LEARNING ERPS FOR LANGUAGE RESEARCH!

A two-days introductory course

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Thursday 10/01/09

&

Thursday 10/08/09

Most of the slides are:

Overview

- A bit of history
- Neural origins of ERPs
- Comparison of ERPs with other techniques

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Pre-History

- 1929: The Berger Rhythm
- 1934/35: Confirmation by the labs of Adrian, Jasper, & Davis
- 1939: Single-trial ERPs reported by Pauline & Hallowell Davis
- 1940-1960: Sensory ERPs recorded with primitive methods
- 1962: First publication of computer-averaged ERPs by Galambos

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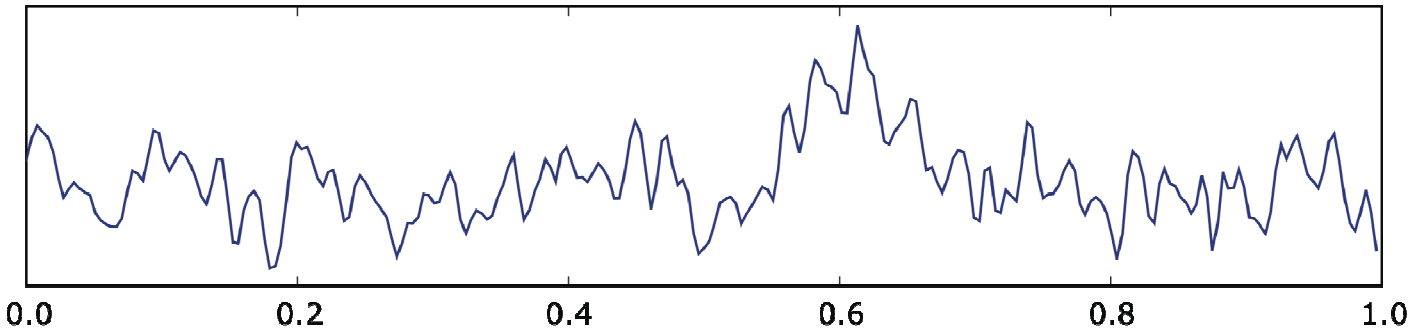
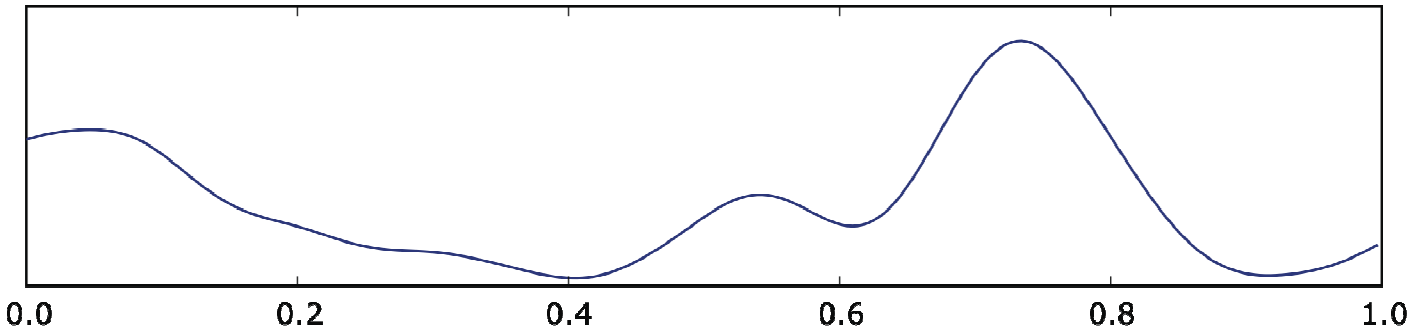
Basic EEG (ElectroEncefaloGraphy)

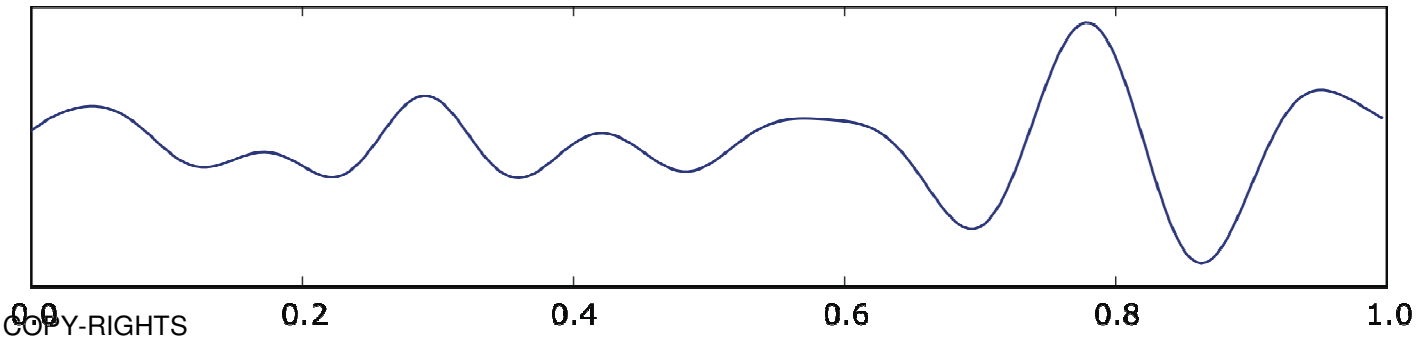
Raw EEG



Delta (1-3 Hz)
Slow Wave Sleep



Theta (4-7 Hz)
Non-REM Sleep



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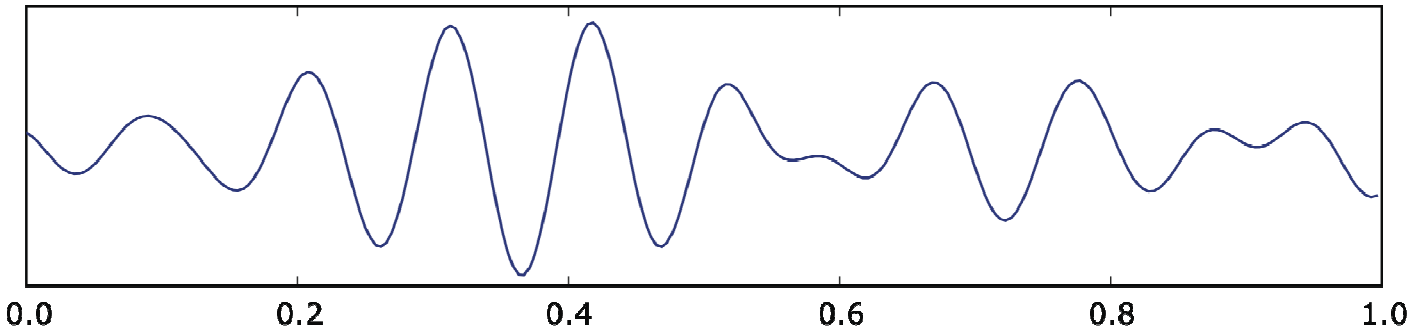
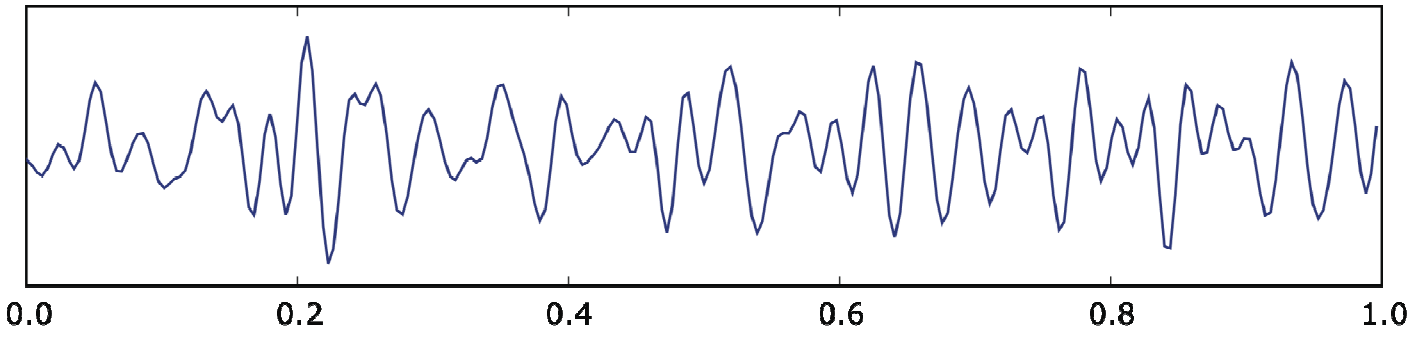
Basic EEG

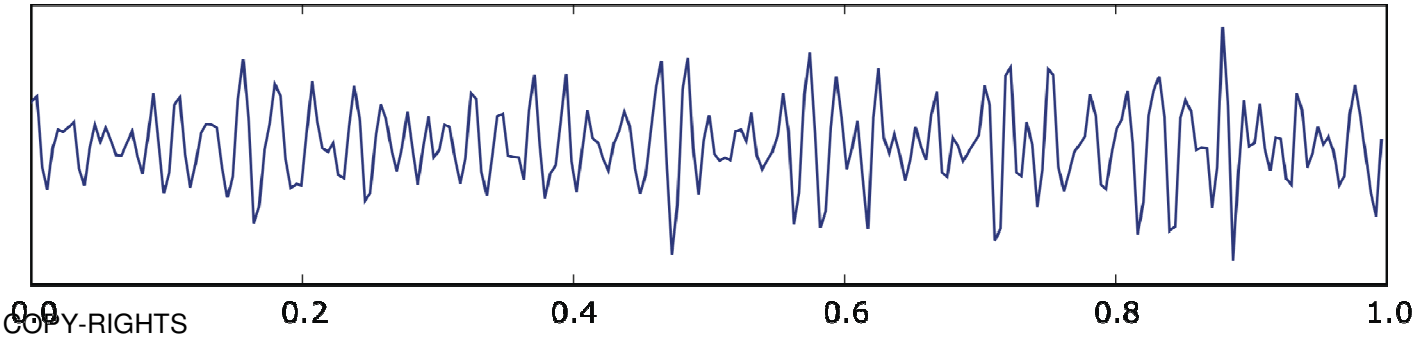
Alpha (8-12 Hz)
Awake, Relaxed
(Zoning)



Beta (12-25 Hz)
Mentally Active



Gamma (25+ Hz)
Binding?



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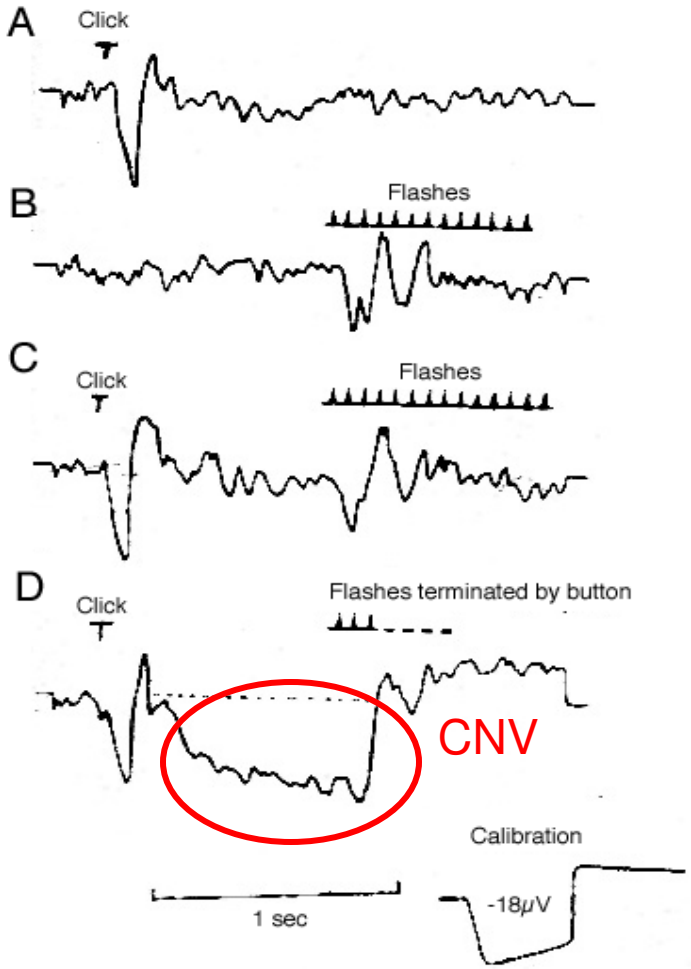
The Dawn of History

- 1964: Gray Walter and the CNV (Contingent Negative Variation)



No Task: Click Only

No Task: Flashes Only

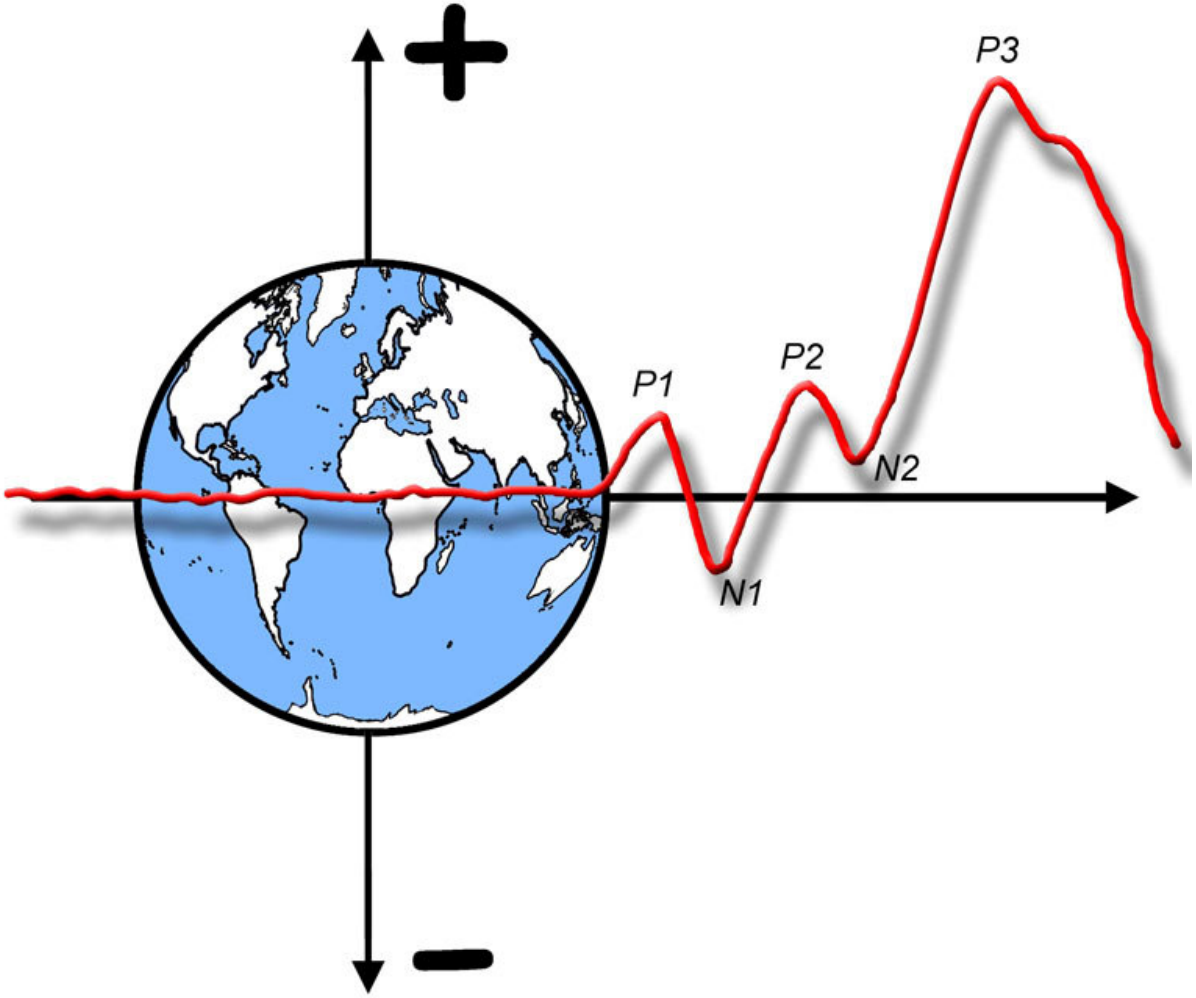
No Task: Click followed by flashes

Task: Press button when flashes start

Walter, W. G., Cooper, R., Aldridge, V. J., McCallum, W. C., & Winter, A. L. (1964). © Macmillan Publishers

Which Way is Up?

René Descartes



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1970s: Methods & Components

- Development and standardization of methods
  - Artifacts, filters, electrode types, impedance
  - Grand averages
  - PCA, epsilon adjustment
  - “Multichannel recordings” (3+ electrodes)
- The ubiquitous oddball paradigm
  - Donchin’s lab and models of P3 amplitude and latency
  - P3a and P3b (Squires, Squires, & Hillyard, 1975)
  - Application to psychopathology
- Selective attention
  - Hillyard, Näätänen, and Harter
  - Exogenous modulation & selection negativities
- The **N400** (Kutas & Hillyard, 1980) (First Language component)

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1980s: Cognitive Science

- Development of ERP (Event-Related-Potentials)
- Cognitive scientists and neuroscientists start to question the value of ERPology
- ERPers get serious about cognitive science
  - Hillyard and attention (Posner paradigm, visual search)
  - Coles and response selection, executive control
  - Kutas and psycholinguistics
- Cognitive scientists start recording ERPs
  - Allen Osman
  - Jeff Miller
  - Jim Hoffman
- The beginning of serious multichannel recordings (32+ channels)

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1990s: Cognitive Neuroscience

- Tucker and the geodesic sensor net
- Large-scale MEG systems come on line
- Integration of ERPs/ERMFs with PET and fMRI
- Use of structural MRI to constrain ERP/ERMF localization

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Some basic concepts from neuroscience & electricity

Some Basics of Electricity

- Current (I for Intensity; Amperes)
  - Movement of charges across space (coulombs per second)
  - Like rate of water coming out of a hose (liters per second)
- Voltage (E for Electromotive Force; Volts)
  - Electrical pressure (electric potential)
  - **Potential for charges to move**
  - Like water pressure
- Resistance (R; Ohms [Ω])
  - Ability to keep charged particles from passing
  - Inverse of *conductance*
  - Like having a skinny or blocked hose segment
- Impedance (Z)
  - Resistance to the flow of alternating current (AC)
  - Combines resistance, capacitance, and inductance
  - Resistance is used to describe the resistance to the flow of Direct Current (DC)

Electricity in the brain?

- Electricity in the brain (EEG) is produced by the movement of ions moving across cell membrane
  - Ion: an atom or particle in which the number of protons is not equal to the number of electrons, giving it either a positive or negative charge!
- What we measure in the EEG is the summation of many of these processes
- EEG (measured on the scalp) are an indirect measure of the direct electrical activity in the brain cells

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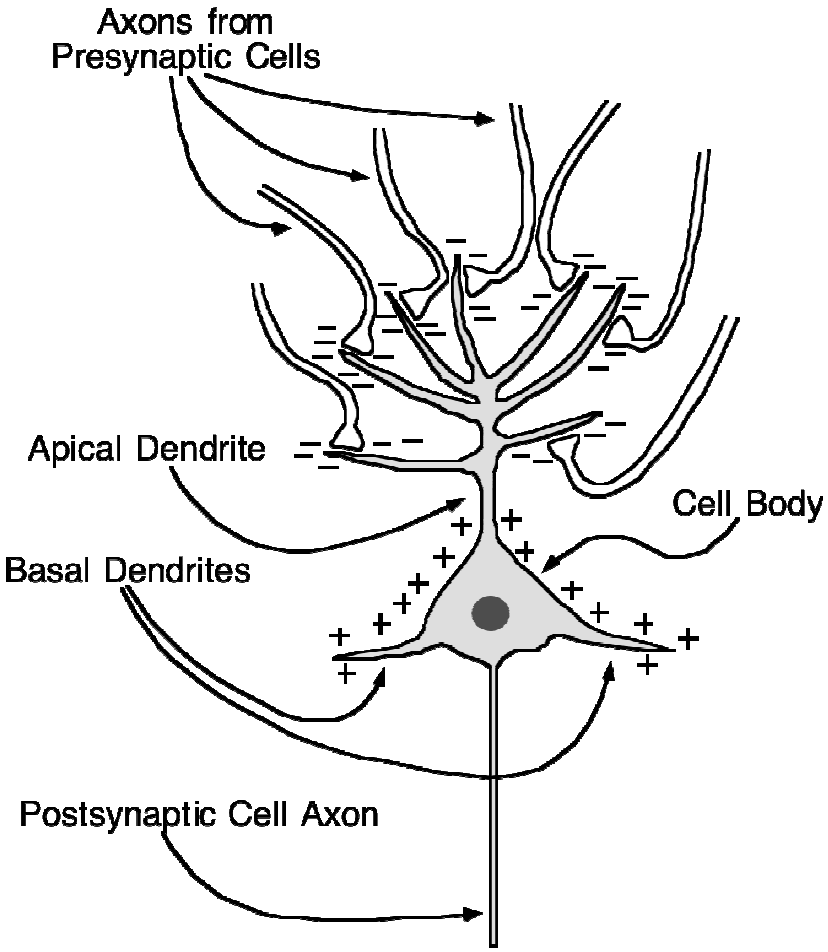
Some Neuronal basic
Where Do ERPs Come From?



Cortical pyramidal cell (basic input-output cell of cerebral cortex)

1) Excitatory neurotransmitters released on apical dendrites causes positive charges to flow into dendrites. Net negative on outside of cell

Current flows through cell at the basal , yielding a net positivity in that area, completing the circuit

A dipole is created (a pair of positive and negative electrical charges separated by a small distance

Polarity reverses with inhibitory transmitter

Polarity reverses with PSP (Post Synaptic Potentials) on cell body and basal dendrites

Polarity at scalp also depends on orientation of the cortical surface and position of reference electrode

Some Basics of Neuroscience

- Resting membrane potential
  - -70 mV on inside of cell
- Action potentials
  - Triggered when membrane potential goes sufficiently positive
  - Starts at axon hillock and travels down axon
  - Rarely contributes to scalp ERPs
- Postsynaptic potentials (PSPs)
  - Neurotransmitter binds with receptor, opens ion channels
  - Excitatory: Positive charges move into cell
  - Inhibitory: Negative charges move into cell
  - The origin of most ERPs
  - They are longer respect to action potentials. PsP can last for hundreds of ms

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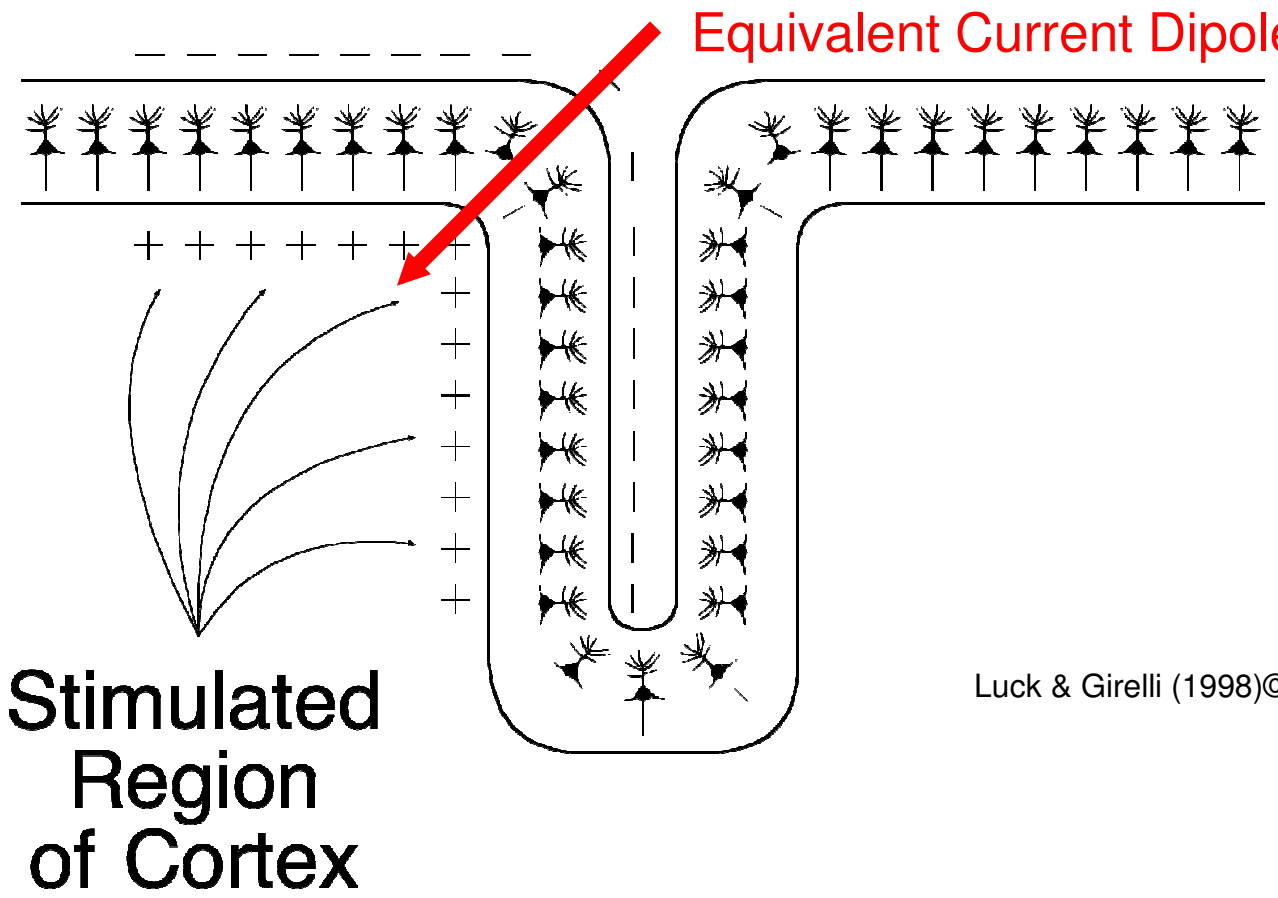
Where Do ERPs Come From?

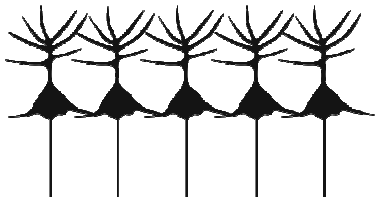


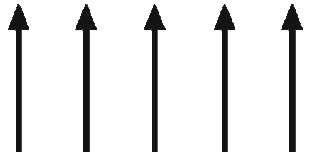
Luck & Girelli (1998)© MIT Press

To be recorded at a distance, large numbers of neurons must have similar voltage fields

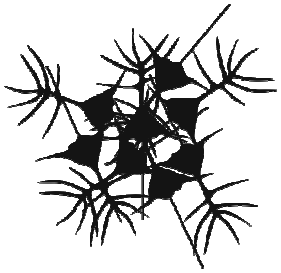
Where Do ERPs Come From?

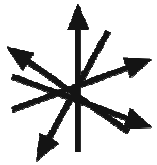
Open Field





Closed Field





Recordings of post-synaptic potentials from large group of neurons is called:

Local Field Potentials recording

Scalp-recorded potentials are possible only for layered structures with <u>consistent orientations</u>

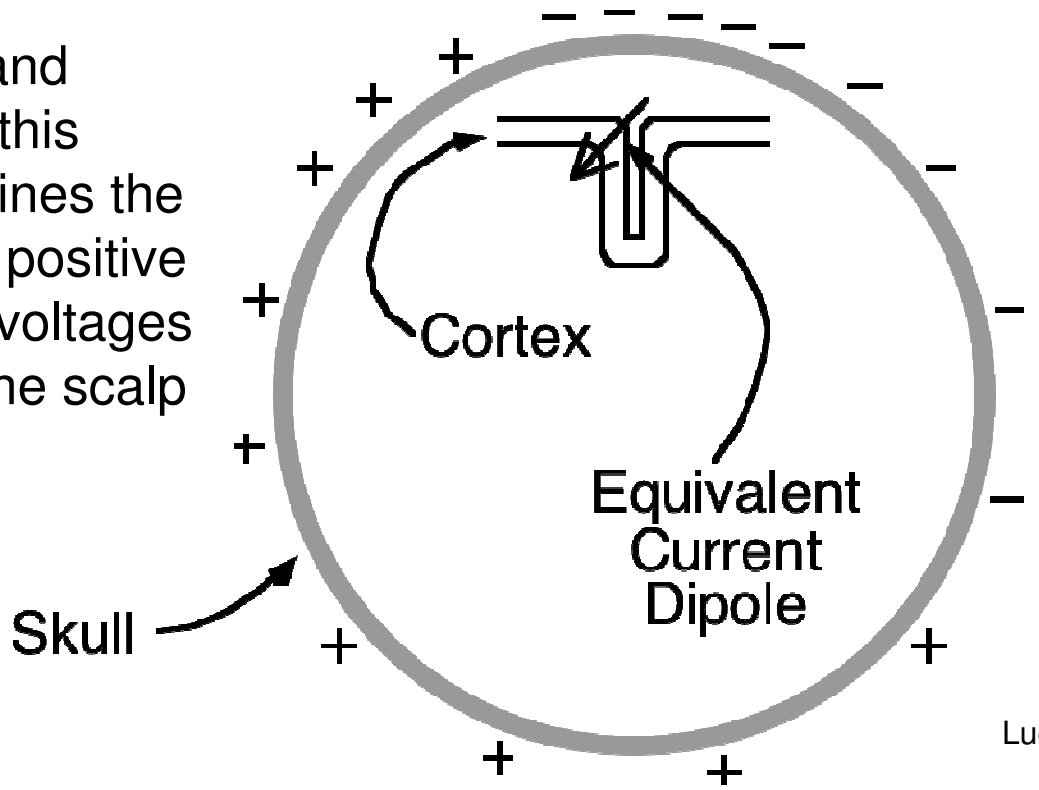
Primarily cerebral cortex

What about:
Cerebellum?
Brainstem nuclei?

Possible role of radial glia

Where Do ERPs Come From?

The position and orientation of this dipole determines the distribution of positive and negative voltages recorded on the scalp



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Voltages spread through the brain by “volume conduction”

Nearly speed of light

Voltage everywhere except at positive-negative transition

Skull causes lateral spread (like spraying hose on cardboard)

What are ERPs Good For?

- Reaction time for the 21st Century
  - Continuous measure of processing between a stimulus and a response
- Determine which process was influenced by an experimental manipulation
  - Which ERP component was influenced by the manipulation?
- Covert monitoring of processing
  - Processing can be measured under conditions that do not involve a behavioral response (or from subjects who cannot easily be trained to respond)
  - Did the brain do something that was not evident in behavior?
- Link to the brain
  - Under some conditions, neural systems can be identified

What are ERPs Good For?

- In language research ERPs are good if we are interested in the time course of a particular linguistic process
- + Time resolution BUT – Space resolution

- If your research question aims at answering a question on language localization, ERP is not the best technique to use (better fMRI, MEG)
  - The voltage distribution observed on the scalp is an *indirect* reflection of the activity that is somewhere generated at the (sub)cortical level.
  - It is possible to infer the source of the electrical activity, (Source Localization Analysis), but this is a field that is still for few specialized people!

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Comparison of Techniques

	Microelectrode Measures	Hemodynamic Measures	Electromagnetic Measures
Invasiveness	Poor	Good (PET) Excellent (fMRI)	Excellent
Spatial Resolution	Excellent	Good	Undefined/Poor (ERPs) Undefined/Better (ERMFs)
Temporal Resolution	Excellent	Poor	Excellent
Cost	Fairly Expensive	Expensive (PET) Expensive (fMRI)	Inexpensive (ERPs) Expensive (ERMFs)

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ERP components and Language related components

Most of the slides are:

What is an ERP component?

- Early definition: Combination of polarity, latency, and scalp distribution
  - C1: Polarity varies with upper/lower position
  - P3: Latency varies with stimulus evaluation time
- Circular definition: The effect produced by a given experimental manipulation
  - “N400 is the difference produced by a semantic mismatch”
- My definition: Scalp-recorded neural activity that is generated in a given neuroanatomical module when a specific computational operation is performed

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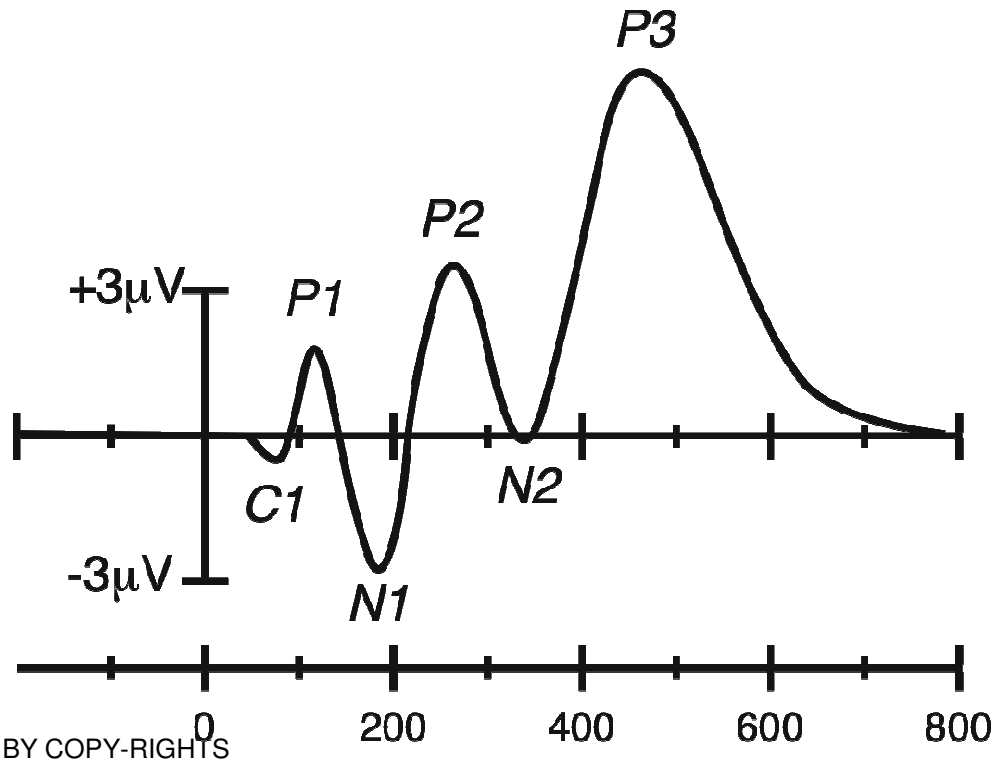
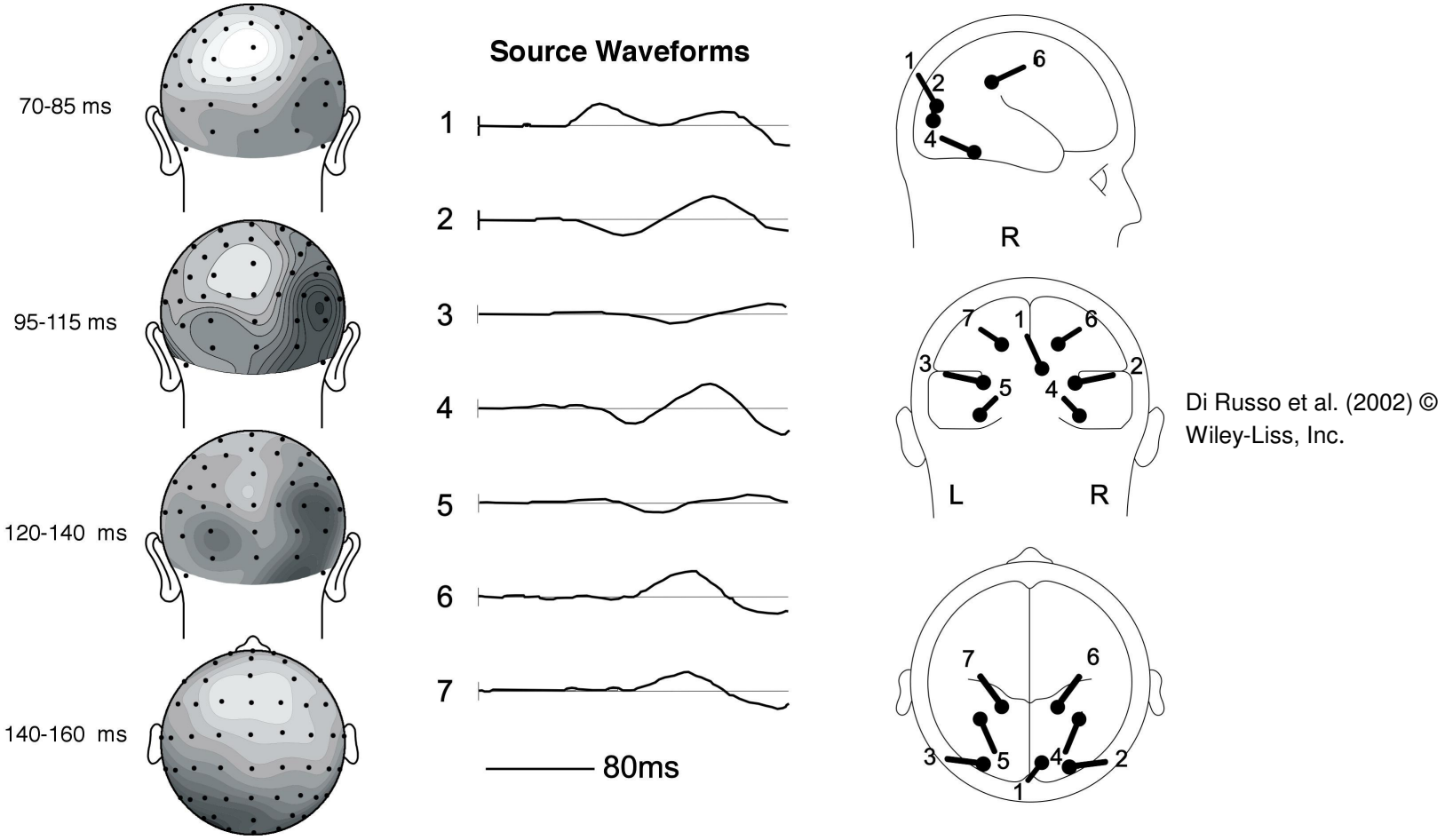
Peaks and Components

- An ERP waveform contains several peaks
- People typically assume that each peak corresponds to a single underlying “latent” component



Peaks and Components

- The scalp ERP consists of a set of summed and scaled intracranial “source” waveforms



Di Russo et al. (2002) © Wiley-Liss, Inc.

Peaks and Components

- The scalp ERP consists of a set of summed and scaled intracranial “source” waveforms
- Unfortunately, there is no foolproof way to recover the source waveforms from the scalp waveforms
  - There is an infinite number of sets of hypothetical source waveforms that could sum together to produce a given set of scalp waveforms
- The relationship between the observed peaks and the latent components may violate one’s naïve expectations
  - Experts can do fairly well when they see waveforms from multiple electrodes and multiple experimental conditions

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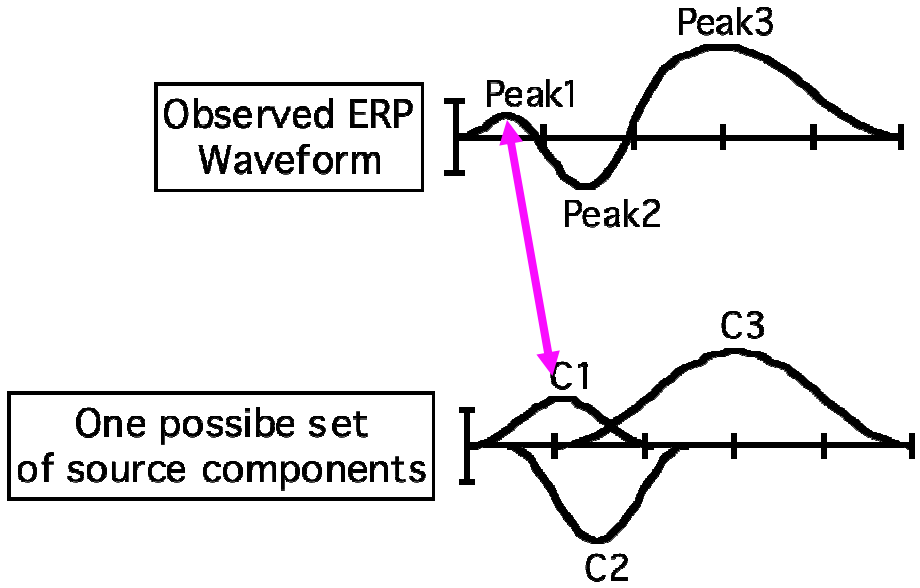
Peaks and Components



Rule #1- Peaks and components are not the same thing. There is nothing special about the point at which the observed waveform reaches a local maximum.

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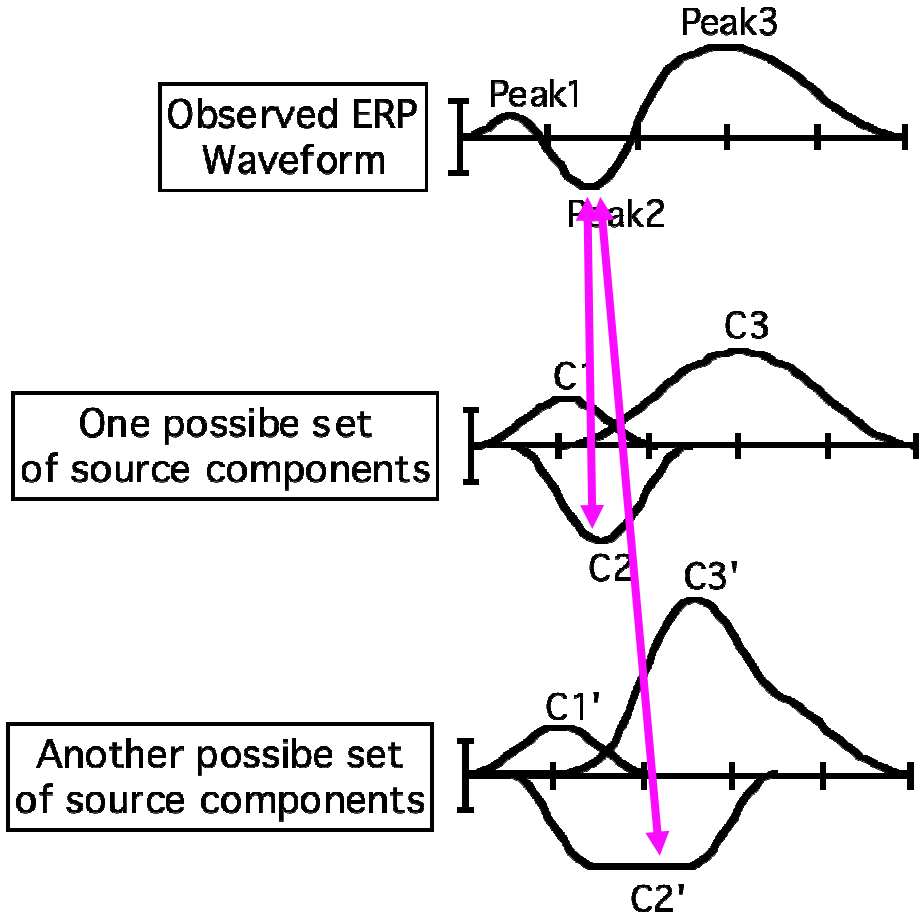
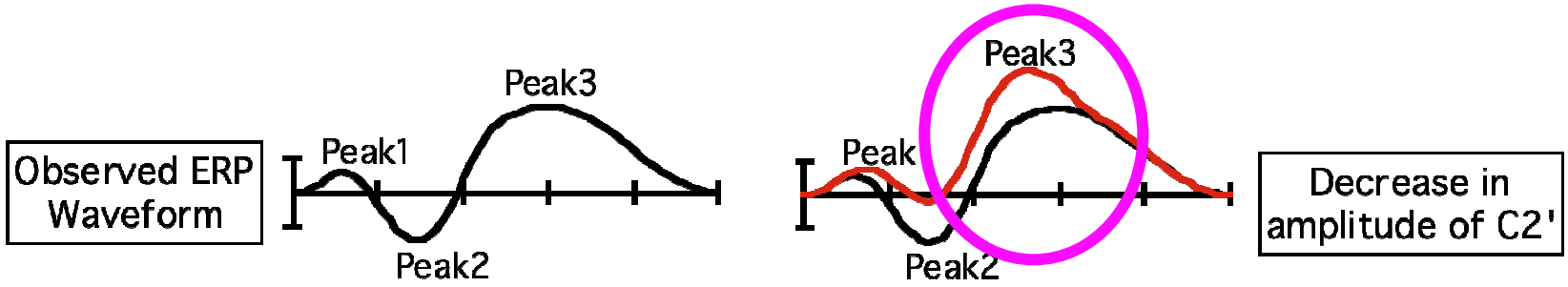
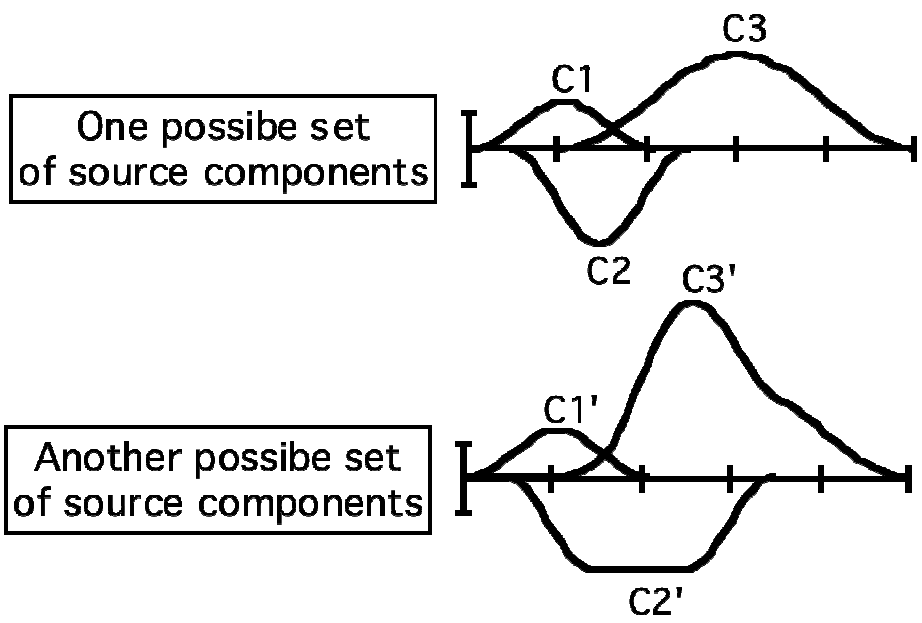
Peaks and Components



Rule #2- It is impossible to estimate the time course or peak latency of a latent ERP component by looking at a single ERP waveform—there may be no obvious relationship between the shape of a local part of the waveform and the underlying components.

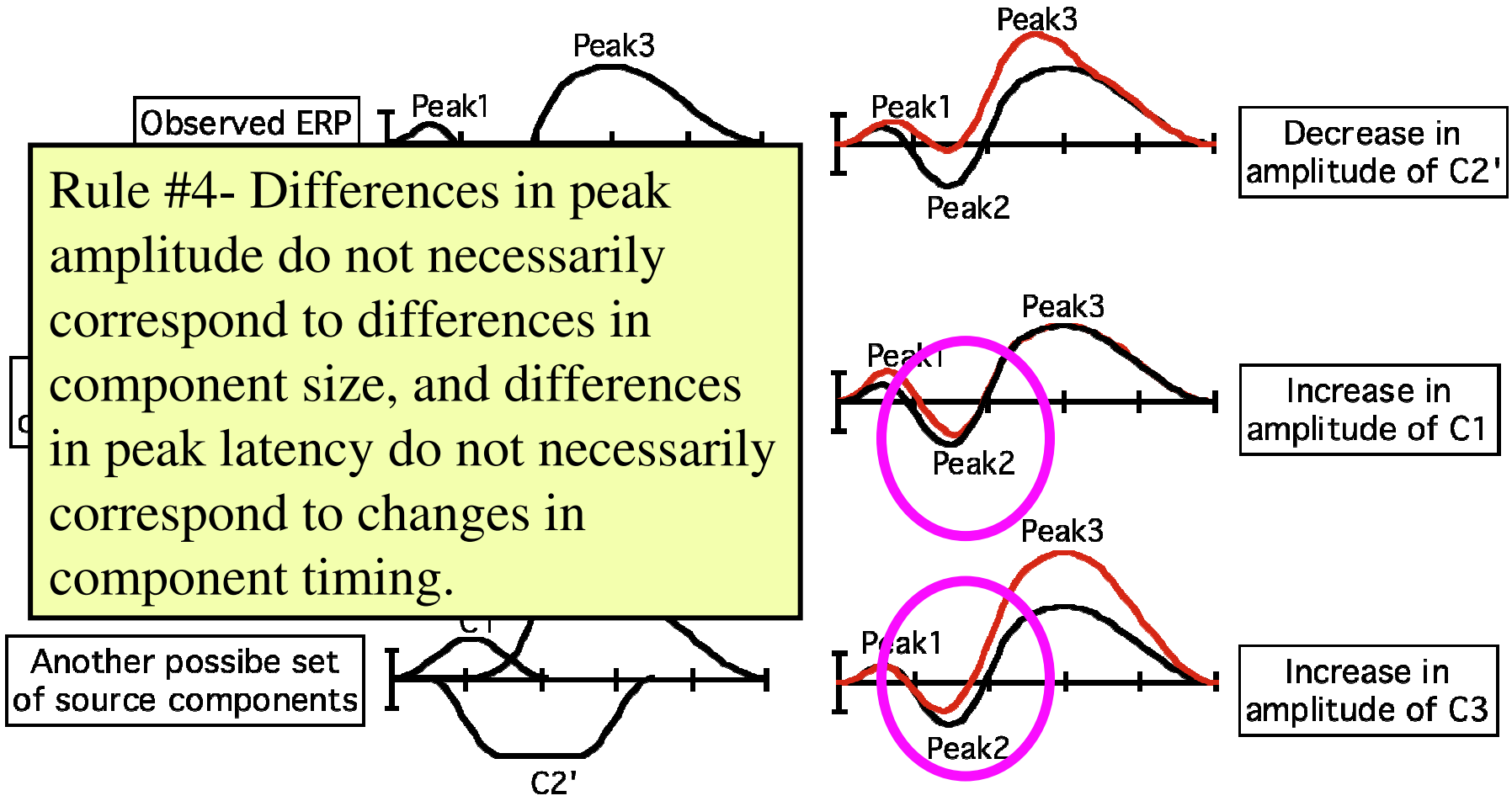
Peaks and Components



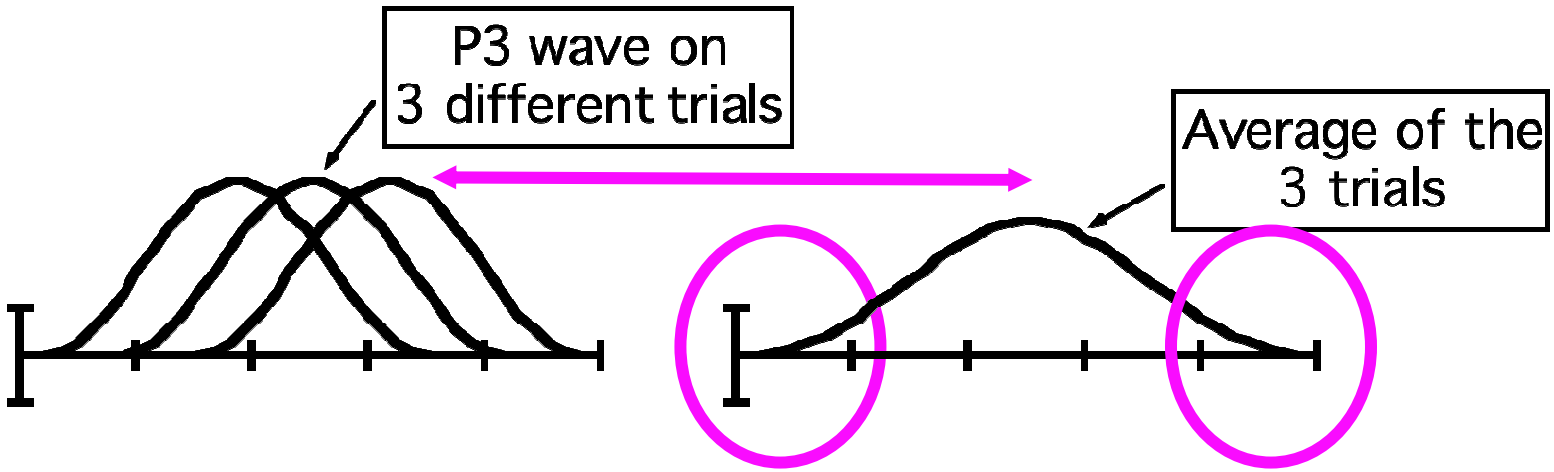


Rule #3- An effect during the time period of a particular peak may not reflect a modulation of the underlying component

Peaks and Components



Peaks and Components



Rule #5- Never assume that an averaged ERP waveform accurately represents the individual waveforms that were averaged together. In particular, the onset and offset times in the averaged waveform will represent the earliest onsets and latest offsets from the individual trials or individual subjects that contribute to the average.

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Another Problem

- Not only is it hard to know what component changed when a given peak was observed to change, it's also hard to know if the same components are being tapped in different experiments
- How do we know that the N400 elicited by a semantically incongruous word is the same as the N400 elicited by a low-frequency word?
- We never know for sure

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What to do?

Strategy #1- Focus on a specific component

Strategy #2- Use well-studied experimental manipulations

Strategy #3- Focus on large components

Strategy #4- Isolate components with difference waves

Strategy #5- Focus on components that are easily isolated

Strategy #6- Use component-independent experimental designs

Strategy #7- Hijack useful components from other domains

Strategy #8- Use a component to assess the processes that came before it

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Additional Rules

Rule #11- Never assume that the amplitude and latency of an ERP component are linearly or even monotonically related to the quality and timing of a cognitive process. This can be tested, but it should not be assumed.

Rule #12- Don't forget about behavior in ERP experiments. Dissociations between behavior and ERPs are sometimes troubling, but they are often informative

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What to do?

- A different approach: Use a technique that can recover the underlying latent components from the observed data
  - Source localization approaches (BESA)
  - Principal components analysis (PCA)
  - Independent components analysis (ICA)
- My opinion: A good experimental design is always better than mathematical hocus-pocus

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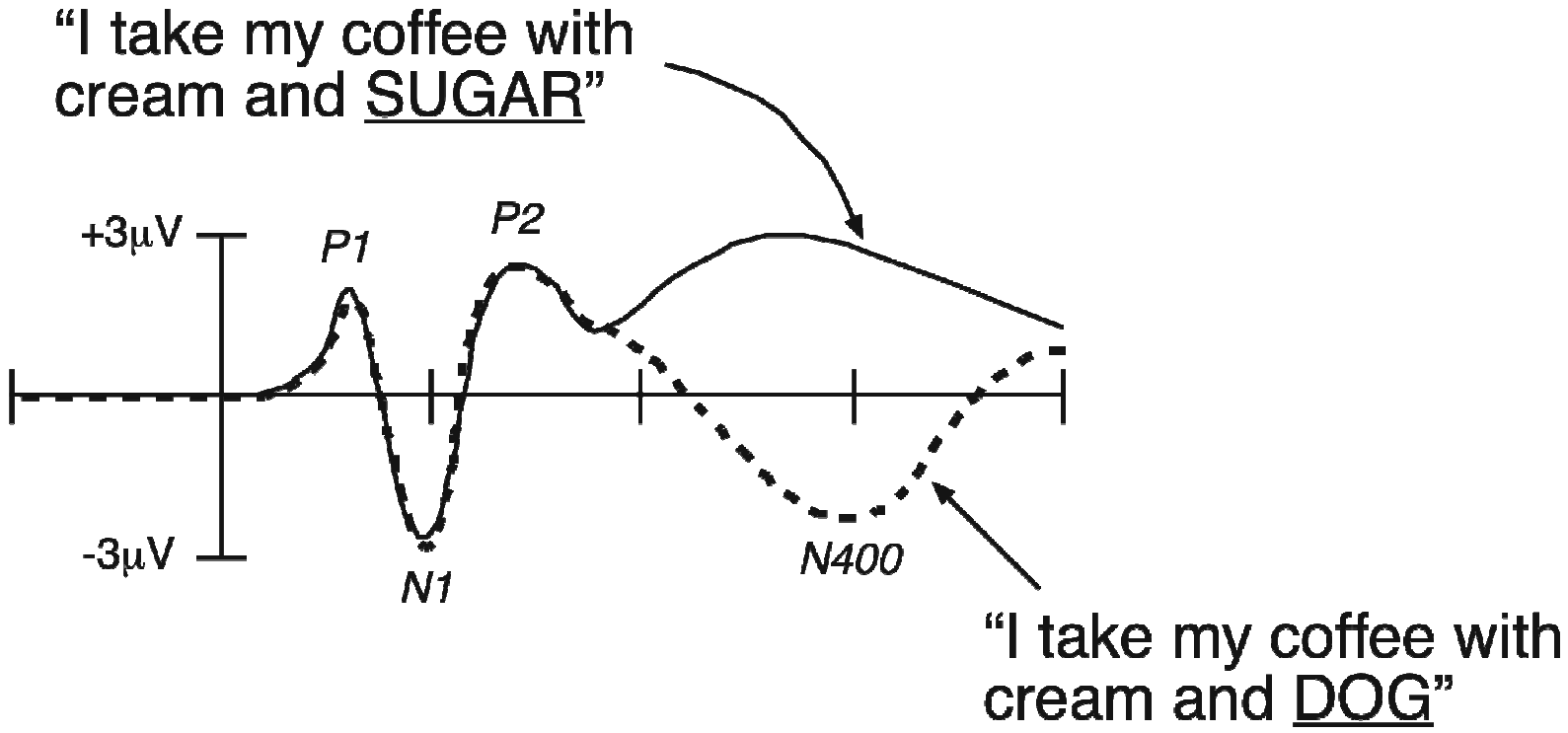
N400

- Typical paradigm: Establish a semantic context and then violate it



N400

- N400 is found for semantic violations, but not syntactic or musical violations
- N400 is primarily found with word stimuli, but it can be found with pictures
- N400 is large for orthographically regular nonwords but not consonant strings, false fonts, etc.
- N400 is larger for uncommon than common words
- N400 appears to be generated primarily in the floor of the left temporal lobe
  - Slightly larger over right hemisphere due to tilt of dipole
  - Possibly also a PFC source
- Kutas: N400 reflects work done to form a semantic interpretation of a stimulus
- Hagoort: N400 reflects work done to integrate stimulus into current conceptual context

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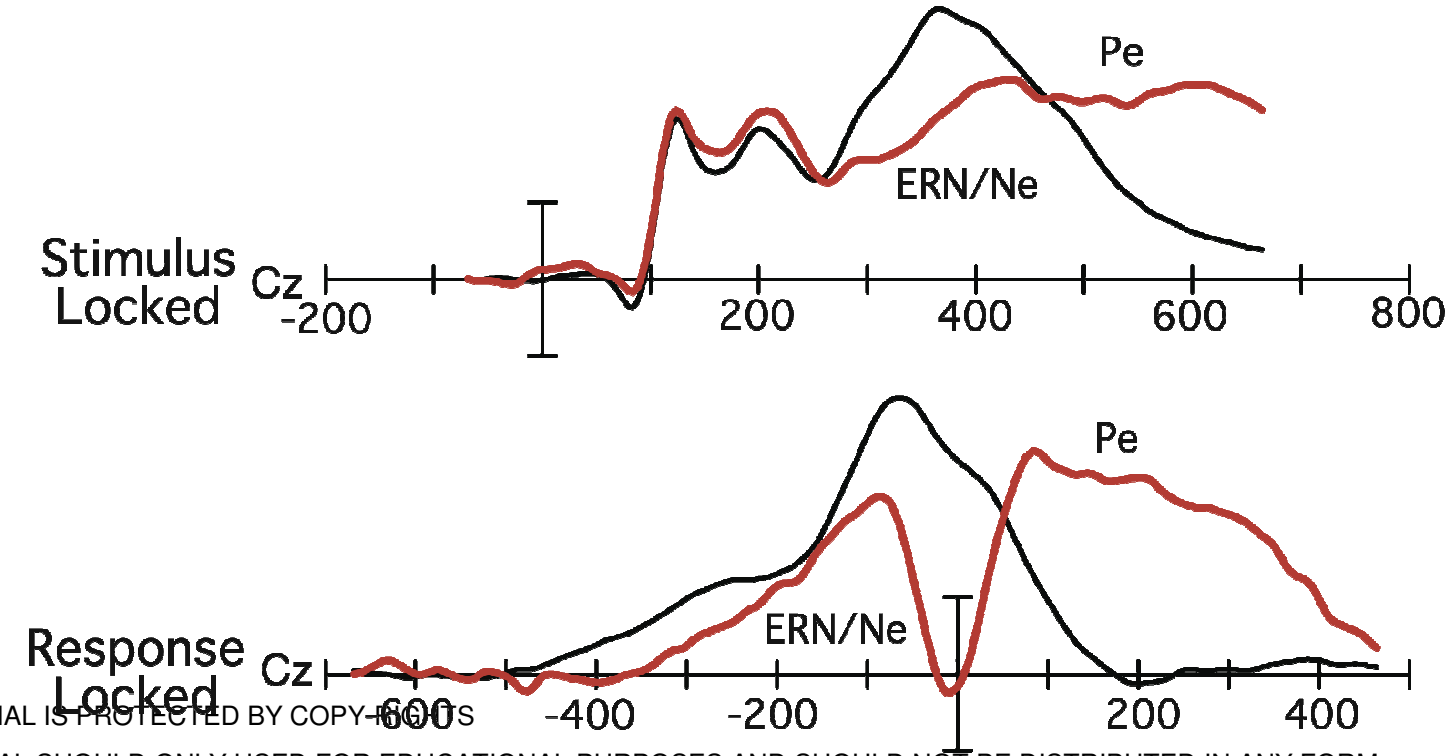
The Error-Related Negativity

- Independently discovered by Falkenstein and Gehring

Flankers paradigm: Respond to Central Letter (X or O)
XXXXX OOOOO XXOXX OOXOO



The Error-Related Negativity

- ERN thought to be generated in anterior cingulate cortex
  - But an intracranial study finds many active sites
- Theories:
  - Error detection
  - Conflict detection
  - Emotional response
- May be the same as the anterior N2 component
  - Anterior N2 larger for incompatible trials in flankers and Stroop tasks
  - Anterior N2 larger when search array contains pop-out

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P600 (or Syntactic positive shift)

- Originally related to the processing of grammar and syntactic anomalies
- It is a positive ongoing deflection
- Its peak amplitude is generally observed around 600 ms from the onset of the critical stimulus
- No clear peak, generally widespread
- First observed by Osterhout & Holcomb, 1992
- Hagoort et al (1993)
  - Violations of Subject-verb number agreement in Dutch
  - Het verwende kind ***gooien** het speelgoed op de grond

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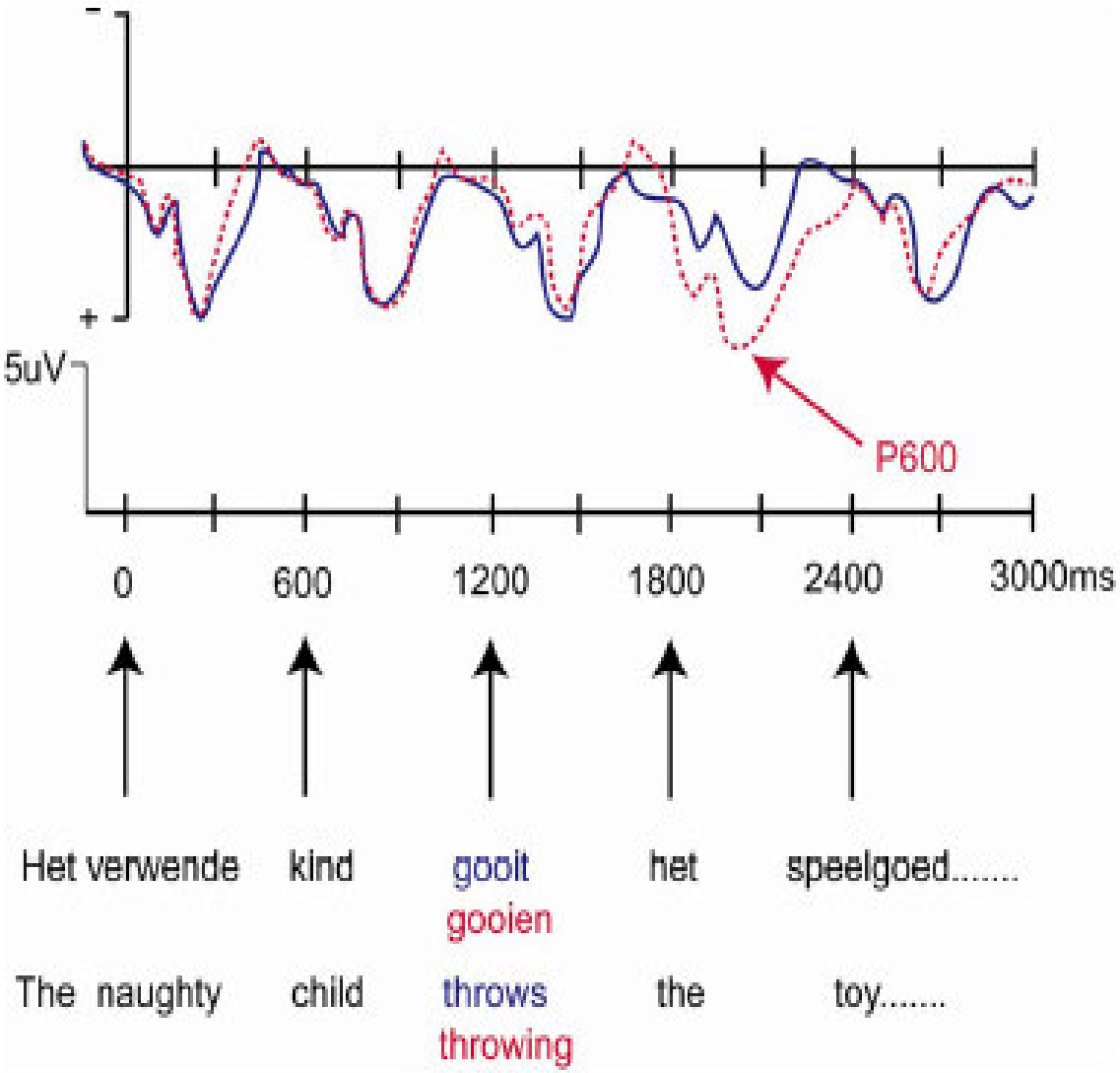

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P600 (or Syntactic positive shift)

- Recently, the P600 component has been found to be sensitive to semantic integration (among others Kupergerb et al, 2003)
- .... The finger print for the P600 is not so clear as the one for the N400…
- Mm

- E-LAN (Early, Left Anterior Negativity)
  - Print mark for syntactic anomalies as well

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Data Signal & Averaging

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Importance of Clean Data

- ERPs are tiny
  - Many experimental effects are less than a millionth of a volt
- ERPs are embedded in noise that is 20-100 μV
- Averaging is a key method to reduce noise
  - S/N ratio is a function of sqrt(# of trials)
  - Doubling # of trials increases S/N ratio by 41% [sqrt(2)=1.41]
  - Quadrupling # of trials doubles S/N ratio [sqrt(4)=2]

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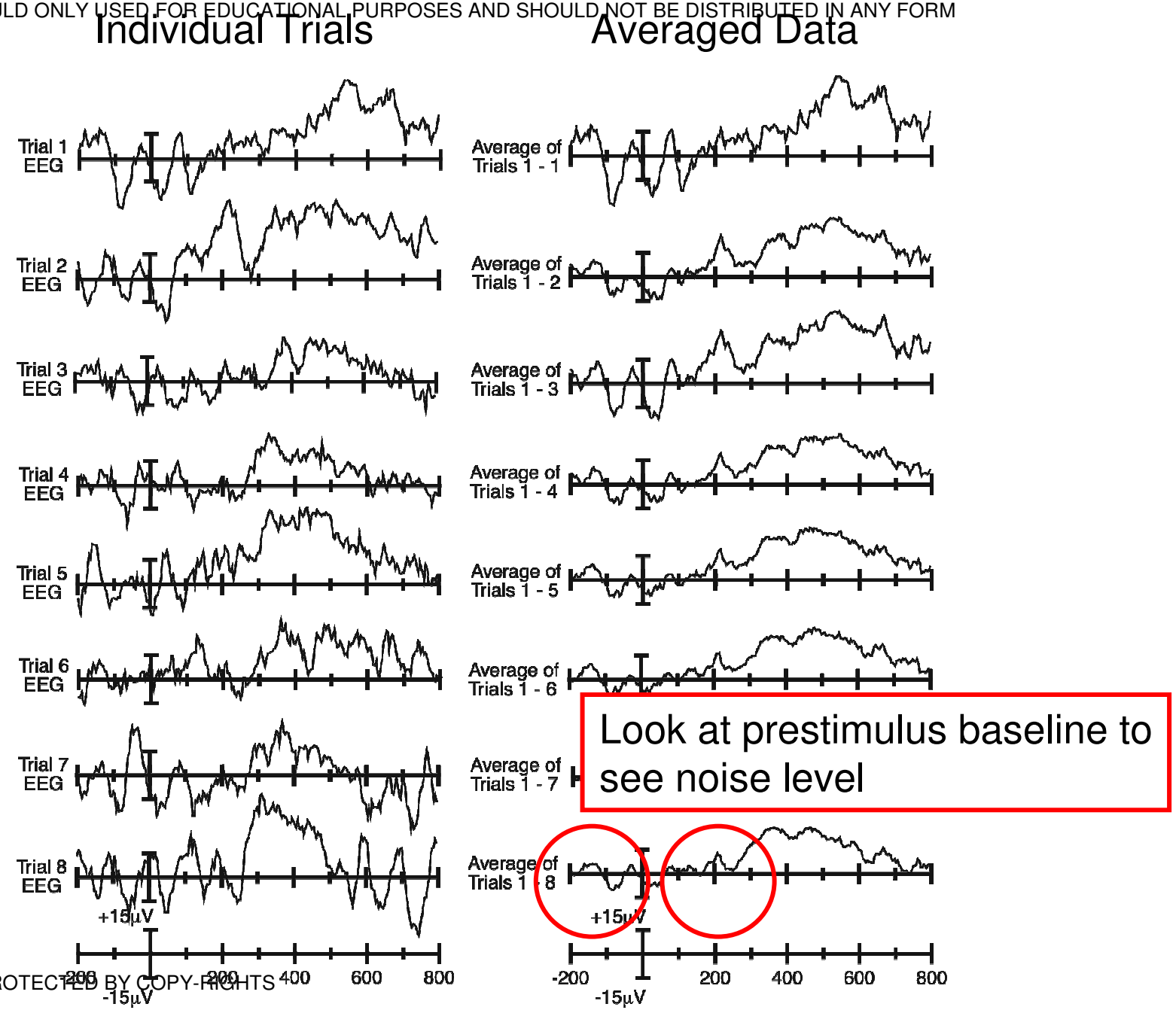
Importance of Clean Data

- Just having a lot of trials is often not enough to get clean data
- It pays to reduce sources of noise before the noise is recorded
- Hansen's Axiom: There is no substitute for clean data
- Cleaning up noise in the recordings has a cost
  - Averaging requires lots of trials (lots of time)
  - Filters distort the time course of the ERPs
- Spending a few days tracking down and eliminating noise sources could allow you to cut an hour off every recording session and cut the number of subjects in each experiment by 25%



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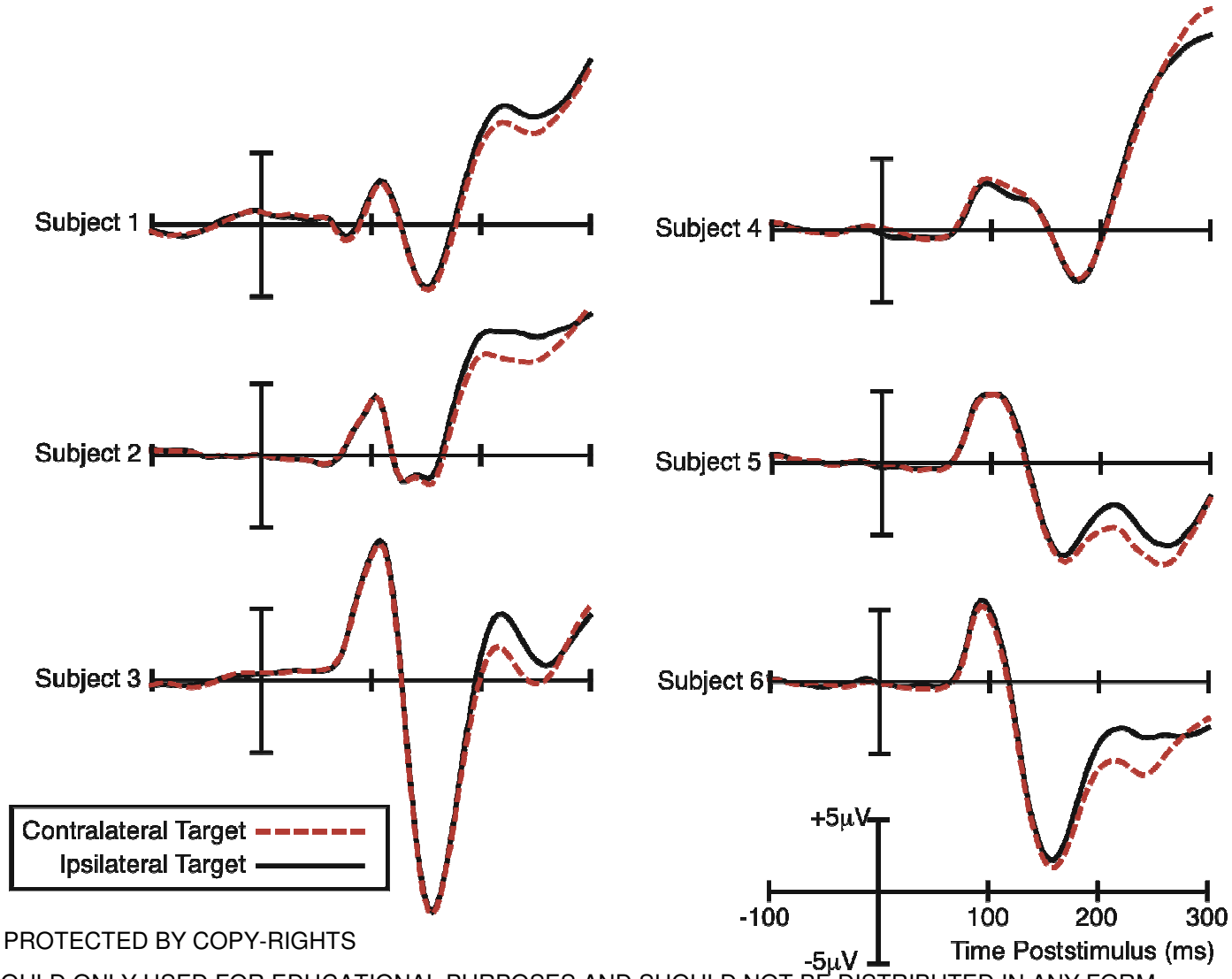
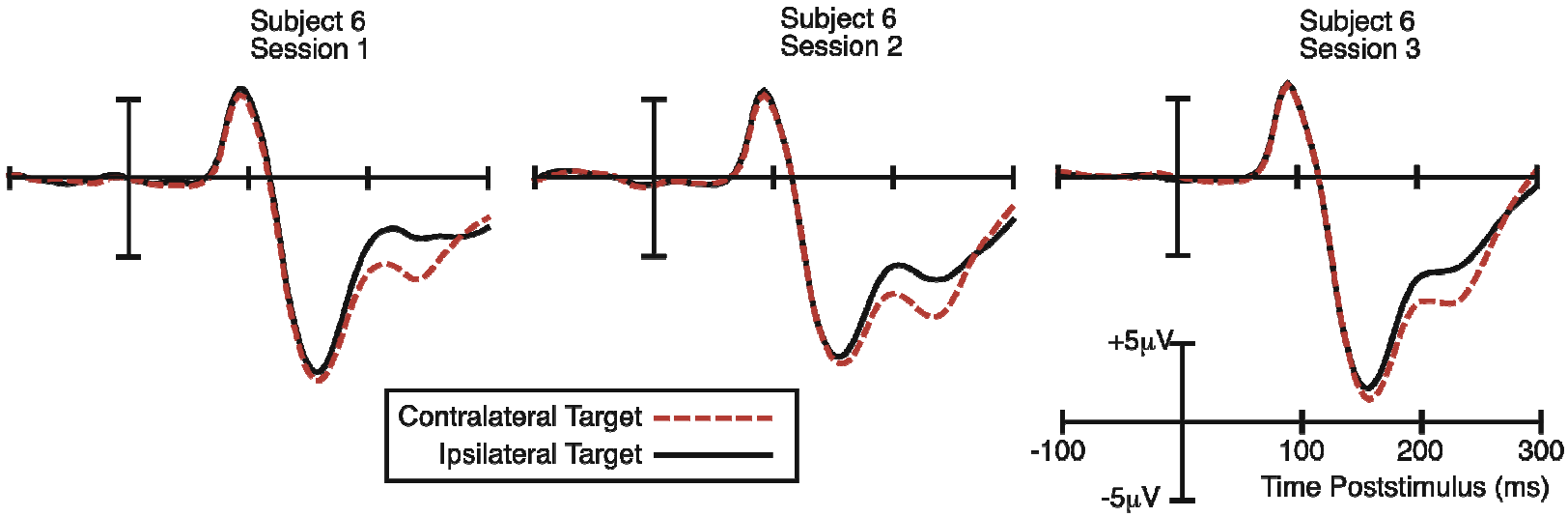
Averaging and S/N Ratio

- S/N ratio = (signal size) ÷ (noise size)
  - 0.5 µV effect, 10 µV EEG noise -> 0.5:10 = 0.05:1
  - We typically want a value that is at least 1:1
  - Acceptable S/N ratio also depends on number of subjects
- Averaging increases S/N according to sqrt(N)
  - Doubling N multiplies S/N by a factor of 1.41
  - Quadrupling N doubles S/N (because sqrt(4) = 2)
  - If S/N is .05:1 on a single trial, 1024 trials gives us a S/N ratio of 1.6:1
    - Because sqrt(1024) = 32 and .05 x 32 = 1.6
  - Ouch!!!

Individual Differences



Individual Differences



Good reproducibility across sessions
(assuming adequate # of trials)

Assumptions of Averaging

- Assumption 1: All sources of voltage are random with respect to time-locking event except the ERP
  - This should be true for a well-designed experiment with no time-locked artifacts
- Assumption 2: The amplitude of the ERP signal is the same on each trial
  - Violations of this don't matter very much
  - We don't usually care if a component varies in amplitude from trial to trial
  - However, two components in the average might never occur together on a single trial
  - Techniques such as PCA can take advantage of less-than-perfect correlations between components

Assumptions of Averaging

- Assumption 3: The timing of the ERP signal is the same on each trial
  - Violations of this matter a lot
  - The stimulus might elicit oscillations that vary in phase or onset time from trial to trial
    - These will disappear from the average
  - The timing of a component may vary from trial to trial
    - This is called “latency jitter”
    - The average will contain a “smeared out” version of the component with a reduced peak amplitude
  - Response-locked averaging can sometimes solve this problem

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Potential problems with ERP signal

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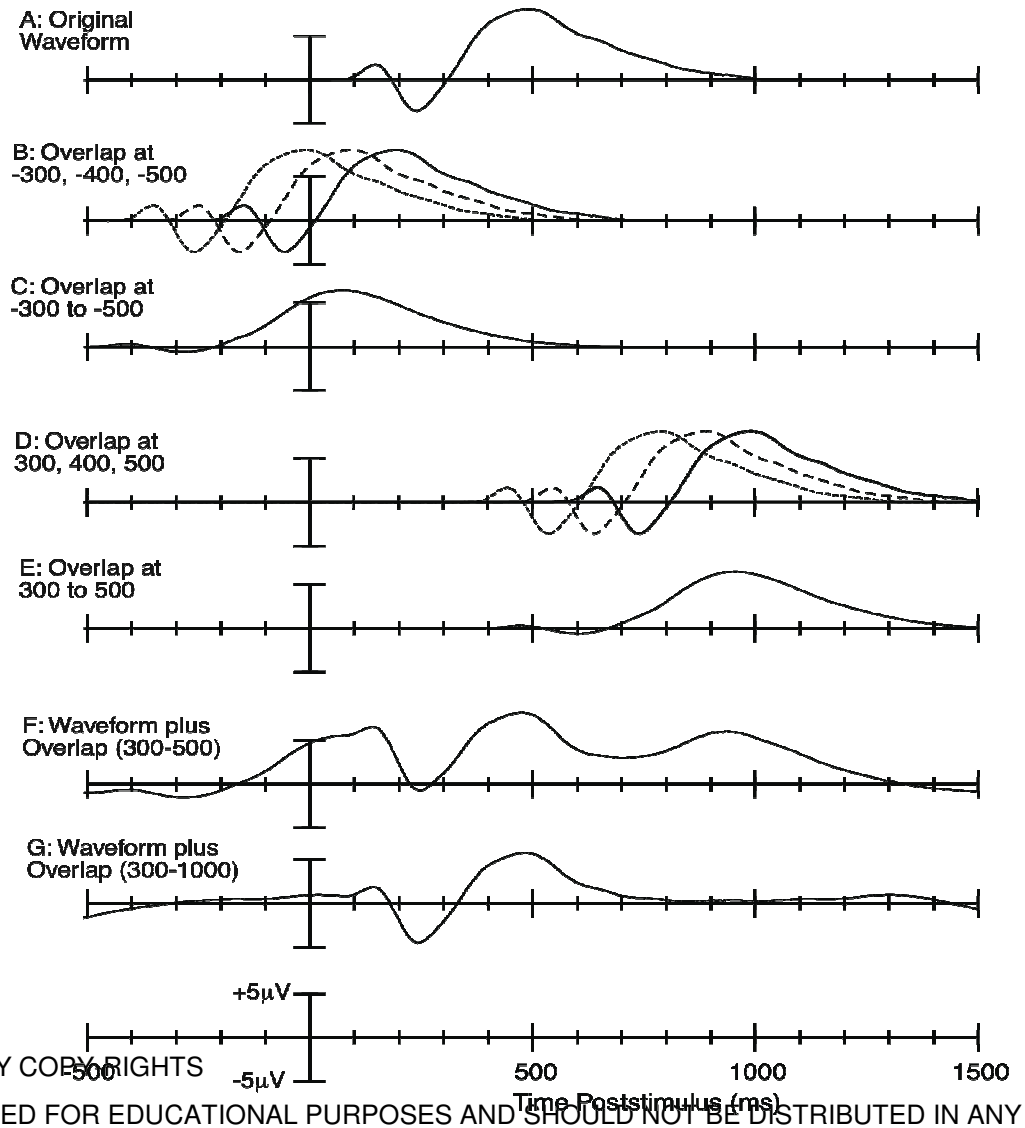
The Overlap Problem



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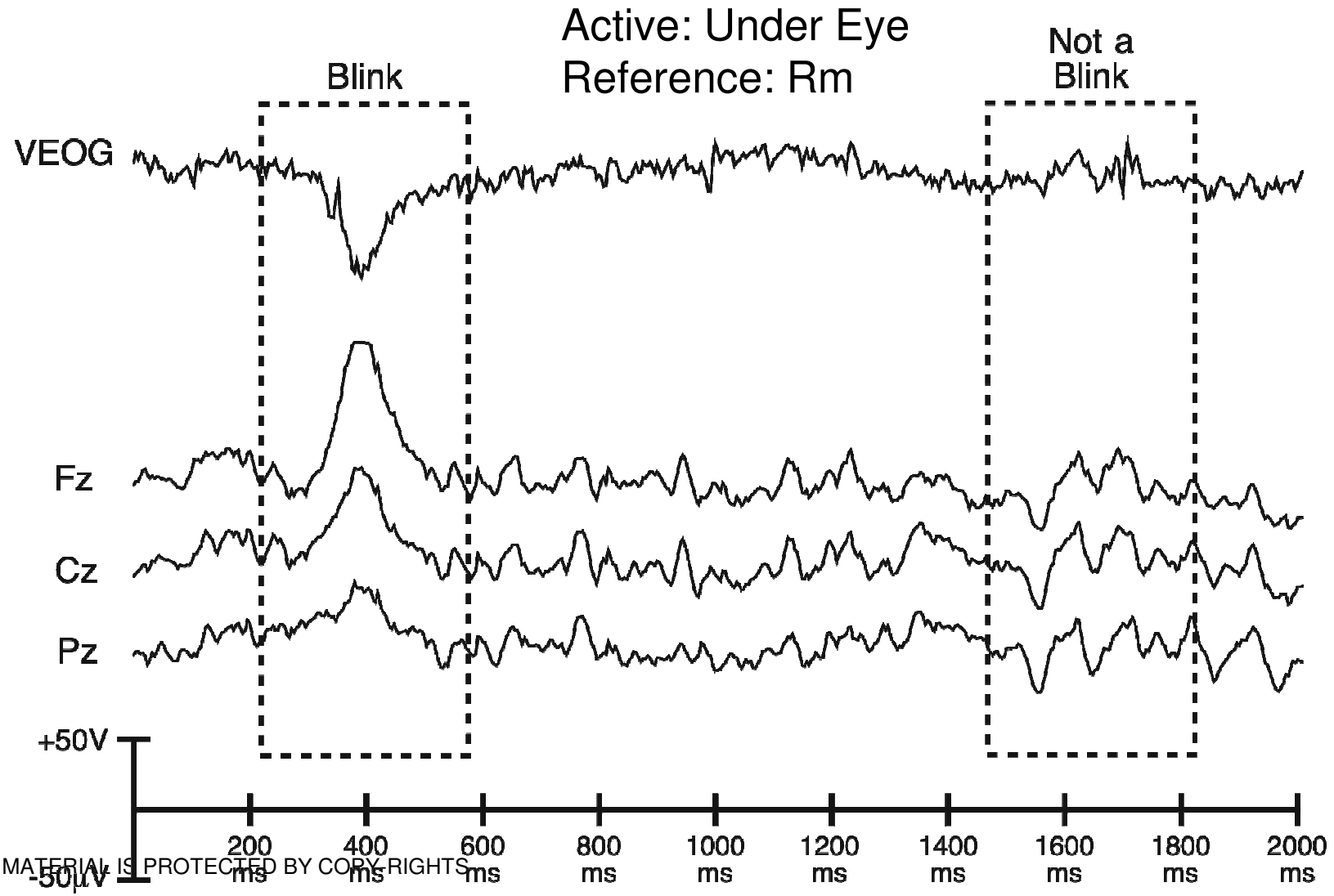
Artifacts: Blinks



Artifacts: Blinks

- To minimize blinks
  - No contact lenses
  - Frequent breaks
  - Times when blinks are OK
    - But be careful of blink offsets

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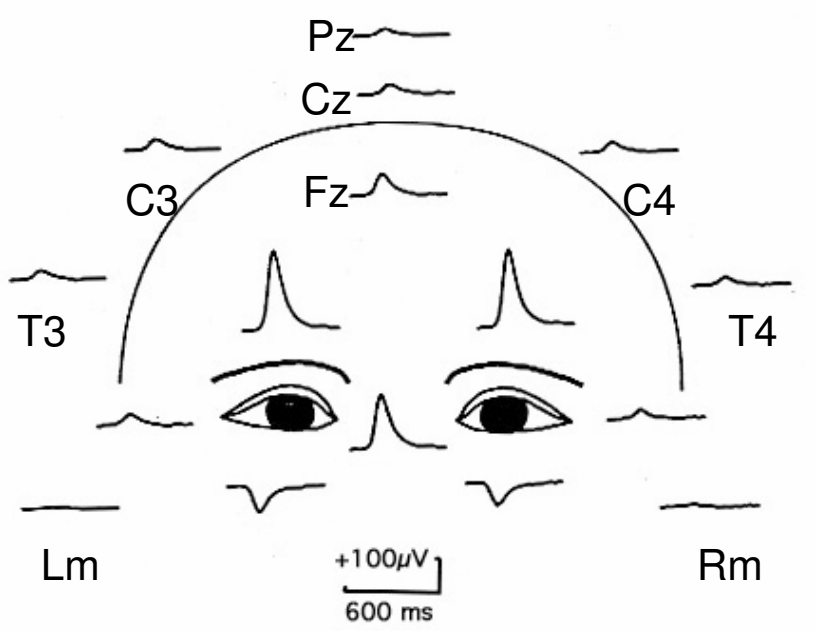
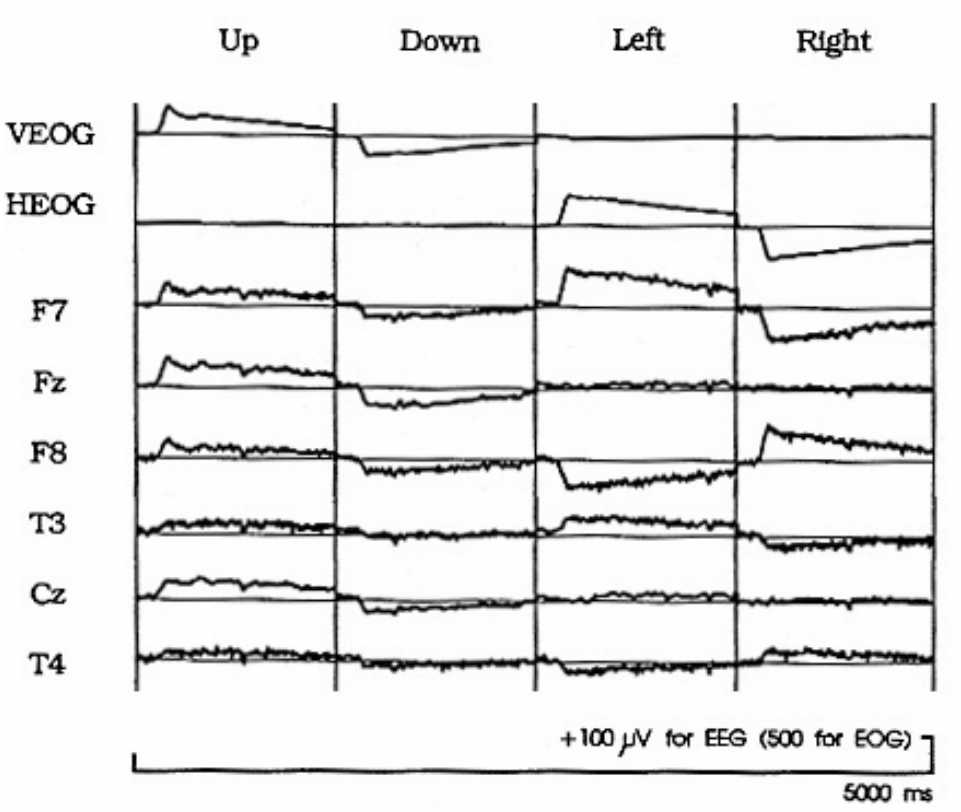
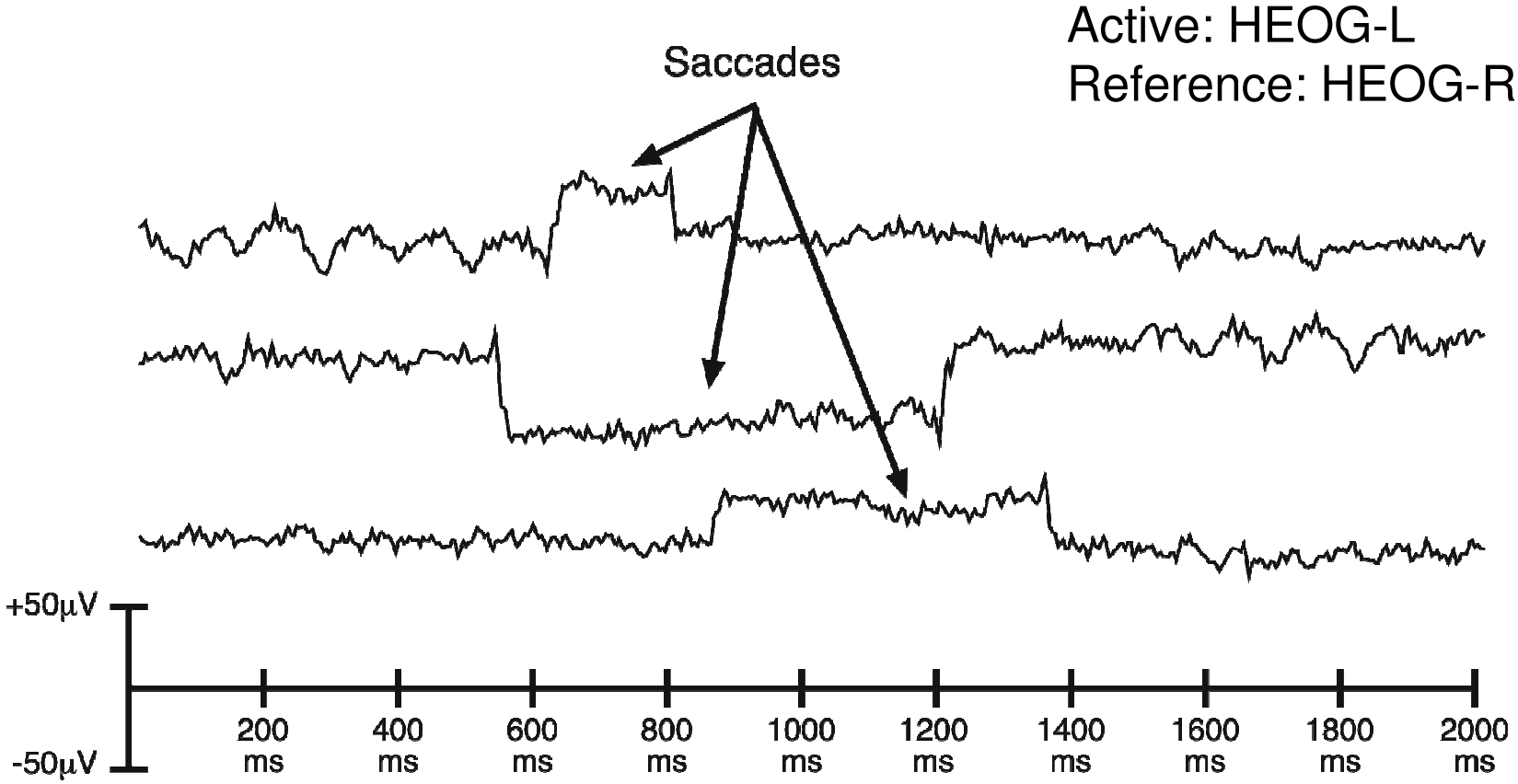
Ocular Artifact Propagation





Lins, Picton, Berg, & Scherg (1993) © Springer

Artifacts: Saccades



Eyes contain dipole with positive end pointing toward front of eye

Amplitude linearly related to size of eye movement (16 μV/degree)

Artifacts: Saccades

- To minimize and detect eye movements
  - Design experiment so that subjects don't have any reason to deviate from fixation at beginning of each trial
  - An event code should demarcate the event that might lead to a deviation of fixation
  - Provide feedback
    - Pretend you know more than you actually do

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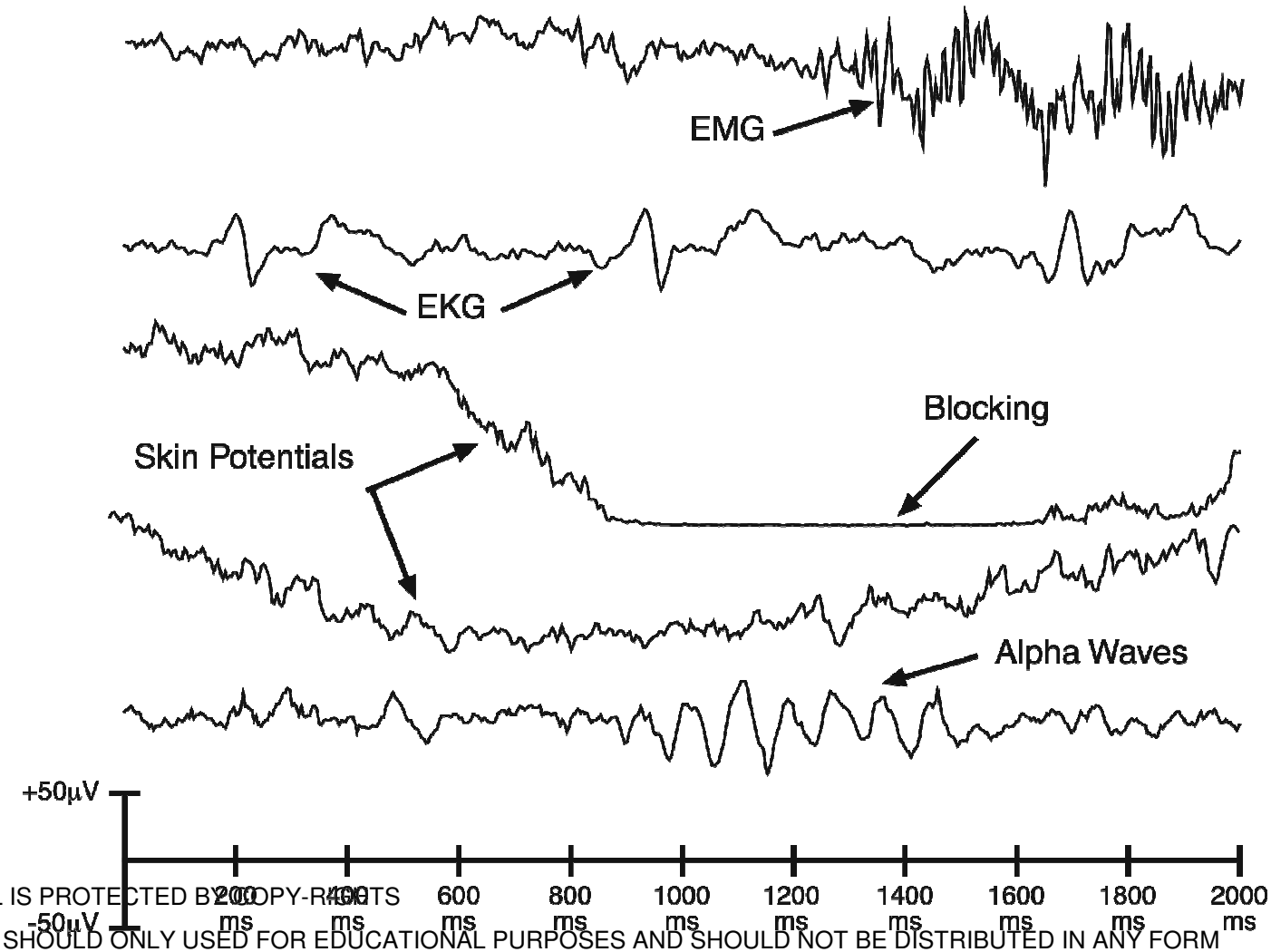
Artifacts: C.R.A.P.

(Commonly Recorded Artifactual Potentials)



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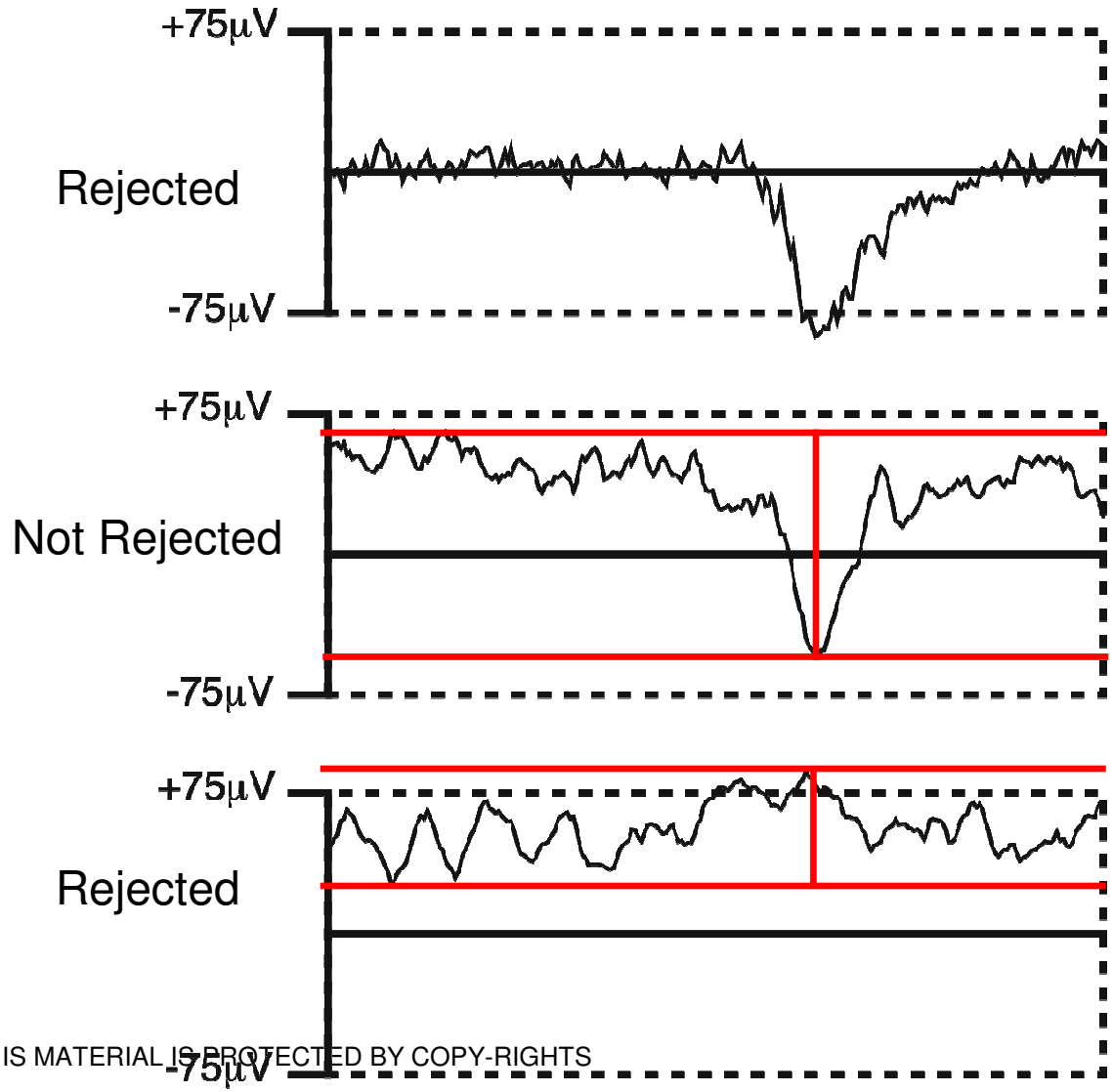
Artifact Rejection

- Goal: Throw out trials with problematic artifacts; don't throw out "good" trials
  - Throw out all channels if an artifact is detected in any channel
- Problem: There is a continuum of "goodness"
- Signal detection problem
  - We have a measure of strength of artifact
    - Tends to be bigger when artifact is actually present
    - A good measure is big for present, small for absent
  - We set a rejection criterion
  - Any trials that exceed this criterion are thrown away
  - Best criterion depends on relative costs of misses and false alarms

Artifact Rejection: Blinks



Better:
Peak-to-peak amplitude

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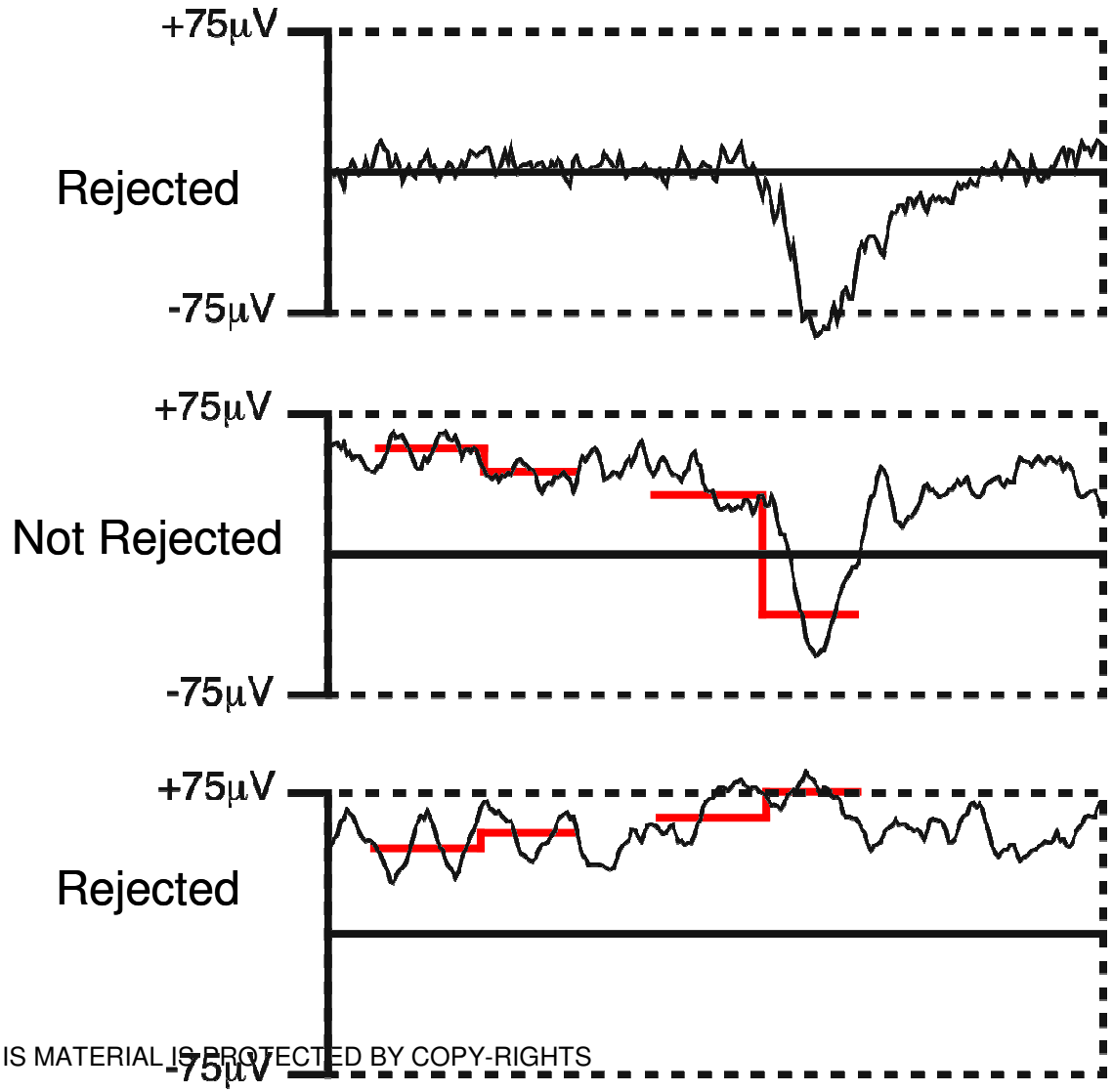
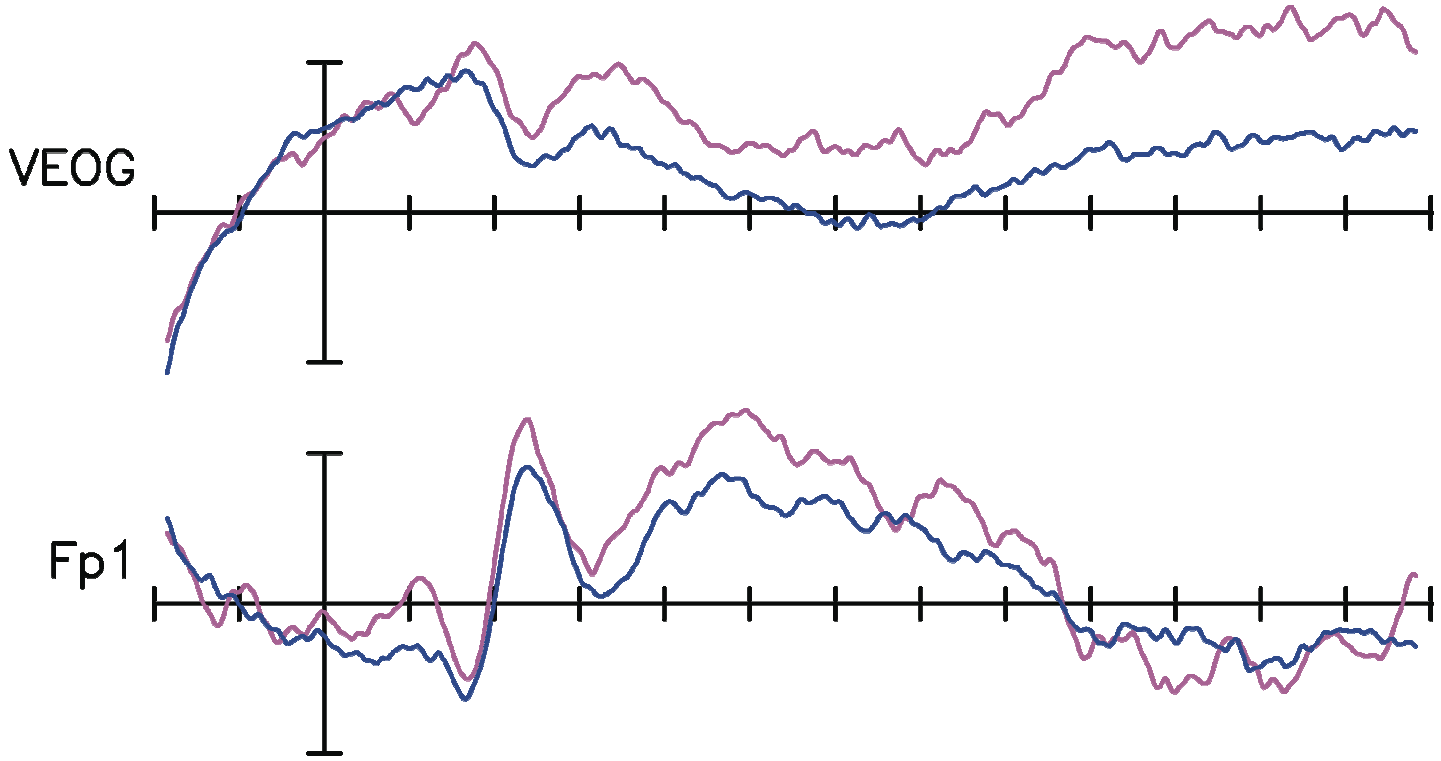
Artifact Rejection: Blinks



Better:
Peak-to-peak amplitude

Even better:
Step Function

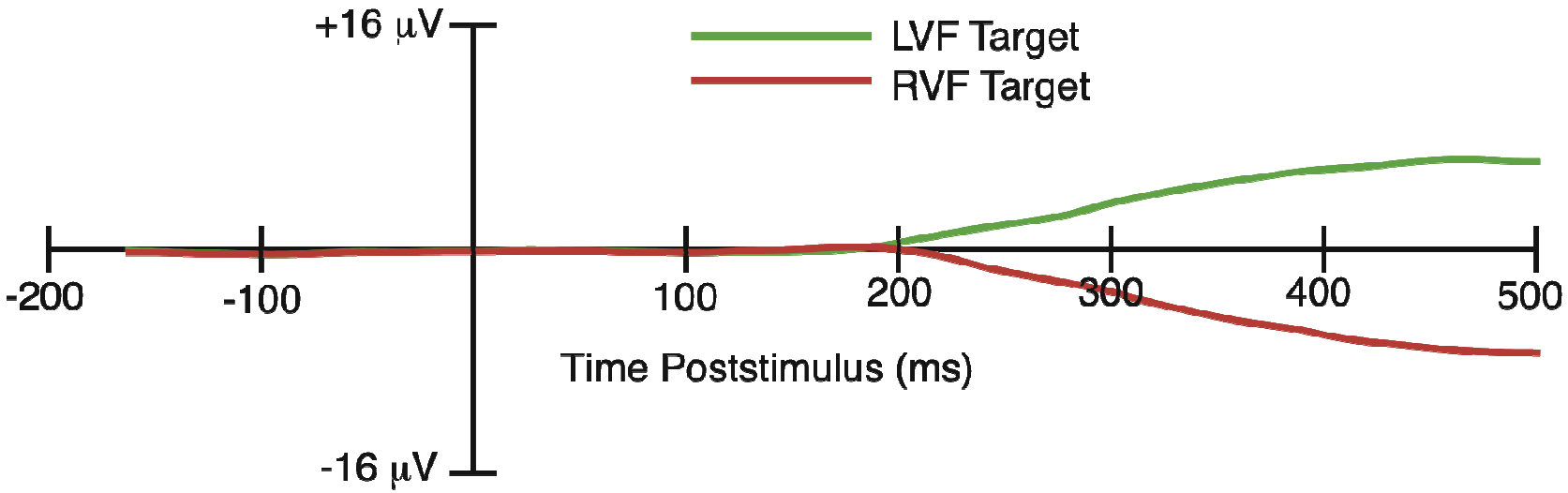
Artifact Rejection: Blinks



- Was blink rejection successful?
  - Look for polarity inversions
  - Baseline impacted by blinks in this example
  - Experimental effect not due to blinks

Artifact Rejection: Saccades

- Small saccades (< 1°) are hard to detect
- Two-tiered strategy:
  - Throw out trials with large, obvious eye movements
  - Compute averaged HEOG waveforms for L and R stimuli
  - Throw out subjects with residual HEOG > some threshold



Artifact Correction

- Goal: Estimate contribution of artifact at each EEG channel and subtract it
  - Fairly easy to compute propagation factors
- Problem #1: Signal at EOG electrodes contains non-artifact activity as well as artifact activity
  - The most common technique (Gratton et al., 1983) "overcorrects" and distorts the scalp distribution of the ERP components
- The best approaches use more sophisticated ways of estimating the actual ocular activity
  - Dipole source localization
  - Independent component analysis

Artifact Correction

- Problem #2: Eye movements and blinks are accompanied by sensory and motor potentials that are not removed by correction techniques
  - This can be a problem if blinks or saccades are triggered by the stimulus in a time-locked manner
- Problem #3: Eye movements and blinks change the sensory input
  - This can confound many experiments, especially experiments using peripheral stimuli
- Recommendation: Use rejection unless correction is absolutely necessary
  - And think about the effects of the correction procedure

Next Thursday in the LAB!

- We will actually try to see how an EEG signal looks like!

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