CSI5180. Machine Learning for Bioinformatics Applications

Kernel methods in bioinformatics

by

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Preamble

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Kernel methods in bioinformatics

In this lecture, we continue our exploration of **kernel methods** in bioinformatics. After an informal presentation of **support vector machines**, we now more formally investigate kernel methods. Still, the aim is to give you the intuition behind these methods. Specifically, you should understand how the data is implicitly embedded into a higher-dimensional space.

General objective :

- **Discuss** applications of kernel methods in bioinformatics

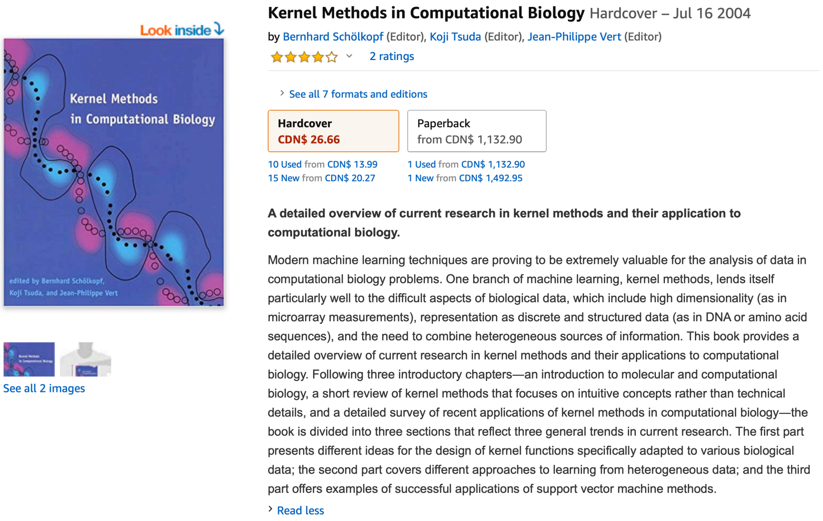
Learning objectives

- **Discuss** applications of kernel methods in bioinformatics

Reading:

- Berhhard Schölkopf, Koji Tsuda, and Jean-Philippe Vert (eds.), Kernel methods in computational biology, MIT Press, 2004. §2.

Kernel methods in computational biology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edited by Bernhard Schölkopf, Koji Tsuda, and Jean-Philippe Vert
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Kernel Methods in Computational Biology Hardcover – Jul 16 2004

by Bernhard Schölkopf (Editor), Koji Tsuda (Editor), Jean-Philippe Vert (Editor)

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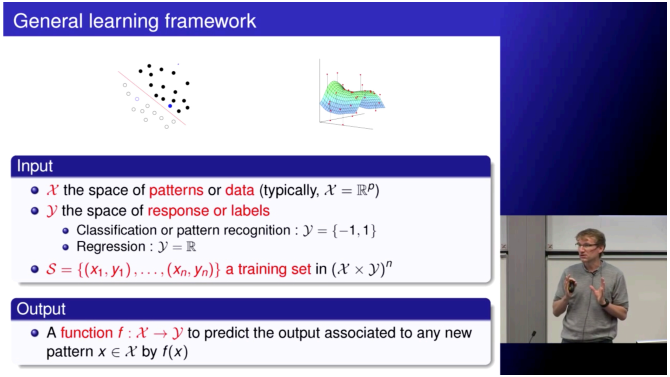
A detailed overview of current research in kernel methods and their application to computational biology.

Modern machine learning techniques are proving to be extremely valuable for the analysis of data in computational biology problems. One branch of machine learning, kernel methods, lends itself particularly well to the difficult aspects of biological data, which include high dimensionality (as in microarray measurements), representation as discrete and structured data (as in DNA or amino acid sequences), and the need to combine heterogeneous sources of information. This book provides a detailed overview of current research in kernel methods and their applications to computational biology. Following three introductory chapters—an introduction to molecular and computational biology, a short review of kernel methods that focuses on intuitive concepts rather than technical details, and a detailed survey of recent applications of kernel methods in computational biology—the book is divided into three sections that reflect three general trends in current research. The first part presents different ideas for the design of kernel functions specifically adapted to various biological data; the second part covers different approaches to learning from heterogeneous data; and the third part offers examples of successful applications of support vector machine methods.

Read less

Kernel methods in computational biology



General learning framework

Input

- $\mathcal{X}$ the space of patterns or data (typically, $\mathcal{X} = \mathbb{R}^p$)
- $\mathcal{Y}$ the space of response or labels
  - Classification or pattern recognition : $\mathcal{Y} = \{-1, 1\}$
  - Regression : $\mathcal{Y} = \mathbb{R}$
- $\mathcal{S} = \{(x_1, y_1), \ldots, (x_n, y_n)\}$ a training set in $(\mathcal{X} \times \mathcal{Y})^n$

Output

- A function $f : \mathcal{X} \to \mathcal{Y}$ to predict the output associated to any new pattern $x \in \mathcal{X}$ by $f(x)$

- `https://www.youtube.com/watch?v=svXc382Y3aw` (Part 1 - 1 hour 23 minutes)
- `https://www.youtube.com/watch?v=9QRVG1wB-ds` (Part 2 - 1 hour 31 minutes)
- `https://www.youtube.com/watch?v=KPpFc2OASIo` (Part 3 - 1 hour 38 minutes)

Plan

Introduction

Summary

- Just like **hidden Markov models** (**HMM**), **support vector machines** (**SVM**) have a strong theoretical foundation. **Kernel methods** are grounded into **statistical learning theory**.

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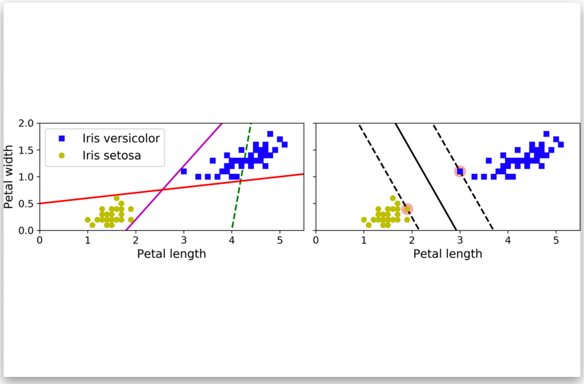
- **Combining** kernels for **data fusion**.

Summary

- The **support vectors** are the examples **closest** to the **separating hyperplane**.



Source: [19] Figure 5.1

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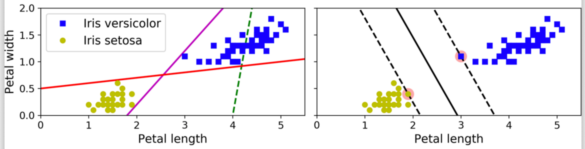

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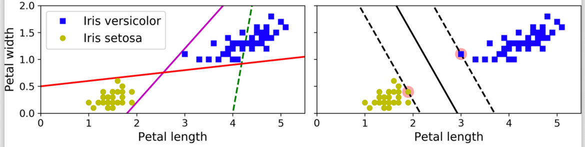
- The **support vectors** are the examples **closest** to the **separating hyperplane**.
- The **margin** is the distance between the **separating hyperplane** (decision boundary) and the **support vectors**.
- **Problem:** of all possible **separating hyperplanes** find the one with the **largest margin**.



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- However, **SVM** algorithms also rely on the concept of **maximum margin hyperplane** as a mechanism to lower generalization errors.
- In order to handle a **small number of classification errors**, the algorithms introduce the concept of **soft margin**.
- Finally, because the data is **not always linearly separable**, these algorithms project the data to **higher dimensions** using a **kernel function**.

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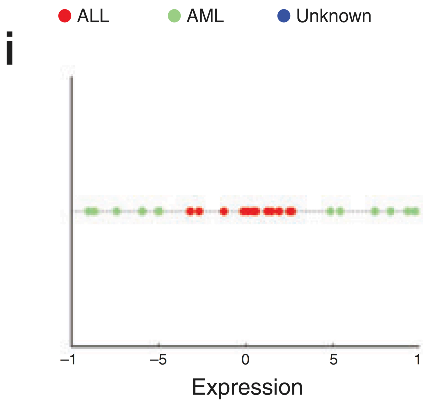
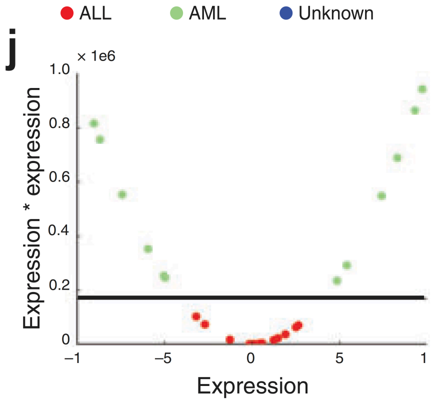


Source: [20] Figure 1i

- **No** single point can separate the two classes!

Summary



Source: [20] Figure 1j

- Adding a **new dimension** to our data.

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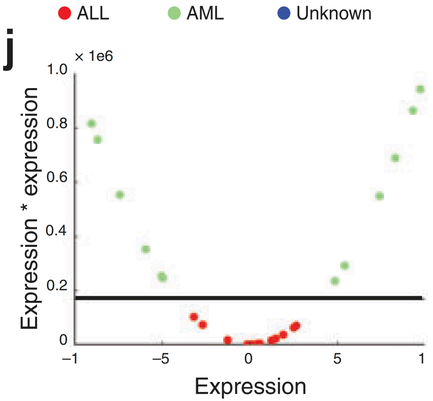

Source: [20] Figure 1j

- Adding a **new dimension** to our data.
- Here, simply taking the square values of our feature.

Support vector machines

Support vector machines (SVM)

- Bernhard E. Boser, Isabelle Guyon, and Vladimir Vapnik, A training algorithm for optimal margin classifiers, *COLT, ACM*, pp. 144152, 1992.

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- Let $\mathcal{S} = \{x_1, x_2, \ldots, x_N\}$ be a **data set**, each $x_i \in \mathcal{X}$.
- Let $\mathcal{Y} = \{y_1, y_2, \ldots, y_N\}$ be the **labels** associated with each object.

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- To **predict** the label of an $x \in \mathcal{X}$, evaluate $f(x)$.

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- Let use the label **1** for **positive examples** and -**1** for **negative examples**.
- Consequently, each y_i belongs to the set $\{-1, 1\}$.

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- We want to assign the label **+1** to points $x \in \mathcal{X}$ such that $f(x) \geq 0$, and **-1** to points $x \in \mathcal{X}$ such that $f(x) < 0$.

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  - For the other two cases, the example is misclassified.

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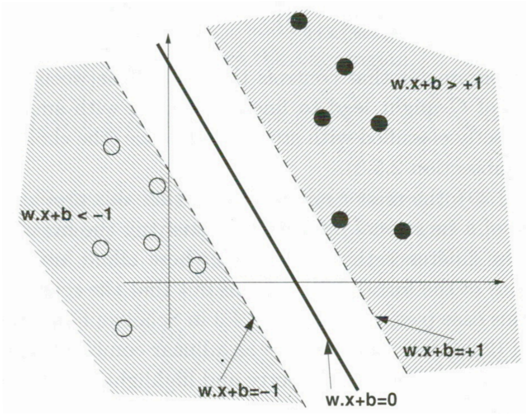
- A principled, termed **empirical risk minimization** suggests selecting the function $f(x)$ that makes the **fewer number of classification errors** on the training set $\mathcal{S}$.
- As we have seen, when the data is **linearly separable**, there could be infinitely many such hyperplanes (decision boundaries).

Support Vector Machine (SVM)

- Two **half-spaces**:



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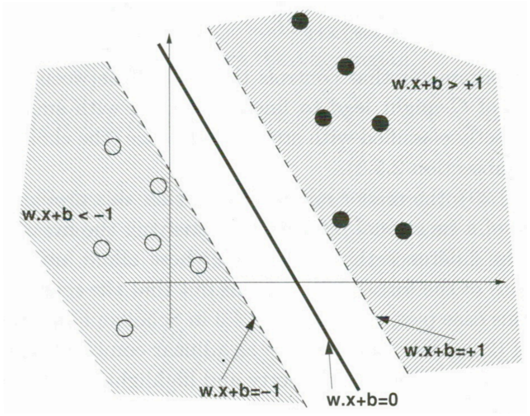

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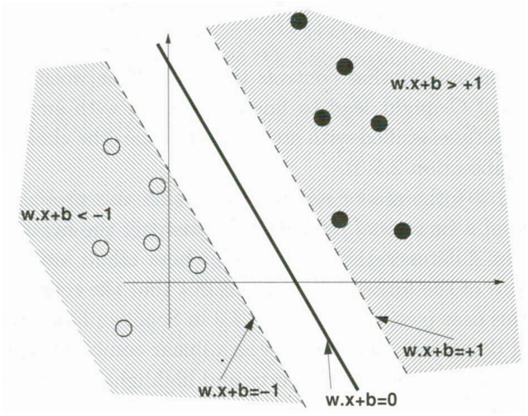

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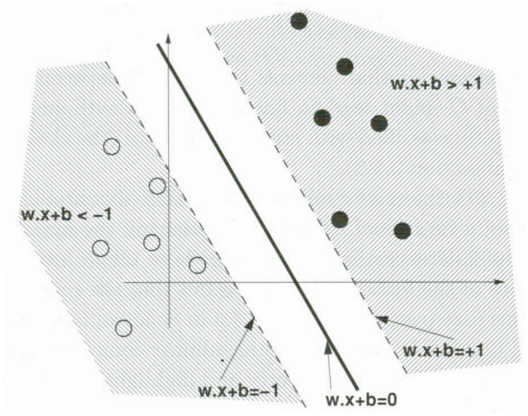

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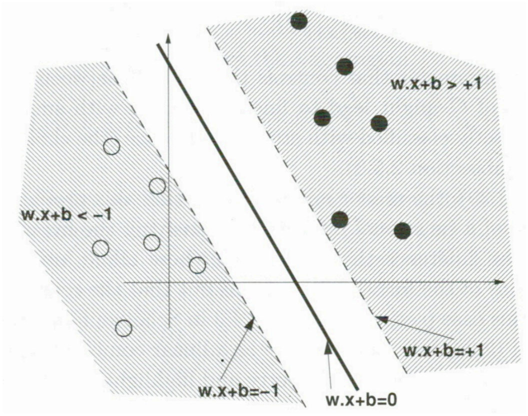

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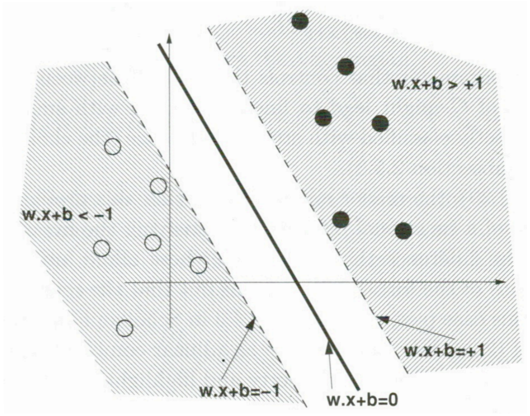
Large margin

- **Optimization**: maximize $\frac{2}{||w||}$ subject to

$$y_i(w^T x + b) \geq 1 \text{ for } i = 1, \ldots, N$$



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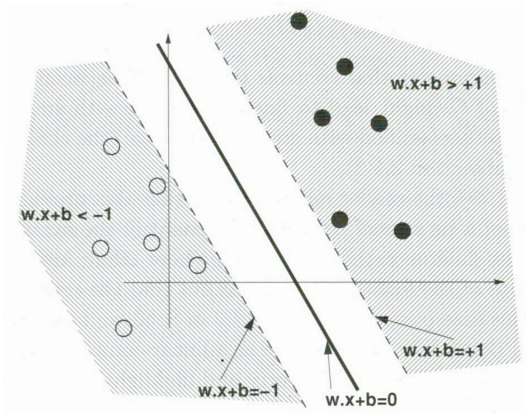
- There will be a solution only if the data set is **linearly separable**.



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Hinge loss function

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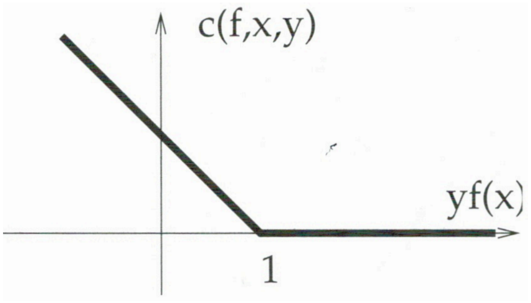
$$c(f,x,y) = \max(0, 1 - yf(x))$$



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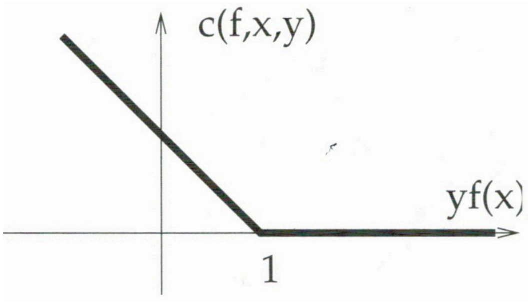

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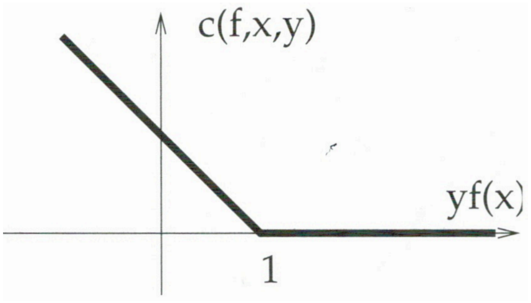

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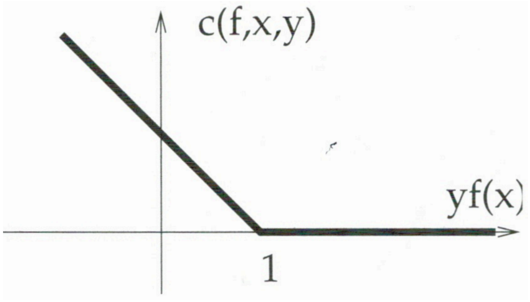

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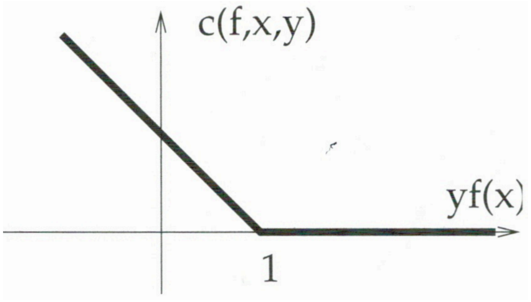

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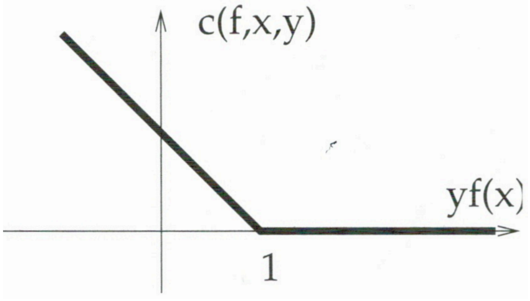
- if $yf(x) \leq 0$, the example is **misclassified** and the **cost** is $1 - yf(x)$.



Source [1] Figure 2.9

Support Vector Machine

- **Optimization**

$$\operatorname{argmin}_{f(x)=w^T x+b}\ \frac{1}{2}||w|| + C\sum_{i=1}^{N} c(f, x_i, y_i)$$

where C is a user-defined parameter controlling the tradeoff between having a **large margin** and **classification errors**.

Kernel representation

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  - **Vectors.** For a given application, each object $x_i \in \mathcal{X}$ could represent the level of expression of D genes for the i^{th} sample , in this case $\mathcal{F} = \mathbb{R}^D$.

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    - **Vectors.** For a given application, each object $x_i \in \mathcal{X}$ could represent the level of expression of D genes for the i^{th} sample , in this case $\mathcal{F} = \mathbb{R}^D$.
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Representation - traditional learners

- Let $\mathcal{S} = \{x_1, x_2, \ldots, x_n\}$ be a **data set**, the objects to be analyzed, each $x_i \in \mathcal{X}$.
- In order to apply a machine learning algorithm, we need a **representation** for each object, $\phi(x) \in \mathcal{F}, \forall x \in \mathcal{X}$.
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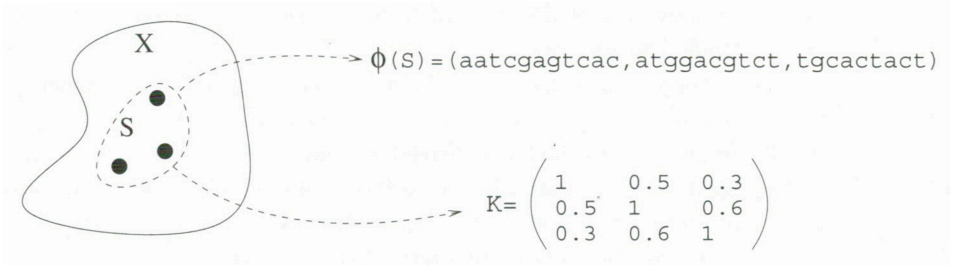
X
S
φ(S) = (aatcgagtcac,atggacgtct,tgcactact)
$K = \begin{pmatrix} 1 & 0.5 & 0.3 \\ 0.5 & 1 & 0.6 \\ 0.3 & 0.6 & 1 \end{pmatrix}$

Source: [1] Figure 2.1

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- The **data representation** as a square matrix is **independent** of the nature of the objects!
    - Algorithms are **modular**. The same algorithm can work **strings** or **graphs**, as long as a **function** k is defined for those objects (DNA, RNA, or protein sequences, graph connectivity, phylogenetic trees, RNA structures, molecular pathways, . . .).

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  - Even if each sample comprises **thousands** of gene expression levels.
  - This is **computationally** attractive.

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  - Pairwise comparison methods are often readily available.
    - **Pairwise sequence comparison** (alignment)
    - **Pairwise tree comparison** (Robinson-Foulds, RFL, etc.)
- This enables **data fusion/integration**.

Representation - kernel methods

- “Most kernel methods [. . .] can only process square matrices, which are **symmetric *positive semidefinite***. This means that if k it is a $n \times n$ matrix of pairwise comparisons, it should satisfy $k_{i,j} = k_{j,i}$ for any $1 \leq i, j \leq n$, and $c^T kc \geq 0$ for any $c \in \mathbb{R}^n$." [1] page 38.

Representation - kernel methods

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- "**Theorem** *For any kernel k on a space $\mathcal{X}$, there exists a Hilbert space $\mathcal{F}$ and mapping $\phi : \mathcal{X} \to \mathcal{F}$ such that*

$$k(x, x') = \langle \phi(x), \phi(x') \rangle, \text{for any } x, x' \in \mathcal{X}$$

where $\langle u, v \rangle$ represents the dot product in the Hilbert space between any two points $u, v \in \mathcal{F}$." [1] page 40.

Kernel trick

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- Finding the optimal value of $f(x)$ for a **support vector machine** requires solving a **quadratic programming problem**.
- After many mathematical transformations, buried into the equation to be solved, there is a **dot product of the transformed vectors**.
- Thanks to the previous theorem (Mercer's theorem), the dot product can be replaced by the value of the kernel in the original space.

Prologue

Summary

- Kernel methods use as input a $N \times N$ matrix, representing all **pairwise comparisons** between examples.

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- This allows kernel methods to handle a greater range of data types than most learning algorithms.

Next module

- Fundamentals of **deep learning**

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