An Efficient Method for Computing Synaptic Conductances Based on a Kinetic Model of Receptor Binding

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Synaptic events are often formalized in neural models as stereotyped, time-varying conductance waveforms. The most commonly used of such waveforms is the $\alpha$-function (Rall 1967):

$$g_{syn}(t) = \frac{(t - t_0)}{\tau} \exp\left[-\frac{(t - t_0)}{\tau}\right], \quad t \geq t_0$$  \hspace{1cm} (1)

where $g_{syn}$ is the synaptic conductance and $t_0$ is the time of transmitter release. This function peaks at a value of $1/e$ at $t = t_0 + \tau$, and decays exponentially with a time constant of $\tau$. When multiple events occur in succession at a single synapse, the total conductance at any time is a sum of such waveforms calculated over the individual event times.

There are several drawbacks to this method. First, the relationship to actual synaptic conductances is based only on an approximate correspondence of the time-course of the waveform to physiological recordings of the postsynaptic response, rather than plausible biophysical mechanisms. Second, summation of multiple waveforms can be cumbersome, since each event time must be stored in a queue for the duration of the waveform and necessitates calculation of an additional exponential during this period (but see Srinivasan and Chiel 1993). Third, there is no natural provision for saturation of the conductance.

An alternative to the use of stereotyped waveforms is to compute synaptic conductances directly using a kinetic model (Perkel et al. 1981). This approach allows a more realistic description of neurotransmitter...
uration and summation of multiple synaptic events, obviating the need for event queuing.

Following the arrival of an action potential at the presynaptic terminal, neurotransmitter molecules, $T$, are released into the synaptic cleft. These molecules are taken to bind to postsynaptic receptors according to the following first-order kinetic scheme:

$$ R + T \xrightleftharpoons{\alpha}{\beta} TR^* $$

where $R$ and $TR^*$ are, respectively, the unbound and the bound form of the postsynaptic receptor, $\alpha$ and $\beta$ are the forward and backward rate constants for transmitter binding. Letting $r$ represent the fraction of bound receptors, these kinetics are described by the equation

$$ \frac{dr}{dt} = \alpha [T] (1 - r) - \beta r $$

where $[T]$ is the concentration of transmitter.

There is evidence from both the neuromuscular junction (Anderson and Stevens 1973) and excitatory central synapses (Colquhoun et al. 1992) that the concentration of transmitter in the cleft rises and falls very rapidly. If it is assumed that $[T]$ occurs as a pulse, then it is straightforward to solve equation 3 exactly, leading to the following expressions:

1. During a pulse ($t_0 < t < t_1$), $[T] = T_{\text{max}}$ and $r$ is given by

$$ r(t - t_0) = r_\infty + [r(t_0) - r_\infty] \exp\left[-(t - t_0)/\tau_r\right] $$

where

$$ r_\infty = \frac{\alpha T_{\text{max}}}{\alpha T_{\text{max}} + \beta} $$

and

$$ \tau_r = \frac{\beta}{\alpha T_{\text{max}} + \beta} $$

2. After a pulse ($t > t_1$), $[T] = 0$, and $r$ is given by

$$ r(t - t_1) = r(t_1) \exp\left[-\beta (t - t_1)\right] $$

If the binding of transmitter to a postsynaptic receptor directly gates the opening of an associated ion channel, then the total conductance through all channels of the synapse is $r$ multiplied by the maximal conductance of the synapse, $g_{\text{syn}}$. Response saturation occurs naturally as $r$
approaches 1 (all channels reach the open state). The synaptic current, $I_{\text{syn}}$, is given by the equation

$$I_{\text{syn}}(t) = g_{\text{syn}} \ r(t) \ |V_{\text{syn}}(t) - E_{\text{syn}}|$$  \hspace{1cm} (6)

where $V_{\text{syn}}$ is the postsynaptic potential, and $E_{\text{syn}}$ is the synaptic reversal potential.

These equations provide an easily implemented method for computing synaptic currents and have storage and computation requirements
events obtained using these values. Figure 1A and B show fast, excitatory currents resulting from a single synaptic event and a train of four events. Note that the time course of the postsynaptic potential resembles an \( \alpha \)-function even though the underlying current does not. Figure 1C and D show the time courses of the same variables for a slower, inhibitory synapse. In this case the rates for \( \alpha \) and \( \beta \) were slower, allowing a more progressive saturation of the receptors.

We have presented a method by which synaptic conductances can be computed with low computational expense using a kinetic model. The kinetic approach provides a natural means to describe the behavior of synapses in a way that handles the interaction of successive presynaptic events. Under the same assumption that transmitter concentration occurs as a pulse, more complex kinetic schemes can be treated.
in a manner analogous to that described above (Destexhe et al. in preparation). The “kinetic synapse” can thus be generalized to give various conductance time courses with multiexponential rise and decay phases, without sacrificing the efficiency of the first-order model.

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References


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