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

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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:

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

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).
approaches 1 (all channels reach the open state). The synaptic current, $I_{syn}$, is given by the equation

$$I_{syn}(t) = g_{syn} \ r(t) \ (V_{syn}(t) - E_{syn})$$

(6)

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

These equations provide an easily implemented method for computing synaptic currents and have storage and computation requirements that are independent of the frequency of presynaptic release events. To simulate a synaptic connection, it is necessary only to monitor the state of the presynaptic terminal and switch from equation 5 to equation 4 for a fixed time following the detection of an event. At each time step, this method requires the storage of just two state variables [either $t_0$ and $r(t_0)$ or $t_1$ and $r(t_1)$], and the calculation of a single exponential (either equation 4 or equation 5). This compares favorably to summing $\alpha$-functions, which requires storage of $n$ release times and $n$ corresponding exponential evaluations, where $n$ is the product of the maximum frequency of release events and the length of time for which the conductance waveform is calculated.

The parameters of the kinetic synapse model can be fit directly to physiological measurements. For instance, duration of the excitatory neurotransmitter glutamate in the synaptic cleft has been estimated to be on the order of 1 msec at concentrations in the 1 mM range (Clements et al. 1992; Colquhoun et al. 1992). Figure 1 shows simulated synaptic

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Figure 1: Facing page. Postsynaptic potentials from receptor kinetics. Presynaptic voltage, $V_{pre}$ (mV); concentration of transmitter in the synaptic cleft, [T] (mM); fraction of open (i.e., transmitter-bound) postsynaptic receptors, $r$; synaptic current, $I_{syn}$ (pA); and postsynaptic potential, $V_{syn}$ (mV), are shown for different conditions. (A) A single transmitter pulse evokes a fast, excitatory conductance $G_{syn} = 2 \ \text{pA M}^{-1} \ \text{mM}^{-1}$. (B) A train of pulses.---
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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