Evoked Potentials

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  - 4-4.3.7

- Introduction

- Modalities (4.1)
  - Auditory EP’s (AEP)
  - Visually EP’s (VEP)
  - Somatosensory EP’s (SEP)

- Noise reduction by ensemble averaging (4.3)
  - Homogenous samples (4.3.1)
  - Exponential averaging (4.3.3)
  - Inhomogenous ensembles (4.3.4)
    - Varying variance
    - Varying amplitude
    - Latency shifts

Introduction

- Electrical brain/ brainstem responses due to triggering by
  - Auditory signal (AEP)
  - Visual stimulation (VEP)
  - Somatosensory nerve stimulation (SEP)
The cerebral cortex
• EP are transient waveforms amplitude 0.1 - 10 uV
• Background EEG amplitude 10 – 100 uV
• Signal extraction by: Repetitive stimulation and noise reduction by ensemble averaging

Figure 4.1: Various morphologies of evoked potentials. The duration, amplitude, and morphology differ considerably from potential to potential.
Diagnostics example, VEP

- **Amblyopia**, or lazy eye, is a disorder of the eye that is characterized by poor or indistinct vision in an eye that is otherwise physically normal.

- The problem is caused by either no transmission or poor transmission of the visual image to the brain for a sustained period of dysfunction or during early childhood. Amblyopia normally only affects one eye.

- Amblyopia is a developmental problem in the brain. The part of the brain corresponding to the visual system from the affected eye is not stimulated properly, and develops abnormally.
Figure 4.2: (a) Auditory evoked potentials obtained at different positions on the scalp. (b) Scalp distribution maps of voltages, calculated at four different latencies, for three of the AEPs shown in (a). The heavy lines in the maps represent the zero voltage level. The dashed lines represent contours for negative voltages, and the thin lines represent contours for positive voltages. The maps were computed for latencies at which the waveforms either had a peak or a trough.
EP modalitites

Figure 4.3: Auditory evoked potentials. (a) Recording setup and (b) typical morphology of a brainstem auditory evoked potential.

Figure 4.4: Somatosensory evoked potentials. (a) Recording setup and (b) typical SEP morphology when the peroneal nerve of the leg is stimulated. Note the reversed amplitude plotting convention!
Figure 4.5: Visual evoked potentials. (a) Recording setup where pattern reversal is used as the stimulation method and (b) typical VEP morphology.

Noise characteristics

- EEG
- Non-EEG
  - Eye blinks
  - Eye and eyelid movement
  - Muscle activity
  - 50 Hz powerline interference
  - Poor electrode attachment

- Linear phase response bandpass filtering
  - BAEP, 25-2000 Hz
- EOG subtraction, ECG heart rate adapted stimulus
Noise reduction by ensemble averaging

Figure 4.7: Formation of an ensemble with EPs of somatosensory origin. The stimulus is elicited periodically at the instants indicated by the arrows. The signal $x_1$ contains 40 ms of data preceding the first stimulus (pre stimulus data), 40 ms of data following the first stimulus, and so on. Stimulation can, if required, be done aperiodically.

An ensemble with $M$ different potentials, each $x_i$ having $N$ samples:

$$x_i(n), i = 1, \ldots, M; n = 0, \ldots, N - 1$$

$$X = [x_1, x_2 \ldots x_M]$$

$$x_i = \begin{bmatrix} x_i(0) \\ x_i(1) \\ \vdots \\ x_i(N-1) \end{bmatrix}$$
Signal model: \( x_i \) is the evoked signal \( s \) + random noise \( v_i \)

\[
x_i(n) = s + v_i
\]

The noise is a stationary zero-mean process:

\[
E[v_i] = 0
\]

\[
r_k(n) = E[v_i(n) v_i(n-k)]
\]

\[
r_k(0) = E[v_i^2(n)] = \sigma_v^2
\]

\[
E[v_i(n) v_j(n-k)] = r_k(n) \delta(i-j)
\]

\[
\hat{s}_a = \frac{1}{M} (x_1 + x_2 + \ldots + x_M) = \frac{1}{M} \mathbf{X} \mathbf{1} = s + \frac{1}{M} \mathbf{V} \mathbf{1}
\]

Each component of \( s \):

\[
\hat{s}_a(n) = \frac{1}{M} \sum_{i=1}^{M} x_i(n)
\]

\[
E[\hat{s}_a(n)] = s(n)
\]

\[
V[\hat{s}_a(n)] = \frac{1}{M^2} \sum_{i=1}^{M} \sum_{j=1}^{M} E[v_i(n) v_j(n)] = \frac{\sigma_v^2}{M}
\]
Figure 4.8: Noise reduction by ensemble averaging. (a) Four of the $M$ different VEPs contained in the ensemble and (b) the resulting ensemble average based on different ensemble sizes.

Model assumptions/ violations

-Solutions

- Large slowly changing EEG components
  - Highpass filtering, decrease stimulus rate
- Non-stationary EEG activity
  - Weighted averaging
- Response (s) morphology varies between potentials
  - Latency shift estimation
Estimating ensemble variance

Sample by sample:

$$\sigma^2(n) = \frac{1}{M} \sum_{i=1}^{M} (x_i(n) - \hat{s}_{\Delta M}(n))^2$$

Split trial assessment (grouping odd- and even-numbered potentials):

$$\hat{s}_d(n) = \frac{2}{M} \sum_{i=1}^{M/2} x_{a,i}(n), l = 0,1$$

$$\Delta \hat{s}_a(n) = \hat{s}_d(n) - \hat{s}_{al}(n)$$

$$\text{var}[\Delta \hat{s}_a(n)] = \frac{4\sigma^2(n)}{M}$$

$$\hat{\sigma}^2 = \frac{M}{4} \hat{\sigma}^2_{\Delta s} = \frac{M}{4} \sum_{l=0}^{N/4} \left( \Delta \hat{s}_a(n) \right)^2$$

$$\rho = \frac{\hat{s}_d^T \hat{s}_a}{\sqrt{\hat{s}_d^T \hat{s}_d} \sqrt{\hat{s}_a^T \hat{s}_a}}$$
Exponential averaging

\[ \hat{s}_{x,M} = \frac{1}{M} X_M I_M \]

\[ = \frac{1}{M} (X_{M-1} I_{M-1} + x_M) \]

\[ = \hat{s}_{x,M-1} + \frac{1}{M} (x_M - \hat{s}_{x,M-1}), M \geq 1 \]

\[ \hat{s}_{x,0} = 0 \]

\[ \hat{s}_{e,M} = \hat{s}_{e,M-1} + \alpha (x_M - \hat{s}_{e,M-1}), M \geq 1 \]

\[ \hat{s}_{e,0} = 0 \]

Figure 4.12: The performance of exponential averaging for a sudden increase in amplitude occurring at \( M = 250 \).
(a) The amplitude of the trough of \( s_{e,M} \) for \( \alpha \) equal to 0.005, 0.01, and 0.0275, respectively, has been computed from (b) the signal estimate \( s_{e,M} \).
Weighted averaging

- The noise varies between potentials
- The amplitude varies between potentials

\[ \hat{s}_w = Xw \]

\[ w = \begin{bmatrix} w_1 \\ w_2 \\ \vdots \\ w_M \end{bmatrix} \]

\[ X = sa^T + V \]
\[ a = \begin{bmatrix} a_1 \\ a_2 \\ \vdots \\ a_M \end{bmatrix} \]
\[ R_v = E[V^TV] \]

Signal part in weighted average: \( sa^Tw \)
Noise: \( Vw \)

\[ \text{SNR} = \frac{w^Tas^Tsa^Tw}{E[w^TV^TVw]} = \frac{w^Tas^Tsa^Tw}{w^TR_vw} \]
Varying noise variance, indendent between potentials, fixed amplitude for the stimulus response:

\[
a = a_0 \mathbf{1}
\]

\[
\mathbf{R}_v = N
\begin{bmatrix}
\sigma_{v1}^2 & 0 & \cdots & 0 \\
0 & \sigma_{v2}^2 & \cdots & 0 \\
\vdots & \vdots & \ddots & \vdots \\
0 & 0 & \cdots & \sigma_{vM}^2
\end{bmatrix}
\]

\[
w = \frac{1}{N} \sum_{i=1}^{n} \frac{1}{\sigma_i^2}
\frac{1}{\sigma_{v1}^2}
\frac{1}{\sigma_{v2}^2}
\vdots
\frac{1}{\sigma_{vM}^2}
\]

\[
a^T \mathbf{R} v = \mathbf{w}^T \mathbf{a}
\]

**Figure 4.14:** (a) The weighted average \( s_w \_{100} \) and (b) the ensemble average \( s_{a_{100}} \) using the data of Figure 4.8, but with the amplitude of the added noise (i.e., the background EEG) scaled such that \( \sigma_{vA}^2 = 1 \) for 80 EPs and \( \sigma_{vA}^2 = 20 \) for the remaining ones. The noise-free EP is indicated by the thin line.
Varying signal amplitude with fixed noise variance:

\[
a = \begin{bmatrix}
    a_1 \\
    a_2 \\
    \vdots \\
    a_M
\end{bmatrix}
\]

\[
R_v = N\sigma_v^2 I
\]

\[
w = \frac{1}{a^\top a}
\]

\[
\hat{a} = X^\top \hat{s}_n
\]

Figure 4.15: Weighted averaging of AEPs recorded from two different subjects. Each diagram shows the results of four trials of each subject. The ensemble average and the weighted average are plotted with dotted and solid lines, respectively.
Latency shifts

Figure 4.19: The effect of latency shifts on the ensemble average. The shifts are introduced in a simulated, noise-free signal, and the size of the shifts are shown by the horizontal bars to the right. At the bottom, the resulting ensemble average $s_d(t)$ is shown together with the true signal $s(t)$ superimposed (thin line).

The model (white Gaussian noise) and the Woody algorithm:

\[
x_i(n) = \begin{cases} 
 v_i(n), & n = 0, \ldots, \hat{\theta}_i - 1 \\
 s(n - \hat{\theta}_i) + v_i(n), & n = \hat{\theta}_i, \ldots, \hat{\theta}_i + D - 1 \\
 v_i(n), & n = \hat{\theta}_i + D, \ldots, N - 1 
\end{cases}
\]

\[
\hat{\theta}_i = \arg \max_{\hat{\theta}_i} \left( \sum_{n=0}^{\hat{\theta}_i+D-1} x_i(n)s(n-\hat{\theta}_i) \right)
\]

\[
\hat{s}_i^{(0)}(n) = \hat{s}_i(n)
\]

\[
\hat{s}_i^{(1)}(n) = \frac{1}{M} \sum_{i=1}^{M} x_i(n + \hat{\theta}_i^{(1)})
\]

\[
\hat{s}_i^{(\beta)}(n) = \frac{1}{M} \sum_{i=1}^{M} x_i(n + \hat{\theta}_i^{(\beta)})
\]
Figure 4.22: The performance of the Woody method illustrated at different SNRs: (a) a high SNR, (b) an intermediate SNR, and (c) a low SNR. For each of the three SNRs, one of the EPs in the ensemble is displayed together with the corresponding ensemble average, obtained either before or after latency correction. The averages are based on an ensemble of 100 EPs.

Summary EP morphology estimation

- Homogenous samples (Eq. 4.33-4.34)
  \[
  \hat{s}_{s,M} = \hat{s}_{s,M-1} + \frac{1}{M} (x_M - \hat{s}_{s,M-1}), M \geq 1
  \]
  \[
  \hat{s}_{s,0} = 0
  \]

- Exponential averaging (Eq. 4.35)
  \[
  \hat{s}_{e,M} = \hat{s}_{e,M-1} + \alpha (x_M - \hat{s}_{e,M-1}), M \geq 1
  \]
  \[
  \hat{s}_{e,0} = 0
  \]

- Inhomogenous ensembles
  - Weighted averaging (4.3.4)
    - Varying variance (Eq. 4.67)
    - Varying amplitude (Eq 4.78)
  - Latency shifts (Eq. 4.125, 4.131)
  \[
  \hat{\theta}_i = \arg \max \left( \sum_{n=0}^{i-1} x_i(n) s(n - \hat{\theta}_j) \right)
  \]
  \[
  s_{s,i}^{(0)}(n) = \hat{s}_s(n)
  \]
  \[
  s_{s,i}^{(j)}(n) = \frac{1}{M} \sum_{i=1}^{M} x_i(n + \hat{\theta}_j)
  \]
  \[
  w = \frac{1}{\hat{a}^T \hat{a}}
  \]
  \[
  \hat{a} = X^T \hat{s}_s
  \]