



ALMA MATER STUDIORUM
UNIVERSITY OF BOLOGNA

DEPARTMENT OF COMPUTER SCIENCE AND ENGINEERING

SECOND CYCLE DEGREE/TWO YEAR
MASTER IN ARTIFICIAL INTELLIGENCE

Course

**COGNITION AND
NEUROSCIENCE**

Held by

Prof. Francesca Starita

Prof. Giuseppe Di Pellegrino

Written by

Giorgio De Simone

Academic Year 2021-2022

© 2024 Giorgio De Simone

Contents

Preface	1
I Module 1	3
1 A neuroscience course in an AI degree	4
1.1 Cognition and Neuroscience	4
1.2 Using the (human) brain as model for AI	7
1.3 The neuroscience side of the story	8
1.4 The cognitive side of the story	14
2 The nervous system	19
2.1 Individual cells	20
2.2 From individual neurons to neural circuit	28
2.3 From neural circuits to neural systems	32
3 Neuronal signaling	60
3.1 Signaling units of the nervous system	60
3.2 Information transfer within a neuron	63
3.3 Information transfer between neurons	71
4 Intro to Reinforcement learning	79
4.1 Introduction to reinforcement learning	79
4.2 Classical conditioning	83
4.3 Neural bases	91
4.4 Instrumental conditioning	103
5 Reinforcement learning: part one	109
5.1 Associate stimuli/actions to outcomes	110
5.2 Formalization of learning theories	119
5.3 Prediction errors in neurons	123
6 Reinforcement learning: part two	129
6.1 A brief recap	129
6.2 The reward prediction error hypothesis of dopamine	131
7 Model-based & Model-free	156
7.1 Learning strategies	156

II Module 2	188
8 Neural mechanisms of vision	189
8.1 Vision: a general overview	189
8.2 Low-level visual processing	228
8.2.1 Retina	229
8.2.2 LGN	254
8.2.3 V1	254
8.3 Visual motion	266
Bibliography	314

Preface

The idea of writing these notes born with the intention of collecting the entire material of the *Second Cycle Degree/Two Year Master in Artificial Intelligence* offered by *University of Bologna*, dividing it in different volumes depending on the different courses held with the purpose of creating a true series of books.

Specifically here I wrote the notes related to the *Cognition and neuroscience* course – held by Professor Francesca Starita and Professor Giuseppe Di Pellegrino – which concerns rudiments of cognition and neuroscience.

How do neurons in the brain give rise to mind – to our abilities to sense and perceive the world, to act and think about it, to learn and remember it? This book will provide an accessible but highly challenging survey of the empirical evidence, theories and methods in cognitive neuroscience exploring how cognition is instantiated in neural activity. Drawing on a wide variety of investigative tools available to cognitive neuroscience, the book explores the neural mechanisms underlying complex cognitive processes, including visual perception, selective attention, learning and emotion, cognitive control and decision-making. Importantly, the book examines the logic and assumptions that permit us to interpret brain activity in psychological terms.

Prerequisite involves high-school knowledge of the biology of the *central nervous system*. In addition, it is highly recommended to attend to online video lectures on Neuroscience Core concepts, freely available at the *Society for Neuroscience* website: <https://www.brainfacts.org/core-concepts>.

The book itself is essentially divided in two modules.

Below it is shown a very preliminary schedule of the book content, schedule that is suggested to follow.

1. Topics of module 1:
 - (a) Neuroanatomy: from single neurons to the nervous systems.
 - (b) Neurophysiology: mechanisms of neuronal signaling:
 - i. within a neuron;
 - ii. between neurons: neural networks.
 - (c) Reinforcement learning: Pavlovian and instrumental conditioning.
 - (d) Mechanisms of reinforcement learning 1: prediction error:
 - i. Rescorla-Wagner and temporal difference models;
 - ii. prediction error signals in the brain: dopamine, feedback related negativity.

CONTENTS	2
----------	---

(e) Mechanisms of reinforcement learning 2: Model-free & Model-based learning.

2. Topics of module 2:

- (a) Vision.
- (b) Visual object recognition.
- (c) Visual selective attention.

At the end of the book, the reader knows the state of the art of human and animal research that uses neuroscience techniques to understand the cognitive and emotional aspects of the human mind and behavior. The reader is able to critically read experimental and theoretical studies of cognitive and affective neuroscience, to evaluate their methods and results, explain their significance, and apply such notions in the study and development of artificial intelligence systems.

So, more schematically, at the end of the book the reader is be able to:

- get in-depth understanding of the neural substrates and functional mechanisms of mental processes;
- get knowledge of the-state-of-the-art methodologies and novel approaches of current research in cognitive neuroscience;
- critically review and discuss the theoretical and empirical contributions of the current literature, understand and analyse the methods employed, interpret their results and critically assess their conclusions;
- exercise the ability to engage in creative thinking leading to formulations of new hypotheses and planning of their empirical testing.

Part I

Module 1

Chapter 1

A neuroscience course in an AI degree

1.1 Cognition and Neuroscience

What is Neuroscience?

Neuroscience is the study of the *animal nervous system* where we highlight that:

- the term *animal* contains the *human* category;
- we will see that the *nervous system* is divided into a *peripheral* one and a *central* one (the latter containing the *brain*).

We will study its:

- *anatomy* (structure);
- *physiology* (functions);

But also its *computational capacity* which involves both structures and functions (in general functions depends on structures, but not always).

So Neuroscience is more concerning with *structure* but not totally, there is also a study on *functions* but a lower level (physiology) in comparison to what Cognition studies.

It is essentially the study of how the nervous system is organized and functions; it's a multidisciplinary science (from microlevel to macro):

- physiology;
- anatomy;
- molecular biology;
- developmental biology;
- cytology;
- computer science;

- mathematical modeling

It has different levels:

- *molecular*: molecular neuroanatomy, mechanisms of molecular signaling in the nervous system;
- *cellular*: study of neurons at a cellular level including morphology and physiological properties;
- *neural circuits and systems*: how neural circuits are formed and function anatomically and physiologically to generate behaviours, such as:
 - sensory perception (somatosensory, visual auditory *etc.*) and multi-sensory integration;
 - motor reflexes and actions.

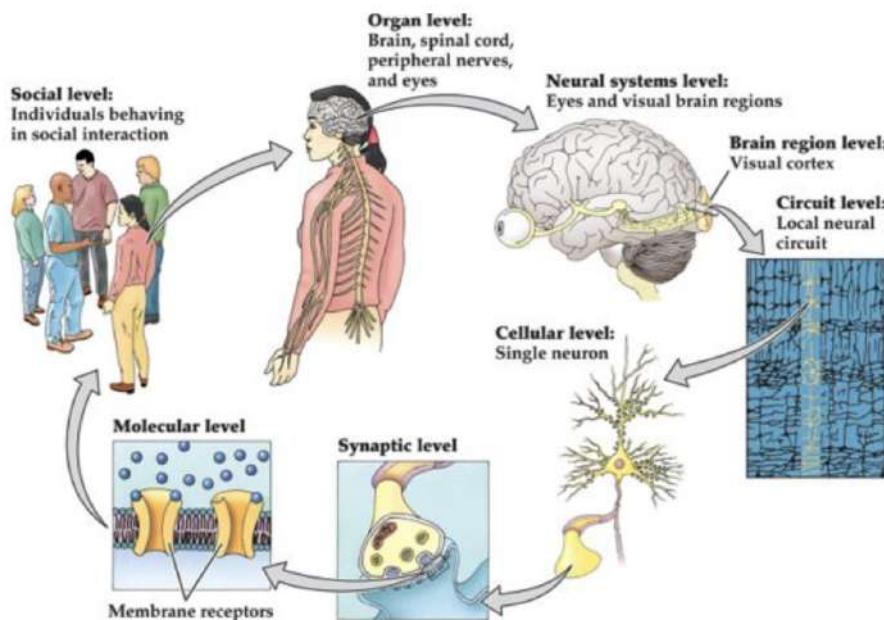


Figure 1.1

What is Cognition?

Cognition is made of lots of different processes. We can say that is the higher level process that brain makes; it is more concerning with the functions that emerge from the brain structure. So cognition is more concerning with what we call *mind*¹, and consists in a series of different processes that include:

- knowledge;

¹We could roughly say that the physiology of the brain (hardware) produce the *mind* (software).

- reasoning;
- thinking;
- learning.

So Cognition is a range of mental processes relating to the:

- acquisition;
- storage;
- manipulation;
- retrieval of information.

The description, explanation and simulation of human thought processes.
Cognition includes multiple processes:

- *perception*: take in information from environment through the senses (sensation);
- *attention*: allows to focus on a specific stimulus in the environment.
- *learning*: manipulating new information, and integrating it with prior knowledge;
- *memory*: encode, store and retrieve information. It is a critical component in the learning process;
- *action*: use perceived information to interact with the environment;
- *language*: the ability to understand and express thoughts through spoken and written words. It allows communication with others;
- *thought/higher reasoning*: allows to engage in decision-making and problem-solving.

Cognitive neuroscience

Cognitive neuroscience is the study of how functions of the physical brain can yield the thoughts and ideas of an intangible mind.

Roughly speaking how *brain* produces *mind*; how the *hardware* produces the *software*.

Below a useful video which introduces to Cognitive neuroscience:

<https://www.youtube.com/watch?v=lfGwsAdS9Dc> (Severed Corpus Callosum)²

²Between parenthesis we insert, when possible, key-words that can be useful to find the video in case the url will change; put them in the default search bar of the server indicated into the url (in this case www.youtube.com).

1.2 Using the (human) brain as model for AI

The (human) brain is the existing proof that general intelligence is even possible. Studying animal cognition and its neural implementation can provide a window into various important aspects of higher-level general intelligence.

There are functional similarities: the '*all-or-none*' nature of the firing of neurons in a nervous system, is analogous to binary computations. But these binary abstractions do not capture all the complexities inherent the brain.

Neuroscience provides a rich source of inspiration for new types of algorithms and architectures, independent of and complementary to the mathematical and logic-based methods and ideas that have largely dominated traditional approaches to AI.

Neuroscience can provide validation of AI techniques that already exist: a known algorithm that is subsequently found to be implemented in the brain gives strong support for its plausibility as an integral component of an overall general intelligence system.

Biomimicry

Biomimicry is that branch in which technologies are inspired by nature.

Emulation of the models, systems and elements of nature for the purpose of solving complex human problems.

Living organisms have evolved well-adapted structures and materials over geological time through natural selection.

Below a useful video which introduces to biomimicry:

<https://www.youtube.com/watch?v=iMtXqTmfta0> (The world is poorly designed. But copying nature helps)

But the animal brain is not *necessarily* a good model for AI

We need not slavishly enforce adherence to biological plausibility. From an engineering perspective, what works is ultimately all that matters.

The human brain does not implement '*intelligence*' in the same way as a computer:

- Machine Learning practitioners use '*statistical learning*' that requires a very large collection of examples on which to generalize implying a vast memory capacity;
- the brain has limited memory capacity, yet humans excel at generalizing or transferring generalized knowledge gained on one context to novel, previously unseen domains.
 - Think to children that for the first time see a flame and they don't know that flame burns; but once they put their fingers to the flame, just one time, they quickly learn that a flame can cause pain. Machine Learning could be very inefficient for surviving.

We still do not know the detailed circuitry of any region of the brain well enough to reproduce its structure.

We model brains and computers on each other, and so prevent ourselves from having deep insights that would come with new models.

Brains differ from computers in a number of key respects:

- they operate in cycles rather than in linear chains of causality, sending and receiving signals back and forth;
- unlike the hardware and software of a machine, the mind and brain are not distinct entities (artificially you can design software and hardware separately, for example);
- living cells process incoming sensory information and generate not just electrical signals but subtle biochemical changes.

Different levels of brain emulation

Structure

Closely mimic or directly reverse engineer the specifics of neural circuits.

Function

Mimic the computational and algorithmic levels of neural systems to gain transferrable insights into general mechanisms of brain function.

Blue brain Project (Markram, 2006) aims to build biologically detailed digital reconstructions and simulations of the mouse brain.

Deep Mind (Hassabis, Legg, 2010) aims to create a general-purpose AI.

Biologically-detailed digital reconstructions and simulations of the mammalian brain to identify the fundamental principles of brain structure and function.

Systems neuroscience-level understanding of the brain, namely the algorithms, architectures, functions and representations it utilizes.

1.3 The neuroscience side of the story

Brain structure gives rise to function

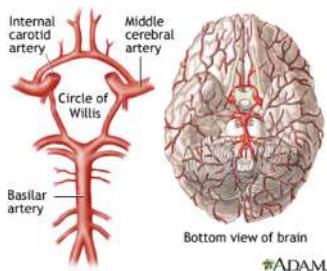


Figure 1.2

Thomas Willis (1621-1675, English physician) was the first anatomist to link abnormal human behaviours to changes in brain structure. Forshadowed cognitive neuroscience with the notion that isolated brain damage (neurology) could affect behaviour (psychology).

He coined the term *neurology*.

A pioneer in research into the anatomy of the brain, nervous system and muscles.

Phrenology: localizationism

Phrenology is a pseudoscience (not scientific) invented by Franz Joseph Gall (1758-1828, German neuroanatomist, physiologist).

One of the thesis of this theory was that the brain was the organ of the mind and the innate faculties were localized in specific regions of the cerebral cortex (*localizationism* which is a consistent scientific theory).³

Furthermore hypothesized that if a person used one of the faculties with greater frequency than the others, the part of the brain representing that function would grow, causing a bump in the skull.

A careful analysis of the skull could describe the personality of the person inside the skull.

A scientific approach: aggregate field theory

Gal was not a scientist. He observed *correlations* and sought only to *confirm his hypotheses*, not disprove, them.

Napoleonic government asked physiologist Marie Jean Pierre Florens (1794-1867, French physiologist) to test the validity of phrenology by collecting evidence using the scientific method.

He destroyed parts of the brain of pigeons and rabbits and observed what happened. He was the first to show that indeed certain parts of the brain were responsible for certain functions.

He could not, however, find any areas for advanced abilities such as memory or cognition, concluding that the whole brain participated in behavior giving rise to *aggregate field theory*.⁴

A debate that is still going on today: aggregate field theory vs localizationism.

Evidence in favor of localizationism

In 1836 (France) Marc Dax (French neurologist), reported about three patients, noting that each had speech disturbances and similar left-hemisphere (part responsible of language) lesions found at autopsy.

John Hughlings Jackson (1835–1911, English neurologist) noticed that epilepsy⁵ progressed in an orderly manner from one part of the body to another; proposed a topographic organization of the cortex.

³This basic idea was right in the sense that specific functions depend on specific regions of the brain; Phrenology was in the right direction, but after lost it.

⁴The whole brain is greater of the sum of its parts' is the aggregate field theory motto: in the sense that is true that specific parts are related to specific functions, but it is also true that all the parts together contribute to macro-functions.

⁵Epilepsy is manifest when electrical activity spread through the brain in an abnormal way. Usually and normally electrical activity is localized, but when there is epilepsy electrical activity can spread in specific regions. Jackson noticed that when patients had seizures they involved different parts of the body orderly; so he deduced from this and other evidences that the cortex has a topographic organization. Topographic organization of the cortex: different parts of the brain are represented by different parts of the cortex. Jackson was right but his intuitions were confirmed almost 100 years later.

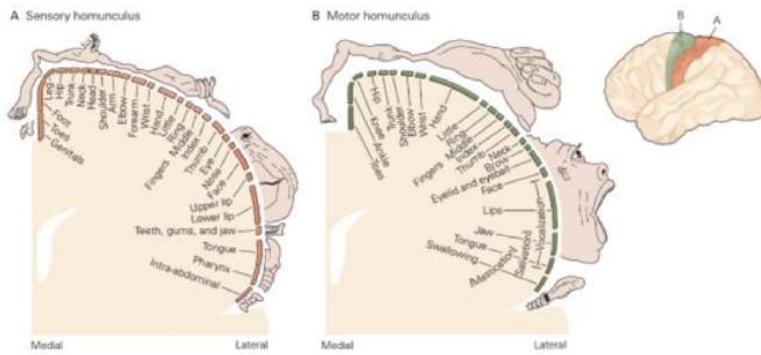


Figure 1.3

In 1861 (France) Paul Broca (1824-1880, French physician) published the results of his autopsy on a patient who had been nicknamed Tan.⁶

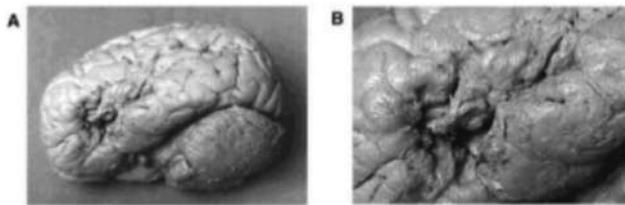


Figure 1.4

Tan had a lesion in his left hemisphere in the inferior frontal lobe
Tan had developed *expressive aphasia*:

- could understand language;
- could not speak.

Below a usefull video which explains *Broca's aphasia*:

<https://www.youtube.com/watch?v=JWC-cVQmEmY> (Broca's Aphasia (Non-Fluent Aphasia))

In 1876 (Germany) Carl Wernicke (1848-1905, German physician) reported on a stroke victim who had *fluent aphasia*:

- could talk but made little sense when he spoke;
- could not understand spoken or written language.

Below a usefull video which explains *fluent aphasia*:

<https://www.youtube.com/watch?v=3oef68YabD0> (Fluent Aphasia (Wernicke's Aphasia))

We saw that specific aspects of language were impaired by specific lesions and a focal brain damage causes specific behavioral deficits.

⁶This nickname was given because the only thing that he was able to say after a lesion of its brain was 'Tan'.

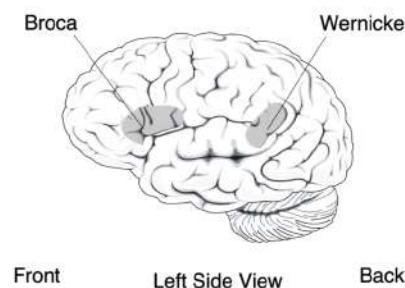


Figure 1.5

Evidence in favor of aggregate field theory

But also brain gave proofs of being *plastic*, meaning that it can create new connections in order to perform some functions; it changes with experience: the connection between neurons change with experience, it is possible to ‘train’ the brain.

For example when the brain has some damage, people can try with training to recover the skills lost and sometimes they succeed. During the rehabilitation, brain can perform new connection in order to reacquire the function lost.

For people that born blind it was proved that parts that corresponds to the visual cortex respond to signal which are not visual.

Different regions of the brain are made of different neurons

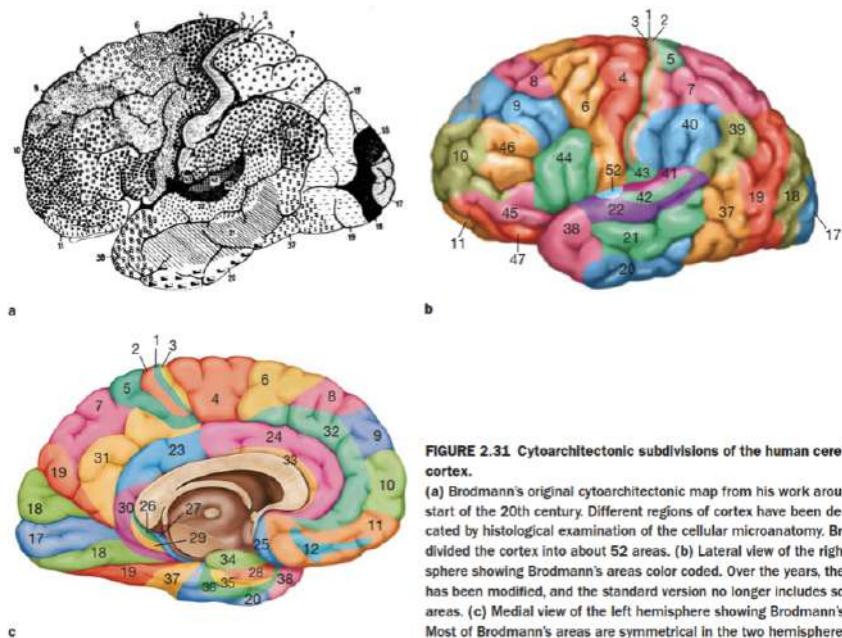


FIGURE 2.31 Cytoarchitectonic subdivisions of the human cerebral cortex.
 (a) Brodmann's original cytoarchitectonic map from his work around the start of the 20th century. Different regions of cortex have been demarcated by histological examination of the cellular microanatomy. Brodmann divided the cortex into about 52 areas. (b) Lateral view of the right hemisphere showing Brodmann's areas color coded. Over the years, the map has been modified, and the standard version no longer includes some areas. (c) Medial view of the left hemisphere showing Brodmann's areas. Most of Brodmann's areas are symmetrical in the two hemispheres.

Figure 1.6

In 1909 Korbinian Brodmann (1868-1918, German neurologist) used tissue stains that permitted him to visualize the different cell types in different brain regions.

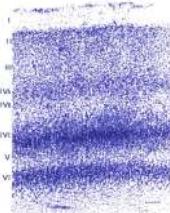


Figure 1.7

Characterized 52 distinct regions.

Started cytoarchitectonics: the study of cellular architecture or how cells differ between regions.

The rise of molecular neuroscience

Camillo Golgi (1843-1926, Italian biologist and pathologist) invented the silver method for staining neurons, in Italian called '*la reazione nera*' – '*the black reaction*' – with which impregnated individual neurons with silver chromate stains and so permitted visualization of individual neurons in their entirety.

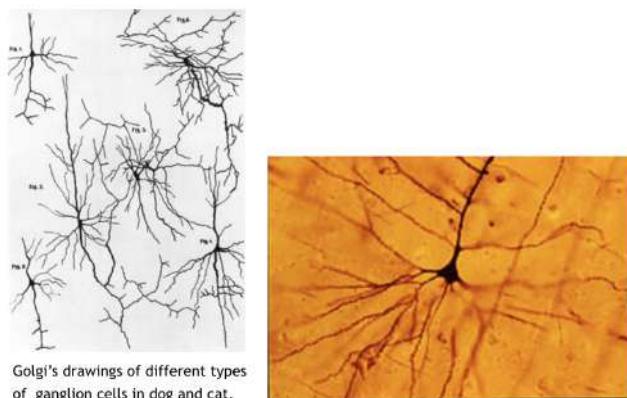


Figure 1.8

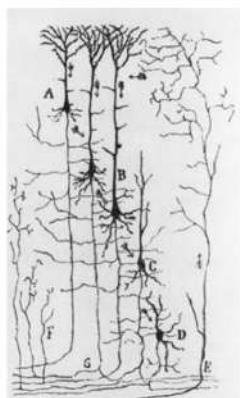
The neuron doctrine

Santiago Ramón y Cajal (1852-1934, Spanish neuroscientist, pathologist, and histologist) was the first to identify the unitary nature of neurons.

Invented the *neuron doctrine*: the nervous system is made up of individual cells. Neurons are discrete entities.

Challenged Golgi which had believed that the whole brain was a *syncytium*, a continuous mass of tissue that shares a common cytoplasm.

Cajal also recognized that the transmission of electrical information within neurons went in only one direction.



Ramón y Cajal's drawing
of the afferent inflow to
the mammalian cortex

Figure 1.9

The synapse enables neuronal communication

Charles Scott Sherrington (1857-1952, English neurophysiologist) realized that reflexes were not as fast as they should be if the nervous system was a continuous mass of tissue (syncytium)

He coined the term *synapse*⁷ referring to the structure that enables communication between neurons.

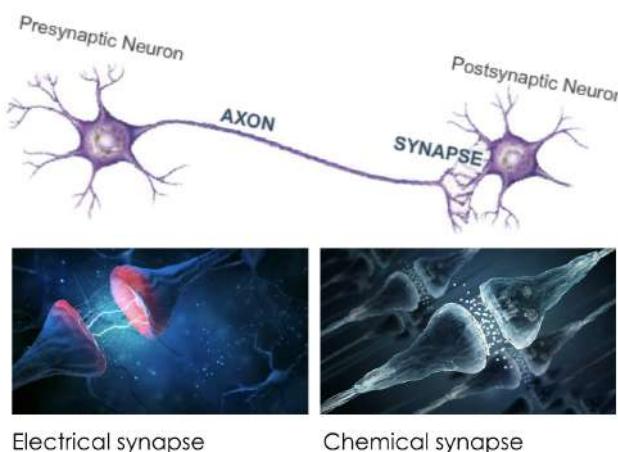


Figure 1.10

⁷Today we know that we have both *electrical* and *chemical* synapses. At the beginning it was believed that the majority of synapses were electrical, but after was proved that the majority is chemical. Chemical synapses are advantageous because they work with different substances and each of them can do specific things (consider that there are also *receptors* that respond differently to different chemicals); so they are powerful from the point of view of the variety and with them it is easier to modulate the signal *i.e.* how much signal has to be transferred from one part to the other. While the advantage of electrical synapse is that they are faster.

A debate that is still going on today

So *localizationism* or *aggregate field theory*?

A reasonable answer could be: the knowledge of the parts (the neurons and brain structures) must be understood in conjunction with the whole (*i.e.* what the parts make when they come together: the *mind*).

1.4 The cognitive side of the story

The Greeks

800 BC the Homeric Greeks believed that multiple souls were associated with different aspects of cognition, each located in different parts of our body (logic similar to *localizationism*)

500 BC two fields of thought:

- *cardiocentrism*;
- *encephalocentrism*:
 - Theon of Croton discovered the nerves and notice that the nerves were sending information to the brain;
 - Hippocrates localized intellect and neurological diseases in the brain.

Cartesian dualism (1600s)

Two kinds of foundation: mental and physical.

The mind and body are distinct and separable.

The body is a machine controlled by the soul.

The soul is located in the *pineal gland*, the only non-bilateral brain structure.

Monism (1700s)

Body and mind are not separable.

The body produces the mind (the brain produces our cognition).

Rationalism and empiricism (17th century)

17th century was divided into two main theories:

- *Rationalism*: all knowledge could be gained through the use of reason alone: Truth was intellectual, not sensory. Among intellectuals and scientists, rationalism replaced religion and became the only way to think about the world.
- *Empiricism*: all knowledge comes from sensory experience, the brain began life as a blank slate. Direct sensory experience produces simple ideas and concepts. When simple ideas interact and become associated with one another, complex ideas and concepts are created in an individual's knowledge system.
 - Empiricism which was a particular philosophy gave rise to *Associationism* and *Behaviorism* that are branches of psychology.

Associationism

Associationism asserted that individual experiences are associated to produce learning.

In 1800s Hermann Ebbinghaus (1850-1909, German psychologist) discovered that complex processes like memory could be measured and analyzed.

In 1911 Edward L. Thorndike (1874-1949, American psychologist) published the monograph '*Animal Intelligence: An Experimental Study of the Associative Processes In Animals*' in which formalized the first general statement about the nature of associations:

- *Law effect*: a behaviour response followed by a reward will be repeated. If no reward followed a response, the response would disappear.⁸

Behaviorism

Behaviorism asserted that only observable behavior can be studied.

John B. Watson (1878–1958, American psychologist) proposed that psychology could be objective only if it were based on *observable behavior*. All talks of mental processes which cannot be publicly observed, should be avoided.

Learning was the key, everybody had the same neural equipment on which learning could build.

The brain as a *blank slate* upon which to build through learning and experience. A fundamental historical experiment was the '*little Albert experiment*' in which was used the '*classical conditionism*'⁹ procedure:

1. Are shown different animals to the baby; the baby has no fear;
2. Animals are shown again, but this time when are shown white rats they are presented with a loud noise.
3. Animals are shown again, but when are shown animals similar to rats (the experiment introduced also proofs of *generalization*) the baby start crying, furthermore when the baby see a white mask he starts crying too. He starts to cry in response of the view of the rats or something similar, he anticipates that with the view of the rats or similar comes the noise.

Below a usefull video which shows the *little Albert experiment*:

<https://www.youtube.com/watch?v=FMnhyGozLyE> (Baby Albert Experiments)

Cognitivism

Cognitivism asserted that mental processes can be studied because the brain gives rise to them.

Wilder Penfield (1891–1976, American-Canadian neurosurgeon) introduced the '*Montreal procedure*' to treat epilepsy¹⁰:

- surgically destroyed the neurons in the brain that produced the seizures;¹¹

⁸It is possible to experience this everyday: if you train a dog ... or if you consider that money and sex can be judged as the most powerful rewards.

⁹It essentially consists in associating a stimulus to an outcome.

¹⁰Not only, also to remove tumors.

¹¹Obviously there would be an hight possibility of side effects.

- stimulated various parts of the brain with electrical probes and observed the results on the patients, to determine which cells to destroy.¹²

From these observations, he created maps of the sensory and motor cortices in the brain (Penfiel & Jasper, 1954).¹³

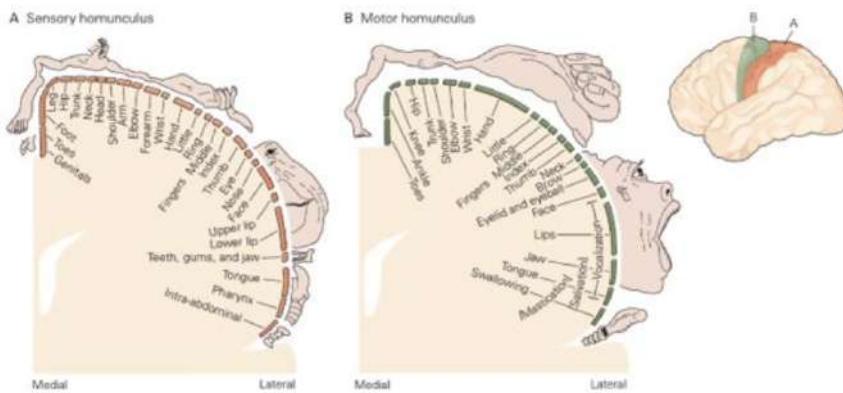


Figure 1.11

Below a usefull video which shows the '*Montreal procedure*' which is still used today.

<https://www.youtube.com/watch?v=nVvuGaIMvQI> (Awake brain surgery (Inside Out longer film))

Donald O. Hebb (1904–1985, Canadian psychologist) worked with Penfield studying the effects of brain surgery and injury on the functioning of the brain. Hebb thought that the workings of the brain explained behavior and that the psychology and biology of an organism could not be separated.

Learning has a biological basis: '*cells that fire together, wire together*'. Neurons can combine together into a single processing unit and the connection patterns of these units make up the ever-changing algorithms determining the brain's response to a stimulus.

Hebb's theory was subsequently used in the design of artificial neural networks.

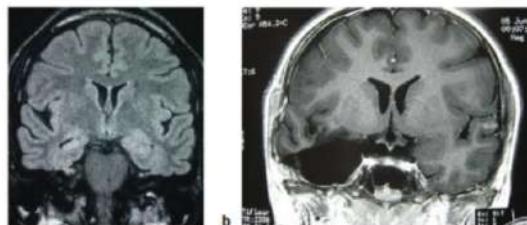


Figure 1.12

¹²Note that there are no pain receptors in the brain, so it is possible to remove parts of the brain without anesthesia.

¹³Just to know some differences between the two consider that the '*hand part*' is greater in the motor cortex while smaller in the sensory cortex.

Penfield's patients began to complain about mild memory loss after surgery. Brenda Milner (1918–, British-Canadian neuropsychologist) provided anatomical and physiological proof that there are multiple memory systems.¹⁴ The extent of the memory deficit depended on how much of the medial temporal lobe had been removed. The more posterior the resection was made, the worse the amnesia was (Scoville & Milner, 1957). Only bilateral re-section of the hippocampus resulted in severe amnesia.

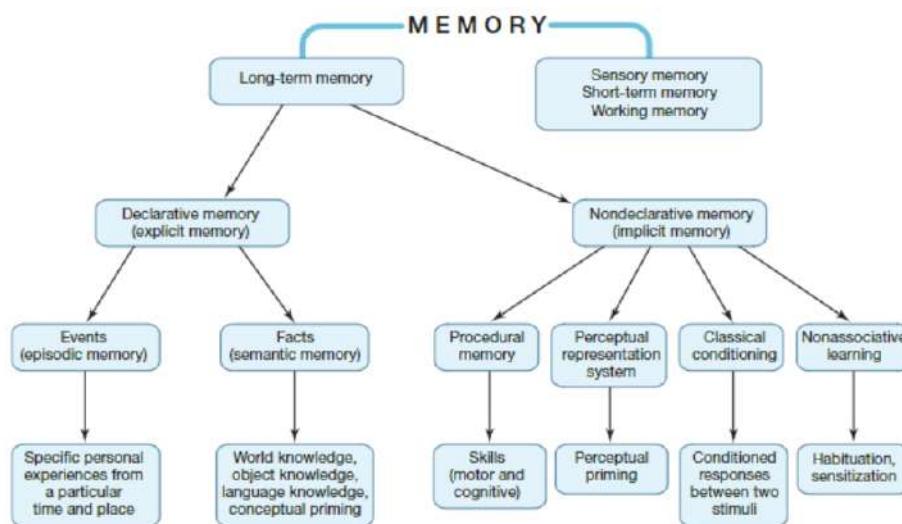


FIGURE 9.2 The hypothesized structure of human memory, diagramming the relationships among different forms of memory.

Figure 1.13

Below a usefull video which shows a case in which a man was deprived of his hippocampus.

<https://www.youtube.com/watch?v=KkaXNvzE4pk> (What happen when you remove the hippocampus? - Sam Kean)

A usefull website in which is described the previous case and that represents a public observatory for the human brain:

<https://www.thebrainobservatory.org/projecthm>

The fall of behaviorism and associationism

Noam Chomsky (1928–, American public intellectual) showed that behaviorism and associationism cannot explain all learning.

In particular, learning theory (associationism) could in no way explain how language was learned.

The complexity of language was built into the brain, and it ran on rules and principles that transcended all people and all languages. It was innate and it was universal.

¹⁴As example we can consider the so called *long-term memory* which is split in *declarative memory* ('Remember that': e.g. story life) and *nondeclarative memory* ('Remember how': e.g. once you learned how to drive a car you don't have to think explicitly in order to remember how and you can do other things at the same time, as talking to the phone).

Chomsky demonstrated that children that are learning to speak just don't have enough information to form complex grammatical blocks that allow them to generate unlimited new and original sentences.

Below a useful video which shows Chomsky theory.

<https://www.youtube.com/watch?v=7Cgpfw4z8cw> (Noam Chomsky on Language Acquisition)

Cognitive neuroscience

Neuroscientists and psychologists reached the conclusion that:

- there is more to the brain than just the sum of its parts;
- the brain must enable the mind.

But how?

Understanding brain function depends on an understanding of both structure and function, and crucially, of the relation between the two.

The major goal of cognitive neural science is to understand neural representations of mental processes.

Chapter bibliography

Gazzaniga, Ivry, Magnum, *Cognitive Neuroscience: the biology of the mind, Fifth Edition*, W. W. Norton & Company, 2018. Chapter 1.

Chapter 2

The nervous system

From individual cells to circuits to systems

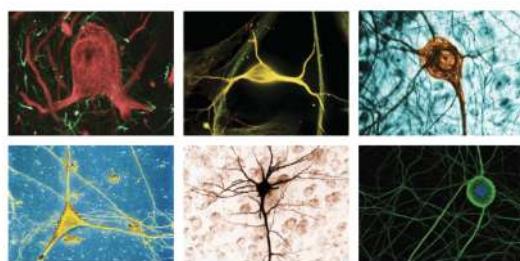


FIGURE 2.2 Mammalian neurons show enormous anatomical variety.

Figure 2.1

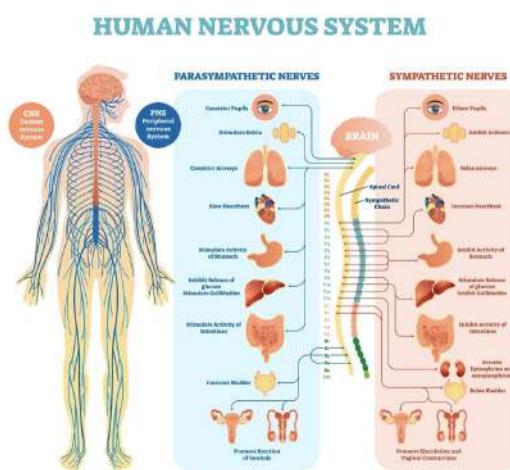


Figure 2.2

2.1 Individual cells

Nervous system classes of cells

The nervous system has two classes of cells:

- Nerve cells, or *neurons*.¹

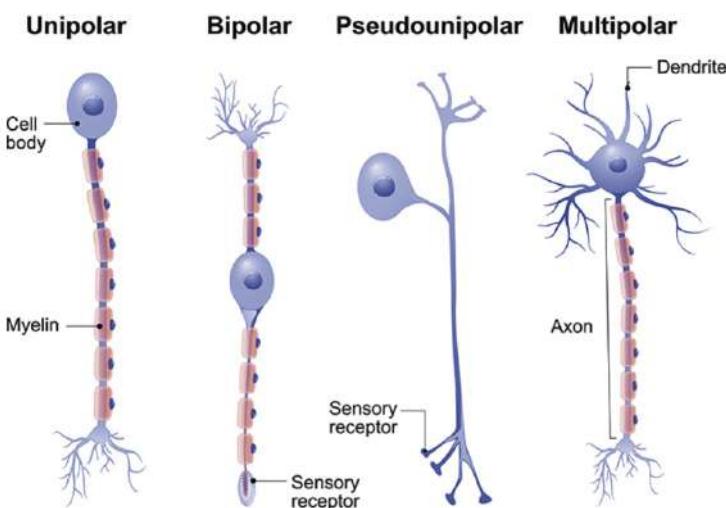


Figure 2.3

- Glial cells, or *glia*.²

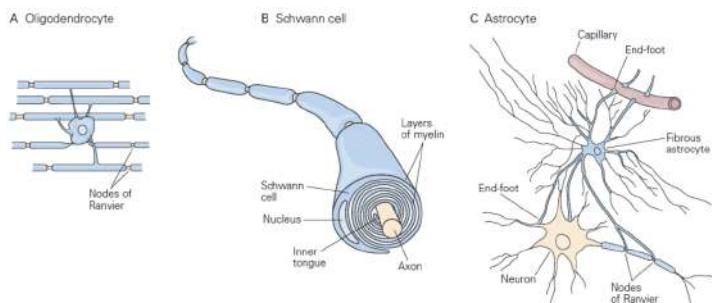


Figure 2.4

¹What neurons do? Functional activity: they transmit signals from the environment perception or within the body and then they transmit these signals to the brain which produces an output that also travels through neurons; so neurons are the transmitting cells from the periphery to the central nervous system and from here to the peripheral nervous system, and also to muscles and glands. More later.

²Considering the images above and focusing on the axon, you can consider a glia as that unit enveloping the axon; in particular if we are in the central system the glia is called *oligodendrocyte* while if we are in the peripheral is called *Schwann cell*. Functional activity: they are supportive cells; they support neural transmission, help neurons transmitting signals. They are also immune system cells: help neurons and nervous system to defend cells from pathogens. They also help neurons eat and support nourishing neurons.

Glial cells support nerve cells

Glial cells greatly outnumber neurons; there are 2 to 10 times more glia than neurons in the vertebrate central nervous system.

Microglia are immune system cells that are mobilized to present antigens³ and become phagocytes⁴ cells during injury, infection, or degenerative diseases.

There are three main types of *macrogli*: oligodendrocytes, Schwann cells, and astrocytes. In the human brain about 80% of all the cells are macrogli.

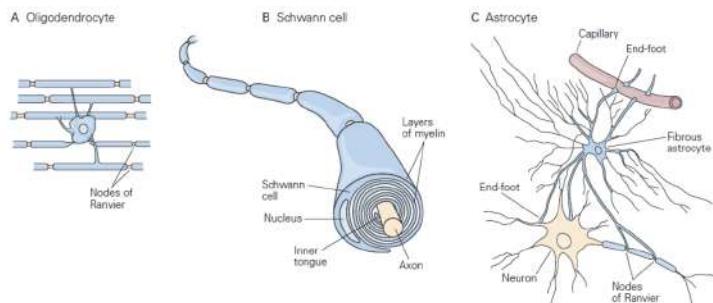


Figure 2.5

In particular *oligodendrocytes* and *Schwann cells*:

- provide the insulating material along the axon;
- produce thin sheets of myelin that wrap concentrically, many times, around the axon of neurons to allow rapid conduction of electrical signals along the axon;⁵
- Schwann cells are in the peripheral nervous system;
- oligodendrocytes are in the central nervous system.

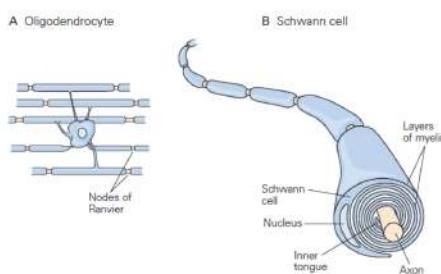


Figure 2.6

³Any substance that induces the immune system to produce antibodies against it is called antigen. Any foreign invades, such as pathogens (bacteria and viruses), chemical toxines can be antigen. Under pathological condition, normal cellular proteins can become self-antigens.

⁴Eat other cells.

⁵They assure that the *action potential* does not dissipate and is transferred from the beginning to the end with the same intensity; they behave like an electrical cable.

Multiple sclerosis is a disease that involves oligodendrocytes; the immune system attack the myelin sheets and so electrical message can't travel efficiently through neurons.

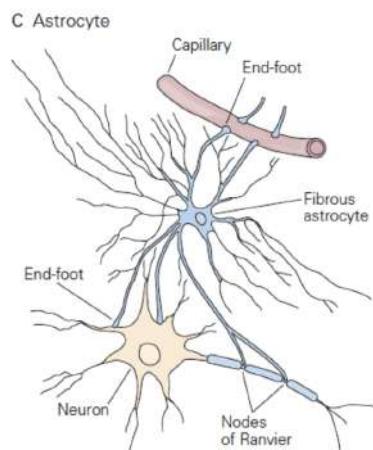


Figure 2.7

Finally, *astrocytes*:

- star-shaped glia found in all areas of the brain;
- they constitute nearly half the number of brain cells;
- important roles in nourishing neurons and in regulating the concentrations of ions and neurotransmitters⁶ in the extracellular space.⁷
- astrocytes and neurons communicate with each other to modulate synaptic signaling in ways that are still poorly understood.

Signaling units of the nervous system

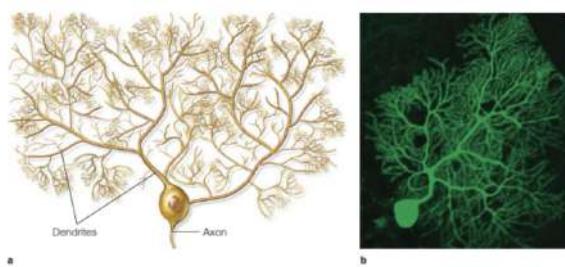


FIGURE 2.4 Soma and dendritic tree of a Purkinje cell from the cerebellum.

Figure 2.8

⁶This is important to generate the action potential, the electrical signal which transmits the message from one neuron to the other.

⁷Extracellular space is not empty, there is fluid which contains various chemicals.

Neurons are the signaling units of the nervous system:

- 100 billion neurons in the nervous system;
- 100 distinct types of neurons;
- each neuron receives and gives rise to thousands of connections;
- some of these connections are formed nearly a meter from the cell body of the neuron.

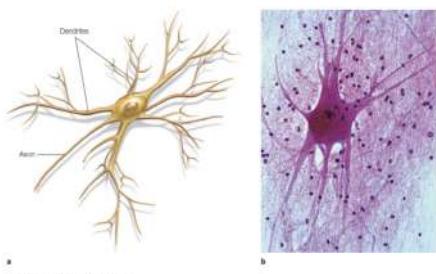


Figure 2.9

Neurons defined regions

Neurons have four morphologically defined regions. Each region has a distinct role in generating signals and communicating with other nerve cells.

1. The *cell body* or *soma* is the metabolic center of the cell. It contains the nucleus⁸, which contains the genes of the cell, and the endoplasmic reticulum, where the cell's proteins are synthesized. The cell body usually gives rise to two kinds of processes: several short dendrites (input) and one long, tubular axon (output).
2. *Dendrites* are the main apparatus for receiving incoming signals from other nerve cells.
3. The *axon* extends some distance from the cell body and carries signals to other neurons. An axon can convey electrical signals over distances ranging from 0.1 mm to 2 m. These electrical signals, called *action potentials*, are initiated at a specialized trigger region near the origin of the axon called the *initial segment* from which they propagate down the axon without failure or distortion at speeds of 1 to 100 m/s.⁹
4. Near its end the axon divides into fine branches that contact other neurons at specialized zones of communication known as *synapses*.

⁸Almost every cell has a nucleus, the part in which resides the genetic material.

⁹In particular, the *axon hillock* is responsible to process incoming signal and if it passes a certain threshold the signal is transmitted. Think like so: all the receiving signals contributes to a unique number; if this number satisfies the threshold, then the signal passes.

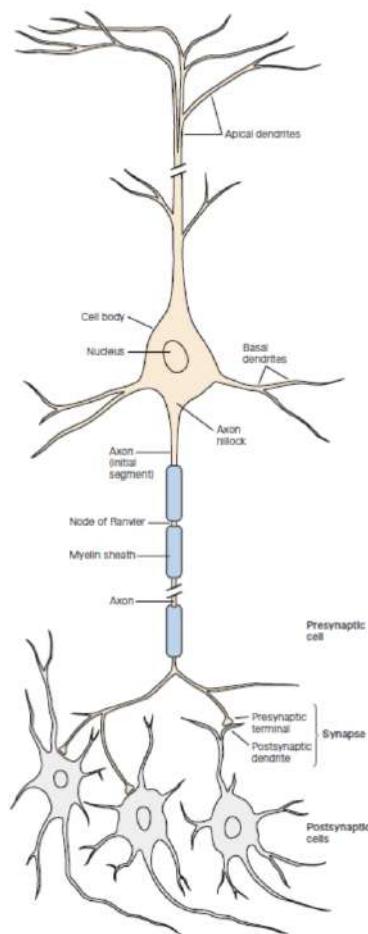


Figure 2.10

Synapses: neurons communication

(Refer to the image above).

Synapses enable communication between neurons.

Presynaptic cell:

- the nerve cell transmitting a signal;
- from presynaptic terminals or nerve terminals, *i.e.* specialized enlarged regions of its axon's branches.

Postsynaptic cell:

- the cell receiving the signal.

Synaptic cleft:

- the narrow space separating the presynaptic and postsynaptic cell.

Most presynaptic terminals end on the postsynaptic neuron's dendrites; but the terminals may also terminate on the cell body or, less often, at the beginning or end of the axon of the receiving cell.

Types of synapses

There are three types of synapses:

- **Axosomatic:** synapses that are made onto the soma or cell body of a neuron.
- **Axodendritic:** synapses that one neuron makes onto the dendrite of another neuron. The most common type.
- **Axoaxonic:** synapses made by one neuron onto the synapse of another neuron. Axoaxonic synapses mediate presynaptic inhibition and presynaptic facilitation.¹⁰

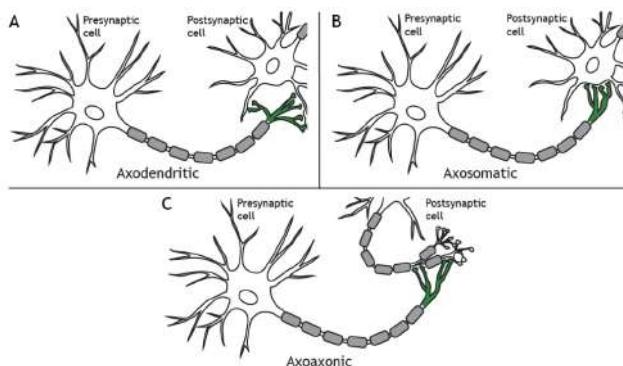


Figure 2.11

Note: plasticity of nervous system on brain: synapses that we don't use die in time while the synapses that we use live; this explain why somebody that had an injury (*e.g.* a stroke) can recover the function lost; not only, *e.g.* who plays piano has a different plastic model brain from one that doesn't play.

Functional classification of nerve cells

Nerve cells are also classified into three major functional categories:

1. *Sensory neurons* carry information from the body's peripheral sensors¹¹ into the nervous system¹² for the purpose of both perception and motor coordination.

Note: some primary sensory neurons are called *afferent neurons*, and the two terms are used interchangeably. The term *afferent* (carried toward

¹⁰With the last sentence we mean: when a signal is transmitted from one cell to another, at the synaptic point of transmission the signal itself can be amplified or decreased. Focusing on just after the synapses green highlighted of the Figure C of the image below (Axoaxonic): for example the signal is already passed from the postsynaptic cell and at this point the presynaptic can be responsible of decreasing or amplifying the signal.

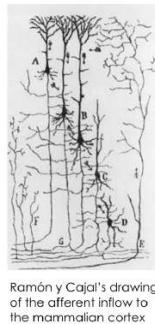
¹¹Pay attention that they not only take information from outside the body but also inside. For example if you are hungry, your intestine is moving; or also there are sensors to perceive the position of our body.

¹²In particular up to the central nervous system, which process and generate a response; the majority of the time is a motor response.

the central nervous system) applies to all information reaching the central nervous system from the periphery, whether or not this information leads to sensation. The term *sensory* should, strictly speaking, be applied only to afferent inputs that lead to perception.

2. *Motor neurons* carry commands from the brain or spinal cord to muscles and glands¹³ (*efferent*¹⁴ information).
3. *Interneurons* which are the most numerous and are subdivided into two classes:
 - (a) *Relay* or projection interneurons have long axons and convey signals over considerable distances, from one brain region to another.
 - (b) *Local* interneurons have short axons because they form connections with nearby neurons in local circuits.

The neuron doctrine



Ramón y Cajal's drawing of the afferent inflow to the mammalian cortex

Figure 2.12

Santiago Ramón y Cajal (1852-1934, Spanish neuroscientist, pathologist, and histologist) was the first to identify the unitary nature of neurons.

Invented the *neuron doctrine*: the nervous system is made up of individual cells. Neurons are discrete entities.

Challenged Golgi which had believed that the whole brain was a *syncytium*, a continuous mass of tissue that shares a common cytoplasm.

Cajal also realized that the feature that most distinguishes one type of neuron from another is form, specifically the *number of the processes* arising from the cell body.

Electrical signals within a nerve cell flow *only in one direction*: from the receiving sites of the neuron, usually the dendrites and cell body, to the trigger region at the axon.

Neurons classification according to processes

Neurons are classified into three large groups according to the number of processes that originate from the cell body:

¹³For example they communicate at some glands to sweat (activate some glands).

¹⁴From the central to out (periphery); afferent: from out to in.

1. *Unipolar cells* they are the simplest, they have a single process¹⁵ emanating from the cell.¹⁶ Different segments serve as receptive surfaces or releasing terminals. They predominate in the nervous systems of invertebrates; in vertebrates they occur in the autonomic nervous system.¹⁷
2. *Bipolar cells* have an oval soma that gives rise to two distinct processes that are functionally specialized: the dendrite receives electrical signals and the axon transmits signals to other cells. Many sensory cells are bipolar, where the dendritic structure receives signals from the periphery of the body and the axon carries information toward the central nervous system.
 - (a) *Pseudo-unipolar cells* are variants of bipolar cells. These cells develop initially as bipolar cells but during development the two processes of the embryonic bipolar cell fuse and emerge from the cell body as a single process that has two functionally distinct segments. Both segments function as axons; one extends to peripheral skin or muscle, the other to the central spinal cord.
3. *Multipolar cells*: a single axon and many dendrites. The most common type of neuron in the mammalian nervous system. Large diversity of these cells:
 - (a) *Spinal motor neurons* innervate skeletal muscle fibers.
 - (b) *Pyramidal cells* have a roughly triangular cell body; dendrites emerge from both the apex (the apical dendrite) and the base (the basal dendrites). Pyramidal cells are found in the hippocampus and throughout the cerebral cortex.
 - (c) *Purkinje cells* of the cerebellum are characterized by a rich and extensive dendritic tree that accommodates an enormous synaptic input.

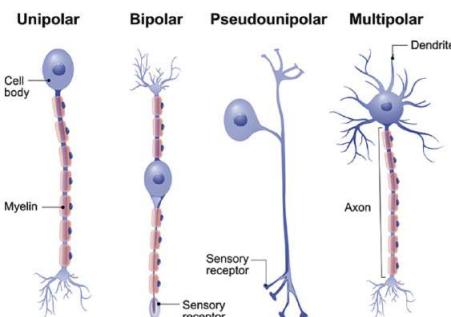


Figure 2.13

¹⁵The important key to understand what is a process: how many (unit) branches generates from cellular body. Keep in mind always that electrical signal flows only in one direction.

¹⁶The cell body can be a sensor (light, pressure); from that they perceive the environment and then transmit the information.

¹⁷Autonomic nervous system is part of the peripheral (which perceive the info).

Which kind of neuron is this?

Note: dendrites are the input, axon is the output part. Always!
 Cell body integrates all the input and if the threshold is passed the output is generated and goes through the axon.

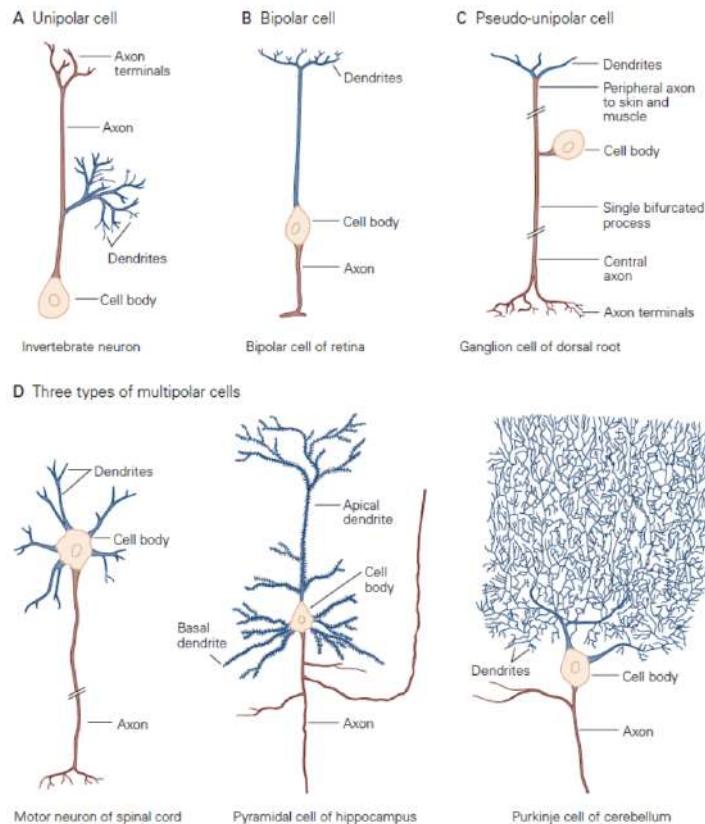


Figure 2.14

2.2 From individual neurons to neural circuit

Combination of neurons creates a neural circuit.

Neural circuits

Groups of interconnected neurons that process specific kind of information.¹⁸

1. Take in information (afferent inputs).
2. Evaluate the input either at a synapse or within one or a group of neurons¹⁹ (local circuit neurons).

¹⁸Sensory information: light, pressure, smell, temperature, etc.

¹⁹Inter-neurons: intermediate part that evaluates the informations and then an output is produced.

3. Convey the results to other neurons, muscles, or glands (efferent outputs).

Every behavior is mediated by specific sets of interconnected neurons, and every neuron's behavioral function is determined by its connections with other neurons.²⁰

Principle of connectional specificity

Nerve cells do not connect randomly with one another in the formation of networks. Rather each cell makes specific connections²¹ – at particular contact points – with certain postsynaptic target cells but not with others.

A simple neural circuit: the knee-jerk reflex

The knee-jerk reflex dynamic is the following:

1. Sensory information is conveyed to the central nervous system (the spinal cord) from muscle.
2. Motor commands from the central nervous system are issued to the muscles that carry out the knee jerk.
3. Inhibitory²² commands are issued to motor neurons that innervate opposing (antagonist) muscles, providing coordination²³ of muscle action.

The combination of excitatory and inhibitory activity produces the reflex.

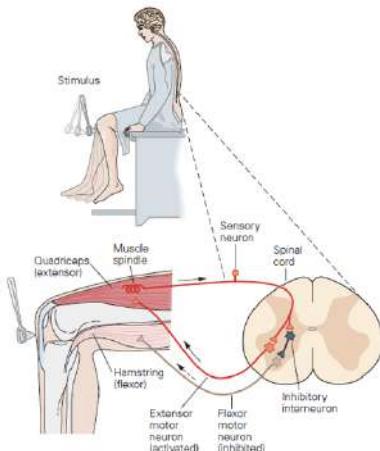


Figure 2.15

²⁰Circuits don't form randomly but, depending on how the message has to be sent, neurons make connections with each other; connections that are useful are formed while connections that are not useful are thrown (they die). The environment shapes the circuits which change in time; we are born with a certain amount of circuits but structured in a certain way, but then the environment shapes our circuits, our experiences through learning determining connections.

²¹Depends on where the information needs to go. Cells that fire together wire together.

²²Inhibition: means that decreases the probability that the post-synaptic neurons go to fire.

Excitation: means that increases the probability that the post-synaptic neurons go to fire.

²³We have coordination muscles (a couple): agonist and antagonist, they do opposite actions.

Referring to the image above we do some considerations:

- each *extensor* and *flexor* motor neuron represents a population of many cells;
- look at the *muscles spindle*: is a sensor at the end of the sensory neuron;
- look at the *sensory neuron*: its form is a pseudounipolar;
- look at the *spinal cord*: it is a part of the central nervous system; in this case the signal does not go to the brain.

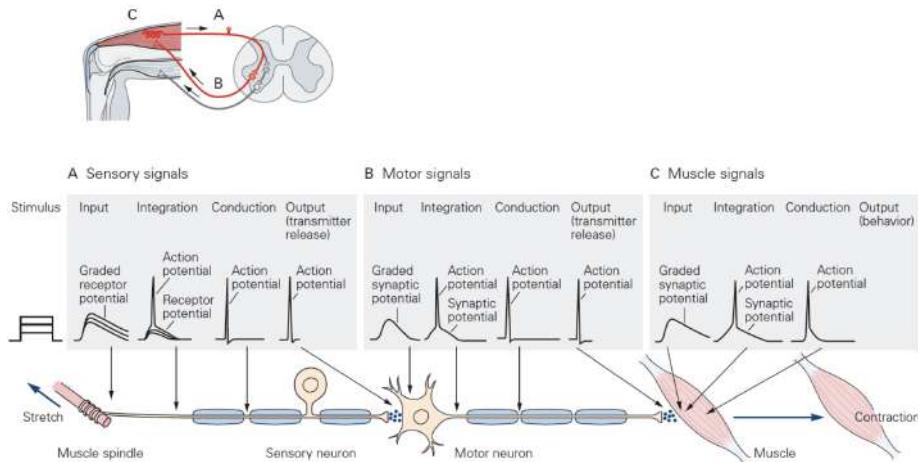


Figure 2.16

Looking to the image above we can see the *glia cells* as the azure envelopping units that go from the muscle spindle to the muscle and the *chemicals* released as the small blue circles.

Divergence and convergence

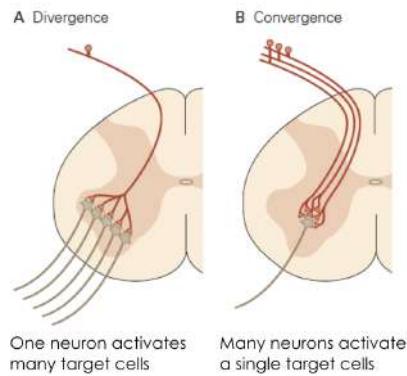


Figure 2.17

Divergence: observed in the input stages of the nervous system:

- a single neuron can exert wide and diverse influence.

*Convergence:*²⁴ observed at the output stages of the nervous system:

- a target motor cell that receives information from many sensory neurons is able to integrate information from many sources;
- ensures that a motor neuron is activated only if a sufficient number of sensory neurons become activated together.

Neurons are both excitatory and inhibitory

Excitatory neurons produce signals that increase the likelihood of firing of the postsynaptic neurons.

Not all important signals in the brain are excitatory.

Many neurons produce inhibitory signals that reduce the likelihood of firing.

We have two kinds of *inhibition*:

- *feed-forward inhibition* enhances the effect of the active pathway by suppressing the activity of pathways mediating opposing actions.
- *feedback inhibition* dampens activity within the stimulated pathway and prevents it from exceeding a certain critical level.
 - A functional advantage of feedback inhibition is that it is a self-regulating mechanism.²⁵

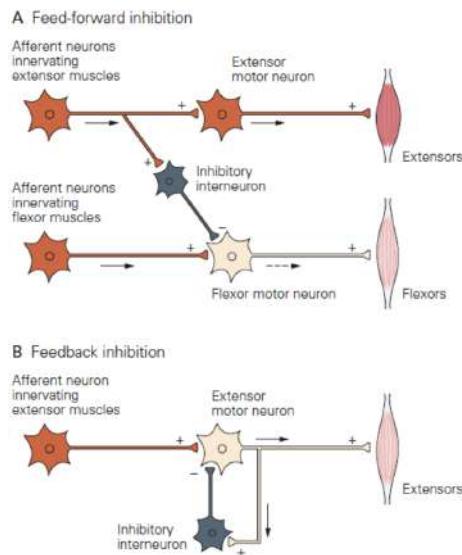


Figure 2.18

²⁴Convergence is important because it gives the possibility to integrate informations that come from different sources.

²⁵It prevents a continuing firing.

Parallel processing

No complex human behavior is initiated by a single neuron. Each behavior is generated by the actions of many cells. Three components of the neural control of behavior:

- sensory input;
- intermediate processing;
- motor output.²⁶

In vertebrates each component is:

- mediated by a single group or several distinct groups of neurons;
- has multiple neural pathways that simultaneously provide the same or similar information.²⁷

Evolutionary advantage: it increases both the speed and reliability of functions²⁸ within the central nervous system.²⁹

Plasticity & learning

Neural connections can be modified by experience.
Neuroplasticity can be:

- chemical;
- structural;
- functional.

Below a usefull video which shows Neuroplasticity.

<https://www.youtube.com/watch?v=dmEOJyWVQj4> (Neuroplasticity, Animation.)

2.3 From neural circuits to neural systems

Combination of neural circuits creates a neural system.

The bigger picture: neural systems

The entire system is divided into two main entities:

- Central nervous system (CNS):
 - brain;
 - spinal cord.
- Peripheral nervous system (PNS):

²⁶Mostly motor.

²⁷This is called parallel processing.

²⁸And more generally of signals.

²⁹Parallel processing is an advantage.

- nerves: bundles of axons and glia;
- ganglia: clumps of nerve cell bodies outside of the CNS;
- delivers sensory information to the CNS;
- carries the motor commands from the CNS to the muscles;
- supplies the CNS with a continuous stream of information about both the external environment and the internal environment of the body;
- has somatic and autonomic division (see ahead).

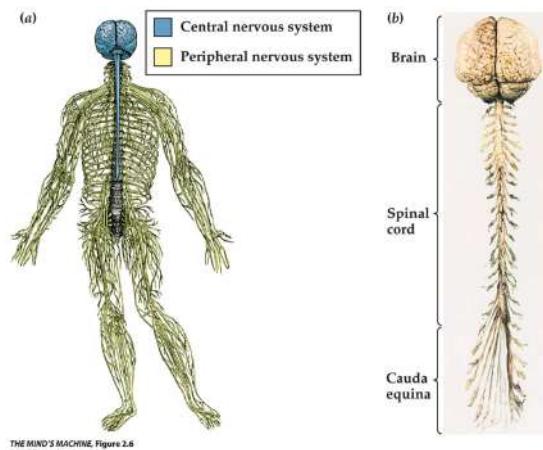


Figure 2.19

PNS: the somatic nervous system

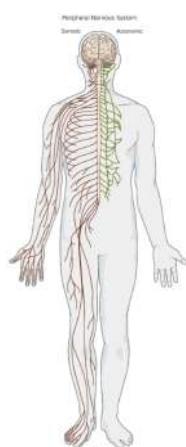


Figure 2.20

The somatic nervous system consists in:

- sensory neurons that receive information from the skin, muscles, and joints;

- receptors associated with these cells provide information about muscle and limb position and about touch and pressure at the body surface;
- receptors transduce different types of physical energy (such as deep pressure or heat) into the electrical signals used by the nervous system.

PNS: the autonomic nervous system

The autonomic nervous system:

- mediates visceral sensation as well as motor control of the viscera, vascular system (*e.g.* blood pressure), and exocrine glands (*e.g.* sweating, how fast the heart beats *etc.*);
- sympathetic system: participates in the body's response to stress;
- parasympathetic system: acts to conserve body resources and restore homeostasis;
- enteric system: controls the function of smooth muscle of the gut.

The sympathetic and parasympathetic systems

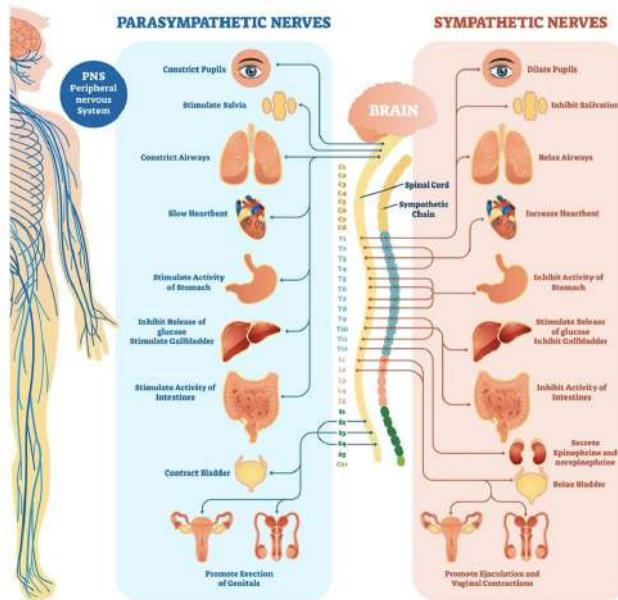


Figure 2.21

They operate antagonistically:

- sympathetic system uses norepinephrine;

- parasympathetic system uses acetylcholine;³⁰

Example:

- the sympathetic system:

- prepares the body for action (fight or flight) by stimulating the adrenal glands to release adrenaline;
- increases heart rate;
- diverts blood from the digestive tract to the somatic musculature.

- The parasympathetic system:

- helps the body with functions germane to maintaining the body;
- slows heart rate;
- stimulates digestion.

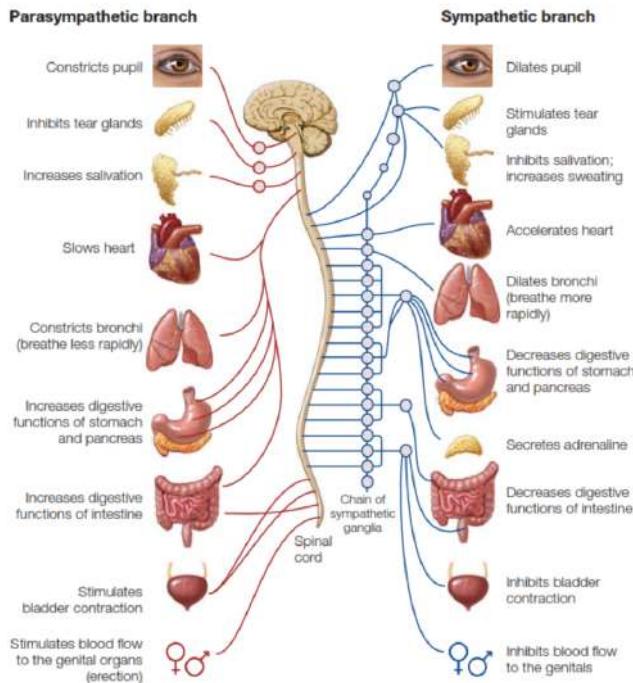


FIGURE 2.17 Organization of the autonomic nervous system, showing sympathetic and parasympathetic branches.

Figure 2.22

Note that in the figure above every action has a parallel in the two systems except for *Secretes adrenaline* (look at *Sympathetic branch, right*).

³⁰Norepinephrine and acetylcholine are two different (chemical) neurotransmitters, and different chemicals would lead to different functions. Remember that the advantage to have chemical synapsis (compared to electrical) is that we can release different chemicals and different chemicals lead to different functions.

CNS is protected by the meninges

CNS (brain and spinal cord) is protected by the meninges; in particular we have three protective membranes:

- Dura mater:³¹
 - outermost;
 - thickest.
- Arachnoid mater:
 - middle
- Pia mater:
 - inner;
 - most delicate;
 - firmly adheres to the brain surface.

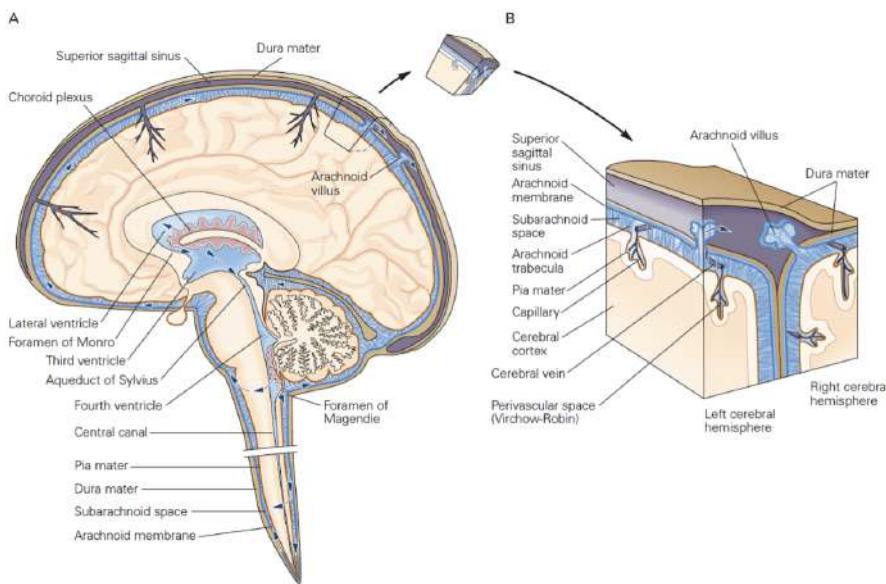


Figure 2.23

Brain & spinal cord float in the cerebrospinal fluid

Cerebrospinal fluid³² occupies:

- the space between the arachnoid membrane and the pia mater;

³¹'Dura' because it is the hardest one.

³²It is the pale blue parts in the figure above. It is very important that is liquid: for example when moving the brain absorbs the movements or shocks, so the brain is protected. There are also other advantages, see below.

- the brain ventricles;
- cisterns and sulci;
- central canal of the spinal cord.

Cerebrospinal fluid allows:

- the brain to float to help offset the pressure that would be present if the brain were merely sitting on the base of the skull;
- reduces shock to the brain and spinal cord during rapid accelerations or decelerations, such as when we fall or are struck on the head.

CNS: the spinal cord

The spinal cord³³ takes in sensory information from the body's peripheral sensory receptors.

Relays it to the brain.

Conducts the final motor signals from the brain to muscles.

Runs from the brain stem at about the first spinal vertebrae to its termination in the *cauda equina* (meaning "horse's tail").

Enclosed in the *vertebral column* (which protects it):

- a stack of separate bones, the vertebrae;
- extend from the base of the skull to the fused vertebrae at the coccyx (tailbone);
- divided into sections: cervical, thoracic, lumbar, sacral, and coccygeal.

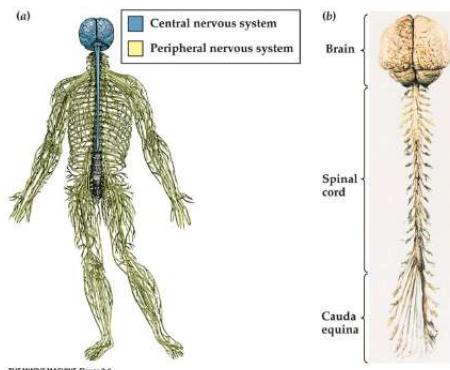


Figure 2.24

Note: looking at the image above (part (b)) we can see that the nerves that arise from different sections do not expand them randomly but they go to the *closest region*.

For example, lesions to different parts of the spinal cord leads to different functional problems.

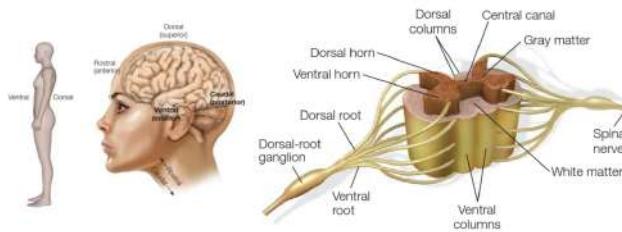


Figure 2.25

Upper (to the brain) we go and more severe will be the consequences of the lesions because there are more connections.

The spinal cord is divided into 31 segments.

Each segment has a right and a left³⁴ spinal nerve that enters and exits from the vertebral column through openings called '*foramen*'.

Each spinal nerve has:

- sensory axon: afferent neuron, input through the dorsal root (*IN*) into the spinal cord;
- motor axon: efferent neuron carries motor output through the ventral root (*OUT*) away from it.

Dorsal root ganglion³⁵ contains cell bodies of peripheral sensory neurons;
Grey matter³⁶ contains cell bodies of peripheral motorneurons.

The opposite functional system of the brain

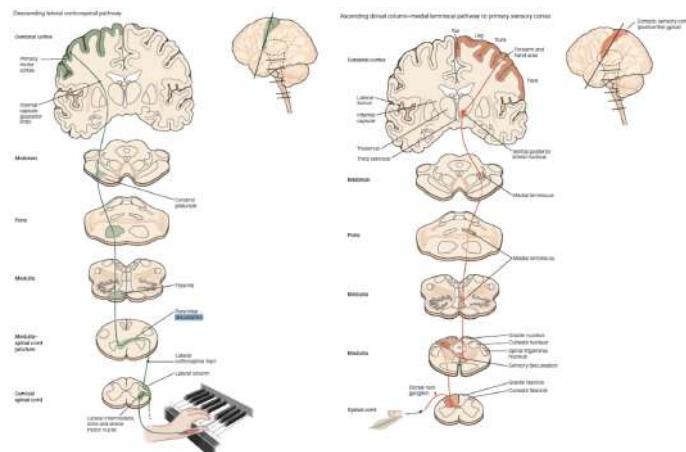


Figure 2.26

³³Part of nervous system which is made of nerves and glia.

³⁴It's bilateral.

³⁵Groups of cell bodies; in particular it contains the cell bodies of the sensory neuron.

³⁶In general, nervous system has grey and white matter and, in particular, also the brain.

Functional systems on one side of the brain control the other side of the body.³⁷ Most pathways in the central nervous system are bilaterally symmetrical and cross over to the opposite (contralateral) side of the brain or spinal cord.

Sensory and motor activities on one side of the body are mediated by the cerebral hemisphere on the opposite side.

The pathways of different systems cross at different anatomical levels within the central nervous system.

Looking at the image above we can see that that the crossing from one part of the brain to the opposite part of the body is at the *Medulla* level.

Note: in the last video proposed (regarding ‘*plasticity*’) we saw, for example, that in right-handed people the motor cortex of the left side of the brain is more developed than the right one.

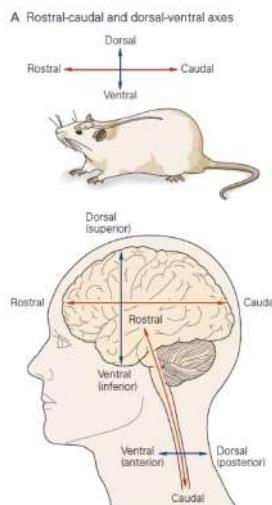


Figure 2.27

Neurons bunching

In the CNS neurons are bunched together in various ways:

- Nucleus:³⁸
 - compact arrangement of nerve cell bodies and their connections, ranging from hundreds to millions of neurons, with functionally similar inputs and outputs;
 - located throughout both the brain and the spinal cord.
- Layer:³⁹

³⁷Remember that we saw that the pineal gland is the unique element which is not bilateral (everithing else instead is bilateral and mostly simmetrical.)

³⁸It is the equivalent of ganglia – that are groups of cell bodies in the pheipheral nervous system – but in the CNS.

³⁹Another way to regroup cells is by layering them. Important thing: do you think that they group randomly? Obviusly not! Nothing happen by chance: they are regrouped functionally (group of neurons that have the same function).

- thin sheets, folded across the surfaces of the cerebral hemispheres like a handkerchief;
- found in the cerebral cortex.

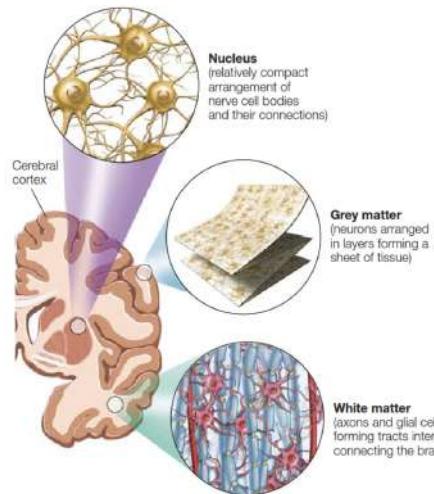


Figure 2.28

The brain

We propose below a website which shows a dynamic 3D representation of the brain:

<https://www.brainfacts.org/3d-brain#intro=true>

Regarding the brain we highlight that there are two emispheres.

Furthermore, it is important to know that there are structures that go in between the two emispheres (in the center) like *pons*, *medulla oblongata*, *diencephalon*, etc.

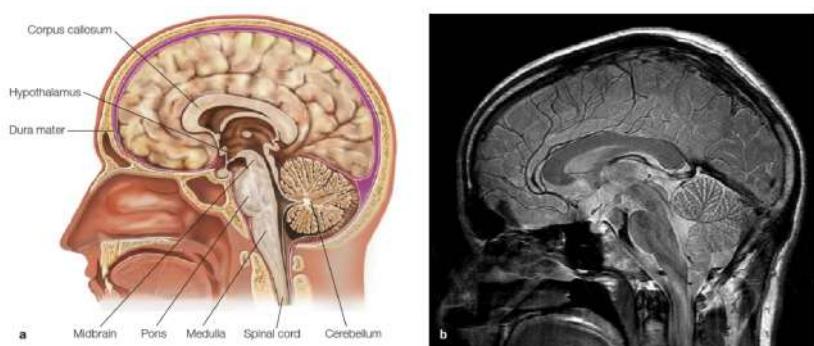


FIGURE 2.20 Gross anatomy of a brain showing brain stem.
 (a) Midsagittal section through the head, showing the brainstem, cerebellum, and spinal cord. (b) High-resolution structural MRI obtained with a 4-tesla scanner, showing the same plane of section as in (a).

Figure 2.29

The brain lies rostral to the spinal cord.

It is composed of six subdivisions:

- Medulla;
- Pons;
- Midbrain;
- Cerebellum;
- Diencephalon,⁴⁰
- cerebral hemispheres or telencephalon.⁴¹

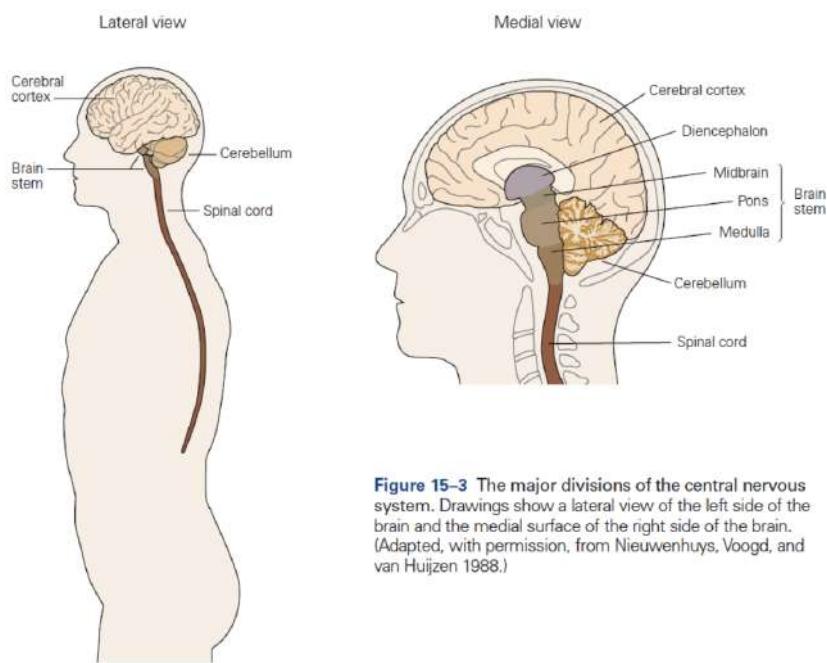


Figure 15–3 The major divisions of the central nervous system. Drawings show a lateral view of the left side of the brain and the medial surface of the right side of the brain. (Adapted, with permission, from Nieuwenhuys, Voogd, and van Huijzen 1988.)

Figure 2.30

The brain stem

Let's go from the cord to the cortex.

The *brain stem*⁴² is the first structure that we meet after the spinal cord. Components:

- *Medulla*: prolongation of spinal cord. Regulates blood pressure and respiration;

⁴⁰The previous elements plus the Diencephalon are evolutionary older.

⁴¹It is evolutionary younger. More specifically cerebral hemispheres and cortex are evolutionary younger; in particular, speaking evolutionary, the cortex is what makes us human.

⁴²Note that if you damage the brain stem you're basically dead or that at least in vegetative state. That's because being *evolutionary older* is responsible of most of basic tasks (it is important for respiration, to regulate sleep, blood pressure, etc.).

- *Pons*: main connection between the brain and the cerebellum:⁴³
 - ventral portion contains the pontine nuclei, groups of neurons that relay information about movement and sensation from the cerebral cortex to the cerebellum;
 - dorsal portion contains structures involved in respiration, taste, and sleep.
- Mid brain: nuclei in the midbrain provide important linkages between components of the motor system, particularly the cerebellum, basal ganglia, and cerebral hemispheres.

Damage to the brainstem is life threatening: controls respiration and global states of consciousness such as sleep and wakefulness.

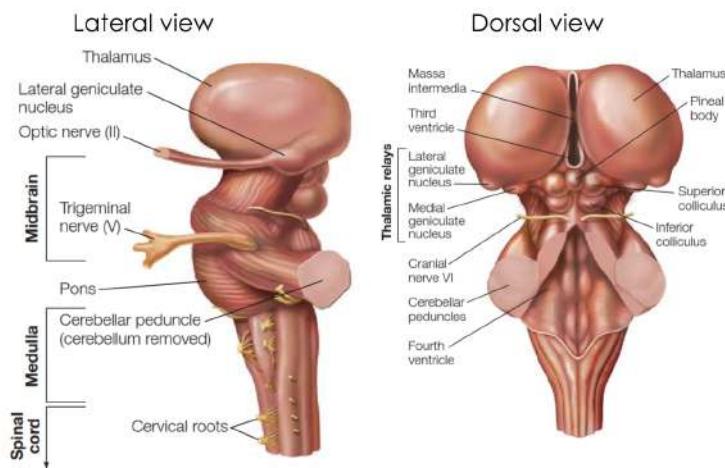


Figure 2.31

The cerebellum

The cerebellum⁴⁴ is divided into several lobes by distinct fissures. Contains far more neurons than any other single subdivision of the brain, including the cerebral hemispheres.

Its internal circuitry is well understood because relatively few types of neurons are involved.

Receives information about:

⁴³It is important for movement, for action. Regarding *movement* we can say that is one of the main function of the brain: there is a female neuroscientist who discovered that there is an organism in the sea that when born is able to move and go throughout the world but, at a certain point, it becomes sedentary and, at this point, it eats its brain (brain \Rightarrow movement). It's like it says: 'When I don't need to move anymore I don't need brain anymore'. We will see during these notes that a lot of structures are important to movement: this highlights the importance of this function.

⁴⁴It's important for *procedural memory*: it's about procedures, it's related to long term memory, it's related to things that we do automatically '*without thinking about*' and become automatic (*e.g.* driving a car, diving, *etc.*)

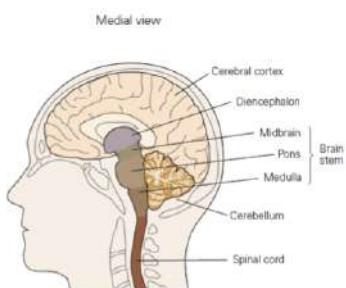


Figure 2.32

- somatic sensation from the spinal cord;
- balance from the vestibular organs of the inner ear;
- motor and sensory information from various areas of the cerebral cortex via the pontine nuclei.

Important for:

- maintaining posture;
- coordinating head, eye, and arm movements;
- regulation of motor output;
- learning motor skills.

Considered a purely motor structure, new anatomical information about its interconnections with the cerebral cortex and functional imaging studies have shown that it is also involved in language and other cognitive functions.⁴⁵

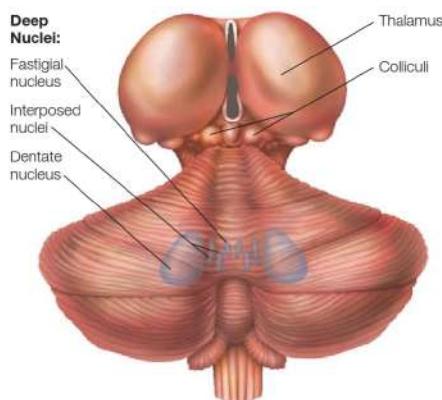


FIGURE 2.22 Gross anatomy of the cerebellum.

Figure 2.33

⁴⁵So the cerebellum is mostly anything related to *action*.

The diencephalon

The diencephalon is composed of *thalamus* and *hypothalamus*.⁴⁶

Thalamus that is ‘gateway to the cortex’:⁴⁷

- essential link in the pathway of sensory information from the periphery to sensory regions of the cerebral hemispheres;
- determines which sensory information reaches the neocortex;
- interconnects the cerebellum and basal ganglia with regions of the cerebral cortex concerned with movement and cognition.

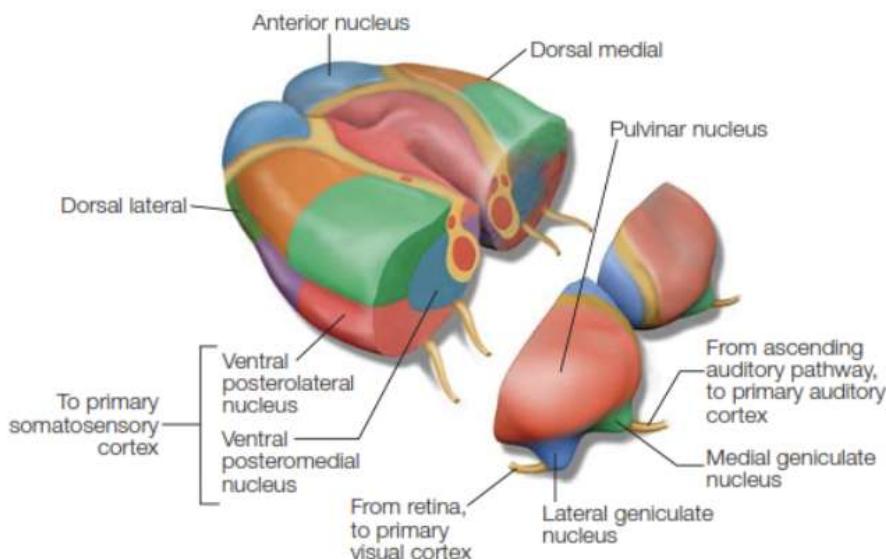


Figure 2.34: Thalamus.

Hypothalamus:

- ventral to the thalamus;
- link between the nervous and the endocrine system;
- regulates⁴⁸ homeostasis by regulating body temperature, thirst and hunger, and the circadian rhythm;
- essential component of the motivational systems of the brain, initiating and maintaining behaviors the organism finds aversive or rewarding.

⁴⁶Out (sensory info) → spinal cord → thalamus → cortex; in particular we highlight that thalamus it's not passive; it has an active role to choose which information can reach the cortex and, at that point, we become aware of; otherwise not.

⁴⁷Mostly any information that comes in goes through the thalamus. It is subdivided into different parts depending on the info that comes and neurons (different sensory neurons are grouped by different receptors and info that they have to process). Obviously neurons don't interconnect randomly; there are different parts: neurons that process vision, neurons that process temperature.

⁴⁸By secreting chemicals for example.

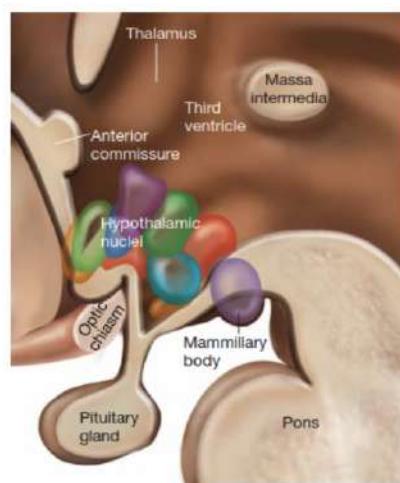


FIGURE 2.25 Midsagittal view of the hypothalamus.

Figure 2.35

A brief recap: the brain stem is important for respiration and wakefulness. The thalamus is a relay center, a ‘*gateway to the cortex*’. The hypothalamus it’s important to regulate homeostasis. The cerebellum is important for basic motor coordination.

The telencephalon or cerebral hemispheres



Figure 2.36

This is the largest part of the human brain; it consists of:

- the cerebral cortex;
- the underlying white matter;
- three deep-lying structures that regulate cortical activity:
 - Basal ganglia;
 - Amygdala;
 - Hippocampal formation.

Note in the image below (at right) that the most exterior part is the cortex; furthermore we have that the most exterior darker part is the *grey matter*: essentially cell bodies; while inside of that part we have a pale part which is the *white matter*: it is white because composed of axons and axons are enveloped

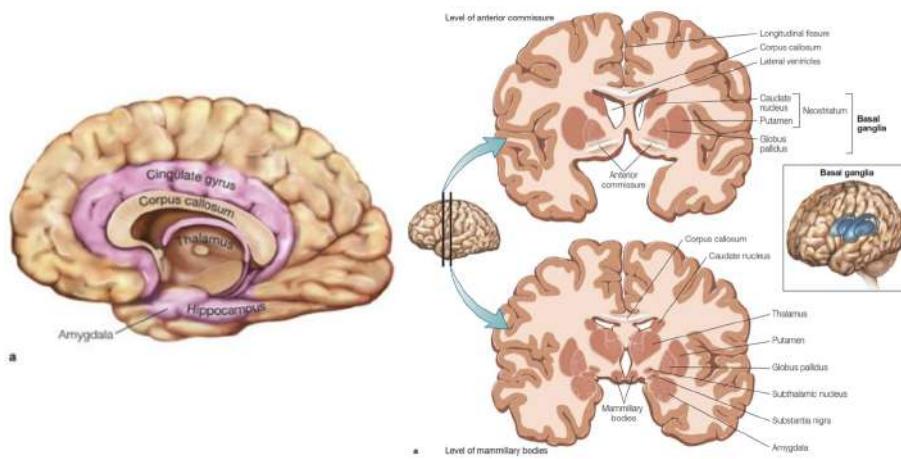


Figure 2.37

in myelin and myelin is white, remembering that myelin is essential to transmit correctly the signal without dissipating it.

Note also that when we talk about brain it's important to highlight that we don't only talk about the cortex or the hemisphere, but also of the other structure that we have seen.

Basal ganglia

Basal ganglia are:

- a collection of subcortical nuclei;⁴⁹
- bilaterally located deep in the brain beneath the anterior portion of the lateral ventricles, near the thalamus;
- receive inputs from sensory and motor areas;
- send output largely through the thalamus⁵⁰ to the frontal lobe;
- extensively interconnected.

Include:

- Caudate nucleus;
- Putamen;
- Globus pallidus;⁵¹
- Subthalamic nucleus;
- Substantia nigra.

⁴⁹ Nuclei that are cell bodies of neurons in the CNS; generally bodies of neurons in the CNS lie in the grey matter but, if they lie in some subcortical structure (*i.e.* below the cortex) then they lie in the *nuclei*.

⁵⁰ Remember that everything goes through the thalamus.

⁵¹ These first three are components of *striatum*.

Basal ganglia have crucial role in motor control:

- action selection;
- action gating;
- motor preparation;
- Timing;
- fatigue;
- task switching.⁵²

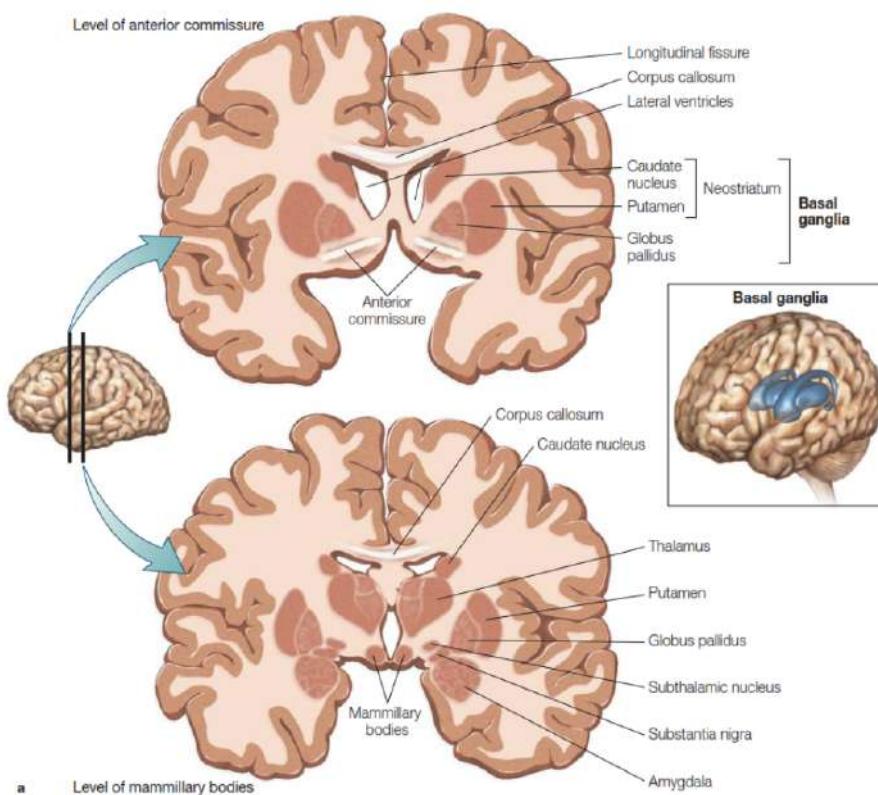


Figure 2.38

Physiologically (see the figure below):

- the direct pathway (green line) participates in the activation of movement, so excites movement;

⁵²They are also important for action: motor control in particular; it is a little more sophisticated than cerebellum because cerebellum is important to coordinate the action, to balance while basal ganglia are more important for '*action selection*' (*action selection* is also for more abstract tasks e.g. problem solving, decision making) i.e. they are important for making decisions. So when you have different options you have to decide what option you are going to select, what action you take.

- the indirect pathway (red line) participates in the inhibition of movement, so inhibits movement.

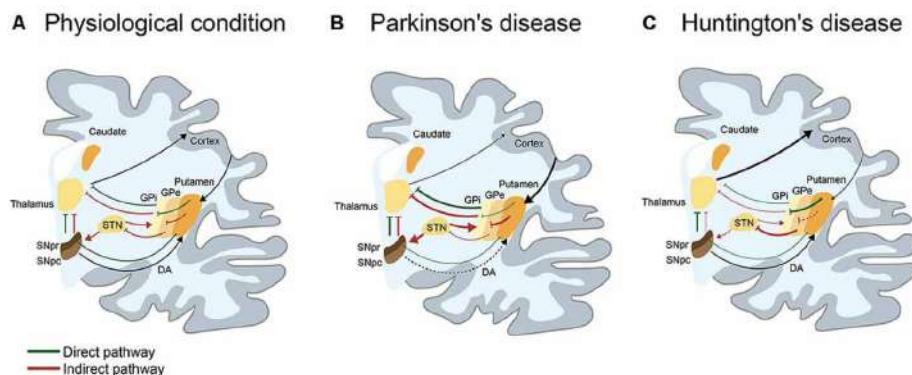
Parkinson's disease:

- the loss of dopaminergic neurons of the SNpc, induces an overactivation of the indirect pathway and a decrease of movement (hypokinesia).⁵³

Huntington's disease (early stage):

- MSNs of the indirect pathway appear to be affected before the MSNs of the direct pathway.⁵⁴

So we have seen that essentially Parkinson's disease implies a movement decrease while Huntington's disease implies a movement increase. But how is possible that the damage of the same structure leads to two different diseases? We saw that neural circuits can have both *inhibitory* and *excitatory* components and this is valid also for basal ganglia; so it depends on what circuits is affected.



Troncoso-Escudero, Paulina et al. "On the Right Track to Treat Movement Disorders: Promising Therapeutic Approaches for Parkinson's and Huntington's Disease." *Frontiers in aging neuroscience* vol. 12 571185. 3 Sep. 2020, doi:10.3389/fnagi.2020.571185

Figure 2.39

Basal ganglia have a crucial role in reinforcement learning.⁵⁵

Play a big role in reward-based learning and goal-oriented behavior:

- Combine an organism's sensory and motor context with reward information;
- Passes this integrated information to the motor and prefrontal cortex for a decision (Chakravarthy et al., 2009)

⁵³It is affected the *direct pathway*. The trembles are the most known symptoms but not the most characteristic of this disease: slow movements and the difficulty of initiating the movement by themselves ('internally generate the motor command') are the most characteristic; for example if somebody else gives the signal to start a movement it is easier to start a movement rather than by themselves.

⁵⁴It is affected the *indirect pathway*. It is the opposite of the Parkinson's disease: if Parkinson is characterized of slow movements and difficulty to start a movement, the Huntington is characterized by an activation of not controlled movements.

⁵⁵Basic dynamic of reinforcement learning: you have a stimulus, the stimulus conveys some info and you produce the action or select the action that is coherent with the stimulus that you get and that generally leads to a reward or make you avoid a punishment; do this thanks to *dopamine* (see below).

Have many *dopamine*⁵⁶ receptors:

- monitoring reinforcements and rewards;
- changes in dopamine represents the error between predicted future rewards and actual rewards (Shultz et al., 1997).⁵⁷

Note that in general the most important thing of basal ganglia is that they not only permit to move around the world but they permit to move in a way that consents to gain rewards and avoid punishments.

Interesting question: so can we say that the basal ganglia are the center of *consciousness*? No. All the brain contributes to consciousness; in the sense that basal ganglia contributes for some parts and other brain's components for others. So in general there is no center of consciousness. When you read some articles which says 'found the center of happiness etc.' they are not true informations.

The amygdala

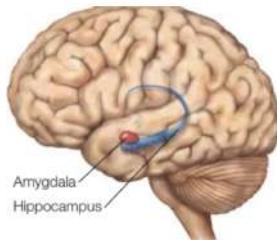


Figure 2.40

Small, almond shaped structure in the medial temporal lobe adjacent to the anterior portion of the hippocampus.⁵⁸

Collection of thirteen nuclei.

Luiz Pessoa (2011) boils down the amygdala's job description by suggesting that it is involved in determining what a stimulus is and what is to be done about it. Involved in:

- attention;
- perception;
- value representation;

⁵⁶It is another neurotransmitter.

⁵⁷It is called '*the prediction error*' (we will see also later). There is a process related in order to minimize the error: we do an action expecting a reward but we don't reach this reward (there is an error!) so next time we change the action in order to minimize the error. We also have an history of all these processes, an history of errors, rewards, etc. that involves a certain period of time.

⁵⁸The amygdala is also important for *reinforcement learning* and in particular, when we detect a stimulus in the environment it is important to process stimulus that are salient (meaning how important is for our survival), it tells us how salient the stimulus is. Also is crucial for life threatening: when something is threatening the amygdala is activated and relays information to the rest of the brain; patients that have lesions to amygdala have difficulty to perceive angry faces and fearful faces; that in particular because when somebody has a fearful face it's because mostly there is a danger in the environment.

- decision making;
- learning;⁵⁹
- memory.

The hippocampus

Small, curved formation (see figure above).
Infolding of inferomedial part of temporal lobe.
Crucial for:

- memory formation;⁶⁰
- spatial memory.⁶¹

Cerebral cortex

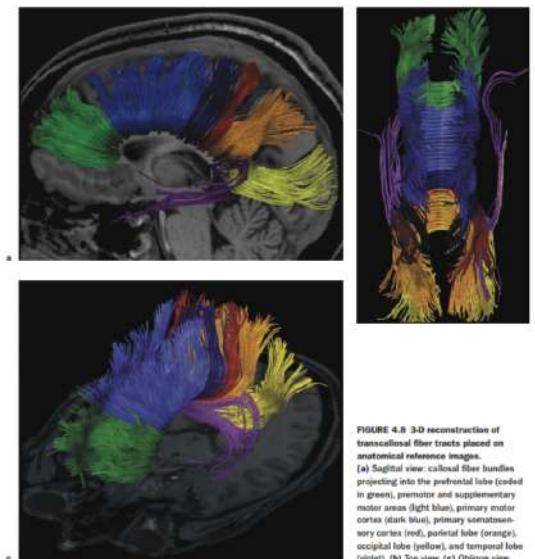


Figure 2.41

⁵⁹As already mentioned in the previous note in particular for *reinforcement learning*. Specifically to associate environment stimuli with something adverse, adverse consequences. Who has problem of amygdala has difficulty to predict that a certain stimulus is going to lead to something dangerous.

⁶⁰In particular in translating short term memory in long term memory. The info from the environment is processed by the hippocampus in short term memory and then the hippocampus transmit it to the cortex where it can be translated, stored in long term memory. So is mainly important for *short term memory*. Remember the patient that (we saw in a video) had lesions to hippocampus: he remembered who he was, his past, but wasn't able to form new memory.

⁶¹When you have to navigate in the environment or remember the path to go somewhere; there is an important study conducted in the UCL: they studied London taxi drivers before they became taxi drivers; in particular to become a London taxi driver you have to memorize a lot of London streets and paths without smartphone, GPS etc. and they found that before becoming taxi drivers their hippocampus was bigger than after (structure plasticity).

The cerebral cortex is the evolutionary younger part of our brain.
 Outermost tissue of the telencephalon.
 Made up of large sheets of (mostly) layered neurons.
 Two symmetrical hemispheres.
 Connections between the cerebral hemispheres are via axons from cortical neurons that travel through the *corpus callosum*.⁶²
 Contains many infoldings, or convolutions:

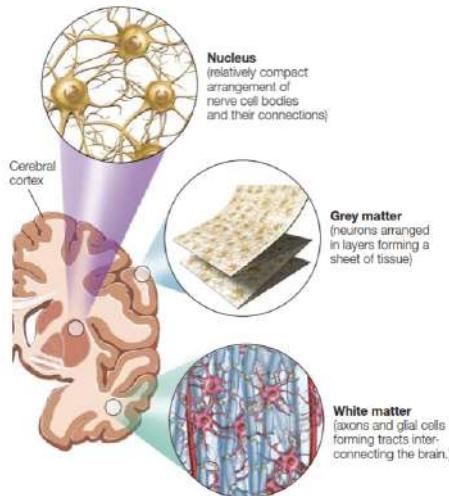


Figure 2.42

- sulci: crevices (infoldings);
- gyri: crowns (convolutions);⁶³
- total surface area of the human cerebral cortex is about 2.2 to 2.4 m^2 ;
- about 2/3 confined within the depths of the sulci;
- highly folded cortex brings neurons into closer three-dimensional relationships with one another;⁶⁴
- reducing axonal distance and hence neuronal conduction time between different areas:
 - possible because the axons that make long-distance corticocortical connections run under the cortex through the white matter and do not follow the foldings of the cortical surface.⁶⁵

⁶²Corpus callosum is essentially a bundle of axons which connects the two hemispheres (remember the patient that we saw in a past video that for epilepsy had the two hemispheres separated by cutting the corpus callosum with surgery.)

⁶³It has many infoldings and convolutions because we need to put 2.2 to 2.4 m^2 in our head; it's a lot of material!

⁶⁴And three-dimensional is a lot more efficient than the two-dimensional that we would have had without infoldings and convolutions; so three-dimensional leads to a large number of convolutions.

⁶⁵Remember that cell bodies are in the grey matter and axons are in white matter but in particular the axons do not follow the infoldings and they can travel freely in the white matter (see figure above).

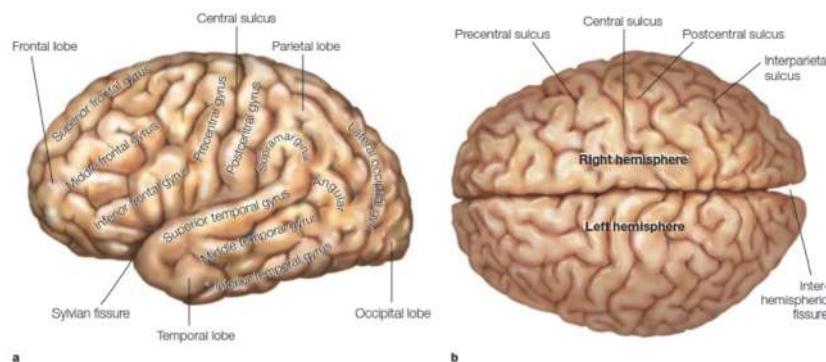


Figure 2.43

Contains:

- cell bodies of neurons, dendrites, some of their axons;
- axons and axon terminals of neurons projecting to the cortex from other brain regions, such as the subcortical thalamus;⁶⁶
- blood vessels;⁶⁷
- gray matter and white matter.

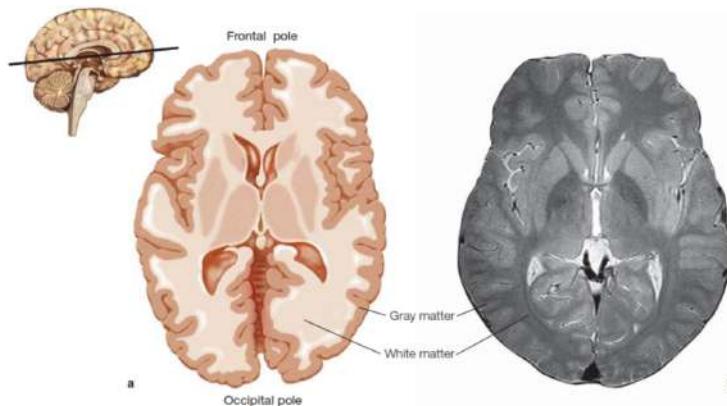


Figure 2.44

Cerebral cortex: anatomical division

Divided⁶⁸ in 4 lobes distinguished from one another by pronounced sulci:⁶⁹

- Central sulcus: divides the frontal lobe from the parietal lobe.

⁶⁶Connection are also from one area of the cortex to the other.

⁶⁷The blood needs to go to the brain in order to nourish the components.

⁶⁸The division is not only structural but also functional; see next section.

⁶⁹Very long sulci in comparison to the others.

- Sylvian (lateral) fissure: separates the temporal lobe from the frontal and parietal lobes.
- Parieto-occipital sulcus: divides the occipital lobe from the parietal and temporal lobes on the dorsal surface.
- Preoccipital notch: divides the occipital lobe from the parietal and temporal lobes on the ventrolateral surface.

Interhemispheric (longitudinal) fissure:

- runs from the rostral to the caudal end of the forebrain;⁷⁰
- separates the left and right cerebral hemispheres.

Some parts of the cortex are not included in the lobes:

- Insula: between the temporal and frontal lobe.

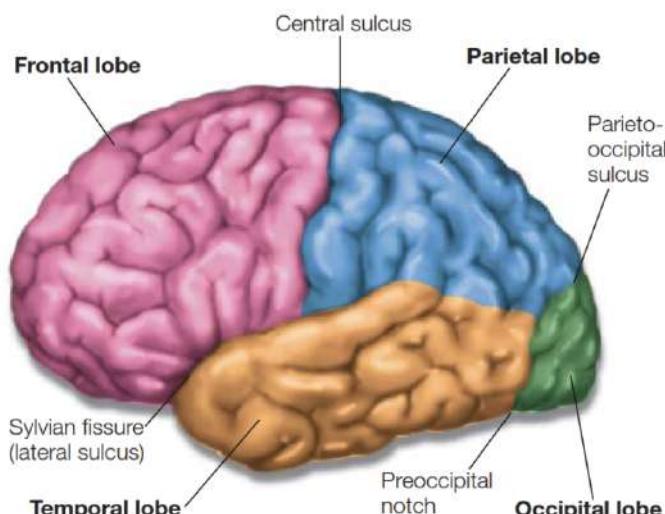


Figure 2.45

Cerebral cortex: functional division

The lobes of the cerebral cortex have a variety of functional roles in neural processing.⁷¹

Cognitive brain systems are often composed of networks whose component parts are located in different lobes of the cortex.

Most functions in the brain rely on both cortical and subcortical components. Each functional system is hierarchically organized:

- areas of the cerebral cortex are designated as primary, secondary, or tertiary areas, depending on their functional sequence within the pathway.

⁷⁰Front part of the brain.

⁷¹Mostly, different lobes have different functions but they communicate also with each other in order to perform particular functions; that's why for example we said that there is no a single center of consciousness.

Cerebral cortex: functional division – Frontal lobe

Frontal lobe is essentially related to movement.

Motor cortex:

- planning and execution of movements;
- M1:⁷² contains neurons that directly activate somatic motor neurons in the spinal cord.⁷³

Prefrontal cortex:

- Long-term planning & organizing;
- executive functions;
- decision making;⁷⁴
- Motivation and value.

Looking at the figure below note that: from posterior to anterior the movement control becomes more abstract in the sense that the frontal part is important for long term movement, for planning the sequence of movements we need to take.

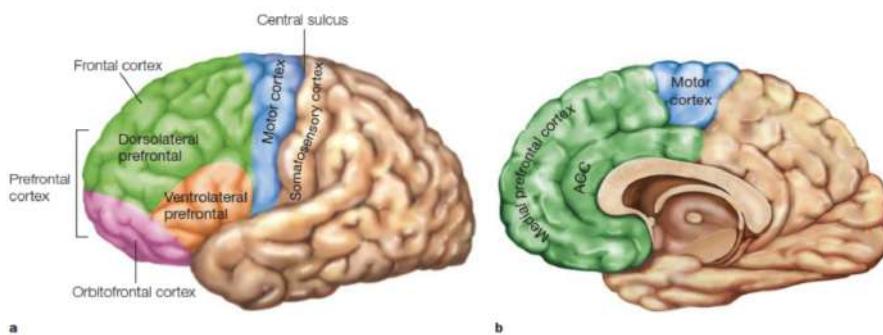


FIGURE 2.33 The human frontal cortex.
 (a) Divisions of the frontal cortex. The frontal lobe contains both motor and higher order association areas. For example, the prefrontal cortex is involved in executive functions, memory, decision making, and other processes. (b) Midsagittal section of the brain showing the medial prefrontal regions, which include the anterior cingulate cortex (ACC). Also visible is the supplementary motor area.

Figure 2.46

Cerebral cortex: functional division – Parietal lobe

Receives sensory information from:

- the outside world;
- within the body;

⁷²M1 stands for ‘primary’, M2 for ... (see previous pages)

⁷³And then there are other motor neurons that from the spinal cord go to the muscles; for example if we stimulate electrically M1 we generate movements of fingers.

⁷⁴And also action selection.

- memory.

And integrates it.

Includes the somatosensory cortex:

- S1: information about touch, pain, temperature sense, and limb proprioception (limb position) is received via receptor cells on the skin and converted to neuronal impulses that are conducted to the spinal cord and then to the somatosensory relays of the thalamus.
- Higher-order sensory area: sends its outputs to multimodal association areas that integrate information from two or more sensory modalities.

Looking at the figure below note that the Frontal and Parietal lobes are divided by the *central sulcus* which is very deep. More precisely the two lobes are connected in 3D but if we think in 2D (extending the surfaces) they would be very distant.

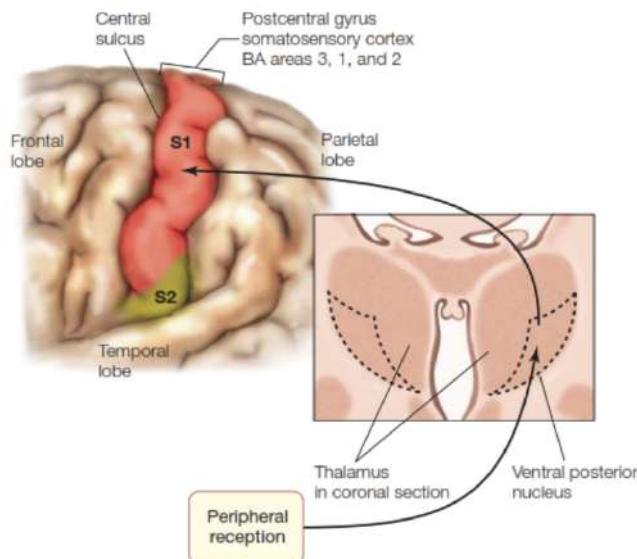


FIGURE 2.34 The somatosensory cortex, which is located in the postcentral gyrus.

Inputs from peripheral receptors project via the thalamus (shown in cross section) to the primary somatosensory cortex (S1). Secondary somatosensory cortex (S2) is also shown.

Figure 2.47

Neurons are organized into a neural map of the body

Topographic correspondence between cortical regions and body surface with respect to somatosensory and motor processes.

The neurons that regulate particular body parts are clustered together.

Somatotopy: mapping of specific parts of the body to areas of the cortex.

Homunculus: map of the body surface on the cortex.

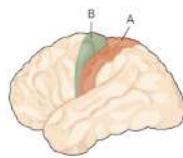


Figure 2.48

There is an indirect relation between the actual size of body's parts and the cortical representation of the body's parts.

The extent of the representation of a body part reflects the density of innervation of that part.

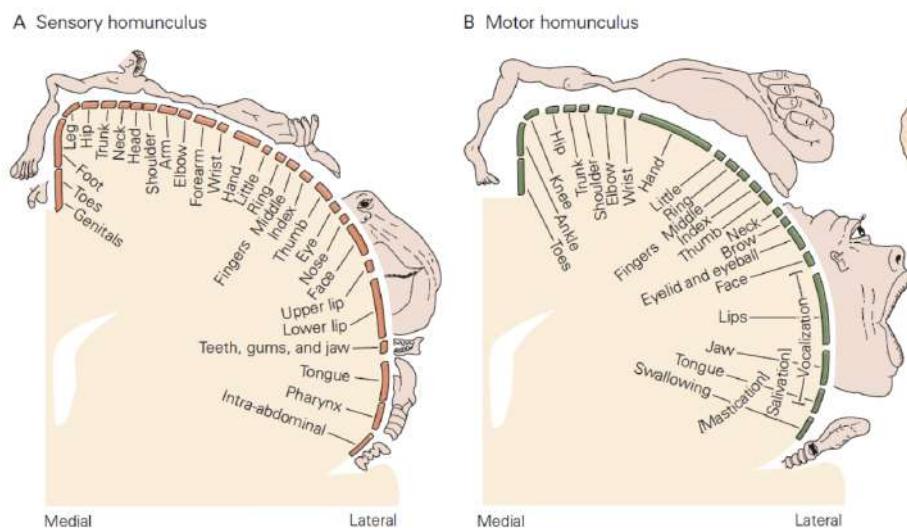


Figure 2.49

Cerebral cortex: functional division – Occipital lobe

Occipital lobe processes vision information.

Visual cortex:⁷⁵

- the cells do not respond randomly or with the same intensity to different stimuli or, in particular, to different locations, but our cells respond preferentially to some locations of the stimulus in comparison to others (think about of vision field exam.)

Primary visual cortex: begins the cortical coding of visual features like:

- luminance;
- spatial frequency;
- orientation;

⁷⁵Information from our eyes is received from visual cortex

- motion.

Retinotopic maps:⁷⁶

- the receptive fields of visual cells form an orderly mapping between spatial location and the neural representation of that dimension.⁷⁷

Looking at the figure below (at right) we see here also that info that comes from the right goes to the left and viceversa; they cross in the *optic chiasm*; we already saw another cross at Medulla level.

In the same figure below we can see the *information path*: from the eyes to visual cortex and back through the thalamus (which is located at the bord of the triangle between eyes and cortex.)

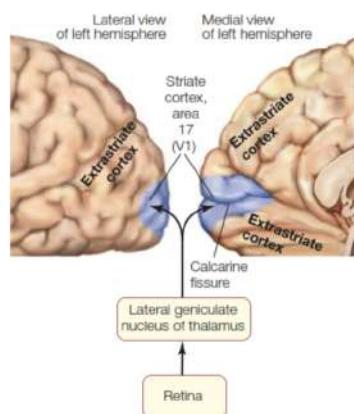


FIGURE 2.35 The visual cortex, which is located in the occipital lobe. Brodmann area 17, also called the primary visual cortex, visual area 1 (V1), and striate cortex, is located at the occipital pole and extends onto the medial surface of the hemisphere, where it is largely buried within the calcarine fissure.

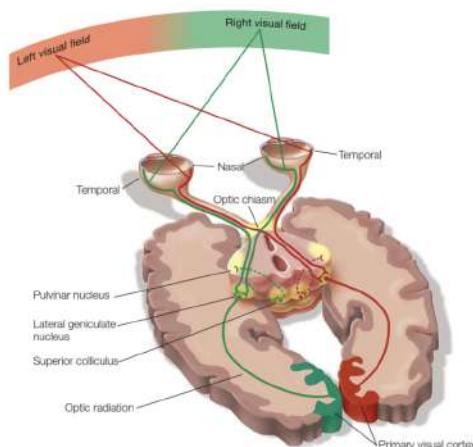


FIGURE 5.23 The primary projection pathways of the visual system.

Figure 2.50

Cerebral cortex: functional division – Temporal lobe

Includes the auditory cortex:

- sound processing;
- from the cochlea in the ear proceeds through the subcortical relays to the thalamus to reach primary auditory cortex;
- Tonotopic organization:⁷⁸
 - layout of the neurons based on sound frequency.⁷⁹

⁷⁶Retinotopic is the equivalent of *somatotopy* (see previous pages).

⁷⁷What it means is that there are some cells in our visual cortex that respond preferentially (they fire more) to specific location of visual stimuli, they encode position of the stimuli.

⁷⁸It is the equivalent of Retinotopic, Somatotopic etc. (see previous pages).

⁷⁹From lower to higher frequency they go from posterior to anterior.

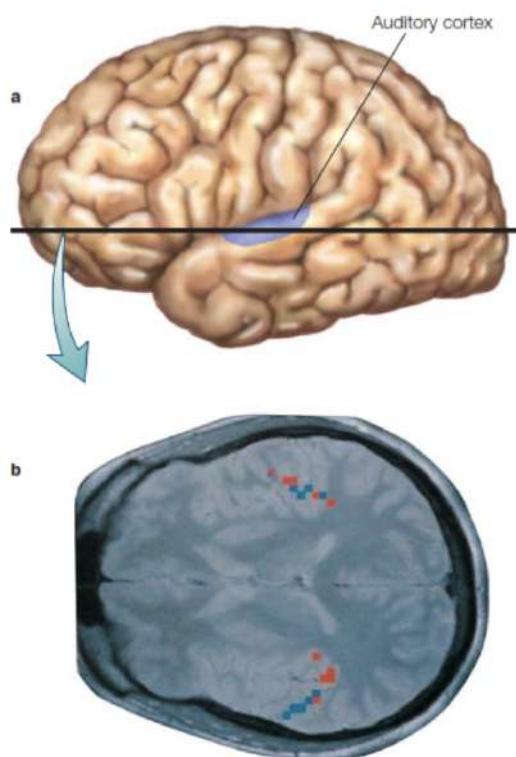


FIGURE 2.36 The human auditory cortex.
 (a) Primary auditory cortex, which is located in the superior temporal lobe. The primary auditory cortex and surrounding association auditory areas contain representations of auditory stimuli and show a tonotopic organization. (b) This MRI shows areas of the superior temporal region in horizontal section that have been stimulated by tones of different frequencies (shown in red vs. blue) and show increased blood flow as a result of neuronal activity.

Figure 2.51

Cerebral cortex: functional division – Association cortex

Portion of the neocortex that is neither sensory nor motor.

Contains cells that may be activated by more than one sensory modality.

Receives and integrates inputs from many cortical areas to produce integrated experience of the world.⁸⁰

Responsible for all our high-end human abilities, such as language, abstract thinking.

Each sense has a sensory association area:

- visual association cortex: *e.g.* from individual features to a face;
- auditory association cortex.

⁸⁰We don't have sequentially separated experiences and processes of the world, but they come in mostly together. We don't have unitary experiences.

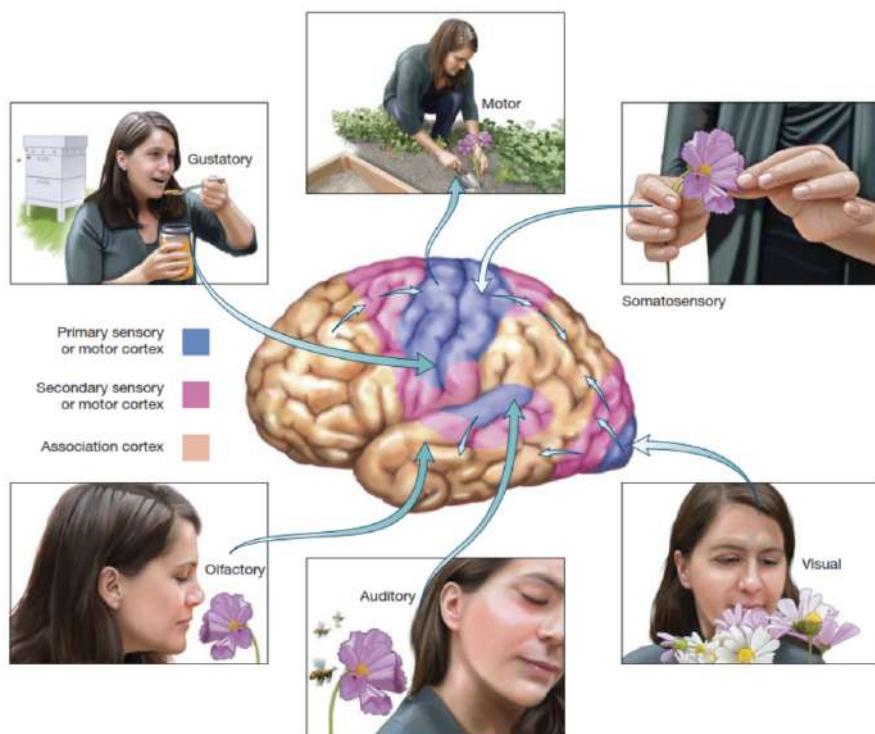


FIGURE 2.37 Primary sensory and motor cortex and surrounding association cortex.
The blue regions show the primary cortical receiving areas of the ascending sensory pathways and the primary output region to the spinal cord. The secondary sensory and motor areas are colored pink. The remainder is considered association cortex.

Figure 2.52

Chapter bibliography

Kandel, *Principles of Neural Science, Sixth Edition*, McGraw-Hill, 2021. Chapter 2.

Kandel, *Principles of Neural Science, Sixth Edition*, McGraw-Hill, 2021. Chapter 15.

Gazzaniga, Ivry, Magnum, *Cognitive Neuroscience: the biology of the mind, Fifth Edition*, W. W. Norton & Company, 2018. Chapter 2.

Chapter 3

Neuronal signaling

Below a usefull video which gives a view of an introduction to the nervous system.

https://www.youtube.com/watch?v=qPix_X-9t7E (The Nervous System, Part 1: Crash Course Anatomy & Physiology #8)

3.1 Signaling units of the nervous system

Neurons are the signaling units of the nervous system

Each neuron receives and gives rise to thousands of connections.

Neurons receive, evaluate, and transmit information

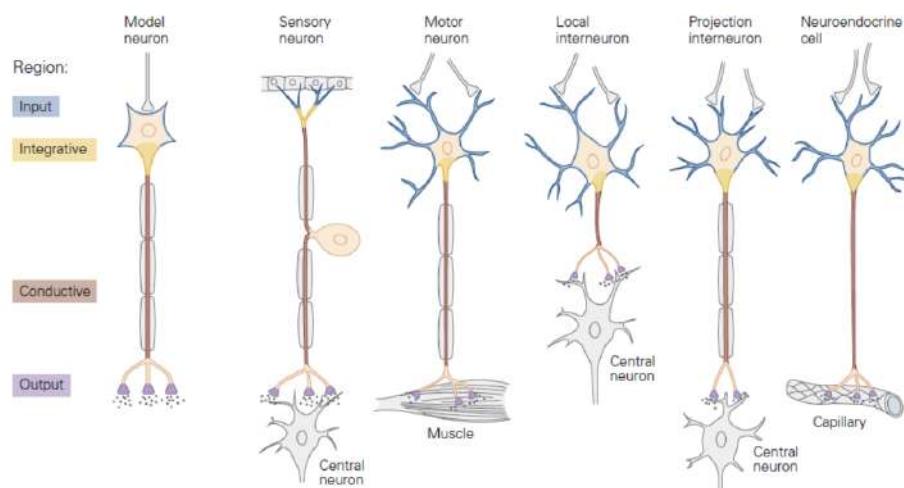


Figure 3.1

Information is transferred:

1. Within a neuron:

- (a) received at synapses on dendrites;
 - (b) conducted within the neuron;
 - (c) transmitted down the axon;
 - (d) passed along at synapses on the axon terminals.
2. Between a neuron and:
- (a) another neuron;
 - (b) a non-neuronal cell: *e.g.* muscles or glands;

Neurons have four morphologically defined regions

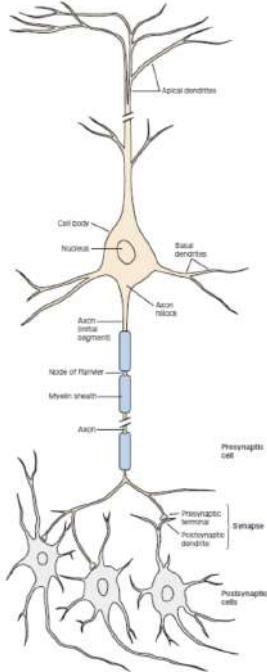


Figure 3.2

Each region has a distinct role in generating signals and communicating with other nerve cells:

1. The *cell body or soma* is the metabolic center of the cell. It gives rise to two kind of processes: several short dendrites and one long, tubular axon;
2. *Dendrites* are the main apparatus for receiving incoming signals from other nerve cells;
3. The *axon* extends over some distance from the cell body and carries signals to other neurons;
4. Near its end the axon divides into fine branches that contact other neurons at specialized zones of communication known as *synapses*.

Now we are going to see:

- how the messages are conducted along the axon;
- when they arrive to the end, how they are transmitted from one neuron to the others.

Signaling is organized in the same way in all nerve cells

Four components:

1. Input signal (receptive);
2. trigger signal (summing or integrative);
3. conducting signal (signaling);
4. output signal.

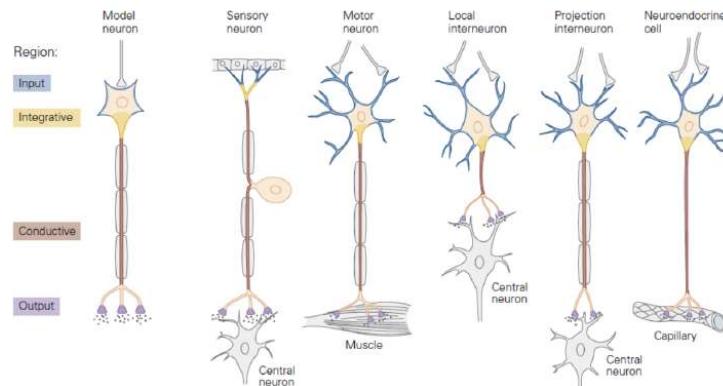


Figure 3.3

Regardless of cell size and shape, transmitter biochemistry, or behavioral function.

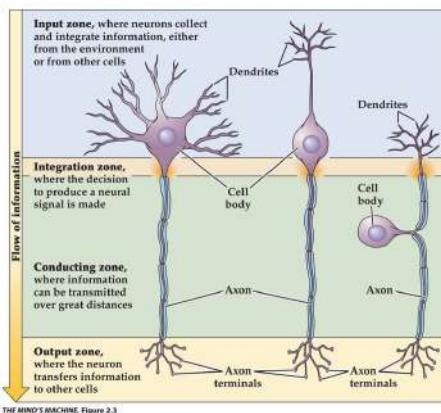


Figure 3.4

Signaling within and between neurons is handled differently

Within a neuron:

- transferring information involves changes in the *electrical state* of the neuron;
- electrical currents flow through the volume of the neuron \Rightarrow neuronal spikes.

Between neurons:

- information transfer occurs at synapses.¹



Figure 3.5

3.2 Information transfer within a neuron

Signaling within a neuron

Transferring information involves transient changes in the *electrical state* of the neuron.

Produced by temporary changes in the electric current into and out of the cell.

Resting membrane potential

Arises from the asymmetric distribution of ions across the neuron's cell membrane.²

In the image below an idealized neuron is shown with intracellular recording electrode penetrating the neuron. The electrode measures the difference between the voltage inside versus outside the neuron and this difference is amplified and displayed on an oscilloscope screen (top). The oscilloscope screen shows voltage over time, and shows that prior to the electrode entering the neuron, voltage between the electrode and the extracellular reference electrode is zero, but when the electrode is pushed into the neuron, the difference becomes -70 mV , which is the resting membrane potential.

Note that what said is valid also along the axon of a neuron (when the myelin breaks at the Nodes of Ranvier).

In a resting neuron the voltage of the inside of the cell is about *70 mV more negative* than the voltage outside the cell.

¹Remember: at the beginning was thought that most synapses were electrical but after was discovered that most are chemicals.

²A possible question could be why myelin doesn't wrap around dendrites: the answer is that myelin insulates and dendrites need to communicate with other cells and it would be reduced the number of processes of the dendrites; furthermore usually the dendrites aren't so long in order that the myelin sheets could improve the conduction.

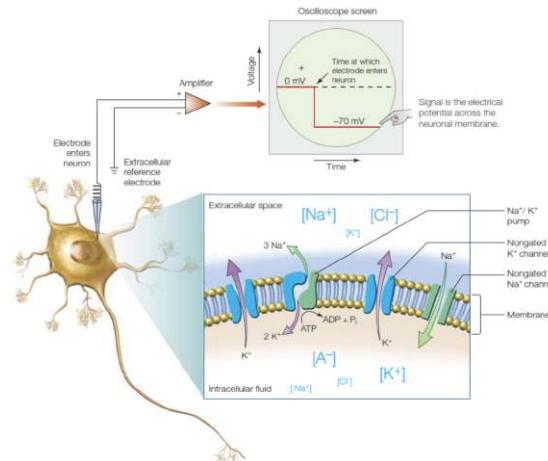


Figure 3.6

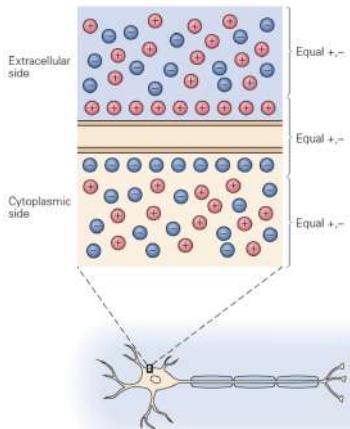


Figure 3.7

This electrical potential difference means that the neuron has at its disposal a kind of battery.

Like a battery, the stored energy can be used to do work *i.e.* signaling work.
All of the substances that we see in the first figure above at the right are chemicals (in our body there is a lot of sodium and potassium).

After the Extracellular side there is the Membrane and after it the Citoplasmic³ side in the Intracellular space.

Two mechanisms enables the difference in potential, that create the above mentioned difference in potential:

1. Na^+/K^+ pump (see figure above):⁴

- High Na^+ concentration *out vs in* cell;

³Cytoplasm: the fluid inside a cell but outside the cell's nucleus.

⁴Na sodium, K potassium.

- high K⁺ concentration *in vs out* cell;
- 3 Na⁺ vs 2 K⁺;
- Creates a concentration gradient:⁵
 - Na⁺ wants to enter the cell;
 - K⁺ wants to escape the cell.⁶

2. *Ion channels:*

- are more permeable to K⁺ and less to Na⁺;
- K⁺ exit the cell, they leave behind a cloud of negative charge on the inner surface of the membrane;
- *the net charge inside the membrane is more negative than that outside:*
-70 mV difference.

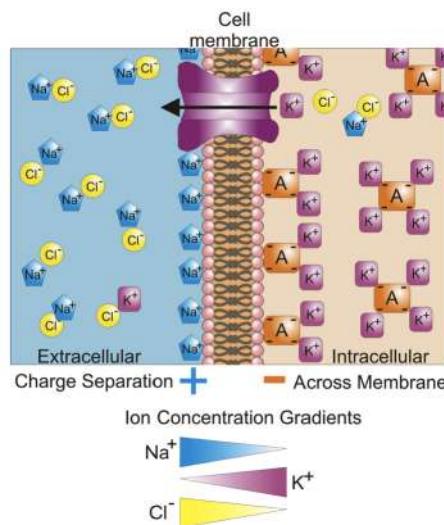


Figure 3.8

-70 mV:

- the energy source that neurons can use for signaling;
- it is the baseline on which all signaling occurs.

Neurons are excitable

The membrane potential can be quickly and significantly altered.

Alteration serves as a signaling mechanism.⁷

The alteration in membrane potential can be either:

⁵Difference in concentration.

⁶Because the principium is to gain equilibrium of concentration between inside and outside of the cell.

⁷Scenario: i) many signals arrives from other cells through dendrites; ii) these signals determine a decrease or an increase.

- a decrease *i.e.* depolarization:⁸
 - enhances the ability to generate action potential;⁹
 - excitatory.
- an increase *i.e.* hyperpolarization:
 - reduces the ability to generate action potential;
 - inhibitory.

Action potential

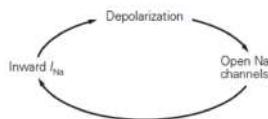


Figure 3.9

When the alteration in membrane potential is:

- a decrease *i.e.* depolarization:
 - enhances the ability to generate action potential;
 - excitatory.

If the depolarization is strong enough to reach -55 mV an *action potential* is triggered.

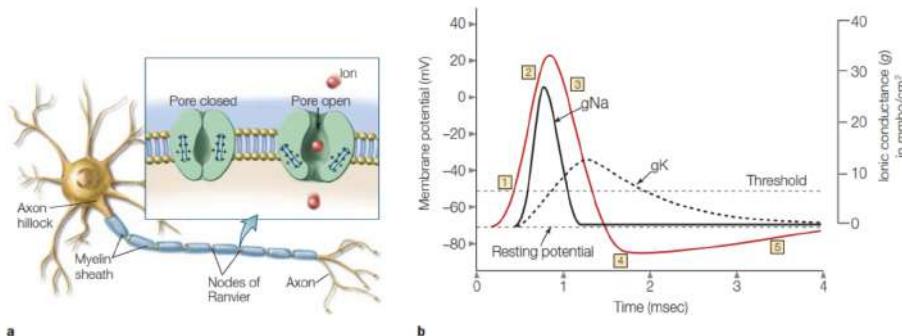


Figure 3.10

The figure **b** above shows action potential in time (note that there is an error in the graph: the red line should grow up to 40 not to 20); it is the same in all cells: the behaviour has the same shape and the same magnitude in all cells. So

⁸Means that the membrane becomes more positive: decrease the negativity.

⁹Action potential is what transfers the message; increase the probability that a neuron fires *i.e.* that a message that it is received pass (or it is generated) between the neuron and goes to other cells.

a natural question would be: if it is the same what determine the *intensity* of the message? (We'll see later).

Depolarization makes the membrane much more permeable to Na^+ than to K^+ . The resultant influx of positively charged Na^+ neutralizes the negative charge inside the cell and causes a brief and explosive change in membrane potential to +40 mV.

Action potential: the first portion (1 & 2)

When the threshold is reached, voltage-gated Na^+ channels open and Na flows rapidly into the neuron.

This influx of positive ions further depolarizes the neuron, opening additional voltage-gated Na^+ channels; thus, the neuron becomes more depolarized.

This causes more Na channels to open, in a cycle.

Until the equilibrium potential for Na^+ is reached.

Action potential: the first portion (3 & 4)

Voltage gated K^+ channels open, allowing K to flow out of the neuron down its concentration gradient (3).

This shifts the membrane potential back toward:

- its resting potential;
- to the K^+ equilibrium potential (4).

Action potential: hyperpolarization (4) & return to rest (5)

The K^+ equilibrium potential is more negative than the resting potential: this causes an hyperpolarization.

K^+ channels close.

The membrane potential can return to its resting state.

Hyperpolarization & Refractory period

During hyperpolarization the Na^+ channels cannot open \implies refractory period.
Two consequences:

1. Limits the number of action potentials that a neuron can generate in a given time.
2. Unidirectional current flow: from the axon hillock toward the axon terminal:
 - the current cannot reopen the channels that generated it;
 - it can depolarize the membrane a bit farther on opening channels in this next portion of the membrane.

Principle of dynamic polarization

Electrical signals within a nerve cell flow only in one direction:¹⁰

¹⁰This principle was discovered by Santiago Ramón y Cajal (1852-1934, Spanish neuroscientist, pathologist, and histologist).

- received at synapses on dendrites;
- transmitted down the axon;
- passed along at synapses on the axon terminals.

Seizures: the misfiring of neurons

Below a usefull video which explains the seizures misfiring neurons dynamic.
<https://www.youtube.com/watch?v=Lc09YU-PdwS> (What causes seizures, and how can we treat them? - Christopher E. Gaw)

Action potential: travelling far

The action potential is actively propagated along the axon:¹¹

- self-regenerative feature;
- its amplitude does not diminish by the time it reaches the axon terminal.

Action potential: travelling fast

Action potentials must travel quickly.

Glial Cells Support Nerve Cells

Oligodendrocytes (in CNS) and Schwann cells (in PNS):

- produce thin sheets of myelin that wrap around the axon of neurons;
- provide the insulating material along the axon:
 - resistance to voltage loss;
 - allows *rapid conduction* of electrical signals along the axon;
 - action potentials do not have to be generated as often, and can be spread out along the axon (see ahead).

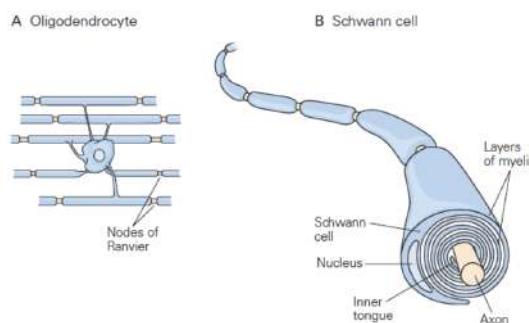


Figure 3.11

¹¹It has to travel far, possibly without dissipating.

Nodes of Ranvier & Saltatory conduction

Action potentials in myelinated axons need occur only at the nodes of Ranvier, where myelination is interrupted.

Saltatory conduction: appearance that the action potential is jumping down the axon.¹²

All-or-none action potential

Action potentials have always similar amplitude and duration.

The size and shape of an action potential initiated by a large depolarizing current is the same as that of an action potential evoked by a current that just surpasses the threshold.

Implication: the strength of the action potential does not communicate anything about the strength of the stimulus.¹³

The firing rate of the action potential

The firing rate of the action potential is proportional to stimulus intensity. More intense stimuli elicit higher action potential firing rates.

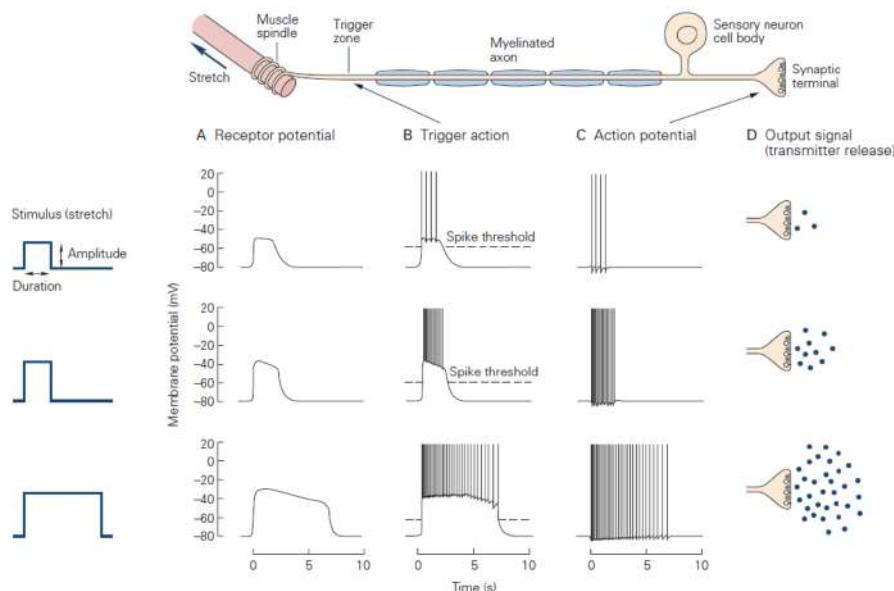


Figure 3.12

Referring to the image above we can see that in the second line of the group of graphs we have same duration but an increased amplitude in comparison to the first line; while in the third line we have both increased duration and increased amplitude in comparison to the first line.

¹²Fast conduction.

¹³So how a neuron can perceive the strength of the stimulus? By *frequency* of the action potential (see ahead).

Action potential properties for neuronal signaling

Action potential has four properties important for neuronal signaling:

1. Threshold for initiation.
2. All-or-none nature.
3. Conducted without decrement.
4. Refractory period.

Signaling is organized in the same way in all Nerve Cells

Four components:

1. Input signal (receptive).
2. Trigger signal (summing or integrative).
3. Conducting signal (signaling).
4. Output signal.

Regardless of cell size and shape, transmitter biochemistry, or behavioral function.

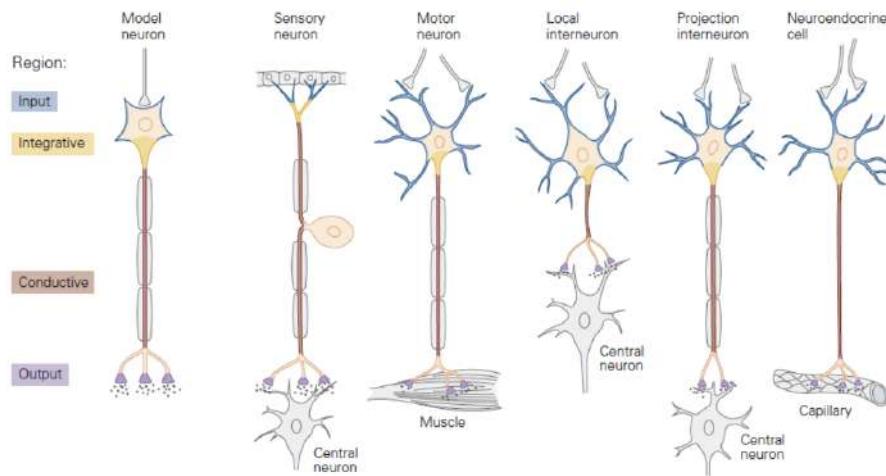


Figure 3.13

Characteristic signal of each signaling components

Refer to Figure 3.12. Each of the neuron's four signaling components produces a characteristic signal:

1. The input signal (A) is graded in:
 - (a) Amplitude.
 - (b) Duration.

- (c) Proportional to the amplitude and duration of the stimulus.
2. The trigger zone sums the depolarization generated by the input signal:¹⁴
 - (a) An action potential is generated only if the input signal exceeds a certain voltage threshold.
 - (b) Once the threshold is surpassed an action potential is generated.
 - (c) Any further increase in amplitude of the input can only increase the frequency of action potentials.
 - (d) The duration of the input determines the duration of the train of action potentials.

The graded amplitude and duration of the receptor potential is translated into a *frequency code* in the action potentials generation. All action potentials are propagated along the axon.

3. Conducting signal: action potentials:
 - (a) Action potentials are all-or-none: they all have a similar amplitude and duration.
 - (b) The frequency and duration of firing represents the information carried by the signal.
4. Output signal:
 - (a) The frequency of action potentials determines exactly how much neurotransmitter is released by the cell.¹⁵

Concluding this section we propose below a usefull video which gives a view of action potential.

https://www.youtube.com/watch?v=0ZG8M_1dA1M (The Nervous System, Part 2 - Action! Potential!: Crash Course Anatomy & Physiology #9)

3.3 Information transfer between neurons

Synapses enable communication between neurons

Presynaptic cell:

- the nerve cell transmitting a signal;
- from presynaptic terminals or nerve terminals, i.e. specialized enlarged regions of its axon's branches.

Postsynaptic cell:

- the cell receiving the signal.

Synaptic cleft:

¹⁴Referring to the penultimate figure the trigger zone appears very simple, but it can be much more complicated: can be associated to multiple dendrites.

¹⁵Note that the signal goes from electrical to chemical.

- the narrow space separating the presynaptic and postsynaptic cell.¹⁶

Most presynaptic terminals end on the postsynaptic neuron's dendrites; but the terminals may also terminate on the cell body or, less often, at the beginning or end of the axon of the receiving cell.

Three types of synapses

1. *Axosomatic*: synapses that are made onto the soma or cell body of a neuron.
2. *Axodendritic*: synapses that one neuron makes onto the dendrites of another neuron. The most common type.
3. *Axoaxonic*: synapses made by one neuron onto the synapses of another neuron. Axoaxonic synapses mediate presynaptic inhibition and presynaptic facilitation.

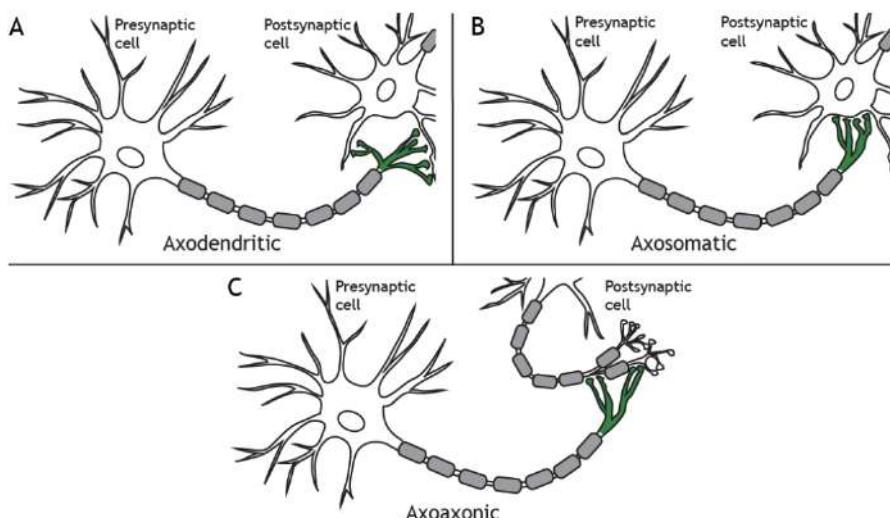


Figure 3.14

Below we propose an interactive website that permits starting from one neuron to make an your own network (using the different types of neurons and matching them together logically) and watch the signal travel. Use it as an exercise tool.
<https://www.fi.edu/your-brain/interactives/build-your-network>

Synaptic transmission

The transfer of a signal from the axon terminal to the next cells that can be:

- other neurons;
- muscles;

¹⁶Here most of the synaptic communication happens.

- glands.

There are two major kinds of synapses:

- electrical synapse;
- chemical synapse.

Electrical and chemical synapses are structured differently

Electrical synapses: neuronal membranes are touching at gap junctions, and the cytoplasms of the two neurons are essentially continuous.¹⁷

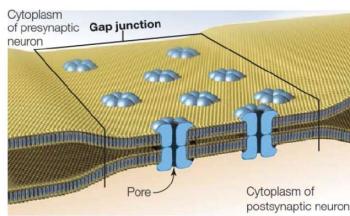


FIGURE 2.14 Electrical synapse between two neurons.

Figure 3.15

Chemical synapses: no structural continuity between presynaptic and postsynaptic neurons, synaptic cleft separates the neurons.¹⁸

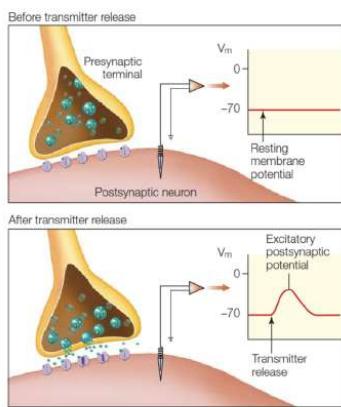


FIGURE 2.13 Neurotransmitter leading to postsynaptic potential.

Figure 3.16

¹⁷The intracellular spaces of the two cells are connected; this leads to a faster transmission, but notice that since the pores are open the signal can't be modulated (as, instead, in the chemical transmission). Input and output are the same and it is transmitted directly (whatever arrives, it passes).

¹⁸It is slower (in comparison to the electrical) but this structure is able to *modulate* the message: the input message can have different consequences on the postsynaptic cell. Input and output can be different, depending on what receptors.

Electrical and chemical synapses function differently

Electrical synapses: electrical synaptic transmission depends on the instantaneous transmission of the flow of ions from the presynaptic to the postsynaptic neuron.

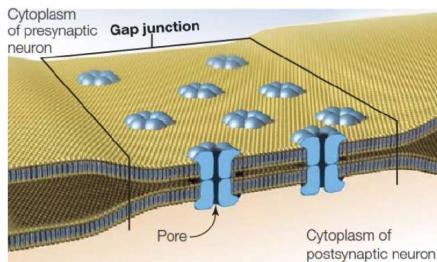


FIGURE 2.14 Electrical synapse between two neurons.

Figure 3.17

Chemical synapses: chemical synaptic transmission depends on the diffusion of a neurotransmitter across the synaptic cleft.¹⁹

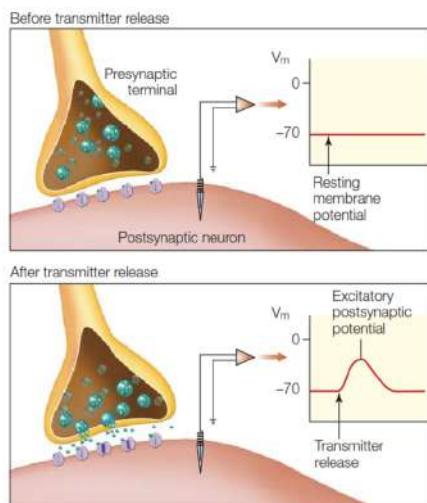


FIGURE 2.13 Neurotransmitter leading to postsynaptic potential.

Figure 3.18

Electrical synapses provide instantaneous signal transmission

Gap junction channels create pores connecting the cytoplasm of the two neurons. The two neurons are isopotential.

Electrical changes in one neuron are reflected instantaneously in the other.

¹⁹Another important thing is that here (referring to the image below before of the Presynaptic terminal) an electrical message (the action potential is electrical) has to be converted into a chemical message (after the Presynaptic terminal). We note also that at the Postsynaptic neuron level, if an action potential is triggered, the signal becomes again electrical.

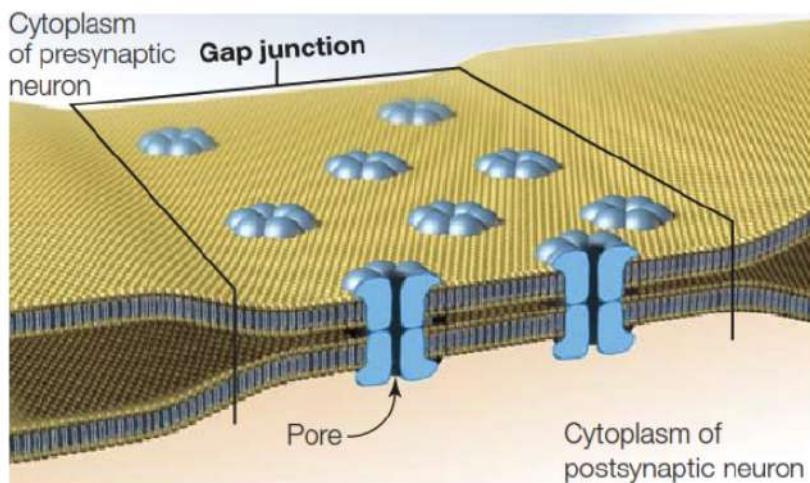


FIGURE 2.14 Electrical synapse between two neurons.

Figure 3.19

Electrical synapses

Advantages:

- fast transmission (*e.g.* Invertebrate escape reflex);
- synchronous operation of groups of neurons (*e.g.* hypothalamus).

Disadvantages:

- less plastic than chemical synapses;
- cannot modulate signal;
- less specific.²⁰

Chemical synapses

Chemical synaptic transmission depends on the diffusion of a neurotransmitter across the synaptic cleft.

Neurotransmitter: a chemical substance that binds receptors in the postsynaptic membrane of the target cell.

Presynaptic terminals: specialized swellings of the axon, which typically contain synaptic vesicles.

Synaptic vesicles: vesicles filled with several thousands of molecules of the neurotransmitter.

Referring to the image below, in the second row of images, looking at the first image (from the left) we highlight that the group of receptors can consist of different types of receptors. Looking instead at the third row, second image (from

²⁰Modulating/Plasticity/Specificity can depend on the amount of neurotransmitters released or the amount of receptors present *etc.*

the left), we highlight that we can have depolarization (+) vs hyperpolarization (-).

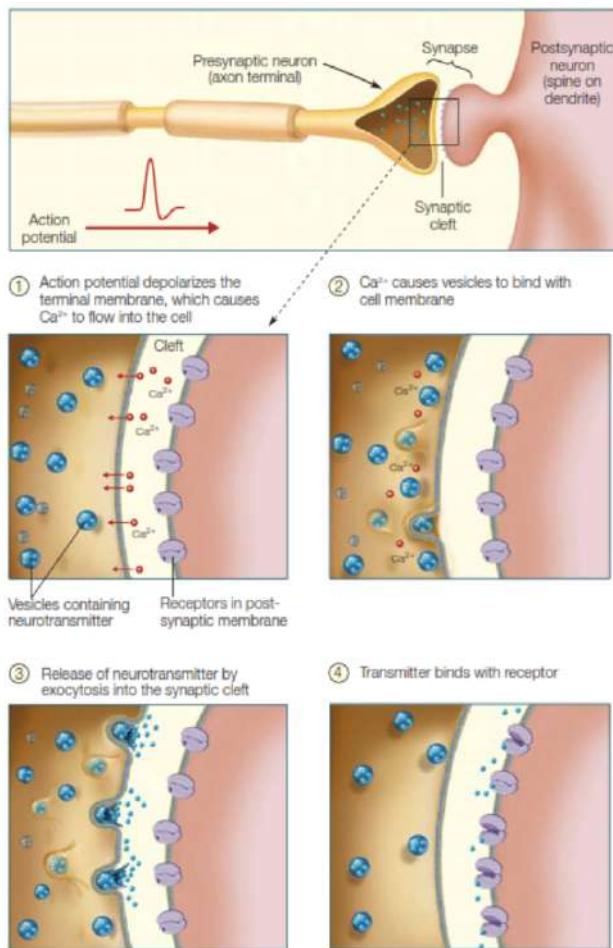


FIGURE 2.12 Neurotransmitter release at the synapse, into synaptic cleft.
The synapse consists of various specializations where the presynaptic and postsynaptic membranes are in close apposition. When the action potential invades the axon terminals, it causes voltage-gated Ca^{2+} channels to open (1), which triggers vesicles to bind to the presynaptic membrane (2). Neurotransmitter is released into the synaptic cleft by exocytosis and diffuses across the cleft (3). Binding of the neurotransmitter to receptor molecules in the postsynaptic

Figure 3.20

There is the possibility that the same type of neurotransmitter can be bound to different types of receptors; so it can be possible that one neurotransmitter is transmuted in positive charge (+) and another of the same type (but that goes in a different receptor) is transmuted in negative (-).

After that neurotransmitters are bound to their receptors, it is necessary to return to a normal status (they can't stay on receptors forever, otherwise neurons will fire forever conducting to the death), so we have *inactivation of neurotransmitters* that can be accomplished by:

1. Active reuptake of the substance back into the presynaptic terminal.

2. Enzymatic breakdown or degradation of the transmitter in the synaptic cleft.²¹
3. Diffusion of the neurotransmitter away from the site of action (*e.g.* in the case of hormones that act on target cells distant from the synaptic terminals).

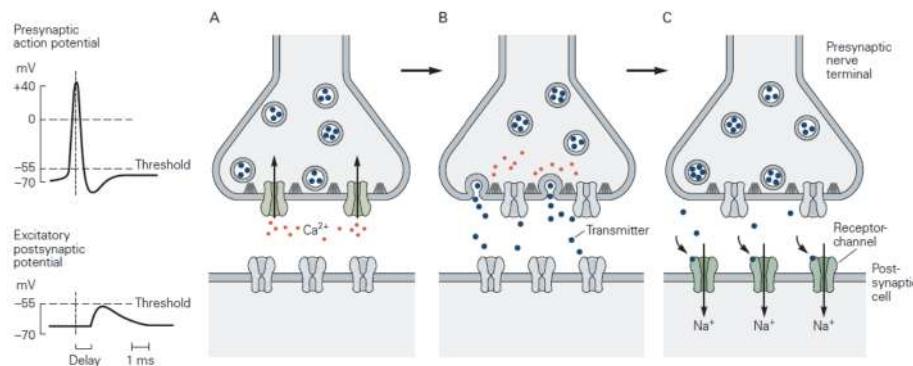


Figure 8-8 Synaptic transmission at chemical synapses involves several steps. The complex process of chemical synaptic transmission accounts for the delay between an action potential in the presynaptic cell and the synaptic potential in the postsynaptic cell compared with the virtually instantaneous transmission of signals at electrical synapses (see Figure 8-2B). A. An action potential arriving at the terminal of a presynaptic axon causes voltage-gated Ca²⁺ channels at the active zone to open. The gray filaments represent the docking and release sites of the active zone.

B. The Ca²⁺ channel opening produces a high concentration of intracellular Ca²⁺ near the active zone, causing vesicles containing neurotransmitter to fuse with the presynaptic cell membrane and release their contents into the synaptic cleft (a process termed exocytosis).

C. The released neurotransmitter molecules then diffuse across the synaptic cleft and bind specific receptors on the postsynaptic membrane. These receptors cause ion channels to open (or close), thereby changing the membrane conductance and membrane potential of the postsynaptic cell.

Figure 3.21

Neurotransmitter

The effect of a neurotransmitter on the postsynaptic neuron is determined by the postsynaptic receptor rather than by the transmitter itself.

The same neurotransmitter released from the same presynaptic neuron onto two different postsynaptic cells might cause one to depolarize (excitation) and the other to hyperpolarize (inhibition).

Although most of the time neurotransmitters have a typical effect, either inhibitory or excitatory.

Below a useful video which describes some synapses functionalities.

<https://www.youtube.com/watch?v=VitFvNvRIIY> (The Nervous System, Part 3 - Synapses!: Crash Course Anatomy & Physiology #10)

We already talked about different parts of the cortex and how they are specialized in different functions; see the following link in order to see how they work.

<https://www.fi.edu/en/your-brain/interactive/turn-off-your-perception>

We conclude this chapter proposing below a useful video which summarizes some of what we have seen.

https://www.youtube.com/watch?v=q8NtmDrb_qo (Central Nervous System: Crash Course Anatomy & Physiology #11)

²¹The first two are the most common.

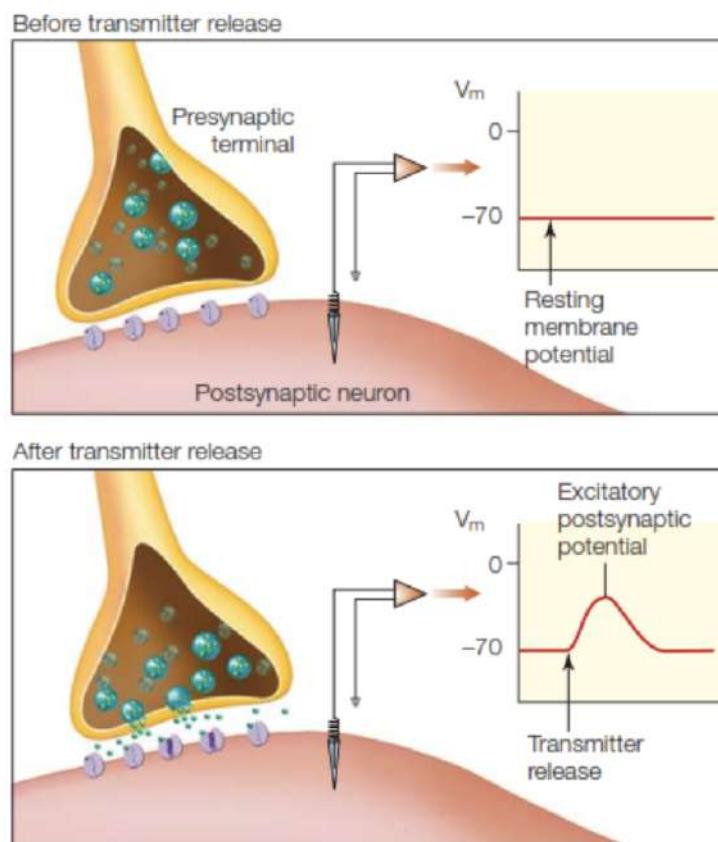


FIGURE 2.13 Neurotransmitter leading to postsynaptic potential.
The binding of neurotransmitter to the postsynaptic membrane receptors changes the membrane potential (V_m). These postsynaptic potentials can be either excitatory (depolarizing the membrane), as shown here, or inhibitory (hyperpolarizing the membrane).

Figure 3.22

Chapter bibliography

Kandel, *Principles of Neural Science, Sixth Edition*, McGraw-Hill, 2021. Chapter 2.

Gazzaniga, Ivry, Magnum, *Cognitive Neuroscience: the biology of the mind, Fifth Edition*, W. W. Norton & Company, 2018. Chapter 2.

Chapter 4

Intro to Reinforcement learning

Below a usefull video which gives a view of an introduction to the nervous system.

https://www.youtube.com/watch?v=qPix_X-9t7E (The Nervous System, Part 1: Crash Course Anatomy & Physiology #8)

4.1 Introduction to reinforcement learning

Reinforcement in psychology

Reinforcement learning:

- used to describe learning in both classical and instrumental conditioning.¹

Reinforcer:

- a stimulus that causes a change in response;
- a stimulus that increases or decreases the probability of emitting a response.

Response can be:

- physiological;²
- behavioral;³
- change in subjective experience.

Looking at the image below we have that the animal represents the *stimulus* while the two men show the same *physiological response* (shivering) but different *behavioural response*; the difference (response A of the first man on the left, response B of the second man running on the right), may depend on changing in subjective experiences.

¹We'll see both.

²How our body reacts to the stimulus.

³For example change in motor reflexis.



Figure 4.1

Learning

Enduring change in response or behavior that occurs as a result of experience.
Two broad classifications of learning:

1. non-associative;
2. associative.

Non-associative learning

Learning about the properties of a *single stimulus*: subject is exposed once or repeatedly to a single type of stimulus:

1. *habituation*:

- a *decrease* in an innate response to a stimulus that is presented repeatedly;
- less likely for the subject to respond to innocuous stimuli.



or work noise, traffic noise

Figure 4.2

2. *sensitization*:

- an *increase* in an innate response to a stimulus that is presented repeatedly;
- more likely for the subject to respond to potentially noxious stimuli.⁴

⁴Note that habituation and sensitization have opposite consequences.



warns you to stop the rubbing because it may cause injury

Figure 4.3

Associative learning

Change in response is caused by learning about the association of at least two stimuli or events.

Associative learning is the way in which an animal learns to predict events.

Maximize rewarding outcomes and minimize aversive outcomes to increase chances of survival.⁵

Below we propose two useful video about associative learning.

The first one trains a reflexive behaviour using two stimuli or events (pc noise and gum)

https://www.youtube.com/watch?v=xnf8i_IRCcw (The Office Pavlov Experiment)

The second one trains a more complex behaviour using two stimuli or events (chocolat and 'be quiet!')

https://www.youtube.com/watch?v=5XUvm_smWHY (Big Bang Theory operant conditioning)



Figure 4.4

In the image above we talked about *unconditioned* and *conditioned* stimuli. See ahead to understand better. We can think of the term *unconditioned* as a synonymous of 'biological programmed'.

The animal learns about the relationship between:

⁵In associative learning is possible to use rewards or punishments in order to induce the learning, but most likely we give rewards because they are ethically correct.

- A stimulus and an outcome: Pavlovian or classical conditioning;



Figure 4.5

- a behavior and an outcome: instrumental or operant conditioning.



Figure 4.6

Associative Learning is constrained by the biology of the organism



Figure 4.7

Animals generally learn to associate stimuli that are relevant to their survival.
Conditioned taste aversion:

- occurs only when certain tastes are associated with nausea/sickness;
- develops poorly if a taste is followed by a stimulus that does not produce nausea (*e.g.* painful stimulus, such as chili pepper taste);
- does not develop for a visual or auditory stimulus that has been paired with nausea.

4.2 Classical conditioning

Classical conditioning involves associating a stimulus with an outcome

Look at the figure below.

When a stimulus is presented that has no meaning to an animal, such as the sound of a bell (CS), there is no response (NR) (a). In contrast, presentation of a meaningful stimulus like food (US) generates an unconditioned response (UR) (b). When the sound is paired with the food, however, the animal learns the association (c); and later the newly conditioned stimulus (CS) alone can elicit the response, which is now called a conditioned response (CR) (d).

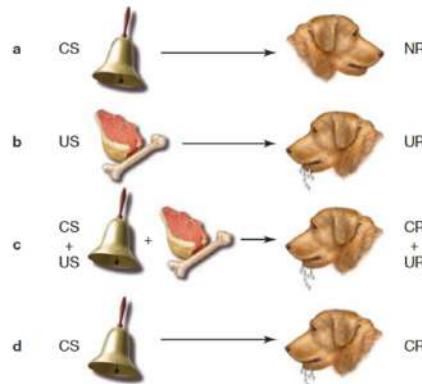


Figure 4.8

Ivan Pavlov (1849–1936, Russian and Soviet experimental neurologist and physiologist) received a Nobel Prize after first demonstrating this type of learning with his dogs.

Appetitive vs aversive conditioning

Appetitive.

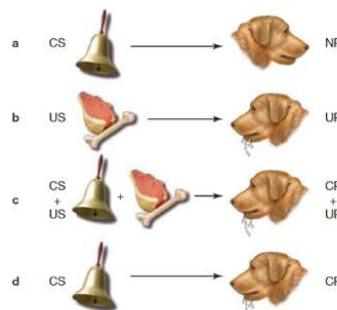


Figure 4.9

Aversive conditioning.

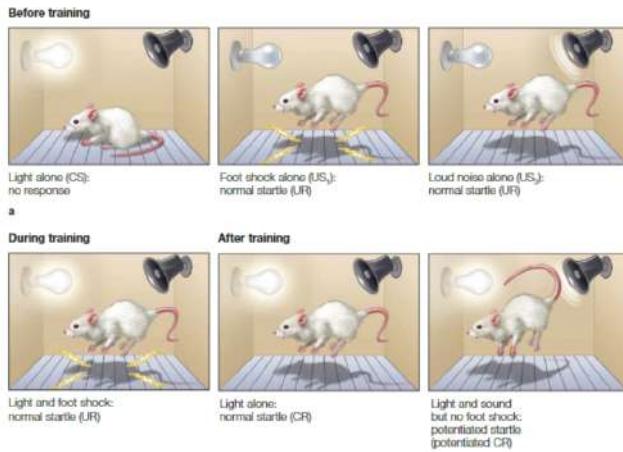


Figure 4.10

Classical conditioning in everyday life

Some examples.



Figure 4.11



Figure 4.12

Classical conditioning involves associating a stimulus with an outcome

The CS *anticipates* the US (look at *Trace Conditioning* in the image below). The CS to become an *anticipatory stimulus* for the US (look at the *Delay Conditioning* in the image below).

Looking at the image below we can say that *Simultaneous conditioning* (and *Delay Conditioning* which is an its specific case) is learned faster in comparison to *Forward conditioning* (and *Trace Conditioning* which is an its specific case) because it is to associate a phenomenon simultaneous rather than sequential (here you have to remember).

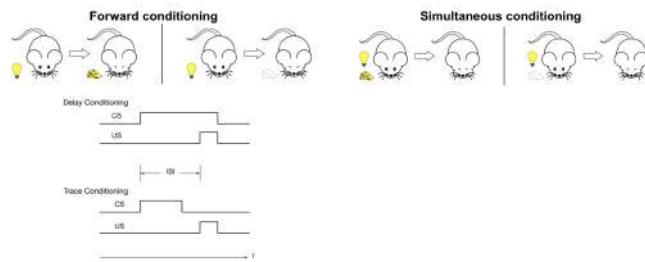


Figure 4.13

Primary and secondary reinforcers

Reinforcers other than in *rewards* or *punishments*, can be classified in:

1. Primary:⁶
 - (a) Food.
 - (b) Pain.
 - (c) Sex.
2. Secondary:⁷
 - (a) Money.
 - (b) Social approval (praise)/disapproval.

Classical conditioning in the lab

- Animal:

See <https://app.jove.com/v/5417/fear-conditioning>.⁸

The typology of the example is called ‘*fear conditioning*’ (it is a type of classical conditioning).

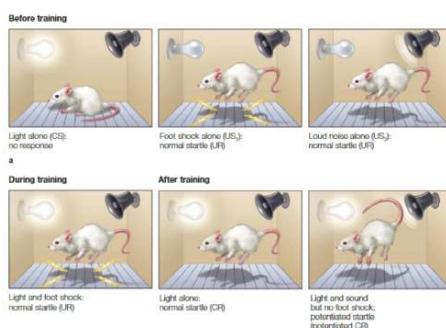


Figure 4.14

⁶Biologically programmed to be reinforcing; related to unconditioned response (US).

⁷Those we learn to be associated with *Primary*; they become reinforcers after learning.

⁸If this url doesn't work go to *jove.com*, log in with institutional credentials and search ‘*fear conditioning*’.

- Human:

See <https://app.jove.com/it/v/3893/extinction-training-during-the-reconsolidation-window-prevents-recovery-of-fear>.⁹

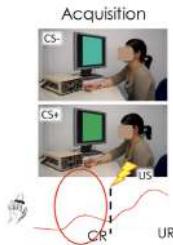


Figure 4.15

The experiment consists:

1. A person is seeing a monitor black and his skin conduction is monitored through sweating.
2. When a green screen appears (CS+) a shock is given.
3. When a blue screen appears (CS-) a shock is not given.¹⁰

Where:

- CR: (conditioned skin conduction response) sweating without shock (only seeing the green screen);
- US: shock;
- UR: sweating implied by the shock.

Note: sweating implies a skin conduction increment.

The image above shows the ‘*Acquisition*’ phase; as it can be seen from the videos there are different phases during an experiment. ‘*Acquisition*’, ‘*Extinction*’ (go back to normality) etc.

In particular, regarding this experiment, after a period, what is seeing here is that during the ‘*Acquisition*’ phase we have an increment of sweating before the shock is given, only seeing the green screen (note the red circle in the image above).

Different types of conditioned responses

The CR must be learned, while the UR takes place with no learning.

CR are *anticipatory responses*.

Response can be:

- physiological (e.g skin conduction response);

⁹If this url doesn't work go to *jove.com*, log in with institutional credentials and search ‘reconsolidation window prevents ...’.

¹⁰In general during an experiment is used always a CS- because it is necessary to have a base in comparison to the other.



Figure 4.16

- behavioral (*e.g.* running away);
- change in subjective experience.

Conditioned responses involves both *Parasympathetic branch* and *Sympathetic branch*.

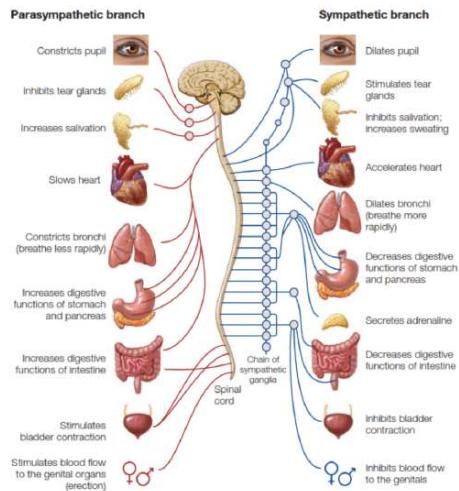


FIGURE 2.17 Organization of the autonomic nervous system, showing sympathetic and parasympathetic branches.

Figure 4.17

See <https://app.jove.com/it/v/52151/disrupting-reconsolidation-of-fear-memory-in-humans-by-a-noradrenergic.¹¹>

They measured the US expectancy in terms of blinking.

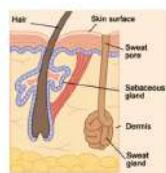
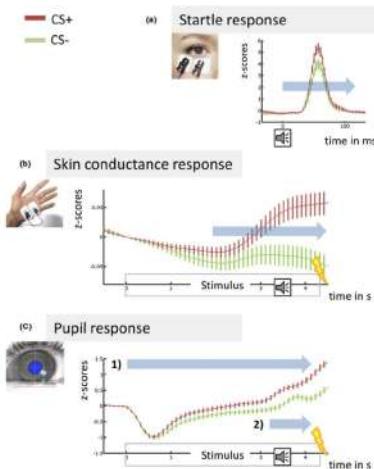


Figure 4.18

¹¹If this url doesn't work go to *jove.com*, log in with institutional credentials and search 'disrupting reconsolidation of fear memory ...'.

Let's see some different types of *physiological responses*.
 CR are *anticipatory, predictive* responses.



Leuchs, L., Schneider, M., & Spooraker, V. I. (2019). Measuring the conditioned response: A comparison of pupillometry, skin conductance, and startle electromyography. *Psychophysiology*, 56(1), e13283. <https://doi.org/10.1111/pyps.13283>

Figure 4.19

Adaptive nature of CR: predictive response

Regarding the *response* what is important is that has an *anticipatory nature*: if is a reward I prepare to catch it; if is a punishment I prepare to avoid it.

The animal respond to the CS with a CR that *prepares the animal for, or protects it from*, the predicted US.

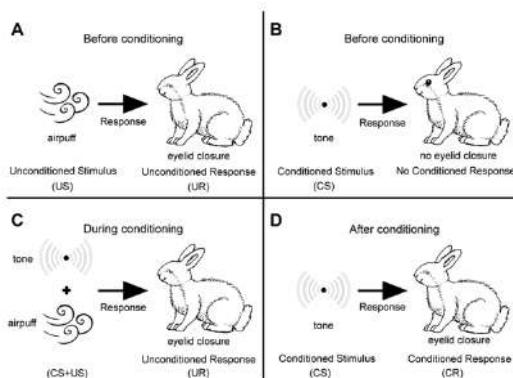
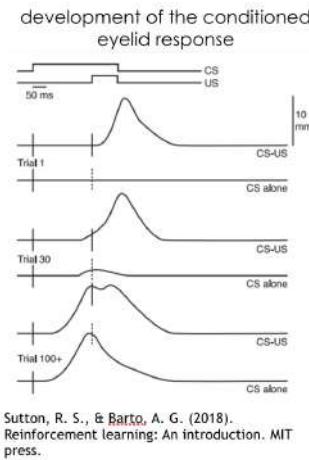


Figure 4.20

Looking at the image above the tone comes to trigger a CR consisting of membrane closure that begins before the air puff and eventually *becomes timed* so that peak closure occurs just when the air puff is likely to occur. This CR,

being *initiated in anticipation* of the air puff and appropriately timed, offers better protection than simply initiating closure as a reaction to the irritating US.



Sutton, R. S., & Barto, A. G. (2018). Reinforcement learning: An introduction. MIT press.

Figure 4.21

Looking at the image above starting from the top:

- CS \longleftrightarrow duration of the tone;
- US \longleftrightarrow airpuff comes;
- on the y-axis closure of eyes is measured;
- pay attention that the vertical line in the figures – which represent the trials – corresponds to the moment in which the US arrives;
- note at the end that also the timing changed, it is set automatically when the US was expected.

Classical conditioning depends on the stimuli degree correlation

Classical conditioning depends on the degree to which two stimuli are correlated.

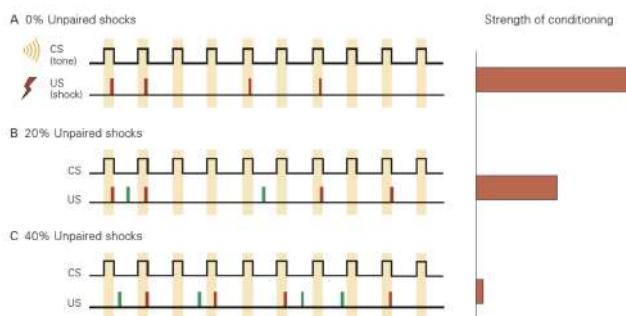


Figure 4.22

With *Strength of conditioning* in the image above we mean *Strength of CR*.

Acquisition

Before we saw and talked about different phases of the conditioning. Let's see them starting from *Acquisition*.

The probability of occurrence of a conditioned response increases if the CS is repeatedly presented with the US.

Adaptive mechanism ensures that an animal responds to cues that are meaningful to survival.

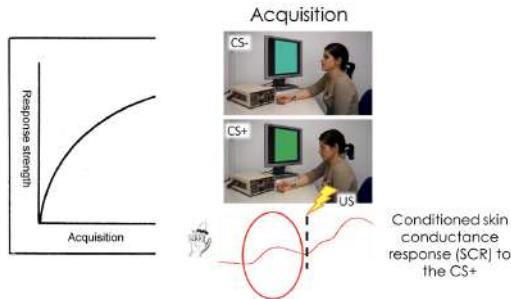


Figure 4.23

Extinction

The probability of occurrence of a conditioned response decreases if the CS is repeatedly presented without the US.

Why adaptive?¹²

Adaptive mechanism ensures that an animal stops responding to cues that are no longer meaningful to it.

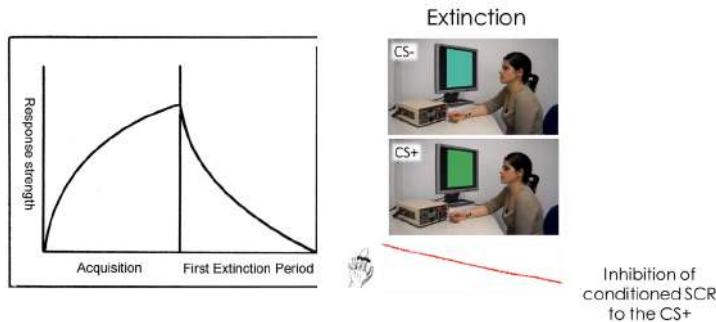


Figure 4.24

Extinction is not the same as forgetting, it is new learning

But how would you show that?

After extinction, the original CR can return under specific circumstances.

Let's see three different cases.

¹²If there is no more danger or no more food there is also no more need to spend energy.

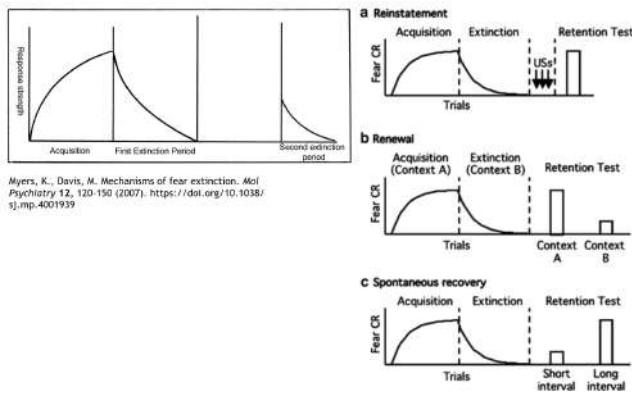


Figure 4.25

4.3 Neural bases

Functional magnetic resonance imaging (fMRI)

*Functional magnetic resonance imaging (fMRI)*¹³ measures the ratio of oxygenated to deoxygenated hemoglobin; this value is referred to as the blood oxygen level-dependent signal, or *BOLD signal*.¹⁴

Correlational evidence.¹⁵

Appropriate to know where things happen: high spatial resolution.

Inappropriate to know when things happen: poor temporal resolution.¹⁶

Below a useful video which introduces to Cognitive neuroscience:

<https://www.youtube.com/watch?v=4U0eBM5BwdY> (Understanding MRI: What is functional MRI (fMRI)?)

Lesional method

Study of the consequences resulting from brain lesions:

- natural occurring (*e.g.* tumor, stroke, degenerative disease);
- surgically induced to treat epilepsy;
- experimentally caused (only done in animals).

Causal evidence: which region is necessary for a given behavior or response.¹⁷

Regarding Figure 4.26 below remember that *white matter* contains axons (not cell bodies) which have myelin which is white.

¹³It shows essentially the brain activity; what parts of the brain are active under certain circumstances when brain does different things. Different from *Structural magnetic resonance* which shows the structure.

¹⁴Note that we're not measuring directly the neurons activity – for seeing this directly we should see electrical activity – but we infer it analyzing the oxygen level.

¹⁵Tells us about *correlation* not *causation*; doesn't tell us if a certain part is necessary for certain activity, but only that a part is active during an activity.

¹⁶Change in oxygen happens in relatively long interval of time.

¹⁷The fMRI seen in the previous subsection was a *correlation* method while this is a *causation* method.



FIGURE 3.7 Vascular disorders of the brain.
 (a) Strokes occur when blood flow to the brain is disrupted. This brain is from a person who had an occlusion of the middle cerebral artery. The person survived the stroke. After death, a postmortem analysis shows that almost all of the tissue supplied by this artery had died and been absorbed. (b) Coronal section of a brain from a person who died following a cerebral hemorrhage. The hemorrhage destroyed the dorsomedial region of the left hemisphere. The effects of a cerebrovascular accident 2 years before death can be seen in the temporal region of the right hemisphere.

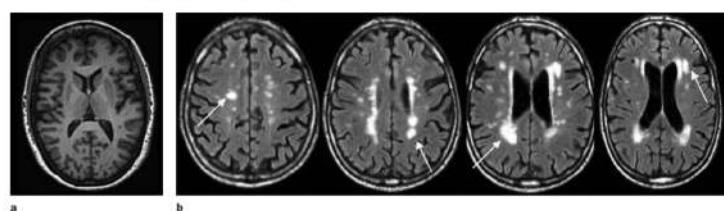


FIGURE 3.8 Degenerative disorders of the brain.
 (a) Normal brain of a 60-year-old male. (b) Axial slices at four sections of the brain in a 79-year-old male with Alzheimer's disease. Arrows show growth of white matter lesions.

Figure 4.26

Neural bases of aversive conditioning

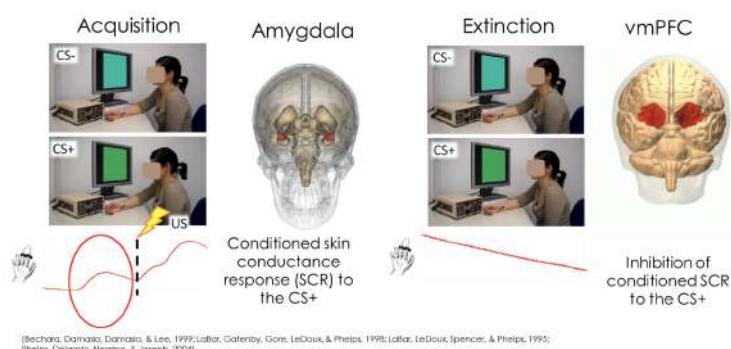


Figure 4.27

With *vmPFC* we refer to *ventral medial prefrontal cortex*.

Neural bases of aversive conditioning acquisition: the amygdala

Looking at the image below we can see an *high road* (yellow and orange lines passing through the cortex, related to *consciousness*) and a *low road* (yellow and orange lines not passing through the cortex and arriving directly to the amygdala, related to *unconscious/subconscious*).

Remember that sensations come from peripheral nervous system to the central and remember that everything passes through the thalamus before going to other

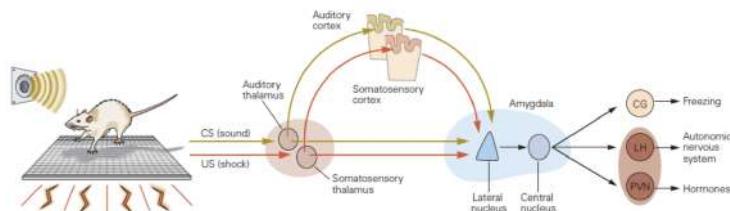


Figure 48-5 Neural circuits engaged during fear conditioning. The conditioned stimulus (CS) and unconditioned stimulus (US) are relayed to the lateral nucleus of the amygdala from the auditory and somatosensory regions of the thalamus and cerebral cortex. Convergence of the CS and US pathways in the lateral nucleus is believed to underlie the synaptic changes that mediate learning (see Figure 49-6). The lateral nucleus communicates with the central nucleus both directly and through intra-amygdala pathways (not shown) involving the basal and intercalated nuclei. The central nucleus then connects with regions that control various motor responses, including the central gray region (CG), which controls freezing behavior, the lateral hypothalamus (LH), which controls autonomic responses, and the paraventricular hypothalamus (PVN), which controls stress hormone secretion by the pituitary-adrenal axis. (Reproduced, with permission, from Medina et al. 2002.)

Figure 4.28

zones.

We have *redundancy*: the same type of information is processed in two different ways (high and low roads in fact).

See next subsection to understand why the amygdala receives inputs from two different pathways.

The amygdala receives sensory input along two pathways

The *low road* allows for the amygdala to receive information quickly in order to prepare the amygdala for a rapid response if the information from the *high road* confirms that the sensory stimulus is the CS.

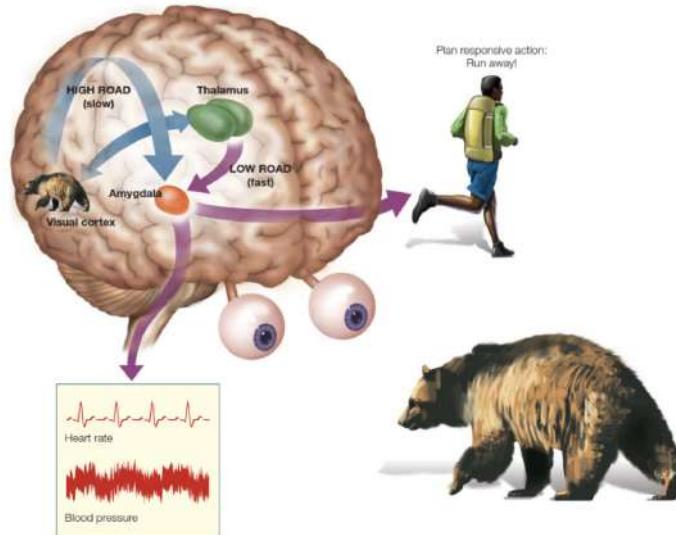


FIGURE 10.10 The amygdala receives sensory input along two pathways. When a hiker chances upon a bear, the sensory input activates affective memories through the cortical "high road" and subcortical "low road" projections to the amygdala. Even before these memories reach consciousness, however, they produce autonomic changes, such as an increased heart rate, blood pressure, and a startled response such as jumping back. These memories also can influence subsequent actions through the projections to the frontal cortex. The hiker will use this emotion-laden information in choosing his next action: Turn and run, slowly back up, or shout at the bear?

Figure 4.29

Neural bases of aversive conditioning acquisition: the amygdala

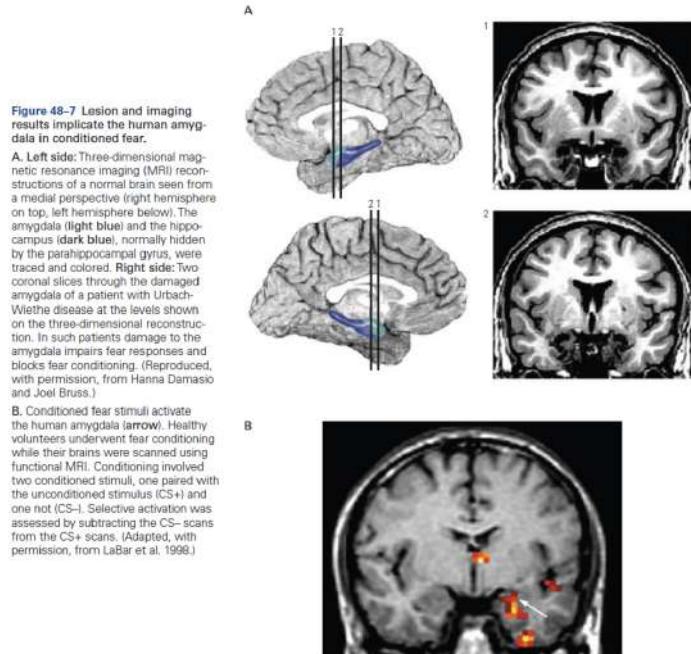


Figure 4.30

Till now we saw that amygdala is involved in conditioning. But is it necessary? Reading also the final part of explanation *A*. *Left side* of the above figure, the answer to the previous question seems to be ‘yes’ for fear conditioning. See also the next experiment.

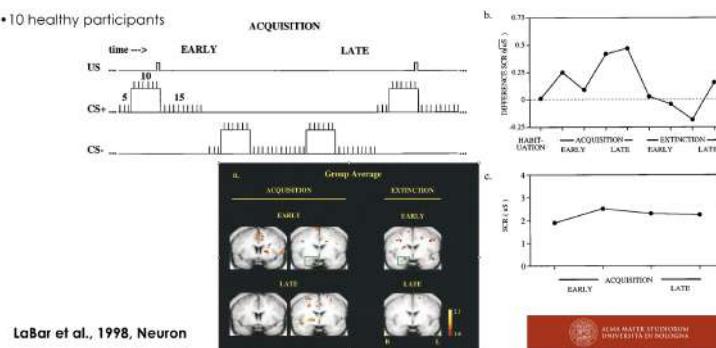


Figure 4.31

In the above experiment we have 10 healthy participants that are involved in a fear conditioning process.

We have a CS+ (paired with the US) and a CS- ‘control stimulus’ (not paired with the US).

Conditioned skin conductance response (SCR) is monitored.

In the black figure we highlight that the green square points to the amygdala. In particular looking at the *b.* graph on the right we can see the *DIFFERENCE SCR*: I measure how much you sweat to the conditioned stimulus subtracted how much you sweat to the control stimulus; so difference in the response to the conditioned stimulus and control. So if the difference is:

- above 0: we are responding more to the conditioned stimulus;
- below 0: more to the control stimulus.

Let's see another experiment. This other experiment to understand if the amygdala is only activated or it is necessary for the conditioning; for this scope we put both healthy and non healthy participants (this last is the so called control group, to have a reference); to have a more complete experiment another group is missing: not healthy people that have lesions in other parts of the brain for seeing if other parts other than amygdala participate to inactivate fear conditioning. In particular, here we have:

- 26 participants with temporal lobectomy;
- 23 healthy control participants;
- Pavlovian fear conditioning task:
 - CS: 2 tones;
 - US: white noise burst;
- No deficit when explicitly reporting the CS-US association.

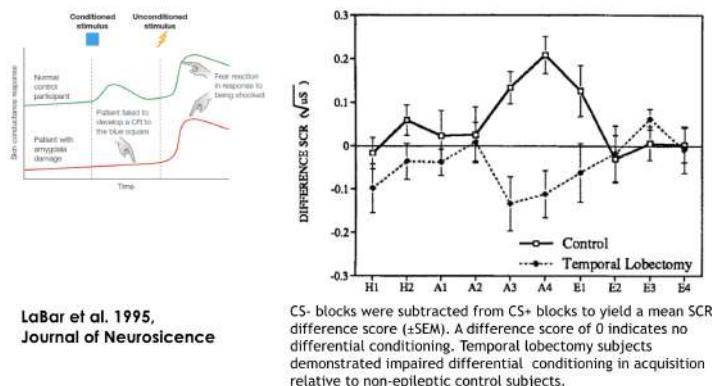


Figure 4.32

Looking at the image above at right we have that A1, A2, A3, A4 temporal segment is related to acquisition while E1, E2, E3, E4 temporal segment is related to extinction.

In this case patients with temporal lobectomy (amygdala involved) don't show difference in skin conduction but they are able to recognize the stimulus paired with the shock and the other that is not paired.

Instead patients with *hippocampal* lesions show the opposite behaviour/pattern: they are not able to recognize what stimulus shocks them but they show *DIFFERENCE SCR* (see next subsection).

These last two considerations imply that different aspects of conditioning are controlled from different brain region.

Neural bases of aversive conditioning acquisition: the hippocampus

In patients who had bilateral damage to the hippocampus but an intact amygdala, the opposite pattern of performance emerged. These patients showed a normal skin conductance response to the CS, indicating acquisition of the conditioned response. When asked what had occurred during conditioning, however, they were unable to report that the CS was paired with a US.

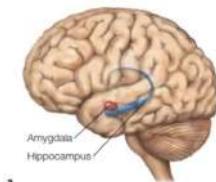


Figure 4.33

Neural bases of aversive conditioning acquisition

Double dissociation between patients who have amygdala lesions and patients with hippocampal lesions.¹⁸

The amygdala is necessary for the implicit¹⁹ expression of conditioning.

The hippocampus is necessary for the explicit or declarative expression of conditioning.

Neural bases of aversive conditioning

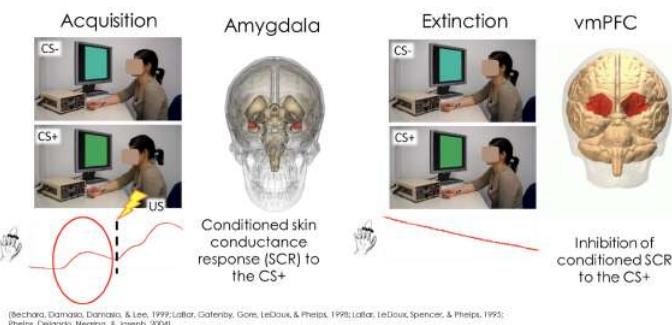


Figure 4.34

¹⁸When we find that a region is responsible for one process but not another and the other region shows the opposite pattern we call this *Double dissociation*.

¹⁹Because they don't show difference in sweating?

The *vmPFC* is related to *inhibition* (see next subsection).

Neural bases of aversive conditioning: the vmPFC

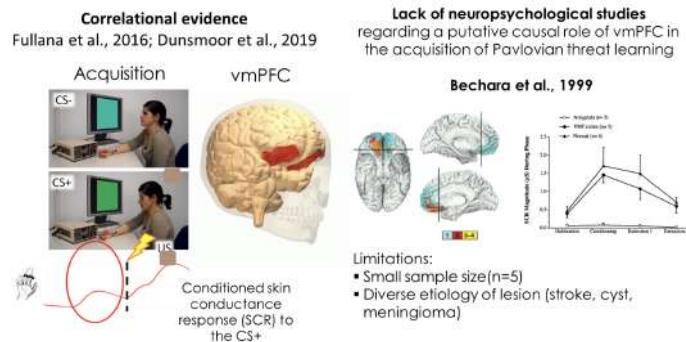


Figure 4.35

Regarding the left part of the image above we saw that the *vmPFC* was active during the extinction phase (correlational evidence).

Regarding the right part of the image above we can say that is a rough study: as it can be seen we have only 5 patients for the group that had lesions to the amygdala, 5 patients for the group that had lesions to the VMF cortex and 6 normal patients; furthermore, if we look at the graph paying attention to the normal group and the VMF cortex group, we can see a very similar behaviour, so nothing very important can be deducted; finally, if we look at the amygdala group behaviour in the graph, we can see that patients don't show any conditioning response.

Methods: Participants

Table 1. Demographic characteristics and neuropsychological assessment for all groups.

Demographics		vmPFC (n = 8)	BDC (n = 10)	HC (n = 10)	test	df	p	η_p^2
Age (yrs)		57.25 ± 6.25	51.10 ± 14.37	67.90 ± 7.87	F=6.69	2, 25	0.005 ⁺	0.34
Education (yrs)		10.5 ± 2.67	13.30 ± 4.37	13.00 ± 2.45	F=1.83	2, 25	0.18	0.12
Chronicity (yrs)		5.87 ± 4.94	2.80 ± 2.20	-	F=3.13	1, 16	0.09	0.16
Sex (m/f)		6/2	6/4	4/6	X ² =1.27	2	0.32	-
Neuropsychological assessment								
	vmPFC (n = 8)	BDC (n = 6)	-	F	df	p	η_p^2	
Raven Progressive Matrices*	3.05 ± 0.75	3 ± 1.09	-	1.02	1, 12	0.33	0.07	
Stroop Test*	2.25 ± 1.91	2.5 ± 1.04	-	0.08	1, 12	0.77	0.007	
Towers of London [#]	99.14 ± 16.40	104 ± 13.56	-	0.33	1, 11	0.57	0.02	
Digit Span*	3.75 ± 0.46	3.16 ± 1.60	-	0.97	1, 12	0.34	0.07	
Phonemic Fluency*	3.25 ± 1.16	3.16 ± 1.32	-	0.02	1, 12	0.90	0.001	
Semantic Fluency*	3.75 ± 0.74	3.66 ± 0.81	-	0.48	1, 12	0.49	0.03	

All measures are reported as mean ± standard deviation, except for Sex, reported as frequency. vmPFC = ventromedial prefrontal cortex lesion group; BDC = brain damaged control group; HC = healthy control group. *Equivalent score.

[#]Standard score. Post-hoc analysis reported a significant difference between BDC and HC p=0.01 and vmPFC vs HC p=0.02; vmPFC vs BDC was not significant p=0.8.

Figure 4.36

This experiment aim was to show that vmPFC was not responsible for acquisition but in the end showed that this is not true (see ahead also); so whether vmPFC is only necessary for extinction and not for acquisition is still an open question: because we have one study (this) that contrast with the previous evidence (*e.g* Fullana 2016; Dunsmoor 2019); but to confirm this we should have replications.

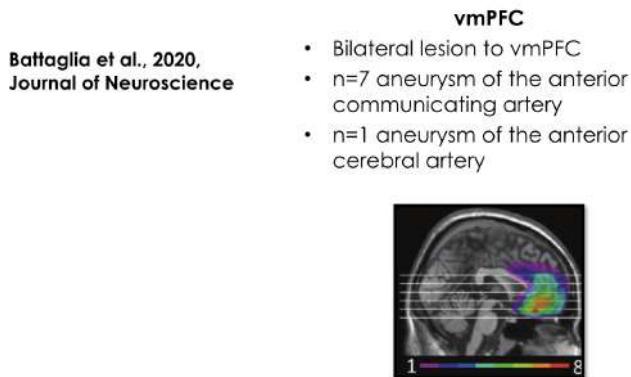


Figure 4.37

Methods: Pavlovian threat learning task

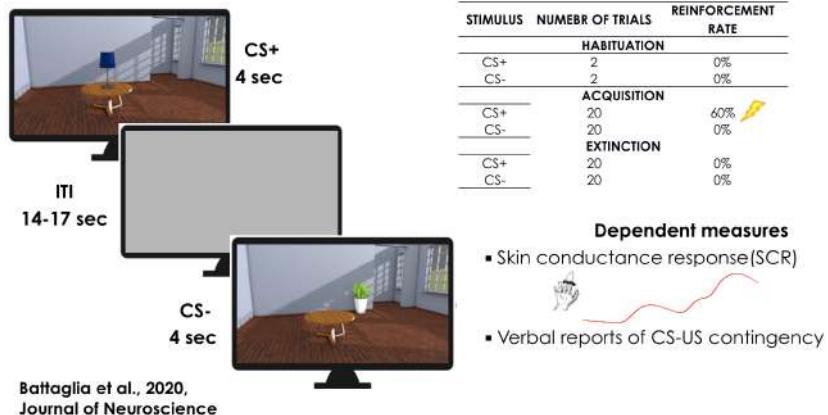


Figure 4.38

Referring to the image above we have:

- CS+ ↔ associated with shock;
- CS- ↔ not associated with shock;
- the experiment measured the skin conductance response;
- with '*Verbal reports*' we mean that we asked to report what stimulus was associated to the shock.

Results: conditioned SCR during acquisition

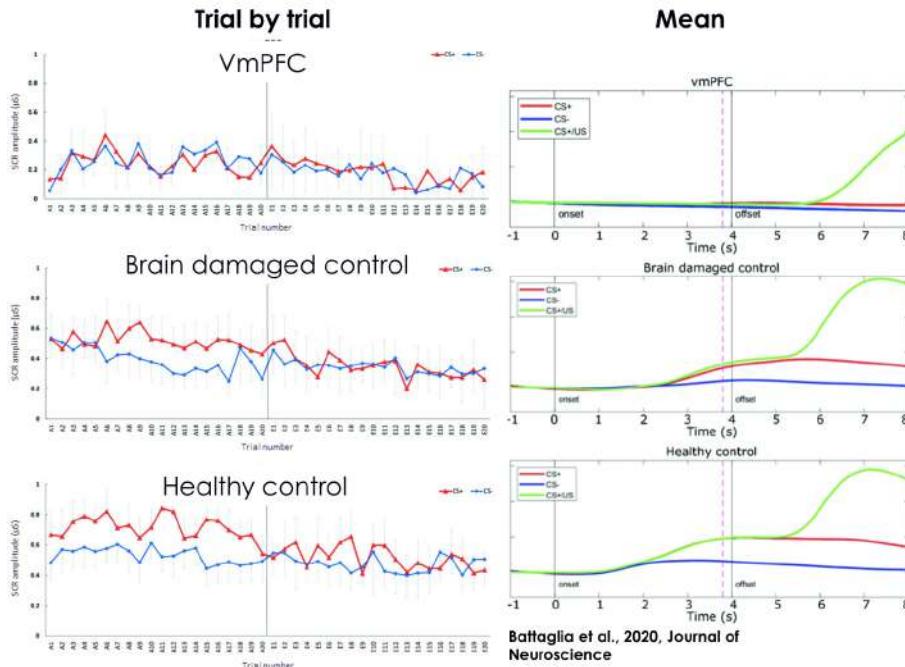


Figure 4.39

Looking at the image above, paying attention to the left side graphs, we have that for the first graph (from up to bottom) we have that here doesn't happen the same as below: no difference in the response of CS+ and CS-.

For the other two graphs: here basically the red line is above the blue one; they respond more at CS+.

Paying attention to the right side graphs, we have that the vertical lines indicate the moment in which the shock is given.

The first graph shows that the members of the vmPFC group produce a response to the shock but, before it was given, notice the difference with the other two graphs (and so with the Brain damaged control group and the Healty control group): they are not able to learn.

Regarding the other two graphs we can see a very similar behaviour, noticing that at the end of acquisition (look at the time interval from 1 to 4) there is a response before the shock.

Generalization

Other stimuli that are not involved in the initial learning process and that resemble the original CS come to elicit a CR.

Adaptive or maladaptive?

Below a usefull video which regards '*fear generalization*:

<https://www.youtube.com/watch?v=G5QAKnMf4Xc> (Fear generalization)²⁰

²⁰Note that generalization regards not only fear but also rewards; more generally: all the

Generalization: perceptual similarity

Generalization starts when a person begins to produce a CR not only in response to the CS but also to stimuli that are similar to it. This generalization can happen along different dimensions: one is *perceptual similarity* (stimuli are similar in perceptual properties *e.g.* colors, emotional expressions, as in the following experiment).

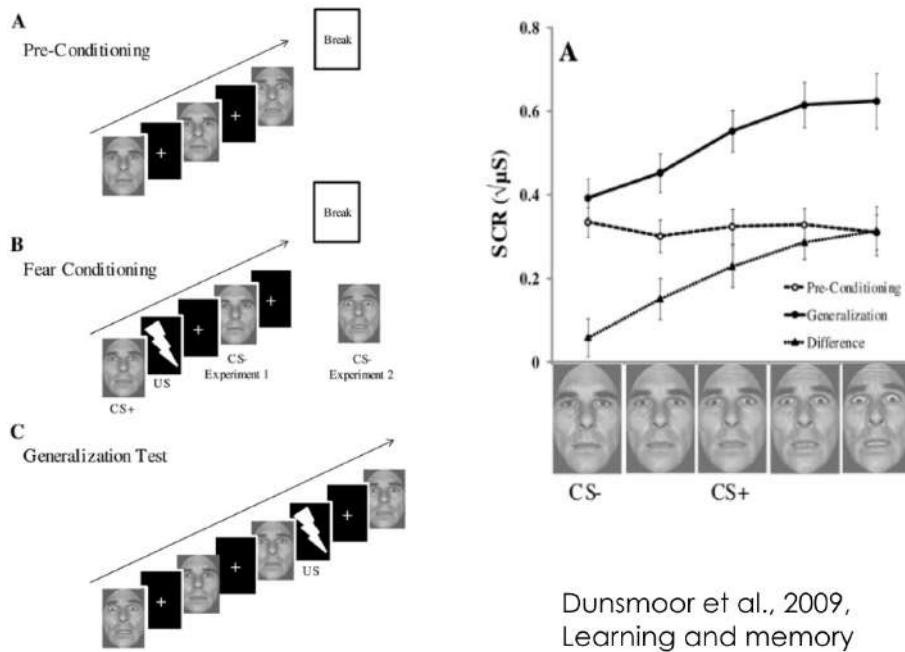


Figure 4.40

Regarding the figure above, focusing on the graph on the right: the Generalization trend responds less to the CS- (look at the initial segment part), responds more to the CS+ (look at the middle segment part), but also responds significantly to stimuli that are similar to the CS+ (look at the final segment part).

Instead the Pre-Conditioning trend shows no significant skin conductance response depending on what face/expression.

Generalization: conceptual similarity

Referring to the image below, figure at the left, we have that for the first case (the top case) the shock is given together with the tools: here we have a *semantic* category of objects (tools) which are perceptually very different but conceptually very similar.

For the second case the shock is given together with the animals: here we have a *semantic* category of animals.

The conceptual similarity capacity is probably related to intelligence; probably a mouse is not able to do that.

processes we talked about for aversive stimuli in fear conditioning also apply for rewards.

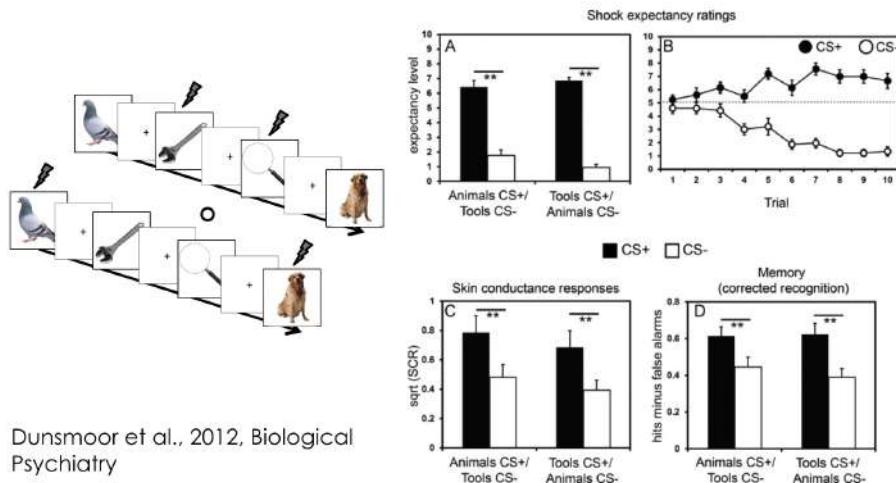


Figure 4.41

Another experiment.

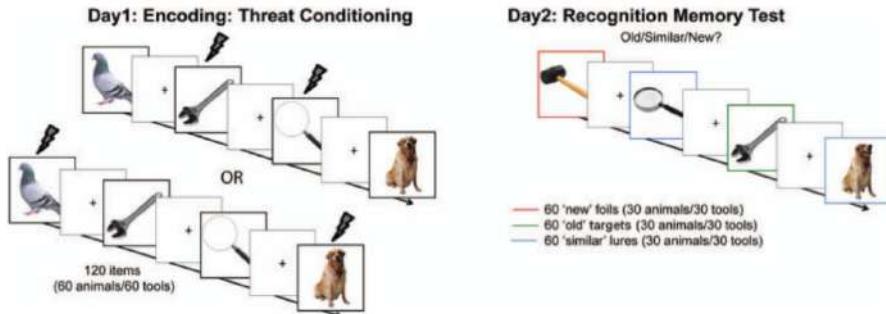


Figure 1. Behavioral task paradigm. During conditioning, participants rated shock expectancy; shocks were paired with 30 out of 60 animal or tool pictures (counterbalanced across participants). During the memory test, participants indicated whether the presented picture was new, old or similar. Colored borders are for illustrative purposes, and not part of the stimuli shown to subjects. See the online article for the color version of this figure.

Figure 4.42

This is a memory test: after a certain period of time the experiment with CS are repeated.

What emerged was:

- from one side the response is ‘*stronger*’;
- but memory get confused: also object that wasn’t shown during the experiment (but belonging to the same category) are able to induce a response and the subject believed to have seen them during the experiment.

See also next images.

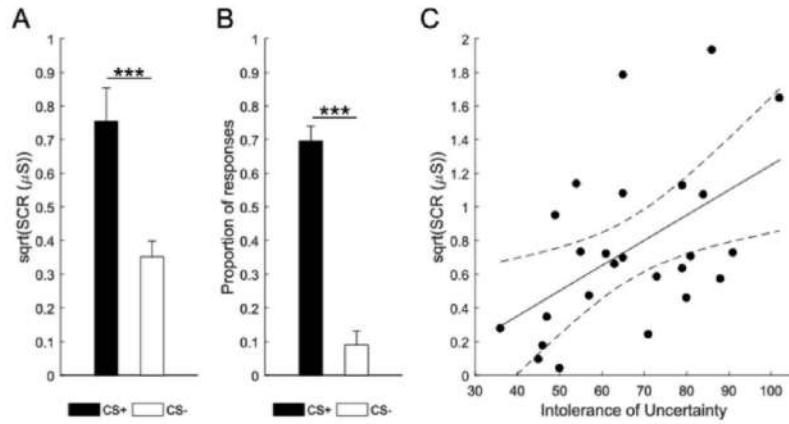


Figure 2. Acquisition of threat conditioning and correlation between intolerance of uncertainty and skin conductance response (SCR). Acquisition of threat conditioning was shown by higher mean square-root-normalized SCR in μS (A) and higher shock expectancy (B) on CS+ than CS- trials. Error bars represent standard error of the mean, *** $p < .001$, two-tailed paired-samples t test. In addition, intolerance of uncertainty predicted mean square-root-normalized SCR in μS to the conditioned category (C). Dashed lines represent 95% confidence interval, $p < .05$, simple linear regression.

Starita et al., 2019, Journal Experimental Psychology: General

(a)

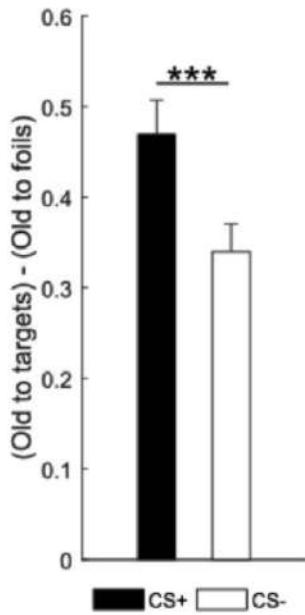


Figure 3. Recognition memory. Bias corrected item recognition score (i.e., responding old to targets minus responding old to foils) showed better recognition of items from the CS+ than CS- category. Error bars represent standard error of the mean. *** $p < .001$, two-tailed paired-samples t test.

(b)

Figure 4.43

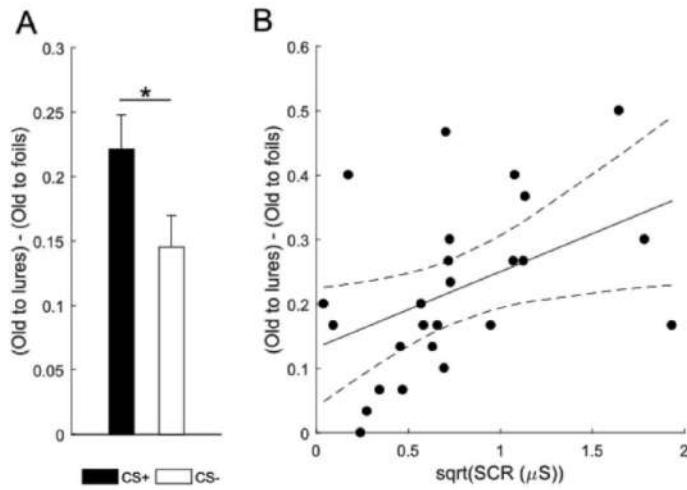


Figure 4. Episodic memory generalization and its correlation with arousal for the conditioned category. (A) Episodic generalization score (i.e., responding old to lures minus responding old to foils) was greater for items from the CS+ than the CS- category. Error bars represent standard error of the mean. * $p < .05$, two-tailed paired-samples t test. (B) Mean square-root-normalized SCR in μS to the conditioned category predicted episodic memory generalization score for the conditioned category. Dashed lines represent 95% confidence interval, $p < .05$, simple linear regression.

Figure 4.44

4.4 Instrumental conditioning

Associative learning

The animal learns about the relationship between:

- A stimulus and an outcome: Pavlovian or classical conditioning;



Figure 4.45

- a behavior and an outcome: instrumental or operant conditioning.



Figure 4.46

Instrumental conditioning involves associating an action with an outcome

Discovered by Edgar Thorndike (1874 – 1949, was an American psychologist) and systematically studied by B. F. Skinner (1904 – 1990 was an American psychologist, behaviorist, author, inventor, and social philosopher) and others. Thorndike's Law of effect:

'Of several *responses* made to the same situation, those which are accompanied or closely *followed by satisfaction* to the animal will, other things being equal, be more firmly connected with the situation, so that, when it recurs, they *will be more likely to recur*; those which are accompanied or closely *followed by discomfort* to the animal will, other things being equal, have their connections with that situation weakened, so that, when it recurs, they *will be less likely to occur*. The greater the satisfaction or discomfort, the greater the strengthening or weakening of the bond.' (Thorndike, 1911)

Skinner Box



Figure 4.47

Below a useful video that explain the '*Skinner Box*'.

<https://www.youtube.com/watch?v=PQtDTdDr8vs> (Skinner Box - Lever Press)

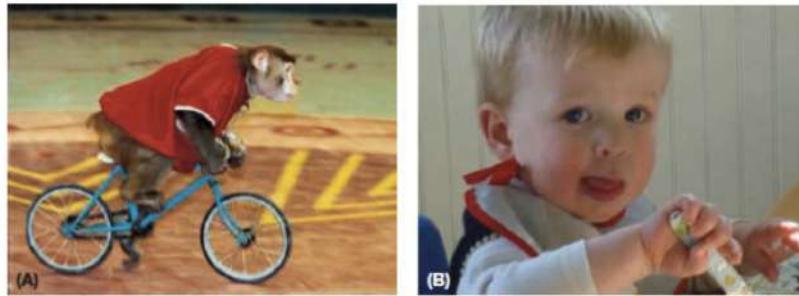
At the beginning the rat is put in the chamber.

After exploring, after some time he discoveres that pressing the lever gets food; so he learns (obviously after a certain number of repetition) that doing this action he obtains a reward.

From the video is not properly visible but the rat gets food any time that do the action, pressing the lever.

Shaping

An existing response is gradually changed across successive trials towards a desired target behavior by reinforcing exact segments of behavior.
Reinforcement of successive approximations (of the behaviour).²¹



7.23 Shaping (A) Nhat, a four-year-old monkey with the Hanoi Circus, was trained using techniques essentially identical to those described in the text—a process of gradual shaping that leads to the desired response. (B) Parents use shaping to teach their children to eat with utensils. As the parents' demands gradually increase, the child's behavior comes closer and closer to the "standard" pattern of using the spoon and fork.

https://www.brainkart.com/article/Instrumental-Conditioning--The-Major-Phenomena-of-Instrumental-Conditioning_29319/

Figure 4.48

The nature of the reinforcement shapes behavior

Remember: reward increases the probability of behaviour performance; punishment decreases the probability of behaviour performance.

Positive: we deliver something.

- Positive reinforcement:²²
 - delivery of rewarding outcome increases the probability of emitting the action.
- Positive punishment:²³
 - delivery of aversive outcome decreases the probability of emitting the action.²⁴

²¹If we want to train a complex behaviour it is unlikely that it will be learned immediately; so we use *shaping*: in order to teach the complex behaviour we divide it in smaller steps and we gradually reinforce each step. For example if we want to teach a child to use a fork: at the beginning he eats with hands and we say: 'No it's bad! Take the fork!'; when he takes the fork we say: 'Good boy! Take the fork!' (reinforcement).

²²Note the word '*reinforcement*' means '*increase the probability*'.

²³Note the word '*punishment*' means '*decrease the probability*'.

²⁴For example if we drive too fast we get traffic ticket.

Negative: we take something away.

- Negative reinforcement:
 - omission of aversive outcome increases the probability of emitting the action.²⁵
- Negative punishment:
 - omission of rewarding outcome decreases the probability of emitting the action.

Activity: everyday life examples.



Figure 4.49

The frequency of the reinforcement also shapes behavior

Continuous reinforcement:²⁶

- the desired behavior is reinforced every single time it occurs;
- most effective when trying to teach a new behavior.²⁷

Partial reinforcement:

- the response is reinforced only part of the time;²⁸
- behaviors are acquired more slowly with partial reinforcement, but the response is more resistant to extinction.²⁹

²⁵For example when we are in the car and we don't put the seatbelt usually an annoying sound begins repeatedly and putting the seatbelt stop the sound.

²⁶Previous mouse example (Skinner Box).

²⁷But it extinguishes fast: for example if I give you food every time you do something, after a little bit you don't want food anymore because you are full, and then 'food' lose its value and the 'power' to shape the behaviour

²⁸Some time is reinforced, some time not.

²⁹Essentially because you have to work harder in comparison to continuous to get reward (see ahead).

Four schedules of partial reinforcement

1. *Fixed-ratio*: a response is reinforced only after a *specified number of responses*. This schedule produces a high, steady rate of responding with only a brief pause after the delivery of the reinforcer.



First learning ratio training, 2 lever presses for 1 food

Pressing the lever 10 times to get 1 reward

Figure 4.50

Looking at the image above, figure at left, we can see the related video here:

<https://www.youtube.com/watch?v=Edf1yDFrBSk> (Eddy - ratio training, beginning)

In the video is clear that the mouse understood that he needed to press 2 times the lever after getting food; so he pressed 2 times consecutively and then he goes to see if there is the food.

Looking at the image above, figure at right, we can see the related video here:

https://www.youtube.com/watch?v=QTweW_LVR3Y (Eddy - ratio training)

The same as the previous in this video: the rat repeats compulsively the action many times and only after then he goes to the food.

2. *Variable-ratio*:³⁰ a response is reinforced after an *unpredictable number of responses*. This schedule creates a high steady rate of responding.³¹
3. *Fixed-interval*: a response is reinforced only after a *specified interval of time*. This schedule causes high amounts of responding near the end of the interval but slower responding immediately after the delivery of the reinforcer.³²
4. *Variable-interval*: a response is reinforced only after an *unpredictable interval of time*. This schedule produces a slow, steady rate of response.

³⁰For example lottery.

³¹But a risk is that it can create compulsively behaviours.

³²Animals can encode time.

Partial reinforcement everyday life

Can you think about some examples?

- *Fixed-ratio*: Supermarket points, videogames.
- *Variable-ratio*: gambling, lottery games.



Figure 4.51

Conclusion

Before concluding this chapter we propose an useful video which resumes what we've seen.

https://www.youtube.com/watch?v=qG2SwE_6uVM (How to Train a Brain: Crash Course Psychology #11)

Chapter bibliography

Kandel, *Principles of Neural Science, Sixth Edition*, McGraw-Hill, 2021. Chapter 48, Section *The Amygdala Emerged as a Critical Regulatory Site in Circuits of Emotions*. Chapter 65, Section *Implicit Memory Can Be Associative or Non-associative*, Section *Classical Conditioning Involves Associating Two Stimuli*, Section *Operant Conditioning Involves Associating a Specific Behavior with a Reinforcing Event*.

Sutton, R. S. & Barto, A. G. *Reinforcement learning: An introduction.*, MIT press, 2018. Chapter 14.

Chapter 5

Reinforcement learning: part one

Behavior can be controlled by reward or punishment, and environmental stimuli that predict them

Associative learning is learning about the association of at least *two stimuli or events*.



Figure 5.1

Associative learning is the way in which an animal learns to predict events

Change in response is caused by learning about the association of at least *two stimuli or events*.

Maximize rewarding outcomes and minimize aversive outcomes to increase chances of survival.

Conditioned responses are anticipatory, predictive responses

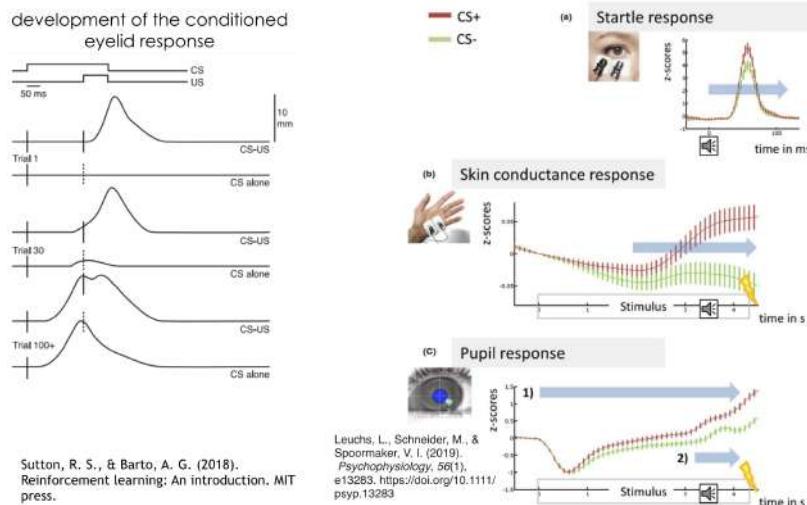


Figure 5.2

5.1 Associate stimuli/actions to outcomes

Associative learning is learning about contiguity and contingency

- **Contiguity:** closeness in time between stimulus/behavior and outcome. Stimuli that are close to one another in time become associated.¹
- **Contingency:** causal relationship between stimulus/behavior and outcome. When one stimulus depends on the other, they will become associated → Predictive value critical.

Temporal contiguity: the temporal relation between the CS and US is critical for learning

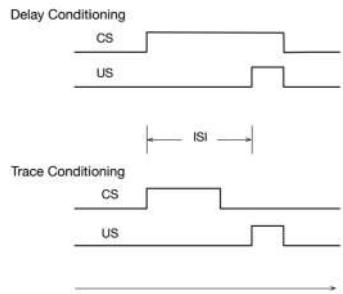


Figure 5.3

¹At the beginning was thought that only *Contiguity* contributed to associative learning.

The closer in time two events occur, the more likely they will become associated.
Delay vs trace conditioning.

- *Delay conditioning:*

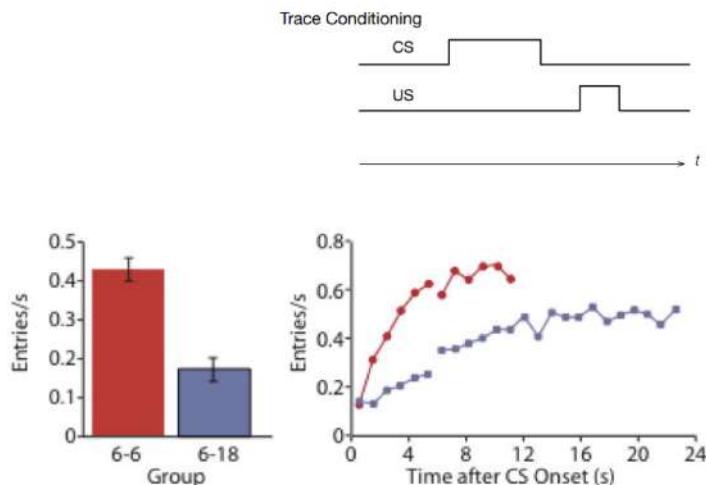
- the CS extends throughout the interstimulus interval (ISI), which is the time interval between the CS onset and the US onset (often with the CS and US ending at the same time as shown here).²

- *Trace conditioning:*

- there is a time interval, called the trace interval, between CS offset and US onset;
- assumes that a trace of the CS remains when the US arrives. So, learning occurs through the simultaneous presence of the trace and the US;
- *learning does not occur across long trace intervals.*³

Evidence for contiguity learning: delay vs trace conditioning

When this CS-US interval⁴ is lengthened, a decrement in conditioning is observed. Meaning that it takes more trials for the conditioned response (CR) to appear, and CR strength is often reduced.



Balsam, P. D., Drew, M. R., & Gallistel, C. R. (2010). Time and Associative Learning. *Comparative cognition & behavior reviews*, 5, 1–22. <https://doi.org/10.3819/ccbr.2010.50001>

Figure 5.4

Experiment:

²Generally the strength in the response is greater in *Delay conditioning*.

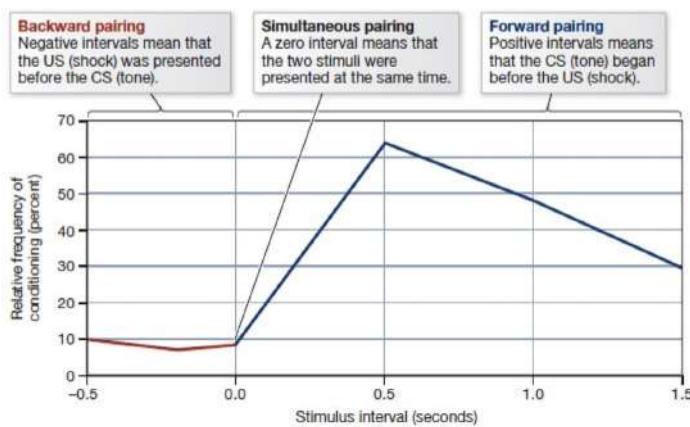
³Look at image above at the CS part of the *Trace conditioning* graph: after the CS terminates we have a trace there which makes in some way the CS still present in our perception.

⁴With CS-US interval we refer to the interval that goes from the end of the CS to the beginning of US.

- 2 groups of rats were exposed to a 6 s tone CS, followed by pellet delivery after:
 - 6s (red data);
 - 18s (purple data).
- Anticipatory head entries into the feeding hopper were recorded.

Evidence for contiguity learning

(Rescorla, 1988)



7.10 The CS-US interval in classical conditioning The figure shows the results of a study of the effectiveness of various CS-US intervals in humans. The CR was a finger withdrawal response, the CS a tone, and the US an electric shock. The time between CS and US is plotted on the horizontal axis; negative values indicates that the CS arrived after the US. The vertical axis indicates the strength of conditioning.

https://www.brainkart.com/article/Classical-Conditioning--The-CS-as-a-Signal-_29311/

Figure 5.5

Early theories of Pavlovian conditioning took for granted that CS-US contiguity was the critical determinant of learning

Contiguous relations are important because *only closely spaced presentations of the CS and US allow for their mental representations to be simultaneously active and learned about*.

If a long trace interval is introduced, then the CS representation will have decayed by the time the US is presented and thus the CS will not be learned about. (McNally & Westbrook, 2006).

Contiguity learning in the nervous system: the case of Hebbian plasticity

We've seen how closeness in time between CS and US is important for learning; let's see how this is implemented in the nervous system.

Plasticity:

- neural connections can be modified by experience and learning;
- learning is the result of changes in the strength of synaptic interactions among neurons in neural networks;
- changes in the strength of synaptic interactions can be:
 - Functional alterations, physiological changes,⁵ are typically short-term and result in changes in the efficacy of existing synaptic connections.⁶
→ Hebbian plasticity;
 - anatomical alterations are typically long-term and consist of the growth of new synaptic connections between neurons.

In 'The Organization of Behaviour' (1949) Hebb (Donald Hebb, 1904-1985, Canadian psychologist) proposed a mechanism to explain synaptic plasticity. Hebb's Law: *Neurons that fire together, wire together.*

It describes how, when a cell persistently activates another nearby cell, the connection between the two cells becomes stronger.

Below an useful video that talks about '*Habituation/Sensitization*' that are type of learning but they are *not associative* because we have only one stimulus: in this case we only repeatedly touch the *Siphon of the Aplysia* and response of the *Aplysia Gill withdrawal* becomes weaker (habituation).

In general you repeatedly do something/stimulate and the response to that stimulus decreases.

But in addition to this the *Gill withdrawal* response can be conditioned, we can apply another stimulus: *e.g.* the touching of *Siphon* associated to another stimulus is going to conditionate the response of the *Gill*.

See the following until 3'05".

<https://www.youtube.com/watch?v=D-OLQaujK68&t=141s> (Sensitization in Aplysia)

Classical conditioning of withdrawal reflexes in Aplysia (see the figure below).

- (A) Learning. Activity in one sensory neuron (SN1) is paired (CS1) with the reinforcing stimulus (US). Activity in SN2 is unpaired (CS2) with the US. The US itself acts 2-fold by activating the motor neuron directly, thus producing the unconditioned response (UR), and by activating a modulatory system (facilitatory neuron) that nonspecifically enhances the synaptic strength of both sensory neurons. The paired activity in SN1 results in a selective amplification of the facilitation caused by the US.⁷

⁵For example change in the amount of neurotransmitter released.

⁶There is already connection between neurons.

⁷Referring to the previous video we describe specifically what the description above means. CS+ could be for example the electric shock which stimulate SN1; CS- is the *controll condition* (I don't apply a conditioned stimulus, thus -); SN2 is a neuron which is not stimulated by a CS, it is a *controll neuron*, (it is only stimulated by the *Facilitatory neuron*); UR is the *Gill*

- (B) Memory. As a result of paired activity in (A), the synaptic strength in the SN1 is enhanced, which increases its probability to activate the motor neuron and to produce the conditioned response (CR). Because activity in SN2 was unpaired with the US, the connection of SN2 is not specifically enhanced.

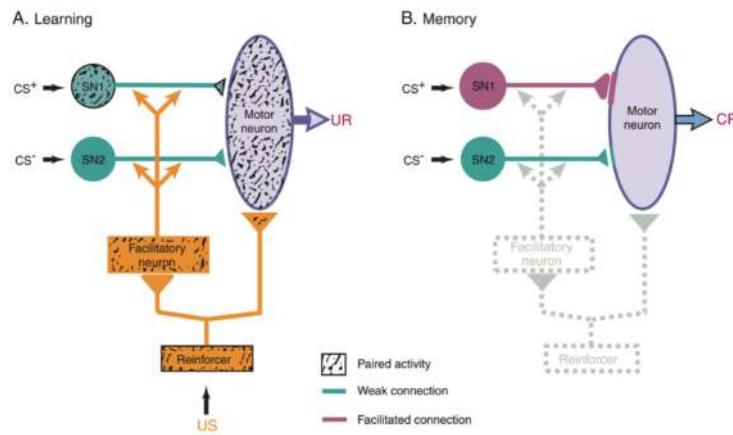


Figure 5.6

Hebbian plasticity and classical conditioning

The conditioned eyelid response.

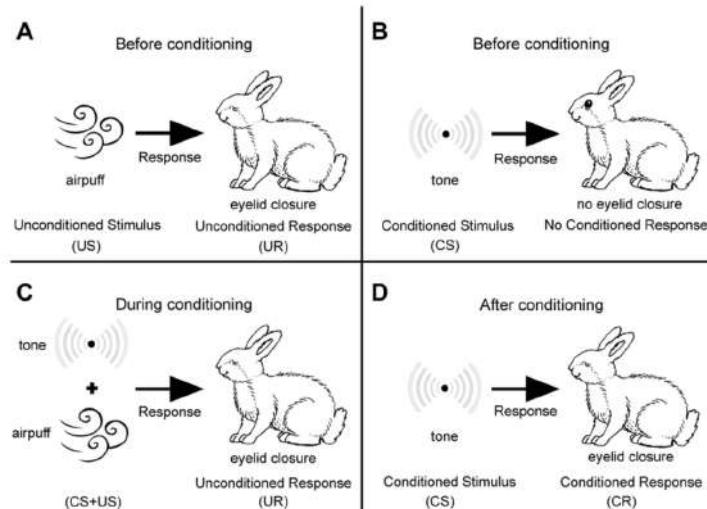


Figure 5.7

withdrawal response; Reinforcer: touch of the *Syphon* is gonna activate neuron that directly acts on motoneuron (right flow triggered by reinforcer), at the same time the touch activate another neuron which is associated to sensory neurons (left flow triggered by reinforcer).

The tone comes to trigger a CR consisting of membrane closure that begins before the air puff and eventually becomes timed so that peak closure occurs just when the air puff is likely to occur.

Below a video that presents the explanation of *what* happens.

<https://www.youtube.com/watch?v=-wakk5Iwqj8&t=7s> (PSY210 CH13PT5: Hebbian Plasticity)

To see *how* (at the cellular level) happens see the next video (from 3'40" to 11'38").

<https://www.youtube.com/watch?v=W0H32ISbk0w> (PSY210 CH13PT6: Long Term Potentiation)

Associative learning is learning about contiguity and contingency

- *Contiguity*: closeness in time between stimulus/behavior and outcome. Stimuli that are close to one another in time become associated.⁸
- *Contingency*: causal relationship between stimulus/behavior and outcome. When one stimulus depends on the other, they will become associated → Predictive value critical.

They are both necessary.

Challenging the contiguity assumption

In the 1960's and 70's, evidence began to accumulate that posed a challenge to the simple contiguity assumption.

The phenomena of:

- The truly random control (Rescorla, 1968);
- Blocking (Kamin, 1968).

Showed that repeated *temporal contiguity* between a conditioned stimulus (CS) and an unconditioned stimulus (US) *did not necessarily lead to learning*.

Challenging the contiguity assumption: the truly random control

Experiment (Rescorla, 1968).

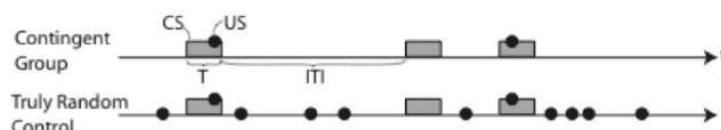
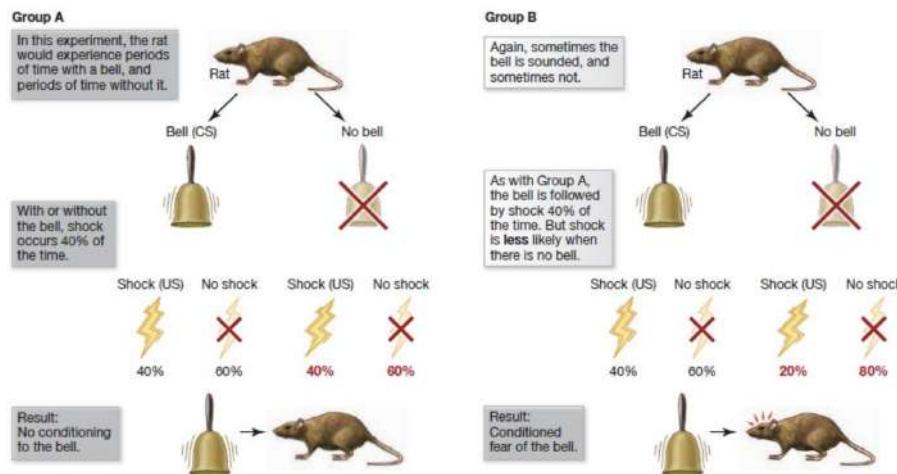


Figure 5.8

The temporal pairing of CS and US is identical in the two groups, but there is no CS-US contingency in the second group (the truly random control), because the US occurs as frequently in the absence of the CS as in its presence. The subjects in the Group 1 develop a conditioned response to the CS; the subjects in Group 2 do not.

⁸We've mostly seen this so far.



7.11 The effect of contingency on classical conditioning For both groups, there's only a 40% chance that bells will be followed by shock. However, for Group B, shock is less likely when no bell is sounded, and, for this group, the bell becomes a fearful stimulus.

Figure 5.9

Regarding the figure above we have that for the Group A, first description, specifically 50% of time with bell, 50% of time without bell.

In general:

- *Contiguity is the same:* the two groups experienced the same number of bell-shock pairings.
- *Contingency differs:* for group B the shock is more likely with the bell than without the bell.

Whether the bell is *informative* or not is what matters for conditioning.⁹

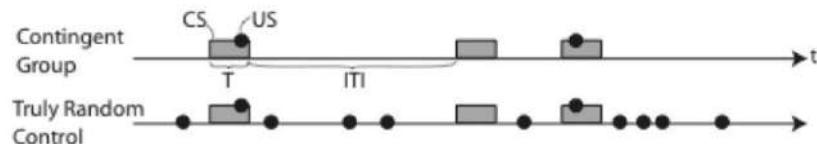


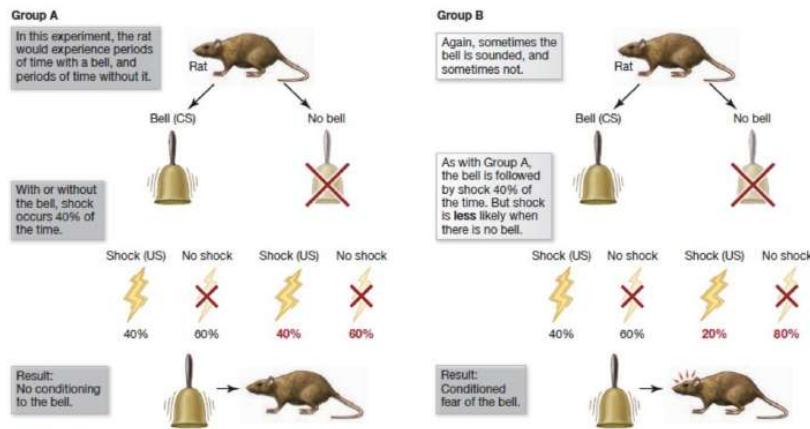
Figure 5.10

The temporal contiguity between the predictor (the CS) and the predicted (the US) is not the key.

But rather the information that the predictor provided about the predicted event.

The article can be found here: https://www.brainkart.com/article/Classical-Conditioning--Contingency_29312/

⁹Note that the shock percentage (40%) is the same but the 40% Group B is *informative* while the 40% Group A not.



7.11 The effect of contingency on classical conditioning. For both groups, there's only a 40% chance that bells will be followed by shock. However, for Group B, shock is less likely when no bell is sounded, and, for this group, the bell becomes a fearful stimulus.

Figure 5.11

Challenging the contiguity assumption: blocking

Let's analyze the following experiment (full info here: https://www.brainkart.com/article/Classical-Conditioning--Role-of-Surprise_29314/)

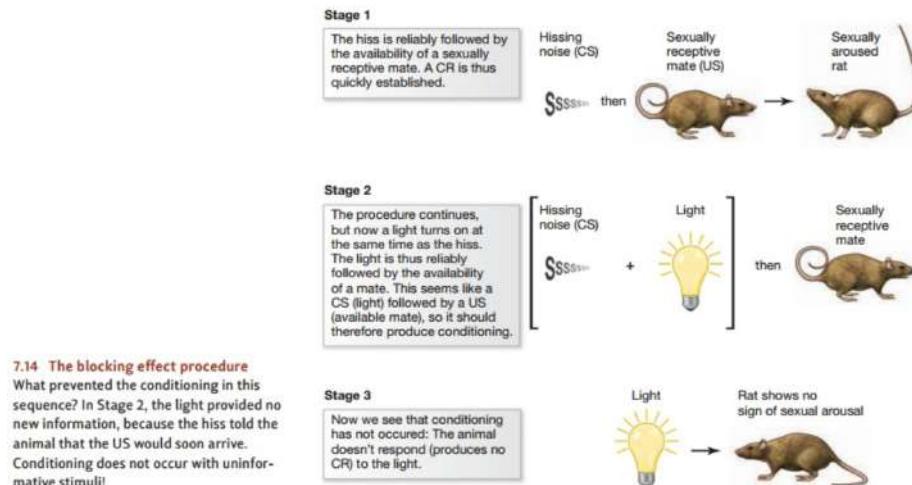


Figure 5.12

Focusing on the image above - Stage 2 one could be tempted to say that the light would imply a CR but note that this kind of pairing occurs at Stage 2, when there was already a pairing.

No learning occurs to a stimulus if it is combined with a previously conditioned stimulus during conditioning trials.

The light provided only redundant information. The rat already knew from the hissing noise that the US was about to be presented, and so it wasn't at all surprised when the US did arrive.

Associative learning is more than learning about contiguity. It's learning about contingency

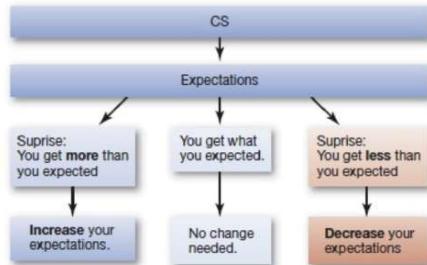
Learning about *predictive relations* involves learning about more than just the contiguous pairing between the CS and US.

It involves learning about the *causal relationship* between the two events (Dickinson 1980; Rescorla 1988).

CS-US *contingency*, *not the temporal contiguity* of the CS and US, produces a CR.

We learn only from surprising/unpredicted events

We refer again to this article https://www.brainkart.com/article/Classical-Conditioning--Role-of-Surprise_29314/



7.13 The role of expectations and surprise This figure shows the (automatic, unconscious) process through which expectations can be adjusted, trial by trial, in a classical conditioning experiment. The one complication not shown here is that bigger surprises (greater departures from expectations) will trigger larger adjustments; smaller surprises will lead to smaller adjustments.

Figure 5.13

The image above recall something already seen: *Acquisition/Extinction*; in particular:

- *Acquisition* ↔ Increase expectation;
- *Extinction* ↔ Decrease expectation.

Expectations are related to learning.

More percisely:

- predictive learning depends on what is already known about those events;
- if little is known about the relation between the events, so that the US is not predicted by the CS, then learning occurs;
- if much is known about this relation, so that the US is adequately predicted by the CS, then learning fails.

Look at the image above, we can pair:

- *Acquisition* ↔ Increase expectation: during the acquisition phase different trials implies that the CS predicts the US, e.g. CS followed by a US (always in probabilistic terms).

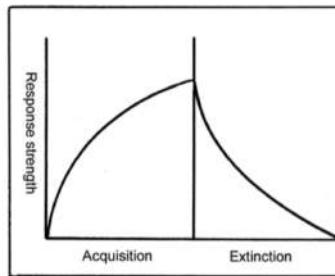


Figure 5.14

- *Extinction* \longleftrightarrow Decrease expectation: CS not followed by US, for example for some change in the environment the US is stopped.

Learning theories have posited that conditioning is not instructed by a simple sensory representation of the outcome, but instead by an *error signal measuring the difference between the outcome actually present and that expected*. (McNally, 2011)

Prediction error

For learning to occur we need a prediction error (what we saw so far). Error signal measuring the difference between the outcome actually present and that expected.¹⁰

Occurs when the outcome of a conditioning trial is different from that which is predicted by the conditioned stimuli that are present on the trial (*i.e.*, when the US is surprising).

Prediction error is *necessary for associative learning*:

- dictates variations in the effectiveness of the US in supporting learning;
- if the difference is large, predictions did not match observations, there is a need for more learning to update those predictions;
- If predictions match observations, there is no prediction error and no learning occurs.

5.2 Formalization of learning theories

The Rescorla-Wagner model

If the actual US is denoted as R and the expected US as V , then the error signal is computed as $R - V$. ($R = 1$ if reward is delivered and $R = 0$ if reward is omitted).

Prediction error:

$$\delta_t = R_t - V_t \quad (5.2.1)$$

¹⁰It can be *positive i.e.* more than expected or *negative i.e.* less than expected.

The expected value V of a given CS is updated based on the sum of the current expected value V and the prediction error at trial t .¹¹

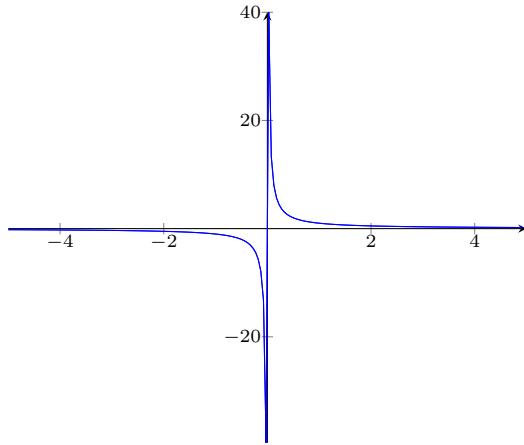
Where α is a learning rate parameter, which determines the size of the update step:

$$V_{t+1} = V_t + \alpha \delta_t \quad (5.2.2)$$

Note that:

$$\delta_t = \frac{V_t - V_{t+1}}{\alpha} \approx \frac{c}{\alpha} \approx \frac{1}{\alpha} \implies \delta_t \approx \frac{1}{\alpha}$$

Which is:



Prototypical acquisition and extinction learning curves for Pavlovian conditioning as predicted by the Rescorla-Wagner model.

The filled circles show the time evolution of the value V of a CS over 200 trials:

- In the first 100 trials, a reward R was paired with the CS (acquisition);
- in trials 100-200 no reward was paired (extinction).

Learning is proportional to prediction error δ , which is larger at the start of training when reward is unexpected, and gets smaller, eventually 0, as training progresses and reward is fully predicted.

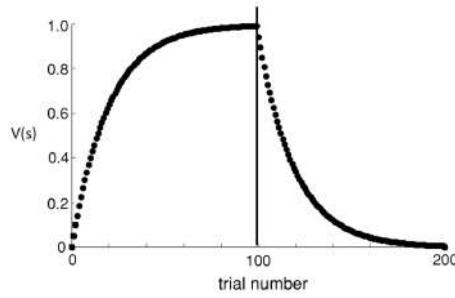


Figure 5.15

¹¹it is important to notice that this is a trial by trial model: so the ‘trial’ is the temporal unit.

Notice that the above graph is equal to the acquisition/extinction model. Let's analyze it considering the (5.2.1) prediction error formula seen with this view:

$$V_t = R_t - \delta_t$$

Acquisition:

- $R_t = 1$;
- prediction error δ_t is positive (I'm acquiring something) and becomes smaller in time (when time passes is logic that the prediction error becomes smaller in absolute value).

So:

$$\begin{cases} V_t = 1 - \delta_t \\ \delta_t \geq 0 \end{cases}$$

Extinction:

- $R_t = 0$;
- prediction error δ_t is negative and becomes smaller in time (when time passes is logic that the prediction error becomes smaller in absolute value).

So:

$$\begin{cases} V_t = 0 - \delta_t \\ \delta_t \leq 0 \end{cases}$$

Learning is proportional to prediction error δ :

- δ is *positive* (more than expected) and larger at the start of acquisition when reward delivery is unexpected;
- δ gets smaller, eventually 0, as acquisition progresses and reward delivery is fully predicted.
- δ is *negative* (less than expected) and larger at the start of extinction when reward omission is unexpected;
- δ gets smaller, eventually 0, as extinction progresses and reward omission is fully predicted.

Looking at the image below:

- Use prediction: beginning.
- Generate error: can be positive or negative.

As already anticipated it is a *trial-level* model:

- it deals with how associative strengths change from trial to trial without considering any details about what happens within and between trials;

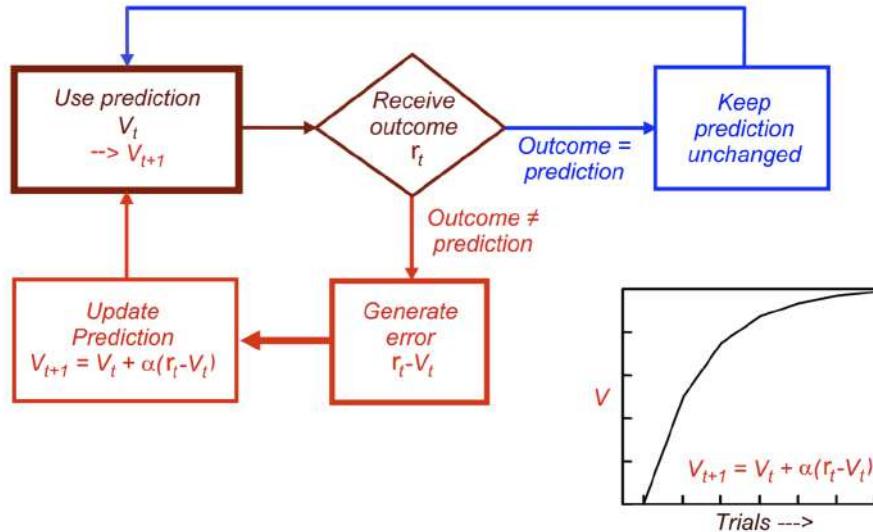


Figure 5.16

- the model does not apply to details about what happens during the time a trial is taking place, or what might happen between trials.
- Within each trial an animal might experience various stimuli whose onsets occur at particular times and that have particular durations. These timing relationships strongly influence learning.¹²

The temporal difference model

From the point of view of the animal, a trial is just a fragment of its continuing experience interacting with its world.

The temporal difference model instead:

- is a real-time model;
- t now labels time steps within or between trials instead of complete trials;
- the prediction error here (see the formula below):
 - sums the actual and expected US value;
 - then compares the momentary value of this sum against the value of the prior moment of the expected US value.
- The error signal arises from a comparison that is made across successive moments in time, t versus $t - 1$.

Prediction error:

$$\delta_t = R_t + V_t - V_{t-1} \quad (5.2.3)$$

The expected value:

$$V_{t+1} = V_t + \alpha \delta_t \quad (5.2.4)$$

¹²But this model doesn't consider them; if you want to take in consideration them see the next model.

Rescorla-Wagner and TD model rely upon signed prediction errors

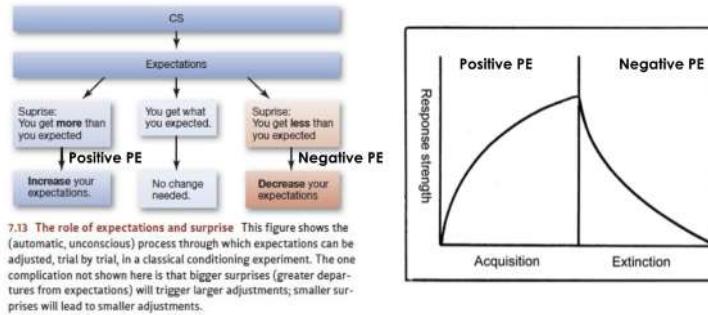


Figure 5.17

5.3 Prediction errors in neurons

How could signed prediction errors be implemented in neurons?

Neurons could:

- increase their firing rates when the error is positive;
- decrease their firing rates when the error is negative.

Synaptic plasticity:

- changes in synaptic efficacy through changes in the amount:
 - of neurotransmitter that is released, directly affecting excitation or inhibition of postsynaptic neuron;
 - of neuromodulator, which is a neurotransmitter having effects other than, or in addition to, direct neural excitation or inhibition.

The parameters, or weights, adjusted by learning algorithms correspond to synaptic efficacies.

The reward prediction error hypothesis of dopamine neuron activity

In the next chapter we will see that the reward prediction error hypothesis of dopamine¹³ was formulated thanks to the interaction between neuroscientists and mathematicians.

Resulted from the convergence of computational reinforcement learning and results of neuroscience experiments.

Modulation of synaptic plasticity via the neuromodulator dopamine is a plausible mechanism for how the brain might implement learning algorithms.

¹³It is a neuromodulator: neurotransmitter plus something. It is thought to encode – or at least to be crucial – the prediction error (PE) in the brain. So AI took the idea of PE directly from the brain.

There is strong evidence that the dopaminergic system is the major neural substrate of reward and reinforcement for both natural rewards and addictive drugs.

Below a useful video which introduces to this:

https://www.youtube.com/watch?v=Wa8_nLwQIpg (2-Minute Neuroscience: Dopamine)

Dopamine

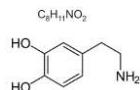


Figure 5.18

It's a neuromodulator, *i.e.* a neurotransmitter having effects other than, or in addition to, direct neural excitation or inhibition.

Plays essential roles in many processes:

- motivation;
- learning;
- action-selection, decision-making;
- most forms of addiction;
- Parkinson's disease;
- Huntington's disease.

The dopaminergic pathways

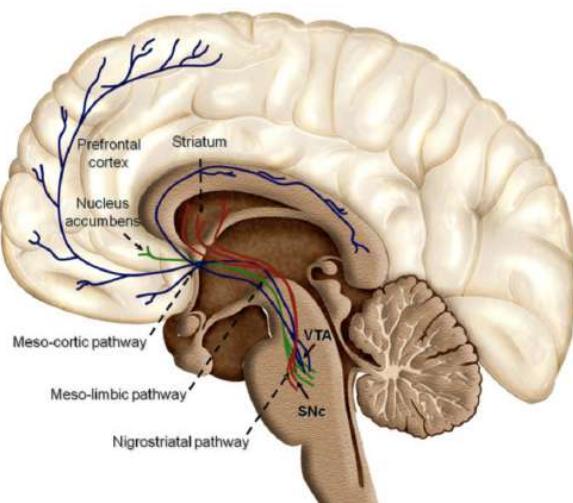
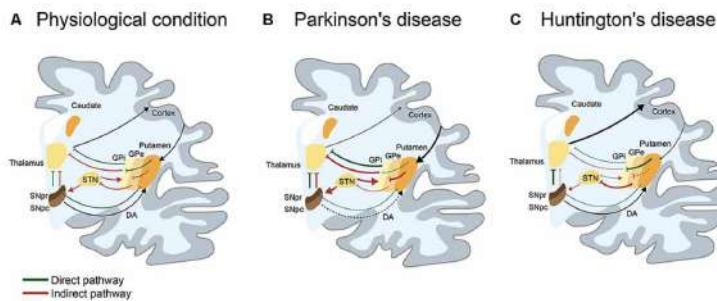


Figure 5.19

Looking at the image above for the three different pathways (red, green and blue) we have that the cell bodies start at the SNc level and then their axons go through the different parts of the brain releasing dopamine at the synapses level that are represented from the lines ramifications.

1. Nigrostriatal pathway (red pathway):

- originates in the substantia nigra pars compacta (SNc);
- projects primarily to the caudate–putamen (dorsal striatum in rodents);
- it is critical in the production of movement as part of the *basal ganglia motor loop*; remember that *basal ganglia* have a crucial role in motor control:



Troncoso-Escudero, Paulina et al. "On the Right Track to Treat Movement Disorders: Promising Therapeutic Approaches for Parkinson's and Huntington's Disease." *Frontiers in aging neuroscience* vol. 12 571185. 3 Sep. 2020, doi:10.3389/fnagi.2020.571185

Figure 5.20

– Physiologically:

- * the direct (green line) pathway participates in the activation of movement;
- * the indirect pathway (red line) participates in the inhibition of movement.

– Parkinson's disease:

- * the loss of dopaminergic neurons of the SNpc, induces an overactivation of the indirect pathway and decrease of movement (hypokinesia).

– Huntington's disease (early stage):

- * MSNs of the indirect pathway appear to be affected before the MSNs of the direct pathway (it is essentially the opposite of Parkinson's disease).

2. Mesolimbic pathway (green pathway):

- originates in the VTA (Ventral Segmental Area);
- projects to the nucleus accumbens, septum, amygdala¹⁴ and hippocampus.¹⁵

¹⁴It is involved in emotion, we talked about amygdala when we talked about fear conditioning; in general the entire limbic system is crucial for emotion.

¹⁵It is related to memory.

3. Mesocortical pathway (blue pathway):

- originates in the VTA;
- projects to the medial prefrontal, cingulate, orbitofrontal and perirhinal cortex.

These two last pathways are important for *motivational function*:¹⁶ reinforcement learning.

It is possible to see the involved parts in the following website:

<https://www.brainfacts.org/3d-brain#intro=false&focus=Brain>

The early view: dopamine neurons broadcast a reward signal

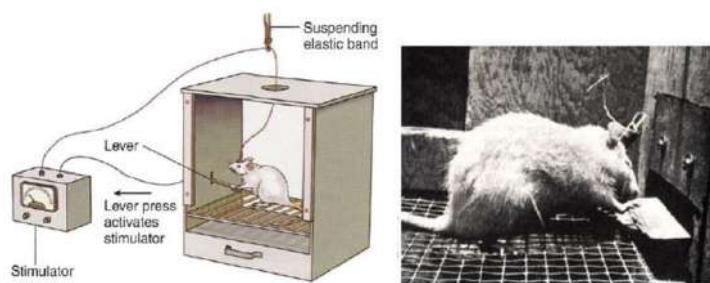


Figure 5.21

At the beginning was taught that dopamine was important for movement; after for movement and reward.

1954: James Olds and Peter Milner publish a paper that describes the effects of electrical stimulation on certain areas of a rat's brain.

'... the control exercised over the animal's behavior by means of this reward is extreme, possibly exceeding that exercised by any other reward previously used in animal experimentation.'

The sites at which stimulation was most effective in producing this rewarding effect excited dopamine pathways, either directly or indirectly, that ordinarily are excited by natural rewarding stimuli.¹⁷

In the following video it is shown that this rewarding effect was so strong that the mouse wanted to go to the stimulator despite a painful road before the stimulator itself; this can be related to drugs addiction.

<https://www.youtube.com/watch?v=uofQPLuLV9A> (Study by James Old of Brain Reward Center)

Activation by unconditioned rewarding (and aversive) stimuli:

- About 75% of dopamine neurons show phasic activation when animals touch a small piece of hidden food, or when drops of liquid are delivered to the mouth outside of any task.

¹⁶Wanting to do something; liking to do something.

¹⁷So essentially the experiment was: the elastic band was attached to some areas of the brain; when the lever was pressed an electrical stimulation started which involved a reward producing. Experimenting this on different areas was found that the dopaminergic pathways were most affected.

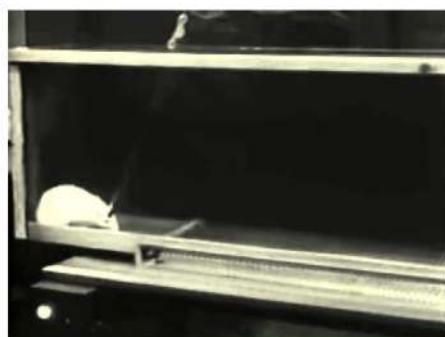


Figure 5.22

- They do not discriminate between different food or liquid rewards; however, their responses distinguish rewards from non-reward objects.
- Only 14% of dopamine neurons show phasic activations when aversive stimuli are administered, such as pain pinch or electrical shock. However, they are not entirely insensitive to aversive stimuli, as they show depressions or activations with slower time courses following pain pinch.
- The phasic activations of dopamine neurons report preferentially environmental events with rewarding value, whereas aversive events may be signaled primarily with a slower time course.

Source: Schultz, Wolfram. 'Getting formal with dopamine and reward.' *Neuron* vol. 36,2 (2002): 241-63. doi:10.1016/s0896-6273(02)00967-4

The reward prediction error hypothesis of dopamine neuron activity



Figure 5.23

'for their multidisciplinary analysis of brain mechanisms that link learning to reward, which has far-reaching implications for the understanding of human behaviour, including disorders of decision-making in conditions such as gambling, drug addiction, compulsive behaviour and schizophrenia.'

Wolfram Schultz discovered that dopamine was not only related to movement, but only after meeting Peter Dayan – Mathematician, AI researcher – was formalized the concept of PE (*prediction error*).

Ray Dolan applied what discovered from Schultz and Dayan to clinical researches.

Next time we're gonna see *how* dopamine produces a prediction error signal.

Chapter bibliography

Papers cited in the chapter.

Chapter 6

Reinforcement learning: part two

6.1 A brief recap

In the last chapter we looked at the difference between *contiguity* and *contingency* and we saw that we only learn when we are *surprised*, and this surprise is computed as *prediction error signal*.

We get surprised, and so we get a prediction error; when there is a discrepancy between what we have predicted and what actually happened in the environment. The brain is constantly making hypothesis about the world, about what is going to happen and compares its hypothesis with reality, and every time hypothesis is different from reality there is an error signal that is computed by the brain as prediction error.

During this chapter we are going to see that the neuromodulator *dopamine* seems to be a chemical that is used by the brain to compute this prediction error.¹

Learning is regulated by prediction error

Prediction error:

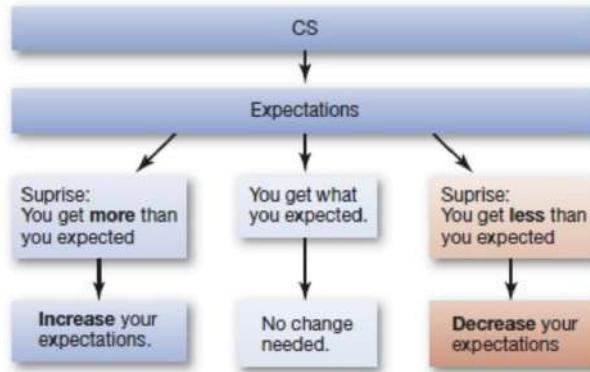
- is a quantitative discrepancy between the outcome expected² when the cue was presented, and the outcome that was actually experienced;
- functions as teaching signal to update expectations and reduce following prediction errors.³

Remember also that the PE is signed: it can be positive (more than you expect) or negative (less than you expect). This increase/decrease changes also our behaviour: *e.g.* we study for an exam and we get a lower grade than we expected; then next time we are going to study more.

¹There are also others but we focus on dopamine; dopamine prediction error is just one of the many prediction error signals that the brain computes.

²Basically divided in reward or punishment, on this we make hypothesis.

³If there is a prediction error we need to change our mind adapting it to our environment. We change constantly our hypotheses making them more coherent with our environment.



7.13 The role of expectations and surprise This figure shows the (automatic, unconscious) process through which expectations can be adjusted, trial by trial, in a classical conditioning experiment. The one complication not shown here is that bigger surprises (greater departures from expectations) will trigger larger adjustments; smaller surprises will lead to smaller adjustments.

Figure 6.1

Prediction error in reinforcement learning algorithms (e.g. Rescorla-Wagner)

Prediction error:

- difference between the expected and delivered outcome:

$$\delta_t = R_t - V_t$$

- Used to update predicted value:

$$V_{t+1} = V_t + \alpha \delta_t$$

- the value signal produced by the reward itself transfers back to events that reliably precede reward delivery (*e.g.* CSs);
- thus, the rewarding value transfers from the reward to the CS that predicts reward.

In this manner, reinforcement learning algorithms explicitly state that the quantitative value inherent in reward transfers back to the antecedent cue predicting its delivery. That is, the predictive cue becomes endowed with the scalar value of the reward.⁴

⁴See ahead to understand better, but essentially this tell us that after learning the value of R is transferred to CS and, with a formula like this, experimental evidence is encoded by the math formula. *E.g.* in the case of a dog that receives the food after the sound of a bell (CS) at the beginning the reward is only the food but after a while the bell itself becomes a reward. So the formula is coherent with Pavlov experiments and with the fact that we look around in our environment and cues that predict a certain reward; this works also for punishment or aversive stimuli: *e.g.* I look for cues that signal if there is a predator around so that I can run away before the predator arrives: the cues enable me to prepare my body to respond, I don't have to respond directly to the predator (survival increased).

What's important about reinforcement learning algorithms that involves prediction error like Rescorla-Wagner and Temporal difference is that both have to compute the value we give (V_t) to a certain stimulus or cue and this value is updated (V_{t+1}) on every trial (Rescorla-Wagner) or on instances of time (Temporal difference); it is updated based on a *learning grade* (α) which multiplies the prediction error (δ_t). Finally what's important is that algorithms include the prediction error and this is computed by the difference between what actually happens (R_t reward or not) and what I expect (V_t), and this difference is constantly updated.

How could signed prediction errors be implemented by neurons?

Neurons could change their firing rate when *predictions do not meet reality*:

- increase their firing rates when the error is positive;
- decrease their firing rates when the error is negative.

Prediction error signals in the brain

The reward prediction error hypothesis of *dopamine* neuron activity.

6.2 The reward prediction error hypothesis of dopamine

Dopamine

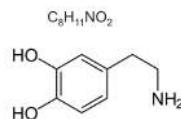


Figure 6.2

It's a neuromodulator, *i.e.* a neurotransmitter having effects other than, or in addition to, direct neural excitation or inhibition.

Plays essential roles in many processes:

- motivation;
- learning;
- action-selection, decision-making;
- most forms of addiction;
- Parkinson's disease;
- Huntington's disease.

Regarding the last two items remember that dopamine acts on basal ganglia.

The dopaminergic pathways

There is always a certain amount of dopamine released (*tonic level* see ahead for a precise definition) and when there is a prediction error it decreases or increases suddenly depending on the expectations (+ or -).

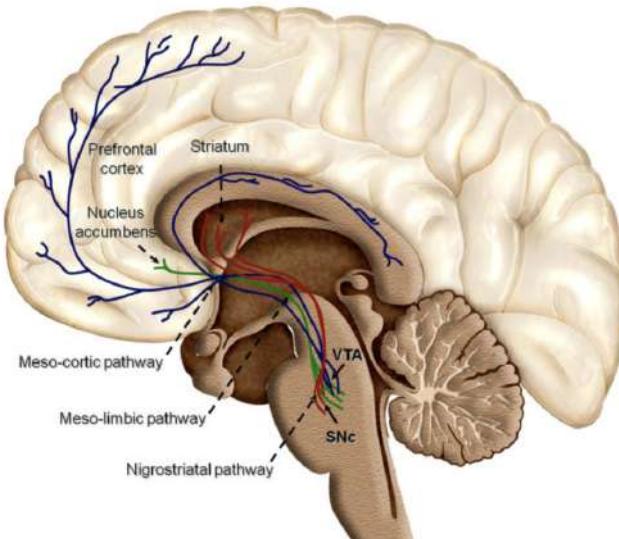


Figure 6.3

What's important is that dopamine produced in these neurons is released in different parts of the brain (many many parts).

In the case of Nigrostriatal pathway, for example, neurons have cell bodies in substantia nigra and release dopamine in the Striatum (which is made of caudate-putamen).

1. Nigrostriatal pathway (red pathway):

- originates in the substantia nigra pars compacta (SNC);
- projects primarily to the caudate-putamen (dorsal striatum in rodents);
- it is critical in the production of movement as part of the *basal ganglia motor loop*.

2. Mesolimbic pathway (green pathway):

- originates in the VTA (Ventral Segmental Area);
- projects to the nucleus accumbens, septum, amygdala and hippocampus.

3. Mesocortical pathway (blue pathway):

- originates in the VTA;
- projects to the medial prefrontal, cingulate, orbitofrontal and perirhinal cortex.

These two last pathways are important for *motivational function*: reinforcement learning.

It is possible to see the involved parts in the following site:

<https://www.brainfacts.org/3d-brain#intro=false&focus=Brain>

The early view: Dopamine neurons broadcast a reward signal

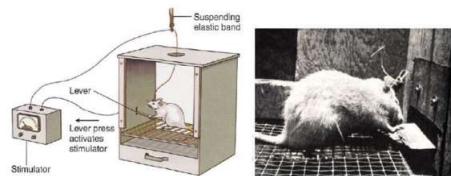


Figure 6.4

1954: James Olds and Peter Milner publish a paper that describes the effects of electrical stimulation on certain areas of a rat's brain.

'... the control exercised over the animal's behavior by means of this reward is extreme, possibly exceeding that exercised by any other reward previously used in animal experimentation.'

The sites at which stimulation was most effective in producing this rewarding effect excited dopamine pathways, either directly or indirectly, that ordinarily are excited by natural rewarding stimuli.

But pay attention!

At the beginning was taught that dopamine neurons \longleftrightarrow reward signal.

But now we know that dopamine neurons \longleftrightarrow reward prediction error signal which is very different (refer to past and next chapters).

The reward prediction error hypothesis of dopamine neuron activity



Figure 6.5

'for their multidisciplinary analysis of brain mechanisms that link learning to reward, which has far-reaching implications for the understanding of human behaviour, including disorders of decision-making in conditions such as gambling, drug addiction, compulsive behaviour and schizophrenia.'

Wolfram Schultz discovered that dopamine was not only related to movement, but only after meeting Peter Dayan – Mathematician, AI researcher – was formalized the concept of PE (*prediction error*).

Ray Dolan applied what discovered from Schultz and Dayan to clinical researches.

In the following video the *Brain Prize* winners explain their results:

https://www.youtube.com/watch?v=8n1-lv1_wCY (Meeting The Prize Winners - The Brain Prize 2017)

While the following video shows the presentation of the *2017 Brain Prize* and the scientific motivations of assigning this prize (look from 10'10" to 21'18").

https://www.youtube.com/watch?v=8n1-lv1_wCY (Meeting The Prize Winners - The Brain Prize 2017)

How could signed prediction errors be implemented by dopamine neurons?

Neurons could change their firing rate when *predictions do not meet reality*.

Increase their firing rates when the error is positive (more than expected).

Decrease their firing rates when the error is negative (less than expected).

Dopamine neurons show phasic changes in firing rate when predictions do not meet reality.

Increase firing rate when:

- Reward is unexpectedly delivered.
- Reward is better than expected.

Suppress firing rate when:

- Reward is unexpectedly omitted.
- Reward is worse than expected.

Phasic responses (vs Tonic response which is the standard response related to a standard neurons firing rate) of dopamine neurons signal reward prediction errors, not reward itself (in the sense that dopamine responds when there is $\delta_t = R_t - V_t \neq 0$ not when only $R_t \neq 0$).

Focusing on the explanations presented on the right column we referred always to *reward*.

Theoretically these dynamics could be similar also to aversive learning (remember when we talked about associative learning) when you have to learn about *punishment*.

This could also work for punishment, however, for punishment is a little bit more complicated. It is still not clear if dopamine encodes a prediction error

also for punishment; some evidences do, other not. We are going to focus only on *reward*.

Measuring neuronal signalling

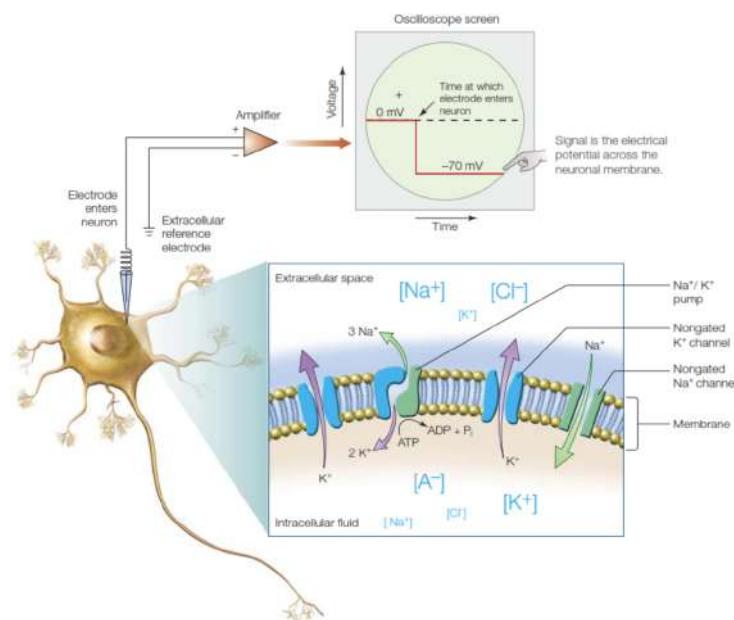


Figure 6.6

Idealized neuron shown with intracellular recording electrode penetrating the neuron. The electrode measures the difference between the voltage inside versus outside the neuron and this difference is amplified and displayed on an oscilloscope screen (top). The oscilloscope screen shows voltage over time, and shows that prior to the electrode entering the neuron, voltage between the electrode and the extracellular reference electrode is zero, but when the electrode is pushed into the neuron, the difference becomes -70 mV, which is the resting membrane potential.

So, during next experiments with animals (obviously not with humans), we essentially measured with this modality over time.

Dopaminergic neurons exhibit a strong phasic response to an unexpected reward ... Discriminate between reward & non-reward

Activity of single dopamine neurons⁵ is recorded in alert monkeys while they perform behavioral acts and receive rewards.

- (A) Dopamine responses to touch of food in absence of any stimuli predicting the reward. The food inside the box is invisible (so unexpected) but is touched by the hand underneath the cover.⁶

⁵In particular motor response.

⁶Looking at the image and in particular at the graph: the 'white' (bottom) part shows the response of the single cells (neurons), while the 'black' (top) part shows the sum of the response of the single cells.

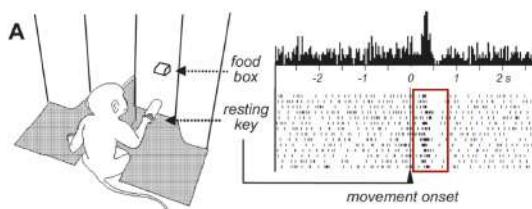


Figure 6.7

- (B) Differential response of dopamine neuron to touch of a wire holding a piece of apple (top), or touch of a wire holding an inedible objects (bottom, control condition).⁷

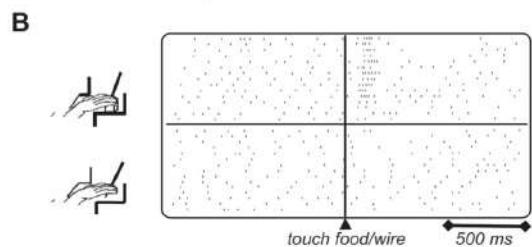


Figure 6.8

Reference: 'Romo & Schultz, *J. Neurophysiology*, 1990'.

... Discriminate between reward magnitude

Not only able to distinguish reward or not reward, but also how much.
Neural discrimination of liquid volume.

- (A) (Top) Rasters and histograms of activity from a single dopamine neuron.
(Bottom) Population histograms of activity from all neurons tested ($n = 55$ neurons). Three volumes of liquid were delivered in the absence of any explicit predictive stimuli.

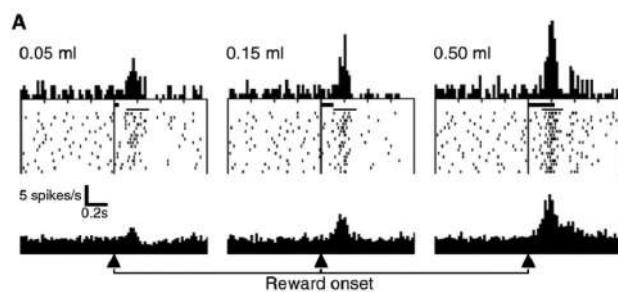


Figure 6.9

⁷Note the difference in intensity from the image.

- (B) Neural response as a function of liquid volume. Median ($\pm 95\%$ confidence intervals) percentage change in activity for the population of neurons ($n = 55$ neurons) was calculated for responses to each volume after normalization in each neuron to the response after delivery of 0.5 ml, which itself elicited a median activation of 159% above baseline activity.⁸

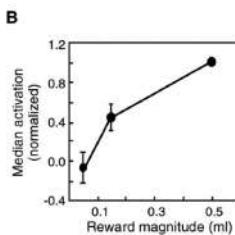


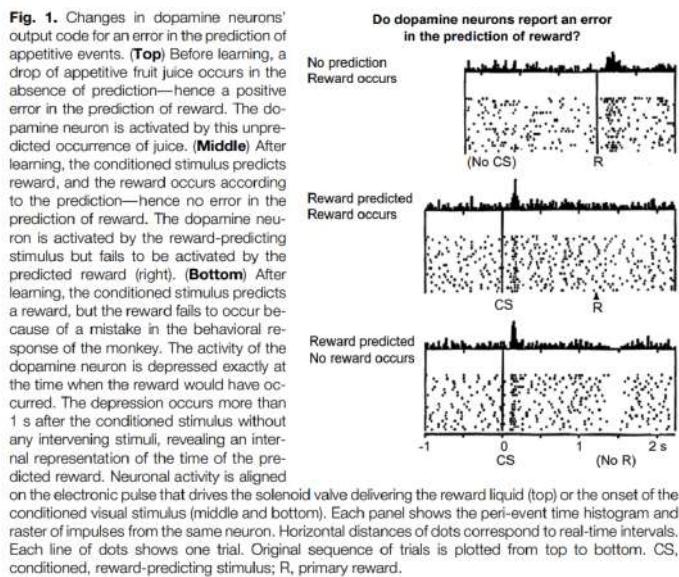
Figure 6.10

Reference: 'Tobler, Fiorillo and Schulz, *Science*, 2005'.

... Transfers back to a cue which predicts reward occurrence (i.e. CS)

A Neural Substrate of Prediction and Reward

Wolfram Schultz, Peter Dayan, P. Read Montague*



1594 SCIENCE • VOL. 275 • 14 MARCH 1997 • http://www.scie

Figure 6.11

⁸The image shows essentially the increase on average.

The learning mentioned in the explanation of the figure above is *Pavlovian learning*.

Referring to the graphs of the figure above, and focusing on the instant t in which is expected the reward R , respectively from top to bottom we have:

- $\delta_t = R_t - V_t = 1 - 0 = 1$ (here increase at the reward time).
- $\delta_t = R_t - V_t = 1 - 1 = 0$ (here increase at the CS time which inherits – after learning – the value of R).
- $\delta_t = R_t - V_t = 0 - 1 = -1$ (here no reward is given).

Before learning:

- unexpected rewards occurs $\implies +\text{PE}$.
 - Dopamine neuron firing is increased following reward.

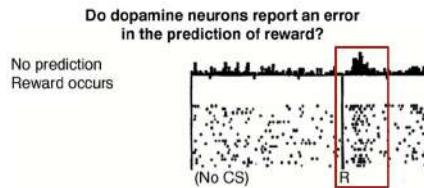


Figure 6.12

After learning (CS endowed the value of R):

- the CS predicts reward, and the reward occurs \implies no PE.
 - Dopamine neuron firing is increased following CS but *not following reward*. So, *dopamine \neq reward signal* (as already highlighted).

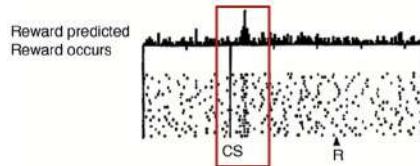


Figure 6.13

- the CS predicts reward, and the reward does not occur $\implies -\text{PE}$.
 - Dopamine neuron firing is increased following CS but decreased following omitted reward.
 - Exactly at the time when reward was expected.⁹

⁹Neurons not only are able to respond to stimuli or not, but they encode time also, and if a given encoded time does not obtain what expected, change their firing rate.

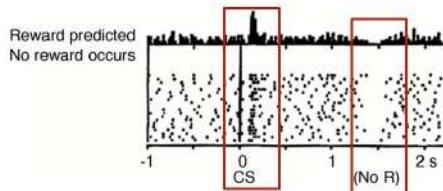


Figure 6.14

How can we measure the firing of neurons? It is possible, for example, to monitor the sound of neurons firing.

Below a video which shows their sound, hear it!

<https://www.youtube.com/watch?v=8bxpz-YEua0> (Sound of Neurons)

Refer to the image below.

A dopamine neuron that responds initially to a liquid or food reward acquires a response to the CS after some tens of paired CS-reward trials.

Each line of dots represents a trial, each dot represents the time of the discharge of the dopamine neuron, the vertical lines indicate the time of the stimulus and juice reward, and the picture above the raster shows the visual conditioned stimulus presented to the monkey on a computer screen. Chronology of trials is from top to bottom. The top trial shows the activity of the neuron while the animal saw the stimulus for the first time in its life, whereas it had previous experience with the liquid reward.¹⁰

Data from Waelti (2000).

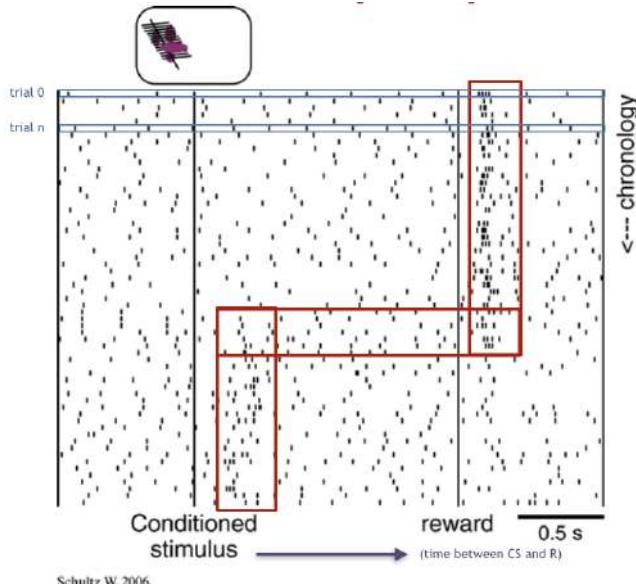


Figure 6.15

¹⁰The horizontal red square shows the trials in which the monkey is learning; there is an overlap. *R* is transferring back to CS.

Dopaminergic neurons response conforms to blocking

Referring to the image below.¹¹ Neural learning is blocked¹² when the reward is predicted by another stimulus (left) but is intact in the same neuron when reward is unpredicted in control trials with different stimuli (right).

- The neuron has the capacity to respond to reward-predicting stimuli (top left)¹³ and discriminates against unrewarded stimuli (top right).
- The addition of a second stimulus results in maintenance and acquisition of response, respectively (middle).¹⁴
- Testing the added stimulus reveals absence of learning when the reward is already predicted by a previously conditioned stimulus (bottom left).¹⁵

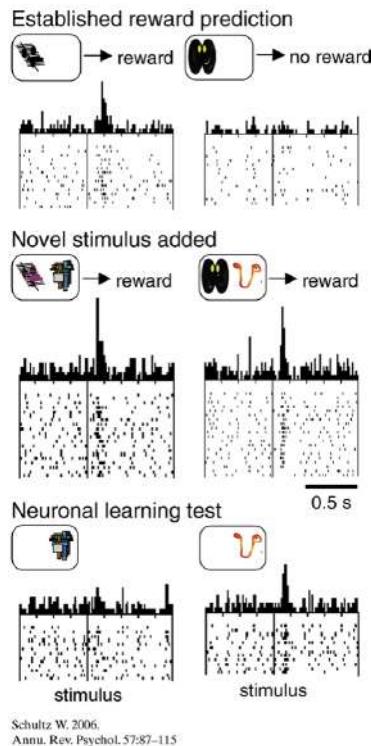


Figure 6.16

Data from Waelti et al. (2001).

¹¹The horizontal line indicates the instant in which the CS recurs.

¹²Blocking experiments told us that we learn only when we are surprised (so when there is a prediction error). Remember that we saw that blocking affirms that *contiguity* is not enough (CS close in time with US is not enough to learning) but we need also *contingency*; we learn only when we are surprised.

¹³ t indicates the CS instant; $\delta_t \neq 0 = R_t - V_t = 0 - 1$.

¹⁴ t indicates the CS instant; $\delta_t \neq 0 = R_t - V_t = 0 - 1$.

¹⁵Looking at the left image we can see that the second symbol is redundant: $\delta_t = 0 = R_t - V_t = 0 - 0$.

Dopaminergic neurons firing to the CS increases with expected reward value

Scientist here measured behaviour of monkeys.

- (A) Anticipatory licking responses during the 2 s delay between the conditioned stimuli and liquid delivery.¹⁶
- (B) Single-neuron (top) and population responses (bottom) ($n = 57$ neurons) from the experiment in (A). Visual conditioned stimuli with their expected magnitude of reward are shown above the rasters.¹⁷

Source: Tobler, Fiorillo and Schulz, Science, 2005.

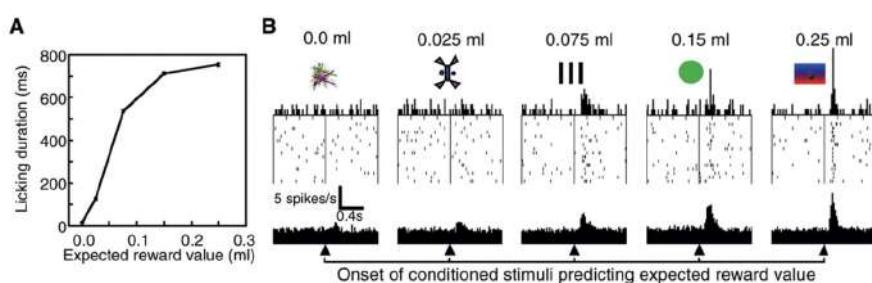


Figure 6.17

Dopaminergic neurons exhibit a signed (bidirectional) response to unexpected reward ...

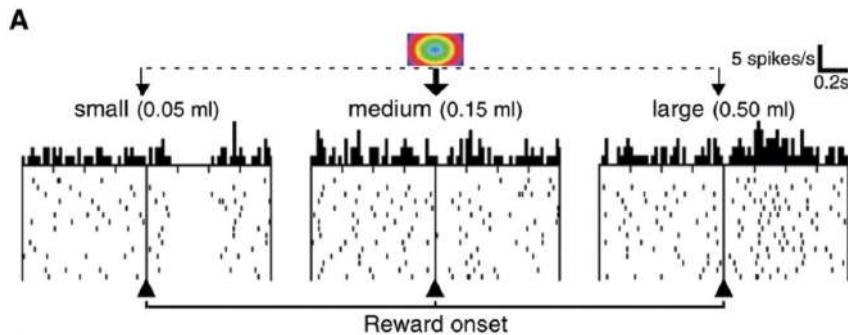


Figure 6.18

A single CS was usually followed by an intermediate volume of liquid (0.15 ml) that elicited no change in the neuron's activity (center). However, on a

¹⁶Along the x-axis is shown the CS, while along the y-axis the conditioned response CR.

¹⁷Dopaminergic neuron firing is relative to the difference between the values. Neurons does not encode the absolute quantity of liquid delivered but the fact that at a time t was greater or lower than the quantity at the $t - 1$; specifically neurons do not encode the specific quantities 0.15 ml or 0.25 ml, but the *relation* $0.25 > 0.15$ and the *gap in intensity* between 0.15 and 0.25. See ahead to integrate better.

small minority of trials, *smaller* (0.05 ml) or *larger* (0.50 ml) volumes were unpredictably substituted, and neural activity decreased (left) or increased (right), respectively.

Source: Tobler, Fiorillo and Schulz, Science, 2005.

... Which is relative to a predicted magnitude

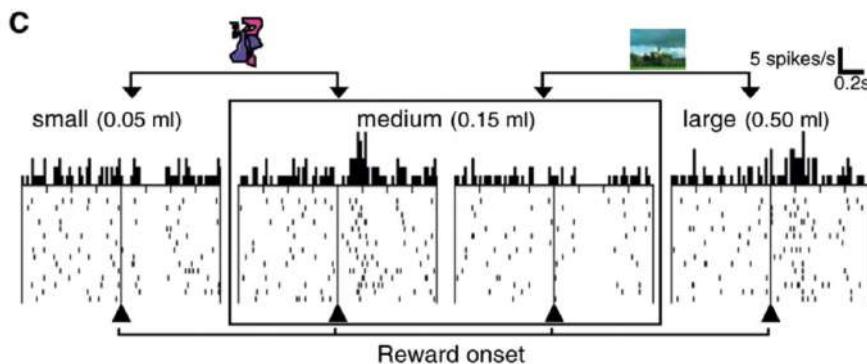


Figure 6.19

Responses of a single neuron to three liquid volumes, delivered in the *context of two different predictions*. One stimulus predicted small or medium volume with equal probability, whereas another stimulus predicted medium or large volume. The medium volume activated the neuron in one context, but suppressed activity in the other.

- Dopamine neurons process reward magnitude relative to a predicted magnitude.
- *A reward outcome that is positive on an absolute scale can nonetheless suppress the activity of dopamine neurons.*

Dopaminergic neurons encode reward probability (or uncertainty)

We have seen that dopaminergic neurons encode:

- magnitude;
- time.

Here we see also that encode *probability*.

Phasic activation of dopamine neurons vary monotonically with reward probability.

Refer to the image.

Rasters and histograms of activity in a single cell, illustrating responses to the conditioned stimuli and reward at various reward probabilities, increasing from top to bottom.¹⁸

¹⁸What is shown here is a test phase after a learning phase.

Reward at $P = 0.0$ was given in the absence of any explicit stimulus at a rate constant of 0.02 per 100 ms and thus presumably occurred with a low subjective probability. Only rewarded trials are shown at intermediate probabilities. Bin width = 20 ms.

Source: Fiorillo, Tobler and Schulz, Science, 2003.

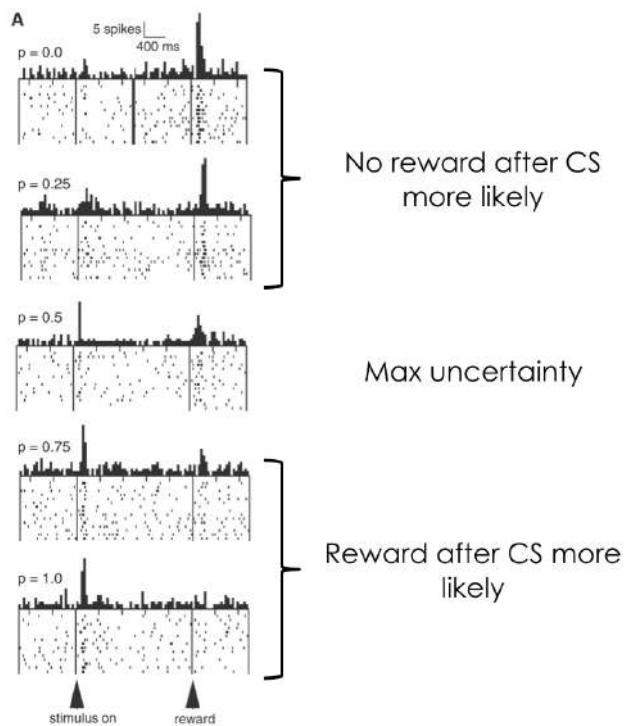


Figure 6.20

Looking at the image above notice the following aspects:

- Focusing on the first two graphs from the top: in correspondence of the two peaks at this stage ('reward' level) you don't expect to have the reward.
- Focusing on the last two graphs from the top:
 - in correspondence of the two peaks at this stage ('stimulus on' level) we have $\delta_t \neq 0 = R_t - V_t = 0 - 1$;
 - in correspondence of the 'reward' level, here we have $\delta_t = 0 = R_t - V_t = 1 - 1$ (here $V_t = 1$ because I have the CS before).

Tonic activation vs Phasic activation (of dopamine neurons):

- Tonic activation:
 - in general neurons have a certain firing rate, a basal activity (their are not completely silent for a long time). In the case of dopamine neurons we have always a certain amount of dopamine floating in our

brain and in our synapses and that is our basal level of dopamine and, to have this certain amount we need that neurons always fire with a *certain frequency* and this is the tonic activity.

- Phasic activation:

- with the phasic activity we mean the *sudden increase/decrease of the basal activity* (*i.e.* graphically a great increase/decrease in a very short interval of time). This, for example, happen when we have a positive prediction error or when it is presented a CS that predicts a reward; when we have a negative prediction error ...

Tonic activation¹⁹ of dopamine neurons varies with reward probability in a ramp-like fashion.

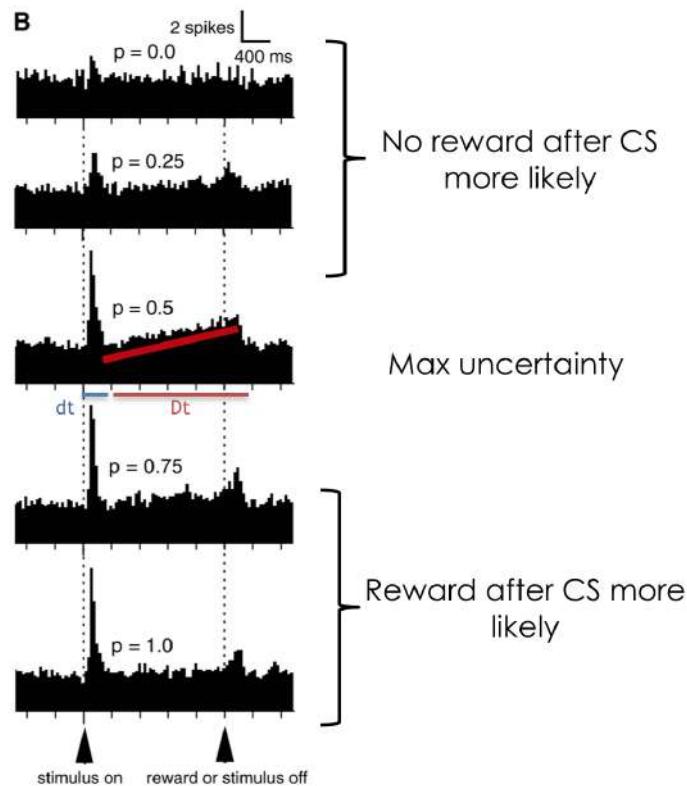


Figure 6.21

¹⁹So we have *Tonic activation* (which is the basic, continuous level of activation): generally speaking, *tonic firing* refers to a sustained response, which activates during the course of the stimulus; while *Phasic activation* refers to a transient response with one or few action potentials at the onset of stimulus followed by accommodation. Until now we looked only at the phasic activation and we saw that violation of our expectations changes not so much the basic level of dopamine in our brain but it induces a phasic firing; however in this paper Schulz realized that there is a change also on tonic activation/firing and that it encodes also probability.

Some dopamine neurons show a sustained increase in activity that grows from the onset of the conditioned stimulus to the expected time of reward.

The peak of the sustained activation occurs at the time of potential reward, which corresponds to the moment of greatest uncertainty (when the monkey expects the reward).

Population histograms at reward probabilities ranging from 0.0 (top) to 1.0 (bottom). Histograms were constructed from every trial in each neuron in the first picture set in monkey A (35 to 44 neurons per stimulus type; 638 total trials at $P = 0$ and 1200 to 1700 trials for all other probabilities). Both rewarded and unrewarded trials are included at intermediate probabilities. At $P = 0.5$, the mean ($\pm SD$) rate of basal activity in this population was 2.5 ± 1.4 impulses per second before stimulus onset and 43.9 ± 2.74 in the 500 ms before potential reward.

Looking at the figure ('Max uncertainty' level) notice that the delta dt (blue) related to phasic activation is very less than the delta Dt (red) related to the tonic activation: $dt << Dt$. At the end of Dt the neuron encode also the time that passes from the CS to R (US).

Source: Fiorillo, Tobler and Schulz, Science, 2003.

Dopaminergic neurons encode expectations of reward timing

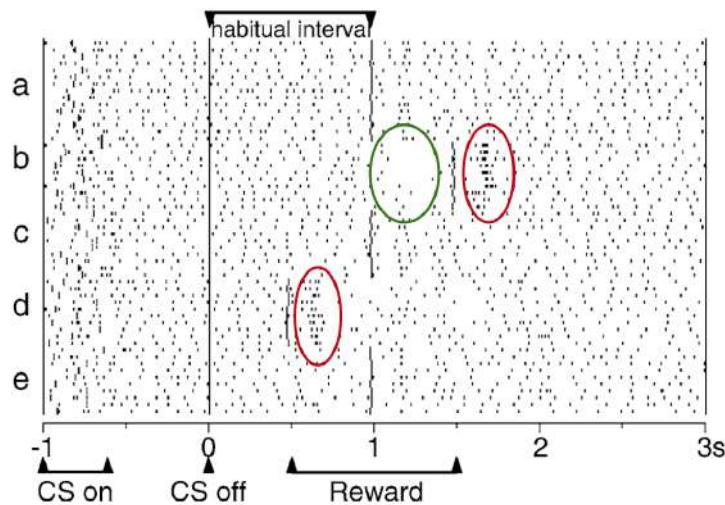


Figure 6.22

Referring to the image above let's explain:

- Note the 'a' level (vertical) segment corresponds to the trial phase.
- *habitual interval*: lenght of 1s; it is called 'habitual interval' because here the CS disappears and the reward happens most of the time;
- *CS off*: CS disappears at this time;

- *Reward*: reward can arrive in this interval but as it can be seen from the vertical line arrives mostly at 1s. Notice that just before the vertical segment at 1.5 s we have a negative prediction error; instead in correspondence of the vertical segment at 1 s (aligned at the ‘c’ level) prediction is satisfied, we restore the expectation created during the trial phase (‘a’ segment).

Following a correct response:

- Expected time: the reward was delivered after 1.0 s.
- Unexpected delay: 1.5 s.
- Unexpected anticipation: 0.5 s.

Firing of a dopamine neuron was:

- depressed (green) when reward failed to occur at the expected time.
- Increased (red) when reward unexpectedly occurred at a new time, either earlier or later.

Temporal prediction error:

- unexpectedness, is not limited to event occurrence (*e.g.*, a reward is delivered or omitted unexpectedly), but also includes the *time of reward*.
- Rewards elicit transient activations when they are delivered *earlier or later than predicted, even though it is certain that the reward will occur*.
- Firing is depressed exactly at the time of the usual occurrence of reward when a predicted reward is omitted.
- The *depression occurs even in the absence of any stimuli* at the time of the omitted reward.
- The depression does not constitute a neuronal response to a stimulus but reflects an *expectation process based on an internal clock tracking the precise time of predicted reward*.

Source: Hollerman and Schulz, Nature Neuroscience, 1998.

Summary

Dopamine neurons:

- *DO NOT* broadcast a *reward signal*.
- *DO* broadcast a *prediction error signal*.

Dopaminergic neurons exhibit a strong phasic response to:

- an unexpected reward:
 - discriminating between reward & no-reward;
 - discriminating between reward magnitude (more or less reward).
 - * In a relative way, rather than absolute.

- Discriminating between reward probability (more or less likely to get reward).
- Timing (earlier or later reward).
- In a signed manner.
 - * Increase firing to unexpected delivery (positive PE).
 - * Pause firing to unexpected omission (negative PE).
- transfers back to a cue which predicts reward occurrence (*i.e.* CS)
 - enabling associative (reinforcement) learning.

Implications of the reward prediction error hypothesis of dopamine

Dopamine:

- is not the feel-good chemical;
- does not make us feel good;
- does not tell us how much we like something.

Dopamine:

- teaches us where to find things we need or like.
- by conveying PEs.

Prediction errors make events that predict rewards relevant (and disregard events that did not).

We saw till now evidences regarding animals, in the following video are presented some evidences regarding humans that show that dopamine in human brain presents a similar response to what we have seen in monkeys.

<https://www.youtube.com/watch?v=UEWRBRq29II> (The Brain Prize Presents: Ray Dolan)

What about humans?

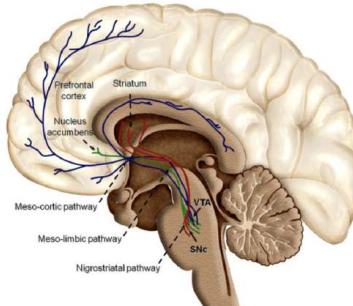


Figure 6.23

Human studies also demonstrate reward prediction error signals in the human brain.²⁰

²⁰And this have also been related to *dopamine activity* (better: *changes in dopamine activity*).

What about humans? Electrophysiological evidence

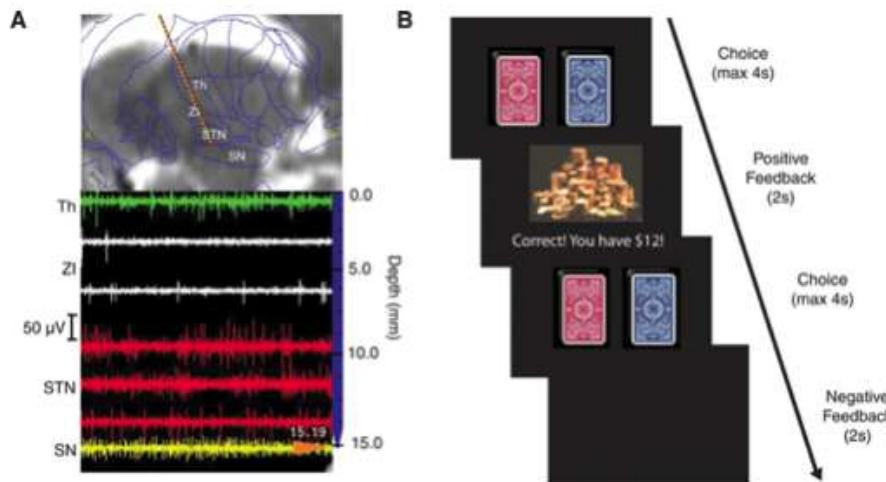


Figure 6.24

Microelectrode recordings²¹ during deep brain stimulation surgery to study neuronal activity in the human substantia nigra (SN)²² while patients with Parkinson's disease²³ engaged in a probabilistic learning task motivated by virtual financial rewards.

Participants are presented with two decks of cards on a computer screen. They are instructed to repeatedly draw cards from either deck to determine which deck yields the higher reward probability.²⁴

Referring to the image below:

- (A) *Expected loss/win*: spike raster for a single experiment from one participant. Individual spike activity recorded from SN for trials during positive (blue) and negative (black) feedback is shown for each trial as a function of time. Below each spike raster is the average z-scored continuous-time firing rate (continuous trace) and histogram (bars, 75 ms intervals). The red vertical line indicates feedback onset.
- (B) *Unexpected loss/win*: individual spike activity, recorded from the same cell, for trials in response to unexpected gains (blue) and losses (black) is shown for each trial as a function of time.²⁵
 - Raw spike count increased in response to positive feedback and decreased in response to negative feedback during this interval.

²¹In the image A above the highlighted line penetrating brain represents the electrode.

²²Contains the cell bodies of *dopaminergic neurons* (see previous image, Nigrostriatal pathway).

²³When drugs are no more efficient with this patients, it is possible to implant surgically electrodes to stimulate parts involved in dopamine production. Remember that Parkinson is also related with lack of dopamine.

²⁴Referring to the image B: after different choiches the patients can elaborate expectations from both the decks (one brings more likely to win, the other not), so after a while we can have with more intensity unespected gains or losses.

²⁵Note that – when unexpected – the trend is more accentuated which reflexed the firing rate.

- The difference in activity between responses to unexpected gains and losses was clearer than the difference between positive and negative feedback.

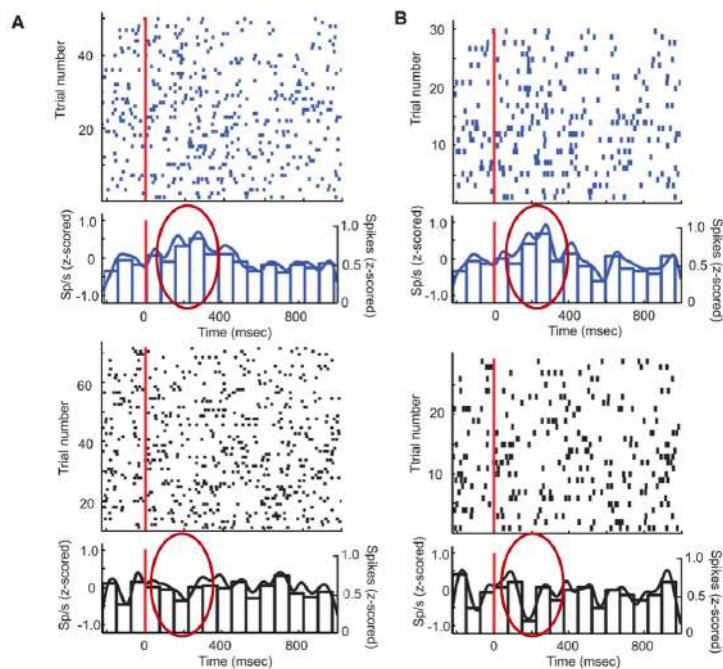


Figure 6.25

Source: Zaghloul, Blanco, Weidemann, et al. Science. 2009.

What about humans? Neuroimaging evidence

Predictability Modulates Human Brain Response to Reward

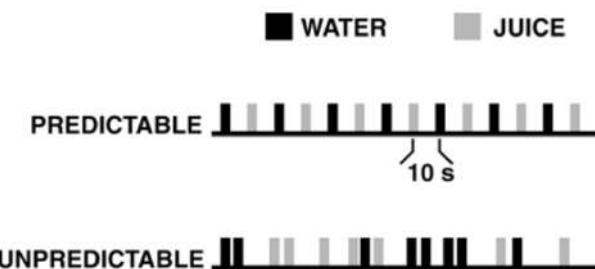


Figure 6.26

Design of the fMRI experiment. A 2×2 factorial design was used, with factors of preference (juice or water) and predictability (predictable or unpredictable). Subjects received 0.8 ml boluses of juice and water in either a predictable or unpredictable sequence. Using event-related fMRI, brain activation was analyzed in terms of preference and predictability, as well as the interaction between them.

Reward-related regions had a greater BOLD response to the unpredictable stimuli.

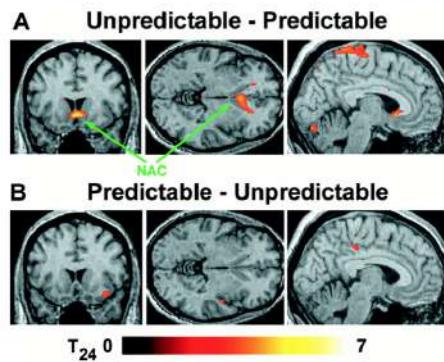


Figure 6.27

Refer to the image above:²⁶

- (A) Planes centered at (0, 4, -4) show that bilateral *nucleus accumbens/ventral striatum (NAC)*²⁷ and bilateral superior parietal cortex were more active in the *unpredictable condition*.
- (B) A small region in the right superior temporal gyrus was relatively more activated by the predictable stimuli.²⁸

Source: Berns, G. S., McClure, S. M., Pagnoni, G., & Montague, P. R. (2001). Journal of neuroscience.

*Predictability in time Modulates Human Brain Response to Reward.*²⁹

Refer to the image below:

- (A) In the previous experiment, juice and water were delivered to subjects in two separate (predictable and unpredictable) sequences. Stimuli delivered during the unpredictable sequence were associated with greater changes in brain activity in the ventral striatum compared with stimuli delivered during the predictable sequence.
- (B) However, stimuli can be unpredictable in character (what stimulus arrives next), unpredictable in time (when the stimulus arrives), and unpredictable in amount (how much arrives). We sought to separate the effects of *temporal prediction errors* only. Subjects were trained to expect juice at a fixed time following a flash of light (normal events) and then changes in brain response were probed when juice was delivered at an unexpected time (catch events).

²⁶In the formulas shown in the image the symbol ‘-’ (e.g. Unpredictable – Predictable) is the minus sign: we subtract the Predictable activity to the Unpredictable and what we see is what remains. In fMRI we need always to subtract two conditions to see what remains.

²⁷Remember that striatum was part of dopaminergic pathways.

²⁸Note that the active zones are not touching the NAC zone (at least with the same intensity), so they are not touching dopaminergic pathways (with the same intensity).

²⁹With the previous experiments done on monkeys we've seen that they encode time. The following kind of learning is Pavlovian (association).

- (C) *Normal events* consisted of brief (1 s) flashes of a yellow light centered in their visual field and orally delivered fruit juice (in 0.8 ml boluses). The time between individual events was randomly selected from between 4 and 14 s.³⁰
- (D) After 49 consecutive light-juice pairings, several *catch events* were randomly inserted among normal events. For the catch events, *the time of juice delivery was extended* to 10 s beyond the preceding flash of light.

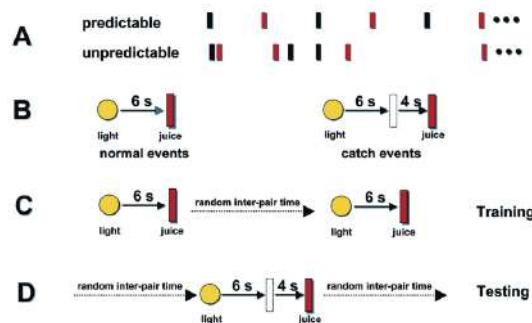


Figure 6.28

Refer to the image below:³¹

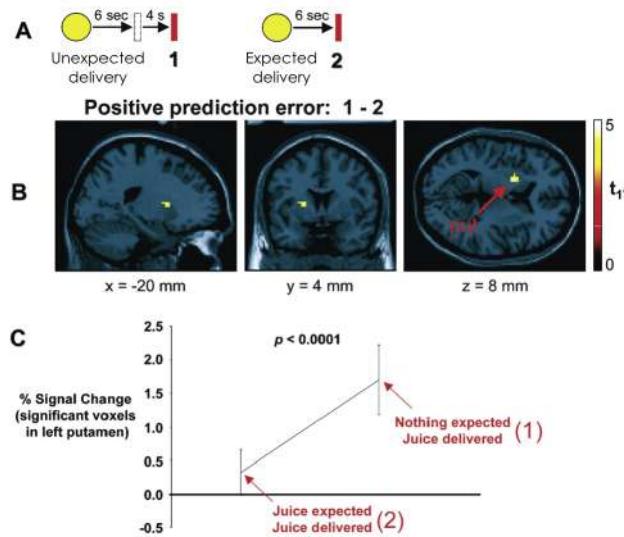


Figure 6.29

³⁰This last interval is made random to avoid that the deliver of juice could be interpreted as the light (the our reference regarding timing the CS) if also that interval would be constant we would make time prediction/expectation also after the delivering of juice, instead we want only after the delivery of light.

³¹In the formulas shown in the image the symbol ‘-’ is also here the minus sign.

- (A) Comparing the brain response to juice delivered during catch and trained events reveals the effect of predictability on the induced brain response.
- (B) *Unpredictable juice delivery* is associated with significantly greater activity in the left putamen (put)³² and parts of the left globus pallidus.
- (C) Combining the average response amplitude across subjects shows that *predicted juice delivery induces essentially no change in fMRI signal, whereas unpredicted juice delivery induces a significantly positive change.*

Refer to the image below:

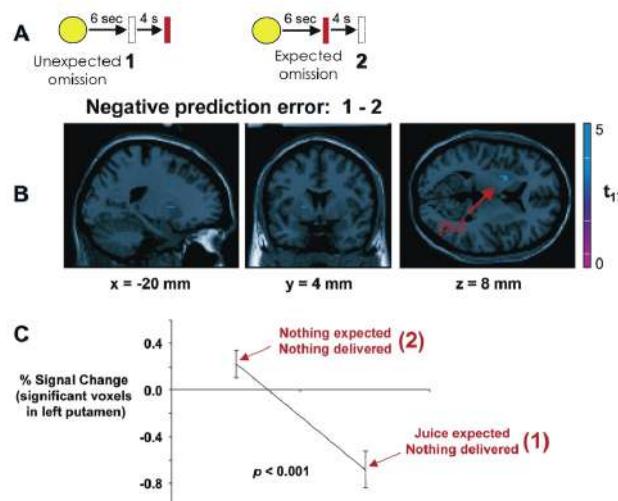


Figure 6.30

- (A) Comparing the brain response at 6 s following the light in catch events versus a period of no juice delivery in normal events (10 s following light) reveals brain regions that correlate with the negative prediction error.
- (B) The failure of juice delivery during catch events correlated with decreased activity selectively in the left putamen.
- (C) *There is a significant decrement in BOLD signal following the absence of juice delivery at expected times.*

Source: McClure, Samuel & Montague. *Neuron* (2003).

Notice that so far

We showed evidence that striatal/putamen, accumbens³³ activity changes to unexpected events but no direct evidence of a link with dopamine and of an effect on behavior.

³²Remember that caudate and putamen are parts of the striatum (together make the striatum.)

³³Are parts of the brain related to dopamine activity.

What about humans? Behavioral & pharmacological evidence

Here we show that, during instrumental learning,³⁴ the magnitude of reward prediction error expressed in the striatum is modulated by the administration of drugs enhancing³⁵ (3,4-dihydroxy-L-phenylalanine; L-DOPA) or reducing³⁶ (haloperidol) dopaminergic function.

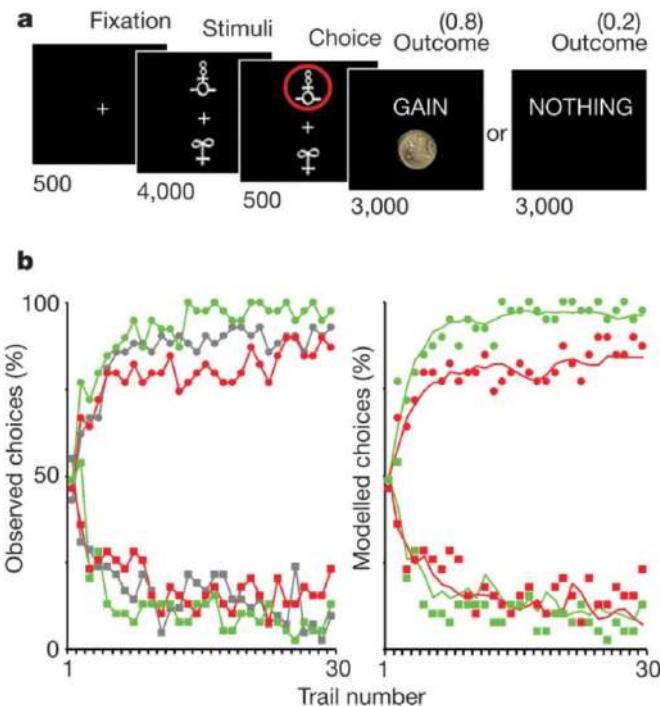


Figure 6.31

Looking at the figure (b-part) above we have:

- group with agonist administration: green;
- placebo (neutral) group: grey;
- group with antagonist administration: red;
- circles (top) for the right choice;
- square (bottom) for the wrong choice.
- So, resuming, we have 3 groups which make 2 choice (right/wrong) each.

³⁴Instrumental learning because there is association between a behaviour and an outcome.

³⁵Agonist.

³⁶Is an antagonist: antagonist substance in general mimics the structure of neurotransmitters so that they can combine with receptors but without inducing any effect, so that the real neurotransmitter can't combine with receptors that are already full. Here haloperidol for example combine with receptors of dopamine without any effect.

Subjects performed an instrumental learning task involving monetary gains and losses, which required choosing between two novel visual stimuli displayed on a computer screen, so as to maximize payoffs. Each stimulus was associated with a certain probability of gain or loss: one pair of stimuli was associated with *gains* (£1 or nothing), a second pair was associated with *loss* (– £1 or nothing), and a third pair was associated with *no financial outcomes*. Thus, the *first pair* was designed to assess the *effects of the drugs* on the ability to learn the most rewarding choice. The *second pair* was a *control condition for the specificity of drug effects*, because it required subjects to learn from punishments (losses) instead of rewards (gains), with the same relative financial interests. The *third pair* was a *neutral condition* allowing further control, in which subjects could indifferently choose any of the two stimuli, because they involved no monetary gain or loss.

Looking at the figure above:

- (a) Experimental task. Subjects selected either the upper or lower of two abstract visual stimuli presented on a display screen, and subsequently observed the outcome. In this example, the chosen stimulus is associated with a probability of 0.8 of winning £1 and a probability of 0.2 of winning nothing. Durations of the successive screens are given in milliseconds.
 - The effects of haloperidol (an antagonist of dopamine receptors) and L-DOPA (a metabolic precursor of dopamine) on both brain activity and behavioural choice in groups of healthy subjects was assessed.
- (b) Behavioural results. Left: observed behavioural choices for initial placebo (grey), superimposed over the results from the subsequent drug groups: L-DOPA (green) and haloperidol (red). The learning curves depict, trial by trial, the proportion of subjects that chose the ‘correct’ stimulus (associated with a probability of 0.8 of winning £1) in the gain condition (circles, upper graph), and the ‘incorrect’ stimulus (associated with a probability of 0.8 of losing £1) in the loss condition (squares, lower graph). Right: modelled behavioural choices for L-DOPA (green) and haloperidol (red) groups. The learning curves represent the probabilities predicted by the computational model. Circles and squares representing observed choices have been left for the purpose of comparison.³⁷

A standard algorithm of action-value learning was then fitted to the observed behaviour. Outcome prediction errors estimated by the model were then used as a statistical regressor in the imaging data.

³⁷It is important to notice that in the first half (circles - right choice) dopamine makes a huge difference (notice how distant and distinct are the 3 trends) while in the second half (square) the 3 trends are overlapping almost all the time. All this \Rightarrow dopamine is more related to reward/gain than loss: so more related to learning from reward than learning from punishment/loss; assuming an antagonist does not modify significantly the behaviour performance as assuming an agonist substance. Note also that at the beginning of the trial number there is quite the same trend for all the 3 groups: the percentage starts from 50 (fifty-fifty for circles and squares); after some period the trends become distinct and, in particular, after a longer period the trends of the circles become distinct in turn. In the first half (circles) the green group makes choice that *maximize the gain* while in the second half (squares) always the green group makes choice that *minimize the loss*: so participants with L-DOPA make more correct choices, they learn better than the haloperidol group. Note in the end that the red group makes the higher percentage in choosing the wrong (see the bottom half, at trial 30, red squares).

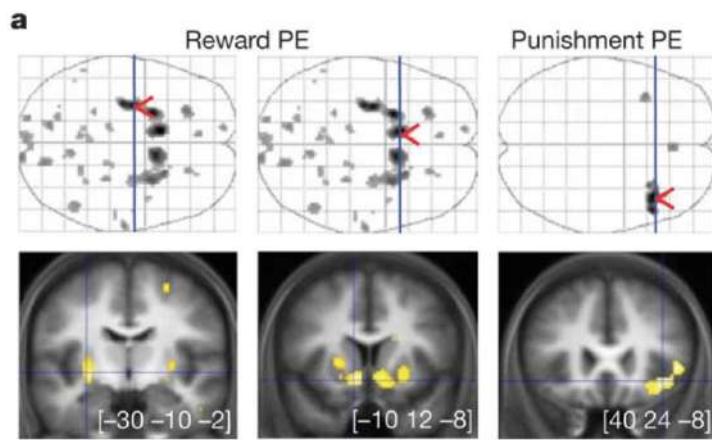


Figure 6.32

Looking at the figure above:

- (a) Brain activity correlated with prediction errors derived from the computational model. *Reward prediction errors* (positive correlation) were found by conjunction of gain and loss conditions (left panels), whereas *punishment prediction errors* (negative correlation) were found in the loss condition alone (right panel). From left to right, MNI (Montreal Neurological Institute) coordinates are given for the maxima found in the *left posterior putamen*, *left ventral striatum* (reward PE) and right anterior insula (punishment PE).

Source: Pessiglione, Seymour, Flandin, Dolan & Frith. Nature (2006). <https://doi.org.ezproxy.unibo.it/10.1038/nature05051>.

What about humans?

- Human studies also demonstrate reward prediction error signals in the human brain;
- the signal reflects the dopamine response;
- occurs in *striatal and frontal dopamine terminal areas* rather than in mid-brain cell body regions, presumably because it reflects summed *postsynaptic potentials*.

Dopamine and addiction

We suggest to see the following video:

https://www.youtube.com/watch?v=aqXm0b_fuN4 (Misunderstanding dopamine: Why the language of addiction matters | Cyrus McCandless | TEDxPortsmouth)

Chapter bibliography

Papers cited in the chapter.

Chapter 7

Model-based & Model-free

7.1 Learning strategies

Everyone at least one time in his/her life experienced to get lost in a place like a train station or a hospital: a place that looks the same in all its part.

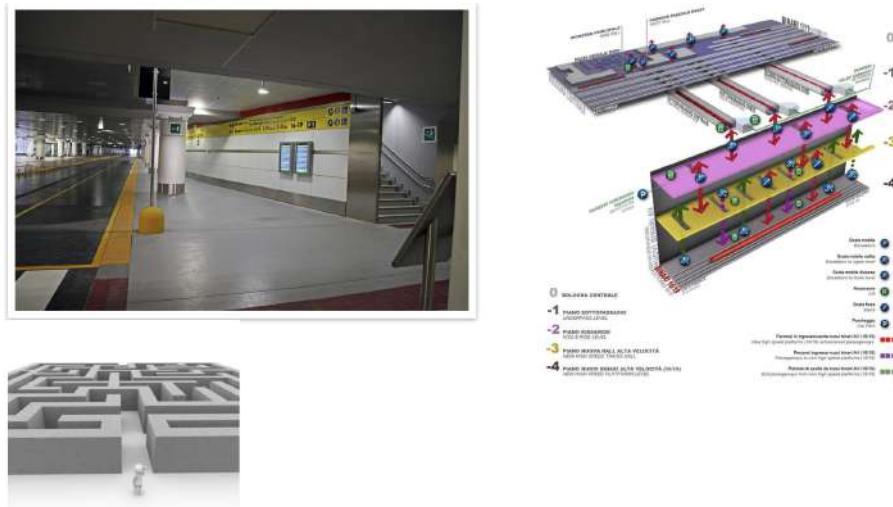


Figure 7.1

Different learning strategies: place/map vs response strategy

In a plus or T maze, animals start in a particular location (say a south arm) and from there they must enter a different arm, say the west arm to find a food reward. In such a situation, the animals could use one of two strategies to solve the task:

- *place/map*: they could form a *cognitive map*¹ and learn that *reward is located in the west location* and so travel there to find it;

¹Imagine the entire structure or part of the location.

- *response strategy*: they could learn that a particular sequence of motor responses, ultimately *turning left*, *leads to reward*.

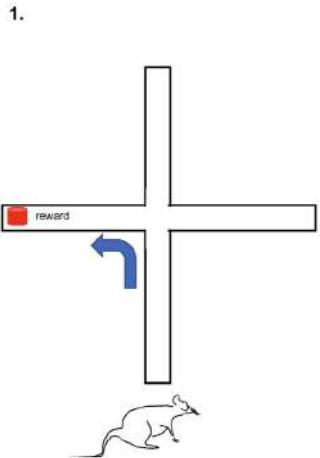


Figure 7.2

To find out what strategy was used, in a probe trial, the animals are placed in a novel location, the north arm, and allowed to choose between arms from there:

- if they had learned to solve the maze using a so-called place strategy, they should use the available cues from the maze to navigate to the west arm;
- if they learned based on a so-called response strategy, they should perform the same response that led to reward in the past, that is, turn left delivering them now to the east arm.

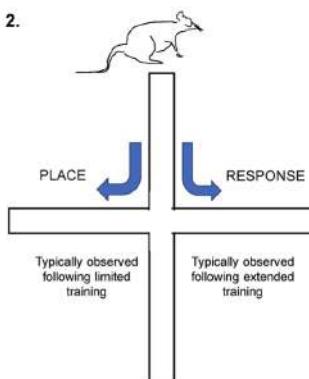


Figure 7.3

Early studies found that *rats learned more readily about places than about the*

particular response sequence.²

Nonetheless, given sufficient training, rats come to rely on a response strategy.³

Source: Corbit, Laura H. 'Understanding the balance between goal-directed and habitual behavioral control.' Current opinion in behavioral sciences 20 (2018): 161-168.

Associative learning

The animal learns about the relationship between:

- A stimulus and an outcome: Pavlovian or classical conditioning;



Figure 7.4

- a behavior and an outcome: instrumental or operant conditioning.



Figure 7.5

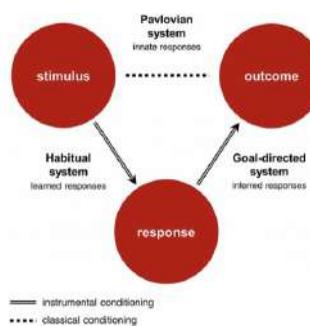


Figure 7.6

In the case of the instrumental conditioning, for example (see the figure above), the rat sees the lever (stimulus) and understands that has to press the lever (response) in order to get the food (outcome).

²Less experience, more imagination. At the beginning the rat does not know the environment, it's a new place, so has to figure the environment; for example just to survive.

³More experience, less imagination. After a period the environment becomes well-known, so the rats follow the response strategy.

Instrumental learning (or operant conditioning) involves associating an action with an outcome

Thorndike's Law of effect (Thorndike, 1911):

'Of several responses made to the same situation, those which are accompanied or closely *followed by satisfaction* to the animal will, other things being equal, be more firmly connected with the situation, so that, when it recurs, they *will be more likely to recur*; those which are accompanied or closely *followed by discomfort* to the animal will, other things being equal, have their connections with that situation weakened, so that, when it recurs, they *will be less likely to occur*. The greater the satisfaction or discomfort, the greater the strengthening or weakening of the bond.'

We act to produce outcomes that are desirable or to avoid those that are harmful or aversive.



Figure 7.7

But how do we select/decide which is the appropriate action to take?

- Are we flexible in the actions we take?
- Do we choose the action to take with the goal in mind or do we automatically select actions based on previous experiences?
- Are our choices directed by the goal we want to achieve or are they automatically/habitually triggered based on our past experiences?⁴

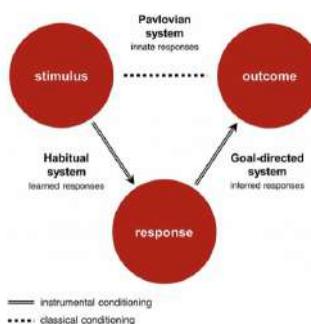


Figure 7.8

⁴E.g. a rat (but also a man) presses a button and then gets the food. After several experiences, when the rat sees the button, does he press it because want the food or just because experienced this action and then repeat it automatically? Or another example could be that sometimes humans open social networks like Instagram and scroll the activity just for habit.

Ray J. Dolan and Peter Dayan in the following paper – which is the main reference of this lecture – identified six *generation of studies* (that disconnected from instrumental learning).

It's interesting because these different generations involves different types of studies: from experimental psychology to computational neuroscience.



Goals and Habits in the Brain

Ray J. Dolan^{1,*} and Peter Dayan²

¹Wellcome Trust Centre for Neuroimaging, Institute of Neurology, University College London, London WC1 3BG, UK

²Gatsby Computational Neuroscience Unit, University College London, London WC1N 3AR, UK

*Correspondence: r.dolan@ucl.ac.uk

<http://dx.doi.org/10.1016/j.neuron.2013.09.007>

This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use,

distribution, and reproduction in any medium, provided the original author and source are credited.

Open access under [CC-BY license](#).

Figure 7.9

Here we cover four of them:

- *Generation 0*: cognitive maps vs stimulus-response (experimental psychology).
- *Generation 1*: goal-directed vs habitual actions (experimental psychology).
- *Generation 2*: goal-directed vs habitual actions in the human brain (cognitive neuroscience).
- *Generation 3*: model-based vs model-free computational analyses (computational neuroscience).

Generation 0: cognitive maps vs stimulus-response

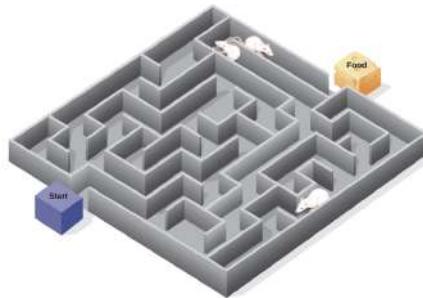


Figure 7.10

How does the animal learn to solve the maze?⁵

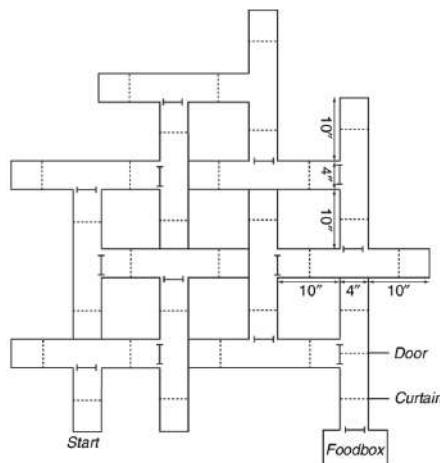
⁵It is essentially what we saw at the beginning of the chapter. A generic experiment is (with animals, not with human) put rats in a maze and see how them reach the end where usually there is food; food is essential because is the *reward* and the reward motivates the behaviour (it is difficult to do anything if at the end there is no reward).

- *Stimulus-response (S-R) theories:*

- the bedrock of psychology in the first half of the 20th century.
- Solving the maze is a matter of *individual stimulus-response one-to-one connections*.
- Learning depends on strengthening of some connections and weakening of others.
- the animal helplessly responds to a succession of external and internal stimuli that callout the actions to take (*e.g.* turnings: turning left - turning right ... seen as separate actions) and the like that follows.

- *Field theories:*

- Solving the maze is a matter of creating a mental/cognitive map that includes multiple sets of connections.
- The mental map then guides what responses the animal will perform.
- The mental map acts as a representational template that enables an animal to find the best possible action at a particular state.⁶



Maze used by Tolman and Honzik (1930) to study latent learning in rats. From Tolman EC (1948) Cognitive maps in rats and men. Psychol. Rev. 55: 189-208

Figure 7.11

Tolman's maze (see the figure above):

- The maze had lots of doors and curtains to make it difficult for the rats to master.

⁶For example: turning left - turning right - go ahead ... are not seen as separate action (are connected to the others) as described in the previous page but they are seen together. It is learned the entire map: if you start in another place you are able to reach the end too; you just not repeat the sequence from the start point but you adapt it to the place in which you are.

- *Doors* swung both directions, which prevented the rat from seeing most of the junctions as it approached. This forced the rat to go through the door to discover what was on the other side.
- *Curtains* hung down and prevented the rat from getting a long distance perspective and it also meant that they could not see a wall at the end of a wrong turn until they had already made a choice and moved in that direction.
- The rat was always in a small area, unable to see beyond the next door or curtain, so learning the maze was a formidable task.

Experiment:

- Hungry⁷ rats have to find their way out through a maze.
- Group 1: no reward for solving the maze.
- Group 2: food reward for solving the maze.

Which group completed the maze faster?

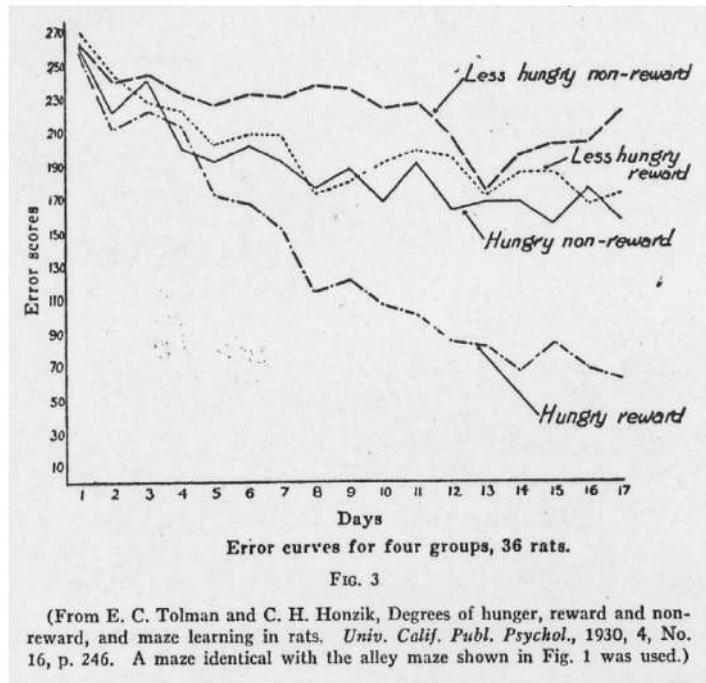


Figure 7.12

In the above figure we have:

- along the y-axis: number of errors in order to solve the maze (less errors made, faster you get the reward).

⁷To motivate the rats to solve the maze.

- along the x-axis: put the rat in one day in the maze *etc.*
- as it can be seen the group 2 completed faster.

Note: the S-R theories argues that no learning occurs when there is no reward.⁸
Experiment:

- Hungry⁹ rats have to find their way out through a maze.
- Group 1: no reward for solving the maze.
- Group 2: food reward for solving the maze.
- Group 3: food reward for solving the maze provided only at day 11.¹⁰

What do you think happens to performance?

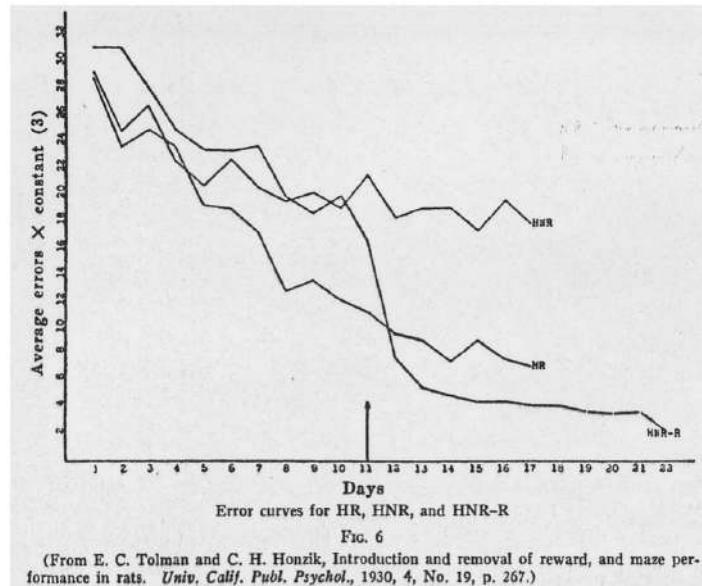


Figure 7.13

Looking at the figure above we have the following correspondence:

- HNR (hungry never rewarded) \longleftrightarrow Group 1;
- HR \longleftrightarrow Group 2;
- HNR-R \longleftrightarrow Group 3;

As soon as the rats in Group 3 became aware of the food, they were able to find their way through the maze quickly, just as quickly as the comparison group, which had been rewarded with food all along.¹¹

⁸Look at the previous image: group 1 seems to have a better behaviour but not so much as the group 2 with the time passing (no learning).

⁹To motivate the rats to solve the maze.

¹⁰According to S-R theories so far for the group 3 no learning occurs till the day 11. See ahead.

¹¹So if Group 3 hadn't learnt until the day 11, how is it possible a performance like this (focus at the day 11 on the graph: after only 1-2 days Group 3 was better than Group 2; so this is not coherent with the S-R theories)? There should be a sort of *latent learning*.

Latent learning & cognitive maps

*Latent learning:*¹²

- Learning that is not shown behaviorally until there is sufficient motivation.
- It occurs without any obvious reinforcement of the behavior or associations that are learned.

*Cognitive map:*¹³

- Rats¹⁴ behaved as if they were responding to a mental representation of the overall layout of the maze rather than blindly exploring different parts of the maze through trial and error.
- Mental representation of the space field that can guide what actions should be performed at any stage to achieve a particular goal.

Generation 0: implications for the field

- Challenged the constraints of behaviorism, which stated that processes must be directly observable and that learning was the direct consequence of conditioning to stimuli.
- Challenged the prevailing stimulus-response (S-R) view of learning and behavior, which corresponds to the simplest model-free (model free learning) way of learning policies.
- Conditioning involves more than the simple formation of associations between sets of stimuli or between responses and reinforcers. It includes learning and representing other facets of the total behavioral context.

Generation 0 studies established a dichotomy between decision behavior controlled by a cognitive map and by S-R associations.¹⁵

Generation 1: Goal-Directed vs Habitual actions

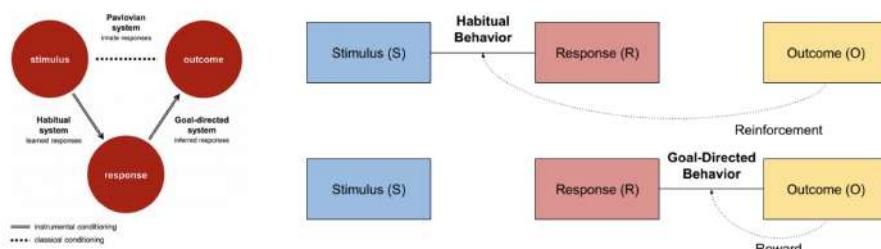


Figure 7.14

¹²The experiment in the previous section tells us that this kind of learning exists.

¹³Mental representation is called *cognitive map*; term used by Tolman for the first time.

¹⁴Of the Group 3 of the previous experiment.

¹⁵We learn through both of them (depending from the case and the conditions).

Operationalized the use of cognitive maps for learning to choose appropriate actions (*i.e.* that maximize rewards/minimize punishments) in non-spatial domains.¹⁶

Termed this as *goal-directed behavior/actions*.¹⁷

Contrasted it with *habitual behavior/actions*.¹⁸

Focused on animal studies to identify the neural bases of the two types of behaviors.¹⁹

So:

- Generation 0: *S-R strategy* vs *Cognitive Map* \longleftrightarrow [SPATIAL].
- Generation 1: *Habitual behavior/actions* vs *Goal-directed behavior/actions* \longleftrightarrow [NON SPATIAL].
- Generation 0 \longrightarrow Generation 1 (Generation 0 mapped in non-spatial domains) \implies *S-R strategy* \longrightarrow (drop the term) *Habitual behavior/actions* and *Cognitive Map* \longrightarrow *Goal-directed behavior/actions*.

Goal-directed behavior/actions

The action is made because we think that they will lead to outcomes that we desire.

Two criteria make an action goal-directed:

1. There must be *knowledge of the relationship between an action* (or sequence of actions) and its *consequences* \longrightarrow response-outcome or R-O control.
2. The *outcome should be motivationally relevant* or desirable at the moment of choice/action.²⁰

Goal-directed behavior:

- involves active deliberation;
- has high computational cost;
- shows adaptive flexibility to changing of environmental contingencies (*e.g.* the behavior stops if no reward follows the action).²¹

¹⁶Generation 0 of studies was concern with *spatial navigation*, but after scientists wondered if *S-R strategy* and *cognitive map* could be used for learning about non spatial task.

¹⁷When the behaviour is *goal-directed behavior/actions* what is strength any time you get the reward is the relationship between the R (response) and the O (outcome); in this case you see the *Stimulus* but you're going to do the R or not because you have in mind your Outcome or what you want to achieve. In this case you press the lever (R) only if you want the food (O).

¹⁸In *habitual behavior/actions* is more strength (every time you get the outcome) the relation between *Stimulus* and the *Response* than *Response-Outcome*: the *Outcome* is seen as *reinforcement* of S-R relationship (S: see the lever, R: press the lever, O: get food); induce a more *compulsive response*, it's an habit, you see the stimulus, you do the action.

¹⁹We can have and study these two kinds of behaviour.

²⁰The food is relevant when you're hungry.

²¹You don't search any more food if is finished in a place.

Habitual behavior/actions

The action is:

- made automatically, just because it has been rewarded in the past;
- not influenced by the current value of the outcome it leads to;²²
- continues to be enacted even when the outcome is undesired.

Habitual behaviour:

- automatic (no active deliberation);
- has low computational cost;
- is inflexible to changing of environmental contingencies (*e.g.* the behavior does not stop even if no reward follows the action).²³

IT'S NOT THAT SIMPLE



www.ninaamir.com NINA AMIR
INSPIRATION TO COACH

Figure 7.15

Testing if a behavior is goal-directed (vs habitual)

1. Training session: the animal undergoes instrumental learning (learns that some actions will lead to rewards).²⁴
2. Post-training manipulation:
 - (a) reinforcer *devaluation*,²⁵
 - (b) contingency degradation.²⁶
3. Testing session: the animal repeats the actions learned during instrumental training under extinction:²⁷
 - (a) If the action associated to the devalued reinforcer is performed less, then the behavior is goal-directed;
 - (b) if not, it's habitual.

²²Obviously we see what reported in these first two items after a trial period.

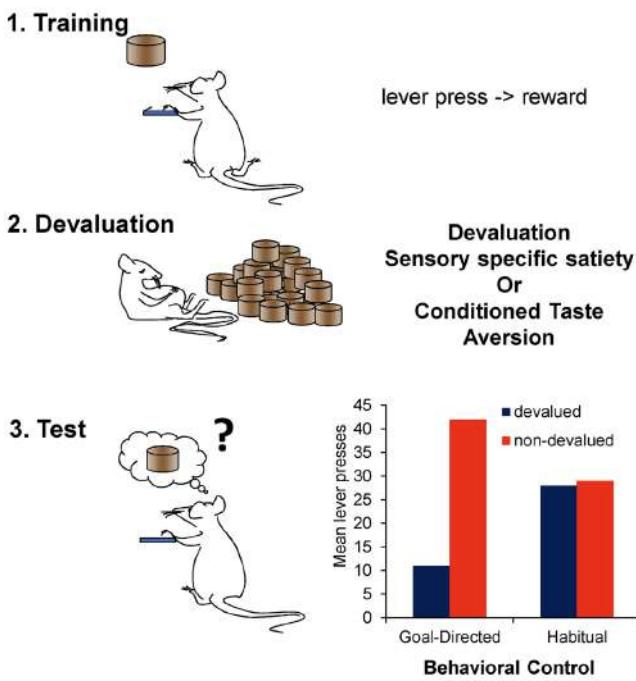
²³You see the food and you eat it even if you're not hungry.

²⁴Lever press → reward (is instrumental).

²⁵Devaluation example: we give a lot of food until the rat stops eating, it is stuffed.

²⁶An example of this typology is when you teach the rat that pressing the lever don't let to food any more.

²⁷*I.e.* without giving the outcome; we mean this with 'under extinction'.



Corbit, Laura H. "Understanding the balance between goal-directed and habitual behavioral control." *Current opinion in behavioral sciences* 20 (2018): 161-168.

Figure 7.16

Testing if a behavior is habitual (vs goal-directed)

1. Extensive training session or *overtraining*:²⁸
 - (a) the animal undergoes instrumental learning (learns that some actions will lead to rewards);
 - (b) this time the training is extensive.
2. Post-training manipulation:
 - (a) reinforcer *devaluation*;
 - (b) contingency degradation.
3. Testing session; the animal repeats the actions learned during instrumental training under extinction:²⁹
 - (a) if the action associated to the devalued reinforcer is performed less, then the behavior is goal-directed;
 - (b) if not, it's habitual.

²⁸Training over time a lot. In this case results show that the behaviour is gonna turn from goal-directed to habitual; which means: at the beginning is goal-directed, after is habitual.

²⁹I.e. without giving the outcome; we mean this with 'under extinction'.

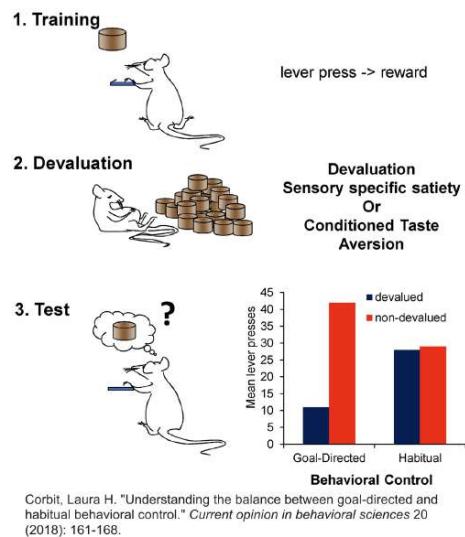


Figure 7.17

Dissociation of goal-directed vs habitual behaviour in the striatum

This Generation 1 of studies looked also at the *neural basis* (it is very important that there is a neural correspondence) of this distinction and they found that the striatum was important for these two kinds of behaviours.

- *Dorsomedial striatum*: supports goal-directed behaviour.
- *Dorsolateral striatum*: supports habitual behaviour.

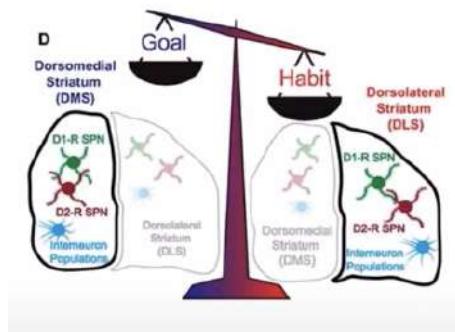


Figure 7.18

Another thing very important is that with overtraining the behaviour goes from goal-directed to habitual, there is a *continuum*; and at a neural level this is seen passing from DMS to DLS.

Source: Lipton, David M., Ben J. Gonzales, and Ami Citri. 'Dorsal striatal circuits for habits, compulsions and addictions.' *Frontiers in systems neuroscience* (2019): 28.

From goal-directed to habitual behavior: a continuum

Generation 1 results show that the need for *overtraining to make a behavior habitual* implies that behavior is initially goal directed but then becomes habitual over the course of experience.

In the brain, there is a dynamic *inter-dependency* between goal-directed and habitual systems, which may *act simultaneously and competitively*.

If habit and goal-directed processes act concurrently, we may wonder what are the factors that influence the integration and competition between the two systems.

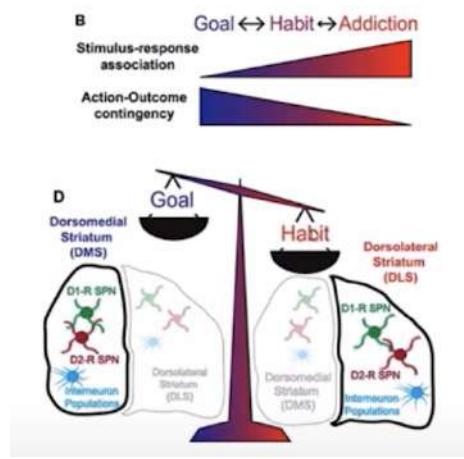


Figure 7.19

Looking at the image above we can see that the two systems *Stimulus-response association* and *Action-Outcome contingency* are in competition. There is a continuum: if we strength SR we go from goal to habitual; if we strength Action-Outcome we have a more goal directed behaviour.

Striatum linking motivation-action

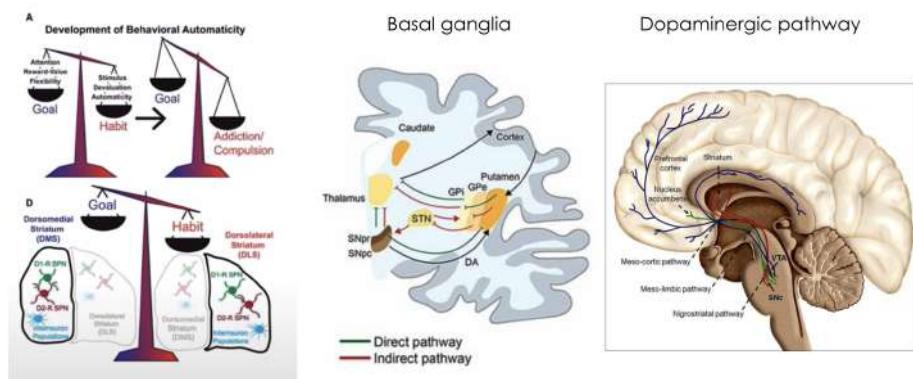


Figure 7.20

Remember that Striatum is linked to dopamine reward prediction error; Striatum receives input from dopamine neurons about PE, where dopamine is released. Striatum is part of Basal ganglia which are important for action/movement: remember Parkinson's disease that affects Basal Ganglia.

But Striatum is important also to turn PE in action.

So, Striatum is an important structure that connects PE (and motivation, and learning) and turn them into *action*.

We learn something and we act upon that learning.

Generation 2: Actions (Goal directed) and Habits in the Human Brain

What we've seen in Generation 0 and Generation 1 is valid for humans? Generation 2 translates animal research into human research and they adopted animal paradigms to human experiments.



Figure 7.21

Successful animal paradigms were adapted for human experiments.

Use of fMRI in order to investigate the neural bases of:

- Goal-directed actions.
- Habitual actions.

Neural substrates of the goal-directed behavior in humans

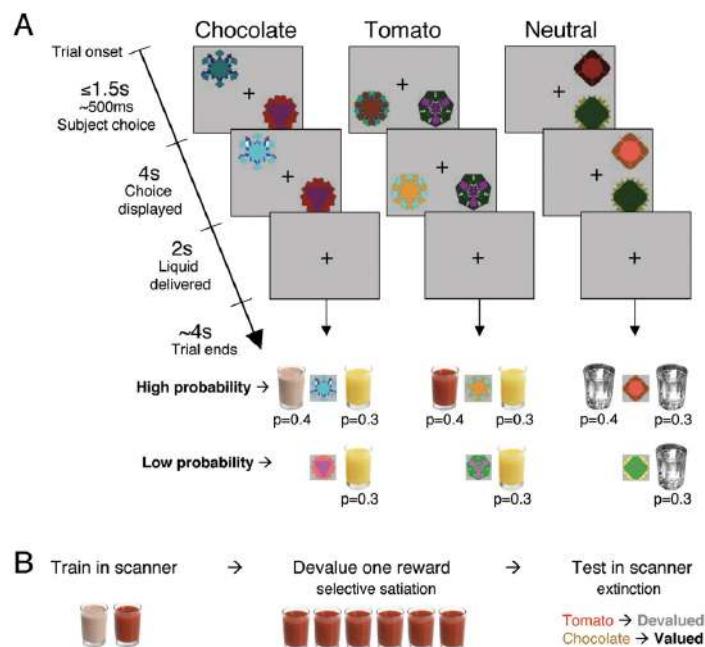
Method:³⁰

- human subjects were trained on a task in which two different actions resulted in two distinct food reward outcomes (*i.e.* instrumental conditioning);
- one of the outcomes was then devalued (by feeding subjects that food to satiety *i.e.* until they would consume no more of it);
- the values of other foods not eaten remained high;
- after devaluation participants performed the instrumental actions (choice of stimuli) under extinction.³¹

³⁰Some paradigms seen for animals.

³¹*I.e.* without giving the outcome; we mean this with 'under extinction'.

- fMRI was recorded at train and test to examine brain areas responding during action selection:
 - looking for areas that showed sensitivity to the change in value of the associated outcomes;
 - such area(s) would be candidate regions for implementing goal-directed behavior in humans.



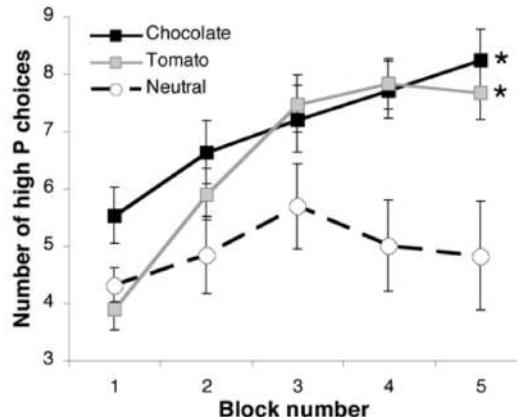
Valentin, V.V., Dickinson, A., and O'Doherty, J.P. (2007). Determining the neural substrates of goal-directed learning in the human brain. *J. Neurosci.* 27, 4019–4026.

Figure 7.22

Looking at the figure above we can see that the A part shows in particular the *training*:

1. Human sees the two fractal figures.
2. If choose the blue one has an high probability (40% to have chocolate and 30% to have orange juice; 70% total having something).
3. If choose the red one has a low probability (30% to have orange juice).
4. Over time human should choose the blue one (70% reward)

The *Neutral* part in the figure is relative to the so-called *control stimulus*: it is important having it to make sure that the experiment induces humans to choose a reward and not just to receive a glass which stands for whatever.



Valentin, V.V., Dickinson, A., and O'Doherty, J.P. (2007). Determining the neural substrates of goal-directed learning in the human brain. *J. Neurosci.* 27, 4019–4026.

Figure 7.23

Focusing on the B-part of the Figure 7.22 we highlight that after devaluation we expect changes in performance.

Results: behavioral (look at the image above).

Learning curves. Total number of high-probability action choices over five 10-trial blocks shown averaged across 19 subjects during training. Over the course of training, subjects increasingly favored the high-probability actions associated with tomato juice or chocolate milk over their low-probability counterparts, but this was not the case for the neutral condition where subjects were indifferent between the high- and low-probability actions ($*p < 0.0005$, one-tailed). Error bars indicate SEM.

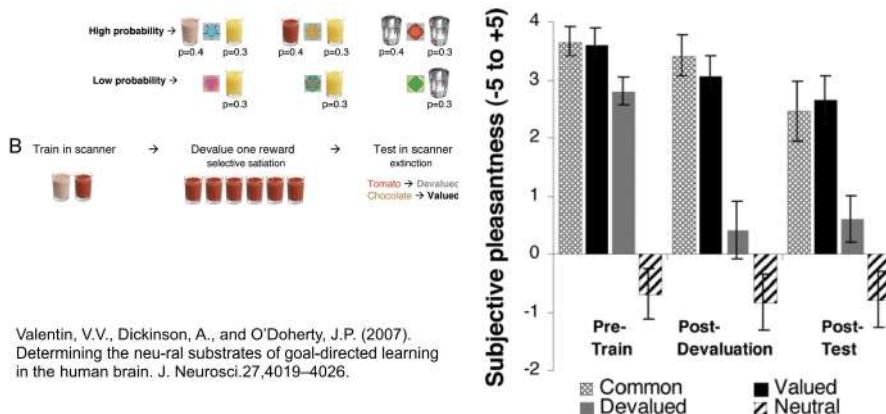


Figure 7.24

Results: behavioral (look at the image above).

Subjective pleasantness ratings on a scale of -5 (very unpleasant) to $+5$ (very pleasant) before training, after devaluation, and after test. The rating for the

food eaten (devalued) significantly decreased compared with the food not eaten (valued) after the selective devaluation procedure (interaction at $p < 0.01$). Error bars indicate SEM.

From the graph is clear that the behavior is goal directed.

Note also that for the *Common* one (orange juice, while the *Devalued* is tomato and the *Valued* is chocolate) there is a decrease because during time you can drink it too and so pleasure goes down too a little bit.

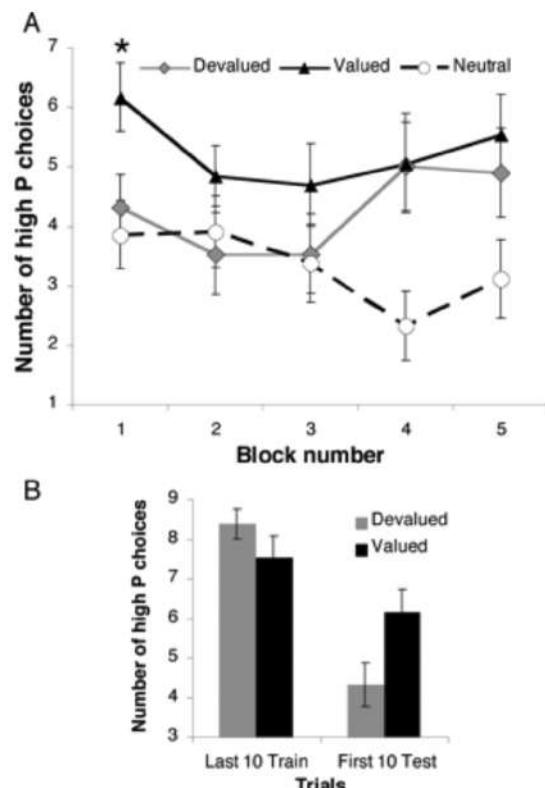


Figure 7.25

Results: behavioural (look at the image above).

- (A) At testing, the number of choices of the high-probability action in the first block was significantly greater in the valued compared with the devalued condition, indicating that subjects modulated their instrumental responses as a function of the change in value of the associated food outcomes ($*p < 0.05$, one-tailed).³²
- (B) After devaluation, subjects reduced their choices of the high-probability action associated with the devalued food significantly more than that of the valued food (interaction with $p < 0.01$). Error bars indicate SEM.³³

³²The graph A shows the trend under extinction. Note also the gap at block 1 (where is the point where there are inputs to evaluate): the devalued is comparable with the neutral and there is a huge gap with the valued.

³³Looking at the B graph remember that train comes before than tests.

Goal-directed behavior/actions

The action is made because we think that they will lead to outcomes that we desire.

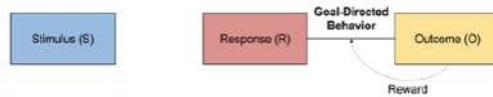


Figure 7.26

Two criteria make an action goal-directed:

1. There must be *knowledge of the relationship between an action* (or sequence of actions) and its *consequences* —→ response-outcome or R-O control.
2. The *outcome should be motivationally relevant* or desirable at the moment of choice/action.

Neural substrates of the goal-directed behavior in humans



Figure 7.27

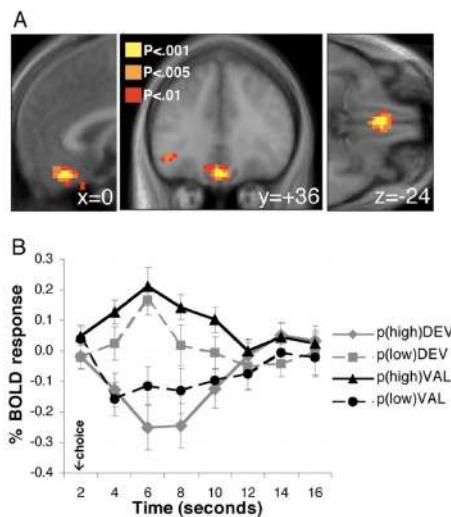
Are there brain areas that respond differently between the still motivationally relevant outcome (*i.e.* valued) and the devalued one?

Results: neural (looking to the figure below).

- (A) A region of the medial OFC³⁴ showing a significant modulation in its activity during instrumental action selection as a function of the value of the associated outcome (mOFC; $x = -3$, $y = 36$, $z = -24$ mm; $Z = 3.29$; $p < 0.001$).
- (B) Time-course plots derived from the peak voxel (from each individual subject) in the mOFC during trials in which subjects chose each one of the four different actions (choice of the high vs low-probability action in either the valued or devalued conditions).³⁵

³⁴OFC stands for orbital frontal cortex. Remember that one of the dopamine pathways goes also to frontal cortical area, so make sense to hypothesize that this also is connected to *dopamine*.

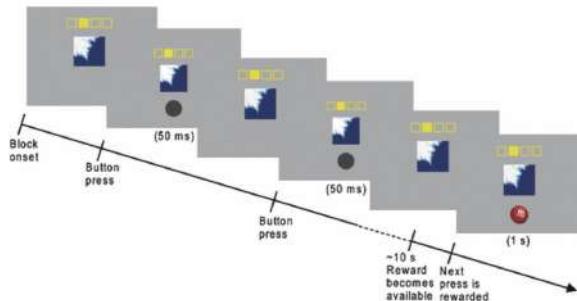
³⁵What emerge is that OFC is more active in response to the devalued outcome than to the valued one (see the graph).



Valentin, V.V., Dickinson, A., and O'Doherty, J.P. (2007). Determining the neural substrates of goal-directed learning in the human brain. *J. Neurosci.* 27, 4019–4026.

Figure 7.28

Neural substrates of habitual behavior in humans



Tricomi, E.M., Balleine, B.W., and O'Doherty, J.P. (2009). A specific role for posterior dorsolateral striatum in human habit learning. *Eur. J. Neurosci.* 29, 2225–2232

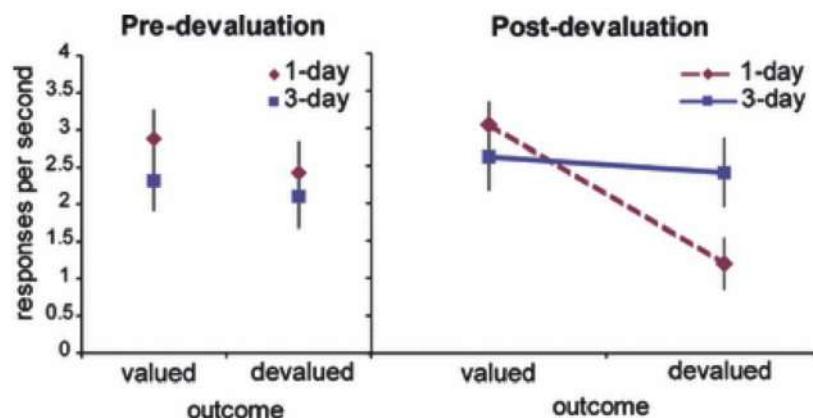
Figure 7.29

Method:

- Group 1: extensive training³⁶ (6 times more than group 2)
- Group 2: little training.

³⁶habitual behaviour ↔ overtraining.

A fractal image was shown on the screen, along with a schematic indicating which button to press.³⁷ Participants were instructed to press the indicated button as often as they liked; after each button press either a gray circle briefly appeared (50 ms), indicating no reward, or a picture of an M&M or Frito appeared (1000 ms), indicating a food reward corresponding to the picture. Only presses of the indicated button led to the display of the gray circle or food picture. Rewards were delivered on a variable interval 10 s schedule.



Tricomi, E.M., Balleine, B.W., and O'Doherty, J.P. (2009). A specific role for posterior dorsolateral striatum in human habit learning. *Eur. J. Neurosci.* 29, 2225–2232

Figure 7.30

Results: behavioral.³⁸

During the last session of training, prior to the devaluation procedure (left), there were no significant differences in response rates between groups or when responding for the two food rewards (one which will be devalued through selective satiation and one which will not). During the test following the devaluation procedure, response rates for the still-valued outcome remained high, as did response rates for the devalued outcome for the 3-day group. In contrast, response rates for the 1-day group for the devalued outcome were reduced.

Results: neural (see the figure below).

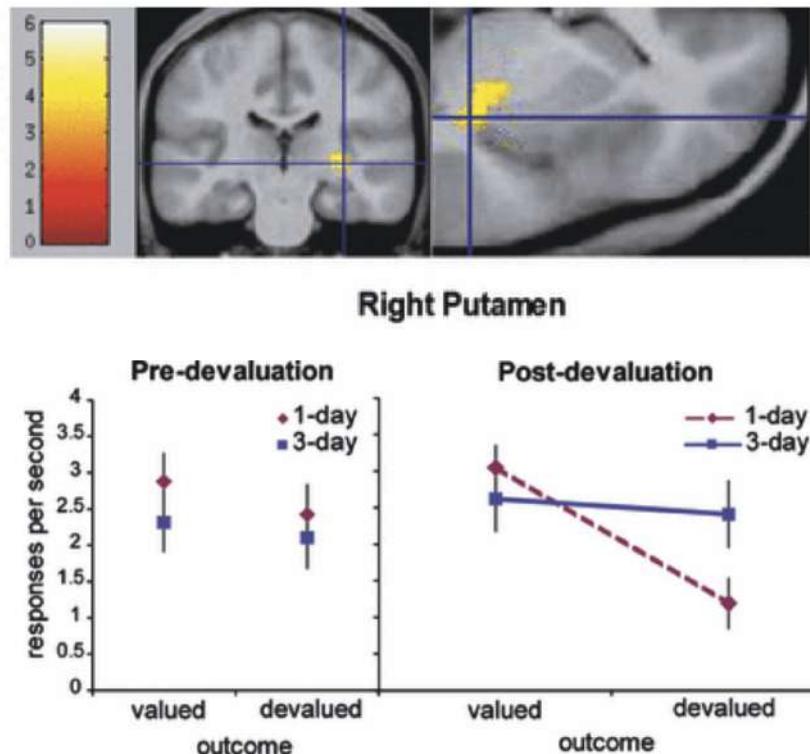
Our within-subjects analysis of the last two sessions of training versus the first two sessions in the 3-day group revealed several significant voxel clusters, including a region within the dorsolateral striatum (DLS),³⁹ in the right posterior

³⁷The yellow square among the schematic indicates the button to press; below there is the fractal image.

³⁸Looking at the image above we have that on the y-axis the responses per seconds corresponds to the action of pressing the button; 1-day is referred to the short training group while the 3-day to the long training group; the term 'devalued' in the Pre-devaluation part should be intended as 'will be devalued'. Focusing on the Post-devaluation part we can see that the 3-day performed habitual behaviour while the 1-day performed goal-directed behaviour; note also the passing (with time) from goal directed to habitual.

³⁹Here Striatum is important for habitual behaviour. This paper presented for the first time that the Striatum that we saw being important for passing from goal-directed to habitual behaviour in rats (more general animals), is important for habitual behaviour for humans: habitual behaviour is also under Striatum for humans.

putamen–globus pallidus.



Tricomi, E.M., Balleine, B.W., and O'Doherty, J.P. (2009). A specific role for posterior dorsolateral striatum in human habit learning. *Eur. J. Neurosci.* 29, 2225–2232

Figure 7.31

Generation 3: model-based vs model-free computational analyses

Computational formalization of:

- Goal-directed actions → model-based:⁴⁰
 - A model-based algorithm selects actions by using a model to predict the consequences of possible courses of action in terms of future states and the reward signals expected to arise from those states.
- Habitual actions → model-free.
- Their interaction.

Model means anything an agent can use to predict how its environment will respond to its actions in terms of state transitions and rewards.

⁴⁰ Model-based is the name of goal-directed in generation 3 which is viewed under an algorithmic point of view; so the computational formalization of goal-directed is named ‘model-based’.

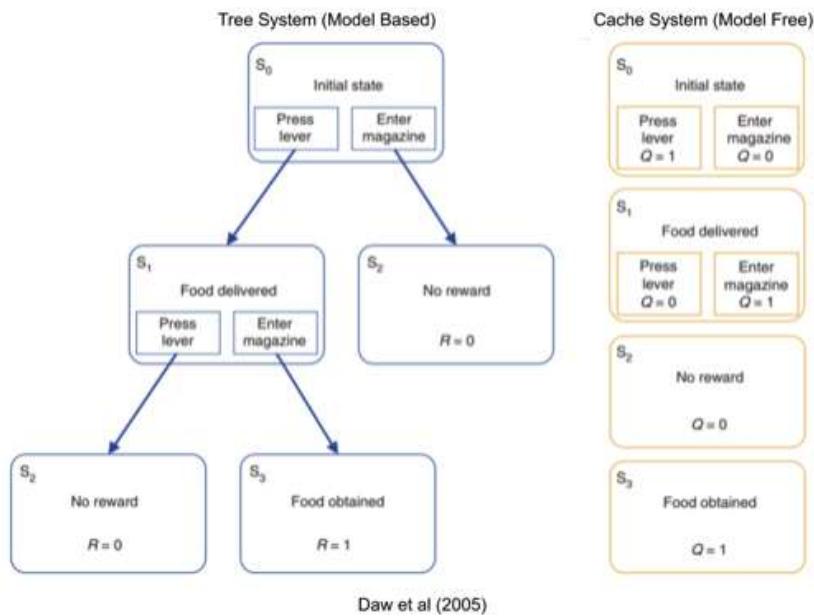


Figure 7.32

Looking at the figure above we can see that:

- Tree System (Model Based):
 - Looking at the model is clear that it is more complex – in comparison to the other – and that it costs more from a computational point of view; each level of the tree depends on the other ones: you don't only compute (and/or keep in memory) if a specific action in a state gives you a reward or not, but each state is connected to the other, behaviour in the previous states affect behaviour in the current and future states.
 - Is an algorithm that includes a full representation of the various different contingencies, different states. It has a model of reward *i.e.* what was called at the beginning a cognitive map and that after became goal directed.
- Cache System (Model Free):
 - each state is separate from the others and you only compute whether that state is going to lead you to a reward or not, to the outcome that you wanted or not.
 - It doesn't have a model of the environmental contingencies or what's happening in the environment; so the term *model* – as already anticipated above – doesn't exactly mean *computational model* because both model free and model based are two different *computational models* but *model free* means *free* of a model of reward, environment, environmental contingencies.

Sequential two-choice Markov decision tasks

The two computational models – mentioned before – were applied to test experimental evidences and to see if the different types of behaviour (goal directed vs habitual) indeed fit with the two different types of model, and after see what are the neural bases of the two types of learning. Experiments became much more sofisticated: it is not only looked simply the behaviour but they used the data from behaviour and apply them to the models, and also looked learning in terms of the two computational models.

Developed to:

- discern the influence of model-free vs model-based controller on behavior;
- to determine whether neural signals are correlated with predictions and prediction errors specific to each controller.

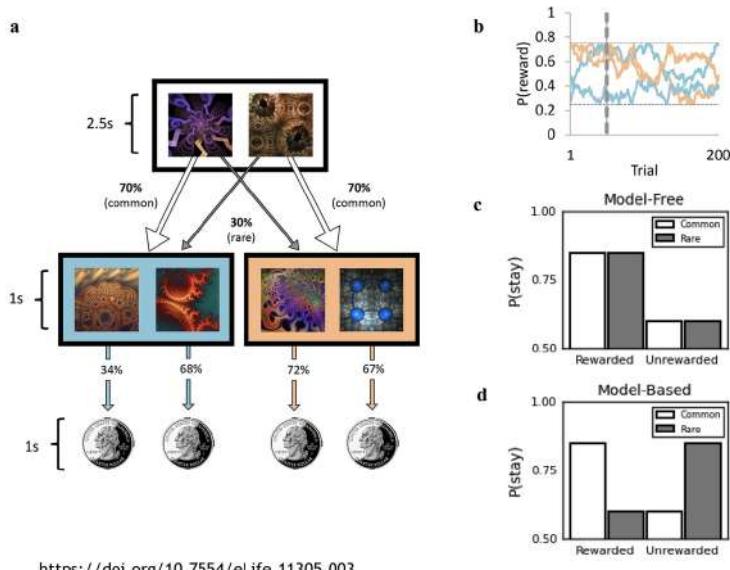


Figure 7.33

Some aspects regarding the figure above waiting the experiment explanation:

- the first percentages in the tree in *figure a* (70% (common), 30% (rare)) are fixed (so after some time can be learned, just because they are fixed);
- the second percentages in the tree in *figure a* (34%, 68%, 72%, 67%) vary in time (see the first graph from top of the *figure b*);
- metrics explanation of the *figure c*, *figure d*:
 - $P(\text{stay})$: probability to repeat – in the actual trial – the same actions of the previous trial;
 - $P(\text{stay})$ and Rewarded: the probability to repeat the same actions of the previous trial if the previous trial was rewarded;

- $P(\text{stay})$ and Unrewarded: ...
- $P(\text{stay})$ and Rewarded and Common: the probability to repeat the same actions of the previous trial if the previous trial was rewarded and the first transition was common;
- $P(\text{stay})$ and Unrewarded and Common: ...

Let's explain the experiment and the results reported in the figure above:

'Your task is to maximize the reward'.⁴¹

- (a) Subjects chose between two fractals, which probabilistically determined whether they would transition to the orange or blue second stage state. Action at the first state is associated with one likely and one unlikely transition. For example, the fractal on the left⁴² had a 70% chance of leading to the blue second stage state ('common' transition) and a 30% chance of leading to the orange state ('rare' transition). These transition probabilities were fixed and could be learned over time. In the second stage state, subjects chose between two fractals, each of which was associated with a distinct probability of being rewarded with a 25 cents coin. The probability of receiving a reward associated with each second stage fractal could also be learned, but (unlike the transition structure) these drifted slowly over time ($0.25 < P < 0.75$, panel b). This meant that *in order to earn the most rewards possible, subjects had to track which second stage fractals were currently best as they changed over time*. Reward probabilities depicted (34%, 68%, 72%, 67%) refer to example trial 50, denoted by the vertical dashed line in (b).
- (b) Drifting reward probabilities determined by Gaussian Random Walks for 200 trials with grey horizontal lines indicating boundaries at 0.25 and 0.75. To incentivize subjects to continue learning throughout the task, the chances of pay off associated with the four second-stage options were changed slowly and independently.

Model-free and model-based agents differ in the action selected after a *rare transition*:

- Model-free control prefers to repeat actions that lead to reward, irrespective of the likelihood of that first transition.⁴³
- Model-based control instead can ascribe those rewards following a rare transition to an alternative (non-selected) action which, despite not predicting reward on the current trial, will be more likely to lead to reward on future trials.⁴⁴

⁴¹The goal is to earn much more money as you can.

⁴²The fractal on the right has the opposite.

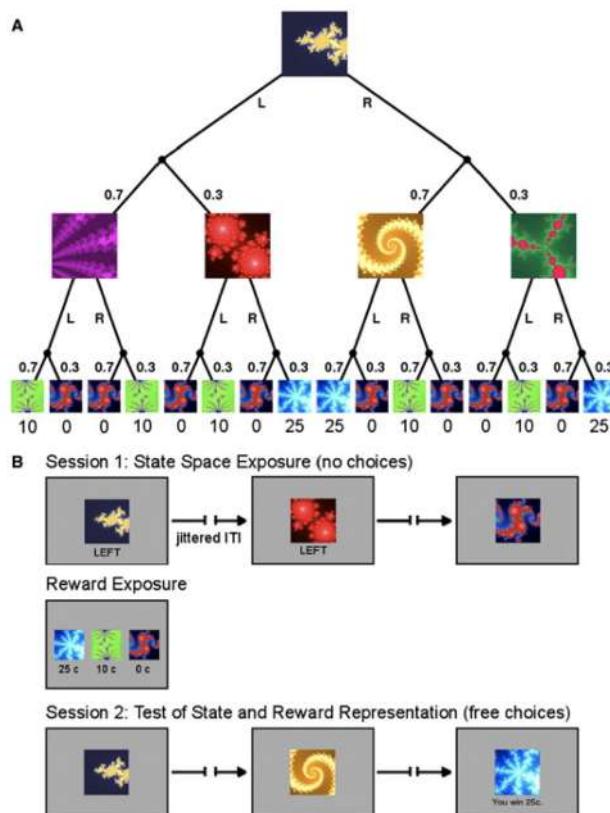
⁴³In fact $P(\text{stay})$ is higher when the previous trial was rewarded and lower if not (so is higher the probability to change actions): Trial $n - 1$ had a rare scenario – choosing the yellow fractal leads to the blue box – and leads to a reward; trial n repeats exactly the same actions, choose the yellow fractal. For model-free the second transition is separated from the first.

⁴⁴In fact $P(\text{stay})$ is lower when the previous scenario was rewarded (*i.e.* is higher the probability to change actions if the choice lead to a reward): Trial $n - 1$ had a rare scenario choosing the violet fractal and lead to a reward; trial n change the action – because the scenario of the previous trial was rare – choosing the yellow fractal.

- (c) Schematic representing the performance of a purely ‘model-free’ learner, who only exhibits sensitivity to whether or not the previous trial was rewarded vs unrewarded, and does not modify their behavior in light of the transition that preceded reward.
- (d) Schematic representing the performance of a purely ‘model-based’ learner, who is more likely to repeat an action (*i.e.* ‘stay’) following a rewarded trial, only if the transition was common. If the transition to that rewarded state was rare, they are more likely to switch on the next trial.

Latent learning in humans?

Experiment to test whether humans exhibit latent learning or not; meaning with ‘latent’ when you learn something but you only show it (the learning) when there is a motivation.



Gläscher J, Daw N, Dayan P, O'Doherty J. States versus rewards: dissociable neural prediction error signals underlying model-based and model-free reinforcement learning. *Neuron*. 2010;66:585–595

Figure 7.34

Method:

- (A) The experimental task was a sequential two-choice Markov decision task in which all decision states are represented by fractal images. The task design

follows that of a binary decision tree. Each trial begins in the same state. Subjects can choose between a left (L) or right (R) button press. With a certain probability (0.7/0.3) they reach one of two subsequent states in which they can choose again between a left or right action. Finally, they reach one of three outcome states associated with different monetary rewards (0\$, 10\$, and 25\$).

(B) The experiment proceeded in two fMRI scanning sessions of 80 trials each:

- In the *first session*, subject *choices were fixed* and presented to them below the fractal image. However, subjects could still learn the transition probabilities.⁴⁵
- *Between scanning sessions* subjects were presented with the *reward schedule* that maps the outcome states to the monetary payoffs. This mapping was rehearsed in a short choice task.
- Finally, in the *second scanning session*, subjects were *free to choose* left or right actions in each state. In addition, they also received the payoffs in the outcome states.⁴⁶



Figure 7.35

Results: Behavioral from free-choice session.

Test if participants were able to make optimal choices by combining the knowledge they acquired about state transitions (session 1) and reward contingencies (between sessions).

*Any successful learning would be possible with model-based, but not model-free, learning.*⁴⁷

Can you tell why?

Model-free learning focuses exclusively on predicting rewards without building a model of the environment and therefore learns nothing during session 1.

In state 1, at the first trial, of all 18 subjects:

- 13 made the optimal choice;⁴⁸
- 5 made the wrong choice in state.

⁴⁵According to *stimulus response theory* participants should not learn anything because there is not a reward; according to cognitive map or goal directed or model based the learning instead can happen also when there is no reward, we learn all the time but we are just not showing it.

⁴⁶If there is latent learning we expect that they have learned to choose the picture that are more likely to lead to a reward.

⁴⁷Theoretically; according to the theory under them.

⁴⁸The majority took the optimal choice showing that there is latent learning.

Indicating that their choice of behavior *cannot* be explained by model-free learning theory.

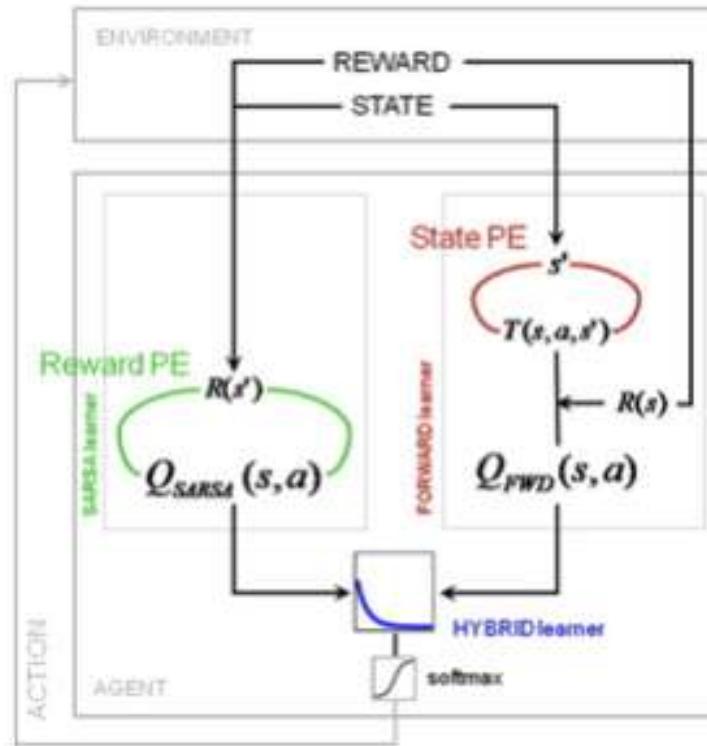


Figure 7.36

Results: Computational from free-choice session.

Choice behavior during the entire session was best explained by hybrid model that integrates both:

- Reward PE: model-free (similar TD model);⁴⁹
- State PE: model-based.⁵⁰

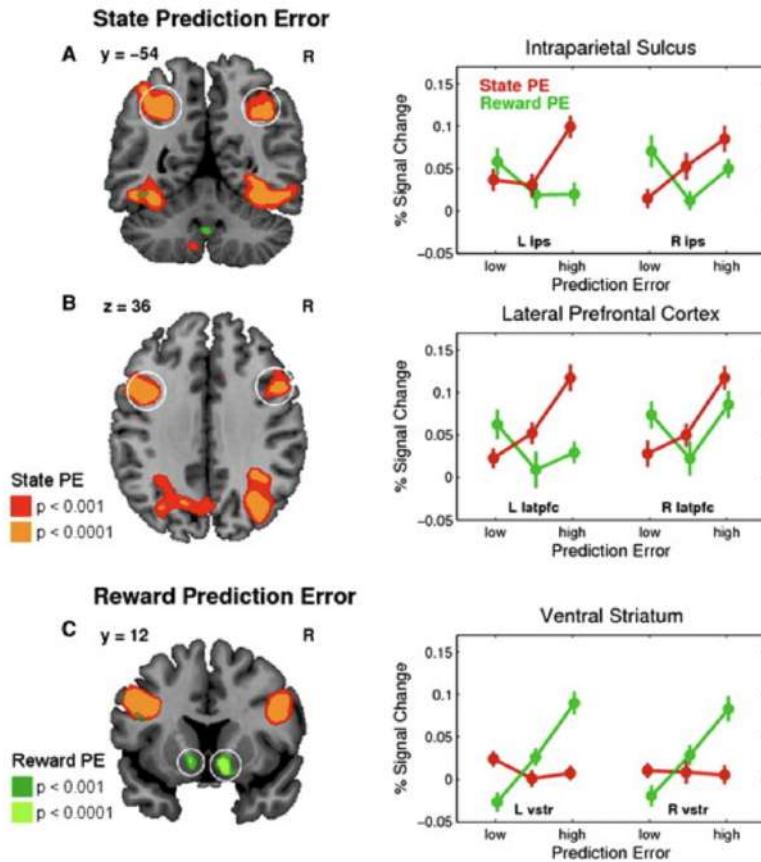
So the best is the *hybrid model*; if you think it makes sense because in relation to this experiment:

- first session: was related to transition probabilities (and the correlation of states);
- between scanning sessions: subjects were presented with the reward schedule;
- second session: subjects were free to choose and received the payoff.

⁴⁹TD stands for ‘temporal difference’.

⁵⁰PE stands for ‘prediction error’; ‘State’ because it correlated the various states: coherent with the model-based logic that links states one to the other.

Neural Signatures of Reward PE and State PE



Gläscher J, Daw N, Dayan P, O'Doherty J. States versus rewards: dissociable neural prediction error signals underlying model-based and model-free reinforcement learning. *Neuron*. 2010;66:585–595.

Figure 7.37

Results: neural

Parameters estimated from computational models were used to find activations that correlated with SPE & RPE.⁵¹

(A and B) Significant effect for SPE bilaterally in the intraparietal sulcus (ips) and lateral prefrontal cortex (lpfc).

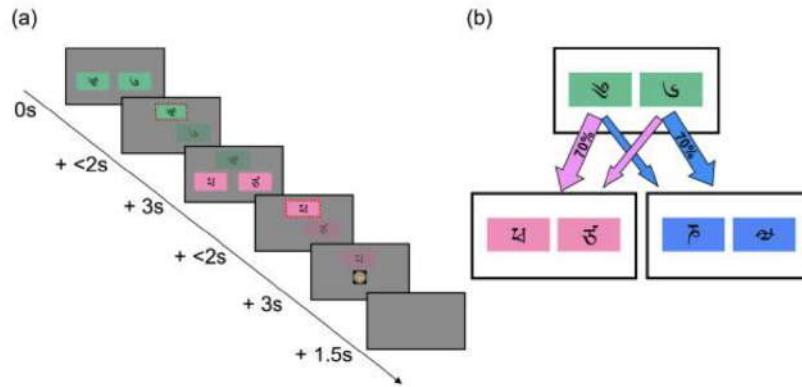
(C) Significant effects for RPE in the ventral striatum (vstr).⁵²

Detecting simultaneous correlates of model-free and model-based systems

Barring one recent exception (Gläscher et al., 2010), previous studies investigating the neural substrates of model-free and model-based control have not attempted to detect simultaneous correlations of both as these systems learn concurrently.

⁵¹SPE stands for *State prediction error* while RPE for *Reward prediction error*.

⁵²This should not surprise us; we already saw it when we talked about dopamine.



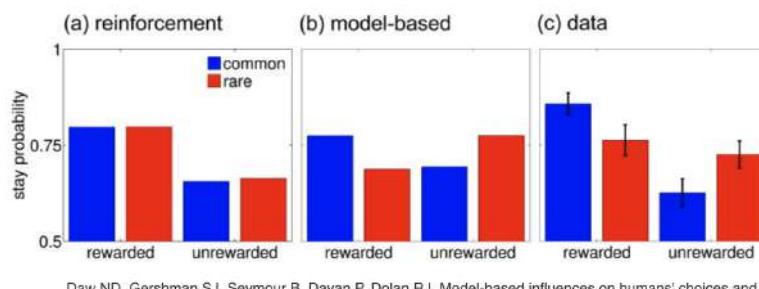
Daw ND, Gershman SJ, Seymour B, Dayan P, Dolan RJ. Model-based influences on humans' choices and striatal prediction errors. *Neuron*. 2011;69(6):1204-1215. doi:10.1016/j.neuron.2011.02.027

Figure 7.38

Method:

- (a) Timeline of events in trial. A first-stage choice between two options (green boxes) leads to a second-stage choice (here, between two pink options), which is reinforced with money.
- (b) State transition structure. Each first-stage choice is predominantly associated with one or the other of the second-stage states, and leads there 70% of the time.

To incentivize subjects to continue learning throughout the task, the chances of pay off associated with the four second-stage options are changed slowly and independently.⁵³



Daw ND, Gershman SJ, Seymour B, Dayan P, Dolan RJ. Model-based influences on humans' choices and striatal prediction errors. *Neuron*. 2011;69(6):1204-1215. doi:10.1016/j.neuron.2011.02.027

Figure 7.39

Results: Analysis of choice behavior.⁵⁴

⁵³Same logic of the previous experiment.

⁵⁴Same logic seen in the previous experiment.

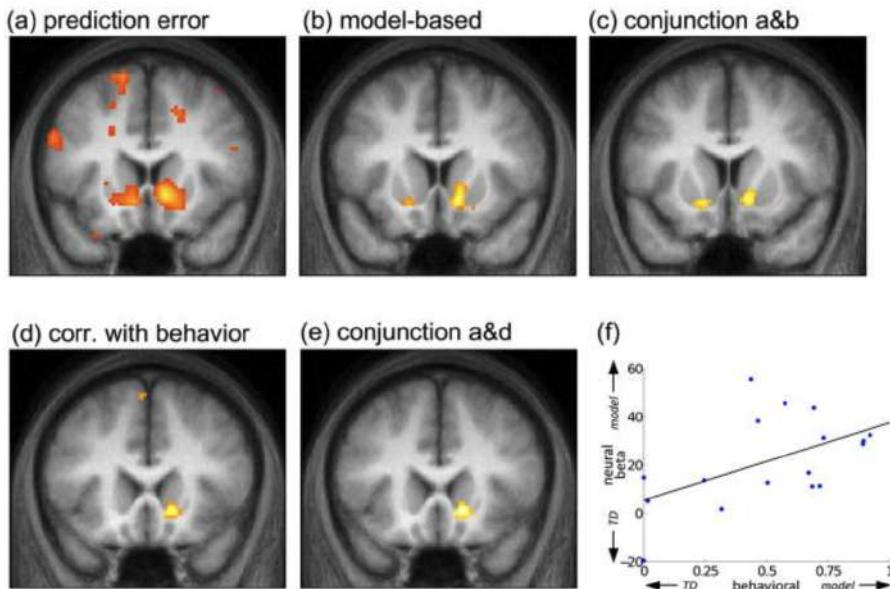
- (a) Simple reinforcement⁵⁵ predicts that a first-stage choice resulting in reward is more likely to be repeated on the subsequent trial, regardless of whether that reward occurred after a common or rare transition.
- (b) Model-based prospective evaluation instead predicts that a rare transition should affect the value of the other first-stage option, leading to a predicted interaction between the factors of reward and transition probability.
- (c) Actual stay proportions, averaged across subjects, display hallmarks of both strategies. Error bars: 1 SEM.

Looking at the image above: (a) reinforcement and (b) model-based are *ideal agent* while (c) data are *real agent*.

Results: computational.

Choice behavior during was best explained by hybrid model that integrates both:

- Reward PE: model-free (similar TD model);
- State PE: model-based.



Daw ND, Gershman SJ, Seymour B, Dayan P, Dolan RJ. Model-based influences on humans' choices and striatal prediction errors. *Neuron*. 2011;69(6):1204-1215. doi:10.1016/j.neuron.2011.02.027

Figure 7.40

Results: neural.

Parameters estimated from computational models were used to find activations that correlated with SPE/model-based & RPE/model-free.

Activity in Striatum occurred both for model-free and model-based prediction error.

This activity correlated with the extent to which that subject's behavior was model based.

⁵⁵Model free ↔ reinforcement.

Goal-directed/model-based habitual/model-free behavior are integrated

- *Generation 3 results* challenge the notion of a separate model-based vs model-free learner and suggest a more *integrated computational and neural architecture* for high-level human decision-making.
- In the brain, there is a dynamic *inter-dependency* between goal-directed/model-based and habitual/model-free systems, which may *act simultaneously and competitively*.

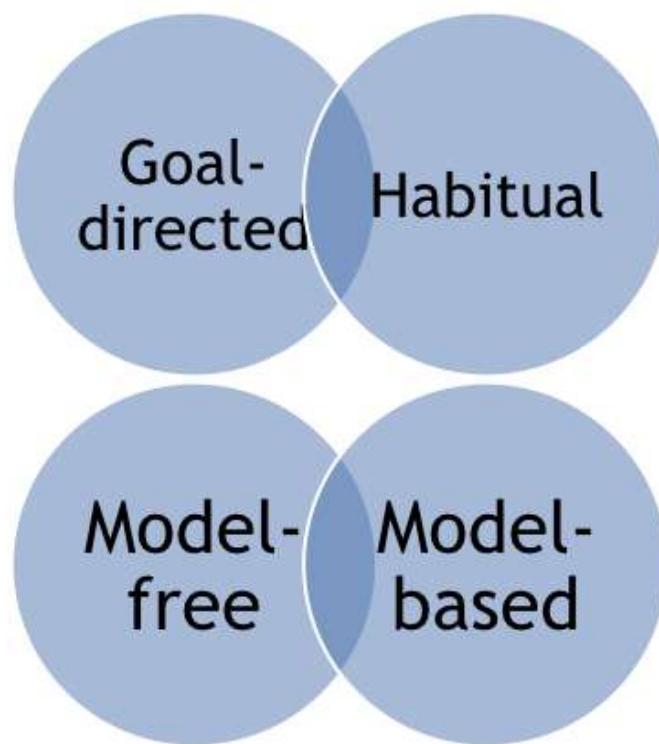


Figure 7.41

Chapter bibliography

Dolan, R. J., & Dayan, P. (2013). Goals and habits in the brain. *Neuron*, 80(2), 312–325.
<https://doi.org/10.1016/j.neuron.2013.09.007>.

Part II

Module 2

Chapter 8

Neural mechanisms of vision

Chapter outline

- The anatomical and functional organization of vision.
- Low-level visual processing: the retina.
- Then we will go into the Visual Cortex, specifically we will see the Primary Visual Cortex, the place where the cortical processing of visual information starts in the cortex.
- Then we will see other cortical areas.
- We will terminate with Object Recognition.

So we are going to start at a low level *i.e.* ‘low level vision’ (elementary analysis of simple features) up to how subjects recognize uncategorized objects (it is one of the major aim of the visual system).

8.1 Vision: a general overview

Outline

- The anatomical and functional organization of vision.
- Low-level visual processing: the retina.

What is vision?

What does it mean, to see? The plain man’s answer (and Aristotle’s, too) would be, to know what is where by looking. In other words, vision is the process of discovering what is present in the world, and where it is. (D. Marr¹, Vision, 1982).

Vision is a process that produces from images of the external world a description that is useful to the viewer and not cluttered with irrelevant information.² (Marr and Nishihara, 1978).

¹One of the first computer scientists that tried to integrate computer science with neurophysiology.

²Not simple copying and representing everything in the same number. There is an *interpretation*.

Simple definition but very complex mechanisms: one major complexity is that just when we see there are many different objects (*what*) located in different areas (*where*), some hidden from others ... the same object can be seen from different perspectives giving different images (in principle can be infinite images of the same object on the retina).

So it is clear that the question how animals and humans are able to identify one object among all these possible representations of the objects on the retina it is a very complex aim: we still don't know how vision accomplishes this.

Vision: perception, memories and even action

Vision dominates our perceptions and memories of the world and appears even to frame the way we think.

Vision is used not only for object recognition³ but also for guiding our movements. *Vision for action; vision motor transformation; action (event more important of vision for perception.)* These separate functions are mediated by at least two parallel and interacting pathways.⁴

Vision, and more generally the brain, is a system that analyzes information (information processing device): receives inputs and transforms them into outputs.

Marr's 'tri-level hypothesis'

Information-processing systems can be analysed (at least) in terms of the problems that they solve, the representations and processes by which they solve them, and their physical instantiation.

1.2 Understanding Complex Information-Processing Systems		
Computational theory	Representation and algorithm	Hardware implementation
What is the goal of the computation, why is it appropriate, and what is the logic of the strategy by which it can be carried out?	How can this computational theory be implemented? In particular, what is the representation for the input and output, and what is the algorithm for the transformation?	How can the representation and algorithm be realized physically?

Figure 1–4. The three levels at which any machine carrying out an information-processing task must be understood.

Marr, Vision (1982)

Figure 8.1

As illustrated in the image above Marr reported the so called 'tri-level hypothesis' in his book *Vision* (1982):

1. Computational theory (First [higher] level):

³Vision for perception; perception side of vision. In this book we cover only this theme.

⁴They are – two main goals in neuroscience – separated in the brain: Vision for perception ↔ Ventral (part of the brain); Vision for action ↔ Dorsal (part of the brain).

- What is the goal of the computation, why is it appropriate, and what is the logic of the strategy by which it can be carried out?⁵
2. Representation and algorithm (Second level):
- How can this computational theory be implemented? In particular, what is the representation for the input and output, and what is the algorithm for the transformation?
3. Hardware implementation (Third level):
- How can the representation and algorithm be realized physically?⁶

A central element in Marr's view was that a higher - level was largely independent of the levels below it, and hence computational problems of the highest level could be analyzed independently of understanding the algorithm that executes the computation. For the same reason the algorithmic problem of the second level was thought to be solvable independently of an understanding of the physical implementation.⁷

In contrast to the doctrine of independence of computation from implementation, current research suggests that considerations of implementation play a vital role in the kind of algorithms that are devised and the kind of computational insights available to the scientists.

It would be convenient if we could understand the nature of cognition without understanding the nature of the brain itself. Unfortunately, it is difficult if not impossible to theorize effectively on these matters in the absence of neurobiological constraints. The primary reason is that computational space is consummately vast, and there are many conceivable solutions to the problem of how a cognitive operation could be accomplished.⁸ Neurobiological data provide essential constraints on computational theories, and they consequently provide an efficient means for narrowing the search space (Churchland e Sejnowski, *Science*, 1988).⁹

Vision is not just simple camera reproduction

Vision is often incorrectly compared to the operation of a camera.

A camera simply reproduces point-by-point the light intensities in one plane of the visual field.

The visual system, in contrast, does something fundamentally different. It interprets the scene and parses it into distinct components, separating foreground from background.

⁵You can think of a philosophical/psychological questions or problems independently on how it is represented and/or solved. It is a Philosophical/Psychological level.

⁶So, for example, we can: (1) think of a problem; (2) solve the problem in many ways (abstract level); (3) implement the physical solution suggested from the higher level or even implement with a new solution (practical level).

⁷So you could focus on one level forgetting the other ones.

⁸Conversely Marr thought that just for this reason *i.e.* computational level is vast (it comprehends so many functions that are independently defined and realized from how they are realized on a lower level [you can think of a philosophical/psychological questions or problem independently on how it is represented and/or solved]); you can define and realize a function in so many ways independently from how is implemented on a lower level.

⁹The actual brain is the result of thousands of years of evolution. Maybe evolution found the best way and pattern and we need to look at them (and they work!).

The visual system is less accurate than a camera at certain tasks, such as quantifying the absolute level of brightness or identifying spectral colors.¹⁰ However, it excels at tasks such as recognizing objects (a charging animal or a speeding car) whether in bright sunlight or at dusk, in an open field or partly occluded by trees (or other cars).¹¹ And it does so rapidly¹² (< 200 ms) to let the viewer respond and, if necessary, escape.

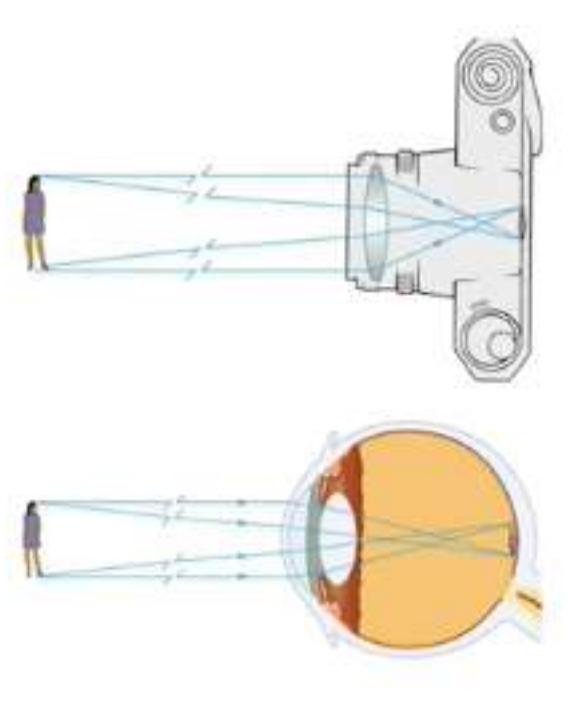


Figure 8.2

Vision is an active and bidirectional process

Vision is a generative process that involves more than just the information provided to the retina.¹³ The brain has a way of looking at the world, a set of expectations about the structure of the world that derives in part from experience and in part from built-in neuronal wirings.¹⁴

¹⁰Simply the brain does not care of these details so accurately. It does not encode values in *absolute terms*, it encodes values in *relative terms*.

¹¹What the brain cares is the *contrast*, the *difference* (subtraction); e.g. always compare the brightness of the objects with the brightness of the environment.

¹²There are studies in the so called ‘Social Neuroscience’ field which explain that humans are able in only 1 ms to know, to categorize looking to a face if that face is friendly or not; in only 1 ms you know if you want to stay with that person, to trust or not; it’s just an impression. We are very quickly to *make decision* (slower in other things that machines can perform better.)

¹³It is not a simple copying, is not passive. It is an active process (generative).

¹⁴And we use this kind of knowledge to shape, to select, to confirm or discard (particularly important when the stimulus is ambiguous, something difficult to see – which is the majority of the cases – we use a lot of this background information). It is not a completely bottom-up

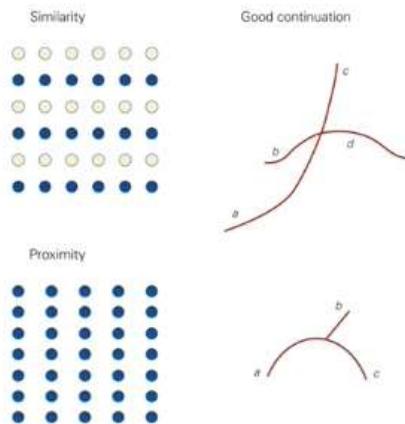


Figure 8.3

To link the elements of a visual scene into unified percepts, the visual system relies on organizational rules such as similarity, proximity, and good continuation. Referring to the image above:

- Looking to the *Similarity principle* figure we spontaneously say that the figure represents rows of dots (rather than columns of dots); we use *similarity* between white and blue dots in order to separate the segment.
- Looking to the *Proximity principle* figure instead we say that the figure represented by the set of dots is made of columns of dots because the dots into a column are closer on the vertical line than on the horizontal of a row.
- Looking to the *Good continuation principle* figure seems obvious, for example, that the segment *c* is a *continuation* of the segment *a*, so *a* \longleftrightarrow *c* appears a distinct object and *b* \longleftrightarrow *d* segment is another one just superimposed on *a* \longleftrightarrow *c*. We intuitively don't see that for example *a* \longleftrightarrow *d* can be another object and so *b* \longleftrightarrow *c*; and this because we use the *Good continuation principle* that relies on some statistical metrics that tell us that, for example, that the two segments *a* and *c* are better connected than *a* and *d*.

The psychologists already knew since the 60s of the last century that we use some *principles* to capture the essence of the image; the so called *Gestalt principles*:¹⁵

- similarity;
- continuation;
- proximity;
- closure;

process but is also a feedback top-down process. The role of this feedback from higher levels to lower: it is not only from the retina to the brain but also from the brain to the retina.

¹⁵From the *Gestalt school of psychology* (german).

- figure/ground;
- symmetry;
- order.

These principles are like some rules that we apply when we see to understand what we have in front of us. All of these derive both on our experience and innate abilities developed through evolution.

Contour saliency

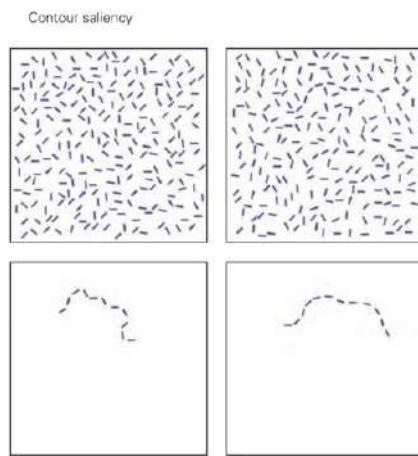


Figure 8.4

The principle of good continuation is also seen in contour saliency. On the right, a smooth contour of line elements pops out from the background, whereas the jagged contour on the left is lost in the background.

Visual priming



Figure 8.5

Higher-order representations of shape (in memory, see the figure below) guide lower-order processes of surface segmentation (see the figure above).¹⁶

¹⁶It is difficult to recognize the girl and the horse from the black and white image without



Figure 8.6

Bayesian theories

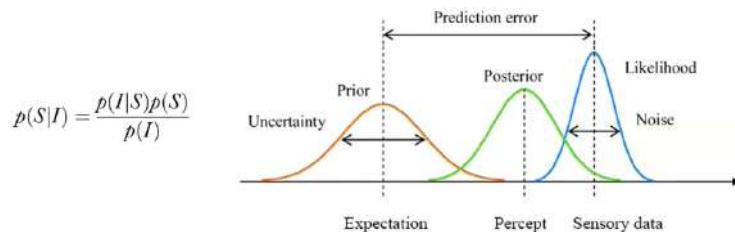


Figure 8.7

Bayesian theories treat the visual system as an ideal observer that uses prior knowledge about visual scenes and information in the image to infer the most probable interpretation of the image.

The posterior probability ($p(S|I)$) of a possible real-world stimulus S (*i.e.*, percept) is proportional to the product of the prior probability of S (that is, the probability of S ($p(S)$) before receiving the stimulus I, *e.g.* expectation) and the likelihood (the probability of I given S ($p(I|S)$), *i.e.*, sensory data).

Is it reasonable to assume that the visual system knows the probability calculus and operates according to it?

$$p(S|I) = \frac{p(I|S)p(S)}{p(I)}$$

Where:¹⁷

- $p(S|I) \longleftrightarrow$ Percept posterior probability.
- $p(I|S) \longleftrightarrow$ Likelihood (Sensory data).
- $p(S) \longleftrightarrow$ Prior probability (Expectation).

having seen the complete image before. But once seen is obligatory to see the horse and the girl. From that emerge that we use informations present in our memory to shape, to modulate what we see, input on our system. *Visual priming* is named for this reason: we use primary information.

¹⁷Note that we have gaussian functions because we're representing probabilities. Obviously the weights of the factors of this formula can vary in some range depending on individuals and environments. Some give more weights to prior information rather than the actual and viceversa.

Prior probability ($p(S)$) distributions in typical applications of the Bayesian strategy represent knowledge of the regularities governing object shapes, constituent materials, and illumination, and likelihood ($p(I|S)$) distributions represent knowledge of how images are formed through projection on the retina. Some examples of prior knowledge are that solids are more likely to be convex than concave and that the light source is above the viewer.

The more ambiguous the image, the greater the influence of prior knowledge in yielding a nonambiguous percept. Some perceptions may be more data-driven, others more prior knowledge driven.

Three levels of analysis

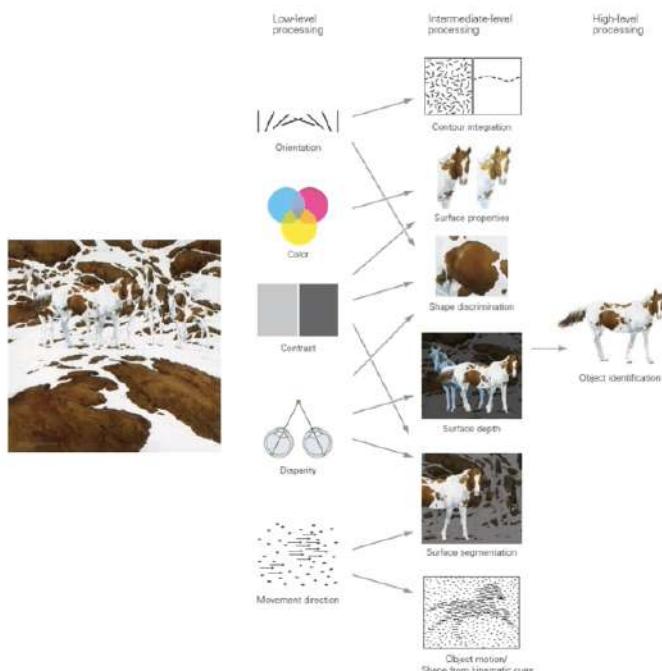


Figure 8.8

Traditionally, a visual scene is analyzed at three levels: low, intermediate and high:¹⁸

- Low-level processing:¹⁹ simple attributes²⁰ (contrast, orientation, motion, depth, and color) of the visual environment are first analyzed.

¹⁸This categorization is a didactic separation: in the brain these levels are not completely separated. It's just easier for us to follow this.

¹⁹So called because begins in the retina and in the first part of the primary visual cortex.

²⁰Are caught local features, crucial for understanding; not general. They are all features that are able to be caught *in parallel* just in the retina, just immediately; and this parallel mechanism-processing is a '*continuous*' mechanism: it starts in the retina and continues in the other components of analysis like primary visual cortex and also the others.

- Intermediate-level processing: low-level features are used to parse the visual scene. Local orientation is integrated into global contours (contour integration); local visual features are assembled into surfaces, objects are segregated from background (surface segmentation), surface shape is identified from depth, shading and kinematic cues.
- High-level processing: surfaces and contours²¹ are used to identify the object.

Mediation of the retino-geniculo-striate pathway

Visual processing²² is mediated by the retino-geniculo-striate pathway

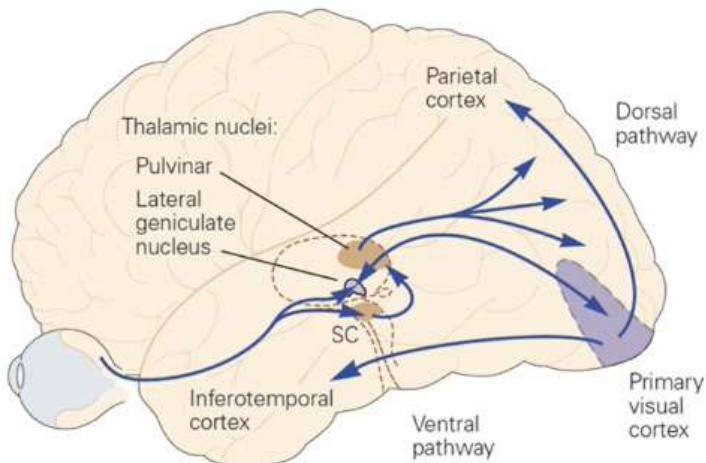


Figure 8.9

This pathway (Primary Visual Pathway)²³ includes:²⁴

- the retina,²⁵

²¹Here plays a crucial role also our experience, our semantics: the composition of surface and contours is equal or similar to what already seen? This is crucial to identify objects already seen, new objects, or identify nothing.

²²The *Primary Visual Pathway*: the pathway used to understand *what is where*; and eventually acts upon the recognized objects.

²³It is also called *Retina Geniculate Striate* pathways, so called to mention each of the three parts involved.

²⁴Three major locations.

²⁵In the retina (which is in the eye, so we have two retinas, one for each eye) starts everything; what is lost in the retina is lost forever, there is no way we can recover informations that are lost in the retina. Retina is made in order to catch as much as possible in the environment. Vision can be explicit and implicit: explicit when we are conscious of what we see, we identify something clearly; implicit when we don't see clearly something, maybe because it moves fast in the environment, or there are shadows but we are able to reconstruct subsequently or to use that information: for example in some experiments patients are asked to perform a task and we can see that the way by which they perform a task shows that they have seen objects that weren't able to report. So we are also able to recover information implicitly, or using information implicitly. So visual information is not processed only at the level in

- The lateral geniculate nucleus (LGN) of the thalamus;²⁶
- the primary visual cortex (V1) or striate cortex;

The beginning: the retina

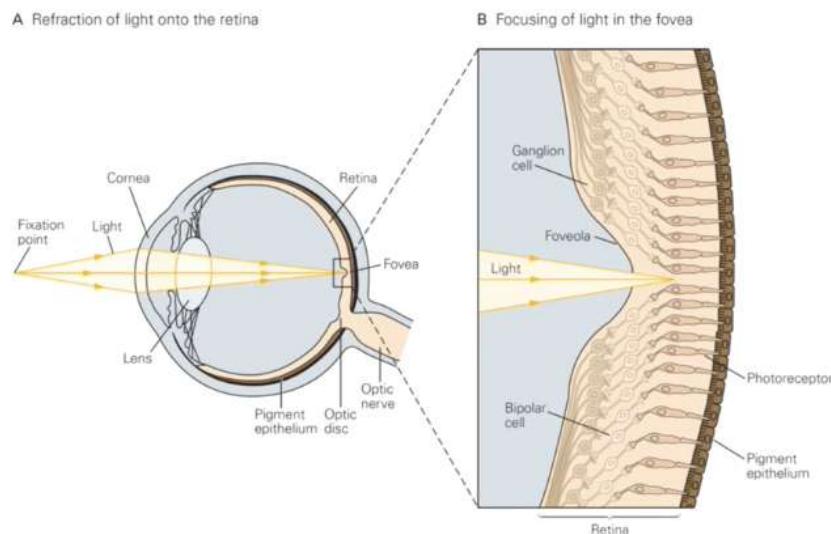


Figure 8.10

The brain's analysis of visual scene begins in the two retinas, which transform the visual input into neural signals, a process known as phototransduction.²⁷

which we are able to recognize 'what' and so we are conscious of what we are seeing. This implicit processing (without awareness, consciousness) is not obvious: a lot of experiments were needed. There is this kind of implicit processing also in animals, but for them we can't say exactly if they recognize something consciousness or not like humans (because we don't have discovered if animals are conscious or not) but we are able to determine if they are or were aware of something or not. Finally, implicit vision is particularly important in pathologies: for example, in the so called 'visual neglect': is a neurophysiological condition characterized by the inability to pay attention to, or be aware of, objects or stimuli on one side of space, typically the left side. This condition is often associated with brain injuries, particularly in the right hemisphere of the brain. Nevertheless there are experiments that tell us that they process that information, they are not aware but the information is still processed; the experiments show implicitly that the patients show a lot of things of those objects present in the affected side on that the patients are not able to report explicitly. There is another similar phenomenon in which patients show *Cortical Blindness*: i.e. a neurological condition in which the visual cortex of the brain is damaged or doesn't work correctly, causing a partial or total loss of vision, even if eyes can be structurally healthy. This kind of patients cannot see, but if you present a stimulus in the environment the patient is able to locate the stimulus in the environment much more than a simple guess. So in some way the visual input arrives in the brain (the retina is healthy, the visual cortex is damaged) and is processed (we don't know how). The processing does not follow the canonical way, bypassing consciousness, nevertheless is processed in some way.

²⁶Remember that Thalamus (which is in the center of the brain) is a relay station, intermediate between the retina and the cortex; useful in order to transmit the informations from the retina to the cortex.

²⁷In the phototransduction process energy of the light is transformed in neural signal.

As you can see from the image there are structures that work in order to make the light converge on the retina and in particular on a specific part of the retina called '*Fovea*' because this part is designated to see with high resolution: what terminates in this part of the retina is seen well, what terminates elsewhere is seen blurry. *Fovea* controls high resolution vision.

In the retina there are something like 200 millions of receptors²⁸ (pixels) subdivided in *rows*²⁹ and *columns*.³⁰

So the strategy is to concentrate as much as possible information on a part of the retina and that part is the *Fovea*.

The output of the eye converges in the *Optic nerve* (unique per each eye) and this is transmitted ahead.

The output layer of the retina

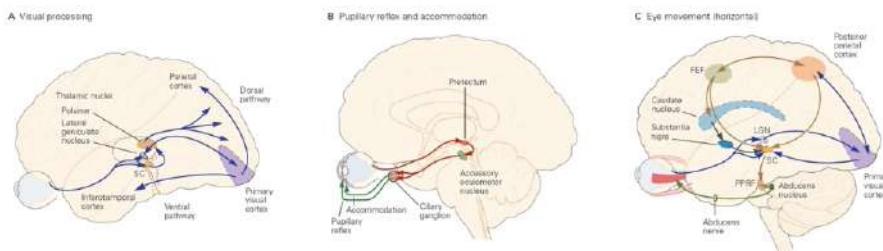


Figure 8.11

Retinal ganglion cells (RGC) constitute the output layer of the retina. The axons of RGCs form the optic nerve which projects:

- lateral geniculate nucleus (LGN) of the thalamus;
- pretectal nuclei of the midbrain;
- superior colliculus of the mid brain;

There are different pathways that extend from the retina:

- The primary visual pathway is also called the geniculostriate pathway³¹ because it passes through the LGN on its way to the primary visual cortex (V1), also known as the striate cortex because of the myelin-rich stripe that runs through its middle layers;

²⁸Retina is 'part' of the brain, is like brain outside the brain (in the eyes); is made of the same substance of the brain i.e. neurons, there are neurons in the eyes; the components have the same structure of neurons. Retina and the brain have the same neurogenetic origin.

²⁹Are the majority and they use nocturnal lights, so when the light is weak, not strong.

³⁰Are very few and are all concentrating on the *Fovea*, there are no rows here.

³¹The Retina Geniculate Striate (see the first image on the left) is the major pathway, almost 90% of visual information pass through this pathway; but there are other pathways: the 'wake-sleep' cycle for example is regulated by structures that depend on the light (we are diurnal creature).

- A second pathway extends from the retina to the pretectal area of the midbrain,³² where neurons mediate the pupillary reflexes that control the amount of light entering in the eyes;³³
- A third pathway from the retina runs to the superior colliculus and is important in controlling eye movements;³⁴

So there are others pathways that have other functionalities than perceiving objects.

NOTE: Vision is an *exteroceptive sense* (sensory perception of external stimuli or information from the external environment) like the other 4 traditional sense: audition, tactile perception, gustation, olfaction. But we also have *interoceptive sense* which refers to the body's ability to sense and interpret internal physiological sensations and processes. It involves perceiving signals and information from within the body such as hunger, thirst, heart rate, breathing or feeling of fullness or discomfort.

Visual field



Figure 8.12

³²Midbrain because is in the middle of the brain, midbrain area is between brain and spinal cord; is a very short area (more or less 1 cm) in the center of the brain; we saw in the first module that is related to dopamine.

³³It is known that the size of the pupil (the black circle in our eyes) is not fixed; it becomes smaller or larger depending on the light: when there is darkness is very very large while with a great amount of light is very very small. This change is automatic, is an ocular reflex: there is a muscle that restricts or relaxes the pupil regulating the amount of light which enters on the eyes. There is another muscle called 'lens' (italian 'cristallino', see the previous page) that can be made more or less tense and consequently its curvature can change, this activity happens for example when we stare a far object in our hand and that gradually we put it closer and closer near our eyes; this just to say that visual informations that arrives to the brain have also other uses rather further perceiving objects.

³⁴It is very important to control eyes movement because we saw that we see well only in the center of the retina, so we need to put what is important in the center all the time.

We are visual animals, primates are visual animals, vision is our dominant sense: more than half of the brain is devoted to vision, there are more vision neurons than other type of neurons; we use vision for everithing, we use vision so much that we use vision also for metaphors: when we understand something we say ‘I see it’ or when a great discovery occurs we say ‘that man had a vision’, or just think about memory: most of our memory is visual (not auditory). Basically there is almost every area of the brain which has visual neurons.

Visual field refers to the area that can be seen as you fixate (without moving) your eyes on a central point (cross).

It is usually divided in two parts:

- Left hemifield.
- Right hemifield.

That’s because the two brain hemispheres (where there is the primary visual cortex) are able to ‘see’ one hemifield each:

- Right hemisphere → Left hemifield.
- Left hemisphere → Right hemifield.

There is a complete subdivision.

We don’t perceive this subdivision (we see continuously from left to right and viceversa) because there is the Corpus Callosum made of white matter that connects the two hemispheres.

Human vision vs pigeon vs owl

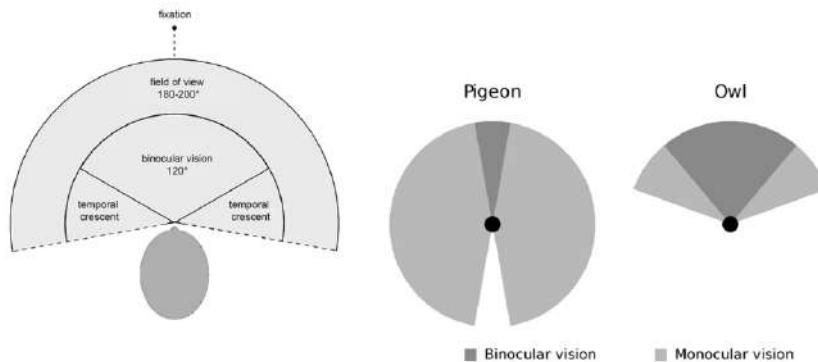


Figure 8.13

Let’s compare the human vision with that of pigeons and owls:

- Human: we have a very large vision, more than 180°. The majority of this field is seen in both eyes: binocular vision (120°).³⁵ Just a small part (both on the left and on the right) is seen by one eye (monocular).

³⁵This is not in contraddition to what seen in the previous subsection: Left hemisphere → Right hemifield, because in this case we are talking of part of the brain (Left hemisphere) while above we talked about *eyes*. Remember we have an unique optic nerve for each eye which conveys informations from the eye and realys them to the brain (see also *hemiretinas* ahead).

- Pigeon: they are almost able to see 360° which is a very useful for a prey but they reach this ability in a monocular way losing for example the depth (for seeing the depth is necessary integrate informations from both the eyes) but for them is enough to survive.
- Owl: instead there are the so called birds of prey like owl or eagle that have a smaller vision field but almost all *binocular* in order to see very well the depth, and they are the best in this: an eagle is able to see 5 kilometers away from its position. Predators have a very good binocular vision.

Visual angle

Visual field is measured in degrees $^\circ$ or *visual angle*.

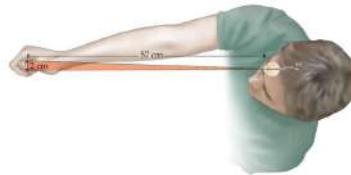


Figure 8.14

Visual angle of the width of the thumb held at arm's length is about 2° .³⁶

The retina of each eye can be divided

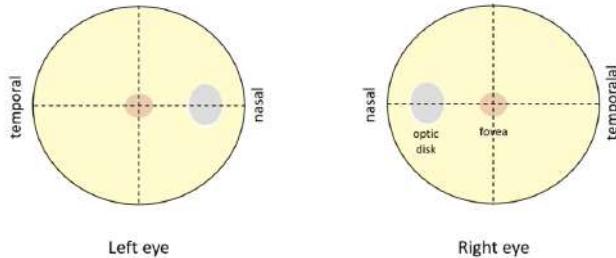


Figure 8.15

The retina of each eye can be divided into:

- Nasal (close to the nose) hemiretina, medial to the fovea.
- Temporal (close to the temple) hemiretina, lateral to the fovea.³⁷

Furthermore:

³⁶Moving the arm this convention can be used to measure. In the vision experiments it is usual to put the screen to 6 cm from the subject so, doing the right proportion, we know exactly the size of the objects presented (in terms of visual angle).

³⁷Furthermore we have also a conventional vertical (vertical meridian, the vertical dashed line) and horizontal (horizontal meridian, the horizontal dashed line) subdivision.

- The left hemiretinas (temporal of the left eye, and nasal of the right eye) see the right (opposite) visual hemifield (they see exactly the same thing: redundancy).³⁸
- The right hemiretinas (nasal of the left eye, and temporal of the right eye) see the left (opposite) visual hemifield.

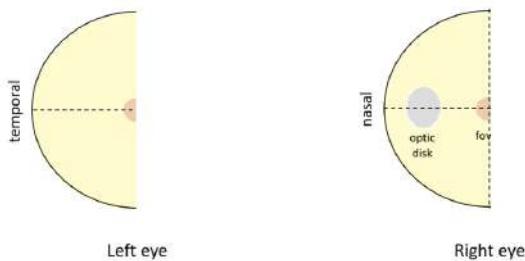


Figure 8.16

The optic disc, or optic nerve head, is the site where ganglion cell axons converge and exit from the eye³⁹ forming the optic nerve.⁴⁰

Partial decussation

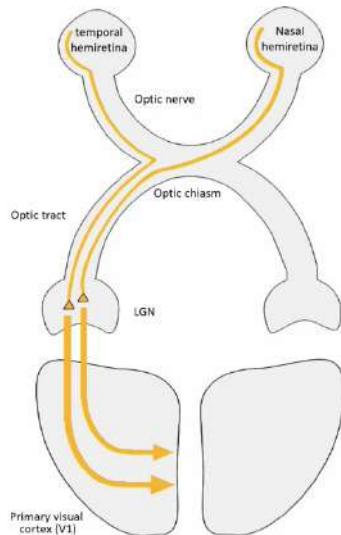


Figure 8.17

³⁸This is due to the so called *partial decussation* phenomenon (see next subsection).

³⁹All the neurons of the retina need to go out from the retina and they converge in the optic disk.

⁴⁰In the optic disk there are not photoreceptors: we cannot see here, but obviously we can't see that we cannot see.

Because the temporal hemiretina of one eye sees the same visual hemifield as the nasal hemiretina of the other eye, partial decussation⁴¹ of the optic nerve fibers at the chiasm ensures that all information related to each hemifield is processed in the visual cortex of the contralateral hemisphere.

From the eye, the optic nerve extends to a midline crossing point, the optic chiasm.

Beyond the chiasm, the fibers from each temporal hemiretina proceed to the ipsilateral⁴² hemisphere along the ipsilateral optic tract; fibers from the nasal hemiretinas cross to the contralateral⁴³ hemisphere along the contralateral optic tract.

In the figure above is the nasal decussation to be highlighted; both the left optic nerve and the right optic nerve are visible; at the end of the Optic tract there is the LGN (Left Geniculate) which *sees* only the right visual hemifield; then the confluence ends in the Primary visual cortex (V1) that can only *see* things from the right visual hemifield.

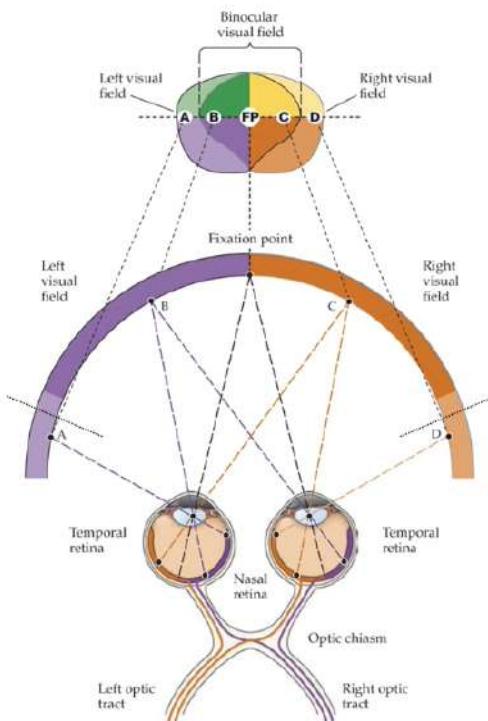


Figure 8.18

⁴¹Decussation refers to the anatomical or neurological phenomenon where nerve fibers or pathways cross from one side of the body to the other, typically at a specific point in the central nervous system. This crossing results in patterns that resemble an 'X' or an intersection. *E.g. Motor decussation:* right motor cortex is able to move the muscles on the left; so neurons start from the right and end on the left.

⁴²Stands for 'same side'.

⁴³Stands for 'opposite side'.

- points in the binocular portion of the left visual field fall on the nasal retina of the left eye and temporal retina of the right eye.
- points in the binocular portion of the right visual field fall on the nasal retina of the right eye and the temporal retina of the left eye.
- points in the monocular portion of the left visual fields fall on the left nasal retina.
- points in the monocular portion of the right visual fields fall on the right nasal retina.

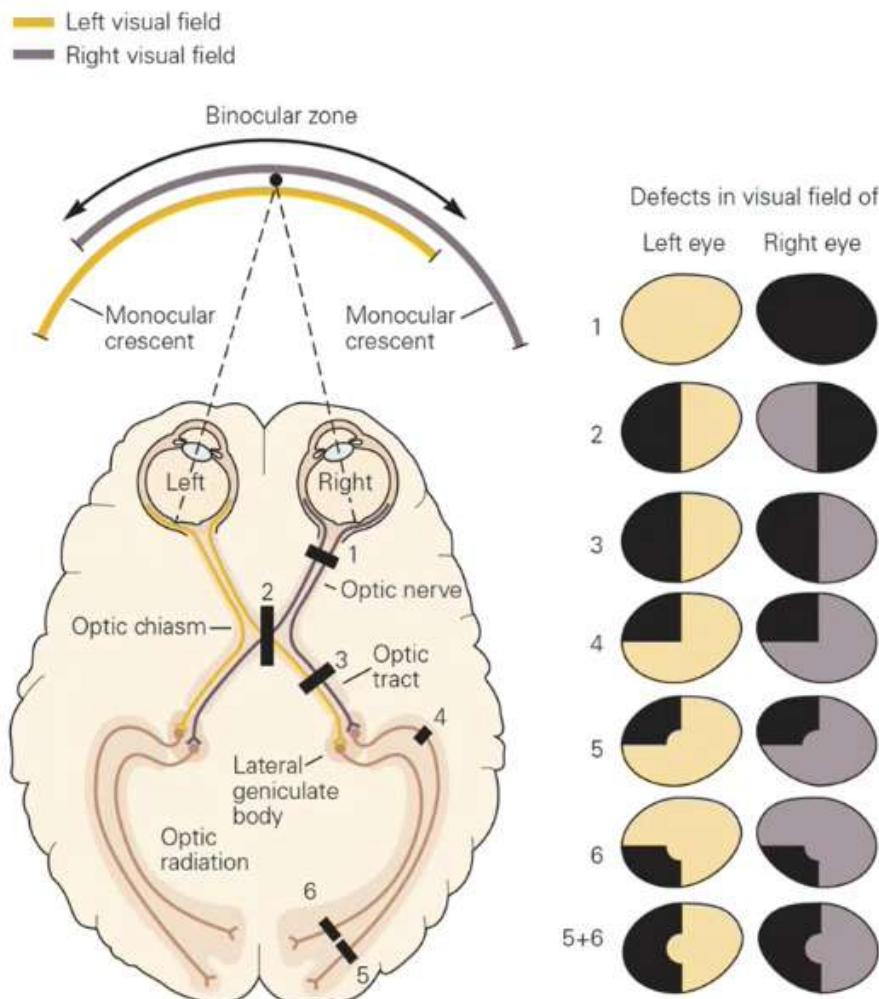


Figure 8.19

Each eye sees most of the visual field, with the exception of a portion of the peripheral contralateral visual field known as the monocular crescent. Lesions along the visual pathway produce specific visual field deficits, as shown above.

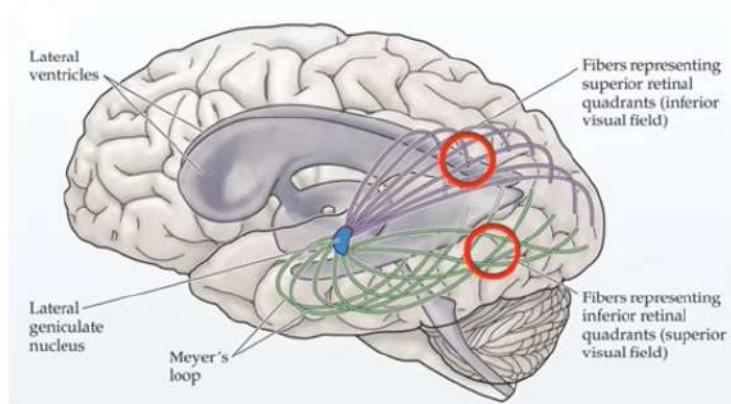


Figure 8.20

So, we see each visual hemifield with both eyes. With only one eye we can see almost everything; obviously with only one eye we lose the ability to see depth; we use both eyes to see in stereo, 3D. At the origin the image is 2D because in the retina we only have pixels but from the 2D the image is completely reconstructed the 3D structure of the environment from the brain.

So losing one eye is not a big problem instead if you lose the *optic tract* or have a lesion (where the fibers of both eyes converge) you lose completely the visual opposite hemifield. For example if you lose the lateral geniculate from one side (*e.g.* the right) you cannot see anymore the left visual hemifield and this is a big problem! But still you're able to see depth because you have both eyes and so you have still two images of what you see (even if it is only one hemifield).

Right hemianopia

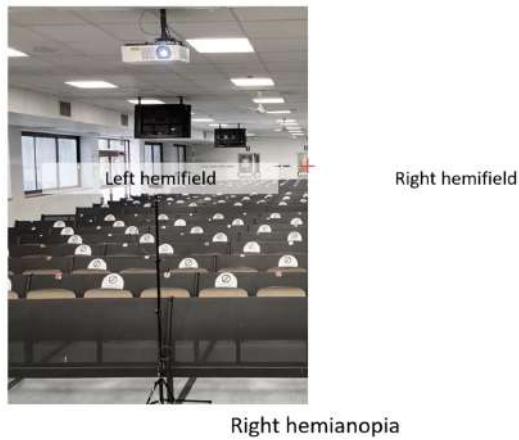


Figure 8.21

Right hemianopia: left primary visual cortex is damaged. It is possible to see depth: right hemiretinas of both eyes are used.

NOTE: When you don't see – in general – for example the right hemifield does not mean that you see ‘dark’ but simply your visual field is restricted; you're not aware that you don't see that part, it's just restricted. You just lose this information from consciousness.

Retina blind spot



Figure 8.22

The optic disc is where the axons of retinal ganglion cells leave the eye to reach the LGN of the thalamus. This region of the retina does not contain photoreceptors and, because it is insensitive to light, produces the perceptual phenomenon known as a blind spot.

Given the lack of photoreceptors, a defect or scotoma (blind area) of the visual field should be noticed by the observer. However, the blind spot goes unnoticed for two reasons:

1. Since the optic disc (blind spot) is nasal to the fovea of each eye, light from a single point in the visual field never falls on both blind spots at the same time.⁴⁴ Thus, In binocular vision to compensate for the missing information in the blind spot of one eye, the brain uses information from the homologous region (temporal hemiretinas) of the other eye.
2. In monocular vision, the visual system simply ‘fills-in’ the missing part of the scene (the filling-in phenomenon) using information from the surrounding areas to the blind area.⁴⁵

To find your right eye's blind spot (look at the figure above):

- Close your left eye.
- Stare at the cross.
- Move closer to the screen (2530 cm), then farther away. Keep doing this until the green circle disappears.

When it disappears, you found your right eye's blind spot.

⁴⁴For example a light from a single point of the right side of the visual field goes in the two left hemiretinas (nasal retina of the right eye [has the blind spot] and temporal retina of the left eye [has not the blind spot]) and viceversa; refer to page 208.

⁴⁵So the brain itself fills in the missing part (green circles) with the information surrounding (white portion).

Lateral Geniculate Nucleus (LGN)

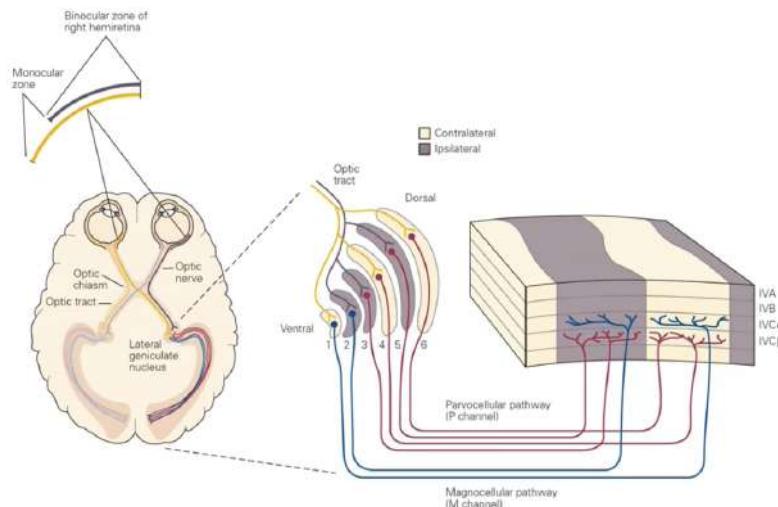


Figure 8.23

Beyond the optic chiasm, the axons from nasal and temporal hemiretinas carrying input from one hemifield join in the optic tract, which extends to the LGN⁴⁶ of the thalamus.⁴⁷



Figure 8.24

In primates, LGN is a layered structure consisting of six layers, of which two

⁴⁶Lateral Geniculate Nucleus (LGN) is the *second station*; first station is the retina; is just one part of the Thalamus. Why we call it *nucleus*? In anatomy we call *nucleus* anything that is an aggregate of neurons, there are many neurons, they converge in that place and becomes a grey area in the brain which is almost made entirely of white matter. So the very small grey matter parts are called *nucleus*.

⁴⁷The Thalamus is a sort of *Gate* to the cortex; if you want to arrive up to the cortex you need necessarily to pass through the thalamus. Any information that comes from outside in order to arrive to the cortex has to stop in the *Thalamus* (for vision, somato sensation, pain, smell ... any sensation stops to the thalamus and then is transmitted to the cortex). So vision stops in LGN; LGN is pretty large, is one of the largest nucleus in the thalamus, this because *vision* is very important; as we said before large part of the brain is devoted to *vision*.

Magnocellular layers (layers 1 and 2), and four Parvocellular layers (layers 3 to 6).⁴⁸ Each layer receives input from either the ipsilateral eye (temporal hemiretina, layers 2, 3, 5) or the contralateral eye (nasal hemiretina, layers 1, 4, 6).

Since each layer contains a map of the contralateral hemifield, the six maps are stacked on top of each other and in spatial register.⁴⁹

The magnocellular layers project to the IVC α layer while the Parvocellular layers project to the IVC β layer of V1. The Koniocellular intercalated layers project to the blobs (layers 1-2) of V1.⁵⁰

Interspersed (white in the figure) between the Magno and Parvo layers, are thin but (smaller than Parvo) dense layers called Koniocellular which receive from the K retinal ganglion cells.

The parallel channels established in the retina remain anatomically segregated even in LGN.

- Parvocellular layers receive input from midget retinal ganglion cells, which are most numerous in the primate retina (~70%) and carry red-green contrast information.⁵¹
- The magnocellular layers receive input from parasol retinal ganglion cells (~10%), which carry achromatic contrast information;
- Finally, the Koniocellular layers receive input from retinal ganglion cells K (~10%), which carry blue-yellow opponent information;

So, for example, color informations, motion informations ... they are separated since from the retina and this separation propagates (parallel processing) creating channels of informations; three major channels:

- Parvocelluar (color contrast, details, static ∴ *What*):
– (*parvo* means *small*) this channel – as its name suggests – is made of small cells, neurons; they are able to intercept information very precisely, they see a lot of details but are not very performant with *motion* (static, e.g. are important when we read) and they are able to see colors.
- Magnocellular: (acromatic contrast, general global image, motion movement ∴ *Where*; functional separations in comparison to Parvocellular):

⁴⁸From the image is pretty clear that Parvocellular has more neurons (because has to be precise, has to catch the details, details of *What* thing) than Magnocellular (general infos, *Where* things are.)

⁴⁹Remember that right LGN sees left visual hemifield, sees the same hemifield with both eyes (and viceversa). Each of these 6 layers has a complete ordered map of the visual hemifield they're referring; because each layer is staked on top of each other, they are in spatial register meaning that each layer sees something; infact if I have an electrode and I record neurons (of each layer) that are on the same parallel line trasversal to the layers, they fire together at the same time when they see the same pixel in the space, the same point; and from that point they elaborate with parallel processing different informations following the layer division cathegory.

⁵⁰Remember V1 indicates the primary visual cortex. Till this level, brain mantains informations separated (what comes from the right and what comes from the left; two different channels; for integrating info we need to reach V2).

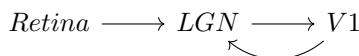
⁵¹Each neuron does not see a single color but it is able to measure one color relative to the opposite color (only red-green the parvo).

- made by large neurons; they are not able to see colors, they see only black and white, only difference in luminosity (black small luminosity, white great luminosity).

- Koniocellular:

- see above.

Finally:



There is almost 40 x feedback from V1 to LGN: the number of cells that connect back V1 to LGN is much more larger than the number of the first connection LGN to V1.

We don't know yet exactly in detail what this feedback projection does but something related to controlling the information flow through filters and integration of the cortex.

Primary visual cortex (V1)

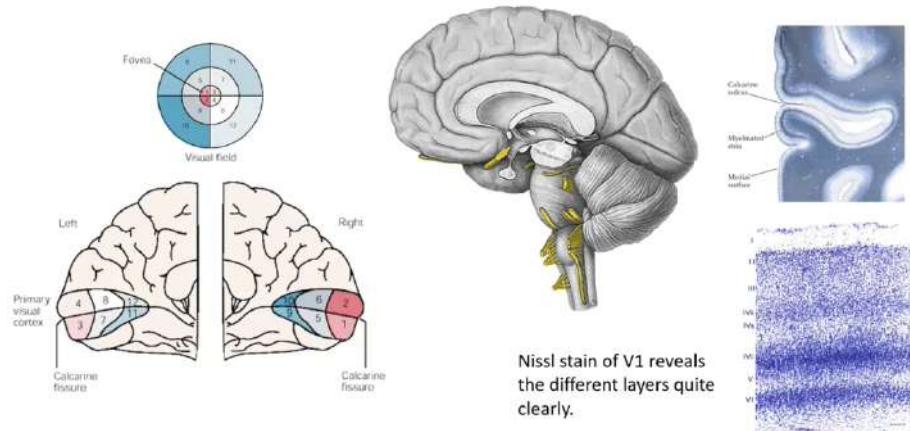


Figure 8.25

In humans, V1 (BA17) is located in the occipital portion of the brain along the calcarine fissure of the brain.

V1 constitutes the first level of cortical information processing.

Visual field is mapped in V1 (and viceversa) in a very ordered manner (look at the left part of the figure): what is close in the visual field is close also in V1 and what far in the visual field is far in V1 too. It is maintained a topographical map. Note almost half V1 is devoted to Fovea while the periphery is much smaller.

The name striate cortex⁵² derives from the Gennari (1782) stripe⁵³, a distinctive

⁵²Striate cortex ≡ V1; so when we say *striate cortex* we refer to V1; when we say *extra-striate cortex* we refer to all the other visual cortices (V2, V3, V4 ...) all the other visual areas that are not V1; there are almost 30-35 *extra-striate* cortices.

⁵³V1 is called *striate* because it presents a stripe well visible; see top right figure above.

line (visible to the naked eye) composed of terminations of myelinated axons from the LGN entering into the IV cortical layer of V1.⁵⁴

The primary visual cortex is a koniocortex (sensory cortex) divided into six distinct functional layers, numbered from 1 to 6. Layer 4, which receives most of the visual inputs from the LGN, is in turn divided into four layers, called 4A, 4B, 4C α , and 4C β .⁵⁵ Sublayer 4C α receives magnocellular inputs from the LGN, while 4C β receives parvocellular inputs.⁵⁶

Visual area V1 has a visuotopic map of the visual field. For example, the upper bank of the calcarine fissure responds to the lower half of the visual field, the lower bank responds to the upper half of the visual field.

In humans, V1 contains about approximately 140 million neurons per hemisphere (Wandell, 1995), i.e. about 40 V1 neurons per LGN neuron.

Receptive field

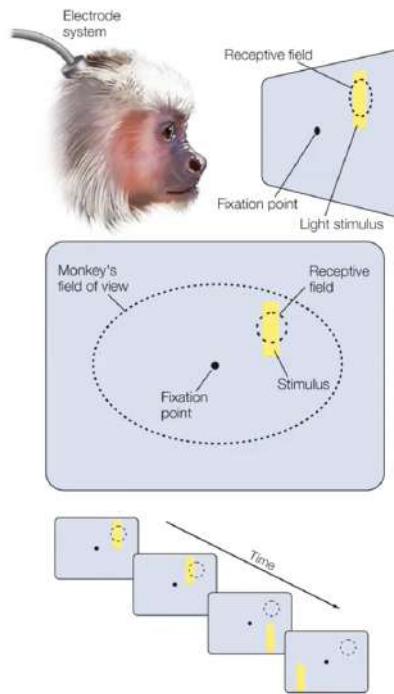


Figure 8.26

⁵⁴The input in V1 is very large: there is 1 million neurons carrying from the optic nerve which is the largest nerve in our body, there is no other nerve that has more neurons than the optic nerve. Think about that: there are 200 millions of photoreceptors (which are neurons) and 1 million is in each optic nerve; so there is a very efficient compression of informations: from 200 millions (retina) to 2 millions (optic nerves) without losing informations. How this efficient compression is done remains a matter of study.

⁵⁵Layer 4 is striped.

⁵⁶All cortices in cerebral cortex that we have are made of 6 layers (see the bottom right of the figure above) except very few that are the phylogenetically older (called *archi-cortices*) for example hippocampus is a region that has 3 layers.

Before going into V1 we need to see few things about the concept of *Receptive Field* (RF) and the functional properties of neurons, because we are going to focus on a single neuron in our tractation.

In experiment we can record, we can analyze the activity of a single cell (it's rare to have an human subject because the recording use very invasive techniques, for example we need to put a needle (very small but still is a needle) in the brain). There are other methodologies of analisys like fMRI that are not invasive but they don't allow to follow the activity of a single cell (neuron) and its properties. In general the needle is made of platinum, you need to insert it in the brain, specifically in the cerebral cortex (see ahead). Usually the patients are Macaque monkeys called also macaques, small and very clever monkeys, not antropomorphic (for ethical reason). Looking at the image above we put the electrode in extra cellular space, near the neuron, not inside (see ahead).

Visual neurons respond to stimuli in only a limited region of space. This region of space is referred to as that cell's receptive field (RF).

Monkey is required to maintain fixation, and stimuli are presented at various positions in the field of view.

The neuron below fires vigorously only when the stimulus is presented in the upper right quadrant, thus defining the upper right region as the RF for this cell.⁵⁷

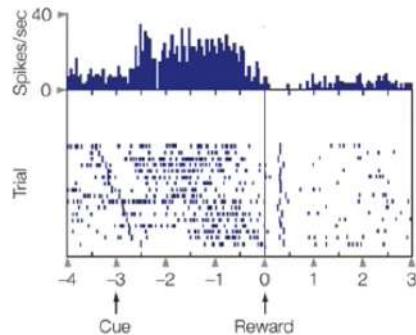


Figure 8.27

The concept of RF was introduced in 1906 by Charles Sherrington. The receptive field is a characteristic of all neurons and, in vision, indicates the region of the visual scene where the stimulus must fall to excite or inhibit the neuron being studied.

⁵⁷When we fix the electrode we don't know yet where is the receptive field (the resolution is so high!); we intercept it by the firing of neuron that is the RF of the neuron. Neuron encodes the position (generating RF), it is just one (but crucial) property, we will see others. The neuron does not respond randomly to the position varying. It's important to make the monkey fixate a point, we need to train the animal presenting a reward which has to be also in the trial phase. Stimulus is presented inside the receptive field at different time causing a firing rate increment (see the figure below, trials are almost 50). As you can see in the figure below the firing is not regular, it follows statistical logic and distribution (Poisson) what we can say is that neurons fire more when the signal is inside RF rather than if is outside.

Single-cell recording

This technique allows recording signals (firing rate) from single neurons. A fine-tipped, usually metal (platinum), electrode is inserted in the animal brain to record extracellularly change in electrical activity called action potential (AP, 1 ms duration) or spike. Collected signals are appropriately amplified, filtered, viewed through an oscilloscope, and saved to a computer for offline analysis. Since spikes are all-or-none highly stereotyped signals, most information is encoded in the brain as neuron firing rate, *i.e.*, the number of AP in 1 s. The primary goal of single-cell recording experiments is to determine what experimental manipulations produce a consistent change in the firing rate of an isolated neuron.

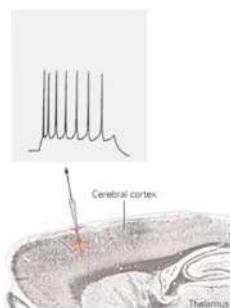


Figure 8.28

Disadvantages:

- invasive.

Advantages:

- high spatial and temporal resolution;
- differentiation between excitation and inhibition.

Organization of receptive fields in the visual system

The receptive field size varies based on:

- position of the neuron along the visual pathway;⁵⁸
- eccentricity, *i.e.*, RF position relative to the fovea.⁵⁹

At each eccentricity, receptive fields are relatively small at the first levels of visual processing and become progressively larger at later levels.

The amount of cortex devoted to one degree of viewing angle changes with eccentricity.

⁵⁸If you're in the retina for example the RF is very very small much less than 1 degree. If you go in LGN is larger; if you go in V1 larger; V2 ... and so on. So along the hierarchy of the *visual pathway* the RF becomes larger and larger till reaching V4 and eventually arrive to the end (here is the end of the object recognition pathway) of the *ventral* (infero-temporal cortex) pathway the RF becomes all the visual field; the entire visual field in the RF.

⁵⁹Distance to the Fovea.

Accordingly, more cortical space is dedicated to the central part of the visual field, where the receptive fields are smaller and densely packed and the visual system has the highest spatial resolution.

Eccentricity

The receptive fields of the retinal ganglion cells that monitor portions of the fovea subtend about 0.1° (equal to 6 min of arc), while those in the visual periphery reach up to 1° of visual angle or more.

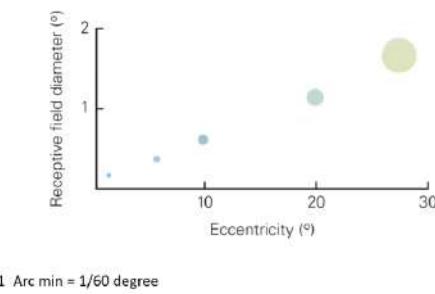


Figure 8.29

The amount of cortex devoted to one degree of viewing angle changes with eccentricity.

Accordingly, more cortical space is dedicated to the central part of the visual field, where the receptive fields are smaller and densely packed and the visual system has the highest spatial resolution.

Retinotopy

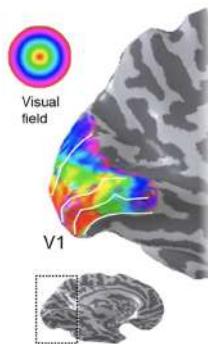


Figure 8.30

In early visual areas (*e.g.*, V1 to V5), neuron RFs reveal an ordered organization, termed a retinotopic or visuotopic map.

This refers to the existence of a non-random relationship between the position of neurons in the visual areas.

Neuron RFs form a 2D map of the visual field, such that neighbouring regions in the visual image (and therefore on the retinal surface) are represented by adjacent regions of the visual cortical area (*i.e.*, orderly mapping of RF positions in retinotopic coordinates).

Note also this: more neurons are devoted to processing images that are in the center of the visual field than what are in the peripheral; in fact looking above the red zone in the cortex which corresponds to the small red circle in the visual field is much greater in comparison to the violet-red in the peripheral. Remember that the center of the visual field is what requires the highest resolution (and so more neurons). So the size of the parts of the visual field is not isomorphic to the size of the parts of the visual pathway (in the sense they have proportional size).

Receptive fields on the retina

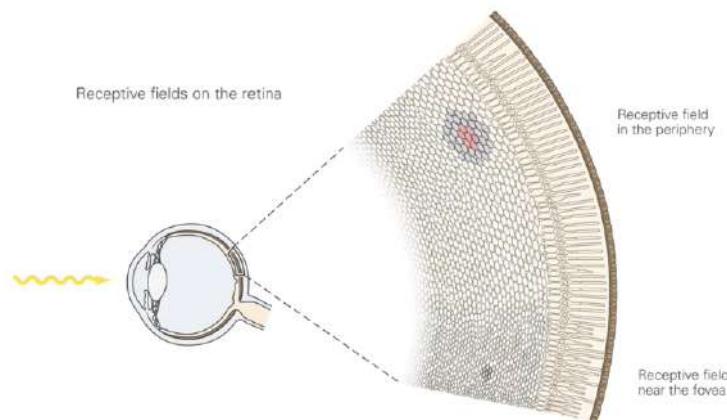


Figure 8.31

A retinal ganglion cell near the fovea receives input from fewer receptors covering a smaller area, while a cell further away from the fovea receives inputs from many more receptors covering a larger area.

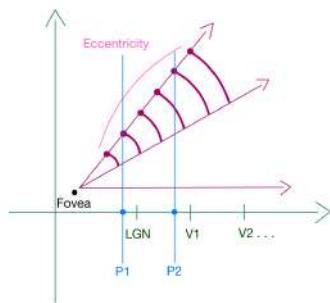


Figure 8.32

In the figure above P1, P2 (denoting position of the neurons along the pathway) have same *Eccentricity* but different *Position* along the pathway.
And RF is directly proportional to both *Eccentricity* and *Position*.

Spatial resolution

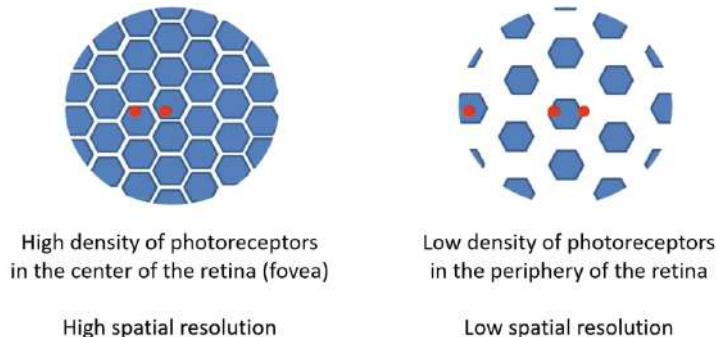


Figure 8.33

Spatial resolution: minimum distance at which it is possible to recognize as distinct two stimuli presented simultaneously in the visual field.

Looking at the figure above:

- in the left figure we can see that two receptors are activated with two near signals;
- in the center of the right figure we have the same distance between signals of the left figure but only one receptor is activated; in order to activate two receptors you have to put more distance between signals.

Cortical magnification

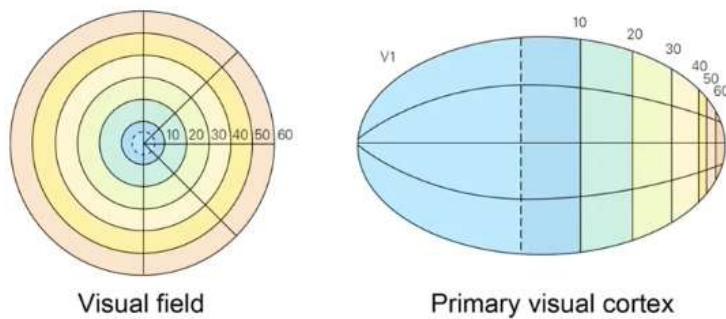


Figure 8.34

The amount of cortical area devoted to each degree of the visual field, known as the magnification factor, varies with eccentricity (*i.e.* the neural maps of the visual field are not isometric).

In fact, the central part of the visual field controls the largest area of the cortex. For example, in V1 more cortex is dedicated to the central 10° of the visual space than to everything else.

Receptive field properties

Properties change from relay to relay along a visual pathway.

By determining these properties, one can assay the function of each relay nucleus and how visual information is progressively analysed.

Whereas retinal ganglion cells and neurons in the LGN have concentric center-surround receptive fields, those in the primary visual cortex, although equally sensitive to contrast, analyse oriented contours (orientation selectivity).⁶⁰

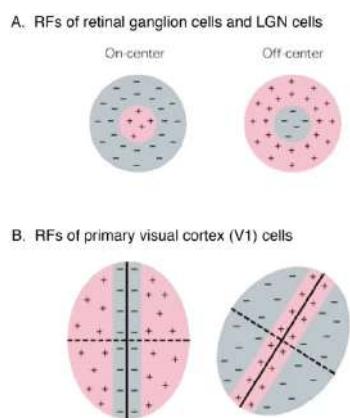


Figure 8.35

We saw RF size, magnification, retinotopic of visual map (remember that this is true for early visual area *e.g.* V1, ..., V5 of the object recognition pathway; we will see that we don't have retinotopic for the other more advanced areas). So not all the visual map is retinotopic *e.g.* in the hippocampus which also responds to visual stimulus the coding is not retinotopic, but is allocentric: it does not depend by the viewer, by the observer, but is coded according to certain landmarks that are fixed in the environment (it's a very different part of coding). But in the ventral visual pathway (the pathway that is related to object perception) the coding, when present, is until the infero-temporal cortex where the RF there is not anymore, disappears (the RF ≡ entire visual field) with also the concept of retinotopy.

We saw that some *selectivity* is related to position in the visual field; neurons respond only if the stimulus is in a certain location but '*select*': the neurons does not respond to all the location, but to the location of the receptive field. However this is not enough, it is needed to present inside the receptive field the correct appropriate stimulus which is called '*optimal*' stimulus; basically not all stimuli are optimal for each neuron (*e.g.* V4 wants colored stimuli).

Looking at the figure above:

⁶⁰They select bars.

- A. They prefer concentric type of stimuli, the stimulus has to be circular, the On-center type of cell for instance should fill (with light) the center part of RF whereas dark should be around (if you illuminate the entire RF or larger you don't get any type of response, they need a little spot of light in the center of the RF in order to activate. For the Off-center is the opposite: they need dark in the center and light in the periphery surround.)
- B. This type needs elongate stimuli (not spot as the previous). They select bars: vertical dark bar on light theme (left figure), light oblique bar on dark theme (right figure). This long stimuli probably address edges, border of objects, contours; because the RF is small each cell has a small part of an edge; so not only the stimulus has to be an elongated bar, but also has to have the right orientation (orientation selectivity).

Cortical columns

If you're in V1 and you insert an electrode perpendicularly it is possible to see going in deep micron per micron till the white matter (2 mm) that neurons along the same perpendicular line respond all to the same orientation (we still don't know why). Instead if you go tangential with unit of 50-75 μm , the diameter of columns, you see a change in direction and this change is not random.

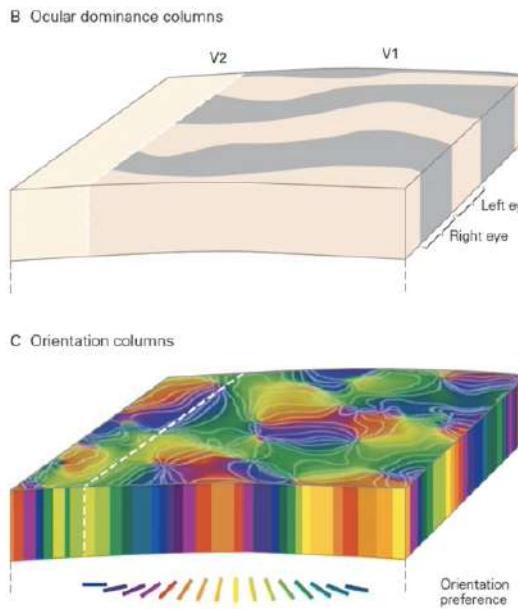


Figure 8.36

In V1, neurons with similar functional properties are found close together in columns or functional modules (about 50-75 μm in diameter) that extend from the cortical surface to the white matter (about 2 mm high).

V1 includes specific columns for stimulus orientation, and ocular dominance.

There are also proposals for maps of direction selectivity (Weliky et al., 1996; Ohki et al., 2005), selectivity for spatial frequency (Issa et al., 2000) and for

disparity (Kara and Boyd, 2009).

Orientation columns

Neurons with the same orientation preference (*i.e.*, vertical) are grouped together into orientation columns. Each column contains a few hundred cells and is 50-75 μm wide.

Moving from one column to the adjacent one, orientation preference changes systematically by 10-15°, both clockwise and counterclockwise, completing a 180° cycle (12 steps) every 750-1000 μm .

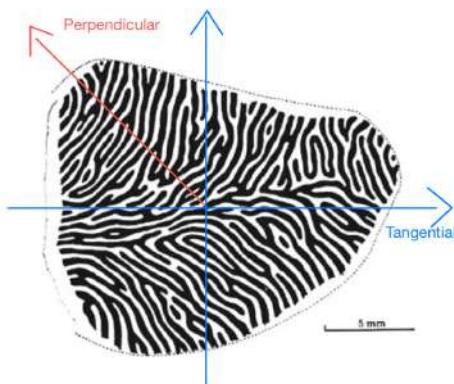
The set of columns corresponding to a complete sequence of orientations (a period) is called a hypercolumn.

There are approximately 3-4 thousand hypercolumns, each monitoring a position of the visual field, in accordance with the retinotopic topology.

Hubel & Wiesel (1962, 1968) observed that when they advanced a microelectrode along a penetration perpendicular to the cortical surface, successively recorded cells shared an identical orientation of their receptive field axis.

By contrast, when they advanced a microelectrode along a penetration tangential to the cortical surface, they observed that the preferred orientation of cells shifted in steps of 10-15° approximately every 65 μm .

Ocular dominance columns



Ocular dominance columns in primary visual cortex (V1) of macaque monkey shown in tangential section. Regions receiving input from one eye are shaded black and regions receiving input from the other eye are unshaded. The dashed line signifies the border between areas V1 and V2 (taken from Hubel and Wiesel, 1977).

Figure 8.37

In addition to orientation columns we have also ocular dominance columns.

The ocular dominance columns group⁶¹ neurons that respond more vigorously to stimuli presented to one of the two eyes.⁶² They are stripes with an average

⁶¹An alternative name of columns group neurons is *hypercolumns*.

⁶²Remember: the two eyes see each – almost – the same thing, the same location.

width of approximately $750 \mu\text{m}$, running tangentially for various mm. The ocular dominance columns⁶³ reflect the segregation of inputs from different layers of the LGN, which receive inputs from retinal ganglion cells located in the ipsilateral or contralateral retina.

In tangential penetrations of V1, the dominance columns of the left and right eye have been found to alternate regularly with a periodicity of 750 to $1000 \mu\text{m}$.

The function of ocular dominance columns remains an enigma. One candidate function for ocular dominance columns has been stereopsis (binocular vision). However, it has been reported that squirrel monkeys, which lack ocular dominance stripes have a stereoacuity comparable to that of human observers (Livingstone et al. 1995).

If you move tangentially we find the same orientation of those columns but for the other eye: left-eye, right-eye, left-eye ... and in each stripe we have orientation columns.

Blob e interblob

D Blobs, interblobs (V1), and stripes (V2)

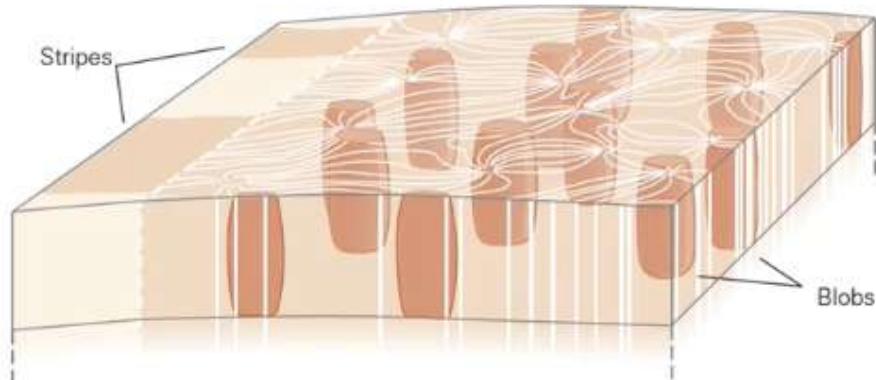


Figure 8.38

The columns of orientation and ocular dominance include groups of neurons that are poorly selective for orientation (they have circular receptors) but with strong preferences for the color of the stimulus.

These cell groups are located in the superficial layers II and III of V1. They are detectable by a specific marker for the cytochrome oxidase (CO) enzyme,⁶⁴ distributed in a regular pattern of regions defined as blobs (CO rich and color responsive) separated by interblob areas (CO poor and orientation responsive). In blobs there are neurons that respond to colours (red-green, blue-yellow).

So putting all this together ...

⁶³They are in V1 like cortical columns.

⁶⁴An enzyme that can be colored. You can inject this substance, obviously this is done in vitro or when the subject is dead.

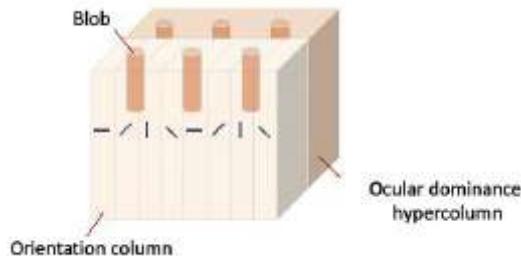


Figure 8.39

The functional organization of the primary visual cortex is therefore based on two systems running orthogonally to each other:

- orientation system;
- ocular dominance system.

The figure represents a complete model called '*eyes cube model*'; we have this model for each possible location of the visual field.⁶⁵

This is all the machinery that is needed to see in a specific location all the possible orientations and all possible colors.

We still don't know why we have this minimum complete organization but it is a reasonable thing that this organization implies optimization for time processing, functional processing *etc.* ... *e.g.* having cells that process orientation closer each other is more advantageous in an optimization logic rather than being distant; if you send one input from LGN, the same input is received for all cells \Rightarrow more efficient.

Pinwheels

More recently, optical imaging technique⁶⁶ has enabled to visualize a surface representation of the orientation and ocular dominance columns in living animals. The cycles of orientation columns form various structures, from parallel stripes to pinwheel-like shapes.



Figure 8.40

⁶⁵It is easy to see the orientation system and the ocular dominance system; the grey stripe is related to one eye and the white stripe to the other eye.

⁶⁶It is enough just to be able to project light on the brain (after removing protective bones) and the reflected light depend on the metabolic activity of neurons.

Sharp jumps or singularities (discontinuities) in orientation preference occur at the pinwheel centers and cause ‘fractures’ in the orientation map.⁶⁷

Developed for studies of cortical organization by Amiram Grinvald, this technique visualizes changes in surface reflectance associated with the metabolic requirements of active groups of neurons, known as intrinsic signal optical imaging, or changes in fluorescence of voltagesensitive dyes.

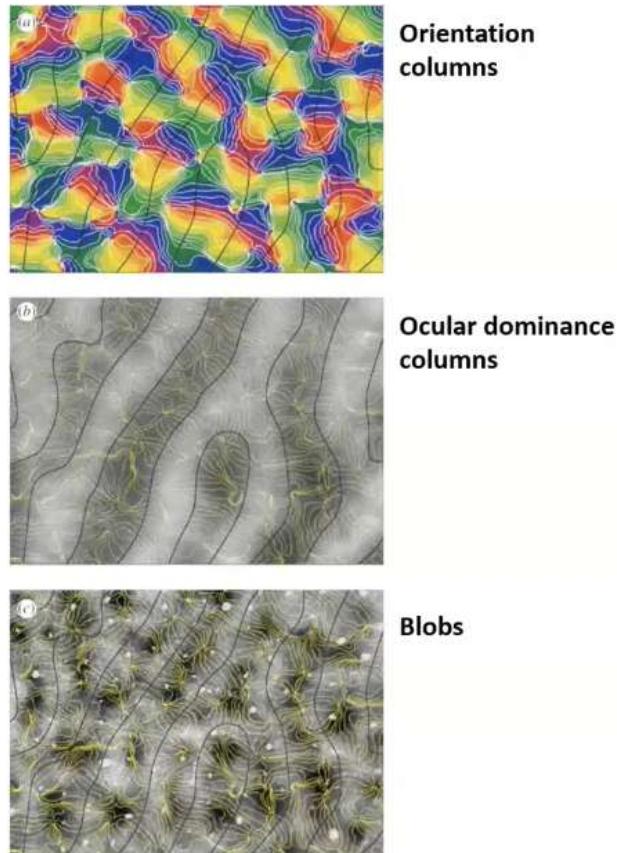


Figure 8.41

Looking at the image above (top-down order):

- (a) Optical imaging map of orientation preference in macaque striate cortex. The black lines represent the borders of ocular dominance columns.⁶⁸
- (b) Iso-orientation contours from (a) superimposed on an optical imaging map of the ocular dominance columns. Note that orientation singularities tend to be situated in the centres of ocular dominance columns.

⁶⁷There is a very sharp jump of orientation; in this point is broken the linear progressive change in orientation.

⁶⁸Obviously the colors of the image are given to highlight better, to make you understand (each color is for one particular orientation) e.g. in this image blue is referred to vertical orientation, red oblique to the left, green oblique to the right, yellow horizontal ... and so on.

- (c) Comparison between iso-orientation contours and CO patches (blobs). In some instances, singularities and blobs coincide. (from Horton and Adams, 2005).⁶⁹

Also in humans

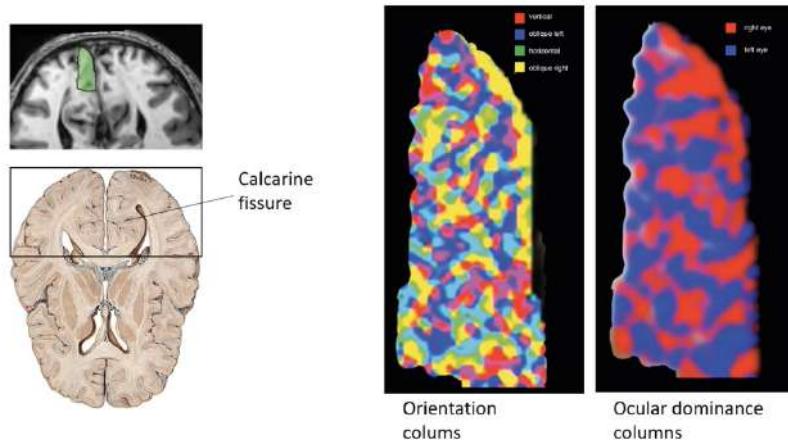


Figure 8.42

Yacub et al. (PNAS, 2008) demonstrated, by using highfield (7-T)⁷⁰ fMRI, the existence and spatial features of orientation selective columns in humans. Striking similarities were found with the known spatial features of these columns in monkeys. In addition, it was found that a larger number of orientation columns are devoted to processing orientations around 90° (vertical stimuli with horizontal motion).⁷¹

Looking at the figure above note that V1 is positioned at the top of the square that highlights the Calcarine fissure (bottom left figure).

Note that there are certain types of monkeys, very simple primates, that don't have ocular dominance columns; these columns are associated with the ability to see depth (as said before) but they see depth very well.

In general if we consider:

rats —→ *cats* —→ ... —→ *monkeys* —→ *humans*

the organization of the cells increases, in rats for example the organization is very caotic.

Ice cube model (Hubel e Wiesel, 1977)

A region of cortical tissue of about 1 mm contains two orientation hypercolumns (a complete cycle of selective vertical columns for orientation), one for the left eye and one for the right that alternate regularly, blob and interblob. This computational module contains all the anatomical-functional types of V1 neurons,

⁶⁹Note that the white circles in the figure represent the *blobs*.

⁷⁰T stands for *TESLA*.

⁷¹Maybe because we are essentially *biped* beings.

and would be repeated thousands of times to cover the entire surface of the visual field.

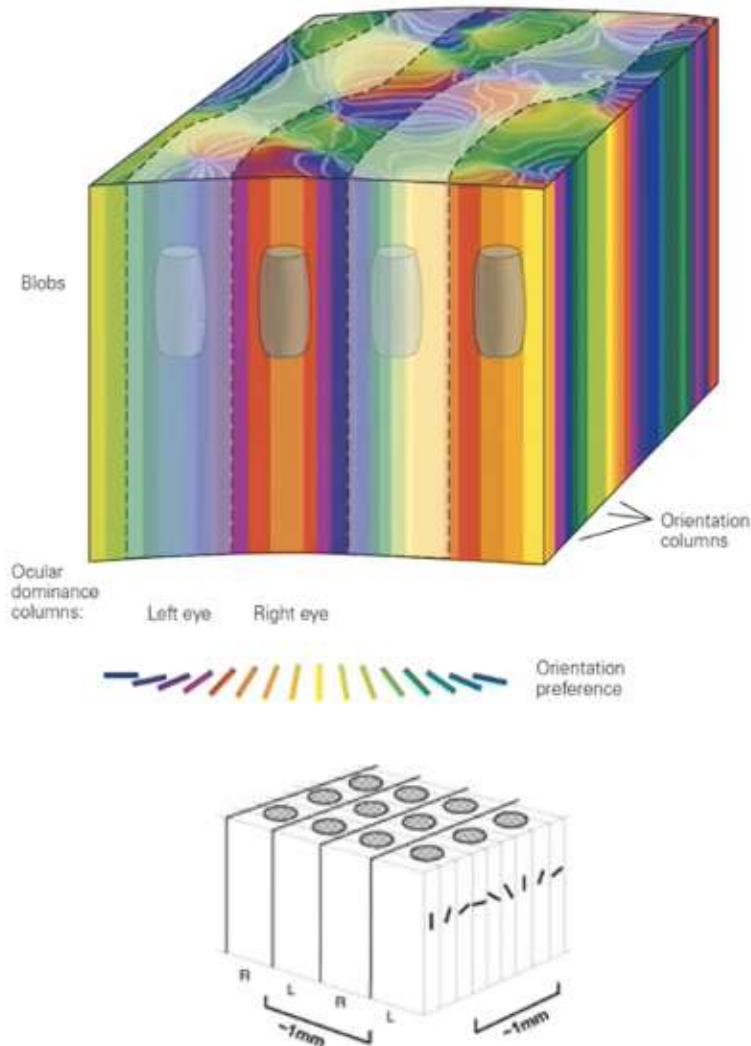


Figure 8.43

However, it remains unclear what advantage, if any, is conveyed by this form of columnar segregation. One candidate function for cortical columns is the minimization of connection lengths and processing time, which could be evolutionarily important.

General overview

The ‘*next-level*’, the next area close to V1 is V2 which corresponds to area 18 in the *Brodmann classification* (Brodmann was a neurologist who classified using the

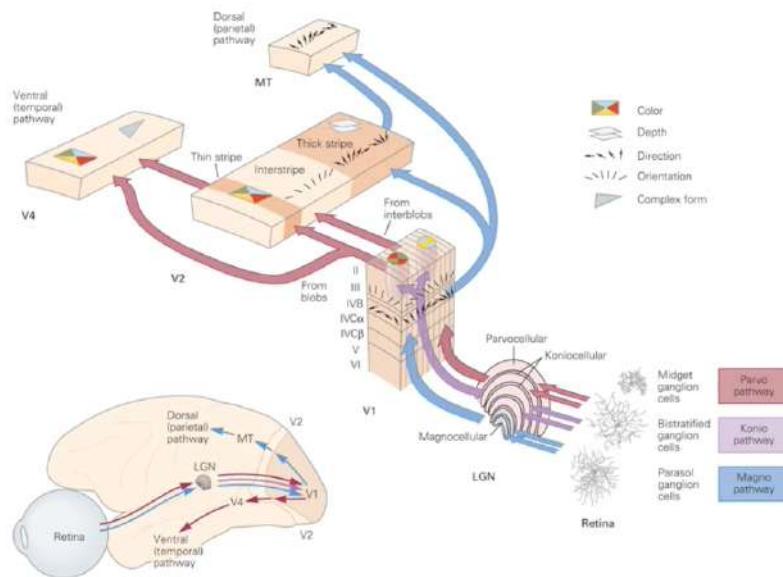


Figure 8.44

microscope the different possible cortices in primate and human brain from 1 to 52⁷² and usually neuroscientists use these numbers to indicate a specific brain area: $V1 \longleftrightarrow 17$, $V2 \longleftrightarrow 18$, ...). There is a huge correspondence between primate brain areas and human brain areas.

In these groups of lectures we will see the following major groups and pathway (light goes): RETINA \rightarrow LGN \rightarrow V1 \rightarrow :

- *Dorsal pathway* (goes up): specialized in analyzing motions of the stimulus, movement \longleftrightarrow ‘Where pathway’.
- *Ventral pathway* (goes down): specialized in analyzing *what* is the object, what are the characteristics of the object \longleftrightarrow ‘What pathway’.

They are *parallel pathways*, there are a lot of intercommunications between them. We will see how they process time which is different: *Dorsal pathway* is faster while *Ventral pathway* is relatively slow, this means that the brain is able to extract first information about *Position* and then *What* is the stimulus in that position. It seems that *Position/Location* has a priority or it is faster because the type of processing is simpler than what relative to *What* object which requires a higher detail level. These are experiments in primates and humans. Or maybe because to recognize *Position* faster is more important for *Survival* (think to the *Escape* action; distance is very important).

In LGN there are essentially three types of layers. Remember:

- *Magnocellular* are completely acromatic (so the informations that they carry go to the dorsal pathway).

⁷²When we say *Visual Area* we are referring to those areas that have neurons which respond to visual stimuli. There are more than 30 Visual areas: V1, V2, ..., V30, ...

- *Parvocellular* analize the details of the stimulus.
- *Koniocellular* are in between Parvocellular and Magnocellular and include cells that are important to encodes colors (blu-yellow in particular).

Note the cube model for V1. We have:

- *BLOBS* (neurons) which encode *colors*.
- *INTERBLOBS* encode *orientations* (for left and right eyes).

In V2 there are also parts characterized by the cytochrome oxidase (CO) enzyme (CO rich and color responsive) but are not anymore *BLOBS*, they are *STRIPES* (blobs are replaced by stripes). In particular also here we have a specific geometric organization:

- Thin stripe \longleftrightarrow colors.
- Thick sripe \longleftrightarrow direction of motion.
- Interstripe \longleftrightarrow orientation (for shape, it is important for encoding contours of objects).

Colors, stimulus orientation, stimulus direction of motion; we have *parallel processing* also in V2 (we already saw in V1).

Area V2

In area V2, thick and thin dark stripes separated by pale stripes are evident with cytochrome oxidase labeling.

- The thick stripes contain neurons selective for direction of movement and for binocular disparity;
- The thin stripes contain cells specialized for color.
- The pale stripes contain orientation-selective neurons.

For every visual attribute to be analyzed at each position in the visual field, there must be adequate tiling, or coverage, of neurons with different functional properties.

Any given position in the visual field can therefore be analysed adequately in terms of the orientation of contours, the color and direction of movement of objects, and stereoscopic depth by a single computational module.

Beyond V1

Beyond V1 are the extrastriate visual areas (more than 30 areas in macaques), a set of higher-order visual areas organized as neural maps of the visual field.

Visual areas are organized in two hierarchical pathways, a ventral pathway involved in object recognition and a dorsal pathway dedicated to the use of visual information for guiding movements.

The ventral or object recognition pathway extends from V1 to the temporal lobe. The dorsal or movement-guidance pathway connects V1 with the parietal lobe and then with the frontal lobe.

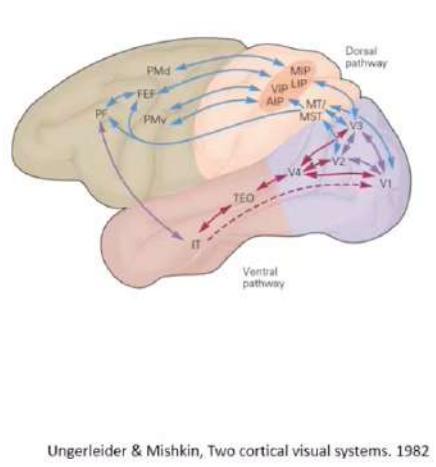


Figure 8.45

The dorsal and ventral pathways are highly interconnected so that information is shared.

For example, stimulus movement information in the dorsal pathway (area V5) can contribute to object recognition through kinematic cues. Information about movements in space derived from areas in the dorsal pathway is therefore important for the perception of object shape and is fed into the ventral pathway. Note: all connections between areas in the ventral and dorsal pathways are reciprocal: each area sends information to the areas from which it receives input. Reciprocity is an important feature of connectivity between cortical areas.

The figure above refers to monkey brain. There is a strong parallel organization between human and monkey (macaques in particular) brain (is just a little bit simpler); macaques monkey brain is what we know better.

Here below we show instead human brain:

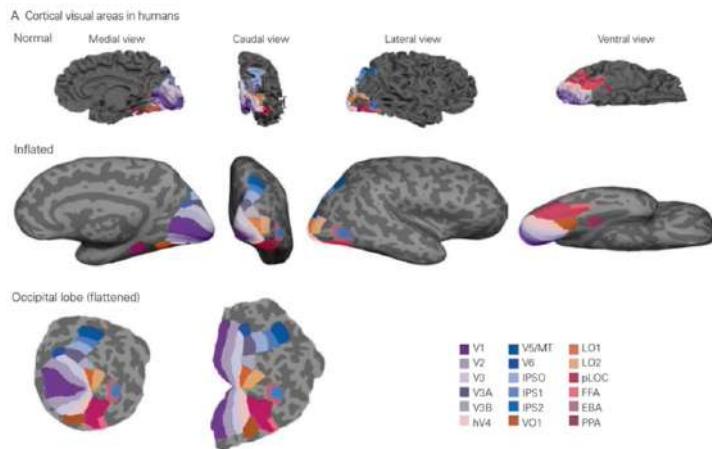


Figure 8.46

From lowest to highest level



Figure 8.47

At the lowest level, visual attributes such as local contrast, orientation, color and motion are processed.

The intermediate level involves the separation of the visual image into surfaces and outlines (contours), and figures from background distinction.

The highest level concerns object recognition.

Once a scene has been analyzed by the brain and the objects have been recognized, the objects can be associated with memories of shapes and their meanings.

8.2 Low-level visual processing

Components

Low-level visual processing involves:

- retinal circuits;
- LGN;
- some (but not all) of the neurons of V1

This level allows you to extract some elementary characteristics from the visual image.

8.2.1 Retina

Retina

The eye projects the visual scene onto the retina's photoreceptors.

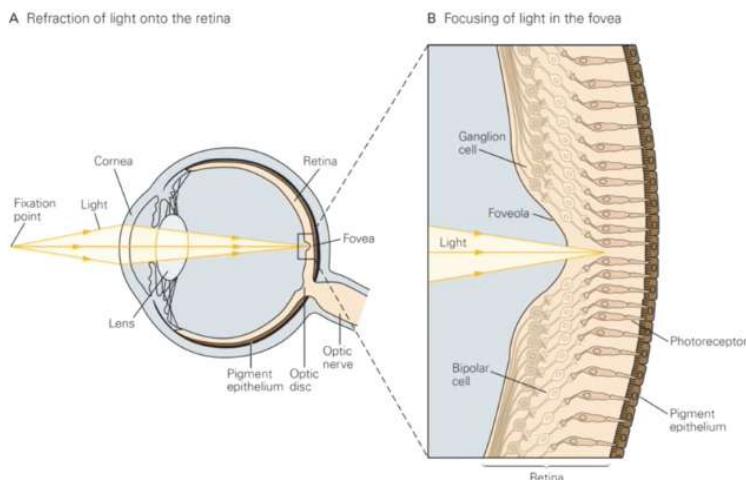


Figure 8.48

The retina is a thin (0.5 mm) sheet of neurons at the back of the eye, made up of five main types of cells arranged in three layers.⁷³

The fovea corresponds to the gaze center that we direct towards the objects we pay attention to.

The optic disc is an area of the retina without a receptor and is therefore a blind area.

Referring at the image above:

- A Light from an object in the visual field is refracted by the cornea and lens and focused onto the retina.
- B In the foveola, corresponding to the very center of gaze, the proximal neurons of the retina are shifted aside so light has direct access to the photoreceptors. The fovea is the area of the retina where the density of photoreceptors, bipolar cells, and ganglion cells is greatest, and where vision is sharpest (higher two-point resolution).⁷⁴

⁷³Types of cells: ganglion cells, bipolar cells, photoreceptors (see in detail in the next section)
... Layers: ganglion layer, bipolar layer, photoreceptor layer. Light has to go through 3 layers before arriving to photoreceptors, so there is possibility of refraction/aberration of the light, but in the *foveola* has direct access to the photoreceptors. Note that the photoreceptors layer (the most external layer: looking to the image above we refer to the *internal* part of the retina as the beginning at the left, while to the *external* part as the end at the right) is the part of the retina which is sensitive to light; why the sensitive part to the light is put in the most external part? It could be at the very beginning of the retina; the best probably reason is that if we focus on the adjacent dark epithelium (layer of cells), since light alters continuously photoreceptors, this epithelium makes continuously new photoreceptors, is important for renovation, avoiding the photoreceptors to get too old.

⁷⁴Note that *Fovea* and *Foveola* are different: *Foveola* is part of the *Fovea*.

Note: if the images are not focused exactly on the retina (using the refraction system of the eye) you have some distortion like miopia etc..

Basic circuitry of the retina

A three-neuron chain *i.e.* photoreceptor, bipolar cell, and retinal ganglion cell⁷⁵ provides the most direct route for transmitting visual information to the brain.

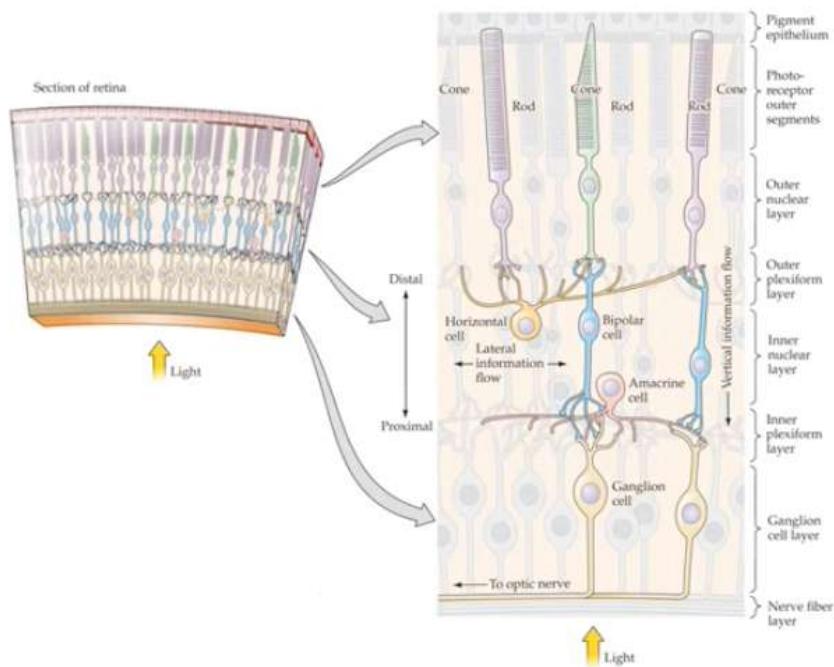


Figure 8.49

Looking at the image above (In particular focusing to the right bottom part) we can see that *Retinal ganglion cells* (RGC) axons goes out of the eye forming the optic nerve going to the thalamus in the LGN; so the RGC layer is the output layer, the output layer of the entire processing of the retina. So what the retina does is ‘seen’ through RGC cells (are very important) by the brain.

Types of photoreceptors

Humans, like most vertebrates, possess two types of photoreceptors, rods and cones, differing in shape, function, connectivity and distribution in the retina. Rods and Cones are so called because of the form of their *outer segment* (look at the image above), rod shape and cone shape respectively. In the outer segment there are mini disks (continuously renovated/updated by the black epithelium seen previously when they break; they are made by proteins and liquids which are the main structure of life) stacked one above the other and among these disks – in the shape between – there are *photopigment*, the part sensitive to light.

⁷⁵The other two types of cells are for integration (Amacrine cell, Horizontal cell).

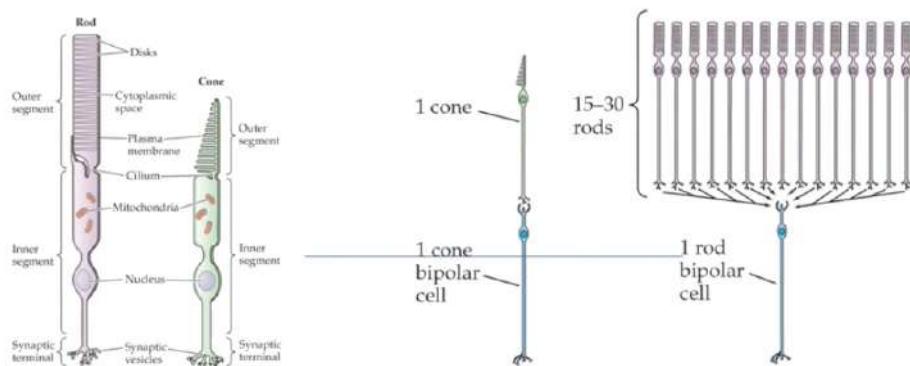


Figure 8.50

Difference in the amount of convergence for the rod and cone system.⁷⁶

In the rod system, the bipolar cell receives synapses from 15 to 30 rods. In the cone system, in the center of the fovea in particular, each bipolar cell receives its input from a single cone and synapses with a single ganglion cell (1-1 associations).

Photoreceptors sensitivity to light

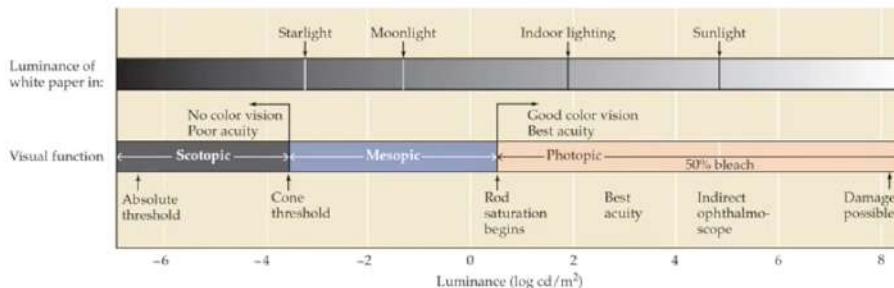


Figure 8.51

Rods and cones differ in their sensitivity to light.⁷⁷

Rods (100 million) are mainly for night (or scotopic) vision. They can signal the absorption of 1 single photon;⁷⁸ their response saturated in daylight, and they cease to respond to variation of intensity.

Cones (5 million) are only for daytime (or photopic) vision. They are much less sensitive to light, make no contribution to night vision, but have higher spatial and temporal resolution (their response is considerably faster than that of rods).

At very low light levels, vision is scotopic: light is detected by the rods of the retina. Rods⁷⁹ are extremely sensitive to wavelengths close to 500 nm

⁷⁶Higher convergence for rods. No convergence for cones. So there is a huge difference among RGC that connect with bipolar cells connected to rods (huge receptive field) and RGC that connect with bipolar cells connected to cones (very small receptive field).

⁷⁷In the figure above we refer to the word *threshold* as threshold for activation.

⁷⁸Very sensitive to light! While we need many more photons to activate a cone.

⁷⁹In practise they see only black and white.

(blue-green)⁸⁰ and play little, if any, role in color vision.

In brighter light conditions, such as daylight, vision is photopic: the light is detected by the cones responsible for color vision.

Cones are sensitive to a range of wavelengths, but are most sensitive to wavelengths close to 555 nm (green-yellow).⁸¹

In mesopic view, both rods and cones provide signals to the retinal ganglion cells.

Distribution of photoreceptors in the human retina

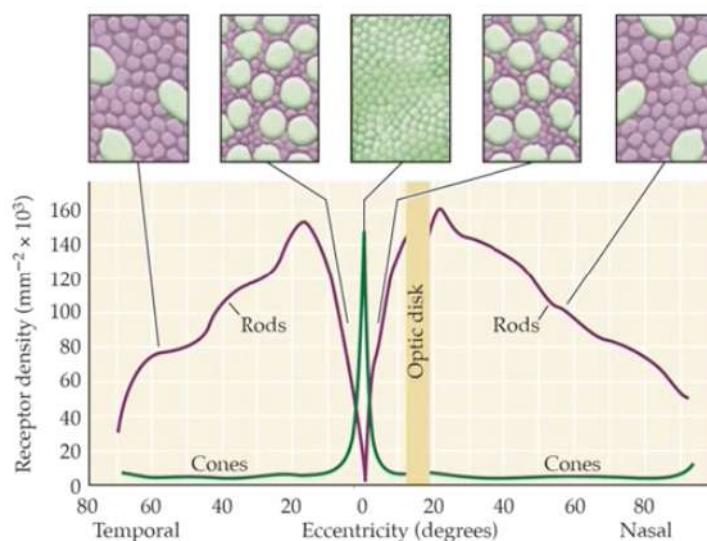


Figure 8.52

Cones are present at a low density throughout the retina, with a sharp peak in the center of the fovea (the foveola).

Conversely, rods are present at high density throughout most of the retina, with a sharp decline in the fovea; rods are absent in the foveola.

Spectral sensitivity curves of retinal photoreceptors

Curiosity: actually we don't know much about color processing⁸² in the brain, is a very complex topic. But we know that much more important for life is *Contrast*: black vs white essential to distinguish. Colors give us more details but they are not fundamental. It is possible to live without colors. Probably at the beginning there was only one type of photoreceptor and animals saw only in black and white. Then were developed at least two types of photoreceptors, with two types you can see colors because with two you have the possibility to compare (when one is activated and the other not you can discriminate

⁸⁰Colors are just an invention of our brain.

⁸¹See ahead for details. Note that since in our cities there is always a great amount of light it is difficult not using cones.

⁸²We have about no models, there is no agreement in the processing

colors). But still using two receptors there are some surfaces which can have some strange distribution of colors that with two receptors you see exactly the same thing and we need a further photoreceptor; with three photoreceptors you can essentially see/discriminate all possible colors, although you can still make mistakes. Initially probably there was the blue-yellow and then from yellow developed red and green; note that the red and green combined give yellow; note below the green is close to yellow.

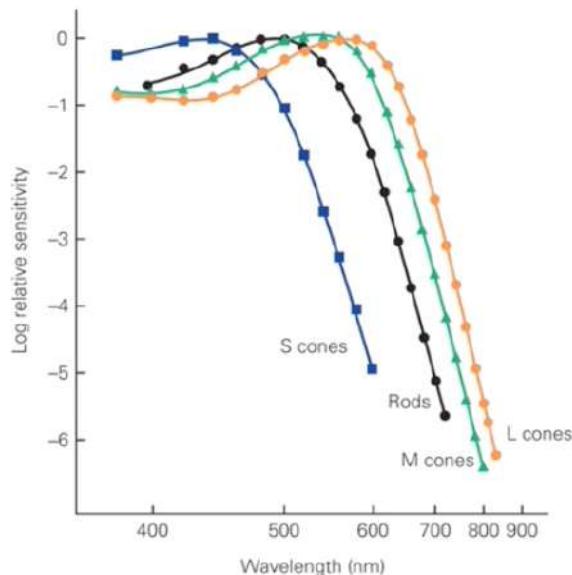


Figure 8.53

For each wavelength, the greater the sensitivity the lower the intensity of light⁸³ required to evoke the response in the photoreceptor.

Primates have only one type of rod⁸⁴ and three types of cones, distinguishable on the basis of the different photopigments (S, M and L) and, consequently, of the range of wavelengths to which they respond: L (long waves), M (medium waves) and S (short waves).

At each wavelength, the sensitivity is inversely proportional to the intensity of light required to elicit a criterion response in the sensory neuron.

Sensitivity varies over a large range and thus is shown on a logarithmic scale. The different classes of photoreceptors are sensitive to broad and overlapping ranges of wavelengths.

⁸³Is the intensity of light measured by lengthwaves? No, the intensity of light is not measured in terms of wavelengths (lengthwaves). Wavelength refers to the physical distance between successive crests or troughs of a wave, and it is a characteristic of the wave itself. It describes the color or frequency of light but does not directly measure its intensity. The intensity of light is typically measured in units such as lux (for illuminance, which is the amount of visible light incident on a surface per unit area) or watts per square meter (for radiant flux). These units quantify the amount of light energy arriving at a particular location or the brightness of the light.

⁸⁴It has one pigment called *rodopsin*, the pigment important to catch the light.

Distribution of cone cells in the fovea

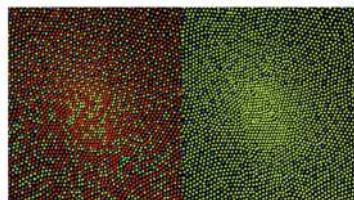


Figure 8.54

Distribution of cone cells in the fovea of an individual with normal color vision (left), and a color blind (protanopic) retina (right).⁸⁵ Note that the center of the fovea holds very few blue-sensitive S cones.

The S cones make up only 10% of all cones and are absent from the central fovea.

Analysis of colours

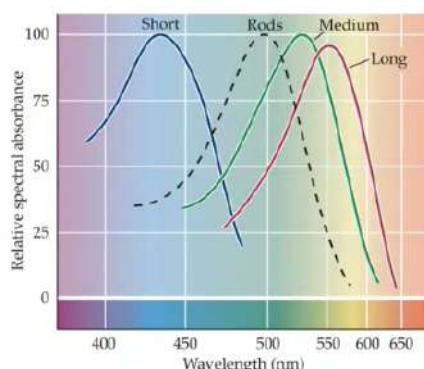


Figure 8.55

Because a single photoreceptor cannot distinguish between a change in the wavelength of light and a change in its intensity, the analysis of colour requires the comparison of signals from different types of cones.

In night vision, when only rods are active, a green light consequently has exactly the same effect on the visual system as a red light of a greater intensity.⁸⁶

⁸⁵Protanopia is a type of color vision deficiency, often referred to as 'red-green color blindness' it's more common in males than females. People with protanopia have a specific defect in their retinal cones, which are the light-sensitive cells in the eye responsible for perceiving color. In this case, the red cone cells (L-cones) are missing or not functioning correctly. The primary characteristic of protanopia is a reduced ability to distinguish between red and green colors. People with this condition may see the world in a range of muted, desaturated colors, as the spectrum of light they can perceive is limited. For them, many red and green hues may appear as shades of brown, gray, or sometimes even completely indistinguishable.

⁸⁶When you are in the dark, you don't see colors (if you see something you see grey for instance [you don't differentiate spectral composition from intensity]; all cats are the same, all stimuli are the same); if there are things red and green, you cannot discriminate between the two, but you can put the things according to their intensity for instance. A green stimulus is

Phototransduction in rod photoreceptors

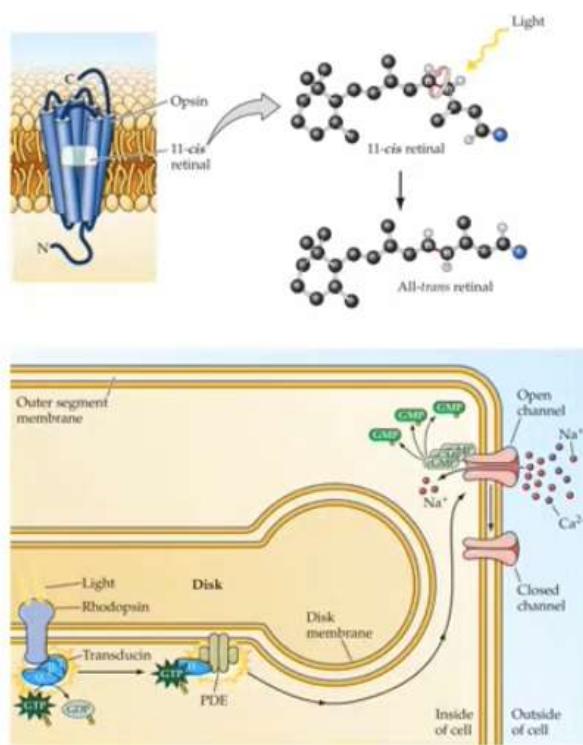


Figure 8.56

Rhodopsin (is a protein) resides in the disk membrane of the photoreceptor.⁸⁷ The opsin molecule enclose the light-sensitive retinal molecule.⁸⁸

Absorption of a photon of light by retinal leads to a change in configuration from the 11-cis to the all-trans isomer.

This in turn activates a phosphodiesterase (PDE) which then hydrolyzes cGMP, reducing its concentration and leading to the closure of channels in the outer segment membrane.

Detailed: the so called ‘economic molecule of our cells’, the GTP⁸⁹ is used to keep the channel of photoreceptors open, so if there is a lot of GTP the channel are open and sodium (Na^+) continuously goes inside the photoreceptor and depolarize the photoreceptors, so the *photoreceptor* is *active*; this is a first

perceived as more intense (think to nocturnal visors, they project green because the rods perceive green with more intensity.) from the *rod system* than a red stimulus (red is far away from the rods in comparison to green, see the image above). So in night vision you see red things lighter than green things (you are not distinguishing colors, but only perceiving, we mean this saying ‘see’). However if the intensity of the red things is increased, you see something redder, the green and red things appear of the same lightness.

⁸⁷We already talked about disks staked; inside the disks there is liquid except for the protein.

⁸⁸Which is a vitamine A; *vitamine* is a substance that we cannot produce ourselves, we need to get it from the diet.

⁸⁹Similar to ATP, both molecule involved in energy transfer and various cellular processes.

paradox for vision: the receptor *in dark* is continuously *active!* When we close our eye the photoreceptors are active! The sodium that goes inside is very very rich of GTP which carries energy!⁹⁰

We don't know exactly why but probably we evolved from *nocturnal animals* and initially was more important to see in dark; the receptor is very active in dark (Dark current of Sodium). When light comes the consequences is that 'the GTP get lower and channel close'; light comes and the receptors stop; is hyperpolarized when you see things.

Dark current

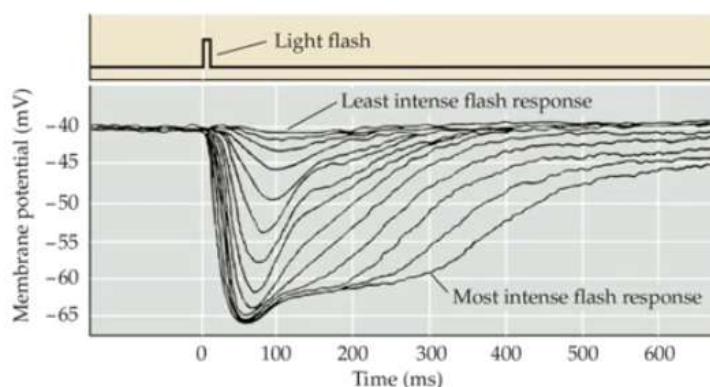


Figure 8.57

In the dark, the receptor is in a state of continuous depolarization, with a membrane potential of approximately -40 mV (current in the dark).⁹¹

The presentation of a light flash of increasing intensity produces an ever greater (*i.e.*, more negative) hyperpolarization that becomes saturated when the membrane reaches about -65 mV.

In the retina, photoreceptors do not exhibit action potentials;⁹² rather, light activation causes a graded change in membrane potential and a corresponding change in the rate of transmitter release.⁹³

⁹⁰It should be coherent with the fact that rods are saturated during the daylight and are active in nocturnal vision. Does it happen also for cones? Yes, the concept of *dark current* apply in both rods and cones, in photoreceptors in general, see ahead.

⁹¹So -40 mV should be the *rest state*.

⁹²The beginning of an action potential is that the channel open (from a closure state), the sodium goes in (we get depolarized) and cell fires; here we have the *opposite*: light arrives, channel close and photoreceptors get more hyperpolarized. So when the light comes, instead of being depolarized, they are hyperpolarized.

⁹³It is more continuous (see the figure above), more adjustable signal than a simple *action potential* firing rate (more intense: higher discrete frequency; less intense: less discrete frequency), more gradable. We can think: the code is analogic, is not digital anymore (fire or not fire, 1 or 0). Most neurons use, by means action potential, a digital type of information transmission. For example, if I am in V1, neurons in V1, I present a stimulus which is weakly illuminated, neuron fires a little, increasing the intensity of the stimulus the neuron fires more; so the *intensity* of the stimulus is translated in *firing rate*. In the retina instead the *intensity* of the stimulus is translated in *graduation* of hyperpolarization; is more continuous, you can continuously represent all possible graduation. With digital

Dark current: in the dark, the cytoplasmic concentration of GMPc is high, the channels activated by the GMPc are open and allow a constant current of Na^+ to pass inside the cell, called the dark current.

Therefore, in the dark, the membrane potential of the receptor is around -40 mV and is much more depolarized than that of most neurons (they are almost -70 mV at rest).

When the light stimulus reduces the concentration of GMPc by closing the channels controlled by the GMPc, the incoming current of Na^+ decreases and the cell becomes hyperpolarized (-70 mV).

So two exceptions:

- *Dark current*: current at rest. In other words a photoreceptor is continuously releasing a neurotransmitter (when a neuron is active it releases neurotransmitters at the synapse); neurotransmitters make synapse contact with *bipolar cells*, they continuously release glutamate in dark which is an activating (not inhibiting) neurotransmitter to/for the bipolar cell.
- *Graduation of Potential* instead of Action Potential.

Photoreceptors simple neural representation of the visual scene

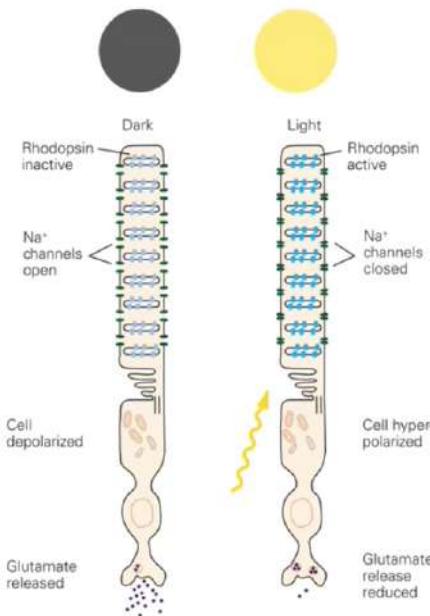


Figure 8.58

Photoreceptors produce a relatively simple neural representation of the visual scene.

Neurons in the bright regions are hyperpolarized, while those in the dark regions are depolarized.

signals and processes (discrete) we cannot cover all type of graduation; our eyes are exposed at an incredibly variation of light and you need to have a system that catch this.

At this point we have: different receptors, very simple pattern of activity; each receptor has a very small receptive field (smallest RF we have in our visual system) 1/60 of a degree, each cone. We saw also that the intensity of the light corresponds to a graduated hyperpolarization response.

So from here: Photoreceptors → Bipolar → (Retinal) Ganglion Cells → Optic Nerve (which is formed by RGC cells) [then → LGN (Thalamus) → V1].

Retinal Ganglion Cells

RGCs respond to light with action potentials, unlike photoreceptors and bipolar cells.

There are several types of RGCs that differ in shape, connectivity and function:

- Midget or P (parvo) cells are the most numerous (70%), have smaller cell bodies and dendritic fields, and supply the parvocellular layers of LGN.
- Parasol or M (magno) cells, about 10%, have large-diameter cell bodies and large dendritic fields supply the magnocellular layers of LGN.
- K cells, about 10%, have small cell bodies and intermediate-sized dendritic fields. They supply the koniocellular layers of LGN.

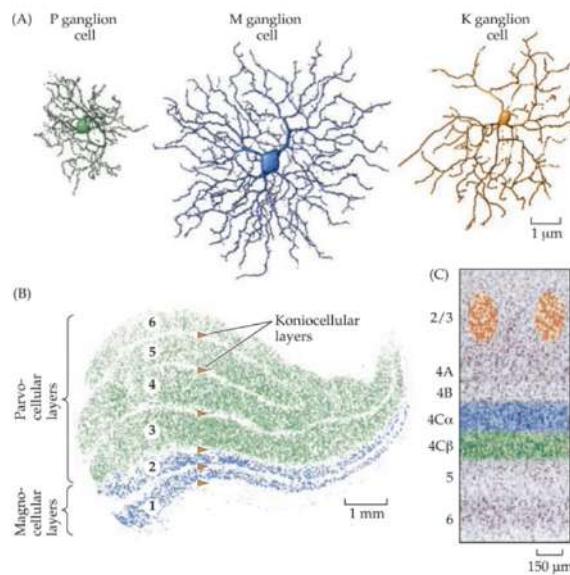


Figure 8.59

The mechanisms by which the brain deciphers the spatial patterns of light and dark that fall on the photoreceptors have been a vexing problem.

To understand what the complex neural circuits within the retina accomplish during this process, it is useful to begin by considering the responses of individual

retinal ganglion cells to small spots of light.⁹⁴

RGCs constitute the last level of retinal processing and project information, through the optic nerve, directly to the LGN of the thalamus.

In the figure above we can see:

- (A) Types of retinal ganglion cells.
- (B) LGN.
- (C) Termination of lateral geniculate axons in striate cortex. Magnocellular layers terminate in layer 4C α , parvocellular layers terminate in layer 4C β , and koniocellular layers terminate in layers 2 and 3.

RGCs receptive field

RGCs have concentric circular RFs and fall into one of two categories:

- ON-center;
- OFF-center.

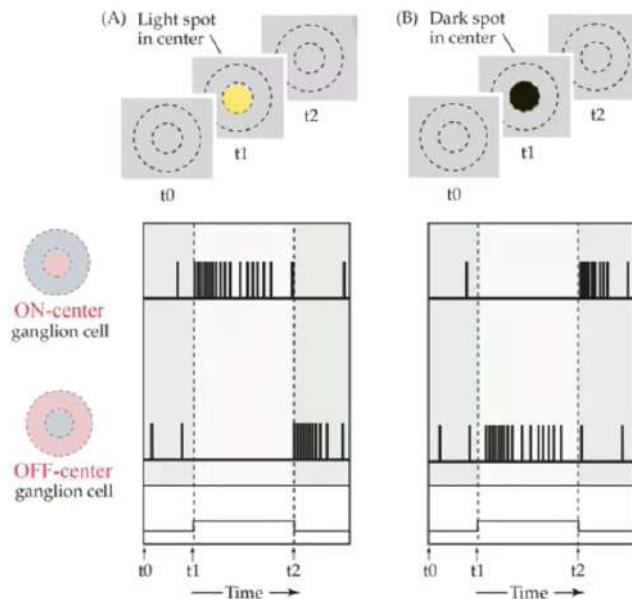


Figure 8.60

The ON-center cells discharge in response to the increase in brightness in the center of the receptive field, while the OFF-center cells discharge in response to the reduction of brightness in the center of the receptive field.⁹⁵

⁹⁴For photoreceptors is pretty simple: light in the receptive field \Rightarrow photoreceptor non active; no light in the receptive field \Rightarrow photoreceptor active. But things become much more complicated when we record from retinal ganglion cells (see ahead).

⁹⁵The system separates sensibility to increase in brightness and decrease in brightness in two different channels in order to have a faster parallel processing in comparison to have only

ON-Center ganglion cells are excited by a light stimulus in the center of the receptive field; OFF-Center ganglion cells are excited by a dark stimulus in the center of the receptive field.

Note that the firing rate of ON-Center ganglion cells increases soon after the dark stimulus disappears.

Similarly, the discharge rate of OFF-Center ganglion cells increases soon after the disappearance of the light stimulus.

Center vs Surround

The other characteristic is the *contrast* (in time and in space) between center and surround; they encode the contrast (see ahead).

In the image below there is an ON-Center type of cell.

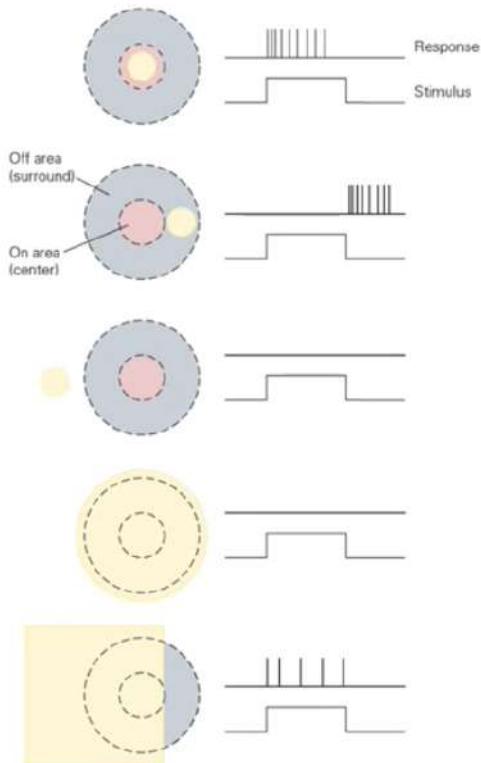


Figure 8.61

one channel that does a lot of things; we would have a linear (slower) process. In general the retina cares a lot changing things, things that change suddenly; is not important for the retina a thing that start and stay there forever, for the retina is important when it starts and when it goes away, is signalling the beginning and the end of something: if we look at the upper left graph of the figure we can see that, for example, the ON-Center cell fires when light comes and doesn't fire when goes out and the OFF-Center does the opposite, so we have informations on both when the stimulus comes and when goes out. The ON-Center signals that the stimulus of light comes (fires at the presence of this stimulus); The OFF-Center signals that the stimulus of light goes away (fires at the absence of this stimulus). So, working they together they can signal the *movement* of the stimulus across the retina.

Center and surround reveal opposite response (lateral inhibition) mutually antagonistic.

A uniform stimulus that activates the center and surround simultaneously causes a weak or no response.

Note that ganglion cells are not selective for the orientation of lines or edges.

The retinal ganglion cells have an organization of the receptive field with two concentric circular areas with opposite and antagonistic response.

In ON-center cells, the illumination of the central part of the receptive field causes an excitatory response, i.e. an increase in the discharge of the cell, while the illumination of the surrounding part of the receptive field causes an inhibitory response (mechanism of lateral inhibition).

The OFF-center cells are instead organized in the opposite way: the illumination of the surrounding area causes an excitatory response, while the illumination of the central part of the receptive field causes an inhibitory response.

The simultaneous illumination (or darkness) of the center and surround does not evoke a variation in the discharge frequency.

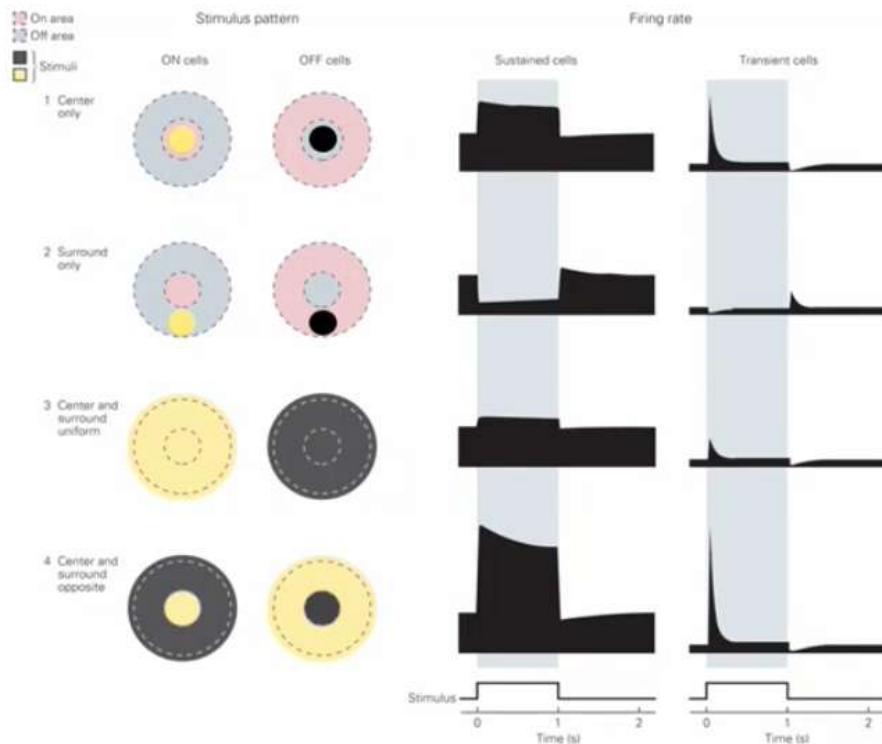


Figure 8.62

Stimulation of the center combined with the opposite stimulus in the boundary produces the strongest response.⁹⁶

⁹⁶The last case (number 4) in the figure above represent the best response situation.

Therefore, the output produced by a population of retinal ganglion cells emphasizes luminance contrast regions in the input, such as a border between two areas of different intensity, and gives less emphasis to the regions of homogeneous illumination.

Transient ganglion (M cells) cells produce a spike discharge only at the start of the stimulus.⁹⁷

Sustained neurons (P cells) maintain the discharge almost constant for several seconds during light stimulation.⁹⁸

In general, however, ganglion cell output favors temporal changes in visual input over periods of constant light intensity. The visual image that is stabilized on the retina with an eye-tracking device disappears from view in a few seconds. However, this does not happen in normal vision; even when we keep our gaze fixed, since small automatic eye movements (microsaccades) continuously scan the image through the retina to prevent the disappearance of the visual image.

RGCs resume

RGCs respond only weakly to uniform stimulation.

RGC mainly emphasize the contrasts⁹⁹ of brightness present in the visual scene, and not the absolute intensity of the lighting itself.¹⁰⁰

Most of the useful information in a visual scene lies in the distribution of brightness contrasts (edges).

In fact, the absolute light values reflected by the different objects give very little information as they depend on the intensity of the lighting source.

ON-center and OFF-center responses mechanism

The mechanism responsible for generating ON-Center and OFF-Center responses of retinal ganglion cells depends on bipolar cells.¹⁰¹

There are two classes of bipolar cells: ON- and OFF-center bipolar cells.

The selective response of ON- and OFF-center bipolar cells to light increments and decrements is explained by the fact that they express different types of glutamate receptors.

ON-center bipolar cells express metabotropics receptor that cause the cells to hyperpolarize in response to glutamate (sign-inverting synapse). OFF-center bipolar cells have ionotropic receptors that cause the cells to depolarize in response to glutamate (sign-conserving synapse).

Thus, glutamate has opposite effects on these two classes of cells, depolarizing OFF-center bipolar cells and hyperpolarizing ON-center cells.

The ON-center bipolar cells are activated by the light stimulus, while the OFF-center bipolar cells are inhibited by the light stimulus.

⁹⁷Has both ON-Center, OFF-Center.

⁹⁸Has both ON-Center, OFF-Center. Generally retinal ganglion cells associated to the cones have *sustained response*.

⁹⁹In space and in time (temporal and spatial contrast).

¹⁰⁰It is not encoded the absolute value of the single pixel. To understand why see the next rows.

¹⁰¹In the figure below the receptive field shown is of either ON-Center or OFF-Center ganglion cells. In the section (A) of the figure below the sign ‘minus’ in black represents the *sign inverting*. In the section (B) the green graph at the level of the center cone shows hyperpolarization.

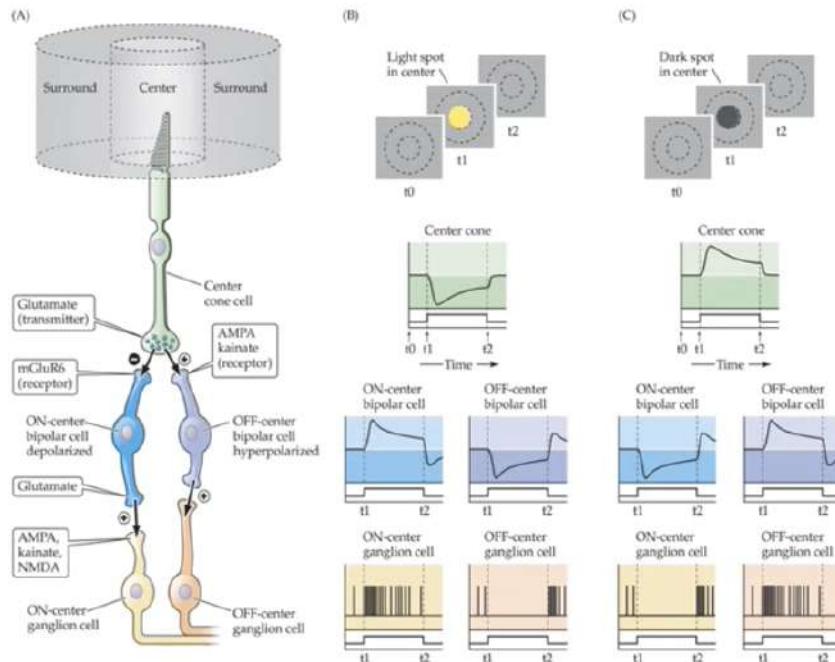


Figure 8.63

Better explained:

- Center cone cell → (light) → center cone hyperpolarized → (channel closed) → glutamate release reduced → ON-Center bipolar depolarized → neurotransmitter released → ON-Center ganglion activated.
- Center cone cell → (light) → center cone hyperpolarized → (channel closed) → glutamate release reduced → OFF-Center bipolar hyperpolarized → neurotransmitter not released → OFF-Center ganglion not activated.
- The opposite for dark.

Lateral inhibition of retinal ganglion cells mechanism

The mechanism responsible for the lateral inhibition of retinal ganglion cells depends on the horizontal cells.¹⁰²

The center-surround antagonism (lateral inhibition) observed in RGCs is thought to be mediated by horizontal cells.

Horizontal cells receive synaptic inputs from photoreceptors. Although the mechanism of their action is not entirely clear, horizontal cells are thought to exert their influence on the photoreceptor terminals, by regulating the amount of transmitter that the photoreceptors release onto the bipolar cell.

¹⁰²Refer also to the second figure of the ‘Center vs Surround’ section (Figure 8.62). In the figure below instead note the form of the section in which the horizontal cells are present, this form is called ‘Mexican hat profile’.

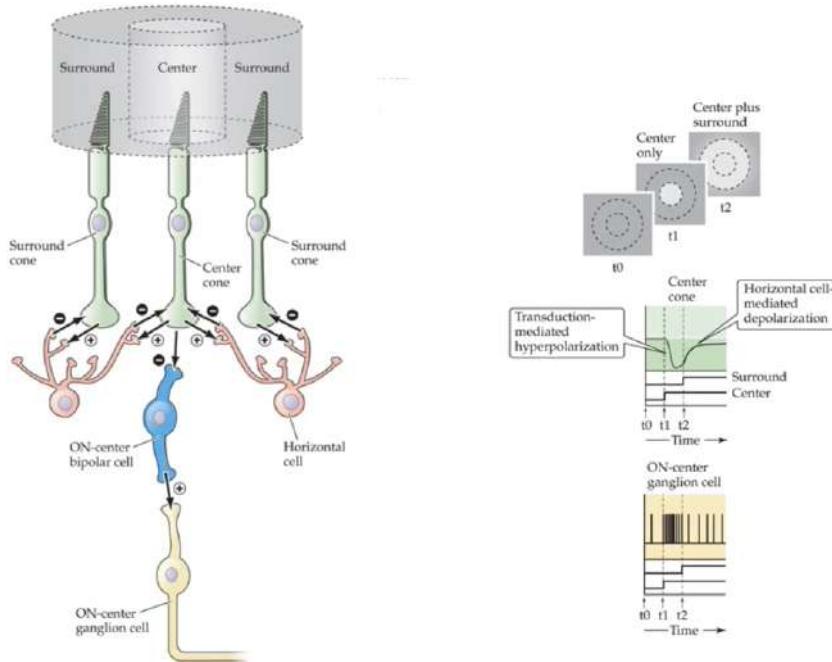


Figure 8.64

The release of glutamate from the photoreceptor terminals has a depolarizing effect on the horizontal cells (synapse which preserves the sign), while the horizontal cells have a hyperpolarizing influence on the terminals of the photoreceptors (synapse which reverses the sign). Consequently, the net effect of the horizontal cell is to oppose light-induced changes in the photoreceptor membrane potential (inhibitory effect).

The figure shows how these events lead to an inhibitory peripheral ring surrounding the receptive field center of the ON-center ganglion cell.

A light stimulus circumscribed and centered on a photoreceptor, which provides input to the center of the receptive field of the ON-center ganglion cells, produces a hyperpolarization in the photoreceptor. Under these conditions, the inhibitory effects produced by the horizontal cells are relatively small and the response of the photoreceptor to light remains very high.¹⁰³

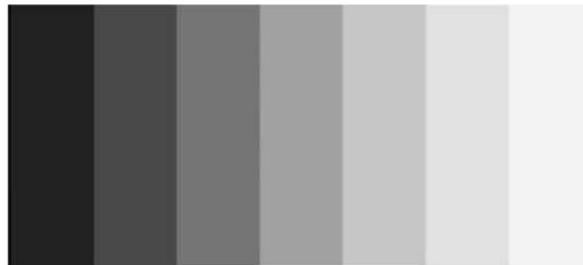
With the addition of light in the peripheral ring, however, the inhibitory impact of the horizontal cells becomes significantly greater. In fact, a large light stimulus involving photoreceptors that provide input to the center and periphery of the receptive field of the ON-center ganglion cells produces a strong hyperpolarization of the horizontal cells that converge on the photoreceptor terminal connected with the center of the receptive field. The reduction in activity (hyperpolarization) of horizontal cells has a depolarizing effect on the central photoreceptor, reducing

¹⁰³Light in the center and dark surround: dark surround effect wins (2 surround cones (\leftrightarrow 2 horizontal cells) $>$ 1 center cone). So Dark surround \rightarrow channel open \rightarrow photoreceptors depolarized \rightarrow glutamate released \rightarrow depolarization effect on Horizontal cell \rightarrow photoreceptors hyperpolarization \rightarrow glutamate release reduced \rightarrow bipolar cells depolarization \rightarrow many neurotransmitters released \rightarrow ganglion cell activated.

the effect evoked by light and, ultimately, the discharge frequency of the ON-center ganglion cell.¹⁰⁴

The lateral inhibition mechanism enhances the contrast at each border

The lateral inhibition mechanism mediated by the horizontal cells enhances the contrast at each border, thus increasing the ability to see objects that contrast only weakly with the background, as in the image below.



Chevreul-Mach bands

Figure 8.65

Chevreul-Mach band phenomenon (1865) is an optical illusion that makes the band at the edge with the next lighter band appear darker (and the band at the margin with the previous darker band lighter),¹⁰⁵ although each band is of a uniform gray color.



Figure 8.66

It is due to the lateral inhibition mechanism that exaggerates the contrast between figure and background, highlighting the margin ('edge-detection' mechanism).¹⁰⁶

¹⁰⁴Light everywhere → channel closed → photoreceptors hyperpolarization → glutamate release reduced → hyperpolarization effect on Horizontal cell → photoreceptors depolarization → glutamate released → bipolar cells hyperpolarization → few neurotransmitters released → ganglion cell not activated.

¹⁰⁵For example if we look at the image above and we focus on the middle bar (the fourth from the left and from the right) we can see that at the left border seems lighter while at the right border seems darker.

¹⁰⁶It's the retina responsible of lateral inhibition and so, consequently, of this phenomenon; not the brain.

A neural network of the Chevreul-Mach band phenomenon

The following is a very small neural network capable to explain the Chevreul-Mach band phenomenon.

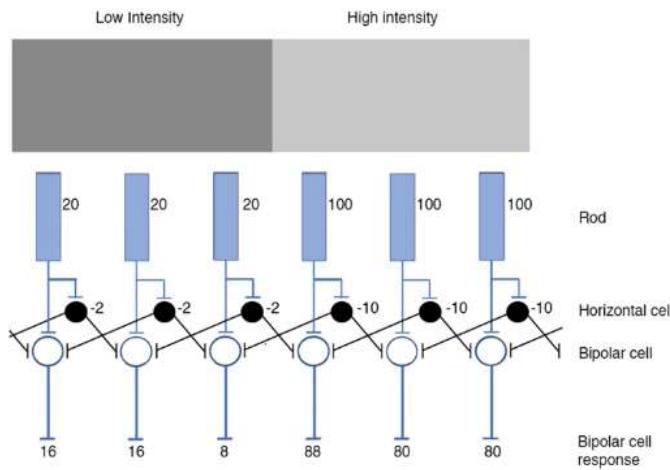


Figure 8.67

There is a formal error in reproducing the real anatomical model: in the figure *horizontal cells* connect to *Bipolar cell* instead they should be connected only to photoreceptors (*rods* in this case) modulating their output with the sign inverting activity that they (the horizontal cells) are capable to perform on photoreceptors; for semplicity we connected directly *horizontal cells* with *bipolars*.

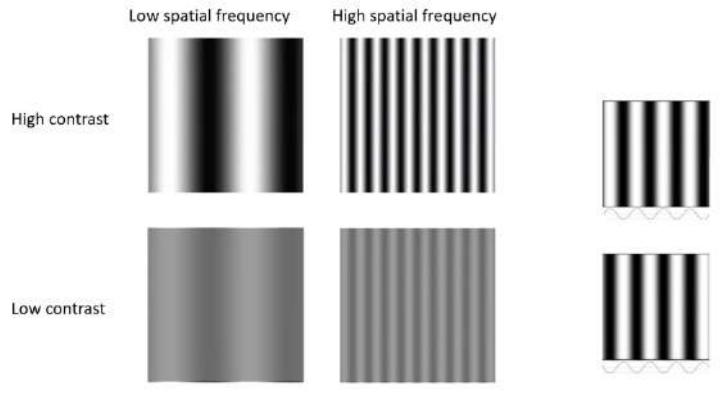
Anyway the network works correctly: looking at the figure above¹⁰⁷ and in particular to the *bipolar cell response* we can see that at the border from *low intensity* to *high intensity* (left to right) we pass from the uniform 16 to the darker 8 (more the number is high more the color is light) and viceversa from *high intensity* to *low* (right to left) we pass from the uniform 80 to the lighter 88. What is dark becomes darker, what light become lighter.

Sinusoidal gratings

Sinusoidal gratings are stimuli commonly used for the study of the visual system in animals (properties of the receptive field of neurons) and in humans (psychophysics).¹⁰⁸ In the gratings, the intensity (brightness) of the stimulus varies in a sinusoidal way, creating light and dark bands that are repeated in space.

¹⁰⁷The numbers referred to rods are 100 indicating the lighter color and 20 indicating a darker one. Note at the black circles the *inhibitory effect of the horizontal cell*. In particular the model is coherent with the previous pages because the negative number -2 is in correspondence of the darker color while the negative number -10 is where there is more light (clear color) \implies horizontal cells induce hyperpolarize more the bipolar cell). Note also in the figure that we should move the synapses (of the horizontal cells) to be connected with rods in the real model, not with bipolar cells. Finally, the numbers at the end of the figure are units of activation.

¹⁰⁸In real experiments are not used bars but sinusoidal gratings. They are a kind of stimuli much more flexible because allow to change several parameters which make the possibility to manipulate and changing experiments.



Sinusoidal gratings used for the study of contrast sensitivity in humans

Figure 8.68

For each grating it is possible to vary independently:

- orientation of the bands (light and dark areas, arranged vertically, obliquely, etc.);
- contrast (the difference in brightness between light and dark bands);¹⁰⁹
- spatial frequency (the width of a pair of light and dark bands or cycle), is measured in cycles per degree of visual angle;
- phase (the position of the light and dark bands in the stimulus, i.e. whether the grating begins with a light or dark band) is measured in radians.

The two gratings on the right in the figure are identical in orientation, contrast and spatial frequency but have opposite phase.

We are just at the level of retina, not in the brain; the retina is sensible to this parameters.

Determining human sensitivity



Figure 8.69

To determine the sensitivity of a human observer to different spatial frequencies, the threshold is measured.

¹⁰⁹Contrast is very important.

The contrast of the sinusoidal gratings is progressively reduced until the observer stops perceiving the stimulus.¹¹⁰

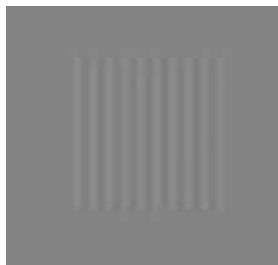


Figure 8.70

Sensitivity is given by the inverse of the threshold ($1/\text{threshold}$).

Contrast sensitivity function

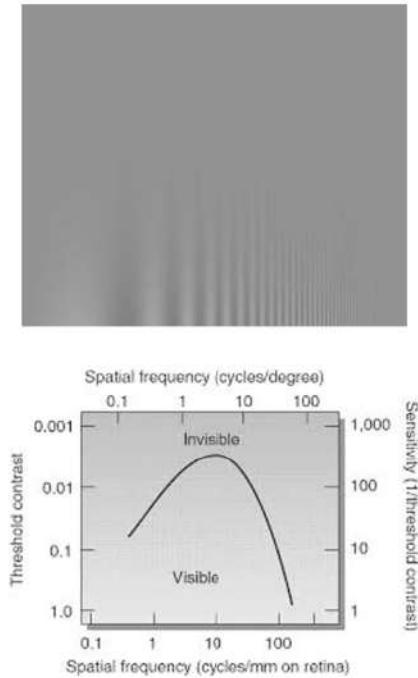


Figure 8.71

The contrast sensitivity function (CSF) describes an observer's sensitivity to sinusoidal gratings as a function of their spatial frequency.

This is measured using a contrast detection experiment in which the minimum (threshold) contrast required to detect sinusoidal gratings of various spatial

¹¹⁰Threshold is determined establishing for example a certain error percentage by the human observer.

frequencies is determined.

Sensitivity is defined as $1/(\text{threshold contrast})$ (so if the threshold is low, the sensitivity is high).

Humans are more sensitive to an intermediate range of spatial frequencies (about 4-6 cycles/degree) and less sensitive to both lower and higher space frequencies. Gratings with a frequency of about 5 cycles per degree are the most visible. The visual system is said to have bandpass behavior because it rejects everything but a narrow band of spatial frequencies.

In the figure above, the stimulus contrast increases from top to bottom, while the spatial frequency increases from left to right.

The central bars in the figure (medium spatial frequency) are visible even at low contrast, while the wide bars and narrow bars are visible only at high contrast.¹¹¹

Center-surround concentric model

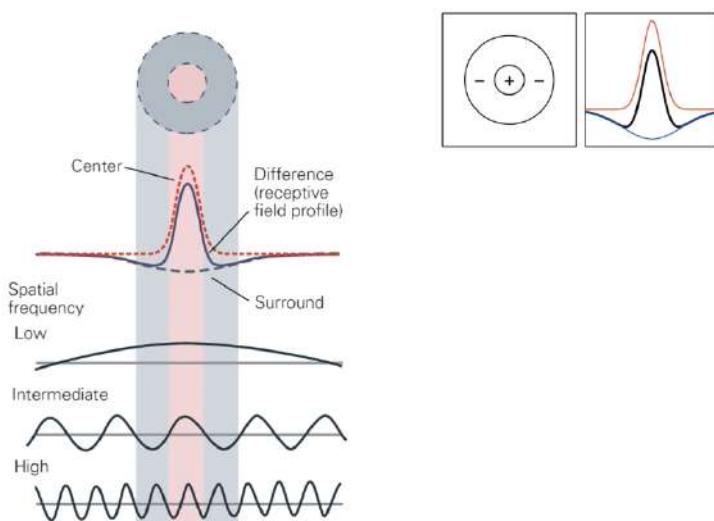


Figure 8.72

The response of the center-surround concentric RF is modeled as two Gaussian curves, a positive with a narrow base corresponding to the center of the receptive field, and a negative with a wide base, corresponding to the center and surround. The neuron's response is given by the difference of the two Gaussian curves.¹¹² In daylight, contrast sensitivity declines both at high and low spatial frequencies (band-pass behavior).¹¹³

¹¹¹See next section to see the explanation to this phenomenon or better the hypothesis explanation that is coherent with several experiments.

¹¹²Looking at the figure above we have that the red gaussian represents the *center*, the light blue gaussian represents *center and surround* and the dark blue gaussian represents the *difference*.

¹¹³*Low spatial frequency*: looking at the figure you can see the curve cover both the center and the surround positively activating both the area and inhibiting. *High spatial frequency*: looking at the figure you can see the curves are positive also in both center and surround positively and equally activating both area and inhibiting. *Intermediate spatial frequency*:

In humans, if sinusoidal gratings are used, sensitivity is greater for spatial frequencies around 5-8 cycles / visual degree, and is attenuated both for higher frequencies (up to acuity around 30-50 cycles / degree) and for frequencies less than 1 cycle / degree.

Multiplying the profile of the grating stimulus (intensity vs position) with the profile of the receptive field (sensitivity vs position) and integrating over all space calculates the stimulus strength delivered by a particular grating.

In day light, contrast sensitivity declines sharply at high spatial frequencies, with an absolute threshold at approximately 50 cycles per degree.

Interestingly, sensitivity also declines at low spatial frequencies. The attenuation at low frequencies reflects the inhibitory and antagonistic action of the periphery (surround) of the receptive fields of the retina, geniculate and cortex. Patterns with a frequency of approximately 5 cycles per degree are most visible. The visual system is said to have band-pass behavior because it rejects all but a band of spatial frequencies.

At night

What we have seen is valid during the day (day-light). Instead at night.

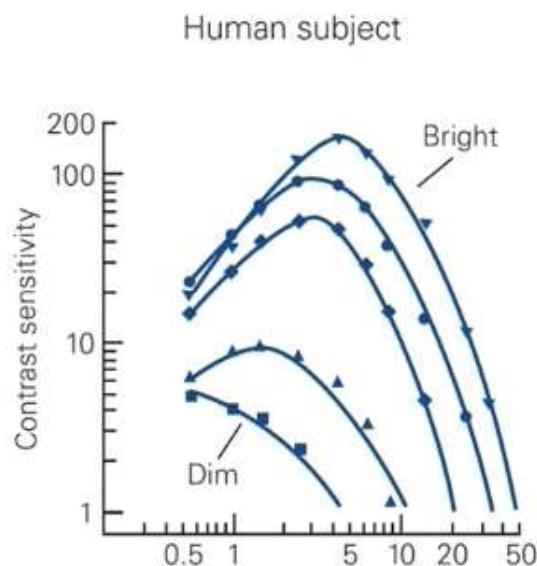


Figure 8.73

In dim light, the visual system's contrast sensitivity declines, but more so at high than at low spatial frequencies.

Thus, the peak sensitivity shifts to lower spatial frequencies.

In this state, the visual system has so-called low-pass behavior, for it preferentially encodes stimuli of low spatial frequency.

The fact that in dim light the receptive fields of ganglion cells lose their antagonistic surrounds explains the transition from bandpass to low-pass spatial

here instead the curve cover positively only the center (surround negatively) \Rightarrow so we have the best vision thanks to intermediate frequency, so 5-8 cycles.

filtering.¹¹⁴

RGCs recap

At the beginning we said that retinal ganglion cells are of three types (considering also K cells) but two are essential the main: P cells that go to the *Parvocellular layers of LGN* and M cells that go to the *Magnocellular layers of LGN*:

- P cells:¹¹⁵

- dense in central retina (fovea);
- narrow dendritic trees and thin axons;¹¹⁶
- cone inputs;¹¹⁷
- small receptive fields;
- slow and sustained responses;
- color opponency;¹¹⁸
- low contrast sensitivity;¹¹⁹
- respond to high spatial frequencies from small areas of the visual field,

- M cells:

- more common in peripheral retina;
- large dendritic trees and thick axon;
- rod inputs;
- wide receptive fields;
- fast and transitory responses;
- no color opponency;¹²⁰
- high contrast sensitivity;¹²¹
- respond to low spatial frequencies from large areas of the visual field.

¹¹⁴This lose because during night the difference between center and surround (of RGC) becomes weaker and weaker; lose this due to the rods: RGCs are driven more by the rods (are 100 millions in general) than by cones (are 5 millions in general) during night (during night is more important just to see things than distinguishing colors or contrasts; the center-surround antagonism is lost, all the cell receptive fields cooperate to see things, no more antagonism between center and surround). So since cones are less active and cones are responsible of seeing colors and detecting contrasts, the receptive field of ganglion cells loses their antagonistic surround.

¹¹⁵So they are for analyzing details, small things, very slowly for small parts of the visual field.

¹¹⁶Narrow dendritic trees neurons ≡ small RF; thin axons ≡ slow conducting infos; large dendritic trees ≡ large RF; thick axons ≡ fast conducting infos. Parvocellular dominates the ventral pathway for recognizing objects and we know / we saw the ventral visual pathway is slower in processing information because all axons are thinner probably because there are more informations to transmit accurately and larger one probably would be faster but less precise.

¹¹⁷Receive inputs.

¹¹⁸They show color sensitivity/ opponency; color opponency means that they encode colors in an opponent way e.g there are ‘red-green cells’ and ‘blue-yellow cells’; ‘red-green cells’ can be of two types: cell activated by red and inhibited by green and viceversa. In this way there is the opponency.

¹¹⁹They are not very good in contrast sensitivity.

¹²⁰Colors blind.

¹²¹They find anything in the environment.

Magnocellular	Parvocellular
Large RF	Small RF
ON- and OFF-center	ON- and <u>OFF</u> -center
High contrast sensitivity	Low contrast sensitivity
Color blind	Color sensitive
Transient	Sustained
Low spatial resolution	High spatial resolution
High temporal resolution	Low temporal resolution
Global aspect	Local aspect
Fast and raw	Slow and detailed

Figure 8.74

Selective P/M cell lesion

Selective P cell lesion:

- complete loss of color perception;
- deficits high spatial frequencies discrimination (reduced visual acuity).¹²²

Selective M cell lesion:

- reduced perception of movement;
- Deficits high temporal frequencies discrimination.

The contribution to the visual perception of the magno and parvocellular systems was experimentally tested by examining the visual abilities of monkeys after selective lesion of the magno or parvocellular layers of LGN.

The lesion of the magnocellular layers has little effect on visual acuity or color vision but drastically reduces the ability to perceive the rapid change of stimuli.¹²³ On the contrary, the lesion of the parvocellular layers has no effect on the perception of movement but seriously compromises visual acuity and color perception.¹²⁴

These observations suggest that the visual information conveyed by the parvocellular system is particularly important for high spatial resolution - the detailed analysis of an object's shape, size and color. *Recognize object*

The magnocellular system, on the other hand, appears critical for activities that require high temporal resolution, such as assessing the position, speed and direction of a rapidly moving object. *Analyzing movement*.

¹²²You cannot read for example.

¹²³They mainly support/supply dorsal visual pathway.

¹²⁴They mainly support/supply ventral visual pathway.

Retinal ganglion cells have adjustable operating range (on varying illumination)

Retinal ganglion cells have an amazing ability to adapt in changing illumination,¹²⁵ and again here they use possibly neurons like the horizontal and bipolar to adjust.

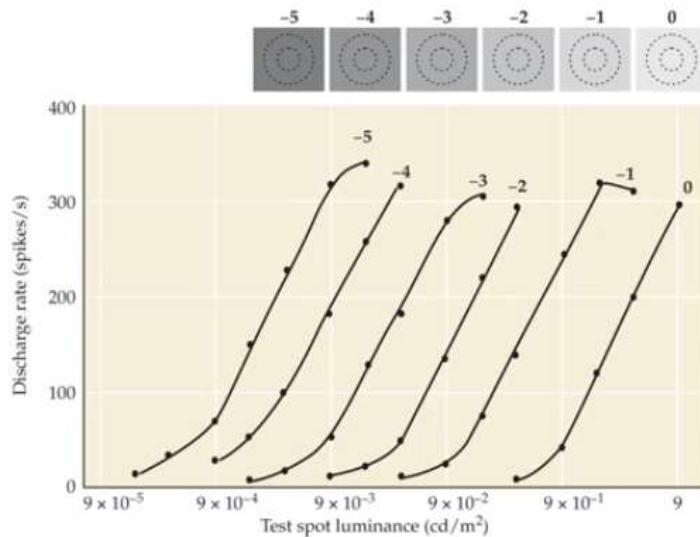


Figure 8.75

Sigmoid curves illustrating the discharge rate of a single ON-center ganglion cell to the onset of a small test spot of light in the center of its receptive field.

Each curve represents the discharge rate evoked by spots of varying intensity at a constant background level.

The response rate is proportional to stimulus intensity over a range of 1 log unit, but the operating range shifts to the right as the background level of illumination increases.¹²⁶

By scaling the ganglion cell's response to prevailing levels of illumination (adjusting the gain), the entire dynamic range of a ganglion cell's firing rate can be used to encode information about intensity differences over the range of luminance values relevant for visual scene.

¹²⁵Looking at the figure below (Sakmann and Creutzfeldt, Pflugers Arch, 1969) and focusing on the x-axis we can notice that the variation of illumination is huge! (the spot luminance change from 9×10^{-5} to 9). Note that the discharge rate remains pretty the same varying illumination, in this sense cells show an amazing ability to adapt in changing illumination showing that retinal ganglion cells have adjustable operating range. Focusing instead on the y-axis we can note that the variation in discharge rate is pretty the same (0-350) for each level (at 350 saturates) which is a relatively limited range of firing.

¹²⁶If you look at the figure the discharge rate is proportional to Test spot luminance value, for each background level (-5, -4, ..., 0). Note that it makes sense that spots have more intensity (if we project on the x-axis the circles points on the lines graph we can intercept spots of increasing intensity) when the background becomes more clear; otherwise they would be not perceived.

8.2.2 LGN

LGN

We've finished to study the retina.

Then there is LGN (lateral geniculate nucleus); its cells are practically the same of the RGC (retinal ganglion cells), there is no apparent difference in the RGC cells and LGN cells.

Again the RF (receptive field) is concentric, with a center and surround, more or less of the same size, they are ON-Center, OFF-Center more or less the same, very very similar.

One difference is that the brain, the cortex is able to control the LGN but not the retina.

The brain cannot process all the information that arrives continuously from the retina, it needs to select, to filter; so it makes sense that LGN is a replica of the retina but that can be controlled by the brain and where all the information that comes from the retina can be selected, filtered. Then, after LGN, there is V1 (see ahead).

8.2.3 V1

V1

V1 has a large number of cells, it's huge if compared to LGN and the cortex, and it is very difficult at the moment for the neuroscientists to reproduce a circuit of the V1 processing and precisely tracking the mechanism at the moment. Neuroscientists extracted some cellular mechanism hoping in the future to reconstruct all.

First studies were conducted in the 50s/60s of the last century on cats basically immobilized and anesthetized (with eyes kept open), presenting them spots of light inside the RF and recording because at that time the concept of RF was already there, neuroscientists already knew that if you want to drive, to manage visual cells inside the brain you need to present small pieces of light on a dark background (spots of light) they already knew the mechanisms of retina and LGN.

At the beginning when neuroscientists started to record from V1 were quite frustrated because they were not able to drive any cells by spot of light: illuminating all the room triggered no activity, illuminating small spots triggered nothing. So techniques that worked for retina and LGN not worked. Then they used *slide projectors*. They noticed the following: when you project slides, for example one by one, the slide presents borders that usually are dark thin and elongated bars (and consequently adjacent elongated bars of light), and when they change one slide with another one they noticed that just moving the slide (so moving the elongated bars) these movements triggered the firing of the cells in V1. So they found this by chance. So they understood that they don't need to use spots of light but long light stimulus.

The primary visual cortex (V1) has several functional categories of cells:

- simple cells;¹²⁷
- complex cells;

¹²⁷We have similar cells of this type in cats, monkeys and humans.

- end-stopped cells.

V1 - Simple cells

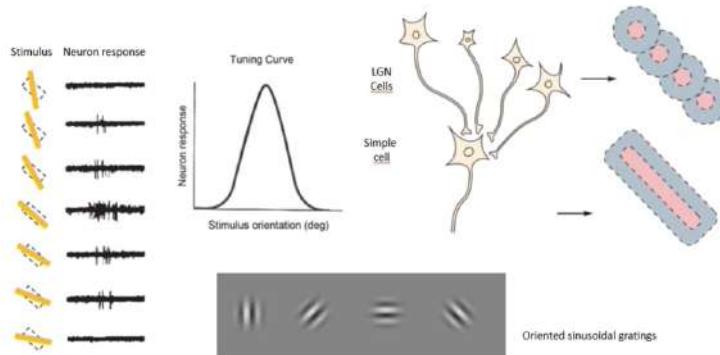


Figure 8.76

In V1, neurons selectively respond to oriented bars or gratings.¹²⁸ In simple cells, the receptive fields have separate ON and OFF areas.¹²⁹

Neurons in area V1 are classically divided into two types: simple and complex (Hubel and Wiesel, 1959). Neurons have elongated RFs and respond to a narrow range of orientations. Different neurons respond optimally to distinct orientations (orientation tuning curve). Example of a neuron in area V1 that selectively responds to lines that adapt to the orientation of its receptive field. This selectivity is the first step in the brain's analysis of the shape of an object. The orientation of the receptive field is thought to result from the alignment of the center-surround circular receptive fields of different LGN cells.

In the monkey, the neurons of the LGN have non-oriented circular receptive fields. However, projections of adjacent LGN cells onto a simple cell create a receptive field with a specific orientation.

Simple cells respond well to sinusoidal gratings (Gabor patches) of specific spatial frequencies and phases.

Receptive field of simple cells

The receptive fields of the simple cells of the primary visual cortex are different (we have different typologies.) and less homogeneous than those of the ganglion cells of the retina and the LGN.

¹²⁸So it emerge a new parameter to be considered: the *orientation* (this property hasn't emerged before in both retina and LGN). In the figure above note that the fourth stimulus on the left (forth both from top and bottom) represents the orientation that has the maximum response, as it can be seen in both neuron response and tuning curve. About tuning curve: tuning curve tells us also about *selectivity* of the neuron: the larger the base of a tuning curve, the less the neuron is selective, the smaller ... So we can see that they are not very much selective.

¹²⁹In the figure above, at right, we can see cells that present light in the center and dark in the surround. If you present the opposite you don't get any activation (inhibition like in the LGN) and also if you illuminate all the entire RF you don't get any response (like in the LGN).

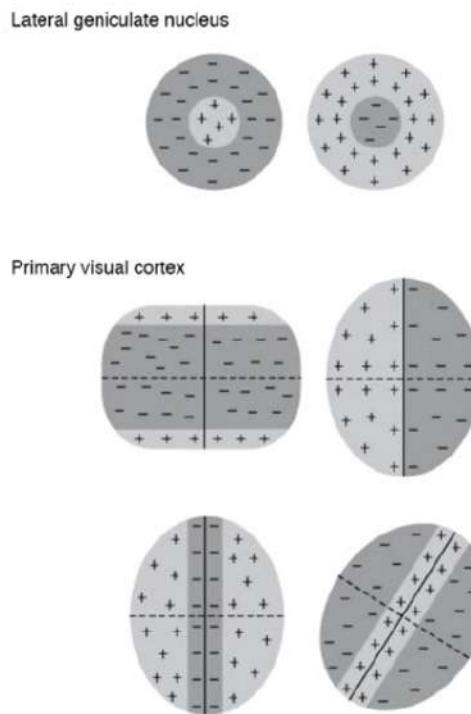


Figure 8.77

The linear receptive fields of simple cells of the primary visual cortex arise from the convergence of multiple cells of the lateral geniculate nucleus on a single simple cell.

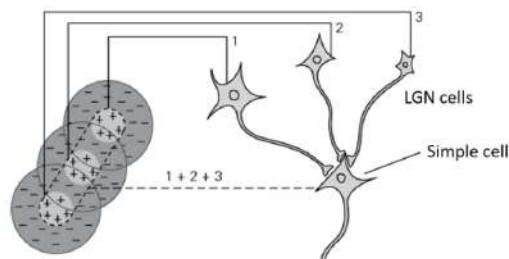


Figure 8.78

Complex cells

Have rectangular receptive fields, larger than those of simple cells.

Respond to linear stimuli with specific orientation.

The position of the stimulus within the receptive field is not critical as the demarcation between on and off zones is not so clear.

Movement of the stimulus in the receptive field is particularly effective in activating the cells.

Complex cells selectively respond to stimuli that move in particular directions.

Complex cells: superimposed ON and OFF regions

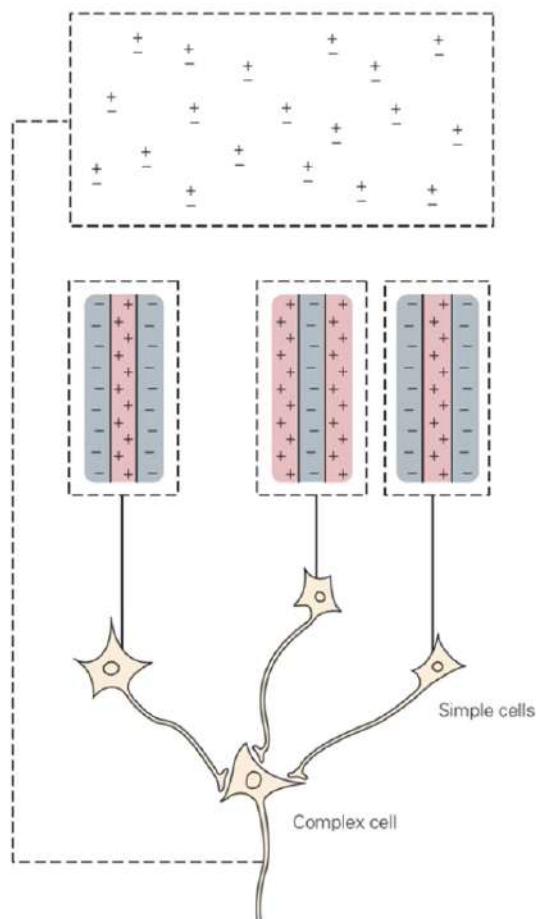


Figure 8.79

In complex cells, the ON and OFF regions are superimposed, *i.e.* each position in the receptive field responds to both white and black bars, and the cells respond when a line or edge crosses the receptive field along an axis perpendicular to the orientation of the receptive field.¹³⁰

This constancy in the response to variations of stimulus location in the RF is commonly called position invariance.

Complex cells are less selective for the position of the stimulus in the receptive field.

¹³⁰Instead in simple cells the ON and OFF regions are completely separated: the sign \pm in the figure above indicates there is no more ON-OFF regions in the receptive fields.

The receptive field has no defined ON and OFF regions and responds similarly to light (on a dark background) or dark (on a light background) stimuli in all positions of the receptive field.

They are activated as a linear oriented stimulus crosses their receptive fields in one direction.

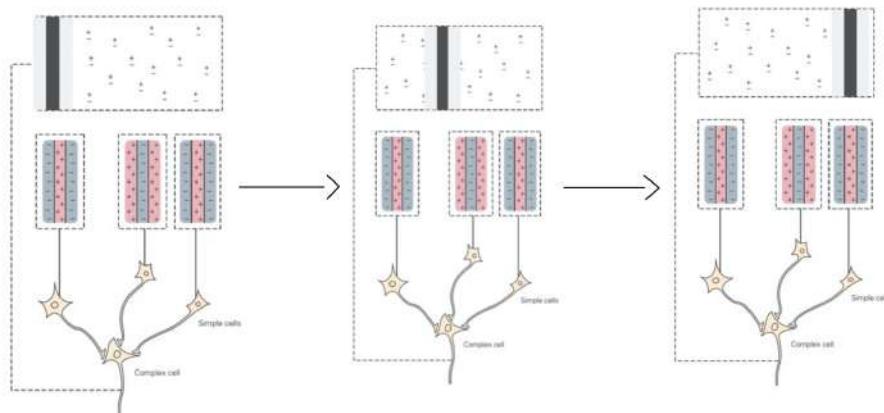


Figure 8.80

Response Characteristics of Neurons to Orientation in the Primary Visual Cortex

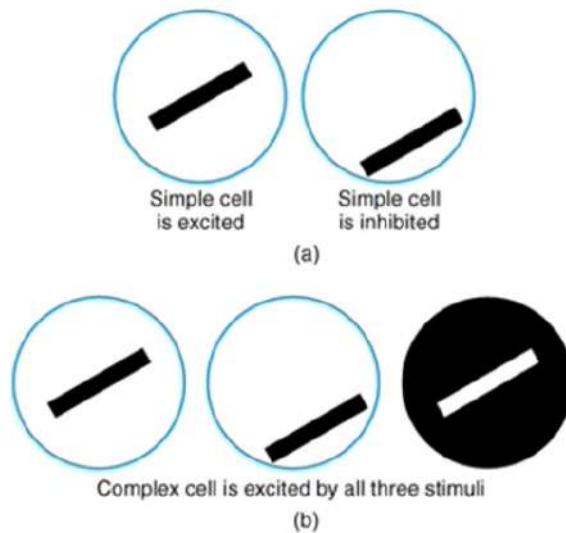


Figure 8.81

Hierarchical model of the receptive field

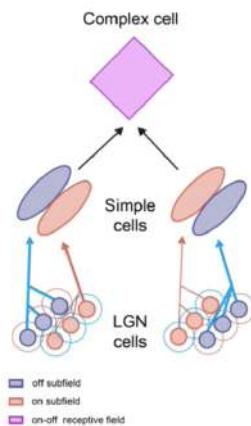


Figure 8.82

The processing of some characteristics of the visual images is performed through a progressive convergence of information within the visual system.

Each RF at one level of the visual processing hierarchy emerges from the convergence of inputs from many neurons of the previous level.

The size of the RF increases along the visual hierarchy.

According to the hierarchical model (Hubel and Wiesel, 1962), simple cell receptive fields are constructed from the convergence of geniculate inputs with receptive fields aligned in the visual space. In turn, complex receptive fields arise from the convergence of simple cells with similar orientation preferences.

End-stopped cells

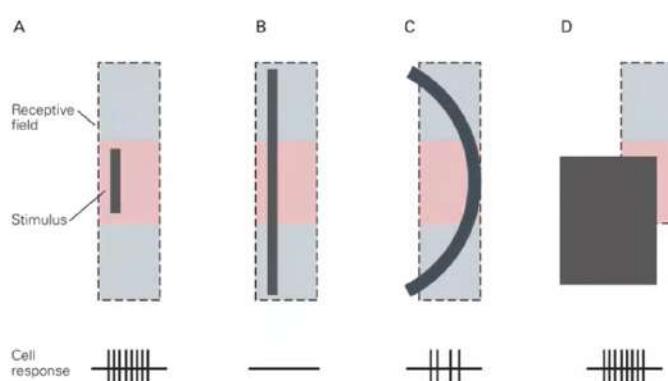


Figure 8.83

The receptive fields of some cells have a central excitatory region flanked by inhibitory regions that have the same preferential orientation.

A short linear segment (A) or a long curved line (C) will be effective in activating the neuron, but not a long straight line (B).

A neuron with a receptive field that has only one inhibitory region in addition to the excitatory region can signal the presence of angles (D).¹³¹

Respond better to linear stimuli of a certain length, or that have an end that does not extend beyond a specific portion of the cell's receptive field. End-stopped may serve to detect angles ("angle-detectors") or curved lines of visual images. ON and OFF regions of the RF have the same preferred orientation (vertical, in the neuron illustrated in the figure). Therefore, the inhibitory effect is greater if the same oriented contour is presented both in the ON and OFF regions. A short linear segment (A), or a long curved line (C) will be effective in activating the neuron, because excitation will be greater than inhibition. On the contrary, a long straight line (B) will not be effective, because excitation will be canceled by the inhibitory effect.

We suggest to see the following video in which you will hear the neuron firing when the stimulus is inside the receptive field:

<https://youtu.be/jw6nBW021Zk?si=01YmMZZ7Je9EZNcm> (Hubel & Wiesel's demonstration of simple, complex and hypercomplex cells in the cat's visual cortex)

Simple and complex cells model

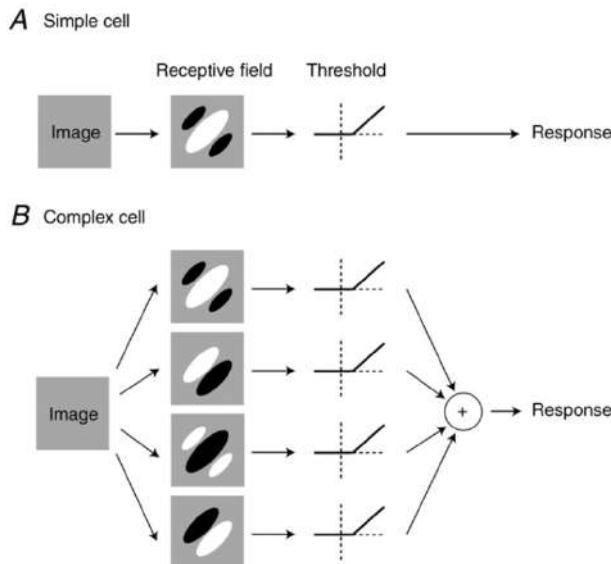


Figure 8.84

There are many models: the one above is one of the most common.

The models of simple and complex cells proposed by Movshon, Thompson and Tolhurst (Movshon et al. 1978):

¹³¹It has to mark a sort of corner, edge; for this only two zones because has to end.

- A Simple cells: the first stage is linear filtering,¹³² *i.e.* a weighted sum of the image intensities, with weights given by the receptive field. The second stage is rectification: only the part of the responses that is larger than a threshold is seen in the firing rate response.¹³³
- B Complex cells: the first stage is linear filtering by a number of receptive fields such as those of simple cells (here we show four of them with spatial phases offset by 90 deg). The subsequent stages involve rectification, and then summation.

V1 neurons selective attributes

In addition to stimulus position, V1 neurons are selective for a number of attributes:

- *Orientation:* this selectivity must arise from computations that take place within cortex, because LGN responses are not selective for orientation.
- *Spatial frequency:* V1 neurons are typically sharply selective for the spatial frequency of a stimulus. *Spatial frequency* is best defined for a grating pattern, where frequency is the inverse of the distance between bars. This selectivity arises naturally from the shape of the receptive fields that have multiple ON and OFF regions.
- *Direction:* cells in area V1 are commonly selective for direction of stimulus motion.
- *Temporal frequency:*¹³⁴ is the inverse of the period between temporal oscillations between dark and light. V1 neurons typically prefer lower temporal frequencies than those that can drive LGN neurons.
- *Disparity:* in animals with front-facing eyes (such as carnivores and primates), much of the visual field is covered jointly by both eyes. This poses a challenge as signals need to be integrated, but also an opportunity for computing binocular depth (stereoscopy). The signals from corresponding regions in the two eyes are kept separate in the LGN, and are combined in V1.
- *Color:* retinal ganglion cells respond along one of three ‘cardinal directions’, known informally as red-green, blue-yellow, and black-white. V1 neurons are also organized along ‘cardinal directions’.

3D vision

How the brain is capable to reconstruct 3D images starting from the retina? Psychophysical studies indicate that 3D vision is based on:

¹³²Anithing that is not in the *receptive field* region, or that not have the orientation shown, or that not has the right intensity is thrown away by filtering: image intensity (if the image fit the geometric properties of the RF) is multiplied by RF sensitivity $\sum_{k,z} I_{k,z} RF_{k,z} > T \quad \forall z(zone) \in RF$.

¹³³Referring to the image above: *the image* is, for example, an elongated bar; *the receptive field* presents a central region (ON-region) and two surround regions (OFF-regions), so the good stimulus should be a white bar oriented to the right associated with a dark surround.

¹³⁴Change in time.

- monocular elements;
- stereoscopic elements (binocular elements).

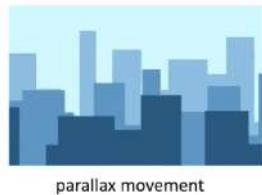


Figure 8.85

Monocular elements are able to create the sense of depth for distances greater than 30 meters:¹³⁵

- familiarity with the object;
- interposition;
- linear perspective;
- size of objects;
- distribution of shadows and lighting;
- parallax movement.¹³⁶

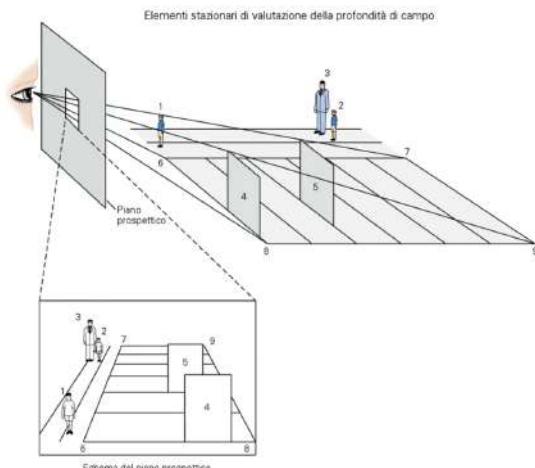


Figure 8.86

¹³⁵These are monocular elements (you don't need both eyes); but you can also use informations from both eyes: they are able to encode the so called *disparity* (see ahead for understanding how disparity works).

¹³⁶Things that are closer from you are moving faster than things farther.

The following experiments carried out by Bela Julesz with random dot stereograms¹³⁷ show that stereopsis is a visual faculty separate from the perception of forms.¹³⁸

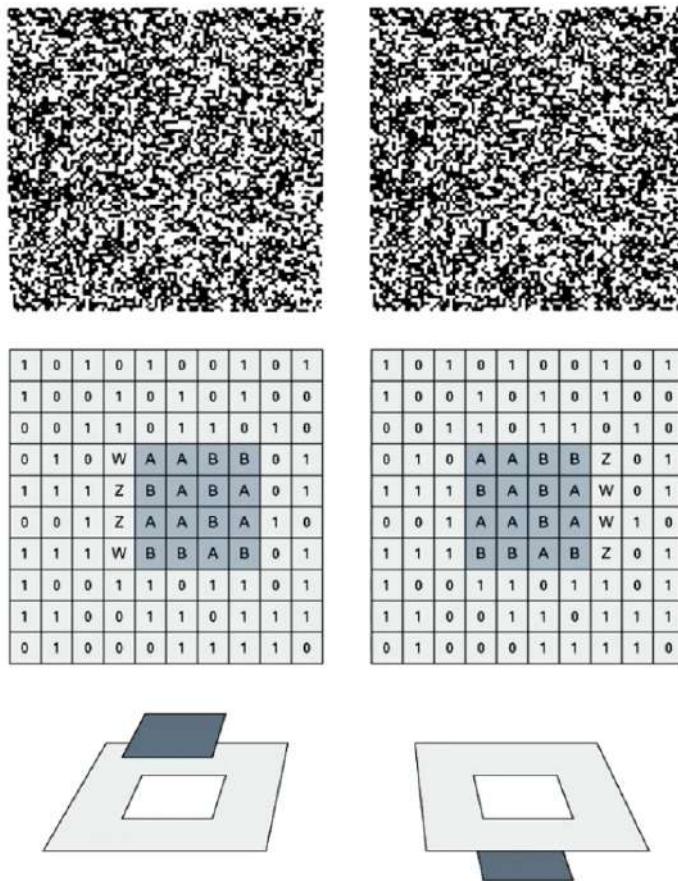


Figure 8.87

Looking at the figure above:

- figure at the left: in this case moving the figure closer and farther (from a specific and precise position)¹³⁹ continuously (with both eyes open), emerges a square from the background.
- figure at the right: here instead a square sinks into the background.

¹³⁷They are not random, neuroscientists know that this conformation implies, or could imply, precise effects.

¹³⁸It is a behavioral experiment: just asking the patient what he sees; not recording anatomical components directly.

¹³⁹You don't see this effect if you are not in the exact position; if, for example, the figure is put far away, the disparity is so large that the brain discharges that information; but if disparity is relatively small the brain is able to encode that information to see depth of the stimulus from you. Disparity is detected within a certain range.

Disparity

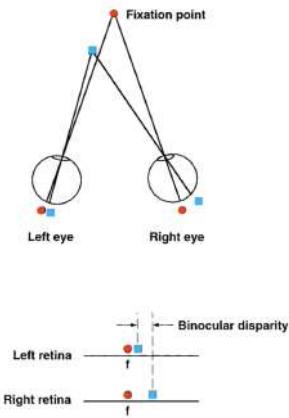


Figure 8.88

When we fix our eyes on a point, the convergence of the eyes causes the fixed point to fall on identical areas of both retinas. Points lying outside the fixation plane stimulate slightly different parts of each eye's retina creating binocular disparity.

So looking at the figure above, the brain is able to recover the difference (binocular disparity): it retrieves information from one eye and from the other eye, compare them and calculate the disparity: if informations are the same then disparity is zero and image is exactly in the fixation plane; otherwise if there is a negative/positive disparity is either in front/behind the fixation plane.

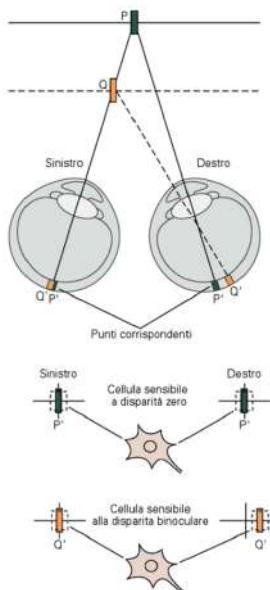


Figure 8.89

The primary visual cortex is the first site of the central nervous system where information from the two eyes converges on a single neuron.

Some neurons of V1 (simple and complex cells) are specifically selective for the horizontal disparity of the retinal images, that is, they respond better to stimuli localized to particular depths of the visual field.

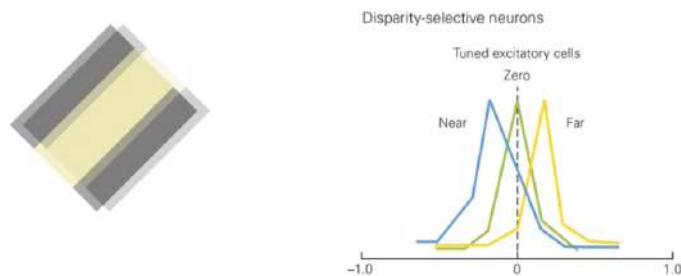


Figure 8.90

Note the three tuning curves in the figure above.

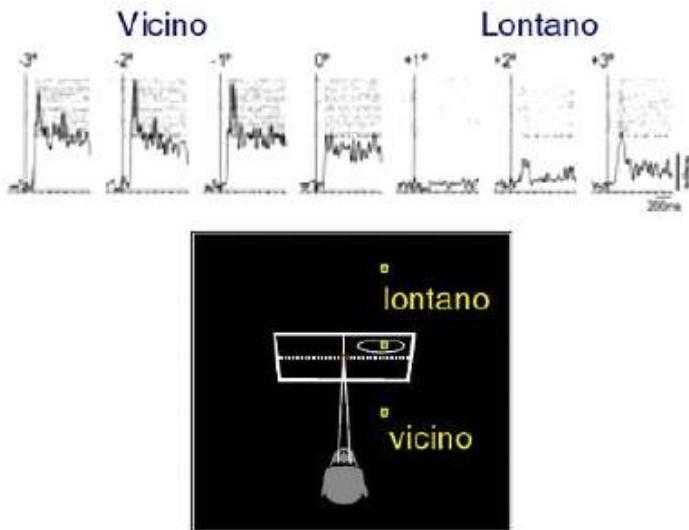


Figure 8.91

In addition to V1, neurons sensitive to retinal disparity are also observed in V2, V3 and particularly in MT and MST.¹⁴⁰

MST neurons appear sensitive to stimuli that move in particular direction at specific depths of field.

¹⁴⁰It means that (from all these areas) ‘*depth*’ is extracted from informations from two eyes that are encoded separately in the retina and that remains separate in LGN and also V1, but after V1 you find neurons that are sensitive to disparity but you don’t find any more neurons one or the other image presented twice, the ocular dominance is reduced beyond V1, only up to V1 there is segregation of left and right areas. MT and MST are related to V5, beyond no neurons sensitive to retinal disparity are observed.

8.3 Visual motion

For *visual motion* we have one specific area that is V5 (or MT) that is particularly selective for that process which is not strictly dorsal nor ventral, but in between dorsal and ventral streams (see images ahead); it is a conjunction point of the two because has to do with *direction, position, location*, which are properties that are processed by the dorsal stream, and it is important also for ventral stream because from *cinematic cues, motion*, we are able to recover the shape of the objects (*WHERE* and *WHAT*). MT is so called because stands for *middle temporal* in the monkey and V5 for humans.

Characteristics

Visual motion:

- Contributes to the recognition of objects (background figure segregation);
- It is used to establish the depth or distance of an object (parallax);
- Helps in navigation and interaction with the outside world;
- It serves to direct attention.

Movement of visual images

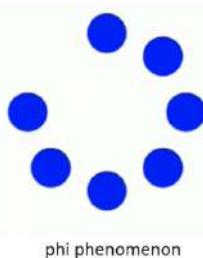


Figure 8.92

The movement of visual images is essentially analyzed from the dorsal visual pathway.

The (illusory) perception of apparent movement constitutes proof of the existence of specific mechanisms for the analysis of visual movement.¹⁴¹

The neurons of the IVB layer of V1 are particularly sensitive to the direction of movement of a stimulus within the receptive field.¹⁴²

¹⁴¹The image above shows the so called *phi phenomenon*: intermittent activation of circles causes an (illusory) perception of movement. Fixating the entire figure while there is the intermittent activation generate a white circle (of the same size of the blue ones) which is moving anti-clockwise jumping from one blue circle to the other. From static stimulus, brain is able to extract motion, movements. Why we perceive this illusion is still unknown. This kind of (apparent) motion, movement is called ‘*pure motion*’ (stimulus doesn’t change position).

¹⁴²Note in the figure below that IVB of V1 can go also directly to MT without passing through V2.

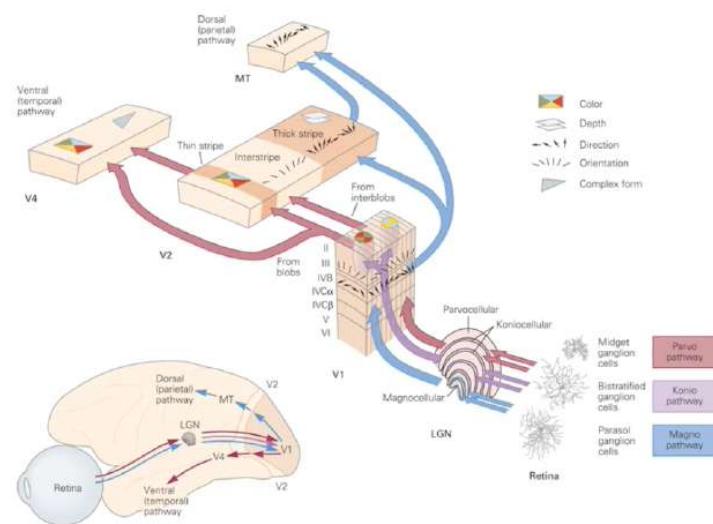


Figure 8.93

MT area

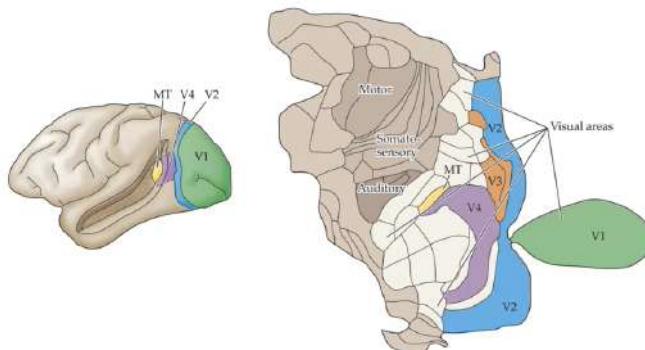


Figure 8.94

A key role in the perception of movement¹⁴³ is played by the MT area, (Middle Temporal) a small region of the dorsal path,¹⁴⁴ located in the posterior part of the superior temporal sulcus, and first described in 1971 independently by J. Kaas and S. Zeki.

About 95% of MT neurons selectively respond to stimuli that move in a specific direction (preferred direction). The MT area contains a topographic, retinotopic representation of the visual field.¹⁴⁵

¹⁴³See also the last figure of the previous section.

¹⁴⁴Remember that we saw that MT for its ‘middle position’ has also properties that characterize the ventral pathway.

¹⁴⁵In a retinotopic map, adjacent neurons or regions in the visual processing areas of the brain

MT columnar cortical organization

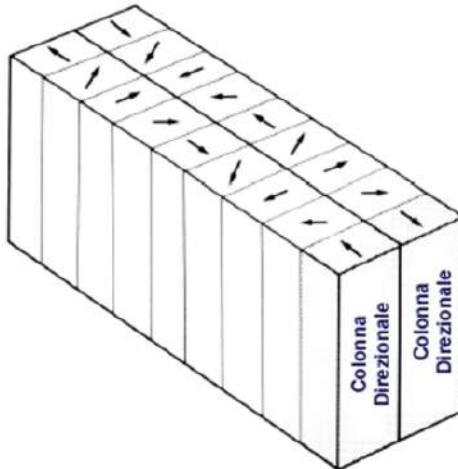


Figure 8.95

MT¹⁴⁶ shows a columnar cortical organization (analogous to V1). ¹⁴⁷

The neurons present in each column selectively respond to stimuli in the same region of the visual field (same RF)¹⁴⁸ and with the same direction of movement. The preferred direction changes gradually from one column to the contiguous one (ordered organization).

In addition to the direction¹⁴⁹ of movement, MT cells are selective for the speed of the stimulus. Conversely, they do not selectively respond to shape and colors. So:

- speed of motion;
- position of the stimulus inside the RF;
- orientation of the stimulus;
- direction of the stimulus;
- depth;
- width (how large is the stimulus).¹⁵⁰

respond to adjacent areas on the retina. This organization is crucial for maintaining the spatial details of visual stimuli, and it occurs in several stages of the visual pathway, from the retina to higher visual cortex areas.

¹⁴⁶This also in V5.

¹⁴⁷This can be seen penetrating the cortex tangentially/obliquely with an electrode; we can see the difference from one column to the next.

¹⁴⁸RFs in MT are relatively larger in comparison to RFs in V1; each RF, not the entire visual field is relatively larger, so that the entire object can be seen from a single cell; one problem that V1 has is that its RFs are so small that each RF can see only a part of an object (see the so called '*aperture problem*', see ahead) and MT can – with its larger RFs – compensates (there is a higher probability that a single object can fall into a single RF).

¹⁴⁹Direction, motion; also static direction: orientation.

¹⁵⁰Because the RF has a center-surround characteristic (central area, surround area) and can be antagonism between the twos, so the size of the stimulus can be encoded because it should fall, for instance, in the ON part and not in the OFF part (surround).

MT neuron response

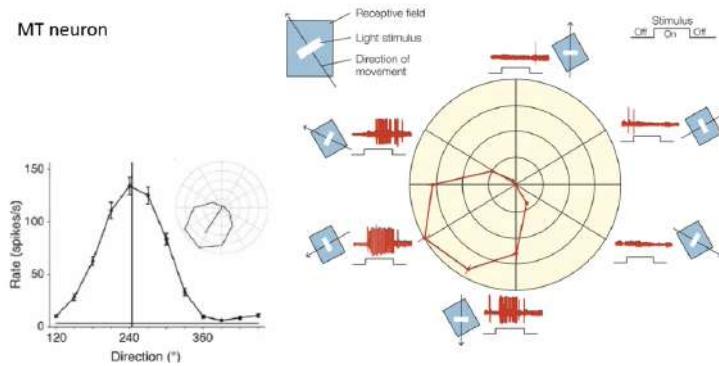


Figure 8.96

In the figure above an example of MT neuron responding maximally to downward and leftward directions of movement (225° = preferred direction). Note that the neuron also responds, but less, to directions contiguous to the preferred one.

Intro to the ‘aperture problem’

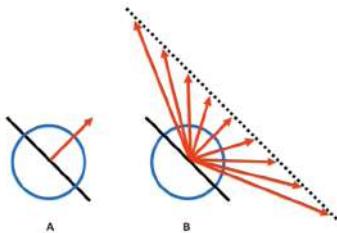


Figure 8.97

If a moving contour is seen (the black long bar in figure A, B above) through a small aperture (the blue circle in figure A, B above), only the velocity component perpendicular to the contour can be detected through the opening (Wallach 1935).¹⁵¹



Figure 8.98

¹⁵¹Looking at the figure above, if we move the black bar – seeing through the blue circle aperture – in all the directions shown in red in figure B, we only perceive the velocity (direction in movement) shown in figure A.

The velocity component parallel to the orientation of the contour can only be observed at the extremes.¹⁵²

Since neurons in the primary visual cortex (V1) have small receptive fields, this 'aperture problem' (Marr, 1982) must be overcome if the visual system is to function properly.¹⁵³

The aperture problem

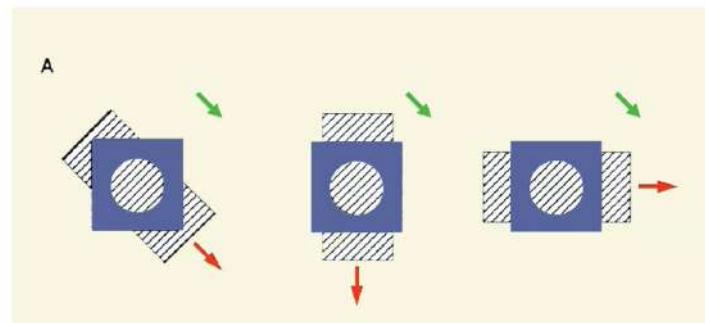


Figure 8.99

Due to the aperture problem, movements of a stimulus in three different directions (red arrows) are always interpreted by the neuron as movement in a single direction (green arrows), perpendicular to the orientation of the contour.

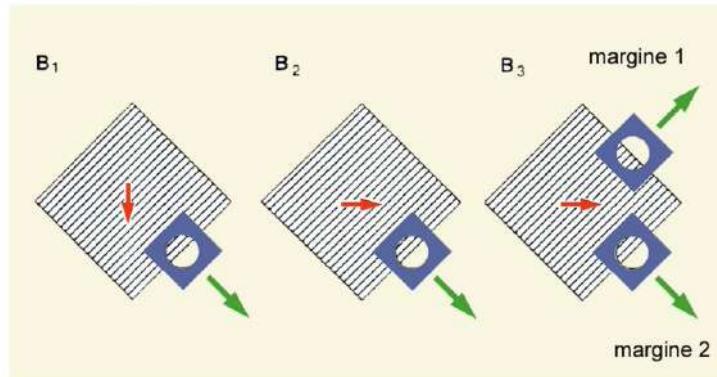


Figure 8.100

The responses of the neurons in B1 and B2 are highly ambiguous, and fail to detect the true direction of the figure's movement.

In B3, the aperture problem is solved by integrating the response of two or more neurons whose receptive fields are placed in different points of the figure.

¹⁵²Remember that the velocity vector has a direction and a direction is the sum of a perpendicular and a parallel component. So the parallel component could be seen only if the black bar fall entirely into the circle aperture, as shown in the figure C above.

¹⁵³So neurons in V1, which have small RFs, are affected by this problem.

Visual motion processing stages

Visual motion processing occurs in two stages.

To solve the aperture problem, it has been hypothesized by some researchers that the visual processing of moving stimuli occurs through two successive cortical stages:

1. In the first stage, the individual components of the stimuli are analyzed, through the responses of neurons capable of signaling only the movement of the local components, perpendicular to the movement of the contour.
2. In the second stage, higher order neurons would integrate the different local components of the stimulus, analyzed by the neurons of the previous stage.

The integrated signal produced by higher-order neurons corresponds to the real direction of motion of the object and to the perception that an observer has of it.

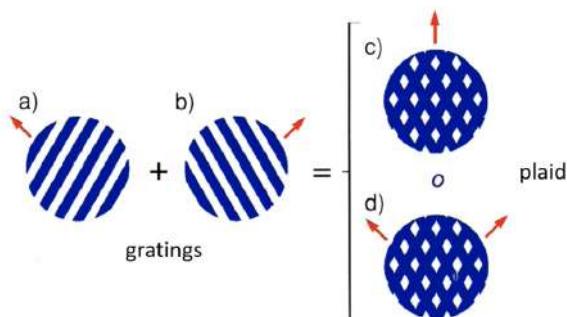


Figure 8.101

This hypothesis was evaluated by Movshon and colleagues (1982) in the MT area of a monkey, through the use of complex stimuli ('PLAID') obtained from the superimposition of sinusoidal gratings directed in opposite directions.

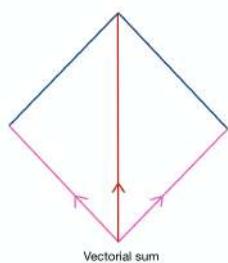


Figure 8.102

By superimposing two gratings (a and b) that move in the opposite direction (topright and top-left) we obtain a gratings or PLAID that appears to move clearly in only one direction (top, resulting from the sum of the directions of the two gratings, as in c).

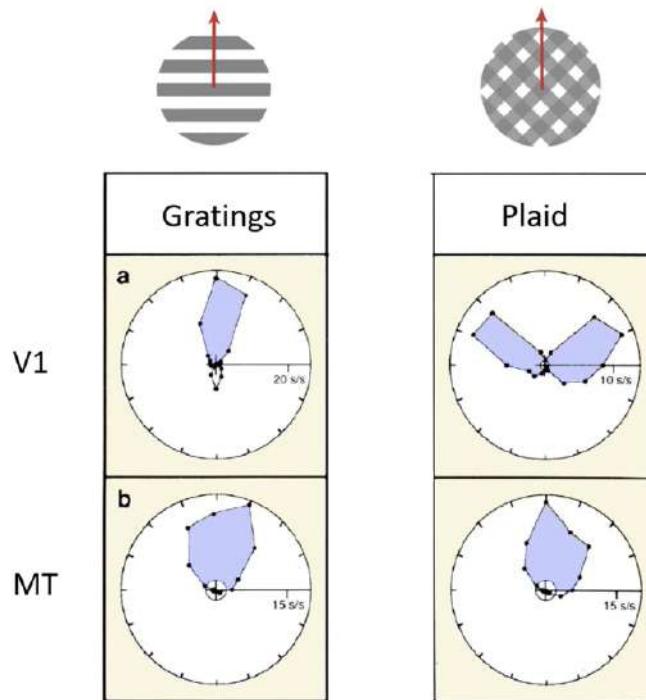


Figure 8.103

It still remains unknown what MT can do with stimulus that arrives through the geniculate nucleus; such stimulus has no motion information, has not orientation information at all because LGN (lateral geniculate nucleus) doesn't encode orientation, doesn't see contours, it just sees dots, spots, because RF is very small.

We know that there is a connection between LGN and MT (so stimulus from LGN arrives to MT) but how MT is able to use LGN information to understand the motion of the stimulus, still remains unknown.

MT response to transparent motion

The following is another example of what MT/V5 is capable of doing.

Note: according to many people the major functional ability of MT is not understanding motion perception indeed, but is *segmentation* in order to understand what is in the environment, so it is most related to *object recognition*. It is true that through MT we are able to report in which direction the stimulus is moving, but this is not the major activity, MT is not active all the time only for this, but mostly is to segment the scene (analyzing all the surfaces that are in front of us, that are changing, moving, that have depth, that have different motion directions) into objects. MT not only integrates multiple informations in order to find the motion, but also *separate*, segregate: *e.g.* in the environment could be a main object in which we are interested in and MT is crucial to intercept its motion, but also there are other objects, surfaces, things moving all around and

MT is crucial to separate them into different entities different each other. So is very important to *structure the scene* and *motion perception* can be seen as a subtask of structuring the scene.

So one of the problems that MT area has to solve is that at the same time multiple objects can move at different levels, positions, even *superimposed* as in the case of the so called '*transparent motion*': look at the experiment which represent a situation that is usually used to study MT (when MT is studied it is often used this kind of stimuli):

- *Random dots pattern stimuli:*

- black dots on white surface;
- or white dots on black surface;¹⁵⁴

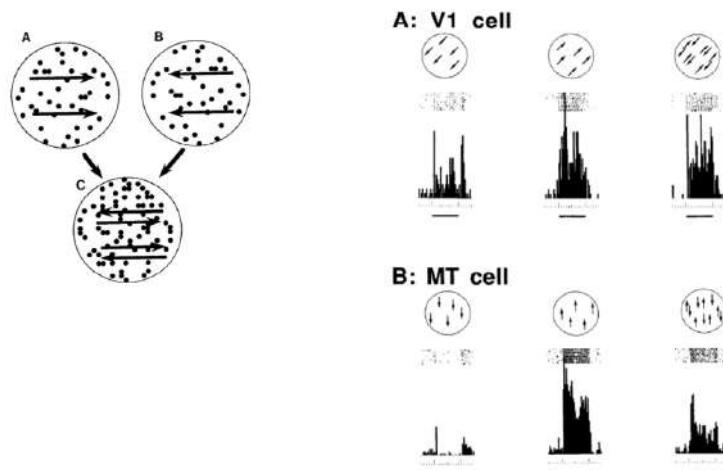


Figure 8.104

In the case of the figure above we present dots that are appearing moving to some direction and firing rate of the cells in V1 and MT is recorded:

- A. V1 cell: by analyzing the firing rate of the cell we can see that the *preferred direction* (we already talked about of this) is upper right while in the down-left direction the firing rate decreases. However by superimposing the two stimuli doesn't interfere with the firing of the cell.
- B. MT cell: here we can see that the *preferred direction* is to the top while to the bottom the firing rate decreases. By superimposing the two opposite stimuli we can see interference¹⁵⁵ because the firing rate decreases in comparison to what registered during the preferred direction.¹⁵⁶

¹⁵⁴What is the advantage in comparison to using sinusoidal gratings? We can manipulate the number of dots, size of dots, the *coherence of the dots* (i.e. *all dots can go in one direction or only one part can go in one direction, all dots can go randomly etc.*).

¹⁵⁵It is the similar mechanism of the noise cancellation.

¹⁵⁶Depth plays a crucial role: opposite directions have to be in the same depth to have the maximum suppression, if opposite directions belong to different depths the suppression is less intense because different depths would suggest that we are referring to different objects.

So our perception, what in the end we ‘see’ is closer to MT than to V1 (that is capable to perceive something of what we are not conscious) and in general is closer going up with the structures of our brain.

Visual attention

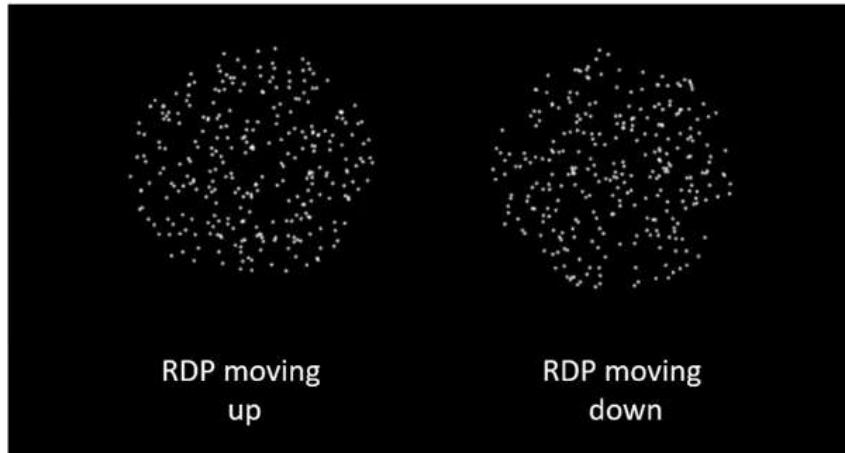


Figure 8.105

Selective *visual attention*¹⁵⁷ can be directed toward a specific region of space (*i.e.* space-based attention), but also be guided by feature information indicating some non-spatial properties of the target, such as color, shape, direction of motion, etc. (*i.e.* object-based attention).

Middle temporal (MT) area is crucial for the perception of visual motion. MT neurons show direction tuning curves (bell-shaped response profiles) depending on the direction of motion of the stimulus (random dot pattern, RDP).¹⁵⁸

Spatial attention modulates¹⁵⁹ the responses of neurons selective to direction of motion in area MT and MST.

The figure below shows a typical visual direction tuning curve from a neuron in the monkey visual cortex (area MT) in response to a moving dot stimulus.

¹⁵⁷Visual attention is the ability to select information in order to process that information more precisely (you focus all the means only on one thing, so for that thing you have more power in analyzing); you can think of it as the ability of seeing better few things (among others). *Selection* is an intrinsic concept of attention, so you process less but with an higher grade of resolution; and you can do this *voluntary e.g.* when you read. But also *involuntary* (when something catch your attention for instance). So the same scope (pay attention on something, selecting) can be done *voluntary* or not *voluntary*.

¹⁵⁸Very few people that had injuries only in MT area developed the so called ‘achinetopsia’. They lost the ability to perceive things moving, they have static vision, meaning that if something in the environment is moving they perceive only static changes, like photograms, all this causing very big problems: imagine to cross a street while a car is arriving, you are not able to calculate the velocity of the car and consequently how fast you need to move in order to avoid an incident.

¹⁵⁹Changing amplitude of the curve, not quality. See also the experiment explained in the next section.

The vertical line indicates the preferred direction of motion, and the inset shows the mean spiking responses in polar plot form, showing clear direction selectivity.

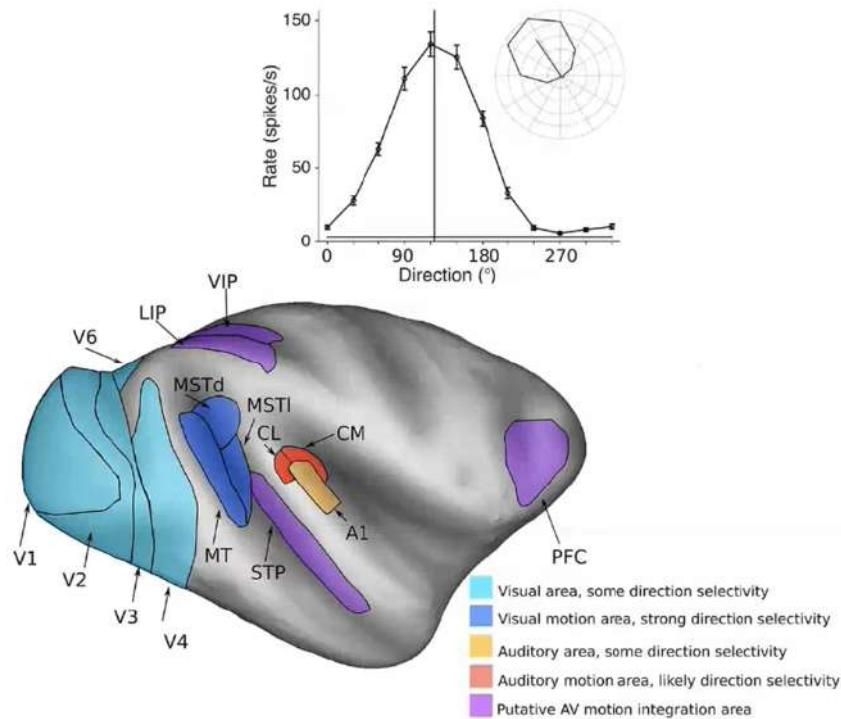


Figure 8.106

Experiment: Effect of spatial attention

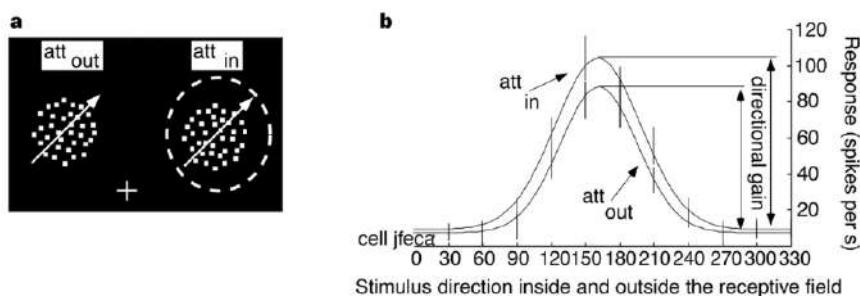


Figure 8.107

- We have a fixation cross which separates the left hemifield to the right hemifield; the same neuron is recorded, the two RDPs moved at the same time. One RDP was presented inside the RF (dashed circle) while the

other was presented in the opposite hemifield. In a given trial, both RDPs moved in the same of 12 possible directions.¹⁶⁰

- b. The upper curve shows the response when the monkey was attending to the stimulus inside the receptive field (marked ‘att in’), and the lower curve plots the responses when the monkey was attending to the stimulus outside the receptive field (marked ‘att out’). These tuning curves show an increase in directional gain in the attended condition.

So I have a fixation cross, and in the two visual hemifield I present random dots pattern; the dashed circles line represents the RF of the neuron you’re recording; so you’re recording a neuron whose RF is in the right visual hemifield; the animal is fixating in the center and you see RDP both in the right visual hemifield and in the left. You ask the animal (through some methods/signals) to pay attention either to the left stimulus or to the right one (while the animal is still fixating). What emerges is that the tuning curves are the same in quality: the only difference regards amplitude (stronger response when the animal is paying attention to the stimulus inside the RF). So attention in both cases amplified the responses (in the sense that the respective tuning curves without asking of paying attention [tuning curves built at level of description a.] will show a wicker response in comparison to the tuning curves at level b. – which are shown above – when is asked to pay attention).

These results demonstrate a physiological correlation of non-spatial, feature-based attention by showing neuronal response modulations in the absence of spatial shifts of attention.

Thus, attending to a given direction enhances the responses of neurons whose preferred direction aligns with the attended direction and reduces the responses of those neurons preferring the opposite direction.

These findings shows that spatial and feature-based attention represent separate (and summable) processes that have a multiplicative effect on the responses of neurons.

Such attentional modulations resemble changes to a neuron’s sensory gain and thus can be mimicked by sensory effects, such as reducing the luminance contrast of a stimulus, which similarly does not change the tuning width of direction-selective neurons, suggesting that response modulation based on attentional and sensory aspects employ common mechanisms.

Ventral visual pathway

The colored labels of the figure below indicate the *ventral visual pathway* (in particular the yellow parts represent the *infero temporal cortex* also named *IT*). The not colored parts indicate the *dorsal visual pathway*.

Focusing on the *ventral visual pathway* we observe that:

- V1 is characterized by 2-3 types of cells, the so called ‘end-stop’ cells important for corners, curvatures of objects;
- V2 is just the next area, we saw something about thick/thin stripes (inter stripes etc.); so there are compartments in V2 and each compartment is

¹⁶⁰So that we can build the relative tuning curves understanding also what is the preferred direction.

dedicated to specific processes (*e.g.* color processing, direction of motion and depth, shape orientation); these compartments respect a specific connectivity with V1 (meaning that compartments in V1 are specifically connected to compartments of V2);

- When we move from V1 to the other areas, before arriving in the *inferior temporal cortex*, in general what we know till today about the function of the areas is not completely clear, in the sense that we're still not good in characterizing exactly what is the difference between *e.g.* V1 and V2 or V1 and V4;
- It is a little easier (even if also here we do not have yet a complete and precise description of operations/mechanisms) to differentiate V1/V2 and *inferior temporal cortex* because there are striking differences between the response of neurons in IT and in V1/V2 (striking difference that there is not between V1 and V2, *e.g.* both have retinotopic map – topographic representation – of the entire visual field).

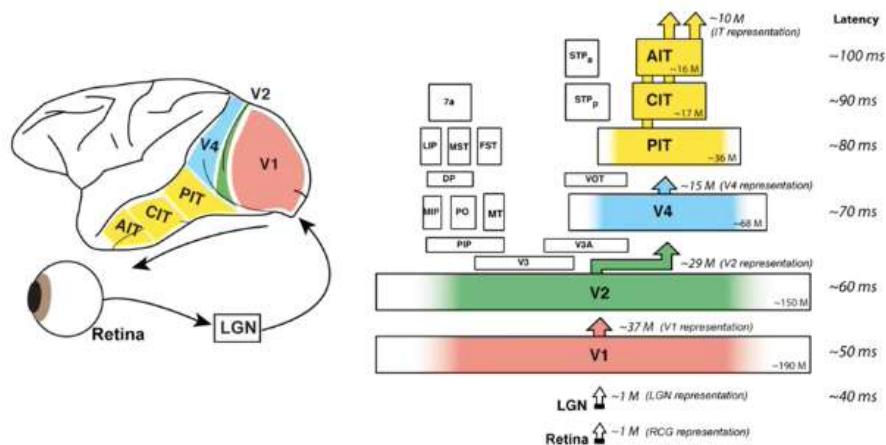


Figure 8.108

In general it is thought that going up (along hierarchy) things become more complicated; for example RFs of LGN are concentric and neurons respond to spot of light in a dark background or viceversa (very simple response to simple stimuli). When you go from V1 to V2 what is the major difference?

Neural responses to illusory contours

Initially, one idea that could represent a striking difference between V1 and V2 was the following:

- Figures in which humans perceive illusory contours evoke responses in cells of area 18 (V2) in the monkey visual cortex. Modifications that weakens the perception of contours also reduces the neuronal responses.

- In contrast, cells in V1 (area 17) were apparently unable to see these contours.



Figure 8.109

Looking at the figure above:

- In the image it seems that there is a triangle above the three black circles, we perceive also the illusory contours that are in between two circles and that form the sides of an ‘illusory’ triangle that doesn’t exist (we have only the small three triangle aperture inside the black circles that form three black packman).
- In this image, instead, the illusory triangle disappears by filling the arc base of the mini white triangle inside each black circle.

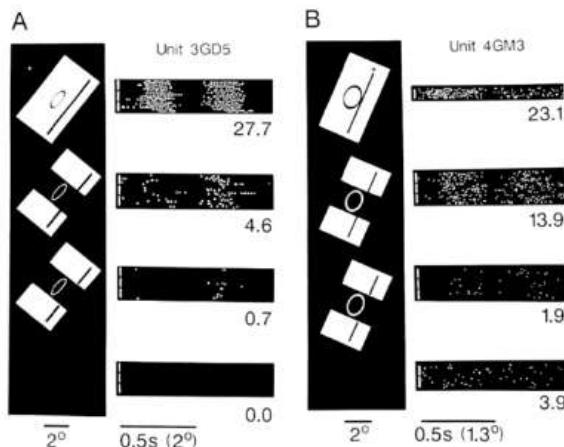


Figure 8.110

Looking at the figure above:

- The oval shape represents the RF of the neuron and at the top is completely filled with a white background; imagine that the long black bar is passed orthogonally along the RF and at the side we can see the neuron firing; this behaviour is exactly the same in V1 and V2. What is surprising is the image below: the background of the RF is completely black, there is no *real bar* crossing the RF, but only an illusory contour bar (the segment

that theoretically would fill the two black segments – one above and one below the oval RF – making so a unique black bar), anyway the cell fires, even if less in comparison to the first case, but still fires. In the third case the two black segments are a little detached from the border of the white rectangles, making lose the sense of contiguity with the black background and consequently making lose ‘illusory contours’, and so, crossing the RF, the neuron fires very very weakly. So when you perceive the illusion \Rightarrow there is activity; when you don’t perceive the illusion \Rightarrow the activity is transcurable. This was the behaviour found in V2 (able to respond to illusory contours).

Initially (1984) this behaviour of V2 was not found in V1 and scientists were happy to having found a behaviour that characterize V2 and not V1 (not able to respond to illusory contours). But years after scientists – with more consistent experiments – were able to find that also neurons in V1 are able to respond to illusory contours. Find this in V1 is very more difficult because V1 is very basic, primary visual cortex, and is difficult to find kind of modulation like what shown above, but scientists found it.

Reference: ‘Von der Heydt et al., Science, 1984’

So what could be another possible difference between V2 and V1 – something that V2 has and V1 not – having seen that the previous cannot be considered a difference? It was thought that the following phenomenon could represent that difference but it was experienced – in part – in V1; anyway it is important to report what was thought to be exclusively of V2.

Coding of border ownership in monkey area V2

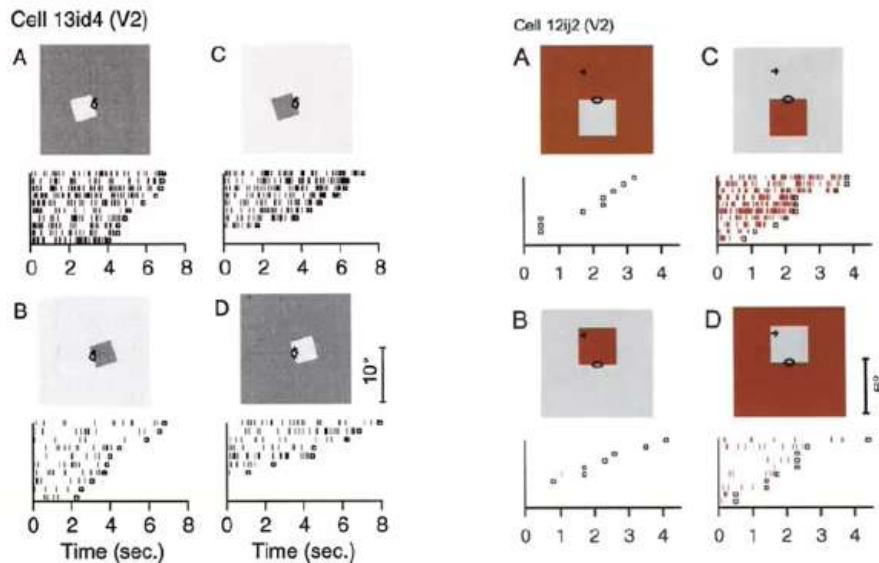


Figure 8.111

Cells of V2 respond to the *ownership of the border*.

What does it mean? In the images above the small black circles represent the RF of the cell, and, as you can see, although the stimulus inside the receptive field is quite the same for all the cases (A, B, C, D) of the two groups of images (Cell 13id4, Cell12ij2) the cell responds differently according to the different objects presented of which only a very small part falls inside the RF.

So although inside the small RF falls a small part of the entire object, the cell is able to recognize informations regarding the *entire* object (*e.g.* in the first block on the left response in A is greater than the response of the others; the second block response in C is greater than the response of the others).

This is due to the fact that the particular cell receive informations also from other cells that tell to the particular cell if the line/part inside the receptive field belong to one object or to another object. The particular cell integrates information of a grater visual scene, not only responds to the stimulus inside the RF but also to informations that are contextual. So we do not call anymore this RF ‘classical RF’ but ‘contextual RF’.

So the neuron is responding to the stimulus inside the RF but also is computing the context in which the stimulus appears. If the context outside the RF changes, this context affects the response inside the RF.

The influence of visual stimulation far from the receptive field center indicates mechanisms of global context integration. The short latencies and incomplete cue invariance suggest that the border-ownership effect is generated within the visual cortex rather than projected down from higher levels.

Reference: ‘*Zhou et al., J Neurosci, 2000*’

Neuronal responses to naturalistic textures differentiate V2 from V1 in macaques.

There is no generally accepted account of the function of V2, partly because no simple response properties robustly distinguish V2 neurons from those in V1. Recently (2013) has been discovered that *neural responses to naturalistic texture* differentiate V2 from V1 in macaques.

So what is done here is the following: given an *original texture photographs*, from them – following particular criteria – *spectral matched noise* images (more simple) and *naturalistic texture* images (more complex, in the sense that are more similar to the originals) are extracted. Then these two typology are presented to V1 and V2.

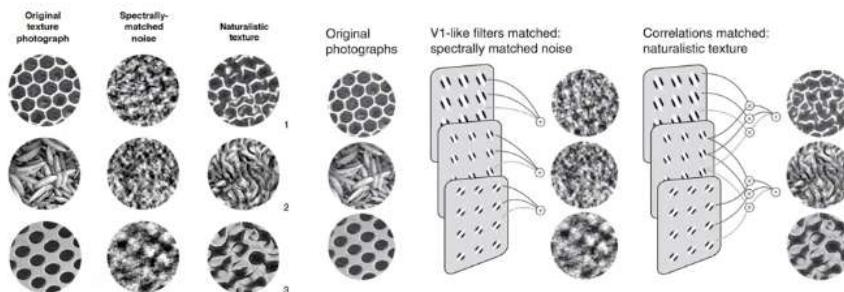


Figure 8.112

Stimuli replicating the higher-order statistical dependencies found in natural texture images were used to stimulate macaque V1 and V2 neurons.

- Spectrally matched noise images (look at the second image above, from the right):
 - The original texture is analyzed with linear filters and energy filters (akin to V1 simple and complex cells, respectively) tuned to different orientations, spatial frequencies and spatial positions. Noise images contain the same spatially averaged orientation and frequency structure as the original but lack many of the more complex features.
- Naturalistic texture images (look at the first image above, from the right):
 - Correlations are computed by taking products of linear and energy filter responses across different orientations, spatial frequencies and positions. Images are synthesized to match both the spatially averaged filter responses and the spatially averaged correlations between filter responses. The resulting texture images contain many more of the naturalistic features of the original.

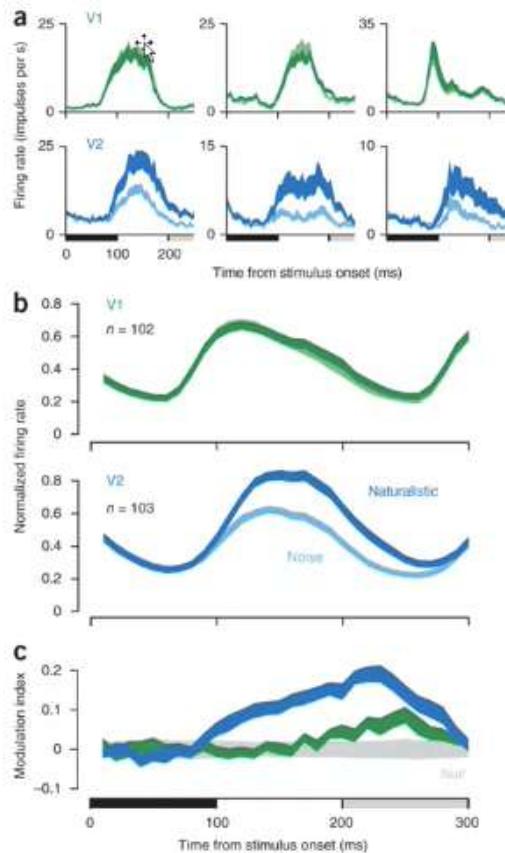


Figure 8.113

Looking at the image above:

- Time course of firing rate for three single units in V1 (green) and V2 (blue) to images of naturalistic texture (dark) and spectrally matched noise (light). Black bar indicates the presentation of the stimulus; gray bar indicates the presentation of the subsequent stimulus.
- Time course of firing rate averaged across neurons in V1 and V2. Each neuron's firing rate was normalized by its maximum before averaging.¹⁶¹
- Modulation index, computed as the difference between the response to naturalistic and the response to noise, divided by their sum. Modulation was computed separately for each neuron and texture family, then averaged across all neurons and families.¹⁶²

A similar effect has been found also in human, also human V2 is sensitive to statistical regularities in the properties of the images. If the images contain these statistical regularities V2 responds modulating.

Naturalistic texture stimuli modulate the responses of neurons in area V2, while having only a minimal effect on neurons in area V1. These modulations were similar and substantial in both macaques and humans (both primates).

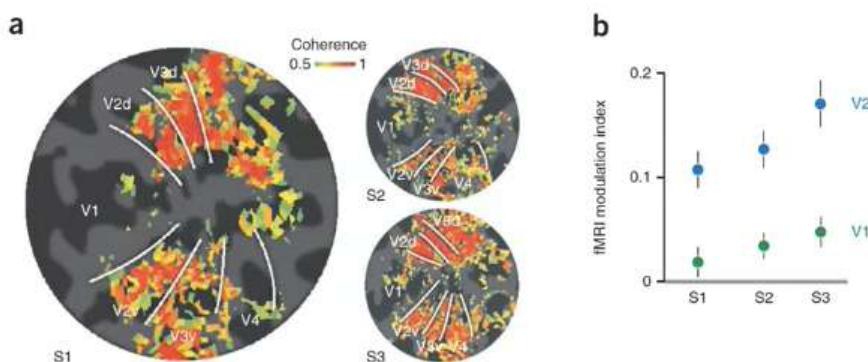


Figure 8.114

fMRI responses to naturalistic textures differentiate V2 from V1 in humans.
Looking at the figure above:

- Responses in subjects 1–3 (S1–S3) to alternating blocks of naturalistic texture images and spectrally matched noise shown on a flattened representation of the occipital pole. Color indicates coherence,¹⁶³ which captures the extent to which the fMRI responses to naturalistic and noise stimuli

¹⁶¹What emerges here is that neurons in V1 respond exactly the same to both *spectrally* and *naturalistic* (the green light and green dark are overlapping) while neurons in V2 are able to differentiate the images with different responses.

¹⁶²The modulation is high for neurons in V2 because the difference between naturalistic and noise is high while the modulation is low for neurons in V1 because the difference between naturalistic and noise is low (overlapping).

¹⁶³Colors represent response to naturalistic minus response to noise (Modulation). Notice that in V1 we have almost no colors. Difference in colors represent how strong is the difference.

differ, computed voxel by voxel¹⁶⁴ after averaging responses to all texture families. White lines indicate boundaries between visual areas, identified in an independent retinotopic mapping experiment.

- b. fMRI modulation averaged across voxels and texture families in V1 and V2 for the three subjects. Error bars indicate s.e.m. across texture families.

Reference: 'Freedman et al., Nat. Neurosci., 2013'

Up to V4 and then IT

Now we go to V4 (and then we go to *inferior temporal cortex* which is subdivided into: *posterior infero temporal cortex or PIT, central infero temporal cortex or CIT* and *anterior infero temporal cortex or AIT*; look at the image below). V4 (as the other parts seen so far) is another 'mysterious' area in the sense that we have many studies, many data but we are not able to characterize simply differences with other areas. We certainly know that is in a higher level in comparison to V1 for example.

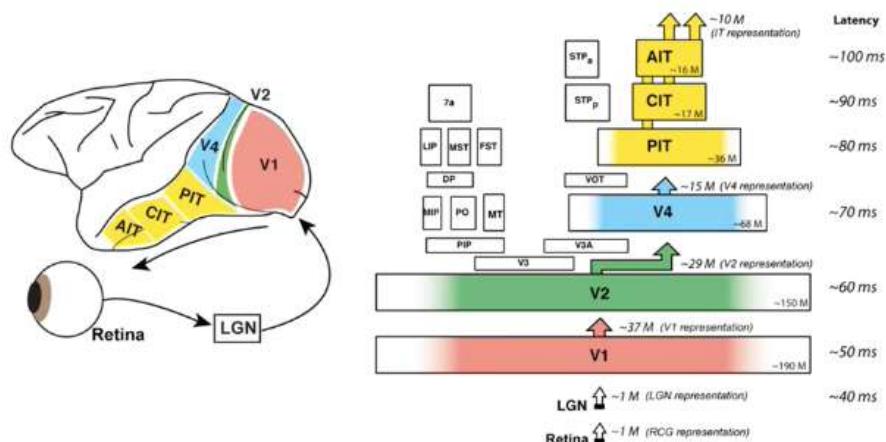


Figure 8.115

Visual area V4 is an intermediate¹⁶⁵ cortical area in the ventral visual pathway. It is considered to be crucial for visual object recognition and visual attention. A

¹⁶⁴A voxel is the smallest unit of a three-dimensional grid used in computer graphics, medical imaging, and scientific visualization. The term 'voxel' is a combination of 'volume' and 'pixel', reflecting its role as the three-dimensional equivalent of a pixel.

¹⁶⁵V1: early visual area; V2, V4: intermediate visual area; IT (PIT, CIT, AIT): high level visual area. If you remember past sections for *early visual processes* we meant *extraction of simple features* like color, depth, orientation, direction of motion but not *shapes* (and so not object). But when you go into V2-V4 (*intermediate visual processes*), shapes of objects begin to appear because there is integration of different contours in a single shape, touches of colors into surfaces. When you arrive in IT level (*high visual processes*), then you have object processing and object recognition, you are able to associate these shapes to a name, to a label.

primary role of V4 is to facilitate figure-ground¹⁶⁶ segmentation of the visual scene, thus enabling both bottom-up and top-down visual processes.

In the macaque monkey, V4 is located on the prelunate gyrus and in the depths of the lunate and superior temporal sulci and extends to the surface of the temporal-occipital gyrus.

So V4 intermediate level extracts shapes from different cues, from colors of an object (and extract shapes), from depth ..., from contours; so shape representation. But notice it's just a *shape*, there is still *no meaning, no significance*. V4 is also important for *colors*, probably integrate multiple features into a single object (colors and shape into a single object) is the main goal of V4, its general ability. Indeed at this level the best stimulus to activate a neuron should have a specific shape (like a bar with a certain orientation, oriented bar) but the shape has to have a specific color to activate maximally the neurons (it is not enough a – white/black – luminance bar); best stimulus is a colored oriented shape.

V4 is not a homogenous area

Recent advances in fMRI and optical imaging methods have revealed that V4 is not a homogenous area and may comprise segregated functional domains, dubbed globs¹⁶⁷ (in analogy with the color blobs of V1), specialized for color processing, and interglobes, for orientation and shape processing.

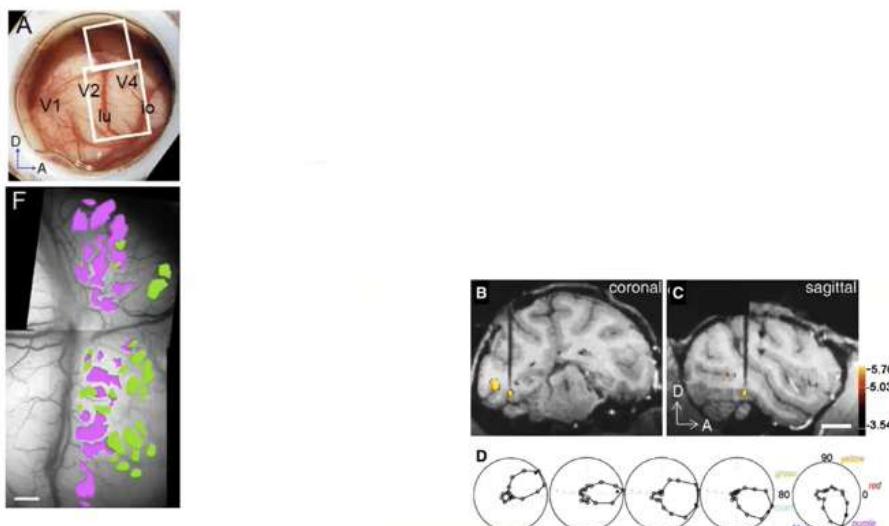


Figure 8.116

Looking at the figure above:

- A, F. Here a portion of the skull of the animal has been opened and, for example, we can see segregation: in green for instance are indicated zones processing

¹⁶⁶Figure-ground segmentation is a perceptual process in visual perception that involves distinguishing between a meaningful object or 'figure' and its background or 'ground' within a visual scene. This segmentation helps individuals organize and make sense of the visual information they encounter.

¹⁶⁷The 'g' stands for indicating a globular region.

color/Lum¹⁶⁸ and in purple zones processing orientations. So (F) illustrates in particular segregation of color/Lum and orientation preference bands in area V4.

- B, C. Several color globs identified with fMRI seen in coronal (B) and sagittal (C) views. Color voxels are better activated by equiluminant color than black and white gratings. Electrode is seen targeting a color glob.
- D. Shift in color preference of neurons along length of an electrode penetration through a glob.

Color-response measurements

Figure shows color-response measurements for a typical cell in a glob (A), and a cell in the interglob (B) region. Left panels show time histograms to an optimally shaped bar of various colors;¹⁶⁹ right panels show the color tuning in polar coordinates.

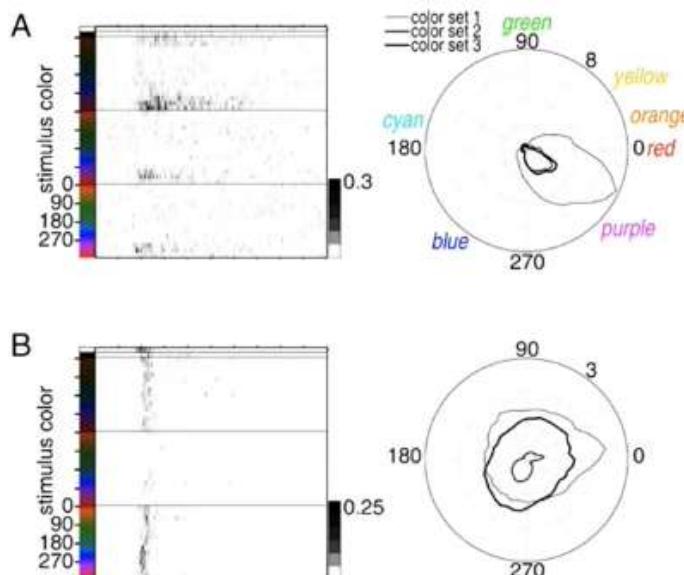


Figure 8.117

Looking at the figure above:

- A. Most glob cells were excited by a specific hue,¹⁷⁰ as shown by hue tuning in the polar plots. This hue selectivity was luminance invariant. That is, hue tuning does not change with change in luminance between stimulus and background.

¹⁶⁸'Lum' stands for 'Unit of Luminance'

¹⁶⁹So as you can see in the graphs A, B below, the orientation is always the same, what change are colors.

¹⁷⁰Refers to the attribute of a color that allows us to distinguish it from other colors. In terms of color theory, hue represents the pure, dominant color of an object as it appears on the color wheel. It is one of the three properties that define a color, the other two being saturation and brightness (or value).

- B. The interglob cell (B), on the other hand, did not show strong hue tuning, to any color set.
- A, B. Note in the figure there are three types of closed lines (different intensity of black) corresponding to the three different parts in which histograms are divided; see also the following explanation.

These measurements were conducted by presenting an optimally configured bar at the center of the response region for each cell, and in each trial changing the color of the bar.

The top two rows in each histogram show the responses to white and black.

The rest of the histogram plot is divided into three sections. The top section shows responses to a set of colors that were equiluminant with each other but lower luminance than the background (top), equiluminant with background (middle), and of higher luminance than the background (bottom).

The glob cell shown in figure was excited by bluish-red, shown by the maximal response density at the bottom of each section of the histogram.

The hue responses can be compressed into polar plots. Despite differences in overall response magnitude to the three color sets, the peak hue response within each color set was the same: each of the three curves in right panels point to 330.

This shows that the hue selectivity was luminance invariant.

Luminance invariance does not imply that luminance does not modulate the responses, just that a change in luminance does not drastically shift or cancel out the hue tuning.

Luminance invariance can be quantified by determining the degree to which the patterns of responses to the different color sets are correlated. The correlation coefficient of the response to color set 1 and color set 2 for was 0.94; between color set 1 and 3, 0.87; and between color set 2 and 3, 0.96; average, 0.92.

The interglob cell (B), on the other hand, did not show strong hue tuning, to any color set.

Reference: ‘Conway et al., *Neuron*, 2007’

Note: remember that V5 (MT) is important for motion direction. V4 is important particularly for colors. V5 is mostly a visual motion area, and is color blind, does not respond very much to color.

So they are quite the opposite:

- Parvocellular pathway \longleftrightarrow color and shape orientation segregation \longleftrightarrow color visual area V4 \longleftrightarrow ventral visual pathway.
- Magnocellular pathway \longleftrightarrow motion direction segregation \longleftrightarrow motion visual area V5 \longleftrightarrow dorsal visual pathway.

So V4 is the ‘color visual area of the brain’ (today scientists would respond so). Colors play a very crucial role in separating shape from the background; it is possible to do that also in black and white but it would be slower, with colors this kind of processing is faster and easier. It’s easier for an animal to distinguish an object from the background if the object is different from the background not only for the luminance but also for the color. So we use two types of informations to separate object/shape from the background:

- luminance: if the shape is darker than the background (degree of blackness over whiteness) or if it is brighter than the background (degree of whiteness over blackness); it is called ‘luminance contrast’.
- color: color contrast or chromatic contrast and acromatic contrast (black and white).

Color is important also¹⁷¹ for social animals – like humans and more generally primates – to display our emotion (think for example when somebody says: ‘I am seeing all black’ or psychologists ask children to paint in order to understand their emotions) and also anatomically referring to our body: when we are angry we become red in face, when we are afraid we became pale and pupils get larger and other people without understanding rationally are able to perceive a larger pupil (the pupil is the black part of the eye).

Up to now we said very little about colors: for all cells that we saw in V1, LGN, retina we spoke about spots of light but didn’t say anything about colors; we said something about that we have 3 different cones and each cone has a molecule/protein that is sensitive to different wavelengths (blue ↔ short wavelength, green ↔ intermediate, red ↔ long) and from these three colors we can combine them and obtain all possible colors; we saw that the fovea is rich of red and green cones but no blue cones, blue cones are outside the fovea and overall blue cones are fewer than red and green cones (only 10% blue cones).

So again colors are important mainly to extract shape/objects from the background; but there is a problem: see ahead the ‘inverse optics problem’ and then we return to see what is called ‘color constancy’.

Retinal luminance in visual stimuli (the inverse optics problem)

The color of an object doesn’t depend only on the ‘reflectance’ (the absorptive properties of the objects which could determine an *absolute colors* of the objects) but also on ‘illumination’ and other factors such as atmospheric transmittance. So the retinal luminance (the spectral light reflected from an object) which determines the retinal stimulus is always something ‘relative’ to the environment, it is not absolute. So we can’t see absolute color, or object always with the same color, the ‘reflectance’ is not the only thing that determines the retinal stimulus.

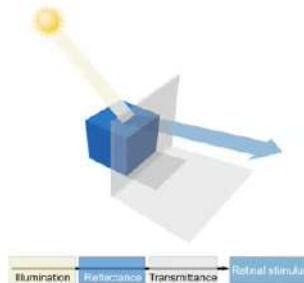


Figure 8.118

¹⁷¹But the following aspects are secondary in comparison to the fact of separating shapes from the background.

Retinal luminance, the spectral light reflected from an object is a product of two variables, illumination (the spectral content of the illuminant, *i.e.* the light source) and reflectance (the absorptive properties of the object), as well as a variety of other factors (*e.g.* atmospheric transmittance).

These physical determinants of retinal luminance values are conflated in visual stimuli and cannot be disentangled by any algorithmic process.

At the beginning we said that visual system does not care about absolute values of things, it cares about contrast, comparison between object and background and through this comparison is able to understand the color of the object. To recognize the color of the object is always subjective to the process of distinguish object and not viceversa.

Color constancy

Color constancy it's a property of the V4 area, neurons.

It refers to the effect whereby the perceived or apparent color of a surface remains constant despite changes in the intensity and spectral composition of the illumination (see ahead the comparison between the images of a pelargonium under sunlight and skylight).

The following shows a striking example in which the same physical patch appears yellow when the scene appears to be illuminated by blue light but appears blue when the scene appears to be illuminated by yellow light.

Surrounded by white, the patch appears gray.

This example illustrates the potency of color contrast in generating color perception.



Figure 8.119

Color constancy illustration: the patches indicated by the asterisks in the images are the same.

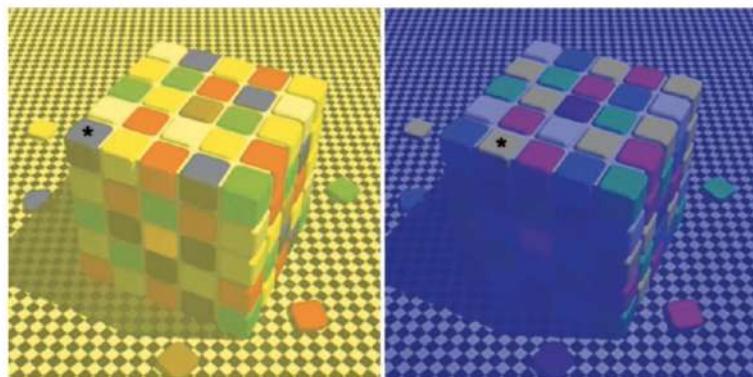


Figure 8.120

What happen here is that the patches are exactly the same, surrounded by white appear grey, but when the surround theme changes they appear different.¹⁷²

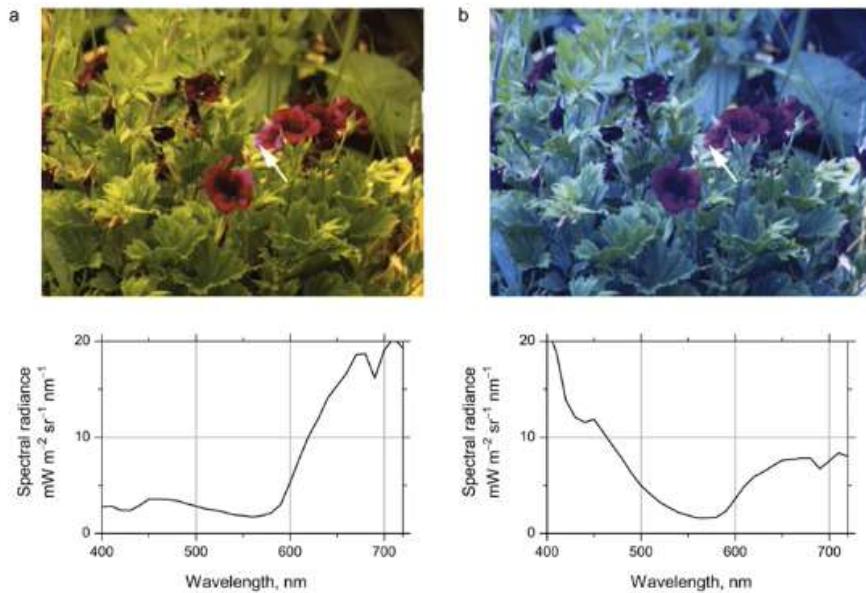


Figure 8.121

Images of a pelargonium under sunlight and skylight with respective correlated color temperatures (a) 4000 K and (b) 25,000 K and the corresponding radiance spectra reflected from the arrowed region of a petal.¹⁷³

Constancy¹⁷⁴ is achieved because the brain determines an object's color from a local comparison of the light reflected from the object with the light reflected from adjacent regions of the scene.

The brain is able to compare, needs to compare the value of the spectral composition coming from the object with the spectral composition of the environment; makes comparison from these two, makes *difference* between the two types of informations. And in order to compare these two informations we need one specific type of cell, a cell that is able to respond to *color contrast*.

Up to now we only saw *luminance contrast* (remember LGN cells, they are all example of luminance contrast, respond to dark over white or white over dark). Now we need *color contrast* to compute *color constancy*, so we need a cell for instance able to respond to green over red or red over green or blue over yellow or yellow over blue; Not anymore a *center-on cell* but a *green-on cell*, *red-on cell* ... a cell that responds to color in the center and different color in the surround.

Where are these cells?

¹⁷²What arrive in our retina is grey, but then brain processes make their job.

¹⁷³In the two graphs above we have different spectral radiance but constant perception of red and green.

¹⁷⁴In the sense that in the two images we perceive in both flowers to be red, even if different reds, on a green background, even if different greens.

Retina and LGN: Color Opponency

Experiments in psychology, in particular psychophysical (we mean behavioral studies, not recording any neural activity, just presenting some stimuli to subject and ask questions concerning those stimuli) show the behavioral evidence that we've three different channels for colors:

- Magnocellular channel: that is acromatic, does not use color but only black and white;
- two other channels that use colors but in opposition (opponent theory): red vs green, blue vs yellow.

There are many evidence of these three channels; *e.g.* the ‘after effect phenomenon’: if I show you a red circle (very large) and you fixate it for one minute and suddenly this circle is taken away, and it is presented in place a white circle, you see some greenish color inside this circle; this because we have saturated the red neurons with the fixating action, the red neurons are completely exhausted, instead the green opposite neurons are fresh, they were not involved before, they were just silent.

It's an after effect (completely illusory); there is a correspondent phenomenon for visual stimuli: *e.g.* if I present stimuli that are going in one direction, and suddenly stop them, you see *illusory* stimuli that go in the opposite direction. In general, if you present something that involves some stimuli for a while making working some kind of neurons and then you stop it, the opposite neurons begin to work for few seconds.

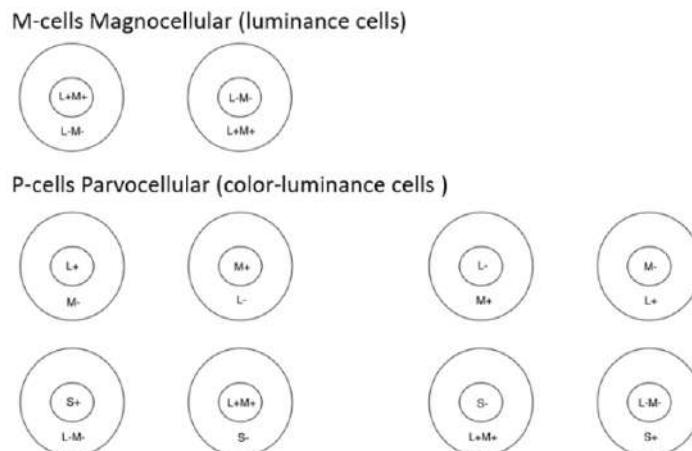


Figure 8.122

Looking at the image above. The principle dimensions in the space of cone excitations produced by natural objects are:

1. A luminance axis where the L and M-cone signals are added (see the first line circles in the figure above);¹⁷⁵

¹⁷⁵The circles represent on-center cell (left) and off-center cell (right). Here essentially we

2. A red-green opponent axis where the difference of L and M-cone signals is taken (see the second line circles in the figure above);¹⁷⁶
3. A blue-yellow color opponent axis where the S-cone signal is differenced with the sum of the L and M-cone signals (see the third line circles in the figure above).¹⁷⁷

All the RFs in the figure above are concentric RFs, so they are either retinal ganglion cells (M-cells, P-cells) or we are in LGN and they are Magnocellular Cells or Parvocellular Cells.

Receptive fields of single-opponent cells in the retina and LGN are not capable of color contrast (see next section to understand why).

So, Psychophysical experiments have revealed that there are three independent channels in color vision, or cardinal directions of color space. (Krauskopf et al., 1982).

All of above are ‘Single-opponent’ type receptive field.

Example of dynamic: ‘L+’ denotes excitatory L cone input; ‘M-’ denotes inhibitory M cone input. The cell thus prefers ‘red’ in the centre maximally stimulating the L cone and a lack of ‘green’ in the surround.

Primary visual cortex: calculating color contrast

The cone just responds to one specific wavelength: either to blue or green or red (three main types of cones).

But which type of cells we have in LGN, or Ganglion cells, or V1 and so on ...?

We have essentially 2 major types of cells:

- *single-opponent* (simple type);
- *double-opponent* (more rare, more interesting, more important).¹⁷⁸

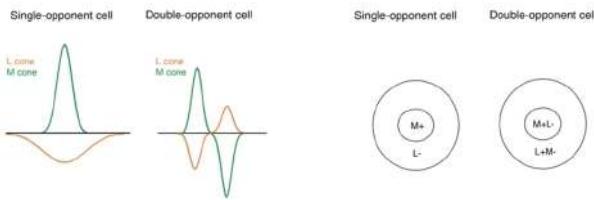


Figure 8.123

have only black and white, but for example from what white comes from? In the case of an on-center cell, the center is white because receive both green-red (and also small blue), all the cones are in the center and the cell is activated when both red and green arrive here and because they are activated by both is not able to differentiate and this is the effect of white color.

¹⁷⁶The couple of circles at the left represent red-on cell (left, + indicates the presence of the color, - indicates the absence) and green-on cell (right).

¹⁷⁷The couple of circles at the left represent blue-on cell and yellow-on cell (note that yellow is similar to white dinamic combining red and green).

¹⁷⁸They are very numerous in V4, there are also in V1 but maybe in V4 there is a great convergence; this why V4 is particularly important to calculate color contrast and color constancy.

Lookign at the figure above – in particular the left circle RF – note that + is related to positive graph, – to negative graph. So + indicates ‘presence’ and – indicates ‘absence’.

- Single-opponent cells cannot resolve color contrast.
- Double-opponent cells may represent the neural basis for color contrast and color constancy.

The optimal stimulus for a Green-on double-opponent cell is a green spot on a red background. Because of their specialized receptive-field structure, double-opponent cells are candidates for the neural basis for color contrast and color constancy.¹⁷⁹

- Single-opponent:¹⁸⁰
 - These cells increase their firing rate above some baseline rate in response to activation of one cone class and decrease their firing rate when a different cone class is activated. Thus, they cannot resolve color contrast.¹⁸¹
- Double-opponent:
 - These cells are so named because their receptive fields are both chromatically and spatially opponent.

Object identification and categorization

Now we move on *infero-temporal-cortex* to see the problem object recognition/perception. In the visual ventral pathway object recognition/perception is the most crucial part of the pathway.

The visual experience of the world is fundamentally centered on objects.

By visual object we mean a set of visual characteristics (*e.g.* visual features) grouped or joined perceptually in discrete units on the basis of the organizational principles of the Gestalt, such as proximity, similarity, closure, good continuation, good form, connection, *etc.*

By visual recognition we mean the ability to assign a verbal label (*e.g.* a name) to objects in the visual scene.

There are at least two possible object recognition tasks, distinguished by level of specificity: identification and categorization.

An object can be recognized at an individual level (*e.g.*, a Siamese cat), or at a more general categorical level, as an object belonging to a given class (a cat, a mammal, an animal, and so on).

¹⁷⁹Look at the figure above: they are maximally activated when there is green in the center (M+) and red in the surround (L+); note M+L– indicates presence of green (M+) and absence of red (L–). So better, the best stimulus is: M+L– ↔ green in the center M+ and absence of red L– in the center; L+M– ↔ red in the surround L+ and absence of green M– in the surround.

¹⁸⁰As anticipated before they are in retina, LGN, V1 (in the BLOBS); the most basic: we have cones and after cones ‘single opponent’.

¹⁸¹In the figure above for instance the cell is activated by green and is inhibited by red (to resolve color contrast the cell should be able to *understand* both colors at the same time); activated by a spot of green, inhibited by a spot of red; the best stimulus is green in the center M+ and absence of red L– in the surround.

It is quite simple for computer vision techniques to identify (rather than categorize) objects.

On the contrary, for the human vision the task of identification (compared to categorization) is more difficult. Categorization: a category exists whenever two or more distinct objects or events are treated equivalently.

For example, when distinct objects or events are labeled with the same name, or when the same action is performed on different objects. Although the stimuli are distinct, organisms do not treat them uniquely; but they respond on the basis of past experience and categorization.

In this sense, categorization can be considered one of the most basic functions of living beings (Mervis and Rosch, 1981).

High-level visual processing is concerned with object recognition

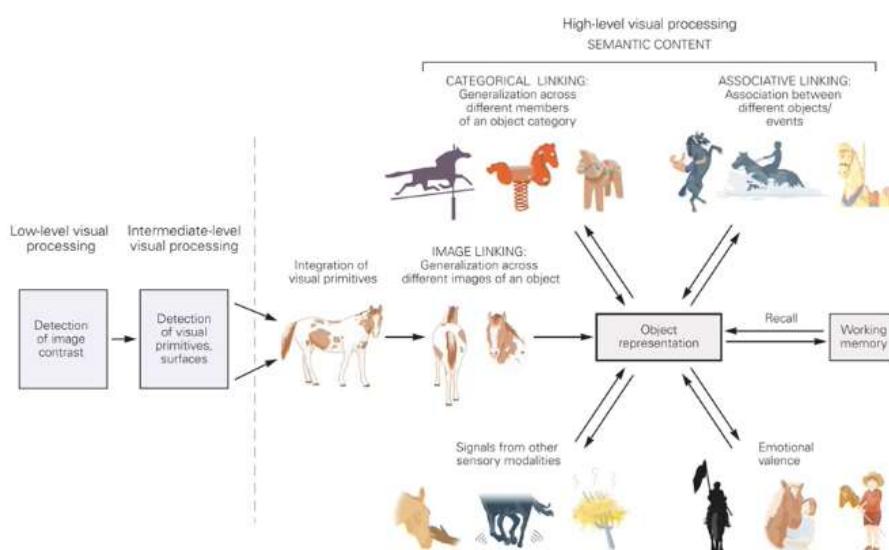


Figure 8.124

We effortlessly and rapidly (100-200 ms) detect and classify objects from among tens of thousands of possibilities despite the tremendous variation in appearance that each object produces on our eyes.

Our daily activities (*e.g.* finding food, social interaction, selecting tools, reading, *etc.*), and thus our survival, depend on our accurate and rapid extraction of object identity from the patterns of photons on our retinas.

The fact that half of the nonhuman primate neocortex is devoted to visual processing speaks to the computational complexity of object recognition.

Object recognition involves integration of visual features extracted at earlier stages in the visual pathways.

This integration requires generalization across different retinal images of an object, as well as generalization across different members of an object category. The representation also incorporates information from other sensory modalities, attaches emotional valence, and associates the object with the memory of other objects or events.

Selectivity and object constancy (or invariance)

One of the major problem is the following.

A computational difficulty of object recognition is that it requires both:

- selectivity (different responses to distinct objects, such as one face with respect to another face);
- invariance with respect to image transformations (similar responses to, for example, rotations or translations of the same face).

In fact, we are able to recognize the same object even when the image it projects on the retina varies considerably.

Object invariance problem

The phenomenon of perceptual constancy, or ‘object invariance problem’, is the crucial point of object recognition, and also the main obstacle for computer vision recognition systems.¹⁸²

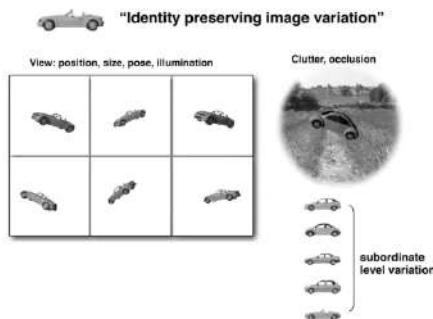


Figure 8.125

Core object recognition

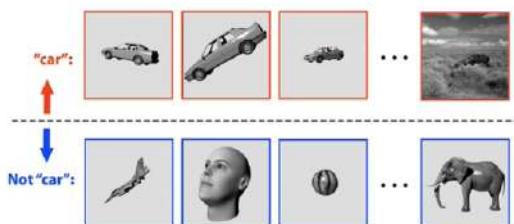


Figure 8.126

¹⁸²For example, for computer vision, information about the background are also processed and become very important; it is very difficult for a machine to recognize a car that is not in a proper environment e.g. a car flying among planets.

Core object recognition¹⁸³ is the ability to rapidly (< 200 ms viewing duration) discriminate a given visual object (*e.g.* a car, top row) from all other possible visual objects (*e.g.* bottom row).

Primates perform this task remarkably well, even in the face of identity-preserving transformations (*e.g.* changes in object position, size, viewpoint, and visual context).

Object recognition

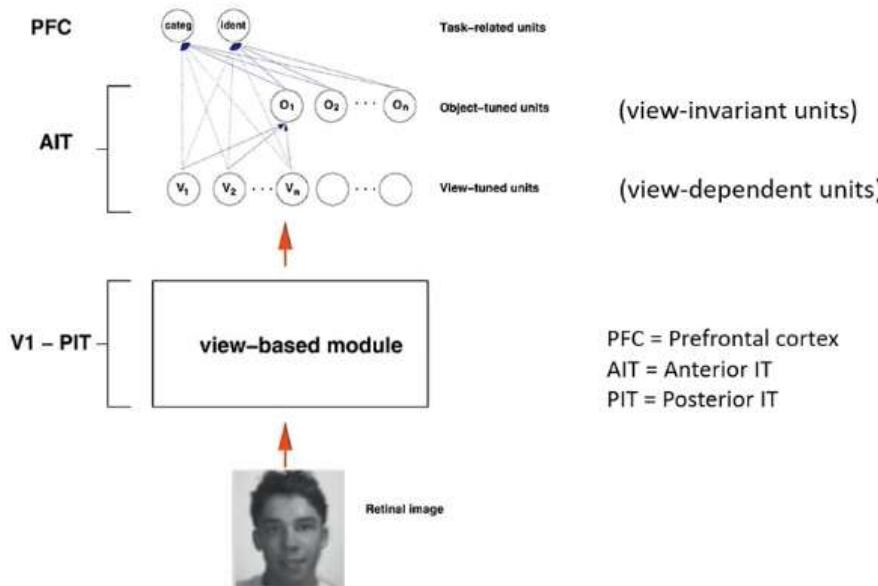


Figure 8.127

In early visual area the representation is very view-based (imagine that in the retina we've just a representation of what is there: here we have a lot of dependencies like distance, position, luminance, size ...).¹⁸⁴

But moving up along the visual pathway the representation gets more and more abstract,¹⁸⁵ less view-based, becomes more view independent, gradually. Until you arrive in PFC. This is a continuous process, a loop.

Reference: '*Riesenhuber & Poggio, Nat. Neurosci. 2000*'.

Object perception and recognition pathway

In the PFC (Prefrontal Cortex) converge both dorsal and ventral pathway (although we saw they're in communication also before), PFC is the only part in which this convergence happens. PFC uses the information coming from infero

¹⁸³A core object recognition task could be sitting in front of a screen and press a button each time a car image appears (also other images are presented sequentially).

¹⁸⁴In V1, for instance, we have simple cells, if the stimulus is not exactly inside the RF you will not see activation of neurons so is very dependent on the position of the stimulus, scale of the object, colors and so on ...

¹⁸⁵More independent from transformations that can involve objects.

temporal cortex IT to understand. Imagine I've to make the decision if an object is car or not; IT should be readable from PFC, PFC receives informations from IT in order to make the decision is a car or not. So probably IT should sent informations made in some explicit from that PFC is able to understand in order to decide.

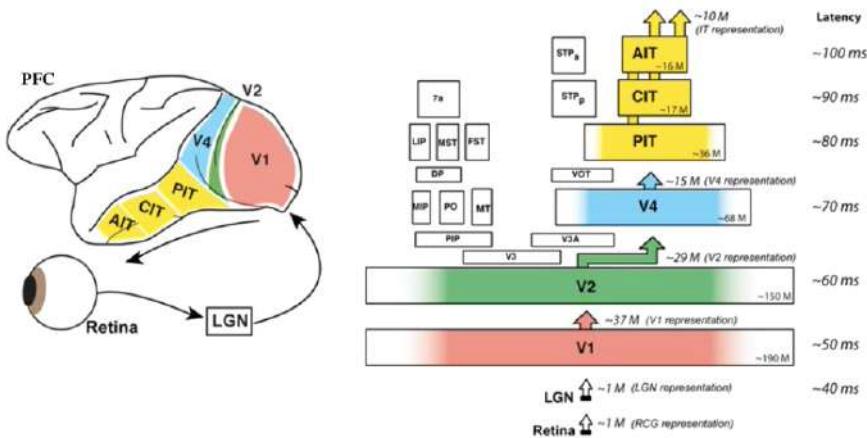


Figure 8.128

Studies in animals (*e.g.*, primates) primarily implicates the inferior temporal cortex in object perception and recognition.

The inferior temporal cortex is a large region of the brain that includes at least two major functional subdivisions - the posterior area, or temporo-occipital cortex (TEO area), and the anterior area, or inferotemporal cortex (IT area). Area V1, V2 and V4 are located in the occipital lobe.

Area TEO (Temporal-Occipital) and IT (Infero-Temporal) are located in the temporal lobe.

Now we go in IT; we don't know yet how IT exactly works; there are different theory and opinion on how IT does its work; if we have lesions in IT area of animals and humans we lose the ability to recognize object; they see something but they don't recognize, identify, categorize; they can even make a perfect drawing, they can copy the object but they don't know anything about (this is called '*visual agnosia*'). It is possible that the subject recognize the object through other senses, but not through vision.

Receptive fields get larger

In contrast to V1, V2, V4 and partly PIT, CIT and AIT show no clear retinotopy.¹⁸⁶

¹⁸⁶When instead we go up in the IT the concept of RF becomes not important anymore: the size of RF of infero temporal cortex neurons is as large as the entire visual field. Retinotopy refers to the mapping of visual space in the brain, specifically in the visual cortex. The term is derived from 'retina' (the light-sensitive tissue at the back of the eye) and 'topography' (the arrangement of the physical features of an area). In retinotopic mapping, neighboring locations in the visual field are represented by neighboring neurons in the visual cortex. This means that adjacent points on the retina correspond to nearby points in the brain's visual processing areas. The primary visual cortex (V1) is organized in a retinotopic manner,

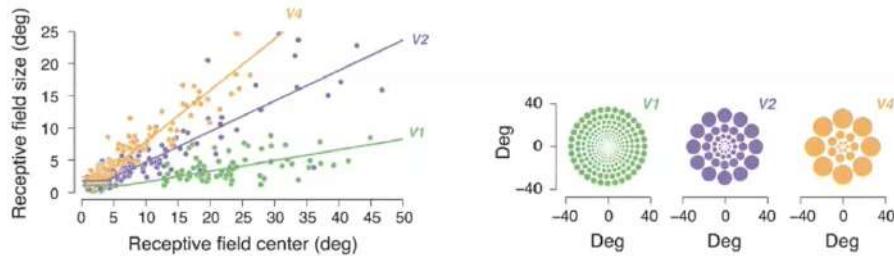


Figure 8.129

Large receptive fields (from 2 to 30 degree). Most of the receptive fields include the fovea. Foveal stimuli evoke stronger responses.

Note that the size of the RF becomes larger going up (V1, V2, V4 ...). Even the stimulus has to be more and more complex in order to activate the neuron: *e.g.* you cannot activate V4 neuron by presenting a white bar on a black background. We need lines and colors and shapes; it is not important it has a meaning but has to be more abstract, complicated. But in any case should be in the RF.

Reference: ‘Freeman and Simoncelli, *Nat. Neurosci.*, 2013’.

Representation of the visual field in the dorsal and ventral visual pathway

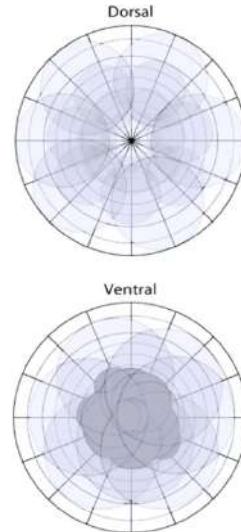


Figure 8.130

and this mapping continues in subsequent visual processing areas. This organization helps maintain the spatial relationships of visual stimuli, allowing the brain to construct a coherent representation of the visual world.

The dorsal visual pathway is characterized by a more complete sampling of the visual field with wide receptive fields, which include the visual periphery, and, in some cases, sparing of foveal regions.

In contrast, the areas of the ventral visual pathway show greater focalization, which always involve coverage of the foveal regions.

This difference would indicate a crucial role of the dorsal pathway in the exploration of salient stimuli of the visual field, while the ventral pathway would be involved in object recognition and use (exploration vs exploitation).

Reference: 'Sheth and Young, *Front Integral Neurosci*, 2016'.

Increased complexity of effective stimuli along the ventral visual path

V2	V4	posterior IT	anterior IT
			
			
			
			

Figure 8.131

Reference: 'Kobatake and Tanaka, *J. Neurophysiol.*, 1994'.

Functional columns in IT



Figure 8.132

Tanaka (1996) suggested that responses to effective stimuli are organized in topographical order, so that two adjacent neurons are much more likely to respond similarly to a set of stimuli than neurons that are more distant. The neurons that respond to the different parts of an object are not randomly arranged in the IT area. Neurons that respond to same elements are grouped in a cortical column, analogous to the orientation columns found in V1. Contiguous columns encode elements related to each other.

Invariances

And also one specific aspect is the *invariances* that we found:

- size invariance;¹⁸⁷
- position constancy (same size – meaning same distance – of the object but different positions);
- form-cue invariance (does not matter if the stimuli are black or white, the stimuli show the same trend – see the figure below).

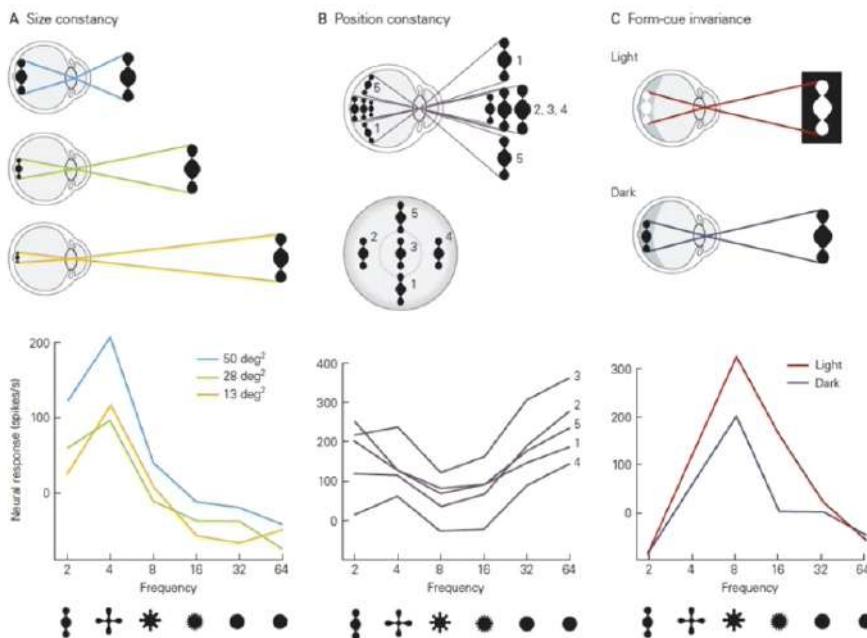


Figure 8.133

Note for each size/distance, position, and form cue we have the same trend for varying the stimulus forms.

¹⁸⁷Imagine you present to your infero temporal cortex (IT) this kind of stimuli (see the figure) we can see *selectivity*: what does it mean selectivity? The greatest response of the neuron/neurons is represented by the peak of the lines when the cross is presented (not when other images are presented), furthermore note that varying the size (note that increasing the distance, the object perception becomes smaller: blue line ↔ big, green line ↔ intermediate, yellow line ↔ small) the *selectivity* for the cross image remains. So we have selectivity (for the cross) and invariance (for the size of the cross).

IT neurons respond selectively

Neurons in the IT respond to relatively complex stimuli, often to biologically relevant objects such as human and other animal faces, hands and other parts of the body.

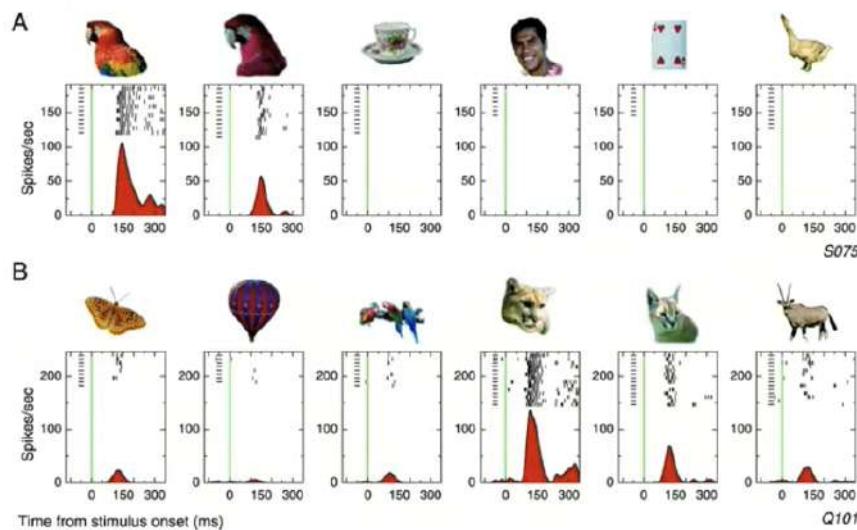


Figure 8.134

Looking at the image above:

- A. Here one neuron recorded; seems that this one neuron responds only to sparrow faces;
- B. Here another neuron recorded; seems that this one neuron responds only to cat/feline faces;

There are theories that tell that we have a neuron that encode only one relevant object (or part of object) of our world.

In the early 1980s, several researchers (Bruce et al., Perrett et al.) identified in the monkey a group of IT neurons that responded selectively to faces.

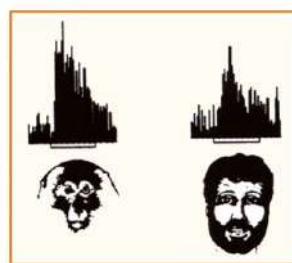


Figure 8.135

Question: Are there in IT, as for faces, selective cells for the different types of objects that can be encountered in the outside world (neurons for chairs, for flowers, for cars, etc. ...)?

Neuron that responds to faces: The neuron responds to faces of different species (1, 4, 5). The discharge is reduced if the elements of the face are mixed (2) or occluded (3). The neuron does not respond to other biologically relevant stimuli (6).

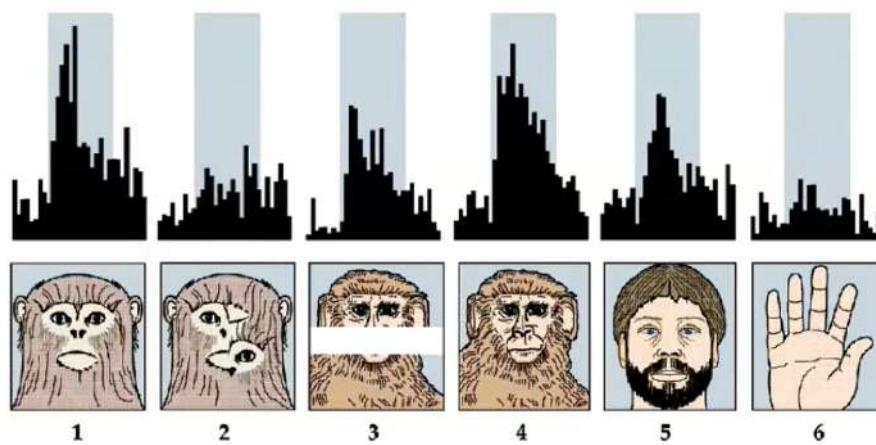


Figure 8.136

Reference: 'Desimone, Albright, Gross and Bruce, J. Neurosci, 1984'.

Recording of a single neuron from monkey IT cortex (Desimone et al., 1984)

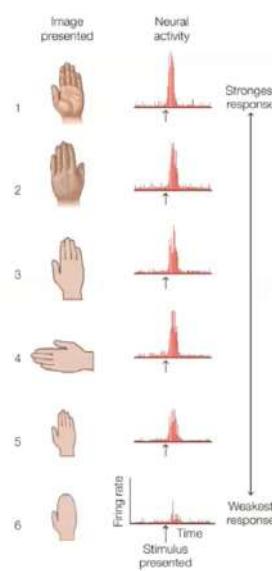


Figure 8.137

This cell is activated by the vision of the human hand.

The first five images in the figure show the cell's response to various perspectives of a hand.

Activity is high regardless of hand orientation and only decreases slightly when the hand is noticeably smaller.

The sixth image shows that the response decreases if the stimulus has the same shape, but does not have well-defined fingers.

Stimuli activating IT neurons

The following is just a list of papers published in different years containing various stimuli that are able to activate IT neurons.

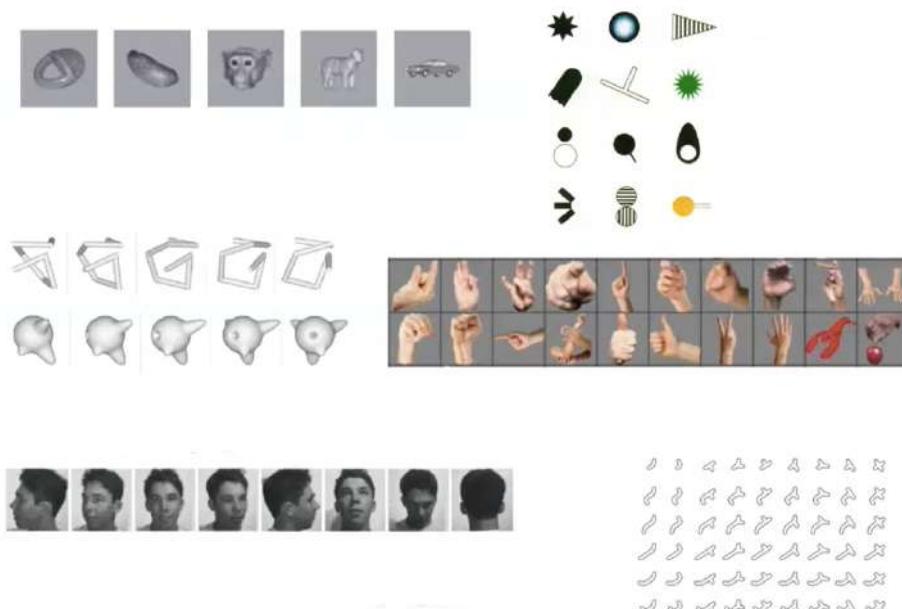


Figure 8.138: Hung et al., Science, 2005; Tanaka, Science, 1993; Logothetis et al., Curr, Biol., 1995; Kiani et al., J. Neurophysiol., 2007; Freiwald and Tsao, Science, 2010; Brincat and Connor, Nat. Neurosci., 2007.

Distributed representation

Tanaka hypothesized that the representation of each object occurs not through the activation of a single neuron but of a population of IT neurons (distributed representation), each of which encodes only one element or a particular (which can be present in several objects) and not the whole object.

Studies by Tanaka have shown that IT neurons that seem selective for a specific object, actually respond to a part or component of the object, and not to the object as a whole. These parts of objects that activate neurons can be found in a variety of different stimuli, and constitute a sort of visual alphabet for the recognition of objects.

In the following image we have a schematic representation of the different elements to which IT neurons respond (from Tanaka, 1996).



Figure 8.139

For example, the neuron shown in the figure below seems to respond to the complex image of a fruit (melon). However, a detailed study (method of progressive reduction) shows that the neuron also responds to simpler stimuli that represent the visual elements of an object to which the neuron is sensitive.

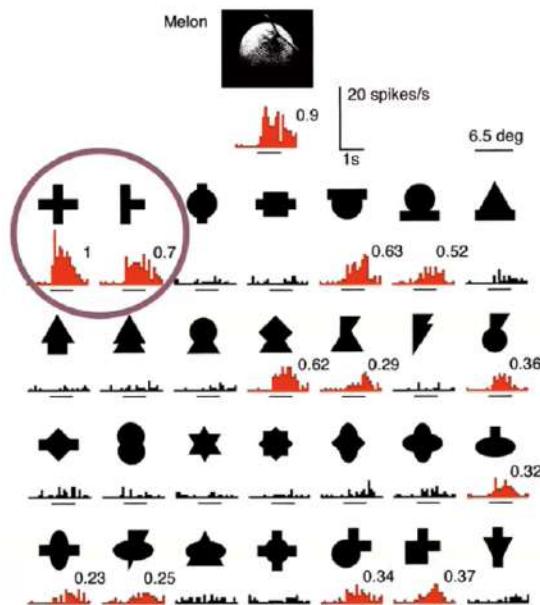


Figure 8.140

View-dependent/independent responses

The majority of IT neurons respond to a stimulus only when it is presented from specific points of view (view-dependent responses).

Some neurons (10%) selectively respond to familiar stimuli regardless of their position with respect to the observer (view-independent responses).

These responses, although rare, indicate that IT is capable of forming a (relatively abstract) representation of the object, rather than responding to one of the different forms that the object can take when its position with respect to the observer changes.

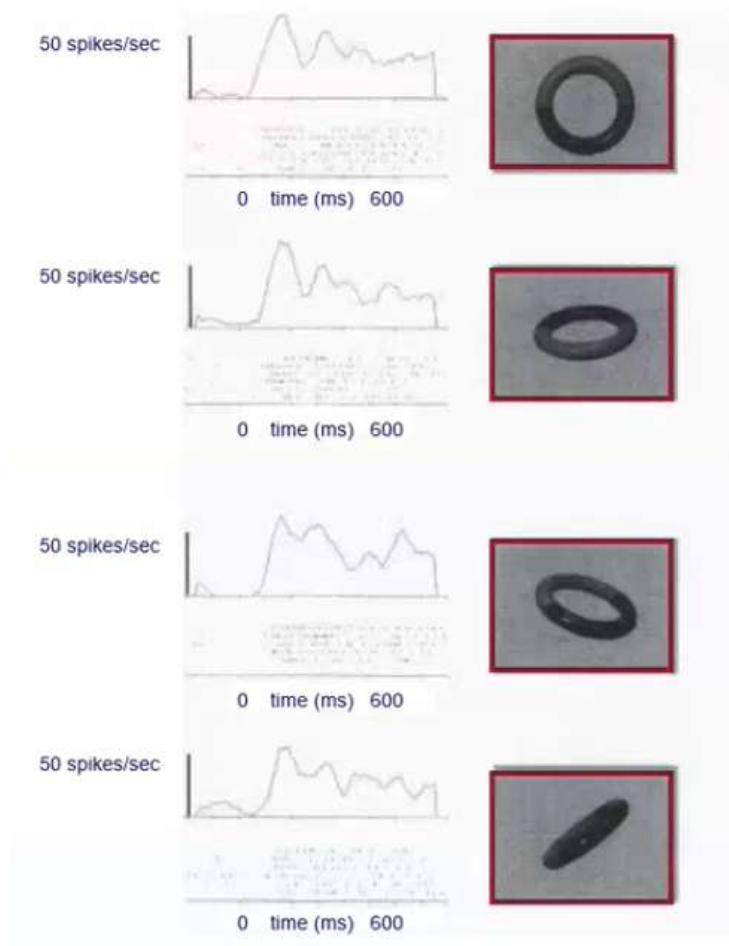


Figure 8.141

Hierarchical model of the object recognition

The finding that IT cells selectively respond to more complex stimuli than V1, V2 and V4 is consistent with a hierarchical model of object perception.

According to this model, each subsequent level encodes more complex combinations from the inputs of the previous level.

The type of neuron that can recognize a complex object has been called the gnostic unit, referring to the idea that the cell (or cells) signals the presence of a complex, highly specific, and significant stimulus: that is, a known object, place or animal that has been encountered in the past.

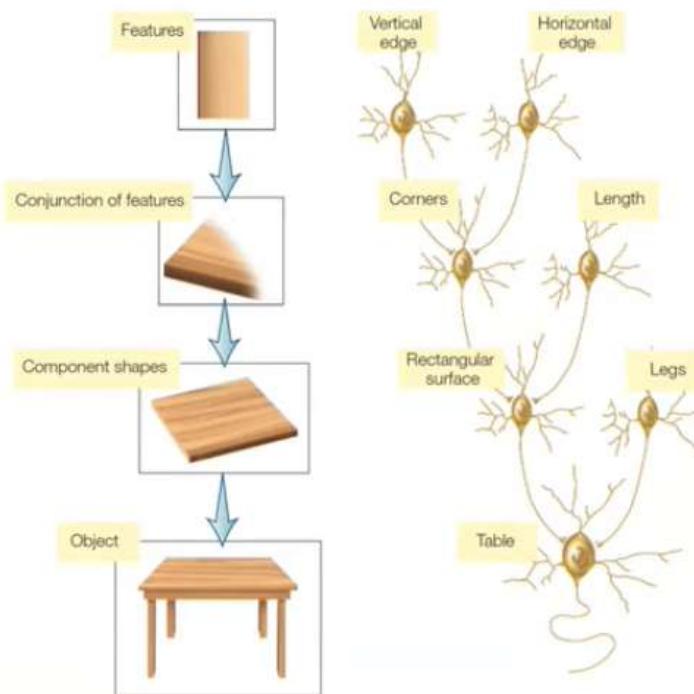


Figure 8.142

Local or distributed coding?

It is tempting to conclude that the cell represented by the activity of IT cells signal the presence of an object (a hand or face), independent of the point of view.

In this regard, the researchers coined the term ‘grandmother cell’ to convey the idea that people’s brains may have a gnostic unity that is activated only when the grandmother comes into view.

Other Gnostic units would specialize in recognizing, for example, a blue Volkswagen or the Golden Gate Bridge.

Distributed code hypothesis

An alternative to the Grandmother cell hypothesis is that object recognition is the result of a distributed activation pattern on the population of IT neurons. According to this hypothesis, recognition is due not to one unit but to the collective activation of many units.

Distributed code theories easily explain why we can recognize similarities between objects (say, a tiger and a lion) and make mistakes between visually similar objects - both objects activate many of the same neurons.

Losing some units may degrade our ability to recognize an object, but the remaining units may be enough.

Distributed code theories also explain our ability to recognize new objects. New objects have a resemblance to familiar things, and our perceptions result from activating units that represent their characteristics.

The results of the studies on single neurons of the temporal lobe are in agreement with the theories of the distributed code of object recognition.

Although it is surprising that some cells are selective for complex objects, the selectivity is almost always relative, not absolute.

Summary

Here some summary points:

- IT neurons respond only to visual stimuli.
- The receptive fields always include the fovea, that is the part of the retina most involved in the fine recognition of a visual stimulus.
- The receptive fields tend to be large, providing the opportunity to generalize the stimulus within the receptive field, and often extend along the midline in both visual hemifields, thus joining the two halves of the space for the first time. This property depends on the interhemispheric connections through the splenium of the corpus callosum and the anterior commissure.
- IT neurons encode complex characteristics of the stimulus (not simple features, such as color, form orientation, depth).

IT neuron selectivity often appears somewhat arbitrary. A single IT neuron could, for example, respond vigorously to a crescent of a particular color and texture. Cells with such selectivity likely provide inputs to higher-order neurons that respond to specific objects. Other summary points:

- A small percentage of IT units are selective for faces. Some are sensitive to emotional expression and others to the direction of gaze. Hand-selective cells are also found.
- Faces and probably other shapes appear to be encoded by a pattern of activity distributed over a set of cells, rather than by gnostic units (grandmother's cell), that is, a cell that responds to complex and highly specific visual stimuli such as one's grandmother.
- The selectivity of IT cells is usually invariant with respect to changes in stimulus size, contrast, color, and exact location on the retina.

- Appears to be a vertical organization for the selectivity of the stimulus of IT neurons.
- The activity of IT neurons can be modulated by the animal's attention.
- IT cells can exhibit both short and long-term memory effects for visual stimuli, and their selectivity can be changed by experience.

Ventral visual pathway gradually ‘untangles’ information about object identity

Note: we know much more V1 (even if we have not yet a complete understanding of all mechanisms) than IT (even if we have many many studies); going up with the structure, the mechanisms becomes very complex and we have to discover a lot.

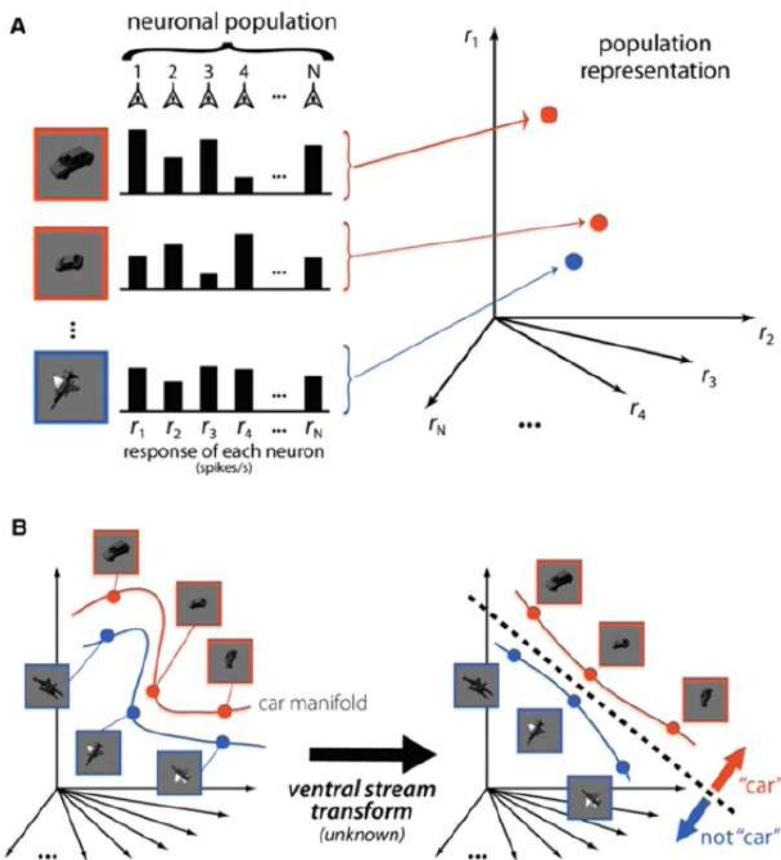


Figure 8.143

Response of a population of neurons to a particular view of one object can be represented by a response vector in a space whose dimensionality is defined by the number of neurons in the population.

When an object undergoes an identitypreserving transformation, it produces a different pattern of population activity, which corresponds to a different response vector.

Together, the response vectors corresponding to all possible identity preserving transformations define a low-dimensional surface in this high-dimensional space, an object identity manifold.

Looking at the figure B above:

- Recording at an early level we can see that the manifolds are almost completely enveloped each other, we have a '*tangled*' representation; so it is difficult to properly distinguish.
- Then we have → *ventral stream transformation*.¹⁸⁸
- But when you move away from V1 and early visual area and you record the representation become '*untangled*'.

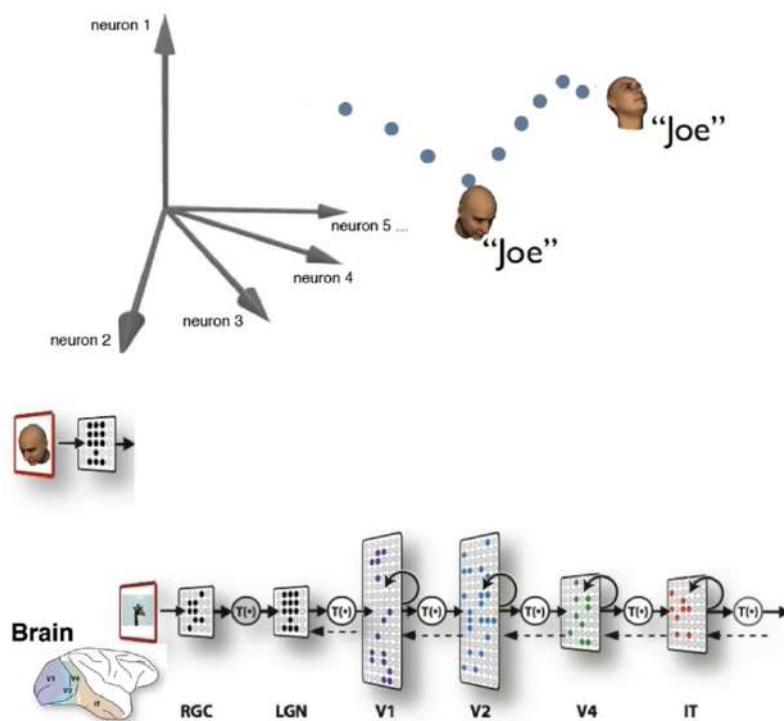


Figure 8.144: ‘Joe’s’ identity manifold.

The response of a population of neurons to a particular view of one object can be considered as a response vector in a space whose dimensionality is defined by the number of neurons in the population.

¹⁸⁸How this transformation happens is still unkown; one of the main problem of object recognition is *untangling* visual representation; from *tangled* to *untangled*.

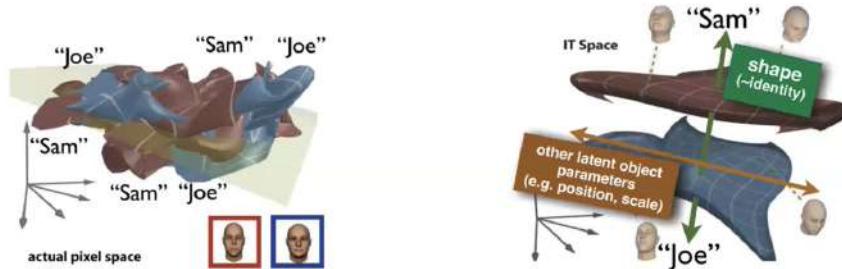


Figure 8.145

Object recognition is the ability to separate representation that contain one particular object from representation that do not.

Thus, object manifolds are thought to be gradually untangled through nonlinear selectivity and invariance computations applied at each stage of the ventral pathway.

At higher stages of visual processing, neurons tend to maintain their selectivity for objects across changes in view; this translates to manifolds that are more flat and separated (more ‘untangled’).

For neurons with small receptive fields that are activated by simple light patterns, such as retinal ganglion cells and V1, each object manifold will be highly curved. Moreover, the manifolds corresponding to different objects will be ‘tangled’ together. Going up the *untangling* could be possible because the RF becomes larger and larger and so cells can have a clear and distinct view of the objects (this is an hypothesis).

Reference: ‘DiCarlo et al., *Neuron*, 2012’.

Distributed vs grandmother representation. Classifier performance.

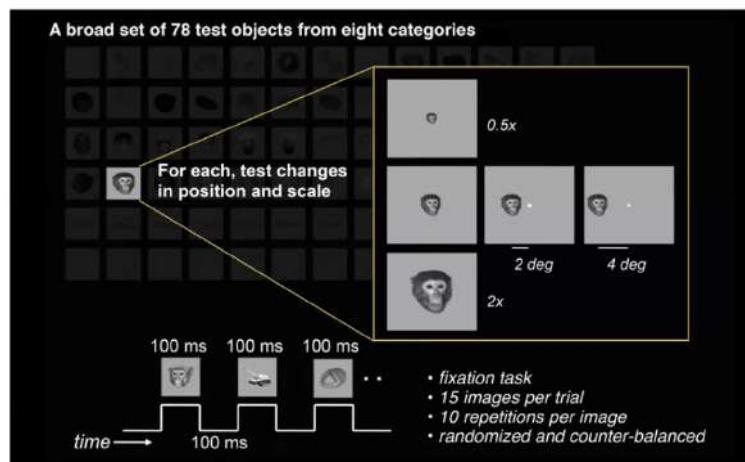


Figure 8.146

Look at the image above.

Is given a set of 78 grey images belonging to 8 categories of object presented in different scale (look in vertical) and in different position (look in horizontal). Then one stimulus was presented for 100 ms followed by 100 ms of nothing, then another image for 100 ms and so on. The animal is just passively (without paying attention) fixating without doing other things and scientists are recording neurons from IT cortex.

By using a classifier-based (see ahead for a detailed explanation) readout technique, Hung et al (2005) investigated the neural coding of selectivity and invariance at the IT population level.

They showed that the activity of small neuronal populations (almost 200 units) over very short time intervals (as small as 12.5 milliseconds)¹⁸⁹ contain accurate and robust information about both object ‘identity’ and ‘category’.

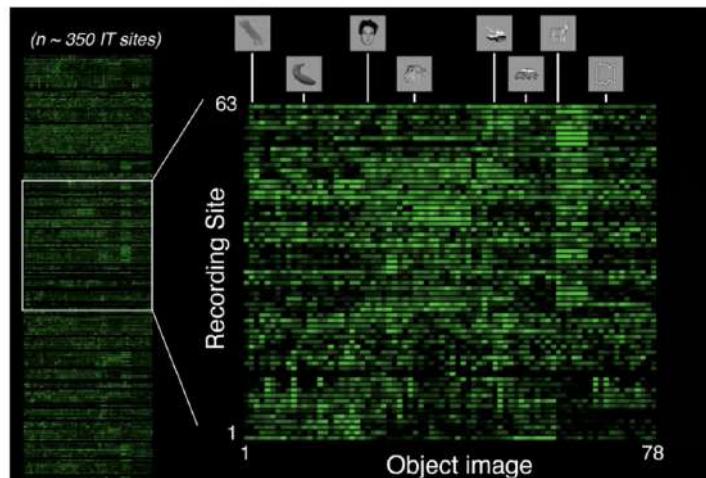


Figure 8.147

Look at the image above.

On the horizontal axis of the image there are at each point the 78 images (so each vertical line represents the response on a specific image) and on the vertical axis are reported the recording IT sites (so each horizontal line represents the response of a specific site varying images).

The readout technique consists of training a regularization classifier¹⁹⁰ to learn

¹⁸⁹These 12.5 milliseconds are referred to the δ after the stimulus was presented (stimulus: 100 ms + δ : 12.5 ms); see ahead.

¹⁹⁰Regularization is a technique used in machine learning, particularly in the context of training models, to prevent overfitting and improve generalization performance. A ‘regularization classifier’ refers to a classifier that incorporates regularization techniques. Common types of classifiers that often use regularization include logistic regression, support vector machines, and neural networks. In the context of neural networks, regularization is a technique used to prevent overfitting, which occurs when a model learns the training data too well, including its noise and outliers, but fails to generalize well to new, unseen data. The regularization term is typically used during the training phase, and it helps to prevent the model from fitting the noise in the training data too closely, resulting in improved generalization to unseen data. Overfitting is a common issue in machine learning where a model learns the

the map from neuronal responses (from the independently recorded neurons) to each object label.

The input consists of the neuronal responses.

The activity of almost 250 randomly selected multi and single-unit activity in response to 78 images of different objects were recorded at 350 IT sites in two monkeys.

So the classifier was trained by these data and then is tested with different sample of object (belong to the same category but are novel object just because they're presented in a different position or different size, anyway object that the animal has not seen while the recording and the classifier was trained).

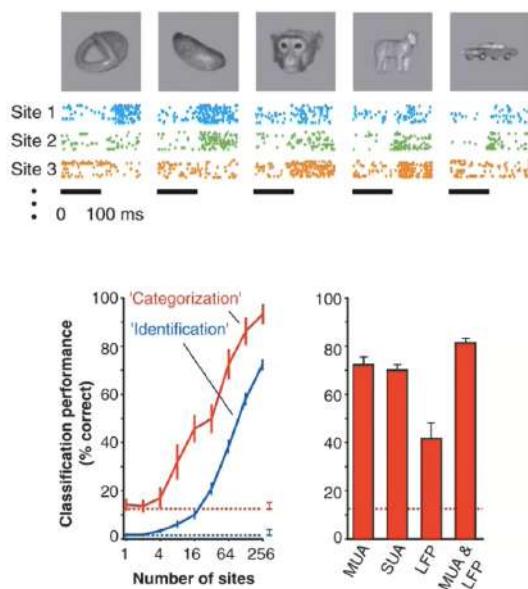


Figure 8.148

training data too well, capturing not only the underlying patterns but also the noise or random fluctuations present in that data. As a result, an overfit model performs well on the training data but fails to generalize effectively to new, unseen data. Key characteristics of overfitting include:

- High Training Accuracy, Poor Generalization: The model achieves high accuracy on the training dataset, correctly predicting the labels for the examples it was trained on.
- Poor Performance on Unseen Data: When applied to new, unseen data (such as a validation or test set), the model's performance is significantly worse than expected. It fails to generalize well.
- Capturing Noise as Signal: Overfitting occurs when a model captures not only the underlying patterns in the data but also the noise, outliers, or random fluctuations specific to the training set.
- Overly Complex Model: The model is too complex relative to the simplicity of the underlying true data distribution. It may have an excessive number of parameters or be too flexible.

The spiking activity of 256 randomly selected multi-unit activity sites was sufficient to categorize the objects with 94% accuracy.

Classifier performance increased approximately linearly with the logarithm of the number of sites, which is indicative of a distributed representation in contrast to a grandmother-like representation.

Looking at the image above focusing on the two graphs we can see the black horizontal bar which represents the stimulus presented (0-100 ms) followed by a period in which the stimulus is gone. Note that the firing rate increase just after the presented stimulus is gone; as mentioned before the 12.5 ms δ are enough to recognize.

Focusing instead on the two graphs below note that the *Categorization* is better than *Identification* for the animal. Furthermore in the right graph the data performance are splitted by type of recording:

- MUA stands for multi-unit recording;
- SUA stands for single-unit recording;
- LFP stands for local feed potential;¹⁹¹

So:

- α. the classifier was trained by the registration of the neural activity of the monkey;
- β. then was tested on new objects not present in the training data (as reported ahead).

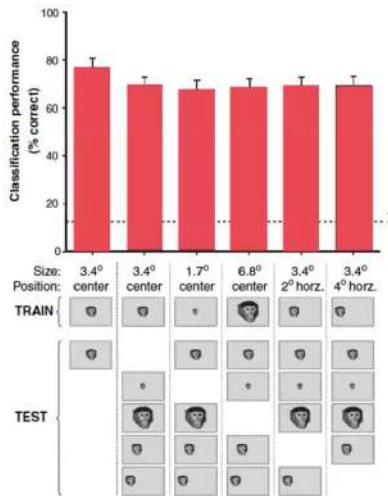


Figure 8.149

After training, the classifier was used to decode the responses to novel stimuli.

¹⁹¹ Neural activity recorded by the cortex directly on the cortex with a surface electrode not on the skull but directly to the cortex.

The classifier performance is maintained high over a range of object positions and scales, even for novel objects.

A one-versus-all approach¹⁹² was used whereby for each class of stimuli (8 classes for categorization, 77 classes for identification, 3 classes for scale and position readout), one binary classifier was trained.

Recognition performance is what downstream neurons (for instance PFC neurons) could, in theory, perform by simply computing a weighted sum of IT spikes over a short time interval (100 to 300 ms interval divided into bins of 50 ms in this case).

This is notable considering the high trial-to-trial variability of cortical neurons. Objects could be reliably categorized and identified (with less than 10% reduction in performance) even when transformed (spatially shifted or scaled), although the classifier only saw each object at one particular scale and position during training.

Reference: '*Hung et al., Science, 2005*'.

¹⁹²The one-versus-all (OvA) approach, also known as one-versus-the-rest (OvR) or one-against-all, is a strategy used in machine learning classification problems, particularly in scenarios where there are multiple classes. In this approach, a single classifier is trained for each class, treating that class as the positive class and all other classes as the negative class. Here's how the one-versus-all approach works:

- Binary Classification for Each Class: For each class in the multi-class problem, a binary classifier is trained. The goal is to distinguish instances of that particular class from all other classes.

Bibliography

- [1] Gazzaniga, Ivry, Magnum, *Cognitive Neuroscience: the biology of the mind, Fifth Edition*, W. W. Norton & Company, 2018.
- [2] Kandel, *Principles of Neural Science, Sixth Edition*, McGraw-Hill, 2021.
- [3] Sutton, R. S. & Barto, A. G. *Reinforcement learning: An introduction.*, MIT press, 2018.
- [4] Papers cited in the chapters.