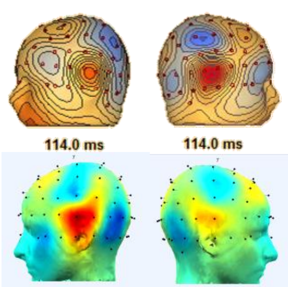
Brain event-related potentials, ERPs, and EEG as a tool for cognition



Basics of Brain Imaging - EEG

Paavo H.T. Leppänen

Jarmo Hämäläinen

Cognitive and Behavioral Neuroscience

https://www.jyu.fi/ytk/laitokset/psykologia/en/research/research-areas/neuroscience

CIBR,
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Finland

Supported by Academy of Finland

Talk plan

- **Information processing in the brain**
- **EEG technique**
- **What does EEG measure from the brain**
- **EEG oscillations**
- **Event-related potentials – typical components**
- **Sources of the brain responses**
- **Time-frequency measures of EEG**

- **Recommended book:**

  Luck, Steven J. *An introduction to the event-related potential technique*. MIT press, 2014.

ERP measurement techniques for dyslexia research - Central Hospital of Central Finland and Department of Psychology

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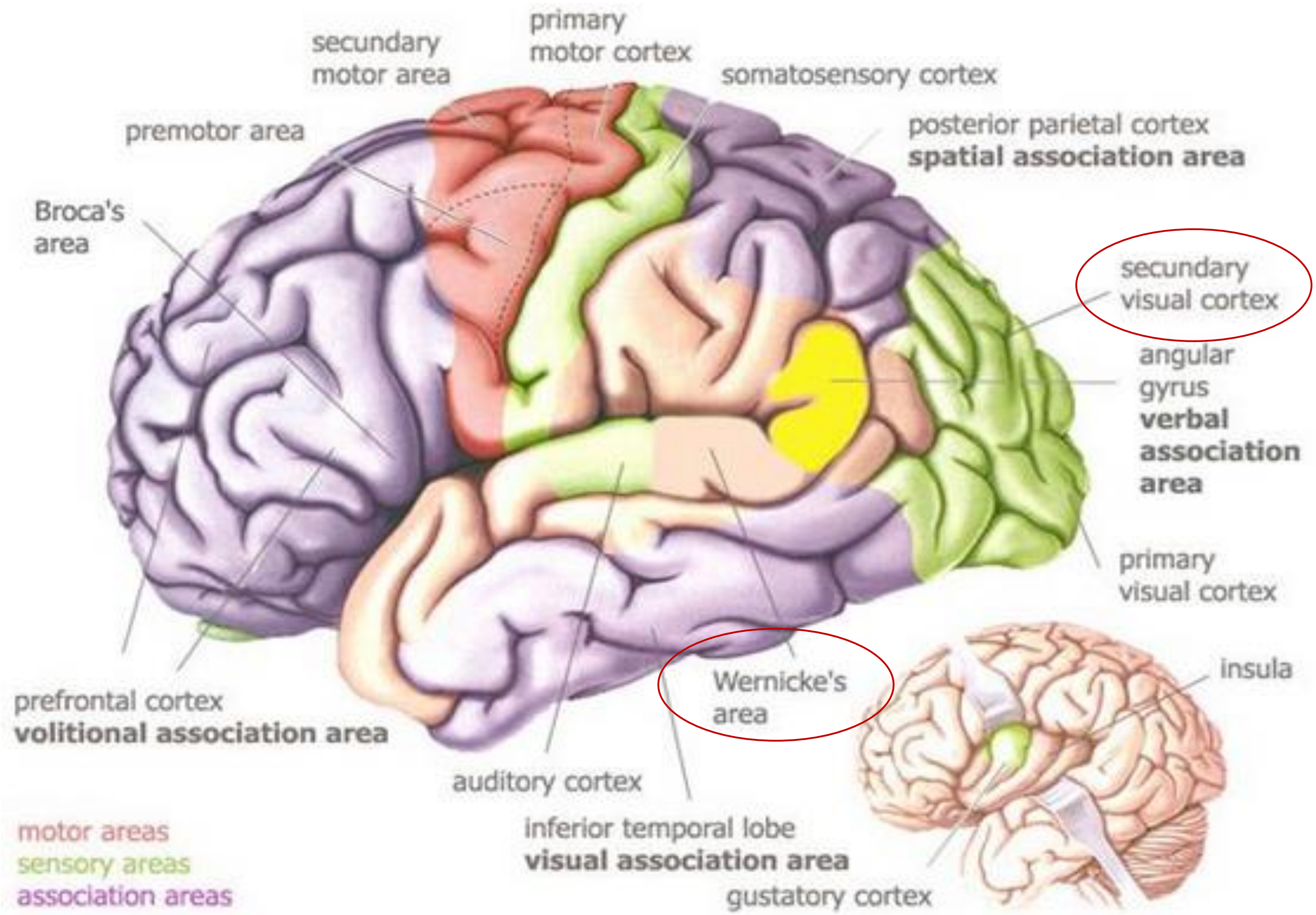
EEG - electroencephalography
ERP- event related potentials
EEG and eye-tracking combined

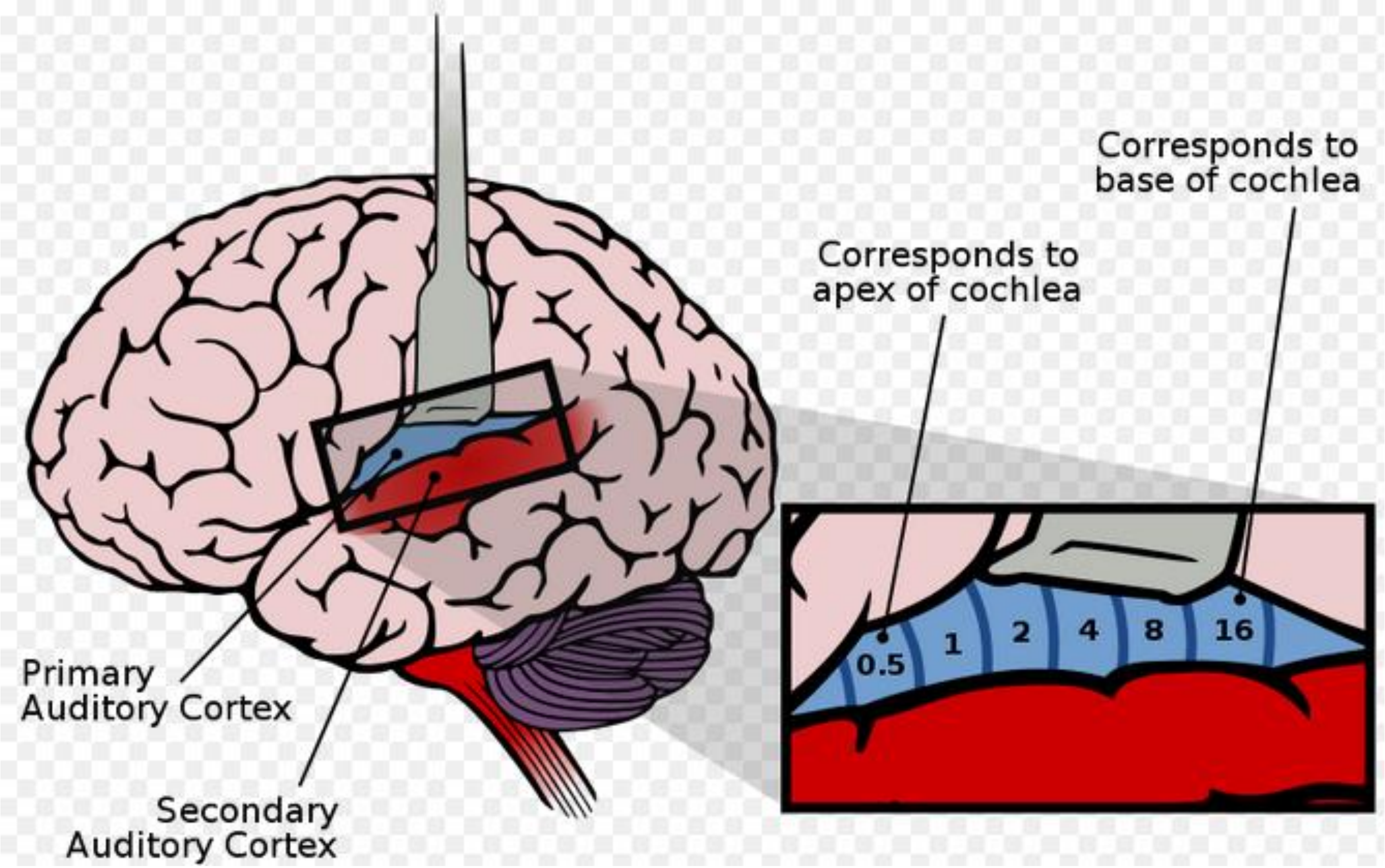
High density EEG recording

Processing units and circuits of the brain

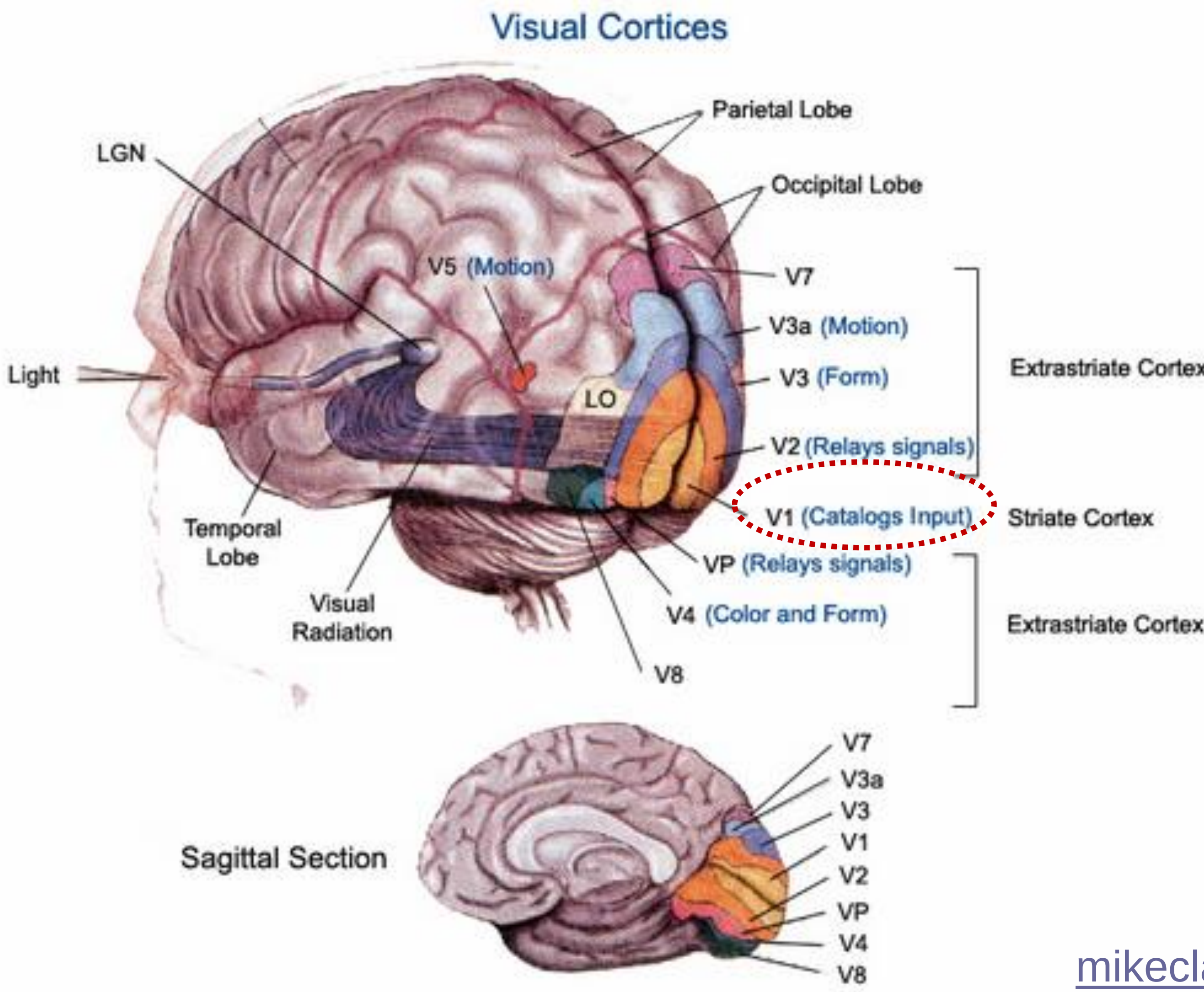


Processing units and circuits of the brain - auditory system

Tonotopicity of the auditory cortex

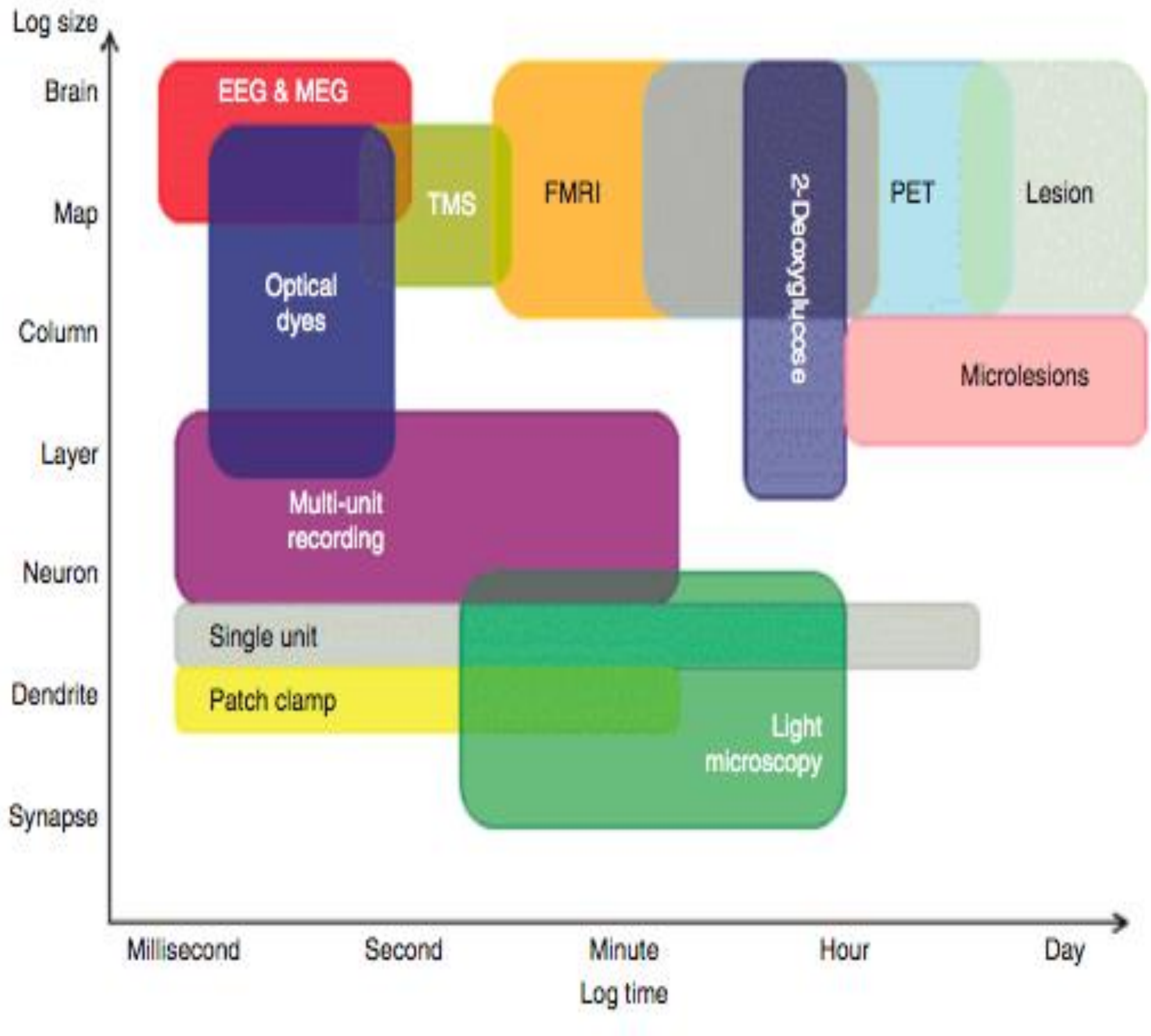


Processing units and circuits of the brain - visual system



mikeclaffey.com

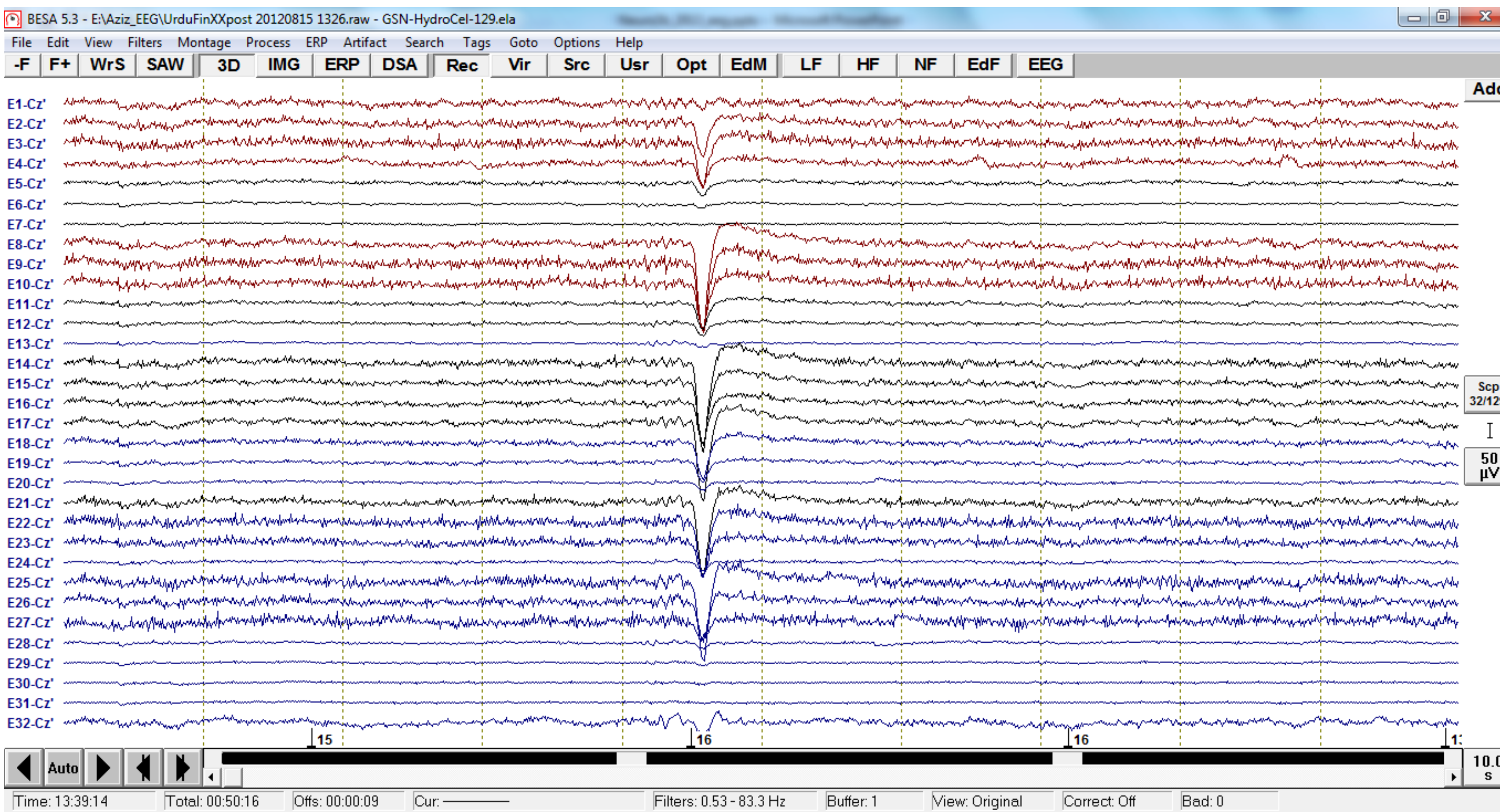
Measuring the brain



Spatial scale

Time scale

EEG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Scp 32/129
50 µV
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Auto
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Time: 13:39:14
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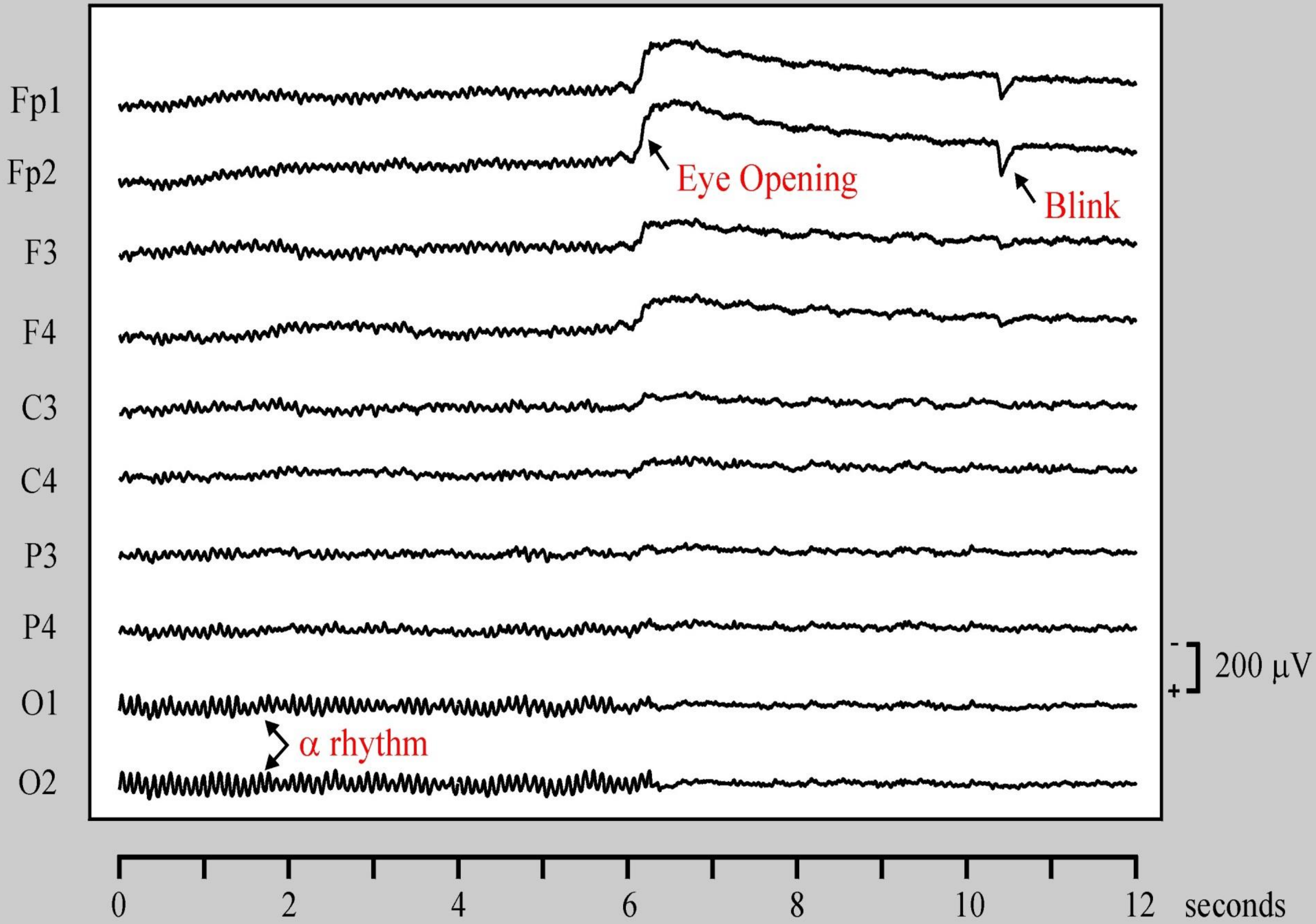
Human Electroencephalogram



Measuring EEG...

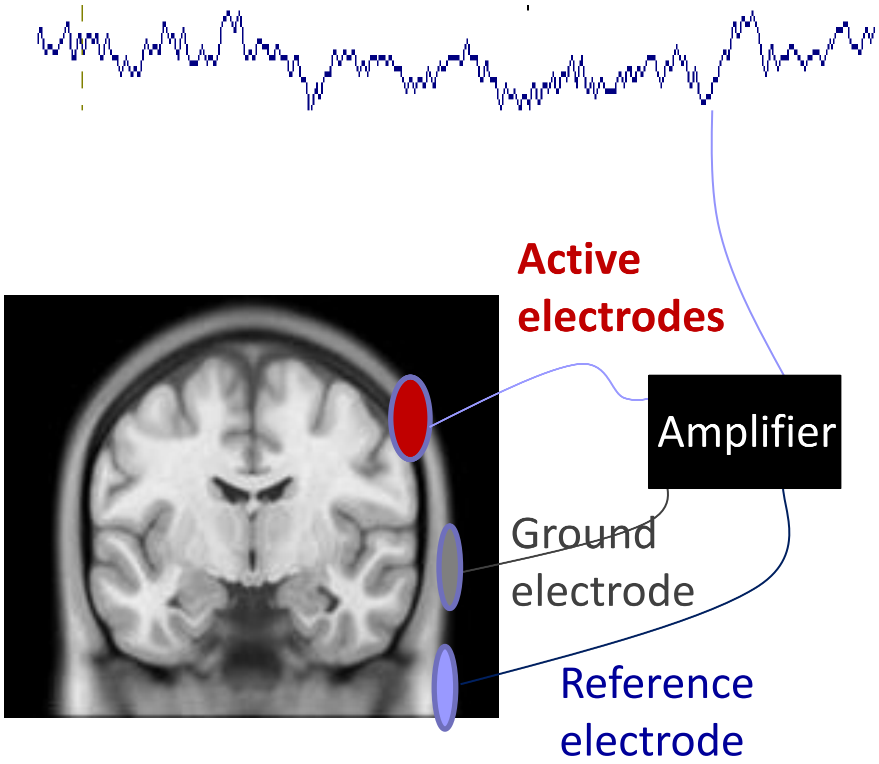
Electric fields affectingmeasurements:

1. Static electric current
2. Electric noise
3. Brain activity

Ground = difference between the participant and the amplifier

➔ Subtracted from the active and reference electrode activity: A-G, R-G

➔ is the reference point in an electrical circuit from which voltages are measured, a common return path for electric current, or a direct physical connection to the Earth



Monopolar configuration =
voltage between active and a reference electrode

Bipolar configuration =
voltage between two active electrodes

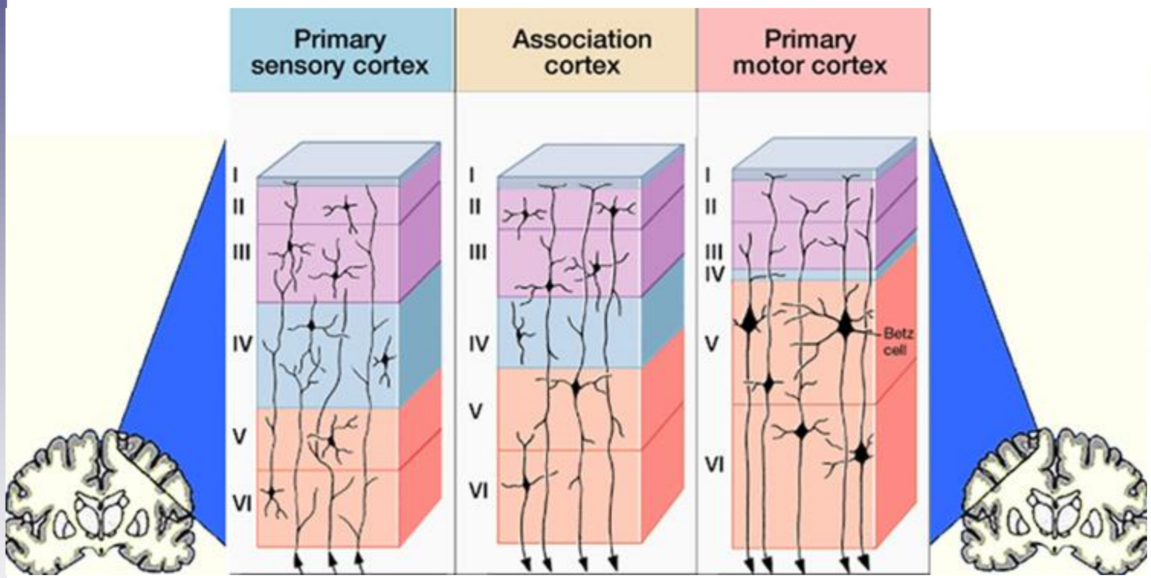
EEG =
(Activity @ AE + noise) –
(Activity @ RE + noise) =
voltage @ AE – voltage @ RE

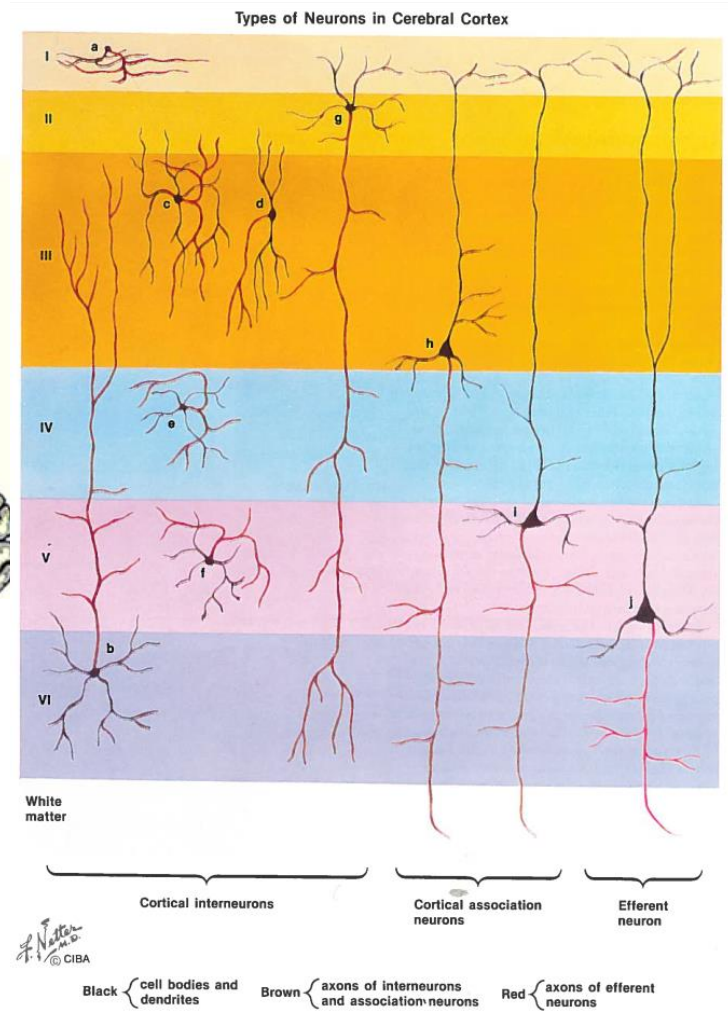
EEG signal

- Signal quality and strength
  - Affected by the tissue outside the brain tissue
  - scall
  - cerebrospinal fluid (likvor)
  - volume conductancy in the tissue
  - resistance between the recording electrode and skin

- Spatial resolution
  - mal-function (e.g. bad contact, high impedance and movement) of several electrodes will reduce the spatial resolution
  - ➔ results in different signal-to-noise ratio in some areas
  - high-density recordings can alleviate partly these problems and increase spatial resolution

Neuron types

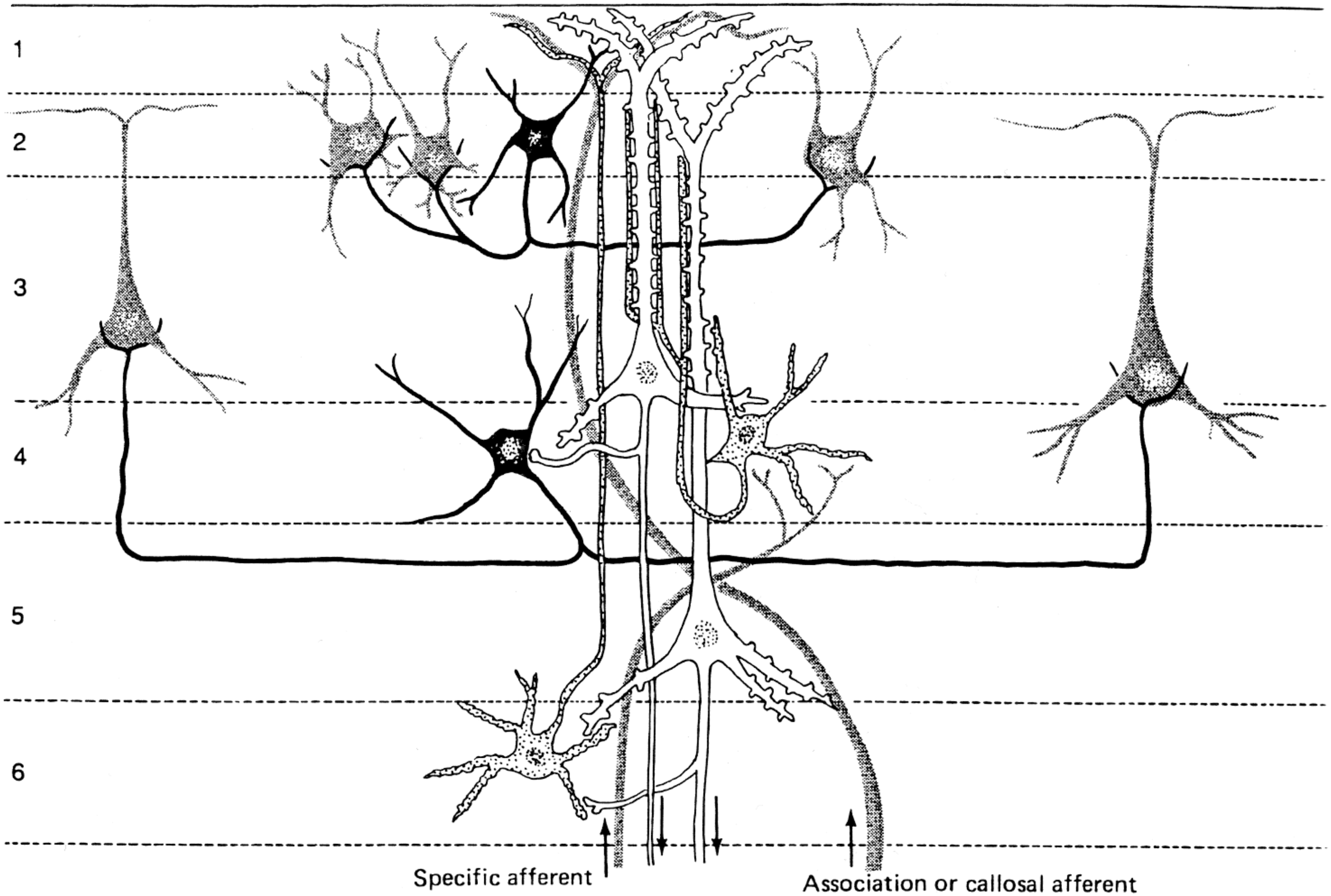




Interneurons – inside the cortex
Associative neurons
Efferent neurons
Afferent neuronal pathways

- from thalamus, project to the layer IV

Origins of EEG activity at neuronal level



From Martin, 1992 In: Kandel *et al.*, *Principles of Neural Science*

Electrical activity of the brain

The neural electric fields

- electric fields and their ‘counterfields’, magnetic fields, are dependent on several factors:
  - geometry of the particles
  - relation to each other
  - volume-conductancy

Open fields

- generated in e.g. in pyramidal cells organized in columns in layers
- can be measured with distance electrodes

Closed fields

- e.g. in nuclei, can be measured only with electrodes near the source

Open fields with spatial summation and closed fields with no spatial summation

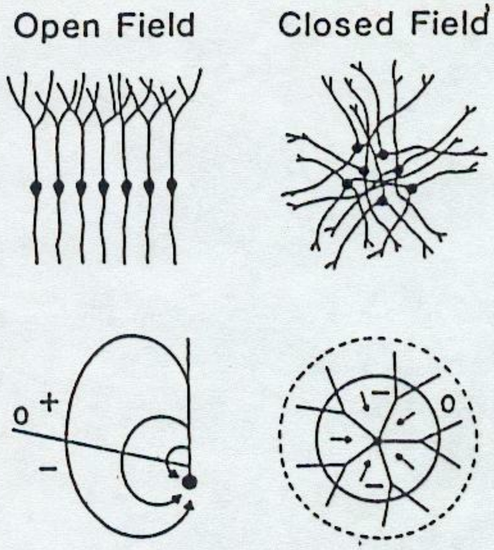


Figure 13.3. Schematic representation of configuration of neurons whose simultaneous polarization does or does not result in potential detectable by distant electrode. Electric fields generated by polarization of neurons organized in layers (such as those shown in the left panel) add together to form powerful fields that can be detected from distant (e.g., scalp) electrodes ("open field"). Fields generated by neurons organized concentrically (such as those shown in right panel) cancel each other to produce very small fields that cannot be detected by scalp electrodes ("closed field"). (Copyright 1947, Alan R. Liss, Inc. Reprinted with permission of author and publisher from Lorente de No, 1947.)

Temporal summation

Spatial summation

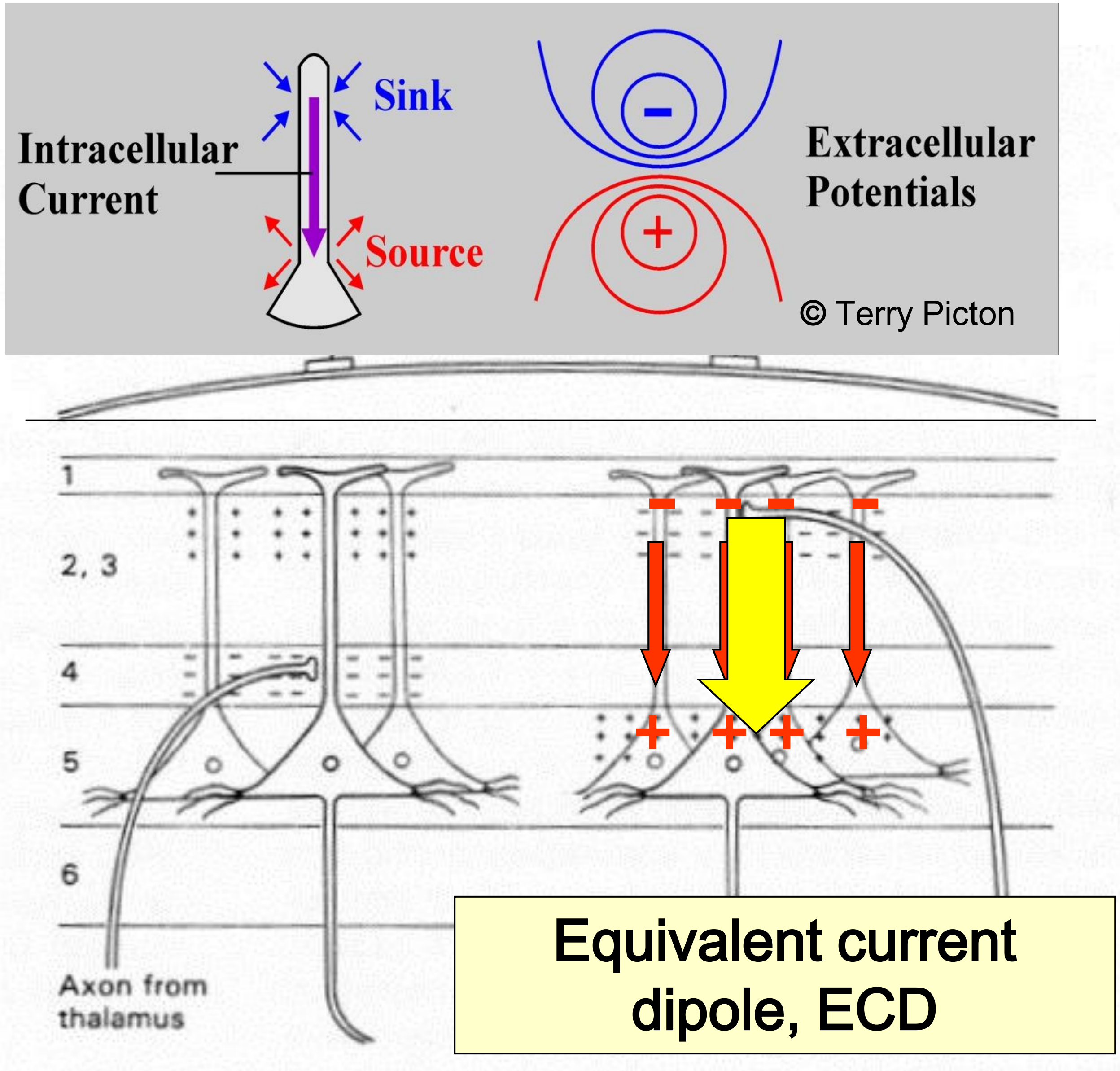
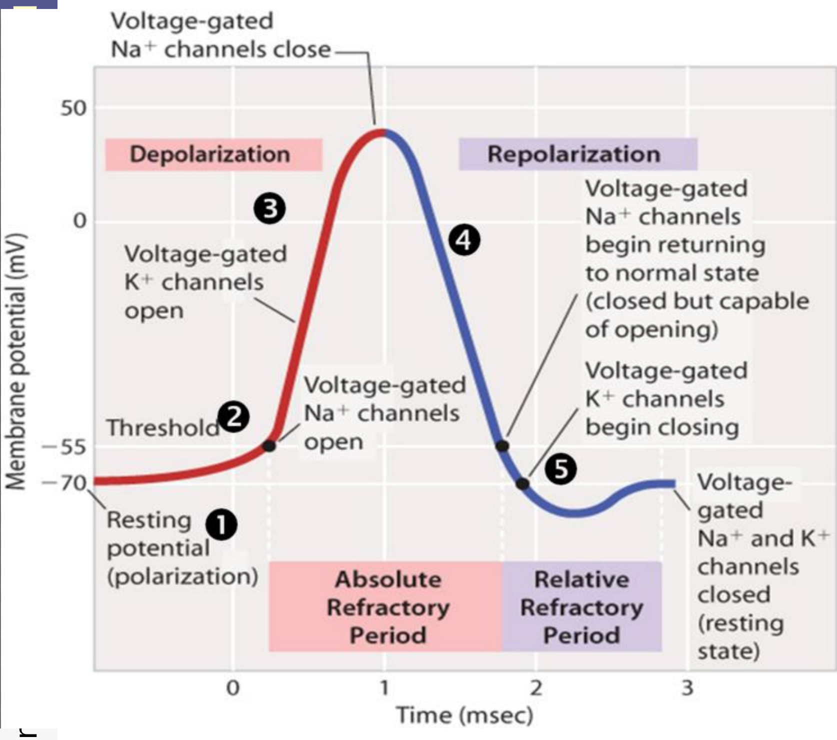


FIGURE 50–10

Leppänen; adapted from Alho; and Martin, 1992 In: Kandel *et al., Principles of Neural Science*

Communication in the brain

Action potentials



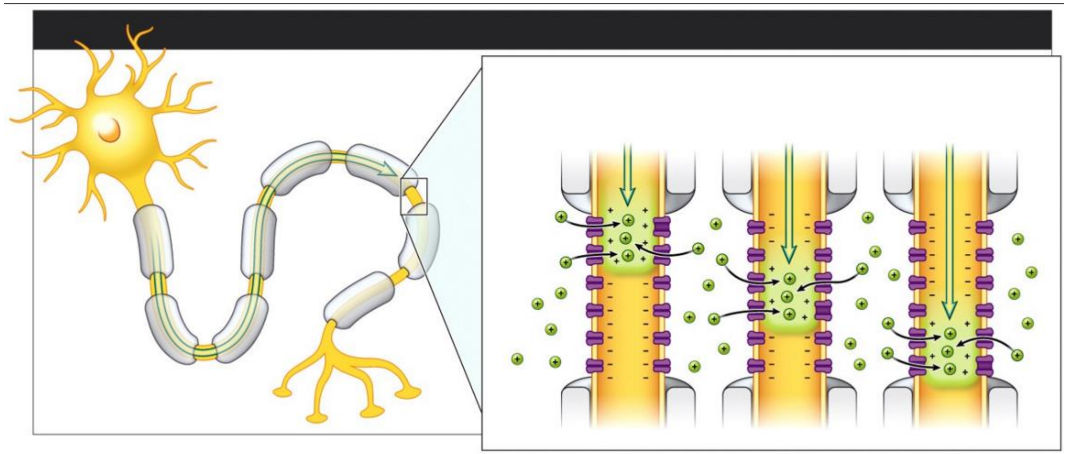
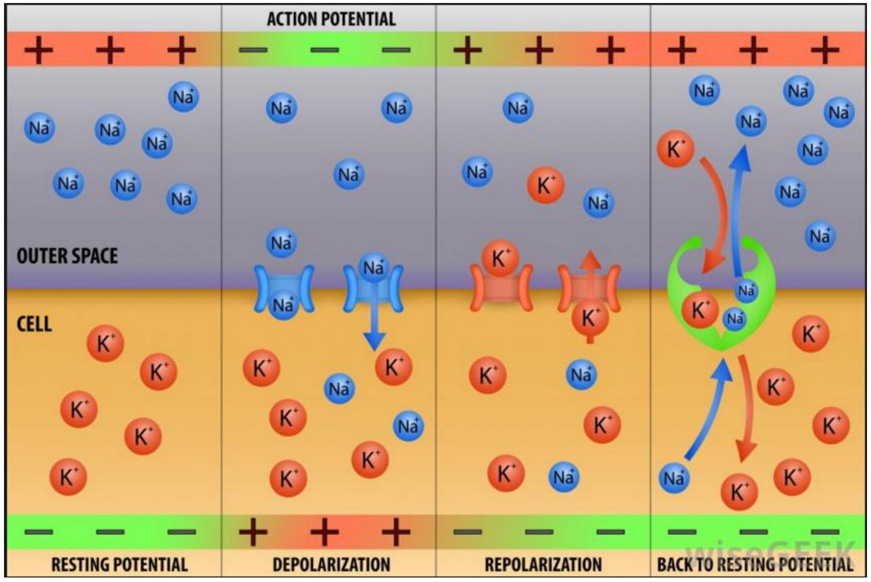
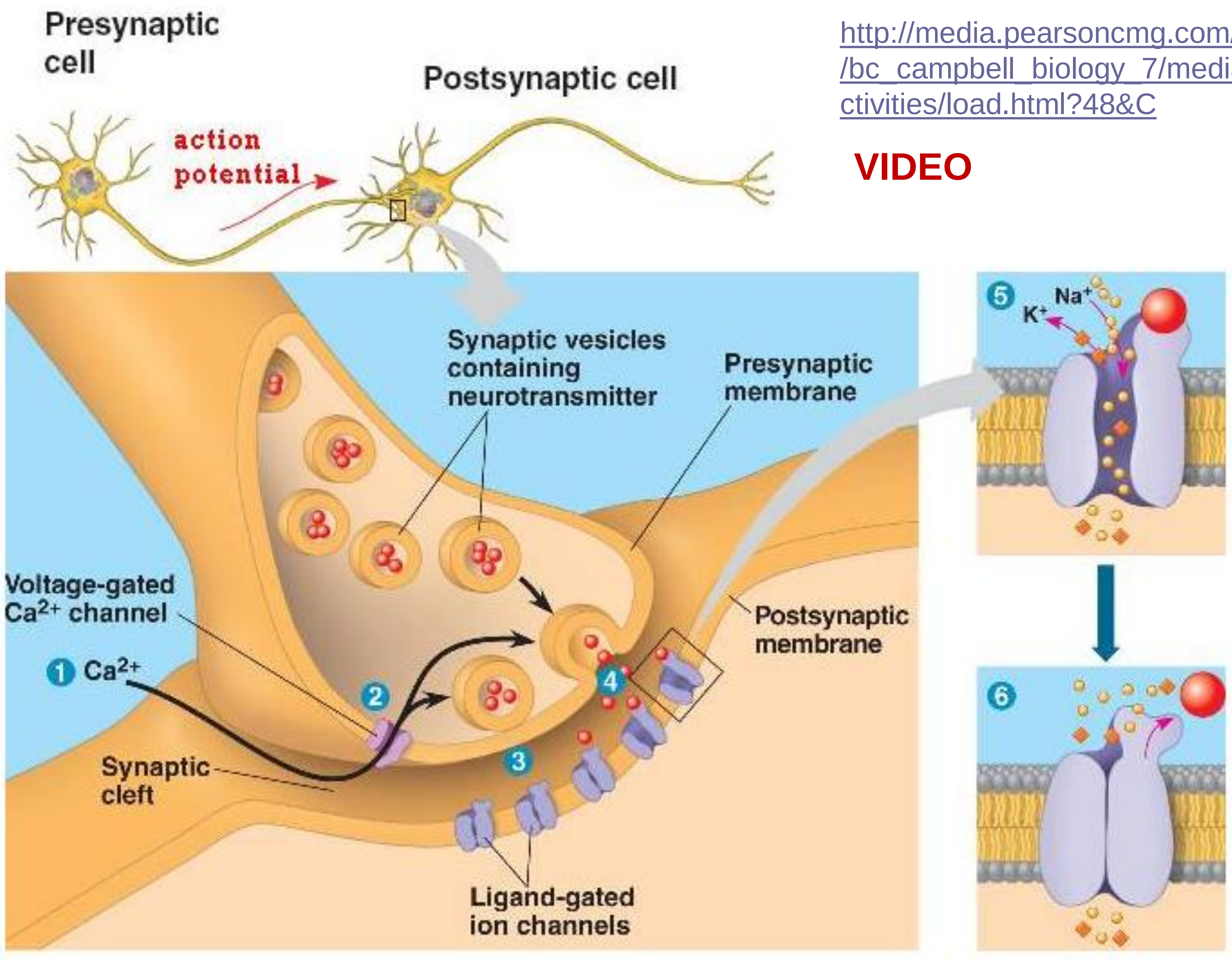


Figure 23-10
What Is Life? A Guide To Biology



Communication in the brain - synapse

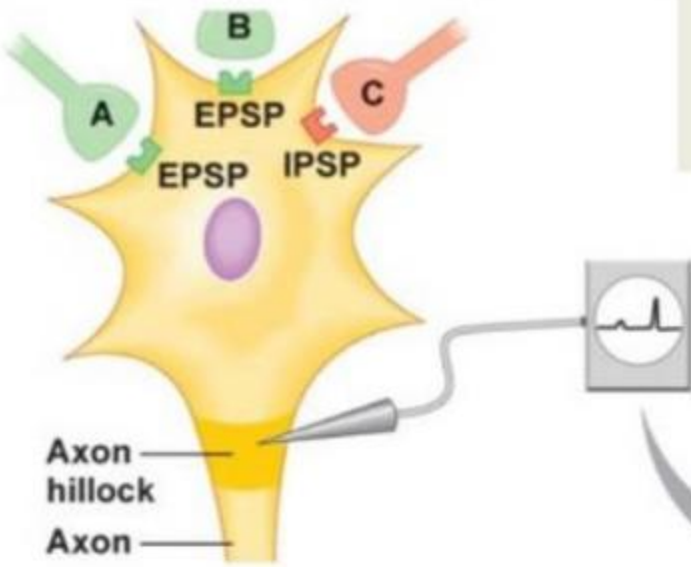


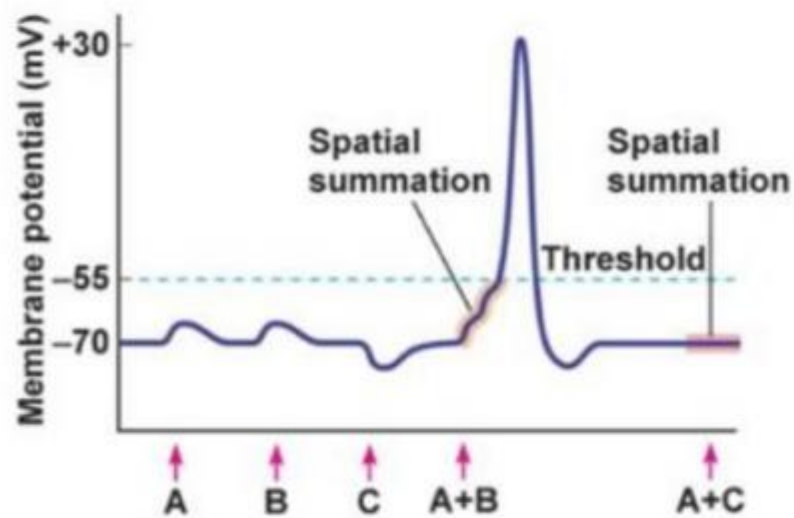
http://media.pearsoncmg.com/bc/bc_campbell_biology_7/media/activities/load.html?48&C

VIDEO

Post-synaptic potentials

- Presynaptic action potentials result in either Excitatory (EPSP) or Inhibitory Post Synaptic potentials (IPSP).





- Changes in potential reflect ionic currents across the membrane.

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

Prerequisites for EEG/ERP

Temporal summation

- postsynaptic potentials slow enough for this
  - ➔ EEG mostly reflects post-synaptic summated potentials

- action potentials also affect indirectly

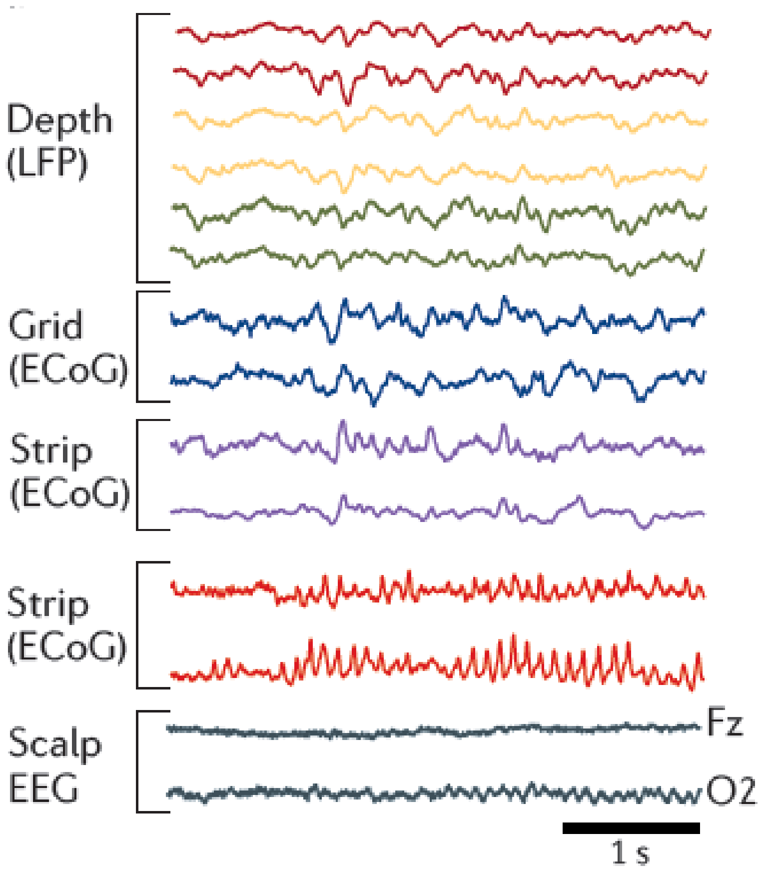
Spatial summation

- with large enough neuronal population, cortical patch, activated
- seen well in pyramidal cell activity
  - pyramidal cells oriented parallel to one another
  - oriented perpendicular to the surface of the cortex
- these form a dipolar activation pattern
- nucleic and interneurons oriented randomly

  ➔ synaptic potentials cancel out themselves in recordings

Electrophysiological Signals at Different Scales

- **Single cell recording**
- **Local filed potential (LFP)**
- **Electrocorticogram (ECoG)**
- **Electroencephalogram (EEG)**



Slide material: Kaushik Majumdar,
Indian Statistical Institute Bangalore Center/
Buzsaki et al., *Nat. Rev. Neurosci*., **13**: 407 – 420, 2012

Neuronal Oscillation: Functions

- Modulates synaptic plasticity.
- Influence reaction time.
- Correlates with attention.
- Modulates perceptual binding.
- Coordinate among brain regions far apart.
- Consolidate memory.

Slide material: Kaushik Majumdar,
Indian Statistical Institute Bangalore Center/
Canolty et al., *Science.*, **313**: 1626 – 1628, 2006

Cortical Oscillation: 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)**

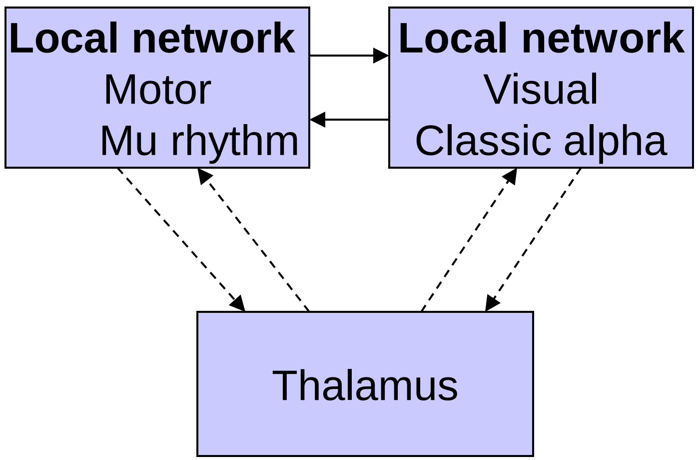
Synchronization of Inputs

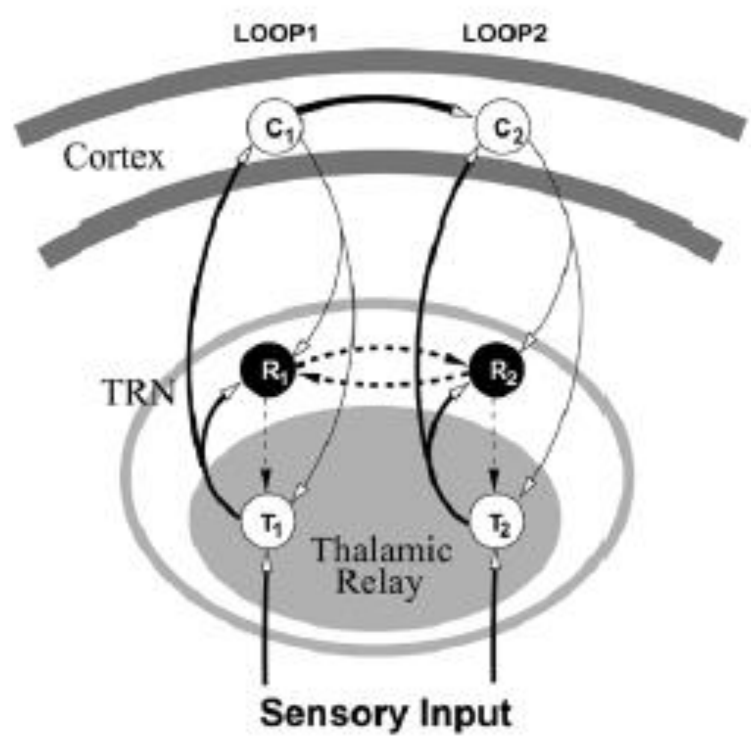
At least three types of synchronies have their electrogenesis in cortex.

1. Those created **locally between neighboring columns** produce high frequency components above 30 Hz (gamma rhythms).
2. **Intermediate or "regional" oscillations between cortical columns** separated by several centimeters produce intermediate frequency components (high alpha/mu : > 10 Hz; and beta: 12-20 Hz).
3. **Global synchronies between cortical regions** that are significantly far apart, such as frontal and parietal or occipital and frontal regions. ➔ These are related to slow frequency components - delta (1-4 Hz), theta (4-8 Hz), and low alpha/mu (8-10 Hz).

http://www.cogsci.ucsd.edu/~pineda/COGS260/cogs260%20lect3.ppt

Local and Global Networks





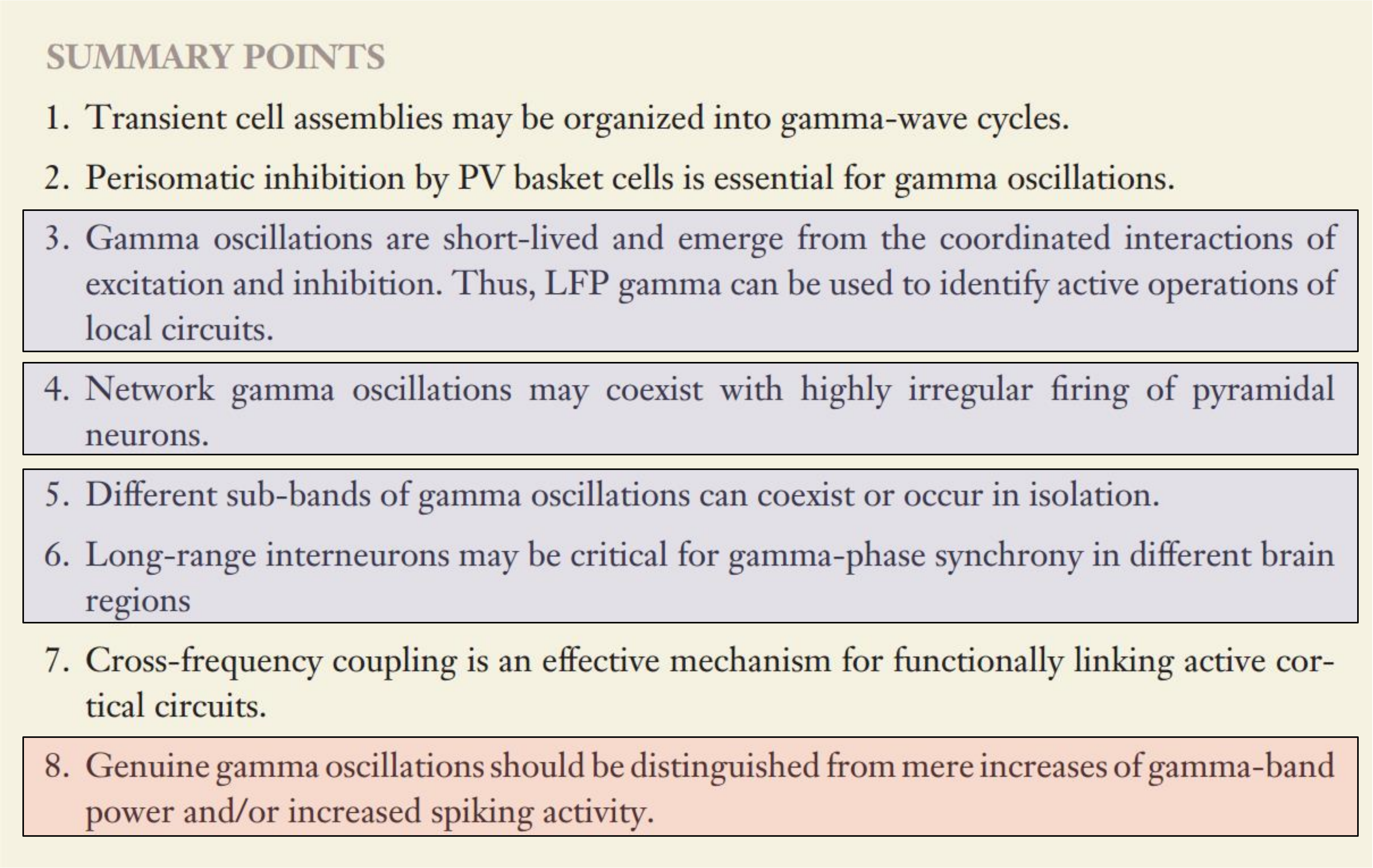
http://www.cogsci.ucsd.edu/~pineda/COGS260/cogs260%20lect3.ppt;
Choe, Y. IEEE Trans. Neural Net., 2003, 15(5): 1480-1485

EEG – oscillations, examples

- Alpha-activity:
  - 8-12 Hz
  - Observed e.g. in eyes-closed recordings and relaxed state
  - Alpha-activity a sign that thalamus is not communication information to the cortex.
  - When the stimulus evokes information processing alpha activity becomes suppressed and desyncronized

- Beta-activity
  - 12-30 Hz
  - Cortical
  - Can increase with increased brain activation
  - Observed in eyes-open recordings and awake arousal state

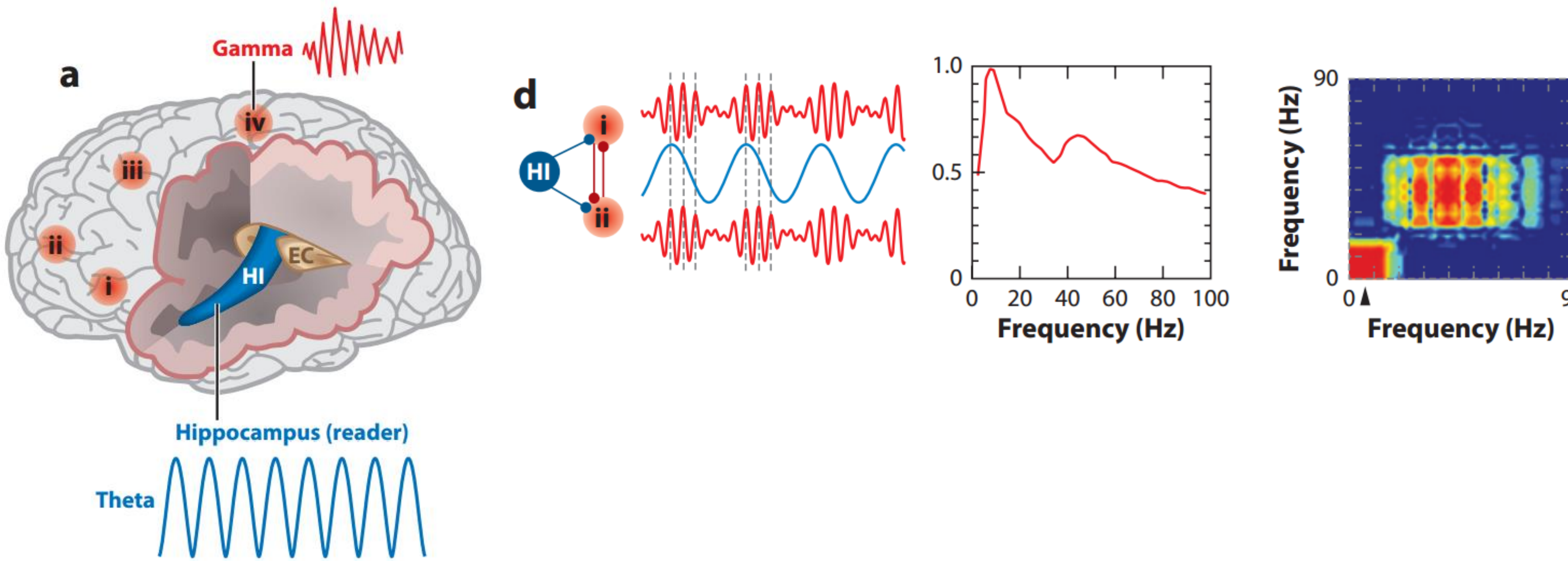
Gamma oscillation functions


SUMMARY POINTS

1. Transient cell assemblies may be organized into gamma-wave cycles.
2. Perisomatic inhibition by PV basket cells is essential for gamma oscillations.
3. Gamma oscillations are short-lived and emerge from the coordinated interactions of excitation and inhibition. Thus, LFP gamma can be used to identify active operations of local circuits.
4. Network gamma oscillations may coexist with highly irregular firing of pyramidal neurons.
5. Different sub-bands of gamma oscillations can coexist or occur in isolation.
6. Long-range interneurons may be critical for gamma-phase synchrony in different brain regions
7. Cross-frequency coupling is an effective mechanism for functionally linking active cortical circuits.
8. Genuine gamma oscillations should be distinguished from mere increases of gamma-band power and/or increased spiking activity.

Buzsaki & Wang, 2012, Annu. Rev. Neurosci. 2012. 35:203–25

Gamma oscillation functions

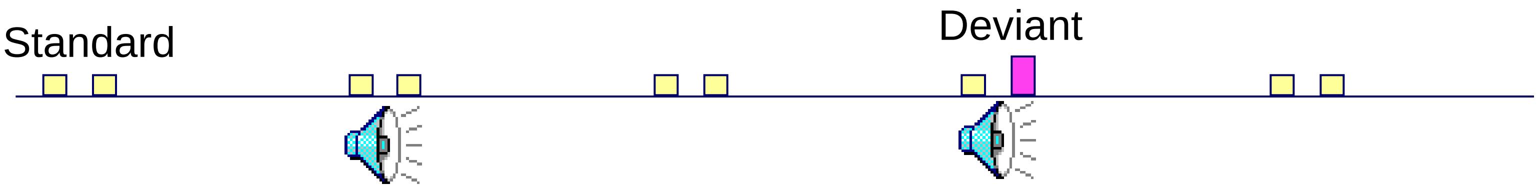


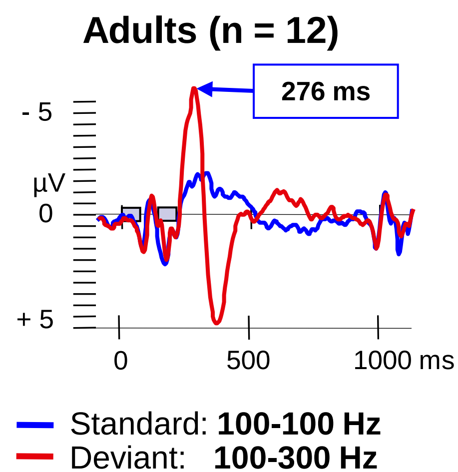
Gamma phase-phase coupling between two cortical sites, whose powers are modulated by the common theta rhythm. Both gamma coherence and gamma power-power coupling are high

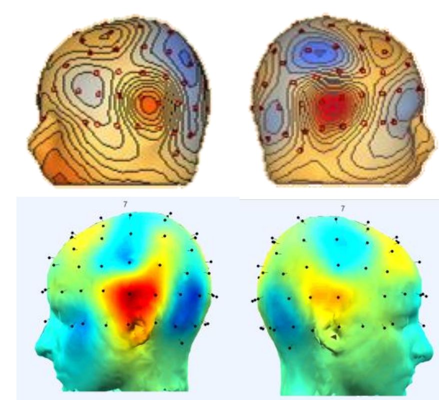
Buzsaki & Wang, 2012, Annu. Rev. Neurosci. 2012. 35:203–25

Brain event-related potentials (ERPs)

- electrical brain responses to events/ stimuli based on time-locked EEG portions
- can measure the time course of processing in tens of ms
- can reveal brain areas related to cortical processing
  - scalp current density and source modeling analyses
  - time-frequency analyses
- allow us to observe how processing changes with development and how it relates to later cognitive outcome

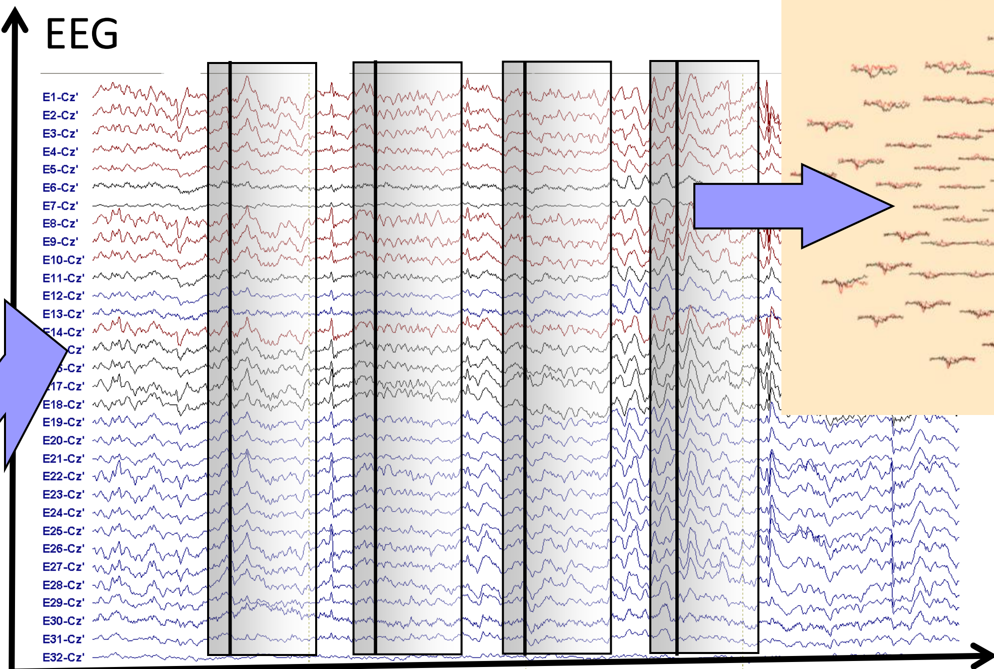


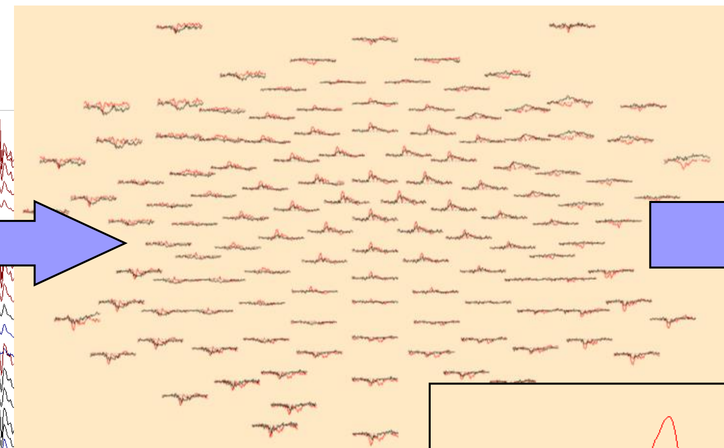


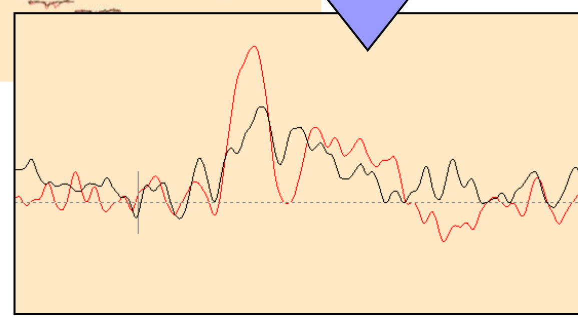


Obtaining averaged ERPs

Averaged across 100 stimulus presentations

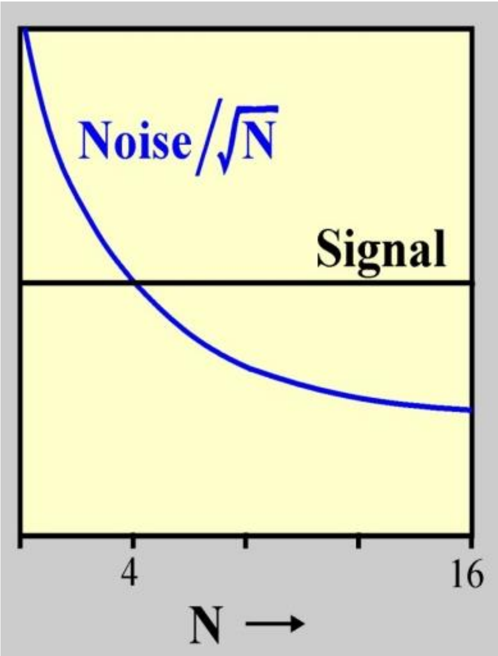


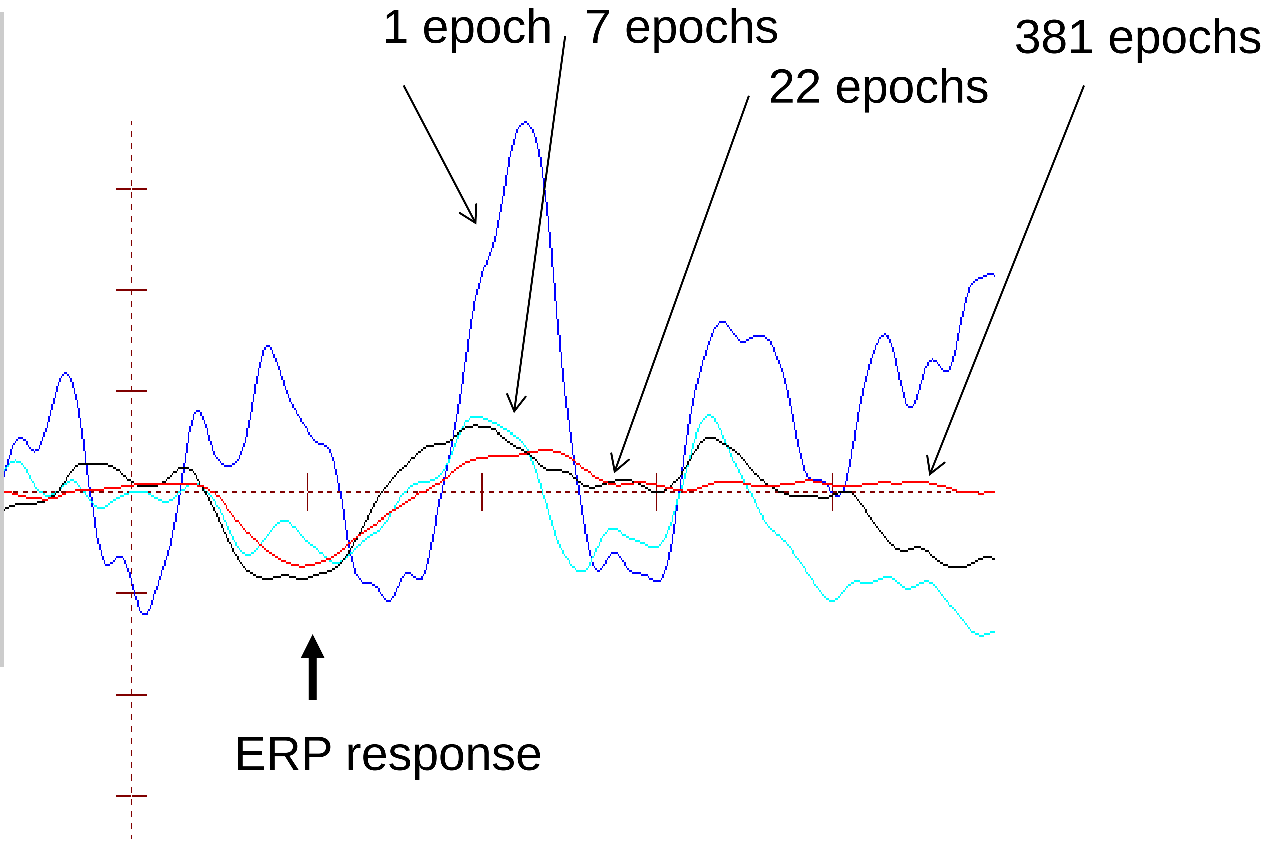




ERP at a single electrode

Effect of nr of stimulus presentations on the signal-to-noise ratio /SN





Ongoing EEG and ERPs obtained by averaging EEG epochs

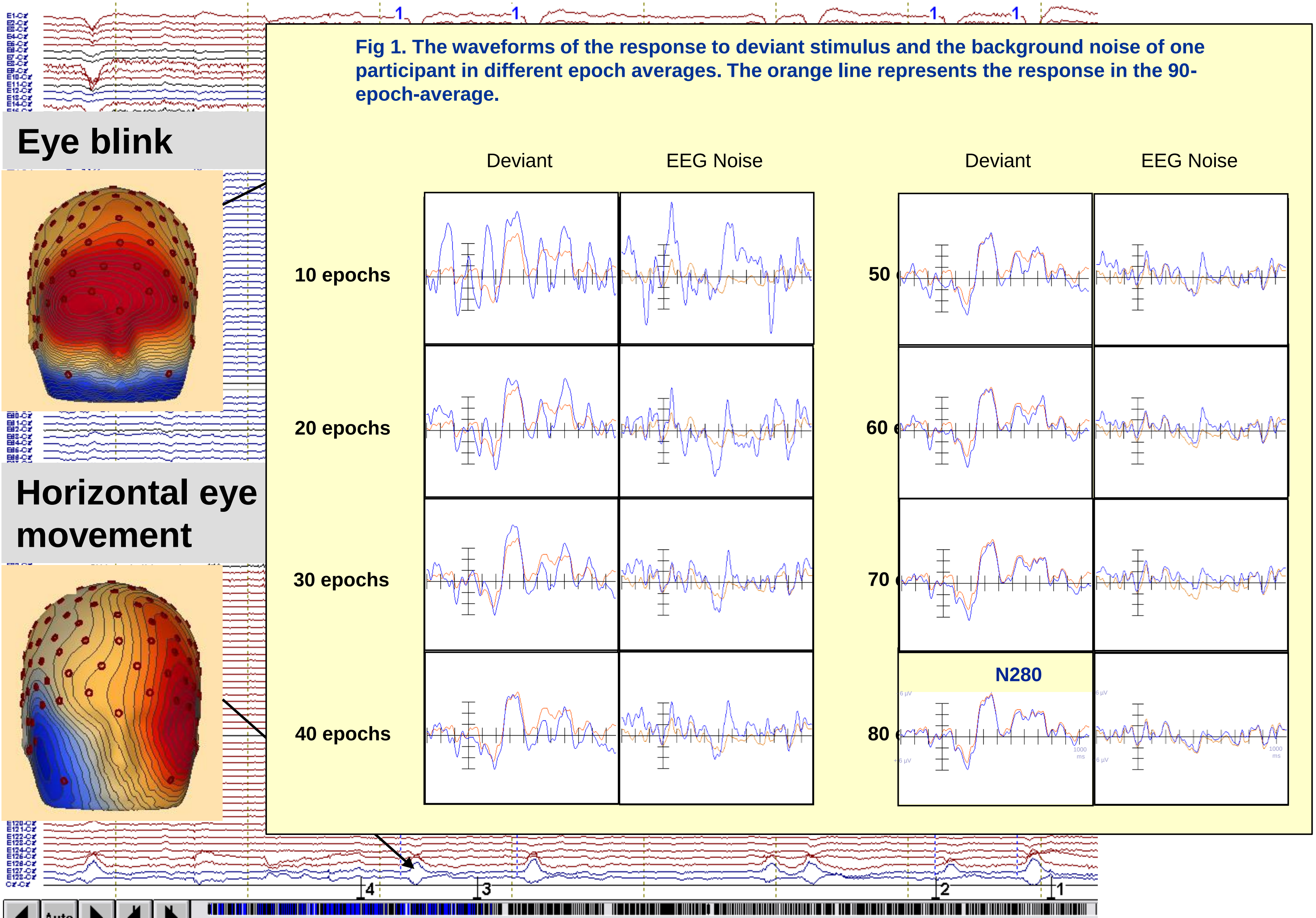


Fig 1. The waveforms of the response to deviant stimulus and the background noise of one participant in different epoch averages. The orange line represents the response in the 90-epoch-average.

ERP – mathematical modeling

ERP-averaging is based on the following assumtions:

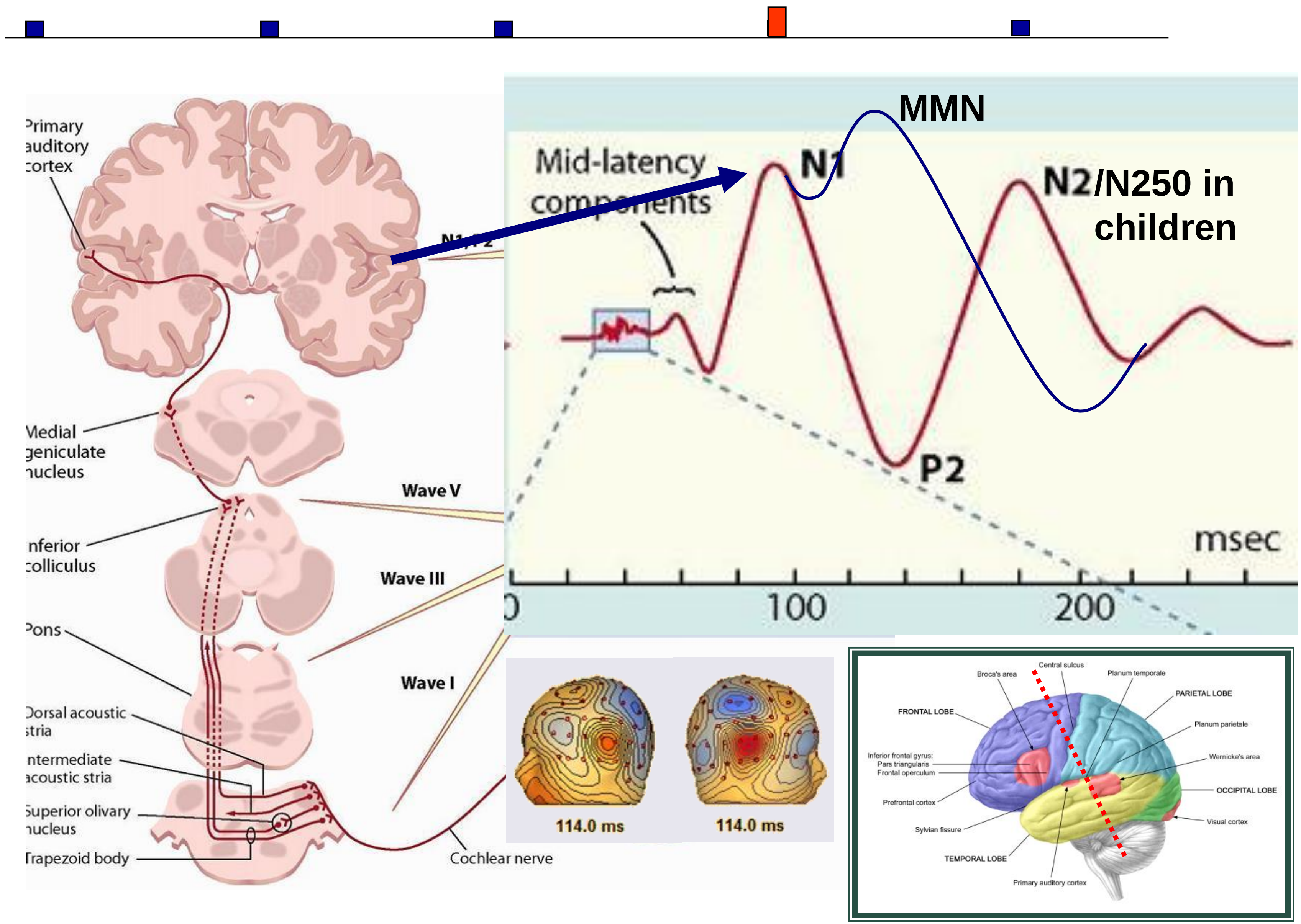
(Regan, 1989)

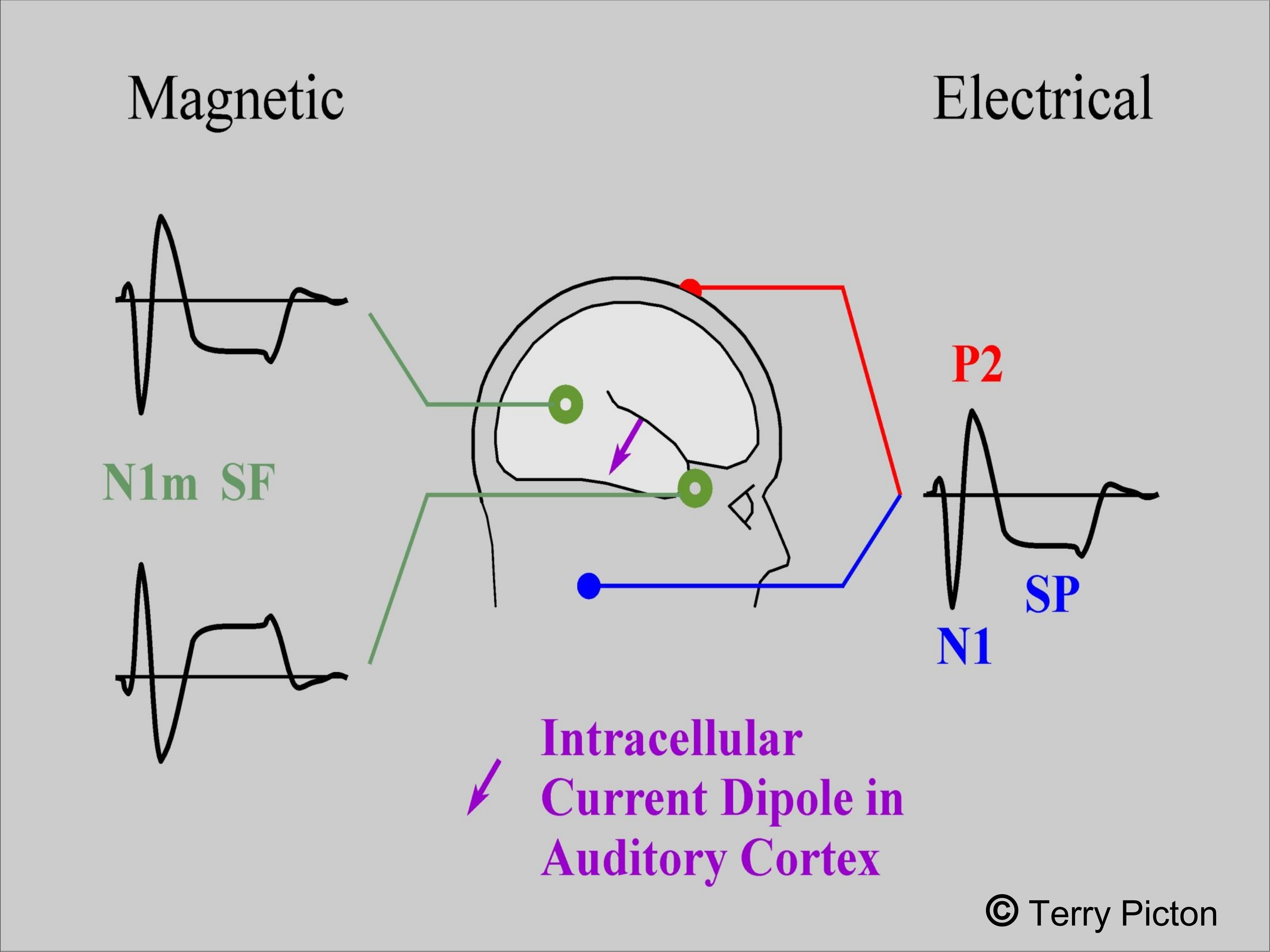
1. The background EEG acts as noise for the ERP-signal
2. The signal waveform is generated by a process that stays stationary from trial to trial
3. The noise, background EEG, is produced by a stationary random process
4. The noise samples are uncorrelated from trial to trial

Possible problems:

- The background EEG is not always random in relation to stimuli.
  - E. g. 50 Hz electric current can create a regular rhythm to the background EEG.
- A psychological process, reflected in ERP-signal, may not remain the same during the entire measurement session, e. g. due to arousal state effects

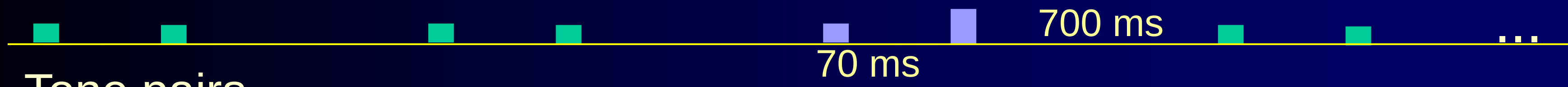
Brain responses to sounds and speech




Magnetic
Electrical
N1m SF
P2
SP
N1
Intracellular
Current Dipole in
Auditory Cortex
© Terry Picton

ERP procedure

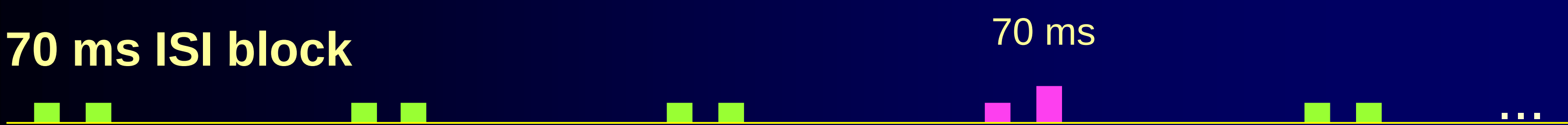
300 ms ISI block



Tone pairs

- standard: 100 Hz - 100 Hz 75 dB 85% (708 trials)
- deviant: 100 Hz - **300 Hz** 15% (125 trials)
- between-pair interval fixed for 700 ms

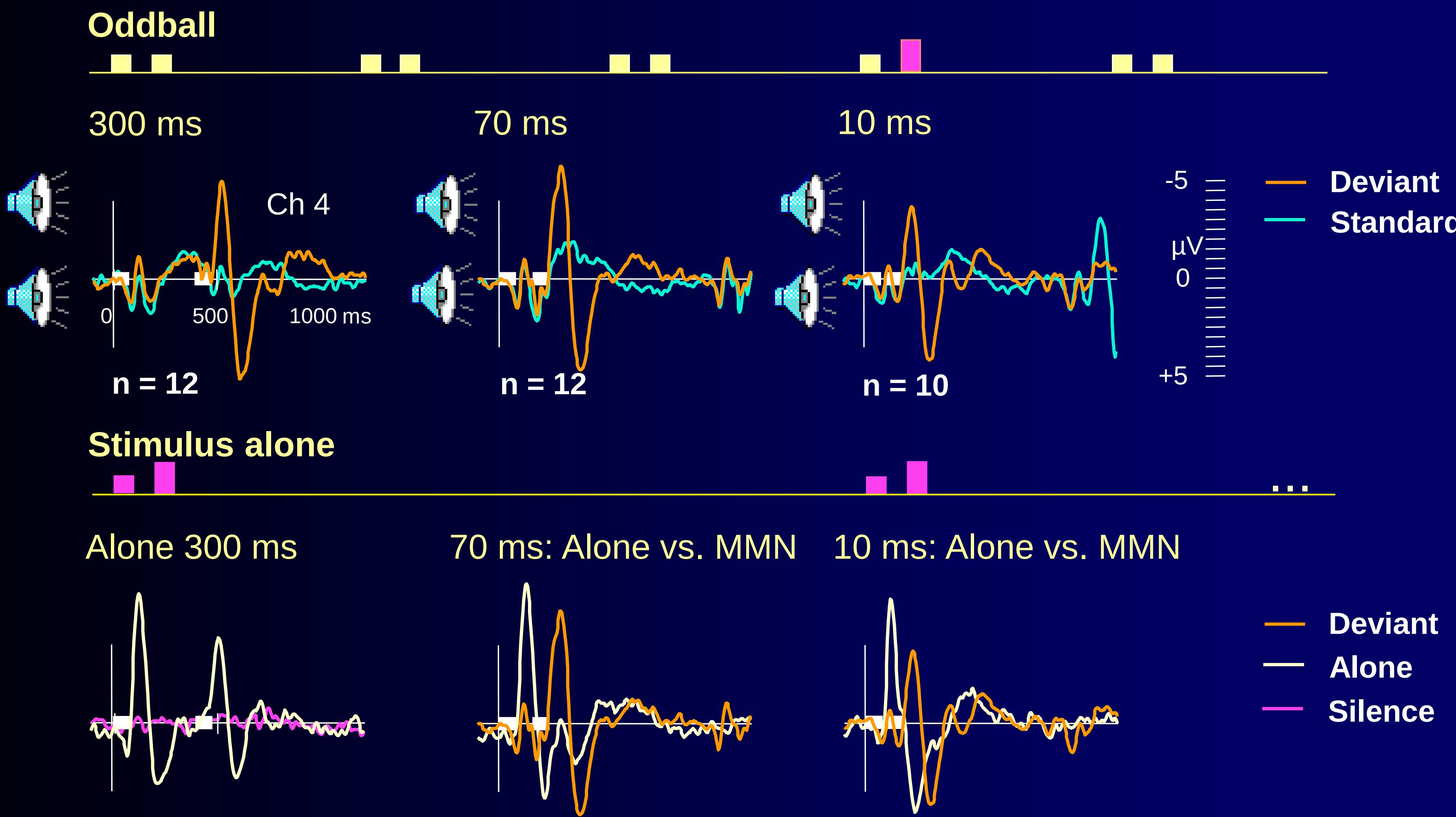
70 ms ISI block



Procedure

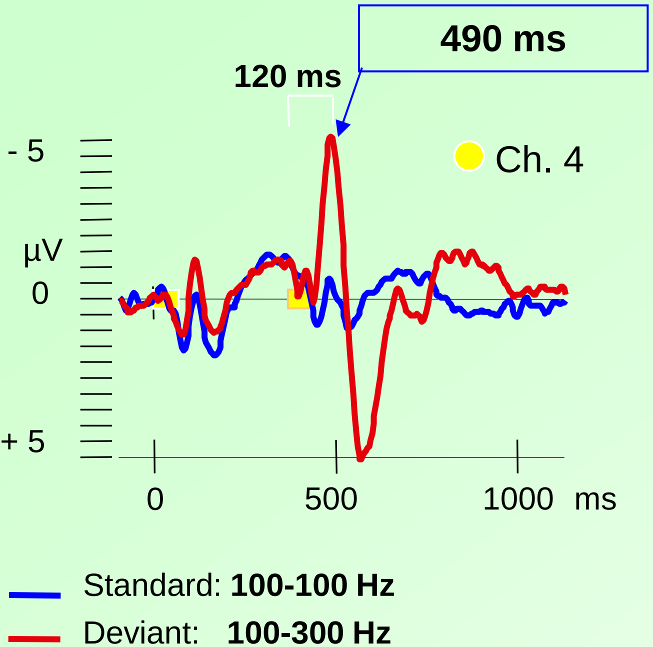
- EEG/ERP were recorded with EGI 62-channel sensor net
- Infants were seated at mother's lap and entertained with toys
- ERPs were re-referenced to the averaged mastoids

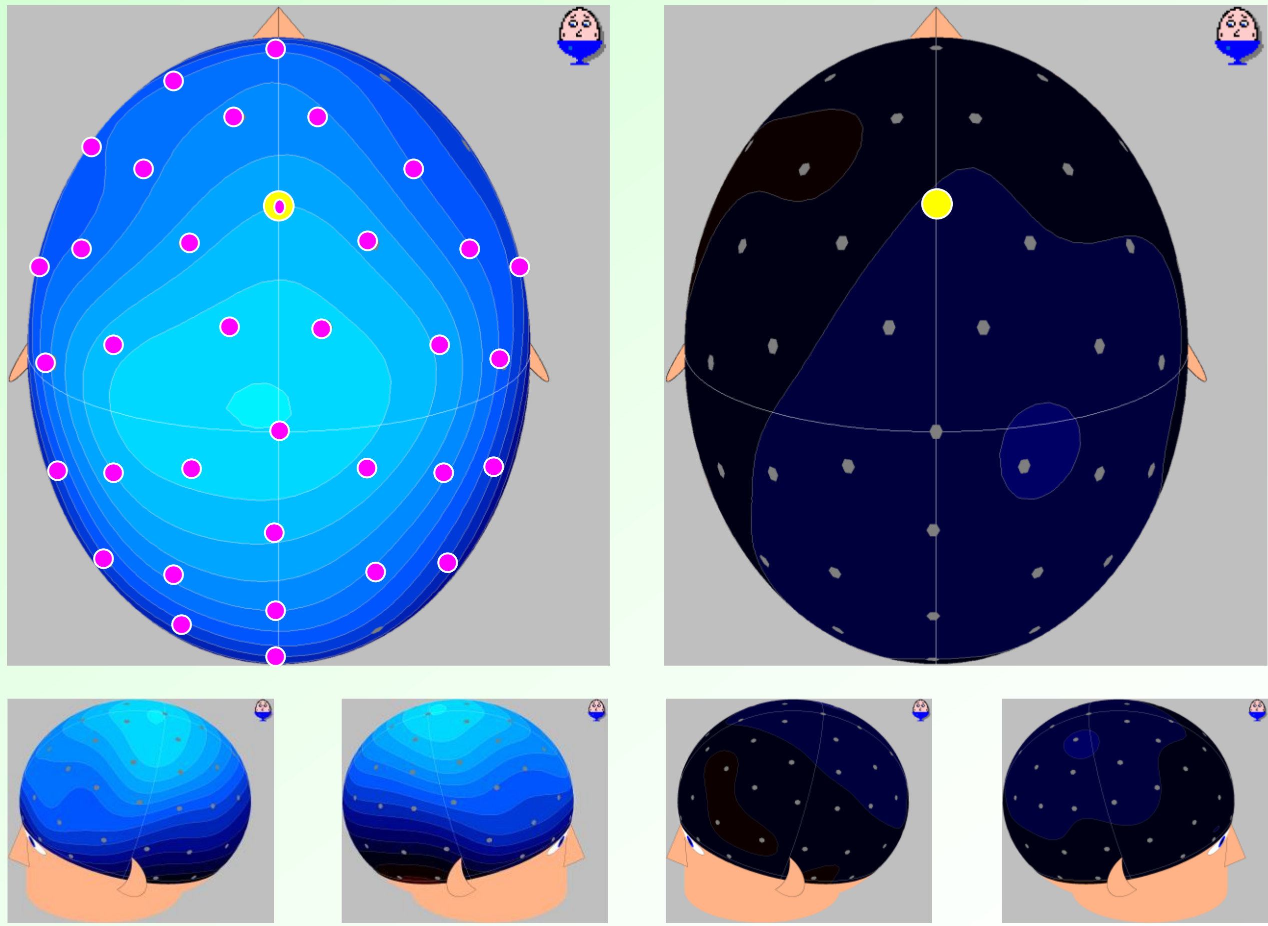
Adult example: ERPs to tone pairs with different ISIs



P.H.T. Leppänen et al., Infancy Studies Lab, CMBN, Rutgers University

Adult ERPs with scalp surface maps in 300 ms ISI condition (N = 12)



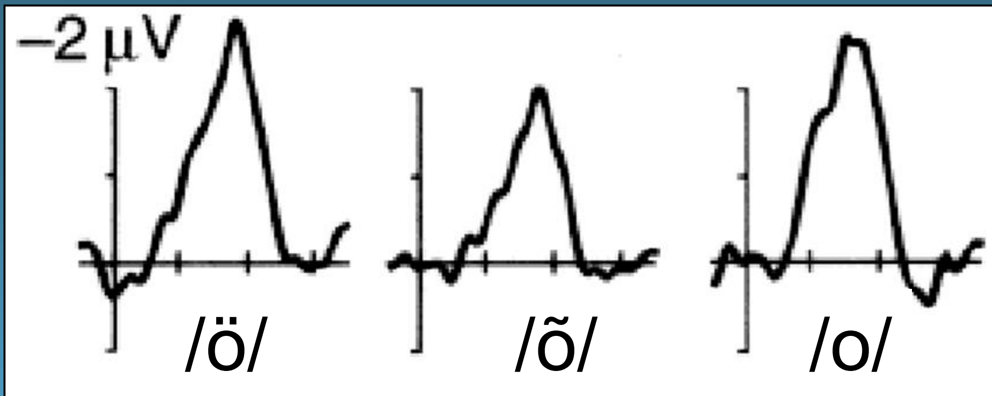


ERPS TO DEVIANT **ERPS TO STANDARD**

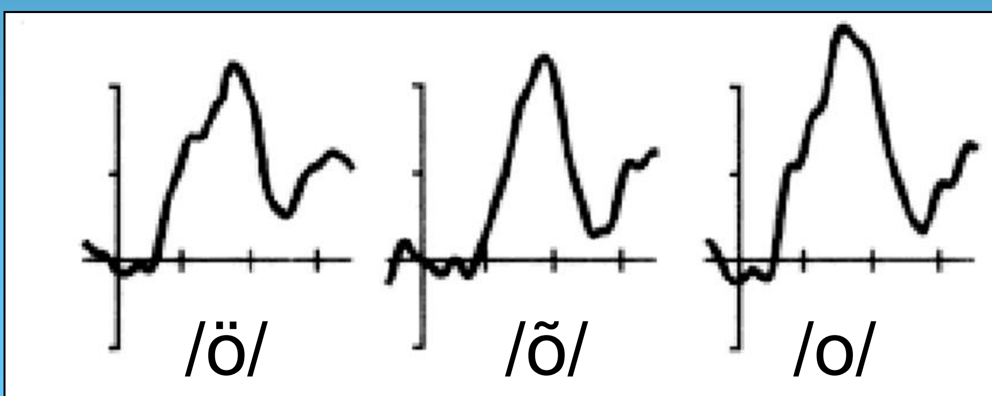
● denote significant difference between deviant and standard responses ($p \leq 0.01$)

- 6.5 µV  **+6.5 µV**

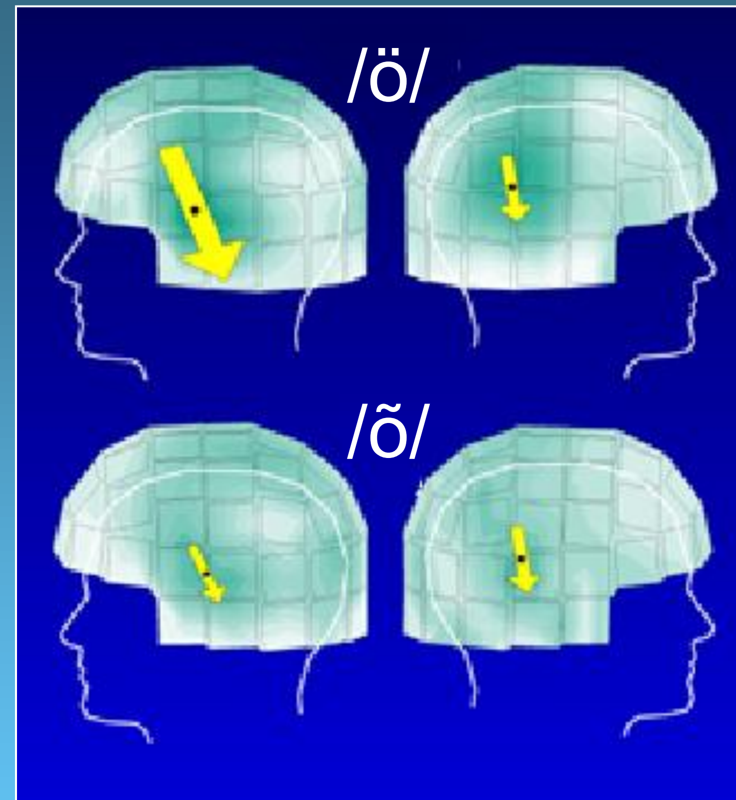
Finns



Estonians



Finn



Näätänen et al., 1997

Mismatch negativity (MMN) – ERP-component for regularity violations

(reviews: Näätänen et al 2012, Paavilainen et al 2013, Sussman et al 2014)

Memory trace explanation (Näätänen et al., 1984, 1992, 1997):

- The generation of MMN to a **change in pitch**:

1. A neuronal population specific and sensitive to a certain frequency is in a homogenous inhibition state upon an arrival of 1st stimulus signal - no MMN is generated
   - unlike afferent neurons (generating N1), which are sensitive to even to 1st stimulus in a sequence

2. By repeating the same stimulus few times, the neurons specific to other than the present stimulus’ frequencies are released from inhibition

3. The neurons specific to the stimulus frequency become refractory

4. Repeating the same stimulus increases stimulus specific refractoriness as well as increases exitability elsewhere in the system.

Mismatch negativity (MMN) ERP-component

Memory trace explanation/ cont. :

- The state of selective inhibition is the basis for neural memory trace for ca. 5-10 secs (Mäntysalo & Näätänen, 1987), after which the system returns to the general homogenous inhibition state

- Interstimulus interval (ISI) by which MMN can be elicited does not reflect the time-span of the memory trace, but
  - it represents the time by which the process, underlying MMN, still considers the preceeding standards as relevant context for the deviant
- Several memory traces can exist at the same time
  - This suggests separate memory traces for a part of sub-standards
  - Suggests also the ecological validity of the MMN as a measure of sensory memory

Mismatch negativity (MMN) ERP-component

Alternative explanation for MMN generation

Cf. Näätänen, 1990, 1992; Jääskeläinen et al 2004; Näätänen et al 2005; Nelken et al 2007; Taaseh et al 2011

- MMN could be explained by sensoric adaptation (or refractoriness)
- MMN to a frequency deviation generated by the neuronal population specific to the frequency of the deviant stimulus
- Neurons specific to the repeated standard stimulus become refractory
- Because deviants occur rarely, the neurons specific to the frequency of these stimuli would remain sensitive
- Thus, N1 and MMN would reflect – functionally – the same process

- More recently the idea of stimulus specific adaptation (Nelken et al)

Mismatch negativity (MMN) ERP-component

Evidence for the memory trace explanation of MMN

(review: Näätänen et al 2005)

- MMN is neither elicited by the first stimulus in a series (Cowan et al., 1993)
- MMN is not obtained with the very long ISIs (Mäntysalo & Näätänen, 1987)
- MMN not generated when the deviant stimuli are presented alone without intervening standard stimuli (Näätänen, 1985; Näätänen et al., 1987; Lounasmaa et al., 1989; Sams et al., 1985)
- MMN can be elicited not only when stimulus intensity, duration, or ISI is increased, but also when they are reduced (Ford & Hillyard, 1981; Näätänen et al., 1989 a,b; 1993)
- MMN can be elicited by the omission of an element of a compound stimulus or of the second of two paired stimuli if the within pair ISI is short (Yabe et al., 1997)
- MMN latency and duration are relatively long for minor stimulus changes, which is atypical to theafferent responses (Näätänen et al., 1989)

Measuring MMN

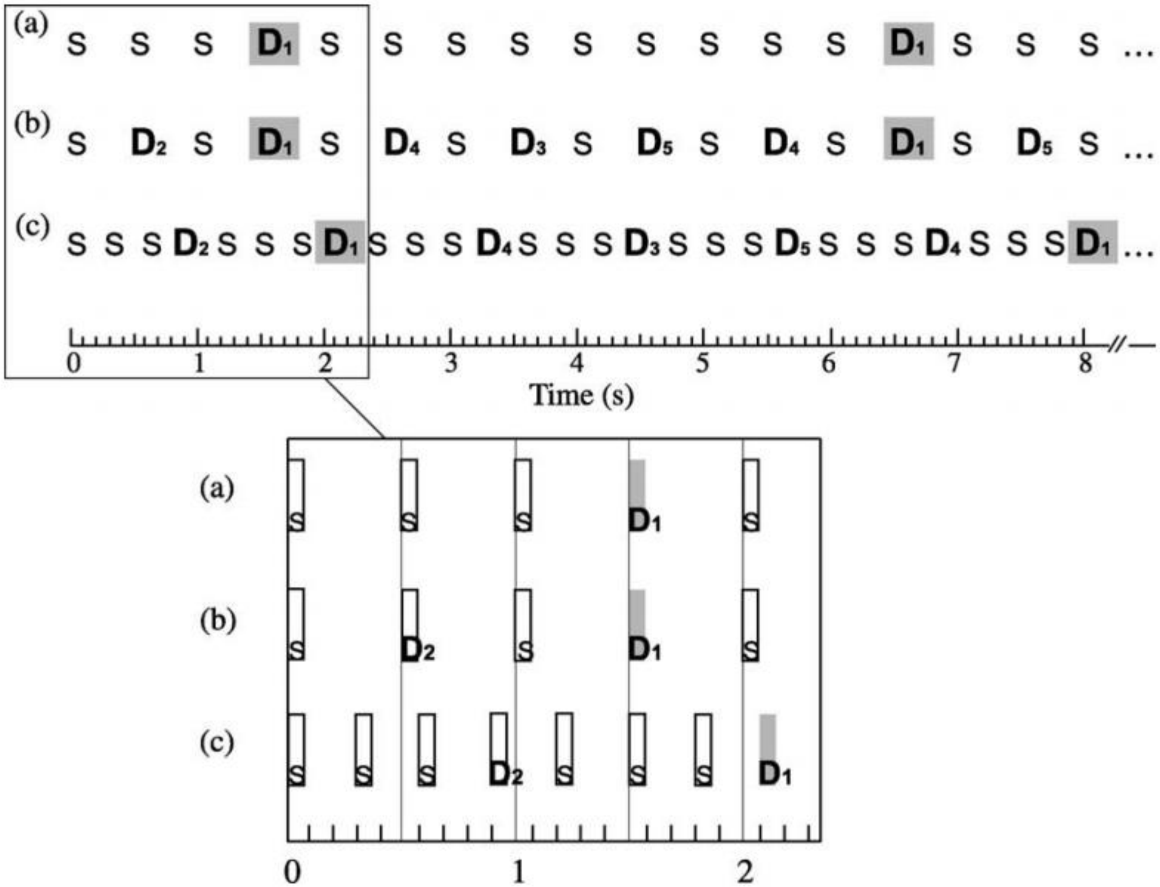


Fig. 1. Schematic illustration of the 3 stimulus conditions used: traditional Oddball (a), Optimum-1 (b), and Optimum-2 conditions (c). S denotes standard tone and Dx tones of different deviant types. Note how D1 (grey area) is positioned in these sequences. Stimulus-onset-asynchrony (SOA) was 500 ms in (a) and (b), and 300 ms in (c).

MMN for auditory features

R. Näätänen et al. / Clinical Neurophysiology 115 (2004) 140–144 143

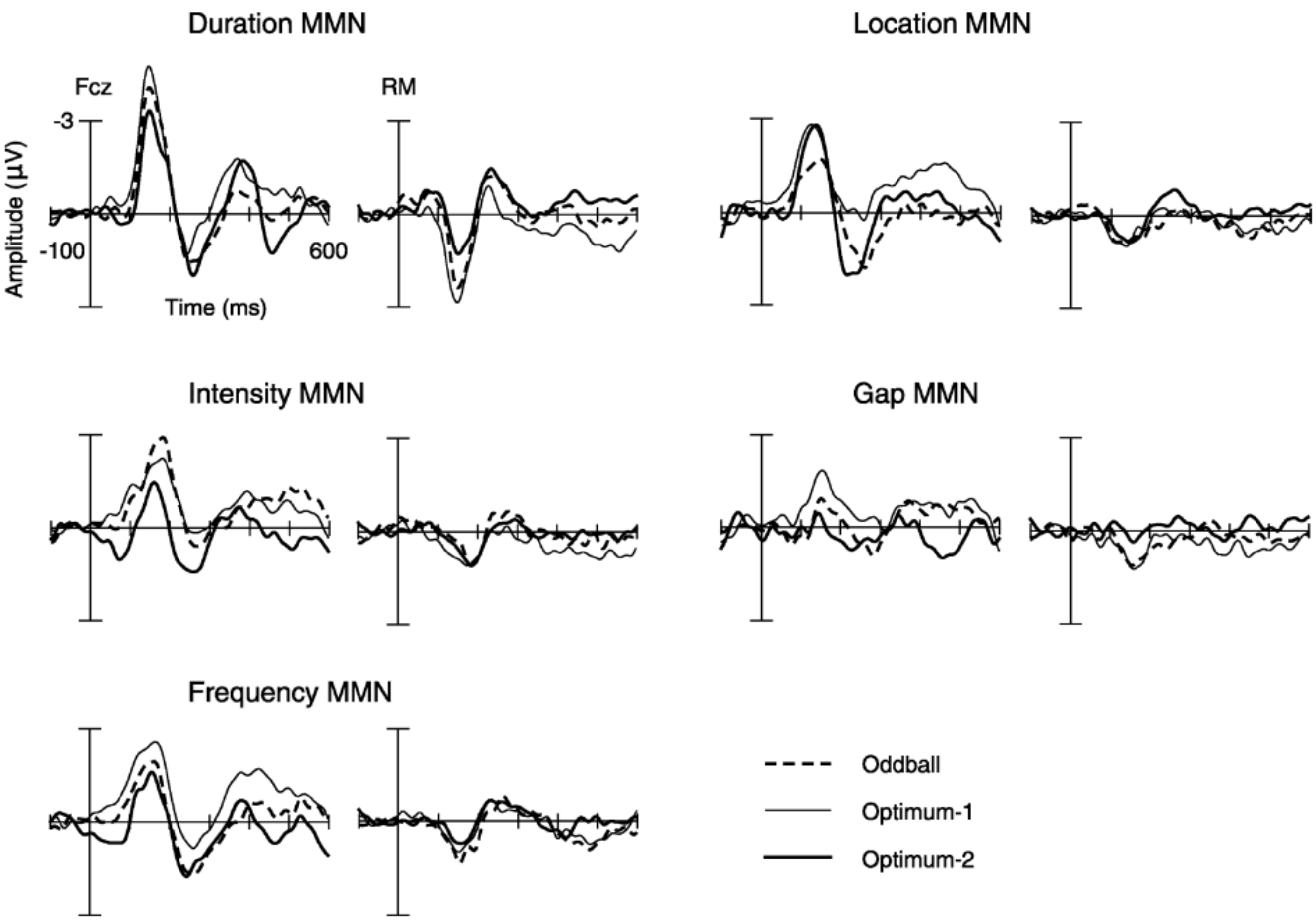


Fig. 2. Grand average difference waves (11 subjects) for 5 types of deviations recorded at a frontocentral (approximately FCz) and a right-mastoid electrode. Overlaid are the MMNs for the same type of deviation in the different conditions. The dotted line indicates the MMN in the traditional Oddball condition, the thin line that in Optimum-1 condition, and the thick line that in Optimum-2 condition. The data were referenced against the nose electrode.

Neurodys WP7 ERP-paradigms

… i i i i i **fh-y** i i i i **fh-y** i i i **fh-y** i i i i **fh-y** i i i…

… i i i i i **ge-y** i i i i **ge-y** i i i **ge-y** i i i i **ge-y** i i i…

… i i i i i **fr-y** i i i i **fr-y** i i i **fr-y** i i i i **fr-y** i i i…

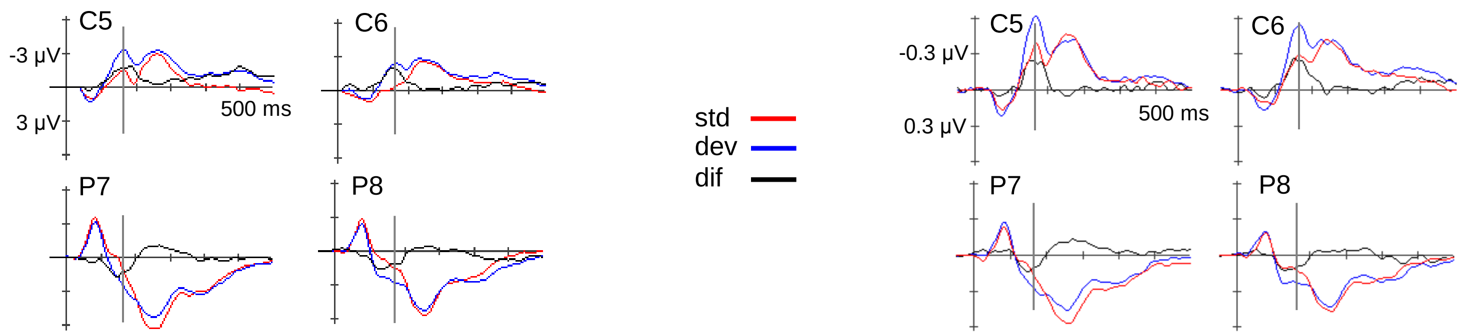
- **ERP studies in different orthographies**
  - Regular: Finland, Hungary
  - More irregular: Germany, France
- **Stimuli:**
  - **Standard (82 %):** euro-/i/
  - **Deviants** (**18 %,** 129 trials each**) in separate blocks**
    - Finnish-Hungarian /y/
    - German /y
    - French /y/
  - **Corresponding complex non-speech tones**
- **Age:** range 8-11 years
- **Grade level:** 2-4th graders

Averaged ERP curves transformed into current source density (CSD) curves

- improves the spatial and temporal resolution

ERPs

CSDs

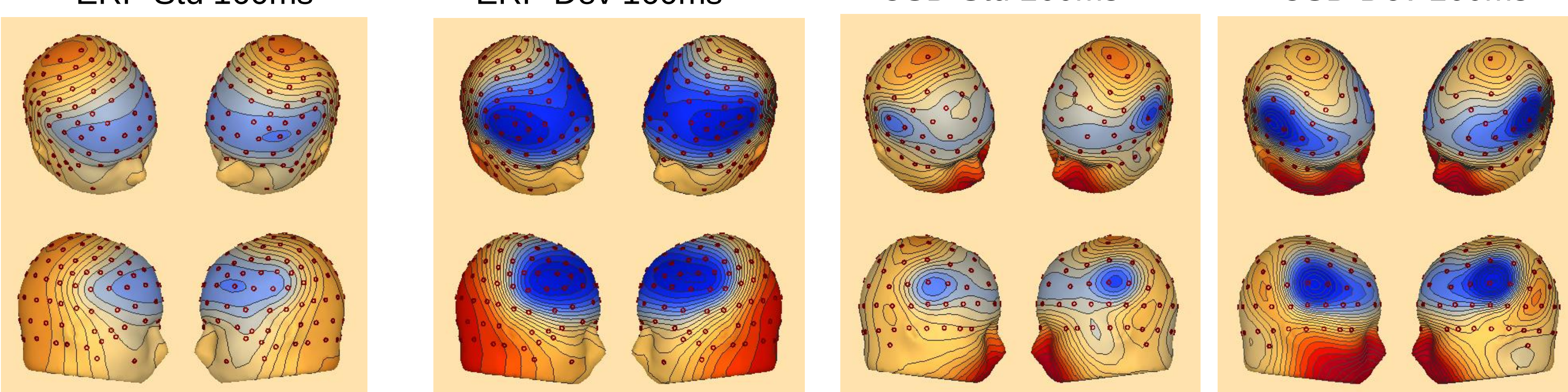


ERP Std 160ms

ERP Dev 160ms

CSD Std 160ms

CSD Dev 160ms



0.25 μV / step

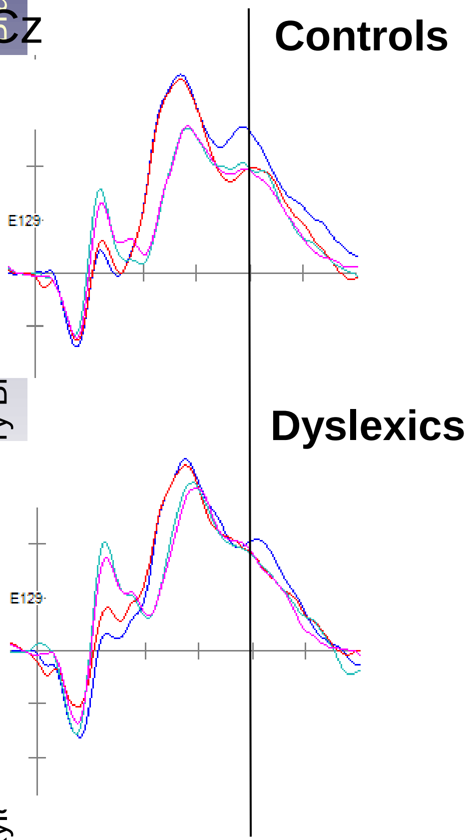
0.02 μV / step

Lohvansuu et al 2013

Children speech vs non-speech – LDN 400 ms

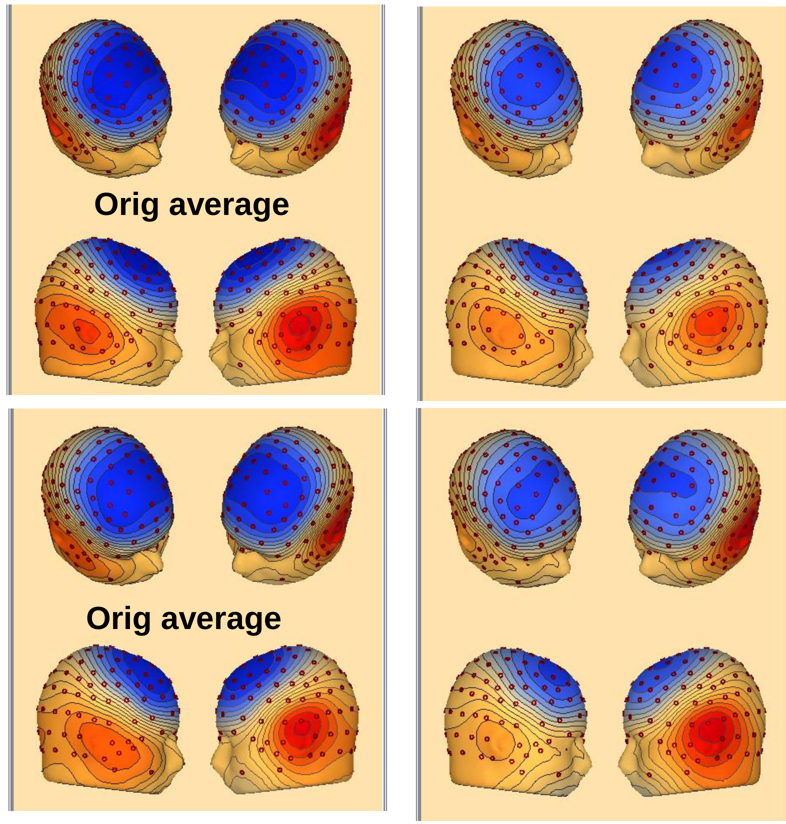
- y-fh-sp
- y-fh-nsp
- y-fr-sp
- y-fr-nsp

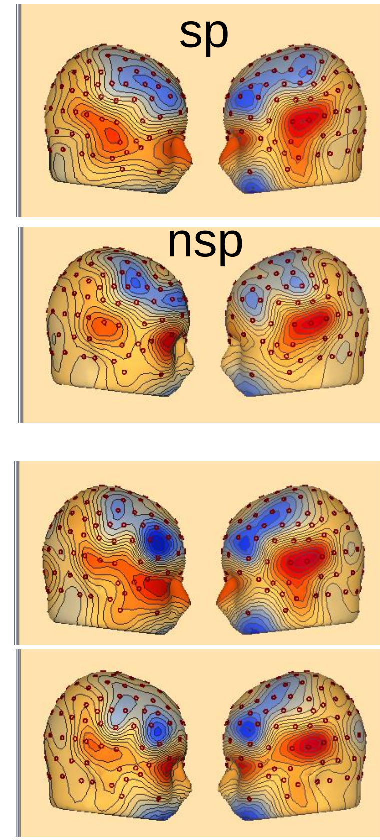
Cz



y-speech 400 ms

y-non-speech 400 ms



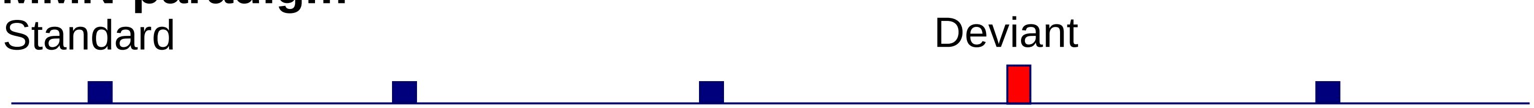


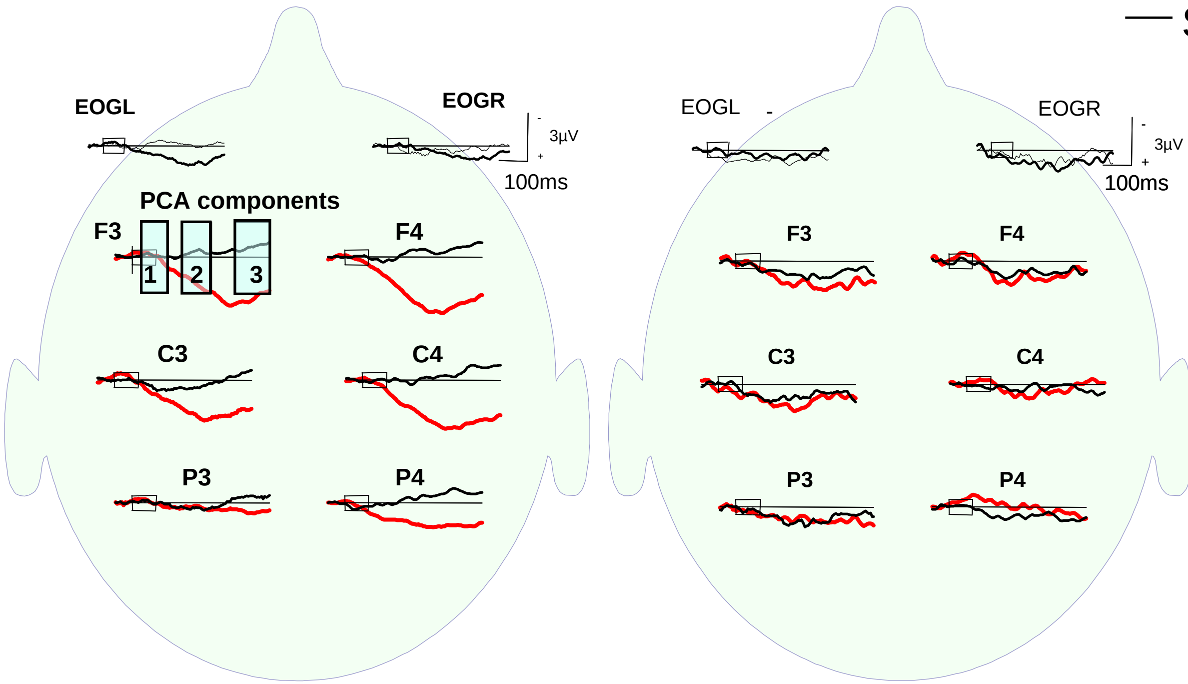
Voltage maps

CSD

Newborn ERPs to tone frequency change differ between 2nd grade typical control and dyslexic at-risk readers

MMN-paradigm

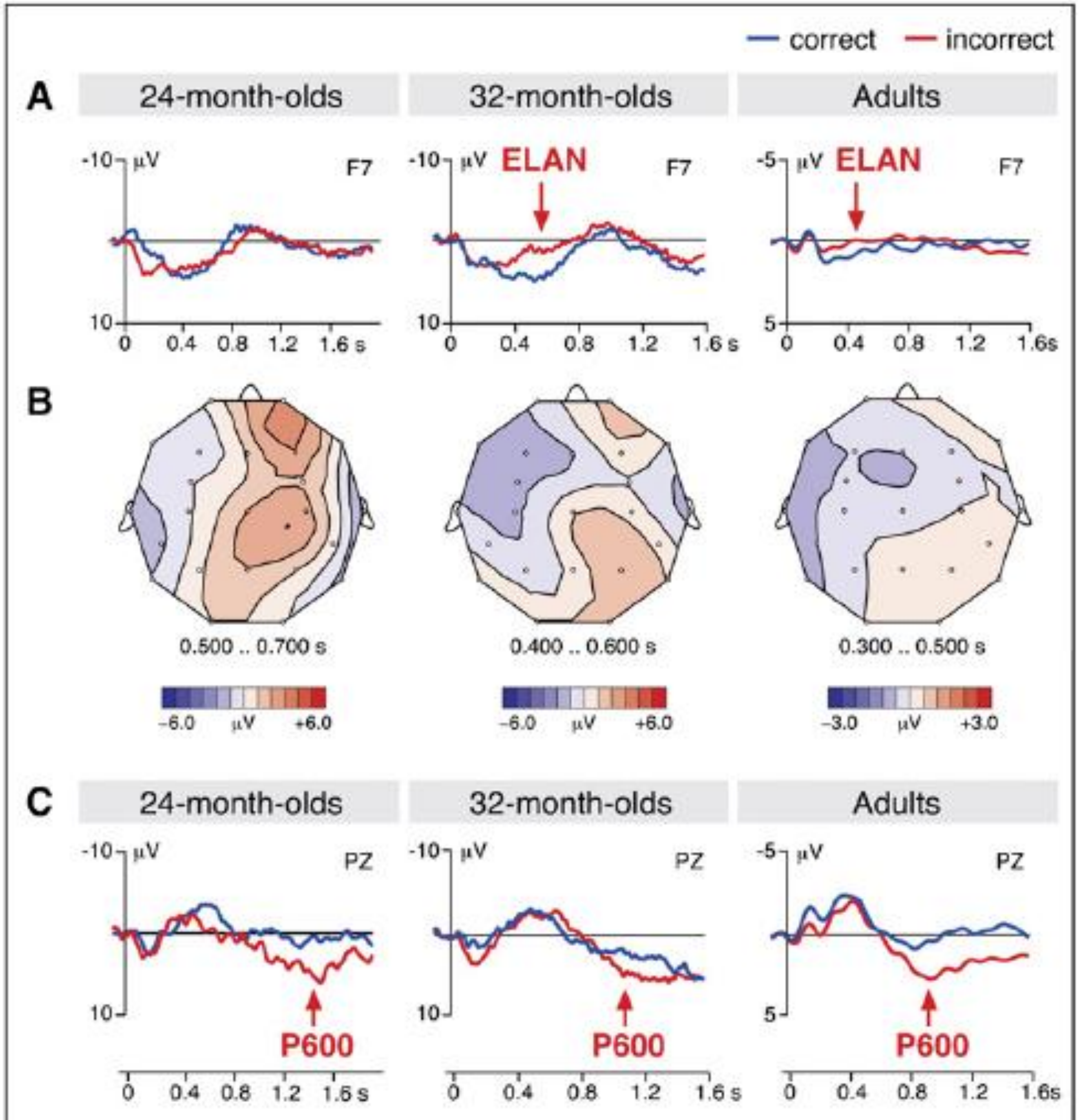




Quiet sleep

Leppänen et al, *2010*, *Cortex*

Higher linguistic processing related ERPs



Adapted from: Oberecker et al., 2005 and Oberecker & Friederici, 2006

Figure 2. Averaged Event-Related Brain Potentials to Auditorily Presented Correct and Syntactically Incorrect Sentences in 24-Month-Olds, 32-Month-Olds, and Adults

Vertical line indicates the onset of the violating word. (A) ERPs at left anterior electrode F_7 for the early syntactic effect (ELAN). (B) Distribution maps for the difference between correct and incorrect sentences in the time windows in which the ELAN effect is expected. Dark blue indicates negativity, which is clearly present at left anterior site for 32-month-olds and for adults. (C) ERPs at centro-parietal electrode PZ for the late syntactic effect (P600).

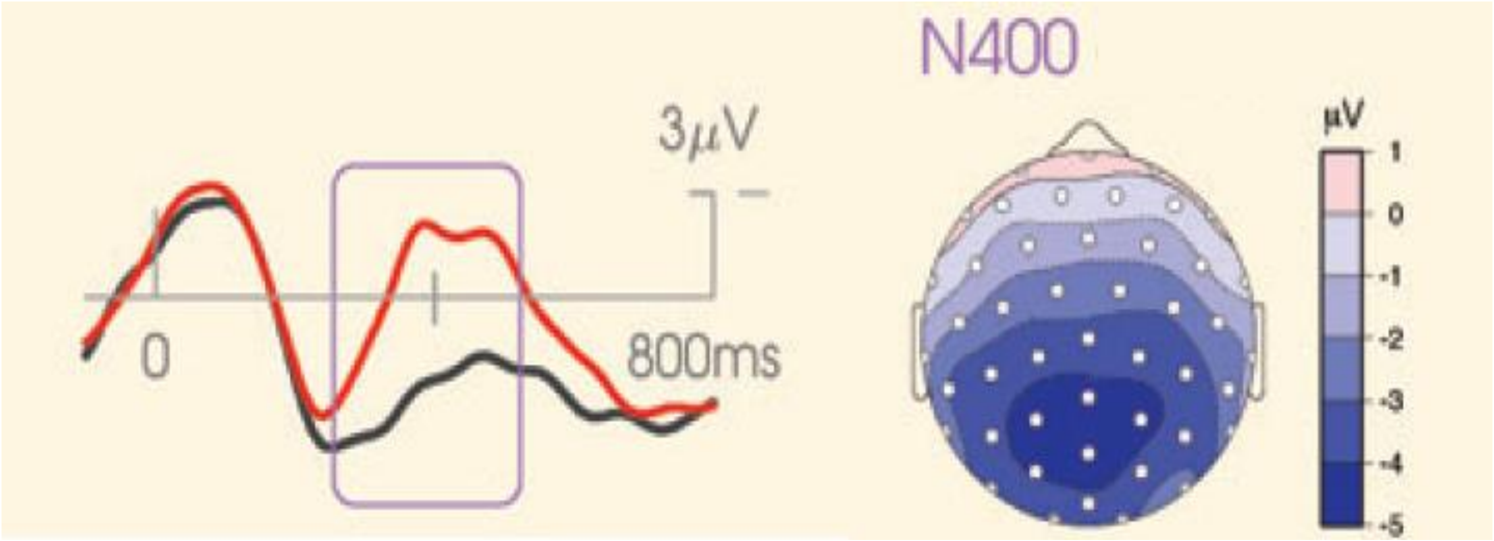
ELAN = Early left anterior negativity

P600 = Syntactic positivity

Semantic processing and reading comprehension at the brain level

3 sentences, the last word is

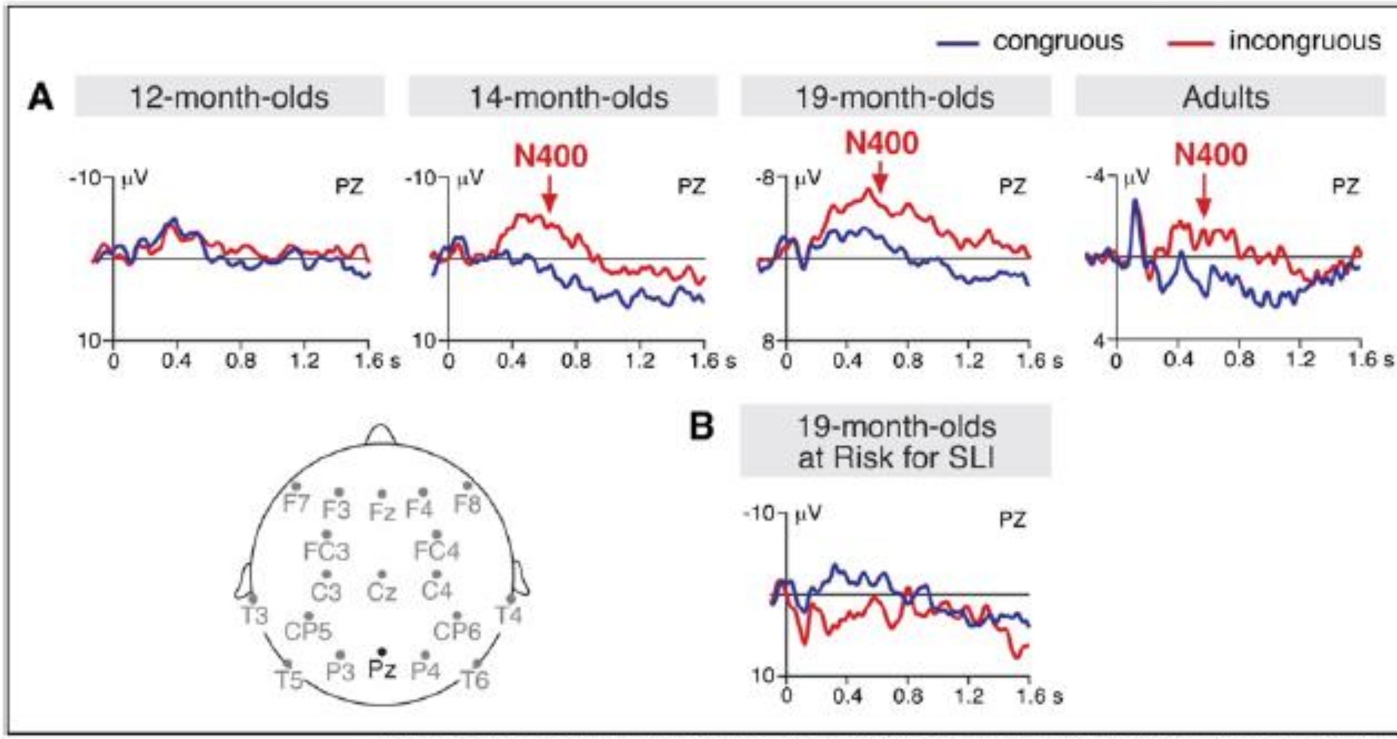
- congruent with the context: *By the blue lake you'll find a red* ***sauna***
- Incongruent: *The car has four round* ***legs***
- lähellä oikeaa ääntöasultaan: *The bright flash was caused by* ***fighting***



Otto Loberg, picture adapted from Kutas & Federmeier 2011

Semantic processing related ERPs – N400

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



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

Figure 3. Averaged ERP for Spoken Words Congruous and Incongruous with a Picture Presented

Vertical line indicates the word onset. (A) ERPs of typically developing children and adults showing a semantic N400 effect except for the youngest group. (B) ERPs of 19-month-old infants who were diagnosed with risk for SLI at the age of 2.5 years.

Processing stages of number comparison in developmental dyscalculia

Soltész et al 2009 Cognitive Development 24 (2009) 473–485

2.2. Experimental setup

The DE was investigated by an experimental paradigm requiring subjects to decide whether the presented number is smaller or larger than 5. The distance of the target number from 5 was manipulated. Stimuli were the Arabic digits 1–4 and 6–9. Black stimuli on light yellow background appeared for 800 ms at the centre of a 17 inch computer monitor (800 × 600 pixels) positioned at about 1 m from the subjects' eyes. 480 stimuli were presented in two blocks, preceded by 72–72 practice stimuli. Responses, counterbalanced across blocks, were given by either the left or right index finger. Reaction times and accuracy were also recorded.

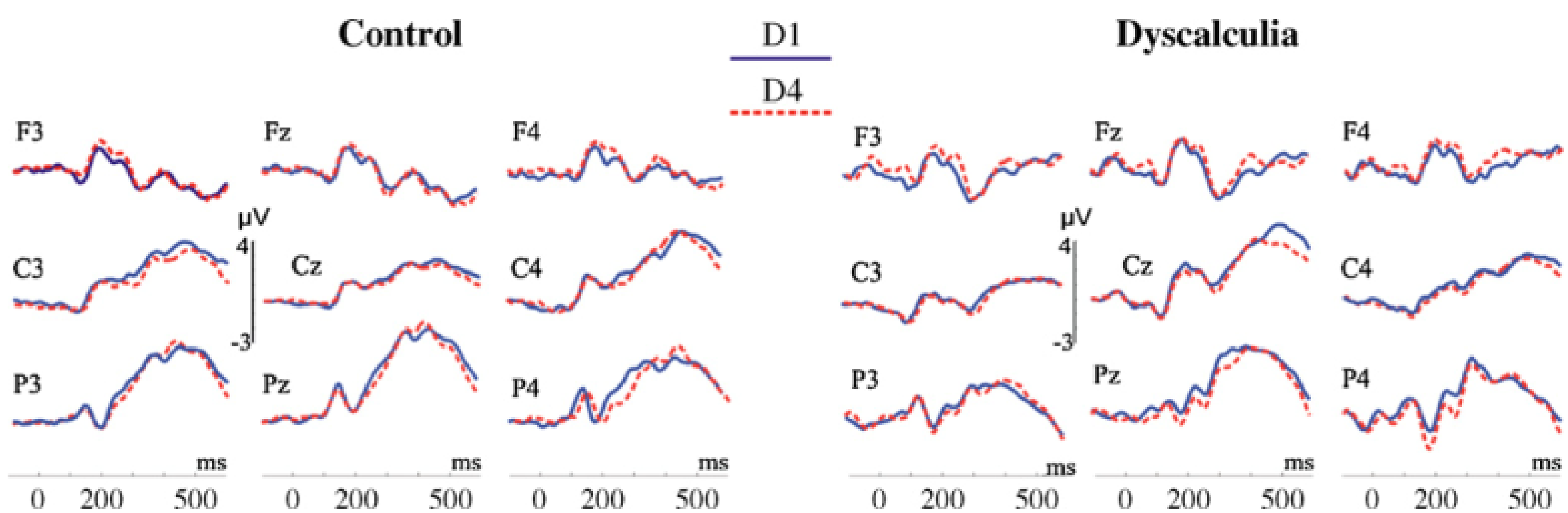
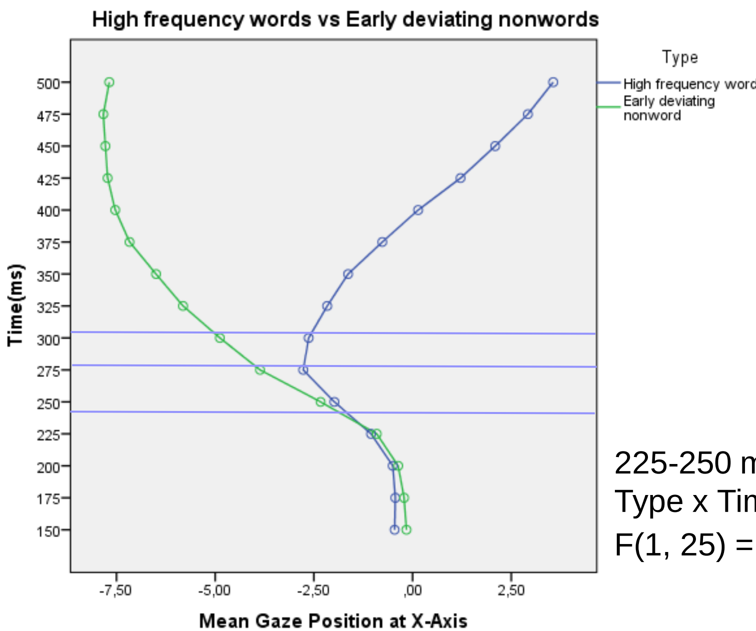


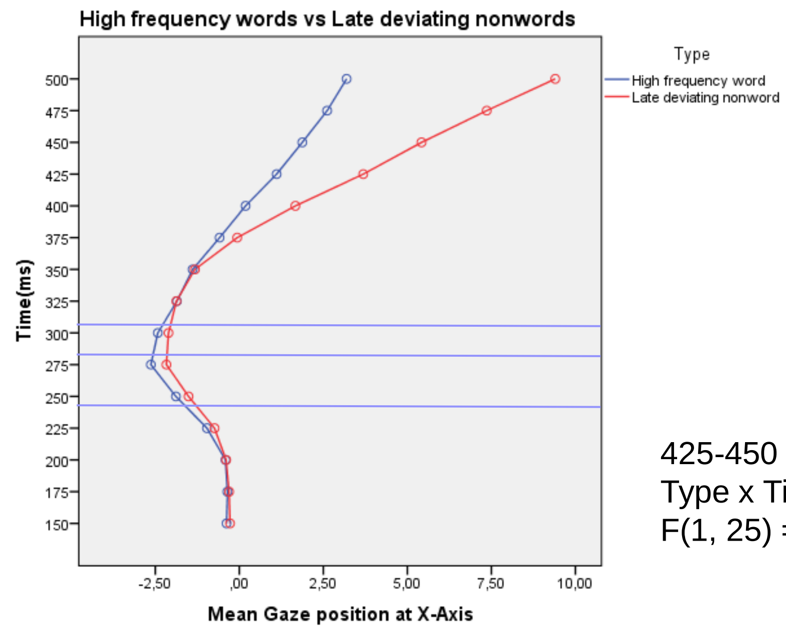
Fig. 1. ERPs for CG and DG in the two experimental conditions at frontal, central and parietal electrodes.

EEG and eye-tracking combined

Comparison of gaze trajectories between high frequency words and nonwords



225-250 ms:
Type x Time,
F(1, 25) = 7.7*



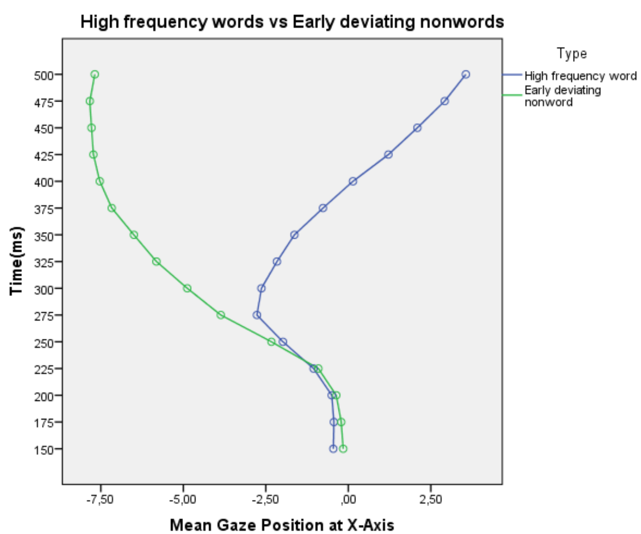
425-450 ms:
Type x Time,
F(1, 25) = 5.9*

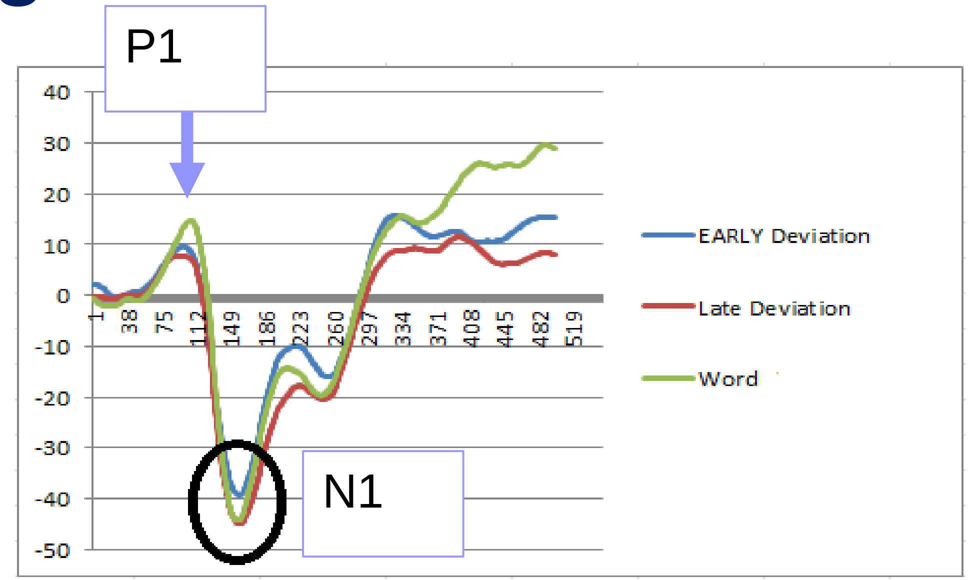
* p <.05, ** p < .001

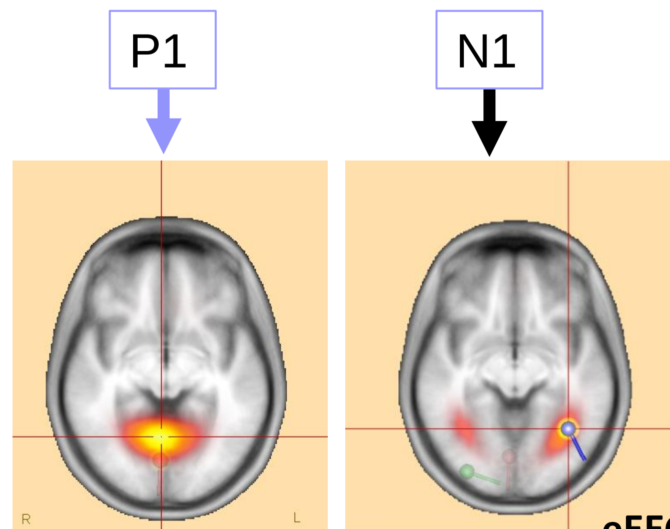
- Response to early deviating nonwords begins at the same time point as in exp 1
- Response to late deviating nonwords is heavily delayed relative to exp 1 – result from placing the anomaly to second last letter instead of last one?

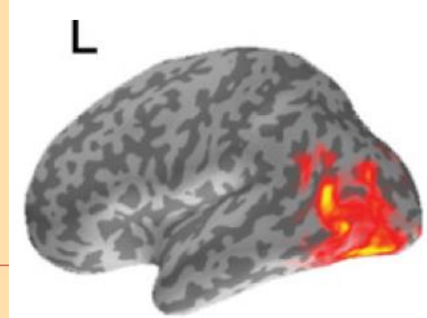
Thanks Otto Loberg

Brain responses to written text – visual word recognition





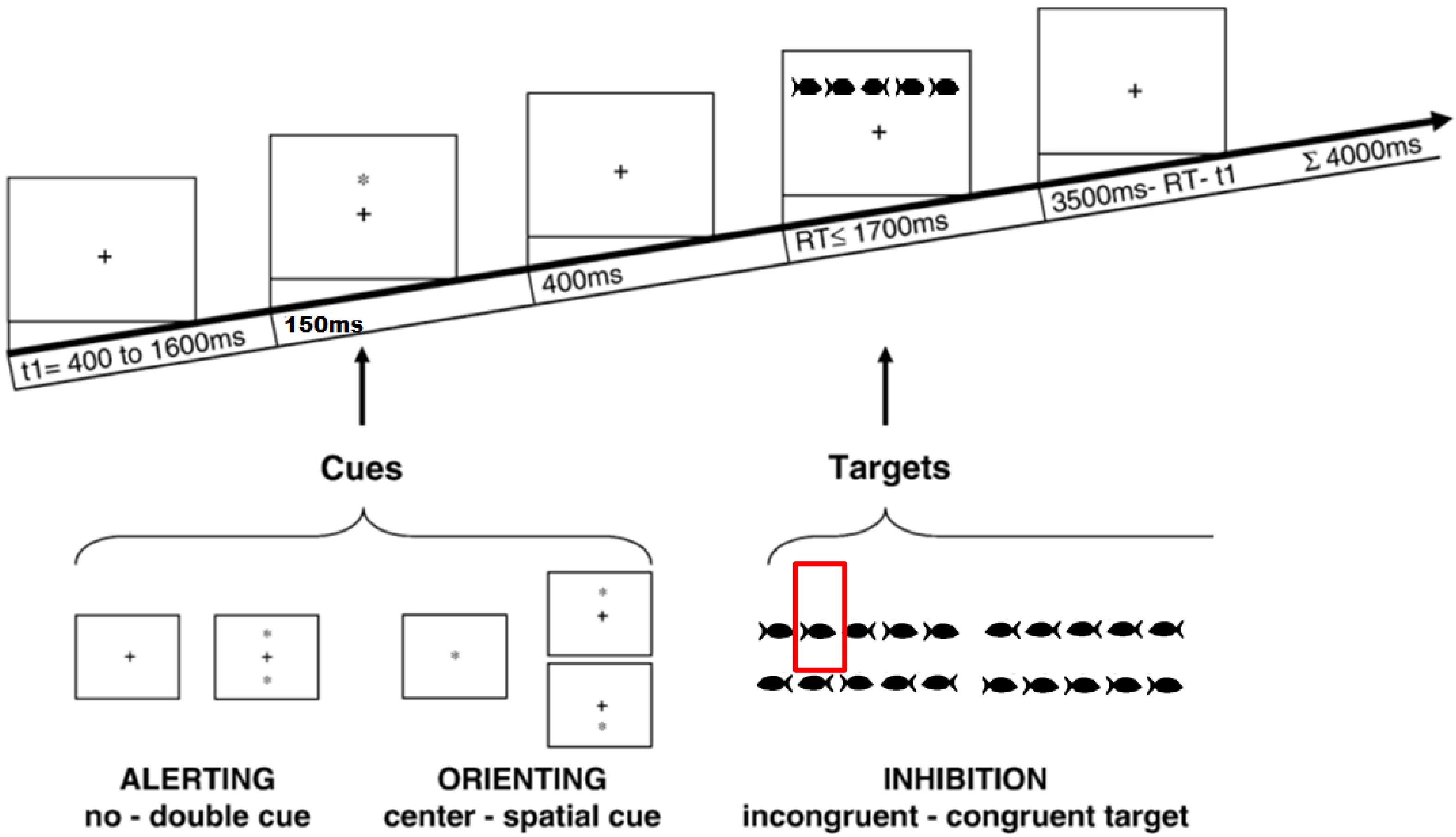




eEEG-ET project, eSeek team

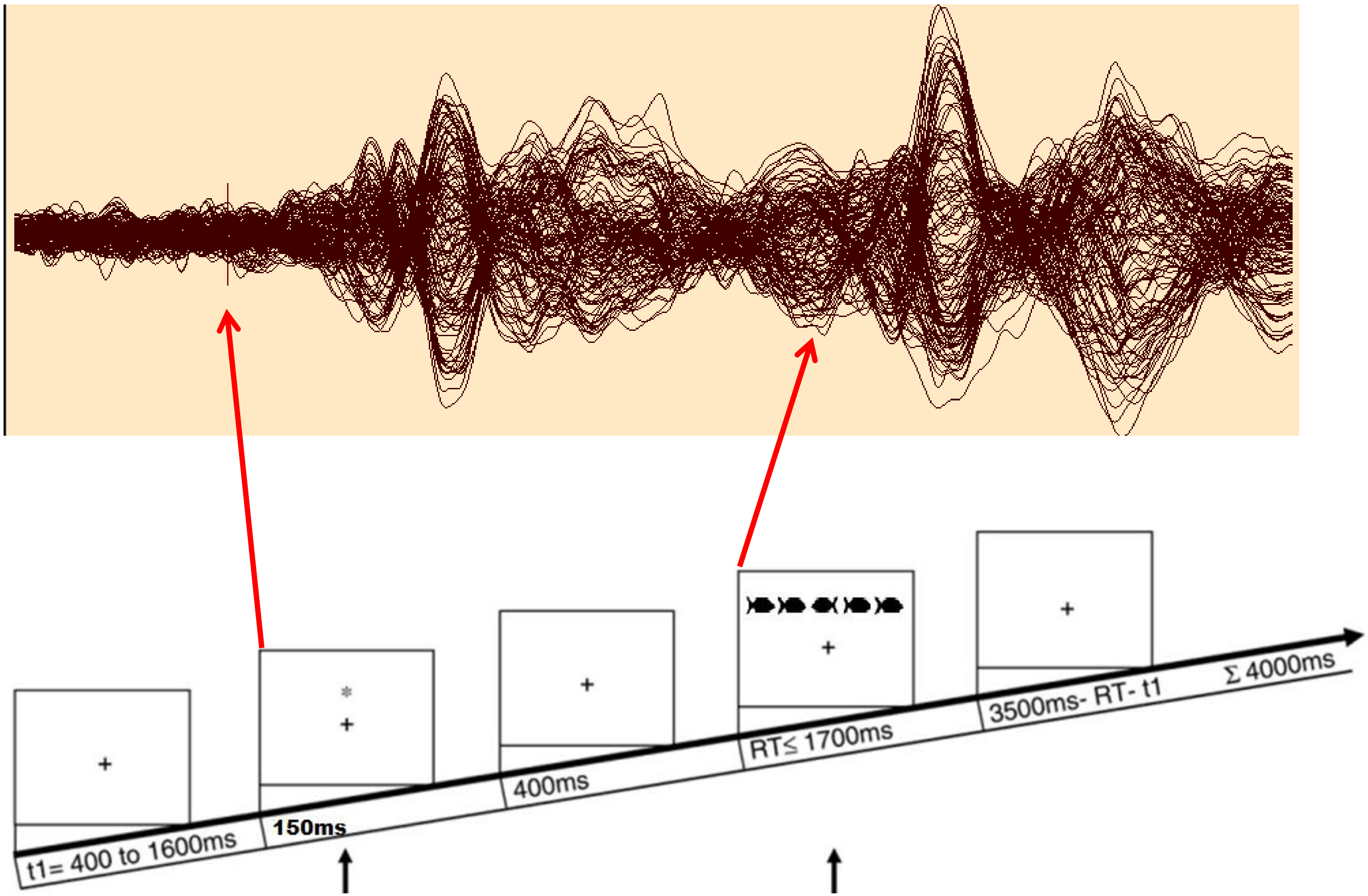
Jyväskylä Centre for Interdisciplinary Brain Research (CIBR) – BrainRead group

ANT - attention network test



Modified from Neuhaus 2010

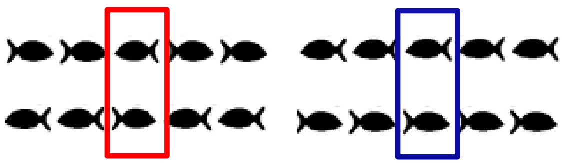
Thanks Otto Loberg



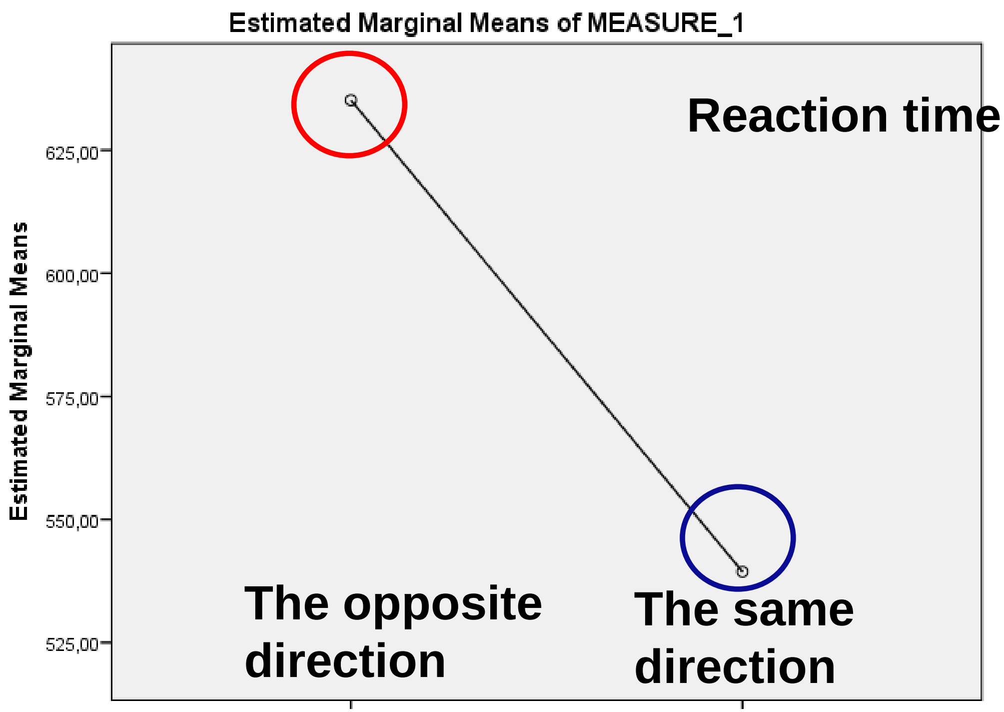
Thanks Otto Loberg

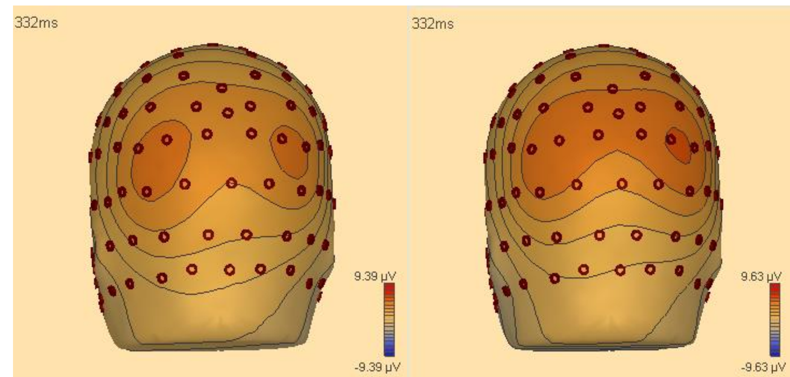
Preliminary results:

- Reaction times shorter
- Brain response larger for the congruent fish



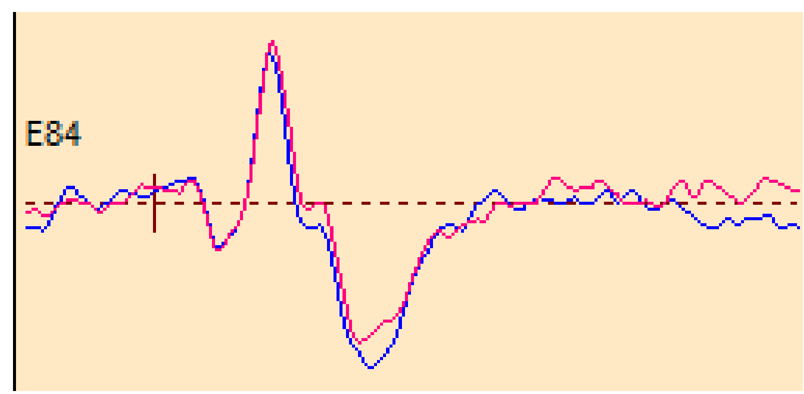
INHIBITION
incongruent - congruent target





The opposite direction

The same direction



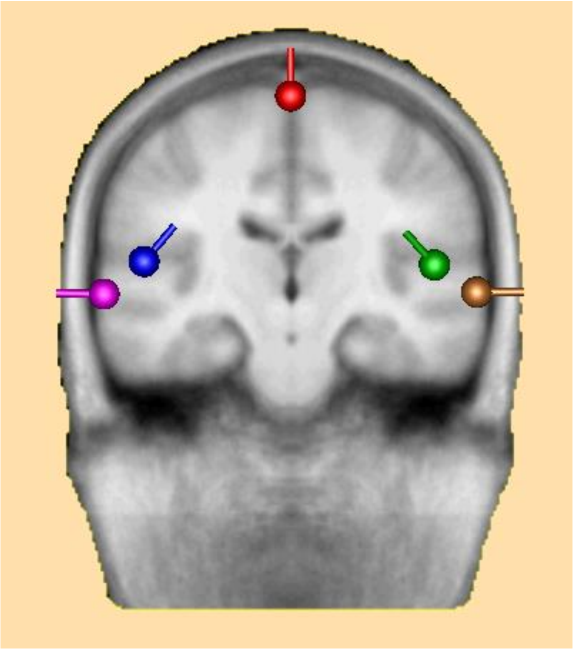
Red: Incongruent
Blue: Congruent

Thanks Otto Loberg

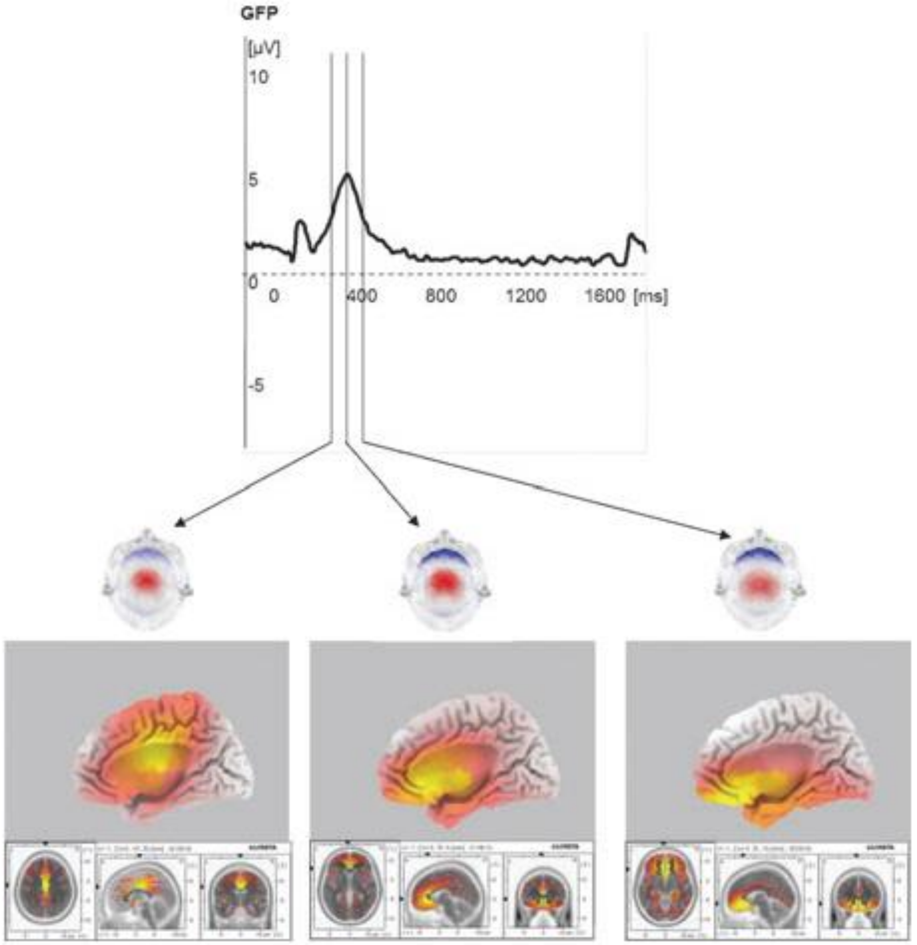
Sources of the brain signal

- **Forward vs. inverse problem**
- **Channel space vs. source space**
- **Source analysis as a spatial filter**
- **Example**
  - Jyväskylä Longitudinal Study of Dyslexia, ERPs of 9-year-olds

ERP source localization

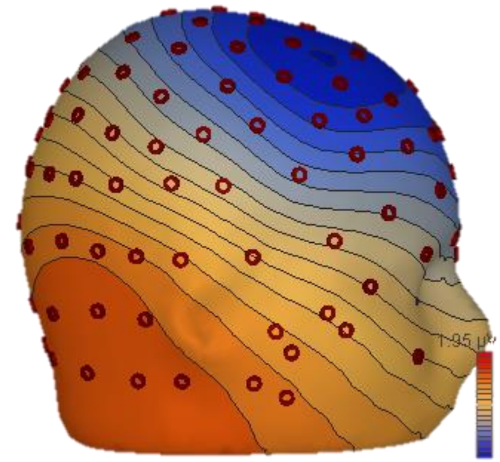


- **Eg. N1 has several sub-components:**
  - supratemporal N1b
  - T-complex (radial lateral sources)
  - vertex potential (motor cortex)



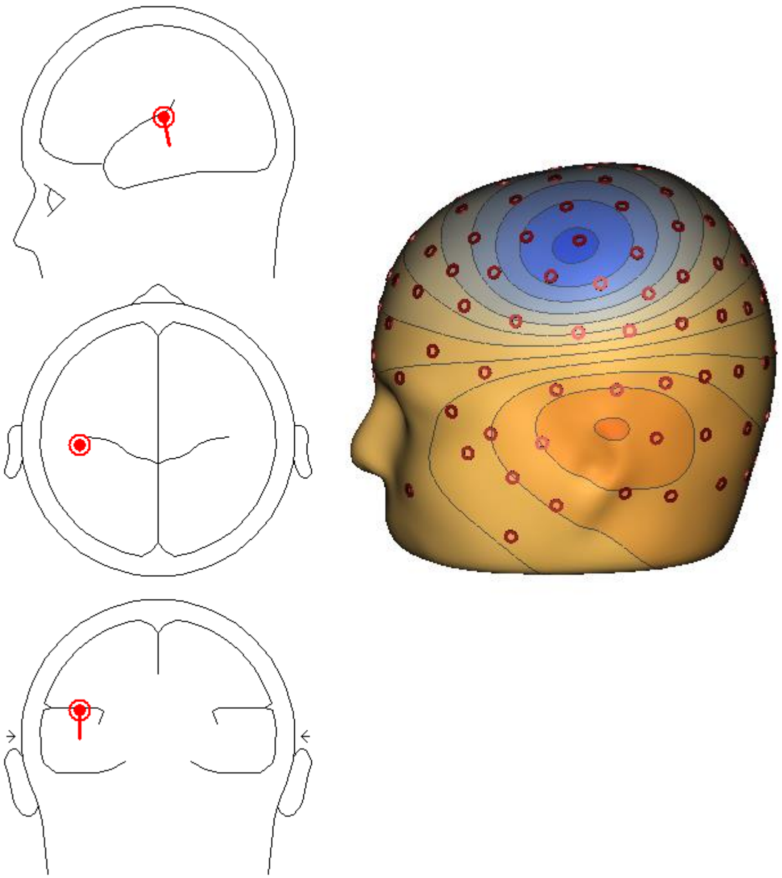
Banaschewski & Brandeis, 2007, Journal of Child Psychology and Psychiatry, 48

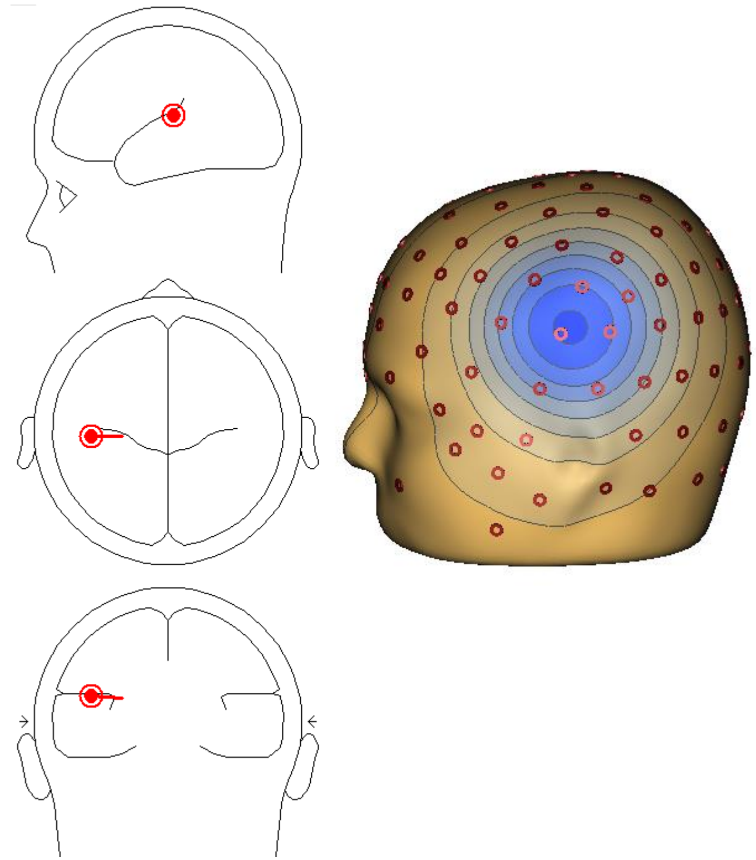
Forward and inverse problem in EEG



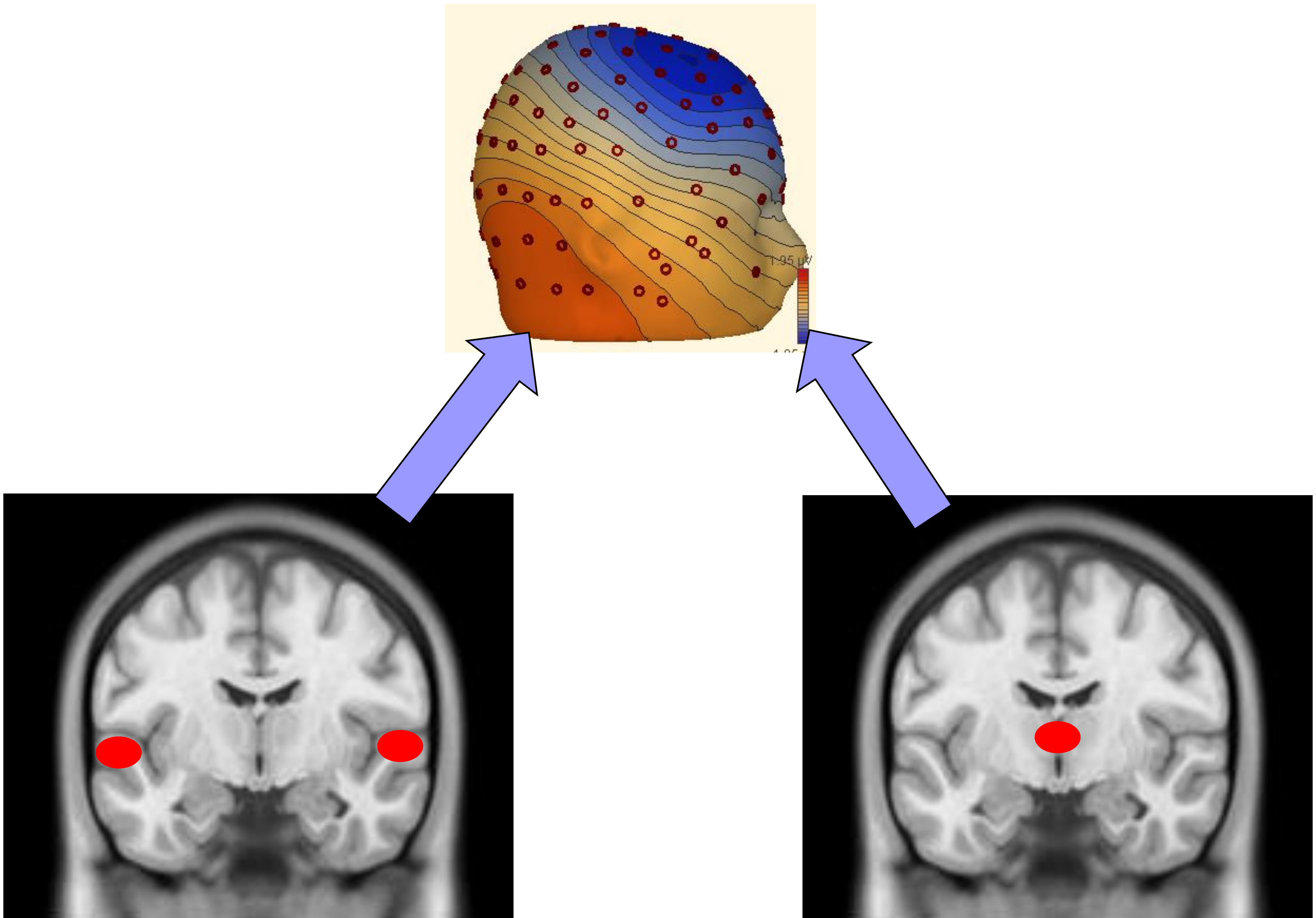
- **Forward problem/solution**
  - Based on the active cortical areas, what is the generated voltage topography?
  - Always has a unique solution
- **Inverse problem/solution**
  - Based on the voltage topography, what are the underlying active cortical areas?
  - Mathematically ill-posed question: no unique solution
  - In practice there are several ways to limit the number of solutions

Forward solution

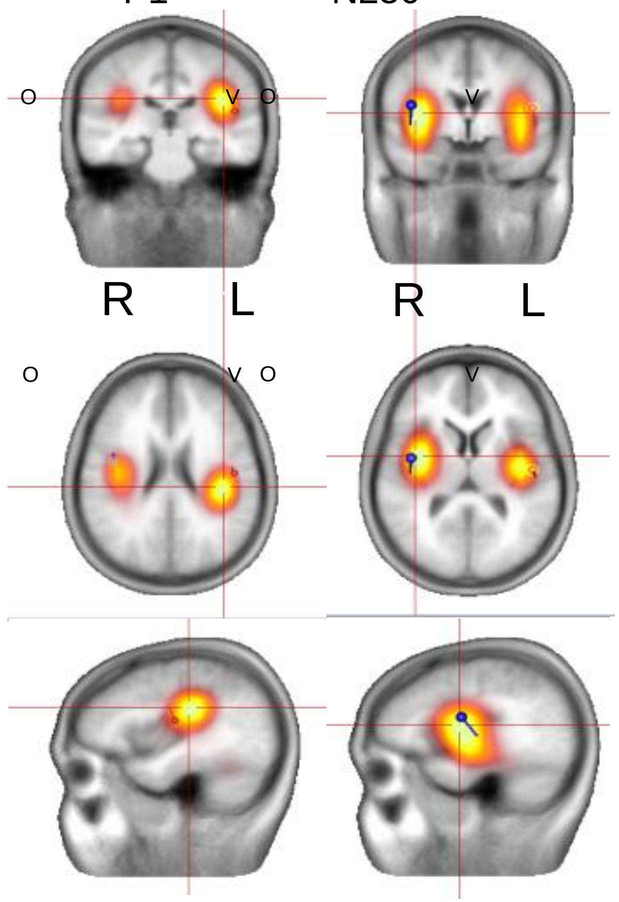


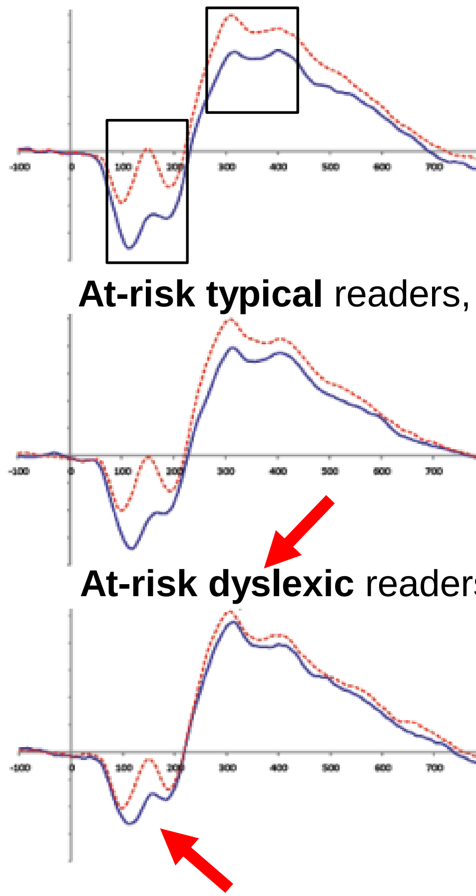


Inverse problem



Using source space waveforms as a spatial filter - ERPs to non-speech sounds at 9 year





Khan, Hämäläinen, Leppänen et al. 2011, Neuroscience Letters