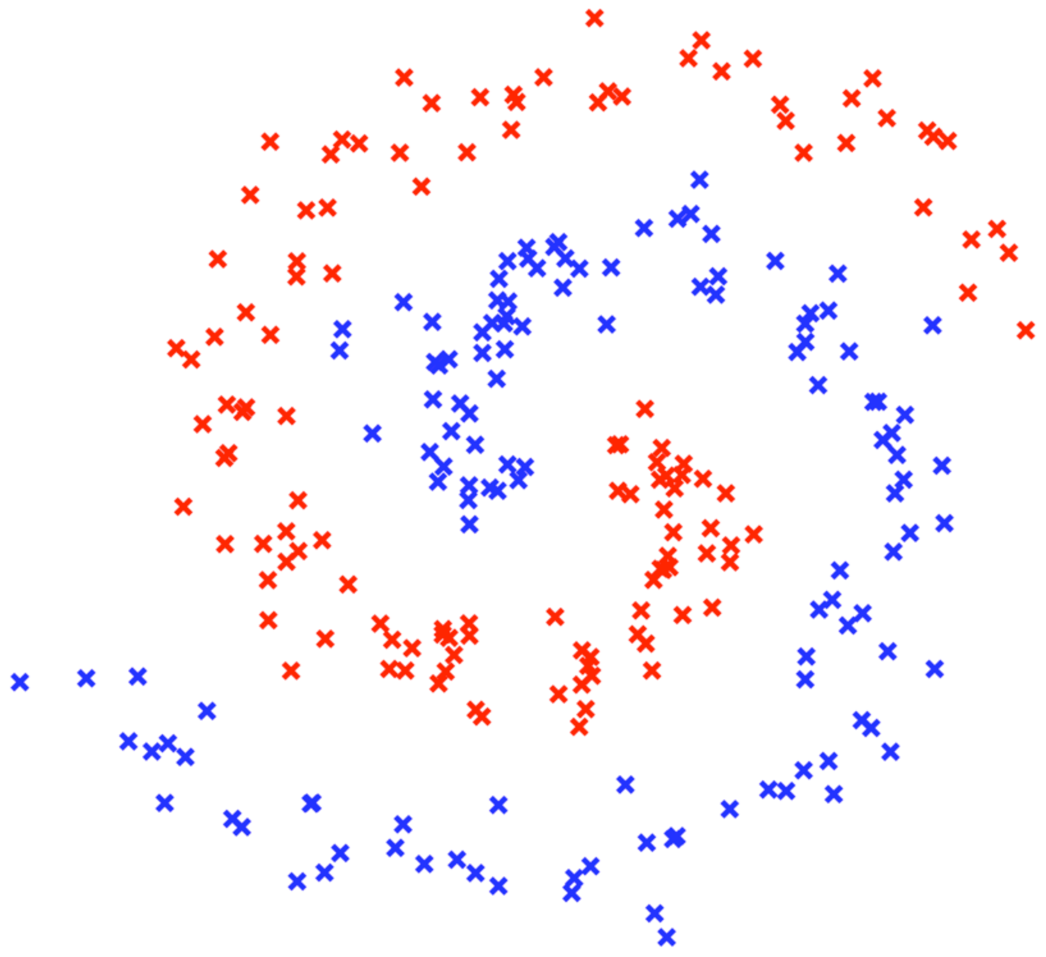
Support Vector Machine

- Find a separating hyperplane with maximal margin to the samples



Non-Linear Classifiers

These classes can not be separated by a linear hyperplane



Feature Transformation

Transform the data with non-linear function, e.g.

$$f(x) = \left(1, x, x^2, x^3, \ldots\right)$$

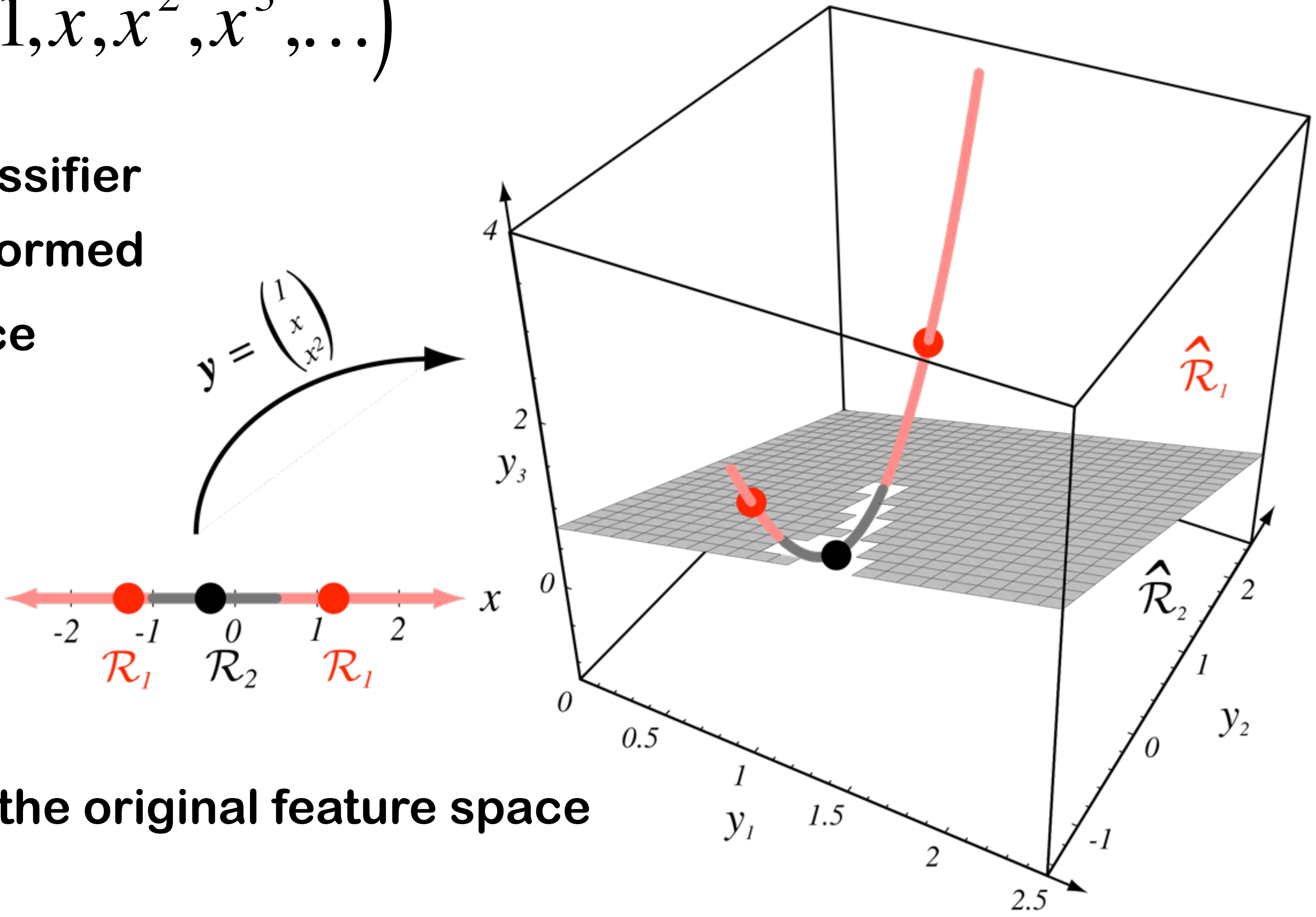
Train linear classifier

in the transformed

feature space

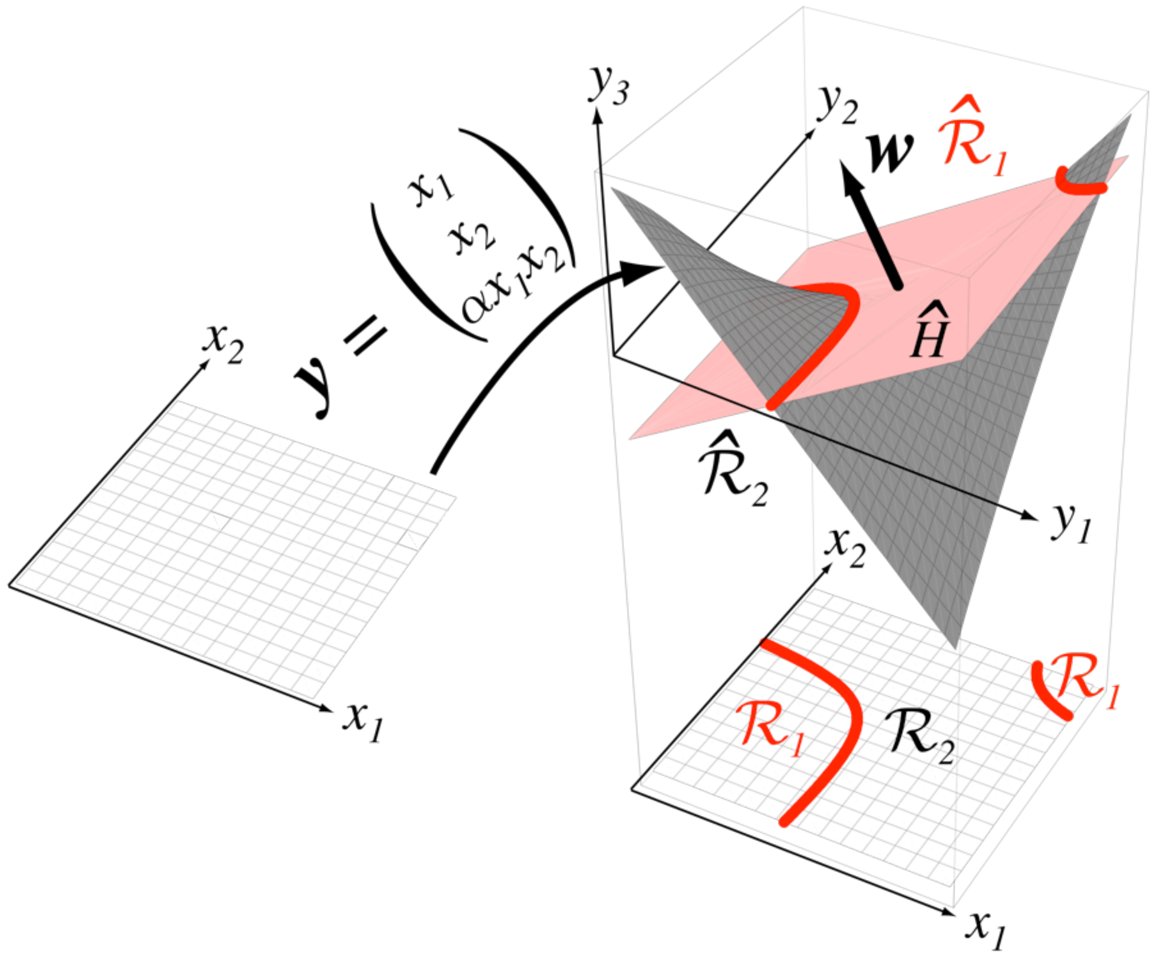
→ non-linear

classifier in the original feature space



Quadratic Extension

- Parabolic decision boundaries can be achieved by extending by the product x_1x_2.



The Kernel Trick

Rewrite the model such that the data *X* no longer appear directly, but only within scalar products.

Example: least squares

$$\sum_i (y_i - \beta \cdot \mathbf{x}_i)^2 \to \min$$

$$\beta = \left(X^t X\right)^{-1} X^t \mathbf{y}$$

The least squares problem can be reformulated as a scalar product.

The matrix *XX*^t^ (i.e. $X_{ik}X_{kj}$) contains all scalar products. Replace it by

$K_{ij} = K(x_i, x_j)$

Implicit feature transformation. The kernel has to be positive semi-definite.

The Kernel Trick

Popular functions :

Linear kernel:

$$K(x_i, x_j) = x_i x_j$$

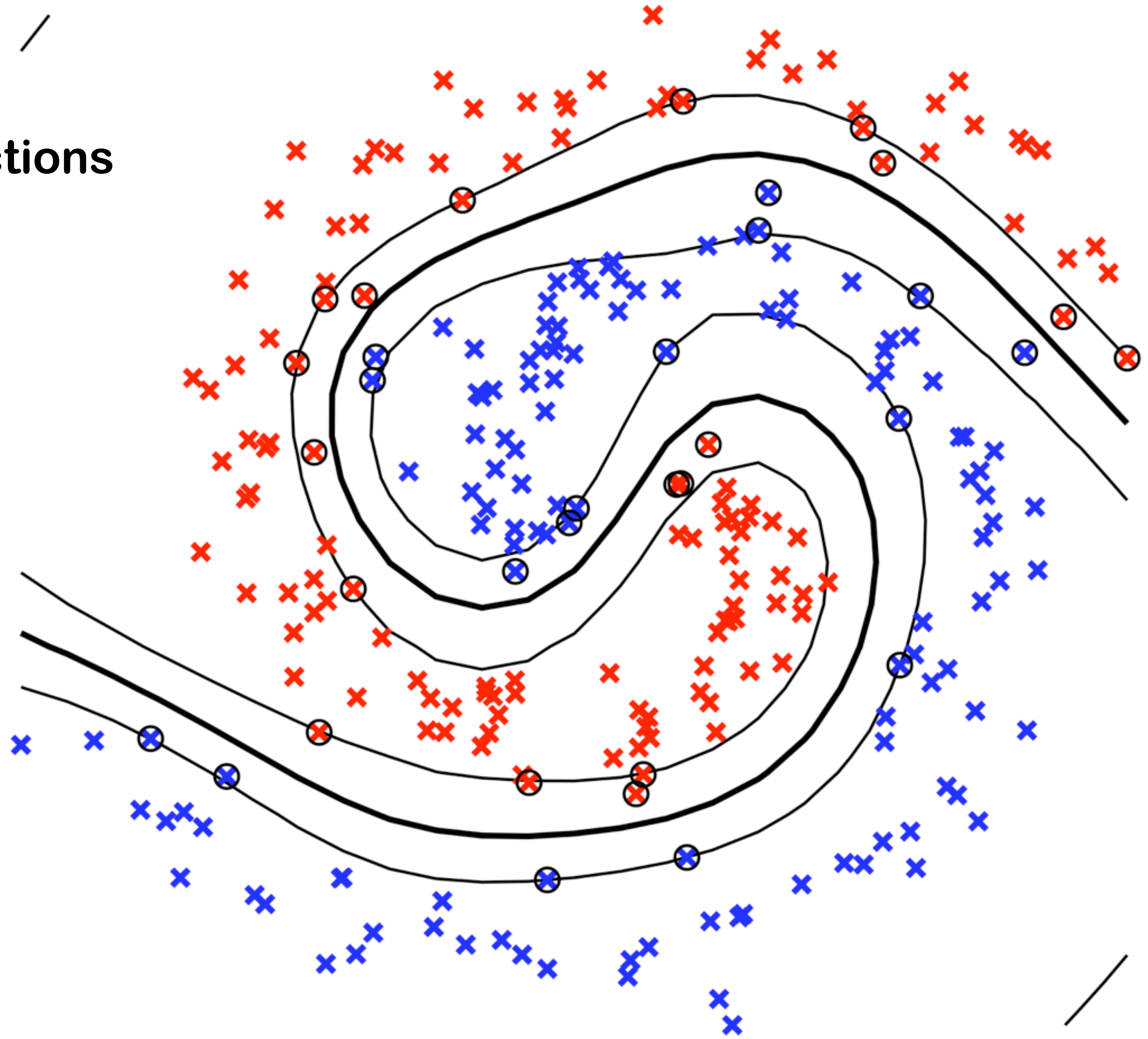
Radial basis functions:

$$K(x_i, x_j) = \exp\left(-\frac{1}{2\sigma^2}\left\|x_i - x_j\right\|\right)$$

$$K(x_i, x_j) = (x_i x_j + 1)^d$$

Examples for SVM-Classification

SVM with
Radial Basis Functions
(RBF-kernel)

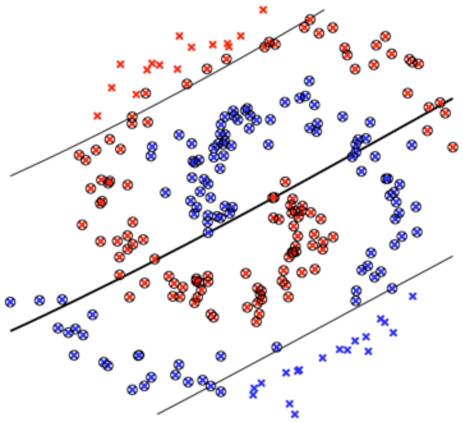


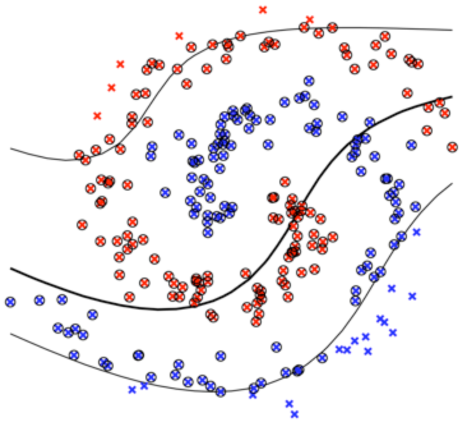
Thick line:
class separating
hyperplane

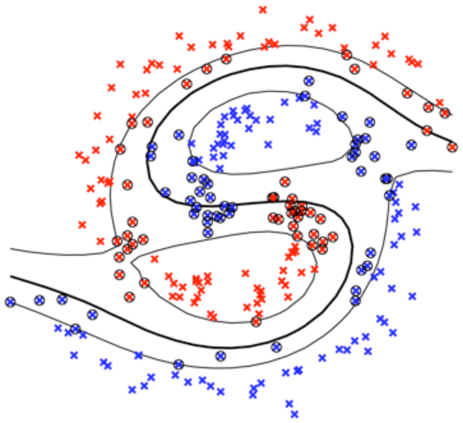
Thin line:
margin

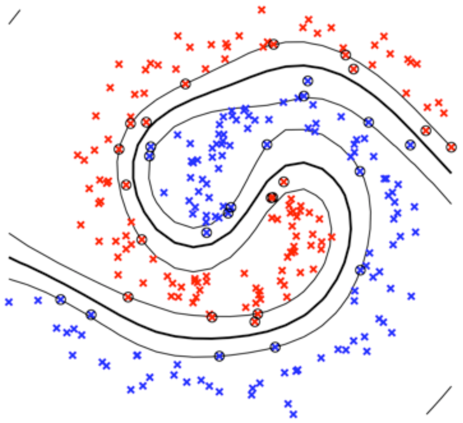
Circles:
support vectors

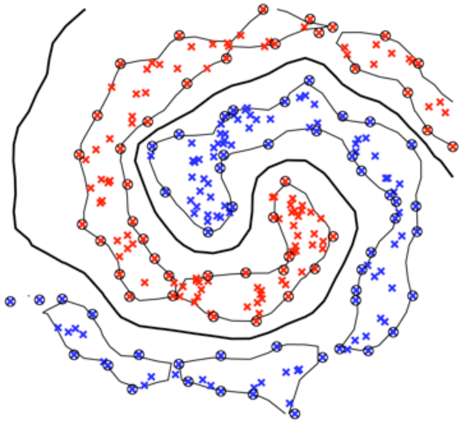
The Influence of the Kernel Parameter

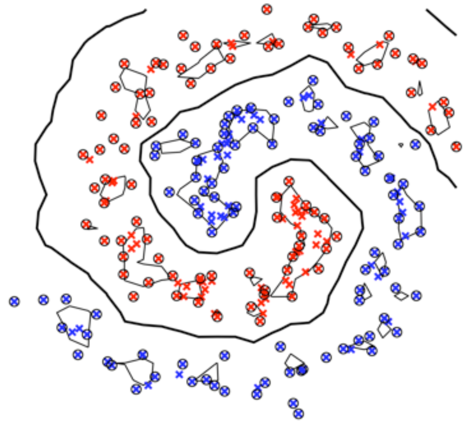

$\gamma = 0.001$

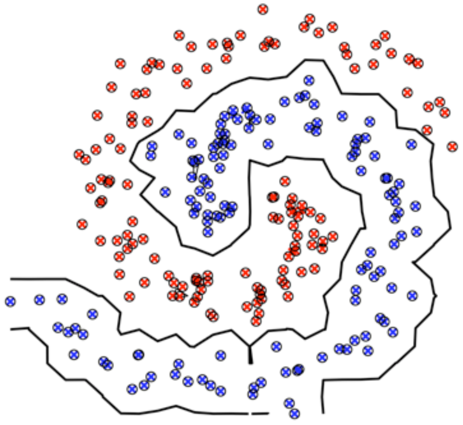

$\gamma = 0.005$

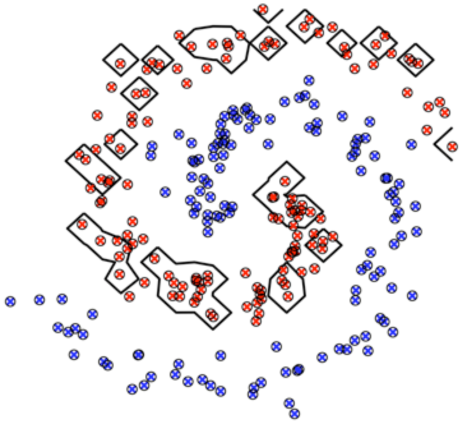

$\gamma = 0.03$


$\gamma = 0.1$


$\gamma = 1$


$\gamma = 2$

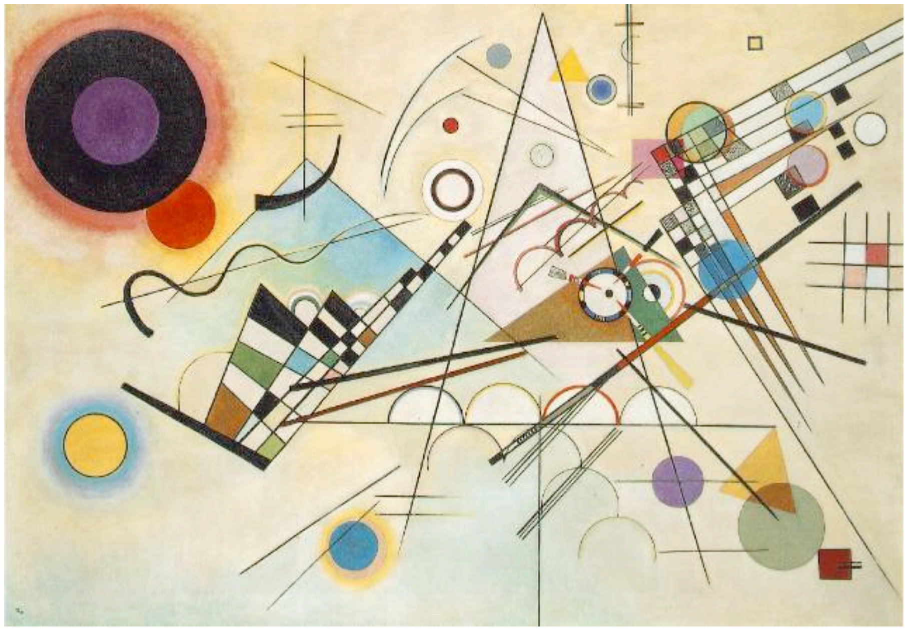

$\gamma = 20$

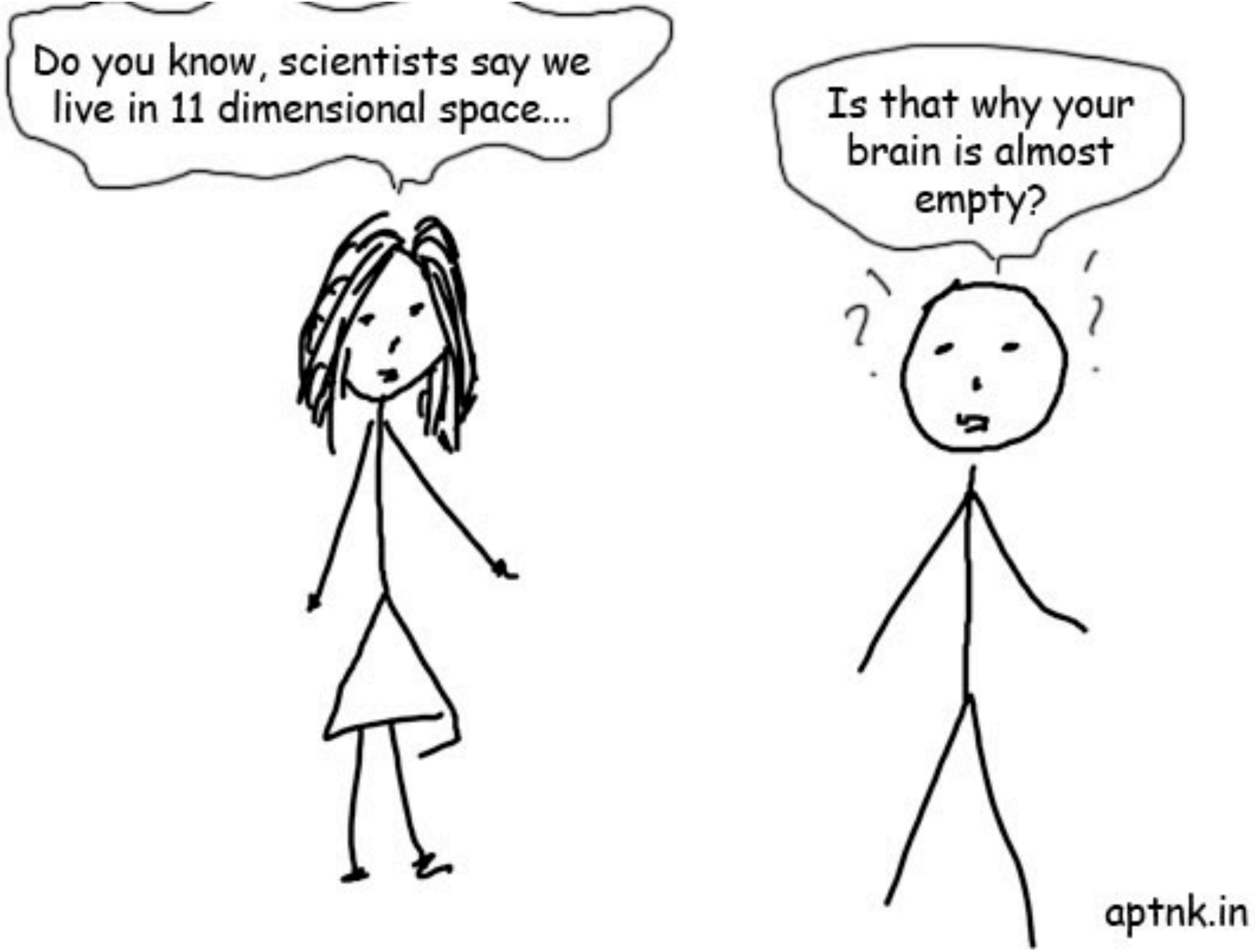

$\gamma = 200$

$\gamma = \sigma^{-2}$, RBF

Curse of Dimensionality

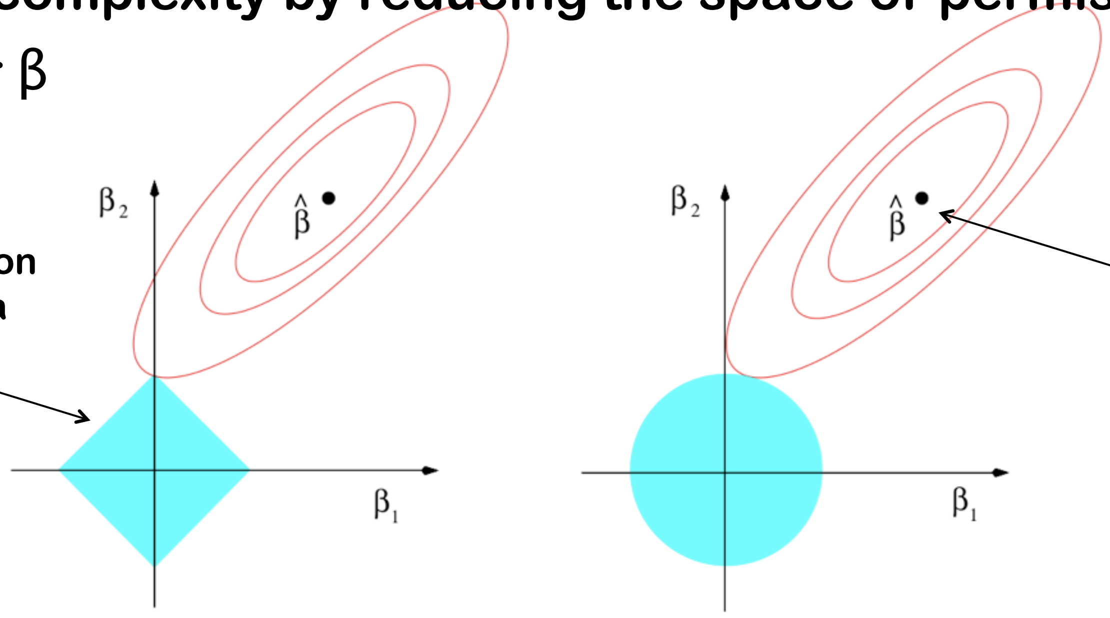
- Consider:
  - 10 samples per class
  - Each sample is characterised by several hundred features.
- Even a linear classifier will be (always) too complex: overfitting
- There is a need to lower the complexity even below that of the linear classifier




Do you know, scientists say we live in 11 dimensional space...
Is that why your brain is almost empty?
aptnk.in

Regularization

- Reduce the complexity by reducing the space of permissible solutions for β


constrain the solution of β to the blue area
β_2
$\hat{\beta}$
β_1
β_2
$\hat{\beta}$
β_1
unconstrained least squares solution

Lasso:

$$\hat{\beta} = \arg\min_{\beta} \|X\beta - y\|_2^2 + \lambda \|\beta\|_1^1$$

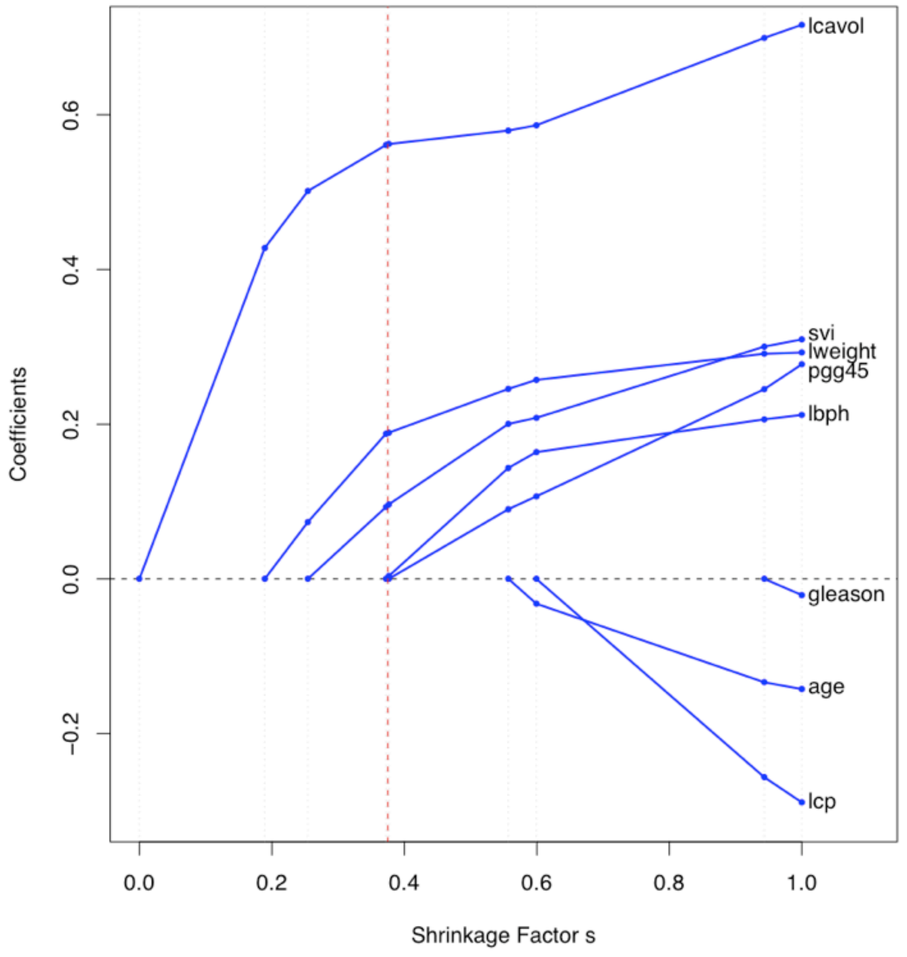
Ridge Regression

$$\hat{\beta} = \arg\min_{\beta} \|X\beta - y\|_2^2 + \lambda \|\beta\|_2^2$$

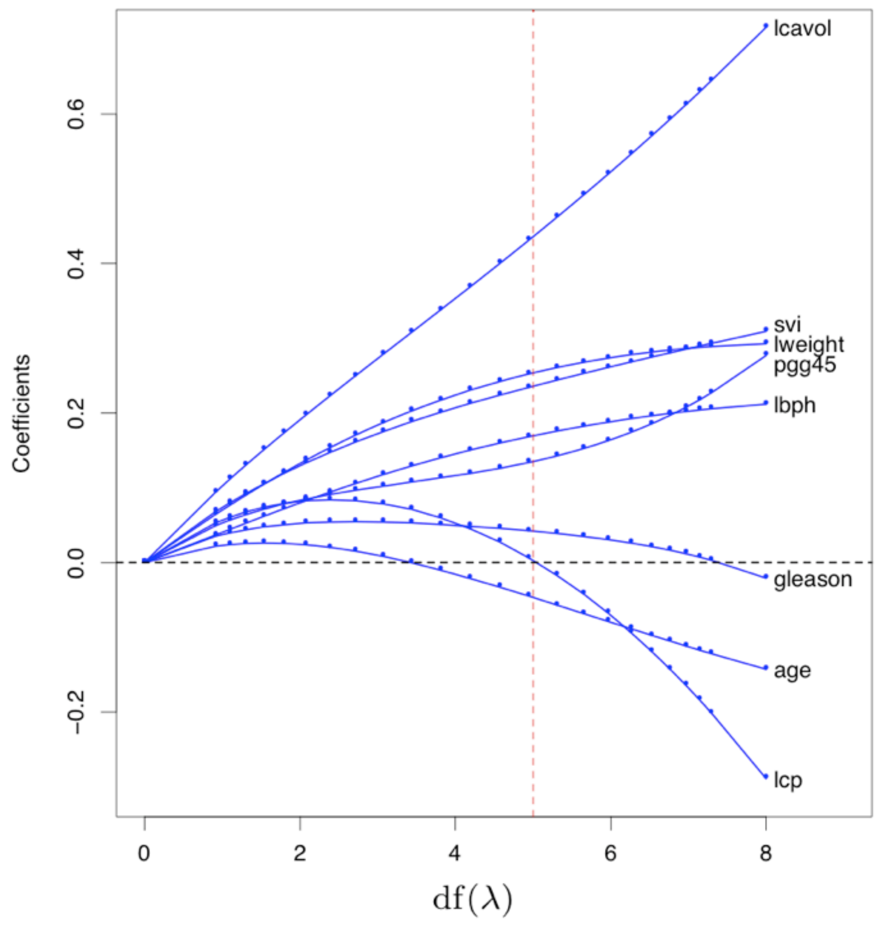
Lagrangian formulation of constrained optimization.
The blue area becomes larger, the smaller λ.
Lasso: sparse solution. Many coefficients βi become 0. Only a few coefficients are used for prediction. Implicitly selects features.

Regularization Path

The coefficients for varying regularization parameter λ

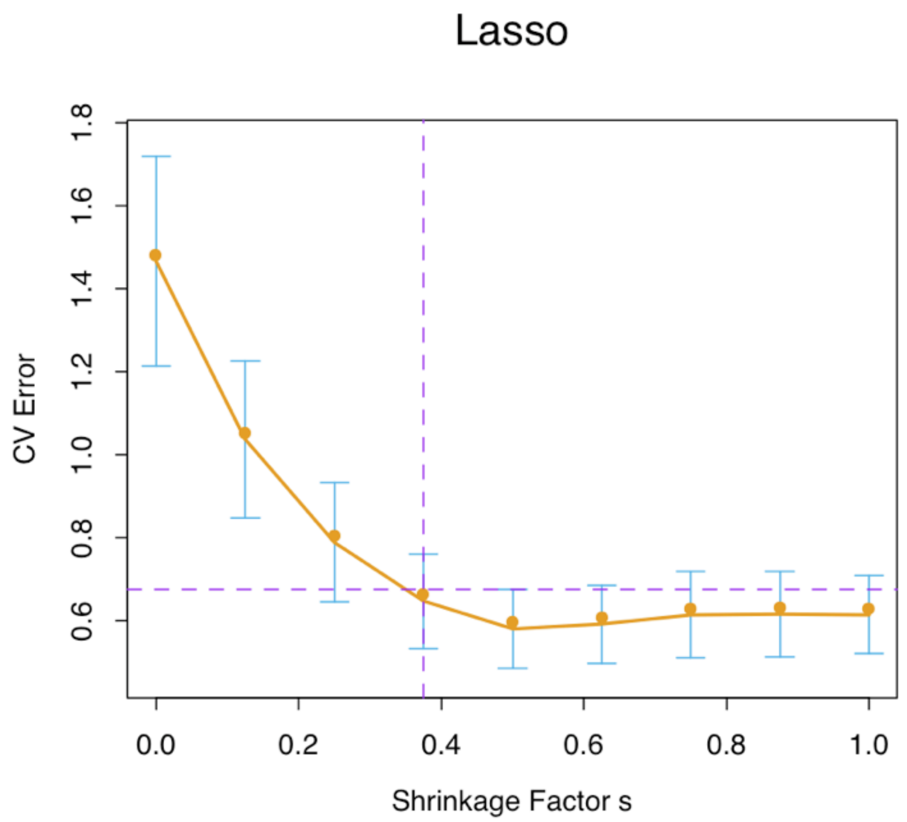


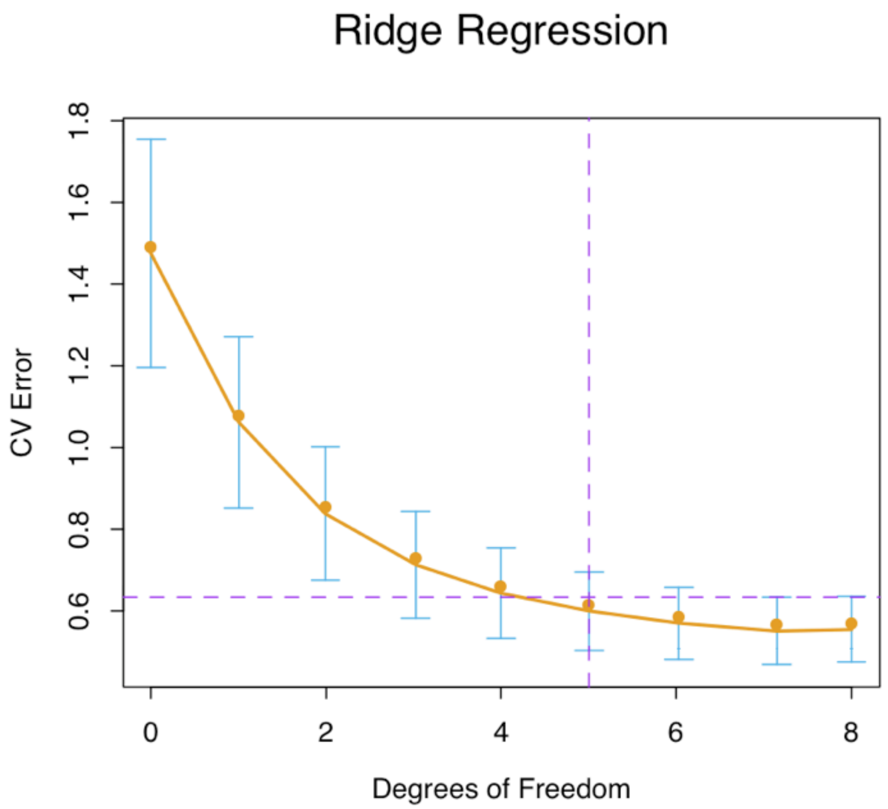
Lasso



Ridge Regression

Cross-Validation for Regularized Regression

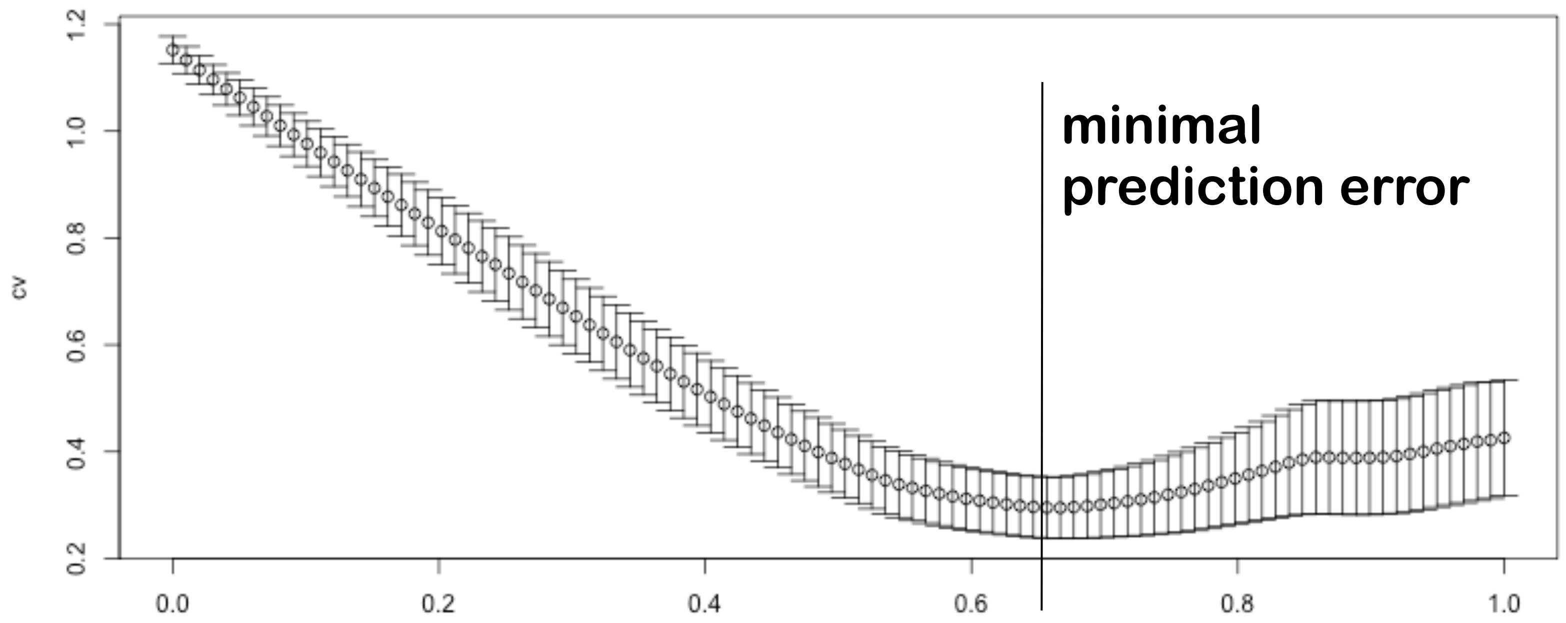




Demo Lasso I

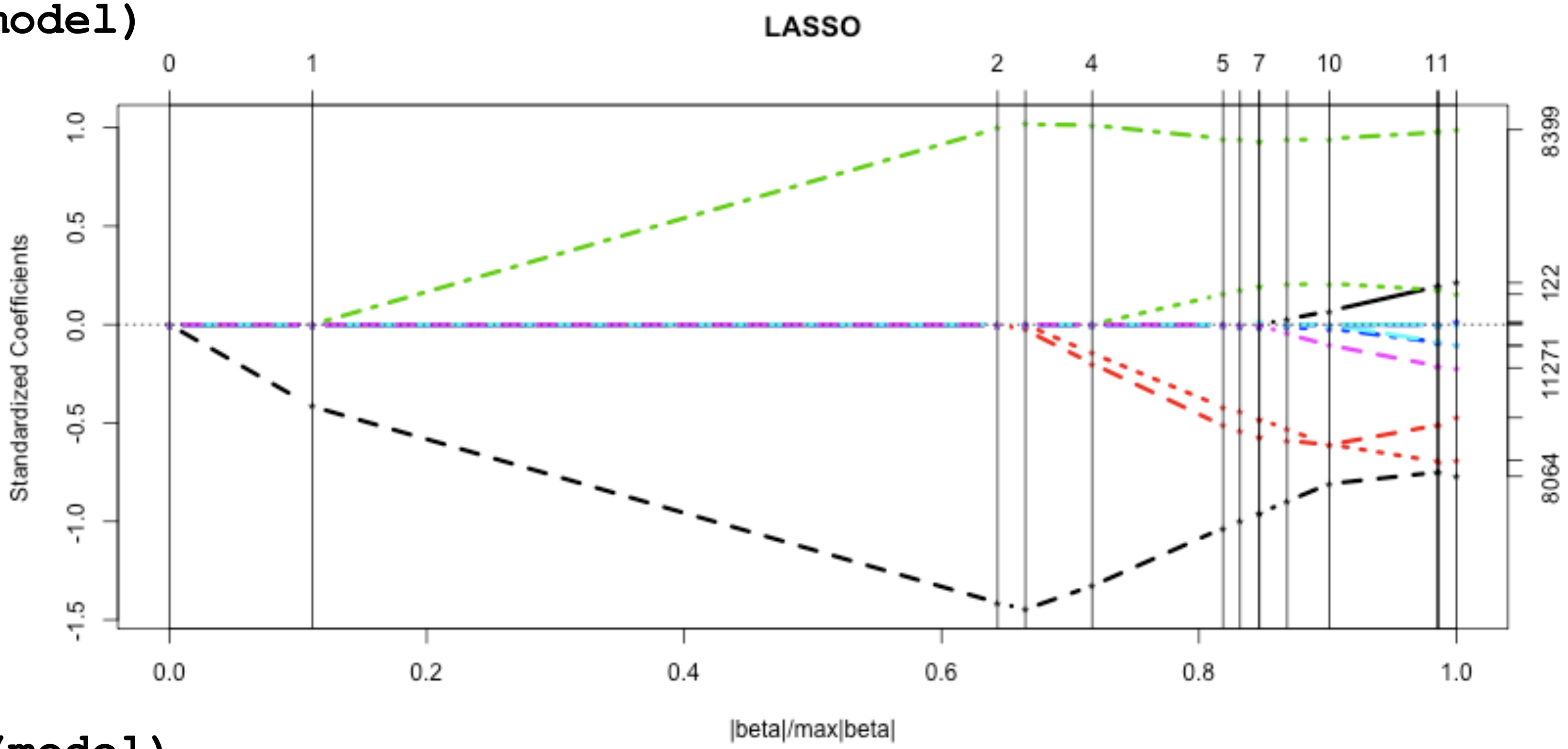
- ALL cancer dataset: gene expression of 12000 genes
- Two classes B-cell ALL and T-cell ALL.
- Cross validation over a range of λ-values

```
# filename: demo-lars.R
>CV <- cv.lars(X,y,use.Gram=FALSE,trace=TRUE)
```



Demo Lasso II

```
> model <- lars(X,y,use.Gram=FALSE,trace=TRUE)
> plot(model)
```

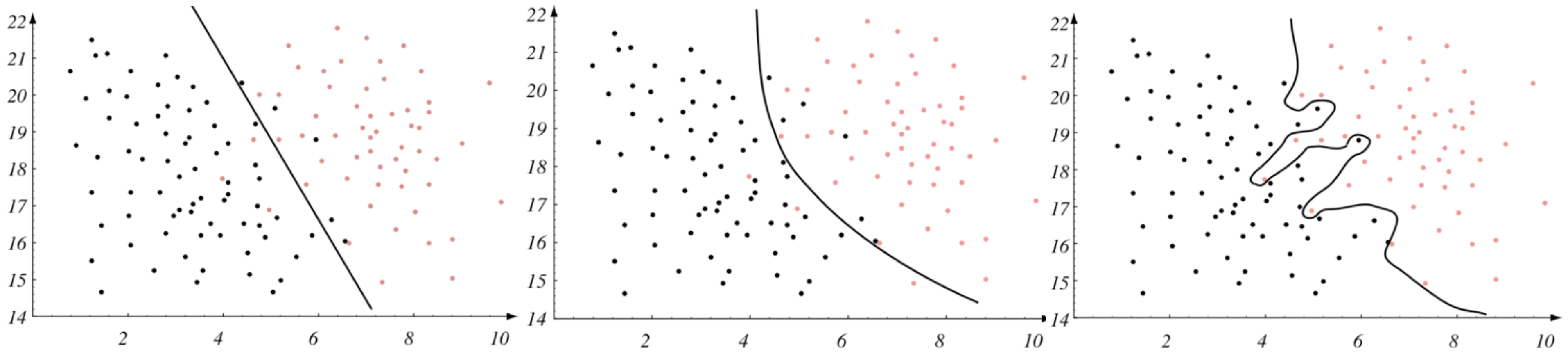


```
> print(model)
Sequence of LASSO moves:
     37988_at 38319_at 2031_s_at 38242_at 34908_at 35434_at …
Var      8064     8399      1144     8321     4955     5486 …
Step        1        2         3        4        5        6 …
```

Summary: It's all about adapting the complexity of the model to that of the data

High bias
Low variance

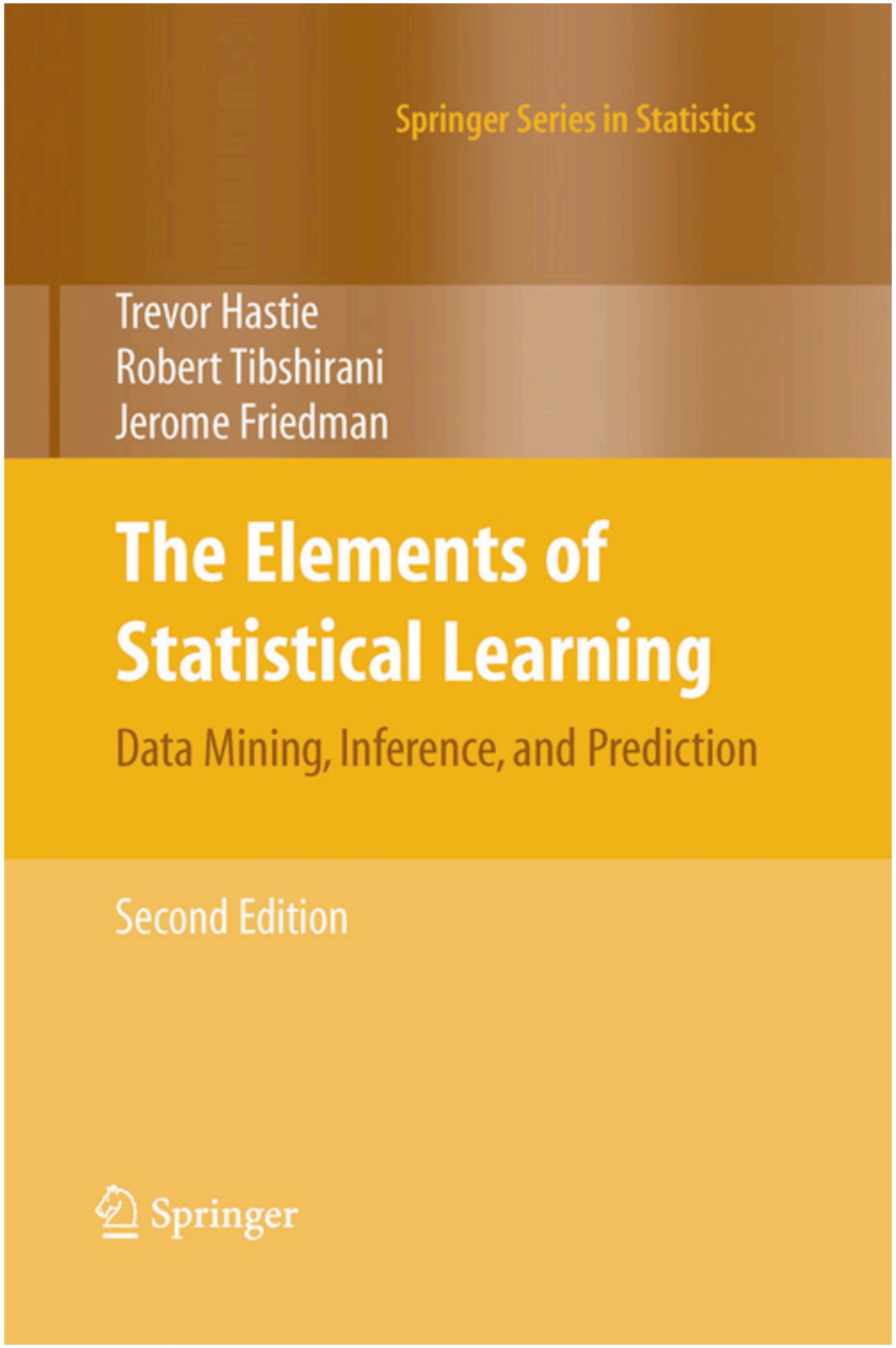
Low bias
High variance



low model complexity
(2 parameters describe the decision boundary)

high model complexity
(hundreds of parameter to describe the decision boundary)

Reduce complexity by regularization (Lasso, ridge, …)
Increase complexity by feature transformation or kernel functions
Always assess classifiers by cross-validation



Springer Series in Statistics

Trevor Hastie
Robert Tibshirani
Jerome Friedman

The Elements of Statistical Learning

Data Mining, Inference, and Prediction

Second Edition

Springer