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A Stochastic Model of the Visual Evoked Response

T. Ward[1], *Member IEEE*

Abstract –**A stochastic model for visual evoked response generation is proposed based on a compound neurological generator approach. Participation of individual generators is stochastically modelled in a physiologically realistic manner that captures the inherent variability in latencies and amplitudes associated with the component phases of the response. The model is invertible such that decomposition of real responses to reveal individual unit generator participation is possible and suggests that conventional averaging techniques may provide a truer picture of the visual evoked response than previously thought.**

Keywords- **Neural modelling, evoked potentials, ensemble averaging.**

I. INTRODUCTION

In this study a specific electrical response of the central nervous system to visual stimuli will be acquired, analysed and modelled in an attempt to yield new measures of nervous system integrity and function. In a similar fashion to nerve conduction studies (NCS) the approach used, is to work up from the single neural response to a macro activity of large ensembles of neurons. Similar approaches have been undertaken for evoked responses by [1] and [2].

The visual evoked response under study in this work is termed the monocular full-field pattern shift reversal visual evoked response (FF-PSR-VER) [3] and is a particular manifestation of a VER, though it is hoped that some of the ideas presented here based on this particular paradigm can be generalised to include whole classes of ER modalities. The clinical value of such responses has been most apparent in the evaluation and diagnosis of degenerative nerve diseases such as multiple sclerosis. A significant body of evidence suggests that patients suspected of such conditions often suffer from demyelinating lesions in the visual pathways that may give rise to 'abnormal' VER patterns. Consequently the accurate recording and analysis of such responses has become more critical and methods by which additional information regarding the integrity of the visual pathways can be ascertained are of significant value, [4][5].

The acquisition of a single ER is a difficult task as the intervening skull structures and tissue serve to substantially attenuate the evoked signal to very low levels (0.2-5μV amplitude) while the significant distances between the electrodes and the response generators result in additional EEG signals of much higher amplitude (20-100μV) swamping the desired signal. To exacerbate matters, motor artefact, ECG activity, ocular potentials and mains 'hum' all serve to contaminate the signal further. Consequently the detection process becomes very difficult, and satisfactory acquisition can only be brought about by means of additional signal processing methods.

One of the earliest successful attempts to enhance the measured response was realised by Dawson [6] in 1947 using the superposition of photographed individual traces in a montage that elucidated the nature and form of the evoked potential. This method also had the advantage of providing a means whereby changes in the latency of the response could be tracked. Since then this process has become more sophisticated in terms of technological implementation e.g. the process is usually done on-line with automatic screening of responses such that samples with excess contamination are excluded from the averaging process, but the principle has remained the same. It is rather unsatisfactory that even though advances in signal acquisition hardware, signal processing algorithms and basic brain science has meant that we now know a lot more about the nature of evoked responses and are thus in a far better position to successfully extract quantitative information regarding brain functioning, the ensemble averaging technique remains the most utilised measure. Is this telling us something about our understanding of the formation of VERs, i.e. does the averaged response contain more information than we think?. In particular is it possible that there is a fundamental flaw in our understanding of the formation of evoked responses particularly with regard to the phenomenon of 'jitter' (i.e. variability in latency and amplitude of the waveform). The model proposed here reconciles the 'jitter' phenomenon with the ensemble averaging approach.

II. MODEL STRUCTURE

The model structure is parallel in nature consisting of an ensemble of neurological generators acting independently of each other in a manner not dissimilar to that responsible for sensory nerve conduction studies [7]. Each generator can be though of as an optical pathway fibre along which action potentials (APs) are propagated with a velocity related to the nerve fibre parameters. For conventional myelinated nerve fibres a linear dependence between nerve diameter and

[1]Department of Computer Science,
National University of Ireland, Maynooth,
Co. Kildare, IRELAND
Email: tward@cs.may.ie

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conduction velocity (CV) has been found [8], but so far as the author knows no such result has been produced for the optical nerve pathways. Therefore, no relationship between the CV and nerve fibre parameters (and/or synaptic parameters) will be used and so the velocity domain will be the starting point in this model.

This idea is not unrelated to the approach of Micheli *et al.* [9], who considered the form of the VER to be attributed to an asynchrony in the arrival times of APs at a focal point in the brain. According to this concept the individual signals are modulated so that at the site each vj has been changed in amplitude k(j) and in phase ϕj. The amplitude change represents the propagation decay and the phases represent the propagation delay according to

$$v_j(i) = k(j).h(i - \phi_j) \qquad (1)$$

for a specific choice of $k(j)$ and ϕ_j , j=1,2,...,N the simulated VEP can be found by

$$VER = b + \sum_{j=1}^{\alpha} v_j^{\alpha} \qquad (2)$$

where k is a scaling factor b is a DC component and alpha a constant.

The VER in the present case is modelled as a weighted sum of biphasic action potentials. The biphasic aspect of these responses stem from the bipolar recording electrode configuration used in the acquisition of the response [10]. Further justification for this approximation lie in the fact that the summated response (the VER) is also biphasic in nature (i.e. the P100-N145 components). Qualitative similarities (e.g. number of phases) between the single fibre response and the compound response have been noted by other researchers and indeed have been used by Barker *et al.* [11] to solve for nerve fibre velocity distributions. As a further consequence of this bipolar configuration the temporal scale of the response is linearly related to the CV for that particular nerve fibre.

It is now appropriate to write down the equations describing the model thus;

$$\boldsymbol{y}=\mathrm{A}\boldsymbol{p} \qquad (3)$$

where

$$A_{ij} = \sin(\pi \frac{v_j}{d_2} t_i) \qquad (4)$$

for $t_1<t_i<2t_2$ where

$$t_1 = \frac{d_1}{v_j} \qquad (5),$$

$$t_2 = \frac{d_2}{v_j} \qquad (6)$$

$\boldsymbol{y}$ is a vector representing the discretized time series of the VER and $\boldsymbol{p}$ is a vector representing the histogram of conduction velocities. The biphasic unit responses are modelled as single cycles of a sinusoid as a first-order approximation. d_1 and d_2 in the conventional NCS approach represent the distances between the stimulation site and the active electrode and the active electrode and reference electrode respectively. Although a bipolar configuration of electrodes is used, the interpretation of the electrode distances is not straightforward as the geometry of the experiment is somewhat different, nevertheless an interpretation in terms of normal electrode distances is tempting and not inconsistent with the timing of the phases of the VER.

Using such a model one can infer how different *P100-N145* waveform features arise due to changes in the underlying nerve fibre distribution. This model also suggests an alternative to averaging and even latency corrected averaging to yield the 'true' *VER*. The problem with latency corrected averaging is that supramaximal stimulation is by no means achieved during the VER experiment therefore the actual participation of the same set of nerve fibres out of all those possible every trial is extremely unlikely. Such variability in the make-up of the actual nerve fibre set involved would obviously give rise to latency variability and varying waveform morphology i.e. 'jitter'. Therefore an alternative averaging method based on the single trial decomposition into *CV* groups could be processed to construct a picture of the full nerve fibre set, from which an ideal *VER* could be constructed.

In the next section a simulation of the *VER* will be attempted based on equation (3) which will also illustrate how the latency and amplitude variability could arise.

III. Modelling the Stochastic Element of the VER

If one considers the stimulation of the retina as per the *FF-PSR-VER* experiment in the context of *NCS* it is not difficult to appreciate that full stimulation of the nerve fibres of the visual pathways is very unlikely. If in a *VER* experiment some form of electrical stimulation of the retina was possible then supramaximal responses could be guaranteed. Unfortunately this is not the case, for it is patterns of light that form the stimulus in *VER* experiments and such a stimulus presentation is not so thorough in its ability to excite the visual pathways. Eyeball-jitter and non-uniform illumination of the retina along with many other factors all contribute to make stimulation of the retina a less than rigorous affair. If one considers the set of direct nerve fibres $\boldsymbol{f}$, then each trial of a *VER* experiment probably only excites a subset $\boldsymbol{f'}$ of $\boldsymbol{f}$ which differs in its makeup from trial to trial. One can rearrange this set $\boldsymbol{f}$ such that it reflects the nerve fibre velocity distribution, $\boldsymbol{p}$ and model single trial stimulation as extracting a smaller set $\boldsymbol{p'}$ from such a distribution. It is unknown how each set $\boldsymbol{p'}$ is extracted from $\boldsymbol{p}$ so for the current preliminary investigation a random function will be used. This random set extraction is based on the following expression

$$p(i)=p(i).\mathrm{mod}(c,1) \qquad (7)$$

where c is a positive random variable taken from a normal distribution characterised by a mean μ and standard deviation σ. Fig. 1 shows three such sets p' and the associated output responses generated. It is immediately apparent that the responses are qualitatively similar to each other but differ slightly in latency times and amplitude. Such responses are certainly exhibiting the 'jitter' phenomenon.

Statistical analysis of the latency and amplitude variations inherent in the visual evoked response has been carried out by Cigánek [12] and the results exhibit a gaussian distribution. One important fact that arose from his work is that the spread of the distribution of latencies increased for the later components i.e. the standard deviation of the N145 peak latency distribution was greater than that for the P100. Given the velocity approach being taken here it is apparent that the proposed model should exhibit this phenomenon and indeed it does as Fig. 2 shows. This figure shows the resultant latency histograms for 1000 responses generated by the model.

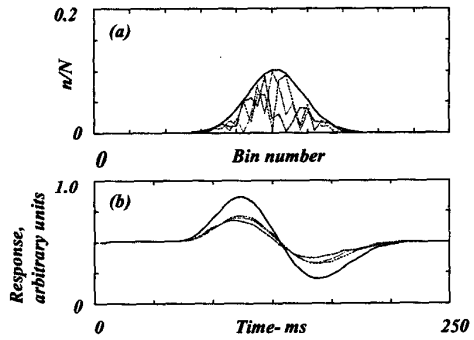

Fig. 1: (a) Model input CV distributions and (b) the corresponding outputs.

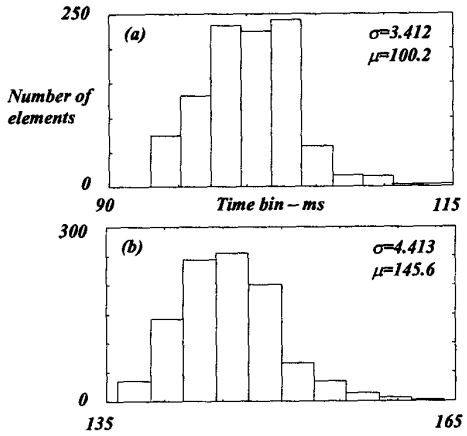

Fig. 2: Latency histogram for (a) P100 and (b) the N145peak.

IV. Reconstruction of the Full VER

Using the real VER data, an attempt was made to carry out the velocity-domain averaging procedure to generate the true VER. Data from one hundred consecutive trials will be used to produce the full VER and this will then be compared with the conventionally averaged response.

The subject from which this data was taken was a healthy 23-year-old male with his left eye covered and visual stimulation is applied to the right eye. For details on the acquisition of this set of data and the protocols observed see [13]. The single trial data is very noisy so 10-15 consecutive trial averages are used for the reconstruction process. As the number of consecutive trials used is very small (ten/fifteen trials) then such averaged responses can be used to reconstruct an average measure of p' over that time frame.

In order to invert the model and derive a measure for the CV histogram the nonnegative least squares method (NNLS) was utilised [14]. The NNLS procedure was applied to these responses and the resultant distributions recorded. From this data set a simple average is constructed and is shown in Fig. 3. This distribution p is assumed to be 'closer' to the potential fibre distribution than any other of the individual distributions found and can now be used to produce a true visual-evoked response. Such a VER generated from the averaged distribution is shown in Fig. 4 along with the ensemble average for the same data.

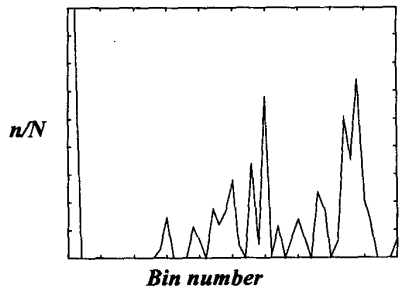

Fig. 3: Averaged decomposition.

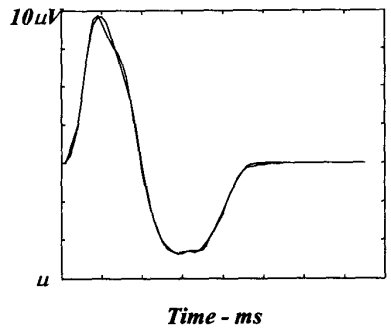

Fig. 4: Ensemble average and reconstructed average response.

IV. CONCLUSION

The VER generated using the decomposition procedure is almost identical to that generated by the averaging procedure. This is to be expected given the linear nature of the model. Whether or not one can assert that the velocity-averaged response is a better measure of the VER than the time-averaged response is impossible to answer in light of current knowledge on the physiological basis of evoked response generation. Nevertheless as the velocity averaging technique is based on a physiologically plausible theory for VER generation that encompasses even latency and amplitude variations, it does stand out among the other techniques such as averaging and decompositions using the Prony method [15], which are lacking in this regard. As further experimental evidence regarding the physiological mechanisms involved emerges, the model outlined here can be refined further. One very important conclusion that may be drawn from this analysis is that the conventional averaging technique does not need processing techniques such as latency correction [16], in fact attempts to correct latency should, according to the theory above, only serve to distort the waveform. The uncorrected ensemble average, which is universally used in ER studies and which is so often criticised, should be one of the most powerful methods for building up a true picture of the visual evoked response, particularly if used in conjunction with other signal processing techniques.

Another interesting aspect to the velocity-domain averaging approach is that additional signal processing operations can be performed on the velocity distribution signal e.g. the possibility of filtering the averaged distribution to smoothen it out would probably yield better results. Other nice properties of the velocity domain method include the reduced representation of the signal that is possible. Such representations are ideal for presentation to pattern classification algorithms such as neural networks and clustering algorithms as well as for providing a method for compression of ER data. Finally, calculation of the true set of nerve fibre velocities may lead to new methods for single trial VER extraction based on velocity domain criteria e.g.. if the decomposition of a single trial is sufficiently correlated with the full velocity domain profile then this can be used as an indicator that an evoked response was present.

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