Lecture 8: Machine Learning III

Regularization, Optimization and Performance

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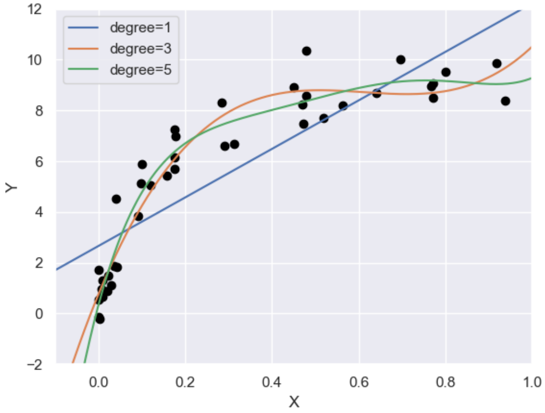
Outline

- Regularization
- Optimization
- Performance Metrics
- Data Leakage
- Nested Cross-validation

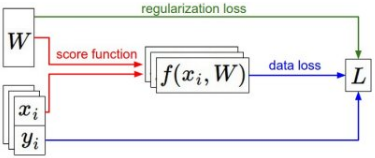
Polynomial Regression

$$y = ax + b$$
$$y = ax^3 + bx^2 + cx + d$$



Regularziation

$$\mathcal{L}_\lambda(\mathbf{w}) = \frac{1}{N}\sum_{i=1}^{N} L_i\big(y_i, f(\mathbf{x}_i;\mathbf{w})\big) + \lambda R(\mathbf{W})$$



- Regularization: prefer simpler models to improve generalization.
- λ is the regularization strength (hyper-parameter).
- L1 regularization: $R(W) = \sum |W|$
- L2 regularization: $R(W) = \sum W^2$
- Elastic net (L1+L2): $R(W) = \sum W^2 + |W|$
- Dropout in neural network

Regularziation

$$\begin{aligned}
\mathbf{x} &= [1,\ 1,\ 1,\ 1] \\
\mathbf{w}_1 &= [1,\ 0,\ 0,\ 0] \\
\mathbf{w}_2 &= [0.25,\ 0.25,\ 0.25,\ 0.25] \\
\mathbf{w}_1^T\mathbf{x} &= \mathbf{w}_2^T\mathbf{x} = 1
\end{aligned}$$

- L2 prefer spread out weights
- L1 tends to have sparse weights

Regularziation

$$
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$$

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Regularziation: Logistic Regression Example

The (regularized) logistic regression objective minimized is:

$$\mathcal{L}(w) = -\frac{1}{n}\sum_{i=1}^{n}\left[y_i \log p_i + (1-y_i)\log(1-p_i)\right] + \lambda R(w)$$

where $p_i = \sigma(w^T x)$ and $R(W)$ is the penalty (L2, L1, elastic-net).

Implement Logistic Regression in scikit-learn

```
clf = LogisticRegression(
        penalty='l2',
        C=C,
        solver='saga',
        max_iter=5000,
        random_state=42
)
scaler = StandardScaler()
Xs = scaler.fit_transform(X)
clf.fit(Xs, y)
```

In `scikit-learn`, the regularization strength is controlled by $C = \frac{1}{\lambda}$

C value	Effect	Genomics interpretation
$C = 0.01$	Very strong regularization	Only strongest signals survive
$C = 0.1$	Strong regularization	Aggressive shrinkage
$C = 1.0$	Moderate regularization	Reasonable default
$C = 10$	Weak regularization	Increased risk of overfitting
$C \to \infty$	No regularization	Ill-posed when $p \gg n$

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The Loss Landscape

Idea 1: Random Search

```
# assume X_train is the data where each column is an example (e.g. 3073 x 50,000)
# assume Y_train are the labels (e.g. 1D array of 50,000)
# assume the function L evaluates the loss function

bestloss = float("inf") # Python assigns the highest possible float value
for num in range(1000):
  W = np.random.randn(10, 3073) * 0.0001 # generate random parameters
  loss = L(X_train, Y_train, W) # get the loss over the entire training set
  if loss < bestloss: # keep track of the best solution
    bestloss = loss
    bestW = W
  print 'in attempt %d the loss was %f, best %f' % (num, loss, bestloss)

# prints:
# in attempt 0 the loss was 9.401632, best 9.401632
# in attempt 1 the loss was 8.959668, best 8.959668
# in attempt 2 the loss was 9.044034, best 8.959668
# in attempt 3 the loss was 9.278948, best 8.959668
# in attempt 4 the loss was 8.857370, best 8.857370
# in attempt 5 the loss was 8.943151, best 8.857370
# in attempt 6 the loss was 8.605604, best 8.605604
# ... (truncated: continues for 1000 lines)
```

Idea 2: Follow the Slope

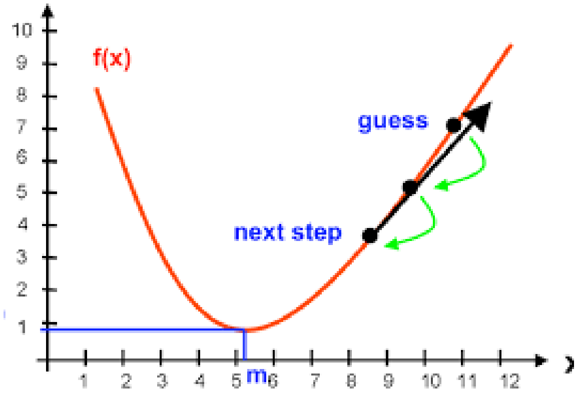
In 1-dimension, the derivative of a function:

$$\frac{\partial f(x)}{\partial x} = \lim_{h \to 0} \frac{f(x+h) - f(x)}{h}$$

In multiple dimensions, the gradient is the vector of (partial derivatives) in each dimension:

$$\nabla f(\mathbf{x}) = \begin{bmatrix} \frac{\partial f}{\partial x_1} \\ \frac{\partial f}{\partial x_2} \\ \vdots \\ \frac{\partial f}{\partial x_d} \end{bmatrix}$$

Gradient



Finding good Ws

$$
\begin{aligned}
s_i &= f(x_i; W) = W^T x_i \\
p_i &= \frac{1}{1+e^{-s_i}} \\
\mathcal{L}(w) &= -\left[\sum_{i=1}^{N} y_i \log p_i + (1-y_i)\log(1-p_i)\right]
\end{aligned}
$$

want $\nabla_W \mathcal{L}(W)$

Gradients

- Numerical gradient: approximate, slow, easy to write
- Analytical gradient: exact, fast, could be error-prone during derivation

Optimizer: Gradient Descent (batch)

Gradient Descent (batch)

$$\mathbf{w}_{t+1} = \mathbf{w}_t - \eta \nabla \mathcal{L}(\mathbf{w}_t),$$

where η is the step size (learning rate).

- Stable, smooth descent
- Uses full dataset each step (expensive)
- Good for small datasets or final fine-tuning

```
  # Vanilla Gradient Descent

while True:
  weights_grad = evaluate_gradient(loss_fun, data, weights)
  weights += - step_size * weights_grad # perform parameter update
```

Stochastic Gradients Descent (SGD)

Stochastic / Mini-batch GD

$$\mathbf{w}_{t+1} = \mathbf{w}_t - \eta\,\widehat{\nabla}_{\mathcal{B}_t}\mathcal{L}(\mathbf{w}_t)$$

- Cheap updates (one sample or mini-batch)
- Noisy gradients — can help exploration
- Requires learning rate schedules / tuning

```
# Vanilla Minibatch Gradient Descent

while True:
  data_batch = sample_training_data(data, 256) # sample 256 examples
  weights_grad = evaluate_gradient(loss_fun, data_batch, weights)
  weights += - step_size * weights_grad # perform parameter update
```

Optimizer: Momentum

Momentum

$$\mathbf{v}_t = \rho\,\mathbf{v}_{t-1} + \nabla\mathcal{L}(\mathbf{w}_t)$$

$$\mathbf{w}_{t+1} = \mathbf{w}_t - \eta\,\mathbf{v}_t$$

- Accumulates a velocity vector from past gradients
- Dampens oscillations in narrow valleys
- Accelerates convergence along consistent directions

Typical settings:

- Momentum coefficient: Default $\rho = 0.9$
- Learning rate: same scale as SGD

Optimizer: RMSProp

RMSProp (per-parameter adaptive)

$$v_t = \rho\, v_{t-1} + (1-\rho)\, g_t^2$$
$$\mathbf{w}_{t+1} = \mathbf{w}_t - \eta\, \frac{g_t}{\sqrt{v_t} + \varepsilon}$$

- Adaptive per-parameter learning rates
- Typical: $\rho = 0.9,\ \varepsilon = 10^{-8}$

Optimizer: Adam

Adam (momentum + adaptive scaling)

$$m_t = \beta_1 m_{t-1} + (1-\beta_1) g_t$$
$$v_t = \beta_2 v_{t-1} + (1-\beta_2) g_t^2$$
$$\widehat{m}_t = \frac{m_t}{1-\beta_1^t}, \quad \widehat{v}_t = \frac{v_t}{1-\beta_2^t}$$
$$\mathbf{w}_{t+1} = \mathbf{w}_t - \eta \frac{\widehat{m}_t}{\sqrt{\widehat{v}_t} + \varepsilon}$$

- Momentum + RMS scaling (fast convergence)
- Defaults: $\beta_1 = 0.9,\ \beta_2 = 0.999,\ \varepsilon = 10^{-8}$
- Often a great default for deep learning

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Accuracy: Definition and Intuition

Accuracy measures the fraction of correctly classified samples:

$$\text{Accuracy} = \frac{\text{TP} + \text{TN}}{\text{TP} + \text{TN} + \text{FP} + \text{FN}}$$

- TP: true positives TN: true negatives
- FP: false positives FN: false negatives

Interpretation:

- Probability that a randomly chosen sample is classified correctly
- Simple and intuitive

Why Accuracy Can Be Misleading

Problem: Class imbalance (common in genomics)

Example:

- 95 healthy samples, 5 disease samples
- Classifier predicts “healthy” for everyone

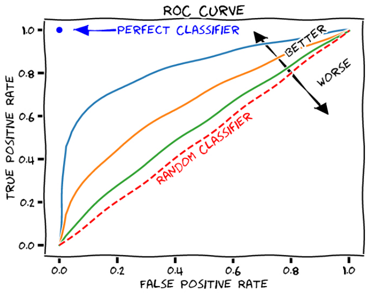
$$\text{Accuracy} = \frac{95}{100} = 95\%$$

But:

- Sensitivity (recall for disease) = 0
- Model is biologically useless

Key takeaway: Accuracy ignores the *decision threshold* and the *cost of errors*.

ROC Curve and ROC-AUC



Most classifiers output a **score or probability**, not just a label.
The **ROC curve** plots:

$$\mathrm{TPR} = \frac{\mathrm{TP}}{\mathrm{TP}+\mathrm{FN}} \quad \text{vs} \quad \mathrm{FPR} = \frac{\mathrm{FP}}{\mathrm{FP}+\mathrm{TN}}$$

as the classification threshold varies.

Interpreting ROC-AUC

ROC-AUC = Area Under the ROC Curve

- Ranges from 0.5 (random guessing) to 1.0 (perfect ranking)
- Threshold-independent

Probabilistic interpretation:

$$\text{ROC-AUC} = P\left(\text{score}_{\text{positive}} > \text{score}_{\text{negative}}\right)$$

That is:

- Probability that a randomly chosen disease sample is ranked higher than a randomly chosen control sample

Precision–Recall Curve and PR-AUC (Rare Disease Genomics)

When the positive class is rare (e.g. disease cases), ROC-AUC can be misleading.

The **Precision–Recall (PR) curve** plots:

$$\text{Precision} = \frac{\text{TP}}{\text{TP} + \text{FP}} \quad \text{vs} \quad \text{Recall} = \frac{\text{TP}}{\text{TP} + \text{FN}}$$

as the classification threshold varies.

PR-AUC = Area Under the Precision–Recall Curve

- Focuses on performance for the *positive (rare) class*
- Sensitive to false positives
- Baseline equals prevalence of the positive class

Why PR-AUC Matters for Rare Disease Genomics

Typical setting:

- Disease prevalence: $< 5\%$
- Goal: identify a small set of high-confidence candidates

Key differences vs ROC-AUC:

- ROC-AUC may appear high even with many false positives
- PR-AUC penalizes false positives directly
- Better reflects experimental validation cost

Interpretation:

- High PR-AUC $\Rightarrow$ predicted positives are trustworthy
- Low PR-AUC $\Rightarrow$ many false leads for follow-up

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Data Leakage: Definition

Data leakage occurs when information from outside the training data is used to build the model.

Formally:

Training procedure has access to information from the test set

Consequences:

- Overly optimistic performance estimates
- Poor generalization to new data
- Irreproducible scientific results

Common Sources of Data Leakage (Genomics)

- Scaling or normalization using the full dataset
- Feature selection performed before cross-validation
- Batch correction using test samples
- Reusing test data for model tuning

Key insight:

> *If the test data influences any step of model construction, performance estimates are invalid.*

Feature Selection Can Cause Leakage

Incorrect workflow:

1. Use all samples to select top k genes
2. Cross-validate classifier on selected genes

Why this is wrong:

- Feature selection uses label information
- Test folds influence which features are chosen

Result: Inflated accuracy, ROC-AUC, PR-AUC

Correct Feature Selection Workflow

Correct principle:

Feature selection must be performed inside the training data only.

Implementation:

- Encapsulate feature selection in a pipeline
- Apply selection separately in each CV fold

This ensures that test data remains truly unseen.

Nested Cross-Validation: Concept

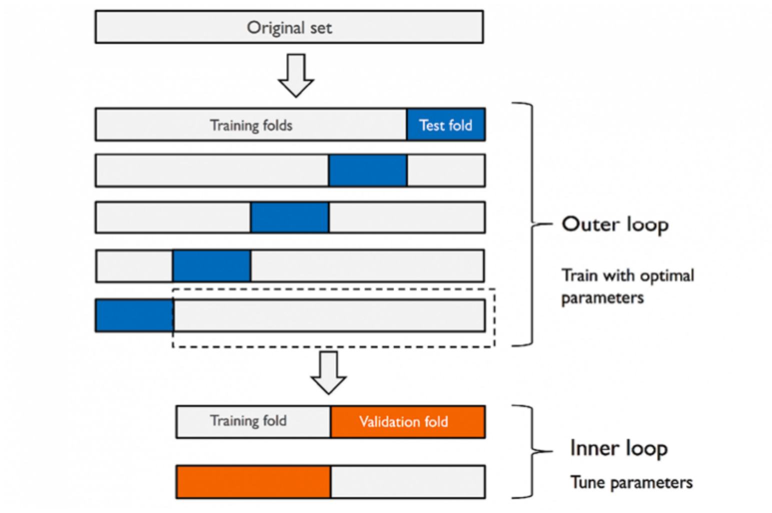
Nested cross-validation separates:

- **Model selection** (hyperparameters, features)
- **Model evaluation** (generalization performance)

Two loops:

- Inner CV: tuning and selection
- Outer CV: unbiased evaluation

Nested Cross-Validation


Original set
Training folds
Test fold
Outer loop
Train with optimal parameters
Training fold
Validation fold
Inner loop
Tune parameters