Evoked Potentials: Modalities and Noise Reduction

Based on course book sections 4.1 - 4.3.4

Juha Raitio
juha.raitio@hut.fi

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Outline

- Evoked potentials (EP)
- Recording EPs
- Analyzing EPs
- EP modalities
- Processing of EPs
  - Characteristics and assumptions on noise
  - Noise reduction by ensemble averaging
    - Homogeneous ensembles
    - Inhomogeneous ensembles
- Summary

Evoked potentials (EP) - short introduction

- EPs are brain activity that occurs as response to sensory stimulation of nervous tissues
- Commonly used stimulation is auditory or visual
- Recorded using electrodes on the scalp
- Responses are weak transient waveforms of electrical potentials
- Analyses of waveform morphology potentially provide information e.g. on
  - sensory pathways abnormalities
  - localization of lesions affecting the pathways
  - disorders related to language and speech
- Many uncontrollable factors that influence response waveform morphology

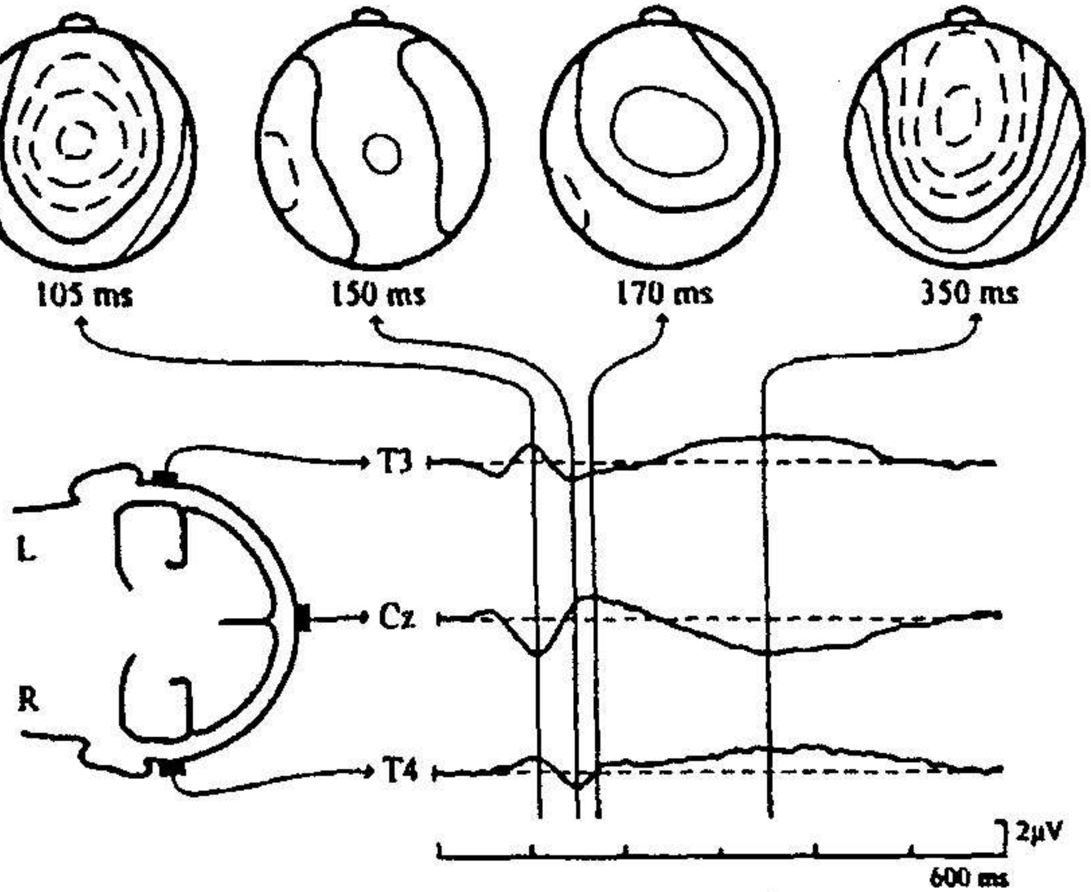
Propagation of evoked potentials

1. Stimulus elicits electrical impulses in sensory nerve cells
2. Impulses propagate along nerve fibers in the brain
3. Complex structures of cortex amplify and slow down the impulses
   - Amplitudes of brains stem responses are order of 1/10 of cortical responses
   - Inter peak latencies are a few milliseconds in brain stem, but over 100 ms in late cortical responses

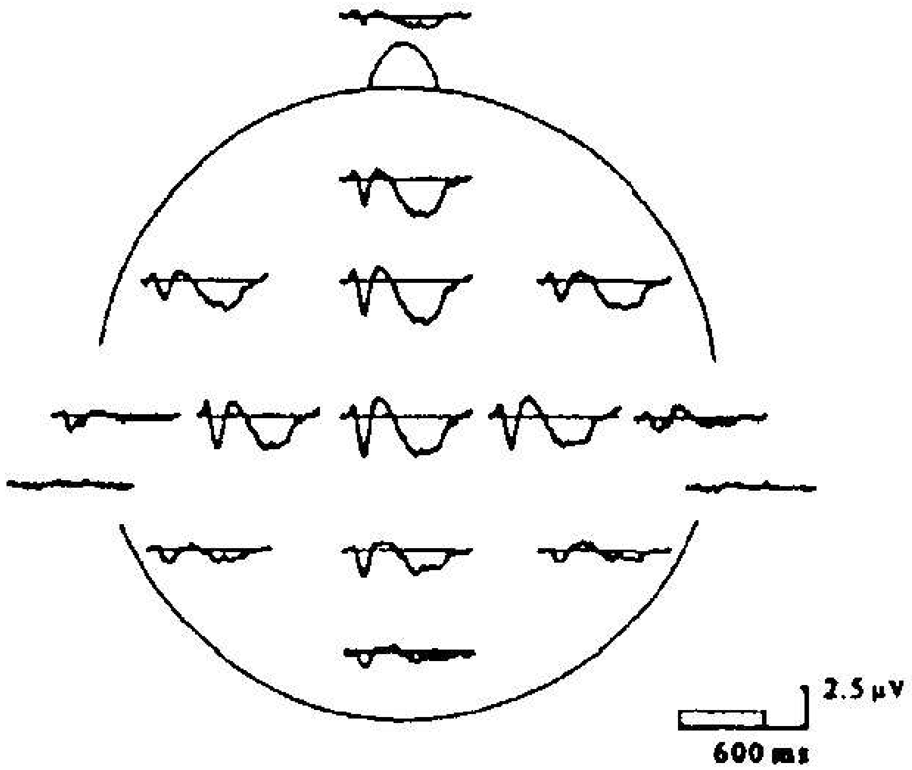
- EPs have very low amplitude $(0.1 - 10\mu V)$
- EEG is seen as loud noise (amplitude $10 - 100\mu V$)

Recording of evoked potentials - general

- EPs are recorded from the scalp similarly to EEG recording



- Electrodes view large areas and thus have rather desynchronized view of impulses
- Multi-channel recording views spatial distribution of EPs



Waveform morphology - transcription

- Peak component of response waveform is referred to by P (positive amplitude)
- Trough component of response waveform by N (negative amplitude)
- Appended number reflects latency in milliseconds e.g.
  - P300 is signifies positive peak 300 ms after stimulus
- If less than 10, appended number reflects temporal order e.g
  - N3 implies that third waveform component has negative amplitude

Analyses of evoked potentials - general

- Characteristic measures of response waveforms are extracted from recordings
- Measurements are compared to normative values to discriminate neurological impairment
  - analyses of individual channels with respect to time and amplitude waveform properties
  - multi-channel analyses may provide additional information on location of impairment e.g. epileptic focus
  - analyses per the age group, as normative values are strongly dependent on age

Auditory evoked potentials (AEP)

- Typically generated in response to short sound waves e.g. 10 clicks per second
- Recorded by electrodes behind ears and at vertex
- Reflects how neural information propagates from acoustic nerve to the cortex
- Response is divided into intervals for analyses purposes
  1. brainstem response
  2. middle cortical response
  3. late cortical response
- Applications
  - diagnosing hearing losses and brainstem disorders
  - monitoring anesthesia
  - monitoring interoperability during brain surgery

Somatosensory evoked potentials (SEP)

- Generated as response to electrical stimulation of peripheral nerve, from arm or leg
- Recorded by electrodes over motor-sensory cortex
- Provides information on nerve conduction functionality via spinal cord to cortex
- Applications
  - identifies blocked or impaired conduction in sensory pathways
  - monitoring interoperability during spine surgery

Visual evoked potentials (VEP)

- Response to visual stimuli - pattern reversal or flashing
- Recorded over visual cortex with reference electrode at vertex
- Characterized by long latency, high amplitude
- Reflects functionality of visual pathway
- Applications
  - diagnosing ocular and retinal disorders
  - detecting visual field defects and optic nerve pathology

Evoked potentials and cognition

- Potentials evoked by cognitive tasks such as recognition of sound stimuli
- Very long latencies compared to exogenous (AEP, SEP, VEP) responses
- Characterized by P300, which is related to the time required for memory updating

Noise characteristics

- Main source of noise is the spontaneous background EEG activity
- Minor sources that has to be taken into account are non-cerebral
  - eye blinks, eye and lid movements
  - muscular activity, heart
  - 50/60Hz interference, instrumentation noise, poor electrode attachment

Noise reduction by ensemble averaging

- EPs are known to be synchronized to stimulus presentation
- Noise occur in more random fashion than EPs
- The approach is to cancel the noise by repeated time-synchronized experiments

Ensemble averaging - notation

- Electrical potential on scalp is measured N times with fixed interval

$$x(n), \quad n = 0, \ldots, N-1 \tag{1}$$

or

$$\mathrm{x}_i = \begin{bmatrix} x_i(0) \\ x_i(1) \\ \vdots \\ x_i(N-1) \end{bmatrix} \tag{2}$$

- Sampling is repeated for M stimuli to form an ensemble

$$\mathrm{X} = [\mathrm{x}_1 \quad \mathrm{x}_2 \ldots \mathrm{x}_M] \tag{3}$$

Averaging of homogeneous ensembles - model

- Observed response x_i is assumed to be composed of evoked signal s and additive random noise v_i

$$\mathrm{x}_i = \mathrm{s} + \mathrm{v}_i, \tag{4}$$

where

$$\mathrm{s} = \begin{bmatrix} s(0) \\ s(1) \\ \vdots \\ s(N-1) \end{bmatrix} \quad \text{and} \quad \mathrm{v}_i = \begin{bmatrix} v_i(0) \\ v_i(1) \\ \vdots \\ v_i(N-1) \end{bmatrix} \tag{5}$$

- Noise is assumed to have zero mean $E\left[v_i(n)\right] = 0$
- Correlation function of noise $r_{v_i}(k) = E\left[v_i(n)v_i(n-k)\right]$ is assumed to decay to zero and be uncorrelated between recordings

Averaging of homogeneous ensembles - estimation

- Estimate of signal s is calculated by averaging the ensembles

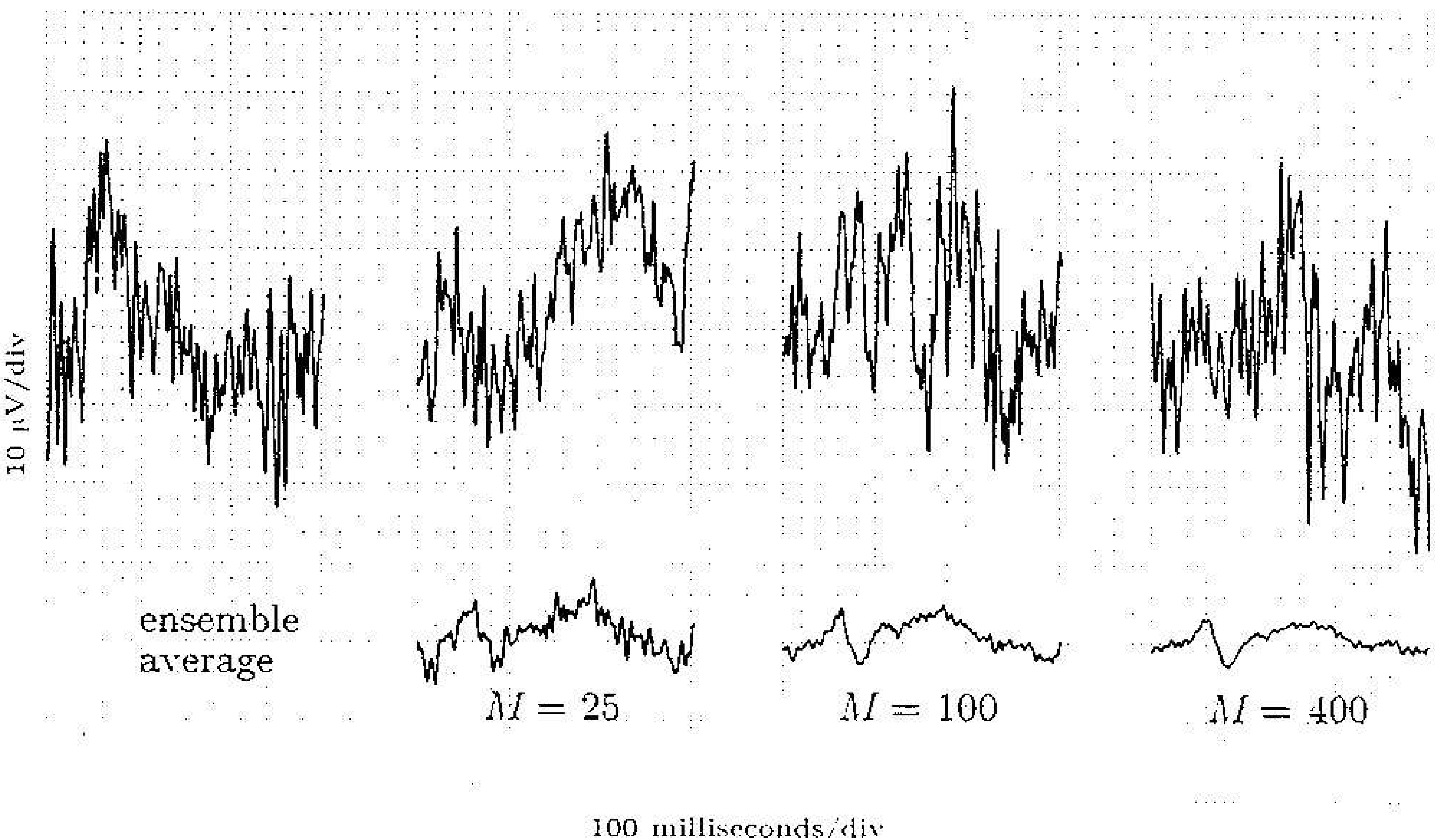
$$\hat{s}_a(n) = \frac{1}{M}\sum_{i=1}^{M} x_i(n) = s(n) + \frac{1}{M}\sum_{i=1}^{M} v_i(n), \quad \text{or} \tag{6}$$

$$\hat{\mathrm{s}}_a = \frac{1}{M}\left(\mathrm{x}_1 + \mathrm{x}_2 + \ldots + \mathrm{x}_M\right) = \frac{1}{M}\mathrm{X}1 = \mathrm{s} + \frac{1}{M}\mathrm{V}1, \quad \text{where} \tag{7}$$

$$\mathrm{V} = \left[\mathrm{v}_1 \quad \mathrm{v}_2 \ldots \mathrm{v}_M\right]$$

Averaging of homogeneous ensembles - properties of estimator

- $\hat{s}_a(n)$ is an unbiased estimator, since $E\left[\hat{s}_a(n)\right] = s(n)$
- $\hat{s}_a(n)$ is a consistent estimator, since $Var\left[\hat{s}_a(n)\right] = \frac{r_v(0)^2}{M} = \frac{\sigma_v^2}{M} \rightarrow 0$, as $M \rightarrow \infty$
- Noise magnitude is reduced by a factor $\sqrt{M}$


10 µV/div
ensemble
average
M = 25
M = 100
M = 400
100 milliseconds/div

Averaging of homogeneous ensembles - problems

1. Assumes zero-mean noise (can be resolved with better model)
2. Assumes noise is uncorrelated between measurements (can be resolved with better model)
3. Assumes noise is white and Gaussian (can be helped with other methods)
4. Assumes noise is uncorrelated from signal
5. Assumes constant waveform morphology, no changes in amplitude or shape, allows no missing responses
6. Assumes perfect time synchronization between stimulus and response

Ensemble averaging viewed as linear filtering

- Signal $x(n)$ is now formulated as concatenation of successive recorded potentials $x_1(n), \ldots, x_M(n)$

$$x(n) = x_{\lfloor \frac{n}{N} \rfloor + 1}(n - \lfloor \frac{n}{N} \rfloor N), \quad n = 0, \ldots, NM - 1 \tag{8}$$

- Ensemble averaging is viewed as filter with impulse response $h(n)$

$$h(n) = \frac{1}{M} \sum_{i=0}^{M-1} \delta(n - iN) \tag{9}$$

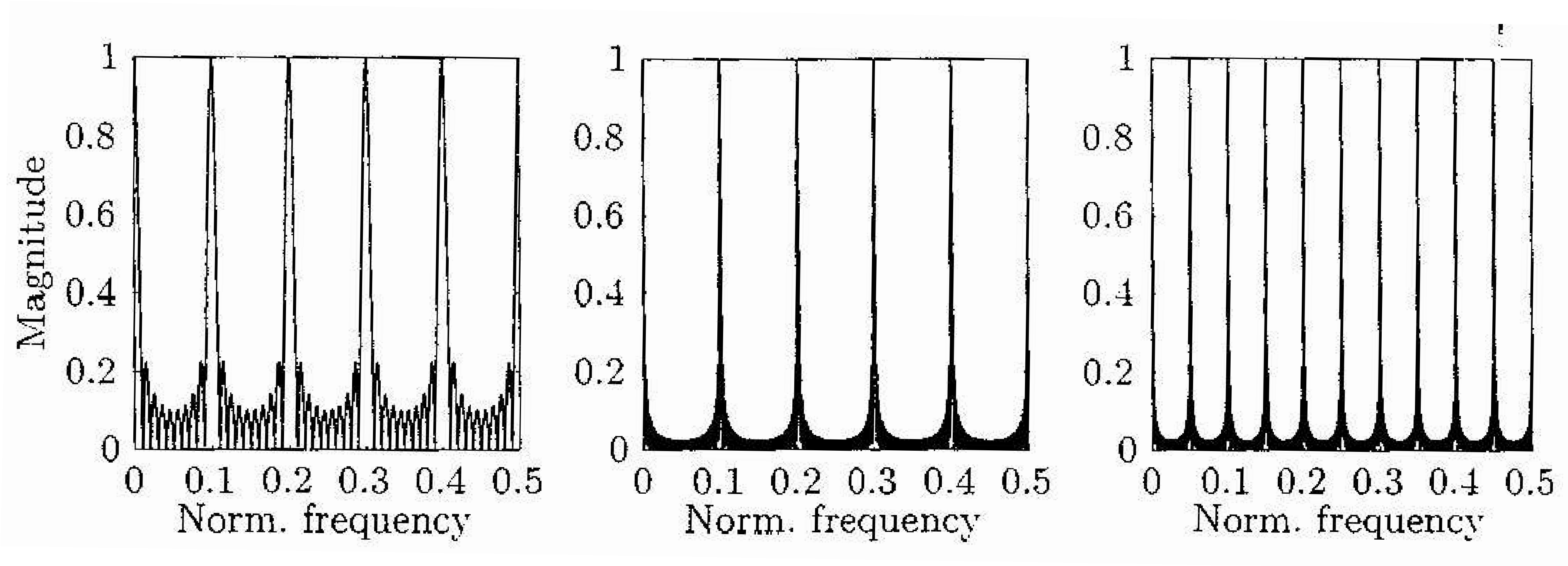
- Signal may be now modeled as

$$\hat{s}_a(n) = \sum_{l=-\infty}^{\infty} x(l)h(n-l) = x(n) * h(n) \tag{10}$$

Frequency response of ensemble averaging

- Frequency response may be used to analyze the properties of ensemble averaging
- Ensemble averaging implements a comb filter with period $2\pi/N$
- Magnitude response of the filter suppress noise inversely proportional to number of recordings M

- Examples of magnitude response for $(M, N) = (10, 10)$, $(40, 10)$ and $(40, 20)$



- Stimulus rate should be chosen so that noise rhythms do not interfere with signal

Exponential averaging

- Ensemble average may be computed recursively at observation M

$$\begin{aligned}\hat{\mathrm{s}}_{a,M} &= \frac{1}{M}\mathrm{X}_M \mathrm{1}_M \\ &= \frac{1}{M}(\mathrm{X}_{M-1}\mathrm{1}_{M-1} + \mathrm{x}_M) \\ &= \hat{\mathrm{s}}_{a,M-1} + \frac{1}{M}(\mathrm{x}_M - \hat{\mathrm{s}}_{a,M-1}), \quad \hat{\mathrm{s}}_{a,0} = 0 \end{aligned} \tag{11}$$

- Exponential averaging is generalization using weight factor α instead of $1/M$

$$\hat{\mathrm{s}}_{e,M} = \hat{\mathrm{s}}_{e,M-1} + \alpha(\mathrm{x}_M - \hat{\mathrm{s}}_{e,M-1}), \quad 0 < \alpha < 1 \tag{12}$$

- α determines how much weight is given to recent versus past values of signal
  - trade-off between low noise level and rapid tracking of amplitude changes

Exponential averaging - properties

- Implements a comb filter
- Unbiased estimator

$$E[\hat{s}_{e,M}(n)] = (1 - (1 - \alpha)^M)s(n) \tag{13}$$

- But not consistent, variance

$$Var[\hat{s}_{e,M}(n)] = \alpha^2 \frac{1 - (1 - \alpha)^{2M}}{1 - (1 - \alpha)^2} \sigma_v^2 \tag{14}$$

- Variance may be approximated using recursion

Averaging of inhomogeneous ensembles

- Noise variance in all EPs is not really constant as assumed previously
- In reality one has to deal with
  - occurrence of short-duration artifacts
  - variations in noise level between measurements
  - non-Gaussian noise distribution
- Occasional artifacts can be dealt with rejection of response in question
- General resolution is to weight responses by their quality

$$\hat{\mathrm{s}}_w = \mathrm{X}\mathrm{w}, \tag{15}$$

where w is to be wisely chosen

Noise reduction by weighted averaging - model

- All observations in ensemble are modeled as

$$\mathrm{X} = \mathrm{s}\mathrm{a}^T + \mathrm{V}, \text{ where} \tag{16}$$

  - s is the evoked signal
  - a assigns evocations individual amplitudes

$$\mathrm{a} = \begin{bmatrix} a_1 \\ a_2 \\ \vdots \\ a_M \end{bmatrix}$$

  - V is additive noise characterized by correlation matrix $\mathrm{R}_\mathrm{V} = E[\mathrm{V}^T\mathrm{V}]$

Weighted averaging - determining weights

- Weights w are now determined from the model

$$\hat{\mathrm{s}}_w = \mathrm{s}\mathrm{a}^T\mathrm{w} + \mathrm{V}\mathrm{w} \tag{17}$$

- Several methods for finding weights w exist
- Maximizing signal energy to noise requires least assumptions

$$\max_{\mathrm{w}} \mathrm{SNR} = \max_{\mathrm{w}} \frac{\mathrm{w}^T\mathrm{a}\mathrm{s}^T\mathrm{s}\mathrm{a}^T\mathrm{w}}{E[\mathrm{w}^T\mathrm{V}^T\mathrm{V}\mathrm{w}]} = \max_{\mathrm{w}} \frac{\mathrm{w}^T\mathrm{a}\mathrm{s}^T\mathrm{s}\mathrm{a}^T\mathrm{w}}{\mathrm{w}^T\mathrm{R}_{\mathrm{V}}\mathrm{w}} \tag{18}$$

- Assume normalized signal energy $\mathrm{s}^T\mathrm{s} = 1$ and fixed $\mathrm{w}^T\mathrm{R}_{\mathrm{V}}\mathrm{w} = 1$
- Best weights w^* are found by standard methods for constraint optimization

Determining weights - varying noise variance case

- Assume fixed amplitude for responses ($\mathrm{a} = a_0 1$) and individual noise variances

$$\mathrm{R_V} = \begin{bmatrix} \sigma_{v_1}^2 & 0 & \dots & 0 \\ 0 & \sigma_{v_2}^2 & \dots & 0 \\ \vdots & \vdots & \ddots & \vdots \\ 0 & 0 & \dots & \sigma_{v_M}^2 \end{bmatrix}$$

- Under these assumptions the best weights for ensemble averaging are

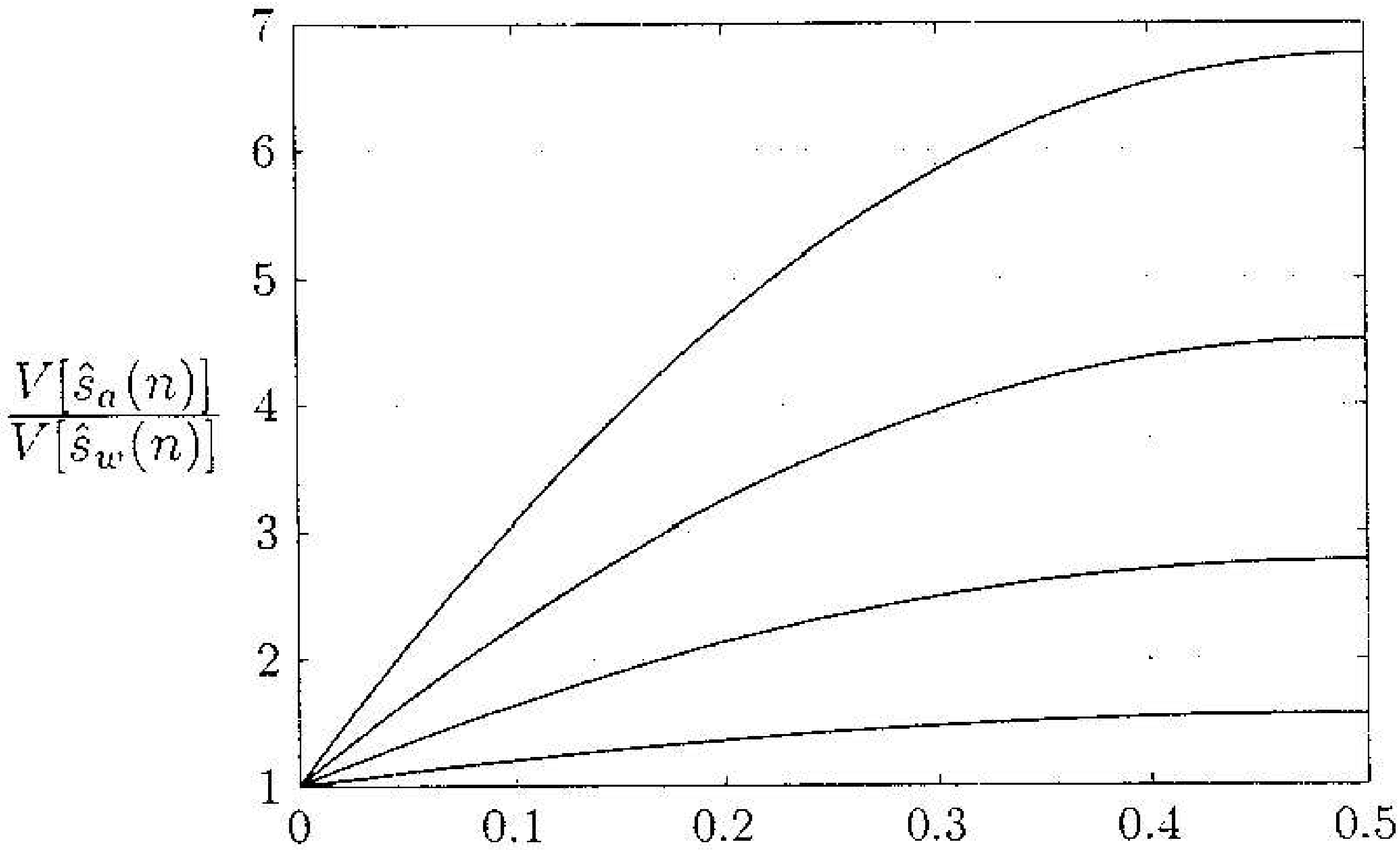
$$\mathrm{w}^* = \frac{\mathrm{R_V^{-1}} 1}{1^T \mathrm{R_V^{-1}} 1} = \frac{1}{\sum_{i=1}^{M} \frac{1}{\sigma_{v_i}^2}} [\frac{1}{\sigma_{v_1}^2} \; \frac{1}{\sigma_{v_2}^2} \; \dots \; \frac{1}{\sigma_{v_M}^2}]^T \tag{19}$$

- Resulting estimator is unbiased with variance $Var[\hat{\mathrm{s}}_w(n)] = \sum_{i=1}^{M} \frac{1}{\sigma_{v_i}^2}$

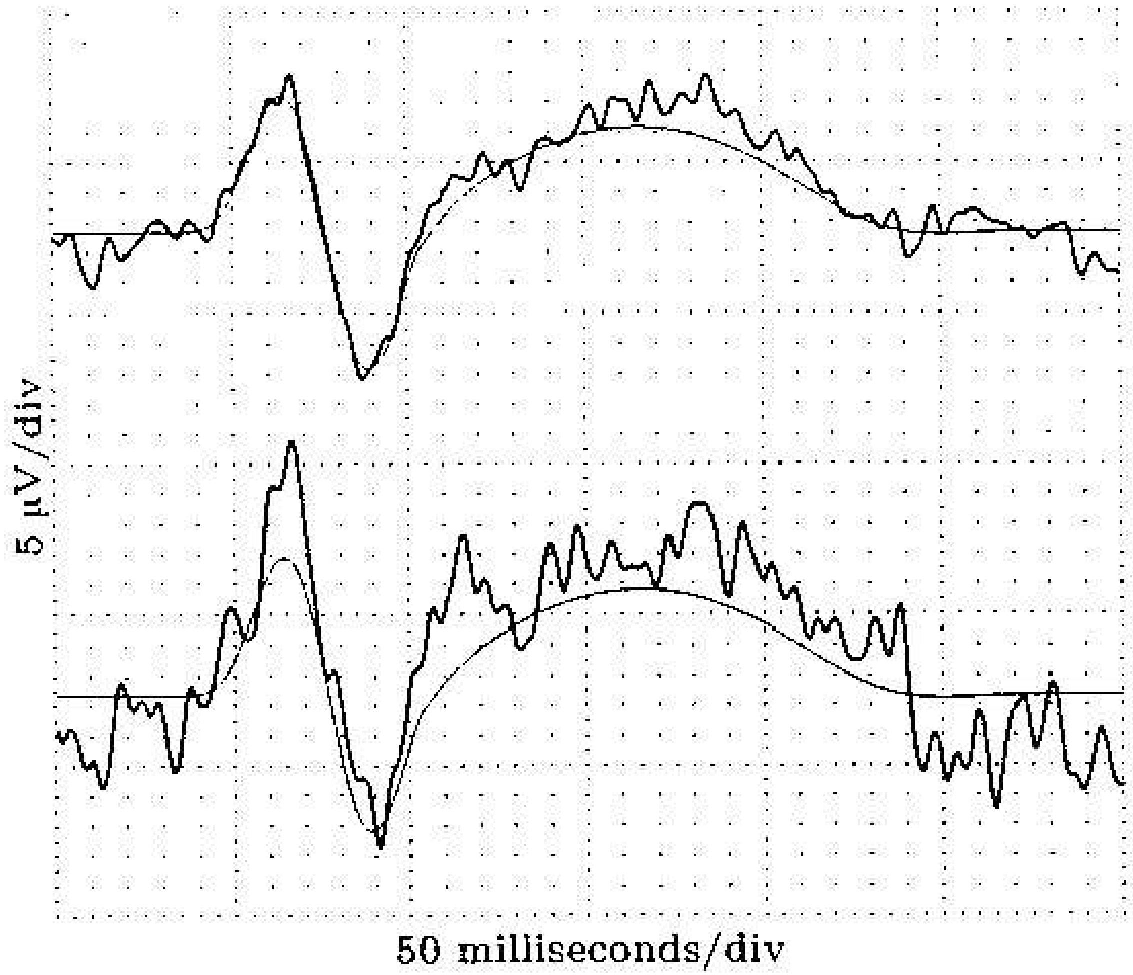
- Prestimulus intervals must be used for estimation of noise variances $\sigma_{v_i}^2$

Comparison of ensemble averaging and weighted averaging

- Ratio of estimator variances $Var[\hat{s}_a(n)]/Var[\hat{s}_w(n)]$ as inhomogeneity increases, curves computed for orders 2, 3, 4 and 5 of difference in ensemble variances



- Estimates of VEP by weighted and ensemble average when 20 of 100 responses have noise amplified of order 20



Summary

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- Commonly used stimulation is auditory or visual
- Responses are weak transient waveforms of electrical potentials
- Analyzing waveform morphology potentially provide information e.g. on
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  - localization of lesions affecting the pathways
  - disorders related to language and speech
- Many uncontrollable factors influence response waveform morphology
- Main source of noise is the spontaneous and loud background EEG activity

- Ensemble averaging aims to cancel any random noise
- Some assumptions of ensemble averaging are hard to satisfy and deal with
  - constant waveform morphology, no changes in amplitude or shape, none missing
  - perfect time synchronization between stimulus and response
- Ensemble averaging may be viewed as linear filtering
- Exponential averaging allows to control trade-off between low noise level and rapid tracking of amplitude changes
- Most general solution for using ensembles is to weight responses so that SNR is maximized
- Optimal weights maybe computed by constraint optimization