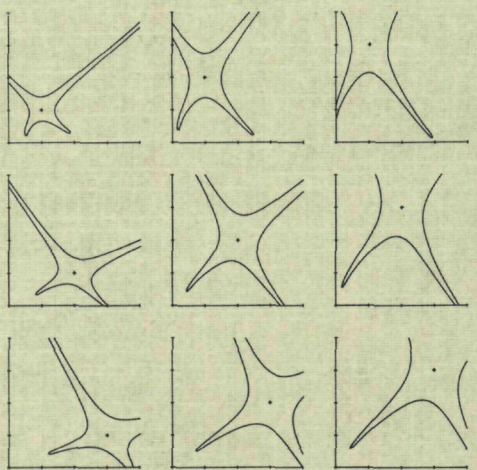

STOCHASTIC NEURAL ACTIVITY
a theoretical investigation

P. I. M. Johannesma

STOCHASTIC NEURAL ACTIVITY

A THEORETICAL INVESTIGATION

PROMOTOR PROF DR A J H VENDRIK

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PROEFSCHRIFT

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A C K N O W L E D G E M E N T

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D A N K Z I J M I J N O U D E R S,

D A N K Z I J C O N S T A N C E.

A B S T R A C T

The activity of a neuron subjected to an input of many small excitatory and inhibitory pulses is analysed. The theoretical model consists of a linear or nonlinear first order system followed by a threshold. Diffusion equations for the transition probability density of the somatic potential are derived.

Analytical results for the stationary activity include expressions for the stationary distribution of the somatic potential and for the moments of the distribution of intervals between action potentials. Applications and numerical data are given for three specific models: an integrator, an imperfect integrator and an equivalent circuit for the membrane, each combined with a threshold. Linear regions of the input-output characteristics are indicated.

The dynamical aspects are discussed in more general terms. A relation between the stochastic switch-response and the expectation density is derived. For small variations of the input a dynamical description is given on the base of a region-dependent stochastic transfer matrix. A general form of stationary and a linearised version of dynamical interaction equations for an ensemble of neurons are proposed.

S T O C H A S T I C N E U R A L A C T I V I T Y

A THEORETICAL INVESTIGATION

P R O L O G U E

1.1 PROBLEM AND MOTIVATION.

Experimental studies of the neural cell have supplied a wealth of data which continues to grow at an increasing rate. Admirable theoretical analyses of the experimental results have been given. A large amount of knowledge exists concerning different aspects of the neuron. Synaptic transmission, decremental conduction in dendrites, the nonlinear properties of the membrane generating the action potential and the propagation of this signal along the axon have all been intensively studied and described. Up till now, however, no theoretical description exists in which these data have been integrated into a model of the signal transmission properties of the neuron as a whole. The same situation exists with regard to neural networks. A large amount of experimental data, but a lack of adequate theoretical concepts and methods for analysis and comparison of these data. It is evident that these two problems, though not identical, are related. If an acceptable formulation of the properties of a single cell could be found, this might serve as a starting point for the theory on networks.

Early theoretical work on neural activity was done by McCulloch and Pitts (1943). They considered a neuron as a logical threshold device with an input of positive or negative unit-impulses, synchronised by an external clock. When the sum of simultaneously arriving excitatory pulses exceeded the threshold and no inhibitory pulse was present, an output pulse was created. An important result was the conclusion that any complete logical expression could be implemented by a network of these elements.

An extension of this work was formed by the study of the possibility of reliable computation using networks consisting of unreliable elements. This problem, first treated by Von Neumann (1956), was extensively analysed by Winograd and Cowan (1963). They were able to extend the coding theorem of Shannon (1948), which treats the transmission of information through a noisy channel, to the computation of information in an automaton with unreliable elements and/or false interconnections. Under the assumption that the probability of malfunction of an element is independent of its complexity it is shown that an arbitrarily high reliability of the network may be reached by a distribution of functions over the elements and a diversification of the computational properties of each element.

The resulting network is a logically distributed system of multiple interconnected and highly complicated elements.

A development towards the incorporation of more realistic properties of the neuron also took place. McCulloch (1957) gave already a more flexible formulation of his model: arbitrary values for excitatory and inhibitory pulses, linear summation of these pulses, afferent inhibition and a variable threshold. A number of different versions by other authors include complete or partial persistence of the effect of pulses until an action potential occurs, synaptic delays and different forms of refractoriness.

Caianiello (1961) formulated his neuronic equations within the framework of this model. Analysis of these equations (Caianiello, De Luca and Ricciardi, 1967, 1968) elucidated the nature of transients and the conditions under which reverberations in these networks occur.

As a whole all these approaches are conceptually related with automata-theory. Mathematically one of the main difficulties is the combination of a continuous description for the somatic potential and the discontinuous threshold condition for spike generation. Physiological shortcomings are the discretisation of time and, usually, a lack of probabilistic descriptions which play such an important role in electrophysiological data from the central nervous system.

A rather different approach to the properties of neural networks is based on a more 'thermodynamical' point of view. In the work of Beurle (1956), Griffith (1963, 1965) and Ten Hoopen (1965) the assembly of cells is regarded as a continuous medium and the active fraction of neurons as a function of space and time is the fundamental variable. An analysis is made of steady states or oscillations of the total activity and the propagation of waves of excitation. This theoretical work appears to be mostly related to experimental data on evoked responses or oscillatory activity of groups of cells as measured with mini-electrodes (tip diameter 0.1-1 mm). A drawback of this description is that up till now no rigorous connection has been made between the dynamics of a single neuron and the equations presenting the activity of the mass of cells.

The reader is referred to Harmon and Lewis (1966) or Reiss (1964) for a general review on neural modeling, both with regard to single cells and to networks, also covering the large amount of investigations by means of sumulation on digital computer or in hardware.

The activity of a single cell in the central nervous system observed with a microelectrode (tip diameter $\sim 1\mu m$) usually contains a stochastic aspect: it is not possible to predict precisely the occurrence of an action potential. Therefore this activity is presented in probabilistic terms. For the stationary activity use is made of the probability density of the occurrence of a spike (average frequency) and of the probability density for the first or an arbitrary spike as a function of time after the occurrence of an earlier one (interval histogram or expectation density). In case of evoked activity the behaviour of a cell is characterised through the probability density of spikes as a function of time after the stimulus (post stimulus time histogram).

A theoretical approach related to these types of data has been propesed by Cowan (1967, 1968). The neural cells are considered as discrete elements; their acitvity is characterised by a function continuous in time, assuming a continuous range of values. This quantity is, essentially, the probability density for the generation of an action potential (event density). A set of nonlinear first order differential equations are postulated to describe the interactions of the cells in the network. Under the condition that the interaction coefficients are ant-symmetric there exists a 'constant of the motion' and the equations can be written in a Hamiltonian form. On this base it is possible to develop by standard methods a 'statistical mechanical' description of the neural net. This theoretical approach appears attractive both with regard to the description of the single-cell properties as for the characterisation of an assembly of a large number of cells.

The aim of this dissertation is an analysis of stochastic input and output signals of a neuron and their interrelation. Moreover, the work is intended as a contribution to the derivation of a continuous type of equation for the description of neural interaction.

After a condensed review of the most relevant biological data in § 1.2, the theoretical viewpoint is presented in § 1.3. When many connections exist between cells, the input to each one is highly complex. This leads naturally

to a stochastic description of the input: average value (m) and power (s^2) emerge as the informationally significant quantities; the other aspects of the signal are obscured by the summation. The behaviour of the somatic potential is described by a first order nonlinear fluctuation equation; diffusion equations result for the transition probability densities. § 1.4 gives some more detailed experimental evidence and a comparison of the model with previous ones.

The stationary activity is analysed in Ch. 2 and Ch. 3. Expressions for the distribution of the somatic potential and for the moments of the distribution of intervals between action potentials are derived in Ch. 2. Applications on more specific models and mumerical data are presented in Ch. 3. The results of this part are such that experimental verification appears feasible. Intra-cellular masurements would supply evidence on the correctness of the invoked assumptions and quantitative tests of the theoretical predictions.

The dynamical input-output relations are much harder to analyse; Ch. 4 is devoted to this subject. Again the detailed properties of the signals are not taken onto account, but attention is focused on the relation between the statistical characteristics: average value and power of the input and event density of the output. Two cases are studied: a stepwise change in the input signal and small variations around a fixed level; the last case leads to the introduction of a region-dependent stochastic transfer matrix. In § 4.4 an attempt is made at the derivation of stochastic interaction equations on the base of the single cell characteristics. Nonlinear stationary and linearised dynamical equations are formulated.

This part of the theory is more of a qualitative nature, no quantitative predictions of experimental results can be given. However, it is possible to design experiments to investigate the applicability of the theoretical description and to measure the properties of the stochastic transfer matrix. A further theoretical and experimental elaboration of this part may, to our view, result in stochastic neural interaction equations of a continuous type.

1.2 THE MORPHOLOGICAL AND PHYSIOLOGICAL BASE

A neuron is a biological cell; its properties are to a large extent determined by the geometrical and functional characteristics of the surrounding membrane. Though there exist several types of neurons, differing both in size and form, a large number of cells in the central nervous system are characterised by the following description.

Morphologically and physiologically the cell consists of three different parts. The soma or cell body contains the nucleus; the axon, an elongated part of the cell, conducts signals away from the soma and may divide into a number of branches; the dendrites form a complicated receptive network with many branches, converging finally on the soma. Types of cells can be characterised by different geometrical structures of these regions and their distribution over the nervous system studied (Ramon-Moliner, 1962; Braitenberg, 1963). In Fig.1.2.1 some types of neurons occurring in the central nervous system are presented.

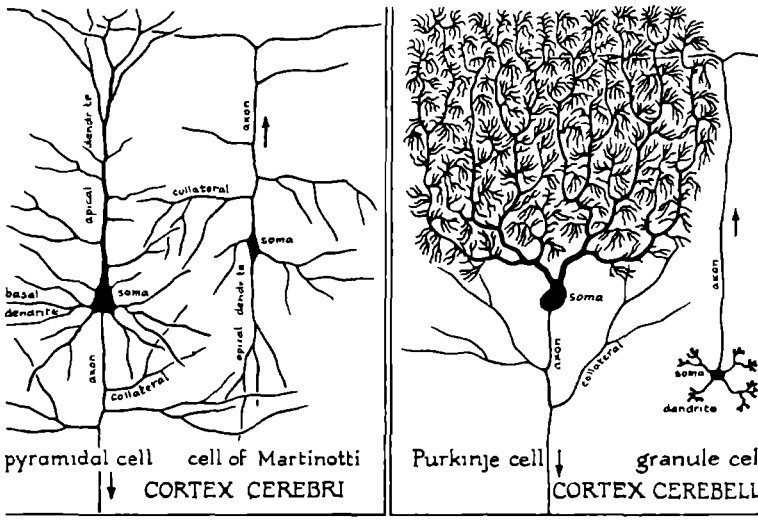


Fig.1.2.1. Some types of neurons in the C.N.S.

Receptor cells and interneurons may be morphologically rather different from cells in the central nervous system, but their functional properties are in many respects analogous.

The synapses are places where axon branches of a neuron seem to touch the dendrites or soma of another neuron. The functional properties of both membranes at the synaptic junctions have been shown to differ from their properties at other places. The number of synapses on cells in the central nervous system is usually more than ten and may be as high as $10^4 - 10^5$.

A basic assumption for the theory, as developed in this paper, is that the processes in which a neuron is involved can be separated in at least two categories:

a. Reception, transformation and emission of signals. This is a relatively fast process and most clearly manifested in electrical phenomena: dendritic and somatic potential, action potential.

b. The relatively slow processes related with long lasting changes in structure and function of the neuron: adaptation, habituation, learning.

This "adiabatic hypothesis" (Caianiello, 1961), usually made implicitly both in theoretical and in experimental work, seems reasonable from a biological point of view; the construction of a mathematical description of neural signal processing is greatly simplified by it. In the following only these physiological aspects are considered which describe the processing of signals by neurons not changing in structure or function.

In the neural cell exists an active metabolism, causing differences in chemical concentrations as well as an electric potential across the membrane. The experimental results for the local dynamical behaviour of the membrane are well described through a set of four coupled nonlinear differential equations: the Hodgkin-Huxley equations. The variables appearing in these equations are the membrane potential and the concentrations of potassium, sodium and of other ions. (For references and review see Nobel (1966) and Kats (1966)). Quantititive analysis is only possible using a computer, qualitative insight is difficult to acquire because of the four interacting variables. However, if only the electrical aspect is considered, the process is well described by one second order nonlinear differential equation: the Bonhoeffer-van der Pol equation (Fitzhugh 1961, 1968). Since this equation contains only two variables, pictures of the phase plane can be drawn and the dynamical behaviour visualised.

A description of the electrical membrane properties is then as follows. In the equilibrium state there exists a potential difference across the membrane: $\sim$ 70 mV, inside negative. The application of a small current

forces the membrane potential away from its equilibrium value: positive outward current induces depolarisation, negative current hyperpolarisation. Termination of the current allows the membrane potential to return to its original value with a rate of change dependent on, and roughly proportional to, the deviation from the equilibrium value.

However, if the depolarizing current is larger and as a consequence the membrane potential reduced further ($\sim$ 55 mV) a completely different behaviour develops. Changes in ionic permeability give rise to ionic currents which cause the membrane potential to decrease and even to change sign, the maximal value being $\sim$ 30 mV, inside positive, then the potential returns to its equilibrium value. This phenomenon, called the generation of an action potential, has a duration of 0.8 - 1.0 msec.; the form of an action potential is only weakly dependent on present or past influences.

Both the subthreshold behaviour during and after stimulation with a constant current and the generation of an action potential are schematically shown in Fig.1.2.2.

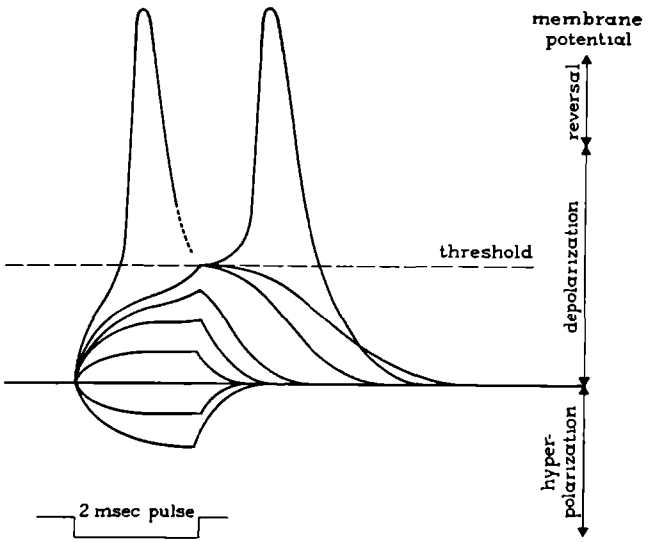


Fig.1.2.2. Subthreshold behaviour and generation of action potential by current pulse of fixed duration but variable ampliyude (Dedrawn from Katz,1966).

The value of the membrane potential at which an action potential is initiated, the threshold potential, forms a separatrix in phase space: a three dimensional hyperplane in the four dimensional H.H.-space or a curve in the two dimensional B.v.d.P.-space. Theoretically partial action potentials might occur; experimentally however, and even in computer simulations, the presence of noise combined with the strongly nonlinear nature of the equations make it an all or none phenomenon (Fitzhugh 1955, 1961).

The local threshold potential varies, depending on the geometrical and functional properties of the membrane. Usually it has a relatively low value at the junction of soma and axon: the axon hillock. At this point the action potential is thought to be initiated. It propagates with a constant velocity and without decrement along the axon. The speed of propagation increases with the diameter of the axon and is larger when a myelin sheath is present (10-100 m/sec). Probably also a backward propagation of the action potential over the somatic membrane occurs and, dependent on the geometry and the presence of synapses, partially into the dendritic tree (Eccles, 1964, Ch. VII).

The signal transmission from one neuron to another takes place at the synapses. The arrival of an action potential at the synaptic endings of the axon causes a quantal release of transmitter substance into the synaptic cleft. The transmitter diffuses across the cleft (0.02-0.05 mμ) to the post-synaptic membrane, where it induces selective changes in ionic permeability. This again causes local hyperpolarisation or depolarisation of the membrane potential. The time course of the synaptic transmission involves a delay of 0.5-1.0 msec, a rise time of the dendritic potential of 1 msec and a decay time depending on the functional and structural properties of the neuron.

Experiments on the neuro-muscular junction have shown that the transmitter substance is transferred in a probabilistic way. The number of molecules contained in a quant is Gaussian distributed, the moments of ejection follow a Poisson process, the mean rate of which is modulated by the value of the presynaptic potential. The quantal changes in muscle end-plate potential have an average value of $\sim$ 0.5 mV with a standard deviation of $\sim$ 0.1 mV; the rate of occurence may vary from 1/sec. to 100/sec. or more. Fig.1.2.3 shows the results of Boyd and Martin (1956) for a mammalian end-plate.

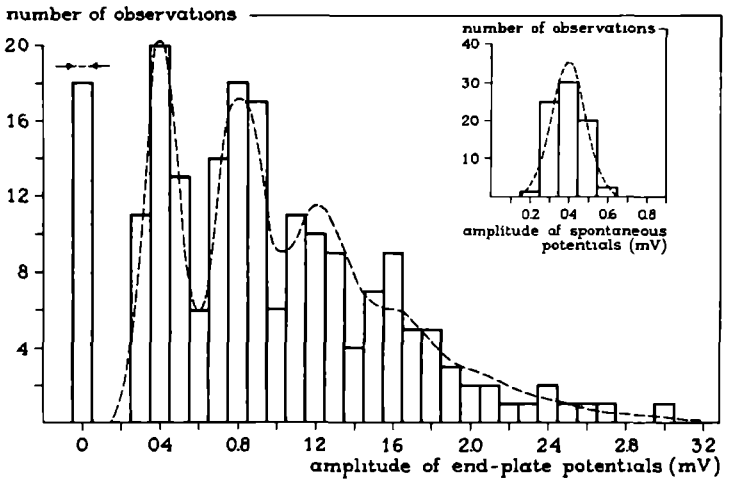


Fig.1.2.3 Histograms of endplate potentials and spontaneous potential amplitudes. Peaks in e.p.p. amplitude distribution occur at 1,2,3 and 4 times the mean amplitude of the spontaneous miniature potentials. Gaussian curve is fitted to spontaneous potential distribution and used to calculate theoretical distribution of e.p.p. amplitude. Arrows indicate expected number of failures of response to nerve stimuli. (From Boyd and Martin(1956)).

Though evidence on neuro-neuronal synapses is incomplete it seems likely that a comparable mechanism of synaptic function exists (Martin,1966, 1968; Kuno and Miyahara, 1968).

Dependent on the polarity of the synapses the selective permeability of the postsynaptic membrane may change in different ways, resulting in either an increase (hyperpolarisation) or a decrease (depolarisation) of the post-synaptic membrane potential, the amount of change of the dendritic potential being dependent on its previous value. At the synapses the membrane seems to be electrically inexcitable; in most of the dendritic tree the threshold potential is usually so high as to exclude initiation of action potentials. The decremental conduction of the changes in potential through dendrites and soma is then described by partial differential equations with varying coefficients. Theoretical analysis and numerical computations (Rall, 1964, 1967) show that the electrotonic distance between synapse and soma has a considerable influence on amplitude and time course of the resulting somatic potential. Moreover, since the equations are nonlinear (varying coefficients!) interactions may occur between potentials generated at different synapses.

To describe the repetitive generation of action potentials refractory properties are important. During and directly after the occurrence of an action potential no other action potential can be generated; this results in an absolute refractory period of $\sim$ 2 msec. The equations describing the local properties of the membrane, the Hodgkin-Huxley as well as the Bonhoeffer-van der Pol equation, show enhancing and depressing after-effects. Moreover, it appears plausible that also the global properties of the neuron contribute refractory effects. The action potential when initiated in the initial segment, propagates back over the somatic membrane and into the larger branches of the dendritic tree. The interaction would annihilate, or at least diminish, the electrotonically conducted potential changes generated at synapses. Persistence of transmitter substance with its influence on the permeability of the membrane and a dependence of equilibrium and threshold potential on preceding action potentials may even more complicate the foregoing description.

1.3 THE THEORETICAL APPROACH: FLUCTUATION AND DIFFUSION.

In the preceding section a brief review was presented of the physiology of a neural cell. In order to be able to construct a mathematical description of the signal processing aspects of neural activity, a simple and unequivocal formulation of the cell properties is required. The basis for the mathematical approach is formulated in the form of five assumptions.

ASSUMPTION 1.

The subthreshold state of a neuron is characterised by one variable only; the somatic potential y(t). *The influence of other neurons and/or external environment is given by the input signal* i(t). *The rate of change of* y(t) *is dependent only on the present values of* y(t) *and* i(t). *This dependence may be nonlinear; its general form is given by the equation*

$$\frac{dy}{dt} = f(y) + g(y)\, i(t) \quad ; \quad g(y) > 0 \qquad (1.3.1)$$

where f *and* g *should be differentiable functions.*

A diagram of Ass. 1 is given in Fig.1.3.1.

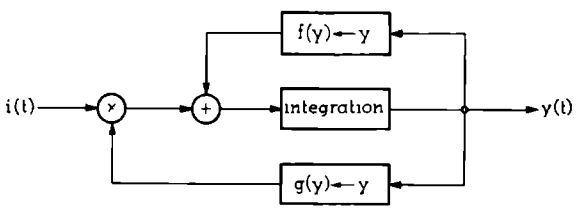


Fig.1.3.1 Diagram of subthreshold behaviour of the somatic potential.

The input i(t) is the current originating from changes in synaptic permeability caused by action potentials arriving from other neurons or current generated through external stimulation. If the cells have many interconnections or if the stimulus is complex, then the detailed structure of the input is also highly complex. Moreover, i(t) may be different in seemingly identical experiments. In this situation it is clearly undesirable to aim at a complete description of the input. Instead of considering all

the, partly irreproducible and unpredictionable, complexities of this signal, we regard the input as a stochastic process, of which only the most important properties are taken explicitly into account.

The simplest and usually the most prominent feature of the input is its average value

$$m(t) = \langle i(t) \rangle \tag{1.3.2}$$

The second characteristic of the input is the correlation function

$$k(t,\tau) = \langle i(t).i(t-\tau) \rangle - \langle i(t) \rangle . \langle i(t-\tau) \rangle \tag{1.3.3}$$

representing the correlation between values of j at a time t and at time τ earlier.

The average in the determination of m(t) and $k(t,\tau)$ may be taken with respect to time if the input i(t) is stationary, that is if $m(t) = m$ and $k(t,\tau) = k(\tau)$ are time independent. If average value and correlation function are time dependent, then the averages should be taken over a suitable ensemble, for instance a number of repetitions of the experiment.

Two important quantities are given by special values of the correlation function. The variance of the input is represented by the value of the correlation function for $\tau = 0$.

$$v^2(t) \equiv k(t,0) = \langle i(t)^2 \rangle - \langle i(t) \rangle^2 \tag{1.3.4}$$

The incremental variance, or intensity (Stratonovich, 1963) of the input is the integral of the correlation function

$$s^2(t) \equiv \int_{-\infty}^{\infty} d\tau \; k(t,\tau) \tag{1.3.5}$$

A normalised signal having zero mean and unit incremental variance is now defined by

$$j(t) = \frac{i(t) - m(t)}{s(t)} \tag{1.3.6}$$

and the input is rewritten as

$$i(t) = m(t) + s(t).j(t) \tag{1.3.7}$$

The equation for the somatic potential, Eq.(1.3.1) reads then

$$\frac{dy}{dt} = \alpha(y,t) + \beta(y,t).j(t) \qquad (1.3.8)$$

where

$$\alpha(y,t) = f(y) + g(y).m(t) \qquad (1.3.8a)$$

$$\beta(y,t) = g(y).s(t) \qquad (1.3.8b)$$

In this description f(y) and g(y) represent the properties of the system and m(t) and s(t) the statistical characteristics of the input; the quantity j(t) may, under certain conditions, be treated as a stochastic carrier.

In order to be able to specify the assumption which allows us to neglect he 'microscopic' properties of j(t), three time constants have to be defined.

- The time constant of the 'microscopical' coherence of the input: τ_c. This correlation time will be defined as

$$\tau_c = \frac{1}{s^2(t)} \int_{-\infty}^{\infty} d\tau/\tau/k(t,\tau) \qquad (1.3.9)$$

The correlation between the value of j(t) and of j(t+τ) can be neglected for τ several times larger than τ_c.

- The time constant of the variation of the statistical characteristics of the input: τ_s. An acceptable estimation of this constant could be

$$\tau_s = \left| \left\{ \frac{\dot{m}(t)}{m(t)} \right\}^2 + \left\{ \frac{\dot{s}(t)}{s(t)} \right\}^2 \right|^{\frac{1}{2}} \qquad (1.3.10)$$

- The time constant for the relaxation of the system: τ_r. The definition of the relaxation time is

$$\tau_r = -\left\langle \left\{ \frac{\partial \dot{y}}{\partial y} \right\}^{-1} \right\rangle = -\left\langle \left| \frac{\partial}{\partial y} \{\alpha(y,t) + \beta(y,t)\ j(t)\} \right|^{-1} \right\rangle \qquad (1.3.11)$$

The definitions of τ_c in Eq.(1.3.9) and of τ_r in Eq.(1.3.11) agree, in the stationary case, with those of Stratonovich (1963; p. 88 and p. 99).

ASSUMPTION 2.

The correlation time of the statistical fluctuations of the input (τ_c) is small, both with regard to the time constant of the variation in the statistical characteristics of the input (τ_s) as with respect to the relaxation time of the system (τ_r):

$$\tau_c \ll \tau_s \text{ and } \tau_c \ll \tau_r.$$

An important conclusion follows from Ass. 2. The 'microscopical' properties of j(t) are under these conditions irrelevant for the behaviour of the system given by Eq.(1.3.8) for time differences Δt which are large with respect to the correlation time τ_c. This implies that, as long as $\Delta t \gg \tau_c$, the signal j(t) may be replaced by another quantity w(t) with the identical statistical characteristics: m = 0, s = 1. The best choice is to take for w(t) a signal with a correlation function of the form of a delta function.

To stress the stochastic nature of the variable y we write Y instead of y. Eq.(1.3.8) is then replaced by the stochastic differential equation

$$dY = \alpha(Y,t)dt + \beta(Y,t)\, dW(t) \qquad (1.3.12)$$

where

W(t) is the integrated process w(t)

$$\langle w(t) \rangle = 0 \qquad (1.3.12a)$$

$$\langle w(t)w(t+\tau) \rangle = \delta(\tau) \qquad (1.3.12b)$$

Eq.(1.3.12) is known as a fluctuation equation or Langevin equation.

The replacement of j(t) by w(t) amounts to the statement that for $\Delta t \gg \tau_c$ the physical process of Eq.(1.3.8) can be described through the first order Markov process of Eq.(1.3.12). Some equivalent descriptions of the process given by Eq.(1.3.12):

w(t) has a delta-type correlation function,
w(t) has a constant spectral density,
w(t) is white noise,
W(t) has independent increments,
Y(t) is a first order Markov process.

References mainly used here were Stratonovich (1963; Ch. 4) and Cumming (1967; Ch. 4)

What has been accomplished up till here is an abstraction of the statistical characteristics m(t) and s(t) from the input i(t) and a formalisation of the lack of knowledge with respect to the rest-signal j(t) through a replacement of this quantity by the white noise w(t). An important advantage of this procedure is that stochastic differential equations of the form of Eq.(1.3.12) occur frequently in physics and have been widely studied. In the remainder of this paragraph the standard theory for analysis of the fluctuation equation is briefly presented.

Since Eq.(1.3.12) contains now the stochastic function w(t), statistical concepts are needed for the analysis of this equation. The fundamental one of these concepts is the transition probability density function:

$f(y,t|x,s)$ = probability density that the stochastic variable Y has the value y at time t given that it was equal to x at time s.

= transition probability density $(x,s) \rightarrow (y,t)$.

The infinitesimal short duration of the correlation of the white noise implies that the transition probability density is independent of the past history. This feature is expressed in the Smoluchowski integral equation.

$$f(y,t + \Delta t|x,s) = \int dz\ f(y,t + \Delta t|z,t)\ f(z,t|x,s) \qquad (1.3.13)$$

from which also a differential form may be derived

$$\frac{\partial}{\partial t} f(y,t|x,s) = \sum_{n=1}^{\infty} \frac{(-1)^n}{n!} \left(\frac{\partial}{\partial y}\right)^n \{A_n(y,t)\ f(y,t|x,s)\} \qquad (1.3.14)$$

where

$$A_n(y,t) = \lim_{\Delta t \to 0} \frac{1}{\Delta t} \int dz\ z^n\ f(y + z,t + \Delta t|y,t) \qquad (1.3.15)$$

(Middleton, 1960: p. 448-450; Stratonovich, 1963: Ch. 4).

The functions $A_n(y,t)$, known as incremental moments or intensity coefficients, characterise a stochastic process completely and are all experimentally measurable. The first incremental moment or <u>drift</u>

$$a(y,t) = A_1(y,t) \qquad (1.3.15a)$$

represents the rate of change of the average value of Y. The second incremental moment or <u>dispersion</u>

$$b(y,t) = A_2(y,t) \qquad (1.3.15b)$$

gives the rate of change of the variance of Y. The higher incremental moments are less significant for the process.

No attention has yet been given to the amplitude distribution of w(t). There exists a relation between this distribution and the continuity of a stochastic process as a function of time. It has been demonstrated that a continuous delta-correlated process has a Gaussian amplitude distribution. If the process is not continuous in time, then the amplitude distribution may have a different form.

ASSUMPTION 3.

The stochastic process w(t) *is continuous:*

$$\lim_{\Delta t \to o} \frac{1}{\Delta t} \int_{|z|>\varepsilon} dz\, f(y + z, t + \Delta t | y, t) = 0 \quad \textit{for all } \varepsilon > 0 \tag{1.3.16}$$

Ass. 2 and Ass. 3 may be combined in the statement: w(t) is a continuous delta-correlated process or, equivalently, Gaussian white noise.

A direct consequence of this property is

$$A_n(y,t) = 0 \qquad \text{for } n \geq 3, \tag{1.3.17}$$

which implies that a continuous first order Markov process is completely determined by drift and dispersion. As a consequence Eq.(1.3.14) simplifies into a second order partial differential equation

$$\frac{\partial}{\partial t} f(y,t|x,s) = -\frac{\partial}{\partial y}\{a(y,t)\, f(y,t|x,s)\} + \left(\frac{\partial}{\partial y}\right)^2 \{\tfrac{1}{2} b(y,t)\, f(y,t|x,s)\} \tag{1.3.18}$$

This equation is known as a <u>diffusion equation</u> and the process described by it as a diffusion process.

Stratonovich has demonstrated that the following relation exists between the system and signal characteristics (α and β) appearing in the fluctuation equation and dispersion and drift (a and b) in the diffusion equation:

$$a(y,t) = \alpha(y,t) + \tfrac{1}{2}\frac{\partial}{\partial y}\{\beta(y,t)\}^2 \tag{1.3.19}$$

$$b(y,t) = \{\beta(y,t)\}^2 \tag{1.3.20}$$

Eq.(1.3.18), also named the forward diffusion equation or Fokker-Planck equation, describes the probability density or transitions from a given 'start-point' (x,s) to all possible 'points' (y,t). Its solution supplies probabilistic knowledge of the future of the variable Y(t).

We may equally well be interested in the probability density of transitions from all 'start-points' (x,s) to a given 'final-point' (y,t): for this we need a related equation describing the past of Y(t). In the theory of stochastic processes it is well known that, under the conditions which allow the derivation of the forward equation, it is possible to derive the corresponding backward, or Chapman-Kolmogorov, equation (see for instance Prabhu (1965))

$$-\frac{\partial}{\partial s} f(y,t|x,s) = a(x,s)\frac{\partial}{\partial x} f(y,t|x,s) + \tfrac{1}{2}b(x,s)\left(\frac{\partial}{\partial x}\right)^2 f(y,t|x,s) \qquad (1.3.21)$$

An important simplification of the diffusion equations occurs when the statistical characteristics of the input do not depend on time:

$$m(t) \rightarrow m \quad , \quad s^2(t) \rightarrow s^2$$

As a direct consequence the incremental moments, including drift and dispersion, become time independent:

$$A_n(y,t) \rightarrow A_n(y)$$

The transition probability density is in the stationary case redefined as

f(y,t,x) = probability density of the transition $x \rightarrow y$ in a time interval with duration t.

The stationary diffusion equations have the form

$$\frac{\partial}{\partial t} f(y,t,x) = -\frac{\partial}{\partial y}\{a(y)\, f(y,t,x)\} + \left(\frac{\partial}{\partial y}\right)^2 \{\tfrac{1}{2}b(y)\, f(y,t,x)\} \qquad (1.3.22)$$

$$\frac{\partial}{\partial t} f(y,t,x) = a(x)\frac{\partial}{\partial x} f(y,t,x) + \tfrac{1}{2}b(x)\left(\frac{\partial}{\partial x}\right)^2 f(y,t,x) \qquad (1.3.23)$$

These equations form the base of the mathematical derivations in Ch. 2 and the numerical computations of Ch. 3.

Fluctuation and diffusion equations are fundamental tools for the description of continuous stochastic processes. Their history is intimately connected with the theory of Brownian motion; at present their applications include problems of diffusion, heat conduction, noise in electrical circuits, neural activity and population genetics. A famous reference is Wax (1954). The Brownian motion language will sometimes be used for the explanation of mathematical operations.

The diffusion equations as presented here are yet incomplete: boundary conditions have to be added. For the forward equation they are formulated in the following way.

Since no changes occur in a zero time interval, the initial condition is:

$$f(y,o,x) = \delta(y - x) \tag{1.3.24}$$

Since only finite distances are traversed in a finite time, the first spatial condition reads simply:

$$f(-\infty,t,x) = 0 \tag{1.3.25}$$

For the formulation of the second spatial condition, a further assumption concerning the properties of a neuron is involved.

ASSUMPTION 4.
There exists a threshold value for the potential: d. When the somatic potential Y(t) *reaches this value an action potential is generated.*

A consequence of Ass. 4 is that Y(t) does not assume values larger than or equal to d. The boundary condition reads then:

$$f(d,t,x) = 0 \tag{1.3.26}$$

Because of the boundary condition for y = d the function f(y,t,x) determined by the forward diffusion equation takes now a somewhat different meaning:
f(y,t,x) = probability density of transition $x \to y$ in time interval t, under the condition that Y has assumed no value larger than or equal to d in this interval.

Though the backward equation is for our work of equal importance we shall not need its boundary conditions. In order to describe the repetitive activity the last assumption concerning the behaviour of a neuron is introduced.

ASSUMPTION 5.
The action potential has an infinitesimal short duration. Directly after this event the somatic potential jumps to a reset potential x_o.

The last assumption excludes all refractory properties. Inclusion of these effects in the traditional way would lead to difficult mathematical problems. However, in § 2.4 a different way is proposed to treat refractoriness.

1.4 EVALUATION OF THE MODEL.

In this section the diffusion model, as formulated in the previous paragraph, is situated among the theoretical approaches to stochastic neural activity. Also some experimental and theoretical evidence is given with regard to the plausibility of the assumptions.

It should be realised that a certain type of description of the stochastic spike generation process is applicable only to certain types of neurons. Moreover, these descriptions are not intended to supply a complete picture of the electrical phenomena inside a cell, but only of these aspects which have a direct influence on the generation of action potentials.

Though many papers on stochastic neural activity have been published, only a few of these contained contributions to the mathematical analysis of the problem. A systematic account of a number of the earlier models is given in Moore, Perkel and Segundo (1966). Also Harmon and Lewis (1966) give in their review-paper on neural modeling a short exposition of theories of the stochastic activity of the single cell. Recent contributions, of a type comparable to our approach, are given in the papers of Gerstein and Mandelbrot (1964), Stein (1965, 1967), Ten Hoopen (1966), Molnar (1966) or Molnar and Pfeiffer (1968) and Gluss (1967).

The assumptions of the diffusion model as given § 1.3 are summarised:

- *below threshold the neuron is described as a linear or nonlinear first order filter* (Ass. 1);
- *the input is a stochastic quantity which, when normalised, has a short correlation time* (Ass. 2) *and a Gaussian amplitude distribtuion* (Ass. 3);
- *when the state variable reaches the threshold an action potential is generated* (Ass. 4) *and the system returns immediately to its initial state* (Ass. 5).

Previous analyses were all characterised by the assumption of linear subthreshold behaviour. In the work of Stein, Molnar and Gluss there is a continuous proportional decay of the somatic potential:

$$\frac{dy}{dt} = - y/\tau + i(t) \qquad (1.4.1)$$

In the random walk model of Gerstein and Mandelbrot no decay of the potential occurs: $\tau = \infty$. Ten Hoopen assumes that the diminution of the potential occurs in jumps, which have a probability of occurrence proportional to the existing value of the potential.

The input is described in either of two ways: a discrete or a continuous formulation. The discrete viewpoint is taken by Stein, Ten Hoopen and Molnar. In this approach the input has the form

$$i(t) = \sum_{k=1}^{K} \sum_{m} c_k \, \delta(t-t_{k,m}) \qquad (1.4.2)$$

Here $\{t_{k,m}\}$, m = 1, 2, ... is the sequence of arrival times of action potentials at synaps k and c_k indicates modality and strength of the effect of this action potential on the somatic potential. Further the assumption is made that the combined sequence of arrival times for all synapses $\{\{t_{k,m}\}\}$, k = 1, ..., K; m = 1, 2, ...; can be regarded as a Poisson-process. Though this is perfectly true under the strong condition that each input sequence $\{t_{k,m}\}$ is a Poisson process, it also serves as a good approximation when a large number of independent but non-Poissonian point processes contribute to the input (high convergence condition).

As a consequence a stationary input can be written

$$i(t) = m + s.w(t) \qquad (1.4.3)$$

where

$$m = \sum_{k} n_k \, c_k \qquad (1.4.4)$$

$$s^2 = \sum_{k} n_k \, c_k^2 \qquad (1.4.5)$$

n_k = event density (frequency) of arrivals of action potentials at synaps k

w(t) = discrete white noise.

So Ass. 2 is shared by these authors, but they do not invoke Ass. 3.

The continuous approach is choosen by Gerstein and Mandelbrot, by Gluss and in our work. The assumptions concerning the input are here of the following form. The input is the sum of independent events, many of these occurring within a time constant of the system, each having only a small effect and a short duration. These properties are rather plausible on the base of the high convergence condition, which was already used to justify Ass. 2. Since the effects of the (normalised) input on the somatic potential are in this case indiscernible from these caused by continuous white noise, this description is equivalent to Ass. 2 and Ass. 3.

When the continuous white noise input is small, so that (nearly) no action potentials are generated, a proportional decay of the somatic

potential results in a Gaussian amplitude distribution and an exponential autocorrelation function of the somatic potential.

Experimental support for this description is given by Calvin and Stevens (1968). Fig.1.4.1 shows one of their measurements on spinal motoneurons in cats. The authors reach the conclusion that, for at least one class of motoneurons, fluctuations in synaptic input (synaptic noise) are the major source of variability in the interspike intervals.

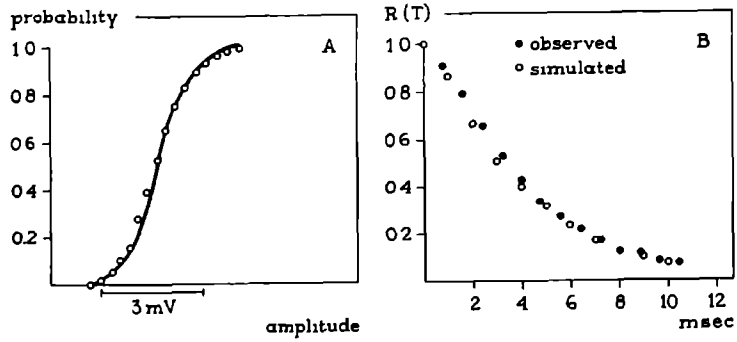


Fig. 1.4.1 Statistical structure of synaptic noise from motoneuron MIV-I. A: amplitude distribution histogram for a 2-sec sample (10.000 sample points) of synaptic noise using a class interval of 300 μV. The superimposed smooth curve is a normal distribution function with a SD of 0,8 mV. B: autocorrelation function for a 30-sec segment of synaptic noise sampled at 5 kHz (filled circles). Open circles represent the autocorrelation function for filtered Gaussian white noise used in the simulation of this cell's behaviour. (from Calvin and Stevens, 1968)

With regard to the mechanism of spike generation the situation is as follows. Ass. 4 is common to all approaches mentioned in this paragraph; both because of its mathematical simplicity and since it is in good agreement with experimental data. Though Ass. 5 is physiologically insufficient, it is widely used as a first starting-point for a mathematical analysis.

A schematic representation of the behaviour of the proportional decay model with a discrete input is given in Fig.1.4.2.

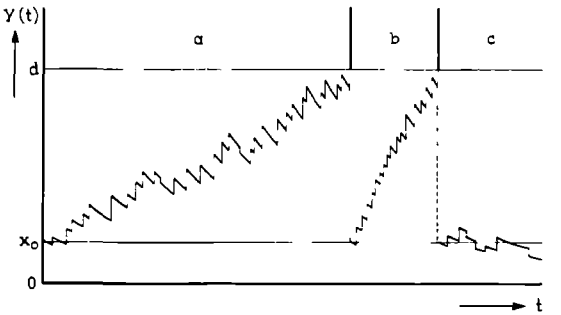


Fig. 1.4.2 Examples of the time course of the somatic potential for the model with discrete input and continuous proportional decay
a) excitation and inhibition
b) high excitation, no inhibition
c) nearly equal intensity of excitation and inhibition.

For all models of somatic signal processing and types of inputs discussed in this paragraph, the Smoluchowski differential equation, given in Eq.(1.3.14), applies to the subthreshold behaviour. It reads for the stationary case

$$\frac{\partial}{\partial t} f(y,t,x) = \sum_{n=1}^{\infty} \frac{(-1)^n}{n!} \left(\frac{\partial}{\partial y}\right)^n A_n(y)\, f(y,t,x) \qquad (1.4.6)$$

However, the incremental moments are different in different situations. Four descriptions and their results are compared.

1. Continuous input, no decay.

   (Gerstein and Mandelbrot, 1964)

   Drift $a(y) = m$

   dispersion $b(y) = s^2$

   higher incremental moments $A_j(y) = 0, \quad j \geq 3$

   where m and s^2 are defined by Eq.(1.3.2) and Eq.(1.3.5).

   Closed expressions exist for transient and stationary distribution of somatic potential and distribution of intervals.

2. Discrete input, continuous proportional decay.

(Stein, 1965, 1967; Molnar, 1966)

drift $a(y) = m - y/\tau$

dispersion $b(y) = s^2$

higher incremental moments $A_j(y) = \sum_k n_k c_k^j, \quad j \geq 3$

where m and s^2 are defined by Eq.(1.4.4) and Eq.(1.4.5). Substitution of these relations in Eq.(1.4.6) leads to the differential-difference equation

$$\frac{\partial}{\partial t} f(y,t,x) = \frac{\partial}{\partial y} \{\frac{y}{\tau} f(y,t,x)\} + \sum_k n_k \{f(y-c_k,t,x) - f(y,t,x)\} \quad (1.4.7)$$

An integrated version of this equation is given by Stein (1965, p. 182, Eq.(13)) and by Molnar (1966, p. 50, Eq.(4.2)). However, under the boundary conditions related to the threshold property no general solutions have been found for the distribution of somatic potential or intervals.

Simulations of the model with propertional decay and a discrete input by Lynn (1969) on a digital computer indicated that the amplitude of the pulses has a neglible influence on the distribution of intervals between action potentials, as long as this amplitude is less than or equal to 10% of the difference between threshold and reset potential.

3. Discrete input, discrete proportional decay.

(Ten Hoopen, 1966).

Under the assumption that all excitatory and inhibitory pulses have the same size ($c_k = \pm c$) the incremental moments are for $y > 0$

drift $a(y) = m - y/\tau$

dispersion $b(y) = s^2 + cy/\tau$

higher incremental moments $A_j(y) = n_e c^n + n_i(-c)^n - (-c)^{n-1} y/\tau$

where $m = (n_e - n_i)c$ and $s^2 = (n_e + n_i)c^2$

and n_e is frequency of excitatory, n_i of inhibitory pulses.

The Smoluchowski equation for the transition probability is for $y > 0$

$$\frac{\partial}{\partial t} f(y,t,x) = \frac{1}{c\tau} \{(y+c) f(y+c,t,x) - y f(y,t,x)\} \quad (1.4.8)$$

$$+ n_e f(y-c,t,x) - f(y,t,x)\} + n_i\{f(y+c,t,x) - f(y,t,x)\}$$

For $y = 0$ and $y > 0$ slightly different equations apply.

Since the distribution is zero everywhere except at $y = mc$, m integer, the differential-difference equation Eq.(1.48) is equivalent with a set of coupled first order differential equations. When an absorbing barrier (threshold) is introduced at $m = d$ and a reflecting barrier at $m = -r$, then the number of equations becomes finite.

Exact solutions can be found for both the distribution of the somatic potential and the distribution of intervals. Ten Hoopen did not succeed in the derivation of a closed expression for average value or variance of the interval distribution.

4. Continuous input, continuous proportinnal decay.

(Gluss, 1967; Johannesma, 1968 and this paper)

drift $a(y) = m - y/\tau$

dispersion $b(y) = s^2$

higher incremental moments $A_j(y) = 0, \quad j \geq 3$

where the average value m is defined by Eq.(1.3.2) and incremental variance s^2 by Eq.(1.3.5).

The Smoluchowski differential realtion, Eq.(1.4.6), takes now the form

$$\frac{\partial}{\partial t} f(y,t,x) = - \frac{\partial}{\partial y} \{(m-y/\tau) f(y,t,x)\} + \tfrac{1}{2}\left(\frac{\partial}{\partial y}\right)^2 \{s^2 f(y,t,x)\} \qquad (1.4.9)$$

This second order partial differential equation is a special form of the forward diffusion equation, Eq.(1.3.22).

Gluss gives a mathematical analysis of Eq.(1.4.9) indicating a number of relations between different functions resulting in directives for numerical computations.

The results presented in this paper and the previous one are expressions for the stationary distribution of the somatic potential and for the moments of the interval distribution. In Ch. 2 these equations are derived for arbitrary drift and dispersion, in Ch. 3 applied on the system without decay (§ 3.2) on the system with proportional decay (§ 3.3) and on the equivalent circuit of the membrane (§ 3.4).

THE STATIONARY SCENE: MATHEMATICAL DERIVATIONS.

2.1 INTRODUCTION

In the previous chapter a theoretical approach, the diffusion model, has been formulated and evaluated with regard to physiological evidence. In this chapter a mathematical analysis is made of the diffusion equations for the stationary situation. The main results are analytical expressions for the distribution of the somatic potential and for the moments of the distribution of intervals between action potentials.

The basic equations for a diffusion process, derived in § 1.3, are

$$\frac{\partial}{\partial t} f(y,t,x) = P(\frac{\partial}{\partial y},y)\ f(y,t,x) \tag{2.1.1}$$

$$\frac{\partial}{\partial t} f(y,t,x) = Q(x,\frac{\partial}{\partial x})\ f(y,t,x) \tag{2.1.2}$$

Here we introduced the forward diffusion operator

$$P(\frac{\partial}{\partial y},y) = -\frac{\partial}{\partial y}a(y) + (\frac{\partial}{\partial y})^2 \tfrac{1}{2}b(y) \tag{2.1.3}$$

and the backward diffusion operator

$$Q(x,\frac{\partial}{\partial x}) = a(x)\frac{\partial}{\partial x} + \tfrac{1}{2}b(x)(\frac{\partial}{\partial x})^2 \tag{2.1.4}$$

Four functions of fundamental importance will occur frequently in the analysis.

1. The first function is already introduced in § 1.3; its definition is here repeated in more neurophysiological terms.

$f(y,t,x)$ = probability density of the somatic potential at the value y a time t after the occurrence of a value x, under the condition that no action potential has been generated in this interval.

This probability density obeys Eq.(2.1.1) and Eq.(2.1.2).

2. The second function defines the distribution of the pulse initiation time.

$g(t,x)$ = probability density for the first action potential to be initiated a time t after the occurrence of a value x of the somatic potential.

This probability density is identical with the distribution of the first passage time.

From the definitions follow

$$\lim_{t\to\infty} f(y,t,x) = 0 \quad \text{and} \quad \lim_{t\to\infty} g(t,x) = 0$$

Conservation of probability leads to the relation

$$\int_{-\infty}^{d} dy\, f(y,t,x) + \int_{o}^{t} du\, g(u,x) = 1 \tag{2.1.5}$$

3. The third function to define is the probability density of the somatic potential under repetitive activity.

$h(y,t,x)$ = probability density of somatic potential at the value y a time t after the occurrence of a value x.

4. The last function is the probability density for the initiation of an action potential under repetitive activity.

$n(t,x)$ = probability density for an action potential to be initiated a time t after the occurrence of a value x of the somatic potential.

After the occurrence of an action potential the somatic potential assumes the value x_o (§ 1.3; Ass. 5). As a consequence $g(t,x_o)$ is identical to the probability density of intervals between action potentials. For the same reason $n(t,x_o)$ is the event density of action potentials a time t after the occurrence of an action potential. This conditional event density has the nature of an autocorrelation function; in neurophysiology it has been awarded the slightly confusing name of expectation density. (Perkel, Gerstein and Moore, 1967).

Since there may have occurred an arbitrary number $k \geq 0$ of action potentials in the interval (0,t), the function $h(y,t,x_o)$ is the convolution of f and the k-fold convolution of g summated over all values of $k \geq 0$. Laplace transformation allows a simple presentation of this relation

$$\hat{h}(y,p,x_o) = \sum_{k=o}^{\infty} \hat{f}(y,p,x_o).\{\hat{g}(p,x_o)\}^k = \frac{\hat{f}(y,p,x_o)}{1-\hat{g}(p,x_o)} \tag{2.1.6}$$

An action potential occurring at t may have been preceded by an arbitrary number $k \geq 0$ of action potentials in the interval (0,t). In the Laplace domain this is expressed by

$$\hat{n}(p,x) = \sum_{k=o}^{\infty} \hat{g}(p,x)\ \{\hat{g}(p,x_o)\}^k = \frac{\hat{g}(p,x)}{1-\hat{g}(p,x_o)} \tag{2.1.7}$$

The last equation is a well known relation for all types of renewal processes.

In the next paragraph the forward equation will be shown to yield the equilibrium distribution of the somatic potential; that is the function

$$h(y) = \lim_{t\to\infty} h(y,t,x) \tag{2.1.8}$$

In § 2.3 the backward equation is used to derive the moments of the interval distribution

$$T_n(x_o) = \int_0^\infty dt\ t^n\ g(t,x_o) \tag{2.1.9}$$

The last paragraph of this chapter indicates a way to take account of refractory influences.

2.2. THE DISTRIBUTION OF THE SOMATIC POTENTIAL.

The forward diffusion equation forms the base for the mathematical operations of this paragraph. Therefore it is repeated

$$\frac{\partial}{\partial t} f(y,t,x) = P(\frac{\partial}{\partial y},y)\ f(y,t,x) \qquad (2.1.1)$$

The initial condition is taken at the end of an action potential, then

$$f(y,o,x_o) = \delta(y-x_o) \qquad (1.3.24)$$

Laplace transforamtion of Eq.(2.1.1) incorporating at the same time the initial condition, gives

$$p\ \hat{f}(y,p,x) - \delta(y-x_o) = P(\frac{\partial}{\partial y},y)\ \hat{f}(y,p,x) \qquad (2.2.1)$$

Division of Eq.(2.2.1) by $1 - \hat{g}(p,x_o)$ and interchange of the order of operations leads for $x = x_o$ to

$$p\ \hat{h}(y,p,x_o) - \frac{\delta(y-x_o)}{1-\hat{g}(p,x_o)} = P(\frac{\partial}{\partial y},y)\ \hat{h}(y,p,x_o) \qquad (2.2.2)$$

The rest of the procedure is as follows:

- multiply Eq.(2.2.2) with p,
- take the limit $p \to 0$,
- use the relation

$$\lim_{p\to o} p\ \hat{h}(y,p,x) = \lim_{t\to\infty} h(y,t,x) = h(y)$$

- make use of

$$\lim_{p\to o} p^2\hat{h}(y,p,x) = \lim_{p\to o} p\ h(y) = 0$$

This results in the equation

$$P(\frac{\partial}{\partial y},y)\ h(y) = -\ \delta(y-x_o)\ \lim_{p\to o} \frac{p}{1-p\hat{g}(p,x_o)} \qquad (2.2.3)$$

The Laplace transform of the first passage time density may be expanded as a power series of p with the moments as coefficients

$$\hat{g}(p,x_o) = \sum_{n=o}^{\infty} \frac{T_n(x)}{n!}\ (-p)^n \qquad (2.2.4)$$

where

$$\frac{T_n(x)}{n!} = (-\frac{\partial}{\partial p})^n\ \hat{g}(p,x) \Big/_{p=o} \qquad (2.2.5)$$

Under the condition that

$$T_o(x) = \int_0^\infty dt\ g(t,x) = 1$$

this expansion leads to

$$\lim_{p\to o} \frac{P}{1-\hat{g}(p,x)} = T_1^{-1}(x) \qquad (2.2.6)$$

Combination of Eq.(2.2.3) and Eq.(2.2.6) gives

$$P(\frac{\partial}{\partial y},y)\ h(y) = -T_1^{-1}\ (x_o)\ \delta(y-x_o) \qquad (2.2.7)$$

Because of the form of the forward diffusion operator, given in Eq.(2.1.3), the second order ordinary differential equation, Eq.(2.2.7) may be integrated directly. Using the boundary condition

$$h(-\infty) = 0$$

the result is a first order differential equation

$$a(y)\ h(y) - \frac{\partial}{\partial y}\ \{\tfrac{1}{2}b(y)\ h(y)\} = T_1^{-1}(x_o)\ \varepsilon(y-x_o) \qquad (2.2.8)$$

in which ε is the unit step function.
After insertion of the boundary condition

$$h(d) = 0$$

the solution of Eq.(2.2.8) yields an expression for the stationary distribution of the somatic potential

$$h(y) = T_1^{-1}(x_o)\ \frac{e^{C(y)}}{\frac{1}{2}b(y)} \int_y^d dz\ \varepsilon(z-x_o)\ e^{-C(z)} \qquad (2.2.9)$$

where

$$C(y) = \frac{a(y)}{\frac{1}{2}b(y)} \quad , \quad C(Y) = \int_y^y dz\ c(z) \qquad (2.2.10)$$

and a(y) and b(y) are the drift and dispersion.

A more direct relation with the fluctuation equation is given in the equivalent expression

$$h(y) = T_1^{-1}(x_o)\ 2\ \frac{e^{\Gamma(y)}}{\beta(y)} \int_y^d dz\ \varepsilon(z-x_o)\ \frac{e^{-\Gamma(z)}}{\beta(z)} \qquad (2.2.11)$$

where

$$\gamma(y) = \frac{\alpha(y)}{\frac{1}{2}\beta^2(y)} \quad , \quad \Gamma(y) = \int_y^y dz\ \gamma(z) \qquad (2.2.12)$$

Since

$$\int_{-\infty}^{d} dy\ h(y) = 1$$

The average interval duration is given by

$$T_1(x_o) = 2\int_{-\infty}^{d} dy\ \frac{e^{\Gamma(y)}}{\beta(y)} \int_{y}^{d} dz\ \epsilon(z-x_o)\ \frac{e^{-\Gamma(z)}}{\beta(z)} \qquad (2.2.13)$$

Partial integration transforms this equation in

$$T_1(x_o) = 2\int_{x_o}^{d} dy\ \frac{e^{-\Gamma(y)}}{\beta(y)} \int_{-\infty}^{y} dz\ \frac{e^{\Gamma(z)}}{\beta(z)} \qquad (2.2.14)$$

This relation forms a special case of the results of the next paragraph.

2.3 THE DISTRIBUTION OF IMPULSE INITIATION.

The backward equation is fundamental for the derivations of this paragraph

$$\frac{\partial}{\partial t} f(y,t,x) = Q(x,\frac{\partial}{\partial x}) f(y,t,x) \tag{2.1.2}$$

The conservation of probability, given in Eq.(2.1.5), reads in the differential form

$$g(t,x) = -\frac{\partial}{\partial t} \int_{-\infty}^{d} dy\, f(y,t,x) \tag{2.3.1}$$

Since the backward diffusion operator does not contain the forward variables y and t, it is allowed to integrate Eq.(2.1.2) with respect to y, to differentiate with respect to t and interchange the order of operations. The following equation results

$$\frac{\partial}{\partial t} g(t,x) = Q(x,\frac{\partial}{\partial x}) g(t,x) \tag{2.3.2}$$

This equation for the distribution of first passage times has the same form as the bakcward equation.

The initial condition for this equation is

$$g(o,x) = 0 \tag{2.3.3}$$

and the boundary conditions are

$$g(t,d) = \delta(t), \qquad \lim_{x\to-\infty} \frac{\partial}{\partial x} g(t,x) = 0 \tag{2.3.4}$$

A solution in closed form of Eq.(2.3.2) has been found only in the case that drift and dispersion are independent of the value of x: $a(x) = a$, $b(x) = b$. This case, known as the Wiener-Einstein model of diffusion is treated in detail in § 3.2.

For a more general analysis we start again with Laplace transformation. Eq.(2.3.2) with its inital condition leads to

$$p\, \hat{g}(p,x) = Q(x,\frac{\partial}{\partial x})\, \hat{g}(p,x) \tag{2.3.5}$$

with transformed boundary donditions

$$\hat{g}(p,d) = 1, \qquad \lim_{x\to-\infty} \frac{\partial}{\partial x} \hat{g}(p,x) = 0 \tag{2.3.6}$$

Substitution of the explicit form of $Q(x,\frac{\partial}{\partial x})$ as given in Eq.(2.1.4) and of the function c(x) as defined in Eq.(2.2.10) gives Eq.(2.3.5) the form

$$p\, \frac{1}{\frac{1}{2}b(x)}\, \hat{g}(p,x) = \{c(x) + \frac{\partial}{\partial x}\} \frac{\partial}{\partial x} \hat{g}(p,x) \tag{2.3.7}$$

Multiplication of both sides with exp {C(x)} leads to

$$p \frac{e^{C(x)}}{\frac{1}{2}b(x)} \hat{g}(p,x) = \frac{\partial}{\partial x} \{e^{C(x)} \frac{\partial}{\partial x} \hat{g}(p,x)\} \tag{2.3.8}$$

The rest of the operations are:

- integrate the equation over x,
- use the boundary conditon for $x = -\infty$,
- multiply both sides with exp {-C(x)},
- integrate the equation over x,
- use the boundary condition for $x = d$.

The result is an integral equation

$$\hat{g}(p,x) = 1 - p\int_x^d dy\, e^{-C(y)} \int_{-\infty}^{y} dz\, \frac{e^{C(z)}}{\frac{1}{2}b(z)}\, \hat{g}(p,z) \tag{2.3.))}$$

or alternatively

$$\hat{g}(p,x) = 1 - 2p\int_x^d dy\, \frac{e^{-\Gamma(y)}}{\beta(y)} \int_{-\infty}^{y} dz\, \frac{e^{\Gamma(z)}}{\beta(z)}\, \hat{g}(p,z) \tag{2.3.10}$$

A simplification of the formulas is caused by the definition of the integral operator

$$L = 2\int_x^d dy\, \frac{e^{-\Gamma(y)}}{\beta(y)} \int_{-\infty}^{y} dz\, \frac{e^{\Gamma(z)}}{\beta(z)} \tag{2.3.11}$$

which gives Eq.(2.3.10) the seemingly simple form

$$\hat{g}(p,x) = 1 - p\, L\, \{\hat{g}(p,z)\} \tag{2.3.12}$$

To our knowledge no general solution of this equation in closed form exists. However, it is possible to derive a recurrence relation, involving the operator L, for the moments of the distribution of intervals between the presence of a value x for the somatic potential and the occurrence of the next action potential. The n^{th} moment defined by Eq.(2.1.9), obeys

$$T_n(x)/n! = -(\frac{\partial}{\partial p})^n\, \hat{g}(p,x)\Big/_{p=o} \tag{2.2.5}$$

Combination of this relation with Eq.(2.3.12) gives the results

$$T_o(x) = 1$$

as should be expected; and

$$T_1(x) = L\{1\} = 2\int_x^d dy\, \frac{e^{-\Gamma(y)}}{\beta(y)} \int_{-\infty}^{y} dz\, \frac{e^{\Gamma(z)}}{\beta(z)} \tag{2.2.14}$$

which was already derived in the previous paragraph;

$$\begin{aligned} T_2(x) &= 2\, L\,\{T_1(z)\} \\ &= 4\int_x^d dy\, \frac{e^{-\Gamma(y)}}{\beta(y)} \int_{-\infty}^{y} dz\, \frac{e^{\Gamma(z)}}{\beta(z)}\; T_1(z) \end{aligned} \tag{2.3.13}$$

for the second moment; and finally

$$T_n(x) = n\, L\,\{T_{n-1}(z)\} = n!\, L^n\{1\} \tag{2.3.14}$$

as the general equation. The numerical values of the moments can be computed from these expressions. For the distribution of intervals between action potentials x_o should be substituted for x.

Experimental results are usually not expressed in the moments, but either through the interval distribution or using the lower cumulants of the distribution. The cumulants are defined through

$$K_n(x_o) = (-\frac{\partial}{\partial p})^n \ln \hat{g}(p,x_o)\Big/_{p=o} \tag{2.3.15}$$

They are in a simple way related to the moments:

$K_1 = T_1 = \mu$ = mean.

$K_2 = T_2 - T_1^2 = \sigma^2$ = variance,

$K_2^{\frac{1}{2}}/K_1 = \gamma_o$ = coefficient of variation,

$K_3 = T_3 - 3T_1T_2 + 2T_1^3$ = third central moment,

$K_3/\sigma^3 = \gamma_1$ = skewness,

$K_4 = T_4 - 3T_2^2 - 4T_1T_3 + 2T_1^2T_2 - 6T_1^4$,

$K_4/\sigma^4 = \gamma_2$ = excess.

Digital computer simulations of Lynn (1969) showed that variation of parameters of a neuron gave marked and systematic changes in μ, σ, γ_1 and γ_2.

The event density (frequency) of action potentials is simply related to the average interval through

$$n = T_1(x_o)^{-1} \tag{2.3.16}$$

The first order conditional event density (expectation density) follows from the distribution of intervals (compare Eq.(2.1.7))

$$\hat{n}(p,x_o) = \frac{\hat{g}(p,x_o)}{1-\hat{g}(p,x_o)} \tag{2.3.17}$$

This relation can also be expressed directly in the moments of the interval distribution

$$\hat{n}(p,x_o) = -\sum_{n=o}^{\infty} \frac{T_n(x_o)}{n!}(-p)^n \qquad \sum_{n=1}^{\infty} \frac{T_n(x_o)}{n!}(-p)^n \tag{2.3.18}$$

As a consequence of the reset-condition (§ 1.3; Ass. 5) the higher order conditional event densities do not contain new information; frequency and expectation density give then a complete description of the stationary output sequence of action potentials.

An approximating function for the interval distribution based on the knowledge of the first four cumulants may be found in the following way. For distributions with a single mode Pearson devised a family of functions, defined by

$$\frac{df(z)}{dz} = \frac{z-a}{b_o + b_1 z + b_2 z^2} f(z), \quad a = \text{mode} \tag{2.3.19}$$

A number of well known distributions belong to this family: normal, beta, gamma distribution. The parameters a, b_o, b_1 and b_2 are in a rather simple way related to the first four cumulants. The type of distribution depends on the value of

$$\kappa = \frac{\gamma_1^2(\gamma_2+6)^2}{4(3\gamma_1^2 - 12 - 4\gamma_2)(3\gamma_1^2 - 2\gamma_2)} \tag{2.3.20}$$

If

$$\kappa = \infty \leftrightarrow \gamma_2 = \frac{3}{2}\gamma_1^2 \leftrightarrow b_2 = 0$$

then the distribution is a generalized gamma distribution (Pearson type III)

$$\gamma_\pi\left(\frac{t-\alpha}{\beta}\right) = \frac{1}{\beta\Gamma(\pi)} \left(\frac{t-\alpha}{\beta}\right)^{\pi-1} \exp\left(-\frac{t-\alpha}{\beta}\right) \tag{2.3.21}$$

which is completely specified by its first three cumulants. The parameters are limited to

$$\alpha \leq t \leq \infty\ , \quad -\infty < \alpha < \infty\ , \quad 0 < \pi < \infty\ , \quad 0 < \beta < \infty$$

and related to the first three cumulants by

$$\alpha = \mu - 2\sigma/\gamma_1, \quad \beta = \tfrac{1}{2}\sigma\gamma_1, \quad \pi = (2/\gamma_1)^2 \tag{2.3.22}$$

When a gamma distribution supplies an acceptable approximation, then

$$\hat{g}(p,x_o) = e^{-\alpha p}\ (\beta p + 1)^{-\pi} \qquad (2.3.23)$$

and

$$\hat{n}(p,x_o) = \{ e^{\alpha p}\ (\beta p + 1)^{\pi} - 1\}^{-1} \qquad (2.3.24)$$

Three special cases of gamma distributions of the intervals are

- no dead time: $\alpha = 0$, β , π
- exponential with dead time: α , β , $\pi = 1$
- exponential without dead time: $\alpha = 0$, $\beta = T_1$, $\pi = 1$

Because of the reset condition (§ 1.3; Ass. 5) the last process is a Poisson process. In this case the expectation density is constant and the frequency $n = T_1^{-1}$ gives a complete description of the sequence of events.

If a gamma function does not fit the interval distribution satisfactorily and values of more moments are available, refinements of the approximation may be produced by adding terms of the associated Lagurerre expansion.

An advantage of this method of curve fitting is that type and parameters of the distribution result from simple algebraical mainpulations of the lower moments. The best approximating curve is in this procedure not defined by a least square deviation, but through an identification of the lower moments of both functions (Kendall Stuart, 1963; Johannesma, 1968).

To what extent this approach is useful depends strongly on the purpose of the investigation. When the interest is concentrated on the intracellular processes causing the action potentials the neglect of fine details of the interval distribution in this approximation is a serious drawback, if however the signal characteristics of the sequence of action potentials are considered this type of description may be satisfactory. An advantage of moments and cumulants is that much is known about their sampling characteristics; moreover, they allow the presentation of comparable results of a large number of experiments in a single graph.

2.4 THE INFLUENCE OF REFRACTORINESS.

A proper treatment of refractory effects should take into account at least all the four variables of the Hodgkin-Huxley equations as well as geometrical properties of the membrane. Mathematically this is too difficult. A widely used procedure is to consider the threshold to be dependent on the time passed since the last action potential.

$$d(t) = d + d_r\,(t - s) \tag{2.4.1}$$

Here s is the moment at which the last action potential occurred and $d_r(u)$ is a function which decreases from infinity at u = 0 to zero at u = ∞. This model implies, in our approach, a time-dependent boundary condition and is not analytically tractable.

An alternative approach is now presented. The function $\lambda(y)$ is defined by

$$\lambda(u) \geq 0 \text{ for all } u \geq 0\ ; \quad \int_0^\infty du\ \lambda(u) = \infty \tag{2.4.2}$$

Usually $\lambda(u)$ will be a function which goes smoothly and monotonic from 0 to 1; for instance

$$\lambda(u) = 1 - \exp(-t/t_o) \tag{2.4.3}$$

(Fuortes and Mantegazzini, 1962).

Refractory properties are described by multiplying the 'spatial' coordinate with a factor $\{\lambda(t-s)\}^{-1}$ for t > s. As a result the threshold potential becomes

$$d(t) = \frac{d}{\lambda(t-s)} \tag{2.4.4}$$

and the reset potential

$$x_o(t) = \frac{x_o}{\lambda(t-s)} \tag{2.4.5}$$

Some reflection leads to the conclusion that this 'space-transformation' is equivalent with a multiplication of drift a with $\lambda(t-s)$ and dispersion b with $\{\lambda(t-s)\}^2$. This means that refractory influences are manifest mainly in a reduction of the amplitude of the input with a factor $\lambda(t-s)$.

This description appears, in the whole of the theoretical approach, an acceptable simplification of the physiological situation. However, also here again we come across complicated mathematical problems.

A more succesful way, not too different from the previous one, to treat refractoriness, is a multiplication of both drift and dispersion with $\lambda(t-s)$

$$a(x,t) = \lambda(t-s).a(x) \tag{2.4.6}$$

$$b(x,t) = \lambda(t-s).b(x) \tag{2.4.7}$$

This amounts to the assumption that at a time u after the last action potential all processes are slowed down with a factor $\lambda(u)$. Roughly, this is equivalent with the assumption that the probability for an incoming pulse to reach the central somatic structure is reduced with a factor $\lambda(u)$.

The mathematical analysis relies on the introduction of a transformed time variable

$$\Lambda(t-s) = \int_0^{t-s} du\ \lambda(u) \tag{2.4.8}$$

in terms of which the diffusion equations can be reformulated as time independent equations. The rest of the mathematical operations for the determinations of (the moments of) the interval distribution is then formally identical with that given in § 2.3. The main result of this procedure is the assertion:

If drift $a(x)$ *and dispersion* $b(x)$ *result in a cumulative distribution of intervals* $G(t)$ *and a probability density function* $g(t)$ *then drift* $\lambda(t).a(x)$ *and dispersion* $\lambda(t).b(x)$ *result in a cumulative distribution of intervals* $G_r(t) = G(\Lambda(t))$ *and a probability density* $g_r(t) = \lambda(t)\ g(\Lambda(t))$.

THE STATIONARY SCENE:
APPLICATIONS AND RESULTS.

3.1 INTRODUCTION

In the first chapter a mathematical framework was constructed which incorporated some of the basic physiological properties of a neuron. The second chapter contained mathematical procedures which derived from the diffusion equations a number of more specific expressions. The main results were formulas for the stationary distribution of the somatic potential and the moments of the interval distribution. In this chapter these formulas are applied on three detailed models.

These three models consist all of first order systems followed by a threshold-reset mechanism. The sections in front of the threshold are in the three cases: an integrator, an imperfect integrator and an equivalent circuit for the membrane. For the first two models analytical expressions and numerical results are presented, for the third only the mathematical formulas.

3.2 THE SIPIT-MODEL

In this model for a neural cell a Stochastic Input enters a Perfect Integrator followed by a Threshold-reset mechanism: this description of a neuron will be named the SIPIT-model. The stationary characteristics are not so much treated here for their own importance, a large amount is already well known, as for the development of a dynamical description in the next chapter.

Following the approach of § 1.3 the subthreshold behaviour is described by the fluctuation equation

$$\frac{dY}{dt} = i(t) = m + s\, w(t) \qquad (3.2.1)$$

where

$$m = \langle i(t) \rangle,$$

$$s^2 = \int_{-\infty}^{\infty} d\tau \{ \langle i(t).i(t+\tau) \rangle - \langle i(t) \rangle^2 \},$$

$w(t)$ = Gaussian white noise.

(compare Eq.(1.3.2) - (1.3.5)).

The important quantities drift and dispersion of the Eqs.(1.3.8), (1.3.19) and (1.3.20) are given by

$$a = \alpha = m, \qquad b = \beta^2 = s^2 \qquad (3.2.2)$$

For this model all functions of interest are known (Bailey, § 14.4). The transient distribution of the somatic potential (§ 2.1, Def. 1) has the form

$$f(y,t,x) = \{\varphi(\frac{y-x}{s\sqrt{t}}) - \varphi(\frac{y-x-2d}{s\sqrt{t}})\} \quad \exp(\frac{my-\frac{1}{2}m^2t}{s^2}) \qquad (3.2.3)$$

where the abbreviation for the normal distribution is used

$$\varphi(\frac{z-\mu}{\sigma}) = \frac{1}{\sigma\sqrt{2\pi}} \exp\{-\tfrac{1}{2}(\frac{z-\mu}{\sigma})^2\} \qquad (3.2.4)$$

The first passage time or interval distribution (§ 2.1,Def. 2) is given by

$$g(t,x_o) = \frac{d-x_o}{t} \varphi(\frac{d-x_o-mt}{s\sqrt{t}}) \qquad (3.2.5)$$

In Fig. 3.2.1 - 3.2.4 a number of interval distributions are presented for $x_o = 0$, $d = 1$; average value m and incremental variance s^2 are the parameters.

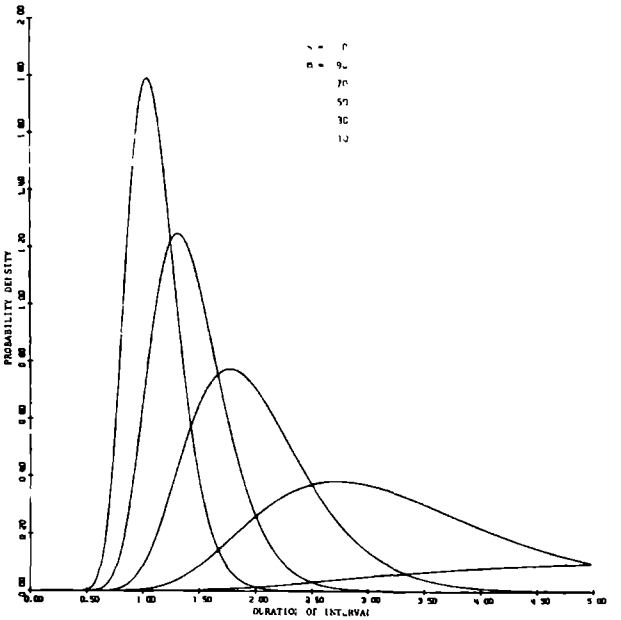


Fig. 3.2.1. Interval distributions for the SIPIT-model for s = .20

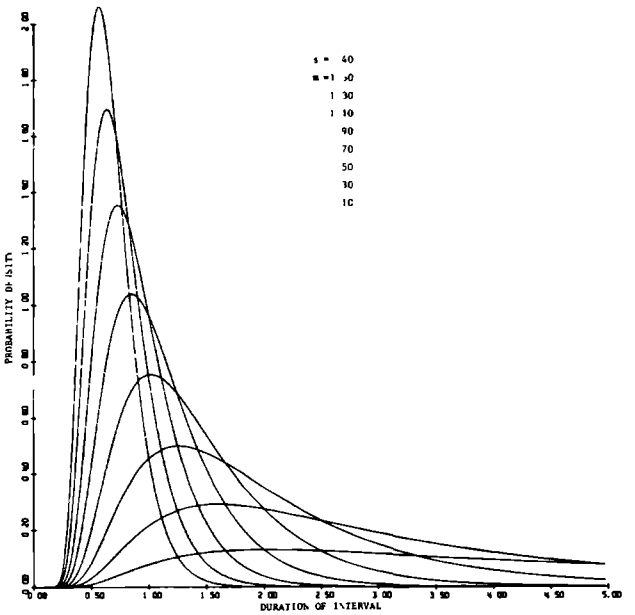


Fig. 3.2.2. Interval distributions for the SIPIT-model for s = .40

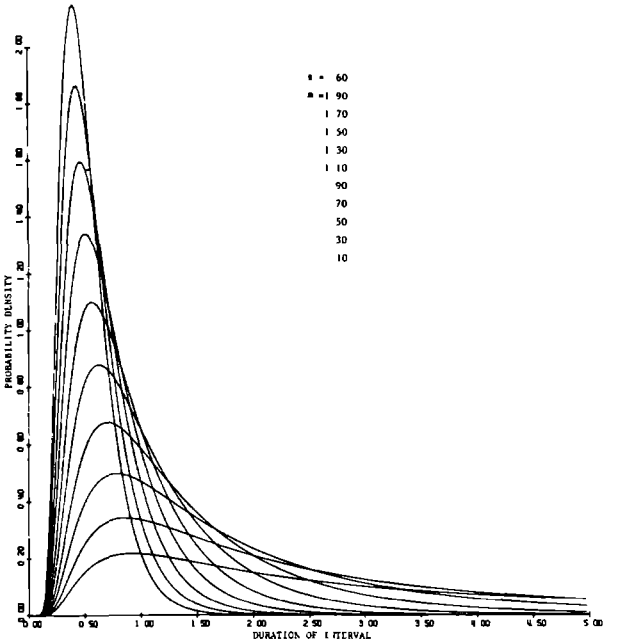


Fig. 3.2.3. Interval distributions for the SIPIT-model for s = .60

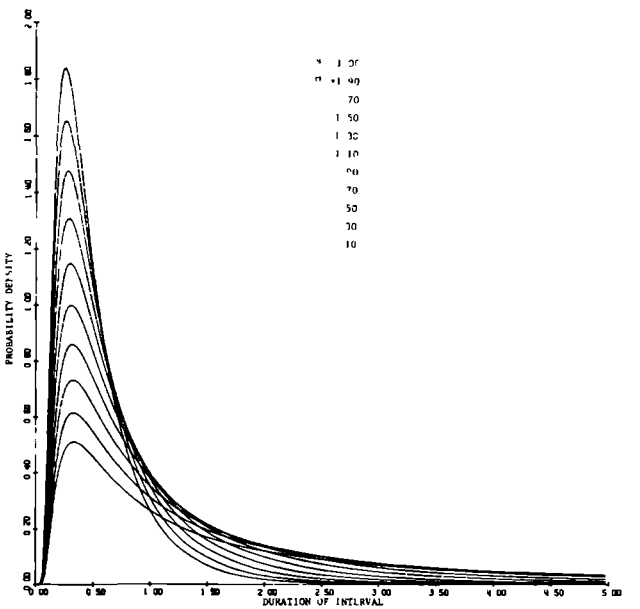


Fig. 3.2.4. Interval distributions for the SIPIT-model for s = 1.00

Without loss of generality the reset potential can be normalised to zero and the threshold potential to one

$$x_o = 0, \qquad d = 1$$

The following relations are then valid:
the mean interval is equal to

$$\mu = T_1 = m^{-1}, \tag{3.2.6}$$

the average frequency

$$n = T_1^{-1} = m,$$

the variance of the interval distribution

$$\sigma^2 = T_2 - T_1^2 = \tfrac{1}{2}s^2/m^3 \tag{3.2.7}$$

and the coefficient of variation, defined as the standard deviation of the intervals divided by the mean interval,

$$\gamma_o = \sigma/\mu = \{\tfrac{1}{2}s^2/m\}^{\frac{1}{2}} \tag{3.2.8}$$

Since drift and dispersion are equal to average value and incremental variance of the input

$$a = m, \qquad b = s^2$$

their ratio, as defined in Eq.(2.2.10), is simply

$$c = \frac{a}{\frac{1}{2}b} = \frac{m}{\frac{1}{2}s^2} \tag{3.2.9}$$

Substitution of this expression in Eq.(2.2.9) gives the equation for the stationary distribution of the somatic potential

$$h(y) = \frac{1}{d-x_o}\left\{ e^{c(y-x_o)} - e^{c(y-d)} + \varepsilon(y-x_o)\left\{1 - e^{c(y-x_o)}\right\}\right\} \tag{3.2.10}$$

The distribution h(y) is a continuous function of y but has a discontinuity in its derivative at the reset value x_o.

For the normalised values $x_o = 0$, $d = 1$ Eq.(3.2.10) becomes

$$h(y) = e^{cy} - e^{c(y-1)} + \varepsilon(y)\ \{1 - e^{cy}\} \tag{3.2.11}$$

A collection of graphs, with $s^2/m = 2/c$ as parameter, is presented in Fig. 3.2.5.

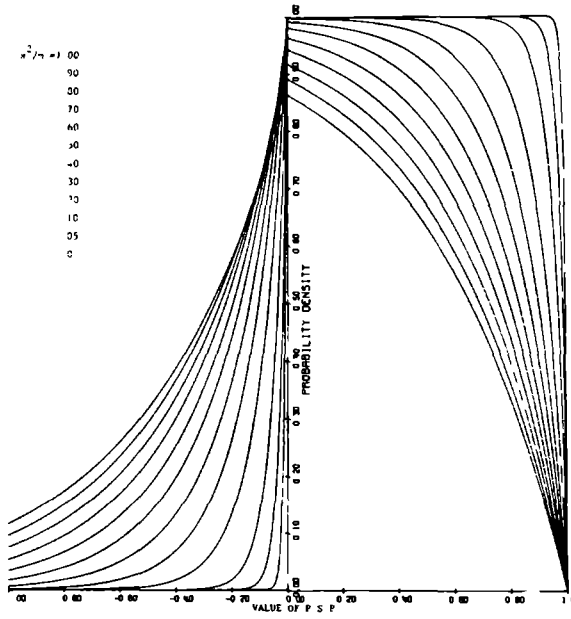


Fig. 3.2.5 The stationary distribution of the somatic potential for the SIPIT-model; at both sides s^2/m *decreases from the left to the right.*

A conclusion with important implications for the dynamical properties (Ch. 4) follows from Eq.(3.2.10) :
the stationary distribution of the somatic potential depends only on the ratio of average value and incremental variance of the input and not on one of them separately.

3.3 THE SILIT-MODEL.

In this description of a neuron a Stochastic Input impinges upon a Leaky Integrator followed by a Threshold-reset mechanism. This model, usually described as the proportional decay model, has been widely studied, mainly with respect to the distribution of intervals between action potentials (for discussion and references see § 1.4).

The fluctuation equation, describing the subthreshold behaviour, is

$$\frac{dY}{dt} = - Y/\tau + i(t) = m - Y/\tau + s\, w(t) \qquad (3.3.1)$$

where

$m = \langle i(t) \rangle$,

$s^2 = \int_{-\infty}^{\infty} d\tau \{ \langle i(t).i(t+\tau) \rangle - \langle i(t)^2 \rangle \}$,

$w(t)$ = *Gaussian white noise.*

Drift and dispersion are given by

$$a(z) = \alpha(z) = m - z/\tau, \qquad b = \beta^2 = s^2 \qquad (3.3.2)$$

From the definitions, given by Eq.(2.2.10) and Eq.(2.2.12), follows

$$c(z) = \gamma(z) = \frac{m-z}{\frac{1}{2}\delta^2}, \qquad C(z) = \Gamma(z) = - \left(\frac{z-m}{\delta}\right)^2 \qquad (3.3.3)$$

where we used the notations

$$m = m\tau \ , \ \delta^2 = s^2\tau \qquad (3.3.4)$$

Closed solutions for the transient distribution of the somatic potential $f(y,t,x)$ and the interval distribution $g(t,x)$ are unknown. The moments of the distribution of intervals between action potentials follow from the substitution of Eq.(3.3.2) and Eq.(3.3.3) in Eq.(2.3.14).

The result is

$$\frac{T_n(x)}{n!} = \tau \frac{2}{\delta^2} \int_x^d dy \, \exp\{(\tfrac{y-m}{\delta})^2\} \int_{-\infty}^{y} dz \, \exp\{-(\tfrac{z-m}{\delta})^2\} \, \frac{T_{n-1}(z)}{(n-1)!} \qquad (3.3.5)$$

A simplification of this equation is caused by the introduction of the dimensionless variables

$$X = \frac{m-x}{\delta}, \quad D = \frac{m-d}{\delta}, \quad \mu_n = \frac{1}{n!} \frac{T_n}{\tau^n} \qquad (3.3.6)$$

The result is the recurrence relation

$$\mu_n(X,D) = 2\int_D^X dy\ e^{y^2}\int_y^\infty dz\ e^{-z^2}\mu_{n-1}(z,D) \qquad (3.3.7)$$

A general conclusion follows from Eq.(3.3.7):
if time is measured in units of the time constant τ, *then all moments of the interval distribution, and as a consequence interval distribution and expectation density, depend only on the two combinations of system and input parameters* X *and* D.

The important equation for the average interval can be given in several equivalent forms.

$$T_1(X,D) = \tau\{\mu(X) - \mu(D)\} \qquad (3.3.8)$$

where

$$\mu(x) = 2\int_0^x dy\ e^{y^2}\int_y^\infty dz\ e^{-z^2} \qquad (3.3.9a)$$

$$= \int_0^\infty du\ e^{-u^2}\ \frac{1-e^{-2xu}}{u} \qquad (3.3.9b)$$

$$= \sum_{n=1}^{\infty}(-2)^{n-1}\ \frac{\Gamma(n/2)}{\Gamma(n+1)}\ x^n \qquad (3.3.9c)$$

Small values of x allow the use of the series representations of Eq.(3.3.9c) for numerical computations. For all positive values of y the integrand of Eq.(3.3.9a) is bounded by

$$(y + \sqrt{y^2 + 2})^{-1} < e^{y^2}\int_y^\infty dz\ e^{-z^2} < (y + \sqrt{y^2 + 4/\pi})^{-1};\ y > 0 \qquad (3.3.10)$$

(Abramowitz and Stegun, 1965; p. 298). For large values of y this gives

$$2e^{y^2}\int_y^\infty dz\ e^{-z^2} \simeq y^{-1};\qquad y >> 1 \qquad (3.3.11)$$

When both X and D are large this results in the approximation

$$T_1(X,D) = \tau\ln(X/D) = \tau\ln\frac{m-x}{m-d};\qquad X >> 1,\qquad D >> 1 \qquad (3.3.12)$$

Eq.(3.3.12) applies exactly in the limit $s \to 0$, that is an input approaching a constant current. In this case this equation can also be derived directly. For $x = 0$, $d = 1$ the average interval for a constant current input is

$$T_1(m,\tau) = -\tau \ln(1 - \frac{1}{m\tau}) \qquad (3.3.13)$$

Numerical results are presented in terms of dimensionless variables. The dependent variable, the output, is given by

$N = \tau/T_1$

= time constant divided by average interval

= average number of pulses within a time constant.

The two independent variables characterising the input are

$M = \frac{m}{d} = \frac{m\tau}{d}$

= product of average value of input current and time constant divided by the threshold potential

= equilibrium value of the somatic potential in the absence of a threshold expressed in units of the threshold potential

$S^2 = \frac{\delta^2}{d^2} = \frac{s^2\tau}{d^2}$

= product of incremental variance of the input and time constant divided by the square of the threshold potential.

The reset potential x_o was for all numerical computations choosen to be equal to the resting potential

$$x_o = 0$$

In Fig. 3.3.1 N is plotted against M with S as parameter.

Remarkable is the strong dependence of N on S for values of M near the threshold. The nearly discontinuous change in N at M = 1 was already dicussed by Stein (1967). For small values of M the dependence of N on M is approximately exponential while for large M the relation between N and M becomes linear. These features are well brought out by an approximative relation

$$N \simeq \exp(aM + b - cN) \qquad (3.3.14a)$$

or alternatively

$$\ln N + cN \simeq aM + b \qquad (3.3.14b)$$

This relation forms a good approximation for $S \geq 0.2$. The constants a, b and c depend on S.

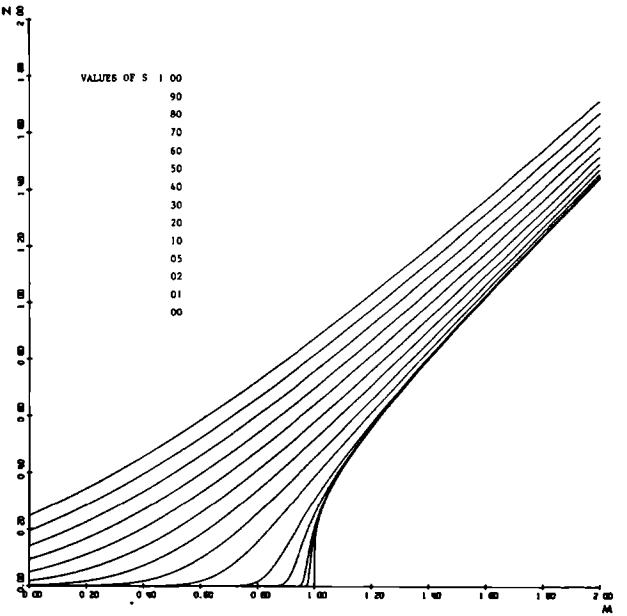


Fig. 3.3.1 Frequency-current relations for the SILIT-model for different amounts of variability of the input.

It is rather unlikely that average value of the input (M) and its incremental variance (S^2) vary independently. Therefore two different presentations of the frequency-current relations, both essentially equivalent to Fig. 3.3.1, are given. In Fig. 3.3.2 S is varied proportionally to M with S/M as an additional parameter. In Fig. 3.3.3 the proportion of S^2 and M is constant for each curve. In both cases large regions occur over which these input-output relations are approximately linear.

In Fig. 3.3.4 attention is concentrated on the functional relation between N and S^2 while M is constant for each curve. A rather different presentation of the relation between N, M and S^2 is given in Fig. 3.3.5. Here M is the horizontal, S^2 the vertical ordinate and the curves are the collection of (M,S^2) values which result in the same output frequency. For $S^2 > 0.2$ the isofrequency curves are rather linear and can be described to a good approximation by

$$N_o = N_o (M + qS^2) \qquad (3.3.15)$$

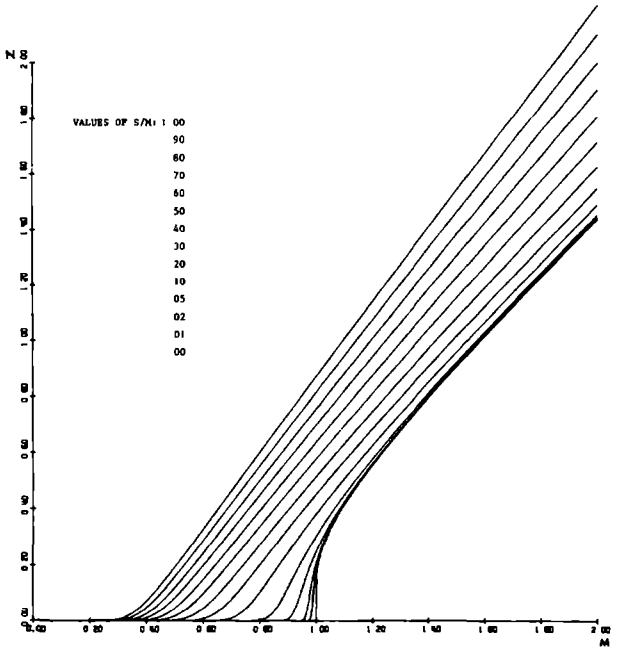


Fig. 3.3.2 Frequency-current relations for the SILIT-model for different values of the proportion S/M.

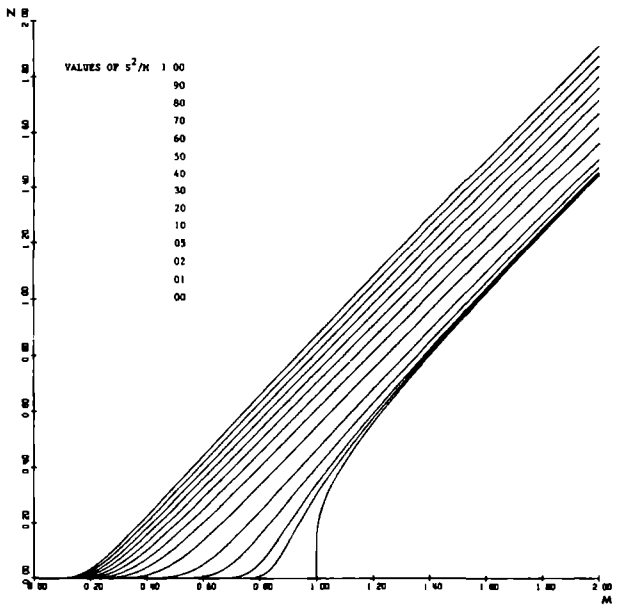


Fig. 3.3.3 Frequency-current relations for the SILIT-model for different values of the proportion S^2/M.

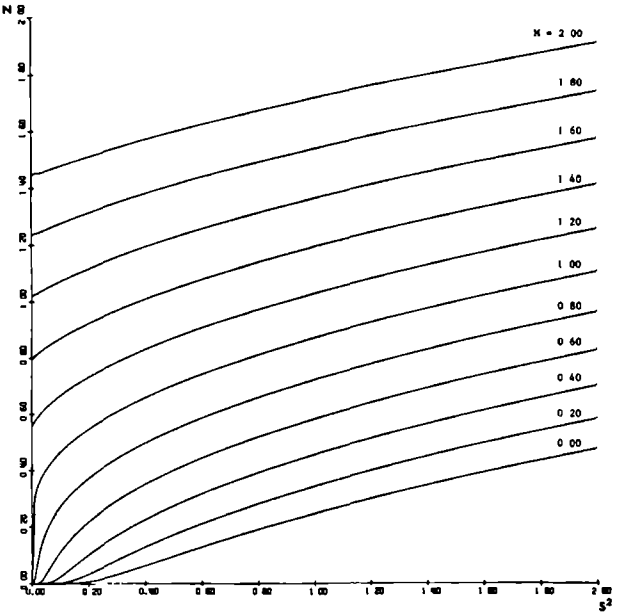


Fig. 3.3.4 Frequency-variability relations for the SILIT-model for different values of the average input current.

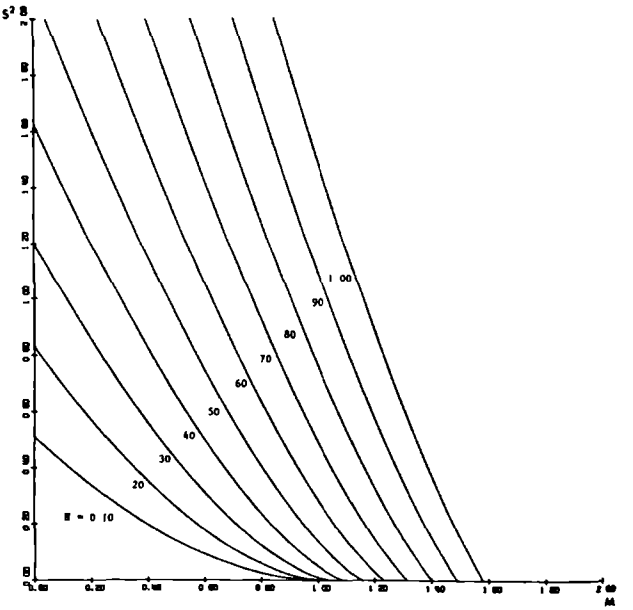


Fig. 3.3.5 Iso-frequency curves for the SILIT-model.

In several of the previous graphs large regions of quasi-linearity were present. In order to investigate this phenomenon more precisely we proceed as follows. In an arbitrary point (M_o, S_o^2) of the (M,S^2)-plane (with the exception of $M = 1$, $S^2 = 0$) an expansion of the function $N(M,S^2)$ is possible.

$$N(M,S^2) = N(M_o,S_o^2) + (M-M_o)\,\frac{\partial}{\partial M}\,N(M,S_o^2)_{/M=M_o} + (S^2-S_o^2)\,\frac{\partial}{\partial S^2}\,N(M_o,S^2)_{/S=S_o} + \Delta(M,S^2;M_o,S_o^2) \qquad (3.3.16)$$

where Δ represents the rest term of this expansion.

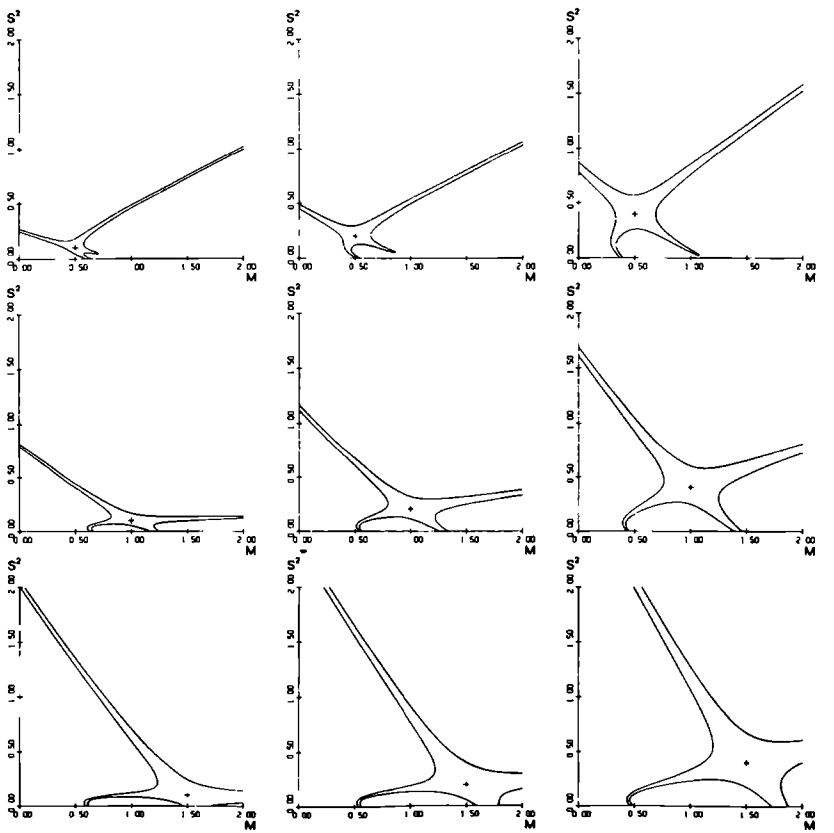


Fig. 3.3.6 Linear ε-regions for the SILIT-model for ε = 0.01
horizontally : S^2 = 0.10; 0.20; 0.40
vertically : M = 0.50; 1.00; 1.50

The (stationary) ε-region of linearity around (M_o, S_o^2) is then defined as the collection of (M, S^2) for which

$$\Delta(M, S^2; M_o, S_o^2) < \varepsilon \qquad (3.3.17)$$

This implies that within this region a linear approximation holds with an error less than ε.

A number of these regions for $\varepsilon = 0.01$ are presented in Fig. 3.3.6 and Fig. 3.3.7. Remarkable is that the regions are not necessarily closed and that form and size depend on the location of the centre. The significance of these regions for a linearised dynamical description based on stochastic transfer functions is pointed out in Ch. 4.

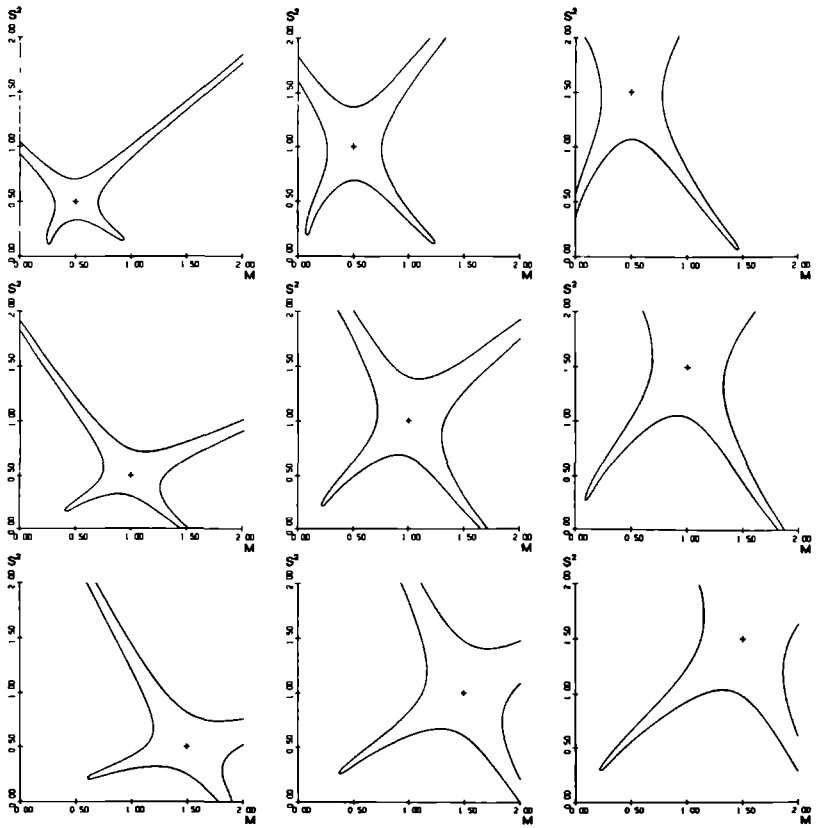


Fig. 3.3.7 Linear ε-regions for the SILIT-model for $\varepsilon = 0.01$
horizontally: S^2 = 0.50; 1.00; 1.50
vertically : M = 0.50; 1.00; 1.50

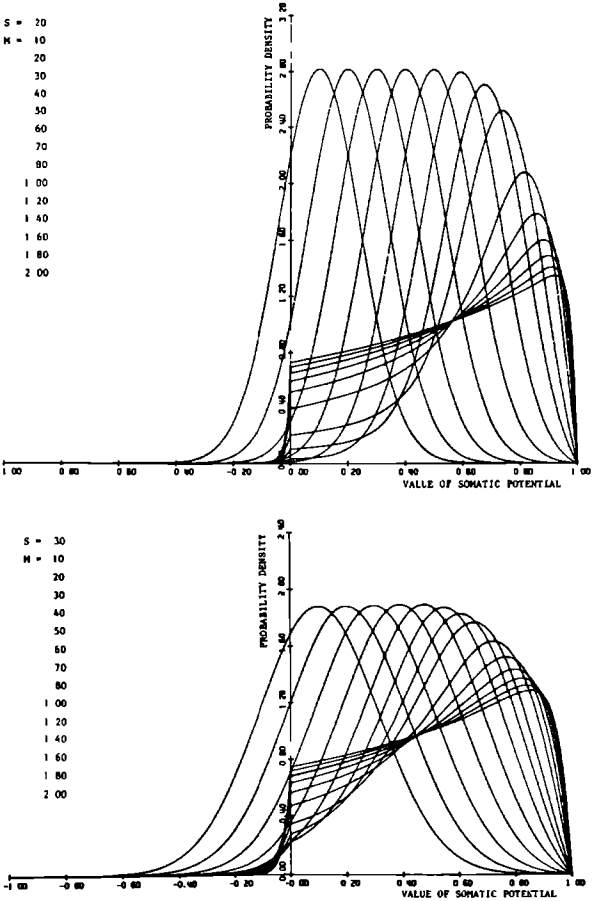
The stationary distribution of the somatic potential follows from the substitution of Eq.(3.3.2), (3.3.3) and (3.3.4) in the general expression given by Eq.(2.2.11). The result is

$$h(y) = \frac{N}{\frac{1}{2}\Delta^2} \exp\{-(\frac{y-m}{\Delta})^2\} \int_y^d dz\ \varepsilon(z-x_o) \exp\{(\frac{z-m}{\Delta})^2\} \qquad (3.3.18)$$

For the case x = 0, d = 1 this expression becomes

$$h(y) = \frac{N}{\frac{1}{2}S^2} \exp\{-(\frac{y-M}{S})^2\} \int_y^1 dz\ \varepsilon(z) \exp\{(\frac{z-M}{S})^2\} \qquad (3.3.19)$$

A number of these distributions are presented in Fig. 3.3.8.



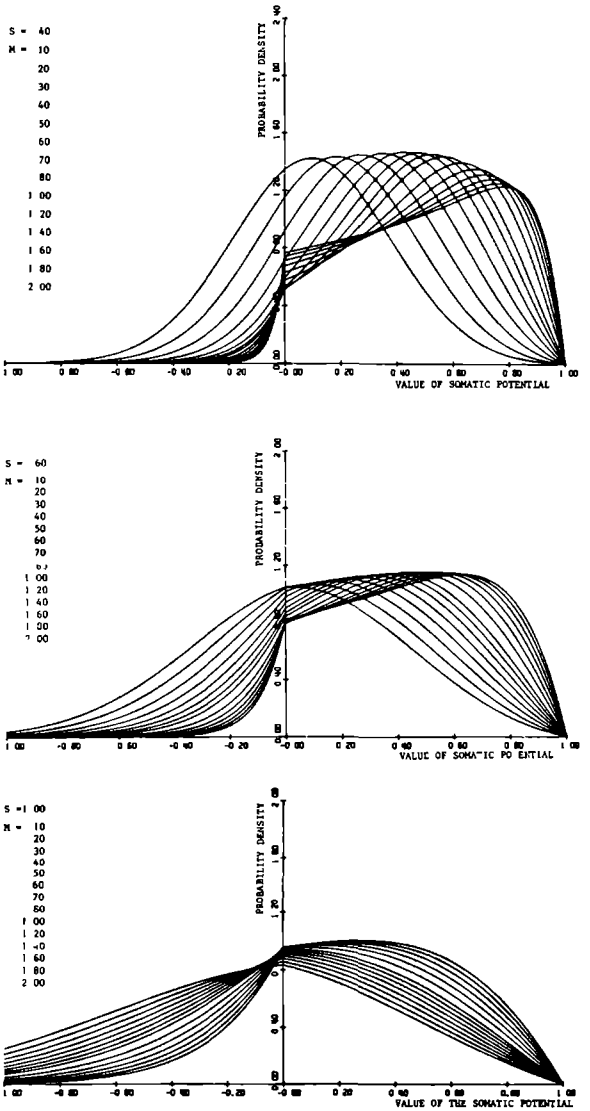


Fig. 3.3.8 Distributions of the somatic potential for the SILIT-model for different values of M and S; M increases from left to right.

The moments of the stationary distribution of the somatic potential are defined as

$$Y_k = \int_{-\infty}^{d} dy\ y^k\ h(y) \qquad (3.3.20)$$

A recurrence relation between these moments can be derived:

$$Y_o = 1$$

$$Y_k = M\ Y_{k-1} + (k-1)\tfrac{1}{2}S^2\ Y_{k-2} - \frac{1}{k}\ N \qquad (3.3.21)$$

It follows directly that the average value of the somatic potential is

$$Y_1 = M - N \qquad (3.3.22)$$

and the variance

$$Y_2 - Y_1^2 = \tfrac{1}{2}S^2 + (M - N - \tfrac{1}{2})N \qquad (3.3.23)$$

In Fig. 3.3.9 - 3.3.11 the average value and in Fig. 3.3.12 - 3.3.14 the standard deviation of the somatic potential are given as functions of the normalised average input M.

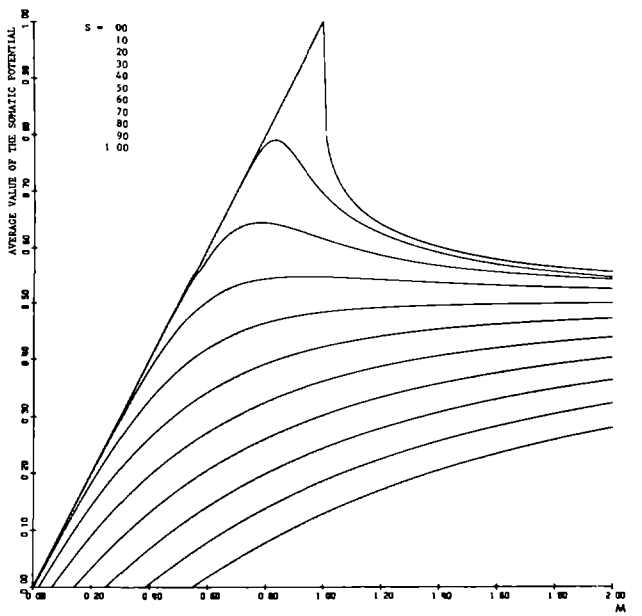


Fig. 3.3.9 Average value of the somatic potential versus normalised average input (M) for different amounts of variability of the input (S).

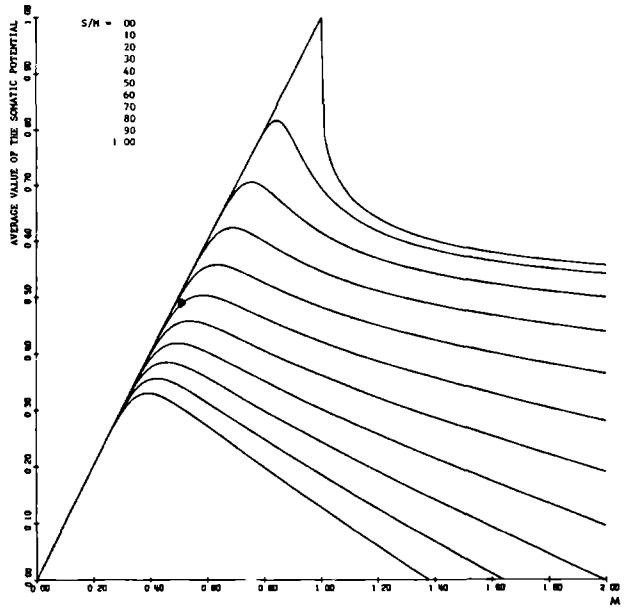


Fig. 3.3.10 Average value of the somatic potential versus normalised average input (M) for different values of the proportion S/M.

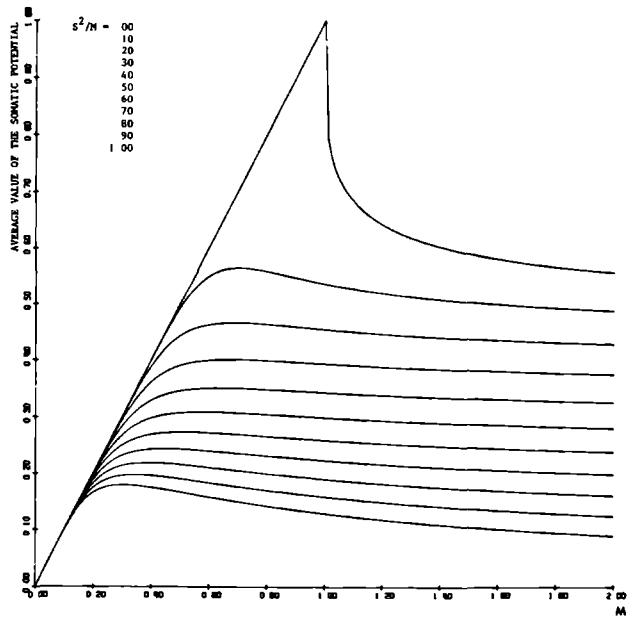


Fig. 3.3.11 Average value of the somatic potential versus normalised average input (M) for different values of the proportion S^2/M.

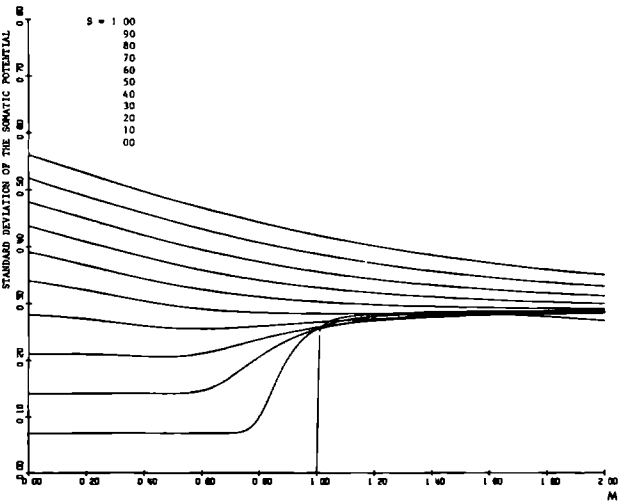


Fig. 3.3.12 Standard deviation of the somatic potential versus normalised average input (M) for different amounts of variability of the input (S).

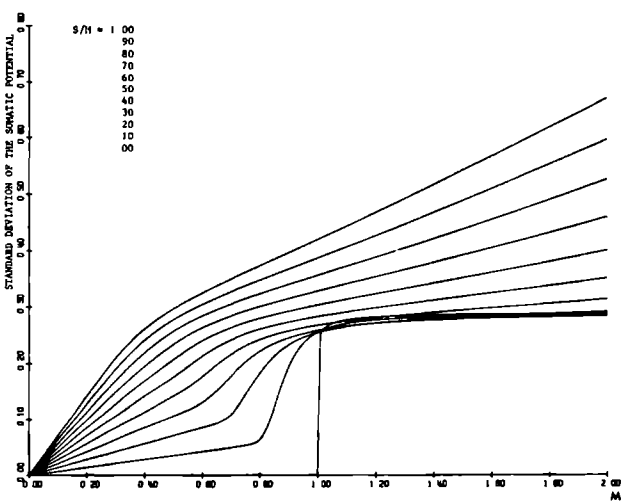


Fig. 3.3.13 Standard deviation of the somatic potential versus normalised average input (M) for different values of the proportion S/M.

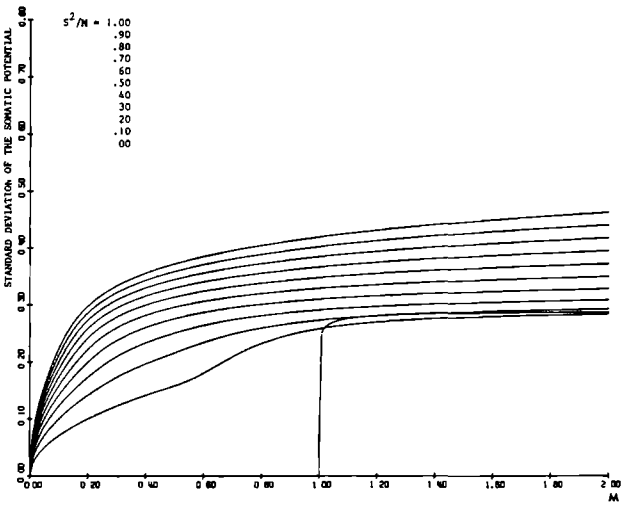


Fig. 3.3.14 Standard deviation of the somatic potential versus normalised average input (M) for different values of the proportion S^2/M.

In the case where the incremental variance (S^2) is proportional to the average value (M) of the input both average value (Fig. 3.3.11) and standard deviation (Fig. 3.3.14) of the somatic potential vary only weakly for $M \gtrsim 0.50$.

If the SILIT-model does apply, which has to be decided on the base of intracellular measurements, the results of this paragraph should correlate with the experimental data. However, all numerical results presented here are based on the assumption that the reset value of the somatic potential (x_o) is equal to its equilibrium value (0). If this is not the case the numerical computations have to be done for the correct value of x_o before a quantitative comparison between experimental and theoretical results can be made.

3.4 APPLICATION OF THE DIFFUSION MODEL ON THE EQUIVALENT CIRCUIT OF THE MEMBRANE

This section is mainly intended as a demonstration of the wide range of possible applications of the diffusion approach and as a first step toward a more accurate description of the stochastic behaviour of the somatic potential and the generation of action potentials.

As long as no action potential occurs a small uniform patch of membrane is represented by the circuit of Fig. 3.4.1. (Rall, 1962).

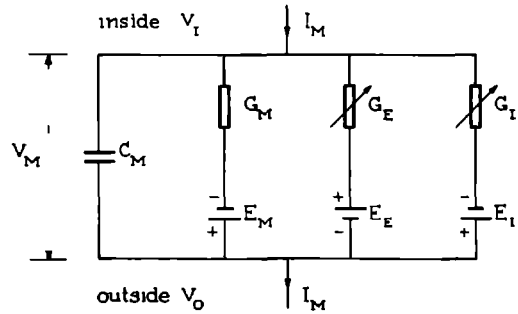


Fig. 3.4.1 The equivalent circuit of the membrane

The equivalent equation reads

$$I_M = C_M \frac{dV_M}{dt} + G_M(V_M - E_M) + G_E(V_M - E_E) + G_I(V_M - E_I) \qquad (3.4.1)$$

or

$$\tau \frac{dV}{dt} = - V + I_M R_M + (E_e - V)e + (E_i - V)i, \qquad (3.4.2)$$

where

$\tau = C_M/G_M = R_M C_M$ = membrane time constant

$V = V_M - E_M$, $\quad E_e = E_E - E_M$, $\quad e = G_E/G_M$,

$V_M = V_I - V_O$, $\quad E_i = E_I - E_M$, $\quad i = G_I/G_M$.

and the membrane current I_M is an arbitrary function of the membrane potential V.

We assume the input signal to consist of unpredictable changes in the relative excitatory and inhibitory conductances G_E/G_M and G_I/G_M, of which only average values and incremental variances are known.

$$m_e = \langle e(t) \rangle, \qquad s_e^2 = \int_{-\infty}^{\infty} d\tau \, \{\langle e(t).e(t+\tau) \rangle - \langle e(t)^2 \rangle\}$$

$$m_i = \langle i(t) \rangle, \qquad s_i^2 = \int_{-\infty}^{\infty} d\tau \, \{\langle i(t)\ i(t+\tau) \rangle - \langle i(t)^2 \rangle\}$$

Eq.(3.4.2) can be written as

$$\frac{dV}{dt} = \alpha(V) + s_e(V)\ n_e(t) + s_i(V)\ n_i(t) \tag{3.4.3}$$

with

$$\alpha(V) = \tau^{-1}\{I_M(V)R_M + m_e E_e + m_i E_i\} - \tau^{-1}\{m_e + m_i + 1\}\ V,$$

$$s_e(V) = s_e\{E_e - V\} \qquad s_i(V) = s_i\{E_i - V\},$$

$$n_e(t) = \frac{e(t) - m_e}{s_e} \qquad n_i(t) = \frac{i(t) - m_i}{s_i}$$

If both excitation and inhibition consist of many small independent contributions, each with a short duration, then Eq.(3.4.3) may be considered as a fluctuation equation. It can be written as

$$\frac{dV}{dt} = \alpha(V) + \beta(V)w(t) \tag{3.4.4}$$

with

$w(t)$ = Gaussian white noise with zero mean and unit variance,

$\beta(V) = s_e(V) + cs_i(V)$, $-1 \leq c \leq 1$,

if $n_e(t)$ and $n_i(t)$ are completely correlated;

$\beta^2(V) = s_e^2(V) + s_i^2(V)$,

if $n_e(t)$ and $n_i(t)$ are totally independent.

Substitution of these quantities in the appropriate equations will supply the expressions for the stationary distribution of the somatic potential and the moments of the interval distribution.

The description of this section takes more proporties of the membrane into account than the proportional decay model of the preceding paragraph; as a consequence it contains also more parameters. It appears that this more precise description will only make sense quantitively, if the values of all parameters and variables can be measured and proper regard is paid to the geometrical properties of the neuron.

SOME ASPECTS OF THE DYNAMICS

4.1. INTRODUCTION

The subject of this chapter is the dynamical behaviour of neurons. While a large amount of theoretical work has been done on the analysis of stationary stochastic activity of neurons, much less insight exists concerning the dynamical aspects.

Consider a situation given by

$$o(t) = T\{i(t)\} \tag{4.1.1}$$

where T is a linear or nonlinear integro-differential operator representing the system. The output o(t) is completely measurable. For the input i(t) two situations are considered: i(t) is completely or i(t) is incompletely measurable. In both cases i(t) is supposed to be controllable to the same extent as it is measurable. An auditory stimulus is usually assumed to be completely measurable, while a visual stimulus should, at least for low intensities, be regarded as incompletely measurable.

For a completely measurable input a first order estimation of the dynamics of the system T is acquired from the correlation between input and output. A number of signals may be used as input: impuls, step, ramp, sinewaves, noise. For a linear system these different signals all lead to the same characterisation: the impulse response or its Laplace transform, the transfer function. For nonlinear systems different classes of input signals usually lead to different descriptions.

In engineering it is well known that in many situations it has advantages to use white noise for the analysis of nonlinear systems. The input is choosen as

$$i(t) = w(t)$$

where $w(t)$ = stationary Gaussian white noise

Values of input and output with a delay τ are multiplied and averaged with respect to time. The resulting quantity is the crosscorrelation function

$$\rho(\tau) = \langle i(t - \tau).\ o(t) \rangle \tag{4.1.2}$$

If the system T is not too strongly nonlinear an approximation by a linear system is useful. The optimal approximation resulting in the least square deviation for this input is the linear system with impulse response $\rho(\tau)$ or transfer function $\hat{\rho}(p)$. A clear exposition of these methods is given in Graham and McRuer, (1961).

It is important to realise that this method makes use of complete knowledge of input and output signal. Only after delay and multiplication the averaging operation is performed. The noise w(t) as used here is unpredictable but measurable; a priori it is unknown but not a posteriori.

A completely different situation arises if the input i(t) is a stochastic quantity which is only partly measurable. Already mentioned is the example of the visual system where the statistical parameters of the stimuli are easily measured and controlled, but the precise times of occurrence of the light quanta cannot be measured without destruction of the signal.

As in § 1.3 we assume that the input may be described as

$$i(t) = m(t) + s(t).w(t) \qquad (4.1.3)$$

The average value of m(t) and incremental variance $s^2(t)$ of the input, defined by Eq.(1.3.2)-(1.3.5), are measurable but the white noise w(t), described by Eq.(1.3.12a)-(1.3.12b), is not measurable.

A rather different approach has to be developed for the analysis of this situation. The input signal is defined as the pair $\{m(t), s^2(t)\}$; it is the $\{m(t), s^2(t)\}$ modulation of a carrier consisting of white noise. This modulation can be additive (m), multiplicative (s^2) or a combination of these. Since the carrier contains equally all frequenties from zero to infinity, there are no limitations on the frequency content of the modulation.

In some situations s(t) may be dependent on m(t). For instance if the input is a frequency modulated Poisson process, or a sum of independent identically modulated Poisson processes, then $s^2(t)$ is proportional to m(t). On the other hand, in the neurophysiologically unlikely situation that the amplitude of the pulses is modulated, s(t) is proportional to m(t). If only additive noise is present $s^2(t)$ is independent of m(t). In the case that s(t) = 0 for all t, this description and the previous one for completely known signal are identical.

A general property of these signals is that the sum of two signals $\{m_1(t), s_1^2(t)\}$ and $\{m_2(t), s_2^2(t)\}$ with uncorrelated white noise carriers

$w_1(t)$ and $w_2(t)$ is a signal $\{m(t), s^2(t)\}$ with

$$m(t) = m_1(t) + m_2(t)$$
$$s^2(t) = s_1^2(t) + s_2^2(t)$$

Because of the stochastic nature of the input, the output is also stochastic. The output signal is therefore defined as

$$n(t) = \langle o(t) \rangle \tag{4.1.4}$$

For neurons the output is a sequence of action potentials. The traditional assumption is that this signal is determined only by the times at which the action potentials occur. As a consequence it may be written

$$o(t) = \sum_i \delta(t-t_i) \tag{4.1.5}$$

The output signal n(t) is then the event density of action potentials. A proper definition of this function is given by the equation.

$$n(t)\, dt = \left\langle \int_t^{t+dt} du \sum_i \delta(u-t_i) \right\rangle \tag{4.1.6}$$

The analysis starts now from the relations between input signal $\{m(t), s^2(t)\}$ and output signal n(t). This type of analysis will be needed if seemingly identical repetitions of an experiment produce different results.

Since $n(t)dt$ represents the probability that an action potential occurs in $(t,t+dt)$, the event density n(t) is the theoretical counterpart of the experimental quantity called the post stimulus time histogram. The input signal $\{m(t), s^2(t)\}$ is then usually an impulse, step, ramp or sinewave. In contrast to the first method described in this paragraph, here the averaging operation is performed before relations between input and output are analysed. Moreover this averaging operation cannot be taken anymore over time, but has to be over a number of repetitions of the experiment.

In this chapter attention is given to the dynamical relations between $\{m(t), s^2(t)\}$ and n(t). Two situations will be analysed. In § 4.2 the response to a stepwise change in the input signal from a level $\{m_o, s_o^2\}$ to another level $\{m_1, s_1^2\}$ is considered: the switch-response. This name is choosen to indicate that this response is, in contrast to the step-response in linear systems, dependent both on initial and final level of the input signal. An important special case is the switch -on response, which occurs

when $\{m_o, s_o^2\} = \{0,0\}$. The second case analysed in § 4.3 is that of small arbitrary variations of the input signal $\{m(t), s^2(t)\}$ around a fixed level $\{m_o, s_o^2\}$. Linearisation leads here to the concept of a stochastic transfer matrix, which supplies an approximative characterisation of the dynamical behaviour in a region around $\{m_o, s_o^2\}$. Combination of a number of the stochastic transfer matrices, guided by the stationary characteristics might finally result in a general dynamical representation of the input-output relations. The last paragraph of this chapter is devoted to the formulation of interaction equations.

4.2. THE STOCHASTIC SWITCH-RESPONSE

On the base of the derivations in Ch. 2 it is assumed that two functions are known.

$h(y)$ = stationary distribution of the somatic potential,

$g(t,x)$ = first passage time distribution for a start at x at time $t = 0$.

In order to be able to make use of these functions for a nonstationary situation, a single stepwise change in the input signal is choosen for analysis.

$$\begin{aligned} m(t) &= m_o, \quad s^2(t) = s_o^2 \quad \text{for } t < 0 \\ m(t) &= m_1, \quad s^2(t) = s_1^2 \quad \text{for } t > 0 \end{aligned} \tag{4.2.1}$$

For negative t the output signal, the event density, is independent of time

$$n(t;m_o,s_o^2) = n(m_o,s_o^2) = \{T_1(m_o,s_o^2)\}^{-1}, \quad t < 0$$

For positive t this event density is explicitly dependent on time. The following line of thought supplies an expression for n(t).

The probability density for the somatic potential at $t = 0$ is stationary and give by $h(x;m_o,s_o^2)$. The probability density that the first pulse occurs at $t > 0$ when the potential has a value x at $t = 0$ is the function $g(t,x;m_1,s_1^2)$ averaged over all initial values x, each with its probability density. Symbolically this may be written as

$$g(t;m_1,s_1^2|m_o,s_o^2) = \int_{-\infty}^{d} dx\, h(x;m_o,s_o^2)\, g(t,x;m_1,s_1^2) \tag{4.2.2}$$

The event density n(t) that an arbitrary pulse occurs at some time $t > 0$ obeys in the Laplace domain the equation

$$\hat{n}(p;m_1,s_1^2|m_o,s_o^2) = \frac{\hat{g}(p;m_1,s_1^2|m_o,s_o^2)}{1 - \hat{g}(p;m_1,s_1^2)} \tag{4.2.3}$$

where $g(t;m_1,s_1^2)$ is the stationary distribution of intervals for an input signal $\{m_1,s_1^2\}$.

Since $h(x;m_o,s_o^2)$ was given in Eq.(2.2.9) and $\hat{g}(p,x;m_1,s_1^2)$forms a power series in p for which the coefficients were derived in § 2.3, the function $\hat{n}(p;m_1,s_1^2|m_o,s_o^2)$ is, at least in principle, fully known.

Two special cases of Eq.(4.2.3) are treated.

In most models, with the exception of the SIPIT-model which contains a perfect integrator, an equilibrium value of the potential exists: x_e. It is evident that in these models for $m_o = 0$, $s_o^2 = 0$ the distribution of the somatic potential at $t = 0$ is concentrated at $x = x_e$

$$h(x;0,0) = \delta(x-x_e). \tag{4.2.4}$$

This simplifies Eq.(4.2.2) to

$$g(t;m_1,s_1^2|0,0) = g(t,x_e;m_1,s_1^2) \tag{4.2.5}$$

and Eq.(4.2.3) becomes

$$\hat{n}(p;m_1,s_1^2|0,0) = \frac{\hat{g}(p,x_e;m_1,s_1^2)}{1-\hat{g}(p;m_1,s_1^2)} \tag{4.2.6}$$

If reset and equilibrium potential would be identical, $x_e = x_o$, Eq.(4.2.6) becomes

$$\hat{n}(p;m_1,s_1^2|0,0) = \hat{n}(p,x_o;m_1,s_1) \tag{4.2.7}$$

Conclusion:

if equilibrium potential x_e and reset potential x_o are identical then the dynamical switch-on response of the event density is identical to the stationary conditional event density (or expectation density) for arbitrary values of average value and incremental variance of the input signal.

The second case is the application of the switch-response on the SIPIT-model. The stationary distribution of the somatic potential depends, as shown in § 3.2 for this model only on the ratio of average value and incremental variance of the input

$$h(y;m,s^2) = h(y;m/s^2). \tag{4.2.8}$$

For the input signal $\{m,s^2\}$ the assumption is made that, though average value and incremental variance change, their ratio is constant

$$m_1/s_1^2 = m_o/s_o^2 \tag{4.2.9}$$

Using Eqs.(4.2.2), (4.2.3) and (4.2.8) it can be shown that the condition of Eq.(4.2.9) leads to the relation

$$n(t;m_1,s_1^2|m_o,s_o^2) = n(t;m_1,s_1^2|m_1,s_1^2) \tag{4.2.10}$$

The right hand side of this equation is the event density in case no change in the input signal occurred; this however, is the stationary event density.

As a consequence

$$n(t;m_1,s_1^2|m_1,s_1^2) = n(m_1,s_1^2) \tag{4.2.11}$$

Eq.(4.2.11) states that the event density is in this situation independent of previous values of input or output signal, Since an arbitrary function of time may be approximation by a sequence of steps, this leads to

$$n(t;\ m(t),\ s^2(t)) = n(m(t)) \tag{4.2.12}$$

From the results of § 3.2 follows

$$n(m) = \lambda.m \tag{4.2.13}$$

$$\lambda = (d - x_o)^{-1},\ m \geq 0$$

which gives finally for the SIPIT-model

$$n(t;\ m(t),\ s^2(t)) = \lambda.m(t) \tag{4.2.14}$$

Conclusion:

if the SIPIT-model is subjected to an input signal $\{m(t),s^2(t) = c.m(t)\}$, $c \geq 0$

then the output signal $n(t)$ *is, apart from the scaling factor* λ, *identical to the input signal* $m(t)$

$$n(t) = \lambda.m(t) \tag{4.2.15}$$

4.3 LINEAR REGION AND STOCHASTIC TRANSFER MATRIX

The purpose of this paragraph is to develop a generalisation of the transfer function. This function, defined as the Laplace transform of the impulse response, has proven extremely useful in linear system theory.

The relation between the input current i(t) and the output sequence of action potentials o(t) is strongly nonlinear. Traditional methods of linearisation will be unsuccesful in this case. However, the redefined input signal $\{m(t), s^2(t)\}$ and output signal n(t) are much more linearly related. This is well illustrated by the stationary N versus $\{M,S^2\}$ graphs in § 3.3.

A linear description, expressed by means of a stochastic transfer function, will serve as a first order approximation of the dynamical properties. The usefulness of this approximation depends on the size of the region in which the linear description applies with a precision ε.

The point of departure is again a stepwisse change in the input signal at t = 0, but now limited to small amplitudes

$$\{m_o, s_o^2\} \rightarrow \{m_o + \Delta m, s_o^2 + \Delta s^2\}$$

The stationary event density for t < 0 is equal to $n(m_o, s_o^2)$. The stochastic step response is

$$u(t;\Delta m,\Delta s^2;m_o,s_o^2) = n(t,m_o + \Delta m, s_o^2 + \Delta s^2 | m_o, s_o^2) - n(m_o, s_o^2) \qquad (4.3.1)$$

If the event density and its derivatives are differentiable, which appears in general to be the case for $s^2 \geq \delta > 0$, then it may be approximated by a power series in both Δm and Δs

$$n(t;m_o + \Delta m, s_o^2 + \Delta s^2 | m_o, s_o^2)$$

$$\simeq \sum_{k=o}^{K} \frac{1}{k!} \{\Delta m \frac{\partial}{\partial m} + \Delta s^2 \frac{\partial}{\partial s^2}\}^k n(t;m,s^2|m_o,s_o^2)_{/m=m_o \atop s=s_o} \qquad (4.3.2)$$

For Δm and Δs^2 small enough the terms with $k \geq 2$ give a contribution less than a given ε; neglecting then terms with $k \geq 2$ gives the linear approximation to the step response. The values of $\{\Delta m, \Delta s^2\}$ around $\{m_o, s_o^2\}$ for which the linear approximation to the stepresponse differs less than ε from the exact response is defined as the ε-region of $\{m_o, s_o^2\}$.

The linear approximation of the stochastic stepresponse is

$$u(t;\Delta m,\Delta s^2;m_o,s_o^2) \approx \{\Delta m \frac{\partial}{\partial m} + \Delta s^2 \frac{\partial}{\partial s^2}\} \; n(t;m,s^2|m_o,s_o^2)_{/\substack{m=m_o \\ s=s_o}} \tag{4.3.3}$$

or in matrix notation

$$u = [u_m, u_{s^2}] \cdot \begin{bmatrix} \Delta m \\ \Delta s^2 \end{bmatrix} \tag{4.3.3}$$

with

$$u_m(t;m_o,s_o^2) = \frac{\partial}{\partial m} n(t;m,s_o^2|m_o,s_o^2)_{/m=m_o} \tag{4.3.4}$$

$$u_{s^2}(t;m_o,s_o^2) = \frac{\partial}{\partial s^2} n(t;m_o,s^2|m_o,s_o^2)_{/s=s_o}$$

An arbitrary function of time can be approximated by a sequence of steps. If $\varepsilon << 1$ then all steps within the ε-region of $\{m_o,s_o^2\}$ have the form of the step response of $\{m_o,s_o^2\}$ as described by $[u_m,u_s^2]$ of Eq.(4.3.4) with an error of the order of ε. A linear description of the input-output relations applies then in the whole ε-region of $\{m_o,s_o^2\}$ with precision ε and methods analogous to linear system theory may be used.

As in linear system theory a transfer matrix is defined; however, here this is a region-dependent stochastic transfer matrix. Its elements are equal to the Laplace transforms of the corresponding elements of the stochastic unit stepresponse matrix multiplied with p

$$\hat{h}_m(p;m_o,s_o^2) = p\,\hat{u}_m(p;m_o,s_o^2) = p \frac{\partial}{\partial m} \hat{n}(p;m,s_o^2|m_o,s_o^2)_{/m=m_o} \tag{4.3.5}$$

$$\hat{h}_{s^2}(p;m_o,s_o^2) = p\,\hat{u}_{s^2}(p;m_o,s_o^2) = p \frac{\partial}{\partial s} \hat{n}(p;m_o,s^2|m_o,s_o^2)_{/s=s_o} \tag{4.3.6}$$

The region dependent stochastic transfer matrix is

$$\hat{H} = [\hat{h}_m, \hat{h}_{s^2}] \tag{4.3.7}$$

The relation between an arbitrary input signal $\{m(t),s^2(t)\}$ within the ε-region of $\{m_o,s_o^2\}$ and the output signal $n(t)$ is then, in the Laplace domain, given by

$$\hat{n}(p) - \hat{n}_o(p) = [\hat{h}_m, \hat{h}_{s^2}] \begin{bmatrix} \hat{m}(p) - \hat{m}_o(p) \\ \hat{s}^2(p) - \hat{s}_o^2(p) \end{bmatrix}$$

or

$$\hat{n}(p) - n_o/p = \hat{h}_m \{\hat{m}(p) - m_o/p\} + \hat{h}_{s2} \{\hat{s}^2(p) - s_o^2/p\} \qquad (4.3.8)$$

where

$$n_o = n(m_o, s_o^2)$$

is the stationary event density for the centre of this domain and $\hat{h}_m$ and $\hat{h}_{s2}$ are as defined in Eq. (4.3.5) and Eq.(4.3.6). Eq.(4.3.8) is valid for arbitrary but fixed $\{m_o, s_o^2\}$.

There are reasons to expect that the dependency of $\hat{h}_m(p;m_o,s_o^2)$ on s_o^2 may, in a number of situations, be quite strong and that in many cases the dependency of $\hat{h}_{s2}(p;m_o,s_o^2)$ on p will be weak.

Form and size of dynamical ε-regions are usually difficult to determine, however, these regions are always contained within the corresponding stationary ε-region. A reasonable estimation of the dynamical ε-region would be the stationary ε/2-region.

For the SIPIT-model, treated in § 3.2, the stationary relation between the input and the output signal is

$$n = \lambda.m, \qquad \lambda = (d - x_o)^{-1}, \qquad m \geq 0 \qquad (4.2.13)$$

The stationary ε-region of linearity is then for arbitrarily small ε

$$m \geq 0 \qquad (4.3.9)$$

Eq.(4.2.15) leads to the conclusion that the dynamical ε-regions of linearity are

$$\{m(t) \geq 0,\ s^2(t) = c.m(t)\},\ c \geq 0 \qquad (4.3.10)$$

Because of the character of the region defined by Eq.(4.3.10), it is permitted to take n_o, m_o and s_o^2 in Eq.(4.3.8) all equal to zero. This results in the equation

$$\hat{n}(p) = \hat{h}_m\, \hat{m}(p) + \hat{h}_{s2}\, \hat{s}^2(p) \qquad (4.3.11)$$

under the constraint

$$\hat{s}^2(p) = c\, \hat{m}(p)\ ,\ c \geq 0 \qquad (4.3.12)$$

Laplace transformation of Eq.(4.2.15) gives

$$\hat{n}(p) = \lambda.\hat{m}(p) \qquad (4.3.13)$$

Combination of the last three equations leads to a relation between the two elements of the stochastic transfer matrix of the SIPIT-model

$$\hat{h}_m(p;c) + c.\hat{h}_{s2}(p;c) = \lambda \qquad (4.3.14)$$

Conclusion:

if the SIPIT-model receives an input signal

$$\{m(t),\ s^2(t) = c.m(t)\},\ c \geq 0$$

then a stochastic transfer function can be defined as

$$\hat{h}(p;c) = \hat{h}_m(p;c) + c\,\hat{h}_{s^2}(p;c) \qquad (4.3.15)$$

which is valid for all $m(t) \geq 0$;

the form of this transfer function is

$$\hat{h}(p;c) = \lambda$$

The stationary ε-regions of linearity for the SILIT-model were presented in § 3.3 for $\varepsilon = 0.01$. The dynamical characteristics of this model are hard to analyse; no general properties could be derived. Intuitively it seems clear that for large values of the input signal the leakage of the somatic potential is relatively unimportant and the behaviour resembels strongly that of the SIPIT-model. For small values of the input such that firing frequency is low, a relation between the transfer function of the linear part of the neuron in front of the threshold and the correlation between a white noise input and the output spike sequence has been established by De Boer (1967, 1968). It appears that this correlation function is tightly related with the transfer function $\hat{h}_m(p;0,0)$. Values of the input comparable to the threshold may lead to much more complex characteristics.

From the stochastic transfer matrix a deterministic transfer function can be derived. In the deterministic situation the input signal does not contain an unknown part, this implies

$$\{m,s^2\} \rightarrow \{m,0\}$$

The stochastic transfer matrix $[\hat{h}_m, \hat{h}_{s^2}]$ becomes a transfer function $\hat{h}_m$ defined as

$$\hat{h}_m(p;m_o) = \lim_{s_o^2 \to o} \hat{h}_m(p;m_o,s_o^2) \qquad (4.3.16)$$

and the input-output relation takes the form

$$\hat{n}(p) - \hat{n}_o(p) = \hat{h}_m(p;m_o)\,\{\hat{m}(p) - \hat{m}_o(p)\} \qquad (4.3.17)$$

For $m_o = 0$ this deterministic transfer function resembles strongly the Laplace transform of the correlation function $\hat{\rho}(p)$ given in § 4.1.

For linear systems stochastic transfer matrix, deterministic transfer function and traditional transfer function are all identical.

4.4. INTERACTION EQUATIONS

The results presented in this paper do not allow a complete specification of general interaction equations. However, it is possible to propose nonlinear equations describing the stationary interaction for a large region of the input and output variables. Moreover, linearised dynamical interaction equations can be formulated which are valid for small variations of the variables within an arbitrary region.

The numerical data for the stationary input-output relations of the SILIT-model are given in graphical form in § 3.3. These results can be described through

$$N = \exp\{\alpha M + \beta S^2 - \gamma N - \delta + c(M,S^2)\} \tag{4.4.1}$$

where $c(M,S^2)$ is a correction function which is small for large regions of the (M,S^2)-plane. The neglection of this function gives the approximation

$$N \approx \exp\{\alpha M + \beta S^2 - \gamma N - \delta\} \tag{4.4.2}$$

Since for constant S^2

$$\lim_{M\to\infty} \frac{N}{M} = 1$$

it follows that

$$\gamma = \alpha \tag{4.4.3}$$

Moreover there exists the relation

$$\delta = \lim_{m\to\infty} \left\{ \frac{m\tau}{d-x_o} - \left(\ln \frac{1-x_o/m\tau - 1}{1-d/m\tau}\right) \right\} = \tfrac{1}{2}\frac{d+x_o}{d-x_o} \tag{4.4.4}$$

When reset and equilibrium potential are equal, as choosen for the computations of § 3.3, then $\delta = \frac{1}{2}$. The results, especially Fig. 3.3.5, indicate that β/α is not really a constant but decreases with N; for $N \gtrsim 0.1$ holds that $0 \leq \beta/\alpha \leq 1$. In spite of this deficiency we shall accept Eq.(4.4.2) as an approximation to the stationary input-output relation.

For a neuron in interaction with other neurons subscripts should be added to all variables. Eq.(4.4.2) reads then

$$N_i = \exp\{\alpha_i M_i + \beta_i S_i^2 - \alpha_i N_i - \delta_i\} \tag{4.4.5}$$

The analysis of § 1.3 and § 1.4 showed that, in the absence of external influences and under the condition of high convergence, the input is to a large extent characterised by average value and incremental variance of this signal.

The relation between M and S^2 and the contributing spike sequences is given by Eq.(1.4.2)-(1.4.5)

$$M_i = \frac{m_i \tau_i}{d_i} = \sum_j \frac{c_{ij}}{d_i} \frac{\tau_i}{\tau_j} N_j \qquad (4.4.6)$$

$$S_i^2 = \frac{s_i^2 \tau_i}{d_i} = \sum_j \left(\frac{c_{ij}}{d_i}\right)^2 \frac{\tau_i}{\tau_j} N_j \qquad (4.4.7)$$

It is desirable to define the dimensionless quantities

$$\gamma_{ij} = \{\alpha_i \frac{c_{ij}}{d_i} + \beta_i \left(\frac{c_{ij}}{d_i}\right)^2\} \cdot \frac{\tau_i}{\tau_j}, \quad i \neq j \qquad (4.4.8)$$

$$\gamma_{ii} = \alpha_i \left(\frac{c_{ii}}{d_i} - 1\right) + \beta_i \left(\frac{c_{ii}}{d_i}\right) \qquad (4.4.9)$$

The equations describing the stationary activity of an ensemble of interacting neurons take then the form

$$N_i = \exp\{\sum_j \gamma_{ij} N_j - \delta_i\} \qquad (4.4.10)$$

or

$$\ln N_i = \sum_j \gamma_{ij} N_j - \delta_i \qquad (4.4.11)$$

A reasonable way to incorporate refractoriness in the stationary equations is the multiplication of the right hand side of Eq.(4.4.10) with

$$1 - r_i n_i = 1 - \rho_i N_i$$

where r_i is the duration of the refractory period and $\rho_i = r_i/\tau_i$. The resulting stationary equations are

$$N_i = (1 - \rho_i N_i) \exp\{\sum_j \gamma_{ij} N_j - \delta_i\} \qquad (4.4.13)$$

or

$$\ln \frac{N_i}{1 - \rho_i N_i} = \sum_j \gamma_{ij} N_j - \delta_i \qquad (4.4.14)$$

Eq.(4.4.14) is formally equivalent to the stationary form of interaction equations used by Cowan (1967, 1968); however, the interpretation of the interaction coefficients is different.

Dynamical interaction equations can only be derived in a linearised form. These equations are based on Eqs.(4.3.5), (4.3.6) and (4.3.8). In order to avoid double indices we define

$$\hat{h}(p;m,s^2) = \hat{h}_m(p;m,s^2) \tag{4.4.15}$$

$$\hat{k}(p;m,s^2) = \hat{h}_{s^2}(p;m,s^2) \tag{4.4.16}$$

The linearised dynamical input-output equation for neuron i reads then

$$\hat{n}_i(p) - n_i/p = \hat{h}_i(p;m,s_i^2)\{\hat{m}_i(p) - m_i/p\} + \hat{k}_i(p;m_i,s_i^2)\{\hat{s}_i^2(p) - s_i^2/p\} \tag{4.4.17}$$

where

$$n_i = \langle n_i(t)\rangle, \qquad m_i = \langle m_i(t)\rangle, \qquad s_i^2 = \langle s_i^2(t)\rangle$$

are the time-averaged levels of these quantities.
A simplification of Eq.(4.4.17) is caused by the introduction of

$$\nu_i(t) = n_i(t) - n; \qquad \mu_i(t) = m_i(t) - m; \qquad \delta_i^2(t) = s_i^2(t) - s_i^2 \tag{4.4.18}$$

Substitution in Eq.(4.4.17) gives

$$\hat{\nu}_i(p) = \hat{h}_i(p;m_i,s_i^2)\ \hat{\mu}_i(p) + \hat{k}_i(p;m_i,s_i^2)\ \hat{\sigma}_i^2(p) \tag{4.4.19}$$

Synaptic delay and transmission time in axon and dendrites result in a delay between the generation of an action potential in neuron j and the arrival of the resulting excitation or inhibition at the central structure of neuron i; this delay is designed as τ_{ij}. The analyses given in § 1.3 and § 1.4 indicate that for a neuron in interaction with many other neurons in the absence of an external stimulus the following relation holds

$$\mu_i(t) = \sum_j c_{ij}\ \nu_j(t - \tau_{ij}) \tag{4.4.20}$$

$$\sigma_i^2(t) = \sum_j c_{ij}^2\ \nu_j(t - \tau_{ij}) \tag{4,4.21}$$

Here the assumption is made that the signaltransmission from the soma of one neuron to the soma of another neuron can be described as an attennation (c_{ij}) and a pure delay (τ_{ij}).

Combination of the last three equations results in the linearised form of the interaction equations

$$\hat{\nu}_i(p) = \sum_j e^{-p\tau_{ij}}\ \hat{\kappa}_{ij}(p;m_i,s_i^2)\ \hat{\nu}_j(p) \tag{4.4.22}$$

where

$$\hat{\kappa}_{ij}(p;m_i,s_i^2) = c_{ij}\ \hat{h}_i(p;m_i,s_i^2) + c_{ij}^2\ \hat{k}_i(p;m_i,s_i^2) \tag{4.4.23}$$

In Eq.(4.4.22) the factor exp ($-p\tau_{ij}$) represents the dynamical aspects of the signal transmission from neuron j to neuron i, where $\hat{\kappa}_{ij}$ describes the transformation of this signal within neuron i.

The theory presented in this chapter is a first order description. The central quantity is n(t), the ensemble-averaged event density of action potentials. Because of the high convergence assumption, made in § 1.3 and § 1.4, higher order conditional event densities are irrelevant. As a consequence the applicability of the equations is limited to networks in which each cell synapses with many other cells.

The theoretical results of this chapter are essentially incomplete. However, a combination of the nonlinear stationary equation (Eq. (4.4.10)) with the linearised dynamical equations (Eq.4.4.22) might lead to more general interaction equations.

E P I L O G U E

5.1. DISCUSSION AND SUMMARY

The subject of this study is a theoretical analysis of the stochastic activity fo certain types of neural cells. The neurons considered are characterised by a large number of connections with other cells. The input signal to a single neuron is described through its average value and incremental variance; the detailed structure of the input is shown to be of less importance and considered as a white noise carrier. The neuron itself is represented by a, linear or nonlinear, first order filter followed by a threshold-reset mechanism.

The time course of the somatic potential turns out to be describable through a transition probability density which obeys a second order partial differential equation (diffusion equation). The threshold acts as an absorbing barrier, while the distribution of output spikes is equivalent to the distribution of first passage times of the somatic potential. An expression for the transition probability density of the somatic potential would supply a complete description of the activity. In general this sort of expression does apparently not exist in closed form. In the stationary case, however, it has been possible to derive the unconditional distribution of the somatic potential (h(y) given by Eq.(2.2.11)) and a recurrence relation between the moments of the interval distribution (given by Eq.(2.3.14)).

Though a way has been indicated to take account of relative refractory effects, this treatment cannot be considered as satisfactory. However, it is expected that insight in the dynamical activity will allow an acceptable description of these effects. The inclusion of absolute refractory properties does not present any mathematical problems.

Specific applications have been presented for three cases: a linear filter without decay (SIPIT-model), a linear filter with proportional decay of the potential (SILIT-model) and the equivalent circuit of the membrane; each of these followed by a threshold-reset mechanism.

The SIPIT-model which is well known and completely solvable, has been treated mainly because of its properties in a nonstationary situation. The most interesting result under stationary conditions is that the unconditional distribution of the somatic potential does not depend on both average value and variance of the input, but is determined only by their ratio.

The SILIT-model is accepted widely as a more realistic description of a neuron. The mathematical analysis showed that its interval distribution does not depend on all its five parameters but only on two combinations of these quantities. The numerical results include graphs for the mean rate of firing as a function of input variables, quasilinear input-output regions and distributions of the potential and its mean and variance.

The large size of the quasi-linear region when the average value and variance vary proportionally is remarkable. It should be realised that frequency modulated pulse trains possess this characteristic. The hypothesis of Mountcastle (1967) that the central nervous system operates in a linear manner on its input, is understandable from a theoretical point of view under of the assumption that the ratio of excitation and inhibition is constant. Another noteworthy feature of the SILIT-model in this situation is the weak dependence of average value and standard deviation of the somatic potential on the value of the input (Fig. 3.3.11 and 3.3.14). This suggests that the contribution of the somatic potential to an evoked potential may be quite small.

The equivalent circuit of the membrane is only treated as an example of a nonlinear system to which the theoretical framework does apply. Because of the large number of parameters of this model a quantitative evaluation should await precise experimental data.

The results of the analysis of the stationary situation are experimentally completely testable. Intracellular measurements, comparable to those of Calvin and Stevens (1968), will supply evidence concerning the applicability of the model and values of relevant parameters. Insertion of these values in the theoretical expressions should produce quantitative predictions of the stationary activity of such a cell.

The investigation into the dynamical aspects of the signal processing

properties is of a more preliminary nature; only a number of qualitative results have been obtained. The input signal is defined as the pair (m(t), s^2(t)), the modulation of average value and incremental variance of a white noise carrier. The output signal is n(t), the event density of action potentials. This approach takes the partial observability of the input explicitly into account. Both input and output are averaged over a suitable ensemble until statistically reproducible results are acquired, then dynamical relations are analysed. Though the procedure is used in many electrophysiological and in a number of psychological experiments, the presence of s^2(t) is not usually recognised. The theoretical analysis is limited to two cases: the response to a stepwise change and to small arbitrary variations of the input signal.

The stochastic switch-response is expressed in terms of the stationary distribution of somatic potential and first passage time. For the SIPIT-model this leads to the conclusion that, for constant ratio of s^2 and m, input and output signal are identical in form. For the SILIT-model this results in a relation between switch-on response and stationary conditional event density (expectation density). This again leads to a prediction of nonlinear oscillations in the post-stimulus-time histogram of a square wave stimulus. The period of these oscillations is strongly dependent on the amplitude of the input, but will in general be of the order of the time constant of the neuron. Experimental evidence of this type of microstructure in the P.S.T.H. of a square wave light modulation with a period of 100 - 1000 msec. has been found by Coenen (1968) in the lateral geniculate body of the cat and by Allen (1968) in ganglion cells of the rabbit; the period of the nonlinear oscillations being 1 - 10 m sec.

The input-output relations for small variations of the input signal (m(t), s^2(t)) are described in a linear approximation. This allows the definition of a stochastic transfer matrix, which forms a generalisation of the (stochastic) transfer function. For the SIPIT-model an important property of this matrix has been established. Conceptually the stochastic transfer matrix is considered to be of great importance; one reason for this is that its use allows a comparison of P.S.T.H.'s for different type of stimuli.

Moreover it suggests precise ways for the embedding of a simple signal in a complex environment. This technique, which generally results in an enlargement of the quasi-linear region, has been successfully applied in engineering and in the analysis of e.e.g. responses in man evoked by sine wave modulated light (Spekreyse, 1966).

A knowledge of the input-output relations for a single neuron allows the formulation of interaction equations for a network of a given structure. Since the stationary single cell relations are known over the complete region, interaction equations for a stationary network could be formulated in a general way. The more interesting equations for a nonstationary network could only be given in a linearised approximation. Theoretical work will be continued and experimental work initiated along these lines with an emphasis upon the investigation of the stochastic transfer matrix.

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STELLINGEN

I

De "momentane frequentie" van een pulsreeks gedefinieerd op basis van de intervallen tussen opeenvolgende pulsen leidt tot theoretische en experimentele problemen. Een acceptabele continue representatie van een pulsreeks wordt gegeven door een lineaire functionaal van deze reeks.

II

In een neuronaal net gekenmerkt door hoge convergentie zijn de hogere orde eigenschappen van de pulsreeksen (bijv. intervalverdeling) irrelevant.

III

De correlatie functie tussen extern aangeboden ruis en de pulsactiviteit in de gehoorzenuw zoals bepaald door de Boer, vormt een speciaal geval van de stochastische overdrachtsfunctie, beschreven in § 4.3 van dit proefschrift.

(E. de Boer. J. of Auditory Research, 7, 209-217 (1967)).

IV

Het is geenszins vanzelfsprekend dat de spontane activiteit van het centraal zenuwstelsel een stationair proces is. Inductie van de stationariteit door gunstig gekozen stimulering lijkt mogelijk.

V

Een stochastische beschrijving van een verschijnsel dient te worden opgevat als een relatie tussen waarnemer en verschijnsel. Dit is in het bijzonder relevant voor de controverse random versus deterministische verbindingen tussen zenuwcellen.

VI

De veel gebruikte analogie tussen hersenen en computer draagt vrijwel niet bij tot het begrip van de eigenschappen van hersenen.

VII

In Nederland bestaat een behoefte aan een postdoctorale opleiding in de biofysica, zowel voor fysici en ingenieurs als voor biologen.

VIII

Een streven naar een grotere zelfstandigheid van een groep of organisatie binnen een democratische samenleving dient gepaard te gaan met een bevordering van de interne democratie.

31 oktober 1969.