PARAMETRIC AND NON-PARAMETRIC MODELS OF SHORT-TERM PLASTICITY

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Abstract—Short-term plasticity (STP) was recorded with voltage-clamp technique and modeled with both parametric and non-parametric approaches. In the parametric approach, we simulated STP by calculating facilitation and refractory depression driven by presynaptic residual calcium; In the non-parametric approach, STP was modeled using Laguerre expansions of Volterra kernels. Our results showed that the 3rd order non-parametric model sufficiently captured the nonlineairities of the parametric model.

Keywords – Synaptic plasticity, Volterra kernel estimation, Non-parametric model

I. INTRODUCTION

STP is the use-dependent plasticity of synaptic transmission with a duration in the range of milliseconds to hundreds of milliseconds. The magnitudes of the post-synaptic responses are dynamically regulated by the history of recent activity. More specifically, trains of pre-synaptic action potentials elicit varying amplitudes of post-synaptic responses (Fig. 1). This temporal filtering property of synapses is important for the signal transmission and information processing in brain [1].

STP was modeled parametrically in a previous study [2]. In our study, we abstracted the input-output properties of their model using a non-parametric, Volterra kernel model.

II. METHODOLOGY

1) Recording: Hippocampal slices were prepared from young, male rats. Stimulating electrodes were placed in the Schaffer collaterals to activate CA1 pyramidal cells. Whole-cell recordings of CA1 pyramidal cells were obtained with HEKA EPC 9 double patch amplifier, which is digitally controlled by a Pentium PC.

2) Parametric model of STP: The parametric model was adopted from [2]. The peak amplitude of EPSCs was modeled as the product of the total number of release sites \( N_\tau \), facilitation factor \( F \) and depression factor \( D \). \( F \) and \( D \) were calculated from the concentrations of two calcium-bound molecules, \( \text{CaX}_F \) and \( \text{CaX}_D \), which were both driven by residual calcium. Model parameters were: initial release probability \( F_1 = 0.24 \), maximum paired-pulse facilitation ratio \( \rho = 2.2 \), \( \tau_F = 100 \text{ ms} \), \( \tau_D = 50 \text{ ms} \), \( k_{\text{max}} = 30 \text{ sec}^{-1} \), \( k_0 = 2 \text{ sec}^{-1} \), \( K_0 = 2 \) for Schaffer collateral - CA1 pyramidal cell synapses (Sch-CA1). \( \alpha N_\tau \) was set to 1 for simplicity. \( \Delta t \) is the sampling interval.

\[
\text{EPSC}(t) = \alpha \cdot N_\tau \cdot F(t - \Delta t) \cdot D(t - \Delta t)
\]

\[
\frac{\partial \text{CaX}_F}{\partial t} = -\text{CaX}_F(t)/\tau_F + \Delta_F \cdot \delta(t - t_0)
\]

\[
\frac{\partial \text{CaX}_D}{\partial t} = -\text{CaX}_D(t)/\tau_D + \Delta_D \cdot \delta(t - t_0)
\]

\[
F(t) = F_1 + \frac{1 - F_1}{1 + K_F/\text{CaX}_F(t)}
\]

\[
\frac{\partial D}{\partial t} = (1 - D(t)) \cdot k_{\text{conv}} \cdot \text{CaX}_D - D(t) \cdot F(t) \cdot \delta(t - t_0)
\]

\[
k_{\text{conv}} \cdot \text{CaX}_D = \frac{k_{\text{max}} - k_0}{1 + K_D/\text{CaX}_D(t)} + k_0
\]

3) Non-parametric model of STP: Action potentials, the input of the system, were simplified as discrete pulses (Fig. 1A,C), while EPSCs, the output of the system, were simplified as discrete pulses with varying amplitudes (Fig. 1B,D). The adapted Laguerre expansion of Volterra kernels could be expressed as below [3]:

\[
y(n) = C_0 + \sum_j C_j V_j(n) + \sum_{j_1, j_2} C_{j_1, j_2} V_{j_1}(n)V_{j_2}(n) + \sum_{j_1, j_2, j_3} C_{j_1, j_2, j_3} V_{j_1}(n)V_{j_2}(n)V_{j_3}(n) + \ldots
\]

\[
V_j(n) = \Delta t \sum_{\tau=0}^M b_j(\tau) x(t - \tau)
\]

\[
b_j(\tau) = \alpha^{j-1/2} (1 - \alpha)^{1/2} \sum_{k=0}^{[\tau]} \left( \frac{\tau}{k} \right) \left( \frac{1}{k} \right) \alpha^{j-k} (1 - \alpha)^k
\]

In the above equations, \( y \) is peak amplitude of EPSC, \( C_0 \), \( C_j \), \( C_{j_1}, C_{j_2}, \ldots \) are kernel expansion coefficients, \( V \) is the convolution of Laguerre basis functions and input epoch values, \( b \) is the Laguerre basis function. The \( t \) in the parametric model is equal to \( n \Delta t \) here. The kernel expansion coefficients were calculated with a least-square fitting method.

III. RESULTS

A. Sch-CA1 synapses show both facilitation and depression

The EPSCs elicited by Poisson random trains (2Hz) were recorded in CA1 pyramidal cells. Consistent with previous
reports [2], evoked EPSCs were first facilitated and then depressed during the stimulus train (Fig. 1B).

B. The 3rd order Volterra kernel model of Sch-CA1 synapse

The Laguerre expansions of Volterra kernels were calculated from the EPSC amplitudes predicted by the parametric model. Our results showed that a 3rd order kernel model was sufficient to replicate the parametric model’s output of a 2Hz Poisson random train (Table 1; Fig. 2).

<table>
<thead>
<tr>
<th>Table I</th>
<th>Predictive Accuracies of the Non-parametric Model</th>
</tr>
</thead>
<tbody>
<tr>
<td>Order of Model</td>
<td>NMSE (%)</td>
</tr>
<tr>
<td>1st</td>
<td>23.43</td>
</tr>
<tr>
<td>2nd</td>
<td>12.86</td>
</tr>
<tr>
<td>3rd</td>
<td>2.66</td>
</tr>
<tr>
<td>4th</td>
<td>1.89</td>
</tr>
</tbody>
</table>

In all predictions, different random trains were used to calculate the kernels and the NMSEs.

![Fig. 2. Prediction of parametric model’s output using the 3rd order non-parametric Volterra kernel model. Bar. EPSC amplitudes simulated by the parametric model; Circle, EPSC amplitudes predicted by the 3rd order non-parametric model.](image)

In the 3rd order kernel model, the 1st order kernel gave the value of $F_1$ in the parametric model. The 2nd and 3rd order kernels described the paired-pulse and triple-pulse responses of the parametric model. We can see facilitation in the 2nd order kernel and depression in the 3rd order kernel (Fig. 3).

![Fig. 3. The 3rd order kernel model of Sch-CA1 synapse. Model parameters were $\alpha = 0.992$, number of basis functions = 4, memory of system = 2000 ms. The 2nd and 3rd order kernels were normalized by the 1st order kernel.](image)

C. The 3rd order Volterra kernel models of three different synapses

Three different forms of STP found in the CNS were modeled by the parametric model (Table II) and non-parametric model (Fig. 4). Sch-CA1 synapses expressed both facilitation and depression; parallel fiber synapses expressed only facilitation; climbing fiber synapses expressed only depression. These three forms of nonlinearities associated with the parameters of the three parametric models were explicitly visualized by the 3rd order kernel models. The shape and magnitude of 2nd and 3rd order kernels were highly sensitive to the parameters determining the form of STP ($\rho$, $F_1$).

<table>
<thead>
<tr>
<th>Table II</th>
<th>Parametric Model Parameters for the Three Synapses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sch-CA1</td>
<td>Parallel Fiber</td>
</tr>
<tr>
<td>$\rho$</td>
<td>2.2</td>
</tr>
<tr>
<td>$F_1$</td>
<td>0.24</td>
</tr>
<tr>
<td>$K_0$</td>
<td>2</td>
</tr>
</tbody>
</table>

Other parameter values were the same as those given in the Methodology. The facilitation ratio ($\rho$) was determined by $K_0$.

![Fig. 4. The 3rd order kernel models of 3 different synapses. Note that facilitation and depression were separated in the 2nd and 3rd order kernels.](image)

IV. DISCUSSION

In this study, we numerically estimated the Volterra kernels of a published parametric model of STP. Our results showed that the 3rd order Volterra kernel model could accurately replicate the input-output properties of the parametric model. The 2nd and 3rd order kernels provided a reliable measurement of the nonlinearities and the associated parameters. The sensitivity of kernels to changes of key model parameters was examined and two of them ($\rho$, $F_1$) were found to be most critical. This high sensitivity suggested that it is possible to evaluate the important physiological parameters, e.g., the release probability of the synapse ($F_1$), using the Volterra kernel model. Experimental data are currently being collected to further validate these model results.

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REFERENCES

