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Wounds as probes of electrical properties of skin

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Abstract
We have built a model where we use a wound as a probe of the dielectric properties of skin. In this way one is able to infer information about skin dielectric properties in situ. We introduce the notion of a skin electrochemical capacitor. This gives good agreement with recent measurements for the electric potential landscape around a wound. Possible diagnostic consequences are briefly touched upon.

Keywords: Wound, skin, electrochemical capacitor, electric field, electric potential, numerical modeling

Introduction

Our skin is the largest body organ and an important interface between the body and the environment. Understanding its dielectric and electrical properties is of key importance both from a physiological as well as clinical perspective. Skin research spans everything from healing of involuntary breaches of the skin barrier to active management of drug delivery through the skin [1] in conjunction with electric stimuli. This has brought together different disciplines and has lead to both questions of how to measure important properties of the skin in the best possible way as well as to model them in an often approximate but most appropriate way. In this paper we concentrate on constructing a dielectric model of skin for calculating electric field and potential profiles when a wound is present.

In many respects our bodies can be described as "Body Electric" [2] and can be probed by external electrodes [3]. These can pick up relevant signals from different parts of the body, such as the heart, brain, eyes or muscles. However not only functioning of many processes in the body are dependent on and giving rise to electrical characteristics one can also use exogenous electric fields to influence the working of e.g. wound healing. We witness a steady increase in therapeutic devices and wound dressing utilizing the presence of static electric and magnetic fields as well as their dynamic counterparts [4-6]. Fundamental processes such as regeneration and embryo development are also discussed in electrical terms [7]. There is a large body of evidence, as reviewed in [8,9], that electrical fields override any other directional cue. This has important implications for the motion, direction and dividing plane of cells as well as possible ways of influencing this with external probes. It also touches upon the basic question if electric field patterns are emerging from a particular biological structure or if they are the cause of it?

Our aim is to gain a better understanding of the dielectric properties of skin by creating a model of wounded skin based on experimental dielectric permittivities. In particular we strengthen our conclusions by comparing them with recent potential measurements based upon a probe which is not in contact with the tissue examined. Such a probe makes it possible for the skin to be in a regular state with respect to environmental conditions while being monitored. From a physical point of view the skin is an extremely complex material. It is anisotropic, inhomogeneous, layered and it has many different types of structures embedded. Charge carriers of various types and an extensive sensitivity to local factors such as humidity, pH and salinity add to the complexity. Where on the body, the epidermis of the soles are 30-40 times thicker than the eye-lids, as well as more general factors such as health status are also important. A key to this complex situation is to gain a better understanding of the static bioimpedance properties of skin in order to fully be able to extract useful, and hopefully clinically valuable, information when using electrical signals in order to probe or manage healing of skin related phenomena [10-12].

A traditional approach in physics, especially with respect to dielectric and optical properties, is to perturb a system in a systematic way and in that manner gain an understanding of the basic response properties. In this aspect we can consider the presence of a wound as a perturbation and by studying this gain information about the electrical properties of the unwounded skin. Recently Nuccitelli et al. [13,14] measured the potential in the wound area of mice and humans using a non-invasive vibrating probe. These experimental results will be compared with our model of the skin. Main factors which determine the field strength in skin are dielectric permittivities and geometrical factors. With a detailed knowledge of the electrical conductivities of various tissue components [15] one can, from our results, also predict and understand generated current patterns.

On a more general level we hope to gain an increased understanding of the possibility of using the potential variation in and around a wound, as it heals, for information about the status of the wound. Given that the epithelium of the skin represents a structure which is also present around the internal body organs our findings should also be of value here. It should be mentioned in this context that the electrical profiles in the corneal epithelium [16,17] predated the corresponding measurements on skin [18,19] by

decades. However the latter lead to important suggestions as to the basic workings of the epithelium and explained it in terms of a so called "skin battery".

In our electrostatic model of the skin we consider a level of description which incorporates many cells by only differentiating between various strata in the skin. In the other spatial end we stay well below a circuit representation with resistors and alike by doing actual calculations based on Poisson equation to generate electric potential and field patterns. In this respect our work has connections to the one of Karba et al. [20, 21]. However, in contrast to them we focus on a more detailed description of the structure of the epidermis and more importantly; we include the dielectric permittivity of the different layers as a major field determining factor. This has drastic consequences implying the total lack of field penetration into deeper tissue layers.

Our paper is outlined in the following manner. In the next section we discuss an alternative way of viewing the skin battery in terms of a skin electrochemical capacitor. After that, we introduce our model of human skin and define the parameters going into our calculations. Then we present our numerical results for electric potential and field patterns and discuss their implications. We also compare our results with recent experimental measurements and discuss possible wound healing monitoring aspects.

Theory

Skin electrochemical capacitor

Bioelectrical signals have been known since long through the ground-breaking work of Galvani and Volta. In the 19th century DuBois-Reymond conducted a more detailed investigation and noticed that a cut in a finger gave rise to a galvanic signal. Later on this and other observations have lead to the development of the skin battery [19,23-25]; an electrical working model of epithelia going back to the membrane model of Kofoed-Johnson and Ussing [26]. Through continuous transport of ions between the upper (apical) surface of the epithelium and its lower (basolateral) surface, a charge separation is achieved. This charge separation gives rise to the so called trans-epithelial potential with the bottom part of the epidermis being more positive than the part just under the stratum corneum. The trans-epithelial potential varies depending on type of epithelia and is in general measured to be in the range of 10-100 millivolts. Depending on the thickness of the tissue at hand this corresponds to electric field strengths up to the order of 100 V/m. However the dielectric screening in skin is substantial bringing down this field strength considerably in deeper layers of tissue as we will see in what follows.

One of the main features of our calculations in this paper is to include the basic charge separation in the epidermis. However, we somewhat disagree with the notion of this being a (biological) battery from the point of view that the main purpose of a battery is to provide a current. In our view the epithelial construction is more like an electrochemical capacitor, where the purpose is to use stored charge to create a particular potential landscape. In this respect we could talk about *electrostasis*. With this we mean the way the skin maintains a constant internal electrical environment, especially with respect to external perturbations. In this respect the trans-epithelial potential has a purpose both when the skin is intact as well as when a wound is inflicted, while the battery model tends to focus or assign a purpose only when a wound is present. In this context it is appropriate to extend a suggestion made by Levin [25] that there is a correspondence between the individual cell trans-membrane potential, and the skin potential. Both are viewed as nature's way of being able to heal disturbances. For the cell, the membrane potential makes it possible to counteract the flow of ions which would start if the membrane is damaged. The trans-epithelial potential is thought to have the same basic functioning. However, in our capacitor description the trans-epithelial potential serves a purpose at all times; not only when the skin is damaged. Furthermore the capacitor model is more amenable to build a skin model with a reasonable resolved internal structure, than a battery model.

Before building our full wound model based on the concept of an electrochemical skin capacitor we will look at a very simplified picture to identify the main physical factors acting. The basic idea of our model is to represent the potential difference in the epidermis in terms of a capacitor and that a wound corresponds to a hole in that capacitor. The simplest realisation of this is then to take an infinite parallel plate capacitor where we take away half of it to make a semi-infinite one. The cut is then representing the damaged epidermis of a wide wound. In electrostatic terms the cut in the capacitor creates a fringing electric field extending out into the part of space where the hole ("wound") is. This simplified model thus means that we effectively look at a semi-infinite piece of epidermis in air. In *Figure 1* we show the fringe electric field pattern where the "epidermis" meet air. The lower capacitor plate potential V_0 is positive in a skin situation. We notice that whereas the unperturbed capacitor has no electric field outside and a field inside being perpendicular to the plates a hole in the capacitor changes the situation in several ways. There is now an electric field pointing towards the hole (our wound) at the lower part of the capacitor (bottom part of epidermis). Furthermore there is an electric field pointing away from the wound at the upper part (just beneath stratum corneum). This field, which would also be there in a full model of the situation (further down) is fundamental for giving direc-

tional cues for ions restoring the trans-epithelial potential as well as for the cell types involved in the inflammatory, proliferative and remodeling phases of wound healing [4,27,28].

We will later compare with measurements when an external probe is passed across a wound at a certain probing depth. In *Figure 1* (lower) we therefore show how the "wound" potential is expected to vary as one moves away from the wound edge, given a certain probe depth under the skin surface (dashed line in upper part of *Figure 1*). It is seen that the potential decays in an almost exponential manner away from the wound edge, with the only length-scale in the problem being the capacitor plate separation (a), i.e. roughly the thickness of the epidermis. This follows directly from a conformal mapping $z \equiv x + iy = 1 + w + \ln w$ which maps complex position z (in units of a/π) and complex potential w (in units of V_0) of the infinite capacitor to the semi-infinite one.

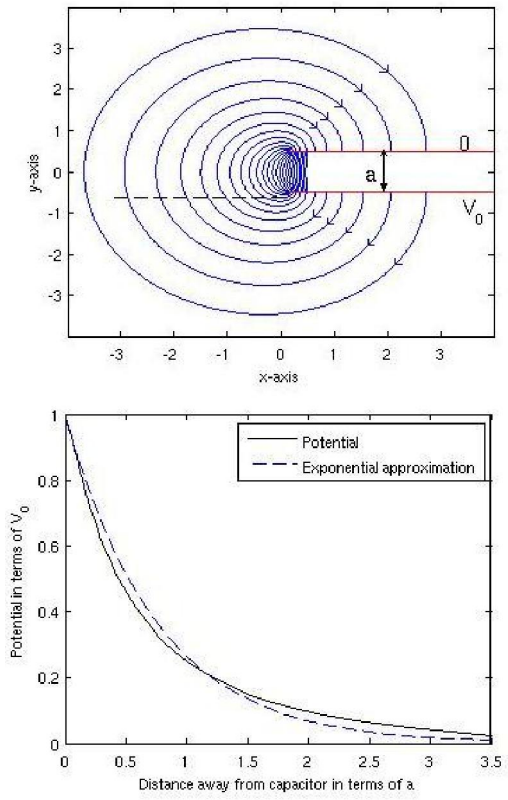

Figure 1: **Electric field pattern at the edge of a semi-infinite capacitor as a very rough model of a "wound" situation.** The "wound" is to the left and the intact skin (the capacitor corresponds to the epidermis) is to the right. Field lines go from the bottom plate of the capacitor (potential V_0) to the upper (at zero potential; just below the stratum corneum). The dashed line (upper) indicates a path along which the potential is studied and is presented in the lower figure as we move into the "wound". Notice how well the potential is approximated by an exponential form with a length-scale being the capacitor plate separation (a).

As we will see in our following calculations, and their comparisons with experimental results, this semi-infinite capacitor captures many of the traits of the field situation in an actual wound.

With a model of the epidermis as a capacitor we can calculate the corresponding time-constant of importance for the replenishing of charge on the capacitor plates, which is a continuously ongoing process in live tissue. From the conductivity σ and permittivity ε of the material between the capacitor plates we find the time-constant $RC = \varepsilon/\sigma$ [20] to be of the order of 0.1 ms using values given in *Table 1* (ε) and [30] (σ). The main reason for the long time-scale is the very large dielectric permittivity of the living epidermis. This has a beneficial effect from the point of view that the energy needed to make the charge separation as well as to uphold it between the capacitor plates is drastically reduced and might be an indication why the epidermis has such a high dielectric permittivity compared to e.g. water. Notice also that this long time-scale and the large charge reservoir at the capacitor plates is our basic motivation for first calculating electro-statically the field distribution which thereafter can be used for calculating what currents are flowing in the system using pertinent conductivities. Naturally an extension and refinement of the present model, which is under way, would need to include the charge redistribution in the epidermis near the wound site and in the wound fluid in a self-consistent manner.

Human skin model

To be able to model a wound and the surrounding skin in a realistic yet calculable manner it is necessary to simplify the physical structure of skin as well as extend the simple semi-infinite capacitor model presented above. We therefore model the wound as rotationally symmetric around an axis perpendicular to the skin. The skin in turn is divided into four layers. In order they describe the stratum corneum (SC), the living epidermis (E), dermis (D) and hypodermis (H). The reason for this separation is that these layers have distinctly different dielectric properties as given in *Table 1* [30]. The interfaces between the skin layers are taken as flat. This is an oversimplification. For example the interface between dermis and epidermis is corrugated as can be seen in a finger-print. However, we find that this simplification does not to any significant degree influence the electric field in and near to the wound. Furthermore, the field penetration in dermis and hypodermis is almost non-existing due to the high dielectric permittivities of these areas. Our model is implemented in the mathematical, finite element-using software *Comsol Multiphysics*

The wound and surrounding tissue can now be defined in terms of a two-dimensional sheet with four layers as shown in *Figure 2*.

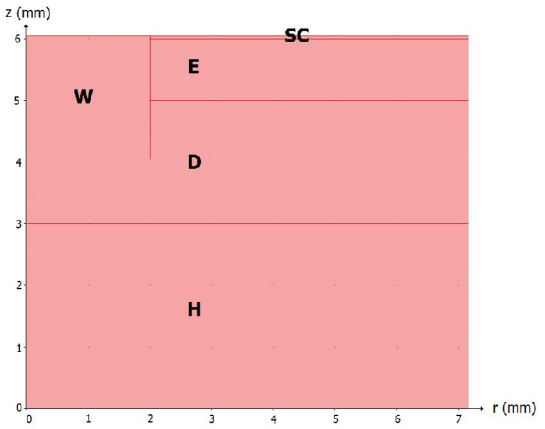

Figure 2: **Model cross section of skin with a wound** (W) as used in our computational scheme. The relevant length-scales and dielectric permittivities are given in *Table 1* for the wound (W), stratum corneum (SC), living epidermis (E), dermis (D), and hypodermis (H). The depth (z) and radius (r) of the wound is set to 2 mm in order to comply with the wound size in the measurements we compare with [14]. The model is rotationally symmetric around the vertical r=0 axis. The actual calculations extend further to the right than shown in the figure (r=50 mm) to assure convergence.

Boundary conditions and parameters

To proceed with the model we need to specify the different areas in terms of their size and dielectric properties and the boundary conditions used. *Table 1* contains values of the relative permittivities ε_r for the different areas as well as their thickness. The relative permittivity of the wound has been set to that of a standard saline solution [31]. Notice that due to a large spread in experimentally established permittivities we use an order of magnitude values relevant to wet skin and we want to stress that our approach is in itself a way of testing the actual dielectric properties at hand providing another way of obtaining these parameters. Furthermore we want to point out that in certain parts of the body the stratum corneum is substantially thicker, especially for soles and palms, while we use a value which is typical for most of the body.

When it comes to boundary conditions we have used:

1. Axial symmetry: The model is rotationally symmetric around an axis that goes through the middle of the wound.

2. Interfaces: In order to make the displacement field continuous over the interfaces we set $\vec{n}\cdot(\vec{D}_1-\vec{D}_2)=0$ where $\vec{n}$ is a normal vector to the interface and $\vec{D}_i$ is the displacement field for neighboring regions *1* and *2*.

3. Outer boundaries: The electric field normal to all the outer boundaries of the model is set to zero; included as $\vec{n}\cdot\vec{D}_i=0$ in an obvious notation.

4. Skin capacitor: The interface between stratum corneum (SC) and living epidermis (E) is assigned a potential V_0 = -20 mV and zero potential is set to the interface between epidermis (E) and dermis (D). Since Poisson equation is linear in the potential the actual value has no significance as to the *form* of our results. When it comes to absolute values one would however have to know the value of tissue under study. We use -20 mV as a typical value for human tissue [4].

Area	Block	Thickness (mm) [1]	ε_r
Wound	W	2.0	80 [31]
Stratum Corneum	SC	0.05	10^4 [32,33]
Epidermis	E	1.0	10^6 [32]
Dermis	D	2.0	10^8 [30]
Hypodermis	H	3.0	10^7 [30]

Table1: **Summary of modeling parameters** used in the different areas. ε_r is the static relative dielectric permittivity for wet tissue.

Model limitations

In our model, the different skin layers are seen as completely homogeneous and isotropic, i.e. the electrical properties are constant in each layer of the skin and do not depend on direction. We have used the values from [30] as applicable for a perturbation applied perpendicular to the interfaces. Needless to say the real anisotropy should be included in a more refined calculation. In this context one should also include a self-consistent description of the charge redistribution at the capacitor plates near the wound.

Furthermore we have used dielectric permittivities for unwounded skin. The slight changes in ε seen experimentally, induced by a wound, are not taken into account [34]. Of far larger importance is the water content of the skin which has enormous influence on the dielectric permittivity [35] and if not stated otherwise we use values for wet skin.

The skin is not homogeneous. It contains hair follicles, nerves, sweat glands/ducts, blood vessels etc. Their electrical properties are very different from those of the surrounding tissue. Hair follicles can be regarded as insulators and sweat ducts as good conductors [36]. It is reasonable to believe that these components of the skin if present at or near a wound site may influence the wound field and should therefore be included in a more extended model than the one presented here.

Electric field and potential around a wound

Electric field pattern

One of the main results from our modeling is the visualization of the electric field around and inside a wound; see *Figure 3*. At the bottom of the wound, field lines point towards the wound but at the top the field lines point in the opposite direction. There is a vanishingly small field penetration beneath the wound due to the high permittivity of dermis (and hypodermis). This leads to, depending on the depth of the wound, that dermis and/or hypodermis could be excluded from the calculations to simplify matters. Notice the close resemblance with the field lines around our simple model system introduced in the previous section; the semi-infinite capacitor (*Figure 1*). Still, an important difference is the fact that the stratum corneum of high dielectric permittivity forces the field to stay away from the capacitor top.

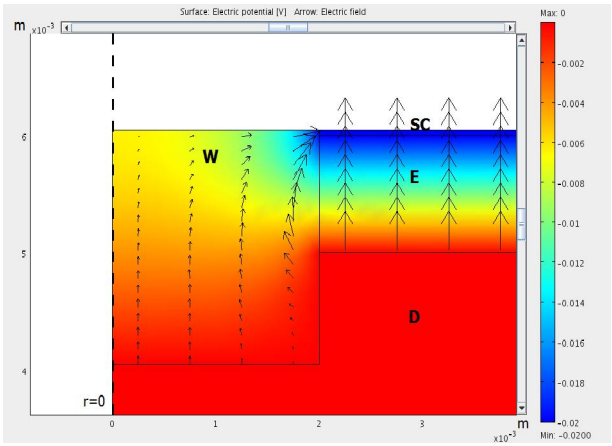

Figure 3: **Calculated electrical field around a wound** (W). The electric field is directed towards the wound in its lower part. At the top of the wound it points in the other direction. The colors represent the electric potential according to the scale to the right (mV). There is a vanishingly small penetration of the field into dermis and hypodermis owing to their large dielectric permittivities.

Potential variation at the wound site

Having established a skin and wound model we now compare it with experimental data from Nuccitelli et al. [14]. They measured the surface potential around and in a wound of mm size following the healing process day by day. [14] contains information about the accuracy of the method with respect to length and voltage scales. We are mainly concerned about the electrical potential map of the wound rather than the wound healing process itself and we therefore compare with the result for the initial wound as reproduced in *Figure 4* below. Experimentally a wound is characterized by drop in the surface potential as compared to surrounding tissue.

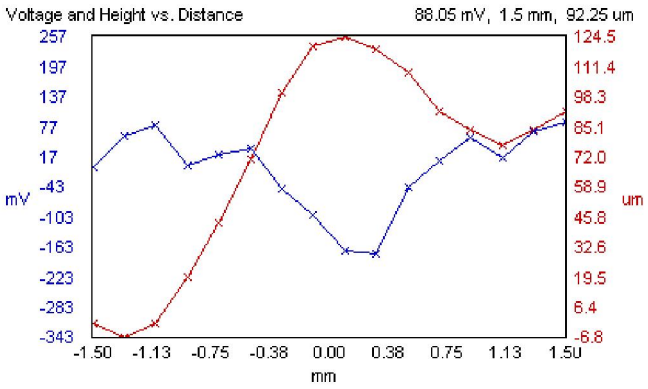

Figure 4: **Experimental surface potential** scanning across a human wound [14]. 0.0 mm corresponds to the middle part of the wound, where the potential has its minimum value. The curve that has a maximum at 0.0 mm (red) is the topographical profile of the wound (swelling makes it peak at wound center). The curve that has a minimum at 0.0 mm (blue) represents the measured potential. Probe size is 0.5 mm.

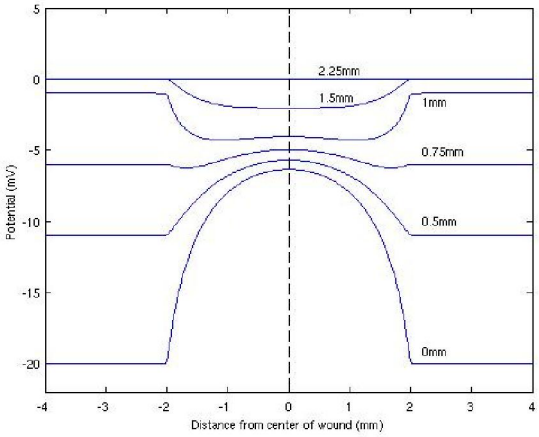

Figure 5: **Calculated wound potential at different probing depths** for a wound 2 mm deep with 2 mm radius. The different curves represent different probing depths (see curve legend), starting from the skin surface (bottom curve) going deeper into the wound. Notice the change in curvature, from convex to concave as we go from a region dominated by the upper epidermis charges to the region dominated by the lower epidermis charges. For an intermediate range of depths we have a more intricate signature related to the high dielectric screening in the dermis.

To see whether our model can account for the measured data we have generated numerical potential data for a wound with a radius and depth of 2 mm, at different probing depths. The size of the wound is chosen to comply with the experimental measurements in [14]. Our results are presented in *Figure 5*. There is clearly a correspondence between our results and the experimental measurements with respect to the signature of the potential provided we are at probing depths of around 1 mm.

Notice that the interplay between the charges of opposite sign, at the two capacitor plates, gives rise to a rich variety of potential curves. These are sensitively depending on the probing depth which determines the final weighting of these charges. The slight maximum appearing at interme-

diate depths is due to the high dielectric permittivity of the dermis as we will see below where we study a wider wound where the measured potential shows a local maximum in the middle of the wound. At present we have no explanation for the large discrepancy in absolute values of measured and calculated potentials. We have used a conservative estimate correponding to -20 mV of the skin electrochemical capacitor. Even using values five times this as reported in the litterature [9], depending of type of tissue and animal, it is not enough to fully bridge the gap. One possible reason for the larger potential measured is that there is a substantial change in the skin capacitor properties next to the wound, which would need a more detailed description since we use unperturbed dielectric values as input. An aspect of this is a possible charge build-up being responsible for a larger potential. A model for this is under development and it would also neccesitate more substantial measurements to corroborate the theoretical modelling as well as trying to understand the large spread in experimental values seen when comparing *Figures 4* and *6*.

Apart from calculating the potential at different probing depths for a given wound important information can be extracted from the calculations for a constant probing depth but varying wound size. In *Figure 6* we therefore show experimental results [14] for the potential corresponding to a wider wound than the one considered above. These results are compared with our prediction in *Figure 7*, where the wound potential has been studied at a constant depth of 1.25 mm in wounds with different radii, going from a very narrow to a much wider wound. They all have the same depth of 2 mm. The potential starts out with a simple minimum for narrow wounds where the upper capacitor plate charges dominate the picture. This is the picture we see in the upper part of *Figure 5*. When widening the wound a cross-over follows when the wound radius is about the same as the wound depth giving a different signature to the potential. The earlier minimum is still present in the outer parts but in the middle a local potential maximum now grows. This maximum is related to the high dielectric permittivity of the dermis making it more favorable for positive charges to stay close to the middle of the wound. Finally it should be mentioned that the variation in *Figure 7* can in a restricted sense be viewed as a wound healing process. In these terms one would have to make a more detailed study to see if the clear signature of the wound potential can be of use in a clinical monitoring of a healing wound without physical contact with the patient.

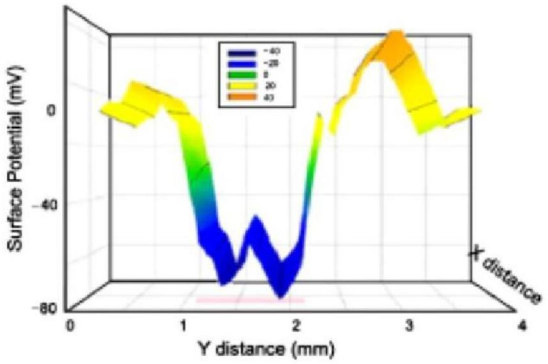

Figure 6: **Experimental potential variation in a wide wound** [14]. (radius much greater than depth). The over-all potential shape resembles that of a narrow wound (Figure 4). However it has in addition a local maximum in the middle of the wound.

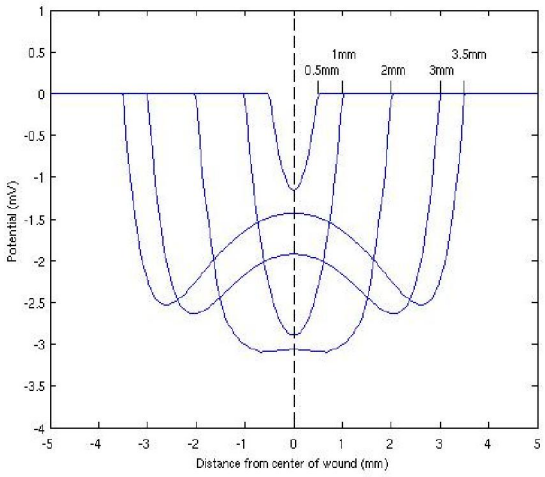

Figure 7: **Calculated potential for wounds of different sizes** at a constant probing depth of 1.25 mm. The wound depth is in all cases 2 mm (*Figure 2*). We go from a 0.5 mm radius (narrow wound) to a 3.5 mm radius (wide) wound. Notice that we can reproduce the experimentally found local potential maximum in the center for wider wounds appearing approximately when the radius exceeds the depth.

Discussion and conclusions

Our model of a skin wound is generated from a very simplified picture of what the skin and wound system looks like in reality. This is a necessary starting point to build upon for further refinements. However, already this simple skin model has good predictive powers when compared to recent experimental results. The model and the consequent interpretation of the experimental findings have led us to introduce the notion of a skin electrochemical capacitor acting in the living epidermis being the prime driving force for the potential patterns set up. We should point out that in a capacitor frame-work description already the simple semi-infinite capacitor captures the main potential patterns. This owes partly to the very high dielectric screening in lower layers. We can therefore conclude that a very simple model,

depending on wound depth, to understand field and potential patterns around wounds would be to include stratum corneum whose interface with the living epidermis is at a certain potential, the wound with pertinent wound fluid and an equipotential surface following wound bottom, interface with dermis and epidermis/dermis boundary.

Knowing potential maps and for that matter the corresponding electric fields we can calculate relevant current patterns given good values for the tissue components contributing are available. It also gives a map of forces acting on relevant cell types involved in both the cleaning up and healing of a wound. There are keratinocytes in the upper area of the epidermis that move in the direction of an electric field [27]. There are also fibroblast cells below the epidermis that move in the opposite direction of the field. Both cell types are present when healing a wound and within our study of a fresh wound they are held back from the wound area. This is important since mechanical cues, like wound edge relaxation, would tend to cover the wound before it has been cleaned out by e.g. lymphocytes, which are found to be attracted by a negative potential [37]. In this context we notice that all our wound potentials are negative sending a clear directional cue. The electric fields (potentials) involved also clearly drive ions participating in setting up the trans-epithelial potential in the right direction; to uphold it. We should also point out that the trans-epithelial potential sets up a preferred direction for the movement of keratinocytes upward in the epidermis already in intact skin. This led us to introduce the notion of *electrostasis*; in other words that the body has a natural built-in system to maintain a potential equilibrium; the skin electrochemical capacitor.

From the model we have also found that there is a transition in an electrical sense from a narrow to a wide wound when the wound radius is about the depth of the wound. The wide wound is characterized by two potential wells close to the wound edges but as these gets closer and start to overlap the whole potential changes into only one potential well. This dependence on wound size can be understood simply in terms of the distribution of dipoles at the wound edge, formed by charges on the upper and lower capacitor plates. It is gratifying to notice that this is a general electromagnetic and solid state phenomena showing up in other fields of physics such as surface trapping of atoms and molecules with dipole rings [38].

The similarities between our theoretical study and the real measurements are promising for both further developments of this first simple model in itself as well as modeling situations where wound dressing with electric properties are present. This is a fast developing area. We are currently undertaking measurements and calculations on the wound dressing Procellera^{TM} to be reported elsewhere with the purpose of understanding if the findings in this paper can have clinical implications beyond that of our basic interest in the dielectric and bioimpedance properties of skin.

Acknowledgments

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