Synapse Models for Neural Networks: From Ion Channel Kinetics to Multiplicative Coefficient $w_{ij}$

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This paper relates different levels at which the modeling of synaptic transmission can be grounded in neural networks: the level of ion channel kinetics, the level of synaptic conductance dynamics, and the level of a scalar synaptic coefficient. The important assumptions to reduce a synapse model from one level to the next are explicitly exhibited. This coherent progression provides control on what is discarded and what is retained in the modeling process, and is useful to appreciate the significance and limitations of the resulting neural networks. This methodic simplification terminates with a scalar synaptic efficacy as it is very often used in neural networks, but here its conditions of validity are explicitly displayed. This scalar synapse also comes with an expression that directly relates it to basic quantities of synaptic functioning, and it can be endowed with meaningful physical units and realistic numerical values. In addition, it is shown that the scalar synapse does not receive the same expression in neural networks operating with spikes or with firing rates. These coherent modeling elements can help to improve, adjust, and refine the investigation of neural systems and their remarkable collective properties for information processing.

1 Introduction

Neural network modeling is concerned with the study of collective properties of large assemblies of interconnected neurons. A special emphasis is placed on interpreting these properties at the global level of information processing in the brain. A useful paradigm of this domain is offered by Hopfield's neural network. This model (Hopfield 1982, 1984) incorporates a few basic properties of biological neurons (nonlinear units with threshold and saturation, densely interconnected, through adaptable couplings), and it demonstrates that at the network level, collective behaviors emerge that allow the storage and retrieval of information through the exploitation of attractor dynamics toward controlled stable fixed points (Amit 1989).
To increase the biological plausibility and significance of such neural networks, efforts are made to introduce more realistic and detailed elements in their modeling (Amit and Tsodyks 1991; Wilson and Bower 1989). However, the complexity of real neural systems is such that no practical models attempt to describe them in full detail. The modeling process has to reduce and simplify reality, and balance between realism and tractability, but this in a controlled and coherent way.

For this purpose it is useful to know important modeling choices that are available, how they relate to one another, and the properties they convey and those they discard. This serves to correctly appreciate the significance and the limitations of the neural models they entail.

An illuminating paper by Abbott and Kepler (1990) discusses how to pass from an elaborate Hodgkin–Huxley neural model to a simple binary neuron, in a series of coherent steps at each of which one controls what is retained and what is neglected in the modeling process. In the present paper, we propose a similar approach for the modeling of synaptic transmission in neural networks. We examine the important successive steps that have to be taken to reduce a synaptic model from the level of the kinetics of ion channels to a simple multiplicative scalar coefficient.

We do not aim at a detailed biophysical and biochemical understanding of every elementary mechanism of function. Instead, in the other direction, we try to pinpoint important features of synaptic transmission that may play a significant role at the level of neuron networks. Only synaptic transmission is considered, for chemical synapses; synaptic plasticity is not explicitly addressed here.

Other authors have considered the modeling of synaptic transmission (Melkonian 1990, see also Shepherd 1990, Abeles 1991 for recent reviews), but their focus was on a given level with a single class of assumptions. In contrast, a specificity of the present work is the coherent perspective of translevel modeling in the context of neural networks, and the relationships between different classes of assumptions.

2 Ion Channel Kinetics

We start the description of synaptic transmission at the level of the kinetics of ion channels. An incoming action potential (AP) at a presynaptic terminal elicits the release of neurotransmitter molecules \( T \) in the synaptic cleft, in quantity whose time evolution is described by a pulse-like function \( q(t) \).

It is then assumed, as done for instance in Destexhe et al. (1994), that these transmitter molecules \( T \) bind to postsynaptic receptors according to the first-order kinetic scheme:

\[
R + T \xrightarrow{\beta} TR^*
\]  
(2.1)

In equation 2.1, \( R \) and \( TR^* \) represent, respectively, the unbound and the bound form of the postsynaptic receptor, and \( \alpha \) and \( \beta \) are the forward and backward rate constants for transmitter binding.

We further assume, as in Destexhe et al. (1994), that the binding of transmitter to a postsynaptic receptor directly gates the opening of an ion channel of electric conductance \( g_c \). A typical order of magnitude for \( g_c \) is \( \sim 10 \text{ pS} \) (Hille 1984). The total synaptic conductance through all channels of a synapse is thus \( G(t) = g_c n_c(t) \), where \( n_c(t) \) is the number of bound receptors (or open channels) at time \( t \).

To obtain the evolution of the conductance \( G(t) \), assumptions have to be made concerning the transmitter pulse \( q(t) \). A convenient possibility is to use the following alpha function \( h(t) \):

\[
h(t) = \frac{t}{\tau_h} \exp \left( -\frac{t}{\tau_h} \right), \quad t \geq 0
\]

(2.2)

that verifies \( \int_0^\infty h(t) \, dt = 1 \), peaks at \( t = \tau_h \), where \( h(\tau_h) = e^{-1/\tau_h} \) and extends over a duration of \( \sim 5\tau_h \) as \( h(5\tau_h)/h(\tau_h) = 0.09 \). In addition, \( h(t) \) tends to the Dirac delta function \( \delta(t) \) when \( \tau_h \) goes to zero.

If \( q(t) \) is to describe a pulse of transmitter that peaks at \( q_{\text{max}} \), starts at time \( t_0 \), and lasts over a duration of \( \sim \tau_q \), we thus write:

\[
q(t) = Q h(t-t_0), \quad \text{with} \quad Q = \tau_q q_{\text{max}} \times c/5, \quad \text{and} \quad \tau_h = \tau_q/5
\]

(2.3)

There is experimental evidence from both central synapses (Colquhoun et al. 1992) and the neuromuscular junction (Anderson and Stevens 1973; Hille 1984) that, following the arrival of an AP at the presynaptic terminal, the concentration of transmitter in the cleft rises and falls very rapidly, and that the duration \( \tau_q \) can be estimated to be of the order of 1 msec or below.

At the level of individual receptors, the kinetic scheme of equation 2.1 can be interpreted in probabilistic terms: At time \( t \), a bound receptor has a probability per unit time \( \beta \) to become unbound, and an unbound receptor has a probability per unit time \( \alpha q(t) \) to become bound. With these probabilities and \( q(t) \) given by equation 2.3, we have performed a Monte Carlo simulation of the kinetics 2.1, where individual transitions between bound and unbound states are monitored for a population of \( N \) receptors. The resulting synaptic conductance \( G(t) = g_c n_c(t) \) is plotted in Figure 1 for various values of \( N \), and with \( G_{\text{sat}} = g_c N \).

In the synaptic conductances \( G(t) \) of Figure 1, the statistical fluctuations that result from the stochastic gating of the channels are progressively smoothed out as their total number \( N \) increases. In biological synapses, the number \( N \) of postsynaptic channels can vary over a relatively wide range, typically from \( N \approx 10 \) to \( N \approx 1000 \) (Korn and Faber 1991; Bekkers and Stevens 1989; Hille 1984).
Figure 1: Normalized synaptic conductance \( G(t)/G_{\text{sat}} = n_e(t)/N \) that results from a Monte Carlo simulation of ion channel kinetics 2.1, with a total of (a) \( N = 10 \), (b) \( N = 100 \), and (c) \( N = 1000 \) channels. The parameter values are \( q_{\text{max}} = 1 \ \text{mmol} \) and \( g_e = 1 \ \text{msec}^{-1} \), \( \alpha = 0.5 \ \text{msec}^{-1} \ \text{mmol}^{-1} \), (A) for a "slow" synapse with \( \beta = 0.1 \ \text{msec}^{-1} \); (B) for a "fast" synapse with \( \beta = 1 \ \text{msec}^{-1} \), \( \alpha = 2 \ \text{msec}^{-1} \ \text{mmol}^{-1} \).

Now, at the level of a population of \( N \) receptors where \( N \) is sufficiently large, the kinetics 2.1 leads to a number \( n_e(t) \) of bound receptors that evolves according to

\[
\frac{dn_e}{dt} = q(t) (N - n_e) - \beta n_e
\]  
(2.4)

For the total synaptic conductance \( G(t) = g_e n_e(t) \) we thus have

\[
\frac{dG}{dt} = -\beta G + (G_{\text{sat}} - G) q(t)
\]  
(2.5)

The solution of equation 2.5 with initial condition \( G(t_0 = G_0) \), reads for \( t \geq t_0 \):

\[
G(t) = \left\{ G_0 + G_{\text{sat}} \int_{t_0}^{t} a q(t') \exp \left[ \beta (t' - t_0) + \int_{t_0}^{t'} a q(t') \, dt' \right] \, dt' \right\}
\]
\[
\times \exp \left[ -\beta (t - t_0) - \int_{t_0}^{t} a q(t') \, dt' \right]
\]
(2.6)

Figure 2 depicts \( G(t) \) of equation 2.6 when \( q(t) \) is described by equation 2.3, and with \( G_0 = 0 \).

Equation 2.6 constitutes the limit expression for the synaptic conductance \( G(t) \) when the number of postsynaptic channels \( N \to +\infty \). Figure 1 illustrates the convergence to this limit as \( N \) is increased from \( N = 10 \) to \( N = 1000 \). For \( N = 1000 \) channels, Figure 2 demonstrates that the synaptic conductance \( G(t) \) that results from the stochastic kinetics 2.1 is very satisfactorily represented by the continuous solution 2.6.

The stochastic kinetics 2.1 is known to be a statistical birth and death process (Goel and Richter-Dyn 1974), and equation 2.6 represents its expectation. The convergence to 2.6 as \( N \) increases can be estimated from Figure 3, which depicts the standard deviation of the process for different \( N \). The decay of this standard deviation is as \( 1/\sqrt{N} \).

It is then clear that the replacement of the discrete stochastic kinetics 2.1 by the continuous deterministic model of equations 2.5–2.6 provides an acceptable representation of the synaptic conductance, only if the number \( N \) of the postsynaptic channels is sufficiently large. Obviously, the value of \( N \) that forms the frontier cannot be settled once and for all. It largely depends on the level of distortion that is admitted, and further on the type and scope of the modeling being developed. To proceed, we maintain that the situation where continuous equations 2.5-
For the description of neural networks can be chosen to start just above $T_r$, and it will be sufficient to capture the fastest firing activities of neurons that occur at around 300 Hz.

For these reasons, for the description of synaptic transmission in a neural network, it is possible to consider that the duration of the transmitter release $\tau_a$ is sufficiently smaller than the temporal resolution, and thus does not need to be temporally resolved. The arrival of an AP at the presynaptic terminal at time $t_0$ is modeled with a Dirac delta function $\delta(t - t_0)$, and it produces the release of $q(t) = Q(t - t_0)$.

The solution given by equation 2.6 with $q(t)$ a rectangular pulse of duration $\tau_a$ is taken to the limit where $\tau_a \to 0$ while the integral $Q$ of $q(t)$ is kept constant. This yields the solution for $q(t) = Q(t - t_0)$ and when $t > t_0$ as

$$G(t) = G_\infty - G_{\text{sat}} = G_\infty - G_{\text{sat}} \left[ \frac{1}{\beta} \right] \left[ 1 - \frac{t - t_0}{\tau_a} \right]$$

This $G(t)$ of equation 2.7 is depicted in Figure 4 together with the $G(t)$ of equation 2.6. This comparison shows that equation 2.7 may constitute an acceptable approximation of equation 2.6 if time scales below ~1 msec do not need to be resolved. The quality of the approximation varies with the characteristic of the synapse; it is good if the synapse has a relatively slow response (slow decay) relative to $\tau_a$, and tends to degrade for fast synapses.

For further use, we write that $G(t)$ of equation 2.7 is the solution to

$$\frac{1}{\beta} \frac{dG}{dt} = -G + \left( G_{\text{sat}} - G \right) \frac{1}{\beta} \alpha Q \delta(t - t_0)$$

When $\alpha Q \approx 2$ the synaptic conductance $G(t)$ of equation 2.7 rises above $G_\infty = 0$ to a peak value of around $0.9 G_{\text{sat}}$, which nearly saturates the synapse. It is thus unlikely that $\alpha Q$ can be found $\gg 1$; this would be functionally useless since $\alpha Q \approx 2$ is enough to drive the synapse to saturation. Furthermore, it is not functionally efficient to drive the synapse to saturation with a single presynaptic spike (Faber et al. 1992). During the time of $\sim 2$ to $\sim 3 \times 1/\beta$ that $G(t)$ persists after arrival of a single spike, a succession of $\sim 2$ or more following spikes can impinge on the synapse. These would have practically no effect if the first spike drives $G(t)$ to saturation. A functionally reasonable maximum value for $\alpha Q$ can be thought to be $\sim 1$. With $\alpha Q = 1$, a single spike drives $G(t)$ of equation 2.7 to a peak value of around $0.66 G_{\text{sat}}$ above $G_\infty = 0$, which leaves the response to respond to immediate successive spikes.

In the present section, the evolution of the synaptic conductance $G(t)$ is derived from mechanisms at the level of ion channels and their kinetics. A simpler alternative in neural modeling is to postulate an appropriate form for $G(t)$ or its variation, at the level of the synaptic membrane itself, as we shall see in the next section.
3 Synaptic Conductance Dynamics

Now let us consider that we want to ground the modeling of a synapse, at the level of the synaptic conductance $G(t)$ itself, with no explicit consideration for the underlying kinetics of ion channels. As we would like to use this synapse model for investigations at the level of a neural network, we assume again that time scales below $\sim 1$ ms do not need to be resolved. We thus represent a presynaptic spike simply as $\delta(t - t_0)$. Subjected to this input, we want a synapse model that will deliver a response $G(t)$ that has to be consistent with the synaptic conductance of equation 2.7 and Figure 4.

A simple possibility that is often adopted is to assume a linear dynamics for $G(t)$ (Wilson and Bower 1989). This can be represented with a linear differential equation for $G(t)$, with a linear action of the driving input that describes the incoming spikes. The response of such a linear system to the Dirac pulse $\delta(t)$ generates a waveform (the impulse response) for $G(t)$. For instance, with a second-order linear system, this impulse response can be made to approximate the waveform of Figure 4 (dotted line) that displays finite rise and fall times. Differences of two exponentials or alpha functions form the basis of the approximation, with times to peak or decay constants that are introduced as parameters but not derived from underlying mechanisms. With a first-order linear system, the impulse response can reproduce the exponential waveform of Figure 4 (solid line) that displays an instant rise time and a finite fall time.

The conductance waveform considered as the impulse response can also be used directly, as a convolution kernel, to obtain the response $G(t)$ to an arbitrary incoming spike train. This method allows us to implement, through the convolution kernel, a large variety of conductance waveforms. At the same time, the storage and computational requirements of this method are known to be relatively high.

An important characteristic of such an approach to the synaptic conductance dynamics is that it assumes a linear superposition of the response to input spikes. Based on the results of Section 2, this assumption appears here as only an approximation. The validity of this approximation degrades when the time interval between successive input spikes is less than the duration of the impulse-response waveform for $G(t)$. This may occur in the relatively high range of the firing rates. The linear superposition assumption then tends to artificially sustain these high firing rates. In contrast, nonlinear superposition as it was authorized by equation 2.8 is efficient to refrain high firing rates, and it offers a source of nonlinear interaction that may be useful at the network level.

An economical implementation of the linear dynamics for synaptic conductance is to directly compute with the linear differential equation instead of a convolution kernel (Wilson and Bower 1989). If we consider that the rise time of the conductance response to an input spike is short enough and does not need to be temporally resolved, a first-order linear dynamics for $G(t)$ is suitable, which we write under the form

$$\frac{dG}{dt} = -G(t) + G_{sat}WE(t)$$

(3.1)

In equation 3.1, $E(t) = \sum \delta(t - t_i)$ is the input spike train (with dimension sec$^{-1}$) that linearly drives $G(t)$. The parameter $W$ (with dimension of a time) is introduced to model the efficacy of the synapse in converting incoming spikes into conductance changes. When the input is zero, $G(t)$ relaxes exponentially with time constant $\tau_G$.

For a single presynaptic spike $E(t) = \delta(t - t_0)$, equation 3.1 reads

$$\frac{dG}{dt} = -G(t) + G_{sat}W\delta(t - t_0)$$

(3.2)

and the change in the synaptic conductance that results from equation 3.2 is, for $t > t_0$:

$$G(t) = \left( G_0 + G_{sat} \frac{W}{\tau_G} \right) \exp \left( -\frac{t - t_0}{\tau_G} \right)$$

(3.3)

where $G_0 = G(t_0)$. 
To preserve a coherent link with the synapse description of Section 2 involves relating equation 3.2 to equation 2.8, and equation 3.3 to equation 2.7. Both of these relations point to the fact that an accurate identification can be made between these two pairs of equations only if the conductance \( G(t) \) operates far below saturation. In such a case \( G_{\text{sat}} - G(t) \approx G_{\text{sat}} \) and equation 2.8 can be reduced to equation 3.2. At the same time, a \( G(t) \) that remains far below \( G_{\text{sat}} \) is associated with \( \alpha Q \ll 1 \), and equation 2.7 can be reduced to equation 3.3. As a result of this identification process between the synapse models of Sections 2 and 3, we deduce that the time constant \( \tau_c \) in equations 3.1 and 3.2 is just \( 1/\beta \), the reciprocal of the rate constant for channel closing. Also, identification of equations 3.3 and 2.7 leads to express the synaptic efficacy \( W \) of equations 3.1 and 3.2 as

\[
W = (1 - e^{-\alpha Q})\tau_c
\]

This expression for \( W \) allows equations 3.1 and 2.5 to have the same impulse response when the initial condition \( G_0 \) equals 0, irrespective of the value of \( \alpha Q \). Expression 3.4 reduces to \( W = \alpha Q \tau_c \) when the conditions for identification of 3.3 and 2.7 (i.e., \( \alpha Q \ll 1 \)) best apply.

In summary, equation 3.2 constitutes a good approximation of the more detailed model of equation 2.8, inasmuch as the synaptic conductance operates far below saturation. When this condition is not well verified, departures may arise with equation 3.2 used in place of equation 2.8. The result is to suppress a source of nonlinear interaction between incoming spikes, and the effect is to unduly favor the growth of \( G(t) \), or to unduly enhance the role of the residual value \( G_0 \) in the response to a new presynaptic spike.

4 Synaptic Coefficient for Spike Dynamics

With a space clamped neuron model (Abbott and Kepler 1990), the change \( G(t) \) of the membrane conductance in a synaptically driven region drives the membrane potential \( V(t) \) of the postsynaptic neuron according to

\[
C_m \frac{dV}{dt} = -C_m V + G(t) \times (V_{\text{rev}} - V)
\]

(4.1)

The zero reference for the potentials is taken, throughout, at the resting potential of the postsynaptic neuron. In equation 4.1 \( C_m \) and \( G_{\text{sat}} \) are, respectively, the membrane capacitance and conductance of the postsynaptic neuron at rest. Equation 4.1 operates in the subthreshold region where voltage-dependent conductances do not come into play. \( V_{\text{rev}} \) is the reference potential of the synapse; it is positive (i.e., above the resting potential) for an excitatory synapse, and negative (i.e., below the resting potential) for an inhibitory synapse. It is at the resting potential for a shunting synapse. Typically, for an excitatory synapse \( V_{\text{rev}} \) is 70 mV above rest, and \( V_{\text{inh}} = -10 \) mV for an inhibitory synapse. With several synapses, the corresponding synaptic conductance changes just add up linearly in the right-hand side of equation 4.1.

At this point, we possess various models to describe the evolution of \( G(t) \) that enters equation 4.1. We wish now to make a connection with simple models such as Hopfield's (1982), where the postsynaptic neuron is directly driven by the incoming spikes mediated by synapses that reduce to simple multiplicative scalar coefficients. From now on we have to discard the case of shunting synapses, because they are ignored by the scalar representation of a synapse as it is used in neural networks.

A first step in our reduction process is to collapse the time dynamics of \( G(t) \), as expressed in equation 3.3, to an instant dynamics. When \( \tau_c \) vanishes, equation 3.3 leads to

\[
G(t) = G_{\text{sat}} W \delta(t - t_0)
\]

(4.2)

Equation 4.2 constitutes a suitable approximation to enter the driving term of equation 4.1 when the duration \( \tau_c \) is sufficiently shorter than the time constant \( \tau_m = C_m/G_m \) of the driven system. This is a similar move that was performed when the duration \( \tau_c \) of the transmitter pulse was neglected in order to go from equation 2.9 to equation 2.8, allowing us to replace a solution of the type of 2.6 where time scales below \( \tau_c \) are resolved, by a solution of 2.7 where time scales below \( \tau_c \) are not resolved.

A second step in the reduction process is to linearize equation 4.1 by replacing \( V_{\text{rev}} - V(t) \) simply by the constant \( V_{\text{rev}} \). This simplification suppresses another source of nonlinear interaction between incoming spikes. In equation 4.1 the excursion of \( V(t) \) is between, at the lowest, \( V_{\text{inh}} \), and, at the highest \( V_{\text{inh}} \approx 20 \) mV the firing threshold above rest. Obviously the replacement of \( V_{\text{rev}} - V(t) \) by \( V_{\text{rev}} \) is more acceptable an approximation for excitatory synapses than for inhibitory ones. The result of this replacement is to unduly favor inhibitory actions.

After this linearization process and the collapse of \( G(t) \), equation 4.1 transforms into, for the response to a single spike,

\[
C_m \frac{dV}{dt} = -C_m V + V_{\text{rev}} G_{\text{sat}} W \delta(t - t_0)
\]

(4.3)

If the membrane potential \( V(t) \) is reduced to a dimensionless variable \( v(t) \) with the natural voltage unit \( V_{\text{inh}} \), we obtain for \( v(t) = V(t)/V_{\text{inh}} \) the following dynamics:

\[
\frac{dv}{dt} = \frac{v}{\tau_m} + w^a \delta(t - t_0)
\]

(4.4)

where \( \tau_m = C_m/G_m \) is the membrane time constant, and

\[
w^a = \frac{V_{\text{rev}}}{V_{\text{inh}} C_m/G_{\text{sat}}}
\]

(4.5)
Equation 4.4 is a classic model for a neuron,\(^1\) where the reduced membrane potential \(v(t)\) is directly driven by input spikes (Cowan 1990). The efficacy of the transduction by the synapse is simply modeled here by the dimensionless coefficient \(w^r\). However, we now may relate \(w^r\) through equation 3.4, to underlying quantities all the way down to the level of ion channel kinetics:

\[
w^r = \frac{V_{\text{rev}} G_{\text{m}} T_c}{V_{\text{th}} G_{\text{m}} T_m} (1 - e^{-\alpha Q})
\]  

(4.6)

where we recall that \(Q\) is the time integral of a single neurotransmitter pulse.

For an excitatory synapse \(V_{\text{rev}} > 0\) leads to a positive \(w^r\), for an inhibitory one \(V_{\text{rev}} < 0\) leads to a negative \(w^r\). We thus capture the synaptic coefficients of neural networks that can be positive or negative.

5 Synaptic Coefficient for Firing-Rate Dynamics

We now examine the derivation of a multiplicative scalar synaptic coefficient for neural networks that operate with continuous firing rates instead of spikes. We introduce \(I(t) = G(t)\left[V_{\text{rev}} - V(t)\right]\), the synaptic current that drives the membrane potential in the right-hand side of equation 4.1. In the conditions where equation 4.1 is linearized, the synaptic current reduces to \(I(t) = G(t)V_{\text{rev}}\). When the dynamics of equation 3.1 is used for \(G(t)\), the synaptic current \(I(t) = G(t)V_{\text{rev}}\) evolves according to

\[
\tau_G \frac{dI}{dt} = -I(t) + V_{\text{rev}} G_{\text{m}} \frac{\partial E(t)}{\partial I(t)}
\]  

(5.1)

With a driving current \(I(t)\), the membrane potential \(V(t)\) can reach the firing threshold \(V_{\text{th}}\) and then be reset, and the neuron can emit output spikes \(S(t) = \sum \delta(t - t_j)\). We now consider a linear time-averaging

\[
\bar{v}(t + \Delta t) = \bar{V}(t + \Delta t) = \frac{1 - \Delta t}{\tau_m} \bar{v}(t) + w^r \delta(t - t_j)
\]

(5.2)

where \(\delta(t)\) is a discretized and reduced version of the Dirac delta function with \(\delta(t) = 1\) when \(t = 0\) and \(\delta(t) = 0\) when \(t = n \times \Delta t\) for integers \(n \neq 0\). Then, it is assumed that \(v(t)\) varies fast enough to be, at each time \(t\), in equilibrium with its driving input, to give

\[
\bar{v}(t + \Delta t) = \frac{\tau_m}{\Delta t} \bar{v}(t - t_j)
\]

(5.3)

and the neuron output at time \(t + \Delta t\) takes the value 1 if \(v(t + \Delta t) > V_{\text{th}}\) and the value 0 otherwise. This is exactly the discrete neuron model of Hopfield (1982), that has to operate with synaptic efficacies that here take the form \(w^r \tau_m / \Delta t\), but whose derivation imposes severe temporal constraints that together appear difficult to strictly satisfy.

process of some type (bin counting, low-pass filtering, etc.). This averaging process applied to the output train \(S(t)\) produces a signal \(\bar{S}(t)\) that provides a definition for the firing rate of the neuron.

It is then usually possible (Antón et al. 1992; Chapeau-Blondeau and Chauvet 1992) to extract a firing function \(f\) that relates the average membrane current \(I(t)\) to the output firing rate \(\bar{S}(t)\) under the form \(\bar{S} = f(I(t))\). The firing function \(f\) can take various analytical expressions. A possibility is the so-called Lapicque form (Tuckwell 1988; Chapeau-Blondeau and Chauvet 1992) derived from a leaky-integrator scheme for the neuron membrane:

\[
f(I(t)) = \begin{cases} 
0 & \text{if } I(t) < I_{\text{th}} \\
\frac{1}{\tau_r} \exp[-(I(t) - I_{\text{th}}) / \tau_r] & \text{if } I(t) > I_{\text{th}} 
\end{cases}
\]

(5.4)

with \(I_{\text{th}} = G_{\text{m}} V_{\text{th}}\) and \(\tau_r\) the refractory period of the neuron. Another simpler possibility is the sigmoid function, postulated this time, at the level of the neuron itself:

\[
f(I(t)) = \frac{1}{1 + \exp[-a(I(t) - I_{\text{th}})]}
\]

(5.5)

with a slope \(a\) that comes as a "free" parameter, whose value is often arbitrarily settled.

The linear time-averaging process applied to equation 5.1, leads to an equation that governs the average membrane current:

\[
\tau_G \frac{dI}{dt} = -I(t) + V_{\text{rev}} G_{\text{m}} \frac{\partial E(t)}{\partial I(t)}
\]

(5.6)

In equation 5.4, the term \(E(t)\) represents the firing rate of the presynaptic neuron.

If the average membrane current \(I(t)\) is reduced to a dimensionless variable \(i(t)\) with the natural current unit \(I_{\text{th}} = G_{\text{m}} V_{\text{th}}\), we obtain for \(i(t) = I(t)/I_{\text{th}}\) the following dynamics:

\[
\frac{di}{dt} = \frac{i - \bar{v} E(t)}{\tau_c}
\]

(5.7)

with:

\[
w^r = \frac{V_{\text{rev}} G_{\text{m}} W}{V_{\text{th}} G_{\text{m}} T_c}
\]

Equation 5.5 is another classic model for a neuron,\(^2\) where the reduced average membrane current \(i(t)\) is directly driven by neuron firing rates (Amit and Tsodyks 1991). The efficacy of the transduction by the synapse is simply modeled here by the dimensionless coefficient \(w^r\). However, we again have a possibility to relate \(w^r\), through equation 3.4, to underlying quantities:

\[
w^r = \frac{V_{\text{rev}} G_{\text{m}}}{V_{\text{th}} G_{\text{m}}} (1 - e^{-\alpha Q})
\]

(5.8)

\(^2\)An additional specification that completes the neuron model is the firing function \(f\) that provides for the output firing rate a constitutive relation of the form \(\bar{S}(t) = f(i(t))\).
Table 1: Numerical Values for Three Examples of an Excitatory Synapse: Slow, Medium and Fast.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Slow</th>
<th>Medium</th>
<th>Fast</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\alpha) (msec(^{-1}) mmol(^{-1}))</td>
<td>0.5</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>(1/\beta = \tau_C) (msec)</td>
<td>10</td>
<td>3.33</td>
<td>1</td>
</tr>
<tr>
<td>(aQ = \frac{1}{2} \tau_T \sigma_{\text{max}})</td>
<td>0.27</td>
<td>0.54</td>
<td>1.09</td>
</tr>
<tr>
<td>(W = (1 - e^{-\alpha T}) \tau_C) (msec)</td>
<td>2.38</td>
<td>1.40</td>
<td>0.66</td>
</tr>
<tr>
<td>(w^\text{syn}) (sec(^{-1}))</td>
<td>0.083</td>
<td>0.049</td>
<td>0.023</td>
</tr>
<tr>
<td>(w^\text{syn}) (sec(^{-1}))</td>
<td>0.083</td>
<td>0.147</td>
<td>0.232</td>
</tr>
<tr>
<td>nb inputs (n^I = n^I)</td>
<td>4</td>
<td>6</td>
<td>13</td>
</tr>
</tbody>
</table>

*In all cases the remaining parameters receive the typical values: \(\sigma_{\text{max}} = 1\) mmol, \(\tau_T = 1\) msec, \(G_{\text{na}} = 1\) nS, \(G_{\text{m}} = 10\) nS, \(\tau_m = 10\) msec, \(V_{\text{rev}} = V_{\text{na}} = 70\) mV, \(V_{\text{th}} = 20\) mV.

6 Quantitative Evaluation of the Synaptic Parameters

The numerical values of the various parameters that model a synapse are given in Table 1, for three examples of an excitatory synapse, that are typical, and that we here call slow, medium, and fast synapses. This is a purely illustrative set, and, for instance, synapses can be found with a significantly larger \(\tau_C\) than our “slow” synapse. This is the case with the NMDA (Daw et al. 1993; Forsythe and Westbrook 1988) and GABA-B receptors (McCormick 1990), characterized by \(\tau_C\)s of hundreds of milliseconds, and synapses can even be found with \(\tau_C\)s of a few seconds (Syed et al. 1990). The quantitative evaluations of Table 1 can readily be extended to these cases. However, as visible in the present treatment, the significance of the reduction of a synapse model to a simple scalar coefficient degrades for large \(\tau_C\).

For a neuron model that operates with spikes or with firing rates, the synaptic coefficients \(w^\text{syn}\) and \(w^\text{mem}\) relate differently to the parameters of the system. Both \(w^\text{syn}\) and \(w^\text{mem}\) increase with \(aQ\), because this corresponds to an increased probability of channel opening. Only \(w^\text{syn}\) increases with \(\tau_C\), because \(w^\text{syn}\) drives the membrane potential \(V(t)\) and a given value of \(G\) that lasts over a time \(\tau_C\) produces a larger increase in \(V(t)\) if \(\tau_C\) is large. In contrast, \(w^\text{mem}\) is independent of \(\tau_C\), because \(w^\text{mem}\) drives the membrane current \(I(t)\) and a given value of \(G\) that lasts over a time \(\tau_C\) produces a given \(I(t)\) insensitive to the duration \(\tau_C\).

Another possibility to derive a neuron model with firing rates would be to linearly average an equation like 4.3 to obtain an average membrane potential \(\bar{V}(t)\) driven by a firing rate \(\dot{E}(t)\), and then look for an appropriate firing function for the output rate \(S = f(t)(\bar{V})\). Such a rate model would use the same \(w^\text{syn}\) as in equation 4.6. However, its derivation requires us to endorse the two assumptions of the linearization of \(\dot{E}(t)\) into \(G(t)\dot{V}_{\text{rev}}\) and of the collapse of \(G(t)\) to an instant dynamics with \(\tau_C \to 0\). This last assumption may be problematic with a \(\tau_C\) that in some cases can be of the order of significant interspike durations (Mason et al. 1991; Forsythe and Westbrook 1988; Rinzel and Frankel 1992). In comparison, the derivation of the rate model of equation 5.5 is less stringent since it assumes only the linearization of \(\dot{E}(t)\).

An assessment of the consistency of the values of \(w^\text{syn}\) and \(w^\text{mem}\) that are derived in Table 1 from equations 4.6 and 5.7, can be obtained if one tries to deduce from them the minimal input activity that is necessary to reach the firing threshold of the postsynaptic neuron. For this, we assume that the neuron governed by equation 4.4 receives its inputs from a “neural bath” of a number \(n^I\) of coherent neurons, that all fire the same spike train \(E(t)\), each mediated by the same synaptic efficacy \(w^\text{syn}\). In such condition, the driving term of the right-hand side of equation 4.4 is just \(n^I w^\text{syn} \dot{E}(t)\). We choose a periodic input train \(E(t) = \sum \delta(t - KT)\) where the neurons of the bath fire at their maximum repetition period \(T\) (of the order of a few milliseconds). For such a \(T\) sufficiently smaller than \(\tau_m\), we approximate in 4.4 the signal \(E(t)\) by the constant \(1/T\). With such a constant input, we now ask for the value of \(n^I\) that allows \(\dot{v}(t)\) in 4.4 to just asymptotically reach the firing threshold \(v_{\text{th}} = 1\). The answer is \(n^I = T/(\tau_m w^\text{syn})\).

We now turn to the neuron governed by equation 5.5, and drive it with the same type of neural bath containing this time \(n^r\) neurons mediated by the synaptic efficacy \(w^\text{syn}\). With the constant input that gives \(E = 1/T\), we now ask for the value of \(n^r\) that allows \(\dot{i}(t)\) in 5.5 to just asymptotically reach the activity threshold \(i_{\text{th}} = 1\). The answer is \(n^r = T/(\tau_C w^\text{mem})\).

From equations 4.6 and 5.7 we have \(w^\text{syn}/w^\text{mem} = \tau_C/\tau_m\) we thus deduce that the numbers of inputs \(n^I\) and \(n^r\) required to reach the threshold of activity of the two neuron models verify \(n^I = n^r\). This outcome unites the two neuron models of 4.4 and 5.5 that at another level operate with different synaptic efficiencies.

The values of \(n^I = n^r\) computed with \(T = 3\) msec are also given in Table 1. They come as consequences of the evaluation of the synaptic efficiencies of equations 4.6 and 5.7, which in turn originate in the level of ion channel kinetics. These values of Table 1 deduced for \(n^I\) and \(n^r\) appear quite realistic and plausible, knowing that they stand for the number of inputs at the maximum firing rate that are necessary to asymptotically reach the activity threshold. With lower input firing rates, and to reach the threshold faster than asymptotically, the necessary number of inputs may be multiplied by several 10. This demonstrates that a quantitative consistency is preserved in our derivation, from the level of ion channels to the level of neural networks.

The synapse models of equations 4.6 and 5.7, although simple, exhibit two special parameters that can form the support of the property of synaptic plasticity. These are \(Q\) and \(G_{\text{mem}}\), that relate to the quantity of neurotransmitter and the number of postsynaptic receptors, and appear...
as natural adaptable parameters. It is known that indefinite increase
in \( Q \) could not infinitely increase the synaptic efficacy because of the
possibility of saturation at the postsynaptic level; this expected behavior
is explicitly conveyed by equations 4.6 and 5.7.

7 Discussion

7.1 Approximations of the Modeling. The kinetic-based framework
that forms the basis of our treatment is in itself simple and neglects
many aspects of synaptic transmission. A first reason for this is that
some degree of simplification is inherent to the modeling process, for
tractability and efficiency. Another reason, more specific, is that we wish
to here to set the conditions that allow us to develop a coherent connection
with the elementary scalar synapse. We discuss in this section important
synaptic properties that have been left out in this process.

An important stage that has not been explicitly considered in the
present description of synaptic transmission is the process of transmitter
release controlled by the kinetics of presynaptic vesicles and the
clearance mechanisms (reuptake, hydrolysis, diffusion out of the cleft). Direct
experimental measurements indicate a stochastic reconstruction of the
dynamics of this process (Clements et al. 1992). To develop a connection
with scalar synapses, the framework of this paper ignores the stochastic
and quantized characters of transmitter release, and considers in place
a deterministic continuous quantity of transmitter \( q(t) \) as introduced in
Section 2. In this context that receives justification when a large number
of presynaptic vesicles are involved (see Section 7.2 below), a reasonable
approach to approximate the dynamics of \( q(t) \) is

\[
\frac{dq}{dt} = -\frac{q}{\tau_e} + (q_{sat} - q)\gamma E(t)
\]  

Equation 7.1 assumes that the variation \( dq/dt \) is made up by two
terms. There is a relaxation term, \(-q/\tau_e\), that as a first approximation is
considered to be proportional to \( q(t) \), the proportionality factor involving
\( \tau_e \) interpreted as a time constant for the clearance processes. There is next
a driving term, \((q_{sat} - q)\gamma E(t)\), that is proportional to the input activity \( E(t) \)
that as before describes the presynaptic spike train. To express again a
possibility of saturation (due to the limited quantity of neurotransmitter
that can be released), the proportionality factor of the driving term is
dependent on \( q \) with the form \((q_{sat} - q)\gamma\), with \( \gamma \) a constant efficacy, that
prevents \( q(t) \) from growing above \( q_{sat} \).

Equation 7.1 is a nonlinear dynamics, whose form has been found at
several levels in the present description of synaptic transmission (equa-
tions 2.5, 2.8, 4.1), and that appears rather generic in this context. From
the previous derivation of an equation like 2.5, we can infer that equa-
tion 7.1 will form a satisfactory approximation when the stochastic and
quantized character of transmitter release tends to vanish in the limit of
a large number of presynaptic vesicles. Also, the evolution of \( q(t) \) deduced
from equation 7.1 in response to a single presynaptic spike can be
reasonably approximated by the alpha function of equation 2.3. The
time constant \( \tau_e \) in equation 7.1 can be expected to be small, of the order
of 1 msec or below, and it enters the determination of the value of \( \tau_e \) in
equation 2.3. At the level of a neural network, presynaptic spikes cannot
impinge on a given synapse with a repetition period shorter than, say
\( \sim 3 \) msec, because of the neuron refractory period. Therefore, it can be
assumed that the excursion of \( q(t) \) that results from a single presynaptic
spike, and that evolves on a time scale of \( \sim 1 \) msec, is sufficiently cleared
out before another presynaptic spike arrives. Thus, there is no significant
nonlinear interaction of the effects of successive presynaptic spikes
that can arise from equation 7.1, and a linear superposition of pulses like
equation 2.3 that we chose to describe the evolution of the quantity of
neurotransmitter appears justified.

Only two-state kinetics were considered for postsynaptic receptors,
as expressed by the discrete stochastic scheme of equation 2.1, or its
continuous limit of equation 2.4. This represents a simplification of the
actual evolution of the receptors. More complicated kinetics, with more
than two states, exist for, e.g., biological synapses (Hille 1984). Their modeling
can be approached by a cascade of schemes like equations 2.1 or 2.4.
These schemes describe transitions between various multiply occupied
states (with more than one transmitter molecule binding to the receptor)
or differing conformational states of the postsynaptic receptors, and they
usually operate with rate constants that are of the same order or faster
than those we used with equation 2.1. The global effect that results,
for the number of open channels or the synaptic conductance variation
in response to a presynaptic spike, is a pulse-like course, characterized
by a rise time and a fall time, that all together form a picture that is
similar to what is shown in Figures 1 and 2 (Faber et al. 1992). Thus,
the simple two-state scheme of equation 2.1 can be thought sufficient,
as a first approximation, to capture the salient features of the kinetics
of postsynaptic receptors that can be significant at the level of neuron
networks. These salient features include the possibility of a stochastic
discrete dynamics that can evolve to a deterministic continuous one in the
limit of a large number of postsynaptic receptors, and the presence of two
dominant time constants for the rise and fall of the synaptic conductance.

A specific synaptic feature that is not accounted for with our simple
kinetic scheme is receptor desensitization (Hille 1984), which usually oc-
curs over time scales of several seconds, and where prolonged exposure
to neurotransmitter gradually suppresses channel responsiveness that is
slowly recovered after the transmitter is removed.

Other synaptic properties that have been left out are the effects, like
facilitation or depression, that can enhance or reduce the efficacy of trans-
mision to spike trains as opposed to individual spikes (Zucker 1989).
Such effects might be due to presynaptic factors, like residual calcium or a limited store of releasable transmitter, that would imply, in our present formalism, an alteration of the transmitter pulse $q(t)$ with successive spikes. Postsynaptic factors also might be involved with these effects.

Synaptic receptors sometimes show a voltage-dependent behavior, for instance the NMDA receptor (Daw et al. 1993; Flattman et al. 1986). A possible way to introduce this property into the present framework is to consider that the single channel conductance $g_e$ of Section 2 ceases to be a constant to bear a voltage dependence $g_e(V)$. Then, $G(t)$ in equation 4.1 has to be separated into $g_e(V) n_e(t)$. $n_e(t)$ alone can be described by equation 2.4 or a kinetic scheme like 2.1. And $g_e(V)$ can be given as an empirical dependence for instance. The resulting set of coupled equations is more complex to theoretically analyze. It may give rise to new interesting capabilities. A trace of these capabilities could even be preserved, possibly, up to the scalar synaptic coefficient, if a voltage dependence is introduced in its expression. But this is a feature that is usually not considered in current neural networks with scalar synapses.

In the present treatment of synaptic transmission, we have discarded the passive transport of the membrane potential that may occur in dendritic regions of the neuron (Jack et al. 1975). Passive dendritic transport can be described with cable theory (Rall 1989). Addition of a Laplacian term $\Delta V$, in an equation like 4.1 for instance, allows us to take into account spatial variations of the membrane potential. Another possibility is to use the current computed in a synaptic region for a convolution with the dendritic Green’s function (Tuckwell 1988). The main features that passive dendritic transport adds to the situation of the space clamped neuron, at a level of examination, are propagation delays, and lengthening and decay of spatiotemporal variations with propagation. Such alterations can be quantitatively evaluated with the aforementioned formalism, and, if needed, they would complement the description of synaptic transmission that we developed here, but this would retain significance in their presence. The simple scalar synapse in which our reduction process terminates can even be made to incorporate a reminiscence of the attenuation during passive transport. It is not the case with propagation delays, that fail to be conveyed by a simple scalar synapse as such.

Our treatment of synaptic transmission, as presented here, is appropriate for somatic synapses or for dendritic inputs at small electrotonic distances (the spatial distance in units of the space constant of the passive transport) to the axon hillock. This forms a relatively broad range of significantly interesting synaptic inputs, and also constitutes the conditions that are most of the time adopted in current neural network models.

7.2 A Summary of Important Assumptions. We summarize and discuss in the following, important conditions that we found in the way of the derivation of a simple neuron model like equation 4.4, where the synaptic transmission is simply modeled by a scalar multiplicative coefficient $\omega$.

1. To begin with, the stochastic and quantized characters of transmitter release (Hesseler et al. 1993) have to be ignored to introduce a deterministic description of the transmitter pulse $q(t)$ as in equation 2.3. Such an approximation receives justification in the limit where a large number of synaptic vesicles are involved in the response to a single presynaptic spike. The average number of quanta released by a single presynaptic spike is estimated to be about 200 for the neuromuscular junction (Trimble et al. 1991; Korn and Faber 1991; Holmes 1993). For central synapses, this average number of quanta may possibly differ from this estimate. Moreover, it is known that an important variability exists in the release process (Hesseler et al. 1993), and that sometimes it even fails. This source of unreliability in synaptic transmission is not present in our treatment. Part of this synaptic feature could be conveyed here, up to the simple scalar synapse of equations 4.6 and 5.7, if the parameter $Q$ was made a quantized random variable.

2. The number $N$ of postsynaptic receptors must be large enough to allow a deterministic continuous description of the synaptic conductance $G(t)$ instead of a stochastic quantized evolution. Experimental reports indicate that typical $N$s can vary between 10 and 1000 for different synapses (Korn and Faber 1991; Bekkers and Stevens 1989; Hille 1984). Small $N$s are another source of variability and unreliability in synaptic transmission. These features fail to be conveyed by the deterministic description of $G(t)$, but they gradually diminish as $N$ increases. An intermediate modeling possibility is to adopt the deterministic continuous description of $G(t)$ supplemented by an additive synaptic noise. This noise can represent stochastic fluctuations of $G(t)$ around its expectation as they appear in Figures 1 and 2. However, the statistical properties of this noise are not simple, because its standard deviation varies with time as demonstrated in Figure 3, and only when $N$ is large can it be considered as gaussian.

3. The synaptic conductance $G(t)$ must remain far from saturation to introduce a synaptic efficacy as in equation 3.1, that will mediate the driving input $E(t)$ in a way independent of the instant value of $G(t)$ itself. Such conditions are not unrealistic, but at the same time situations are known where synapses operate in the vicinity of saturation (Faber et al. 1992; Clements et al. 1992). The neglect of saturation effects suppresses nonlinear interactions that may be useful at the network level. It enhances the impact of successive spikes that come close to one another, and as a consequence artificially maintains high firing rates.
4. The time durations of both neurotransmitter release \( q(t) \) and synaptic conductance change \( G(t) \) in response to a single presynaptic spike have to be considered sufficiently brief to fall below the temporal resolution of the description. However, the time durations that are discarded here (especially the decay of \( G(t) \)) can sometimes lie of the order of significant interspike intervals (Forsythe and Westbrook 1988; Syed *et al.* 1990; Rinzel and Frankel 1992) that may critically influence the behavior of a neural network.

5. The synaptic current \( G(t)V_{m} - V(t) \) has to be linearized into \( G(t)\Delta V \). This constitutes an approximation that distorts the time integration at the membrane potential, and also unduly favors the action of inhibitory inputs compared to excitatory ones.

The above conditions are not unrealistic in themselves. They constitute approximations in the modeling process, that have to be controlled, to correctly appreciate the significance and the limitations of the neural models they entail. Very simple models like equation 4.4, with scalar synaptic coefficients, can bring useful insight of some qualitative capabilities of neural networks. But, as exhibited here, such models ignore many features of synaptic transmission. They discard stochastic as well as temporal properties. They suppress sources of nonlinear interactions, in the evolution of \( G(t) \) where they neglect saturation, and in the evolution of \( V(t) \). Such stochastic, dynamic, and nonlinear attributes may play important roles at the level of neuron networks. Yet, it is not easy to accurately assess their importance with only a priori considerations. A clear perception of their impact demands direct examination and study of their implications in neural networks.

To enhance our understanding of neural networks and their collective properties for information processing we must progressively include more biophysical details in neural network models, and seek increased quantitative significance. At the same time, some control of this complication of the models has to be maintained, for the study of collective behaviors among large populations of interacting neurons. The modeling elements for synaptic transmission that we have presented here in a coherent perspective may be useful in this direction.

References


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