Machine Learning Methods for Gene Expression Data

Day 4

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Outline

Support vector machines (SVMs)

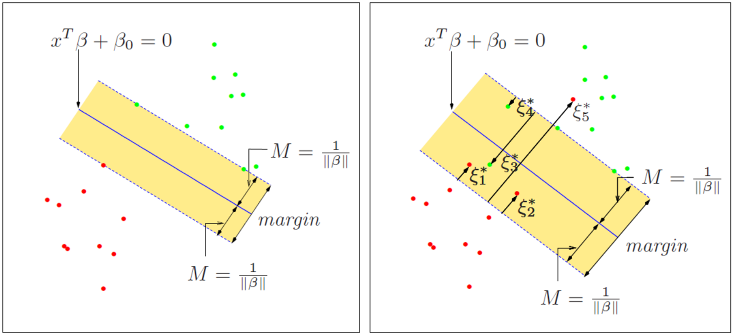


FIGURE 12.1. *Support vector classifiers. The left panel shows the separable case. The decision boundary is the solid line, while broken lines bound the shaded maximal margin of width $2M = 2/\|\beta\|$. The right panel shows the nonseparable (overlap) case. The points labeled ξ_j^* are on the wrong side of their margin by an amount $\xi_j^* = M\xi_j$; points on the correct side have $\xi_j^* = 0$. The margin is maximized subject to a total budget $\sum \xi_i \leq$ constant. Hence $\sum \xi_j^*$ is the total distance of points on the wrong side of their margin.*

Taken from Hastie *et al.* (2009).

Fitting SVMs

Here follow convention $y \in \{-1, 1\}$ instead of $y \in \{0, 1\}$ convention I've been adhering to.

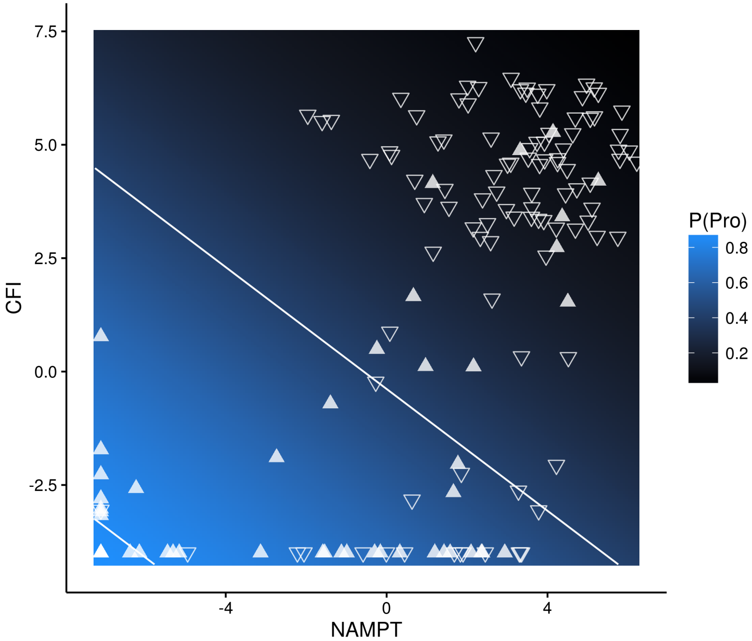
SVM parameters $\beta_0, \boldsymbol{\beta}$ fit by optimization:

$$\underset{\beta_0, \boldsymbol{\beta}}{\arg\min} \left\{ \frac{1}{2} \|\boldsymbol{\beta}\|^2 + C \sum_{i=1}^{n} \xi_i \right\}$$

subject to constraints

$$y_i(\boldsymbol{\beta} \cdot \mathbf{x}_i + \beta_0) \geq 1 - \xi_i$$
$$\xi_i \geq 0$$

Linear SVM



Nonlinear SVMs

Can fit SVM in nonlinearly transformed feature space.

For certain transformations, so-called “kernel trick” can be used to do this in very computationally efficient manner. Given a particular transformation h, the kernel

$$k(\mathsf{x}, \mathsf{x}') = \langle h(\mathsf{x}), h(\mathsf{x}') \rangle$$

is actually all that is needed to fit SVM.

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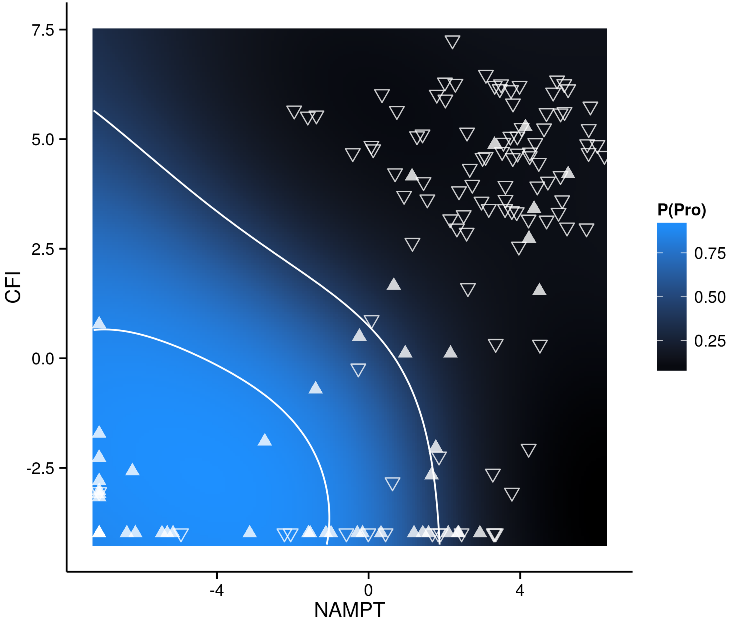
Most popular *h* is rather involved transformation designed to produce the radial basis kernel

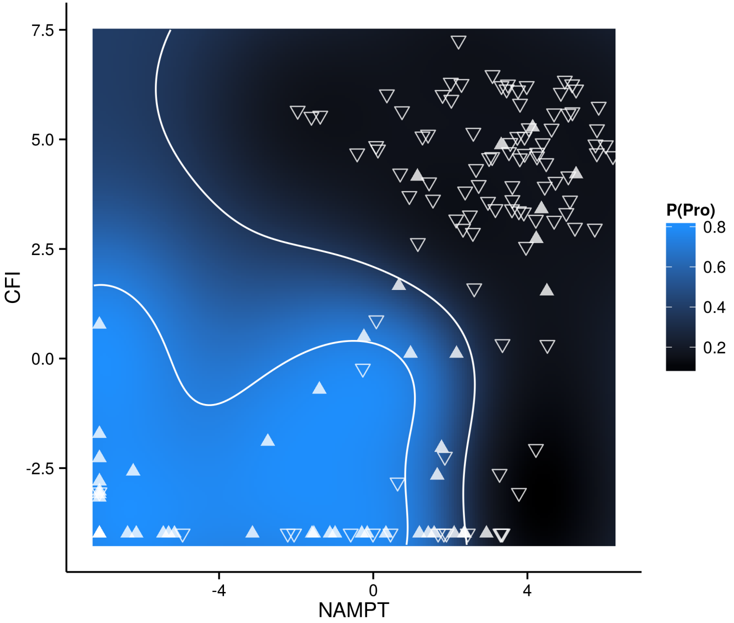
$$k(\mathsf{x}, \mathsf{x}') = \exp\left(-\gamma \|\mathsf{x} - \mathsf{x}'\|^2\right)$$

SVMs may be intuitively thought of as classifying a sample with features x based on the (known) classes of similar training data x_i, where “similarity” is quantified by the kernel $k(\mathsf{x}, \mathsf{x}_i)$.

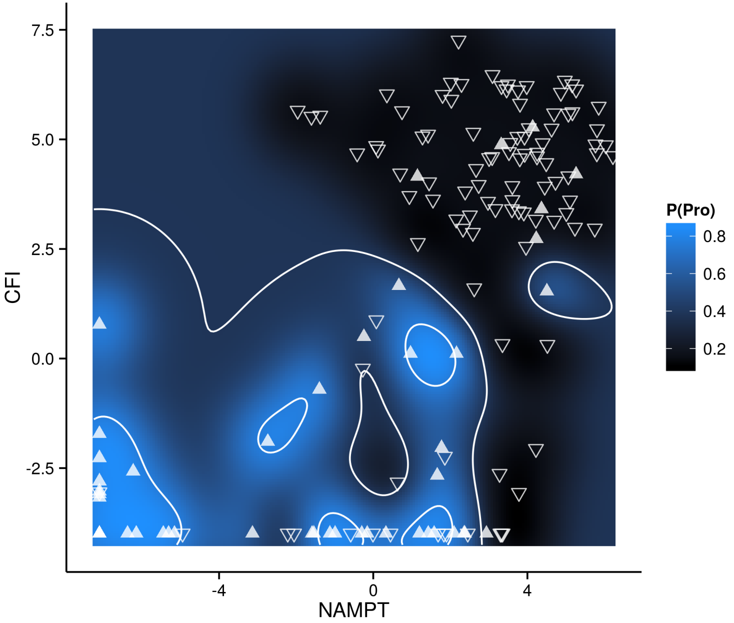
Radial SVM: $C = 1, \gamma = 0.5$



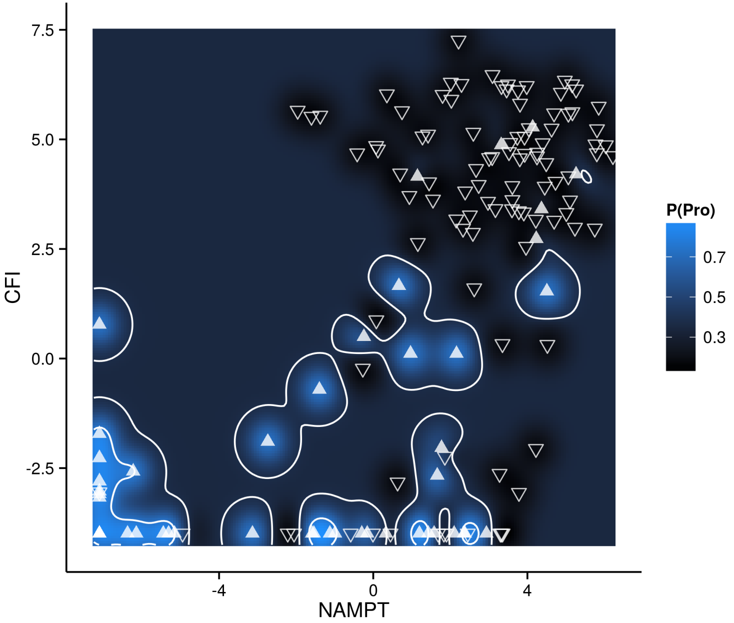
Radial SVM: $C = 1, \gamma = 2.5$



Radial SVM: $C = 1, \gamma = 12.5$



Radial SVM: $C = 1, \gamma = 62.5$



Uncertainty in Model Parameters

We often want to have some idea what the uncertainty in model parameters might be.

While for linear models there are many useful analytical results on confidence intervals, other modeling strategies are not so lucky.

If gathering data were sufficiently cheap, we could just replicate both the experiment which generated data and the modeling process many times and empirically estimate the distribution of fit model parameters.

Bootstrapping

Bootstrapping is an approach to simulate such replication using just the one data set we actually have.

Usually bootstrapping consists of:

1. Generate a case-resampled data set $\underline{\mathbf{X}}^{\text{boot}}$ by drawing n random integers $R = \{r_i \in \{1, \ldots, n\}\}$ with replacement and setting
$$x_{gi}^{\text{boot}} = x_{gr_i}$$
$$y_i^{\text{boot}} = y_{r_i}$$
Note that the r_i will generally not be unique!
2. Apply modeling strategy M to $(\underline{\mathbf{X}}^{\text{boot}}, \underline{y}^{\text{boot}})$ to obtain fitted parameters $\boldsymbol{\theta}^{\text{boot}}$.
3. Use model $(M, \boldsymbol{\theta}^{\text{boot}})$ to estimate parameter or statistic $\hat{\Omega}^{\text{boot}}$ of interest.
4. Repeat steps 1-3 B times, obtaining values Ω_b^{boot} for $b \in \{1, \ldots, B\}$ using models $(M, \boldsymbol{\theta}_b^{\text{boot}})$.

Bootstrapping for Performance Estimation

Bootstrapping can be used as an alternative to cross-validation for estimation of prediction error Ω.

How to do this? One approach would be to estimate distribution of prediction error $\{\hat{\Omega}_b^{\text{full}}\}$ on full (original) training set $\underline{\mathbf{X}}$.

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However, since bootstrap training sets were drawn from $\underline{\mathbf{X}}$, $\{\hat{\Omega}_b^{\text{full}}\}$ will suffer from resubstitution bias.

Instead we could follow cross-validation methodology and use only models $(M, \boldsymbol{\theta}_b)$ for which sample i was not used in the resampled training set R_b to calculate

$$\hat{\Omega}^{\text{loo-boot}} = \frac{1}{n} \sum_i \frac{1}{|\{b \mid i \notin R_b\}|} \sum_{\{b|i \notin R_b\}} \hat{\Omega}(M, \boldsymbol{\theta}_b, y_i)$$

.632 Bootstrap

While $\{\hat{\Omega}_b^{\text{full}}\}$ are generally overly optimistic, $\hat{\Omega}^{\text{loo-boot}}$ may be too pessimistic ...

Why? Because each bootstrap case-resampled training set

$$R_b = \{r_{bi} \mid i \in \{1, \ldots, n\}\}$$

generally contains only a fraction $1 - \frac{1}{e} \approx 0.632$ of the true training samples (albeit with some showing up multiple times!).

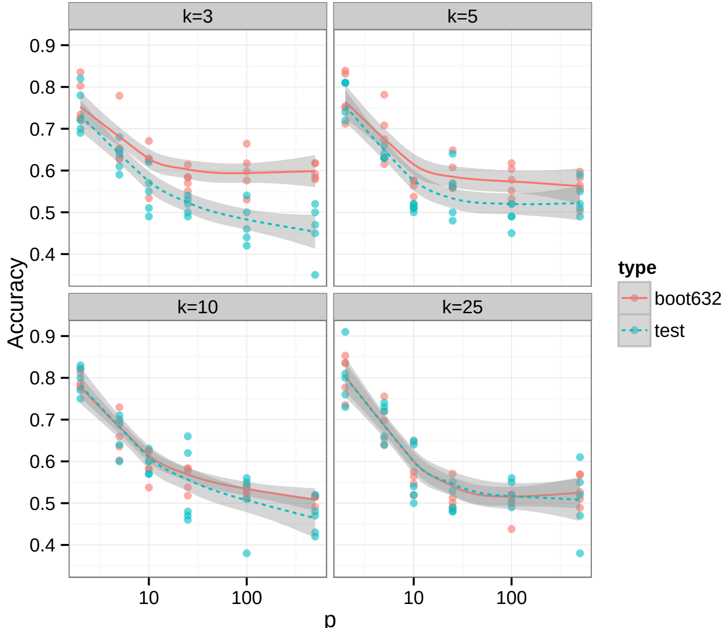
Repeating some training samples doesn't generally improve the performance of the built models ... so we're basically learning models using only $\approx 63.2\%$ of the available data.

Efron & Tibshirani (1997) showed that

$$\Omega^{.632} = 0.368\,\Omega^{\text{resub}} + 0.632\,\Omega^{\text{loo-boot}}$$

works well in some situations.

.632 Bootstrap



.632+ Bootstrap

However, in cases where overfitting is more severe, Efron & Tibshirani (1997) recommend

$$\Omega^{.632+} = (1 - \hat{w})\,\Omega^{\text{resub}} + \hat{w}\,\Omega^{\text{loo-boot}}$$

where $\hat{w} \in [1 - \frac{1}{e}, 1]$ depends on the degree of overfitting.

There is a standard formula for calculating $\hat{w}$ for estimating prediction error using the .632+ bootstrap which you can look up; aside from Efron & Tibshirani (1997), Hastie *et al.* (2009) has a nice treatment.

Bagging: **B**ootstrap **Agg**regat**ing** Models

One might consider using a set of B bootstrap case-resample trained models in place of a single model for making predictions.

For a modeling strategy M which, after fitting parameters $\boldsymbol{\theta}$, yields predictions $f_{M,\boldsymbol{\theta}}(\mathbf{x})$:

Repeat for $b \in \{1, \ldots, B\}$:

1. Generate $\underline{\mathbf{X}}_b$ by drawing n random integers $R_b = \{r_{bi} \in \{1, \ldots, n\}\}$ with replacement and setting $X_{bgi} = X_{gr_{bi}}$, $y_{bi} = y_{r_{bi}}$.
2. Fit M to $(\underline{\mathbf{X}}_b, \underline{y}_b)$ to obtain fitted parameters $\boldsymbol{\theta}_b$.

Bagged predictions for new data $\mathbf{x}$ using $(M, \{\boldsymbol{\theta}_b\})$:

$$f_{M,\{\boldsymbol{\theta}_b\}}(\mathbf{x}) = \frac{1}{B} \sum_{b=1}^{B} f_{M,\boldsymbol{\theta}_b}(\mathbf{x})$$

Bagging: What is it Good For?

From Breiman (1996):

> For unstable procedures bagging works well . . . The evidence, both experimental and theoretical, is that bagging can push a good but unstable procedure a significant step towards optimality. On the other hand, it can slightly degrade the performance of stable procedures.

In this context, "stability" is of the fit model parameters $\boldsymbol{\theta}$ with respect to the training data $\{\mathbf{x}_i, y_i\}$.

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Perhaps the most celebrated application of bagging is in its application to generate **random forests** of **decision trees** . . .

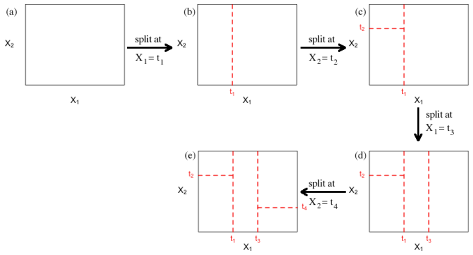
Decision Trees

$$\mathbb{P}(Y = y \mid \mathbf{X} = \mathbf{x}) = \sum_{k=1}^{K} p_k \, [\mathbf{x} \in R_k]$$

where the Iverson bracket expression

$$[\mathbf{x} \in R_k] = \begin{cases} 1 & \text{if } \mathbf{x} \in R_k, \\ 0 & \text{otherwise} \end{cases}$$

and the regions $R_k \in \mathbb{R}^p$ are defined by *recursive partitioning*.



Images from http://www.unc.edu/courses/2010spring/ecol/562/001/images/lectures/lecture21

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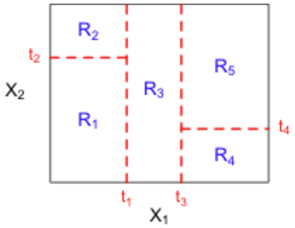

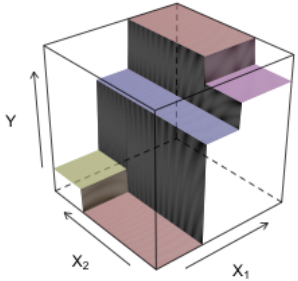

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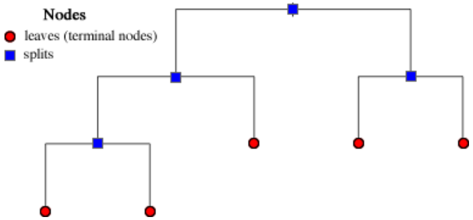

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Fitting a Decision Tree

Recursive partitioning generally selects both the variable X_g to split on and the value t at which to split that variable by minimizing an impurity measure Q such as

$$\begin{aligned} Q_{\text{misclassification}} &= \min(p_<, 1 - p_<) \\ &\quad + \min(p_>, 1 - p_>) \\ Q_{\text{gini}} &= p_<(1 - p_<) \\ &\quad + 2p_>(1 - p_>) \\ Q_{\text{deviance}} &= -p_< \log p_< - (1 - p_<)\log(1 - p_<) \\ &\quad - p_> \log p_> - (1 - p_>)\log(1 - p_>) \end{aligned}$$

where

$$\begin{aligned} p_< &= \frac{|\{i \mid y_i = 1, x_{ig} < t\}|}{|\{i \mid x_{ig} < t\}|} \\ p_> &= \frac{|\{i \mid y_i = 1, x_{ig} \geq t\}|}{|\{i \mid x_{ig} \geq t\}|} \end{aligned}$$

Random Forests

A random forest is constructed by:

Repeat for $b \in \{1, \ldots, B\}$:

1. Generate $\underline{\mathbf{X}}_b$ by drawing n random integers $R_b = \{r_{bi} \in \{1, \ldots, n\}\}$ with replacement and setting $X_{bgi} = X_{gr_{bi}}$.
2. Recursively partition $\underline{\mathbf{X}}_b$ with the modification that for each partitioning step, $m < p$ of the features are randomly selected from a uniform distribution and the best split is selected from only this set of variables.
   - m random features redrawn for each new split.
   - Commonly $m \approx \sqrt{p}$.

Boosting

An alternative approach to model aggregation is boosting; one variant (Discrete AdaBoost, Friedman *et al.* (2000)) consists of:

1. Observation weights w_{1i} ($i \in \{1, \ldots, n\}$) are initialized: $w_{1i} = \frac{1}{n}$.
2. For each $b \in \{1, \ldots, B\}$, fit M to $(\underline{\mathbf{X}}, \underline{y}, \underline{w})$ and set

$$\mathrm{err}_b = \frac{1}{\sum_i w_{bi}} \sum_i w_{bi} \left[y_i \neq f_{M,\boldsymbol{\theta}_b}(\mathbf{x}_i) \right]$$

$$\alpha_b = \log \left(\frac{1 - \mathrm{err}_b}{\mathrm{err}_b} \right)$$

$$w_{(b+1)i} = w_{bi} \exp \left(\alpha_b \left[y_i \neq f_{M,\boldsymbol{\theta}_b}(\mathbf{x}_i) \right] \right)$$

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- Requires M to be able to fit weighted data set.

Boosting

Training of b^{th} tree fit focused on those samples misclassified by first $b-1$ trees.

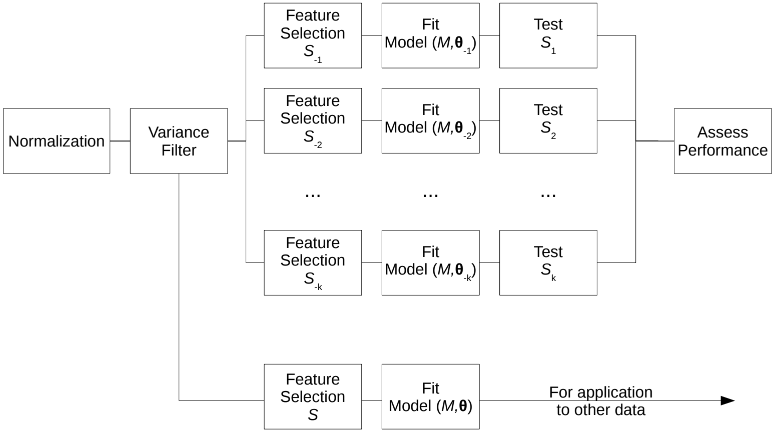
Individual trees cast votes weighted by α_b to determine outcome of final classifier.

Friedman *et al.* (2000) showed that from a statistical point of view boosting can be seen as a form of additive modeling with similarities to logistic regression.

Key concept which emerges across many variations of boosting is the importance of **slow learning**.

- often use very shallow trees (e.g., stumps)
- may be further facilitated by shrinkage and randomization

Cross-Validation Flow


Normalization
Variance Filter
Feature Selection S_{-1}
Fit Model $(M,\boldsymbol{\theta}_{-1})$
Test S_1
Feature Selection S_{-2}
Fit Model $(M,\boldsymbol{\theta}_{-2})$
Test S_2
...
...
...
Feature Selection S_{-k}
Fit Model $(M,\boldsymbol{\theta}_{-k})$
Test S_k
Assess Performance
Feature Selection S
Fit Model $(M,\boldsymbol{\theta})$
For application to other data

References I

Breiman, Leo. 1996. Bagging predictors. *Machine Learning*, **24**(2), 123–140.

Efron, Bradley, & Tibshirani, Robert. 1997. Improvements on cross-validation: the 632+ bootstrap method. *Journal of the American Statistical Association*, **92**(438), 548–560.

Friedman, Jerome, Hastie, Trevor, Tibshirani, Robert, *et al.* . 2000. Additive logistic regression: a statistical view of boosting. *The Annals of Statistics*, **28**(2), 337–407.

Hastie, Trevor, Tibshirani, Robert, & Friedman, Jerome. 2009. *The Elements of Statistical Learning*. Springer.