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Bayesian Quantitative Electrophysiology and Its Multiple Applications in Bioengineering

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Abstract

Bayesian interpretation of observations began in the early 1700s, and scientific electrophysiology began in the late 1700s. For two centuries these two fields developed mostly separately. In part that was because quantitative Bayesian interpretation, in principle a powerful method of relating measurements to their underlying sources, often required too many steps to be feasible with hand calculation in real applications. As computer power became widespread in the later 1900s, Bayesian models and interpretation moved rapidly but unevenly from the domain of mathematical statistics into applications. Use of Bayesian models now is growing rapidly in electrophysiology. Bayesian models are well suited to the electrophysiological environment, allowing a direct and natural way to express what is known (and unknown) and to evaluate which one of many alternatives is most likely the source of the observations, and the closely related receiver operating characteristic (ROC) curve is a powerful tool in making decisions. Yet, in general, many people would ask what such models are for, in electrophysiology, and what particular advantages such models provide. So to examine this question in particular, this review identifies a number of electrophysiological papers in bio-engineering arising from questions in several organ systems to see where Bayesian electrophysiological models or ROC curves were important to the results that were achieved.

Index Terms

Bayes procedures; bioelectricity; electrophysiology; modeling

I. Introduction

Bayesian interpretation of observations is a powerful method of relating measurements to their underlying sources and of great potential use in electrophysiology. This review gives a brief historical context, a few examples, identifies publications across a range of electrophysiological situations arising from different organ systems where Bayesian interpretation or analysis is used, and presents some comments about the advantages and disadvantages of a Bayesian framework for bioengineering models. As most readers of this review are likely to have considerable expertise in biomedical engineering and electrophysiology, the challenge addressed in this review is to show where and how

Bayesian analysis, and more broadly a Bayesian outlook, has come to be significant within this field. A primary aim of this review is to motivate readers with an electrophysiology background with little exposure to Bayesian methods to try it. More experienced readers may enjoy some of the historical flavor as well as be informed about the range of electrophysiological topics where Bayesian analysis now is used, whether in a simple or complex way. Conversely, it is beyond the scope of this review to examine Bayesian methodology itself across the range of fields in which it now is used or to give examples of the use of Bayesian strategies, except where that use is described in an electrophysiology-related publication.

In electrophysiology the use of Bayesian analysis is growing rapidly, as is seen in Table I.

The table shows the number of citations returned by Google advanced scholar when the index terms are “Bayesian Models Electrophysiology.” This measure is imperfect, returning some unintended citations (e.g., other scholars named Bayes) and omitting others, e.g., if the topic is discussed as “electrogram” but not using the word “electrophysiology.” Nonetheless, using Google scholar consistently across papers for several decades shows unequivocally that use of Bayesian models in electrophysiology has increased rapidly over the last four decades. The question of how it happened that Bayesian models had two centuries of gestation that suddenly was followed by the recent period of rapidly growing requires a brief historical discussion, as presented in Section II.

II. Brief History

In the late 1700s, Galvani’s seminal observations on frogs [1] and the mechanism of action of frog nerves [2] formed the beginning of scientific electrophysiology. (Electrophysiology was originally called *Galvanism*.) Galvani was an important member of the scientific establishment of his day and had many famous arguments with Alessandro Volta, for whom the electric unit Volt is named. In the earlier years of the 1700s, Bayes Theorem [3], [4] was published posthumously, and soon after Laplace [5] published similar ideas in a different mathematical form. For two centuries electrophysiology and Bayesian analysis developed separately, with electrical science and electrophysiology being much more visible, with rapid progress.

In the two centuries following its origin, the theory of Bayesian models and its usefulness for interpretation seems to have been preserved quietly by a relatively few scholars in mathematical statistics, working largely outside the realm of medical or other application issues. In the introduction (and Appendix 6) of his textbook on Bayesian statistics, S. James Press [6] gives results from a poll, apparently taken around the turn of the millennium, of 24 senior researchers in statistics. The poll identified six people as members of the *Bayesian Hall of Fame*, that is, as the principal founders of modern Bayesian statistical science. These six identified were (listed alphabetically) Thomas Bayes [3], Bruno de Finetti [7], Morris DeGroot [8], Harold Jeffreys [9], Dennis Lindley [10], and Leonard Savage [11]. It is notable that five were active in the mid to late 1900s. E. T. Jaynes, well known for infusing statistical mechanics with information theory [12], made clear some of the ways that de Finetti’s work contributed to the technical solutions of real problem [13] and was an early promoter of Bayesian thinking.

Concurrent with computer systems becoming widespread in the latter 1900s, Bayesian understanding and operational use began to move from the province of mathematical statisticians into applications in science, engineering and medicine, and into electrophysiological modeling in particular. Computer power was needed in part because the expressions for Bayesian evaluation, as given by mathematical statisticians, often involved

integrals of joint probability density functions, which could be evaluated for realistic situations using numerical methods.

Remarkably, the flow of ideas since the mid 1900s from abstract concept to specific application, even up to the present day, has often passed through a relatively small number of people (that is, there have been only “a few degrees of separation” [14]). As an example, consider one of the threads that began with Leonard Savage, one of the members of the Bayesian Hall of Fame. Savage was professor of mathematical statistics at the University of Michigan, an advocate of Bayesian thinking (and later founder of the Statistics Department at the University of Chicago). Savage’s textbook, *The Foundations of Statistics* [11], incorporated the viewpoint that Bayesian models were that foundation. While auditing one of Savage’s courses, Ted Birdsall (later professor of electrical engineering at the University of Michigan) recognized the potential importance and relationship of Bayesian theory to a paper he and Wes Peterson (later known for coding theory) had published on the theory of signal detectability [15]. Birdsall, along with some of his graduate students, discovered that when signal detection theory was viewed from a Bayesian perspective, it could be extended to include adaptivity and learning in a natural and meaningful way. In addition, estimation and detection could now be viewed as simultaneous operations, i.e., one did not have to estimate first and then detect [16]–[19]. John Swets, David Green, and Wilson (“Spike”) P. Tanner, who were psychologists at the University of Michigan, recognized the applicability of the just-developed signal detection theory of Peterson, Birdsall and Fox to psychology, involving hearing and vision initially [20], [21]. Out of that work grew a strong theoretical foundation for experiments involving human decision making in the face of uncertainties [22].

One of Birdsall’s students was Loren Nolte, who became well known for contributions to detailed Bayesian physical models that included uncertainty [23], to tracking sound sources underwater [24]–[26], for optimum Bayesian detection as applied across disciplines [27], [28], and for decision fusion principles as related to breast cancer diagnosis [29]–[31]. Results established in [27] provided one of the bases for models of visual detection put forward by Eckstein *et al.* [32], Shimozaki *et al.* [33], by Itti [34] and others. Remus and Collins [35] have also demonstrated that Bayesian techniques can expedite the measurement of psychophysical variables in hearing, and in particular cochlear implant research. Such analysis is broadly related to other Bayesian models in hearing, such as that of Mark and Miller [36], who studied auditory nerve discharge rates.

III. Bayes Theorem

A. General Form for Events

Bayes Theorem is given in many different forms, as shown, for example, in the texts by Bishop [37] and by Press [6]. One form for continuous random variables is

$$f(\Theta|M) = \frac{f(M|\Theta)f(\Theta)}{f(M)} \quad (1.1)$$

where Θ is a vector of unknown parameters and M is the measurement or data vector. In words, $f(\Theta|M)$, the *a posteriori* probability density function of the unknown parameter(s) given the measurement vector, equals $f(M|\Theta)$, the forward probability which is often called the likelihood function, times the *a priori* probability of the unknown parameter(s) $f(\Theta)$, divided by the normalizing factor $f(M)$, the *a priori* probability density function of M . The normalizing factor $f(M)$ can be obtained by integrating the numerator of (1.1) over all Θ , i.e.,

$$f(M) = \int_{\Theta} f(M|\Theta) f(\Theta) d\Theta. \quad (1.2)$$

Historically, considerable effort and discussion have been given to choosing the *a priori* probability density function $f(\Theta)$. One approach is to try to model the *a priori* probability density function to represent as much uncertainty as possible. For example, Jaynes [38] showed how the concept of maximum entropy from information theory could be used to specify the *a priori* probability density function when little physical information was available. Jaynes argued that if expressing maximum uncertainty was desired, the *a priori* probability density function could be chosen to have the maximum entropy. A contrasting approach to selecting the *a priori* probability density function, especially relevant for electrophysiology, is to recognize that physiology or medicine often has established or limited the relationships between unknown parameters that are known in a probabilistic sense. In these cases selecting the prior on the uncertain parameters is an opportunity to express this knowledge and “get it into the problem”. Doing so is, in general, rewarded by improved performance in estimating the unknown parameters from the measurement data.

Another critically important part of Bayes theorem is the likelihood function. This function provides the opportunity, especially in specific applied problems, to include electrophysiological models which now are often highly developed. For example, one often knows the probability of the measurement data if the specific parameter values were known, but in the specific problem of interest these parameter values are uncertain. Historically, the likelihood function was often chosen for mathematical convenience and often “softly” modeled the problem. Now the availability of models of physiologically realistic structure coupled with the computational power of modern computers provides a powerful Bayesian approach to real electrophysiological problems involving uncertainties.

In the context of electrophysiology, a mathematical form that is frequently useful arises from considering discrete sets of sources, which be anatomical, electrical or medical (as in the frequency of different patient populations) in nature, that give rise to measurements, which often (but not always) are electrical. Suppose k different possible sets of sources are denoted $S_1 \dots S_k$ and suppose one of these sets (the “true set”) gives rise to a set of measurements M . What is the probability that source S_j set is the set that gave rise to the measurements? S. James Press [6] gives the appropriate discrete form of Bayes Theorem as

$$P\{S_j|M\} = \frac{P\{M|S_j\}P\{S_j\}}{P\{M\}}. \quad (1.3)$$

As a first step in expansion of (1.3), note that in the denominator of (1.3), $P\{M\}$ is the *a priori* probability of observing the set of measurements M . This term may be found by the summation

$$P\{M\} = \sum_{j=1}^k P\{M|S_j\}P\{S_j\}. \quad (1.4)$$

That is, the *a priori* probability of obtaining measurements M is a weighted sum of the probabilities of obtaining those measurements from any one of the possible source configurations.

In (1.3) or (1.4), S_j is the j th configuration of the sources, M is a set of one or more measurements, and $P\{\}$ is the probability of the quantity in braces. Accordingly, (1.3) can be

read as the probability that the true source is S_j , given that the measurements are M . (This idea is written as $P\{S_j|M\}$, where the vertical bar expresses the conditional.)

Consider now the individual terms that appear in (1.3). $P\{S_j\}$ is the *a priori* probability, a set of probabilities known before measurements are taken. Such a probability may involve records or numbers found in earlier experience or analysis and in the use of Bayes' Theorem is taken to be a given quantity. In biomedical situations, investigators sometimes avoid thinking about this term and assume that all possible source configurations are equally likely, though often previous experience makes some values consistent with references, others possible but less likely, and still others impossible physiologically. However it might be determined, this term expresses that knowledge, and it is a strength of a Bayesian method that such prior knowledge is explicitly included.

$P\{M|S_j\}$ is the probability that the measurement set M will be observed if the true source is S_j , the source set j . As an example, suppose the measurement set M is the set of three voltage measurements m_1, m_2 and m_3 . In the absence of noise these measurements would be exactly equal to $v_{1,j}, v_{2,j}$, and $v_{3,j}$, the exact voltages arising from source set j if the true source was source set j . Additionally, for independent measurements $P\{M|S_j\}$ is

$$P\{m_1, m_2, m_3|S_j\} = P\{m_1|S_j\}P\{m_2|S_j\}P\{m_3|S_j\}. \quad (1.5)$$

If the noise is Gaussian with a standard deviation σ one might make use of the Gaussian probability density function

$$f\{m_i|S_j\} = \frac{1}{\sqrt{2\pi}} \exp \left[-\frac{|m_i - v_{i,j}|^2}{2\sigma^2} \right]. \quad (1.6)$$

It may of course be the case that the measurements are not independent or the noise Gaussian, in which case (1.5) and (1.6) would be replaced by other equations that were suitable.

1) Computational Aspects—For computational purposes it is useful to rewrite (1.3) using a forward probability term F_j defined by

$$F_j \equiv P\{M|S_j\}P\{S_j\} \quad (1.7)$$

and a normalization value N defined by

$$N \equiv P\{M\} = \sum_{i=1}^k P\{M|S_i\}P\{S_i\}. \quad (1.8)$$

With these definitions, the inverse probabilities of (1.3), which in most problems are quantities to be determined, can be written with the simplified notation of (1.7), as

$$P\{S_j|M\} = \frac{P\{M|S_j\}P\{S_j\}}{P\{M\}} \equiv \frac{F_j}{N}. \quad (1.9)$$

2) Computation Sequence—In computationally simple questions, one can evaluate (1.3) directly by hand or with a calculator, as in Example 1 as follows. More often analysis is done by means of computer code, as in Example 2. To do the latter, it is helpful to look back upon the equations given previously to see how they can be structured in terms of a computational sequence. One possible sequence is as follows., as

1. Prepare to use (1.6) by making a table of the differences $(m_i - v_{ij})$ between each measurement m_i measurements and the corresponding value v_{ij} that arises from the j th source configuration.
2. Use (1.6) or other appropriate equation to make a table of each of the component probabilities $P\{m_i/S_j\}$. The resulting array will give the probability of observing each one of the measurements for each of the possible source configurations. The array of values will have a row for each measurement and a column for each source. (All i and j combinations will be included in the table.)
3. Use (1.8) to find each forward probability (probability of getting the set of measurements) (as a whole) from each source and the normalization value.
4. Use (1.9) and find the inverse probability for each source being considered, the goal of the computation.

One's understanding of these equations is greatly aided by working through examples.

IV. Examples

Here we give two computationally simple examples of use of Bayesian calculations in easily framed questions so that the reader who is unfamiliar with Bayesian analytical methods can have an entranceway into the subject. As these examples are only a secondary aspect of a review of how Bayesian models are used in electrophysiology, more complicated examples are not included here. In contrast, in the review sections that follow, articles are identified without restriction as to degree of complexity of the Bayesian methods used. The careful reader will nonetheless detect that some deeper considerations come to the surface even in these simple examples.

A. Example 1—Screening Test

Bayes Theorem, as given by (1.1), can seem elusive and hardly intuitive. An example of its use is given in the following example, adapted from Yudkowsky [39]:

Suppose 1% of people at age 40 who participate in routine screening have condition X. Suppose also that 80% of people with condition X will get a positive screen score. Suppose further that 9.6% of people without condition X will also get a positive screening score. A person in this age group had a positive score in a routine screening. What is the probability that this person actually has condition X?

Using (1.3) for Bayes' Theorem, one finds the probability that the patient has condition X. The resulting probability of only 7.8% is lower than would seem intuitively correct to many people (and perhaps some physicians [40]–[42]) in view of the positive outcome of the test. Looking at the individual terms of the numerator of (1.3), one sees that the low percentage reflects the low prior probability of abnormality when combined with the accuracy of the screening. Yudowsky [39] discusses this outcome in “excruciating detail.”

The context of the screening test as presented here is used to show a computationally simple Bayesian calculation. It is suggestive but not a realistic example in that it ignores many other aspects important to real screening tests, such as family history. Technically, it is worth noting that implicit in the question and procedure as described above is the idea of a single

test threshold, an idea at variance with the range of possibilities incorporated into the concept and practice of receiver operating characteristic (ROC) curves, discussed below. Even so, this example is similar in fundamental respects to the much more sophisticated classification system used by Ishikawa, Pipberger and associates [43] for the P-wave of the electrocardiogram, one of the first uses of Bayesian models in electrophysiology, in that one must bring together the prior probabilities of a condition with the data obtained from electrophysiological measurement.

1) Example 2—Inverse Electrocardiography—The question of “what are the sources” of cardiac and neural wave forms cuts across these fields of study. Answering such questions requires consideration of the available measurements, their limitations, the nature of the sources and how they are modeled, and of the intervening medium.

2) Electrocardiographic Inverse Problem—As an example of historical significance in electrocardiography, cardiac electrical activity has been widely modeled by current dipoles. A detailed report in which dipole models were used to portray cardiac electrical sequences was presented by Rogers, Pilkington, Boineau and Spach [44], [45]. There is a long history of cardiac electrical activity being represented by dipole models, as reviewed and extended by Geselowitz [46]. A comprehensive discussion of both electrical and magnetic cardiac models has been given by Gulrajani [47]. A detailed derivation of the relation between segments of heart muscle and potentials away from the heart has been given by Plonsey [48].

As a computational example taken from that context (but here highly simplified), suppose the cardiac source is represented by two dipoles. At one moment, either or both of the dipoles may be active (generating current) or inactive (that is, the magnitude of the dipole moment is 1 or 0). Conceptually, dipole activity corresponds to a wave of excitation that is (or is not) passing through the portion of the cardiac muscle represented by the dipole, at the time considered. (In its most simple form, one dipole represents the whole heart, but here two are used.)

Suppose potentials from the dipoles are measured at each of two sites on the body surface (Fig. 1). The potential ϕ_i at site i on the body surface from the dipole moment d_j of dipole j can be found, with significant simplifying assumptions, as

$$\phi_i = \frac{R_e}{4\pi} \frac{\hat{d}_j \bullet \hat{r}_{i,j}}{r_{i,j}^2} \quad (1.10)$$

where $r_{i,j}$ is the distance to body site i from dipole j , and the hat mark signifies a unit vector. As seen in Fig. 1, the differences between potentials at adjacent points on the body surface may be small or large, depending mainly on the cosine of the angle θ . The results are often expressed as a matrix equation

$$[\phi] = [Z][d] \quad (1.11)$$

where $[\phi]$ is a vector of potentials on the body surface, computed as the product of the matrix of transfer coefficients $[Z]$ times the vector of dipole moments. Repeated use of (1.10), or a more complicated calculation taking into account regions of different conductivity and the 3-D shape of each structure [44], [45], allows each element of the transfer coefficient matrix $[Z]$ to be determined.

For the purposes of creating a simple example, suppose that transfer matrix for two closely spaced body points is

$$[Z] = \begin{pmatrix} z_{11} & z_{12} \\ z_{21} & z_{22} \end{pmatrix} = \begin{pmatrix} 1 & 0.95 \\ 0.95 & 0.90 \end{pmatrix}. \quad (1.12)$$

The *forward problem* of electrocardiography is computing the potentials on the body surface from sources in the heart. If the amplitudes of the dipoles representing the heart are

$$[d] = \begin{pmatrix} 1 \\ 0 \end{pmatrix} \quad (1.13)$$

then using (1.11) one finds the potentials on the body surface as

$$[\phi] = \begin{pmatrix} 1.0 \\ 0.95 \end{pmatrix}. \quad (1.14)$$

3) Failure of Direct Inverse Method—The *electrocardiographic inverse problem* is to find the sources in the heart from the potentials on the body surface. The direct way to approach the inverse problem is to invert the transfer matrix. The result here (as rounded) is

$$[Z]^{-1} = \begin{pmatrix} -360 & 380 \\ 380 & 400 \end{pmatrix}. \quad (1.15)$$

Making use of the inverse to find estimates d' the dipole magnitudes from the surface potentials, one has

$$[d'] = [Z]^{-1}[\phi]. \quad (1.16)$$

This plan works perfectly if the inverse matrix in (1.16) is expressed without roundoff, if the model is perfect, and if the body surface potentials are without noise (none of which is ever true with real data). Under these conditions, performing the calculation (1.16) gives

$$[d'] = \begin{bmatrix} 1.0 \\ 0.0 \end{bmatrix}. \quad (1.17)$$

The results (1.17) are the same as the true sources as given in (1.14). But, there always is noise.

4) Noise in Measurements and Uncertainty in the Model—Potentials measured from the body surface are affected by noise. In electrocardiography the term "noise" is used for electronic noise in the measurements of the potentials on the body, such as random or 60-Hz interference. Perhaps more importantly, the term "noise" is sometimes used to mean uncertainty about the differences between, on the one hand, the electrical sources in the heart and the volume conductor in reality, as compared, on the other hand, to the sources,

volume conductor and measurements as modeled. Often the latter category is more significant, and both categories can be included in a Bayesian model. Here, so as to maintain a relatively simple example, suppose the “true” values of potential are the values of (1.14) as modified to include noise of whatever origin to get a set of “measurements” ϕ' , as shown

$$[\phi'] = \begin{pmatrix} 1.0+0.1 \\ 0.95-0.09 \end{pmatrix} = \begin{pmatrix} 1.1 \\ 0.86 \end{pmatrix}. \quad (1.18)$$

Note that each noise term has a magnitude of about 10% of the measured value.

5) Direct Inverse Calculation—Executing the inverse calculation using $[\phi']$ in (1.16) gives

$$[d'] = [Z]^{-1}[\phi'] = \begin{bmatrix} -69.2 \\ 74.0 \end{bmatrix}. \quad (1.19)$$

This result is a disaster. The first element of estimated dipole amplitudes $[d']$ shows an error of about 7000%, as compared to an error in the body potentials of about 10%. Perhaps even worse, the sign is wrong, so interpretation of the result indicates that excitation in the heart proceeded in the wrong direction. The value 74, the second element of d' , also is wrong qualitatively as well as quantitatively. That is, the noise in the body surface data resulted in a large estimated value for the current being generated from a segment that in fact is generating no current. As shown by Rogers, Pilkington, Boineau, and Spach [44] (using a considerably more detailed and realistic model and analysis), the direct inverse method of calculation does not give the hoped-for results, even when many body surface measurements are included.

6) Bayesian Reformulation of Inverse Calculation—Bayesian reformulation allows one to make use of one’s *a priori* knowledge of the nature of the source terms, and the approximate value of the noise. As simplified here, there are four possible source configurations, as shown in the columns of Table II. In each column there are two rows indicating whether, for the source set described by that column, each dipole is generating current, or not. The last row of the table gives an *a priori* probability of each source being the true source. The values in this row indicate that “both off” or “both on” have higher probability than either mixed case.

The measured values of the body surface potentials that are analyzed are the same as those used in the standard inverse approach above (1.18). For Bayesian analysis, we assume further that the noise values are samples from a normal distribution with $\sigma = 0.1$ as the standard deviation. This standard deviation reflects the measurement noise. Its specification gives the Bayesian analysis a scale to judge the significance of a particular deviation between a given measurement and the corresponding value from one of the sources. (It does not characterize the differences in measured values that occur from source to source in the absence of noise, though sometimes those are chosen with measurement noise in mind.)

Following the steps in the Bayesian calculation the inverse (Bayesian) probability of each possible source, as computed with (1.9), is presented in Table III.

Examining the results presented in Table III, we can make the following observations.

1. Source 2 has the highest probability (0.57). It is in fact the true source.

2. Source 3, a source similar to the true source in that it also has one dipole on and one off, has a lower probability of being the true source (0.43), but still a substantial probability. This result is useful information, for it indicates that the noise level is high enough than an alternative to source 3 may be the true source.
3. Source sets 1 and 4 have virtually zero probabilities. Neither is the true source.
4. The *a priori* probability (Table II) of source 2 was a somewhat lower value than sources 1 or 4. Nonetheless, source 2 was identified as having highest probability because it best matched the measurements.

Table III is “the end” of the Bayesian analysis, in that a full set of probabilities are shown. It is also the full Bayesian result, i.e., the full set of *a posteriori* probabilities. It is at this point interesting to examine the observations above and think about what an investigator or analyst might do next with this result. One possibility is to look at Table III and accept the source with the highest probability as “the answer.” Another is to find a weighted average of the outcomes, with the results (here dipole magnitudes) being weighted by the computed probabilities. In this example that would end in giving both dipoles a strength of about 0.5. A third possibility is to consider these results and use them as input into another Bayesian procedure, where additional measurement data has been obtained that might be structured to differentiate between sources 2 and 3.

To a newcomer, it might at first seem that the Bayesian procedure has somehow failed by not producing a single clear-cut answer. However, further reflection gives rise to the realization that the Bayesian procedure is showing that not enough information is available in the original measurements to know, without significant ambiguity, a final answer. Then the investigator can use the probabilities in the table and rationally choose a suitable follow up.

V. Decisions and ROC Curves

The use of ROC curves is intimately linked with Bayesian models and has taken on increasing importance in the design of medical equipment for electrophysiology, and more broadly. For example, largely due to the influence of Robert F. Wagner [49], in the USA the Food and Drug Administration (FDA) requires the submission of ROC curves for consideration for approval of any new medical imaging device.

The ROC curve is a plot of the probability of detection or true positive rate on the y-axis, versus the probability of false alarm or false positive rate on the x-axis. According to Swets [50], the term “receiver operating characteristic (ROC)” was first used by Peterson and Birdsall. Both Peterson, Birdsall and Fox [15] and Middleton and VanMeter [51] used the concepts expressed on ROC’s in seminal papers at the 1954 Information Theory Symposium. As they noted, the ROC provides a systematic method of evaluating decision making for a two hypothesis decision situation, for both optimal as well as *ad hoc* decision making strategies and experiments. Swets [52] noted that two hypothesis situations are often important even when more detailed estimation of multiple parameters in complex problems are involved and desired.

The ROC has particularly interesting, unique, and powerful properties when it is connected to Bayesian analysis and the concept of optimality in decision making, e.g., such an ROC is always convex. For example, it is known that for a variety of reasonable decision criterion (e.g., minimizing probability of error, minimizing average cost of a decision) that the likelihood ratio algorithm followed by a threshold setting that depends on the criterion (in some contexts called the ideal Bayesian observer) is optimum. Furthermore, what is remarkable is that one can relate a particular decision criterion to a particular point on the

ROC and from that determine a quantitative result for the best possible decision performance for that criteria, all on one curve [53]. That relationship, for Bayesian likelihood ratio algorithms, is that the corresponding operating point on the ROC is where the slope on the ROC equals the threshold setting on the likelihood ratio.

VI. Bayesian Models in Vision, Hearing and Brain

Some of the earliest experiments in vision and hearing involved uncertainties in regard to both the signals as well as how a human observer was making decisions. They were not formally designed from a Bayesian perspective [21], [22] but encompassed much of what is now thought of as Bayesian concepts.

The original application of ROC curves involved radar and sonar systems. ROC curves are now used widely in vision, hearing, and electrophysiology more broadly, and in many medical fields where decision making is required. (A 2010 Google scholar search on the terms “electrophysiology receiver operating characteristic” returned 5160 items.) One use of the ROC is the quantitative evaluation of ideal Bayesian observers, a term that usually refers to the optimum likelihood ratio algorithm for making decisions between two hypotheses in the face of uncertainty and noise. The seminal paper by Peterson, Birdsall and Fox [15] presented a very broad fundamental Bayesian framework (although the authors at that time did not use the term Bayesian), based on likelihood ratio and *a priori* probabilities and Bayes Theorem, for deriving what the psychology community now calls the ideal Bayesian observer. However, the story is even better than that. Their paper also presented the framework for deriving the ROC of ideal Bayesian observers. The power of using the ROC in that way is that it provides an upper bound on the best decisions possible for uncertainties in various parameters as well as the noise. Furthermore, the ROC presents this decision-making performance for a very wide variety of possible decision criterion.

An early biomedical use of ROC curves occurred in the fields of hearing and vision [22]. Prior to use of the ROC, the goal for over almost a century (according to Swets [50]) of experimental psychologists had been to develop a precise 1-D measure of sensor (e.g., hearing, vision) discrimination between two stimuli. Their measures had great variability due to individual differences and other parameters of the experimental situation. In particular, performance measures used prior to the ROC confounded sensor discrimination and response bias (decision criterion). With the introduction of the ROC, psychologists were able to separate sensor discrimination from response bias in their experiments on sensory processes (hearing, vision) as well as in vigilance and other areas. Over time the ROC has become an essential decision-making performance metric in medical fields including radiology, anesthesiology, cancer diagnosis and detection, and in the process of medical decision making generally [53]–[57]. A caution is, however, in order. An ROC curve appears simple. Interpretation of what it shows, however, is more complex and comparative, and often requires careful thinking. Fawcett [54] provides an illuminating discussion on “some common misconceptions and pitfalls when using them in practice”.

In hearing, many of the early experiments involved detection, i.e., trying to determine at what levels signals and tones of various frequencies, amplitude, phase and duration could be heard by human observers when these signals were obscured in white Gaussian noise. Although the signals presented to the listener in various experiments had uncertainties in their frequencies, phases, etc., the ROC’s from their experimental results were primarily compared to an “ideal observer” model that assumed that the signal or tone was known exactly (SKE) in white Gaussian noise. When the experimental ROC from the human observer experiments fell short of the ideal observer, as it almost always did, this difference was attributed to “internal noise” of the observer. ROC curves were obtained for the human

observer and compared with the SKE ROC curve to see how closed to the ideal performance a human observer to come. Although the SKE ROC provided an upper bound, this approach added little insight into how a human observer processed information with uncertainties.

Subsequently, a class of ideal observers (now sometimes called Bayesian ideal observers) was developed which incorporated *a priori* knowledge of various signal uncertainties. The advantage of these models was that by incorporating the uncertainties optimally and getting their corresponding ROC's, one could determine a more realistic bound on decision performance as a function of different uncertain parameters of the signals. The early Bayesian ideal observers were obtained for signals with very fundamental parameters unknown such as phase, unknown frequency, unknown amplitude [15], one of M orthogonal signals [15], [27], unknown location in time and/or space [15], [22], and some others. Typically, the experimenter would then design an experiment which presented audio or visual signals with different uncertainties and compare the ROC with the performance of the Bayesian ideal observer. If the match in performance was good, this suggested that perhaps human hearing or visualization was done in a way similar to how the Bayesian ideal observer processed uncertain information.

More recently, there has been interest in getting a better understanding of the relationships between the psychophysics of hearing and the underlying physiology. One approach is to incorporate a physiological-based modeling approach, along with its uncertainties. Similar modeling approaches, physics-based, have successfully addressed statistical decision making in a variety of fields, including underwater acoustic communications [23].

In order to get a better understanding of the relationship between hearing and its underlying electrophysiology, Huettel and Collins [58]–[60] incorporated known as well as proposed new computational auditory models that predict neurophysiological data such as neural firing rates. Their Bayesian approach modeled both uncertainty in the stimulus as well as in their auditory models. Using this approach they were able to relate the gains in performance in using a simple hearing aid for the hearing impaired to the physiological bases of the impairments [61].

Vision research involving Bayesian statistical decision theory followed along similar lines of development with respect to including Bayesian models and eventually simple neuroscience models. Initially the Bayesian ideal observer models available were fundamental and very important, but relatively few [15], [22], [27] and not particularly tied to physiology. For example, Cohn and Lasley [62] studied the visual impact of the uncertainty of a luminance-increment on the detectability of that increment by a human observer and found general agreement with the Bayesian ideal observer for one of M orthogonal signals as a predictor. Clarkson and Barrett [63] developed Bayesian ideal observers for visual situations with amplitude, scale, orientation and position uncertainty. Shimozaki, Eckstein, and Abbey [33] compared two models for a cueing task in visual detection. Their human observer experimental results in combination with models suggest that human observers approximate a Bayesian ideal observer model.

As Eckstein, Peterson, Pham and Droll [32] point out, integration of results from neuroscience with the classic theories of human decision making is not simple. This difficulty arises in part because each field historically has had its own questions, terminology and established approaches to research. Nevertheless, Geisler [64] by using a sequential ideal-observer analysis was able to include physiological processing components of human spatial vision. Eckstein, Peterson, Pham and Droll [32] were able to use statistical decision theory and computational modeling to relate classic theories of attention in

psychological research to neural observables such as mean firing rate, tuning functions, Fano factor, neuronal index of detectability and area under the ROC.

As more broadly related to the brain, a pioneering figure has been Peter Dayan [65]–[68]. His work on Helmholtz machines has come to be extended into Bayesian analysis in brain–machine interfaces, a very active research community in recent years, by authors such as Nicolelis *et al.* [69], Darmanjian *et al.* [70], and Cunningham *et al.* [71]; Friston and colleagues have published extensively [72]–[74] and especially with Moran and colleagues have actively investigated neural populations, spectral responses of the structures of the brain, as deduced using Bayesian models [75]–[80]. Other Bayesian structural models have been presented by Jepna [81] and by Rao [82].

Structure also has been deduced using Bayesian models with functional MRI [83]–[85] and by Bayesian modeling with Markov chain analysis [86]. Bayesian analysis has allowed multisensory integration [87], and the concentration dependent effect of sevoflurane on the EEG [88]. Inverse prediction of potentials on a sphere around the brain from EEG data, using a Bayesian model, has been accomplished by Riera *et al.* [89].

VII. Bayesian Evaluation and Cardiology

1) Electrocardiographic Interpretation

In the late 1800s electrical waveforms were first measured from the body surface of dogs and humans and were identified as arising from the heart. It took a number of years to improve the method of measurement, including especially the invention of the sensitive string-galvanometer device, and considerable further discussion as well as investigation to standardize what was recorded and the nomenclature used to describe it. After years of organizing wave forms from many patients, Einthoven won the Nobel prize in 1925 for demonstrating that in fact electrocardiograms measured from the body surface in humans could be used to identify patients who were electrocardiographically normal and to identify those individuals suffering from several types of heart disease.

In the later 1900s, Hubert Pipberger, Al Berson and other colleagues, working in Washington DC with one of the first large digital computers in that city, organized a research project to accumulate ECG data, much of it in the form of Vectorcardiograms, from thousands of individuals who were seen at Veterans Administration (VA) hospitals in the U.S., along with corollary clinical data. These investigators and this project had many ground-breaking achievements, especially in relation to mathematically sophisticated analysis of numerous wave form features across large numbers of recordings. Many accomplished international investigators worked for periods of several years in the Pipberger laboratory, making use of the accumulated data and the computer facilities, which were very powerful for that time. In 1973, a paper in the influential journal *Circulation* by Ishikawa, Kim, and Pipberger [43] used Bayesian analysis in relation to P-wave analysis in normal subjects and patients with atrial overload, marking one of the first uses of formal Bayesian evaluation in the electrocardiographic field. The Ishikawa paper cited as the basis for its analysis the report “Multigroup Diagnosis of Electrocardiograms,” [90], by Cornfield, Dunn, Batchlor, and Pipberger, which details the rationale for use of Bayes Theorem for ECG classification. Interestingly, Cornfield was a member of the faculty in the statistics department at George Washington University, and likely in direct contact with those members of the Bayesian Hall of Fame who were active at that time.

The purpose of the Ishikawa study was to establish limits of normal for P wave measurements and to propose criteria for routine electrocardiographic readings and for multivariate analysis to recognize left atrial overload (LAO) and right atrial overload (RAO)

in the orthogonal electrocardiogram (ECG). From the ECGs, 15 key measurements were identified. These 15 measurements were then used for a simultaneous three-group analysis utilizing a Bayesian likelihood ratio. The Bayesian approach did not however find much success with its intended beneficiaries, for, as pointed out by Rautaharju in his penetrating review [91], Pipberger's approach was doomed because cardiologists found it difficult to accept the Bayesian approach to diagnostic ECG classification, presumably because they felt it compromised the "objectivity" of the ECG recording.

Although Pipberger's specific computer code did not become widely used, the well-known papers by Pipberger and colleagues, appearing in prominent journals, led to Bayesian evaluation being considered by many other investigators in the broader electrocardiographic community. In recent years Bayesian models have been used, for example, in relation to electrophysiology and exercise testing [92], unexplained syncope [93], intensive care monitoring [94], atrial tachyarrhythmias [95], ST-segment elevation [96], and broad complex tachycardia [97].

2) Inverse Problem

Cardiac electrophysiology's *inverse problem*, as it is called, might be considered to be electrocardiography in a more comprehensive, physically based form. The approach is to use physical and physiology information about the nature and size of the volume conductor between the heart together with information about the geometry of the structures of the heart and a specification of the locations of electrodes on the body surface. The goal then is to begin with recordings made on the body surface (or in other variants of the inverse problem, on or within the heart itself) and from these recordings to predict the nature of the cardiac sources. Sometimes the predictions are of specific time-varying voltages. Bayesian models are used so as to take into account uncertainties in the given information and to limit the results to those that are physiologically within the realm of possibility. Recent inverse reports that use a Bayesian approach include those of Greensite [98], Wang [99], [100], focusing on cardiac arrhythmias, and Efstratios [101], who integrated several sources of data. Bin He incorporated Bayesian concepts while focusing on visualizing cardiac arrhythmias [102]. Khoury, Taccardi and Rudy [103] have dealt with similar ideas in localizing electrical activity from a ventricular probe. Wang and co-workers [104] have used Bayesian analysis to address functional imaging of volumetric cardiac electrical activity, another form of inverse procedure.

Studies of heart-rate variability are another kind of inverse problem that involves hypothesized interactions of the nervous system with the heart, resulting in readily observed changes in heart rate, over time. Bayesian concepts naturally arise in the need to deduce how the neural sources affect the heart rate as an observed variable. Such studies include those of Lake *et al.* [105], Fallen [106], and Mohammadzadeh and co-workers [107].

3) Models of Mechanisms

Recent students by Pollard *et al.* [108], [109] have dealt directly with physical and physiological properties of the heart muscle itself. The goal is to measure the conductances within and around cardiac cells, including those of cell to cell connections, as these are recognized contributors to arrhythmia development. The strategy evaluated uses a comprehensive 3-D simulation. As was presented in a recent report [109], interstitial, intracellular and membrane components are included in the model and coupled to one another in a realistic fashion. The cell array was interrogated using a set of eight electrodes, of which six were used as three pairs of stimulating electrodes at spacings of 75, 125, and 175 μm , and the center two were used as voltage sensing electrodes. Bayesian analysis is used to determine the probability of each one of thousands of possible combinations of cell

parameters being the actual source of the responses observed, judged as a comprehensive set.

The general procedure of associating reciprocal cases of underlying model parameters with records obtained during the experimental case in which potential differences are recorded during stimulation, with low amplitude supplied currents, provides an opportunity to expand the set of parameters one might consider measuring. That is, the measurements might allow a richer source set than first imagined. This strategy has not yet been validated comprehensively experimentally, but within the simulation worked well. It seems to provide a means of measuring both intracellular and intracellular resistances, along and across cell axes, and of doing so within a few seconds in living tissue.

4) Cardiac Devices

Bayesian models have been used for the design of a number of kinds of cardiac devices. Woo *et al.* [110] report on multimodal data integration in relation to ablation of atrial fibrillation. Here the action taken is removing the ability of tissue in a small region in the hopes that occurrences of atrial fibrillation will be diminished or eliminated. Goodman, Idriss, Wolf and coworkers [111] use Bayesian statistics to set shock levels to stop atrial fibrillation. Swerdlow *et al.* [112] use a Bayesian model in connection with biphasic defibrillation. Several reports deal with stimulation or defibrillation of cardiac tissue for specific patient groups, including Khairy *et al.* in relation to defibrillation [113] and stimulation [114] in patients with tetralogy of Fallot, and Abhimanyu in relation to statin therapy [115].

Along different lines, Laufs *et al.* [116] have used a Bayesian model in simultaneously recording electrophysiological data with magnetic resonance imaging, and Sermesant and co-workers [117] used Bayesian analysis for image analysis and simulation. Wang *et al.* [118] have used Bayesian models in noninvasive functional imaging of “volumetric cardiac electrical activity.”

A number of other reports involve Bayesian models where electrophysiological considerations play a secondary role to the primary medical conditions involved. Among these are reports on congestive heart failure [119], coronary stents [120], cardiac hypertrophy [121], and dexmedetomidine hemodynamics in children after heart surgery [122].

VIII. Genomics and Microarrays

Among the powerful experimental tools for identifying protein sequences are microarrays. A Bayesian framework for the analysis of microarray expression data, a powerful tool for genetic identification, was presented by Baldi and Long [123]. Le Bouter *et al.* [124] made use of this framework in cardiac electrophysiology. In particular, they used a combination of patch clamp experiments, ECG recordings and cDNA microarrays that contained murine probes to investigate functional and molecular remodeling accompanying altered thyroid status. Male C57BL/6 mice fed 5-propyl-2-thiouracil for 5 weeks developed hypothyroidism, and mice treated with intraperitoneal T3 hormone developed hyperthyroidism. In comparison to control, the hypothyroid animals showed significant reductions in two sarcolemmal potassium currents (I_{to,f} and I_K, slow) that are pronounced in mice, as well as an increase in the potassium current governing the action potential plateau (I_{Ks}). Analyses of ECG recordings showed prolonged QT intervals, consistent with the reduced densities for the potassium currents that largely govern the repolarization time course. Connections between functional changes of these type and the changes in expression for 98 mouse genes were made possible through an elegant analysis using Cyber-T (Baldi

and Long, 2001). RNA extracted from hearts was split into sample pairs that were reverse-transcribed and labeled with either Cy3 or Cy5. Fluorescence intensities were measured, normalized to Cy3 and presented as %-change in gene expression for all 98 genes. The Bayesian procedure allowed statistical comparisons between hypothyroid samples that demonstrated marked differences in a set of expression levels that were largely unaffected by the noise, variability and low replication associated with measurements of this type.

More broadly related to the use of Bayesian models at the genomic level are models for gene expression as related to retinal aging [125], hERG-related liability by Sun [126] and its relation to QT prolongation Raschi *et al.* [127]. Related to cardiac electrophysiology, Smith *et al.* [128] have extended studies of electrocardiographic conduction to genome-wide association.

Working outward from the genomic size scale, Schmid [129] has investigated cardiac modeling for multi-scale models, McCulloch and Paternost have included Bayesian analysis in a comprehensive view of cardiac systems biology [130]. Bassingthwaighe, Hunter, and Noble have taken a comprehensive and forward looking view that includes Bayesian model in their paper “The cardiac physiome: Perspectives for the future” [131].

IX. Bayesian Models in Broader Electrophysiological Context

Bayesian models have come to be included in a range of books on topics from those virtually philosophical essays of Sobel [132] to rational deliberation [133], to decision making [134], to highly technical [135]–[137]. Across this range one rarely sees any mention of electrophysiology as a field of application (though a thoughtful reader knowledgeable about electro-physiology in medicine or biomedical engineering would have little difficulty in identifying such a connection). In contrast, in professional applications a specialized literature is available discussing Bayesian evaluation, especially as related to arrhythmias [138], [139]. It is notable that such knowledge has come to be included in an European professional accreditation report on the core curriculum for heart rhythm specialists [140].

Experimental studies involving Bayesian models and electrophysiology include a fascinating report about reverse engineering of signaling, metabolic or gene regulatory pathways by reconstructing them from experimental observations. Such reconstruction is a central theme in systems biology including its electrophysiological aspects, and use of Bayesian models to this end is described by Rice and Stolovitzky [141]. Other reports include those evaluating subchronic exposures to concentrated ambient particles in mice [142], [143]. A different kind of report involving Bayesian models and electrophysiology is the human–computer interaction study on user interruptability [144].

X. Discussion

Looking again at Table I, one sees that use of Bayesian models has grown exponentially since 1970. What are the advantages of using Bayesian models that have driven this growth? An immediately evident advantage to a Bayesian formulation is that it allows the investigator’s prior experience to be taken into account. That experience is formulated as the probability of one outcome as compared to another. Stated quantitatively such prior experience becomes a part of the mathematical expressions and thus the quantitative outcome. In electrophysiology, the most obvious use of prior probabilities is to exclude outcomes that are physiologically impossible but otherwise mathematically acceptable. Exclusion of impossible findings allows some questions to be answered with a Bayesian model that, as a practical matter, cannot be solved by a direct method, as in example 2.

More generally, Bayesian questions and models have the advantage that they allow one to take into account, explicitly and formally, the range of uncertainties that are known to be present. The most obvious is noise in the measurements themselves. Perhaps more important is that uncertainty in the underlying model can be included; that is, uncertainties in the mechanisms by which different possible causes of a set of measurements come to be observed by including different sources to be based on variants of the model in those evaluated, or by including their effects into the description of the noise. Such model unknowns often can be included by using alternative sets of sources in the Bayesian analysis.

A substantial advantage with a Bayesian framework occurs in complex problems where the data are insufficient to resolve observations into a single, clear-cut “solution.” Here a Bayesian framework may provide an organized way to evaluate the whole range of possible solutions, with a probability assigned to each one. Procedurally, an advantage of Bayesian methods is that they lend themselves readily to sequential evaluation, when initial measurement and evaluation is followed by further measurement and then improved evaluation. Noble and Rudy, in their excellent summary [145] of the series of improving cardiac cell membrane models developed over the last 50 years, have emphasized the importance of such sequential development.

Finally, a Bayesian framework provides a measure of the quality of a solution that comes from noting how close its probability is to one. That is, if a set of measurements is thought to derive from a particular source, one learns whether that source is virtually certain to be the true source. There is at the same time a comprehensive picture of all the possibilities, as the full Bayesian solution determines a probability for every source. Sometimes the comprehensive picture shows one source as highly likely and the other sources as having probabilities close to zero, but sometimes not. In the latter situation one learns which other sources also have a significant probability of explaining the observations. Perhaps there is one other likely source, or perhaps more than one. Engineers, scientists and physicians with expertise in a field already do such a weighing of alternative explanations as a mental process; what the Bayesian analysis brings is the opportunity to make that process systematic and quantitative. Such a Bayesian framework provides one a quantitative basis that might be used to focus further work on significant alternatives.

The reports cited in this review extend across a wide range of electrophysiological topics, in keeping with the aim of a broad overview. Conversely, the list of reports given here is by no means exhaustive. One might argue that separate reviews of the use of Bayes Theorem in vision, in hearing, in brain research, and in relation topics such as machine learning also are warranted. The community of investigators developing brain-machine interfaces uses Bayesian analysis in an intense and technically sophisticated one that is only lightly mentioned here. In this regard, PubMed searches in preparation of this review using “Bayes AND vision” and “Bayes AND brain” produced 109 and 755 responses, respectively. While a fraction of those reports are cited here, it is worth noting that Bayesian models are associated with problem areas as diverse as gene expression (Chen [125]), interpretation of functional MRI measurements (Smith [128]), design of neural signal processors for brain machine interfaces (Darmanjian [70], Cunningham [71]), analyses of dose-response and toxicity (Wang [146]), point processes (Brown [147]) and particle filtering (Brockwell [148]).

In looking across the range of reports that are cited here, one may divide them very broadly into two categories. The category that might be most readily anticipated by a newcomer to Bayesian models has an original question, most often involving medical diagnosis, that is framed in terms of probability. For example, that was the case for the first example and for

the electrocardiographic evaluations of Pipberger and co-workers. The category that might not have been anticipated are the numerous reports that deal with questions about structure, where alternative structures are evaluated by examining outcomes. This second category includes, for example, the reports about populations and structures in the brain, the plan for measuring impedances of tissue in the heart, and inverse solutions in the heart and brain.

Those most committed to a Bayesian outlook sometimes argue philosophically that any question can be framed from a Bayesian point of view. That may be true abstractly, but a Bayesian framework or model still enters into only a small fraction of publications—less than 5%—on electrophysiological topics over the last decade. What factors limit more widespread use? The most obvious is that in many studies the quantities of interest can be directly measured with satisfactory precision, so a Bayesian framework brings extra overhead without additional benefit. For example, if one wishes to measure the transmembrane action potential in a certain ventricular cell, and if the right access to the tissue and equipment for measurement is available, a few direct measurements of such cells may be sufficient and comprehensive. Conversely, when the question becomes how to administer stimulation or defibrillation shocks to affect a sequence of action potentials over time following shock administration, the pathway between cause and consequence becomes longer, and a Bayesian model becomes more valuable.

Moreover, a Bayesian framework may show that different sources could give rise to a given set of measurements. Acknowledging that possibility may be disconcerting, and at first misunderstood. Here another factor becomes significant: There is a measure of complexity involved in framing the question in a Bayesian fashion and possibly an initial steep learning curve. There also may be the need for computer support. With experience, such barriers are found to be small, but on first use they are significant. And, as a corollary, one also may be hesitant to adopt a procedure that seems different from those used previously by colleagues in the field.

Comparing the advantages and disadvantages above, the advantages seem to be ones that will be true for decades to come and of increasing value as Bayesian models in electrophysiology become a part of addressing more and more complicated questions. Conversely, some of the limitations will diminish as knowledge of what is possible and familiarity with its use becomes more widespread. Further, with more and more questions best approached using multiple observations that have to be merged together to reach an integrated decision about many source parameters as a group, so the need for a comprehensive framework is increasing. Moreover, increasingly powerful computer capabilities make the computational aspects less and less of a barrier. The tide rolls on.

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Biographies

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Andrew E. Pollard received the B.S., M.S., and Ph.D. degrees in biomedical engineering from Duke University, Durham, NC, in 1983, 1985, and 1988, respectively.

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Fig. 1.

In schematic form, two dipoles (large arrows), having dipole moments p_1 and p_2 , represent electrical activity of two segments of cardiac ventricular muscle, drawn as double lines below. At a particular time, these dipoles generate potentials ϕ_1 and ϕ_2 at points S_1 and S_2 on the body surface (represented by the horizontal line at top). Angle θ between each dipole and line from dipole to each body point has a major role in the *electrocardiographic forward problem*, which is determining potentials on the body from a description of electrical sources in the heart. For *inverse electrocardiography*, the question is whether, knowing ϕ_1 , ϕ_2 the approximate geometry, one can deduce values for p_1 , p_2 . Although a great deal of knowledge has been developed over time about both forward and inverse problems, there is no comprehensive and satisfactory solution for either forward or inverse problems (small differences between theory and experiment) that has been achieved so far.

TABLE I

Reports Using “Bayesian Models Electrophysiology”

Decade Starting Jan 1	Number Indexed ‘Bayesian Models Electrophysiology’
1970	22
1980	91
1990	588
2000	3690

About 450,000 papers appeared in ‘Electrophysiology’ during this 40 years.

TABLE II

Source Specification

Configuration	Source 1	Source 2	Source 3	Source 4
Dipole 1	0 (off)	1 (active)	0	1
Dipole 2	0	0	1	1
<i>A Priori</i>	0.30	0.20	0.20	0.30

TABLE III

Bayesian Results

Configuration	Source 1	Source 2	Source 3	Source 4
Dipole 1	0(off)	1 (active)	0	1
Dipole 2	0	0	1	1
<i>Bayesian probabilities</i>	0.0000	0.5744	0.4256	0.0000