Send Orders of Reprints at reprints@benthamscience.net

The Open Cybernetics & Systemics Journal, **2013,** *7,* **11-22** **11**

Open Access

Dynamics of the Eyeblink EMG at Global and Microscopic Scales

Dmitriy Melkonian[*,1,2] and Terry D. Blumenthal[3]

[1]*Western Clinical School, University of Sydney, North Paramatta, NSW 2151, Australia*

[2]*Kaoskey Pty Limited, 3 Central Avenue, Thornleigh, NSW 2120, Australia*

[3]*Department of Psychology, Wake Forest University, Winston-Salem, NC 21709, USA*

Abstract: Eyeblink electromyogram (EMG) is a noninvasive and reliable tool for evaluating information processing at different levels of the central nervous system.The recently developed method of fragmentary decompositioncreates the model of a single trial eyeblink EMG as the series of consecutive, partly overlapping components, with the generic mass potential being the basis element. Here we express this model in terms of underlying cellular processes. To our knowledge, this is the first study where the dynamics of a mass potential at global scale is deduced from a stochastic particle model of the ion movements at microscopic scale. We consider generation of the eyeblink EMG as a stimulus-induced creation of an extracellular dipole by the movements of ions at the microscopic scale. These processes are described in terms of an equivalent circuit which is composed of novel circuit elements named sourceoid, sinkoid, and dipoloid. The corresponding equations are formulated in terms of nonhomogeneous birth-and-death processes. The theory brings together the deterministic and stochastic factors underlying the genesis of eyeblink EMG with the minimum number of free parameters. No matter how complex are the particle systems, just a few global scale parameters accumulate essential aspects of microscale activities which appear as significant variables at the global scale. Numerical experiments revealed that the mass effect of multiple elementary dipoles is expected to settle down into a behavior that qualitatively remains unchanged at different levels of a volume conductor. We summarize these findings as the principle of the conservation of the mass potential distributions.

Keywords: Fragmentary decomposition, generic mass potential, birth-and-death process, equivalent circuit, sourceoid, sinkoid and dipoloid.

1. INTRODUCTION

The startle reflex is a brainstem response to a sudden stimulus, such as a sound, a flash of light, a tap to the forehead, a puff of air to the side of the face, or an electrical pulse to the forehead [1]. The most common measure of the eyeblink response in human studies is the EMG from surface electrodes placed on the skin overlaying the orbicularis oculi [2]. Eyeblink EMG is an indicator of motor unit action potentials that are caused by activity of the facial nerve (CN7) [3].

As a noninvasive and reliable tool for evaluating information processing at different levels of the central nervous system, eyeblink EMG has been used in a wide variety of research and clinical applications in humans, to study basic stimulus processing [4-6], attentional factors [7, 8], emotion [9], personality variables [10], and dysfunction in clinical populations [11].

However, interpretation of EMG waveforms is largely empirical, and so an explicit mathematical model of their generation would be of great value. The major problem in modeling of the cellular sources of surface EMG is how to deal appropriately with the functional complications posed by the multiplicity of underlying muscle cells. In this context the numerical simulations of single cells are not feasible, as the number of functional elements required is too high and the details of cellular machinery are too intricate.

In order to avoid the large number of microscale variables it is necessary to distinguish those aspects of cellular machinery that are significant on the global scale from those that are not. In the context of this problem, the model based signal processing method of fragmentary decomposition provides a means to decompose the eyeblink EMG into a series of consecutive, partly overlapping transient potentials, each of which may be associated with a specific cellular ensemble underlying generation of positive or negative deflections (peaks) in the EMG waveform [12-14]. An appealing feature of this approach is its conceptual consent with current methods of eyeblink quantitative evaluation, which regard "peak" as synonymous with a functional component of the measured potential [2]. Almost without exception, EMG quantification is performed by different peak picking procedures that identify and measure the peak amplitude relative to either a point of onset or the mean of a baseline period [1]. A critical limitation of peak picking procedures is that reduction of EMG to peak amplitudes and latencies at isolated time points is unable to

*Address correspondence to this author at the Western Clinical School, University of Sydney, North Paramatta, NSW 2151, Australia;
Tel: +61-2-82677302; Fax: +61-2-92645154;
E-mail: dmitri@med.usyd.edu.au

1874-110X/13

characterize the waveform dynamics which may possess important functional and cognitive information.

By contrast, the technique of fragmentary decomposition regards a functional component of eyeblink EMG as being not just a peak in the waveform, but a whole deflection (positive or negative) described by the model termed as the generic mass potential (GMP). The parameters of GMPs are estimated by the time-frequency analysis of each peak in the time course of single trial EMG. A very satisfactory agreement of numerical solutions with empirical data suggests the GMP as an adequate component from which an eyeblink EMG is composed [13].

Physically, the GMP may be regarded as a summary global scale effect of intermittent synchronization of specific ensembles of the muscle cells in a local conductance volume. Preliminary analysis suggests that modeling of this form of collective behaviour of muscle cells necessitates an account of statistical properties of relevant cellular processes [12, 13].

The study we present here was performed in an attempt to support the global scale model of an eyeblink EMG in terms of GMPs by the physically tractable models of relevant cellular machinery. The emphasis is on identifying the critical cellular processes underlying the genesis of the GMP and, accordingly, the functional waveforms.

2. STATISTICAL THEORY OF AN ELEMENTARY DIPOLE

2.1. Generic Mass Potential

A single-trial eyeblink EMG is a mass action potential, referred to in the following text as a mass potential that develops as a succession of positive and negative deflections (peaks) generally accepted as functionally meaningful components.

Fig. (**1**) illustrates three single-trial EMGs recorded in different trials. It is clear that the general pattern of reaction, including the timing and amplitude of components, substantially varies between trials. Consequently, single trial EMGs recorded in different trials, $u^1(t),...,u^k(t),...,u^K(t)$ (superscript k indexes a particular single trial), may be regarded as realizations of the non-stationary random process **u**(t).

The method of fragmentary decomposition [14] provides a means to express single trial EMG as the sequence of consecutive, partly overlapping components of the following form

$$u^k(t) = \sum_{i=1}^{N_k} g_i^k(t), \qquad (1)$$

where $g_i^k(t)$ is a GMP, and N_k is the number of GMPs identified at the *k*th trial.

The GMP is defined economically by the set of three parameters: κ_i^k (amplitude constant), ρ_i^k (shape constant), and ψ_i^k (onset time), in the form

$$g_i^k(t) = \kappa_i^k \cdot \mathrm{bud}\left[\left(t-\psi_i^k\right)/\rho_i^k\right], \qquad (2)$$

where

$$\mathrm{bud}(t) = \begin{cases} \frac{1}{\sqrt{2\pi}}\left(e^{-(t-1)^2/2} - e^{-(t+1)^2/2}\right) \text{ at } t \geq 0 \\ 0 \quad \text{at} \quad t < 0 \end{cases} \qquad (3)$$

is a standard GMP.

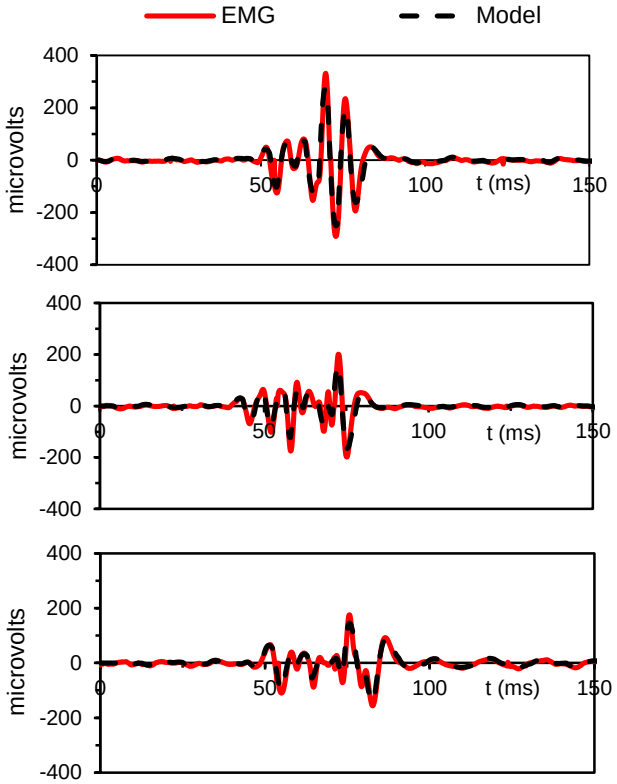

Fig. (1). Three examples of experimental startle eyeblink EMG responses elicited in different trials (redlines), and their model reconstructions (dotted black lines) estimated by the method of fragmentary decomposition. Description of the procedures may be found in the previous work [13].

As illustrated in Fig. (**2**), this function has a steeply rising left flank and a slowly decreasing right flank. The peak value indicated by the vertical dotted line corresponds to t=1.2 at which bud(1.2)≈0.356.

The number of GMPs in (1) and their parameters are specific for each trial. However, independently of the parameters of individual trials, all GMPs may be regarded as elements of the ensemble of self-similar functions. In this context the equation (2) serves as a similarity relationship, and the standard GMP is a basis element.

The self-similarity of eyeblink EMG functional components indicates universal mechanisms of underlying cellular sources. Our key objective is to reconcile the GMP

waveform with the underlying source machinery. A major difficulty is that creation of a quantitative model is a highly under-determined task. The traditional approach consists of the representation of significant elements of the system producing the mass potential by conventional circuit elements and the synthesis, on these grounds, of the global model. In this context, the electrical properties of muscle cells are usually simulated using cable equations as building blocks for formulation of the models of the volume conductor [15]. However, the transition from the global to the microscopic scale using these strictly deterministic notions has no unique solution because it is impossible to exactly delineate a distinctive pattern of the cellular and molecular phenomena involved. In the face of such uncertainty, numerous efforts to create models of the cellular machinery that gives rise to the mass potentials are supported by a remarkable variety of heuristic approaches that differ widely not only in physiological and anatomical details of the models, but also in the basic mathematical tools. The extent to which the models are in contradiction is unknown.

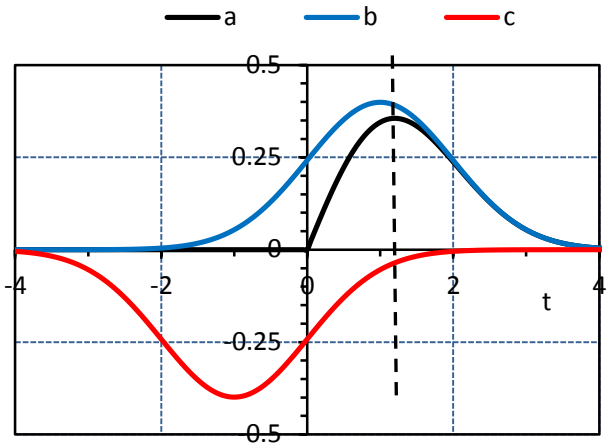

Fig. (2). The standard GMP (curve a) is defined at t≥0 as the sum of shifted positive (curve b) and negative (curve c) Gaussian functions.

In contrast to deterministic notions of the previous theories of mass potentials, our approach takes account of the variability of the cellular sources as a factor that may have a significant effect on the development of mass potentials. To support the stochasticity on a phenomenological basis, we refer to the finding of the normalization effect [12], the empirically based evidence that the summary activity of multiple synchronized current sources may reflect statistical regularities which are independent of the physical nature of the source machinery. In this context, we become involved in a joint consideration of deterministic and stochastic processes underlying the generation of mass potentials. The deterministic aspects of the theory are concerned essentially with the physical conditions underlying the creation of extracellular dipoles. We approach this problem using equivalent circuit concepts of the network theory of external performance.

2.2. Physical Basis of GMP

Physically, we regard the GMP as a mass potential created by an extracellular dipole, the poles of which correspond to different spatial locations. In its most common form, the system in question is indicated schematically in the upper panel of Fig. (**3**), where the "black boxes" A and B are two terminal electrical networks. We consider these networks as the generators of the electromotive forces (EMFs) E_A and E_B at the poles of the dipole, respectively.

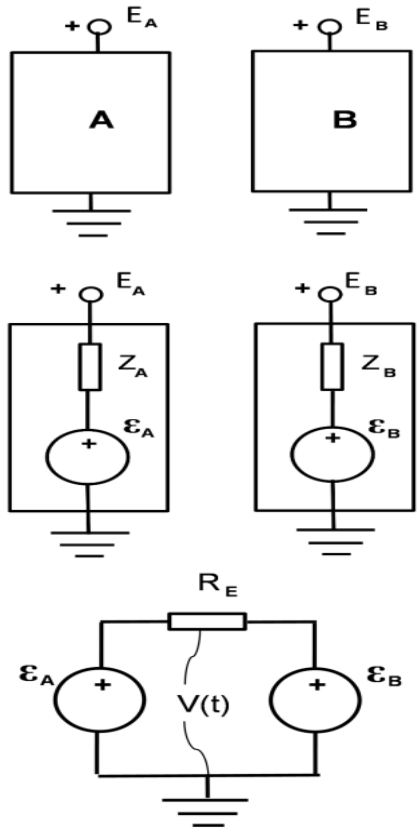

Fig. (3). Schematic overview of the major steps the use of which reduces the sources of the EMFs E_A and E_B at the poles of the dipole to the equivalent circuit with ε_A, ε_B and R_E elements.

In this context, we deal with the external performance of monumentally complex systems of molecular and cellular elements, the machinery of which remains largely an enigma. Obviously, there is no means to delineate exactly the internal structure and function of the networks in question. Despite this, we may address the mass potential in a sufficiently general fashion using the concept of the equivalent circuit: no matter how complex the underlying machinery, from the viewpoint of *any* pair of surface electrodes the network behaves as if it consisted *only* of a source and an impedance [16]. Given two terminal networks A and B, we refer to the circuit equivalents in the form of Thevenin's (voltage-source) equivalent circuits in the middle panel of Fig. (**3**). Z_A and Z_B are the equivalent impedances which are in series with the corresponding sources of equivalent EMFs ε_A and ε_B.

To support the circuit equivalents with a physical basis, we associate the passive circuit elements Z_A and Z_B with a volume conductor created by the extracellular space, and active circuit elements ε_A and $\varepsilon_B$with the machinery of trans-membrane ion pumps which use the energy derived from metabolic processes to move the ions (charged particles) through the cell membrane.

With regard to the passive elements, our approach refers to the following two assumptions, which constitute a widely accepted basis of the theories of field potentials [17]. First, extracellular space is electrically isolated from intracellular space by the cellular membrane, which has high resistance compared with the resistance of the extracellular and intracellular space. Second, within the range of frequencies of physiological interest, capacitive, inductive, magnetic, and propagative properties of the extracellular medium can be neglected.

The first assumption defines the volume conductor as a specific system the electrical parameters of which may be treated separately from the parameters of the cell membrane and cytoplasm. The second assumption means that *quasi-static* conditions apply to the volume conductor created by the extracellular space, i.e. the volume conductor is purely resistive. Consequently, at a given instant in time, the voltage-current relationships correspond to those found under static conditions. This allows us to consider Z_A and Z_B as ideal fixed resistors, the resistance values of which are constant across time. We denote these entities by R_A and R_B, respectively.

By exactly the same reasoning as above, we may regard the volume conductor through which the current flows between the poles of the dipole as a resistor with the time invariant resistance value R_{AB}. On these grounds we present the major elements generating the mass potential in the form of the equivalent circuit depicted in the lower panel of Fig. (**3**), where $R_E = R_A + R_B + R_{AB}$. Here, the equivalent resistance R_E is a time invariant parameter. Therefore, to treat the mass potential as a function of time, we must consider both EMFs as the functions of time, $\varepsilon_A(t)$ and $\varepsilon_B(t)$, respectively.

Physically, R_E is a circuit equivalent of the volume conductor, the two points of which serve for recording of the mass potential in question. Taking one of the points as the ground of the system, the mass potential is indicated in the lower panel of Fig. (**3**) as the voltage V(t), the potential difference between the points of recordings.

In terms of EMFs, $V(t) = k\left(\varepsilon_A(t) - \varepsilon_B(t)\right)$, where k is a dimensionless coefficient the value of which may range from 0 to 1.

Our goal in the next sections is to construct microscale models of particle systems, the external performances of which are consistent with the global scale circuit model of a mass potential considered above.

2.3. Stochastic Ion Compartment

The cellular processes which create different charges at the spatial locations corresponding to the poles of the dipole are associated with the movements of ions, both positively and negatively charged particles, which cross the cell membrane in both directions.It is realistic to regard a thin layer distributed over the entire exterior membrane surface as the container of ions that were released from the cell and have the possibility to cross the membrane in the opposite direction, i.e. to return to the interior of the cell.Let us divide this layer into small volume elements of equal size, each termed a stochastic ion compartment (SIC). Such compartment normally contains both positively charged ions (cations) and negatively charged ions (anions).

Let integer-valued random variables $\mathbf{N}_+(t)$ and $\mathbf{N}_-(t)$ measure at time *t* the numbers of cations and anions, respectively. From the point of view of a distant point in the extracellular medium, the SIC can be envisaged as having a positive charge if $\mathbf{N}_+(t)>\mathbf{N}_-(t)$, or a negative charge if $\mathbf{N}_+(t)<\mathbf{N}_-(t)$. The net charge of the SIC is proportional to the $\mathbf{X}(t)= \mathbf{N}_+(t)-\mathbf{N}_-(t)$. Let the constant ν be the value of the voltage produced at the extracellular point of interest by an elementary charge. Then, the summary EMF produced by the SIC may be expressed in the form $\varepsilon(t) = \nu \cdot \mathbf{X}(t)$. Therefore, the estimation of the EMF dynamics is reduced to the study of the particle population described by $\mathbf{X}(t)$.

Given the complex nature of molecular mechanisms underlying the time evolution of $\mathbf{X}(t)$, we need to avoid detailed description of the internal processes responsible for changes in the population size.We address this problem using the theoretical framework of stochastic models of the quanta turnover developed in the context of the theory of chemically mediated synaptic transmission [18, 19]. The theory describes the time evolution of the quanta (neurotransmitter particle) population in terms of the postulated probabilities of elementary trans-membrane particle transfers occurring in a small interval of time. Using this approach, we regard SIC as a container of $\mathbf{X}(t)$ identical particles that leave or enter the compartment according to a probabilistic mechanism. After the manner of [20], we describe the particle population in terms of the birth-and-death process (BDP). In this context, the BDP is a continuous time Markov process the state of which at time t is defined by the number of particles $\mathbf{X}(t)$.

Conceptually, a Markov process is the probabilistic model of a physical process, where the future development depends on the present state, but not on the manner in which the present state has emerged from the past [21]. This property considerably simplifies the mathematical analysis of stochastic processes, but the theory remains pertinent to various applications, particularly the modeling of the performance of different kinds of *ion channels* [22]. This and relevant studies of membrane channels address such problems as the probabilities of opening and closing of various types of ion channels, and the distributions and

variance of the timing of the corresponding events. A central assumption is that transition of ion channel from one state to another is a constant, independent of time [23].

Our preference for particular classes of Markov processes defined as BDPprovides a new approach to the treatment of ion transport mechanisms which extends the modelling capabilities in two aspects. First, instead of distinct entities such as a single ion channel, we deal with ensembles of ions, the particle populations with specific functional abilities to create extracellular EMFs. Second, the physical processes underlying the time evolution of particle populations can be treated in terms of the transition probabilities that are permitted to vary in time (nonhomogeneous BDP).

Since inter-state transitions are governed by probabilistic mechanisms, the future of BDP is not uniquely determined. A major condition is that during a sufficiently small element of time, Δ, the probability of the change of the **X**(t) by more than one particle is negligibly small:

$$\Pr[\mathbf{X}(t+\Delta)=\mathbf{X}(t)+k]=o(\Delta) \quad \text{if} \quad |k|>1, \tag{4}$$

where Pr denotes probability and k is an integer.

Therefore, the particle system changes only through transitions from states to their nearest neighbours. An increase of the population size by a unit represents birth, $\mathbf{X}(t+\Delta)=\mathbf{X}(t)+1$, whereas a decrease by a unit represents death, $\mathbf{X}(t+\Delta)=\mathbf{X}(t)-1$. The probabilities of these events for nonhomogeneous BDP are [21]:

$$\Pr\left[\mathbf{X}(t+\Delta)=\mathbf{X}(t)+1\right]=\lambda(t)\mathbf{X}(t)\Delta+o(\Delta) \quad (\text{birth}) \tag{5}$$

$$\Pr\left[\mathbf{X}(t+\Delta)=\mathbf{X}(t)-1\right]=\mu(t)\mathbf{X}(t)\Delta+o(\Delta) \quad (\text{death}) \tag{6}$$

where $\lambda(t)$ and $\mu(t)$ are the birth and death rates, respectively. We use these general relationships as a framework for the probabilistic treatment of dipole creation. A major step in this regard is to specify the birth and death rates in physical terms.

2.4. Sourceoid and Sinkoid

According to the theory of field potentials, it is well accepted to consider an extracellular dipole as a source and a sink of electrical charge. These components of the dipole must have different spatial locations. Therefore, distinct systems of the source creation may be involved. To support our theory by this physical basis, we introduce the two novel circuit elements named *sourceoid* and *sinkoid*. The circuit representations of these elements are given in the upper panel of Fig. (**4**) (the sourceoid is shown at left). The arrows B and D indicate the birth and death processes, respectively.

Both elements are voltage-controlled voltage sources that produce the EMFs $\boldsymbol{\varepsilon}_A(t)$ and $\boldsymbol{\varepsilon}_B(t)$, respectively. Using the probabilistic notions considered above, we describe these EMFs in terms of BDPs $\mathbf{X}_A(t)$ and $\mathbf{X}_B(t)$ which develop in SICs at different spatial locations indexed by subscripts "A" and "B". The assumption is that

$$\varepsilon_A(t)=\nu\cdot\mathbf{X}_A(t) \text{ and } \varepsilon_B(t)=\nu\cdot\mathbf{X}_B(t).$$

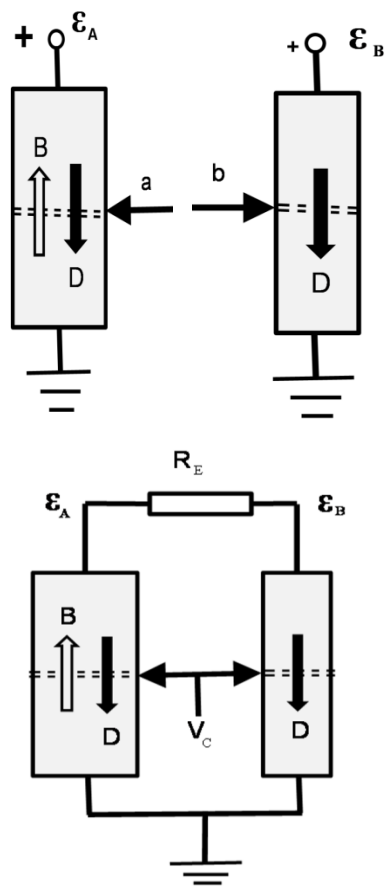

Fig. (4). Circuit representations of the novel circuit elements: soursoid, sinkoid and dipoloid.

We regard performance of the sourceoid and sinkoid in the absence of controlling voltage as the resting conditions. Stimulus application forces simultaneous transition of the sourceoid and sinkoid from the resting to the transient conditions. As a marker of the time instant at which the stimulus is applied, the controlling voltage is described in the form of $V_C(t)=\delta(t-\tau)$, where δ(t) is the Dirac delta function and τ is the time of the stimulus application. Without loss of generality, we assume that τ=0. Therefore, the system is switched from the resting to transient conditions at t=0.

We define the rates of birth and death that govern the corresponding time evolution of $\mathbf{X}_A(t)$ and $\mathbf{X}_B(t)$ by the following rules.

Sourceoid: a non-homogenous BDP with the constant birth rate

$$\lambda_A=1/\mathrm{T} \tag{7}$$

and the time dependent death rate

$$\mu_A(t)=\begin{cases} 1/\mathrm{T} \text{ at } t<0 \\ t/\mathrm{T}^2 \text{ at } t\geq 0 \end{cases} \tag{8}$$

where T is a time constant.

Sinkoid: a non-homogenous BDP with the time dependent birth rate

$$\lambda_{\mathrm{B}}(t)=\begin{cases} 1/\mathrm{T} \text{ at } t<0 \\ 0 \text{ at } t\geq 0 \end{cases} \tag{9}$$

and the time dependent death rate

$$\mu_{\mathrm{B}}(t)=\begin{cases} 1/\mathrm{T} \quad \text{at} \quad t<0 \\ (t+\mathrm{T})/\mathrm{T}^2 \text{ at } t\geq 0 \end{cases} \tag{10}$$

General solutions of the equations governing non-homogenous BDP $\mathbf{X}(t)$ with the birth and death rates regarded as arbitrary functions of time $\lambda(t)$ and $\mu(t)$ have been developed by Kendall [24]. Given t=0 as the reference point, the mean as a function of time (expected trajectory) has the form

$$\mathrm{m}(t)=\mathrm{E}\{\mathbf{X}(t)\}=\xi \mathrm{e}^{-\rho(t)}, \tag{11}$$

where

$$\rho(t)=\int_0^t [\mu(x)\text{-}\lambda(x)]\,\mathrm{d}x, \tag{12}$$

and ξ is an initial size of the particle population.

We use these equations as a point of departure to obtain the transient solutions on the basis of the introduced birth and death rules (7)-(10).

Solution of (12) for $X_A(t)$ using the birth and death rates defined at t≥0 by (7) and (8) gives $\rho_{\mathrm{A}}(t)=\left(t^2-2Tt\right)/2T^2$ (the subscript indicates the circuit element in question). After replacement of ρ(t) in (11) by this formula, we obtain the mean trajectory of $\mathbf{X}_{\mathrm{A}}(t)$ at t≥0 in the form

$$\mathrm{m}_{\mathrm{A}}(t)=\xi \mathrm{e}^{-\rho_{\mathrm{A}}(t)}=\sqrt{\mathrm{e}}\cdot\xi\cdot \mathrm{e}^{-\frac{(t\text{-}\mathrm{T})^2}{2\mathrm{T}^2}}. \tag{13}$$

An initial value, $\mathrm{m}_{\mathrm{A}}(0)=\xi$, develops under the resting conditions when the particle population behaves as a simple BDP with equal birth and death rates. Thus, $\mathrm{m}_{\mathrm{A}}(t)=\xi$ at $t<0$.

Solution of (12) for sinkoid using the rate of the death from (10) for t≥0 gives $\rho_{\mathrm{B}}(t)=\left(t^2+2Tt\right)/2T^2$. Inserting this formula into (11) instead of ρ(t) gives the mean of $\mathbf{X}_{\mathrm{B}}$(t) at t≥0 in the form

$$\mathrm{m}_{\mathrm{B}}(t)=\xi \mathrm{e}^{-\rho_{\mathrm{B}}(t)}=\sqrt{e}\cdot\xi\cdot \mathrm{e}^{-\frac{(t+\mathrm{T})^2}{2\mathrm{T}^2}}. \tag{14}$$

At t<0 (resting conditions) $\mathrm{m}_{\mathrm{B}}(t)=\xi$.

2.5. Dipoloid

A dipole is produced by coherent performance of the sourceoid and sinkoid, which means that one and the same controlling voltage V_C(t) is applied to both elements. The corresponding circuit composed from sourceoid and sinkoid is depicted in the lower panel of Fig. (**4**). We term this circuit the dipoloid.

The resistance between the poles of the dipole is represented in the circuitry of the dipoloid by the resistor R_E. We regard the corresponding EMF $\varepsilon_{\mathrm{D}}(t)=\varepsilon_{\mathrm{A}}(t)-\varepsilon_{\mathrm{B}}(t)$ as the output function of the dipoloid. Accordingly, the integer-valued random variable $\mathbf{X}_{\mathrm{D}}(t)=\mathbf{X}_{\mathrm{A}}(t)-\mathbf{X}_{\mathrm{B}}(t)$ serves for description of the dipoloid's performance. The mean of this process follows from (13) and (14):

$$\mathrm{m}_{\mathrm{D}}(t)=\begin{cases} \sqrt{e}\cdot\xi\left(\mathrm{e}^{-\frac{(t-T)^2}{2\mathrm{T}^2}}-\mathrm{e}^{-\frac{(t+T)^2}{2\mathrm{T}^2}}\right) \quad \text{at} \quad t\geq 0, \\ 0 \quad \text{at} \quad t<0. \end{cases} \tag{15}$$

The corresponding EMF produced by the dipoloid is $\varepsilon_{\mathrm{D}}(t)=\nu\cdot\mathbf{X}_{\mathrm{D}}(t)$. The mean of this function is compatible with the GMP. The standard GMP (3) is produced by a dipoloid with T=1 and $\xi=\frac{1}{\pi\sqrt{2\pi e}}$. We regard this element as a generic dipoloid which gives rise to different sets of self-similar dipoloids.

2.6. Numerical Simulations

In a manner analogous to [20], we now use numerical simulations to estimate the time evolution of particle population in various trials. The number of particles X(t) is computed step by step for consecutive points $t_i=i\cdot\Delta\,(i=-M,..,0,..,N-1)$, where Δ is a small element of time the size of which should comply with (4). Accordingly, we deal with discrete samples $x_i=\mathrm{X}(t_{\mathrm{i}})$. The time t_0=0 is an instant from which the resting conditions are changed to the transient conditions.

According to the condition (4), the permitted size of the particle population at time t_{i+1} is: $x_{i+1}=x_i+1$ (birth), $x_i=x_i$ (unchanged size) or $x_{i+1}=x_i-1$ (death). We denote the corresponding birth and death probabilities by $\mathrm{p}_{\mathrm{b}}(i)$ and $\mathrm{p}_{\mathrm{d}}(i)$, respectively.

It is clear from (7)-(10) that under the resting conditions the particle populations in both sourceoid and sinkoid behave as simple BDPs with constant rates of birth and death $\lambda=\mu=1/\mathrm{T}$. With reference to (5) and (6), the corresponding birth and death probabilities are:

$$\mathrm{p}_{\mathrm{b}}(\mathrm{i})=\mathrm{p}_{\mathrm{d}}(i)=x_i\Delta/T. \tag{16}$$

Transient performance of the sourceoid develops as a nonhomogeneous BDP. Substituting the birth rate from (7) into (5), and the death rate from (8) into (6), we obtain the following probabilities of particle transitions in $[t_i,t_{i+1}]$ interval:

$$\mathrm{p}_{\mathrm{b}}(i)=x_i\Delta/T,\ \mathrm{p}_{\mathrm{d}}(i)=x_i\Delta^2 i/T^2. \tag{17}$$

With regard to the transient performance of sinkoid, we deal with a nonhomogeneous death process. Given absence

of the birth processes, by substituting the death rate from (10) into (6), we obtain the following probabilities:

$$p_b(i)=0, p_d(i)=x_i\Delta(i\Delta+T)/T^2. \quad (18)$$

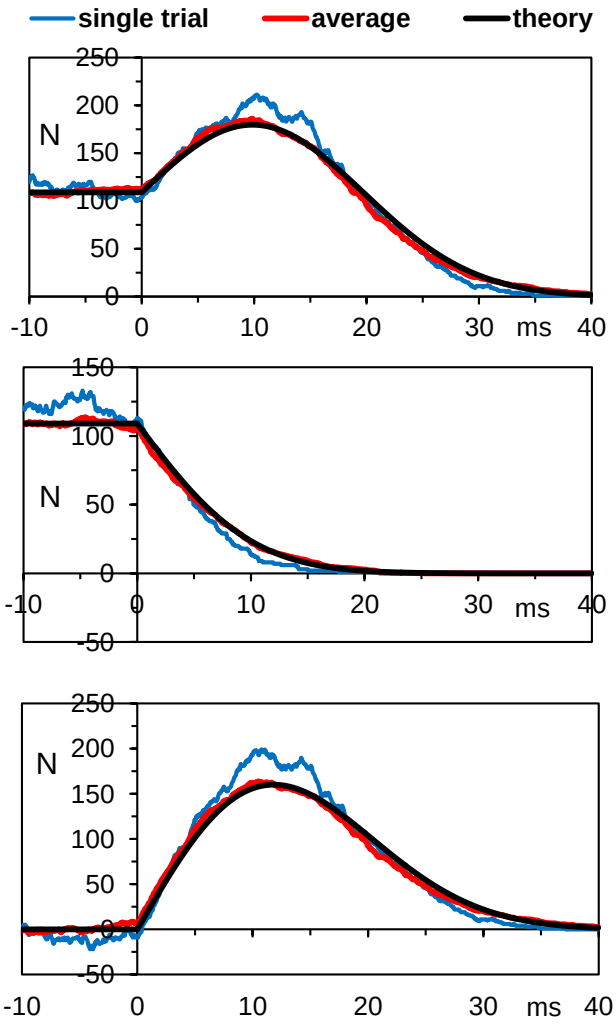

Fig. (5). Result of a numerical simulation that illustrates dynamics of particle populations under the resting and transient conditions. The y-axis units are the numbers of particles.

The calculations were organized as the succession of standard steps dealing with the time intervals $[t_i,t_{i+1}](i=-M,..,0,..,N-1)$. Given the step beginning from t_i, the x_i serves as the initial condition. The value x_{i+1} which **X**(t) takes at the end of the interval was computed using Monte Carlo simulations.

The procedure for each step was as follows:

1. Estimate relevant probabilities $p_b(i)$ and $p_d(i)$ from (16)-(18).
2. Pick out random real numbers R_b and R_d using a random number generator to produce real numbers in the range from 0 to 1.
3. Estimate the size of the particle population at the end of the interval.

$$x_{i+1}=x_i+b-d,$$

where *b* and *d* are binary numbers defined as follows:

$b=1$ if $R_b<p_b(i)$ and is zero otherwise,

$d=1$ if $R_d<p_d(i)$ and is zero otherwise.

Numerical experiments have been supported by a specially designed computer program written in the object Pascal language of Embarcadero Delphi 2010.

Typical results of numerical simulations of single trial samples of $\mathbf{X}_A(t), \mathbf{X}_B(t)$ and $\mathbf{X}_D(t)$ on the interval from -10 to 40 ms are exemplified by Fig. (**5**). An important point is the choice of the value Δ under which the probabilities $p_b(i)$ and $p_d(i)$ are low enough to be consistent with condition (4). Based on a number of numerical experiments with different parameters, the value Δ=0.002 ms was chosen. Consequently, $t_i=i\cdot 0.002$ (ms) where *i* takes values from -5,000 to 20,000. For the sake of illustration the time constant was set to be T=10 ms, a value compatible with the time scale of the signals under consideration.

In the time interval from -10 ms to 0 the particle populations were simulated as simple BDPs with the birth and death probabilities from (16). As an initial condition it was supposed that the sizes of both $X_A(t)$ and $X_B(t)$ at t=-10 ms are equal to N_0=100. The transition from the resting to transient condition was simulated as the change of the resting state probabilities (16) to the transient state probabilities from (17) and (18). This change occurs in a "smooth" fashion without alteration of the basic condition (4). This means that $X_A(0)$ and $X_B(0)$, developed under the resting conditions, serve as the initial conditions for the transient regimes.

To define the limits to which statistical solutions converge, the averages of single trial samples were computed. The red lines in Fig. (**5**) A-C show the averages of ten samples obtained in independent trials. These statistical averages are compared with theoretical solutions provided by analytical formulas (13)-(15). The agreement of numerical and theoretical solutions is very satisfactory and may be regarded as a strong support of computational aspects of our theory.

2.7. Nonlinear Dynamics of GMP

Conventional circuit theoretical approach uses the time domain description of a dynamic circuit element in the form of an impulse function, i.e. the circuit response to the application of a delta impulse. Conceptually, the impulse function is a deterministic transient. Accordingly, we associate impulse functions of novel circuit elements with deterministic trends, the means or expected trajectories of stochastic processes $\varepsilon_A(t), \varepsilon_B(t)$ and $\varepsilon_D(t)$ after application of controlling voltage, i.e. at t≥ 0. In this context, we refer to (12)-(14), and define impulse functions of sourceoid, sinkoid and dipoloidas $g_A(t)=\nu\cdot m_A(t), g_B(t)=\nu\cdot m_B(t)$ and $g_D(t)=\nu\cdot m_D(t)$, respectively.

Given the impulse function in the form of a deterministic solution (15), we present the description of underlying dynamic system in terms of the following system of nonlinear differential equations:

$$\dot{g}_A(t) = -\frac{t-T}{T^2} g_A(t), \quad (19)$$

$$\dot{g}_B(t) = -\frac{t+T}{T^2} g_B(t), \quad (20)$$

$$g_D(t) = g_A(t) - g_B(t), \quad (21)$$

where $\dot{g}_A(t), \dot{g}_B(t)$ and $\dot{g}_D(t)$ denote the derivatives of the corresponding impulse functions.

The form of these equations allows us to qualify the system as a nonautonomous system; that is, a system driven by time-varying signals.

3. MASS EFFECT OF MULTIPLE ELEMENTARY DIPOLES

3.1. Simulations of Mass Action Effects

The role of deterministic trends in statistical samples increases with the increase in the number of particles involved. Single trials shown in Fig. (**5**) develop from initial populations of 100 particles. A tenfold increase of N_0 to 1000 significantly reduces variability and brings single trial samples to a closer agreement with expected trajectories. On purely theoretical grounds we may regard the bell-shaped waveform (15) as the limit to which the transients converge with an infinite increase in the size of the population.

The important point that we wish to stress is that model parameters must be consistent with the physics of the underlying processes. A free parameter that allows us to keep the values of probabilities at low levels is the sampling interval Δ. Physically, the value of this parameter should be compatible with the time interval that is necessary for an ion channel to change its state; this event allows an ion to move through the membrane. Since such a transition usually takes a fraction of a millisecond, the value Δ=0.002 ms used in the simulations above may be regarded as a sensible estimate. However, the corresponding size of the particle population (100-200 units) is small compared with an actual number of ions participating in the trans-membrane transport processes. Even in the case of a single cell, the number of excitable channels is estimated to be large (on the order of tens of thousands of ion channels). To keep the birth and death probabilities at reasonably low levels in the case of such large particle populations, we need to reduce Δ to physically unrealistic values.

To approach the problem in a physically acceptable way, we divide the whole particle population into sub-populations with equal initial sizes and time constants. Under these conditions, we actually deal with the same realizations of relevant stochastic process as those reproduced in numerical experiments. Indeed, note that the red lines in Fig. (**5**) are the averages of 10 independent samples of stochastic processes produced by a single particle population. We could just as well interpret these results as the averages of single trial samples produced by 10 independent populations with equal parameters.

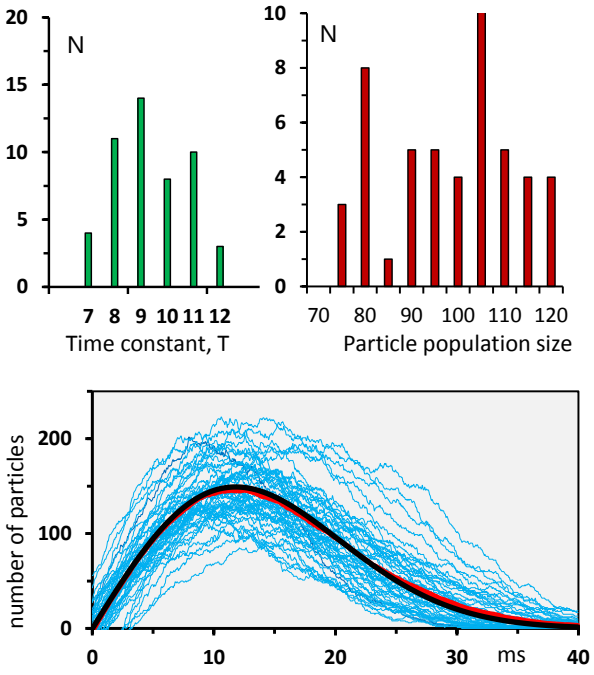

Fig. (6). Result of numerical simulations of 50 particle populations with different ξ (initial size of particle population) and T (time constant) parameters. The histograms show the distributions of these parameters. The blue curves show the time evolution of individual populations. The average of these traces is shown by the red line. The black line is the theoretical solution suggested by the principle of the conservation of the mass potential distributions.

Typical results, illustrated by Fig. (**6**), deal with the model composed of 50 sub-systems with different parameters. The minimum and maximum values of parameters were 7.6 and 12.5 ms (mean 9.83 ms) for the time constants, and 77 and 123(mean 102) for the initial size of the population at t=0. The parameter distributions between these extremes are illustrated by the histograms.

Being supported by exactly the same simulation technique as above, Fig. (**6**) refers to the single trial samples of $\mathbf{X}_D(t)$. Given the parameter values indicated by the histograms, each of the 50 systems under analysis is presented by a single sample. The red line is the average of these traces. The black line is the expected theoretical solution $g(t) = \bar{\xi}_0 \, \mathrm{bud}(t/\bar{T})$, where $\bar{\xi}_0$ and $\bar{T}$, are the means of ξ_0^k and T^k parameters; $\bar{\xi}_0 = 102$, $\bar{T} = 9.83$ ms.

This and similar numerical experiments show that differences in the sizes of particle populations and time constant T do not affect the form of statistical solutions from the microphysical scale to the global level.

3.2. Postulated Effects of the Mass Action

The essential outcome of numerical simulations is that the mass effect of multiple elementary dipoles, all produced in the same way by synchronously activated dipoloids with different parameters, is expected to settle down into a

behavior that essentially remains unchanged with regard to the general rules (7)-(10), that govern the performance of the dipoloid. This result may be viewed from various angles, and here we shall consider it as the heuristic basis for the following hypotheses.

Principle of the conservation of the mass potential distributions (CMPD). Let dipoloid with T_i and ξ_i parameters be characterized at a certain extracellular location by EMF $\varepsilon_D^i(t)$. At the same location, the cumulative effect of the EMFs $\varepsilon_D^1(t),...,\varepsilon_D^i(t),...,\varepsilon_D^N(t)$ from N synchronously activated distinct dipoloids is equal to the EMF of a single dipoloid with the following parameters:

$$T_E = \frac{1}{N}\sum_{i=1}^{N} T_i, \quad \xi_E = \frac{1}{N}\sum_{i=1}^{N} \xi_i$$

This principle differs drastically from conventional deterministic treatment of mass potentials in that, whereas previous theories assume that the global scale activity is an algebraic sum of the outputs of elementary cellular generators, the above principle denies this possibility, the prime factors being the spreads of the probability distributions of elementary sources.

According to the deterministic framework, the surface EMG is produced by linear summation of the membrane potentials of the contributing muscle fibres [25]. Suppose that the number of parameters in the cable model chosen for a fiber simulation is M. Therefore, for simulations of J fibers, the global model must include J cable equations, and contain JM free parameters. In this context, the extension of the range and number of microscale biophysical and biochemical parameters leads to an enormous increase in the number of model elements. This is a highly under-determined task. Actually, the large number of details and free parameters contained in the model can often obscure rather than illuminate the essentials of the underlying physical processes.

By contrast to the deterministic approaches, our theory deals with the summary effect of simultaneously developing stochastic processes with a common statistical distribution following from the defined rules (7)-(10) of the birth and death processes. Probabilistically, the effects of the superposition of stochastic processes relate to a general problem of the limiting behavior of random events. With regard to random variables, the central limit theorem states that any process of random sampling tends to produce a normal distribution of sample values, even if the whole population from which the samples are drawn does not have a normal distribution. This approach deals with time invariant statistical distributions.

Consideration of mass potentials in our theory in terms of random processes introduces time as an additional variable, which suggests that the statistical distributions may be time dependent. Physically, the time dependency of the statistical distributions appears as the result of stimulus application. The corresponding expected trends converge on the transient solution (1) that was suggested in the previous studies as a global model of eye blink EMG.

3.3. A Tentative Multiscale Model of Eyeblink EMG Generation

Eye blink EMG belongs to the category of oscillatory electrophysiological signals. Besides different types of electromyograms, the models of such processes have been widely researched with regard to the electrical activity of the brain [26]. The fundamental question is whether an oscillatory waveform is generated by a single generator, like a harmonic oscillator in physical systems, or a number of relatively independent generators.

Our theory suggests that mass potential is a composite of consecutive monopolar waveforms which may be regarded as an ensemble of self-similar functions with the standard GMP (3) being a basic element. This rejects the existence of specialized oscillatory systems, and allows us to consider the eyeblink EMG as a mass electrical potential produced by the sequence of serially activated cellular networks.

A universal model of single trial EMG has the form of equation (1). The probabilistic basis of our theory views this mass potential as the realization of a stochastic process governed by the introduced equations of non-homogenous BDPs. Though the details of cellular processes to which these results are relevant are not yet clear, the theory provides the means to distinguish those aspects of microscale activities that are significant on the large scale from those that are not.

To approach this problem we should take full advantage of *the principle of the conservation of the mass potential distributions* which takes into account the source variability and its relationship to the functional organization of relevant structures. In this regard, an essential aspect of the geometric cell arrangements is that muscle fibers are organized as muscle units (MUs). In a normal muscle, each MU consists of hundreds of muscle fibers and each muscle consists of multiple MUs. Depending on the type of muscle the actual number of MUs varies, and is typically in the order of 50-250.

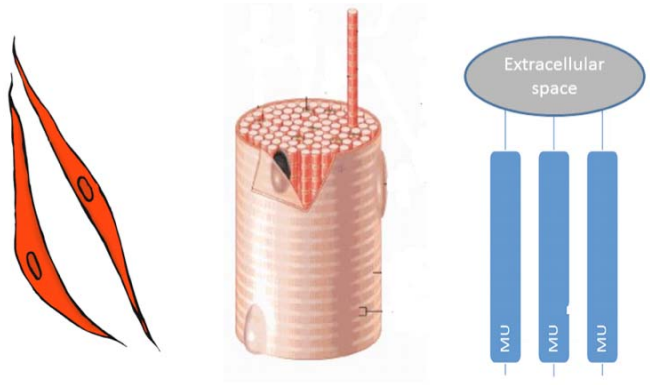

Fig. (7). The functional elements that produce dipoloids at the three stages of the development of surface EMG: muscle fiber, muscle unit, and the volume conductor.

The diagram in Fig. (**7**) provides a schematic summary of the three levels of abstraction of EMG generation. The functional element of the first level is the muscle fiber which is shown schematically at far left. In principle, due to the spatially distributed mechanisms of ion transport, the fiber

may produce multiple dipoles. However, the principle of CMPD allows us to regard a muscle fiber as an elementary dipole, i.e. the summary of multiple ionic mechanisms in the form of an equivalent dipoloid.

The next diagram shows muscle fibers aggregated into a muscle unit. A crucial role of the principle of CMPD at this level of abstraction is that its application to relevant muscle fibers reduces their summary effect to a single dipole. Accordingly, the parameters of multiple fibers are transformed into the equivalent parameters of a single dipoloid which serves as a model of the MU.

The third diagram shows a chain of distinct MUs the summary potential of which is recorded at a certain point in the extracellular space. We propose that the process underlying the model (1) consists of the stimulus-induced activation of different MUs in successive instants in time. The essential logic is that each GMP is produced by MU, and demands a large degree of synchronization of MFs that compose MU. In terms of the equations (1) and (2), the process of synchronization of the fibers composing the *i*thMU starts at the time instant ψ_i^k (*k*th trial) beginning from which the MU generates transient extracellular current. This current, together with that generated by other MUs, sets up a field of extracellular current flow. Since the extracellular space performs as a purely resistive volume conductor, the corresponding transient voltage develops as the sum of the MU voltages, i.e. has the form of the model (1).

The reference to the synchronized activity of muscle fibers does not imply that at particular MU the activity of one fiber is a replica of the other. The differences in synchronization scenarios among the MFs mean that the summed activity of MU is governed by both deterministic and probabilistic factors, an ample account of which is provided by the equations of the dipoloid and the principle of CMPD. The adequacy of these concepts is directly supported by the results of experimental identification of the GMP as an adequate building block of an eyeblink EMG [12-14]. A satisfactory degree of agreement of theoretical and experimental data are illustrated in Fig. (**1**) by typical modeling results. The dotted lines show graphs of the model eyeblink EMGs identified in terms of the equation (1) using the technique of high resolution fragmentary decomposition.

Given the eyeblink EMG in Fig. (**1**) A, the curve in the upper panel of Fig. (**8**) shows the fragment of the corresponding EMG and the model in the time interval from 65 to 90 ms. The waveform deflections indicated by the numbers from 1 to 5 correspond in the model to the five consecutive GMPs. These elements of the fragmentary decomposition are shown in the lower panel of the figure.

We wish to draw attention to the fact that appearance of specific forms of stochasticity in the behavior of dynamic systems is often qualified as deterministic chaos. This approach has supported quantitative analysis of different aspects of the ion transport phenomena [27, 28].

The phenomenological framework of deterministic chaos is supported by the theory of non-linear systems. In this regard, the nonlinear dynamics of GMP described by equations (19)-(21) are consistent with the notion that equations of deterministic chaos must be non-linear to generate chaotic solutions, but apart from that can be remarkably simple and have a small number of parameters.

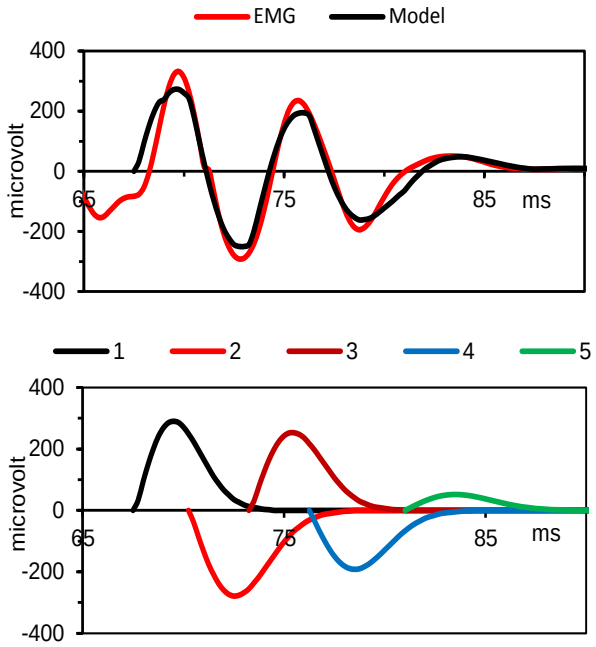

Fig. (8). Typical temporal dynamics of identified GMPs is illustrated using the fragment of the eyeblink EMG from Fig. (**1A**).

Another distinctive feature of the chaos is a short-term predictability. By reference to Fig. (**1**)with different samples of eye blink EMG, we feel that various deflections of this non-stationary signal may appear randomly. In terms of equation (1) this means that onset times ψ_i^k of different GMPs may be regarded as random variables that belong to some range of physically meaningful values of onset times. Therefore, we have no means to predict the exact time of GMP appearance. However, suppose that real time monitoring of the signal indicates the point of the GMP initiation. For example, such judgment may be made on the basis of the measurements of the waveform in the time interval from ψ_i^k to $\psi_i^k + \phi$, where ϕ is the time interval during which the waveform reaches the absolute maximum. On the basis of this information it is possible to evaluate κ_i^k, ρ_i^k and ψ_i^k parameters and make short term predictions of expected signal trajectory after reaching the peak.

This relevance of our theory to deterministic chaos suggests the possibility of enriching the methods employed by a number of recently developed mathematical tools of nonlinear dynamics analysis, for example to implement the formalism of fractal and self-similar geometrical objects. We hope to present a comprehensive consideration of these issues in a separate publication.

4. CONCLUSIONS

As we demonstrate in this paper, a wide range of monolithic deflections identified in the time course of eyeblink EMG may be qualified as self-similar processes

that resemble a geometric form of a standard GMP. Rather than a continuous process, the EMG develops as a series of consecutive, partly overlapping self-similar GMPs, each of which is produced through intermittent synchronization of specific ensembles of muscle cells in a local conductance volume.

Previous theories of different types of EMG signals have been supported by deterministic models. To our knowledge, the description in our theory of the particle movements in terms of non-homogenous BDPs for the first time puts the randomness and determinism in the generation of extracellular dipoles on a common theoretical framework, supported by the introduction of specific circuit elements termed the sourceoid, sinkoid, and dipoloid. These novel models of the cellular sources of electricity not only predict how the extracellular potential evolves over time, but also do this with the minimum number of degrees of freedom. No matter how complex are the systems of ion transport producing the GMP, from the viewpoint of the global scale, a single set of just three parameters, $\langle \kappa, \rho, \psi \rangle$, accumulates all essential aspects of the dynamics of the potential. Being generalized by the statement of the principle of the conservation of the mass potential distributions, this paradigm may be associated with the presence of the Gaussian distribution in the GMP equation. The normal (Gaussian) distribution is well known as the most important probability distribution in the field of probability and statistics because, in accordance with the central limit theorem, any process of random sampling tends to produce a normal distribution of sample values, even if the population from which the samples are drawn does not have a normal distribution. A single Gaussian distribution is not suitable to account of the temporal changes in the system from which the samples come. In the context of non-homogenous BDPs, a specific combination of two Gaussian distributions describes how the mean size of the particle population evolves over time. It is difficult to escape the conclusion that a standard GMP may be regarded as a time dependent statistical distribution relevant to a specific class of physiological processes.

CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

ACKNOWLEDGEMENTS

Declared none.

REFERENCES

[1] W. K. Berg, and M. Balaban, "Startle elicitation: Stimulus parameters recording techniques and quantification", In: *Startle modification: Implications for neuroscience, cognitive science, and clinical science*, M. E. Dawson, A. Schell, and A. H. Böhmelt, (Eds.), Cambridge University Press: New York, 1999, pp. 21-50.

[2] T. D. Blumenthal, B. N. Cuthbert, D. L. Filion, O. V. Lipp, A. van Boxtel, and S. Hackley, Committee report: "Guidelines for human startle eyeblinkelectromyographic studies", *Psychophysiology*, vol.42, pp.1-15, February 2005.

[3] M. Davis, D. L. Walker, and Y. Lee, Neurophysiology and neuropharmacology of startle and its affective modification, In: M. E. Dawson, A. M. Schell, A. H. Böhmelt (Eds.), *Startle modification: Implications for neuroscience, cognitive science, and clinical science*, Cambridge University Press: New York, 1999, pp. 95-113.

[4] T. D. Blumenthal, "Prepulse inhibition of the startle eyeblink as an indicator of temporal summation", *Percept. Psychophys*. vol. 57, pp. 487-494, June 1995.

[5] T. D. Blumenthal, "Short-lead-interval startle modification", In: *Startle modification: Implications for neuroscience, cognitive science, and clinical science*, M. E. Dawson, A. Schell, and A. Böhmelt, Eds., Cambridge, University Press: New York, 1999, pp. 51-71.

[6] A. J. W. Boelhouwer, R. J. M. A. Teurlings, and C. H. M. Brunia, "The effect of an acoustic warning stimulus upon the electrically elicited blink reflex in humans", *Psychophysiology*, vol. 28, pp. 133-139, March 1991.

[7] D. L. Filion, M. E. Dawson, and A. M. Schell, "Modification of the acoustic startle-reflex eyeblink: A tool for investigating early and late attentional processes", *Biol. Psychol*., vol. 35 pp. 185-200, June 1993.

[8] L. W. Hawk, J. S. Redford, and J. S. Baschnagel, "Influence of a monetary incentive upon attentional modification of short-lead prepulseinhibition and long-lead prepulse facilitation of acoustic startle", *Psychophysiology*, vol. 39, pp. 674-677, September 2002.

[9] B. N. Cuthbert, M. M. Bradley, and P. J. Lang, "Probing picture perception: Activation and emotion", *Psychophysiology"*, vol. 33, pp. 103-111, March 1996.

[10] J. C. Franklin, N. Heilbron, J. D. Guerry, K. B. Bowker, and T. D. Blumenthal, "Antisocial and borderline personality disorder symptom atologies are associated with decreased prepulse inhibition: The importance of optimal experimental parameters", *Pers. Individ. Dif*., vol.47, pp.439-443, January 2009.

[11] C. Grillon, and J. Baas, "A review of the modulation of the startle reflex by affective states and its application in psychiatry", *Clin. Neurophysiol*. Vol. 114, pp. 1557–1579, September 2003.

[12] D. Melkonian, T. D. Blumenthal, and E. Gordon, "Numerical Fourier transform spectroscopy of EMG half-waves: Fragmentary-decomposition-based approach to nonstationary signal analysis", *Biol. Cybern*., vol. 81, pp. 457-467, November 1999.

[13] T. D. Blumenthal, and D. Melkonian, "A model based approach to quantitative analysis of eyeblink EMG responses", *J. Psychophysiol*. vol. 17, pp. 1-11, January 2003.

[14] D. Melkonian, T. D. Blumenthal, and R. Meares, "High resolution fragmentary decomposition – a model based method of non-stationary electrophysiological signal analysis", *J. Neurosci. Methods*, vol. 131, pp. 149-159, December 2003.

[15] L. Mesin, and D. Farina, "An analytical model for surface EMG generation in volume conductors with smooth conductivity variations", *IEEE Trans. Biomed. Eng*. vol. 53, pp. 773-779, May 2006.

[16] D.H. Johnson, "Origins of the equivalent circuit concept: The current-source equivalent", *Proc. IEEE*, vol. 91, pp. 636-640, September 2002.

[17] R. Plonsey, *Bioelectric Phenomena*, McGraw-Hill: New York, 1969.

[18] D. Melkonian, "Mathematical theory of chemical synaptic transmission", *Biol. Cybern*., vol. 62, pp. 539-548, June 1990.

[19] D. Melkonian, "Double barrier quantal model of neurotransmitter release", *Neuroreport*, vol. 2, pp. 719-722, November 1991.

[20] D. Melkonian, E. Barin, and H. Bahramali, "Chaotic dynamics of ECG waveforms at global and microscopic scales: theory and applications", *Open Cardiovasc. Med. J*., vol. 5, pp. 16-28, April 2011.

[21] A.T. Bharucha-Reid, *Elements of the theory of Markov processes and their applications*, McGraw- Hill: New York 1960.

[22] M. E. A. Hodgson, and P.J. Green, Investigating Markov model discrimination for ion channels, *Proc. Roy. Soc. Lond. Ser. A*, vol. 455, pp. 3425-3448, October 1999.

[23] D. Colquhoun, and A. G. Hawkes, "On the stochastic properties of single ion channels", *Proc. Roy. Soc. Biol. Sci*., vol. 211, pp. 205-235, March 1981.

[24] D. G. Kendall, "On the generalized "birth-and-death" process", *Ann. Math. Stat*., vol. 19, pp. 1-15, January 1948.

[25] D.F. Stegeman, J.H. Blok, H.J. Hermens, and K. Roeleveld, "Surface EMG models: properties and applications", *J. Electromyogr. Kinesiol*., vol. 10, pp. 313-26, October 2000.

[26] P.L. Nunez, *Neocortical Dynamics and Human EEG Rhythms*, Oxford University Press: New York, 1995.

[27] T.R. Chay, and J. Rinzel, "Bursting, beating, and chaos in an excitable membrane model", *Biophys. J.*, vol. 47, pp. 357-366, March 1985.

[28] L. Liebovitch, and T.Toth, "A model of ionchannelkinetics using deterministic chaotic rather than stochastic processes", *J. Theor. Biol*., vol. 148, pp. 243–267, January 1991.

Received: April 29, 2013 Revised: June 3, 2013 Accepted: June 10, 2013