Physics of the Brain, and Analyzing the Brain Networks with QEEG for Better Treatment of Neural Disorders

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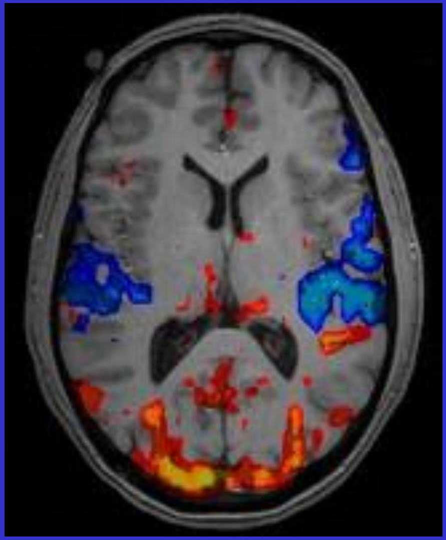
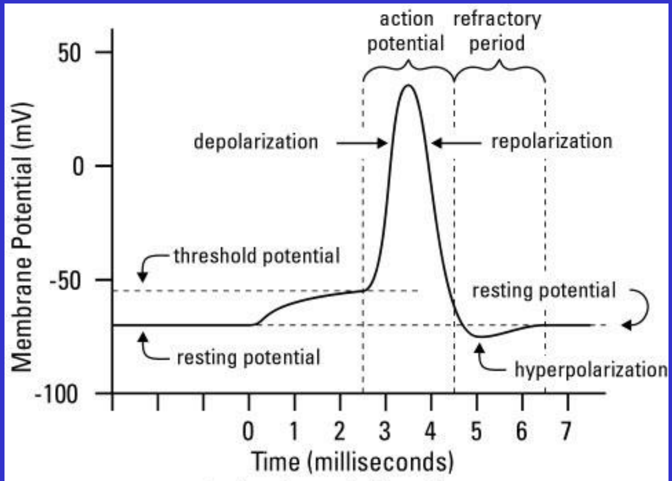
Neuroscience & Neurophysics

- Neuroscience explores the brain and its relationship with mind.
- An interdisciplinary science which applies different approaches and methods to study the nervous system.
- Nervous system (including Brain) is among the most complex systems in nature.



- Physics has the power to simplify complex systems to get them under control and predict their behavior.
- Neurophysics deal with the development and use of physical experimental tools in order to gain information about the nervous system on nuclear, atomic or molecular level.

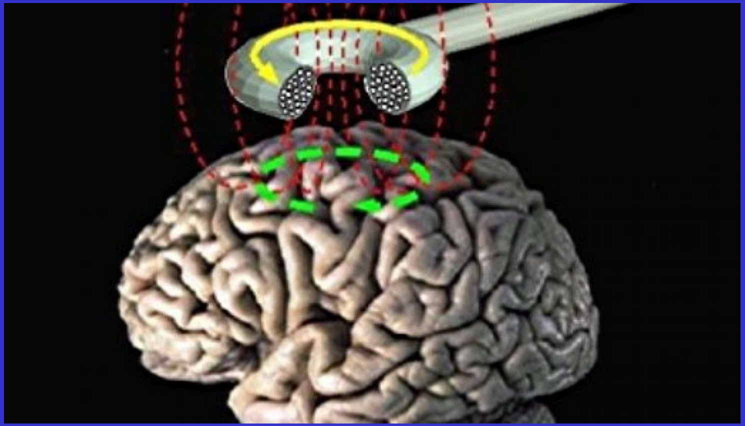


Action Potential in a Neuron

Neurophysics & Neurotechnology

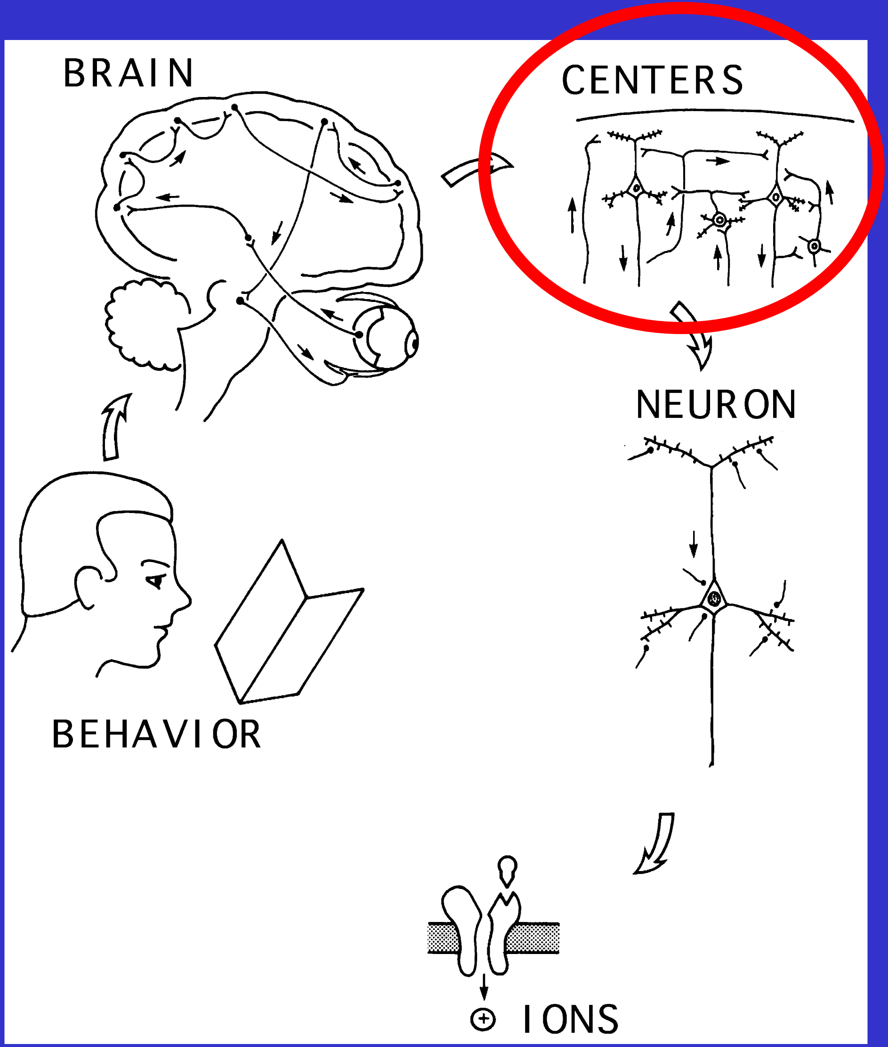
- Neurophysics helps for diagnosis and treatment of neurological disorders.

- Computational Neuroscience employs mathematical models, theoretical analysis and abstractions of the brain to understand the principles that govern the development, structure, information-processing, physiology and cognitive abilities of the nervous system.

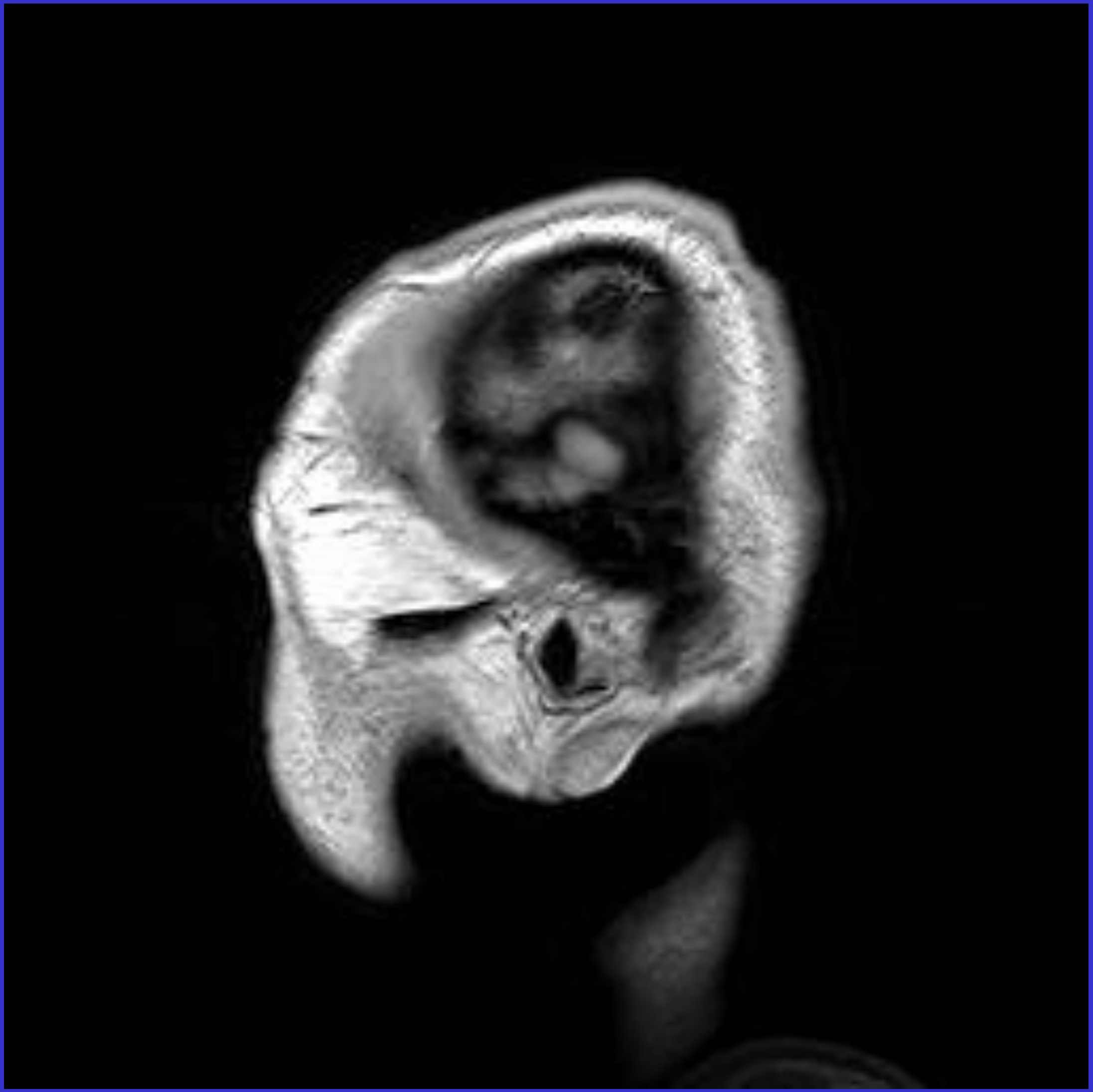


Introduction to Neurophysics

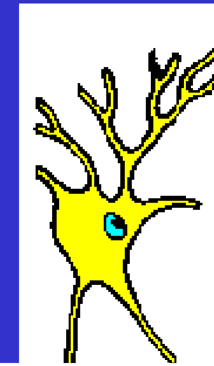
- The fundamental task of the nervous system is to communicate and process information.
- The basic structural units of the nervous system are individual neurons.
- Neurons convey neural information by virtue of electrical and chemical signals.

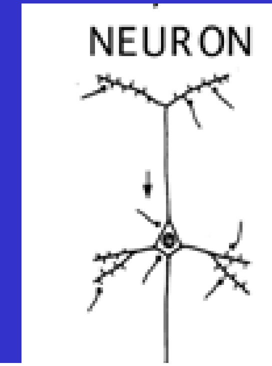


Physics of the Brain

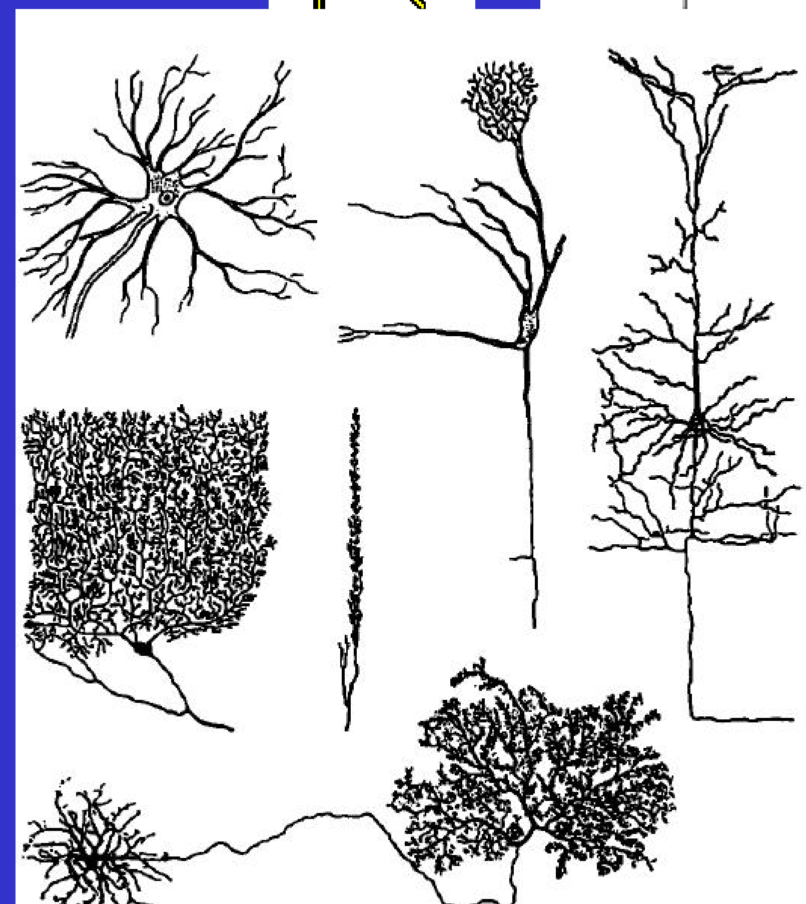


Neurons are the basic structural units of N.S.



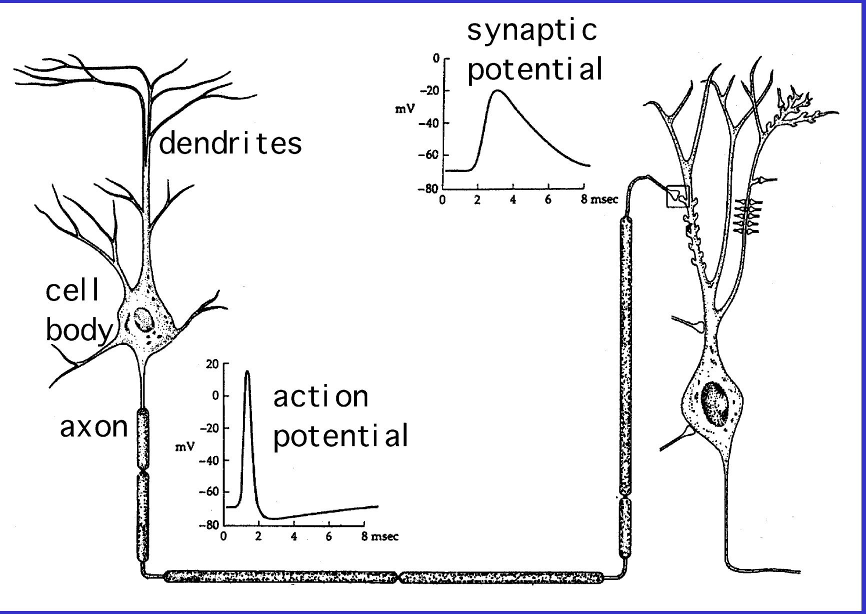


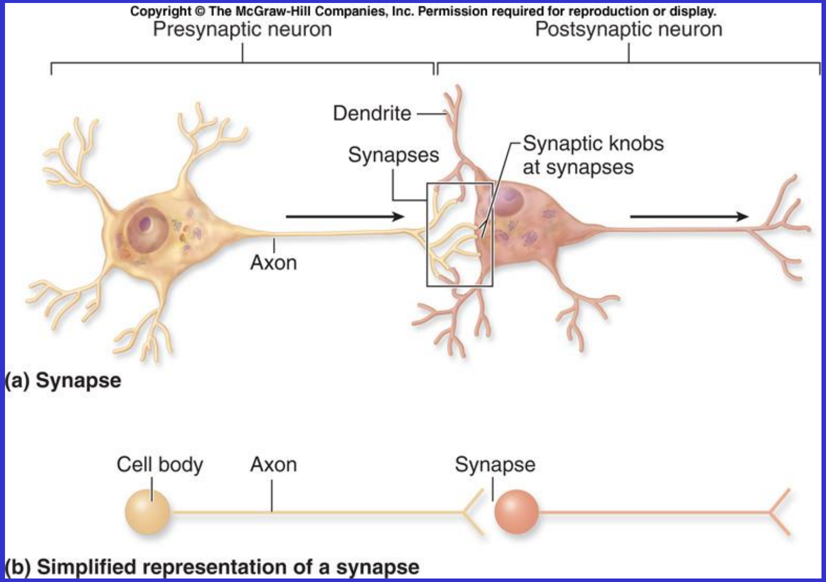
- In the human nervous system there are about 10^{12} neurons.
- Cells in the nervous system exhibit extraordinary morphological and functional diversities (from a few μm to 2 meters).
- Some neurons have large, flamboyant dendrites, whereas others have no dendrites or axons.
- The number of different morphological classes of neurons in the vertebrate brain is estimated to be near 10,000.



Neurons communicate through synapses

- Synapse: specialized contact zone
- There are about 10^{15} synapses in a human brain.
- Two types of synapses: electrical and chemical.

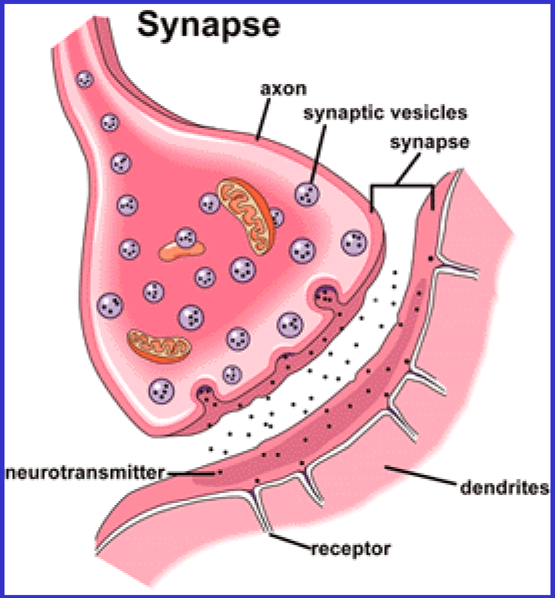


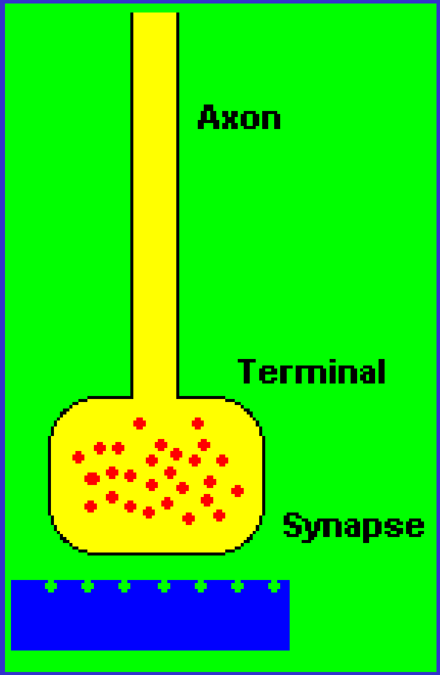


- electrical synapses contain intercellular bridging pores that allow current flow

Chemical synapses

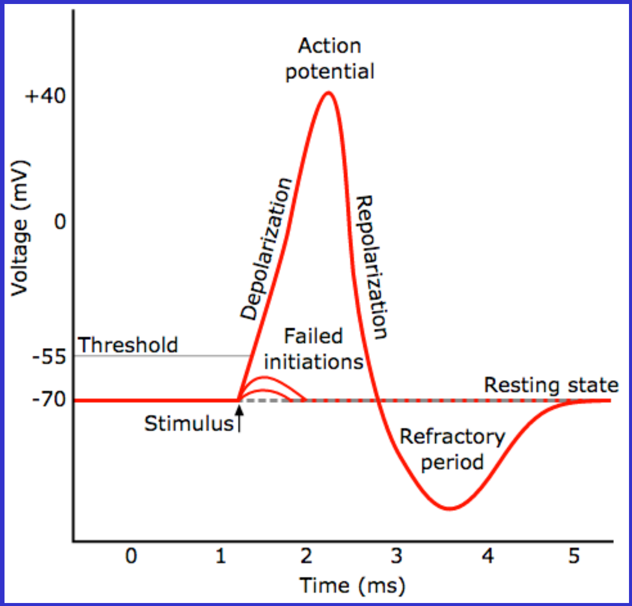
- Chemical Synapse: release chemical messengers or neurotransmitters.
- Electrical and chemical synapses can be observed with the electron microscope.
- The typical chemical synapse consists of synaptic vesicles in the presynaptic neuron and membrane thickening in the presynaptic and postsynaptic membranes (active zones).
- The patterns of synaptic connections in the nervous system are extremely complex.
- The dendrite of a mammalian motor neuron, for example, receives inputs from about 10^4 synapses.





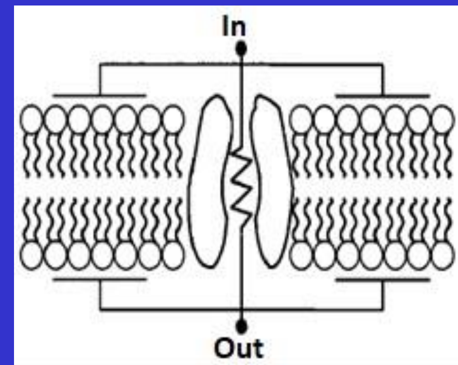
Principles of Neural Signaling

- The primary difference between neurons and most other cells in the body (e.g., liver cells) is that neurons can generate and transmit neural signals.
- In the nervous system four ion species are involved in transmembrane currents: sodium (Na^+), potassium (K^+), calcium (Ca^{2+}), and chloride (Cl^-).
- Concentration gradients set up the electrochemical potential across the membrane, which drives ion flow in accordance with the laws of diffusion and drift (Ohm's law).

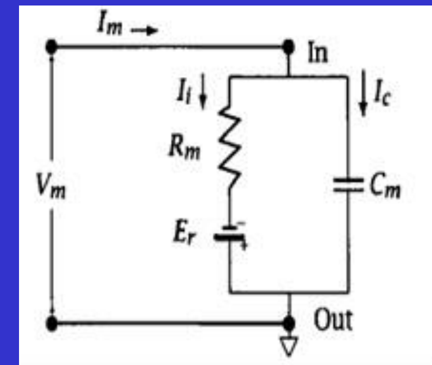


Physics principles that dictate ion movements

Cell Membrane



Model Cell Membrane



1. Fick's law for diffusion:

$$J_{diff} = -D\frac{\partial [C]}{\partial x}$$

2. Ohm's law for drift:

$$J_{drift} = \partial_{el} E = -\mu z[C]\frac{\partial V}{\partial x}$$

3. The Einstein relation between diffusion and mobility:

$$D = \frac{kT}{q}\mu$$

4. Space-charge neutrality:

$$\sum z_i^c e[C_i] = \sum z_j^A e[C_j]$$

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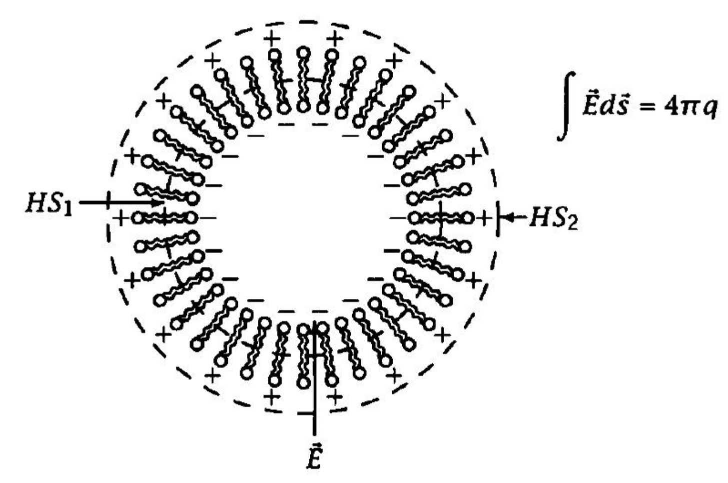
Fundamental laws of Neurophysics



1. The Nernst-Planck equation (NPE):

$$I = J.zF = -(uz^2F[C]\frac{\partial V}{\partial x} + uzRT\frac{\partial [C]}{\partial x})$$

2. The Nernst equation:

$$E_i = V_m(I_i = 0) = V_{in} - V_{out} = \frac{RT}{zF}\ln\frac{[C]_{out}}{[C]_{in}} \rightarrow E_i = 62\log_{10}\frac{[C]_{out}}{[C]_{in}}$$

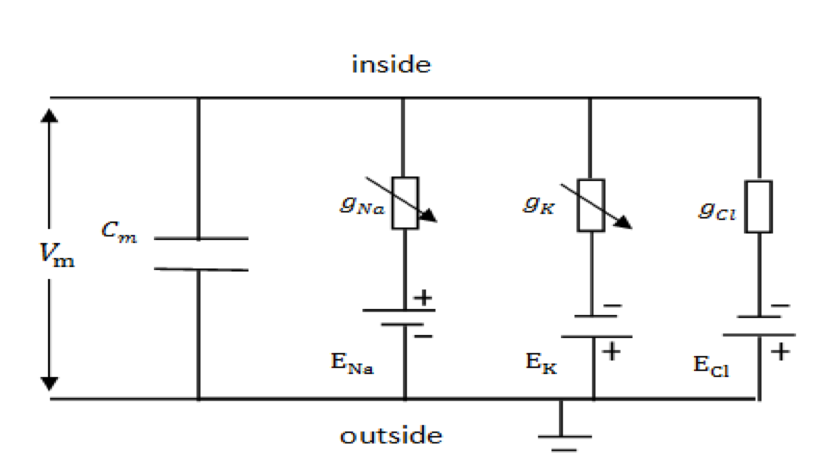
3. Donnan equation:

$$[\frac{C_{out}^{+m}}{C_{in}^{+m}}]^{\frac{1}{m}} = [\frac{A_{in}^{-n}}{A_{out}^{-n}}]^{\frac{1}{n}}.$$

4. Goldman-Hodgkin-Katz (GHK) equation:

$$V_{rest} = \frac{RT}{F}\ln\frac{P_K[K^+]_{out} + P_{Na}[Na^+]_{out} + P_{Cl}[Cl^-]_{in}}{P_K[K^+]_{in} + P_{Na}[Na^+]_{in} + P_{Cl}[Cl^-]_{out}} \rightarrow V_{rest} = \frac{RT}{F}\zeta$$

The parallel conductance model for membrane

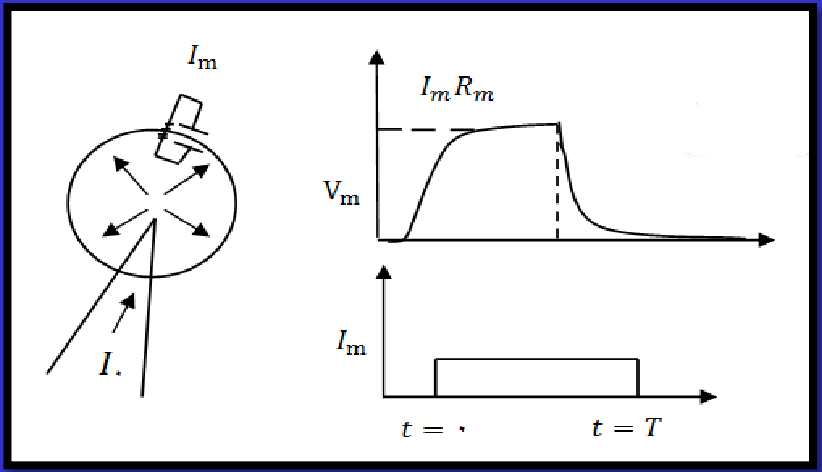


$$I_{total} = I_C + (I_K + I_{Na} + I_{Cl}) = C\frac{dV}{dt} + g_K(V - E_K) + g_{Na}(V - E_{Na}) + g_{Cl}(V - E_{Cl}).$$

At Rest:

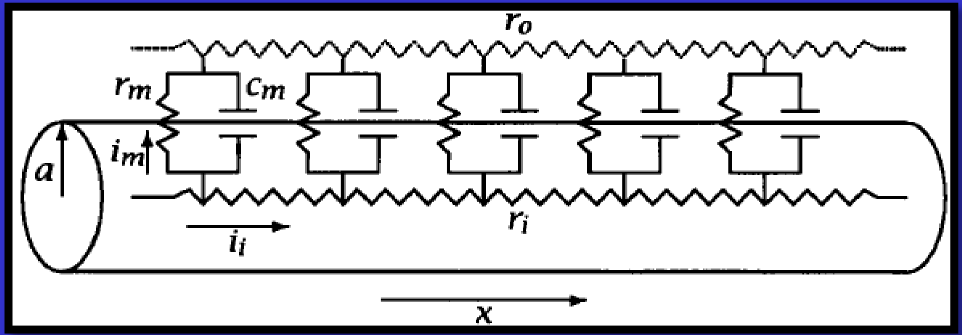
$$V = \frac{g_K E_K + g_{Na} E_{Na} + g_{Cl} E_{Cl}}{g_K + g_{Na} + g_{Cl}}.$$

Isopotential and Non-Isopotential Cell (Cable theory)



$$V_m(t) = I_m R_m (1 - e^{-t/\tau_m}), \qquad 0 < t < T$$

$$V_m(t) = I_m R_m e^{-t/\tau}, \qquad T < t$$

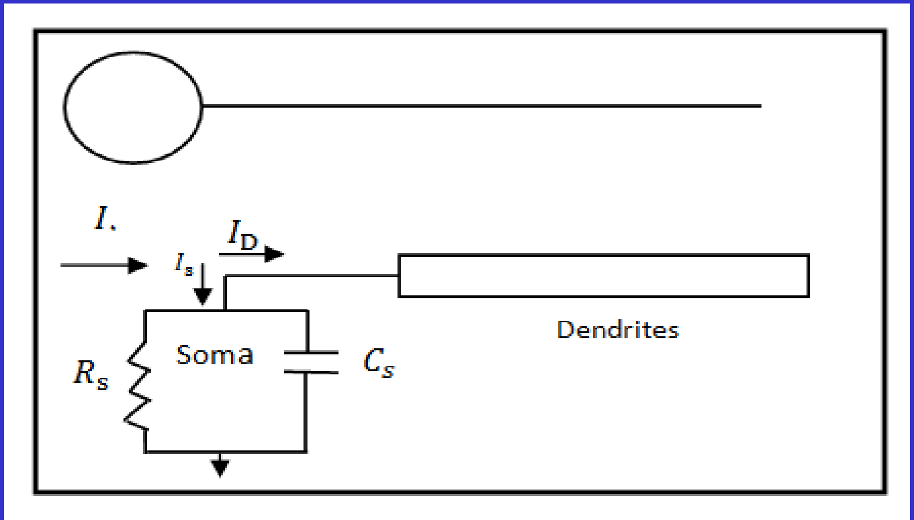


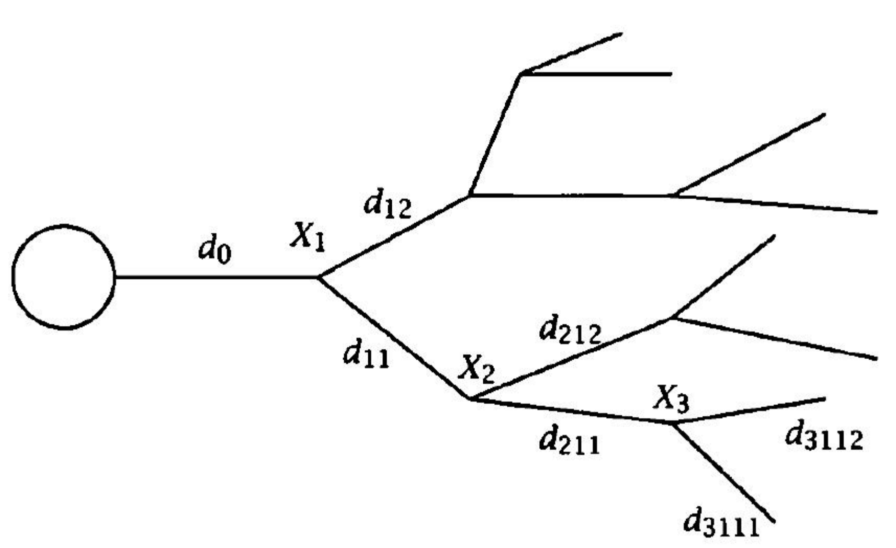
$$\frac{1}{r_i}\frac{\partial^2 V_m(x,t)}{\partial x^2} = c_m \frac{\partial V_m}{\partial t} + \frac{V_m}{r_m}$$

$$V_m(T,X) = \frac{r_i I_0 \lambda}{4}\left[e^{-X} erfc\left(\frac{X}{2\sqrt{T}} - \sqrt{T}\right) - e^{X} erfc\left(\frac{X}{2\sqrt{T}} + \sqrt{T}\right)\right]$$

A simple model for Neuron

- Rall Model





$$d_P^{3/2} = \sum d_D^{3/2}$$

Non-Linear Models for Membrane Rectification

- Sources for membrane non-linearity: voltage dependency and time dependency

- Constant field (GHK) model:

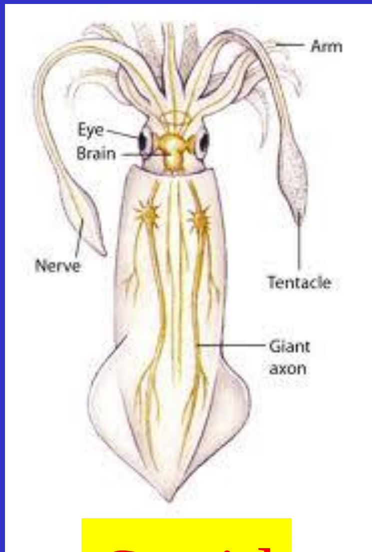
$$I = P\frac{z^2F^2}{RT}V\left(\frac{[C]_{in} - [C]_{out}e^{\frac{-zVF}{RT}}}{1 - e^{\frac{-zVF}{RT}}}\right)$$

- Energy barrier model (Eyring rate theory):

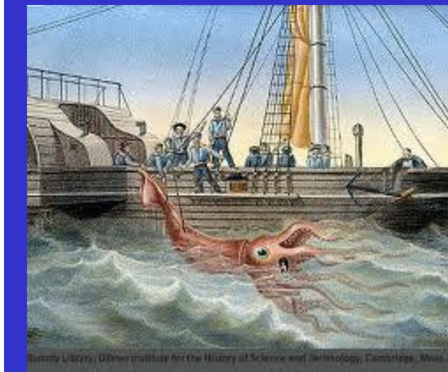
$$I = zF(J_{outward} - J_{inward}) = zF\beta k_0 [[C]_{in} e^{\delta zFV/RT} - [C]_{out} e^{-(1-\delta)zFV/RT}]$$

- The gate model (Hodgkin and Huxley's model):

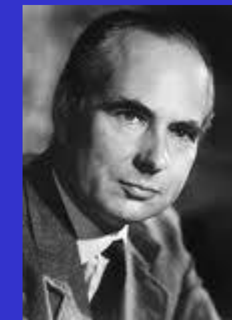
$$\text{open} \underset{\alpha(V)}{\overset{\beta(V)}{\rightleftharpoons}} \text{closed}$$

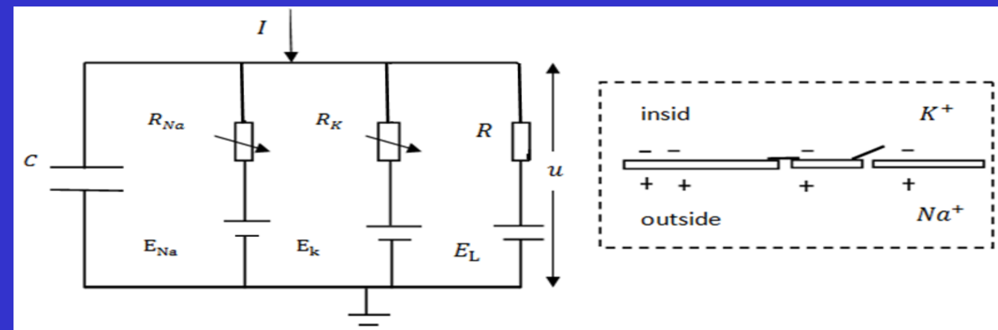


Squid



Hodgkin-Huxley Model (Nobel Prize 1963)





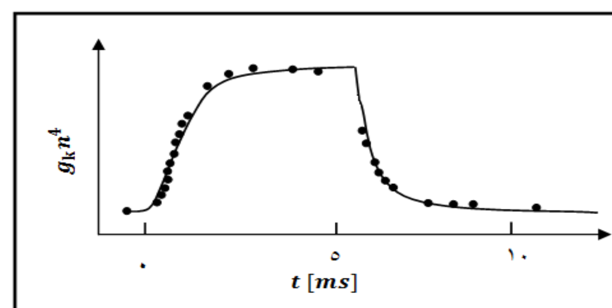
$$C_m \frac{dV}{dt} = -g_L(V - V_L) - \bar{g}_{Na} m^3 h (V - V_{Na}) - \bar{g}_K n^4 (V - V_K)$$

$$\frac{dm}{dt} = \alpha_m(V)(1-m) - \beta_m(V)m$$

$$\frac{dh}{dt} = \alpha_h(V)(1-h) - \beta_h(V)h$$

$$\frac{dn}{dt} = \alpha_n(V)(1-h) - \beta_n(V)n$$

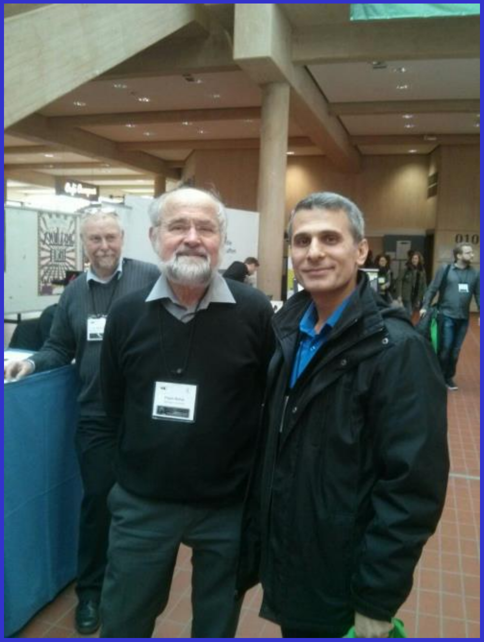
$$\dot{x} = -\frac{1}{\tau_x(u)}[x - x_0(u)]$$



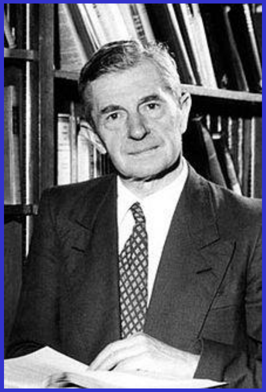
Stochastic Channels

- Patch-Clamp data for the currents of single ion channel has shown that these channels open and close stochastically.

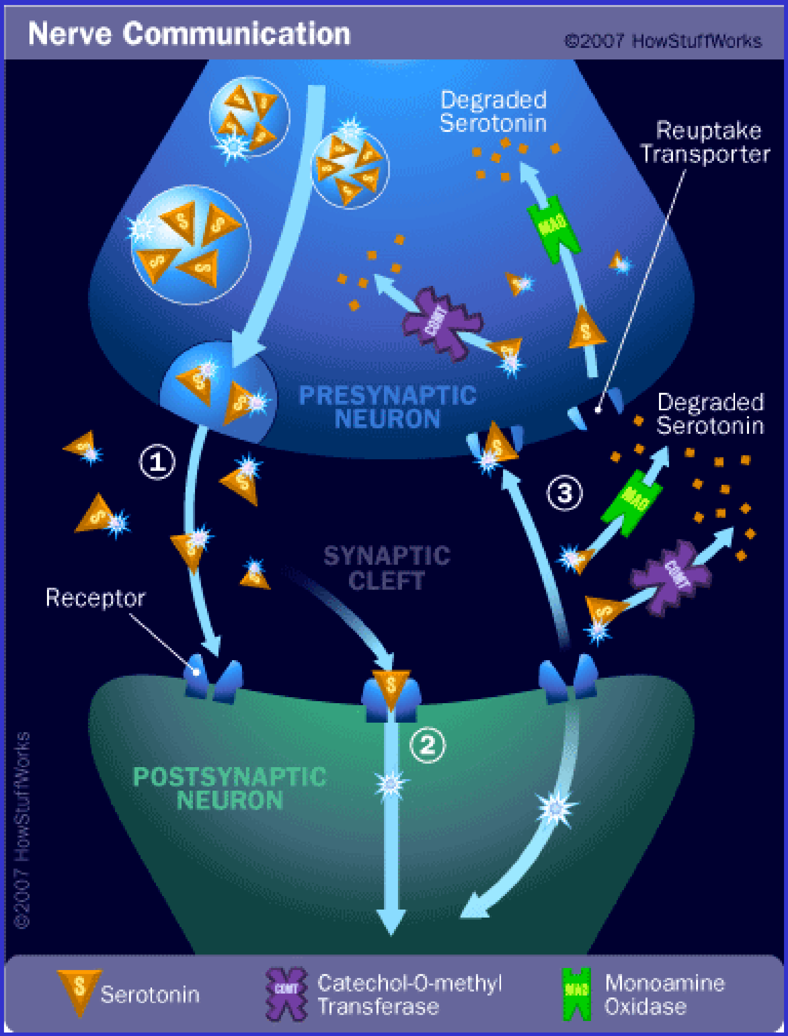
  - Nobel prize to Neher and Sakman, 1991



- Statistical analysis of channel gating: Chapman and Kolmogorov have developed a mathematical base for stochastic analysis of ion channels opening.

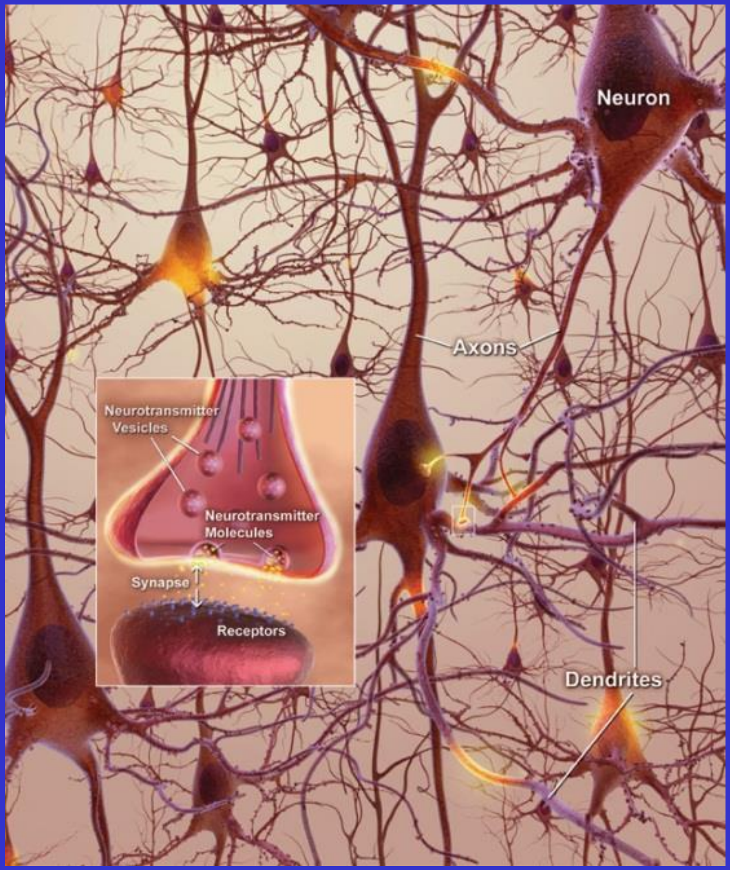


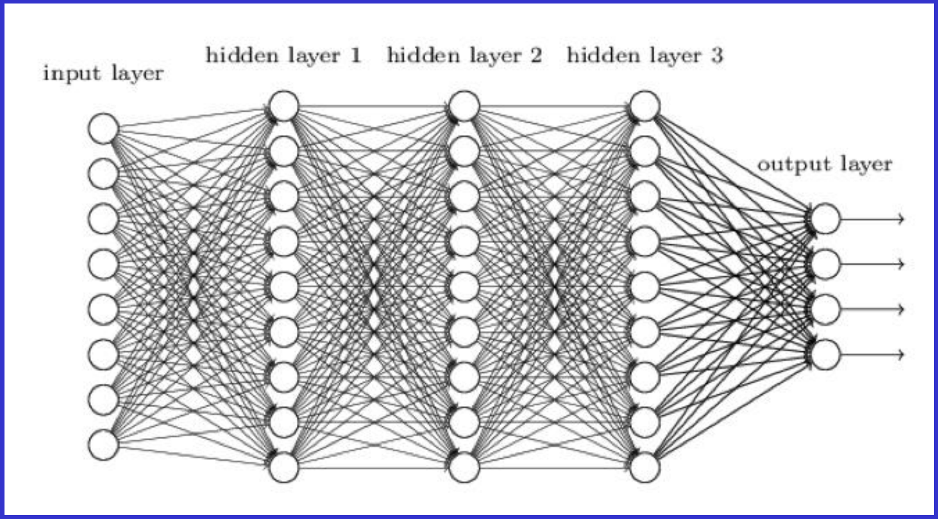
Quantal Analysis for Synaptic Transmission & Memory

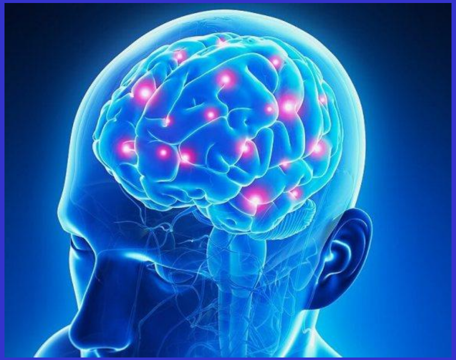


- Bernard Katz introduced the Quantum Hypothesis for transmitter release.
- Neurotransmitters are released from presynaptic terminals in discrete ‘quanta’.
- Long-Term Potentiation of the synapse is the best candidate for the memory.

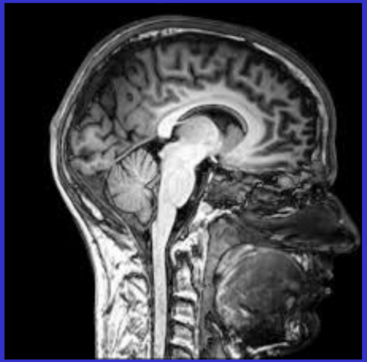
Network of Neurons
Neural Networks





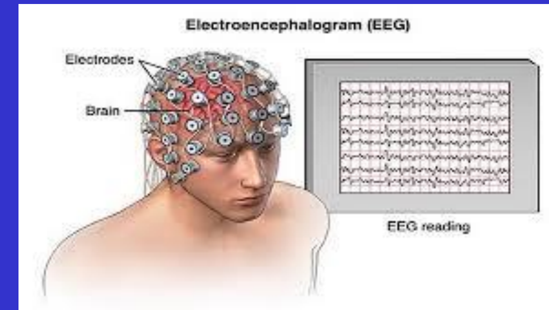


Neuro-technologies

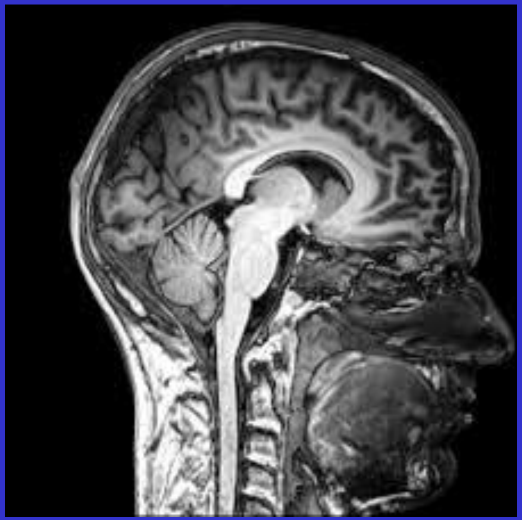


- A century ago, the only way to make a positive diagnosis for many neurological disorders was by performing an autopsy after a patient had died.
- But decades of basic research into the characteristics of disease, and the development of techniques that allow scientists to see inside the living brain and monitor nervous system activity as it occurs, have given doctors powerful and accurate tools to diagnose disease and to test how well a particular therapy may be working (NIH fact sheet).
- Neurotechnologies are helping to improve anatomical images and more detailed functional information for researchers and physicians.

Neurotechnologies



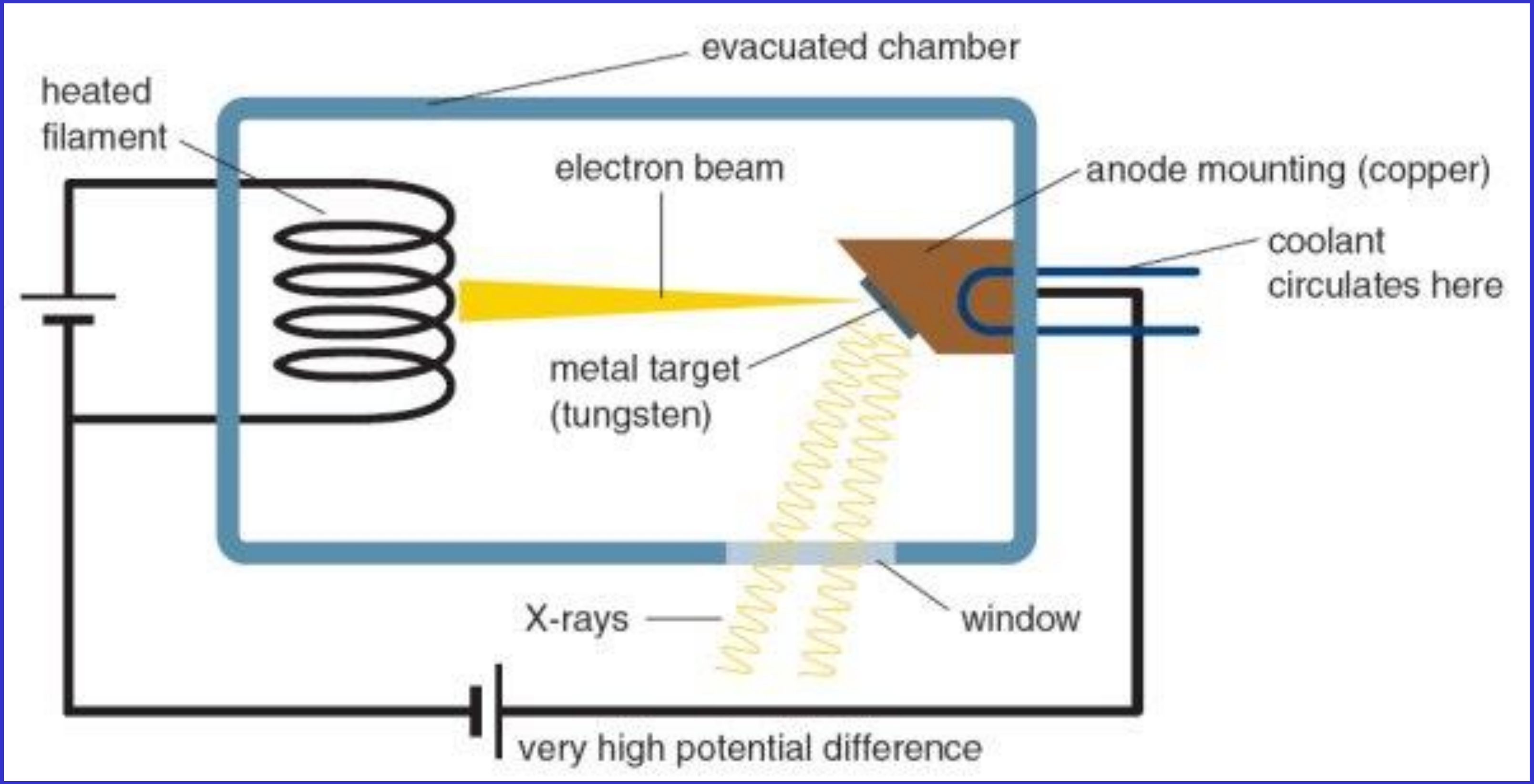
- X-Ray (Angiography, CT Scan, Myelography)
- Electroencephalography (EEG) & Magnetoencephalography (MEG)
- Transcranial Electric Current Stimulation (tECS) & Transcranial Magnetic Stimulation (tMS)
- Magnetic Resonance Imaging (MRI) & Functional MRI (fMRI)
- Functional Near-Infrared Spectroscopy (fNIR or fNIRS)
- Positron Emission Tomography (PET)
- Single photon emission computed tomography (SPECT)



Physics of Neurotechnologies:

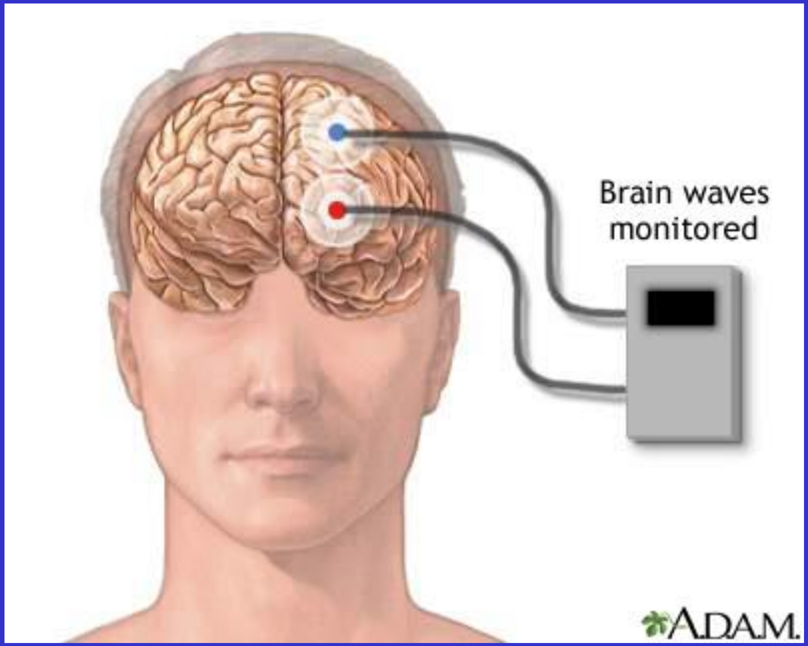
X-Rays

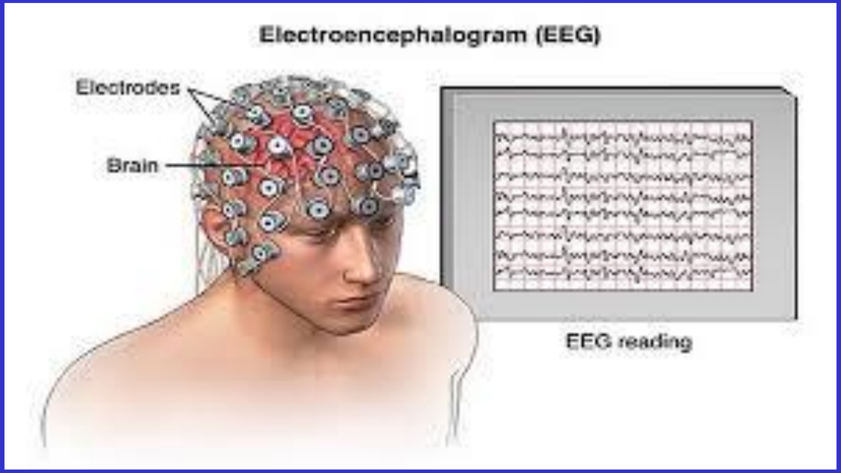
Angiography, CT Scan, Myelography

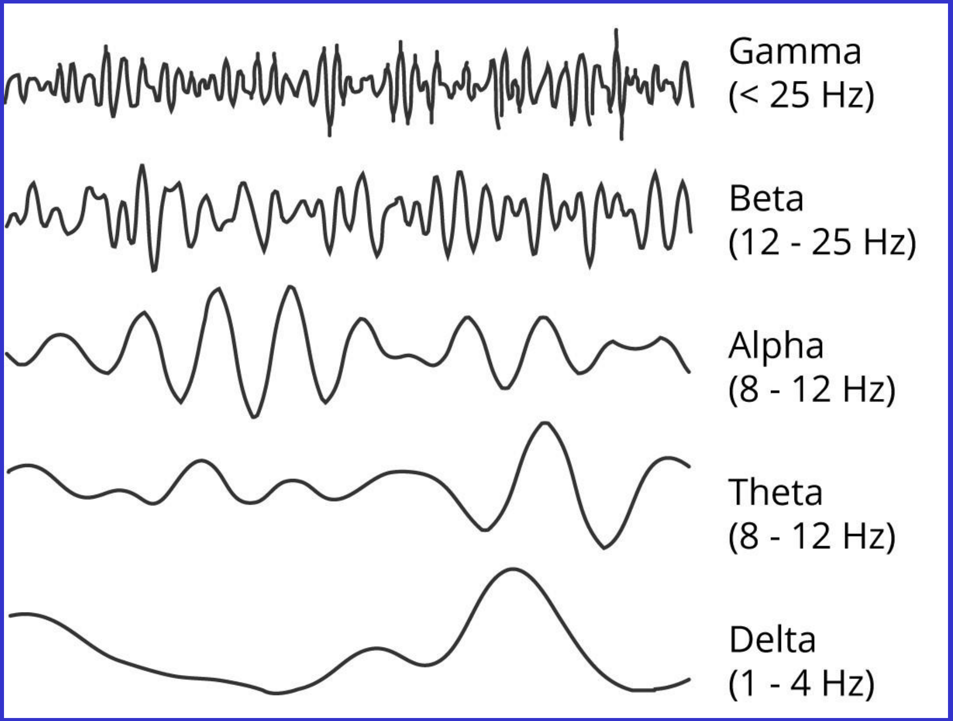


Physics of Neurotechnologies:

EEG & MEG







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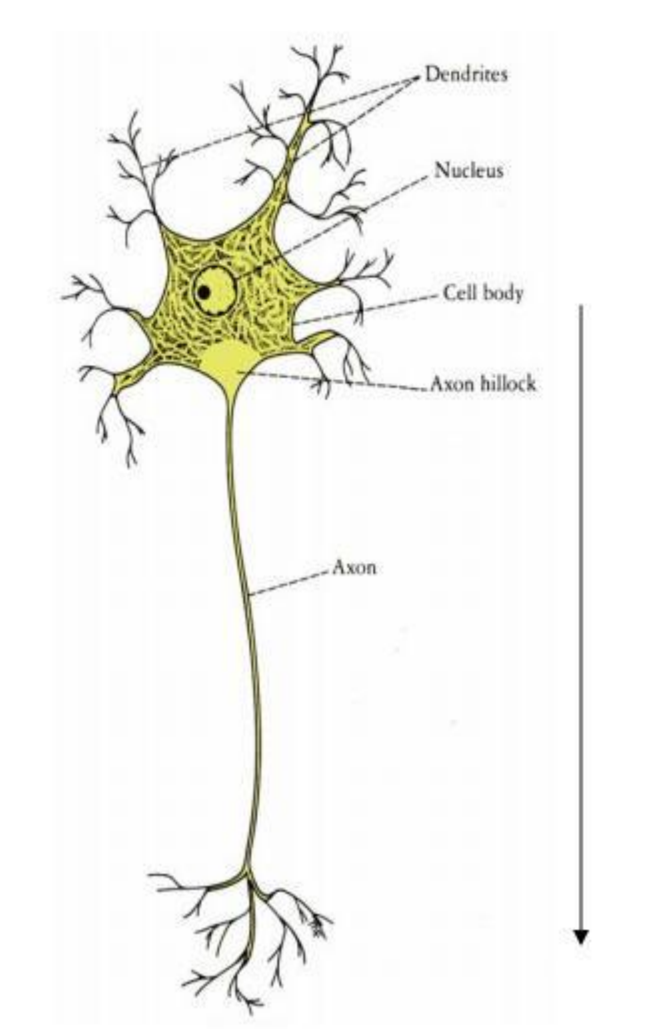
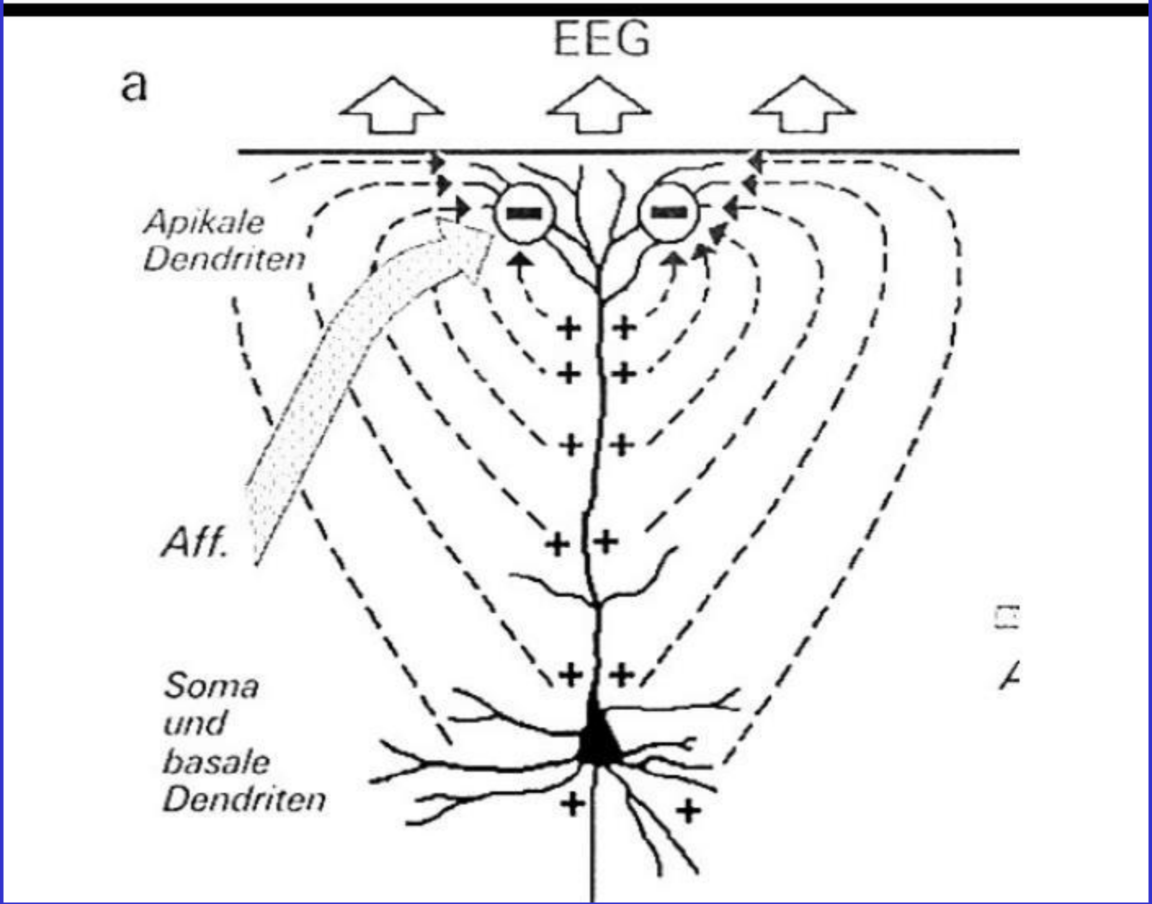


Physics of Neurotechnologies:

EEG & MEG

Pyramidal Neuron as Dipole

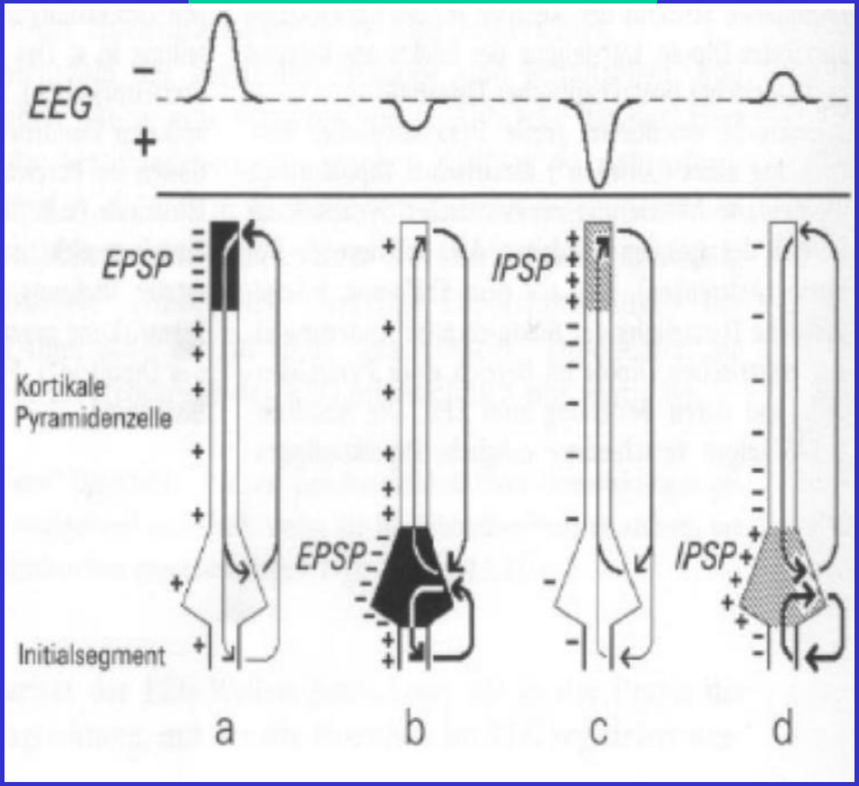


Ionic exchange across the neuron and action potentials create currents and magnetic fields.

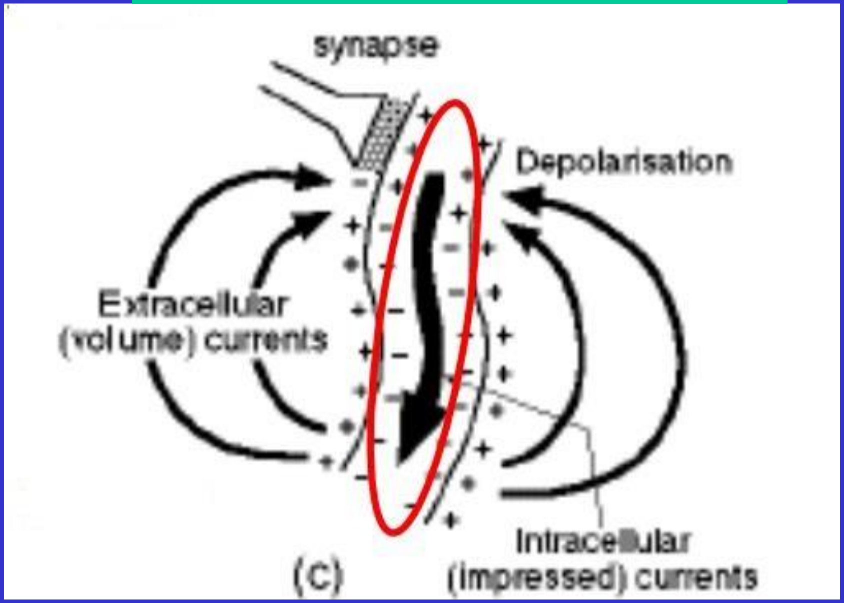
Physics of Neurotechnologies:

EEG & MEG

EPSP and IPSP dipoles



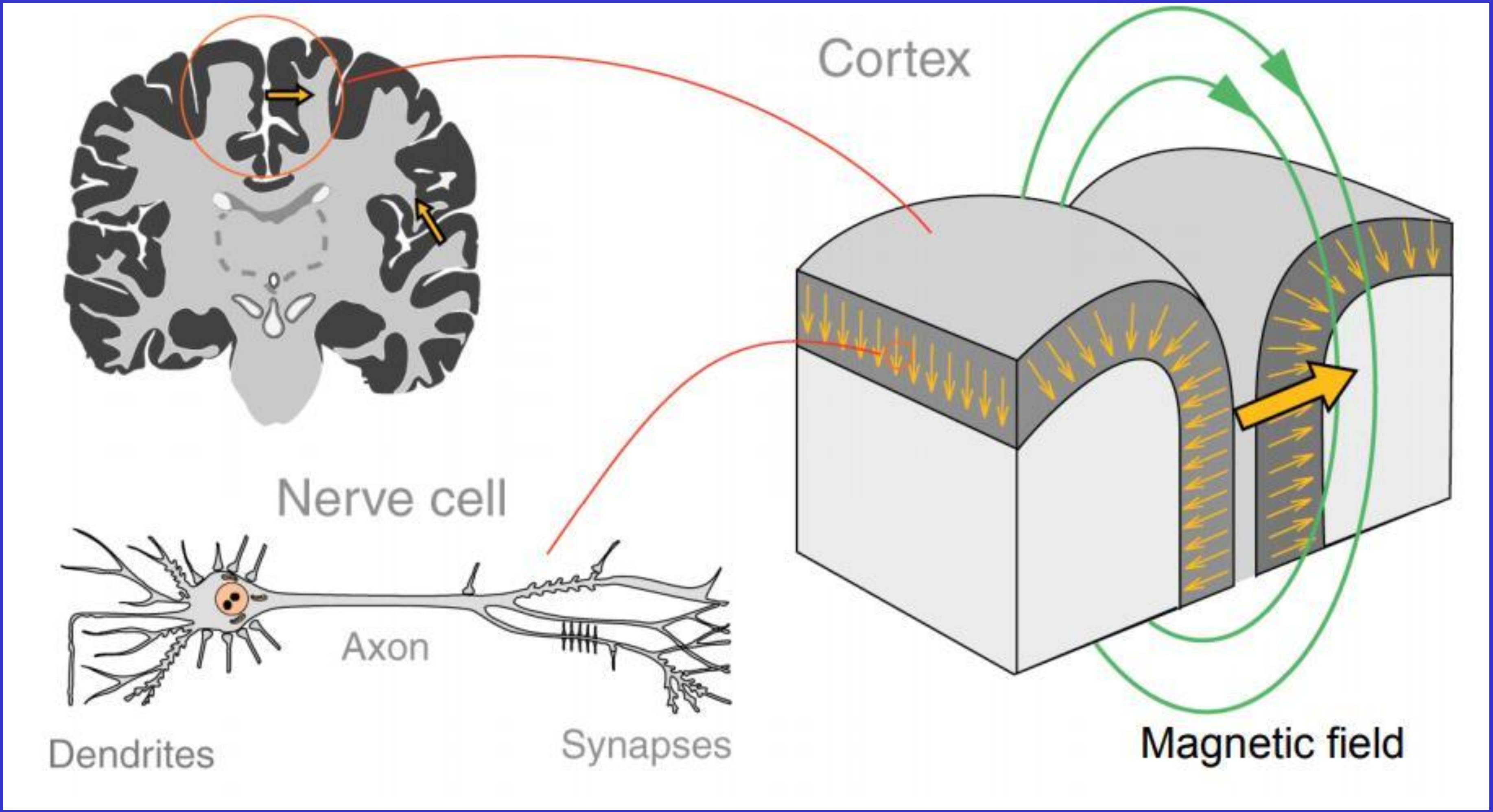
Primary and Secondary Current



- Secondary currents yield potential differences on the scalp of the head that can be measured by EEG
- MEG measures magnetic fields induced mainly by primary currents (Intracellular)

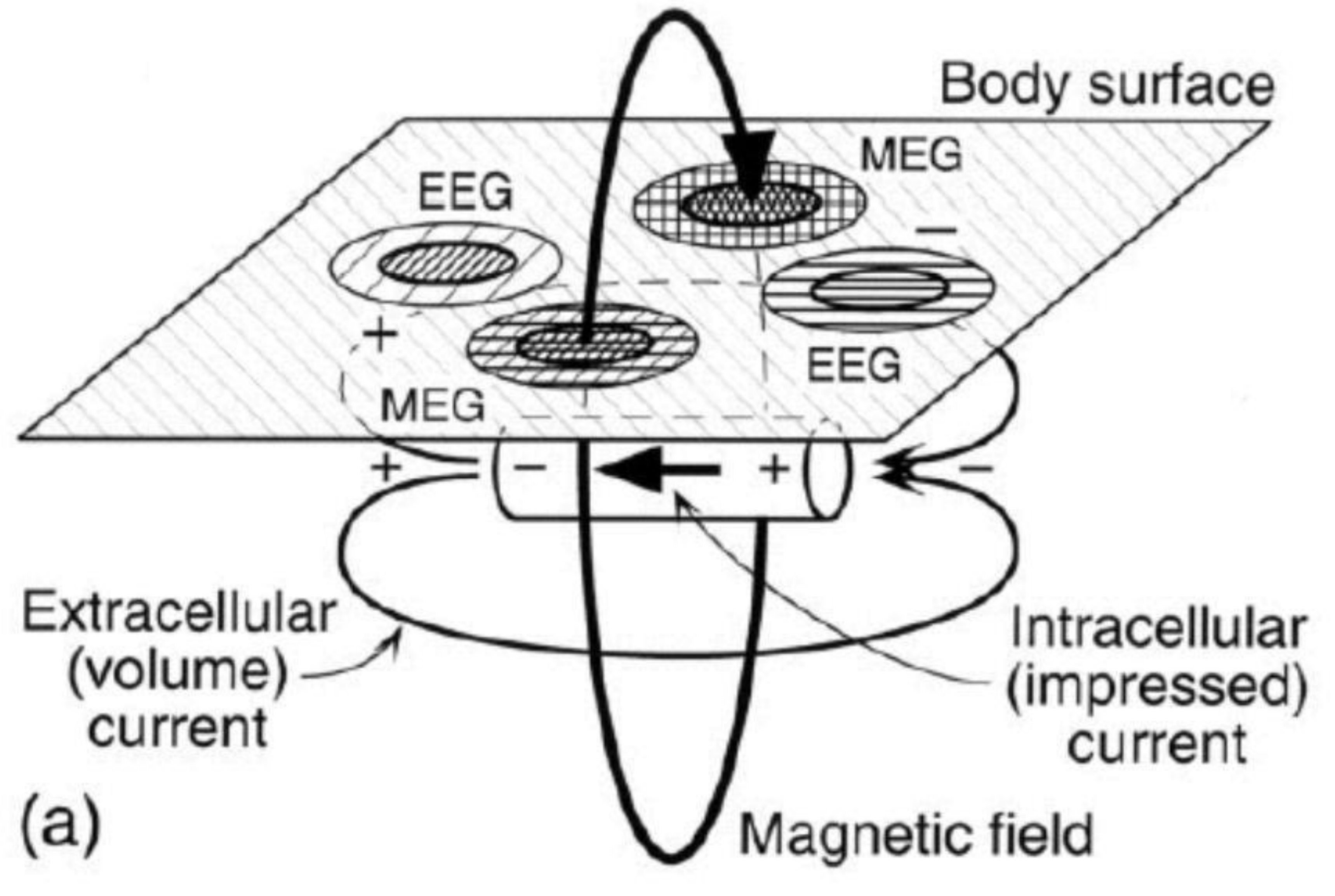
Physics of Neurotechnologies:

EEG & MEG



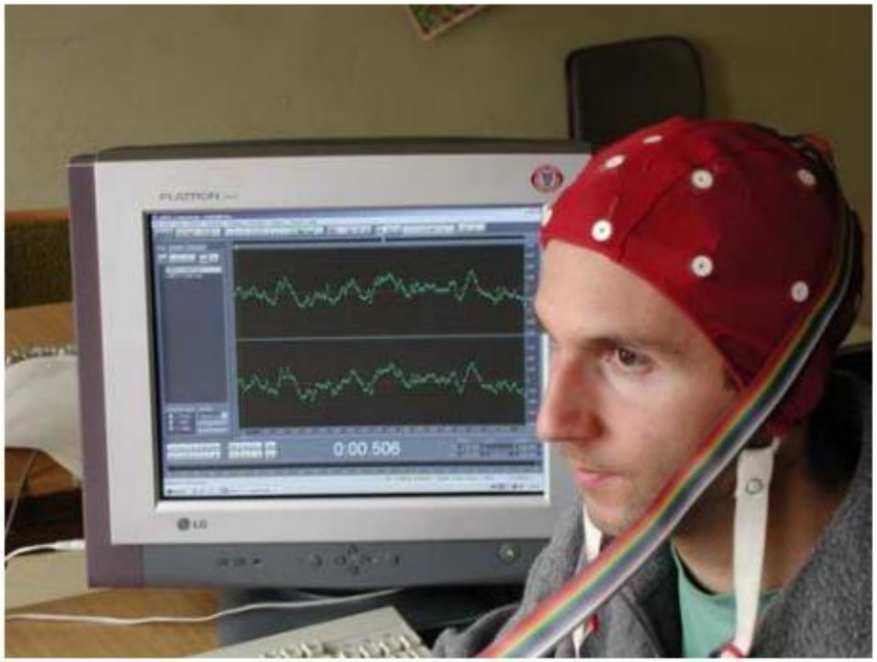
Physics of Neurotechnologies:

EEG & MEG



Physics of Neurotechnologies:

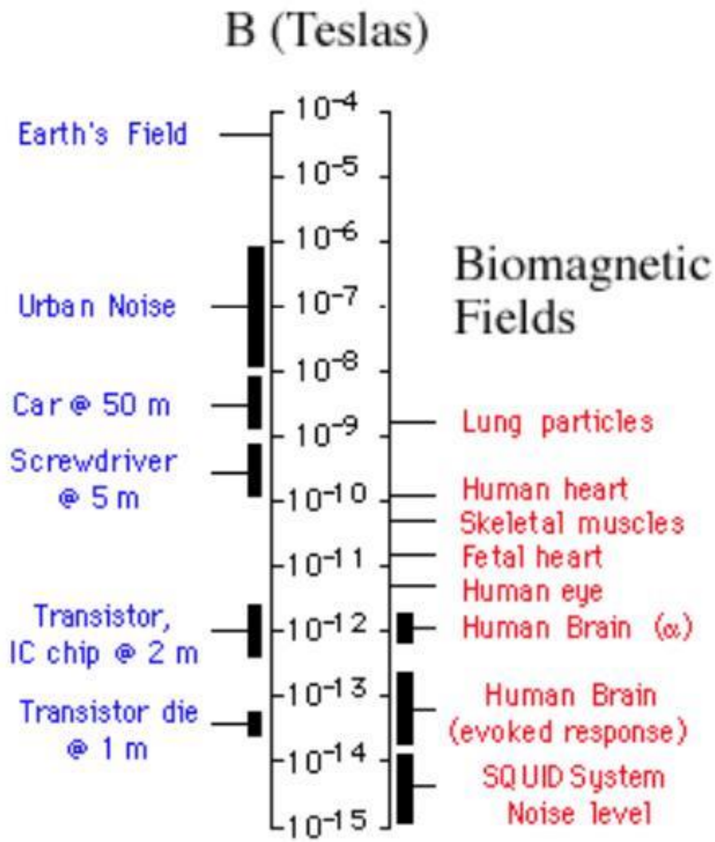
EEG



Physics of Neurotechnologies:

MEG

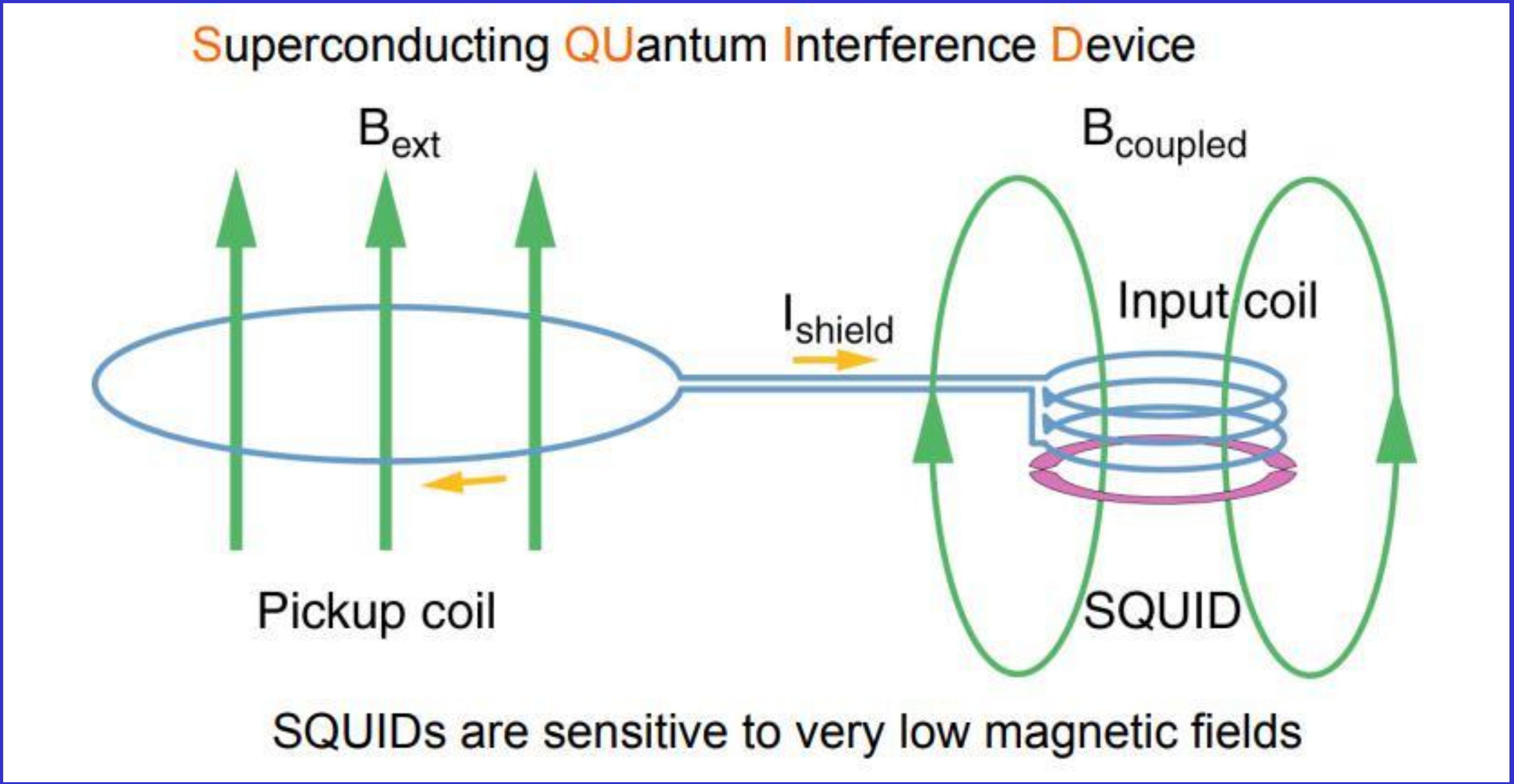
Magnetic Fields



Noise is about a factor of 10^3 to 10^6 larger than the MEG signal

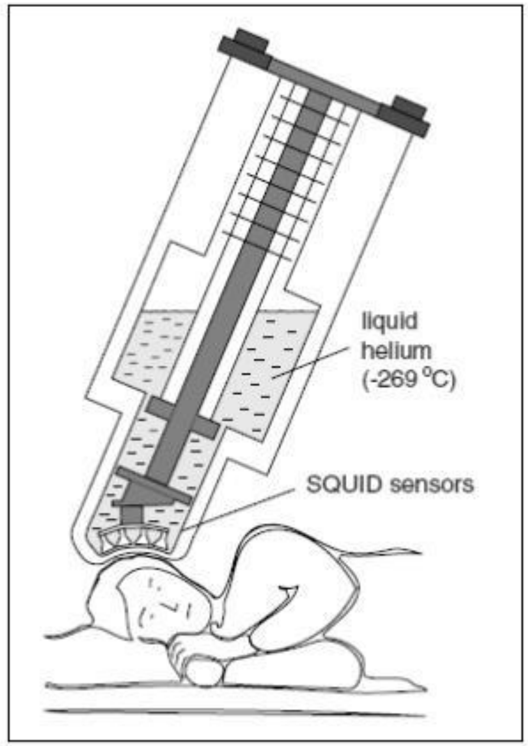
Physics of Neurotechnologies:

MEG

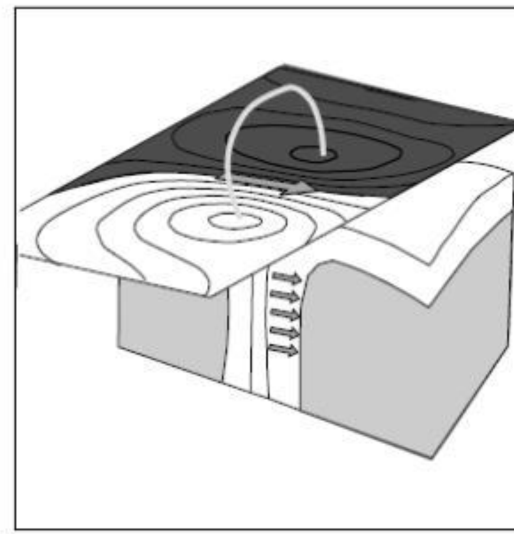


- The SQUIDs "translate" the magnetic field into an electrical current which is proportional to this field.
- To have their superconductive properties, the SQUIDs need to be maintained at-269 °C.

MEG

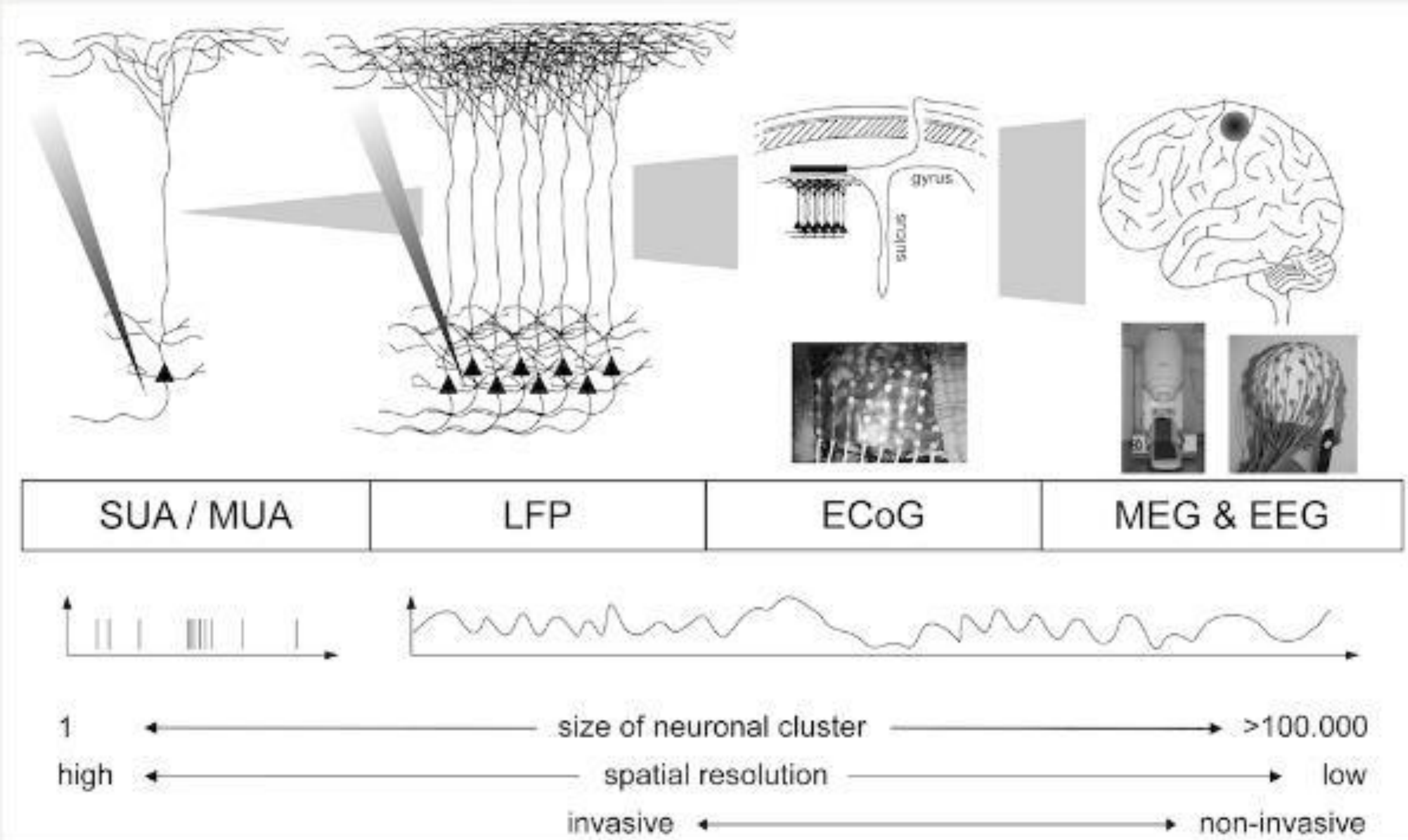


Short set-up time



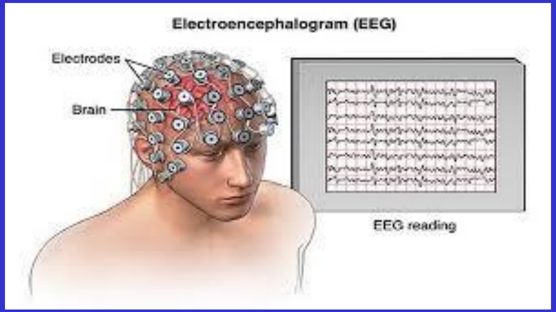
Magnetic shielded room   Hardware and software   Averaging

Physics of Neurotechnologies



Schematic overview of the recording techniques that can be used for the purposes of a brain-machine interface. The scale of recorded neurons increases from left to right, but this happens at the expense of the achieved spatial resolution.

Neurotechnologies



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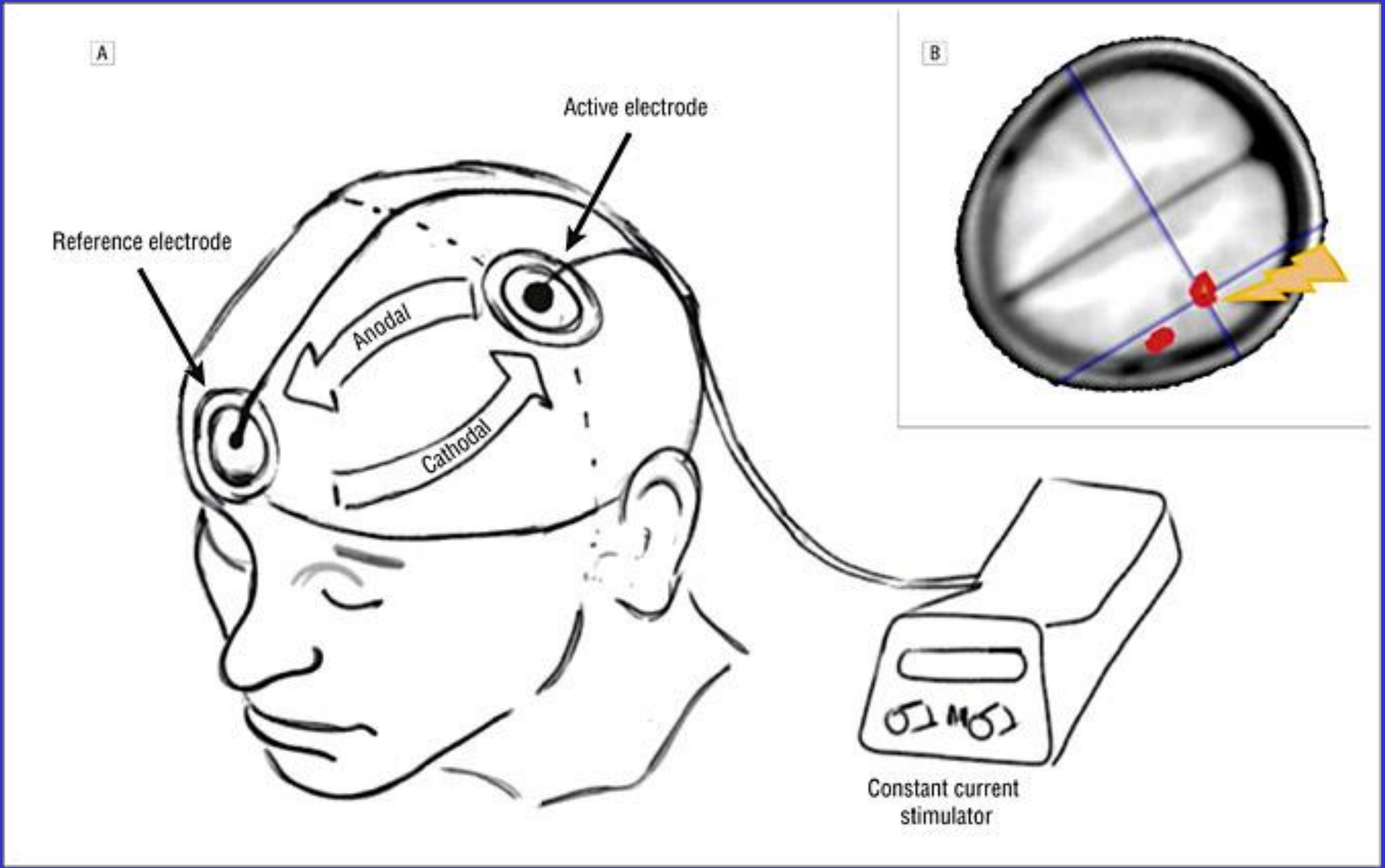
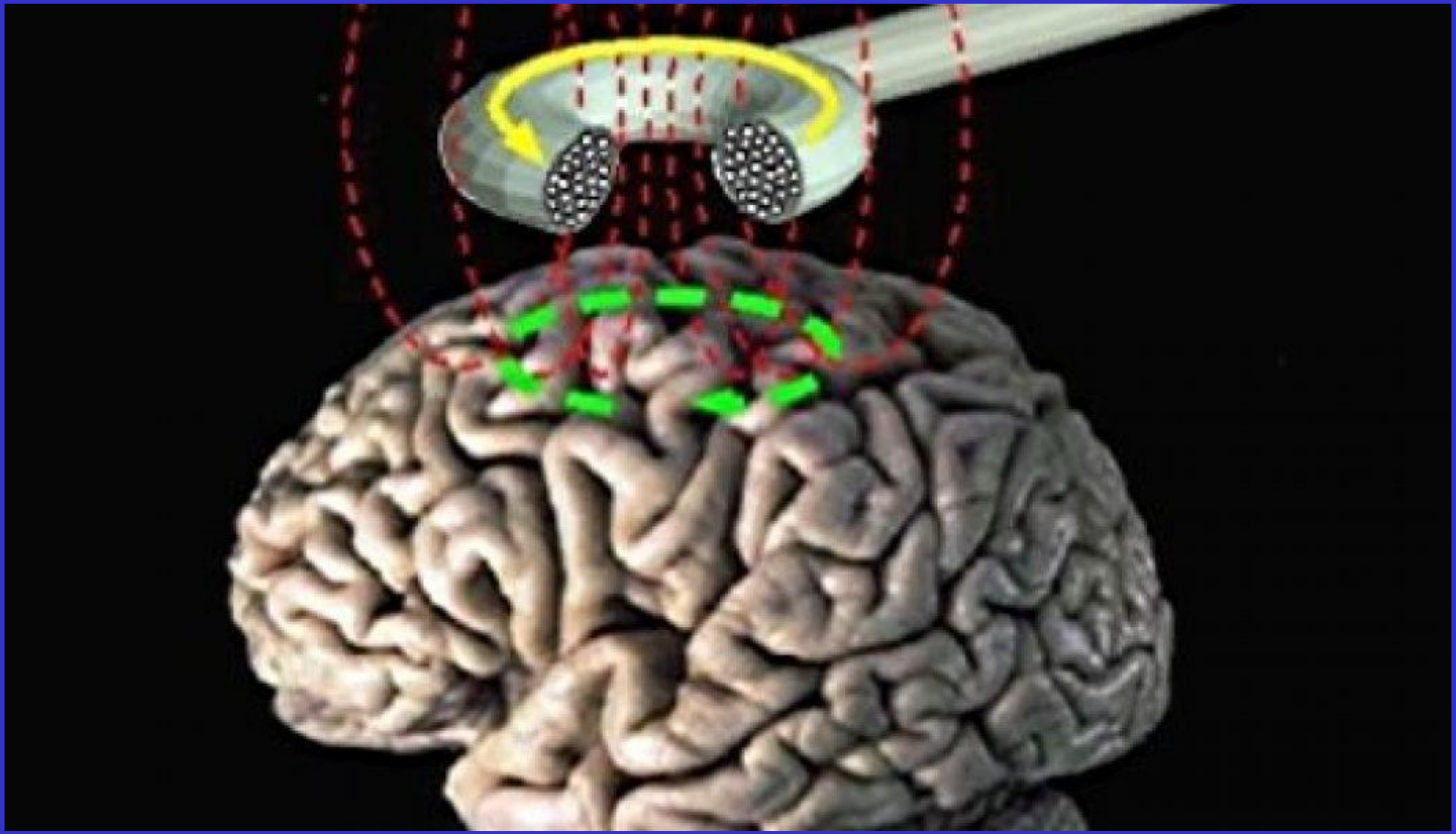
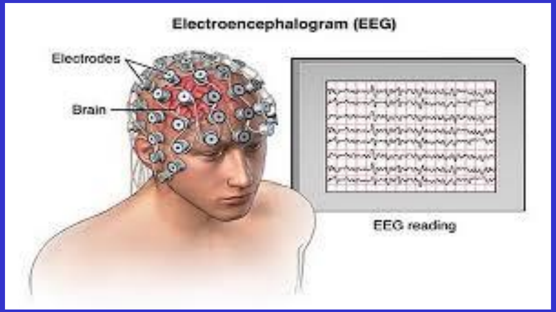
Physics of Neurotechnologies: # tES



Physics of Neurotechnologies: tMS



Neurotechnologies



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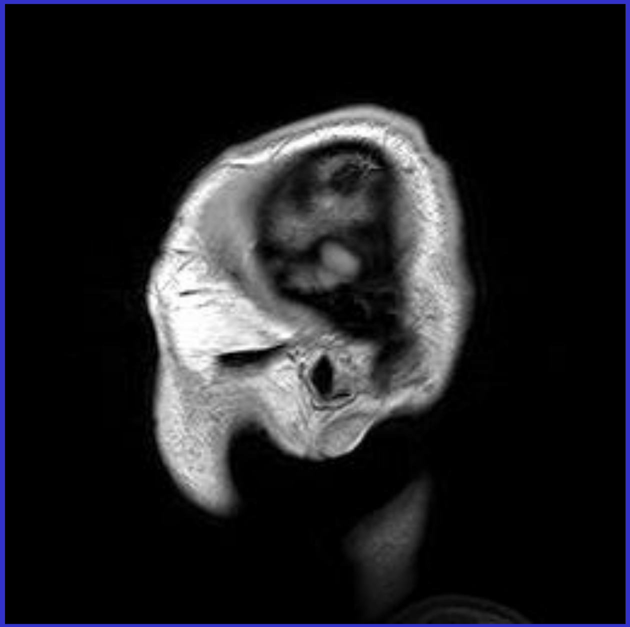
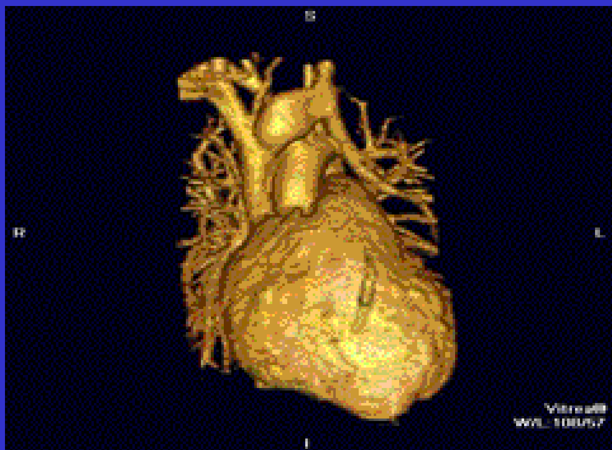
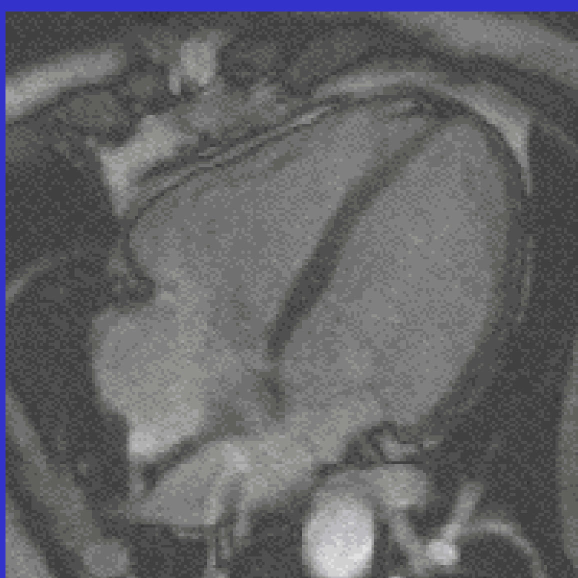
Physics of Neurotechnologies: **MRI**



- MRI scanners use strong magnetic fields, radio waves, and field gradients to generate images of the organs in the body.
- MRI was originally called 'NMRI' (nuclear magnetic resonance imaging). It is based upon the science of nuclear magnetic resonance (NMR).
- Certain atomic nuclei are able to absorb and emit radio frequency energy when placed in an external magnetic field.
- In clinical and research MRI, hydrogen atoms are most often used to generate a detectable radio-frequency signal that is received by antennas in close proximity to the anatomy being examined.
- Water and Fat

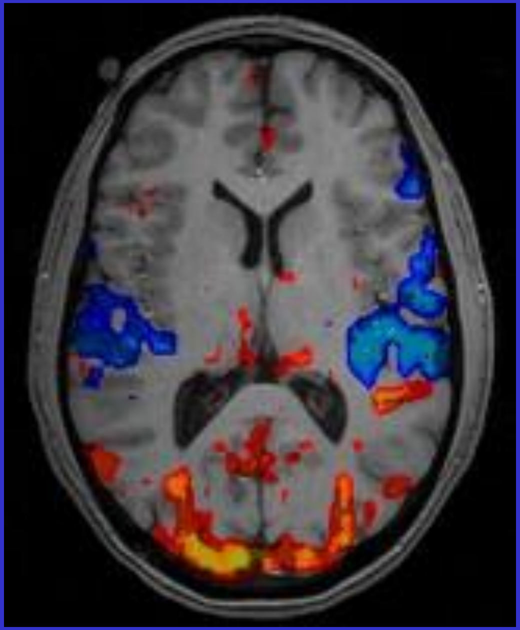
Physics of Neurotechnologies: MRI



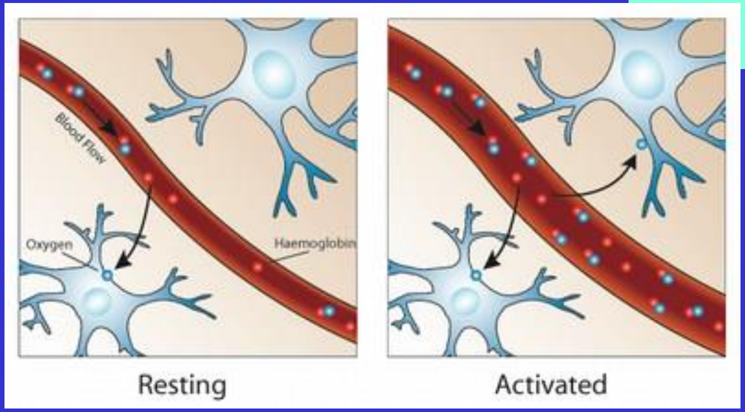


- Pulses of radio waves excite the nuclear spin energy transition, and magnetic field gradients localize the signal in space.
- By varying the parameters of the pulse sequence, different contrasts may be generated between tissues based on the relaxation properties of the hydrogen atoms therein.

Physics of Neurotechnologies: MRI



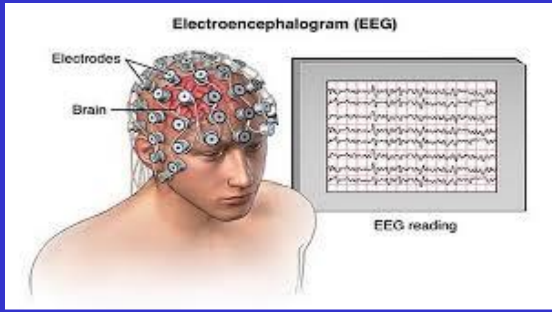
- Functional magnetic resonance imaging, or fMRI, is a technique for measuring brain activity.
- It works by detecting the changes in blood oxygenation and flow that occur in response to neural activity. When a brain area is more active it consumes more oxygen and to meet this increased demand blood flow increases to the active area.
- The development of FMRI in the 1990s, generally credited to Seiji Ogawa and Ken Kwong, is the latest in long line of innovations, including positron emission tomography (PET) and near infrared spectroscopy (NIRS), which use blood flow and oxygen metabolism to infer brain activity.



Physics of Neurotechnologies: MRI

- Normally atomic nuclei are randomly oriented but under the influence of a magnetic field the nuclei become aligned with the direction of the field. The stronger the field the greater the degree of alignment. When pointing in the same direction, the tiny magnetic signals from individual nuclei add up coherently resulting in a signal that is large enough to measure. In fMRI it is the magnetic signal from hydrogen nuclei in water (H_2O) that is detected.
- The key to MRI is that the signal from hydrogen nuclei varies in strength depending on the surroundings. This provides a means of discriminating between gray matter, white matter and cerebral spinal fluid in structural images of the brain.
- Oxygen is delivered to neurons by hemoglobin in capillary red blood cells. When neuronal activity increases there is an increased demand for oxygen and the local response is an increase in blood flow to regions of increased neural activity.
- **Hemoglobin** is diamagnetic when oxygenated but paramagnetic when deoxygenated. This difference in magnetic properties leads to small differences in the MR signal of blood depending on the degree of oxygenation. Since blood oxygenation varies according to the levels of neural activity, these differences can be used to detect brain activity. This form of MRI is known as blood oxygenation level dependent (BOLD) imaging.

Neurotechnologies



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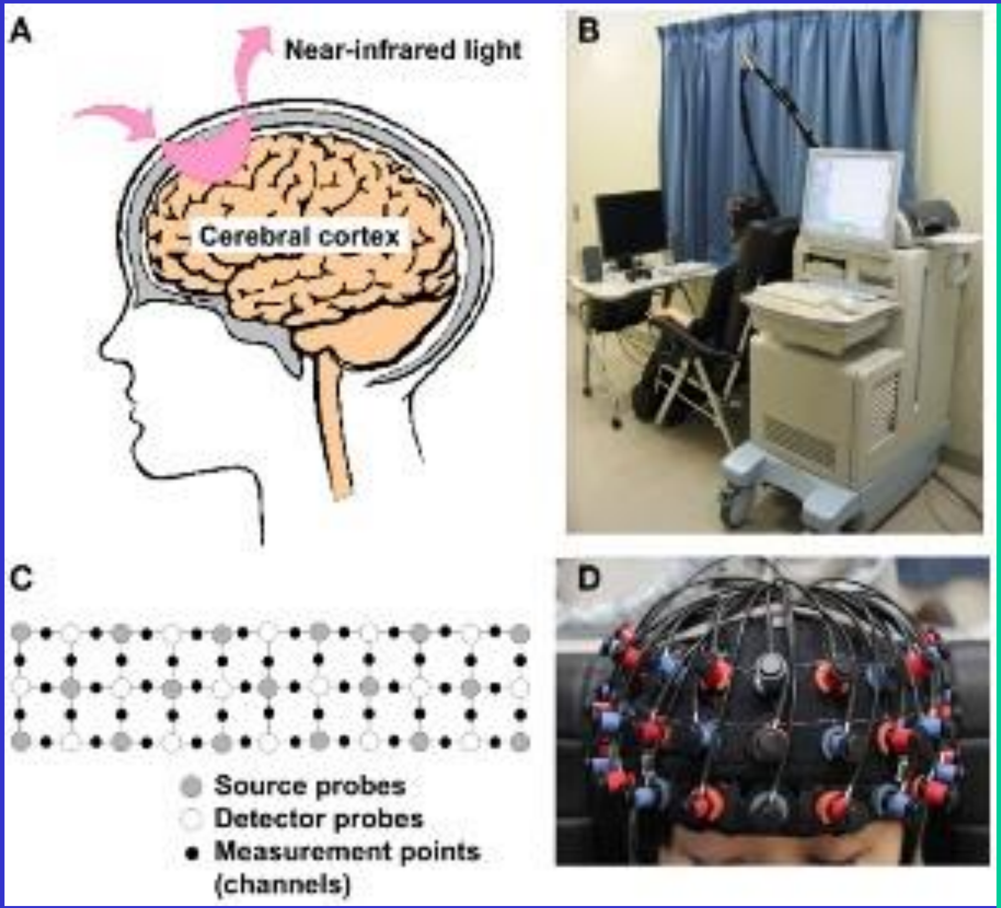
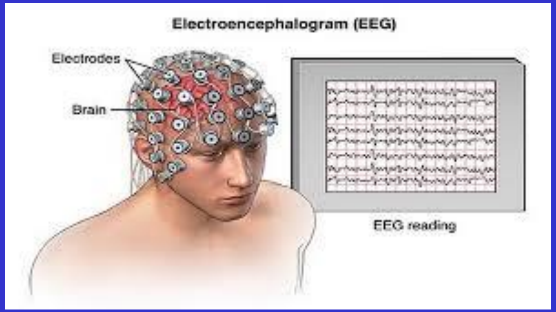
Physics of Neurotechnologies: fNIRS



- NIR (Near-Infrared) spectrum light takes advantage of the optical window in which skin, tissue, and bone are mostly transparent to NIR light in the spectrum of 700-900 nm, while hemoglobin (Hb) and deoxygenated-hemoglobin (deoxy-Hb) are stronger absorbers of light.
- Differences in the absorption spectra of deoxy-Hb and oxy-Hb allow the measurement of relative changes in hemoglobin concentration through the use of light attenuation at multiple wavelengths.
- Using the modified Beer-Lambert law (mBLL), relative concentration can be calculated as a function of total photon path length.

$$I(t) = I_s \exp[-\mu_a \rho]$$

Neurotechnologies



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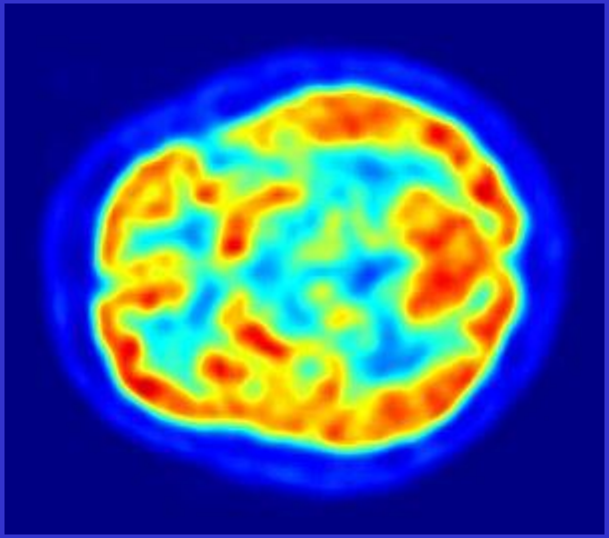
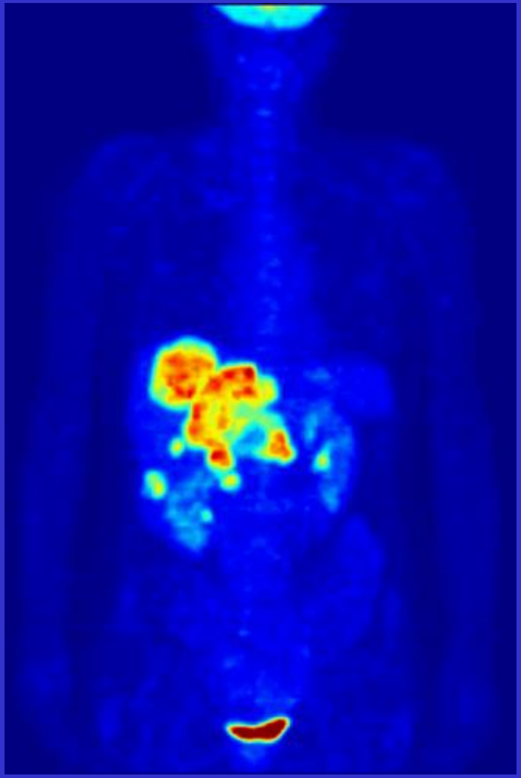
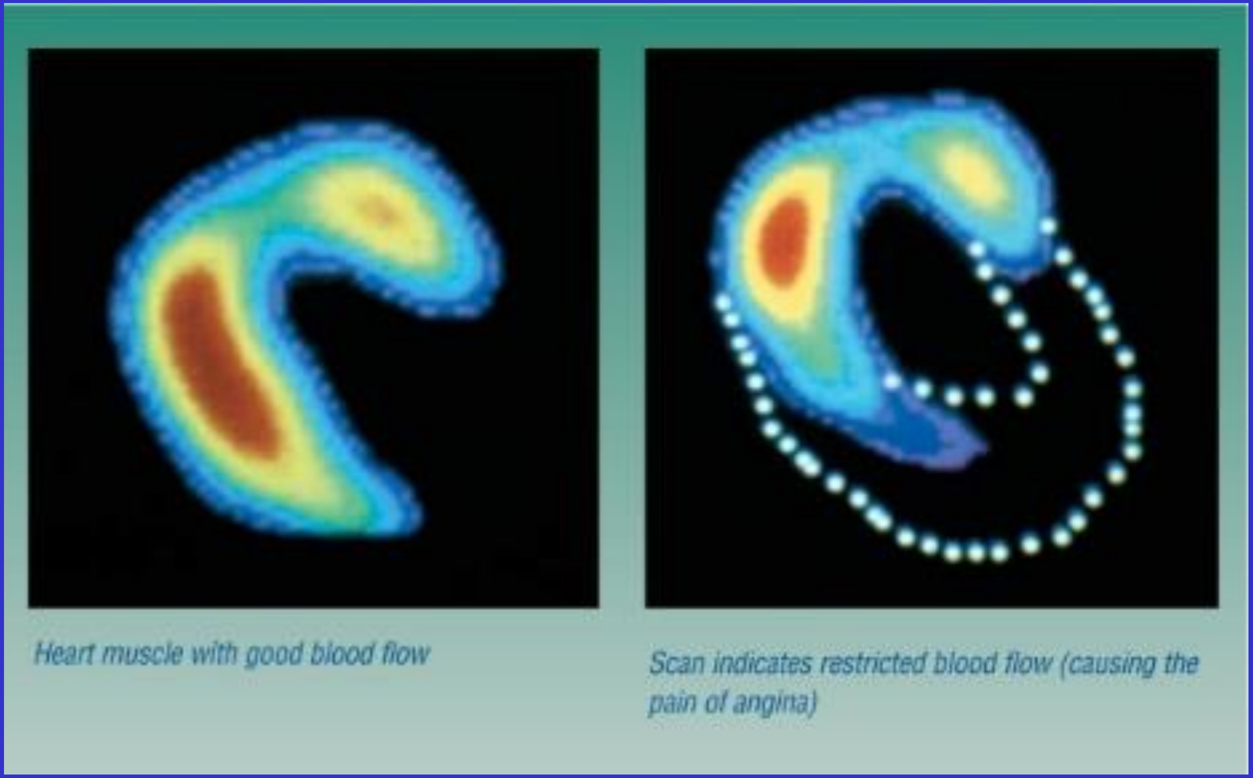




Physics of Neurotechnologies: PET

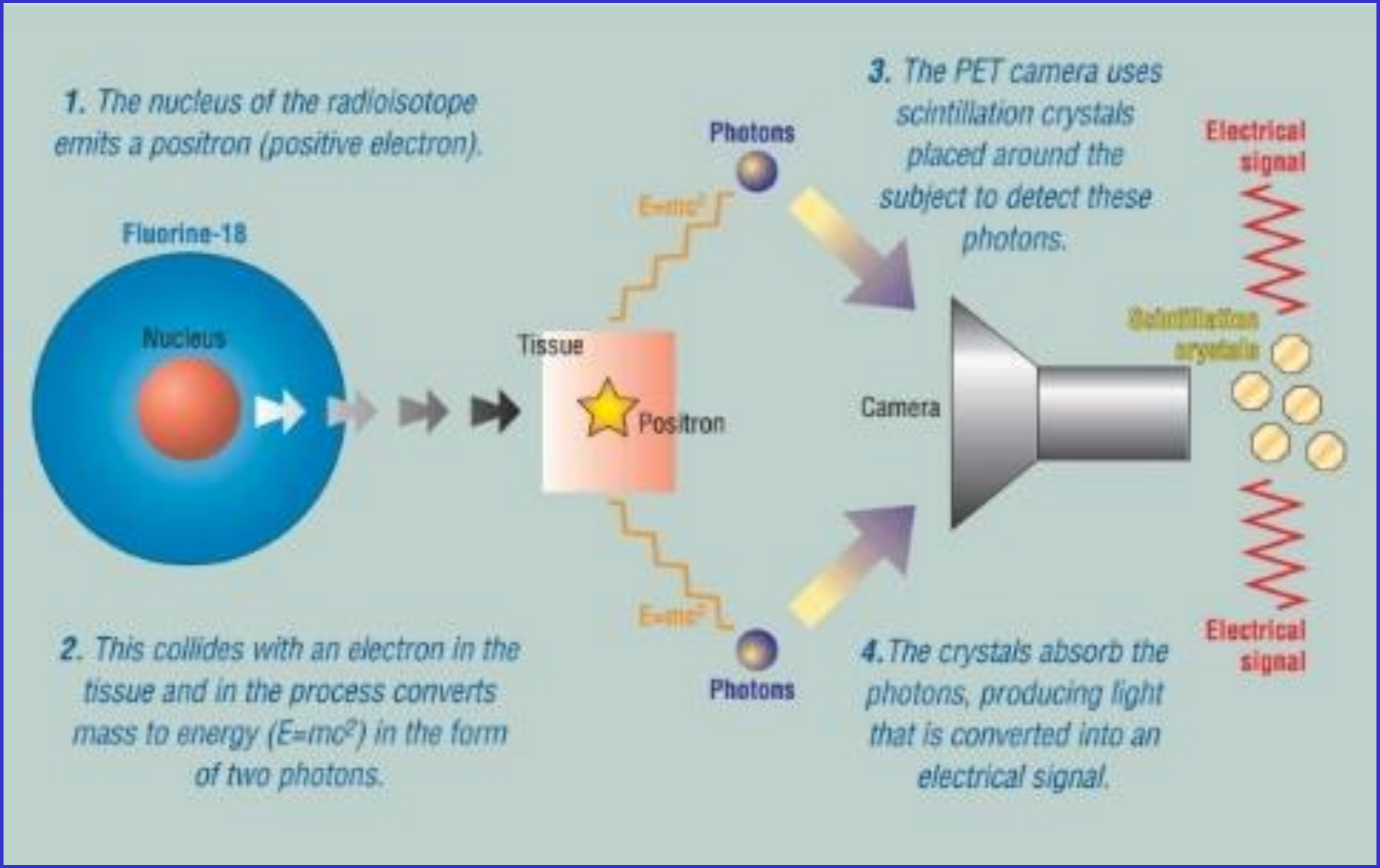
- Positron-emission tomography (PET) is a nuclear medicine functional imaging technique that is used to observe metabolic processes in the body.
- The system detects pairs of gamma rays emitted indirectly by a positron-emitting radionuclide (tracer), which is introduced into the body on a biologically active molecule.
- The tracer is administered as an intravenous injection usually labelled with oxygen-15, fluorine-18, carbon-11, or nitrogen-13. The total radioactive dose is similar to the dose used in computed tomography.
- A common use for PET is to measure the rate of consumption of glucose in different parts of the body.

Physics of Neurotechnologies: PET

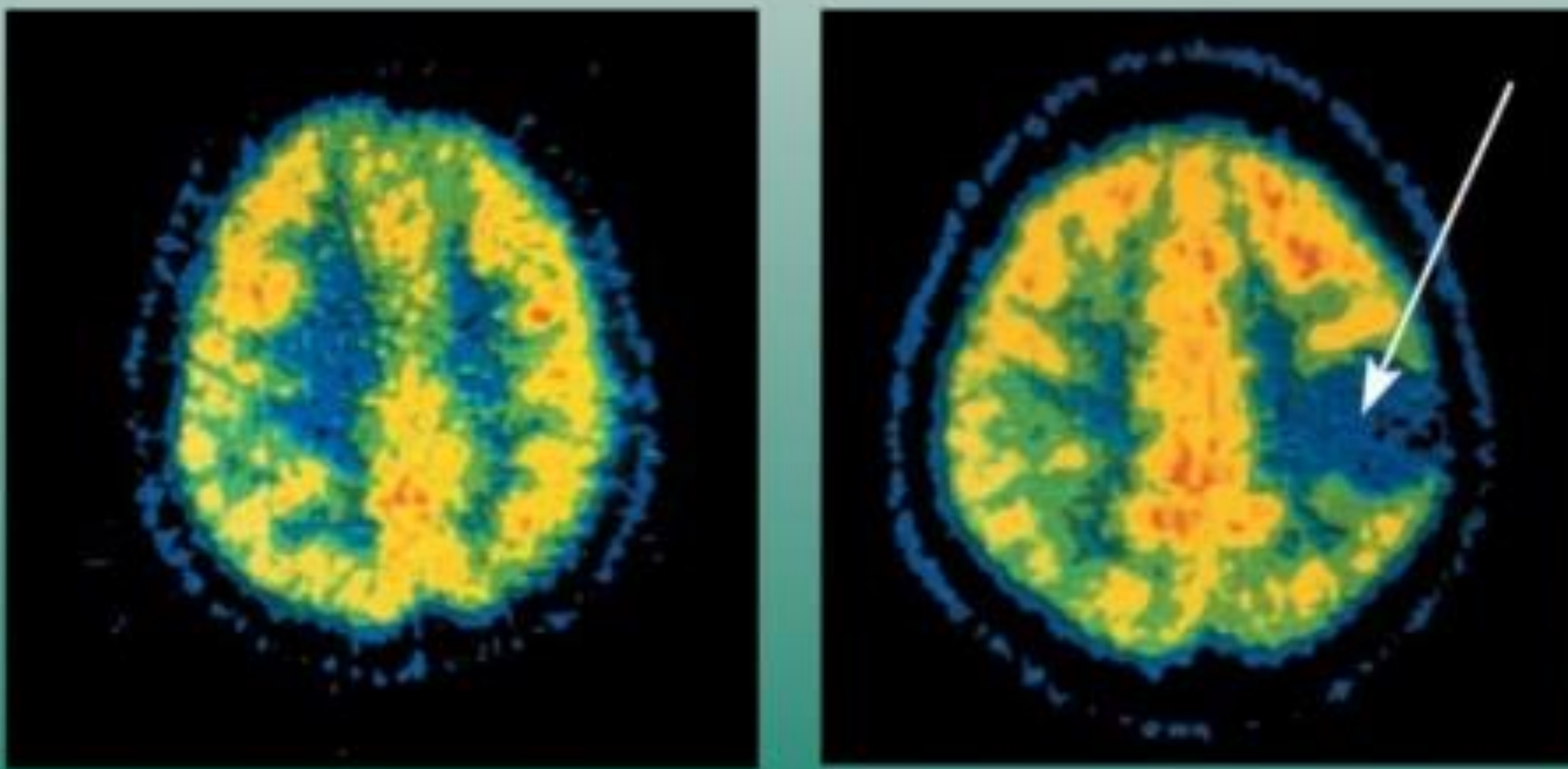


• Positron emission tomography (PET) is a technique that measures physiological function by looking at blood flow, metabolism, neurotransmitters, and radiolabelled drugs. PET offers quantitative analyses, allowing relative changes over time to be monitored as a disease process evolves or in response to a specific stimulus.

Physics of Neurotechnologies: PET



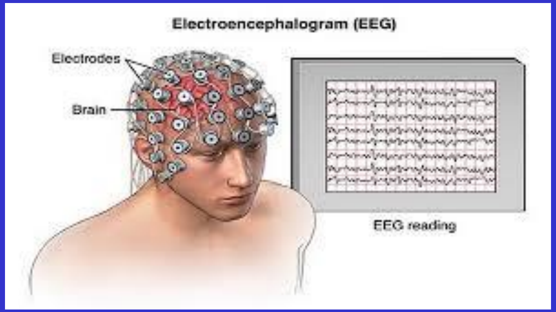
Physics of Neurotechnologies: PET



Normal brain

A brain tumour demonstrated on the right (blue, indicating poor blood flow at the area of tissue damage or tissue death)

Neurotechnologies



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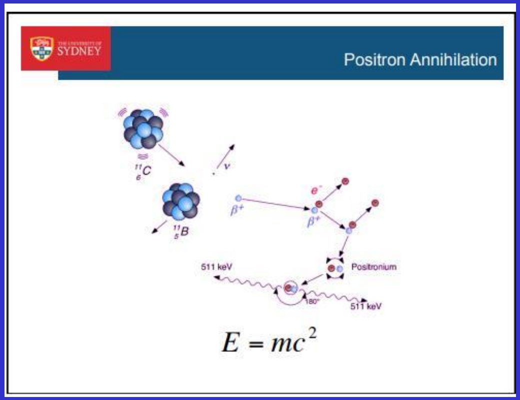
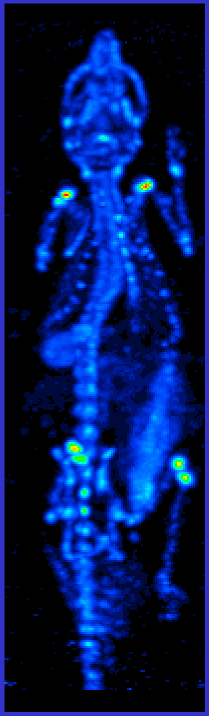
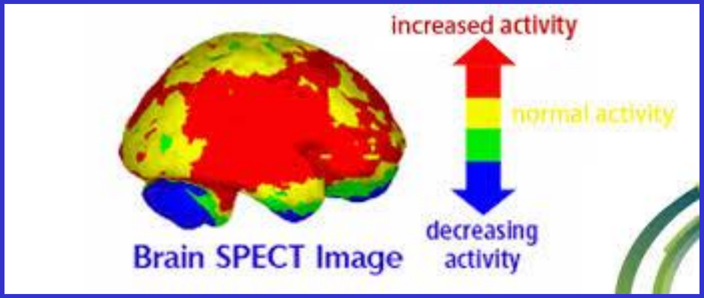
Physics of Neurotechnologies: SPECT





- Single-photon emission computed tomography (SPECT, or less commonly, SPET) is a nuclear medicine tomographic imaging technique using gamma rays.
- A SPECT scan integrates two technologies to view your body: computed tomography (CT) and a radioactive material (tracer). The tracer is what allows doctors to see how blood flows to tissues and organs.
- A SPECT scan is primarily used to view how blood flows through arteries and veins in the brain.



Physics of Neurotechnologies: SPECT

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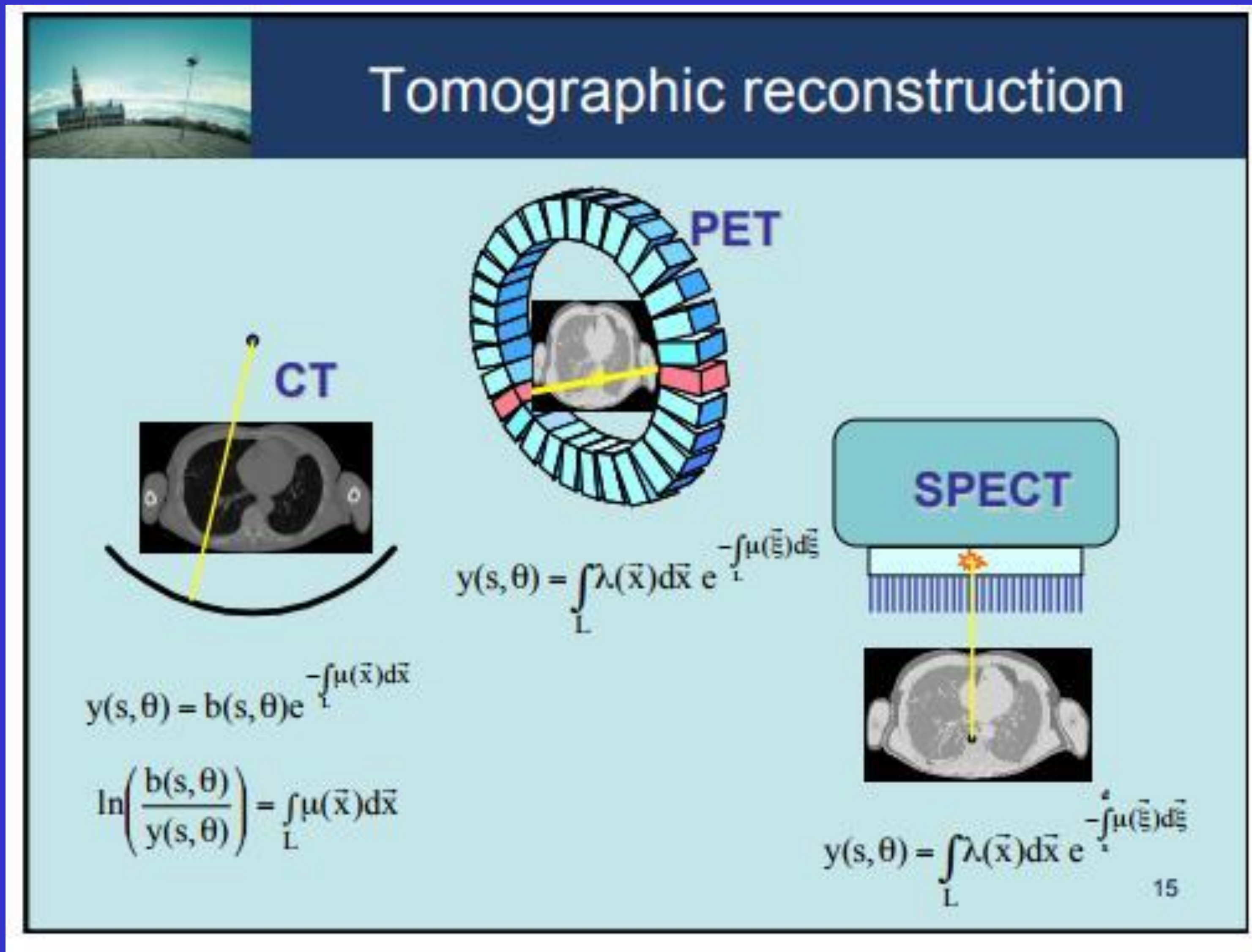
SPECT and PET: Key Features

PET	SPECT
• isotopes are cyclotron produced	• isotopes may be reactor, generator or cyclotron produced
• isotopes typically have short half-lives (min-hrs)	• isotopes typically have longer half-lives (hrs-days)
• 2 γ per nuclear decay (requires coincidence detection)	• 1 γ per nuclear decay (requires collimator)
• electronic collimation (good detection efficiency)	• physical collimation (poor detection efficiency)
• stationary ring detector	• rotating detector/s (usually)

Physics of Neurotechnologies: SPECT & PET



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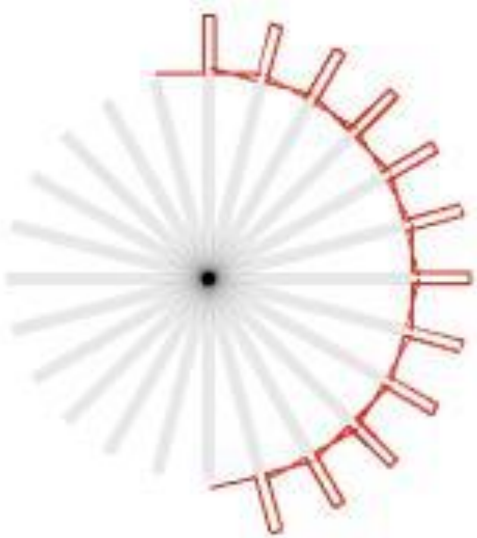
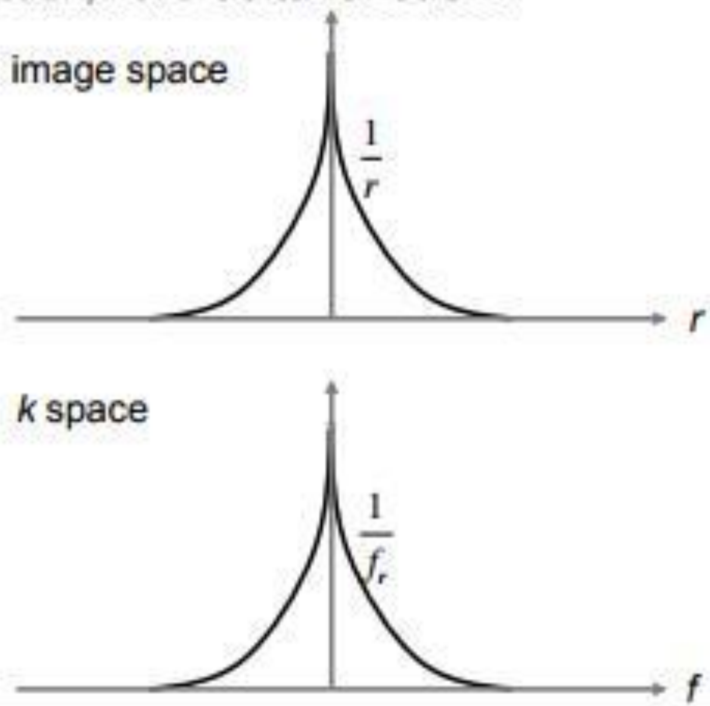
Simple Back Projection

- leads to radial (1/r) blurring in the spatial domain
- this is equivalent to a 1/f function in the frequency domain
- what type of function would we need to multiply 1/f by to result in a perfect point source reconstruction, i.e. a **delta function**?

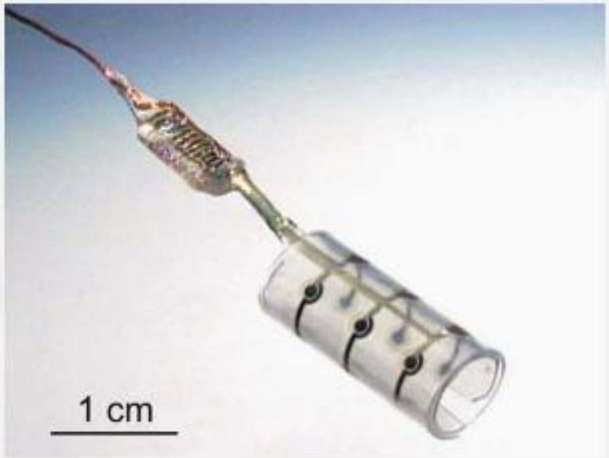




Brain Engineering

Illustration of a cochlear implant (National Institutes of Health).

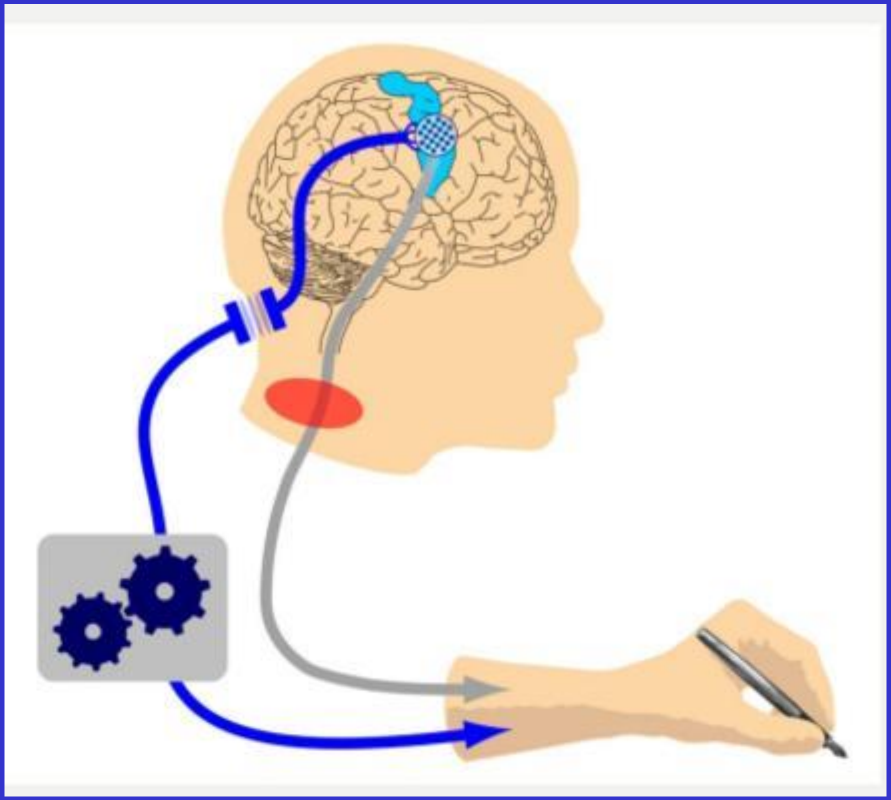
The two main forms of grasping. A neurotechnological prosthesis should be able to elicit both so that a patient can carry out everyday tasks (Tobias Pistohl, BMII).



A "cuff" electrode that is placed around a nerve fiber in the peripheral nervous system (Hassler et al. (2011) Journal of Polymer Science: Part B: Polymer Physics 49, 18–33).

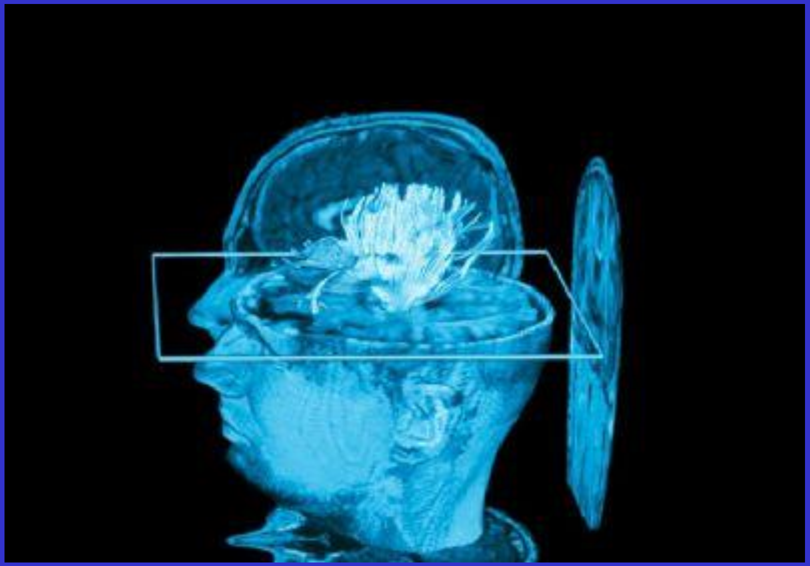
Brain Engineering

Spinal Cord Stimulator

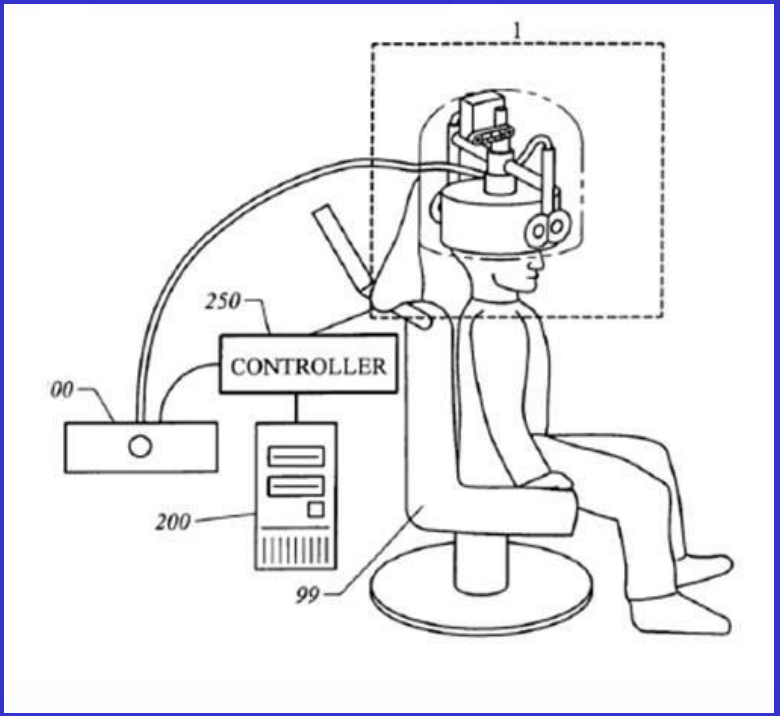


Brain Machine Interface

Brain Engineering



Mind Reading-MRI



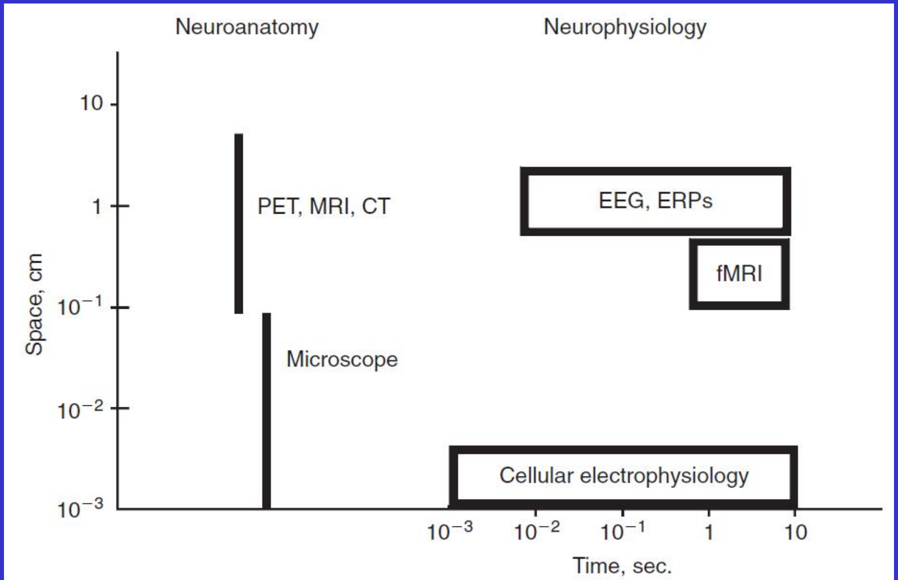
Magnetic Stimulation

Quantitative Electroencephalography (QEEG)
Mapping of the Brain
Modern Renaissance of EEG

- With QEEG it is possible to:
  - See the pattern of the brain activity
  - Evaluate the state of the mind and the brain
  - Map the areas of the brain with different levels of activities
  - Analyze the brain networks
  - Diagnose neural disorders
  - Evaluate the treatment of neural disorders
  - Design efficient artificial neural networks

Modern Renaissance of EEG

- Although EEG was discovered almost 80 years ago, the fastest development of this field was observed only recently, because:



1. New methods of EEG analysis such as spatial filtration techniques in artifact correcting, independent component analysis of ERPs, wavelet analysis, electromagnetic tomography, and some others.

2. Relative cheapness of modern EEG devices.

3. Dramatic increase of our knowledge regarding mechanisms of generation of spontaneous EEG waves and functional meaning of ERPs components.

4. High temporal resolution of EEG and ERPs signals which principally can not be achieved by other neuroimaging techniques. EEG and ERP provide time resolution of few milliseconds, while PET and MRI are limited by few seconds.

Pharmaco-QEEG

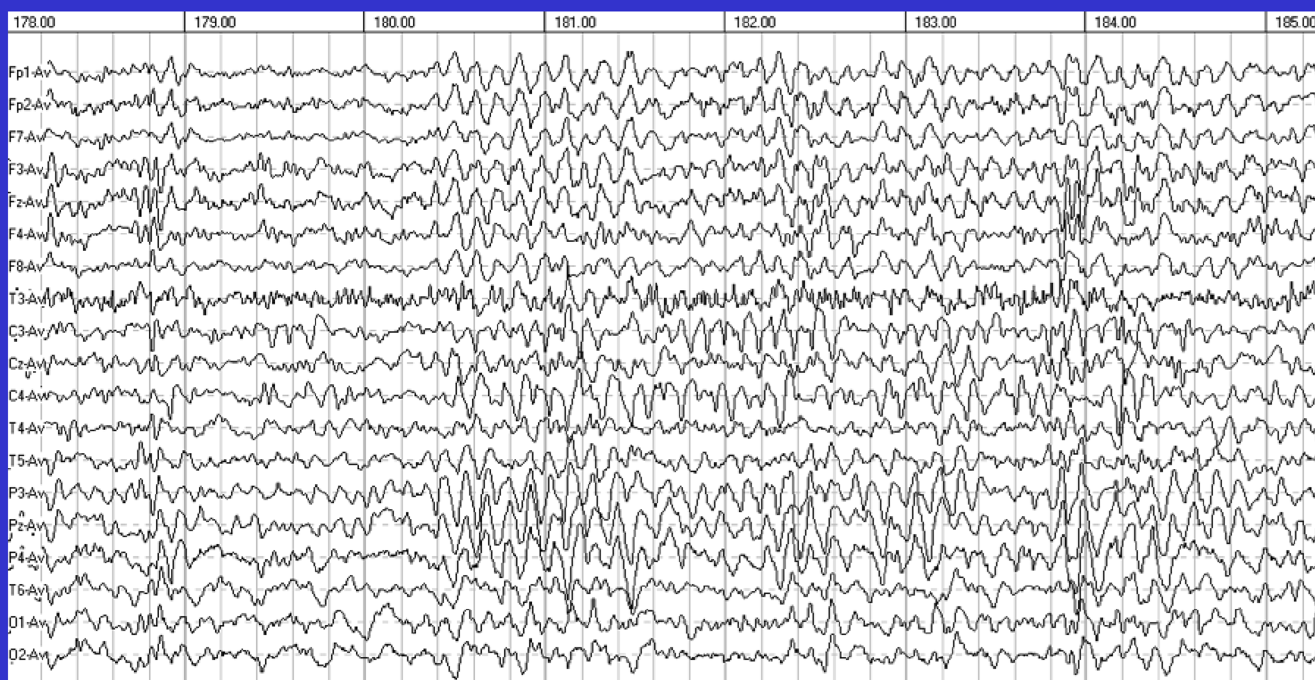
- The idea that QEEG may be applied in pharmacology as an index of brain functioning in response to pharmaceutical agents was born in the early 1960s.
- International Pharmaco-EEG society (IPEG) was established in 1980
- However individual QEEG profiles for different classes of drugs often overlapped with each other, because:

(1) Inappropriate extraction of parameters of QEEG with meaningful functional significance,
(2) Large interindividual differences that are probably exhibited in existence of several classes of QEEG patterns,
(3) Nature sharing of effects of distinct classes of drugs.

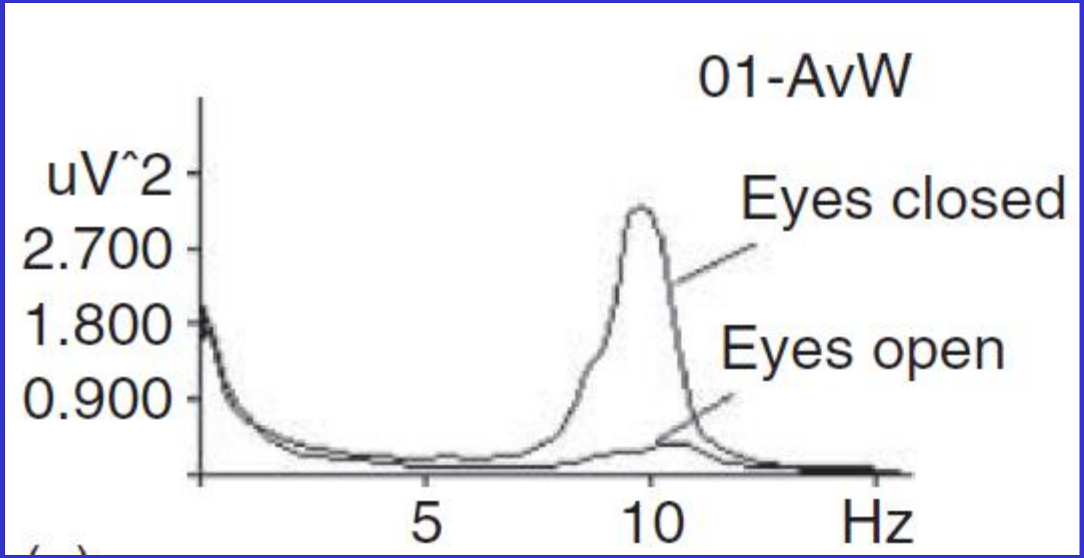
- So: Pharmaco-QEEG was a method with poor theoretical background and without any significant effect on drug industry and on clinical application.

Brain Waves

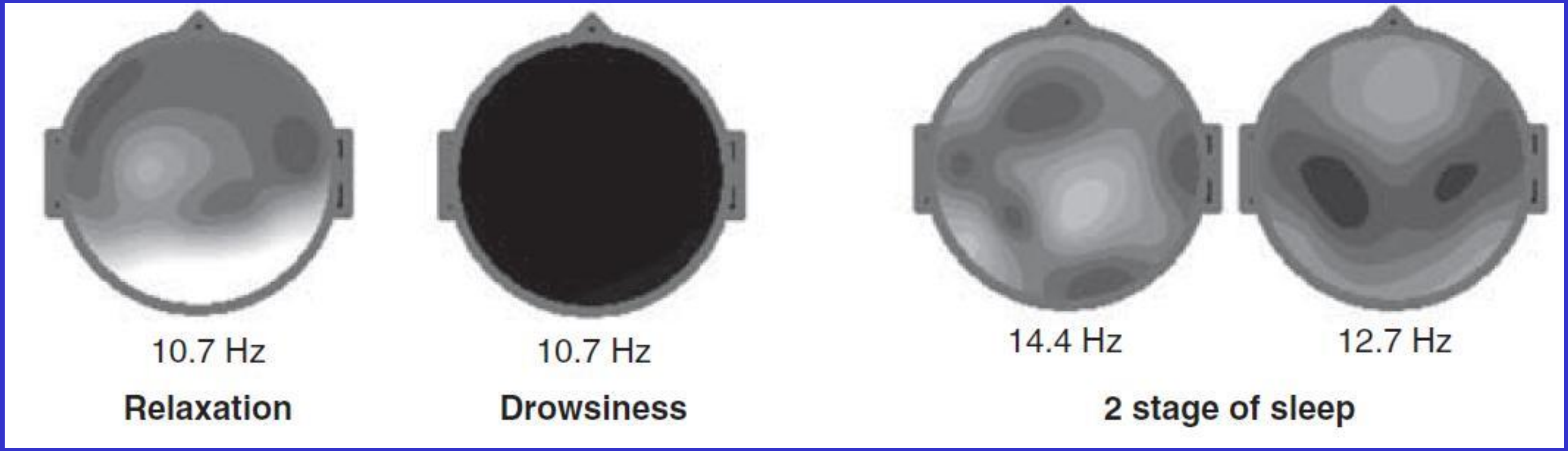
- The roots of all thoughts, learning, emotions, and behaviours is the communication between neurons.
- Synchronized electrical pulses of a group of neurons generate brain waves.
- The brain waves changes according to the state of our feeling and actions.



Brain Rhythm - Alpha

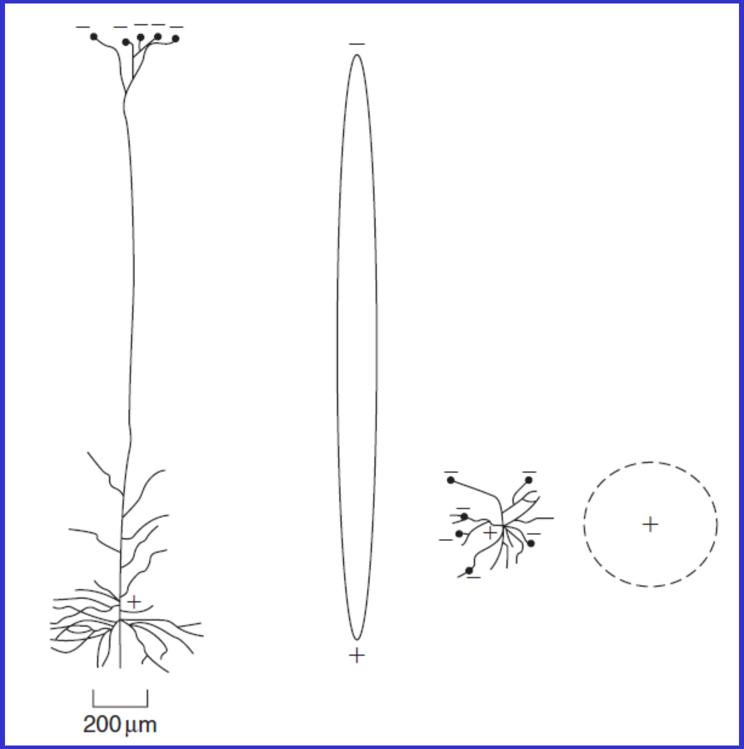


Synchronization of the occipital alpha rhythm during closing eyes.



Source of EEG

- EEG is a result of collective electrical behavior of pyramidal neurons, that is, a sum of hundreds of thousands small dipoles corresponding to those pyramidal cells.
- The dipoles are induced by local currents that are associated with excitatory and inhibitory postsynaptic potentials.
- Excitatory postsynaptic potentials (EPSP) depolarize the membrane, driving its potential toward the threshold of spike generation and making probability of discharging higher.
- Inhibitory postsynaptic potentials (IPSP) hyperpolarize membrane, driving its potential from the threshold, and thus decreasing the probability of discharge.

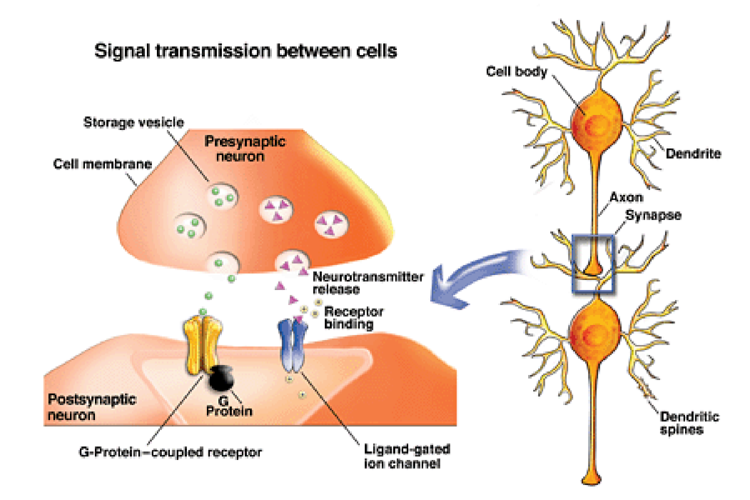


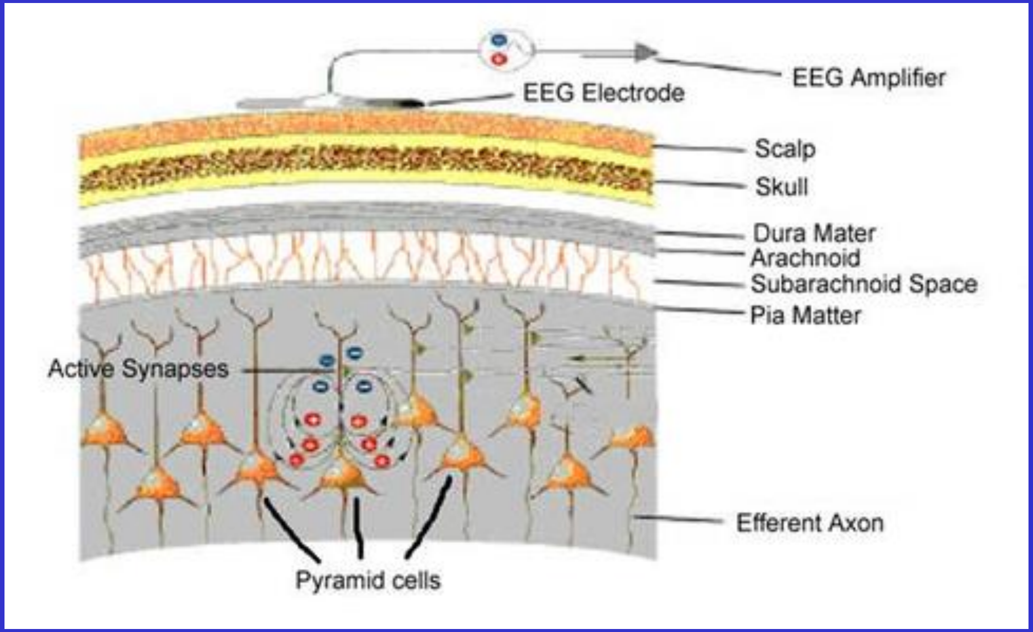
1. The duration of postsynaptic potentials (20-30 ms ~ 30-50 Hz) is 10 times longer than duration of a single spike (1 ms ~ 1000 Hz). The duration of postsynaptic potential depends on the type of receptor-mediator coupling.

Source of EEG

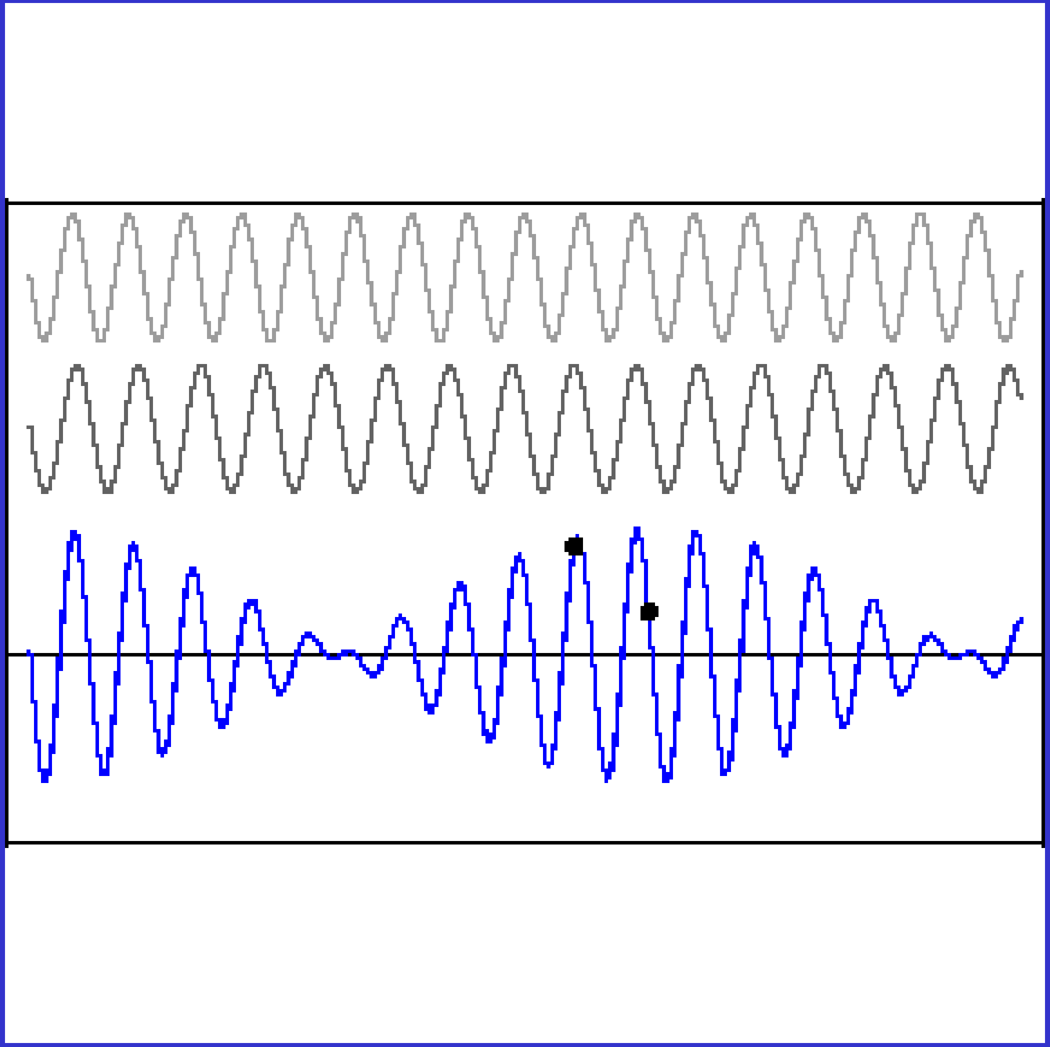
2. In addition, the space occupied by synapses where postsynaptic potentials are generated is much larger than the space occupied by axonal hillocks where spike are generated.

- These two factors make postsynaptic potentials (not impulse activity of neurons) to play a critical role in generation of field potentials recorded at the scalp in 0–70 Hz frequency range (EEG).

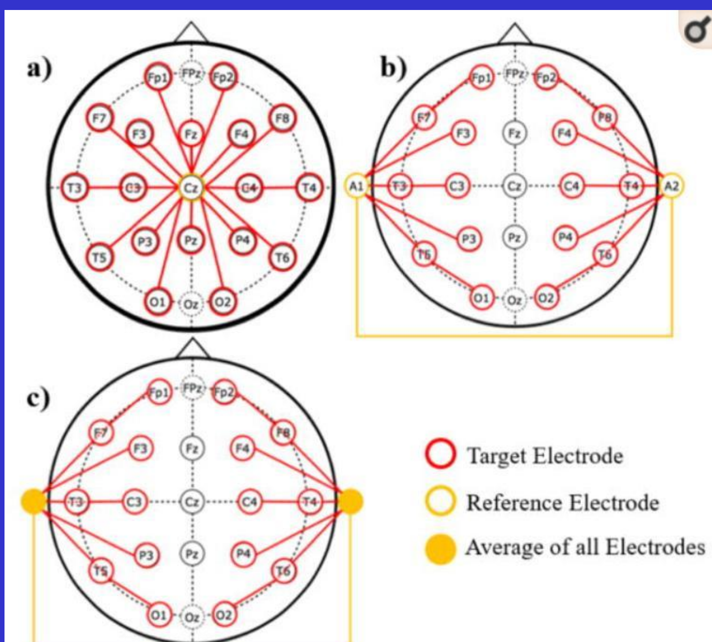


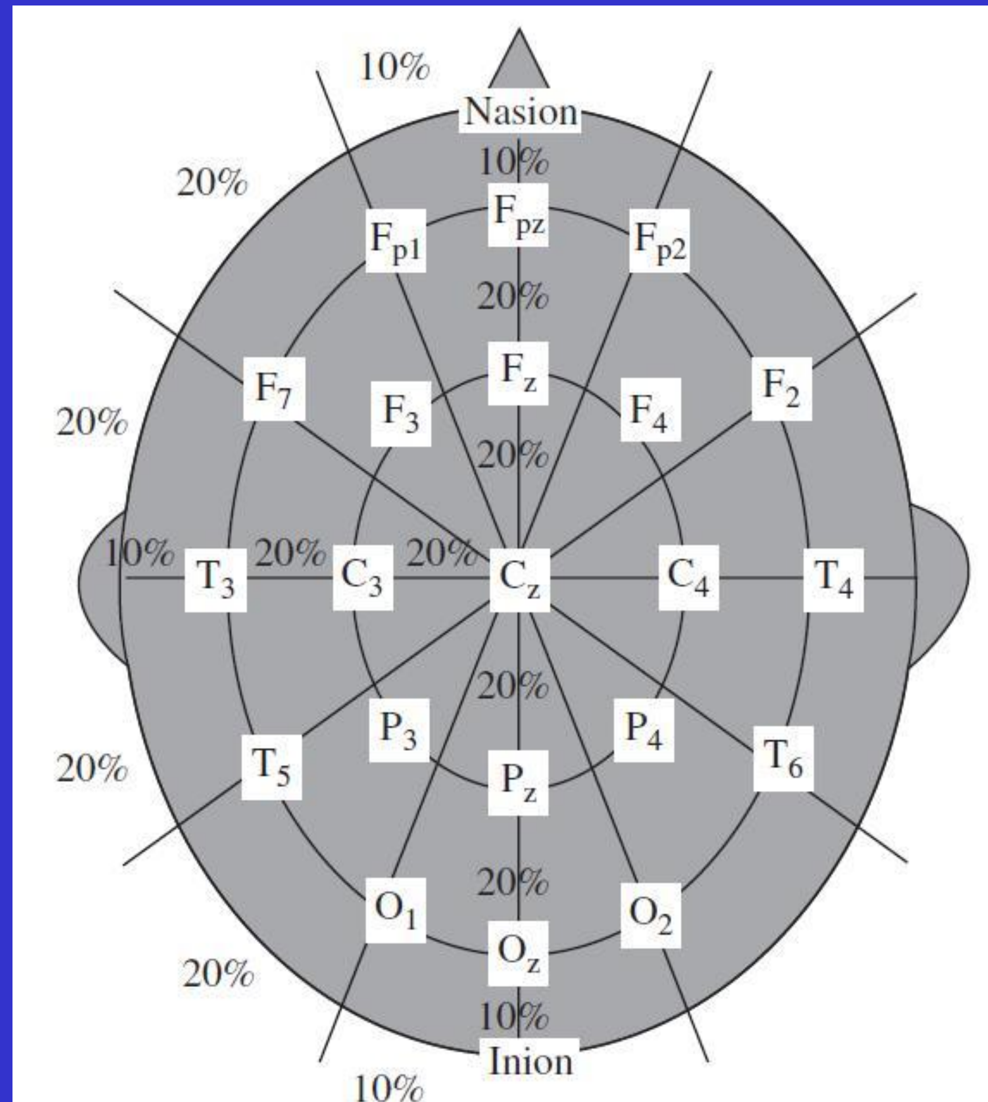


Superposition of Waves



10–20 EEG electrode positions and Montages



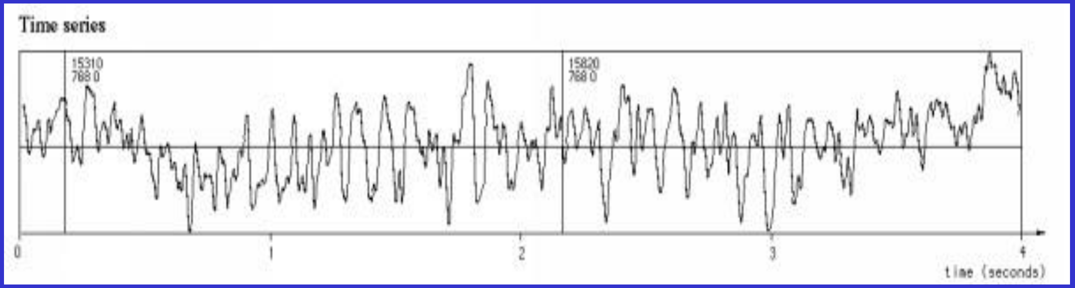


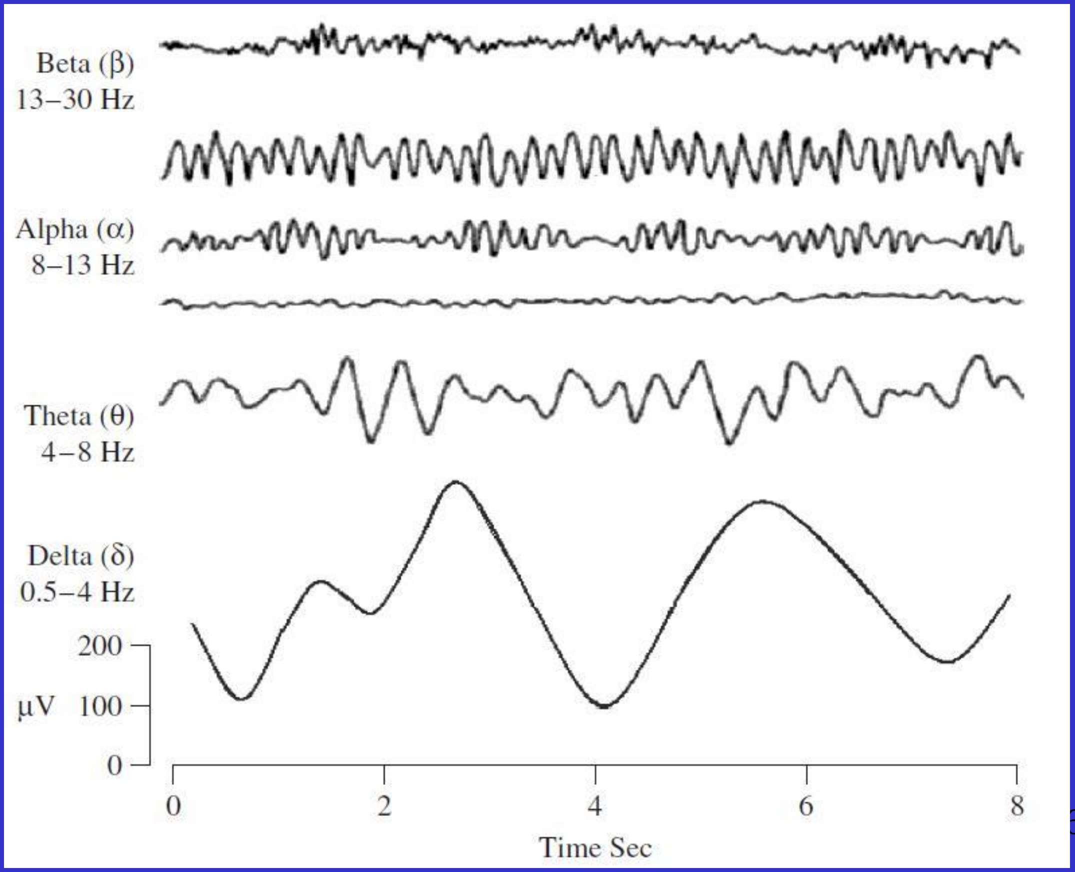
Montages

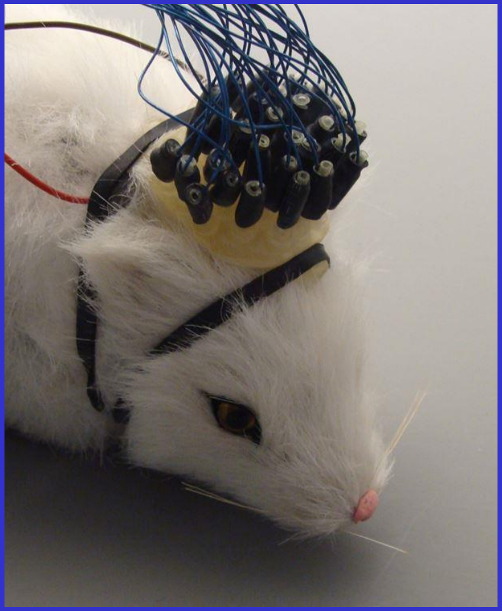
- **Montage** is a rule according to which EEG potentials are computed.
- **Linked ears montage**: Measuring electrodes potentials in reference to two linked electrodes located at left and right earlobes.
- **Common average reference montage** is a computational montage in which electrodes ’ potentials are measured in reference to “common average ” potential, that is, a potential averaged over all electrodes.
- **Local average reference montage** is a computational montage in which a local average potential is averaged over a small number of electrodes in the vicinity of a target electrode and is subtracted from the potential of the target electrode. There are several types of local average montages (Laplacian, Lemos, Hjorth).
- **Referential recording is a recording** of EEG signal when the second (reference) electrode is usually located on the earlobes, mastoids, or the tip of the nose, that is, far away from the neuronal source. This is in contrast to sequential recording when two electrodes are located on the scalp near EEG generators in the cortex.

Brainwaves Decomposition

- An EEG signal is a measurement of currents that flow during synaptic excitations of the dendrites of many pyramidal neurons in the cerebral cortex.

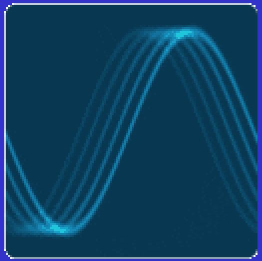




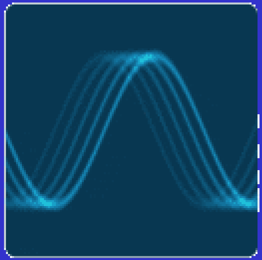


Brainwaves

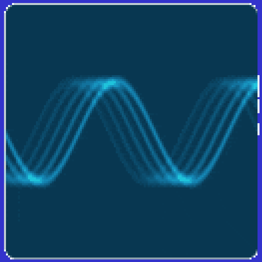
- **DELTA WAVES (0.1-3 Hz)**
  [Occurs in deepest meditation, dreamless sleep, suspending external awareness, source of empathy, healing and regeneration]



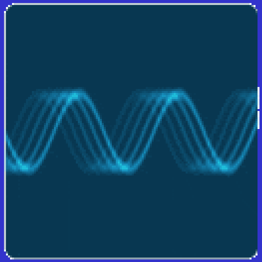
- **THETA WAVES (3.1-8 Hz)**
  [Sleep, deep meditation, learning, memory, and intuition, transition from sleep to waking, drift off to sleep, dream, vivid imagery, fears, troubled history, and nightmares]



- **ALPHA WAVES (8.1-12 Hz)**
  [Quietly flowing thoughts, some meditative states, being in current time, resting state for the brain, mental coordination, calmness, alertness, mind/body integration and learning]

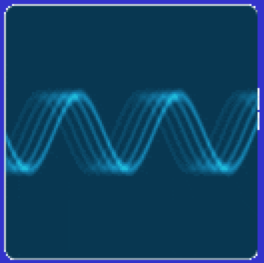


- **BETA WAVES (12.1-30 Hz)**
  [Normal waking state, consciousness, attention toward outside world, engaged in problem solving, judgment, decision making, or focused mental activity]



Brainwaves-cont…

- **BETA WAVES (12.1-38 Hz)** is usually divided into 3 bands:

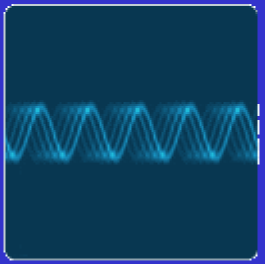


- ➢ Beta1 (12.1-15 Hz):
  [‘fast idle’, musing]

- ➢ Beta2 (15.1-20 Hz)
  [high engagement, actively figuring something out]

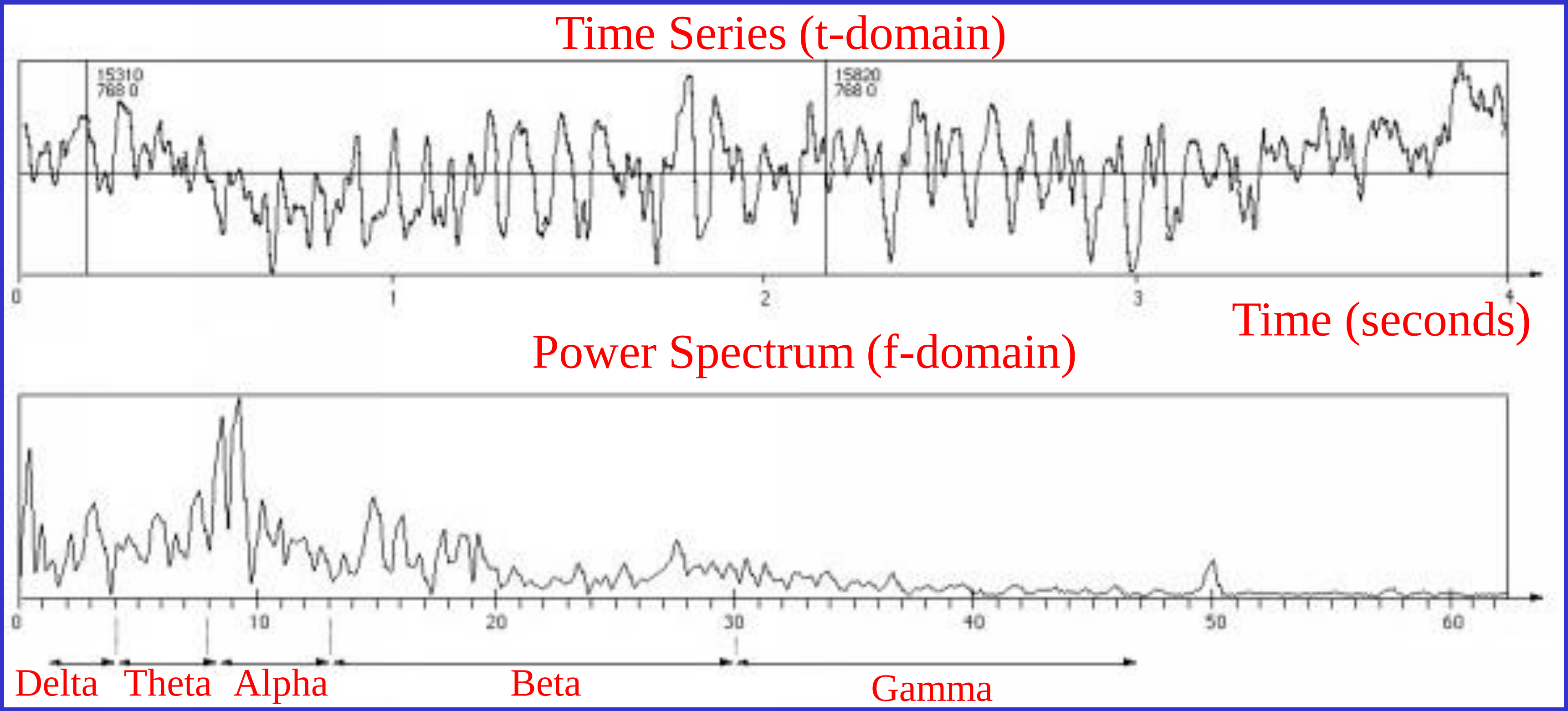
- ➢ Beta3 or High Beta (20.1-30 Hz)
  [highly complex thought, integrating new experiences, high anxiety, or excitement]
  → High energy consumption, not very efficient

- **GAMMA WAVES (30-100 Hz)**
  [simultaneous processing of information from different brain areas, pass information rapidly and quietly, universal love, altruism, higher virtues, expanded consciousness and spiritual emergence]



Brainwaves Analysis

- Time-domain analysis
- Frequency-domain analysis
- Spatial-domain analysis
- Multiway processing.

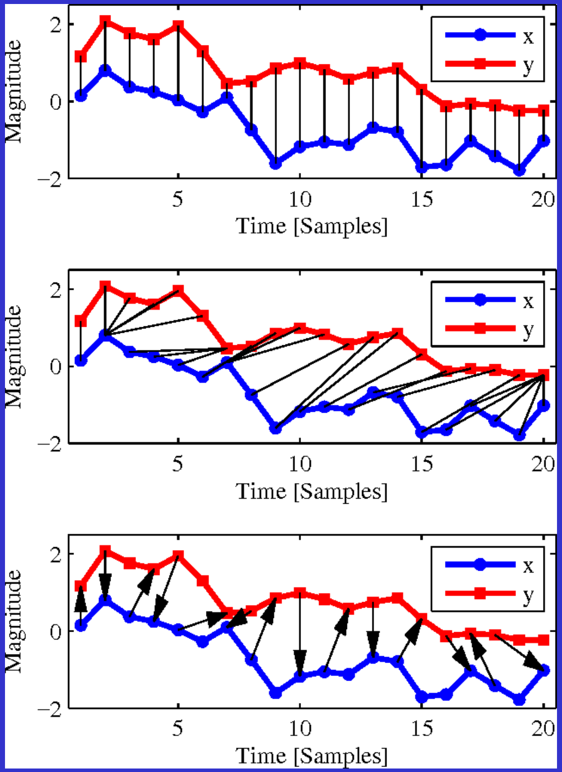


Time-domain Analysis of Brainwaves

- **Auto-Correlation**: a tool for periodicity estimation
  $\emptyset(\tau) = \sum_n x[n]x[n+\tau]$

$$\hat{r}_x(k,m) = \begin{cases} \frac{1}{N} \sum_{l=0}^{N-1-k} x(l+m+k)x(l+m), & k = 0, \ldots, N-1 \\ 0, & k = N, N+1, \ldots \end{cases}$$

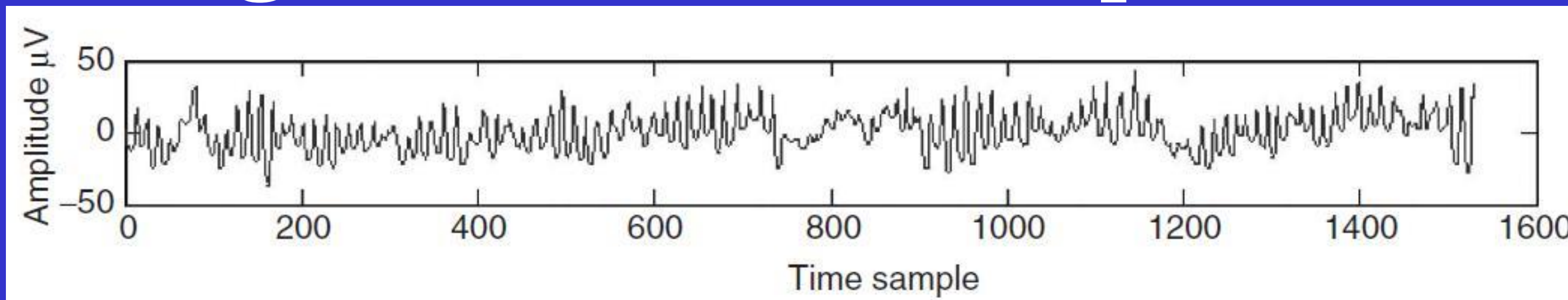
$$d_3(m) = \frac{\int_{-\pi}^{\pi} [S_x(\omega,m) - S_x(\omega,m-1)]^2 \, d\omega}{\int_{-\pi}^{\pi} S_x(\omega,m) d\omega \int_{-\pi}^{\pi} S_x(\omega,m-1) \, d\omega}$$

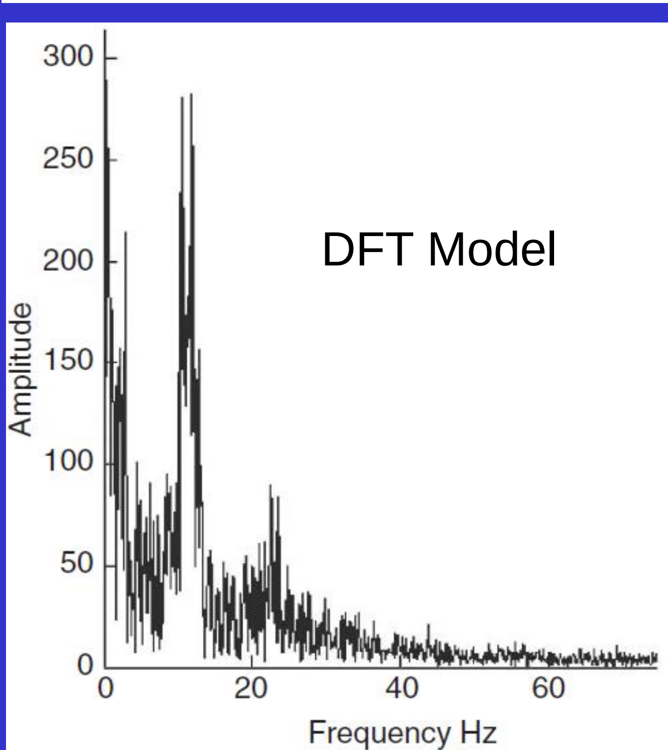


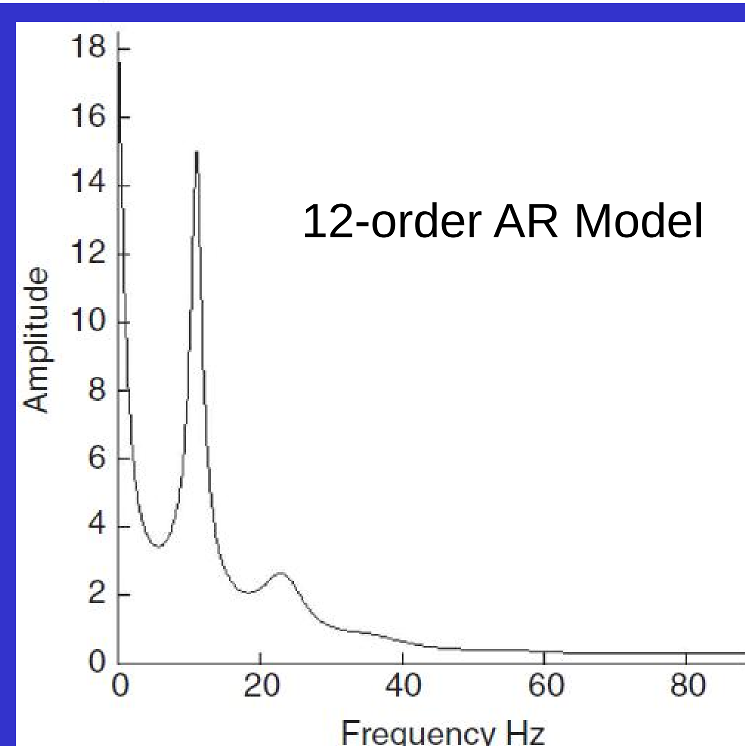
- **Cross-Correlation:** a signal processing tool to investigate temporal relationships between two signals:
  $\emptyset(\tau) = \sum_n x[n]y[n+\tau]$

or with Average Magnitude Difference Function (AMDF): $\emptyset(\tau) = \sum_n |x[n] - y[n+\tau]|$

Single-channel EEG spectrum







Spectrum of the signal using the Discrete Fourier Transform (DFT)

Spectrum using the 12-order Autoregressive (AR) Model

Calculating Spectrogram

Short-time Fourier transform (STFT):

$$X(n,\omega) = \sum_{\tau=-\infty}^{\infty} x(\tau)w(n-\tau)\mathrm{e}^{-\mathrm{j}\omega\tau}$$

Spectrogram:

$$S_x(n,\omega) = |X(n,\omega)|^2$$

Continuous Wavelet Transform:

$$W(a,b) = \frac{1}{\sqrt{a}}\int_{-\infty}^{\infty} f(t)\psi^*\left(\frac{t-b}{a}\right)\mathrm{d}t$$

Coherency

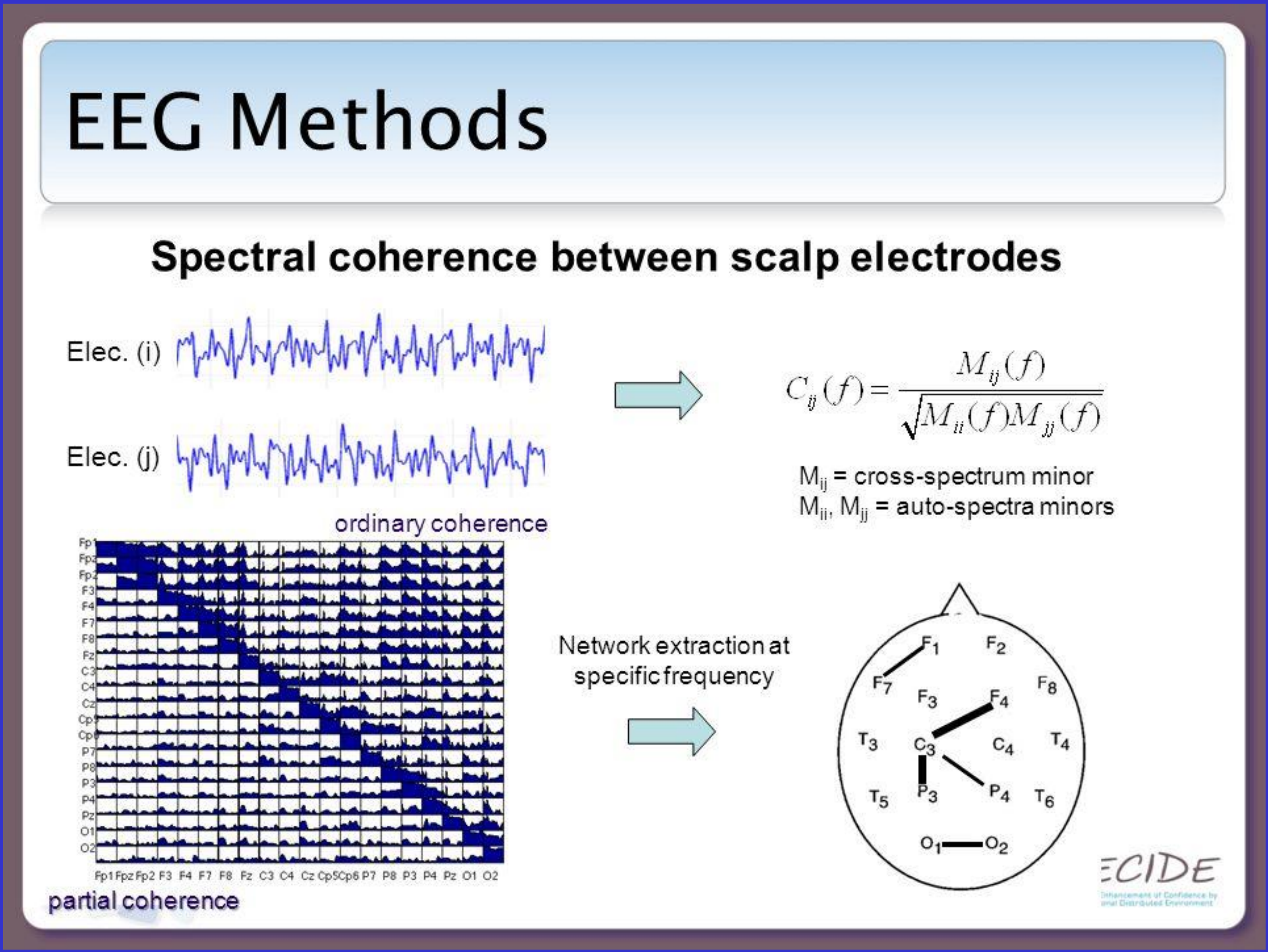
- The spatial statistics of scalp EEGs are usually presented as coherence in individual frequency bands:

$$\mathrm{Coh}_{ij}^2(\omega) = \frac{E[|C_{ij}(\omega)|^2]}{E[C_{ii}(\omega)]E[C_{jj}(\omega)]}$$

$$C_{ij}(\omega) = X_i(\omega)X_j^*(\omega)$$

- Therefore, spectral coherence is a common method for determining the synchrony in EEG activity.
- These coherences result both from correlations among neocortical sources and volume conduction through the tissues of the head, i.e. brain, cerebrospinal fluid, skull, and scalp.
- A measure of this coherency, such as an average over a frequency band, is capable of detecting zero time lag synchronization and fixed time nonzero time lag synchronization, which may occur when there is a significant delay between the two neuronal population sites

Coherence



EEG Methods
Spectral coherence between scalp electrodes
Elec. (i)
Elec. (j)
$C_{ij}(f) = \frac{M_{ij}(f)}{\sqrt{M_{ii}(f) M_{jj}(f)}}$
M_{ij} = cross-spectrum minor
M_{ii}, M_{jj} = auto-spectra minors
ordinary coherence
Fp1 Fpz Fp2 F3 F4 F7 F8 Fz C3 C4 Cz Cp5 Cp6 P7 P8 P3 P4 Pz O1 O2
partial coherence
Network extraction at specific frequency
F_1 F_2 F_7 F_8 F_3 F_4 T_3 C_3 C_4 T_4 T_5 P_3 P_4 T_6 O_1 O_2

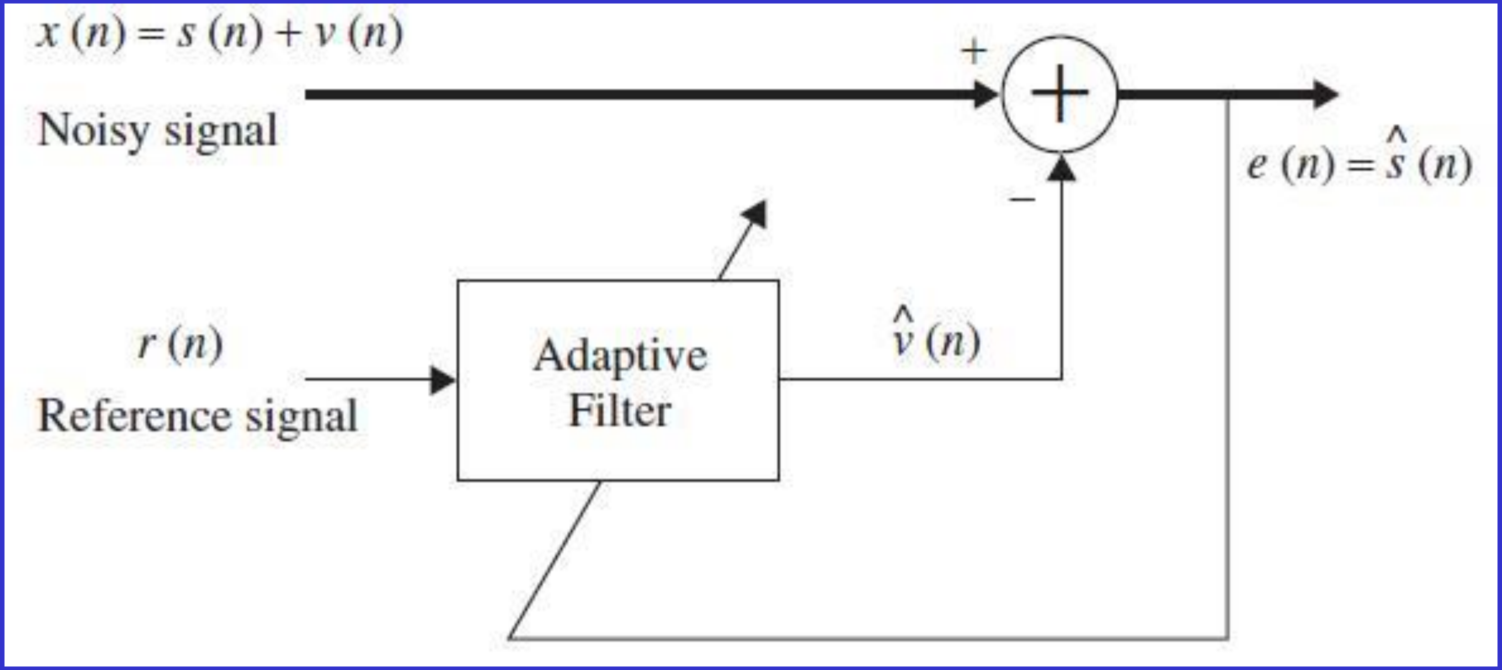
Entropy and Chaos

- Entropy is a measure of uncertainty.
- The level of chaos may also be measured using entropy of the system. Higher entropy represents higher uncertainty and a more chaotic system

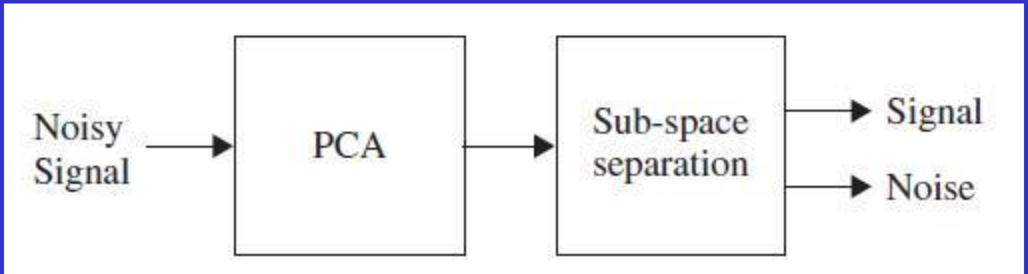
$$\text{Entropy of the signal } x(n) = \int_{\min(x)}^{\max(x)} p_x \log(1/p_x)\, dx$$

- p_x is the probability density function (PDF) of signal x(n).

Filtering and Denoising

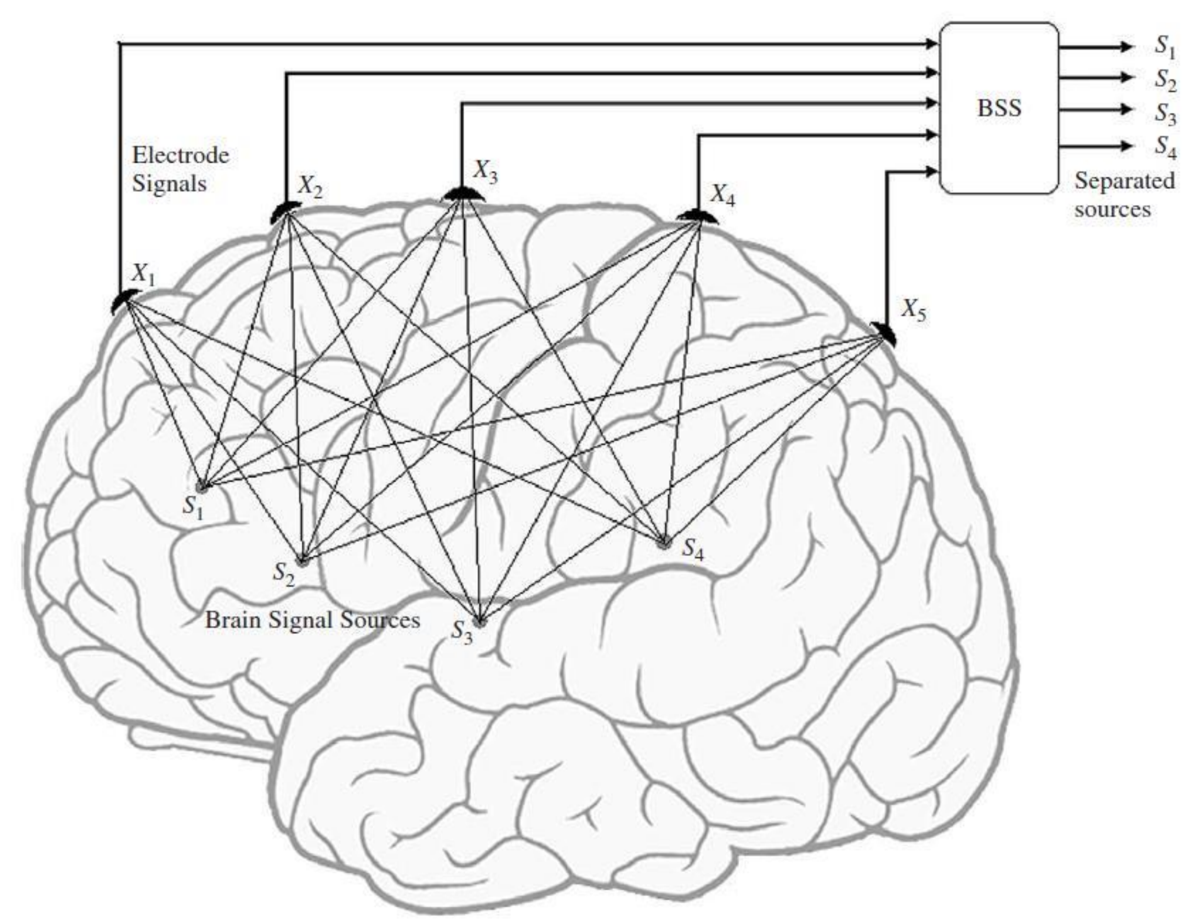


Principal Component Analysis (PCA)



Independent Component Analysis (ICA)

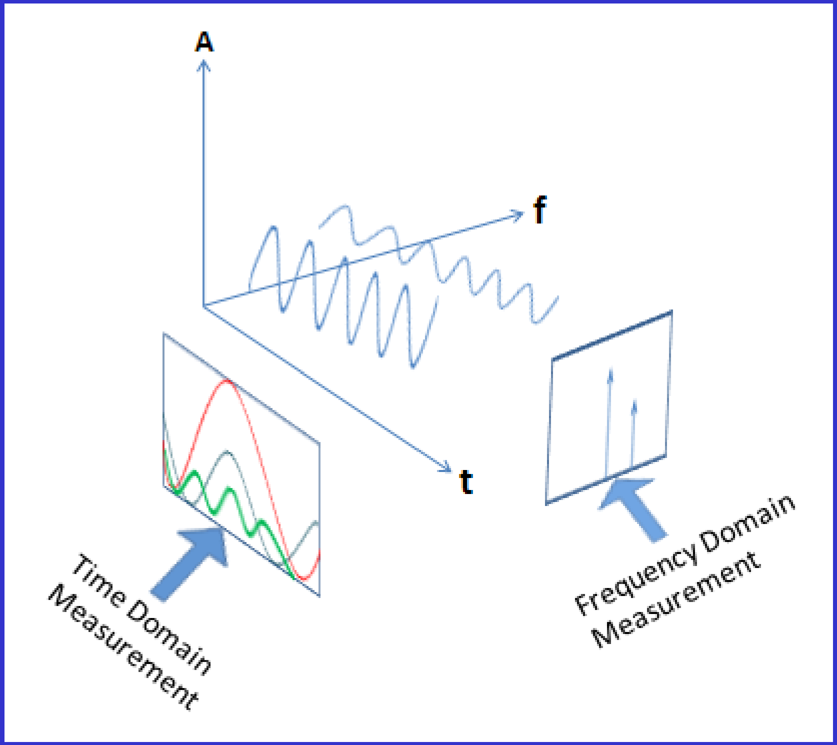
- An important application of ICA is in blind source separation (BSS).



Definitions

- **Notch filter: A** very sharp filter that attenuates a certain frequency in the signal. In EEG a notch filter at 50 (60) Hz is used to filter out the noise from the electrical system in the room.

- **Sampling rate**: The rate at which raw EEG signal is sampled (quantified). According to Naiquist theorem the sampling rate must be twice as much as the highest possible frequency of recorded EEG signal.



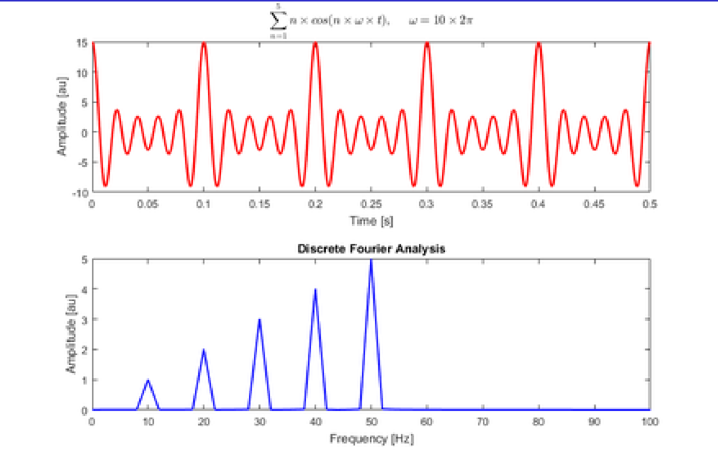
Spectra: Computed by means of fast Fourier transformation that decomposes EEG signals into series of sinusoidal functions with different frequencies, amplitudes, and phases. Spectra show how amplitude, power or phase of the sinusoidal harmonic depends on the sinusoid's frequency in the EEG signal.

Frequency-domain Analysis of Brainwaves

DFT

- Discrete Fourier Transform (DFT): A mathematical tool for estimating the frequency content (i.e. both magnitude and phase) of any sequence of samples.
- DFT is an equation which allows use to analyse a block or frame of samples in order to estimate the component present at ANY particular digital frequency (θ)
- Mathematically speaking, the output of this equation is a complex number which can be represented by a magnitude and a phase value:
  - ➢ The magnitude is the “amplitude” of the component at that frequency.
  - ➢ The phase is the “phase angle” of the component at that frequency (0-π) or (0-fs/2 Hz).

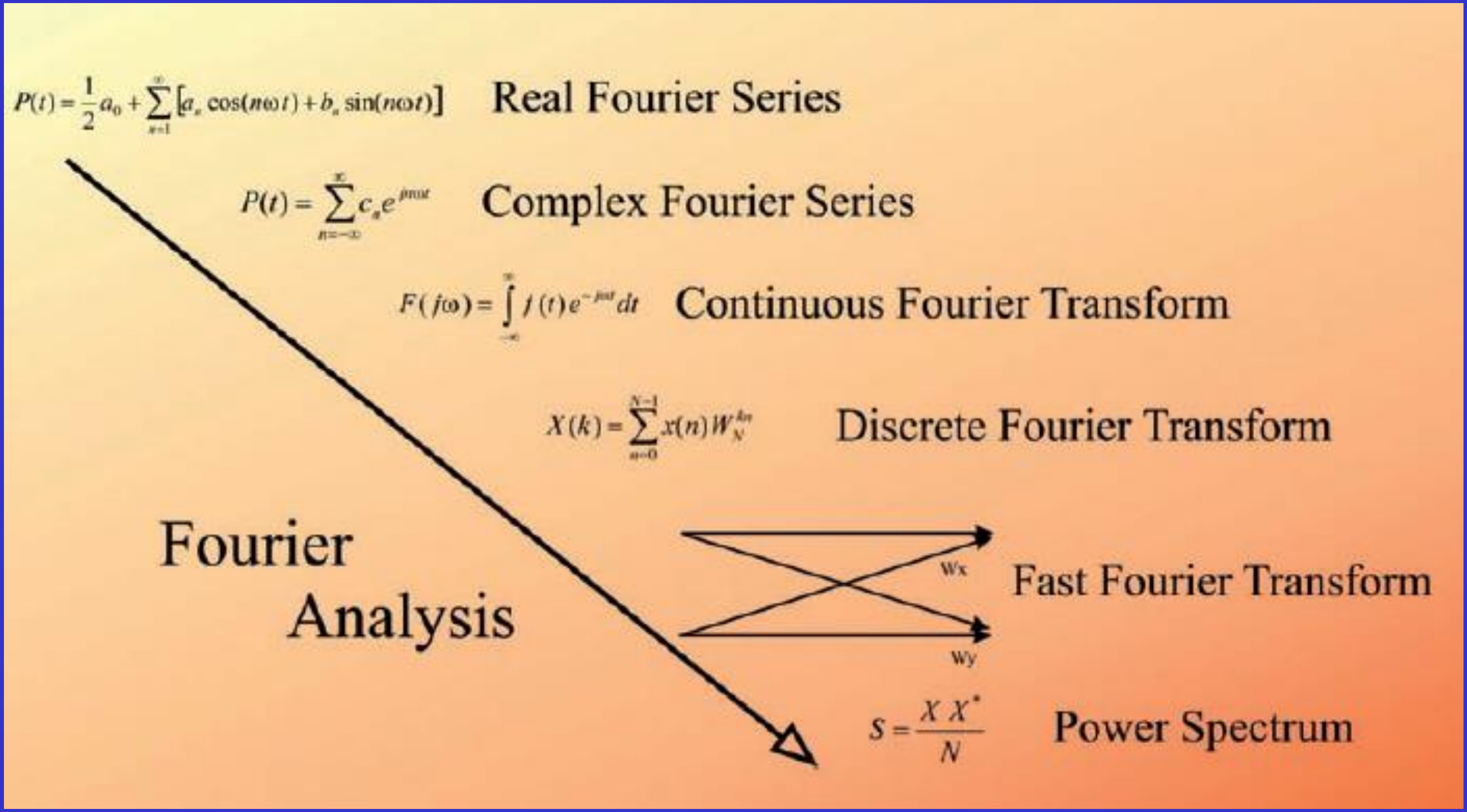
$$X_k = \sum_{n=0}^{N-1} x_n \cdot e^{-\frac{2\pi i}{N} kn}$$



Decomposition of White Light

- A prism performs spectral decomposition of white light in bands with different wavelengths that are perceived by us as different colors.

Fourier Transform



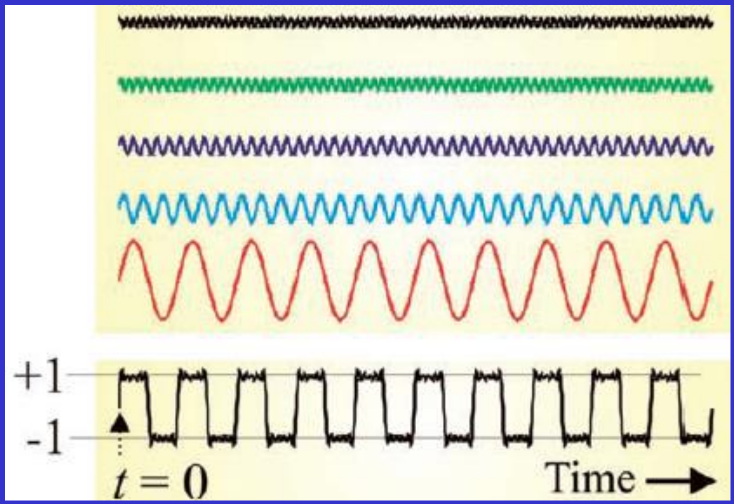
We usually want to quantify the frequency components in a signal for a whole set of discrete frequencies in the range of possible digital frequencies → Computationally very demanding!

Fast Fourier Transform (FFT)

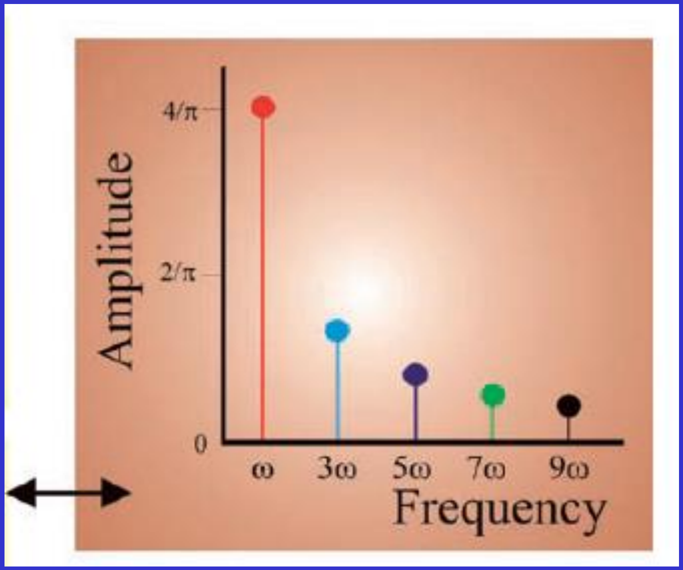
- The Fast Fourier Transform (FFT) addresses this issue by carrying out the DFT calculation for a certain specific set of frequencies in a computationally efficient manner.
- The FFT uses as its input a block or frame of N consecutive samples

- Restriction: $N=2^k$ where k is some integer value!
- N is termed the FFT "order" (e.g. "512 point" (2^9) FFT)
- The output of the FFT will be exact same result that you would have got if you calculated the DFT for these specific set of N digital frequencies.

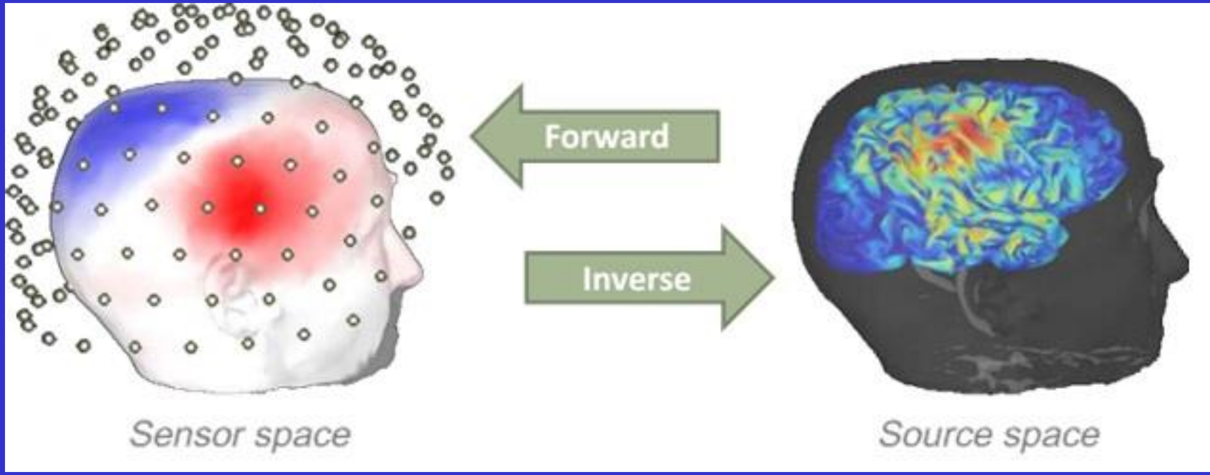
- N points in time → N frequency points after the FFT



Fourier Transform (FFT)



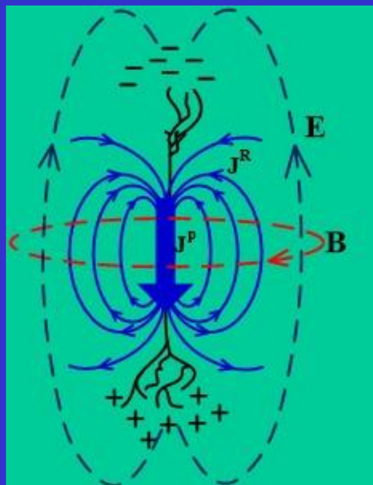
Forward-Inverse Problem



- **Forward problem** is a problem of calculating the scalp potential of a single dipole or a set of dipoles located within the cortex. The forward solution can be expressed in a physical equation and numerically solved by computers.

- **Inverse problem** is a problem of finding multiple elemental dipoles in the cortex (sometimes named density of neuronal generators) that approximate potentials recorded by multiple scalp electrodes. Theoretically this problem does not have a unique solution, that is, a certain scalp distribution can be achieved by infinite number of cortical distributions.

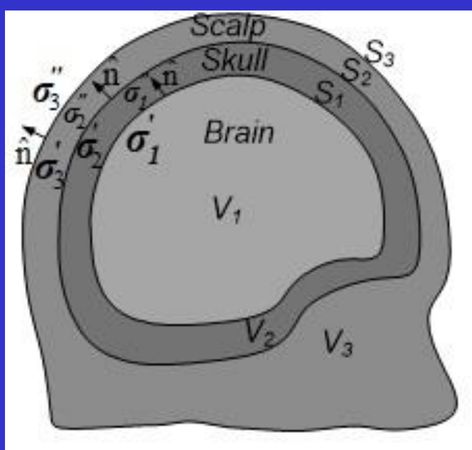
Forward Problem Solution



J(r) ➔ V & B

$$\nabla . \mathbf{J}^p - \sigma \nabla^2 V = 0$$

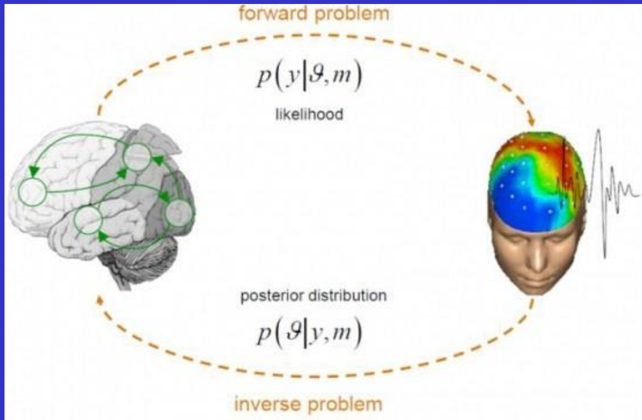
$$\boldsymbol{B}(\boldsymbol{r}) = \frac{\mu_0}{4\pi}\int \mathbf{J}(\boldsymbol{r}') \times \frac{\boldsymbol{r}-\boldsymbol{r}'}{|\boldsymbol{r}-\boldsymbol{r}'|^3} d^3r' = \frac{\mu_0}{4\pi}\int \mathbf{J}(\boldsymbol{r}') \times \nabla' \frac{1}{|\boldsymbol{r}-\boldsymbol{r}'|} d^3r'$$



$$\frac{\sigma'_k + \sigma''_k}{2} V(\boldsymbol{r}_k) = \frac{1}{4\pi}\sum_j (\sigma'_j - \sigma''_j) \int_{S_j} dS'_j \boldsymbol{n}(\boldsymbol{r}') \cdot \frac{\boldsymbol{r}'-\boldsymbol{r}_k}{|\boldsymbol{r}'-\boldsymbol{r}_k|^3} V(\boldsymbol{r}') + \frac{1}{4\pi}\int_V d^3r' \boldsymbol{J}^p(\boldsymbol{r}') \cdot \frac{\boldsymbol{r}_k-\boldsymbol{r}'}{|\boldsymbol{r}_k-\boldsymbol{r}'|^3}$$

$$\boldsymbol{B}^R(\boldsymbol{r}) = \frac{\mu_0}{4\pi}\int \mathbf{J}^p(\boldsymbol{r}') \times \nabla' \frac{1}{|\boldsymbol{r}-\boldsymbol{r}'|} d^3r' - \frac{\mu_0}{4\pi}\sum_j (\sigma'_j - \sigma''_j) \int_{S_j} dS'_j \boldsymbol{n}(\boldsymbol{r}') \times V(\boldsymbol{r}')\nabla' \frac{1}{|\boldsymbol{r}-\boldsymbol{r}'|}$$

Inverse Problem Solution



V & B ⇒ $J(r)$

$$f_i(t) = \int_V \boldsymbol{M}_i(\boldsymbol{r}') \cdot \boldsymbol{J}^p(\boldsymbol{r}', t) d^3r' + \xi_i(t) \quad , \qquad i = 1, \dots, N$$

$$\mathbf{J}^p(\mathbf{r}) = \sum_{j=1}^{M} \mathbf{p}_j \delta^{(3)}(\mathbf{r} - \mathbf{r}_j)$$

$$\mathbf{f} = \mathbf{Kq} + \xi$$

$$\mathbf{f} \equiv (f_1, \cdots, f_N)^T$$

$$\xi \equiv (\xi_1, \cdots, \xi_N)^T$$

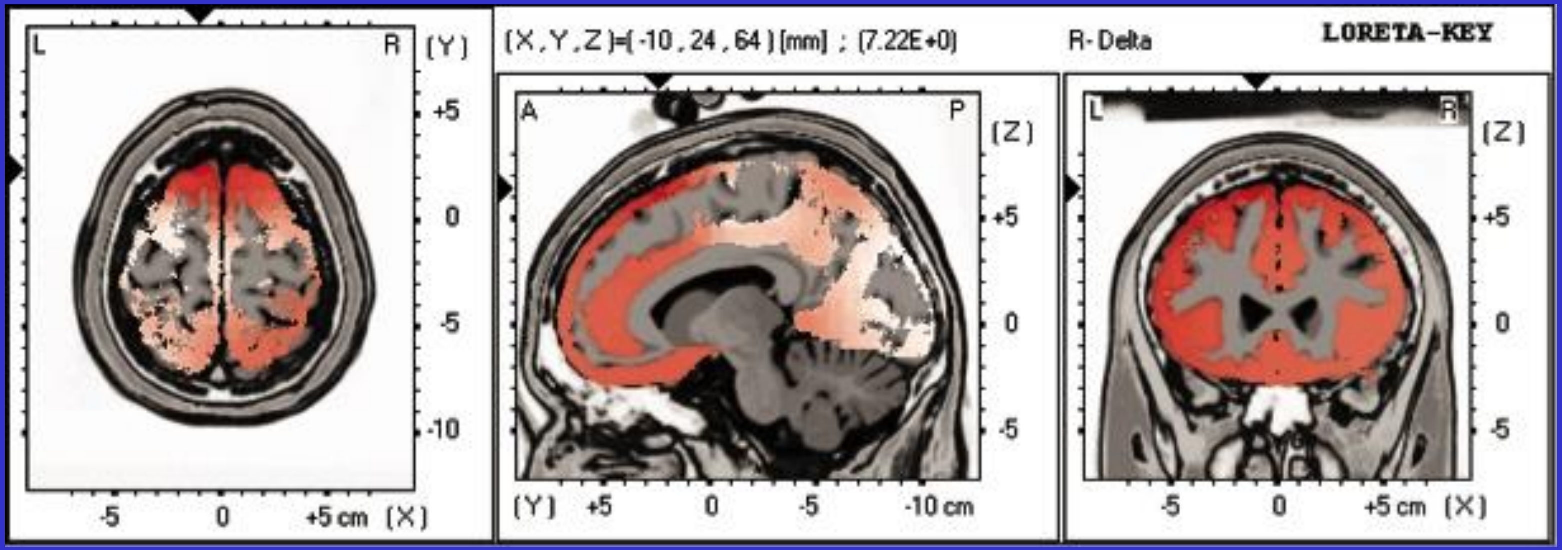
$$\boldsymbol{q} \equiv \left((\boldsymbol{p}_1)_x, (\boldsymbol{p}_1)_y, (\boldsymbol{p}_1)_z, (\boldsymbol{p}_2)_x, (\boldsymbol{p}_2)_y, (\boldsymbol{p}_2)_z, \cdots, (\boldsymbol{p}_M)_x, (\boldsymbol{p}_M)_y, (\boldsymbol{p}_M)_z \right)^{\boldsymbol{T}}$$

$$\boldsymbol{K} \equiv \boldsymbol{K}(\boldsymbol{r}_1, \boldsymbol{r}_2, \cdots, \boldsymbol{r}_M)$$

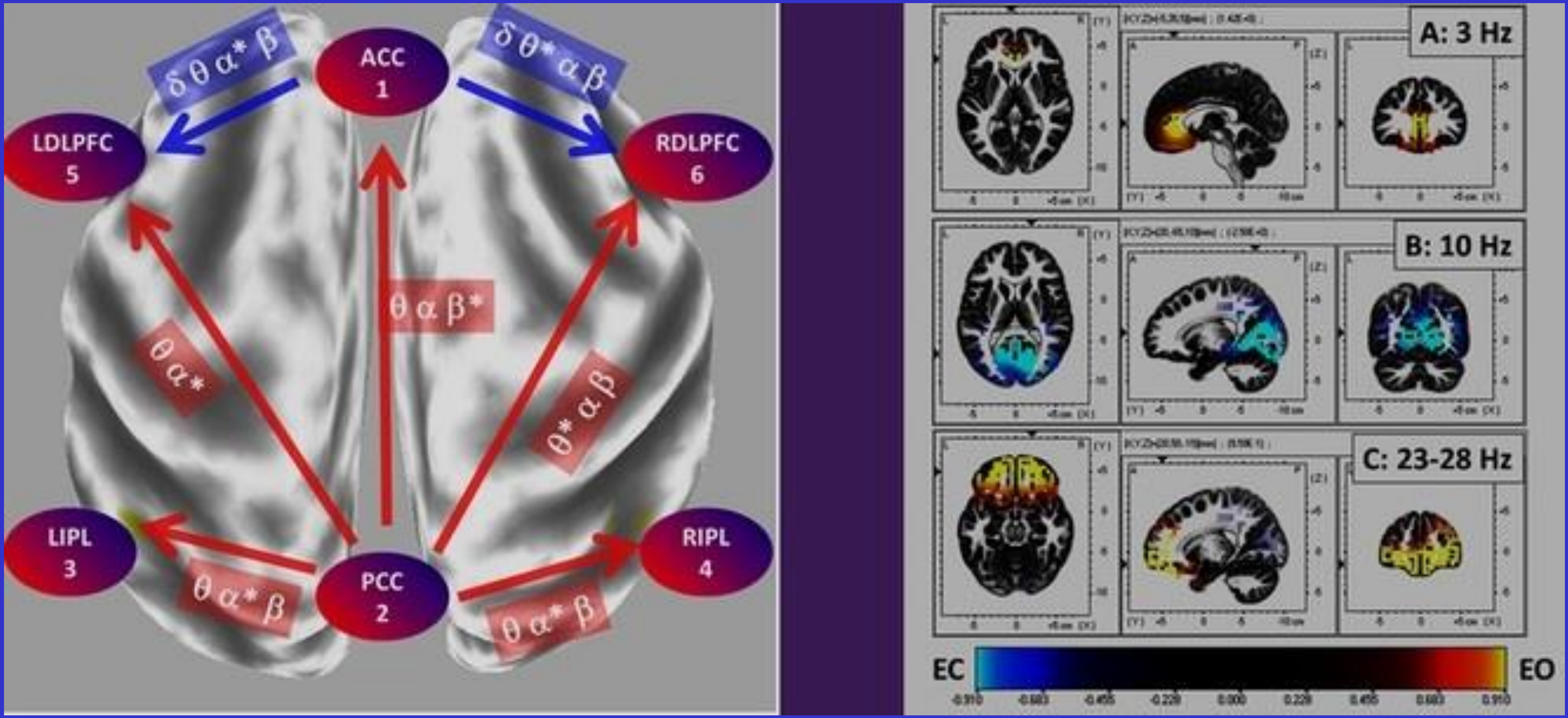
$$\equiv \begin{bmatrix} (\boldsymbol{M}_1(\boldsymbol{r}_1))_x & (\boldsymbol{M}_1(\boldsymbol{r}_1))_y & (\boldsymbol{M}_1(\boldsymbol{r}_1))_z & \cdots & (\boldsymbol{M}_1(\boldsymbol{r}_M))_x & (\boldsymbol{M}_1(\boldsymbol{r}_M))_y & (\boldsymbol{M}_1(\boldsymbol{r}_M))_z \\ (\boldsymbol{M}_2(\boldsymbol{r}_1))_x & (\boldsymbol{M}_2(\boldsymbol{r}_1))_y & (\boldsymbol{M}_2(\boldsymbol{r}_1))_z & \cdots & (\boldsymbol{M}_2(\boldsymbol{r}_M))_x & (\boldsymbol{M}_2(\boldsymbol{r}_M))_y & (\boldsymbol{M}_2(\boldsymbol{r}_M))_z \\ \cdots & \cdots & \cdots & \cdots & \cdots & \cdots & \cdots \\ (\boldsymbol{M}_N(\boldsymbol{r}_1))_x & (\boldsymbol{M}_N(\boldsymbol{r}_1))_y & (\boldsymbol{M}_N(\boldsymbol{r}_1))_z & \cdots & (\boldsymbol{M}_N(\boldsymbol{r}_M))_x & (\boldsymbol{M}_N(\boldsymbol{r}_M))_y & (\boldsymbol{M}_N(\boldsymbol{r}_M))_z \end{bmatrix}$$

Low Resolution Electrical Tomography (LORETA) Source Localization

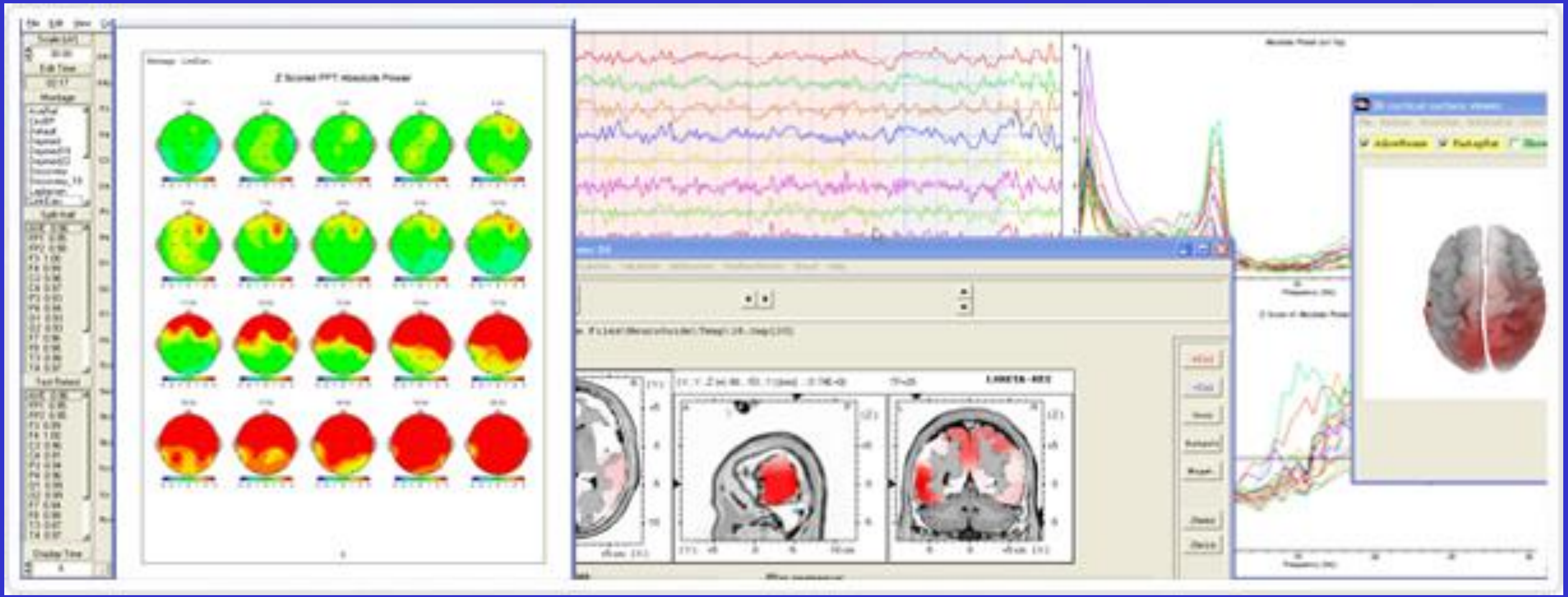
- Brodmann area is a region in the human cortex defined on the basis of its organization observed in microscope when a tissue is stained for nerve cells.
- Brodmann areas were originally defined in 1909 by a German neurologist Korbinian Brodmann and referred to by numbers from 1 to 52.

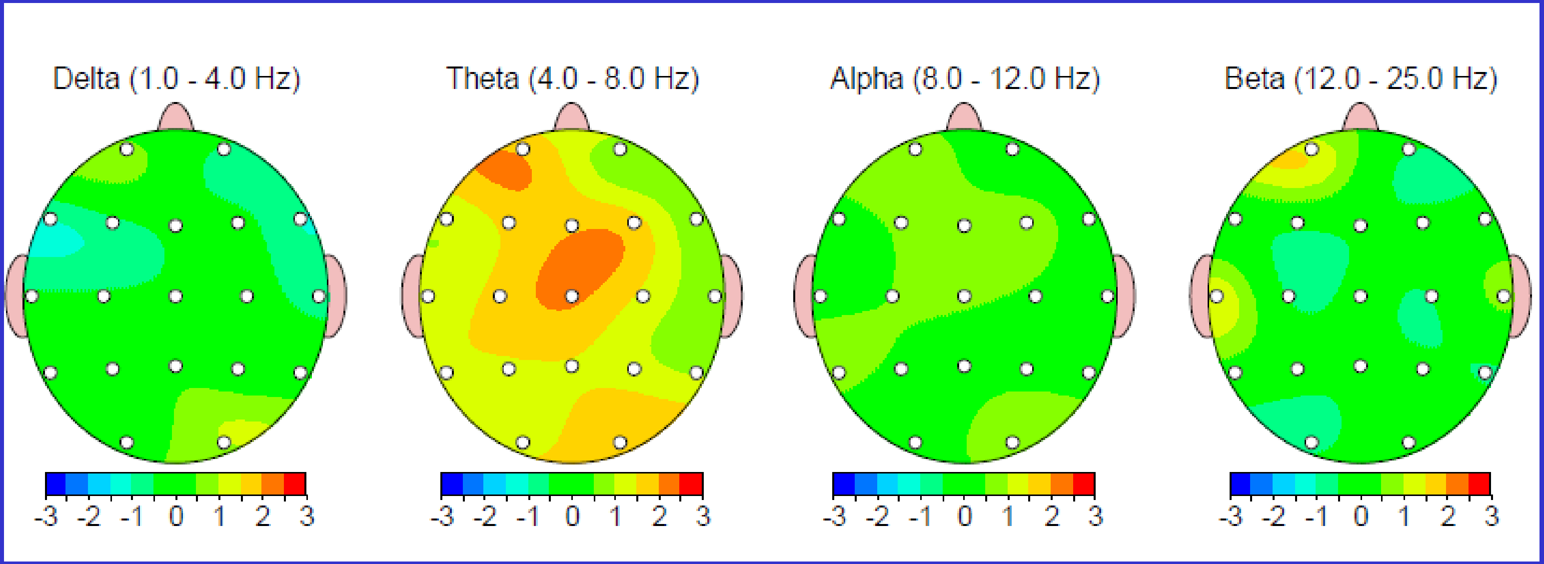


LORETA Source Localization

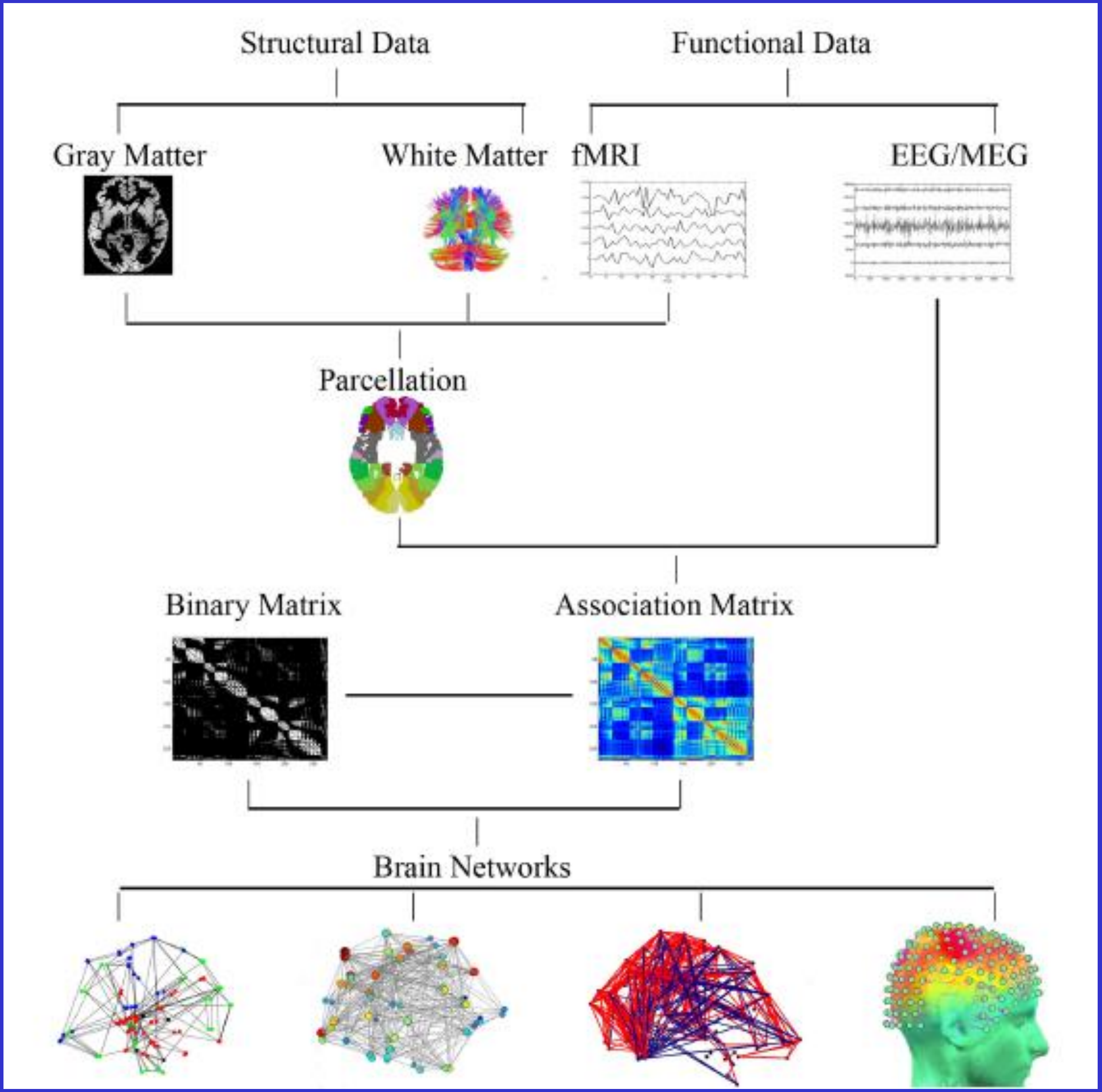


Brain Mapping

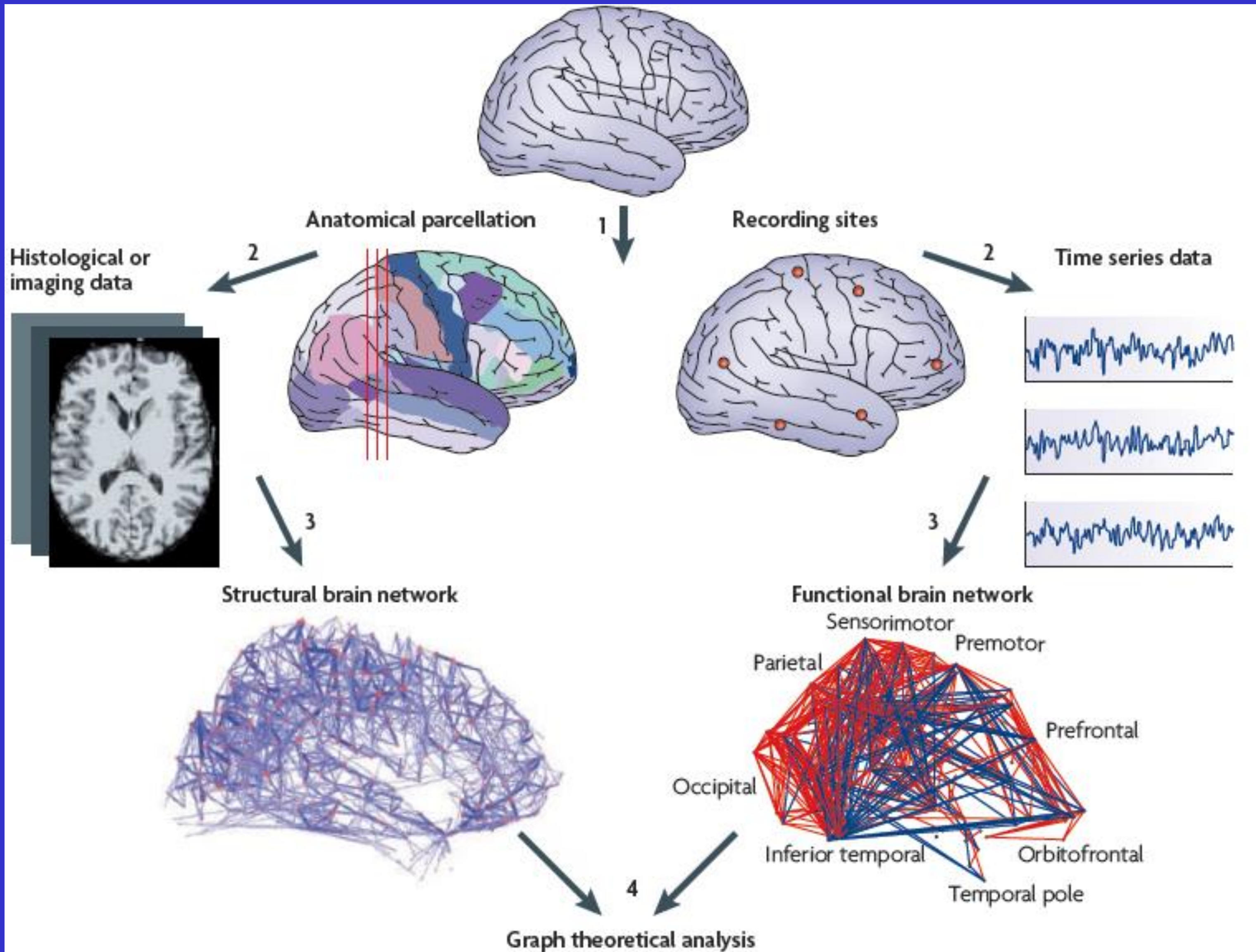




Analyzing Brain Networks

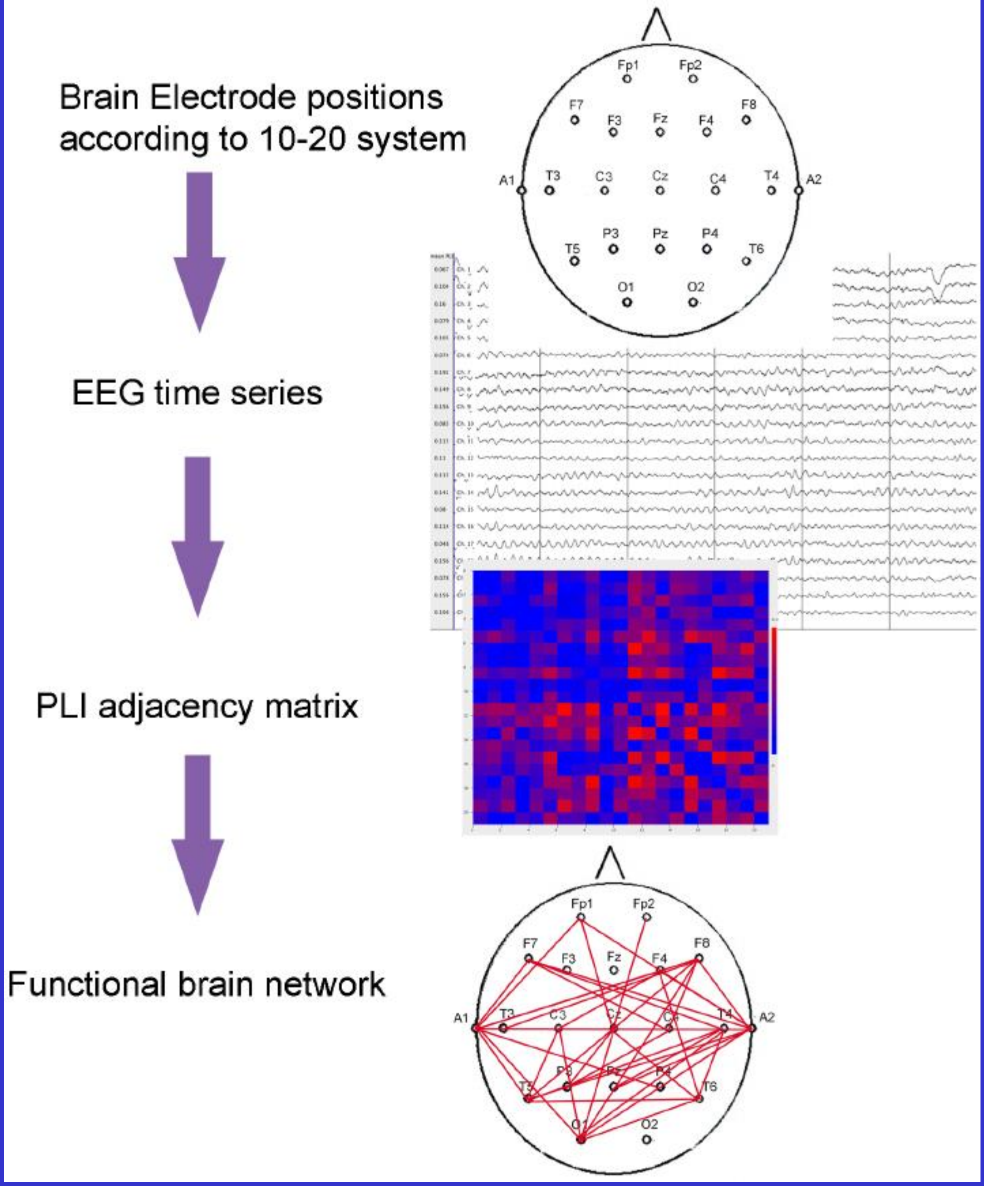


Analyzing Brain Networks

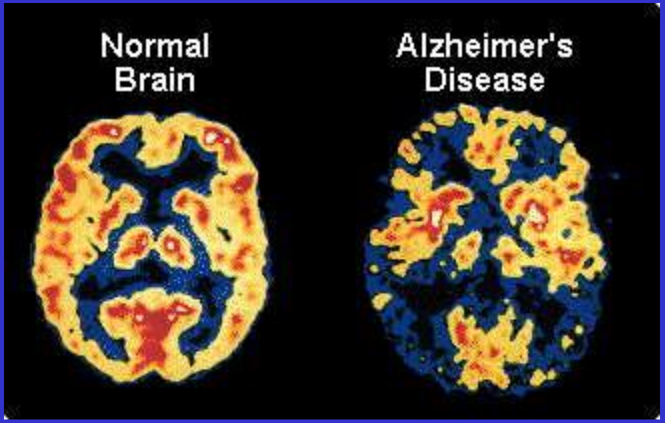


Construction of Graph from EEG

- Schematic representation of construction of graphs from EEG time series



EEG Rhythms in Diseased Brain

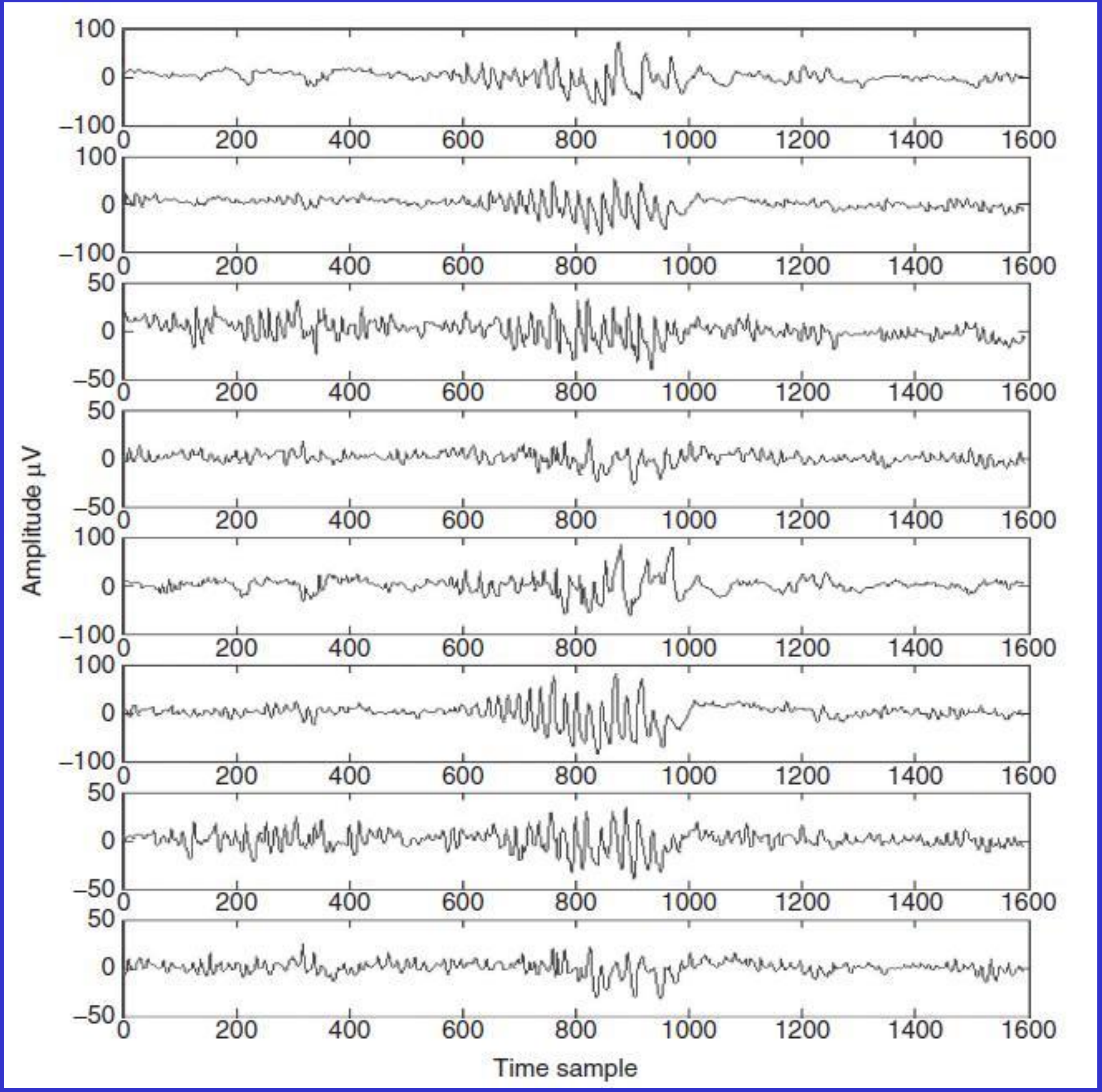


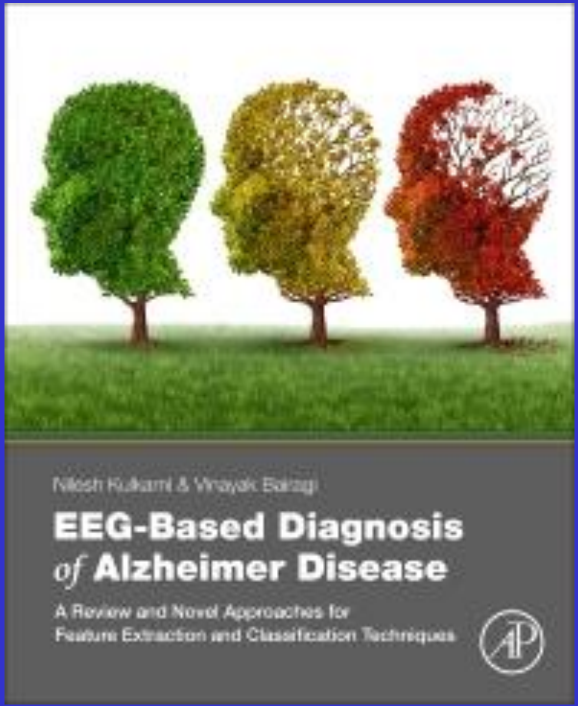
- Impaired EEG rhythms:
  (1) become **slower** in frequency (so-called EEG slowing),
  (2) may appear in **unusual places** (e.g., alpha rhythms at temporal areas),
  (3) may become **higher in amplitude** (hypersynchronization) and in more synchronicity with other areas (hypercoherence),
  (4) in some severe cases (characterized e.g., by disconnection of cortical areas from subcortical structures due to stroke, trauma, or tumor) a **separate slow rhythm in delta frequency** (1–3 Hz) may appear

- Normative databases help an electroencephalographer to recognize those **abnormal patterns** and to assess the level of statistical **significance** of the abnormality.

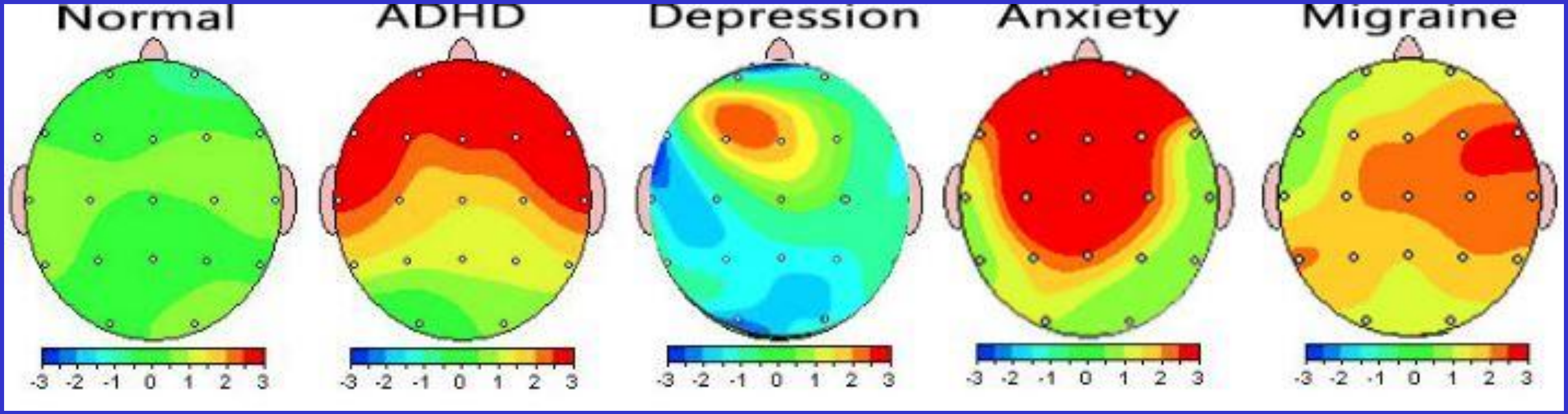
EEG in Diseased Brain

Bursts of 3–7 Hz **seizure** activity in a set of adult EEG signals





EEG and Brain Map in Diseased Brain



Reviewing a Few Researches by our Group

frontiers
in Integrative Neuroscience

Evidence for a Resting State Network Abnormality in Adults Who Stutter

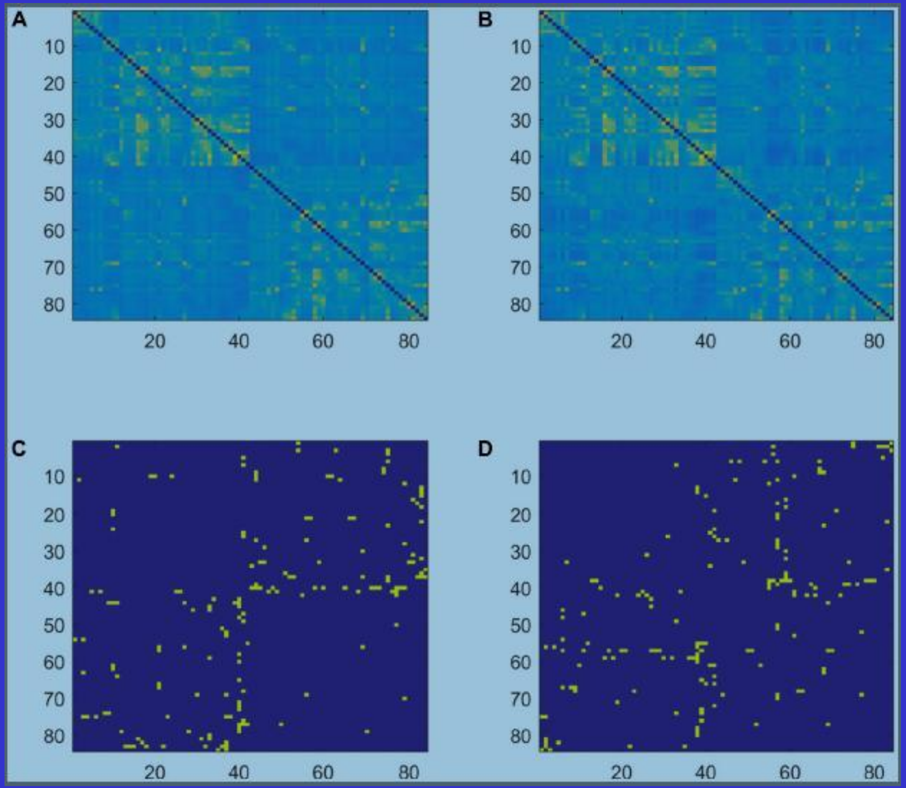


FIGURE 1 | Weighted and sparse (MST) adjacency matrices for the two groups (AWS and control) in the beta2 band. (A) Averaged weighted adjacency matrix for controls. (B) Averaged weighted adjacency matrix for AWS. (C) Average MST adjacency matrix for controls. (D) Average MST adjacency matrix for AWS. Different patterns are visually observable between the MST graphs

Evidence for a Resting State Network Abnormality in Adults Who Stutter

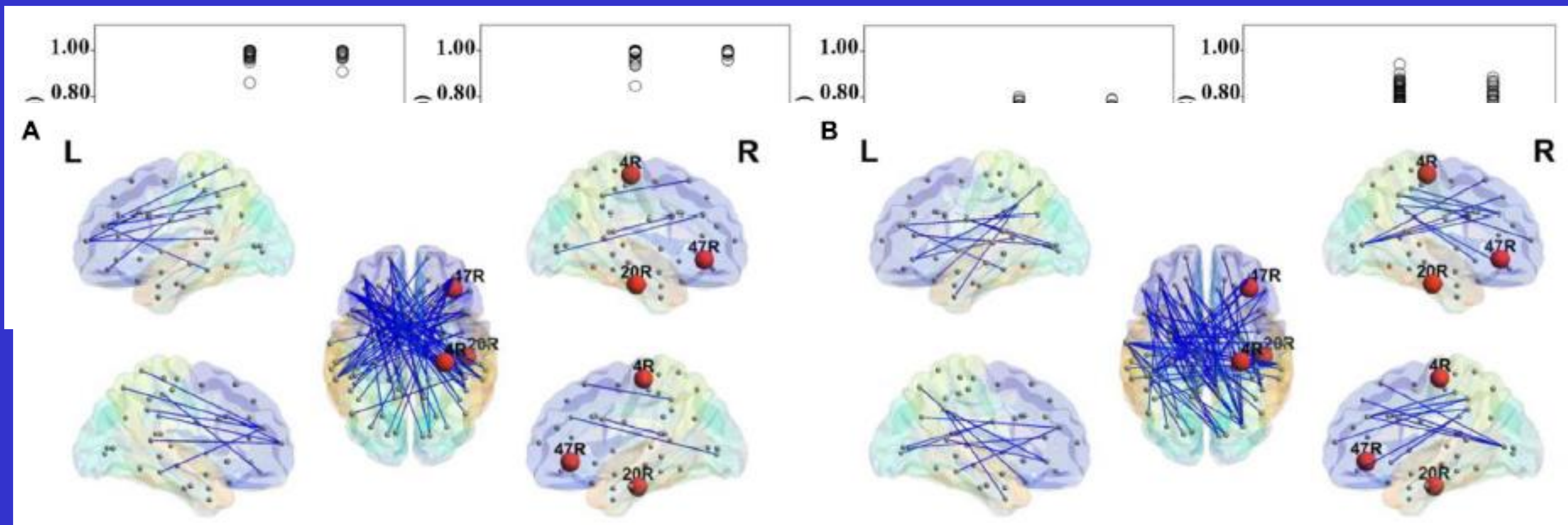


exhibit values less than 0.6.

Evidence for a Resting State Network Abnormality in Adults Who Stutter

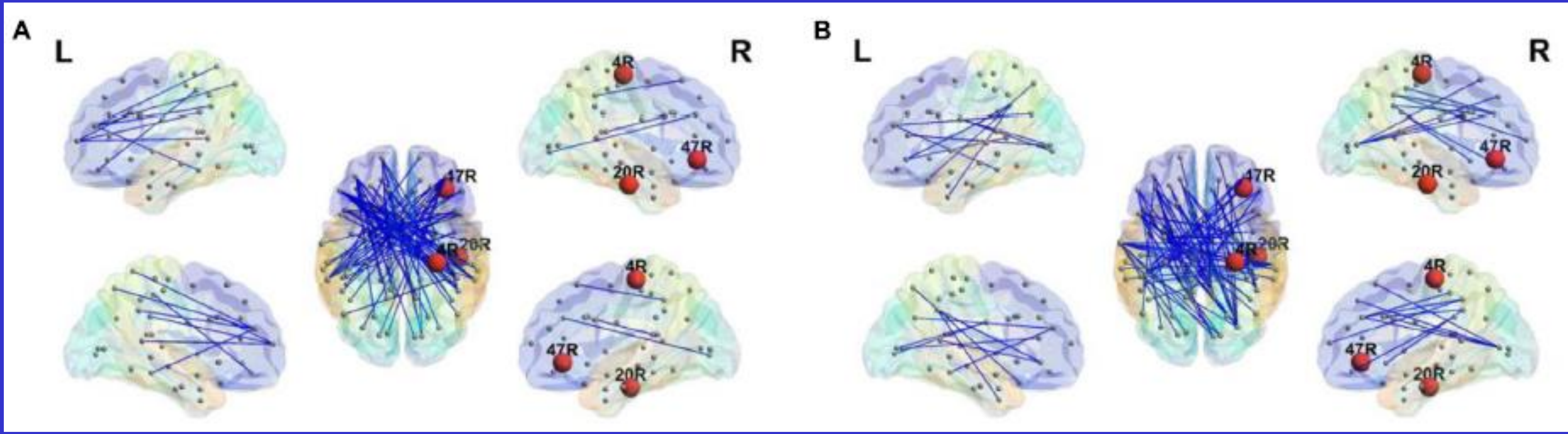


FIGURE 3 | Minimum spanning tree in the beta2 band. Significant differences of BC (red nodes) were observed for right primary motor cortex (4R), right inferior temporal lobe (20R) and right inferior frontal gyrus (47R). The stuttering group (A) shows higher BC than the fluent group (B) in 20R and right 47R. The AWS exhibit lower BC in 4R. The figure was generated using BrainNet viewer toolbox version 1.53 (Xia et al., 2013).

Basic and Clinical NEUROSCIENCE

Functional Brain Connectivity Differences Between Different ADHD Presentations: Impaired Functional Segregation in ADHD-Combined Presentation but not in ADHD-Inattentive Presentation

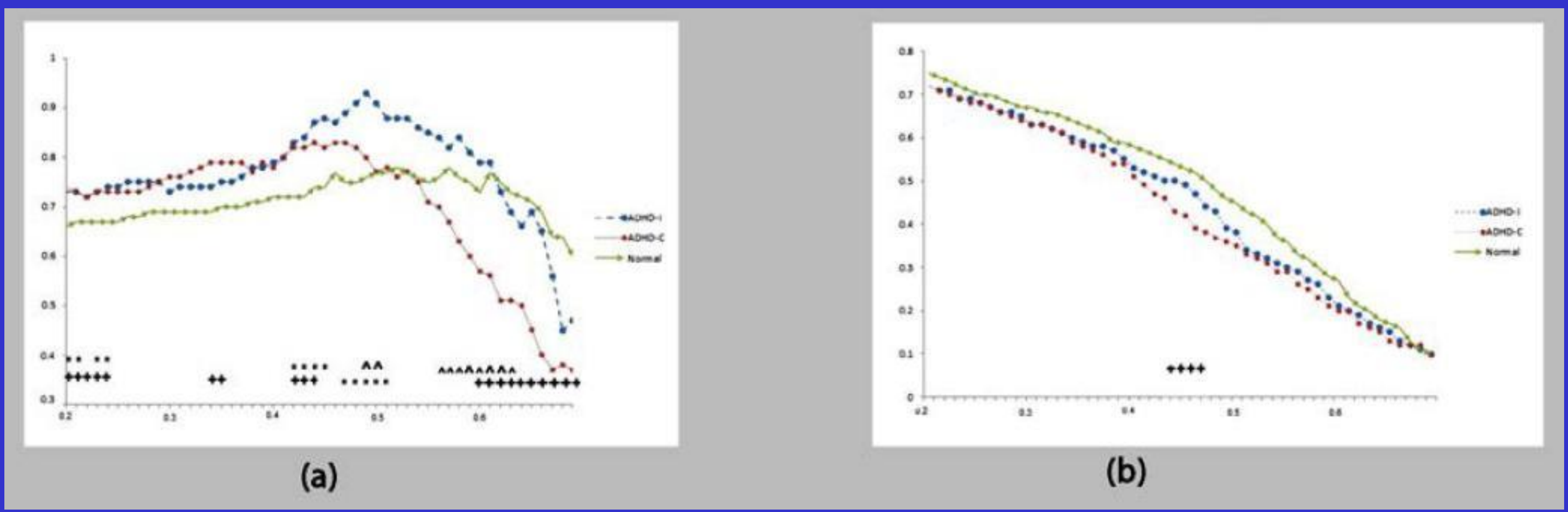
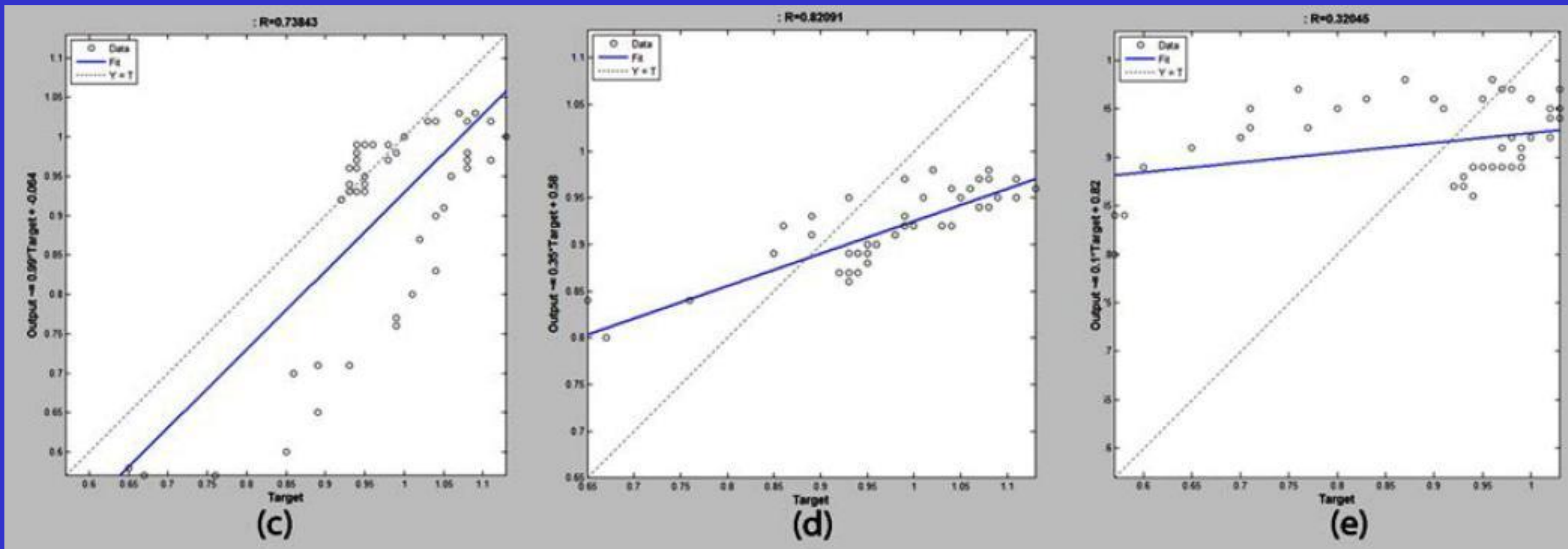


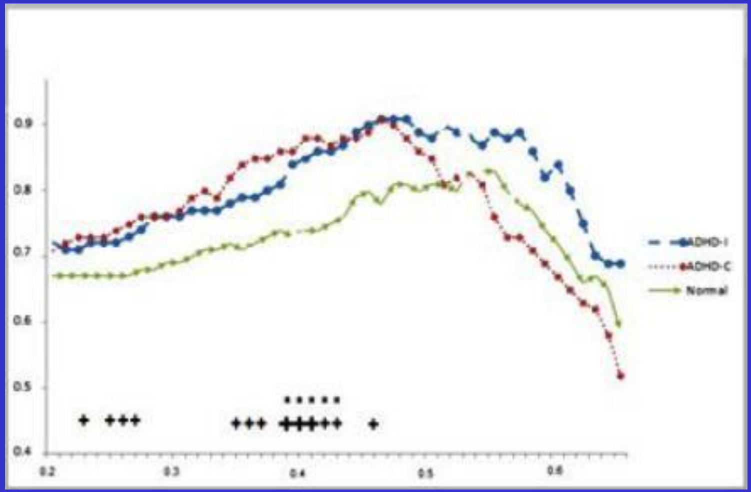
Figure 1. Theta band: (a) Clustering coefficient calculated as a function of threshold. (b) Global efficiency calculated as a function of threshold.

Different ADHD Presentations



(c) The correlation of clustering coefficient graphs between the ADHD-C group and ADHD-I group. (d) The correlation of clustering coefficient graphs between the control group and ADHD-I group. (e) The correlation of clustering coefficient graphs between the control group and ADHD-C group.

Different ADHD Presentations



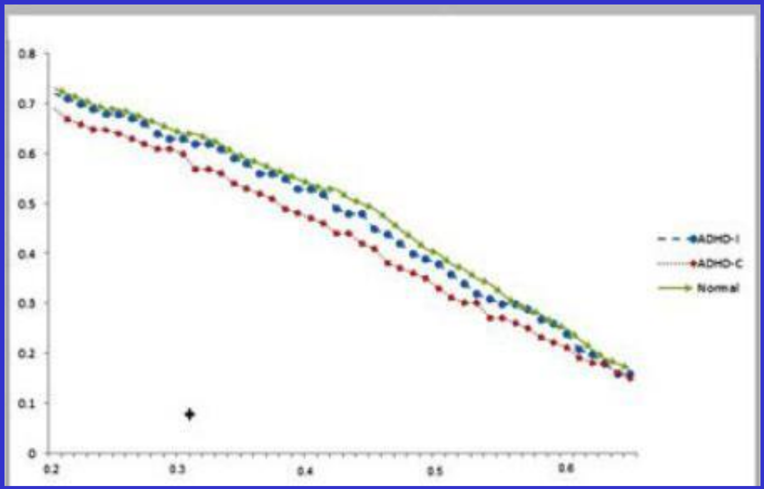


Figure 2. Alpha band: (a) Clustering coefficient calculated as a function of threshold. (b) Global efficiency calculated as a function of threshold.

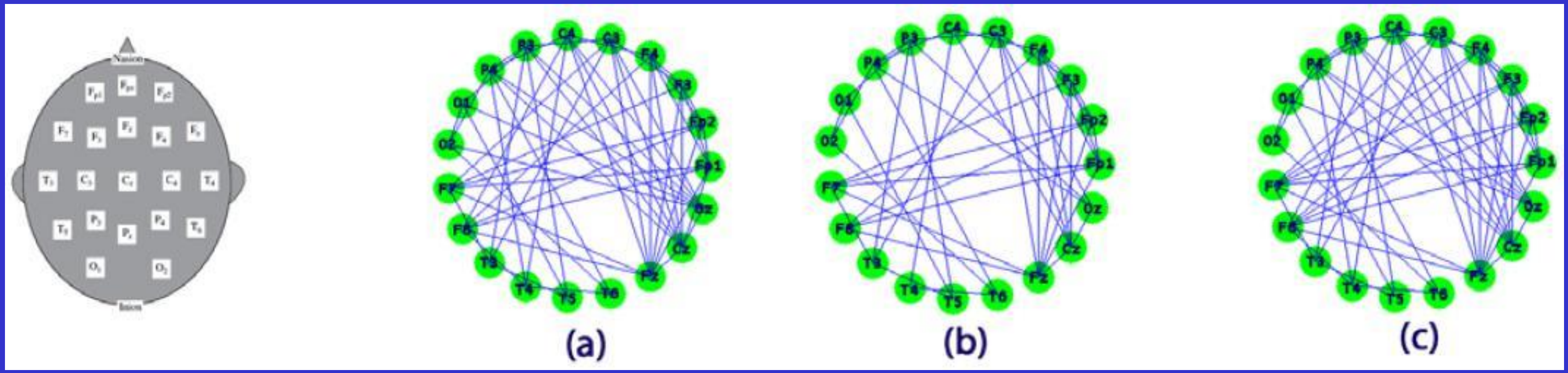


Figure 6. Theta band: Circular graph in T=31. (a) Control group. (b) ADHD-C group. (c) ADHD-I group.

Multiple Sclerosis Brain Network

Addicted Brain Network