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**The Design and Test of A
Millimetre Resolution EEG Amplifier**

by
Oliver Zimmermann, B.Sc.

A thesis submitted to
the Faculty of Graduate Studies and Research
in partial fulfilment of
the requirement for the degree of

Master of Science

Department of Systems and Computer Engineering
Carleton University
Ottawa, Ontario

September 11th 1990
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and Research acceptance of the thesis

"THE DESIGN AND TEST OF A
MILLIMETRE RESOLUTION EEG AMPLIFIER"

submitted by Oliver Zimmermann, B.Sc.
in partial fulfilment of the requirements for
the degree of Master of Science

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Abstract

The spatial resolution of scalp-derived EEG signals is limited by the separation of the cortex from the scalp and the thermal noise of the intervening tissue. Experiments were performed to determine empirically the maximum obtainable scalp resolution, but the input noise of the EEG amplifier used was too high to accurately measure sub-centimetre potentials. A lower-noise circuit based on an excellent commercially available precision instrumentation amplifier with a multiplexed input was designed and tested. The circuit provided a ten fold improvement over the noise levels of the amplifier used in the maximum resolution experiment, but only when the input multiplexers were static. For typical source impedances with the multiplexers dynamically changing the input to the amplifier, noise levels were similar to those of a conventional EEG amplifier. An ultra-low noise preamplifier using parallel differential JFETs was designed to provide essentially maximal scalp resolution. The expected noise level of the amplifier and models of cortex to scalp signal transmission place the optimum attainable resolution at better than 5 mm with a 2 to 1 signal to noise ratio, ten times better than conventional topographic EEG resolutions.

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List of Acronyms and Abbreviations

μ V	microvolts
Ag-AgCl	silver - silver chloride
BJT	Bipolar Junction Transistor
cm	centimetres
CMOS	complimentary metal oxide semiconductor
CMRR	common mode rejection ratio
cps	cycles per second or hertz
CRT	cathode ray tube or oscilloscope
db	decibel
EEG	electroencephalogram
FFT	Fast Fourier Transform
Hz	hertz or cycles per second
JFET	junction field effect transistor
J6	output jack on GRASS model-8 amp
k Ω	kilo ohms; thousands of ohms
mA	milliamps
MHz	mega hertz
mm	millimetres
ms	milliseconds
MUX	multiplexer
NFET	N parallel field effect transistors
nV	nanovolts
O.D.	outside diameter
pA	picoamps
p-p	peak to peak
RMS	root mean square
$\sqrt{N}$	square root of N
SEP	somatosensory evoked potential

CHAPTER 1

INTRODUCTION

1.1 Background and Motivation

Richard Caton detected electrical activity in the brain of a monkey with a galvanometer in 1875 [Caton 1875]. The human electroencephalogram (EEG) was first recorded by Hans Berger fifty-four years later [Berger 1929]. Today EEG is routinely recorded both clinically and experimentally in a variety of applications, including epileptogenic localization [eg. Lesser 1987, Lueders 1982], sleep studies [Caderas 1982], and visual or auditory evoked potential experiments [Thickbroom 1984, MacKay 1984] among many others:

The ongoing EEG is most frequently analyzed in connection with neurological screening and diagnosis, sleep-stage analysis, and the quantification of drug and metabolic effects. [Gevins 1984]

The EEG signal is thought to originate mainly in the billions of largely parallel neurons that occupy only the outermost 3 mm of the brain - the cerebral cortex [Nunez 1981, Niedermeyer 1987]. The activity of the brain on the cortical surface has been recorded frequently and some of the findings of cortical experiments are reviewed in Chapter 5.

Between the neurons in the cerebral cortex and the hair on the head lie 10 to 15 mm of biological tissue and other substances including the scalp, skull, dura mater, pia mater, blood vessels, and cerebrospinal fluid [Liebman 1983]. All of these conduct electricity to varying extents and provide a path for the electric fields created by neural activity to propagate to the surface of the scalp [Nunez 1981]. The advantage of recording scalp potentials without medical incision is compromised by the loss of information inherent in the procedure. The distance from the brain's surface to the sensing electrodes, and the electrical conductivities of intervening tissue cause attenuation and de-focusing of the cortical signal [Nunez 1981]. This is quantitatively examined in chapter 5.

The scalp EEG is usually measured across several cm, has amplitudes in the microvolt range, occupies frequencies between 0 and 30 Hz and emanates from an impedance between 1 and 100 k Ω [Niedermeyer 1987, Nunez 1981]. These signal characteristics, however, are loosely defined. Potentials exceeding 50 μ V are commonly recorded, whereas "close" potentials (across less than a cm of scalp) are often much less than a microvolt. Sensory evoked potentials are usually recorded with a passband up to 1 kHz, because these reactive signals have short rise and fall times, containing frequency components into the hundreds of Hz. Although conventional 5 mm electrodes are generally expected to create a source

impedance of a few $k\Omega$, needle electrodes often present impedances exceeding 100 $k\Omega$. Additionally, the pattern of background activity on the cortical surface is pseudo-random and thus difficult to distinguish from noise [DeMott 1966].

In spite of the difficulties presented by a signal of such small amplitude in an electrically noisy biological environment, scalp recordings of human brain activity have been successfully obtained since 1929. The earliest, and still the most common presentation of these potentials are time versus voltage graphs seen in **figure 1.1a**. The use of multiple-electrode recordings led to iso-potential maps as in **figure 1.1b** and topographic maps as shown in **figure 1.2a**. Sleep and drug studies often make use of "compressed spectral arrays" for the display of EEG information as in **figure 1.2b**, where the changing EEG power spectrum is repeatedly plotted as a function of time. Computerized colour display systems capable of producing colour-coded animations of a changing scalp potential topography have been commercially available for a number of years.

FIGURE 1.1

a) **TOP:** Scalp recorded potentials and associated scalp electrode positions. The traces show changes in amplitude (voltage) and frequency as a function of time. Different electrode positions show significantly different activity. (Adapted from [Caderas 1982]).

b) **BOTTOM:** Isopotential contour maps derived from scalp potentials. Contours are drawn on 2 microvolt increments, a new distribution calculated every millisecond. (Adapted from [Ragot 1978, fig 1a]).

FIGURE 1.2

a) TOP: Map of a Visual evoked potential showing the scalp topography 120 ms after a flash of light. The map represents an average of 32 evoked responses. (adapted from [Buchsbaum 1981]).

b) BOTTOM: Repeated traces of the EEG power spectrum in a subject receiving Diazepam. Spectra are calculated for successive 30 second intervals. (adapted from [Vaz 1986])

Caton's discovery of the electrical nature of the monkey brain has led researchers to view the human brain as a kind of three-dimensional electric circuit, and to study its function through spatial and temporal analysis of the EEG. The animated topographic displays available now represent the state of the art in non-invasive real-time brain function analyzers. Although such machines provide useful information in some contexts, their spatial resolving power is limited to several square centimetres. In contrast, it has been shown [DeMott 1966] that repeatable patterns of synchronous cortical activity often occupy only a few square millimetres. **Figure 1.3** depicts a moment of electrical activity on the cortex of a racoon.

FIGURE 1.3

Cortical potentials recorded from a racoon in response to a white light. These two similar patterns occurred at latencies of 80 (left) and 183 ms (right), the longer latency associated with a weaker stimulus. Areas of similar activity are seen to occupy a few square mm. The recording matrix consisted of 400 electrodes on 0.25 mm centres.

The obvious way to improve the spatial resolving power of topographic EEG equipment is to increase the number of electrodes used to sample the scalp distribution. This has been done to some extent by several researchers...

Placement of the 30 recording electrodes was such as to give an approximately uniform cover of the head above the nasion-inion plane. The standard 10-20 system was used as a basis.
[Thickbroom 1984]

The present paper gives a phenomenology of typical EEG alpha field distributions on the human scalp, using a 48-channel recording system for off-line mapping of the scalp EEG fields...

The inter-electrode distances were between 3.5 and 4.2 cm, depending on the subject's head dimensions and the number of electrodes.
[Lehmann 1971]

Gevins used 128 simultaneous electrodes on the scalp, and recommended more [Gevins 1984]. With 128 electrodes, the inter-electrode spacing is approximately 2.3 cm. Conventional topographic EEG equipment offers 16 channels to which to connect the electrodes. Standard positions for electrode placement have been defined, as for example in the international "10-20" montage which defines 21 electrode positions relative to prominent head-marks. The 10-20 system produces an approximate 7 cm inter-electrode gap on the average adult head.

The question of how tightly to space the electrodes has been considered by a number of researchers, but without a clear consensus. It is accepted that smaller inter-electrode

distances record smaller scalp potentials; Epstein shows that the RMS amplitude in both alpha (8-13 Hz) and beta (14-25 Hz) frequencies is proportional to electrode separation [Epstein 1987]. He positioned electrodes on the scalp across various separations from 1 to 15 cm. Epstein's findings are conclusive. When a sufficiently large area of cortical activity is averaged (as by recordings made from the scalp), the greater the separation of electrodes, the smaller the commonality of the signal, and the greater the average difference in the measured potential. Significantly, Epstein measures an average of over 1 microvolt in both the alpha and beta bands when the 4.5 mm electrodes are only 1 cm apart, suggesting that smaller electrodes, more closely spaced, could record fractions of a microvolt (figure 1.4).

FIGURE 1.4

RMS amplitude of spontaneous human scalp EEG as a function of inter-electrode distance averaged over 20 seconds. (Adapted from [Epstein 1984]).

Perhaps the most comprehensive experiment on the spatial resolution limit of scalp EEG was performed using 6 mm electrodes on 9 mm centres [Spitzer 1989]. Somatosensory evoked potentials were recorded. Figure 1.5 illustrates some of the waveforms obtained by Spitzer when averaging 1000 stimulus-response cycles. Spitzer's results suggest a minimal inter-electrode distance of 1.5 cm is adequate to capture 95% of the power in the EEG spectrum...

In the coronal direction, the cut-off for the component at 16.25 ms corresponded to a Nyquist interelectrode distance of 3.6 cm, while for later components the corresponding distance was calculated to be 2.9 cm. The conservative estimates for the cut-off in the sagittal direction yielded very small distances of 1.5-1.8 cm...

...Any unexpected smaller components that were not adequately sampled would, therefore, have to have been smaller than 1.8 cm in diameter, to be missed by this technique. The physical properties of the physiologic medium between the recording electrodes and the generators make it unlikely that significant components of that small size would be recorded from the scalp.
[Spitzer 1989]

FIGURE 1.5

a) TOP: 32 traces of 1000 averaged somatosensory evoked potentials and their corresponding electrode positions. The top 16 traces represent the coronal (vertical) array, the bottom 16 the sagittal (horizontal) array. Inter-electrode spacing is 9 mm.

b) BOTTOM: Potential distribution along both arrays at a latency of 16.75 ms, and the calculated spatial Fourier Transform for each. (adapted from [Spitzer 1989])

Other experimenters have anticipated higher resolutions than Spitzer's limiting 1.8 cm. MacKay, using 20 ordinary (5 mm) electrodes positioned on 1.5 cm centres concludes:

From the amount of contrast between responses from neighbouring electrodes spaced by 1.5 cm, it is evident that source-density analysis can in principle resolve details of the Auditory Evoked Potential scalp map to better than 1 cm. The practical limit seems likely to be set by the physical size of electrodes rather than by current spread.

[MacKay 1984]

MacKay used averages of 20 to 32 stimulus repetitions and a version of Hjorth's source-derivation or "source density" potential calculations [Hjorth 1975]. In 1983 Sandini found evidence of a limit to scalp resolution which is also in contrast with Spitzer's findings:

In the processing of topographic data, one main problem still unresolved is the measure of the resolution achievable to discriminate regions of activated cortical areas, i.e. the minimum distance between two adjacent cortical areas that produce two distinguishable scalp recorded activities....

Not all the stimuli are discriminated; particularly the stimuli over the horizontal meridian are not well resolved, probably because of the folding of the visual cortex. Nonetheless, the minimum cortical distance discriminated is about 7 mm. Of particular interest, suggesting possible clinical applications, is the fact that the results were obtained from different subjects hinting at a good repeatability of the analysis.

[Sandini 1983]

Spitzer's work requires a further comment. Although it seems unlikely that significant contributions to the scalp EEG would be generated by sources less than 1.8 cm in diameter, it is important that such small sources do exist [DeMott 1966], and clearly must contribute something, albeit a small amount, to the scalp EEG. Spitzer used 1000 somatosensory stimulus-response cycles in an evoked potential study of maximum scalp resolution. Evoked potentials are recorded by repeatedly presenting a stimulus, usually a tone or an image, to the subject and then averaging the brain's electrical response as captured by the electrodes and amplification equipment. Any temporally consistent signals (relative to the time of the stimulus) will be preserved, and noise or stimulus-independent activity will be averaged out. Because the noise is averaged out in this way, any signal, no matter how small, can in principle be recovered by a sufficiently high number of stimulus-response cycles. Hence, the question of maximal scalp resolution must be qualified. The maximal resolution for spontaneous activity will be much poorer than what can be reasonably achieved through the use of evoked potentials.

1.2 Objectives and synopsis of research

The research was intended to investigate the spatial resolution limits of human scalp EEG, and, based on the empirical results of this investigation, an amplifier capable of capturing the sub-microvolt signals found across minimal scalp electrode spacings was to be designed and tested.

In January of 1988 a 16 electrode, one output channel electrode matrix was tested at the Carleton University sleep lab under the supervision of Bob Hoffman. The matrix had electrodes spaced at various separations from 0.5 to 17 mm.

The results obtained at the sleep lab led to the construction of an 8 electrode linear array. The array was constructed with Ag-AgCl electrodes 1 mm in diameter placed on 2 mm centres. In May 1988 it was used on a volunteer at the EEG sector of the Civic Hospital in Ottawa. Eight channels were simultaneously recorded via a Grass instruments model 8 EEG amplifier and a Racal data recorder.

Between June of 1988 and January of 1989 the data was digitized and analyzed at the Carleton University Systems Engineering facility. A Sun computer running the "Matlab" analysis package was used to study the experimental data.

During the summer of 1989, an amplification system intended to improve the obtainable signal resolution was designed and tested. The circuit used a series of Analog Devices 624 instrumentation amplifiers fed by Siliconix DG506 16-channel analog multiplexers. Experiments on the circuit

established its single-channel and multi-channel noise characteristics. A circuit optimizing the one-channel noise level was designed in the Spring of 1990. This circuit remains to be built and tested on the linear electrode array.

The data from the experiments performed in the EEG lab, in conjunction with the technological limit of electronic amplification systems suggest a minimum inter-electrode distance of 5 mm for spontaneous scalp-derived EEG recordings. Evoked potential recordings, however, could benefit from a tighter spacing through the improvement in signal to noise ratio obtainable with that method. The physiological causes of scalp signal attenuation and information loss are investigated in chapter 5.

1.3 Thesis organization

Chapter 2 describes the methods and apparatus used in the sleep lab and Civic Hospital experiments. The findings of the sleep lab experiment are included in this chapter. Chapter 3 describes the procedure and results of the data analysis performed at the Systems Engineering laboratory. Chapter 4 covers the design and testing of the multiplexed analog EEG amplifier as well as the design of the optimal single channel circuit. Chapter 5 presents a physiological model for scalp EEG and reviews some previously performed cortical and scalp EEG experiments. Chapter 6 summarizes and concludes the work of the thesis.

CHAPTER 2

MILLIMETRE RESOLUTION EXPERIMENTS

2.1 Carleton Sleep Lab Experiment; 16 electrodes, sub-millimetre resolution

A group of 16 electrodes attached to a plastic frame was constructed to the dimensions shown in figure 2.1. The electrodes were made from 0.012 inch (0.30 mm) diameter spring steel. Each electrode was bent and formed to provide spring-action contact with the scalp. Standard wire-wrap (0.017 inch O.D.) connections were made to every electrode and then twisted together with the 15 other leads. These 16 wires spliced into two separate banks of switches, each bank used to select any of the 16 inputs as its single output. The switch bank thereby permitted the measure of potential differences between any two electrodes in the matrix. Figure 2.2 is a photo of the complete electrode matrix as used in the experiment.

a)

b)

FIGURE 2.2

a) TOP: Top view of the first electrode matrix with 16 pink wires running in a bundle from electrodes to the banks of selector switches. The two outputs from the selector switches are the orange and red coiled wire at the left.

b) BOTTOM: The underside of the plastic electrode substrate showing the electrodes as they protrude. The electrodes were made to push into the substrate as it was pushed against the scalp.

The two electrodes selected with the switch banks were differentially connected to a "GRASS MODEL P511J" EEG amplifier. A single 5 mm gold-cup electrode, attached to the forehead with Grass Instruments "EC2" electrode cream was used to ground the subject. He lay in a shielded room, protected from radio and line interference. Figure 2.3 illustrates the subject wiring used during the experiment at the sleep lab.

The matrix was attached to the subject's head at a parietal-occipital position (figure 2.3) and held motionless with Collodion and gauze. The room was dim and the subject relaxed. Spontaneous brain potentials were measured between various electrodes for approximately 30 minutes.

When connected through the "HIP511E" input probe, as it was in the experiment, the P511 amplifier has a noise specification of $2.6 \mu\text{V}$ average peak to peak for a 100 Hz bandwidth [GRASS model P511 instruction manual]. The passband in this experiment was set from 0.1 Hz to 100 Hz (-3 dB). A 60 Hz notch filter built into the P511 was also selected. The maximum gain of the amplifier was used and the output displayed on an oscilloscope.

FIGURE 2.3

a) TOP: Diagrammatic representation of subject wiring in sleep lab experiment.
b) BOTTOM: Position of electrode matrix (rectangle) and ground lead (circle) during the experiment.

The experiment was carried out at the Carleton University sleep lab, under the supervision of Bob Hoffman, an expert in electroencephalography. Hoffman monitored the EEG signal as it appeared on the CRT. Even at maximum gain, the output from the amplifiers was "unusually low" when electrode pairs with a spacing of less than one centimetre were selected. Hoffman did feel, however, that the signal obtained with 3 distinct electrode pairs, (#5 to #8, #7 to #9 and #2 to #10 in figure 2.1) each of them with less than a 5 mm inter-electrode distance was "...hard to be sure, but it looks like EEG" [Hoffman, personal communication during experiment]. Several recordings between the wider spaced outer electrodes (eg. #1 to #3, #1 to #4) in the matrix yielded what "...definitely looks like EEG." [Hoffman, during experiment]. The hard-copy device was unavailable on the day of the experiment and so there are no permanent traces of the potentials observed.

Although some experimenters satisfactorily use stainless steel electrodes for scalp EEG [eg. Delucchi 1961], it has been established that Ag-AgCl electrodes produce among the lowest contact noises for biocompatible electrodes [Niedermeyer 1987]. This noise can be generated by movement of the electrode, or by the chemical interaction of the electrode metal with the various substances found on the scalp. The formation of a silver-chloride layer on a silver electrode effectively neutralizes the metal to scalp junction, thereby preventing further chemical reactions between the

scalp and electrode. As mentioned earlier, the electrodes used in the sleep lab experiment were made of steel and may have produced contact-potential artifacts that were read as EEG signals.

The unexpected result of the sleep lab experiment was that electrodes separated by less than 4 mm were seemingly recording EEG signals. There is however some chance that the signals observed at the sleep lab were in fact interference, artifact, or electronic noise. The second experiment, described in the following section, was devised to provide a more rigorous search for maximal EEG resolution.

2.2 Civic Hospital Experiment; 8 electrodes, 2 millimetre resolution

The linear array of 8 electrodes shown in figure 2.4 was constructed to rigorously test the possibility of resolving millimetre-spaced scalp potentials hinted at by the sleep lab experiment. To eliminate contact-potential noise, each silver electrode was chlorided to form the recommended Ag-AgCl interface to the scalp [GRASS instruction manual]. The electrodes were 1 mm in diameter, linearly spaced through a plexiglass substrate on 2 mm centres. The contact ends of the electrodes were flush with the plexiglass. The electrode assembly was connected with a 16 pin ribbon cable header (8 pins unused) to a shielded (with aluminum foil) ribbon cable. The foil was wrapped 3 times around the cable. 8 banana plugs connected the ribbon cable to the "electrode board" of the Grass Model 8 EEG amplifier used at the Civic Hospital. The electrode board is a shielded jack interface to the 16 channels of the amplification system.

The array was strapped to the head of a volunteer with string and elastics. In order to improve contact, a specially prepared cream was applied to the scalp under the electrode matrix. The cream, intended to approximate the impedance of the skull, was rubbed deeply into the scalp such that closely spaced electrodes embedded in the cream were essentially embedded in an extension of the skull. In order to have this effect, the cream had to saturate the skin and provide enough

electrical impedance so as not to short out the recording electrodes.

The impedance of the skull was measured as shown in figure 2.5, using various scalp interfaces. A pair of stainless steel needles inserted firmly into the scalp produced a separation-independent (tested between 5 and 100 mm) 90 k Ω skull impedance ($\pm$ 20 k Ω) with a 40 Hz test signal. A larger (0.025 inch diameter) wire, immersed in salt-saturated "K-Y" lubricant applied to the scalp measured 14 k Ω across 15 mm of scalp (40 Hz test frequency). Standard 5 mm EEG electrodes, applied to the scalp with "Grass EC2" electrode cream, are expected to produce impedances between 1 and 10 k Ω at ordinary EEG frequencies (1 to 30 Hz) [GRASS model 8 instruction manual]. The average human skull is 3 to 4 mm thick [Niedermeyer 1987], so a biocompatible cream with an impedance of approximately 1 k Ω per mm (roughly equivalent to the skull impedance) was synthesized, consisting of salt-saturated K-Y lubricant, mixed 1:1 with vaseline. It was found to have an impedance of 4 k Ω across 10 mm at 60 Hz. This cream was not completely satisfactory, the main problem being its low melting point; when applied to the scalp it liquified in approximately 15 minutes. Nevertheless, it was used in the Civic Hospital experiment. Melted cream was replaced as required.

a)

24

b)

c)

FIGURE 2.4

a) **TOP:** Complete linear array assembly including the banana plugs (red), the shielded ribbon cable, the subject-ground lead (near top of photo), and the array (left of the penny).
b) **BOTTOM LEFT:** Top view of the array when disconnected from ribbon cable showing the cable header.
c) **BOTTOM RIGHT:** Contact-side view of the array showing the 8 electrodes. Black electrical tape was used to insulate electrode connecting set screws from the scalp.

FIGURE 2.5

Test circuit for measuring skull impedance. Wires were applied to the skull using conductive cream (GRASS EC2), or with steel needles inserted into the skin. An oscilloscope was used to measure the voltage across the source (V_s) and the known resistance R_1 (V_m). The skull impedance R_s is given by: $R_s = R_1 * (V_s/V_m - 1)$.

The model 8 is a popular EEG amplifier with an input noise specification of 2 μ V peak to peak, and an optimum common mode rejection ratio (CMRR) of 100,000 [GRASS model 8 instruction manual]. It is difficult to achieve maximal CMRR in EEG measurements due to the difficulty of perfectly balancing the source impedance of the inputs (i.e. the impedance of the skull in two separate positions). With a source imbalance of up to 5 k Ω , the Grass Model 8A5 has a CMRR specified at 1500.

The ribbon cable running between the electrode array and the electrode board was shielded with a triple layer of grounded aluminum foil. The subject ground was established by connecting a 1/4 inch (6 mm) gold-cup electrode between the scalp and the grounded foil shield of the electrode ribbon cable. **Figure 2.6** illustrates the connections made between the subject and the GRASS amplifiers.

FIGURE 2.6

a) TOP: Diagrammatic representation of subject wiring used at the Civic Hospital experiment. No shielded room was used and up to 3 output devices were connected.

b) BOTTOM LEFT: Array position and ground lead used during epochs 1 and 2.

c) BOTTOM RIGHT: Array position and ground lead used during epochs 3 and 4.

The EEG lab in the Civic Hospital does not use a shielded room, making it necessary to use the 60 Hz notch filter for small signal recordings. The passband was set from 5 Hz to 10 kHz (-1.9 dB or 80% amplitude) for the duration of the experiment, later low-pass filtered to prevent aliasing during the analog to digital conversion performed on the recorded data.

The Model-8 amplifier has a pushbutton selector panel allowing the operator to select any pair of electrodes as the input to any of the 16 available channels. Taking advantage of this feature, the separate epochs of EEG recorded used different electrode to channel mappings, and thus different electrode separations for the channels recorded. For example, in epoch one channel 4 was used to amplify the potential difference between electrodes 4 and 5 of the linear array, separated by 2 mm, centre to centre. In epoch two, however, channel 4 was used to amplify differences between electrodes 1 and 3, separated by 4 mm, centre to centre. The electrode pair to channel assignment for all channels and all epochs is given in table 2.1.

A 7 channel Racal data recorder was connected to the "J6" outputs of the Model 8A5 amplifier. The J6 outputs provide a maximal 2.8 volts (peak to peak) through a 500 Ω output impedance [GRASS model 8 instruction manual]. Channels 1,2,3,4,6,7 and 9 of the amplifier were used. Channels 5 had its inputs shorted, channels 8 and 10 through 16 were unused.

The amplifiers were also connected (in parallel with the data recorder) to a GRASS model 8 "writer unit" which recorded the potentials obtained on paper via electro-mechanical pen-deflections. Figure 2.7 shows a sample of the output recorded with the writer unit. Due to the mechanical nature of the pens the writer unit has a high frequency limit of 95 Hz (-3 dB) [GRASS model 8 instruction manual]. The model 8 amplifier was set to its maximum gain of 112,000 (1 microvolt per mm on the control panel) implying that a 1 microvolt input signal produced 0.1 volts at the J6 output jack, which drove the data recorder.

The data recorder was set to a tape speed of 7.5 inches per second, at input sensitivities of 1, 2 and 5 volts peak to peak (epoch dependant, specified below). The frequency response at 7.5 inches per second is DC to 20 kHz (-3 dB), therefore capable of recording all signals produced by the Model-8 amplifiers.

FIGURE 2.7

Sample output from the GRASS writer unit during epoch 3. Channel 1 is at the top, channel 16 at the bottom. In this case channels 1, 2 and 3 are amplifying potential differences between 2 mm spacings; channels 4 and 9 across 4 mm; channel 6 across 6 mm and channel 7 across 14 mm. Channels 5 has short circuited inputs and channels 8, and 10 through 16 are not connected.

All Epochs (unless otherwise noted below)

Tape speed set at 7.5 inches per second

Model-8 amplifier settings at:

1 microvolt per mm

5 Hz high pass

10 KHz low pass

60 Hz notch filter ON

EPOCH NUMBER	CHANNEL ELECTRODE ASSIGNMENT	TAPE POSITION	COMMENT
1	1) 1-2	0-100	MONTAGE A figure 2.6
	2) 2-3		
	3) 3-4		
	4) 4-5		
	5) 5-6		data recorder set to 1 Volt peak-peak
	6) 6-7		
	7) 7-8		
2	1) 1-2	100-250	MONTAGE A figure 2.6
	2) 2-3		
	3) 3-4		
	4) 1-3		
	5) 2-4		data recorder set to 5 volts peak-peak
	6) 1-4		
	7) 1-8		
3	1) 1-2	250-500	MONTAGE B figure 2.6
	2) 2-3		
	3) 3-4		
	4) 1-3		
	5) 2-4		
	6) 1-4		
	7) 1-8		
		310	60 Hz notch filter OFF
		330	data recorder set to 2 Volts peak-peak
		350	60 Hz notch filter ON
		440	5 Hz strobe light
		460	30 Hz strobe light

TABLE 2.1

EPOCH NUMBER	CHANNEL ELECTRODE ASSIGNMENT	TAPE POSITION	COMMENT
4	1) 1-2	500-710	MONTAGE B figure 2.6
	2) 3-4		
	3) 5-6		
	4) 7-8		
	5) 1-4		
	6) 3-6		
	7) 5-8		
		590	40 Hz strobe light
		600	20 Hz strobe light
		620	10 Hz strobe light
		670	20 Hz strobe light
		690	strobe off
		710	experiment over

TABLE 2.1 (continued)

Four separate epochs of data from two different scalp positions were recorded (scalp positions in Figure 2.6). Each epoch lasted approximately 5 minutes. At various times during the recordings filter settings were changed, a strobe light was turned on or off, or the sensitivity of the data recorder was changed. The time and tape position of these events was noted. A summary of the parameters of the four epochs is given in table 2.1. An oscilloscope was used to verify the presence of some signal at the J6 outputs. After the experiment was completed, a second copy of the output data was produced by driving the Model-8 writer unit from the data recorder through the J5 input jacks on the Model-8. The digitization, analysis and interpretation of the experimental data was subsequently carried out at Carleton University and is described in the next chapter.

CHAPTER 3

DATA ANALYSIS

3.1 Data acquisition and digitization

Two copies of the data were simultaneously recorded during the experiment, one on the GRASS EEG paper output device, the other on the Racal data recorder. The hardcopy writer unit has a frequency response between 0 and 95 Hz (-3 dB). The "J6" output to which the data recorder was connected has a bandwidth of 0 to 22 kHz (-3 dB) [GRASS model-8 instruction manual]. When run at 7.5 inches per second, as in the Civic Hospital experiment, the data recorder has a -3 dB response between 0 and 20 kHz [Racal instruction manual]. These limiting frequencies are well over the "normal" EEG frequencies of 0 to 30 Hz. The J6 output band includes the higher frequencies, in the hundreds of Hz, required to capture sensory evoked potentials. The experiment was run with a 3 Hz high pass filter (-3 dB) selected from the GRASS model-8 control panel, as lower frequencies than this were not expected to be of interest.

Data collected on the recorder were filtered, digitized and analyzed at the Carleton University department of Systems Engineering. EEG segments were selected by visual inspection of the paper output, and marked at the corresponding point on the data tape. The data mark was made by dubbing a one-second

step function onto the tape at the point of interest. When subsequently digitized, the computer discarded data until the falling edge of this step function was found. The analog data coming from the data recorder was passed through three cascaded anti-aliasing filters (Krohn-Hite 3550), thereby providing -60 dB attenuation (-20 dB each) at selected frequencies. The filter cutoff frequencies were always set to well below half of the sampling frequency as required by the Nyquist sampling theorem.

After passing through the anti-aliasing filters, the analog signal was sampled and digitized by a 16 channel analog to digital converter connected to a Texas Instruments "Professional Computer", through which the digitized data was stored on floppy diskettes. Finally the floppies were transported to the Sun computer system and processed with the Matlab data analysis software.

3.2 Visual inspection of paper output

In the course of the experiment 112 pages of data representing 18.6 minutes of EEG were recorded. Of this, only 5 minutes were sufficiently artifact-free (see figure 3.2) to be considered for further (computed) analysis. However, the paper trace itself provides important information about the signals recorded. Figure 3.1 is a sample of "clean" (no artifact evident) EEG data as recorded during trial 3 of the experiment, whereas figure 3.2 illustrates some of the common artifacts encountered. In the clean recording, pen 9 was connected to short-circuited inputs and represents an approximate measure of the minimum noise level, roughly 1 microvolt peak to peak as measured from this trace. Pen 8 was not connected. Pen 7 recorded the potential difference between the outermost two electrodes of the array, separated by 14 mm. At this time in the experiment there was a strong 3 to 5 microvolt (peak to peak) 9 Hz signal observable at the scalp between these electrodes. Pen 6 was recording the potential between electrodes 1 and 4, separated by 6 mm, and delivering only about 2 μ V peak to peak. A further reduction in amplitude is evident in traces 1,2 and 3, all of which represent potentials across only 2 mm of scalp. The signals here are so small it is difficult to determine whether the 9 Hz signal clearly recorded by pen 7 is even present. It is clear, however, that these pens were recording something more than the minimum noise level recorded by pen 9.

FIGURE 3.1

A sample of EEG as recorded during the 3rd trial of the Civic Hospital experiment. The data here is seemingly free of artifact. Channel 7 most clearly shows a recognizable EEG pattern, with strong alpha (9 Hz) activity.

FIGURE 3.2

A sample of some of the more common artifacts encountered during the experiment. The upper four traces show evidence of poor electrode contact. The lower four have received electromagnetic interference from the strobe light.

Figure 3.3 illustrates the increase of amplitude with electrode separation. The 14 mm separation generates roughly twice the potential of the 6 mm separation which in turn generates about twice the potential of the 2 and 4 mm separations. The electrodes separated by only 2 mm are generating a potential difference of approximately 1 microvolt peak to peak. Since the nominal input noise of the model-8 amplifier is 2 μ V peak to peak, it is difficult to attribute the wiggles captured across these separations to brain activity. The paper trace suggests that 6 mm scalp separations contain detectable EEG, and, by extension, that smaller inter-electrode spacing could also, with less noisy, higher gain amplifiers. The question of information content across such spacing - is it redundant with respect to adjacent electrodes or not - was investigated by computer analysis of the data tapes.

FIGURE 3.3
Increased electrode separation leads to higher scalp potentials. The lowest trace (2 mm separation) is difficult to distinguish from noise.

3.3 Noise in the data

Figure 3.4a is a sample of unfiltered EEG recorded across 2 mm of scalp. The root mean square (RMS) value of this data segment was $0.65 \mu\text{V}$. The data in the figure has had a zero-frequency or DC offset subtracted out and is presented as multiples of the RMS value. The data was sampled at 10 kHz, the segment shown therefore represents just over 0.8 seconds of EEG. As can be seen in this figure, the data contains frequencies far in excess of 30 Hz. Figure 3.4b is a fast fourier transform (FFT) of a typical data segment, illustrating what was found to be generally true for all data; the spectrum extends well past 4 kHz, with the strongest contributions made between 0 and 50 Hz.

Having discovered that the data had such an unexpectedly wide spectrum forced us to quantify the background noise as seen by the data recorder. Using figure 3.4c as a guide suggests 10% of the strongest frequency as a fair approximation to the average white noise level that extends out to over 4 kHz. The strongest frequency, nearly 10 Hz, is oscillating at roughly 1 microvolt (figure 3.5), implying an approximate white noise level of $0.1 \mu\text{V}$.

FIGURE 3.4

a) TOP: "Pure" EEG as recorded by the data recorder. RMS = $0.65 \mu\text{V}$.

b) MIDDLE: Typical frequency spectrum of recorded data extending beyond 4 kHz.

c) BOTTOM: Expanded view of frequency spectrum shown in (b).

Figure 3.5 provides an indirect measure of the low-frequency noise generated by the amplifiers. The solid line in that figure represents the potential difference measured between electrodes 1 and 3 on the scalp, a separation of 4 mm. The dotted line represent the sum of the potential differences between electrodes 1 to 2, and 2 to 3. If no noise were generated by the amplifier, these two curves would be identical, instead differences in excess of $0.5 \mu\text{V}$ are frequently seen. The noise specifications for the GRASS model-8 amplifier indicate that an RMS value of $0.5 \mu\text{V}$, depending on source impedance, can be expected. This is consistent with the approximations made here and highlights the central difficulty of the experiment. Potentials across the smaller (2 to 4 mm) electrode separations are usually less than 1 microvolt in amplitude, too close to the specified 0.5 RMS noise level to allow precise measurements to be performed.

FIGURE 3.5

Comparison between channel 4 (electrodes 1-3) and the sum of channels 1 (electrodes 1-2) and 2 (electrodes 2-3). Any deviation between the solid and dotted traces is due to noise.

3.4 Frequency spectrum measurements

Figures 3.6a to 3.6g are FFT spectra obtained for each of the 7 recorded channels during the third trial of the experiment. Several significant features are illustrated by these spectra. Channels 1 and 2 (figures 3.6a and 3.6b) have what first appears to be model EEG frequency profiles, i.e. strong activity in the 0 to 20 Hz range, little activity beyond 20 Hz, and the expected notch at 60 Hz (due to the use of a 60 Hz notch filter). However, both these channels indicate maximal contributions from frequencies below 3 Hz, which were being attenuated by the 3 Hz high pass filter used during the experiment. These channels were recording potentials across only 2 mm of scalp, generating potentials close to the RMS noise level of the amplifiers. It is therefore likely that the maximal peaks seen in channels 1 and 2 are just the $1/f$ noise produced by the GRASS model-8. Interestingly, channel 2 (figure 3.6b) displays a strong secondary contribution at about 17 Hz which is more difficult to attribute to noise. Channel 3 (figure 3.6c) seems to contain only noise, possibly due to a non-contacting electrode. The 60 Hz notch is still present. Channel 4 (figure 3.6d), like channels 1 and 2, displays a spectrum suggestive of EEG activity, this time across 4 mm of scalp. Again it is possible that the largest peak represents only $1/f$ amplifier noise. Channels 5, 6 and 7 (figures 3.6e, f, g) are unique in that they all show a significant peak at 180 Hz, the third

harmonic of the power line frequency. It is possible that a source impedance imbalance, due to poorly contacting electrodes, is responsible for the amplifier's failure to reject this harmonic as a common mode signal. Channel 7 (figure 3.6g), recording potentials across 14 mm, shows a strong contribution at 10 Hz, apparently quite distinct from the possibility of $1/f$ noise. Channels 2, 5 and 6 share a strengthened 10 Hz contribution to their spectra, albeit with significantly reduced power.

The spectra for many other epochs were computed and found to be similar to those just presented, except that channel 3 is not usually noticeably different from other channels. Although this analysis suggests that a classical 0 to 30 Hz band might be seen by electrodes separated by as little as 4 mm, the influence of amplifier noise on these measurements is significant and cannot be discounted.

FIGURE 3.6

- a) FFT for channel 1
- b) FFT for channel 2
- c) FFT for channel 3
- d) FFT for channel 4
- e) FFT for channel 5
- f) FFT for channel 6
- g) FFT for channel 8

3.5 Inter-channel comparisons

Having been unable to conclusively determine both the amplitude and frequency range for the smallest (2 mm) electrode separations, a comparison of the signals between adjacent channels was undertaken. By applying filtering techniques based on the characteristics of a signal in more than one channel, a reduction of the noise level beyond what can be achieved by single-channel techniques is possible. **Figure 3.7a** shows the cross-correlation for the 5 to 25 Hz band between channels 1 and 2, as well as between channels 2 and 3 for an epoch of EEG recorded during the 3rd trial. As can be seen in this figure, the correlation coefficient for these channels is high (0.88) and maximal at 0 time shift. This suggests that the channels were recording more than just noise, as the correlation coefficient is close to 1, but that there is little temporal difference in what they were recording, since the correlation is maximal without any relative time shift of the signals.

Figure 3.7b is a plot of the maximum correlation between adjacent channels as a function of frequency. Individual 10 Hz bands were isolated from the Fourier spectrum of the original waveform, inverse-transformed to produce a time varying signal and then cross-correlated with a similarly processed signal in the adjacent channel. The "correlation quotient" plotted in **figure 3.7b** is intended only to display a measure of relative correlation.

FIGURE 3.7

- a) TOP: Cross correlation between channels 1 and 2 (solid line) and channels 2 and 3 (dotted line). The correlation coefficient is high (0.88) and maximum at the origin ($T=0$).
- b) BOTTOM: Maximum correlation as a function of central frequency for 10 Hz bands. Highest correlations are obtained in bands below 40 Hz.

As can be seen in the figure, quotients are maximal in the 3 bands below 40 Hz, and again suggest that even for 2 mm separations EEG can be recorded. If the lower-frequency signals had been due only to $1/f$ amplifier noise, their cross-correlation would have been as low as that in the higher white-noise frequencies. Again, however, the possibility that the tightly spaced electrodes are merely over-sampling a relatively crude underlying signal cannot be discounted.

Figure 3.8a and 3.8b are plots of the cross correlation between two pairs of adjacent channels (2 mm separation) after having been low-pass filtered at 30 Hz. In both cases, the maximum correlation coefficient is attained with significant relative time-shifts, -0.4 seconds (-200 time units) for the channel 5 to channel 6 cross correlation, and +0.07 seconds (+33 time units) for the channel 6 to channel 7 cross correlation. The larger -0.4 second shift is the time required for channel 5 to be maximally correlated with channel 6, however, a much shorter 0.05 second delay would be required to reach the closest positive correlation peak shown in figure 3.8a. It seems likely that the -0.4 second true maximum is a side effect of noise-contaminated data, as it is the 4th correlation peak from time 0. Assuming then that 0.05 seconds were required for the signal in channel 5 to propagate to channel 6, and 0.07 seconds for it to propagate from channel 6 to channel 7, a propagation velocity of (2 mm / 0.05 sec) 40 mm per second might be inferred. This is a neurologically

plausible speed [Niedermeyer 1987], and could suggest that the electrodes were collecting non-redundant information even when separated by only 2 mm. Figure 3.8c is the cross-correlation between a data channel and a synthetic noise source. Except for the compressed time axis, some of the same features as described for figures 3.8a,b are evident here; the periodic oscillations are present in a somewhat less regular form, and a non-zero time shift to maximum correlation is required. Finally it is therefore possible that the propagation velocities deduced above are yet another side effect of noisy data.

FIGURE 3.8

- a) **TOP:** Correlation coefficient between adjacent channels 5 and 6. Maximum correlation occurs at $t=-200$, perhaps due to noise.
- b) **MIDDLE:** Correlation coefficient between adjacent channels 6 and 7. Maximum occurs at $t=+33$ (66 milliseconds).
- c) **BOTTOM:** Correlation between a data channel and a synthetic noise source. Note similarity between this and traces (a) and (b) implying noise could be responsible for time lags seen in those traces.

The cross-correlation curves discussed above share a strengthened rhythmic appearance, due to the enhancement of mutually rhythmic activity by the cross correlation function. The FFT of a cross-correlation curve represents the shared frequency spectrum of the crossed channels and will attenuate frequencies present in only one channel. Since the spectrum of random noise generally differs from moment to moment and channel to channel, the FFT of a cross-correlation provides a spectral profile with reduced noise contributions. **Figures 3.9a to 3.9d** are the spectra of channel 3 cross-correlated with channels 4,5,6 and 7. It was hoped that the cross-spectrum of the further separated channels would be noticeably different from that of adjacent channels, but no such regular trend was found. All spectra do however show relatively strong 8 or 10 Hz activity, further supporting the possibility of detecting 2 mm scalp EEG.

FIGURE 3.9

FFT spectra of cross correlation of channel 3 with 4 other channels. The solid lines represent the average of 16 FFT's calculated for each channel pair. Dots represent spectra of individual epochs. Note strong 8 and 10 Hz contributions in all cases.

- a) TOP LEFT: Channel 3 vs. channel 4, 2 mm separation
- b) TOP RIGHT: Channel 3 vs. channel 5, 4 mm separation
- c) BOTTOM LEFT: Channel 3 vs. channel 6, 6 mm separation
- d) BOTTOM RIGHT: Channel 3 vs. channel 7, 8 mm separation

The elimination of noise frequencies by comparison with other channels was extended with an FFT filtering method wherein frequencies in one channel were removed from the fourier spectrum unless they were also present with some minimum power in other pre-defined channels. Two sets of comparative channels were tried. In one set, the filtered channel had to match frequencies with its adjacent channels. In the second set the filtered channel had to match frequencies with all other recorded channels. To provide additional selectivity of frequencies, a filtered channel lost all frequencies which did not contribute more than a pre-defined fraction of the average contribution to the spectrum. Figures 3.10a to 3.10d illustrate this filtering method. Figure 3.10a is the spectrum of channel 1 prior to any filtering other than the analog anti-aliasing filters used during digitization (200 Hz low pass in this case). Figure 3.10b is the same spectrum after all frequencies which did not exceed 0.99 of the mean contribution were removed. Figure 3.10c is the spectrum of channel 3 after some of its frequencies have been eliminated by comparison with the adjacent channels 2 and 4. Any frequency in channel 3 whose power differed by more than 10% in channels 2 or 4 was removed from the spectrum. Figure 3.10d represents the spectrum of channel 3 after all frequencies whose power differs by more than 35% in any other channel (as opposed to just the 2 adjacent channels) have been removed. Spectra which have been

"cut and matched" in this way are then inverted to produce filtered time-varying signals. Channels which have been filtered in this way are then plotted and visually compared. **Figure 3.11a** compares channel 3 to 4 and channel 4 to 5 after all of them have been filtered as described above. In this case frequencies were chosen in relation to the two adjacent channels only. **Figures 3.11b** and **3.11c** are traces of similarly processed channels, except in this case frequencies were selected by comparison with all other channels. Also, frequencies were not "cut" for the traces in **figures 3.11b,c** (frequencies weren't discriminated on their relative contribution to the spectrum), resulting in the preservation of some higher frequencies and the more jagged appearance of these traces. All the data presented in these figures is for channels recording 2 mm scalp activity. In general the "all channel match" filter produces curves wherein adjacent channels appear more similar than the "adjacent channel match" filter, probably because more of the noise frequencies have been eliminated from the spectra. These figures indicate strong similarities between adjacent channels, to the extent of suggesting redundancy for 2 mm electrode spacing.

FIGURE 3.10

Selective removal of spectral components based on comparisons with the spectra of other channels.

a) **TOP LEFT:** Original spectrum of channel 1 after analog anti-aliasing filters.

b) **TOP RIGHT:** Same spectrum after rejection of any component not greater than 0.99 of the mean contribution.

c) **BOTTOM LEFT:** Spectrum of channel 3 after rejection of components more than 10% different in either of its adjacent channels.

d) **BOTTOM RIGHT:** Spectrum of channel 3 after rejection of components more than 35% different in any of the 6 other channels.

FIGURE 3.11

EEG waveforms after application of the FFT "cut and match" filtering technique.

- a) **TOP 2 TRACES:** Frequencies contributing less than 0.99 of the mean were rejected, as were frequencies that differed by more than 10% with adjacent channels. ("0.99 cut, 0.9 match").
- b) **MIDDLE 2 TRACES:** Frequencies differing by more than 50% in any other channel are rejected.
- c) **BOTTOM 2 TRACES:** Same as (b), but for different channels.

3.6 Analysis summary

The difficulty in drawing absolute conclusions from this experiment stems mainly from the poor signal to noise ratio attained when electrodes are separated by only 2 mm, generating sub-microvolt signals, and the amplifier used has a peak to peak noise specification of 2 μ V. There is a suggestion that such tightly spaced electrodes do in fact detect an EEG signal, although adjacent pairs may not carry significantly different information, thereby defeating their purpose. Sufficient curiosity was aroused to motivate the design of a lower noise amplifier in the hope of finding a better defined limit to attainable EEG scalp resolution.

CHAPTER 4

A high resolution EEG amplifier

4.1 General design constraints

The detection of an apparent EEG signal with 4 mm electrode separation led to the design of an amplification system capable of detecting tiny (0.2 to 1.0 microvolt RMS) voltages over a small scalp area. The system was intended to provide the highest attainable spatial resolution, to be easily applied to the patient, and to be affordable. The system was hoped to be marketed as a clinical replacement for the conventional 16 or 32 channel EEG apparatus now in common use. The maximum spatial resolution is limited by unavoidable input noise, (the thermal noise of the scalp, skull, and other tissue), and by the minimum equivalent input noise generated by the amplifiers. Higher resolution is obtainable in evoked potential recordings, wherein the signal to noise ratio can be improved through response averaging. The actual minimum useful distance between electrodes depends on how often an experimenter repeats the stimulus-response cycle. In the spontaneous EEG recordings taken at the Civic Hospital, an EEG signal was detected between electrodes separated by 4 to 6 mm, suggesting a 5 mm inter-electrode distance may be useful for spontaneous recordings. As little as 2 mm could be used for the evoked potential recordings.

A matrix of electrodes spaced on 3.3 mm centres requires 50 electrodes to cover a square inch (6.3 sq. mm) of scalp. The curvature of the head limits the practical area for a rigid electrode matrix to approximately one square inch, beyond which the edge electrodes are lifted unacceptably far from the scalp. The optimum geometry for such a matrix is a hexagonal chip which could be tiled together with other chips to cover an arbitrary scalp area. A simpler square geometry is almost as good, but leaves bigger gaps when tiled to the scalp. In the design of a prototype the simpler square chip was used.

The mechanical difficulty of constructing a robust matrix with 3 mm inter-electrode spacing is most easily overcome with a surface deposition method such as that used for building integrated circuits. A variation of this procedure, used to construct cochlear implant electrodes, has been developed at Carleton University [van der Puije 1989]. A similar method was to be used to construct the prototype of the EEG matrix. The method ensures a repeatable and accurate process and produces an electrode "circuit" which can be bonded to a rigid (eg. epoxy) supporting plate. It also permits the construction of a hybrid circuit wherein EEG amplifiers and other electronics are bonded directly onto the matrix substrate. This places the amplifiers as close as possible to the signal source, minimizing the pickup of interference. A circuit based on this approach was designed using the ICED graphics tool at Carleton

University (appendix A). The signals obtained by the matrix are potential differences between selected electrodes, or potential differences between a selected electrode and a common or ground electrode. If the potentials are measured relative to ground, a 50 electrode matrix emits just 50 signals, which are subsequently compared to each other to generate the spatial potential distribution map. If potentials are recorded differentially, a matrix of 50 electrodes generates 100 signals (4 potentials for each electrode relative to its 4 nearest neighbours, divided by 2 to eliminate redundancy). If the redundant measures are not eliminated, each potential difference is simultaneously measured by 2 separate amplifiers, which might be used to improve the S/N ratio. In any case, the minimum number of signals generated by a 50 electrode chip is 50, but up to 200 signals may be useful. It is mechanically difficult to build or use a harness of wires carrying 100 extremely low power signals. The cost of a system with the necessary low-noise amplifiers (one per signal) is high and possibly unmarketable. Systems capable of supporting more than a single matrix would require several hundred parallel amplifiers. In light of this, the matrix was designed to share a single amplifier between many electrodes, made possible by the low bandwidth of the EEG signal. Electrode pairs are selected via analog multiplexers, sequentially routing the 100 signals to one low-noise amplifier. Each signal is amplified and sent to a data

acquisition computer where the matrix output is de-multiplexed and the scalp potentials are reconstructed. The electrode matrix then runs from one amplifier, the bank of multiplexers, and the digital circuitry required to control the data routing. Space limitations imposed by mounting the various electronic devices directly on the matrix chip are overcome by using die-form circuits and multi-layering the matrix circuitry.

The availability of all selected components in die form, and the design of the matrix layout with the ICED software suggested a workable approach to building a pre-production prototype. A multiplexed circuit functionally equivalent to this prototype was designed and tested.

4.2 A multiplexed amplifier

The scalp EEG signal has the following characteristics:

TABLE 4.1
Characteristics of EEG signal

Two Possible Frequency Bands:

band 1 uses 0 to 30 Hz, for ordinary EEG activity
band 2 uses 0 to 500 Hz, for evoked potentials

Source Impedance:

minimum of 1 k Ω for large (4 mm) electrodes
up to 300 k Ω for needle electrodes
negligible capacitance

Expected Amplitude:

0 to 10 μ V

A sampling frequency of at least twice the maximum signal frequency, as dictated by the Nyquist sampling theorem, is required to accurately reconstruct a waveform [Malmstadt 1974]. For 100 signals at 30 Hz, the electrode matrix would generate data at (100 * 60) 6000 Hz. When monitoring 500 Hz signals in evoked potential experiments, the matrix output frequency would be 100 kHz. The highest quality, lowest noise commercially available instrumentation amplifier found was the Analog Devices "AD624". Figure 4.1 summarizes the critical specifications of the AD624. The minimum equivalent input noise of the amplifier is obtained when the maximum gain (1000) is used. The 25 MHz gain-bandwidth product of the AD624 limits the unattenuated gain to 250 for a 100 kHz data rate. As can be seen in figure 4.1, the input noise voltage at a gain of 100 is 50% higher than at a gain of 1000 (0.3 instead of 0.2 μ V p-p).

a)

SPECIFICATIONS(typical @ $V_s = \pm 15V$, $R_L = 2k\Omega$ and $T_A = +25^\circ C$)

SPECIFICATIONS (typical @ $V_s = \pm 15V$, $R_L = 1k\Omega$ and $V_{DI} = 0V$)										
Model	AD625A/J/S			AD625B/K			AD625C			Units
	Min	Typ	Max	Min	Typ	Max	Min	Typ	Max	
INPUT CURRENT										
Input Bias Current		± 30	± 50		± 20	± 25		± 10	± 15	nA
vs Temperature		± 50			± 50			± 50		pA/°C
Input Offset Current		± 2	± 35		± 1	± 15		± 1	± 5	nA
vs Temperature		± 20			± 20			± 20		pA/°C
INPUT										
Input Impedance										G Ω
Differential Resistance		1			1			1		G Ω
Differential Capacitance		4			4			4		pF
Common-Mode Resistance		1			1			1		G Ω
Common-Mode Capacitance		4			4			4		pF
Input Voltage Range										V
Differential Input Linear (V_{DI})		± 10			± 10			± 10		V
Common-Mode Linear (V_{CML})		$12V - (\frac{G}{2} \times V_{DI})$			$12V - (\frac{G}{2} \times V_{DI})$			$12V - (\frac{G}{2} \times V_{DI})$		V
Common-Mode Rejection Ratio dc to 60Hz with 1k Ω Source Impedance										dB
G = 1	70	75		75	85		88	90		dB
G = 10	90	95		95	105		100	115		dB
G = 100	90	105		105	115		110	125		dB
G = 1000	110	115		115	125		120	140		dB
OUTPUT RATING										
		$\pm 10V$			$\pm 10V$			$\pm 10V$		
		1.5mA			1.5mA			1.5mA		
DYNAMIC RESPONSE										
Small Signal - 3dB										kHz
G = 1, $R_s = 20k\Omega$		650			650			650		kHz
G = 10		400			400			400		kHz
G = 100		150			150			150		kHz
G = 1000		25			25			25		kHz
Slew Rate		5.0			5.0			5.0		V/ μ s
Settling Time to 0.01% 20V Step										μ s
G = 1 to 100		15			15			15		μ s
G = 100		35			35			35		μ s
G = 1000		75			75			75		μ s
NOISE										
Voltage Noise 1kHz										nV/ $\sqrt{Hz}$
R T I		4			4			4		nV/ $\sqrt{Hz}$
R T O		75			75			75		nV/ $\sqrt{Hz}$
R T I 0.1 to 10Hz										μ V p-p
G = 1		10			10			10		μ V p-p
G = 10		1.0			1.0			1.0		μ V p-p
G = 100		0.3			0.3			0.3		μ V p-p
G = 1000		0.2			0.2			0.2		μ V p-p
Current Noise										pA p-p
0.1Hz to 10Hz		60			60			60		pA p-p

b)

Low Frequency Voltage
Noise, $G=1$

c)

Low Frequency Voltage
Noise, $G=1000$

FIGURE 4.1

Analog Devices DG506 specifications and figures.

a) TOP: Critical specs for selection as an EEG amplifier.

b) BOTTOM LEFT: .1 to 10 Hz input noise at gain of 1.

c) BOTTOM RIGHT: .1 to 10 Hz input noise at gain of 1000.

[adapted from Analog Devices AD624 data sheet]

For a 10 Hz band between 0.1 and 10 Hz, with a relatively low 1 k Ω skull (source) impedance, random fluctuations in the leakage current of the amplifier ("current noise") (60 pA p-p, 15 pA RMS) generates 150 nV RMS of noise. Random low frequency variations of the input voltage offset of the amplifier ("voltage noise"), cause approximately 50 nV RMS of noise, and therefore negligible in comparison with the current noise. These noise level specifications are the lowest we could find, nearly 4 times better than those of the EEG amplifier used in the Civic Hospital.

Noise data on the analog multiplexers are difficult to obtain. The Siliconix DG506 chip was chosen because it offered 16:1 multiplexing, a 1 MHz bandwidth, low on-resistance of 270 Ω (typical), availability in die-form, and its reputation for low-noise performance. Two other analog multiplexers, the Siliconix DG538 and the DG409 were also tested.

A circuit was designed and built around the precision instrumentation amplifier and the 16 channel analog multiplexer. **Figure 4.2** is a schematic of the circuit as implemented. An analog voltage is presented to the multiplexers, one side of the source connected to the "A" mux bank, the other to the "B" mux bank. Low power CMOS logic latches control data sent from the computer. This control information selects appropriate mux channels and connects the analog source to the inputs of the AD624. Two extra channels are used to compare signal waveforms with noise. One noise

channel connects to a 10 k Ω resistor, i.e. a signal-less source with approximately the same impedance as the skull, and the other noise channel connects to a short-circuit. The AD624 amplifies its input voltage and sends it to the SMP11 sample and hold chip. The SMP11 was used to sample the amplified output as late as possible after channel switching, to avoid the MUX's signal-obliterating "switch glitch". Output from the sample and hold chip is low pass filtered and monitored on an oscilloscope and/or spectrometer.

The final version of the test circuit used 4 parallel AD624 amplifiers in an effort to reduce noise levels. The noise reducing effect of paralleling amplifiers is discussed in section 4.4. Digital and analog circuits and wires were maximally separated to minimize digital interference. Separate digital and analog grounds were used, tied together at the power supply. All analog chips had their own ground wire. Originally an automatic auto-zero circuit was used to keep the AD624 close to zero offset, but this proved unnecessary and was replaced by a nulling potentiometer. Many variations on the basic circuit were tried and usually found to have no noticeable impact on its performance. Use of the sample and hold to avoid the mux switch glitches, paralleling the AD624s to partially cancel the voltage noise, and using a steel box to shield the circuit from interference were essential to attain the noise levels described in the next section.

FIGURE 4.2 (next 6 pages)
Block diagram of the multiplexed EEG amplifier. With the exception of the electrode matrix block, each element is drawn in detail in the subsequent pages.

FIGURE 4.2 continued
The circuitry used to generate test signals. The "CH2" output is simply a short circuit, used for voltage noise measurements. The "NOISE" output is a source with roughly the same impedance as the skull, without any signal. "CH1" provides a variable test signal.

FIGURE 4.2 continued
 The analog multiplexers through which the input signals are routed. Control of the multiplexers is sent from latches described in the "control" block. Only 8 mux channels were connected for testing.

FIGURE 4.2 continued
 The primary amplification stage. Signals from the multiplexers are fed to the inputs of 4 parallel instrumentation amplifiers. The output of these is averaged with the OP37 "summing amp" and passed to the sample and hold chip. The final output is low pass filtered.

FIGURE 4.2 continued
Control information sent from the computer is latched, decoded and passed on to the multiplexers and analog switches. The analog switch was used to allow shorting the inputs to the amplifiers, or in some variations to optionally send the amplified output to the sample and hold circuits.

FIGURE 4.2 continued
Two variations of power supplies used, one a conventional line transformer with voltage regulators, the other a pair of car batteries, also using regulators though probably unnecessarily.

4.3 Test of multiplexed amplifier

The multiplexed circuit had its channel control logic connected to the I/O ports of an Analog to Digital conversion board, which was plugged into the backplane of the Texas Instruments Professional Computer. A program executing on the computer defined the switching behaviour of the test circuit. A wave generator (Hewlett Packard 3312A) provided test signals which were fed through an attenuator (Daven T693) en route to the analog multiplexers (Siliconix DG506). The amplified output was sent through 4 analog bandpass filters (Khron Hite 3202), normally set to 30 Hz low pass, providing 80 dB attenuation of unwanted frequencies. The output from these cascaded filters was monitored on an oscilloscope and a spectrum analyzer.

The circuit was first tested on a work bench, but 60 Hz interference finally forced it inside a steel shielding box powered from two car batteries (also in the box). The use of wire-wrap connections increased interference pick up and cross talk, however once in the box this was no longer a problem. Initially the multiplexers were statically set to select a single input channel, eliminating any noise created by electronic multiplexing. Noise levels were obtained by progressively decreasing the input signal amplitude (selecting greater attenuation factors on the Daven T693), until the corresponding output could no longer be seen to decrease, or until an arbitrary signal to noise amplitude was observed on

the oscilloscope. The noise level was then calculated from the known input signal and attenuation factors, and compared to equivalent input noise and amplifier gain calculations. When the circuit was built with 4 parallel amplifiers, it exhibited input noise levels of $0.18 \mu\text{V}$ peak to peak for a 30 Hz bandwidth and a $1 \text{ k}\Omega$ source impedance. **Figure 4.3** compares the noise output of a single amplifier to that of 4 parallel amplifiers. As can be seen, the noise level is approximately halved, suggesting that even greater paralleling might be effective. However, when a larger ($10 \text{ k}\Omega$) source impedance was used, the noise levels became unacceptably large. A $10 \text{ k}\Omega$ source generated nearly $2 \mu\text{V}$ peak to peak. The linear relationship between source impedance and noise level implies that the current noise of the AD624 was responsible for the degradation.

In addition to the serious difficulty presented by the combination of larger source impedances with amplifier current noise, the multiplexing of these sub-microvolt signals proved to be impossible. **Figure 4.4a** compares noise levels when a single mux channel was statically selected to those when the mux was switching at 40 kHz.

FIGURE 4.3

Several sweeps recorded on the digital storage oscilloscope comparing single-amplifier noise levels (sweeps marked Noise1) with four parallel amplifier noise levels (marked Noise2). A source impedance of 1 k Ω and a 0 to 30 Hz band were used.

The mux noise was dependent on the switching frequency. A spectrometer was used to observe the input noise spectrum, which was seen to contain 20 to 40 dB spikes in the tens of kHz. These were being aliased into the signal band by the sampling frequency, which was varied between 60 Hz and 50 kHz. In general, muxing created roughly ten times the low-frequency noise of a continuous sample. 60 Hz interference was reduced by sampling at an exact multiple of the line frequency, thereby aliasing the line interference to a DC or very low frequency noise. The mux noise is caused by a current and voltage glitch generated when switching. Using the sample and hold circuit at the output, out of phase with the switching pulse, helped reduce the problem, but not to an acceptable level. Cancelling the glitch by using a separate dummy mux and subtracting its glitch from the glitch generated in the signal mux also helped a little (30% reduction in glitch amplitude), but the noise spikes did not overlap identically and were therefore not perfectly cancelled. A capacitor across the output of the mux banks also helped somewhat, but the capacitance reduces the bandwidth of the system, which must be capable of amplifying a 100 kHz data rate. **Figure 4.4b** is a sketch of the switching glitch as observed during testing.

FIGURE 4.4

- a) TOP: Noise levels of an unswitched input signal compared to an input signal multiplexed at 40 kHz.
 b) BOTTOM: Sketch of the mux switching glitch responsible for the increased noise levels.

Although the input noise level seemed acceptable when an un-multiplexed $1\text{ k}\Omega$ source was amplified, use of more realistic source impedances and glitches generated by the multiplexers both created noise levels in excess of $2\text{ }\mu\text{V}$ peak to peak. Alternative multiplexers, the DG538 and the DG409 were tested and found to perform slightly worse than the DG506. Four months were devoted to circumventing these problems, but finally it was decided that multiplexing sub-microvolt signals is not viable with current technology. Also, the 60 pA current noise of the AD624, when multiplied by a $10\text{ k}\Omega$ source impedance generated peak to peak noise voltages of more than a microvolt. Paralleling the amplifiers helped to reduce voltage noise, but the current noise was correspondingly increased. It was decided that an un-multiplexed system using amplifiers with much lower current noise specifications had to be used.

4.4 Design of an optimum EEG amplifier

The rejection of the multiplexing methodology implies that signal amplification must be done away from the electrode matrix, as there is insufficient space to build 100 low-noise pre-amplifiers onto a square inch. The electrode chip will consist only of the contact points and the signal cable header. The signal cable provides each electrode with its own conducting path to the amplifier bank. The amplifier bank will house all of the pre-amplifiers in a constant temperature, electrically shielded environment. The space constraints are now mainly aesthetic, and the pre-amplifiers can be designed to minimize the excess noise in the system. The awkwardness of routing 100 signals from the scalp matrix to the amplifier bank must be overcome through a crafty design of a signal cable, not yet undertaken.

Since uncorrelated noise power adds linearly, the noise power in a potential difference calculated by subtracting two common mode signals (adjacent electrodes) is twice the noise power in a single common mode electrode signal [Ott 1988]. Similarly, a differential amplifier generates twice the input noise power of a one sided common mode amplifier, each side of the differential pair contributing half the noise. However, a balanced differential amplifier has a higher common mode rejection than two independent common mode amplifiers [Sedra 1982], and is therefore chosen for the minimum noise circuit.

Figure 4.5 is the circuit designed to minimize noise in the input stage of an EEG amplifier. It is a differential "NFET", using 8 parallel low-noise FETs on each side of the amp. FETs are the chosen transistors due to their unique combination of high input impedance and extremely low current noise. Although the best bipolar junction transistors exhibit lower voltage noise than the best FETs, their current noise is significantly higher. For signals with a high source impedance, like the EEG, FETs produce less total noise than BJTs.

A good low-noise FET has characteristics similar to those shown in **figure 4.6** for the Siliconix U404. The voltage noise density at 10 Hz is specified as 6 nV per $\sqrt{\text{Hz}}$ (upper limit shown in **figure 4.6b**), the current noise density is calculated from **equation 4.1** to produce curves as shown.

EQUATION 4.1 Noise Current in FETs
[Siliconix FET data book 1986].

$$I_{\text{noise}} = \sqrt{[2q \cdot I_g \cdot B]}$$

$q = 1.6 \times 10^{-19}$ coulombs
 $I_g = \text{DC operating gate current}$
 $B = \text{bandwidth}$

The gate current is a function of the drain to gate voltage. **Figure 4.6c** is a graph of gate current vs. drain-gate voltage. For drain-gate potentials of less than 10 volts (the gate current "breakpoint"), the gate leakage is seen to be less than 2 pA. The noise current is therefore approximately 6×10^{-16} amps RMS in a 1 Hz band. A typical 10 k Ω EEG source impedance thereby causes 6 pV RMS of noise voltage. A relatively high 200 k Ω source impedance would cause 120 pV RMS. As the voltage noise is a much larger 6 nV, current noise is seen to be negligible for a single FET in an EEG application.

For a 10 k Ω skull at 37 celsius, random thermal agitation of the electrons generates approximately 13 nV RMS in a 1 Hz band. A 1 k Ω low impedance skull would generate only 4 nV. A differential amplifier built from 2 low-noise FETs would generate roughly 9 nV RMS in a 1 Hz band at 10 Hz.

FIGURE 4.6

Specifications and performance curves of U404 JFET. Quiescent points as calculated for the optimum EEG circuit are marked. a) TOP: FET characteristics for devices with 3 different pinchoff voltages; $-0.6V$ (left), $-1.2V$ (middle) and $-1.7V$ (right).

b) MIDDLE LEFT: Input noise voltage and noise current curves for a FET similar to the U404. Curves of the noise current for the U404 itself were not given in the data book.

c) MIDDLE RIGHT: Gate operating current as a function of drain-gate voltage. The gate current breakpoint is seen to occur at 10 volts.

d) BOTTOM LEFT: Transconductance as a function of drain current.

e) BOTTOM RIGHT: Transconductance as a function of temperature. The equivalent input noise decreases with decreasing temperature, so operation near 120 Kelvin is seen to optimize transconductance and low-noise operation.

These numbers are based on noise voltages specified at 10 Hz for the U404 FET. For FETs, the frequency at which white noise dominates low-frequency or "1/f" noise is generally between 100 and 1000 Hz. At 10 Hz, noise is largely produced by 1/f mechanisms. At 1 Hz, well within the 1/f noise region, the noise power is approximately 10 times greater than at 10 Hz, implying roughly 30 nV RMS for a 1 Hz band at 1 Hz.

When several FETs are connected to a source in parallel (as in **figure 4.5**), their combined RMS noise voltage is divided by $\sqrt{N}$ whereas their RMS current noise is multiplied by the same factor of $\sqrt{N}$ [Motchenbacher 1973]. However, as calculated earlier, noise caused by FET gate current fluctuations is negligible in comparison to the voltage fluctuations, and so an overall reduction in noise level can be expected when paralleling several FETs. **Figure 4.7** illustrates the equivalent voltage and current noise sources for a differential amplifier using 4 parallel FETs on each side. **Equation 4.2** gives the voltage and current noise as a function of the number of paralleled FETs. The current noise in the FETs is so low that even in the worst case shown with a skull impedance of 200 k Ω , it takes 75 parallel FETs for the current noise to exceed the voltage noise.

The amplifier is assumed noiseless after moving its voltage and current noise into the input circuitry as shown.

FIGURE 4.7

Voltage and current noise sources for a differential parallel ($N = 4$) amplifier. The currents and voltages combine as given by equation 4.2.

2

of/de

2

MICROCOPY RESOLUTION TEST CHART
NATIONAL BUREAU OF STANDARDS
STANDARD REFERENCE MATERIAL 1010a
(ANSI and ISO TEST CHART No. 2)

EQUATION 4.2 Comparison of current noise and voltage noise in differential NFETs

Voltage Noise in 1 FET = $E1$

Current Noise in 1 FET = $I1$

$E2$ = Voltage Noise in a differential FET pair
 $= \sqrt{2} \cdot E1$

$I2$ = Current Noise in a differential FET pair
 $= \sqrt{2} \cdot I1$

EN = Voltage Noise in N parallel differential FETs
 $= \sqrt{2} \cdot E1 / \sqrt{N}$

IN = Current Noise in N parallel differential FETs
 $= \sqrt{N} \cdot \sqrt{2} \cdot I1$

EiN = Voltage created by IN current noise
 $= IN \cdot Rsource$

for (Noise due to current) > (Noise due to voltage)
 in a parallel NFET:

$EiN > EN \Rightarrow (IN \cdot Rsource) > (\sqrt{2} \cdot E1 / \sqrt{N})$
 $\Rightarrow N > (E1 / I1 \cdot Rsource)$

using the Siliconix U404,
 at 1Hz with $Rsource = 10 \text{ k}\Omega$
 $I1 \cdot Rsource = 6 \text{ pV RMS}$
 $E1 = 30 \text{ nV RMS}$
 $\Rightarrow N > 5000$

at 10Hz with $Rsource = 10 \text{ k}\Omega$
 $I1 \cdot Rsource = 6 \text{ pV RMS}$
 $E1 = 9 \text{ nV RMS}$
 $\Rightarrow N > 1500$

at 10 Hz with $Rsource = 200 \text{ k}\Omega$
 $I1 \cdot Rsource = 120 \text{ pV RMS}$
 $En = 9 \text{ nV RMS}$
 $\Rightarrow N > 75$

An EEG amplifier is generally intended to be useful down to frequencies near DC, where $1/f$ amplifier noise is strongest. For an average skull, generating 13 nV of thermal noise in any 1 Hz band, an amplifier input noise of 6 nV contributes less than 20% of the total input noise power and is an acceptable design objective. As derived earlier, a 1 Hz band centred at 1 Hz is expected to contain approximately 30 nV of differential amplifier input noise. To reduce these 30 nV down to 6 requires 25 parallel FETs. Less stringently, 1 Hz band centred on 3 Hz contains only a third the noise power as that at 1 Hz, or roughly 17 nV. If the amplifier is designed to operate down to 3 Hz, 8 parallel FETs suffice to maintain less than a 20% contribution to the total input noise power.

The FETs are kept in the active mode by the Siliconix "CRR4300" constant current source (also a FET). The current source chosen generates 4.3 milliamps as long as more than 3 volts are kept across it. From the drain current characteristics of the U404, (figure 4.6a), a quiescent drain current of 0.3 milliamps is seen to be reachable by all devices independent of their pinchoff voltage. Although higher drain currents generate higher transconductances (figure 4.6d), they also lower the limiting value of the drain resistance. This relationship is non-linear in favour of lower drain currents for higher voltage gains. The constant current source shares its 4.3 mA between the 16 input FETs, roughly

0.3 mA for each. In order to maximize the value of the drain resistor, and therefore the gain, the gate is biased to leave as much as possible of the available 24 volts for the (drain current * drain resistor) drain resistor's voltage drop. A gate bias of 4 volts (as in figure 4.5) guarantees proper function of the CRR4300 and maximizes the available drain voltage. Each drain resistor sees a quiescent current of 2.15 mA, and cannot create a voltage drop exceeding 14 volts to keep the FETs actively biased. The drain resistors are therefore chosen at 5.6 k Ω with an additional 1 k Ω potentiometer used to balance the impedance in the two sides of the NFET (and maximize common mode rejection).

The differential gain of the input stage of the amplifier is given by:

EQUATION 4.3 Differential FET gain [Sedra 1982]

$$V_{do} / V_{di} = -g \cdot R_d$$

V_{do} = differential output voltage

V_{di} = differential input voltage

g = transconductance

R_d = drain resistor

From the specifications on the U404 (figure 4.6d), a single FET running at a 0.3 mA drain current is seen to have a transconductance of approximately 1.5 millimhos. 8 parallel FETs generate 8 times the drain current for the same input voltage, implying a parallel transconductance of 12 millimhos. Using equation 4.3 for the gain of a differential amplifier with the drain resistance set at 6.1 k Ω as in figure 4.5 yields an expected value of 73 for the 16 device differential

NFET. A second differential stage provides another gain of 50, while preserving high common mode rejection. Parallel FETs are not required in the second stage as the gain of the first stage lifts the signal well away from the input noise level. Finally a pair of source followers are used as power-gain amplifiers, providing an output impedance of roughly 500 Ω . Low noise metal film or wire wound resistors are used in critical areas. Thermal noise generated by the M Ω bias resistors is in parallel with the much lower source impedance, and does not contribute significantly to the input thermal noise. The coupling capacitors are used to isolate the skull from the bias voltage, although this is not strictly necessary. The values of the coupling capacitors are much larger than required for a 3 Hz lower cutoff, to provide low impedance for low-frequency noise currents. The battery is bypassed to guarantee a signal ground at the power supply end of the drain resistor, and thereby avoid unwanted feedback to the input side of the NFET. Current noise produced by the CRR4300 current source is attenuated by the common mode rejection of the differential configuration. Noise created by temperature fluctuations can be avoided by placing the circuit in a constant temperature bath. All noise sources are reduced by cooling the circuit, the optimum temperature of operation being approximately 120 Kelvin. An optimum implementation of the circuit would run in a liquid-gas cooled housing. Less expensive versions are simply shielded in an air-tight box.

The effect of temperature variations can be minimized by biasing the FETs to run on a zero temperature coefficient drain current, although this was not done in this design.

The "NFET-16" is expected to produce one half the input noise of a single FET, but since a differential measure is taken, potential differences between pairs of electrodes amplified by the NFET contain roughly one third the noise of potential differences calculated from two single-FET common mode measurements (half the noise in the amplifier divided by $\sqrt{2}$ for not having to perform the addition of 2 common mode signals) At 10 Hz, independent of skull impedance (up to several M Ω), the NFET has an equivalent input noise of 3 nV per $\sqrt{\text{Hz}}$. The thermal noise in a 10 k Ω skull was previously given as 13 nV per $\sqrt{\text{Hz}}$. The noise figure of the NFET is therefore 0.2 dB at 10 Hz, and 0.02 dB At 100 Hz...

EQUATION 4.4 Noise Figure of designed amplifier

$$V_{\text{thermal}} = \sqrt{4 \cdot k \cdot T \cdot R_s \cdot B}$$

V_{thermal} = thermal noise voltage
 k = Boltzmann's constant = 1.38×10^{-23}
 T = temperature in degrees Kelvin (310 for body)
 R_s = source resistance (1 to 100 k Ω)
 B = bandwidth

$$NF = 10 \cdot \text{LOG} \left[\frac{(N_d + N_t)}{N_t} \right]$$

NF = noise figure
 N_d = noise power generated by device
 N_t = thermal noise power

For a 1 Hz band at 10 Hz with a 10 k Ω source at body temperature:

$$\begin{aligned}
 N_t &= V_{\text{thermal}}^2 / R_s = 1.7 \times 10^{-20} \\
 N_d &= (3 \text{ nV})^2 / 10 \text{ k}\Omega = 9.0 \times 10^{-22} \\
 \Rightarrow NF &= 0.2
 \end{aligned}$$

For a 1 Hz band at 100 Hz (implying one tenth the noise power in the amp) with a 10 k Ω source:

$$N_t = \text{same as above} = 1.7 \times 10^{-20}$$

$$N_d = 9.0 \times 10^{-23}$$

$$\Rightarrow NF = 0.02$$

The AD624 was specified to have a 0.2 peak to peak noise voltage in a 0.1 to 10 Hz band with a short circuit input, roughly ten times better than the specification for the GRASS EEG amplifier used at the Civic Hospital. However, when used on a 10 k Ω source impedance, the AD624 was found to generate noise in excess of 0.6 μ V peak to peak. The NFET designed here is expected to generate less than .1 μ V peak to peak in the 0.1 to 10 Hz band, independent of source impedance, a twenty fold improvement on the amplifier used in the Civic experiment. This amplifier is expected to be near-optimum for EEG sources, contributing only 20% excess noise power to the unavoidable thermal source noise which ultimately limits attainable scalp resolution.

CHAPTER 5

PHYSIOLOGICAL CONSIDERATIONS

5.1 The cortical signal

The physiological properties of the brain and skull physically define a mathematically limited resolution to the image of cortical potential differences at the scalp. There is loss of information in transition from the cortex. The strength of the originating brain signal, its loss of energy in spreading from the source, and the presence of interfering signals, including thermal noise, are all factors involved in determining the limiting scalp-image resolution. Additionally, the electronic sensors (electrodes and very quiet amplifiers) used to create the scalp image degrade their own input, not being able to listen perfectly quietly.

The electric potential on the cerebral cortex at any point varies its amplitude, frequency, and coherence with other points as a side effect of neural activity [Niedermeyer 1987]. Electroencephalography is sometimes used to investigate spatial characteristics of this activity. The scalp EEG is frequently recorded with several parallel electrodes to produce maps of brain activity as was shown in **figure 1.2a**. These maps generally have a resolution of 4 to 10 square centimetres. Between a source of an electric potential in the cortex and the recording electrodes on the scalp, there are

layers of tissue with varying electric parameters. The electrode material, the electrode-scalp interface, the skull, cerebra-spinal fluid, dura-mater, pia-mater, and parts of the cortex itself intervene between the signal and the amplifier. The loss of information this implies is dependant on the type of brain activity being measured. For some applications it is negligible, whereas for imaging of cortical electric coherence the loss finally limits the image resolution.

Spatial parameters of cortical electric activity have been investigated [DeMott 1966, Livanov 1973]. DeMott recorded cerebral activity on the cortex of Cebus monkeys [DeMott 1970], using a 400 channel parallel vacuum tube amplifier:

consisting merely of four hundred amplifiers operating in parallel, each one driven by a single electrode and displaying the signal as the brightness of a small neon tube.

[DeMott 1970]

The neon tubes were filmed at 250 frames per second, and the resulting films were analyzed for the two dimensional form and amplitude of cortical activity. Figure 5.1 illustrates the cortical electrode positions used by DeMott for the experiments on Cebus monkeys.

FIGURE 5.1
Positions of 400 recording electrodes on the left hemisphere of a Cebus monkey. Electrodes are separated by 1.5 mm. (adapted from [DeMott 1970])

DeMott's 0.8 mm diameter electrodes were positioned on 1.5 mm centres, and were sensitive to signals above 5 Hz (upper cutoff frequency not known) with amplitudes up to 200 μ V. The input noise level of his amplifiers was 20 μ V RMS.

DeMott observed:

In the Cebus monkey, the normal appearance of toposcopic records is a moderately fine-grained flickering. Spatial synchrony seldom extends beyond 2 or 3 mm. Frequencies are normally from the alpha range (10 cycles) upward to around 50 cps.

...[a focus] is distinguished from normal activity primarily by a broader spatial synchrony, usually extending across 4 or 5 mm in the Cebus.
[DeMott 1970]

A focus of 4 or 5 mm implies 3 adjacent channels of the toposcope produced similar intensities for a noticeable length of time. DeMott was recording cortical brain potentials with gradients in the neighbourhood of 100 μ V per mm.

His experiments included a toposcopic "microprobe", constructed from a bundle of 400 stainless steel electrodes. Each electrode measured 0.15 mm in diameter, and was separated by 0.25 mm from its neighbours...

The electrode array covers an area only about 7 by 4 mm, thus any activity without steep voltage gradients will be eliminated....In our experiments cortical areas outside the primary sensory regions show no activity recordable by this technique....When an appropriate stimulus is delivered to the primary sensory areas, a burst of finely patterned activity appears on the output panel of the toposcope. In real time, the effect is very striking, the neutral array of neon lights abruptly erupting into frantic activity which usually outlasts the stimulus by a second or more. On slow-motion films, the activity is seen to consist of highly detailed patterns in a specific sequence which repeats quite reliably when the same stimulus is repeated. ...The use of the closely spaced electrode array, with all 400 electrodes placed on primary sensory cortex, reveals activity which is not comparable to that shown by conventional EEG techniques. From the recorded patterns it is apparent that the maximum interelectrode distance that would reveal even the crude outlines of this activity is about 0.5 mm. [DeMott 1966]

Figure 5.2 is a magnified and encoded view of one of DeMott's racoon cortex recordings. By measuring distances between the approximate centroid of the most positive (pure white) potentials and the most negative (pure black), gradients of 150 μ V per mm are seen. Areas of monotonic increasing potential are often larger than 4 square mm. Comparable studies for human cortex were not found.

FIGURE 5.2

400 channel potential recordings on racoon cortex. The patterns are elicited by a white light. Elapsed time since the onset of the light is given above each pattern. Areas of similar potential often occupy several square mm. (Adapted from [DeMott 1966]).

Lueders et al. studied somatosensory evoked potentials (SEP) on human cortex [Lueders 1983]. The electrodes used were 4X4 or 4X8 matrixes of 4.5 mm diameter stainless steel, spaced on 1 cm centres. Figure 5.3 shows that potentials exceeding 180 μ V were recorded between adjacent channels, implying a gradient of 18 μ V per mm. The potentials were averaged evoked responses from sets of 400 to 1000 stimuli, with amplifiers set to a half-amplitude band of 30 to 250 Hz (-3 dB), outside the normal EEG band, but common for evoked potential work.

FIGURE 5.3

Cortical somatosensory evoked potentials recorded from a matrix of electrodes placed on 1 cm centres. The two superposed lines shown for every trace represent two separate trials of 400 to 1000 evoked responses each. Electrode A1 is adjacent to electrodes A2 and B1, etc. (adapted from [Lueders 1983])

Lee et al. used a technique similar to that of Lueders, a 4X4 matrix of 3.1 mm stainless steel electrodes positioned on 1 cm centres [Lee 1984]. The -6 dB passband was 30 to 250 Hz. The neural source was known to lie hidden within the sylvian fissure, causing attenuation of the auditory evoked potentials recorded. Figure 5.4 indicates that these fissure-attenuated potentials produced as much as 15 μ V across 1 cm, or 1.5 μ V per millimetre.

FIGURE 5.4

Cortical auditory evoked potentials from sources within the sylvian fissure. Electrodes were placed on 1 cm centres and positioned as shown. Dual superimposed traces represent two trials of 1000 stimulus-response averages each. (adapted from [Lee 1984]).

The experiments reviewed and others not mentioned [Lueders 1989, Graf 1984, Lee 1984] indicate that cortical potentials exceeding 50 μ V per mm can be observed on human cortex, and that gradients are smaller when measured with larger electrodes. DeMott presented racoon cortex recordings with coherent activity areas of several square millimetres. Based on cortical sources with these approximate gradients and geometries, expected scalp potentials can be calculated.

5.2 Cortex to scalp signal attenuation

The transmission of cortical signals to the scalp has been studied [Nunez 1981, Peters 1988]. Generators of electric potential are modeled as dipole current sources, i.e. a current source and corresponding sink a short distance away. Such sources operate across volumes of varying impedance, sometimes creating scalp-detectable potentials. The image of cortical activity at the scalp, however, is compromised by several factors:

- 1) The separation of the electrode from the source. For distant dipoles, this results in an inverse square attenuation with distance. [Lorrain 1970]
- 2) The surface area of the cortical source.
Small area sources attenuate as simple dipoles, whereas larger area sources attenuate less quickly. [Nunez 1981]
- 3) The non-homogeneity of the head causes an attenuation of scalp-recorded cortical signals. Experimental and theoretical considerations place this factor between 1 and 4. [Nunez 1981]
- 4) The spatial frequency of cortical sources causes progressively stronger attenuation as that frequency is raised. This is in addition to effect (2) mentioned above. Hypothetical cortical wavelengths of 3 cm suffer sixteen times the attenuation of wavelengths of 21 cm. [Nunez 1981]

It is generally accepted that scalp-measurable potentials are generated in a sort of dipole layer in the cortex of the brain:

It appears that 65 to 75% of cortical neurons in all species of mammals are oriented perpendicular to the cortical surface. Because these neurons have a large number of interconnections, it seems likely that many neurons can also be synchronously active. This latter view has quantitative support from statistical considerations of the spatial coherence of EEG recorded from cortex. Thus, there appear to be both anatomical and physiological bases for the dipole layer as a model for scalp potentials. [Nunez 1981]

The dipoles are pairs of positive and negative current sources in the cortex, separated by approximately 1 mm, and lying in the brain's outermost 3 mm. However, deeper sources of scalp potential do exist and can serve to complicate the interpretation of both scalp and cortical images.

To derive the expected scalp-potential of a group of cortical dipoles, the potential due to hypothetical positive monopoles in an infinite homogenous brain is first calculated. Similar potentials from the corresponding negative monopoles in the dipole group are then integrated and a "homogenous brain" potential is derived. The effects of head inhomogeneity are subsequently applied to improve the accuracy of the model.

The potential generated by a current dipole can be calculated by summing the potentials of its two current monopoles. The electric potential of a current monopole relative to an infinitely distant origin is given by:

EQUATION 5.1 Potential due to a current source in an infinite homogenous medium.

$$V = c1 \cdot (i / r)$$

V = electric potential

$c1 = 1 / (4 \cdot \pi \cdot \text{con})$

con = conductivity of medium

i = current source

r = distance from current source to field point

An area of near-synchronously active cortex is modeled as an extended layer of coherent current dipoles. The potential generated by this layer is calculated by integrating the effect of two layers of current monopoles, separated by the dipole gap (approximately 1 mm). Consider an electrode placed directly above such a coherent layer (figure 5.5).

FIGURE 5.5

Model of an extended layer of current dipoles in the cerebral cortex. The effect of each fragment of the layer adds according to equation 5.1 to produce a net potential at the scalp. (adapted from [Nunez 1981]).

Integrating the effect of a circular layer of current sources as shown in figure 5.5 according to equation 5.1 produces a potential at a distance y from the source given by:

EQUATION 5.2

$$V = C2 \cdot I_density \cdot \int_0^R [r \cdot dr / \sqrt{(y^2 + r^2)}]$$

$C2 = 1 / \text{conductivity of medium}$
 $I_density = \text{current density in the layer}$
 $r = \text{distance from origin to integration point}$
 $R = \text{radius of layer}$
 $y = \text{distance from source to field point}$

This is a standard integral whose solution is:

$$V = C2 \cdot I_density \cdot (\sqrt{(y^2 + R^2)} - y)$$

Evaluating the integral at $y = .5$ mm (for a current layer half a millimetre below the cortical surface), and then subtracting the effect of the current sink layer at $y = 1.5$ mm gives the cortical potential. Similarly, evaluations at 12 and 13 mm give the scalp potential. The cortex to scalp ratio is then calculated without knowing either the conductivity of the tissue or the actual current density. An infinite homogenous model is being used, and the current density factors out. Table 5.1 summarizes the cortex to scalp voltage ratios for varying current source geometries.

TABLE 5.1

Ratio of potentials on cortex to those on scalp from an extended cortical dipole. Scalp is defined to be 11.5 mm from the cortical surface. For clarification of the geometry see figure 5.5.

current source radius R (mm)	source layer gap D (mm)	upper layer to scalp distance Y (mm)	cortex / scalp voltage ratio (unitless)
1	1	12	98
2	1	12	43
4	1	12	16

FIGURE 5.6

Ratio of cortical to scalp potential for a dipole layer separation of 1 mm (lower curve) and a separation of 0.5 mm (upper curve). (Adapted from [Nunez 1981])

As can be seen in figure 5.6, the ratios of cortical to scalp potentials are less attenuated as the radius of the source is increased. For a 1 mm radius of coherent cortical activity, with dipole sources and sinks separated vertically by 1 mm, the scalp potential is approximately one-hundredth the cortical potential in an infinite homogenous brain.

The various layers of tissue and fluid separating the cortical source from the observing electrode can be reduced to a model consisting of 3 concentric spheres with varying conductivities [Nunez 1981]. For an average human head with normal tissue conductivities, the fact that the source is shielded from the electrode by these layers of tissue results in an approximate 4X attenuation of the electric potential at the scalp [Nunez 1981]. This is in comparison with what might be recorded at an identical source-electrode separation in a homogenous brain of infinite extent, as was used in the cortex to scalp ratio calculations.

The combination of these influences is then to attenuate the scalp potential of a 1 mm radius of cortex activity by a factor of roughly 400. A 2 mm radius area will be attenuated by only 160, and a 4 mm radius by 64. These are crude estimates. If the dipole is modeled at 2 mm below the surface (instead of 1 mm), with a dipole gap of only 0.5 mm (instead of 1 mm), the scalp attenuation is reduced to a factor of 133 from 400.

Smaller sized cortical sources are subject to another form of attenuation. If two 1 mm (radius) areas of cortex are exactly out of phase, (inverted polarity) and adjacent to one another along the cortical surface, each area will reduce the amplitude of the potential seen at the scalp due to the other. This mutual attenuation is maximized for small area adjacent sources, where the source to electrode distances for the areas are nearly identical even as the sensing electrode is moved laterally across the scalp. By calculating the attenuation of scalp potentials as a function of lateral displacement, an estimate of the strength of a signal between a pair of adjacent scalp electrodes can be made. An electrode displaced laterally from its scalp position changes its distance to both the sources and sinks of cortical dipoles. For a source and sink 0.5 mm and 1.5 mm below the cortical surface, a lateral 10 mm scalp displacement changes the distance to the source from 12 to 15.6 mm. Everything else being equal, the activity 10 mm lateral from directly above the source is attenuated as the square ratio of the distances, or $(12 / 15.6)^2$, i.e. down to 60% of the potential of the undisplaced electrode (a 40% attenuation). Laterally displacing the electrode by only 2 mm attenuates the scalp potential by only 3 percent.

A strong somatosensory cortical gradient of 50 μV per mm might have a peak potential of 50 μV over a 2 mm radius area. If the source is modeled as a point (thereby causing the greatest lateral attenuation), the potential difference

between a pair of scalp electrodes 4 mm apart is only 60 nV (an attenuation of 43 for transmission from cortex to scalp, a conservative 2 for head inhomogeneities, and a lateral attenuation of 10% across 2 mm). Similarly, a 10 mm separation yields 230 nV and a 1 mm separation yields 4 nV.

Several experiments have been performed to empirically identify the maximum useful resolution derivable at the scalp. In 1989 Spitzer et al. published data suggesting that in the case of Somatosensory Evoked Potentials (SEP), electrodes are optimally separated by 3 cm, although a conservative experimenter may wish to reduce that to 1.5 cm (the 1.5 CM spacing, however, is only necessary if a relatively small 5% contribution to the spatial frequencies is pursued) [Spitzer 1988]. **Figure 1.5** displayed some of their findings. Spitzer points out that the scalp potential Nyquist distance depends on the type of potential being recorded (eg. somatosensory evoked, or auditory evoked or epileptic, etc.), the component of the potential under investigation (eg. the P100 peak in a pattern-shift evoked potential), and the portion of the scalp being monitored. Standard 6 mm Ag-AgCl paediatric electrodes were used and the signals were bandpassed between 30 and 1000 HZ, outside the usual 0 - 30 Hz band since fast somatosensory evoked potentials were being recorded. The experiment revealed scalp amplitudes of well over 1 microvolt, (often 2 or 3) with an inter-electrode spacing of 9 mm:

In the case of SEPs we recorded with an electrode spacing

of 0.9 cm, none of the transforms had significant components beyond approximately one-half the maximum Fourier coefficient. Any unexpected smaller components that were not adequately sampled would, therefore, have to have been smaller than 1.8 cm in diameter, to be missed by this technique. The physical properties of the physiologic medium between the recording electrodes and the generators make it unlikely that significant components of that small size would be recorded from the scalp. A spacing of 0.9 cm is adequate for over-sampling potentials to determine their Nyquist distance [Spitzer 1989].

Analysis of Spitzer's experiments (see figure 1.5) reveal he was recording 0.5 μ V across 30 mm, or 16 nV per mm. His electrodes were spaced 9 mm apart, so the above estimate of 230 nV for electrodes separated by 10 mm is seen to compare reasonably with the 150 nV recorded by Spitzer.

CHAPTER 6

CONCLUSION

6.1 Summary and closing remarks

The experiments performed at the sleep lab and Civic Hospital suggest that EEG is recordable with electrode separations of less than a centimetre. Visual inspection of the experimental data suggested brain waves were being recorded across as little as 6 mm. Fourier analysis revealed spectra that contained strong alpha wave (near 10 Hz) components with as little as 4 mm between electrodes, as did the spectra of cross correlated channels. Specialized multi-channel filtering techniques were used to extract a possibly redundant signal from electrodes separated by only 2 mm. The 2 microvolt (peak to peak) input noise voltage of the amplifiers used at the Civic made it difficult to clearly establish a lower limit of useful electrode separation, as signals across 4 mm of scalp generally had amplitudes somewhat under 2 μV (p-p). To circumvent this problem, a lower-noise EEG amplifier was designed and tested. The amplifier was unique in that it could service up to 50 electrodes via a bank of input analog multiplexers. Very low voltage noise levels of less than 0.2 μV p-p were achieved in the static mode (no multiplexing, fixed input) for low-impedance (1 k Ω) sources. For more normal 10 k Ω source impedances the current noise

dominated the input, raising the input noise level to just over 1 microvolt. In the dynamic mode, with the primary amplifiers receiving multiplexed inputs from different electrodes, the switching noise raised the amplifier input noise level to over 2 μV p-p. The multiplexing of sub-microvolt signals as are expected in sub-centimetre scalp EEG recordings was thereby shown to be unviable, although this method could be used to reduce the cost of conventional multi-channel EEG systems. An un-multiplexed differential amplifier optimized for EEG signals was subsequently designed. By using parallel JFET input circuitry the difficulties presented by high source impedance (the skull) and operation inside the "1/f" region of the noise spectrum of electronic amplifiers was overcome. In a 3 Hz window in the alpha EEG band (roughly at 10 Hz) the designed "NFET" amplifier is expected to contribute less than 20 percent of the total input noise, the other 80 percent being fundamental, unavoidable thermal noise. This noise level is roughly 20 times quieter than provided by the GRASS model-8 amplifiers used in the Civic experiment.

Experiments reviewed in chapter 5 suggest that cortical coherence occurs on a millimetre scale, coherent cortical regions often having a diameter between 1 and 3 mm. An accurate representation of this activity can only be derived by electrodes spaced at the appropriate Nyquist distance - every millimetre for capture of 2 mm coherence. Cortical signal models imply that electrodes separated by 4 mm are expected to see 60 nV of potential difference at the scalp for a (not uncommon) 50 microvolt, 2 mm diameter cortical source. The thermal noise of the intervening tissue generates roughly 13 nV per $\sqrt{\text{Hz}}$ (a 10 k Ω source at body temperature), a 10 Hz bandwidth creating 41 nV. This implies that for a 10 Hz band, a 50 microvolt cortical source generates as much voltage at the scalp across 3 or 4 mm as does the skull's thermal noise. Four times the Nyquist sampling distance is required just to come even with the thermal noise. Consequently, although improvements in scalp image resolution are possible, theoretical considerations imply the additional information available cannot provide detailed images of spontaneous cortical potentials, the attainable resolution being roughly a factor of five poorer than required. However, higher resolutions are attainable with evoked potential recordings, the average noise being reduced in proportion to the square root of the number of averaged stimulus-response cycles. The quieter the input stage of the EEG amplifier, the fewer the number of repetitions required to attain a given signal to

noise ratio. With the NFET differential amplifier designed, in an evoked potential band of 50 to 250 Hz, it is expected that a 1 to 1 signal to noise power ratio for electrodes separated by 3 mm can be achieved with 30 stimulus response cycles (180 nV thermal noise with a 10 k Ω skull, 30 nV amplifier noise, and 35 nV signal). The amplifier used at the Civic would have required roughly 300 cycles to achieve the same ratio.

The research performed for this thesis has found support for the detectability of 5 mm scalp EEG. The electronic multiplexing of conventional (upwards of 10 μ V) EEG signals, through a bank of analog multiplexers to a single amplifier, was shown to be viable. A circuit designed to maximize the signal to noise ratio for high-resolution EEG measurement, involving sub-microvolt potentials across a few millimetres of the scalp, was designed and is expected to contribute less than 20% excess noise power in frequencies beyond 3 Hz. These contributions made by the research imply that scalp EEG resolution is currently technology limited. The fundamental resolution limit imposed by thermal noise and the separation of the cortex from the scalp could now be attained by technological refinements such as the NFET amplifier designed.

The suggestion that 5 mm scalp resolutions could be recorded with the NFET are partially based on theoretical models of cortex to scalp EEG signal transmission, partially on the results of the Civic experiment, and partially on the

results of other experiments [Spitzer 1989, Sandini 1983, MacKay 1984]. Although imaging detailed cortical coherence at the scalp is seen to be impossible due primarily to the distance of the scalp from the cortex, 5 mm electrode spacing offers a ten-fold improvement over conventional scalp resolutions, but with a reduced signal to noise ratio (approximately one fifth the signal to noise amplitude ratio in a 3 Hz alpha band). The final utility of this resolution is difficult to predict. Five millimetre electrode spacing may provide images of scalp EEG which permit diagnostic judgements that are currently impossible, for lack of resolution. Imaging the finer details of cortical electrical activity, however, will still require exposing the cortex.

Appendix A

A 5 X magnification of a possible layout for sixteen DG506 analog multiplexers in die form (large black rectangles) on the back of a 256 electrode (small black squares) scalp matrix. Space remains for the addition of the analog amplifier and control circuitry. The matrix-forming process is performed according to the method described in [van der Puije 1989]. A magnified view of a portion of the matrix is given on the next page.

Appendix A

A magnification of a portion of the hybrid matrix shown on the previous page (20 X actual size). The red lines indicate the position of the die-form DG 506 muxes. Each electrode (larger red and green squares) is connected to a mux channel. Red electrodes are controlled by one bank of multiplexers, feeding one side of the amplifier, green electrodes by the other. Small rectangles outside the DG506 rectangles represent bonding pads for the hybrid circuit.

REFERENCES

Ashida H, Tatsuno J, Okamoto J, Maru E (1984)
Field Mapping of EEG by Unbiased Polynomial Interpolation
Computers and Biomedical Research (1984) 17:267-276

Barlow J (1986)
Automatic elimination of electrode-pop artifacts in EEG's
IEEE transactions on Biomedical Engineering
BME-33 (5):517-521

Berger H (1929)
On the Electroencephalogram of Man
Unknown Publisher

Buchsbaum MS, Rigal F, Coppola R, Cappelletti J, King C, Johnson J (1982)
A new system for gray-level surface distribution maps of electrical activity
Electroencephalography and Clinical Neurophysiology
(1982) 53:237-242

Caderas M, Niedermeyer E, Uematsu S, Long DM, Nastalski J (1982)
Sleep Spindles Recorded from Deep Cerebral Structures in Man
Clinical Electroencephalography (1982) 13(4):216-226

Caton R (1875)
The electrical currents of the brain.
Br. Med. J., 2:278

Childers DG, Fischler IS, Boaz TL, Perry NW, Arroyo AA (1986)
Multichannel, Single Trial Event Related Potential Classification
IEEE Transactions on Biomedical Engineering
(1986) BME-33 12:1069-1075

Delucchi MR, Garoutte B, Aird RB (1961)
The Scalp as an Electroencephalographic Averager
Electroenceph. clin. Neurophysiol., (1962), 14:191-196

DeMott Donald W (1970)
Toposcopic studies of learning
Charles C Thomas Publisher

DeMott Donald W (1966)
Cortical micro-toposcopy
Med. Res. Engin., 5(4):23-29

Epstein CM, Brickley GP (1985)
Interelectrode distance and Amplitude of the Scalp EEG
Electroencephalography and Clinical Neurophysiology
(1985) 60:287-292

Gevins A (1984)
Analysis of the Electromagnetic Signals of the Human
Brain: Milestones, Obstacles, and Goals
IEEE Transactions on Biomedical Engineering,
BME-31 (12), December 1984: 833

Graf M, Niedermeyer E, Schiemann S, Uematsu S,
Long DM (1984)
Electrocortigraphy: Information Derived from
Intraoperative Recordings during Seizure Surgery
Clinical Electroencephalography, (1984), 15(2):83-91

GRASS model 8 INSTRUCTION MANUAL (1973)
published by Grass Instrument Company
Quincy, Massachusetts, USA

GRASS model P511E-H AC preamplifier
Instruction Manual (1977)
published by Grass Instrument Company
Quincy, Massachusetts, USA

Hallgren RB (1988)
Paralleled transconductance ultralow-noise preamplifier
Rev. Sci. Instrum. (1988), 59(9):2070-2074

Hjorth B (1975)
An on-line transformation of EEG scalp potentials into
orthogonal source derivations
Electroencephalography and Clinical Neurophysiology
(1975) 39:526-530

Kruger J and Bach M (1981)
Simultaneous Recording with 30 Microelectrodes
in Monkey Visual Cortex
Exp Brain Res (1981) 41:191-194

Lee YS, Lueders H, Dinner DS, Lesser RP, Hahn J,
Klem G (1984)
Recording of auditory evoked potentials in Man using
chronic subdural electrodes
Brain, (1984), 107:115-131

Lehmann D (1971)
Multichannel topography of Human Alpha EEG fields
Electroencephalography and Clinical Neurophysiology
(1971) 31:439-449

Lehmann D (1984)
EEG Assessment of Brain Activity: Spatial Aspects,
Segmentation and Imaging
International Journal of Psychophysiology (1984)
1:267-276

Le Men H (1988)
Effects of under-sampling in digital imagery
in
Statistics and Topography in Quantitative EEG
Elsevier (1988), 210-213

Lesser RP, Lueders H, Morris HH, Dinner DS,
Wyllie E (1987)
Commentary: Extracranial EEG Evaluation
Surgical Treatment of the Epilepsies
Raven Press, New York (1987)

Liebman M (1983)
Neuroanatomy made easy and Understandable, 2nd edition
University Park Press, Baltimore (1983)

Livanov MN (1973)
Spatial Organization of Cerebral Processes
Keter Publishing House Jerusalem Ltd. (1977)
QP385 L784

Lorrain P, Corson D (1970)
Electromagnetic Fields and Waves
W.H. Freeman and Company (1970)

Lueders H, Hahn J, Lesser RP, Dinner D, et al. (1989)
Basal Temporal Subdural Electrodes in the Evaluation
of Patients with Intractable Epilepsy
Epilepsia, (1989), 30(2):131-142

Lueders H, Lesser R, Hahn J, Dinner D, Klem G (1983)
Cortical somatosensory evoked potentials in
response to hand stimulation
J Neurosurg (1983) 58:885-894

Lueders H, Hahn J, Lesser RP, Dinner DS, Rothner D,
Erenberg G (1982)
Localization of Epileptogenic Foci: Comparative Study
of Closely Spaced Scalp Electrodes, Nasopharyngeal,
Sphenoidal Subdural, and Depth Electrodes
Advances in Epileptology: XIIIth Epilepsy International
Symposium
Raven Press, New York (1982)

MacKay DM (1984)
Source-Density Mapping of Human Visual Receptive Fields
Using Scalp Electrodes
Exp Brain Res (1984) 54:579-581

Malmstadt, Enke, Crouch (1974)
Electronic Measurements For Scientists
W.A. Benjamin, Inc (1974)

Motchenbacher CD, Fitchen FC (1973)
Low-Noise Electronic Design
John Wiley & Sons (1973)

Niedermeyer E, Lopes da Silva F (1987)
Electroencephalography
Basic Principles, Clinical Applications and Related
Fields (2nd edition)
Urban & Schwarzenberg (1987)

Nunez PL (1988)
Spatial Filtering and Experimental Strategies
in EEG
in
Statistics and Topography in Quantitative EEG
Elsevier (1988), 196-209

Nunez PL (1981)
Electric Fields of the Brain
The neurophysics of EEG
Oxford University Press (1981)

Nuwer MR (1988)
Quantitative EEG: I. Techniques and problems of Frequency
Analysis and Topographic Mapping
Journal of Clinical Neurophysiology (1988) 5(1):1-43

Ott WO (1988)
Noise Reduction Techniques in Electronic Systems
John Wiley & Sons (1988)

Peters MJ, Elias PJH (1988)
On the magnetic field and the electrical potential
generated by bioelectric sources in an anisotropic
volume conductor
Med. & Biol. Eng. & Comput., (1988), 26:617-623

Pfurtscheller G, Cooper R (1975)
Frequency dependence of the Transmission of the EEG
From Cortex to Scalp
Electroencephalography and Clinical Neurophysiology
(1975) 38:93-96

Ragot RA, Remond A (1978)
EEG Field Mapping
Electroencephalography and Clinical Neurophysiology
(1978) (45):417-421

Sandini G, Romano P, Scotto A, Traverso G (1983)
Topography of brain electrical activity:
a bioengineering approach
Medical Progress through technology (1983) 10:5-19

Sedra AS, Smith KC (1982)
Micro-Electronic Circuits
Holt, Rinehart and Winston (1982)

Siliconix Small-Signal FET Data Book (1986)
Siliconix Incorporated (1986)

Spitzer R, Cohen L, Fabrikant J, Hallett M (1989)
A method for determining optimal interelectrode
spacing for cerebral mapping
Electroencephalography and Clinical Neurophysiology
(1989) 72:355-361

Thickbroom GW, Mastaglia FL, Carroll WM, Davies HD (1984)
Source Derivation: Application to Topographic Mapping of
Visual Evoked Potentials
Electroencephalography and Clinical Neurophysiology
(1984) 59:279-285

van der Puije PE, Pon CR, Robillard H (1989)
Cylindrical Cochlear Electrode Array for use in Humans
Ann. Oto. Rhin. and Laryn. (June 1989)
98(6):466-471

Vaz CA, Thakor NV (1986)
Monitoring Brain Electrical and Magnetic Activity
IEEE Engineering in Medicine and Biology Magazine
(1986) September:11-15

Walter DO, Etevenon P, Pidoux B, Tortrat D,
Guillou S (1984)
Computerized Topo-EEG Spectral Maps:
Difficulties and Perspectives
Neuropsychobiology (1984) 11:264-272

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