2. Literature Review

Many facets of bioelectric activity have been investigated using both animal and human models. The scope of bioelectric research is wide, ranging from alterations in skin potentials in response to psychological stress and sleep, through to changes in cell membrane potentials in response to external electrical stimulation. In an attempt to establish some order to the breadth of research, an organisational model was constructed, grouping the research efforts by general headings. This model is inevitably both incomplete and open to interpretation, but aims to provide a background to the scope of the subject from which some elements are reviewed herein. Much of the published research is of peripheral relevance to the current project, and although important in the overall context of bioelectric research, is not considered in detail in this review. There are many cross links that exist within the framework which are not illustrated for the sake of clarity. The organisational structure of the subject is shown in Figure 2.1.

The bioelectric activity which is associated with the skin and underlying soft tissues is of most direct relevance to the current work, and the literature reviewed concentrates on these areas, together with the effect of injury, trauma and disease on this activity. The influence of endogenous signals on morphogenesis, nerve repair and limb regeneration are examples of elements are beyond the scope of the current review.

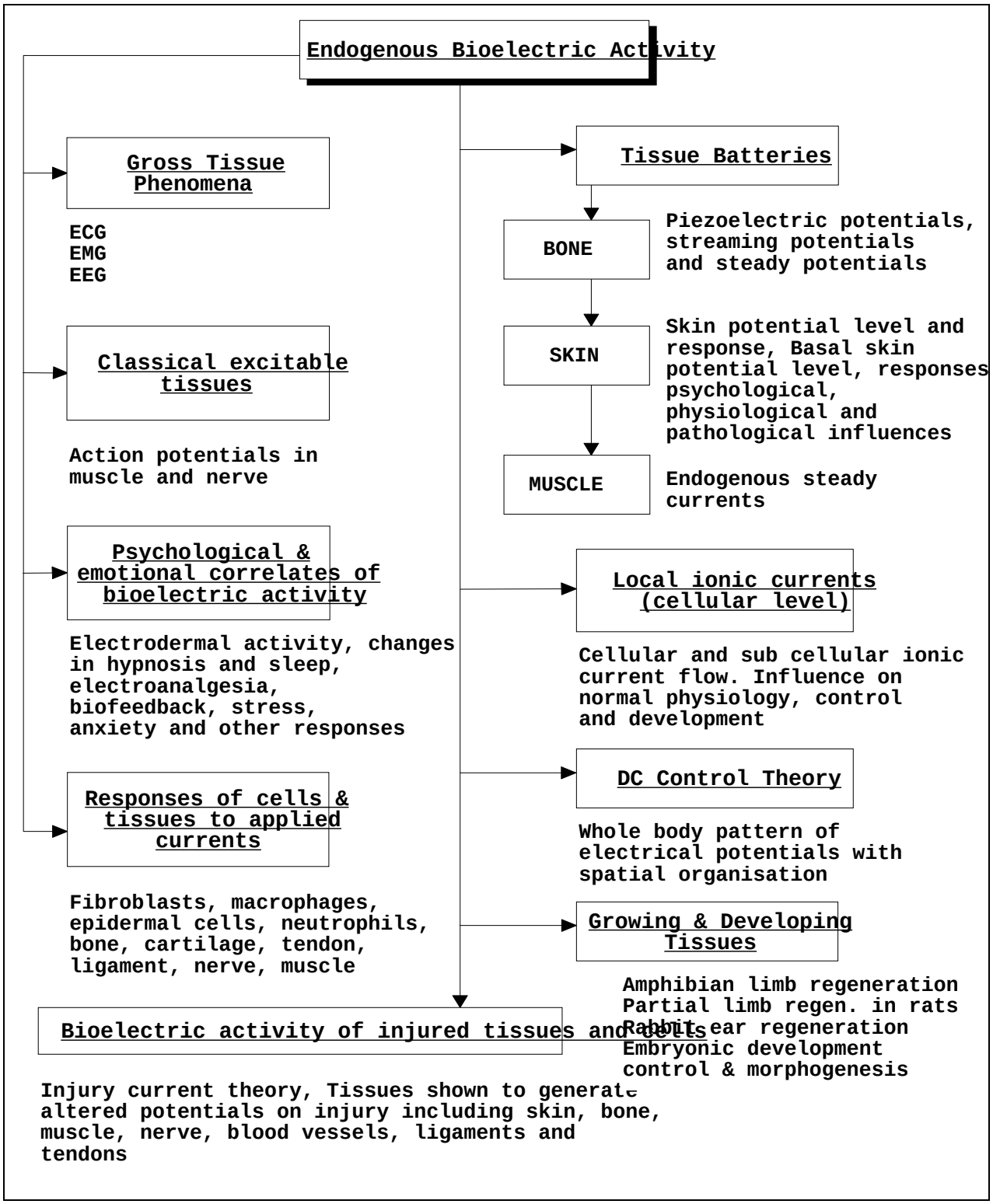

Figure 2.1 : Core elements of the bioelectric research field

2.1 Skin Potentials

Measurement of electrical potentials that are apparently derived from the skin dates back to at least the 19th century, though the level of research activity seems to pass through various phases with the evolution of new measuring equipment and developing physiological science. The main problem encountered in reviewing this work, is that the electrical potential measured from the skin surface is interpreted differently by various groups. The professional disciplines that have primarily concerned themselves with the work include:

a) Psychophysiologists, psychologists and psychiatrists (grouped here as the Behavioural sciences)
b) Physiologists
c) Applied Physiologists and Clinicians

There is a lack of agreement regarding the sources, generation mechanisms and control of endogenous bioelectric phenomena. Some elements are well documented and have been critically reviewed, though they tend to be in the areas most distantly related to the current work (e.g. ECG, EMG, EEG, morphogenesis, amphibian limb regeneration). The more recent upsurge in interest in bioelectric activity has led to a wide research base, but with little depth of cover in many areas. Frequently, workers investigate a particular aspect of bioelectric activity, identify apparent patterns of behaviour and generate hypotheses to explain the mechanisms which may be responsible for the generation and control of the observed phenomena. Although this is not a universal approach, it was commonly encountered in the literature, possibly attributable to the ‘youth’ of this branch of science. Examples of published replication of experimental work have been few, and are noted where appropriate,

Comparison between professional groups has rarely been attempted in the literature consulted, though no groups have claimed mutual exclusivity. The division of bioelectric research into groups is somewhat arbitrary in that there is almost certainly considerable overlap between them. Similar recording methods are used in many cases, and the main difference lies in the interpretation of the data. This is most strongly influenced by the background of the research group (e.g. psychology, physiology, alternative or conventional medicine). It remains possible that the bioelectric activity, and more specifically, bioelectric potentials which arise from within the body have a limited number of physiological sources but are influenced by a wide range of factors (e.g. environmental, psychological, physiological and pathological). This may explain how groups can measure the phenomena by using similar methods yet offer different explanations for the control mechanisms by considering a limited range of influential factors, being those which are most closely allied to their own background or professional training.

The principle work from each group whose work is most directly relevant to the current study is reviewed. The suggested modes of generation are outlined and where possible, the control mechanisms and identified characteristics of the bioelectric potential behaviour. The similarities are highlighted as are the obvious differences between the groups whether of methodology or interpretation. It would be inappropriate to suggest that a novel theme has been identified which runs through all the published work, but the common ground appears to be extensive and the differences not as great as appears at first.

The Behavioural Scientists (both research and clinical) utilise skin potentials for both monitoring and assessment and base their interpretation of the results on various hypotheses centred around higher centre activity, sweat gland activity, arousal and emotional states (Sections 2.1.1 to 2.1.5).

Skin potential activity has been investigated by several groups of physiologists. This has led to theories concerning the generation and control mechanisms of the skin potential that have some essential concepts in common with the Behavioural Scientists (e.g. ionic concentration gradients across membranes), but vary in their interpretation of experimental data. This research has closer links with various aspects of the current work though it is difficult to isolate any one view as being exclusively applicable. A reasonably extensive body of research concerns the behaviour of the skin as a battery, resulting in a measurable skin potential that is allied to the skin potential work of the Behavioural scientists (Section 2.1.6).

Several research groups amongst the physiologists have investigated tissue potentials as a very localised phenomenon concerned with the microscopic changes in cell membranes and small scale ionic flux variations. These small scale changes are thought to be responsible for changes in gross tissue behaviour. Much of this work stems from developmental physiology and morphogenetic studies by Jaffe, Nuccitelli and Robinson and is not directly applicable to the current work which concerns mature tissue responses.

A further group has considered the skin potential to be a measurable phenomenon of a more global, neural based system, thought to monitor and control many body systems, particularly related to post embryonic growth, the response to injury and repair of tissue damage. This work, centred around Beckers' research, takes the emphasis away from local physiological control and concentrates on the role of the central nervous system and DC potentials associated with peripheral nerve pathways. One of the difficulties with this research is that there has been limited reporting of the experimental method and detailed results to support the hypotheses (Section 2.1.7).

A variety of clinical research groups have conducted basic and applied skin potential research with an emphasis on application to clinical problems, primarily, the control of healing and repair in chronic and surgical skin lesions. Their work is of interest as it appears to establish formative links between endogenous bioelectric potentials and the healing processes in musculoskeletal tissues (Section 2.2).

The Behavioural Scientists, concerned with the links between skin potential, anxiety levels and stress have used the potential as a method of dynamically monitoring emotional state and psychological responses. The physiologists have recorded the skin potential in almost an identical way, but have explained the recorded potential in terms of skin battery activity and local ionic exchange. The DC control theory has been derived from physiological experiments with a different emphasis resulting in an alternative explanation for the generation and control of the potential based on CNS activity and system control theory. Each of these approaches is considered in isolation, in the context of the original research. Links between the approaches are considered in Section 2.1.8.

2.1.1 Behavioural Scientists and Clinical Psychologists

Skin potentials, commonly recorded by researchers and clinicians in psychology and psychiatry generally refers to a potential difference between the external surface of the skin and the internal environment of the body (the transcutaneous potential). In line with current terminology, this potential difference can be considered in two forms - a phasic response to some form of stimulation (Skin Potential Response - SPR) or as a tonic (background) level - the Skin Potential Level - SPL. The SPR can be monophasic, biphasic or occasionally triphasic, and is essentially attributed to the relative activity of the sweat gland, the activity of which is blocked by the local introduction of atropine and following sympathectomy (Fowles 1974).

The SPL is most commonly externally negative (Christie 1981, Fowles et al 1974) and although primarily related to sweat gland activity, involves epidermal mechanisms to a greater extent than the SPR's. The SPL is of more direct interest in the current work as it is concerned with a tonic (or background) phenomenon rather than a response to a specific stimulus.

The SPL falls into a wider group of phenomena, collectively known as Electrodermal Activity which is a general term for the electrical activity originating from the eccrine sweat glands (sudorific) and their associated dermal and epidermal tissues (non-sudorific) (Christie 1981). Edelberg (1971) suggests that electrical measures taken from the skin may reflect the level of sweat gland activity, the state of the local blood vessels, and the state of one or more living cell layers.

Two manifestations of the skin potential level (SPL) have been identified. The first is the SPL associated with sweat gland activity and concomitant hydration of the epidermal layers. Edelberg (1968) proposed a skin hydration model to explain the generation of the skin potential based on the relative activities of the sweat gland and epidermal membrane generators. The basic tenets of the model are widely accepted in psychology and psychophysiology, though some of the details of the model remains controversial. A second form of SPL has been investigated by Christie and Venables (1971a,b,c,d) and is concerned with the skin potential recorded in the resting state and which appears to be primarily related to the potassium ion environment of the body fluids. Both SPL types are considered in more detail in subsequent sections.

Both the SPL and BSPL are measured with paired electrodes, one placed on the skin surface (most commonly on the palmar surface of the hand or fingers) with a second ('reference') electrode at a drilled or abraded site which provides contact with the internal environment of the body. This reference electrode is most commonly placed on the volar aspect of the forearm.

2.1.2 Skin Hydration Model after Edelberg (1968)

Edelbergs model sets out to explain the relative contributions made by two different generators to a single electrical phenomenon in the skin. The reason for seeking an explanation appears to be as a model to describe

the Skin Potential Response (SPR) (changes in the skin potential that can be recorded from the skin in response to cognitive or other psychological arousal). It is a model therefore which attempts to describe the phasic changes observed with skin potential behaviour rather than the tonic potentials that are of concern in the current work. It remains relevant however in that it attempts to formalise a relationship that will still exist even under baseline conditions. Martin and Venables (1966) note that the congenital absence of sweat glands results in a total absence of Skin Resistance Responses (SRR's) and this adds strength to the relationship demonstrated between SRR's and non-thermoregulatory sweat gland activity (Wilcott 1967). That there is a relationship between skin resistance and potential measures, and that there is an established relationship between resistance responses and sweat gland activity does not automatically confirm the relationship between skin potential activity and sweat gland activation (Martin and Venables 1966).

Skin potentials recorded by the transcutaneous method are in the mV range, with the palmar skin typically at 0 to -60mV relative to the internal environment of the body, though occasionally may be up to +10mV (Hassett 1978, Edelberg 1972, Brown 1967).

Edelberg hypothesised that there are two dissimilar sources of potential in the skin, a sweat gland generator and an epidermal membrane generator (a concept supported by Fowles 1974). They are arranged in parallel and the electrolyte of the measuring electrode is separated from the generator by a narrow column of saline (i.e. the contents of the sweat gland) or by a layer of corneum (the outermost layer of the epidermis). The resistances, in series with the generators do not act in a simple fashion and variations in these resistances may have a striking effect on the measured potential (Edelberg 1968, 1971).

The skin can be considered as a living semi-permeable barrier of cells covered by a dense layer of cell carcasses (the corneum). Under the skin lies a loose, freely conducting connective tissue - the corion. These layers are perforated by the long narrow ducts of the sweat glands, with their coiled secretary portion lying in the corion.

Electrical potentials originate in biological systems as a result of concentration gradients of ions across the membranes that surround the cells that form the organism. In general such membranes tend to let some species of ions pass readily, but offer much more resistance to other species. This creates a difference in concentration of various ions on either side of the membrane, and a potential difference will develop, the magnitude of which will relate to the concentration difference across the membrane. Eventually, a point of equilibrium will be reached as the potential itself will prevent further movement of ions across the membrane - this being determined mathematically using the Nernst formula (Offner 1984, Guyton 1986).

The corneum is considered to be easily permeated by electrolytes and even by molecules of considerable size. Edelberg suggests that the sweat gland makes a greater contribution to the potential than the epidermal layer (Edelberg 1968). Burbank and Webster (1978) have confirmed the existence of an epidermal generator which is separate from the sweat gland generator.

The electrical equivalent circuit developed by Edelberg is shown in Figure 2.2 below. S represents the sweat gland battery, E the epidermal membrane battery (the two generators). Rs and Re are the combined internal and series resistances of these two batteries respectively. The two sources of potential are arranged in parallel, connected together on the tissue side by the highly conductive corion and on the skin surface by the electrode medium. P represents the transcutaneous potential, monitored by a meter with impedance Rv. As the two generators develop different potentials, and if the sweat gland potential is the more negative (as suggested by Edelberg), a circuit current (i) will flow.

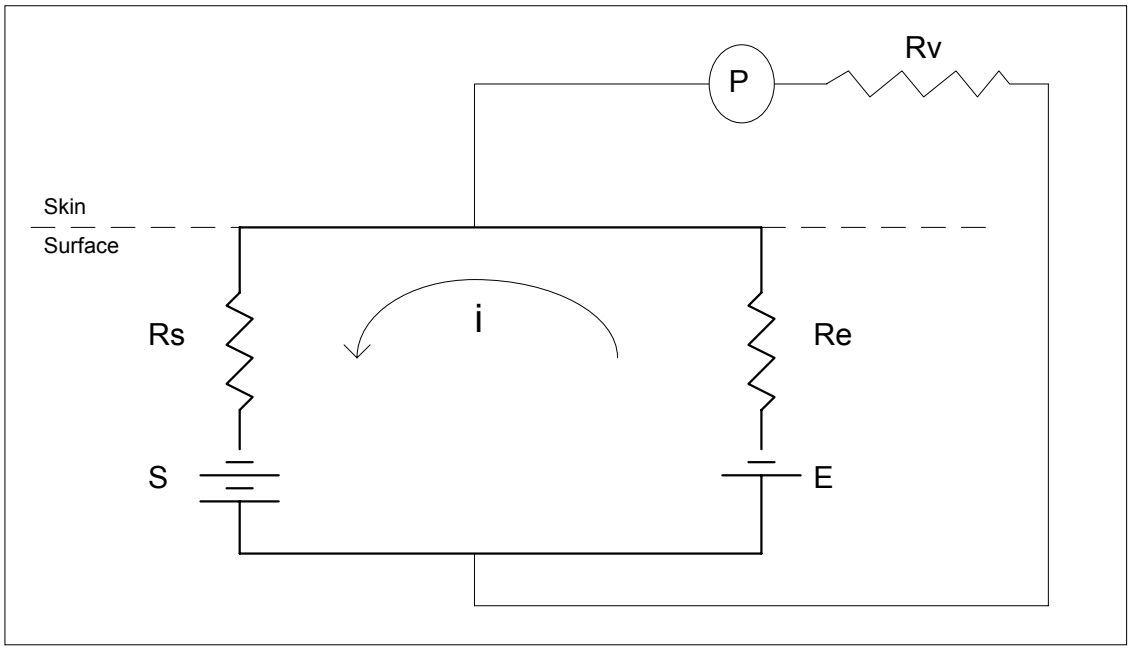

Figure 2.2: Equivalent circuit of Edelbergs Skin Hydration Model

The skin potential (P) can alter as a result of changes in generator potential as well as due to changes in the relative resistances of the sweat ducts and the epidermal membrane.

Rs is determined by the permeability of the sweat gland membrane and upon the height of the column of saline in the duct. Re is determined by the permeability of the layer of cells in the epidermis and the resistance of the corneum between the barrier layer and the surface. Edelberg (1968) suggests that the corneal resistance is the more important of these two factors.

The dynamic behaviour of the generators and their interaction are discussed by Edelberg at some length (Edelberg 1968, 1971). Sweat rising in the duct will reduce Rs causing a negative shift in the potential. If the sweat overflows, it starts to hydrate the adjacent corneum and this causes Re to fall and so causes the potential to fall below the resting level (assuming a sufficiently large fall in Re), i.e. there is an inverse relationship between P and Re. If the corneum dries out, Re rises and the skin potential becomes more negative. If only the hydration of the corneum occurs, Re will fall and the surface potential will become more positive. Despite the emphasis placed on the degree of hydration of the skin in the model, diffusion potentials are also considered to be of

importance. The hydration effects in the epidermis were confirmed by Garwood et al (1981) in a complex study of epidermal hydration and skin potential.

A selectively permeable barrier layer such as that needed for such a process is most likely a combination of a number of relatively impermeable layers acting in series and thus constituting an effective barrier. Edelberg (1971, 1977) proposes that the germinative and granular layers of the epidermis are the prime candidates for this layer. Both Edelberg (1971,1977) and Millington and Wilkinson (1983) consider steric hindrance (limitation of ionic movement due to the relative size of the ion to the available channel) to be an unlikely mechanism for selective permeability in the corneum. This is due to the relative width of the channels compared with the sizes of the principal ions involved. Electrostatic selectivity (limitation to ion movement due to fixed membrane charges) remains a possible mechanism, but there does not seem to be any conclusive evidence to support this process as an explanation for the development of diffusion potentials.

The vascular plexus of the corion may also contribute to the electrical properties of the skin, however the maximum vascular contribution is probably low when compared to the epidermal contribution (Edelberg et al 1960). In addition, when smooth muscles of blood vessels, myoepithelial cells and the piloerectile cells contract, they may set up dipoles, which may in turn make a contribution to the surface potential, but this contribution is also expected to be low (Edelberg 1971,1977).

Edelberg (1968) presents experimental evidence which, it is suggested, validates that hydration model. Both electrical and electro-hydraulic models were utilised. Measurements were also made with microelectrodes at both sweat gland duct and non ductal epidermis. The differences in the recorded potential appeared to confirm the predicted values from the hydration model. Further supportive evidence for the contribution made by the epidermal generator was presented following extensive research into skin deformation potentials (Edelberg 1977) which were derived from the nail bed which has no sweat glands

In his summary of electrodermal activity (Edelberg 1977), it is suggested that in the absence of sweating, surface potential in a wet preparation essentially reflects the diffusion potential across the epidermis which is very similar to the explanations proposed by Christie et al in relation to BSPL (Section 2.1.3).

Edelberg's model is based on the following equation (Edelberg 1968):

$$P = E + Re\left(\frac{SRv - ERv - ERs}{RsRv + Re\,Rv + Re\,Rs}\right)$$

(using the same notation as in Figure 2.2)

From this basic equation, Edelberg has derived two further equations based on the assumption that the impedance of the meter is both constant and can be considered to be infinite. These equations can be used to theoretically predict the magnitude and the polarity of the transcutaneous skin potential under various circumstances.

$$P = E + Re\left(\frac{S - E}{Rs + Re}\right)$$ Equation A

$$P = S - Rs\left(\frac{S - E}{Rs + Re}\right)$$ Equation B

Where P = transcutaneous potential measured at meter V.

Derivation of the Equations

If Edelbergs circuit is considered as in Figure 2.3 below, and Rv is considered to be both constant and effectively infinite, it can be omitted from the calculations.

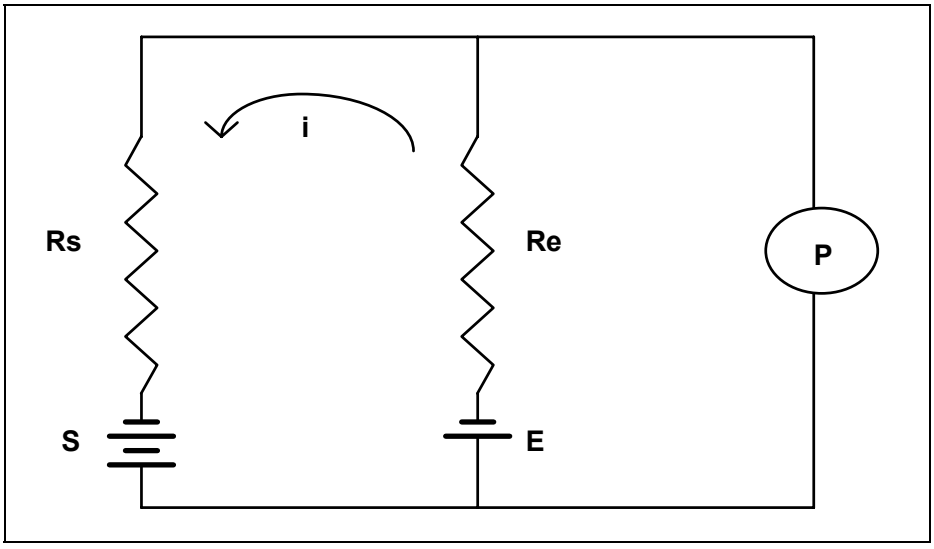

Figure 2.3: Modified Edelberg Skin Hydration Model Circuit

It is assumed that the current direction is as indicated and that the deeper tissues (towards the lower rail) are the most positive point of the circuit, then the voltage drop across Re and Rs will oppose the current i as shown in Figure 2.4. A positive value for P refers to the bottom rail being the more positive point compared with another point.

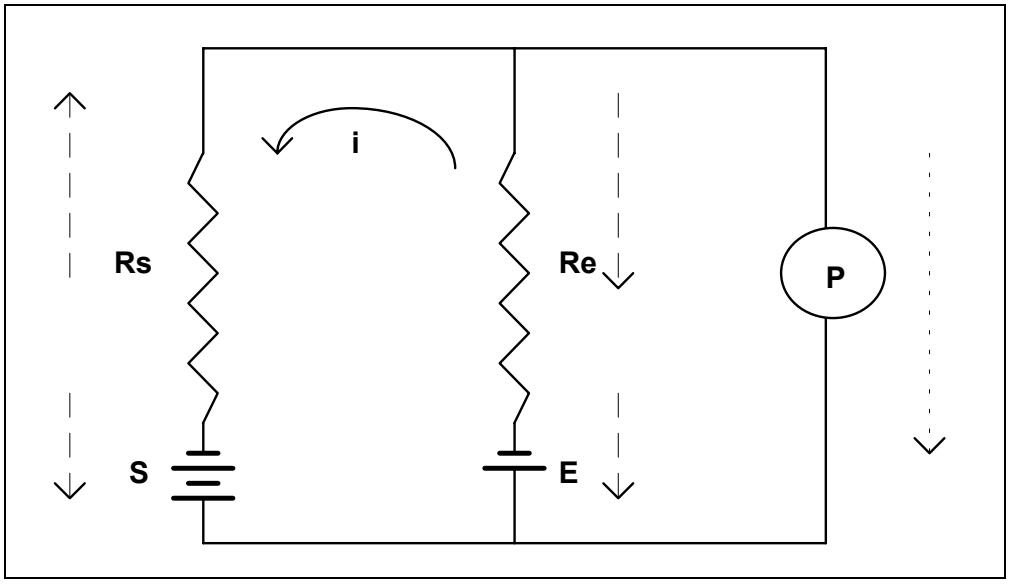

Figure 2.4: Edelberg Model Circuit indicating the direction of the voltage drops

Using Kirchoff analysis, starting at source S:

$$S - E - (Re\,i) - (Rsi) = 0$$

From loop 1 (left side of circuit)

$$S = E + Rei + Rsi \qquad (1)$$

Rearrange (1)

$$i = \frac{S - E}{(Re + Rs)} \qquad (2)$$

From loop 2 (right side of circuit)

$$P - E - Rei = 0 \qquad (3)$$

Rearrange (3)

$$P = E + Rei \qquad (4)$$

Substitute (2) into (4)

$$P = E + Re\frac{(S - E)}{(Re + Rs)} \qquad \text{(Edelberg Equation A)}$$

Now use loop 3 (combined loop 1 and 2)

$$S - P - Rsi = 0 \qquad (5)$$

Rearrange (5)

$$S - Rsi = P \qquad (6)$$

Substitute (2) into (6)

$$P = S - Rs\frac{(S - E)}{(Re + Rs)} \qquad \text{(Edelberg Equation B)}$$

Edelberg assumes that of the 2 generators, S (the sweat gland) is the more powerful when the sweat glands are active. The generators S and E are attributed the polarity of their surface directed side. Edelberg considers changes of P as a result of variation of Re and Rs alone - i.e. he considers that the generator function remains unchanged.

The Skin Hydration Model provides a useful, if incomplete analysis of the relationship between the generators and modulators (resistances) of the skin potential. It is acknowledged that the model was developed to explain

the events associated with the skin potential response (SPR) and as such does not aim to explain changes in baseline potential. Even so, the discussion of the hydration model does not consider the relationship between the two generators and their resistance in any detail which seems to be a somewhat narrow approach. Even as a relatively simple model, Edelbergs' examples concerning changes in Re and Rs alone are not realistic as changes in generator function would seem to be as likely as changes in their resistances. A more detailed consideration of the model is presented in Section 3.6 along with possible changes associated with injury and repair.

2.1.3 Basal Skin Potential Model (BSPL) (after Christie and Venables 1971)

In 1971, Christie and Venables, published a series of papers concerning the Basal Skin Potential Level (BSPL) which they suggested was fundamentally different from the Skin Potential Level (SPL) reported by Edelberg. Both could be recorded in essentially the same way (i.e. using a transcutaneous method), but that the BSPL related to a non-sudorific skin potential as opposed to the 'normal' SPL to which a significant contribution is made by sudorific activity.

The overall results of their experimentation with electrode electrolyte concentrations and measurement of the internal ion concentrations of the body, resulted in the generation of a hypothesis for a relationship between the skin potential when recorded in the basal state, and the internal potassium ion concentration of the epidermal and subdermal tissues. Their work is relevant to the current study in that they were directly concerned with the potential in the basal (non stimulated) state whereas Edelberg was primarily concerned with the SPR.

2.1.4 BSPL as a membrane phenomenon

Venables and Martin (1967) demonstrated that after blocking the action of the sweat glands with hyoscyamine, the SPL was reduced by only 25% of its pre-treatment value, leaving a significant part of the potential to be accounted for in terms of non sudorific generation. Several reports in the literature had identified that the magnitude of the SPL varied with electrode electrolyte concentration and also that there were individual differences that could not be explained by the existing theory. The epidermal membrane had been implicated as a contributor to the generation of the SPL in previous research (Venables and Sayer 1963, Edelberg 1968) and it was this membrane function of the epidermis which Christie and Venables investigated.

Christie and Venables (1971c) suggested that if the absence of sudorific activity (as in the Martin and Venables 1967 research) resulted in a membrane oriented skin potential mechanism, then instead of using a drug based block of the glands, the use of habituated subjects could provide similar data as their arousal levels would not be overtly increased by the circumstances of the testing procedures. Habituated subjects were therefore tested under resting conditions to achieve a similar absence of sudorific activity. The absence of phasic electrodermal activity (i.e. SCR's and SPR's) were taken as indicators of the absence of sweat gland activity.

In summary, the results of the experiments with habituated subjects (N=20 males between 21 and 45 years) demonstrated that in the absence of electrodermal responses (phasic activity) the SPL recorded with Ag/AgCl electrodes and 0.5% KCl electrode electrolyte had specific characteristics that distinguished them from the 'normal' SPL recorded in a non basal state. The skin potential was recorded using a standard transcutaneous method with an active electrode(s) on the palmar surface of the finger(s) and a punctured forearm reference electrode site (after Venables and Sayer 1963, Venables and Martin 1967). A divergence was demonstrated between the SPL and SCL on prolonged recording. Under normal recording the SPL and SCR are expected to change in parallel with each other. This divergence was taken to represent the cessation of the sudorific contribution to the skin potential. The mean SPL recorded under these basal conditions was -18mV (skin surface electronegative in relation to the internal environment of the body) and the mean time taken to achieve this basal state was 12 minutes (73% of subjects achieved the basal state in less than 12 minutes). The lower, resting skin potential level was referred to as the Basal Skin Potential Level (BSPL).

The experiments were repeated with a group of non habituated subjects (N=20 males matched as closely as possible with members of first group). This second group also achieved the basal skin potential condition though it took longer on average to achieve (only 27% of the group achieved BSPL in less than 12 minutes). There was no statistically significant difference in the magnitude of the mean BSPL potential achieved in either group once the baseline had been achieved (Christie and Venables 1971c).

Further experimental work involved measurement of the BSPL under less ideal conditions. The BSPL was recorded under restful conditions, but allowing the subject to read non arousing material. This was immediately followed by a repeat of the standard (bed rest) BSPL recording protocol. No significant difference was noted between the reading BSPL and bed rest BSPL. It appears therefore that this BSPL state can be achieved in less than optimal conditions and with non habituated subjects.

In the discussion to their initial paper, Christie and Venables (1971c) suggest that BSPL could be dependent on the K^+ gradient between the electrolyte (0.5% KCl) and a source of K^+ in the tissue fluids. From existing physiological data, the K^+ concentration (convention is to use the abbreviation $[K^+]$ to represent the concentration of a particular ion - in this case potassium) in the tissue fluids would be expected to fall in the range of 4 - 140 mEq/l (being the values for the extracellular fluid (ECF) and muscle tissue fluid (Woodbury 1966). The Nernst equation can be used to predict the EMF generated across a biological membrane separating solutions with differing concentrations of a single ion. The Nernst equation for the epidermal membrane potential (BSPL) can be described with the following equation :

$$\text{BSPL} = \text{constant} \times \log_{10} \frac{[K^+] \text{ electrode electrolyte}}{[K^+] \text{ tissue source}}$$

where: constant = 61 at 37°C and $[K^+]$ is the potassium ion concentration

Christie and Venables acknowledge that the consideration of a single ion is a probable oversimplification, but if the hypothesis is in any way tenable, on substitution of the BSPL values obtained experimentally, the calculation should give tissue [K^+] values which are within the physiological range. Working on this principle, the BSPL ranges obtained from the experiments give a predicted tissue fluid [K^+] of between 21 and 47.6 mEq/l when 0.5% KCl is used as the electrolyte, which falls in the expected range. Individual differences in potassium ion concentrations may be partly responsible for the differences in recorded BSPL when an electrode electrolyte of constant concentration is used.

Two further experimental avenues were considered following this initial work. Firstly, plasma potassium levels had been previously correlated with ECG T wave magnitude (Turner 1967, Laks and Elek 1967). If the BSPL magnitude was related to potassium ion concentration in the plasma, and if the suggested relationship between BSPL and body [K^+] was reasonable, there should also be a correlation between BSPL and ECG T wave magnitude. Secondly, the effect of varying the electrode electrolyte concentrations was studied as the model predicts that this should result in an alteration in the BSPL value recorded, and was a phenomenon that had been reported previously by Edelberg 1971 , Venables and Sayer 1963 although these previous workers had not fully explained the relationship.

Christie and Venables (1971d) review the correlations between ECG T wave magnitude and the plasma potassium ion concentration. The ECG T wave amplitude has been shown to increase as the plasma potassium ion concentration increases This relationship is reported as fulfilling the equation (after Papadimitriou et al 1970):

$$K = 3t / 2$$

where: K = the plasma [K+]
t = the T wave amplitude

Working from the Nernst equation with potassium as the sole ion of concern, it is predicted that a high (more negative) BSPL would be expected to occur with a low plasma (and therefore ECF) [K^+]. The expected relationship would be a negative correlation with BSPL $\propto$ 1/ECG T Wave amplitude.

The experimental work reported in (Christie and Venables 1971d) tested the relationship between BSPL and ECG T wave amplitude in 21 male habituated subjects aged 21-45 years. The electrodes (Ag/AgCl) and electrolyte (0.5% KCl) were as used previously. Subjects were tested in sitting and in supine lying, and both results produced a significant negative correlation between the variables ($r=-0.70$, $p<0.001$ in lying and $r=-0.61$, $p<0.01$ in sitting). No significant relationship was demonstrable between the ECG T wave amplitude and SPL before BSPL had been achieved.

If the ion concentration of the external electrolyte was related to the magnitude of the BSPL as predicted by the Nernst relationship, then an increased ion concentration in the electrolyte would result in an increased BSPL

(more negative) a finding which had been reported previously by Venables and Sayer (1963). The experimental work involved varying the electrolyte ion concentration within physiological limits to establish the strength of the relationship (Christie and Venables 1971b). The skin [K^+] could not be identified from the literature, but had been established by Christie (PhD Thesis, University of London 1970)

Three sets of results were collected from the palmar surface fluid:

1) 14 subjects during the summer months, tested around midday
   4.7 - 28.2 mEq/l Mean 16.2 mEq/l

2) Same 14 subjects tested at 6pm of the same day
   3.6 - 27.2 mEq/l Mean 16.7 mEq/l

3) 20 subjects at midday during the winter months
   7.8 - 33.3 mEq/l Mean 20.8 mEq/l

The palmar surface fluid that was used for the testing arose from a variety of sources including sweat (even though the subjects were not in a state of arousal), transepidermal fluid and keratinisation products (Christie 1970). Instead of using these values directly, Christie and Venables (1971b) combined the sample data with the results of calculations based on the Nernst equation (the [K^+] of the extracellular fluid was expected to be in the range of 21 to 67mEq/l based on the typical BSPL range of 0 to -30mV) and subsequently tested electrolyte concentrations of 67 mEq/l that had been used in the previous work, a similar but slightly different value of 60 mEq/l to see what effect small changes in electrolyte concentration had on the BSPL and two further concentrations of 40 mEq/l and 2 mEq/l.

The electrolytes were tested on a group of 16 male habituated subjects aged 20 - 45 years using the methods previously described by the author, with the exception that the external electrolyte concentration was varied. Ag/AgCl electrodes were placed on the palmar surface of 4 fingers of one hand. The varying electrolyte concentrations were randomly allocated to different fingers and data recorded simultaneously from electrodes paired with 4 reference electrodes (using a matched electrolyte) at a punctured site on the ipsilateral forearm.

The mean experimental potentials together with the predicted values from the Nernst equation were plotted for the subjects and it was shown that a change in BSPL was obtained by varying the electrolyte concentration of potassium ions. The direction and magnitude of the change agreed favourably with the potentials predicted by the Nernst equation (Christie and Venables 1971b).

The results obtained by Christie and Venables appear to establish the relationship between the electrolyte ion concentration and the ECF ion concentration by means of the BSPL. The relationship appears to fit a theoretical model based on the Nernst equation for single ion concentration gradients across a biological membrane. The results and predictions suggest that with a constant INTERNAL [K^+], reduction of the electrolyte [K^+] will

result in a smaller BSPL (less negative) which may in fact become positive. These findings are in keeping with Edelbergs' observation that two surface electrodes with different concentrations of KCl as the electrolyte will produce a surface skin potential, which will be more negative at the site with higher electrolyte concentration (Edelberg 1971). This relationship is represented graphically in Figure 2.5. The two graphs are symbolic in that they represent the direction of the relationship rather than a real linear regression line. The left graph shows the effect of varying the ion concentration in the electrode electrolyte and the right graph, the effect of variation in the ECF potassium ion concentration.

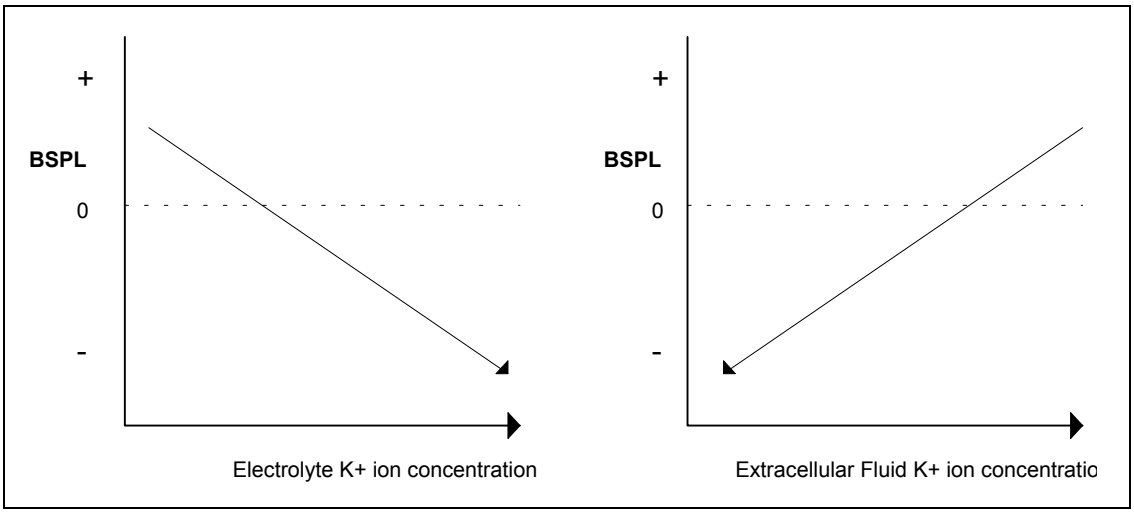

Figure 2.5: Representation of the relationships between electrolyte ion concentration and BSPL magnitude based on the experimental results of Christie and Venables 1971b

With a constant $[K^+]$ in the electrolyte, variation of the internal ECF $[K^+]$ will also change the magnitude of the recorded potential, with lower ECF concentrations being associated with a larger (more negative) BSPL.

2.1.5 BSPL calculations in relation to the Nernst equation.

The essential factor that determines the theoretical value of the BSPL when using the Nernst equation is the ratio of the external and internal ion concentrations. If the ratio produces a low value (i.e. the INTERNAL (ECF) CONCENTRATION >> EXTERNAL (ELECTROLYTE) CONCENTRATION) then the BSPL that results will be more positive. If the external ion concentration was maintained at a constant level, and a series of BSPL readings were taken when the internal (ECF) ion concentration varied (but other factors remain constant), then the measured BSPL would vary inversely with the ECF ion concentration.

The typical $[K^+]$ of the ECF based on a mean BSPL of 19.9mV (Christie and Venables 1971b) and an external electrolyte concentration of 67mEq/l (0.5% KCl) can be derived from the Nernst equation by substitution thus:

$$\text{BSPL} = \text{constant x } \log_{10} \frac{[K^+] \text{ electrode electrolyte}}{[K^+] \text{ tissue source}}$$

where: constant = 61 at 37°C and $[K^+]$ is the potassium ion concentration
thus:

$$19.9 = 61 \log_{10} \frac{67}{x}$$

where x represents the ECF K^+ concentration

This gives a typical $[K^+]$ in the ECF of 31.6 mEq / l

From Christie and Venables (1971), the 'normal' ion concentration ratio can be approximated at 2:1 when the standard 0.5% KCl is used as an electrolyte. In these circumstances, and by substitution into the formula, a BSPL value of 18.3mV would be produced. The Nernst equation gives the magnitude of the membrane potential, and the polarity is that taken by the internal membrane potential in relation to the external. In the case of the epidermal membrane and BSPL calculations therefore, this potential of 18.3mV is the potential of the internal tissues compared with the external surface of the skin. In the convention used for BSPL and similar measurements, the potential is given the polarity of the external surface in relation to the internal environment of the body, thus this calculated value would be equated to a transcutaneous BSPL of -18.3mV. A simple manipulation of this ratio offers a theoretical model for altered ratios between the internal and external ion concentrations. By altering the ratio from 2:1 to 2:1.5 (as would occur with the same electrolyte being used to record the potential from tissue with an elevated potassium ion concentration), the BSPL calculated value would be 7.62mV, externally negative. An increase in ECF $[K^+]$ would therefore reduce the BSPL - i.e. to induce a positive shift. If the ECF ion concentration was increased sufficiently to become greater than the electrolyte concentration, the calculated BSPL achieves a positive value for the external surface. For example, using a ratio of 2:3 (external:internal), the calculated BSPL value would be -10.7 (for the internal membrane potential, giving a SPL of +10.7mV when using the conventional terminology. The essential relationship therefore, when considering a single ion type (potassium), based on the Nernst equation and using an external electrolyte of 67mEq/l for potassium is that the larger the ratio of external:internal ion concentration, the more negative the BSPL.

An informative secondary analysis of the ion concentration of the external electrolyte was conducted by Christie and Venables (1971a) in which the applicability of the Nernst model was considered by the use of a different electrolyte salt. The study used physiologically equivalent concentrations of KCl and NaCl as the electrolyte based on the data obtained during palmar surface fluid analysis (Christie 1970). In the non aroused state (and depending on the time of day and the time of year), the ratio of sodium to potassium ions in the palmar fluid was found to be approximately 2:1. Thus, BSPL values with physiologically equivalent electrolyte concentrations of 40mEq/l KCl and 80mEq/l NaCl on both male and female subjects were compared.

The results of the experimentation (with 40 subjects) suggest that for physiologically equivalent electrolyte concentrations (based on palmar fluid collection values and Nernst equation calculations), NaCl has properties which are similar to those of KCl when used as an external electrolyte, and therefore, the Nernst model appears to be as applicable to Na ions as it is for K ions (Christie and Venables 1971a).

When measuring BSPL, it appears therefore that the particular ion used in the electrolyte is possibly less critical than the concentration of that ion relative to its ECF concentration. It is the ratio of the external:internal concentrations which will determine the magnitude and the polarity of the BSPL.

This conclusion by Christie and Venables has been challenged by Fowles (1974) who suggests that if the epidermal membrane is selectively permeable to K^+ ions alone, the results obtained with NaCl as the electrolyte could be attributed to a potential produced across the sweat duct wall rather that across the epidermal membrane. If this were the case, then changes in NaCl concentration in the electrolyte would have little or no effect on the potential generated across the epidermal membrane, though a change in potential may actually be recorded due to the altered function of the sweat gland generator function.

The Nernst equation describes an electrochemical relationship for a single ion species at different concentrations on either side of a biological membrane. The difference in concentration provides a diffusion gradient down which ions from the more concentrated solution will pass. Taking potassium ions as an example (with a net positive charge), the rapid initial passage of a number of +ve ions across the membrane will lead to a deficit of positive ions on the more concentrated side, thus creating a potential that opposes the passage of the ions. As the ion transfer continues, a point is reached where the concentration gradient (i.e. the drive for the diffusion) is matched exactly by the opposite electrical gradient that inhibits ion movement. This then is the state of equilibrium described by the Nernst equation where the passage of ions in one direction by diffusion is matched by the passage of ions in the opposing direction by the electrical gradient. The equation ascribes a magnitude for the resulting potential which in the case of the single positively charged ion, will result in a negative potential on the side of the membrane which initially has the greater +ve ion concentration (Fowles 1974, Guyton 1986).

As mentioned previously, the Nernst relationship for the epidermal membrane is almost certainly an oversimplification of the situation as it only considers the behaviour of a single ion. A more thorough calculation

could be achieved by using the Goldman equation for the most likely significant ions - Potassium (K^+), Sodium (Na^+) and Chloride (Cl^-):

$$Ei - Eo = \text{constant} \log_{10} \frac{PK^+[K^+]_o + PNa^+[Na^+]_o + PCl^-[Cl^-]_o}{PK^+[K^+]_i + PNa^+[Na^+]_i + PCl^-[Cl^-]_i}$$

where P = membrane permeability coefficient for the ion and
Ei - Eo = potential inside the membrane - potential outside the membrane

The Goldman equation provides a more detailed model of the membrane behaviour as it not only takes account of the relative ion concentrations, but also includes membrane permeability differences between the ions that is necessary for a model that considers multiple ion interactions. Both Guyton (1986) and Passmore and Robson (1976) describe the Goldman equation in relation to the nerve and muscle membrane resting potentials. For these membranes, there is a concentration difference between the ions which results in a net excess of positive ions on the internal aspect of the membrane, though the membrane potential is described as being internally negative. The concentration gradient causes the outward passage of positively charged ions. In moving across the membrane, the ions leave a deficit of positive charge internally, effectively causing an internal electronegativity. The degree of importance of each of the ions in determining the membrane potential is proportional to the membrane permeability for that particular ion. The complex pumping actions at the nerve or muscle membrane mean that more than a single ion is involved. The sodium-potassium pump is primarily responsible for the generation of the resting membrane potential in nerve and muscle. The Na^+ ion concentration is greater outside the membrane whilst the K^+ ion concentration is greater on the inside of the membrane. The sodium-potassium (Na-K) pump actively transports 3 Na^+ ions from the inside to the outside of the membrane whilst transporting 2 K^+ ions from out to inside. For each pump cycle therefore, 3 positive ions are expelled for every 2 allowed in, with a net transfer of positive ions to the outside of the membrane. The membrane is almost impermeable to chloride (Cl^-) ions that are held in greater concentration inside the membrane. The result of the pump action together with membrane permeability, is that there is a net internal negative potential that can be up to -90mV achieved by outward diffusion of potassium, but contributions also being made by the slight inward diffusion of sodium, and the combined active transport of both ions by the Na-K pump.

The generation of the nerve and muscle membrane potential has been extensively researched and values for the various ion concentrations have been established. When attempting to use the Nernst and Goldman models for the epidermal membrane as a generator of the skin potential there are several important differences. The ionic concentrations of the fluids involved are not nearly as clearly documented as for nerve and muscle. Secondly, the permeability of the membrane to the essential ions is not reported in the literature. Thirdly, it would seem unlikely that there are active transport mechanisms in operation, but although none have been identified, they can not be completely eliminated. It is possible (Vanable 1989, Fowles 1974) that the epidermal sheet of cells could function as a complex membrane, with the individual cells acting in unison and under some form of control, such that the cell membrane pumping actions are co-ordinated to produce an effect similar to an active transport mechanism in a single cell.

The structural location of the epidermal membrane is not easily identified. It has been suggested by several authors (Edelberg 1968, 1973, 1977, Venables and Sayer 1963, Millington and Wilkinson 1983) that rather than a single cell layer, the epidermal membrane is most likely a combination of several (2 or 3) relatively impermeable cell layers, which in combination act as a selectively permeable membrane. The germinative and granular layers of the epidermis are cited as the most likely sites for this membrane function (Edelberg 1971,1977).

Edelberg (1977) suggests that membrane potentials arise commonly because of unequal mobilities of oppositely charged ions due to either steric hindrance (i.e. limited mobility due to size) or electrostatic drag imposed by the membrane. The ion permeable channels of the corneum are thought to be too large to exert any steric effect, but that the fixed charge may have an electrostatic effect. Martin and Venables (1966) outline the membrane function of the epidermis as a generator of the transcutaneous potential. They suggest that the potential is a function of the characteristics of the membrane and the internal body ion concentration in relation to the ion concentration in the external electrolyte. The epidermal membrane behaves as if it had a fixed negative charge. It is permeable to cations (+ve) which pass through it and leave an excess of anions (-ve) in the electrolyte external to the surface. A potential difference appears across the membrane, the outer skin surface appearing negative. Experimental evidence (Rein 1924 cited in Martin and Ven 1966) confirms the passage of positively charged ions (dyes) into the corneum whereas anionic (-ve ion) dyes do not penetrate the corneum. Edelberg et al (1960) demonstrated that small cations (Na^+ and K^+) can penetrate the corneum whilst the larger cations (e.g. Ca^{++} and Al^{+++}) are unable to do so. Millington and Wilkinson report that K^+ and Cl^- ions in aqueous solution have a similar size, but that the K^+ ions will diffuse into the epidermis far more readily than will the Cl^- ions. This evidence appears to support the electrostatic hindrance rather than steric effects at the membrane. Rothman (1954 cited in Martin and Venables 1966) has suggested that the effective barrier layer exists between the cornified and non-cornified parts of the epidermis, a concept supported by Leonesio and Chen (1987) and which is in agreement with the germinative/granular layer barrier suggestion by Edelberg.

In the absence of overt sweat gland activity, the generation of a skin potential by some type of membrane function of the epidermis appears to be supported on both a theoretical and experimental basis. Modelling of the generation is difficult in the absence of specific data for the relative permeability of the epidermis to the major

ions (Na^+ K^+ Cl^-), though there is some evidence that anions (-ve) are unable to penetrate the epidermal barrier at an equivalent rate to small cations (Edelberg 1971, Fowles 1974).

When considering a single cation, e.g. potassium, the Nernst equation can be used to predict the magnitude of the transcutaneous potential if the ion concentrations in the body fluids and electrode electrolyte are known, at least as a ratio. Modelling with more than a single ion species involves the Goldman equation which besides concentration ratios, requires permeability characteristics of the membrane to particular ions to be known, which do not appear in the literature. Christie and Venables (1971 a,b,c,d) have highlighted the correlation between potassium ion concentration in the electrolyte and body fluids with the basal skin potential level and also report the limited experimental evidence for the involvement of the other major cation (sodium). A model for potential changes in injured tissues based on potassium concentration gradients is presented in Section 3.5.

Despite the differences between the Skin Hydration and BSPL models of skin potential generation, there are a significant number of common features. Both acknowledge that the epidermal membrane plays an essential role in potential generation. Changing the concentration of the electrode electrolyte ion concentration is known to result in an alteration of the SPL. When recording SPR's (phasic potential changes in response to stimuli), the sweat gland generation mechanisms appear to dominate, and this is confirmed by Edelbergs model. In quiescent conditions, when the sudorific activity is minimised, the membrane generator becomes dominant. In these circumstances, the ratio of external to internal potassium (and sodium) ion concentrations appears to be the most significant contributor to the potentials produced. This can be equated to a change in E in Edelbergs model (Section 2.1.2).

2.1.6 Skin Battery Potentials according to the Physiologists

When considering of the skin potential in situations other than those which are based on psychological or psychophysiological research, there remains a body of literature which has considered the `normal' physiological or pathological correlates of skin potential measurements.

Work with amphibian limb regeneration has established that local potentials following amputation are derived from the skin that acted as a current generator (or battery) (Borgens 1977, 1982, Vanable 1989). In amphibian skin, the outer epidermal cells demonstrate a quite specific ion transport mechanism with sodium channels that are radically different to those in almost all other plasma membranes. These outer epidermal cells allow Na^+ ions to diffuse from the environment into the cells. The cells maintain a very low internal Na^+ ion concentration by the active onward transport of the Na^+ ions to the subepidermal tissues by way of the adjacent cells of the epidermis (Vanable 1989). Essentially, the special channels in the outermost cells allow Na^+ ions to enter these cells by diffusion. The continuing movement of the ions is by an active transport mechanism with each cell moving ions to and from the gap junctions between the cells and hence, ever deeper into the tissues. By continuously passing the ions deeper, the cells maintain a low internal sodium ion concentration, and thereby maintain the gradient. The overall result of this ion flux across a complex membrane is a net inward movement

of positive sodium ions and therefore the generation of an electrical potential across the epidermis (in the region of 50mV), with the body fluids positive with respect to the outside of the skin.

Although the skin battery is best understood in amphibians, numerous research groups have more recently investigated other vertebrates including mammals and man. The discovery that skin injury induces a steady flow of current out of the wound (by DuBois Reymond in 1849) preceded the confirmation of the skin battery by some considerable time. Additionally, electrical (exogenous) stimulation of skin wounds has become established as an acceptable method of clinical management even though it is not currently possible to fully detail the mechanisms of the skin battery or its changes on injury.

An important milestone in the field was the report by Barker et al (1982) who demonstrated the epidermal battery in the guinea pig. The transepidermal potential (TEP) was shown to range between 0-10mV in hairy skin and 30-100mV in hair and gland free skin (both externally negative). The TEP is equivalent to the transcutaneous SPL reported in earlier sections. The research largely concerned the effect on the potential of skin wounds (Section 2.2), but the clear demonstration of a resting skin potential in mammals is important. The location of the epidermal potential generator was determined by progressively increasing the depth of the 'surface' electrode. The outer corneal layers appeared to make no contribution to the potential generated, though they did make a substantial contribution to the skin resistance. The generator appears to be located in the living epidermal layers immediately deep to the corneum. This finding is consistent with the work of Edelberg and Christie and Venables.

Barker et al (1982) demonstrated in addition, that the skin battery appears to be sodium dependent as in the frog and other amphibian skin. The frog skin battery can be inhibited by amiloride that blocks the Na^+ ion channels. Similarly, in guinea pig skin, the epidermal potential was reduced by 50% when exposed to amiloride supporting the contention that mammalian skin not only has a battery function that is similar in relative magnitude to the amphibian skin, but which appears to be related physiologically (Barker et al 1982, Venables 1989). It was concluded that the hair and gland free skin of the guinea pig has a battery comparable in power and character to that of frogs though it is suggested that rather than a primary function concerning salt uptake (as in amphibians), that this mammalian battery may primarily subserve epidermal wound healing.

Whilst conducting the experimental work with guinea pigs, the authors measured the TEP from their own bodies. The potentials recorded were consistently externally negative (with reference to a single punctured forearm electrode), with hair free regions producing higher (more -ve) potentials than the hairy regions (Barker et al 1982). In a more detailed investigation of the human skin battery potential, Foulds and Barker (1983) measured the transcutaneous voltage of 17 normal volunteers. A consistent anatomical variation was observed, but no correlation could be established between the battery voltage, age and sex.

Potentials were recorded at 121 surface sites in each volunteer. Electrodes were of cotton wool soaked in 0.9% saline connected via an agar-saline bridge to calomel electrodes immersed in 3M KCl. These were used with a high impedance voltmeter (10^{12} ohms). A single reference electrode, making contact with the internal

environment of the body completed the measuring circuit. It was shown that the difference in potential between any two punctured sites was less than 1mV, thereby justifying the use of a single reference electrode site (Foulds and Barker 1983).

The average potential (for all locations, all subjects) was -23.4mV (SD 8.6mV), with the hands and feet demonstrating the higher (more negative) potentials and other regions (e.g. head, upper arm) demonstrating much lower potentials (i.e. closer to zero). The anatomical variation of skin battery potentials appears to be a complex combination of several factors (including sweat gland concentration and hair density) and did not appear to be related to dermatome distribution.

The general thrust of this research was to consider the role of skin potentials in relation to skin lesions and wounds. An attempt was made to model the changes in skin potential following injury and how this was related to repair and regeneration. Little further work appears to have been conducted to establish the exact mechanism of generation in the non injured human skin. An outline of the skin wound model in included in Section 2.2.2.

This physiological demonstration of a transcutaneous human skin potential at rest, with the external surface being electronegative with relative to the internal environment of the body is consistent with the SPL and BSPL demonstrations by the behavioural scientists cited previously. The explanations offered by the physiologists appear to be dependent on a comparison with the amphibian skin potential generation that has been reasonably well researched. The reliance on a sodium diffusion and active transport mechanism for the potential generation leaves one essential problem that does not seem to have been investigated. For the amphibian, there is clearly a diffusion gradient between the fluid bathing the external surface of the skin (i.e. the pond water) and the internal fluid environment of the body. The magnitude of the potential will alter with changes in this concentration ratio. If the mammalian, and particularly, the human epidermal generator is also sodium ion dependent, from where does the concentration gradient arise? Clearly, in placing an electrode on the skin surface with an electrolyte, there will be a difference in ion concentration between the two environments, and therefore a skin potential can be measured. If the electrode and therefore the electrolyte were not in contact with the skin, would the potential actually exist, or can it be considered an artefact of the measurement process itself?

The skin potential has been measured in subjects by using dry electrodes (i.e. with no electrolyte) in a series of experiments investigating the relationship between skin potential, resistance and capacitance (Grimes 1982). Although no electrode electrolyte was used in these tests, Grimes suggests that the skin is not actually dry, but has a water content in balance with the humidity of the surrounding air plus a supply from sweat gland activity and insensible perspiration. Fowles (1974) highlights that the epidermis remains at least partially hydrated under normal physiological conditions which together with the hydrophilic nature of the corneum would help to maintain the fluid levels in the outer layers of the skin. With the epidermis in a constant damp if not wet condition, the ion diffusion and active transport mechanisms described by Vanable (1989) could be applied to human skin without the need for an electrolyte to be present in order to generate the potential.

None of the experimental work by physiologists investigating the skin potential appears to have considered the role of ions other than sodium in the potential generation. The surface fluid in the epidermis is unlikely to contain only sodium ions. Sweat has an ionic composition that is similar to that of plasma without the plasma proteins (Guyton 1986) though Fowles (1974) suggests that the initial secretion is actually slightly hypertonic. The sweat secretion is modified however as it passes up the duct towards the surface depending on the sweat rate. The initial secretion (the precursor secretion) has a typical Na^+ ion concentration of some 142mEq/l with 104mEq/l of Cl^- ions. The concentrations of other plasma constituents are much smaller though Guyton does not offer exact concentrations. In a situation where the sweat rate is slow, most of the Na^+ and Cl^- ions will be reabsorbed during the passage through the duct. The concentrations of both of these ions may reach as low as 5mEq/l once the sweat has reached the skin surface. Following this reabsorption, the osmotic pressure of the secretion is reduced, and a considerable amount of the water is reabsorbed by the duct lining. The consequence of this reabsorption is to increase the concentration of the other sweat constituents such that at the skin surface, urea, lactic acid and potassium concentrations can be very high, though again no exact values are offered (Guyton 1986).

In circumstances where the sweat rate is high, there is a greater quantity of the precursor secretion and less time for both ionic and water reabsorption, thus the Na^+ and Cl^- ion concentrations are only reduced to approximately 60mEq/l and there is less concentration of the other constituents as less water has been reabsorbed. Guyton (1986) cites a typical concentration for potassium during rapid sweating of only 1.2 times greater than the plasma concentration.

In the resting, unstimulated conditions ascribed to basal or quiescent skin potential testing, stress is deliberately minimised and it is suggested therefore that sweat gland activity should be minimal. Under these conditions, slow sweating should predominate and therefore the potassium concentration in the surface fluid should be greater than that of the plasma (4mEq/l) (Guyton 1986). The skin fluid investigation by Christie (1970) (Section 2.1.4) gave potassium ion concentrations which were higher than those generally found in plasma, with a mean potassium ion concentration of 17.9 mEq/l for all subjects.

According to the BSPL model (Section 2.1.3) in a situation where the external ion concentration was greater than the ECF ion concentration, the potential developing across the biological membrane would be externally negative, such as that recorded from the skin even with 'dry' electrodes (Grimes 1982).

There is a consistency therefore between the physiological mechanisms associated with both the behavioural scientists and the physiologists explanations of the skin potential recorded under resting conditions. Both groups ascribe the primary generating function to a membrane based potential, with the sweat gland contribution becoming more dominant following stimulation. The explanations offered by the Edelberg, BSPL and Foulds & Barker models vary in their interpretation rather than in their fundamental elements.

2.1.7 DC Control Theory (after Becker)

A more global consideration of the bioelectric potentials measured from the skin has been advanced by numerous researchers, Burr and co workers beginning in the 1930's and Becker and co workers in the 1960's. Both groups have developed a concept of the skin potential being a measurable phenomenon of a DC control system that plays an essential role in monitoring and controlling growth and healing. At the present time, no evidence has been identified which refutes the basic concepts, and several research groups have used them as a fundamental theoretical underpinning of their own work (e.g. Rowley 1974, Shibib et al 1988, Wilber 1978). This appears to be particularly true in the area of electrical stimulation of skin and bone to enhance healing.

The essential difference between the transcutaneous electrical potentials (see above) and the DC potentials recorded by Burr and Becker is that the latter attribute the potentials to a nerve related phenomenon, anatomically distributed and not to local epidermal membrane or psychological episodes.

Measuring the DC potentials from the same level of the epidermis (i.e. not the transcutaneous potential) Becker has demonstrated that both in amphibians and in man, there is a pattern of equipotential lines which follows a predictable arrangement (Becker 1962a). These investigations demonstrated the presence of a complex electrical field with a spatial configuration that had a close relationship to the gross distribution of the central and peripheral nervous system. Both in the Salamander and in man, the cranial, brachial and lumbar neuraxes were found to be positive, with increasing negative potentials along the peripheral outflows (Becker 1962a). On further investigation, it was proposed that the peripheral nerves were responsible for the distribution of this electric field, with DC gradients extending longitudinally throughout the neural network. The dendrites (sensory components) were found to be distally positive and the axons (motor components) distally negative resulting in an axiodendritic polarisation model for the DC control system (Becker 1962). A representation of Beckers polarisation concept is shown in Figures 2.6 and 2.7.

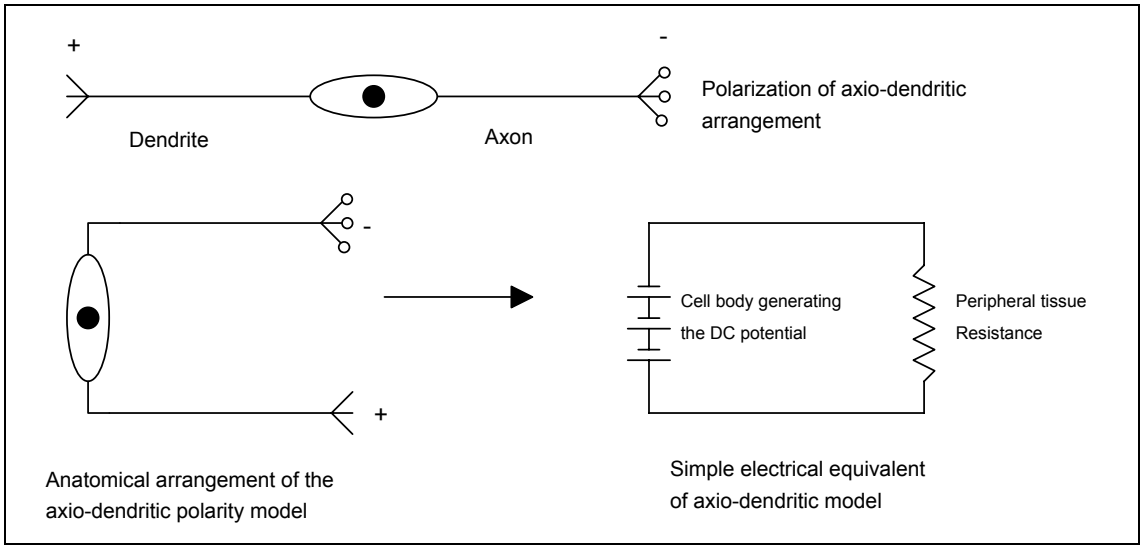

Figure 2.6 Axiodendritic Polarisation of Nerves (after Becker)

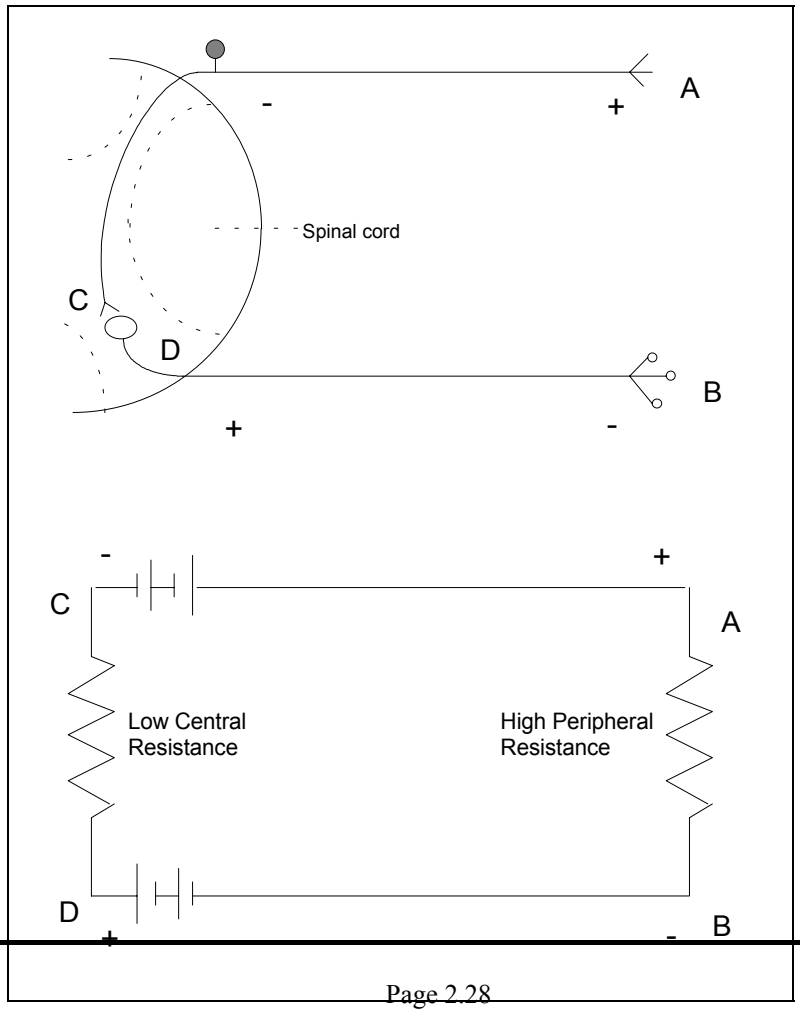
A
-
+
Spinal cord
C
D
B
+
-
-
+
C
A
Low Central
Resistance
High Peripheral
Resistance
D
+
-
B

Figure 2.7 : Physiological and electrical model of a neurone pair forming an elementary circuit (after Becker 1962)

The role of the peripheral nerves in the transmission of these DC potentials was strengthened when it was observed that the potentials were reduced to zero after sectioning the nerves to the extremity (Becker et al 1962a).

The DC potentials were shown to be independent of the action potentials. The DC potentials are related to a longitudinal continuous movement of charges in the nerve whilst the action potential is a travelling wave of membrane depolarisation - a radial movement of ions in and out of the nerve fibre with no longitudinal transmission of electric charges (Becker 1962a, 1974).

Beckers experimentation suggested that the charge carriers were not ionic, but were units the size of electrons, implying that a phenomenon such as semiconduction was occurring in the nerve fibre (Becker et al 1962b). Becker (1974) cites numerous examples of semiconductor like behaviour of biological tissues including nerve (Becker 1961), collagen and bone (Becker and Brown 1965).

Becker (1974a,b) concludes that two data transmission and control systems coexist in most present day animals. One is a sophisticated action potential, digital type system and secondly, a more basic/primitive analogue type system that antedated the former, thought to be solid state in nature. Becker (1974b) proposes that these currents are both generated and transmitted by the Schwann cells that surround the peripheral neurones and the glial cells in the central nervous system. This hypothesis is compatible with the demonstration (Lowestein 1981) of cell to cell conductances and junctional communications in glial and epithelial cells. Evidence is presented (O'Leary and Goldring 1964, Becker et al 1962b) to support the steady state of varying dc fields within the central and peripheral nervous systems and that these DC potentials have a controlling function over the general level of the digital (action) potential - that it acts as a `bias control' over the functions of the action potential system (Becker 1974a,b). In addition to the modulation influence on the peripheral nervous system, Beckers research group propose that the DC potentials, exert a control over growth and repair processes (Becker et al 1962a). The latter is considered in more detail in a subsequent section.

Beckers DC Control theory has gained popularity with those concerned with the electrical stimulation of damaged tissues in order to facilitate or promote repair. There remains a degree of scepticism amongst the purists due in part to the lack of published experimental data and also due to the absence of replicated work. Several significant studies have produced results that appear to support Beckers proposal (including Chakkalakal 1988a,b, Chang and Snellen 1982, Weiss et al 1990) and these are considered in Section 2.2 concerning the relationship between injury and tissue potentials.

2.1.8 Links between the Skin Potential Models

From the models and experimental work outlined, the various approaches to measurement and theoretical generation of the resting skin potential have several features in common.

1) The skin potential is described as an electrical difference in potential between the external skin surface and the internal environment of the body. Under resting conditions, the external skin surface is always electronegative with respect to a reference electrode in contact with the internal body fluid.

2) Despite the variety of explanations offered to account for the generation of the skin potential, the epidermal membrane, located in the living, deeper epidermal layers is implicated in both the behavioural scientists and physiologists theories, though not specifically with Beckers DC Control Theory.

3) The difference in ion concentration on either side of this membrane is considered the most significant factor. Sodium and potassium ions are those most commonly identified as being the most likely contributors to the generation mechanism.

4) The relationships demonstrated between external electrolyte concentration and the magnitude of the skin potential are consistent whether calculated using Edelbergs equations, the Nernst formula identified by Christie and Venables or the active ion transport mechanisms proposed by Vanable. In each case, the ratio of external to internal ion concentration is related to the magnitude (and therefore the polarity) of the skin potential. With a greater external ion concentration, the skin potential will present as externally negative, a situation confirmed by the experimental evidence of all groups.

5) When using a constant external electrolyte concentration, a change in the internal ion concentration will effect a change in the measured potential whatever the external ion concentration is in absolute terms.

Current hypotheses suggest that the nonsudorific skin potential might be due to different factors depending on how it is measured. It might be due to an ionic concentration gradient between the electrode electrolyte and the interstitial fluid when the electrodes are placed at different levels of the epidermis or it might be related to a DC current control system when the electrodes are placed at the same level of the epidermis. These mechanisms are not necessarily mutually exclusive (Leonesio and Chen 1987) and may complement one another.

Beckers' DC Control Theory does not model the skin potential in the same way as the other research groups and it is therefore difficult to incorporate his hypotheses into such models. Some experimental (particularly clinical) work does support the general hypotheses. For example, the human skin battery work of Foulds and Barker (1983) has produced a map of human skin potentials that is grossly consistent with Beckers increasing peripheral negativity predictions. The two models explain the phenomena on different grounds, Becker on the basis of DC neural conduction whilst Foulds and Barker are more concerned with sweat gland distribution and epidermal membrane phenomena. It does not appear to be possible to equate the models given the different

approaches used and the fundamental lack of substantive data published from Beckers experiments. Some replication of Beckers work concerning injured tissues is considered in Section 2.2.1 below along with the injured tissue correlates of the other models

2.2 Injury Potentials

The current of injury is in essence, the potential difference and subsequent current flow between wounded and normal tissue (Harrington and Meyer 1974). Injury currents were recorded as long ago as the 1700's by Galvani, though following the demonstration of the action potential in 1849 by Du Bois Reymond, the DC injury potentials were no longer considered to be of any great interest. A useful historical review of injury current measurements appears in Borgens (1981). The early concept of this current of injury was that it was derived from the summation of the membrane potentials of the damaged cells. Becker (1967) suggests that this explanation is untenable as the current can still be measured days after the injury, long after the damaged cells have either died or restored their membrane function though Becker does not offer an alternative explanation. Thakor and Webster (1978) have proposed an injury current model based on altered membrane potentials in individual cells. Damage to one aspect of the cell will allow an influx of sodium ions at that point, and it is assumed that the sodium pump continues to function in other parts of the membrane. The sodium ion influx will be countered by the pumping action elsewhere in the cell, thus causing a movement of charged particles across the cell and return path via the extracellular fluid - the current of injury.

A similar problem is encountered with this hypothesis in that although it offers an explanation for the immediate current following injury, it offers no explanation with regards the longer lasting injury currents (or bioelectric disturbance) noted for days/weeks after injury.

Work continues to identify possible mechanisms which can explain the presence of these long term changes. At the present time it would appear that the immediate changes can be explained in terms of local membrane potential disturbances, and that the longer term effects are most likely mediated by altered tissue battery function following the injury.

Nordenstrom (1983) has proposed a complex account of the endogenous tissue potentials and injury currents following a 30 year study of the subject. His concept of `Biologically Closed Electric Circuits' postulates (in brief) that the blood within the insulated vascular system acts as a fixed reference potential and that extravascular tissues vary in their electropotential relative to the blood. Local metabolic differences and/or tissue injury will alter the magnitude of these normal potentials. Current flow as a result of these potential differences occurs in a multitude of local closed circuits which the author suggests play a major role in the body response to an injury. Despite an extensive publication, these concepts do not appear to have gained widespread acceptance in the biomedical science community and evaluation of the research continues. Both Taubes (1986) and Charman (1990c) have reviewed the work of Nordenstrom and suggest that the ideas are worthy of further investigation.

2.2.1 Beckers DC Control System and Injured Tissue

The greater part of Beckers DC Control theory is concerned with the response of the body to trauma and its ability to resolve the lesion whether by regenerative or reparative events. The comparison between the bioelectric events following trauma in regenerative and non regenerative species provided the starting point for Becker. The current of injury (e.g. after limb amputation) in a non regenerative species (frog) is seen to be strongly positive at the time of injury, and to gradually return to non injured levels over a 2-3 week period. Regenerative species (Salamander) however show a different response after the initial strongly positive phase. Within the first few days, the strongly positive current undergoes a polarity reversal and becomes strongly negative before returning to the pre injured level (Becker 1967, 1974b). The peak negative polarity was measured preceding the maximum cellular proliferation. A representation of the two injury current patterns is shown in Figure 2.8.

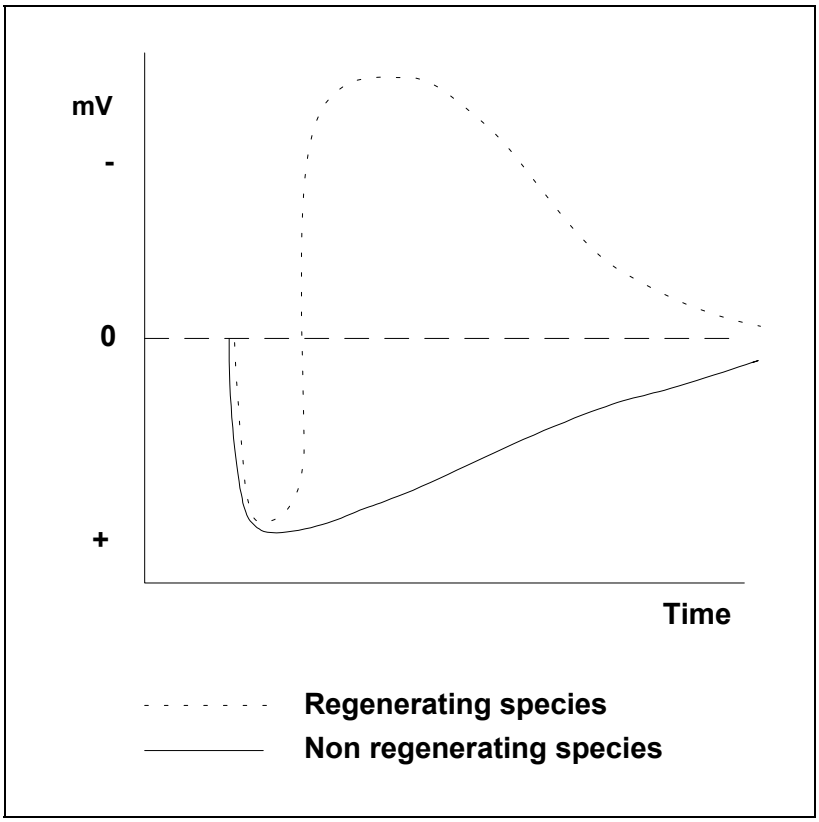

Figure 2.8 : Difference between injury currents from regenerating and non regenerating species (after Becker 1974)

Chang and Snellen (1982) demonstrated a similar potential profile in a series of experiments with regenerating tissue in mammalian tissue (rabbit ear). The initial positive potential changed to a strong negative potential which reduced over the regenerative period. In ears where regeneration was inhibited the negative potential was considerably smaller.

Becker further suggests that the DC control system plays an essential role in the reparative process in that it is responsible for injury detection and control of the repair process - thus providing a bioelectric monitoring and control system. The process has been developed as a system control theory and is shown in Figure 2.9.

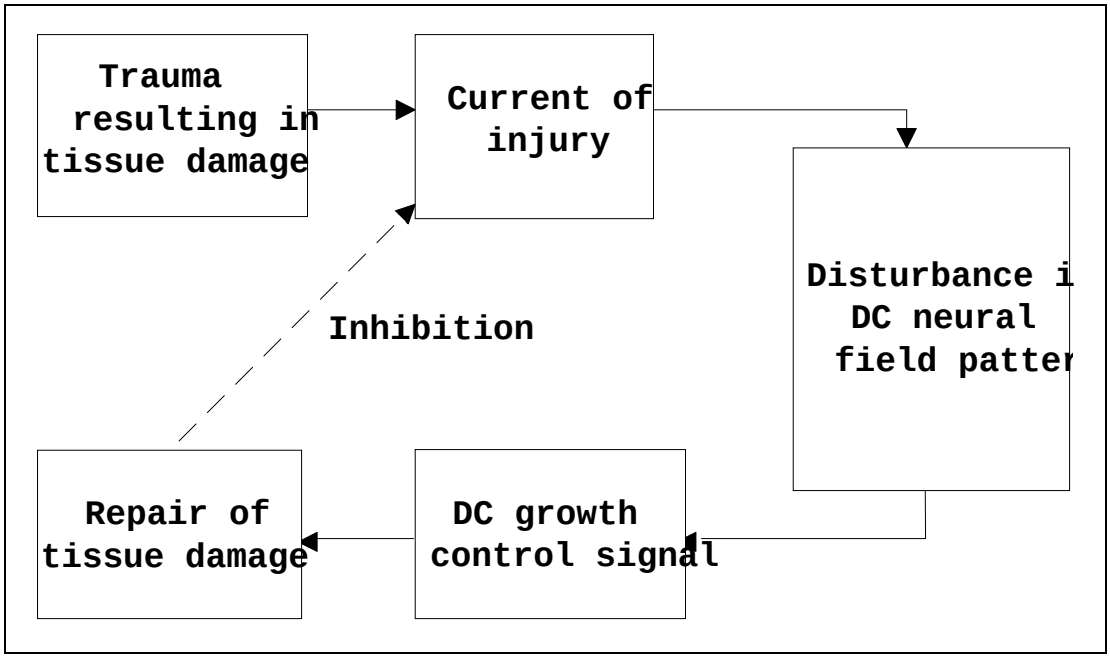

Figure 2.9 : Theoretical DC control system with the response to injury (after Becker 1967)

Becker suggests that the current of injury produces a disturbance in the DC field on both an electronic basis and also by producing an input signal directly to the brain (though the specific mechanism through which this operated is not detailed). Whether the system model is a realistic representation of the physiological mechanism associated with repair or should be interpreted more figuratively is an issue which has yet to be resolved. Many research groups have used this basic concept as the initiator for their work, and in particular, those concerned with the facilitation of wound and tissue healing by means of electrical stimulation. Becker discusses the DC control system at length with examples from clinical medicine, especially bone repair after fracture. The proposed control system has not received universal acceptance and many are sceptical, partly based on a lack of direct supportive evidence and partly due to its challenge of the established chemical control theory of wound healing. This is a complex issue, and one which can not be resolved with the current evidence. If Beckers model is in any way realistic, the measurement of skin surface potentials in the current project should demonstrate changes following injury which are progressive with time. This project was proposed and the basic ideas formulated before the DC Control theory had been investigated. The research is not designed to specifically challenge or provide support for the control theory, though the results of the injured subject trials may make a contribution to the debate.

In support of Beckers DC Control theory, two published pieces of research deserve consideration. Borgens (1984) suggests (without making specific reference to Beckers work), that surface detected injury potentials may help to control the response to damage and that these are not restricted to bone. Acknowledging that this has been a fertile area of research since the mid 19th century, he observes that with the recent development of techniques to measure currents and potentials at the cellular level, surface detection has largely been rendered obsolete. He further suggests that with the renewed interest in the idea that electrical phenomena may help to control tissue response to injury, this measurement modality is undergoing a renaissance.

Shibib et al (1988a) in a complex series of experiments with regenerating nerves, considered Beckers DC control as a possible model for the results obtained. By virtue of the experimental protocol it would not be possible for action potentials to be carried by the nerves involved, leaving the DC potentials and their associated biomagnetic counterparts as the primary bioelectric source. The authors hypothesise with regards possible mechanisms by which either (or both) of these might exert an effect on a severed nerve. They were unable to offer conclusive proof to support either theory, yet considered this to be an area worthy of further investigation. In a follow up paper later the same year, (Shibib et al 1988b), they considered the only electrical factor possibly involved in nerve fibre regeneration (under their experimental conditions) is the DC potential (after Becker) acting as an axial voltage gradient and as a DC current.

It was found that when motor nerves were forced to grow towards other motor nerves (or sensory to sensory) a charge barrier originated at the confrontation zone and growth of the neurons was inhibited. Under conditions where sensory neurons grow towards motor neurons, according to Beckers theory, the distal charges (i.e. the distal voltage gradients) would be of opposite polarity and this would promote regenerative development. The

experimental results uphold the hypothesis, though the authors acknowledge that the exact mode of action of these electromagnetic phenomena remains unknown (Shibib et al 1988b).

2.2.2 Injury potentials in Musculoskeletal Tissues

To continue initially with Beckers DC theory, Becker (1974a,b) reports (in brief) the experimental evidence with regards fracture healing and denervation. It was noted that there was retardation of fracture healing in peripherally denervated extremities and that when the nerve transection gap is bridged by the supporting (Schwann) cells, but not yet by the neurons themselves, the fracture healing rate was returned to normal. This, it is suggested, supports the concept of the DC potentials being conducted through the sheath as opposed to the neurons themselves. The details of this work are not reported in full and all attempts to identify repeat experimentation or collaborative evidence in the literature has failed. The results are reported here as a matter of interest rather than as a confirmed piece of evidence.

Many workers over recent years have considered the change in electrical activity of the tissues on injury, most commonly as a precursor to considering the electrical enhancement of the repair/healing of that tissue. Research by Becker shows that trauma produces an alteration in the whole body field pattern which is detectable as the current of injury (Becker et al 1962a,1974).

O'Leary and Goldring (1964) suggest that an injury potential will develop between injured and uninjured parts of a nerve, muscle, skin and theoretically at least, of any living tissue or cell that presents a membrane vulnerable to depolarisation as a result of trauma.

The bioelectric model of skin lesion repair is complex and largely beyond the scope of this review. The relationship between the activity of the skin battery and the altered potentials measured at a wound is strong, and it is widely considered that the relationship is important to the healing process. Although subjects in the current research will be those who have experienced subcutaneous soft tissue injuries, the electrical changes associated with skin wounds are briefly considered.

The mammalian skin potential work of Barker et al (1982) and Jaffe and Vanable (1984) using a skin injury model in guinea pigs has demonstrated that there is a current flow (movement of positive ions) out from a skin lesion due to an altered skin battery function. The skin potential at the wound site is zero as the battery has been short circuited, though a few millimetres away, a normal transcutaneous potential exists. There is a lateral voltage gradient in the superficial tissues, the mean strength of which was 140mV/mm in guinea pig skin. The lateral gradient was not present if the wound was allowed to dry. The model predicts a current flow from the intact skin battery into the deep wound, with a return path through the wound and to the tissue layer between the dead and living layers of the epidermis. The wound current is illustrated in Figure 2.10 (after Barker et al 1982, Jaffe and Vanable 1984, Vanable (1989)).

Close to the wound, the outer surface of the living layer would be electrically positive with respect to the outer surface of the same layer far from the wound.

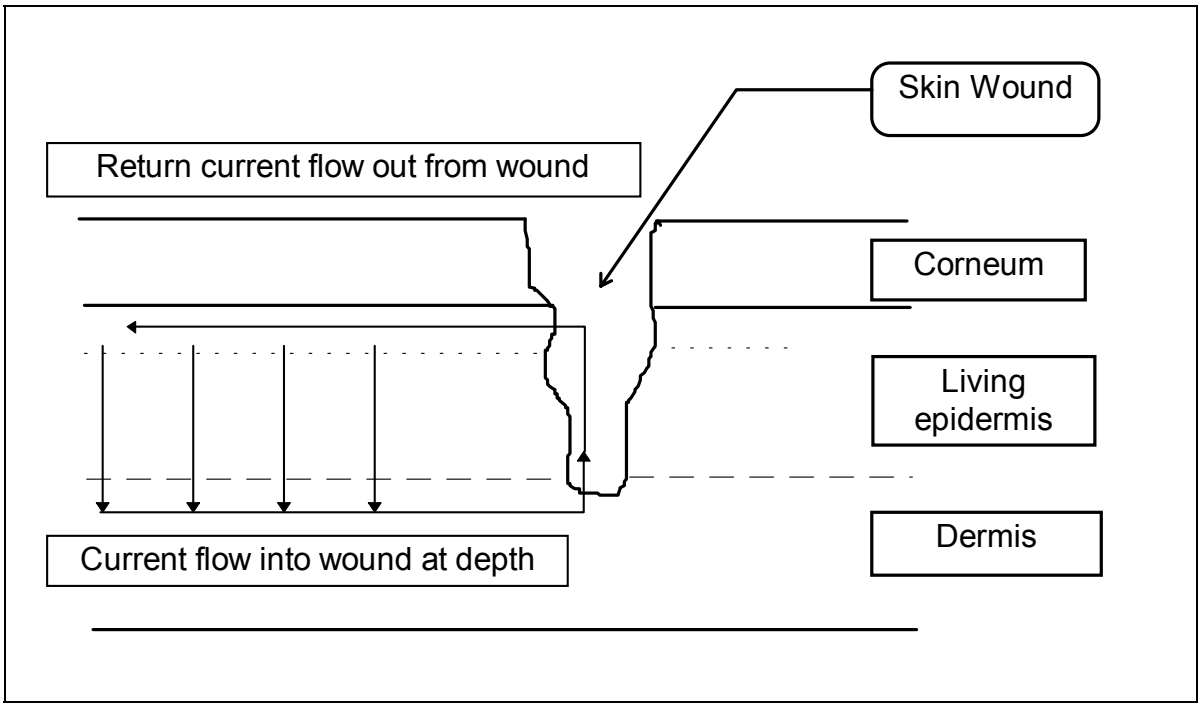

Figure 2.10 : Current path with full thickness wound in mammalian skin after Jaffe and Vanable 1984 (current represents the movement of positive ions)

The strength of the lateral voltage gradients associated with mammalian wounds is within the range of fields found to influence development (Jaffe and Vanable 1984). It is suggested that these wound currents could be

responsible for stimulating wound cover by epithelial cells (Foulds and Barker 1983, Jaffe and Vanable 1984). The stimulation of skin lesions by externally applied electrical currents is gaining clinical acceptance and is in itself a considerable field of study (Vanable 1989, Watson 1994).

Illingworth and Barker (1980) have demonstrated local currents associated with amputated fingertips in children. The current density was on average 22μA cm^{-2} and reached its peak approximately 1 week after the injury. The fingertips regenerated if left unsutured and the battery function of the skin was found to be comparable to that involved in amphibian limb regeneration. The skin battery current driving capacity is in the order of 1μA/mm of wound length (Borgens 1982, Jaffe and Vanable 1984, Vanable 1989).

Much of the experimental work in the area of endogenous electrical changes following injury are related to bone. Some of these studies have in addition considered soft tissue injury associated with the skeletal damage and this is clearly more pertinent to the present study. The activity of bioelectric potentials in relation to bone growth and fracture repair is not considered in detail in this review.

Friedenberg and Brighton (1966), Friedenberg et al (1973) are among those who have shown that there is an increased electronegativity on the bone surface in the vicinity of an injury. Borgens (1984) has measured current densities at the surface of injuries to mice metatarsals in vivo. He concluded that there was a metabolic powered ionic pump in the vicinity of the bone marrow which was the source of the stable, persistent current (referred to as the plateau current). The experimental evidence rules out the periosteum as the source of the potential. It is suggested that these endogenous currents are actively involved in fracture repair, remodelling and possibly growth rather than just being an 'epiphenomenon'. The replication or simulation of the natural injury currents to induce/enhance fracture healing, when applied in the same direction, seems to substantiate this hypothesis.

Chakkalakal et al (1988) present evidence to support the hypothesis that musculoskeletal injuries in humans and in animals cause an increase in endogenous electrical activity in the injured region. The aim of the experimental work they carried out was to determine the source(s) of the endogenous activity and to determine the distribution of the electric fields and currents in the injured limb.

The research measured the change in voltage and current in dog forelegs during progressive stages of surgically created injury, ranging from skin incision to radial osteotomy. The results show that the skin injury activated an epidermal battery of an effective open circuit voltage of 17-42mV. Injury to the subdermal soft tissues (without injuring the muscles) was not associated with any significant increase in endogenous electrical activity. Bone injury activated an endosteal battery of 15-56mV.

The epidermal battery was determined to be the primary source for the injury currents in the extraosseous compartment, including that on the periosteal surface of the bone. The current in the medullary cavity and the net outward flow of current through the osteotomy gap were deemed to be primarily due to the endosteal battery. The authors suggest that evidence from these experiments, together with evidence obtained by Borgens (1984)

indicate that the cell layer of the periosteum has no electrogenic properties. Evidence is presented that the bone battery may be anatomically associated with the endosteal layer of cells lining the bone surface.

The voltages and currents measured in the wound following the skin incision were significantly higher than the variable baseline values measured on the skin surface before injury. The variable baseline results were comparable with those found in animals and humans in other studies (Friedenberg and Brighton 1966, MacDonald and Watson 1982).

The endogenous currents noted in this study were comparable or even greater than those induced by exogenous signals in electrical osteogenesis studies. It is expected therefore that the endogenous activity would be physiologically significant. Large currents on the soft tissue surface (10-32μA) from the epidermal battery were detected and these support Barker et al's (1982) hypothesis that these are important for wound healing. It is suggested (Sevitt 1981) that endogenous electrical activity influences fracture healing and acts as a trigger for proliferation of osteogenic cells in the periosteum, with the bone surface acting as a pathway for currents arising from muscle injury potentials. The currents along the periosteal surface, in the medullary cavity and through the osteotomy gap are such that migration of negatively charged cells towards and into the gap would be enhanced.

The extensive experimentation by Ckakkalakal et al avoided the problem of muscle damage by carefully dissecting between the muscle planes. Lokietek et al (1974) however investigated the effects of several forms of soft tissue damage on the potentials measured from an undeformed tibia in rabbit. They conclude that muscle injury was the dominant factor in generating the voltage detected. It is hypothesised that the bone acts as a pathway for the injury currents produced in the damaged muscle.

MacDonald and Watson (1982) used an array of Ag/AgCl skin surface electrodes overlying the tibial shaft to produce a quasi-three dimensional display of voltage vs position vs time following tibial fracture. It was hypothesised that the detectable skin surface potentials may be indicative of the progress of bone healing. The full details of the work have not been published and the authors were contacted in order to determine the outcome of the research, but the work has been suspended until further funding can be achieved.

In the one research report which investigates a problem analogous to the proposed experimentation, Wilber (1978) measured direct current bioelectric potentials from normal and injured thighs. He utilised a differential skin surface electrode technique, with a reference electrode over the greater trochanter of the femur and an active wandering electrode along the lateral aspect of the thigh. Using pre-gelled commercial electrodes (Ag/AgCl) with an offset potential of 2mV or less, he took a series of readings from normal and injured subjects in order to determine the surface potential pattern. The readings obtained from normal (i.e. non injured) subjects followed one of 4 patterns. The two largest groups were found to be those with similar potentials left and right (i.e. left and right both negative or left and right both positive - groups of 36 and 40 respectively). Two smaller groups (12 in each) presented with opposite polarities (i.e. left positive, right negative or vice versa).

Three injury groups were subsequently investigated: acute femoral fracture, delayed/non union and contusion. The patient numbers in each group were small (7, 4 and 3 respectively) and although the results tended to show differences between injured and non injured limbs, the small numbers make any statistical analysis difficult.

Meaningful interpretation of the results is difficult as no details of the patients medical management are offered and the actual values of the measured potentials are not included in the report. Scant details are available with regards the methodology and an important series of questions remain unanswered. It would appear that this paper was intended to serve as a preliminary report, but no further work by the author has been identified.

Numerous studies have produced results which compare favourably with those cited above. There would seem to be a general agreement that injury to bone causes a significant and relatively predictable alteration in the electrical state of the tissues. Most workers also express with considerable confidence, that this increased endogenous electrical activity is most likely to have a role in stimulating and/or controlling the repair process itself.

In addition to bioelectric activity changes associated with bony injury, there is a substantial volume of research concerned with bioelectric activity changes associated with skin lesions. and the principal studies are summarised below.

Woodrough et al (1975) investigated the relationship between skin potential level and facial skin lesions (malignant, benign and inflammatory). They demonstrated measurable differences between them, but the overlap between groups precluded use of the measurement device in clinical diagnosis.

More recently, Marino et al (1989) have investigated the relationships between skin potentials overlying carcinomatous breast lesions compared with those obtained over benign lesions both in mice and in humans. In both cases significant differences were measured between malignant lesions and controls, but no such difference was demonstrated between benign lesions and controls. The study is still at an early stage and the authors have not yet proceeded to a full scale clinical trials.

Williamson et al (1985) successfully used skin potential and conductance measurements to discriminate between cystic fibrosis and asthmatic patients, with a group matching accuracy of 92.7%. This is likely to be related to the effect of altered sweat gland activity in the generation of the SPL in line with Edelbergs model.

Edelberg (1971) notes that there are electrical changes in the skin of patients with dermatoses, but he questions whether these changes are due to structural alterations, or are linked to the emotional components that often accompany dermatological conditions.

Bioelectric changes following injury have been demonstrated in several tissue types (predominantly bone, skin and nerve). These potentials are different from those normally present in these tissues, though there does not appear to be any universally accepted explanation for the generation of such potentials. Their existence is

generally accepted as being significant rather than just an epiphenomenon (after Borgens 1984) and additionally it is considered by most authors, that these potentials and subsequent current flow has a major role to play in initiating, controlling and terminating the repair process.

2.2.3 Changes in injury potential with recovery/repair

The bioelectric disturbances that occur on injury persist for various lengths of time depending on the tissue involved and the extent of the injury. Burr (1938), Barnes (1945), Friedenberg and Brighton (1966), Wilber (1978), Illingworth and Barker (1980), Chang and Snellen (1982) and Chakkalakal et al (1988) are amongst those who have monitored the electrical activity of damaged tissues as it progresses through its proliferative and healing processes. Each of these groups have reported progressive changes associated with the healing process and have obtained results from mammalian tissue. The greatest difference from the baseline potential occurs during the early proliferative phase and tails off during the subsequent reparative and remodelling phases. Whether these potentials are coincidental, instrumental for the repair or a consequence of the physiological process is an issue which has yet to be resolved. Barker et al (1982), Weiss et al (1990), Becker (1974a,b), Borgens and McCaig (1989), Vanable (1989) are amongst a growing body of researchers who present evidence to support the initiator/control concept. Further evidence to support the initiator/control theory is derived from studies (in animal models) where the natural electrical activity associated with tissue repair is inhibited or subjected to polarity reversal. The effect of this type of manipulation is to either significantly slow down, or more usually to completely inhibit the normal repair process (Vanable 1989).

Many workers have considered the bioelectric correlates of injury/repair/regeneration in amphibians and other lower vertebrates. Borgens (1982, 1984) has established clear patterns of behaviour in amphibians following limb amputation and subsequent regeneration (Section 2.1.5). Becker (1961) has demonstrated a difference in electrical behaviour in regenerating and non-regenerating species (considered in Section 2.2.1).

The use of exogenous electrical potentials, fields and currents in order to facilitate tissue healing (in bone, nerve and skin) has become a clinically accepted technique. More than 40 papers have been identified which report research in this area. The results vary with tissue type, subjects and type of applied stimulus, but a high proportion claim significant enhancement of tissue healing.

One is led to the conclusion that musculoskeletal tissues (not just muscle and nerve) are electrically active, that following injury, the behaviour of this electrical activity is modified and that as the repair process proceeds, there is a progressive return to a normal pattern of bioelectric behaviour. Without necessarily considering the wider implications of the initiator/control concept, the physiological evidence is strong and gaining widespread acceptance.

2.3 Implications for the Current Study

The current study does not aim to identify either the source or physiological effects of the biopotentials. The experimental work aims to establish the background levels for surface potentials in non injured subjects and compare them with equivalent potentials from recently injured soft tissue. If the DC control theory proposed by Becker et al or the tissue repair potential theories proposed by Foulds and Barker (1983), Chakkalakal (1988), Borgens (1982, 1984), Jaffe and Vanable (1984) and many others are in any way applicable to soft tissue injury without specific skin lesions, the surface measurement of skin potentials might reasonably be expected to show different values between injured and non injured subjects.