Design and Development of an Event Related Potential Measurement System

Andrew South

A thesis submitted in partial fulfilment of the requirements of

Sheffield Hallam University

for the degree of Doctor of Philosophy

October 1999

Collaborating Organisation: University of Sheffield

TABLE OF CONTENTS

ABSTRACT

Event-related potentials have been found to be a useful indicator of brain states and brain abnormality. The contingent negative variation, P300 and bereitschaftspotential are well researched event-related potentials of particular interest. Many factors have to be considered in the design of measurement systems to record multiple channels of these signals accurately. The correlation between channels must be high and channel noise and distortion must be minimal, whilst the system as a whole must meet the requirements of the medical safety standards. For further research there was found to be a requirement for a dedicated thirty-two channel ERP measurement system that met these criteria. This has been achieved in a PC based system that utilises simultaneous sampling of all channels, and filters that extend to very low frequencies. Software control of the system enables user adjustment of recording parameters and paradigm implementation. Data processing using high level software enables digital signal processing techniques to be applied for further noise removal and signal analysis. The system has been tested using synthetically generated signals and by limited recording of the three ERPs. The results prove that the system is a suitable tool for high accuracy, multi-channel recording of ERPs.

1 INTRODUCTION

1.1 Aims and Objectives

The aim of this work is to design, manufacture and test a 32 channel event-related potential measurement system, for initially recording the contingent negative variation, P300 and bereitschaftspotential, but with the ability to be developed further to record alternative event-related potentials. The design is to be targeted to measure and record low frequency event-related potentials with maximum accuracy and minimum distortion. The correlation between channels is to be maximised and the susceptibility to interference minimised. Commercial measurement systems do not meet all of these requirements necessary for event-related potential research. Alternatively research systems are usually not designed to be practical in terms of use and little attention seems to be paid to the relevant medical safety standards required for equipment to be used in hospitals. This system is to be designed to be a dedicated research tool, that is easy to use and modify and meets the relevant hospital safety standards that enable it to be used on a wide variety of subjects.

The development of such a piece of equipment to perform multi-channel recording of these event-related potentials will enable further research to give greater insights into their spatial distribution leading to better understanding of their origins and possibly functional representation.

1.2 Outline

Chapter 1 gives an introduction to event-related potentials, their origins and what they may represent. The contingent negative variation, P300 and bereitschaftspotential are then described, along with their method of generation, clinical applications and recording parameters.

Chapter 2 covers the technological problems of EEG recording including standing electrode potentials, electrode impedance, movement artefacts, noise and interference. The principles of EEG amplification and filtering are covered leading on to a detailed description of requirements and finally an event-related potential measurement system specification.

Chapter 3 describes the hardware implementation of the measurement system. The overall system is described first and divided into sections that are then covered in more detail.

Chapter 4 describes the system control program and data analysis software. Flow charts show the overall program structure and key functions are described.

Chapter 5 details the system tests performed to prove the validity of the measurement system and its accuracy. The system is tested first with synthetically generated waveforms to quantify its performance followed by limited subject tests.

Chapter 6 compares the achievements of the work with the initial aims and objectives and concludes with areas for further work.

1.3 EEG and Event-related Activity

It was Berger who discovered that brain electrical activity (electroencephalogram (EEG)) could be measured at the human scalp [1]. Since then it has been assumed that in these voltage fluctuations are hidden the mysteries of the workings of the human mind. While classical neurophysiologists questioned the likelihood that such simple 'fluctuations' could be the key to the complexities of understanding, talking, reasoning, imagining and supposing, the past 70 years have proven otherwise. A large body of evidence has shown that electrical and magnetic activity of the brain (human or otherwise) encodes information about brain states and brain processes and, by inference, about mental states and mental processes. The exact mapping from neural structures to sensory, perceptual and cognitive processes and states is not at all transparent, but all neuroimaging techniques are based on the assumption that such mappings exist and are decipherable.

Event-related potentials (ERPs) are the result of brain electrical activity that is time-locked to some form of external stimulus or event. An ERP experiment requires a willing participant, electrodes for recording the brain wave activity, amplifiers, a digitizer that turns the analogue signals into digital form, a digital storage device for saving the data and some means of presenting stimuli and recording any subject responses.

Since the evoked response to a single stimulus is quite small (5-10μV), it must be extracted from the background activity somehow. Averaging is one method that enhances the signal (or whatever is invariant from trial to trial) and reduces what is random (noise) to nearly zero, improving the signal-to-noise ratio by a factor proportional to the square root of the number of trials.

1.3.1 How ERPs are generated by the brain

The net flow of current across the neural membrane generates an electrical potential in the conductive media both inside and outside the cells. It is this electric potential that forms the basis for the electrophysiological recordings both invasively, by lowering electrodes into the brain, and non-invasively, by placing electrodes on the scalp for EEG/ERP [2]. The same transmembrane current flows are also responsible for the magnetic fields recorded outside the head for MEG (the magnetoencephalogram). Viewed from outside the neurons, each patch of membrane acts as a tiny current source or sink, depending on whether the net local current flow is inward or outward, respectively.

The electric potential and magnetic field generated by a particular spatial distribution of current sources and sinks can be computed either by adding up the individual contributions of each current source and sink in the entire space or, alternatively, by partitioning the source space into a number of regions, calculating the contributions of all the sources and sinks within each region, and then adding together the contribution of each region. In either case, the resultant field is the same.

The potential produced by any arbitrary collection of sources and sinks can be expressed in terms of a multipole expansion:

$$\Phi \approx \Phi_1 + \Phi_2 + O(r^{-3})$$

where Φ_1 is a monopolar term, Φ_2 is a dipolar term and $O(r^{-3})$ represents so-called quadropolar, octopolar and higher order terms which fall off with distance r at the rate of r^{-3} or faster. Hence, we see that the electric potential produced by a collection of sources and sinks within a region can be approximated closely by considering only the monopolar and dipolar terms, as long as the size of the region is small relative to the

distance to which the measurements are made. Since the total amount of current leaving a cell must equal the total amount of current entering the cell, the monopolar term in the multipole expansion of the source-sink distribution of a cell must equal zero. Thus, under these circumstances, where activity of neurons in a patch of tissue is observed at a distance much greater than the linear extent of the patch, only the dipolar term of the multipole expansion need be considered. In short, the distribution of sources and sinks within such a patch can be represented by a single so-called 'equivalent dipole' located in the middle of the patch [3].

If the sources and sinks are distributed in an approximately radially symmetric fashion within a patch of tissue, the dipole term vanishes. This is known as 'closed field' source configuration. Two examples of closed fields, where the net dipole moment of a collection of cells is zero are shown in Figure 1.1. They can occur when the cells are orientated in a random fashion and when the activity of the cells is not synchronised. In fact a patch of brain tissue only produces an externally observable electric potential or magnetic field if, and only if:

(a) The average distribution of sources and sinks within the neuron in the patch is distributed in a non-radially symmetric fashion.

(b) The neurons are aligned in some systematic fashion.

(c) The neurons are activated in a synchronised fashion.

This is illustrated in Figure 1.2.

Figure 1.1 Examples of pyramidal neurons in closed field source configurations

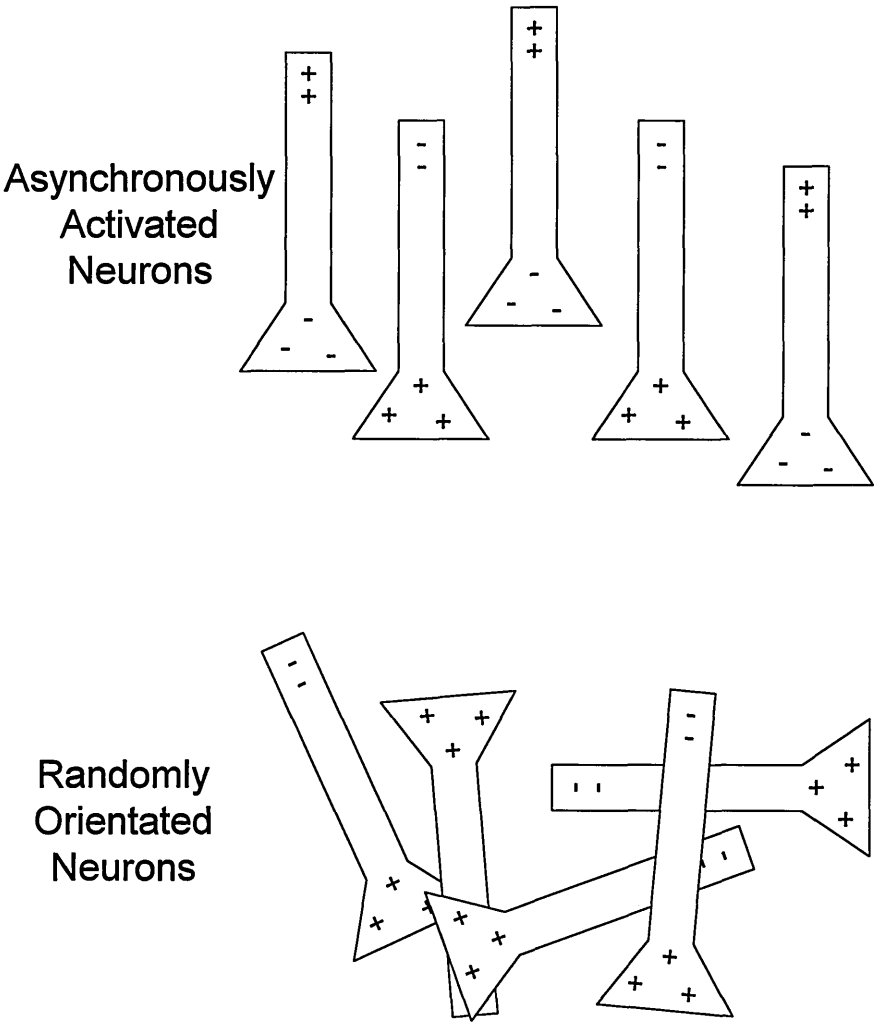
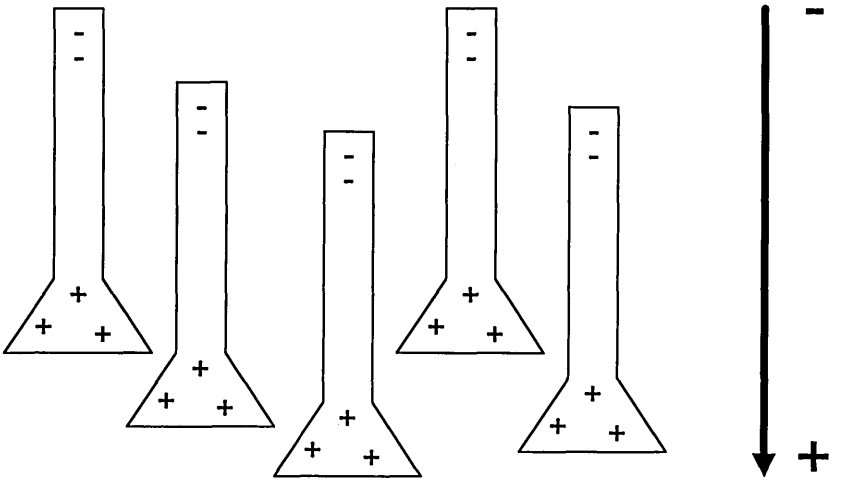


Figure 1.2 Pyramidal neurons in open field source configuration



The neocortex is one of the main structures of the brain that satisfies all these constraints. It is organised as a large folded sheet a few millimetres thick. About 70 % of the cells in the neocortex are pyramidal cells that have apical dendrites extending from the soma toward the surface of the sheet, which gives the cortex a columnar appearance. When the proximal parts of the apical dendrites of a cell are activated, currents flow into the cell around the soma, and currents flow out of the cell at more distal sites, thus creating an approximately dipolar source-sink configuration oriented perpendicular to the cortical sheet. Similarly, if the distal parts of the dendrites are activated, a dipole field of the opposite orientation is generated. Of course, the potential and magnetic field produced by a single cortical pyramidal neuron are quite weak, but those produced by a patch of cortex containing hundreds of thousands of such cells may be strong enough to be detected even at a considerable distance from the patch. These are believed to be the primary source of scalp-recorded ERPs.

1.3.2 What can be inferred from ERPs?

The classical approach to ERP analysis has been to identify so-called 'components' of the ERP, usually positive or negative peaks with characteristic scalp distributions and latencies, which can be shown to be reliably correlated with particular experimental manipulations. It is often assumed that, since such a peak is correlated with a particular cognitive process, it can in fact be used as a physiological index of that process. Based on this reasoning it follows that the timing of the process can be inferred from the latency of the corresponding peak, and the degree of activation or 'strength' of the process can be inferred from the amplitude of or area under the peak.

When the origins of the underlying processes that generate the waveforms are ignored, if differences are found to exist between subjects, they alone prove that differences in mental activity exist that must be accounted for, and give insight into the nature of the associated mental activity.

ERPs are thought to be the consequence of brain functions such as cognition, perception, pre-motor activity etc. and may be modified in cases of abnormal brain conditions. For instance it has been observed that the three ERPs; CNV, P300 and Bereitschaftspotential, are all affected by parkinsonism and that the severity of the disease is related to abnormalities in the waveforms [4] [5] [6]. A greater understanding of the relationship between abnormalities of the different waveforms and the characteristics of different Parkinson's disease sub-groups may allow the use of these electrophysiological methods for condition monitoring, individual prognoses and the monitoring of different drug treatments. By using all three ERPs it may be possible to determine separate electrophysiological feature sets corresponding to movement and cognition. This is important because both of these are affected in Parkinson's disease.

Recording 32 channels of ERPs will enable a study of ERP topography with the possibility of locating the source of origin of the different ERPs in normal subjects and aberrations in abnormal subjects, thus enhancing understanding of both the ERPs and of the abnormality.

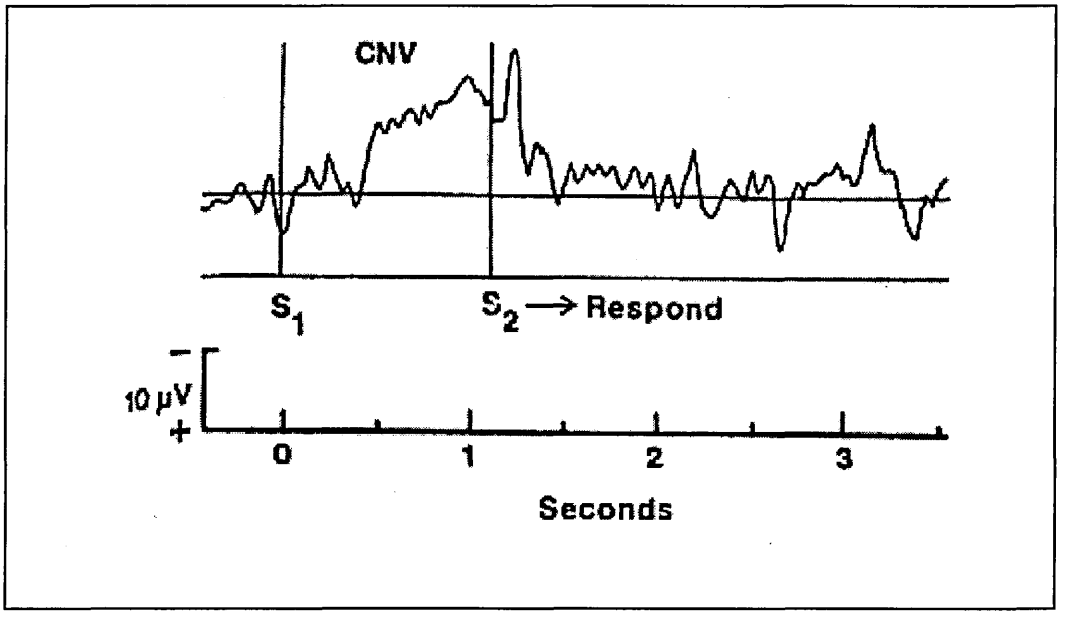
1.4 Contingent Negative Variation

1.4.1 Description and Generation

Grey Walter first reported the CNV [7]. It is a negative waveform that depends upon the association or contingency of two successive stimuli. The basic paradigm is that of a constant foreperiod, reaction time experiment. A first stimulus (S1) serves as a preparatory signal for an imperative stimulus (S2), to which a motor response is made.

Negativity is seen to begin following the warning stimulus reaching a maximum of approximately 15 μV at the imperative stimulus before returning to the baseline (Figure 1.3). In some cases the return to the baseline is delayed giving post-imperative negativity (PINV).

Figure 1.3 Typical CNV waveform



Although the CNV typically occurs in a reaction time paradigm it can be generated by paired stimuli alone [8]. However its magnitude is increased when a motor

response is made to S2. This is partly due to the addition of the BP and partly due to enhanced attentiveness due to greater task involvement.

Traditionally the CNV is thought to represent a state of anticipation [9] [10]. However, increasing the inter-stimulus-interval (ISI) to up to 4 s has shown that the CNV splits into an early and late component. The early CNV is thought to be associated with the warning stimulus whilst the late component is associated with the response. It has therefore been argued that the CNV is related less to higher cognitive states than to sensory and motor functions [11].

1.4.1.1 Topography

In normal subjects the CNV has a central focus with reduced magnitude both frontally and parietally. CNV is largest at Cz (~ 13 μV) (Figure 2.7) and larger at Pz (~ 9 μV) than at Fz (~ 5 μV). The CNV shows slight asymmetry in the S1-S2 paradigm, probably due to the affect of the bereitschaftspotential.

1.4.1.2 Individual differences

Recent work suggests that anxiety, extroversion, and anhedonia are important psychological variables influencing CNV development. High anxiety subjects show lowered CNV magnitude [12]. Extroverts have higher CNV's than introverts, and neuroticism is related to lower CNV, a finding interpreted as due to 'disrupted focused attention' and in terms of a 'heightened arousal internal distraction explanation'.

1.4.1.3 Pharmacological Studies

The effects of psychotropic drugs upon CNV parameters have been reviewed by Thompson et al [13]. Generally, when recorded with the standard short ISI paradigm (< 3 s), CNV amplitude decreases with sedative drugs and increases with stimulants. These effects are not clearly observed with longer ISI and are affected by individual differences. Dopamine has been shown to enhance the initially reduced CNVs of Parkinsons disease patients [14].

1.4.2 Clinical Studies

1.4.2.1 Ageing and Dementia

Normal elderly persons show CNV changes in both magnitude and shape, particularly a selective frontal reduction in CNV amplitude [15]. Age-related attenuation in frontal CNV has been interpreted as reflecting reduced ability to switch attention and fits the views that the elderly have both extensive frontal neuronal loss [16] and functionally significant frontal lobe damage [17]. Frontal CNV diminution in the elderly has been replicated [18]. Of particular interest is the finding in older groups of lowered CNV, lengthened reaction time, elevated heart rate, and increased eye blink rate, suggesting that the ageing process is characterised by distraction-arousal states and not simple physiological hypoactivity. In some studies, age-related CNV differences were limited to association with difficult tasks and extended S1-S2 intervals; other studies have found no age-CNV associations.

Dementia patients have been characterised by a CNV shape with a fast rise time as well as by lowered amplitude and heightened PINV, whereas control individuals show a CNV shape with a more gradual rise time [19]. The pattern of CNV reduction

and attention impairment found in Alzheimers patients resembles that of schizophrenics. Furthermore, the conceptualisation of schizophrenics in terms of distraction-arousal processes has been applied to Alzheimers disease.

1.4.2.2 Psychopathology

The CNV has potential uses in psychiatry. Depresssed patients have been found to display disrupted CNV development, as have adult schizophrenics and schizophrenic children [20]. Schizophrenics also show increased frontal CNV [21], something that has also been observed in obsessive-compulsive individuals and migraine patients. Frontal CNV magnitude also increases in head injury patients, and may reflect disinhibition [22].

The PINV characterises schizophrenia, depression and dementia, although it decreases in neurotics [20]. Clinically demonstrated reversal of CNV disruption by drug treatment has received little attention, although in one report schizophrenics showed elevated CNVs after treatment with mesoridazine and thioridazine [23]. Depressed patients who experience hopelessness and suicidal thoughts have lowered CNVs. Reduced CNV has been reported in alcoholics [24].

1.4.2.3 Pathophysiology

CNV has also proven useful in studying patients with cerebral palsy, head injury, Huntingtons disease, and various neurological disorders. In another study the CNV at Fz and Cz was found to be smaller in blind subjects than in normal subjects while Pz and Oz were found to be equivalent [25]. Reduced CNV has been found during prolonged epileptic EEG discharges in both centrencephalic and temporal lobe patients; the effect

was also clear during brief discharges in the temporal lobe group but not in the centrencephalic group [26]. The CNV of Parkinsons disease subjects has been found to be longer and of smaller amplitude than normal subjects [27].

1.4.3 Recording parameters

Typical recording parameters of the CNV are:

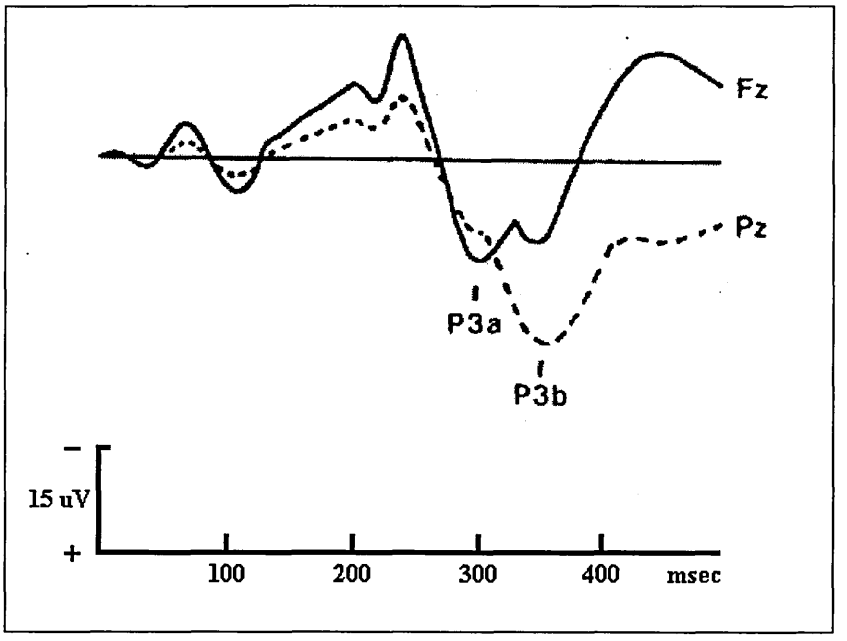
Warning stimulus	Click
Stimulus	1 kHz tone terminated by a button press
Inter-stimulus-interval	1 s
Bandpass frequencies	0.016 - 30 Hz

1.5 P300

1.5.1 Description and generation

The P3 (P300) is a symmetric positive wave, maximal over the midline central and parietal regions, with a latency that varies from 250 to 600 ms depending on stimulus and subject parameters, Figure 1.4 shows the shape of a typical P300 waveform. The P3 can be elicited with a stimulus of any modality. The most commonly used method to obtain the P3 is referred to as the 'oddball' paradigm. This involves the presentation of unexpected or infrequent stimuli randomly interspersed among more frequent stimuli. In most studies the unexpected stimuli differ from the more common stimuli in terms of frequency (pitch) or intensity. The unexpected stimulus may be simply the absence of a stimulus among a train of regularly spaced stimuli or a change of the inter-stimulus interval among a train of regularly spaced stimuli. A method that augments the P3 and is generally used in conjunction with the 'oddball' paradigm consists of attending to task relevant stimuli and ignoring non-target stimuli. A P3 is seen following the target but not the non-target stimuli [28].

Figure 1.4 Typical P300 waveform



These two factors, stimulus infrequency or unexpectability and attention or task relevance operate independently. In fact there is evidence that they produce quite different P3s. Independent of task relevance, an infrequent stimulus elicits a P3 that N.K. Squires and colleagues referred to as a P3a [29]. This component occurs slightly earlier and has a more frontal distribution than the parietal maximum P3b component wave that is best elicited by attending to task relevant stimulus. Presumably, the routinely obtained P3 represents a sum of these two component waves.

1.5.1.1 Subject Parameters

The subject must be awake and alert to obtain the P3. There are a series of related variables that affect the P3: level of attention, vigilance, and response accuracy. Decreasing vigilance is associated with a decrease in the amplitude of some cortical evoked potentials. Drowsiness or inattention will decrease the amplitude or obliterate

the P3. In addition, the P3 amplitudes are larger following a stimulus that is correctly identified than one incorrectly identified. Thus an assessment of behavioural response to the stimuli is important to enable estimation of the subjects vigilance or degree of attention. The subject can be asked to mentally count the number of target stimuli or to respond to each target stimulus (e.g. by pushing a button). Then one can record the accuracy of response. If a motor response is used, one can average only those recordings where a correct response was given. The P3 may be slightly different depending on whether or not the subject produces a motor response, but the P3 does not depend on the presence of a motor response. In fact the P3 latency may be longer than the reaction time.

The specific task that is given to the subject will affect the P3. In the 'oddball' paradigm, when a subject is instructed to specifically attend to the rare stimulus, the P3 amplitude increases. An identical rare stimulus to which the subject is not told to attend will elicit a lower amplitude response.

The difficulty of the discrimination task used to obtain the P3 affects the latency of the P3. The P3 latency increases as the task becomes harder. For example as the pitch of the rare auditory stimulus becomes more similar to the frequency of the frequent stimulus, the task of identifying the rare stimulus becomes more difficult and the P3 latency increases.

The P3 latency has a positive correlation with age for auditory, visual and somatosensory stimuli [30] [31]. There is an increase in mean latency by approximately 1 to 1.5 ms per year after age 20. The standard error estimate of the age-latency regression line has ranged from 20 to 50 ms in various studies. This degree of variability is a problem if one is trying to establish a clinical test and compare patients to a normative data base. The regression line for age and P3 latency has been found by some

researchers to increase in slope with increasing age, although others have not found this. There is also a gradual decline of P3 latency in children, with a minimum latency being achieved age 15 and 25. The correlation between adult age and P3 amplitude is uncertain because of conflicting findings.

1.5.1.2 Stimulus Parameters

While most studies have used auditory or visual stimuli, somatosensory stimuli can also elicit a P3. The P3 is fairly similar following stimuli of different modalities although there may be slight differences in latency or topography. The P3 component is also relatively independent of other physical properties of the stimulus e.g. stimulus loudness, but slight changes in P3 latency may be seen with significant changes in stimulus intensity.

The amplitude of the P3 is affected by the probability of occurrence of the target stimulus. The probability of occurrence can be given by the probability within the global sequence of target and non-target stimuli, the probability within the local sequence (e.g. the last five stimuli), or by the temporal probability, which is affected by the interstimulus interval as well as the sequence probability.

The P3 amplitude increases as the target stimulus frequency in the global sequence decreases. An average occurrence rate below 10-15 % does not improve test results and in clinical studies a rate of 15-20 % is commonly used.

Another factor peculiar to the P3 is its dependence on preceding stimuli or local sequence probability. A target stimulus that is preceded by another target stimulus will elicit a lower amplitude P3 than if it is preceded by a non-target stimulus. The P3 is enhanced by increasing the number of consecutive non-target stimuli preceding the

target stimulus. For example, a target stimulus that is preceded by only one as compared to four non-target stimuli will elicit a lower amplitude P3.

The amplitude of the P3 is increased as the temporal probability of target stimulus occurrence decreases, that is, as the interstimulus interval (ISI) is increased whilst the sequence probability remains unchanged. This factor appears to be more significant than the global sequence probability. A P3 may be obtained with very short ISIs, as small as 300 ms, although the latency is slightly prolonged and the amplitude mildly decreased compared to longer ISIs.

The sequence of presentation of the target and non-target stimuli is important for a reason in addition to the previous ones. If the infrequent stimuli occur at fixed intervals (e.g. every sixth stimulus in the oddball paradigm), then the rare stimulus is not unexpected and the P3 amplitude decreases. Therefore it is important to use a random or pseudorandom sequence . A pseudorandom sequence contains a random sequence of targets and non-targets with limiting conditions on the stimuli sequence e.g. no two target stimuli appear consecutively. A pseudorandom sequence is preferred to a random sequence because of the effects of local sequence probability.

1.5.1.3 Technical Factors

To record the P3, 0.2 to 1Hz high pass and 30 to 100Hz low pass filters are commonly used, although lower frequency high pass filters or dc amplifiers are needed to accurately measure the slow wave. At least three channels of EEG activity should be used (Fz, Cz, Pz), in part to delineate the P3a and P3b components. The electrodes can be referenced to linked-ear, linked-mastoid electrodes, nose or non-cephalic electrodes. The ears, mastoids, and nose are somewhat active references.

Eye movement needs to be monitored because eye movements may be time locked to the stimuli, especially the target (oddball) stimuli, and the field of distribution of the eye movements may include the recording electrode sites. Other sources of extracerebral artefacts, such as cranial muscle, may also need to be monitored.

The stimulus rate is generally about 1 s and may be randomly varied. It is important to standardise the sequence of target and non-target stimuli because variations in the sequence will increase the variability of the P3. The sweep duration should be 600 to 1000 ms and a pre-stimulus period is important in assessing the baseline for amplitude measures.

The P3 is a variable response, even within a subject, and as with other ERPs, it is necessary to repeat trials to ensure reproducibility. Skare and Lynn [32] studied 9 subjects serially and found up to an 18 ms difference between trials 1 and 2, and up to a 12 ms difference between the average of two trials performed at each of two sessions 2 to 4 weeks apart. There was a very high correlation between the two trials and two sessions. Polich (33) studied 100 subjects and found no significant differences in P3 amplitude or latency comparing trials 1 and 2. However, correlation coefficients for P3 latency were significantly lower than those obtained by Skare and Lynn.

There is a significant problem in determining the precise latency and amplitude. One cause is that the P3 is composed of two separable component peaks, P3a and P3b. Measurement of both peaks is probably the best solution. Another source of error in determining the peak for P3 latency measurement is the variable morphology and broadness of the P3. Methods for determining the P3 latency include measuring the P3 latency as the pint of maximum amplitude or as the intersection of the lines extended from the leading and trailing edges of the P3 wave. More complex peak detection paradigms have been used for research purposes but have not been used widely used for

clinical applications. P3 amplitude measurements are best made in comparison to a pre-stimulus baseline because of the superimposed slow wave component. In general P3 amplitude increases as latency increases.

1.5.2 Clinical Studies

Researchers have attempted to correlate changes in cognitive ERPs with clinical changes in cognitive function. In general, changes in the P3 can be seen in cognitive dysfunction but the sensitivity and specificity of the test have not been as high as for some of the earlier latency ERPs.

1.5.2.1 Dementia

One goal of cognitive ERP research has been to develop a useful tool to aid in the diagnosis of dementia. Studies suggest that P3 latency in a group of patients with dementia is prolonged compared to a group of healthy controls. In addition, the P3 latency is prolonged in a percentage of individual patients with dementia. However, there are several limitations of the studies and of the potential clinical application of P3 testing for dementia. Demented patients, especially moderately to severely impaired patients, tend to produce more incorrect responses in the P3 testing than normal controls. This impaired response accuracy may alter the P3 latency more than the dementia itself. In addition the sensitivity of the test is not that high. The important clinical differential diagnosis rest in cases with mild as opposed to moderate or severe dementia. There is a very significant overlap between normal subjects and mildly demented patients, especially in the older age groups. Some controls may not have a

well defined P3; thus patients with a poorly defined P3 cannot be considered to have an abnormal test result.

1.5.2.2 Schizophrenia

Multiple investigators have reported a lower amplitude P3 in groups of schizophrenics compared to controls [34] [35]. Most of these studies have not reported a change in P3 latency. Alteration of the P3 topography has also been reported. Many of the patients in these studies were on neuroleptic drugs. In addition, schizophrenics often had less correct responses in the P3 task, longer reaction times and may have been less motivated to perform the task. Even if the differences between schizophrenics and controls are not related to these factors, there is little clinical significance of the difference because there is so much overlap of the P3 amplitude between the two groups.

1.5.2.3 Parkinson's Disease

The P300 is found to have an increased latency in Parkinson's disease patients compared to normal subjects [36] [37]. Prolonged latencies are also reported in demented compared to non-demented Parkinson's disease patients and there is some evidence that treatment with L-dopa leads to an improvement in latency [38]. Prolonged latency of the P300 is thought to be a consequence of cognitive impairment in patients with Parkinson's disease rather than motor disability. De novo patients have been found to exhibit normal P300 waveforms.

1.5.3 Recording Parameters

Typical recording parameters of the P300 are:

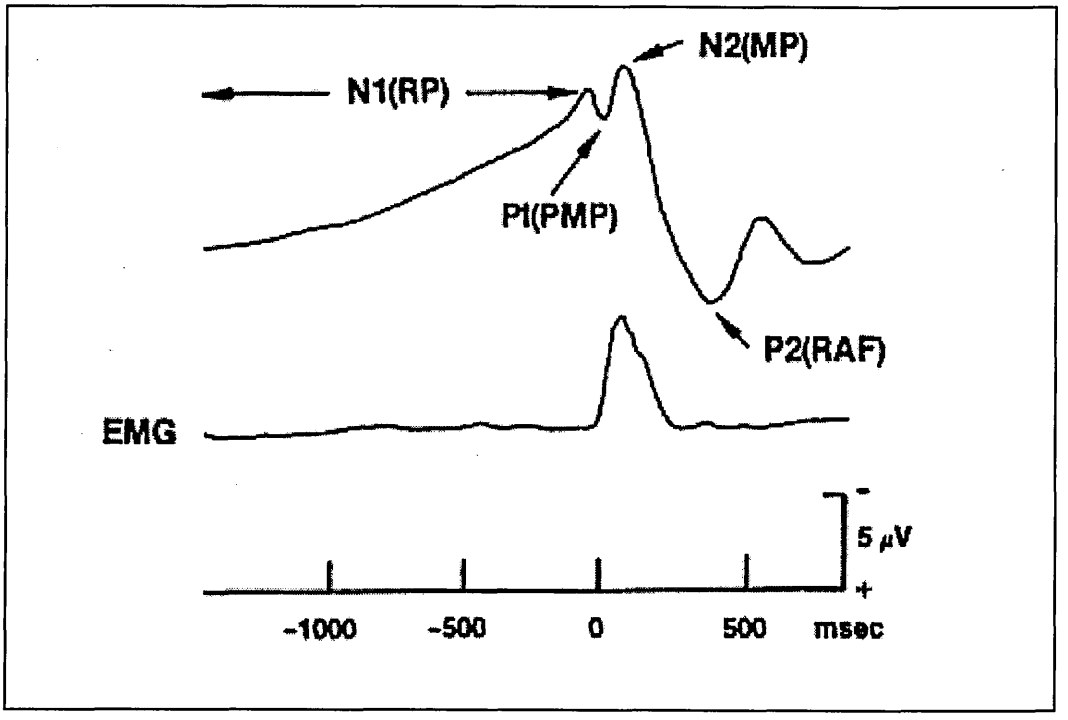
Target tone frequency	2 kHz
Non-target tone frequency	1 kHz
Target tone occurrence	20 %
Non-target tone occurrence	80 %
Tone duration	50 ms
Inter-stimulus interval	2 s
Bandpass frequencies	0.016 - 30 Hz

1.6 Bereitschaftspotential

1.6.1 Description and generation

The Bereitschaftspotential is a slow negative shift, maximal over the vertex, that begins approximately one second prior to the onset of electromyographic (EMG) activity. The wave is similar in morphology to the CNV. The slope of the BP increases several hundred milliseconds prior to the EMG onset (Figure 1.5). This wave is asymmetric, with greater amplitude over the hemisphere contralateral to the limb performing the motor task.

Figure 1.5 Typical BP waveform



1.6.1.1 Technical Factors

Back averaging is required to record the BP. This requires recording of EEG activity from 1 to several seconds prior to motor activity. As with the CNV, DC or very low frequency filters are required to record the slow potential shift. The amplitude of the BP is only 5 to 10 μV which is significantly lower than the EMG which is about 50 to 100 μV.

1.6.1.2 Subject Parameters

The amplitude of the bereitschaftspotential has been found to be reduced in older subjects particularly those over the age of 40 [39]. Latency has also been found to increase with age whilst the slope decreases [40].

1.6.2 Clinical Studies

The Bereitschaftspotential is thought to represent pre-motor activity [9]. One indicator for this is that it is always maximal over the side of the brain contralateral to the side of movement. The amplitude of the Bereitschaftspotential is normally the same in Parkinson's disease patients compared to normal subjects but rises later and more steeply to form a sharper peak [41] [42]. Peak negativity has been found to be reduced in schizophrenics that display both positive and negative symptoms [43].

1.6.3 Recording Parameters

Typical recording parameters are:

Bandpass frequencies	0.016 - 30 Hz
Recording length	-2 to 1 s
Response method	Button press

[1] On the electroencepahalogram of man, H. Berger, Archiv. Psychiatrie Nervenkrankheiten, 87, 527-570, 1929.

[2] Electric fields of the brain, P.L. Nunez, Oxford University Press, 1981.

[3] Theory of current source-density analysis and determination of conductivity tensor for Anuran cerebellum, C. Nicholson, J.A. Freeman, Journal of Neurophysiology, Vol. 38, pp 356-368, 1975.

[4] Contingent negative variation (CNV) in psychopharmocology, M. Timsit-Berthier, Event-related Brain Research (EEG Suppl. 42), Eds. C.H.M. Brunia, G. Mulder, M.N. Verbaten, Elsevier, 1991.

[5] P300 event-related potentials in de novo Parkinsons disease, J.S. Graham, C. Yiannikas, E. Gordon, S. Coyle, J.G.L. Morris, Clinical and Experimental Neurology

[6] The Bereitschaftspotential is abnormal in parkinsons disease, J.P.R. Dick, J.C. Rothwell, B.L. Day, R. Cantello, O. Buruma, M. Gioux, R. Benecke, A. Beradelli, P.D. Thomson, C.D. Marsden, Brain, Vol. 112, pp 233-244, 1989.

[7] Contingent negative variation: an electric sign of sensorimotor association and expectancy in the human brain, W.G. Walter, R. Cooper, V.J. Aldridge, W.C. McCallum, A.L. Winter, Nature, Vol. 203, pp 380-384, 1964.

[8] Surface-negative, slow potential shift associated with conditioning in man, M.D. Low, R.P. Borda, J.D. Frost, P.Kellaway, Neurology, Vol. 16, pp 771-782, 1966.

[9] Endogenous event-related potentials, B.S. Oken, Evoked Potentials in Clinical Medicine, Ed. K.H. Chiappa, Raven Press Ltd, New York, 1989.

[10] Contingent negative variation (CNV), J.J. Tecce, L. Cattanach, Electroencephalography: Basic Principles, Clinical Applications and Related Fields, Eds. E. Niedermeyer, F. Lopes da Silva, Urban and Schwarzenberg, pp 657-679, 1986.

[11] Sensory and motor aspects of the contingent negative variation, J.W. Rohrbaugh, Tutorials in ERP research: Endogenous components, Eds. A.W.K. Gaillard, W. Ritter, North Holland Publishing Company, 1983.

[12] The effects of anxiety and expectancy on the CNV, G.B. Proulx, T.W. Picton, Brian and Information. Event-related potentials, Eds., R. Karrer, J. Cohen, P. Tueting, pp 617-622, New York Academy of Sciences.

[13] Pharmacology of event-related potentials in humans, J.W. Thompson, H. Ashton, J.F. Golding, V.R. Marsh, Cerebral Psychophysiology: Studies in Event-related

Potentials and Behaviour, Eds., W.C. McCallum, R. Zappoli, F. Denoth, pp 374-380, Amsterdam: Elsevier.

[14] Parkinsons disease: Electrophysiological (CNV) analysis related to pharacological treatment, A. Guiseppe, F. Fattapposta, G. Pozzessere, G. Albani, L. Sanarelli, P.A. Rizzo, C. Morocutti, Electro. and Clin. Neuro., pp 521-524, Vol. 64, 1986.

[15] Contingent negative variation and attention functions in the aged, Event-related Brain Potentials in Man, Eds., E. Callaway, P.Tueting, S.H. Koslow, p 626, New York: Academic Press.

[16] Cell counts in cerebral cortex and brainstem, H.Brody, Alzheimers Disease. Senile Dementia and Related Disorders, Eds., R Katzman, R.D. Terry, K.L. Bick, pp 345-351, New York: Raven Press.

[17] Organic implications of neuropsychological deficits in the elderly. M.S. Albert, E. Kaplan, New Directions in Memory and Aging, Eds., L.W.Poon, J.L. Fozard, L.S. Cermak, D. Arenberg, L.W. Thompson, pp 403-432, Hillsdale, NJ: Lawrence Erlbaum.

[18] Age differences in the contingent negative variation (CNV): Reduced frontal activity in the elderly, H.J. Michalewski, L.W. Thompson, D.B.D. Smith, J.V. Patterson, T.E. Bowman, D.Litzelman, G. Brent, J.Gerentol., Vol. 35, pp 542-549, 1980.

[19] Slow potential correlates of attention dysfunction in senile dementia, K.P. O'Connor, International Biol. Psychol., Vol. 11, pp193-202, 1980.

[20] An international pilot study of CNV in mental illness. Second report. M. Timsit-Berthier, A. Gerono, J.C. Rousseau, H. Mantanus, P. Abraham, F.H.M. Verhey, T. Lamers, P. Edmonds, Brain and Information. Event-related Potentials, Eds., R. Karrer, J. Cohen, P.Tueting, pp 629-637, New York Academy of Sciences, 1984.

[21] Contingent negative variation: Components ans scalp distribution in psychiatric patients, van der Bosch, Biol. Psychiatry, pp 963-972, Vol. 19, 1984.

[22] Event-related potentials as indicants of structural and functional damage in closed head injury, S.H. Curry, Motivation, Motor and Sensory Processes of the Brain. Electrical Potentials, Behaviour and Clinical Use. Progress in Brain Research, Vol 54, Eds., H.H. Kornhuber, L. Deecke, pp 507-515, Elsevier.

[23] A CNV typology of chronic schizophrenics and response to drug treatment, J.J. Tecce, G. Gardos, J.O. Cole, P.A. Bowers, Psychopharmacol. Bull., Vol. 15(1), pp39-41, 1979.

[24] Alcoholism, organicity and event-related potentials, J.A. Skerchock, J.Cohen, Brain and Information, Eds., R. Karrer, J.Cohen, P.Tueting, pp 623-628, New York Academy of Sciences, 1984.

[25] Cortical slow potentials and the occipital EEG in congential blindness, J.L. Noebels, W.T. Roth, B.S. Kopell, Journal of Neurological Science, Vol. 37, pp 51-58, 1978.

[26] Spontaneous generalised and focal temporal epileptic EEG discharges and contingent negative variation, R. Zappoli, M. Papini, P.L. Cabras, Riv. Patol. Nerv. Ment., Vol. 91 pp 157-168, 1970.

[27] P3 and contingent hegative variation in Parkinsons disease, F. Pulvermueller, W. Lutzenberger, V. Mueller, B, Mohr, J. Dichgans, N. Birbaumer, Electro. and Clin. Neuro., Vol. 98, pp456-467, 1996.

[28] P300 in clinical applications: Meaning, method and measurement, J. Polich, American Journal of EEG Technology, Vol. 31, pp 201-231, 1991.

[29] Two varieties of long-latency positive waves evoked by unpredictable auditory stimuli in man, N.K. Squires, K.C. Squires, S.A. Hillyard, EEG in Clinical Neurophysiology, Vol. 38, pp 387-401, 1975.

[30] Age differences in P3 reaction time associations, A. Pfefferbaum, J.M. Ford, W.T. Roth, B.S. Kopell, EEG in Clinical Neurophysiology, Vol. 49, pp 257-265, 1980.

[31] Age-related changes in auditory event-related potentials, A. Pfefferbaum, J.M. Ford, W.T. Roth, B.S. Kopell, EEG in Clinical Neurophysiology, Vol. 49, pp 266-276, 1980.

[32] Latency of the P3 event-related potential: Normative aspects and within-subject variability, D.A. Skare, G.E. Lynn, Electroencephalograhy and Clinical Neurophysiology, Vol. 59, pp 251-259, 1986.

[33] Attention, probability and task demands as determinants of P300 latency from auditory stimuli, J. Polich, Electroencephalograhy and Clinical Neurophysiology, Vol. 63, pp 420-424, 1984

[34] Clinical application of the P3 component of event-related potentials. II. Dementia, depression and schizophrenia, A. Pfefferbaum, B.G. Wenegrat, J.M. Ford, W.T. Roth, B.S. Kopell, EEG in Clinical Neurophysiology, Vol. 59, pp 104-124, 1984.

[35] Auditory evoked potentials, clinical vs. research applications, N. Boutros, H. Nasrallah, R. Leighty, M. Torello, P. Tueting, S. Olson, Psychiatry Research, Vol. 69(2-3), pp 183-195, 1997.

[36] Electrophysiological differences between demented and non-demented patients with parkinsons disease, D.S. Goodin, Annals of Neurology, Ed. M.J. Aminoff, Vol 21, No. 1, Jan. 1987.

[37] Cognition in parkinsons disease: an event-related perspective, E.C. Hansch, Z.I. Goldberg, A.R. Potvin, W.W. Tourtellote, Ann. Neurol. Eds. K. Syndulko, S.N. Cohen, Vol. 11, pp 599-607, 1982.

[38] P300 variations in parkinsonian patients before and during dopaminergic monotherapy: a suggested dopamine component in P300, P. Stanzione, F. Fattapposta, P. Giunti, C. D'Alessio, M. Tagliati, C. Affricano, G. Amabile, Electroencephalograhy and Clinical Neurophysiology, Vol. 80, pp 446-453, 1991.

[39] Age-dependence of the bereitschaftspotential, L. Deecke, H.G. Englitz, G. Schmitt, Multidisciplinary perspectives in event-related brain potential research, Ed. D.A. Otto, U.S. government printing office, pp 330-332, 1978.

[40] Age-related changes in movement-related cortical potentials, H. Ishizuka, H. Tomi, N. Sunohara, Japanese journal of geriatrics, Vol. 33, pp 586-591, 1996.

[41] The Bereitschaftspotential is abnormal in parkinsons disease, J.P.R. Dick, J.C. Rothwell, B.L. Day, R. Cantello, O. Buruma, M. Gioux, R. Benecke, A. Beradelli, P.D. Thomson, C.D. Marsden, Brain, Vol. 112, pp 233-244, 1989.

[42] Bereitschaftspotential preceeding voluntary saccades is abnormal in patients with parkinsons disease, N. Shimizu, R. Okiyama, Advances in Neurology, Vol. 60, pp 398-402, 1993.

[43] Beritschaftspotential in schizophrenia, T. Karaman, S. Ozkaynak, C. Buyukberker, British journal of psychiatry, Vol. 171, pp 31-34, 1997.

2 THE TECHNOLOGY OF EEG RECORDING

2.1 Measurement Theory

EEG are recorded from the scalp using electrodes. A basic property of any type of electrode is that there exists a metal/electrolyte junction in the electrical connection between tissue and apparatus. It is common for the electrode not to be in direct contact with the scalp but rather that indirect contact is established by an electrolyte bridge formed by an electrode jelly applied between the electrode and the skin. The electrochemical properties of the metal/electrolyte junction and the skin/electrolyte cause both a dc potential and an electrical impedance in the connection between tissue and apparatus. Both of these can restrict the performance of the recording system.

2.1.1 DC Offset Voltage

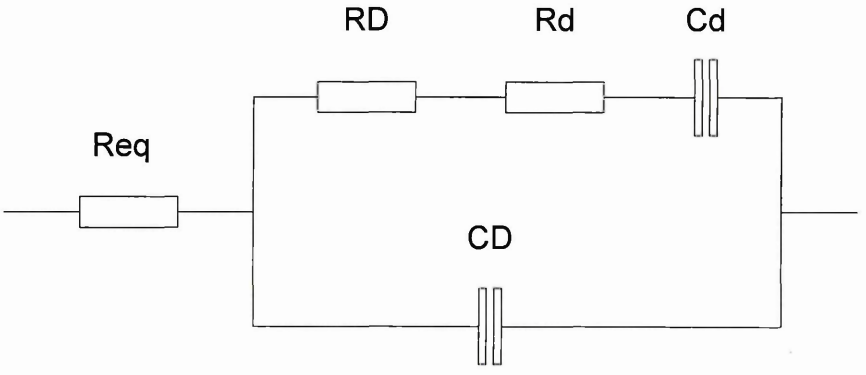
When an electrode comes into contact with an electrolyte, in the absence of any current, an electrical potential exists between the electrode and the electrolyte. This electrode potential results from a difference between the rate of flow of ions from the metallic surface of the electrode into the electrolyte and the flow of ions from the electrolyte into the metallic surface of the electrodes. The ionic imbalance also leads to an accumulation of electrolyte ions in the vicinity of the electrode forming an electrical double layer. In this way equilibrium is established [1]. The value of the electrode potential is a function of electrode material, the electrolyte composition, and temperature. It may have values ranging from millivolts to volts. When scalp electrodes are used a similar dc potential is generated at the skin/electrolyte junction depending on the electrolyte composition and the condition of the skin.

These steady potentials generated at the electrodes cannot be eliminated and result in a dc offset at the amplifier input that can be larger than the magnitude of the EEG signals. EEG amplifiers must therefore be designed so that their performance is not compromised by these dc offset voltages. The maximum value they are assumed to be is ± 300 mV [2] though they are normally much less than this.

2.1.2 Electrode Impedance

When a DC voltage is applied between electrodes placed in an electrolytic solution, the electrical double layers associated with the electrodes are disturbed and an electric current flows. The magnitude of the current is dependent primarily on the transport of ions at the metal/electrolyte junction. The relation between voltage and current can be represented by a time dependent electrode impedance. A simplified model is shown in Figure 2.1

Figure 2.1 Simplified model of an electrode/electrolyte junction



RD and CD signify the resistive and capacitive components of the transport mechanisms due to the electrical double layer. Rd and Cd in series represent the time dependent, and

thus frequency-dependent, diffusion impedance or Warburg impedance [3]. The resistance Rd and capacitance Cd are a function of $1/\sqrt{\omega}$. Req represents the electrolyte resistance, which in a practical situation involves the resistances of the body fluid, the skin and the electrode jelly.

If the application of an external DC voltage to an electrode causes the flow of a steady current, the pathway formed by RD, Rd and Cd is only resistive and the electrode is said to be non-polarised, reversible or inert. The silver/silver chloride (AgAgCl) electrode is an example of a reversible electrode that has a low resistance for DC and low frequency signals, because it allows equal migration of ions both in and out of solution, regardless of current direction. This type of electrode is commonly used for EEG recording [4]. Many metal/electrolyte junctions do not have this property. In these cases dc current flow results in an ionic imbalance at the electrical double layer related to the direction of the current flow. Consequently, the current caused by a voltage step presents an initial transient onset but drops rapidly to a very small value. This can be explained by an initial impedance drop followed by an increase of the impedance component related to diffusion (Rd and Cd) to a large value of the order of megaohms. This type of electrode is said to be polarised or non-reversible and cannot be used for the recording of DC potentials. Amplifiers with low input impedance ($<1M\Omega$) allow greater current flow for a given potential difference and more easily produce electrode polarisation. Testing electrode impedance with a DC meter (which passes a small current to obtain a reading of resistance) will similarly cause such electrodes to become polarised. It is therefore preferable to use an AC impedance meter to reduce electrode polarisation.

The electrode impedance is determined to a large extent by the double layer capacitance CD. The value of CD is proportional to the size of the electrode surface.

The metal used for electrodes cannot always be chosen on the basis of properties of the electrical impedance. Other factors such as toxicity, mechanical strength, or scalp irritation that may be caused by electrode application, may play a role and thus impose restrictions on the choice of the optimal electrode characteristics. Well prepared AgAgCl electrodes are generally considered to be the most suitable for the recording of all types of surface potentials [5].

The ultimate electrical impedance depends on the electrical resistance of the skin/electrolyte junction (Req in Figure 2.1). This can have values from kilohms to hundreds of kilohms depending on the condition and preparation of the skin, the concentration of the electrode jelly, and the time elapsed after the application of the jelly. To obtain an initial low resistance of reasonable stability, an electrode jelly with a high concentration of sodium chloride (5-10%) should be used in conjunction with a well-prepared skin from which the most superficial horny layer is scraped off. This can be achieved by rubbing the skin with a specially formulated compound such as Omniprep Skin Pure.

2.1.3 Electrode Movement Artefacts

The movement of an electrode in relation to the scalp causes changes in the electrical double layer and thus alters the DC offset voltage. This causes an artefact in the EEG. These artefacts can be reduced by using AgAgCl electrodes which, when properly prepared and handled with care, produce a relatively small but stable potential. The effect is also reduced by using electrodes that are not in direct electrical contact with the skin but via an electrode jelly. This minimises the effects of motion at the electrolyte/metal junction.

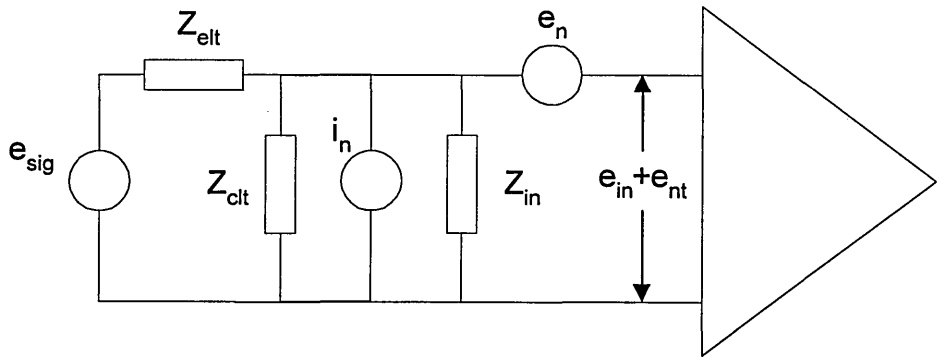
Another source of movement artefacts, however, is the skin/electrolyte junction. The resistance and the DC potential generated at this junction may also change due to motion, which may cause additional artefacts [6]. This effect is more pronounced if the amplifier draws a significant input current. Lowering the resistance at this junction by abrading the skin reduces this type of artefact.

The provisions that can be made to reduce electrode movement artefacts can be summarised as follows. Care should be taken that DC offset potentials and resistance in the pathway from skin to electrode surface are minimal. This implies proper choice of electrodes and good skin preparation. The mechanical design of the electrodes and the way in which they are fixed to the scalp should provide minimal motion at the skin/electrolyte and the electrolyte/metal junctions. To ensure relative mechanical stability of the electrode and the skin region in its vicinity, the mechanical load on the electrode should be kept as small as possible by using lightweight and flexible electrode leads.

2.1.4 Signal Attenuation and Accuracy

Unwanted signal attenuation at the input of an amplifier is determined in general terms by the ratio of the electrode impedance and that of the EEG amplifier input stage. This interaction can be explained on the basis of the circuit given in Figure 2.2 in which Z_{elt} is the sum of the electrode impedances. Z_{clt} represents the impedance of the shunting capacitance of the cable connection between the electrode and the amplifier. Z_{in} is the amplifier input impedance and i_n and e_n represent, respectively, noise current and voltage sources inherent in the amplifier.

Figure 2.2 Input circuit of an EEG recording channel



In this way a noise voltage e_{nt} at the amplifier input has to be taken into account. The signal attenuation is defined by the ratio between the amplifier input voltage e_{in} and the electrode open circuit voltage e_{sig}. The ratio between e_{in} and e_{sig} is given by the expression:

$$\frac{e_{in}}{e_{sig}} = \frac{1}{1 + \frac{Z_{elt}}{Z_{in}} + \frac{Z_{elt}}{Z_{clt}}}$$

From this expression it can be seen that e_{in} approximates e_{sig} if the total electrode impedance Z_{elt} is sufficiently small compared to the amplifier input impedance Z_{in} and the cable impedance Z_{clt} . In order to obtain attenuation as small as 0.99, the values of Z_{in} and Z_{clt} must be larger than 100 times Z_{elt}. Because EEG scalp electrodes may easily have an electrical impedance of many kilohms, EEG amplifiers must have an input impedance of several megohms to prevent appreciable signal attenuation. This requirement becomes even more stringent if electrodes are used which, because of size

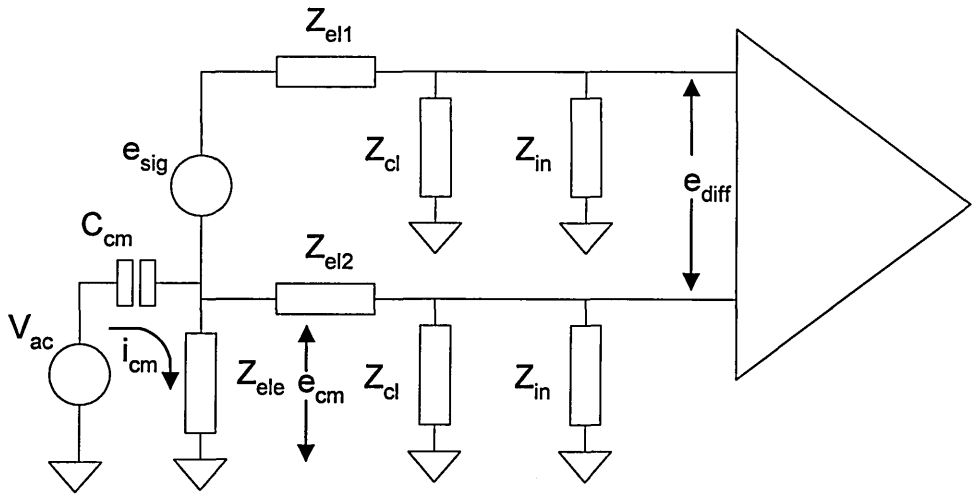
and type of metal, have a relatively high impedance and/or frequency-dependent impedance. If the cable capacitance has a value of 1 nF or more the shunting impedance Z_{clt} will cause considerable attenuation at high frequencies if the electrodes have a relatively high impedance. This drawback can be overcome by locating input amplifiers close to the subject thus minimising cable lengths.

The accuracy of measurement depends primarily on the magnitude of the noise voltage e_{nt}. This noise component is added to the amplifier input signal e_{in}. In this way the accuracy of the measurements cannot be better than the magnitude of the noise. This accuracy can be expressed as the signal to noise ratio SNR = e_{sig}/e_{nt}. The noise voltage source is independent of the electrode/amplifier connection. The noise current source i_n, on the contrary, causes a current flow in the circuit Z_{elt} // Z_{clt} // Z_{in}. Thus the magnitude of the resulting noise voltage will depend on the electrode impedance Z_{elt}.

2.1.5 Interference from external sources

Mains power interference at the electrode/amplifier interface may produce an artefact in EEG recordings. The effect of this interference on the electrodes can be explained on the basis of the circuit of Figure 2.3.

Figure 2.3 Schematic showing the characteristics of an EEG amplifier



Owing to capacitive coupling (C_{cm}) between the subjects' body and power conductors in the environment, an alternating current i_{cm} flows via the subjects earth electrode of impedance Z_{ele} to earth. This current causes an AC voltage ($e_{cm} = i_{cm} \times Z_{ele}$) between the ground and the subjects body. In this way, both recording electrodes have a potential with respect to the earth that is, at each moment, equal in amplitude and polarity. As regards the interference caused by this common mode AC electrode potential, the magnitude of the resultant AC potential difference e_{diff} at the amplifier input is of interest and should be small compared to the EEG signal e_{sig} being measured. If the two parallel impedances formed by the amplifier input impedances Z_{in} and the cable capacitance impedances Z_{cl} are assumed to be large compared with the electrode impedances Z_{el1} and Z_{el2}, then e_{diff} can be approximated by:

$$e_{diff} \approx \frac{Z_{el1} - Z_{el2}}{Z_{cl} Z_{in} / Z_{cl} + Z_{in}}$$

From this expression if follows that in order to minimise e_{diff}, the difference between the two electrode impedances should be as small as possible. The impedance properties of the skin/electrolyte interface, however, may often result in impedance difference of several kilohms at mains frequency. Therefore, taking into account that the common mode voltage e_{cm} can easily have an amplitude of mV, the parallel impedance Z_{cl}, Z_{in} must be many megohms in order to keep e_{diff} sufficiently small. Z_{in} should be at least 10 megohms at mains frequency. A cable capacitance of 1-2 nF, which is realistic, corresponds at mains frequency to an impedance of a few mohms. A cable capacitance of this order will impose a limitation on the obtainable reduction of mains interference. In certain circumstances additional provisions such as electrostatic shielding of the patient may be necessary.

EEG equipment with amplifier input stages located inside the electrode terminal box are favoured in this respect, because in such apparatus mains interference is not affected by cable capacitance.

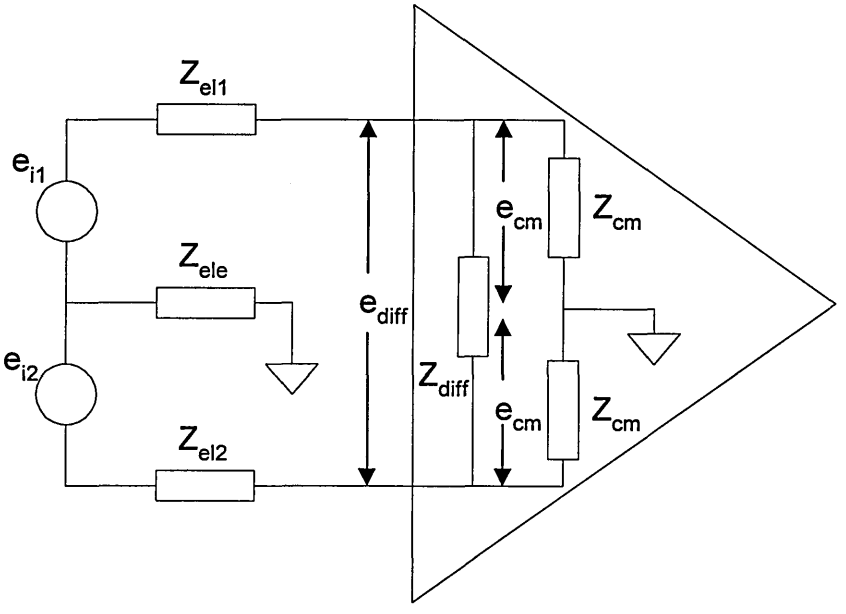
2.2 Principle of Amplification of EEG Signals

2.2.1 Basic Characteristics of EEG Apparatus

2.2.1.1 Input Circuit

The characteristics of the input amplifiers of the EEG apparatus are of great importance for accuracy of measurement. The discriminatory power of the differential measurement performed at this stage depends to a large extent on the values of the amplifier input impedances as compared to those of the electrodes. This can be explained by considering the schematic diagram of the amplifier input circuit in Figure 2.4.

Figure 2.4 Input circuit of an EEG amplifier



Z_{el1}, Z_{el2}, and Z_{ele} represent, respectively, the impedances of the recording and the ground electrode; ei_1 and ei_2 are the voltages at the two recording electrodes with respect to ground; e_{diff} represents the resultant voltage difference at the amplifier input

terminals. Two flows of current into the amplifier input circuit can be distinguished. One current, caused by e_{diff}, flows in the amplifier differential input impedance Z_{diff}; the other current, owing to the common mode component e_{cm} of ei_1 and ei_2, flows in the common mode input impedances Z_{cm}. Assuming that $Z_{cm} >> Z_{el1}$, $Z_{cm} >> Z_{el2}$, and $Z_{diff} >> (Z_{el1} + Z_{el2})$, the voltage difference e_{diff} at the amplifier input can be approximated by:

$$e_{diff} \approx \frac{ei_1}{1+\frac{Z_{el1}+Z_{el2}}{Z_{diff}}+\frac{Z_{el1}}{Z_{cm}}} - \frac{ei_2}{1+\frac{Z_{el1}+Z_{el2}}{Z_{diff}}+\frac{Z_{el2}}{Z_{cm}}}$$

From this expression it can be seen that the values of the input impedances Z_{diff} and Z_{cm} as compared to the electrode impedances Z_{el1} and Z_{el2} determine the accuracy of differential measurement at this stage. An accurate measurement of the voltage difference ei_1 - ei_1 requires that the two denominators in the expression approach unity; thus the sum of the impedance ratios $(Z_{el1} + Z_{el2})/Z_{diff}$ and Z_{el1}/Z_{cm} must be very small. If, for example the electrode impedances have values of about 10 kilohms, the input impedances Z_{diff} and Z_{cm} must have values of several megohms in order to achieve an accuracy of at least 10%. An imbalance of the electrode impedances results in unequal denominators and therefore imposes a further restriction on the accuracy of measurement. This is accentuated if ei_1 and ei_2 have relatively large common mode components. Owing to this inequality, an additional unwanted voltage difference is caused at the amplifier input. The disadvantageous effect of electrode impedance unbalance will be much less if the relative contribution of Z_{el}/Z_{cm} to the denominators is sufficiently small (e.g. $Z_{cm} >> Z_{diff}$).

2.2.2 Frequency Response and Analogue Filtering

The bandwidth of an EEG signal is determined by the highest and lowest frequency components of the signal. If the frequency response of a recording channel is narrower than the frequency range of the signal, information will be lost. If however, the frequency range of the channel is wider than that of the signal, owing to noise, the recorded data will contain additional irrelevant information. When recording ERP signals it is therefore necessary to match the frequency response characteristics of the equipment with those of the signals without inducing unacceptable amplitude distortion. That is the equipment must have a flat frequency response over the signal bandwidth.

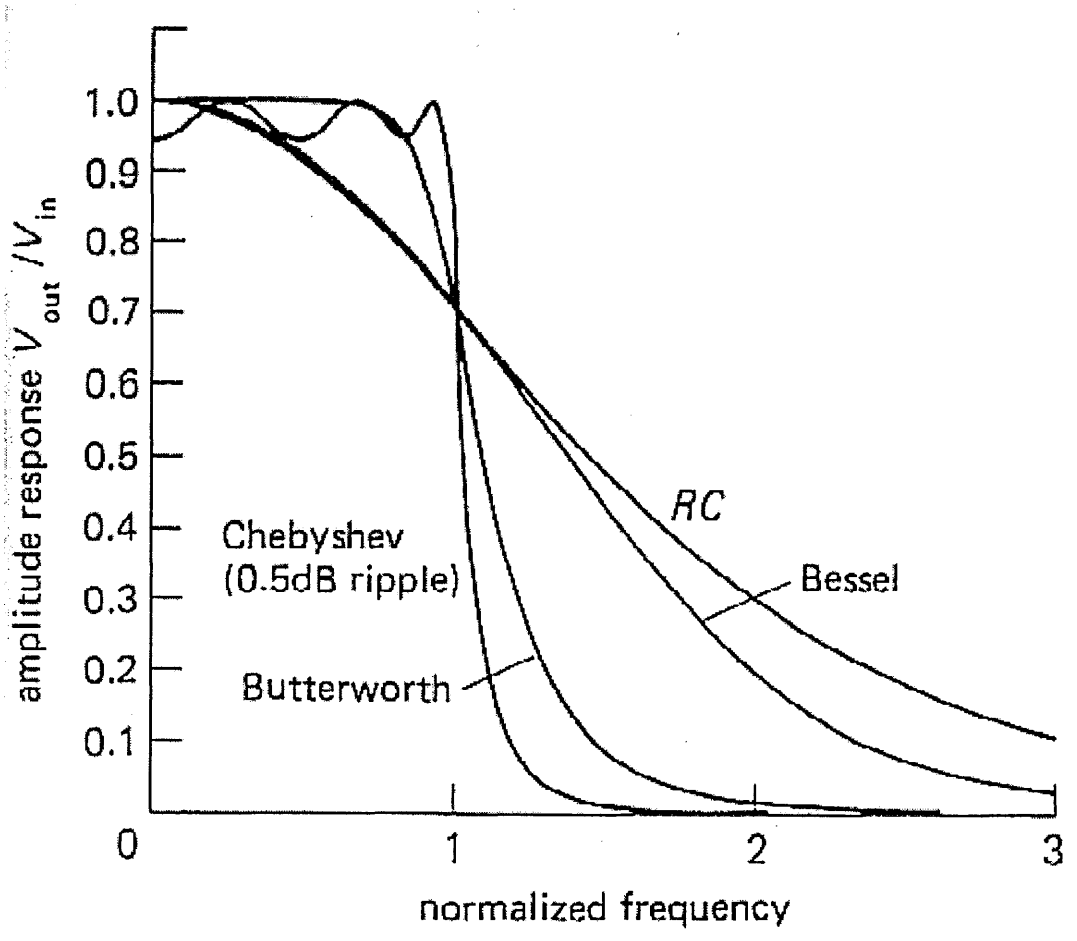
2.2.2.1 Filter Characteristics

Ideal high and low pass filters would have a flat non-zero output amplitude until the cut-off frequency at which the output amplitude would fall instantaneously to zero. However real analogue filters do not exhibit these ideal characteristics. Instead the signal amplitude will start to drop sometime before the cut-off frequency and fall gradually thereafter. The non-ideal properties of the filter are determined by the filter type and generally the more ideal they are the more complex the filter is. Different filter types are also designed to maximise certain ideal characteristics at the expense of others [7]. These are listed for three of the most common filter types:

Butterworth	Passband response flatness
Chebyshev	Cut-off response
Bessel	Linear phase response

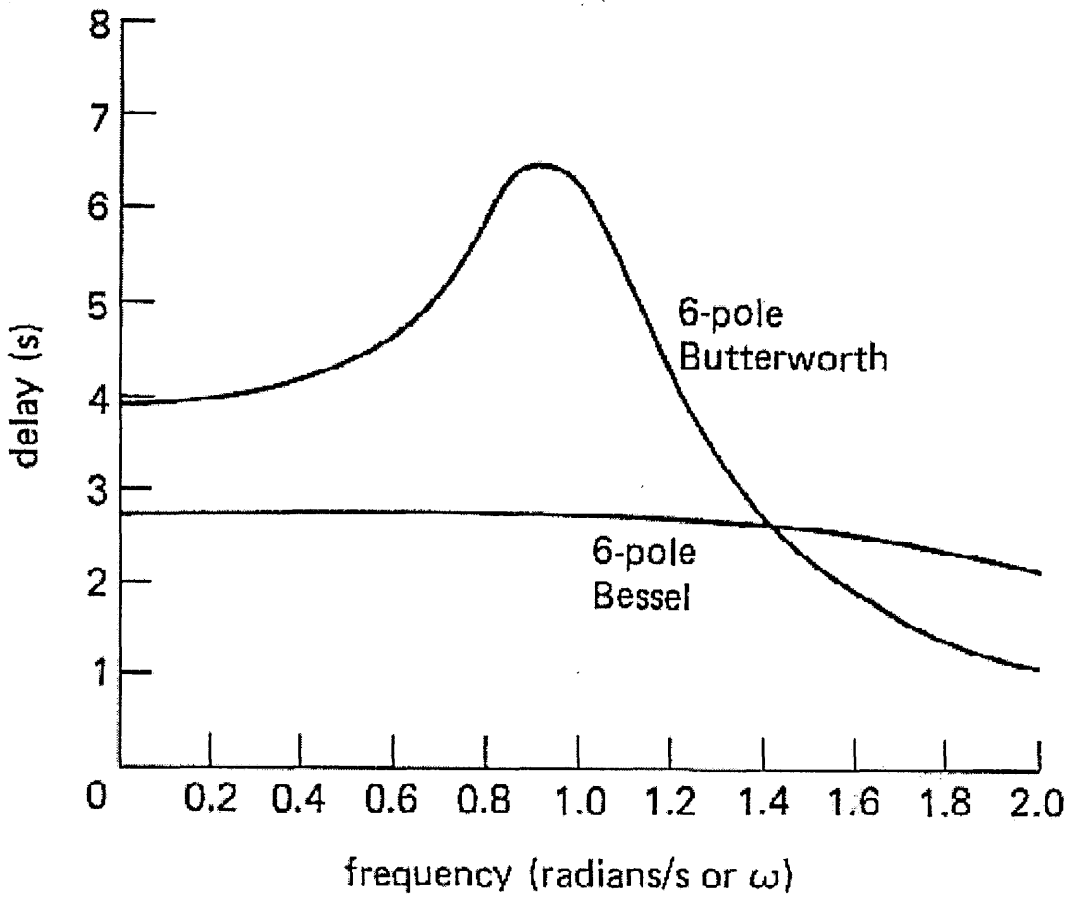
The amplitude response characteristics for low pass versions of these three filter types are shown in Figure 2.5.

Figure 2.5 Amplitude response characteristics of Butterworth, Chebyshev and Bessel filters



The Bessel filter optimises phase response characteristics in the passband. All filters cause a phase difference as a function of frequency between the input and output signal. The difference in characteristics for different filter types is illustrated in Figure 2.6.

Figure 2.6 Phase vs frequency characteristics of Butterworth and Bessel filters



Such a phase difference corresponds to a time displacement between input and output signals whereby the output signal is 'leading' if the phase difference is positive and 'lagging' if it is negative. It is therefore apparent that high pass filters induce a time lag in the region of the cut-off frequency and low pass filters a time lead. The relation between frequency f, phase difference Φ and the corresponding time displacement T is:

$$T = \frac{\Phi}{f \times 360} \qquad \text{if } \Phi \text{ is in degrees}$$

$$T = \frac{\Phi}{f \times 2\pi} \qquad \text{if } \Phi \text{ is in radians}$$

From this it can be established that the time displacement introduced by high pass filters is strongly dependent on frequency, whereas with the low pass filter the time displacement is reasonably frequency independent in the frequency range of interest ($f \leq f_c$). Thus, if a complex signal, composed of several components at different frequencies, is passed through a high pass filter, the original time relations between the several components will be modified, and the output waveform will be distorted compared to the input waveform. The low pass filter will not cause such distortion but there will be a constant time displacement between the input and output signal.

To minimise the distorting affects of high and low pass filters it is best to select generous high and low settings with cut-off points well beyond twice the highest ERP component and half the lowest ERP component of interest respectively. However too wide a bandwidth results in additional noise in the form of unwanted signals. Using filters with linear phase characteristics such as the Bessel filter minimises distortion with minimal bandwidth and hence minimal noise.

2.3 ERP Measurement System Requirements

2.3.1 General Description of Requirements

Previous work by Reza Saatchi lead to the design of an 8-channel system to record the CNV [8]. The aim of this project was to extend this work to develop a portable system that will record 32 channels of not just the CNV, but of the P300 and Bereitschaftpotential as well. The system was also intended to eliminate the need of a conventional EEG machine and its paper recording system, which was required in the previous design.

2.3.2 Recording Bandwidth

The recording bandwidth is to be 0.016 - 10 Hz. ERPs are low frequency waveforms with a first harmonic frequency component of approximately 1Hz. The recording bandwidth was chosen to be 0.016 - 10 Hz to provide additional range to accommodate the non-linear characteristics of the high and low pass filters about their cut-off frequencies. As the high pass filter is to be a single pole design more bandwidth still is provided.

The frequency range does not extend down to dc in order to remove both standing electrode potentials and dc offsets generated by the amplifier circuitry.

It is advantageous to keep the upper frequency limit less than 50 Hz and as low as possible in order to remove any mains noise interference present in the recordings.

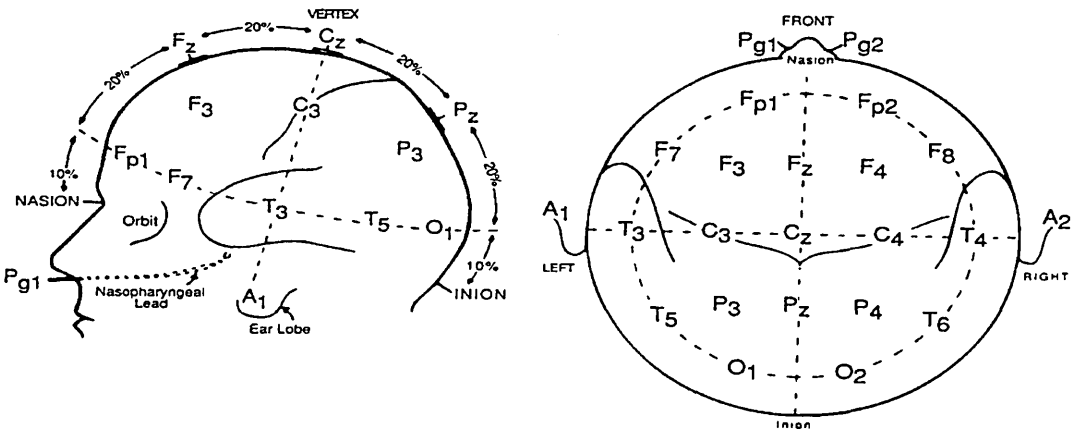
2.3.3 Recording Range

The 32 channels must be capable of recording not only EEG but also electro-oculogram (EOG). EOG are the electrical signals generated by eye movements and blinks, which may be detected between pairs of electrodes placed about the eyes. These can be up to 1 mV in magnitude [9] and must be recorded for use in the removal of ocular artefacts in the EEG using digital signal processing techniques [10].

2.3.4 Number of channels

There exists a standard montage of 21 electrode recording sites called the 10-20 system, see Figure 2.7 [11]. This system specifies the position of 21 evenly spread locations across the scalp. The sites are determined as a percentage (mostly 10% or 20%) of distances between definitive landmarks such as the nasion, inion and the ear tragus. 32-channels will enable recording from all of these sites. In addition five electrodes are required to measure EOG [12] leaving six extra electrodes to record from sites of specific interest.

Figure 2.7 International 10-20 system of electrode placement



Left side of head Top of head

2.3.5 Simultaneous Sampling vs Multiplexing

EEG signals must be recorded simultaneously from different scalp locations for the purposes of signal averaging and the study of topographical distribution. Most commercial EEG machines multiplex the analogue signals into an ADC. This leads to a phase shift error between the signals recorded at different electrode sites, the degree of error depending on the number of channels recorded and the sampling speed of the system.

The error can be calculated as a difference between two identical signals recorded on different channels caused solely by the time difference between conversions of identical sample numbers. This error is a maximum when the rate of change of the signals is largest. That is when the signal frequency and magnitude are maximal. This can be calculated as follows:

If a single component of an EEG signal is represented by a sine wave, its variation V with time t can be described by the following equation:

$$V = A\sin 2\pi ft$$

where A is the amplitude of the signal and f the frequency of the signal.

Its rate of change with time is described by the differential of this equation, which is given by:

$$\frac{dV}{dt} = 2\pi fA\cos 2\pi ft$$

By rearranging this equation the time required to perform a conversion of two signals of frequency 10 Hz and amplitude 1 mV to achieve a maximum difference between signals of 1 μV can be calculated as:

$$dt = \frac{dV}{2\pi fA} = 15.92\ \mu s$$

If 32 channels are to be converted with less than 1 μV of conversion error between them then the total conversion time for all channels would have to be:

$$\frac{15.92 \times 10^{-6}}{32} = 497.5 \times 10^{-9} \quad \text{or approx. 500 ns.}$$

This is very fast when consideration is given to the fact that this time period has to include not only the ADC conversion time but multiplexer settling time and any other stabilisation periods required for circuitry such as programmable gain amplifiers.

The alternative to having a fast conversion time is to re-synchronise the data after recording if the time period between consecutive samples is constant. One method of achieving a constant time difference is to use a sampling signal whose frequency depends upon the number of channels to be recorded and will therefore be a maximum of 32 times greater than that of a simultaneous system. If this is also the interrupt frequency then there will be a lot less time to perform inter-sample functions such as stimulus generation or response recording. Alternatively two sampling signals could be used, one to set the overall sampling and interrupt rate and another to convert all channels rapidly when an interrupt occurs. Having two time locked signals will increase system complexity though.

If the inter-channel conversion period is known the waveforms of different channels could be re-aligned by interpolation of the data. A simple graphical display of the waveforms could be drawn by plotting the true recording time of each sample, that would be dependent on both channel and sample. However interpolation must be performed if inter-channel data manipulation, such as reference subtraction, EOG removal or differential waveform display, is to be performed. This will significantly increase data processing and make it more difficult to display ERP waveforms during recording.

If multiplexed recording was to be used it also raises the question as to where the multiplexing should be performed. To minimise hardware duplication it should be performed as early as possible, however the signals need to be amplified sufficiently so as to make multiplexing errors negligibly small. Pre-amplification would certainly be required and probably secondary amplification also. Ideally the multiplexing should occur prior to the isolation stage so as to remove the need for numerous isolation stages. These are relatively expensive and require safety critical PCB layout. This means that

the digital multiplexing signal would also have to be coupled into the isolated circuit.. This could be a problem as the signal is digital and could therefore potentially transmit noise onto the analogue ERP signals. As the digital signal would require power, this would have to be provided by the isolated analogue supply, which is undesirable, or by a separate isolated digital supply with increased hardware overheads.

The disadvantage of simultaneous sampling is the requirement for duplicate channel hardware leading to increased system cost, power consumption and size. It was envisaged that careful design of both the channel circuitry and PCBs would keep all of these factors within reasonable limits. Duplicate circuitry also means that each channel will have slightly different gain and phase response characteristics. However each channel could be calibrated in software if necessary.

One advantage of duplicate channel hardware is the fact that it makes the system very modular. Channel hardware can be built and tested individually and the possibility of developing alternative channel processing hardware in the future exists.

2.3.6 Stimulus Generation

The audio and/or visual stimuli necessary for the paradigms must be generated. Audio stimuli are the preferred choice as visual stimuli can generate ocular artefacts from blinks. Patient responses must be recognised and recorded accurately relative to the measured EEG.

2.3.7 Data Storage and Display

Storage medium capable of storing up to 32 waveforms of up to 8 s duration per subject is required. Preferably one that can be removed and transferred to other PC's for

analysis. The ability to display the waveforms as they are recorded is also necessary. This enables the operator to monitor the recording process and correct any problems that may occur.

2.3.8 Standing Electrode Potentials

DC electrode potentials of up to 300 mV in amplitude, generated by polarisation at the electrode scalp interface, need to be removed [13]. Although these are more likely to be 100 mV in amplitude, they are still very much larger than the ERP signals, and will swamp them if they are not removed.

2.3.9 Hospital Safety Standard IEC 601

All equipment used in hospitals must conform to hospital safety standards IEC601-1/BS5724 Part 1 [14]. They specify certain design criteria and also require a series of tests to be performed on the equipment used to ensure patient safety. It is of particular importance that there is no dc path between the subject and any mains supply voltages. To achieve this the subject must be isolated from the system to an isolation voltage of at least 240 V a.c.

IEC601-1/BS5724 Part 1 is the safety standard for all medical electrical equipment. Its scope includes electrical safety, mechanical safety, operational safety, labelling and documentation. Regarding ERP measurement equipment, the most challenging aspects are the electrical safety criteria. The following parameters are particularly important:

Earth leakage current

Enclosure leakage current

Patient leakage current

Patient auxiliary current

1) Earth leakage current is the current flowing from the instrument through its protective earth conductor. This must be less than a specified maximum in case the earth conductor becomes detached from the equipment and the operator accidentally becomes the path to earth.

2) Enclosure leakage current is the current flowing from any part of the instrument enclosure to earth or any other part of the enclosure. This must be less than a specified maximum in the event the operator acts as a conductor for this current.

3) Patient leakage current is the current flowing from the instrument via an applied part (e.g. an electrode) to earth. This is particularly important as it specifies the maximum current allowed to flow through a subject if they are connected to earth, intentionally or otherwise. This is measured under normal conditions and in the presence of an applied mains voltage and must not exceed a specified maximum. It is a measure of the degree of isolation of the patient and it is particularly important with EEG equipment that this is small as any measured current will flow through the head. In design terms this parameter mean that either the entire instrument or the input circuitry has to be isolated from ground.

4) Patient auxiliary current is the current flowing between different applied parts such as two electrodes or an electrode and the ground electrode. This must be less than a specified maximum as this current will flow through the head of the subject.

2.3.10 ERP Measurement System Specification

Existing commercial ERP measurement equipment generally has limitations in the number of channels available, bandwidth and method of sampling. The system described in this thesis is designed to provide the optimal solution to measurement and provide an instrument that can be used as a research tool to investigate ERPs further. To record the ERPs the measurement system must meet the following specification:

Number of Channels	32 Simultaneous Sampling
Signal Range	± 1 mV
Frequency Range	0.016 to 10 Hz
Noise	< 1 μV
Resolution	0.024 %
Accuracy	± 0.5 μV
Data Storage	Removable mass storage device
Stimulus Generation	1 kHz & 2 kHz tones
Safety	IEC601-1/BS5724 Part 1

2.3.11 Specification of Commercial ERP Equipment

Before deciding to design a 32 channel ERP system the ERP systems available commercially were reviewed for their suitability.

Biopac MP100+EEG100A

Number of Channels	16 Multiplexed
Bandwidth	1-100 Hz

This is a modular system that is designed to be operated from a standard PC. It uses a single 16 channel data acquisition unit and one biopotential amplifier per channel. Recording systems can therefore be tailored for individual needs. A stimulator unit is available for generating audible stimuli. This system is unsuitable because it can only record a maximum of 16 channels and the high pass cut-off frequency of 1 Hz is too high for our requirements.

Nihon Kohden Neuropack

Number of Channels	8 Multiplexed
Bandwidth	N/A

This is a dedicated ERP measurement system including headbox, control unit, monitor, data storage device, printer and stimulator. The high and low pass filter cut-offs are not stated in the literature but in any case the number of channels is limited to eight and therefore makes it unsuitable.

Bio-logic Systems Ceegraph

Number of Channels	22 Simultaneous Sampling
Bandwidth	0.1-20 kHz

This is a 22 channel simultaneous sampling EEG system. A stimulator unit is available for recording ERPs but this generates visual rather than auditory stimuli. The high pass filter cut-off is really too high but it is the limited number of channels that makes this system unsuitable for our requirements.

Medelec Sapphire/Premiere

Number of Channels	4 Multiplexed
Bandwidth	0.1-10 kHz

This is a 2/4 channel EMG/ERP recording system comprised of headbox, control unit, monitor, data storage device and stimulator. Again the limited number of channels is a problem but the high pass filter cut-off is also too high.

RC Electronics RP-EP/SYS

Number of Channels	16 Multiplexed
Bandwidth	0.1-250 kHz

This system comprises of a headbox and PC interface card. Stimulator outputs are available but a stimulator is not included with the system. Channel number and high pass filter cut-off preclude this system.

Walter Graphtek PL-EEG

Number of Channels	21 Multiplexed
Bandwidth	0.05-140 Hz

This system is available as a fixed or portable system. The limited number of channels is a problem and the high pass filter cut-off of 0.05 Hz is increased to 0.5 Hz on some models.

None of the commercial ERP system come close to meeting the required specification in terms of number of channels and bandwidth alone. The majority are also

multiplexed rather than simultaneous sampling systems. Regarding other factors such as accuracy, there is a large difference in the detail provided by the different manufacturers. Further research would enable better comparison of different parameters, but only direct testing of the systems would demonstrate their true characteristics. This highlights a problem in purchasing a commercial system in that one has little or no control over important characteristics such as not just filter cut-off frequency but filter type. Design of ones own system enables one to pay attention to such detail and also has advantages in terms of flexibility for future development.

[1] Principles of Applied Biomedical Instrumentation, L.A. Geddes, L.E. Baker, New York: John Wiley and Sons, 1968.

[2] EEG instrumentation standards (Revised 1977): Report of the commitee on EEG instrumentation standards of the international federation of societies for electroencephalograhy and clinical neurophysiology, J.S. Barlow, A. Kamp, H.B. Morton, A. Ripoche, H.Shipton, D.B. Tchavdarov, Electroencephalograhy and Clinical Neurophysiology, Vol. 45, pp 144-150, 1978.

[3] Interface design for bio-electrode systems, L.A. Geddes, IEEE Spectrum, pp 41-47, 1972.

[4] EEG Technology, R. Cooper, J.W. Osselton, J.C. Shaw, 3 rd Edition, Butterworths, 1980.

[5] Monitor artefacts and streaming potentials in relation to biological electrodes, A. Kahn, Digest of 6th International Conference in Medical Electronics and Biological Engineering, pp 562-563.

[6] Voltage fluctuations of metal-electrolyte interfaces in electrophysiology, A.H. Flasterstein, Medical and Biological Engineering, 4, 586, 1966.

[7] The Art of Electronics, P. Horowitz , W. Hill, Cambridge University Press, Chapter 9, pp 152-156, 1980.

[8] PC-based integrated system developed to diagnose specific brain disorders, M.R. Saatchi, B.W. Jervis, Computing and Control Engineering Journal, March 1991.

[9] Developments in signal processing for computerised diagnosis in clinical neurophysiology, M.R. Saatchi, Ph.D., 1992

[10] Investigation and comparison of some models for removing ocular artefacts from EEG signals, E.C. Ifeachor, B.W. Jervis, E.M. Allen, E.L. Morris, D.E. Wright, N.R. Hudson, Medical and Biological Engineering and Computing, 26, 584-598, Nov 1988.

[11] The ten-twenty system of the International Federation. Electroencephalography and Clinical Neurophysiology, 10, 371-375, 1958.

[12] Investigation and comparison of some models for removing ocular artefacts from EEG signals, E.C. Ifeachor, B.W. Jervis, E.M. Allen, E.L. Morris, D.E. Wright, N.R. Hudson, Medical and Biological Engineering and Computing, 26, 584-598, Nov 1988.

[13] Technological basis of EEG recording, A. Kamp, F.L. da Silva, Electroencephalography Basic Principles, Clinical Applications and Related Fields, Eds. E. Niedermeyer, F. Lopes da Silva, Urban and Schwarzenberg, pp 43-55, 1986.

[14] IEC601-1 1988/BS7724 Part1 1989, British Standard for Medical Electrical Equipment, Part 1, General requirements for safety.

3 HARDWARE DESIGN

3.1 Overall design of the system

The measurement system is comprised of the following:

Instrumentation PC

Headbox

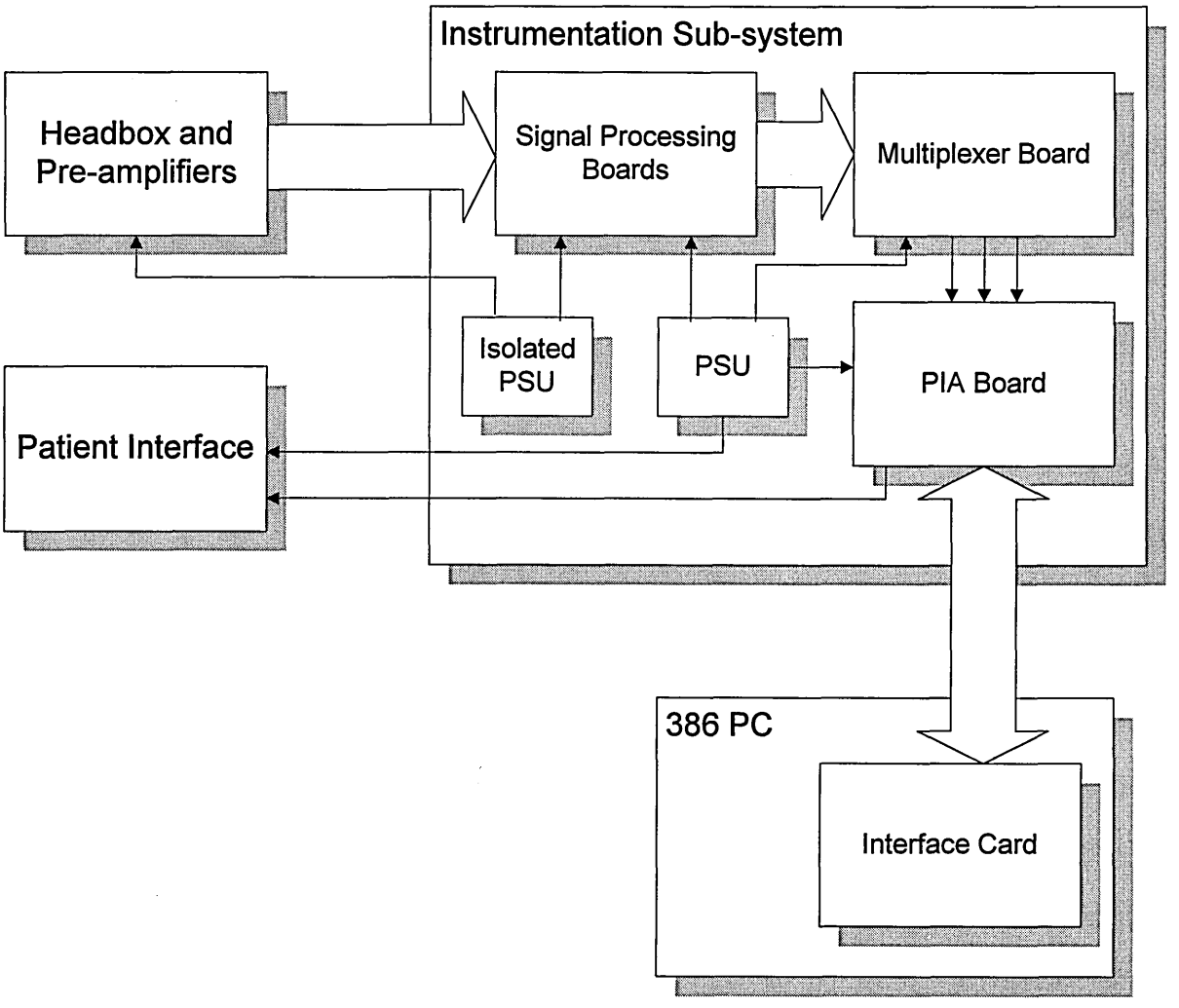
Patient Interface

Instrumentation sub-system

During recording the headbox and patient interface are sited near the subject. The headbox provides the termination point for the scalp electrodes and pre-amplification of the signals. The patient interface generates the audible stimuli required for the paradigms and records patient responses. Both of these units are fitted with trailing leads that connect to the instrumentation sub-system sited further away from the subject. The instrumentation sub-system contains the electronics required for the amplification, filtering and digitisation of the signals. Signal processing boards (SPBs) amplify and filter the signals and a multiplexer board switches each channel into an analogue to digital converter (ADC) on the peripheral interface adaptor (PIA) board. All circuitry in the instrumentation sub-system is powered by either an isolated or non-isolated power supply unit (PSU). Next to the instrumentation sub-system and connected by a ribbon cable is a personal computer (PC) that controls the recording and storage of the signals. The instrumentation PC is fitted with an interface card that enables communication between the PC and PIA board in the instrumentation sub-system.

Figure 3.1 is a block diagram of the measurement and recording system.

Figure 3.1 Measurement and recording system



3.2 Instrumentation PC

The PC is used to control the recording of the ERPs and to display them on screen. To enable the PC to do this an interface card is fitted into one of its internal expansion slots to enable it to communicate with the instrumentation sub-system. This interface card has decoding, timing and buffer circuits on-board and is connected to the instrumentation circuits by a 37-way ribbon cable. The instrumentation system is not dependent on the type of PC used as long as it is a 386 or better. The interface card will fit into the

expansion slot of any PC and will operate up to the maximum I/O bus speed of 8 MHz, which is independent of PC clock speed [1].

3.2.1 PC Interface Card

The interface card is an IBM PC prototyping board which is designed to fit into one of the expansion sockets of a PC motherboard. It provides on board track layout for signal buffering and decoding, together with a grid matrix area for the addition of electronic circuits. Ground and power distribution buses are available throughout the board area and there is space for a 37-way D-type I/O connector. The board is designed to buffer the PC data bus and other I/O lines and to provide an I/O address map as recommended by IBM [2]. IBM has allocated addresses $300 to $31F to prototyping board devices and the prototyping board decodes the high address lines to give an interface card enable, leaving the low A0 -A4 lines available for additional decoding in the range $300-$31F. These address allocations are given in Table 3.1.

Table 3.1 PC memory address allocations

Address Lines					Address in Hex	Device
A4	A3	A2	A1	A0		
0	0	0	0	0	300	Timer 1 Counter 0
0	0	0	1	0	302	Timer 1 Counter 1
0	0	1	0	0	304	Timer 1 Counter 2
0	0	1	1	0	306	Timer 1 Control
0	1	0	0	0	308	Timer 2 Counter 0
0	1	0	1	0	30A	Timer 2 Counter 1
0	1	1	0	0	30C	Timer 2 Counter 2
0	1	1	1	0	30E	Timer2 Control
1	0	0	0	0	310	PIA Port A
1	0	0	1	0	312	PIA Port B
1	0	1	0	0	314	PIA Port C
1	0	1	1	0	316	PIA Control
1	1	0	0	0	318	ADC
1	1	0	1	0	31A	ADC
1	1	1	0	0	31C	ADC
1	1	1	1	0	31E	ADC

Timer 1 and timer 2 are located on the interface card itself whilst the PIA and ADC are inside the instrumentation sub-system. The intention was to locate digital circuitry inside the PC and analogue circuitry inside the instrumentation sub-system, so that the analogue circuitry is subjected to as little digital noise as possible. However it was necessary to locate the PIA inside the instrumentation sub-system because of the limited number of I/O lines available. This is limited by the 37-way connector on the interface card. The circuit diagram for the interface card is in Appendix 7.1.

3.2.1.1 PC/Instrumentation sub-system interface

This interface is unusual in that the PC data bus is buffered and expanded outside the PC to the instrumentation sub-system, to effectively enable the two to communicate as if the instrumentation sub-system were internal to the PC. The advantage of this arrangement is in reducing the number of data and control lines between the two whilst

enabling the ADC to be sited in the instrumentation sub-system as opposed to the more noisy environment of the PC.

If the PIA was located inside the PC and the ADC inside the instrumentation sub-system, a total of 36 I/O lines would be required between the PC and instrumentation sub-system. 24 for the PIA, if all the I/O lines were allocated, and 12 for the ADC if it was operating with a 12-bit parallel output data format With a maximum of 37 lines available this does not leave enough for other functions such as the S&H signal and DGND. Therefore it was decided to buffer and expand the PC data bus outside the PC to the instrumentation sub-system. This way only 14 data lines, 4 address lines and 2 control lines are required to operate both the PIA and ADC.

To do this 74LS245 tri-state octal bus transceivers were used to buffer the data bus lines between the PC and instrumentation system. These are only enabled when either a read or write operation is to be performed on the PIA or ADC. The address and control lines between the PC and instrumentation sub-system are buffered by 74LS244 octal line drivers. All I/O lines are held at approximately 3.2 V by a combination of a 150 Ω pull-up resistor and a 270 Ω pull-down resistor on the interface card. This reduces the voltage swing during a logic transition [3]. The parallel impedance of the two resistors also matches the characteristic impedance of the ribbon cable, which is 108 Ω, which should help reduce reflection of the transmitted signals. Both these design features are included to minimise the effects of transmission noise on the signals.

3.2.1.2 Timer 1 and Timer 2

The circuitry for these timers is shown in Figure 3.2. Their functions are:

1) Generate the sample and hold signal.

2) Measure the random inter-trial interval between successive ERPs.

3) Measure subject reaction times.

The timers are 8254 software programmable timer/counters. Each one contains three counters which can be individually programmed in several modes [4]. The operation of each counter is programmed by writing to the corresponding control register, the two most significant bits of the control word determining which counter is to be programmed. The value in each 16-bit count register is set by writing the low byte first, followed by the high byte, to the corresponding counter address. The counters are also read by two consecutive read operations, yielding first the low byte and then the high byte. The functions of each counter are as follows:

Timer1, Counter 0 This counter divides the 2 MHz clock signal by 2000 to generate a 1 kHz signal that is used by counter 1 of timer 1 and counter 0 of timer 2. It is programmed to operate in mode 3 by writing the control word $36 to the timer 1 control register. This makes the counter operate as a frequency divider, dividing the input clock signal by the value stored in its count register. This is therefore programmed with the value $07D0 which is the hexadecimal equivalent of 2000.

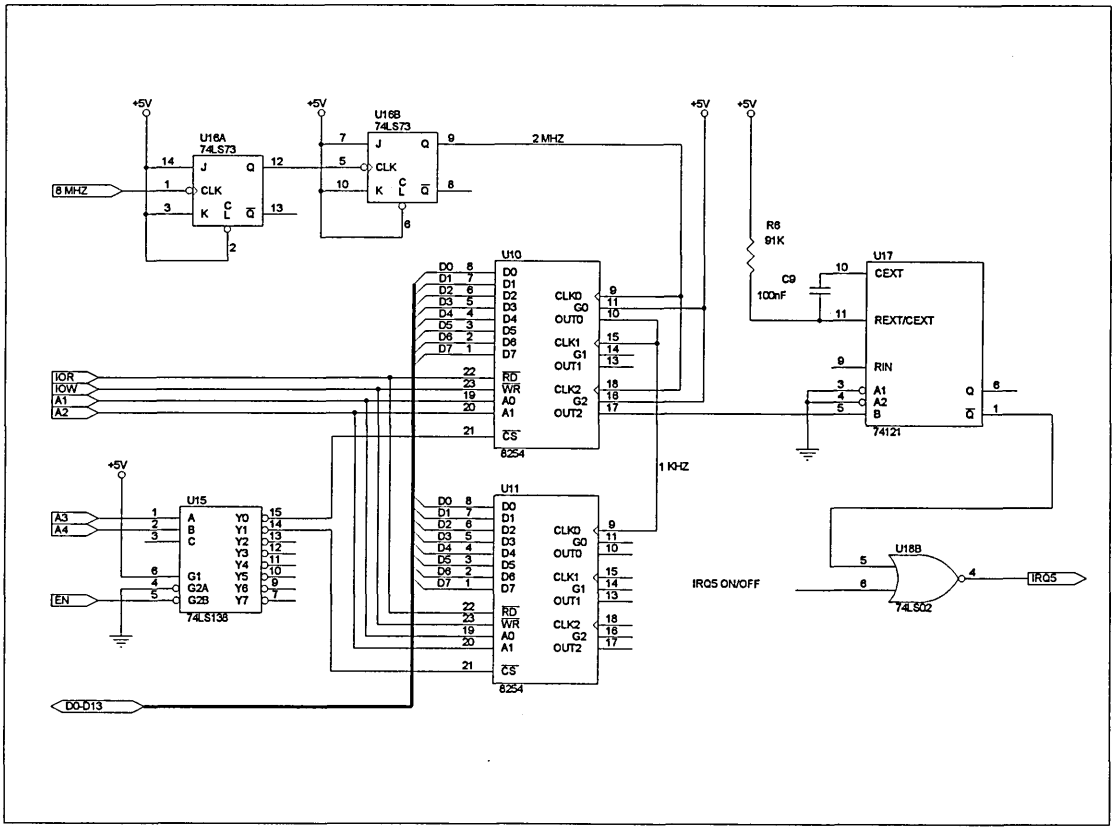
Timer 1, Counter 1 This counter generates the random inter-trial interval between successive ERP recordings. It is programmed to operate in mode 0 by writing the control word $70 to the timer 1 control register. This makes the counter decrement the value stored in its count register each time it is clocked. First the counter is loaded with a random number generated in software, representing the inter-trial interval in

milliseconds. When G1 goes high the contents of the register are decremented each clock pulse until the contents of the clock register reach zero. At this point OUT1 goes high. The value of the inter-trial interval in milliseconds is generated in software. By initiating the count and then monitoring the state of OUT1 it is possible to generate accurate but random delay periods between trials.

Timer 1, Counter 2 This counter divides the 2MHz clock signal by 16000 to generate a 125 Hz square wave that is used to generate the sample and hold signal. It is programmed to operate in Mode 3 by writing the control word $B6 to the timer 1 control register. This makes the counter act as a frequency divider, dividing the input clock signal by the value stored in its count register. This is therefore programmed with the value $3E80.

Timer 2, Counter 0 This counter is used to measure subject reaction times. It is programmed to operate in Mode 0 by writing the control word $30 to the timer 2 control register. This makes the counter decrement the value stored in its count register each time it is clocked. First the counter is loaded with the value $FFFF. When a long low tone is generated G0 goes high which enables the counter and so it starts to decrement the number every millisecond. When the response switch is pressed to stop the tone G0 returns low and the counter is disabled. If the number in the counter is then read it will represent the reaction time of the subject.

Figure 3.2 PC interface card timing circuitry



3.2.1.3 Sample and Hold Signal

This signal is generated from the output of Timer1, Counter 2. This produces a 125 Hz square wave that has to be converted into a narrow sampling pulse and a long hold period. It is therefore used to trigger a 74121 monostable configured to generate a pulse period of approximately 7 ms. The width of the output pulse is described by the equation below, where R_6 and C_9 are the components shown in Figure 3.2 and k is a parameter constant of the 74121 device.

$$t_W = k \times R_6 \times C_9$$

where $R_6 = 91\ k\Omega$

$C_9 = 100\ nF$

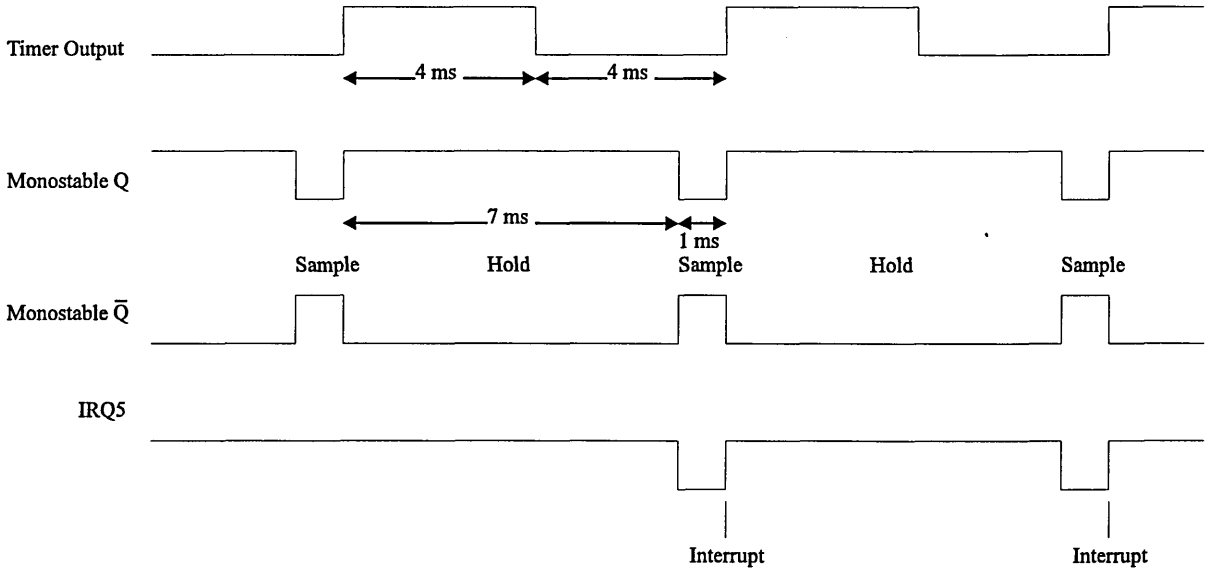
$k \approx 0.7$

Therefore $t_W \approx 6.4\ ms$

The pulse width was actually measured as being 7 ms with these component values, the difference probably being due to component tolerances.

The monostable is triggered on the rising edge of the input square wave. Therefore the inverting output of the monostable will be low for approximately 7 ms then high for approximately 1 ms before being retriggered. See Figure 3.3. This output is used as the control signal for the sample and hold amplifiers. The ERP signals are sampled whilst the output is high and are held for conversion whilst it is low. The inverting output of U17 is also used to generate interrupts. These must occur at the beginning of a hold period so that the PC can convert all signals during this period. So that the interrupt signal can be disabled the inverting output of U17 is logically ORd with a sample enable control signal to generate the interrupt signal. When the sample enable signal is low the interrupt signal is enabled and when it is high it is disabled. The interrupt used is the PC IRQ5 interrupt. When there is a low to high transition on this line the software halts whatever it is doing, converts all the ERP signals into digital format, and stores them in memory.

Figure 3.3 Sample and hold signal timing diagram



3.2.1.4 Data Storage

The PC is fitted with a 650 Mbyte re-writable optical disc for the storage of the recorded ERP data. This is necessary because of the large amounts of data recorded per subject. For example an 8 s CNV paradigm recorded 32 times per subject requires the following memory:

Memory required = Sample frequency × Paradigm length × Channel number × Number of trials × Data size (bytes)

= $125 \times 8 \times 32 \times 32 \times 4$

= 4.096×10^6 bytes

A conventional floppy disc is only capable of storing 1.44 Mbytes and would therefore be unsuitable for the storage of such large amounts of data per subject. The hard drive of the system is also unsuitable for storing the data because it is fixed to the system and

recorded data cannot therefore be analysed on another PC. The optical disc system used is the Panasonic PD system, which is installed as drive D on the PC. The optical disc can be accessed as a conventional hard disc drive except it has the advantage that the discs themselves can be removed.

3.3 Headbox and pre-amplifier board

Sited near the patient the headbox and pre-amplifier board provide a common connection point for the electrodes to the system and also provide the first stage amplification. It is good practice to amplify the signals close to the electrodes to reduce the affect of interference noise [5]. To minimise the affect of interference noise on the signals the headbox should ideally be made of a conductive material and connected to ground. However to be effective it would have to be connected to isolated ground and if this were done patient safety would be compromised and the system would not meet the requirement s of IEC601-1. An alternative would be to spray the inside of the box with a conductive material and connect that to ground but a simpler solution was to fit a double-sided copper PCB, connected to ground, underneath the pre-amplifier PCB to act as a dual ground plane. This protects the sensitive electronics from interference noise. The circuit diagram for the pre-amplifier board is in Appendix 7.2 and the circuit board layout in Appendix 7.3.

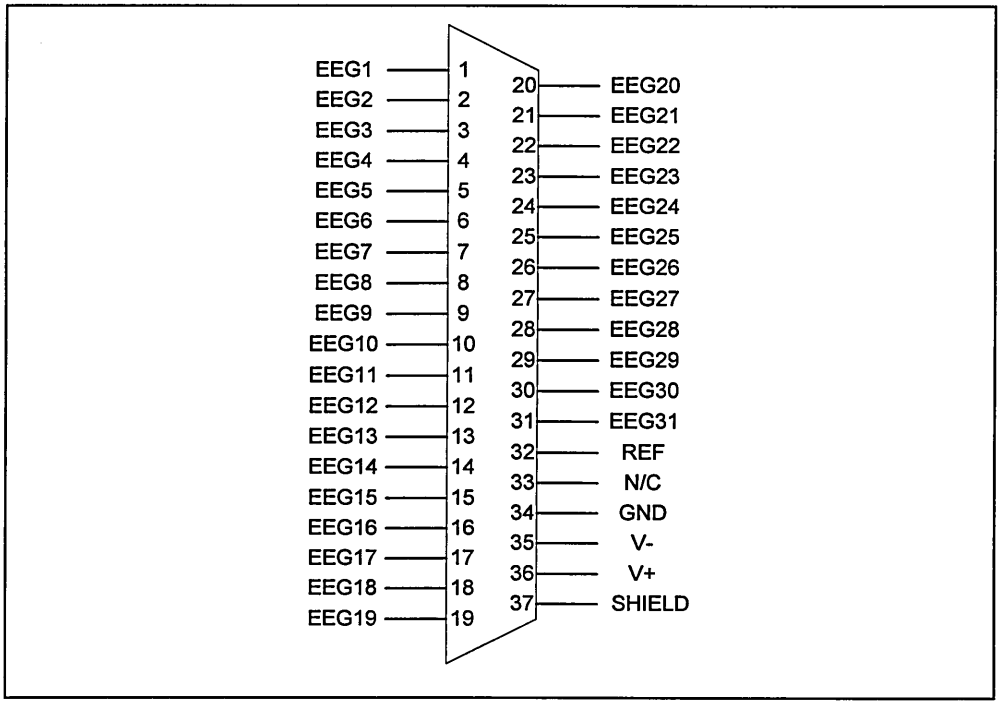
3.3.1 Headbox

The headbox itself is a 200 × 150 × 75 mm ABS box. The electrodes plug into 2 mm sockets arranged in a 5 × 7 grid on the top surface. This size was chosen because it is a

common standard at the moment. The 35 electrode sockets are 31 × EEG, 1 × REF, 1 × GND and 2 × SPARE.

The headbox is connected to the instrumentation sub-system by a 36 core shielded cable and connector. This takes the output of the pre-amplifiers to the instrumentation sub-system and the power supply lines to the pre-amplifier circuitry. The cable is double insulated by fitting an external layer of heat shrink sleeving, and the 37-way miniature connector is made of plastic to maintain safety isolation. For this reason the mating connector on the instrumentation system is also made of plastic and is mounted in a 6 HP [6] traffolyte panel instead of the conventional anodised aluminium ones. This maintains the minimum creepage distance of 8 mm required by IEC601 for 240VAC voltages [7]. The pin out for the headbox connector is shown in Figure 3.4.

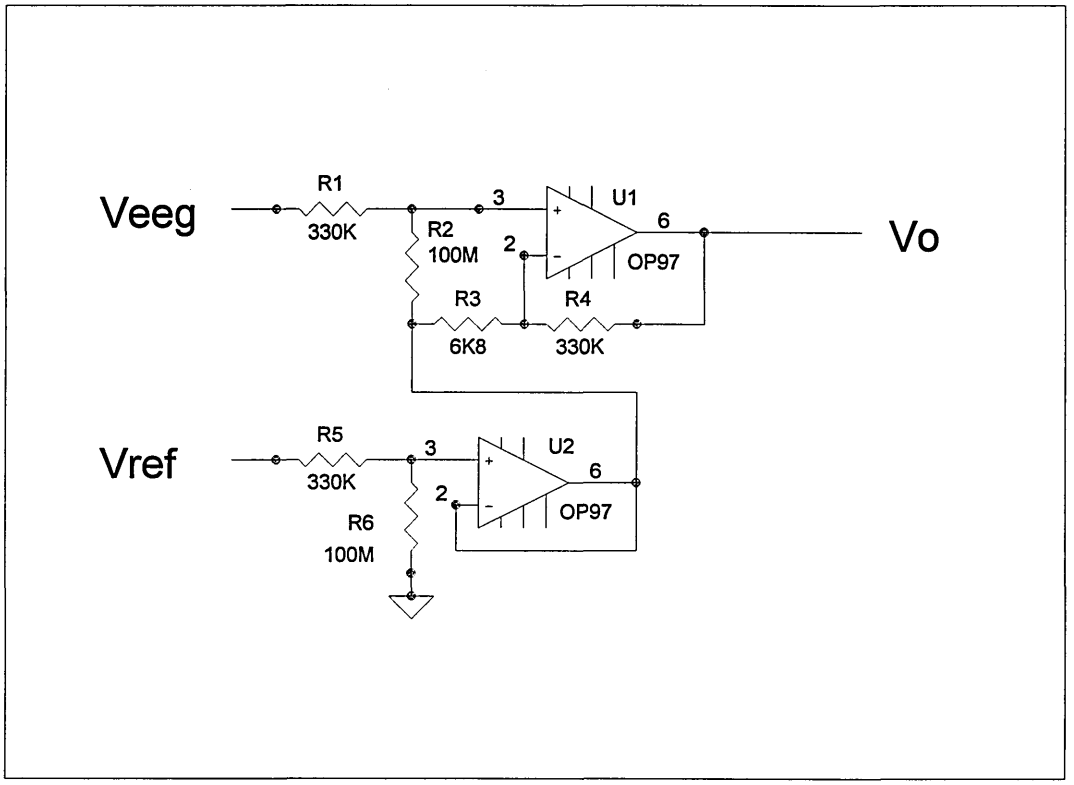
Figure 3.4 Headbox connector pin allocations



3.3.2 Pre-amplifier circuit design

The pre-amplifier circuit employs novel circuit design to achieve differential amplification of all channels whilst minimising component cost and hardware overheads. 31 pre-amplifiers are configured as non-inverting amplifiers except that instead of the resistor network being connected to ground it is fed a buffered reference signal, see Figure 3.5.

Figure 3.5 Pre-amplifier circuit configuration



The effect of this is to make them act as a form of differential amplifier, all signals being amplified with respect to the reference. If V_{EEG} is the EEG input signal and V_{REF} is the reference input signal, the output voltage (V_O) for this circuit configuration is:

$$V_O = (V_{EEG} - V_{REF}) \times \frac{R_4}{R_3} + V_{EEG}$$

From this equation it is apparent that the differential input signal is amplified by a factor of R_4/R_3 relative to any common mode signals. The advantage of using this circuit is that any common mode noise on the input signals is effectively reduced by a factor of R_4/R_3 compared to the EEG signals, without using more expensive instrumentation amplifiers. A differential amplifier configuration cannot be used because of the requirement for a very large input impedance.

Resistor R_1 and R_5 are used to limit the current that could flow into a subject in the unlikely event of a single fault condition where the amplifier supply voltage appeared at the input. IEC 601 specifies this as being a maximum of 50 μA, that is the patient auxiliary current is specified as 50 μA in a single fault condition [8]. Therefore, as the power supply voltage V_s is ± 15 V and the current limiting resistor R_1 is 330 kΩ:

$$\text{Maximum patient auxiliary current} = \frac{V_s}{R_1}$$

$$= 15 / 330 \times 10^3$$

$$= 4.55\ \mu A$$

The electrode impedance would also reduce this current further. One disadvantage of having a relatively large input impedance in series with the amplifier input is that it increases the susceptibility of the circuit to mains interference. This was minimised by placing the current limiting resistors as close as possible to the PCB ground plane.

Resistors R_2 and R_6 are used to bias the pre-amplifier input in the event of the input being unused. If this is not done the amplifier picks up interference noise and amplifies this. If many channels are unused a situation can arise where the unconnected channels all amplify mains noise and generate large surges on the power supply voltage rails. This in turn can generate noise on the channels in use to such a degree as to render them unusable. A resistance value as large as 100 MΩ is used to maintain the high input impedance of the circuit. An alternative solution would be to make the operator connect any unused channels to ground, However this solution was chosen to make the system more convenient to use.

The amplifiers used are OP97 integrated circuits. They are bipolar amplifier, chosen because they have a low input noise voltage of 0.5 μV_{p-p} and yet a relatively high input impedance of 30 MΩ (differential) [9] compared to the impedance of the electrodes which is typically less than 5 kΩ. This is required for minimum signal attenuation. FET amplifiers would have provided much greater input impedance but are generally much noisier than bipolar versions. For example the AD548 has an input noise voltage of 2 μV_{p-p}. which means the amplifier noise would be greater than the minimum signal voltage, making it unsuitable as a pre-amplifier.

The gain of the pre-amplifiers is set by R_3 = 6K8 and R_4 = 330K to 49.5. This is the maximum allowable gain for a system powered with a ± 15 V supply, as a 300 mV standing electrode potential [10][11] will just saturate the amplifier at this gain. [12].

Because all EEG signals are to be referenced to a single reference signal, the signal must be fed into the feedback networks of all 31 pre-amplifiers. To prevent attenuation of the reference signal by loading affects the reference must therefore be buffered. In Figure 3.5 U2 is configured as a unity gain amplifier to perform this

function. On the pre-amplifier board there are six such amplifiers. One is used to buffer the reference signal initially and its output is then fed into five others. Four of these supply the reference to four groups of eight pre-amplifiers, and the fifth feeds the signal back to the instrumentation sub-system where the remaining common mode signal can be removed from the EEG signals.

The number of pre-amplifiers each buffer amplifier can supply is limited by the load impedance seen by the buffer amplifiers. The impedance seen by the buffer amplifiers looking into the feedback network of eight pre-amplifiers is:

$$\text{Total impedance} = \frac{R_1}{8} = \frac{6.8 \times 10^3}{8} = 832.5\ \Omega$$

According to the OP97 data sheet [13] this impedance limits the output swing of the buffer amplifiers to ± 10V. The dc errors generated by each pre-amplifier are calculated from the OP97 data sheet parameters as follows:

$$\text{Input offset voltage} = 200\ \mu V$$

$$\text{Bias current error} = \text{Impedance seen at non-inverting input} \times \text{Bias current}$$

$$= \frac{R_1 \times R_2}{R_1 + R_2} \times I_B$$

$$= \frac{330 \times 10^3 \times 100 \times 10^6}{330 \times 10^3 + 100 \times 10^6} \times 750 \times 10^{-12}$$

$$= 329 \times 10^3 \times 750 \times 10^{-12}$$

= 247 μV

Input offset current error = Impedance seen at non-inverting input ×

Input offset current

$$= \frac{R_1 \times R_2}{R_1 + R_2} \times I_{OS}$$

$$= \frac{330 \times 10^3 \times 100 \times 10^6}{330 \times 10^3 + 100 \times 10^6} \times 750 \times 10^{-12}$$

$$= 329 \times 10^3 \times 750 \times 10^{-12}$$

= 247 μV

Total dc error = Input offset voltage + Bias current error +

Input offset current

= 200 + 247 + 247

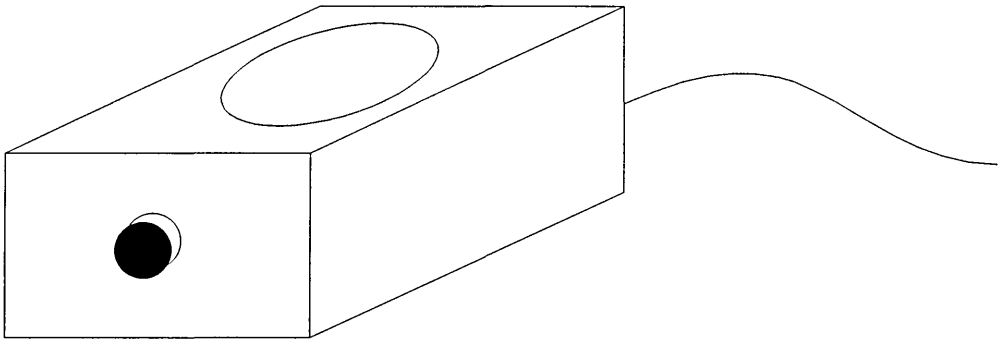
= 694 μV

This error seen at the input is much larger than the minimum signal size of 1 μV but smaller than the maximum signal size of 1 mV. It can be ignored because it is much smaller than the maximum dc electrode potential of 300 mV and will be removed at the next amplification stage.

3.4 Patient Interface Unit

This comprises a small hand held box containing tone generation circuitry and a loudspeaker to produce the patient stimuli, see Figure 3.6. A pushbutton switch on the outside of the box is used to record the response of the patient to the stimuli and a single turn potentiometer is also fitted to enable adjustment of the volume of the stimuli. Short 1 kHz and 2 kHz tones, a click and a long 1 kHz tone can be produced by the internal circuitry. The long 1 kHz tone is terminated by pressing the response switch. The circuit diagram for the internal tone generator board is in Appendix 7.4 and the board layout in Appendix 7.5.

Figure 3.6 Patient interface unit



The unit is designed to fit in the subjects hand enabling them to both comfortably hear any audio stimuli and make appropriate responses. A 9-way connector and flying lead approximately 2 m in length, is used to connect the unit to the instrumentation sub-system when it is in use. The pin out for the connector is detailed in Table 3.2.

Table 3.2 Patient interface connector pin allocation

Pin number	Function	Cable colour
1	Long low tone	Yellow
2	Short low tone	Orange
3	Short high tone	White
4	Click trigger	Green
5	Response output	Blue
6	Reaction output	Brown
7	+5 V supply	Red
8	0 V supply	Black
9	Not used	N/C

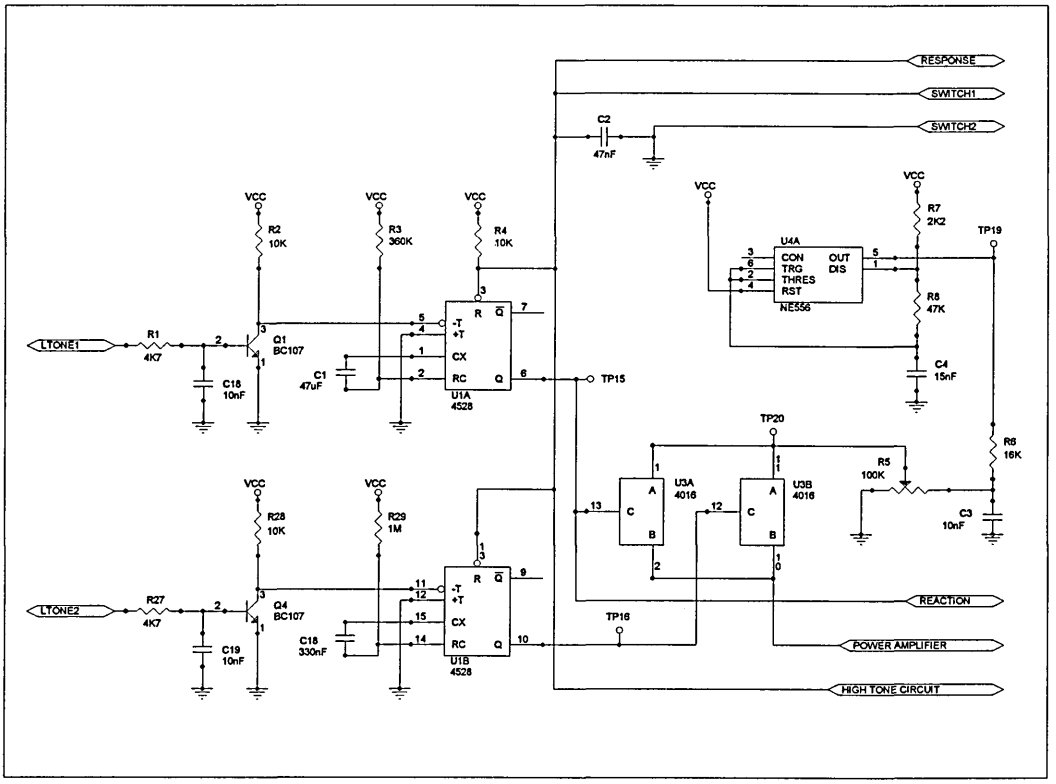
3.4.1 Low tone generator circuit

This circuit can generate a long or short tone of frequency 1 kHz. The long tone is required for the CNV paradigm and the short tone for the non-target stimuli in the P300 paradigm. The low tone generator circuit is shown in Figure 3.7. The tone frequency is generated by one half of a 556 timer. This is configured to produce a square wave of amplitude +Vcc and frequency 1 kHz. The output of the circuit is described by the following equation taken from the 556 data sheet [14]:

$$f = [0.693 \times (R_7 + 2R_8) \times C_4]^{-1}$$

$$f = 1 \text{ kHz}$$

Figure 3.7 Low tone generator circuit



The signal is then fed into a single pole low pass filter which is used to attenuate the high order harmonics to convert it into a sine wave of frequency 1 kHz. The cut-off frequency of this filter is described by the following equation [15]:

$$f_c = \frac{1}{2\pi R_6 C_3}$$

$$f_c = 995 \text{ Hz}$$

The signal is then fed into a 100 kΩ potentiometer which is used to adjust the amplitude of the waveform and hence set the volume of the tone. The signal is then fed into two analogue switches controlled by the output of two 4528 monostables. The outputs of the switches are connected to the input of the power amplifier. U1A is configured to

generate an output pulse period of approximately 5 s, which will close switch U3A for this period and so the power amplifier will be driven by the 1 kHz sine wave for this length of time. The duration of the pulse is given by the following equation:

$$t_W = 0.3 \times R_3 \times C_1$$

$$t_W = 5.08 \text{ s}$$

U2 is configured to generate a pulse period of approximately 100 ms.

$$t_W = 0.3 \times R_{29} \times C_{18}$$

$$t_W = 99 \text{ ms}$$

Both tones are terminated by the pressing of a single pole normally open switch. When pressed this shorts capacitor C_2 to ground, so both monostables are reset, their output goes low and the analogue switches are open. Realistically only the long low tone is terminated by the pressing of the switch as it is not intended for subjects to terminate the short low tone, since they normally have response times much larger than the duration of the tone. In both cases the response to the tones is recorded though, by monitoring the 'RESPONSE' output. For the long low tone the subjects' reaction times can also be measured by monitoring the 'REACTION' output which is connected to the output of U1A.

Both monostables are triggered by pulling low their active low trigger inputs. For U1A this is done by sending a logically high input to R_1. This charges up capacitor C_{18} through resistor R_1 and turns on transistor Q1. The collector of Q1, which normally high, is thus pulled to ground and so U1A is triggered. This arrangement is used to

prevent false triggering of the monostables. Because these are edge triggered it was thought false triggering may occur due to noise on the digital control signals.

3.4.2 High tone generator circuit

This circuit produces a short 2 kHz tone when a logic high pulse is sent to the input. A short low tone is required as the target tone in the P300 paradigm. The high tone generator circuit is shown in Figure 3.8.The tone frequency is generated by the second half of a 556 timer. This is configured to generate a square wave of amplitude +Vcc and frequency 2 kHz. The output frequency of the circuit is given by the following equation:

$$f = [0.693 \times (R_{14} + 2R_{15}) \times C_7]^{-1}$$

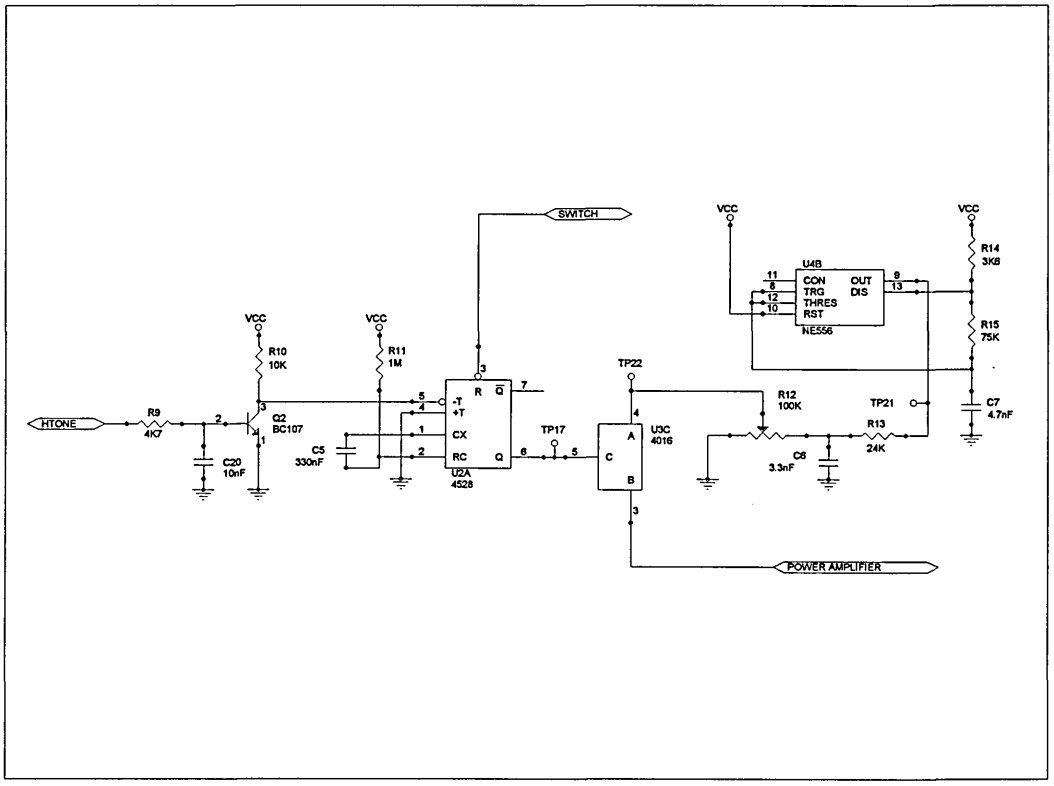
$$f = 2\ \text{kHz}$$

The signal is then fed into a single pole low pass filter which is used to attenuate the high order harmonics to convert it into a sine wave of frequency 2 kHz. The cut-off frequency of this filter is described by the following equation [14]:

$$f_c = \frac{1}{2\pi R_{13} C_6}$$

$$f_c = 2010\ \text{Hz}$$

Figure 3.8 High tone generator circuit



The signal is then fed into a 100 kΩ potentiometer which is used to adjust the amplitude of the waveform and hence set the volume of the tone. The signal is then fed into an analogue switch controlled by a 4528 monostable. The output of the switch is connected to the input of the power amplifier. Therefore the output pulse period of the monostable sets the duration of the tone by controlling how long the 2 kHz signal is input to the power amplifier. The duration of the pulse is given by the following equation:

$$t_W = 0.3 \times R_{11} \times C_5$$

$$t_W = 99 \text{ ms}$$

The monostable is triggered using identical input circuitry as the low tone generator circuit, that is activated by a logically high input pulse.

3.4.3 Click generator circuit

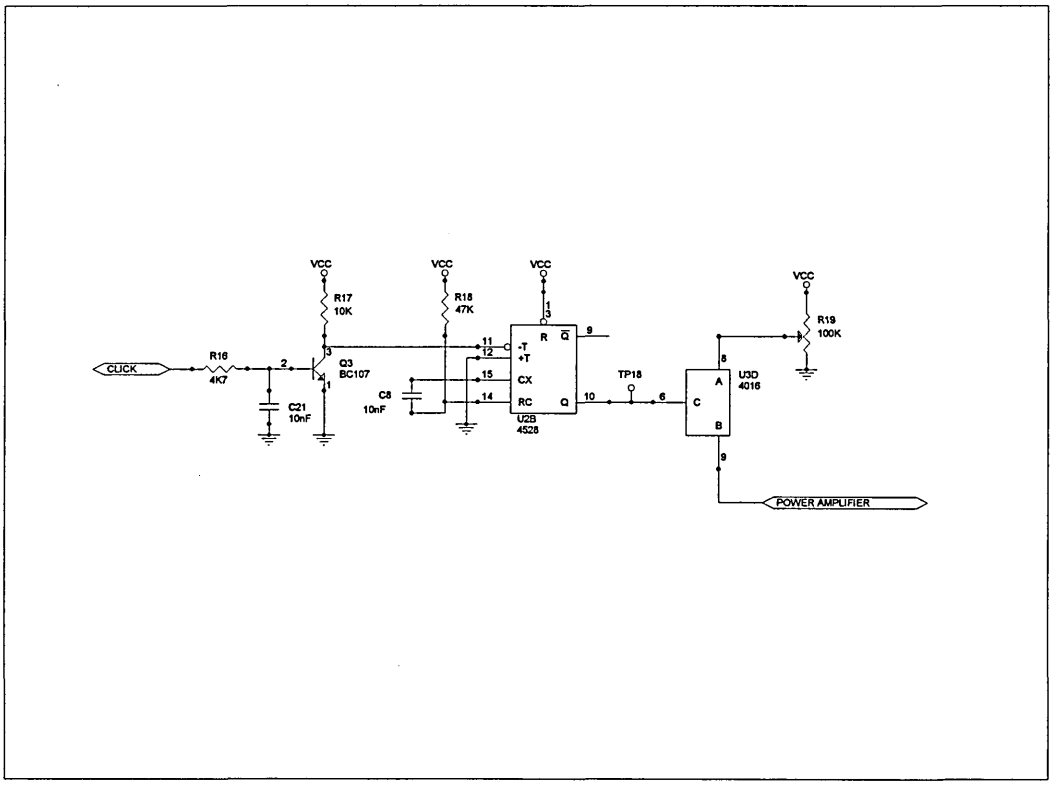
This circuit produces the audible click required as the warning stimulus for the CNV paradigm. The click generator circuit is shown in Figure 3.9. The click is generated by inputting a dc voltage into the power amplifier. The magnitude of the dc voltage and hence the volume of the click is set by potentiometer R_{19}. This acts as a potential divider and its output is connected to the input of the analogue switch U3D. The output of the switch is connected to the power amplifier input and the switch is controlled by the output of the monstable U1. The monostable is configured to generate a narrow output pulse. The duration of the pulse is given by the following equation:

$$t_W = 0.3 \times R_{18} \times C_8$$

$$t_W = 141\ \mu s$$

The monostable is triggered using the same input circuitry as the high and low tone generator circuits and requires a logically high input signal to be activated. The pulse width generated connects the dc voltage level from the potentiometer to the power amplifier long enough to generate a recognisable click.

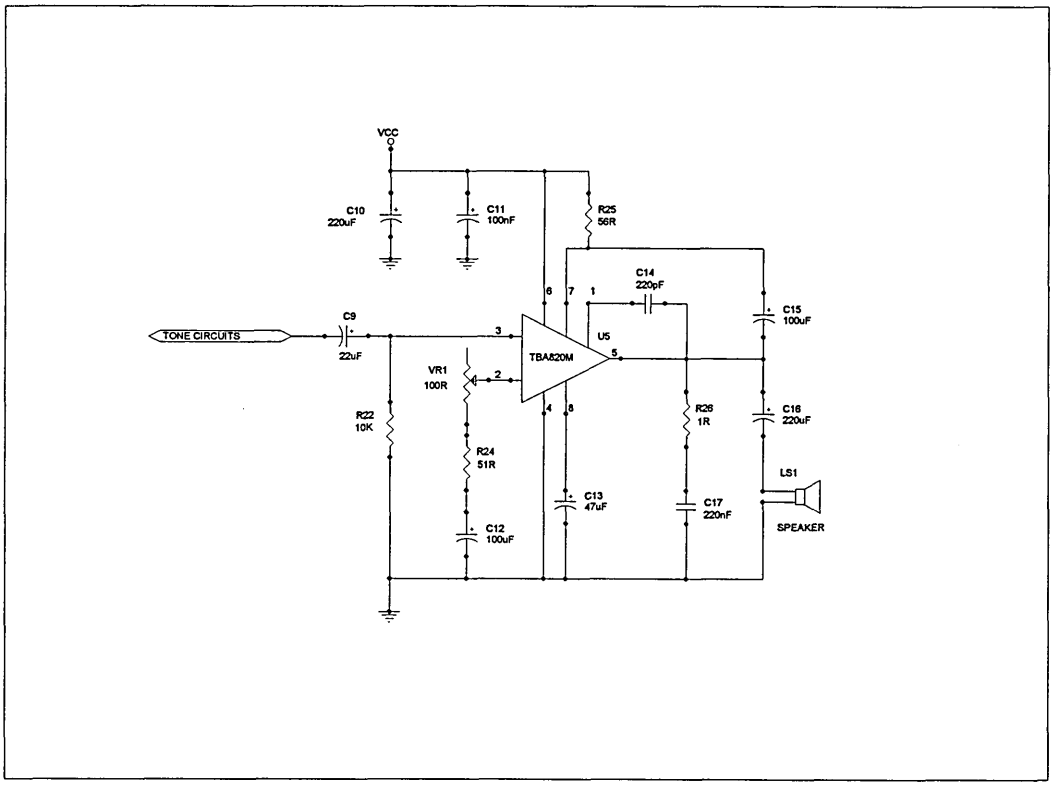
Figure 3.9 Click generator circuit



3.4.4 Audio Power Amplifier

This circuit, shown in Figure 3.10, is based on the TBA820M. This device can operate from a wide supply voltage range and can deliver up to a maximum 0.5 W into an 8 Ω speaker at a supply voltage of + 5V. This was thought sufficient for this application. The circuit is taken from the manufacturers data sheet. The gain of the circuit and hence the output volume can be adjusted using the 100 Ω potentiometer VR1. This varies the total value of the feedback resistance between 51 and 151 Ω. The potentiometer is mounted on one end of the patient interface enclosure so the volume can be adjusted without having to open the box.

Figure 3.10 Audio power amplifier

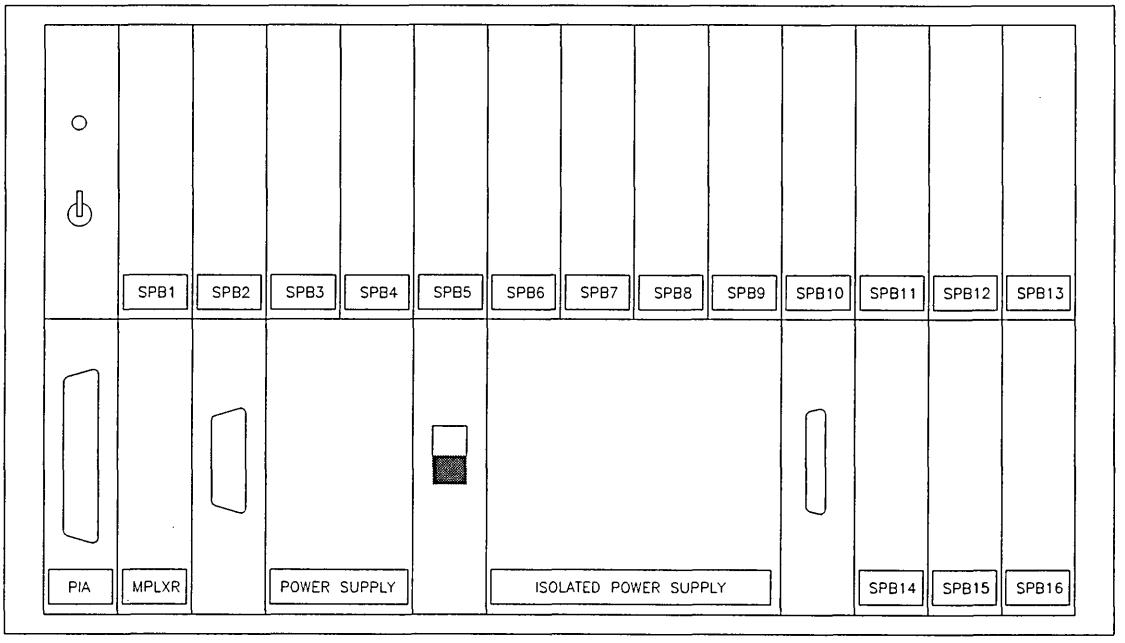


3.5 Instrumentation sub-system

3.5.1 Overview

The instrumentation sub-system contains the majority of the circuitry required to process the ERPs and convert them into digital format. The PCBs are mounted vertically in two horizontal layers in a 19" × 6U sub-frame. This is enclosed in a 19" racking case, see Figure 3.11. The PCB's are supplied with power from two in-situ power supplies, one isolated from earth and the other connected to earth, both of which are also mounted in the sub-frame. Connections to the headbox, patient interface and PC are made at the front of the sub-system through the front panels. Also at the front are an operator switch, a system status LED and power supply switch. The operator switch enables the operator to suspend data recording temporarily. The LED indicates whether the system is recording or not and the power supply switch switches the mains input to the two internal power supplies. The mains power supply input is made through the rear of the enclosure via a twin fused IEC inlet.

Figure 3.11 Instrumentation sub-system



Eighteen PCB's hold the majority of the instrumentation circuitry contained within the instrumentation enclosure. These are all extended Eurocard size (100 × 220 mm). The PCBs comprise: 16 signal processing PCB's, 1 multiplexer PCB and 1 PIA PCB. They are supplied with power from the two power supplies. All PCB interconnections are made through DIN41612 connectors on the rear of the boards. These are 2 × 32 pin connectors that mate with a rack mounted connector of the opposite gender when the board is inserted into the sub-frame.

3.5.2 Signal Processing boards

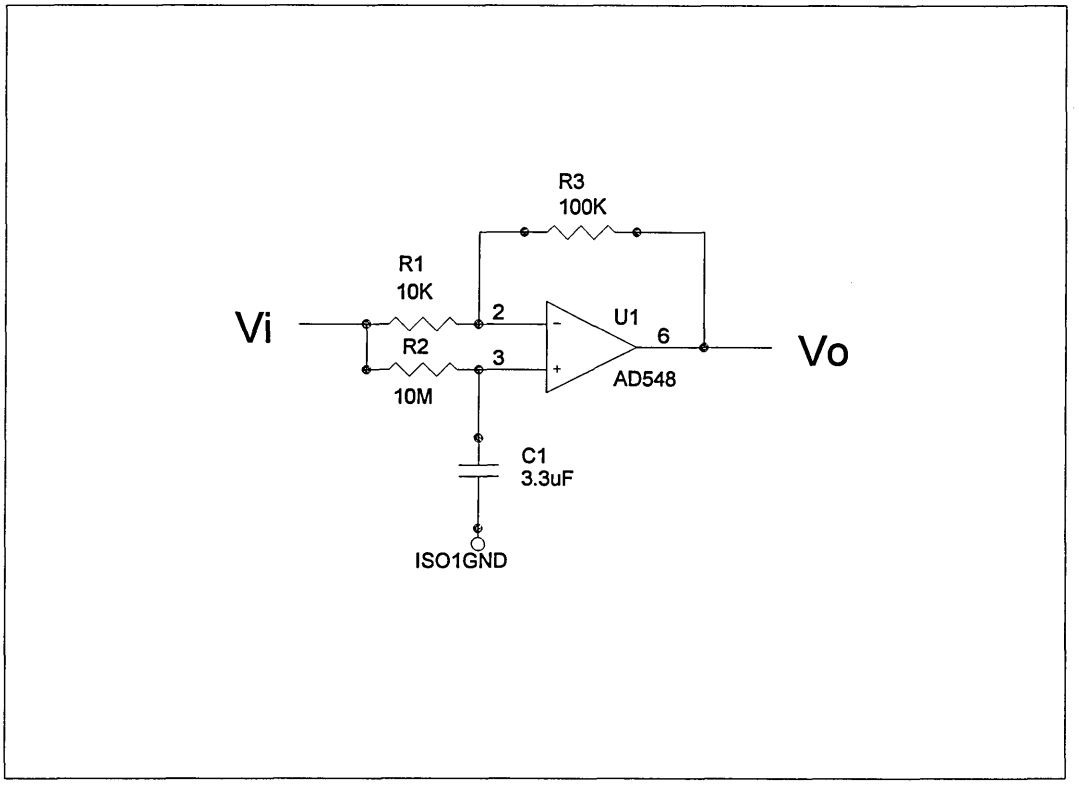
Each signal processing board includes the analogue signal processing circuitry for two channels. This consists of an ac amplifier, isolation circuitry, high and low pass filters, and a sample and hold amplifier. The board has been designed so there is a minimum creepage distance of 8 mm between all isolated and non-isolated circuitry [16]. The

circuit diagram for the signal processing boards is in Appendix 7.6 and the board layout in Appendix 7.7.

3.5.2.1 The a.c. amplifier

This amplifier is used to remove any standing electrode potentials generated at the electrode scalp interface. If there is a dc voltage level of 300 mV at the scalp, after pre-amplification by a gain of 49.5 the dc signal level will be 14.85 V. If this dc signal is not removed it will therefore saturate further amplification stages. The ac amplifier circuit is an operational amplifier configured as an inverting amplifier with a high pass filter also feeding the signal into the non-inverting input, see Figure 3.12.

Figure 3.12 AC amplifier circuit



The amplifier is configured with a gain of -10 set by R_1 and R_3. The high pass filter has a time constant of 33 s so that it has minimal affect on the high pass filter used to set the low frequency cut-off of the measured signals. The low frequency cut-off is given by the following equation:

$$f_c = \frac{1}{2\pi R_2 C_1}$$

$$= \frac{1}{2\pi \times 10 \times 10^6 \times 3.3 \times 10^{-6}}$$

$$f_c = 0.00482 \text{ Hz}$$

C_1 is a boxed polyester capacitor chosen because it was the smallest high value capacitor found with good stability and accuracy. The high input impedance and low bias currents of a FET amplifier [17] combine to reduce the errors generated by the source impedance mismatch necessary for this circuit. The dc errors generated by this circuit are:

Input offset voltage = 2 mV

Bias current error = Impedance seen at non-inverting input × Bias current

$= R_2 \times I_B$

$= 10 \times 10^6 \times 20 \times 10^{-12}$

$= 200\ \mu V$

Input offset current error = Impedance seen at non-inverting input × Bias current

$= R_2 \times I_{OS}$

$= 10 \times 10^{6} \times 20 \times 10^{-12}$

$= 200\ \mu V$

Total dc error generated = Input offset voltage + Bias current error + Input offset current error

$= 2\ mV + 200\ \mu V + 100\ \mu V$

$= 2.3\ mV$

This error could have been reduced by trimming the input offset voltage but was thought unnecessary as it will be removed at a later stage by the high pass filter. A 1 mV EEG signal will have the following amplitude at this stage

$Vi_{MAX} = EEG_{MAX} \times$ Pre-amp Gain

$= 1 \times 10^{-3} \times 49.5$

$= 49.5\ mV$

So the total dc error is much smaller than the maximum input signal. A 1 μV input signal will have the following amplitude at this stage:

$$Vi_{MIN} = EEG_{MIN} \times \text{Pre-amp Gain}$$

$$= 1 \times 10^{-6} \times 49.5$$

$$= 49.5\ \mu V$$

This is considerably larger than the input noise voltage of the amplifier, which is 2 μV p-p.

3.5.2.2 Isolation circuit

This is required to protect the patient should component failure result in mains voltage accidentally reaching the main circuitry. It is conventional to use dedicated isolation amplifiers designed for this purpose, these use either capacitive coupling or transformer coupling to transfer the signal. However accurate versions of these are very expensive and because this is a simultaneous sampling system, and so would require many more isolation amplifiers than a multiplexed system, an alternative device was chosen to provide isolation. IL300 linear optocouplers isolate the signals measured at the electrodes from the main circuitry used to process them. These devices are linear to an accuracy of 12-bits and can withstand test voltages of up to 7500 VAC [18] and yet are a fraction of the cost of conventional isolation amplifiers. The circuit is configured with a gain of 10.

The IL300 is a linear optocoupler that consists of a AlGaAs infra-red LED irradiating both an isolated feedback photodiode and an output photodiode in a bifurcated arrangement. The feedback photodidode captures a percentage of the LED's flux and generates a servo photocurrent (IP1) that can be used to control the LED drive

current (IF). This technique compensates for the LEDs non-linear, time, and temperature characteristics. The servo gain (K1) is defined as:

$$K1 = IP1 / IF$$

The output photodiode also produces an output photocurrent (IP2), that is linearly related to the servo optical flux created by the LED. The output forward gain (K2) is defines as:

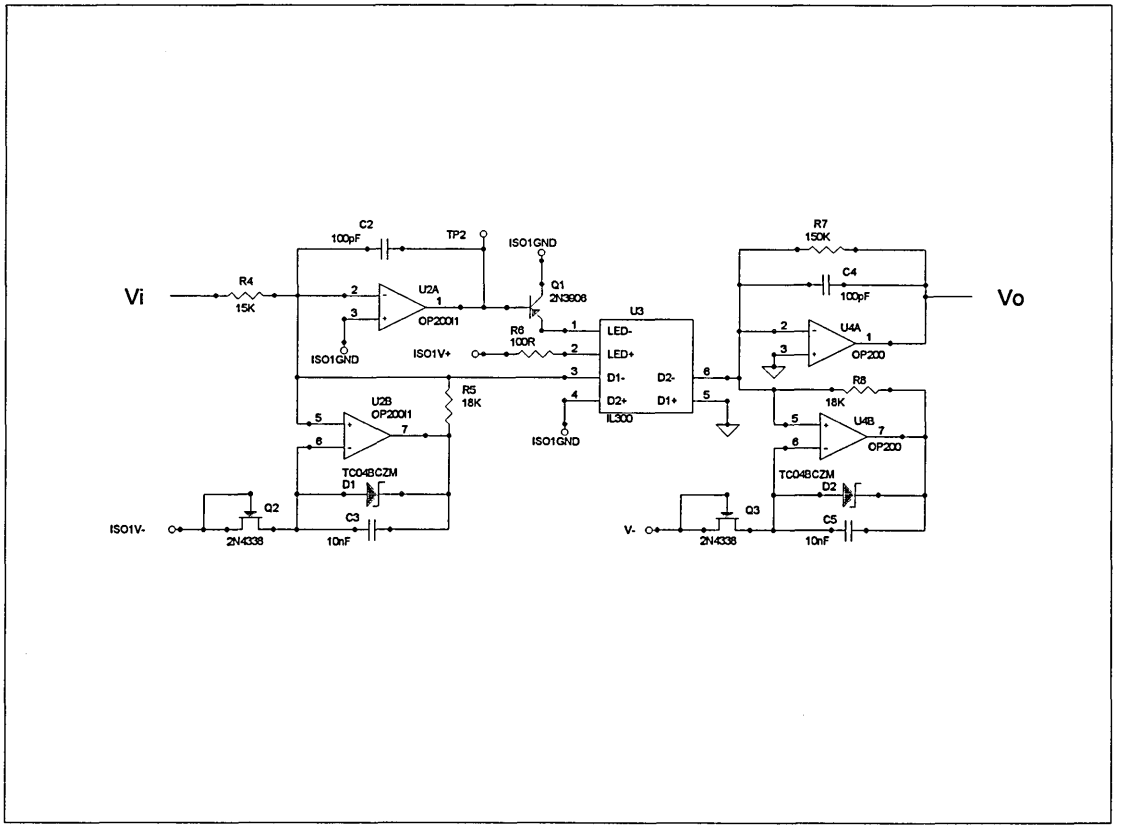
$$K2 = IP2 / IF$$

It is the ratio of the output forward gain and the servo gain that determine the transfer gain (K3) between input and output, where:

$$K3 = K2 / K1$$

The time and temperature stability of the input-output coupler gain (K3) is insured by using matched PIN photodiodes that accurately track the output flux of the LED.

Figure 3.13 Isolation circuit



The IL300 is configured as a pre-biased photovoltaic isolation amplifier, see Figure 3.13. The photovoltaic topology offers the best linearity, lowest noise and drift performance. Isolation amplifiers using this circuit configuration meet or exceed 12 bit AD performance. The circuit has to be pre-biased so that it accepts bipolar rather than just unipolar signals. The design procedure for the circuit is as follows:

The LED can be operated with drive currents from 500 μA to 40 mA but best linearity can be obtained at drive currents between 5 mA and 20 mA. It is intended to set I_F to 10 mA nominal and allow it to swing between 5 mA and 15 mA for an input signal range of ± 500 mV. Now according to the IL300 data sheet K1 = 0.007 and if IF is to be set to 10 mA then:

$$IP1 = K1 \times IF$$

$$= 0.007 \times 10 \times 10^{-3}$$

$$= 70\ \mu A.$$

If a 70 μA current source is used to pre-bias U2A at its inverting input, then for an input voltage Vi = 0 V, IF = 10 mA as required. Now if the minimum LED drive current (IF_{MIN}) is set at 5 mA then the minimum servo photocurrent (IP_{MIN}) generated will be:

$$IP_{MIN} = K1 \times IF_{MIN}$$

$$= 0.007 \times 5 \times 10^{-3}$$

$$= 35\ \mu A$$

So a full-scale negative input Vi = - 500 mV should generate - 35 μA at U2As inverting input. Therefore:

$$R_4 = \frac{Vi}{IP_{MIN}}$$

$$= \frac{0.5}{35 \times 10^{-6}}$$

$$= 14.3\ k\Omega$$

$$R_4 = 15\ k\Omega$$

Pre-bias current source

The pre-bias current (IPB) necessary for the circuit is generated by U2B, which is configured as a modified Howland current source. JFET Q2 acts as a current sink for the zener reference diode D1, generating a reference voltage (VREF) across it. U2B acts to

generate the same voltage as VREF across R5 so that both its inputs see the same voltage. In the process the pre-bias current is generated and fed into U2As inverting input where:

$$IPB = \frac{VREF}{R_5}$$

Therefore

$$R_5 = \frac{VREF}{IPB}$$

$$= \frac{1.25}{70 \times 10^{-6}}$$

$$= 17.9\ \text{k}\Omega$$

$$= 18\ \text{k}\Omega$$

An identical Howland current source based around U4B is fed into output amplifier U4As non-inverting input to match the input pre-bias and hence remove it from the output signal. This arrangement achieves the best stability and minimises offset drift.

Gain

The gain of the circuit is defined by the following equation, where the IL300 data sheet specifies K3 as 1.00:

$$\text{Gain} = \frac{R_7}{R_4} \times K_3$$

$$= \frac{150 \times 10^3}{15 \times 10^3} \times 1$$

$$\text{Gain} = 10$$

3.5.2.3 High pass filter

The high pass filter, shown in Figure 3.14, is a simple RC filter followed by a buffer amplifier to prevent the high impedance of the filter loading the following circuitry. It is used to remove amplifier offsets and to set the lower frequency limit of the signals of interest. The RC filter has a time constant of 10 s, equating to a cut-off frequency of 0.016 Hz. The cut-off frequency is given by the following equation:

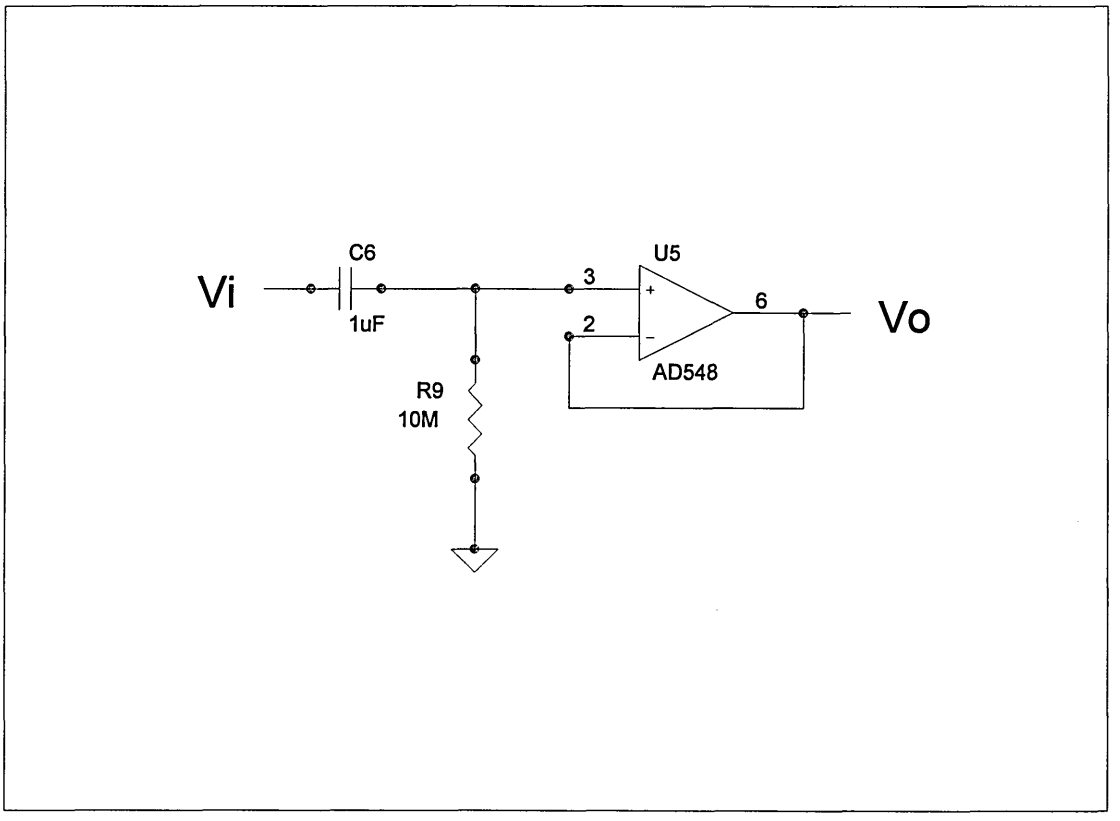
$$f_c = \frac{1}{2\pi R_9 C_6}$$

$$= \frac{1}{2\pi \times 10 \times 10^6 \times 1 \times 10^{-6}}$$

$$f_c = 0.0159 \text{ Hz}$$

A single pole filter is used for design simplicity. Because an operational amplifier is used a two pole filter could have been made to improve the characteristics of the filter but this was thought unnecessary as a steep roll-off is not required and additional components would have increased costs. A two pole filter would also require a high impedance in the feedback path which would make the circuit more susceptible to interference noise.

Figure 3.14 High pass filter circuit



An AD548 FET amplifier [17] was chosen to buffer the filter because of its high input impedance of 1000 GΩ differential and 3000 GΩ common mode. If a bipolar amplifier such as the OP77 were used its input impedance of 18.5 MΩ differential would mean that the input signal would be significantly attenuated by the 10 MΩ input impedance seen by the amplifier.

The low bias current of the AD548 also means that the offset voltage generated by the impedance mismatch seen at the two inputs is also kept to a minimum. The maximum dc errors generated by this circuit are calculated from the worst case AD548 data sheet parameters as:

Input offset voltage = 2 mV

Bias current error = Impedance seen at non-inverting input × Bias current

= R_9 × I_B

= 10×10^6 × 20×10^{-12}

= 200 μV

Input offset current error = Impedance seen at non-inverting input ×
Input offset current

= R_9 × I_{OS}

= 10×10^6 × 20×10^{-12}

= 200 μV

Total dc error generated = Input offset voltage + Bias current error +
Input offset current error

= 2 mV + 200 μV + 100 μV

= 2.3 mV

A 1 μV EEG signal will have the following amplitude at this stage:

Vi_{MIN} = EEG_{MIN} × Pre-amp Gain × AC-amp Gain × Optoisolator Gain

= $1 \times 10^{-6} \times 49.5 \times 10 \times 10$

= 4.95 mV

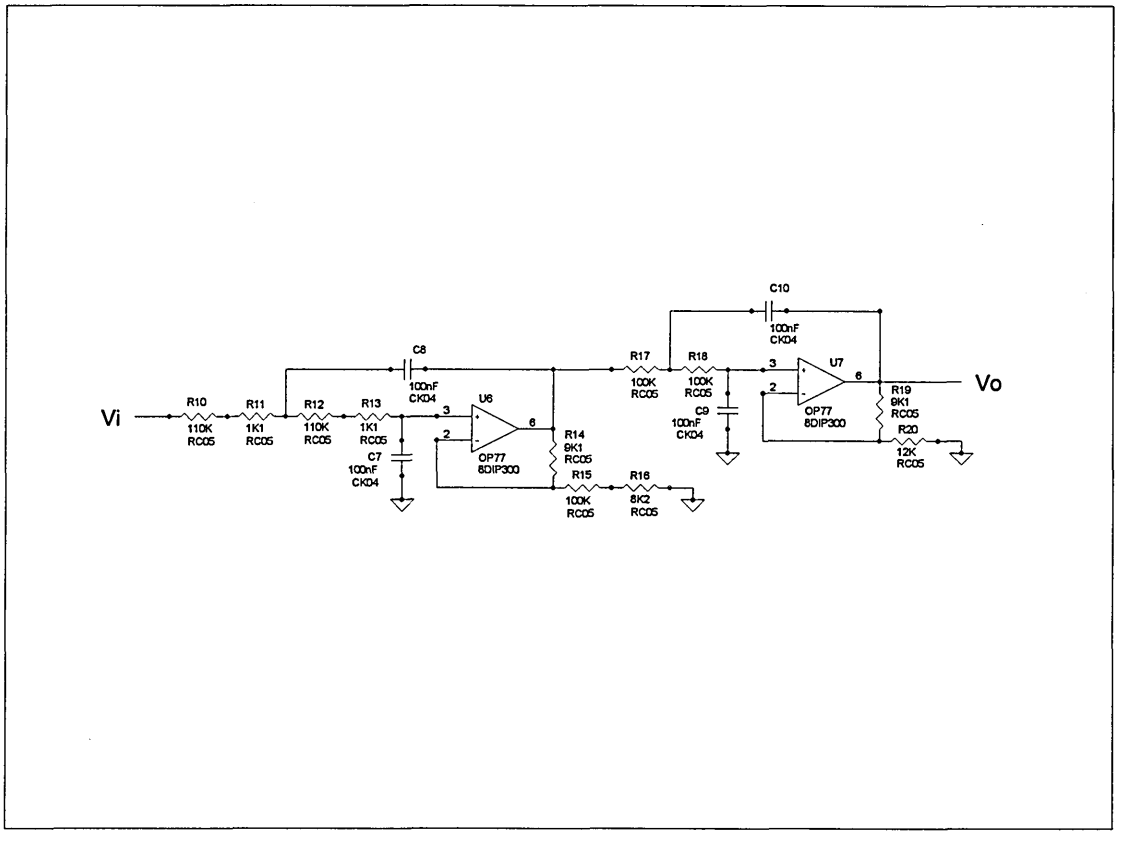
So the minimum EEG signal is more than twice the size of the worst case dc error.

C_6 is a polycarbonate capacitor chosen because of its tolerance of ± 5 % and low temperature coefficient of ± 100 ppm/°C.

3.5.2.4 Low pass filter

The low pass filter, shown in Figure 3.15, is a fourth order Bessel filter based on the VCVS configuration with a cut-off frequency of 30 Hz. This filter is required as an anti-aliasing filter prior to the ADC and to attenuate the 50 Hz mains frequency noise from the signals.

Figure 3.15 Low pass filter circuit



A Bessel filter is used because of its good phase characteristics leading to minimal signal distortion. A VCVS implementation was chosen because of its simplicity of design [19]. The overall gain of the filter is set by the combination of the gains (G1 and G2) of the two operational amplifiers U6 and U7. These are:

$$G1 = 1+\frac{R_{14}}{R_{15}+R_{16}}$$

$$= 1.084$$

$$G2 = 1+\frac{R_{19}}{R_{20}}$$

$$= 1.759$$

Therefore the overall gain is $1.084 \times 1.759 = 1.91$.

The operational amplifiers used in the circuit are OP77s. These are low cost precision bipolar operational amplifiers [20]. The maximum dc errors generated by the first stage of this circuit are calculated from the worst case OP77 data sheet parameters as:

Input offset voltage = 200 μV

Bias current error = Difference in impedance seen at the inputs × Bias current

$$= \left(R_{10}+R_{11}+R_{12}+R_{13}-\left(\frac{R_{14}\times(R_{15}+R_{16})}{R_{14}+R_{15}+R_{16}}\right)\right)\times I_B$$

$$= 213.8\times 10^{3} \times 750\times 10^{-12}$$

$$= 160\ \mu V$$

Input offset current error = Difference in impedance seen at the inputs × Input offset current

$$= \left(R_{10} + R_{11} + R_{12} + R_{13} - \left(\frac{R_{14} \times (R_{15} + R_{16})}{R_{14} + R_{15} + R_{16}} \right) \right) \times I_{OS}$$

$$= 213.8 \times 10^{3} \times 750 \times 10^{-12}$$

$$= 160\ \mu V$$

Total dc error generated by the first filter stage = Input offset voltage + Bias current error + Input offset current error

$$= 200\ \mu V + 160\ \mu V + 160\ \mu V$$

$$= 520\ \mu V$$

The dc errors generated by the second filter stage are:

Input offset voltage = 200 μV

Bias current error = Difference in impedance seen at the inputs × Bias current

$$= \left(R_{17} + R_{18} - \left(\frac{R_{19} \times R_{20}}{R_{19} + R_{20}} \right) \right) \times I_{B}$$

$$= 194.8 \times 10^{3} \times 750 \times 10^{-12}$$

$$= 146\ \mu V$$

Input offset current error = Difference in impedance seen at the inputs × Input offset current

$$= \left(R_{17} + R_{18} - \left(\frac{R_{19} \times R_{20}}{R_{19} + R_{20}} \right) \right) \times I_{OS}$$

$$= 194.8 \times 10^{3} \times 750 \times 10^{-12}$$

$$= 146\ \mu V$$

Total dc error generated by the second filter stage = Input offset voltage + Bias current error + Input offset current error

$$= 200\ \mu V + 146\ \mu V + 146\ \mu V$$

$$= 492\ \mu V$$

The total dc error generated at the output of the lowpass filter is the sum of the dc error generated at the first stage (DC1) multiplied by the gain of the first stage (G1). This is then added to the dc errors generated at the second stage (DC2) all multiplied by the gain of the second stage (G2).

Total dc error = $((G_1 \times DC1) + DC2) \times G_2$

$$= ((1.084 \times 520 \times 10^{-6}) + 492 \times 10^{-6}) \times 1.759$$

Total dc error = 1.86 mV

A 1 μV EEG signal will have the following amplitude at this stage:

Vi_{MIN} = EEG_{MIN} × Pre-amp Gain × AC-amp Gain × Optoisolator Gain

× Lowpass filter Gain

= $1 \times 10^{-6} \times 49.5 \times 10 \times 10 \times 1.91$

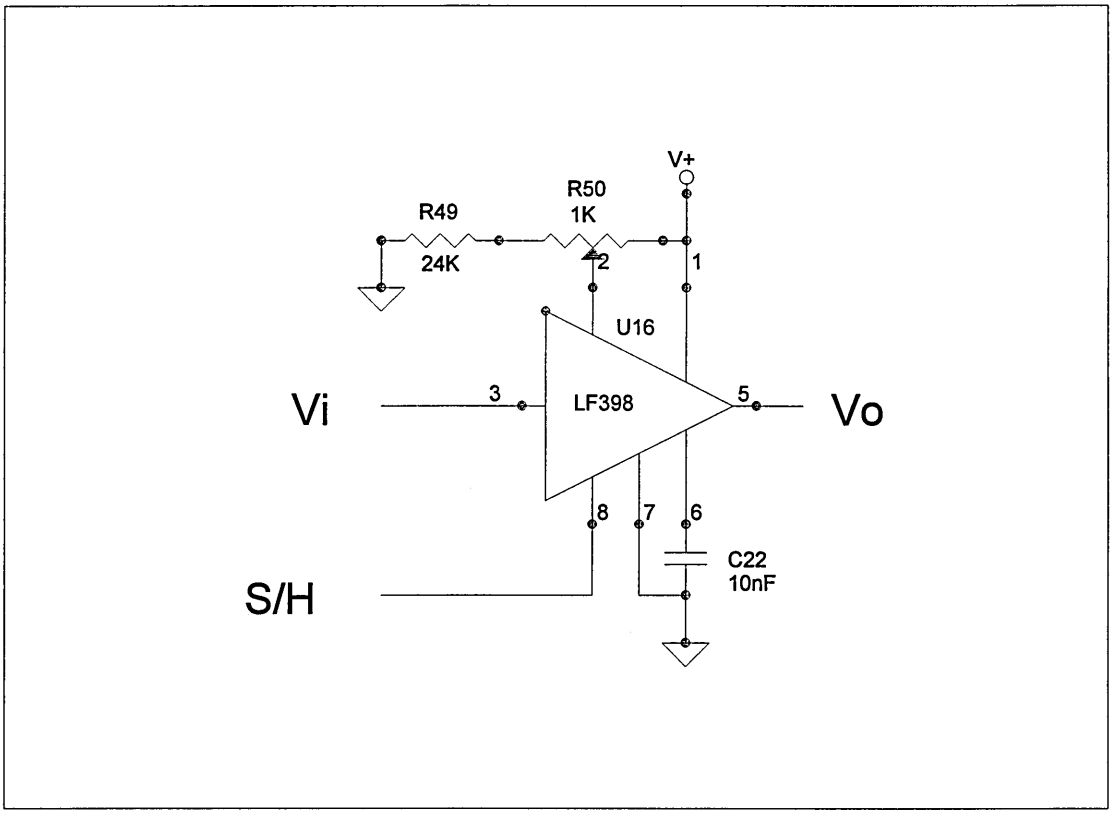
= 9.45 mV

So the minimum EEG signal is much larger than the dc error.

3.5.2.5 Sample and hold amplifiers

There are sample and hold amplifiers on each channel to capture the signals simultaneously prior to digitisation by the ADC. LF398 amplifiers were chosen because of their fast acquisition time (16 μs) and low droop rate [21]. The circuit is shown in Figure 3.16.

Figure 3.16 Sample and hold amplifier circuit



In designing this circuit a decision as to what size of external hold capacitor (C_1) was to be used had to be made. The larger the capacitor the smaller the hold step and droop errors become. By using a 1 ms sample time and a 7 ms hold time a relatively large capacitor could be used to minimise errors whilst still providing sufficient time for signal conversion. The capacitor must be made from a low loss dielectric such as Teflon or Polystyrene. It was decided to use a polystyrene capacitor because these are readily available and inexpensive. The largest value available in this material was 10 nF so this was chosen as its value

Errors

A 1 μV EEG signal will have the following amplitude at this stage:

$$Vi_{MIN} = EEG_{MIN} \times \text{Pre-amp Gain} \times \text{AC-amp Gain} \times \text{Optoisolator Gain} \times \text{Lowpass filter Gain}$$

$$= 1 \times 10^{-6} \times 49.5 \times 10 \times 10 \times 1.91$$

$$= 9.45 \text{ mV}$$

The following is a list of error sources at this stage and their magnitudes:

Dynamic sampling error

There are two sources of dynamic sampling error namely, digital delay and analogue delay. Digital delay is caused by a delay in switch opening which is approximately 150 ns. Analogue delay is the difference in input signal and capacitor voltage. The RC product of the hold capacitor and the effective series resistance determines it, which in the case of the LF398 is about 150Ω. For a 10 nF capacitor this is 1.5 μs or ten times the delay of the switch. An input signal of amplitude A and frequency f has a maximum slew rate of:

$$\frac{dV}{dt} = A \times 2\pi f$$

$$= 10 \times 2\pi \times 10$$

$$= 628 \text{ Vs}^{-1}$$

$$= 0.628 \text{ mV}\mu\text{s}^{-1}$$

Therefore

Analogue delay error = 0.628×1.5

= 0.94 mV

This is the maximum error for an input signal of magnitude ± 10 V and frequency 10 Hz.

Hold Step

This is an error caused by the actual hold signal transferring charge to the capacitor by internal switching. The data sheet specifies this as being 0.5 mV for a 10 nF capacitor.

DC Offsets

There are two types of dc offset. Input offset voltage, which is the same as any amplifier, and hold step. Input offset is stated as being a maximum of 7 mV for the LF398. Both the input offset and hold step voltages can be reduced to zero using potentiometer R_{50}.

Output Droop Rate

For a 10 nF capacitor at 25 °C the output droop rate is specified as being 8×10^{-4} Vs^{-1}. So if the entire 7 ms of the hold period is required to convert all 32 EEG signals the signal voltage will have drooped by:

Droop = $8 \times 10^{-4} \times 7 \times 10^{-3}$

= 5.6 μV

This is negligible compared to the minimum signal size of 10 mV.

Dielectric Absorption

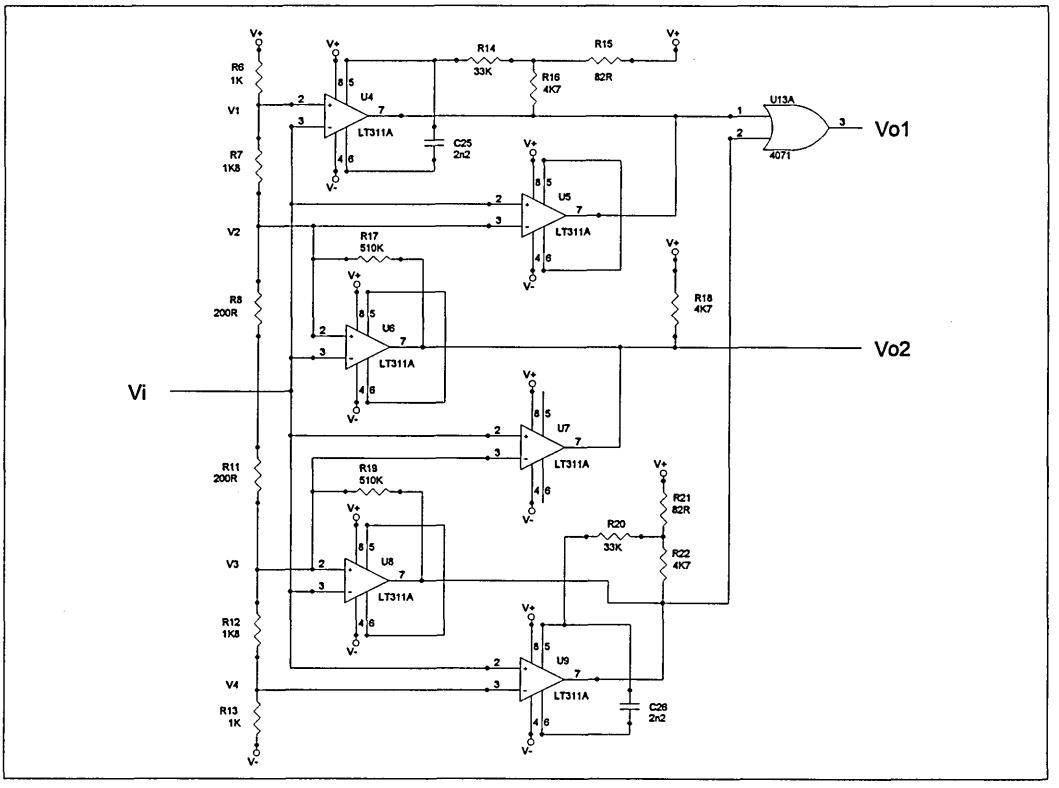
This is a property of the hold capacitor used. Rapid changes in capacitor voltage are not tracked by internal parasitic capacitance because of internal resistance in series with them. This leads to a "sag" effect in the hold capacitor after a sudden change in voltage followed by a rapid switch to the hold mode. The capacitor remembers its previous state via the charge on the internal parasitic capacitance and sags back slightly to the previous voltage. The magnitude of the sag depends on the voltage change and the time spent sampling the new voltage. Sag problems are minimised by long sampling times and short hold times. For a polystyrene capacitor the data sheet specifies a sag of 0.006 % for a sample time of 1 ms and 0.025 % for a hold time of 6 ms.

3.5.3 Multiplexer board

In order to maximise signal resolution this board incorporates automatic gain adjustment circuitry prior to signal conversion. This comprises of a window detector circuit and a programmable gain amplifier. The window detector circuit identifies the magnitude of the signals and generates control signals that program the gain of the amplifier. These control signals are also output as a two bit digital code that is added to the 12-bit digital data after conversion. The automatic nature of the gain adjustment maximises the speed of data conversion, whilst the method of storage of the gain setting enables the data to be stored as one 16-bit word instead of two. The latter reducing the amount of memory required to store the data and the amount of time to read it.

The multiplexer board is comprised of two HI506 16 to 1 multiplexers, which can switch the 32 channels into a window detector circuit and a programmable gain amplifier (PGA). The fact that the device output goes into a high impedance state when disabled allows the two outputs to be connected together [22]. All signals are switched into the window detector which detects whether the signal is in the range ± 100 mV, ± 1 V or ± 10 V. The circuit comprises six LT311 [23] comparators connected to a resistor network that generates the transition voltages. The window detector outputs two digital signals that indicate which range the signal lies in. These signals set the gain of the PGA to 1, 10 or 100 thereby ensuring that all signals make the maximum use of the ADC input range which is ± 10 V. The PGA is a PGA204 which is a high accuracy low cost device [24]. The output signal of the window detector is also added as the MSBs to the 12-bit digital output of the ADC to form a 14-bit word that includes the PGA gain setting and is read and stored by the PC. The circuit diagram for the multiplexer board is in Appendix 7.8 and the board layout in Appendix 7.9.

Figure 3.17 Window detector circuit



3.5.3.1 Window Detector

This circuit is shown in Figure 3.17. A resistor ladder comprised of components R6, R7, R8, R11, R12 and R13 is used to generate four reference voltages V1, V2, V3 and V4 with values 10 V, 1 V, -1 V and -10 V respectively. These reference voltages are calculated as follows:

$$V_1 = \left(\left(\frac{R_7 + R_8 + R_{11} + R_{12} + R_{13}}{R_6 + R_7 + R_8 + R_{11} + R_{12} + R_{13}}\right) \times \left(V_+ - V_-\right)\right) + V_+$$

$$= \left(\left(\frac{5 \times 10^3}{6 \times 10^3}\right) \times 30\right) + 15$$

$$= 10$$

$$V_2 = \left(\left(\frac{R_8 + R_{11} + R_{12} + R_{13}}{R_6 + R_7 + R_8 + R_{11} + R_{12} + R_{13}}\right) \times (V_+ - V_-)\right) + V_+$$
$$= \left(\left(\frac{3.2 \times 10^3}{6 \times 10^3}\right) \times 30\right) + 15$$
$$= 1$$

$$V_3 = \left(\left(\frac{R_{12} + R_{13}}{R_6 + R_7 + R_8 + R_{11} + R_{12} + R_{13}}\right) \times (V_+ - V_-)\right) + V_+$$
$$= \left(\left(\frac{2.8 \times 10^3}{6 \times 10^3}\right) \times 30\right) + 15$$
$$= -1$$

$$V_4 = \left(\left(\frac{R_{13}}{R_6 + R_7 + R_8 + R_{11} + R_{12} + R_{13}}\right) \times (V_+ - V_-)\right) + V_+$$
$$= \left(\left(\frac{1 \times 10^3}{6 \times 10^3}\right) \times 30\right) + 15$$
$$= -10$$

The input voltage Vi is compared with the four reference voltages by the comparators U4 to U9 whose outputs are combined to generate two digital outputs Vo1 and Vo2. These digital signals set the gain of the PGA and are later combined with 12-bit digital data of the ADC to form a 14-bit word.

3.5.4 PIA Board

This is connected to the interface card in the PC and therefore forms part of the instrumentation control circuitry. On the board are an 8255 peripheral interface adapter, a 12-bit analogue to digital converter and buffer circuitry. The circuit diagram for the PIA board is in Appendix 7.10 and the board layout in Appendix 7.11.

3.5.4.1 Peripheral interface adapter (PIA).

An 8255 is used to expand the bus of the PC to provide input/output lines to control the multiplexers, tone generator circuits and other functions. The device is programmed to configure Port A and Port C as output ports, and Port B as an input port by writing the control word $86 to the control register. The port addresses and bit functions are given in Table 3.3.

Table 3.3 PIA port address functions

Port	Address in Hex	Bit	Byte in Hex	Function
A	310	0	01	Multiplexer A0
		1	02	Multiplexer A1
		2	04	Multiplexer A2
		3	08	Multiplexer A3
		4	10	Multiplexer EN
		5	20	Long low tone
		6	40	Unused
		7	80	Click
C	314	0	01	Sampling enable
		1	02	ITI Start
		2	04	Error detect clear
		3	08	LED Control
		4	10	Unused
		5	20	Short low tone
		6	40	Short high tone
		7	80	Unused
B	312	0	01	Error Detect
		1	02	Operator Switch
		2	04	ITI End
		3	08	Unused
		4	10	Unused
		5	20	Unused
		6	40	Unused
		7	80	Unused

3.5.4.2 Analogue to digital converter (ADC).

The ADC converts the processed EEG signals into 12-bit digital format. The ADC must convert 32 signals in 8 ms, the required conversion time is therefore:

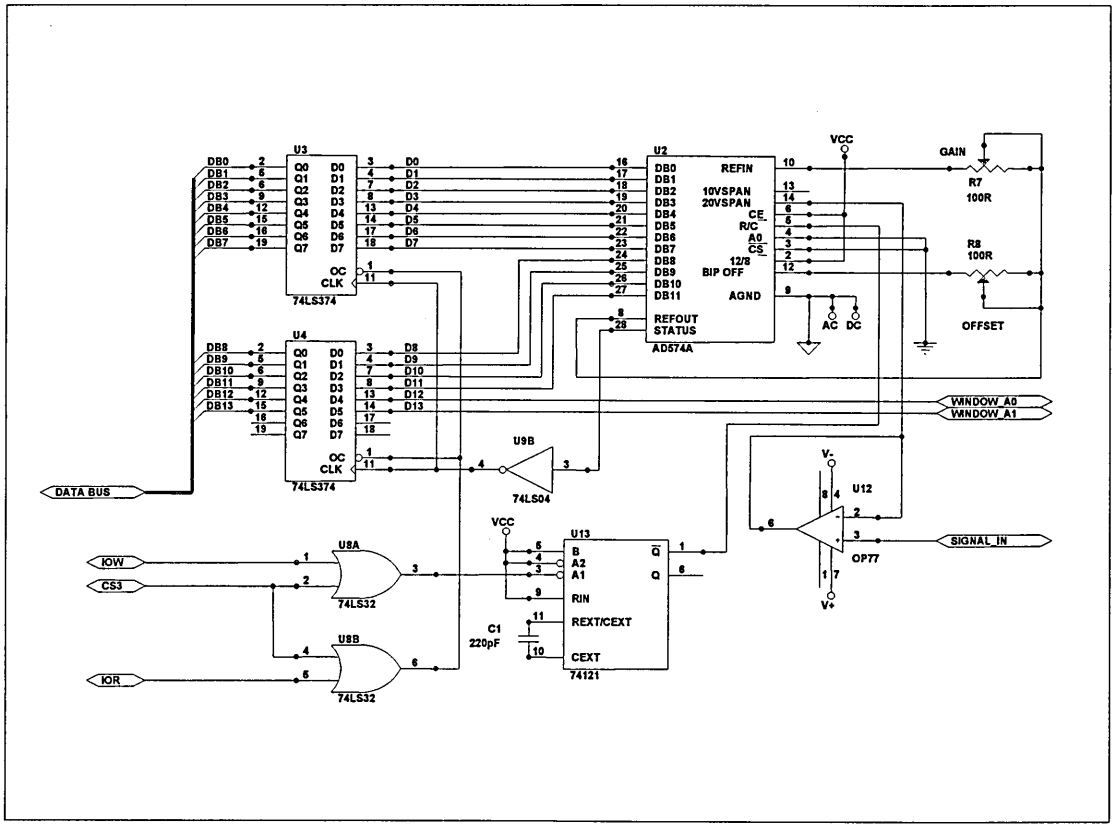
Conversion speed = Sampling interval / Number of channels

= $8 \times 10^{-3} / 32$

= 250 μs

An AD574 was chosen because it is an inexpensive 12-bit ADC with a maximum conversion time of 35 μs. It also has a 12-bit parallel output, can interface directly with a 16-bit PC bus and does not have an internal sample and hold [25]. An OP77 operational amplifier buffers the analogue signal before being fed into the 20 V span input of the ADC.

Figure 3.18 ADC circuit



The ADC is operated by reading and writing to it as though it is an I/O device. It occupies address space $310 - $31E. Writing to these addresses initiates a conversion. When the data is ready the status line of the ADC goes high indicating that a conversion is being performed, returning low when it has been completed. This signal is inverted and used to clock the data into two 374 D-Type transparent latches at the end of a conversion, see Figure 3.18.

A 74121 monostable is used to lengthen the write command of the PC so it can be used as the convert command for the ADC. This is necessary because the write pulse width of the instrumentation PC was measured as 200 ns whereas the AD574 requires a minimum convert pulse width of 250 ns. The 74121 monostable is configured to

generate a pulse of width 300 ns when triggered by the negative going edge of the PC write command. The width of the output pulse is described by the following equation taken from the 74121 datasheet [26]:

$$t_W = k \times R_X \times C_1$$

where R_X = 2 kΩ, which is the value of the internal resistor

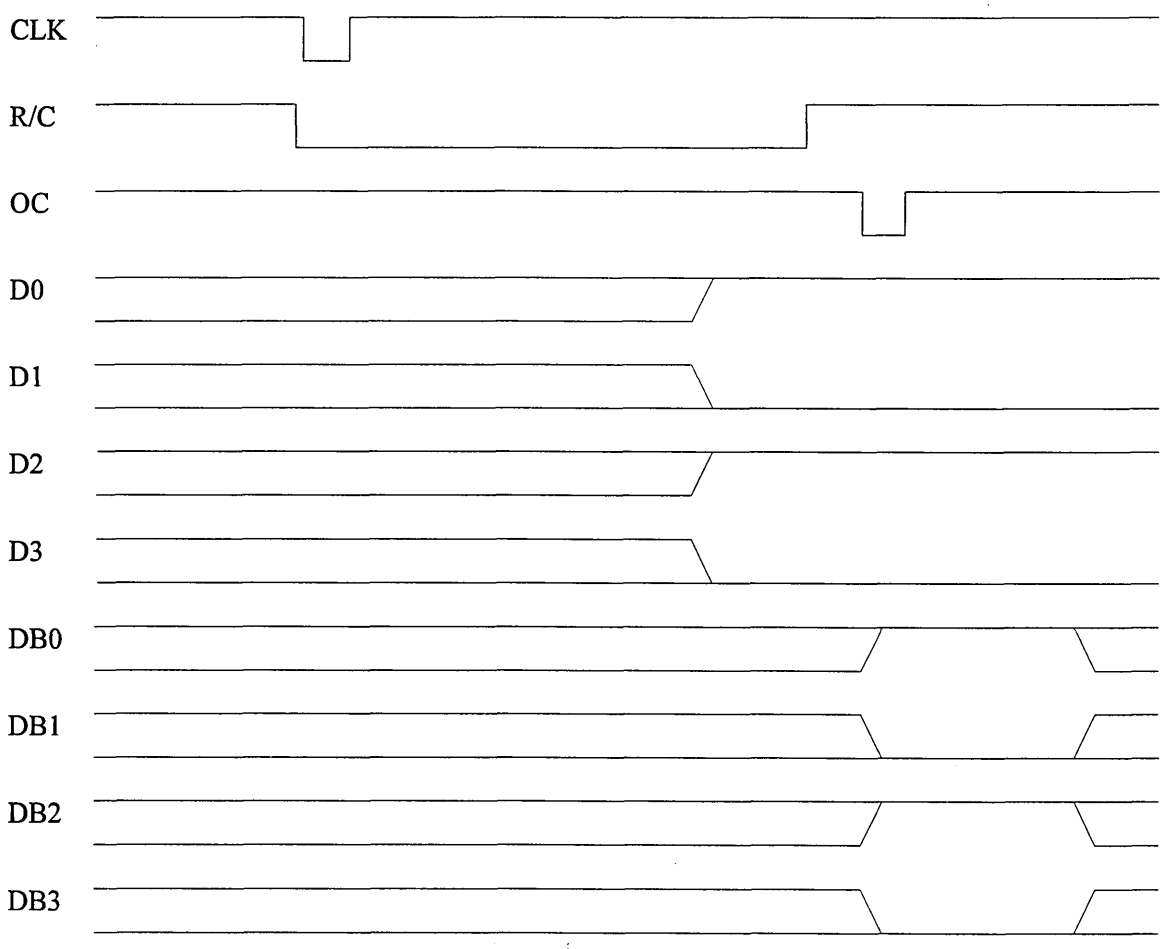
C_1 = 220 pF

$k \approx 0.7$ constant

Therefore $t_W \approx$ 308 ns

The timing diagram for the operation of the ADC is shown in Figure 3.19.

Figure 3.19 Timing diagram for ADC



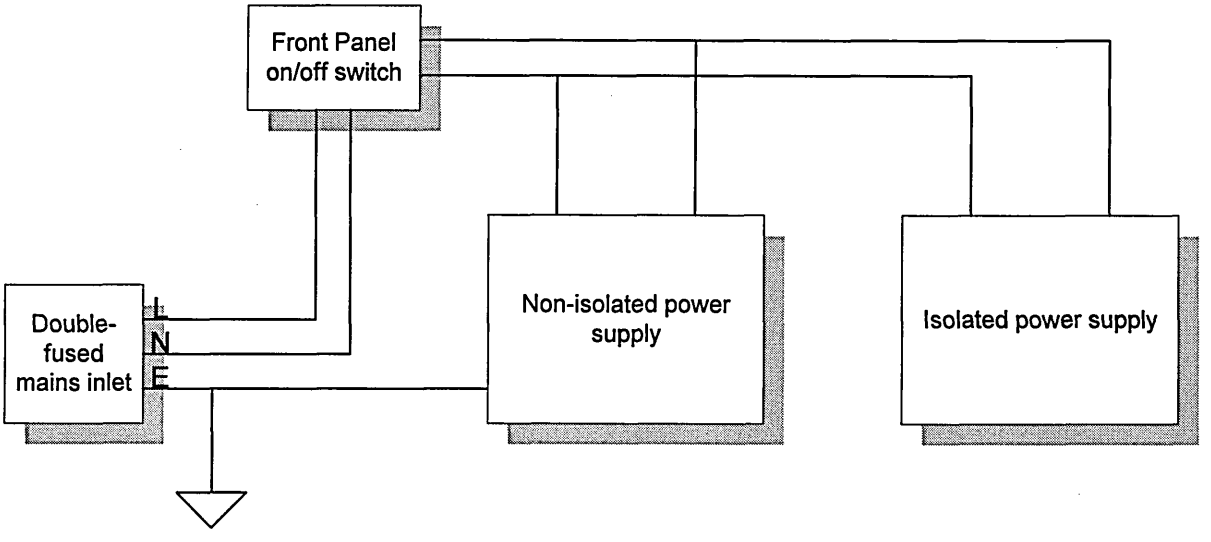
3.5.4.3 Buffer circuitry

Two 74LS245 tri-state octal bus transceivers buffer the data bus between the PC and the PIA board circuitry. These are permanently enabled. A 74LS244 octal tri-state line driver/line receiver buffers the control and address signals from the PC and another buffers the S&H signal from the interface card to all the signal processing boards and all signals output to the interface card timing circuitry.

3.5.5 Power Supplies

The power supply wiring for the instrumentation sub-system is shown in Figure 3.20. The mains input is through a twin fused IEC panel socket. Both the live and neutral wires must be fused in accordance with IEC601 [27]. Both wires are taken to a double pole single throw illuminated mains switch mounted on a 6 HP front panel plate. This switches both the live and neutral supply leads to the isolated and non-isolated power supplies. Both supply leads are double insulated throughout the enclosure. The inclusion of an accessible mains switch is a requirement of medical equipment according to IEC601, as is the ability to tell whether power is being supplied to the equipment or not [28].

Figure 3.20 Power supply wiring diagram



3.5.5.1 Earthing

The mains supply earth is connected from the IEC socket to the sub-rack and the frame of the non-isolated power supply. An earth lead is also used to connect the rear panel to the sub-rack. Thus all metal parts of the system are connected to earth by low impedance connections.

3.5.5.2 Isolated power supply

This power supply provides isolated ± 15 V power to all the isolated circuitry in the system. Namely the pre-amplifiers in the headbox and the isolation circuits on the signal processing boards. All isolated circuitry in the system must be powered from an isolated power source. Isolation amplifier packages tend to have in-built isolated power supplies but these amplifiers aren't used in the system to reduce cost. If they were they would still only generate enough power to drive their own circuitry and no other. Alternately isolated dc-dc converters could be used, but versions that are suitable for medical applications are expensive, and several would be required to generate enough power for the entire system. This system solves the problem by using a standard medical power supply to provide power to the isolated circuitry. However it is not connected to earth and installed so that it is double isolated from the non-isolated parts of the system to meet the isolation requirements.

The power supply is an MAA15-0.8-A built by Condor dc power supplies. This has an output current capability of 0.8 A at ± 15 V. It has a safety leakage current of 6 μA and a safety isolation voltage of 3750 VAC rms. It is double insulated from the rest of the system by not connecting the frame to earth and by mounting it horizontally between two 100 × 220 mm PCBs. Mounting it this way gives it a separation distance of

at least 8 mm between the power supply and the 19" sub-rack or any other PCBs. This is the minimum creepage distance for isolated components at 240 VAC.

The PCBs effectively form a module that can be slid in and out of the 19" sub-rack like any of the other PCBs. Both are fitted with a 96 pin DIN41612 connector that is used to distribute the power to the signal processing boards. These connectors mate with a connector of the opposite gender when the module is slid into the sub-rack. These connectors and all power supply wires are double insulated from the rest of the system

3.5.5.3 Non-isolated power supply

This power supply provides + 5 V and ± 15 V power referenced to earth to all the non-isolated circuitry in the system, namely the circuitry on the non-isolated part of the signal processing boards, the PIA, Multiplexer and Patient interface boards. It is built to IEC 601-1 which enables it to be used in medical equipment.

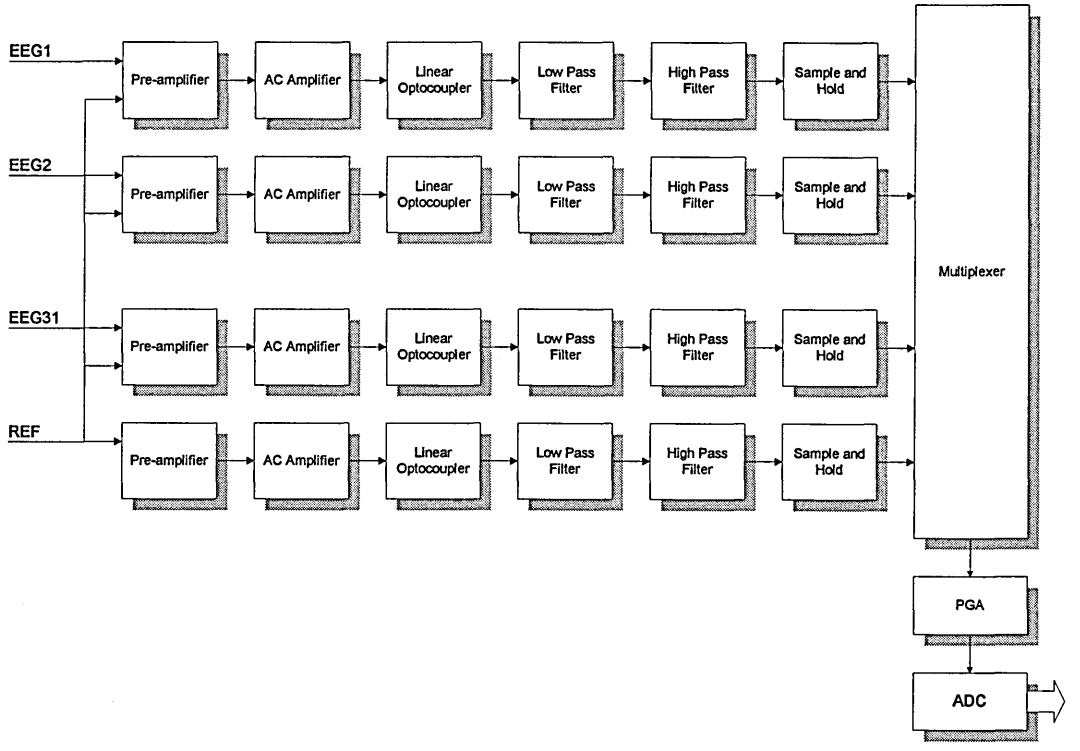
The power supply is an MTAA-16W-A made by Condor dc power supplies. It can provide up to 2 A at +5 V and 0.4 A at ± 15 V. It is mounted vertically on a 100 × 220 mm PCB that slides into the 19" sub-rack. The PCB is fitted with a 96 pin DIN4162 connector that is used to distribute the power supplies to the other PCBs. This connector mates with another of the opposite gender when the PCB is slid into the sub-rack.

3.6 Channel Structure

All signals are measured differentially, in software, against a reference channel. This is so that any common mode signals not removed in previous stages and any common mode noise induced in the circuitry during processing is removed.

The advantage of measuring all signals relative to a single reference electrode is that any electrode montage can be simulated after recording by mathematical manipulation of the digital signal data. For example either monoploar or bipolar recordings are possible, or any one channel can be referenced against the average of all the other channels. The channel structure is shown in Figure 3.21.

Figure 3.21 Diagram showing the structure of each EEG channel



[1] The Winn L. Rosch Hardware Bible, 2nd Edition, Winn L. Rosch, Brady Publishing 1992.

[2] RS Data Sheet No. A16904, Prototyping boards, March 1994.

[3] The Art of Electronics, P. Horowitz , W. Hill, Cambridge University Press, Chapter 9, pp 406-407, 1980.

[4] Intel Data Book, Section 4, pp 207-220, 1990.

[5] EEG recording and operation of the apparatus, E.L. Reilly, Electroencephalography: Basic Principles, Clinical Applications and Related Fields, Eds. E. Niedermeyer, F. Lopes da Silva, Urban and Schwarzenberg, pp 57-77, 1986.

[6] 1 HP = 5.08 mm.

[7] Table XVI, IEC601-1 1988/BS7724 Part1 1989, British Standard for Medical Electrical Equipment, Part 1, General requirements for safety.

[8] Table IV, IEC601-1 1988/BS7724 Part1 1989, British Standard for Medical Electrical Equipment, Part 1, General requirements for safety.

[9] PMI Analog IC Data Book, Vol 10, Section 5, pp 320-329, 1990.

[10] Technological basis of EEG recording, A. Kamp, F.L. da Silva, Electroencephalography Basic Principles, Clinical Applications and Related Fields, Eds. E. Niedermeyer, F. Lopes da Silva, Urban and Schwarzenberg, pp 43-55, 1986.

[11] EEG instrumentation standards (Revised 1977): Report of the commitee on EEG instrumentation standards of the international federation of societies for electroencephalograhy and clinical neurophysiology, J.S. Barlow, A. Kamp, H.B. Morton, A. Ripoche, H.Shipton, D.B. Tchavdarov, Electroencephalograhy and Clinical Neurophysiology, Vol. 45, pp 144-150, 1978.

[12] EEG Technology, R. Cooper, J.W. Osselton, J.C. Shaw, 3 rd Edition, Butterworths, 1980.

[13] PMI Analog IC Data Book, Vol 10, Section 5, pp 320-329, 1990.

[14] National Semiconductor Databook, Section 5, pp 46-49, 1984.

[15] National Semiconductor Logic Databook, Vol 2, Section 6, pp 148-151, 1984.

[16] IEC601-1 1988/BS7724 Part1 1989, British Standard for Medical Electrical Equipment, Part 1, General requirements for safety.

[17] Analog Devices Amplifier Reference Manual, Section 2, pp 81-88, 1992.

[18] Siemens Optoelectronic Databook, Section 5, pp 115-122.

[19] The Art of Electronics, P. Horowitz , W. Hill, Cambridge University Press, Chapter 4, pp 148-161, 1980.

[20] PMI Analog IC Data Book, Vol. 10, Section 5, pp 285-296, 1990.

[21] Linear Technology Data Book, Section 9, pp 97-112, 1990.

[22] Analog Devices Data Converter Reference Manual, Vol. 2, Section 5, pp 79-86, 1992.

[23] Linear Technology Data Book, Section 9, pp 97-112, 1990.

[24] Burr Brown Linear Products Data Book, Section 4, pp 155-168, 1994.

[25] Analog Devices Data Converter Reference Manual, Vol. 2, Section 2, pp 41-51, 1992.

[26] National Semiconductor Logic Databook, Vol 1, Section 5, pp 275-280, 1984.

[27] Sub-clause 57.6, IEC601-1 1988/BS7724 Part1 1989, British Standard for Medical Electrical Equipment, Part 1, General requirements for safety.

[28] Sub-clause 57.1, IEC601-1 1988/BS7724 Part1 1989, British Standard for Medical Electrical Equipment, Part 1, General requirements for safety.

4 CONTROL AND ANALYSIS SOFTWARE

The system software controls the operation of the instrumentation system. This is written in Borland C that is compiled to generate the executable code. The function of this software is to control the acquisition and recording of the EEG signals and to generate the required ERP paradigms. The software also displays the ERP waveforms as they are recorded so the operator has some indication as to what is being recorded in case there are any problems. The control software does not process the waveforms, however, it is simply raw data that is recorded and saved for analysis later. Analysis is performed after recording using programs written in Matlab. This is a higher level language compared to Borland C and more suited for performing functions such as signal averaging and artefact removal as well as providing useful graphical display functions.

4.1 System Control Program

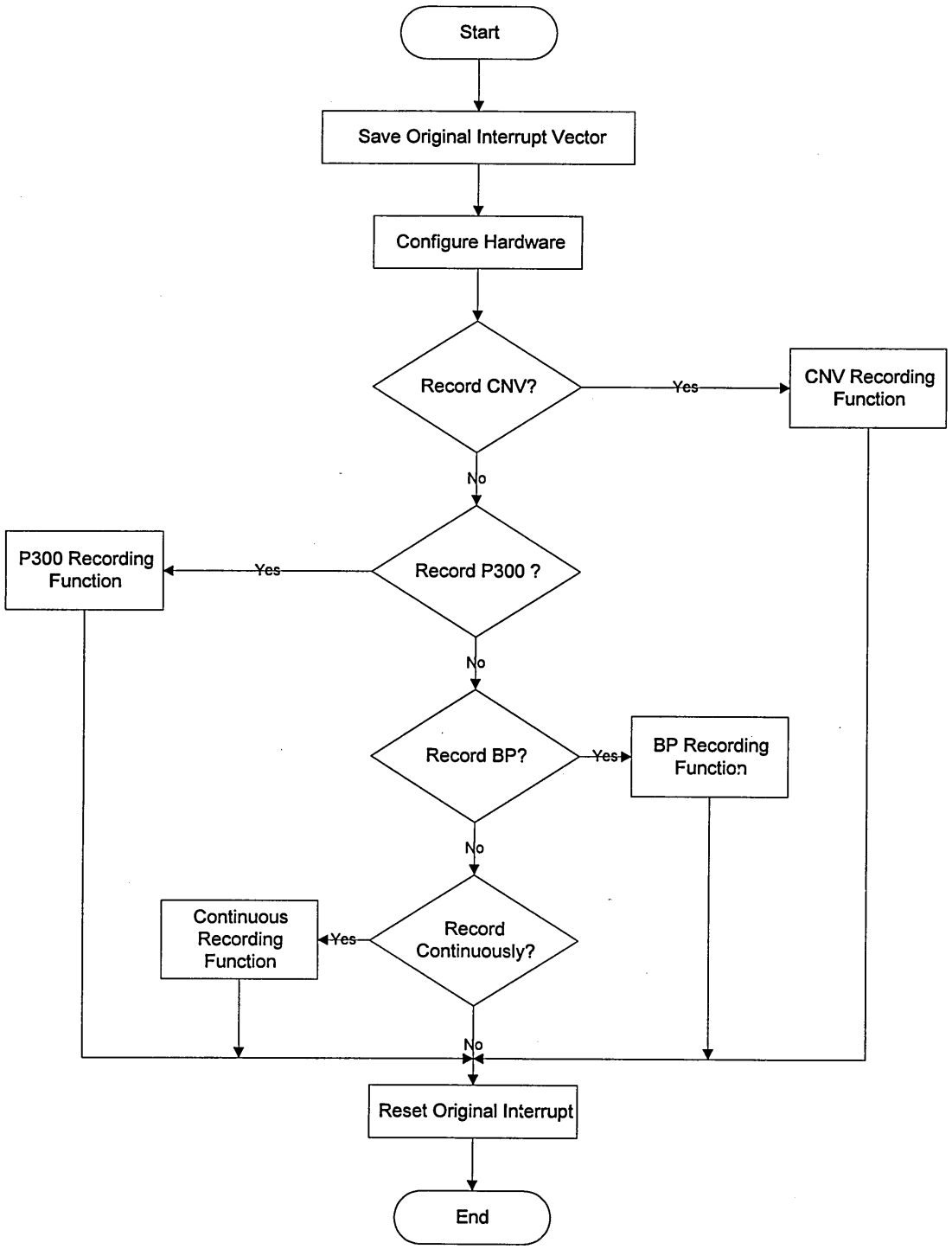
The system control program is called ERP20.C and is written in a structured manner so the program code is divided into functions. The program comprises a main program and four ERP recording functions. These are the CNV, P300, BP and Continuous recording functions. These functions call smaller functions that perform common tasks such as displaying and saving recorded data. The source code listing for ERP20.C is in Appendix 7.12 and is heavily commented for readability.

4.1.1 Main program

The main program configures Timers 1 and 2 of the PC interface card, the PIA of the PIA board and PC interrupt controller 1 which controls IRQ5, which is the interrupt used during recording. The screen display is also set and the operator asked to select which paradigm they wish to record or whether they wish to record continuously. The continuous recording facility is a useful option to use prior to recording to ensure that the system is functioning correctly. Large eye movements and blink artefacts are easily recognisable when superimposed on background EEG so asking the subject to move their eyes and/or blink is a good method of validating the system.

The flow diagram of Figure 4.1 represents the operation of the main program that determines which ERP paradigm is to be recorded.

Figure 4.1 Flow diagram of main program

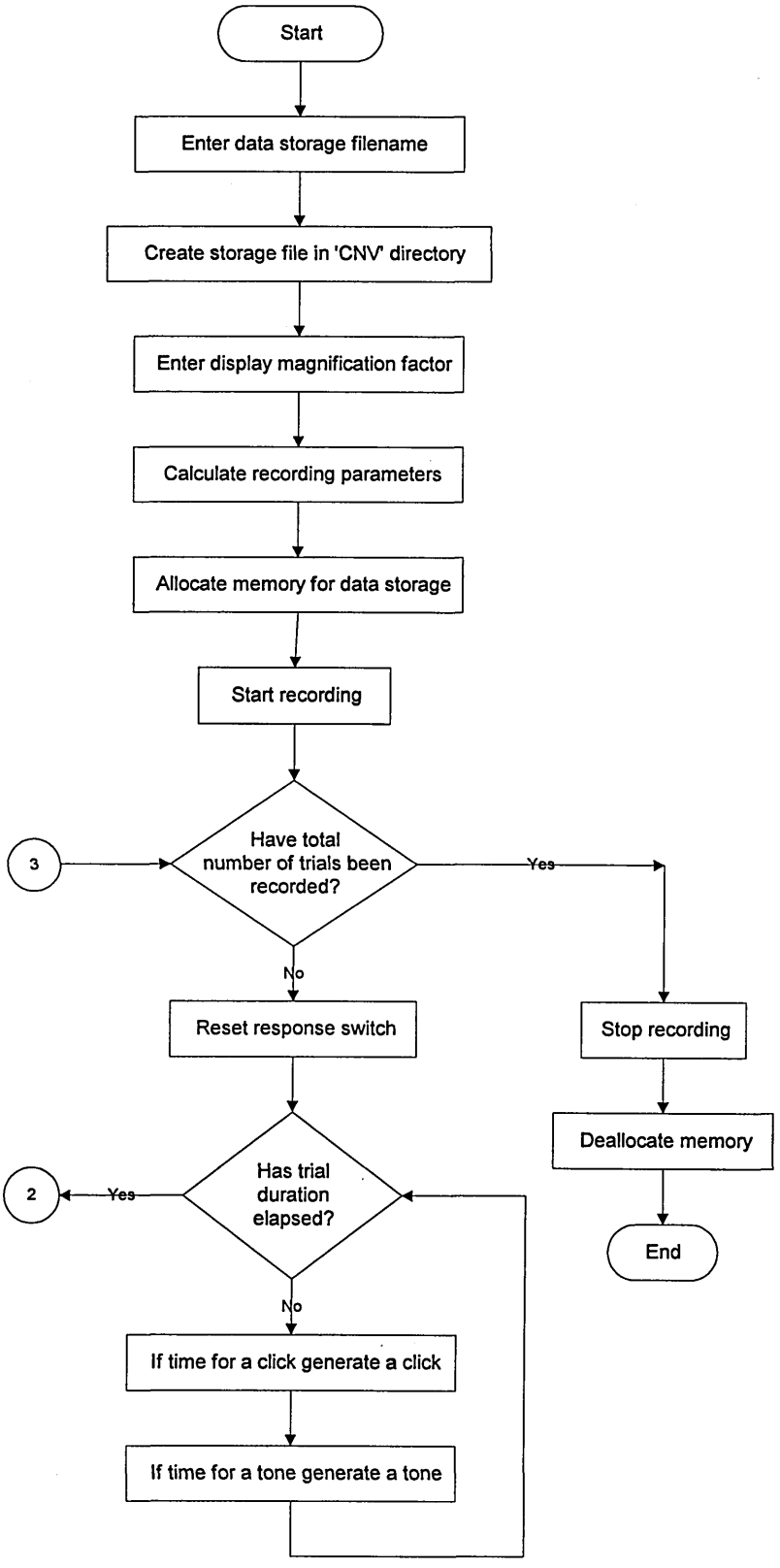


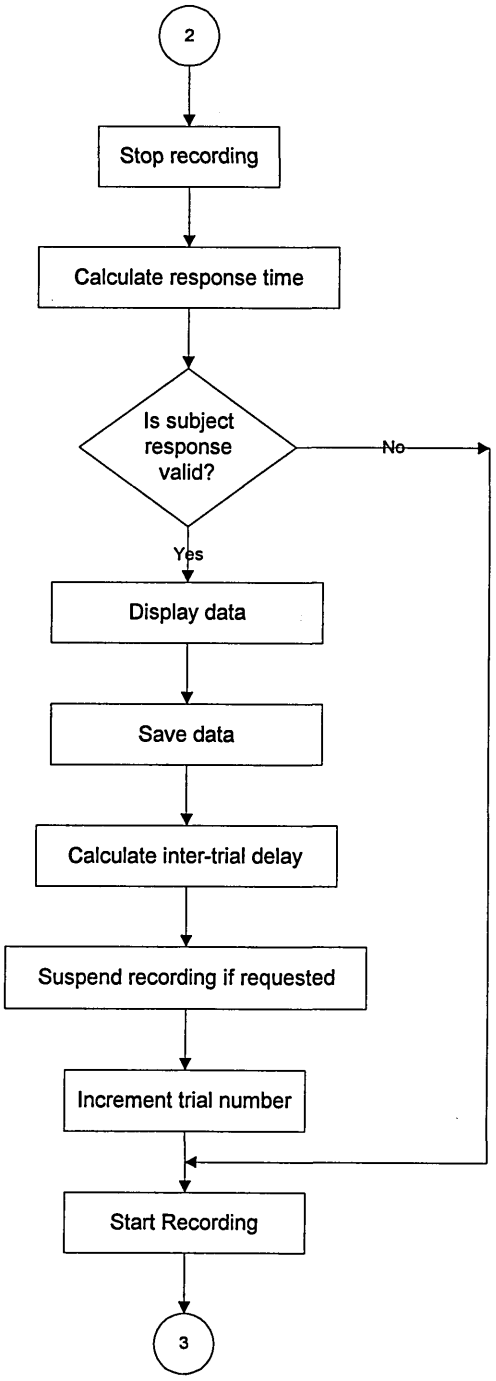
4.1.2 CNV recording function

The flow diagram of Figure 4.2 shows how the function that controls the recording of the CNV paradigm is implemented. This function has to generate a warning stimulus and a target stimulus and record data prior to, in between, and after the stimuli. The program both displays and saves to disk the recorded data after a trial, provided there was a valid response to the target stimulus. The validity of the response is determined by monitoring the response switch circuit in order to ascertain whether a response was made before or after a target stimulus. If a response is made before the target stimulus the trial is deemed invalid as the subject has anticipated the stimulus rather than respond to it. Invalid trials are neither displayed nor saved to disk. The function also measures the subject reaction times, that is the time between the target stimulus and the response. The response times are displayed on screen with each trial.

The inter-trial interval is made random to prevent subjects anticipating the warning stimulus but is set to a minimum of 2 s and a maximum that can be set in software.

Figure 4.2 Flow diagram of CNV function





4.1.2.1 Function Description

At the beginning of the CNV function the function variables are defined. These include the number of trials to be recorded, the duration of each trial, the time the click and tone

occur within each trial and the maximum time between trials. If the operator wishes to change any of these parameters they must edit the source code to do so.

The operator is first asked the filename they wish to store the CNV data in. This must be no more than eight characters long but may have a three-digit extension. This is defined by the DOS operating system the program runs under. The operator must then enter a display magnification factor. This is typically an integer number between ten and hundred that is used to enable the operator to view the recorded data in greater or lesser detail whilst recording is in progress.

Prior to actual recording the recording parameters used by the function are calculated. These parameters represent the trial length, click and tone times in terms of the sample number at which they are to occur. If at the start of a trial sample zero is said to occur at time zero, then with a sample rate of 125 samples/second, a four second trial will equate to 500 samples. Based on the trial recording parameters and the number of channels to be recorded the total amount of memory required to store the recorded data can be calculated. This amount of memory is then allocated for this purpose.

Recording begins by first enabling interrupts to occur. Then the subject response switch is reset. The switch can detect whether a premature response has been made i.e. one that is made prior to tone and must be reset at the beginning of every trial. Every time an interrupt occurs data for each channel is converted and stored in memory by the 'interrupt' function. At the end of this function the variable 'sample' is incremented and hence at any time represents the number of samples to have occurred. The CNV function monitors the value of this variable and generates the click and tone of the paradigm when its value is equivalent to the relevant recording parameters. Similarly the function also checks for the end of trial and when reached disables interrupts.

After the data has been recorded and saved in memory interrupts are disabled and the function calculates the subjects reaction time by calculating the time between when the tone was generated and when the subject response switch was pressed. The response switch is also checked to see if it was pressed prior to the tone and hence if a false response was made. If this is found to be the case the function starts to records another trial straight away. However, if the response was made after the tone the data is first displayed on the VDU using the 'display_waveform' function and then saved to optical disk using the 'save_waveform' function.

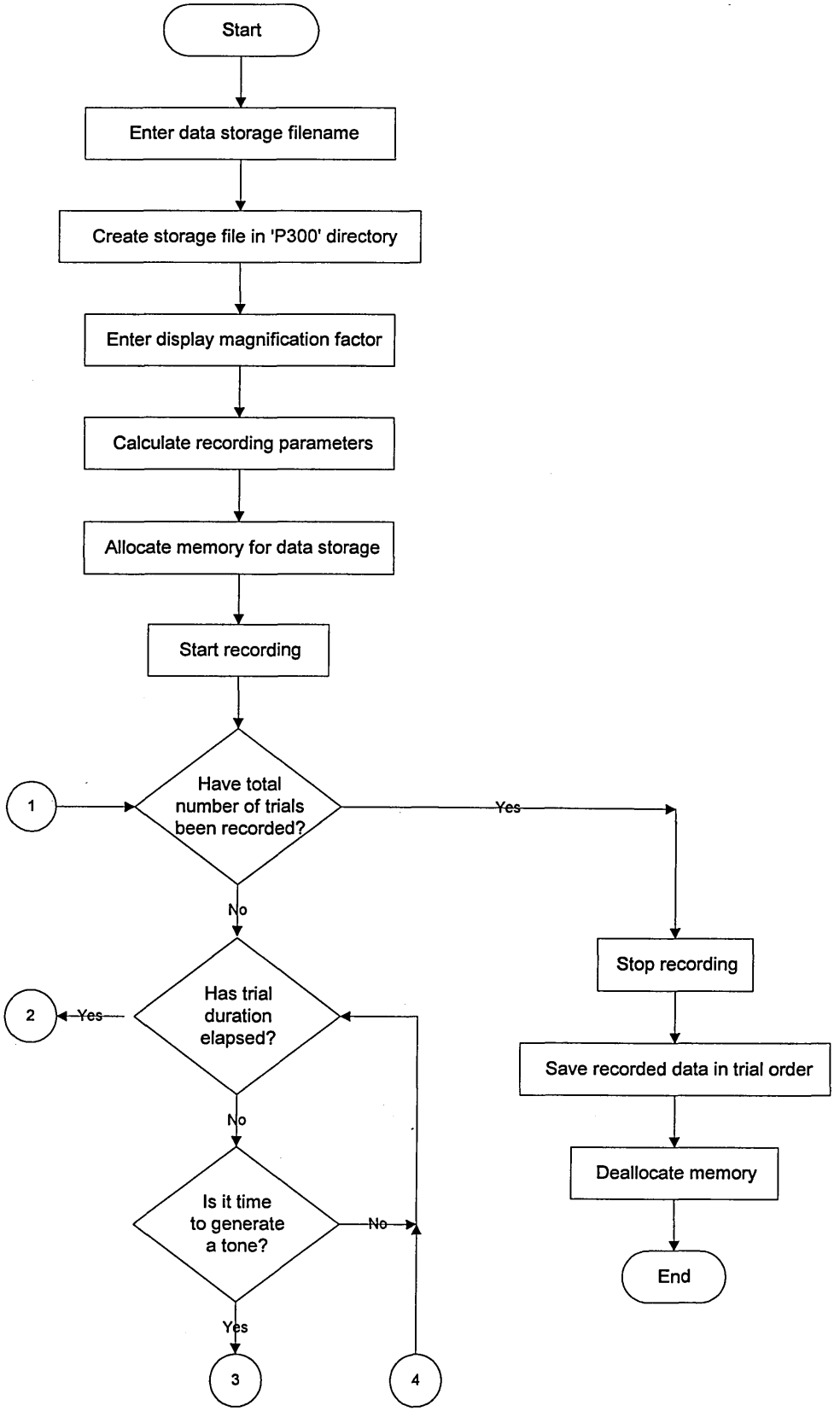
Preparation for the next trial now begins with the calculation of a random inter-trial interval. The operator switch is also checked to see if the operator wishes to suspend recording and the 'trial' variable incremented. Then interrupts are enabled and recording of the next trial begins.

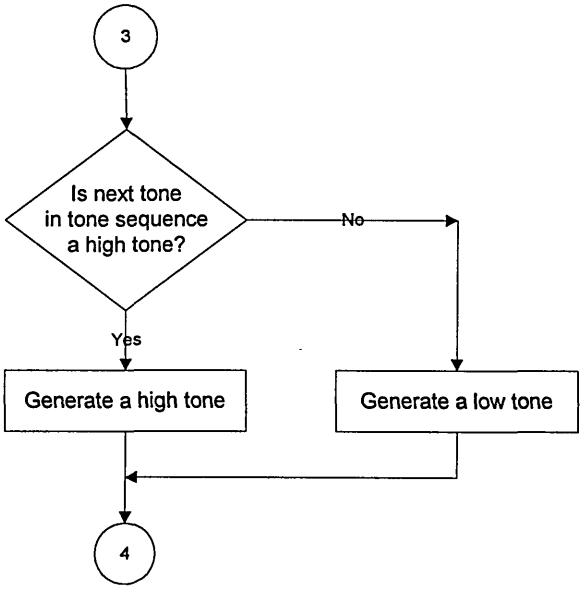
After the required number of trials have been recorded the memory allocated to data storage is deallocated.

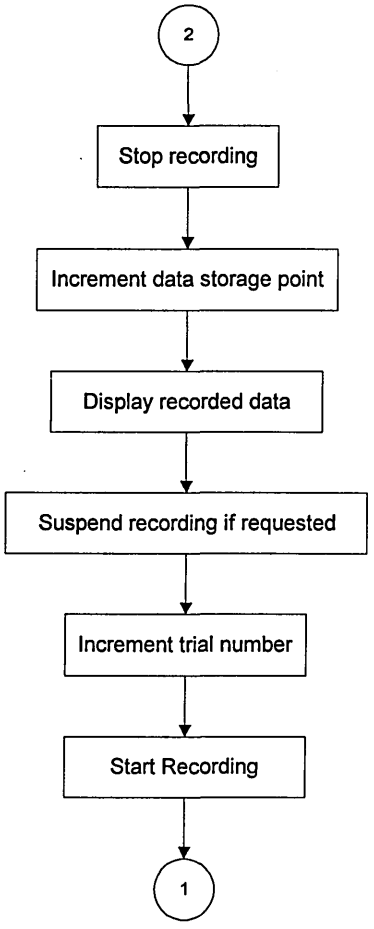
4.1.3 P300 recording function

The flow diagram of Figure 4.3 represents the operation of the function that controls the recording of the P300 paradigm. This function has to generate a sequence of high and low tones at fixed periods of time and is therefore limited in the number of operations it can perform in between. This means that there is not enough time to store trial data after it has been recorded following a target stimulus. Therefore the data is displayed, but stored in memory rather than to disk. It is only after all trials have been recorded that the trial data is finally saved to disk in trial order. The sequence of high and low tones is determined by a pre-defined string of 1's and 0's, where a '1' represents a high tone and '0' a low tone. The order of the 1's and 0's in the string is pseudo-random with a ratio of 0's to 1's of 5:1. The format of this string was generated by another program written for this task.

Figure 4.3 Flow diagram of P300 function




3
Is next tone in tone sequence a high tone?
No
Yes
Generate a high tone
Generate a low tone
4


2
Stop recording
Increment data storage point
Display recorded data
Suspend recording if requested
Increment trial number
Start Recording
1

4.1.3.1 Function Description

At the beginning of the P300 function the function variables are defined. These include the number of trials to be recorded, the duration of each trial and the time the tones are to occur within each trial. A character string that comprises of a pseudo-random sequence of '1s' and '0s' is also defined. This string determines the sequence of high and low tones that are generated during recording. If the operator wishes to change any of these parameters they must edit the source code to do so.

The operator is first asked the filename they wish to store the P300 data in. This must be no more than eight characters long but may have a three-digit extension. This is defined by the DOS operating system the program runs under. The operator must then enter a display magnification factor. This is typically an integer number between ten and hundred that is used to enable the operator to view the recorded data in greater or lesser detail whilst recording is in progress.

Prior to actual recording the recording parameters used by the function are calculated. These parameters represent the trial length and tone times in terms of the sample number at which they are to occur. If at the start of a trial sample zero is said to occur at time zero, then with a sample rate of 125 samples/second, a two second trial will equate to 250 samples. Based on the trial recording parameters and the number of channels to be recorded the total amount of memory required to store the recorded data can be calculated. This amount of memory is then allocated for this purpose.

Recording begins by enabling interrupts. Every time an interrupt occurs data for each channel is converted and stored in memory by the 'interrupt' function. At the end of this function the variable 'sample' is incremented and hence at any time represents the number of samples to have occurred. The P300 function monitors the value of this variable and generates a tone when its value is equivalent to the relevant recording

parameters. Whether the tone is a high or a low one is determined by reading the character string. Similarly the function also checks for the end of trial and when reached disables interrupts.

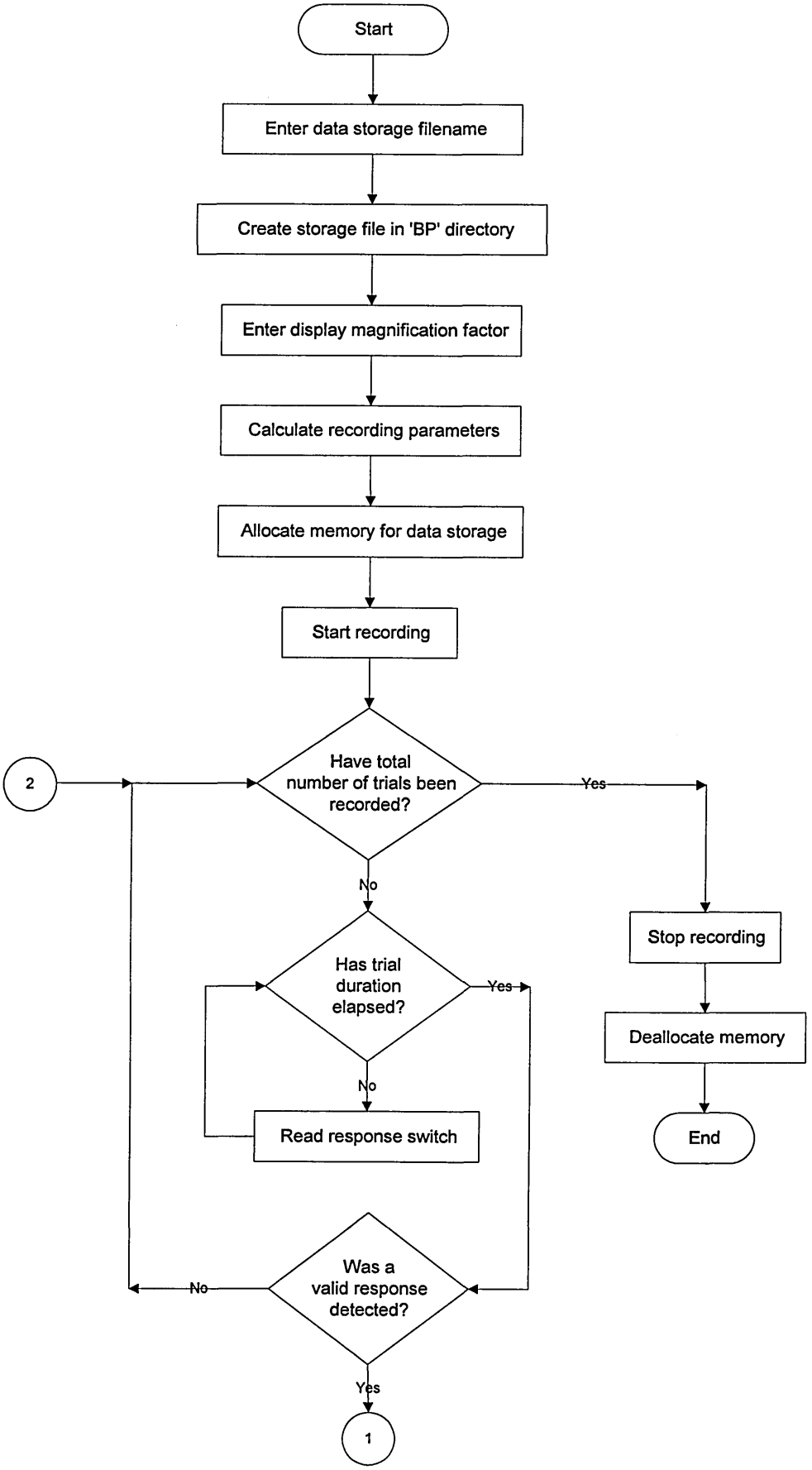
After each target stimulus (high tone) interrupts are disabled and the recorded data is displayed using the 'display_waveform' function. However, unlike the CNV function, the data is not saved to optical disk as there is not sufficient time to do so within the paradigm without disrupting the sequence of high and low tones. Instead the location in memory where recorded data is stored is advanced so that successive trial data is stored consecutively. Before interrupts are enabled once more the operator switch is checked to see if the operator wishes to suspend recording and the 'trial' variable is incremented.

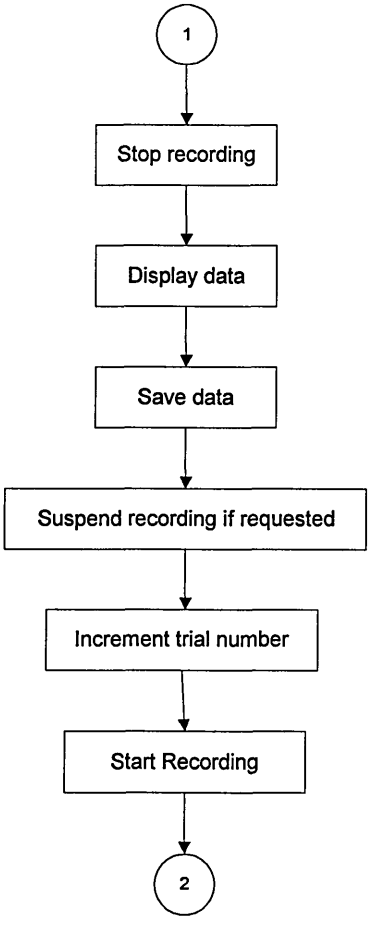
After the specified number of trials have been recorded interrupts are disabled and all the trial data stored in memory is saved to optical disk. Finally memory used to store the trial data is deallocated.

4.1.4 BP recording function

The flow diagram of Figure 4.4 represents the operation of the function that controls the recording of the BP paradigm. This function has to record a fixed period of time prior to a button press and a fixed period of time after it. Because the program cannot anticipate the subject response it must record continuously, detect the response and display and save the data recorded before and after the response. Recording continuously presents problems in that memory has to be allocated prior to recording for data storage and yet the subject effectively determines the recording period necessary. The BP recording function achieves a solution to this problem by repeatedly recording over a fixed period of time several times larger than the trial length. When a button press is detected it's position within the recording period is noted and only the data recorded prior to it and after it that constitutes the required trial length is displayed and saved. A problem with this solution is that if the subject responds at the start or end of the recording period there is a possibility that the required pre-response or post-response data will not have been recorded. The likelihood of this occurring is dependent on the relative lengths of the trial and recording periods. If this does occur the trial data is simply discarded. As the subject is not told how many responses they are to make in a session they will be unaware of this process.

Figure 4.4 Flow diagram of BP function





4.1.4.1 Function Description

At the beginning of the BP function the function variables are defined. These include the number of trials to be recorded, the duration of each trial and the pre-response period. If the operator wishes to change any of these parameters they must edit the source code to do so.

The operator is first asked the filename they wish to store the BP data in. This must be no more than eight characters long but may have a three-digit extension. This is defined by the DOS operating system the program runs under. The operator must then enter a display magnification factor. This is typically an integer number between ten and hundred that is used to enable the operator to view the recorded data in greater or lesser detail whilst recording is in progress.

Prior to actual recording the recording parameters used by the function are calculated. These parameters represent the trial length and pre-response recording period in terms of the sample number at which they are to occur. If at the start of a trial sample zero is said to occur at time zero, then with a sample rate of 125 samples/second, a two second trial will equate to 250 samples. Based on the trial recording parameters and the number of channels to be recorded the total amount of memory required to store the recorded data can be calculated. This amount of memory is then allocated for this purpose.

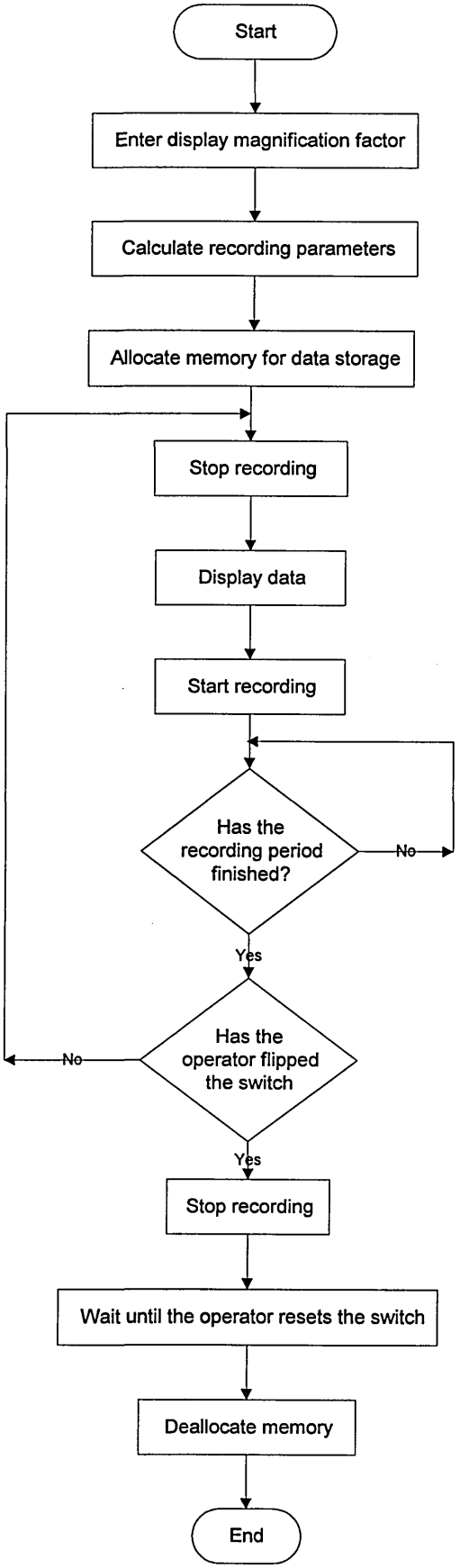
Recording begins by enabling interrupts. Every time an interrupt occurs data for each channel is converted and stored in memory by the 'interrupt' function. At the end of this function the variable 'sample' is incremented and hence at any time represents the number of samples to have occurred. The BP function records for a fixed period of time several times larger than the trial length whilst monitoring the subject response switch to see if it has been pressed. At the end of the recording period the function checks to see if a response was made. If there was no response the function records for another fixed period of time. However, if a response was made, the function checks to see if a complete trial was recorded within the recording period. If a complete trial was not recorded the function continues to record for another fixed period. If a complete trial was recorded interrupts are disabled and the recorded trial is displayed on the VDU using the 'display_waveform' function and then saved to optical disk using the 'save_waveform' function.

Before interrupts are enabled once more the operator switch is checked to see if the operator wishes to suspend recording and the 'trial' variable is incremented. After the specified number of trials have been recorded interrupts are disabled and memory used to store the trial data is deallocated.

4.1.5 Continuous recording function

The flow diagram of Figure 4.5 represents the operation of the function that enables continuous recording and display of a subjects EEG. This function does not save recorded data. The EEG is recorded for a fixed period of time and then displayed whilst the next sample of EEG is recorded. Once selected, continuous recording can only be halted by setting and then resetting the user switch on the front of the instrumentation sub-system.

Figure 4.5 Flow diagram of continuous recording function



4.1.5.1 Function Description

At the beginning of the Continuous recording function the recording time is defined. If the operator wishes to change any of these parameters they must edit the source code to do so.

The operator is first asked to enter a display magnification factor. This is typically an integer number between ten and hundred that is used to enable the operator to view the recorded data in greater or lesser detail whilst recording is in progress.

Prior to actual recording the number of samples per recording period is calculated. Based on this and the number of channels to be recorded the total amount of memory required to store the recorded data can be calculated. This amount of memory is then allocated for this purpose.

Recording begins by enabling interrupts. Every time an interrupt occurs data for each channel is converted and stored in memory by the 'interrupt' function. At the end of this function the variable 'sample' is incremented and hence at any time represents the number of samples to have occurred. After recording for the pre-defined recording period the operator switch is read to see if continuous recording is to be stopped. If it is not, interrupts are disabled, the recorded data displayed on the VDU and then interrupts enabled to record for another fixed period. If recording is to be stopped interrupts are disabled then a message is displayed on screen telling the operator to reset the switch. Once this is done the recording memory is deallocated.

4.2 Data Analysis Software

The purpose of this software is to organise, process and display data recorded using the ERP measurement system. The programs are written in the Matlab programming language. This application software was chosen because it is a very powerful tool for performing data analysis and for displaying data.

Two main programs were written for data analysis. 'Plotrial' for processing and displaying the data for a single trial and 'Plotall' for performing averaging on a number of selected trials. The programs described are sample programs that can easily be modified to perform more complex processing of the data such as ocular artefact removal or alternative methods of graphical presentation.

4.2.1 Matlab Plotrial Program

The Matlab 'Plotrial' program is used to process and display recorded ERP data for a single trial and is listed in Appendix 7.13. The program must be edited by the operator for each data file. First the recording parameters for the data must entered. This includes the number of trials recorded, the duration of each trial, the sample frequency and the number of channels recorded. The program needs these parameters for each data file in order to read the data correctly.

The display parameters must then be entered. This includes a scaling factor, which is either 1 or -1 to invert the data if necessary. The first and last channels to be included in the display must also be entered. Then there are x and y axis parameters which are used if automatic scaling is not to be used, for instance if the operator wishes to zoom in on a particular part of a waveform.

The initialisation code begins with a path being opened to the recorded data file. This must be entered by the operator. The parameters of a data matrix in which to store the data are then calculated from the recording parameters and the recorded data is then read from the data file into this matrix.

Data processing is performed only on the channels that are to be displayed. It begins by the gain of each channel being multiplied by its individual gain correction factor. The reference channel is then subtracted from each channel and the data multiplied by the scaling factor. Dc removal is then performed on each channel by calculating the mean value of each channels data and then subtracting it from each sample. Finally the processed data is stored in a display matrix.

After processing each channel is plotted on the same graph. A grid, title and x and y-axis labels can be added to the graph by the operator if required.

4.2.2 Matlab Plotall Program

The Matlab program 'Plotall' is similar to the 'Plotrial' program except that instead of processing and displaying the data for a single trial the data for a number of selected trials is processed, averaged and then displayed. This means that in addition to the 'Plotrial' recording parameters the trials selected for averaging must also be entered. Data processing is performed identically in both programs except that now it is performed on the data for all of the selected trials, which are then averaged to generate a single trial. It is this trial which is finally displayed. The program is listed in Appendix 7.14.

5 SYSTEM TEST RESULTS

5.1 Parameter Tests

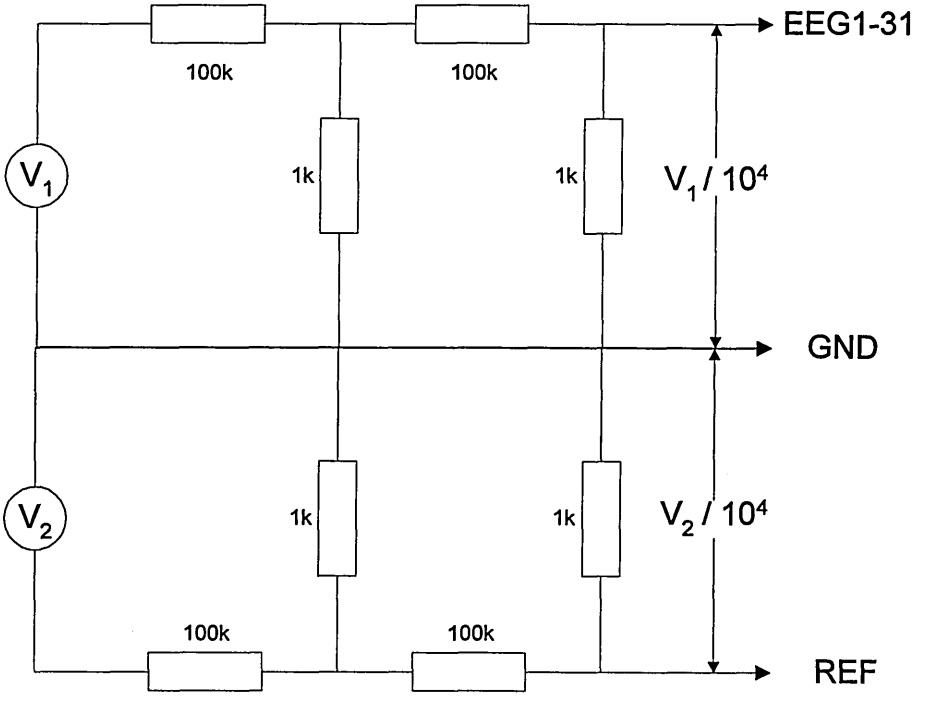
Before the measurement system was used to record event-related potentials, its ability to record synthetically generated signals was first tested. By changing the amplitude and frequency of the signals and analysing the recorded waveforms, the recording characteristics of the equipment can be compared with those required in the original specification.

5.1.1 Test signal recordings at different frequencies and amplitudes

The ability of the system to record low frequency signals of small magnitude was tested by applying sine wave test signals of amplitudes 10 μV and 100 μV and frequencies 0.1 Hz, 1 Hz and 10 Hz, into all 32 channels and recording over an appropriate period of time. The standard ERP recording programs could easily be made to do this by adjusting their recording parameters. The test signals were generated using a Thurlby Thander TG230 signal generator with a potential divider network on its output. The potential divider network was required to attenuate the signal generator output sufficiently to generate the small amplitude of the signals. As the signal generator output was a minimum of approximately 0.1 V, the potential divider had to have an attenuation of 10000 to generate a 10 μV signal. This was achieved using the network in Figure 5.1. V1 is the applied signal generator signal that is successively reduced in amplitude by two potential divider networks, each with an attenuation of approximately 100, to give a total signal attenuation of approximately 10000. Thus an applied signal of magnitude 0.1 V will result in an output signal of 10 μV, and an input signal of 1 V will result in

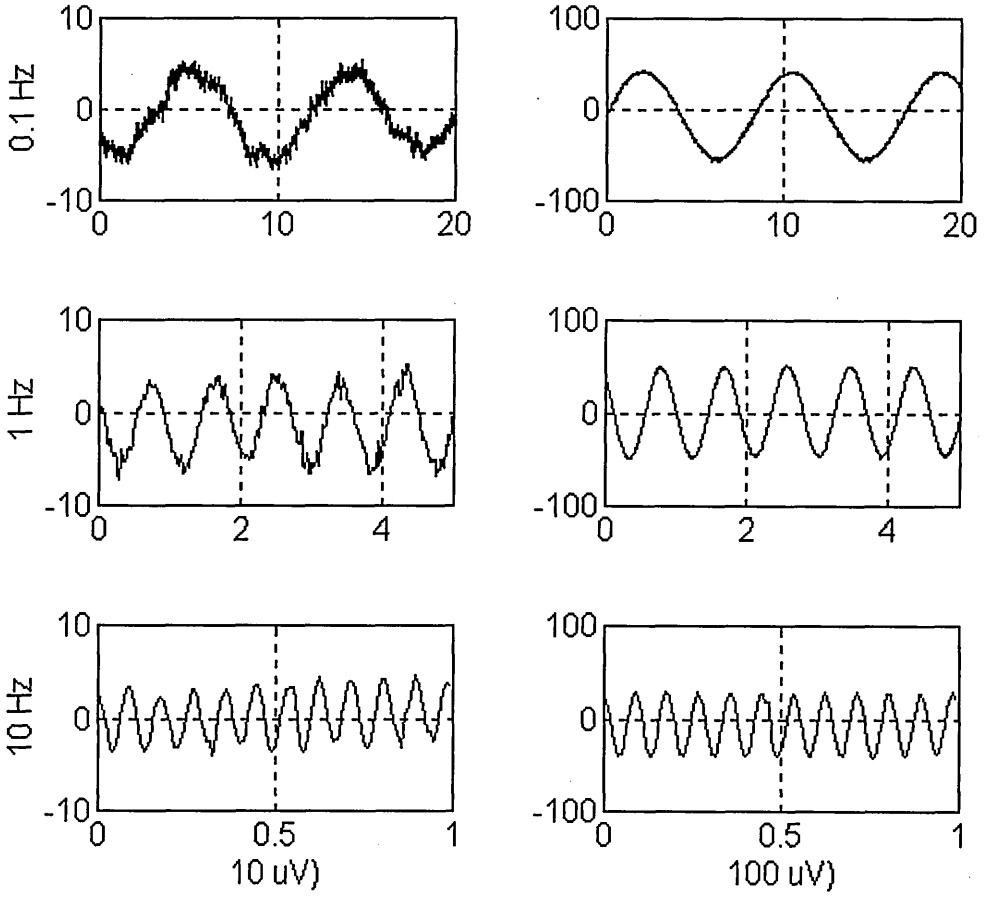
an output signal of 100 μV. V2 and its associated resistor network is a signal generator input used to represent reference signals for common mode tests.

Figure 5.1 Resistor network used to generate low voltage test signals



The test signal recordings for channel 1 at input frequencies of 0.1, 1 and 10 Hz and at amplitudes of 10 μV and 100 μV are shown in Figure 5.2. This was one of 31 simultaneously recorded signals.

Figure 5.2 Test signal recordings for channel 1



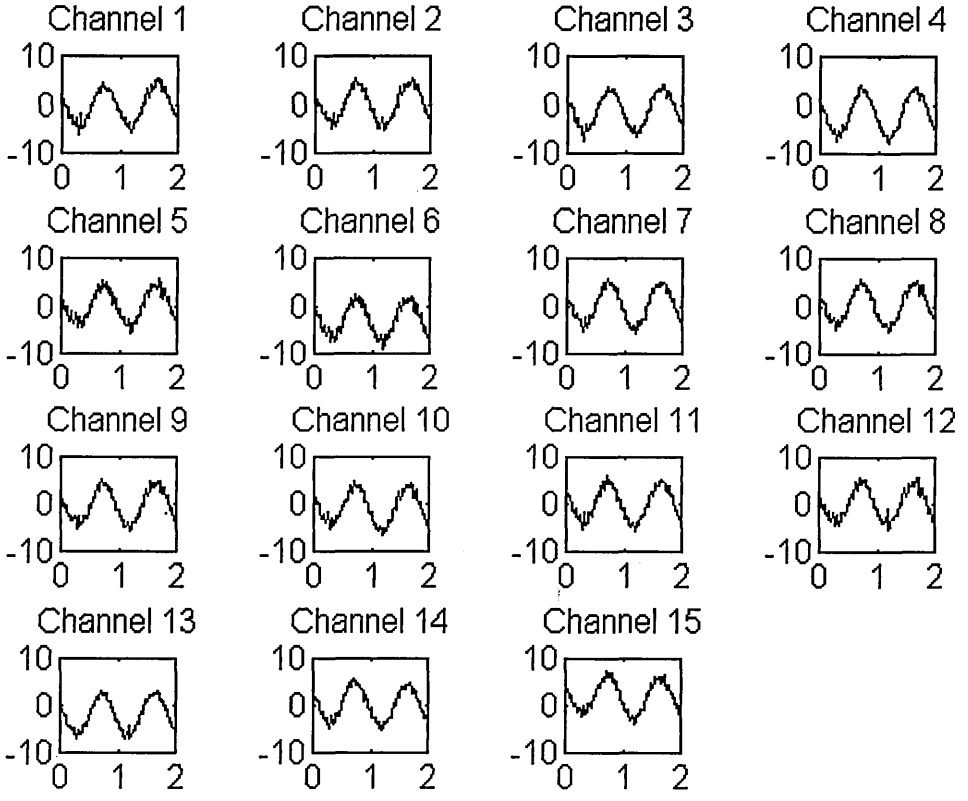
All test signals are clearly recognisable as sine waves. The 1 Hz 100 μV signal has the best signal quality. At higher frequencies there are less samples recorded per signal period leading to a slight reduction in signal quality. More noticeable however is the affect of noise on the 10 μV signals leading to a 'fuzzy' outline for the 0.1 Hz signal and a variation in amplitude for the 10 Hz signal.

The affect of the high pass filter on the amplitude of the 10 Hz signal is also apparent. As this is the cut-off frequency a 10 Hz signal should be attenuated by 3dB.

5.1.2 Channel comparison

To prove that all channels have similar gain and phase characteristics for a given signal, channels 1 to 16 were all connect directly to the test signal generator circuit. A recording was then made with an input signal of magnitude 10 μV and frequency 1 Hz. Figure 5.3 shows the resultant waveforms.

Figure 5.3 Test signal recording comparison for channels 1 to 16

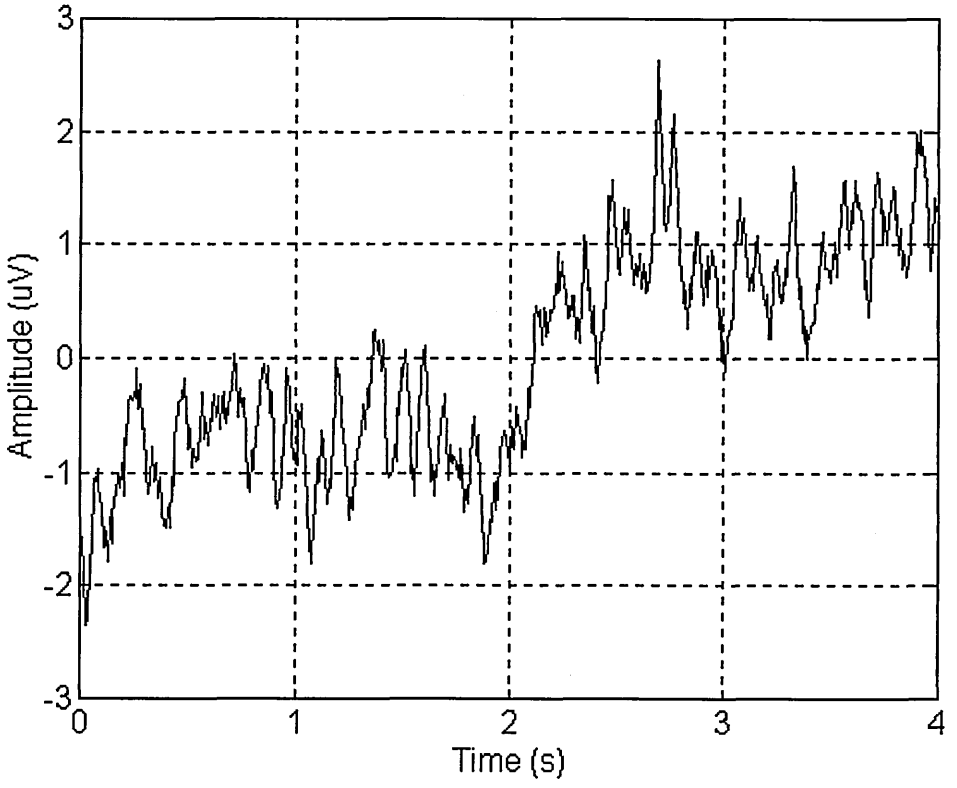


From these plots it is apparent that the waveforms recorded from each channel do not differ significantly from each other.

5.1.3 System noise

The system noise was recorded by connecting the electrode inputs to ground and recording for a period of 4 s. The waveform recorded for a typical channel is shown in Figure 5.4.

Figure 5.4 System noise for channel 1

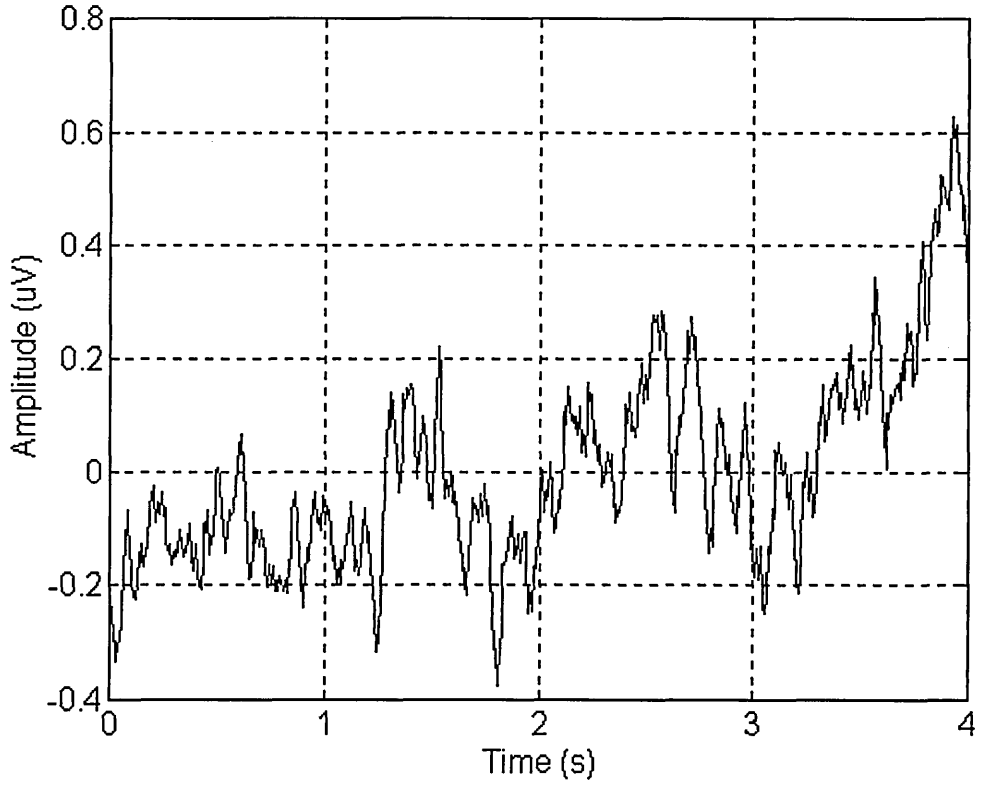


The high frequency noise is of approximate amplitude 1 μV pk-pk and there is also some drift in the recorded signal of 3 μV over the 4 s interval. The minimum value the system noise could be is determined by the pre-amplifier input noise voltage, which for the OP97 operational amplifier is stated as being typically 0.5 μV pk-pk.

In ERP recording it is standard practice to average a number of trials to obtain the final waveform in order to remove recorded noise further. In order to test the

effectiveness of this technique on the system noise the system noise was recorded for 16 trials and the data processed and averaged as if it were ERP data using the Matlab program 'Plotall'. Figure 5.5 shows the resultant waveform.

Figure 5.5 System noise for channel 1 averaged over 16 trials

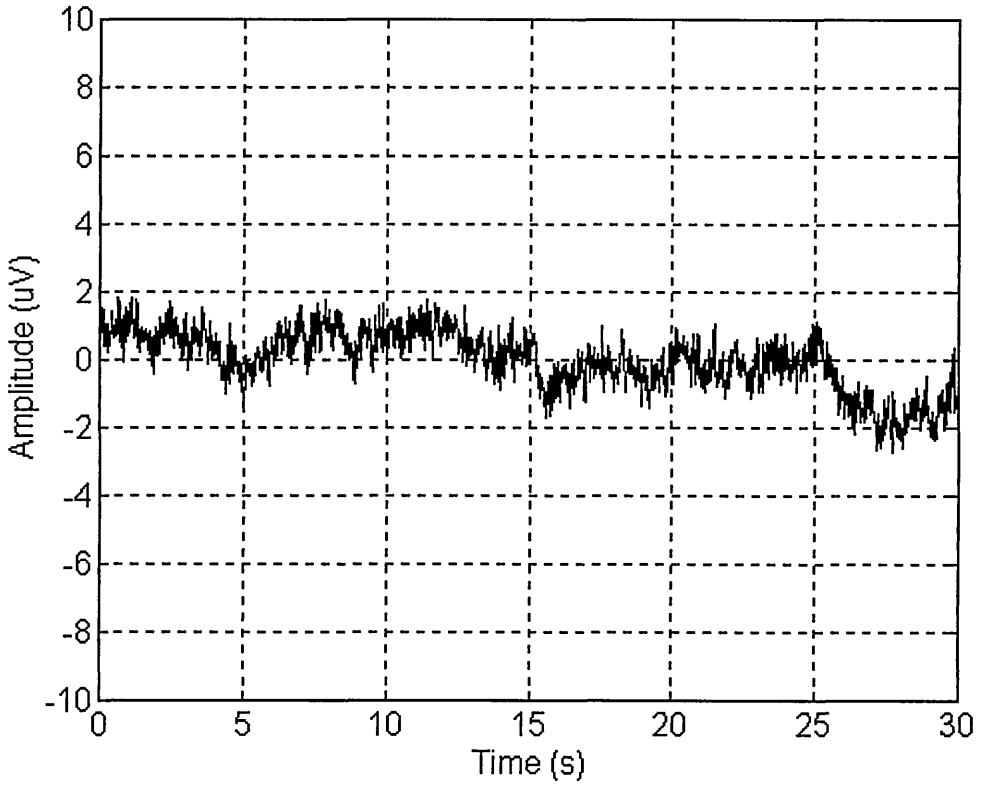


The high frequency noise has now been reduced in magnitude to 0.2 μV and the low frequency drift to 0.7 μV. This demonstrates both the effectiveness of the technique and that the system noise is random. If the system noise were not random, averaging would have no affect on the noise level. The relative reductions in signal magnitude correlate well with the rule that averaging N trials improves the signal to noise ratio by a factor of $\sqrt{N}$, which means that in this instance any random signals would be expected to decrease by a factor of $\sqrt{16} = 4$.

5.1.4 Channel Drift

Channel drift with time was recorded by connecting all channels to ground and recording over a 30 s period The waveform recorded for a typical channel is shown in Figure 5.6.

Figure 5.6 Drift for channel 1



The waveform drifts by approximately ± 2 μV over the 30 s period. This was found to be typical of all the channels recorded.

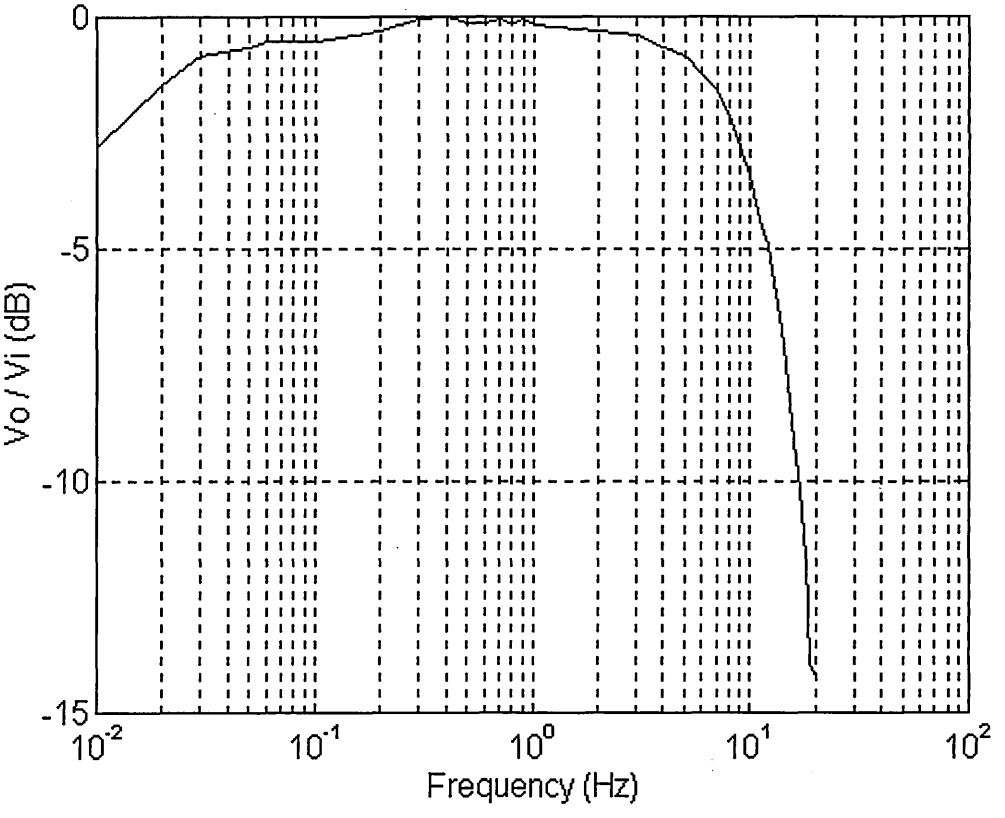
To calculate the total root-mean-square noise of each channel the mean and standard deviation of each channel was calculated for recordings taken over a 30 s period. This figure then includes both drift and high frequency noise. The mean and standard deviation of all the channel noise figures was then calculated and found to be:

Mean channel noise = $0.88 \pm 0.13\ \mu V_{rms}$

5.1.5 Amplitude response of the system

The amplitude response of the system was determined by recording 100 μV test signals over the frequency range 0.01 Hz to 20 Hz. The amplitudes of the recorded signals were then measured relative to the amplitude of the test signal and plotted against frequency to give the graph in Figure 5.7.

Figure 5.7 Amplitude response of channel 1

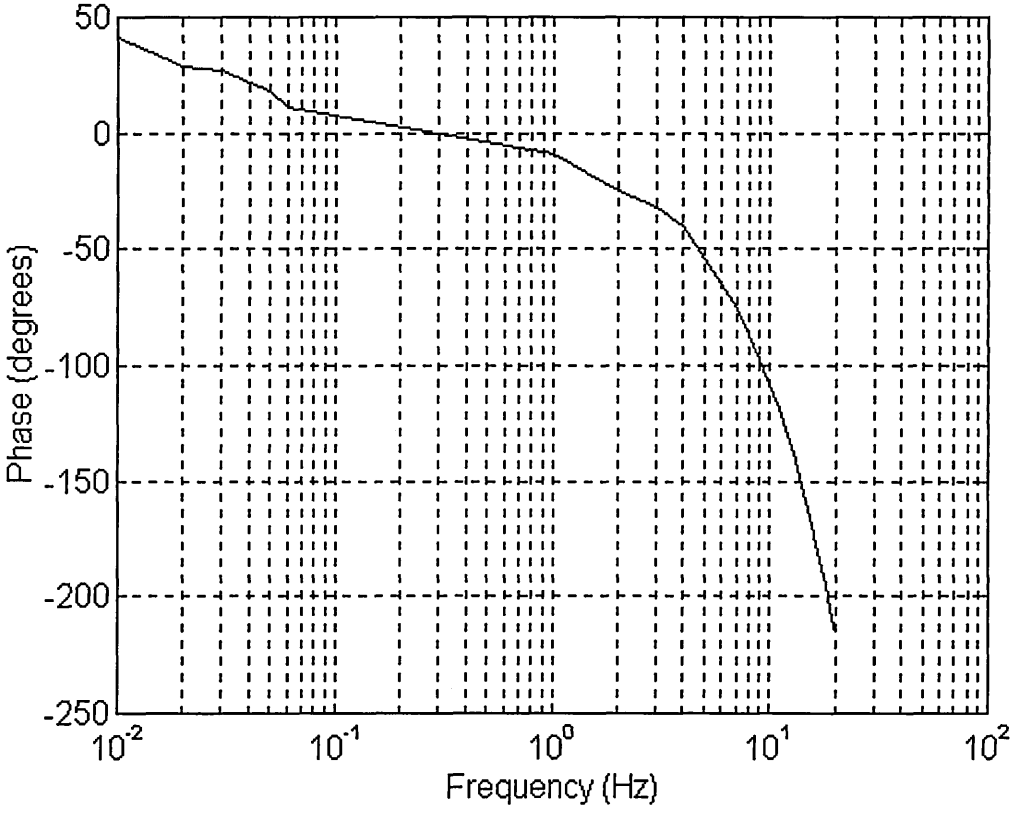


The steep roll-off of the 4 pole low pass Bessel filter is clearly visible at higher frequencies, the output being –3 dB at the cut-off frequency of 10 Hz. In contrast the roll-off of the single pole high pass filter is much more gradual at lower frequencies.

5.1.6 Phase response of the system

The phase response of the system was determined by recording 100 μV test signals over the frequency range 0.01 Hz to 20 Hz. The phases of the recorded signals were then measured and plotted against frequency to give the graph in Figure 5.8.

Figure 5.8 Phase response of channel 1



The results show the system has linear phase characteristics over its bandwidth inducing a constant time delay of 30 ms.

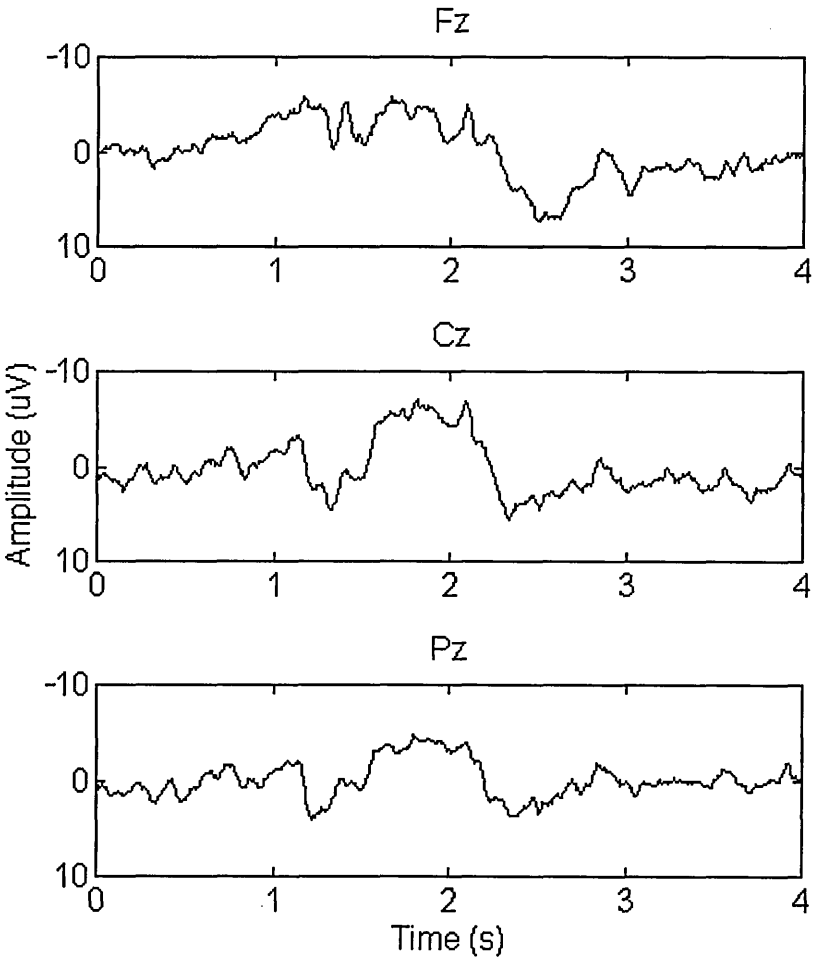
5.2 ERP Recordings

The ultimate test of the ERP system is its ability to record ERPs, specifically the CNV, P300 and BP (of subjects). As these are well defined waveforms, if the system is functioning correctly it should be possible to acquire them from any subject, although there will be some variation between individuals. The recorded waveforms should be comparable to those reported in current literature.

5.2.1 Contingent negative variation

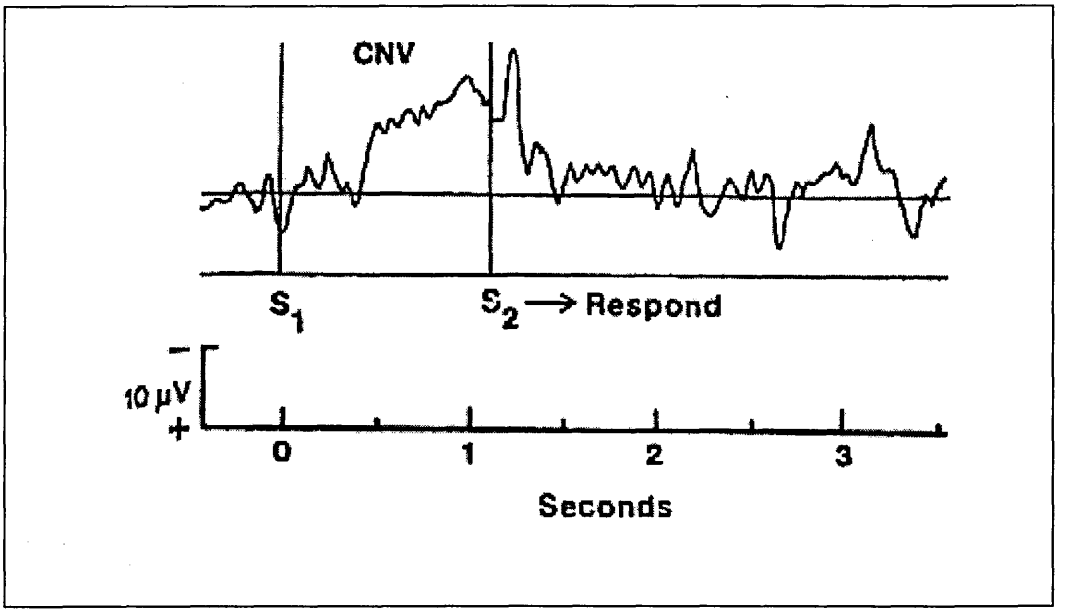
The waveforms of Figure 5.9 were generated from trials recorded from subject FOY1010 using the CNV recording program. Channels 1, 2 and 3 were connected to electrodes attached at sites Fz, Cz and Pz. The reference channel was attached to linked mastoids and isolated ground to a point equidistant between Cz and Pz. A total of 16 trials were recorded of 4 s duration. The warning stimulus was set to occur after 1 s and the target stimulus after 2 s. All of the recorded trials were used in the Matlab program 'Plotall' to generate the final waveforms.

Figure 5.9 CNV recorded from subject FOY1010



The waveforms recorded from all three sites follow the general shape expected of a CNV waveform shown in Figure 5.10. The warning stimulus occurs at 1 s after which the waveforms peak. This is followed by the negative shift characterised by the CNV prior to the target stimulus at 2 s, which leads to a further peak in the waveform, followed by a levelling off. It is apparent that the CNV is largest at Cz, then Pz with Fz showing the waveform of smallest amplitude. This is in accordance with standard literature.

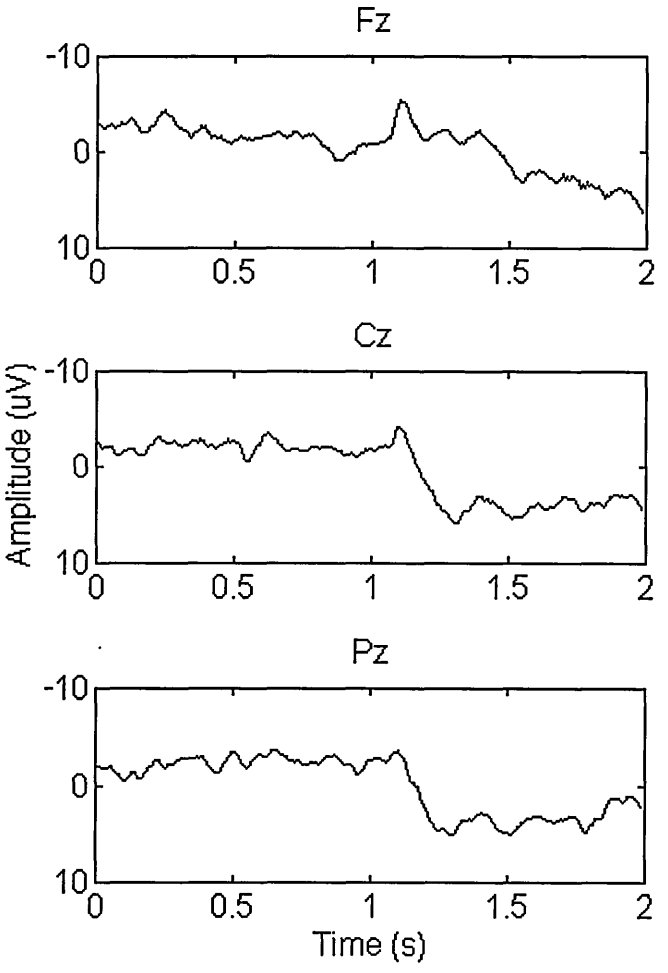
Figure 5.10 Typical CNV waveform



5.2.2 P300

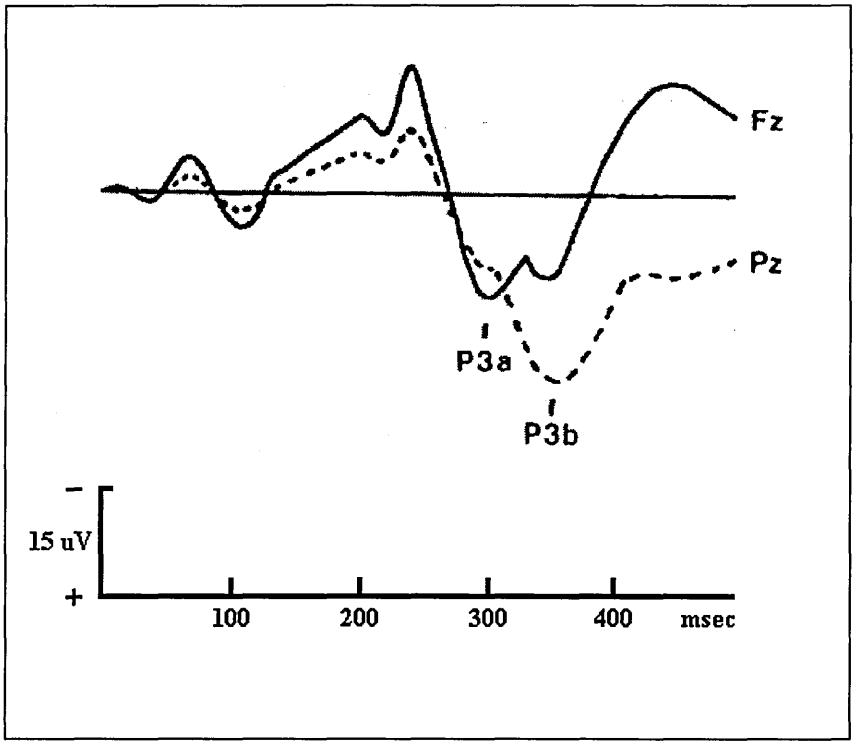
The waveforms of Figure 5.11 were generated from trials recorded from subject FOY1010 using the P300 recording program. Channels 1, 2 and 3 were connected to electrodes attached at sites Fz, Cz and Pz. The reference channel was attached to linked mastoids and isolated ground to a point equidistant between Cz and Pz. A total of 16 trials were recorded of 2 s duration with the target stimulus occurring after 1 s. All of the trials were used in the Matlab program 'Plotall' to generate the final waveforms.

Figure 5.11 P300 recorded from subject FOY1010



The waveforms recorded from all three sites follow the general shape expected of a P300 waveform shown in Figure 5.12. The negative N2 peak is the first feature that is recognisable after the subject response at 1 s. This followed the positive peak of the P300 occurring approximately 300 ms after the response. According to published literature the P3 increases in amplitude from the frontal to parietal scalp areas. There are indications of this distribution with the recorded waveforms in that the recording at Fz, although displaying N2 doesn't have a significant P3 component. Sites Fz and Pz however display a significant P3 component of magnitude 8-9 μV.

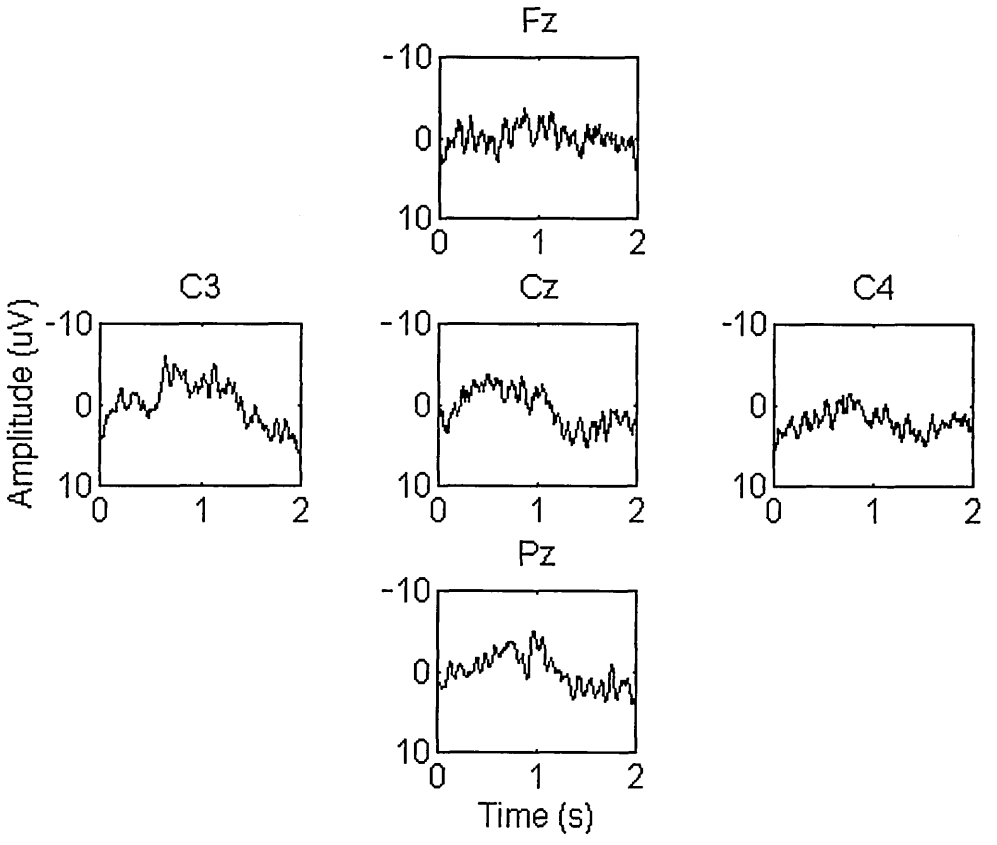
Figure 5.12 A typical P300 waveform



5.2.3 Bereitschaftpotential

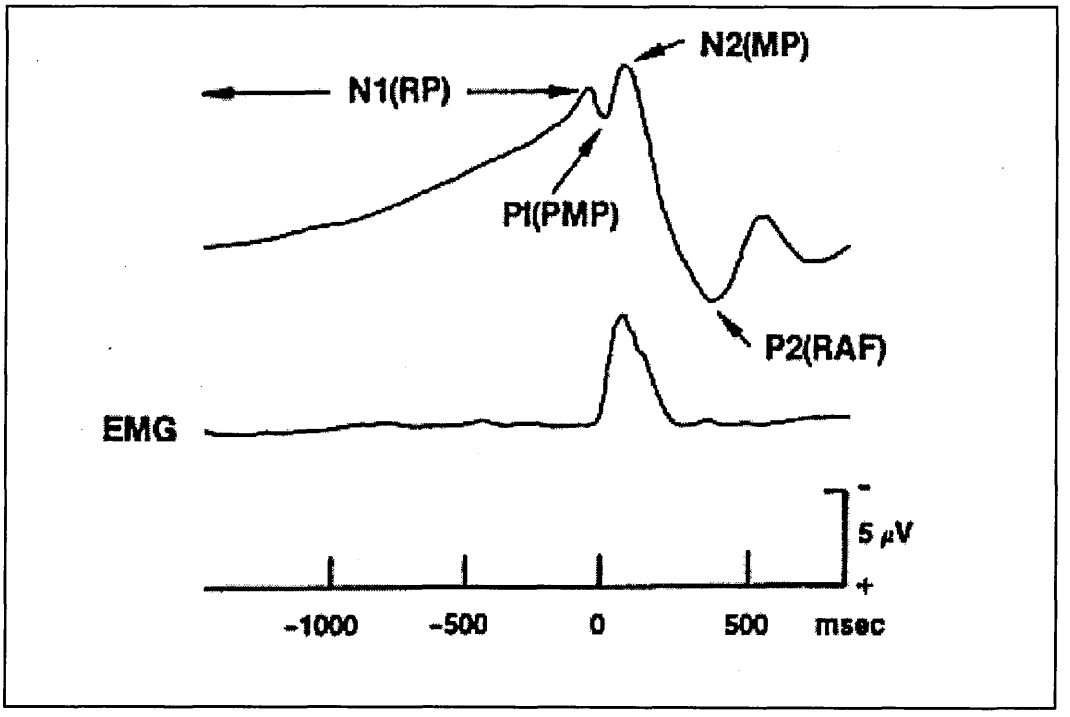
The waveforms of Figure 5.13 were generated from trials recorded from subject ANDY1110 using the BP recording program. Channels 1, 2, 3, 4 and 5 were connected to electrodes attached at sites Fz, Cz, Pz, C3 and C4 respectively. The reference channel was attached to linked mastoids and isolated ground to a point equidistant between Cz and Pz. A total of 16 trials were recorded of 2 s duration with the button press occurring at 1 s. All of the trials were used in the Matlab program 'Plotall' to generate the final waveforms.

Figure 5.13 BP recorded from ANDY1110



Five channels instead of three were recorded for this paradigm to demonstrate the contralateral nature of the waveform. The BP is normally maximal over the vertex and larger over the side of the brain contralateral to the side of movement. Figure 5.13 shows the BP to be larger at Cz than at Fz or Pz and larger at C3 than at C4. As subject ANDY1110 was right-handed this is in accordance with previous findings. Figure 5.14 is a typical BP waveform to compare the recording with.

Figure 5.14 A typical BP recording

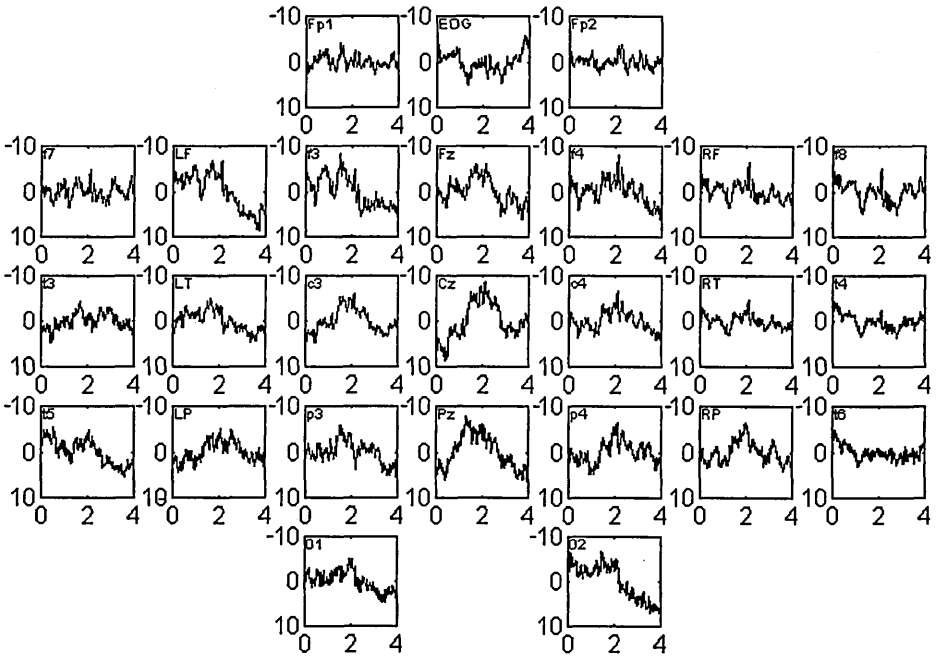


This really just shows shape of the waveform. That is, that it rises gradually to form a peak at the time of movement, which for this recording was at 1 s. Also that the magnitude of the waveform is approximately 5 - 10 μV. Again the shape and magnitude of the BP recorded from subject ANDY1110.bp is comparable with this example.

5.2.4 Twenty eight channel Recording

All previous ERP recordings were made with conventional glued electrodes. This method takes a prohibitively long time to attach large numbers of electrodes. To test the ability of the measurement system to record from a large number of sites simultaneously a head cap with twenty eight fixed electrode positions was used to record the CNV from a subject. Figure 5.15 is a topographical picture of the CNV waveforms recorded from subject ANDY28.cnv.

Figure 5.15 CNV recorded from ANDY28



The CNV waveform is maximal over the midline and seems to show slight asymmetry biased towards the left side of the scalp.

6 CONCLUSION

A dedicated event related potential measurement system has been developed that can simultaneously record waveforms from thirty two separate scalp locations. The simultaneous method of recording ensures maximum correlation between channels, which in addition to the large number of channels enables a more comprehensive study of these waveforms than with commercial systems. Commercial ERP systems currently measure a maximum of eight channels which this is insufficient when investigating ERP topography and current trends are for recording from an increasing numbers of scalp locations generally.

The system can accurately record signals as small as 1 μV and as large as 1 mV. Thus small amplitude ERPs can be recorded accurately as well as larger amplitude signals such as EOGs. The wide dynamic range of the system enables DSP techniques to be applied to ERP recordings containing ocular artefacts in order to remove them, rather than reject contaminated trials.

All channels are simultaneous sampled to maintain the cross-correlation between channels which is essential when performing DSP techniques such as ocular artefact removal and when investigating ERP topography. The bandwidth of the system is also tailored to the recording of these low frequency waveforms. A high pass cut-off frequency of 0.016 Hz ensures that distortion of low frequency components is minimised whereas the low pass cut-off frequency of 10 Hz ensures that any 50 Hz mains interference present is removed. Commercial equipment does not normally record to such low frequencies and little attention seems to be given to signal distortion such as induced time delays. This is important when measuring ERP latencies.

Simultaneous sampling systems would be expected to cost more and be physically larger than multiplexed systems because of hardware duplication. This system is of comparable size to other systems and relatively cheap. Small size is achieved by careful system and PCB design, and cost is reduced by using inexpensive components throughout.

The system meets the relevant safety standard for medical electrical equipment, IEC601-1/BS5724 Part 1, which enables it to be used in hospitals to take recordings from patients with different neurological disorders. Thus it can be used to give insights into the relationship between event-related potentials and different brain diseases or brain abnormalities. This distinguishes the system from being a pure research system to a dedicated research tool. This is also reflected in the fact that the system is portable, low cost/channel and easy to modify for different applications. The system incorporates a number of novel design features that enable it to meet its overall objectives:

1) The pre-amplifiers are inexpensive low noise operational amplifiers configured as non-inverting amplifiers. However a reference signal recorded from the patient is buffered and fed into the amplifier feedback network to give differential amplification of each channel. By amplifying differentially at the input stage any external interference noise is removed immediately. Using conventional operational amplifiers in this configuration instead of instrumentation amplifiers reduces cost.

2) It is common practice to use expensive isolation amplifiers in medical equipment to provide the signal isolation between the patient and the equipment. These use either capacitive coupling or transformer coupling to transfer the signal. This system uses linear optocouplers. These provide 12-bit accuracy and isolation of 4 kV and yet are a lot less expensive in comparison.

3) In order to maximise signal resolution the system incorporates automatic gain adjustment circuitry prior to signal conversion. This comprises of a window detector circuit and a programmable gain amplifier. The window detector circuit identifies the magnitude of the signals and generates control signals that program the gain of the amplifier. These control signals are also output as a two bit digital code that is added to the 12-bit digital data after conversion. The automatic nature of the gain adjustment increases the speed of data conversion and the method of storage of the gain setting enables the data to be stored as one 16-bit word instead of two. The latter reducing the amount of memory required to store the data and the amount of time to read it.

4) All isolated circuitry in the system must be powered from an isolated power source. Isolation amplifier packages tend to have in-built isolated power supplies but these amplifiers are not used in the system to reduce cost. If they were they would still only generate enough power to drive their own circuitry and no other. Alternately isolated dc-dc converters could be used, but versions that are suitable for medical applications are expensive, and several would be required to generate enough power for the entire system. This system solves the problem by using a standard medical power supply to provide power to the isolated circuitry. However it is not connected to earth and installed so that it is double isolated from the non-isolated parts of the system to meet the isolation requirements.

5) Ideally in a system that contains both analogue and digital electronics the two should be kept separated as far as possible to prevent contamination of the analogue signals with digital noise. The placement of the ADC is critical in this respect as it forms the transition between the analogue and digital circuits. It was desirable to site this in the instrumentation system as opposed to the PC because the PC is a very noisy environment. Transferring the analogue signals from the instrumentation system to the

PC would also subject them to external noise sources as well. However having the ADC internal to the instrumentation system requires more signal lines between the PC and the instrumentation system. To reduce the total number of lines required, the PC data bus was buffered and extended to the instrumentation system. This enables the ADC and PIA, which are internal to the instrumentation system, to be operated as if they are internal to the PC.

The equipment can record signals as small as 1 μV enabling the accurate comparison of signals recorded from different locations or different subjects. However the equipment can also record signals as large as 1 mV enabling any artefacts that occur during recording to be recorded for the purposes of ocular artefact rejection.

The equipment can also generate stimuli in the form of tones and clicks and record subject responses via a pushbutton. The functions are provided in the form of a detachable hand held patient interface. If necessary alternative forms of this device can be developed to generate alternative stimuli or record alternative responses.

The system is portable and is controlled by a standard PC fitted with a mass storage device on which to store the data. This enables the instrument to be moved to different sites and used with alternative PCs if necessary.

The system software has been developed to record the standard ERPs: the CNV, P300 and BP. Tests have shown that the system can record these accurately and reliably from different subjects as the recorded waveforms match the standard waveforms found in current literature.

6.1 Future work

The recording system could be enhanced by developing the software to improve the user interface and graphical display features. Both of these are very basic as they were developed from test programs and found to be sufficient for recording standard paradigms.

The user interface could include more user selectable program parameters such as the number of trials to be recorded, the duration of each trial and inter-stimulus intervals. These currently have to be edited in the source code and therefore require the operator to have some knowledge of the program. If these parameters were to be entered in the user interface prior to recording more error checking code would also have to be added to check the validity of the parameters. The P300 recording function could be improved by the addition of a pseudo-random sequence generator. This could be initiated prior to recording to generate a unique sequence of 1's and 0's, representing the sequence of high and low tones to be presented during the recording. The operator could set the proportion of high to low tones along with the other recording parameters. The operation of the BP recording function could also be improved by recording continuously over a fixed area of memory, and then using the subject response to give a reference point from which to re-organise the data to give the required pre-response and post-response recording periods.

The graphical display could be improved by the addition of x and y-axes representing amplitude and time displacement. Waveform labels could also be included to show the topographical location of each displayed signal. A real time display of the waveforms should also be possible, particularly if the control PC was upgraded to a faster microprocessor so that it executed instructions faster. It would then also be

possible to perform real-time digital signal processing of the recorded data. For instance signal averaging could be performed at the end of each trial and the averaged waveforms displayed and updated. This could be useful to an operator as it would enable them to decide when enough trials had been recorded from a particular subject to give a useable waveform. If ocular artefact removal were also performed at the end of each trial, prior to displaying the waveforms, this could also assist in minimising the number of recorded trials per subject. A topographical display of the waveforms could also be shown in real-time. This could display individual trials, the average of all trials or variation in amplitude as a change in colour at each recording site.

In addition to improved graphical displays ERP data such as peak amplitude and latency could also be presented at the end of each trial as well as response times. Running averages could also be calculated if required. All of these functions require the PC to perform additional digital signal processing during the recording process which requires a faster microprocessor to execute the additional instructions if the recording process is not to be compromised.

For a much more modern interface the control software would have to be re-written in a visual programming language such as Visual Basic, Visual C or Delphi. This would present the operator with a windows based graphical user interface that is becoming more common on all instrumentation. Recording parameters could then be entered in a configuration menu prior to recording and any variation of user selectable displays presented in windows during the trials.

Additional software could also be written to generate alternative paradigms, either variants of the existing ones, or to record different ones. For instance visual stimuli may be required for more complex differentiation testing in the P300 paradigm. This could be achieved by using another PC to present the subject with visual stimuli

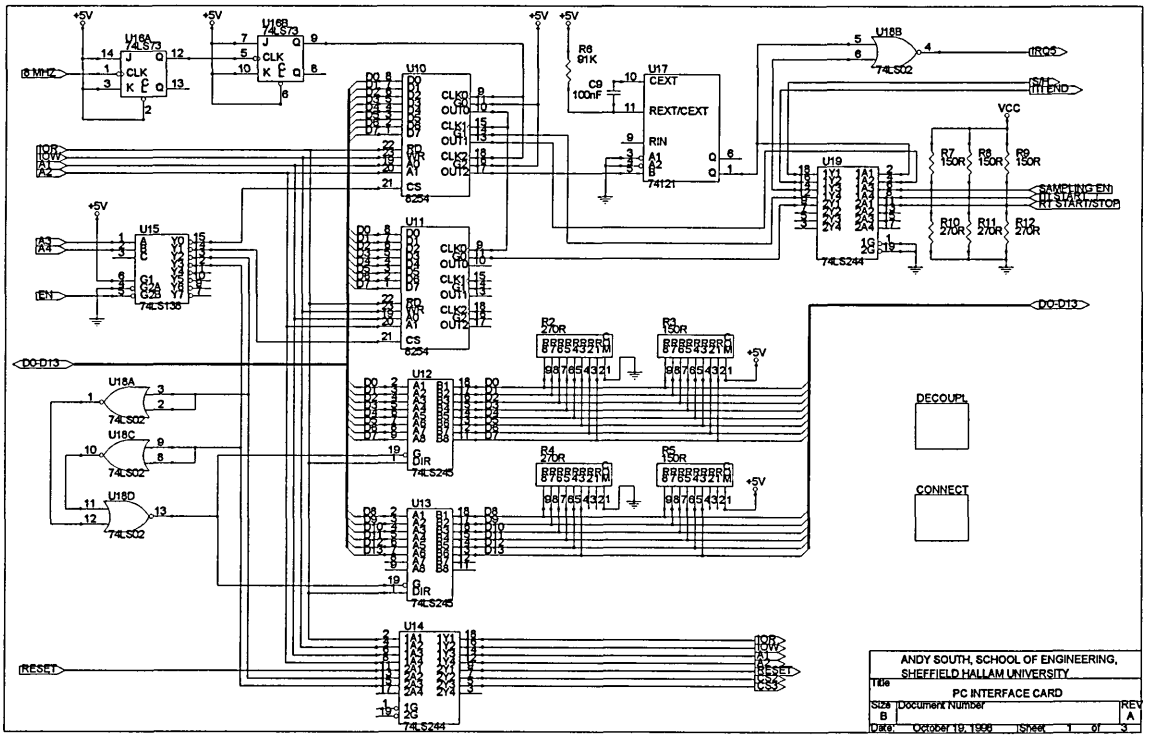
when requested by the instrumentation PC. If alternative paradigms are required alternative forms of the patient interface may also be required to generate the stimuli and record subject responses.

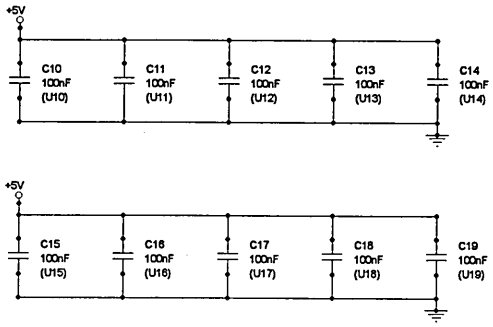
Changes to the instrumentation system hardware could take the form of reducing the overall size of the system by using surface mount components throughout rather than conventional types. This would reduce the size of each PCB and hence the size of the enclosure required to house them. The head-box, instrumentation sub-system and patient interface could be substantially reduced in size if this were done. The latter is particularly important as some subjects found it difficult to hold the patient interface because of its size and shape. The use of surface mount components on all boards would also enable the PCB ground planes to be improved that would minimise the affect of interference noise.

The noise immunity of the headbox may also be improved if the inside of the box was coated with a conductive paint that is connected to ground. This would act as protective shield around the sensitive pre-amplifier circuitry. The internal wiring of the instrumentation sub-system could be improved by using a back-plane to provide the inter-board connections With low cost instrumentation amplifiers now being widely available the pre-amplifier board could now be re-designed with these as direct replacements for the OP97 pre-amplifiers. This would have the beneficial affect of increasing the common mode rejection ration at this stage.

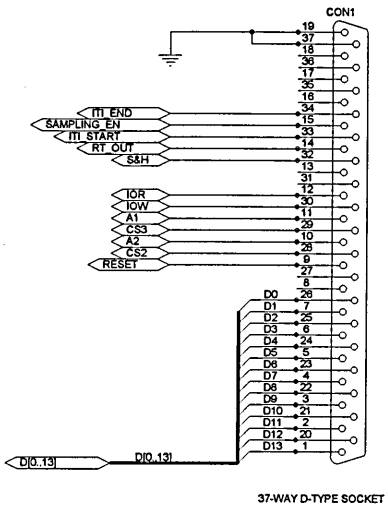
7 APPENDICES

7.1 PC Interface Card Circuit Diagrams





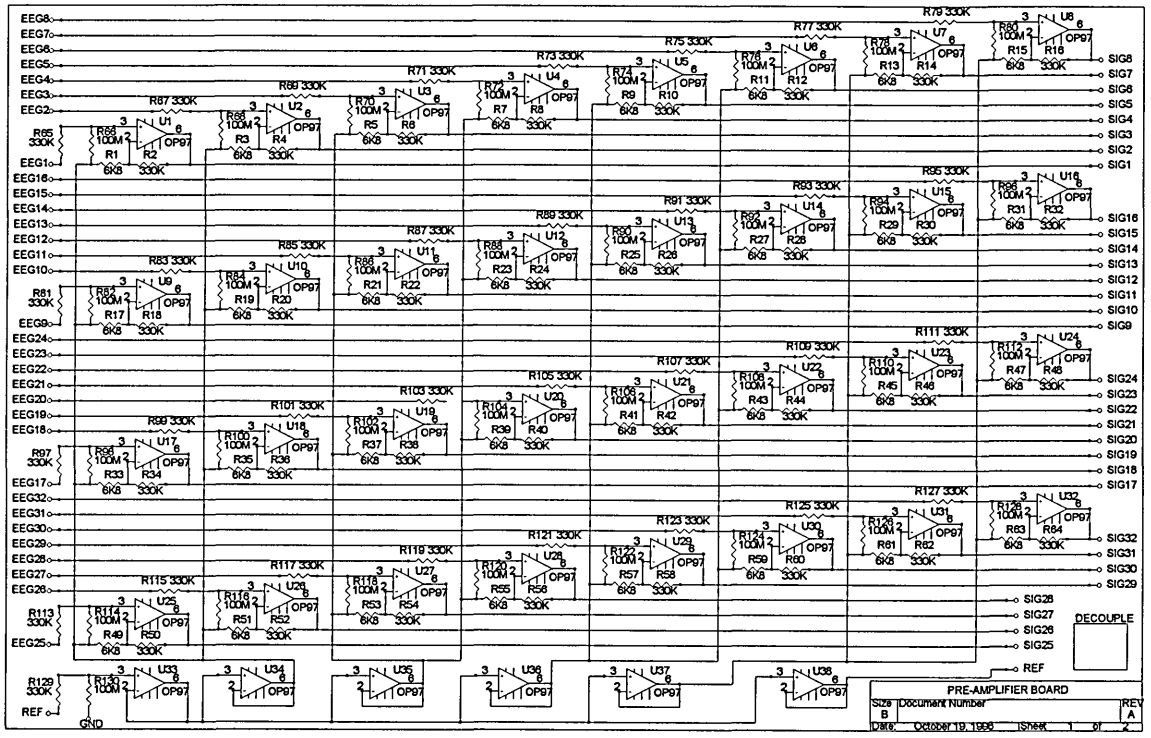
ANDY SOUTH, SCHOOL OF ENGINEERING, SHEFFIELD HALLAM UNIVERSITY				
Title: INTERFACE CARD ELECTRICAL DECOUPLING				
Size: A	Document Number			REV: A
Date: October 19, 1998	Sheet 2 of 3			

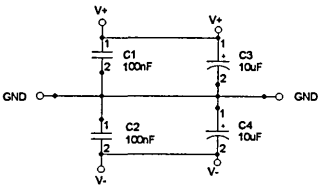


37-WAY D-TYPE SOCKET

ANDY SOUTH, SCHOOL OF ENGINEERING, SHEFFIELD HALLAM UNIVERSITY					
Title: INTERFACE CARD EXTERNAL CONNECTIONS					
Size: A	Document Number				REV: A
Date: October 19, 1998		Sheet 3	of	3	

7.2 Pre-amplifier Board Circuit Diagrams

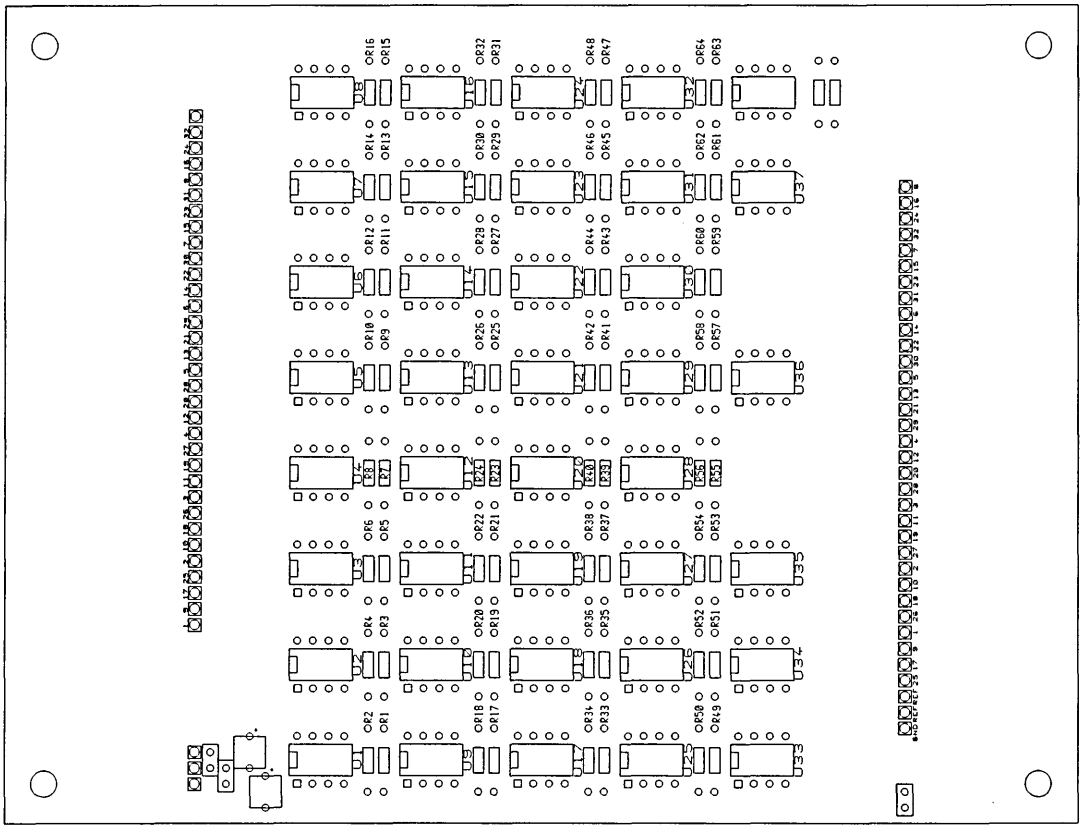




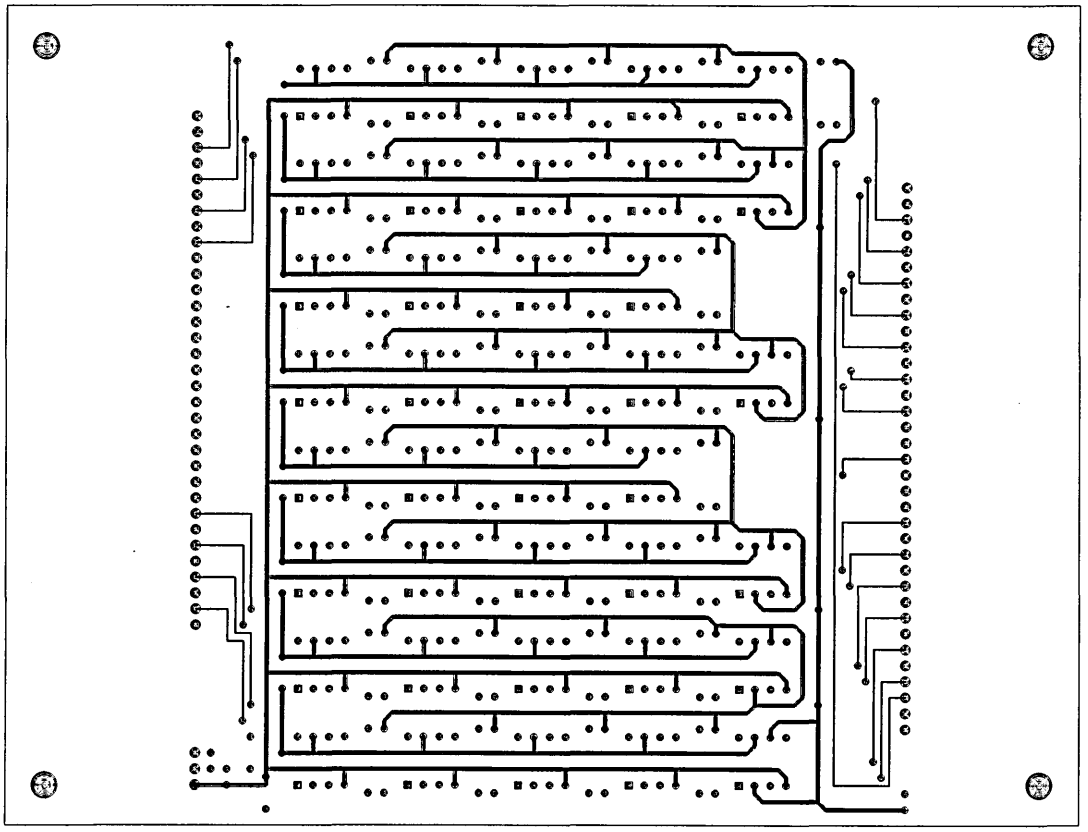
ANDY SOUTH, SCHOOL OF ENGINEERING, SHEFFIELD HALLAM UNIVERSITY			
Title: PRE-AMP BOARD ELECTRICAL DECOUPLING			
Size: A	Document Number:		REV: A
Date: October 18, 1998	Sheet 2 of 2		

7.3 Pre-amplifier Board Layout

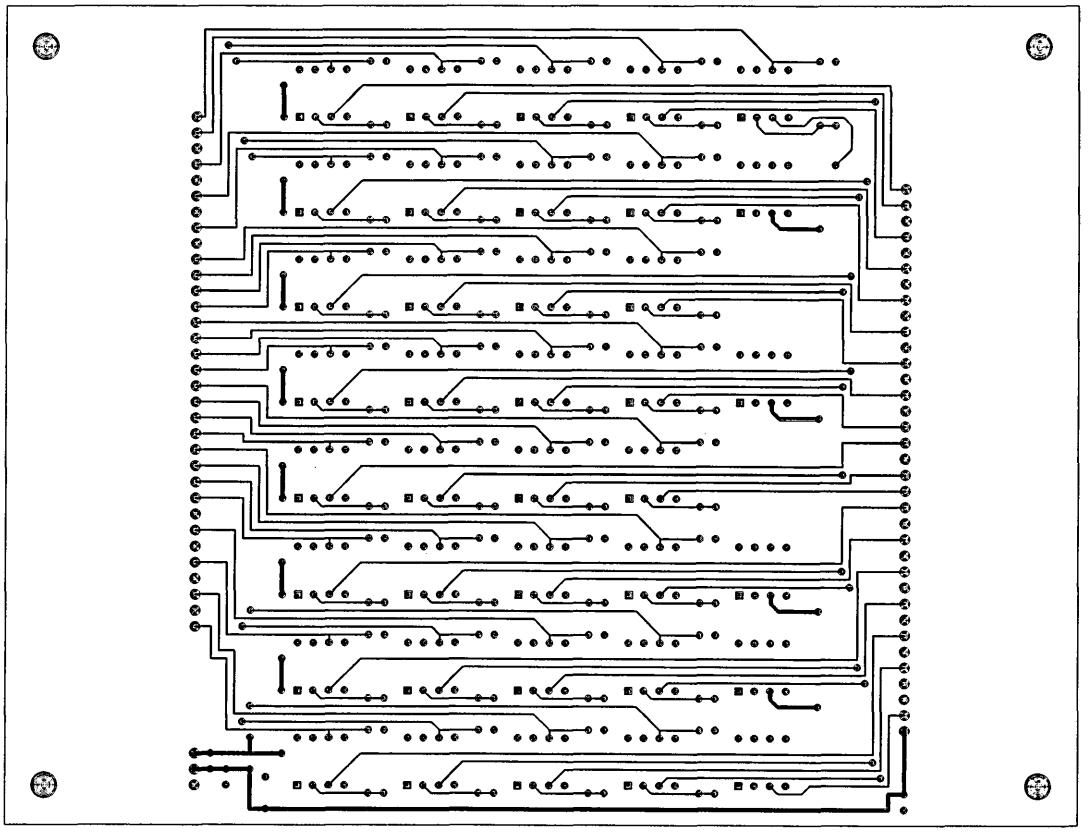
Component Side Silk Screen



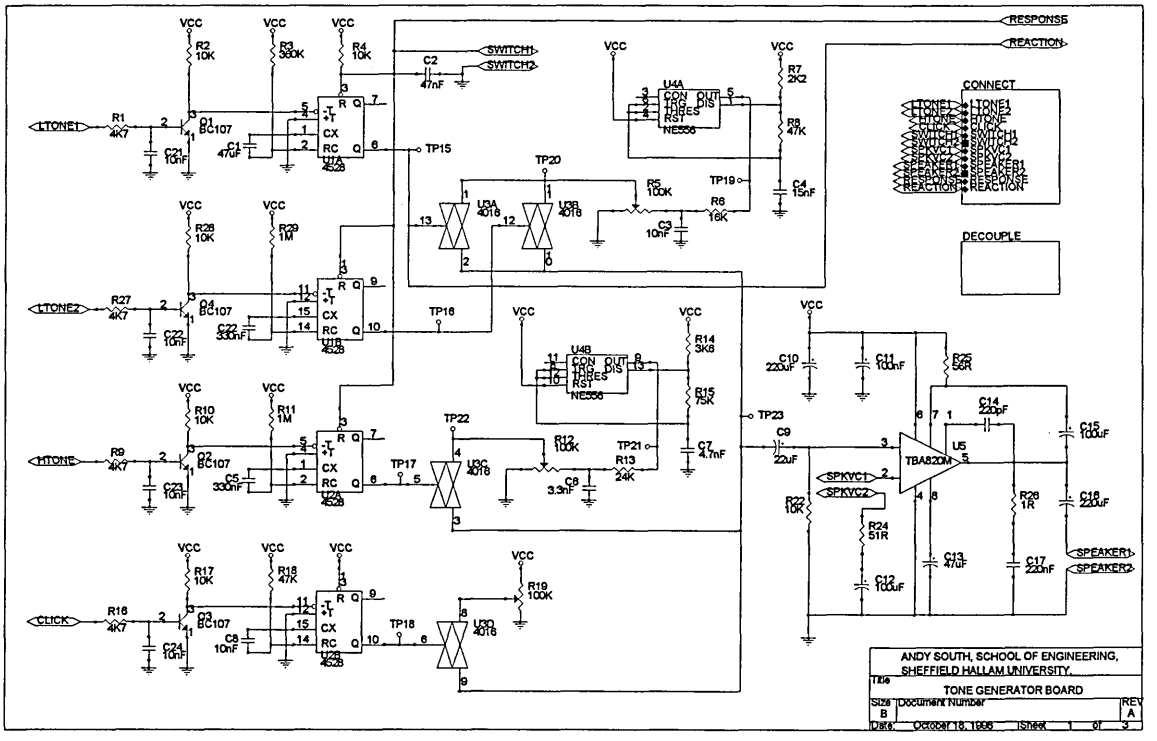
Component Side Copper

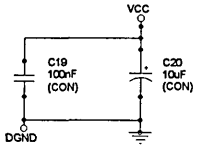


Solder Side Copper

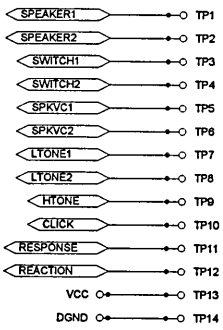


7.4 Tone Generator Board Circuit Diagrams





ANDY SOUTH, SCHOOL OF ENGINEERING, SHEFFIELD HALLAM UNIVERSITY.			
Title: TONE GENERATOR BOARD ELECTRICAL DECOUPLING			
Size: A	Document Number:		REV: A
Date: October 18, 1996	Sheet 2 of 3		



ANDY SOUTH, SCHOOL OF ENGINEERING,
SHEFFIELD HALLAM UNIVERSITY.

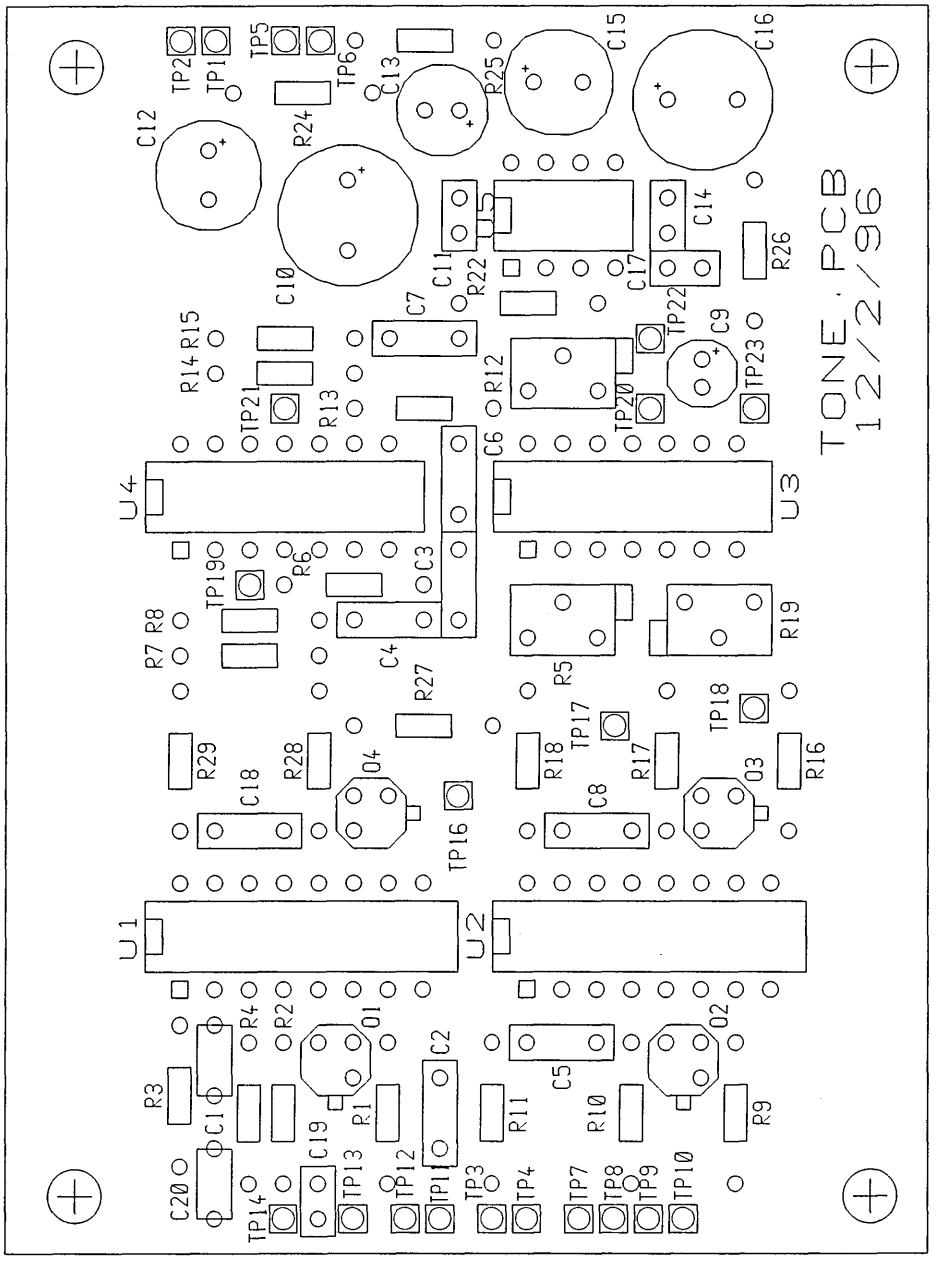
Title
TONE GENERATOR BOARD EXTERNAL CONNECTIONS

Size	Document Number	REV
A		A

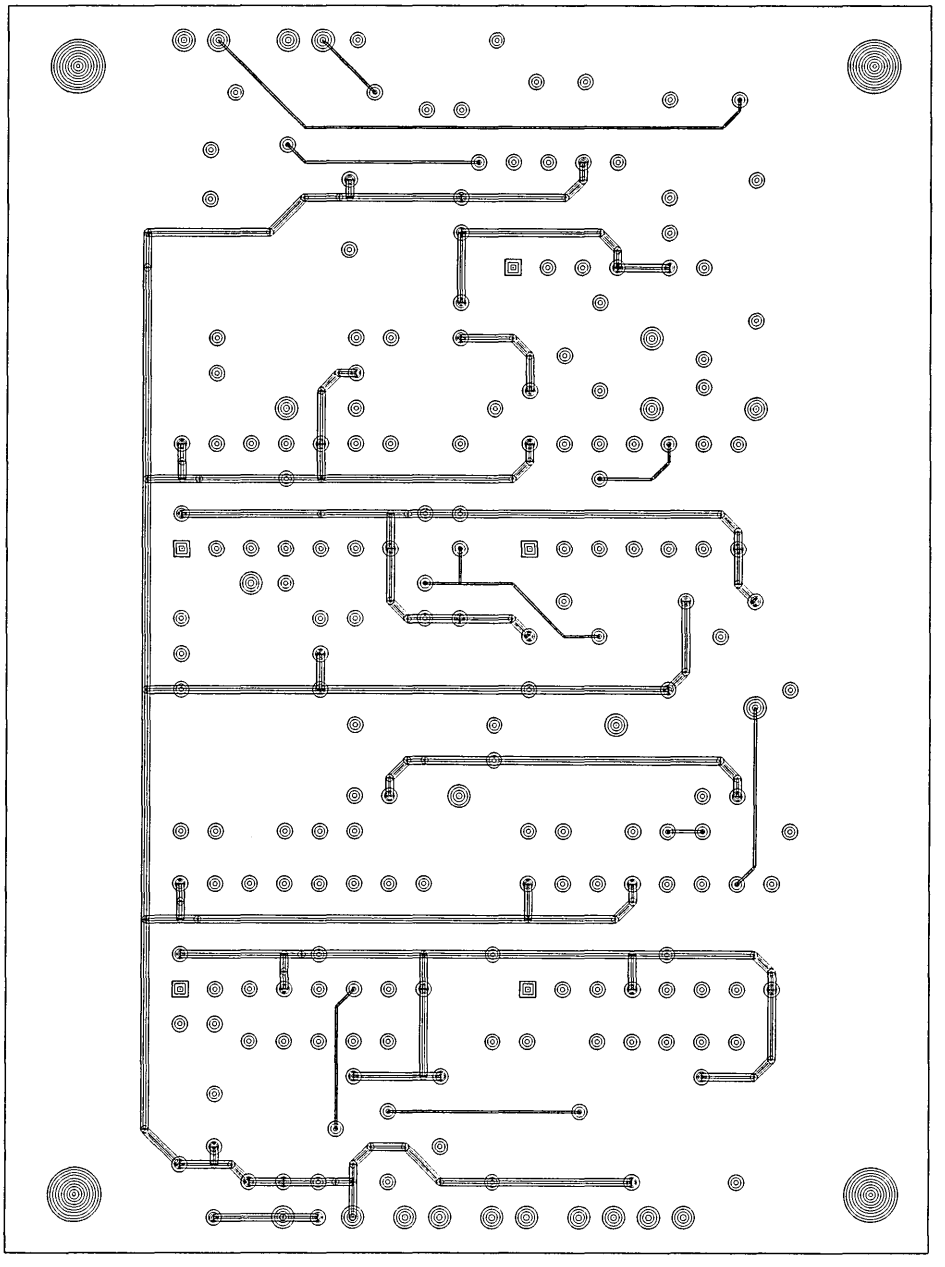
Date: October 18, 1998 Sheet 3 of 3

7.5 Tone Generator Board Layout

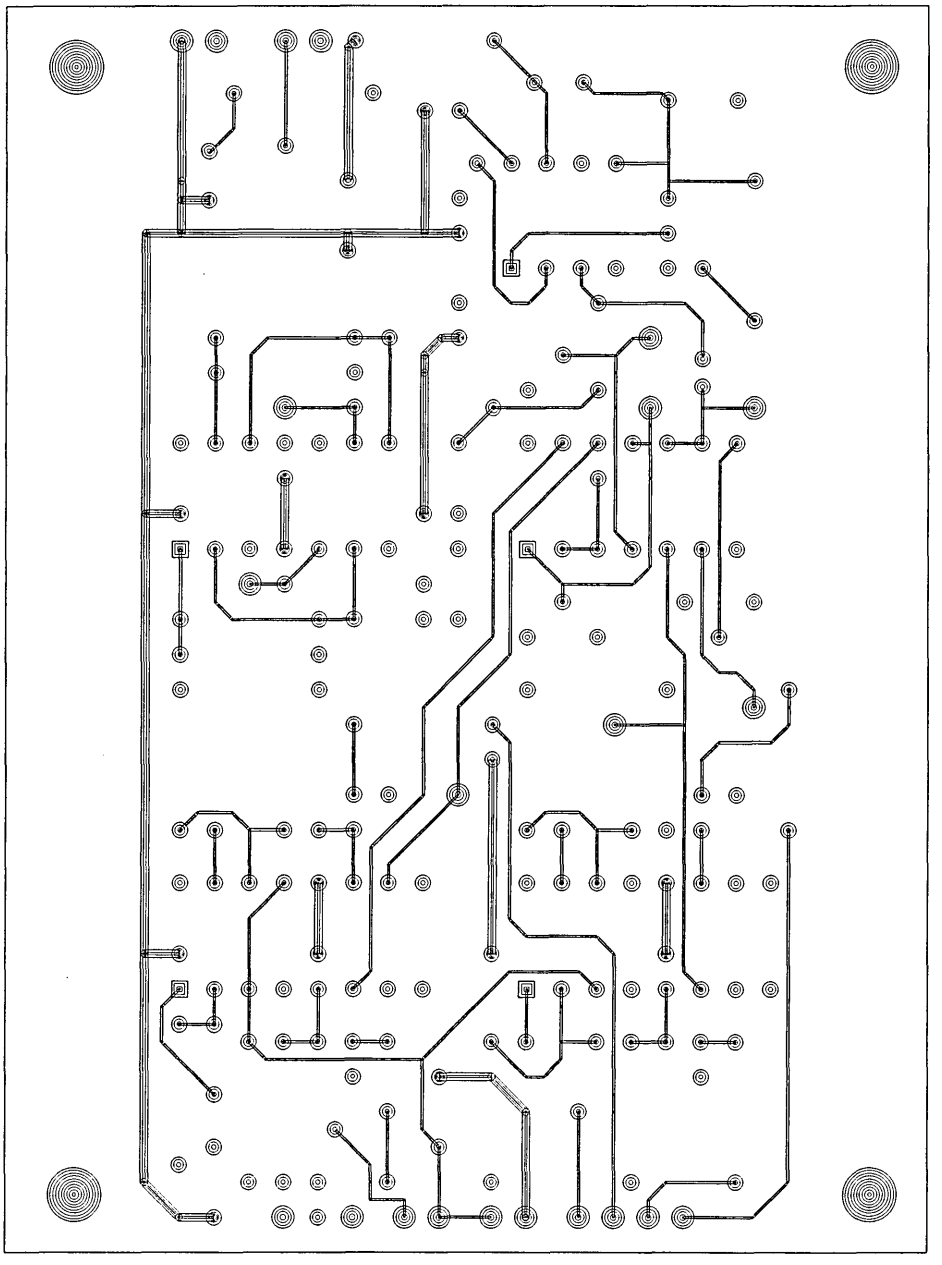
Component Side Silk Screen



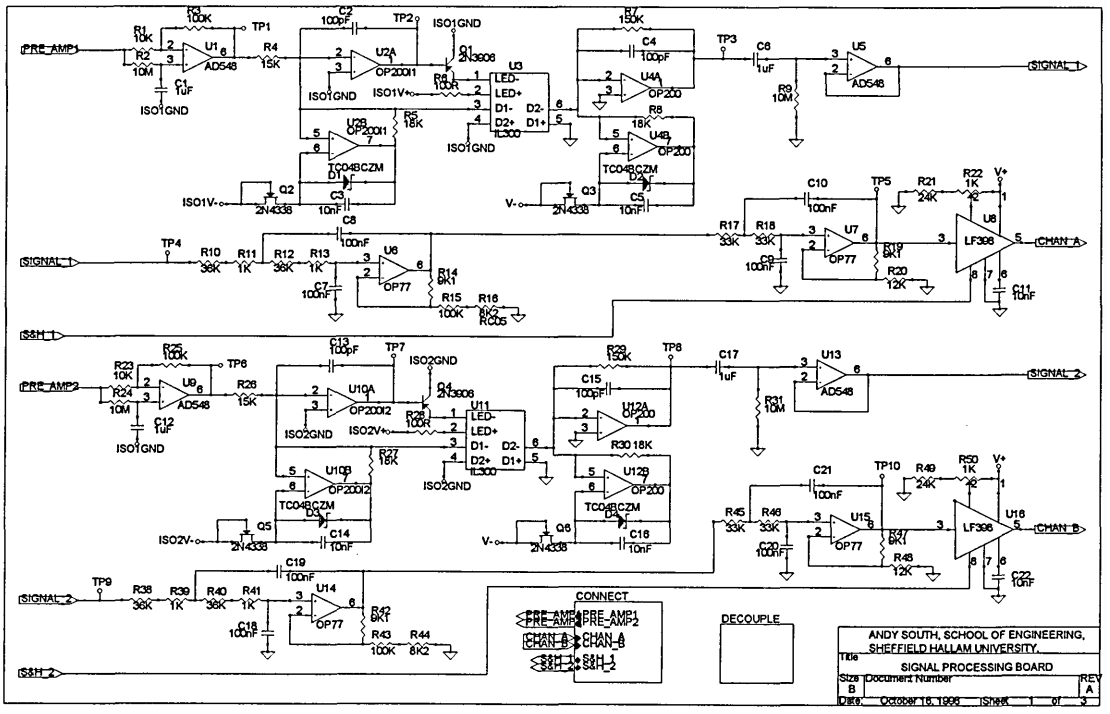
Component Side Copper

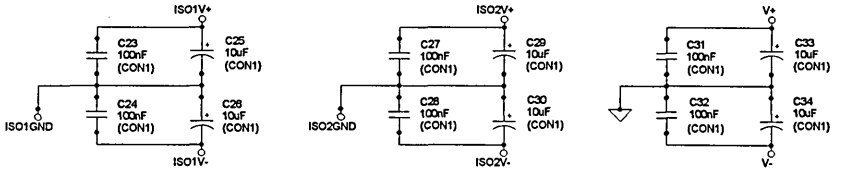


Solder Side Copper

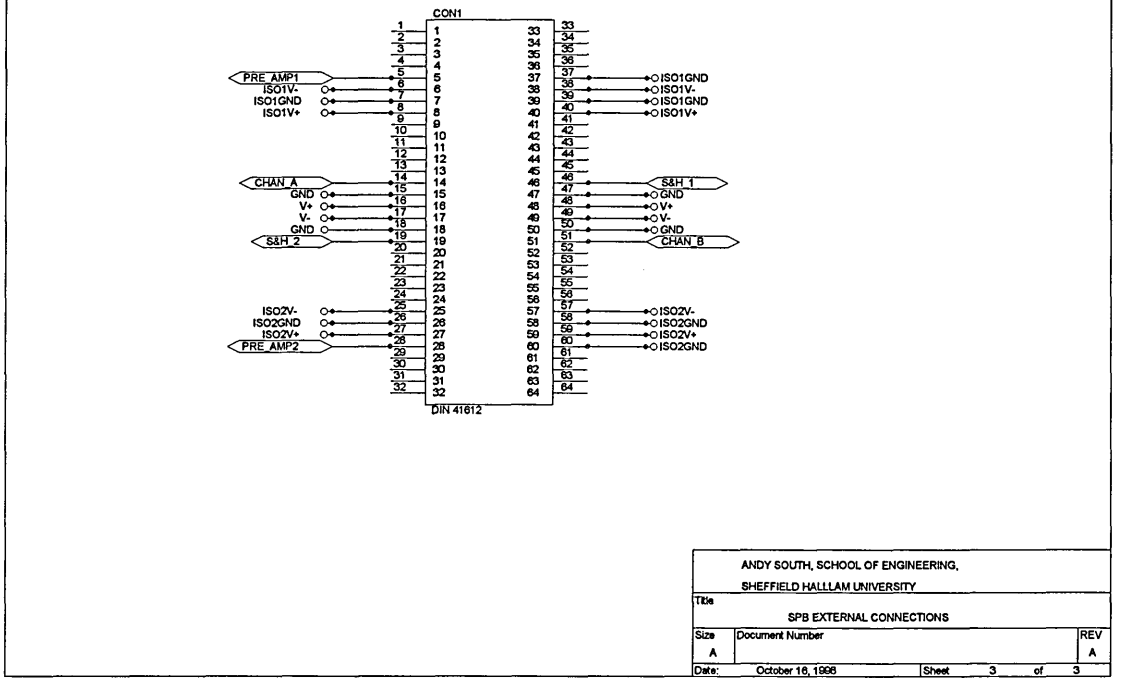


7.6 Signal Processing Board Circuit Diagrams





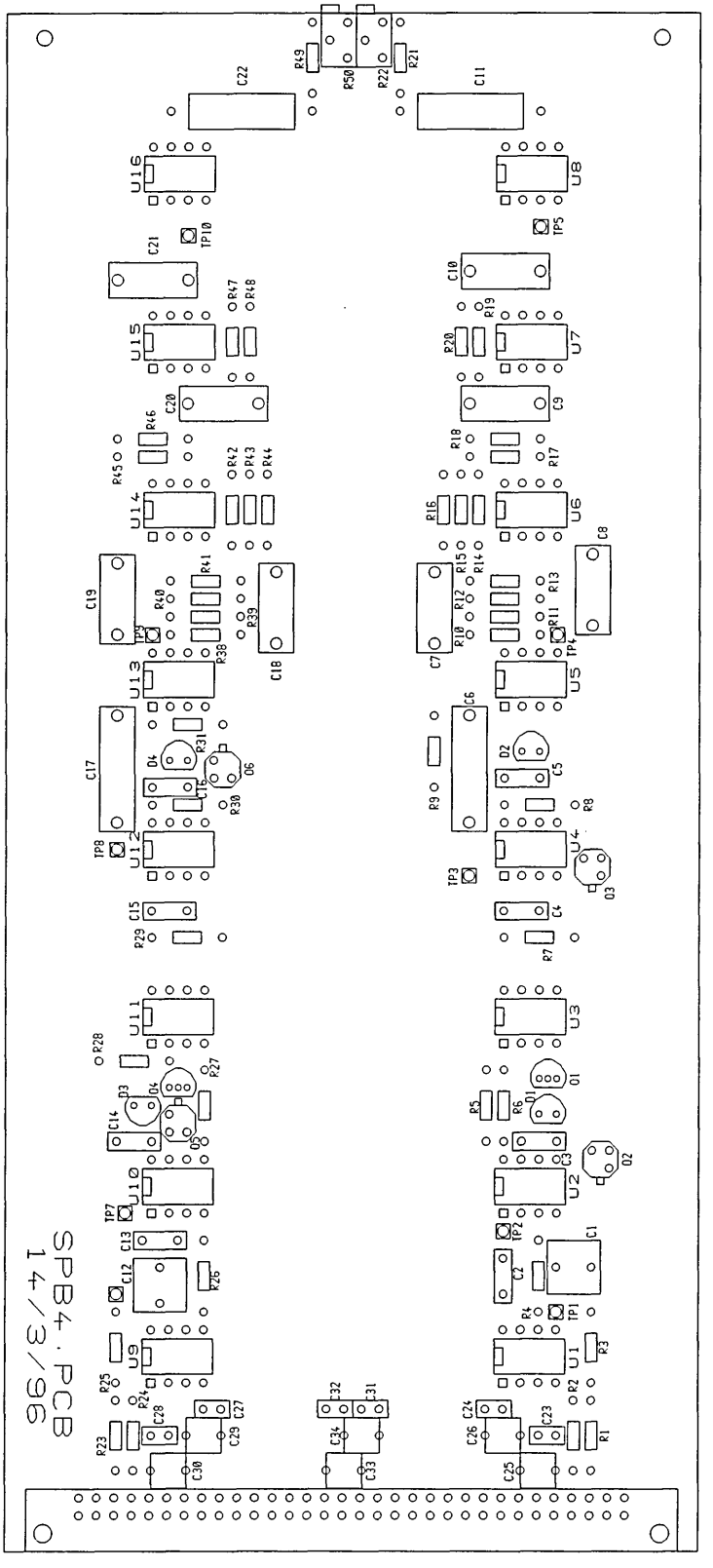
ANDY SOUTH, SCHOOL OF ENGINEERING, SHEFFIELD HALLAM UNIVERSITY.			
Title: SPB ELECTRICAL DECOUPLING			
Size: A	Document Number		REV: A
Date: October 16, 1998	Sheet 2 of 3		



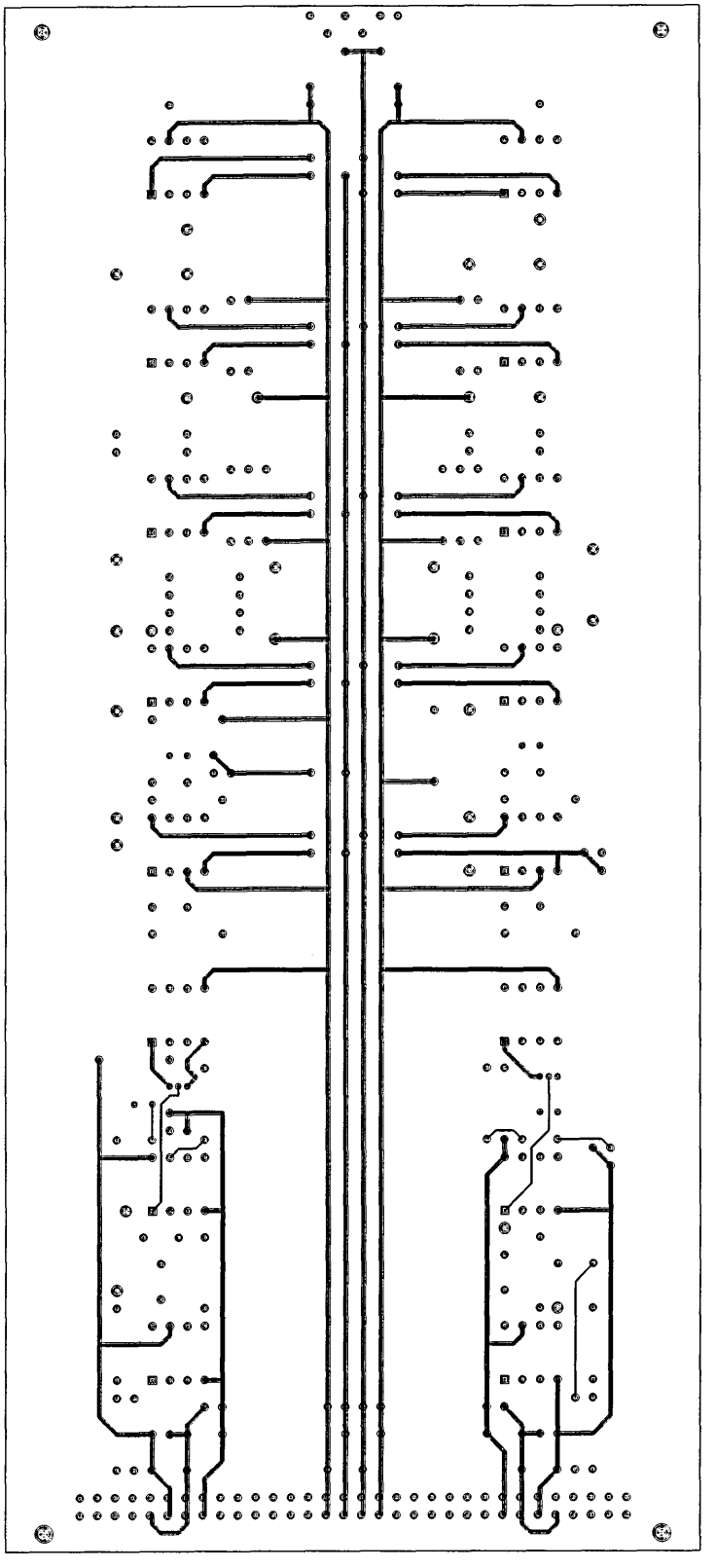
ANDY SOUTH, SCHOOL OF ENGINEERING, SHEFFIELD HALLLAM UNIVERSITY			
Title: SPB EXTERNAL CONNECTIONS			
Size: A	Document Number		REV: A
Date: October 16, 1998	Sheet 3 of 3		

7.7 Signal Processing Board Layout

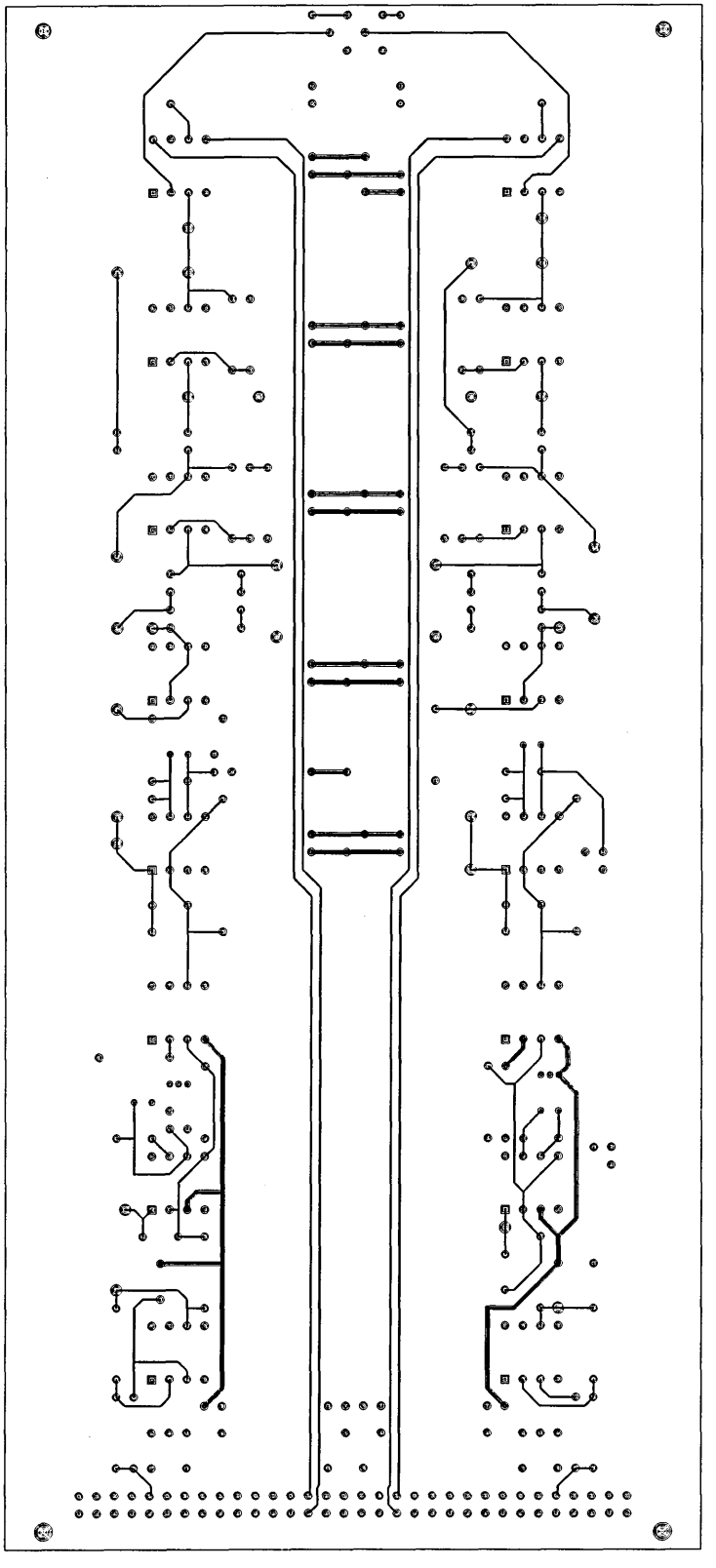
Component Side Silk Screen



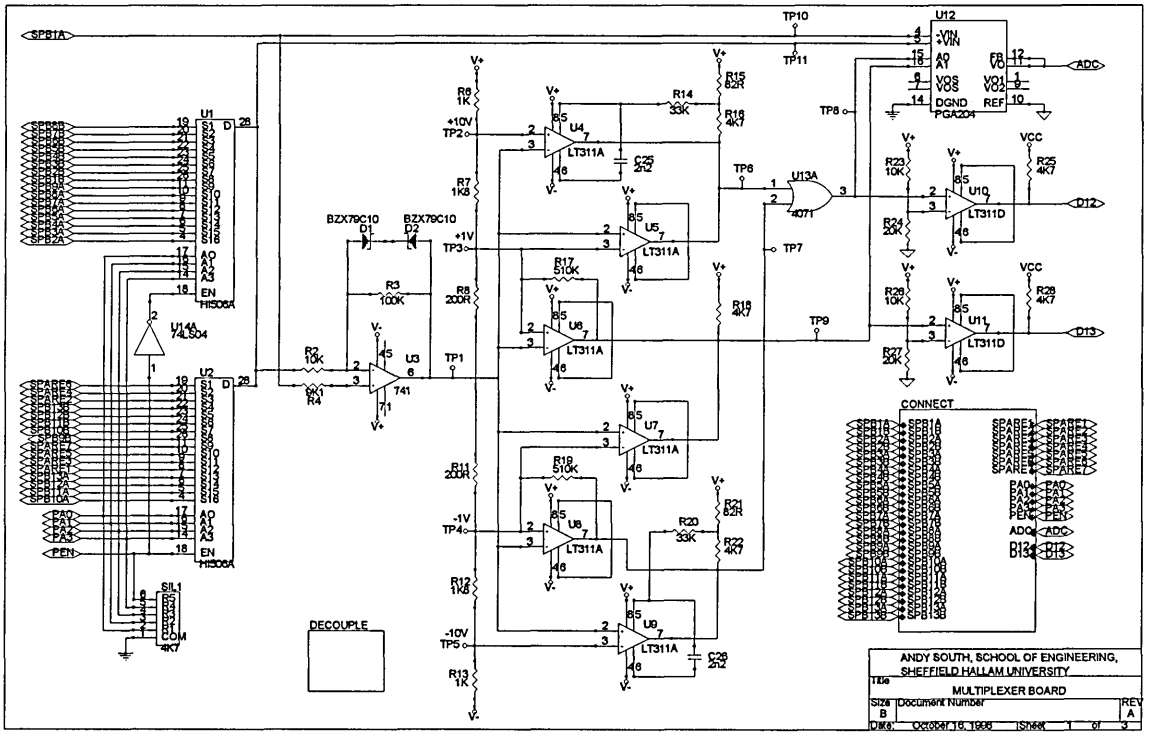
Component Side Copper

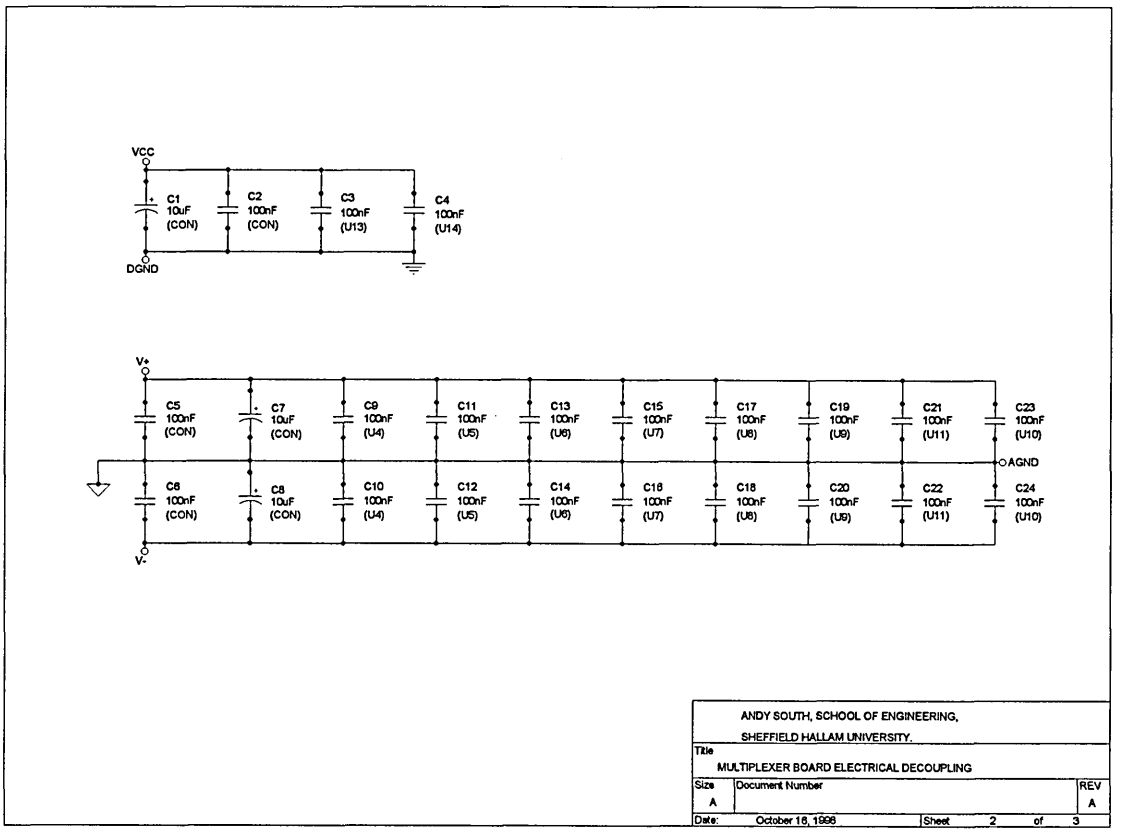


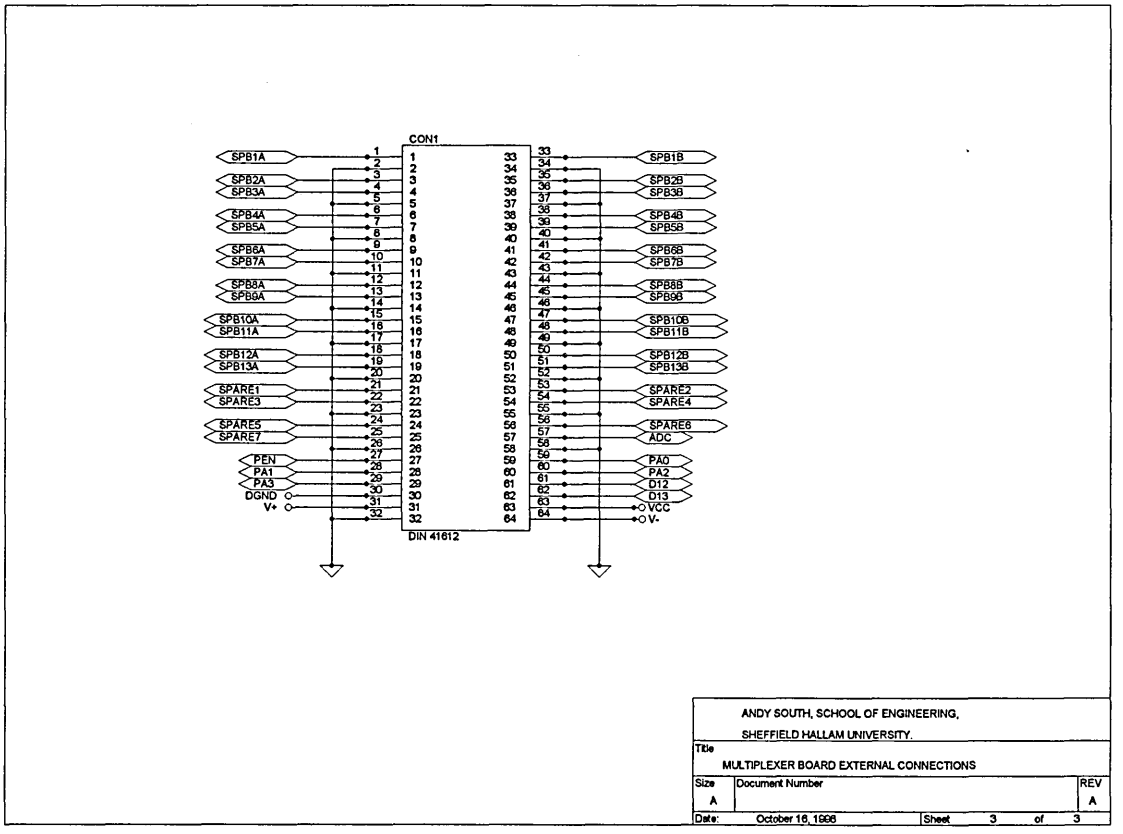
Solder Side Copper



7.8 Multiplexer Board Circuit Diagrams



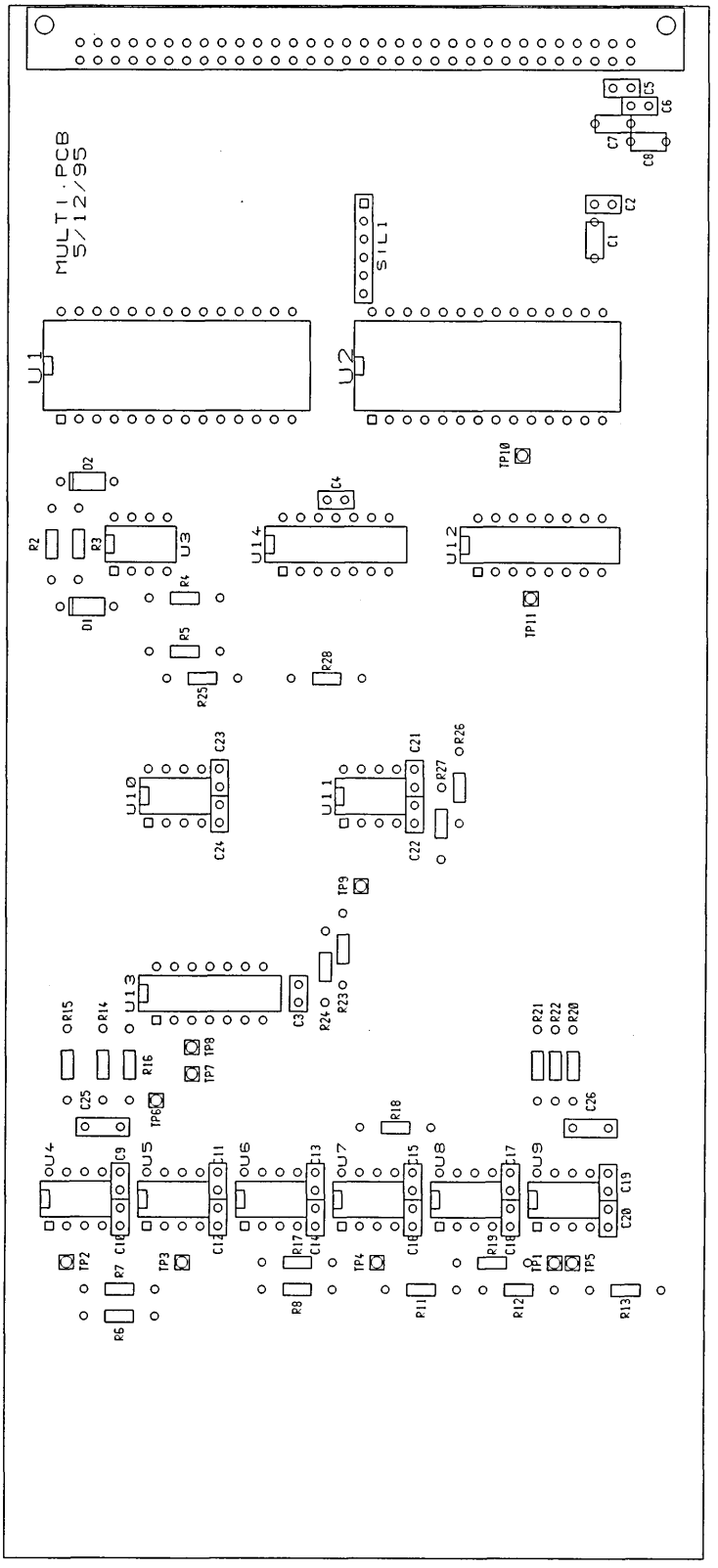

VCC
C1
10uF
(CON)
C2
100nF
(CON)
C3
100nF
(U13)
C4
100nF
(U14)
DGND
V+
C5
100nF
(CON)
C7
10uF
(CON)
C9
100nF
(U4)
C11
100nF
(U5)
C13
100nF
(U6)
C15
100nF
(U7)
C17
100nF
(U8)
C19
100nF
(U9)
C21
100nF
(U11)
C23
100nF
(U10)
AGND
C6
100nF
(CON)
C8
10uF
(CON)
C10
100nF
(U4)
C12
100nF
(U5)
C14
100nF
(U6)
C16
100nF
(U7)
C18
100nF
(U8)
C20
100nF
(U9)
C22
100nF
(U11)
C24
100nF
(U10)
V-
ANDY SOUTH, SCHOOL OF ENGINEERING,
SHEFFIELD HALLAM UNIVERSITY.
Title
MULTIPLEXER BOARD ELECTRICAL DECOUPLING
Size
A
Document Number
REV
A
Date:
October 16, 1998
Sheet
2
of
3



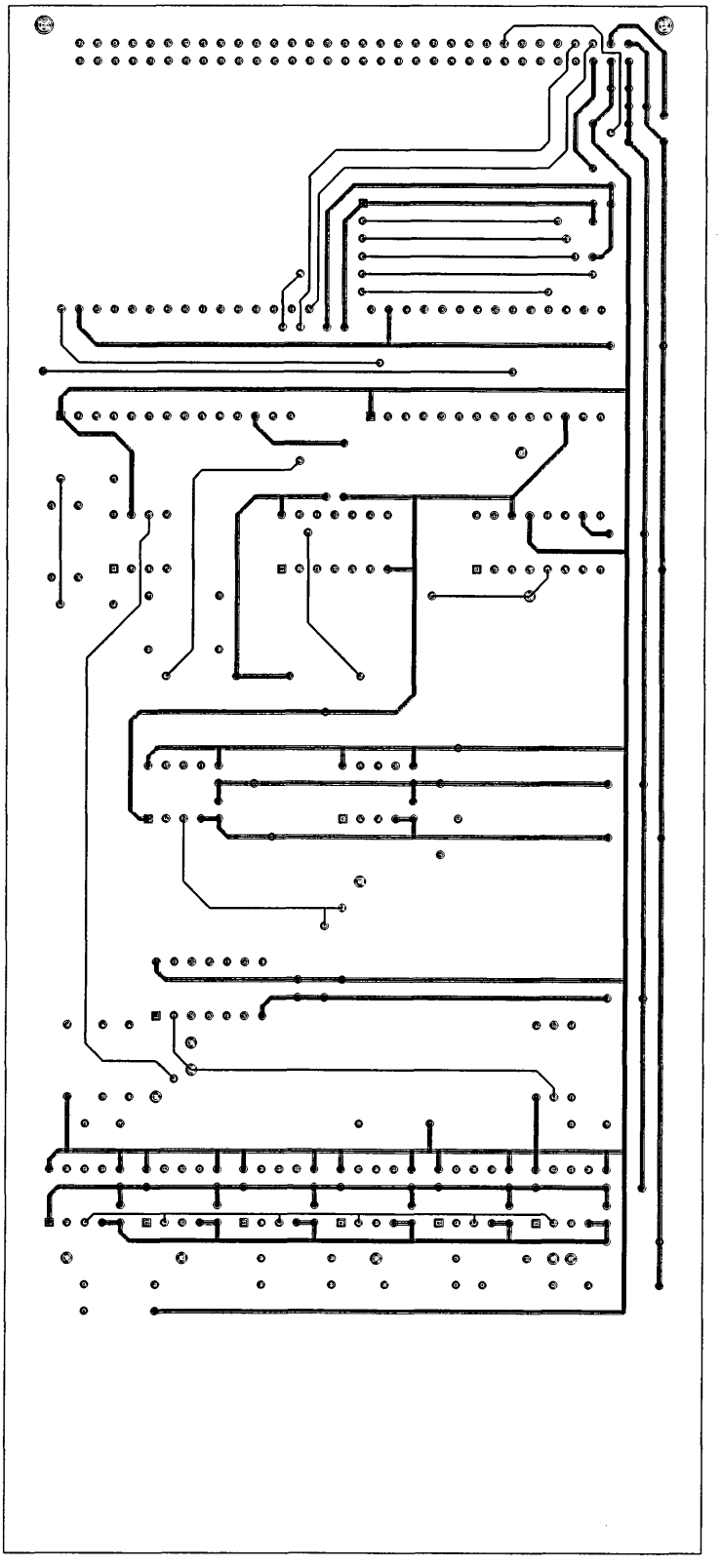
ANDY SOUTH, SCHOOL OF ENGINEERING, SHEFFIELD HALLAM UNIVERSITY.			
Title: MULTIPLEXER BOARD EXTERNAL CONNECTIONS			
Size: A	Document Number		REV: A
Date: October 16, 1998	Sheet 3 of 3		

7.9 Multiplexer Board Layout

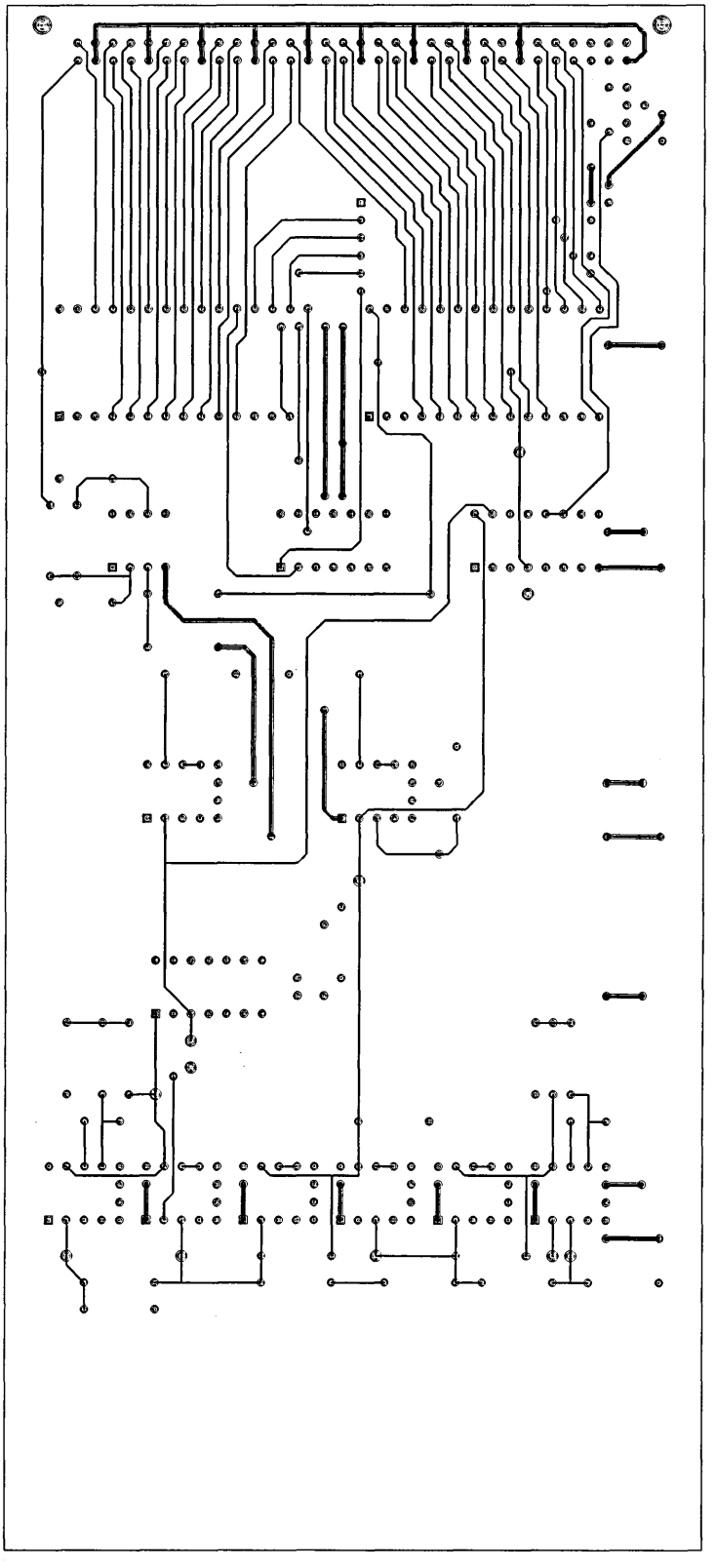
Component Side Silk Screen



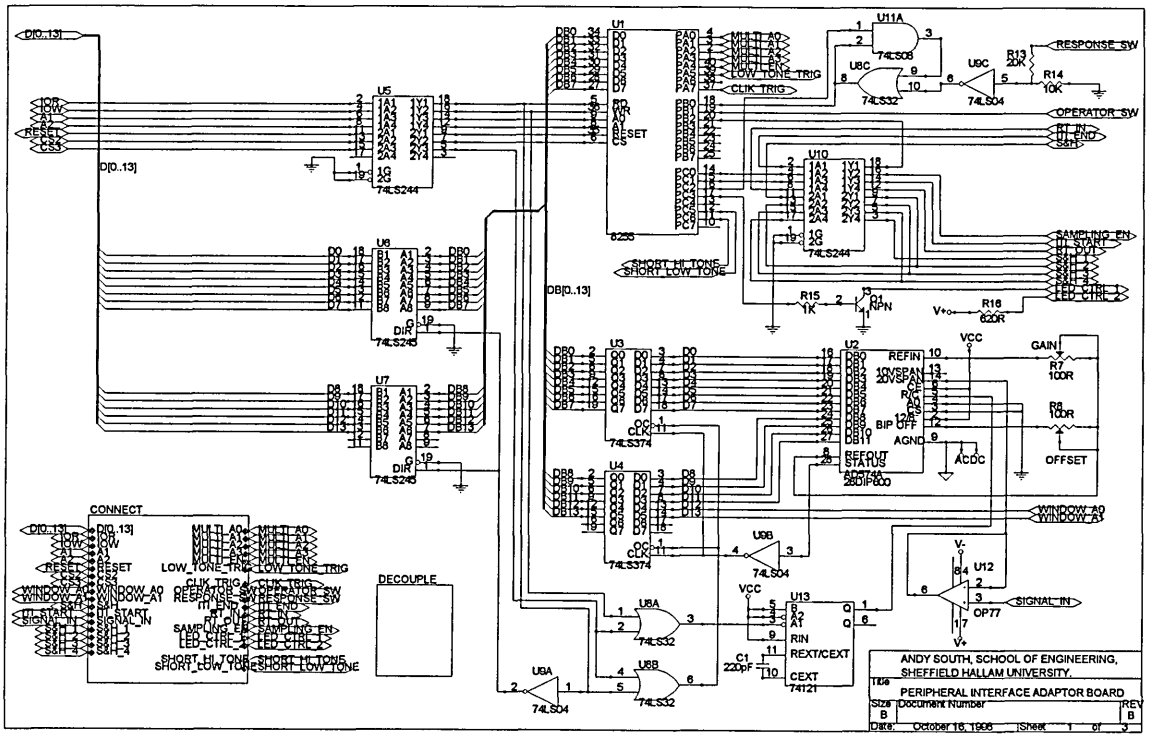
Component Side Copper

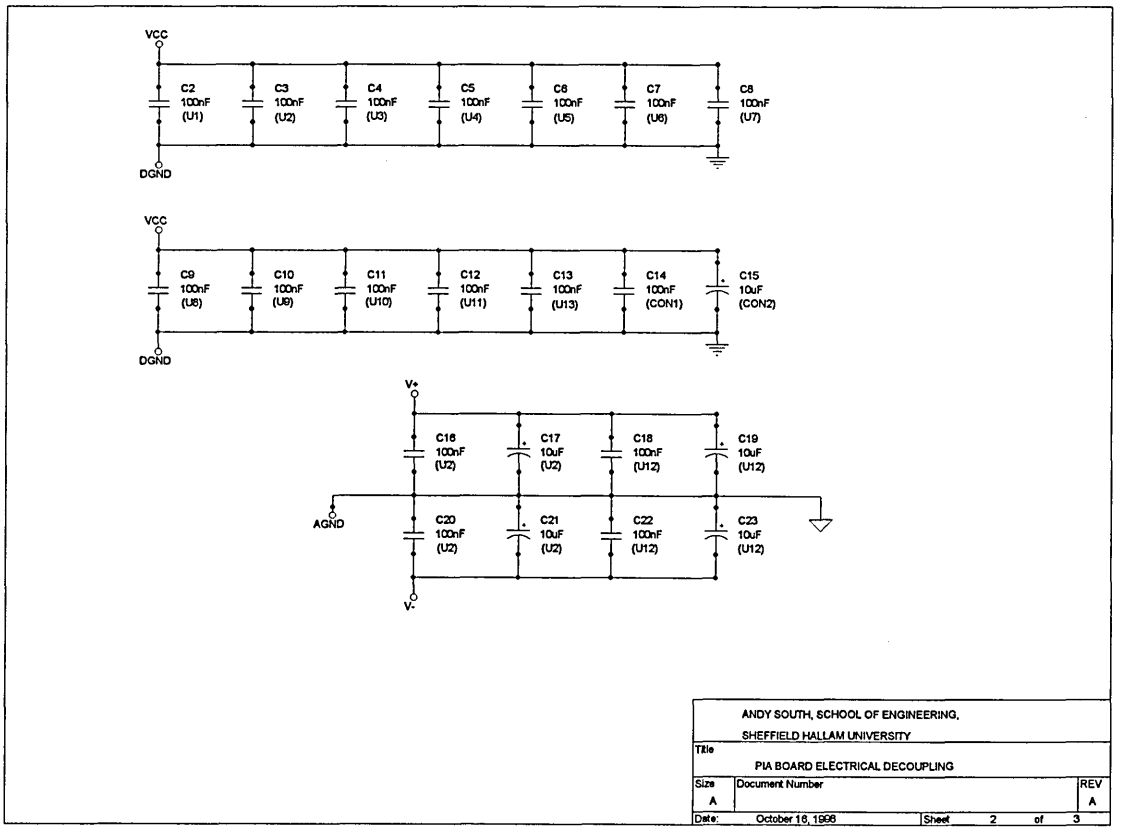


Solder Side Copper

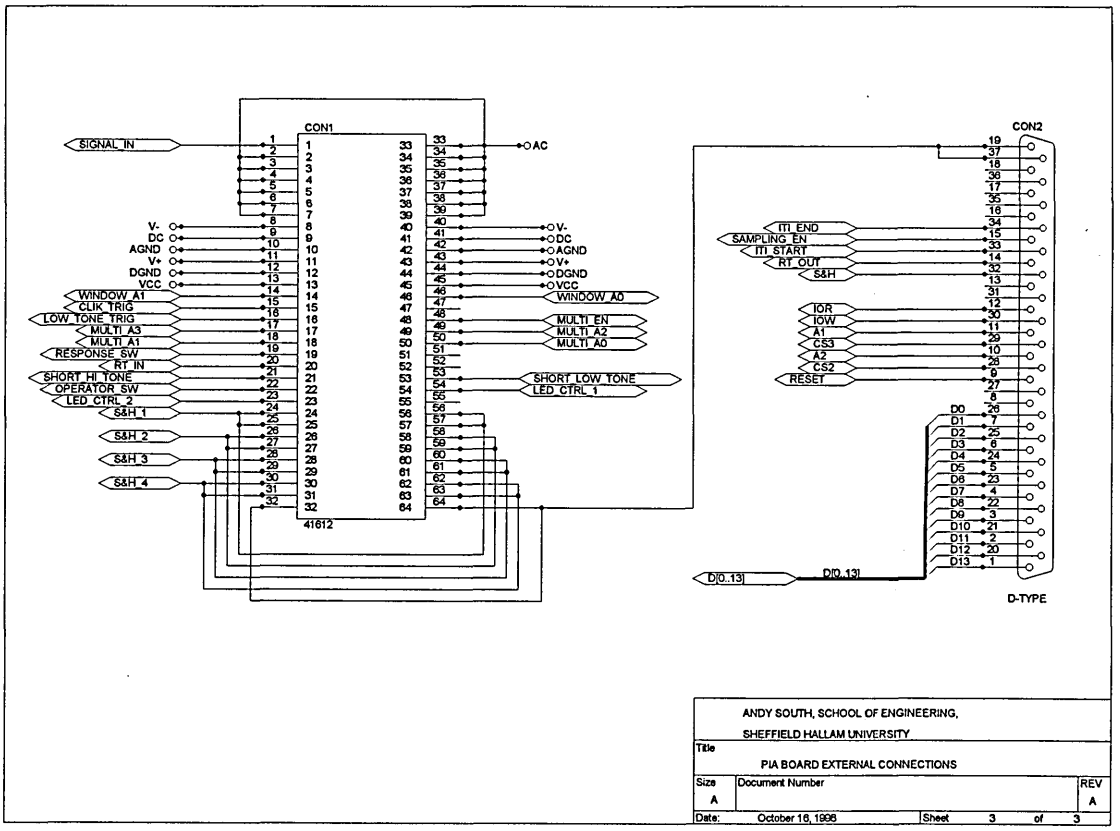


7.10PIA Board Circuit Diagrams



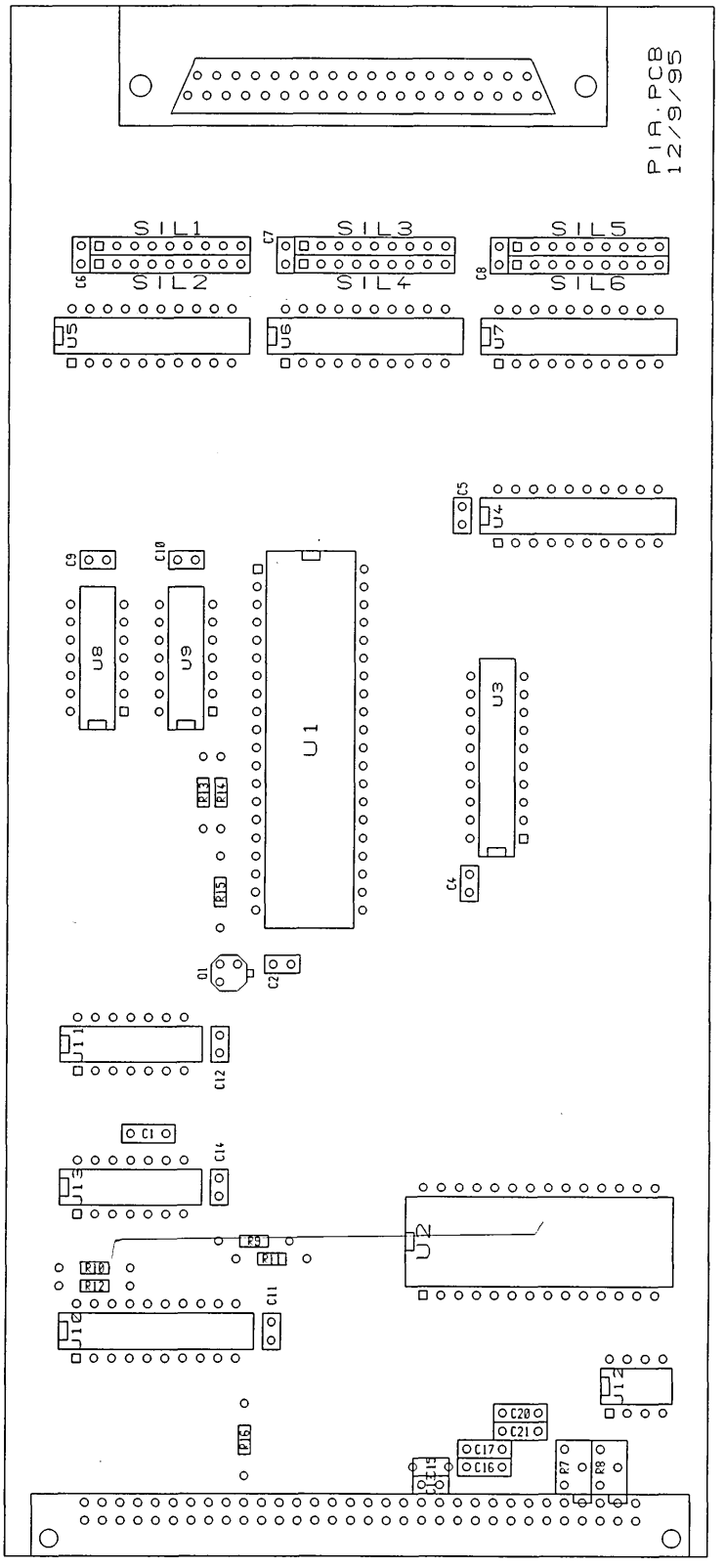


ANDY SOUTH, SCHOOL OF ENGINEERING, SHEFFIELD HALLAM UNIVERSITY			
Title: PIA BOARD ELECTRICAL DECOUPLING			
Size: A	Document Number		REV: A
Date: October 16, 1996	Sheet 2 of 3		

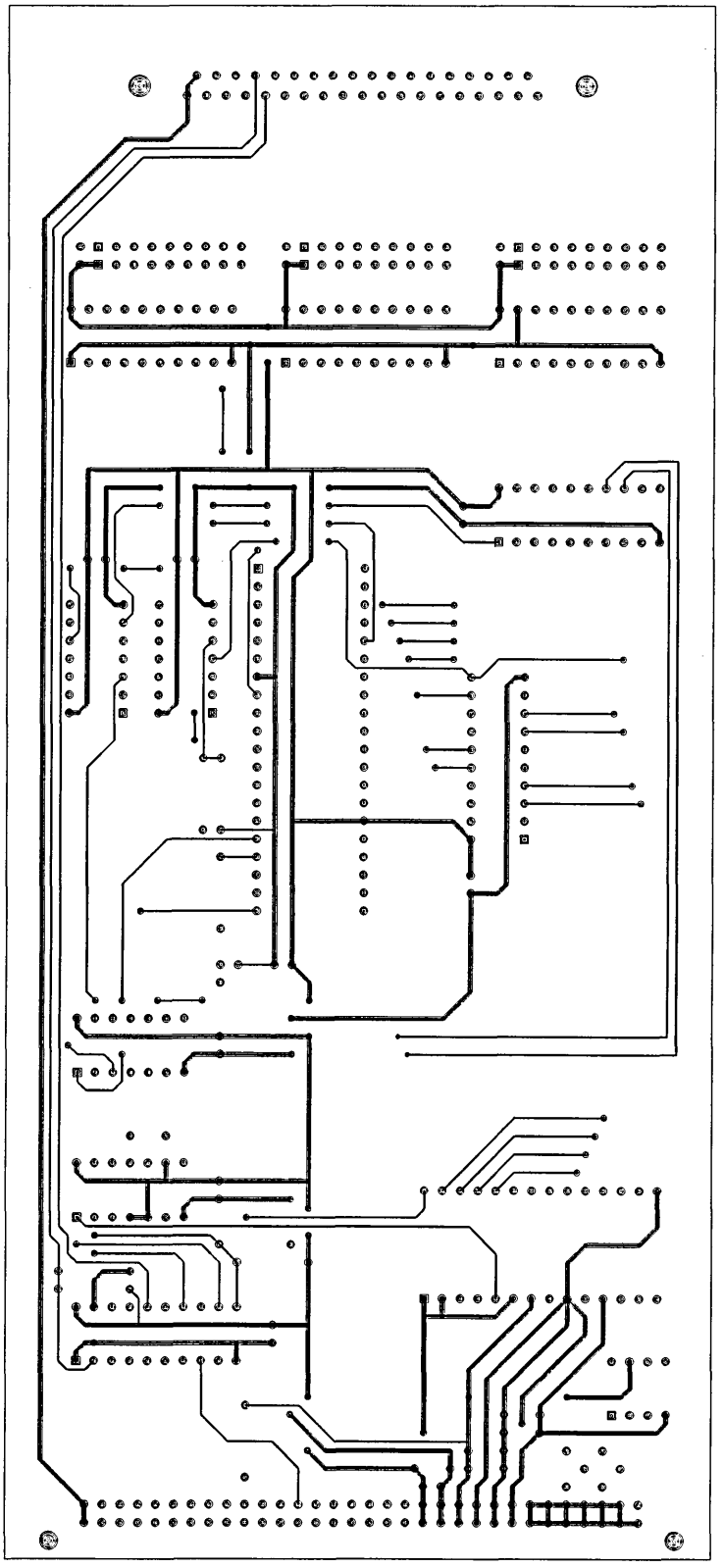

CON1
SIGNAL_IN
AC
V-
DC
AGND
V+
DGND
VCC
WINDOW_A1
CLK_TRIG
LOW_TONE_TRIG
MULTI_A3
MULTI_A1
RESPONSE_SW
RT_IN
SHORT_HI_TONE
OPERATOR_SW
LED_CTRL_2
S&H_1
S&H_2
S&H_3
S&H_4
WINDOW_A0
MULTI_EN
MULTI_A2
MULTI_A0
SHORT_LOW_TONE
LED_CTRL_1
41612
CON2
ITI_END
SAMPLING_EN
ITI_START
RT_OUT
S&H
IOR
IOW
A1
CS3
A2
CS2
RESET
D0
D1
D2
D3
D4
D5
D6
D7
D8
D9
D10
D11
D12
D13
D[0..13]
D[0..13]
D-TYPE
ANDY SOUTH, SCHOOL OF ENGINEERING,
SHEFFIELD HALLAM UNIVERSITY
Title
PIA BOARD EXTERNAL CONNECTIONS
Size
A
Document Number
REV
A
Date:
October 16, 1996
Sheet
3
of
3

7.11PIA Board Layout

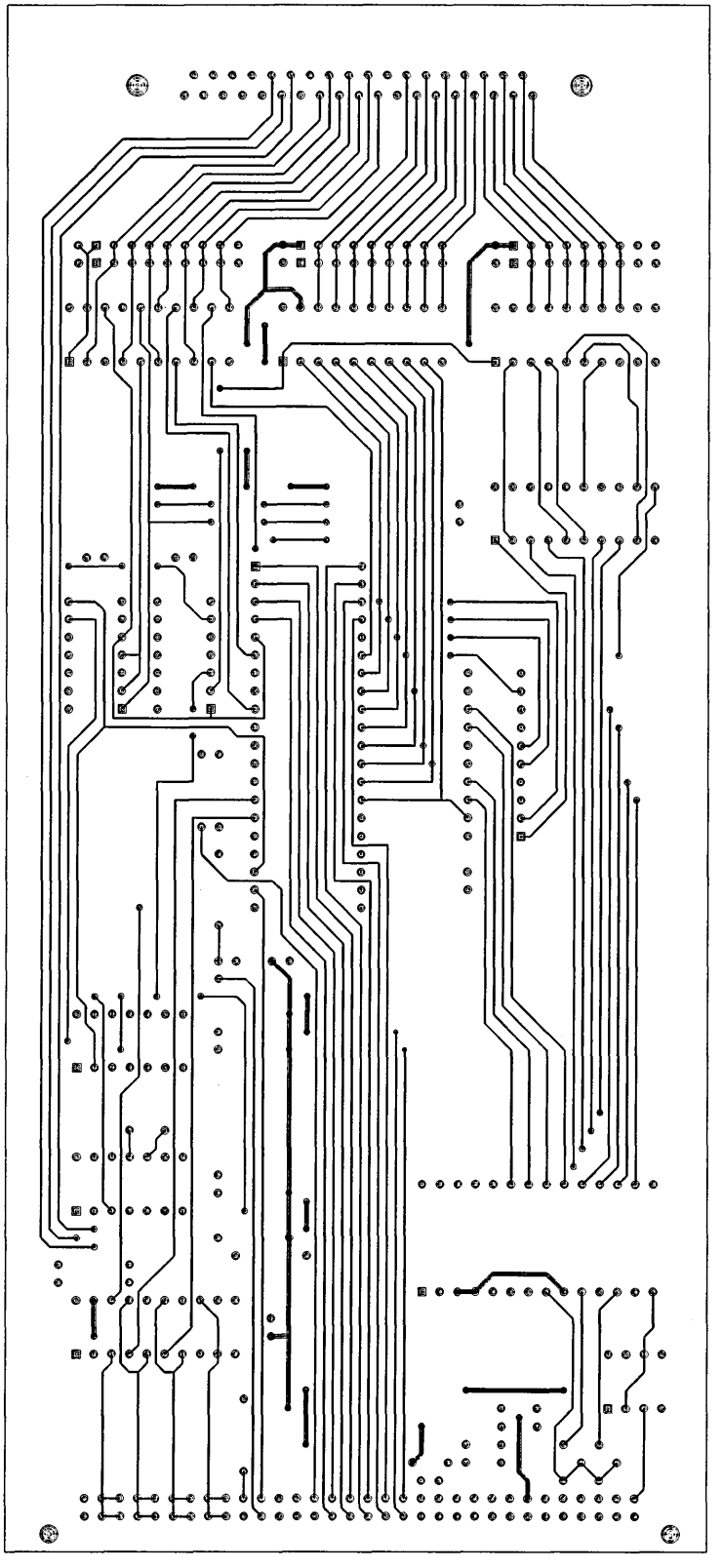
Component Side Silk Screen



Component Side Copper



Solder Side Copper



7.12System Control Program Source Code

The following is the source code listing for the 'C' program ERP20. This is the latest version of the control program software. This software controls the operation of the system hardware and is therefore responsible for the generation of the ERP paradigms and the recording, display and storage of the EEG of the subject.

```
/*
Program name: ERP20.C
Author     : Andy South
Date       : 12/2/98
Description :

This program generates the paradigms required for the CNV,
P300 and BP. It records each waveform for a set number of
trials and displays each one after it has been recorded.


*/

#include      <dos.h>
#include      <alloc.h>
#include      <stdlib.h>
#include      <stdio.h>
#include      <string.h>
#include      <graphics.h>
#include      <math.h>
#include      <time.h>

// Interrupt controller 1 data

#define       interrupt_control_0          0x20
#define       interrupt_control_1          0x21
#define       interrupt_vector             0x0D
#define       ICW1                         0x11
#define       ICW2                         0x08
#define       ICW3                         0x04
#define       ICW4                         0x03

//Timer 1 addresses

#define       timer1_control               0x306
#define       timer1_counter0              0x300
```

```
#define     timer1_counter1          0x302
#define     timer1_counter2          0x304

// Timer 1 program data

#define     timer1_counter0_word     0x36   // Mode 3
#define     timer1_counter0_lo_byte  0xD0
#define     timer1_counter0_hi_byte  0x07
#define     timer1_counter1_word     0x70   // Mode 0
#define     timer1_counter1_lo_byte  0x00
#define     timer1_counter1_hi_byte  0x00
#define     timer1_counter2_word     0xB6   // Mode 3
#define     timer1_counter2_lo_byte  0x80
#define     timer1_counter2_hi_byte  0x3E

// Timer 2 addresses

#define     timer2_control           0x30E
#define     timer2_counter0          0x308
#define     timer2_counter1          0x30A
#define     timer2_counter2          0x30C

// Timer 2 program data

#define     timer2_counter0_word     0x30   // Mode 0
#define     timer2_counter0_lo_byte  0xFF
#define     timer2_counter0_hi_byte  0xFF

// PIA control data

#define     pia_control              0x316
#define     pia_port0                0x310
#define     pia_port1                0x312
#define     pia_port2                0x314
#define     pia_control_word         0x82
#define     sample_enable            0x08   // LED on = 0x08
#define     sample_disable           0x01
#define     multi_channel            0x00   // Multiplexer channel 1
#define     click                    0x80
#define     high_tone                0x40
#define     low_tone                 0x20
#define     no_stimulus              0x00
#define     switch_on                0x00
#define     switch_off               0x04

// ADC control data

#define     adc                      0x318
#define     start_conversion         0x0A
```

```
#define     settling_time           100
#define     conversion_time         40

// Data aquisition constants

#define     channel_total           4       // Number of recorded
channels
#define     sample_freq             125     // Recording frequency in
hertz
#define     bits_volts_factor       2.048   // ADC conversion factor
#define     ref_channel             0       // First channel
#define     start_delay             3       // Delay in recording in
seconds

// Display control data

#define     blue                    1
#define     yellow                  14
#define     xmax                    640
#define     ymax                    480
#define     first_display_channel   0       // Reference channel = 0
#define     last_display_channel    4       // Last EEG channel = 31

// Largest difference between two consecutive displayed data points

#define  max_spike_mag              100


void    interrupt ISR (void);
int     read_adc (void);

void    read_switch_status(void);
void    set_screen(int x_coord, int y_coord);
void    initialisation (void);
void    record_cnv (char *cnv_filename);
void    record_p300 (char *p300_filename);
void    record_bp (char *bp_filename);
void    continuous(void);

float   convert_data(int compressed_data);

void    deallocate_memory(int *array_name[], int channel_number);
void    allocate_memory(int *array_name[], int channel_number, int data_size);

void    display_waveform (int magnify, int time, int *plot_data[channel_total],
                          int sample_min, int sample_max);
void    save_waveform (char *save_filename, int *save_data[channel_total],
                          int sample_min, int sample_max);
void    create_file (char *create_filename);
```

```
void    wait(int delay_time);


int record_start = 0;
int sample = 0;
int stimulus0 = 0;
int stimulus2 = 0;
int sample_status = 0;
int switch_control = 0;
int *adc_data[channel_total];


// Main Program

void main()
{

char choice;
char *erp_filepath="d:\\erps\\";
void interrupt (*old_ISR)();
int channel;

// Save original interrupt vector

        old_ISR = getvect(interrupt_vector);

        initialisation();

        set_screen(14,8);
        printf("This program records the CNV, P300, BP or Continuously");
        gotoxy(14,10);
        printf("Which would you like to record?");
        gotoxy(14,12);
        printf("1. CNV\n");
        gotoxy(14,13);
        printf("2. P300\n");
        gotoxy(14,14);
        printf("3. BP\n");
        gotoxy(14,15);
        printf("4. Continuously\n");
        gotoxy(14,16);
        printf("5. None\n");
        gotoxy(14,18);
        printf("Enter your choice: ");

        do {
```

```
                gotoxy(34,18);
                scanf("%c",&choice);
                switch(choice) {
                 case '1':
                        record_cnv(erp_filepath);
                        break;
                 case '2':
                        record_p300(erp_filepath);
                        break;
                 case '3':
                        record_bp(erp_filepath);
                        break;
                 case '4':
                   continuous();
                   break;
                 case '5':
                   set_screen(1,1);
                   break;
                }
        } while (choice!='1' && choice!='2' && choice!='3'
                        && choice!='4' && choice!= '5');

// Reset original interrupt vector

        disable();
        setvect(interrupt_vector,old_ISR);
        enable();


}  // End of main program



// This function initialises timers 1 and 2, the PIA,
// interrupt controller 1 and screen display

void initialisation (void)
{
int Graphdriver, Graphmode;
int i, channel;


// Initialise Timer 1, Counter 0

        outportb (timer1_control, timer1_counter0_word);
        outportb (timer1_counter0, timer1_counter0_lo_byte);
        outportb (timer1_counter0, timer1_counter0_hi_byte);

// Initialise Timer 1, Counter 1
```

```
        outportb (timer1_control, timer1_counter1_word);

// Initialise Timer 1, Counter 2

        outportb (timer1_control, timer1_counter1_word);
        outportb (timer1_counter2, timer1_counter2_lo_byte);
        outportb (timer1_counter2, timer1_counter2_hi_byte);

// Initialise Timer 2, Counter 0

        outportb (timer2_control, timer2_counter0_word);
        outportb (timer2_counter0, timer2_counter0_lo_byte);
        outportb (timer2_counter0, timer2_counter0_hi_byte);

// Initialise the PIA

        outportb (pia_control, pia_control_word);
        outportb (pia_port2, sample_disable);
        outportb (pia_port0, multi_channel);

// Initialise Interrupt contoller 1

        disable();
        outportb(interrupt_control_0,ICW1);
        outportb(interrupt_control_1,ICW2);
        outportb(interrupt_control_1,ICW3);
        outportb(interrupt_control_1,ICW4);
        outportb(interrupt_control_1,inportb(interrupt_control_1)&0xDF);
        setvect(interrupt_vector,ISR);
        enable();

// Initialise the screen display

        Graphdriver=DETECT;
        initgraph(&Graphdriver, &Graphmode, "c:\\tc\\bgi");
        setbkcolor(blue);
        setcolor(yellow);


} // End of 'initialisation' function




// Function that records the CNV

void record_cnv (char *cnv_filename)
```

```
{
unsigned int react_time_lo_byte;
unsigned int react_time_hi_byte;
int trial = 0;                          // Trial number
int react_time = 0;                     // Reaction time
int magnification;                      // ERP display magnification factor
int record_number;                      // Number of samples per trial
int click_number;                       // Sample number at which click occurs
int tone_number;                        // Sample number at which tone occurs
int delay_number;                       // Number of samples between trials
int false_response = 0;                 // Detects premature subject response
const trial_total = 4;                  // Number of recorded trials
const record_time = 4;                  // Trial length in seconds
const pre_stimulus_time = 1;            // Time before click
const inter_stimulus_interval = 1;      // Time between click and tone
int max_inter_trial_interval = 6;       // Maximum time delay between trials
char *filename;


// Reset random number generator used to generate inter-trial interval

        randomize();

// Create storage file for CNV data in 'CNV' directory

        strcat(cnv_filename,"cnv\\");
        set_screen(18,13);
        printf("Enter the data storage filename: ");
        scanf("%s", filename);
        strcat(cnv_filename, filename);
        create_file(cnv_filename);

// Request waveform display magnification factor

        set_screen(22,13);
        printf("Enter display magnification: ");
        scanf("%d",&magnification);
        set_screen(28,13);
        printf("Recording CNV");

// Calculate trial parameter sample numbers

        record_start = 0;
        record_number = record_time*sample_freq;
        click_number = pre_stimulus_time*sample_freq;
        tone_number = inter_stimulus_interval*sample_freq+click_number;
        delay_number = max_inter_trial_interval*sample_freq;

// Allocate memory for data storage
```

```
        allocate_memory(adc_data, channel_total, record_number+delay_number);

// Enable sampling at start of recording

        sample_status = sample_enable;
        outportb (pia_port2, sample_status);

// Start of main control loop

        while (trial < trial_total){

// Reset subject response switch

                switch_control = switch_on;
                outportb(pia_port2, sample_status+switch_control);
                switch_control = switch_off;
                outportb(pia_port2, sample_status+switch_control);

// Start of trial control loop

                sample = 0;
                while (sample < record_number+delay_number){
                        if (sample == click_number+delay_number) stimulus0 = click;
                        else if (sample == tone_number+delay_number){
                                stimulus0 = low_tone;
                                false_response = (inportb(pia_port1) & 0x01);
                        }
                        else stimulus0 = no_stimulus;

                } // End of trial control loop

// Disable sampling after trial

                sample_status = sample_disable;
                outportb (pia_port2, sample_status);

// Calculate subject response time

                react_time_lo_byte = inportb (timer2_counter0);
                react_time_hi_byte = inportb (timer2_counter0);
                react_time_lo_byte = 0xFF - react_time_lo_byte;
                react_time_hi_byte = 0xFF - react_time_hi_byte;
                react_time = (0x100*react_time_hi_byte + react_time_lo_byte);
                outportb (timer2_counter0, timer2_counter0_lo_byte);
                outportb (timer2_counter0, timer2_counter0_hi_byte);

// If response is valid perform the following
```

```
            if (!false_response){

// Display trial data

                    display_waveform(magnification, react_time, adc_data,
                                                                    delay_number,
delay_number+record_number);

// Save trial data

                    save_waveform(cnv_filename, adc_data, delay_number,
                                                delay_number+record_number );

// Calculate inter-trial delay

                    delay_number = (((random((max_inter_trial_interval-2)*1000))
                                                    *sample_freq)/1000)+250;

// Suspend recording ?

                    read_switch_status();

// Increment trial number

                    trial++;

                    } // End of valid data code

// Enable sampling for next trial

            sample_status = sample_enable;
            outportb (pia_port2, sample_status);

        } // End of main control loop

// Disable sampling at end of recording

        sample_status = sample_disable;
        outportb (pia_port2, sample_status);

// Deallocate memory used for data storage

        deallocate_memory(adc_data, channel_total);


} // End of 'record_cnv' function
```

```
// Function that records the P300

void record_p300(char *p300_filename)
{
char                                    tone_sequence[]                                    =
"0001000101000100001001000100001010001000100000101000101001000 1";
int trial = 0;                  // Trial number
int number = 0;                 // Tone sequence number
int magnification;              // ERP display magnification factor
int record_number;              // Number of samples per trial
int sample_number;              // Total number of samples for all trials
int tone_number;                // Sample number at which tone occurs
const record_time = 2;          // Trial length in seconds
const tone_time = 1;            // Time at which tone is to occur
const trial_total = 4;          // Number of recorded trials
char *filename;


// Create storage file for p300 data in 'p300' directory

        strcat(p300_filename,"p300\\");
        set_screen(18,13);
        printf("Enter the data storage filename: ");
        scanf("%s", filename);
        strcat(p300_filename, filename);
        create_file(p300_filename);

// Request waveform display magnification factor

        set_screen(22,13);
        printf("Enter display magnification: ");
        scanf("%d",&magnification);
        set_screen(28,13);
        printf("Recording P300");

// Calculate trial parameter sample numbers

        record_start = 0;
        record_number = record_time*sample_freq;
        sample_number = record_number*trial_total;
        tone_number = tone_time*sample_freq;

// Allocate memory for data storage

        allocate_memory(adc_data, channel_total, sample_number);

// Enable sampling at start of recording
```

```
        sample_status = sample_enable;
        outportb (pia_port2, sample_status);

// Delay recording for 1 second

        while (sample < sample_freq*start_delay);
        sample = 0;

// Start of main control loop

        while (trial < trial_total){
                sample = 0;

// Start of trial control loop

                while (sample < record_number){
                        if (sample == tone_number){
                                if (tone_sequence[number] == '1') stimulus2 = high_tone;
                                else stimulus2 = low_tone;
                                }
                        else stimulus2 = no_stimulus;
                        }
                        if (tone_sequence[number] == '1'){

// Disable sampling after trial

                        sample_status = sample_disable;
                        outportb (pia_port2, sample_status);

// Display trial data

                        display_waveform(magnification, 0, adc_data,
                                                                        record_start,
record_start+record_number);

// Increment data storage point

                        record_start += record_number;

// Suspend recording ?

                        read_switch_status();

// Increment trial number

                        trial++;

// Enable sampling for next trial
```

```
                    sample_status = sample_enable;
                    outportb (pia_port2, sample_status);

                } // End of trial control loop

// Increment tone sequence number

                number++;

        } // End of main control loop

// Disable sampling at end of recording

        sample_status = sample_disable;
        outportb (pia_port2, sample_status);

// Save recorded data in trial order

        record_start = 0;
        for (trial=0;trial<trial_total;trial++){
                save_waveform(p300_filename, adc_data, record_start,
                                                record_start+record_number);
                record_start += record_number;
        }

// Deallocate memory used for data staorage

        deallocate_memory(adc_data, channel_total);


}  // End of 'record_p300' function




// Function that records the Bereitschaftspotential

void record_bp(char *bp_filename)
{
int magnification;              // ERP dislplay magnification factor
int record_number;              // Number of samples per trial
int pre_response_number;        // Number of samples prior to response
int headroom_number;            // Additional number of samples
int response;
int channel;
int erp_start;
int sample1;
int data_valid;
```

```
int trial = 0;                          // Trial number
const pre_response_time = 1;            // Recording time prior to response
const headroom_time = 5;                // Additional recording period
const record_time = 2;                  // Length of trial in seconds
const trial_total = 4;                  // Number of recorded trials
char *filename;


// Create storage file for bp data in 'bp' directory

        strcat(bp_filename,"bp\\");
        set_screen(18,13);
        printf("Enter the data storage filename: ");
        scanf("%s", filename);
        strcat(bp_filename, filename);
        create_file(bp_filename);

// Request waveform display magnification factor

        set_screen(22,13);
        printf("Enter display magnification: ");
        scanf("%d",&magnification);
        set_screen(28,13);
        printf("Recording BP");

// Calculate trial parameter sample numbers

        record_start = 0;
        record_number = record_time*sample_freq;
        pre_response_number = pre_response_time*sample_freq;
        headroom_number = headroom_time*sample_freq;

// Allocate memory for data storage

        allocate_memory(adc_data, channel_total, record_number+headroom_number);

// Enable sampling at start of recording

        sample_status = sample_enable;
        outportb (pia_port2, sample_status);

// Start of main control loop

        while (trial<trial_total){
                sample = 0;
                sample1 = 0;
                data_valid = 0;

// Start of trial control loop
```

```
            while (sample < headroom_number + record_number){

 // Ensures switch status is read only once per sample

                    if (sample1 < sample){

// Read response switch

                            response = inportb(pia_port1);
                            response = inportb(pia_port1);
                            response = response & 0x01;

// If a response is detected check it occured at a valid time

                            if (response == 1 && pre_response_number <= sample
                                    && sample <= headroom_number){
                                erp_start = sample-pre_response_number;
                                data_valid = 1;
                            }
                            sample1 = sample;
                    }

            } // End of trial control loop

// If button press occured at a valid time process trial data

            if (data_valid){

// Disable sampling after trial

                    sample_status = sample_disable;
                    outportb (pia_port2, sample_status);

// Display trial data

                    display_waveform(magnification, 0, adc_data, erp_start,
                                                        erp_start+record_number);

// Save trial data

                    save_waveform(bp_filename, adc_data, 0, record_number);

// Suspend recording ?

                    read_switch_status();

// Increment trial number
```

```
                    trial++;

// Enable sampling for next trial

                    sample_status = sample_enable;
                    outportb (pia_port2, sample_status);
                }

        } // End of main control loop

// Disable sampling at end of recording

        sample_status = sample_disable;
        outportb (pia_port2, sample_status);

// Deallocate memory used for data storage

        deallocate_memory(adc_data, channel_total);


} // End of 'record_bp' function




// Function that continuously displays EEG waveforms

void continuous(void)
{
int record_number;              // Number of samples in the recording period
int magnification;              // ERP dislplay magnification factor
int switch_status = 0;          // On = 1, Off = 0
const record_time = 2;          // Length of recording period in seconds


// Request waveform display magnification factor

        set_screen(22,13);
        printf("Enter display magnification: ");
        scanf("%d",&magnification);
        set_screen(28,13);
        printf("Continuous recording");

// Calculate number of samples in the recording period

        record_number = record_time*sample_freq;

// Allocate memory for data storage
```

```
        allocate_memory(adc_data, channel_total, record_number);

// Enable sampling at start of recording

        sample_status = sample_enable;
        outportb (pia_port2, sample_status);

// Start of main control loop

        do  {    // Do until operator flips switch

// Disable sampling at the end of the recording period

                sample_status = sample_disable;
                outportb (pia_port2, sample_status);

                display_waveform(magnification, 0, adc_data, 0, record_number);

// Enable sampling for start of next recording period

                sample_status = sample_enable;
                outportb (pia_port2, sample_status);

// Recording period

                sample = 0;
                while (sample < record_number);

// Read switch status

                switch_status = ((inportb(pia_port1) & 0x02)>>1);

        } while (!switch_status);       // End of main control loop

// Disable sampling at end of recording period

        sample_status = sample_disable;
        outportb (pia_port2, sample_status);

// Wait until operator resets switch

        gotoxy(33,13);
        printf("Turn switch on!");
        while (switch_status){
                switch_status = ((inportb(pia_port1) & 0x02)>>1);
        }

// Deallocate memory used for data storage
```

```
        deallocate_memory(adc_data, channel_total);

// Clear screen

        set_screen(1,1);


} // End of 'continuous' function




// Interrupt function for sampling data

void interrupt ISR (void)
{
int i;
int channel;


// Select each channel in sequence

        for (channel=0;channel<channel_total; channel++){

                outportb (pia_port0, channel);

// Wait for multiplexer, window detector and PGA to settle

                for (i=0;i<settling_time;i++);

// Read adc data

                *(adc_data[channel]+sample+record_start) = read_adc();
        }

// Generate stimuli

        outportb (pia_port2, sample_status+stimulus2+switch_control);
        outportb (pia_port0, stimulus0);
        sample++;

} // End of 'interrupt' function
```

```
// Function that performs an ADC conversion

int read_adc (void)
{
int adc_data, j;

// Start adc conversion

        outportb (adc,start_conversion);
        outportb (adc,start_conversion);

// Wait until adc had finished conversion

        for (j=0;j<conversion_time;j++);

// Read adc data

        adc_data = inport (adc);

return (adc_data);
}




// Function that displays ADC data

void    display_waveform (int magnify, int time, int *plot_data[last_display_channel],
                                int sample_min, int sample_max)
{
int channel, sample, scale, data, i;
int display_channel_total;
int sample_total;
unsigned int xcoord, ycoord;
long int dc_offset;
float x_max, display_point;
int *display_data[last_display_channel];
int last_display_data;

x_max=xmax;             // Needs to be a floating point number for display calculations
display_channel_total = last_display_channel-first_display_channel;
sample_total = sample_max-sample_min;

        set_screen(1,1);
        printf("Reaction time is %d", time);

// Allocate memory for display data
```

```
        allocate_memory(display_data, last_display_channel, sample_total);

// Convert data into floating point numbers

        for (channel=0;channel<last_display_channel;channel++){
                for (sample=0; sample<sample_total; sample++){
                        *(display_data[channel]+sample)                         =
convert_data(*(plot_data[channel]+sample+sample_min));
                }
        }

// Subtract reference channel from data

        for (channel=first_display_channel;channel<last_display_channel;channel++){
                if (channel != ref_channel){
                        for (sample=0; sample<sample_total; sample++){
                                *(display_data[channel]+sample)                 -=
*(display_data[ref_channel]+sample);

//Simple spike filter

                                if      (sample==0)     last_display_data       =
*(display_data[channel]+sample);
                                if              (abs(*(display_data[channel]+sample)-
last_display_data) > max_spike_mag){
                                        *(display_data[channel]+sample)         =
last_display_data;
                                }
                                last_display_data =  *(display_data[channel]+sample);
                        }
                }
        }

// Start of main display loop

        for (channel=first_display_channel;channel<last_display_channel;channel++){
                dc_offset =0;

// Calculate mean data value

                for (sample=0; sample<sample_total; sample++){
                        dc_offset += *(display_data[channel]+sample);
                }
                dc_offset = dc_offset/sample_total;

// Start of channel display loop

                for (sample=0; sample<sample_total; sample++){
```

```
                    display_point = *(display_data[channel]+sample) - dc_offset;
                    display_point *= magnify;
                    display_point /= 100;

// Create xcoord from sample number

                    xcoord = (sample*x_max)/sample_total;
                    display_point    +=    (channel-first_display_channel+1)*(ymax-
40)/display_channel_total;   // Display offset
//                  ycoord  =  ymax-((display_point*display_channel_total)/80);    //
Create ycoord from data
                    ycoord = ymax-display_point;

// Move to first data point

                    if (sample==0) moveto(xcoord, ycoord);

// Draw line to data point

                    else lineto(xcoord, ycoord);

               } // End of channel display loop

        } // End of main display loop

// Deallocate memory used for display data

        deallocate_memory(display_data, last_display_channel);


} // End of 'display_waveform' function




// Function that saves recorded data to a specified file

void save_waveform (char *save_filename, int *save_data[channel_total],
                    int sample_min, int sample_max)
{
int channel,sample;
int sample_total;
float *process_data;
FILE *fp;

        sample_total = sample_max-sample_min;

// Open data storage file
```

```
        if (!(fp = fopen(save_filename,"ab"))){
                puts("Cannot open file");
                exit(0);
        }

// Allocate memory for processing data

        if ((process_data = farcalloc(sample_total, sizeof(float)))==NULL){
                puts("Memory allocation error whilst saving to disc");
                farfree(process_data);
                exit(0);
        }

// Process data

        for (channel=0;channel<channel_total;channel++){
                for (sample=0; sample<sample_total; sample++){

// Convert data into floating point numbers

                        *(process_data+sample)                                  =
convert_data(*(save_data[channel]+sample+sample_min));

// Convert data into microvolts

                        *(process_data+sample) /= bits_volts_factor;

                }

// Write data to disc

        fwrite(process_data, sizeof(float), sample_total, fp);

        }

        fclose(fp);
        farfree(process_data);

} // End of 'save_waveform' function




// Function that clears screen and moves cursor to specified coordinates

void set_screen(int x_coord, int y_coord)
{
```

```
        cleardevice();
        gotoxy(x_coord,y_coord);
}



// Function that creates a data storage file

void create_file(char *create_filename)
{

FILE *fp;


        if (!(fp = fopen(create_filename,"wb"))){
                puts("cannot open file");
                exit(0);
        }
        fclose(fp);

}



// Function that converts data in recorded format into floating point numbers

float convert_data(int compressed_data)
{
int scale,data;
float expanded_data;
float scaled_data,scaling_factor;


        data = compressed_data;

// Convert 4 MSB's into scale

        scale = (data & 0x3000)>>12;

// Make scale into scaling factor

        scaling_factor = pow(10,scale);

// Remove 4 MSB's to make 12 bit
```

```
        data = (data & 0xFFF);

// Convert data from unipolar to bipolar format

        scaled_data = data-0x800;

// Down scale the data

        scaled_data = (scaled_data)/scaling_factor;

// Invert data

        expanded_data = - scaled_data;

return (expanded_data);
}



// Function that allocates space in memory for the storage of data

void allocate_memory(int *array_name[], int channel_number, int data_size)
{
int channel, i;

        for (channel=0; channel<channel_number; channel++){
                if ((array_name[channel] = farcalloc(data_size, sizeof(int)))==NULL){
                        puts("Memory allocation error");
                        for(i=0;i<channel;i++){
                                farfree(array_name[i]);
                        }
                exit(0);
                }
        }
}



// Function that deallocates memory storage space

void deallocate_memory(int *array_name[], int channel_number)
{
int channel;

        for (channel=0; channel<channel_number; channel++){
                farfree(array_name[channel]);
```

```
        }
}


// Function that reads the status of the operator switch to determine whether
// recording is to be suspended and suspends recording if requested

void read_switch_status(void)
{
int switch_status;


        switch_status = ((inportb(pia_port1) & 0x02)>>1);
        if (switch_status){
                set_screen(24,13);
                printf("Recording suspended by operator");
                while (switch_status){
                        switch_status = ((inportb(pia_port1) & 0x02)>>1);
                }
        }
}
```

7.13Matlab Plotrial Program

```
function plotrial(trial_num)

% Andy South
% 12/2/98

% This program reads bp trial data from a file into a matrix,
% where each column represents one channel of data from a trial,
% and then plots selected channels from a selected trial.
%
% Use the command 'whitebg' before running to set the background
% colour to white for graphs to be imported into 'word'
%
% Yellow = EEG1
% Magenta(Purple) = EEG2
% Cyan(Blue) = EEG3



% *** Program Parameters ***


% Recording parameters

trial_total = 2;
trial_duration = 1;
sample_frequency = 125;
channel_total = 16;          % Include reference channel in total number

% Display parameters

scaling_factor = 1;          % For +ve or -ve displays of waveforms
first_display_channel = 3;   % Channel 0 is reference
last_display_channel = 3;
xmin = 0;
xmax = 1;
ymin = -100;
ymax = 100;

% Gain factors for each channel

gain_factor = 1.3*[0.92 0.95 0.9 0.82 1.05 1 0.92];
```

```
% *** Initialisation code ***


% Open path to trial data file

file_path = fopen('c:\phd\erpdata\test\16ch10f.tst');
if file_path ==-1 disp('File name error'); end;

% Calculate data matrix parameters

sample_total = trial_duration*sample_frequency;
channel_data_total = channel_total*trial_total;

% Read trial data into data matrix

[data total] = fread(file_path,[sample_total channel_data_total],'float');
if total ~= sample_total*channel_data_total disp('Error while reading data!'); end;

% Close path to trial data file

fclose(file_path);



% *** Start of averageing and processing code ***


for display_channel = first_display_channel:last_display_channel

% Calculate display data position in data matrix

        trial_data_num = ((trial_num-1)*channel_total)+display_channel+1;

% Calculate reference data position in data matrix

        trial_ref_num = ((trial_num-1)*channel_total)+1;

% Store trial data as vector 'eeg'

        eeg = data(:,trial_data_num);

% adjust channel gain

%       eeg = eeg*gain_factor(display_channel);

% subtract reference channel

        eeg = eeg - data(:,trial_ref_num);
```

```
% Subtract mean value from data (dc removal)
        eeg = eeg - mean(eeg);
% Filter spikes from data
        eeg = filt(eeg,sample_total);
% Store processed trial data in a display channel matrix
        erp_channel(display_channel,:) = eeg';
end;
% This is used for the display of phase data
% erp_channel(2,:) = -erp_channel(2,:);

% *** Graphical display code ***

% New graph to be displayed
% figure;
% Plot time on x-axis
time = 0:1/sample_frequency:trial_duration-1/sample_frequency;
% Plot each display channel on y-axis
plot(time,erp_channel([first_display_channel:last_display_channel],:));
% Plot grid on graph
grid;
% Title of graph
% title('Plot of system noise for channel 1');
% Label of x-axis
 xlabel('100 uV)');
% Label of y-axis
```

```
% ylabel('10 Hz');

% Dimensions of x and y axes if autoscale isn't to be used

axis([xmin xmax ymin ymax]);
```

7.14Matlab Plotall Program

```
function plotall

% Andy South
% 11/2/98

% This program reads trial data from a file into a matrix,
% where each column represents one channel of data from a trial.
% Selected trials are then averaged and the data for each channel
% displayed on the same graph.
%
% Use the command 'whitebg' before running to set the background
% colour to white for graphs to be imported into 'word'
%
% Yellow = EEG1
% Magenta(Purple) = EEG2
% Cyan(Blue) = EEG3


% *** Program parameters ***


% Recording parameters

trial_total = 16;
trial_duration = 4;
sample_frequency = 125;
channel_total = 4;              % Include reference channel in total number

% Display parameters

scaling_factor = 1;             % For +ve or -ve displays of waveforms
first_display_channel = 1;      % Channel 0 is reference
last_display_channel = 1;
xmin = 0;
xmax = 4;
ymin = -50;
ymax = 50;

% Trials to be included in averageing process

selected_trials = [1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16];
```

```
% *** Initialisation code ***


% Open path to trial data file

file_path = fopen('c:\phd\erpdata\test\noise4.tst');
if file_path ==-1 disp('Unable to open data file'); end;

% Calculate data matrix parameters

sample_total = trial_duration*sample_frequency;
channel_data_total = channel_total*trial_total;

% Read trial data into data matrix

[data total] = fread(file_path,[sample_total channel_data_total],'float');
if total ~= sample_total*channel_data_total disp('Error while reading data!'); end;

% Close path to trial data file

fclose(file_path);

% Convert into a column matrix

selected_trials = selected_trials';

% obtain the largest trial number

trial_max = size(selected_trials,1);



% *** Start of averageing and processing code ***


eeg_sum = 0;

for display_channel = first_display_channel:last_display_channel

        eeg_sum = 0;
        for num = 1:trial_max

                trial_num = selected_trials(num);

% Calculate trial data position in data matrix

                trial_data_num = ((trial_num-1)*channel_total)+display_channel+1;

% Calculate reference data position in data matrix
```

```
                trial_ref_num = ((trial_num-1)*channel_total)+1;
% Store trial data as vector 'eeg'
                eeg = data(:,trial_data_num);
% subtract reference channel
                eeg = eeg - data(:,trial_ref_num);
% Scale trial data by scaling factor
                eeg = eeg * scaling_factor;
% Subtract mean value from data (dc removal)
                eeg = eeg - mean(eeg);
% Filter spikes from data
                eeg = filt(eeg,sample_total);
% Add the trials together
                eeg_sum = eeg_sum + eeg;
        end;
% Calculate the mean of the trials
        eeg_mean = eeg_sum/(trial_max);
% Store processed trial data in a display channel matrix
        erp_channels(display_channel,:) = eeg_mean';
end;


% *** Graphical display code ***

% Create new display graph
figure;
% Plot time on x-axis
```

```
time = 0:1/sample_frequency:trial_duration-1/sample_frequency;

% Plot each display channel on y-axis

plot(time,erp_channels([first_display_channel:last_display_channel],:));

% Plot grid on graph

grid;

% Title of graph

title('Plot of system noise for channel 1 averaged over 16 trials');

% Label of x-axis

xlabel('Time (s)');

% Label of y-axis

ylabel('Amplitude (uV)');

% Dimensions of x and y axes if autoscale isn't to be used

% axis([xmin xmax ymin ymax]);
```