Functional Properties of Electrical Synapses Between Inhibitory Interneurons of Neocortical Layer 4

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INTRODUCTION

There is strong anatomical and electrophysiological evidence for electrical synapses between inhibitory interneurons of neocortex (Bozhilova Pastiurova and Ovtscharoff 1995; Galarreta and Hestrin 1999; Gibson et al. 1999; Sloper and Powell 1978; Tamas et al. 2000). Electrical synapses mediate direct electrical communication between neurons. They are composed of clusters of ion channels that span the plasma membranes of 2 neurons, thereby directly connecting their cytoplasmic compartments. Each of these channel clusters is called a gap junction (Bennett 1977). Gap junctions between inhibitory neurons in neocortex tend to be dendrodendritic or dendrosomatic (Fukuda and Kosaka 2003; Szabadics et al. 2001; Tamas et al. 2000), and their channels require Cx36 in cell expression (Deans et al. 2001; Hormuzdi et al. 2001). Electrical synapses in neocortex mostly occur between cells whose somata are within 75 μm of each other, they interconnect about 20 to 60 neighboring inhibitory neurons, and they may account for almost half of the input conductance of single interneurons (Amatii et al. 2002).

Different modes of synchronous activity occur in neocortex in vivo, and some forms of synchrony are hypothesized to play a role in sensory perception, motor control, or cognition (Anderson et al. 2000; Gray 1999; Jones et al. 2000; Kandel and Buzsaki 1997; Macdonald et al. 1998; Murthy and Fetz 1996; Singer 1999; Steriade 1997). Experimental data obtained from both neocortical and hippocampal slices suggest that inhibitory synaptic transmission is critical for many forms of synchronous activity (Buhl et al. 1998; Cobb et al. 1995; Jefferys et al. 1996; Traub et al. 1996b). In a variety of neuronal systems, electrical synapses are also hypothesized to promote network synchrony (Bennett 1977; Dermietzel and Spray 1993). Consistent with this, experiments on neocortical slices have shown the importance of electrical synapses among inhibitory neurons for synchronous network activity (Beierlein et al. 2000; Deans et al. 2001; Galarreta and Hestrin 2001; Tamas et al. 2000). Recent work in connexin36 (Cx36) knockout mice supports a role for electrically coupled inhibitory neurons in gamma oscillations in the hippocampus (Buhl et al. 2003; Hormuzdi et al. 2001). Theoretical studies demonstrate that, in principle, an inhibitory network interconnected by both chemical and electrical synapses can produce synchronous network activity (Bartos et al. 2002; Golomb and Rinzel 1993; Pfeuty et al. 2003; Traub et al. 2001; van Vreeswijk et al. 1994; Wang and Buzsaki 1996; White et al. 1998).

To understand how electrical synapses mediate synchrony, it is necessary to know precisely how a presynaptic action potential in one neuron generates an electrical postsynaptic potential (ePSP) in another. The signal pathway includes not only the electrical synapse itself, but also the somata and dendrites of each cell. Gap junctions formed by Cx36 in cell expression systems are electrically linear over a range of ±80 mV (Srinivas et al. 1999). In neocortical inhibitory neurons, electrotocnic communication appears to be linear as well because it is voltage independent and nonrectifying over a range of at least ±40 mV (Galarreta and Hestrin 1999; Gibson et al. 1999). Thus most theoretical models examining how electrical communication influences cortical synchrony assume a simple linear rule for communication, or assume neuronal properties conducive to linear communication (i.e., mostly passive dendrites, proximal location of electrical synapses) (Bartos et al. 2002; Lewis and Rinzel 2003; Pfeuty et al. 2003; Traub et al. 2001).

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No measurements examining linearity have been made at potentials close to threshold and faster timescales comparable to an action potential, so the possibility that electrical synapses display nonlinear properties under realistic conditions has not been ruled out. Furthermore, because gap junctions often interconnect dendrites (Fukuda and Kosaka 2003; Szabadics et al. 2001), electrical synaptic signals originating at the soma may be transformed by active conductances in dendritic membranes (Goldberg et al. 2003; Martina et al. 2000; Stuart and Sakmann 1994).

Here we examine the properties of electrical synaptic communication between inhibitory interneurons in layer 4 of somatosensory neocortex. At least one type of inhibitory interneuron in layer 4 has been observed to fire together in precise synchrony in vivo (Swadlow et al. 1998), and it is likely that electrical synapses play a role in this synchrony. Among the variety of inhibitory interneuron subtypes in neocortex (Cauli et al. 2000; Gupta et al. 2000; Kawaguchi and Kubota 1997; Thomson and Deuchars 1997), we focus here on 2: fast-spiking (FS) and low threshold-spike (LTS) cells. We have found that electrical synapses tend to interconnect FS cells to other FS cells, or LTS cells to other LTS cells, but they rarely connect the 2 subtypes to each other. FS cells and LTS cells form 2 distinct inhibitory networks with different electrophysiological properties and functionally different chemical synaptic connections (Beierlein et al. 2003; Gibson et al. 1999). Here we demonstrate that the transmission of an action potential from one interneuron soma to another by an electrical synapse is passive and linear. We also demonstrate that electrical synapses between layer 4 inhibitory interneurons promote firing synchrony among neuron pairs over a wide range of firing frequencies, and that this property opposes the antisynchrony promoted by GABAergic synapses at lower firing frequencies.

METHODS

Slice preparation and recording

Thalamocortical slices (Agmon and Connors 1991) 250–450 μm thick were obtained from Sprague–Dawley rats aged P15–P20. After dissection, slices were incubated at 32°C for 1 h, and then kept at room temperature until they were transferred to a submersion-type recording chamber for recordings. The bathing solution contained (in mM): 126 NaCl, 3 KCl, 1.25 NaH2PO4, 2 MgSO4, 26 NaHCO3, 10 dextrose, and 2 CaCl2, saturated with 95% O2-5% CO2. Recordings were performed at 32°C.

Whole cell recordings were performed on layer 4 inhibitory interneurons in primary somatosensory (barrel) cortex. Data from a subset of the cell pairs presented here were also included in a previous study (Gibson et al. 1999). Micropipettes were made from 1.5 mm OD/0.86 mm ID glass (Sutter) and filled with (in mM): 130 K-glucorinate, 4 KCl, 2 NaCl, 10 HEPES, 0.2 EGTA, 4 ATP-Mg, 0.3 GTP-Tris, 7 phosphocreatine-Tris, 10 sucrose (pH 7.25, 290 mOsm). Series resistance was typically between 12 and 22 MΩ and continually monitored. Liquid junction potential was −11 mV and was not corrected for. Most recordings were made in current-clamp mode (Axoclamp 2A, Axoclamp1A, or Axoprobe 1A; Axon Instruments). Recordings were performed with IR-DIC visualization (Stuart et al. 1993) using a Zeiss Axioskop and a CCD camera (Hamamatsu).

Where indicated, some experiments were performed with drugs to block fast synaptic transmission: the N-methyl-D-aspartate (NMDA) receptor antagonist d-2-amino-5-phosphopentanoic acid (AP5; 50 μM, Sigma), the AMPA/kainate receptor antagonist 6,7-dinitroquinoxaline-2,3-dione (DNQX; 20 μM, Sigma), the GABA<sub>A</sub> receptor antagonists bicuculline methiodide (BMI; 50 μM, Sigma), or picrotoxin (100 μM, Sigma). In some experiments, voltage-dependent sodium currents were blocked with tetrodotoxin (TTX; 2 μM, Sigma) and voltage-dependent potassium currents were blocked with tetraethylammonium chloride (TEA; 1 mM, Sigma) and 4-aminopyridine (4-AP; 400 μM, Sigma).

Data analysis

Recordings were filtered at 10 kHz and acquired and analyzed using software written in LabVIEW (National Instruments) by J.R.G. Statistical significance was defined at the 5th percentile, and unless otherwise stated was determined by an unpaired t-test. All statistics were calculated using Statview (SAS Institute). For multiple comparisons, a one-way ANOVA was performed followed by a Fisher’s protected least-significant difference test for all possible pairwise comparisons. Averages are given as means ± SE.

CELL TYPES. To record from inhibitory interneurons in layer 4, we selected large, vertically oriented somata with 2 primary dendritic processes. Electrophysiological criteria reliably categorize FS and LTS neurons in layer 4, which are further distinguished by differential protein expression, afferent and efferent synaptic properties, and specificity of synaptic connections (Beierlein et al. 2003). In brief: FS cells fired at rates ≤300 Hz, had high minimum firing rates at spike threshold, and displayed no frequency adaptation. FS cells generated very brief action potentials with fast, deep, monophasic afterhyperpolarizations (AHPs). LTS neurons had distinctly lower maximum and minimum firing rates, showed spike frequency adaptation, had action potentials that were longer in duration, and generated more complex AHPs. Excitatory neurons showed more pronounced adaptation than LTS neurons, had the broadest spikes, and displayed distinctly different AHP waveforms. Our LTS cells may correspond to the interneurons called “regular-spiking nonpyramidal cells” (RSNs) or “adapting cells” (ADs) reported in other studies (Cauli et al. 2000; Goldberg et al. 2003). The distance between neurons in simultaneously recorded pair was measured as the center-to-center distance between their cell bodies.

COUPLING COEFFICIENT. The steady-state coupling coefficient (CC) (Bennett 1977) was determined in current clamp by injecting a current step into one cell and observing the voltage deflection in both cells. The following equation was used: CC = V1/V2, where V1 refers to the potential change of the current-injected cell and V2 is the potential change of the other cell. The CC was measured at a latency of 300 ms into the current step. In addition, an action potential (AP) coupling coefficient was also determined, where V1 is the presynaptic spike amplitude and V2 is ePSP amplitude. Unless stated otherwise, ePSP amplitude refers to the peak amplitude of the early depolarizing phase.

JUNCTIONAL CONDUCTANCE. An effective junctional conductance (Gj) was calculated to estimate the strength of electrical synapses (Bennett 1977). This calculation assumed a model of 2 isopotential neurons coupled directly by a single junction. Three conductances (the junctional and 2 input conductances) were calculated from simultaneous equations using the current injection values and voltage responses (300 ms after step onset) of each cell. The model does not account for complexities arising from junctions on dendritic or axonal cables, it does not incorporate nonlinear membrane properties, and it does not include effects of multiple current pathways through additional coupled cells in the network (Amitai et al. 2002).

CROSS-CORRELATIONS. Cross-correlations for action potential firing were based on counts of the number of spikes that fell into bins 0.2 ms wide. These numbers were normalized to the reference trace for the correlation; thus the y-axis of the cross-correlograms represents the probability of a spike occurring in a bin given a single spike in the
reference trace. Synchronous firing was defined as a peak in the cross-correlogram within 1.5 ms of zero.

FREQUENCY-TRANSFER FUNCTION. Frequency-transfer functions were derived from postsynaptic responses evoked by presynaptic sine-wave current injections at various frequencies. Baseline membrane potential was maintained at ~63 mV and induced presynaptic sine-wave voltages were about 12 mV (peak-to-peak) at all frequencies. Data from cell pairs were used only if the coupling was strong enough to make measurements up to 200 or 500 Hz (Gj >1.2 nS; series resistance <18 MΩ). All data were corrected for contamination and phase lags that occur between the current injection pipette and the second recording pipette, as determined from simultaneous patch recordings on single FS and LTS cells (n = 4, Fig. 2B, dashed line). The corner frequency was defined as the intersection of a straight line drawn along the asymptotic course at high frequencies, with a horizontal line representing the DC attenuation (Schwarz and Oldham 1984).

IMPULSE FUNCTION. Impulse functions were calculated from experimentally obtained frequency-transfer functions of electrically coupled neurons. This was done by taking the inverse Fourier transform of the attenuation and phase lag data obtained experimentally from sine-wave current injections (Stark and Woods 1986) (LabVIEW software, National Instruments). An impulse function with higher time resolution was obtained by extrapolating the experimental sine-wave data to higher frequencies. Points at 750, 1,000, and 2,000 Hz were added by averaging the 2 nearest compartmental model-derived frequency-transfer functions surrounding the 500-Hz experimental point (see Fig. 4). The former is referred to as the “data only” impulse function, and the latter the “extrapolated” impulse function. All impulse functions were scaled to a coupling coefficient of 0.1 (Fig. 7A), and then rescaled based on the experimentally derived coefficient for each electrical synaptic connection.

ERROR MEASUREMENTS. The accuracy of the linear models was sometimes described by the percent of variance (POV) in an experimental waveform that could be accounted for by a predicted waveform. POV is directly proportional to $R^2$, which is used in linear compartmental modeling software Neuron (Hines 1989; www.neuron.yale.edu). Purely passive neurons were created with 3 dendritic branches and no axon (Fig. 3). Only a passive leak conductance was included, which had a reversal potential of ~75 mV. The properties of FS cell and LTS cell models were identical except for their specific membrane resistances (5,000 Ω cm$^{-2}$ for FS and 7,000 Ω cm$^{-2}$ for LTS). These values were derived from experimental measurements of input resistance and time constants (mean $R_{input} = 54$ and 81 MΩ and mean $\tau_{decay} = 10$ and 17 ms for FS cells and LTS cells, respectively). These specific membrane resistances are similar to those used in a previous modeling study of dentate inhibitory neurons (10,000 Ω cm$^{-2}$; Bartos et al. 2002), and if electrical synapses can account for up to half the total conductance in a single neuron (Amitai et al. 2002), then our specific resistances essentially match those of Bartos et al. (2002). The resulting model cells had input resistances of 58 MΩ for FS cells and 77 MΩ for LTS cells (i.e., within about 8% of experimental data). The specific membrane capacitance (1.2 μF/cm$^2$) was chosen based on values reported in the literature (Cole 1968) and on the input resistances and time constants actually measured experimentally. Internal axial resistivity was 150 Ω cm$^{-1}$, which was also based on values previously reported for other types of central neurons (Segev et al. 1998).

The somatic and dendritic geometry of the modeled neurons was designed to approximate the dimensions of inhibitory neurons observed under living conditions (IR-DIC optics) and with reconstructions from biocytin-filled neurons. Cells filled with biocytin in this study were described anatomically in another study (Amitai et al. 2002), and here we used the cell dimensions obtained there with light microscopy. We also referenced electron microscopic data of neocortical inhibitory neurons (Tamas et al. 2000). Under IR-DIC, soma size typically ranged from 20 to 40 μm vertically and from 8 to 15 μm horizontally. The model soma was made slightly smaller (18 × 12 μm) to compensate for the large proximal upper dendrites in the model. The 2 upper dendritic branches (Fig. 3A) were enlarged to increase the membrane area of the cell. The lengths of the branches were 200 μm for oblique, 130 μm for upper horizontal, and 135 μm for lower horizontal branches. Their diameters tapered to 1 or 1.5 μm at their distal terminations (depending on the particular branch). The lower dendritic branch had realistic morphological parameters, derived from biocytin reconstructions, and had an important effect on the simulation results. It was composed of 4 segments with these dimensions (in μm: length, proximal diameter, distal diameter), starting from the soma boundary: 10, 5.5, 2.5; 10, 2.5, 1.5; 80, 1.5, 1.0; 100, 1.0, 0.5. Electrical synapses were modeled as simple resistive elements between 2 identical cells and were placed various distances from the soma on the lower dendrite (in μm: 0, 30, 50, 100, 150, 200; Fig. 3A).

A micropipette was also added to the model to estimate analysis error attributable to the recording electrode. The pipette was a single compartment 2 mm long, tapering from 1 μm where it contacted the soma to 1 mm at the other end. The series resistance was set to 17 MΩ (the average in our experiments). The specific capacitance of the pipette (0.0002 μF/cm$^2$) was set so that the model approximated real recordings in 2 ways: 1) capacitive transients observed during current-step injections, and 2) attenuation of sine-wave current injections at 500 Hz observed with 2 pipettes patched onto one cell. This resulted in a 6.4-pF pipette. The specific resistance of the pipette glass was infinite and axial resistivity was the same as that of the model cell: 150 Ω cm$^{-1}$. All data from the simulations were obtained through this pipette to more closely approximate experimental conditions.

CORRECTED ACTION POTENTIALS. Model simulations also required voltage clamping presynaptic neurons with a “corrected” version of the action potential (see Fig. 6). Correction refers to the fact that our experimentally measured action potential was a filtered version of the signal occurring in the soma (attributed to the recording pipette). We made the correction by initially shifting the measured action potential back in time and increasing its amplitude such that when the soma was clamped to this corrected action potential, the waveform measured in...
the model pipette closely matched the experimental waveform. Subsequent arbitrary modifications were made to the corrected version until the error in action potential amplitude was <3% and the average voltage error was <1.5 mV (between model pipette and experimental waveforms). This latter error was measured in a time window where maximum differences existed between corrected and experimental waveforms (the spike itself and the initial AHP, average error about 7 mV).

RESULTS

Simultaneous paired recordings were performed on layer 4 inhibitory cells (n = 136 pairs; see Table 1 for detailed summary). Vertically oriented nonpyramidal cells were specifically targeted, since these were usually inhibitory, and the somata of these cells were often distinctly larger than the majority of surrounding cells (Simons and Woolsey 1984). There are numerous classification systems for neocortical inhibitory interneurons (Cauli et al. 2000; Gupta et al. 2000; Kawaguchi and Kubota 1997; Thomson and Deuchars 1997). We focused on FS cells and LTS cells, which were identified by their distinctive spike shapes and repetitive firing characteristics (Beierlein et al. 2003; Cauli et al. 2000; Connors and Gutnick 1997; Gibson et al. 1999). There are numerous classification systems for neocortical inhibitory cells (Beierlein et al. 2003; Cauli et al. 2000; Gupta et al. 2000; Kawaguchi and Kubota 1997; Thomson and Deuchars 1997). We focused on FS cells and LTS cells, which were identified by their distinctive spike shapes and repetitive firing characteristics (Beierlein et al. 2003; Cauli et al. 2000; Connors and Gutnick 1997; Gibson et al. 1999). The differences in firing properties strongly correlated with a number of synaptic and histochemical features (Beierlein et al. 2003; Cauli et al. 2000; Gibson et al. 1999).

Basic properties of electrical synapses

When a current step was used to evoke membrane potential changes in one cell, an attenuated version of that potential change occurred in the electrically coupled cell (Fig. 1A). Action potentials in one cell led to attenuated, low-pass–filtered signals in the other cell; we termed the latter electrical postsynaptic potentials (eSPs). Electrical synapses occurred mainly between inhibitory cells of the same type, and rarely between interneurons of different types (Gibson et al. 1999). Coupling coefficients (CC) and junctional conductances (Gj) for homotypic (same cell type) pairs were: FS: CC = 0.094 ± 0.014, Gj = 2.41 ± 0.42 nS, n = 45; LTS: CC = 0.129 ± 0.019, Gj = 2.35 ± 0.46 nS, n = 18. Electrical synaptic signaling for both inhibitory cell types was independent of the direction of current flow and voltage polarity over a transjunctional range of ±40 mV.

TABLE 1. Frequency table for chemical and electrical synaptic connections among FS and LTS neurons.

<table>
<thead>
<tr>
<th>Cell Types</th>
<th>Total Pairs</th>
<th>≥1 Chemical</th>
<th>2 Chemical</th>
<th>Electrical +1 Chemical</th>
<th>Electrical +2 Chemical</th>
</tr>
</thead>
<tbody>
<tr>
<td>FS-FS</td>
<td>57</td>
<td>42</td>
<td>17</td>
<td>33</td>
<td>29</td>
</tr>
<tr>
<td>LTS-LTS</td>
<td>24</td>
<td>2</td>
<td>0</td>
<td>16</td>
<td>0</td>
</tr>
<tr>
<td>Mixed</td>
<td>55</td>
<td>37</td>
<td>16</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>FS→LTS</td>
<td>55</td>
<td>20</td>
<td>4</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>LTS→FS</td>
<td>55</td>
<td>34</td>
<td>4</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

All pairs were within 100 μm. “≥1 chemical” indicates a chemical synapse in at least one direction. “Electrical +1 chemical” indicates a chemical synapse in at least one direction plus an electrical synapse. “Electrical +2 chemical” indicates chemical synapses in both directions, plus an electrical synapse. FS, fast spiking; LTS, low threshold spiking.

Both the strength and prevalence of electrical coupling between pairs of interneurons fall sharply with intercellular distance. In both layers 2/3 and 4, average coupling strength decreases to roughly half-maximum between 75 and 100 μm (Amitai et al. 2002; Galarreta and Hestrin 1999). We examined whether electrical coupling strength had an orientation preference by comparing coupling along the radial axis (operationally defined as being within ±35 ° of a line normal to pia) versus other axes. We restricted our analysis to FS cell pairs 25–100 μm apart (including uncoupled pairs), for which we had an adequate sample size. Radially oriented pairs had larger average coupling strengths than those of horizontally oriented pairs (1.9 ± 0.6 vs. 0.5 ± 0.2 nS, P < 0.05, n = 16, 18; average distance = 56 and 59 μm, P < 0.65). This difference is consistent with the radially biased orientation of the dendritic trees of the targeted interneurons (Amitai et al. 2002; Gibson et al. 1999).

Frequency-transfer characteristics

To measure the transfer characteristics of electrical synapses, sine-wave currents of different frequencies were injected into one cell of a coupled pair, and amplitude attenuation and phase lag were measured (Fig. 2A). Average attenuation and phase data for frequencies between 1 and 500 Hz for both FS and LTS pairs were obtained (Fig. 2B). Corner frequencies for FS and LTS pairs were 30 and 19 Hz, respectively, and at
these frequencies attenuation was 0.6 for each. Significant
differences in attenuation between FS and LTS pairs occurred
at 40 and 100 Hz ($P = 0.002$; $n = 8$, FS; $n = 5$, LTS).
Intercellular distances were not statistically different between
the 2 groups (38.9 ± 8.7 and 26.4 ± 5.0 μm for FS and LTS
pairs, respectively, $P = 0.35$), and there was no correlation
between intersomatic distance and filtering among FS cells
($n = 8$). Thus the average electrical connection between FS
cells transmits high frequencies more effectively than connec-
tions between LTS cells do.

To better understand electrical synaptic transmission, we
tested whether the frequency-transfer functions for FS and LTS
cells could be explained by a purely passive process. We
simulated the sine-wave injection experiments with compart-
mentally modeled interneuron pairs with passive membranes.
A dendrodendritic electrical synapse was placed at variable
distances from the somata (Fig. 3; see METHODS for model
details). Simulations in which the electrical synapse was placed
along the dendrites within 30–50 μm of the 2 somata most
closely approximated the average experimental transfer func-
tions for both FS and LTS cells (Fig. 4). Thus the frequency-
transfer properties of coupled interneurons are consistent with
entirely passive signal transmission through proximally located
electrical synapses.

**Electrical and inhibitory postsynaptic potentials**

The shape and time course of an ePSP will have an impor-
tant influence on the postsynaptic firing pattern or subthreshold
integration of inputs. Average action potential and ePSP wave-

![Fig. 2](http://jn.physiology.org/)

**FIG. 2.** Frequency-transfer characteristics of electrical coupling from
paired cell recordings. **A:** current ($I_{Pre}$) was injected presynaptically to evoke
oscillations of cell membrane potential ($V_{Pre}$) at various frequencies. Postsyn-
aptic attenuation and phase lag at each frequency were measured ($V_{Post}$). **B:**
average attenuation (top) and phase lag (bottom) for both FS ($n = 8$) and LTS
($n = 5$) cells are plotted. Values are modified from actual data based on the
attenuation and phase advance that occurred in the recording pipette with
respect to a current injection pipette in the same neuron ($n = 4$, dashed lines).
Attenuation values for all curves are normalized to measurements at 2 Hz. Data
points with statistically significant differences between FS and LTS pairs are
marked (*). Scale bar for $I_{Pre} = 1100$ pA.

![Fig. 3](http://jn.physiology.org/)

**FIG. 3.** **A:** diagram of a single-model neuron used for compartmental
calculations. Soma is represented by the center rectangle. Lower dendrite
is relevant to simulations. Parallel lines represent breaks in the pictorial rep-
resentation because of space limitations. All compartments are scaled to the
actual size used in the model (see METHODS for dimensions). **B:** scaled-up
diagram of the model depicting both cells and all possible locations for
electrical synapses (zigzags). Solid zigzag indicates a single electrical synapse
located at the soma, and dashed zigzags indicate the alternate electrical
synaptic locations examined. Vertical line between **A** and **B** is a scale bar.

![Fig. 4](http://jn.physiology.org/)

**FIG. 4.** Frequency-transfer characteristics of electrical coupling in the com-
partmental models for FS (**left**) and LTS (**right**) pairs. Along with somasomatic coupling (**(c)**), dendrodendritic coupling was simulated for various distances
from the soma as indicated in Fig. 1: 30 μm (**(c)**), 50 μm (**(c)**), and 100 μm (**(c)**).
Experimental data (bold lines with error bars) were best matched by models in
which electrical coupling was within 50 μm of the soma. Coupling strength in
the model was held constant at 2 nS. Attenuation is normalized to the 2 Hz
value.
forms (aligned to presynaptic spike peak; Fig. 5A) were derived from a random subset of FS and LTS cell pairs from which an ePSP was clearly measured and inhibitory postsynaptic potentials (IPSPs) were either nonexistent or blocked pharmacologically \((n = 8, \text{FS–FS}; n = 10, \text{LTS–LTS}; G_J > 0.6 \text{ nS})\). Cells were depolarized to evoke spikes at an average rate of 50 Hz, and ePSP latencies were measured with respect to the peak of the presynaptic action potential. ePSPs were recorded when the postsynaptic resting potential was at \(-60 \text{ mV}\) to minimize voltage-dependent, nonlinear conductances that might be activated at more depolarized or hyperpolarized potentials.

Consistent with the spike shapes of the presynaptic cells, ePSPs between FS cells were distinctly faster compared with those of LTS cells (Fig. 5A). At 50 ± 20 Hz, ePSPs of FS cells were biphasic, with a short-latency depolarizing phase (latency-to-peak = 405 ± 30 \(\mu s\), \(n = 17\)) followed by a longer hyperpolarizing phase (latency-to-trough = 8.48 ± 0.29 ms, \(n = 17\)). LTS ePSPs were more monophasic at the same frequency, with a single depolarizing phase (latency-to-peak = 1054 ± 148 \(\mu s\), \(n = 17\)). The width at half-height of the early depolarizing phase was 1.27 ± 0.07 and 5.04 ± 0.47 ms for FS and LTS cells, respectively. These differences in ePSP time course were not explained by differences in the intersomatic distances between FS and LTS pairs. Overall, ePSP amplitude (early depolarizing phase) was linearly proportional to the steady-state CC for both cell types (Fig. 5B). Both \(y\)-intercepts and slopes derived from linear regression fits were not statistically different between the 2 cell types \((y = -0.002 \text{ and } -0.004 \text{ and } m = 0.113 \text{ and } 0.137 \text{ for FS and LTS, respectively})\). This simple linear relationship suggests that no significant amplification or dendritic propagation of action potentials influences electrical synaptic signaling.

In addition to electrical synapses, FS cells form inhibitory chemical synapses with each other (Table 1; chi square, \(P < 0.05\); average distance not different). Consistent with previous studies, LTS cells made very few inhibitory synapses with each other (Gibson et al. 1999; Venance et al. 2000). Inhibitory synapses between FS cells had an average latency of 507 ± 33 \(\mu s\) \((n = 19)\) with respect to the peak of the presynaptic action potential. This is significantly longer than the peak latency of the ePSP mentioned earlier \((P < 0.05)\). In addition, the GABA\(_A\) receptor antagonists bicuculline and picrotoxin had no effect on either the latency-to-peak or the magnitude of the early depolarizing phase of a dual chemical–electrical synapse (Fig. 5C). Thus IPSPs have negligible effects on the early depolarizing phase of the ePSP, but add to the hyperpolarizing effect of the later phase of the ePSP in FS cells.

**Passive compartmental modeling accurately predicts ePSP waveforms**

The data described above suggest that subthreshold electrical synaptic transmission is largely a passive and linear process. We used 2-cell compartmental models with electrically passive membranes to determine whether the shape and magnitude of the average ePSPs obtained experimentally (Fig. 5A) could be predicted by passive signal transmission. The electrical synaptic conductances were the same as the average conductances estimated from the pairs used in Fig. 5 (i.e., FS = 2.38 nS, LTS = 1.54 nS), and we examined the effects of electrical synapses at 3 different locations (soma, 30 \(\mu m\), and 50 \(\mu m\)). The presynaptic soma was voltage clamped to the experimentally obtained action potential waveforms (from Fig. 5A). The model reproduced the general shape and magnitude of average ePSPs in both cell types reasonably well (Fig. 6A1). The biphasic FS–ePSP and the monophasic LTS–ePSP were best simulated by electrical synapses located at the soma; these
had POV values of 94.9 and 96.7%. The peak amplitudes of these same model ePSPs (somasomatic) displayed 6.5 and 8.1% error compared with experimental data.

At a faster timescale, however, errors in the onset kinetics of the ePSP were apparent (Fig. 6A2). The times-to-peak of the model ePSPs were markedly delayed compared with the experimental data. We reasoned that these delays could be artifactual, stemming from errors in our experimental measurements of the action potentials. Recordings of somatic action potentials are slightly delayed and attenuated by the micropipette used to measure them, so simply clamping the model presynaptic soma to the experimental waveform is not accurate. To remedy this, corrected versions of the average FS and LTS action potentials were calculated (Fig. 6; see METHODS), such that when the model soma was clamped to the corrected action potential (\(V_{\text{soma}}\)) the signal in the model micropipette (\(V_{\text{pip}}\)) closely mimicked the experimentally measured AP (\(V_{\text{exp}}\)). Model and experimental data were well matched (A2), and inconsistencies at the faster timescale (A2) were minimized (B2). Dendritic locations for model synapses that most closely approximated the data are consistent with those found for the sine-wave data in Fig. 5: about 30 \(\mu\)m from the soma.

**Linear transfer functions accurately predict ePSP waveforms**

If electrical signal transmission is truly linear, then an analytical model using the frequency-transfer functions should predict the shape and size of the ePSP. “Data only” impulse functions (Fig. 7A; see METHODS) were derived from the experimental frequency-transfer functions in Fig. 2. To improve time resolution, an “extrapolated” impulse function was also derived by extrapolating the transfer functions to higher frequencies (Fig. 7A; see METHODS). Simply convolving an impulse function with the presynaptic signal should reproduce the shape and size of the ePSP. “Data only” functions (errors for data only and extrapolated functions, respectively: FS: 20.5 and 10.2%; LTS: 0.25 and 0.5%). The complete waveform was also accurately predicted (FS: POV = 94.1 and 97.3%; LTS: 95.7 and 96.4%; data only and extrapolated functions, respectively). The largest error was associated with the early, fast component of the FS–ePSP (Fig. 7B, bottom) perhaps reflecting recording micropipette filtering at higher frequencies.
The ePSPs from samples of individual pairs of electrically coupled neurons were also well predicted using the “data only” impulse function (Fig. 7C). Linearity predictions for FS–ePSPs and LTS–ePSPs had POVs of 87.8 ± 1.8 and 83.2 ± 3.7%, respectively (n = 21, 15). The predicted ePSP amplitudes had average errors of 28.6 ± 2.8 and 13.7 ± 3.5%, whereas the average predicted/experiment ratios were 0.81 ± 0.06 and 0.94 ± 0.05. The greater error for the FS cells originated from the higher-frequency components that constituted their onsets because the predicted/experiment ratio for the ePSP trough (the later hyperpolarization) was 1.00 ± 0.05 (P < 0.005 when compared with ePSP amplitude ratio; paired t-test). We also observed less error in trough measurements, but this was not statistically significant (20.7 ± 2.6%; P < 0.06; paired t-test). The predicted ePSP peak for each connection was highly correlated with the experimental peak (R² = 0.87 and 0.89; P < 0.0001 for both, Fig. 7C).

Although no significant nonlinearities appeared to influence electrical synaptic transmission, we tested whether coupled interneurons could be manipulated to promote nonlinear transmission. In inhibitory neurons, potassium channels strongly affect action potential shape and regulate action potential backpropagation through proximal dendrites (Goldberg et al. 2003; Hoffman et al. 1997; Lau et al. 2000). Therefore if potassium channels are blocked, any possible nonlinear processes occurring in the dendrites, such as backpropagation, will be enhanced. Depending on the location of electrical synapses, this could unmask nonlinearities in electrical synaptic communication. We blocked potassium channels with either 1 mM TEA (FS, n = 4; LTS, n = 2), or with 1 mM TEA +400 μM 4-AP (FS, n = 1; LTS, n = 2) applied to the bath. Presynaptic action potentials widened, and ePSPs broadened and slightly enlarged, but transformations of these altered signals through electrical synapses were very well simulated using the “data only” impulse function. The average POV value for these predictions was 89.6 ± 1.7%. Thus no significant nonlinear effects were uncovered.

Taken together, these results suggest that ePSPs in response to presynaptic action potentials can be accurately predicted by the transfer function obtained from subthreshold sine-wave stimuli, thus representing a linear process. This strongly implies that voltage-gated membrane conductances are not significantly involved in the transformation of presynaptic action potentials into ePSPs.

**FIG. 7.** Impulse functions derived from experimentally measured sine-wave data can be used to predict both FS– and LTS–ePSPs accurately. Lines in all panels are as follows: experimental data (solid black), prediction based on “data only” transfer function (dashed black), and prediction based on “extrapolated” transfer function (solid gray). A: impulse functions derived from “data only” and “extrapolated” transfer functions (CC = 0.1; units = s⁻¹). B: convolving the canonical action potentials (from Fig. 6A) with the impulse functions produced linear predictions that accurately reflected the canonical ePSPs. As seen on an expanded timescale (bottom), ePSPs predicted from extrapolated impulse functions improved the temporal resolution of the response peak. C: performing the same convolution for each individual cell pair produced accurate linear predictions (based on “data only” impulse). Bottom: predicted ePSP peak was plotted against the experimental peak for individual cell pairs. For FS cells, ePSP trough was predicted more accurately than peak. Diagonal line represents equal peak amplitudes. Arrows on the FS trace delineate ePSP peak and trough measurements. Vertical scale bars in C; FS/LTS.

**Linearity predicts ePSP shape at different presynaptic firing rates**

Because the shapes of presynaptic action potentials depend on firing rate, ePSP waveforms should also change with rate. Examples of individual FS– and LTS–ePSPs are shown during low (<18 Hz) and high (about 90 Hz) spiking rates in Fig. 8, A1 and A2. Note the biphasic ePSP shapes at low frequencies and the monophasic shapes when spiking approached 90 Hz. A switch from biphasic to monophasic occurred between 20 and 50 Hz for LTS–ePSPs and between about 70 and 90 Hz for FS–ePSPs. Using the “data only” impulse functions from Fig. 7, the ePSP shapes and amplitudes in these individual cells were well approximated (Fig. 8A3). Electrical PSP peak-to-trough amplitudes decreased with firing rate, and for LTS electrical synapses the decrement occurred at lower frequencies (Fig. 8B). There was no striking change in ePSP width with increasing frequency, and we observed a statistically significant change in FS–ePSPs only when comparing <25 Hz with 25–50, 50–75, and 75–100 Hz (ANOVA: 0.9 ms for the former and 1.1 ms for the latter 3). Dependencies of ePSP amplitude on both firing frequency and interneuron subtype were well predicted over the sample of coupled pairs using the same “data only” impulse function (Fig. 8B).

Even though we have focused on the transmission characteristics of one or a few action potentials, transmission at
longer timescales also appeared to be a linear process. A random sample of responses to current steps (700 ms) applied to one cell was obtained from electrically coupled cell pairs (CC/H11022 0.06). The average impulse functions (“data only” from Fig. 7A) accurately predicted the postsynaptic signals with an average POV of 91.4% (n = 17 traces from 3 FS and 3 LTS pairs, see METHODS; Fig. 9). Typically, errors were at the very lowest frequencies (Fig. 9C). Because of these errors, we cannot exclude a contribution by nonlinear processes, but our data suggest that a large fraction of slow signals can be explained by linear transmission through electrical synapses.

**Nonlinear effects of postsynaptic membrane potential on ePSPs**

The experiments described above were all performed with the postsynaptic cell near resting potential. However, chemical PSPs can be altered in shape and size by voltage-activated currents when the postsynaptic membrane potential is near or above spike threshold (Magee et al. 1998; Stuart and Sakmann 1995). We observed distinctly nonlinear effects of electrical synaptic transmission under similar conditions. Electrical PSPs were amplified and prolonged when the postsynaptic membrane potential was near firing threshold, even though the

[FIG. 8. PSP shape depends on presynaptic AP frequency. A: data from a single FS pair (left) and a single LTS pair (right). A1: action potentials from single traces during trains of low (<15 Hz) and high (about 90 Hz) spiking frequency. A2: average electrical PSPs in response to the action potential trains. Bipolar nature of the PSP at low frequencies disappeared at higher frequencies for both cell pairs. A3: ePSP predictions using the “data only” impulse function in Fig. 7. B: ePSP amplitude plotted as a function of frequency for the population of cell pairs. Amplitudes refer to the peak-to-trough amplitude of the ePSP, and were normalized to those measured at 25 Hz or below. LTS ePSPs decreased in amplitude at lower frequencies than FS cells (* marks statistical significance, *P < 0.05). Data were plotted in 25-Hz bins (FS, n = 3–10; LTS, n = 3–11). Dashed lines plot values for the linear prediction based on the “data only” impulse functions from Fig. 7. Vertical scale bars refer to FS/LTS data.]

[FIG. 9. Linear and passive electrical communication at longer timescales. A: electrical synaptic signals between FS cells were accurately modeled by “data only” impulse functions derived from average data (from Fig. 7A). POV is 98.2%. B: impulse functions also accurately modeled LTS-to-LTS coupling. The LTS cell illustrated here displayed bursting attributed to the bath application of ACPD (100 μM). POV is 95.4%. C: another LTS pair. When noticeable errors occurred, they were at the longer timescales. POV is 76.9%. Scale bars: 20 and 3 mV for each trace pair.]
presynaptic action potential was not significantly changed (Fig. 10; ePSP amplitudes were $2.3 \pm 0.3$ and $1.5 \pm 0.3$ mV when evoked from threshold and subthreshold levels, respectively; $P < 0.0008$; FS = 3; LTS = 3). In addition, the accuracy of predicting the ePSP with the average “data only” impulse functions decreased from a POV of $91.2 \pm 1.5$ to $60.5 \pm 5.5\%$ ($P < 0.009$; paired $t$-test) when the postsynaptic membrane was depolarized. Thus even though subthreshold signaling appears very linear at resting membrane potential, postsynaptic depolarization can contribute nonlinearities to electrical communication.

**Functional consequences of electrical synapses**

Electrical coupling can promote precisely synchronous firing among pairs of interneurons (Galarreta and Hestrin 1999; Gibson et al. 1999; Szabadics et al. 2001; Tamas et al. 2000). However, no studies have investigated the robustness or magnitude of this synchrony as a function of the strength of the electrical synapses or of the firing frequency of the neurons. We tested the synchronizing properties of electrical synapses in isolated cell pairs by simultaneously injecting long, suprathreshold current steps into both cells (Fig. 11A). Although synaptic noise provided by inputs from other neurons will affect neuronal synchrony, we restricted our analysis to a relatively noiseless 2-cell system by blocking all fast synaptic transmission pharmacologically, unless stated otherwise.

Electrical synapses promoted synchronous firing over the entire frequency range that the cells were capable of sustaining for a 800-ms test interval: =225 Hz for FS cells and 110 Hz for LTS cells. Firing was most synchronous when the mean rates of the 2 cells were very similar, and synchrony fell very sharply when the cells’ firing rates differed significantly (Fig. 11A). Across cell pairs, the precision of synchrony increased with coupling strength, as determined by the widths of the central peaks in cross-correlograms, measured at half-height (Fig. 11B). Generally, coupling strengths above 3 nS resulted in synchronous firing with a precision of <2 ms at all frequencies tested (Fig. 11C).

There is considerable indirect evidence that networks of neurons with mutually inhibitory connections can promote synchronized oscillations in the cerebral cortex (Golomb and Rinzel 1993; Jefferys et al. 1996; Lewis and Rinzel 2003). Because we observed pairs of interneurons interconnected by reciprocal inhibitory chemical synapses, electrical synapses, or both types of synapses, we examined how the 2 types of synapses modify spiking interactions. When 2 FS cells were reciprocally connected by inhibitory synapses and their electrical synapse strength was weak or zero ($<1$ nS, $n = 5$ pairs), firing was out of phase (antisynchronous) when the cells were driven at lower frequencies, but switched abruptly to synchrony when the cells were driven at higher frequencies (Fig. 12A). The transition between antisynchrony and synchrony occurred at a mean of $102 \pm 10$ Hz. Reciprocally connected FS–LTS pairs displayed only out-of-phase behavior ($n = 5$) perhaps because the LTS cells were limited to a maximum steady-state firing rate of about 100 Hz. The antisynchronous relationship of all the reciprocally inhibitory pairs was usually $180 \pm 30^\circ$, and only rarely displayed phases extending to 90 or $270^\circ$. This antisynchronous behavior is consistent with the
fast-decay constants of the IPSCs measured in voltage clamp (mean $\tau = 2.3 \pm 0.23$ ms, $n = 3$ FS pairs) (but see van Vreeswijk et al. 1994; Wang and Buzsaki 1996; White et al. 1998 and DISCUSSION).

Our analysis was mainly restricted to mutually inhibitory pairs of neurons firing at similar rates. We did notice, however, that reciprocal inhibition could promote limited synchrony when one cell in a pair was firing just above threshold and the other cell was firing at a moderately high rate (Fig. 13).

Some FS–FS pairs had both reciprocal inhibitory synapses and electrical connections. Among such pairs with strong electrical synapses (>3.6 nS), synchronous firing occurred at all frequencies, and antisynchronous firing was not observed at lower frequencies as it was in pairs with purely inhibitory connections ($n = 3$; Fig. 12B). Two FS–FS pairs with both inhibitory connections and electrical synapses of moderate strength (1.9 and 2.3 nS) displayed antisynchrony–synchrony transitions at frequencies of 35 and 60 Hz, respectively. This was considerably lower than the mean transition frequency of 100 Hz observed in pairs with purely inhibitory connections. Thus electrical synapses appear to stabilize the synchronous state of neuron pairs, even in the presence of reciprocal inhibitory connections.

**DISCUSSION**

**Passive and linear electrical communication**

We studied electrical synaptic communication between inhibitory neurons using simultaneous recordings from neighboring neurons and realistic modeling. Our data imply that the transformation of subthreshold signals and action potentials as they propagate from one coupled soma to another is a passive and linear process; linearity can explain the differences in shape of ePSPs between FS and LTS cells and the change in ePSPs observed during repetitive firing. Furthermore, our data suggest that electrical communication on longer timescales is also linear. These results validate the assumption used in many theoretical models that electrical synaptic communication is linear and, in addition, suggest that the use of a computationally simple impulse function is adequate for modeling electrical synaptic function under many conditions.

The linear properties of electrical synapses found in this study are consistent with previous data involving connexin36-
mediated electrical communication. First, the directional symmetry of current flow and the relative voltage independence of the electrical synapses are similar to observations from cell lines transfected with connexin36 (Teubner et al. 2000). Second, electrical synaptic communication between cortical inhibitory neurons is linear and symmetric over a range of ±40 mV when tested with step-current injections (Galarreta and Hestrin 1999; Gibson et al. 1999). Third, gap junctions between FS neurons of layer 2/3 are located in proximal portions of the dendrite (Tamas et al. 2000), and this makes it unlikely that propagating action potentials in the dendrites would be able to influence signaling significantly (Goldberg et al. 2003; Kaiser et al. 2001; Martina et al. 2000). Our estimates of synapse location based on compartmental modeling are also consistent with this conclusion.

Linearity accounted for most of the variance in a 20-ms window around the ePSP in both FS and LTS cells (POVs of 87 and 83% for individual ePSPs), although we found that a linear process was less accurate in predicting the early peak of the FS ePSP when compared with that of the LTS–ePSP. This probably originates from the filtering of higher frequencies that is not accounted for in our methods. Higher frequencies exist in FS signaling because of their very fast spikes (0.36- vs. 0.56-ms half-widths for FS and LTS, respectively; Beierlein et al. 2003). Transfer functions based on experimental data included only frequencies ≤500 Hz, and therefore error may have resulted by not including higher frequencies. Consistent with this, the model prediction for the early peak of canonical FS–ePSPs was improved when we used impulse functions that were extrapolated ≤2000 Hz. Any remaining error may be attributable to greater micropipette filtering than we estimated. Because of this error, we cannot exclude the possibility of nonlinear effects on the early FS–ePSP peak but, if this occurs, it still contributes less than the linear component.

We cannot rule out the possibility that nonlinear communication occurs when a large network of inhibitory neurons is activated because we studied communication only between pairs of neurons in isolation. Furthermore, our analysis using compartmental models and impulse functions was biased by not including weaker connections (<0.6 nS) where signals were too small for analysis. With this in mind, we argue that our data are most relevant to the individual electrical synapses that are most likely to influence the precise synchrony and timing of action potential generation.

**Proximal Electrical Communication**

Soma-to-soma electrical coupling appears to be a distinctly local process. A previous study demonstrated that electrical synapses connect inhibitory neurons locally, with the half-maximal decrement in overall coupling strength occurring at an intersomatic distance of about 75 μm (Amitai et al. 2002). Our data further demonstrate that neurons are not only coupled locally, but that their electrical synapses are also proximal and local (30–50 μm from the soma).

It is very likely that coupling at more distal locations occurs as well because we observed coupling between neurons spaced ≤175 μm apart (Amitai et al. 2002) and because anatomical studies have demonstrated gap junctions in more distal dendrites (Fukuda and Kosaka 2003). However, these connections are much weaker and are either rare or undetectable with somatic recordings. Therefore they may be irrelevant in the context of soma-to-soma communication. Proximally located synapses provide signals that undergo relatively little dendritic filtering, which enables rapid signaling and perhaps sharper synchrony between neurons.

Using our compartmental models, we find that junctional conductances measured at the soma are 80 and 60% of their true value if synapses are located on dendrites 50 and 100 μm away, respectively. The proximal location of electrical synapses (Tamas et al. 2000) makes it possible to reasonably estimate the number of Cx36 channels involved in cell-to-cell communication. Assuming our measured electrical synaptic conductances are 80% of true value, and assuming a single-channel conductance of 14 pS (Teubner et al. 2000), roughly 200 channels are open in the average electrical connection between interneurons.

**Functions of electrical synapses**

We found that electrical synapses promote synchronous firing at all frequencies, and that this property is directly related to synaptic strength. If electrical synapses are strong enough, they counteract the antisynchrony induced by reciprocal inhibitory connections at low frequencies (<100 Hz).

If it is possible to extrapolate the properties of a 2-cell system to a network (White et al. 1998), our data suggest that electrical synapses are necessary for promoting synchronous rhythms in the gamma range (30–60 Hz) among layer 4 inhibitory neurons. Based on our 2-cell data, layer 4 inhibitory synapses do not appear suited for generating gamma-range synchrony, as has been reported for the hippocampus or other layers of neocortex (Tamas et al. 2000; Traub et al. 1996a). This could be a result of the much faster decay rates of the IPSCs measured in this study compared with other studies (2.3 vs. 8–10 ms; van Vreeswijk et al. 1994; Wang and Buzsáki 1996; White et al. 1998). At higher frequencies, both electrical and chemical inhibitory synapses promote firing synchrony, and this may play a role in high-frequency synchronous rhythms observed in neocortex (Jones et al. 2000; Kandel and Buzsáki 1997; Timofeev et al. 2001). Using the same 2-cell to network extrapolation, our data suggest that FS and LTS inhibitory networks would tend to fire in antisynchrony because they are coupled only by inhibitory synapses. Such antisynchronous clustering of inhibitory subpopulations has been reported in one theoretical model examining heterogeneity among inhibitory synapses (Wang and Buzsáki 1996).

One study examining synchronous oscillations among parvalbumin–positive inhibitory neurons of the dentate gyrus, which are similarly interconnected by electrical and fast decaying inhibitory synapses, suggests that gamma-range network synchrony is emergent with inhibitory synapses alone and that electrical synapses simply enhance synchrony (Bartos et al. 2002). Other studies similarly suggest that electrical synapses enhance synchrony mediated by inhibitory synapses (Traub et al. 2001; White et al. 1998). Alternatively, in some model networks, the existence of both synapse types reduces the amount of synchrony, compared with the presence of only one synapse type (Lewis and Rinzel 2003; Wang and Buzsáki 1996). Clearly, further theoretical study is required to determine how the connection scheme and the 2-cell synchrony we
describe here for neocortical FS and LTS neurons influence synchrony at the network level.

The maximal precision of synchrony in this study was on the order of 2 ms, whereas synchrony in another study of electrically coupled inhibitory interneurons was less precise, at about 10 ms (Tamas et al. 2000). This discrepancy could be attributable to differences between layer 4 FS neurons (this study) compared with layer 2/3 FS neurons (Tamas et al. 2000). For instance, in the previous study ePSPs were much longer lasting and more monophasic, and electrical coupling was weaker. One potential source of error in our measure of synchrony among FS neurons was the relatively negative reversal potential for IPSPs (about –82 mV, corrected for junction potential) ascribed to low chloride concentration in our recording pipettes. The reversal potential in FS neurons at this age is unknown, but in slightly older animals, it has been reported to be –54 mV (Martina et al. 2001). Therefore IPSPs may have been enhanced in our experiments. Modeling studies have suggested that when IPSP reversal potential is more positive than the most negative potential attained by the action potential (AHP trough), network firing becomes asynchronous (Wang and Buzsáki 1996). Therefore the polarity of IPSP reversal potential to AHP trough at lower firing frequencies in our study (<100 Hz; –82 mV vs. about –70 mV) may not reflect native conditions (–54 mV vs. about –70 mV). How this discrepancy affects synchrony in our 2-cell recordings is unclear.

**Linear electrical synapses and synchrony**

Linear signaling in our study implies that the presynaptic waveform is the main determinant of the ePSP shape when the postsynaptic cell is subthreshold, and the main determinant of electrical postsynaptic currents (ePSCs) in all conditions. We demonstrated that differences in FS– and LTS–ePSPs are attributed to differences in presynaptic action potential waveform. Similarly we showed that frequency-dependent alterations in presynaptic action potentials distinctly change the shape and amplitude of the ePSP. These differences in ePSP shape resulting from different action potential waveforms may have profound effects on network synchrony. For instance, the fast, biphasic FS–ePSPs appear to be important in precisely synchronizing firing (Galarreta and Hestrin 2001). With this in mind, neuromodulators may have a dramatic impact on network synchrony by their ability to simply alter the presynaptic action potential waveform (Atzori et al. 2000). Specific alterations in membrane currents that affect action potentials have been shown to alter network synchrony among electrically coupled inhibitory neurons in a theoretical model (Pfeuty et al. 2003). Therefore based on the linearity of electrical synaptic communication, modulation of action potential shape in the soma has predictable consequences on ePSP shape and, in principle, predictable consequences on synchrony at the network level. Further study is required to determine what these consequences are and how they might differ between FS and LTS inhibitory neurons.

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