HACETTEPE UNIVERSITY

FACULTY OF HEALTH SCIENCES

SYSTEMS ANALYSIS OF THE RELATION BETWEEN BRAIN'S SPONTANEOUS AND EVOKED ACTIVITIES

BIOPHYSICS PROGRAM

DOCTORAL DISSERTATION

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ABBREVIATIONS

a : Amplification factor

DFT : Discrete Fourier Transformation

EEG : Electroencephalogram

EP : Evoked Potential

FFT : Fast Fourier Transform

FSAEP : Filtered Selectively Averaged Evoked Potential

GEA : Anterior Ectosylvian Gyrus

HI : Hippocampus

IC : Inferior Colliculus

MG : Medial Geniculate Body

RF : Reticular Formation

S : Frequency stabilization factor

SAEP : Selectively Averaged Evoked Potential

SPL : Sound Pressure Level

TRFC : Transient Response-Frequency Characteristics

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ABSTRACT

In this study, a series of mathematical methods are applied alternativ-ely to the spontaneous activity and evoked potentials of the brain stem structures of the cat, such as IC and RF, in order to investigate the high frequency resonance phenomena in a large scale of frequencies up to 1000 Hz in the responses of the reticular formation and of the inferior colliculus. A complete realization of this objective is attained by comparing the spontaneous activity recorded immediately before stimulation with the single evoked potentials both in the frequency domain and in the time domain.

Studies are carried out on the epochs, which contain spontaneous activities (EEGs) recorded immediately before the stimulation and single evoked potentials (EPs), recorded from 8 chronically implanted cats during the waking stage. The stimulation consists of auditory step functions in the form of tone bursts of 5000 Hz and 90 dB (SPL). High-pass filtering with a cut-off frequency of 80 Hz provides high frequency analysis of the spontaneous and evoked activities of the RF and IC, and approximately 18 dB attenuation is obtained on alpha activity (8-15 Hz).

Frequency domain analysis of the spontaneous activity and evoked potentials is done as follows: (1) power spectral density function is obtained from the epoch of the spontaneous activity (EEG) recorded prior to the stimulation; (2) the single evoked potential of the same epoch is transformed to the frequency domain with the Fourier transform in order to obtain the instantaneous frequency characteristic of the studied brain structure; (3) the distribution of the amplitude maxima which are seen in the instantaneous

frequency characteristic is compared with the distribution of the peaks seen in the power spectral density function; (4) in order to describe frequency distribution as revealed by the power spectra and instantaneous frequency characteristics, the histograms are obtained by plotting the frequency peaks (and/or amplitude maxima) seen in the power spectra and in the instantaneous frequency characteristics. During the frequency domain analysis of the epochs, frequency stabilization of the response upon stimulation is observed.

In the time domain, the direct comparison of the voltages of maximal amplitudes of the frequency components existing in the on-going activity and in the evoked potential is done as follows: (1) selectively averaged evoked potentials (SAEPs) are obtained from the recorded EPs ; (2) amplitude frequency characteristics are computed from the SAEPs by means of Fourier transform; (3) the single EEG-EP sweeps are theoretically pass-band filtered with adequate band limits determined according to the selectivities revealed by the amplitude characteristics; (4) the EEG and EP components obtained in this way are compared with regard to the amplification in the population response upon the application of the stimulus. The results of this analysis show strong resonances in a large scale of frequencies up to 1000 Hz in the responses of the RF and IC. The amplification factor related to resonance phenomena has probabilistic nature.

The selectively averaged evoked potentials of the RF and IC which are obtained from the freely moving cats during the waking stage show short latency waves. The most prominent short latency wave seen in the SAEPs of the IC is a positive wave with a 5-5.5 msec latency. Similarly SAEPs of the

ÖZET

Bu çalışmada, kedi beyin kökünün formatio reticularis ve colliculus inferior gibi bölgelerinden kaydedilen spontane aktivite ve uyarılma potansiyellerine değişik matematiksel yöntemler zinciri uygulayarak, bu bölgelerin 1000 Hz e kadar olan frekanslardaki cevaplarında yüksek frekanslı rezonans olayları araştırılmıştır. Bu amacın tam olarak gerçekleştirilmesi uyarmadan hemen önce kaydedilen spontane aktivitelerin uyarmadan sonra kaydedilen uyarılma potansiyelleri ile hem frekans alanında hem de zamansal alanda karşılaştırılmaları ile mümkün olmaktadır.

Çalışmalar, kronik elektrodlu 8 kediden uyanık konumunda kaydedilen, uyarmadan önceki spontane aktivite ve uyarmadan sonraki uyarılma potansiyelleri kayıtları üzerinde yapılmıştır. Uyarma sinyali olarak adım fonksiyonları şeklindeki 5000 Hz ve 90 dB (SPL) lik ses sinyalleri kullanılmıştır. Kesme frekansı 80 Hz olan yüksek geçiren bir filtre yardımı ile reticular formation ve inferior colliculus'un spontane aktivite ve tek uyarılma potansiyelleri kayıtları filtrelenmiş, böylece bu kayıtların yüksek frekans analizi mümkün olabilmiştir. Bu filtreleme işlemi sonucunda alfa bandında (8-15 Hz) yaklaşık olarak 18 dB lik bir zayıflama elde edilmiştir.

Spontane aktivite ve tek uyarılma potansiyelleri kayıtlarının frekans alanı analizleri şu şekilde yapılmaktadır: (1) uyarmadan önce kaydedilen spontane aktivite kaydından güç spektrumu elde edilir; (2) aynı kayıdın tek uyarılma potansiyeli kısmından Fourier dönüşümü yardımı ile çalışılan beyin bölgesinin ani (instantaneous) frekans karakteristiği hesaplanır; (3) ani frekans karakteristiğinde görülen genlik zirvelerinin dağılımı güç

spektrumu zirvelerinin dağılımı ile karşılaştırılır; (4) güç spektrumları ve ani frekans karakteristiklerindeki zirvelerin frekanslarının dağılmasının gösterilmesi, güç spektrumları ve ani frekans karakteristiklerindeki frekans zirvelerinin ayrı ayrı çizilmesiyle elde edilen histogramlar yardımıyla yapılır. Kayıtların frekans alanı analizleri, cevap sinyallerinin uyarma sonucunda frekans kararlılığı (frequency stabilization) gösterdiğini ortaya çıkarmıştır.

Zamansal alanda spontane aktivite ve tek uyarılma potansiyelleri bileşenleri voltajlarının maksimum genliklerinin doğrudan karşılaştırılması aşağıda gösterildiği gibi yapılmaktadır: (1) kaydedilen tek uyarılma potansiyellerinden seçmeli ortalama yöntemi ile ortalama uyarılma potansiyelleri elde edilir, (2) Fourier dönüşümü yardımıyla ortalama uyarılma potansiyellerinden genlik frekans karakteristikleri hesaplanır; (3) tek spontane aktivite ve uyarılma potansiyelleri kayıtları, genlik frekans karakteristiklerinde görülen genlik zirvelerine uygun olacak şekilde seçilen teorik band geçiren filtreler yardımı ile filtrelenir; (4) spontane aktivite ve tek uyarılma potansiyelleri bileşenleri, uyarmaya karşılık cevap potansiyellerinde görülen amplifikasyon tanımına göre karşılaştırılmaktadır. Zamansal alanda yapılan bu analizler sonucunda, reticular formation ve inferior colliculus'un cevap potansiyellerinde 1000 Hz e kadar uzanan çeşitli frekanslarda kuvvetli rezonans olayları görülmüştür. Kuvvetli rezonans olaylarında gözlenen amplifikasyon katsayıları ihtimali davranış göstermektedirler.

Uyanık konumunda, serbestçe hareket edebilen kedilerin formatio reticularis ve colliculus inferior bölgelerinden elde edilen seçmeli ortalama uyarılma potansiyellerinde kısa latensli dalgalar bulunmaktadır. Colliculus inferior bölgesinden elde edilen seçmeli ortalama potansiyellerinde görülen en kısa latensli dalga, 5-5.5 ms de oluşan belirgin bir positif dalgadır. Aynı şekilde formatio reticularis bölgesinden elde edilen seçmeli ortalama potansiyelleri, 4.5-5 ms de belirgin bir negatif dalga göstermektedirler. Reticular formation ve inferior colliculus'un ortalama uyarılma potansiyellerinden elde edilen genlik frekans karakteristiklerinde 1000 Hz e kadar uzanan çeşitli yüksek frekans bandları ortaya çıkmaktadır. Reticular formation ve inferior colliculus'un ortalama genlik frekans karakteristikleri yüksek frekans bölgelerinde oluşan değişmez seçici bandları (consistent selectivities) ortaya çıkarmaktadır. Bu yüksek frekanslı değişmez seçici bandlar reticular formation'da; 60 Hz, 110 Hz, 240 Hz, 320 Hz ve 410 Hz, inferior colliculus'ta; 80 Hz, 160 Hz, 210 Hz, 300 Hz ve 700 Hz dir. Reticular formation'ın 500 Hz ve 700 Hz deki genlik maksimumları ortalama genlik frekans karakteristiğinde daha az belirgin zirveler olarak ortaya çıkmaktadır.

1.1 INTRODUCTION

The discovery of the brain's low-level electrical activity has led to the establishment of a neurophysiological speciality known as electroencephalography, and this spontaneous electrical activity of the brain (which can be recorded either superficially or through the surgically implanted deep electrodes) was called electroencephalogram (EEG). Following the technological advances, which provided low-noise, high-gain amplifiers and suitable recording techniques, it became possible to obtain reliable EEG patterns. The EEG of different nuclei of the brain (or that recorded from the various locations on the scalp by means of surface electrodes) under different behavioral or pathological conditions and in different sleep stages reveal different kinds of rhythmic activities which, on analysis, show several characteristic peaks of energy in their frequency spectra. Consequently, some frequency bands, such as delta (0.5-3 Hz), theta (3-8 Hz), alpha (8-13 Hz), beta (13-35 Hz), have been assumed conventionally in order to identify the various types of EEG patterns (Brazier, 1968).

One of the most widely used experimental EEG technique involves the study of responses evoked by sensory stimuli. If these stimuli are presented through their natural receptors (e.g. the eyes and the ears), much can be learned about the functional anatomy of the nervous system. Direct or peripheral stimulation (electrical, optical, acoustical, etc.) of the sense organ induces detectable electrical changes in the electrical activity of the sensory pathway or any related structure of the sensory system. These induced potentials which form definite response pattern characteristics of specific system in the sensory pathway are called Evoked Potentials (EP). Averaging techniques are often used to detect evoked responses in the EEG. The EPs obtained in response to identical successive stimuli are averaged to obtain Averaged Evoked Potential (AEP).

The method of averaged evoked potentials (AEPs) is common in the study of electrical activity of the brain. Usually the averaged evoked response is described in terms of several arbitrarily defined components such as peak (wave) latencies, wave magnitudes, etc. These arbitrarily defined components depend generally upon the location of the recording electrode, behavioral state or sleep stage of the subject under study and upon nature of the stimulating signal. Therefore, the interpretation of these arbitrarily defined components is very difficult and generally does not allow comparisons between evoked potentials of different brain structures or between evoked potentials obtained under different experimental conditions (Başar, 1976).

In the previous years, a set of systems theoretical analysis methods such as method of Transient Response-Frequency Characteristics (TRFC) (Başar and Weiss, 1968), the method of ideal filtering (Başar and Ungan, 1973), selective averaging (Başar et al., 1975a) and power spectra as proposed by Welch (1967) were presented and used successfully in the dynamics of brain rhythmic and evoked potentials. These methods, which are more useful amplitude characteristics and which are clearly revealed by mean value curves (in spite of information reduction), the consistent maxima or the consistent selectivities. In other words, the probability for maximal signal transfer through the consistent selectivity channels mentioned above is always existent in all experimental conditions, during the waking stage.

Various authors describe the relationship between the evoked potentials and the spontaneous activity of the brain. Anninos (1973) states that the spontaneous activity (i.e., the level of the activity which is unrelated to specific sensory event) carries no information, on the other hand this activity may be depressed or enhanced or generally modulated by sensory signal. Acording to Harth et al. (1970) neural activity is viewed as a stochastic point process, in which information resides in the modulation of a background of spontaneous activity. According to one interpretation, the spontaneous activity is the "carrier that is without information until modulated" (Perkel and Bullock, 1968). Başar et al. (1975b) describe the relationship between the brain evoked potentials and the spontaneous activity from a systems analytical point of view: "Since the brain is a system which shows spontaneous electrical activities, it is expected that the signal evoked in the brain by external stimuli must undergo some interactions with these spontaneous activities. Amplitude characteristics of a system containing intrinsic oscillations must contain responses which originate through these interactions. Resonance phenomena can be expected when an oscillatory physical or biological system is forced by external input signals."

comparison of absolute magnitudes of EEG and evoked potential (EP) components. Comparison of absolute magnitudes of EEG and evoked potential (EP) components can be attained by the application of adequately chosen pass-band theoretical ideal filters to the single evoked potentials and the spontaneous activity recorded prior to each stimulus of the brain nuclei under study. These methods will be described in the section of material and methods.

Major emphasis will be given to the high frequency resonance phenomena in the brain stem structures (such as IC and RF). The preliminary results, which confirm the existence of the high frequency mechanisms, were observed previously during the studies of dynamics of rhythmic and evoked potentials of the inferior colliculus and of the reticular formation of the cat brain (Başar et al., 1975b; Başar, 1974). The averaged evoked potentials (AEPs) of the reticular formation and of the inferior colliculus revealed marked short latency waves (latencies between 3-12 msec). An introductory report, which showed the existence of the strong resonances in the various frequency bands up to 1000 Hz of the RF was presented by (Başar, Gönder and Ungan) (1976a). In the present work the recordings from the RF and IC, which were taken during the periods of no stimulation (EEG) and immediate auditory stimulation (EP) will be investigated. High frequency analysis, up to frequencies of 1000 Hz in the electrical activities of the RF and IC, will be performed both in the frequency domain and in the time domain. The methodology for the comparison of brain's spontaneous activity and evoked potentials will be described in section 2.3.

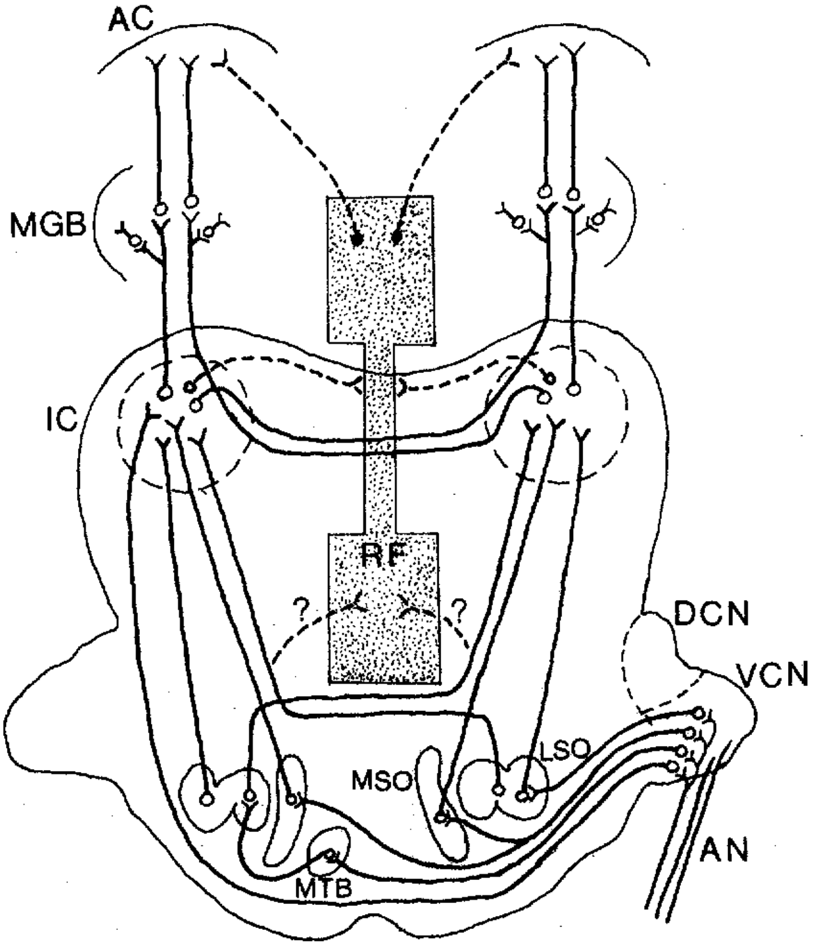


Fig. 2 Schematic drawing of the principal ascending connections of the auditory system with respect to the acoustic nerve of the right side (adopted from Harrison and Howe, 1975). Possible connections of the reticular formation are shown by dashed lines. AC: acoustic cortex; MGB: medial geniculate body; IC: inferior colliculus; RF: reticular formation; MSO: medial superior olivary nucleous; LSO: lateral superior olivary nucleous; MTB: medial nucleous of the trapezoid body; DCN: dorsal cochlear nucleous; VCN: ventral cochlear nucleous; AN: acoustic nerve.

2.1.2. Experimental Set-up and Procedures

A block diagram of the equipment used for generating the acoustic stimulation signals as well as for recording and evaluation of the data is shown schematically in Fig. 3. The stimulus signals were in the form of tone bursts (acoustical step functions) of 5000 Hz and 90 dB (SPL) which were timed and triggered with the Varian 620/L computer which is the most important device for control and evaluation in the experimental set-up. The rise time of the step function was sharp enough to cover the dynamic ranges of brain nuclei under study.

The program called RDSD was written for the Varian 620/L computer with 16 K core memory, sixteen channel analog-to-digital converter, two channel digital-to-analog conversion, eight status control input, eight control output, a high capacity disc memory, a digital magnetic tape recorder, a storage scope display and teletype. This program generated the trigger signals and also collected the data. The timing of the sampling process was controlled also by this program. Trigger signals were obtained from the control output of the computer with a random inter-stimulus interval not less than 16 sec. The pulse adjustment device was used to maintain a delay between the stimulus on-set and the beginning of data recording which allowed for recording the EEG just prior to the stimulation. The duration of the stimulus was also adjusted by this device. When triggered, the function generator (Data pulse 410) elicited sound signals with a duration of 3 sec over a power amplifier and loudspeaker.

Cats were freely moving in a comfortable cage placed in a fully sound proof and electrically isolated echofree room. The movements and the different waking and sleep stages of the cat were monitored using a closed circuit television scope. EEG time histories of the cat brain nuclei under study were preamplified and recorded with the help of the EEG recorder (Schwarzer Encephysioscript E1230).

Preamplified electrical activity of the brain nucleus under study was first high-pass filtered then further amplified by a Tektronix 122 differential preamplifier, and fed to the analog input of the computer. The filter had a high frequency response of 2000 Hz, low frequency response of 80 Hz for the EEG recorded from IC and RF. High-pass filtering with a cut-off frequency of 80 Hz provided high frequency analysis of IC and RF and approximately 18 dB attenuation was obtained on alpha activity (8-15 Hz).

Recordings were taken during the periods of no stimulation (EEG) and immediate auditory stimulation (EP). Both EEG and EP records were sampled with the same sampling interval over the same recording period. EEG and EP records from RF and IC the sampling interval was 0.1 msec and recording period was 102.4 msec. Thus, a Nyquist rate of 5000 Hz was attained as the upper limit for the data processing.

Each record, which contained a pair of EEG and EP, was first stored in core memory then transfered to the digital magnetic tape controled by the computer. Five files, each containing fifteen records, were taken during an experiment. Diverse computational methods were applied to the recorded data after the experimental session. These methods will be described in the next section.

EEG and EP recordings were obtained from the brain nuclei under study during the waking stage only. If there was a stage change or a continuous movement artifact during the recording session, the recording was stopped temporarily by the switch connected to the status input of the computer. However, this measure alone could not prevent the recording of short transition states and instant movement artifacts. This problem was solved most effectively by *a posteriori* selective averaging (see section 2.2.2). For monitoring purposes conventional average evoked potentials were also obtained by on-line averaging technique with the second computer (Fabri-Tek Instruments FT-1072) during the recording sessions. The FT-1072 computer served also for the monitoring of all the results obtained with the Varian computer and to drive the X/Y recorder (HP-7005 B) to plot all the evaluated data.

2.2. Mathematical Methods

2.2.1. Power Spectral Analysis

In order to obtain power spectral density functions, fast Fourier transform (FFT) techniques were used. FFT is an algorithmic process for calculating with great computational efficiency the Fourier coefficients of a given discrete time series. A method proposed by Bingham (1967) was used to estimate power spectra. This method consisted of the following steps which were accomplished by means of the computer. Power spectral analysis was applied to all the EEG time histories which were recorded on a magnetic tape during the experiment.

1. The mean of the measured values was subtracted prior to analysis.
2. A data window of the following form was applied to each data over a period of T.

$$\frac{1}{2}\left(1-\mathrm{Cos}\ 2\pi\frac{t}{T}\right) \qquad 0 \leqq t \leqq T$$

3. Windowed data were Fourier transformed using a FFT algorithm and Fourier periodogram of this modified time series was obtained.
4. Smoothed power spectrum was obtained by filtering the periodogram itself to improve the statistical stability of the power estimate.

2.2.2. Selective Averaging

Since the spontaneous activity of the brain has a nonstationary character, the conventional averaging method is not the ideal method for the investigator interested in analyzing evoked responses in brain states during almost invariable experimental conditions. In order to eliminate the disadvantages of the conventional averaging method, which are due to the nonstationarity of EEG, a posteriory selective averaging method was presented by Başar et al. (1975a). The method presented permits the experimenter to select single evoked potentials after the experiments and to eliminate perturbations and stage changes which could occur during the recording of evoked potentials.

An averaging procedure can be effective if the stationarity of background EEG is maintained and identical responses are evoked by repeated presentations of the same stimulus. However, neither of these conditions seem fully to be met for EEG and evoked potentials generally. A posteriori selective averaging method enables the investigator to select evoked potentials during defined waking and sleep stages and allows averaging in almost stationary periods. As far as the amplitude characteristics are concerned, always better results are obtained by taking into account only the selected epochs (Başar et al., 1975a, b, c).

Selectively averaged evoked potentials are obtained after the recording sessions. The individual sweeps or EPs are averaged, taking into account the following criteria:

1. the EPs, where a movement artifact is observed and
2. the EPs, during which a transition from one stage to another is observed, are discarded (see Başar et al., 1975a; Ungan and Başar, 1976; Başar, 1976; Başar et al., 1975d for more information on the selective averaging).

2.2.3. Method of Transient Response- Frequency Characteristics

In order to obtain frequency characteristics of the systems under study, the step responses (transient averaged or single evoked potentials) are transformed to the frequency domain with Laplace transform.

The general systems theory states that any linear system can be fully described in the time domain or in the frequency domain (with frequency characteristics). All information concerning the frequency characteristics of a linear system is contained in the transient response of the system,

2.2.4. Theoretical Ideal Filtering Method

Ideal filters are defined as transmission systems which (within a pre-determined band of frequencies) transfer the input signal without any change in amplitude and with a fixed (independent of frequency) time shift. Outside this band, they have zero transmission (or vice versa, depending on whether the filter has a band-pass or a band-stop characteristic). Theoretical filtering method gives the possibility to choose amplitude and phase frequency characteristics of the filter separately. Therefore, the investigator can apply ideal filters without phase shift. The detailed theory and application of ideal filtering were given by Başar and Ungan (1973), Başar et al. (1975a) and Başar (1976). In the present discussion the practical realization of ideal digital filtering will be emphasized.

Consider a signal $x(n\ \Delta t)$, where $x(n\ \Delta t)=0$ for $n<0$, so that the signal consists of a sequence of numbers $x(0)$, $x(\Delta t)$, $x(2\ \Delta t)$, etc. where Δt is the sampling interval. A linear digital filter can now be defined via the principle of superposition as follows:

$$y(n\ \Delta t)=\sum_{m=0}^{n} g_F(n\ \Delta t-m\ \Delta t)\ x(m\ \Delta t) \qquad (2.3)$$

Numerically, the output sequence $y(n\ \Delta t)$ is a weighted sum over all previous values of the input sequence. The weights $g_F(n\ \Delta t)$ define the filter.

An algorithm based on the discrete Fourier transformation (DFT) was used to obtain theoretical filtering of signals. This method is almost always computationally more efficient than the direct convolution (2.3), because the practical application of this algorithm makes use of the fast Fourier transform (FFT). Since multiplication of Fourier transforms corresponds to convolution of the transformed functions, the process of convolution can be exchanged for three Fourier transforms and a multiplication (Gold and Rader, 1969).

The process used consisted of the following steps.

1. The discrete Fourier transform (DFT) of the signal $x(n\,\Delta t)$ was computed by using a FFT algorithm. The DFT of a signal $x(n\,\Delta t)$ is defined as

$$\chi(k\Omega)=\sum_{n=0}^{N-1} x(n\,\Delta t)\ \exp(-j\Omega\Delta tnk) \qquad k=0,1,2,\ldots,N-1 \qquad (2.4)$$

In this equation, $j=\sqrt{-1}$, $\Omega=2\pi\Delta f$ and $\Delta f=1/N\Delta t$, where N is the number of signal samples to be transformed and Δf is the chosen increment between samples in the frequency domain.

2. $\chi(k\Omega)$ was multiplied by $G_F(k\Omega)$, where $G_F(k\Omega)$ was the desired frequency response of the filter at the frequencies $2\pi k\Delta f$, $k=0,1,2,\ldots,N-1$

3. The inverse DFT of the product $G_F(k\Omega)\ \chi(k\Omega)$ was computed by using the same FFT algorithm, which yielded the desired output

$$y(n\,\Delta t)=\frac{1}{N}\sum_{k=0}^{N-1} \chi(k\Omega)\ G_F(k\Omega)\ \exp(j\Omega\Delta tnk) \qquad (2.5)$$

2.3. The Methodology Used in this Work for the Comparison of the Brain's Spontaneous Activity and the Evoked Potentials

As mentioned in Section 2.1.2., all the recordings were taken during the periods of no stimulation (EEG) and immediate auditory stimulation (EP). Each records, which contained spontaneous activity recorded immediately before the stimulation (stimulation was acoustical step function of 5000 Hz and 90 dB (SPL) for the high frequency analysis of the RF and IC) and a single evoked potential (EP), was stored in a magnetic tape. During a single experiment approximately 75 epochs (EEG and EP) were taken. Comparison of the brain's spontaneous activity and the evoked potentials was done both in the frequency domain and in the time domain.

<u>Frequency Domain Analysis</u>: The frequency domain analysis of the spontaneous activity and the evoked potentials was done as follows:

1. Power spectral density function was obtained from the epoch of the spontaneous activity (EEG) recorded prior to the stimulation by using the method described in Section 2.2.1.

2. The single evoked potential of the same epoch was transformed to the frequency domain with the Fourier transform in order to obtain the instantaneous frequency characteristic (which described the response to a single stimulus) of the studied brain structure. This method which was called TRFC-Method was given in Section 2.2.3.

3. The distribution of the amplitude maxima which were seen in the instantaneous frequency characteristic was compared with the distribution

of the peaks seen in the power spectral density function. The comparison described above gave information about the frequency domain organisation of the system under study before and after each stimulus. It should be noted here that the amplitude frequency characteristic is a different function from the power spectrum. In order to find the frequency characteristics of a system, input signals must be applied, while the power spectrum is obtained by measuring the intrinsic oscillations in the output of the system. The power spectrum is able to show maxima of the power spectral density function in different frequencies without application of input signals (stimulation signals). The amplitude characteristic reflects the signal transfer or the selectivities in the system under study, while the power spectrum depicts only the spontaneous oscillatory behavior of the system.

4. The procedure explained in steps #1-#3 was repeated for all the stored epochs.

5. In order to describe frequency distribution as revealed by the power spectra and instantaneous amplitude frequency characteristics, the histograms were obtained by plotting the frequency peaks (and/or amplitude maxima) seen in the power spectra and in the instantaneous frequency characteristics. After an experimental session more than 60 epochs of EEG and EP were analyzed to obtain the power spectra and instantaneous frequency characteristics of the brain nucleus under study. In all the power spectra and instantaneous frequency characteristics, the frequency peaks (and /or amplitude maxima) were routinely determined by plotting them on a seperate

paper. Each frequency peak (or amplitude maximum) was represented by an approximate bandwidth (horizontal line segment) and a center frequency marked on it. The number of center frequencies fall into each of a set of slots around frequencies up to 1000 Hz were determined. The histograms were presented by plotting the number of center frequencies versus frequency.

The methodology described in steps #1-#5 was the extention of the earlier usage of the power spectral density functions and the frequency characteristics given by Başar et al. (1975a, b, and c). In this work, however, the same functions were applied to single EEG-EP epochs each consisting of the spontaneous activity recorded immediately before stimulation and the evoked potential recorded right after the stimulus onset.

Time Domain Analysis (Magnitude Analysis): In the frequency domain a direct comparison of the magnitudes of various peaks revealed by power spectrum and amplitude characteristic was not possible, since the power spectrum reflects the intrinsic activity of a system whereas the amplitude characteristic represents the response of the system to an excitation. The direct comparison of the voltages of maximal amplitudes of the frequency components existing in the on-going activity and in the evoked potential was done in the time domain as follows:

1. The evoked potential sections of the epochs stored in the magnetic tape of the computer were averaged using the selective averaging method described in section 2.2.2.

2. Amplitude frequency characteristic of the studied brain structure was obtained from the selectively averaged evoked potential mentioned in #1. The amplitude frequency characteristic obtained from the SAEP reflected the most probable frequency selectivities in the system under study. (See TRFC-Method given in section 2.2.3.)

3. One of the single epochs was picked out to begin with.

4. One of the most probable selectivities determined in step #2 was chosen.

5. The epoch under study was inspected to see if it contained the selectivity chosen.

6. If no, the next most probable selectivity was chosen and step #5 was repeated.

7. If yes, the band limits of the stable selectivity chosen were determined according to the instantaneous amplitude characteristic which had already been computed during the frequency analysis of the epoch under study.

8. Both the spontaneous activity (EEG) and the EP sections of the same epoch were filtered by means of an ideal pass-band filter having the band limits determined in step #7.

9. The voltage of the maximal amplitude existing in the filtered spontaneous activity was compared with that existing in the filtered evoked potential and the amplification in the EP was computed as the ratio of these two voltages.

3. RESULTS

3.1. A Typical Example of Strong Resonance

The strong resonance was defined (see Başar et al., 1976) as the occurrence of time-locked responses in the filtered single evoked potentials showing amplification factor greater than 1. The amplification factor was defined, in a given experimental record, as the ratio of the maximal time-locked response amplitude to the maximal amplitude recorded in the spontaneous activity, both signals (spontaneous and evoked activities) being filtered within the same band limits. Fig. 4A shows a typical amplitude frequency characteristic of the cat mesencephalic reticular formation. This amplitude frequency characteristic was obtained from the selectively averaged evoked potential illustrated in Fig. 5 with the help of Fourier transform (TRFC-Method briefly explained in Section 2.2.3). Along the abscissa is the input frequency in logarithmic scale and along the ordinate is the potential amplitude, $|G(j\omega)|$, in relative units and decibels. The curves are normalized in such a way that the amplitude at 0 Hz is equal to 1 (or $20 \log 1=0$). The amplitude characteristic has selectivities (or maxima) in frequencies around 2 Hz, 12 Hz, 30 Hz and 60 Hz. These amplitude maxima were already defined as consistent selectivities of the reticular formation, since the results from 19 experiments using 9 cats gave mean value amplitude frequency curves with the same selectivities (Fig. 4B, after Başar et al., 1975b). Fig. 5 illustrates a typical comparative analysis of on-going and evoked activities in the reticular formation. At the top of the illustration a selectively averaged potential

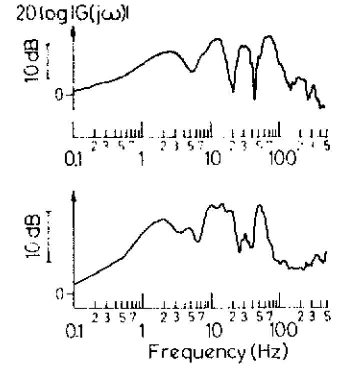


Fig. 4 (A): A typical amplitude characteristic of the cat reticular formation determined by Fourier transform and using the SAEP shown in Fig. 5. (After Başar, Gönder and Ungan, 1976a.) (B): Mean value curve of the cat reticular formation amplitude characteristics obtained from 19 experiments on 9 cats. (After Başar et al., 1975b.)

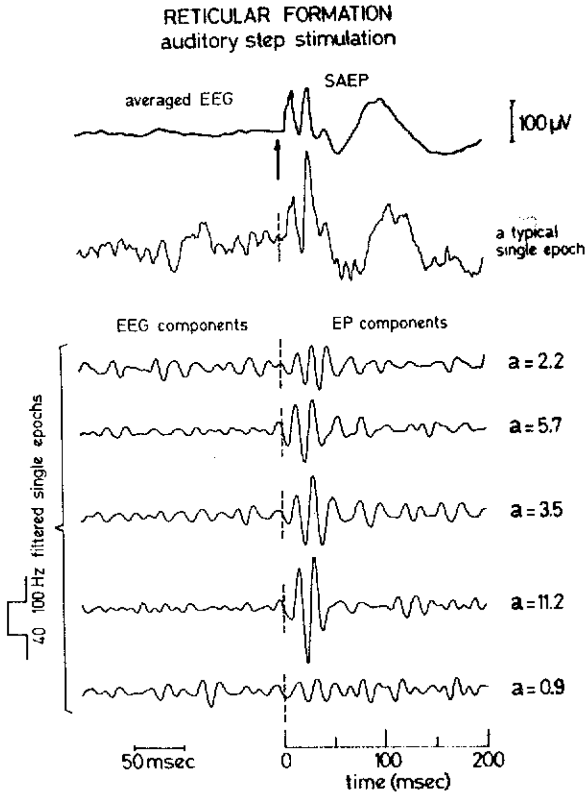


Fig. 5 Strong resonance phenomena in the brain as demonstrated by comparison of evoked potential components with the spontaneous activity components in the time domain. At the top of the illustration a selectively averaged evoked potential (SAEP) is shown together with the average of the preceding spontaneous activity. A typical single epoch which contains the unfiltered spontaneous activity and unfiltered single EP is illustrated below the averaged EEG and SAEP. The spontaneous activity was recorded just prior to the stimulus application (indicated by an upward arrow). Further, five randomly chosen filtered single epochs of EEG and EP components are shown. The theoretical pass-band filters applied had band limits of 40-100 Hz. At the right side of the EP components, the amplification factor a determined for the corresponding epoch is also given. Direct computer plottings. Negativity is upwards. (After Başar, Gönder and Ungan, 1976a.)

Background masking of low frequency high amplitude EEG and EP components usually created difficulty in observing the relatively low-magnitude high-frequency electrical activities of the brain. High pass filtering provided attenuated transmission below 80 Hz and allowed for high frequency analysis in the electrical activities of the RF and IC. The typical examples of the RF and IC high frequency responses were chosen from similar observations during experiments with 8 cats. The stimulation consisted of auditory step functions in the form of tone bursts of 5000 Hz and 90 dB (SPL).

3.2.1. Selectively Averaged Transient Evoked Potentials

Fig. 6 A and B show two typical examples of the SAEPs of the RF and Fig. 7 A and B show two typical SAEPs of the IC during the waking stage. The SAEPs of both RF and IC depict marked short latency waves with steep slopes or large slope changes. A positive short latency wave around 3 msec following a marked negative wave of 4.5-5 msec latency were the most prominent waves of the SAEPs of the RF (see Fig. 6A and B). The SAEPs of the inferior colliculus (Fig. 7A and B) depicted a negative short latency wave between 3-3.5 msec following a marked positive wave between 5-5.5 msec. In this study the detailed analysis of the latencies and waveforms of the transient evoked potentials are not elaborated. As stated earlier, "slope and slope and slope changes and the entire time course of evoked potentials carry the whole information concerning different activities and frequency selectivities of brain structures rather than the number and latencies of the waves" (Başar and Özesmi, 1972; Başar and Ungan, 1973).

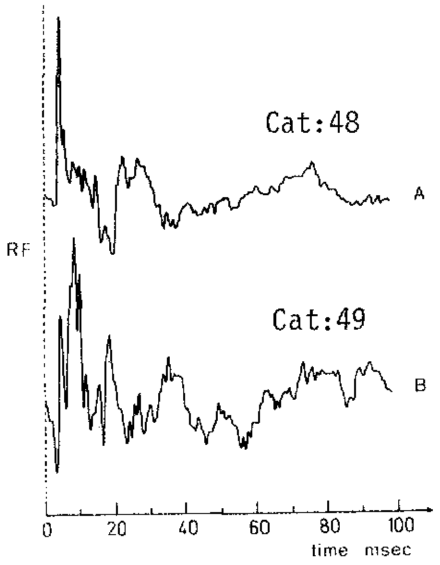


Fig. 6A and B. Two typical examples of the SAEPs of the RF obtained from two awake cats. The number of averaged responses are (A) 5, (B) 6. The negativity is upward. The stimulation consists of auditory step functions in the form of tone bursts of 5000 Hz and 90 dB (SPL).

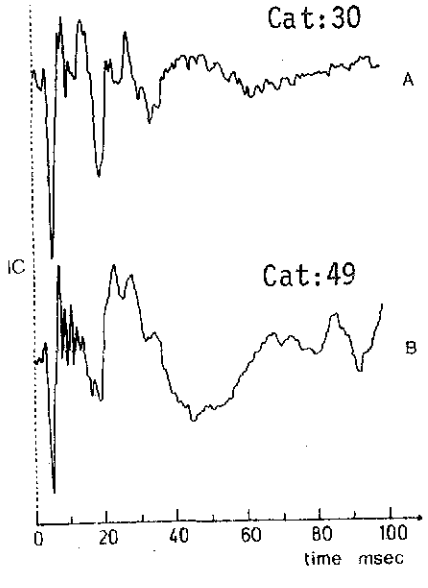


Fig. 7A and B. Two typical examples of the SAEPs of the IC obtained from two awake cats. The number of averaged responses are (A) 8, (B) 10. The negativity is upward. The stimulation consists of auditory step functions in the form of tone bursts of 5000 Hz and 90 dB (SPL).

3.2.2. Amplitude Frequency Characteristics

Fig. 8A and B show two typical amplitude characteristics obtained from the RF during the waking stage. These amplitude frequency characteristics were computed using the SAEPs presented in Fig. 6A and B, respectively, with the help of the Fourier transform (refer to Section 2.2.3 for the TRFC-Method). Along the abscissa is the input frequency in logarithmic scale and along the ordinate is the potential amplitude, $|G(j\omega)|$, in relative units and decibels. The curves are normalized in such a way that the amplitude at 0 Hz is equal to 1 (or 20 log 1=0). Various numbers of distinct amplitude maxima, which were centered at 60 Hz, 120 Hz, 180 Hz, 240 Hz, 310 Hz, 400 Hz, 500 Hz and 700 Hz, were seen in the frequency characteristic of the RF shown in Fig. 8A. The second amplitude characteristic shown in Fig. 8B reflects also the same amplitude maxima except that the maximum around 60 Hz is centered at 50 Hz and that the amplitude maxima at 180 Hz and 500 Hz are missing (or show irrelevant peaks). It has already been defined that the amplitude maximum seen at 50-60 Hz was the consistent selectivity of the RF (see Fig. 1). 50-60 Hz amplitude maximum was observed in all the experiments which were carried out in this study.

Inferior colliculus amplitude characteristics shown in Fig. 9A and B exhibited also distinct maxima in higher frequency ranges similar to the characteristics of the RF. Amplitude maxima around 75 Hz, 170 Hz, 220 Hz, 300 Hz and 700 Hz were the most prominent maxima seen in Fig. 9A and B. A small amplitude maximum around 20-25 Hz (beta range) was highly attenuated due to high pass filtering. Minor peaks around 400-500 Hz were also identified in the amplitude characteristics of the IC. Amplitude maxima around 70 Hz and 180-200 Hz were defined by Başar et al. (1975b) as the consistent selectivities of the inferior colliculus (see Fig. 1). These selectivities were observed also as the most prominent maxima in the amplitude characteristics of the IC which were obtained in this study.

Consistent selectivities: The mean value amplitude characteristic curves of the RF and IC of all the experiments were computed. The mean value curves were obtained by averaging the amplitude frequency characteristics of different cats and experiments. Fig. 10 shows the mean value amplitude characteristic curves of the RF and IC. The mean value curve of the RF is the result of 6 experiments on 6 cats. The mean value curve of the IC is the result of 3 experiments on 3 cats. Three experiments with the IC gave similar results. Therefore, the number of experiments with different cats was kept lower. The amplitude frequency characteristics obtained from the RF showed less consistency. Therefore, more experiments were done with the RF.

Various distinct maxima are seen in the curves of Fig. 10: 60 Hz, 110 Hz, 240 Hz, 320 Hz and 410 Hz in the RF; 80 Hz, 160 Hz, 210 Hz, 300 Hz and 700 Hz in the IC. We call these maxima, which always exist in the amplitude characteristics and which are clearly revealed by mean value curves (in spite of information reduction), the consistent maxima or the consistent selectivities. In other words, the probability for maximal signal transfer through the consistent selectivity channels mentioned above is always existent

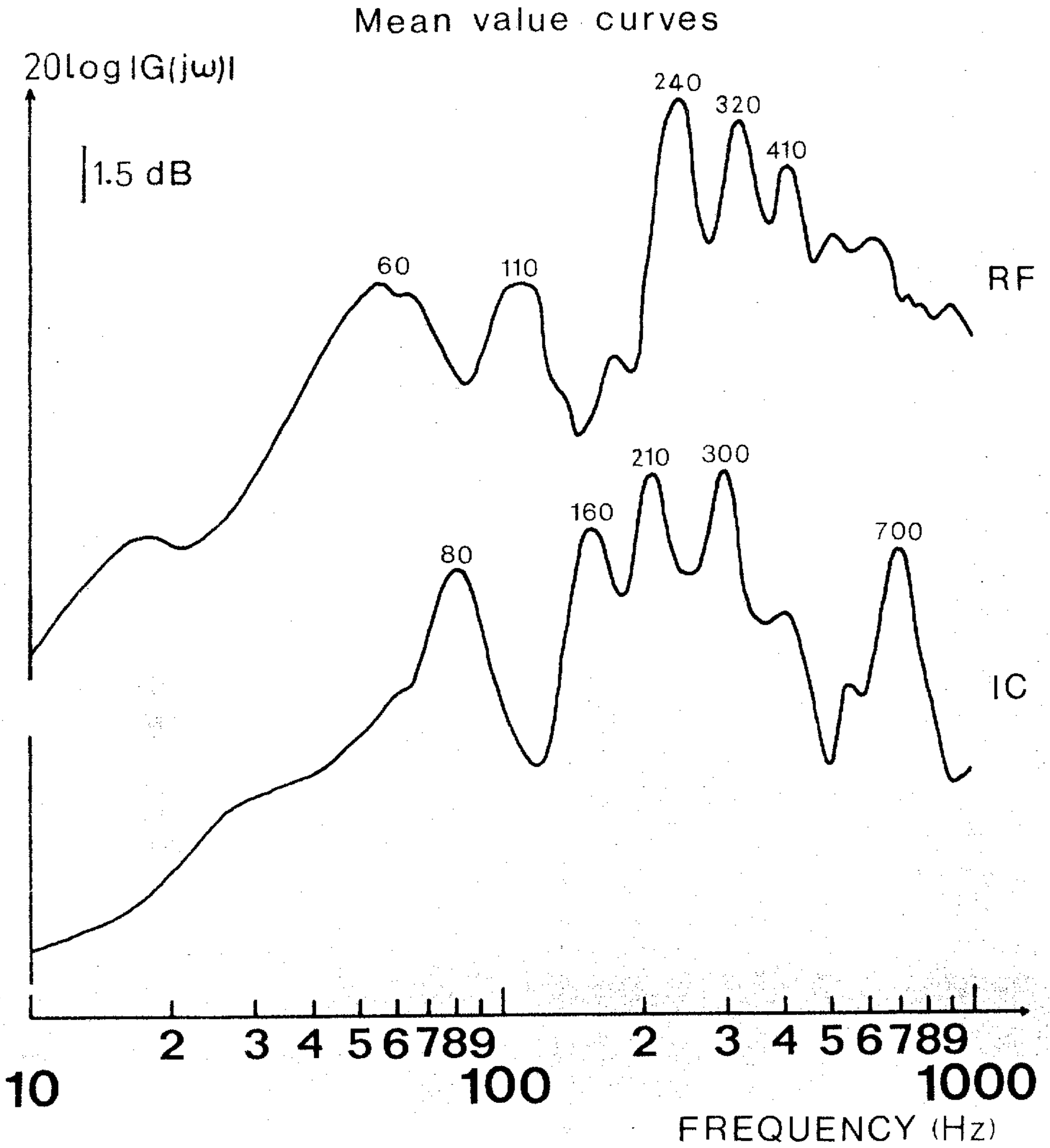


Fig. 10. Mean value curves of amplitude characteristics of the RF obtained from 6 experiments on 6 cats and the IC obtained from 3 experiments on 3 cats with auditory stimulation during the waking stage. Along the abscissa is the input frequency in logarithmic scale, along the ordinate the mean value potential amplitude, $|G(j\omega)|$, in decibels.

in all the experimental conditions, during the waking stage.

The higher frequency selectivities of the RF and IC presented above were the extention of the previous results (concerning the amplitude frequency characteristics of the RF and IC) obtained by Başar et al. (1975b).

3.2.3. Information Obtained from Application of Pass-Band Filters to Transient Evoked Potentials

Figs. 11 and 12 show the application of adequately chosen pass-band filters to the SAEP of the RF (Fig. 6A) and the SAEP of the IC (Fig. 7A) respectively. Fig. 8A and Fig. 9A show the amplitude characteristics of the RF and IC obtained using the transient evoked potentials of Fig. 6A and Fig. 7A. According to the RF and IC amplitude characteristics (see Fig. 8A and Fig. 9A), different frequency pass-bands in which the transmission reached maximum values were chosen. (For the filtering method refer to section 2.2.4.)

The information obtained with pass-band filtering was approximately the same information obtained by means of amplitude characteristics. Each amplitude maximum seen in the amplitude characteristics had a defined frequency band which was characterized by a center frequency where the transmission reached maximum value and a band width around the center frequency in which the transmission was allowed (see Fig. 8A and Fig. 9A). According to systems theory, each amplitude maximum depicted by a frequency characteristic should result from a damped oscillatory waveform in the time domain. As a matter of fact, pass-band filtered components show in the time domain

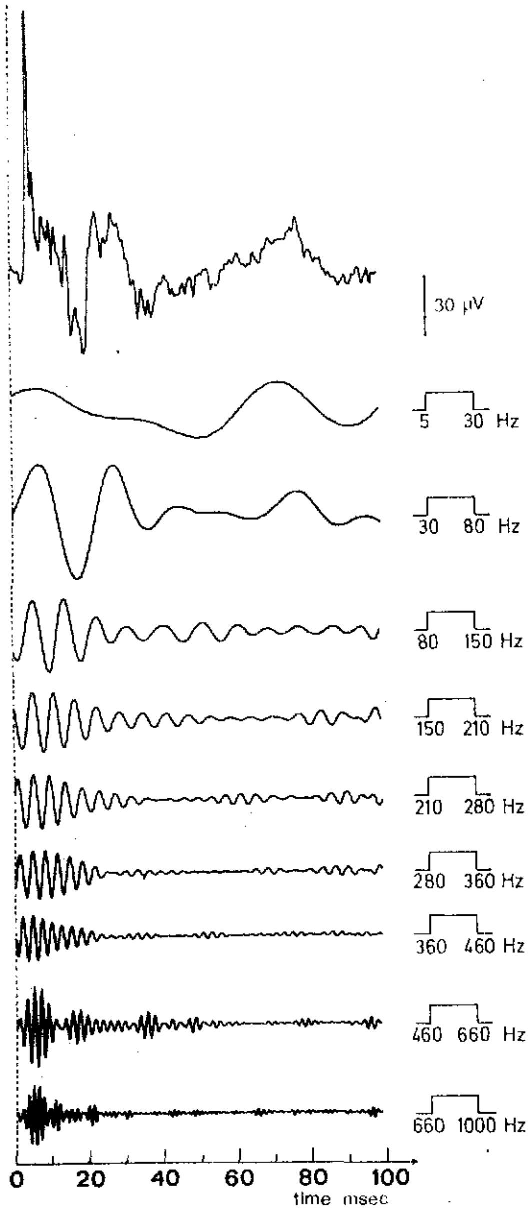


Fig. 11. Filtering of the SAEP of the RF shown in Fig. 6A with pass-band filters. The band limits of the filters applied are shown in the right side of the filtered SAEPs (FSAEPs). The original SAEP is shown at the top of the figure.

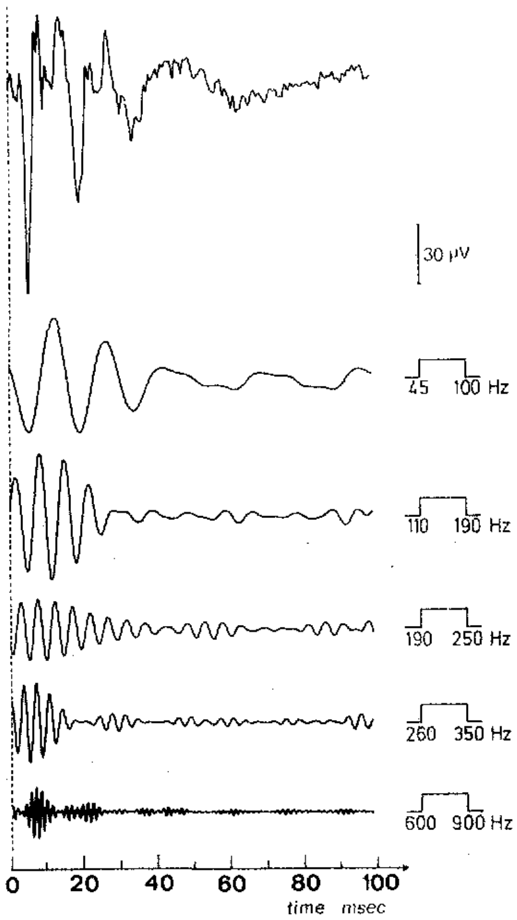


Fig. 12. Filtering of the SAEP of the IC shown in Fig. 7A with pass-band filters. The band limits of the filters applied are shown in the right side of the filtered SAEPs (FSAEPs). The original SAEP is shown at the top of the figure.

similar characteristics such as: a) they have oscillatory transient waveforms with a determined frequency of oscillation (which is exactly the same frequency as the center frequency of the corresponding amplitude maximum); b) these oscillatory signals reach their maximum value then decrease to reach zero within a finite duration (see Figs. 11 and 12). One important advantage of the time domain representation of the filtered components is that, they give additionally phase information, whereas amplitude characteristics alone do not give phase information.

3.2.4. Typical Power Spectral Density Functions and Instantaneous Amplitude Frequency Characteristics of the RF and IC

In section 2.3 a procedure was given for the frequency analysis of the brain's spontaneous activity and evoked potentials. In the above procedure the power spectral density functions obtained from the spontaneous activity recorded immediately before stimulation were compared with the instantaneous amplitude frequency characteristics obtained from the single evoked potentials to each stimulus. Fig. 13A and B show two typical sets of power spectral density functions and instantaneous amplitude frequency characteristics of the RF. The same kind of illustrations obtained from the IC are presented in Fig. 14A and B. The results given in Figs. 13 and 14 reflected single responses of the RF and IC. The amplitude characteristic of the RF in Fig. 8A and the amplitude characteristic of the IC in Fig. 9A were obtained from the same experiments which gave the results presented in Figs. 13 and 14. However, the amplitude frequency characteristics seen in Figs. 8A and 9A were computed from the selectively averaged evoked potentials

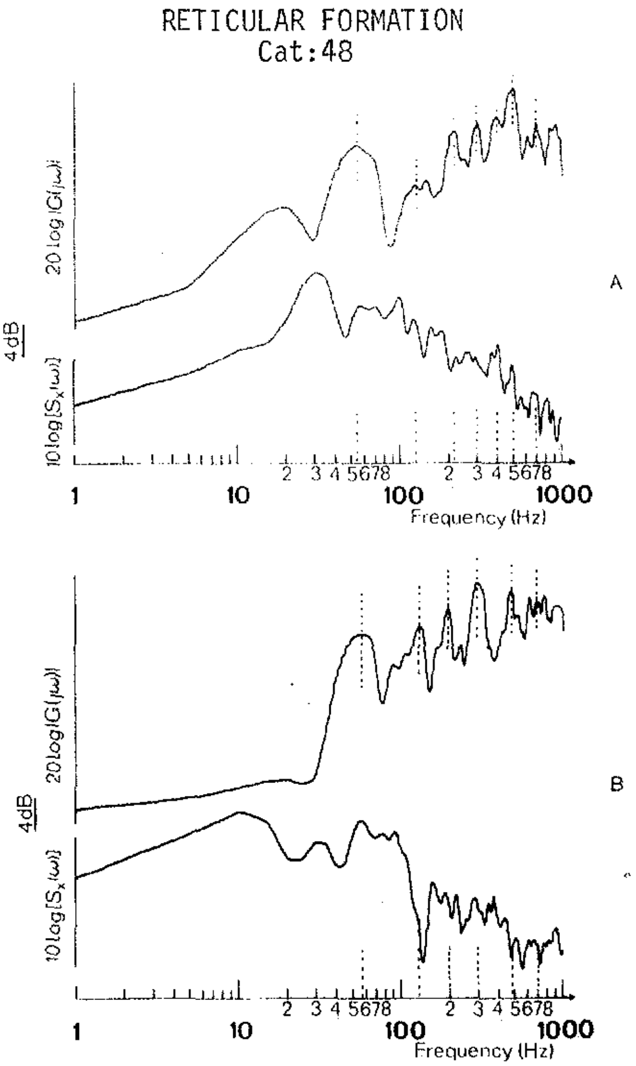


Fig. 13A and B. Two typical sets of power spectral density functions and instantaneous amplitude frequency characteristics of the RF. The power spectral density functions obtained from the spontaneous activity recorded immediately before stimulation are compared with the instantaneous amplitude frequency characteristics obtained from the single EPs of the RF. These two epochs are selected from 64 epochs of a single experimental session with cat no:48.

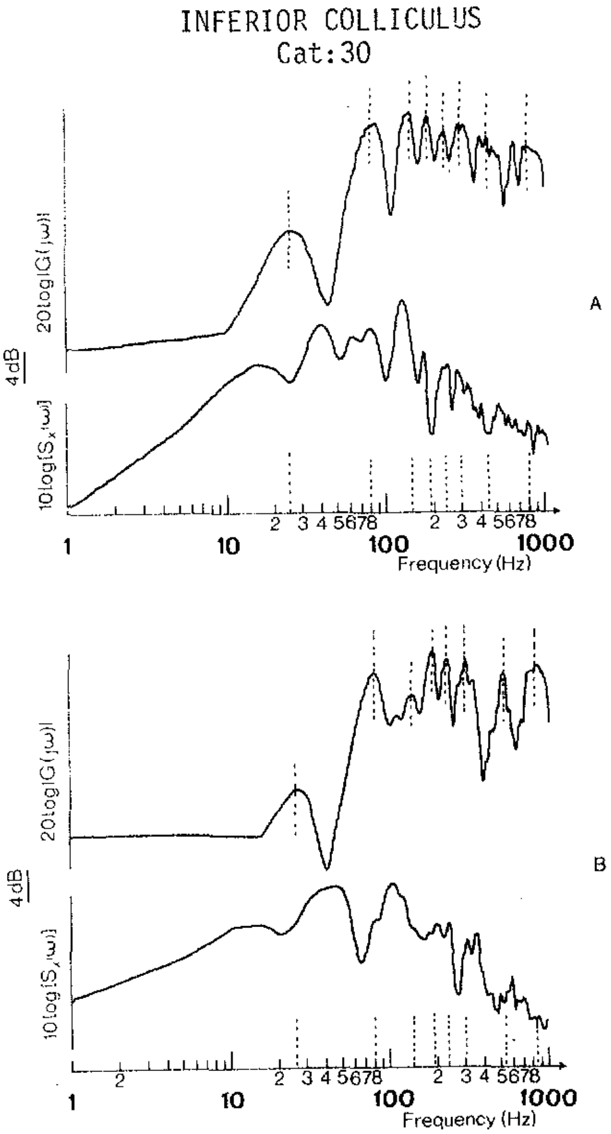


Fig. 14A and B. Two typical sets of power spectral density functions and instantaneous amplitude frequency characteristics of the IC. The power spectral density functions obtained from the spontaneous activity recorded immediately before stimulation are compared with the instantaneous amplitude frequency characteristics obtained from the single EPs of the IC. These two epochs are selected from 59 epochs of a single experimental session with cat no:30.

and reflect an averaged response to a number of identical stimuli whereas the instantaneous amplitude frequency characteristics presented in this section were obtained from the single evoked potentials and describe the responses to each single stimulus. The instantaneous amplitude characteristics of the RF (Fig. 13A and B) and the IC (Fig. 14A and B) show various distinct maxima. These maxima show relative differences in both magnitude and frequency for each single case. Fluctuations in both magnitude and frequency lead to important dissimilarities between the instantaneous amplitude frequency characteristics. Although there are some frequency fluctuations in the occurrence of the individual amplitude maxima, the results obtained in this section show that the most of the amplitude maxima observed in the instantaneous amplitude characteristics tend to occur at rather fixed frequencies. These frequencies, where the most of the amplitude maxima centered at, correspond to the frequency selectivities of the RF and IC described in section 3.2.2.

Power spectral density functions obtained from the RF and IC spontaneous activities recorded immediately before stimulation show also distinct peaks at various frequencies up to 1000 Hz (Figs. 13 and 14). However, these peaks and some minor spiky peaks are distributed randomly along the frequency axis rather than having consistent frequencies. The excitation of the system (in this case, RF and IC) with an input signal seemed to regularize and also increase the magnitude of the existing and randomly distributed spontaneous power spectral spikes. Probabilistic nature of the power spectral density functions and the frequency regularization reflected by the instantaneous amplitude frequency characteristics due to stimulation will be discussed extensively in the next section. Investigation of the amplitudes will be done in the time domain by comparing the frequency components existing in the on-going activity and in the evoked potential. High frequency resonances of the RF and IC of the cat brain is the subject of section 3.2.6.

3.2.5. Histograms Showing Frequency Distribution as Revealed by the Power Spectra and Instantaneous Amplitude Frequency Characteristics

Since the power spectra and instantaneous frequency characteristics have randomly varying frequency peaks (and/or amplitude maxima), reasonably obvious classification scheme is to plot the respective number of events which fall into each of a set of frequency ranges (slots). The methodology of obtaining the histograms was described in section 2.3.

In the previous section we have given some typical power spectrum-instantaneous frequency characteristic curves of the RF and IC. Figs. 15 and 16 show the histograms obtained from the power spectra and instantaneous frequency characteristics of the RF and IC respectively. At the bottom of Fig. 15A the frequency peaks seen in the power spectra, at the bottom of Fig. 15B the amplitude maxima seen in the instantaneous frequency characteristics of the RF are illustrated. Each frequency peak (or amplitude maximum) was represented by an approximate bandwidth (horizontal line segment) and a center frequency marked on it. The number of center frequencies fall into each of a set of 20 Hz slots around 50 Hz, 70 Hz, 90 Hz, etc were determined. The histograms shown at the top of Fig. 15A and B were presented

RETICULAR FORMATION
Cat:48

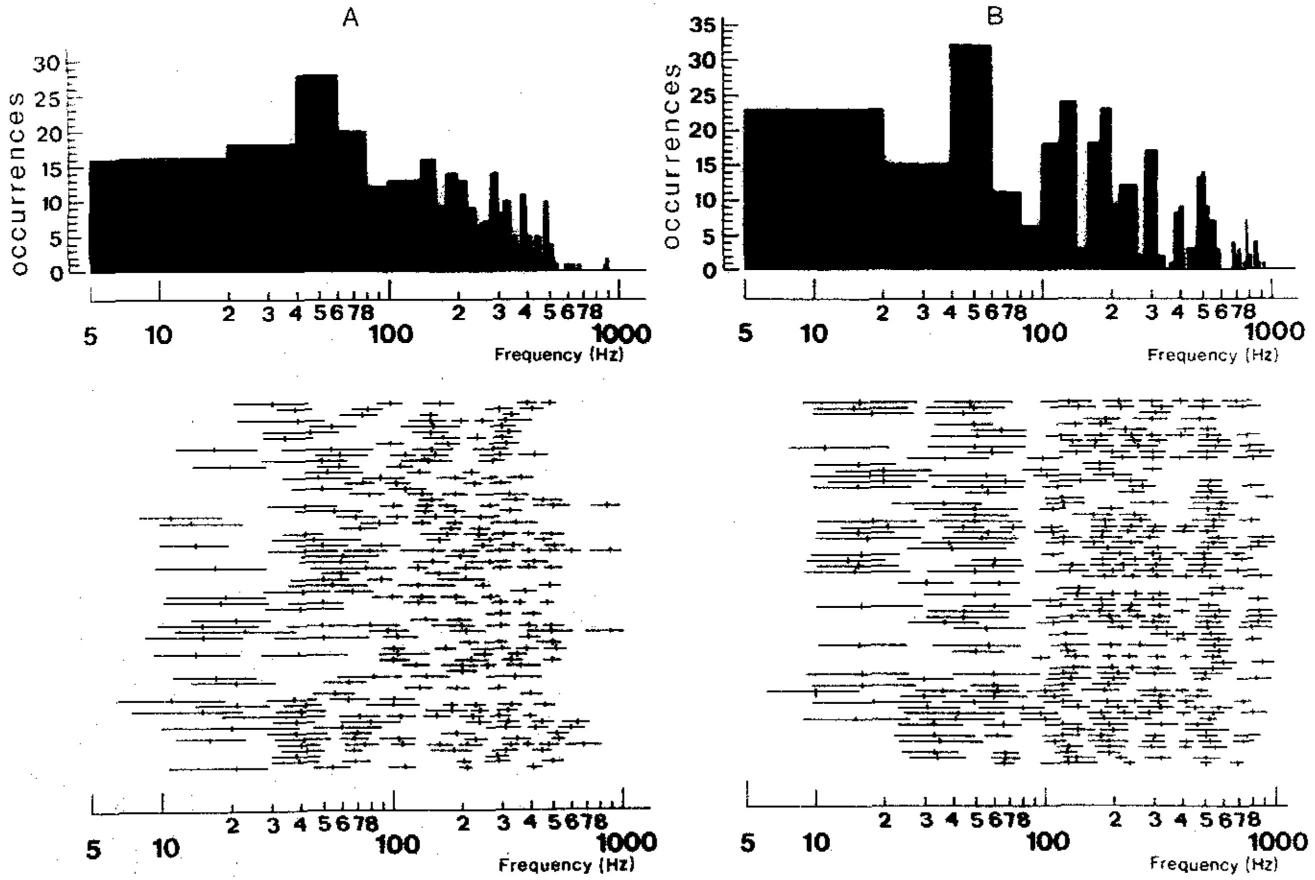


Fig. 15A and B. Histograms showing frequency distribution as revealed by (A): the power spectra, (B): the instantaneous frequency characteristics of the RF. At the bottom of the figure, each frequency peak (or amplitude maximum) was represented by an approximate bandwidth (horizontal line segment) and a center frequency marked on it. The histograms shown at the top of the figure were presented by plotting the number of center frequencies fall into each of a set of 20 Hz slots versus frequency. The number of power density function-instantaneous frequency characteristic pair which were used to obtain the histograms is 64.

by plotting the number of center frequencies versus frequency. The same kind of illustrations were obtained for the IC shown in Fig. 16A and B.

The histogram of the RF shown in Fig. 15B was the results of 64 instantaneous frequency characteristics. The same number of power spectra curves obtained from the corresponding EEG epochs of the RF were used to obtain the histogram shown in Fig. 15A. The histogram of the instantaneous frequency characteristics shows quantitatively that the substantial frequency stabilization achieved by appropriate frequency control imposed on rather randomly occurring frequency peaks of the power spectra. Some frequency channels are easily determined in Fig. 15B where the response amplitude maxima tend to occur most frequently. These are; 40-60 Hz, 100-140 Hz, 160-200 Hz, 200-260 Hz, 280-320 Hz, 380-420 Hz, 490-530 Hz and 700-900 Hz.

The frequency domain analysis of the spontaneous activity and evoked potentials of the IC, shown in Fig. 16A and B, was done using 59 epochs. It is apparent from the histograms that frequency stabilization takes place also in the frequencies of the responses of the IC. The frequency channels are determined in Fig. 16B. These frequency channels, in which response amplitude maxima are seen most frequently, are as follows; 20-40 Hz, 60-80 Hz, 140-180 Hz, 180-240 Hz, 280-320 Hz and 600-900 Hz.

In order to understand the frequency stabilization of amplitude maxima in the instantaneous frequency characteristics, we have to try to find a quantitative description between power spectra and instantaneous frequency characteristics. Such kind of analysis will be done in section 4.3.2 by comparing the results of different experiments with other cats.

3.2.6. High Frequency Resonances in the Reticular Formation and the Inferior Colliculus of the Cat Brain

In Fig. 5 strong resonance phenomena was demonstrated giving only the 60 Hz selectivity of the RF. In the previous sections the amplitude characteristics of the RF and IC proved that a number of selectivities existed also in relatively higher frequency ranges up to 1000 Hz. Therefore the resonances up to frequencies of 1000 Hz in the RF and IC will be searched in this section. The methodology used for comparing the absolute magnitudes of the frequency components existing in the EEG and in the EP was given in section 2.3.

At the top of Fig. 17 a typical EEG-EP pair recorded from the RF is shown. The vertical dashed line indicates the time of arrival of the sound stimulation to the cat's ears. Fig. 17 contains also the filtered EEG components and EP components obtained with the use of theoretical pass-band filters. The band limits of the pass-band filters are shown at the right side of the corresponding potentials. The filtered components in the frequency bands of (5-30 Hz), (30-80 Hz), (160-250 Hz), (460-580 Hz) and (580-800 Hz) were obtained from the successive pass-band filtering of the single epoch illustrated at the top of Fig. 17. Amplitude characteristic computed from this single EP and the spectral density function obtained from the spontaneous activity prior to the stimulation were already presented in Fig. 13A. The filtered components in the frequency

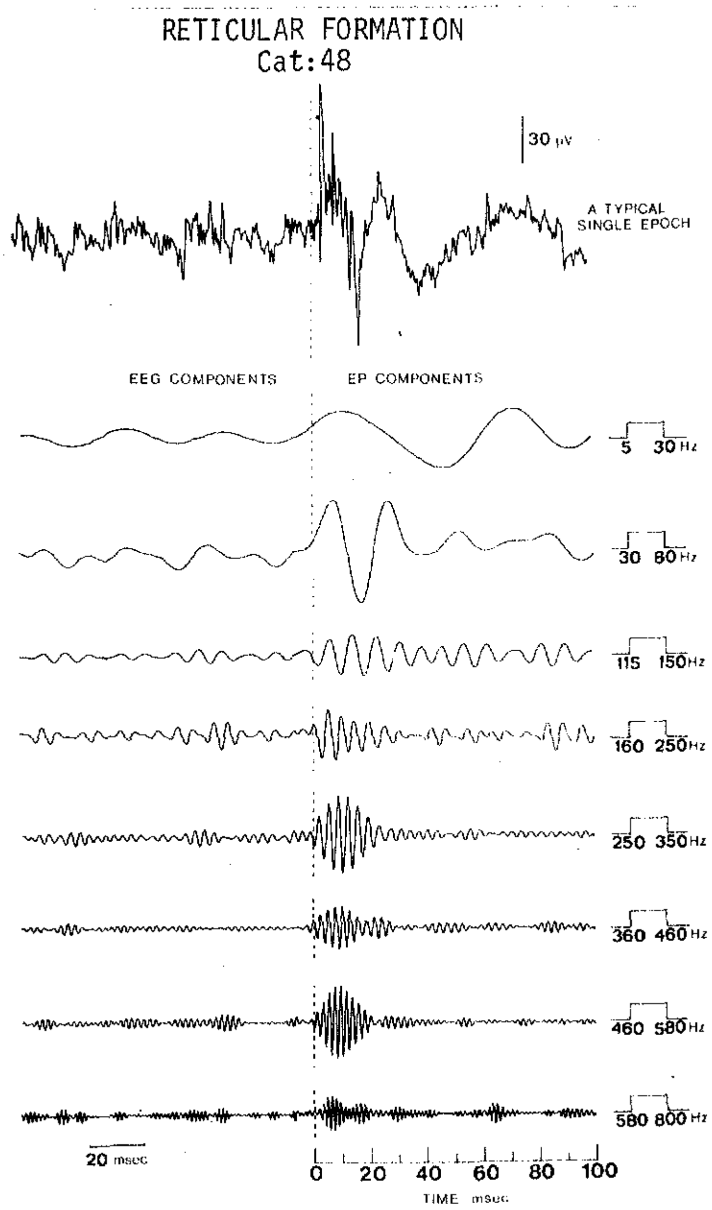
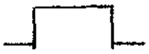
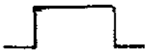
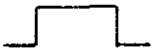


Fig. 17. A typical comparative analysis of on-going and evoked activities in the RF. The upper curve shows a typical EEG-EP pair recorded from the RF. Components in various frequency bands were obtained by using theoretical pass-band filters with the band limits given at the right side of each component. The spontaneous activity was recorded just prior to the stimulus application at 0 msec. The negativity is upward.

the pass-band of the filter applied	maximal amplitude of filtered EEG component	maximal amplitude of filtered EP component	amplification factor
1. (45-110 Hz)	29.1 µV	82.8 µV	a=2.9
2. (120-190 Hz)	21.1 µV	76.5 µV	a=3.6
3. (190-250 Hz)	15.3 µV	50.2 µV	a=3.3
4. (260-350 Hz)	18.6 µV	44.5 µV	a=2.4
5. (600-900 Hz)	24.2 µV	36.5 µV	a=1.5

In Table 1 the fluctuations of the maximal amplitude in the filtered EEG and EP components together with their amplification factors in various channels of the RF and IC were given in order to show, how fluctuations in the amplitudes of the spontaneous activity and evoked potential components were observed.

	Maximal amplitudes (μV)		
The pass-band filter applied	EEG components	Time-locked EP components	Amplification factor
 45 110 Hz	34.0 50.1 29.1 36.7 24.7	68.7 57.2 82.8 73.5 85.1	2.02 1.14 2.90 2.00 3.44
 110 190 Hz	31.9 19.0 38.2 34.9 21.1	49.8 69.6 64.1 72.5 76.5	1.56 3.66 1.68 2.07 3.60
 190 250 Hz	15.8 17.5 18.4 15.3 24.2	35.7 44.4 42.1 50.2 22.3	2.26 2.54 2.29 3.30 0.92
 250 350 Hz	18.6 33.5 21.5 24.8 22.4	44.5 32.2 43.4 42.8 53.5	2.40 0.96 2.02 1.72 2.39
 600 900 Hz	24.2 17.8 18.0 16.0 28.0	36.5 38.6 40.1 51.5 30.9	1.50 2.17 2.23 3.22 1.10

B

Table 1A and B. Fluctuation of the amplification factor and its relation to the voltage of the spontaneous activity just preceding the stimulus. (A): Observation in various frequency channels of the RF from an experimental session on a single cat no:48. (B): Observation in various frequency channels of the IC from an experimental session on a single cat no:30. Note that high-pass analog filtering with a cut-off frequency of 80 Hz caused attenuated (6 dB per octave) transmission below 80 Hz.

4. DISCUSSION

4.1. A Discussion on the Methodology Used in this Study

The accuracy and the reliability of the mathematical methods such as selective averaging, power spectral analysis, TRFC-method and ideal filtering, were discussed in detail in previous studies (Başar and Ungan, 1973; Başar et al., 1975a; Başar, 1974; Ungan, 1974; Başar, 1976). Therefore, in the present discussion, there will be no further comment about the accuracy and reliability of the mathematical methods mentioned above.

In this study a new methodology was applied alternatively to the spontaneous activity and evoked potentials of the brain. The methodology for comparison of the brain's spontaneous activity and the evoked potentials consisted of two sections: frequency domain analysis and time domain analysis.

Frequency domain analysis was done by the comparison of the peaks seen in the power spectral density function (which was obtained from the EEG recorded prior to the stimulation) with the amplitude maxima revealed by the instantaneous frequency characteristic (which was obtained from the EP section of the same epoch under study).

Several features are to be noted in order to explain the methodology concerning the frequency domain analysis.

1. Power spectrum reflects the intrinsic activity of the brain structure under study just before the stimulation. The instantaneous

amplitude frequency characteristic represents the response of the same system to an excitation. Therefore, the method of power spectra which was given in section 2.2.1 and the method of frequency characteristics which was described in section 2.2.3 have been used alternatively for each EEG and EP pair.

2. Instantaneous amplitude characteristic is obtained from a single evoked potential (a response to a single stimulus) rather than an averaged evoked potential. An averaged evoked potential is a response obtained by signal averaging. According to the results presented in the previous section, the information contained in neural responses to a single stimulus was somewhat different than that obtained from signal averaging. The most important fact was that repeated presentations of the same stimulus did not yield identical responses in the electrical activities of the brain, although the experimental conditions were kept as invariable as possible. More could be learned from the information available in each individual response than the information obtained from the averaged response of the same individual responses.

3. We must emphasize that the instantaneous amplitude characteristic curves presented in Figs. 13 and 14 are not frequency characteristic curves in the classical system theory configuration. Since the stages of the brain change continuously, it is very difficult (and sometimes impossible) to get homogeneously measured, invariant instantaneous amplitude characteristics. The spontaneous activity of the brain also shows time varying character. The power spectral density functions measured at different times do not

characteristics is not possible. The exact determination of the absolute magnitudes of the EEG and EP components are possible only by filtering of each EEG and EP components of the brain structure under study.

2. When one examines the unfiltered EEG data and compares it with the filtered data (EEG components), he can immediately recognize that filtered components do exist in the unfiltered EEG data in form of instantaneous frequencies (Figs. 17 and 18). The power density functions of the unfiltered EEG data have already given in Figs. 13 and 14. The same observations can be done on examination of the single EPs in Figs. 17 and 18. The filtered components do exist in the unfiltered EPs as instantaneous frequency components (instantaneous frequency characteristics shown in Figs. 13 and 14).

3. Frequency components analyzed in the single EPs do exist in the averaged evoked potentials (SAEPs shown in Figs. 11 and 12). In other words, high frequency components existing in single EPs are not resulting from sporadic transient events as the SAEPs of Figs. 11 and 12, and the amplitude characteristics of Figs. 8A and 9A show, but are resulting from consistent phenomena.

4. It should be emphasized that in the time domain analysis the band limits of the theoretical filters are not chosen arbitrarily. The band limits are chosen according to the selectivity bands revealed from the amplitude characteristics of evoked potentials. In other words, one filters the spontaneous activity after defining the frequency bands of components which exist in a very stable manner in the response. Only

in this way, it is possible to analyze whether the EEG contains the same frequency components as the EPs.

4.2. Demonstration of the Relationship Between EEG and Evoked Potentials

Without any peripheral stimulation, the brain has intrinsic spontaneous activity. When the brain is stimulated peripherally, for instance, by means of an acoustic stimulus, this stimulus is transduced in lower structures of the auditory pathway to an electrical signal, and an additional electrical activity is evoked at the brain output which is called the evoked potential. This evoked activity undergoes an interaction with the ongoing (spontaneous) activity. Resonance phenomena which explain the relationship between EEG and EPs was first classified by Başar et al. (1975b, c). This classification was based on relative comparisons. In the present study comparison of filtered EPs with filtered EEG was done in the time domain. The demonstration of the dependence of EPs on EEG was performed using the absolute magnitudes of EEG and EP components.

The evoked potentials reflect in a different manner (and/or with different weights) the spontaneous activity. This fact was described by Başar, Gönder and Ungan (1976a) and also partly presented in section 3.1. During the experiments described above, at least four types of evoked potentials which were related to the spontaneous activity were encountered.

1. <u>Weak time-locking</u> of the response signal with the stimulus. In this case the filtered averaged evoked potential components are smaller than the components of the spontaneous activity in the same frequency band.

2. Perfect time-locking, with amplification factor of single EPs around 1. In this case the filtered averaged evoked potentials have comparable magnitudes with components of the spontaneous activity in the same frequency band.

3. Perfect time-locking, with amplification factor of single EPs greater than 1 (strong resonance). In this case the filtered averaged evoked potentials have magnitudes greater than the magnitudes of the spontaneous activity components in the same frequency band (example: the 50-60 Hz component of the reticular formation; see Fig. 5).

4. Frequency stabilization or frequency-locking with amplification factor of single EPs greater than 1. Often, in the spontaneous activity various components depict frequency spread as it is the case of the 70 Hz component of the inferior colliculus illustrated in Fig. 14. In such cases the frequency of the response is stabilized during a short period after stimulation (filtered 70 Hz component of the IC was shown in Fig. 18). As the explanation in the coming section will also show, this response component of the inferior colliculus has a more stable frequency, while the power spectra of the same nucleus depict frequency spread with multiperiodicities and often broad band character in the same selectivity channel. Frequency stabilization of the response upon stimulation will be discussed more systematically during the high frequency analysis of the RF and IC in section 4.3.2. (See also section 4.3.3.)

4.3. Discussion of the Results Concerning the High Frequency Analysis of Electrical Signals from the Reticular Formation and the Inferior Colliculus.

4.3.1. Transient Evoked Potentials

A direct comparison of the results presented in section 3.2.1 with previous reports is not possible since the evoked potentials obtained in this study reflect mainly high frequency components. Low frequency components were filtered out by high-pass filtering with a cut-off frequency of 80 Hz. Moreover, evoked potentials of the studied nuclei were obtained by selective averaging method. Selective averaging provided us with more consistent and stable data. Also the responses were more smooth although we used a minimum number of sweeps.

The SAEPs of the RF and IC which were presented in section 3.2.1 showed short latency waves. The most prominent short latency wave seen in the SAEPs of the IC (Fig. 7) was a positive wave with a 5-5.5 msec latency. The existence of such a wave (peak) is consistent with other studies (Ades and Brookhart, 1950; Jungert, 1956; Rosenblitz, 1954; Starr, 1964). Similarly SAEPs of the RF (see Fig. 6) showed a marked negative wave of 4.5-5 msec latency.

4.3.2. Frequency Domain Analysis of Spontaneous Activity and Evoked Potentials: Frequency Stabilization, Transmission Probabilities

The histograms presented in section 3.2.5 were chosen from similar observations during 6 experiments with 4 cats. During these experiments fre-

RETICULAR FORMATION	Distribution factor given by spectral peaks	Distribution factor given by amplitude maxima	Frequency stabilization factor
Cat:48	1.76	5.90	S=3.35
Cat:30	1.18	2.74	S=2.32
Cat:49	1.69	1.61	S=0.95
Cat:47	0.84	1.71	S=2.04

Frequency channels

Cat:48 (5-20Hz, 40-60Hz, 100-140Hz, 160-260Hz, 280-320Hz, 380-420Hz, 480-580Hz, 680-900Hz)
Cat:30 (5-20Hz, 40-60Hz, 100-140Hz, 160-200Hz, 220-280Hz, 320-360Hz, 460-520Hz, 680-900Hz)
Cat:49 (5-20Hz, 40-60Hz, 100-140Hz, 160-240Hz, 260-320Hz, 360-400Hz, 620-720Hz)
Cat:47 (5-20Hz, 40-60Hz, 80-120Hz, 200-260Hz, 280-340Hz, 500-580Hz)

INFERIOR COLLICULUS	Distribution factor given by spectral peaks	Distribution factor given by amplitude maxima	Frequency stabilization factor
Cat:30	0.95	3.12	S=3.28
Cat:49	1.18	3.60	S=3.00

Frequency channels

Cat:30 (20-40Hz, 60-80Hz, 140-240Hz, 280-320Hz, 620-800Hz)
Cat:49 (10-30Hz, 60-80Hz, 140-240Hz, 280-320Hz, 580-700Hz)

Table 2. Demonstration of the frequency stabilization in the frequency distribution of the amplitude maxima seen in the instantaneous frequency characteristics with respect to the frequency distribution of the spectral peaks seen in the power spectra. The distribution factor is obtained in a given histogram by the ratio of the number of all the amplitude maxima (or frequency peaks) in the frequency channels to the number of all the amplitude maxima (or frequency peaks) outside the frequency channels, both amplitude maxima and frequency peaks being counted according to the same frequency channels. Frequency channels are determined by choosing the distinct frequency ranges seen in the instantaneous frequency characteristics. The frequency stabilization factor is obtained by, in a given experimental session and over a whole frequency range, the ratio of the distribution factor given by amplitude maxima to the distribution factor given by spectral peaks. Frequency domain analysis of the recordings over four hundred EEG-EP epochs from the RF and IC during 6 experiments with 4 cats were done. (See Figs. 15 and 16 for the typical histograms of the RF and IC.)

quency stabilization of the response upon stimulation was observed. Some frequency channels were determined where response amplitude maxima tend to occur most frequently. A quantitative description of the histograms will be done as follows. The distribution factor in a given histogram is defined as the ratio of the number of all the amplitude maxima (or frequency peaks) in the frequency channels to the number of all the amplitude maxima (or frequency peaks) outside the frequency channels, both amplitude maxima and frequency peaks being counted according to the same frequency channels. Frequency channels are determined by choosing the distinct frequency ranges seen in the histogram of the instantaneous frequency characteristics (see Figs. 15 and 16). We define the frequency stabilization factor, in a given experimental session and over a whole frequency range, as the ratio of the distribution factor given by amplitude maxima to the distribution factor given by spectral peaks.

Table 2 shows the distribution factors and frequency stabilization factors obtained from the results of various experiments with different cats. Frequency stabilization factors are changing between 0.95 to 3.35. For a particular experiment, a frequency stabilization factor around 1 means there is no improvement in the frequency distribution of the amplitude maxima seen in the instantaneous frequency characteristics with respect to the frequency distribution of the spectral peeks seen in the power spectra. A frequency stabilization factor greater than 1 indicates that there exists a frequency stabilization immediately after the stimulus onset. An example of frequency stabilization on histograms obtained from the RF of the cat: 48 was presented in Fig. 15. For the above experiment

4.3.3. Probabilistic Nature of the Strong Resonances

An important feature of the observations on strong resonances is their probabilistic behaviour as seen in the occurrance of the amplitude maxima together with the amplification factors. The statistical analysis of amplitude maxima of instantaneous frequency characteristics showed a significant frequency stabilization while the statistical analysis of spectral peaks of EEG gave more random distribution over the frequency axis. Time domain analysis of the single epochs presented in section 3.2.6 showed that the maximal amplitudes of the filtered single evoked potentials displayed a fluctuation in the amplification factors (Table 1). Thus we have two statistical variables. One is the frequency, the other is the amplification factor. Both variables should be considered simultaneously for a given frequency channel. In this section we will confine our attention to a single frequency band of the IC which is determined between 50 and 100 Hz. In Fig. 19A the percentage histogram showing the distribution of frequencies of amplitude maxima is plotted between 50-100 Hz frequency band of the IC. In Fig. 19B the distribution of spectral peaks between the same frequencies is presented. These distributions are obtained by counting the number of center frequencies falling into each of a set of 4 Hz slots between 50-100 Hz frequency bands of the histograms shown in Fig. 16B and A. The mean frequency of amplitude maxima is 72 Hz. The standard deviation is 6 Hz. The mean frequency of spectral peaks is 76 Hz. The standard deviation is 13 Hz. The spectral peaks depict flat distribution in the range under study. The distribution of amplitude maxima in the same frequency range shows Gaussion-like distribution.

Fig. 20A gives the percentage histogram showing the distribution of amplification factors which are obtained from the filtered EEG-EP epochs of the IC. The band limits of the theoretical pass-band filters are 50-100 Hz. The mean amplification factor is 2. The standard deviation is estimated as 0.72.

Fig. 20B shows an estimated curve of the relationship between the amplification factor and the peak-to-peak amplitude of the spontaneous 50-100 Hz activity just preceding the stimulus. In this diagram we see that the amplification factor reaches maximal values for low spontaneous voltage around 25-35 μV while the minimal amplification factor are in spontaneous activities with higher voltages (50-60 μV).

Frequency stabilization of response amplitude maxima rapidly increase when amplification factor take values greater than 1. This fact is illustrated in Fig. 20C. In this figure ordinate shows standard deviation from the mean frequency, abscissa gives amplification factor, in 0.5 divisions. In the scope of the illustrations given above, we will try to understand the cause of the probabilistic nature of strong resonance phenomena.

1. The amplification factor shows a strong dependence on the voltage of spontaneous activity which precedes immediately the stimulation. Minimal amplification factors are seen during high magnitude spontaneous activity (see Fig. 20B).

2. Spontaneous oscillations with smaller magnitudes can be frequency stabilized more efficiently by the excitation signals than the spontaneous oscillations with larger magnitudes (see Figs. 20B and C).

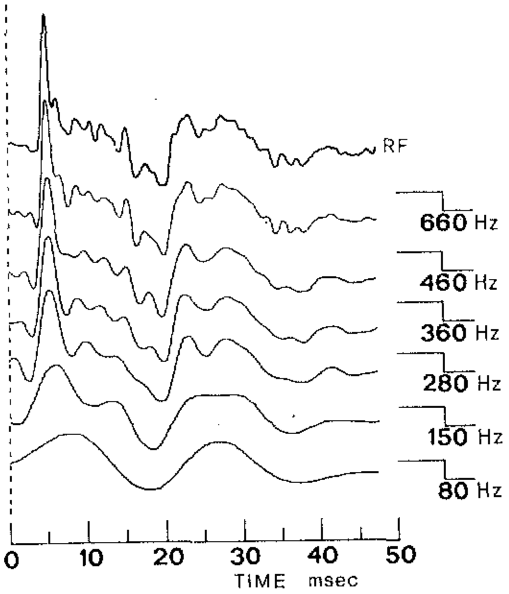


Fig. 21. The formation of short latency waves of the RF as demonstrated by successive application of low-pass filters to the SAEP of Fig. 6A. The cut-off frequencies are indicated for each FSAEP..

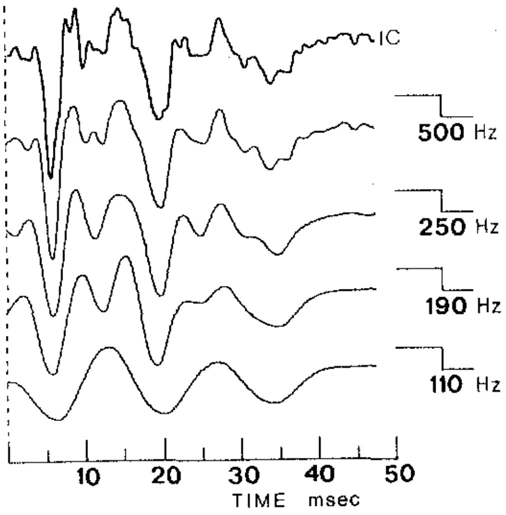


Fig. 22. The formation of short latency waves of the IC as demonstrated by successive application of low-pass filters to the SAEP of Fig. 7A. The cut-off frequencies are indicated for each FSAEP.

250 Hz), (260-350 Hz), and (600-900 Hz). All these oscillatory components have time-coincident minimal values giving a positive wave at approximately 5.5 msec. Similarly negative short latency wave at 5 msec of the SAEP of the RF in Fig. 11 is the result of many oscillatory components described with various frequency bands as shown in the figure. Therefore, the short latency peaks of the RF and IC evoked potentals should not necessarily reflect single mechanisms, but indeed have very complicated structures. It must be emphasized here once more that, the evoked potentials were not decomposed into some arbitrarily chosen Fourier components; with pass-band filtering we selected components which were already detected in the amplitude frequency characteristics. The filters were chosen adequate to the amplitude characteristics.

In Fig. 21 and Fig. 22 successive application of low-pass filters to the same SAEPs of the RF and IC are given. In these figures the formation of short latency waves are clearly demonstrated. Those oscillatory components having frequencies higher than 150 Hz are the most effective ones for the formation of the short latency wave at 5 msec of the SAEP of the RF. Similar oscillatory components having frequencies higher than 110 Hz are more effective for the formation of the short latency wave at 5.5 msec of the SAEP of the IC.

Some degree of synchronization of the activity of individual oscillatory components of an evoked potential is necessary if there is to be a clear electric response with a definite latency. If the activity of individual oscillatory components is random in phase, in magnitude and complex of the RF evoked potential) in the typical response pattern will usually cause significant loss of amplitude and often serious changes in waveform and latency-to-peak of the averaged evoked potential. At the bottom of the same figure average evoked potential is given. It is an average of five single evoked potentials (two of them are illustrated in the figure above). One can easily see the differences between the single evoked potentials and the average evoked potential. Averaging caused significant loss of amplitude and serious changes in waveform. N2 was significantly reduced in magnitude relative to N1. Amount of magnitude reduction was also obvious in the 600-950 Hz component of the averaged evoked potential.

Random fluctuations, of the order of 0.25 msec, occur physiologically in the latency of the initiation of nerve impulses in single auditory units (Tasaki, 1954) and they must be presumed to occur at other synaptic junctions as well. In the example given in Fig. 23, one quarter of the duration of the peak N1 is approximately 0.3 msec. How serious is the problem of jittering becomes obvious when comparing this number with Tasaki's measurement.

4.3.5. Comparison of the Evoked Potentials of the RF and IC with the Far-Field Acoustic Response

Short-latency evoked potentials recorded from humans with electrodes on vertex and earlobe have been published by various authors (Jewett et al, 1970; Sohmer and Feinmesser, 1970; Jewett and Williston, 1971; Picton et al, 1974). The early components consisted of 5 or 6 waves originating within the first 8 msec after the stimulus onset. These early waves, which clear yet, there is good evidence that the superior olivary complex, for example, discharges into surrounding reticular nuclei (Ades and Brookhart, 1950).

The evoked potential of the IC shown in Fig. 24C depicts a positive wave at P1. P1 is in the range of latencies for the positive wave in the averaged evoked potentials of the IC recorded by Jewett (1970) of 5 msec. The negative wave N2 of the IC evoked potential occurs at about the same time with wave 5 of the far field evoked potential.

4.3.6. Oscillatory Components of the Evoked Potentials of the Brain

In the time domain the filtered EP components showed stimulus enhanced oscillatory transient responses. Within a finite duration these oscillatory responses reached their maximum value then decreased to reach zero. During this period the phase angle of the oscillations behaved deterministically, after which fluctuations set in again (Figs. 17 and 18). In the frequency domain the instantaneous frequency characteristics which were obtained from single EPs depicted amplitude maxima. Each amplitude maximum gave information about the frequency band which was characterized by a center frequency where the transmission reached maximum value and a band width around the center frequency in which the transmission was allowed (Figs. 13 and 14).

In 1944 Gabor described certain "elementary signals" which occupy the smallest possible area in the frequency-time domain (information diagram). They are harmonic oscillations amplitude modulated by a gaussian distribution curve. The derivation of this signal form is established in Gabor (1946). "The signal which occupies the minimum area $\Delta t \, \Delta f = 1/2$ is the modulation product of a harmonic oscillation of any frequency with a pulse of the form of a probability function." A cosine type elementary signal and its spectrum are illustrated in Fig. 25. It has a finite band width and a finite duration with 76.8 % of its energy inside the band Δt or Δf, and only 11.6 % on either side.

When the oscillatory components of the evoked potentials are compared with elementary signals, remarkable similarity between the fine details of evoked potential components and elementary signals is often observed (see Figs. 17, 18 and 25). Numerous examples have been presented here in showing that such different waveshapes can be elicited by presentation of a stimulus, and that the released waveshapes are excellent facsimiles of the elementary signals. According to this interpretation, evoked potential components resembling elementary signals are predicted. The search for the biological correlates of these very stable oscillatory components of evoked potentials will remain as an important research subject for the feature. There are a number of studies in the literature related to the evoked oscillatory components of the brain mechanisms. Such components were recorded in the olfactory bulb (Freeman, 1972), and in the hippocampus of the cat (Horowitz, 1972).

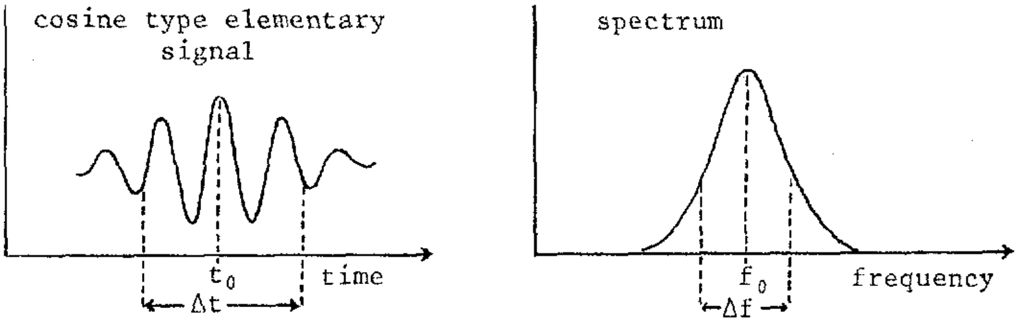


Fig. 25. Cosine type elementary signal and its spectrum.

probabilities, each selectivity channel shows consistent phenomena which is called strong resonance. The elements of the matrix are either 1 or 0 depending on whether a specific selectivity channel exists in the corresponding nuclei or not. Hence, the sum of identical columns gives the number of common selectivities of the RF and IC. The ratio of common selectivities is computed as follows from the rough considerations on the histograms of Fig. 15 and Fig. 16; R=8/18=0.44 (44%).

Accordingly, there exist considerably significant common regulative processes between the RF and IC in the high frequency bands. The filtered components of the EPs of the RF and IC, in the common selectivities, show resembling oscillatory transient responses (Fig. 17 and Fig. 18). Existence of such oscillatory responses give a hope for the neural networks with the same design and frequency selectivity may exist in the RF and IC.

5. CONCLUSIONS

Major emphasis has been placed in this study on the high frequency resonance phenomena in the brain stem structures such as IC and RF, by allowing the comparison of the spontaneous activity recorded immediately before stimulation with the single evoked potentials both in the frequency domain and in the time domain. In this chapter the conclusions drown from the experimental results and theoretical arguments are summarized.

1- The selectively averaged evoked potentials of the RF and IC which are obtained from the freely moving cats during the waking stage show short latency waves. The most prominent short latency wave seen in the SAEPs of the IC is a positive wave with a 5-5.5 msec latency. Similarly SAEPs of the RF show a marked negative wave of 4.5-5 msec latency.

2- Amplitude frequency characteristics obtained from the SAEPs of the RF and IC show various frequency bands up to 1000 Hz. Mean value amplitude frequency characteristic curves of the RF and IC show consistent selectivities in the high frequency range. The high frequency consistent selectivities of the RF are: 60 Hz, 110 Hz, 240 Hz, 320 Hz and 410 Hz. The high frequency consistent selectivities of the IC are: 80 Hz, 160 Hz, 210 Hz, 300 Hz and 700 Hz. Less consistent amplitude maxima around 500 Hz and 700 Hz are also noted in the amplitude frequency characteristics of the RF.

3- Frequency domain analysis of the recordings over four hundred EEG-EP epochs from the RF and IC during 6 experiments with 4 cats are done. During the analysis, frequency stabilization of the response upon stimulation is observed. Frequency stabilization factor is obtain for a particular experitime-coincident minimal values giving the short latency waves of the SAEPs. Therefore, the short latency peaks of the RF and IC evoked potentials should not necessarily reflect single mechanisms, but indeed have very complicated structures.

8- The effect of jitter or of systematic time differences creates more synchronization problems for the very fast responses than the slower responses of the brain evoked potentials. Averaging may cause significant loss of amplitude and serious changes in the short latency waves.

9- When comparing the evoked potentials of the RF with the far-field evoked potentials recorded from the vertex of the cat, the negative wave N1 (in latency about 4.5-5 msec) coincides in time with P4 of the far-field evoked potentials. Therefore, the wave 4 of the far-field potential thus seems to represent a composite potential which might originate from the RF.

10- The oscillatory components of the RF and IC, which are measured for an interval of only up to 100 msec, indicate two facts. One is that at least up to about 1000 Hz, and for durations at least within the limits of 50-7 msec, the information area is a characteristic of the RF and IC in case of auditory stimuli. The other fact arises from the first one is that the RF and IC appear to have an adaptive time constant at least between 50-7 msec. This last fact enables us to estimate the threshold area for very short durations of stimulus. Unless the inter-stimulus interval of a paired stimulus is at least 7 msec, the RF and IC can not regognize them as two separate stimuli independent and distinguishable from each other.

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