Applying maths to understand biological systems

Magdalene College outreach residential

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Aim of lecture

- Introduce you to problems where maths can be applied to Biological systems.
- Example of interdisciplinary research.
- Neuroscience –> artificial intelligence/machine learning

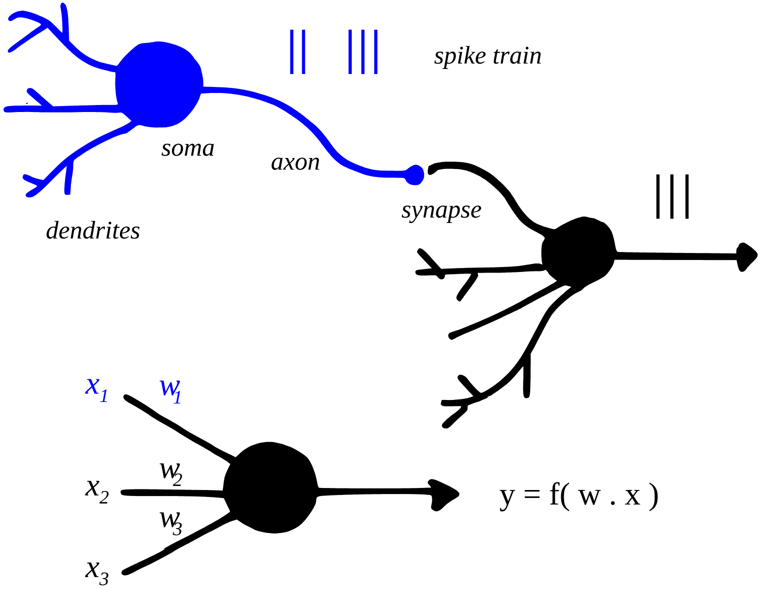
Please ask questions.
Slides available at: `http://bit.ly/eglen-mag17` with links to literature.

My background

What is mathematical biology?

- Mathematics Is Biology's Next Microscope, Only Better; Biology Is Mathematics' Next Physics, Only Better. Cohen (2004) `http://doi.org/journal.pbio.0020439`
- Rich history in Cambridge:
- Disease dynamics
- Cancer research
- Neuroscience (Hodgkin-Huxley)

Neurophysiology 101



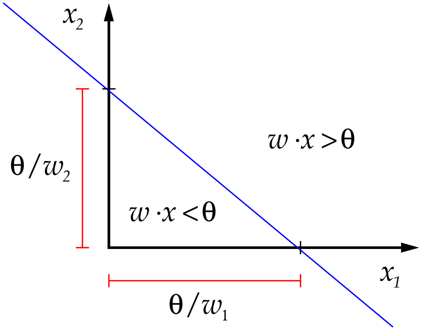
Perceptrons

Whether a perceptrons output is 0 or 1 depends on whether $\sum_{i=1}^{N} w_i x_i$ is less or greater than θ.

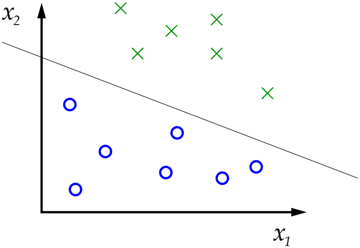
The equation $\sum_{i=1}^{N} w_i x_i = \theta$ defines a hyperplane in N-dimensional space.

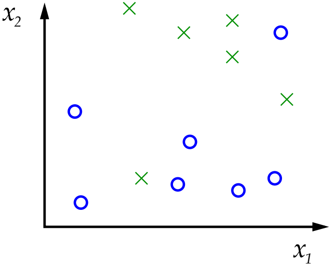
This hyperplane cuts the space in two.

$$w_1 x_1 + w_2 x_2 = \theta \Rightarrow x_2 = \left(\frac{-w_1}{w_2}\right) x_1 + \frac{\theta}{w_2}$$



Linearly separable problems





Learning involves adjusting the values of w and θ so that the decision plane can correctly divide the two classes.

What can they do?

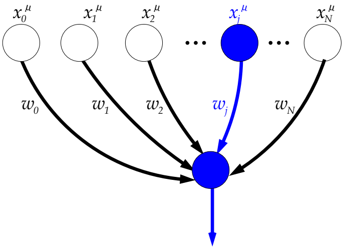
Generate simple building blocks, like logic gates.

1. OR
2. AND

Systematic “training” of weights

Intuitive and mathematical approach …

Intuitive explanation



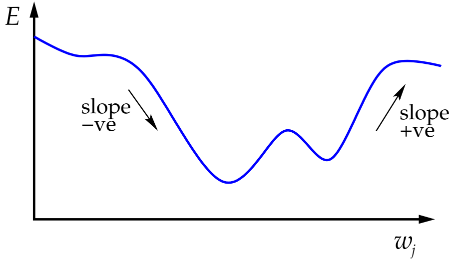
$y^\mu = \text{step}\left(\sum_{i=0}^{N} w_i x_i^\mu\right)$

Consider w_j's contribution to $\sum_i w_i x_i^\mu$ in different cases:

1. $y^\mu = t^\mu$ Perceptron has classified input μ correctly – change nothing
2. $x_j^\mu = 0$ Changing w_j will not affect the $\sum_i w_i x_i^\mu$ – change nothing
3. $x_j^\mu \neq 0, y^\mu < t^\mu$ The sum $\sum_i w_i x_i^\mu$ is too low – so increase it
4. $x_j^\mu \neq 0, y^\mu > t^\mu$ The sum $\sum_i w_i x_i^\mu$ is too high – so decrease it

The local rule: $\boxed{\Delta w_j \propto (t^\mu - y^\mu)\, x_j^\mu}$

Perceptron learning rule



$$y = f(\mathbf{w} \cdot \mathbf{x}) \qquad \text{e.g.} \quad f(z) = 1/(1+\exp(-z)), \quad f(z) = z$$

$$E = \frac{1}{2}(t-y)^2 \qquad t \text{ is target output}$$

$$\Delta w_j = -\epsilon \frac{\partial E}{\partial w_j} = -\epsilon \frac{\partial E}{\partial y} \frac{\partial y}{\partial w_j} = \epsilon (t-y) f'(\mathbf{w} \cdot \mathbf{x}) x_j$$

This is the method of gradient descent.

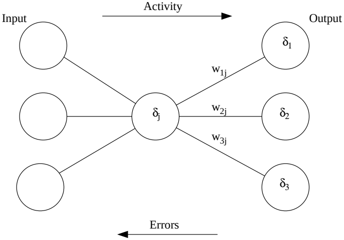
Limitations of perceptrons

Inability to solve “simple” problems like XOR.
Signalled the end of studying these in the 1960s.

Multilayer perceptrons: backpropagation algorithm

(Werbos PhD thesis, 1974)

Solving the **credit assignment problem** to generate “deltas” for hidden units.



But how to decide number of layers? Convergence?

Interest waned in 1990s, but now computers/GPUS are much faster …

Deep learning

Deep learning is everywhere. [New Scientist, April 2017]

https://www.newscientist.com/article/
2126738-google-uses-neural-networks-to-translate-without-trans

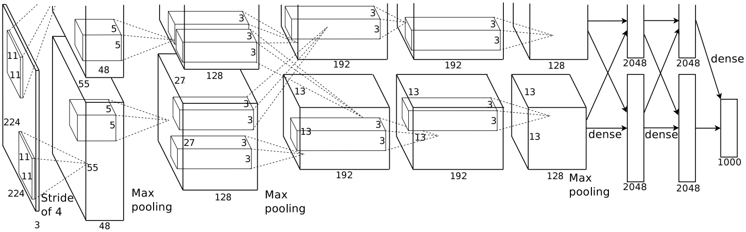
DAILY NEWS 4 April 2017

Google uses neural networks to translate without transcribing

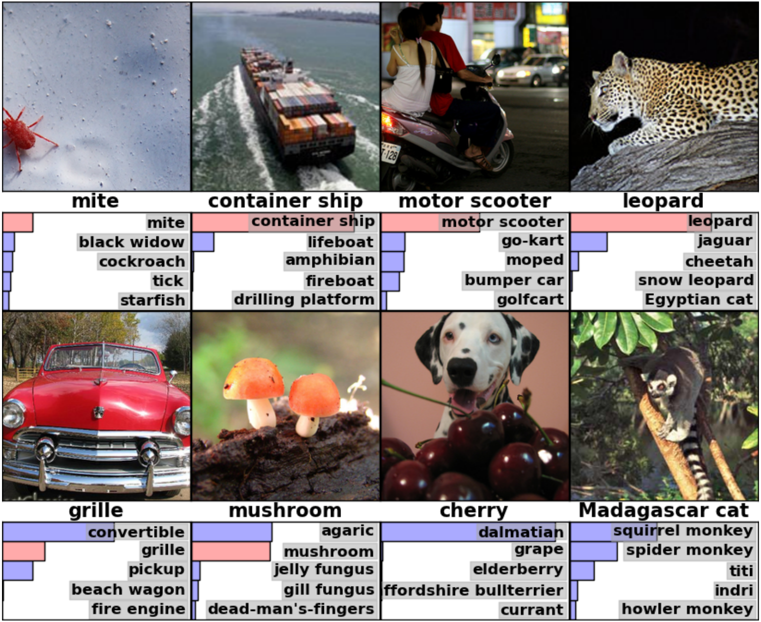
Image classification

2012 competition. 1,000 examples of 1,000 classes. Top-1 (37.5%) and top-5 (17.0%) error rate exceed previous state of the art. Won 2012 competition with top-5 test error rate of 15%; second had error rate of 26%.

Imagenet architecture



Imagenet performance



Reinforcement learning

Basic idea: limited feedback from a critic to say how well you did.
Two problems with reinforcement learning:

1. No specific signal on what the desired outputs should be. “It is as if each person in the United States tried to decide whether he or she had done a useful day’s work by observing the gross national product [GNP] on a day by day basis” (Hinton, p220).
2. Reinforcement signal can occur long time after action. (e.g. one bad move in a game of chess, causing eventual loss of game.) “If … a person wants to how their behavior affects the GNP, they need to know whether to correlate today’s GNP with what they did yesterday or with what they did five years ago.” (Hinton, p220).

Hinton (1989) Connectionist learning systems, *Artificial Intelligence*, 40:185-234.

Classic control problem

Pole balancing problem.

`https://www.youtube.com/watch?v=Lt-KLtkDlh8`

Playing Go

Silver et al (2016) Nature 529:484–489

`http://doi.org/10.1038/nature16961`

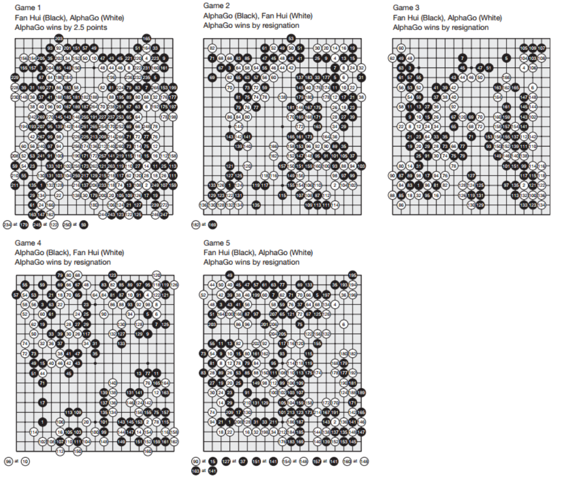
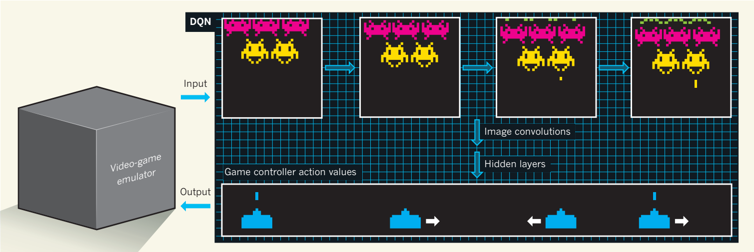


Figure 6 | Games from the match between AlphaGo and the European champion, Fan Hui. Moves are shown in a numbered sequence corresponding to the order in which they were played. Repeated moves on the same intersection are shown in pairs below the board. The first move number in each pair indicates when the repeat move was played, at an intersection identified by the second move number (see Supplementary Information).

Playing Atari video games

Mnih et al (2015) Human-level control through deep reinforcement learning. Nature 518:529–533.



System played better than professional human on 49 Atari 2600 games.
`https://www.youtube.com/watch?v=V1eYniJ0Rnk`

Summary

1. Maths/computing can be applied to interesting areas in the life sciences.
2. Interdisciplinary sciences are the future.
3. Careers in machine learning/data science/artificial intellgience are BIG.