A PREDICTION OF TEMPLATES IN THE AUDITORY CORTEX SYSTEM

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To my dear family
Abstract

In this study variation of human auditory evoked mismatch field amplitudes in response to complex tones as a function of the removal in single partials in the onset period was investigated. It was determined: 1-A single frequency elimination in a sound stimulus plays a significant role in human brain sound recognition. 2-By comparing the mismatches of the brain response due to a single frequency elimination in the “Starting Transient ” and “Sustain Part” of the sound stimulus, it is found that the brain is more sensitive to frequency elimination in the Starting Transient.

This study involves 4 healthy subjects with normal hearing. Neural activity was recorded with stimulus whole-head MEG. Verification of spatial location in the auditory cortex was determined by comparing with MRI images. In the first set of stimuli, repetitive (‘standard’) tones with five selected onset frequencies were randomly embedded in the string of rare (‘deviant’) tones with randomly varying inter stimulus intervals. In the deviant tones one of the frequency components was omitted relative to the deviant tones during the onset period. The frequency of the test partial of the complex tone was intentionally selected to preclude its reinsertion by generation of harmonics or combination tones due to either the nonlinearity of the ear, the electronic equipment or the brain processing.

In the second set of stimuli, time structured as above, repetitive (‘standard’) tones with five selected sustained frequency components were embedded in the string of rare (‘deviant’) tones for which one of these selected frequencies was omitted in the sustained tone. In both measurements, the carefully frequency selection precluded their reinsertion by generation of harmonics or combination tones due to the nonlinearity of the ear, the electronic equipment and brain processing. The same considerations for selecting the test frequency partial were applied.

Results- By comparing MMN of the two data sets, the relative contribution to sound recognition of the omitted partial frequency components in the onset and sustained regions has been determined.

Conclusion- The presence of significant mismatch negativity, due to neural activity of auditory cortex, emphasizes that the brain recognizes the elimination of a single frequency of carefully chosen anharmonic frequencies. It was shown this
mismatch is more significant if the single frequency elimination occurs in the onset period.
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Introduction

Recognizing objects in the environment from the sounds they produce is one of the primary functions of the auditory system. Recognition is possible, in part, because acoustic features of sounds often represent physical properties of their sources. As a simple example, one distinguishes and recognizes immediately a tone heard from a playing guitar than a piano. This is because, although both sounds originate from thin tensioned vibrating strings, the harmonics generated by the guitar’s resonator differ from those of the piano resonator. Exciting resonances in large objects, produces mostly lower frequency partial waves relative to those produced by a small resonating object. This has led the researchers to speculate the significance of the contribution of frequency distributions of complex waveforms into sound recognition.

The overall detection of frequency change in human auditory cortex has been studied. This present study is the first to investigate whether a single omitted frequency component in the onset period produces significant differentiation.

Neuromagnetic imaging is vastly used for the study of human auditory cortex. In this study, neural activity of 4 human subjects is recorded coincident with the sound stimulus by whole-head Magneto-encephalography (MEG). This is an imaging technique used to measure the magnetic fields produced by electrical activity in the brain via extremely sensitive devices such as superconducting quantum interference device (SQUIDs).

The magnetic fields were analysed by mismatch negativity (MMN) or mismatch field (MMF) which is a component of the the event related potential (ERP). It arises from electrical activity in the brain which can occur in any sensory system, but has most frequently been studied for audition and for vision. In the case of auditory stimuli, the MMN occurs after an infrequent change in a repetitive sequence of sounds. For example, a rare deviant sound can be interspersed among a series of frequent standard sounds. The deviant sound can differ from the standards in one or more perceptual features such as pitch, duration, or loudness. The MMN can be elicited regardless of whether the subject is paying attention to the sequence. During auditory sequences, a person can be reading or watching a silent subtitled movie, meanwhile show a clear MMN.
In this study, the presence of significant mismatch negativity, due to neural activity of auditory cortex, emphasizes that the brain recognizes the elimination of a single frequency of carefully chosen anharmonic frequencies.
Part I

Theory of the Study
Chapter 1

Physics of Sound and Hearing

In this chapter acoustic or physics of sound and its close application in human auditory study has been introduced. The basic understanding of sound and hearing requires knowledge on the physics of generation, transmission and reception of sound. In a media such as air these happen due to the two properties of it: inertia and elasticity. If the atoms or molecules of the air are displaced from their normal configuration it must be subject to a restoring force, and if the air is to be capable of transmitting vibration, it must posses inertia so that when it is restored to its normal configuration, the momentum which it has gained may carry it through that position to a displacement opposite to the original one. However the sound heard by human is generated by a source, transmitted through air, and received by the mechanical and chemical mechanism of the auditory system. Its reception or perception occurs by chemical and electrical activities in the brain. In the following sections I will discuss the fundamentals of physics involved in this study in detail.

1.1 Physics of Sound
Experiments have shown that a healthy young person interprets a vibration disturbance as sound, if its frequency lies approximately between 20 to 20,000 HZ. Sound waves are generated in many forms such as the sinusoidal vibrations produced by a tuning fork, a complex form produced by a violin and a non-periodic form associated with an explosion. In studying the fundamentals of vibration it is common to begin with the simplest type: a linear one-dimensional harmonic oscillation that has only a single frequency component. A point mass oscillating only in one dimension where damping or forcing does not exist is represented by the following equation:

$$\ddot{x} + \omega^2 x = 0$$

$$x = Acos(\omega t + \phi)$$

The frequency of the vibration $\omega$ depends on the mass in kg and stiffness in N/m. $\phi$ and $A$ the initial phase angle and the amplitude of the motion depend on the initial condition of the vibration.

However most vibration systems are not as simple as a point mass, but are extended systems. For example in a violin it is strings which are vibrated and in a drum it is a surface. By studying the ear carefully later in the next section we will find the process of sound delivery in an ear happens through multiple systems, which in some parts it involves the vibration of diaphragms, and bone structures. The vibration of a clamped bar at one end which resembles a
section of the inner ear called basilar membrane will be discussed. In studying the fundamentals of vibration of an extended system it is common to begin with the simplest extended system which is a vibrating string. Although the generation of waves on a string is transverse, its study yields to the general form of wave equation:

\[
\frac{\partial^2 y}{\partial x^2} = \frac{1}{c^2} \frac{\partial^2 y}{\partial t^2} \quad (1.1)
\]

Where: \( c^2 = \frac{T}{\mu} \)

The tension in string is represented by T. \( \mu \) is the mass per unit length and c is in m/s.

Other extended systems which are the interest of our particular study are: 1-a transverse vibrating bar clamped at one end which resembles a basilar membrane, 2-longitudinal vibrating bar clamped at two ends (ossicles) and 3-symmetric vibration of a circular membrane fixed at the rim(tympanic membrane). To find the wave equation of a bar clamped at one end it is common to start from deriving the wave equation of a free-free bar and apply the boundary condition off a free-clamped bar. Consider a segment of a bar where a force acts on one end so shear force associated with it exists on the other end. By applying the static equilibrium conditions of the net force and torque on a segment of the bar, and some simplifications, the wave equation is found to be [1,2]:

\[ \text{6} \]
\[
\frac{\partial^4 y}{\partial^4 x} = -\frac{1}{c^2 k^2} \frac{\partial^2 y}{\partial^2 t^2}
\]

Where: \( c^2 = \sqrt{\frac{Y}{\rho}} \), \( Y \) being the young modulus. \( k \) is the radius of the gyration of the cross section which commonly used in this topic is defined as: \( k^2 = \frac{\int r^2 dS}{S} \), where \( S \) is the cross section of the bar.

The significant difference between this equation and the string wave equation is the presence of the fourth partial derivative with respect to \( x \) rather than a second partial. Therefore the transverse waves do not travel along the bar with a constant speed \( c \). However by solving this equation by separation of variables one finds the transverse displacement as follow:

\[
y = \Psi(x) e^{i\omega t}
\]

\[
\frac{d^4 \Psi}{dx^4} = \frac{\omega^2}{k^2 c^2} \Psi
\]

or letting \( \nu = \sqrt{\omega ck} \)

\[
\frac{d^4 \Psi}{dx^4} = \frac{\omega^4}{\nu^4} \Psi
\]
If $\Psi$ can be expressed in terms of $\Psi = A \exp(\gamma x)$ by substitution into the previous equation it is found:

\[
\gamma = \pm \omega/v, \pm j\omega/v
\]

So the complete solution is given by:

\[
y = e^{j\omega t} (A e^{\omega x/v} + B e^{-(\omega x/v)} + C e^{j\omega x/v} + D e^{-j\omega x/v})
\]

None of the above individual terms in the above equation represents waves moving with speed of $c$, but they move with a phase speed $v$, where $v$ is a function of frequency.

By applying the boundary conditions of $y=0$ and $\frac{\partial y}{\partial x} = 0$ to the above wave equation the first five fundamental resonance frequencies are found to be:

\[
f = ck(j)^2 /2\pi L^2
\]

where the values of $j$ which determines the first five fundamental frequencies are: $j=1.875, 4.694, 7.855, 10.996, 14.137$

The reason the frequencies of a free-clamped bar are discussed in detail is because I have
adopted these frequencies to structure the synthetic sound signals of this study which will be discussed further later.

1.1.1 Energy distribution in sound waves

In the previous section wave equation was found through a vibrating string as a simple representative of a transverse wave. Transverse waves propagate only in solids, since gas and liquid cannot sustain the transverse shear necessary for transverse waves. However sound waves are longitudinal waves and can propagate in all phases of matter. Studying sound waves in gas which requires knowledge in thermodynamics leads to energy distribution in sound waves and definition of acoustic impedance which is an acoustic property of a medium.

Let us consider a fixed mass of gas. Kinetic energy in sound waves is found by considering the motion of the individual gas elements of thickness $\Delta x$. Each element will have a kinetic energy where the average is $\frac{1}{4}\rho_0 \dot{x}^2$, with $\rho_0$ being the density of gas. The average potential energy density is $\frac{1}{4}\rho_0 \dot{x}^2$ therefore the total energy is as follow [3]:

$$E = \frac{1}{2} \rho_0 \dot{x}^2$$
Intensity or energy flux is the product of energy density and velocity

\[ I = \frac{1}{2} \rho_0 c x^2 \]

Assuming a harmonic solution for wave equation similar to the one in section (1.1)

\[ I = \frac{1}{2} \rho_0 \omega^2 x^2 \]

A commonly used standard of sound intensity is given by the average of the softest audible tone.

\[ I_0 = 10^{-16} \text{Wcm}^{-2} \]

Sound density is measured in terms of “decibels” which is a dimensionless unit measuring the ratio of a given sound to the value of \( I_0 \) above.

\[ db = 10 \log(I / I_0) \]
By definition acoustic impedance is the opposition to the flow of sound through a medium. It is related to the density of the medium and velocity of the sound

\[ Z = \rho_0 c \]

Sound waves can be described in terms of amplitude, frequency, velocity and wavelength. The original amplitude and frequency of the sound depend on the characteristic of the sound source, however speed of sound through a medium depends on the physical properties of the medium. By analogy of the speed of a transverse wave defined in (1.2) to the longitudinal sound speed in fluid it is shown \( c^2 = B/\rho \) where B is the bulk modulus. In the discussion of a vibrating bar, it was shown that \( c^2 = Y/\mu \) is the speed in a longitudinal vibrating bar, where Y is the Young modulus.

1.2 Physics of Hearing

The physics of hearing requires understanding of the mechanical and electrochemical processes of auditory system. The mechanical structure involves the study of the ear anatomy, which in brief consists of 1-external ear: pinna, auditory canal, ear drum, 2-middle ear: ossicles(malleus,
incus, stapes) and 3-inner ear: oval window, cochlea, basilar membrane and round window. The electrochemical process of auditory system requires understanding the physiology of hearing which involves the study of neurons. This will be discussed in the next chapter.

1.2.1 External Ear

External ear consists of pinna, ear canal and eardrum. Pinna is the most outer section of the external ear. Some of the sound from a given source enters the ear canal directly, but some enters after reflection from one or more of the folds in the pinna. As the speed of sound in air is about 330 m/s, sound waves which their wavelength is in the order of the dimension of the external ear will resonate. There are also reflections from external ear, the upper part of torso such as the head and shoulders. The interference of the reflected waves with the direct ones will result in modification of the original spectrum of the sound waves. Due to these effects for humans, the enhancement of hearing sensitivity to the sounds in the range of 1.5 to 7 kHz from the free-field region to the eardrum is 5 to 20 dB. While some of this increase is due to
reflection of sound from the body, together with diffraction of sound by the head, most of the increase arises from two mechanisms: a) resonance of the concha (the opening of the ear canal) around 5 kHz; and b) resonance of the ear canal (meatus) acting as an organ pipe around 3 kHz.

The external ear acts as a directional amplifier of sound. Thus, the shifts in the structure of the spectrum with changes in sound direction provide important cues for sound localization. The complex structures of the pinna and ear canal are now recognized as significant components in the mechanisms that underlie the capacity of a listener to recognize and localize sounds in space. The physics of this will be discussed below:

**Pinna**

On the account of its shape and dimension, pinna contributes to the enhancement of the stimulus strength due to diffraction within 2-7 kHz. At higher frequencies, above about 6 kHz, the shape of the sound spectrum shifts systematically as the location of a sound source is
changed, both vertically and horizontally. Differences in the spectral shape of sounds, especially when they occur at low frequencies are often heard as changes in timbre, or tone quality. However, the spectral changes introduced by interference in the meatus are not usually heard as changes in timbre, especially when they occur at high frequencies. Rather, they are associated with the perceived location of the sound source [4]. Human listeners probably do not use changes in spectral shape at low frequencies for sound localization, because these changes are produced by reflections from the shoulders and torso (and perhaps nearby surfaces), and the position of these relative to the head is not fixed; therefore, the spectral changes at low frequencies do not provide consistent information about the location of a sound relative to the head. However, the pinna is fixed relative to the head, so spectral changes produced by reflections from the pinna are reliable indicators of source location. These changes occur mainly at frequencies above 6000 Hz, since it is only at high frequencies that the wavelength of sound is sufficiently short for it to interact strongly with the pinna. Since it is the spectral patterning of the sound which is important, the information provided by the pinna is most effective when the sound has spectral energy over a wide frequency range. When sounds at the eardrum include the type of spectral patterning that would normally be provided by the pinna, the sounds are usually heard as outside the head [5]. However, when the sounds lack such patterning (as can happen for sounds presented by insert earphones, for example), the sounds
may be heard as inside the head. If the listener is to make efficient use of spectral cues associated with the direction of a sound source, then it is necessary to distinguish spectral peaks and dips related to direction from peaks and dips inherent in a sound source or produced by reflections from nearby surfaces. Thus one might expect that a knowledge of the sound source and room conditions would also be important. However, knowledge of the spectrum of the sound source might not be essential, since, the two ears provide separate sets of spectral cues, so the difference between the sound at the two eardrums can be used to locate unfamiliar sound sources. Even for sound sources in the median plane (all points equidistant from the two ears), asymmetries in pinna shape may result in spectral shifts, which can be used for localization if the stimuli contain audible components with frequencies above 8 10 kHz [6].

**Ear Canal**

The ear canal consists of two parts: concha, which is the opening of the ear canal, the ear canal, which is in the form of a pipe, approximately 2-cm in length, leading to the tympanic membrane and finally the tympanic membrane, which encloses the ear canal. The ear drum is
coupled to the middle ear and isolates the middle ear from the world outside.

The opening, concha, is physically and mathematically modeled. These models confirm that the concha operates over a broad-band of frequencies and a large dynamic range of input while maintaining a low power consumption. An approximated physical model of the human concha is developed by Lopez and Meddis [7].

The simplest physical model of an ear canal is a pipe enclosed in one end, which the first resonance harmonic due to its length is around 3000 kHz. It is not until the sound reaches the eardrum that the energy of the mechanical wave becomes converted into vibrations of the inner bone structure of the ear.

After passing through the external ear a sound wave causes the vibration of the ear drum which is a tightly stretched membrane separating the external and the inner ear. The physical model of the tympanic membrane is a circular membrane fixed at its rim. To solve for its resonance frequencies, it is best to solve the wave equation for a free membrane then apply the boundary condition of a fixed rim as below:

In a two dimensional situation (1.1) the wave equation is extended to the form of:

\[
\frac{\partial^2 y}{\partial x^2} + \frac{\partial^2 y}{\partial z^2} = \frac{1}{c^2} \frac{\partial^2 y}{\partial t^2}
\]
By writing this equation in a polar coordinate system and applying the boundary condition of \( y(a, \theta, t) = 0 \). The solutions are found to be in the form of Bessel functions as below:

\[
y_{0a} = A_{0n} J_0 (k_{0n} r) e^{j \omega_0 t}
\]

Therefore the first few fundamental frequencies are:

\[
f = (j) f_1, f_i = \frac{2.405}{2\pi a} \sqrt{\frac{\tau}{\rho}}
\]

where \( j = 2.29 f_1, 3.598 f_1, 4.90 f_1 \) and \( a \) is the radius of the membrane.

1.2.2 Middle Ear

Vibration of the ear drum (tympanic membrane) causes vibration of the three small connected bones of the middle ear named the ossicles malleus, incus, and stapes. They all move as a unit, in a type of lever-like action. The first bone, the malleus, is attached to the tympanic membrane, and the back-and-forth motion of the tympanic membrane sets all three bones in motion. The final result of this bone movement is pressure of the footplate of the last (smallest) bone, which is the stapes, on the oval window. The oval window is one of two small membranes which allow communication between the middle ear and the inner ear. It also prevents the inner ear
from leaking. The three bones act as a piston and couple the vibrations of the tympanic membrane to the oval window.

The Middle ear is a mechanical structure which provides the energy necessary to compensate for the acoustic impedance mismatch of the outer and the inner ear. Its function is significant because it transfers sound signals from the external ear which is an air filled medium, air being compressible, to the inner ear which is a liquid or simply water field medium, water being a relatively incompressible medium. This physical property in sound is defined as acoustic impedance. The ratio of the acoustic impedance of water to air is 3400. This means if the middle ear did not exist according to the reflection property of sound energy at the boundary: \[ \frac{2Z_a}{Z_a + Z_w} \] the energy transmitted to the oval window which is the opening of the inner ear would have been \(10^{-4}\) of the energy incident to the ear drum. However the middle ear is nearly compensating for this acoustic mismatch by the means of amplifying the air pressure which causes the vibration of the tympanic membrane through its lever function, which is associated with the length difference of mainly the two levers of malleus and incus (their length ratio is 1.3). The second cause for this amplification is due to the hydraulic action of the middle ear, which is associated with the area difference of the ear drum and the oval window (their area ratio is 30). Therefore the pressure on the oval window is 40 times greater then the pressure on the ear drum. This is about a 25dB gain in pressure.
1.2.3 Inner Ear

The inner ear is responsible for transforming the sound waves into nerve impulses that the brain can analyze. The portion of the inner ear that deals with hearing is known as the cochlea (in Latin it means snail). The shape of the cochlea resembles a tube of decreasing diameter which is coiled sharply upon itself two and three quarter times ending blindly at the apex (fig 2.1-A). The cochlear spiral begins at the vestibule.

The Scala Vestibuli and Tympani which are continues in the apex, are filled with watery fluid called perilymph (high concentration in Na\(^+\), low in K\(^+\)) the Scala Media is a self-contained sac filled with endolymph (low concentration in Na\(^+\), high concentration in K\(^+\)) the Scala media houses the transducer cells resting on the basilar membrane (contains the sensory receptors of the auditory system called organ of corti).

Pressure changes produced by the to-and-fro movements of the stapedia footplate causes the bending of the basilar membrane, which is a flexible membrane lying in the cochlea. This bending is due to the phase difference of the pressure changes of the fluid. This bending is communicated to the receptor structures that lie within the scala media.
Since the acoustic properties of the perilymph and endolymph are sufficiently similar, this
transmission through one canal to the other is effective. At the end these pressure changes are relieved by the movements of the membrane within the round window as no one has found resonances due to the round window in the cochlea area.

**Effect of the non-linearity of the inner ear on hearing**

An Italian violinist, Tartini (1692-1770) discovered a difference tone could be distinctly heard by double-stopping on the violin [8]. If two tones are sounded strongly together a series of tones can be heard whose frequencies are a combination of the two generating tones. This phenomenon is not observed if the two frequencies are played on each ear individually. It is the superposition of the two frequencies on the basilar membrane, which acts as a nonlinear system, that generates a series combination of the two frequencies.

**Mechanical limitations of the inner ear are the reasons for non-linearity of the hearing**

Limitation due to the speed of opening and closing of the ion channels (ms) of the hair cells on
the basilar membrane, and the rate at which action potentials are transmitted through the nerve (ms) are the reasons for incapability of the inner ear to linearly encode sounds that vary on a time scale significantly faster than a millisecond. Action potentials are sudden changes in the potential of the neurons, which will be discussed in more detail in the physiology chapter. A second reason for non-linearity of hearing is the range of sound intensities that is sufficient to stimulate the nerve membrane receptors and not yet overload.

The problem of coding a wideband acoustic signal when only very low pass (speed and range) channels are available may be solved by breaking the wideband signal up to many narrowband signals and transmitting each signal separately on an independent narrowband channel. Thus the wideband acoustic signal could be analyzed by parallel overlapping of the narrowband filters [9]. This is where the non-linearity of the hearing comes into consideration.

**Combination Tones**

The physical effect of the non-linearity of the hearing is an interesting matter to study. In the discussion of physics of sound, we confined ourselves to linear harmonic oscillations, however since we are dealing with non-linearity of the ear, we might as well find the solutions to a nonlinear harmonic system; where the relationship between acceleration and displacement is
defined to be nonlinear as the following:

\[ \ddot{x} + \omega^2 x + ax^2 + bx^3 + \ldots = 0 \]

The first two terms are what we saw in the linear harmonic discussion. The rest of the terms are what it defines the non-linearity of the system. In usual derivations the coefficients are are assumed to be such that we can neglect the terms in \( x^2 \) and higher powers. However, as \( x \) increases the \( x^2 \) term is likely to become effective.

The frequencies of a nonlinear vibrating system, which is subject to two forces is obtained through the solution of the following equation:

\[ \ddot{x} + \omega^2 x + ax^2 + F_1 \sin n_1 t + F_2 \sin(n_2 t + \theta) = 0 \]

The frequencies are: \( 2f_1, 2f_2, f_1, f_2, f_1 - f_2, f_1 + f_2, 3f_1, 2f_1 + f_2, f_1 + 2f_2, 2f_1 - f_2, f_1 - 2f_2 \).

The existence of the combination tones has been shown by simultaneously introducing into the ear a strong pure tone of frequency \( f \) and another pure tone of variable intensity and frequency. It has been shown when the frequency of the exploring tone is in the vicinity of \( 2f \), \( 3f \), \( 4f \), beats are heard [8].
Chapter 2

Physiology of Hearing

There have been many different theories to define how the cochlea transforms sound information, including frequency, amplitude, and phase, into signals, which the brain perceives and recognizes. To study this matter understanding the physiology of the hearing is of great importance. So far mainly the physics of hearing involved in mechanical energy transportation of the sound signals was discussed. Sound energy in hearing appear in the form of mechanical energy until it arrives at the inner ear and more specifically, the organ of corti. Then the energy of sound appears as chemical energy. In the following sections what is discussed is the physiology of the hearing which is mainly focused on the mechanical energy transduction to chemical energy and its transportation until it is perceived by the higher levels of the brain.
2.1 Transducing Mechanical to Electrochemical Energy

As discussed in the inner ear section, the organ of corti lies on the surface of the basilar membrane, fig(2.1-B), it serves as a system to transduce mechanical energy into electrochemical forms. The actual sensory receptors in the organ of corti are two types of hair cells; inner hair cells which are about 3000 in number extending in a single row from a base to apex and outer hair cells which are about 12000 in number extending in three or four rows. From the upper surface of each hair cell, 50 hairlike stereocilia emerge, which increases in length along the radial axis of the hair cells[11]. The basilar membrane is displaced due to the phase difference of the pressure waves in the liquid which fills the cochlea. This displacement of the basilar membrane is communicated to the organ of corti, so the hair cells move in relation to the stationary tectorial membrane. The bending of the hairlike extensions of the hair cells causes a mechanical transduction to trigger. This effect opens 200-300 cation-conducting channels allowing rapid movement of positively charged potassium ions into the tips of the stereocilia, which causes depolarization of the entire hair cell membrane. Due to the polarization of the membrane chemical messengers called neurotransmitters are released into the space connecting the nerves called synaptic cleft. These neurotransmitters are capable of stimulating the dendrites of the auditory nerve fibers called cochlear nerves that are responsible for carrying the information from the receptor to the processing units in the brain.

Based on one theory outer hair cells are responsible for sharpening the resonance peak. If
so, the passing wave stimulates the hair cells and in response some mechanism feeds mechanical energy back into the sound wave, causing it to become more sharply tuned and allowing for better discrimination. Outer hair cells are known as the Q-enhancement in the membrane since when damage occurs to the outer hair cells the sharper tuning disappears.

### 2.2 Physics of Membrane Potentials

A nerve cell consists of four major sections: input end (dendrites), cell body (soma), long conducting portion (axon), output end (synapse). A threshold mechanism is built into the input end; when an input signal exceeds a certain level, the nerve fires and an impulse or action potential of fixed size and duration travels down the axon. The diameter of the axons in a human ranges from a few μ to about 2 meters. The pulses travel with speed ranging from .6-100 m/s.

The axons are surrounded by either a thin membrane (5-10 nm) called unmyelinated or a thick membrane called myelinated (in order of μ m) membrane [10].

A micrometer inserted inside a resting axon shows a potential of 70mV less than the potential outside of the axon. The magnitude of this potential is determined by thermodynamics: the ratio of the ions concentration on the two sides of the membrane. When
the membrane is permeable to several different ions, the potential across depends on three factors: 1) the polarity of each ion, 2) the permeability of the membrane to each ion, 3) the concentration of the respective ions on the inside and outside of the membrane. Overall, the concentration $C$ of each ion type tends toward thermal equilibrium between the two compartments according to the Boltzmann expression; this is named Nernst equation which finds the membrane potential on the inside of the membrane according to the following:

$$
emf = \frac{k_B T}{|e|} \log \frac{\text{Concentration}_{\text{inside}}}{\text{Concentration}_{\text{outside}}} = -70\text{mV}
$$

When using this equation the extracellular fluid outside the membrane remains at zero, and the above equation is the potential inside the membrane.

To calculate the potential when the membrane is permeable to several different ions the Goldman-Hodgkin-Katz equation, as follows, is applied based on the polarity of the charge, permeability of the membrane and the concentration of the respective ions on the inside($i$) and outside($o$) of the membrane:

$$
emf = -61 \log \frac{C_{Na_i} P_{Na_i} + C_{K_i} P_{K_i} + C_{Cl_i} P_{Cl_i}}{C_{Na_o} P_{Na_o} + C_{K_o} P_{K_o} + C_{Cl_o} P_{Cl_o}}
$$
2.3 Nerve Action Potential

Signals through nerves are transmitted by action potentials, which are rapid changes in the membrane potential. A typical action potential is shown as a function of time in the figure (2.3-A). As seen in the figure the potential inside of a resting nerve is -70mV. Due to the stimulation of nerve by an input signal which causes concentration difference of the ions on both sides of the membrane the potential of the nerve rises to +40mv in a few ms. This is called depolarization. Then it falls down to -90mV (repolarization) and then it recovers slowly to its resting value of -70 mV. To conduct a nerve signal, the action potential moves along the nerve fiber until it comes to the end of the nerve.
Fig. 2.3-A. This is a typical figure of action potential, which represents the superposition of potential change due to Na+ and K+ ion movements. Fig.2.3-B represents the two individual peaks due to the Na+ and K+ movements. Adopted from wikipedia.
Otherwise the depolarization stage fails to initiate. When an action potential is generated, it causes the adjacent regions of the membrane to trigger, therefore the next action potential is generated. This is how a signal is transported from input of a neuron toward the dendrites(output). Rearrangement of the ions after action potentials are generated occur to rearrange the ions for equilibrium.

2.4 Transport Properties of the Resting Nerve Membrane for Sodium Potassium

To understand the level of the normal resting membrane potential it is important to study the sodium-potassium pumps. These pumps are actively pumping sodium ions in the extracellular fluid and potassiums in the intracellular fluid. The number of Na pumped out is always more than the K inside therefore when the nerve is at rest inside the membrane the potential is negative with respect to the potential outside and that is -90mV. Bellow is the table of the concentration:

\[
\begin{align*}
Na^+ & \text{ 142 m mol/l outside} & Na^+ & \text{ 14 m mol/l inside}
\end{align*}
\]
\[ K^+ \text{ 4 m mol/l outside } K^+ \text{ 140 m mol/l inside} \]

Leak channels exist on the nerve membrane through which sodium and potassium ions can leak. On average the channels are far more permeable to potassium than to sodium ions.

Which is important in determining the level of the resting membrane potential.

2.5 Determination of sound frequency

In physiology literature, it is greatly accepted that the frequency in a non-linear form is transduced based on the stiffness of the basilar membrane. Basilar membrane is a fibrous membrane that separates the scala media from scala tympani. Because the fibers are stiff near the base and free in one end they can vibrate. The stiffness due to the diameter and width change of the fibers decreases exponentially from base to the free end by a factor of 100, since the overall width of the basilar membrane increases by a factor of about 6 (the narrowest at the base is .08mm the widest at the apex is .5 mm). As a result basilar membrane is acting as a frequency analyzer, resonating high frequencies near the base and low frequency resonance occurs at the apex.
2.6 Determination of Sound Amplitude

As the sound becomes louder, the magnitude of vibration of basilar membrane and hair cells also increases, so that the hair cells amplitude is determined by the amount of the hair cell bending or the number of bent hair cells. This effect is transferred to the nerve signals by increasing the frequency of the firing of the action potentials. A high firing rate indicates high amplitude of the sound signal and vice versa. Also an increase in the number of hair cells activated, increases the firing rate.

2.7 Central Auditory Mechanism

Studying the central auditory mechanism (fig 2.7) indicates how specific information in sensory signals is dissected out as the signals passing through different levels of neural activity.

The role of the brainstem is divisible into three broad categories. The first is to provide transit and processing nuclei for ascending and descending pathways that convey influences to and from the cerebrum, cerebellum, and spinal cord. The second is to play a part in a range of activities such as consciousness, the sleep-wake cycle, and respiratory and cardiovascular
The third relates to actions of the cranial nerves, which are comprised of sensory fibers terminating in brainstem nuclei and motoneurons originating in brainstem nuclei. Cranial nerves are nerves that emerge directly from the brain stem. Although thirteen cranial nerves in humans fit this description, twelve are conventionally recognized. The 8th nerve carries auditory information from the cochlea and vestibular information from the semicircular canals, utricle, and saccule. It is really two nerves running together, the auditory (cochlear) nerve and the vestibular nerve. The auditory nerve carries the signal from spiral ganglion of corti into the cochlear nucleus located in the upper part of the medulla. At this point all the fibers synapse and second order fibers pass mainly to the opposite side of the brain stem to terminate in the superior olivary nucleus(some also pass to the superior olivary on the same side. From superior olivary nucleus, the auditory pathway then passes upward through the lateral lemniscus; some of the fibers terminate here others bypass this and pass on to the inferior colliculus where almost all fibers terminate. From here the pathway passes to the medial geniculate nucleus, where all the fibers synapse. Finally the pathway proceeds to the auditory cortex located in the superior gyrus of the temporal lobe.
The principal central connections of hearing.

Solid coloured lines show the ascending pathways to the primary auditory cortex. Descending connections are represented by broken lines.

Fig. 2.7- Central Auditory Mechanism. Adopted from: instruct.uwo.ca/anatomy/530/530notes.htm
A high degree of spacial orientation is maintained in the fiber tracts from the cochlea all the way to the cortex. In fact there are three spacial representations of sound frequencies in cochlear nuclei, two representations in the inferior colliculi, one precise representation for discret sound frequencies in the auditory cortex and at least five other less precise representations in the auditory cortex and the association areas(Guyton). Therefore frequency recognition mainly happens in the auditory cortex.

2.8 Sound Frequency Perception In the Primary Auditory Cortex

Auditory cortex is tonotopicly mapped such that each specific area dissect out some specific feature of the sounds. For instance, one of the large maps in the primary auditory cortex discriminates sound frequencies and gives the person a perception of sound pitches. Another one of the maps is used to detect the direction from which the sound comes from and other areas of the auditory cortex detect special qualities such as sudden onset of sounds and so forth.
2.9 Discrimination of Sound Patterns by the Auditory Cortex System

It has been shown that the complete removal of the auditory cortex does not prevent a monkey from detecting sounds. However, it does greatly reduce or abolish its ability to discriminate different sound pitches and specially patterns. For instance, an animal that has been trained to recognize a combination or sequence of tones, one following the other in a particular pattern, loses this ability when the auditory cortex is destroyed; furthermore, it cannot relearn this type of response. Therefore, the auditory cortex is important in the discrimination of tonal and sequential sound patterns [10].
Chapter 3

Biomagnetism

Bio-magnetic fields are caused by electric currents in conducting body tissues like the brain, the heart, skeletal muscles or by magnetized material. In this chapter we will discuss the details of how magnetic fields are generated in the brain.

3.1 Magnetic field of a single nerve

The effect of a current carrying wire on a compass was discovered by Oersted on 1820. This discovery explains the existence of neurons’ magnetic field due to the ion transportation through the neurons.

The long cylindrical body of the nerve called axon has the properties that are similar to electrical cable. Its diameter may range from 1μm to meters. The shape of signals depending
on the diameter of the axons and few other reasons which will be discussed later may be conserved in a range from .6 to 100 ms. The axon core is either surrounded by a membrane (unmyelinated) or by an electrically-insulating dielectric phospholipid layer (myelinated). Myelinated fiber has its sheath interrupted at intervals by a short segment of membrane to make ion transportation possible. The type of surrounding of axon affect the speed of electrical signal transportation. A typical unmyelinated axon might have a radius of .7 μm where myelinated ones have a radius of up to 10μm, with nodes spaced every 1-2 mm.

It is valid to assume a nerve cell membrane with a thickness of about 6 nm and 6μm of radius acts as a capacitor. The electric field of this capacitor can be calculated since the membrane acts as an insulator separating the two conductors of the ions inside and outside of the membrane. To ignore nonuniform electric fields of the edges, it is assumed that the sheets of the electric charges of ions on both sides of the membrane are infinite. By insertion of a microelectrode inside an axon, the membrane resting potential is found to be about -70 mV, therefore the electric field within the membrane is assumed to be constant:

\[ E = -\frac{dV}{dx} = -(70 \times 10^{-3} V / (6 \times 10^{-9} m) = 1.17 \times 10^7 Vm^{-1} \]

Therefore electric charge density is:

\[ \sigma = \frac{E}{4 \pi (1/4 \pi \varepsilon)} = 1.03 \times 10^{-4} Cm^{-2} \]
\[ \sigma / e = 6.4 \times 10^{14} \] charged atoms in one square meter

To get an estimate of the number of the ions that are in contact with the surface of the membrane one can start from the diameter of an atom that is \(10^{-10}\). So in one square meter, \(10^{20}\) atoms are in contact with the surface, which means the charged atoms in one square meter are \(10^{14}/10^{20}\) \([10]\).

The existence of the potential difference in axons is due to the contribution of potassium and sodium diffusion through the membrane and the NA-K pumps. As discussed in the previous sections, when a sudden change stimulates a normal resting potential an action potential is generated. The successive resting, depolarization and repolarization of an action potential is associated with ion transportation to extracellular(out going current) and from intracellular(return current) fluid. One model to describe this is to divide the axon into many small segments, where the length of each segment is in the order of the magnitude of the length of an action potential (a few mm).

The outcome of the outgoing and return current is a loop of current which in biophysics is modeled as a current dipole. This current dipole generates a magnetic field. If the axons are symmetric the generation of the magnetic field is week due to the cancellation effect of the magnetic field generated on both sides of the membrane. Therefore axons, which are usually asymmetrically organized, generate a stronger magnetic field. This is because the path of ion movement on one side of the membrane is longer than the other side.
A postsynaptic potential is a sudden potential change similar to an action potential due to the ion transportation but this occurs in synapses. A postsynaptic potential lasts about 10 ms which is longer than an action potential (1-2 ms), therefore it is believed the magnetic field detected outside is due to the synapses.

Fig 3.1-A. Schematic figure of a single neuron. *Adopted from: www.ccs.neu.edu*

Fig 3.1-B. Auditory cortex at the temporal lobe and Sylvan fissure. *Adopted from: www.ccs.neu.edu*
The other possibility for this is that since axons are usually symmetric the generation of the magnetic field is mainly due to the synapses which are the branched projections from an axon. Synapses are usually densely branched and appear in asymmetric shapes (fig 3.1-A) so it is thought the detectable neuron’s magnetic field is due to the ion transportation in synapses rather than the axons.

Since we are following the model of segmented currents, it is convenient to apply Bio-Savart law to estimate the magnitude of the generated magnetic field due to these segments or as it is put in physiology field the "current dipoles".

\[ B(r) = \frac{\mu_0}{4\pi} \int \frac{d\Gamma \times \hat{r}}{r^2} \]

By applying this to a loop of current (current dipole) the magnetic field is:
\[ B(r) = \frac{\mu_0}{4\pi} \frac{IR}{R^2 + d^2} \hat{r} \]

where \( R \) is the radius of the current loop and \( d \) is the distance of the loop to the SQUID sensor.

Due to the obvious fact that SQUID sensors will detect the radial component of the magnetic field and they are blind to the tangent component of fields to them therefore only the radial components of the magnetic fields of the brain are detectable with the SQUID configurations which are tangent to the head surface. This is possible if the neurons themselves are aligned tangent to the head surface. Fortunately the neurons of the Silvian Fissure which is in the auditory cortex are also positioned tangent to the head surface (fig 3.1-C).

### 3.2 The cable model of a segment of Axon

Assuming electric signal propagation inside axons obey Ohm’s law and membrane has capacitance, Kirchhoff’s law (conservation of energy and charge) is applied to a small segment of the axon. It is valid to assume a membrane has capacitance since it is a dielectric which separates two conductors, intracellular and extracellular fluids. Therefore the membrane
behaves as a capacitor.

The result is a differential equation that is independent of any particular model for the cell membrane. This is called the cable model for an axon.

In the resting state there is a tendency for leakage; negative ions move out and the positive ions move in if their concentration ratio is unity. Based on the Kirchhoff’s law, the sum of all the ion currents is the current through the membrane, \( i_m \). If there is no mechanism to maintain the charge on the capacitor’s plates it discharges it so:

\[
-i_m = \frac{dQ}{dt} = C \frac{dv}{dt}
\]

This equation was derived by making the assumption that this segment is an isolated axon and there is no mechanism to maintain the charge on the membrane or the plates of the capacitor. By applying ohms’ law and rearranging this equation, the familiar equation for exponential decay of voltage is obtained as follows:

\[
v = v_0 e^{-t/\tau}
\]
One model, which is used to explain the propagation of the electrical signals through an axon, is the cable model. This divides the axon up into many small segments, each with capacitance C. A resistance is designated to the extracellular and intracellular fluids, which separates the capacitance of each segment of the membrane. When the neuron is at rest the potential across the membrane or the capacitor is –70mv. However when the neuron is activated all it depolarizes and then repolarizes the cell and eventually goes back to the resting potential. During these stages current will flow across the membrane and along the axon. According to the cable model the current through the membrane shortens the capacitor. The current along the axon and the return current is represented by the current flow through the resistors.

According to the fig 3.2 for a small portion of an axon the equation above is corrected to the form of
\[ i_m(x) - i_m(x + dx) - i_m = \frac{dQ}{dt} = C \frac{d(v_i - v_0)}{dt} \]

or

\[ \frac{1}{2\pi ar g_m} \frac{\partial^2 v}{\partial x^2} - v - \frac{c_m}{g_m} \frac{\partial v}{\partial t} = -v_r \]

In the above equation it is simply assumed \( j_m = g_m(v - vr) \)

\[ \lambda^2 = \frac{1}{2\pi ar g_m} \]

\[ -\tau = \frac{c_m}{g_m} \]

Where \( \lambda \) and \( \tau \) play the role of scale length and scale time of the described process [10].

3.3 Magnetostatics

3.3.1 Forward Problem

It is possible to locate an unknown electric current source in the brain by analyzing brain magnetic field (MEG) measurements. The study of the field source is called inverse
problem. However before one can estimate the source of a field it is important to understand the forward problem, i.e. how the magnetic field arises from a known source. First let us assume the magnetic and electric fields are generated from a source current density $I'$. This current is due to the electromotive force of biological activity in a conducting tissue of conductivity $\sigma$ and it is called induced current. The magnetic permeability is assumed to follow $\mu = \mu_0$, everywhere in the brain. To compute the electric field $E$ and the magnetic induction $B$ caused by the bioelectric source $I'$, the use of the quasistatic approximation of the Maxwell’s equations is justified [12] and this approximation is stated by the equations below [13]

$$
E = -\nabla V
$$

$$
\nabla \times B = \mu_0 J
$$

$$
\nabla \cdot B = 0
$$

$$
I = I' + \sigma E
$$

where $V$ is the electric potential. $I$ is the total current density and $\sigma E$ is the Ohmic or volume current.

The Biot-Savart law of a steady state line current was shown in the previous section. Below shows the magnetic field due to the volume currents:

By applying the curl on the above equation Ampere’s law is simply driven in the form of

$$
\nabla \times B = \mu_0 I
$$
Introduction of a vector potential $A$ in magnetostatics $B = \nabla \times A$ and its combination with Ampere’s law is led into the multiple expansion where in the absence of any monopole contribution, the dominant term is the dipole term:

$$A_{\text{dep}}(r) = \frac{\mu_0 I}{4\pi r^2} \oint r' \cos \theta' dl'$$

This equation could be written as

$$A_{\text{dep}}(r) = \frac{\mu_0 m \times r}{4\pi r^2}$$

Where $m$ is magnetic dipole moment. However, using useful vector identities, Stokes’ theorem and the boundary condition for an unbounded homogeneous medium (Sarvas) is written:

$$B(r, Q) = \frac{\mu_0 Q \times r}{4\pi r^2}$$

Where $B$ is the magnetic field due to a dipolar source of current dipole. In the above equation $Q$ is defined as dipole moment where concentration of the induced current to a single
point is defined as \( r_0 : I(r) = \sigma(r - r_0)Q \); \( \sigma(r) \) is the Dirac delta function. A current dipole is a good approximation for a small source viewed from a remote field point. As seen from the last equation for magnetic field the effect of volume currents is eliminated. This is because we are assuming the brain to be an unbounded homogeneous medium. Since we are interested in finding dipoles, the magnetic field expression above is written explicitly as a function of the dipole location and moment, and the dependency of the magnetic field on the measurement location \( r \) is to be implicit. It is important to mention the equipment I used to measure the magnetic field of the brain does not record all the 3 dimensions of the field, but only a scalar component of the field which is the radial component of dipoles that are tangentially oriented with respect to the skull.

### 3.3.2 Inverse Problem

The inverse problem is to estimate the location and orientation of the dipole current source within the head. In this study an integrated free MATLAB toolkit named "BrainStorm" was applied. This software is dedicated to Magnetoencephalography (MEG) and Electroencephalography (EEG) data visualization and processing. From the documentation of the software it is found that the name of the method used to solve this inverse problem is called: Recursively Applied and Projected -MUltilple Signal Classification(RAP-MUSIC). The basic method of estimation of the RAP-MUSIC relies on a dipole fit algorithm. It is important to note
that even with the assumption that all the electrical activity is a localized and dipolar source, the inverse problem has a non-unique solution. The efficient technique to solve the inverse problem is a "least squares fit". However a least squares fit performs best when provided with a reasonable initial guess about the location of the dipole. In order to get a reasonable initial guess for the location of a dipole, a trial and error search of a few hundred dipoles works well. The initial location and orientation could be estimated by guessing and testing the accuracy of it, they are plugged into the forward equation(Bio-savart) to find if the corresponding field pattern is generated. Figure 3.3.2 shows the ability of inverse problem to localize the source of the neurons activity in the auditory cortex system at the time a stimulus is presented to the ear. The dots shows 3σ for the location of the electric dipoles and the line shows the direction of the dipoles at the time the stimulus is put to the ear.
Fig 3.3.2 represents the localization of the neurons activity of the auditory cortex at the time the sound stimulus was presented to the human ear. These were generated by using BrainStorm. The dot represents standard deviation of the location of neurons’ activity and the line represents the direction of the current dipole in three dimensions.
3.3.3 Measurements of Brain Magnetic field

The magnetic field generated by a single neuron is almost negligible; thus, when several thousands of nearby cells are synchronously active, the sum of extracranial magnetic field typically achieves a magnitude of only a few hundred femto Tesla \((1 \text{fT} = 10^{-15} \text{Tesla})\). Even the strongest neuromagnetic signals, those associated with epileptic spikes, are only a thousand femto Tesla \((10^{-13} \text{Tesla})\) in magnitude. This is still more than one billion times smaller than the earth’s steady magnetic field and the noise fields generated by even distant moving metal objects (e.g., cars and elevators) and power lines.

The detection and isolation of neuromagnetic signals is a challenging problem, the signals are very small and the background noise is nearly overwhelming. To reduce the amount of magnetic noise reaching the biomagnetometer, the system is operated in a magnetic and radiofrequency shielded room. The recording dewar contains magnetic detection coils which are continuously bathed in liquid helium to superconducting temperatures of 4.2K degrees Celsius.

During the Brain magnetic field recording, the subject is lying on a bed and the sensor is placed close to the subject’s head. Even applying all the precocious procedures, the data of a brain magnetic field measurement is contaminated by several sources of noise, which its reduction requires application of special techniques to make any use of the data. This will be
3.3.4 Magnetoencephalography

The non-invasive technique used to measure the magnetic fields produced by electrical activity in the brain via extremely sensitive device of superconducting quantum interference devices (SQUIDs) is called Manegoencephalography or MEG. This technique is a direct measure of brain function and has a very high temporal resolution. Events with time scales in the order of milliseconds can be resolved, differentiating MEG from other imaging techniques such as fMRI, PET and SPECT, which have much longer time scales. Also its spatial resolution is within millimeter precision.

The magnetic field passes unaffected through brain tissue and the skull, so it can be recorded outside the head. This is the feature of MEG which differentiates it from electromagnetoeencephalography (EEG). By analyzing the spatial distributions of magnetic fields, it is possible, by using a model such as a single equivalent current dipole, to estimate the intracranial localization of the generator source and superimpose it on an MRI.

The main drawback of MEG is that the signals of interest are extremely small, several orders of magnitude smaller than other signals in a typical environment that can obscure the
The first successful attempt to measure the magnetic field generated by bioelectric activity was made by Baule and McFee in the mid-60s using resistive induction coils. At that time they measured the magnetic field generated during human heart contraction [13]. In fact it is also possible to detect the most intense biomagnetic fields, like that generated by the heart during left ventricle contraction, using conventional coils coupled to a conventional amplifier. However most of the information contained in a biomagnetic signal is confined to the low frequencies: all electric cell activities are limited to frequencies below a few kilohertz, and most of the useful information for the successive clinical diagnosis is below 50 Hz. In this frequency range the only devices able to measure magnetic fields are the SQUIDs. The machinery which includes SQUIDs consists of several elements which must be specifically designed for this purpose: (i) the SQUID, which is the active element of the instrument; (ii) the SQUID electronics; (iii) the detection coil that actually senses the field; (iv) the dewar that keeps the inset in a superconducting state; and (v) the shielded room that attenuates external magnetic fields interfering with the measurement. In order to determine the current distribution in a specific body region and finally obtain information about its functionality, it is necessary to sample the magnetic field on as many spatial points as possible. Thus, for instance, all neuromagnetic systems used for brain activity measurements are today obtained from 100 or more SQUIDs. Moreover, in using such a large number of detectors, the mean performance of all the sensors is more important than the peak quality of the best ones. All the efforts in the
development of clinically oriented biomagnetic instrumentation are therefore aimed at producing very stable SQUIDs, with simple electronics (fewer parts, less trouble). Finally, noise reduction plays a role at least as important as SQUID tuning, and a working device cannot overlook the importance of this point.

3.3.5 SQUIDs

The Super Conducting Quantum Interference Device (SQUID) combines the physical phenomena of flux quantization and Josephson tunneling. The flux contained in a closed superconducting loop is quantized in units of the flux quantum $\phi_0 = \hbar/2e \approx 2.07 \times 10^{-15} \text{Wb}$.

Flux quantization is driven from the wave equation:

$$\psi(\vec{r}, t) = |\psi(\vec{r}, t)| \exp[i\phi(\vec{r}, t)]$$

If we take a ring of superconductor, as shown in fig 3.3.5-A, we get a condition on the magnetic flux through the center. Consider two different paths from $r_0$ to $r$.  

54
The difference between the two calculations of $f$ is the flux. Now $f$ is not a physical observable so the $f_1 - f_2$ does not have to be zero, but, $\psi$ does have to be single valued.

$$\psi_1 = \psi_2$$
$$e^{-i\frac{e}{\hbar c} f_1} = e^{-i\frac{e}{\hbar c} f_2}$$

$$\frac{e}{\hbar c} (f_1 - f_2) = 2n\pi$$
$$\varphi = f_1 - f_2 = \frac{2n\pi\hbar c}{e}$$

The flux is quantized. The observed magnetic flux is quantized in a region enclosed by a superconductor. However, the fundamental charge is seen as cooper pairs of $2e$. 
Fig 3.3.5-A represents two different paths around a magnetic flux through a superconducting ring. *Adopted from* www.quantummechanics.ucsd.edu

\[ \phi \] must be single valued in a superconducting loop. Considering a one dimensional geometry where the current flows through a barrier region connecting two superconductors, the supercurrent across the barrier has a simple sinusoidal dependence on the difference of the phase \( \varphi(z) \) of the wave functions of the two superconductors near the barrier.

The supercurrent density is written as
\[ j_s = \sum_{k=1}^{\infty} j_{sk} \sin(k\delta). \]

This equation is the most general form of the supercurrent across the barrier fulfilling the fundamental symmetry principles. Usually for all junction types the first term of the above equation is considered:

\[ j_s = j_0 \sin\delta \]

The Josephson current and the flux quantization effect which is in the order of femto-Tesla is the basic principles of the SQUID measurement in MEG. The DC SQUID was invented in 1964 by Arnold Silver, Robert Jaklevic, John Lambe, and James Mercereau of Ford Research Labs after B. D. Josephson postulated the Josephson effect in 1962. Practically in order to measure magnetic fields of biological activities squids of two kinds: dc and rf are designed which a brief introduction of them is found below.

**The dc SQUID**

If two identical Josephson junctions are connected in parallel, forming a super conducting
loop the device is called a dc SQUID. In this device a steady current bias can be used to operate it. The development of the dc SQUIDs is one of the most remarkable applications of superconductivity, in fact the dc SQUID is the most sensitive magnetometer presently available. By using a dc SQUID it is possible to build the fastest amplifiers with the lowest noise (close to the quantum limit). Figure 3.3.5-B shows a schematic diagram of a dc SQUID. In a more naive picture, let us suppose that a biasing current $I_b$ is fed through the ring according to the figure. Since the two junctions are identical, the current splits into two halves. If the current is equal to twice the critical current of the junctions, the voltage output is zero. If the biasing current exceeds the critical current, the two junctions are in a voltage state, i.e. the phase of the wavefunction oscillates in time according to Josephson equations.

When an external magnetic flux $\varphi$ is threading the loop a circular current is induced ($J = -\varphi/L$), changing the current flowing in the two branches and modifying the frequency of oscillation of the phase, eventually affecting the interference between the two currents. The result of this is that the critical current of the device is modulated by the external flux as discussed. The critical current modulation induces a voltage change across the SQUID related to the magnetic flux coupled to the loop. The sensitivity of this device is measured as voltage versus applied field: $V\varphi = \partial V/\partial \varphi$. 


Fig 3.3.5-B Schematic figure of a dc SQUID. Adopted from: rich.phekda.org/squid/technical/part3.htm

Fig 3.3.5-C Schematic figure of an rf SQUID. Adopted from: rich.phekda.org/squid/technical/part3.htm
The rf-SQUID

The rf-SQUID consists of a superconducting loop interrupted by a single Josephson junction [21](figure 3.3.5-C) Actually the rf-SQUID is mis-named, since there is no quantum interference of the phase across the junction. In fact the device behaves differently from the dc-SQUID, and may be considered as a parametric amplifier. The basic principle of operation of the rf-SQUID may be briefly outlined as follows. If the tank circuit is energized, a magnetic flux $\varphi$ is linked to the SQUID, and a superconducting current $I$ circulates in the ring, trying to maintain the total flux coupled to the ring $\varphi_t$ as constant as possible. Flux quantization imposes the following constraint on the total flux threading the loop $\varphi_t$:

$$\delta + 2\pi \varphi_t/\varphi_0 = 2\pi n$$

where $\delta$ is the phase difference across the barrier as defined in section 3.1. The phase difference is related, through the critical current of the junction, to the total current circulating in the ring as discussed before: $j_s = j_0 \sin \delta$
Part II

Experiment of the study
Chapter 4

Highlights of the Experiment

4.1 Motivation

Recognizing objects in the environment from the sounds they produce is one of the primary functions of the auditory system. Recognition is possible, because acoustic features of sounds often represent physical properties of their sources. As a simple example, one distinguishes and recognizes immediately a tone heard from a playing guitar versus a piano. This is because, although both sounds originate from thin tensioned vibrating strings, the harmonics generated by the guitar’s resonator differ from those of the piano resonator. Exciting resonances in large objects produce mostly lower frequency partial waves relative to those produced by a small resonating object. This has led us to speculate the significance of the contribution of frequency distributions of complex waveforms into sound recognition. The
overall detection of frequency change in the human auditory cortex has been studied in the past[14], but in this study we are interested in the onset period of the sound. Detection of sudden changes is also an important survival advantage for animals or humans, as it is a precondition for a rapid flight response. Detection of changes in auditory input has been studied in the form of the orienting response, described by Pavlov [15] and Sokolov [16]. However, despite several decades of experimental research, the exact neural mechanisms underlying sound recognition have still remained unclear.

4.2  Goal of the study

The goal of this study is to find how we are sensitive to changes in sound. In particular for example in a complex tone will we recognize if a single component of this complex tone is removed from its initial phase (first few ms), defined as onset period. The change which was selected to study in this work was removal of a single frequency from its first 10 ms. The philosophy of the work is that since a human is sensitive to fast changes in a sound signal, one must be more sensitive to changes in the physical structure of the onset period rather than the rest of the sound period named: sustain period. I studied the effect of this change on the magnetic fields generated in the auditory cortex.
4.3 Sound Stimuli Structure

To study the sensitivity of the auditory cortex to the changes in the onset period and compare this effect to the same changes made in the sustain period, two sets of audio signals were generated which were time structured exactly the same, each 15 min in duration.

The two sets of monaural right-ear auditory stimuli were presented in a paradigm of both random insertion of differing stimuli, and random inter-stimuli intervals. In the first set of stimuli, repetitive strings of ’standard’ tones with five selected frequencies had an occasional stimulus replaced with a single occurrence of a ’deviant’, fig(4.3-A). The random replacement and inter-stimulus intervals (ISI) were chosen to avoid brain anticipation while retaining identification of the ’standard’ tone in the memory cache. At the onset of the ’deviant’ tone a single frequency component was omitted relative to the same region of the ’standard’ tone. A single stimulus of the first set of stimulus is shown in fig (4.3-B). The frequencies of the partial waves of the complex tone onset were intentionally selected to be not harmonically related. This precluded reinsertion of the omitted test frequency by the generation of harmonics or combination tones due to either the non-linearity of the ear and electronic equipment, or due to brain processing. In the second set of stimuli, following the same paradigm as above (fig 4.3-A), the omitted frequency in the deviant tone was confined to the latter part of the stimulus, normally termed as the ’sustain’ region, rather than at the stimulus onset. A single stimulus of the second set of stimulus is shown in fig 4.3-C. The same
considerations for selecting the test frequency partial were applied. The total duration of each epoch is .5 sec. The onset period is 10 ms followed by the sustain part which dies away smoothly toward the end to avoid discontinuity.
Fig 4.3-A represents a segment of a typical 15min stimuli applied in this study.

Fig 4.3-B represents a single stimulus called epoch designed for the first experiment.

Fig 4.3-C represents a single stimulus designed for the second experiment.
4.3.1 First Sound Stimulus Structure

The fourier spectrum of the reference epoch of the first set of the sound stimuli is presented in fig.4.3.1-A. From the figure it is found that the frequencies of the reference onset that are anharmonically related are : 70, 440, 1234, 2418, 3997 Hz. These are the resonance frequencies of a clamped bar resembling the basilar membrane discussed before. The duration of each onset is 10ms and the amplitudes of each of the frequencies follow the Fletcher-Munson curves of the 80dB loudness. This is the maximum loudness, permitted by Occupational Safety and Health Administration (OSHA) standards to which a human subject can be exposed. The sustained period of each epoch is 490 ms and the frequencies are the first 5 harmonics of 440Hz, which are 440, 880, 1320, 1760, 2200 frequencies. These frequencies are carefully chosen to avoid combination tones, which was explained in the previous sections. The amplitudes of these frequencies, as the ones of onset, follow the Fletcher-Munson curves of the 80dB loudness. From the fourier spectrum figure it is found that the frequencies of the deviant epochs are similar to that of the reference epochs, only the onset of the deviant epochs are missing the single frequency of 1234 Hz relative to that of the reference signal. This was selected to be an anharmonic frequency relative to the rest of the frequencies in order to avoid the brain’s reinsertion of this frequency, as the brains are known to be capable of reinserting a missing frequency which is harmonically related to the rest of the frequencies. In addition the frequencies were carefully selected to avoid generation of combination tones as previously discussed.
Fig 4.3.1-A represents the fourier spectrum of an epoch in the first experiment. The dotted line represents the missing anhormonic frequency from the onset period of the deviant epoch.

Fig 4.3.1-B represents the fourier spectrum of an epoch in the second experiment. The dotted line represents the missing anhormonic frequency from the sustain period of the deviant epoch.
4.3.2 Second Sound Stimulus Structure

The fourier spectrum of the reference epoch of the second set of the sound stimuli is presented in fig(4.3.1-B). From the figure one will find the frequencies of the reference onset which are harmonically related: 440, 880, 1320, 1760, 2200. However the sustained period contains the anharmonic frequencies which are the same as the resonance frequencies of a clamped bar (these formed the onset period frequencies of the first sound stimulus structure previously explained). The duration of each onset is 10ms and the sustain part is 490ms. The amplitudes of each of the frequencies follow the Fletcher-Munson curves of the 80dB loudness. These are carefully chosen to avoid generation of combination tones.

From the fourier spectrum of the deviant epochs representing the second set of the sound stimuli in fig (4.3.1-B) it is found that the onset frequencies of the deviant epoch are similar to those of the reference epoch, only missing the single 1234 Hz frequency.

Inter-stimulus intervals (ISI) are randomly distributed from 250 ms to 750 ms periods. The minimum is limited by OSHA standards and the maximum is limited by the cache memory time limit. The minimum inter-stimulus interval is limited by cache memory time since the temporary information is stored in the cortex. The magnetometer I use at the VA hospital is suitable to make measurements of the cortex.

Studying the combination of these two experiments will allow us to conclude whether
in a recognition process the auditory cortex is sensitive to a single omitted frequency in the onset period of a 500ms epoch.

The total duration of each sound stimulus file is 15 min. This will allow us for 505 reference epochs and 81 deviant epochs. Each epoch was 500ms in duration.

4.4 Synthetic sound stimulus preparation

Synthetic sound stimuli were computer programmed using FORTRAN and saved as .TXT files. The audio files in the form of .WAV files were also generated by using FORTRAN.

Trigger signals are needed when preparing an audio file in these studies. Since the amplitude of the brain signals is in the order of femto Tesla, the raw magnetic field brain data appears as white noise due to the environmental noise contamination.

In this stimulus the start of the trigger signals are aligned with start of each sound epoch. To distinguish between the brain response to the reference and deviant epochs, the amplitude of the reference triggers were chosen to be half of those of the deviant triggers.
4.5 Sound delivery system

The synthetic audio files are recorded on audio CD and delivered to the VA hospital. They are played on a high quality sound card and delivered to the magnetically shielded room through plastic tubing available at the VA hospital. The plastic tubing is inserted into the human ear. This sound delivery system at the VA hospital is designed for such auditory studies.

4.6 Testing of the Equipment

As it is important how to design an experiment, it is also crucial to test the equipment for accuracy of the acquired data. For example, it is crucial to find whether the data is contaminated due to the electrical, thermal or mechanical artifacts of the equipment. Therefore careful attention was given to study the details of the sound delivery system and the MEG equipment.
4.6.1 Testing of the Sound Delivery System

The played audio file through the sound card, amplifier and the tubing was recorded by the radio shack sound-pressure-level meter and oscilloscope to calibrate the outcome of the plastic tube based on the frequency spectrum of the syntactically generated sound signals. In order to do this, an audio file containing pure multiple sin waves, with frequencies ranging from 10 to 50Hz in 10 Hz intervals, was delivered with the same technique in which the stimuli is delivered to the subject’s ear. The output sound was read through the radio shack sound pressure level meter and oscilloscope to monitor the possible amplitude or frequency deviation due to the disturbance of the delivery system.

4.6.2 Testing of the SQUIDs Responses

Since this study involves the sensitivity of the auditory cortex to the frequencies of the sound signals, it was essential to test the validity of the SQUID response to the detected cortex signals. To do this a loop of diamagnetic material was built in such a way that the generated magnetic field for a 10nAm current was in the order of fT (this is in the order of the magnitude of the field generated by human brain). This loop, which represents the replica of a dipole current, was taken to the VA hospital and was taped to a head phantom. The end of the dipole current replica was connected to the PC computer with which an auditory sound signal
of pure sine was played. The length of the pure sine waves were 10sec, and 11 frequencies of 10-50HZ in 10Hz intervals and 100-600Hz in 100Hz intervals, were played. However in data analysis of brain signals for this auditory study only the waves which are below 30HZ provided information. By doing this test it was confirmed that the response of the SQUID to various frequencies of our interest was uniform.

4.7 Subject preparation

The completion of Good Clinical Practice and Human Subjects Protection(GCP) training was required by the VA hospital to be permitted to take human subject data. The documentation, which can be found on-line, is a complete training session which familiarizes one with all the regulations to deal with the needed ethical responsibilities.

Demagnetization of the subjects is necessary to minimize the magnetic activities. This was done by applying a randomized magnetic field to demagnetize the head area of the subjects. The metal belongings of the subjects were removed prior to demagnetization.
4.8 Experimental sessions

4.8.1 Data acquisition

The brain’s magnetic field response was received as an ASCII format data in two separate files for each run. One contained the brain response information and the other contained trigger information. The ASCII file was loaded in MATLAB and analyzed.

4.8.2 Noise reduction and data analysis

As discussed in the previous sections the MEG data are contaminated with various noises such as that of distant or local sources. The noise reduction is significantly important in this field since the magnetic field that the biomagnetometer measures is in order of fT or $10^{-15}$ T. For example there are noises due to the biological activities of the body which are not the interest of our study. Also there are noises due to the non biological activities such as electrically powered devices, power lines, earth and ionosphere magnetic files. These all need to be removed from data by applying careful techniques.
Cardiac Removal

The cardiac activity (or other involuntary activities) need to be tolerated. These activities are usually in the order of few hundred femto tesla. In my study the cardiac signals were removed by the method of synchronized event subtraction. It means the cardiac signals were detected at the same time as the brain signals were detected. Then the signal due to cardiac activities was removed from the data at the time a heartbeat occurred.

Large uniform magnetic fields

Earth’s magnetic field for example, is $10^{-4} T$ which is significantly larger than the magnitude of biological signals. At the VA hospital data is acquired using gradiometers which consist of two coils wrapped in opposite directions. Therefore what is registered as signal is the effect of the net signal passing through both coils. By using a gradiometer, the effect of a distant uniform magnetic field background, such as earth magnetic field, is reduced. The deep brain activities are also removed by using gradiometers. This is an advantage for this study since the recognition, which is lower level processing, happens in the auditory cortex of the brain where its thickness is about a few millimeters.
4.8.3 Double Ferromagnetic Shielded Room

Subjects are put in a double ferromagnetic shielded room to remove the fluctuations of the surrounding magnetic fields due to the movement of large metal objects (cars, elevators,..) or due to the fluctuations of the earth’s magnetic field. The earth’s magnetic field fluctuations due to the solar wind effect, is in order of nT. As a typical ferromagnetic shield will attenuate in the order of nT, therefore a double shield is necessary to bring the earth’s magnetic field fluctuation in the order of fT, which is in the same order of our measurements.

Baseline Removal

As the SQUIDs are not time stable over the fraction of an hour, which is the duration of my data acquisition, the baseline of the magnetic field response wonders in value. Sometimes the baseline oscillation appears due to the fact the SQUID sensors jump from one flux quanta to the next one. The baseline drift was removed by designing fitting models. This model was designed using the method of clamping, where the difference of the averages of ISI before and after each epoch was subtracted from the epoch.
Grand Averaging

This is associated with Johnson noise discussed before; the thermal-electrical activation noise associated with the SQUIDs amplifier. This is inevitable so it is removed by averaging. The average of reference and deviant files were stored in two separate files for each channel and plotted for comparison and study. The grand averaging of the reference signals was done by adding up all the reference signals except the first one after each deviant signal. The effect of the first one was intentionally removed to eliminate the possibility that the first reference epoch could be detected as a deviant signal.

4.8.4 Mismatch Negativity

The mismatch negativity (MMN) is a component of the auditory event related potential (ERP) which is obtained task-independently by comparing the grand average of brain response to standard and deviant sound signals. Usually deviant signals rarely occur in the string of many standard signals. Auditory sensory memory, which stores information about a stimulus or a series of stimuli for some seconds [17], is indirectly reflected in the so-called mismatch negativity. MMN is what the deviant stimuli elicits as a negativity in the
100300 msec latency range, which could not be seen in response to the standard stimuli[18]. This negativity, usually described by the deviant-minus-standard difference wave[17,19-21], is very similar for both the attended and ignored input sequences, suggesting that attention is not required when studying a mismatch negativity. Ntnen et al [22] proposed that “it may well be that a physiological mismatch process caused by a sensory input deviating from the memory trace formed by a frequent background stimulus is such an automatic basic process that it takes place irrespective of the intentions of the experimenter and the subject, perhaps even unmodified by the latter...” .Mismatch negativity is generated in response to changes in stimulus parameters such as frequency [23], intensity [24], and duration [25], as well as to differences in the phonetic, rhythmic, and temporal structure of the stimuli [2831]. In other words, neuronal traces may contain information about both simple and complex features of acoustic signals.

The MMN is a quantifiable method to study the structure of sound characteristics and their effects on the ability of the human sound recognition process. Recently MMN has been widely used in studying the human auditory deficits. In clinical research MMN offers opportunities for basic information processing on disease such as Alzheimer’s, Parkinson’s, schizophrenia, dyslexia and alcoholism.
4.9 Methodology

Neural activity is recorded synchronized with the auditory stimulus by a whole-head 248-channel MEG equipment. The magnetoencephalography system, which I used at the Brain sciences center at the VA hospital in Minneapolis, is a Magnet 3600 WH. Verification of spatial location in the auditory cortex is determined, as needed, by comparing location reconstruction of the MEG data with MRI images using 'Brainstorm' software. Two sets of monaural right-ear auditory stimuli were presented in the paradigm described above. In each case the sound level presented was adjusted to be at a C weighted level of 80dB as determined by a commercial loudness meter.

A total measuring sequence consisted of 15 minutes of auditory signals. In this period, about 586 stimuli were presented to the subject, 505 signals represented the standard and 81 stimuli were of the deviant tone. In no case were deviant tones presented as adjacent stimuli. The MMNm operation of auditory sensory memory, the earliest memory system that encodes physical features of auditory stimuli was assumed to represent the mismatch of auditory respond to the standard and deviant signals.
Chapter 5

Experiment

5.1 Methods

I investigated the generation of MMNm in the human auditory cortex produced by the removal of a single partial wave of a complex frequency structure presented in different measurements in both the onset and sustained portions of the auditory stimulus. The figure (5.1-A) in the next page shows the differences in the cortical MEG signal between interpretations of the ’standard’ and the ’deviant’ stimuli when deviation was presented in the onset and sustain period of the auditory signal. This deviation was due to a single anharmonic frequency missing in the onset portion of the tone. Figure 5.1-B shows the brain response to the missing frequency in the sustain period. In both cases, the MEG sampling rate was set to 250 samples per second and no post sampling filtering of the signals were performed.
**Fig 5.1-A** represents the overlapped graphs of brain response to the standard and deviant sound signals of the first experiment. The shaded region is the MMN region for sound recognition.

**Fig 5.1-B** represents the overlapped graphs of brain response to the standard and deviant sound signals of the second experiment. The shaded region is the MMN region for sound recognition.
Filtering at this point was avoided since the mismatch was significant enough to be observable even in the presence of the high frequency noise. However as it is seen in the figures of the discussion section, the filtered data is presented overlapped with the raw data to confirm no artifact was introduced due to the application of the filters. Following normal practice all epochs of the standard and of the deviant signals were added and averaged after removal of baseline drifts. Since the brain responses are correlated with the number of the designed sound signals, and the noise is correlated with the squared root of the designed sound signals, by doing averaging, the signal to noise ratio is improved by $\sqrt{N}$, where $N$ is the number of designed sound signals.

The figures of 5.1-A and B are interesting for several reasons. The presence of delayed processing activity by the auditory cortex, and later memory access activity is so marked that post averaging filtering is unnecessary in order to distinguish the differences. This would imply that the removal of one of the five partial waves from the combined sound of the onset period of the tone causes a complete reanalysis, rather than a minor modification of the tone recognition necessary to associate the deviant tone as being of the same familial type as the standard tone. The data presented in figures 5.1 also has notable features. Although the delayed processing of the deviant information in the sustained part of the tone is still very visible, there is also delayed processing signals present when the standard tone is stimulating the subject. This may be explained that the brain, after processing the onset information has 'identified' the familial class of the signal and is now expecting variations in the sustained
part of the tone. Taking our initial thesis example of two musical instruments, this is a normal situation as the onset information to be characteristic of the structure of the instrument (in musical terms the instrument’s formants) whereas the sustained information is associated with the pitch of the sound being played.

5.2 Results of the Experiment

In this experiment 5 subjects were involved in the study. Each subject underwent two sets of data acquisition procedures. As discussed before, the first experiment involved a 15 minute repeat of the sound stimulus. Each stimulus was randomly repeated in periods of in order of a second. The time interval between each stimulus was randomized to avoid anticipation of the brain for the arrival of the new stimulus. Deviant epochs were randomly inserted in the string of many standard epochs. The difference between deviant and reference epochs of the first experiment was a single anhormonic frequency missing in the onset period. The output of the brain to this stimuli shows the brain is sensitive to a single missing frequency from the onset period for all the 5 subjects. This was revealed by comparing the mismatch processor region of the averages of standard to deviant signals.
The second experiment was time structured exactly as the first experiment. The difference between the deviant and reference epoch of this experiment was the same single anharmonic frequency missing this time from the sustain period of the deviant epoch. This will provide us the opportunity to compare the brain’s sensitivity between the changes in the onset and sustain periods.
5.2.1- A Magnetic field response of the auditory cortex to the experiment #1 for subject 2. This figure represents the overlap of the unfiltered deviant and reference signals.
5.2.1- B Magnetic field response of the auditory cortex to the experiment #1 for subject 2. This figure represents the overlap of the filtered deviant and reference signals.
5.2.1- C Magnetic field response of the auditory cortex to the experiment #1 for subject 2. This figure represents the overlap of the filtered and unfiltered reference signals.
5.2.1- D Magnetic field response of the auditory cortex to the experiment #1 for subject 2. This figure represents the overlap of the filtered and unfiltered deviant signals.
5.2.2- A Magnetic field response of the auditory cortex to the experiment #2 for subject 2. This figure represents the overlap of the unfiltered deviant and reference signals.
5.2.2- B Magnetic field response of the auditory cortex to the experiment #2 for subject 2. This figure represents the overlap of the filtered deviant and reference signals.
5.2.2- C Magnetic field response of the auditory cortex to the experiment #2 for subject 2. This figure represents the overlap of the filtered and unfiltered reference signals.
5.2.2. Magnetic field response of the auditory cortex to the experiment #2 for subject 2. This figure represents the overlap of the filtered and unfiltered deviant signals.
5.2.3- A Magnetic field response of the auditory cortex to the experiment #1 for subject 3. This figure represents the overlap of the unfiltered deviant and reference signals.
5.2.3- B Magnetic field response of the auditory cortex to the experiment #1 for subject 3. This figure represents the overlap of the filtered deviant and reference signals.
5.2.3- C Magnetic field response of the auditory cortex to the experiment #1 for subject 3. This figure represents the overlap of the filtered and unfiltered reference signals.
5.2.3- D Magnetic field response of the auditory cortex to the experiment #1 for subject 3. This figure represents the overlap of the filtered and unfiltered deviant signals.
5.2.4- A Magnetic field response of the auditory cortex to the experiment #2 for subject 3. This figure represents the overlap of the unfiltered deviant and reference signals.
5.2.4- B Magnetic field response of the auditory cortex to the experiment #2 for subject 3. This figure represents the overlap of the filtered deviant and reference signals.
5.2.4- C Magnetic field response of the auditory cortex to the experiment #2 for subject 3. This figure represents the overlap of the filtered and unfiltered reference signals.
5.2.4- **D** Magnetic field response of the auditory cortex to the experiment #2 for subject 3. This figure represents the overlap of the filtered and unfiltered deviant signals.
5.2.5- A Magnetic field response of the auditory cortex to the experiment #1 for subject 2. This figure represents the overlap of the unfiltered deviant and reference signals.
5.2.5- B Magnetic field response of the auditory cortex to the experiment #1 for subject 4. This figure represents the overlap of the filtered deviant and reference signals.
5.2.5- C Magnetic field response of the auditory cortex to the experiment #1 for subject 4. This figure represents the overlap of the filtered and unfiltered reference signals.
5.2.5- D Magnetic field response of the auditory cortex to the experiment #1 for subject 4. This figure represents the overlap of the filtered and unfiltered deviant signals.
5.2.6- A Magnetic field response of the auditory cortex to the experiment #2 for subject 4. This figure represents the overlap of the unfiltered deviant and reference signals.
5.2.6- B Magnetic field response of the auditory cortex to the experiment #2 for subject 4. This figure represents the overlap of the filtered deviant and reference signals.
5.2.6- C Magnetic field response of the auditory cortex to the experiment #2 for subject 4. This figure represents the overlap of the filtered and unfiltered reference signals.
5.2.6- D Magnetic field response of the auditory cortex to the experiment #2 for subject 4. This figure represents the overlap of the filtered and unfiltered deviant signals.
5.3 Discussion

The first goal of this experiment as discussed was to find the sensitivity of the auditory cortex to single frequency elimination. This goal was obtained by detection of mismatch response of the magnetic field due to auditory cortex activities.

The mismatch responses produced by the fundamental frequency deviations as well as the deviations in the harmonic contents of the sound level has investigated [16]. However this work studies the effect of single frequency elimination.

The second goal of this work was to compare the effect of a single frequency elimination of the onset period from the sustain part. This goal was also achieved by studying the mismatch response of the magnetic field due to auditory cortex activities.

The mismatch figures of 5.1 and 5.2.1-24 reveals the sensitivity of the human brain to a single missing frequency of all the four subject.

In order to confirm this activity is due to the auditory cortex the magnetic fields detected were localized and overlapped with MR images.

Since it takes about 100ms for the sound signals to reach the auditory cortex after its arrival to the eardrum, the MMNm figures show there is a MMN100 peak in the 100ms region of the data, which is
due to the fact that the signals have reached the auditory cortex. It is known that recognition happens after the MMNm100 peak (Naatanen 1975:286). By comparing the averages of the brain’s responses to the standard and deviant signals of both experiments, it is found that a MMNm occurs in the region of 250-350ms. The MMNm data shown are the outputs of the squids only located directly above the auditory cortex for all the 4 subjects. The graphs depict the MEG data of the best squid in terms of the signal to noise ratio for all the 4 subjects. For each subject two sets of figures are shown, which represent the MEG data for the two experiments.

The ”A” graphs represent the overlap of the filtered human brain response to standard and deviant sound stimuli. The thick lines represent the magnetic field response of the brain to the standard sound signals. From the observation of the 250-350 ms regions, it is found that there are less magnetic field fluctuations relative to the thin lines, which is the magnetic field response of the brain to the deviant sound signals. It means that the brain analyzes the standard signals as similar, but it analyzes the deviant signals as signals carrying ”new” information. This is concluded due to the existence of a mismatch in the 250-350 ms regions.

The ”B, C and D” graphs do not carry further information; they only confirm the goodness of the fitting model (Butterworth filter), which was applied. The B graphs show the overlap of the unfiltered standard and deviant data. The C and D graphs show, in order, the overlap of the filtered and unfiltered reference and deviant data.

The activities of the brain beyond the mismatch region at this time are unexplained and remain for future investigation.
From the figures it is found that a mismatch exists due to the variations of deviants in both experiments, however it seems the mismatch due to the first experiment (deviation in the onset period) is more significant. By studying these graphs it is concluded: a single frequency elimination in a sound stimulus plays a significant role in human brain sound recognition. Meanwhile, by comparing the mismatches of the brain response due to a single frequency elimination in the ”Starting Transient ” and ”Sustain Part” of the sound stimuli, it is found that the brain is more sensitive to frequency elimination in the Starting Transient.

5.4 Conclusion

The study of the sensitivity of the human auditory cortex based on MMNm responses depicts that the human brain is sensitive to the start of sound signals. In this study the duration of this starting transient was 100ms. Therefore the time scale for the recognition of a sound source based on the frequency spectrum is more likely to happen in about a 100ms. Obtaining more advance information about a sound signal is more likely to happen beyond the time scale of the starting transient. For example distinction of the sound of a musical instrument from a non-musical instrument happens within the time scale of the starting transient, however to recognize what kind of an instrument is
being played needs further information which is probably obtained by analyzing the rest of a sound signal which in this study is referred to as the sustain part. The optimum time scale to which the auditory cortex is sensitive in this course of the work was not studied which remains for future investigation. Therefore to conclude this discussion, by comparing MMNms of auditory cortex, the relative contribution to sound recognition of the omitted partial frequency components in the onset and sustained regions determines the presence of significant mismatch negativity, due to neural activity of auditory cortex, which emphasizes that the brain recognizes the elimination of a single frequency of carefully chosen anharmonic frequencies.
References


