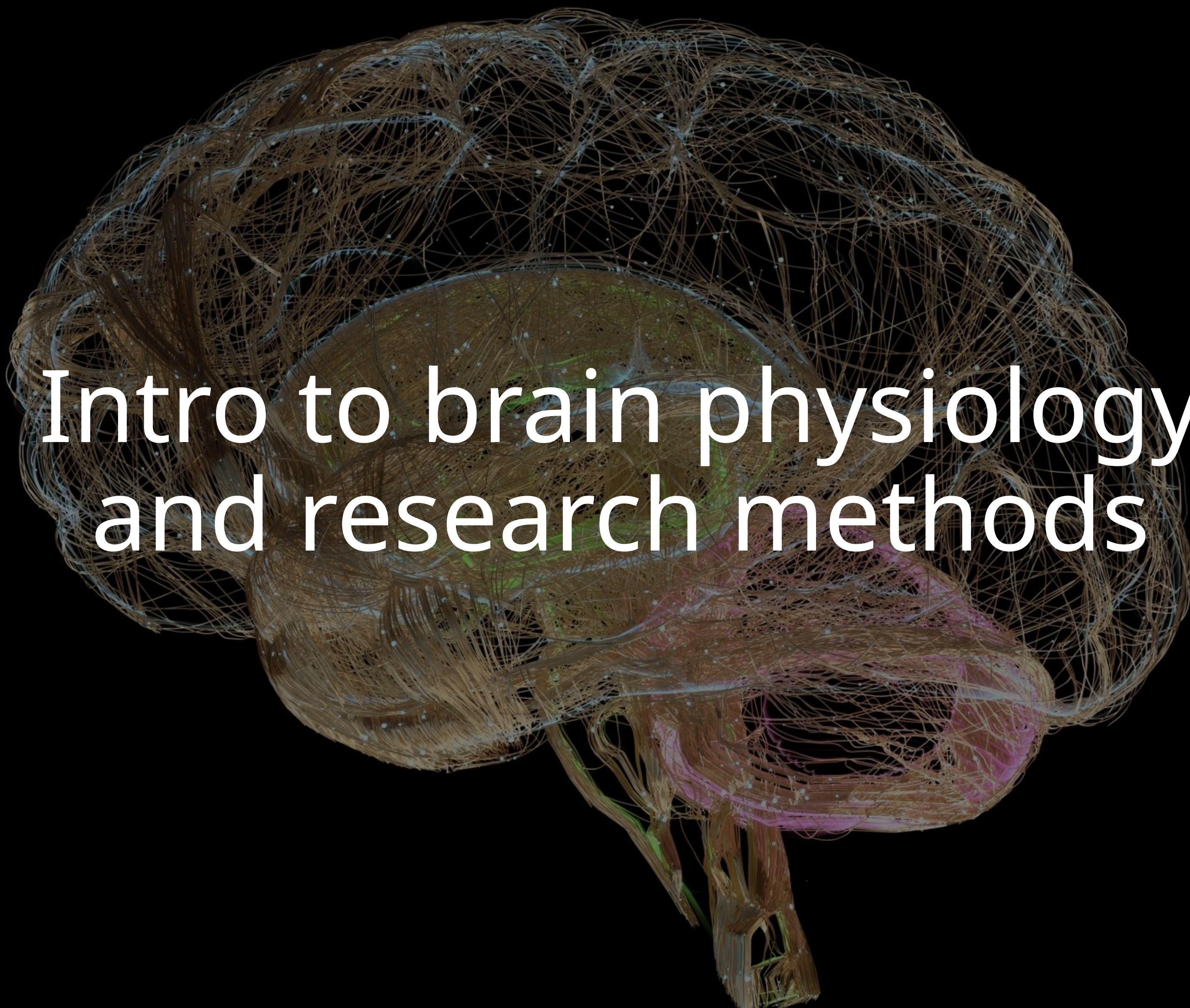
Course Technicalities

- Following the course Moodle is important
- The course grade is determined by a single written exam at the end of the course
  - Seminar Paper is an alternative to the exam. These include a review and small programming project related to the course content
- There will be group assignments that include a series of questions about the course content and readings
  - You will upload your responses to the assignments to Moodle and they will discussed in class
  - The grading of assignments is pass/fail, and the group might be asked to do a better job if necessary.

Course Outline

- A first (short) part of the course includes:
  - Presentation of facts about the human brain
  - Introduction to methods for studying the brain
  - General overview of types of machine learning approaches to Cognitive neuroscience
- The following parts will cover:
  - Modeling of individual concepts and relationships between concepts (representational geometry)
  - Core topics of human cognition, including:
    - Learning
    - Prediction and surprise
    - Language processing
  - Merging information from minds and machines to make machines work better and to better understand the human mind

Intro to brain physiology and research methods

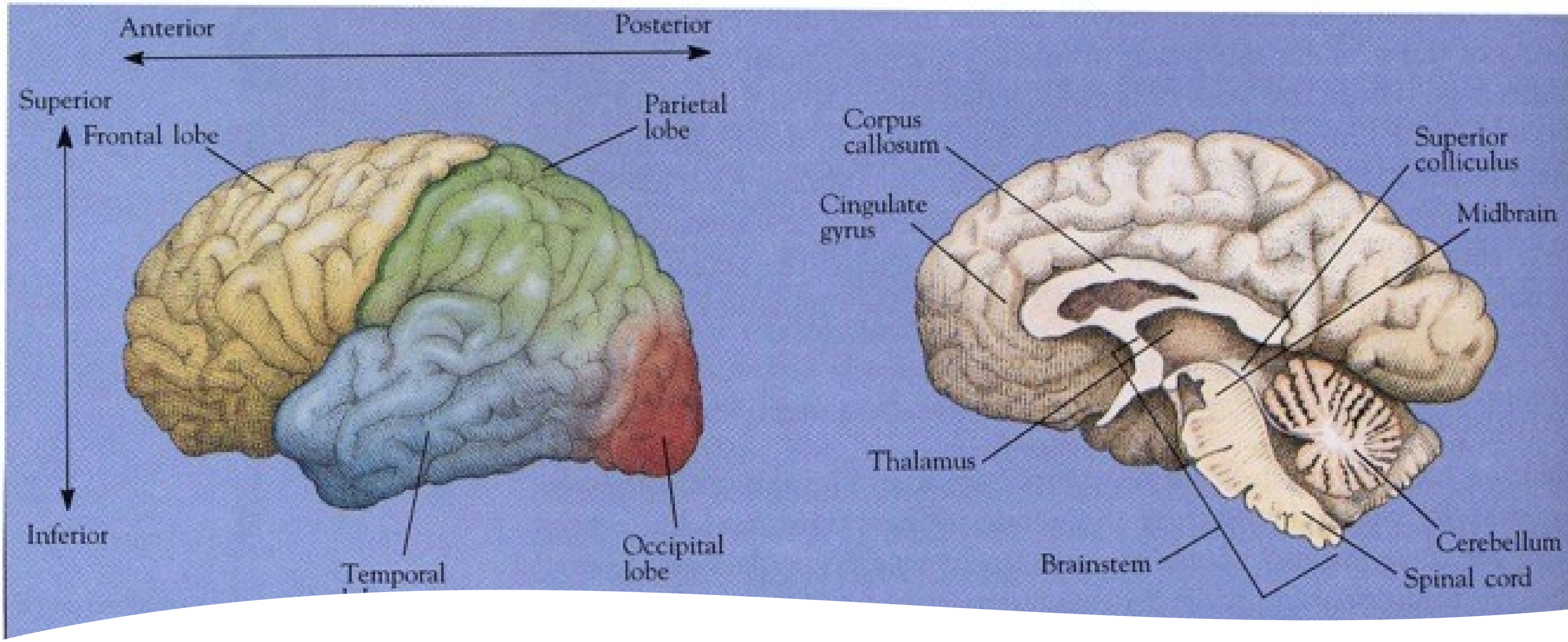


Outline

- Section 1: Basic facts about the human brain
- Section 2: Studying the human brain (tools, and basics of experimentation)

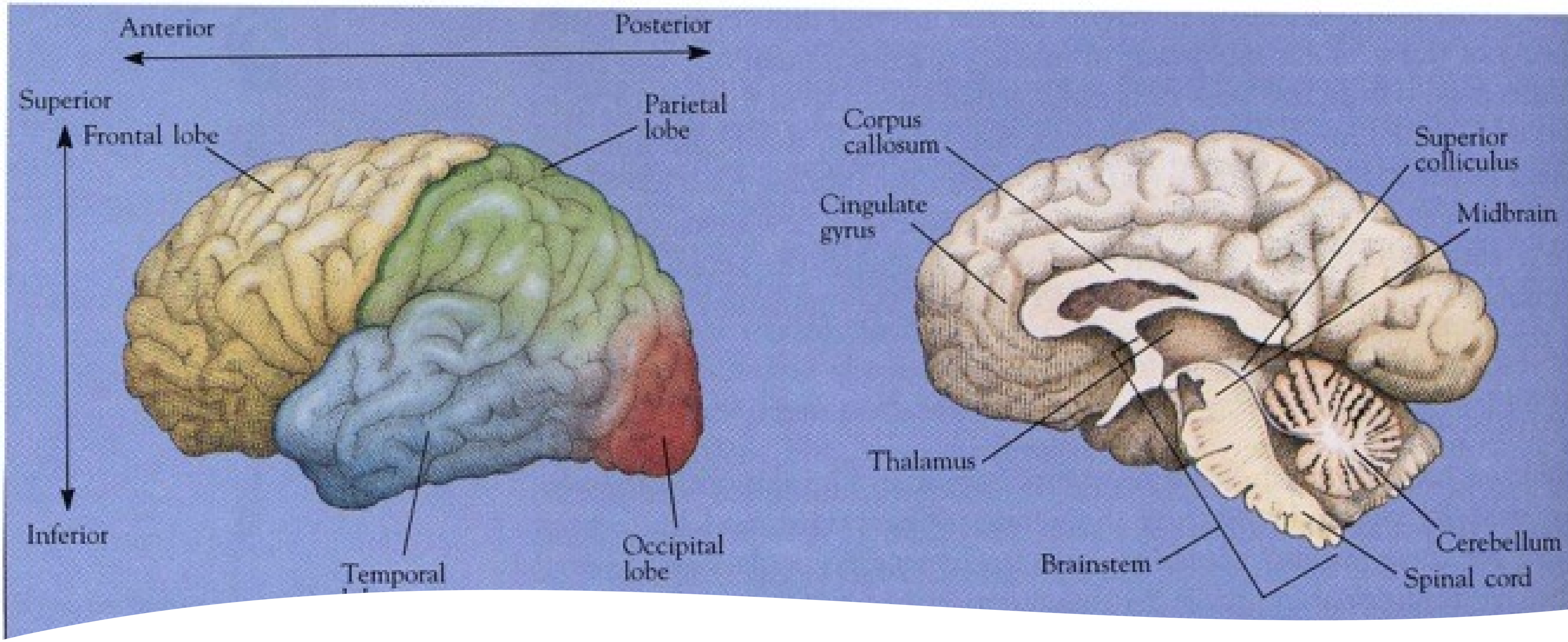
Section 1: Basic facts about the human brain

- What are the main lobes and subcortical structure
- What is a neuron
- What is the difference between gray and white matter



Gross partitioning and function: Cortex

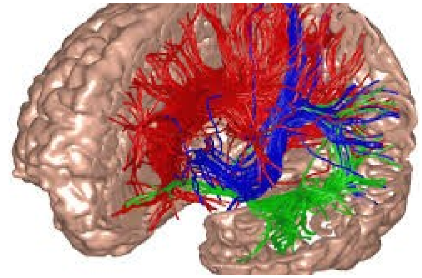
- Temporal lobe: **Auditory processing** (hearing and language)
- Parietal lobe: **Attention**, touch, saccade planning
- Frontal lobe: Planning, execution, **higher level** cognition, high level language processing and language production
- Occipital lobe: **Vision**: perception of visual features, categories and location

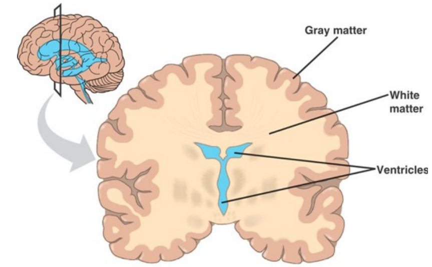


Gross partitioning and function: other structures

- <u>Cerebellum</u>: Fine motor control, implicated in emotional responses
- <u>Thalamus</u>: Major gateway for sensory processing. One of the final stops before sensory information arrives at the cortex
- <u>Hippocampus</u>: implicated in construction of memories; these are later transferred to other cortical regions
- <u>Corpus Callosum</u>: A main “highway” of white matter tracks that connects the two hemispheres

Gray matter

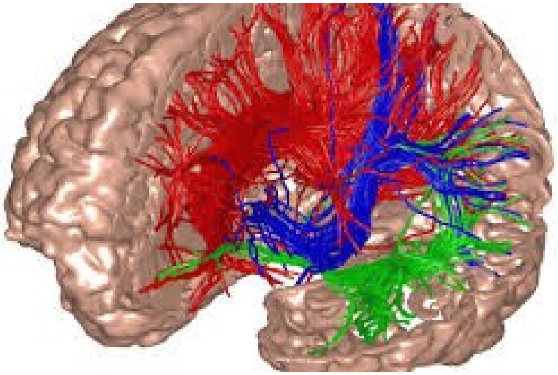


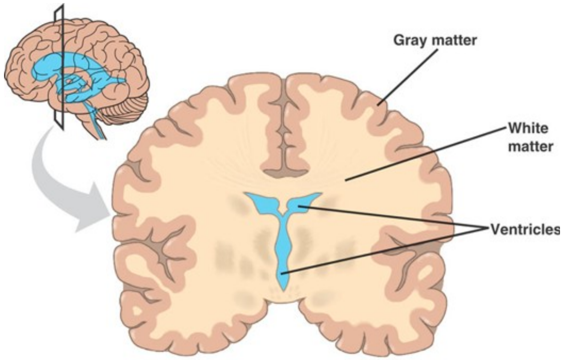


- Gray matter (GM) gets its name from its color, which is mainly due to the high density of cell bodies with relatively fewer myelinated axons.
- The gray matter regions of the brain are involved in various important functions, such as sensory processing and cognition, and include not only the cerebral cortex but also the cerebellum, basal ganglia, thalamus, and several other regions.
- Techniques for measuring brain activity often reflect the function of gray matter regions, which are responsible for the majority of cognitive processing.
- As a result, understanding the role and function of gray matter in the brain is essential for gaining insight into various neurological and psychiatric conditions.

White matter

- White matter consists mainly of long-range axon pathways, or tracts, that connect different regions of the brain.
- Unlike gray matter, there is no direct information processing within white matter itself, but it is essential for efficient communication between different regions of the brain.
- The structure of white matter can change with learning because it reflects the long-range neural pathways that carry nerve impulses and facilitate the communication between different regions of the brain.
- Damage to white matter, such as the loss of myelin in conditions like multiple sclerosis, can have significant impacts on communication between different regions of the brain, leading to various neurological and psychiatric symptoms.
- Therefore, understanding the role and function of white matter is critical for studying brain function and identifying potential targets for interventions in various neurological and psychiatric disorders.





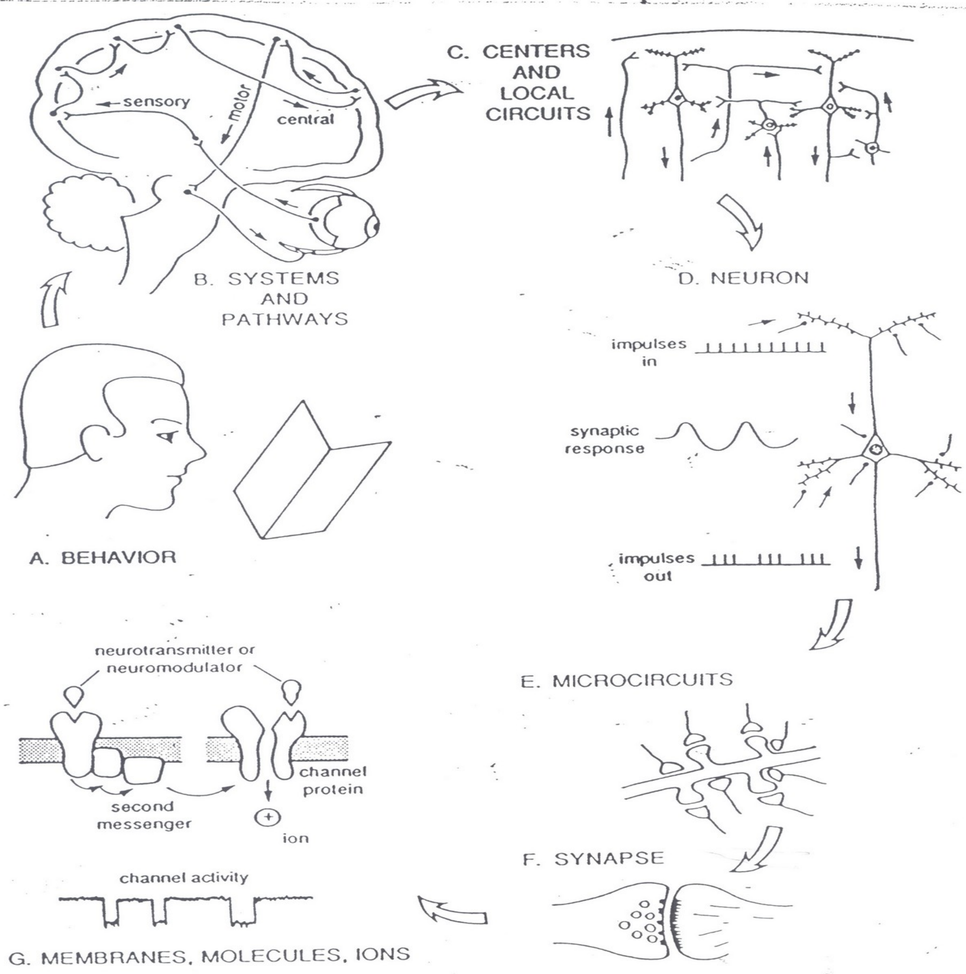


Figure 2.1 Levels of organization in the nervous system, as characterized by Gordon Shepherd (1990).

•The human brain can be studied at different levels of organization, from *systems and pathways* to *synapses* and *membranes*.

•Systems and pathways refer to large-scale neural networks responsible for specific functions, such as sensory perception, motor control, and cognition. These may be topographically distributed.

•Circuits and neurons: networks of interconnected neurons that underlie information processing within the brain.

•Synapses and membranes: molecular and cellular mechanisms that govern the transmission of signals between neurons, such as the release of neurotransmitters and activation of ion channels.

•Studying the brain at different scales provides insights into organization of function from the macroscopic to the microscopic level.

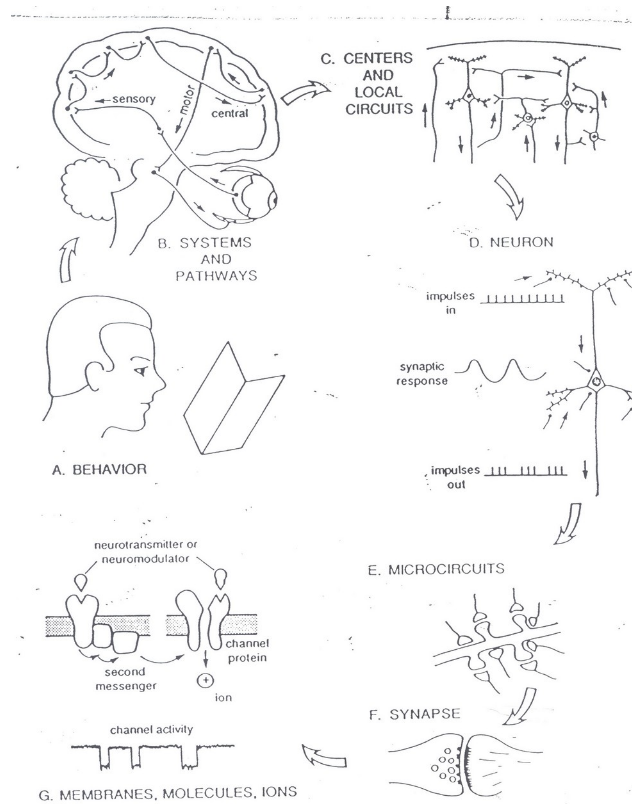


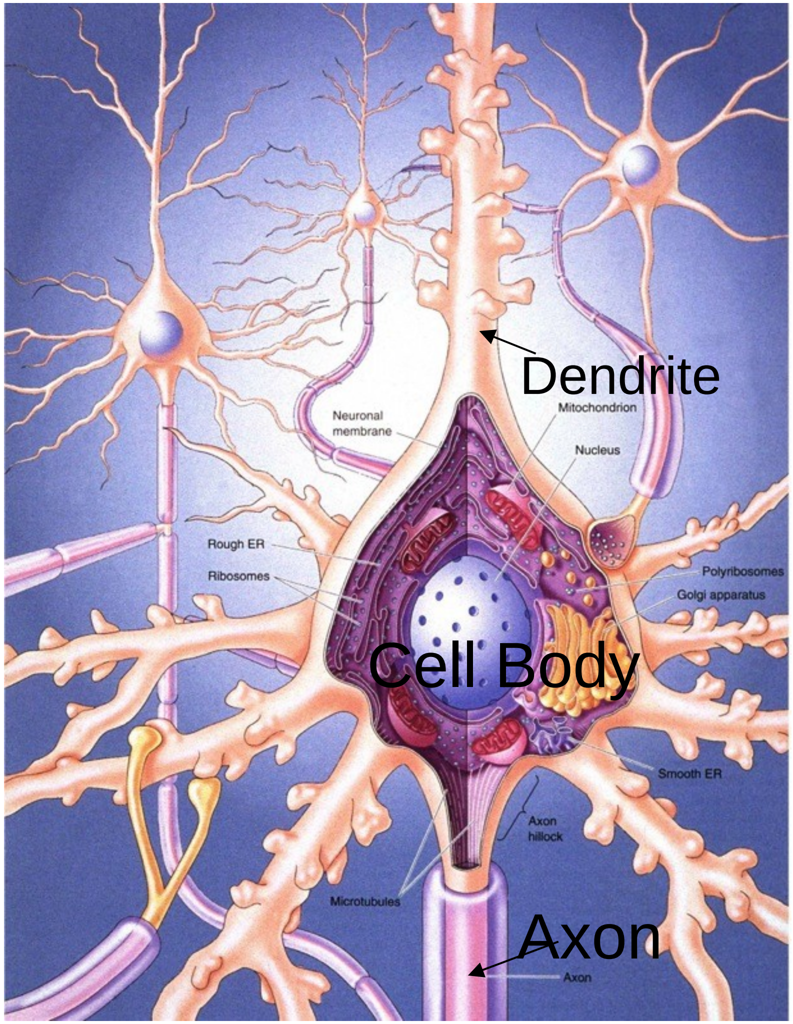
Figure 2.1 Levels of organization in the nervous system, as characterized by Gordon Shepherd (1990).

A word about the Neuron

A Neuron consists of dendrites,
a cell body and an axon.

Connections between
neurons are called **synapses**, and occur on a neuron's **dendrites**, who receive synaptic signals. Synapses are **chemical**, not electrical. Other neurons will connect on **dendrites** and in some cases on soma.

A neuron will 'fire' (generate an action potential) depending on the the number of signals it receives on its dendrites and their **strength**, which are 'summed' in the the neuron's body.

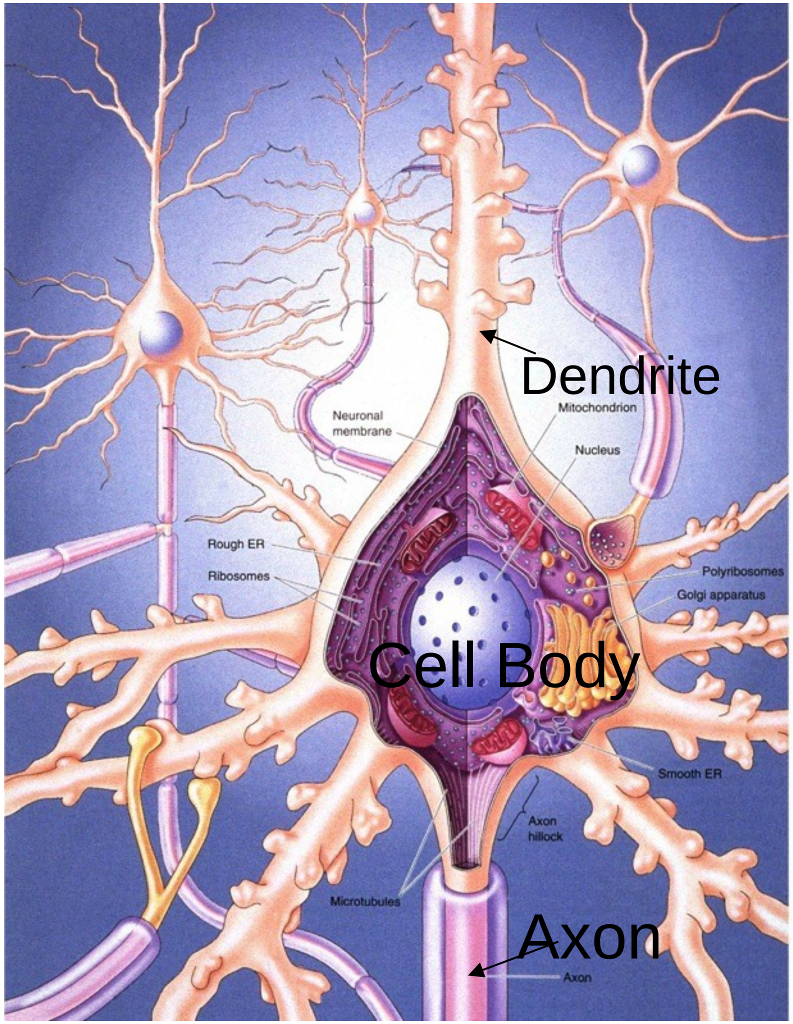


A word about the Neuron

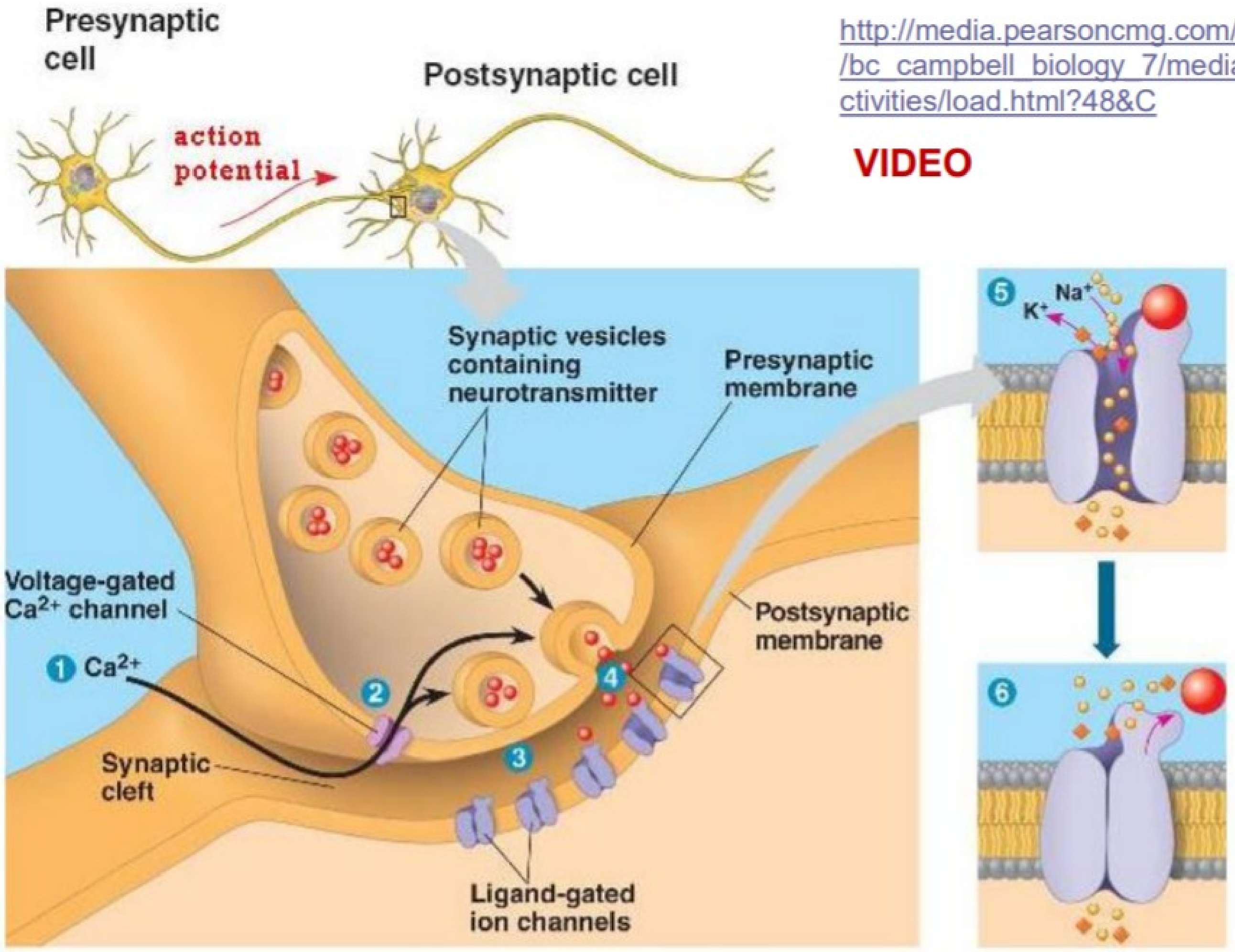
A Neuron consists of dendrites,
a cell body and an axon.

Connections between
neurons are called XX, and occur on a neuron's XX, who receive synaptic signals. Synapses are XX, not electrical. Other neurons will connect on XX and in some cases on soma.

A neuron will 'fire' (generate an action potential) depending on the the number of signals it receives on its dendrites and their XX, which are 'summed' in the neuron's body.



More words about the Synapse: communication



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VIDEO

More words about the Synapse: communication

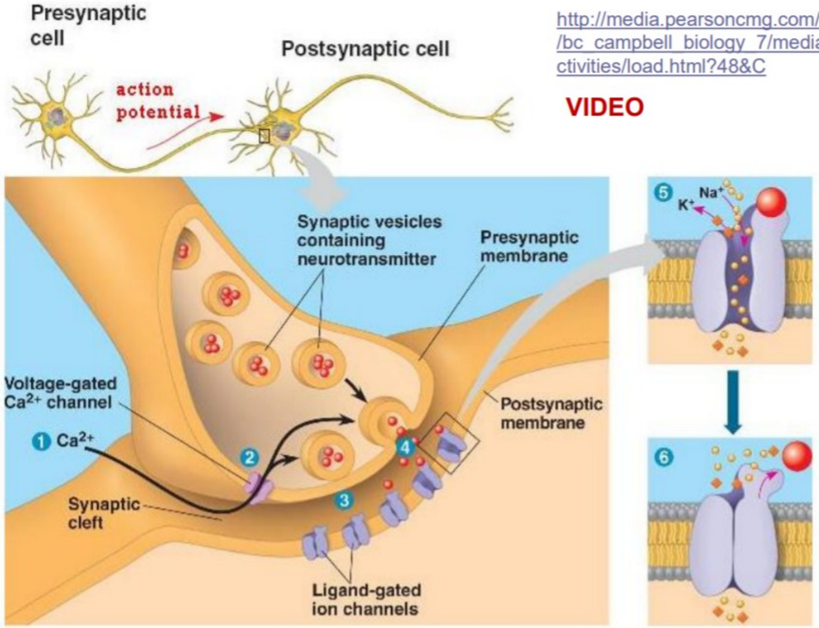
•Synaptic communication is the process by which neurons communicate with each other through the **release and reception of chemical signals called neurotransmitters**.

•The presynaptic cell contains several elements that are involved in the release of neurotransmitters, including vesicles and voltage-gated channels.

•When an action potential reaches the presynaptic terminal, it triggers the opening of voltage-gated calcium channels, triggering the release of neurotransmitters from the vesicles.

•Neurotransmitters diffuse across the synaptic cleft and bind to receptors on the postsynaptic membrane, which triggers the opening of ion channels and the generation of a postsynaptic potential.

•The postsynaptic potential can either be excitatory, causing the postsynaptic neuron to depolarize and fire an action potential, or



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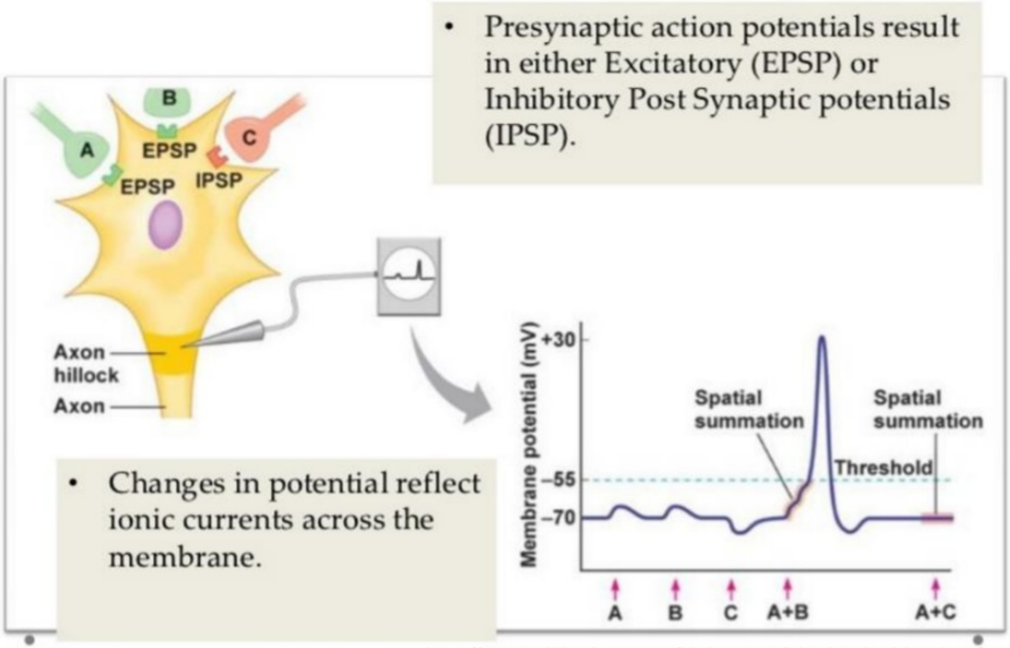
VIDEO

Depolarization produces an ‘all or nothing’ signal. No partial firing.



http://www.slideshare.net/kj_jantzen/biophysical-basis-of-eeg

If we had to say 1 word on plasticity..

- Synapses can be *strengthened* or *pruned*
- Connections between neurons are consistently removed (or created) depending on use.
- Weak or ineffective connections are ‘pruned’
- Plasticity (in one sense) refers to the development and pruning of connections to adapt to the environment.
- A large % of neurons that develop die
- Some principles of neuronal survival:
  - A ‘hub’ Neuron, which receives inputs from many neurons is more likely to survive.
  - When many neurons connect to a target neuron, this decreases their survival rate.
  - This calibration is thought to be associated with generating an optimal degree of synaptic connection.
- Brain volume triples between birth and adulthood.
  - This is mostly *not* due to addition of neurons.
  - It is due to an increased number of connections (synapses), myelineation

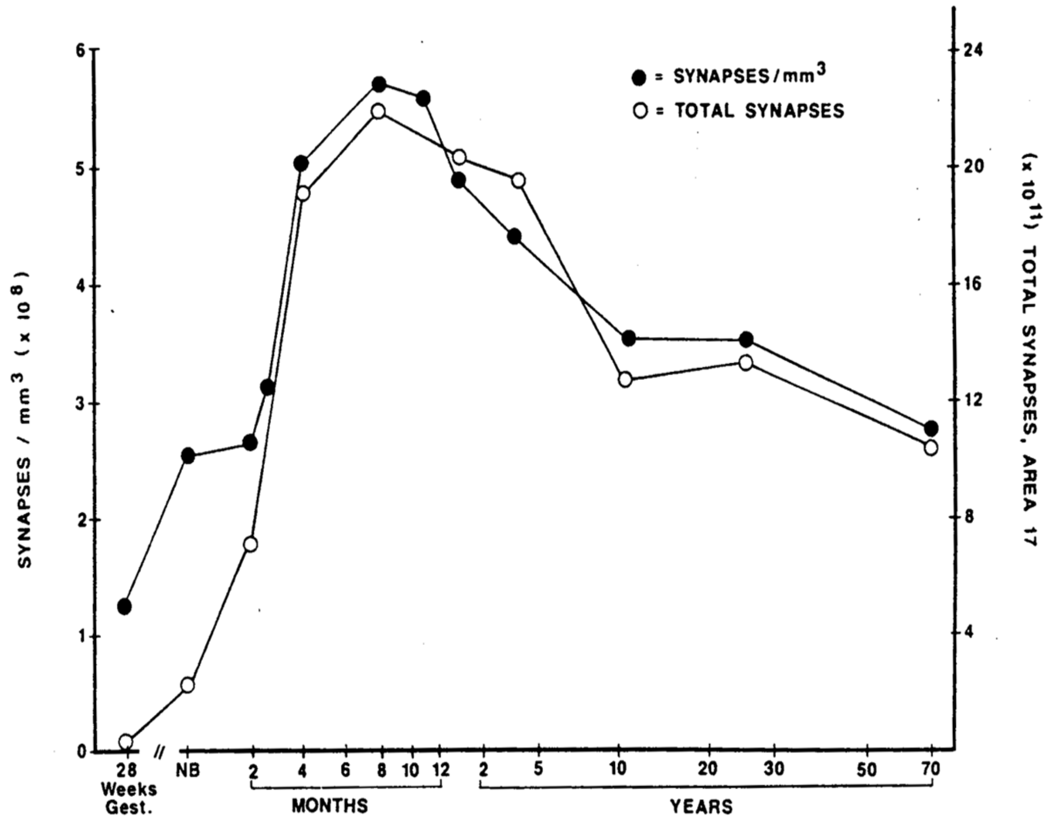


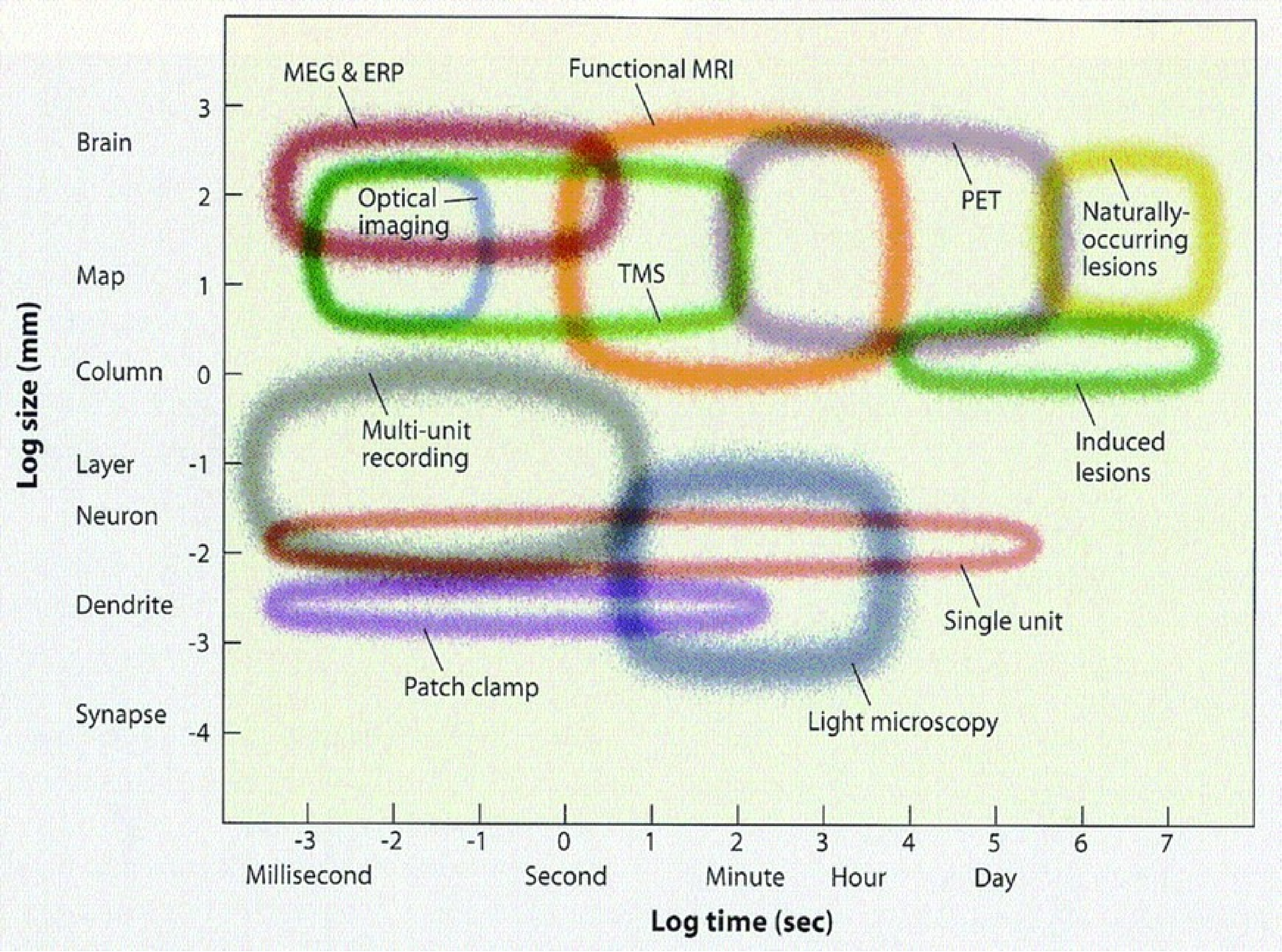
Fig. 1. Synaptic density and total synapses in visual cortex as a function of age.

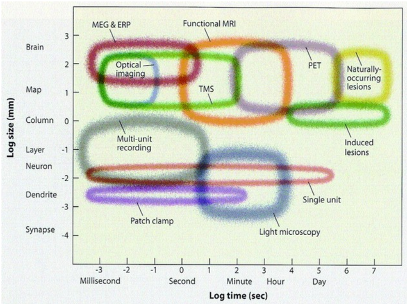
(from Huttenlocher, 1990)

Section 2: Studying the brain

- There are several non-invasive tools available for studying brain activity and structure, including *electroencephalography*, *structural imaging*, *functional magnetic resonance imaging* (fMRI), and diffusion-weighted imaging.
- These tools provide insights into different aspects of brain function and structure: electrical activity of neurons, the structural connectivity of brain regions, and the metabolic activity associated with specific tasks or behaviors.
- *Experimental procedures* are used to analyze the data collected by these tools, which typically involves designing and conducting studies that involve manipulating variables of interest and collecting and analyzing data from participants.
  - In neuroscience, an *experiment* or study is a systematic investigation of a research question or hypothesis that involves manipulating variables and measuring their effects on some outcome of interest.
- Conclusions from experiments are drawn by analyzing the data collected from participants and testing whether there are statistically significant differences between groups or conditions.
  - Typically involves using statistical methods to quantify the strength and direction of effects and assessing the probability that the observed effects are due to chance.

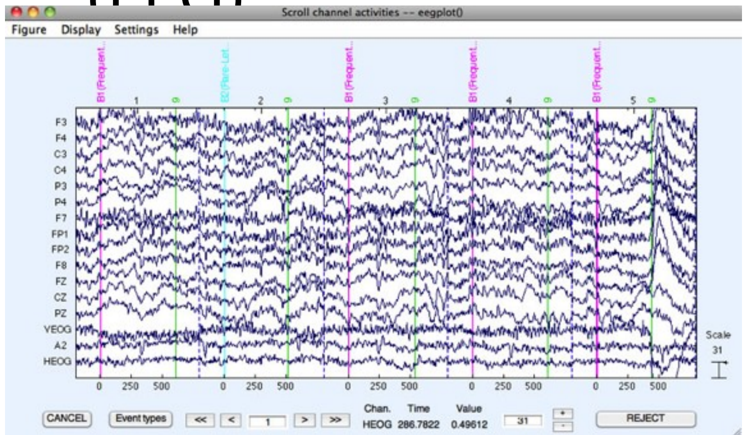
Temporal and spatial scales of common tools

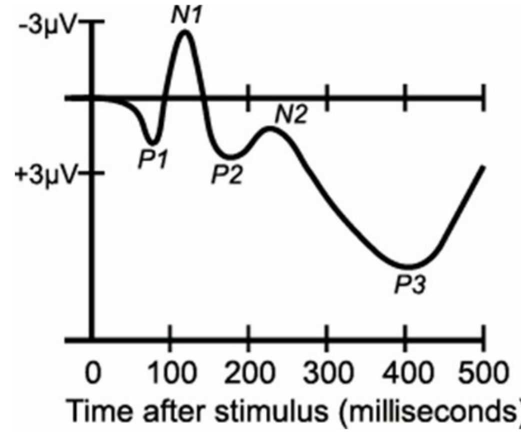




- fMRI:
    - Spatial resolution: typically several millimeters or larger, depending on the voxel size and field strength of the scanner.
    - Temporal resolution: relatively slow, typically several seconds or longer, due to the sluggish hemodynamic response that fMRI measures.
- TMS (transcranial magnetic stimulation):
    - Spatial resolution: relatively poor, typically on the order of centimeters or larger, depending on the location and size of the coil.
    - Temporal resolution: relatively fast, on the order of milliseconds or shorter, since TMS can directly stimulate neurons and induce changes in neural activity.
- Induced lesions:
    - Spatial resolution: depends on the size and location of the lesion, which can vary widely.
    - Temporal resolution: relatively slow, since the effects of the lesion may take days or weeks to become apparent.
- MEG:
    - Spatial resolution: relatively good, on the order of millimeters or less, depending on the number and location of the sensors.
    - Temporal resolution: very fast, on the order of milliseconds or shorter, since MEG measures the magnetic fields generated by neural activity directly.
- Patch clamp (current recording from ion channels in cell membrane):
    - Spatial resolution: very good, on the order of micrometers or less, since the patch clamp technique can record from individual neurons or even subcellular compartments.
    - Temporal resolution: very fast, on the order of milliseconds or shorter, since the patch clamp technique

Electroencephalography (EEG)





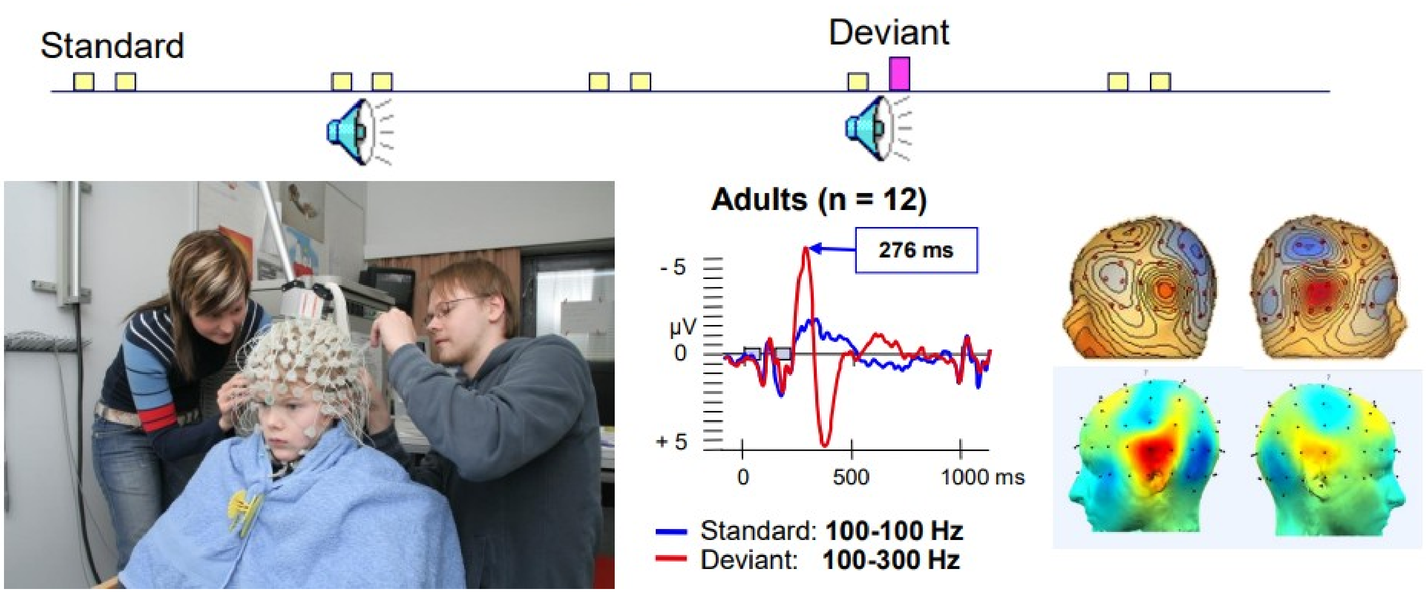
1. EEG is a non-invasive method used to study patterns of brain activity with high temporal resolution.
2. The principle behind EEG is that it is sensitive to very subtle changes in electric potentials below the sensors, which are propagated to the scalp. These changes reflect alterations in the electrical environment of thousands of neurons that fire in synchrony.
3. It is difficult to pinpoint the brain regions causing the fluctuations, but the timing of the signals is very precise.
4. Tasks can generate stereotyped evoked potentials that can be averaged to obtain an "event-related potential".
5. EEG provides a powerful tool for investigating the dynamics of neural activity in the brain, and is widely used in both research and clinical settings

From EEG time series to ERP

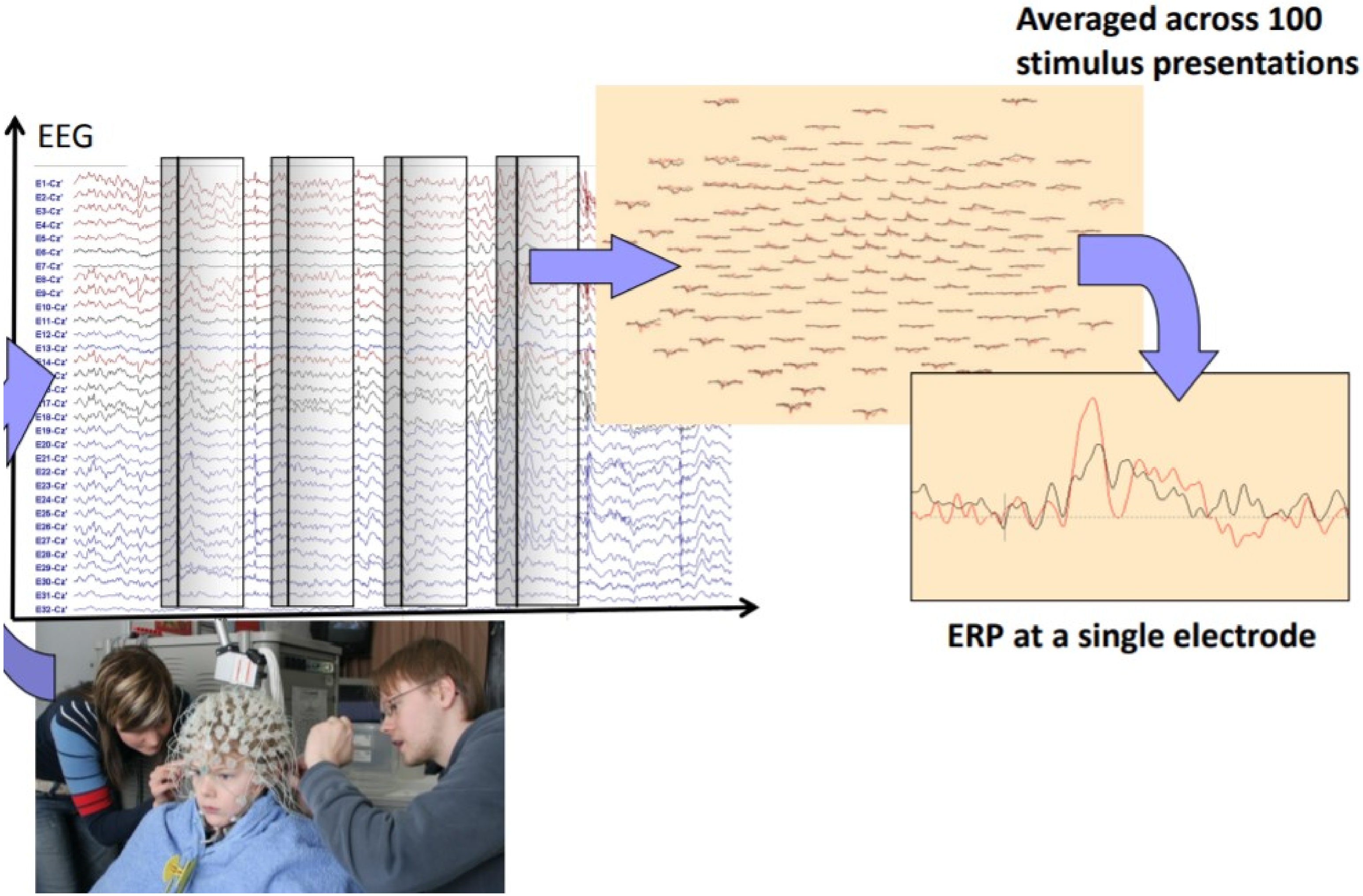
An Evoked-Response-Potential analysis quantifies electrical brain responses to events/ stimuli based on time-locked EEG portions.

Presents an analysis of time-locked brain activity at resolution of ms.

Can be used as the basis for more sophisticated analysis such as source localization.

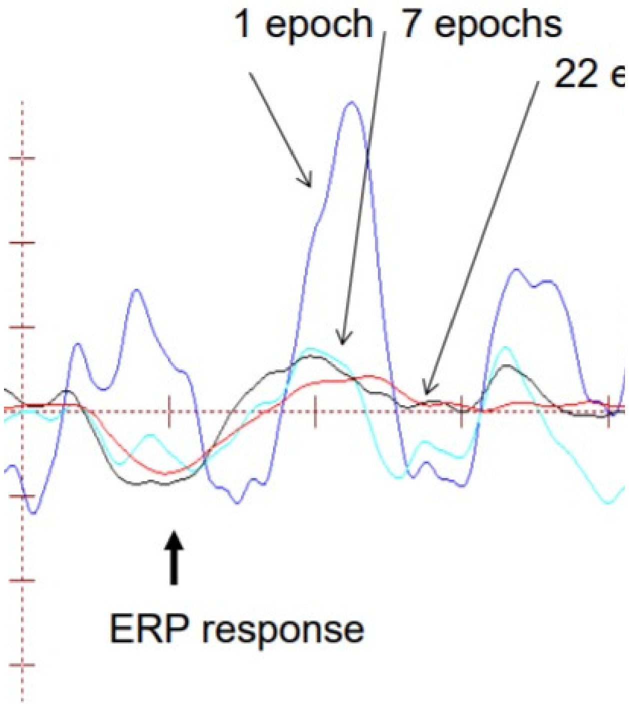


From EEG time series to ERP

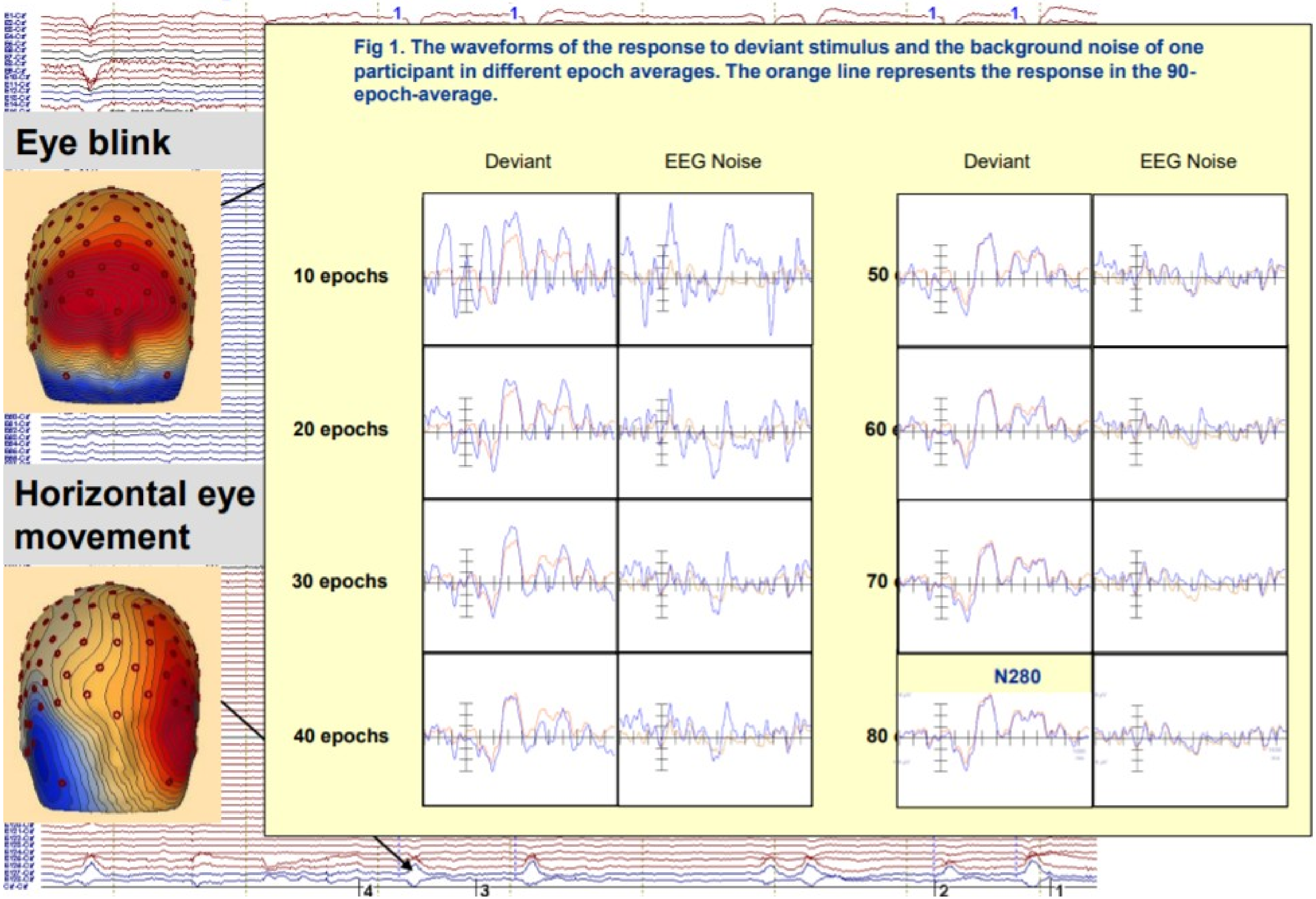


‘Signal’ in brain low. Noise high.

- The impact of noise on computing ERPs scales down (or reduces) as a function of the square root of the number of observations (N). For example, for 381 observations, the noise reduction factor would be approximately 1:19.
- This noise reduction applies to each timepoint measured.
- For accurate results, many repetitions of each condition are needed.
- The need for many repetitions can be challenging and time-consuming, but it is necessary for obtaining reliable and statistically significant results.
- In addition to repetition, other techniques such as filtering and artifact rejection can also help reduce noise in EEG recordings.

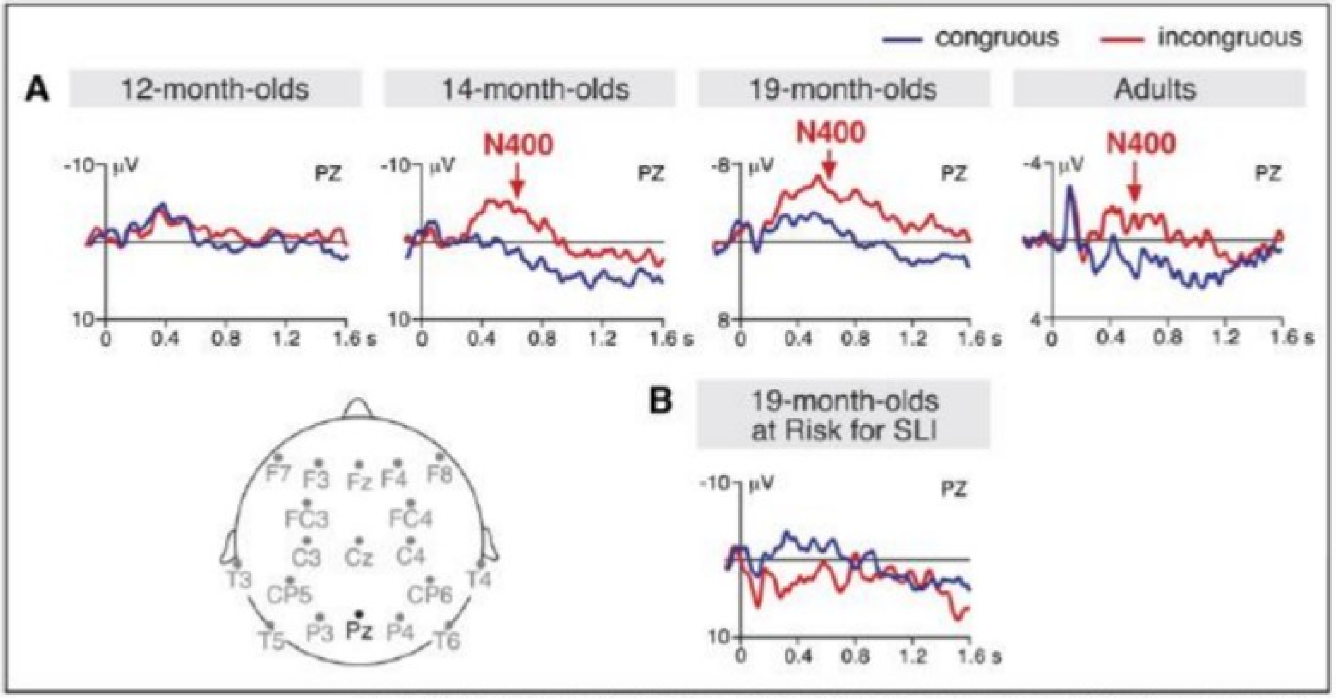


Repetitions: cancel noise, increase signal



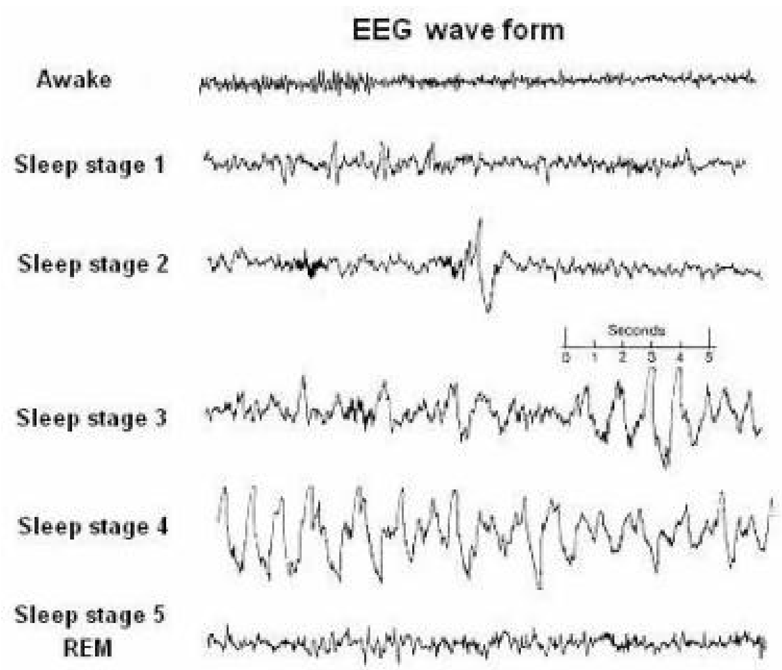
ERP in practice: surprising words.

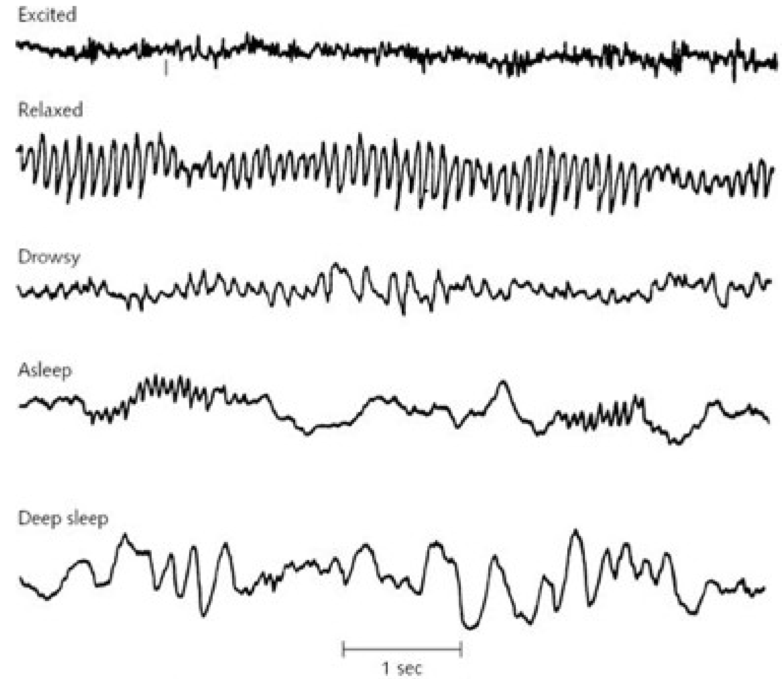
N400 – congruent: ‘*pizza was too hot to eat*’, incongruent: ‘… too hot to sit’



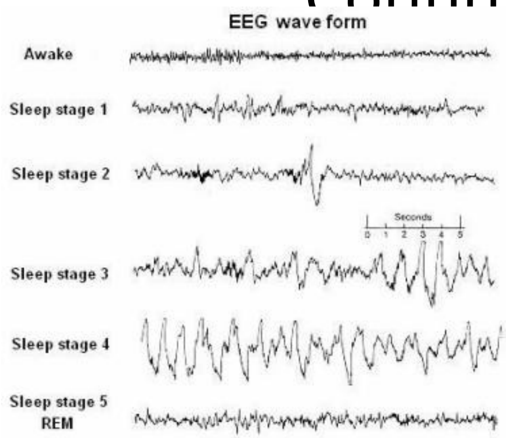
Adapted from: Friedrich & Friederici, JOCN, 2004 and Friedrich & Friederici, NeuroReport, 2005

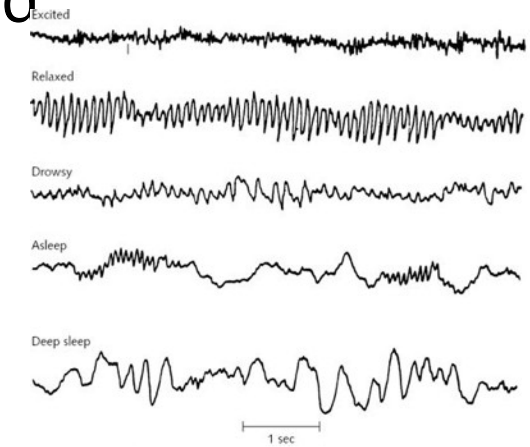
Electroencephalography (EEG)

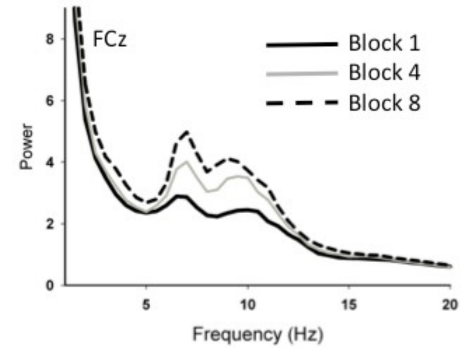


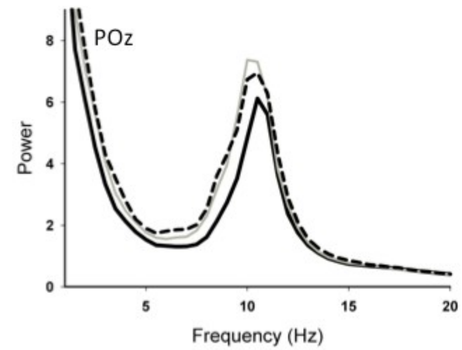


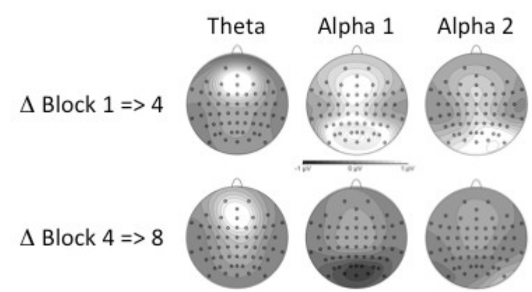
Electroencephalography (EEG) Continued











1. EEG also contains important information in form of frequency characteristics (cycling rate)
2. Differentiates sleep stages from awake, and drowsy from alert.
3. Power plots can show the relative strength of each frequency. To the right: practice (block) effects on power in different frequency bands, sampled at different sensors.

Electroencephalography (EEG)

Frequency bands

- Delta (0 – 4 Hz)
- Theta (4 – 8 Hz)
- Alpha (8 – 12 Hz), Mu (8 – 12 Hz)
- Beta (12 – 30 Hz)
- Gamma (30 – 80 Hz)
- High gamma (80 – 150 Hz)

Understanding the Alpha Band in EEG: An Example of Frequency Band Interpretation

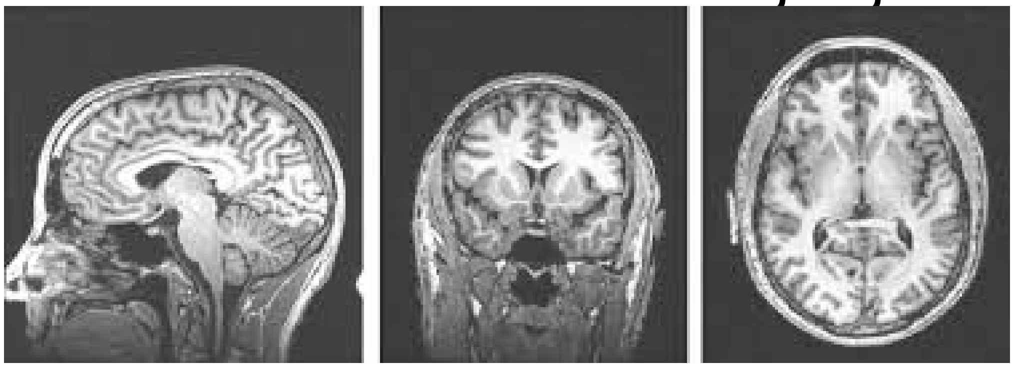
The alpha band in EEG has a frequency range of 8-12 Hz.

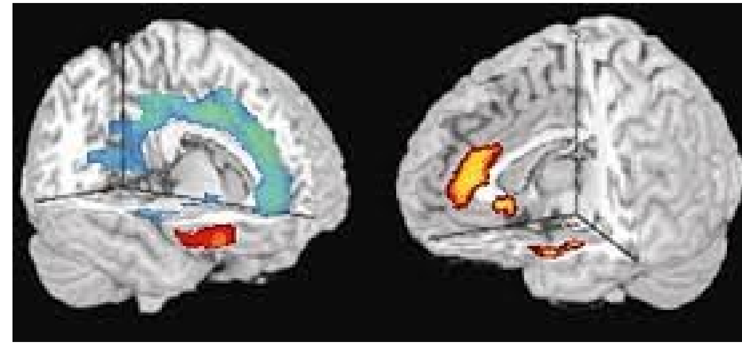
It is commonly observed during eyes-closed recordings and relaxed states.

Alpha oscillations are associated with reduced communication between the cortex and thalamus.

During externally oriented attention and stimulus processing, the alpha activity is suppressed.

Structural Imaging

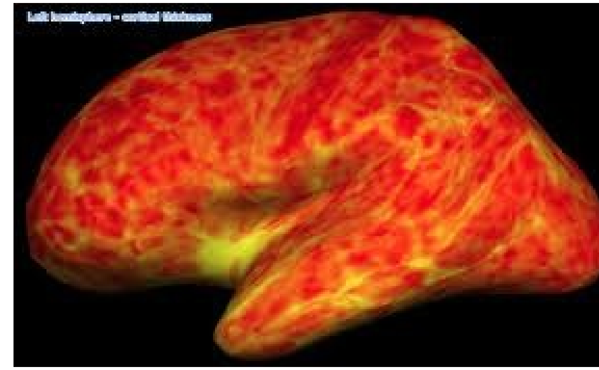


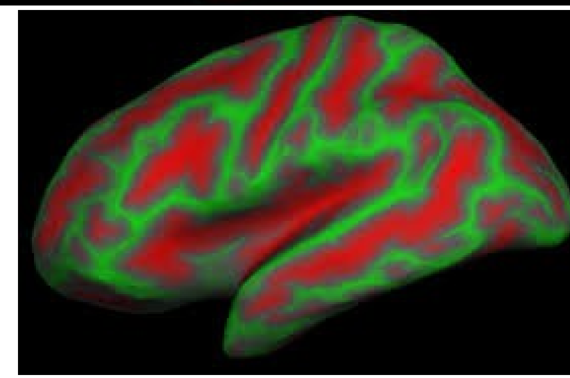


- Structural imaging involves collecting 3D images of the brain, similar to the images obtained in a medical setting.
- This type of imaging can provide information about various aspects of brain structure, such as:
  - Gray matter volume (i.e., the overall size of the gray matter in the brain).
  - The density of gray matter in specific regions, which can approximate the concentration of neurons.
  - Cortical thickness at a resolution of a few millimeters.
  - Surface area of particular brain regions.

Structural Imaging (2)

1. Calculation of cortical thickness is usually done by converting the brain's 3D representation to a 2D sheet representation.
2. The curvature map shows the gyri and sulci.
3. The upper right image shows a thickness map for a sample participant.





SARS-CoV-2 is associated with changes in brain structure in UK Biobank (2022)

Gray matter thickness (left) and diffusivity (right) effects

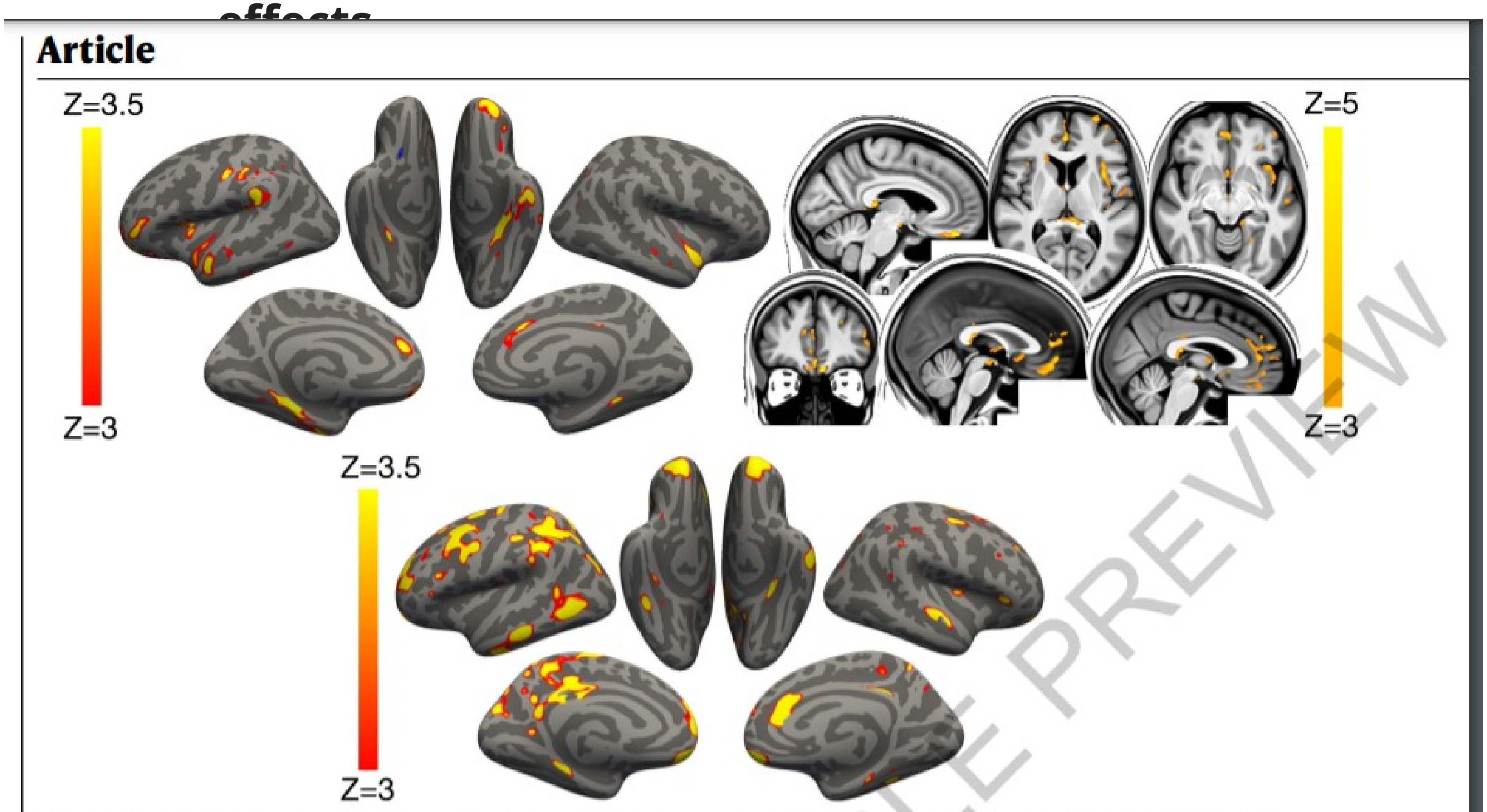


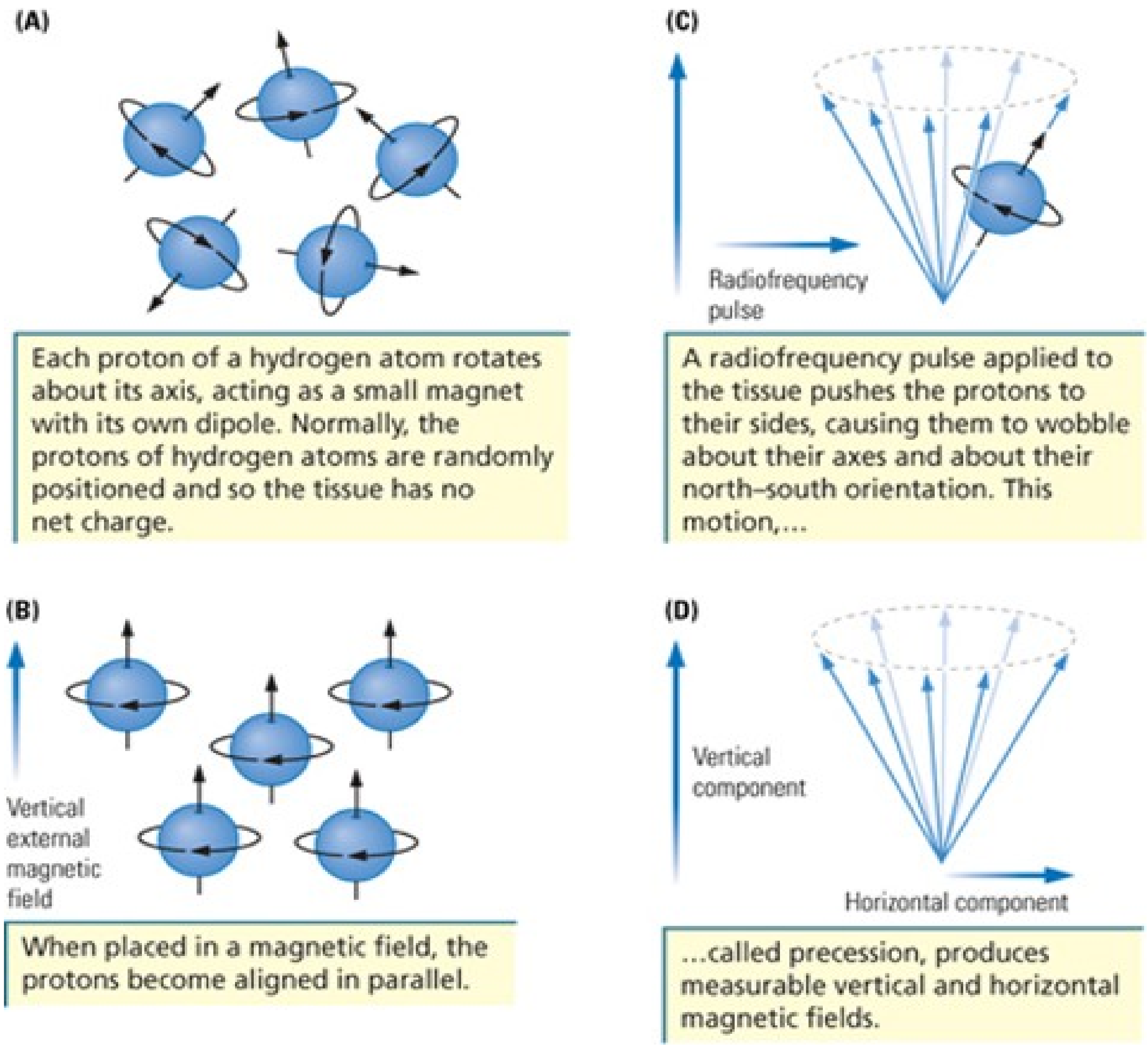
Fig. 2 | Vertex-wise and voxel-wise longitudinal group differences in grey matter thickness and mean diffusivity changes. Top row. Main analysis (Model 1): The thresholded map (|Z|>3) shows that the strongest, localised

insula and amygdala. **Bottom row.** Secondary analysis (Model 4): The thresholded cortical thickness map (|Z|>3) demonstrated longitudinal differences between the 15 hospitalised and 386 non-hospitalised SARS-CoV-2

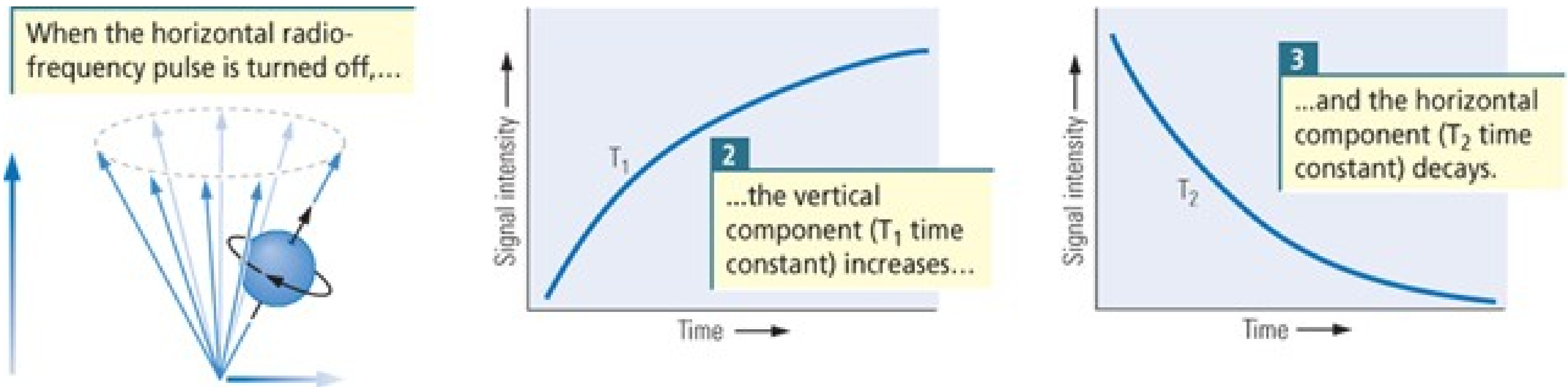
Functional MRI

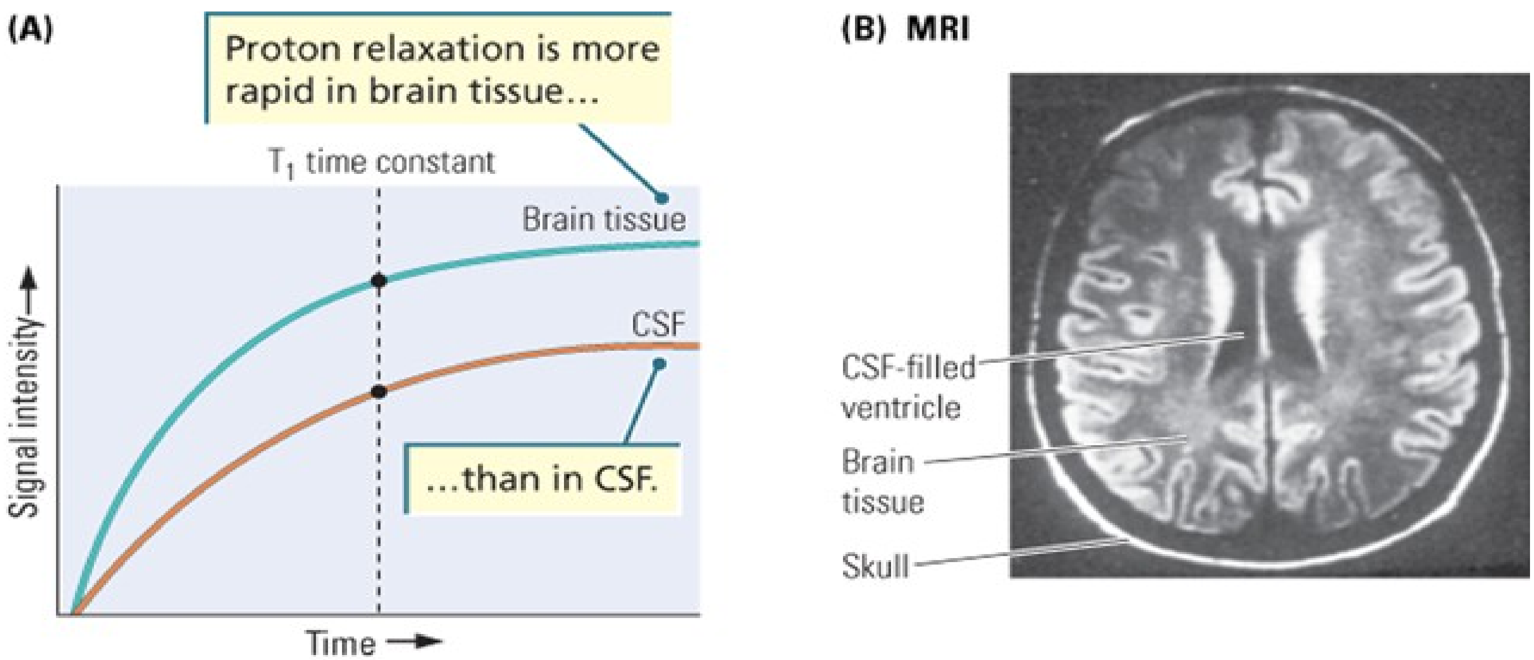
- Functional MRI is allows observing which parts of the brain work when we do things like thinking or perceiving.
  - ‘work’ means: are involved in metabolic activity (cell reactions involved in energy release)
  - In Neuro’, metabolic activity is often as a proxy for neural activity; active neurons require more energy to function and can increase their metabolic rate
- fMRI uses a big magnet to affect protons in the brain and then measures how they behave as they return to their original state.
- By analyzing the patterns of proton behavior, we can identify which brain areas are more active during certain tasks.
- This method gives us very detailed information about where activity is happening in the brain and can help us understand how different regions contribute to complex processes like thinking and perception.

Functional MRI (not for exam)



functional MRI (not for exam)

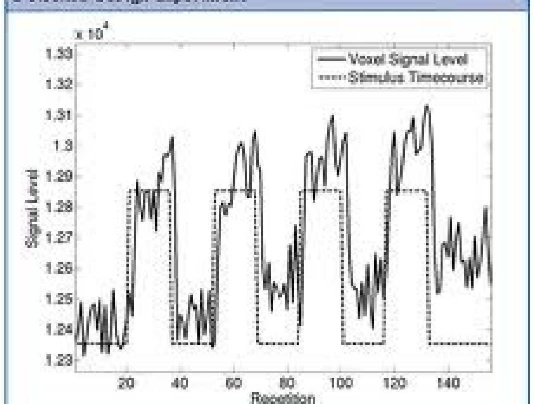




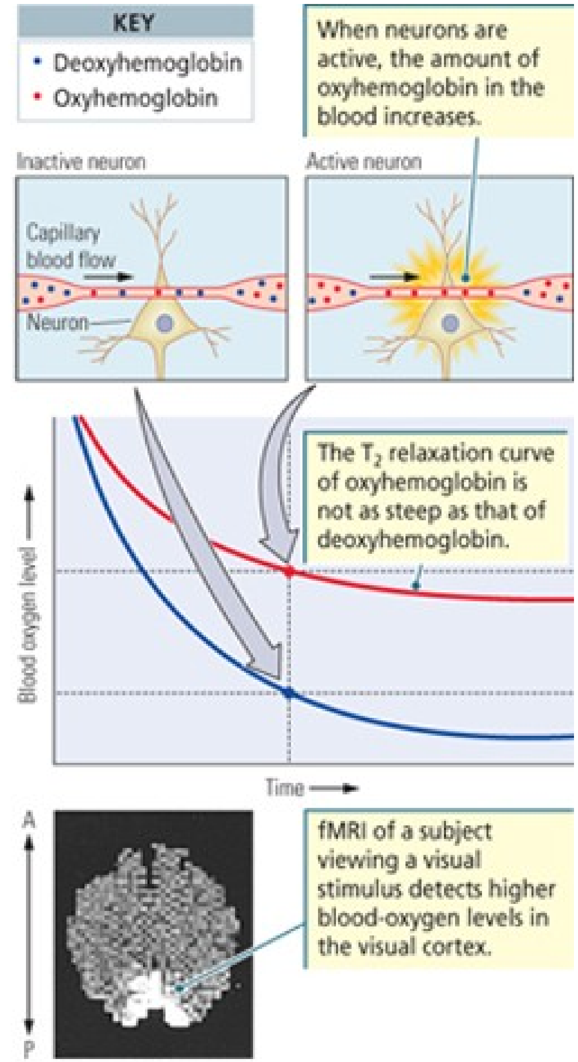
functional MRI (not for exam)

1. Detects differences in oxygen demand in different brain regions during a task, which results in T2 contrast and identifies active areas.
2. Provides a time series of brain activity in every brain region, usually at a resolution of 3x3x3mm.
3. fMRI can also measure the synchronization between different brain regions

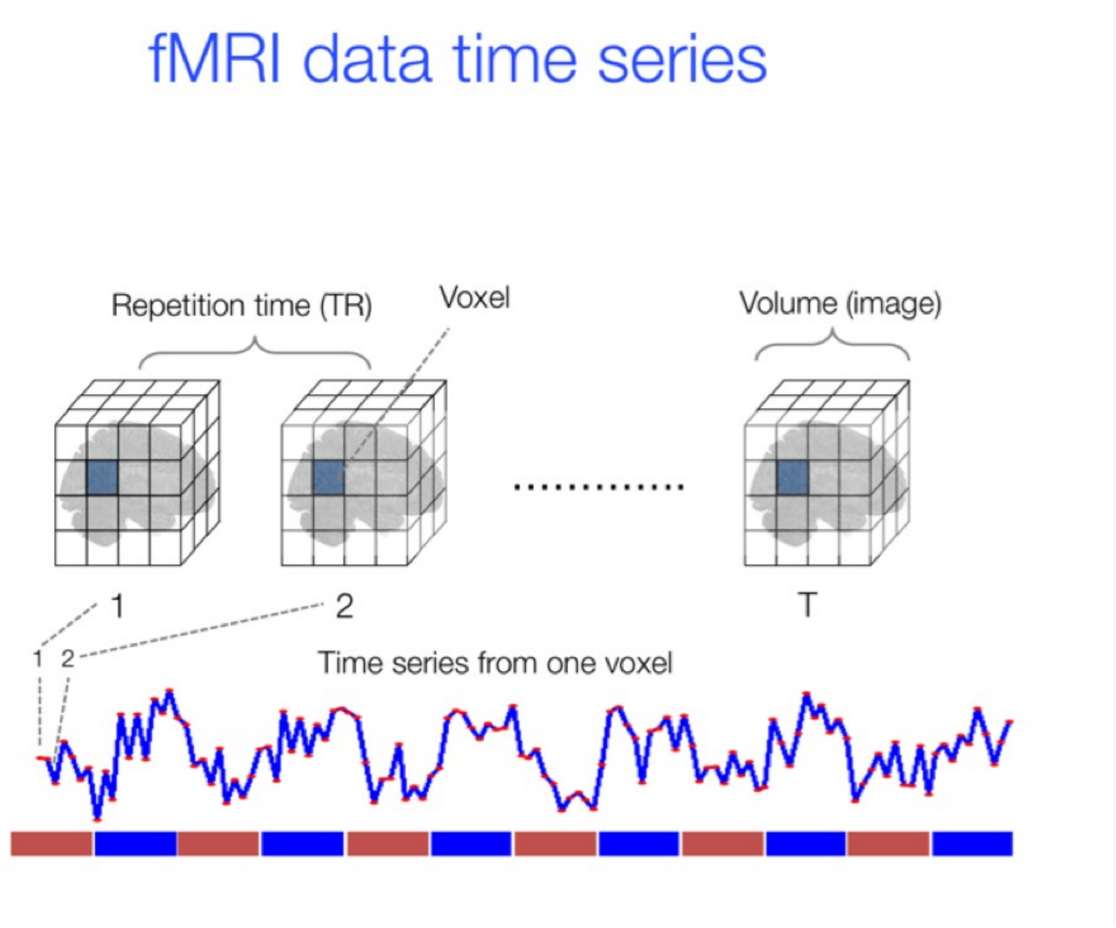
Figure 1. fMRI Time Course from a Single Activated Voxel in a Blocked-Design Experiment



Stimulus is represent as either off (low) or on (high) by the dotted line.
fMRI = functional magnetic resonance imaging.
Courtesy Dr Erik Beall at Cleveland Clinic.



Functional MRI: the time series



Functional MRI: In an experimental context

- FMRI analysis often fits a (convolved) activation model to **each voxel’s time series separately** (“massively univariate” analysis)
- Pre-processing techniques are applied to reduce noise, including spatial smoothing across nearby voxels.
- The outcome of model fitting is a collection of parameters estimated from each voxel's data. The Activation Amplitude (Beta) is the most critical parameter, and it is related to the correlation between the model and activity.
- At the group level, the voxel-level estimates are pooled together to reach a group-level conclusion per voxel

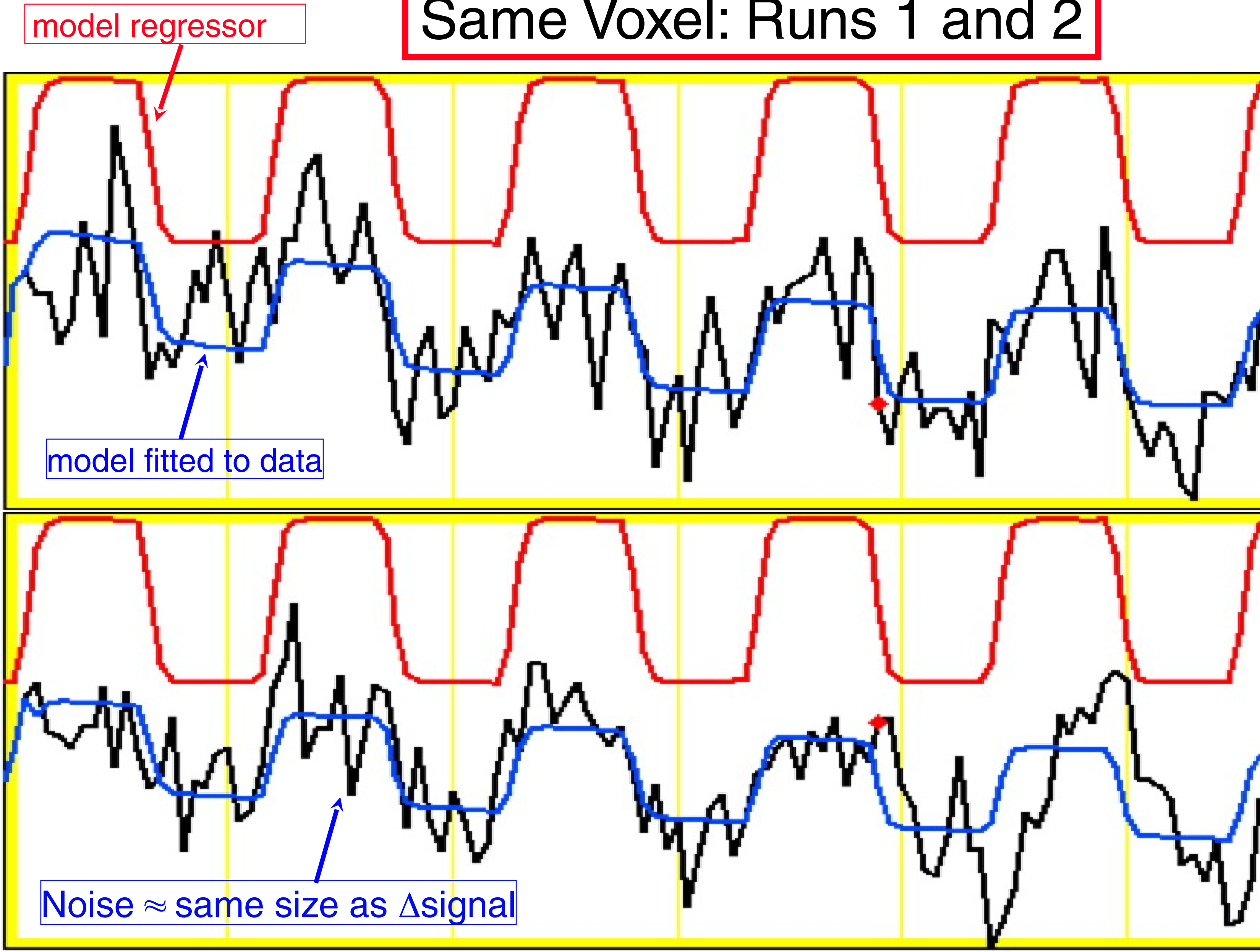
Functional MRI: In an experimental context

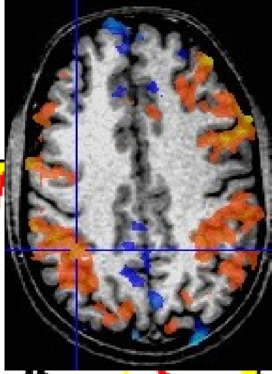
- FMRI measures changes in neural activity, not absolute magnitudes.
- The baseline signal level in a voxel does not provide information about neural activity.
- An experiment using fMRI requires at least two conditions to detect changes in neural activity.
  - Minimally, experiments use a "task" and "rest" condition.
- In a two-task experiment intermixed with rest, a beta value is estimated per task, and their values are contrasted to determine the difference between the two tasks

Functional MRI: In an experimental context (not for exam)

- Example: Block-trial FMRI data
- A long train of stimuli is presented to drive brain activity for extended period, with rest—in between . E.g .10sec on/off cycle.
- BOLD (hemodynamic) response accumulates from multiple close-in-time neural activations and is large
- Noise magnitude can be similar to BOLD response
- Next 2 slides: same brain voxel in 3 (of 9) EPI runs
- black curve (noisy) = data
- red curve (above data) = ideal model response
- blue curve (within data) = model fitted to data
- somatosensory task (finger being rubbed)

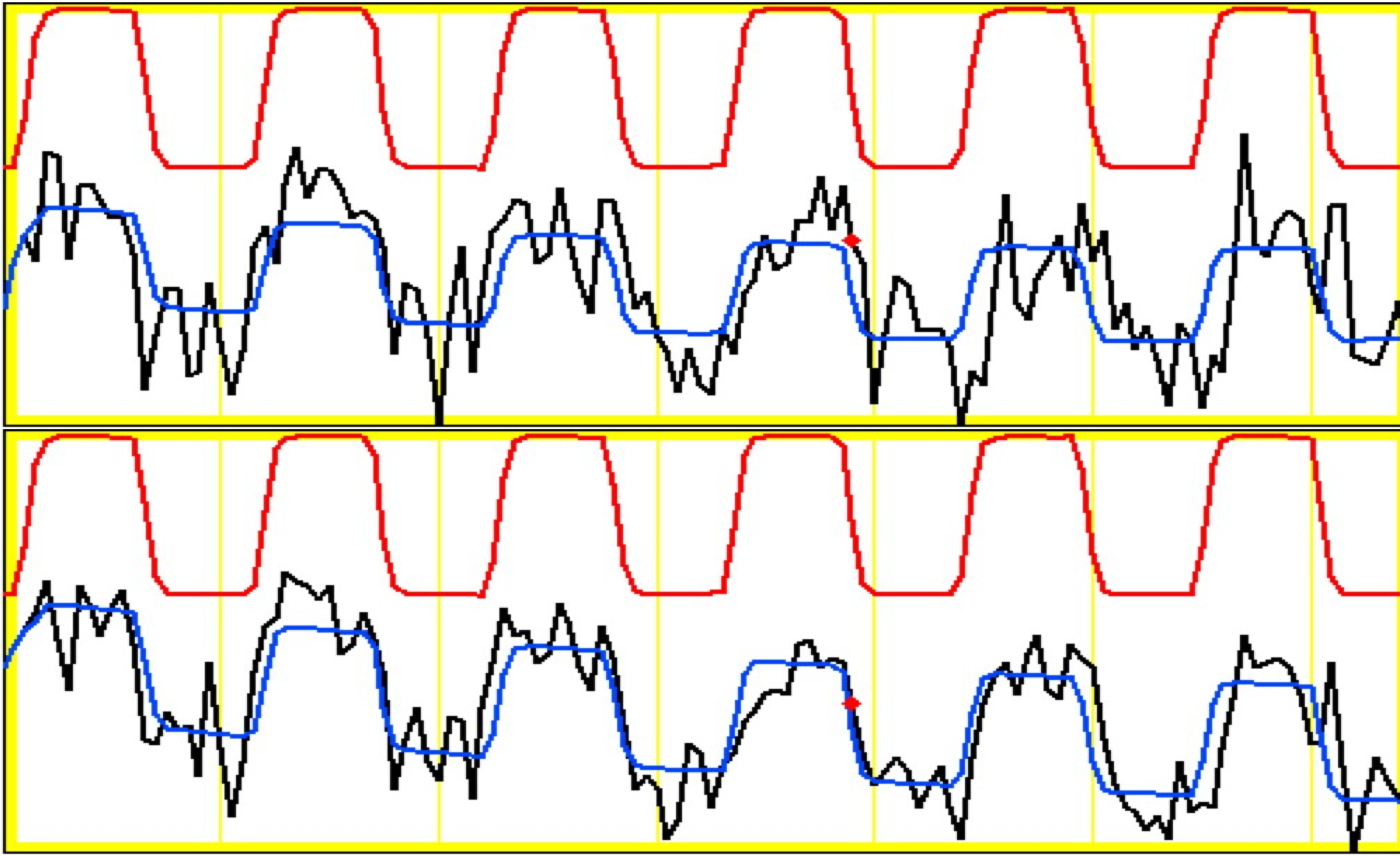
Same Voxel: Runs 1 and 2





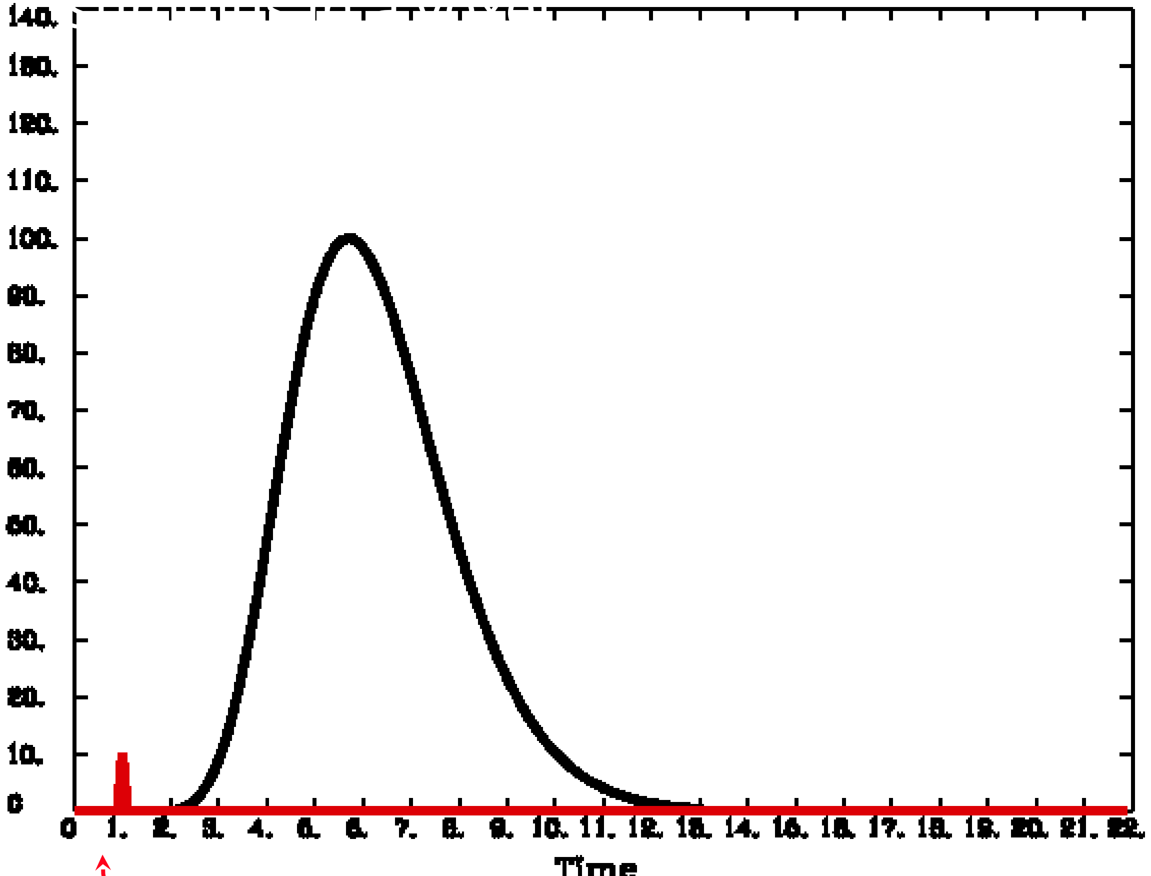
Block-trials: 27 s “on” / 27 s “off”; TR=2.5 s; 130 time points/run not for exam

Same Voxel: Run 3 and Average of all 9



Activation amplitude & shape vary among blocks! Why???

Hemodynamic Response Function (HRF)



Response to brief activation (< 1 s):

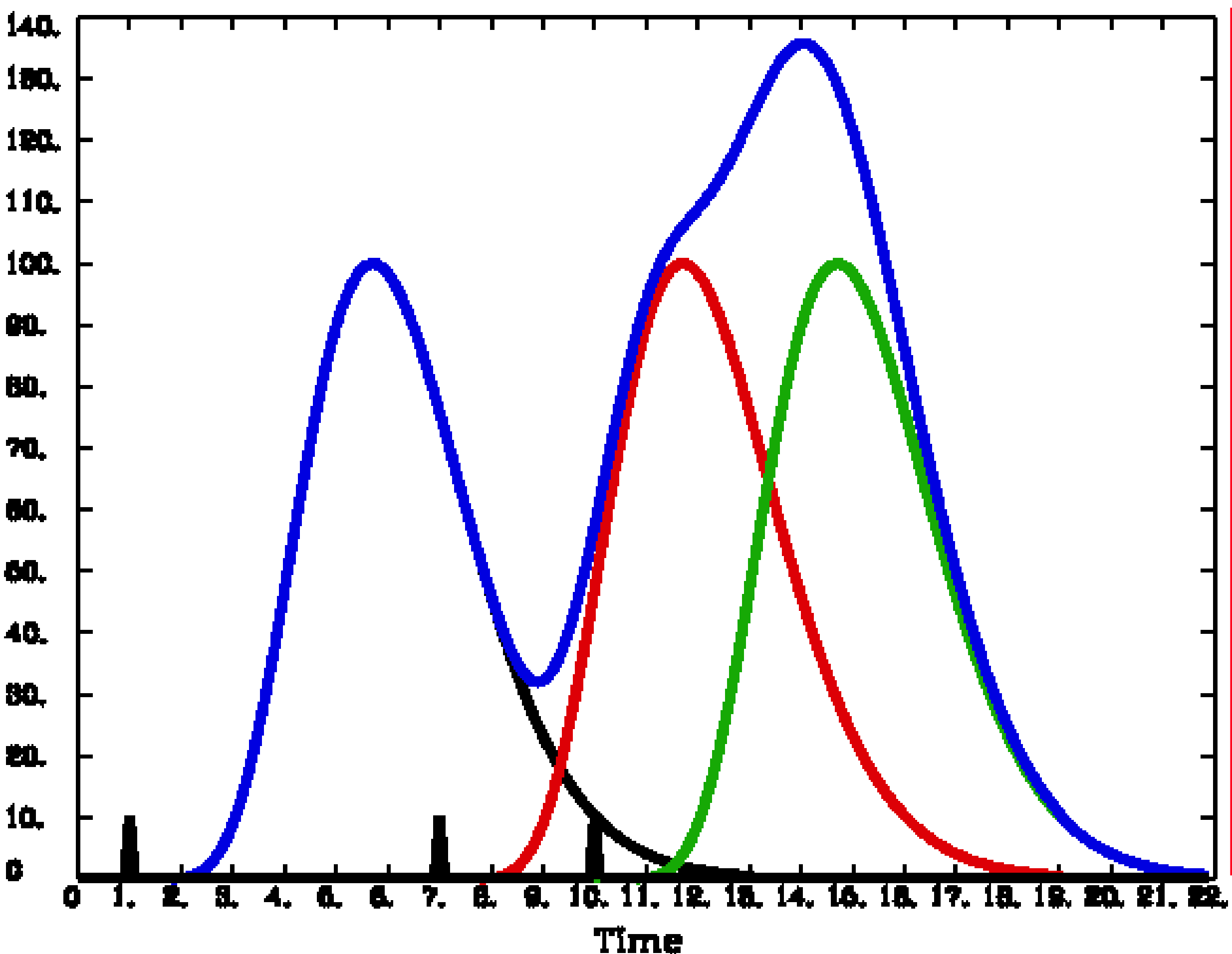
- delay of 1-2 s
- rise time of 4-5 s
- fall time of 4-6 s
- model equation:

- $h(t)$ is signal change t seconds *after* activation

1 Brief Activation (Event)

Linearity (Additivity) of HRF

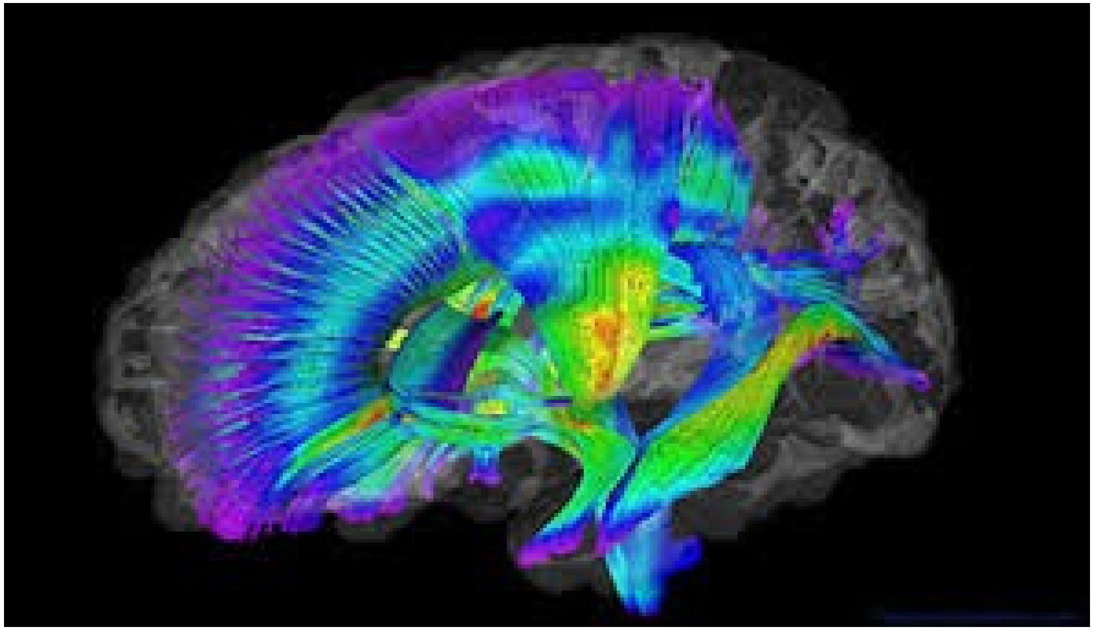
not for exam



3 Brief Activations

- Linearity is a pretty good assumption
- But not apparently perfect — about 90% correct
- Nevertheless, is widely taken to be true and is the basis for the “general linear model” (GLM) in FMRI analysis

Diffusion weighted imaging (DTI)



- Diffusion weighted imaging, also known as Diffusion MRI or Diffusion Tensor Imaging, is used to examine the *structure of white matter fibers*.
- For each voxel, the preferred direction of diffusion and the strength of diffusion are estimated to determine white matter tracts.
- These connections are considered ‘hardwired’ connections. They can be cross-referenced against functional connectivity.