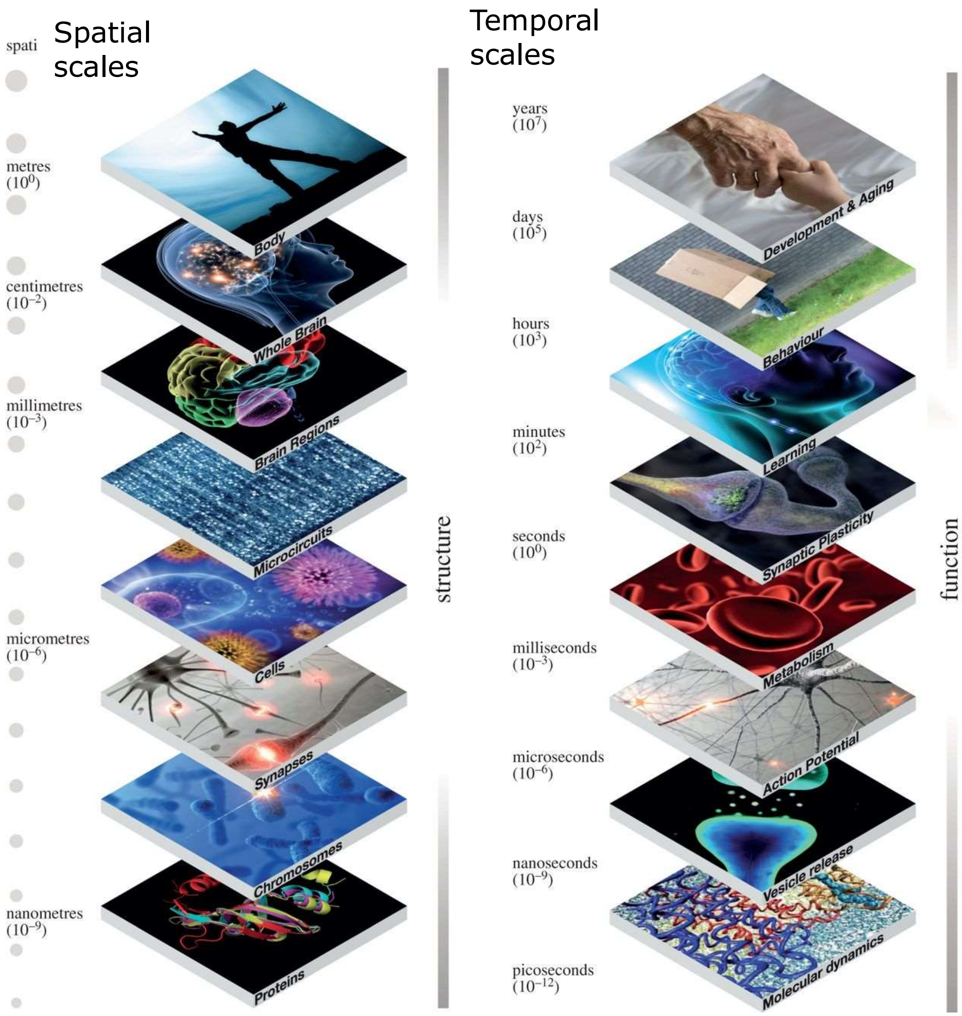
Week 6: The multiscale brain



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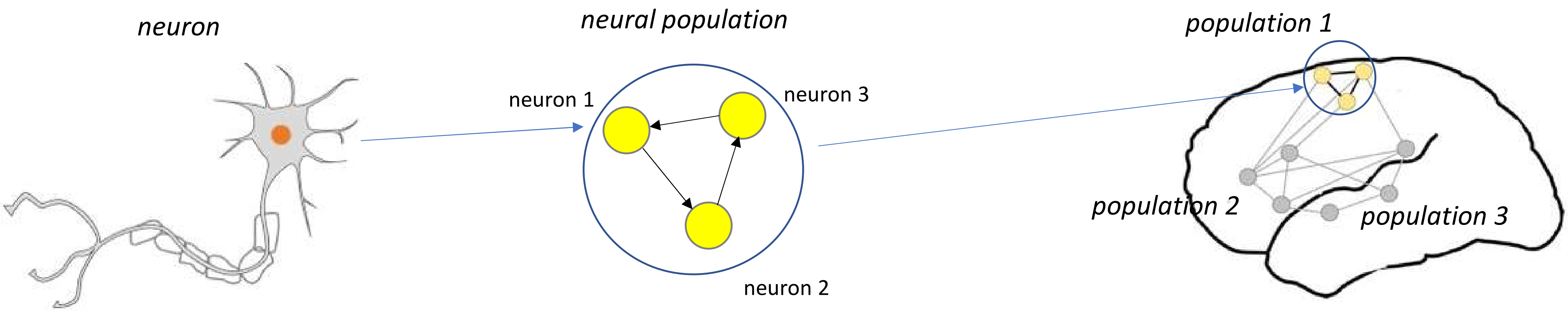
Examining the brain at micro-, meso- and macro-scale

Last week

This week



microscale

cellular mechanisms
e.g. membrane & action potential
neurotransmitters,..

mesoscale

circuits within
neural populations,
local neural networks

macroscale

interactions between networks:
"networks of networks"

Lecture overview

Part 1: *Imaging the brain at work*

1. Brief overview of main neuroimaging methods

2. MRI, fMRI
   - *A. Network neuroscience*
   - *B. Special network characteristics of the Brain*

3. Neuromodulation
   - *A. Transcranial Stimulation*
   - *B. Microstimulation in neurological patients*
   - *C. Optogenetics*

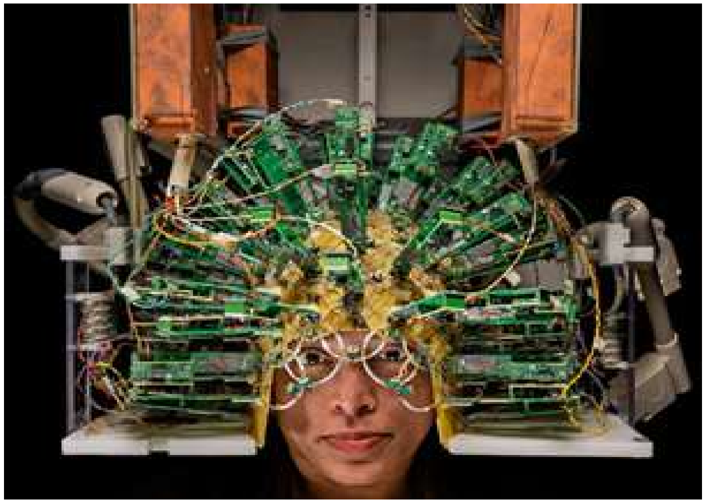


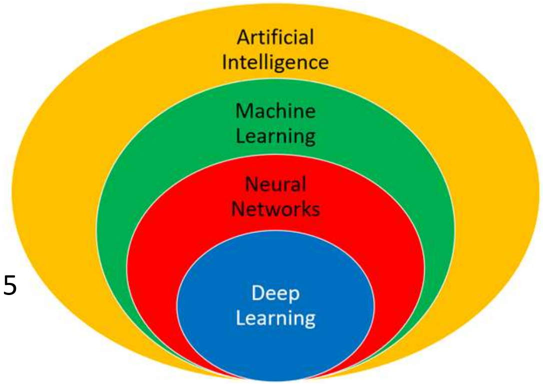
Photo: National Geographic

Part 2: *Computational neuroscience applications*

1. Brain-Machine Interfaces
   Neuroprosthetics

2. Brain-inspired improvements of Artificial Intelligence
   - *A. Intro to neural networks*
   - *B. Neural nets as learning machines*
   - *C. Deep learning applications*

   applications in practical 5



1. Overview of main neuroimaging methods

- Broad **classification** of methods based on their:

  1) capacity to establish ***correlational*** or ***causal*** relations between brain activity and behavior

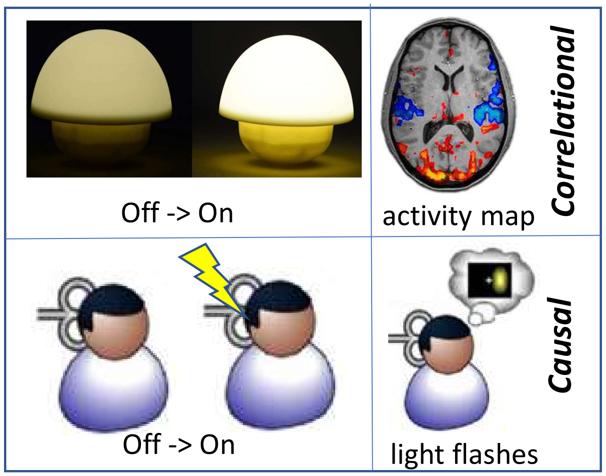
Example: how to study light perception?

Experimental manipulation *Results*

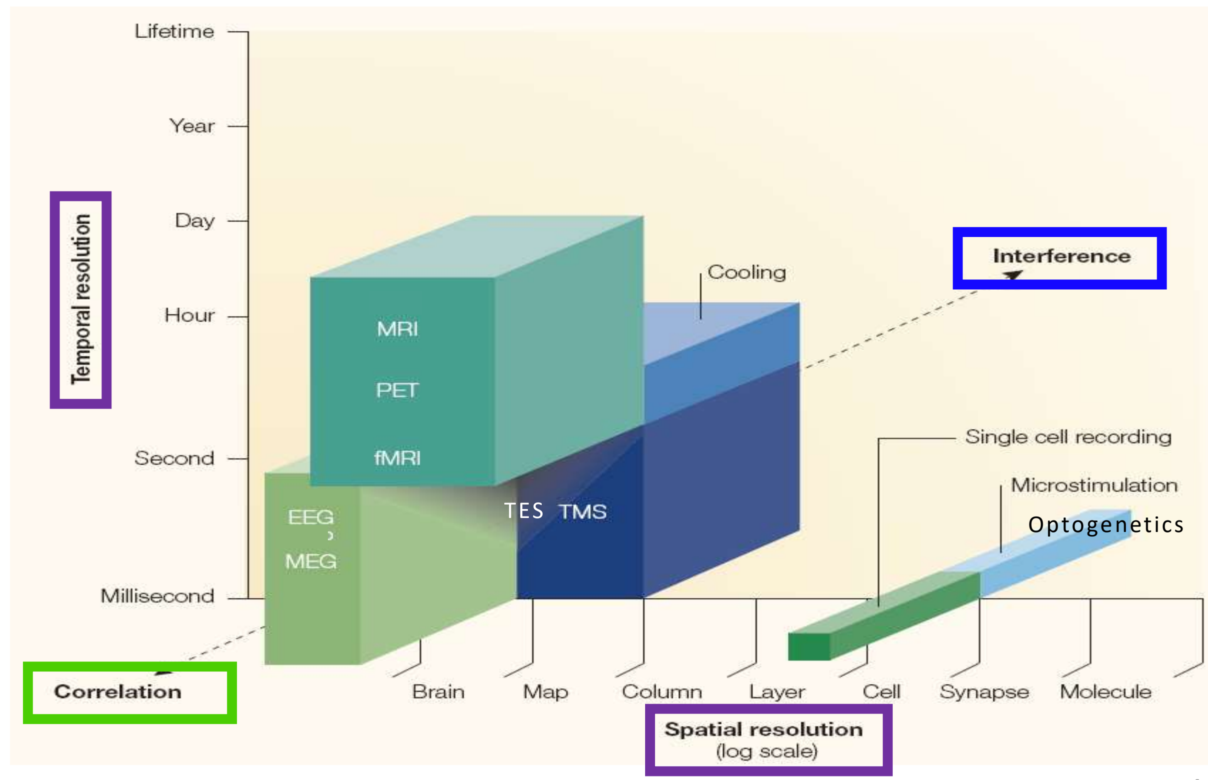
brain activity is:

monitored

modulated
(interfered)



  2) their spatial and temporal ***resolution***



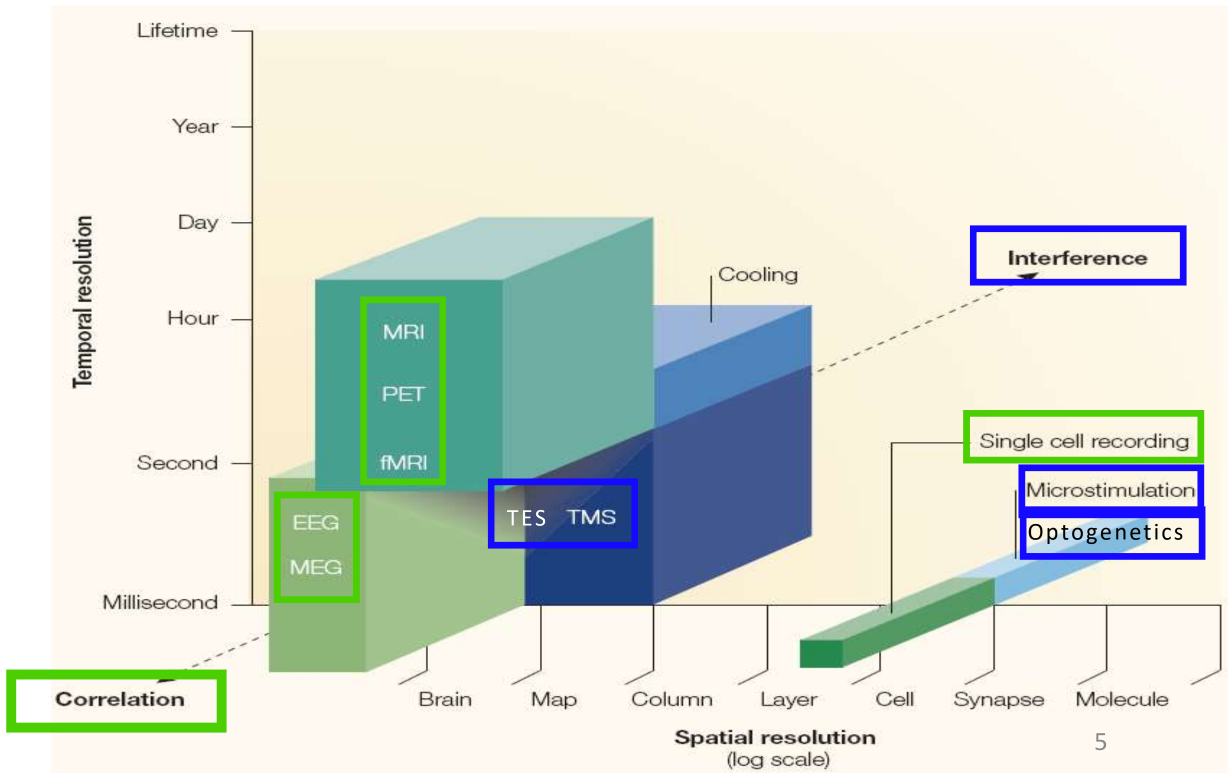
✓ Correlational measures
(monitor brain activity)

1. **High spatial resolution:**
   indirect measures of neural activity
   1. Magnetic Resonance Imaging (MRI)
   2. functional Magnetic Resonance Imaging (fMRI)
   3. Positron emission tomography (PET)
   4. intracranial electrophysiological recordings

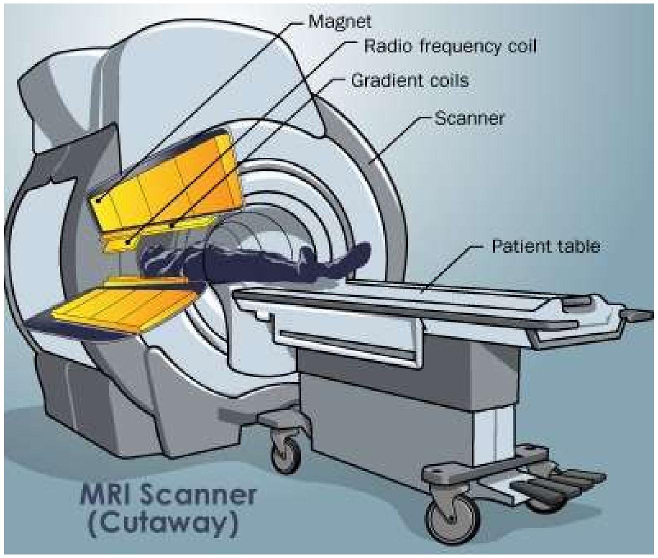
2. **High temporal resolution:**
   direct measures of neural activity
   1. Electroencephalography (EEG)
   2. Magnetoencephalography (MEG)
   3. Intracranial electrophysiological recordings

✓ Modulation measures
(interfere with ongoing brain activity)

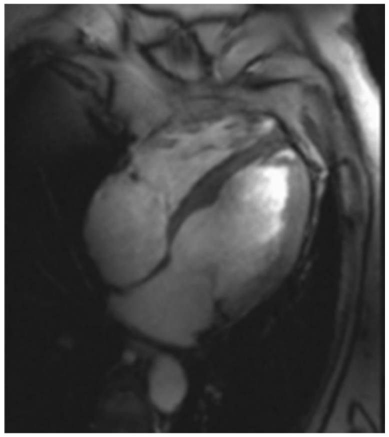
1. Transcranial Stimulation (TES/TMS)
2. Microstimulation
3. Optogenetics



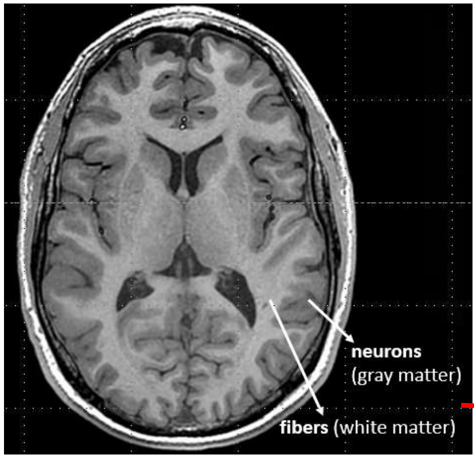
2.1 Magnetic Resonance Imaging (MRI)



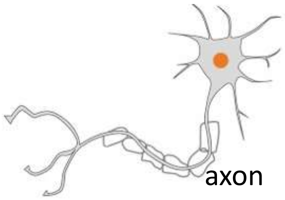
Diverse range of *anatomical* imaging techniques:

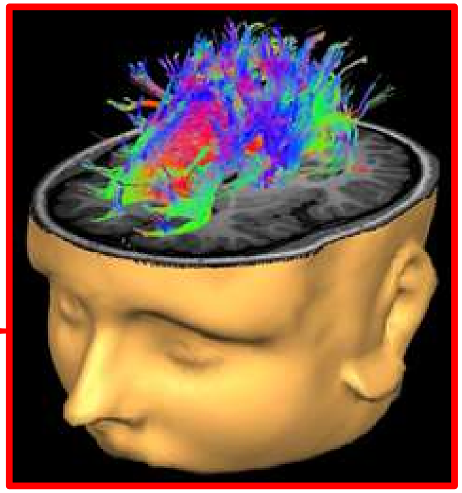


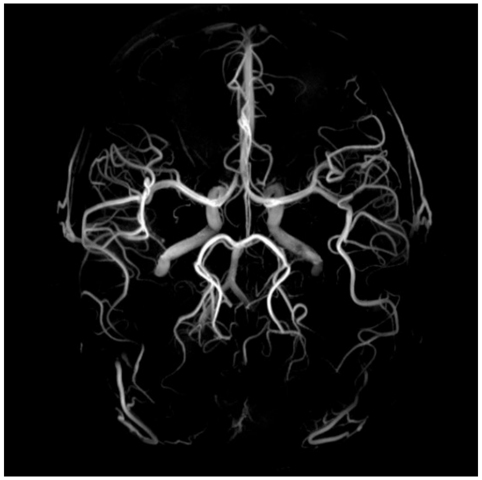
Heart pumping blood



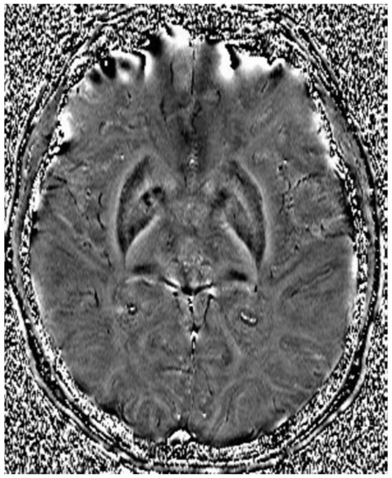
Brain tissue



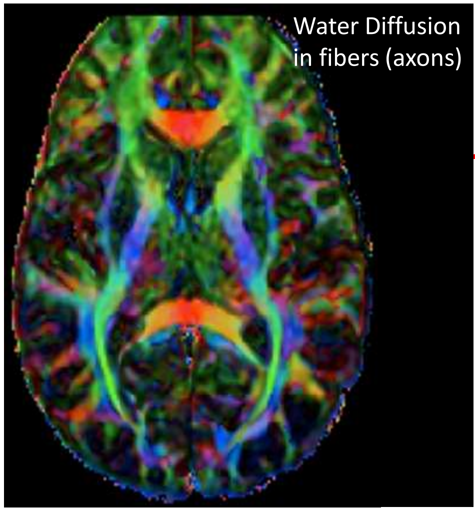




vasculature



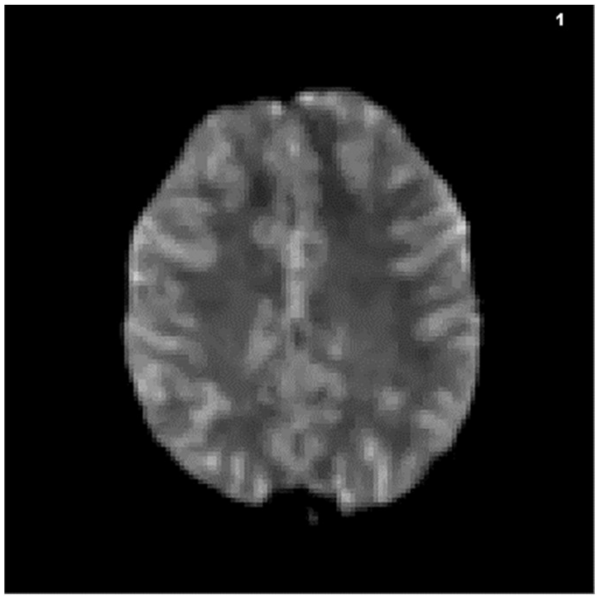
iron accumulation

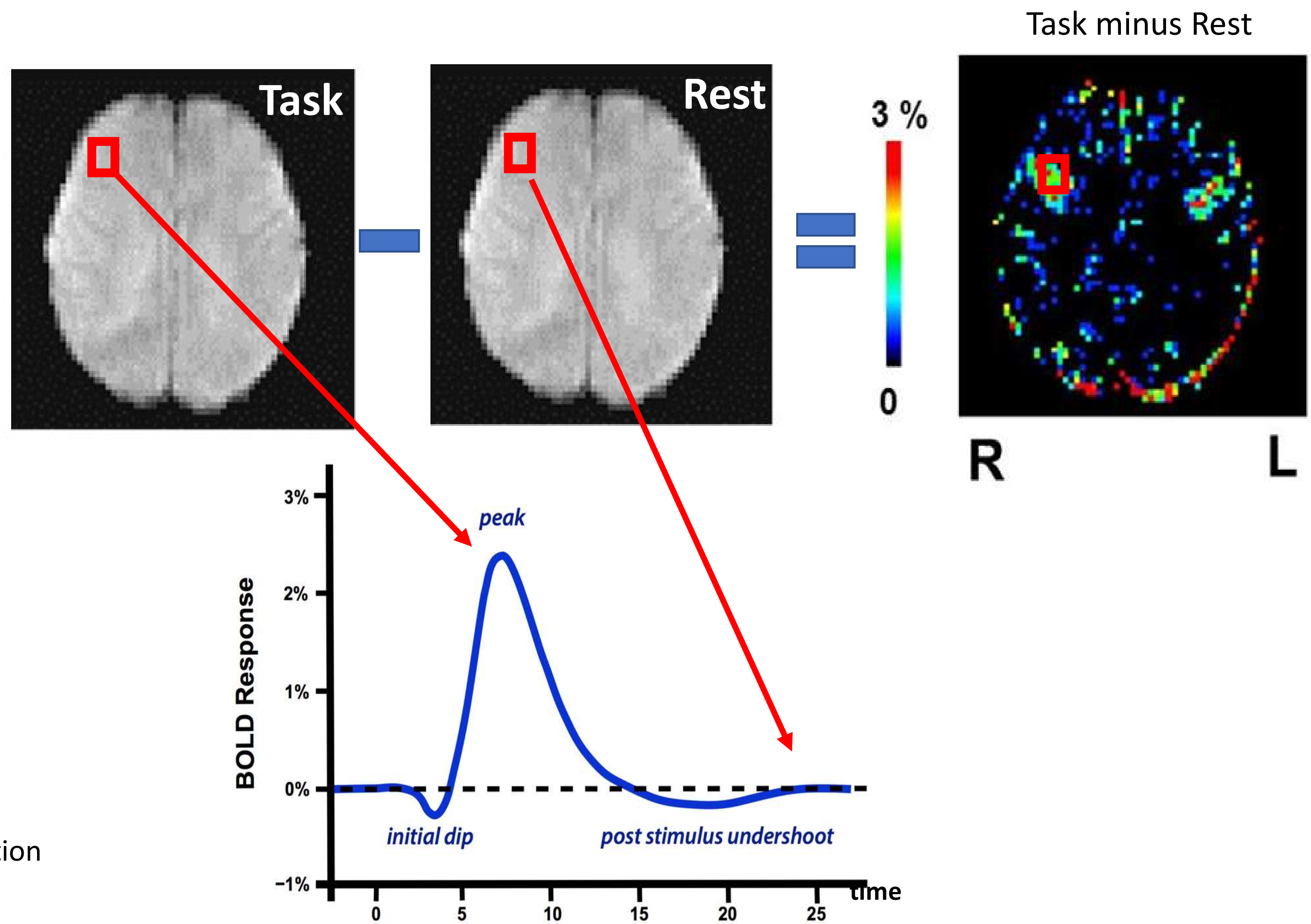


Diffusion Weighted Imaging (DWI)

2.2 *FUNCTIONAL* Magnetic Resonance Imaging (fMRI)

Acquired sequence of fMRI images





BOLD =
blood oxygen level–dependent

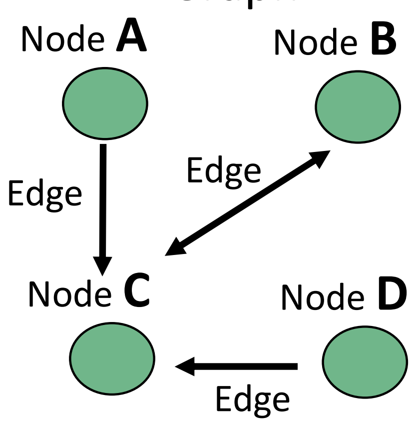
fMRI signal intensities (grey values)
~
deoxygenated / oxygenated blood

-> ratio changes due to oxygen consumption

2A. Network neuroscience: analyzing brain networks applying graph theory to neuroimaging data

Graph

Week 1

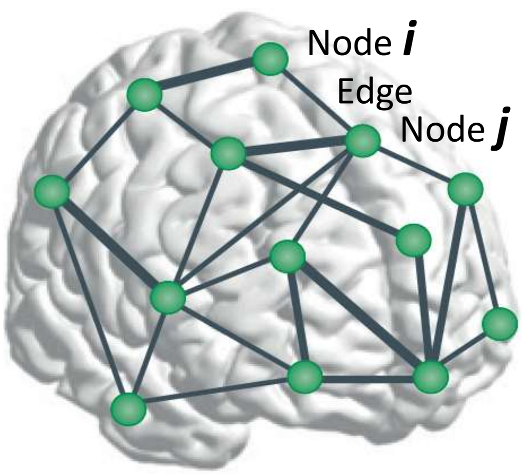


Adjacency matrix

	A	B	C	D
A	0	0	1	0
B	0	0	1	0
C	0	1	0	0
D	0	0	1	0

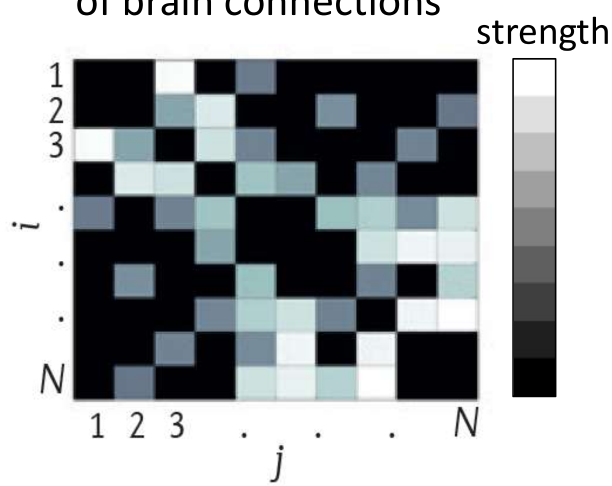
unweighted

Brain network (graph)



Undirected graph (edges no direction)

Adjacency matrix
of brain connections



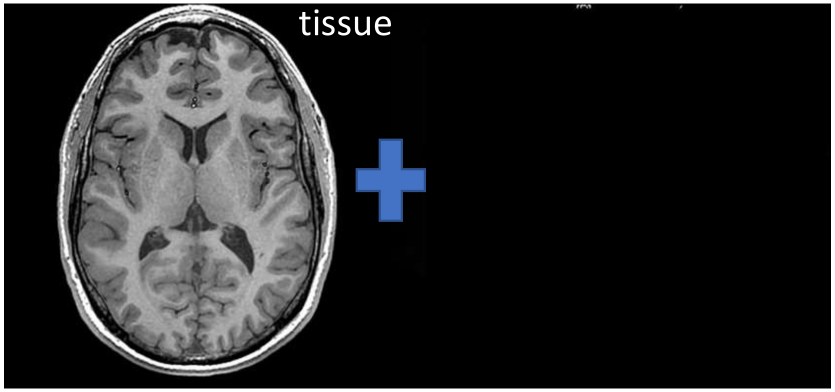
Undirected (symmetric), weighted

Graphs & adjacency matrices can represent:

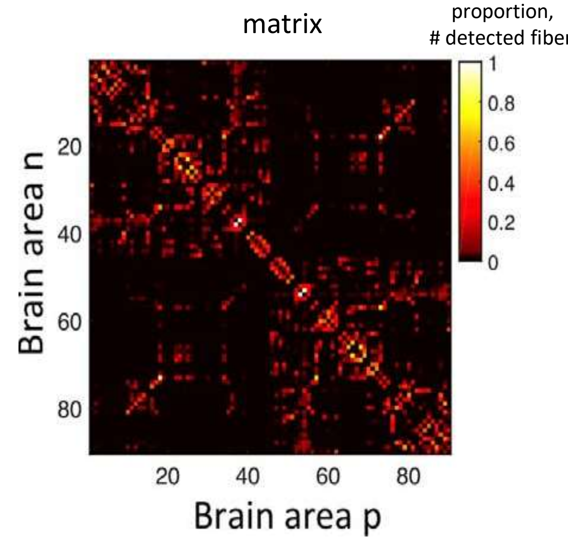
1. Anatomical (structural) connectivity
2. Functional connectivity

2A.1. Mapping *Anatomical* Connectivity

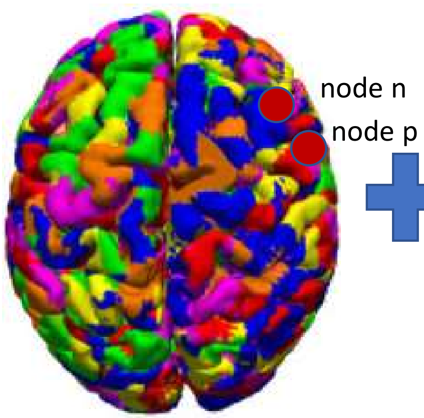
Original
dataspace



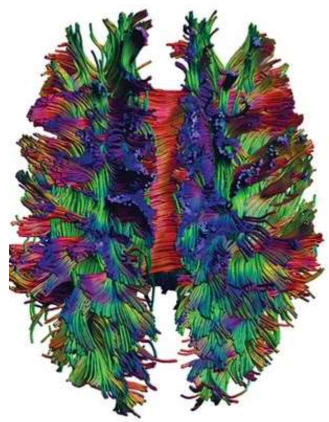
Fiber connections
matrix



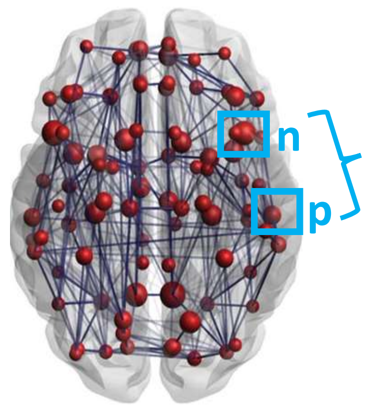
Model
space



brain regions (nodes)



axonal tracts (“fibers”, edges)

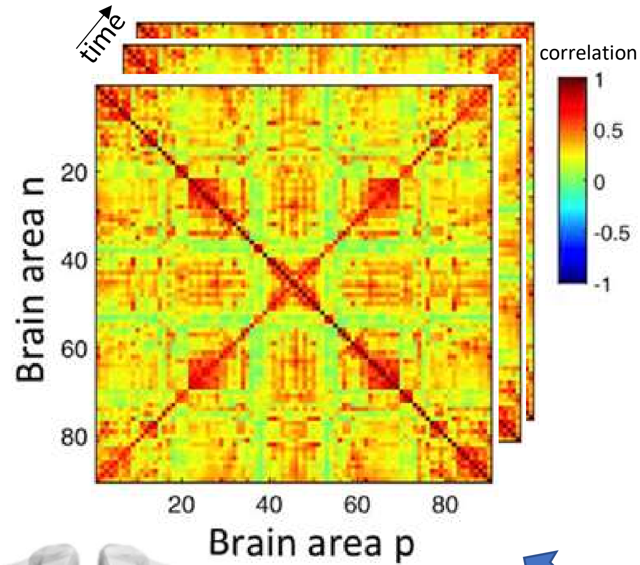


fiber tracts

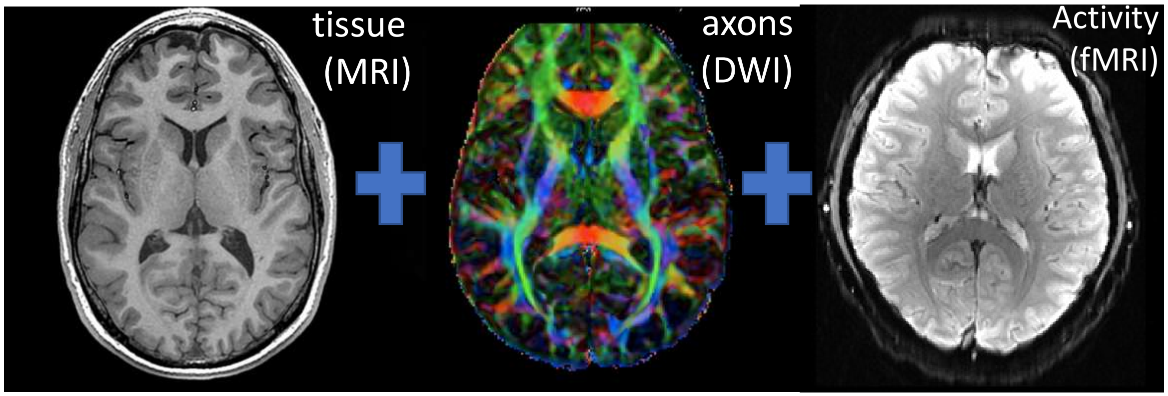
anatomical network model
(undirected graph)

2A.2. Mapping *Functional* Connectivity

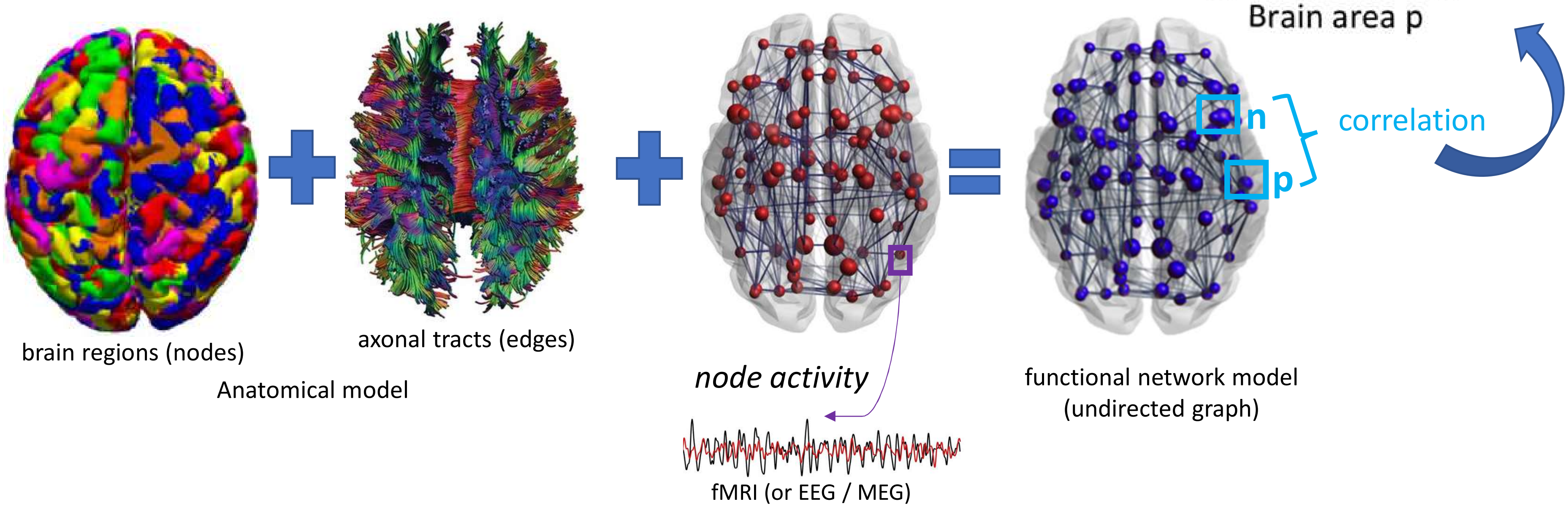
Activity correlation matrix



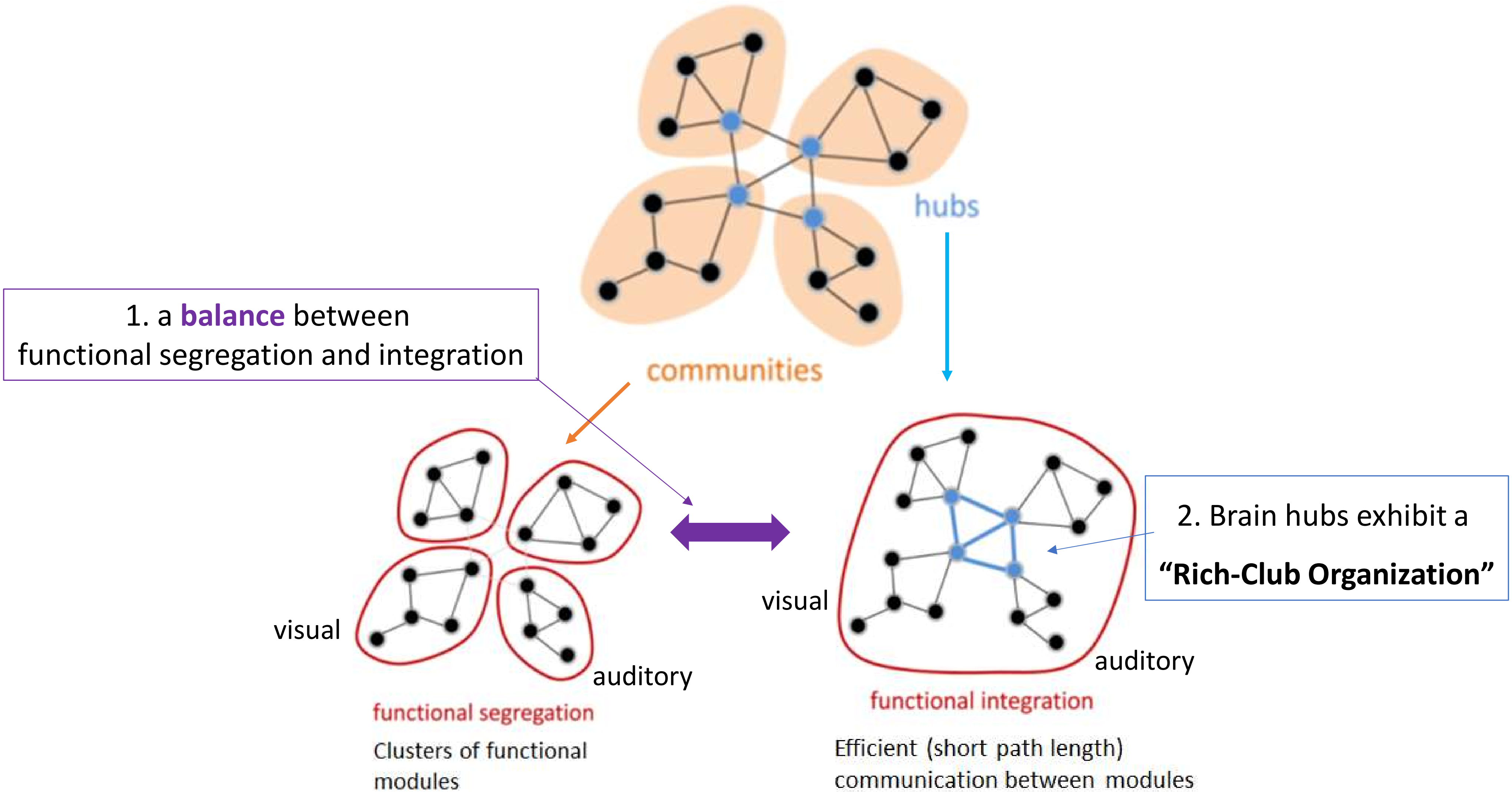
Original
dataspace



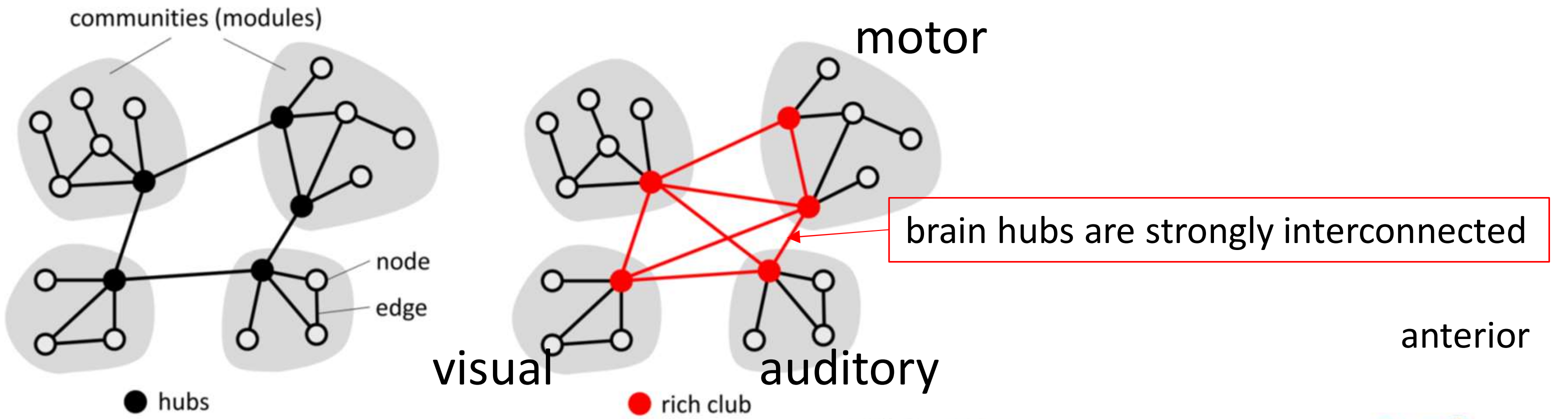
Model
space

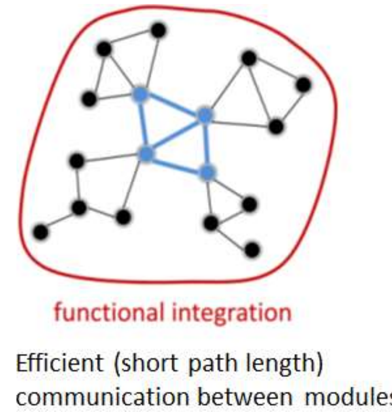


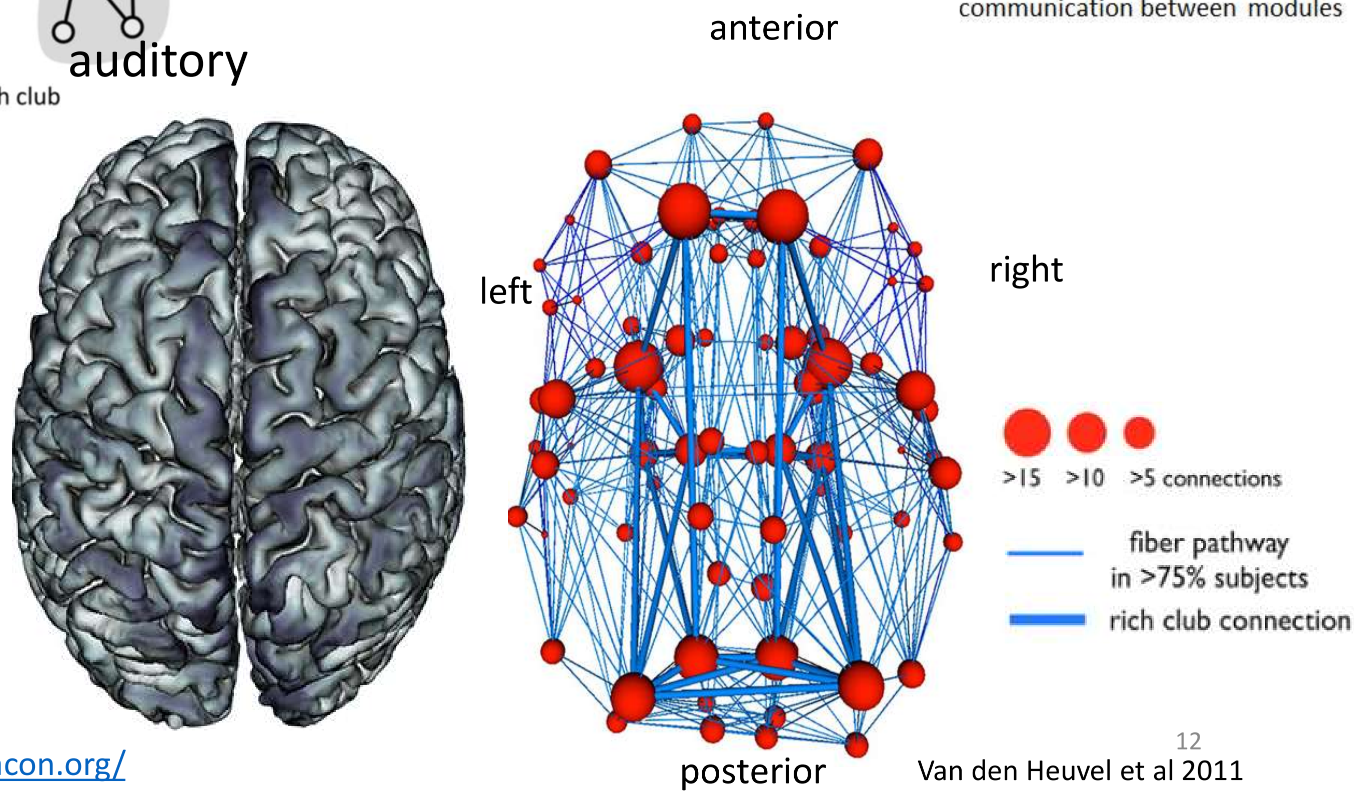
2B. Two characteristics of the Brain's Network Structure:



2B The Brain's network has a Rich-Club Organization*







Van den Heuvel et al 2011

*e.g. social networks of celebrities http://oracleofbacon.org/

3. Neuromodulation

✓ Correlational measures
(monitor brain activity)

1. **High spatial resolution:**
    1. Magnetic Resonance Imaging (MRI)
    2. functional Magnetic Resonance Imaging (fMRI)
    3. Positron emission tomography (PET)
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2. **High temporal resolution:**
    1. Electroencephalography (EEG)
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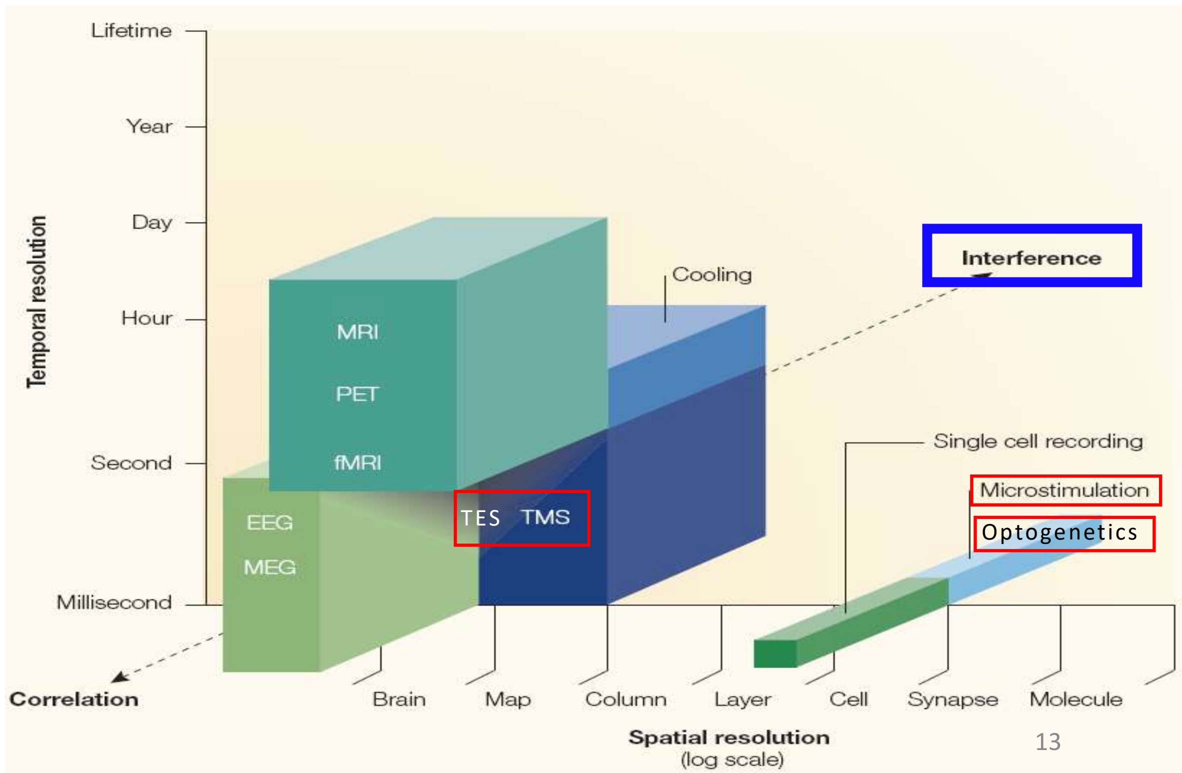
✓ Modulation measures
(interfere with ongoing brain activity)

1. Transcranial Stimulation (TES/TMS)
2. Microstimulation
3. Optogenetics



3A. Transcranial Stimulation

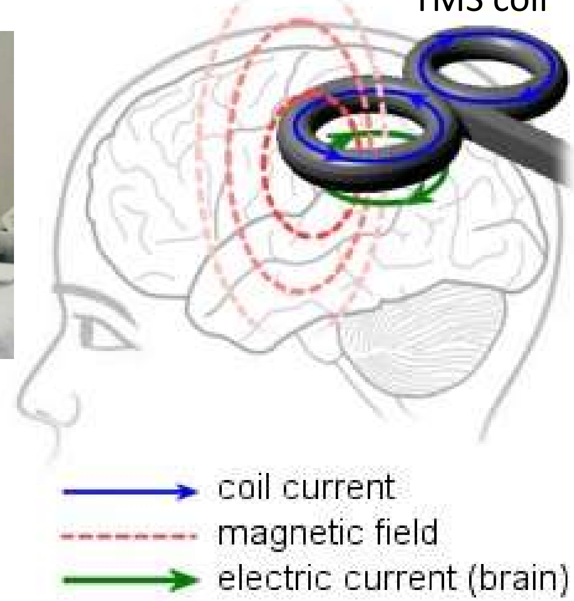
Transcranial Electric Stimulation (TES)

- ❑ Weak, continuous electric current (1–2 mA)
- ❑ Current induces changes in neuronal *excitability* (i.e., shift in membrane potential)

Transcranial Magnetic Stimulation (TMS)

- ❑ Strong, brief magnetic field with accompanying current
- ❑ Electric current generates action potentials


TMS coil

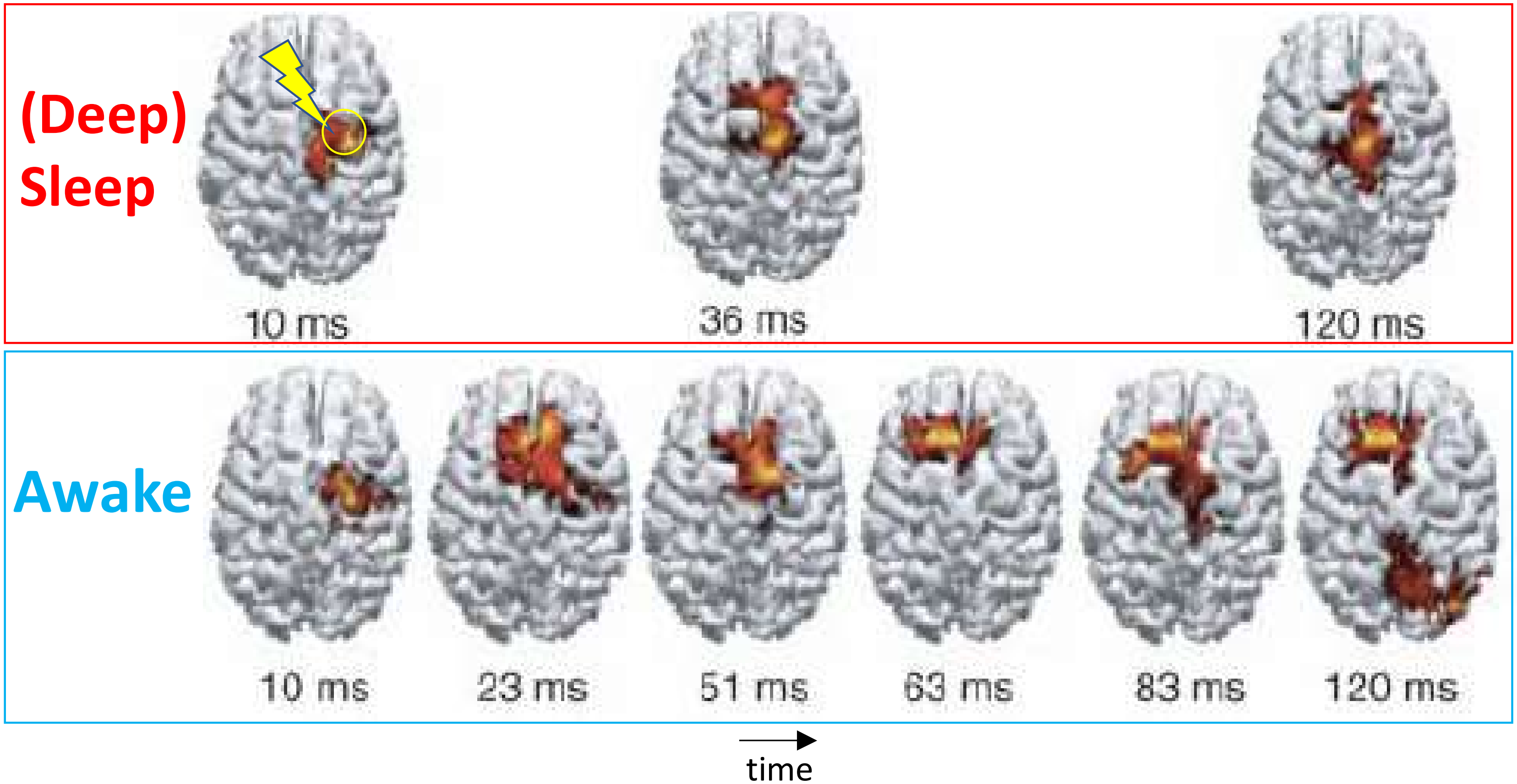
TMS coil


TMS example: Creating a temporary virtual lesion in motor cortex

source: BBC ©
The Brain: A Secret History

TMS Example: Network perturbation to test cortical information flow during sleep

Tracking energy propagation (induced by transcranial magnetic stimulation [TMS]) with EEG:

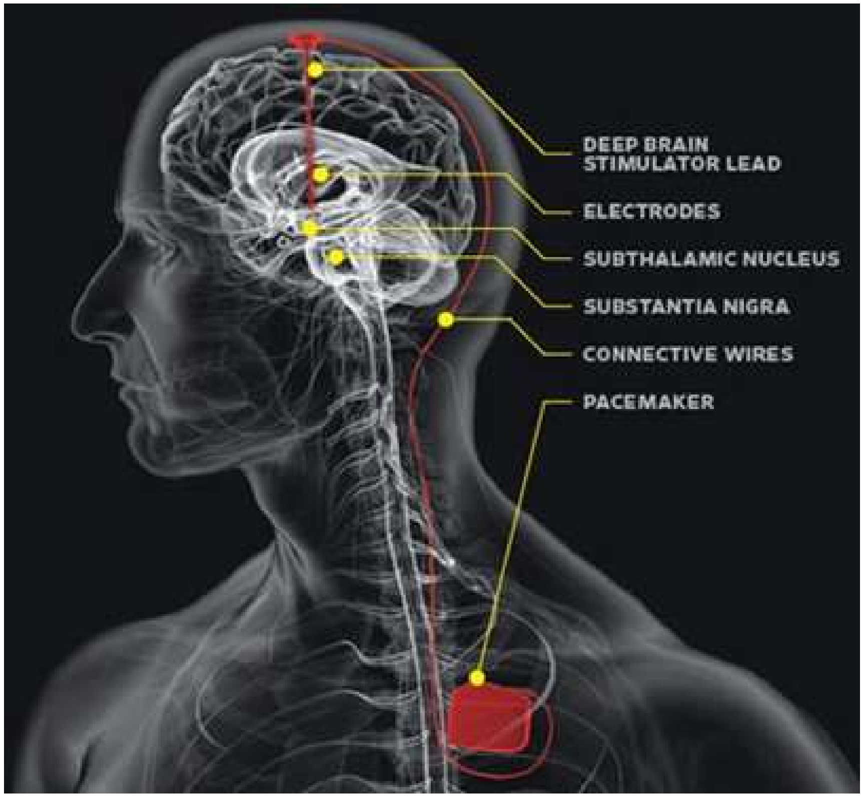


Massimini et al., 2005, *Science*

3B. Microstimulation

- Electric currents via electrodes implanted in the brain

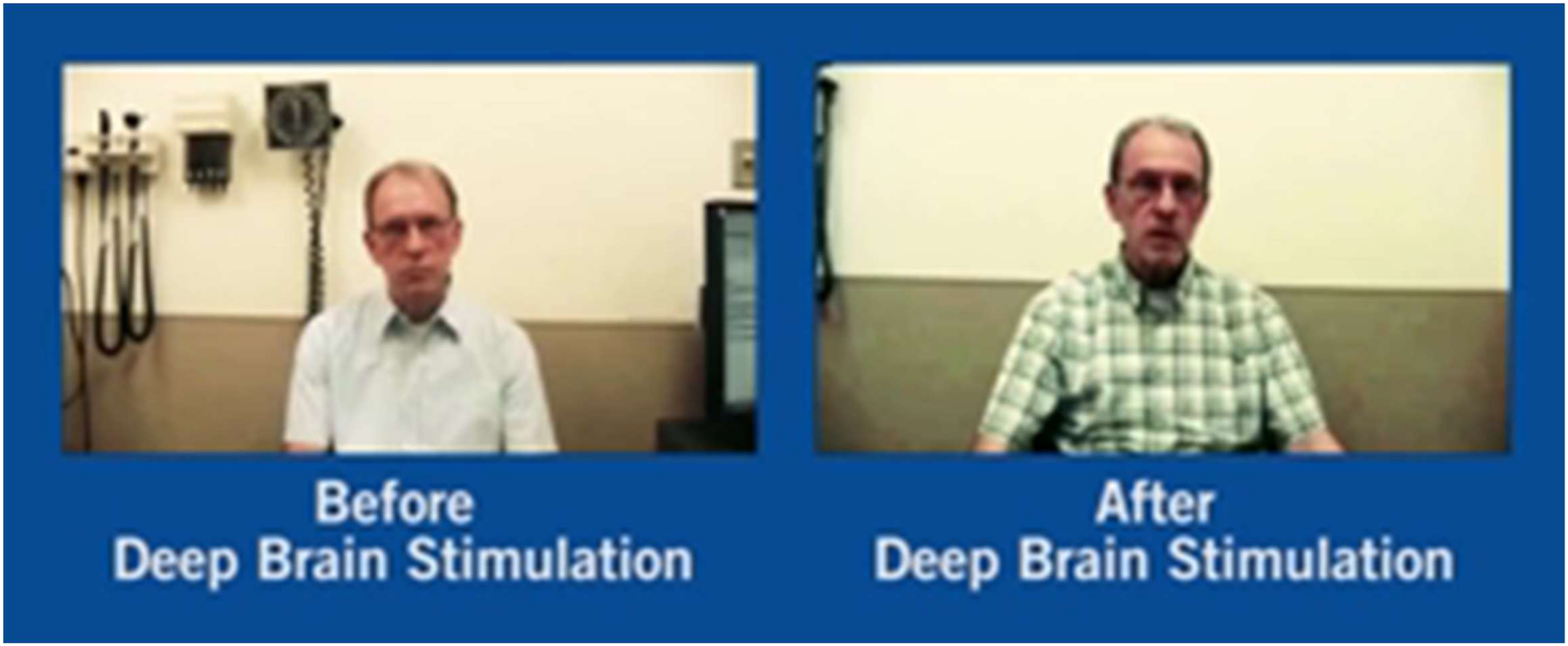
- in humans, **deep brain stimulation (DBS)** treatments for:
  - **Parkinson's Disease** (common)
  - Depression
  - OCD
  - Epilepsy
  - Addiction (experimental)



Action potentials of a subthalamic nucleus neuron

Microstimulation in Parkinson’s Disease

effects on fine motor skills:

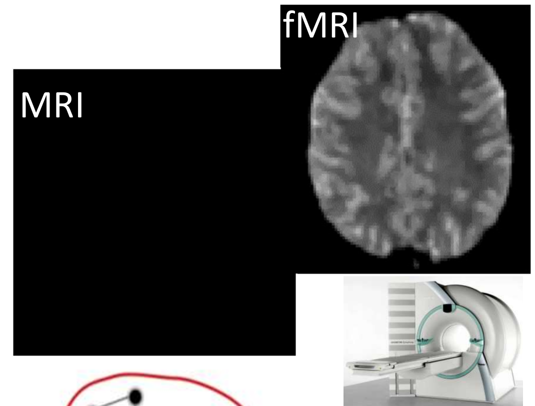


source: ©Medical College of Wisconsin

Microstimulation in Parkinson's Disease has instant, systemic effects (motoric, speech, cognition):

3C. Optogenetics Precise manipulation of Action Potentials by modulating light-sensitive ion channels

Recap lecture Part 1: *Imaging the brain at work*



1. Brief overview of main neuroimaging methods

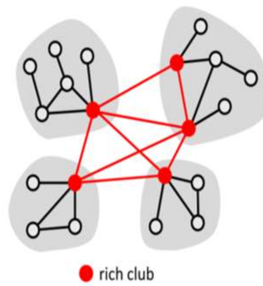
✓ **Correlational measures**

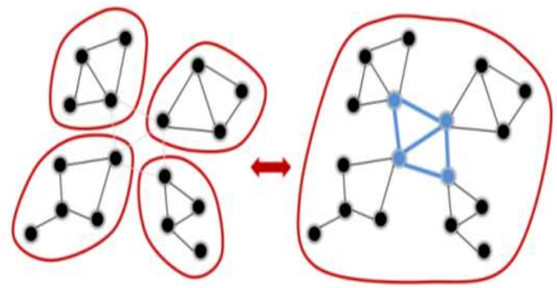
High spatial resolution
High temporal resolution

✓ **Modulation measures**

2. MRI, fMRI

A. Network neuroscience
B. Special network characteristics of the Brain





functional segregation
Clusters of functional modules

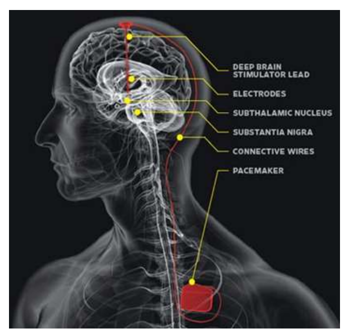
functional integration
Efficient (short path length) communication between modules

3. Neuromodulation

A. TMS sleep research
B. microstimulation in neurological patients
C. Optogenetics

TES

TMS



microstimulation

optogenetics

Lecture overview

Part 1: *Imaging the brain at work*

1. Brief overview of main neuroimaging methods

2. MRI, fMRI

    A. Network neuroscience
    B. Special network characteristics of the Brain

3. Neuromodulation

    A. TMS sleep research
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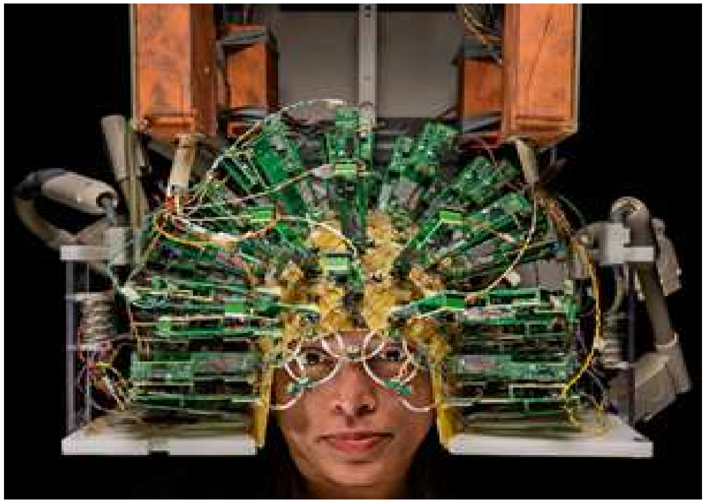


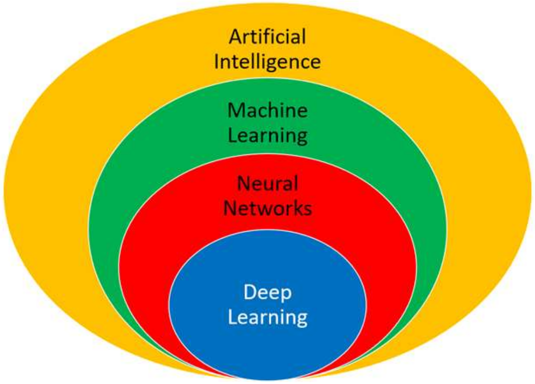
Photo: National Geographic

Part 2: *Computational neuroscience applications*

1. Brain-Machine Interfaces
    Neuroprosthetics

2. Brain-inspired improvements of Artificial Intelligence
    A. *Intro to neural networks*
    B. *Neural nets as learning machines*
    C. *Deep learning applications*

applications in practical 5

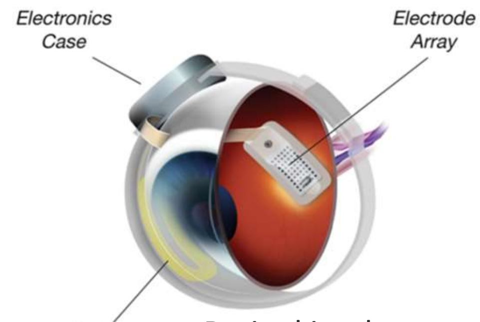


1. Brain-Machine Interfaces

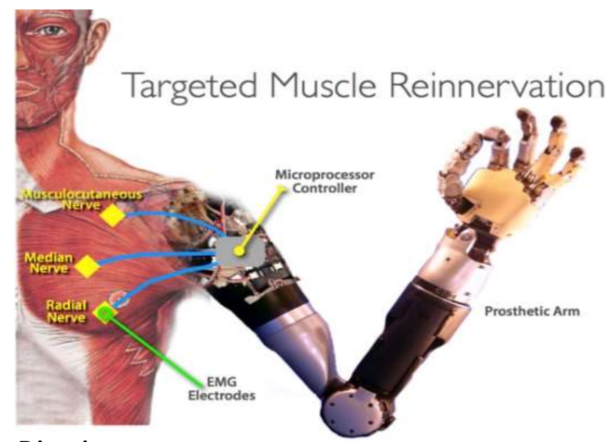
- Neuroprosthetic: device that can enhance (or replace) the input or output of a neural system

- Different types:
  - sensory prostheses (input)
  - motor prostheses (output)
    Devices interfacing with the:
    - peripheral nervous system & spinal cord
    - brain (brain-machine interfaces)
  - hybrid sensory-motor prostheses (in- & output)

Cochlear implant



Retinal implant

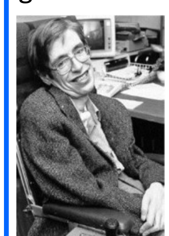


Bionic arm (after amputation)

Bionic arm (after brain or spinal cord injury)

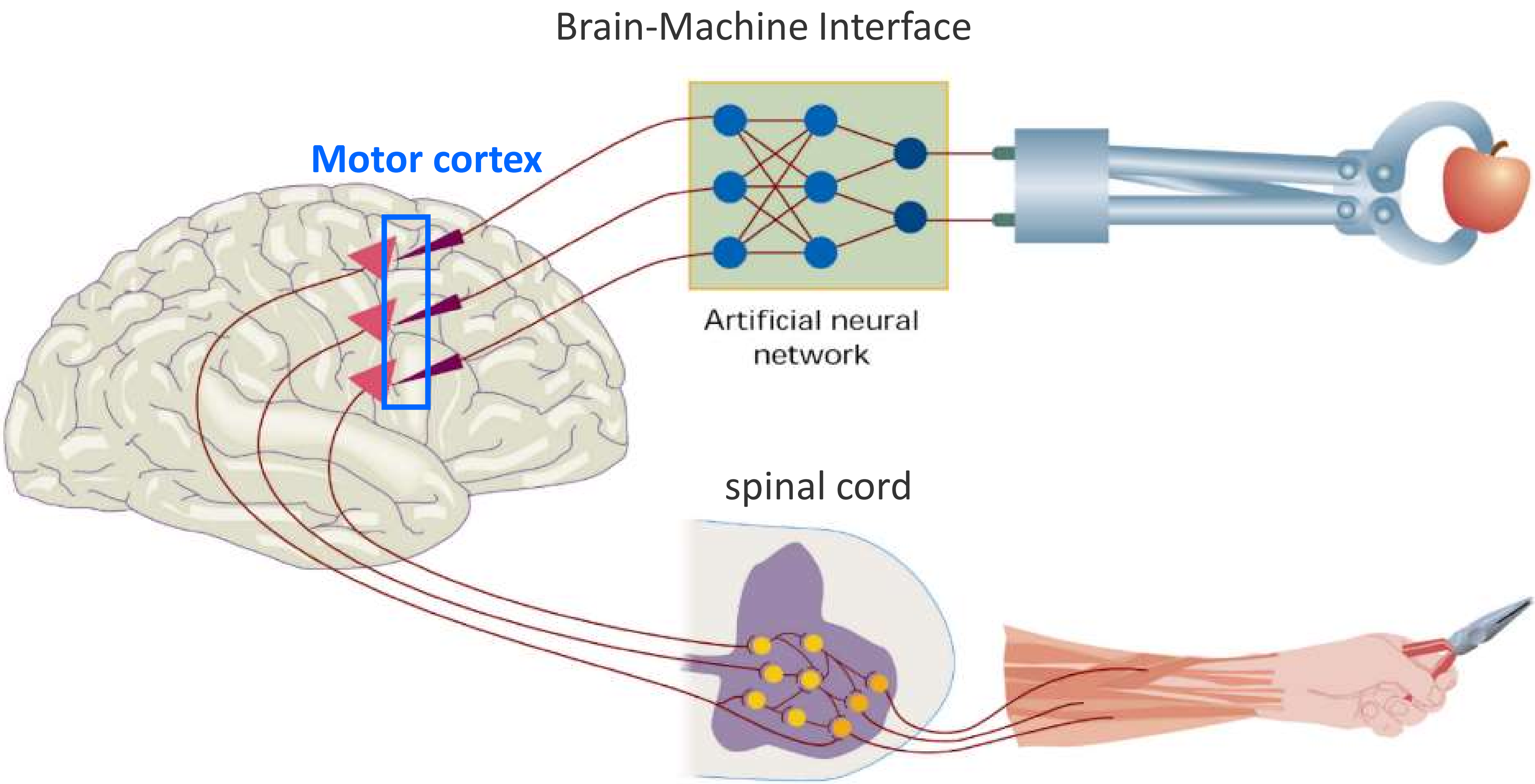
Motorized exoskeleton

Speech generator



Stephen Hawking (1942-2018)

Brain-controlled motor prostheses for paralyzed patients



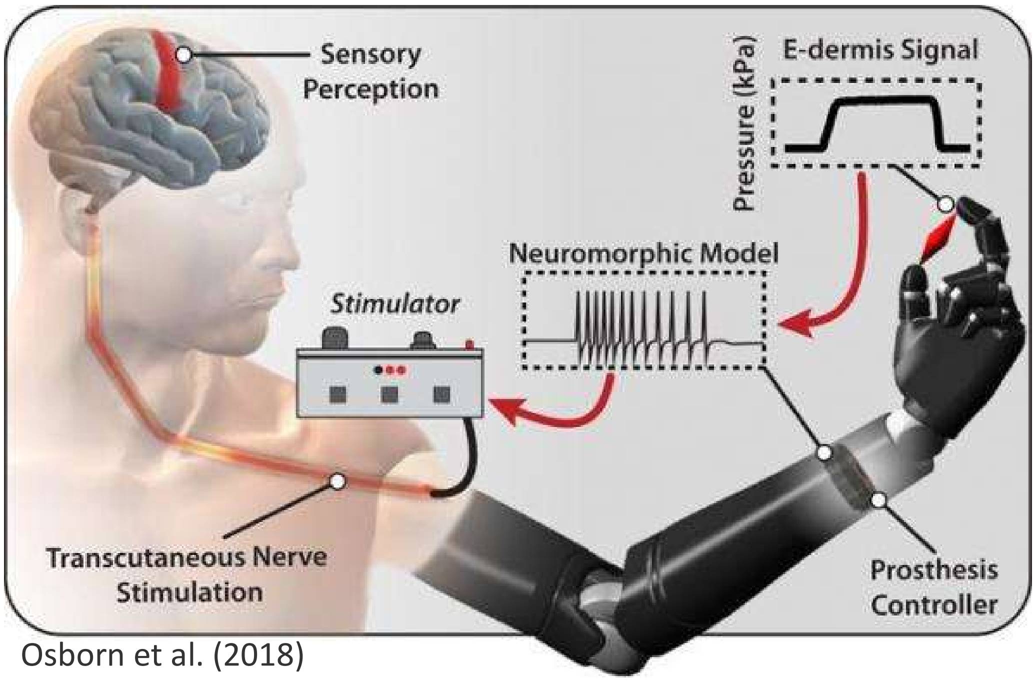
Bionic arm version 1 (2012): **Motor output**

a robotic arm activated by brain activity of paralyzed patient

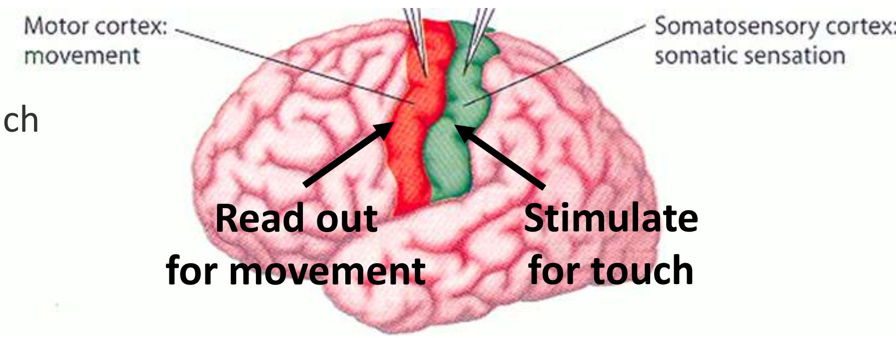
Hochberg et al., 2012

Bionic arm 2.0: ***Sensory Input*** **& Motor output**

Electronic touch receptors in bionic fingertips generate fine-grained touch (and pain) sensations in brain.



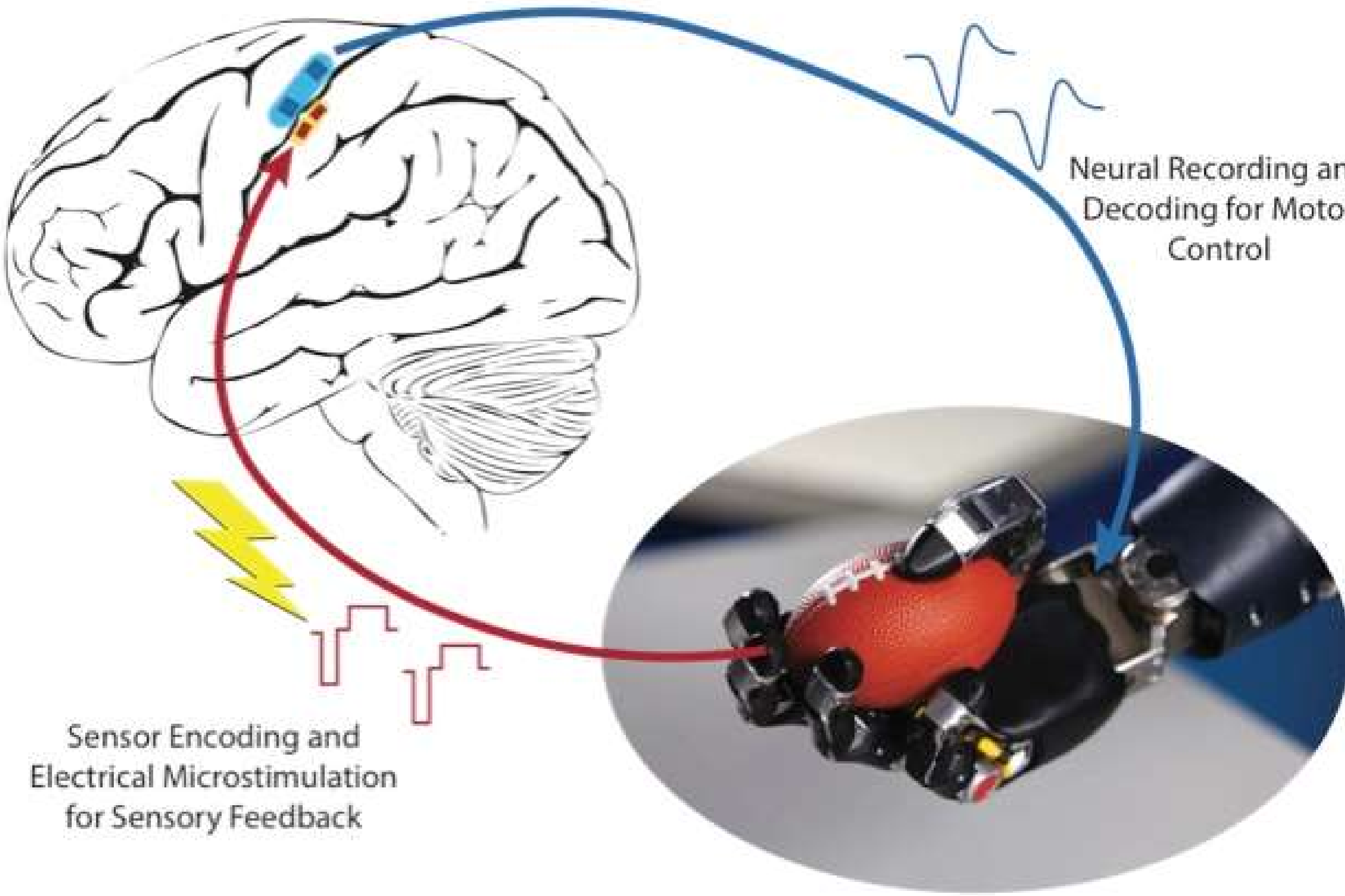
Osborn et al. (2018)



Fine-grained touch perception
(with improved bioinspired touch receptors)

Bao et al (2018)

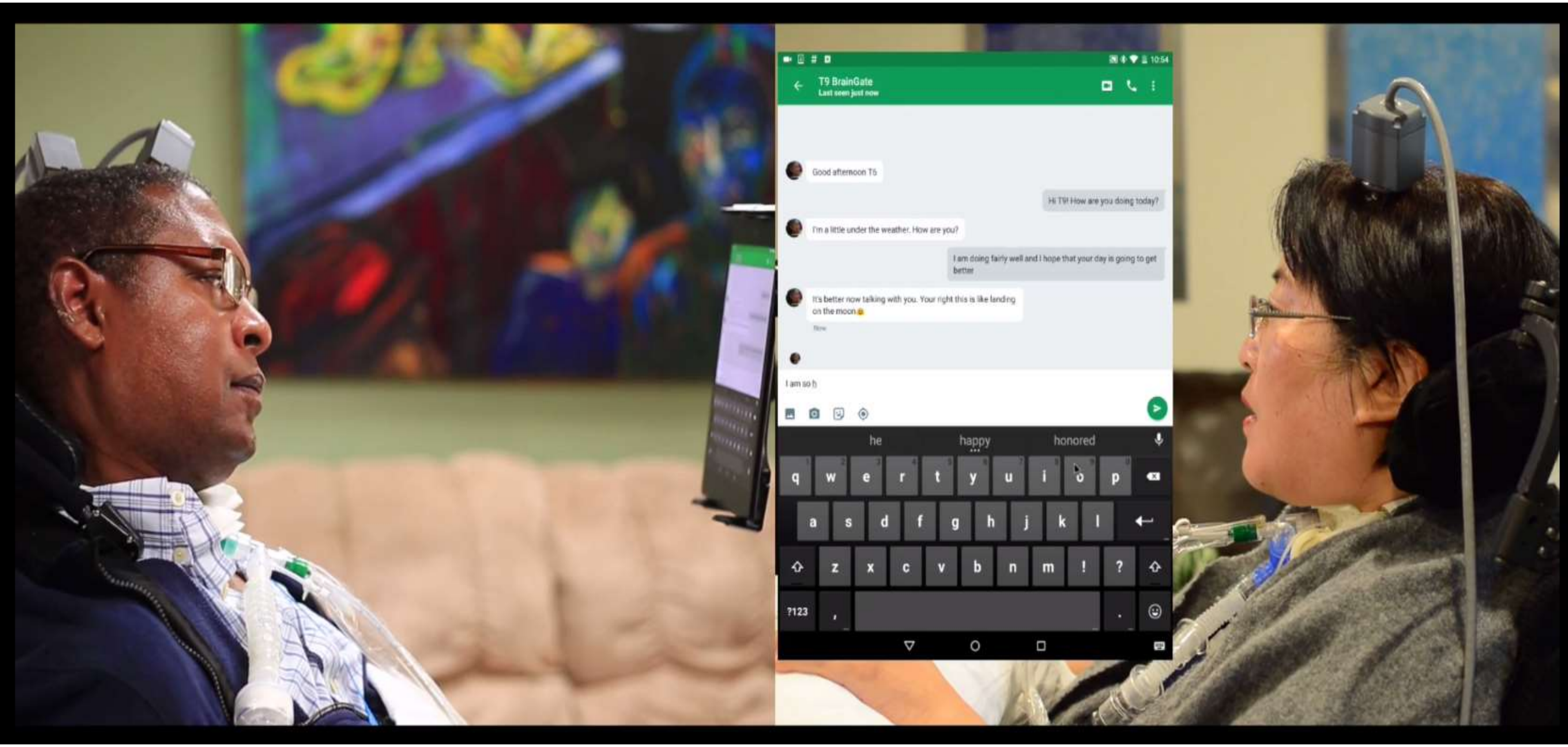
Closing the loop: Brain-Machine-Brain Interface



Sensory-feedback based online movement correction

Brain-Brain-via-Machine Interface

Browsing, emailing, chatting on a computer tablet



Nuyujukian et al., 2018

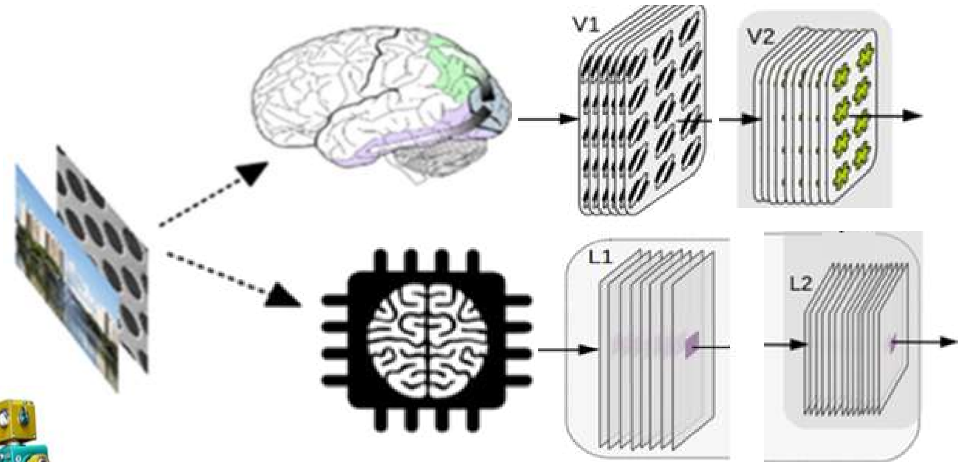
2. Brain-inspired improvements of Artificial Intelligence

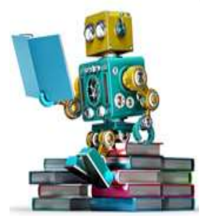
Overview:

- *A. Structure and function of neural networks*

  1. **The basic neural unit**
     - the "Perceptron" neuron
  2. **Multilayer networks**
     - Training a network: weight optimization

  practical 5
  Exercise 1 & 3: Classification
  Exercise 2: Logic operations





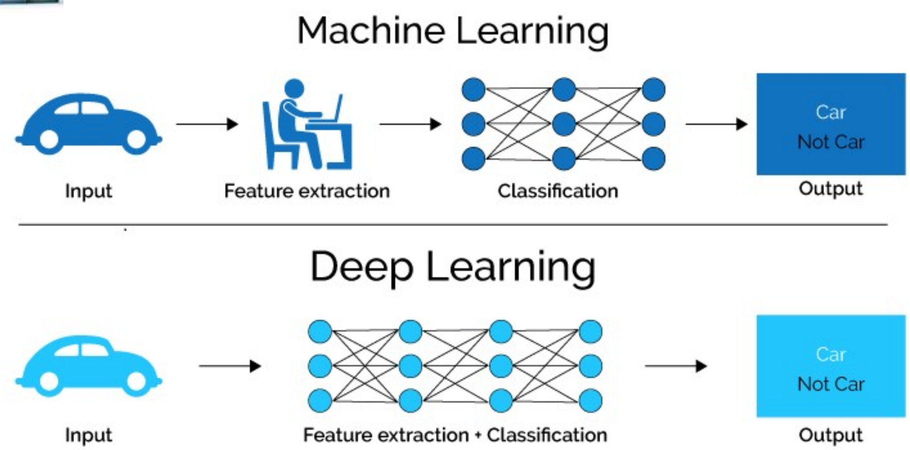
- *B. Neural nets as learning machines*

  3. **Classification** with neural networks
     - the problem of feature extraction:
       which features and how many?

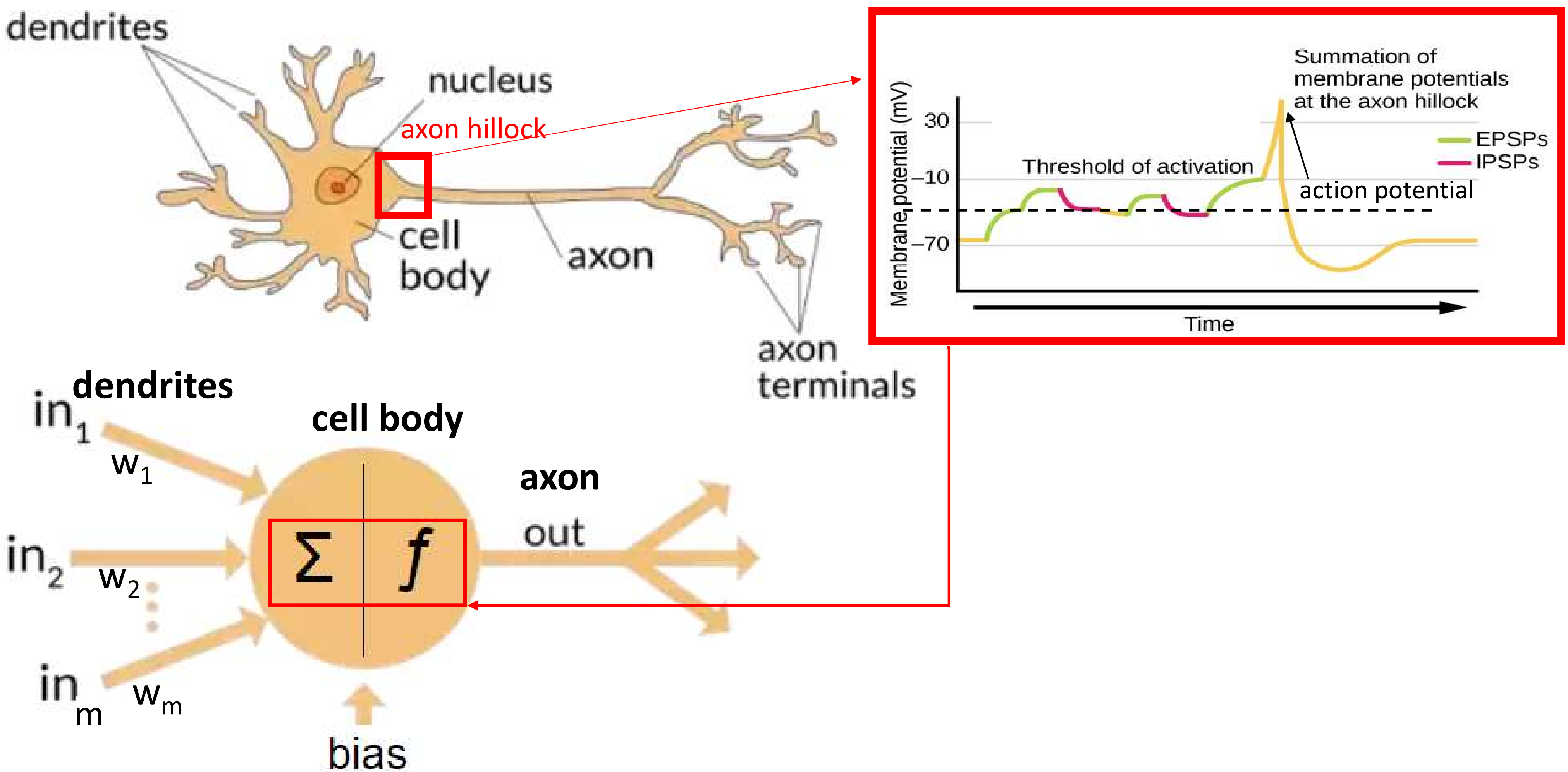
  practical 5
  Exercise 3

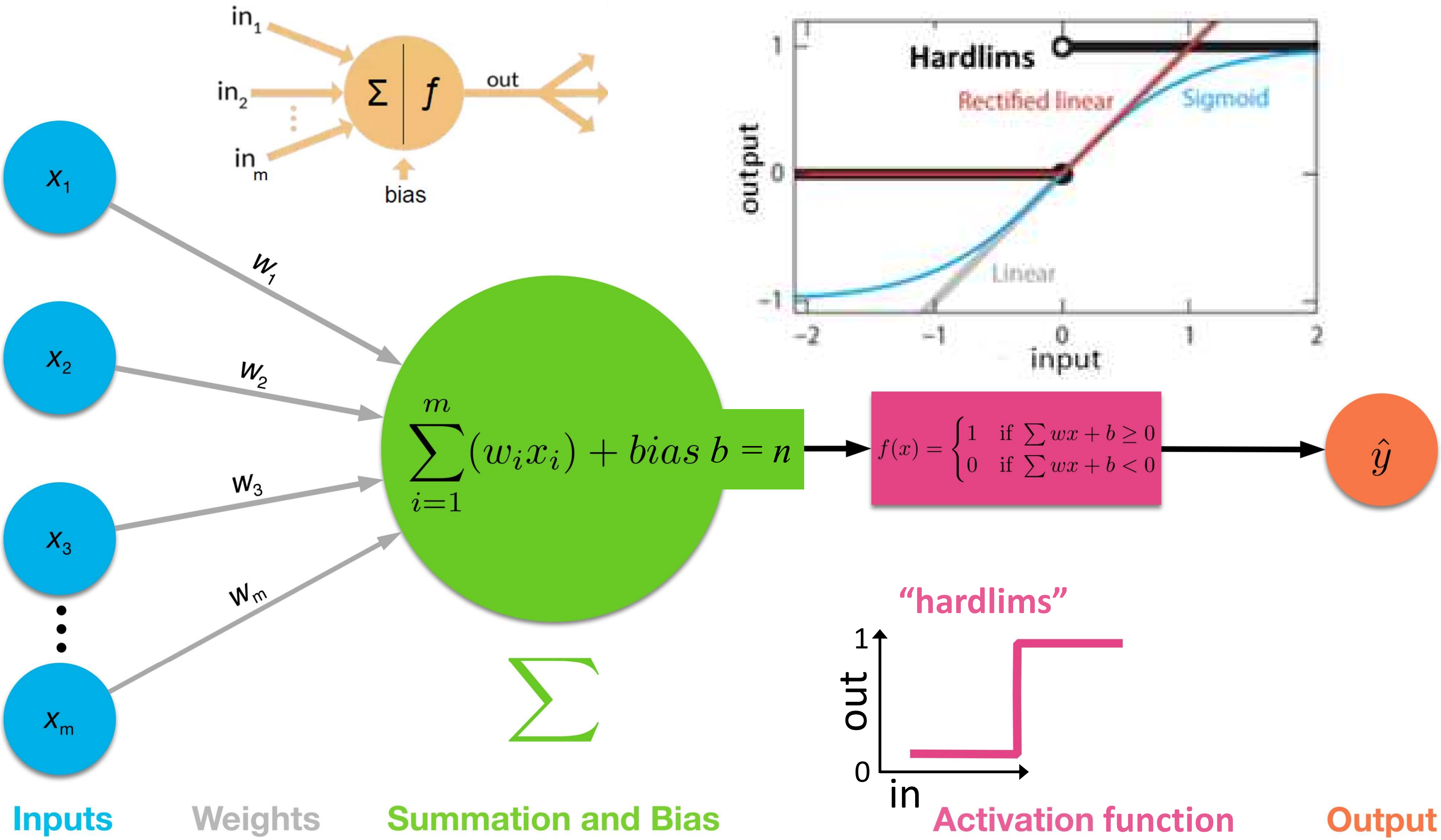
  4. **Deep neural networks**
     - no prior feature selection needed
  5. **Deep learning applications**

  practical 5
  Exercise 4 & 5



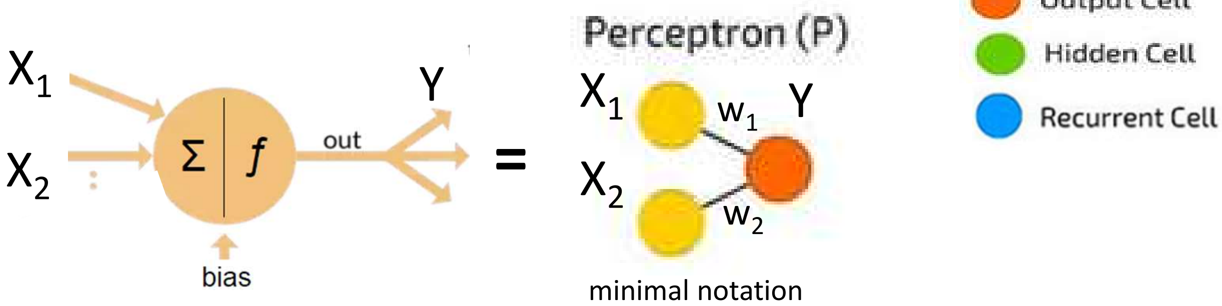
1. The basic neural unit: The Perceptron neuron (Rosenblatt, 1958)

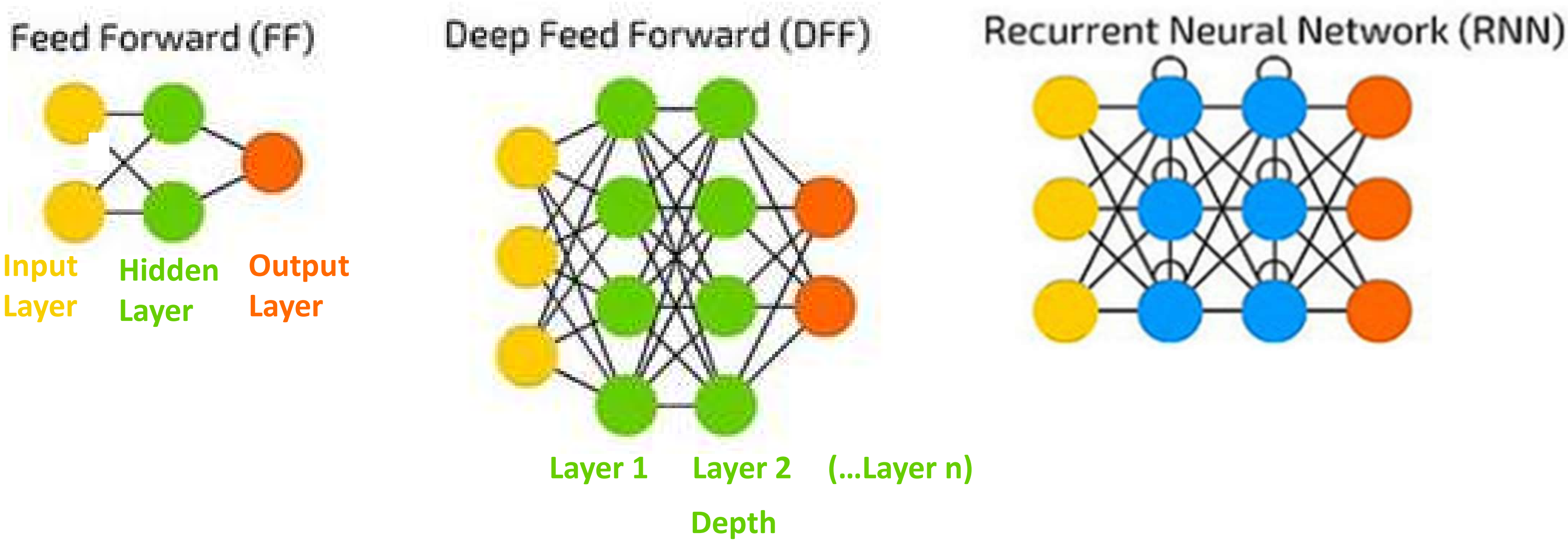




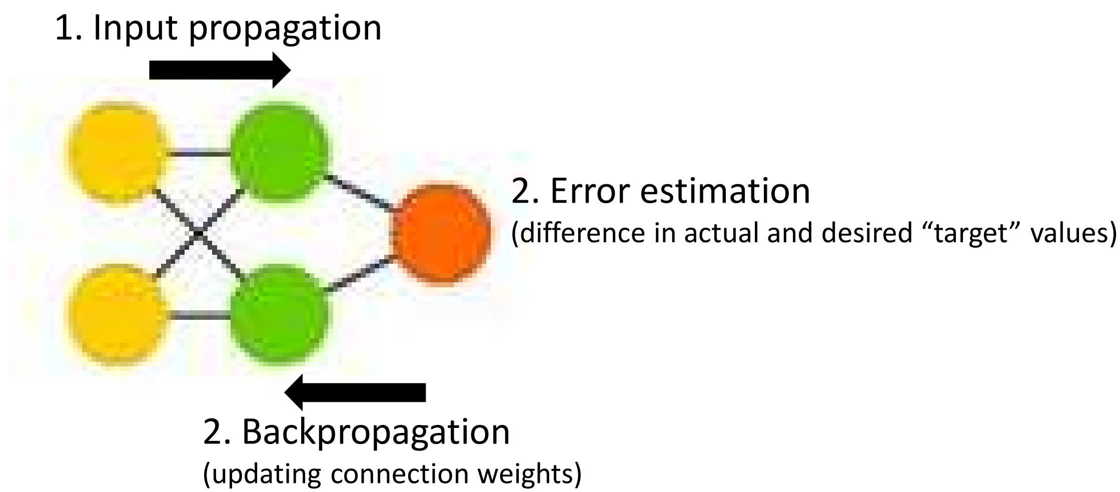
in1
in2
inm
Σ
f
out
bias
Hardlims
Rectified linear
Sigmoid
Linear
output
input
1
0
−1
−2
−1
0
1
2
x1
x2
x3
xm
w1
w2
w3
wm
$\sum_{i=1}^{m}(w_i x_i) + bias\ b = n$
$f(x) = \begin{cases} 1 & \text{if } \sum wx + b \geq 0 \\ 0 & \text{if } \sum wx + b < 0 \end{cases}$
$\hat{y}$
$\sum$
“hardlims”
1
0
out
in
Inputs
Weights
Summation and Bias
Activation function
Output

2. Multilayer networks

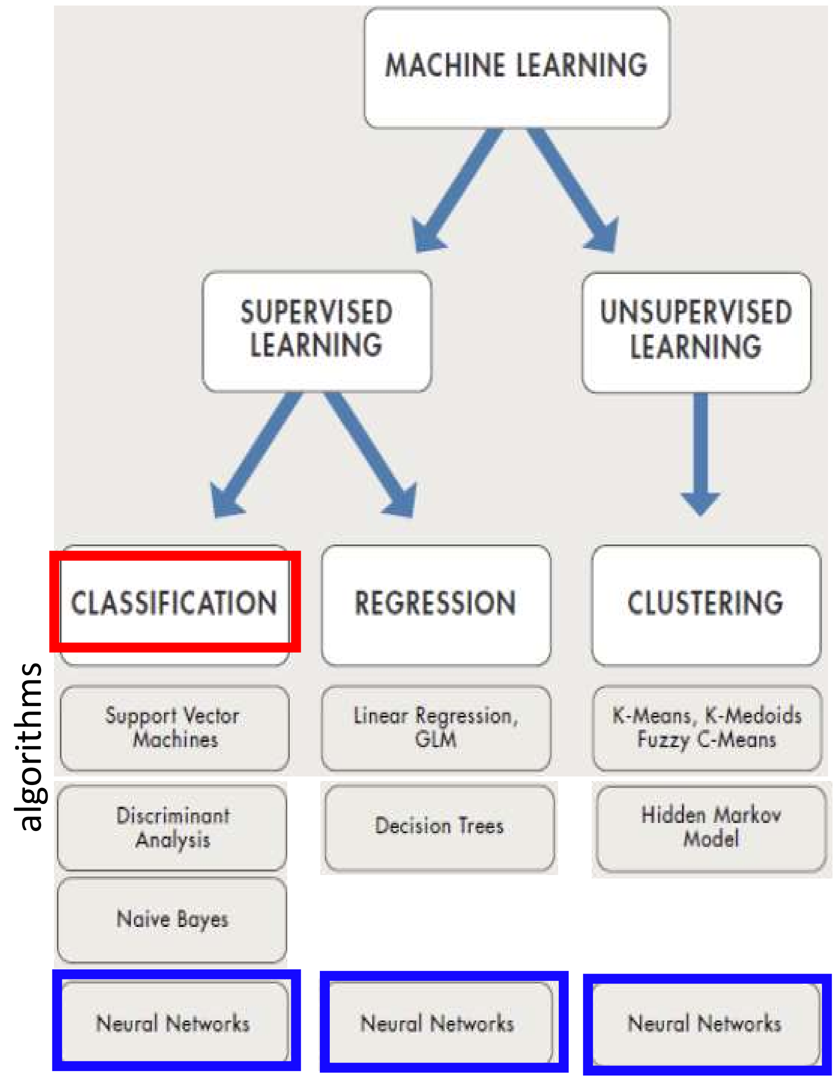




Training a neural network



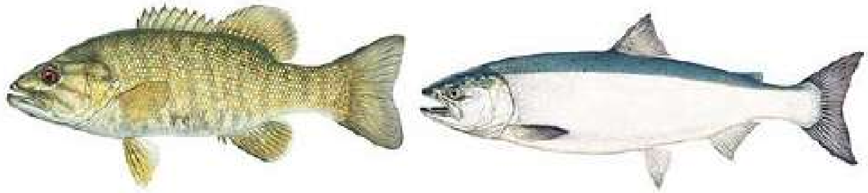
- ➢ *By iteratively adapting weights based on previous inputs, neural network can learn to recognize patterns*



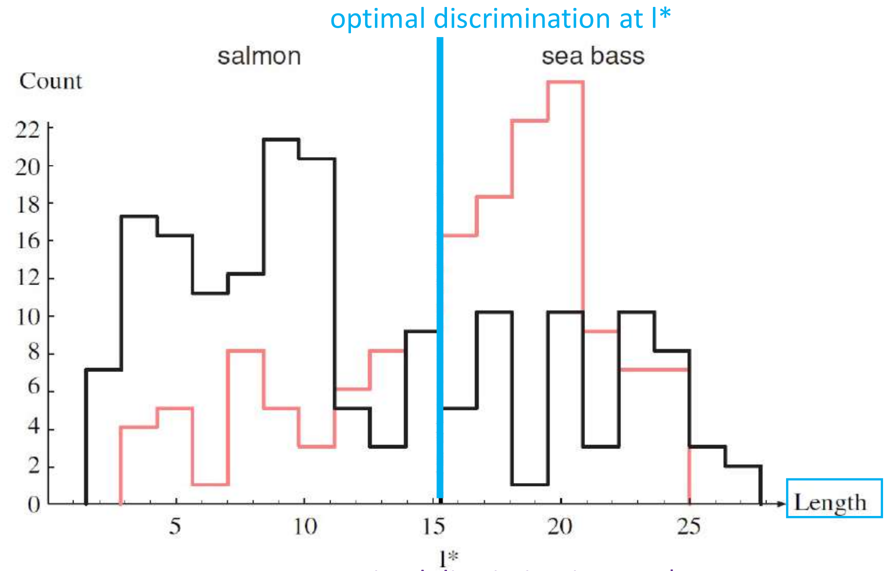
3. Classification

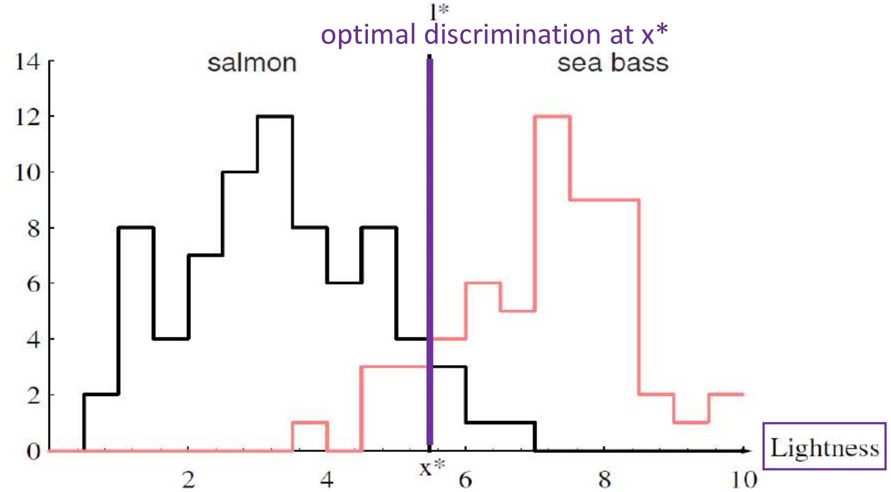
Feature extraction

How to classify?:



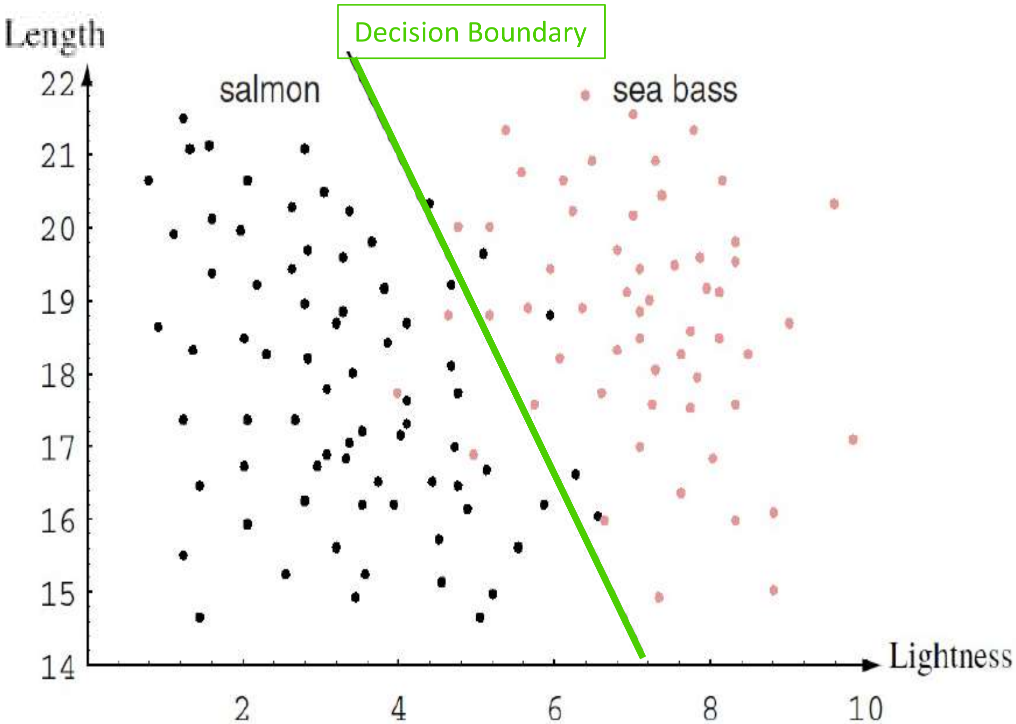
(a) (b)





example adapted from Duda et al. 2001

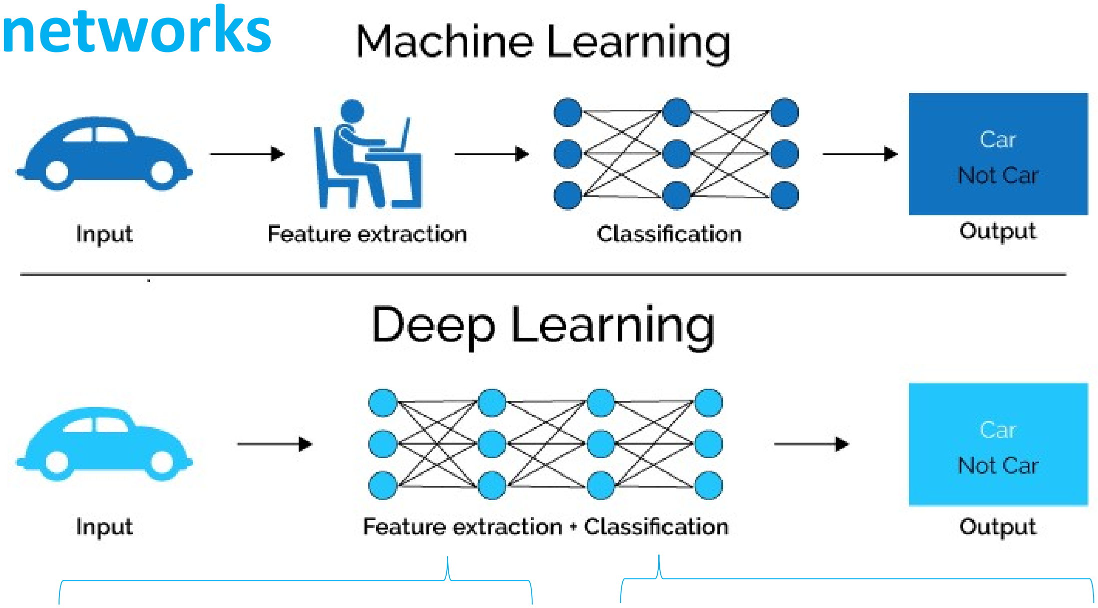
Combining both features improves classification…



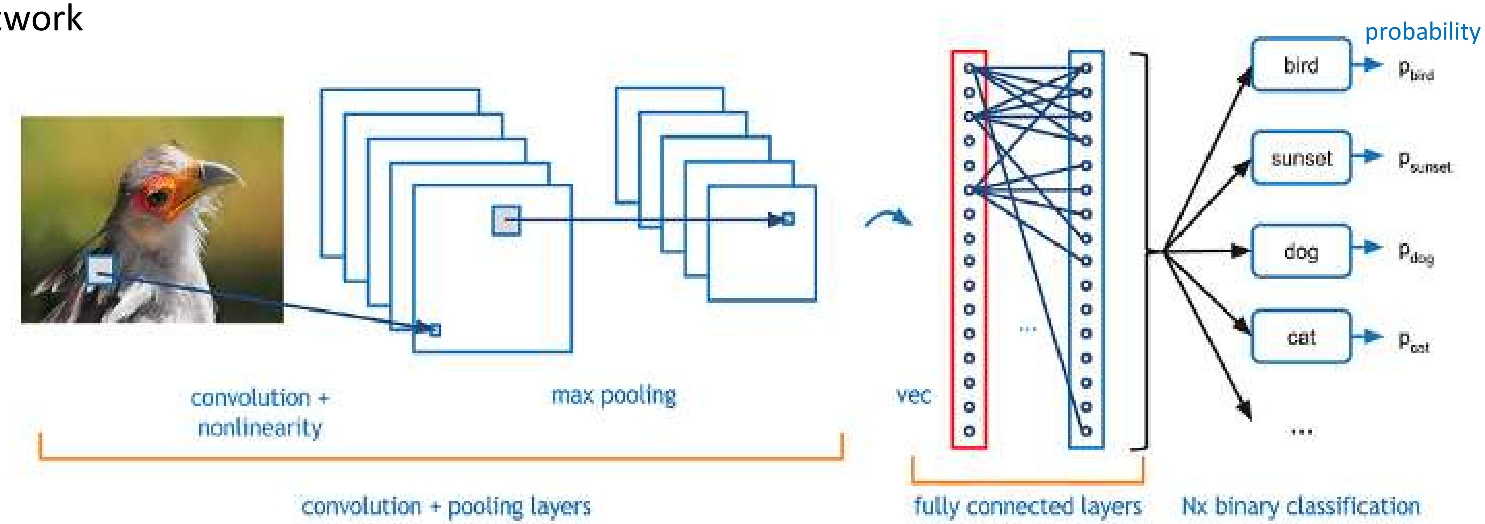
Object variance: What features define a car?

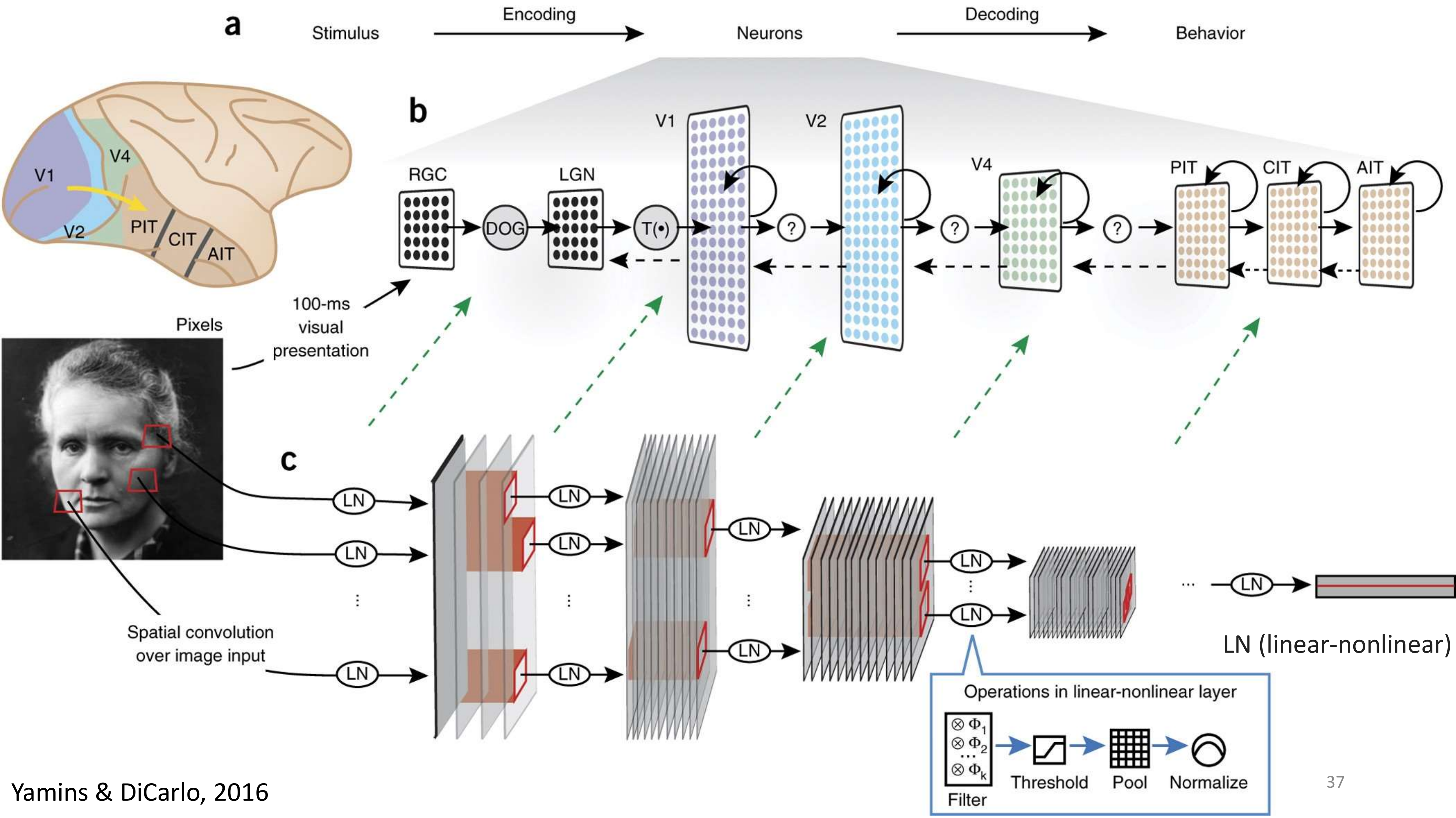
… add more features? Which features? Too many features (overfitting!)?

4. Deep neural networks



convolutional
neural network

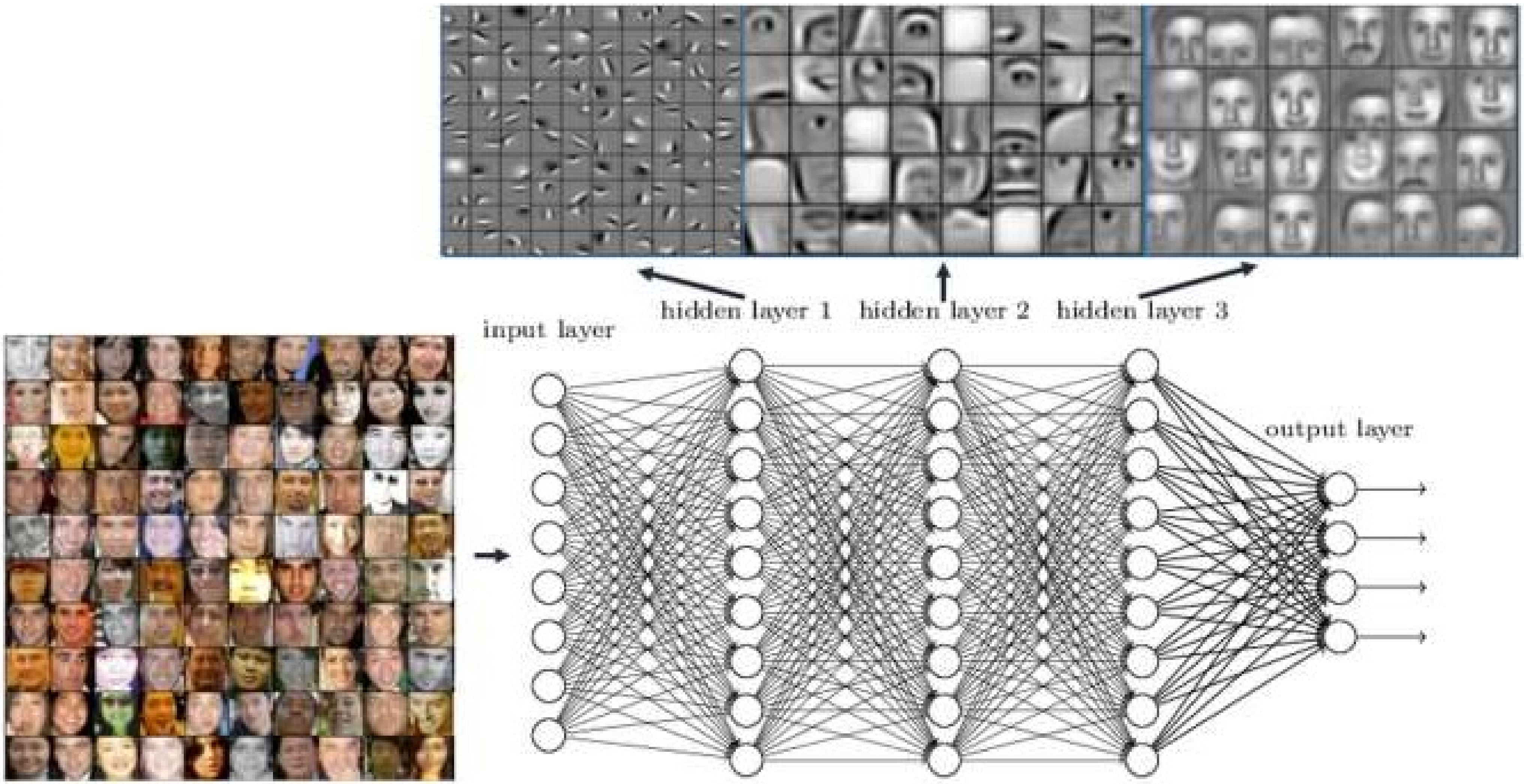




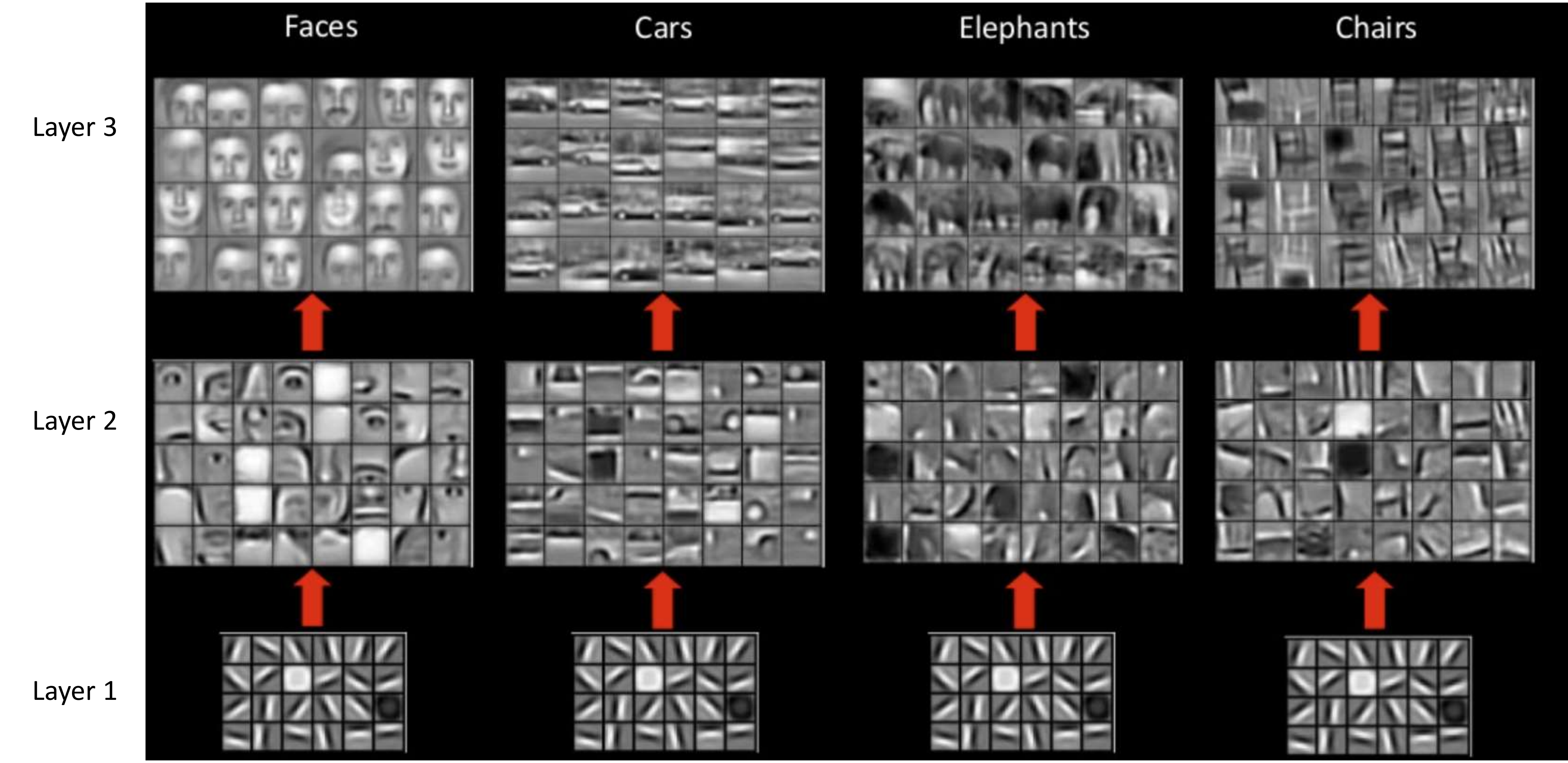
LN (linear-nonlinear)

Yamins & DiCarlo, 2016

Feature representations become increasingly more complex at deeper layers



Examples of feature representations



Generative Networks can use these features to create new data

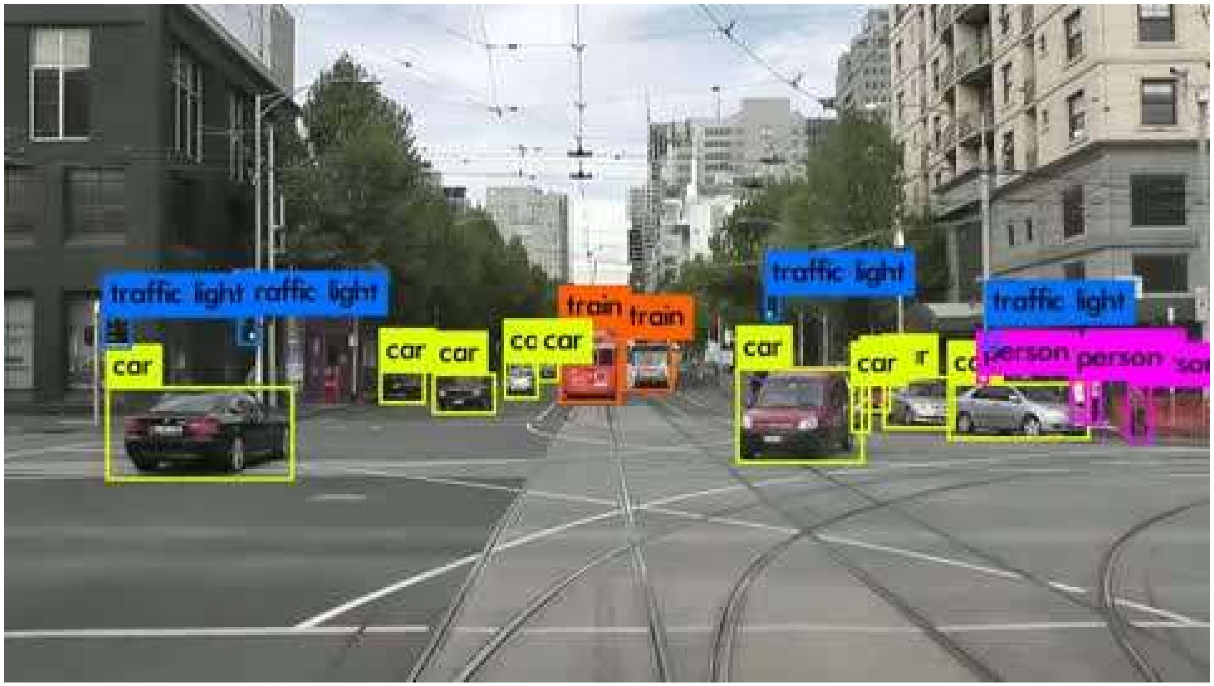
e.g., [pixel-by-pixel generation of a non-existent human face](deepfake picture)

practical 5

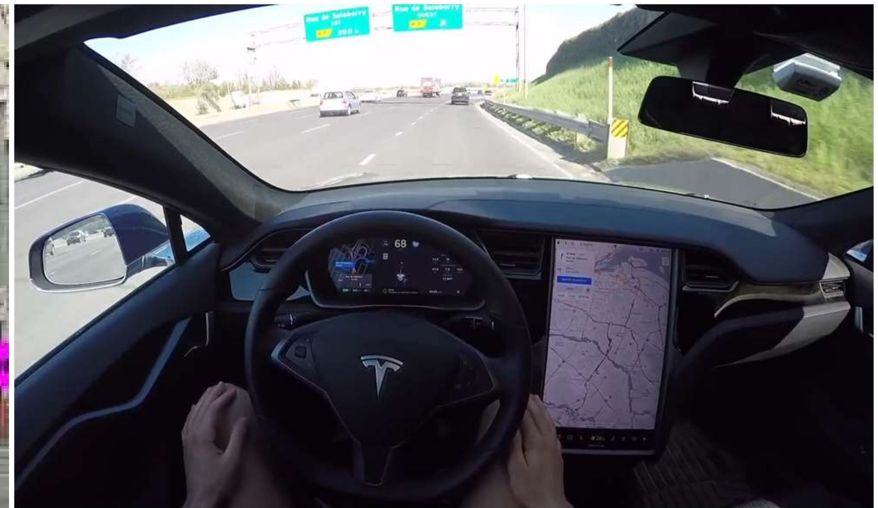
Exercise 5

5. Deep learning applications

Scene analysis (including image classification) in self-driving cars



Autopilot in self-driving cars

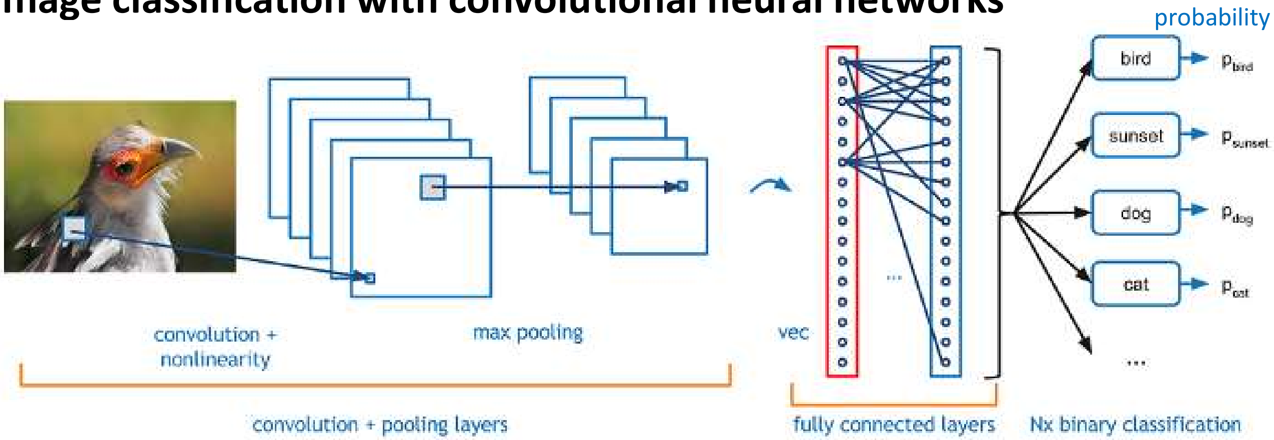


© Tesla (2020)

see also [“Paris streets in the eyes of Tesla”]

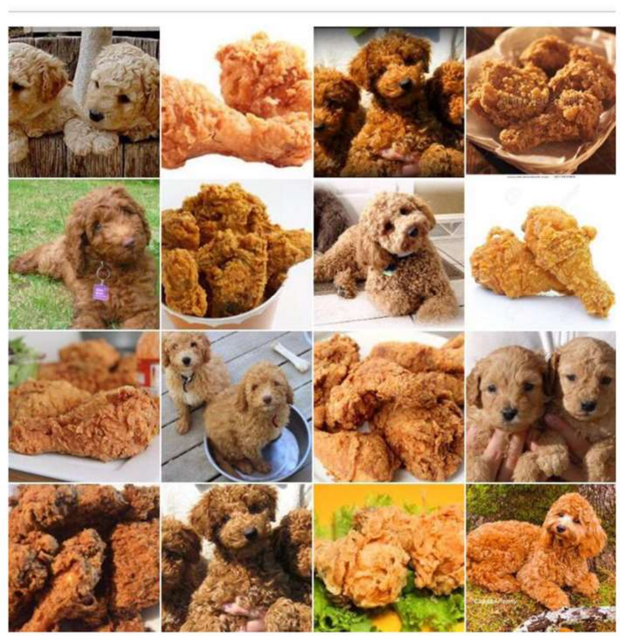
Image classification with convolutional neural networks

practical 5
Exercise 4



Sheepdog or mop

Labradoodle or fried chicken



Puppy or bagel

5. Deep learning applications

(this slide is *not* exam material)

- Image and sound analysis (recognition of objects, speech, fingerprints…)

- Self-driving cars

- Natural Language Processing

  e.g., internet chatbots, text and code completion

- *Analyzing heterogeneous 'Big Data'*

  for example:

  - Web trac analysis
  - Consumer preferences

    e.g., recommendation systems in Tiktok, Youtube, Spotify, Amazon etc.

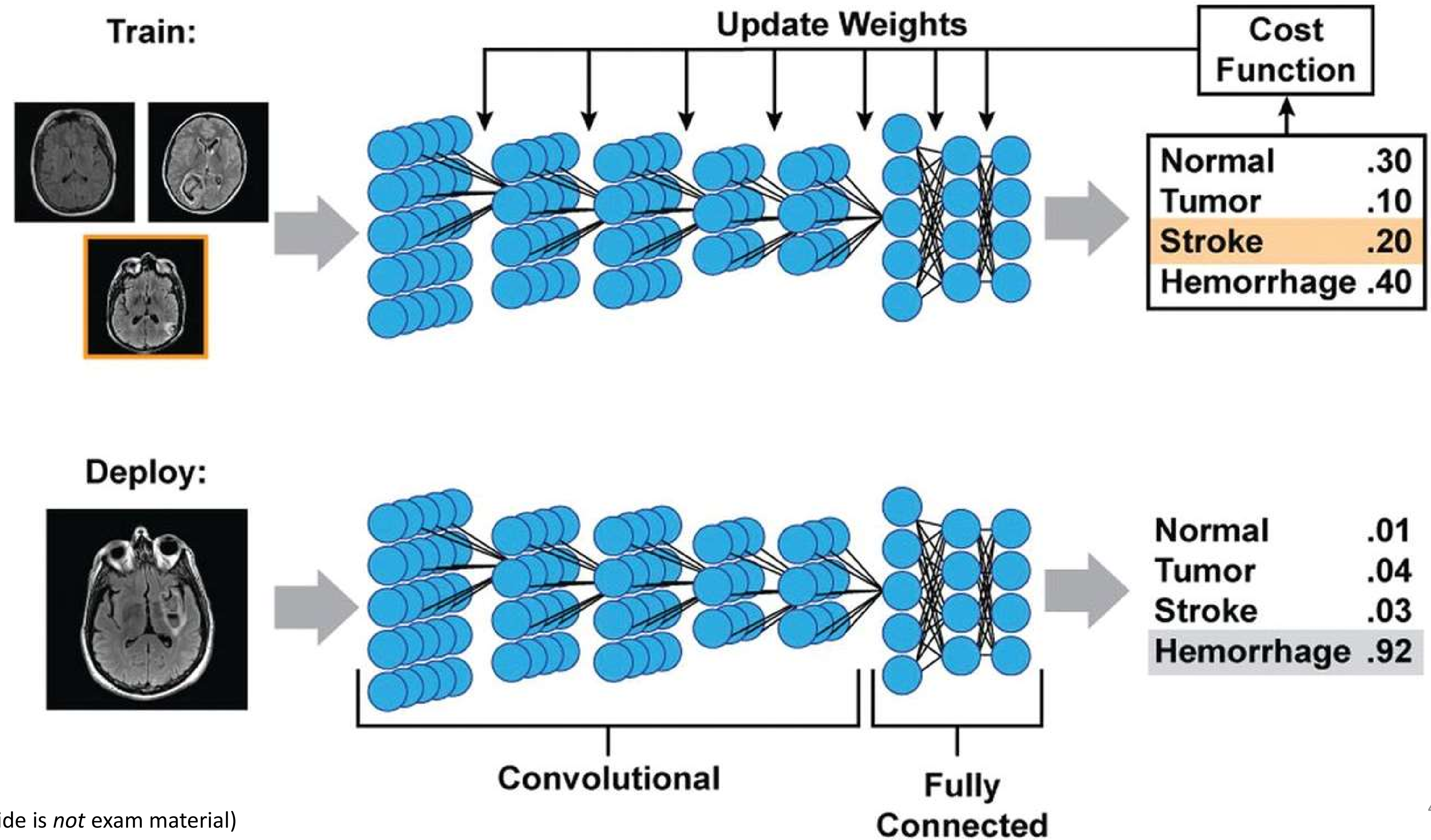
  - Biomedical data:
    - Clinical diagnosis

      e.g., stratifying clusters of symptom characteristics from diverse information sources like health tracking apps, smartwatches, etc.

    - Systems biology research

      e.g., Genome wide association studies and neuroimaging population studies

Example of **AI-supported clinical diagnoses:** Deep Neural Network to classifying brain pathology (Zaharchuk, 2018)

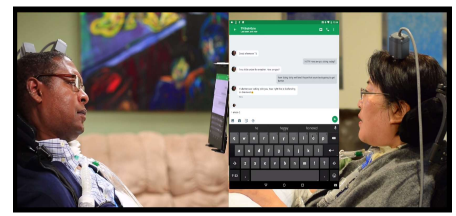


(this slide is *not* exam material)

Lecture Recap Part 2

Computational neuroscience applications:

D



Brain-Brain-via-Machine Interface

1. Brain-Machine Interfaces

A. Overview neuroprosthetics

B. Read out brain activity to control bionic arm

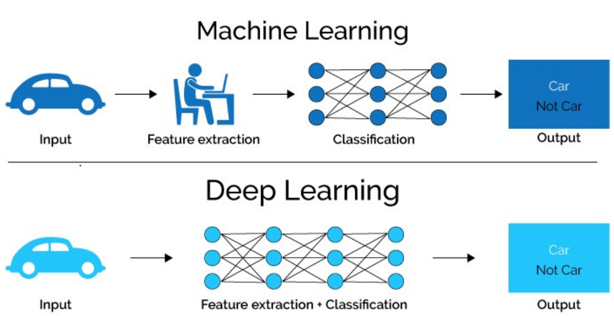
C. Prosthetic-based brain stimulation enables touch and pain perception

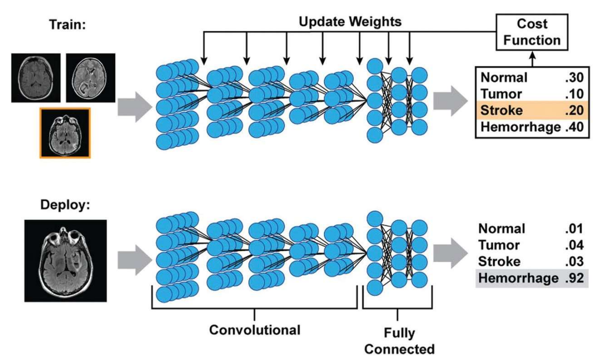
D. Intersubject communication interfaces (Brain-Brain-Machine)

2. Brain-inspired improvements of Artificial Intelligence

❖ Neural Networks (Practical 5)

❖ Convolutional Neural Networks and Deep learning





Lecture Recap

Part 1: *Imaging the brain at work*

1. Brief overview of main neuroimaging methods

2. MRI, fMRI

   A. Network neuroscience
   B. Special network characteristics of the Brain

3. Neuromodulation

   A. Transcranial Stimulation
   B. Microstimulation in neurological patients
   C. Optogenetics

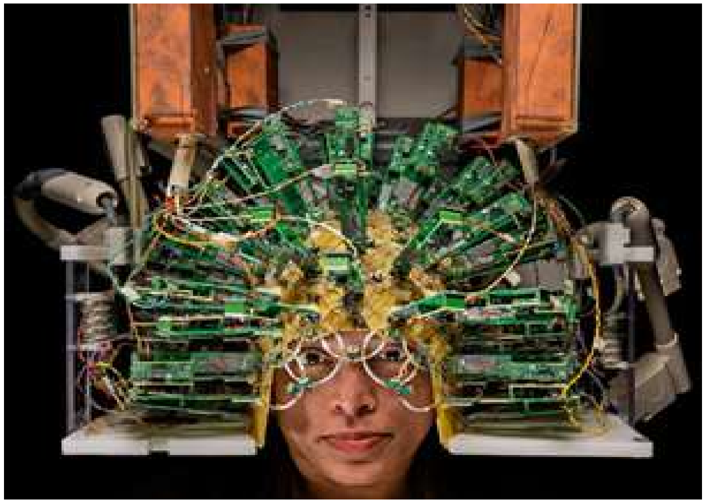


Photo: National Geographic

Part 2: *Computational neuroscience applications*

1. Brain-Machine Interfaces

   Neuroprosthetics

2. Brain-inspired improvements of Artificial Intelligence

   A. Intro to neural networks
   B. Neural nets as learning machines
   C. Deep learning applications

   applications in practical 5