The Use of Local Amplifier and MOSFET Sensor Array in Measuring Bioelectric Signals and Its Clinical Applications

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ABSTRACT

Tissue electrode interface is common to all forms of biopotential recording (e.g., ECG, EMG, EEG) and functional electrical stimulation (e.g., pacemaker, cochlear implant, deep brain stimulation).The proposed new technology of employing local amplification by means of a MOSFET sensor at the bioelectric site is introduced and demonstrates substantial reduction in Signal-to-Noise Ratio (SNR), while improving Spurious-Free Dynamic Range (SFDR).

Methods: A test apparatus capable of simulating a QRS signal, generated and transmitted such through a standard decapolar catheter where one pair of electrodes is configured so as to amplify the native signal with ADC and amplifier in the form of ADS1148EVM. An identical QRS signal is transmitted through a second pair of electrodes where the electrode was modified to incorporate a MOSFET sensor array in a form of amplifier circuit placed on the inner surface of the electrode(s).

Results: The operation of the MOSFET sensor is described. These measurement results of the first electrode pair is compared with the results of a computer simulation, in which the signal of the standard electrode is further compared with the electrode-MOSFET sensor array output. The post-amplified path (using standard electrode technology) is measured to show that the reference signal is nearly imperceptible at this level due to noise degradation. The final result shows a Spurious-Free Dynamic Range (SFDR) of 9.3dB with a Signal-to-Noise Ratio (SNR) of -50dB. In contrast, when the same signal is run through the pre-amplified MOSFET path, it is shown to be well-formed and the cardiac properties are clear, and the final result shows a vastly improved SFDR of 24.9dB and SNR of only -13dB.

Conclusions: The increase in signal quality of the MOSFET sensor array as a local amplifier serves as a new standard in measuring bioelectric signals and outweighs the performance of the current electrode technology.

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Some Observations on the Art of Electrophysiology Measurement

During the Warsaw Conference of 1962, Richard Feynman wrote a letter to his wife, Gweneth, commenting on the status of the theory of gravitational waves: *"I was surprised to find a whole day at the conference devoted to this question, and that 'experts' were confused. That is what comes from looking for conserved energy tensors, etc., instead of asking* ***'Can the waves do work?'"*** [1].

Feynman felt an undisguised contempt for much of the relativity community in the late 1950's and early 1960's. Our sentiments towards the current methods by which "*Bioelectric potential*" is captured and analyzed echo those of Feynman's notes. *Electrograms* are a manifestation of the underlying electrochemical activity of a biological substrate, and the attempt to functionalize and fashion a diagnostic value upon such graphical representation must first assume that the fidelity of the measured native signal is a true representation of an "energetic event," as energy with its vectorial direction and magnitude is the appropriate setting for a diagnostic measure. Paraphrasing Feynman's sentiment, we ask, "***Can the electrogram path represent the underlying substrate composition?"***

Shortcomings of Electrode Technology and Post-Processing of the Native Signal

What we demonstrate in the following patent and applications is centered on the ability of a measuring apparatus employing a catheter fitted with ***electrode technology*** (i.e. at the site of biopotential activity) to capture the signal in its native form. We contend that the current technology with its post-processing algorithms distorts and masks the true nature of the complex wavefronts and "washes out" substantial clinical details, resulting in a non-unique diagnosis as to the underlying nature of the disease mechanism.

Our approach to the existing measuring apparatus (employing electrode(s) with amplifier at the distal end of the catheter shaft), is compared with use of the novel

technology we term in general as **local amplifier-MOSFET sensor array**, with capabilities enabling an accurate "one-to-one" correlation while forming an electrophysiological map. The biopotential measurement using such technology substantially improve the representation of the energy contents on the spatial and time domains of the complex waveform, leading to a recursive relationship between the graphical representation and the underlying biopotential **substrate** which causes such electrical activity.

Electrode technology utilizing post-processing algorithms has tried with limited success to resolve the diagnostic discrepancy between the bottom-up causal representation (i.e., substrate mapping) and the top-down causal description of the underlying mechanism generating the pathology observed. This limitation is cited in many clinical publications and is most clearly evident in the diagnosis and treatment of complex arrhythmias.

As indicated by the current status of clinical results, there are presently at least two (2) approaches to determining the underlying mechanism for modeling the disease: the reductionist approach, which advocates for "substrate mapping" [27] correlations with ECG, and the anatomical approach, which supports "anatomical mapping." [28] However, in contrast, we argue that the true discussion should be centered on the nature of the ***measuring apparatus's fidelity*** and the establishment of a "standard model" in electrophysiology (EP) while employing an apparatus which will enable both methodologies to form a uniform mapping manifold. A standard model would provide for a common method of assessing the data and its "elementary building blocks," which will improve not only the diagnostic and mapping procedures but also the therapeutic outcome.

One of the foremost goals of the EP community is to develop a comprehensive mapping technique so as to characterize the global dynamics of wavefront activation. This must, first, be anchored in a bottom-up consensus where the elementary building blocks are accepted and agreed upon metrically, and whereby the cellular etiology and its electrical

counterparts – e.g., ***dielectric (κ)*** and ***conductivity (σ)*** – are defined. The complexity and inter-relationships of the "avalanche" dynamics which are translated through the myocardial space, due to ionic potential on the spatial as well as time domains, can be resolved by the use of heuristic top-down causal theory, when employing the local amplifier-MOSFET sensor array.

Clearly, there is a relationship between the quality of the measuring apparatus and its ability to resolve the signal accuracy and its signal-to-noise ratio (SNR), as well as the fidelity and repeatability of the data generated. The monograph and its accompanying citations will address the shortcoming of the current electrode technology and the improvement provided by the use of local amplifier with its embodiments, as a solution to the limitations noted by the existing art.

Current attempts to resolve the myriad of abovementioned issues utilize the method of post-production processing which employs, subsequent to the native measurement, algorithmic tools such as the Fast Fourier Transform (FFT) technique or recursive methods. As a result, the EP community is currently faced with a state of affairs as described and exemplified in the sample of published clinical journals cited herein.

The Proposed Solution: MOSFET Sensor Technology

The MOSFET technology that we advocate herein utilizes ***impedance spectroscopy*** at the event site of the biopotential signal. Just as microscopy provided for magnification which produced a novel view of matter at orders of magnitude which were then imperceptible, impedance spectroscopy provides an additional tool in the armamentum of the electrophysiologist that can resolve the distortions caused by the noise of the current art and further in order to study the inherent relationship between the substrate and its electrical activity counterpart.

We advocate employing a local amplifier in the form of a MOSFET sensor array as a solution to such shortcomings. Furthermore, as indicated by the patents and the

exemplary apparatus presented in this monograph, we aim to achieve the following outcomes using such technology:

- That the native bioelectrical signal in the form of ionic electrochemical avalanche dynamics can be addressed by locating the preamplifier (MOSFET) element adjacent to the measurement site; and

- That measurement using such technology is capable of "mining" the "energetic event" by relating its inherent characteristics of *time*, *magnitude* and *direction*, without post-processing of the native signal, as is customary in the current art.

These aims are best achieved by employing a local pre-amplification with the characteristic signal fidelity as it is demonstrated below.

The shortcoming of the current electrode technology is emphasized by compression with the substantial improvements provided by the novel technology presented herein, which we title in a generic form as "MOSFET." Simply stated, a local amplifier which acts as variable resistor, and its on-site electrical ground (i.e., a ground not subject to the 5-ft. antenna/conductor, formed out of the catheter shaft, acting as a receiver/ carrier for equipment located at the operating room with frequencies ranging from 50-60 Hz to 5-10 kHz, and where such an antenna is the origin for some of these noise-generating sources). The novel approach employs pre-amplification technology which substantially improves Signal-to-Noise Ratio (SNR), Spurious-Free Dynamic Range (SFDR), signal fidelity, sampling rate, bandwidth, differentiation of far-field from near-field components, further outlined in this introduction and the accompanying patents provided.

Those familiar with the art of measuring small bioelectrical signals understand that this MOSFET technology provides for new grounds in a wide variety of medical applications. For example, electrophysiological maps can be formed to establish accurate diagnostic maps which improve the subsequent therapeutic outcome. New platforms can open up for the detection of axonal nerve endings for applications such as **renal denervation**

and the measurement of **ganglionic plexus activities** and **neuronal cellular matrices**. The electrical characteristics of MOSFET can resolve many of the existing problems emanating from the electrode technology interface, where the ratio of signal magnitude compared to the noise impairs the ability of the clinician to form an adequate and reliable diagnosis. The MOSFET sensor array can supplement existing technologies used in Implantable Cardioverter Defibrillator (**ICD**) and other implantable devices, **neuromodulation**, and **pacemaker leads**, where the fidelity of the signal is essential for its optimal performance.

Electrode technology is limited in providing uniform diagnostic metrics, and thus the clinical observations provided are oftentimes merely anecdotal indications due to the current state of the technology. The MOSFET sensor array, as a model for local pre-amplification in supplement to the current electrode technology, provides benefits by *complementing* the existing technology when incorporated therein. The current architecture of leading mapping apparatuses such as CARTO™ or EnSite®, as well as their tool sets (e.g., catheters), need not be modified as to their generic metrics (e.g., bipolar, quadripolar, decapolar, balloon, basket), and are not altered as the MOSFET amplifier and its associated circuitry is adopted within the existing catheter shaft, rather, this novel MOSFET technology can be seamlessly incorporated into the existing hardware – and, to the operator, the change would be essentially invisible.

Signal Fidelity of Pre-Amplified (MOSFET) vs. Post-Amplification (Electrode)

Experimental application of the technology is shown in order to demonstrate the proof of concept and the superior performance of a MOSFET sensor array in detecting bioelectric potential. A comparison of the local amplifier employing MOSFET versus the remote amplifier was conducted.

Figure 1

Simulated cardiac (QRS) signals are generated by a programmable generator (Agilent Trueform Wave Generator, 33500B Series) and measured along two (2) different signal paths, one employing a post-amplified (using current electrode technology) and the second channel containing a locally amplified MOSFET sensor array. In the *unamplified* pathway, a standard decapolar geometry catheter is post-amplified using ADCPro computer software, simulating the current method of electrode technology. In the *amplified* pathway, the identical geometry and metric layout is employed using a common, single catheter shaft for both configurations, with the only difference being that the amplification now occurred at the site of the electrodes using the MOSFET sensor array. Thus, the only variable measured was the fidelity of the simulated QRS, enabling a comparative evaluation of the resultant signals from each amplification method.

The signal is first attenuated to under 50μVpp by adding series attenuators to the input signal of the current electrode technology with a total signal gain of 128. The post-amplified path is measured to show that the reference signal is ***nearly imperceptible*** at this level due to noise degradation. The final result

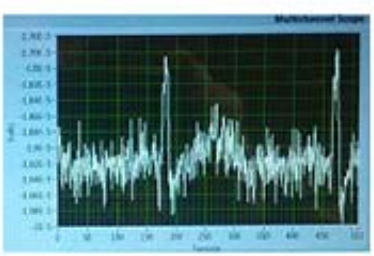

Figure 2

shows a ***Spurious-Free Dynamic Range (SFDR) of 9.3dB with a Signal-to-Noise Ratio (SNR) of -50dB***.

In contrast, when the same signal is run through the pre-amplified MOSFET path, it is shown to be well-formed and the cardiac properties are clear. Here, the total signal gain is only 100, with the location of the gain block having been moved from one end of the catheter to another – and the final result shows a ***vastly improved SFDR of 24.9dB and SNR of only -13dB***.

Figure 3

	Original Catheter	Prototype Catheter
Total Signal Gain	128	100
SFDR	9.3dB	24.9dB
SNR	-50dB	-13dB

When the QRS-simulated signal is captured by the locally amplifier at the site of the electrodes, linked to a local MOSFET sensor, the result is substantially identical to the "pure" standard. The cardiac signal, replicated using True*form* waveform generator technology, is then repeated while the amplifier is located at the distal end of the catheter connector with post-amplification. The signal quality is due to the ***pre-amplified*** embodiment of locating the measurement at the site of the signal source. These and other features relating to the use of MOSFET inherent ***local ground*** with its ***variable resistor*** matching characteristics of the biopotential at the measurement site is the mainstay of the novel technological circuitry.

Application of MOSFET sensor array, Clinical Observations

The application of local pre-amplification to measure bioelectrical potential, with sufficient SNR reduction as well as bandwidth, will transform the art of measurement in electrophysiological studies from its current state of *phenomenological correlations* to a bottom-up discipline, where observations are anchored in a common mode application

of the biological substrate and the measuring apparatus, and where matrices of such measurements are defined by what we term as a "standard model" employing addressable and measurable "elementary building blocks."

Many studies have demonstrated that fibrillatory rhythms are not random phenomena, but rather have definable patterns. [16] However, standard mapping techniques may have limitations in their ability to identify the *organization of fibrillation*. The purpose of this collection of patents, applications, and technical observations is to develop and apply a method for detecting the energetic event by the ability of local amplifier with its inherent variable resistor (MOSFET sensor module) to generate, for example, an "ensemble vector mapping" to characterize the spatiotemporal organization of fibrillation.

Nademanee summarizes in an editorial paper a promising advancement in current trials of electrogram-guided ablation of chronic atrial fibrillation stating that:

> *"Catheter-based ablation has revolutionized arrhythmia management by offering the most definitive treatment for virtually all types of tachyarrhythmias. The reasons behind the success of ablation are many, but chief among them is the ability of the electrophysiologists to identify underlying mechanisms and to precisely localize and eliminate the tachycardia foci or circuits... Unfortunately, mapping of high-dominant-frequency areas has been shown not to be effective in chronic AF patients. On the other hand, mapping of CFAE as target sites for AF ablation has shown great promise. During sustained AF, CFAEs often are recorded in specific areas of the atria and exhibit surprisingly remarkable temporal and spatial stability. CFAEs usually are low-voltage electrogram (0.05 to 0.25 mV) with highly fractionated potential or with a very short cycle length (≤120 ms)."* [17]

This is an important observation that a complex arrhythmia cannot be assumed to be defined as well as treated unless the underlying mechanism and precise identification of the vectorial direction as well as its magnitude can be established.

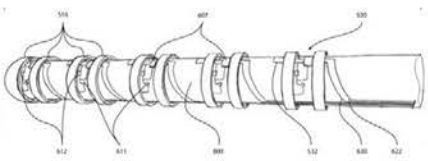

Figure 4

The notion that the native signal-measurement can somehow be improved through a smart algorithm or a sophisticated mathematical filtering, manipulated by recursive methods, and/or wavelet analysis, is a misleading one. The native signal cannot be improved beyond its energy domain on its time scale or its geometric spacing. The signal noise components (SNR) and their representations cannot be altered by a post-processing approach. We advocate a radical departure from the current approach to the art of EP and bioelectrical potential measurement technique. We teach a technological departure from the electrode technology with its post-processing approach, which is the mainstay of the current art of biopotential data acquisition.

The operative departure of the novel technology is the incorporation of ***local amplification*** at the source using, for example, a MOSFET sensor module in an array form with geometry configurations such as bipolar, quadripolar, decapolar, or any array with 64 or more electrodes, to enable a multitude of electrodes/pads to simultaneously capture the complex electropotential energetic event, with the improved SNR and sampling rate commensurable with the bandwidth and accuracy on the spatio-temporal domain. One of our heuristic arguments is the ability of a mature scientific theory is its predictable *power*, and to uniquely project an outcome based on boundary conditions that can be reproduced, where specificity of the well-formed question results in a well-defined answer. As we are to demonstrate in this monograph, the art of EP is in need of radical review of its methodologies with regard to the relationship between its diagnostic findings and its loosely correlated clinical observations.

As an example of the current clinical literature describing the underlying mechanism of patients with supraventricular tachycardia and proxysmal atrial fibrillation:

> *"Each patient underwent a baseline electrophysiologic study closely spaced electrode catheters... Paroxysmal atrial fibrillation (PAF) frequently occurred in patients with paroxysmal supraventricular Tachycardia (PSVT). However, the mechanisms responsible for the occurrence of PAF were not fully understood. Although previous studies have suggested that atrioventricular (AV) accessory pathway or slow AV node pathway itself may play an important role in the genesis of PAF, disturbed atrial electrophysiology during PSVT may be the other mechanism of initiation of PAF. Klein et al. have shown increased atrial refractoriness during PSVT and considered mechano-electrical feedback a cause of PAF during."* [15]

It is clear from the article and other publications that while the underlying cause is nested within multiple potential explanations relating to the mechanism that might lead to such conditions, *no unique* underlying mechanism was cited. The literature is typically repeating such assessment, simply stated, the explanations in many of the clinical studies are fashioned along the general outline shown in the paper above.

Our approach for clarifying the complexity of why such conditions manifest themselves in the specific class of PAF is as follows: a ***standard model*** for any assessment of the boundary conditions must be first subject to the ability of the measurement and its methodology including its measuring apparatus to yield a consistent and repeatable data under similar conditions. The ambiguity and non-unique distinction of the mechanism generating the condition is a typical narrative in many clinical discussions and intellectual chatter of the various conferences on the topic of the underlying mechanisms of arrhythmogenic causes. In order to improve the art of measuring apparatus, we propose a novel platform comprising of *local amplifier* using MOSFET sensor array located at the target site so as to enable the mining of bioelectrical

potential with fidelity and repeatability not currently available in the discipline of EP studies.

The aim to form a standard model for EP is centered on the fact that the etiological as well as morphological elements forming the substrate of a biostructure must obey unique boundary conditions and where their specificity can be studied and reconstructed as well as predicted. The fact that most of the EP studies are a collection of phenomenological observations supports the contention that EP as a scientific discipline must undergo a change which must first be organized under the tool set and the ability of the physician community to recognize a generally accepted standard of data capture as well as a data format. The fact that many researchers and their publication tend to exhibit a colorful plates with interesting isochrones does not constitute a "standard model," as the collection methods vary and its solution has a low predictability and reproducibility value.

MOSFET technology will improve the art of EP by creating such a *standard model,* unifying the diagnostic observations under a measurement technique able to define the EGM as energetic events, distinguishing such applications from the massive digital signal processing (DSP) manipulation customary in the current art.

Feynman's sentiments at the Warsaw Conference of 1962 was a reaction to the fact that most activities in the published as well as the practitioner of general relativity were intellectual deliberations on the mathematical complexity of tensor analysis without the underlying facts that energetic event defining the gravitational waves must account for the ability of the wave to do "work."

As we survey the field of EP, we see a landscape of phenomenological collections of data with little to no specificity associated with the fact that the cellular excitable matrix is the result of specific etiological characteristics of the underlying substrate. If these data points were anchored by a robust physical and biological model, such as that

which is presented here, it will enable a simple translation between the electrical map and its substrate. Hence, the substrate will be directly correlated to the pathophysiology.

This state of affairs is centrally dependent on the ability of the roaming catheter to collect the electrical potential and place such data on its anatomical target synchronously. Additionally, the signal must be distinguished from its noise components so as to separate the native signal effect of the far-field component and its near-field contributing element.

The fundamental technique of local amplification provides the user with native local signal where the near-field as well as its far-field component can be distinguished without post-processing employing algorithmic "gimmicks" and other sophisticated DSP manipulations.

This patent collection is devoted to a novel technology for capturing bioelectric potential data, which is anchored in measurement techniques that reveal the physical nature of a biological substrate's electrical properties. This technology allows for the interpretation of the phenomenological expression of the electrogram (EGM) and its graphical representation in the context of an energetic event, based on the dielectric (κ) and conductivity (σ) measurements of underlying tissues.

Figure 5

Electrophysiology studies employ a variety of devices, specifically catheters with different electrical configurations of electrodes using magnetic as well as electrical impedance techniques to form an electroanatomical map. The fact that electroanatomical mapping fails to connect the inherent physical relationship between an energy transfer function and its causal dependency on the substrate, as represented by the electrogram, is the foundation for the utility of the *local amplifier* invention, exhibited herein via the use of a MOSFET sensor array for conducting electrophysiological studies.

The method and exemplary apparatus which is presented enables the creation of an electroanatomical map with high fidelity and accuracy while depicting a *local* electrogram with its native dynamics, its geometrical as well as its time domain specificity, and further providing for reconstruction of the anatomical and the extrapolated etiological characteristics of the cellular matrix by employing the MOSFET sensor array apparatus.

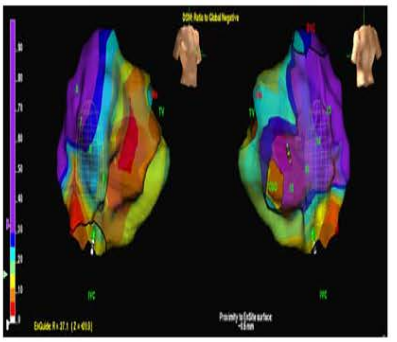

Figure 6

The aim and utility of this *local amplifier* technology is to connect the phenomenological data with clinical observations.

The electrical properties of the conduction path within the substrate and its etiological constituents (e.g., cellular matrix composition and its electrical counterparts) are **correlated without the need to create a causal dependency after the fact**. This allows for the formation of a robust and coherent *standard model* in forming the diagnostic basis for defining a disease model, as noted by Tusscher et al.'s study presented at Europace. The study notes, "*During ageing, after infarction, in cardiomyopathies and other cardiac diseases, the percentage of fibrotic (connective) tissue may increase from 6% up to 10–35%. The presence of increased amounts of connective tissue is strongly correlated with the occurrence of arrhythmias and sudden cardiac death.*" [2]

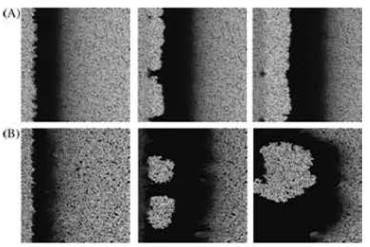

Figure 7

Vulnerability to wave break and spiral wave formation due to diffuse fibrosis.

(A) Snapshots of progression of two wavefronts initiated in a medium with 10% fibrosis and with a coupling interval of 321 ms between them.

(B) Snapshots of progression of two wavefronts initiated in a medium with 30% fibrosis and with a coupling interval of 320 ms between them.

Because of its high success and low morbidity rates, radiofrequency (RF) catheter ablation has become first line of treatment for many arrhythmias. In this procedure, one or more electrode catheters are advanced percutaneously through the vasculature to

contact cardiac tissues. A diagnostic study is performed to define the arrhythmia mechanism, and subsequently an ablation catheter is positioned adjacent to the arrhythmogenic substrate. Radiofrequency energy of up to 50W is delivered in the form of a continuous unmodulated sinusoidal waveform, typically for 60 seconds. The arrhythmia is eliminated via the destruction of arrhythmogenic tissues (e.g., accessory pathways) and its subsequent replacement with scars.

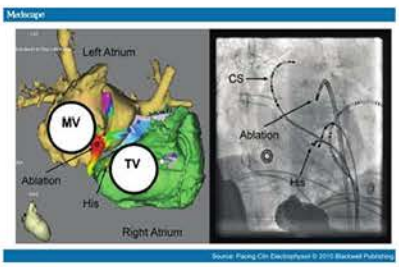

Figure 8

In the electrogram approach, because precise lesion placement is required, arrhythmias for which ablation are most effective (e.g., accessory pathways, atrioventricular nodal re-entry tachycardia [AVNRT]) have *largely anatomically based or directed substrates*. An electrode catheter in the coronary sinus outlines the mitral annulus fluoroscopically, and is used to guide ablation catheter position. The relative amplitude of the atrial and ventricular components of the bipolar electrogram recorded by the ablation catheter further defines the tip position relative to the annulus. The earliest atrial or ventricular activation during pathway conduction identifies pathway location along the annulus. The target for catheter ablation of AVNRT occurs even more predictably in the posteroseptum. Ablation may be guided entirely by anatomic location relative to the His bundle and coronary sinus catheter positions, which serve as fluoroscopic landmarks, or by a combined anatomical and electrophysiological mapping, such as those generated by CARTO™ or EnSite®.

Complex Arrhythmias, Limitations of the current art of Electrophysiology

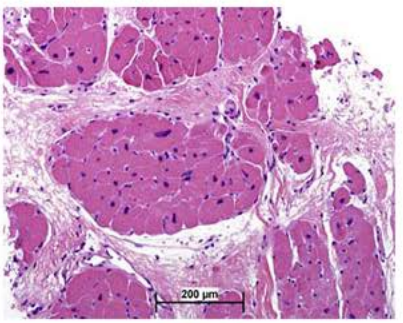

Figure 9

However, ablation of more ***complex arrhythmias*** – including some atrial tachycardia, many forms of intra-atrial re-entry, most ventricular tachycardia, and atrial fibrillation – continue to pose a major challenge. [3] This challenge stems, in part, from the limitations of fluoroscopy as well as in the construction of current mapping catheter and sensory apparatuses, which cannot accurately locate both the geometry and time domain of the wavefronts activity generated by the "avalanche" of the cellular excitable matrix. Thus, the primary disadvantage of the existing and prior art of electrode technology is in its inability to account for the cellular biopotential transfer with the resolution necessary to capture the energetic event, and the insufficiency of the current electrode technology to account for ionic transfer time depicting the actual energetic event, measuring and representing the "avalanche" dynamics of this bioenergetic event.

The aim of the novel technology using transistorized electrodes (i.e., the MOSFET local amplifier circuit) is to accurately identify the conduction path. An ideal conductor might, in general, satisfy the accuracy representation employed by the current art, but in a disease modeling, most of our assumptions relating to linear behavior of the conduction path (the cable theory) cannot be reproduced by such modeling, due to the impact of secondary and significant noise generating phenomena such as *vectorial multiplicity* of sources generating the EGM, *magneto-electric anisotropy*, *conduction* in cardiac strand where gap-junction-mediated mechanisms alternate, and where the standard 'cable theory' does not satisfy the ionic conservation law, and where Navier-Stokes equations with its Diffusion modeling, might be a better approximation of the ionic conduction – its energetic vector with its magnitude and direction then the description provided by the cable theory.

An obvious problem in separating the noise component from the native signal is the inability of the system to identify which is which. If we know that a signal is smooth – changing slowly – and that the noise is fluctuating rapidly, we can filter out noise by averaging adjacent data to eliminate fluctuations while preserving the trend. Noise can also be reduced by filtering out high frequencies.

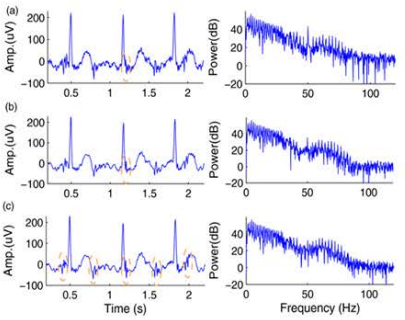

Figure 10

For smooth signals, which change relatively slowly and therefore are mostly lower frequency, this will not blur the signal too much. Many interesting signals are not smooth; they contain high-frequency peaks. Eliminating all high frequencies mutilates the message – "cutting the daisies along with the weeds," in the words of Victor Wickerhauser of Washington University in St. Louis, adequately expresses the main drawback of post-processing such signal wavefronts. [20]

Signal to Noise Ratio

High signal-to-noise ratios (SNR) thus requires the use of a very low-noise amplifier with a limited bandwidth. The current technologies provide a differential amplifier with voltage noise of less than 10nV $\sqrt{1}$Hz and current noise less than 1pA. However, both parameters are frequency-dependent and decrease approximately with the square root of frequency; the exact relationship depends on the technology of the amplifier input stage. Field-Effect Transistor (FET) preamplifiers exhibit about 5 times the voltage noise density compared to bipolar transistors and a current noise density that is about 100 times smaller.

In summary, the problem of reconstruction of the electrophysiological activity in the current art is two-fold: first, in the architectural design of the use of electrodes and their associated electrical circuit design, and secondly, in the further handicap caused by modeling the biopotential activity as a physical phenomenon, whereby excitable cells are modeled by employing the cable theory with isotropic behavior. The use of

electrodes and cable theory is a good approximation of idealized conditions of such energetic events, but suffers from the inability to associate accurately the intracardiac electrogram with a specific endocardial site which also limits the reliability with which the roving catheter tip can be placed at a site that was previously mapped. This results in limitations when the creation of long linear lesions is required to modify the substrate, and when multiple isthmuses or "channels" are present. Additionally, since in conventional endocardial mapping a single localization is made over several cardiac cycles, the influence of beat-to-beat variability on overall cardiac activation cannot be known. The novel sensory apparatus and methods we teach in this collection of patents captures the complexity, as well the time domain, of such energetic events synchronously. The MOSFET sensor array and its fidelity further mimics the underlying dynamics, and will improve conventional catheter-based mapping techniques by localizing and identifying precisely the arrhythmogenic substrates that are removed from fluoroscopic landmarks and lack characteristic electrogram patterns.

Modeling of Bioelectrical Activity and Diffusion, Ricci Flow Modeling

The need to improve modeling of cellular electrical activity is central to physiology and electrophysiological studies. Biopotential recording and mapping of such electrical activity enables the physician or researcher to form and fashion his or her understanding of the fundamental data gathering and analysis of such diverse biological activities as sensory perception, communication between neurons, initiation and coordination of skeletal-muscle contraction, synchronization of the heartbeat, and the secretion of hormones. Most mathematical models of cellular electrical activity are based on the cable model, which can be derived from a current continuity relation on a one-dimensional ohmic cable. As such, its derivation rests on several assumptions: ionic concentrations are assumed not to change appreciably over the time of interest, and a one-dimensional picture of cell geometry is assumed to be adequate for purposes of describing cellular electrical activity. These assumptions, however, may not hold in many systems of biological significance, especially in the central nervous system and

within cardiac tissue, where micro-histological features may play an essential role in shaping physiological responses.

The first and far most assumption of electrophysiological mapping is the notion of linearity as well as homogeneous conduction path, both are refuted in light of the clinical observations associated with Ephaptic coupling effect on the conduction path well as Magnetic Heart vector anisotropy, both affect the ECG representation and its informative content. The corruptive measure of the electrogram fidelity and its true nature as to the native signal is highlighted herein.

Signal Anisotropy, Modeling Biopotential Activity – Ephaptic Coupling

There are many contributions to the resultant signal shown by the electrogram, in this monograph we will mention two of the organizing principles which if accounted for under the current method of capturing the electrogram, it will clearly demonstrate the shortcomings of the existing art. The first principle of organizing the electrogram set is the 'cable theory' and the second principle of organizing the biopotential activity is the ability of the representation system to account for the complementary 'magnetic vector' impact on the ionic cellular matrix. In both of these principles and their accompanying observations, we can see that no filtering methods of any sort would improve the native fidelity of the signal. It is further shown by observations and analytical methods that any attempts to reconstruct such activity artificially by post-programming activity are doomed to fail, as these inherent bioelectrical activities (ephaptic, electromagnetic) are fundamental elements of the native signal. Simply stated the cable theory representation is an ideal depiction of the conditions generating the biopotential cellular avalanche, and it properly accounts for and describes the isotropic influences, but lacks the ability to discern influences such as magnetic heart vector and ephaptic coupling.

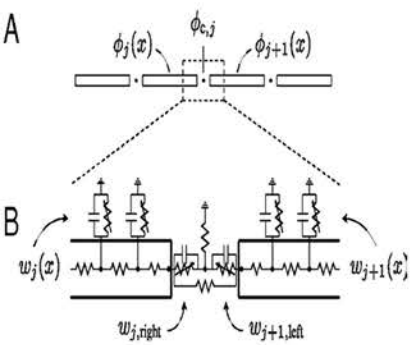

Figure 11

Ephaptic coupling can't be 'washed' by some filter; its effects must be accounted for by measuring its influence on the conduction path. This major drawback of the existing art, whereby the dynamics of the ionic potential with the necessary fidelity mimicking the actual energetic event are not accounted for, example of such influence is the contribution of the gap junctions which play a pivotal role for the velocity of impulse propagation in cardiac tissue. Under physiologic conditions, the specific sub-cellular distribution of gap junctions together with the tight packaging of the rod-shaped cardiomyocytes underlies *anisotropic conduction*, which is continuous at the macroscopic scale. However, when breaking down the three-dimensional network of cells into linear single cell chains, gap junctions can be shown to limit axial current flow and to induce saltatory conduction at unchanged overall conduction velocities. In two- and three-dimensional tissue, these discontinuities disappear due to lateral averaging of depolarizing current flow at the activation wavefront. [18] In this theory, the cellular path is represented as a cable, and hence it is referred to as "cable theory" [4], or the mathematical modeling of bioelectrical current along passive neuronal fibers. Existing hardware employing electrode technology, coupled with the general algorithmic representation of the biopotential dynamics under such theory (both hardware and cable theory) suffer from the abovementioned limitations, which are eliminated by the use of a local amplifier, such as a MOSFET sensor array, and its method of map reconstruction.

As outlined above the effect of ephaptic coupling as an inherent source of anisotropic behavior, impacting the conduction path of the bioelectric signal and its influence, is well expressed in cases such as described by Mori Y. et al. [21] This and other examples in vitro, as well as in vivo animal studies, demonstrate that conduction velocity and gap junction parametrics as expressed play a significant role in the formation of the conduction path and its origin, and can be shown as the result of the etiology of the cellular matrix change due to fibrotic formation. The ephaptic coupling is only one

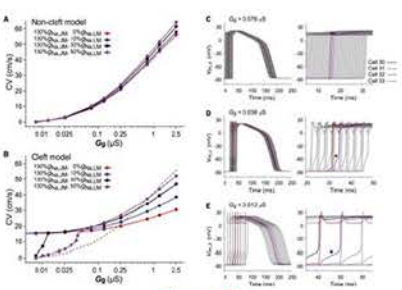

Figure 12

argument out of many cited above in support of our advocacy of using the MOSFET sensor array in acquiring the biopotential signal. The use of Impedance spectroscopy in the form of a MOSFET sensor array provides for accurate representation of the bioelectric signal, due to its inherent electrical characteristics such as shall be described in the accompanying patents.

Signal Anisotropy, Modeling Biopotential Activity – Poynting Energy Vector (PEV)

A second argument cited directly by analytical and clinical observations is a study by Shachar and Farkas [23], demonstrating analytically the relationship between conduction path and the vectorial representation of anisotropic influence of the magnetic dipole vector on the conduction path. The preceding argument will clarify the behavior of the ***Poynting energy vector (PEV)*** further indicating the fact that representation of the ECG signal with its post-processing modality is a very crude approximation of the native bioelectric signal.

The argument outlined in this manuscript as to the ephaptic coupling influence on the conduction velocity is supplemented by the argument of the magnetic heart vector's (MHV) contribution to the conduction path geometry and its timing, including synchronicity.

Analytical evidence for anisotropy is noted when we employ Maxwell's equation. The data analysis and extraction of additional diagnostic (and as a corollary, the pathological diagnostic) information of the substrate is revealed when we create a map where we superimpose the electric and energy wave as shown in the SPICE simulation converging the electric with the magnetic heart vector influence by computing the impedance (**Z**) value generated from the substrate.

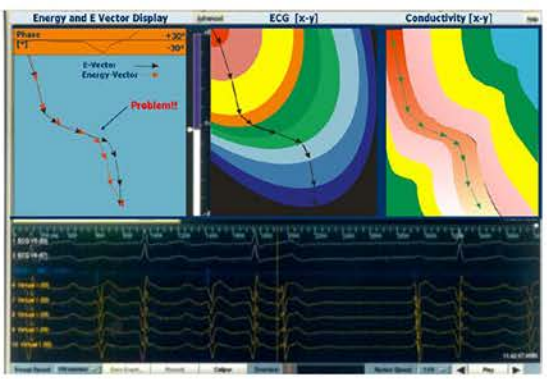

Figure 13

To overcome the measurement limitations and supplement the clear clinical findings of myocardial anisotropy, we observed that production of slam magnetic fields during the cellular activation sequence uncovers the magnetic dipole (MHV) by computing a vector derived from Maxwell's equations, a process of data collection available only if we derive the PEV from the impedance vector (**Z**) using the MOSFET sensor array supplemented with a computational algorithm. Clinical observations reported [22] that measuring the angle between vectors of an equivalent electric dipole (electric heart vector, EHV) and magnetic dipole (MHV) provides significant corollary information about the myocardium conductivity. The overall anisotropic case of the myocardium conductivity is represented by a tensor. [23] The degree of anisotropic conductivity manifestation is characterized by the angle along the transversal and axial conductivity paths, as shown in the figure above of such a simulation.

The solution for measuring and deriving the relationship between the EHV and its respective MHV (supplementing the analytical mapping with additional information about the myocardium conductivity and anisotropy) is derived from Maxwell's equation as the PEV. The PEV is constructed from the multiple potential and impedance vectors of the measurements. In one application of the MOSFET sensor array, a mapping catheter is used for biopotential sensing. A matrix arrangement for phase rotation of the angle β is measured and derived between the PEV and EHV and is used to infer the features of anisotropy in the myocardium. The anisotropy of the conductivity is uniform; that is to say, the activation energy change generated and consumed by the ionic diffusion process is within the activation region of the measurement. Thus, the volume integrations are accurate, with a margin of error reduction based on independent statistical methods by sampling the measured site over multiple heartbeats.

The PEV derivation is based on the law of energy conservation when used for the time period between 2 QRS cycles to acquire the initial baseline data foundation to form the map. The validity of the PEV derivation is corroborated by the fact that the activation spread obeys the mathematical identity, that the PEV is directly exhibiting the **E** and **B** fields' *phase angle* relationship. The integral form of Maxwell's equations leads to the

PEV, and to the substitution of **E** and **Z** derivations of this vector. The following set of derivations of Maxwell's second set of time varying equations provides a formal extraction of additional clinical observations by the application of a MOSFET sensor array to derive **Z** impedance vector, hence demonstrating that the *conduction path* influenced is measurable. The inverse method further supports the argument that the nature of the resultant electrogram supplemented by the use of the proposed novel apparatus (MOSFET sensor array) enables a clinical derivation of PEV from Maxwell's second set of time-varying equations. The availability of **Z** impedance vector by the proposed apparatus is further evidence that ***the complex fractionated wavefront cannot be resolved by post-processing methodology*** as currently practiced by the use of electrode technology.

The argument is shown below using Maxwell's second set of time-varying equations:

1 $$\nabla \times E = -\frac{dB}{dt}$$

2 $$\nabla \times \mathrm{B} = \varsigma\mu\frac{dE}{dt} + \mu J$$

3 $$B \bullet (\nabla \times E) = -B \bullet \frac{dB}{dt}$$

4 $$E \bullet (\nabla \times B) = \varsigma\mu(E \bullet \frac{dE}{dt}) + \mu(E \bullet J)$$

5 $$\nabla \bullet (E \times B) = B \bullet (\nabla \times E) - E \bullet (\nabla \times B)$$

6 $$\nabla \bullet (E \times B) = -\frac{d}{dx}(\frac{1}{2}B \bullet B) - \frac{d}{dx}(\varsigma\mu E \bullet E) - \mu JE$$

7 $$\nabla \bullet \left[\left(\frac{1}{\mu}E \times B\right)\right] + \frac{d}{dx}\left[\frac{\varsigma}{2}E^2 + \frac{1}{2\mu}B^2\right] + J \bullet E = 0$$

8 $$\int_\gamma \frac{1}{\mu}(E \times B) \cdot dS + \frac{d}{dx}\int_v \left(\frac{\varsigma}{2}E^2 + \frac{1}{2\mu}B^2\right)d\tau + \int_v (J \bullet E)d\tau = 0$$

9 $$\mathbf{E} = \frac{1}{\mu}(E \times B) + s \quad \text{where } \nabla \bullet \mathrm{s}=0$$

10 $$(\nabla \bullet \sigma)\nabla V_m = 0 \text{ and } B = -\nabla \bullet V_m$$ **Poisson Equation**

11 $$\mathbf{E} = \frac{1}{\mu}((E \bullet E)\frac{1}{Z}) + c$$ **Poynting Energy Vector**

12 $90° - \alpha = \beta$ **Measure of Anisotropy**

13 $$\nabla \times E = -\frac{dB}{dt}$$

14 $$\nabla \times \nabla \times E = -\frac{d}{dx}(\nabla \times B)$$

15 $$\nabla(\nabla \bullet E) - \nabla^2 E = -\frac{d}{dx}\left(\varsigma\mu\frac{dE}{dt}\right)$$

16 $$\nabla^2 E - \varsigma\mu\frac{\partial^2 E}{\partial t^2} = 0$$ **Wave Function**

By multiplying **B** and **E** respectively and subtracting Equation (2) from (1) and using vector identities yields (3) and (4). Subtracting, rearranging and using vector identities yields Eq. (5) which simplifies as (6). Integrating both sides of Eq. (7) over the volume V and within the boundary Y gives (8), which is a representation of the energy equation in which the first term is the energy flux out of Y boundary of V. The second term in Eq. (8) is the rate of change of the sum of the electric and magnetic fields; the third term is the rate of work within V done by the fields on the ionic charges. This third term in Eq. (8) assumes the inclusion of the energy of the multiple sources of cellular ionic charge exchanges, thus (9) leads to the PEV, as shown in (11). The parameter of interest is the angle β between the electric field and energy field; Eq. (12). The vector **E** is obtained from energy vector field measurements by calculating the **Z** impedance vector; Eq. (11). By using the measured potentials V_m and by employing Poisson equation, the **E** electric field is obtained, Eq. (10). Then, the PEV can be written as Eq. (11). The **E** vector and impedance **Z** can be calculated from the

measured data points. This is where the novel application of the MOSFET sensor array is playing its role of uncovering the substrate using the calculated impedance value **Z** that plots the *conduction path* generated due to the secondary effects associated with ephaptic coupling as well as the Magnetic Heart Vector (MHV), both are inherent characteristics of the underlying substrate and cannot be manipulated by employment of post–processing filtering techniques. One can further calculate the angle ß between the E field and **E** energy vector, where the difference is such that a display of the **E** energy vector is useful for cardiac disorder identification. In one aspect of the proposed use of the MOSFET sensor array the measurements of **E** energy data and **Z** conductivity data are collected from the electrocardiographic mapping and ablation catheter further processing and displaying the resultant anisotropic data, enhancing the current method. The PEV indicates that there is a flux of energy where **E** and **B** are simultaneously present. The spread of the energy flux in the case of Maxwell's derivation is further defined by the wave equation (13). Taking the curl of each side, Eq. (14), yields Eq. (15), which is the wave equation (16).

Utilizing the above-described technique, the electrophysiological map can be accurately tailored using post-processing methodologies, such as diffusion tensor and geometric representation (e.g., Ricci flow geometry). [25, 26] The data generated by the MOSFET sensory array, in contrast, can serve to enhance the existing formation of electrophysiological maps and provide substantial improvement in the art of biopotential measurement and analysis.

Why do we need to capture, amplify and model the signal at the bioelectric site?

The improvement proposed by the novel MOSFET sensor array for mapping of electrophysiological attributes is centered on the formation of a junction by bipolar electrodes/pads between the cellular matrix and the contact surface of the bioelectrical signals generated by nerves and muscles, recorded as potentials, voltages, and electrical field strengths. The measurements involve voltages at very low levels,

typically in the vast range from 1μV–100mV, with high source impedances and superimposed high level interference signals and noise. Furthermore, the signals are amplified for compatibility with devices such as displays, recorders, or A/D converters for computerized equipment. To adequately measure these signals, an amplifier must satisfy very specific requirements: (1) to provide selective amplification to the physiological signal, and (2) to reject superimposed noise and interference signals.

Biopotential, Local Amplifier-MOSFET Technology

The basic requirements that a biopotential amplifier such as the MOSFET sensor array must satisfy are:

- The physiological process to be monitored should not be influenced in any way by the amplifier: no galvanic contact exists between the cellular surface and the conducting part of the sensor, thus preventing the occurrence of any faradic current.

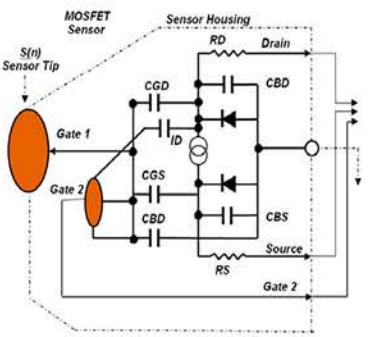

Figure 14

- The measured signal should not be distorted; ephaptic coupling as well as PEV must be accounted for by synchronously measuring such effects with suitable quality as noted by the MOSFET sensor array.
- The amplifier should provide the best possible separation of signal and interferences; near-field versus far-field phenomenon must be separated by mining the inherent differentiating elements without averaging such contributions.
- The amplifier must offer protection to the patient from any hazard of electrical shock: isolated FET and circuit architecture.

MOSFET Sensor Module dimensions: 1x1.2x0.3mm

Figure 15

- The amplifier itself has to be protected against damages that might result from high input voltages as they occur during the application of defibrillators or electrosurgical instrumentation and application of RF energy during ablation.

Renal Denervation and the Use of a MOSFET Sensor Array

The inventions and applications collected in this volume relate generally to an electroanatomical mapping method and an apparatus using a catheter, and more particularly a mapping catheter, having an embedded MOSFET sensor array for detecting local electrophysiological parameters such as biopotential signals within an excitable cellular matrix geometry, for determining the physiological as well as electrical characteristics of the conduction path and its underlying substrate within the endocardial and epicardial spaces, the arterial structure, and in the ganglionic plexus.

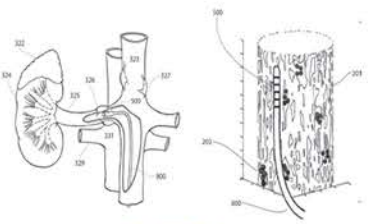

Figure 16

Another major application of this technology is in the field of ***renal denervation***. The renal sympathetic nervous system has been identified as a major contributor to the complex pathophysiology of hypertension, heart failure, and progressive renal disease[5,6]. It is now widely accepted that essential hypertension is commonly neurogenic, both initiated and sustained by sympathetic nervous system overactivity[7,8,9].

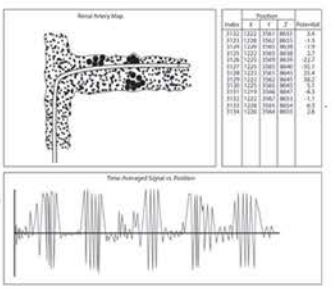

Figure 17

Surgical renal denervation has been shown to be an effective means of reducing sympathetic outflow to the kidneys[10] without adversely affecting other bodily functions[11]. On the basis of these findings and in view of the demand for alternative treatment options, targeting the renal sympathetic nerves as a major player in the pathophysiology of hypertension, kidney disease, and heart failure is a very attractive therapeutic approach.

The current treatment method involves the application of RF energy within the lumen of both renal arteries, which has been shown to reduce blood pressure in selected patients. In essence, the RF catheter is advanced into the renal arteries and discrete low-power RF energy applications are applied along the length of both arteries.

The disadvantage of this method is that it is done on a *purely anatomical basis*, without acute physiologic or electric endpoints for energy application. For example, it is currently unknown whether the ablative energy destroys the afferent or efferent nerve endings, neither, or both. Long-term complications from random application of RF energy into the renal arteries, such as late renal artery stenosis, are an obvious concern. [12]

Therapeutic renal denervation, furthermore, does not currently permit the physician to perform the procedure in an optimal and safe mode, with consistent and repeatable outcomes. The irregular success of the procedure, notably in the reduction of blood pressure, might appropriately be attributed to the occasional renal denervation that was affected by the surgical procedure. The occasional dramatic success of the unproven surgical strategy fuels enthusiasm for the development of a safe, effective, and targeted procedure to functionally denervate the human kidneys. To that extent we project that the use of MOSFET sensor array as the initial formation of an electroanatomical map shall be conducted by identifying the axonal nerve ending potential by detecting and locating such foci and thereafter performing the renal denervation procedure.

Additionally, the current method of renal denervation is limited by the anatomy of the ganglionic plexuses themselves. Renal sympathetic nerves are derived from numerous spinal ganglia, and paraspinal ganglionectomy has been associated with severe and systemic adverse effects. The sympathetic renal nerves arborize throughout the adventitia of the renal artery, eliminating convenient anatomic access.

Thus, a compelling need for additional or alternative therapies exists. Renal denervation potentially offers a more direct, organ-specific strategy by targeting a mechanism crucially involved in initiating the vicious cycle whereby the overactivity of the sympathetic nerves in the renal plexus leads to hypertension.

In spite of these many obstacles, recent developments appear to have the potential to overcome these anatomic and technical difficulties and to provide new hope for the treatment of resistant hypertension.

In summary, catheter-based therapeutic renal denervation appears to be a quick and safe procedure which results in a large and persistent decrease in blood pressure in patients resistant to multiple existing antihypertensive drug classes. Taken together, the safety and efficacy findings of these initial studies confirm the importance of renal sympathetic nerves in resistant hypertension and suggest that renal sympathetic denervation has the potential of therapeutic benefit in this patient population. The procedure of identifying the specific location(s) of renal nerves arborized throughout the adventitia of the renal artery is the mainstay of the MOSFET sensor array, and the advantage of such measuring technology relative to the clinical outcome is clear.

Pacemaker Leads and the Use of a MOSFET Sensor Array

The use of local amplifier employing MOSFET sensor can be seen as an important augmentation to the arsenal of EP, as such sensory apparatus will enable the differentiation of far-field from near-field signal sources. Such ability will enable the current bipolar electrode technology to effectively prevent false positive events as described by a case study, Dirk Vollmann et al.[13]:

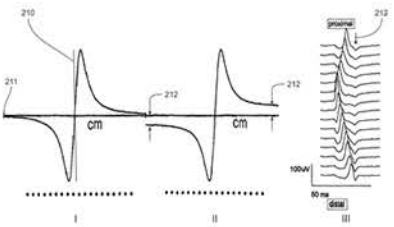

Figure 18

"Implantable cardioverter defibrillator lead failure is a significant problem that may result in potentially fatal inappropriate device therapy. If the structural lead defect is incomplete at first, the electrical integrity of the system may be lost only for brief moments. If this is the case, lead failure will not necessarily manifest with inappropriate ICD therapy because of over sensing of electrical noise and is unlikely to be detected by single measurements of lead impedance and pace-sense performance. The SIC enhances the early detection of ICD lead failure in this situation because it also detects very brief, sporadic episodes of noise over sensing. The algorithm continuously counts the number of short V–V intervals (120 and 130ms) that are typically seen during over sensing of electrical noise. An increment in the total SIC to more than 300 events since last follow-up is considered as a specific indicator of system dysfunction. We previously reported that ICD leads with integrated bipolar sensing appear to be more susceptible for false positive increases of the SIC (in the absence of lead failure). Recently, we also found that in a normally functioning true bipolar ICD lead, an increase of the SIC may occur if intermittent T-wave over sensing and premature ventricular complexes co-exist. The present case illustrates another so far unidentified cause for an increase of the SIC in a true bipolar ICD lead, namely far-field over sensing of atrial signals during sinus tachycardia. In general, over sensing of atrial signals in the ventricular channel is a rare event that has been linked to integrated bipolar sensing and to the automatic adjusting."

A fundamental aspect of clinical EP, the discipline of diagnosing and treating cardiac arrhythmias, is the interpretation of intracardiac electrical signal electrograms. All EGMs represent a voltage difference between two electrodes, whether the electrodes are in close proximity (e.g., bipolar EGMs) or at a relatively great or theoretically infinite distance (e.g., unipolar EGMs). A major disadvantage of unipolar recordings is that they contain a significant amount of **"far-field"** signal, i.e.: signals generated by depolarization of tissue remote from the recording electrode. As shown in Figure 17 above, the near-field signal exhibits a decay to zero potential along the X-axis, while the far-field indicates that the signal does not decay to zero potential, and is asymptotically parallel to the X-axis, hence the use of the MOSFET local amplifier with its variable resistor and ground at the site of measurement will enable a clean separation between the far-field and near-field contribution so as to prevent the averaging of the resultant signal from the native measured potential. This advantage has an enormous contribution to the diagnostic value of the electrogram and can clearly improve the behavior of the ICD leads' optimal performance when detecting such a composite signal.

For example, EGMs from pulmonary vein ostia frequently manifest large far-field atrial signals recorded from regions that are at the border between the atrium and the pulmonary vein. Separating the signal of interest, in this case the pulmonary vein fiber potential (high-frequency signal) from the far-field atrial signal (lower-frequency, usually much larger signal) can sometimes be difficult, and requires pacing maneuvers and empiric RF energy application. In addition, differences in electrode sizes, for example a large ablation distal electrode compared to a smaller proximal electrode, might exaggerate the potential differences between the two electrodes and distort the resultant EGM signal amplitude, which is important for recording scar voltage. In addition, the direction of wavefront propagation influences the amplitude of the bipolar EGM (but not that of the unipolar EGM). Theoretically, a wavefront that propagates in a direction that is exactly perpendicular to the axis of the recording dipole would produce no potential difference, hence no EGM signal. The clinical significance of this scenario

in mapping scarred tissue is unknown, as these maps are dependent on displaying areas of low voltage as areas of scarred myocardium.

Existing intracardiac recording techniques, while they have served the clinician and basic scientists reasonably well over the past three to four decades, suffer from several inherent limitations, which this patent collection seeks to address, such as:

- By the very nature of utilizing electrodes connected by long cables to a distant differential amplifier, these systems are subject to line "noise," ambient EMI, cable motion artifacts, and faulty connections.
- Local signals are subject to recording of far-field signals, which at times render the interpretation of complex, rapid arrhythmias very difficult, if not impossible.
- The conflation of far-field and signals of real interest, such as pulmonary vein fiber potentials, accessory pathway signals, and slow pathway potentials, can sometimes be the cause of failed ablations. The ability to record local electric activity with great precision and to the exclusion of far-field signals would be of paramount importance.
- Current recording systems frequently cannot differentiate low-amplitude, high-frequency signals from background noise. Extremely low-amplitude signals, such as those generated during slow conduction within a myocardial scar, are frequently missed or lost in the background noise when amplifier gain is made sufficiently high to attempt to record such signals.
- Continuous, low amplitude, fractionated high-frequency signals such as those frequently seen in the atria of patients with chronic atrial fibrillation, cannot be further characterized using existing recording technologies. These signals may contain important biologic and electrophysiologic information. For example, these signals may represent important areas of scarring that are responsible for formation of rotors. Alternatively, they may be manifesting discharges from contiguous epicardial parasympathetic ganglionated plexi.

In this illustration, graph I represents a *near-field waveform* characteristic, where the horizontal axis denotes distance; the vertical axis, voltage. It is clear that the potential decreases monotonously with distance along the horizontal axis, therefore the profile shown in graph II indicates the presence of additional *far field source* components for the potential, as it is constant and non-vanishing, representing the difference in potential between far-field and near-field.[14] This difference between the waveform relative to the horizontal axis does not decrease over time, and can be subtracted by using the fast-acting local bipolar measurement available through the use of the novel MOSFET sensor array.

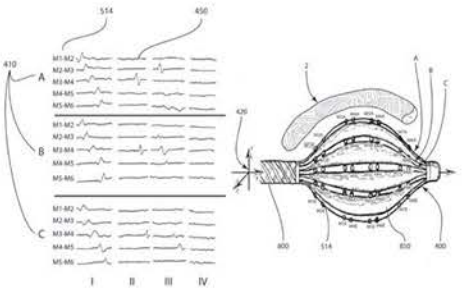

Figure 19

In conclusion, the limitations in the current art of electrode technology, as cited above and detailed in this patent collection, indicate the need to supplement the existing technology with local amplifier technology, such as exhibited in the use of our MOSFET sensor array. This apparatus may be geometrically configured as unipolar, bipolar, quadripolar, decapolar, and other linear arrays, and optionally as, for example, an 8x8 sensor matrix placed on a basket- or balloon-like structure, as well as incorporated into other related devices in various arrayed and matricular configurations.

These applications of the Magnetecs novel MOSFET sensor technology offer great potential in the furthering of electrophysiological studies, including the understanding of the mechanisms of complex arrhythmias.

Citations

1 Feynman, Richard P., as told to Leighton, Ralph (1988). "What Do You Care What Other People Think?" W. W. Norton, New York.
2 Tusscher, Panfilov. "Influence of diffuse fibrosis on wave propagation in human ventricular tissue." Europace (2007) 9(suppl 6): vi38-vi45 doi:10.1093/europace/eum206.
3 Paul A Friedman Heart. 2002 June; 87(6): 575–582.
4 PNAS. December 7, 2010; 107(49): 20935-20940.
5 DiBona GF, "The sympathetic nervous system and hypertension: recent developments," Hypertension, 2004; 43:147–150
6 Zanchetti AS. "Neural regulation of renin release: experimental evidence and clinical implications in arterial hypertension." Circulation, 1977; 56:691–698.
7 DiBona GF. "Sympathetic nervous system and the kidney in hypertension," Curr Opin Nephrol Hypertens. 2002; 11:197–200.
8 Esler M, et al. "Norepinephrine, Release and the pathophysiology of primary human hypertension." Am J Hypertens. 1989; 2:140S–146S.
9 Schlaich MP, et al. "Sympathetic augmentation in hypertension: role of nerve firing, norepinephrine reuptake, and angiotensin neuromodulation." Hypertension, 2004; 43:169–175.
10 Markus P. Schlaich, et al. "Renal Denervation as a Therapeutic Approach for Hypertension: Novel Implications for an Old Concept." Hypertension 2009, 54:1195-1201.
11 Krum H, et al. "Catheter-based renal sympathetic denervation for resistant hypertension: a multicentre safety and proof-of-principle cohort study." Lancet. 2009; 373: 1275–1281.
12 Smithwick RH, Thompson JE, "Splanchnicectomy for essential hypertension; results in 1,266 cases," JAMA. 1953; 152:1501–1504
13 Dirk Vollmann, et al. "Far-field over sensing of atrial signals: an unusual cause for very short V–V intervals and inappropriate implantable cardioverter defibrillator therapy." doi:10.1093/europace/eun103.
14 Cracco RQ, et al. "Somatosensory Evoked in Man: Far-field Potentials." Electroenceph Clin Neurophysiol 1976; 41:460-46.
15 Chen Y, et al. "Role of atrial electrophysiology and autonomic nervous system in patients with supraventricular tachycardia and paroxysmal atrial fibrillation." J Am Coll Cardiol. 1998;32(3):732-738.
16 Kadish A, et al. Characterization of fibrillatory rhythms by ensemble vector directional analysis. Am J Physiol Heart Circ Physiol. 2003 Oct; 285(4):H1705-19. Epub 2003 Jun 5.
17 Koonlawee Nademanee, Trials and Travails of Electrogram-Guided Ablation of Chronic Atrial Fibrillation, Circulation.2007; 115: 2592-2594 doi: 10.1161/Circulation AHA.107.700187
18 Stephan Rohr Cardiovasc Res (2004) 62 (2): 309-322. doi: 10.1016. j.cardiores.2003.11.035
19 Nademanee K, MD Mapping of Complex Fractionated Atrial Electrograms (CFAE) as Target Sites for AF Ablation, The Bangkok Medical Journal Vol. 2 : September 2011
20 Hubbard, Barbara B.. The World According to Wavelets: The Story of a Mathematical Technique in the Making (2nded), Natick, MA: A K Peters, 1998
21 Mori Y, et al. Proc Natl Acad Sci U S A. 2008 Apr 29;105(17):6463-8. Epub 2008 Apr 23. Ephaptic conduction in a cardiac strand model with 3D electrodiffusion.
22 J. Malmivuo, et al. Bioelectromagnetism, Oxford University Press 1995
23 Gerardo I et al. Knowledge-based tensor anisotropic diffusion of cardiac magnetic resonance images, Medical Image Analysis (1999) volume 3, number 2, pp 1–25 :Oxford University Press.
24 Korn, Henri, et al. (Neurobiology, Vol. 77 No. 10: 6244–6247.). *"Electrical inhibition of Purkinje cells in the cerebellum of the rat"*
25 Bakas, I. (2005). The algebraic structure of geometric flows in two dimensions. arXiv:hep-th/0507284

26 Vladimir G. Ivancevic, Ricci Flow and Nonlinear Reaction–Diffusion Systems in Biology, Chemistry, and Physics. arXiv:0806.2194v6 [nlin.PS] 19 May 2011.
27 Marius Volkmer et al. Substrate mapping vs. tachycardia mapping using CARTO in patients with coronary artery disease and ventricular tachycardia: impact on outcome of catheter ablation. Oxford Journals Medicine EP Europace Volume 8, Issue 11Pp. 968-976
27 Deepak Bhakta et al. Principles of Electroanatomic Mapping, Indian Pacing Electrophysiol J. 2008 Jan-Mar; 8(1): 32–50.Published online 2008 February 1.

Figures used by the author for illustration

Figure 1	Magnetecs Corp. Test set- up for comparison study of Electrode technology and MOSFET sensor array.
Figure 2	Image of attenuated QRS signal through catheter electrodes.
Figure 3	Image of attenuated QRS signal through catheter with MOSFET sensor Module.
Figure 4	Schematic representation of a decapolar catherer with embedded MOSFET sensor array.
Figure 5	http://www.theeplab.com/A-Open-EP-Lab-Areas/B000-The-EP-Lab/B-Tools-of-the-Trade/G-Mapping-Systems/BBG0-Mapping-Systems.php
Figure 6	Tools of the Trade - Cardiac Mapping Systems - The EP Lab www.theeplab.com › The EP Lab ›
Figure 7	Oxford Journals Medicine EP Europace Volume 9, Issue suppl 6Pp. vi38-vi45
Figure 8	Pacing Clin Electrophysiol. 2010;33(11):E106-E109.
Figure 9	Cardiovascular Pathology, Volume 18, Issue 1, January–February 2009, Pages 44–48
Figure 10	Physiological Measurement Volume 33 Number 7 Guojun Li et al 2012 Physiol. Meas. 33 1151 doi:10.1088/0967-3334/33/7/1151
Figure 11	PNAS August 17, 2010 vol. 107 no. 33 14603-14608
Figure 12	Biophysical Journal Volume 100, Issue 3, 2 February 2011, Pages 554–563
Figure 13	Shachar Y. Farkas L., Gang E. US Patent No. 7,869,854
Figure 14	Shachar Y. Farkas L., Gang E. US Patent No. 7,869,854
Figure 15	MOSFET Sensor Bi-polar array module (Magnetecs Corp.)
Figure 16	Shachar Y. Gang E. US Patent Application No. 13/549,341
Figure 17	Shachar Y. Gang E. US Patent Application No. 13/549,341
Figure 18	Shachar Y. Gang E. US Patent Application No. 13/621,727
Figure 19	Shachar Y. Gang E. US Patent Application No. 13/621,727