#### **Machine Learning in Healthcare**

#### **#C05 Linear Models for Classification**

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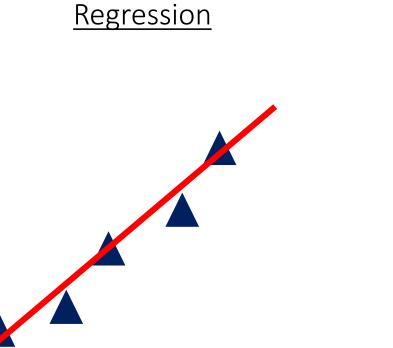




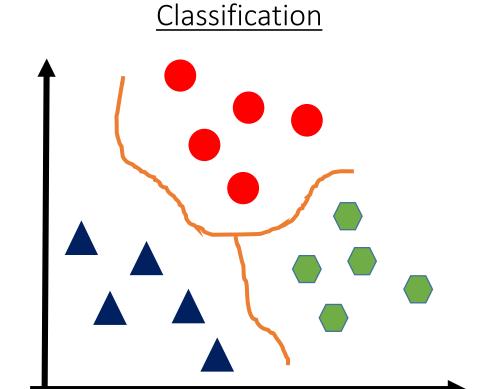
# Classification versus Regression



# Regression versus classification



Estimate relationships among usually continuous variables.



Identify decision boundary between examples of different classes.



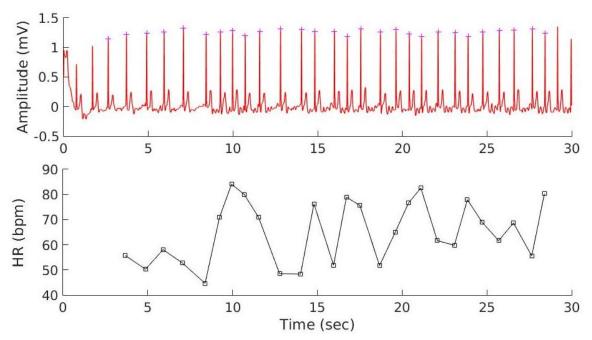
#### Classification

- Examples:
  - Tumor: Malignant/benign?
  - Rhythm: Atrial fibrillation/normal sinus?
- Let's consider a binary classification problem for now:

$$y \in \{0,1\}$$

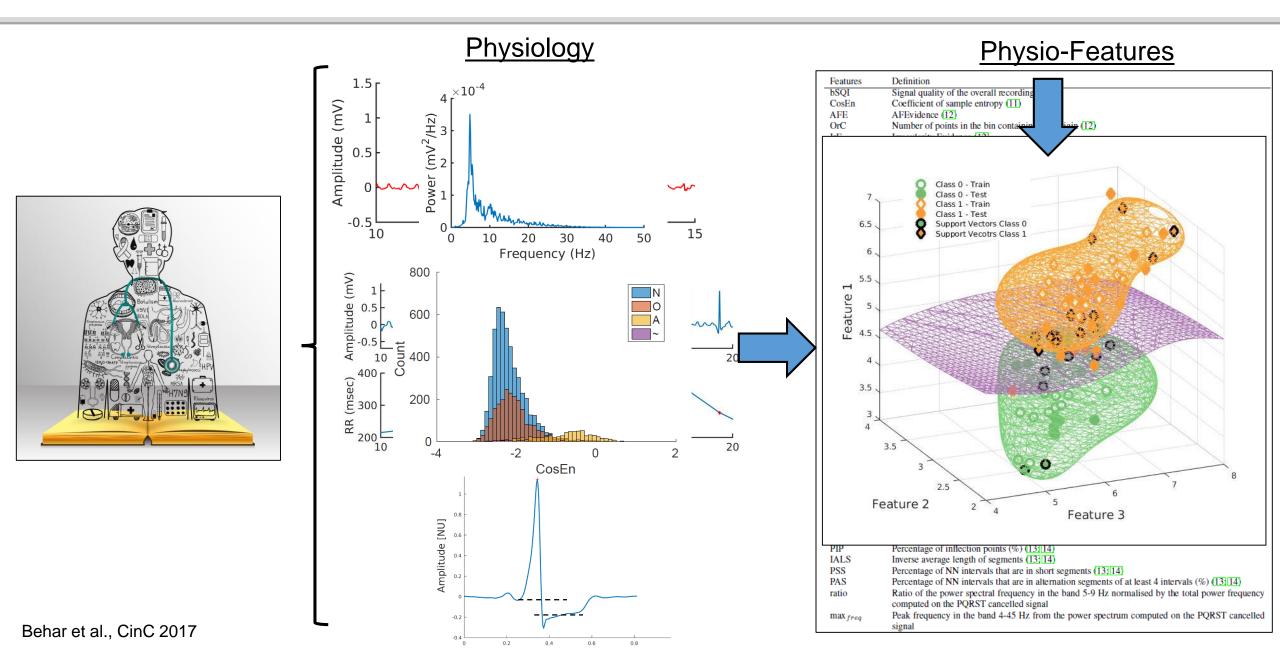
0: negative class (non-AF)

1: positive class (AF)



Behar et al., CinC 2017







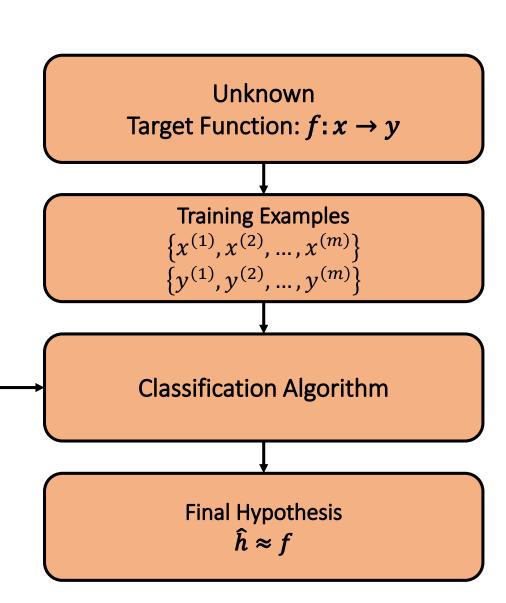
#### Classification

What do we chose?



Hypothesis Class

$$H = \{h\}$$





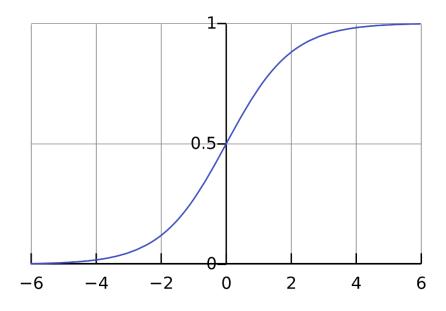
# LR Hypothesis Representation



# Hypothesis representation

- Linear regression:  $h_w(x) = w^T x$
- Logistic regression:  $h_w(x) = g(w^T x)$ 
  - With  $g(z) = \frac{1}{1+e^{-z}} = \sigma(z)$  the sigmoid function.

  - g(0) = 0.5.



Remark: "Logistic regression" is not a "regression" algorithm but a classification one. The naming is just historical!

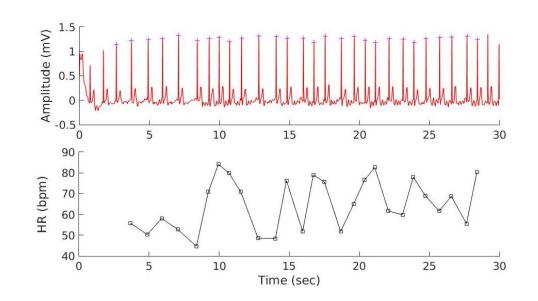


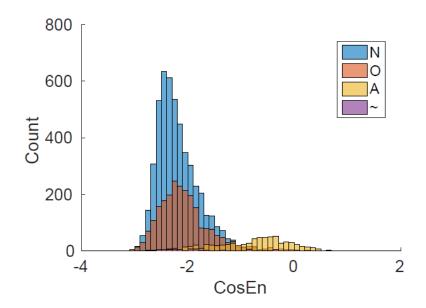
# Hypothesis representation

• Interpretation of the probabilistic output:

• 
$$x = \begin{bmatrix} x_0 \\ x_1 \end{bmatrix} = \begin{bmatrix} 1 \\ CosEn \end{bmatrix}$$
,

- $h_w(x) = 0.7 = P(y = 1|x, w),$
- This individual has 70% change to have AF.

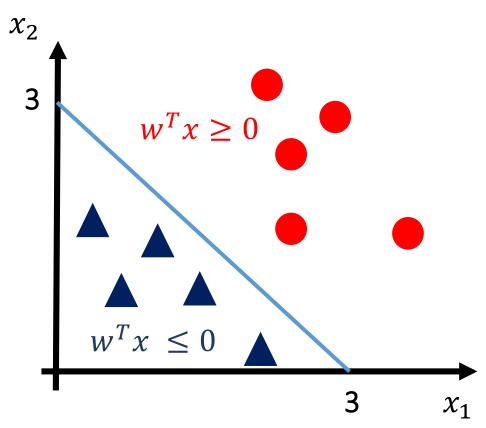






# Hypothesis representation

- Interpretation of the decision boundary:
  - $h_w(x) = g(w^T x) = \frac{1}{1 + e^{-w^T x}}$
- Example:
  - y = 1 if  $h_w(x) \ge 0.5 \iff w^T x \ge 0$
  - Conversely, y = 0 if  $h_w(x) \le 0.5 \iff w^T x \le 0$ .
  - This gives the decision boundary.
- e.g.  $h_w(x) = g(-3 + x_1 + x_2)$





# **LR Cost Function**



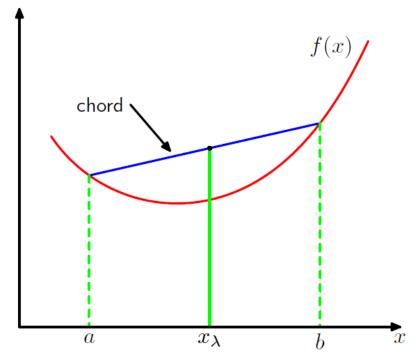
#### **Cost function**

- We have a training set of
  - $m \text{ examples: } \{x^{(1)}, x^{(2)}, ..., x^{(m)}\}$
  - With target labels:  $\{y^{(1)}, y^{(2)}, ..., y^{(m)}\}$
- How do we find the weights w of the LR model?
  - Reminder
    - Linear regression:  $J(w) = \frac{1}{m} \sum_{i=1}^{m} (h_w(x^{(i)}) y^{(i)})^2$
  - In LR we have  $h_w(x) = \sigma(z)$  and the resulting cost function J(w) is **non-convex**. Thus we need to find for another cost function that is convex.



#### Reminder: convex function

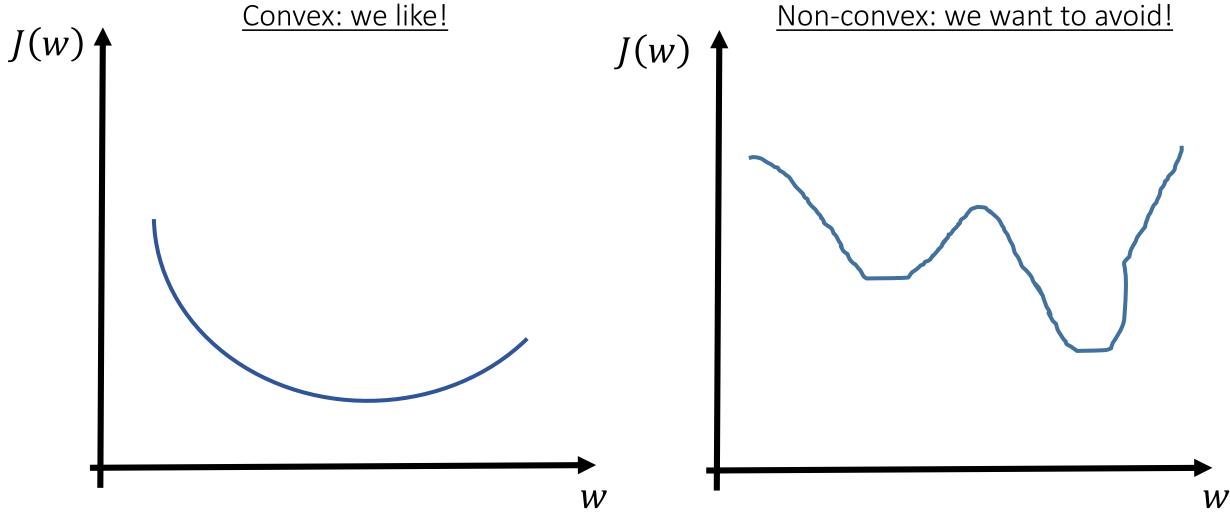
Figure 1.31 A convex function f(x) is one for which every chord (shown in blue) lies on or above the function (shown in red).



$$f(\lambda a + (1 - \lambda)b) \le \lambda f(a) + (1 - \lambda)f(b).$$



#### **Reminder: convex function**





#### Cost function in LR

We define the following error:

$$E_{w}(x,y) = \begin{cases} -\log(h_{w}(x)), & \text{if } y = 1\\ -\log(1 - h_{w}(x)), & \text{if } y = 0, \end{cases}$$

- If y = 1 and  $h_w(x) \to 0$  then  $E_w(x, y) \to \infty$
- If y = 1 and  $h_w(x) \to 1$  then  $E_w(x, y) \to 0$ .
- Ibid y = 0.



#### **Cost function in LR**

We define the error:

$$E_w(x,y) = \begin{cases} -\log(h_w(x)), & \text{if } y = 1\\ -\log(1 - h_w(x)), & \text{if } y = 0, \end{cases}$$

- We can re-write it:
- $E_w(x,y) = -y\log(h_w(x)) (1-y)\log(1-h_w(x))$
- The cost function:
  - $I(w) = \frac{1}{m} \sum_{i=1}^{m} E_w(x^{(i)}, y^{(i)})$

- It is possible to show that the cost function J(w) is convex.
- This is called the Cross-Entropy cost function or log loss.



#### **Cost function in LR**

- Why do we choose this particular error definition?
  - Maximum likelihood estimate.
    - $argmax_w \mathcal{L}(w|Y,X) = argmax_w (\prod_{i=1}^m \mathcal{L}(w|y^{(i)},x^{(i)}))$



Convex cost function.

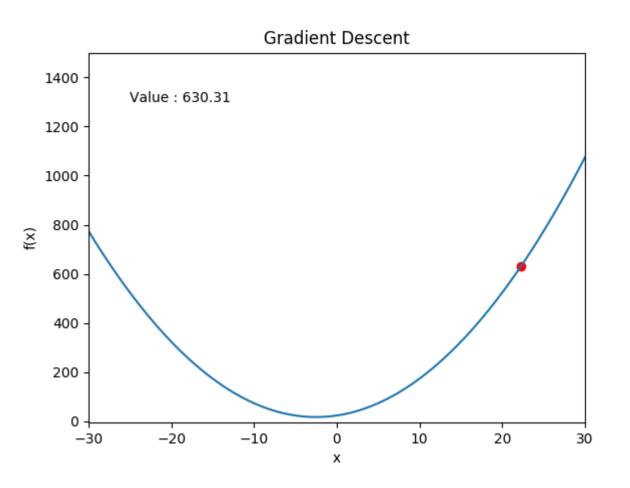


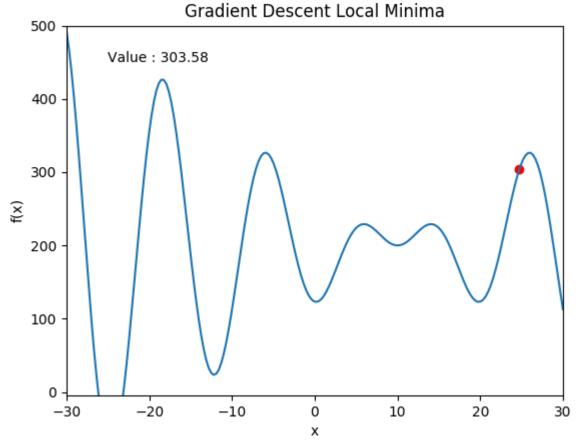
# **Gradient Descent**



- We now want to use some optimization algorithm to solve our optimization problem given the cost function we defined.
- We want to find  $min_w(J(w))$
- For that purpose we will use gradient descent.
- Given w we compute
  - *J(w)*
  - $\bullet \frac{\partial J(w)}{\partial w_j} \text{ for } j \in [1, ..., n]$
- Gradient descent, update  $w_i$ 
  - $w_j := w_j \alpha \frac{\partial J(w)}{\partial w_j}$
- More sophisticated alternative to gradient descent exist: conjugate gradient, BFGS, L-BFGS etc.









- How do we use gradient descent with LR?
  - Snapshot here more in details in the coming slides.
- The overall cost function:

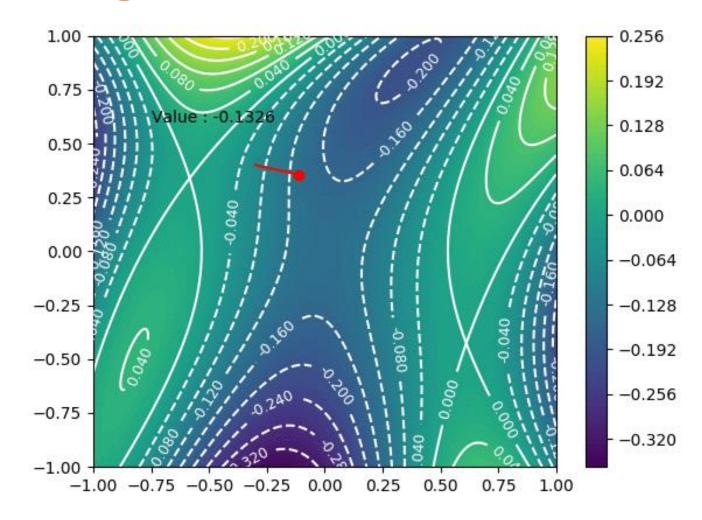
■ We need to compute  $\frac{\partial J(w)}{\partial w_j}$  for  $j \in [1, ..., n]$ 

• Gradient descent, update  $w_i$ 

$$w_j := w_j - \alpha \frac{\partial J(w)}{\partial w_j} = w_j - \alpha \frac{1}{m} \sum_{i=1}^m (h_w(x^{(i)}) - y^{(i)}) x_j^{(i)}$$

What about feature scaling? Yes, we need it!





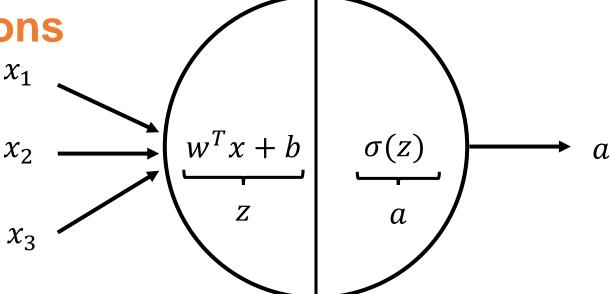


# Logistic Regression Gradient Descent



# Logistic regression equations

- Equations:
  - $z = w^T x + b$
  - $a = h_w(z) = \sigma(z)$

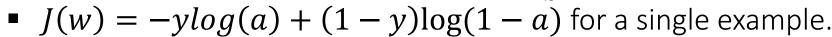




# Logistic regression equations

$$z = w^T x + b$$

$$a = h_w(z) = \sigma(z)$$



■ Forward propagation: →

$$z = w^T x + b$$

• 
$$a = \sigma(z)$$

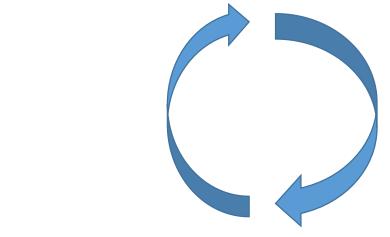
■ Backward propagation: ←

• 
$$w_1 \coloneqq w_1 - \frac{\partial J(w)}{\partial w_1} = w_1 - \alpha(a - y)x_1$$

• 
$$w_1 \coloneqq w_1 - \frac{\partial J(w)}{\partial w_1} = w_1 - \alpha(a - y)x_1$$
  
•  $w_2 \coloneqq w_2 - \frac{\partial J(w)}{\partial w_2} = w_2 - \alpha(a - y)x_2$ 

• 
$$b \coloneqq b - \frac{\partial J(w)}{\partial b} = b - \alpha(a - y)$$

Iterate between forward and backward step.



 $z = w_1 x_1 + w_2 x_2 + b \quad \Longrightarrow a = \sigma(z)$ 



# Logistic regression equations $w_1$

- Now consider m examples
  - Forward propagation,

$$z^{(i)} = w^T x^{(i)} + b, \forall i \in [1, m]$$

■ 
$$a^{(i)} = \sigma(z^{(i)}), \forall i \in [1, m]$$

Backward propagation:

• 
$$w_1 := w_1 - \frac{1}{m} \sum_{i=1}^m \alpha (a^{(i)} - y^{(i)}) x_1^{(i)}$$

• 
$$w_2 := w_2 - \frac{1}{m} \sum_{i=1}^m \alpha (a^{(i)} - y^{(i)}) x_2^{(i)}$$

• 
$$b := b - \frac{1}{m} \sum_{i=1}^{m} \alpha (a^{(i)} - y^{(i)}).$$

$$z = w_1 x_1 + w_2 x_2 + b \qquad \Rightarrow a = \sigma(z) \qquad \Rightarrow J(w)$$



 $a = \sigma(z)$ 

 $z = w_1 x_1 + w_2 x_2 + b$ 

# Logistic regression equations $w_1$

- Now consider n input features:
  - Forward propagation:

$$z^{(i)} = w^T x^{(i)} + b, \forall i \in [1, m]$$

$$a^{(i)} = \sigma(z^{(i)}), \forall i \in [1, m]$$

Backward propagation:

• 
$$w_j := w_j - \frac{1}{m} \sum_{i=1}^m \alpha (a^{(i)} - y^{(i)}) x_j^{(i)}, \forall j \in [1, n]$$

• 
$$b := b - \frac{1}{m} \sum_{i=1}^{m} \alpha (a^{(i)} - y^{(i)}).$$

• So if we perform k iterations of gradient descent we need to go through two loops of m (forward) and then n (backward) steps. In LR this might be viable but as we will see later on with neural network this becomes not a viable option when there are many training examples and features. We have to vectorise these steps.



#### How can we vectorise?

Forward propagation

$$z^{(1)} = w^T x^{(1)} + b$$

$$a^{(1)} = \sigma(z^{(1)})$$

$$z^{(2)} = w^T x^{(2)} + b$$

$$a^{(2)} = \sigma(z^{(2)})$$

- •
- Vectorized form of forward propagation:

$$z = w^T X + b$$

• 
$$z \in \mathbb{R}^m, z = [z^{(1)}, ..., z^{(m)}]$$

• 
$$w \in \mathbb{R}^{n_x}, w = [w_1, \dots, w_n]$$

$$X \in \mathbb{R}^{n_{\chi} \cdot m}, X = [x^{(1)}, ..., x^{(m)}]$$

• 
$$b \in \mathbb{R}^m, b = [b, b, ..., b]$$



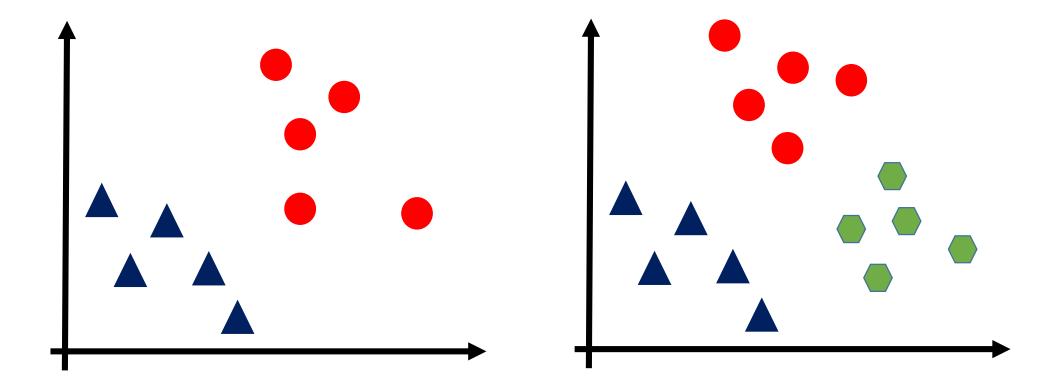
#### How can we vectorise?

- Backward propagation:
  - $w_j := w_j \frac{1}{m} \sum_{i=1}^m \alpha (a^{(i)} y^{(i)}) x_i^{(i)}, \forall j \in [1, n]$
- Vectorized backward propagation:
  - $w \coloneqq w \frac{1}{m} X \left( \underline{a} y \right)$
  - $a \in \mathbb{R}^m, y \in \mathbb{R}^m, X \in \mathbb{R}^{n_x \cdot m}$
- In conclusion, the Vectorized form of LR gradient descent:
  - $z = w^T X + b$ (forward step)
  - $w \coloneqq w \frac{1}{m} X \left( \underline{a} \underline{y} \right)$   $b \coloneqq b \frac{1}{m} \sum_{i=1}^{m} \alpha \left( a^{(i)} y^{(i)} \right)$ (backward step)
    - (backward step)



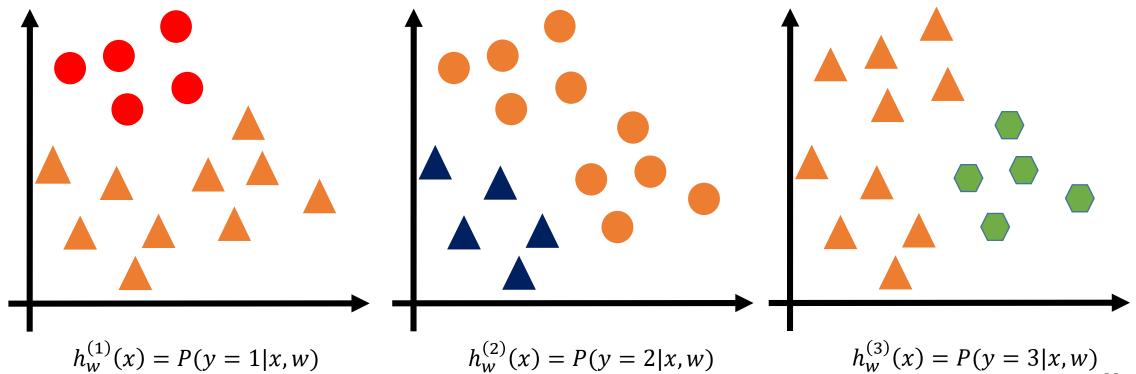


- We are now interested in a problem where the output is not binary.
- Consider the arrhythmia example. Say we now want to distinguish between categories: AF, other ARR and NSR.



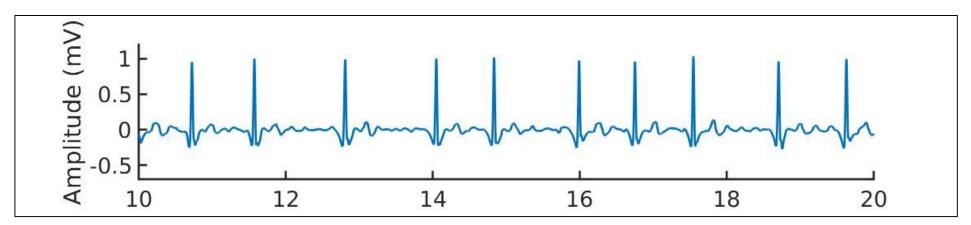


- How do we do that?
- "One vs. all" also called "one vs. the rest" approach.
- Transform the problem into a set of 2-class classification problems:





- So we come up with 3-classifiers, each classifier is trained to recognize one of the three classes.
- How do we classify a new observation x?
  - $max_i\left(h_w^{(i)}(x)\right)$
- This is called the **one-vs-all approach**.
- There a exist other approaches.





https://scikit-learn.org/stable/auto\_examples/linear\_model/plot\_logistic\_multinomial.html

- We saw the one-vs-all approach.
- Another option is using a multinomial LR:
  - Two class classification:  $z = w^T x + b$
  - Multinomial: z = Wx + b
    - $z, b \in \mathbb{R}^{n_y}$ ,
    - $W \in \mathbb{R}^{n_y \cdot n_x}$ ,
- From the z vector how do we classify? Softmax activation function:
  - The usual: z = Wx + b
  - Now activation function: a = softmax(z)
  - $a = e^z / \sum_{i=1}^K e^{z_i}$
- The softmax is also called normalized exponential function. It is a function that takes an input vector of size K and normalizes it into K probability distribution proportional to the exponentials of the input numbers.



Cost function we add for the two-class classification:

- For the multinomial LR:
  - $J(w) = \frac{1}{m} \sum_{i=1}^{m} \sum_{k=1}^{n_y} \left[ 1\{y^{(i)} = k\} \log(h_{w_k}(x^{(i)})) \right],$

- Thus two differences with what we had previously:
  - The cost function sums over the number of classes.
  - We use the softmax activation function and not  $\sigma$ .



# Odds and odds ratio



- Say we learned our model:
  - $h_w(x) = \sigma(w^T x) = \frac{1}{1 + e^{-w^T x}}$
  - This means that we have learned the weights w from the dataset.
- How do we interpret the weights value?
- Let's take the former example of AF diagnosis and the positive class as AF and negative class as no-AF.
- Let's write  $p = \frac{1}{1 + e^{-w^T x}}$
- Then we have:
  - $\frac{p}{1-p} = \frac{1}{e^{-w^T x}}$   $\log\left(\frac{p}{1-p}\right) = w^T x$



- If we assume a single feature, say blood pressure (BP) then
- Let's define the following quantity  $\frac{p}{1-p}$  that we will call the *odds*.
  - p is the probability of AF and p-1 is the probability of non-AF.
  - $\frac{p}{1-p}$  is the **likelihood of some events to happen** e.g. the likelihood of AF.
- On a more perhaps intuitive example, if we roll an even dice and look for the chance of obtaining a 4 then we can say that the probability of 4 is 1/6=17% or equivalently that the odds of a 4 is (1/6)/(5/6)=0.2 or odds is 1:5.
  - Probabilities: "The probability of rolling a four is 17%"
  - Odds: "For one roll of a 4 you will have 5 non-4." The odds is 1:5.
- On the AF example, say p = 20% then:
  - Probabilities: "The probability of a patient being AF is 20%".
  - Odds: "For 1 patient having AF 3 will be non-AF." The odds is 1:4



- With the previous definition of the odds, we can write:
- If we write this equation for a given value of BP and one increment to the variable i.e. BP + 1.
  - $\bullet (1) \log(odds_{BP}) = w_0 + w_1 \cdot BP,$
  - (2)  $\log(odds_{BP+1}) = w_0 + w_1 \cdot (BP + 1)$ .
  - $(2) (1) = \log(odds_{BP+1}) \log(odds_{BP}) = w_1$ 
    - Thus  $w_1$  corresponds to the difference between the log odds for one unit increase in BP.
  - $e^{W_1} = \frac{odds_{BP+1}}{odds_{BP}} = odds$  ratio
    - Odds ratio: relative chance of an event happening under different conditions (here one unit increase of BP).



- Say  $e^{w_1} = 1.06$ , how do we read that?
  - "For one increase in BP the odds of having AF will increase by 6%."
- Why do we use odds and odds ratio?
  - We use the concept of odds and odds ratio here to provide some interpretation to the weights we have learned in the LR model.
- What if we standardize features?
  - In this case the "one unit increase" will read as "one standard deviation increase".
- What about if you have many features?







Contents lists available at ScienceDirect

### Clinical Nutrition

journal homepage: http://www.elsevier.com/locate/clnu



### Original Article

Chocolate consumption is inversely associated with prevalent coronary heart disease: The National Heart, Lung, and Blood Institute Family Heart Study

Luc Djoussé a,b,\*, Paul N. Hopkins c, Kari E. North d, James S. Pankow e, Donna K. Arnett f, R. Curtis Ellison g

**Table 2**Prevalence odds ratios (95% confidence intervals) of coronary heart disease according to chocolate consumption in 4970 participants in the NHLBI Family Heart Study<sup>a</sup>.

Frequency of chocolate intake	Cases/N	Crude	Model 1 <sup>b</sup>	Model 2 <sup>c</sup>
0	168/1093	1.0	1.0	1.0
1–3 per month	147/1167	0.79 (0.62-1.01)	1.01 (0.76-1.37)	1.05 (0.77-1.43)
1–4 per week	182/1931	0.57 (0.46-0.72)	0.74 (0.56-0.98)	0.75 (0.56-1.01)
5+ per week	43/779	0.32 (0.23-0.45)	0.43 (0.28-0.67)	0.43 (0.27-0.68)
P for linear trend		< 0.0001	<0.0001	0.0002

<sup>&</sup>lt;sup>a</sup> Coronary heart disease was defined as history of myocardial infarction, PTCA, or CABG.

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g Section of Preventive Medicine & Epidemiology, Evans Department of Medicine, Boston University School of Medicine, Boston, MA, USA

b Adjusted for age, sex, and risk group (random vs. high risk) using generalized estimating equations (GEE).

<sup>&</sup>lt;sup>c</sup> Variables in Model 1 plus additional adjustment for dietary linolenic acid, education, exercise (min/d), smoking (yes/no), alcohol intake (yes/no), fruit and vegetables, energy intake, and non-chocolate candy (4 groups) consumption.



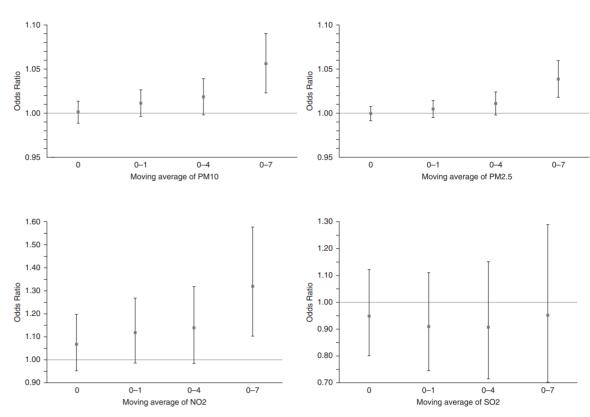


Figure 1. The association between air pollution and bronchiolitis: case—cross-over data showing the results of single-pollutant models of the association between bronchiolitis and moving average concentrations of the pollutants 0, 0–1, 0–4, and 0–7 days before the event. Each exposure was modeled separately and was adjusted for the average temperature that corresponds to the period of the exposure tested. Results are presented as odds ratios and 95% confidence intervals for interquartile range increase in particulate matter (PM) less than 10  $\mu$ m (PM<sub>10</sub>; 25  $\mu$ g/m³), PM less than 2.5  $\mu$ m (PM<sub>2.5</sub>; 5  $\mu$ g/m³), nitrogen dioxide (NO<sub>2</sub>; 13  $\mu$ g/m³), or sulfur dioxide (SO<sub>2</sub>; 3.14  $\mu$ g/m³).

### **ORIGINAL RESEARCH**

## Air Pollution and Hospitalization for Bronchiolitis among Young Children

Maayan Yitshak-Sade<sup>1,2\*</sup>, Dror Yudovitch<sup>1\*</sup>, Victor Novack<sup>1,2</sup>, Asher Tal<sup>3</sup>, Itai Kloog<sup>4</sup>, and Aviv Goldbart<sup>3</sup>

<sup>1</sup>Clinical Research Center, Soroka University Medical Center, Beer Sheva, Israel; <sup>2</sup>Department of Medicine, Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer Sheva, Israel; <sup>3</sup>Department of Pediatrics, Soroka University Medical Center, Beer Sheva, Israel; and <sup>4</sup>Department of Geography and Environmental Development, Faculty of Humanities and Social Sciences, Ben-Gurion University of the Negev, Beer Sheva, Israel

#### **Abstract**

**Rational:** Several studies have found higher risks for childhood respiratory illness, associated with exposure to particulate matter (PM) less than  $10 \mu m$  in diameter (PM<sub>10</sub>) and PM<sub>2.5</sub> and gaseous pollution.

**Objectives:** We analyzed the association between air pollution and hospitalizations due to bronchiolitis, an obstructive pulmonary disorder, commonly caused by respiratory syncytial virus infant infection.

**Methods:** Data were obtained from a local tertiary medical center providing services for a population of 700,000 comprising two ethnic groups: predominantly urban Jews and rural Bedouin Arabs. The latter

**Results:** We identified 4,069 bronchiolitis hospitalizations (3,889 children), with 55.3% being Bedouin Arabs, of whom 16.8% resided in temporary dwellings. An increase in interquartile range of average weekly air pollutants was associated with an increased odds of bronchiolitis (odds ratio [95% confidence interval]):  $PM_{10}$  (1.06 [1.02–1.09]),  $PM_{2.5}$  (1.04 [1.02–1.06]) and nitrogen dioxide (1.36 [1.12–1.65]). Higher effect-estimates for PM were observed among Bedouin Arabs residing in temporary dwellings (1.14 [1.01–1.30] and 1.07 [1.01–1.15]) compared with Jewish individuals (1.05 [0.99–1.11] and 1.03 [1.01–1.07]) and other Bedouin Arabs (1.05 [1.01–1.10] and 1.03 [1.01–1.07]), and among males (1.11 [1.06–1.16] and 1.06 [1.03–1.09]) compared with females (0.99 [0.94–1.05] and 1.01 [0.97–1.04]).



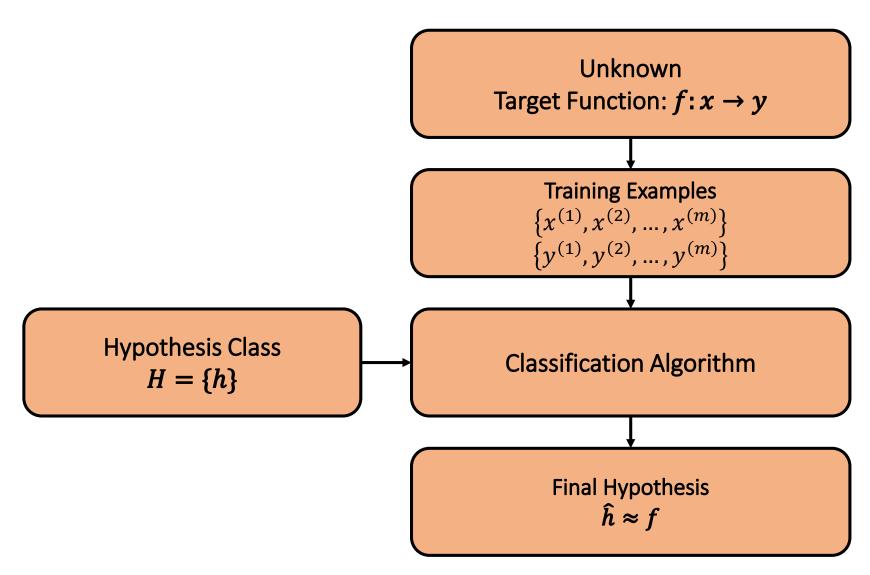
# **Linear Discriminant Analysis**



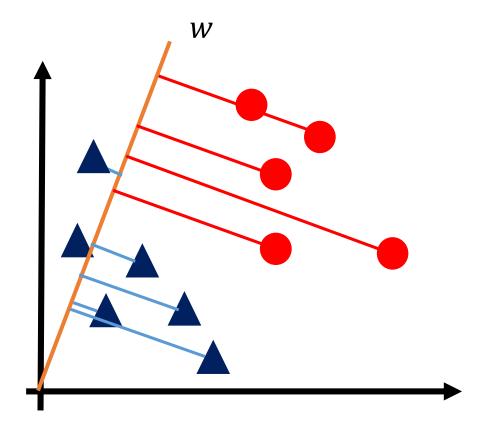
- LDA is used for classification and dimensionality reduction.
- It aims to preserve as much of the class discriminatory information as possible.
- It is often used for dimensionality reduction followed by a classification step.
- We have a training set of:
  - $m \text{ examples } \{x^{(1)}, x^{(2)}, \dots, x^{(m)}\},$
  - With target labels:  $\{y^{(1)}, y^{(2)}, ..., y^{(m)}\}$ .
- Hypothesis function:  $h_w(x) = w^T x$
- We need to find the w that maximize the separability of the observations.

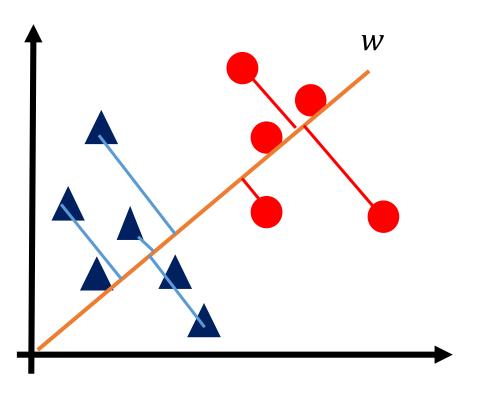






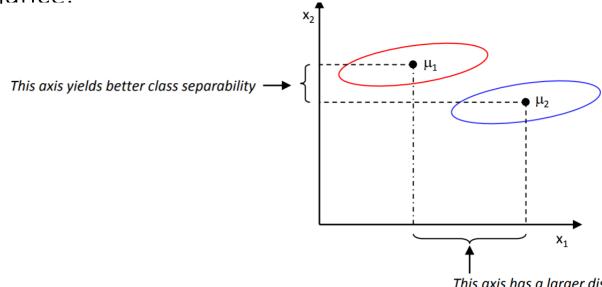








- How do we measure the separation?
- We need to define a measure of separation
- Let's try the difference between the means of the projected observations:
  - $J(w) = |\widetilde{\mu_1} \widetilde{\mu_2}| = w^T(\mu_1 \mu_2)$
  - But not so good because it does not take into account the intra classes variance.



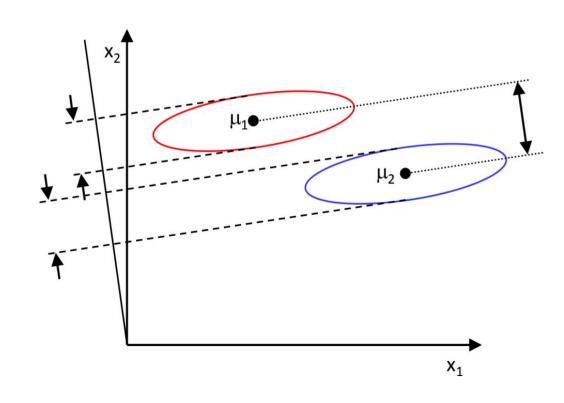


- We can do better.
- Fisher suggested maximizing the difference between the means, normalized by a measure of the within-class scatter.
- For each class:

$$\tilde{s}_j^2 = \sum_{i=1}^{m_j} (y_j^{(i)} - \tilde{\mu}_j)^2$$

Overall cost function:

 We look for a projection where observations from the same class are projected very close to each other but where the projected means are as far as possible from each other.

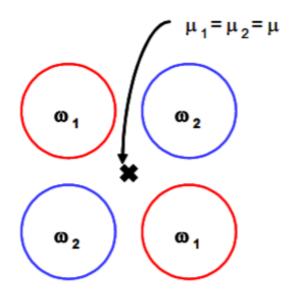


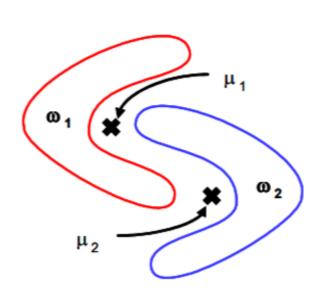


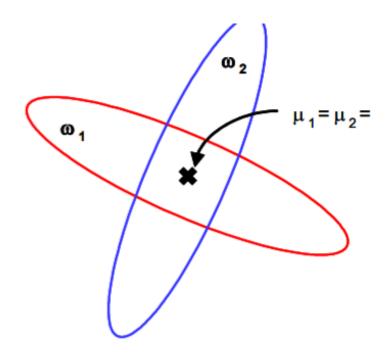
- Now that we have defined the overall cost function, how do we solve for w?
- We can show (make the demo) that the solution is given by:
  - $w = S_w^{-1}(\mu_1 \mu_2)$
  - $S_w = S_1 + S_2$
  - $S_j = \sum_{i=1}^{m_j} (x_j^{(i)} \mu_j)(x_j^{(i)} \mu_j)$
  - So we have a closed form solution of the LDA problem.
- If we want to use LDA for classification"
  - $h_w(x) = w^T x$
  - An example x belongs to class c if  $h_w(x) > t$  where t is the decision threshold.
- Limitation. By assuming  $J(w) = \frac{|\tilde{\mu}_1 \tilde{\mu}_2|^2}{\tilde{s}_1^2 + \tilde{s}_2^2}$  we intrinsically assumed that the independent variables are normally distributed and this is a fundamental assumption of LDA and a fundamental limitation of it!
- LDA can be generalized to multiple classes.



## **LDA Limitations**









### Take home

- Classification versus regression
- Logistic Regression (LR) hypothesis representation, cost function
- Convexity of the overall cost function
- Gradient descent
- Multiclass classification: one vs. all
- LR is one of the most popular classification algorithm. Use it as a baseline before moving to more complex models.
  - Advantages: efficient, interpretable, outputs probabilities.
  - Drawback: cannot solve non-linear problems since the LR decision surface is linear.
- Linear Discriminant Analysis (LDA)
  - Reduce dimensionality while preserving as much of the class discriminatory information as possible.
  - Used for dimensionality reduction and classification.
  - Assumes independent variables are normally distributed.





### References

- [1] Andrew Ng, Coursera, Machine Learning. Coursera.
- [2] Andrew Ng, Coursera, Neural Networks and Deep Learning. Coursera.
- [3] CSCE 666 Pattern Analysis | Ricardo Gutierrez-Osuna | CSE@TAMU

URL: <a href="http://research.cs.tamu.edu/prism/lectures/pr/pr l10.pdf">http://research.cs.tamu.edu/prism/lectures/pr/pr l10.pdf</a>



# **Classification versus Regression**

- Given HRV features decide whether the individual has AF or not.
- Regression model and threshold at the hypothesis function being 0.5 i.e.  $h_w(x) = 0.5$ ?
- Sometime it may be ok.
- But most of the time this is not appropriate.

