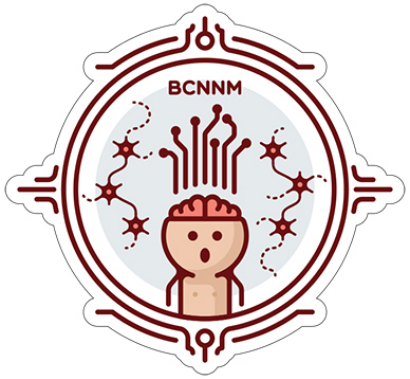

Computational Neuroscience

Lecture 1: Introduction

| Dmitry Bozhko | Georgy Galumov | Sofia Kolchanova | Vladislav Myrov |

Course team

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Agenda

- What is neuroscience
- What we do need to compute here
- Scope of interest
- What will be in the course

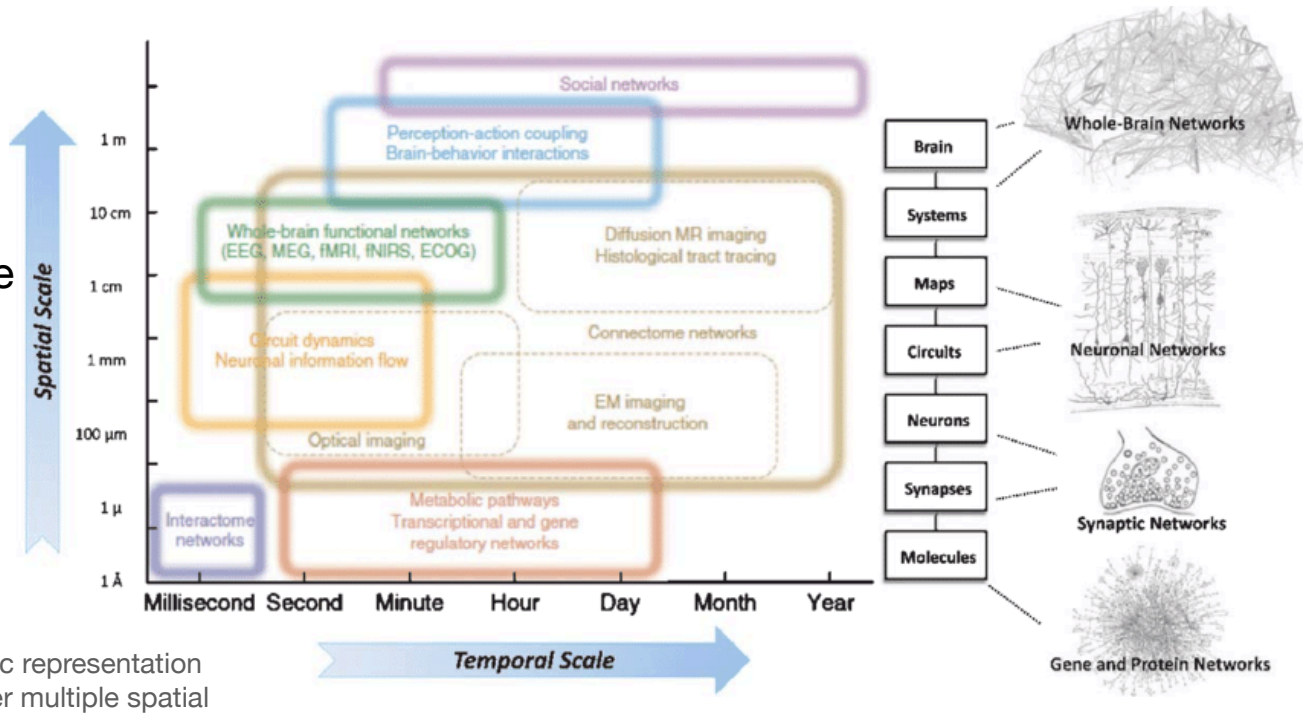
Definitions

Neuroscience

Neuroscience is the scientific study of the nervous system. It is an interdisciplinary field of science that combines physiology, anatomy, molecular biology, developmental biology, cytology, mathematical modelling and psychology to understand the fundamental and emergent properties of neurons and neural circuits.

Modern neuroscience:

- Molecular and cellular neuroscience
- Neural circuits and systems
- Cognitive and behavioural neuroscience
- Computational neuroscience
- Translational research and medicine



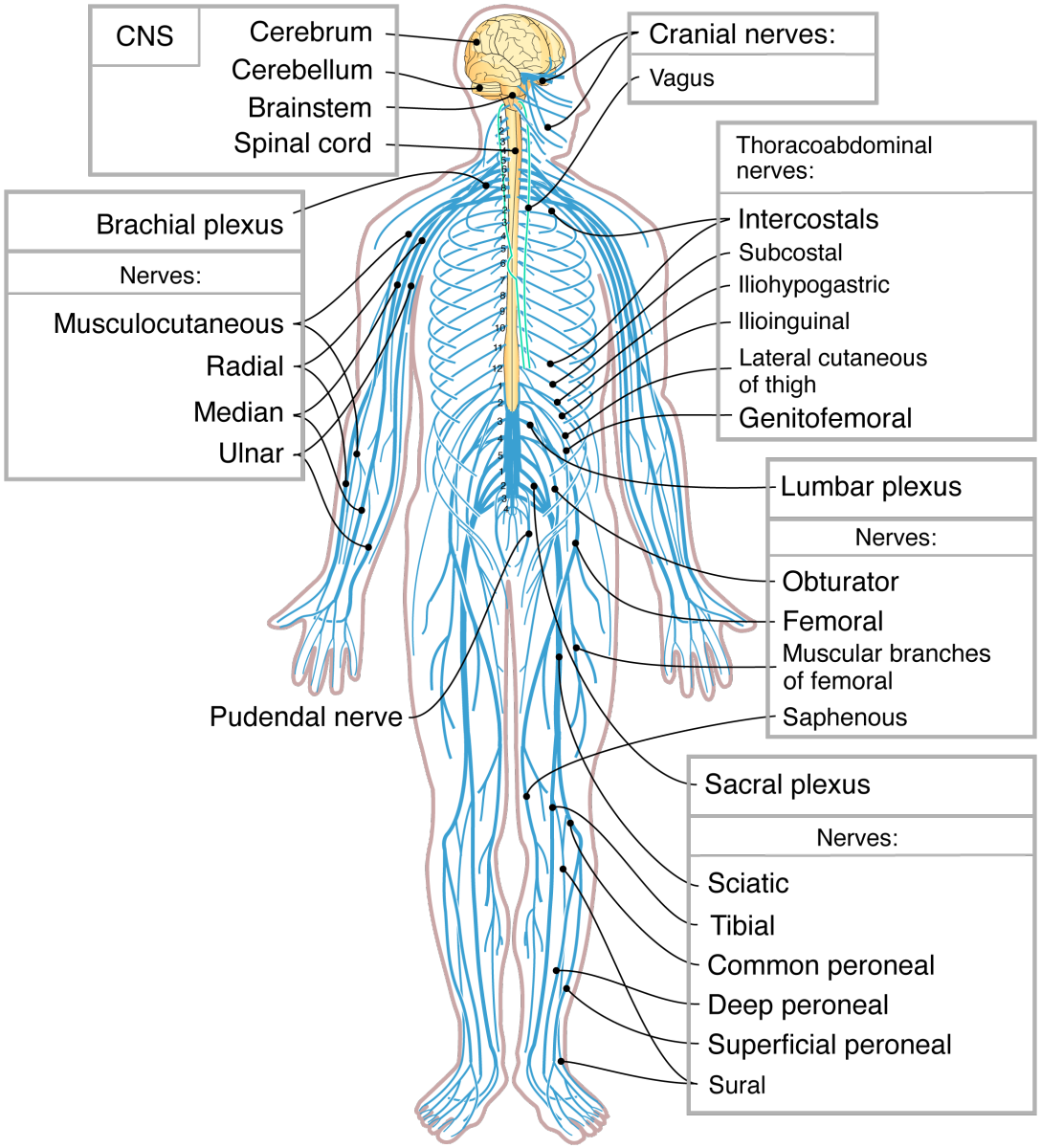
Systems neurophysiology and network neuroscience: schematic representation of how structural levels within the nervous system integrate over multiple spatial and temporal scales. doi:10.3233/JAD-179932.

Neurobiology

Neurobiology is the study of cells of the nervous system and the organisation of these cells into functional circuits that process information and mediate behaviour. It is a sub-discipline of both biology and neuroscience.

The scientific study of the nervous system increased significantly during the second half of the 20th century, principally due to advances in molecular biology, electrophysiology, and computational neuroscience.

- How it is structured?
- How it works?
- How it develops?
- How it malfunctions?
- How it can be changed?



Computations

What and Why

What

- **Theoretical neuroscience** - capturing the essential features of the biological system at multiple spatial-temporal scales, from membrane currents, and chemical coupling via network oscillations, columnar and topographic architecture, all the way up to behaviour
- **Neural data science** - electrophysiological or imaging data, the fitting of models to data, and the comparison of models

Why

- Insight
- Prediction
- Integration

Computations

Approaches

Typically sensory input is considered "**bottom-up**", and higher cognitive processes, which have more information from other sources, are considered "**top-down**".

Top-Down — is characterised by a high level of direction of sensory processing by more cognition, such as goals or targets.

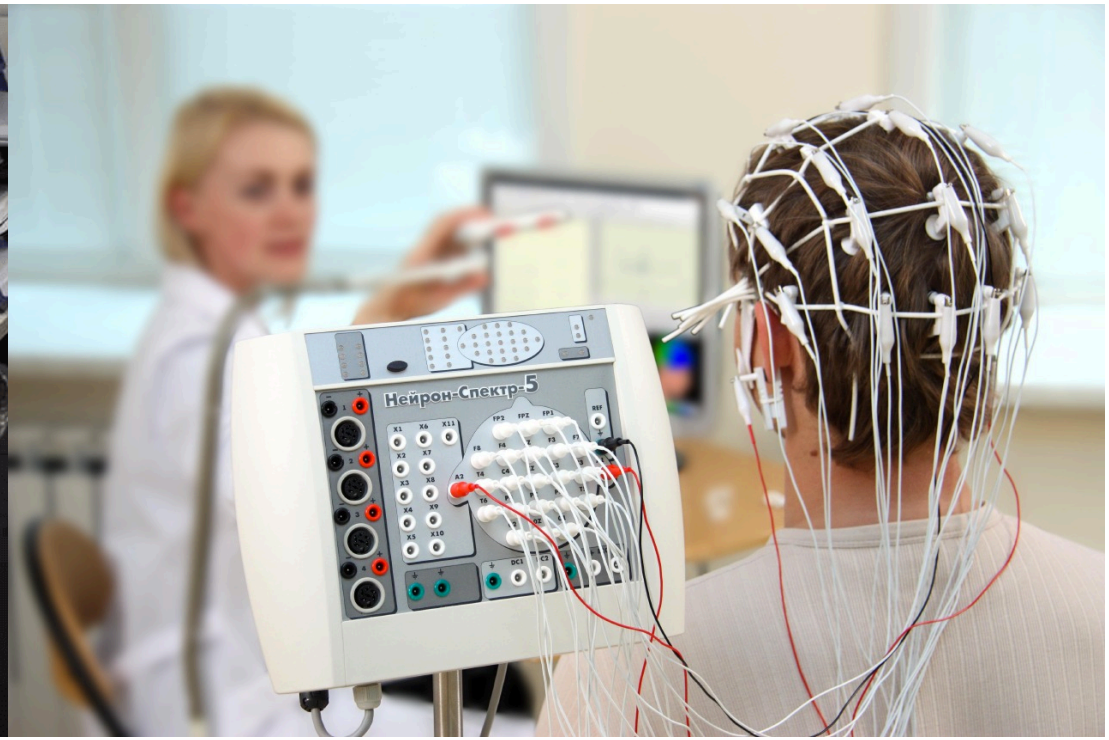
Bottom-Up - is characterised by an absence of higher level direction in sensory processing. Psychology defines bottom-up processing as an approach wherein there is a progression from the individual elements to the whole.

Computations
Scope of interest

- Data processing and analysis (EEG, PET, fMRI)
- Modelling: neuron, development, pathology, tissue & behaviour of networks
- Sensory processing and motor control
- Connectomics and structures mapping
- Memory and synaptic plasticity
- Learning and cognition
- Consciousness
- Clinical neuroscience

Data acquisition

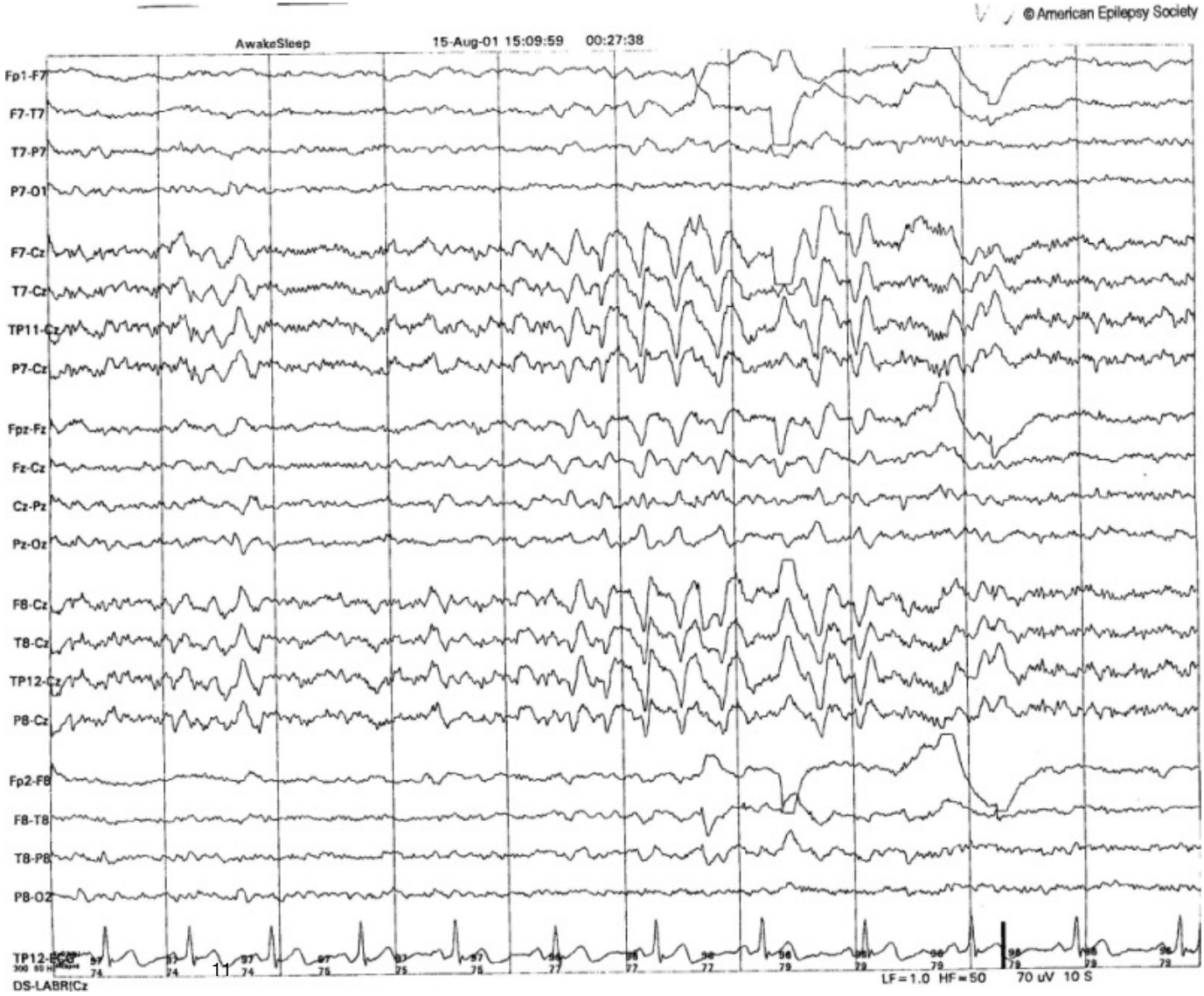
EEG



Data sources
EEG

Electroencephalography (**EEG**) is an electrophysiological monitoring method to record electrical activity of the brain.

It is typically *noninvasive*, with the electrodes placed along the scalp, although invasive electrodes are sometimes used, as in *electrocorticography*, sometimes called *intracranial EEG*.



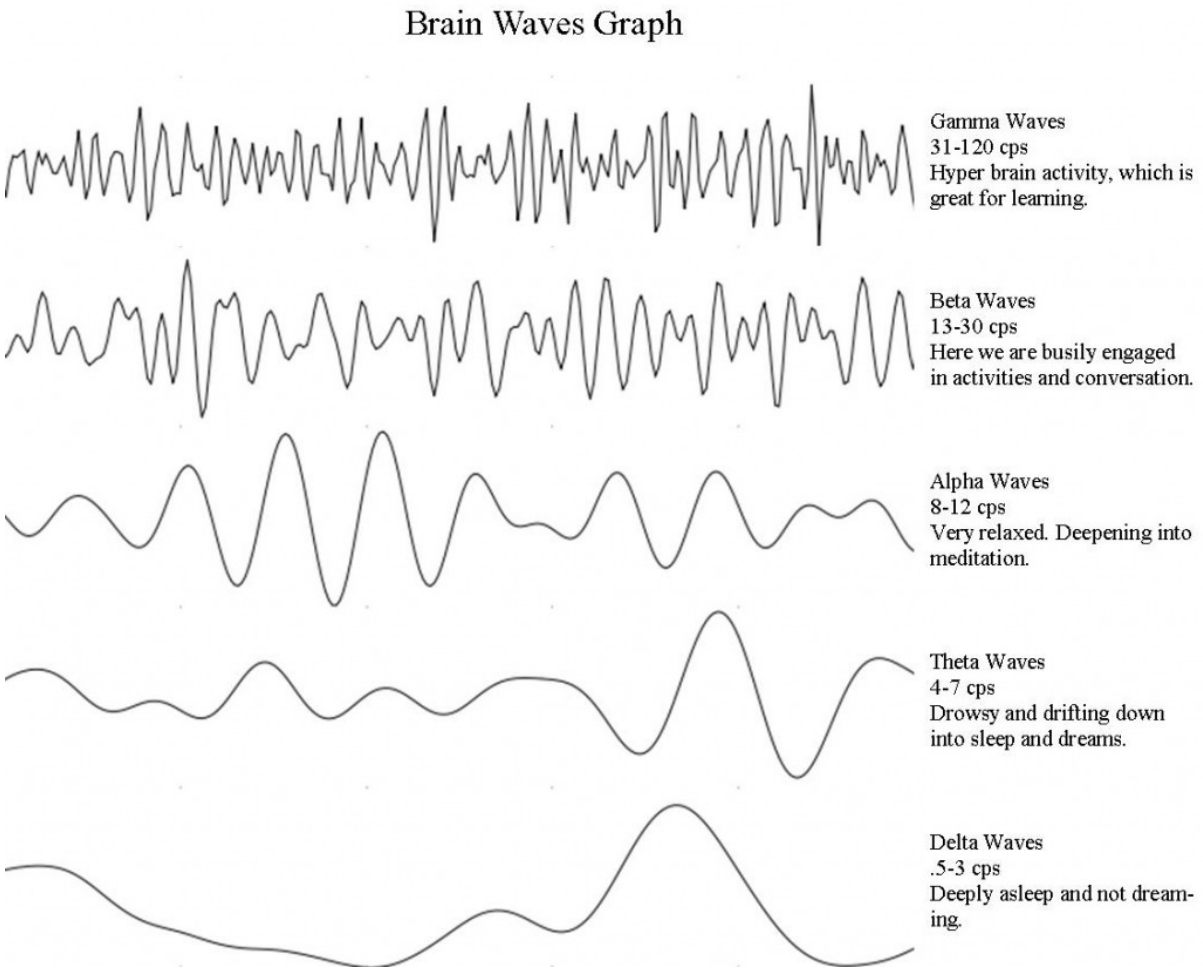
REM sleep EEG

© Electroencephalography (EEG): An Introductory Text and Atlas of Normal and Abnormal Findings in Adults, Children, and Infants

Data sources

Brain waves

- α-waves (alpha) - resting wakefulness
- β-waves (beta) - active wakefulness, active concentration, ¿REM-sleep?
- γ-waves (gamma) correlated with large scale brain network activity, working memory, attention. Altered γ observed in Alzheimer's, epilepsy and schizophrenia patients.
- δ-waves (delta) - natural deep sleep, drugs deep sleep, coma.
- θ-waves (theta) - hyppocampal waves (not cortical), correlated with REM sleep.

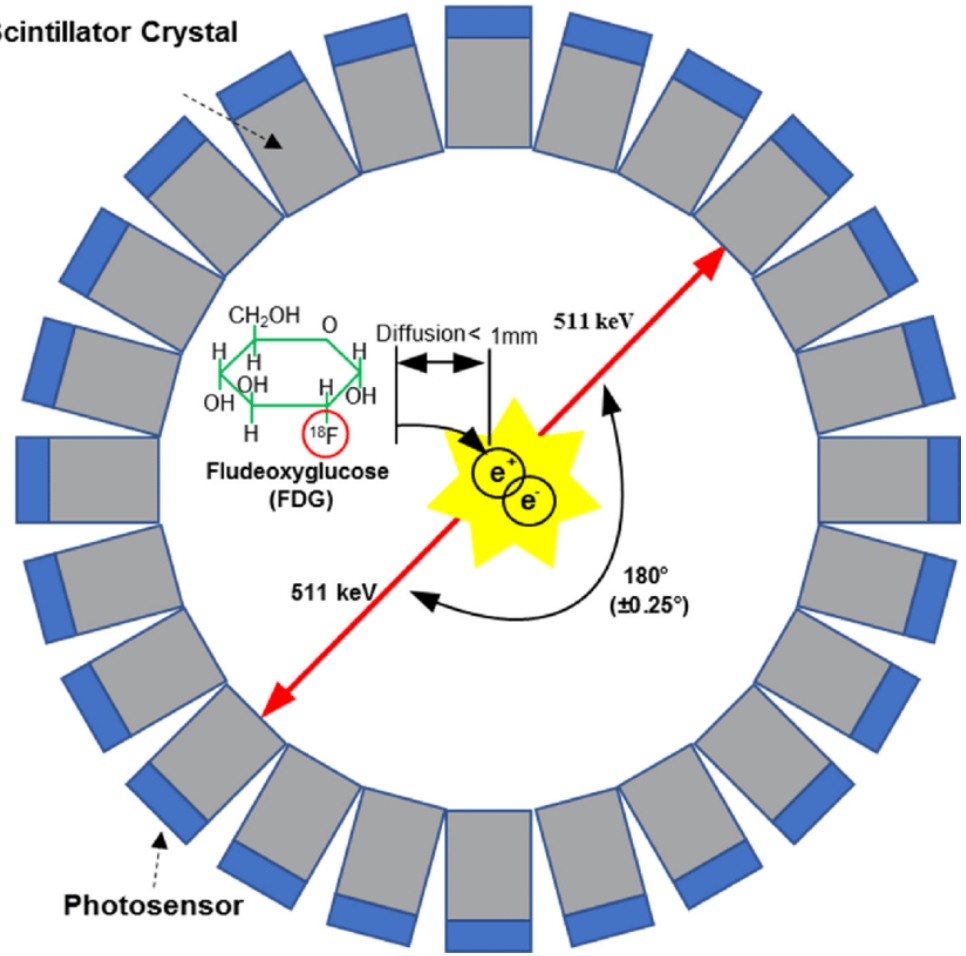


Data processing
PET

Positron-emission tomography (PET) is an imaging technique that uses radioactive substances to visualize and measure metabolic processes in the body.

The longest-lived radioisotope is 18F; it has a half-life of 109.739 minutes.

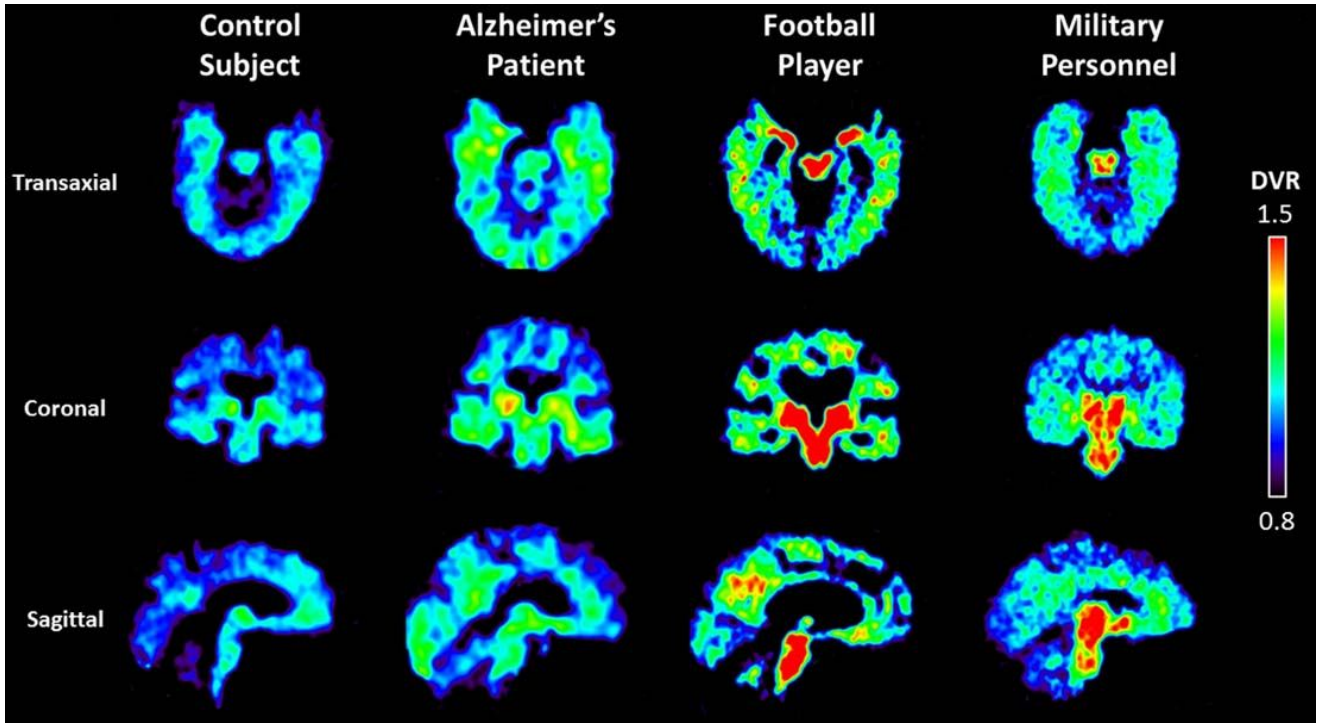
FDG, is a radiopharmaceutical used in the medical imaging modality positron emission tomography (PET). Chemically, it is 2-deoxy-2-[18F]fluoro-D-glucose, a glucose analog, with the positron-emitting radionuclide **fluorine-18** substituted for the normal hydroxyl group at the C-2 position in the glucose molecule.



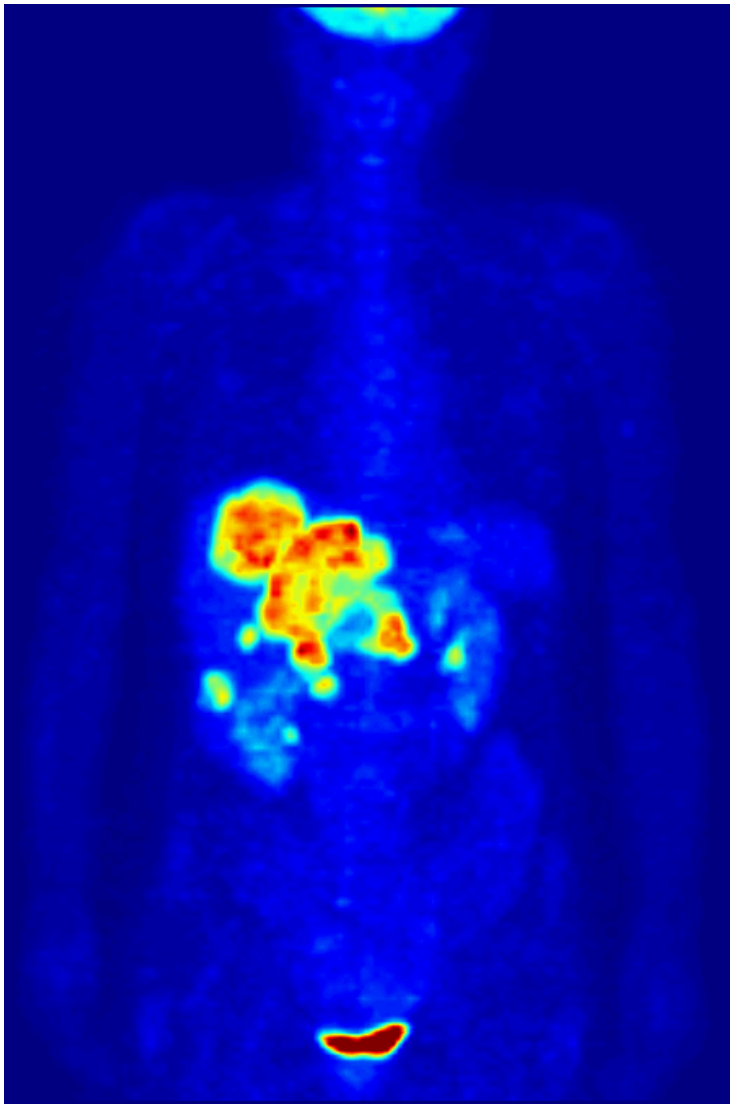
© Jiang, Chalich, Deen
Sensors for Positron Emission Tomography Applications

PET

Examples



Examples of FDDNP-PET DVR transaxial, coronal, and sagittal images
of a cognitively healthy individual, Alzheimer's disease patient, football player, and a military subject.
© J Alzheimers Dis. 2018; 65(1): 79–88.doi: 10.3233/JAD-171152

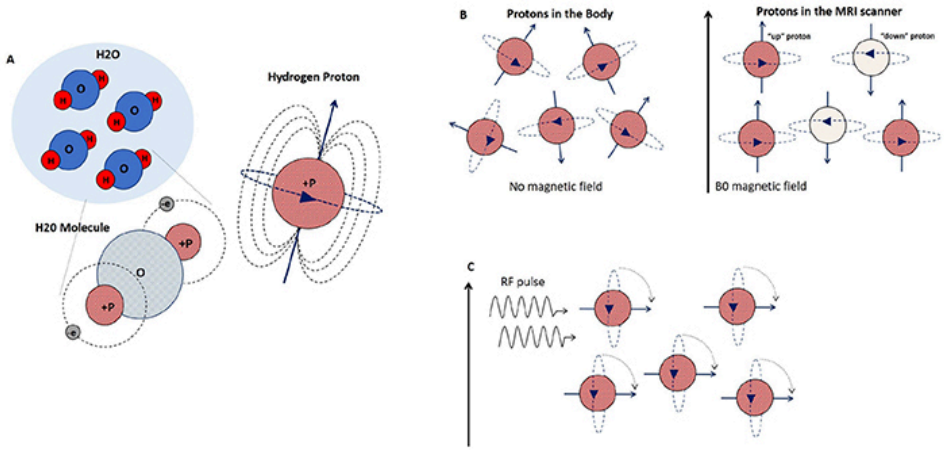


Whole-body PET scan using ^{18}F-FDG. © Public domain

Data processing

MRI

Magnetic resonance imaging (MRI) is a medical imaging technique used in radiology to form pictures of the anatomy and the physiological processes of the body. MRI scanners use strong magnetic fields, magnetic field gradients, and radio waves to generate images of the organs in the body. MRI does not involve X-rays or the use of ionizing radiation, which distinguishes it from CT and PET scans.

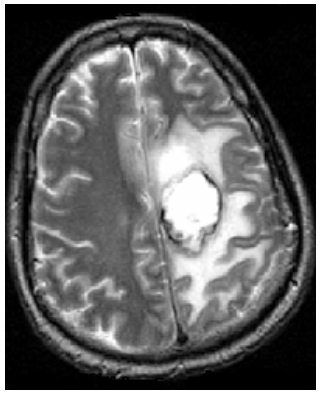


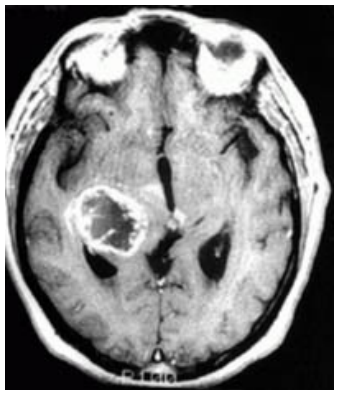
There are many types of MRI exist. High-resolution MRI is used for imaging of tissue, functional MRI is used for continuous monitoring of tissue functioning.

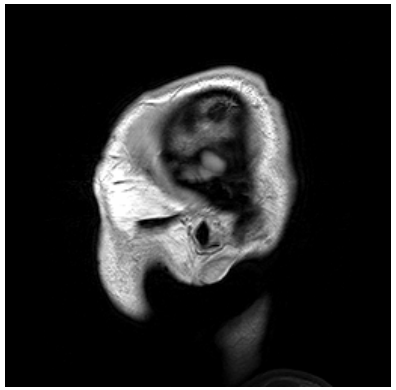
Hydrogen protons and how they behave in a magnetic field. doi: 10.3389/frym.2019.00023

MRI

Examples

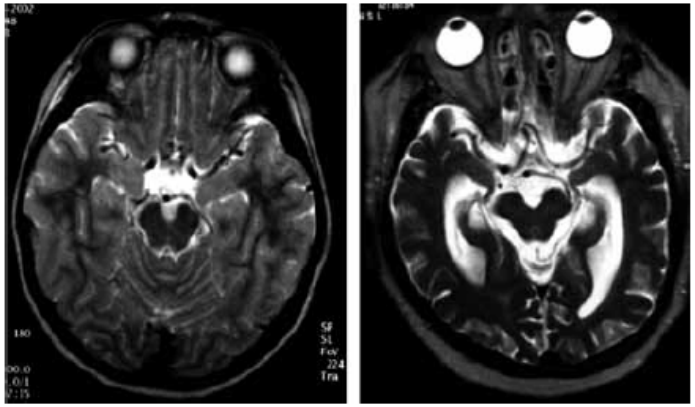




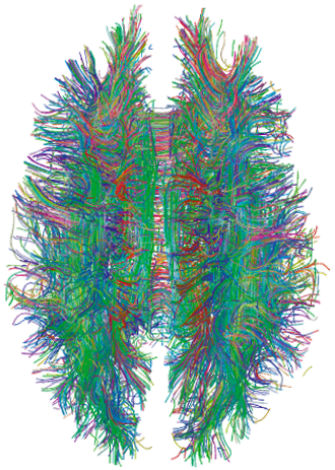


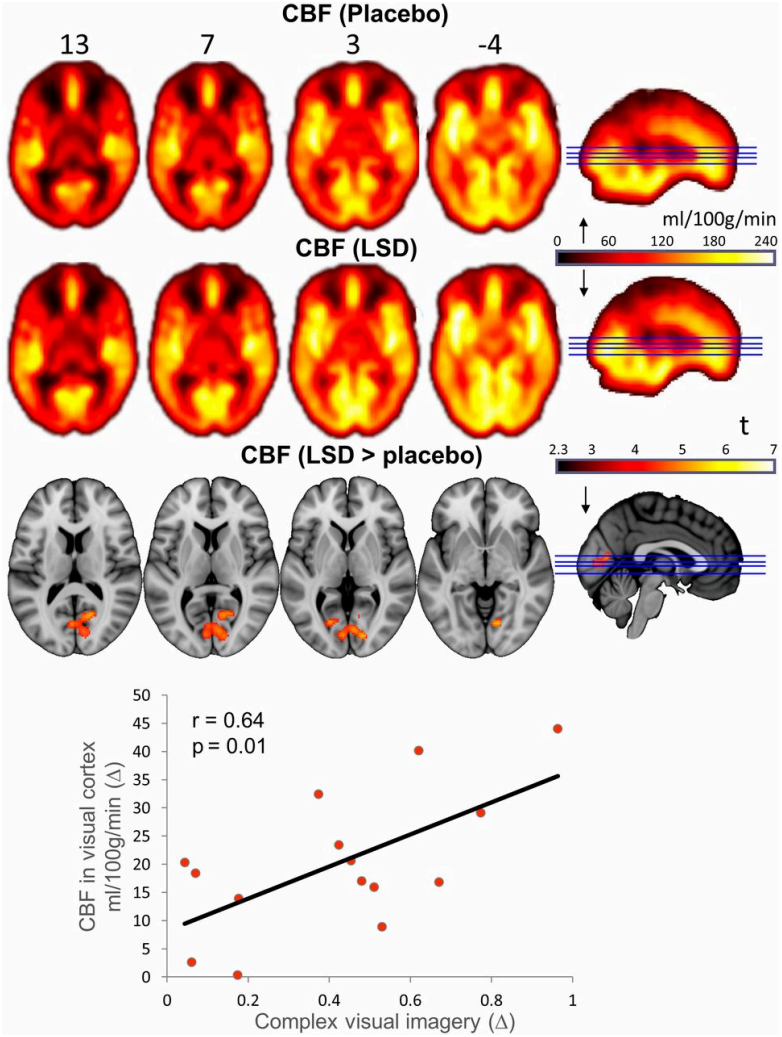
Normal

AD



Compliment of Scanning Department, St. Teresa's Hospital





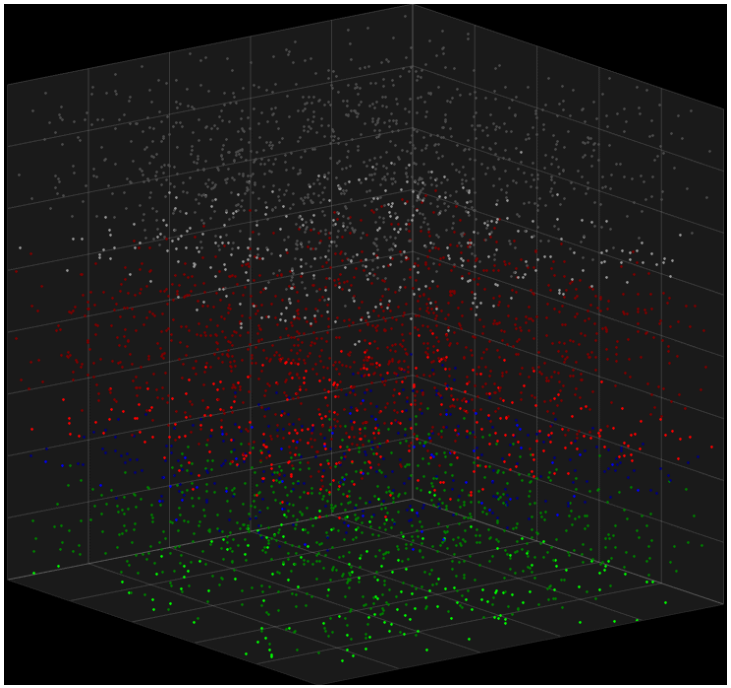
L1-1, L1-2: MRI of glioblastoma. https://www.oncolink.org/print/pdf/8858
L1-3: An animated gif of MRI images of a human head. © Dwayne Reed
L2-1: MRI comparison between a normal control and patient with AD.
The affected individual shows atrophy of brain tissues. https://www.stepwards.com/?page_id=6128
L2-2: MRI diffusion tensor imaging of white matter tracts. doi:10.1371/journal.pone.0004006
R: Whole-brain cerebral blood flow maps for the placebo and LSD conditions, plus the difference map (cluster-corrected, P < 0.05; n = 15). https://doi.org/10.1073/pnas.1518377113

Modelling

Modelling

Electrical input–output membrane voltage models

- Integrate-and-fire/Leaky integrate-and-fire (1907 by Louis Lapicque)
- Hodgkin–Huxley (1952; Nobel Prize by 1963)
- Galves-Löcherbach (2013 by Antonio Galves and Eva Löcherbach)
- Compartmental models

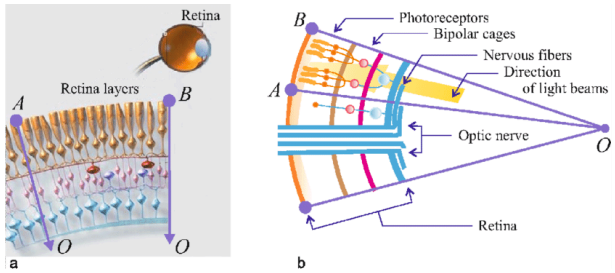


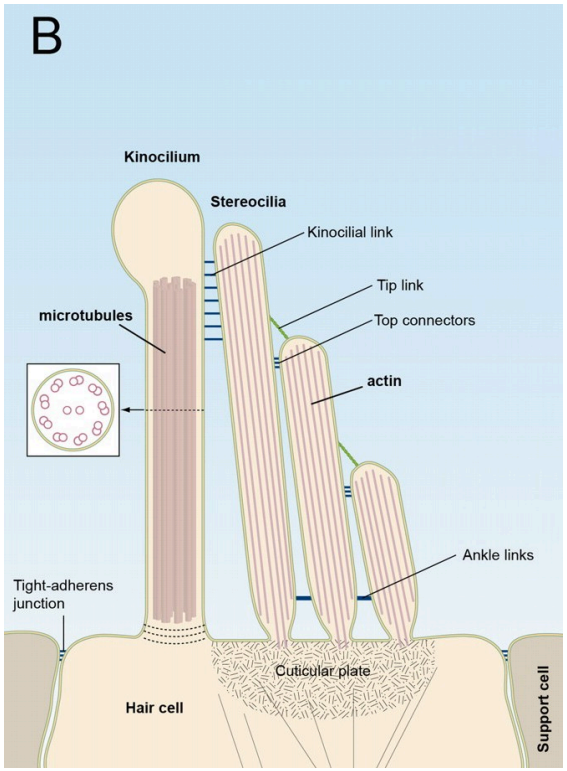
3D visualization of the Galves–Löcherbach model for biological neural nets. This visualization is set for 4,000 neurons (4 layers with one population of inhibitory neurons and one population of excitatory neurons each) at 180 intervals of time.

Modelling

Natural input stimulus neuron models

- The non-homogeneous Poisson process model (Siebert)
- The two state Markov model (Nossenson & Messer)





Modelling

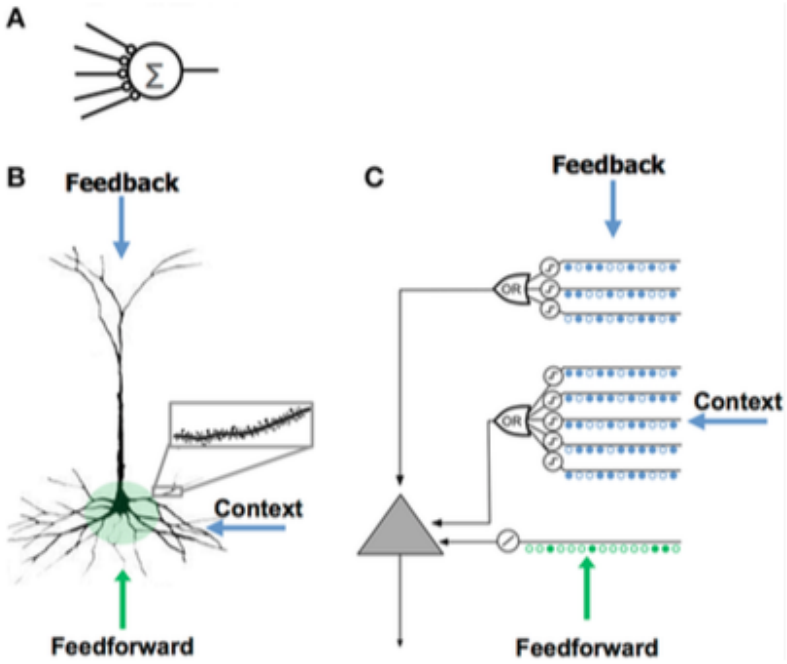
Pharmacological input stimulus neuron models

Pharmacological input stimulus neuron models

- Synaptic transmission (Koch & Segev)
- The two state Markov model (Nossenson & Messer)

Modelling

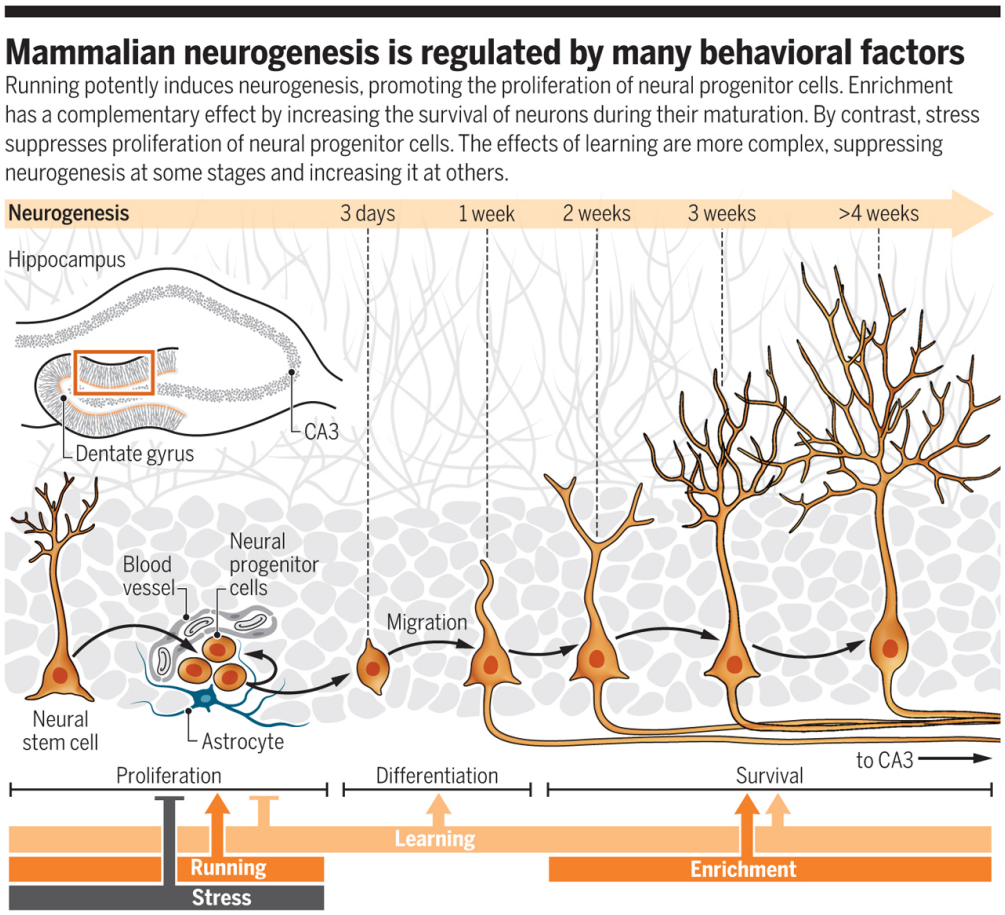
Hierarchical temporal memory



Modelling

Development

- How do neuron precursor cells know how to differentiate?
- How do neurons migrate to the proper position in the central and peripheral systems?
- How do axons and dendrites form during development?
- How do axons know where to target and how to reach these targets?
- How do synapses form?



Adult neurogenesis in mammals. doi: 10.1126/science.aav6885

Modelling

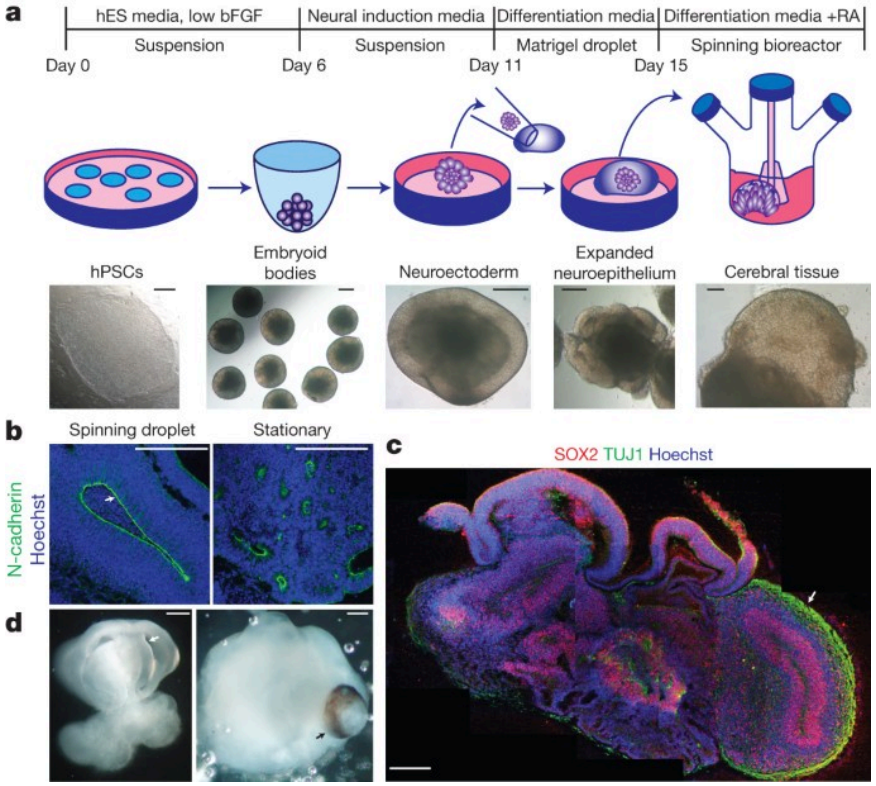
Pathology

- Cellular level pathologies (osmosis, signaling pathways, gene expression etc.)
- Tissue pathologies (proliferation, differentiation, apoptosis etc.)
- Infectious diseases
- Chemicals/drugs interaction

Modelling

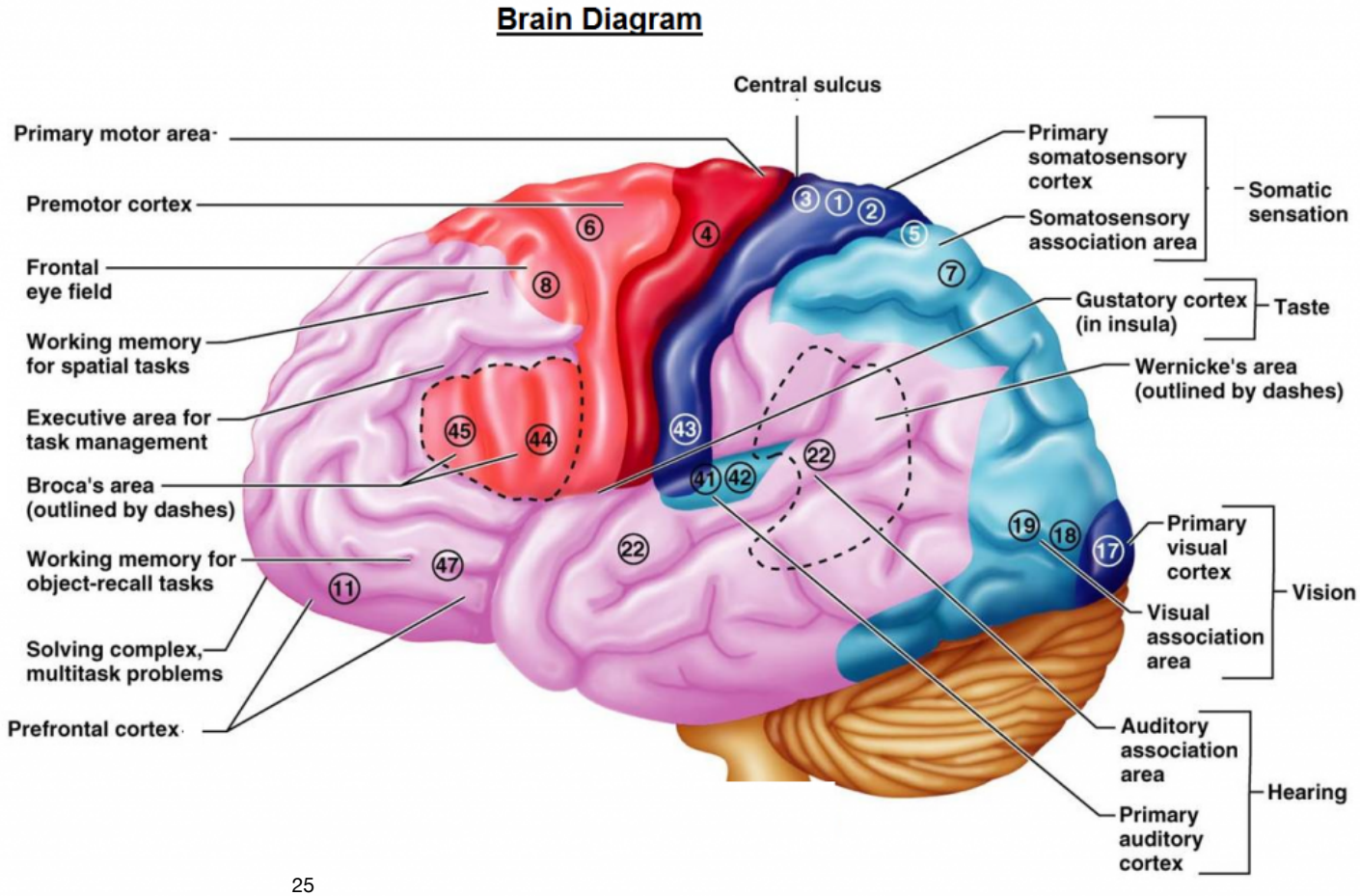
Tissue and behaviour of networks

- Mean field theory (Ising model)
- Population model (Wilson–Cowan model)
- Neural tissue simulation (organoids)
- Spiking neural networks



Connectomics and structures mapping

Model organisms



Connectomics and structures mapping

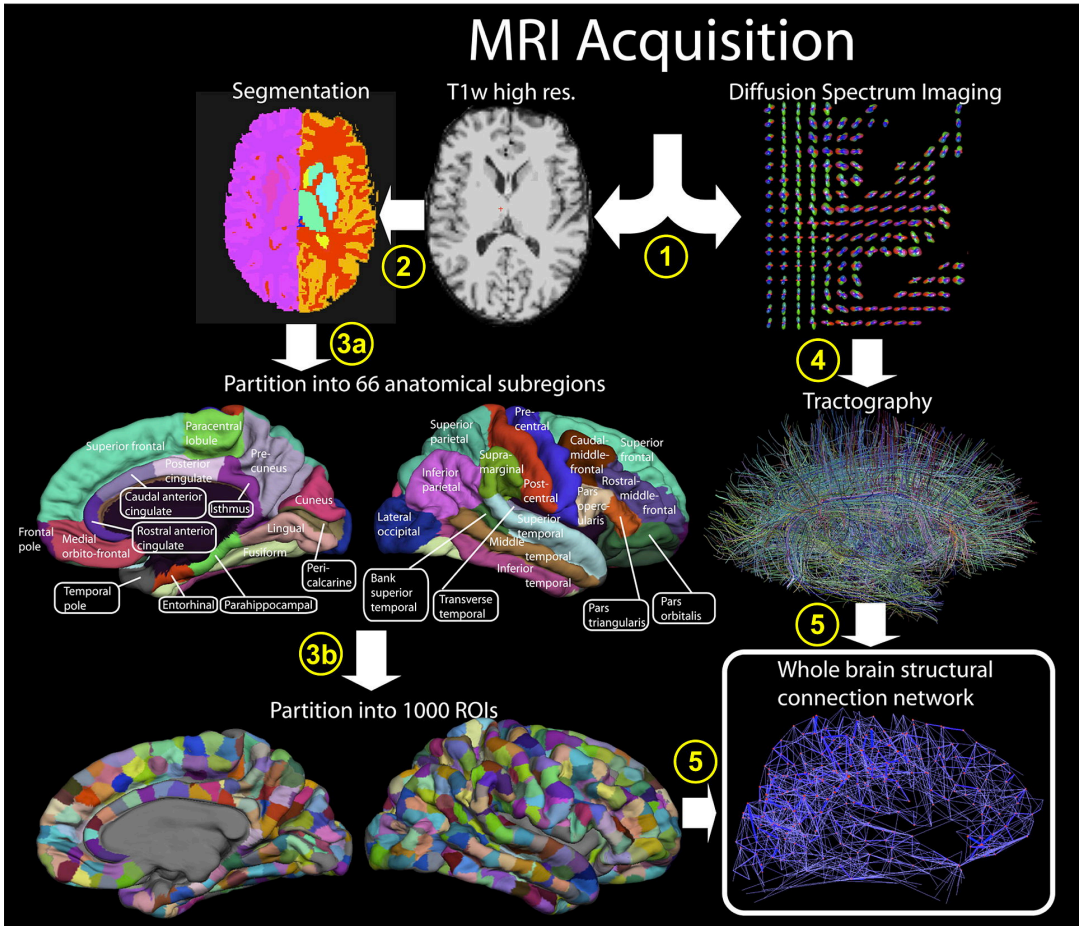
Connectomics is the study of the brain's structural and functional connections between cells, which is visualised as a *connectome*.

Model systems

- Nematode C. elegans
- Fruit fly
- Barn owl
- Mouse/rat
- Human BRAIN!

Instruments

- Neural imaging
- 3D electron microscopy
- Graph theory



Procedure for the extraction of a Whole Brain Structural Connectivity Network followed by the authors in the article *Mapping the Structural Core of Human Cerebral Cortex*, Published in PLoS Biology, Vol.6, No. 7
http://biology.plosjournals.org/archive/1545-7885/6/7/figure/10.1371_journal.pbio.0060159.g001-L.jpg

Memory and synaptic plasticity research

Hebb's postulate

When an axon of cell A is near enough to excite a cell B and repeatedly or persistently takes part in firing it, some growth process or metabolic change takes place in one or both cells such that A's efficiency, as one of the cells firing B, is increased.

Directions of research

- Hebbian learning
- Working memory or short-term memory models (Baddeley and Hitch, Prefrontal cortex basal ganglia working memory)
- Short-term + long-term memory (Atkinson–Shiffrin memory model)
- Search of associative memory (SAM) models
- Stereochemically detailed models of the acetylcholine receptor-based synapse

Learning and Cognition

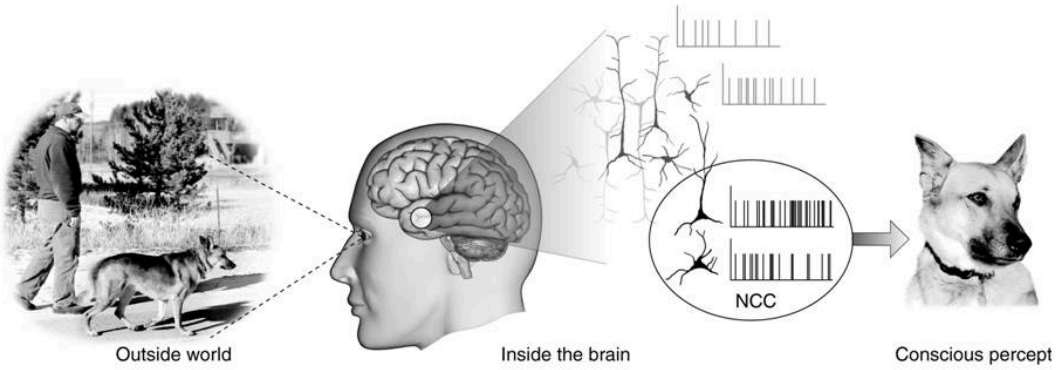
- Visual attention
- Identification
- Categorisation
- Decision making
- Reaction
- Reinforcement (molecular level)
- Default-mode networks

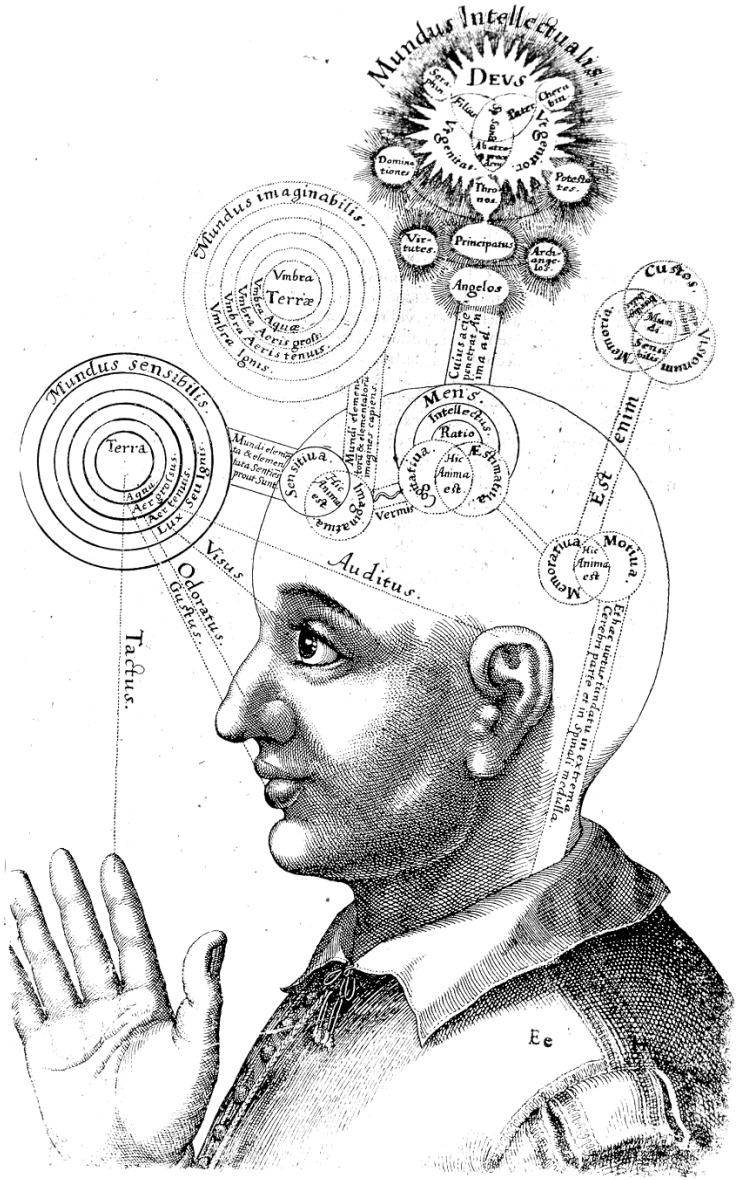
Consciousness

Ultimate goal: explain the everyday experience of conscious life.

Francis Crick, Giulio Tononi and Christof Koch made some attempts to formulate consistent frameworks for future work in **neural correlates of consciousness (NCC).**

Much of the work in this field remains speculative.





L: Schema of the neural processes underlying consciousness, Christof Koch
R: Representation of consciousness from the 17th century by Robert Fludd, an English Paracelsian physician.

Clinical neuroscience

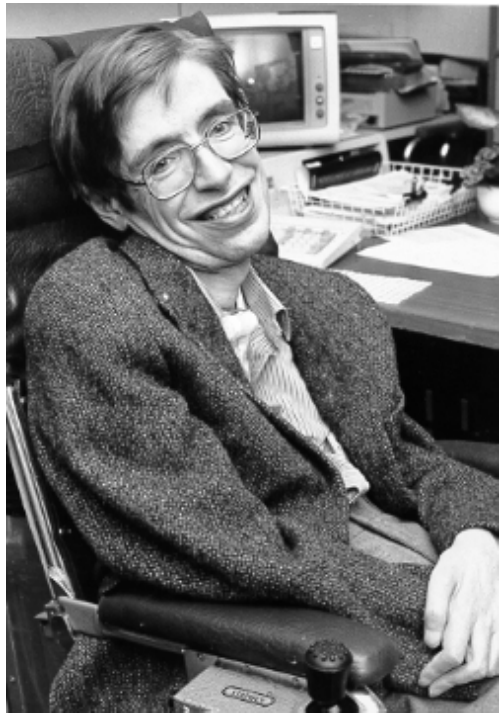
Clinical neuroscience

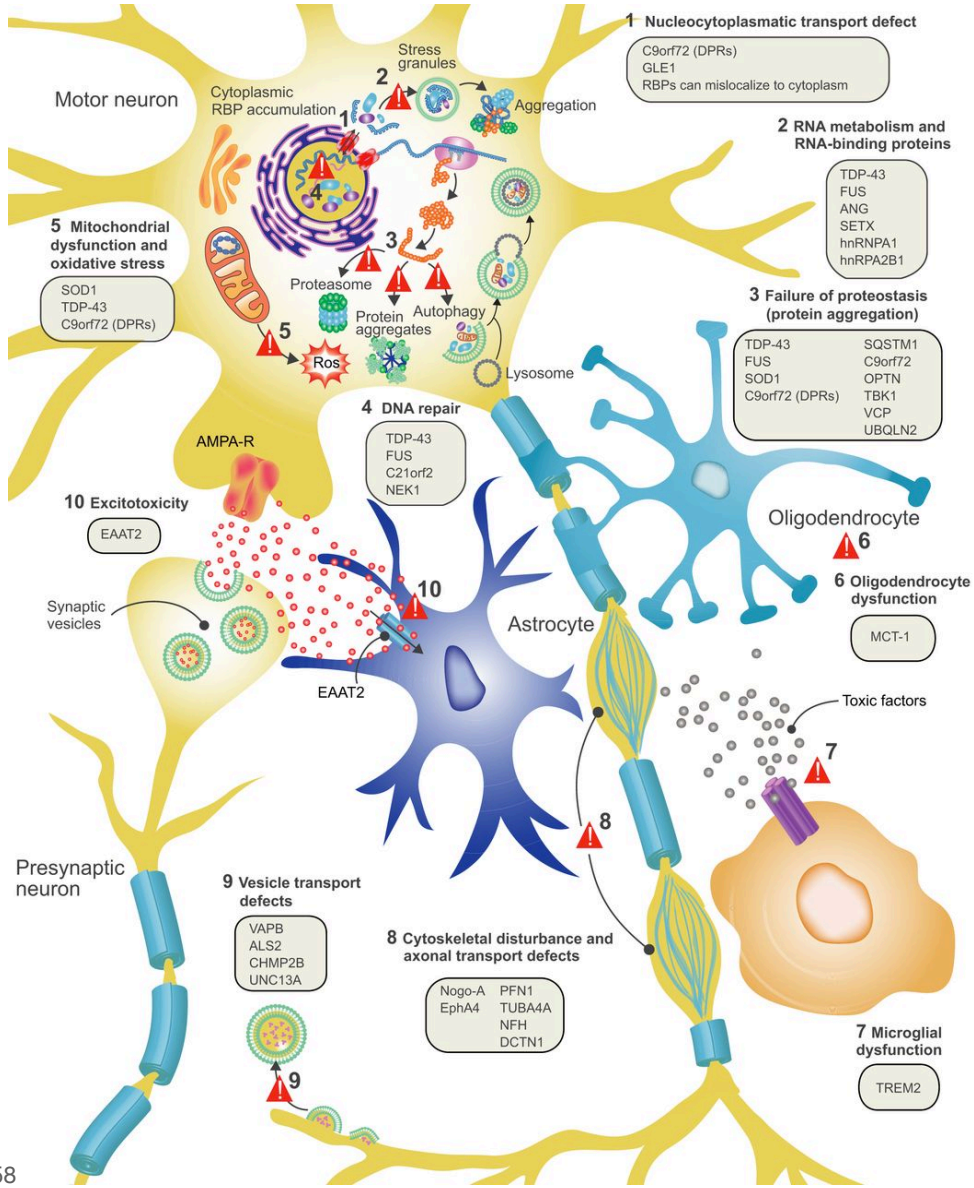
Mental & psychiatric diseases

- Mortal neurological diseases (ALS, AD, PD, Hantington)
- Neurodevelopmental disorders (autism spectrum disorders, motor disorders, ADHD)
- Anxiety disorders (panic disorder, PTSD, OCD)
- Personality disorders (odd or eccentric disorders, dramatic, emotional or erratic disorders, anxious or fearful disorders)
- Psychotic disorders (schizophrenia, bipolar disorder, sleep deprivation)

Neurodegenerative diseases

Amyotrophic lateral sclerosis

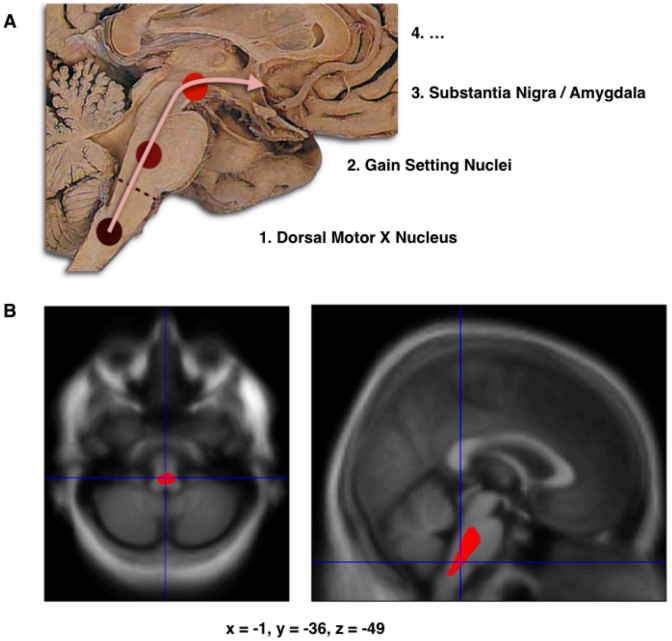




L: The French neurologist Jean-Martin Charcot coined the term amyotrophic lateral sclerosis in 1874.
C: Stephen Hawking had a rare early-onset slow-progressing form of ALS.
R: Ten proposed disease mechanisms for ALS and the genes associated with them. doi:10.1242/dmm.029058

Neurodegenerative diseases

Parkinson's disease



L-A: Schematic initial progression of Lewy body deposits in the first stages of Parkinson's disease, as proposed by Braak and colleagues. doi/10.1371/journal.pone.0008247.g001
L-B: Localization of the area of significant brain volume reduction in initial PD compared with a group of participants without the disease in a neuroimaging study, which concluded that brainstem damage may be the first identifiable stage of PD neuropathology.
C1: Handwriting of a person affected by PD.
C2: First page of James Parkinson's landmark 1817 work.
R: A man with Parkinson's disease displaying a flexed walking posture pictured in 1892.

Catherine Metzger
13 Octobre 1869

AN

ESSAY

ON THE

SHAKING PALSY.

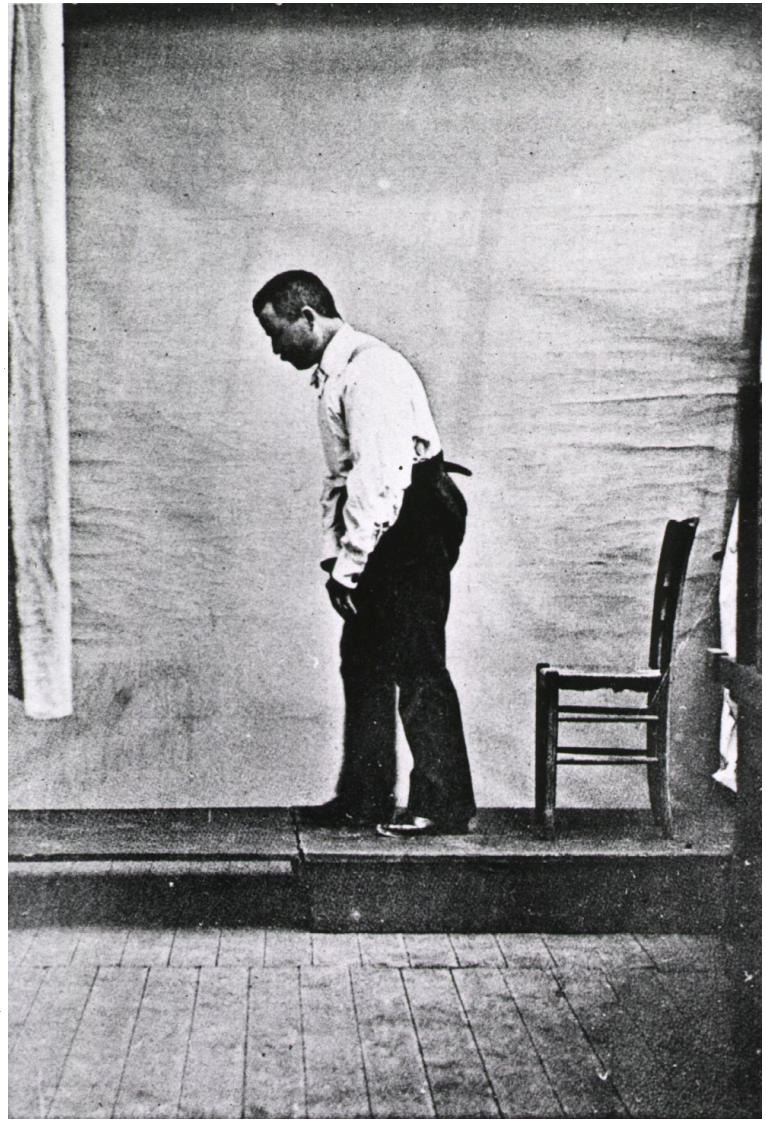
CHAPTER I.

DEFINITION—HISTORY—ILLUSTRATIVE CASES.

SHAKING PALSY. (*Paralysis Agitans.*)

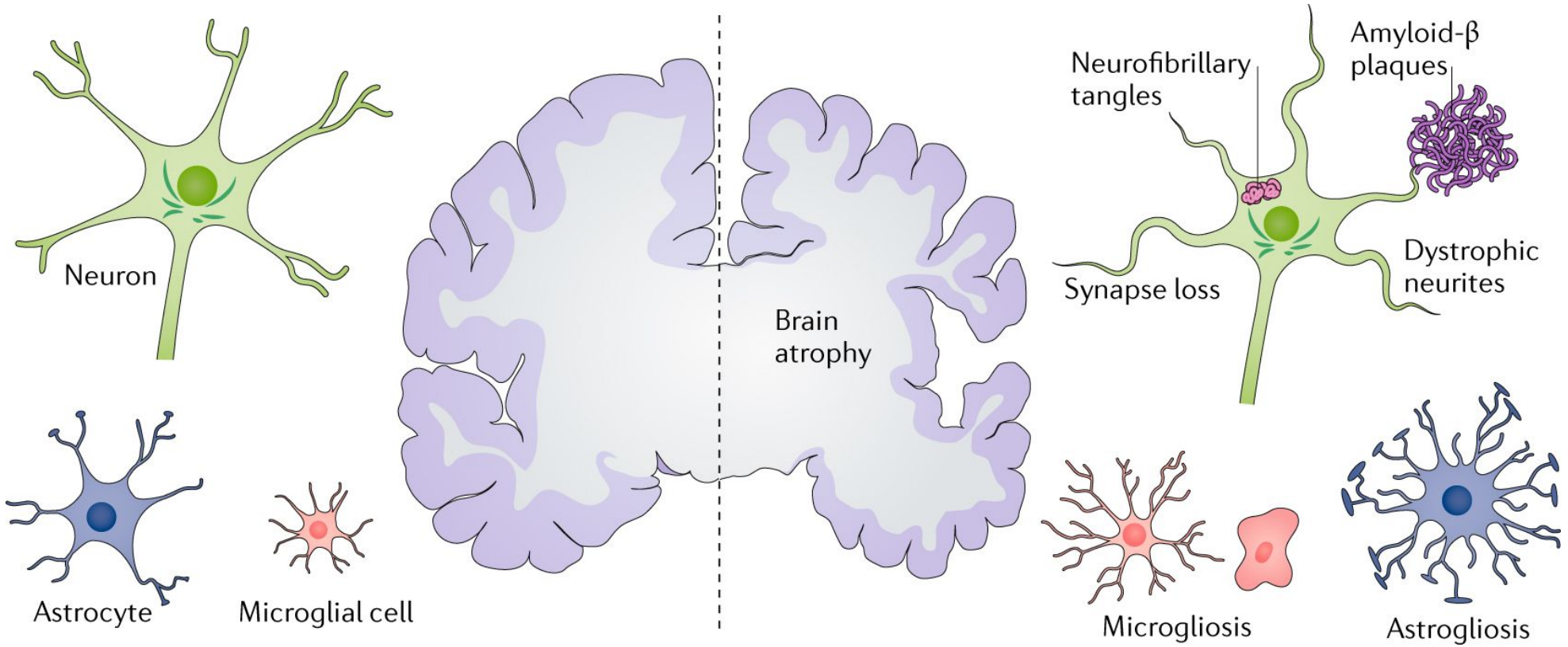
Involuntary tremulous motion, with lessened muscular power, in parts not in action and even when supported; with a propensity to bend the trunk forwards, and to pass from a walking to a running pace: the senses and intellects being uninjured.

33



Neurodegenerative diseases

Alzheimer's disease



Neurodegenerative diseases

Huntington's disease

THE

MEDICAL AND SURGICAL REPORTER.

No. 789.] PHILADELPHIA, APRIL 13, 1872. [Vol. XXVI.—No. 15.

ORIGINAL DEPARTMENT.

Communications.

ON CHOREA.

By George Huntington, M. D.,

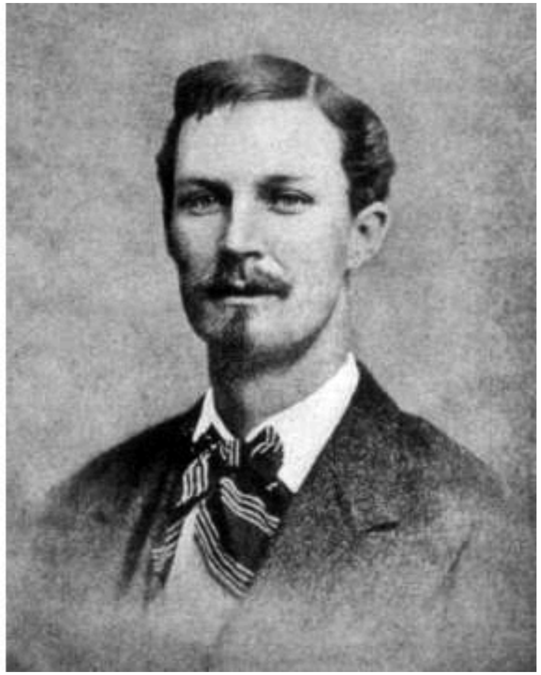
Of Pomeroy, Ohio.

Essay read before the Meigs and Mason Academy of Medicine at Middleport, Ohio, February 15, 1872

Chorea is essentially a disease of the nervous system. The name "chorea" is given to the disease on account of the *dancing* propensities of those who are affected by it, and it is a very appropriate designation. The disease, as it is commonly seen, is by no means a dangerous or serious affection, however distressing it may be to the one suffering from it, or to his friends. Its most marked and char-

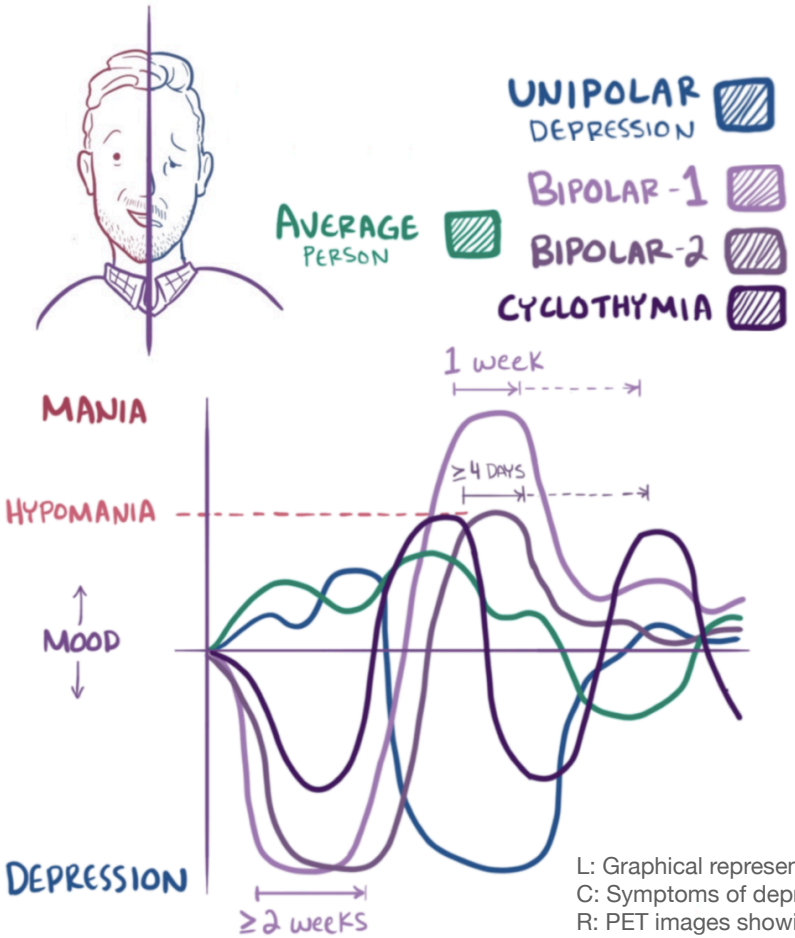
The upper extremities may be the first affected, or both simultaneously. All the voluntary muscles are liable to be affected, those of the face rarely being exempted.

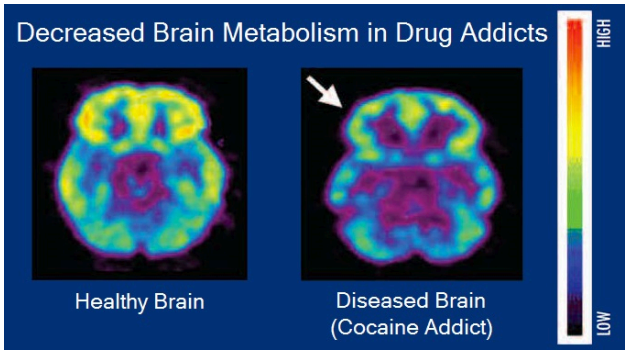
If the patient attempt to protrude the tongue it is accomplished with a great deal of difficulty and uncertainty. The hands are kept rolling—first the palms upward, and then the backs. The shoulders are shrugged, and the feet and legs kept in perpetual motion; the toes are turned in, and then everted; one foot is thrown across the other, and then suddenly withdrawn, and, in short, every conceivable attitude and expression is assumed, and so varied and irregular are the motions gone through with, that a complete description of

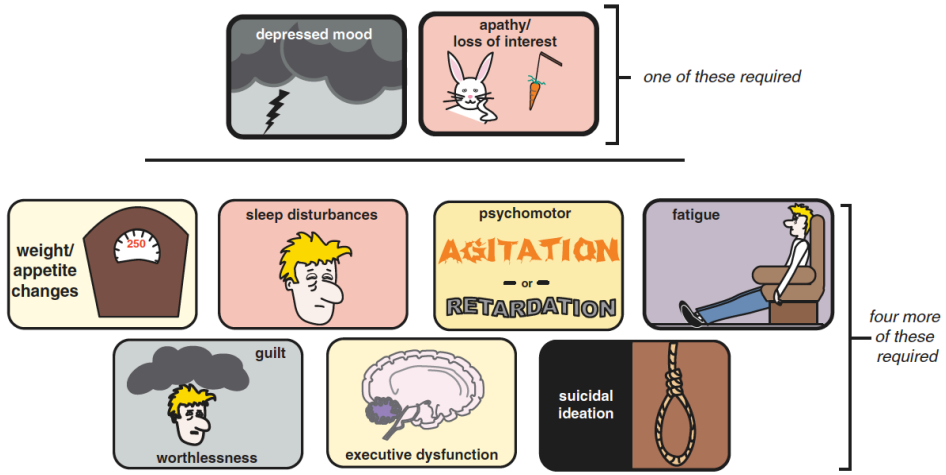


L: Coronal section from an MR brain scan of a patient with HD, showing atrophy of the heads of the caudate nuclei, enlargement of the frontal horns of the lateral ventricles (hydrocephalus ex vacuo), and generalized cortical atrophy. https://radiopaedia.org/articles/huntington-disease
R: In 1872 George Huntington described the disorder in his first paper "On Chorea" at the age of 22.

Psychopharmacology







L: Graphical representation of Bipolar disorder and Cyclothymia.
C: Symptoms of depression. Stahl's essential psychopharmacology. Cambridge University Press.
R: PET images showing brain metabolism in drug addicts vs controls. Drs. Nora Volkow and Heinrich Schelbert, National Institutes of Health (NIH).

The course

Lectures

1. Introduction (Georgy G.)
2. Biological perspective (Sofia K.)
3. Neuron physiology and biophysics (Dmitriy B.)
4. Neuron models (Dmitriy B.)
5. EEG: how to work with it (Vladislav M.)
6. Conductances and morphology models (Dmitriy B.)
7. Neurotransmitters and receptors (Georgy G.)
8. Seminar
9. Neural encoding (Dmitriy B.)
10. Plastisity and learning (Dmitriy B.)
11. Spiking networks: biology and application (Vladislav M.)
12. Regulation of neuron functioning (Georgy G.)
13. Neural tissue development (Sofia K.)
14. ML and computational neuroscience (Vladislav M.)
15. Final exam/Final Q&A

Quizes & Homeworks

There will be quiz after every lecture.

Homeworks:

1. Hodgkin-Huxley Model
2. Practice with EEG data
3. Chemical synapse model
4. Spiking network model

Contacts

Course repository: https://github.com/JetBrains-Research/cncourse2020

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Questions?